Synthesis and Photochemistry of Phenyl Substituted-1,2,4-Thiadiazoles; 15N-Labeling Studies

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Synthesis and Photochemistry of Phenyl Substituted-1,2,4-Thiadiazoles; \textsuperscript{15}N-labeling Studies

by

Chuchawin Changtong

A Dissertation

Submitted to the Faculty of the

Worcester Polytechnic Institute

in partial fulfillment of the requirements for the

Degree of Doctor of Philosophy

in

Chemistry

by

_______________________________

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ABSTRACT

Photochemistry studies of phenyl substituted-1,2,4-thiadiazoles have revealed that 5-phenyl-1,2,4-thiadiazoles 31, 90, 98, 54 and 47 undergo a variety of photochemical reactions including photofragmentation, phototransposition, and photo-ring expansion while irradiation of 3-phenyl-1,2,4-thiadiazoles 46, 105 and 106 leads mainly to the formation of photofragmentation products. The formation of the phototransposition products has been suggested to arise from a mechanism involving electrocyclic ring closure and sigmatropic sulfur migration via a bicyclic intermediate: phenyl-1,3-diaza-5-thiabicyclo[2.1.0]pentene (BC). 15N-Labeling experiments confirm that sulfur undergoes sigmatropic shifts around all four sides of the diazetine ring. Thus, irradiation of 31-4-15N or 54-4-15N leads to the formation of 31-2-15N or 54-2-15N and to an equimolar mixture of 46-2-15N and 46-4-15N or 57-2-15N and 57-4-15N. Work in this laboratory on 15N-labeling of 46-2-15N also shows that 46 does not undergo electrocyclic ring closure but reacts exclusively by photofragmentation of the thiadiazole ring. 15N-Scrambling in the photofragmentation products observed after irradiation of 31-4-15N or 54-4-15N is greater than 15N-scrambling in the starting thiadiazoles suggesting that these products cannot arise only from direct fragmentation of the thiadiazole rings. An additional pathway for the formation of these products is required.

The formation of phenyltriazines, the photo-ring expansion products 39 and 40 or 65 and 66 from photolysis of 31 or 54 is proposed to arise via phenyl Diazacyclobutadienes (CB), generated from elimination of atomic sulfur from the bicyclic intermediates. It is suggested that phenyl Diazacyclobutadienes then undergo [4+2] cycloaddition self-coupling resulting in the formation of unstable tricyclic intermediates which finally cleave to give phenyltriazines.
and nitriles. The observed $^{15}$N distribution in the phenyltriazine photoproducts formed after photolysis of $31\cdot4\cdot^{15}$N or $54\cdot4\cdot^{15}$N and the formation triazine 72 after irradiation of a mixture of $31+54$ are consistent with this mechanism. The formation of nitriles by this pathway would account for the additional $^{15}$N-scrambling in the photofragmentation products.

The photochemically generated phenyl-1,3-diaza-5-thiabicyclo[2.1.0]pentenes are the key intermediates in this suggested mechanism. In the presence of furan, these intermediates are expected to be trapped as Diels-Alder adducts. Irradiation of phenylthiadiazoles 31, 54 and 47 in furan solvent lead to increased consumption of these thiadiazoles, to quenching of the known photoproducts, and to the formation of new products suggested to result from furan trapping of the thiadiazoles followed by elimination of sulfur. Irradiation of 46 in furan solvent leads only to the formation of the photofragmentation product; no furan trapping adduct is observed. This result is consistent with the $^{15}$N-labeling experiment indicating that 46 does not undergo electrocyclic ring closure after irradiation.

The photoreactivity of these phenylthiadiazoles in acetonitrile is substantially decreased when the phenyl ring at position 4 is substituted with an electron donating or withdrawing group. However, they are more photoreactive in cyclohexane solvent than in acetonitrile. The fluorescence emission spectra of these (4′-substituted)phenyl-1,2,4-thiadiazoles exhibit moderate - large Stokes’ shifts in acetonitrile. The magnitudes of these Stokes’ shifts decrease in cyclohexane. This suggests a charge transfer character associated with the excited states of these thiadiazoles. In acetonitrile, these charge transfer excited states would be stabilized and become the lowest energy excited state. These charge transfer excited states would not be photoreactive and, thus, fluorescence emission becomes an effective deactivation process. In cyclohexane solvent, the charge transfer excited states
would be less stabilized and, thus, the relaxed $S_{1(v0)}(\pi,\pi^*)$ would, then, become the lowest excited state. The relaxed $S_{1(v0)}(\pi,\pi^*)$ would be the state from which the observed photoproducts originate and the observed fluorescence with the smaller Stokes’ shifts compared with the Stokes’ shifts observed in acetonitrile.
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CONTENTS

<table>
<thead>
<tr>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABSTRACT</td>
</tr>
<tr>
<td>ACKNOWLEDGEMENT</td>
</tr>
<tr>
<td>CONTENTS</td>
</tr>
<tr>
<td>LIST OF FIGURES</td>
</tr>
<tr>
<td>LIST OF SCHEMES</td>
</tr>
<tr>
<td>LIST OF TABLES</td>
</tr>
</tbody>
</table>

CHAPTER 1 INTRODUCTION

1.1 Photochemistry of isothiazoles and thiazoles .......................... 1
1.2 Photochemistry of 1,2,4-thiadiazoles ................................... 7

CHAPTER 2 RESULTS AND DISCUSSION

2.1 Photochemistry of 5-phenyl-1,2,4-thiadiazole ......................... 8
2.1.1 Synthesis of 5-phenyl-1,2,4-thiadiazole ............................. 8
  2.1.1.1 Synthesis of N-[(dimethylamino)methylene]thiobenzamide .... 9
  2.1.1.2 Synthesis of 5-phenyl-1,2,4-thiadiazole ...................... 15
2.1.2 Synthesis of 2-phenyl- and 2,4-diphenyl-1,3,5-triazine ........... 21
2.1.3 Photochemistry of 5-phenyl-1,2,4-thiadiazole ...................... 27
2.2 Photochemistry of 3-phenyl-1,2,4-thiadiazole ........................ 47
2.2.1 Synthesis of 3-phenyl-1,2,4-thiadiazole ........................... 47
  2.2.1.1 Synthesis of 5-phenyl-1,3,4-oxathiazole-2-one ............... 47
  2.2.1.2 Synthesis of ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate 51
2.2.1.3 Synthesis of 3-phenyl-1,2,4-thiadiazole .......................... 55
2.2.2 Photochemistry of 3-phenyl-1,2,4-thiadiazole .......................... 59

2.3 Photochemistry of 3-methyl-5-phenyl-1,2,4-thiadiazole ................. 67
  2.3.1 Synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole ...................... 67
    2.3.1.1 Synthesis of N-[(dimethylamino)ethylidene]thiobenzamide ... 68
    2.3.1.2 Synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole ............. 74
  2.3.2 Synthesis of 5-methyl-3-phenyl-1,2,4-thiadiazole ................. 78
    2.3.2.1 Synthesis of 5-chloro-3-phenyl-1,2,4-thiadiazole ............. 79
    2.3.2.2 Synthesis of diethyl 3-phenyl-1,2,4-thiadiazole-5-malonate .. 84
    2.3.2.3 Synthesis of 5-methyl-3-phenyl-1,2,4-thiadiazole ............. 92
  2.3.3 Synthesis of 2,4-dimethyl-6-phenyl-1,3,5-triazine and
    2-methyl-4,6-diphenyl-1,3,5-triazine .................................. 97
    2.3.3.1 Synthesis of N-[(dimethylamino)ethylidene]benzamide ..... 98
    2.3.3.2 Synthesis of 2,4-dimethyl-6-phenyl-1,3,5-triazine .......... 104
    2.3.3.3 Synthesis of 2-methyl-4,6-diphenyl-1,3,5-triazine .......... 109
  2.3.4 Photochemistry of 3-methyl-5-phenyl-1,2,4-thiadiazole ........... 113

2.4 Photochemistry of 5-phenyl-1,2,4-thiadiazole-4\(^{15}\)N ................ 123
  2.4.1 Synthesis of 5-phenyl-1,2,4-thiadiazole–4\(^{15}\)N ................. 123
    2.4.1.1 Synthesis of thiobenzamide–4\(^{15}\)N ......................... 123
    2.4.1.2 Synthesis of N-[(dimethylamino)methylene] thiobenzamide–4\(^{15}\)N ..................................................... 129
    2.4.1.3 Synthesis of 5-phenyl-1,2,4-thiadiazole – 4\(^{15}\)N .......... 134
2.4.2 Photochemistry of 5-phenyl-1,2,4-thiadiazole – $^{15}$N

2.4.3 Preparative scale photolysis

2.4.3.1 Preparative gas chromatography

2.4.3.2 Preparative layer chromatography

2.5 Photochemistry of 3-methyl-5-phenyl-1,2,4-thiadiazole – $^{15}$N

2.5.1 Synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole – $^{15}$N

2.5.2 Photochemistry of 3-methyl-5-phenyl-1,2,4-thiadiazole – $^{15}$N

2.5.3 Preparative scale photolysis

2.6 Photolysis of 5-phenyl-1,2,4-thiadiazole in the presence of ethyl cyanoformate

2.7 Photolysis of 3-phenyl-1,2,4-thiadiazole in the presence of ethyl cyanoformate

2.8 Photolysis 3-methyl-5-phenyl-1,2,4-thiadiazole and 5-phenyl-1,2,4-thiadiazole mixture in acetonitrile

2.8.1 Synthesis of 2-methyl-4-phenyl-1,3,5-triazine

2.8.1.1 Synthesis of N-[(dimethylamino)methylene]benzamide

2.8.1.2 Synthesis of 2-methyl-4-phenyl-1,3,5-triazine

2.8.2 Irradiation of 5-phenyl- and 3-methyl-5-phenyl-1,2,4-thiadiazole mixture in acetonitrile
2.9 Photochemistry of phenyl substituted-1,2,4-thiadiazoles in furan solvent  
2.9.1 Photochemistry of 5-phenyl-1,2,4-thiadiazoles in furan solvent....  
2.9.1.1 Irradiation of 5-phenyl-1,2,4-thiadiazole in furan solvent...  
2.9.1.2 Irradiation of 3-methyl-5-phenyl- and diphenyl-1,2,4- 
thiadiazole in furan solvent................................. 260  
2.9.1.3 Preparative scale photolysis of diphenyl-1,2,4-thiadiazole 
in Furan.............................................................. 269  
2.9.2 Irradiation of 3-phenyl-1,2,4-thiadiazole in furan solvent........ 278  
2.9.3 Irradiation of 3-phenyl-1,2,4-thiadiazole in tetrahydrofuran solvent  283  

2.10 Photochemistry of 5-(4′-substituted)phenyl- and 
3-(4′-substituted)phenyl - 1,2,4-thiadiazoles.............................. 290  
2.10.1 Photochemistry of 5-(4′-substituted)phenyl-1,2,4-thiadiazole...... 290  
2.10.1.1 Synthesis of 5-(4′-methoxy)phenyl-1,2,4-thiadiazole....... 290  
2.10.1.1.1 Synthesis of 4-methoxythiobenzamide....................... 291  
2.10.1.1.2 Synthesis of N-[(dimethylamino)methylene] 
4-methoxythiobenzamide........................................... 296  
2.10.1.1.3 Synthesis of 5-(4′-methoxy)phenyl-1,2,4-thiadiazole... 300  
2.10.1.2 Synthesis of 2-(4′-methoxy)phenyl-1,3,5-triazine.......... 305  
2.10.1.2.1 Synthesis of N-[(dimethylamino)methylene] 
4-methoxybenzamide................................................. 305  
2.10.1.2.2 Synthesis of 2-(4′-methoxy)phenyl-1,3,5-triazine...... 310
2.10.1.3 Synthesis of 5-(4′-cyano)phenyl-1,2,4-thiadiazole............. 315
2.10.1.3.1 Synthesis of 4-cyanobenzamide........................................... 316
2.10.1.3.2 Synthesis of 4-cyanothiobenzamide................................. 320
2.10.1.3.3 Synthesis of N-[(dimethylamino)methylene] 4-cyanothiobenzamide................................................................. 324
2.10.1.3.4 Synthesis of 5-(4′-cyano)phenyl-1,2,4-thiadiazole...... 329

2.10.1.4 Photochemistry of 5-(4′-substituted)phenyl- 1,2,4-thiadiazoles................................................................. 336
2.10.2 Photochemistry of 3-(4′-substituted)phenyl-1,2,4-thiadiazoles... 358
2.10.2.1 Synthesis of 3-(4′-methoxy)phenyl-1,2,4-thiadiazole...... 358
2.10.2.1.1 Synthesis of 5-(4′-methoxy)phenyl-1,3,4- oxathiazole-2-one................................................................. 359
2.10.2.1.2 Synthesis of ethyl 3-(4-methoxy)phenyl-1,2,4- thiadiazole-5-carboxylate......................................................... 363
2.10.2.1.3 Synthesis of 3-(4′-methoxy)phenyl-1,2,4-thiadiazole. 367
2.10.2.2 Synthesis of 3-(4′-cyano)phenyl-1,2,4-thiadiazole.......... 371
2.10.2.2.1 Synthesis of 5-(4′-cyano)phenyl-1,3,4- oxathiazole-2-one................................................................. 372
2.10.2.2.2 Synthesis of ethyl 3-(4′-cyano)phenyl-1,2,4- thiadiazole-5-carboxylate......................................................... 376
2.10.2.2.3 Synthesis of 3-(4′-cyano)phenyl-1,2,4-thiadiazole.... 380
2.10.2.3 Photochemistry of 3-(4'-substituted)phenyl-1,2,4-thiadiazoles

2.11 Spectroscopic data of phenyl substituted-1,2,4-thiadiazoles

2.11.1 5-Phenyl-1,2,4-thiadiazole

2.11.2 5-(4'-Methoxy)phenyl-1,2,4-thiadiazole

2.11.3 5-(4'-Cyano)phenyl-1,2,4-thiadiazole

2.11.4 3-Methyl-5-phenyl-1,2,4-thiadiazole

2.11.5 3-Cyano-5-phenyl-1,2,4-thiadiazole

2.11.6 3-Amino-5-phenyl-1,2,4-thiadiazole

2.11.7 Diphenyl-1,2,4-thiadiazole

2.11.8 3-Phenyl-1,2,4-thiadiazole

2.11.9 3-(4'-Methoxy)phenyl-1,2,4-thiadiazole

2.11.10 3-(4'-Cyano)phenyl-1,2,4-thiadiazole

2.10.11 5-Cyano-3-phenyl-1,2,4-thiadiazole

2.10.12 5-Amino-3-phenyl-1,2,4-thiadiazole

2.10.13 Summary on spectroscopic properties of phenyl substituted-1,2,4-thiadiazoles

2.12 Triplet sensitizations

2.12.1 Triplet sensitization of 5-phenyl-1,2,4-thiadiazole

2.12.2 Triplet sensitization of 5-phenyl-1,2,4-thiadiazole
2.13 Photochemistry of phenyl substituted-1,2,4-thiadiazoles in the presence of tri-n-butylphosphine

2.13.1 Synthesis of tri-n-butylphosphine sulfide

2.13.2 Photochemistry of 5-phenyl-1,2,4-thiadiazole in the presence of tri-n-butylphosphine

2.13.3 Photochemistry of 5-(4′-methoxy)phenyl-1,2,4-thiadiazole in the presence of tri-n-butylphosphine

2.13.4 Photochemistry of 5-phenyl-1,2,4-thiadiazole in the presence of tri-n-butylphosphine

2.14 Photochemistry of phenyl substituted-1,2,4-thiadiazoles in the presence of triethylamine or propylamine

2.14.1 Irradiation of 5-phenyl-1,2,4-thiadiazole in the presence of triethylamine or propylamine

2.14.2 Irradiation of 3-phenyl-1,2,4-thiadiazole in the presence of triethylamine or propylamine

CHAPTER 3 EXPERIMENTAL

3.1 Synthesis of the phenyl-1,2,4-thiadiazoles and some expected photoproducts

3.1.1 General procedure

3.1.2 Synthesis of 5-phenyl-1,2,4-thiadiazole

3.1.3 Synthesis of 3-phenyl-1,2,4-thiadiazole

3.1.4 Synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole
3.1.5 Synthesis of diphenyl-1,2,4-thiadiazole

3.1.6 Synthesis of 5-phenyl-1,2,4-thiadiazole-4-\(^{15}\)N

3.1.7 Synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole-4-\(^{15}\)N

3.1.8 Synthesis of 5-(4′-methoxy)phenyl-1,2,4-thiadiazole

3.1.9 Synthesis of 5-(4′-cyano)phenyl-1,2,4-thiadiazole

3.1.10 Synthesis of 3-(4′-methoxy)phenyl-1,2,4-thiadiazole

3.1.11 Synthesis of 3-(4′-cyano)phenyl-1,2,4-thiadiazole

3.1.12 Synthesis of 5-methyl-3-phenyl-1,2,4-thiadiazole

3.1.13 Synthesis of 2-phenyl-1,3,5-triazine and 2,4-diphenyl-1,3,5-triazine

3.1.14 Synthesis of 2,4-dimethyl-6-phenyl-1,3,5-triazine and 2-methyl-4,6-diphenyl-1,3,5-triazine

3.1.15 Synthesis of 2-(4′-methoxy)phenyl-1,3,5-triazine

3.2 Photochemistry

3.2.1 Photolysis of 5-phenyl-1,2,4-thiadiazole

3.2.2 Photolysis of 5-phenyl-1,2,4-thiadiazole

3.2.3 Photolysis of 3-methyl-5-phenyl-1,2,4-thiadiazole

3.2.4 Photolysis of 5-phenyl-1,2,4-thiadiazole-4-\(^{15}\)N

3.2.5 Photolysis of 3-methyl-5-phenyl-1,2,4-thiadiazole-4-\(^{15}\)N

3.2.6 Photolysis of 5-phenyl-1,2,4-thiadiazole in the presence of ethyl cyanoformate

3.2.7 Photolysis of 3-phenyl-1,2,4-thiadiazole in the presence of
ethyl cyanoformate

3.2.8 Photolysis of a mixture of 3-methyl-5-phenyl-1,2,4-thiadiazole and 5-phenyl-1,2,4-thiadiazole

3.2.9 Photochemistry of phenyl substituted-1,2,4-thiadiazoles in furan solvent

3.2.10 Photochemistry of 5-(4′-substituted)phenyl- and 3-(4′-substituted)phenyl-1,2,4-thiadiazoles

3.2.11 Spectroscopic data of phenyl-1,2,4-thiadiazoles

3.2.12 Triplet sensitization of phenyl-1,2,4-thiadiazole

3.2.13 Photochemistry of phenyl substituted-1,2,4-thiadiazoles in the presence of triethylamine or propylamine

3.2.14 Photochemistry of phenyl substituted-1,2,4-thiadiazoles in the presence of tri-n-butylphosphine

CHAPTER 4 CONCLUSION

REFERENCES

APPENDIX A – Calibration Curves

APPENDIX B – Ground States Geometry Optimization by AM1

APPENDIX C – List of Structures
## LIST OF FIGURES

<table>
<thead>
<tr>
<th>Figures</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a. GC-trace of the synthesized 32</td>
<td>10</td>
</tr>
<tr>
<td>1b. Mass spectrum of the compound eluted at a retention time of 33.9 min from the synthesis of 32</td>
<td>10</td>
</tr>
<tr>
<td>2. $^1$H-NMR spectrum of the synthesized 32</td>
<td>11</td>
</tr>
<tr>
<td>3. $^{13}$C-NMR spectrum of the synthesized 32</td>
<td>12</td>
</tr>
<tr>
<td>4. $^1$H–$^{13}$C-NMR correlation spectrum of the synthesized 32</td>
<td>14</td>
</tr>
<tr>
<td>5a. GC-trace of the synthesized 31</td>
<td>16</td>
</tr>
<tr>
<td>5b. Mass spectrum of the compound eluted at a retention time of 6.6 min from the synthesis of 31</td>
<td>17</td>
</tr>
<tr>
<td>5c. Mass spectrum of the compound eluted at a retention time of 10.9 min from the synthesis of 31</td>
<td>17</td>
</tr>
<tr>
<td>6. $^1$H-NMR spectrum of the synthesized 31</td>
<td>20</td>
</tr>
<tr>
<td>7a. GC-trace of the white solid A from the synthesis of 39 and 40</td>
<td>22</td>
</tr>
<tr>
<td>7b. Mass spectrum of the white solid A</td>
<td>23</td>
</tr>
<tr>
<td>8a. GC-trace of the white solid B from the synthesis of 39 and 40</td>
<td>23</td>
</tr>
<tr>
<td>8b. Mass spectrum of the white solid B</td>
<td>24</td>
</tr>
<tr>
<td>9. $^1$H–NMR spectrum of the white solid A</td>
<td>25</td>
</tr>
<tr>
<td>10. $^1$H–NMR spectrum of the white solid B</td>
<td>25</td>
</tr>
<tr>
<td>11a. UV–absorption spectrum of 31 in acetonitrile</td>
<td>27</td>
</tr>
<tr>
<td>11b. UV-overlay spectrum of the photolysis of 31 in acetonitrile</td>
<td>28</td>
</tr>
<tr>
<td>12a. UV–absorption spectrum of 31 in cyclohexane</td>
<td>27</td>
</tr>
<tr>
<td>12b. UV-overlay spectrum of the photolysis of 31 in cyclohexane</td>
<td>28</td>
</tr>
<tr>
<td>13a. GC-trace of solution of 31 before irradiation</td>
<td>31</td>
</tr>
<tr>
<td>13b. GC-trace of solution of 31 after irradiation</td>
<td>31</td>
</tr>
<tr>
<td>14a. GC-trace of the concentrated photolysate of 31 after 210 min of irradiation</td>
<td>32</td>
</tr>
<tr>
<td>14b. Mass spectrum of the photoprocess eluted at retention time 4 min</td>
<td>32</td>
</tr>
<tr>
<td>Figures</td>
<td>Pages</td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>14c. Mass spectrum of the photoproduct eluted at retention time 10 min.</td>
<td>35</td>
</tr>
<tr>
<td>14d. Mass spectrum of the photoproduct eluted at retention time 10.6 min.</td>
<td>36</td>
</tr>
<tr>
<td>14e. Mass spectrum of the photoproduct eluted at retention time 12.1 min.</td>
<td>37</td>
</tr>
<tr>
<td>14f. Mass spectrum of the photoproduct eluted at retention time 23.3 min.</td>
<td>39</td>
</tr>
<tr>
<td>14g. Mass spectrum of the photoproduct eluted at retention time 40 min.</td>
<td>40</td>
</tr>
<tr>
<td>14h. Mass spectrum of the photoproduct eluted at retention time 40.6 min.</td>
<td>42</td>
</tr>
<tr>
<td>14i. Mass spectrum of the photoproduct eluted at retention time 42.7 min.</td>
<td>42</td>
</tr>
<tr>
<td>14j. Mass spectrum of the photoproduct eluted at retention time 48.9 min.</td>
<td>43</td>
</tr>
<tr>
<td>15a. GC-trace of an authentic sample of 43</td>
<td>33</td>
</tr>
<tr>
<td>15b. Mass spectrum of an authentic sample of 43</td>
<td>34</td>
</tr>
<tr>
<td>16a. GC-trace of an authentic sample of 39</td>
<td>35</td>
</tr>
<tr>
<td>16b. Mass spectrum of an authentic sample of 39</td>
<td>36</td>
</tr>
<tr>
<td>17. Mass spectrum of the synthesized 46</td>
<td>38</td>
</tr>
<tr>
<td>18a. GC-trace of an authentic sample of 40</td>
<td>40</td>
</tr>
<tr>
<td>18b. Mass spectrum of an authentic sample of 40</td>
<td>41</td>
</tr>
<tr>
<td>19a. GC-trace of an authentic sample of 47</td>
<td>44</td>
</tr>
<tr>
<td>19b. Mass spectrum of an authentic sample of 47</td>
<td>44</td>
</tr>
<tr>
<td>20a. GC-trace of the white crystals from synthesis of 51</td>
<td>48</td>
</tr>
<tr>
<td>20b. Mass spectrum of the white crystals</td>
<td>48</td>
</tr>
<tr>
<td>21. $^1$H-NMR spectrum of the white crystals</td>
<td>50</td>
</tr>
<tr>
<td>22a. $^{13}$C-NMR spectrum of the white crystals</td>
<td>50</td>
</tr>
<tr>
<td>22b. $^{13}$C-DEPT 135 spectrum of the white crystals</td>
<td>50</td>
</tr>
<tr>
<td>23a. GC-trace of the synthesized 50</td>
<td>51</td>
</tr>
<tr>
<td>23b. Mass spectrum of the synthesized 50</td>
<td>52</td>
</tr>
<tr>
<td>24. $^1$H–NMR spectrum of the synthesized 50</td>
<td>53</td>
</tr>
<tr>
<td>25a. $^{13}$C-NMR spectrum of the synthesized 50</td>
<td>54</td>
</tr>
<tr>
<td>25b. $^{13}$C-DEPT 135 spectrum of the synthesized 50</td>
<td>54</td>
</tr>
<tr>
<td>26a. GC-trace of the synthesized 46</td>
<td>55</td>
</tr>
<tr>
<td>26b. Mass spectrum of the peak at RT 13.2 min</td>
<td>56</td>
</tr>
<tr>
<td>Figures</td>
<td>Pages</td>
</tr>
<tr>
<td>---------</td>
<td>-------</td>
</tr>
<tr>
<td>27. $^1$H–NMR spectrum of the synthesized 46</td>
<td>57</td>
</tr>
<tr>
<td>28a. $^{13}$C-NMR spectrum of the synthesized 46</td>
<td>58</td>
</tr>
<tr>
<td>28b. $^{13}$C-DEPT 135 spectrum of the synthesized 46</td>
<td>58</td>
</tr>
<tr>
<td>29a. UV–absorption spectrum of 46 in cyclohexane</td>
<td>60</td>
</tr>
<tr>
<td>29b. UV overlay spectrum of the photolysis of 46</td>
<td>60</td>
</tr>
<tr>
<td>30a. GLC analysis of 46 in acetonitrile before irradiation</td>
<td>62</td>
</tr>
<tr>
<td>30b. GLC analysis of 46 in acetonitrile after 120 min of irradiation</td>
<td>62</td>
</tr>
<tr>
<td>31a. GC-trace of the concentrated photolysate of 46 after 120 min of irradiation</td>
<td>63</td>
</tr>
<tr>
<td>31b. Mass spectrum of the peak at a retention time of 17.7 min</td>
<td>63</td>
</tr>
<tr>
<td>31c. Mass spectrum of the peak at a retention time of 7.5 min</td>
<td>64</td>
</tr>
<tr>
<td>31d. Mass spectrum of the peak at a retention time of 34.5 min</td>
<td>65</td>
</tr>
<tr>
<td>32a. GC-trace of 55</td>
<td>69</td>
</tr>
<tr>
<td>32b. Mass spectrum of the peak eluted at a retention time of 23.9 min; 55</td>
<td>69</td>
</tr>
<tr>
<td>33. $^1$H–NMR spectrum of 55</td>
<td>70</td>
</tr>
<tr>
<td>34a. $^{13}$C–NMR spectrum of 55</td>
<td>71</td>
</tr>
<tr>
<td>34b. $^{13}$C– Scale expansion exhibits the two singlets at δ 39.5 and 39.7</td>
<td>71</td>
</tr>
<tr>
<td>35. $^1$H–$^{13}$C correlation spectrum of 55</td>
<td>73</td>
</tr>
<tr>
<td>36a. GC-trace of 54</td>
<td>75</td>
</tr>
<tr>
<td>36b. Mass spectrum of 54</td>
<td>75</td>
</tr>
<tr>
<td>37. $^1$H–NMR spectrum of 54</td>
<td>76</td>
</tr>
<tr>
<td>38a. $^{13}$C–NMR spectrum of 54</td>
<td>77</td>
</tr>
<tr>
<td>38b. $^{13}$C–DEPT 135 spectrum of 54</td>
<td>78</td>
</tr>
<tr>
<td>39a. GC analysis of 58</td>
<td>81</td>
</tr>
<tr>
<td>39b. Mass spectrum of 58</td>
<td>81</td>
</tr>
<tr>
<td>40. $^1$H–NMR spectrum of 58</td>
<td>82</td>
</tr>
<tr>
<td>41a. $^{13}$C–NMR spectrum of 58</td>
<td>83</td>
</tr>
<tr>
<td>41b. $^{13}$C–DEPT 135 spectrum of 58</td>
<td>83</td>
</tr>
<tr>
<td>42a. GC analysis of the yellow solid obtained in the synthesis of 59</td>
<td>85</td>
</tr>
<tr>
<td>Figures</td>
<td>Paes</td>
</tr>
<tr>
<td>---------</td>
<td>------</td>
</tr>
<tr>
<td>42b. Mass spectrum of the component eluted at 18.5 min</td>
<td>85</td>
</tr>
<tr>
<td>43. $^1$H–NMR spectrum of 59</td>
<td>87</td>
</tr>
<tr>
<td>44. $^1$H–$^1$H coupling (COSY) spectrum of 59</td>
<td>88</td>
</tr>
<tr>
<td>45a. $^{13}$C–NMR spectrum of 59</td>
<td>89</td>
</tr>
<tr>
<td>45b. $^{13}$C–DEPT 135 spectrum of 59</td>
<td>90</td>
</tr>
<tr>
<td>46. $^{13}$C–$^1$H correlation spectrum of 59</td>
<td>91</td>
</tr>
<tr>
<td>47a. GC-trace of the white solid from the synthesis of 57</td>
<td>92</td>
</tr>
<tr>
<td>47b. Mass spectrum of the component at RT of 9.5 min</td>
<td>93</td>
</tr>
<tr>
<td>48. $^1$H–NMR spectrum of 57</td>
<td>95</td>
</tr>
<tr>
<td>49. $^{13}$C–NMR spectrum of 57</td>
<td>96</td>
</tr>
<tr>
<td>50a. GC-trace of the dark viscous liquid expected to be 67</td>
<td>99</td>
</tr>
<tr>
<td>50b. Mass spectrum of the peak eluted at a retention time of 17.4 min</td>
<td>99</td>
</tr>
<tr>
<td>51. $^1$H–NMR spectrum of the dark liquid from the synthesis of 67</td>
<td>100</td>
</tr>
<tr>
<td>52a. $^{13}$C–NMR spectrum of the dark liquid from the synthesis of 67</td>
<td>101</td>
</tr>
<tr>
<td>52b. $^{13}$C-scale expansion spectrum of the dark liquid</td>
<td>102</td>
</tr>
<tr>
<td>53. $^1$H–$^{13}$C correlation spectrum of the dark liquid</td>
<td>103</td>
</tr>
<tr>
<td>54a. GC-trace of the crude product from the synthesis of 65</td>
<td>106</td>
</tr>
<tr>
<td>54b. Mass spectrum of the peak eluted with a retention time of 16.3 min</td>
<td>106</td>
</tr>
<tr>
<td>55. $^1$H–NMR spectrum of the yellow liquid expected to be 65</td>
<td>107</td>
</tr>
<tr>
<td>56a. $^{13}$C – NMR spectrum of the yellow liquid expected to be 65</td>
<td>108</td>
</tr>
<tr>
<td>56b. $^{13}$C–DEPT 135 spectrum of the yellow liquid expected to be 65</td>
<td>109</td>
</tr>
<tr>
<td>57a. GC-trace of the white solid expected to be 66</td>
<td>110</td>
</tr>
<tr>
<td>57b. Mass spectrum of the peak eluted at a retention time of 32.4 min</td>
<td>110</td>
</tr>
<tr>
<td>58. $^1$H–NMR spectrum of the white solid from the synthesis of 66</td>
<td>111</td>
</tr>
<tr>
<td>59a. $^{13}$C–NMR spectrum of the white solid from the synthesis of 66</td>
<td>112</td>
</tr>
<tr>
<td>59b. $^{13}$C–DEPT 135 spectrum of the white solid from the synthesis of 66</td>
<td>112</td>
</tr>
<tr>
<td>60a. UV-absorption spectrum of 54 in acetonitrile before irradiation</td>
<td>114</td>
</tr>
<tr>
<td>60b. UV–overlay spectrum of the photolysis of 54 in acetonitrile</td>
<td>114</td>
</tr>
<tr>
<td>Figures</td>
<td>Pages</td>
</tr>
<tr>
<td>---------</td>
<td>-------</td>
</tr>
<tr>
<td>61a. GLC analysis of 54 in acetonitrile before irradiation</td>
<td>115</td>
</tr>
<tr>
<td>61b. GLC analysis of the reaction mixture after 150 min of irradiation</td>
<td>116</td>
</tr>
<tr>
<td>62a. GC-analysis of the concentrated reaction mixture</td>
<td>117</td>
</tr>
<tr>
<td>62b. Mass spectrum of the peak eluted at a retention time of 4.1 min</td>
<td>117</td>
</tr>
<tr>
<td>62c. Mass spectrum of the peak eluted at a retention time of 29.2 min</td>
<td>118</td>
</tr>
<tr>
<td>62d. Mass spectrum of the peak eluted at a retention time of 13.0 min</td>
<td>119</td>
</tr>
<tr>
<td>62e. Mass spectrum of the peak eluted at a retention time of 14.0 min</td>
<td>122</td>
</tr>
<tr>
<td>63. Mass spectrum of an authentic sample of 65</td>
<td>120</td>
</tr>
<tr>
<td>64a. GC-trace (HP588) of 54 before irradiation</td>
<td>121</td>
</tr>
<tr>
<td>64b. Mass spectrum of 54 after irradiation</td>
<td>121</td>
</tr>
<tr>
<td>63a. Mass spectrum of 34-15N</td>
<td>125</td>
</tr>
<tr>
<td>63b. Mass spectrum of 34-14N</td>
<td>125</td>
</tr>
<tr>
<td>64a. 1H–NMR spectrum of the synthesized 34-15N</td>
<td>126</td>
</tr>
<tr>
<td>64b. 1H-scale expansion spectrum of the synthesized 34-15N</td>
<td>127</td>
</tr>
<tr>
<td>65. 13C-NMR spectrum of the synthesized 34-15N</td>
<td>128</td>
</tr>
<tr>
<td>66. 15N–NMR spectrum of the synthesized 34-15N</td>
<td>128</td>
</tr>
<tr>
<td>67. 1H–NMR spectrum of 3215N</td>
<td>130</td>
</tr>
<tr>
<td>68. 13C–NMR spectrum of 3215N</td>
<td>130</td>
</tr>
<tr>
<td>69. Two-dimensional 1H–13C correlation spectrum of 32-15N</td>
<td>132</td>
</tr>
<tr>
<td>70. 15N-NMR spectrum of 32-15N</td>
<td>133</td>
</tr>
<tr>
<td>71a. GC-trace of the synthesized 31–415N</td>
<td>135</td>
</tr>
<tr>
<td>71b. Mass spectrum of the peak eluted at a retention time of 11.1 min</td>
<td>136</td>
</tr>
<tr>
<td>71c. Mass spectrum of the peak eluted at a retention time of 6.6 min</td>
<td>136</td>
</tr>
<tr>
<td>72. Mass spectrum of the synthetic 37</td>
<td>137</td>
</tr>
<tr>
<td>73a. GC-trace of the purified 31–415N</td>
<td>138</td>
</tr>
<tr>
<td>73b. Mass spectrum of the peak eluted at a retention time of 11.1 min</td>
<td>139</td>
</tr>
<tr>
<td>74a. 1H–NMR spectrum of the purified 31–415N</td>
<td>140</td>
</tr>
<tr>
<td>74b. 1H–scale expansion spectrum of the purified 31–415N</td>
<td>140</td>
</tr>
<tr>
<td>75a. 13C–NMR spectrum of the purified 31–415N</td>
<td>141</td>
</tr>
<tr>
<td>Figures</td>
<td>Pages</td>
</tr>
<tr>
<td>---------</td>
<td>-------</td>
</tr>
<tr>
<td>75b. $^{13}$C–scale expansion spectrum of purified $31-4^{15}$N showing the signal at $\delta$ 188.8 as singlet</td>
<td>142</td>
</tr>
<tr>
<td>75c. $^{13}$C–scale expansion spectrum of purified $31-4^{15}$N showing the signal at $\delta$ 164.7 as doublet</td>
<td>142</td>
</tr>
<tr>
<td>76. Two-dimensional $^1$H–$^{13}$C correlation spectrum of purified $31-4^{15}$N</td>
<td>144</td>
</tr>
<tr>
<td>77. $^{15}$N–NMR spectrum of the purified $31-4^{15}$N</td>
<td>145</td>
</tr>
<tr>
<td>78a. GC-trace of solution of $31-4^{15}$N before irradiation</td>
<td>148</td>
</tr>
<tr>
<td>78b. Mass spectrum of $31-4^{15}$N before irradiation</td>
<td>148</td>
</tr>
<tr>
<td>79. GC-trace of the un-consumed reactant after 180 min of irradiation</td>
<td>150</td>
</tr>
<tr>
<td>80. GLC trace (PE9000) of $31-4^{15}$N solution after 16 min of irradiation</td>
<td>151</td>
</tr>
<tr>
<td>81a. GC trace (HP588) of $31-4^{15}$N solution after 16 min of irradiation</td>
<td>151</td>
</tr>
<tr>
<td>81b. Mass spectrum of the un-consumed reactant</td>
<td>152</td>
</tr>
<tr>
<td>81c. Mass spectrum of benzonitrile-photoproduct</td>
<td>154</td>
</tr>
<tr>
<td>81d. Mass spectrum of 3-phenyl-1,2,4-thiadiazole – photoproduct</td>
<td>157</td>
</tr>
<tr>
<td>81e. Mass spectrum of 2-phenyl-1,3,5-triazine photoproduct</td>
<td>158</td>
</tr>
<tr>
<td>81f. Mass spectrum of 2,4-diphenyl-1,3,5-triazine photoproduct</td>
<td>162</td>
</tr>
<tr>
<td>82. Plot of the ratio of the intensities of the 135/136 peaks</td>
<td>153</td>
</tr>
<tr>
<td>83. Plot of the ratio of the intensities of the 103/104 peaks</td>
<td>154</td>
</tr>
<tr>
<td>84. Mass spectrum of un-labeled 3-phenyl-1,2,4-thiadiazole</td>
<td>156</td>
</tr>
<tr>
<td>85. Plot of the ratio of the intensities of 135/136 peaks of 3-phenyl1,2,4-thiadiazole–$^{15}$N</td>
<td>156</td>
</tr>
<tr>
<td>86. Plot of the ratio of the intensities of the 158/159 peaks-phenyltriazine–$^{15}$N</td>
<td>158</td>
</tr>
<tr>
<td>87. Mass spectrum of un-labeled 2-phenyl-1,3,5-triazine</td>
<td>159</td>
</tr>
<tr>
<td>88. Mass spectrum of regular 2,4-diphenyl-1,3,5-triazine</td>
<td>163</td>
</tr>
<tr>
<td>89. $^1$H-NMR spectrum of the isolated un-consumed 5-phenyl-1,2,4-thiadiazole–$^{15}$N</td>
<td>166</td>
</tr>
<tr>
<td>90a. $^{15}$N-NMR spectrum of $31-4^{15}$N before irradiation</td>
<td>167</td>
</tr>
<tr>
<td>90b. $^{15}$N-NMR spectrum of the isolated un-consumed reactant after irradiation</td>
<td>167</td>
</tr>
<tr>
<td>91. $^1$H-NMR spectrum of the isolated 3-phenyl-1,2,4-thiadiazole–$^{15}$N</td>
<td>169</td>
</tr>
<tr>
<td>Figures</td>
<td>Pages</td>
</tr>
<tr>
<td>---------</td>
<td>-------</td>
</tr>
<tr>
<td>92. $^{15}$N-NMR spectrum of the isolated 3-phenyl-1,2,4-thiadiazole-$^{15}$N</td>
<td>170</td>
</tr>
<tr>
<td>93. $^1$H-NMR spectrum of the isolated un-consumed reactant after irradiation</td>
<td>172</td>
</tr>
<tr>
<td>94. $^1$H-NMR spectrum of a mixture of 46-4$^{15}$N and 46-2$^{15}$N</td>
<td>173</td>
</tr>
<tr>
<td>95a. $^1$H – NMR spectrum of 34-$^{15}$N</td>
<td>175</td>
</tr>
<tr>
<td>95b. $^1$H–NMR spectrum of 34-$^{15}$N; scale expansion at δ 7.12-7.92</td>
<td>176</td>
</tr>
<tr>
<td>96. $^{13}$C – NMR spectrum of 34-$^{15}$N</td>
<td>176</td>
</tr>
<tr>
<td>97. $^1$H – NMR spectrum of 55-$^{15}$N</td>
<td>177</td>
</tr>
<tr>
<td>98a. $^{13}$C – NMR spectrum of 55-$^{15}$N</td>
<td>179</td>
</tr>
<tr>
<td>98b. $^{13}$C–scale expansion spectrum of 55-$^{15}$N</td>
<td>179</td>
</tr>
<tr>
<td>99. $^1$H–$^{13}$C correlation spectrum of 55-$^{15}$N</td>
<td>180</td>
</tr>
<tr>
<td>100. $^{15}$N-NMR spectrum of 55-$^{15}$N</td>
<td>181</td>
</tr>
<tr>
<td>101a. GC-trace of orange crystals from synthesis of 55-$^{15}$N</td>
<td>182</td>
</tr>
<tr>
<td>101b. Mass spectrum of the peak eluted at a retention time of 39.5 min</td>
<td>182</td>
</tr>
<tr>
<td>102a. GC-trace of 54-4$^{15}$N</td>
<td>183</td>
</tr>
<tr>
<td>102b. Mass spectrum of 54-4$^{15}$N</td>
<td>184</td>
</tr>
<tr>
<td>103. $^1$H – NMR spectrum of 54-$^{15}$N</td>
<td>185</td>
</tr>
<tr>
<td>104a. $^{13}$C – NMR spectrum of 54-$^{15}$N</td>
<td>187</td>
</tr>
<tr>
<td>104b. $^{13}$C – DEPT 135 spectrum of 54-$^{15}$N</td>
<td>188</td>
</tr>
<tr>
<td>105. $^{15}$N–NMR spectrum of 54-4$^{15}$N and the scale expansion showing an un-resolved quartet</td>
<td>189</td>
</tr>
<tr>
<td>106a. GC-trace of 54-4$^{15}$N before irradiation</td>
<td>191</td>
</tr>
<tr>
<td>106b. Mass spectrum of 54-4$^{15}$N before irradiation</td>
<td>191</td>
</tr>
<tr>
<td>107. GLC analysis (PE9000) of the solution of 54-4$^{15}$N after 18 min of irradiation</td>
<td>194</td>
</tr>
<tr>
<td>108a. GC-trace (HP588) of the reaction solution at 18 min of irradiation</td>
<td>194</td>
</tr>
<tr>
<td>108b. Mass spectrum of the peak eluted at a retention time of 5 min</td>
<td>195</td>
</tr>
<tr>
<td>108c. Mass spectrum of the un-consumed reactant</td>
<td>197</td>
</tr>
<tr>
<td>108d. Mass spectrum of the peak eluted at a retention time of 40.5 min</td>
<td>198</td>
</tr>
<tr>
<td>108e. Mass spectrum of the peak eluted at a retention time of 42.7 min</td>
<td>201</td>
</tr>
<tr>
<td>Figures</td>
<td>Pages</td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
<td>--------</td>
</tr>
<tr>
<td>108f. Mass spectrum of the peak eluted at a retention time of 57.7 min</td>
<td>204</td>
</tr>
<tr>
<td>109. Plot of 103/104 ratio as a function of irradiation</td>
<td>195</td>
</tr>
<tr>
<td>110. Plot of ratio of the 186/187 peaks as a function of irradiation</td>
<td>198</td>
</tr>
<tr>
<td>111. Mass spectrum of regular 2,4-dimethyl-6-phenyl-1,3,5-triazine</td>
<td>199</td>
</tr>
<tr>
<td>112. Mass spectrum of an authentic sample of 57</td>
<td>202</td>
</tr>
<tr>
<td>113. Formation of 66 contains 1 and 2 15N atoms</td>
<td>203</td>
</tr>
<tr>
<td>114. Mass spectrum of 2-methyl-4,6-diphenyl-1,3,5-triazine</td>
<td>204</td>
</tr>
<tr>
<td>117. 1H-spectrum of fractions 16-18</td>
<td>208</td>
</tr>
<tr>
<td>118a. 13C-spectrum of fractions 16-18</td>
<td>208</td>
</tr>
<tr>
<td>118b. 13C-scale expansion of a doublet at δ 18.0</td>
<td>209</td>
</tr>
<tr>
<td>118c. 13C-scale expansion of a doublet at δ 129.4 and 129.5</td>
<td>210</td>
</tr>
<tr>
<td>119. Mass spectrum of the un-consumed reactant at 640 min of irradiation</td>
<td>210</td>
</tr>
<tr>
<td>120. 15N-NMR spectrum of fractions 16-18</td>
<td>212</td>
</tr>
<tr>
<td>121a. GLC analysis of solution of 31 containing 49 before irradiation</td>
<td>216</td>
</tr>
<tr>
<td>121b. GLC analysis of solution of 31 containing 49 after irradiation</td>
<td>216</td>
</tr>
<tr>
<td>121c. GLC analysis of the reaction solution spiked with an authentic 50</td>
<td>217</td>
</tr>
<tr>
<td>122a. GC-trace of the concentrated solution after 210 min of irradiation</td>
<td>218</td>
</tr>
<tr>
<td>122b. Mass spectrum of a suspected peak to be 50</td>
<td>218</td>
</tr>
<tr>
<td>123. Mass spectrum of an authentic sample of 50</td>
<td>219</td>
</tr>
<tr>
<td>124a. GLC analysis of the solution of 31+49 before irradiation</td>
<td>221</td>
</tr>
<tr>
<td>124b. GLC analysis of the solution of 31+49 after irradiation</td>
<td>222</td>
</tr>
<tr>
<td>124c. GLC analysis of the solution of 31+49 after irradiation spiked with an authentic 50</td>
<td>222</td>
</tr>
<tr>
<td>125a. GC-trace (HP588) of the un-concentrated reaction solution after irradiation</td>
<td>223</td>
</tr>
<tr>
<td>125b. Mass spectrum of the suspected product at RT 17 min</td>
<td>224</td>
</tr>
<tr>
<td>126. Mass spectrum of an authentic sample of 50</td>
<td>224</td>
</tr>
<tr>
<td>127a. GC (HP588) analysis of 31</td>
<td>229</td>
</tr>
<tr>
<td>127b. Mass spectrum of 31</td>
<td>230</td>
</tr>
<tr>
<td>Figures</td>
<td>Pages</td>
</tr>
<tr>
<td>---------</td>
<td>-------</td>
</tr>
<tr>
<td>128. ¹H-spectrum of 31.</td>
<td>231</td>
</tr>
<tr>
<td>129a. ¹³C-spectrum of 31.</td>
<td>232</td>
</tr>
<tr>
<td>129b. ¹³C-DEPT 135 of 31</td>
<td>233</td>
</tr>
<tr>
<td>130a. GC analysis of the 72</td>
<td>234</td>
</tr>
<tr>
<td>130b. Mass spectrum of the 72</td>
<td>235</td>
</tr>
<tr>
<td>131. ¹H-spectrum of 72</td>
<td>236</td>
</tr>
<tr>
<td>132a. ¹³C-spectrum of 72</td>
<td>237</td>
</tr>
<tr>
<td>132b. ¹³C-DEPT 135 of 72</td>
<td>237</td>
</tr>
<tr>
<td>133a. GLC analysis of 31 in acetonitrile before irradiation</td>
<td>239</td>
</tr>
<tr>
<td>133b. GLC analysis of 31 in acetonitrile after 650 min of irradiation</td>
<td>239</td>
</tr>
<tr>
<td>134a. GLC analysis of 54 in acetonitrile before irradiation</td>
<td>240</td>
</tr>
<tr>
<td>134b. GLC analysis of 54 in acetonitrile after 650 min of irradiation</td>
<td>240</td>
</tr>
<tr>
<td>135. GLC analysis of the mixture solution after 650 min of irradiation</td>
<td>241</td>
</tr>
<tr>
<td>136. GLC analysis of an authentic sample of 72</td>
<td>241</td>
</tr>
<tr>
<td>137. GLC analysis of the irradiated mixture solution spiked with an authentic sample 72</td>
<td>243</td>
</tr>
<tr>
<td>138a. GC-trace (HP588) of the mixture solution after 650 min of irradiation</td>
<td>244</td>
</tr>
<tr>
<td>138b. Mass spectrum of the component eluted with a retention of 19.2 min</td>
<td>244</td>
</tr>
<tr>
<td>139. GC-trace (HP588) of the irradiated mixture spiked with an authentic sample of 72</td>
<td>245</td>
</tr>
<tr>
<td>140a. GC analysis of the concentrated 1 photolysate after irradiation</td>
<td>246</td>
</tr>
<tr>
<td>140b. Mass spectrum of the Unk2 eluted with a retention time of 35 min</td>
<td>247</td>
</tr>
<tr>
<td>140c. Mass spectrum of the Unk1 eluted with a retention time of 18 min</td>
<td>248</td>
</tr>
<tr>
<td>141. GC (HP588) and mass spectrum of an authentic sample of 34</td>
<td>249</td>
</tr>
<tr>
<td>142a. GC-trace of 31+Furan before irradiation</td>
<td>255</td>
</tr>
<tr>
<td>142b. GC-trace of 31+Furan after 120 min of irradiation</td>
<td>255</td>
</tr>
<tr>
<td>143a. GC-trace of 31 in AcCN before irradiation</td>
<td>256</td>
</tr>
<tr>
<td>143b. GC-trace of 31 in AcCN after 120 min of irradiation</td>
<td>256</td>
</tr>
<tr>
<td>144a. GC-trace (HP588) of 31+Furan solution after 120 min of irradiation</td>
<td>257</td>
</tr>
</tbody>
</table>
### Figures

<table>
<thead>
<tr>
<th>Figures</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>144b. Mass spectrum of <strong>Unk1</strong> (24.7 min)</td>
<td>258</td>
</tr>
<tr>
<td>144c. Mass spectrum of <strong>Unk2</strong> (26.2 min)</td>
<td>258</td>
</tr>
<tr>
<td>145a. GC trace of photoreaction of <strong>54</strong> in furan after 210 min of irradiation</td>
<td>260</td>
</tr>
<tr>
<td>145b. Mass spectrum of <strong>Unk3; 54+Furan</strong> reaction</td>
<td>261</td>
</tr>
<tr>
<td>145c. Mass spectrum of <strong>Unk4; 54+Furan</strong> reaction</td>
<td>261</td>
</tr>
<tr>
<td>146a. GC-trace of photoreaction of <strong>47</strong> in furan after 210 min of irradiation</td>
<td>262</td>
</tr>
<tr>
<td>146b. Mass spectrum of <strong>Unk5; 47+Furan</strong> reaction</td>
<td>263</td>
</tr>
<tr>
<td>146c. Mass spectrum of <strong>Unk6; 47+Furan</strong> reaction</td>
<td>263</td>
</tr>
<tr>
<td>146d. Mass spectrum of <strong>Unk7; 47+Furan</strong> reaction</td>
<td>264</td>
</tr>
<tr>
<td>147a. Furan quenching of the formation of <strong>43</strong> in the photoreaction of <strong>31</strong></td>
<td>267</td>
</tr>
<tr>
<td>147b. Furan quenching of the formation of <strong>46</strong> in the photoreaction of <strong>39</strong></td>
<td>267</td>
</tr>
<tr>
<td>147c. Furan quenching of the formation of <strong>39</strong> in the photoreaction of <strong>31</strong></td>
<td>267</td>
</tr>
<tr>
<td>147d. Furan quenching of the formation of <strong>40</strong> in the photoreaction of <strong>31</strong></td>
<td>268</td>
</tr>
<tr>
<td>148a. GC-trace of the concentrated fraction <strong>54</strong></td>
<td>269</td>
</tr>
<tr>
<td>148b. Mass spectrum of the concentrated fraction <strong>54</strong></td>
<td>270</td>
</tr>
<tr>
<td>149a. $^1$H-NMR spectrum of the unknown sample <strong>F7</strong>; the expected adduct</td>
<td>272</td>
</tr>
<tr>
<td>149b. $^1$H-NMR scale expansion of spectrum of the unknown sample <strong>F7</strong></td>
<td>272</td>
</tr>
<tr>
<td>150a. $^{13}$C-NMR spectrum of the unknown sample <strong>F7</strong>; the expected adduct</td>
<td>277</td>
</tr>
<tr>
<td>150b. $^{13}$C-DEPT 135 spectrum of the unknown sample <strong>F7</strong>; the expected adduct</td>
<td>277</td>
</tr>
<tr>
<td>151. GLC analysis of <strong>46+Furan</strong> solution before irradiation</td>
<td>279</td>
</tr>
<tr>
<td>152. GC-trace of <strong>46+Furan</strong> solution after 120 min of irradiation</td>
<td>280</td>
</tr>
<tr>
<td>153. Furan quenching of the formation of <strong>43</strong> in the photoreaction of <strong>46</strong></td>
<td>281</td>
</tr>
<tr>
<td>154. Plot between irradiation time $\nu$s consumption of <strong>46</strong> in acetonitrile solvent</td>
<td>282</td>
</tr>
<tr>
<td>155. Plot between irradiation time $\nu$s consumption <strong>46</strong> in furan solvent</td>
<td>282</td>
</tr>
<tr>
<td>156a. GC-trace of <strong>46+THF</strong> solution before irradiation</td>
<td>283</td>
</tr>
<tr>
<td>156b. GC-trace of <strong>46+THF</strong> solution after 90 min of irradiation</td>
<td>284</td>
</tr>
<tr>
<td>157a. GC trace of the concentrated <strong>46+THF</strong> photolysate</td>
<td>285</td>
</tr>
<tr>
<td>157b. Mass spectrum of the component at retention time of 7 min</td>
<td>285</td>
</tr>
</tbody>
</table>
### Figures

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>157c</td>
<td>Mass spectrum of the component at retention time of 17 min</td>
<td>286</td>
</tr>
<tr>
<td>157d</td>
<td>Mass spectrum of the component at retention time of 34.5 min</td>
<td>286</td>
</tr>
<tr>
<td>158</td>
<td>THF quenching of the formation of 43 in the photoreaction of 46</td>
<td>288</td>
</tr>
<tr>
<td>159</td>
<td>THF quenching of the consumption of 46</td>
<td>289</td>
</tr>
<tr>
<td>160a</td>
<td>GC analysis of the synthesized 91</td>
<td>292</td>
</tr>
<tr>
<td>160b</td>
<td>Mass spectrum of 91</td>
<td>292</td>
</tr>
<tr>
<td>161</td>
<td>$^1$H-NMR spectrum of 91</td>
<td>293</td>
</tr>
<tr>
<td>162a</td>
<td>$^{13}$C-NMR spectrum of 91</td>
<td>295</td>
</tr>
<tr>
<td>162b</td>
<td>$^{13}$C-DEPT 135 spectrum of 91</td>
<td>295</td>
</tr>
<tr>
<td>163</td>
<td>$^1$H-NMR spectrum of 93</td>
<td>297</td>
</tr>
<tr>
<td>164a</td>
<td>$^{13}$C-NMR spectrum of 93</td>
<td>299</td>
</tr>
<tr>
<td>164b</td>
<td>$^{13}$C-DEPT 135 spectrum of 93</td>
<td>299</td>
</tr>
<tr>
<td>165a</td>
<td>GC analysis of the synthesized 90</td>
<td>301</td>
</tr>
<tr>
<td>165b</td>
<td>Mass spectrum of the synthesized 90</td>
<td>301</td>
</tr>
<tr>
<td>166</td>
<td>$^1$H-NMR spectrum of 90</td>
<td>302</td>
</tr>
<tr>
<td>167a</td>
<td>$^{13}$C-NMR spectrum of 90</td>
<td>304</td>
</tr>
<tr>
<td>167b</td>
<td>$^{13}$C-DEPT 135 spectrum of 90</td>
<td>304</td>
</tr>
<tr>
<td>168a</td>
<td>GC analysis of the colorless crystals from synthesis of 96</td>
<td>306</td>
</tr>
<tr>
<td>168b</td>
<td>Mass spectrum of the synthesized 96</td>
<td>307</td>
</tr>
<tr>
<td>169</td>
<td>$^1$H-NMR spectrum of 96</td>
<td>308</td>
</tr>
<tr>
<td>170a</td>
<td>$^{13}$C-NMR spectrum of 96</td>
<td>309</td>
</tr>
<tr>
<td>170b</td>
<td>$^{13}$C-DEPT 135 spectrum of 96</td>
<td>309</td>
</tr>
<tr>
<td>171a</td>
<td>GC analysis of the colorless crystals B1 from synthesis of 94</td>
<td>311</td>
</tr>
<tr>
<td>171b</td>
<td>Mass spectrum of the colorless crystals B1</td>
<td>311</td>
</tr>
<tr>
<td>171c</td>
<td>$^1$H-NMR spectrum of the colorless crystals B1</td>
<td>312</td>
</tr>
<tr>
<td>172a</td>
<td>GC analysis of the colorless crystals B2 from synthesis of 94</td>
<td>313</td>
</tr>
<tr>
<td>172b</td>
<td>Mass spectrum of the colorless crystals B2; 94</td>
<td>313</td>
</tr>
<tr>
<td>173</td>
<td>$^1$H-NMR spectrum of the colorless crystals B2; 94</td>
<td>314</td>
</tr>
<tr>
<td>174a</td>
<td>GC analysis of 100</td>
<td>316</td>
</tr>
<tr>
<td>Figures</td>
<td>Pages</td>
<td></td>
</tr>
<tr>
<td>---------</td>
<td>-------</td>
<td></td>
</tr>
<tr>
<td>174b. Mass spectrum of 100</td>
<td>317</td>
<td></td>
</tr>
<tr>
<td>175. $^1$H-NMR spectrum of 100</td>
<td>318</td>
<td></td>
</tr>
<tr>
<td>176a. $^{13}$C-NMR spectrum of 100</td>
<td>319</td>
<td></td>
</tr>
<tr>
<td>176b. $^{13}$C-DEPT 135 spectrum of 100</td>
<td>319</td>
<td></td>
</tr>
<tr>
<td>177a. GC analysis of 99</td>
<td>320</td>
<td></td>
</tr>
<tr>
<td>177b. Mass spectrum of 99</td>
<td>321</td>
<td></td>
</tr>
<tr>
<td>178. $^1$H-NMR spectrum of 99</td>
<td>322</td>
<td></td>
</tr>
<tr>
<td>179a. $^{13}$C-NMR spectrum of 99</td>
<td>323</td>
<td></td>
</tr>
<tr>
<td>179b. $^{13}$C-DEPT 135 spectrum of 99</td>
<td>323</td>
<td></td>
</tr>
<tr>
<td>180a. GC analysis of 102</td>
<td>325</td>
<td></td>
</tr>
<tr>
<td>180b. Mass spectrum of 102</td>
<td>325</td>
<td></td>
</tr>
<tr>
<td>181. $^1$H-NMR spectrum of 102</td>
<td>326</td>
<td></td>
</tr>
<tr>
<td>182a. $^{13}$C-NMR spectrum of 102</td>
<td>328</td>
<td></td>
</tr>
<tr>
<td>182b. $^{13}$C-DEPT 135 spectrum of 102</td>
<td>328</td>
<td></td>
</tr>
<tr>
<td>183a. GC analysis of the light yellow solid from the synthesis of 98</td>
<td>330</td>
<td></td>
</tr>
<tr>
<td>183b. Mass spectrum of the major component at 13.1 min</td>
<td>330</td>
<td></td>
</tr>
<tr>
<td>183c. Mass spectrum of the minor component at 25.2 min</td>
<td>331</td>
<td></td>
</tr>
<tr>
<td>184a. GC analysis of the synthesized 98</td>
<td>331</td>
<td></td>
</tr>
<tr>
<td>184b. Mass spectrum of 98</td>
<td>332</td>
<td></td>
</tr>
<tr>
<td>185. Infrared absorption spectrum of 98</td>
<td>333</td>
<td></td>
</tr>
<tr>
<td>186. $^1$H-NMR spectrum of 98</td>
<td>334</td>
<td></td>
</tr>
<tr>
<td>187a. $^{13}$C-NMR spectrum of 98</td>
<td>335</td>
<td></td>
</tr>
<tr>
<td>187b. $^{13}$C-DEPT 135 spectrum of 98</td>
<td>335</td>
<td></td>
</tr>
<tr>
<td>188a. UV–absorption spectrum of 90 in acetonitrile</td>
<td>337</td>
<td></td>
</tr>
<tr>
<td>188b. UV–absorption overlay spectra of photolysis of 90 in acetonitrile</td>
<td>337</td>
<td></td>
</tr>
<tr>
<td>189a. UV–absorption spectrum of 90 in cyclohexane</td>
<td>338</td>
<td></td>
</tr>
<tr>
<td>189b. UV–absorption overlay spectra of photolysis of 90 in cyclohexane</td>
<td>338</td>
<td></td>
</tr>
<tr>
<td>190a. UV–absorption spectrum of 98 in acetonitrile</td>
<td>339</td>
<td></td>
</tr>
<tr>
<td>190b. UV-absorption overlay spectra of photolysis of 98 in acetonitrile</td>
<td>339</td>
<td></td>
</tr>
</tbody>
</table>
Figures

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>191.</td>
<td>UV-absorption spectrum of an authentic sample of 103 in acetonitrile.</td>
<td>340</td>
</tr>
<tr>
<td>192a.</td>
<td>GLC analysis of 90 in acetonitrile before irradiation.</td>
<td>342</td>
</tr>
<tr>
<td>192b.</td>
<td>GLC analysis of 90 in acetonitrile after 120 min of irradiation.</td>
<td>342</td>
</tr>
<tr>
<td>193a.</td>
<td>GLC analysis of 98 in acetonitrile before irradiation.</td>
<td>343</td>
</tr>
<tr>
<td>193b.</td>
<td>GLC analysis of 98 in acetonitrile after 120 min of irradiation.</td>
<td>343</td>
</tr>
<tr>
<td>194a.</td>
<td>GC trace (HP588) of concentrated photolysate of 90.</td>
<td>344</td>
</tr>
<tr>
<td>194b.</td>
<td>Mass spectrum of the component at RT of 13.9 min.</td>
<td>345</td>
</tr>
<tr>
<td>194c.</td>
<td>Mass spectrum of the component at RT of 23.2 min.</td>
<td>346</td>
</tr>
<tr>
<td>194d.</td>
<td>Mass spectrum of the component at RT of 24.5 min.</td>
<td>347</td>
</tr>
<tr>
<td>194e.</td>
<td>Mass spectrum of the component at RT of 26.7 min.</td>
<td>348</td>
</tr>
<tr>
<td>194f.</td>
<td>Mass spectrum of the component at RT of 55.2 min.</td>
<td>350</td>
</tr>
<tr>
<td>195.</td>
<td>Mass spectrum of an authentic sample of 104.</td>
<td>345</td>
</tr>
<tr>
<td>196.</td>
<td>Mass spectrum of an authentic 94.</td>
<td>346</td>
</tr>
<tr>
<td>197.</td>
<td>Mass spectrum of an authentic 105.</td>
<td>347</td>
</tr>
<tr>
<td>198a.</td>
<td>GC trace (HP588) of concentrated photolysate of 98.</td>
<td>350</td>
</tr>
<tr>
<td>198b.</td>
<td>Mass spectrum of the component at RT of 12.5 min.</td>
<td>351</td>
</tr>
<tr>
<td>198c.</td>
<td>Mass spectrum of the component at RT of 17.3 min.</td>
<td>354</td>
</tr>
<tr>
<td>198d.</td>
<td>Mass spectrum of the component at RT of 18.1 min.</td>
<td>353</td>
</tr>
<tr>
<td>198e.</td>
<td>Mass spectrum of the component at RT of 19.3 min.</td>
<td>354</td>
</tr>
<tr>
<td>199.</td>
<td>Mass spectrum of an authentic 103.</td>
<td>352</td>
</tr>
<tr>
<td>200.</td>
<td>Mass spectrum of an authentic 106.</td>
<td>355</td>
</tr>
<tr>
<td>201a.</td>
<td>GC analysis of 109.</td>
<td>360</td>
</tr>
<tr>
<td>201b.</td>
<td>Mass spectrum of the component at RT of 4.4 min.</td>
<td>360</td>
</tr>
<tr>
<td>202.</td>
<td>$^1$H-NMR spectrum of 109.</td>
<td>361</td>
</tr>
<tr>
<td>203a.</td>
<td>$^{13}$C-NMR spectrum of 109.</td>
<td>362</td>
</tr>
<tr>
<td>203b.</td>
<td>$^{13}$C-DEPT 135 spectrum of 109.</td>
<td>362</td>
</tr>
<tr>
<td>204a.</td>
<td>GC analysis of 111.</td>
<td>363</td>
</tr>
<tr>
<td>204b.</td>
<td>Mass spectrum of 111.</td>
<td>364</td>
</tr>
<tr>
<td>205.</td>
<td>$^1$H-NMR spectrum of 111.</td>
<td>365</td>
</tr>
<tr>
<td>Figures</td>
<td>Pages</td>
<td></td>
</tr>
<tr>
<td>---------</td>
<td>-------</td>
<td></td>
</tr>
<tr>
<td>206a. 13C-NMR spectrum of 111</td>
<td>366</td>
<td></td>
</tr>
<tr>
<td>206b. 13C-DEPT 135 spectrum of 111</td>
<td>366</td>
<td></td>
</tr>
<tr>
<td>207a. GC analysis of 105</td>
<td>367</td>
<td></td>
</tr>
<tr>
<td>207b. Mass spectrum of 105</td>
<td>368</td>
<td></td>
</tr>
<tr>
<td>208. 1H-NMR spectrum of 105</td>
<td>369</td>
<td></td>
</tr>
<tr>
<td>209a. 13C-NMR spectrum of 105</td>
<td>370</td>
<td></td>
</tr>
<tr>
<td>209b. 13C-DEPT 135 spectrum of 105</td>
<td>370</td>
<td></td>
</tr>
<tr>
<td>210a. GC analysis of 114</td>
<td>372</td>
<td></td>
</tr>
<tr>
<td>210b. Mass spectrum of the component at RT of 8 min</td>
<td>373</td>
<td></td>
</tr>
<tr>
<td>211. 1H-NMR spectrum of 114</td>
<td>374</td>
<td></td>
</tr>
<tr>
<td>212a. 13C-NMR spectrum of 114</td>
<td>375</td>
<td></td>
</tr>
<tr>
<td>212b. 13C-DEPT 135 spectrum of 114</td>
<td>375</td>
<td></td>
</tr>
<tr>
<td>213a. GC analysis of 115</td>
<td>376</td>
<td></td>
</tr>
<tr>
<td>213b. Mass spectrum of 115</td>
<td>377</td>
<td></td>
</tr>
<tr>
<td>214. 1H-NMR spectrum of 115</td>
<td>378</td>
<td></td>
</tr>
<tr>
<td>215a. 13C-NMR spectrum of 115</td>
<td>379</td>
<td></td>
</tr>
<tr>
<td>215b. 13C-DEPT 135 spectrum of 115</td>
<td>379</td>
<td></td>
</tr>
<tr>
<td>216. Infrared spectrum of 116</td>
<td>381</td>
<td></td>
</tr>
<tr>
<td>217a. GC analysis of 106</td>
<td>382</td>
<td></td>
</tr>
<tr>
<td>217b. Mass spectrum of 106</td>
<td>382</td>
<td></td>
</tr>
<tr>
<td>218. 1H-NMR spectrum of 106</td>
<td>383</td>
<td></td>
</tr>
<tr>
<td>219a. 13C-NMR spectrum of 106</td>
<td>384</td>
<td></td>
</tr>
<tr>
<td>219b. 13C-DEPT 135 spectrum of 106</td>
<td>384</td>
<td></td>
</tr>
<tr>
<td>220a. UV-absorption spectrum of 105 in acetonitrile before irradiation</td>
<td>385</td>
<td></td>
</tr>
<tr>
<td>220b. UV-absorption overlay spectra of photolysis of 105 in acetonitrile</td>
<td>386</td>
<td></td>
</tr>
<tr>
<td>221. UV-absorption of an authentic sample of 104 in acetonitrile</td>
<td>387</td>
<td></td>
</tr>
<tr>
<td>222. The overlay spectra between authentic 104 on the photolysis of 105 in acetonitrile</td>
<td>387</td>
<td></td>
</tr>
<tr>
<td>223a. UV-absorption spectrum of 106 in acetonitrile before irradiation</td>
<td>388</td>
<td></td>
</tr>
<tr>
<td>Figures</td>
<td>Pages</td>
<td></td>
</tr>
<tr>
<td>---------</td>
<td>-------</td>
<td></td>
</tr>
<tr>
<td>223b. UV-absorption overlay spectra of photolysis of 106 in acetonitrile</td>
<td>388</td>
<td></td>
</tr>
<tr>
<td>224. UV-absorption of an authentic sample of 103 in acetonitrile</td>
<td>389</td>
<td></td>
</tr>
<tr>
<td>225. GC-trace of the solution of 105 in acetonitrile before of irradiation</td>
<td>390</td>
<td></td>
</tr>
<tr>
<td>226. GC-trace of the solution of 106 in acetonitrile before irradiation</td>
<td>390</td>
<td></td>
</tr>
<tr>
<td>227a. GC-trace of concentrated photolysate of 105</td>
<td>391</td>
<td></td>
</tr>
<tr>
<td>227b. Mass spectrum of the component at RT 7.5 min</td>
<td>392</td>
<td></td>
</tr>
<tr>
<td>227c. Mass spectrum of the component at RT 15.5 min</td>
<td>391</td>
<td></td>
</tr>
<tr>
<td>228a. GC-trace of concentrated photolysate of 106</td>
<td>393</td>
<td></td>
</tr>
<tr>
<td>228b. Mass spectrum of the component at RT 8 min</td>
<td>394</td>
<td></td>
</tr>
<tr>
<td>228c. Mass spectrum of the component at RT 15.8 min</td>
<td>395</td>
<td></td>
</tr>
<tr>
<td>228d. Mass spectrum of the component at RT 16.2 min</td>
<td>393</td>
<td></td>
</tr>
<tr>
<td>229. UV-absorption spectrum of 31 in acetonitrile</td>
<td>399</td>
<td></td>
</tr>
<tr>
<td>230. UV-absorption overlay spectra of 31 in acetonitrile at various concentrations</td>
<td>399</td>
<td></td>
</tr>
<tr>
<td>231. Fluorescence spectrum of 31 in acetonitrile</td>
<td>400</td>
<td></td>
</tr>
<tr>
<td>232. UV-absorption spectrum of 31 in acetonitrile</td>
<td>402</td>
<td></td>
</tr>
<tr>
<td>233. Fluorescence spectrum of 37 in acetonitrile</td>
<td>402</td>
<td></td>
</tr>
<tr>
<td>234a. Phosphorescence emission spectrum of 31 in methanol/ethanol</td>
<td>404</td>
<td></td>
</tr>
<tr>
<td>234b. Phosphorescence excitation overlay spectra of 31 in methanol/ethanol</td>
<td>405</td>
<td></td>
</tr>
<tr>
<td>235. Infrared spectrum of 31 (neat liquid)</td>
<td>405</td>
<td></td>
</tr>
<tr>
<td>236. State diagram of 31</td>
<td>406</td>
<td></td>
</tr>
<tr>
<td>237. UV-absorption spectrum of 90 in acetonitrile</td>
<td>408</td>
<td></td>
</tr>
<tr>
<td>238. UV-absorption overlay spectra of 90 in acetonitrile at various concentrations</td>
<td>408</td>
<td></td>
</tr>
<tr>
<td>239. Fluorescence spectrum of 90 in acetonitrile</td>
<td>410</td>
<td></td>
</tr>
<tr>
<td>240. UV-absorption spectra of 90 in acetonitrile and cyclohexane</td>
<td>410</td>
<td></td>
</tr>
<tr>
<td>241. Fluorescence spectrum of 90 in cyclohexane</td>
<td>411</td>
<td></td>
</tr>
<tr>
<td>242a. Phosphorescence emission spectrum of 90 in methanol/ethanol</td>
<td>412</td>
<td></td>
</tr>
<tr>
<td>242b. Phosphorescence excitation overlay spectra of 90</td>
<td>414</td>
<td></td>
</tr>
<tr>
<td>Figures</td>
<td>Pages</td>
<td></td>
</tr>
<tr>
<td>---------</td>
<td>-------</td>
<td></td>
</tr>
<tr>
<td>243. Infrared spectrum of 90 (neat solid)</td>
<td>413</td>
<td></td>
</tr>
<tr>
<td>244. State diagram of 90</td>
<td>414</td>
<td></td>
</tr>
<tr>
<td>245. UV-absorption spectrum of 98 in acetonitrile</td>
<td>416</td>
<td></td>
</tr>
<tr>
<td>246. UV-absorption overlay spectra of 98 in acetonitrile at various concentrations</td>
<td>416</td>
<td></td>
</tr>
<tr>
<td>247a. Fluorescence spectrum of 98 in acetonitrile</td>
<td>417</td>
<td></td>
</tr>
<tr>
<td>247b. Fluorescence emission overlay spectra of 98 at various excitation wavelengths</td>
<td>419</td>
<td></td>
</tr>
<tr>
<td>248a. Phosphorescence emission spectrum of 98 in methanol/ethanol</td>
<td>420</td>
<td></td>
</tr>
<tr>
<td>248b. Phosphorescence excitation overlay spectra of 98</td>
<td>420</td>
<td></td>
</tr>
<tr>
<td>249. Infrared spectrum of 98 (neat solid)</td>
<td>421</td>
<td></td>
</tr>
<tr>
<td>250. State diagram of 98</td>
<td>422</td>
<td></td>
</tr>
<tr>
<td>251. UV-absorption spectrum of 54 in acetonitrile</td>
<td>424</td>
<td></td>
</tr>
<tr>
<td>252. UV-absorption overlay spectra of 54 in acetonitrile at various concentrations</td>
<td>424</td>
<td></td>
</tr>
<tr>
<td>253a. Fluorescence spectrum of 54 in acetonitrile</td>
<td>425</td>
<td></td>
</tr>
<tr>
<td>253b. Fluorescence emission overlay spectra of 54 at various excitation wavelengths</td>
<td>425</td>
<td></td>
</tr>
<tr>
<td>254. UV-absorption spectrum of 117 in acetonitrile</td>
<td>428</td>
<td></td>
</tr>
<tr>
<td>255. UV-absorption overlay spectra of 117 in acetonitrile at various concentrations</td>
<td>428</td>
<td></td>
</tr>
<tr>
<td>256. Fluorescence spectrum of 117 in acetonitrile</td>
<td>430</td>
<td></td>
</tr>
<tr>
<td>257. UV-absorption spectrum of 118 in acetonitrile</td>
<td>432</td>
<td></td>
</tr>
<tr>
<td>258. UV-absorption overlay spectra of 118 in acetonitrile at various concentrations</td>
<td>432</td>
<td></td>
</tr>
<tr>
<td>259. Fluorescence spectrum of 118 in acetonitrile</td>
<td>434</td>
<td></td>
</tr>
<tr>
<td>260. UV-absorption spectrum of 47 in acetonitrile</td>
<td>436</td>
<td></td>
</tr>
<tr>
<td>261. UV-absorption overlay spectra of 47 in acetonitrile at various concentrations</td>
<td>436</td>
<td></td>
</tr>
<tr>
<td>Figures</td>
<td>Pages</td>
<td></td>
</tr>
<tr>
<td>---------</td>
<td>-------</td>
<td></td>
</tr>
<tr>
<td>262. UV-absorption spectra of 47 in acetonitrile and cyclohexane</td>
<td>437</td>
<td></td>
</tr>
<tr>
<td>263. Fluorescence spectrum of 47 in acetonitrile</td>
<td>438</td>
<td></td>
</tr>
<tr>
<td>264. 259. Fluorescence spectrum of 47 in cyclohexane</td>
<td>439</td>
<td></td>
</tr>
<tr>
<td>265. UV-absorption spectrum of 46 in acetonitrile</td>
<td>440</td>
<td></td>
</tr>
<tr>
<td>266. UV-absorption spectra of 46 at various concentrations</td>
<td>441</td>
<td></td>
</tr>
<tr>
<td>267. UV-absorption spectra of 46 after re-purification in various solvents</td>
<td>442</td>
<td></td>
</tr>
<tr>
<td>268a. Fluorescence spectrum of 46 in acetonitrile</td>
<td>444</td>
<td></td>
</tr>
<tr>
<td>268b. Fluorescence emission overlay spectra of 46 in acetonitrile</td>
<td>444</td>
<td></td>
</tr>
<tr>
<td>268c. Fluorescence spectrum of 46 in methanol at various excitation wavelengths</td>
<td>445</td>
<td></td>
</tr>
<tr>
<td>269a. Phosphorescence emission spectrum of 46 in methanol/ethanol</td>
<td>447</td>
<td></td>
</tr>
<tr>
<td>269b. Phosphorescence excitation spectra of 46 at various emission wavelengths</td>
<td>447</td>
<td></td>
</tr>
<tr>
<td>269c. Phosphorescence emission spectra of 46 at various excitation wavelengths</td>
<td>448</td>
<td></td>
</tr>
<tr>
<td>270. State diagram of 46</td>
<td>448</td>
<td></td>
</tr>
<tr>
<td>271. UV-absorption spectrum of 105 in acetonitrile</td>
<td>450</td>
<td></td>
</tr>
<tr>
<td>272. UV-absorption overlay spectra of 105 at various concentrations</td>
<td>450</td>
<td></td>
</tr>
<tr>
<td>273. Fluorescence spectrum of 105 in acetonitrile</td>
<td>451</td>
<td></td>
</tr>
<tr>
<td>274. UV-absorption overlay spectra of 105 in acetonitrile and cyclohexane</td>
<td>452</td>
<td></td>
</tr>
<tr>
<td>275. Fluorescence spectrum of 105 in cyclohexane</td>
<td>452</td>
<td></td>
</tr>
<tr>
<td>276a. Phosphorescence emission spectrum of 5 in methanol/ethanol</td>
<td>454</td>
<td></td>
</tr>
<tr>
<td>276b. Phosphorescence excitation spectra of 105 in methanol/ethanol</td>
<td>454</td>
<td></td>
</tr>
<tr>
<td>277. State diagram of 105</td>
<td>455</td>
<td></td>
</tr>
<tr>
<td>281. UV-absorption overlay spectra of 106 before and after purification in acetonitrile</td>
<td>457</td>
<td></td>
</tr>
<tr>
<td>282. UV-absorption overlay spectra of 106 after purification at various concentrations</td>
<td>457</td>
<td></td>
</tr>
<tr>
<td>283. Fluorescence spectrum of 106 in acetonitrile after purification</td>
<td>458</td>
<td></td>
</tr>
</tbody>
</table>
284a. Phosphorescence emission spectrum of 106 in methanol/ethanol… 459
284b. Phosphorescence emission overlay spectra of 106 in methanol/ethanol.
285. State diagram of 106………………………………………………………… 460
286. UV-absorption spectrum of 119 in acetonitrile………………………… 462
287. UV-absorption spectra of 119 in acetonitrile at various concentrations.. 462
288. Fluorescence spectrum of 119 in acetonitrile………………………… 463
289. UV-absorption spectrum of 120 in acetonitrile………………………… 466
290. UV-absorption spectrum of 120 in acetonitrile at various concentrations 466
291a. Fluorescence spectrum of 120 in acetonitrile………………………… 467
291b. Scale expansion of fluorescence spectrum of 120 in acetonitrile… 467
292. UV-absorption overlay spectra of 5-phenyl-1,2,4-thiadiazoles in acetonitrile………………………………………………………………………… 471
293. UV-absorption overlay spectra of 3-phenyl-1,2,4-thiadiazoles in acetonitrile………………………………………………………………………… 475
294. UV-absorption spectra of butyrophenone in acetonitrile at various concentrations…………………………………………………………………… 491
295. UV-absorption spectrum of 31 in acetonitrile…………………………… 491
296a. GLC analysis of butyrophenone solution before irradiation…………… 493
296b. GLC analysis of butyrophenone solution after 90 min of irradiation… 493
297a. GLC analysis of solution of 31 before irradiation…………………… 494
297b. GLC analysis of solution of 31 after 90 min of irradiation……………… 494
298a. GLC analysis of solution of 31+Butyrophenone before irradiation… 495
298b. GLC analysis of solution of 31+Butyrophenone after irradiation…… 495
299. UV-absorption spectrum of 46 in acetonitrile………………………… 498
300a. GLC analysis of solution of 46 before irradiation…………………… 499
300b. GLC analysis of solution of 46 after 120 min of irradiation…………… 499
301a. GLC analysis of butyrophenone solution before irradiation…………… 500
301b. GLC analysis of butyrophenone solution after irradiation…………… 500
302a. GLC analysis of solution of 46+Butyrophenone before irradiation….. 501
302b. GLC analysis of solution of 46+Butyrophenone after irradiation…… 501
303a. GC-trace of the viscous liquid product from synthesis of 128……… 507
<table>
<thead>
<tr>
<th>Figures</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>303b. Mass spectrum of the viscous liquid product</td>
<td>507</td>
</tr>
<tr>
<td>304. $^1$H-NMR spectrum of the viscous colorless liquid</td>
<td>509</td>
</tr>
<tr>
<td>305a. $^{13}$C-NMR spectrum of the viscous colorless liquid</td>
<td>510</td>
</tr>
<tr>
<td>305b. $^{13}$C-NMR spectrum of the viscous colorless liquid; scale expansion</td>
<td>511</td>
</tr>
<tr>
<td>305c. $^{13}$C-DEPT 135 spectrum of the viscous colorless liquid</td>
<td>512</td>
</tr>
<tr>
<td>306. GC-trace of $^{31+127}$ mixture in acetonitrile before irradiation</td>
<td>513</td>
</tr>
<tr>
<td>307. UV-absorption spectrum of $^{31}$ in acetonitrile</td>
<td>515</td>
</tr>
<tr>
<td>308. UV-absorption spectrum of $^{127}$ in acetonitrile</td>
<td>516</td>
</tr>
<tr>
<td>309. UV-absorption spectrum of a mixture of $^{31+127}$ in acetonitrile</td>
<td>516</td>
</tr>
<tr>
<td>310a. GC-trace of $^{31+127}$ mixture after 180 min of irradiation</td>
<td>517</td>
</tr>
<tr>
<td>310b. Mass spectrum of the component at RT 26.7 min</td>
<td>518</td>
</tr>
<tr>
<td>311. GC-trace of $^{90+127}$ mixture before irradiation</td>
<td>520</td>
</tr>
<tr>
<td>312. GC-trace of $^{90+127}$ mixture after 180 min of irradiation</td>
<td>521</td>
</tr>
<tr>
<td>313. Fluorescence quenching of the excited state of $^{90}$ by $^{127}$</td>
<td>522</td>
</tr>
<tr>
<td>314. GC-trace of a mixture of $^{46+127}$ before irradiation</td>
<td>525</td>
</tr>
<tr>
<td>315a. GC-trace of a mixture of $^{46+127}$ after 120 min of irradiation</td>
<td>526</td>
</tr>
<tr>
<td>315b. Mass spectrum of the component at RT of 26.7 min</td>
<td>526</td>
</tr>
<tr>
<td>316. Cyclic voltametry of $^{31}$ in acetonitrile</td>
<td>529</td>
</tr>
<tr>
<td>317. Cyclic voltametry of $^{46}$ in acetonitrile</td>
<td>529</td>
</tr>
<tr>
<td>318. Cyclic voltametry of $^{90}$ in acetonitrile</td>
<td>530</td>
</tr>
<tr>
<td>319. Cyclic voltametry of $^{47}$ in acetonitrile</td>
<td>530</td>
</tr>
<tr>
<td>320. GC-trace of the Solution $^{31+TEA}$ after 30 min of irradiation</td>
<td>536</td>
</tr>
<tr>
<td>321. GC-trace of Solution $^{31+PA}$ after 30 min of irradiation</td>
<td>536</td>
</tr>
<tr>
<td>322. GC-trace of the $^{31+TEA}$ mixture after 30 min of irradiation</td>
<td>539</td>
</tr>
<tr>
<td>323. GC-trace of $^{31+PA}$ mixture after 30 min of irradiation</td>
<td>539</td>
</tr>
<tr>
<td>324. GLC analysis of the $^{46+TEA}$ mixture after 120 min of irradiation</td>
<td>543</td>
</tr>
<tr>
<td>325. GLC analysis of the $^{46+PA}$ mixture after 120 min of irradiation</td>
<td>543</td>
</tr>
<tr>
<td>326. GC-trace of the $^{46+TEA}$ mixture after 120 min of irradiation</td>
<td>545</td>
</tr>
<tr>
<td>327. GLC analysis of the $^{4+PA}$ mixture after 120 min of irradiation</td>
<td>54</td>
</tr>
</tbody>
</table>
# LIST OF SCHEMES

<table>
<thead>
<tr>
<th>Schemes</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Phototransposition of isothiazoles <em>via</em> tricyclic zwitterionic intermediates..</td>
<td>2</td>
</tr>
<tr>
<td>2. Phototransposition of phenylisothiazoles and phenylthiazoles <em>via</em> tricyclic zwitterionic intermediates</td>
<td>2</td>
</tr>
<tr>
<td>3. Electrocyclic ring closure heteroatom migration mechanism of thiazoles and isothiazoles</td>
<td>4</td>
</tr>
<tr>
<td>4. Photocleavage of the S–N bond in isothiazoles</td>
<td>6</td>
</tr>
<tr>
<td>5. Particular pathway for the synthesis of 1,2,4-thiadiazole ring system</td>
<td>8</td>
</tr>
<tr>
<td>7. Mechanism for the formation 5-phenyl-1,2,4-thiadiazole</td>
<td>15</td>
</tr>
<tr>
<td>8. Major fragmentation pathways of 1,2,4-thiadiazoles</td>
<td>18</td>
</tr>
<tr>
<td>9. Possible fragmentation pathway of 3-amino-5-phenyl-1,2,4-thiadiazole and 5-phenyl-1,2,4-thiadiazole</td>
<td>19</td>
</tr>
<tr>
<td>10. Synthesis of 2-phenyl- and 2,4-diphenyl-1,3,5-triazine</td>
<td>21</td>
</tr>
<tr>
<td>11. Photochemistry of 5-phenylthiazole and 5-phenylisothiazole</td>
<td>26</td>
</tr>
<tr>
<td>12. The photoreaction of 5-phenyl-1,2,4-thiadiazole</td>
<td>45</td>
</tr>
<tr>
<td>14. Synthesis of 5-phenyl-1,3,4-oxathiazole-2-one</td>
<td>47</td>
</tr>
<tr>
<td>15. Synthesis of ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate</td>
<td>51</td>
</tr>
<tr>
<td>16. Synthesis of 3-phenyl-1,2,4-thiadizole</td>
<td>55</td>
</tr>
<tr>
<td>17. Synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole</td>
<td>67</td>
</tr>
<tr>
<td>18. Synthesis of N-[(dimethylamino)ethylidine]thiobenzamide</td>
<td>68</td>
</tr>
<tr>
<td>19. Synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole</td>
<td>74</td>
</tr>
<tr>
<td>20. Synthesis of 5-methyl-3-phenyl-1,2,4-thiadiazole</td>
<td>79</td>
</tr>
<tr>
<td>21. Synthesis of 5-chloro-3-phenyl-1,2,4-thiadiazole</td>
<td>80</td>
</tr>
<tr>
<td>22. Synthesis of diethyl 3-phenyl-1,2,4-thiadiazole-5-malonate</td>
<td>84</td>
</tr>
<tr>
<td>23. Synthesis of 5-methyl-3-phenyl-1,2,4-thiadiazole</td>
<td>92</td>
</tr>
<tr>
<td>24. Fragmentation pathways of 7 and 53</td>
<td>94</td>
</tr>
<tr>
<td>Schemes</td>
<td>Pages</td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>25. The recent synthetic method of un-symmetrically substituted-s-triazines..</td>
<td>97</td>
</tr>
<tr>
<td>27. Synthesis of 2,4-dimethyl-6-phenyl-1,3,5-triazine</td>
<td>105</td>
</tr>
<tr>
<td>28. Possible synthetic method of 2-methyl-4,6-diphenyl-1,3,5-triazine</td>
<td>109</td>
</tr>
<tr>
<td>29. Synthesis of thiobenzamide-$^{15}$N</td>
<td>124</td>
</tr>
<tr>
<td>30. Synthesis of N-[(dimethylamino)methylene]thiobenzamide-$^{15}$N</td>
<td>129</td>
</tr>
<tr>
<td>31. Synthesis of 5-phenyl-1,2,4-thiadiazole – $^{15}$N</td>
<td>135</td>
</tr>
<tr>
<td>32. The plausible pathway for the formation of 5-phenyl-1,2,4-oxadiazole – $^{15}$N</td>
<td>146</td>
</tr>
<tr>
<td>33. The proposed mechanism for the formation of the phototransposition product</td>
<td>146</td>
</tr>
<tr>
<td>34. Possible fragmentation pathways of 5-phenyl-1,2,4-thiadiazole-4-$^{15}$N</td>
<td>149</td>
</tr>
<tr>
<td>35. Major possible fragmentation pathways of regular 2-phenyl-1,3,5-triazine</td>
<td>160</td>
</tr>
<tr>
<td>36. Possible structures and fragmentation patterns of 2-phenyl-1,3,5-triazine containing one $^{15}$N and two $^{15}$N atoms</td>
<td>161</td>
</tr>
<tr>
<td>37. Possible fragmentation pathways of 2,4-diphenyl-s-triazine-$^{15}$N.</td>
<td>164</td>
</tr>
<tr>
<td>38. Synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole</td>
<td>174</td>
</tr>
<tr>
<td>39. Synthetic pathway of 3-methyl-5-phenyl-1,2,4-thiadiazole-$^{15}$N</td>
<td>175</td>
</tr>
<tr>
<td>40. The N-scrambling mechanism</td>
<td>190</td>
</tr>
<tr>
<td>41. Two major fragmentation pathways of $^{15}$N</td>
<td>192</td>
</tr>
<tr>
<td>42. Possible fragmentation pathways for the triazine containing one and two $^{15}$N atoms</td>
<td>200</td>
</tr>
<tr>
<td>45. Possible fragmentation pathways of 2-methyl-4,6-diphenyl-1,3,5-triazine-$^{15}$N</td>
<td>206</td>
</tr>
<tr>
<td>46. N-2 and C-3 interchange photochemical pathway of isothiazoles</td>
<td>213</td>
</tr>
<tr>
<td>47. N-2 and C-3 interchange photochemical pathway of 5-phenyl-1,2,4-thiadiazole</td>
<td>213</td>
</tr>
<tr>
<td>Schemes</td>
<td>Pages</td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>48. Possible mechanism for the formation of benzonitrile sulfide</td>
<td>214</td>
</tr>
<tr>
<td>49. Trapping of thermally generated 13 by 1,3-dipolar cycloaddition</td>
<td>215</td>
</tr>
<tr>
<td>reaction</td>
<td></td>
</tr>
<tr>
<td>50. The predicted mechanism for the formation of 13</td>
<td>220</td>
</tr>
<tr>
<td>isothiocyanic acid</td>
<td></td>
</tr>
<tr>
<td>51. The proposed mechanism for the formation of 13 upon irradiation of</td>
<td>225</td>
</tr>
<tr>
<td>4</td>
<td></td>
</tr>
<tr>
<td>52. The proposed mechanism for phenyl-s-triazaines formation</td>
<td>226</td>
</tr>
<tr>
<td>53. The proposed formation of unsymmetrical phenyltriazine via [4+2]</td>
<td>227</td>
</tr>
<tr>
<td>cycloaddition cross-coupling of phenyldiazacyclobutadiene intermediates</td>
<td></td>
</tr>
<tr>
<td>54. The possible photoproducts predicted to observe upon irradiation of</td>
<td>228</td>
</tr>
<tr>
<td>a mixture of 5-phenyl-1,2,4-thiadiazole and 3-methyl-5-phenyl-1,2,4-</td>
<td></td>
</tr>
<tr>
<td>thiadiazole</td>
<td></td>
</tr>
<tr>
<td></td>
<td>228</td>
</tr>
<tr>
<td>55. Total synthesis of 2-methyl-4-phenyl-1,3,5-triazine</td>
<td>228</td>
</tr>
<tr>
<td>56. Synthesis of N-[(dimethylamino)methylene]benzamide</td>
<td>229</td>
</tr>
<tr>
<td>57. Synthesis of 2-methyl-4-phenyl-1,3,5-triazine</td>
<td>233</td>
</tr>
<tr>
<td>58. The proposed formation of benzamide upon irradiation of 1</td>
<td>250</td>
</tr>
<tr>
<td>59. 1,3-Diaza-5-thiabicyclo[2.1.0]pentene; Key intermediate upon</td>
<td>251</td>
</tr>
<tr>
<td>irradiation of 5-phenyl-1,2,4-thiadiazole</td>
<td></td>
</tr>
<tr>
<td>60. Photochemistry of 3-cyanothiophene in furan solvent</td>
<td>252</td>
</tr>
<tr>
<td>61. Photochemistry of 1-methyl-5-phenylpyrazole in methanol</td>
<td>252</td>
</tr>
<tr>
<td>62. Irradiation of 1-methyl-5-phenylpyrazole in furan solvent</td>
<td>253</td>
</tr>
<tr>
<td>63. Formation of furan-phenyldiazacyclobutadiene adduct upon</td>
<td></td>
</tr>
<tr>
<td>irradiation of 10+Furan</td>
<td>259</td>
</tr>
<tr>
<td>64. Formation of furan-phenyldiazacyclobutadiene adduct upon</td>
<td></td>
</tr>
<tr>
<td>irradiation of 7+Furan</td>
<td>262</td>
</tr>
<tr>
<td>65. Formation of furan-phenyldiazacyclobutadiene adduct upon</td>
<td></td>
</tr>
<tr>
<td>irradiation of 12+Furan</td>
<td>264</td>
</tr>
<tr>
<td>66. Possible formation of the observed adducts</td>
<td>265</td>
</tr>
<tr>
<td>67. The expected 15N-scrambling in 3-phenyl-1,2,4-thiadiazole-2-15N</td>
<td>278</td>
</tr>
<tr>
<td>68. Possible formation of banzamide upon irradiation of 4</td>
<td>287</td>
</tr>
<tr>
<td>Schemes</td>
<td>Pages</td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>69. Total synthesis of 5-(4′-methoxy)phenyl-1,2,4-thiadiazole</td>
<td>291</td>
</tr>
<tr>
<td>70. Synthesis of 4-methoxythiobenzamide</td>
<td>291</td>
</tr>
<tr>
<td>71. Synthesis of N-[(dimethylamino)methylene]4-methoxythiobenzamide</td>
<td>296</td>
</tr>
<tr>
<td>72. Synthesis of 5-(4-methoxy)phenyl-1,2,4-thiadiazole</td>
<td>300</td>
</tr>
<tr>
<td>73. Total synthetic scheme of 2-(4′-methoxy)phenyl-1,3,5-triazine</td>
<td>305</td>
</tr>
<tr>
<td>74. Synthesis of N-[(dimethylamino)methylene]4-methoxybenzamide</td>
<td>305</td>
</tr>
<tr>
<td>75. Synthesis of 2-(4′-methoxy)phenyl-1,3,5-triazine</td>
<td>310</td>
</tr>
<tr>
<td>76. Total synthesis of 5-(4′-cyano)phenyl-1,2,4-thiadiazole</td>
<td>315</td>
</tr>
<tr>
<td>77. Synthesis of 4-cyanobenzamide</td>
<td>316</td>
</tr>
<tr>
<td>78. Synthesis of 4-cyanothiobenzamide</td>
<td>320</td>
</tr>
<tr>
<td>79. Synthesis of N-[(dimethylamino)methylene]4-cyanothiobenzamide</td>
<td>324</td>
</tr>
<tr>
<td>80. Synthesis of 5-(4′-cyano)phenyl-1,2,4-thiadiazole</td>
<td>329</td>
</tr>
<tr>
<td>81. Photoreaction of 5(4′-methoxy)- and 5(4′-cyano)-phenyl-1,2,4-</td>
<td>357</td>
</tr>
<tr>
<td>thiadiazole</td>
<td></td>
</tr>
<tr>
<td>82. Total synthesis of 3-(4-methoxy)phenyl-1,2,4-thiadiazole</td>
<td>358</td>
</tr>
<tr>
<td>83. Synthesis of 5-(4′-methoxy)phenyl-1,3,4-oxathiazole-2-one</td>
<td>359</td>
</tr>
<tr>
<td>84. Synthesis of ethyl 3-(4′-methoxy)phenyl-1,2,4-thiadiazole-5-</td>
<td>363</td>
</tr>
<tr>
<td>carboxylate</td>
<td></td>
</tr>
<tr>
<td>85. Synthesis of 3-(4′-methoxy)phenyl-1,2,4-thiadizole</td>
<td>367</td>
</tr>
<tr>
<td>86. Total synthesis of 3-(4′-cyano)phenyl-1,2,4-thiadiazole</td>
<td>371</td>
</tr>
<tr>
<td>87. Synthesis of 5-(4′-cyano)phenyl-1,3,4-oxathiazole-2-one</td>
<td>372</td>
</tr>
<tr>
<td>88. Synthesis of ethyl 3-(4′-cyano)phenyl-1,2,4-thiadiazole-5-carboxylate</td>
<td>376</td>
</tr>
<tr>
<td>89. Synthesis of 3-(4′-cyano)phenyl-1,2,4-thiadizole</td>
<td>380</td>
</tr>
<tr>
<td>90. Photoreaction of 3(4′-methoxy)- and 3(4′-cyano)-phenyl-1,2,4-</td>
<td>396</td>
</tr>
<tr>
<td>thiadiazole</td>
<td></td>
</tr>
<tr>
<td>91. Solvent reorganization resulting in lowering of the excited state</td>
<td>479</td>
</tr>
<tr>
<td>energy level</td>
<td></td>
</tr>
<tr>
<td>92. Energy difference between absorbing and emitting states due to</td>
<td>480</td>
</tr>
<tr>
<td>geometry change upon excitation</td>
<td></td>
</tr>
<tr>
<td>Schemes</td>
<td>Pages</td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>93. Photostability of Tinuvin P (reprinted from ref. 32)</td>
<td>481</td>
</tr>
<tr>
<td>94. A large Stokes’ shift due to emission from a TICT excited state</td>
<td>482</td>
</tr>
<tr>
<td>95. Photoinduced intramolecular charge transfer in biaryl systems</td>
<td>485</td>
</tr>
<tr>
<td>96. Possible energy diagram of phenylthiadiazoles in acetonitrile or cyclohexane solvent</td>
<td>486</td>
</tr>
<tr>
<td>97. Major photochemical reaction of butyrophenone</td>
<td>492</td>
</tr>
<tr>
<td>98. Triplet sensitization of 1 by butyrophenone photosensitizer</td>
<td>497</td>
</tr>
<tr>
<td>99. Triplet sensitization of 4 by butyrophenone photosensitizer</td>
<td>503</td>
</tr>
<tr>
<td>100. Possible pathway for the formation of irradiation of 92 in the presence of 90</td>
<td>504</td>
</tr>
<tr>
<td>101. <strong>BC-1</strong> intermediate – the key intermediate in the photoreaction of 1</td>
<td>505</td>
</tr>
<tr>
<td>102. Synthesis of tri-n-butylphosphine sulfide</td>
<td>506</td>
</tr>
<tr>
<td>103. Possible fragmentation pathway of tri-n-butylphosphine sulfide</td>
<td>508</td>
</tr>
<tr>
<td>104. A possible ground state interaction between 1 and 90</td>
<td>514</td>
</tr>
<tr>
<td>105. Thermodynamic feasibilities of electron transfer between <strong>TEA</strong> and some thiadiazoles</td>
<td>533</td>
</tr>
<tr>
<td>106. Thermodynamic feasibilities of electron transfer between <strong>PA</strong> and some thiadiazoles</td>
<td>534</td>
</tr>
<tr>
<td>107. Possible mechanism for the formation of the phototransposition product</td>
<td>614</td>
</tr>
<tr>
<td>108. Possible formation of the observed adducts</td>
<td>615</td>
</tr>
<tr>
<td>109. Phenyldiazacyclobutadiene formation</td>
<td>616</td>
</tr>
<tr>
<td>110. Possible orientations for this cycloaddition-cleavage pathway</td>
<td>617</td>
</tr>
<tr>
<td>111. [4+2] cycloaddition cross-coupling of phenyldiazacyclobutadiene intermediates</td>
<td>618</td>
</tr>
<tr>
<td>112a. Possible photofragmentation pathways of 3-phenyl-1,2,4-thiadiazole...</td>
<td>619</td>
</tr>
<tr>
<td>112b. Possible photofragmentation pathways of 3-phenyl-1,2,4-thiadiazole-2-^{15}N...</td>
<td>619</td>
</tr>
<tr>
<td>113. Evidences for the intermediacy of benzonitrile sulfide upon irradiation of 4</td>
<td>620</td>
</tr>
</tbody>
</table>
# LIST OF TABLES

<table>
<thead>
<tr>
<th>Tables</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. $^{13}$C-chemical shifts of 7-oxabicyclo[2.2.1]hept-2-ene and some derivatives</td>
<td>273</td>
</tr>
<tr>
<td>2. UV-absorption properties of 5-phenyl-1,2,4-thiadiazoles in acetonitrile</td>
<td>470</td>
</tr>
<tr>
<td>3. Fluorescence properties of 5-phenyl-1,2,4-thiadiazoles in acetonitrile</td>
<td>472</td>
</tr>
<tr>
<td>4. Phosphorescence properties of 5-phenyl-1,2,4-thiadiazoles in ethanol/methanol (4:1) at 77 K</td>
<td>473</td>
</tr>
<tr>
<td>5. UV-absorption properties of 3-phenyl-1,2,4-thiadiazoles in acetonitrile</td>
<td>475</td>
</tr>
<tr>
<td>6. Fluorescence properties of 3-phenyl-1,2,4-thiadiazoles in acetonitrile</td>
<td>477</td>
</tr>
<tr>
<td>7. Phosphorescence properties of 3-phenyl-1,2,4-thiadiazoles in ethanol/methanol (4:1) at 77 K</td>
<td>478</td>
</tr>
<tr>
<td>8. Quantitative analysis of triplet sensitization reaction of 31</td>
<td>496</td>
</tr>
<tr>
<td>9. Quantitative analysis of triplet sensitization reaction of 46</td>
<td>502</td>
</tr>
<tr>
<td>10. Reduction potentials and $E_{00}$ (eV) of some phenyl-1,2,4-thiadiazoles in acetonitrile</td>
<td>531</td>
</tr>
<tr>
<td>11. Quantitative analysis of the photoreaction of 31 in AcCN with the presence of TEA or PA</td>
<td>538</td>
</tr>
<tr>
<td>12. Quantitative analysis of the photoreaction of 31 in acetonitrile and methanol with the presence of TEA or PA</td>
<td>541</td>
</tr>
<tr>
<td>13. Quantitative analysis of irradiation of 46 in the presence of TEA or PA in acetonitrile or methanol solvent</td>
<td>546</td>
</tr>
<tr>
<td>14. Photolysis of 5-phenyl-1,2,4-thiadiazole in acetonitrile</td>
<td>584</td>
</tr>
<tr>
<td>15. Photolysis of 5-phenyl-1,2,4-thiadiazole in cyclohexane</td>
<td>585</td>
</tr>
<tr>
<td>16. Photolysis of 3-phenyl-1,2,4-thiadiazole in acetonitrile</td>
<td>586</td>
</tr>
<tr>
<td>17. Photolysis of 3-methyl-5-phenyl-1,2,4-thiadiazole in acetonitrile</td>
<td>588</td>
</tr>
<tr>
<td>18. Photolysis of 3-methyl-5-phenyl-1,2,4-thiadiazole in methanol</td>
<td>588</td>
</tr>
<tr>
<td>Tables</td>
<td>Pages</td>
</tr>
<tr>
<td>--------</td>
<td>-------</td>
</tr>
<tr>
<td>19. Time (min) Vs ratio of 103/104 peaks of benzonitrile-photoproduct……</td>
<td>589</td>
</tr>
<tr>
<td>20. Time (min) Vs ratio of 158/159 peaks of 2-phenyl-1,3,5-triazine-photoproduct</td>
<td>590</td>
</tr>
<tr>
<td>21. Time (min) Vs ratio of 135/136 peaks of un-consumed 5-phenyl-1,2,4-thiadiazole-4$^{15}$N</td>
<td>590</td>
</tr>
<tr>
<td>22. Time (min) Vs ratio of 135/136 peaks of 3-phenyl-1,2,4-thiadiazole-photoproduct</td>
<td>591</td>
</tr>
<tr>
<td>23. Time (min) Vs ratio of 234/235 peaks of 2,4-diphenyl-1,3,5-triazine-photoproduct</td>
<td>591</td>
</tr>
<tr>
<td>24. Time (min) Vs ratio of 103/104 peaks of benzonitrile-photoproduct</td>
<td>595</td>
</tr>
<tr>
<td>25. Time (min) Vs of 186/187 ratio of 2,4-dimethyl-6-phenyl-1,3,5-triazine-photoproduct</td>
<td>595</td>
</tr>
<tr>
<td>26. Time (min) Vs of 135/136 ratio of un-consumed 3-methyl-5-phenyl-1,2,4-thiadiazole-4$^{15}$N</td>
<td>596</td>
</tr>
<tr>
<td>27. Time (min) Vs of 135/136 ratio of 5-methyl-3-phenyl-1,2,4-thiadiazole-photoproduct</td>
<td>596</td>
</tr>
<tr>
<td>28. Time (min) Vs of 248/249 ratio of 2-methyl-4,6-diphenyl-1,3,5-triazine-photoproduct</td>
<td>597</td>
</tr>
</tbody>
</table>
CHAPTER 1

INTRODUCTION

1.1 Photochemistry of isothiazoles and thiazoles

The photoreaction of isothiazole (1) was first reported to undergo phototransposition to yield thiazole (2). The reverse transposition of isothiazole (2) was, however, reported not to take place.

\[
\text{\textbf{1}} \xrightarrow{h\nu} \text{\textbf{2}}
\]

Lablache-Combier and co-workers\(^2\) reported that 3- and 4-methylisothiazole (3) and (4) each transposes to a single N2-C3 interchanged thiazole product (6) and (7). But 5-methylthiazole (5) transposes to the thiazole (8), and isomeric isothiazoles (3) and (4). These methylisothiazoles were suggested to result from a mechanism involving tricyclic zwitterionic intermediates, as shown in Scheme 1, based on the known phototransposition reaction of 2-phenylthiophene.\(^3\)
Research groups in France\textsuperscript{4} and Japan\textsuperscript{5} further extended the study to phenylisothiazoles and phenylthiazoles and proposed that the phototransposition of phenylisothiazoles and phenylthiazoles takes place by a mechanism, which involves tricyclic zwitterionic intermediates as shown in Scheme 2.

Scheme 1: Phototransposition of isothiazoles \textit{via} tricyclic zwitterionic intermediates

Scheme 2: Phototransposition of phenylisothiazoles and phenylthiazoles \textit{via} tricyclic zwitterionic intermediates
Pavlik and colleagues later found several ambiguities in those previous reports. Thus, a reinvestigation of the photochemistry of phenylisothiazoles and phenylthiazoles was carried out.\textsuperscript{6} Their studies revealed that the mechanism involving tricyclic zwitterionic intermediates did not correspond to some of their results. They reported that isothiazoles transposed by four different transposition patterns, which can be labeled as P\textsubscript{4}, P\textsubscript{5}, P\textsubscript{6} and P\textsubscript{7}, respectively leading to the isomeric thiazoles and isothiazoles.\textsuperscript{6}

Similarly, thiazoles were observed to transpose to isomeric isothiazoles and thiazoles by the P\textsubscript{5}, P\textsubscript{6} and P\textsubscript{7} transposition patterns.\textsuperscript{6}

Although the P\textsubscript{5}, P\textsubscript{6} and P\textsubscript{7} pathways involve the largest number of atom interchanges, the formation of all of these products were explained by the electrocyclic ring closure–heteroatom migration mechanism,\textsuperscript{6} as shown in Scheme 3.
Pavlik and colleagues suggested that sulfur migration in the initially formed 1-aza-5-thiabicyclopentane intermediate, $I_1$, occurred by successive 1,3-sigmatropic shifts of sulfur in both directions allowing sulfur to migrate around all four sides of the azetine ring. Thus, sulfur migration followed by rearomatization allows sulfur insertion into all four different sites in the carbon–nitrogen sequence resulting in the formation of the $P_5$, $P_6$ and $P_7$ phototransposition products.

Although the $P_4$ phototransposition involves the interchange of fewer ring atoms (i.e. $N_2$ and $C_3$) than the $P_5$, $P_6$ and $P_7$ pathways, it is mechanistically more complicated, involving both photocleavage and photo-ring contraction pathways. $^7$ 4-Substituted-isothiazoles react exclusively via these pathways while the photochemistry of 3- and 5-substituted-isothiazoles involve a competition between this pathway and the electrocyclic ring closure heteroatom migration mechanism. $^8$

According to Pavlik and Tongcharoensirikul, $^6$-$^8$ electrocyclic ring closure (the first step of the electrocyclic ring closure heteroatom migration pathway) is in competition with cleavage of the S–N bond in the isothiazole reactant. This cleavage results in the formation of a species $I_5$ (Scheme 4). It can be viewed as a $\beta$-thioformylvinyl nitrene.

**Scheme 3:** Electro cyclic ring closure heteroatom migration mechanism of thiazoles and isothiazoles
Vinyl nitrenes are known to rearrange to nitriles. Therefore, as expected, upon irradiation 4-substituted-isothiazoles undergo this photocleavage reaction to yield a substituted cyanothiol (23), which can be detected spectroscopically, trapped and characterized as their benzyl thioether derivatives (24).

Vinyl nitrenes are also known to be in equilibrium with their isomeric azirines. The β-thioformylvinyl nitrene, 15, formed from 4-substituted-isothiazoles (22), would be in equilibrium with the substituted thioformylazirines (25). In the presence of an external base such as triethylamine, ammonia or aqueous bicarbonate, Pavlik and Tongcharoensirikul suggested that the azirine (25) undergoes deprotonation by the added base resulting in the formation of an isocyanosulfide, 26.

The fate of isocyanide 26 depends on the natures of the substituent originally at C-4 of the isothiazole ring. If the substituent is aromatic (26; R = Ph), the extended conjugation of the sulfide and aryl group lowers the basicity of the sulfide, leaving the isocyanide carbon as the more basic site. The effect of protonation at this position to form 27 and to render the carbon more susceptible to nucleophilic attack by the negative sulfur. As the result, these substituted isocyanides cyclize spontaneously to 4-arylthiazoles (30; R = Ph) and cannot be detected or chemically trapped.

If the C-4 substituent is allyl or substituted allyl (26, R = PhCH2 or CH3), the reduced conjugation raises the energy of the sulfide so that sulfide is more basic. Thus, protonation at this position leads to 28, which reduces the nucleophilic character of the sulfur and leaves the negative charged isocyanide carbon less susceptible to nucleophilic attack. As a result, cyclization requires a higher energy of activation, and hence, the allyl-substituted isocyanothiols can be detected spectroscopically, trapped and characterized as their N–formylaminobenzyl thioether derivatives (29).
Scheme 4: Photocleavage of the S–N bond in 4-substituted isothiazoles
1.2 Photochemistry of 1,2,4-thiadiazoles

Although the photochemistry of thiazoles and isothiazoles has been extensively studied in this and other laboratories, no reports concerning the photochemistry of 1,2,4-thiadiazoles were available in the literature at the beginning of this research project. The photochemistry of 1,2,4-thiadiazoles is of interest because the ring system can be viewed as a combination of a thiazole and an isothiazole. Therefore, 1,2,4-thiadiazoles would be expected to undergo phototransposition reaction, via sulfur migration around four sides of the photochemically generated bicyclic intermediates, and photocleavage of the S-N bond similar to those of thiazoles and isothiazoles.

In order to extend the knowledge on photochemistry of five-membered ring heterocycles containing sulfur and nitrogen atoms, the goal of this research is to investigate the primary photochemical reaction of phenyl substituted-1,2,4-thiadiazoles.
2.1 Photochemistry of 5-phenyl-1,2,4-thiadiazole

2.1.1 Synthesis of 5-phenyl-1,2,4-thiadiazole

The 1,2,4-thiadiazole ring can be synthesized by the four following methods; (1) oxidative cyclization of an N-thioacyl amidine\(^9\) (method A), (2) cycloaddition of nitrile sulfides with a nitrile\(^9\) (method B), (3) oxidation of thioamides or thouraes\(^9\) (method C), (4) condensation of amidines with halogenated methylmercaptans\(^9\) (method D).

\[
\begin{align*}
\text{(A)} & & \text{(B)} & & \text{(C)} & & \text{(D)} \\
\text{N} & \text{C} & \text{N} & \text{C} & \text{N} & \text{C} & \text{N} & \text{C} & \text{N} & \text{C} & \text{S} & \text{N} \\
\text{C} & \text{S} & \text{C} & \text{N} & \text{C} & \text{S} & \text{C} & \text{N} & \text{C} & \text{S} & \text{C} & \text{N} \\
\end{align*}
\]

Scheme 5: Particular pathway for the synthesis of 1,2,4-thiadiazole ring system

These methods, however, do not allow the preparation of 5-monosubstituted-1,2,4-thiadiazoles. Therefore, 5-phenyl-1,2,4-thiadiazole (31) was synthesized by the method described by Yang-i Lin and colleagues.\(^9\) According to this approach, the amination cyclization of N-[(dimethylamino)methylene]thiobenzamide (32) with the aminating agent,
hydroxylamine-O-sulfonic acid (33), resulted in the formation of 31 as a colorless viscous liquid in 70% yield.

2.1.1.1 Synthesis of N-[(dimethylamino)methylene]thiobenzamide

According to the synthetic method for 1 described by Yang-i Lin and colleagues,\textsuperscript{9} N-[(dimethylamino)methylene]thiobenzamide (32) was required as the starting material. Therefore, 32 was synthesized in 87.5% by the condensation between thiobenzamide (34) and N,N-dimethylformamide dimethylacetal (35) as shown in Scheme 6.

\[ \text{Scheme 6: Synthesis of N-[(dimethylamino)methylene]thiobenzamide} \]

The orange crystalline product was identified by GC-MS, \textsuperscript{1}H- and \textsuperscript{13}C-NMR spectroscopy. The GC-trace of the sample, shown in Figure 1a, [140°C (5 min), 10°C/min to 240°C (50 min)] indicated the presence of some impurities. The mass spectrum of the major peak, which eluted with a retention time of 33.9 min (Figure 1b), exhibits the molecular ion at m/z 192 corresponding to the molecular weight of 32 (MW 192). It also
Results and Discussion

shows a base peak at m/z 44 due to the \([\text{CH}_3]_2\text{N}^+\) fragment, which is consistent with the structure of this compound, \textit{32}.

\[ \text{Figure 1a: GC-trace of the synthesized N-[(dimethylamino)methylene]thiobenzamide} \]

\[ \text{Figure 1b: Mass spectrum of the peak at retention time 33.9 min} \]
The $^1$H-NMR spectrum of this amidine 32, as shown in Figure 2, exhibits a singlet (1H) at $\delta$ 8.73 due to the imine proton. The two non-equivalent methyl groups are shown as two singlets (3H) at $\delta$ 3.24 and 3.25. The phenyl ring protons appear as two multiplets at $\delta$ 7.32-7.36 (3H) and 8.39-8.41 (2H) due to the meta-, para- and ortho-ring protons, respectively.

Figure 2: $^1$H–NMR spectrum of the synthesized N-[(dimethylamino)methylene]thiobenzamide
The $^{13}$C–NMR spectrum, shown in Figure 3, exhibits signals due to the two non-equivalent methyl carbons at $\delta$ 36.81 and 42.37. The four singlets at $\delta$ 128.12, 129.27, 132.33 and 143.47 were assigned to phenyl ring carbons. The imine carbon absorbs at $\delta$ 159.49. The thiocarbonyl carbon appears downfield at $\delta$ 216.66.

Figure 3: $^{13}$C–NMR spectrum of the synthesized N-[(dimethylamino)methylene]thiobenzamide
In order to confirm the $^1$H- and $^{13}$C-NMR spectral assignments, the two dimensional $^1$H-$^{13}$C correlation spectrum was recorded. The spectrum, shown in Figure 4, reveals that the two carbon signals at $\delta$ 36.8 and 42.4, that were assigned to the non-equivalent methyl carbons, correlate with the two singlets at $\delta$ 3.24 and 3.25 in the $^1$H-spectrum, that were assigned to the protons of the two non-equivalent methyl groups. In addition, the signal in the $^{13}$C-spectrum at $\delta$ 159.5, assigned to the imine carbon, correlates with the downfield singlet in the $^1$H–spectrum at $\delta$ 8.74, assigned to the imine proton. The signal at $\delta$ 143.47 in the $^{13}$C-spectrum, which was assigned to one of the phenyl ring carbons, is not present in the two dimensional spectrum. This shows that this signal is due to the quaternary carbon of the phenyl ring at position 1. As expected, the three additional signals in the $^{13}$C-spectrum due to the phenyl ring carbons still appear in the two dimensional spectrum. The signals in the $^{13}$C–spectrum at $\delta$ 128.1 and 132.3 can be assigned to the meta- and para-carbons of the phenyl ring, respectively, since they correlate with the multiplet (3H) at $\delta$ 7.32-7.36 in the $^1$H–spectrum assigned to the meta- and para-protons. Finally, the last signal at $\delta$ 129.3 in the $^{13}$C–spectrum can be assigned to the ortho carbons of the phenyl ring since this signal correlates with the multiplet (2H) at $\delta$ 8.39–8.41 in the $^1$H–spectrum assigned to the ortho protons.
**Figure 4:** Two dimensional $^1$H-$^{13}$C correlation spectrum of the N-[(dimethylamino)methylene]thiobenzamide
2.1.1.2 Synthesis of 5-phenyl-1,2,4-thiadiazole

The amination cyclization of N-[(dimethylamino)methylene]thiobenzamide (32) using hydroxylamine-O-sulfonic acid (33) and pyridine as basic catalyst led to the formation of 5-phenyl-1,2,4-thiadiazole (31) as shown in Scheme 7.

Scheme 7: Mechanism for the formation 5-phenyl-1,2,4-thiadiazole

5-Phenyl-1,2,4-thiadiazole (31) was obtained as a light yellow viscous liquid and characterized by GC-MS, $^1$H- and $^{13}$C-NMR spectroscopy.
According to the synthetic method described by Yang-i Lin,\textsuperscript{9} \textit{31} was reported as a colorless liquid. But in this synthesis, \textit{31} was obtained as a light yellow viscous liquid. Therefore, there might be an impurity in this product.

The GC-trace (Figure 5a) indicates the presence of an impurity which eluted at a retention time of 6.6 min. Its mass spectrum (Figure 5b) exhibits a molecular ion at m/z 146 and a base peak at m/z 103. The major gc-volatile component eluted with a retention time of 10.9 min. The mass spectrum (Figure 5c) of this compound exhibits a molecular ion at m/z 162, corresponding to the molecular weight of \textit{31} (MW 162). Moreover, the spectrum exhibits a base peak at m/z 135 and an intense peak at m/z 104 which indicates that \textit{31} undergoes fragmentation in the mass spectrometer to yield [C\textsubscript{6}H\textsubscript{7}CNS]\textsuperscript{+} and [C\textsubscript{6}H\textsubscript{7}CNH]\textsuperscript{+} fragments, respectively.

\textbf{Figure 5a:} GC-trace of the synthesized 5-phenyl-1,2,4-thiadiazole
Results and Discussion

Figure 5b: Mass spectrum of the peak at retention time 6.6 min

Figure 5c: Mass spectrum of the peak at retention time 10.9 min
Interestingly, based on the reported fragmentation pathways of phenyl-1,2,4-thiadiazoles\textsuperscript{10} (shown in Scheme 8), the cleavage of $[C_6H_5CN]^+$ was expected to be one of the major fragments. But according to the mass spectrum, shown in Figure 5c, the peak at m/z 104 is much more intense than the peak at m/z 103.

Scheme 8: Major fragmentation pathways of 1,2,4-thiadiazoles

However, the mass spectrum of 3-amino-5-phenyl-1,2,4-thiadiazole was also reported to reveal a peak at m/z 104 as one of intense peaks.\textsuperscript{10} This was suggested to be due to the cleavage of $[C_6H_5CNH]^+$ fragment with a proton from the amino group at position 3 on the thiadiazole ring, as shown in Scheme 9.

Consequently, based on these suggestions, the intense peak at m/z 104 is due to the $[C_6H_5CNH]^+$ fragment and the base peak at m/z 135 is due to the $[C_6H_5CNS]^+$ fragment which can also be expected as a major fragmentation pathway for 5-phenyl-1,2,4-thiadiazole (31) ($R_1 = \text{Ph}$, $R_2 = \text{H}$), as shown in Scheme 9,
Results and Discussion

The $^1$H–NMR spectrum (Figure 6) also shows the presence of an impurity that was also observed by GC-MS. The spectrum shows a singlet at $\delta$ 8.53 due to the proton at position 3 of the thiadiazole ring and 3H and 2H multiplets at $\delta$ 7.32-7.38 and $\delta$ 7.80-7.82 due to the meta-, para-protons and the ortho-protons of the phenyl ring, respectively. In addition, the spectrum also exhibits a singlet of low intensity at $\delta$ 8.31 and a multiplet of low intensity in the phenyl region, which must be due to the observed impurity in the sample.

Based on the observed molecular ion at m/z 146 and the $^1$H–NMR spectrum, this impurity was suspected to be 5-phenyl-1,2,4-oxadiazole (37). In order to investigate this possibility, 37 was synthesized by the same procedure that was used to synthesized 1 except that benzamide (38) was used as the starting material instead of thiobenzamide (34).
Figure 6: $^1$H-NMR spectrum of the synthesized 5-phenyl-1,2,4-thiadiazole
2.1.2 Synthesis of the photoproducts: 2-phenyl-1,3,5-triazine and 2,4-diphenyl-1,3,5-triazine

It has been reported that 1,3,5–triazines can be prepared via cyclotrimerization of nitriles\[^{11}\] where the R group can be hydrogen, alkyl, aryl, halogen or other substituent groups. This method is not effective, however, when the substituents are different.

\[
\begin{align*}
3RCN & \rightarrow \\
\text{R} & \text{N} & \text{N} & \text{R} \\
\text{R} & \text{N} & \text{N} & \text{R} \\
\text{R} & \text{N} & \text{N} & \text{R}
\end{align*}
\]

F.C Schaefer and I. Hechenbleiner reported\[^{11}\] the synthesis of sym-triazines with different substituent groups by trimerization and co-trimerization of amidines. According to their report, 2-phenyl- and 2,4-diphenyl-1,3,5-triazine (39) and (40) can be prepared in 20% and 50 %, respectively, by the co-trimerization of formamidine hydrochloride (41) and benzamidine hydrochloride (42), shown in Scheme 10.

\[
\begin{align*}
\text{H} & \text{N} & \text{H} & \text{C} & \text{Cl} & \text{H} & \text{N} & \text{H} & \text{C} & \text{Cl} \\
\text{H} & \text{N} & \text{H} & \text{N} & \text{H} & \text{C} & \text{Cl} & \text{H} & \text{N} & \text{H} & \text{N} & \text{H} & \text{C} & \text{Cl} \\
\text{Ph} & \text{NH}_2 & \text{Ph} & \text{NH}_2 & \rightarrow & 250^\circ \text{C} & \text{Ph} & \text{N} & \text{N} & \text{H} & \text{Ph} & \text{N} & \text{N} & \text{H} & \text{Ph} & \text{C} & \equiv & \text{N} \\
\text{Ph} & \text{N} & \text{N} & \text{H} & \text{Ph} & \text{N} & \text{N} & \text{H} & \text{Ph} & \text{N} & \text{N} & \text{H} & \text{Ph} & \text{C} & \equiv & \text{N} \\
\end{align*}
\]

\textbf{Scheme 10:} Synthesis of 2-phenyl- and 2,4-diphenyl-1,3,5-triazine
Results and Discussion

By employing their procedure, both triazines 39 and 40 were obtained as a mixture and separated by steam distillation. Both isolated triazines (39) and (40) were obtained as white solids which were different in their melting points (white solid A; mp 62-64 °C and white solid B; mp 80-82°C).

The GC-analysis of the white solid A [isothermal 170 °C (30 min)] (Figure 7a) shows only one component, which eluted with a retention time of 8.5 min. The mass spectrum of this peak (Figure 7b) exhibits a molecular ion at m/z 157 corresponding to the molecular weight of 2-phenyl-1,3,5-triazine (39; MW 157) which was additionally supported by a base peak at m/z 104 due to the [C₆H₃CNH]⁺ fragment, which could be expected as the major fragmentation pathway of 39 rather than the cleavage of benzonitrile fragment (m/z 103).

Figure 7a: GC-trace of the white solid A
Results and Discussion

The GC-trace of the white solid B [isothermal 240°C (30 min)] (Figure 8a) also shows only one gc-volatile component which eluted with a retention time of 16.2 min. As expected, the mass spectrum of this peak exhibits (Figure 8b) a molecular ion at m/z 233, which is consistent with the molecular weight of 2,4-diphenyl-1,3,5-triazine (40; MW 233). In this case the base peak that is observed at m/z 103 instead of m/z 104, which was observed in the mass spectrum of 2-phenyl-1,3,5-triazine (39). This base peak at m/z 103 is probably due to the cleavage of [C₆H₅CN]⁺ fragment.

Figure 7b: Mass spectrum of the white solid A

Figure 8a: GC-trace of the white solid B
The $^1$H–NMR spectrum of the white solid A, shown in Figure 9, exhibits a downfield singlet (2H) at $\delta$ 9.14 and two multiplets at $\delta$ 7.43-7.54 (3H) and $\delta$ 8.43-8.45 (2H). In the case of the white solid B, the $^1$H–NMR spectrum exhibits a singlet (1H) at $\delta$ 9.28 and two multiplets at $\delta$ 7.56-7.63 (6H) and $\delta$ 8.66-8.68 (4H). The $^1$H–NMR spectrum of white solid A is consistent with the assignment as 2-phenyl-1,3,5-triazine (39), in which, the two equivalent triazine ring protons appear downfield as a singlet (2H) and the phenyl ring protons appear as two multiplet (2H due to meta protons and 3H due to ortho-para protons). Also the $^1$H–NMR spectrum of the white solid B, shown in Figure 10, is consistent with the assignment as 2,4-diphenyl-1,3,5-triazine (40), in which the triazine ring proton absorbs at $\delta$ 9.28 as a singlet (1H) and the two multiplet at $\delta$ 7.56-7.63 (6H) and $\delta$ 8.66-8.68 (4H) were assigned to the two sets of equivalent phenyl ring protons of 2,4-diphenyl-1,3,5-triazine (40).
Consequently, according to the above mass spectra and $^1$H–NMR spectra, the white solid A can be identified as 2-phenyl-1,3,5-triazine (39) and the white solid B can be identified as 2,4-diphenyl-1,3,5-triazine (40).

Figure 9: $^1$H–NMR spectrum of the white solid A

Figure 10: $^1$H–NMR spectrum of the white solid B
2.1.3 Photochemistry of 5-phenyl-1,2,4-thiadiazole

5-Phenyl-1,2,4-thiadiazole (31) can be viewed as a combination between 5-phenylthiazole (44) and 5-phenylisothiazole (9). 5-Phenylthiazole (44) and 5-phenylisothiazole (9) have been reported to undergo the phototransposition reactions, shown in Scheme 11. Therefore, the photochemistry of 31 might be expected to exhibit the same type of photochemistry.

\[
\begin{align*}
\text{Ph} & \quad \text{N} \\
\text{S} & \quad \text{N} \\
\text{44} & \quad \text{hv} \\
\end{align*}
\]

\[
\begin{align*}
\text{Ph} & \quad \text{N} \\
\text{S} & \quad \text{N} \\
\text{45} & \\
\end{align*}
\]

Scheme 11: Photochemistry of 5-phenylthiazole and 5-phenylisothiazole

The photolysis of 31 was first monitored by ultraviolet absorption spectroscopy. Solutions of 31 (5×10⁻⁵ M) in acetonitrile and cyclohexane were prepared. The solutions were irradiated with three > 290 nm lamps and monitored by ultraviolet absorption spectroscopy at 60 seconds intervals. Figure 11a and 12a show the UV–absorption spectra of 31 in acetonitrile and cyclohexane, respectively. The λ_max is shown at the same wavelength of 273.2 nm in both solvents with an extinction coefficient of 13,880 L mol⁻¹ cm⁻¹ in cyclohexane and 13,873 L mol⁻¹ cm⁻¹ in acetonitrile.
Figure 11a: UV–absorption spectrum of 31 in acetonitrile

Figure 12a: UV–absorption spectrum of 31 in cyclohexane
The UV overlay spectrum of the photolysis in acetonitrile (Figure 11b) exhibits the decreasing in the absorption band at the $\lambda_{\text{max}}$ 273.2 nm from 0.76 to 0.68 after 240 sec. After 1,560 sec of irradiation, the UV-absorption overlay spectrum (Figure 11b) reveals the absorption band at the $\lambda_{\text{max}}$ 273.2 nm shifted to $\lambda_{\text{max}}$ 260.2 nm. The spectrum also reveals the increasing in the absorption band at $\lambda$ 230 nm.

The UV overlay spectrum of the photolysis in cyclohexane exhibits (Figure 12b) the same spectral pattern. But the absorption band at $\lambda_{\text{max}}$ 264.4 nm was being formed slower than the absorption band observed from the photolysis in acetonitrile. Also the absorption band at $\lambda$ 230 nm is increasing more slowly than during the photolysis in acetonitrile.
Results and Discussion

Figure 11b: UV-overlay spectrum of the photolysis of 31 in acetonitrile

Figure 12b: UV-overlay spectrum of the photolysis in cyclohexane
The photochemical reaction of 31 was also monitored by gas chromatography. A solution of 31 in acetonitrile (2.0×10^{-2} M; 17 mL) was placed in a Pyrex tube (20 cm × 0.7 cm). The GLC analysis of this solution [140 (4 min), 20°C/min to 180°C (14 min), 20°C/min to 240 (30 min)] shows (Figure 13a) one major peak with a retention time of 12 min and a small peak with a retention time of 8 min due to the presence of an impurity. The tube was sealed with a rubber septum, purged with argon for 15 min, and irradiated with sixteen > 290 nm lamps for 210 min. The GLC analysis of the resulting solution (Figure 13b) shows the consumption of 33.4% of the reactant and the appearance of six new peaks with retention times of 4, 11, 18, 39 and 40 min.
Figure 13a: GC-trace of solution of 31 before irradiation

Figure 13b: GC-trace of the solution of 31 after 210 min of irradiation
The reaction solution was concentrated by rotary evaporation at room temperature and analyzed by the GC interfaced with a mass spectrometer.

The GC-trace, shown in Figure 14a, [140 (5 min), 20°C/min to 200°C (20 min), 10°C/min to 240 (20 min)] exhibits seven gc-volatile components with retention times of 4, 7.5, 10, 10.6, 12.1, 23.3 and 40 min.

Figure 14a: GC-trace of the concentrated photolysate of 31 after 210 min of irradiation time

![Figure 14a: GC-trace of the concentrated photolysate of 31 after 210 min of irradiation time](image)

Figure 14b: Mass spectrum of the photoproduct eluted at retention time 4 min

![Figure 14b: Mass spectrum of the photoproduct eluted at retention time 4 min](image)
The mass spectrum of the first peak with a retention time of 4 min (Figure 14b) shows a base molecular ion peak at m/z 103. This product was assumed to be benzonitrile (43).

In order to prove this assumption, an authentic sample of 43 was analyzed by the GC interfaced with a mass spectrometer under the same temperature program (Figure 15a-b). Figure 15a shows that 43 was eluted with the same retention time as the first eluted photoproduct. Furthermore, Figure 15b shows that the fragmentation pattern and molecular ion from both the photoproduct and authentic benzonitrile (43) are also identical. Therefore, based on these chromatographic and mass spectroscopic results, the first eluted photoproduct was identified as benzonitrile (43), a photofragmentation product.

Figure 15a: GC-trace of an authentic sample of 50
The peak at retention time of 7.5 min was identified as 5-phenyl-1,2,4-oxadiazole (37) which was formed as a minor product during the synthesis of 31 (as discussed in the synthesis of section). The GLC analysis showed no significant decrease in the peak area of this compound after irradiation. Therefore, none of the observed photoproducts could result from a reaction of this compound.

The mass spectrum of the product that eluted with a retention time of 10.0 min (Figure 14c) exhibits a molecular ion at m/z 157, consistent with the molecular formula of C₉H₇N₃, and a base peak at m/z 104, consistent with the elimination of [C₆H₅CNH]⁺ as the major fragment. This photoproduct was suggested to be 2-phenyl-1,3,5-triazine (39), a unique ring expansion product. This was confirmed by a direct comparison with the retention time and mass spectrum of an authentic sample of 39, shown in Figure 16a-b.
Results and Discussion

Figure 14c: Mass spectrum of the product eluted at a retention time of 10.0 min; expected to be 39

Figure 16a: GC-trace of an authentic sample of 39
The peak with a retention time of 10.6 min is the starting material since it has a retention time and a mass spectrum (Figure 4d) identical to the reactant, 31.

Figure 14d: Mass spectrum of the component at a retention time of 10.6 min; the reactant
The mass spectrum of the next photoproduct, which eluted with a retention time of 12.1 min, also exhibits a molecular ion at m/z 162 (Figure 14e) which is also consistent with the molecular formula of C₈H₆N₂S, identical to the formula of the reactant, 31. Comparison of these mass spectra clearly shows, however, that although the mass spectrum of the photoproduct is different than the mass spectrum of 31, Figure 14d, it is identical to the mass spectrum of 3-phenyl-1,2,4-thiadiazole (46), shown in Figure 17. This photoproduct is thus the phototransposition product, 3-phenyl-1,2,4-thiadiazole (46).

Figure 14e: Mass spectrum of the peak eluted with a retention time of 12.1 min; expected to be 46
Figure 17: Mass spectrum of the synthesized 46

![Mass spectrum of the synthesized 46](image)

The mass spectrum of the peak that eluted with a retention time of 23.3 min (Figure 14f) exhibits a base molecular ion at m/z 172 and two medium intensity peaks at m/z 103 and 104. Due to the presence of these two peaks, the structure of this product is suggested to contain a system similar to 5-phenyl-1,2,4-thiadiazole (31) which can cleave to give two fragments; [C₆H₅CN]+ and [C₆H₅CNH]+, as discussed previously. However, the absolute structure of this product has not been identified.
Figure 14f: Mass spectrum of the peak eluted with a retention time of 23.3 min

The mass spectrum of the photoproduct that eluted with a retention time of 40 min (Figure 14g) exhibits a molecular ion at m/z 233, which is consistent with a molecular formula of C_{15}H_{11}N_{3}, and a base molecular peak at m/z 103, consistent with the formation of [C₆H₅CN]⁺ as the major fragment. Based on this information the photoproduct was suggested to be 2,4-diphenyl-1,3,5-triazine (40), a ring expansion product, This was confirmed by direct comparison of the retention time and the mass spectrum of an authentic sample of 40, shown in Figure 18a-b.
Results and Discussion

Figure 14g:  Mass spectrum of the peak eluted with a retention time 40 min; expected to be 40

Figure 18a: GC-trace of an authentic sample of 40
Figure 18b: Mass spectrum of an authentic sample of 40

Beside the four major photoproducts shown in Figure 14a, the trace also shows three minor peaks which eluted with retention times of 40.6, 42.7 and 48.9 min. Their mass spectra, shown in Figure 14h, i, j, exhibit molecular ions at m/z 187, 238, 205, respectively. These peaks could be due to some impurities in the solvent. However, their mass spectra exhibit peaks at m/z 77, 103 and 104 which could be due to the cleavage of [C₆H₅]⁺, [C₆H₅CN]^{2⁺} and [C₆H₅CNH]⁺ fragments as previously discussed. Especially, the mass spectra of the peaks that eluted with retention times of 42.7 and 48.9 min also exhibit a peak at m/z 135 as a base peak. This peak has been previously assigned due to [C₆H₅CNS]^{2⁺} fragment. Therefore, these three minor peaks can also be expected as photoproducts formed upon irradiation of 5-phenyl-1,2,4-thiadiazole (31) (in acetonitrile).
Results and Discussion

Figure 14h: Mass spectrum of the peak eluted with a retention time of 40.6 min

Figure 14i: Mass spectrum of the peak at a retention time of 42.7 min
Figure 14j: Mass spectrum of the peak eluted with a retention time of 48.9 min

The mass spectrum of the peak eluted with a retention time of 42.7 min (Figure 4i) exhibits a molecular ion at m/z 238 which corresponds to the molecular weight of diphenyl-1,2,4-thiadiazole (47; MW 238). By direct comparison between the GC-retention time and fragmentation pattern of this product and the GC-retention time and fragmentation pattern of an authentic sample of 47 (shown in Figure 19a-b), this photoproduct was identified as diphenyl-1,2,4-thiadiazole (47).
Figure 19a: GC-trace of an authentic sample of 47

Figure 19b: Mass spectrum of an authentic sample of 47
These results conclusively show that irradiation of 5-phenyl-1,2,4-thiadiazole (31) in acetonitrile solvent at > 290 nm leads to the formation of eight gc-volatile products. Five of these products have been identified as benzonitrile (43; photofragmentation product), 2-phenyl- and 2,4-diphenyl-1,3,5-triazine [(39) and (40); photo ring expansion products], 3-phenyl-1,2,4-thiadiazole (46; phototransposition product) and diphenyl-1,2,4-thiadiazole (47). The three minor photoproducts have not been identified.

In order to determine the chemical yield of these photoproducts, a solution (4 mL, 2×10⁻² M) of 31 in acetonitrile was irradiated with sixteen > 290 nm lamps and monitored by gas–liquid chromatography every 30 min for a total of 150 min. The GC- calibration curves for the four identified photoproducts were constructed by plotting concentration Vs peak area. Scheme 12 shows the photoreaction of 5-phenyl-1,2,4-thiadiazole (31).

**Scheme 12:** Photoreaction of 5-phenyl-1,2,4-thiadiazole
3-Phenyl-1,2,4-thiadiazole (46), the phototransposition product was found to be formed in 10% yield. Benzonitrile (43), the photofragmentation product, was formed in 22.4% yield. The two unique ring expansion photoproducts, 2-phenyl- and 2,4-diphenyl-1,3,5-triazine (39) and (40), were formed in 3% and 1% yield, respectively. The GC-trace obtained from the GC-HP588 interfaced with a mass spectrometer of the concentrated reaction solution revealed the presence of trace amount of three unidentified photoproducts which were not observed in the GC-analysis on GC-PE9000 of the reaction mixture before concentration.
2.2 Photochemistry of 3-phenyl-1,2,4-thiadiazole

2.2.1 Synthesis of 3-phenyl-1,2,4-thiadiazole

The 1,2,4-thiadiazoles can be prepared from a 1,3-dipolar cycloaddition reaction of a nitrile sulfide with a nitrile as described by Howe and Franz.\(^\text{12}\)

In the case of 3-phenyl-1,2,4-thiadiazole (46), a cycloaddition of benzonitrile sulfide (48) with ethyl cyanoformate (49) led to the formation of ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate (50). Base catalyzed ester hydrolysis of 50 followed by decarboxylation of the resulting carboxylic acid produced 46 in 72% as a white solid.

2.2.1.1 Synthesis of 5-phenyl-1,3,4-oxathiazole-2-one

According to the method described by Howe and Franz\(^\text{12}\), 46 could be synthesized by cycloaddition of benzonitrile sulfide (48), which can be in situ generated by decarboxylation of 5-phenyl-1,3,4-oxathiazole-2-one (51). 5-Phenyl-1,3,4-oxathiazole-2-one (51) was prepared by a coupling between chlorocarboxsulfenyl chloride (52) and benzamide (38) in refluxing chloroform under anhydrous condition, described by Howe and Franz\(^\text{12}\) to yield the desired oxathiazole in 95.5% yield as white crystals. Scheme 14 shows the synthesis of 51.

![Scheme 14: Synthesis of 5-phenyl-1,3,4-oxathiazole-2-one](image)
The GC analysis of the white crystals (Figure 20) exhibited two components eluted with a retention time of 4.1 min and 17.2 min. The mass spectrum of the major peak at retention time 17.2 min (Figure 20b) exhibits a molecular ion at m/z 179 which is consistent with the molecular formula of $C_8H_5NO_2S$ and a base peak at m/z 105 which is also consistent with $[C_6H_3CNS]^{+}$ fragment which is due to the loss of CO$_2$.

**Figure 20a:** GC-trace of the white crystals
The $^1$H-NMR spectrum of this compound (Figure 21) exhibits two multiplets: δ 7.45-7.54 (2H), which is assigned to the ortho phenyl-ring protons, and δ 7.93-7.95 (3H), which is assigned to the meta-para phenyl-ring protons.

![1H-NMR spectrum of the white crystals](image)

**Figure 21:** $^1$H-NMR spectrum of the white crystals

The $^{13}$C-NMR spectrum (Figure 22a) exhibits the carbon signals corresponding to the structure of 5-phenyl-1,3,4-oxathiazole-2-one (51). The carbonyl carbon on the oxathiazole ring absorbs downfield at δ 174.3. The carbon at position 5 of the oxathiazole ring appears at δ 157.8. The phenyl ring carbons appear as four singlets at δ 126.2, 127.8, 129.4 and 133.1. These assignments are consistent with the $^{13}$C–DEPT 135 spectrum (Figure 22b). The two signals at δ 157.8 and 174.3 disappeared in the $^{13}$C–DEPT 135 spectrum, which were consistent with the assignment of the two signals to the two quaternary carbons on the oxathiazole ring.
Results and Discussion

Figure 22a: $^{13}$C-NMR spectrum of the white crystals

Figure 22b: $^{13}$C-DEPT 135 spectrum of the white crystals
2.2.1.2 Synthesis of ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate

Decarboxylation of 51 has been reported to result in in situ generation of benzonitrile sulfide (48). Thus, ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate (50) was prepared in 80% as light brown crystals by trapping of 48, formed upon decarboxylation of 51, with ethyl cyanoformate (49) as shown in Scheme 15.

Scheme 15: Synthesis of ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate

The GC-trace [isothermal 220°C (30 min)] of the cycloaddition product shows only one gc-volatile component, which eluted with a retention time of 12.4 min (shown in Figure 23a). The mass spectrum (Figure 23b) of this compound exhibits a molecular ion at m/z 234 which corresponds to the molecular weight of ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate (50) (MW 234). The spectrum also shows a base peak at m/z 135 due to the \([C_{6}H_{5}CNS]^+\) fragment.

Figure 23a: GC-trace of the synthesized 15
The $^1$H–NMR spectrum of this synthesized 15 (Figure 24) exhibits the phenyl ring protons as two multiplets at $\delta$ 7.43-7.44 (3H) and $\delta$ 8.28-8.29 (2H) due to the meta-para and ortho ring protons, respectively. The ethyl ester protons are shown at $\delta$ 4.51 as a quartet (2H; $J = 7.07$ Hz) and at $\delta$ 1.41 as a triplet (3H; $J = 7.07$ Hz).
The $^{13}$C–NMR spectrum (shown in Figure 25a) exhibits the two carbons of the ethyl ester group at $\delta$ 14.6 (CH$_3$-) and 63.8 (-CH$_2$-). The ring phenyl carbons appear as four singlets at $\delta$ 128.9, 129.2, 131.3 and 132.4. The signal at $\delta$ 179.4 is assigned to the ester carbonyl carbon. The two carbons of the thiadiazole ring appear at $\delta$ 158.9 for the carbon at position 3 and at $\delta$ 175.1 for the carbon at ring position 5. These assignments can be supported by the $^{13}$C–DEPT 135 spectrum, shown in Figure 25b. The signals at $\delta$ 14.6 and 63.8 absorb in positive and negative directions in the $^{13}$C–DEPT 135 spectrum, respectively, which is consistent with their assignments as methyl and methylene carbons, respectively. Three signals at $\delta$ 158.9, 175.1 and 179.4 disappeared in the $^{13}$C–DEPT 135 spectrum confirming that they are all quaternary carbons.
Results and Discussion

Figure 25a: $^{13}$C – NMR spectrum of the synthesized 50

Figure 25b: $^{13}$C – DEPT 135 spectrum of the synthesized 50
2.2.1.3 Synthesis of 3-phenyl-1,2,4-thiadiazole

Base catalyzed ester hydrolysis of 50 led to the formation of 3-phenyl-1,2,4-thiadiazole-5-carboxylic acid (53). Decarboxylation of 53 produced 3-phenyl-1,2,4-thiadiazole (46) as a white solid in 72% yield as shown in Scheme 16.

![Scheme 16: Synthesis of 3-phenyl-1,2,4-thiadiazole](image)

The GC-trace [150°C (5 min), 30°C/min to 180°C (17 min)], as shown in Figure 26a, shows that only one component eluted with a retention time of 13.2 min. The mass spectrum (Figure 26b) of this product exhibits a molecular ion at m/z 162 and the base peak at m/z 135, which corresponds to both its molecular weight (MW 162) and to the possible fragment \([\text{C}_6\text{H}_5\text{CNS}]^{+}\) as the base peak. The mass spectrum also corresponds with the reported molecular ion of this compound.12

![Figure 26a: GC-trace of the synthesized 46](image)
The $^1$H–NMR spectrum, as shown in Figure 27, exhibits a very clear spectrum. The proton of the thiadiazole ring at position 5 absorbs downfield at $\delta$ 10.27 as a singlet (1H). The phenyl ring protons appear as two multiplets at $\delta$ 7.49-7.55 (3H) assigned to the meta- and para-ring protons and $\delta$ 8.33-8.36 (2H) assigned to the ortho-ring protons.
The $^{13}$C–NMR spectrum, as shown in Figure 28a, shows that the two carbons of the thiadiazole ring absorb at $\delta$ 174.9 and 175.0. The former signal was assigned to the carbon at ring position 3, while the latter signal was assigned to the carbon at ring position 5. These assignments are consistent with the $^{13}$C–DEPT 135 spectrum (Figure 28b), which confirms that the signal at $\delta$ 174.9 is due to a quaternary carbon. The signal at $\delta$ 175.0 still appears in the $^{13}$C–DEPT 135 spectrum and that must be due to the carbon at ring position 5 of the thiadiazole ring.
Results and Discussion

Figure 28a: $^{13}$C–NMR spectrum of the synthesized 46

Figure 28b: $^{13}$C–DEPT 135 spectrum of the synthesized 46
2.2.2 Photochemistry of 3-phenyl-1,2,4-thiadiazole

This study has shown that 5-phenyl-1,2,4-thiadiazole (31) undergoes phototransposition to 3-phenyl-1,2,4-thiadiazole (46) in 10% yield and to the formation of other photofragmentation and photo ring-expansion products. In order to determine the effect of changing the position of the phenyl substituent from position 5 to 3, the photochemistry of 46 has also been studied.

\[
\begin{align*}
\text{N} & \quad \text{S} \\
\text{H} & \quad \text{Ph} \\
\text{N} & \quad \text{S} \\
\text{H} & \quad \text{Ph}
\end{align*}
\]

The photolysis of 46 was first monitored by ultraviolet–absorption spectroscopy. A solution of 46 (5.0×10⁻⁵ M) in cyclohexane was placed in a quartz cell and irradiated with three > 290 nm lamps through a Pyrex filter. The solution was monitored by ultraviolet absorption spectroscopy at 40 sec intervals.

Figure 29a shows the UV–absorption spectrum of 46 in cyclohexane before irradiation. The UV overlay spectrum (Figure 29b) shows the continuous consumption of the reactant, as indicated by the decrease in the optical density of the absorption band at λ 263.60 nm from 0.51 to 0.34 after 280 sec of irradiation and also shows an increase in the optical density at λ_{max} 229.8 nm. This new absorption maximum suggests the formation of benzonitrile (43) in this reaction since 43 is known to absorb at λ_{max} 224 nm in acetonitrile.
Figure 29a: UV–absorption spectrum of 46 in cyclohexane

Figure 29b: UV overlay spectrum of the photolysis of 46
The photoreaction of 46 was also monitored by gas–liquid chromatography. A solution of 46 (2.0×10^{-2} M) in acetonitrile was placed in a Pyrex tube, sealed with a rubber septum and purged with argon gas for 15 min. GLC analysis [140°C (4 min), 15 min/°C to 180°C (14 min)] of this solution (Figure 30a) indicated the presence of only one component in the sample, which eluted with a retention time of 18 min. The solution was irradiated with sixteen > 290 nm lamps and monitored by gas–liquid chromatography every 15 min. Figure 30b shows the GC-chromatogram of the reaction after 120 min of irradiation. The chromatogram exhibits two volatile components in this sample. One component which eluted with a retention time of 18 min, is the reactant 46. The second component, which eluted with a retention time of 4 min is the only photoproduct observed upon irradiation of 46. The GLC analysis was carried out at a higher oven temperature but no sign of any other photoproduc was observed.
The reaction solution after 120 min of irradiation was concentrated by rotary evaporation at room temperature and analyzed by the GC interfaced with a mass spectrometer. The GC trace (Figure 31a) again exhibits two components in the sample. The mass spectrum of the compound, which eluted with a retention time of 17.7 min (Figure 31b), reveals a molecular ion at m/z 162 and a fragmentation pattern identical to the mass spectrum of the reactant, 46. Therefore, this peak is due to the reactant 46. The mass
spectrum of the peak, which eluted with a retention time of 7.5 min (Figure 31c), reveals a molecular ion at m/z 103.

Figure 31a: GC-trace of the concentrated photolysate of 46 after 120 min of irradiation

Figure 31b: Mass spectrum of the peak at a retention time of 14.3 min, the reactant 46
By direct comparison of the mass spectrum and GC-trace of this peak with the mass spectrum and GC-trace of an authentic sample of benzonitrile (43), it was determined that both fragmentation patterns and retention times are identical. This shows that the only photoproduct observed upon irradiation of 3-phenyl-1,2,4-thiadiazole (46) is benzonitrile (43). This result also indicates that 5-phenyl-1,2,4-thiadiazole (31) is not formed as a phototransposition product as expected.
Unlike the GLC analysis of the solution before concentration, Figure 31 also reveals trace quantity of a gc-volatile material which eluted at high oven temperature with a retention time of 34.5 min. The mass spectrum of this component (Figure 31d) exhibits a molecular ion at m/z 238 and a base peak at m/z 135. Comparison of its mass spectrometric and chromatographic properties with those of the available authentic samples of phenyl-1,2,4-thiadiazoles indicates that this trace quantity product is diphenyl-1,2,4-thiadiazole (47). The observed formation of 47 upon irradiation of 46 in acetonitrile was proposed to arise from a 1,3-dipolar cycloaddition of benzonitrile sulfide (48) with benzonitrile (43), the observed major product in this photoreaction.
The percent yield of 43 was determined by using the same benzonitrile calibration curve previously constructed. After 120 min of irradiation, the trace showed 81.6% consumption of the reactant 46 and the formation of benzonitrile (43) in 74.1% yield.
2.3 Photochemistry of 3-methyl-5-phenyl-1,2,4-thiadiazole

2.3.1 Synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole

5-Phenyl-1,2,4-thiadiazole (31) can be synthesized by the amination cyclization of N-[(dimethylamino)methylene]thiobenzamide (32) with hydroxylamine-O-sulfonic acid (33). This synthesis not only allows the synthesis of 5-monosubstituted-1,2,4-thiadiazole but it also allows the synthesis of 3,5-disubstituted-1,2,4-thiadiazoles.

Therefore, 3-methyl-5-phenyl-1,2,4-thiadiazole (54) was synthesized the amination cyclization of the corresponding amidine, N-[(dimethylamino)ethylidene]thiobenzamide (55). Scheme 17 shows the total synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole (54).

![Scheme 17: Synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole](image_url)
2.3.1.1 Synthesis of N-[(dimethylamino)ethylidine]thiobenzamide

N-[(dimethylamino)ethylidine]thiobenzamide (24) was prepared in 89.8% as an orange crystalline solid by the condensation between thiobenzamide (22) and N,N-dimethyacetamide dimethylacetal (27), as shown in Scheme 18.

Scheme 18: Synthesis of N-[(dimethylamino)ethylidine]thiobenzamide

The obtained orange crystals were characterized by $^1$H-, $^{13}$C-NMR and mass spectrometry.

The product from this reaction was analyzed by GC-MS [140°C (5 min), 20°C/min to 180°C (10 min), 20°C/min to 240°C (30 min)] (Figure 32a). The mass spectrum of the peak that eluted with a retention time of 23.9 minutes (Figure 32b) exhibited a molecular ion at m/z 206, which corresponds to the molecular weight of the desired product, 55. The trace also exhibits the presence of some impurities.
This orange crystalline solid, expected to be 55, is different from N-[(dimethylamino)methylene]thiobenzamide (32) since the substituent at the imine carbon in this case is methyl group instead of hydrogen. Therefore, as expected, the $^1$H-NMR spectrum of this orange solid (Figure 33) exhibits a 3H singlet at $\delta$ 2.45, which can be assigned to the methyl protons of the methyl group attached to the imine carbon. The two singlets (3H) at $\delta$ 3.20 and 3.22 are the absorptions due to the two non-equivalent methyls...
bonded to the amino group. The two multiplets at $\delta$ 7.31-7.41 (3H) and $\delta$ 8.22-8.28 (2H) were assigned to para-meta and ortho-phenyl ring protons, respectively.

**Figure 33**: $^1$H–NMR spectrum of N-[(dimethylamino)ethylidine]thiobenzamide

In the $^{13}$C–NMR spectrum (Figure 34a), the most down field signal at $\delta$ 202.8 is assigned to the thiocarbonyl carbon. The imine carbon absorbs at $\delta$ 168.3. The four signals at $\delta$ 128.0, 128.9, 131.3 and 142.7 were assigned to the phenyl ring carbons. The spectrum reveals the two non-equivalent methyl carbons of the amino group as two singlets at $\delta$ 39.5 and 39.7. Figure 34b shows the scale expansion revealing the two singlet signals. The methyl carbon attached to the imine carbon appears at $\delta$ 18.4.
Figure 34a: $^{13}$C–NMR spectrum of N-[(dimethylamino)ethylidene]thiobenzamide

Figure 34b: Scale expansion exhibits the two singlets at $\delta$ 39.5 and 39.7
The above $^{13}$C–spectral assignments are consistent with the $^1$H–$^{13}$C correlation spectrum (Figure 35). The carbon signal at $\delta$ 18.4, which was assigned to the methyl carbon attached to the imine carbon, correlates with the 3H singlet proton signal at $\delta$ 2.48, which was assigned to the protons of the methyl group attached to the imine carbon. The two singlet at $\delta$ 39.5 and 39.7, which were assigned to the two non–equivalent methyl carbons of the amino group, correlate with the two 3H singlet protons assigned to the two non-equivalent methyl protons of the amino group. Although, the GC-analysis of this sample exhibited the presence of some impurities, all NMR results are consistent with the structure of the desired product, N-[(dimethylamino)ethylidine]thiobenzamide (55).
Figure 35: $^{1}\text{H} - ^{13}\text{C}$ correlation spectrum of N-[(dimethylamino)ethylidine]thiobenzamide
2.3.1.2 Synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole

3-Methyl-5-phenyl-1,2,4-thiadiazole (54) can be synthesized by the same method as described by Yang-i Lin and colleagues\(^9\) for the synthesis of 5-phenyl-1,2,4-thiadiazoles. But in the case of 54, the amination cyclization will employ 55 as the starting material instead of 32, as shown in Scheme 19.

![Scheme 19: Synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole](image)

3-Methyl-5-phenyl-1,2,4-thiadiazole (54) was obtained in 75 % as white colorless crystals. This crystalline solid was characterized by \(^1\)H-, \(^{13}\)C-NMR and mass spectroscopy.
The GC-trace (isothermal 170°C) of these colorless crystals (Figure 36a) exhibits a major peak with a retention time of 15.6 min. The mass spectrum of this peak (Figure 36b) exhibits a molecular ion at m/z 176, which is consistent with the molecular weight of 54 (MW 176). The spectrum also exhibits a base peak at m/z 135 and a peak at m/z 73, which are consistent with the cleavage of $[C_6H_5CNS]^{+}$ and $[CH_3CNS]^{+}$, respectively.

Figure 36a: GC-trace of 3-methyl-5-phenyl-1,2,4-thiadiazole

Figure 36b: Mass spectrum of the peak eluted at a retention time of 15.6 min
Results and Discussion

The $^1$H–NMR spectrum (Figure 37) shows the methyl group as a 3H singlet at $\delta$ 2.70. The phenyl ring protons appear as two multiplets at $\delta$ 7.46-7.51 (3H) assigned to para-meta phenyl ring protons and $\delta$ 7.90-7.93 (2H) assigned to ortho phenyl ring protons.

Figure 37: $^1$H–NMR spectrum of 3-methyl-5-phenyl-1,2,4-thiadiazole

The $^{13}$C–NMR spectrum (Figure 38a) reveals the methyl carbon at $\delta$ 19.5. The two thiadiazole ring carbons at positions 3 and 5 absorb at $\delta$ 174.6 and 188.5, respectively. The four signals at $\delta$ 127.8, 129.7, 130.9 and 132.3 are assigned to the phenyl ring carbons. These spectral assignments were confirmed by the $^{13}$C–DEPT 135 spectrum, shown in Figure 38b. The signal at $\delta$ 19.5 still appears in the $^{13}$C–DEPT 135 spectrum, which is consistent with the assignment to the methyl carbon. The two signals at $\delta$ 174.6 and 188.5, which were assigned to the two carbons at positions 3 and 5 of the thiadiazole ring, are not
Results and Discussion

observed in the $^{13}$C–DEPT 135 spectrum since these signals are due to quaternary carbons. Three of the four singlets, which absorb in the phenyl region, still appear in the $^{13}$C–DEPT 135 spectrum. Thus, these signals can be assigned to the ortho-, meta- and para-phenyl ring carbons. The signal at $\delta$ 130.9 was however not observed in the $^{13}$C–DEPT 135 spectrum and, therefore, can be assigned to the phenyl carbon at the ring position 1.

Figure 38a: $^{13}$C–NMR spectrum of 3-methyl-5-phenyl-1,2,4-thiadiazole
2.3.2 Synthesis of 5-methyl-3-phenyl-1,2,4-thiadiazole

The synthesis of 5-methyl-3-phenyl-1,2,4-thiadiazole (57) has been reported by Goerdeler and Hammen\textsuperscript{16} involving a nucleophilic substitution of a malonate ester group at the ring position 5 of 5-chloro-3-phenyl-1,2,4-thiadiazole (58) followed by acid catalyzed hydrolysis of 59 and decarboxylation of 60 to give 57 in high yield. Scheme 20 shows the total synthetic route of 57. Thus, 57 was prepared by this method to give the desired thiadiazole as a white solid, however, in very low yield.
Results and Discussion

2.3.2.1 Synthesis of 5-chloro-3-phenyl-1,2,4-thiadiazole

According to the synthetic route shown in Scheme 20, 58 is required as a starting material. 5-Chloro-3-phenyl-1,2,4-thiadiazole (58) could be synthesized by a procedure described by Goerdeler and co-workers\textsuperscript{16} via a coupling between benzamidine (62) with perchloromethyl mercaptan (63) in the presence of a base leading to the formation of 58 as a white solid in 41 % yield. The white solid was characterized by $^1$H- and $^{13}$C-NMR and mass spectroscopy. Scheme 21 shows the synthesis of 58.
**Scheme 21:** Synthesis of 5-chloro-3-phenyl-1,2,4-thiadiazole

GC analysis of this white solid (Figure 39a) shows a single gc-volatile component that eluted with a retention time of 10.3 min. The mass spectrum (Figure 39b) of this compound exhibits a molecular ion at m/z 196 which is consistent with the molecular weight of 58 (MW 196.5). A base peak at m/z 135 corresponds to the cleavage of [ClCN] from the molecular ion. The cleavage that results in the formation of \([\text{C}_6\text{H}_5\text{CNS}]^{2+}\) is a characteristic fragmentation pathways of 5- and 3-phenyl-1,2,4-thiadiazoles as presented in other synthesis sections of this thesis. Furthermore, the presence of a chlorine atom in a molecule can be characterized by the presence of a P+2 peak, which is due to a fragment containing natural abundance of isotopic \(^{37.5}\text{Cl}\) atom. The intensity of the P+2 peak will appear as 1/3 less intense than of the molecular ion for the existence of one chlorine atom in the molecule.
The mass spectrum in Figure 39b reveals a P+2 peak at m/z 198 with an intensity approximately 1/3 less intense than of the peak at m/z 196. Thus, this confirms that this compound contains one chlorine atom in the molecule.

**Figure 39a:** GC analysis of 5-chloro-3-phenyl-1,2,4-thiadiazole

**Figure 39b:** Mass spectrum of 5-chloro-3-phenyl-1,2,4-thiadiazole
The $^1$H–NMR spectrum, as shown in Figure 40, exhibits a clear spectrum. The phenyl ring protons appear as two multiplets at $\delta$ 7.36-7.43 (3H) assigned to the meta and para ring protons and $\delta$ 8.15-8.22 (2H) assigned to the ortho ring protons.

![Figure 40: $^1$H-NMR spectrum of 5-chloro-3-phenyl-1,2,4-thiadiazole](image)

The $^{13}$C–NMR spectrum, as shown in Figure 41a, shows that the two carbon atoms of the thiadiazole ring absorb at $\delta$ 172.5 and 173.4. The former signal was assigned to the carbon at ring position 3, while the latter signal was assigned to the carbon at ring position 5. These assignments were based on the previous spectral assignments of 3-phenyl-1,2,4-thiadiazole (46). The signals at $\delta$ 128.4, 129.2, 131.3 and 132.2 were assigned to the phenyl ring carbons. The signal at $\delta$ 132.2 disappears in the $^{13}$C–DEPT 135 spectrum and that must be due to the carbon on phenyl ring at position 1. The signals at $\delta$ 128.4, 129.2 and 131.3 still remain in the $^{13}$C–DEPT 135 spectrum. Thus, this confirms
that these signals are due to absorption of phenyl ring carbons at position 2 and 6, 3 and 5, and 4, respectively.

**Figure 41a:** $^{13}$C-NMR spectrum of 5-chloro-3-phenyl-1,2,4-thiadiazole

**Figure 41b:** $^{13}$C-DEPT 135 spectrum of 5-chloro-3-phenyl-1,2,4-thiadiazole
2.3.2.2. Synthesis of diethyl 3-phenyl-1,2,4-thiadiazole-5-malonate

In this synthesis, a malonate ester anion was generated in situ by a reaction of sodium metal with the malonate ester (61) in toluene at room temperature. Addition of 58 to the solution of the malonate ester anion and subsequent refluxing in toluene for 8 hours gave the thiadiazole malonate ester (59) as light yellow crystals in 20% yield.

Scheme 22: Synthesis of diethyl 3-phenyl-1,2,4-thiadiazole-5-malonate

GC analysis of the yellow crystals (Figure 42a) shows a major component eluted at a retention time of 18.5 min. The mass spectrum of this component (Figure 42b) exhibits a molecular ion at m/z 240 which is not consistent with a molecular weight of the desired thiadiazole malonate ester 59 (MW 320). The spectrum, however, reveals a base peak at m/z 135 which is a characteristic fragmentation of 3-phenyl-1,2,4-thiadiazoles. Thus, this may indicate that 59 would undergo a reaction under the GC-MS analytical condition to give a product with a structure corresponding to the ester 64 (MW 248; Figure 42b). This GC-MS analysis result, however, is still unclear and, thus, structural determination of 59 cannot be confirmed by this GC-MS analysis.
Results and Discussion

Figure 42a: GC analysis of the yellow solid obtained in the synthesis of 59

Figure 42b: Mass spectrum of the component eluted at 18.5 min
Although, mass spectral analysis of the yellow crystals did not provide fragmentation information corresponding to the structure of 59, the $^1$H-NMR analysis shown in Figure 43 exhibits a clear spectrum consistent with the structure of 59. The spectrum reveals a broad singlet (1H) very downfield at $\delta$ 13.78. This broad downfield signal is a characteristic signal for a proton of a hydroxyl group. Thus, it indicates that the structure of this compound contains a hydroxyl group which corresponds to the structure of 59 in an enol form in CDCl$_3$ solution. A typical keto-enol equilibrium is fast and would not be observed on NMR time scale at room temperature. The $^1$H-NMR of this product clearly shows that the structure of this product in CDCl$_3$ would be dominated at only one form. If 59 is in an enol form in chloroform-d solution associated with a hydrogen bonding with a nitrogen on thiadiazole ring as shown, the protons on ethyl ester groups will become non-equivalent. The absorption in the region of $\delta$ 1.33-.140 were assigned to absorptions of two overlapping triplets at $\delta$ 1.355 (J = 7.07 Hz) and 1.375 (J = 7.07 Hz) due to the two non-equivalent methyl protons of the ethyl ester groups. This assignment corresponds to the signal integration of six protons. The absorption in the region of $\delta$ 4.25-4.35 were assigned to absorptions of two overlapping quartets at $\delta$ 4.30 (J = 7.07 Hz) and 4.315 (J = 7.07 Hz) due to the two non-equivalent methylene protons of the ethyl ester groups. This assignment corresponds to the signal integration of four protons. The two multiplets at $\delta$ 7.46-7.52 (3H) and $\delta$ 7.89-7.92 (2H) are due to absorptions of the phenyl ring protons. Figure 44 shows a two-dimensional $^1$H-$^1$H coupling (COSY) spectrum. This spectrum confirms that the protons which absorb in the region of $\delta$ 1.33-.140 (6H) coupled only with the protons that absorb in the region of $\delta$ 4.25-4.35 (4H) and vice versa without any additional coupling from the other protons.
Figure 43: $^1$H-NMR spectrum of diethyl 3-phenyl-1,2,4-thiadiazole-5-malonate
The $^{13}$C–NMR spectrum, shown in Figure 45a, exhibits signals due to the two non-equivalent methyl carbons at $\delta$ 14.3 and 14.4 and the two non-equivalent methylene carbons at $\delta$ 60.7 and 61.0. The $\alpha$-carbon of the malonate ester group absorbs at $\delta$ 85.7. The singlets at $\delta$ 126.8, 127.5, 129.2 and 131.7 were assigned to phenyl ring carbons. The carbons on thiadiazole ring at position 3 and 5 appear at $\delta$ 155.2 and 167.9, respectively. Since the enol equilibrium is fast, thus, the carbonyl carbon and enol carbon will become equivalent on the NMR time scale and appears as a singlet at $\delta$ 178.0. These assignments are consistent with the $^{13}$C–DEPT 135 spectrum (Figure 45b). The four signals at $\delta$ 127.5, 155.2, 167.9 and 178.0 disappear in the $^{13}$C–DEPT 135 spectrum which is consistent with
their assignment to the four quaternary carbons of phenyl ring carbon at position 1, the carbons on the thiadazole ring at positions 3 and 5, and the equivalent carbonyl-enol carbon, respectively. The two singlets at $\delta$ 14.3 and 14.4 appear in the positive direction while the signals at $\delta$ 60.7 and 61.0 appear in negative direction in the $^{13}$C–DEPT 135 spectrum. These are consistent to the assignments to the two non-equivalent methyl carbons and the two non-equivalent methylene carbons of the malonate ester group, respectively.

**Figure 45a:** $^{13}$C-NMR spectrum of diethyl 3-phenyl-1,2,4-thiadiazole-5-malonate
Results and Discussion

Figure 45b: $^{13}$C-DEPT 135 spectrum of diethyl 3-phenyl-1,2,4-thiadiazole-5-malonate

Figure 46 shows the two dimensional $^1$H-$^{13}$C correlation spectrum of the yellow crystals. This spectrum exhibits correlation between $^1$H and $^{13}$C supporting the previous $^1$H and $^{13}$C-spectral assignments. The spectrum reveals that the two carbon signals at $\delta$ 14.3 and 14.4, which were assigned to the non-equivalent methyl carbons, correlate with the quartet (6H) at $\delta$ 1.36 in the $^1$H-spectrum, which was assigned to the protons of the two non-equivalent methyl groups. In addition, the signals in the $^{13}$C-spectrum at $\delta$ 60.7 and 61.0, assigned to the two non-equivalent methylene carbons, correlate with the multiplet (4H) in the $^1$H–spectrum at $\delta$ 4.31, assigned to the protons of the two non-equivalent methylene groups. The spectrum also reveals no correlation of the broad down filed singlet in the $^1$H-spectrum with any carbon signal confirming that this proton is not attaching to any carbon and corresponds to absorption of the hydroxyl proton in enol form of 59.
Figure 46: $^{13}$C-$^1$H correlation spectrum of diethyl 3-phenyl-1,2,4-thiadiazole-5-malonate
2.3.2.3 Synthesis of 5-methyl-3-phenyl-1,2,4-thiadiazole

Acid catalyzed hydrolysis of the ester 59 followed by decarboxylation led to the formation of 5-methyl-3-phenyl-1,2,4-thiadiazole (57) as a white solid, however, in a very low yield.

![Scheme 23: Synthesis of 5-methyl-3-phenyl-1,2,4-thiadiazole](image)

**Figure 47a:** GC-trace of the white solid
The white solid was characterized by $^1$H-, $^{13}$C-NMR and mass spectroscopy. The GC-trace (Figure 47a) of this white solid shows the presence of one gc-volatile component eluted with a retention time of 9.5 min. The mass spectrum (Figure 47b) of this component shows a molecular ion peak at m/z 176 which corresponds to a molecular weight of the desired thiadiazole 57 (MW 176). The spectrum also exhibits a base peak at m/z 135. Unlike, the mass spectrum of 3-methyl-5-phenyl-1,2,4-thiadiazole (54), no peak at m/z 73 was observed in Figure 47b. In the case of 54, the peaks at m/z 73 and 135 were suggested to result from fragmentation pathways A and B, respectively, as shown in Scheme 24. Fragmentation pathway A in 54 would give a fragment with m/z 135 that could be stabilized by the phenyl group leading to a stable radical cation (m/z 135) which could be detected by the mass spectrometer. In contrast, under this similar fragmentation pathway for 57, the
peak at m/z 73 could not be detected in the mass spectrometer which was possibly due to the lack of stabilization of the generated radical cation and, thus, it might undergo further fragmentation before detection by the mass spectrometer. Thus, the absence of the peak at m/z 73 is characteristic fragmentation pathway of 57. Therefore, it can be concluded that this white solid is 5-methyl-3-phenyl-1,2,4-thiadiazole (57).

\[
\text{Scheme 24: Fragmentation pathways of 54 and 57}
\]

The \(^1\text{H–NMR}\) spectrum (Figure 48) shows the methyl group as a 3H singlet at δ 2.84. The phenyl ring protons appear as two multiplets at δ 7.34-7.48 (3H) assigned to para- and meta-phenyl ring protons and δ 8.17-8.27 (2H) assigned to ortho phenyl ring protons.
The $^{13}\text{C}$–NMR spectrum (Figure 49) reveals the methyl carbon of 57 at $\delta$ 16.9 which is slightly upfield compared with the methyl carbon that attaches to the thiadiazole ring carbon at position 3. The two thiadiazole ring carbons at positions 3 and 5 absorb at $\delta$ 186.4 and 173.1, respectively. The four signals at $\delta$ 128.1, 128.7, 130.2 and 132.7 are assigned to the phenyl ring carbons.
Figure 49: $^{13}$C–NMR spectrum of 3-methyl-5-phenyl-1,2,4-thiadiazole
2.3.3 Synthesis of 2,4-dimethyl-6-phenyl-1,3,5-triazine and 2-methyl-4,6-diphenyl-1,3,5-triazine

The procedure for the synthesis of sym-triazines by the cotrimerization of amidines described by Schaefer and colleagues\(^\text{10}\) is suitable for the synthesis of mono substituted-sym-triazines. Additional studies by these same researchers also revealed that the cotrimerization of amidines and imidates also allows the synthesis of un-symmetrically substituted-s-triazines. Since the cotrimerization is a random process, this procedure leads to mixtures of sym-triazines products.

However, more recently, a new synthesis of unsymmetrically substituted-s-triazines was reported. This method involves the condensation of N-acylamidines and amidines or guanidines in aprotic solvent,\(^\text{13}\) as shown in Scheme 25. Therefore, both 2,4-methyl-6-phenyl-1,3,5-triazine (65) and 2-methyl-4,6-diphenyl-1,3,5-triazine (66) were synthesized by this more recent method.

Scheme 25: The recent synthetic method of un-symmetrically substituted-s-triazines
2.3.3.1 Synthesis of N-[(dimethylamino)ethylidene]benzamide

In order to synthesize 2,4-dimethyl-6-phenyl-1,3,5-triazine (65) and 2-methyl-4,6-dimethyl-1,3,5-triazine (66) by the method described by Raymond Dengino and colleagues, required the acylamidine, N-[(dimethylamino)ethylidene]benzamide (67). This amidine was prepared in 90% as a dark viscous liquid by the condensation of benzamide (38) and N,N-dimethylacetamide dimethylacetal (56), as shown in Scheme 26.

\[
\begin{align*}
\text{Scheme 26: Synthesis of N-[(dimethylamino)ethylidene]benzamide}
\end{align*}
\]

The product was identified by \(^{1}H\)-, \(^{13}C\)-NMR and mass spectroscopy. The GC-chromatogram of this dark liquid [180°C (5min), 10°C/min to 240°C (30 min)] shows (Figure 50a) the presence of only one component with a retention time of 17.4 min. The mass spectrum (Figure 50b) of this material exhibits a molecular ion at m/z 190, a base peak at m/z 105, and two strong intensity peaks at m/z 44 and 77. The molecular ion at m/z 190 is consistent with the molecular weight of 67 (MW 190). Furthermore, the base peak at m/z 105 corresponds to the cleavage of \([C_{6}H_{5}CO]^{+}\) and the two strong intensity peaks at m/z 44 and 77 correspond to the cleavage of \([C_{2}H_{6}N]^{+}\) and \([C_{6}H_{5}]^{+}\), respectively.
Results and Discussion

Figure 50a: GC-trace of the dark viscous liquid expected to be \( \text{C}_6\text{H}_5\text{CNCH}_3 \)

Figure 50b: Mass spectrum of the peak eluted at a retention time of 17.4 min
The $^1$H–NMR spectrum of this liquid (Figure 51) exhibits two multiplets at $\delta$ 7.31-7.39 (3H) and $\delta$ 8.07-8.12 (2H) and three singlets at $\delta$ 2.23 (3H), 2.97 (3H) and 3.07 (3H). This spectrum is consistent with the structure of N-[[(dimethylamino)ethyldine]benzamide (67). The two multiplets at $\delta$ 7.31-7.39 and $\delta$ 8.07-8.12 were assigned to the meta-para and ortho-phenyl ring protons, respectively. The 3H singlet at $\delta$ 2.23 can be assigned to the methyl protons bonded to the imine carbon. The additional two 3H singlets were assigned to the two non-equivalent methyl groups bonded to the amino group.

Figure 51: $^1$H–NMR spectrum of the dark liquid
The $^{13}$C–NMR spectrum of this liquid (Figure 52a) also reveals signals consistent with the structure of 67. The methyl carbon bonded to the imine carbon appears at $\delta$ 18.7. The two non-equivalent N-methyl carbons were observed to absorb at $\delta$ 38.6 and 38.7. In the normal scale spectrum, these two absorptions appear as only one signal. But upon scale expansion (Figure 52b), this signal is resolved into two peaks. The signals at $\delta$ 128.2, 129.7, 131.7 and 137.9 were assigned to the phenyl ring carbons. Also the signals at $\delta$ 165.7 and 176.4 were assigned to the imine carbon and the carbonyl carbon, respectively.

Figure 52a: $^{13}$C–NMR spectrum of the dark liquid
In order to confirm the above spectral assignments, the $^1\text{H}$–$^{13}\text{C}$ NMR correlation spectrum was recorded. This spectrum (Figure 53) reveals that the signal at $\delta$ 18.7 in the $^{13}\text{C}$-spectrum, which was assigned to the methyl carbon bonded to the imine carbon, correlates with the singlet (3H) at $\delta$ 2.23 in the $^1\text{H}$–spectrum, which was assigned to the protons of the methyl group bonded to the imine carbon. The signals at $\delta$ 38.63 and 38.68 in the $^{13}\text{C}$-spectrum, which were assigned to the two non-equivalent methyl carbons of the amino group, correlate with the two singlets (3H) at $\delta$ 2.97 and 3.07 in the $^1\text{H}$-spectrum, which were also assigned to the two non-equivalent methyl groups bonded to the amino group. The spectrum also reveals that the signals at $\delta$ 128.2, 129.7 and 131.7 in $^{13}\text{C}$-spectrum correlate with the two multiplets at $\delta$ 7.31-7.39 and $\delta$ 8.07-8.12 in the $^1\text{H}$-spectrum, which were assigned to the protons of the phenyl group. The spectrum also allows to assign the signals at $\delta$ 128.2 and 131.7 in the $^{13}\text{C}$-spectrum to the para-meta phenyl ring carbons. Thus, the signal at $\delta$ 129.7 can be assigned to the ortho-phenyl ring carbons.

**Figure 52b:** $^{13}\text{C}$-scale expansion spectrum of the dark liquid
The signal at $\delta$ 137.9 in the $^{13}$C–spectrum disappears in the $^1$H–$^{13}$C spectrum, this indicates that this signal is due to the phenyl ring carbon at position 1. The signals at $\delta$ 165.7 and 176.7 in the $^{13}$C–spectrum also disappear in the $^1$H–$^{13}$C spectrum, this is consistent with the assignment of these two quaternary carbons to the imine carbon and the carbonyl carbon.

Figure 53: $^1$H–$^{13}$C correlation spectrum of the dark liquid
According to the literature, the melting point of this compound was reported at 47°C, thus, in this synthesis the amidine product was expected to obtain as a solid. But in this synthesis, even though the product was obtained as a dark viscous liquid, however, all the NMR and mass spectroscopic results are consistent with the assignment of this product to N-[(dimethylamino)ethylidine]benzamide (67).

2.3.3.2 Synthesis of 2,4-dimethyl-6-phenyl-1,3,5-triazine

The condensation between 67 and acetamide (68) in refluxing anhydrous tetrahydrofuran led to the formation of 2,4-dimethyl-6-phenyl-1,3,5-triazine (65) in 14.6% as a light yellow liquid. Scheme 27 shows the proposed mechanism for the formation of 2,4-dimethyl-6-phenyl-1,3,5-triazine (65).
Scheme 27: Synthesis of 2,4-dimethyl-6-phenyl-1,3,5-triazine

The GC-trace [110°C (10 min), 10°C/min to 240°C (30 min)] of the crude product (Figure 54a) indicates the presence of more than one product. The mass spectrum of the peak that eluted with a retention time of 16.3 min (Figure 54b) exhibits a molecular ion at m/z 185, thus, this peak was expected to be the desired triazine 65 (MW 185).
This crude product was purified by preparative thin-layer chromatography. The highest band with a R_f of 0.79 was removed and extracted with ethyl acetate. The solvent was removed to give a light yellow viscous liquid. This liquid was analyzed by the GC interfaced with a mass spectrometer. The GC-chromatogram exhibited a major component with a retention time of 16.3 min. The mass spectrum of this component was identical to the mass spectrum shown in Figure 54b, which showed a molecular ion at
Results and Discussion

m/z 185 which is consistent with the molecular weight of 65. The spectrum also showed a base peak at m/z 103 and a peak at m/z 82, which corresponded to the cleavage of [C₆H₅CN]⁺⁺ and [C₄H₆N₂]⁺, respectively, from 65.

The ¹H–NMR spectrum of this yellow liquid (Figure 55) exhibits a singlet at δ 2.67, which is expected due to the absorption of the protons of the two equivalent methyl groups substituted on the triazine ring. The two multiplets at δ 7.44-7.55 (3 H) and δ 8.47-8.49 (2H) were assigned to para-meta and ortho-phenyl ring protons, respectively.

Figure 55: ¹H–NMR spectrum of the yellow liquid expected to be 65
The $^{13}$C–NMR spectrum of this yellow liquid (Figure 56a) also reveals the signals correspond to the structure of 65. The signal at $\delta$ 25.7 was assigned to the two equivalent methyl carbons on the triazine ring. The signal at $\delta$ 171.2 was assigned to the triazine ring carbon at position 6. The two equivalent triazine ring carbons at positions 2 and 4 absorb at the same chemical shift of $\delta$ 176.3. The four signals at $\delta$ 128.6, 128.8, 132.5 and 135.5 were assigned to the phenyl ring carbons. This assignment also corresponds to the signals appear in the $^{13}$C–DEPT 135 spectrum (Figure 56b). The signal at $\delta$ 25.7 still appears in the $^{13}$C–DEPT 135 spectrum. This is consistent with the assignment to the two equivalent methyl carbons. The two signals at $\delta$ 171.2 and 176.4 disappear in the $^{13}$C–DEPT 135 spectrum, which corresponds to the assignment of the three quaternary triazine ring carbons.

**Figure 56a:** $^{13}$C – NMR spectrum of the yellow liquid expected to be 65
2.3.3.3 Synthesis of 2-methyl-4,6-diphenyl-1,3,5-triazine

Raymond Dengino and colleagues did not report the synthesis of 2-methyl-4,6-diphenyl-1,3,5-triazine (66). However, by analogy with the synthesis of 65, it should be possible to synthesize 66 by the reaction of N-[(dimethylamino)ethylidine]benzamide (67) with benzamidine (62) instead of acetamidine (68), as shown in Scheme 28.

Scheme 28: Possible synthetic method of 2-methyl-4,6-diphenyl-1,3,5-triazine
Thus, by using this procedure, 2-methyl-4,6-diphenyl-1,3,5-triazine (66) was synthesized from 67 and 62. The product was obtained in 12.5 % as a white solid and was characterized by $^1$H-, $^{13}$C-NMR and mass spectrometry.

The GC-analysis [110°C (5 min), 10°C/min to 240°C (30 min)] of the white solid (Figure 57a) shows the presence of two components. The mass spectrum of the major peak (Figure 57b), which eluted with a retention time of 32.4 min, exhibits a molecular ion at m/z 247, which corresponds to the molecular weight of 66 (MW 247). The spectrum also exhibits a base peak at m/z 103, which is consistent with the cleavage of [C$_6$H$_3$CN]$.^{++}$.

Figure 46a: GC-trace of the white solid expected to be 66

Figure 46b: Mass spectrum of the peak eluted at a retention time of 32.4 min
The $^1$H–NMR spectrum of this white solid (Figure 58) exhibits a 3H singlet at $\delta$ 2.77, which was assigned to the proton of the methyl group substituted on the triazine ring. The two multiplets at $\delta$ 7.46-7.57 (6H) and $\delta$ 8.61-8.64 (4H) were assigned to the meta-para and ortho-phenyl ring protons, respectively.

Figure 58: $^1$H–NMR spectrum of the white solid

The $^{13}$C–NMR spectrum (Figure 59a) reveals the methyl signal at $\delta$ 26.5. The two equivalent phenyl ring carbons absorb at $\delta$ 129.1, 129.3, 132.9 and 136.3. The triazine ring carbon at position 2 appears at $\delta$ 177.5 while the two equivalent triazine ring carbons at positions 4 and 6 absorb at $\delta$ 171.6. These $^{13}$C- spectral assignments can be confirmed by the $^{13}$C–DEPT 135 spectrum. The spectrum (Figure 59b) still reveals the signal at $\delta$ 26.5 as expected for a signal due to a methyl carbon. The two signals at $\delta$ 171.6 and 177.5, however, disappear in the $^{13}$C–DEPT 135 spectrum. This is consistent with the assignment
of these signals to the three quarternary carbons of the triazine ring. In the phenyl region, the signal at $\delta$ 136.3 disappears in the $^{13}$C–DEPT 135 spectrum and can, therefore, be assigned to the carbon at position 1 of the phenyl ring.

**Figure 59a:** $^{13}$C–NMR spectrum of the white solid

**Figure 59b:** $^{13}$C–DEPT 135 spectrum of the white solid
2.3.4 Photochemistry of 3-methyl-5-phenyl-1,2,4-thiadiazole

The studies presented in this thesis have indicated that 5-phenyl-1,2,4-thiadiazole (31) undergoes phototransposition leading to the formation of 3-phenyl-1,2,4-thiadiazole (46). It also undergoes photofragmentation leading to the formation of benzonitrile (43) and photoring-expansion leading to the formation of 2-phenyl- and 2,4-diphenyl-1,3,5-triazine (39) and (40). However, in the case of 46, only 43 was observed in 75% upon irradiation of this compound. There is no evidence indicating the formation of 31, the phototransposition product expected upon irradiation of 46.

This work was also extended to study the photochemistry of disubstituted 3-methyl-5-phenyl-1,2,4-thiadiazole. Based on the observed photochemistry of 31, the photoproducts expected upon irradiation of 54 would be benzonitrile (43), 5-methyl-3-phenyl-1,2,4-thiadiazole (57), 2,4-dimethyl-6-phenyl-1,3,5-triazine (65) and 2-methyl-4,6-diphenyl-1,3,5-triazine (66).

The photochemistry of 54 was first studied in acetonitrile solvent. A solution of 54 (6.0×10⁻⁵ M, 10 mL) was placed in a quartz cuvette. This solution was irradiated with three > 290 nm lamps through a Pyrex filter. The reaction was monitored by ultraviolet absorption spectroscopy at 40 sec intervals. Figure 60a shows the ultraviolet absorption spectrum of the solution before irradiation. The spectrum reveals the λₘₚₓ at 278 nm with an extinction coefficient of 14,100 L mol⁻¹ cm⁻¹. Figure 60b exhibits the UV–overlay spectrum of the photolysis of this compound. The spectrum reveals the decreasing of the absorption band at λ 278 nm from 0.85 to 0.7 which is due to the consumption of the reactant 54. It also reveals the increasing of the absorption band at λ 261 nm from 0.56 to 0.65.
Results and Discussion

Figure 60a: UV-absorption spectrum of 54 in acetonitrile before irradiation

Figure 60b: UV–overlay spectrum of the photolysis of 54 in acetonitrile
The photolysis was also monitored by GLC. A solution of 54 (2.0×10⁻² M, 4 mL) was placed into a Pyrex tube (0.7 cm × 13.5 cm), sealed with a rubber septum and purged with argon for 30 min. The solution was irradiated with sixteen > 290 nm lamps and monitored by gas liquid chromatography [140°C (4 min), 10°C/min to 240°C (20 min)] at 40 min intervals. Figure 61a shows the GLC analysis of the solution before irradiation. The trace exhibits a major peak with a retention time of 12 min, which is due to the reactant 54. Figure 61b shows the GC-trace of the reaction mixture after 150 min of irradiation time. The trace reveals the consumption of 76.4 % of the reactant and the formation of four new peaks with retention time of 5, 11.5, 13.5 and 28 min.

Figure 61a: GLC analysis of 54 in acetonitrile before irradiation
Results and Discussion

Figure 61b: GLC analysis of the reaction mixture after 150 min of irradiation

The reaction mixture was concentrated by rotary evaporation at room temperature and analyzed again by GC-MS [140°C (5 min), 10°C/min to 240°C (30 min)]. Figure 62a exhibits GC-trace of this concentrated reaction mixture. The trace shows four major GC-volatile components with retention times of 4.1, 13.0, 14 and 29.2 min. The mass spectrum of the first eluted component (Figure 62b) exhibits a base molecular ion peak at m/z 103, which could be due to 43. This was confirmed by comparison of the chromatographic and mass spectrometric properties of this component with an authentic sample of 43.
Results and Discussion

Figure 62a: GC-analysis of the concentrated reaction mixture

Figure 62b: Mass spectrum of the peak eluted at a retention time of 4.1 min

By direct comparison of the mass spectrum and GC-retention time of the first eluted photoproduct with those of an authentic sample of 43, it confirms that the first eluted photoproduct is benzonitrile (43).

The mass spectrum of the peak that eluted with a retention time of 29.2 min (Figure 62c) exhibits a molecular ion at m/z 247. This photoproduct was expected, by analogy of the results from the photolysis of 31, to be 2-methyl-4,6-diphenyl-1,3,5-triazine (66). The molecular ion at m/z 247 corresponds to the molecular weight of 66 (MW 247).
In order to confirm the formation of this photoproduct, an authentic sample of 66 was analyzed by GC-MS. This compound eluted with a retention time of 29.3 min, which is the same as the retention time of the product peak. The mass spectrum of this authentic sample also exhibited a molecular ion at m/z 247 and a base peak at m/z 103, which was due to [C₆H₅CN]⁺. The fragmentation pattern of this authentic sample was identical to the fragmentation pattern of the photoproduct. According to this information, the peak that eluted with a retention time of 29.2 minutes can be identified as 2-methyl-4,6-diphenyl-1,3,5-triazine (66).
The mass spectrum of the peak, which eluted with a retention time of 13 min (Figure 62d) exhibits a molecular ion at m/z 185 and a base peak at m/z 103. Based on the molecular weight and the fragmentation pattern, this compound was suspected to be 2,4-dimethyl-6-phenyl-1,3,5-triazine (65), another possible photoproduct. Therefore, an authentic sample of 65 was analyzed by GC-MS in order to compare its chromatographic and mass spectral properties with those of the photoproducts. Authentic 2,4-dimethyl-6-phenyl-1,3,5-triazine also eluted with a retention time of 13 min.

The mass spectrum of an authentic sample of 65 (Figure 63) shows a molecular ion at m/z 185, a base peak at m/z 103 which is due to $[C_6H_5CN]^{++}$ and a peak at m/z 82 with an intensity of 49.1% of the base peak which is due to $[C_4H_6N2]^+$. 
Comparison between Figures 62d and 63, the mass spectrum of an authentic sample of 65 is not totally identical with the mass spectrum of the photoproduct. Although, the mass spectrum of the photoproduct (Figure 62d) exhibits a molecular ion at m/z 185, a base peak at m/z 103, a peak at m/z 82, the spectrum also reveals peaks at m/z 135 and m/z 73. These two peaks are certainly not due to 65. However, it was suspected that this peak may be due to an overlap of the peaks due to 65 and the reactant 54. Since the GC-analysis and the mass spectrum of 54 before irradiation (Figure 64a-b) show that 54 also has a retention time of 13 min. Furthermore, the mass spectrum (Figure 64b) exhibits a molecular ion at m/z 176, a base peak at m/z 135 which is due to [C₆H₅CNS]+, a peak at m/z 73 which is due to [C₂H₃NS]+. All of these major fragments are observed in the mass spectrum of the photoproduct peak.
Results and Discussion

Figure 64a: GC-trace of 3-methyl-5-phenyl-1,2,4-thiadiazole before irradiation

Figure 64b: Mass spectrum of 3-methyl-5-phenyl-1,2,4-thiadiazole
Moreover, according the GC-trace (PE-9000) of the mixture after 150 min of irradiation, which is shown in Figure 61b, reveals two partially resolved peaks at retention time of approximately 13 min. One of these peaks is due to the reactant, 54, and another one is due to a photoproduct. Although these two compounds are resolved in the GC PE-9000, they are not resolved on the gas chromatograph interfaced to the mass detector. Thus, the mass spectrum shown in Figure 62d is the mass spectrum of a mixture of 2,4-dimethyl-6-phenyl-1,3,5-triazine (65) and 3-methyl-5-phenyl-1,2,4-thiadiazole (54).

The mass spectrum of the peak which eluted with a retention time of 14 min (Figure 62e) exhibits a molecular ion at m/z 176, and is therefore isomeric with 54. This product was expected to be 5-methyl-3-phenyl-1,2,4-thiadiazole (57), the expected transposition product. By comparison of GC-retention time and mass spectral pattern of this product with those of an authentic sample of 57, this product could, therefore, be identified as the phototransposition product, 5-methyl-3-phenyl-1,2,4-thiadiazole (57).

![Figure 62e: Mass spectrum of the peak eluted with a retention time of 14 min](image-url)
2.4 Photochemistry of 5-phenyl-1,2,4-thiadiazole-4\(^{15}\)N

2.4.1 Synthesis of 5-phenyl-1,2,4-thiadiazole-4\(^{15}\)N

5-phenyl-1,2,4-thiadiazole (31) was synthesized in two steps according to the procedure described by Yang-I Lin and colleagues.\(^9\) The first step was to synthesize N-[(dimethylamino)methylene]thiobenzamide (32) by the reaction of thiobenzamide (34) with N,N-dimethylformamide dimethylacetal (35). Then, amination cyclization of 32 with hydroxylamine-O-sulfonic acid (33) gave 31 as a colorless viscous liquid.

Thus, in the synthesis of 5-phenyl-1,2,4-thiadiazole-4\(^{15}\)N (31-4\(^{15}\)N), thiobenzamide-\(^{15}\)N (34-\(^{15}\)N) was required. Since this compound was commercially not available, it was synthesized by thionation of benzamide-\(^{15}\)N (38-\(^{15}\)N) with phosphorus pentasulfide.

2.4.1.1 Synthesis of thiobenzamide-\(^{15}\)N

There are several methods for the synthesis of thioamides. The classical method is a thionation of the corresponding carboamide compound by reaction with phosphorus pentasulfide. Up to now, although there are several other thionating agents available for the conversion of a carboamide to thioamide, phosphorus pentasulfide is still one of the most widely used thionating agent.

Thiobenzamide-\(^{15}\)N (34-\(^{15}\)N) was synthesized in 51.3% by the thionation of 38-\(^{15}\)N (Scheme 29) with phosphorus pentasulfide in refluxing benzene solvent. Thiobenzamide-\(^{15}\)N (34-\(^{15}\)N) was identified by \(^1\)H-, \(^13\)C-, \(^{15}\)N-NMR and mass spectrometry.
Scheme 29: Synthesis of thiobenzamide–$^{15}$N

The mass spectrum of the synthetic 34-15N (Figure 63a) exhibits the base molecular ion peak at m/z 138, which corresponds to the molecular weight of 34-15N. The spectrum also exhibits a peak at m/z 137 with an intensity of 17.8% of the peak at m/z 138. This peak at m/z 137 could be due to an M-1 peak resulting from loss of hydrogen from the molecular ion or from the presence of thiobenzamide-14N (34-14N) in the sample. Figure 63b, however, shows that the mass spectrum of 34-14N also exhibits a molecular ion at m/z 137 and an M-1 peak at m/z 136 with an intensity of 18.1% of the molecular ion peak. This confirms that loss of hydrogen is a normal fragmentation pathway for 34-14N and therefore will also be a normal fragmentation pathway for 34-15N. The peak at m/z 137 in the mass spectrum of 34-15N is therefore not due to the presence of 34-14N in the sample.
**Results and Discussion**

**Figure 63a:** Mass spectrum of thiobenzamide - $^{15}$N

**Figure 63b:** Mass spectrum of thiobenzamide - $^{14}$N
The $^1$H–NMR spectrum (Figure 64a-b) of this synthesized thiobenzamide-$^{15}$N ($^{34-15}$N) is more complicated than $^1$H–NMR spectrum of $^{34-14}$N due to the heteronuclear coupling between $^1$H and $^{15}$N. The two protons of the amino group are not equivalent due to the partial double bond character of the C-N bond. Therefore, these two protons will have different chemical shifts. These two signals appear (see Figure 64b) as double doublet at $\delta$ 7.06–7.30 and $\delta$ 7.70–7.94 due to $^1$H–$^1$H coupling ($J = 4.29$ Hz) and $^1$H–$^{15}$N coupling ($J = 89.2$ Hz) for the signal at $\delta$ 7.06–7.30 and $J = 92.7$ Hz for the signal at $\delta$ 7.70–7.94.

**Figure 64a:** $^1$H–NMR spectrum of the synthesized thiobenzamide-$^{15}$N
Results and Discussion

Figure 64b: $^1$H-scale expansion spectrum of the synthesized thiobenzamide-$^{15}$N

In addition to the signals expected for the ring carbon atoms, the $^{13}$C–NMR spectrum of $34$-$^{15}$N (Figure 65) exhibits a doublet for the thiocarbonyl carbon at $\delta$ 202.8 (d; $J = 13.80$ Hz) due to $^{13}$C–$^{15}$N coupling.

The amide nitrogen of $34$-$^{15}$N appears in the $^{15}$N–NMR spectrum (Figure 66) as a triplet ($J = 91.20$ Hz) at $\delta$ 132.88 due to its one bond heteronuclear coupling with the two attached hydrogens. The nitrogen shielding referred to neat nitromethane is at + 279.8 ppm.
Results and Discussion

**Figure 65:** $^{13}$C-NMR spectrum of the synthesized thiobenzamide-$^{15}$N

**Figure 66:** $^{15}$N–NMR spectrum of the synthesized thiobenzamide-$^{15}$N
2.4.1.2 Synthesis of N-[(dimethylamino)methylene]thiobenzamide-\(^{15}\)N

N-[(dimethylamino)methylene]thiobenzamide-\(^{15}\)N (32-\(^{15}\)N) was synthesized in 83% by the condensation of thiobenzamide-\(^{15}\)N (34-\(^{15}\)N) and N,N-dimethylformamide dimethylacetal (35) at room temperature as shown in Scheme 30.

\[
\begin{align*}
\text{Scheme 30: Synthesis of N-[(dimethylamino)methylene]thiobenzamide-^{15}N}
\end{align*}
\]

The \(^1\)H–NMR spectrum (Figure 67) of N-[(dimethylamino)methylene]thiobenzamide-\(^{15}\)N (32-\(^{15}\)N) exhibits a singlet at \(\delta\) 8.78. Although this proton would be expected to couple with the imine \(^{15}\)N nucleus, no sign of any coupling was observed upon scale expansion of this signal. The two non-equivalent methyl protons appear in the spectrum as two singlets at \(\delta\) 3.24 and 3.25. The phenyl protons appear as a 3H multiplet from \(\delta\) 7.29-7.52 assigned to the meta and para protons and 2H multiplet from \(\delta\) 8.36 – 8.41 assigned to the ortho protons.
Figure 67: $^1$H-NMR spectrum of N-[(dimethylamino)methylene]thiobenzamide$^{15}$N

Figure 68: $^{13}$C-NMR spectrum of N-[(dimethylamino)methylene]thiobenzamide$^{15}$N
The $^{13}$C–NMR spectrum shown in Figure 68 exhibits a singlet at $\delta$ 216.1 for the thiocarbonyl carbon. It is surprising that this signal shows no sign of the coupling with the adjacent $^{15}$N nucleus since in $^{32}$-$^{15}$N, the thiocarbonyl carbon appeared in the $^{13}$C–spectrum at $\delta$ 202.8 as a doublet ($J =$13.8 Hz) due to its coupling with the $^{15}$N nucleus. The $^{13}$C- NMR spectrum of $^{32}$-$^{15}$N does exhibit a doublet ($J =$ 10.0 Hz) for the imine carbon at $\delta$ 159.0 indicating that this carbon is coupling with the adjacent $^{15}$N nucleus. The two non-equivalent methyl carbons appear in the spectrum as sharp singlets. The former absorption appears as a doublet ($J =$ 2.3 Hz), presumably due to a long range coupling with the $^{15}$N. The spectrum also exhibits unusual long range couplings between the $^{15}$N and C-1 of the phenyl ring, which appears as a doublet ($J =$ 8.40 Hz) at $\delta$ 143.0 and between $^{15}$N and the two equivalent ortho carbon of the phenyl ring, which appear as a doublet ($J =$ 3.10 Hz) at $\delta$ 128.8.

The two-dimensional $^1$H–$^{13}$C correlation spectrum shown in Figure 69 is consistent with these spectral assignments. Thus, as shown in Figure 60, the doublet at $\delta$ 36.4 and the singlet at $\delta$ 41.9 in the $^{13}$C–spectrum that were assigned to the two non-equivalent methyl groups correlate with the signals in the $^1$H–spectrum at $\delta$ 3.24 and 3.25 assigned to the two sets of methyl hydrogens. Furthermore, the $^1$H–$^{13}$C correlation spectrum allows the assignments of the carbon absorptions of the phenyl ring to be confirmed. Thus, as can be seen in Figure 60, the doublet at $\delta$ 128.8 in the $^{13}$C–spectrum assigned to the two equivalent ortho-ring carbon atoms correlate with 2H multiplet at $\delta$ 8.39-8.44 in the $^1$H–spectrum assigned to the ortho-ring protons. In addition, the singlets in the $^{13}$C – spectrum at $\delta$ 127.7 and 131.9 which were assigned to the meta- and para-ring carbons, respectively, correlate with the 3H multiplet at $\delta$ 7.29-7.46 in the $^1$H–spectrum due to the
meta- and para- protons. As expected, the doublet in $^{13}$C–spectrum at $\delta$ 130.0 assigned to the quaternary carbon of the phenyl ring is not observed in the $^1$H–$^{13}$C correlation spectrum.

**Figure 69:** Two-dimensional $^1$H–$^{13}$C correlation spectrum of 32-$^{15}$N
Finally, the $^{15}\text{N}$–NMR spectrum, shown in Figure 70, exhibits a doublet ($J = 2\text{Hz}$) at $\delta 266.8$ due to the coupling between $^{15}\text{N}$ and the imine proton. The nitrogen shielding is referred to neat nitromethane at $\delta 109.7$. The geometry of this compound could be the trans-isomer since the calculated coupling constant for the trans-isomer has been reported at 2 Hz.$^{15}$

Figure 70: $^{15}\text{N}$-NMR spectrum of $\text{N-}[(\text{dimethylamino})\text{methylene}]\text{thiobenzamide}^{15}\text{N}$
2.4.1.3 Synthesis of 5-phenyl-1,2,4-thiadiazole – 4\textsuperscript{15}N

5-phenyl-1,2,4-thiadiazole–4\textsuperscript{15}N (31-4\textsuperscript{15}N) was synthesized by the reaction of 32-\textsuperscript{15}N with 33 in absolute ethanol and methanol at room temperature using pyridine as basic catalyst (Scheme 31). Amination cyclization of 32-\textsuperscript{15}N resulted in the formation of 31-4\textsuperscript{15}N as colorless viscous liquid.

\begin{center}
\includegraphics[width=\textwidth]{scheme31.png}
\end{center}

**Scheme 31**: Synthesis of 5-phenyl-1,2,4-thiadiazole – 4\textsuperscript{15}N

The GC-chromatogram [150°C (5 min), 30°C/min to 180°C (14 min)] of the synthetic 31-4\textsuperscript{15}N (Figure 71a) indicates the presence of two components. The major product eluted with a retention time of 11.1 min. The mass spectrum (Figure 71b) of this product exhibits a molecular ion at m/z 163 indicating that this component is the desired thiadiazole 31-4\textsuperscript{15}N. The minor component eluted with a retention time of 6.6 min and exhibits a molecular ion in the mass spectrum (Figure 71c) at m/z 147 and a base peak at m/z 104. This impurity was expected to be 5-phenyl-1,2,4-oxadiazole–4\textsuperscript{15}N (37-4\textsuperscript{15}N). It was presumed to be formed by the reaction of benzamide-\textsuperscript{15}N (38-\textsuperscript{15}N) present in the thiobenzamide-\textsuperscript{15}N (34-\textsuperscript{15}N) (Scheme 32).
Results and Discussion

Scheme 32: The plausible pathway for the formation of 5-phenyl-1,2,4-oxadiazole $^{15}$N

Figure 71a: GC-trace of the synthesized 5-phenyl-1,2,4-thiadiazole $^{15}$N
Results and Discussion

Figure 71b: Mass spectrum of the peak eluted at a retention time of 11.1 min

Figure 71c: Mass spectrum of the peak eluted at a retention time of 6.6 min
By direct comparison of the mass spectrum of this impurity with the mass spectrum of the previously synthesized 5-phenyl-1,2,4-oxadiazole (37), it revealed that the fragmentation of this impurity was identical to the fragmentation pattern of the synthetic 5-phenyl-1,2,4-oxadiazole. Some fragments of in the mass spectrum of this impurity were different due to the presence of $^{15}$N-atom in those fragments. For example, the molecular ion was exhibited at m/z 147 and the base peak was exhibited at m/z 104. These results indicated that the impurity in the synthesized 5-phenyl-1,2,4-thiadiazole–$^4{^{15}}$N (31–$^4{^{15}}$N) was 5-phenyl-1,2,4-oxadiazole – $^4{^{15}}$N (37–$^4{^{15}}$N).

![Figure 72: Mass spectrum of the synthetic 5-phenyl-1,2,4-oxadiazole](image)
Results and Discussion

After the synthesized $31-4^{15}\text{N}$ was purified by preparative gas chromatography, the GC-analysis (Figure 73a) indicates the presence of only the desired product with a retention time of 11.1 min and no sign of any peak at retention time 6.6 min where the impurity was expected to be eluted. The mass spectrum (Figure 73b) exhibits a molecular ion at m/z 163 and two intense peaks at m/z 136 and 105 due to $[\text{C}_6\text{H}_5\text{C}^{15}\text{NS}]^+$ and $[\text{C}_6\text{H}_5\text{C}^{15}\text{NH}]^+$ fragments, respectively, which confirm the presence of only $31-4^{15}\text{N}$. The mass spectrum also exhibits a peak at m/z 162 with relative intensity of 9% and a peak at m/z 135 with relative intensity of 11%. This indicated the presence of 5-phenyl-1,2,4-thiadiazole-14N (31).

Figure 73a: GC-trace of the purified 5-phenyl-1,2,4-thiadiazole – 415N
Figure 73b: Mass spectrum of the peak eluted at a retention time of 11.1 min

The $^1$H–NMR spectrum of the synthetic 31-4$^{15}$N is shown in Figure 74a. In addition to 3H and 2H multiplets due to the phenyl protons at δ 7.58-7.61 and at δ 8.06–8.08, respectively, the spectrum exhibits a doublet ($J = 13.90$ Hz) at δ 8.84 due to the C-3 proton of the thiadiazole ring coupling with the $^{15}$N at ring position 4. Interestingly, scale expansion of this signal shown in Figure 65b reveals the presence of a small amount of 5-phenyl-1,2,4-thiadiazole–4$^{14}$N (31) in the sample as shown by mass spectrometry. Thus, in the absence of $^{15}$N, the C-3 proton appears only as a singlet.
Figure 74a: $^1$H–NMR spectrum of purified 5-phenyl-1,2,4-thiadiazole – $^{15}$N

Figure 74b: $^1$H–scale expansion spectrum of purified 5-phenyl-1,2,4-thiadiazole – $^{15}$N
Results and Discussion

The $^{13}$C–NMR spectrum, shown in Figure 75a, exhibits a singlet at $\delta$ 188.8 assigned to the carbon at position 5 of the thiadiazole ring. The carbon at position 3 of the ring appears as a doublet at $\delta$ 164.7 ($J = 3.80$ Hz) due to the coupling with $^{15}$N atom at the ring position 4 (Figure 75c). Surprisingly, the C-5 carbon signal does not appear as a doublet (Figure 75b), which was expected due to the coupling of this C-5 with $^{15}$N.

Figure 75a: $^{13}$C–NMR spectrum of purified 5-phenyl-1,2,4-thiadiazole – $^{15}$N
Figure 75b: $^{13}$C–scale expansion spectrum of purified 31-4$^{15}$N showing the signal at $\delta$ 188.8 as singlet

Figure 75c: $^{13}$C–scale expansion spectrum of purified 31-4$^{15}$N showing the signal at $\delta$ 164.7 as doublet
As shown in Figure 75a, the doublet in the $^{13}$C–spectrum at $\delta$ 164.6 ($J = 3.80$) that was assigned to the carbon in position 3 of the thia diazole ring correlates with the doublet in the $^1$H–spectrum at $\delta$ 8.80 ($J = 13.90$ Hz) that was assigned to the proton at position 3 of the thia diazole ring. Furthermore, the ring phenyl carbon signals in the $^{13}$C–spectrum can also be assigned from the correlation spectrum. Thus, the signal at $\delta$ 128.2 in the carbon spectrum can be assigned to the two equivalent ortho-ring carbons since this signal correlates with the 2H multiplet due to the ortho-protons at $\delta$ 8.05–8.08 in the $^1$H–spectrum. In addition, the two signals in the $^{13}$C–spectrum at $\delta$ 130.3 and 133.0 can be assigned to the meta- and para-carbons, respectively, since these signals correlate with the 3H multiplet in the $^1$H–spectrum at $\delta$ 7.59–7.61 that is due to the meta- and para-protons. Furthermore, the doublet in the $^{13}$C–spectrum at $\delta$ 131.05 ($J = 6.3$ Hz) can be assigned to the quaternary phenyl carbon since it is not observed in the $^1$H–$^{13}$C correlation spectrum (Figure 76).
Figure 76: Two-dimensional $^1$H–$^{13}$C correlation spectrum of purified 31-4$^{15}$N
The $^{15}\text{N}$–NMR spectrum (Figure 77) exhibits the signal of $^{15}\text{N}$–$4$ at $\delta$ 302.2 as doublet ($J = 13.90$ Hz) due to the coupling between $^{15}\text{N}$–$4$ and $^{1}\text{H}$–$3$. The signal of this $^{15}\text{N}$–$4$ in the term of nitrogen shielding is at $+74.2$ ppm, which corresponds to the reported nitrogen shielding of $^{15}\text{N}$–$4$ on 1,2,4-thiadiazole at $+70$ ppm (in dimethyl ether).$^{15}$

Figure 77: $^{15}\text{N}$–NMR spectrum of the purified 5-phenyl-1,2,4-thiadiazole–$4^{15}\text{N}$
2.4.2 Photochemistry of 5-phenyl-1,2,4-thiadiazole-4-\(^{15}\)N

In the previous photochemistry study of 5-phenyl-1,2,4-thiadiazole (31), the results indicated that five photoproducts were formed upon irradiation of this compound. They were identified as benzonitrile (43), 3-phenyl-1,2,4-thiadiazole (46), diphenyl-1,2,4-thiadiazole (47), 2-phenyl-1,3,5-triazine (39), and 2,4-diphenyl-1,3,5-triazine (40). Scheme 33 shows the proposed mechanism for the formation of 46 upon irradiation of 31.

Scheme 33: The proposed mechanism for the formation of the phototransposition product
The phototransposition of 31 can be rationalized by the mechanism shown in Scheme 33. According to this mechanistic pathway, upon photochemical excitation, 31 is predicted to undergo electrocyclic ring closure leading to the formation of bicyclic intermediate, BC-31. One or two sigmatropic shifts of sulphur would lead to an equilibrium mixture of BC-46 and BC-46', which are identical except for the scrambling of the two nitrogens. Rearomatization of either BC-46 or BC-46' would lead to the observed phototransposition product, 46. In addition, BC-31 would be expected to be in equilibrium with BC-31' via sulfur migration in the opposite direction. Again, BC-31 and BC-31' are identical except for the scrambling of the two nitrogen atoms. Rearomatization of either of these two bicyclic species would lead back to the starting heterocycle, 5-phenyl-1,2,4-thiadiazole (31). Since, it is not possible to distinguish between the two nitrogen atoms in an unlabelled reactant 31, it is not possible to distinguish between formation of 46 by the one or two sulfur migrations. Similarly, it is not possible to detect sulfur migration in the opposite direction leading back to 31.

Scheme 33 shows, however, that nitrogen labelling can resolve these ambiguities. Thus, if the $^{14}$N at ring position 4 is replaced with $^{15}$N, then the one and two step sulfur migrations lead to the formation of 3-phenyl-1,2,4-thiadiazole-4-$^{15}$N (46-$^{15}$N) and 3-phenyl-1,2,4-thiadiazole-2-$^{15}$N (46-2$^{15}$N), respectively. Furthermore, sulfur migration in the opposite direction will result in the formation of 5-phenyl-1,2,4-thiadiazole-2-$^{15}$N (31-2$^{15}$N).

Figure 78a-b show GC trace and mass spectrum of the solution of 31-$^{15}$N before irradiation, respectively.
The mass spectrum of the starting material 31-4$^{15}$N before irradiation (Figure 78b) exhibits a molecular ion peak at m/z 163, which is consistent with the molecular weight of 31-4$^{15}$N (MW 163). The spectrum also exhibits an intense peak at m/z 136 due to the loss of HC$^{14}$N but no signal at m/z 135, which would result if HC$^{15}$N was lost from the molecule. The mass spectrum also exhibits peaks at m/z 104 and 105 due to the formation of [PhC$^{15}$N]$^+$ and [PhC$^{15}$NH]$^+$, respectively, but no significant signal at m/z 103, which would indicate the formation of [PhC$^{14}$N]$^+$. Scheme 34 shows the possible fragmentation pathways of 31-4$^{15}$N.

Figure 78a: GC-trace of 5-phenyl-1,2,4-thiadiazole-4-$^{15}$N solution before irradiation

Figure 78b: Mass spectrum of 5-phenyl-1,2,4-thiadiazole-4-$^{15}$N before irradiation
Results and Discussion

Scheme 34: Possible fragmentation pathways of 5-phenyl-1,2,4-thiadiazole-4-$^{15}$N

In the initial photochemical experiment, a solution of 31-$^{14}$N (4 mL, $3 \times 10^{-2}$ M) was placed in a Pyrex tube (12 cm × 0.7 cm). The tube was sealed with a rubber septum, purged with argon for 15 min, and irradiated with sixteen > 290 nm mercury lamps for a total of 180 min. The mass spectrum of the unconsumed reactant (Figure 79), which eluted with a retention time of 11.5 min, again shows a molecular ion at m/z 163 and an intense signal at m/z 136 due to the loss of HC$^{14}$N. In addition, however, the mass spectrum also shows a peak at m/z 135 due to the loss of HC$^{15}$N. This peak was not observed in the mass spectrum of 31-$^{15}$N before irradiation. This reveals that 31-$^{15}$N has been converted to 31-$^{2}$N during the irradiation. The corrected ratio of the 135:136 signals is 1:2.47. This shows that after 180 min of irradiation the unconsumed reactant is a mixture of 29% of 31-$^{2}$N and 71% of 31-$^{15}$N.
Mass spectrum analysis of the $^{15}$N-labelled 3-phenyl-1,2,4-thiadiazole and 2-phenyl-
and 2,4-diphenyl-1,3,5-triazine photoproducts obtained after this prolong irradiation also
exhibited $^{15}$N scrambling. The origin of this scrambling is unclear, however, due to the
extensive scrambling in the reactant $^{31-415N}$.

![Mass spectrum analysis](image)

**Figure 79:** GC-trace of the un-consumed reactant after 180 min of irradiation

In order to minimize the extent of $^{15}$N scrambling in the reactant, the irradiation was
carried out for a shorter period of time. In this experiment the sample (4 mL, $3 \times 10^{-2}$ M)
was irradiated with sixteen $> 290$ nm lamps for a total of 16 min. Aliquots of the reaction
solution were removed after every four min of irradiation, concentrated, and analyzed by the
GC (HP588) interfaced with a mass spectrometer [140°C (5 min), 20°C/min to 240°C
(20 min)].

GLC analysis on GC-PE9000 (Figure 80) shows that only a trace quantity of the
reactant had been consumed after 16 min of irradiation and that only a trace amount of
photoproducts had been formed. Although the consumption of the starting material and
the formation of the products are clearly observed by the GC-PE9000 analysis, the quantities consumed and formed are too small for accurate measurement. The GC-trace (HP588) of this irradiated solution (Figure 81a) shows five volatile components with retention times of 4.2, 10.7, 11.7, 14.0, and 33.5 min.

**Figure 80:** GLC trace (PE9000) of $31-4^{15}$N solution after 16 min of irradiation

**Figure 81a:** GC-trace (HP588) of $31-4^{15}$N solution after 16 min of irradiation
The un-consumed 5-phenyl-1,2,4-thiadiazole-\textsuperscript{15}N eluted with a retention time of 11.7 min. The mass spectrum of this compound (Figure 81b) exhibits a molecular ion at m/z 163 and a base peak at m/z 136 due to the loss of HC\textsuperscript{14}N from the molecular ion. Moreover, the spectrum also reveals the presence of a peak at m/z 135 with an intensity of 7.8 % of the base peak, which is due to the loss of HC\textsuperscript{15}N from the molecular ion. This signal was not present in the mass spectrum of 3\textsuperscript{14}N\textsuperscript{415}N before photolysis. The formation of this peak during irradiation indicates that some 3\textsuperscript{14}N\textsuperscript{415}N has been photochemically converted to 3\textsuperscript{12}N\textsuperscript{215}N. Figure 82 is a plot of the ratio of the observed intensities of 135/136 peaks as a function of irradiation time, which shows that the ratio slowly increase from 0 before irradiation to 0.07 after 16 min of irradiation. This indicates that at this point the un-consumed reactant consists of 93.5% 3\textsuperscript{14}N\textsuperscript{415}N and 6.5% 3\textsuperscript{12}N\textsuperscript{215}N.

\textbf{Figure 81b:} Mass spectrum of the un-consumed reactant
Figure 82: Plot of the ratio of the intensities of the 135/136 peaks

The mass spectrum of the compound that eluted with a retention time of 4.2 min (Figure 81c) exhibits peaks at m/z 103 and 104, which are consistent with the molecular ions of benzonitrile-$^{14}$N (43-$^{14}$N) and benzonitrile-$^{15}$N (43-$^{15}$N). Figure 83 is a plot of the ratio of the observed intensities of the 103/104 peaks as a function of irradiation time. It reveals that the ratio gradually increased from a value of 0.17 after two min of irradiation to a ratio of 0.31 after 16 min of irradiation. The corrected ratio at this time is 0.32.
Results and Discussion

Figure 81c: Mass spectrum of benzonitrile-photoproduct at 16 min of irradiation

Figure 83: Plot of the ratio of the intensities of the 103/104 peaks
Results and Discussion

It should be pointed out that if the benzonitrile formed in this photoreaction came only directly from 5-phenyl-1,2,4-thiadiazole-$^{15}$N, the benzonitrile-$^{14}$N to benzonitrile-$^{15}$N ratio should also be 0.07. As previously stated, however, the observed corrected ratio is 0.32. This indicates that the benzonitrile formed consists of 24% $^{14}$N and 76% $^{15}$N.

The photoproduct which eluted with a retention time of 11.7 min was identified as 3-phenyl-1,2,4-thiadiazole-$^{15}$N, the phototransposition product. As previously discussed (see synthetic section), the mass spectrum of 3-phenyl-1,2,4-thiadiazole 46 (Figure 84) exhibits major fragmentation pathways involving the loss of HCNS to form [PhCN]$^{\bullet+}$ with an intense signal at m/z 103 and the loss of HCN to form [PhCNS]$^{\bullet+}$ which has an intense signal at m/z 135.

The mass spectrum of the $^{15}$N-labelled 3-phenyl-1,2,4-thiadiazole photoproduct, shown in Figure 81d, exhibits a molecular ion at m/z 163 and two intense peaks at m/z 135 and 136 with a corrected 135/136 ratio of 1.13. Whereas the peak at m/z 135 is consistent with the loss of HC$^{15}$N from the molecular ion, the signal at m/z 136 results from the loss of HC$^{14}$N. This mass spectral data indicates that the $^{15}$N-labelled phototransposition product is a mixture of 53% 46-$^{14}$N and 47% of 46-$^{15}$N.

Figure 85 is a plot of the ratio of the m/z 135 and 136 peak as a function of irradiation time. This plot shows that the ratio is constant over the entire time monitored. Thus, even very early in the photoreaction when the product can first be detected, it is formed with essentially complete scrambling of the $^{15}$N between position 2 and 4.
Results and Discussion

![Mass spectrum of un-labelled 3-phenyl-1,2,4-thiadiazole](image)

**Figure 84:** Mass spectrum of un-labelled 3-phenyl-1,2,4-thiadiazole

![Plot of the ratio of the intensities of 135/136 peaks of 3-phenyl1,2,4-thiadiazole-15N (photoproduct)](image)

**Figure 85:** Plot of the ratio of the intensities of 135/136 peaks of 3-phenyl1,2,4-thiadiazole-15N (photoproduct)
Figure 81d: Mass spectrum of 3-phenyl-1,2,4-thiadiazole - photoproduct upon irradiation of 5-phenyl-1,2,4-thiadiazole-4-$^{15}$N

The photo ring-expansion products, 2-phenyl- and 2,4-diphenyl-1,3,5-triazine eluted with retention times of 10.7 and 35.5 min, respectively. The mass spectrum of the first eluted triazine, shown in Figure 81e, exhibits molecular ions at m/z 158 and 159 which indicate the formation of 2-phenyl-1,3,5-triazine molecules containing one $^{15}$N and two $^{15}$N atoms. Figure 86 shows a plot of the ratio of the intensities of the 158/159 peaks as a function of irradiation time. This plot reveals that the ratio of the 158:159 peaks is constant at a value of 0.8 from 8 min to 16 min of irradiation. The observed corrected ratio at 16 min is 0.84. This indicates that the photoproduct is a mixture with 46% of the 2-phenyl-1,3,5-triazine molecules containing one $^{15}$N atom and 54% containing two $^{15}$N atoms per molecule.
Figure 81e: Mass spectrum of 2-phenyl-1,3,5-triazine photoproduct containing one $^{15}$N and two $^{15}$N atoms

Figure 86: Plot of the ratio of the intensities of the 158/159 peaks
The mass spectrum of the un-labelled triazine 52 (Figure 87) reveals a molecular ion at m/z 157 and a base peak at m/z 104. The major possible fragmentation pathways could be expected as shown in Scheme 35.
According to the fragmentation patterns of the un-labelled triazine 39 in Scheme 35, this could lead to the structures of 2-phenyl-1,3,5-triazine photoprodut containing one $^{15}\text{N}$ and two $^{15}\text{N}$ atoms, which are shown in Scheme 36.
Scheme 36: Possible structures and fragmentation patterns of 2-phenyl-1,3,5-triazine containing one $^{15}$N and two $^{15}$N atoms

The fragmentation patterns in Scheme 36 reveals the ratio of 103 : 104 : 105 peaks at 1 : 2 : 1. However, the formation of 2-phenyl-1,3,5-triazine containing one $^{15}$N and two $^{15}$N atoms was presented with the corrected ratio of 0.84, thus, the actual ratio of 103 : 104 : 105 peaks would be 1 : 2.1 : 1.1. However, the observed corrected ratio is observed at value of 1 : 4.4 : 3.2.
Results and Discussion

The mass spectrum of the second eluted triazine 40, which is shown in Figure 81f, exhibits molecular ions at m/z 234 and 235 which indicate the formation of 2,4-diphenyl-1,3,5-triazine molecules containing one $^{15}$N and two $^{15}$N atoms. This triazine was unable to be detected before 8 min of irradiation. However, at irradiation times from 8 to 16 min the corrected ratio of the 234/235 peaks is constant at a value of 1.2. This indicates that the photoproduct is a mixture with 54% of the 2,4-diphenyl-1,3,5-triazine molecules containing one $^{15}$N atom and 46% containing two $^{15}$N atoms per molecule.

**Figure 81f:** Mass spectrum of 2,4-diphenyl-1,3,5-triazine photoproduct containing one $^{15}$N and two $^{15}$N atoms
The mass spectrum of the un-labelled triazine 40 (Figure 88) reveals a molecular ion at m/z 233 and a base peak at m/z 103. In the mass spectrum of triazine containing $^{15}$N, it reveals a peak at m/z 104 as a base peak. The observed corrected ratio of 103/104 peaks is 1.03. Scheme 32 shows the possible fragmentation pathways of this triazine 40 containing one and two $^{15}$N atoms. According to Scheme 32, the ratio of 103/104 fragments should be 1 : 1. Interestingly, the observed corrected ratio of 103/104 peaks is consistent with the ratio predicted in Scheme 37.

![Mass spectrum of regular 2,4-diphenyl-1,3,5-triazine](image_url)

**Figure 88:** Mass spectrum of regular 2,4-diphenyl-1,3,5-triazine
### Scheme 37: Possible fragmentation pathways of 2,4-diphenyl-s-triazine-$^{15}$N
2.4.3 Preparative scale photolysis

2.4.3.1 Preparative gas chromatography: isolation of the un-consumed reactant and the phototransposition product

A solution of 5-phenyl-1,2,4-thiadiazole-4$^{15}$N (31-4$^{15}$N) in acetonitrile (1.8×10$^{-2}$M; 25 mL) was irradiated with sixteen > 290 nm lamps for 180 min while the solution was continuously purged with a fine steam of argon gas. The resulting reaction solution turned to a light brown clear solution with a fine solid precipitate. This preparative scale photolysis was focused on the isolation of the un-consumed reactant and the phototransposition product, 3-phenyl-1,2,4-thiadiazole-15N, by preparative gas chromatography and preparative thin layer chromatography.

The un-consumed reactant, 5-phenyl-1,2,4-thiadiazole-15N, eluted with a retention time of 9.5 min. TLC analysis indicated the presence of two components which expected to be the un-consumed reactant and 2-phenyl-1,3,5-triazine-15N. Thus, this mixture was subjected to preparative layer chromatography [hexane:chloroform (3:2)]. The un-consumed reactant, which had an $R_f$ of 0.8 (10 runs), was removed from the plate. Figure 89 shows the 1H-NMR spectrum of the isolated un-consumed reactant. The spectrum indicates the presence of 5-phenyl-1,2,4-thiadiazole-15N with two multiplets at δ 7.58-7.62 (m, 3H), δ 8.06-8.09 (m, 3H) and a doublet at δ 8.803 (d, 1H, $J = 13.89$ Hz). The 15N-spectrum of the reactant, 5-phenyl-1,2,4-thiadiazole-4-15N (31-4$^{15}$N), before irradiation (Figure 90a) exhibits a signal due to the 15N atom at position 4 as a doublet at δ 300.9 ($J = 13.9$ Hz) while the 15N-spectrum of the isolated un-consumed reactant (after 180 min of irradiation) (Figure 90b) reveals an additional signal at δ 254.7 as a singlet. Since mass spectral analysis indicated that 31-4$^{15}$N had undergone photo-15N-scrambling to 31-2$^{15}$N, the new signal at δ 254.7 is expected to be due to the 15N at position 2 in 31-2$^{15}$N.
Figure 89: $^1$H-NMR spectrum of the isolated un-consumed 5-phenyl-1,2,4-thiadiazole-$^{15}$N
**Figure 90a:** $^{15}$N-NMR spectrum of 5-phenyl-1,2,4-thiadiazole-4-$^{15}$N before irradiation

**Figure 90b:** $^{15}$N-NMR spectrum of the isolated un-consumed reactant after irradiation
The phototransposition product was isolated from the reaction mixture by preparative gas chromatography with a retention time of 17 min. TLC analysis of this isolated product indicated the presence of at least two components in this sample. The $^1$H-NMR spectrum of this isolated product (Figure 91) exhibits three multiplets at $\delta$ 7.52-7.62, 8.06-8.09, and 8.34-8.78 and three doublets at $\delta$ 8.80 ($J = 13.89$ Hz), $\delta$ 10.27 ($J = 11.62$), and $\delta$ 10.275 ($J = 1.52$ Hz). This $^1$H-NMR spectrum reveals that this sample is a mixture between 5- and 3-phenyl-1,2,4-thiadiazole-$^{15}$N, which indicates an unsuccessful isolation. The doublet at $\delta$ 8.80 ($J = 13.89$ Hz) is due to the presence of the unconsumed reactant. By comparison with the $^1$H-spectrum of 3-phenyl-1,2,4-thiadiazole-$^{14}$N, the ring proton at position 5 of thiadiazole ring is known to appear as a singlet at $\delta$ 10.3. Thus, the two overlapping doublets at $\delta$ 10.27 ($J = 11.62$), and $\delta$ 10.275 ($J = 1.52$ Hz) are due to the presence of 3-phenyl-1,2,4-thiadiazole-4-$^{15}$N ($46\text{-}4^{15}$N) and 3-phenyl-1,2,4-thiadiazole-2-$^{15}$N ($46\text{-}2^{15}$N), respectively, confirming $^{15}$N-scrambling in 3-phenyl-1,2,4-thiadiazole-$^{15}$N. The doublet at $\delta$ 10.27 with the larger coupling constant ($J = 11.62$ Hz) is expected due to the ring proton at position 5 of $46\text{-}4^{15}$N coupling with the $^{15}$N nucleus at ring position 4 while the doublet at $\delta$ 10.275 with smaller coupling constant ($J = 1.52$ Hz) is expected due to the ring proton at position 5 of $46\text{-}2^{15}$N coupling with the $^{15}$N nucleus at position 2. The $^{15}$N-spectrum (Figure 92) also reveals a signal due to the presence of $31\text{-}4^{15}$N as a doublet at $\delta$ 302.3 ($J = 13.9$ Hz) and $31\text{-}2^{15}$N as a singlet at $\delta$ 261.4. The spectrum also reveals a doublet at $\delta$ 307.76 ($J = 11.9$ Hz), which is expected due to the presence of $46\text{-}4^{15}$N based on the corresponding coupling constant in the $^1$H-spectrum, which was proposed due to this compound. However, according to the previous GC analysis results indicated the 50% $^{15}$N-scrambling in the phototransposition, therefore, this $^{15}$N-spectrum should also present a doublet with a small coupling constant due to 3-phenyl-1,2,4-thiadiazole-2-$^{15}$N. But there is no any signal indicates the presence of this product.
Figure 91: $^1$H-NMR spectrum of the isolated 3-phenyl-1,2,4-thiadiazole-$^{15}$N
Figure 92: $^{15}$N-NMR spectrum of the isolated 3-phenyl-1,2,4-thiadiazole-$^{15}$N
2.3.4.2 Preparative layer chromatography: isolation of the unconsumed reactant and the phototransposition product.

A solution of purified 5-phenyl-1,2,4-thiadiazole-4-\(^{15}\text{N}\) (31-4\(^{15}\text{N}\)) \((2\times10^{-2}\text{ M, }8\text{ mL})\) was photolysed to 40\% consumption of the reactant. The reaction solution was concentrated to dryness (42 mg), re-dissolved in small amount of dichloromethane and subjected to preparative layer chromatography. Dichloromethane:hexane (4:1) was employed as a developing solvent. The un-consumed reactant was removed from the plate with a \(R_f\) of 0.39 (4 runs) and the phototransposition product was removed with a \(R_f\) of 0.69 (4 runs).

The \(^1\text{H-NMR}\) spectrum of the band with \(R_f\) of 0.69 (Figure 93) exhibits two multiplets at \(\delta 7.28-7.53\) (m, 3H), \(\delta 7.95-7.98\) (m, 2H) and a doublet at \(\delta 8.69\) (d, 1H, \(J = 13.89\) Hz) which are indicating the presence of the un-consumed reactant, 5-phenyl-1,2,4-thiadiazole-\(^{15}\text{N}\). The \(^1\text{H-NMR}\) spectrum of the band with \(R_f\) of 0.39 (Figure 94) exhibits two multiplets at \(\delta 7.23-7.50\) (m, 3H), \(\delta 7.83-8.34\) (m, 2H) and two overlapping doublets at \(\delta 9.875\) (d, \(J = 11.12\) Hz) and \(\delta 9.875\) (d, \(J = 1.52\) Hz). These signals indicate the presence of 3-phenyl-1,2,4-thiadiazole-\(^{15}\text{N}\) with \(^{15}\text{N}\) atom in both position 2 \((J_{\text{H15N}} = 1.52\) Hz\) and 4 \((J_{\text{H15N}} = 11.12\) Hz\).
Figure 93: $^1$H-NMR spectrum of the isolated unconsumed reactant after 180 min of irradiation
Figure 94: $^1$H-NMR spectrum of a mixture of 46-4$^{15}$N and 46-2$^{15}$N
2.5 Photochemistry of 3-methyl-5-phenyl-1,2,4-thiadiazole-4\textsuperscript{15}N

2.5.1 Synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole-4\textsuperscript{15}N

3-Methyl-5-phenyl-1,2,4-thiadiazole (54) was previously synthesized by the cyclization of 55 with 33 as shown in Scheme 38.

Scheme 38: Synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole

3-methyl-5-phenyl-1,2,4-thiadiazole-4\textsuperscript{15}N (54-\textsuperscript{15}N) was synthesized from commercially available benzamide-\textsuperscript{15}N (38-\textsuperscript{15}N) by the procedure outlined in Scheme 39.
Results and Discussion

Scheme 39: Synthetic pathway of 3-methyl-5-phenyl-1,2,4-thiadiazole-4$^{15}$N

Figure 95a-b and 96 exhibit the $^1$H–NMR and $^{13}$C–NMR spectra of 34$^{15}$N, respectively. The spectra reveal the complicated couplings similar to the $^1$H–NMR spectra of 34$^{15}$N previously synthesized as the starting material for the synthesis of 31-4$^{15}$N.

Figure 95a: $^1$H – NMR spectrum of thiobenzamide-$^{15}$N
Results and Discussion

Figure 95b: $^1$H–NMR spectrum of thiobenzamide-$^{15}$N; scale expansion at $\delta$ 7.12-7.92

Figure 96: $^{13}$C–NMR spectrum of thiobenzamide-$^{15}$N
The second step in this synthetic pathway was the preparation of N-[(dimethylamino)ethylidine]thiobenzamide-\(^{15}\text{N}\) (55-\(^{15}\text{N}\)) by a condensation reaction of \(^{34}\text{N}\) with 56. The desired \(^{15}\text{N}\)-labeled-amidine 55-\(^{15}\text{N}\) was obtained as orange crystals in 82.3% yield with the melting point of 110-113°C. The \(^1\text{H}\)–NMR spectrum of these crystals (Figure 97) exhibits the two multiplets at \(\delta 7.29-7.42\) (3H) and \(\delta 8.22-8.24\) (2H), which were assigned to para-meta and ortho-phenyl protons, respectively. The two singlets (3H) at \(\delta 3.19\) and 3.21 are the absorptions due to the two sets of the non-equivalent methyl protons bonded to the amino group. The protons of the methyl group which is bonded to the imine carbon is revealed as a singlet (3H) at \(\delta 2.47\).

\[\text{Figure 97: } ^1\text{H–NMR spectrum of N-[(dimethylamino)ethylidine]thiobenzamide-}^{15}\text{N}\]
In the $^{13}$C–NMR spectrum (Figure 98a), the most down field doublet at $\delta$ 202.7 (J = 6.90 Hz) is assigned to the thiocarbonyl. It appears as a doublet due to the coupling of this carbon with $^{15}$N atom. The imine carbon absorbs at $\delta$ 168.3. This signal also appears as a doublet (J = 12.30 Hz) due to the coupling of this carbon with $^{15}$N atom. The four signals at $\delta$ 128.0, 128.8, 131.3 and 142.9 were assigned to the ring phenyl carbons. However, upon the scale expansion (Figure 98b) the spectrum also reveals a pair of doublets at $\delta$ 128.8 and 142.9 with coupling constants of 2.30 and 8.40 Hz, respectively. According to the $^1$H–$^{13}$C correlation spectrum (Figure 99), the signal at $\delta$ 128.8 (J = 2.30 Hz) is assigned as ortho-phenyl ring carbon since this signal correlates with the signal at $\delta$ 8.22-8.24 (multiplet,2H) in the $^1$H–spectrum which was assigned to ortho-phenyl ring protons. The signal at $\delta$ 142.9 (J = 8.4 Hz) can also be assigned to the meta-phenyl ring carbon since this signal correlates with the signal at $\delta$ 7.29-7.42 (3H) in the $^1$H – spectrum which was assigned to the para- and meta- phenyl ring protons. The intensity of this signal is also consistent with the assignment to meta-phenyl ring carbons. These two phenyl-carbon signals appear as two doublets, presumably due to a long-range coupling of these carbons with $^{15}$N atom. The spectrum reveals the two non-equivalent methyl carbons of the amino group as two singlets at $\delta$ 39.5 and 39.7. The methyl carbon attached to the imine carbon appears at $\delta$ 18.4.
Results and Discussion

Figure 98a: $^{13}$C–NMR spectrum of N-[(dimethylamino)ethylidene]thiobenzamide-$^{15}$N

Figure 98b: $^{13}$C–scale expansion spectrum of 55-$^{15}$N
Figure 99: $^1$H-$^1^3$C correlation spectrum of 55-$^{15}$N
The $^{15}\text{N}\text{-NMR}$ spectrum (Figure 100) exhibits a singlet at $\delta$ 289.5 which is due to the single $^{15}\text{N}$ atom in the molecule. Surprisingly, the spectrum does not exhibit the splitting of this signal which could be expected due to the coupling of $^{15}\text{N}$ with $^{13}\text{C}$ as showing in $^{13}\text{C}$-NMR spectrum. This is most likely due to the very low concentration of $^{13}\text{C}$ in the compound.

**Figure 100:** $^{15}\text{N}\text{-NMR}$ spectrum of N-[(dimethylamino)ethylidine]thiobenzamide-$^{15}\text{N}$
The orange crystals were also analyzed by GC-MS [120°C (10 min), 20°C /min to 240°C (30 min)] (Figure 101a). The mass spectrum of the peak that eluted with a retention time of 39.5 min (Figure 101b) shows a molecular ion at m/z 207, which corresponds to the molecular weight of the desired product, N-[(dimethylamino)ethylidine]thiobenzamide-$^{15}$N (55-$^{15}$N). The trace also exhibits the presence of some impurities.

**Figure 101a:** GC-trace of N-[(dimethylamino)ethylidine]thiobenzamide-$^{15}$N

**Figure 101b:** Mass spectrum of the peak eluted at a retention time of 39.5 min
The third step of this pathway is the amination cyclization of $^{15}\text{N}_{55}$ with $^{33}$ using pyridine as a basic catalyst. 3-Methyl-5-phenyl-1,2,4-thiadiazole-$^{15}\text{N}_{4}$ ($^{54-4}_{15}\text{N}$) was obtained as a colorless crystals in 80% yield with the melting point of 50-52°C.

The GC-chromatogram [140°C (5 min), 20°C/min to 240°C (20 min)] of these colorless crystals (Figure 102a) exhibits a major peak with a retention time of 10.8 min. The mass spectrum of this peak (Figure 102b) exhibits a molecular ion at m/z 177, which is consistent with the molecular weight of $^{54-4}_{15}\text{N}$ (MW 177). The spectrum also exhibits a base peak at m/z 136, which is consistent with the cleavage of $[\text{C}_6\text{H}_5\text{C}_{15}\text{NS}]^{+}$ and a peak at m/z 73, which is consistent with the cleavage $[\text{CH}_3\text{CNS}]^{+}$.

**Figure 102a:** GC-trace of 3-methyl-5-phenyl-1,2,4-thiadiazole-$^{15}\text{N}_4$
The $^1$H–NMR of this solid (Figure 103) shows two multiplets at $\delta$ 7.46-7.50 (3H) and $\delta$ 7.90-7.92 (2H), which could be assigned to the para-meta and ortho-phenyl ring protons, respectively. The doublet at $\delta$ 2.71 ($J = 2.27$ Hz) is assigned to the protons of methyl group attached to C-3 of thiadiazole ring. This signal appears as a doublet due to a long-range coupling of these protons with $^{15}$N atom at position 4.
Figure 103: $^1$H–NMR spectrum of 3-methyl-5-phenyl-1,2,4-thiadiazole-4\textsuperscript{15}N
The $^{13}$C–NMR (Figure 104a) reveals the signal of carbon at position 5 on the thiadiazole at $\delta$ 188.5. The signal at $\delta$ 174.5, which appears as a doublet ($J = 2.30$ Hz), can be assigned to the carbon at position 3 of the thiadiazole ring. The assignment of these two carbons is based on the previous $^{13}$C–NMR spectral assignment of 5-phenyl-1,2,4-thiadiazole-$^{15}$N (31-$^{15}$N). The doublet at $\delta$ 174.5 ($J = 2.30$ Hz) can be due to the coupling of this carbon with $^{15}$N atom at position 4. Surprisingly, the carbon at position 5 is also bonded to $^{15}$N atom at position 4 but the spectrum does not exhibit the coupling of this carbon with $^{15}$N atom. The four signals at $\delta$ 127.8 (d; $J = 2.30$ Hz), 129.7, 130.9 (d; $J = 6.16$ Hz) and 132.3 were assigned to the phenyl ring carbons. The doublet at $\delta$ 19.5 (d; $J = 8.40$ Hz) was assigned to the methyl carbon bonded to the position 3 of the thiadiazole ring. These spectral assignments were confirmed by the $^{13}$C–DEPT 135 spectrum, shown in Figure 104b. The doublet at $\delta$ 19.5 ($J = 8.40$ Hz) still appears in the $^{13}$C–DEPT 135 spectrum, which is consistent with the assignment to the methyl carbon. The two signals at $\delta$ 174.5 and 188.6, which were assigned to the two carbons at positions 3 and 5 of the thiadiazole ring, are not observed in the $^{13}$C–DEPT 135 spectrum since these signals are due to quaternary carbons. Three of the four signals, which absorb in the phenyl region, still appear in the $^{13}$C–DEPT 135 spectrum. Thus, these signals can be assigned to the ortho-, meta- and para-phenyl ring carbons. The doublet at $\delta$ 130.9 (d; $J = 6.16$ Hz), which was, however, not observed in the $^{13}$C–DEPT 135 spectrum, and therefore can be assigned to the phenyl carbon at ring position 1. The observed splitting in some phenyl carbon signals is presumably due to a long-range couplings with $^{15}$N atom.
Figure 104a: $^{13}$C-NMR spectrum of 3-methyl-5-phenyl-1,2,4-thiadiazole-4$^{15}$N
Figure 104b: $^{13}$C–DEPT 135 spectrum of 3-methyl-5-phenyl-1,2,4-thiadiazole-4$^{15}$N

The $^{15}$N–NMR spectrum (Figure 105) reveals a doublet at $\delta$ 301.7 ($J = 2.00$ Hz), which can be assigned to the $^{15}$N atom at position 4 on the thiadiazole ring. This doublet could be due to a long range coupling of this $^{15}$N atom with the protons of the methyl group bonded to the carbon at position 3 of the thiadiazole ring. If this was true then the $^{15}$N signal should appear as a quartet and, in fact, it does appear to be a quartet with very small coupling constant and unable to be resolved as a clear quartet. This assignment is consistent with the observed coupling constant of the methyl protons in the $^1$H–spectrum ($J = 2.27$ Hz).
Figure 105: $^{15}$N–NMR spectrum of 54-4$^{15}$N and the scale expansion showing an un-resolved quartet
2.5.2 Photochemistry of 3-methyl-5-phenyl-1,2,4-thiadiazole-4-$^{15}$N

In an earlier part of this thesis it was shown that 5-phenyl-1,2,4-thiadiazole-4-$^{15}$N (31-$^{15}$N) undergoes phototransposition to 3-phenyl-1,2,4-thiadiazole-$^{15}$N with complete scrambling of $^{15}$N between position 2 and 4 of the thiadiazole ring. Upon more prolong irradiation, $^{15}$N scrambling between rings position 2 and 4 in the un-consumed reactant was also observed. These observations are consistent with the mechanism shown in Scheme 40.

It has also been previously shown in this thesis that 3-methyl-5-phenyl-1,2,4-thiadiazole (54) undergoes photoreaction to yield benzonitrile (43) in 66%, 5-methyl-3-phenyl-1,2,4-thiadiazole (57) in 10%, 2,4-dimethyl-6-phenyl-1,3,5-triazine (65) in 33% and 2-methyl-4,6-diphenyl-1,3,5-triazine (66) in 6.6%. In this section the results of a study of the photochemistry of 3-methyl-5-phenyl-1,2,4-thiadiazole-4-$^{15}$N (54-$^{15}$N) is presented.

![Scheme 40: The N-scrambling mechanism](image-url)
A solution of 54-4\(^{15}\)N (2.5×10\(^{-2}\) M) in acetonitrile was placed in a Pyrex tube (12 cm × 0.7 cm). The tube was sealed with a rubber septum, purged with argon gas for 30 min, and irradiated with sixteen > 290 nm mercury lamps for a total of 18 min. Aliquots of the reaction solution were removed after every 4 min of irradiation, concentrated, and analysed by GC-MS [130°C (35 min), 10°C/min to 240°C (20 min)]. Figure 106a-b show GC analysis and mass spectrum of the solution of 54-4\(^{15}\)N before irradiation.

**Figure 106a:** GC-trace of 3-methyl-5-phenyl-1,2,4-thiadiazole-4\(^{15}\)N before irradiation

**Figure 106b:** Mass spectrum of 3-methyl-5-phenyl-1,2,4-thiadiazole-4\(^{15}\)N before irradiation
The mass spectrum of the starting material before irradiation (Figure 106b) exhibits a peak at m/z 177, which is consistent with the molecular weight of $\text{54-4}^{15}\text{N}$ (MW 177). The fragmentation pattern of this compound is analogous to the fragmentation of 5-phenyl-1,2,4-thiadiazole-4$^{15}\text{N}$ ($\text{31-4}^{15}\text{N}$) with two major pathways. As shown in Scheme 41, fragmentation pattern $a$ leads to the base peak at m/z 136 due to the loss of CH$_3$$^{14}\text{N}$. No signal, however, is observed at m/z 135, which would result from the loss of CH$_3$$^{15}\text{N}$. Pathway $b$ leads to an intense signal at m/z 73 due to the loss of PhC$^{15}\text{N}$.

\[ \text{Scheme 41: Two major fragmentation pathways of 54-4}^{15}\text{N} \]
GLC analysis (PE9000) (Figure 107) shows that only trace quantity of the reactant $^{54-4}\text{N}^{15}$ had been consumed after 18 min of irradiation and that only trace amounts of the photoproducts had been formed. Although the consumption of the starting material and the formation of the products are clearly observed by the GLC analysis, the quantities consumed and formed are too small for accurate measurement. GC (HP588) analysis of the irradiated solution (Figure 108a) shows five volatile components with retention times of 5.0, 40.2, 40.5, 42.7, and 57.7 min.

The mass spectrum of the compound, which eluted with a retention time of 5.0 min (Figure 108b), exhibits signals at m/z 103 and 104 with an observed 103/104 ratio of 0.77 which are consistent with the molecular ions of benzonitrile-$^{14}\text{N}$ ($^{43-14}\text{N}$) and benzonitrile-$^{15}\text{N}$ ($^{43-15}\text{N}$). After the intensity of the 104 peak is corrected for p+1 contribution (8.03 % of the 103 peak), the ratio is 0.83. Figure 109 is a plot of the ratio of the intensities of the 103/104 peaks as a function of irradiation time. Although it was not possible to detect this photoproduct until after 5 min of irradiation, the plot shows that the 103:104 ratio is essentially constant at a value of 0.83 from 5 min to 18 min of irradiation.
**Results and Discussion**

**Figure 107:** GLC analysis (PE9000) of the solution of $^{54-4}^{15}$N after 18 min of irradiation

**Figure 108a:** GC-trace (HP588) of the reaction solution at 18 min of irradiation
Figure 108b: Mass spectrum of the peak eluted at a retention time of 5 min; benzonitrile-$^{14}$N and benzonitrile-$^{15}$N

Figure 109: Plot of 103/104 ratio as a function of irradiation
Un-converted 3-methyl-5-phenyl-1,2,4-thiadiazole-$^{15}$N eluted with a retention time of 40.2 min. The mass spectrum of this compound (Figure 108c) exhibits a molecular ion at m/z 177 and a base peak at m/z 136 due to the loss of $[\text{CH}_3\text{C}^{14}\text{N}]$. Interestingly, the mass spectrum also exhibits a peak at m/z 135 due to the loss of $[\text{CH}_3\text{C}^{15}\text{N}]$, which was not present in the mass spectrum before irradiation. The corrected 135:136 ratio is 0.1 from 5 to 18 min. The formation of the signal at m/z 135 after irradiation indicates that some of 54-4$^{15}$N has been photochemically converted to 54-2$^{15}$N.

It is of interest to compare the extent of $^{15}$N scrambling in the reactant, 54-4$^{15}$N, with the degree of scrambling in benzonitrile photoproduct. Mass spectral analysis shows that after 18 min of irradiation the un-consumed reactant is 90% 54-4$^{15}$N and 10% of 54-2$^{15}$N. If the observed benzonitrile (43) is being formed only from 3-methyl-5-phenyl-1,2,4-thiadiazole-$^{15}$N, the benzonitrile-$^{14}$N : benzonitrile-$^{15}$N ratio should be 0.1. As previously presented, the actual observed corrected ratio was 0.82 indicating that some or all of benzonitrile is formed from a different source by a pathway, which results in a much greater extent of $^{15}$N scrambling.
The compound which eluted with a retention time of 40.5 min has previously been identified as 2,4-dimethyl-6-phenyl-1,3,5-triazine (65), which has a molecular weight of 185. The mass spectrum of this photoproduce (Figure 108d) exhibits molecular ions at m/z 186 and 187 with an observed 186/187 ratio of 0.76 and a corrected ratio of 0.86. Figure 110 is a plot of the ratio of the intensities of the 186/187 peaks as a function of irradiation time. The plot shows that the ratio of the 186/187 peaks is constant at a value of 0.76 from 5 min to 18 min of irradiation. This reveals that 2,4-dimethyl-6-phenyl-1,3,5-triazine has been formed with both one $^{15}$N and two $^{15}$N atoms per molecule. Although it may be a coincidence, it is also interesting to note that the corrected observed one $^{15}$N : two $^{15}$N ratio of 0.86 is very similar to the benzonitrile-$^{14}$N : benzonitrile-$^{15}$N ratio which was observed to be 0.83.
Figure 108d: Mass spectrum of the peak eluted at a retention time of 40.5 min

Figure 110: Plot of ratio of the 186/187 peaks as a function of irradiation
The mass spectrum of un-labelled 2,4-dimethyl-6-phenyl-1,3,5-triazine (65) is shown in Figure 111. This spectrum exhibits a molecular ion at m/z 185 and major fragments with m/z 103 (base peak) and 82 due to the formation of [PhCN]^+ and [C₄H₆N₂]^+ fragment, respectively. Scheme 42 shows the possible fragmentation pathways for the triazine containing one and two ^1⁵N atoms per molecule. According to Scheme 42, it is expected that the ratio of the m/z 82 : 83 : 84 signals in the mass spectrum would be 1 : 5 : 2. Interestingly, the actual spectrum, shown in Figure 108d, shows that the corrected observed ratio is observed to be 1 : 5.4 : 2.4. Scheme 42 also reveals the expected ratio of 103/104 peaks at value of 1.7. The observed corrected ratio of 103/104 peaks is 1.6, which is consistent with this scheme.
Scheme 42: Possible fragmentation pathways for the triazine containing one and two $^{15}$N atoms.
The mass spectrum of the compound which eluted with a retention time of 42.7 min (Figure 108e) exhibits a molecular ion peak at m/z 177. This indicates that this compound is isomeric with the reactant, 54-4\(^{15}\)N which has a retention time of 40.2 min. This photoproduct was assigned to the structure of the phototransposition product, \(^{15}\)N-labelled 5-methyl-3-phenyl-1,2,4-thiadiazole (57-\(^{15}\)N). The fragmentation pattern of this compound without \(^{15}\)N-labelling, shown in Figure 112, consists of the two major pathways as previously discussed for 3-methyl-5-phenyl-1,2,4-thiadiazole (54). The mass spectrum (Figure 112) of an authentic sample of 57 reveals a molecular ion peak at m/z 176. It also reveals two peaks at m/z 135 (base peak) due to the loss of CH\(_3\)CN and at 103 due to the formation of [PhCN]\(^+\) fragment corresponding to the two major fragmentation pathways.

![Mass spectrum](image)

**Figure 108e:** Mass spectrum of the peak eluted at a retention time of 42.7 min; 5-methyl-3-phenyl-1,2,4-thiadiazole contains \(^{15}\)N atom
The mass spectrum of the 5-methyl-3-phenyl-1,2,4-thiadiazole-15N formed upon photolysis of $\text{54-4}^{15}\text{N}$, shown in figure 108e, also exhibited an intense signal at m/z 135 due to the loss of CH$_3$C$^{14}$N and also a signal of an equal intensity at m/z 136 due to the loss of CH$_3$C$^{15}$N. The corrected ratio of these signals was 1.10. This ratio indicates that the phototransposition product consists of 52% of $\text{57-4}^{15}\text{N}$, which would split out CH$_3$C$^{15}$N leaving a m/z 135 fragment, and 48% of $\text{57-2}^{15}\text{N}$, which would lose CH$_3$C$^{14}$N leaving m/z 136 fragment. The mass spectrum also exhibits a signal at m/z 103 due to the formation of the [PhC$^{14}$N]$^+$ fragment and a signal of almost equal intensity at m/z 104 due to the formation of [PhC$^{15}$N]$^+$ fragment in a corrected ratio of 0.95 consistent with a mixture of 49% $\text{57-4}^{15}\text{N}$ and 51% $\text{57-2}^{15}\text{N}$. These results show that the phototransposition product is very close to a mixture of equal amounts of $\text{57-4}^{15}\text{N}$ and $\text{57-2}^{15}\text{N}$. The $^{15}$N scrambling in the phototransposition of $\text{54-4}^{15}\text{N}$ is identical to the $^{15}$N scrambling that was observed during the phototransposition of 5-phenyl-1,2,4-thiadiazole-4-$^{15}$N ($\text{31-4}^{15}\text{N}$).
By comparison with the photoproducts obtained from un-labelled 3-methyl-5-phenyl-1,2,4-thiadiazole (54), the product which eluted with a retention time of 57.7 min was identified as $^{15}$N–labelled 2-methyl-4,6-diphenyl-1,3,5-triazine. The mass spectrum of this product, shown in Figure 108f, exhibits a molecular ion at m/z 248 and 249 indicating that the triazine has been formed with one or two $^{15}$N atoms per molecule. The ratio of the 248/249 peaks observed in the spectrum is 1 : 1.2. When the intensity of the m/z 249 peak is corrected for p+1 contribution (18.64%), the corrected ratio is 1:1. This shows that 2-methyl-4,6-diphenyl-1,3,5-triazine-$^{15}$N$_1$, and -$^{15}$N$_2$ are being formed in equal amounts. Furthermore, Figure 113 shows that the ratio is consistent over the time monitored.

![Figure 113: Formation of 2-methyl-4,6-diphenyl-1,3,5-triazine contains 1 and 2 $^{15}$N atoms](image-url)
**Results and Discussion**

**Figure 109f:** Mass spectrum of the peak eluted at a retention time of 57.7 min; 2-methyl-4,6-diphenyl-1,3,5-triazine contains 1 and 2 $^{15}$N atoms.

**Figure 114:** Mass spectrum of 2-methyl-4,6-diphenyl-1,3,5-triazine.
The mass spectrum of the un-labelled 2-methyl-4,6-diphenyl-1,3,5-triazine (66) (Figure 114) exhibits a base peak at m/z 103 which is due to [PhCN]* with the loss of PhC\textsubscript{2}N\textsubscript{2}H and a very small peak at m/z 104 (2.9% of the base peak after correcting P+1 contribution of the 103 peak). However, the mass spectrum of the triazine containing 1 and 2 \textsuperscript{15}N atoms (Figure 108f) reveals a peak at m/z 104 as a base peak which is due to [PhC\textsuperscript{15}N]* fragment. The peak at m/z 103 is observed with 91% of the base peak (m/z 104). The observed corrected ratio of 103/104 peaks is 1 : 1.01. Scheme 45 shows the possible fragmentation pathways of this triazine containing one and two \textsuperscript{15}N atoms. According to Scheme 45, the ratio of 103/104 fragments should be 1 : 1. Interestingly, the observed corrected ratio of 103/104 peaks has a value of 1, which is consistent with the ratio predicted in Scheme 45.
Scheme 45: Possible fragmentation pathways of 2-methyl-4,6-diphenyl-1,3,5-triazine-15N
2.5.3 Preparative scale photolysis

The preparative photolysis of 54-415N was also studied. A solution of 54-415N in methanol (2.06×10^{-2} M; 25 mL) was irradiated with sixteen > 290 nm lamps for 640 min while the solution was continuously purged with a fine steam of argon. GLC analysis showed that 50% of the reactant had been consumed. The resulting solution turned to a light brown clear solution with a fine solid precipitate. This preparative scale photolysis focused on the isolation of the un-consumed reactant and the phototransposition product. GLC and TLC analyses indicated that 2,4-dimethyl-6-phenyl-1,3,5-triazine (65) had chromatographic properties close to that of 3-methyl-5-phenyl-1,2,4-thiadiazole (54). Thus, methanol was employed as a solvent for the photoreaction in order to minimize the formation of 65 since previous result showed that the yield of 65 was very low when 54 was irradiated in methanol solvent.

The photolyzed solution was filtered, concentrated and subjected to column chromatography [diameter: 1.5cm, silica gel: 8 g, height: 12 cm, hexane:dichloromethane (3:2)]. The column was eluted with hexane–dichloromethane (3:2) (40 mL) and then 10 mL fractions were collected. The polarity of solvent was 10 % increased from hexane:dichloromethane (1:9) → 100 % dichloromethane → dichloromethane : ethyl acetate → 100% ethyl acetate. Finally, 100 % ethanol was applied to the column to elute a yellow band at the base line with the last fraction (40^{th}).

TLC analysis of fractions 16-18 indicated the presence of only one spot with an R_t corresponding to the un-consumed reactant. The \(^1\)H-NMR spectrum of the residue from these combined fractions (Figure 117) exhibits a doublet at δ 2.65 (3H, J = 2.53 Hz) and two multiplets at δ 7.43-7.49 (3H) and 7.89-7.92 (2H). The \(^{13}\)C-NMR spectrum
(Figure 118a) exhibits major signals at δ 18.0 (d, J = 8.4 Hz), 126.3, 128.2, 129.4, 129.5 (d, J = 6.1 Hz), 130.8, 173.1 (d, J = 3.1 Hz), and 187.0.

Figure 118: $^{13}$C-spectrum of fractions 16-18

Figure 117: $^1$H-spectrum of fractions 16-18 and scale expansion of the doublet at δ 2.65
A $^{13}$C-scale expansion of the doublet at $\delta$ 18.0 (figure 118b) reveals a small singlet between the doublet which does not appear in the $^{13}$C-spectrum of the reactant before irradiation. Since the previous mass spectral results indicated $^{15}$N scrambling in the un-consumed reactant, this small singlet could be due to methyl-carbon of 3-methyl-5-phenyl-1,2,4-thiadiazole-2-$^{15}$N (54-2$^{15}$N). This methyl-carbon, however, is also expected to appear as a doublet as the methyl-carbon of 54-4$^{15}$N does. Furthermore, the mass spectrum of this sample (Figure 119a) indicated that 54-4$^{15}$N underwent 50% photo-$^{15}$N-scrambling to 54-2$^{15}$N. Thus, if this singlet was due to the methyl-carbon of 54-2$^{15}$N, it should appear as a larger singlet.
Figure 119: Mass spectrum of the un-consumed reactant at 640 min of irradiation

Figure 118c: $^{13}$C-scale expansion of a doublet at $\delta$ 129.4 and 129.5
The scale expansion of the signals at δ 129.4 and 129.5 (Figure 118c) reveals a singlet at δ 129.4 which is overlapped with a doublet at δ 129.5 (d, J = 6.1 Hz). It is interesting to note that this signal, which was assigned to the phenyl-ring carbon at position 1 in the reactant, appeared before irradiation as a clean doublet (J = 6.1 Hz) due to long range coupling with the $^{15}$N at position 4. The new carbon singlet at δ 129.4 which formed during irradiation is due to the signal of the phenyl-ring carbon at position 1 which is no longer coupled to the $^{15}$N atom in 3-methyl-5-phenyl-1,2,4-thiadiazole-2-$^{15}$N (54-2$^{15}$N). The doublet at δ 173.1 (d, J = 3.1 Hz) is due to a coupling between the carbon at position 5 of the thiadiazole ring and $^{15}$N at position 4 while the signal at δ 187.0 which still appears as a singlet upon an scale expansion is due to the C-3 carbon. The $^{15}$N-NMR spectrum of this sample (Figure 120) exhibits a singlet at δ 260.5 and a doublet at δ 301.7 (J = 2.0 Hz). This doublet, which was present before irradiation, is assigned to $^{15}$N at position 4 of the reactant 54-4$^{15}$N while the new singlet at δ 260.5 is due to $^{15}$N at position 2 of 54-2$^{15}$N. This result is consistent with the mass spectral results which indicated $^{15}$N-scrambling in the reactant.

TLC analyses and $^1$H-NMR analysis of the other fractions did not exhibit any signal which could indicate the presence of 5-methyl-3-phenyl-1,2,4-thiadiazole-$^{15}$N. $^{15}$N-NMR analysis also did not exhibit any $^{15}$N signal which could either indicate that there was no $^{15}$N atom present in those fractions or due to the low concentration of $^{15}$N atom.
Figure 120: $^{15}$N-NMR spectrum of fractions 16-18 and scale expansion of a doublet at $\delta$ 301.7 and a singlet at $\delta$ 260.5
2.6 Photolysis of 5-phenyl-1,2,4-thiadiazole in the presence of ethyl cyanoformate: attempt to identify the formation of benzonitrile sulfide by 1,3-dipolar cycloaddition reaction

According to the photochemistry of substituted isothiazoles, cleavage of the S—N bond results in the formation of azirine intermediates and eventually to the formation of substituted thiazole products (the N-2 and C-3 interchange product), shown in Scheme 46, has been reported as the major photochemical pathway of 4-substituted isothiazoles. In the case of a 1,2,4-thiadiazole, however, cleavage of the S—N bond and ring contraction would produce a diazirine instead of an azirine (Scheme 47).

Scheme 46: N-2 and C-3 interchange photochemical pathway of isothiazoles

Scheme 47: N-2 and C-3 interchange photochemical pathway of 5-phenyl-1,2,4-thiadiazole
According to the results of the photolysis of 5-phenyl-1,2,4-thiadiazole (31), GLC (PE9000) and GC (HP588) analysis of the reaction solution showed no sign corresponding to the formation of 5-phenyl-1,3,4-thiadiazole (37), the N-2 and C-3 interchange product. According to Scheme 47, 31 could undergo the photocleavage of the S-N bond leading to the formation of a 1,5-diradical. In the case of phenyl substituted isothiazole, cyclization of the 1,5-diradical (Scheme 46) would lead to the formation of a substituted azirine. In this case of 5-phenyl-1,2,4-thiadiazole (Scheme 47), cyclization of the 1,5-diradical would result not to an azirine but to a diazirine intermediate which would be expected to be an anti-aromatic compound, thus, cyclization of this 1,5-diradical to produce a diazirine would be a high energy pathway. This could preclude the formation of a diazirine. However, this 1,5-diradical could undergo loss of HCN to yield a 1,3-diradical. This diradical could cyclize to the formation of phenyl substituted thiazirine which could eventually rearrange to yield benzonitrile sulfide (48), as shown in Scheme 48.

**Scheme 48:** Possible mechanism for the formation of benzonitrile sulfide
The trapping of thermally generated benzonitrile sulfide (48) has been successfully carried out by a 1,3-dipolar cycloaddition reaction using ethyl cyanoformate (49) as a dipolarophile to yield ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate (50),\textsuperscript{12} as shown in Scheme 49.

Scheme 49: Trapping of thermally generated 48 by 1,3-dipolar cycloaddition reaction

In order to investigate the possible formation of 48 upon irradiation of 31, the photolysis of 31 in acetonitrile containing 49 was carried out.

A solution of 31 (2.0×10\textsuperscript{-2} M, 4 mL) and 49 (0.1 mL, 1×10\textsuperscript{-1} M) in acetonitrile was placed in a Pyrex tube and a quartz tube, sealed with rubber septa, purged with argon for 30 min. The solution in the Pyrex tube was irradiated with sixteen > 290 nm lamps and the solution in the quartz tube was irradiated with eight 254 nm lamps. The reactions were monitored by GLC [120°C (5 min), 20°C/min to 160°C (8 min), 20°C/min to 240°C (20 min)] every 30 min of irradiation. Figure 121a exhibits the GC-chromatogram of the reaction solution before irradiation. After 210 min of irradiation, GLC analysis (Figure 121b) reveals the formation of benzonitrile (43), 2-phenyl-1,3,5-triazine (39), 3-phenyl-1,2,4-thiadiazole (46) and 2,4-diphenyl-1,3,5-triazine (40), the known photoproducts with retention times of 3, 9, 13 and 23.5 min, respectively. The unconsumed reactant eluted with a retention time of 11 min. The trace also reveals a very small extra peak with a retention time of 19 min, which was not observed upon irradiation of 31 in an absence of 49.
Figure 121a: GLC analysis of solution of 31 containing 49 before irradiation

Figure 121b: GLC analysis of solution of 31 containing 49 after irradiation
A small amount of the reaction solution was removed and spiked with an authentic sample of the expected cycloaddition product, ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate (50). Figure 121c shows the GLC analysis of the reaction solution spiked with an authentic sample of 50.

GLC analysis of the spiked solution (Figure 121c) reveals a peak due to 50 with a retention time of 19.5 min which is slightly different from the new photoproduct peak observed at retention time of 19 min in Figure 121b. Thus, photoreaction solution was concentrated and analyzed by the GC (HP588) interfaced with a mass spectrometer. The trace (Figure 122a) [140°C (5 min), 20°C/min to 240°C (20 min)] of the concentrated reaction solution exhibits the formation of the known photoproducts with retention times of 4, 9, 11 and 25 min and the un-consumed reactant with a retention time of 10.5 min. The trace also reveals a very small peak, which eluted with a retention time of 15.4 min. The mass spectrum of this peak (Figure 122b) exhibits a molecular ion at m/z 234, which corresponds to the molecular weight of the expected trapping product, 50 (MW 234).
An authentic sample of 50 also eluted with a retention time of 15.4 min under the same GC (HP588) analytical condition.

**Figure 122a:** GC-trace of the concentrated solution after 210 min of irradiation

![GC-trace](image)

**Figure 122b:** Mass spectrum of a suspected peak to be 50

![Mass spectrum](image)

The mass spectrum of the peak which is suspected to be 50 (Figure 122b) exhibits a molecular ion at m/z 234, a base peak at m/z 135 and intense peaks at m/z 104, 103, and 77.

The mass spectrum of an authentic sample of 50 (Figure 123) shows a molecular ion at m/z 234, a base peak at m/z 135 which is due [C₆H₃CNS]⁺ fragment.
By comparison of the fragmentation pattern of the mass spectrum of the suspected product with the fragmentation pattern of the mass spectrum of an authentic sample of 50, it indicates that this suspected product is ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate (50). However, since the presence of this product in the reaction solution before concentration can be detected by GLC (PE9000) analysis in very trace quantity, this indicates that the formation of benzonitrile sulfide (48) can only be a very minor pathway upon photolysis of 5-phenyl-1,2,4-thiadiazole (31). This result is consistent with the proposed mechanism for the formation of 48 upon irradiation of 31, shown in Scheme 48.

This trapping experiment was also irradiated with eight 254 nm lamps. The results also showed trace amount of the formation of the expected cycloaddition product, 50.
2.7 Photolysis of 3-phenyl-1,2,4-thiadiazole in the presence of ethyl cyanoformate: attempt to identify the formation of benzonitrile sulfide by 1,3-dipolar cycloaddition reaction

In an attempt to trap the expected intermediate, benzonitrile sulfide (48), upon irradiation of 31, the results indicated the formation of very trace amount the expected cycloaddition product. However, in the case of 3-phenyl-1,2,4-thiadiazole (46), cleavage of the 1,5-diradical would not finally produce 48. According to Scheme 50, cleavage of the 1,5-diradical would finally lead to the formation of isothiocyanic acid (71), which could be an un-identified photoproduct formed upon irradiation of 46. Therefore, the formation of 50 could be predicted not to observe upon irradiation of 46 in the presence of 49.

![Scheme 50](image)

**Scheme 50:** The predicted mechanism for the formation of isothiocyanic acid

A solution of 46 (2.0×10^{-2} M, 4 mL) in acetonitrile containing 49 (0.1 mL, 1×10^{-1} M) was placed in a Pyrex tube and a quartz tube, sealed with rubber septa, and purged with argon gas for 15 min. The solution in the Pyrex tube was irradiated with sixteen > 290 nm
lamps and the solution in the quartz tube was irradiated with eight 254 nm lamps. The reactions were monitored by GLC [120°C (5 min), 20°C/min to 240°C (20 min)] every 30 min of irradiation. The solution in the Pyrex tube was photolyzed for 300 min while the solution in the quartz tube was photolyzed for 120 min.

Figure 124a exhibits GLC analysis of the solution before irradiation. After 300 min of irradiation, the trace (Figure 124b) shows the formation of two peaks with retention times of 3 and 12 min and the un-consumed reactant with a retention time of 9 min. The peak which eluted with a retention time of 3 min is benzonitrile (43), the known major photoproduct upon irradiation of 46. The peak which eluted with a retention time of 12 min was not observed upon irradiation of 46 without 49.

\[ \text{Figure 124a: GLC analysis of the solution before irradiation} \]
Figure 124b: GLC analysis of the reaction solution after 300 min

Figure 124c: Co-injection GLC analysis of the reaction solution with an authentic sample of 50
Co-injection GLC analysis of the reaction solution after 300 min with an authentic sample of 50 (Figure 124c) reveals that the peak with a retention time of 12 min has been increased. This would indicate that the new observed product which eluted with a retention time of 12 min upon irradiation of 46 in the presence of 49 is ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate (50).

The GC (HP588) analysis of the same un-concentrated reaction solution after 300 min of irradiation (Figure 125a) shows three components in this reaction mixture with retention times of 4, 11.5 and 17 min. The mass spectrum of the first eluted component with a retention time of 4 min exhibited a molecular ion at m/z 103 and fragmentation pattern consistent with that of 43, the known photoproduct. The second eluted component is the un-consumed reactant. The mass spectrum of the third eluted component (Figure 125b), which is strongly suspected to be 50, exhibits a molecular ion at m/z 234 and a base peak at m/z 135.

**Figure 125a:** GC-trace of the un-concentrated reaction solution after 300 min of irradiation
Results and Discussion

Figure 125b: Mass spectrum of the suspected product at RT 17 min

Figure 126: Mass spectrum of an authentic sample of 50
By comparison of the chromatographic and mass spectroscopic properties of the suspected product with the chromatographic and mass spectroscopic properties of an authentic sample of 50, it can be concluded that the suspected product is ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate (50). This result indicates the formation of benzonitrile sulfide (48). This result also corresponds to the observed formation of diphenyl-1,2,4-thiadiazole (47) upon irradiation of 46 which was proposed to arise from a 1,3-dipolar cycloaddition reaction of 48 with benzonitrile (43), the observed major product in this photoreaction.

The detection of 48 would suggest direct photocleavage of the thiadiazole ring with the formation of H-CN and 48. The latter species can undergo cycloaddition with 49 to yield 50. In the absence of the trapping agent, 48 could split out sulfur resulting in the formation of 43 (A) or could undergo a 1,3-dipolar cycloaddition reaction with 43 to give 47 (B), as shown in Scheme 51.

Scheme 51: The proposed mechanism for the formation of 48 upon irradiation of 46
2.8 Photolysis 3-methyl-5-phenyl-1,2,4-thiadiazole and 5-phenyl-1,2,4-thiadiazole mixture in acetonitrile: Identification of phenyltriazines formation via [4+2] cycloaddition reaction of phenyldiazacyclobutadienes by a cross coupling experiment

The formation of triazines was proposed to occur via a [4+2] cycloaddition self-coupling of phenyldiazacyclobutadienes generated upon irradiation of 5-phenyl-1,2,4-thiadiazoles as shown in Scheme 52.

![Scheme 52: The proposed mechanism for phenyl-s-triazines formation](image)

In this proposed mechanism, if two different phenyldiazacyclobutadiene intermediates existed in the reaction, the observed triazines formation would not only come from a [4+2] cycloaddition self-coupling leading to the formation of symmetrical triazines but a [4+2] cycloaddition cross-coupling would also be in competition leading to the formation of an unsymmetrical triazine. This can be envisioned as shown in Scheme 53.
Scheme 53: The proposed formation of unsymmetrical phenyltriazine via \([4+2]\) cycloaddition cross-coupling of phenyldiazacyclobutadiene intermediates.

Therefore, it was proposed that irradiation of a mixture of 5-phenyl-1,2,4-thiadiazole (31) and 3-methyl-5-phenyl-1,2,4-thiadiazole (54) in acetonitrile would lead to the formation of 2-methyl-4-phenyl-1,3,5-triazine (72), a cross coupling product. Scheme 54 shows possible photoproducts that would be observed upon irradiation of a mixture of 31 and 54 in acetonitrile.
Results and Discussion

Scheme 54: The possible photoproducts predicted to observe upon irradiation of a mixture of 5-phenyl-1,2,4-thiadiazole and 3-methyl-5-phenyl-1,2,4-thiadiazole

In order to confirm this proposed mechanism, 2-methyl-4-phenyl-1,3,5-triazine (72) was synthesized and employed as an authentic sample for photoproduct identification upon irradiation of the thiadiazole mixture.

2.8.1 Synthesis of 2-methyl-4-phenyl-1,3,5-triazine

A recent synthesis of un-symmetrically substituted triazines has been reported by Raymond Dengino and colleagues\textsuperscript{13} involving the condensation of N-acylamidines with amidines or guanidines in aprotic solvents. Based on this synthetic method, condensation of N-[(dimethylamino)methylene]benzamide (69) with acetamidine (68) would yield 2-methyl-4-phenyl-1,3,5-triazine (72) as shown in Scheme 55.

Scheme 55: Total synthesis of 2-methyl-4-phenyl-1,3,5-triazine
2.8.1.1 Synthesis of N-[(dimethylamino)methylene]benzamide

In order to synthesize 72 by the synthetic route proposed in Scheme 55, N-[(dimethylamino)methylene]benzamide (69) was required as the starting amidine. This amidine 69 was prepared in 50 % yield as colorless crystals by the condensation of benzamide (38) with N,N-dimethylformamide dimethylacetal (35), as shown in Scheme 56. The colorless crystals were characterized by $^1$H-, $^{13}$C-NMR and mass spectroscopy.

Scheme 56: Synthesis of N-[(dimethylamino)methylene]benzamide

GC analysis of the colorless crystals (Figure 127a) exhibits only one component that eluted with a retention time of 16 min. The mass spectrum of this component (Figure 127b) shows a molecular ion at m/z 176 which is consistent with a molecular formula of C$_{10}$H$_{12}$N$_2$O (MW 176). The base peak at m/z 99 is due to cleavage of [C$_6$H$_5$]$^+$ fragment (m/z 77) from the molecular ion. The peaks at m/z 44 and 105 are consistent with [C$_2$H$_4$N]$^+$ and [C$_7$H$_5$O]$^+$ fragments, respectively.

Figure 127a: GC analysis of N-[(dimethylamino)methylene]benzamide
Figure 127b: Mass spectrum of N-[(dimethylamino)methylene]benzamide

Figure 128 shows $^1$H-NMR spectrum of the colorless crystals corresponding to the structure of 69. The spectrum reveals absorptions of the two non-equivalent amino methyl protons as two singlets at $\delta$ 3.17 (3H) and 3.21 (3H). The imine proton appears as a singlet (1H) downfield at $\delta$ 8.84. The phenyl ring protons are shown as two multiplets at $\delta$ 7.38-7.49 (3H) and 8.06-8.25 (2H).
Figure 128: $^1$H-NMR spectrum of N-[(dimethylamino)methylene]benzamide

The $^{13}$C-NMR spectrum (Figure 129a) is also consistent with the structure of 69. The carbonyl carbon absorbs downfield at $\delta$ 177.6. Based on the previous $^{13}$C–NMR spectral assignments of the amidines synthesized in this laboratory, the signal at $\delta$ 160.6 can be assigned to the absorption of the imine carbon. The phenyl ring carbons at positions 2,6 and 3,5 appear as two singlets at $\delta$ 127.9 and 129.7 while the phenyl ring carbons at positions 1 and 4 absorb at $\delta$ 136.3 and 131.9, respectively. The two singlets at $\delta$ 35.4 and 41.5 were assigned to the two non-equivalent N-methyl carbons. These assignments are consistent with the $^{13}$C–DEPT 135 spectrum (Figure 129b). The two signals at $\delta$ 136.3 and 177.6 disappeared in the $^{13}$C–DEPT 135 spectrum which are consistent with the assignment of the two signals to the two quaternary carbons of the phenyl ring at position 1 and the carbonyl carbon, respectively. The signals at $\delta$ 35.4, 41.5, 127.9, 129.7, 131.9 and 160.6 still appear
in the $^{13}$C–DEPT 135 spectrum which are consistent with the assignment to the two non-equivalent amino methyl carbons, phenyl ring carbons positions 2 and 6, 3 and 5, 4 and the imine carbon, respectively.

Figure 129a: $^{13}$C-NMR spectrum of N-[(dimethylamino)methylene]benzamide
2.8.1.2 Synthesis of 2-methyl-4-phenyl-1,3,5-triazine

2-Methyl-4-phenyl-1,3,5-triazine (72) was synthesized by the method involving a condensation of 68 with amidine 69. The desired triazine 72 was obtained in 20% yield as a colorless viscous liquid. The colorless liquid was characterized by $^1$H-, $^{13}$C-NMR and mass spectroscopy.

Scheme 57: Synthesis of 2-methyl-4-phenyl-1,3,5-triazine
GC analysis of the colorless liquid (Figure 130a) exhibits only one gc-volatile component which was eluted with a retention time of 19 min. The mass spectrum of this component (Figure 130b) shows a molecular ion at m/z 171 corresponding with the molecular weight of 72 (MW 171). The base peak at m/z 103 is due to $[C_7H_5N]^+$ fragment while the moderate intense peak at m/z 104 is due to the m/z 103 fragment with subsequent hydrogen atom abstraction. These fragmentations are characteristic for fragmentation of 2-unsubstituted-4-phenyl-1,3,5-triazines as previously observed in the mass spectra of phenyl- and diphenyl-1,3,5-triazine. The peak at m/z 68 is consistent with elimination of $[C_7H_5N]$ from the molecular ion.

Figure 130a: GC analysis of the colorless liquid; 2-methyl-4-phenyl-1,3,5-triazine
Figure 130b: Mass spectrum of 2-methyl-4-phenyl-1,3,5-triazine

Figure 131 shows the $^1$H-NMR spectrum of the colorless liquid product. The spectrum reveals absorption of the proton on the triazine ring at position 6 as a singlet (1H) at $\delta$ 9.17. The methyl protons appear as a singlet (3H) at $\delta$ 2.71. The phenyl ring protons are shown as two multiplets at $\delta$ 7.47-7.57 (3H) and 8.47-8.51 (2H).
Results and Discussion

Figure 131: $^1$H-NMR spectrum of 2-methyl-4-phenyl-1,3,5-triazine

The $^{13}$C-NMR spectrum (Figure 132a) is also consistent with the structure of 72. The methyl carbon appears at δ 26.3. The phenyl ring carbons at positions 2,6 and 3,5 absorb at δ 129.1 and 129.3 while the phenyl ring carbons at positions 1 and 4 absorb at δ 135.6 and 133.2, respectively. The three singlets at δ 166.5, 171.5 and 177.2 were assigned to the carbons on the triazine ring. These assignments are consistent with the $^{13}$C–DEPT 135 spectrum (Figure 132b). The three signals at δ 135.6, 171.5 and 177.2 disappeared in the $^{13}$C–DEPT 135 spectrum which are consistent with the assignment of the three signals to the three quaternary carbons of the phenyl ring at position 1 and the two carbons on the triazine ring at position 2 and 4, respectively. The signals at δ 26.3, 129.1, 129.3, 133.2 and 166.5 are still present in the $^{13}$C–DEPT 135 spectrum which is consistent with the assignment to the methyl carbon, phenyl ring carbons positions 2 and 6, 3 and 5, 4 and the carbon of the triazine ring at position 6, respectively.
Figure 132a: $^{13}$C-NMR spectrum of 2-methyl-4-phenyl-1,3,5-triazine

Figure 132b: $^{13}$C-DEPT 135 spectrum of 2-methyl-4-phenyl-1,3,5-triazine
2.8.2 Irradiation of 5-phenyl- and 3-methyl-5-phenyl-1,2,4-thiadiazole mixture in acetonitrile

If the formation of triazines occurred via [4+2] cycloaddition self-coupling reaction of phenyldiazyclobutadiene intermediates, as shown in Scheme 52, irradiation of a mixture of 5-phenyl- and 3-methyl-5-phenyl-1,2,4-thiadiazole (31) and (54) in acetonitrile should lead to the formation of the unsymmetrical triazine, 2-methyl-4-phenyl-1,3,5-triazine (72), arising from a [4+2] cycloaddition cross-coupling reaction of phenyldiazyclobutadiene intermediates. In order to explore this possibility, irradiation of a mixture of 5-phenyl- (31) and 3-methyl-5-phenyl-1,2,4-thiadiazole (54) in acetonitrile was carried out. The photoreaction was qualitatively monitored by GLC and GC-MS.

The mixture solution of 31 + 54 (3.5 mL), the solution of 54 (3.5 mL), and the solution of 31 (3.5 mL) in acetonitrile each in sealed Pyrex tubes were purged with argon for 15 min. These solutions were then irradiated simultaneously with fifteen > 290 nm lamps for a total of 650 min. The reactions were monitored by GLC (PE9000) analysis after every 120 min of irradiation. Figure 133 (a-b) and 134 (a-b) show the GC-chromatograms of solutions of 31 and 54 before and after 650 min of irradiation, respectively, revealing the formation of the known photoproducts upon irradiation of these compounds. GC-chromatogram of the mixture before irradiation showed only two components with retention times corresponding to chromatographic properties of each individual thia diazole 31 and 54. This confirms that these two thia diazoles did not undergo any thermal reaction especially leading to the formation of triazines.
Figure 133a: GLC analysis of 31 in acetonitrile before irradiation

Figure 133b: GLC analysis of 31 in acetonitrile after 650 min of irradiation
Results and Discussion

Figure 134a: GLC analysis of 54 in acetonitrile before irradiation

Figure 134b: GLC analysis of 54 in acetonitrile after 650 min of irradiation
Results and Discussion

**Figure 135:** GLC analysis of the thiadiazole mixture solution after 650 min of irradiation

**Figure 136:** GLC analysis of the authentic sample of 2-methyl-4-phenyl-1,3,5-triazine
Figure 136 shows the GLC analysis of the authentic 2-methyl-4-phenyl-1,3,5-triazine (72) under the same analytical condition as employed for the analyses of the photoreactions. The chromatogram reveals the presence of only one gc-volatile component with a retention time of 14.3 min.

After 650 min of irradiation, the solution of 54 and the solution of 31 became yellow brown while the mixture solution appeared as a pale pink-yellow with a colloidal precipitate. Figure 135 shows the GC-chromatogram of the mixture after 650 min of irradiation. The components observed in the mixture reaction after irradiation could be assigned by comparison with the chromatographic properties obtained by GLC analyses of the individual thiadiazole reactions under the same analytical condition (Figure 133b and 134b). Only one component, which eluted with a retention time of 14.3, was not observed in either of the reaction of 54 or 31.

A small amount of the mixture solution after 650 min of irradiation was removed and spiked with an authentic sample of the expected un-symmetrical triazine, 2-methyl-4-phenyl-1,3,5-triazine (72). Figure 137 exhibits the GLC analysis of the irradiated mixture solution spiked with an authentic sample of 72. The GC-trace reveals an increase of the unidentified peak that eluted with a retention time of 14.3 min. This would indicate that the unknown component, which eluted with a retention time of 14.3 min, is 2-methyl-4-phenyl-1,3,5-triazine (72).
The mixture solution after 650 min of irradiation was also analyzed by GC-MS. The GC-trace (Figure 138a) exhibits a new unidentified component, which eluted with a retention time of 19.2 min, which was not observed either in the reaction of 31 or 54. The mass spectrum of this component (Figure 138b) reveals a molecular ion at m/z 171 and its fragmentation pattern corresponding with the molecular ion and fragmentation pattern of an authentic sample of 72.
Figure 138a: GC-trace of the mixture solution after 650 min of irradiation

Figure 138b: Mass spectrum of the component eluted with a retention of 19.2 min
The irradiated mixture solution, which was spiked with an authentic sample of 72, was also analyzed by the GC (HP588) interfaced with a mass spectrometer. The GC-trace (Figure 139a) reveals an increasing of the component that eluted with a retention time of 19.2 min. The mass spectrum of this peak revealed a molecular ion and fragmentation pattern identical to those of an authentic sample of 72.

![GC-trace (HP588) of the irradiated mixture spiked with an authentic sample of 72](image)

By comparison of the chromatographic and mass spectroscopic properties of the new photoproduct with the chromatographic and mass spectroscopic properties of an authentic sample of 72, it can be concluded that this new product is 2-methyl-4-phenyl-1,3,5-triazine (72).
This result, therefore, supports the assumption of triazine formation via a [4+2] cycloaddition reaction of phenyldiazacyclobutadienes as previously proposed based on the results observed upon irradiation of 5-phenyl-1,2,4-thiaidazole-4-\(^{15}\)N (31-\(^{15}\)N).

It is of interest to note that the analysis with the GC (HP588) interfaced with a meaa spectrometer of the concentrated photolysate of 31 (Figure 140a) reveals two unknown peaks that eluted with a retention time of 18.9 min (Unk 1) and 35 min (Unk 2). These peaks were not previously observed in the photolysate of 31.

![Figure 140a: GC analysis of the concentrated 31 photolysate after 650 min of irradiation](image)

The mass spectrum of the broad peak that eluted with a retention time of 35 min (Unk 2; Figure 140b) exhibits a molecular ion at m/z 256 which corresponds to a formula of S\(_8\) (FW 256). The fragmentation pattern of this component appears in a P-32 manner which corresponds to loss of sulfur atom in each cleavage. This indicates the presence of elemental sulfur in this photolysate. Since previous photolysis of 31 was carried out for short periods of irradiation, thus, the concentration of elemental sulfur in the mixture was below the detection limit of the GC-MS analytical condition. Thus, no elemental sulfur was previously detected upon irradiation of 31. This result, therefore, confirms the formation of elemental sulfur upon photolysis of 31 in acetonitrile.
The unknown peak that eluted with a retention time of 18.9 min (Unk1) has a molecular ion at m/z 121 (Figure 140c) which corresponds to a molecular formula of C<sub>7</sub>H<sub>7</sub>NO (MW 121).
Figure 140c: Mass spectrum of the peak eluted with a retention time of 18 min (Unk 1)

Figure 141 show the GC-trace of an authentic sample of benzamide (38). This result shows that the unk 1 in the photolysate of 31 has its chromatographic and mass spectroscopic properties identical to those of an authentic sample of 38. Thus, it can be concluded that the unk 1, which was observed in the photolysis of 31, is benzamide (38).
Figure 141: GC (HP588) and mass spectrum of an authentic sample of benzamide
The formation of 38 upon photolysis of 31 was proposed to arise from a nucleophilic ring opening of the phenyl substituted thiazirine due to the presence of water in the reaction media (pathway A) or a hydrolysis of benzonitrile sulfide (48) via an unclear mechanism (pathway B) as shown in Scheme 58.

Scheme 58: The proposed formation of benzamide upon irradiation of 31
2.9 Photochemistry of phenyl substituted-1,2,4-thiadiazoles in furan solvent: Furan trapping of reactive intermediates

Previous result from the irradiation of 5-phenyl-1,2,4-thiadiazole (31) and $^{15}$N-labeled 5-phenyl-1,2,4-thiadiazole, have suggested that a photochemically generated 1,3-diaza-5-thiabicyclo[2.1.0]pentene (BC-31) is the key intermediate in the photoreaction.$^{14}$

\[ \text{Scheme 59: 1,3-Diaza-5-thiabicyclo[2.1.0]pentene; Key intermediate upon irradiation of 5-phenyl-1,2,4-thiadiazole} \]

There are precedents for trapping such a photochemically generated bicyclic species. Day and Barltrop$^{15}$ have suggested that the phototransposition reaction of cyanothiophenes occur via thiabicyclo[2.1.0]pent-2-ene intermediates (74). The existence of these intermediates was confirmed by isolation of a 1:1 mixture of furan-thiabicyclo[2.1.0]pent-2-ene adducts (75a and 75b) upon irradiation of 3-cyanothiophene (76) in furan solvent as shown in Scheme 60.
Work in our laboratory has also shown that 1-methyl-5-phenylpyrazole (77) undergoes phototransposition to the three different 1-methylimidazoles (78-80) upon irradiation in methanol.\textsuperscript{16} These products were not observed, however, if the reaction was carried out in furan solvent. Instead, irradiation of 77 in furan solvent led to the isolation of the [4+2] adduct (81).\textsuperscript{16} The formation of the product is consistent with furan trapping of 4-phenyl-5-methyl-1,5-diazabicyclo[2.1.0]pentene (82) formed photochemically by electrocyclic ring closure of 77.
Scheme 62: Irradiation of 1-methyl-5-phenylpyrazole in furan solvent

In an attempt to establish the formation of the bicyclic intermediate upon irradiation of phenyl substituted-1,2,4-thiadiazoles, irradiation of phenyl substituted-1,2,4-thiadiazoles in the presence of furan solvent were carried out in an attempt to trap the bicyclic species as a Diels-Alder adduct.
2.9.1 Photochemistry of 5-phenyl-1,2,4-thiadiazoles in furan solvent

2.9.1.1 Irradiation of 5-phenyl-1,2,4-thiadiazole in furan solvent

Solutions of 5-phenyl-1,2,4-thiadiazole (31) in furan (2.4×10^{-2} M; 3.5 mL) and 31 in acetonitrile (1.72×10^{-2} M; 3.5 mL) in sealed Pyrex tubes were purged with argon gas for 20 min. These solutions were simultaneously irradiated with sixteen > 290 nm lamps in a Rayonet reactor for a total of 120 min. Figure 20a and 21a show the GLC analyses of 31+Furan and 31+AcCN solutions before irradiation, respectively. Furan is eluted with a retention time within the solvent delay (2 min) and, thus, will not be observed in this GLC analysis. Figure 142a reveals that no ground state reaction between 31 and furan has occurred.
Results and Discussion

**Figure 142a:** GC-trace of **31+Furan** before irradiation

**Figure 142b:** GC-trace of **31+Furan** after 120 min of irradiation
Figure 143a: GC-trace of 31 in AcCN before irradiation

Figure 143b: GC-trace of 31 in AcCN after 120 min of irradiation
Results and Discussion

Figure 142b shows the GC trace of the 31+Furan solution after 120 min of irradiation. For comparison, Figure 143b shows the GC trace of the 31+AcCN solution after 120 min of simultaneous irradiation on the merry-go-round apparatus. This trace shows that the expected products, benzonitrile (43), 2-phenyl-1,3,5-triazine (39), 3-phenyl-1,2,4-thiadiazole (46), and 2,4-diphenyl-1,3,5-triazine (40) have been formed. Figure 142b reveals, however, that the peaks due 43 and 40 are substantially smaller than the peaks observed in Figure 143b in the absence of furan while the peaks due to the two triazines (39 and 40) are not observed at all in Figure 142b. Thus, Figure 142b shows that during irradiation of 31 in furan, the formation of 43, 46, 39, and 40 have been quenched. In addition to these changes, the GC-trace shows the formation of two new peaks eluting at retention times of 17.9 (Unk2) and 28.8 min (Unk1) that were not observed when the irradiation was carried out in acetonitrile.

The irradiated 31+Furan solution was also analyzed using the gas chromatograph (HP588) interfaced to the mass spectrometer detector. As shown in Figure 144a, this GC trace shows the peaks due to 43, 31 and 46 and two new products eluting at retention times of 24.7 (Unk1) and 26.2 min (Unk2).

![Figure 144a: GC-trace of 31+Furan solution after 120 min of irradiation](image-url)
**Figure 144b:** Mass spectrum of Unk1 (24.7 min)

**Figure 144c:** Mass spectrum of Unk2 (26.2 min)
The mass spectra of these new products are shown in Figure 144b (Unk1) and 144c (Unk2) and reveal molecular ions at m/z 198 and 245, respectively. Although the latter mass is larger than the mass of a 1:1 5-phenyl-1,2,4-thiadiazole-furan adduct, a mass of 198 would be consistent with a 1:1 adduct minus sulfur (87) as shown in Scheme 63.

**Scheme 63:** Formation of furan-phenyldiazacyclobutadiene adduct upon irradiation of 31+Furan

The irradiated 31+Furan solution was also concentrated in a warm water bath (60-70 °C) under vacuum to give a dark brownish viscous liquid and analyzed by GC-MS. No additional product was observed.
2.9.1.2 Irradiation of 3-methyl-5-phenyl- and diphenyl-1,2,4-thiadiazoles in furan solvent

Irradiations of 3-methyl-5-phenyl-1,2,4-thiadiazole (54) (7.1×10^{-2} M, 3.5 mL) in neat furan was carried out with sixteen > 290 nm lamps.

Figure 145a shows GC analysis of the photoreaction of 54 in neat furan after 210 min of irradiation. The trace shows a peak at 18 min due to an unresolved mixture of the reactant (54) and one of the expected photoproducts, 2,4-dimethyl-6-phenyl-1,3,5-triazine (65), very small peaks due to benzonitrile (43) and 5-methyl-3-phenyl-1,2,3-thiadiazole (57), the expected photocleavage and phototransposition products, respectively, and two new peaks due to unknowns 3 and 4, products not observed in the absence of furan. Figure 145b-c show the mass spectra of these unknown products revealing molecular ions at m/z 188 (Figure 145b; Unk3) and m/z 212 (Figure 145c; Unk4).

Figure 145a: GC trace of photoreaction of 54 in furan after 210 min of irradiation
Results and Discussion

**Figure 145b:** Mass spectrum of Unk3; 54+Furan reaction

**Figure 145c:** Mass spectrum of Unk4; 54+Furan reaction
This shows that the major new photoproduct with a retention time of 25.5 min has a mass consistent with a 1:1 adduct of 3-methyl-5-phenyl-1,2,4-thiadiazole (54) and furan minus sulfur (88) as shown in Scheme 64.

\[ \text{Scheme 64: Formation of furan-phenyldiazacyclobutadiene adduct upon irradiation of 54+Furan} \]

Solution of diphenyl-1,2,4-thiadiazole (47) (3.2×10^{-2} M, 3.5 mL) in neat furan was also irradiated with sixteen > 290 nm lamps. Figure 25a shows the GC-analysis of the irradiated 47+furan solution after 210 min of irradiation. In addition to the unconsumed 47, the trace reveals the formation of three new photoproducts labeled Unk5, Unk6 and Unk7 which were not observed in the absence of furan. This GC trace also reveals that 43 and 2,4,6-triphenyl-1,3,5-triazine (86), the photoproducts formed in acetonitrile, were not formed when irradiation was carried out in furan.

\[ \text{Figure 146a: GC-trace of photoreaction of 47 in furan after 210 min of irradiation} \]
Figure 146b: Mass spectrum of Unk5; 47+Furan reaction

Figure 146c: Mass spectrum of Unk6; 47+Furan reaction
The mass spectra of unknowns 5, 6, and 7 are shown in Figure 146b, 146c and 146d, respectively. These new products have molecular ions of m/z 172, 188 and 274, respectively. Of these three products, the major new product (Unk7) has a molecular ion at m/z 274 consistent with the formation of a 1:1 adduct of diphenyl-1,2,4-thiadiazole (47) and furan minus the sulfur atom (89) as shown in Scheme 65.

Scheme 65: Formation of furan-phenyldiazaacyclobutadiene adduct upon irradiation of 47+Furan
These results show that irradiation of 5-phenyl-1,2,4-thiadiazole (31), 3-methyl-5-phenyl-1,2,4-thiadiazole (54) or diphenyl-1,2,4-thiadiazole (47) in furan solvent results in quenching of the formation of the products observed in the absence of furan and in the formation of new products which their molecular weights are consistent with the formation of 1:1 adducts of the thiadiazole and furan with loss of sulfur.

Such adducts could be formed by furan trapping of the initially formed diazathiabicyclo[2.1.0]pentene (BC) to form a sulfur-containing adduct (87-89) which eliminates sulfur, possibly under the condition of our GC-MS analysis, or by furan trapping of the phenyldiazacyclobutadiene (CB) after the initial adduct eliminates sulfur as shown in Scheme 66.

![Scheme 66: Possible formation of the observed adducts](image-url)
Trapping of the initially formed bicyclic intermediate \( \textsc{bc} \) would be accompanied by quenching the formation of the phototransposition, photofragmentation and photo-ring expansion products since these products all arise from this intermediate. Alternatively, trapping of only the phenyldiazacyclobutadiene species \( \textsc{cb} \) would be accompanied by quenching of the photofragmentation and ring-expansion products which are both derived from this species but would not quench the formation of the phototransposition product since that product is derived only from the initially generated bicyclic species.

It should, however, be noted that all previous GC analyses revealed that the formation of the known photoproducts upon irradiation of 5-phenyl-1,2,4-thiadiazoles have been quenched. In order to determine the effect of added furan on the yields of the photoproducts, the irradiation of \( \text{31} \) in acetonitrile containing various concentrations of furan was carried out.

Solutions of \( \text{31} \) (1.7 x 10^-2 M; 5 mL) in acetonitrile with the presence of furan from 0-90% were sealed in Pyrex tubes, purged with a fine steam argon gas for 15 min and simultaneously irradiated with sixteen > 290 nm lamps in a Rayonet reactor. The photoreactions were monitored by GLC at 60 min intervals.

Figure 147a-d show plots that reveal the effect of increasing the furan concentration on the yield of the product in the absence of furan divided by the yield of the product observed at the various furan concentrations. In these plots, a positive slope indicates that the yield of the product decreases with an increase in the furan concentration.
Results and Discussion

267

**Figure 147a:** Furan quenching of the formation of 50 in the photoreaction of 1

**Figure 147b:** Furan quenching of the formation of 4 in the photoreaction of 1

**Figure 147c:** Furan quenching of the formation of 51 in the photoreaction of 1
Results and Discussion

Diphenyl-s-triazine (quenching at 60 min)

\[ y = 1.1576e^{0.0551x} \]

\[ R^2 = 0.9825 \]

Figure 147d: Furan quenching of the formation of 52 in the photoreaction of 1

Figure 147a shows a linear decrease in the yield of benzonitrile (43) with increasing furan concentrations until at 90% furan concentration, the yield of 43 is 80% quenched. The next three plots (Figure 147b-d) show that the yields of 3-phenyl-1,2,4-thiadiazole (46), the phototransposition product, and the yields of phenyl- and diphenyl-1,3,5-triazines (39) and (40) are also substantially quenched by added furan. In these cases, they appear to be a parabolic relationship between product quenching and furan concentration.

Since furan quenches the formation of all products, the quencher must be reacting with a species which is a precursor of all four products, namely the 4-phenyl-1,3-diaza-5-thiabicyclo[2.1.0]pentene (BC-31) as shown in Scheme 59. These results, however, do not rule out the possibility that furan is also reacting with the phenyldiazacyclobutadiene species (CB).
2.9.1.3 Preparative scale photolysis of diphenyl-1,2,4-thiadiazole in furan solvent

In attempts to isolate the furan-trapping adducts, preparative scale photolysis of diphenyl-1,2,4-thiadiazole (47) in neat furan was carried out.

Solution of diphenyl-1,2,4-thiadiazole (47) in neat furan ($2 \times 10^{-2}$ M; 25 mL) in a sealed Pyrex tube was irradiated with sixteen > 290 nm lamps for a total of 360 min resulting in 94% consumption of the starting material. The reaction solution was concentrated by rotary evaporation to give a dark brownish residue. The brown residue (120 mg) was subjected to a column chromatography (column; 0.5 × 30 cm, silica gel 12 g). The column was eluted with ethyl acetate-hexane 3:7. GC (HP588) analysis of each fraction showed that fractions 1-2, 3-5, 7 and 9-10 contained major components with molecular ions at m/z 309, 238, 274 and 172, respectively. Mass spectra analysis indicated that the components in fractions 1-2 and 3-5 were consistent with 2,4,6-triphenyl-1,3,5-triazine (86), the known product in this photoreaction, and the starting thiadiazole, 12, respectively. The molecular ion at m/z 274 corresponds to the molecular ion of the 1:1 adduct of diphenyl-1,2,4-thiadiazole (47) and furan minus the sulfur atom. Thus, fraction 7 was concentrated to give a yellow viscous liquid (F7). This sample was dissolved in CDCl$_3$ and analyzed by $^1$H-, $^{13}$C-NMR, and the GC interfaced with a mass spectrometer.

Figure 148a: GC-trace of the concentrated fraction 7
Figure 148a shows GC trace of the yellow liquid sample \( F_7 \), in CDCl\(_3\). The trace reveals a major component eluted with a retention time of 33.8 min. Figure 148b shows the mass spectrum of this component revealing a molecular ion at \( m/z \) 274 and a base peak at \( m/z \) 245. The molecular weight of this sample \( (F_7) \) is consistent with the molecular weight of the 1:1 adduct of diphenyl-1,2,4-thiadiazole \( (12) \) and furan minus the sulfur atom \( (72; \text{MW 274}) \). For a molecule containing sulfur atoms, its mass spectrum should exhibit a \( M^+ + 2 \) peak due to a natural abundance of \( ^{34}\text{S} \) atom. Since the natural abundance of \( ^{34}\text{S} \)
atom is approximately 4.42 %, thus, the number of sulfur atom in the molecule can also be
determined from the ratio of \([M^+ +2]/[M^+]\) as shown below:

\[
\frac{(M+2)^+}{M^+} = n \frac{(0.042)/(0.9503)}{n \times 0.0442}
\]

\(n = \text{number of } ^{34}\text{S}\)

In Figure 148b, however, no \(M^+ + 2\) peak is observed. This confirms that this molecule does not contain a sulfur atom.

Figure 149a-b shows the \(^1\text{H-NMR}\) spectrum and the scale expansion spectrum of the sample \textbf{F7} in CDCl\(_3\). The \(^1\text{H-NMR}\) spectra of these adducts usually exhibit complicated splitting due to homonuclear long range couplings. Figure 149a shows that the isolated \textbf{F7} is not in a highly pure state and is, therefore, very complicated. In contrast, the \(^{13}\text{C-spectra},\) with complete decoupled, is more simple and characteristic of these adducts. Table 3 shows the \(^{13}\text{C-chemical shifts of 7-oxabicyclo[2.2.1]hept-2-ene and some derivatives.}\)
Results and Discussion

Figure 149a: $^1$H-NMR spectrum of the unknown sample F7; the expected adduct

Figure 149b: $^1$H-NMR scale expansion of spectrum of the unknown sample F7
Table 1: $^{13}$C-chemical shifts of 7-oxabicyclo[2.2.1]hept-2-ene and some derivatives

<table>
<thead>
<tr>
<th>Compound</th>
<th>Assignments (δ in ppm)</th>
<th>Compound</th>
<th>Assignments (δ in ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ref. 17</td>
<td>C1 = 77.7, C2 = 134.6, C3 = 134.6, C4 = 77.7, C5 = 23.4, C6 = 23.4</td>
<td>Ref. 18</td>
<td>C1 = 93.2, C2 = 138.9, C3 = 128.5, C4 = 76.1, C5 = 48.3, C7 = 41.9</td>
</tr>
<tr>
<td>adduct 1</td>
<td></td>
<td>adduct 2</td>
<td></td>
</tr>
<tr>
<td>Ref. 19</td>
<td>C1 = 78.9, C2 = 137.9, C3 = 133.1, C4 = 78.9, C5 = 26.2, C6 = 31.6, CN = 120.8</td>
<td>Ref. 19</td>
<td>C1 = 78.0, C2 = 137.4, C3 = 133.9, C4 = 81.4, C5 = 27.6, C6 = 31.6, CN = 122.8</td>
</tr>
<tr>
<td>adduct 3</td>
<td></td>
<td>adduct 4</td>
<td></td>
</tr>
<tr>
<td>Ref. 16</td>
<td>C1 = 80.0, C2 = 137.4, C3 = 147.4, C4 = 103.5, C5 = 56.5, C6 = 62.1</td>
<td>Ref. 16</td>
<td>C1 = 79.3, C2 = 135.7, C3 = 149.6, C4 = 102.3, C5 = 55.3, C6 = 63.0</td>
</tr>
<tr>
<td>adduct 5</td>
<td></td>
<td>adduct 6</td>
<td></td>
</tr>
</tbody>
</table>
7-Oxabicyclo[2.2.1]hept-2-ene (adduct 1) would be considered as basic structure of the adducts shown in Table 1. Table 1 shows the $^{13}C$-chemical shifts of this compound (adduct 1) revealing the absorption of the two equivalent bridge head carbons at $\delta$ 77.7. The carbons at positions 6 and 5 are shown at $\delta$ 23.4. The two equivalent methylene carbons appear at $\delta$ 134.6. Table 1 shows that when the C6 is replaced with a nitrogen atom, the C1 of the adduct 2 appears downfield of 15.5 ppm, relative to the shift of C1 observed in the adduct 1. This also leads to 4.3 ppm deshielded of the C2 in the adduct 2. In the adduct 5, the C4 is 25.8 ppm deshielded relative to the C4 in the adduct 1. This would be due to a secondary magnetic field from the phenyl ring. The C3s in the adduct 3 and 4 absorb at $\delta$ 133.1 and 133.9, respectively, while the C3s in the adduct 5 and 6 are approximately 10 ppm downfield from the C3s in the adduct 3 and 4. This additional deshield effect of C3s in adduct 5 and 6 would also be expected due to a secondary magnetic field from the phenyl ring. In adduct 5 and 6, the C5s and C6s are shown approximately two-fold further downfiled from the observed shift in C5 and C6 in the adduct 1. The deshielded in these cases would be due to the electronegative nitrogen atom and the phenyl ring in the adduct 5 and 6.

The mass spectrum of the isolated F7 sample (Figure 148b) showed a molecular ion at m/z 274 corresponding with a 1:1 adduct of diphenyl-1,2,4-thiadiazole (47) and furan minus the sulfur atom (89) which the structure of this adduct would be expected as shown below:
Although, the $^1$H-NMR spectrum of this sample, shown in Figure 149a-b, is quite complicated, the $^{13}$C-spectra (Figure 150a-b) show a clearer spectrum. The $^{13}$C-NMR signals of this new product, F7, could be assigned based on the $^{13}$C-chemical shifts analysis of 7-oxabicyclo[2.2.1]hept-2-ene and some derivatives as shown in Table 3. Since the C1 in the adduct 2, which is adjacent to a nitrogen atom, appears downfield at $\delta$ 93.2 while the C4 in the adduct 5 is deshielded, due to an effect from the phenyl ring, to $\delta$ 103.5. Therefore, the singlet at $\delta$ 107.4 would be expected due to the absorption of the C4 in 89 while the C1 would be expected to absorb upfield at $\delta$ 90.4 due to shielding effect of the phenyl ring attached to the C6 as observed in the adduct 5 and 6. Since the C6 in adduct 5 appears at $\delta$ 62.1, the C6 in 89, that is adjacent to two nitrogen atoms and attached to a phenyl ring, would be expected to absorb downfield at $\delta$ 103.8. The sp$^2$ carbons at C2 and C3 of 89 would correspond to the two singlets at $\delta$ 148.5 and 159.0, respectively. The C3 of 89 was expected to appear more downfield than the C3s of adducts shown in Table 3 since nitrogen atom at position 5 and the phenyl ring attached to the C7 would contribute deshielding effect to the C3 more than to the C2 of 89. Although, the cyano carbon of the adduct 3 and 4 are shown at $\delta$ 120.8 and 122.8, respectively.
The carbon chemical shift of cyclobutene at position 1 (as shown above) has been reported at 137.2 ppm.\textsuperscript{21} When the carbon at position 1 is attached with a nitrogen atom as in the azete, shown above, the shift of the carbon at position 1 has been reported at 181 ppm.\textsuperscript{20} Although this azete has one additional double bond in the ring when compared with cyclobutene, the downfield approximately 50 ppm of the carbon at position 1 in the azete relative to cyclobutene would likely be due to a deshield effect of the electronegative nitrogen atom. Based on this information, the signal at $\delta$ 192.0, in Figure 150a, would correspond to the carbon at position 7 of \textbf{89} since it attaches to two nitrogen atoms and a phenyl ring. These assignments corresponded to the $^{13}$C-DEPT 135 spectrum revealing the signals at $\delta$ 90.4, 107.4, 148.5 and 159.0 in positive direction indicating the absorptions of tertiary carbons. The signals at $\delta$ 103.8 and 192.0 appeared in the $^{13}$C-CPD spectrum as the least relative intensity signals and disappeared in the $^{13}$C-DEPT 135 spectrum corresponding to the assignments to the quarternary carbons at C6 and C7, respectively. The signals in the region of $\delta$ 127.0-131.0 would be due to absorption of the phenyl ring carbons.
Results and Discussion

Figure 150a: $^{13}\text{C}$-NMR spectrum of the unknown sample F7; the expected adduct

Figure 150b: $^{13}\text{C}$-DEPT 135 spectrum of the unknown sample F7; the expected adduct
The mass spectral results observed in the photolysis of 5-phenyl-1,2,4-thiadiazole (31), 3-methyl-5-phenyl-1,2,4-thiadiazole (54) or diphenyl-1,2,4-thiadiazole (47) in furan solvent and the $^{13}$C-NMR spectral analysis of the product isolated from the photoreaction of 47 in furan solvent, are strongly evidence for the formation 1:1 adducts of the thia diazole and furan with loss of sulfur. These adducts could result from trapping of the photochemically generated 1,3-diaza-5-thiabicyclo[2.1.0]pentenes (BC) with furan and subsequent elimination of elemental sulfur or from trapping of phenyl-1,3-diazacyclobutadienes (CB) with furan.

### 2.9.2 Irradiation of 3-phenyl-1,2,4-thiadiazole in furan solvent

Previous work in this laboratory has shown that irradiation of 3-phenyl-1,2,4-thiadiazole-2-$^{15}$N (46-2-$^{15}$N) does not lead to $^{15}$N-scrambling in the 3-phenyl-1,2,4-thiadiazole ring. Irradiation of this compound leads only to the formation of benzonitrile-$^{15}$N (43-$^{15}$N), the photofragmentation product. This indicates that 46-2-$^{15}$N does not undergo electrocyclic ring closure. If it did, the initially formed bicyclic species, BC-46-2-$^{15}$N, would be expected to be in equilibrium with the isoenergetic species BC-46-4-$^{15}$N. Rearomatization of the latter species would give 3-phenyl-1,2,4-thiadiazole-4-$^{15}$N (46-4-$^{15}$N). This was not experimentally observed. In view of these results, it was of interest to see if the photochemistry of 46 would be affected by the presence of furan.

**Scheme 67:** The expected $^{15}$N-scrambling in 3-phenyl-1,2,4-thiadiazole-2-$^{15}$N
Results and Discussion

Solutions of 3-phenyl-1,2,4-thiadiazole (46) in furan (1.1×10^{-2} M; 4 mL) and 46 in acetonitrile (1.1×10^{-2} M; 4 mL) in sealed Pyrex tubes were purged with argon gas for 15 min. These solutions were simultaneously irradiated with sixteen > 290 nm lamps in a Rayonet reactor for a total of 120 min. Figure 151 shows the GC trace of the 46+Furan solution before irradiation revealing that no ground state reaction between 46 and furan was observed. Furan is eluted with a retention time within the solvent delay (2 min) and, thus, was not observed in this GLC analysis.

![Figure 151: GLC analysis of 46+Furan solution before irradiation](image)

After 120 min of irradiation, the 46+Furan solution was analyzed by the GC interfaced with a mass spectrometer. The trace reveals (Figure 152) the presence of only two major components which eluted with retention times of 4.3 and 18.5 min. Mass spectra analyses of these components were consistent with the structures of benzonitrile (43), the known photofragmentation product observed upon irradiation of 46 in an absence of furan, and the starting thiadiazole 46, respectively. Even after concentration, the GC-trace did not show the formation of any new GC-volatile components in this concentrated photolysate.
These results show that irradiation of 3-phenyl-1,2,4-thiadiazole (46) in neat furan leads only to the formation of benzonitrile (43). No furan-phenyldiazacyclobutadiene could be detected in this case. These results show that when electrocyclic ring closure does not occur, no reaction occurs with furan. This is further evidence that in the case of 5-phenyl-1,2,4-thiadiazoles 31, 54, and 47, furan reacts with the photochemically generated 1,3-diazacyclo[2.1.0]pentenes (BC) and possibly also with the diazacyclobutadienes (CB) derived from the bicyclic species.

These results are thus consistent with the conclusion reached from $^{15}$N-labeling experiments. These results did show, however, that the yield of benzonitrile (43) formation is decreased upon changing solvent from acetonitrile to neat furan. In order to gain more quantitative information, irradiations of 46 with various furan concentrations were carried out.

Solutions of 46 in acetonitrile ($1.1 \times 10^{-2}$ M; 4 mL) with the presence of furan from 0%-90% were placed in Pyrex tubes, sealed with rubber septa and purged with argon gas for 15 min. The solutions were simultaneously irradiated by sixteen > 290 nm lamps in a Rayonet reactor. The photoreactions were monitored by GLC at 30 min of intervals.
Figure 153 shows a plot of the furan concentrations $Vs$ the yield of $43$ in the absence of furan divided by the yield of $43$ observed at the various furan concentrations after 60 min of irradiation. This plot reveals that, increasing the concentration of furan is initially accompanied by a decrease in the yield of $43$ until the furan concentration reaches approximately 60% which led to 40% quenching of the yield of $43$. After that point continued increasing the furan concentration has no additional effect on the yield of $43$. In classical Stern-Volmer kinetics, such a quenching curve is generally taken to mean that a long-lived species is initially being quenched and is totally quenched by 60% quencher. Beyond that concentration, benzonitrile ($43$) is being formed only from a very short-lived species which cannot be quenched.

![Benzonitrile formation (in Furan)](image)

**Figure 153:** Plot of the furan concentrations $Vs$ the yield of $43$ in the absence of furan divided by the yield of $43$ observed at the various furan concentrations
Figure 154 and 155 show plots between irradiation time $Vs$ consumption of 46 upon irradiation in acetonitrile and furan solvents. These plots clearly indicate that after 60 min of irradiation the consumption of 46 in furan solvent is less than the consumption of 46 in acetonitrile solvent. This change of reactivity could be due to a change in solvent polarity upon changing from acetonitrile to furan or to a direct quenching interaction between 46 and furan.

![Figure 154: Plot between irradiation time $Vs$ consumption of 46 in acetonitrile solvent](image1)

![Figure 155: Plot between irradiation time $Vs$ consumption 46 in furan solvent](image2)

In order to clarify this assumption, irradiation of 46 in tetrahydrofuran solvent was carried out. Tetrahydrofuran is expected to have similar polarity to furan but no interaction between the solvent and either the ground state or excite state of 46 is expected to occur.
2.9.3 Irradiation of 3-phenyl-1,2,4-thiadiazole in tetrahydrofuran solvent

Solutions of 3-phenyl-1,2,4-thiadiazole (46) in tetrahydrofuran (1×10^{-2} M; 3.5 mL) and 46 in acetonitrile (1×10^{-2} M; 3.5 mL) in sealed Pyrex tubes were purged with argon gas for 20 min. These solutions were simultaneously irradiated with sixteen > 290 nm lamps in a Rayonet reactor for a total of 90 min. Figure 156a shows the GLC analysis of 46+THF solution before irradiation revealing that no ground state reaction between 46 with THF was observed.

Figure 156a: GC-trace of 46+THF solution before irradiation
The GC-trace of the \textit{46+THF} solution after 90 min of irradiation (Figure 156b) reveals the formation of \textit{43} eluting at retention time of 3.5 min and the two minor products eluting at retention time of 3.3 and 5.7 min. After concentration, the concentrated photolysate was analyzed by the GC interfaced with a mass spectrometer. Figure 157a exhibits a GC-trace of the concentrated \textit{46+THF} photolysate revealing the presence of two major components, which eluted with retention times of 7.5 and 17.7 min, and three minor components which eluted with retention times of 7, 17 and 34.5 min. Figure 157b-d show mass spectra of the three minor components. Mass spectra analysis of the two major components at 7 and 17 min was consistent with benzonitrile (\textit{43}) and the starting thiadiazole (\textit{46}), respectively. Mass spectra analysis of the three minor products indicates that the components eluting with retention times of 17 and 34.5 min, which have molecular ions at m/z 121 and 238, respectively, are consistent with the structures of benzamide (\textit{38}) and diphenyl-1,2,4-thiadiazole (\textit{47}). The component which eluted with a retention time of 7 min, that has a molecular ion at m/z 86, has not been un-identified.
Results and Discussion

Figure 157a: GC trace of the concentrated 46+THF photolysate

Figure 157b: Mass spectrum of the component at retention time of 7 min
Figure 157c: Mass spectrum of the component at retention time of 17 min

Figure 157d: Mass spectrum of the component at retention time of 34.5 min
Benzamide (38) was also observed as a minor product formed from the photoreaction of 5-phenyl-1,2,4-thiadiazole (31) in acetonitrile solvent. In that case, the formation of 38 was suggested to occur by reaction of either a thiazirine or nitrile sulfide intermediates with water present in the solution. Since 3-phenyl-1,2,4-thiadiazole (46) is not expected to isomerize via a thiazirine intermediate, benzamide (38) would have to result from reaction of benzonitrile sulfide with water in the solution as shown in Scheme 68.

![Scheme 68: Possible formation of benzamide upon irradiation of 46](image)

Irradiation of 46 in acetonitrile with tetrahydrofuran at various concentrations was also carried out. Solutions of 46 in acetonitrile (1.1×10^{-2} M; 4 mL) containing tetrahydrofuran from 0%-90% were placed in Pyrex tubes, sealed with rubber septa and purged with argon gas for 15 min. The solutions were simultaneously irradiated by sixteen > 290 nm lamps in a Rayonet reactor equipped with a merry-go-round apparatus. The photoreactions were monitored by GLC at 30 min of intervals.
Figure 158 shows a plot between tetrahydrofuran concentrations Vs the yield of benzonitrile (43) in an absence of THF divided by the yield of 43 observed at various tetrahydrofuran concentrations after 30 min of irradiation. This plot reveals that tetrahydrofuran has no significant effect on the formation of 43 relative to the formation of 43 observed in the reaction in the absence of tetrahydrofuran.

![Figure 158: Plot of THF concentrations Vs the yield of 43 in the absence of THF divided by the yield of 43 observed at the various THF concentrations](image)

Figure 159 shows a plot between the tetrahydrofuran concentrations Vs the consumption of 46 in the absence of tetrahydrofuran divided by the consumption of 46 observed at various tetrahydrofuran concentrations after 30 min of irradiation. This plot clearly reveals that tetrahydrofuran also has no effect on the consumption of 46 relative to the consumption of 46 in the photoreaction in the absence of tetrahydrofuran.
Results and Discussion

Figure 159: Plot of THF concentrations Vs the consumption of 46 in the absence of THF divided by the consumption of 46 observed at the various THF concentrations

Since tetrahydrofuran and furan are similar in the polarity, if the photoreactivity change of 3-phenyl-1,2,4-thiadiazole (46) upon changing from acetonitrile to furan was due to an effect of solvent polarity, irradiation of 46 in acetonitrile containing tetrahydrofuran at various concentrations should also reveal a similar decrease in the photoreactivity of 46. The result upon irradiation of 46 in acetonitrile with various tetrahydrofuran concentrations, however, indicated that tetrahydrofuran had no effect either on the consumption of 46 or the formation of benzonitrile (43). This indicates that solvent polarity of furan has no effect on the reactivity of 46. Thus, the observed decrease in the photoreactivity of 46 in the presence of furan would be due to a direct quenching interaction between 46 and furan via an unclear mechanism. The $S_1$ and $T_1$ state energies of furan have been reported at 129 and 74 kcal/mol, respectively.\textsuperscript{22} With the observed $S_1$ and $T_1$ state energies of 3-phenyl-1,2,4-thiadiazole (46) at 97 and 68 kcal/mol, respectively, and under the irradiation condition at $> 290$ nm, the possibility that furan may act as a singlet or triplet quencher can be ruled out since these processes are energetically unfavorable.
2.10 Photochemistry of 5-(4’-Substituted)Phenyl- and 3-(4’-Substituted)Phenyl-1,2,4-Thiadiazoles

In order to study the effect of electron donating and electron withdrawing substituents in the phenyl ring on the photochemistry of 1,2,4-thiadiazoles, it was proposed to synthesize and to study the photochemistry of the 3-(4’-substituted)phenyl- and 5-(4’-substituted)phenyl-1,2,4-thiadiazoles shown below.

\[
\begin{align*}
&\text{N} \quad \text{S} \\
&\text{N} \quad \text{S} \\
&\text{X} \\
&\text{X} = \text{OCH}_3 \text{ and CN}
\end{align*}
\]

2.10.1 Photochemistry of 5-(4’-substituted)phenyl-1,2,4-thiadiazole

2.10.1.1 Synthesis of 5-(4’-methoxy)phenyl-1,2,4-thiadiazole

Synthesis of 5-phenyl-1,2,4-thiadiazole (31) can be achieved by base catalyzed amination cyclization of N-[(dimethylamino)methylene]thiobenzamide (32) with hydroxylamine-O-sulfonic acid (33). Therefore, 5-(4’-methoxy)phenyl-1,2,4-thiadiazole (90) was synthesized by this synthetic pathway employing 4-methoxythiobenzamide (91) as the stating material instead of thiobenzamide. 4-Methoxythiobenzamide (91) was synthesized by thionation of 4-methoxybenzamide (92) with Lawesson’s reagent in refluxing tetrahydrofuran. Scheme 69 shows the total synthetic scheme of 90.
Results and Discussion

Scheme 69: Total synthesis of 5-(4’-methoxy)phenyl-1,2,4-thiadiazole

2.10.1.1.1 Synthesis of 4-methoxythiobenzamide

4-Methoxythiobenzamide (91) was prepared in 55 % by thionation of 4-methoxybenzamide (92) with Lawesson’s reagent in refluxing tetrahydrofuran solvent (Scheme 70). The yellow solid product was characterized by $^1$H-, $^{13}$C-NMR and mass spectroscopy.

Scheme 70: Synthesis of 4-methoxythiobenzamide

GC analysis of the synthetic 91 (Figure 160a) shows the presence of one component that eluted with a retention time of 18.8 min. The mass spectrum (Figure 160b) of the synthetic 91 exhibits the base molecular ion peak at m/z 167 which corresponds to the molecular weight of 91. The spectrum also exhibits intense peaks at m/z 151 and 134 due to cleavage of M$^+$-16 and M$^+$-33 fragments from the molecular ion. The loss of these
fragments from the molecular ion is also observed in the fragmentation of the un-substituted thiobenzamide (Figure 63b). This confirms that the loss of these two fragments is a normal fragmentation pathway for thiobenzamides.

**Figure 160a:** GC analysis of the synthesized 4-methoxythiobenzamide

**Figure 160b:** Mass spectrum of 4-methoxythiobenzamide
The $^1$H–NMR spectrum (Figure 161) of this synthetic 91 exhibits a singlet (3H) due to the methoxy protons at $\delta$ 3.84. The phenyl ring protons appear as two doublets at $\delta$ 6.90 (2H; $J = 8.84$ Hz) and $\delta$ 7.92 (2H; $J = 8.84$ Hz). The two protons of the amino group are not equivalent due to the partial double bond character of the C-N bond. Therefore, these two protons have different chemical shifts. The first signal appears as a broad singlet (1H) at $\delta$ 8.34. The second amino proton signal appears as a broad shoulder in the region of $\delta$ 7.9-8.3 where the phenyl ring protons absorb.

![Figure 161: $^1$H-NMR spectrum of 4-methoxythiobenzamide](image)

Figure 161: $^1$H-NMR spectrum of 4-methoxythiobenzamide
In the $^{13}$C–NMR spectrum (Figure 162a), the most down field signal at \( \delta \) 202.8 was assigned to the thiocarbonyl carbon. The phenyl carbon ring position 4 absorbs downfield at \( \delta \) 163.1 while the phenyl carbon ring position 1 appears more upfield at \( \delta \) 130.9. The two signals at \( \delta \) 113.6 and 129.1 were assigned to the two sets of phenyl carbons at ring positions 2,6 and 3,5, respectively. The spectrum also reveals the methoxy carbon at \( \delta \) 55.5. These spectral assignments were confirmed by the $^{13}$C–DEPT135 spectrum, shown in Figure 162b. The signal at \( \delta \) 55.5 still appears in the $^{13}$C–DEPT 135 spectrum which is consistent with the assignment to the methoxy carbon. The three signals at \( \delta \) 130.87, 163.07 and 200.82, which were assigned to the phenyl carbons positions 1 and 4 and the thiocarbonyl carbon, are not observed in the $^{13}$C–DEPT 135 spectrum which confirms that these signals are due to quaternary carbons. The two signals, which absorb in the phenyl region, still appear in the $^{13}$C–DEPT 135 spectrum. Thus, this is consistent with the assignment of these two signals to the two set of phenyl carbons at position 2,6 and 3,5.
Results and Discussion

Figure 162a: $^{13}$C-NMR spectrum of 4-methoxythiobenzamide

Figure 162b: $^{13}$C-DEPT 135 spectrum of 4-methoxythiobenzamide
Results and Discussion

2.10.1.1.2 Synthesis of N-[(dimethylamino)methylene]4-methoxythiobenzamide

N-[(dimethylamino)methylene]4-methoxythiobenzamide (93) was prepared in 95% as a reddish orange crystalline solid by the condensation between 91 and 35, as shown in Scheme 71. The reddish orange crystals were characterized by $^1$H- and $^{13}$C-NMR spectroscopy.

Scheme 71: Synthesis of N-[(dimethylamino)methylene]4-methoxythiobenzamide

The $^1$H-NMR spectrum (Figure 163) of this reddish orange crystalline solid exhibits a singlet (3H) at $\delta$ 3.83 which can be assigned to the methoxy protons. The two singlets at $\delta$ 3.27 (3H) and 3.29 (3H) are the absorptions due to two sets of the non-equivalent methyl protons bonded to the amino group. The two doublets at $\delta$ 6.84 (2H; $J = 9.1$ Hz) and $\delta$ 8.44 (2H; $J = 9.1$ Hz) were assigned to the two set of phenyl ring protons at positions 2,6 and 3,5, respectively. The imine proton absorbs at $\delta$ 9.45.
Results and Discussion

The $^{13}$C-NMR spectrum (Figure 164a) exhibits the carbon signals correspond to the structure of 93. The thiocarbonyl carbon absorbs downfield at $\delta$ 214.66. Based on the previous $^{13}$C–NMR spectral assignment of N-[(dimethylamino)methylene]thiobenzamide (32), the signal at $\delta$ 159.1 can be assigned to the absorption of the imine carbon. The phenyl ring carbons appear as four singlets at $\delta$ 112.8, 131.1, 136.3 and 163.3. The two singlets at $\delta$ 36.3 and 41.8 were assigned to the two non-equivalent N-methyl carbons. The methoxy carbon appears at $\delta$ 55.4. These assignments are consistent with the $^{13}$C–DEPT 135 spectrum (Figure 164b). The two signals at $\delta$ 136.3 and 159.1 disappeared in the $^{13}$C–DEPT 135 spectrum which are consistent with the assignment of the two signals to the two quaternary carbons on the phenyl ring at position 1 and 4, respectively.

Figure 163: $^1$H-NMR spectrum of N-[(dimethylamino)methylene]4-methoxythiobenzamide
The signals at δ 159.1, 131.1, 112.8, 55.4, 41.8 and 36.3 still appear in the $^{13}$C–DEPT 135 spectrum which are consistent with the assignment to the imine carbon, phenyl ring carbons position 2,6 and 3,5, methoxy carbon and two non-equivalent amino methyl carbons, respectively.
Figure 164a: $^{13}$C-NMR spectrum of N-[(dimethylamino)methylene]4-methoxythiobenzamide

Figure 164b: $^{13}$C-DEPT 135 spectrum of N-[(dimethylamino)methylene]4-methoxythiobenzamide
2.10.1.1.3 Synthesis of 5-(4′-methoxy)phenyl-1,2,4-thiadiazole

5-(4′-Methoxy)phenyl-1,2,4-thiadiazole (90) was synthesized by the similar method as for the synthesis of 5-phenyl-1,2,4-thiadiazole. Amination cyclization of 93 with 33 would result in the formation 90, as shown in Scheme 72.

Scheme 72: Synthesis of 5-(4-methoxy)phenyl-1,2,4-thiadiazole

5-(4-Methoxy)phenyl-1,2,4-thiadiazole (90) was obtained in 70 % as white crystals. This crystalline solid was characterized by $^1$H-, $^{13}$C-NMR and mass spectroscopy.
The GC analysis of these colorless crystals (Figure 165a) exhibits a major peak with a retention time of 24.9 min. The mass spectrum of this component (Figure 165b) exhibits a molecular ion at m/z 192 which is consistent with the molecular weight of 90 (MW 192). The spectrum also exhibits an intense peak at m/z 134 which is due to the $[p$-$\text{OMeC}_6\text{H}_3\text{CNH}]^{+}$ fragment resulting from the cleavage of $[p$-$\text{OMeC}_6\text{H}_3\text{CN}]^{+}$ with a subsequent proton transfer. The peak at m/z 165 is consistent with the cleavage of [HCNS].

**Figure 165a:** GC analysis of the synthesized 5-(4'-methoxy)phenyl-1,2,4-thiadiazole

**Figure 165b:** Mass spectrum of 5-(4'-methoxy)phenyl-1,2,4-thiadiazole
The $^1$H–NMR spectrum, as shown in Figure 166, exhibits a very clear spectrum. The proton at ring position 3 absorbs downfield at $\delta$ 8.87 as a singlet (1H). The phenyl ring protons appear as two doublets at $\delta$ 6.99 (2H; $J = 8.6$ Hz) and $\delta$ 7.92 (2H; $J = 8.6$ Hz) assigned to two sets of ring protons at positions 2,6 and 3,5, respectively. The 3H singlet at $\delta$ 3.87 is due to the absorption of the methoxy protons.

**Figure 166:** $^1$H-NMR spectrum of 5-(4'-methoxy)phenyl-1,2,4-thiadiazole
The $^{13}$C–NMR spectrum (Figure 167a) shows that the methoxy carbon absorbs at δ 55.5. The three singlet signals at δ 114.7, 123.1 and 129.3 were assigned to the phenyl ring carbons at positions 2 and 6, 1, and 3 and 5, respectively, while the phenyl ring carbon at position 4 appears further downfield at δ 162.7. The two carbon atoms of the thiadiazole ring absorb at δ 163.2 and 187.8. The former signal was assigned to the carbon at ring position 3, while the latter signal was assigned to the carbon at ring position 5. These assignments are consistent with the $^{13}$C–DEPT 135 spectrum (Figure 167b) which confirms that the signals at δ 123.1, 162.7 and 187.8 are due to quaternary carbons. The signal at δ 55.5, 114.7, 129.2 and 163.2 still appear in the $^{13}$C–DEPT 135 spectrum and thus these are consistent with the assignments to the methoxy carbon, the phenyl ring carbons at positions 2,6 and 3,5 and the carbon at ring position 3 of the thiadiazole ring, respectively.
Figure 167a: $^1$H-NMR spectrum of 5-(4'-methoxy)phenyl-1,2,4-thiadiazole

Figure 167b: $^{13}$C-DEPT 135 spectrum of 5-(4'-methoxy)phenyl-1,2,4-thiadiazole
2.10.1.2 Synthesis of 2-(4′-methoxy)phenyl-1,3,5-triazine

2,4-Dimethyl-6-phenyl-1,3,5-triazine (65) and 2-methyl-4,6-diphenyl-1,3,5-triazine (66) were prepared by the method described by Raymond Dengino and co-workers. This method can be applied to the synthesis of both symmetrical and unsymmetrical triazines which involves the condensation of N-acylamidines with amidines or guanidines. Based on this synthetic procedure, condensation of N-[(dimethylamino)methylene]4-methoxybenzamide (96) with formamidine (97) would yield 2-(4′-methoxy)phenyl-1,3,5-triazine (94) as shown in Scheme 73.

![Scheme 73: Total synthetic scheme of 2-(4′-methoxy)phenyl-1,3,5-triazine](image)

2.10.1.2.1 Synthesis of N-[(dimethylamino)methylene]4-methoxybenzamide

In order to synthesize 2-(4′-methoxy)phenyl-1,3,5-triazine by the synthetic route proposed in Scheme 73, 96 is required as the starting material. The amidine 96 was prepared in 86% yield as a colorless crystals by the condensation of 92 with 35, as shown in Scheme 74.

![Scheme 74: Synthesis of N-[(dimethylamino)methylene]4-methoxybenzamide](image)
The GC-chromatogram of the colorless crystals (Figure 168a) shows the presence of only one gc-volatile component, which eluted with a retention time of 22 min. The mass spectrum (Figure 168b) reveals a molecular ion at m/z 206 and a base peak at m/z 135. The molecular ion at m/z 206 is consistent with a molecular weight of 96 (MW 206) while the base peak at m/z 135 also corresponds to \([\text{C}_3\text{H}_7\text{O}_2]^+\) fragment due to cleavage of \([\text{C}_3\text{H}_7\text{N}_2]\) from the molecular ion.

\[ \text{Figure 168a: GC analysis of the colorless crystals} \]
Figure 168b: Mass spectrum of N-[(dimethylamino)methylene]4-methoxybenzamide

Figure 169 shows that the $^1$H-NMR spectrum of the colorless crystals corresponds with the structure of 96. The methoxy protons are shown as a singlet (3H) at $\delta$ 3.84. The protons of the two non-equivalent methyl amino groups absorb at $\delta$ 3.19 (3H) and 3.23 (3H). The two doublets at $\delta$ 6.89 (2H; $J = 8.59$ Hz) and 8.23 (2H; $J = 8.59$ Hz) are due to absorptions of the phenyl ring protons at position 2,6 and 3,5, respectively. The imine proton appears downfield at $\delta$ 8.82 (1H).
Results and Discussion

Figure 169: $^1$H-NMR spectrum of N-[(dimethylamino)methylene]4-methoxybenzamide

The $^{13}$C-NMR spectrum (Figure 170a) is also consistent with the structure of 96. The carbonyl carbon absorbs downfield at $\delta$ 177.6. The signal at $\delta$ 160.6 was assigned to an absorption of the imine carbon. The phenyl ring carbons at positions 2, 6 and 3, 5 appear as two singlets at $\delta$ 113.6 and 132.2 while the phenyl ring carbons at positions 1 and 4 absorb at $\delta$ 129.9 and 163.1, respectively. The two singlets at $\delta$ 35.7 and 41.8 were assigned to the two non-equivalent N-methyl carbons. The methoxy carbons are shown at $\delta$ 55.8. These assignments are consistent with the $^{13}$C–DEPT 135 spectrum (Figure 170b). The three signals at $\delta$ 129.9, 163.1 and 177.6 disappeared in the $^{13}$C–DEPT 135 spectrum which is consistent with the assignment of the three signals to the three quarternary carbons of the phenyl ring at position 1 and 4 and the carbonyl carbon, respectively. The signals at $\delta$ 35.7, 41.8, 55.8, 113.6, 132.2 and 160.9 still appear in the $^{13}$C–DEPT 135 spectrum in
positive directions which are consistent with the assignment to the two non-equivalent amino methyl carbons, methoxy carbon, phenyl ring carbons positions 2 and 6, 3 and 5, and the imine carbon, respectively.

Figure 170a: $^{13}$C-NMR spectrum of N-[(dimethylamino)methylene]4-methoxybenzamide

Figure 170b: $^{13}$C-DEPT 135 spectrum of N-[(dimethylamino)methylene]4-methoxybenzamide
2.10.1.2.2 Synthesis of 2-(4′-methoxy)phenyl-1,3,5-triazine

By analogy with the triazine synthesis described by Raymond Dengino and co-workers,\textsuperscript{14} 2-(4′-methoxy)phenyl-1,3,5-triazine (94) was prepared by condensation of the acylamidine 96 with 97 in refluxing abs. ethanol under a nitrogen atmosphere. After solvent removal, a crude yellow solid was obtained. The crude yellow solid was subjected to preparative layer chromatography. The two major bands with \( R_f \) of 0.5 and 0.85 were removed and extracted to give colorless crystals B1 and colorless crystals B2, respectively. These solids were characterized by \(^1\)H-NMR and mass spectroscopy.

\[ \text{Scheme 75: Synthesis of 2-(4′-methoxy)phenyl-1,3,5-triazine} \]

GC analysis of the colorless crystals B1 (Figure 171a) exhibits a major component which eluted with a retention time of 14.3 min. The mass spectrum (Figure 171b) reveals a molecular ion at m/z 151 and a base peak at m/z 135. The molecular ion at m/z 151 is consistent with a molecular formula of \( \text{C}_8\text{H}_9\text{NO}_2 \). The chromatographic and mass spectroscopic properties of this sample corresponded to those of an authentic sample of 92.
**Figure 171a:** GC analysis of the colorless crystals B1

**Figure 171b:** Mass spectrum of the colorless crystals B1
Results and Discussion

Figure 171c: $^1$H-NMR spectrum of the colorless crystals B1

Figure 171c shows the $^1$H-NMR spectrum of the colorless crystals B1. The spectrum exhibits two doublets at $\delta$ 6.91 (2H; J = 8.84 Hz) and 7.76 (2H; J = 8.84 Hz), singlet (3H) at $\delta$ 3.84 and a very broad singlet (2H) at $\delta$ 5.89. The 2H broad singlet would suggest the presence of an amino group in the structure of this colorless crystalline solid B1. Comparison of chromatographic, nuclear magnetic resonance and mass spectroscopic properties of this colorless crystalline solid B1 with those of an authentic sample of 4-methoxybenzamide indicating that this solid B1 is 4-methoxybenzamide (92).

GC analysis of the colorless crystals B2 (Figure 172a) exhibits only one component which eluted with a retention time of 11 min. The mass spectrum (Figure 172b) reveals a base molecular ion at m/z 187 and a high intensity peak at m/z 134. The molecular ion at m/z 187 is consistent with a molecular formula of C$_{10}$H$_8$N$_3$O. The high intensity peak at m/z 134 corresponds to the elimination of [C$_8$H$_7$NO] followed by hydrogen atom abstraction to give [C$_8$H$_8$NO]$^+$ fragment (m/z 134). This fragmentation pathway is also observed as the major pathway in fragmentation of 2-phenyl-1,3,5-triazine (39).
**Results and Discussion**

**Figure 172a:** GC analysis of the colorless crystals B2

**Figure 172b:** Mass spectrum of the colorless crystals B2; 2-(4′-methoxy)phenyl-1,3,5-triazine
Figure 173 shows the $^1$H-NMR spectrum of the colorless crystals B2. The spectrum exhibits two doublets at $\delta$ 6.99 (2H; $J = 8.84$ Hz) and 8.46 (2H; $J = 8.84$ Hz) which can be assigned to the absorptions of phenyl ring protons at position 2',6' and 3',5', respectively. The downfield singlet at $\delta$ 9.11 (2H) is due to the two equivalent protons on the triazine ring. The methoxy protons appear as a 3H singlet at $\delta$ 3.87. These $^1$H-NMR spectral assignments and the fragmentation pattern in the mass spectrum of the crystalline solid B2 are consistent with the structure of 2-(4'-methoxy)phenyl-1,3,5-triazine (94).

Figure 173: $^1$H-NMR spectrum of the colorless crystals B2; 2-(4'-methoxy)phenyl-1,3,5-triazine
2.10.1.3 Synthesis of 5-(4′-cyano)phenyl-1,2,4-thiadiazole

The synthesis of 5-(4′-methoxy)phenyl-1,2,4-thiadiazole (90) has shown that 90 can be synthesized by the method described for the synthesis of 5-phenyl-1,2,4-thiadiazole (31) via amination cyclization of the corresponding amidine, 93, with 33. Therefore, it should be also possible to synthesize 5-(4′-cyano)phenyl-1,2,4-thiadiazole (98) by this method. In this synthetic route, 4-cyanothiobenzamide (99) will be required as the stating material instead of thiobenzamide (34). 4-Cyanothiobenzamide (99) is not commercially available and would be prepared by thionation of 4-cyanobenzamide (100) with the Lawesson’s reagent. Thus, 100 would be obtained from 4-cyanobenzoic acid (101) by treatment of 4-cyanobenzoyl chloride with aqueous ammonia as shown in Scheme 76.

Scheme 76: Total synthesis of 5-(4′-cyano)phenyl-1,2,4-thiadiazole
2.10.1.3.1 Synthesis of 4-cyanobenzamide

4-Cyanobenzamide (100) was prepared in 95% as a light brown fine solid by the two steps synthesis shown in Scheme 77. The light brown product was characterized by \(^1\)H-, \(^13\)C-NMR and mass spectroscopy.

\[
\text{Scheme 77: Synthesis of 4-cyanobenzamide}
\]

GC analysis of the synthetic 100 (Figure 174a) shows one component, which eluted with a retention time of 12.4 min. The mass spectrum (Figure 174b) of this component exhibits a molecular ion peak at m/z 146 which corresponds to the molecular weight of 100. The spectrum also exhibits a base peak at m/z 130 due to the loss of [NH\(_2\)] fragment from the molecular ion. The intense peak at m/z 102 is due to [\(p\text{-CNC}_6\text{H}_4\)]\(^+\) fragment.

\[
\text{Figure 174a: GC analysis of 4-cyanobenzamide}
\]
The $^1$H–NMR spectrum (DMSO-$d_6$) of the synthetic 4-cyanobenzamide (100), shown in Figure 175, exhibits two non-equivalent amino protons at $\delta$ 9.61 (1H) and 10.18 (1H). The two sets of phenyl ring protons absorb at $\delta$ 7.94 (d, 2H; $J = 7.3$ Hz) and $\delta$ 8.00 (d, 2H; $J = 7.3$ Hz). The spectrum, however, also reveals a doublet at $\delta$ 8.03 (d, $J = 8.1$ Hz). This signal would be expected due to the presence of an unknown impurity.
The $^{13}$C-NMR spectrum (Figure 176a) exhibits eight carbon signals. Two of these signals are due to the unknown impurity. The carbonyl carbon of 100 absorbs downfield at $\delta$ 167.3. The two sets of phenyl carbons at ring positions 2,6 and 3,5 appear at $\delta$ 129.1 and 133.3, respectively. The phenyl ring carbons at positions 1 and 4 absorb at $\delta$ 119.3 and 139.1, respectively. Thus, the signals at $\delta$ 130.8 and 133.6 were assigned to the carbons of the unknown impurity. These assignments are consistent with the $^{13}$C–DEPT 135 spectrum (Figure 176b). The four signals at $\delta$ 167.3, 139.1, 119.3 and 114.5 disappeared in the $^{13}$C–DEPT 135 spectrum which are consistent with the assignment of the carbonyl carbon and the three signals to the quaternary phenyl ring carbons at positions 4 and 1 and the cyano carbon, respectively. The two small singlets shown in the $^{13}$C–DEPT 135 spectrum at $\delta$ 130.8 and 133.6 are not consistent with any signals of 100. Thus these signals would be consistent with the assignment to the unknown impurity.
Results and Discussion

Figure 176a: $^{13}$C-NMR spectrum of 4-cyanobenzamide

Figure 176b: $^{13}$C-DEPT spectrum of 4-cyanobenzamide
2.10.1.3.2 Synthesis of 4-cyanothiobenzamide

Thionation of 4-cyanobenzamide (100) with Lawesson’s reagent yielded 4-cyanothiobenzamide (99) in 56% as a yellow solid. Scheme 78 shows the synthesis of 99. The yellow solid was characterized by $^1$H-, $^{13}$C-NMR and mass spectroscopy.

\[ \text{NC} \quad \text{O} \quad \text{NH}_2 \quad \xrightarrow{\text{Lawesson’s reagent}} \quad \text{THF, reflux} \quad \text{NC} \quad \text{S} \quad \text{NH}_2 \]

Scheme 78: Synthesis of 4-cyanothiobenzamide

The GC analysis of the yellow solid shows that a gc-volatile product eluted with a retention time of 16.4 minutes (Figure 177a). The mass spectrum (Figure 177b) of this compound exhibits a base molecular ion at m/z 162 which corresponds to the molecular weight of 99. The spectrum also shows two intense peaks at m/z 146 and 129. These two peaks are expected to result from the loss of the m/z 16 and 33 fragments as previously observed in thiobenzamide (34) and 4-methoxythiobenzamide (91).

Figure 177a: GC analysis of 4-cyanothiobenzamide
The $^1$H–NMR spectrum (DMSO-$d_6$; Figure 178) of 4-cyanothiobenzamide (99) exhibits phenyl ring protons as two doublets at $\delta$ 7.90 (2H; J = 8.1 Hz) and $\delta$ 7.96 (2H; J = 8.1 Hz) due to the two sets of phenyl ring protons at positions 2,6 and 3,5, respectively. The two non-equivalent amino protons are shown at $\delta$ 9.75 (1H) and 10.18 (1H). The spectrum also reveals two singlets at $\delta$ 9.60 and 10.00 which would be due to the two non-equivalent amino protons of the starting material, 4-cyanobenzamide (100). The multiplet and doublet at $\delta$ 6.90-7.80 region would also be due to the absorption of the phenyl ring protons of the starting material, 100.
Results and Discussion

Figure 178: $^1$H-NMR spectrum of 4-cyanothiobenzamide

The $^{13}$C–NMR spectrum (Figure 179a) exhibits the two sets of phenyl ring carbon signals at $\delta$ 128.6 and 132.8. The ring phenyl carbon at position 1 appear as a singlet at $\delta$ 119.9 while the ring carbon at position 4 absorbs at $\delta$ 144.2. The signal at $\delta$ 113.9 was assigned to the cyano carbon. The thiocarbonyl carbon absorbs downfield at $\delta$ 199.3. The singlet at $\delta$ 127.6 was assigned to a carbon signal from 100. These assignments can be supported by the $^{13}$C–DEPT 135 spectrum, shown in Figure 179b. The signals at $\delta$ 128.6 and 132.8 appear in positive direction in the $^{13}$C–DEPT 135 spectrum which is consistent with their assignments as two set of equivalent phenyl ring carbons. The four signals at $\delta$ 113.7, 119.2, 144.2 and 199.3 disappear in the $^{13}$C–DEPT 135 spectrum confirming that they are all quaternary carbons.
Results and Discussion

Figure 179a: $^{13}$C-NMR spectrum of 4-cyanothiobenzamide

Figure 179a: $^{13}$C-DEPT 135 spectrum of 4-cyanothiobenzamide
2.10.1.3.3 Synthesis of N-[(dimethylamino)methylene]4-cyanothiobenzamide

N-[(dimethylamino)methylene]4-cyanothiobenzamide (102) was prepared in 85% as a reddish crystalline solid by the condensation between 99 and 35, as shown in Scheme 79. The reddish crystals were characterized by $^1$H- and $^{13}$C-NMR spectroscopy.

Scheme 79: Synthesis of N-[(dimethylamino)methylene]4-cyanothiobenzamide

The GC analysis of the sample, shown in Figure 180a, indicated the presence of some impurities. The mass spectrum of the major component, which eluted with a retention time of 35.6 min (Figure 180b), exhibits a molecular ion at m/z 217 corresponding to the molecular weight of 102. The spectrum also shows a base peak at m/z 44 due to the [(CH$_3$)$_2$N]$^+$ fragment which is consistent with the structure of this compound.
Figure 180a: GC analysis of N-[(dimethylamino)methylene]4-cyanothiobenzamide

Figure 180b: Mass spectrum of N-[(dimethylamino)methylene]4-cyanothiobenzamide
The $^1$H-NMR spectrum (Figure 181) of this reddish crystalline solid exhibits two singlets at very close chemical shift in the region of $\delta$ 3.31-3.32 due to the absorptions the two sets of the non-equivalent methyl protons bonded to the amino group. The two doublets at $\delta$ 7.63 (2H; $J = 8.6$ Hz) and $\delta$ 8.43 (2H; $J = 8.6$ Hz) were assigned to the two set of phenyl ring protons at positions 2,6 and 3,5, respectively. The imine proton appears at $\delta$ 8.75.

**Figure 181:** $^1$H-NMR spectrum of N-[(dimethylamino)methylene]4-cyanothiobenzamide
The $^{13}$C-NMR spectrum (Figure 182a) is also consistent with the structure of 102. The thiocarbonyl carbon absorbs downfield at $\delta$ 213.9. Based on the previous $^{13}$C–NMR spectral assignments of the synthesized amidines, the signal at $\delta$ 159.9 can be assigned to the absorption of the imine carbon. The phenyl ring carbons at positions 2,6 and 3,5 appear as two singlets at $\delta$ 129.5 and 132.0 while the phenyl ring carbons at positions 1 and 4 absorb at $\delta$ 119.4 and 146.5, respectively. The two singlets at $\delta$ 37 and 42.6 were assigned to the two non-equivalent N-methyl carbons. The cyano carbon appears at $\delta$ 114.8. These assignments are consistent with the $^{13}$C–DEPT 135 spectrum (Figure 182b). The two signals at $\delta$ 119.4 and 146.5 disappeared in the $^{13}$C–DEPT 135 spectrum which are consistent with the assignment of the two signals to the two quaternary carbons on the phenyl ring at position 1 and 4, respectively. The signals at $\delta$ 159.9, 132, 129.8, 42.7, and 37 still appear in the $^{13}$C–DEPT 135 spectrum which are consistent with the assignment to the imine carbon, phenyl ring carbons position 2,6 and 3,5, and two non-equivalent amino methyl carbons, respectively.
Results and Discussion

Figure 182a: $^{13}$C-NMR spectrum of N-[(dimethylamino)methylene]4-cyanothiobenzamide

Figure 182b: $^{13}$C-DEPT 135 spectrum of N-[(dimethylamino)methylene]4-methoxythiobenzamide
2.10.1.3.4 Synthesis of 5-(4′-cyano)phenyl-1,2,4-thiadiazole

5-(4′-Cyano)phenyl-1,2,4-thiadiazole (98) was synthesized by the similar method as for the synthesis of 5-phenyl-1,2,4-thiadiazole (31). The amination cyclization of 102 with 33 employing pyridine as a basic catalyst would lead to the formation of 98 as shown in Scheme 80.

![Scheme 80: Synthesis of 5-(4′-cyano)phenyl-1,2,4-thiadiazole](image-url)
The resulting product was obtained as a light yellow solid. GC analysis of this yellow solid (Figure 183a) exhibits the presence of two gc-volatile components which eluted with retention times of 13.1 and 24 min. Figure 183b shows the mass spectrum of the major component with a molecular ion at m/z 187 corresponding with a molecular weight of 98. Figure 183c shows the mass spectrum of the unknown minor component with a molecular ion at m/z 246. Therefore, this yellow solid was subjected to sublimation (120 °C; 0.3 torr) to give a white solid. This white solid was characterized by $^1$H-, $^{13}$C-NMR, infrared and mass spectroscopy.

**Figure 183a:** GC analysis of the light yellow solid

**Figure 183b:** Mass spectrum of the major component at 13.1 min
The GC analysis of the white solid after purification (Figure 184a) exhibits only one gc-volatile component with a retention time of 11.3 min. The mass spectrum of this component (Figure 184b) exhibits a molecular ion at m/z 187 which is consistent with the molecular weight of 98 (MW 187). The spectrum also exhibits a base peak at m/z 160 which is due to the \([p\text{-CNC}_6\text{H}_5\text{CNS}]^+\) fragment. The moderately intense peak at m/z 129 is consistent with the \([p\text{-CNC}_6\text{H}_5\text{CNH}]^{++}\) fragment resulting from the cleavage of \([\text{CNC}_6\text{H}_5\text{CN}]\) with a subsequent proton transfer. The intense peak at m/z 59 is consistent with the \([\text{HCNS}]^{++}\) fragment.

**Figure 184a:** GC analysis of the synthesized 5-(4'-cyanophenyl)-1,2,4-thiadiazole
Figure 184b: Mass spectrum of 5-\((4'\text{-cyano})\text{phenyl-1,2,4-thiadiazole}\)

Figure 185 exhibits the infrared absorption spectrum of the white solid (neat). The spectrum reveals a sharp absorption band at 2231 cm\(^{-1}\) which is a characteristic absorption of a cyano functional group. Thus, this infrared spectrum confirms that this product contains a cyano group in the structure.
Figure 185: Infrared absorption spectrum of 5-(4′-cyano)phenyl-1,2,4-thiadiazole

The $^1$H–NMR spectrum, as shown in Figure 186, exhibits a very clear spectrum. The proton at ring position 3 absorbs downfield at $\delta$ 8.83 as a singlet (1H). The phenyl ring protons appear as two doublets at $\delta$ 7.8 (2H; $J = 8.3$ Hz) and $\delta$ 8.1 (2H; $J = 8.3$ Hz) assigned to two sets of phenyl ring protons positions 2,6 and 3,5, respectively.
The 13C–NMR spectrum (Figure 187a) shows that the cyano carbon absorbs at δ 115.8. The three singlet signals at δ 128.5, 133.6 and 134.4 were assigned to the phenyl ring carbons positions 2 and 6, 3 and 5, and 4, respectively, while the phenyl ring carbon position 1 appears further upfield at δ 118.3. The two carbon atoms of the thiadiazole ring absorb at δ 164.3 and 186.4. The former signal was assigned to the carbon at ring position 3, while the latter signal was assigned to the carbon at ring position 5. These assignments are consistent with the 13C–DEPT 135 spectrum (Figure 187b) which confirms that the signals at δ 115.8, 118.3, 134.4 and 186.4 are due to quaternary carbons. The signals at δ 128.5, 133.6 and 164.3 still appear in the 13C–DEPT 135 spectrum and thus
Results and Discussion

these are consistent with the assignments to the phenyl ring carbons positions 2,6 and 3,5 and the carbon at ring position 3 of the thiadiazole ring, respectively.

**Figure 187a:** $^{13}$C-NMR spectrum of 5-(4′-cyano)phenyl-1,2,4-thiadiazole

**Figure 187b:** $^{13}$C-DEPT 135 spectrum of 5-(4′-cyano)phenyl-1,2,4-thiadiazole
2.10.1.4 Photochemistry of 5-(4′-substituted)phenyl-1,2,4-thiadiazoles

The photochemistry of 5(4′-methoxy)-phenyl-1,2,4-thiadiazole (90) and 5(4′-cyano)-phenyl-1,2,4-thiadiazole (98) were first studied in UV-scale. Solutions of 90 in acetonitrile (8.7×10⁻⁵ M) and cyclohexane (8.7×10⁻⁵ M) and 98 in acetonitrile (5.1×10⁻⁵ M) were prepared. These solutions in quartz cells were irradiated with two > 290 nm lamps through a Pyrex filter. The reactions were monitored by ultraviolet absorption spectroscopy.

Figure 188a and 189a show the UV–absorption spectra of 90 in acetonitrile and cyclohexane before irradiation, respectively, revealing broad absorption bands with the maximum absorptions at 298 nm (ε = 9,500 L mol⁻¹ cm⁻¹) and 296 nm (ε = 9,402 L mol⁻¹ cm⁻¹), respectively. After 240 sec of irradiation, the UV-absorption overlay spectra of the solution of 90 in acetonitrile (Figure 188b) does not show significant consumption of the reactant, 90.

Figure 189b shows the UV-absorption overlay spectra of the photolysis of 90 in cyclohexane solvent. These overlay spectra reveal a decreasing of an absorption band with the λ_max of 296 nm from the optical density of 0.82 to 0.79 after 240 sec of irradiation indicating 3.7 % consumption of the reactant, 90. Figure 189b also reveals an increasing of absorption in the region of 240-260 nm. These results show that 90 is more photoreactive in non-polar solvents.
Results and Discussion

Figure 188a: UV–absorption spectrum of 90 in acetonitrile (8.7×10⁻⁵ M)

Figure 188b: UV–absorption overlay spectra of photolysis of 90 in acetonitrile
Figure 189a: UV–absorption spectrum of 90 in cyclohexane (8.7×10⁻⁵ M)

Figure 189b: UV–absorption spectrum of 90 in cyclohexane (8.7×10⁻⁵ M)
Figure 190a shows the UV–absorption spectrum of 98 in acetonitrile (9.5×10⁻⁵ M) before irradiation revealing the maximum absorption at 280 nm with extinction coefficient of 7,368 L mol⁻¹ cm⁻¹.

Figure 190a: UV–absorption spectrum of 98 in acetonitrile (9.5×10⁻⁵ M)

Figure 190b: UV-absorption overlay spectra of photolysis of 98 in acetonitrile
Figure 190b exhibits the UV-absorption overlay spectra of the irradiation of 98 in acetonitrile for a total of 20 min. The overlay spectra reveal a decrease in the absorption band at the $\lambda_{\text{max}}$ of 280 nm from OD 0.71 to 0.58 and the increasing of absorption in the region of 230-250 nm which has a $\lambda_{\text{max}}$ of 245 nm. The new absorption forming in the region of 230-250 nm could be identified to the formation of 1,4-dicyanobenzene (103), the expected fragmentation product upon irradiation of 98, by comparison with the absorption spectrum of an authentic sample of 103 shown in Figure 191. Figure 191 shows the UV-absorption spectrum of an authentic sample of 1,4-dicyanobenzene (103) in acetonitrile revealing two absorption bands with $\lambda_{\text{max}}$ at 245 and 235 nm.

Figure 191: UV-absorption spectrum of an authentic sample of 103 in acetonitrile
The photochemical reactions of 90 and 98 were also monitored by gas chromatography. Solutions of 90 (1×10^{-2} M; 3.5 mL) and 98 (6×10^{-3} M; 3.5 mL) in acetonitrile were placed in Pyrex tubes. The tubes were sealed with rubber septa, purged with an argon gas for 15 min, and irradiated with sixteen > 290 nm lamps.

Figure 192a and 193a shows the GC-traces [90°C (2 min), 20°C/min to 150°C (10 min), 20°C/min to 250 (15 min)] of the solutions of 90 and 98 before irradiation revealing the starting materials eluted with retention times of 18.7 and 19.3 min, respectively. After 120 min of irradiation, the GC trace of the photoreaction of 90 (Figure 192b) reveals the formation of trace quantities of two new products eluting with retention times of 8.4 and 19.2 min. Figure 193b also reveals the formation of new photoproducts, formed in the reaction of 98, at retention times of 8.2 and 17.6 min in trace quantities. The solutions were then further photolyzed for a total of 600 min. The photolysates of 90 and 98 were concentrated and analyzed by the GC interfaced with a mass spectrometer.
Figure 192a: GLC analysis of 90 in acetonitrile (1×10^{-2} M) before irradiation

Figure 192b: GLC analysis of 90 in acetonitrile after 120 min of irradiation
Figure 193a: GLC analysis of 98 in acetonitrile ($6 \times 10^{-3}$ M) before irradiation

Figure 193b: GLC analysis of 98 in acetonitrile after 120 min of irradiation
Figure 194a shows a GC trace [90 (3 min), 10°C/min to 200°C (10 min), 10°C/min to 250 (100 min), 10°C/min to 280 (15 min)] of the concentrated photolysate of 90 revealing the presence of two major components eluting with retention times of 24.5 and 26.7 min and three minor components eluting with retention times of 13.9, 23.2 and 55.2 min.

The mass spectrum of the first eluted component with a retention time of 13.9 min (Figure 194b) shows a base molecular ion peak at m/z 133. This product was identified as 4-methoxybenzonitrile (104; MW 133) by comparison of the GC-retention times and the mass spectrum of the authentic 4-methoxybenzonitrile (104) shown in Figure 195.
Figure 194b: Mass spectrum of the component at RT of 13.9 min

Figure 195: Mass spectrum of an authentic sample of 4-methoxybenzonitrile
**Figure 194c:** Mass spectrum of the component at RT of 23.2 min

**Figure 196:** Mass spectrum of an authentic 2-(4′-methoxy)phenyl-1,3,5-triazine
The mass spectrum of the product that eluted with a retention time of 23.2 min (Figure 194c) exhibits a molecular ion at m/z 187, which is consistent with the molecular formula of $\text{C}_{10}\text{H}_{9}\text{N}_{3}\text{O}$. The spectrum also reveals an intense peak at m/z 134, which is consistent with the elimination of $[\text{CH}_3\text{OC}_6\text{H}_5\text{CNH}]^+$ as the major fragment. This photoproduct was suggested to be 2-($4'$-methoxy)phenyl-1,3,5-triazine (94), a photo-ring expansion product. This was confirmed by direct comparison with the chromatographic and mass spectroscopic properties of an authentic sample of 94. Figure 34b shows the mass spectrum of an authentic sample of 94 revealing molecular ion and fragmentation pattern identical to those of the product that eluted with retention time of 23.2 min (Figure 194c).

Figure 194d reveals the mass spectrum of the major component at retention time of 24.5 min with a base molecular ion at m/z 192 and two intense peaks at m/z 133 and 134 corresponding with the starting thiadiazole, 90.
The mass spectrum of the photoproduct that eluted with a retention time of 26.7 min also exhibits a molecular ion at m/z 192 (Figure 194e) which is also consistent with the molecular formula of C₉H₈N₂SO, identical to the formula of the reactant, 90. Based on the previous result observed in the photolysis of 5-phenyl-1,2,4-thiadiazole (31) and 3-methyl-5-phenyl-1,2,4-thiadiazole (54), this product was thus expected to be 3-(4′-methoxy)phenyl-1,2,4-thiadiazole (105), the phototransposition product. Comparison of the chromatographic and mass spectroscopic properties of this product with those of an authentic sample of 105 (Figure 197), clearly confirmed that this photoproduct was the phototransposition product, 3-(4′-methoxy)phenyl-1,2,4-thiadiazole (105).

**Figure 194e:** Mass spectrum of the component at RT of 26.7 min
The mass spectrum of the photoproduct that eluted with a retention time of 55.3 min (Figure 194f) exhibits a base molecular ion at m/z 293, which is consistent with a molecular formula of C_{17}H_{15}N_{3}O_{2}, and an intense peak at m/z 133, consistent with the formation of [CH$_3$OC$_6$H$_5$CN]$^+$ as the major fragment. Based on this information and previous results upon photolysis of 1 and 7, the photoproduct was tentatively suggested to be 2,4-di(4′-methoxy)phenyl-1,3,5-triazine (95), a ring expansion product.
Results and Discussion

Figure 194f: Mass spectrum of the component at RT of 55.2 min

Figure 198a shows a GC trace [90 (3 min), 10°C/min to 200°C (10 min), 10°C/min to 250 (100 min), 10°C/min to 280 (15 min)] of the concentrated photolysate of 98 revealing the presence of one major component eluting with retention times of 18.1 and three minor components eluting with retention times of 12.5, 17.3 and 19.3 min.

Figure 198a: GC trace of concentrated photolysate of 98 (after 600 min of irradiation)
The mass spectrum of the component that eluted with a retention time of 12.5 min (Figure 198b) shows a base molecular ion peak at m/z 128. This product was identified as 1,4-dicyanobenzene (103; MW 128) by direct comparison of the GC-retention times and the mass spectrum of the photoproduct with the mass spectrum of an authentic sample of 1,4-dicyanobenzene (103) shown in Figure 199.

**Figure 198b:** Mass spectrum of the component at RT of 12.5 min
The peak that eluted with a retention time of 18.1 min is the starting material, 98, since it has a retention time and a mass spectrum (Figure 198d) identical to 5-(4'-cyano)phenyl-1,2,4-thiadiazole (98).

Figure 199: Mass spectrum of an authentic 1,4-dicyanobenzene
Figure 198d: Mass spectrum of the component at RT of 18.1 min
**Figure 198c:** Mass spectrum of the component at RT of 17.3 min

**Figure 198e:** Mass spectrum of the component at RT of 19.3 min
Results and Discussion

Figure 198c and 198d show mass spectra of the components that eluted with retention times of 17.3 and 19.3 min revealing molecular ion peaks at m/z 182 and 187, respectively. The component with a molecular ion at m/z 187 corresponds to a molecular formula of C₅H₅N₃S (MW 187). This product was expected to be the phototransposition product, 3-(4'-cyano)phenyl-1,2,4-thiadiazole (106). Comparison between the mass spectroscopic and chromatographic properties of this product with these properties of an authentic sample of 6 (Figure 200) confirmed that this product was 3-(4'-cyano)phenyl-1,2,4-thiadiazole (106).

Figure 200: Mass spectrum of an authentic 3-(4'-cyano)phenyl-1,2,4-thiadiazole
The molecular ion at m/z 182 is consistent with a molecular formula of C_{10}H_{6}N_{4} (MW 182) which corresponds to the structure of the expected photo-ring expansion, 2-(4′-cyano)phenyl-1,3,5-triazine (107). The base peak at m/z 129 corresponds to the [C_{8}H_{5}N_{2}]^{+} fragment. This fragment is consistent with the cleavage of [C_{8}H_{4}N_{2}] fragment from the molecular ion of 79 followed by H-abstraction to give [C_{8}H_{5}N_{2}]^{+} fragment. This fragmentation is the major fragmentation pathway as previously observed in the mass spectra of 2-phenyl-1,3,5-triazines. Based on these information, this photoproduct was tentatively identified as 2-(4′-cyano)phenyl-1,3,5-triazine (107).

Since the photoproducts formed in this reaction were observed in trace amounts, thus, the expected 2,4-di(4′-cyano)phenyl-1,3,5-triazine (108) might not be observed in this GC analysis.

These results conclusively show that irradiations of 5(4′-methoxy)- and 5(4′-cyano)-phenyl-1,2,4-thiadiazole (90 and 98) in acetonitrile solvent at > 290 nm lead to the formation of the expected photofragmentation, phototransposition and photo-ring expansion products corresponding with the products observed upon irradiation of 5-phenyl-1,2,4-thiadiazole (31) and 3-methyl-5-phenyl-1,2,4-thiadiazole (54). Quantitative analysis of the photoreactions of 31, 90 and 98 in acetonitrile after 120 min of irradiation showed that 31 was 71% consumed while the consumptions of 90 and 98 were observed at 10% and 20%, respectively. The GLC traces of the solution of 90 and 98 after 120 min of irradiation also revealed the formation of the photoproducts in trace quantities.
This result indicates that introduction of a methoxy or cyano group to the \( p \)-position of the phenyl ring leads to the similar photochemical reactions as observed in the un-substituted compound, 5-phenyl-1,2,4-thiadiazole (31) but 90 and 98 are much less reactive than the un-substituted compound, 31. Scheme 81 shows the photoreaction of 5(4'-methoxy)- and 5(4'-cyano)-phenyl-1,2,4-thiadiazole (90) and (98) in acetonitrile solvent at > 290 nm.

Scheme 81: Photoreaction of 5(4'-methoxy)- and 5(4'-cyano)-phenyl-1,2,4-thiadiazole
2.10.2 Photochemistry of 3-(4'-substituted)phenyl-1,2,4-thiadiazoles

2.10.2.1 Synthesis of 3-(4'-methoxy)phenyl-1,2,4-thiadiazole

In the synthesis of 3-phenyl-1,2,4-thiadiazole (46), cycloaddition of benzonitrile sulfide (48) with ethyl cyanoformate (49) led to the formation of ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate (50). Base catalyzed ester hydrolysis followed by decarboxylation of 50 produced 46 in 72%. Therefore, 3-(4'-methoxy)phenyl-1,2,4-thiadiazole (105) could be synthesized by this synthetic pathway as shown in Scheme 82, employing 4-methoxybenzamide (92) as the starting material instead of benzamide (38).

Scheme 82: Total synthesis of 3-(4-methoxy)phenyl-1,2,4-thiadiazole
2.10.2.1.1 Synthesis of 5-(4′-methoxy)phenyl-1,3,4-oxathiazole-2-one

According to the method described by Howe and Franz\textsuperscript{12} to synthesize 46 by
cycloaddition reaction, 48 is required as an intermediate which can be generated in situ by
decarboxylation of 5-phenyl-1,3,4-oxathiazole-2-one (51). In the synthesis of 105,
5-(4-methoxy)phenyl-1,3,4-oxathiazole-2-one (109) is required for generation of
4-methoxybenzonitrile sulfide (110). Therefore, 109 was prepared by a coupling between 52
and 92 in refluxing chloroform under anhydrous condition to give the desired oxathiazole
109 in 80% yield as white crystals. Scheme 83 shows the synthesis of
5-(4-methoxy)phenyl-1,3,4-oxathiazole-2-one (109).

![Scheme 83: Synthesis of 5-(4′-methoxy)phenyl-1,3,4-oxathiazole-2-one](image)

GC analysis of the white crystals (Figure 201a) exhibits only one component that
eluted with a retention time of 4.4 min. The mass spectrum of this component (Figure 201b)
exhibits a molecular ion at m/z 133 which is not consistent with the molecular formula of
C\textsubscript{9}H\textsubscript{7}NO\textsubscript{3}S (MW 209). The observed gc-volatile component with a molecular ion at m/z 133
would, however, be due to the formation of 4-methoxybenzonitrile (104) (MW 133) from
decarboxylation of 109 and subsequent elimination of sulfur element under this GC analysis
condition.
**Figure 201a:** GC analysis of 5-(4'-methoxy)phenyl-1,3,4-oxathiazole-2-one

**Figure 201b:** Mass spectrum of the component at RT of 4.4 min
Results and Discussion

The $^1$H-NMR spectrum of this compound (Figure 202) exhibits two doublets at $\delta$ 6.99 (2H; $J = 8.8$ Hz) and 7.89 (2H; $J = 8.8$ Hz) which were assigned to the two sets of phenyl ring protons at positions 2,6 and 3,5, respectively. The 3H singlet at $\delta$ 3.86 was assigned to the methoxy protons.

![Figure 202: $^1$H-NMR spectrum of 5-(4'-methoxy)phenyl-1,3,4-oxathiazole-2-one](image)

The $^{13}$C-NMR spectrum (Figure 203a) exhibits the carbon signals corresponding to the structure of 109. The carbonyl carbon on the oxathiazole ring absorbs downfield at $\delta$ 174.7. The carbon at position 5 of the oxathiazole ring appears at $\delta$ 163.4. The phenyl ring carbons appear as four singlets at $\delta$ 114.8, 118.8, 129.7 and 157.7. The signal at $\delta$ 56.0 was assigned to the methoxy carbon. These assignments are consistent with the $^{13}$C–DEPT 135 spectrum (Figure 203b). The four signals at $\delta$ 118.8, 157.7, 163.4 and 174.7 disappeared in the $^{13}$C–DEPT 135 spectrum which are consistent with the assignment to the
two phenyl ring carbon at positions 1 and 4 and to the two quaternary carbons on the oxathiazole ring, respectively.

Figure 203a: $^{13}$C-NMR spectrum of 5-(4′-methoxy)phenyl-1,3,4-oxathiazole-2-one

Figure 203b: $^{13}$C-DEPT 135 spectrum of 5-(4′-methoxy)phenyl-1,3,4-oxathiazole-2-one
Results and Discussion

2.10.2.1.2 Synthesis of ethyl 3-(4-methoxy)phenyl-1,2,4-thiadiazole-5-carboxylate

Benzonitrile sulfide (48) was successfully trapped with ethyl cyanofomate (49), by decarboxylation of 51 in the presence of 4 equivalents of 49, to yield 50 in 80% yield. Thus, trapping of the in situ generated 4-methoxybenzonitrile sulfide (110), from decarboxylation of 109, with 49 would give ethyl 3-(4-methoxy)phenyl-1,2,4-thiadiazole-5-carboxylate (111) as shown in Scheme 84.

![Scheme 84: Synthesis of ethyl 3-(4'-methoxy)phenyl-1,2,4-thiadiazole-5-carboxylate](image)

The GC analysis of the cycloaddition product obtained in this reaction (Figure 204a) shows a single gc-volatile product which eluted with a retention time of 19.5 min. The mass spectrum (Figure 204b) of this component exhibits a base molecular ion at m/z 264 which corresponds to the molecular weight of 111 (MW 264). The spectrum also shows two intense peaks at m/z 165 and 133 due to the \([\text{CH}_3\text{OC}_6\text{H}_5\text{CNS}]^+\) and \([\text{CH}_3\text{OC}_6\text{H}_5\text{CN}]^+\) fragments.

![Figure 204a: GC analysis of ethyl 3-(4'-methoxy)phenyl-1,2,4-thiadiazole-5-carboxylate](image)
Figure 204b: Mass spectrum of ethyl 3-(4′-methoxy)phenyl-1,2,4-thiadiazole-5-carboxylate

The $^1$H–NMR spectrum of this synthesized 111 (Figure 205) exhibits two doublets at δ 6.97 (2H; $J = 8.6$ Hz) and δ 8.28 (2H; $J = 8.6$ Hz) due to absorptions of the phenyl ring protons at positions 2,6 and 3,5, respectively. The ethyl ester protons are shown at δ 4.51 as a quartet (2H; $J = 7.1$ Hz) and at δ 1.45 as a triplet (3H; $J = 7.1$ Hz). The singlet (3H) at δ 3.86 was assigned to the methoxy protons.
Figure 205: $^1$H–NMR spectrum of ethyl 3-(4'-methoxy)phenyl-1,2,4-thiadiazole-5-carboxylate

The $^{13}$C–NMR spectrum (Figure 206a) exhibits the two carbons of the ethyl ester group at $\delta$ 14.6 (CH$_3$-) and 63.7 (-CH$_2$-). The phenyl ring carbons at positions 2,6 and 3,5 appear as two singlets at $\delta$ 114.5 and 130.6 while the phenyl ring carbons at positions 1 and 4 are shown at $\delta$ 125.4 and 159.0, respectively. The signal at $\delta$ 179.1 was assigned to the ester carbonyl carbon. The two carbons of the thiadiazole ring absorb at $\delta$ 162.2 for the carbon at position 3 and at $\delta$ 175.0 for carbon at ring position 5. These assignments can be supported by the $^{13}$C–DEPT 135 spectrum, shown in Figure 206b. The signals at $\delta$ 14.6 and 63.7 absorb in positive and negative directions in the $^{13}$C–DEPT 135 spectrum, respectively, which is consistent with their assignments as methylene and methyl carbons of the ethyl ester group, respectively. Three signals at $\delta$ 125.4, 159.0, 162.2, 175.0 and 179.1 disappear in the $^{13}$C–DEPT 135 spectrum confirming that they are all quaternary carbons. The signal at $\delta$ 55.8 remains in the $^{13}$C–DEPT 135 spectrum with a positive direction which is consistent to the assignment of the methoxy carbon.
Figure 206a: $^{13}$C–NMR spectrum of ethyl 3-(4′-methoxy)phenyl-1,2,4-thiadiazole-5-carboxylate

Figure 206b: $^{13}$C–DEPT 135 spectrum of ethyl 3-(4′-methoxyphenyl)-1,2,4-thiadiazole-5-carboxylate
2.10.2.1.3 Synthesis of 3-(4′-methoxy)phenyl-1,2,4-thiadiazole

Base catalyzed ester hydrolysis of ethyl 3-(4′-methoxy)phenyl-1,2,4-thiadiazole-5-carboxylate (111) led to the formation of 3-(4′-methoxy)phenyl-1,2,4-thiadiazole-5-carboxylic acid (112). Decarboxylation of 112 produced 3-(4′-methoxy)phenyl-1,2,4-thiadiazole (105) as colorless crystals in 90% yield. (Scheme 85)

\[
\begin{array}{c}
\text{H}_3\text{CH}_2\text{CO} \quad 111 \\
\text{1) OH}^- \quad \text{2) H}^+ \\
\text{OMe} \\
\end{array}
\]

\[
\begin{array}{c}
\text{N} \\
\text{S} \\
\text{C} \\
\text{O} \\
\text{H}_3\text{CH}_2\text{CO} \quad 111 \\
\text{1) OH}^- \quad \text{2) H}^+ \\
\text{OMe} \\
\end{array}
\]

\[
\begin{array}{c}
\text{N} \\
\text{S} \\
\text{C} \\
\text{O} \\
\text{H}_3\text{CH}_2\text{CO} \quad 111 \\
\text{1) OH}^- \quad \text{2) H}^+ \\
\text{OMe} \\
\end{array}
\]

\[
\begin{array}{c}
\text{N} \\
\text{S} \\
\text{C} \\
\text{O} \\
\text{OMe} \quad 112 \\
\text{Decarboxylation} \\
\text{H} \\
\text{OMe} \quad 105 \\
\end{array}
\]

Scheme 85: Synthesis of 3-(4′-methoxy)phenyl-1,2,4-thiadiazole

The GC analysis (Figure 207a) shows only one component which eluted with a retention time of 10.5 min. The mass spectrum (Figure 207b) of this product exhibits a base molecular ion at m/z 192 and an intense peak at m/z 165 which correspond both to the molecular weight of 105 (MW 192) and to the possible [CH$_3$OC$_6$H$_5$CNS]$^+$ fragment. The peak at m/z 133 is due to the loss of sulfur from [CH$_3$OC$_6$H$_5$CNS]$^+$ fragment.

Figure 207a: GC analysis of 3-(4′-methoxy)phenyl-1,2,4-thiadiazole
The $^1$H-NMR spectrum (Figure 208) exhibits a clear spectrum. The proton on the thiazole ring at position 5 absorbs downfield at $\delta$ 9.83 as a singlet (1H). The phenyl ring protons at positions 2,6 and 3,5 appear as two doublets at $\delta$ 6.99 (2H; $J = 8.8$ Hz) and 8.27 (2H; $J = 8.8$ Hz), respectively. The methoxy protons are shown at $\delta$ 3.86 as a 3H singlet.
Results and Discussion

Figure 208: $^1$H–NMR spectrum of 3-(4′-methoxy)phenyl-1,2,4-thiadiazole.

The $^{13}$C–NMR spectrum (Figure 209a) shows that the two carbon atoms of the thiadiazole ring absorb at $\delta$ 172.8 and 174.3. The former signal was assigned to the carbon at ring position 5, while the latter signal was assigned to the carbon at ring position 3. These assignments are consistent with the $^{13}$C–DEPT 135 spectrum (Figure 209b) which confirms that the signal at $\delta$ 174.3 is due to a quaternary carbon. The signal at $\delta$ 172.8 still appears in the $^{13}$C–DEPT 135 spectrum and that must be due to the carbon at ring position 5 of the thiadiazole ring. The phenyl ring carbons at positions 2,6 and 3,5 appear at $\delta$ 114.5 and 130.3, respectively, while the carbons at positions 1 and 4 absorb at $\delta$ 125.9 and 161.9, respectively. These assignments are also consistent with the disappearance of the signals at $\delta$ 125.9 and 161.9 due to absorptions of quarternary carbons. The signal at $\delta$ 55.8 appears in a positive direction in the $^{13}$C–DEPT 135 spectrum and thus can be assigned to the methoxy carbons.
Figure 209a: $^{13}$C–NMR spectrum of 3-(4′-methoxy)phenyl-1,2,4-thiadiazole

Figure 209b: $^{13}$C–DEPT 135 spectrum of 3-(4′-methoxy)phenyl-1,2,4-thiadiazole
2.10.2.2 Synthesis of 3-((4′-cyano)phenyl-1,2,4-thiadiazole

3-(4′-Methoxy)phenyl-1,2,4-thiadiazole (105) was synthesized by 1,3-dipolar cycloaddition of 84 with 14 followed by base catalyzed hydrolysis and decarboxylation. Therefore, it should be also possible to synthesize 3-(4′-cyano)phenyl-1,2,4-thiadiazole (106) by this method via the 4-cyanobenzonitrile sulfide intermediate (113). Scheme 86 shows the total synthetic pathway of 3-(4′-cyano)phenyl-1,2,4-thiadiazole (106).

![Scheme 86: Total synthesis of 3-(4′-cyano)phenyl-1,2,4-thiadiazole](image-url)
2.10.2.2.1 Synthesis of 5-(4′-cyano)phenyl-1,3,4-oxathiazole-2-one

In the synthesis of 106, decarboxylation of 5-(4′-cyano)phenyl-1,3,4-oxathiazole-2-one (114) would lead to the formation of the key intermediate, 4-cyanobenzonitrile sulfide (113). Therefore, 114 was prepared by a coupling reaction between 52 and 100 in refluxing toluene. This reaction gave the oxathiazole 114 in 71% yield as light brown crystals. Scheme 85 shows the synthesis of 5-(4′-cyano)phenyl-1,3,4-oxathiazole-2-one (114). The brown crystals were characterized by ¹H-, ¹³C-NMR and mass spectroscopy.

Scheme 87: Synthesis of 5-(4′-cyano)phenyl-1,3,4-oxathiazole-2-one

GC analysis of this crystalline solid (Figure 210a) exhibits a major component that eluted with a retention time of 8 min. The mass spectrum of this component (Figure 210b) exhibits a molecular ion at m/z 128 which is not consistent with the molecular formula of the desired compound 114, C₉H₄N₂O₂S (MW 204). The observed gc-volatile component with a molecular ion at m/z 128 could, however, be due to the formation of 1,4-dicyanobenzene (103) (MW 128) from decarboxylation of 114 and subsequent elimination of sulfur element under this GC analysis condition.

Figure 210a: GC analysis of 5-(4′-cyano)phenyl-1,3,4-oxathiazole-2-one
The $^1$H-NMR spectrum of this product (Figure 211) exhibits two doublets at $\delta$ 7.79 (2H; $J = 8.3$ Hz) and 8.07 (2H; $J = 8.3$ Hz) which were assigned to the two sets of phenyl ring protons at positions 2,6 and 3,5, respectively.
The $^{13}$C-NMR spectrum (Figure 212a) exhibits the carbon signals corresponding to the structure of 114. The carbonyl carbon of the oxathiazole ring absorbs downfield at $\delta$ 172.8. The carbon at position 5 of the oxathiazole ring appears at $\delta$ 155.6. The phenyl ring carbons appear as four singlets at $\delta$ 117.7, 127.9, 129.3 and 132.8. The signal at $\delta$ 116.1 was assigned to the cyano carbon. These assignments are consistent with the $^{13}$C–DEPT 135 spectrum (Figure 212b). The five signals at $\delta$ 116.1, 117.7, 129.3, 155.6 and 172.8 disappeared in the $^{13}$C–DEPT 135 spectrum which is consistent with the assignment to the cyano carbon, the phenyl ring carbons at positions 1 and 4, and to the two quaternary carbons on the oxathiazole ring, respectively.
Figure 212a: $^{13}$C-NMR spectrum of 5-(4′-cyano)phenyl-1,3,4-oxathiazole-2-one

Figure 212b: $^{13}$C-DEPT 135 spectrum of 5-(4′-cyano)phenyl-1,3,4-oxathiazole-2-one
2.10.2.2 Synthesis of ethyl 3-(4’-cyano)phenyl-1,2,4-thiadiazole-5-carboxylate

4-Cyanobenzonitrile sulfide (113) was successfully trapped with 49 to yield ethyl 3-(4’-cyano)phenyl-1,2,4-thiadiazole-5-carboxylate (115) in 66% yield as shown in Scheme 88.

Scheme 88: Synthesis of ethyl 3-(4’-cyano)phenyl-1,2,4-thiadiazole-5-carboxylate

The GC analysis of the cycloaddition product (115) (Figure 213a) shows a single volatile product which eluted with a retention time of 21.8 min. The mass spectrum (Figure 213b) of this component exhibits a base molecular ion at m/z 259, which corresponds to the molecular weight of 115 (MW 259). The spectrum also shows a base peak at m/z 160 corresponding with the cleavage of the [CH$_3$CH$_2$COCN] fragment from the molecular ion. This fragmentation pathway is also a characteristic fragmentation of 3-phenyl-1,2,4-thiadiazoles as previously observed in other sections of this thesis.

Figure 213a: GC analysis of ethyl 3-(4’-cyano)phenyl-1,2,4-thiadiazole-5-carboxylate
Figure 213b: Mass spectrum of ethyl 3-(4′-cyano)phenyl-1,2,4-thiadiazole-5-carboxylate

The $^1$H–NMR spectrum of this synthesized 115 (Figure 214) exhibits two doublets at $\delta$ 7.78 (2H; $J = 8.3$ Hz) and $\delta$ 8.47 (2H; $J = 8.3$ Hz), due to absorptions of phenyl ring protons at positions 2,6 and 3,5, respectively. The ethyl ester protons absorb at $\delta$ 4.54 as a quartet (2H; $J = 7.1$ Hz) and at $\delta$ 1.47 as a triplet (3H; $J = 7.1$ Hz).
The $^{13}$C–NMR spectrum (Figure 215a) exhibits the two carbons of the ethyl ester group at $\delta$ 14.6 (CH$_3$-) and 64.0 (-CH$_2$-). The phenyl ring carbons at positions 2,6 and 3,5 appear as two singlets at $\delta$ 129.4 and 133.1 while the phenyl ring carbons at positions 1 and 4 are shown at $\delta$ 118.8 and 136.0, respectively. The singlet at $\delta$ 114.7 was assigned to the cyano carbon. The further downfield signal at $\delta$ 180.1 was assigned to the ester carbonyl carbon. The two carbons of the thiadiazole ring absorb at $\delta$ 158.6 for the carbon at position 3 and at $\delta$ 173.0 for carbon at ring position 5. These assignments are supported by the $^{13}$C–DEPT 135 spectrum, shown in Figure 215b. The signals at $\delta$ 14.6 and 64.0 absorb in positive and negative directions, respectively, which is consistent with their assignments as methylene and methyl carbons of the ethyl ester group, respectively. The signals at $\delta$ 114.7,
118.8, 136.0, 158.6, 173.0 and 180.1 disappear in the $^{13}$C–DEPT 135 spectrum confirming that they are all quaternary carbons.

**Figure 215a:** $^{13}$C–NMR spectrum of ethyl 3-(4′-cyano)phenyl-1,2,4-thiadiazole-5-carboxylate

**Figure 215b:** $^{13}$C–DEPT 135 spectrum of ethyl 3-(4′-cyano)phenyl-1,2,4-thiadiazole-5-carboxylate
2.10.2.2.3 Synthesis of 3-(4′-cyano)phenyl-1,2,4-thiadiazole

The cyano functional group in 115 is expected to undergo a base-catalyzed hydrolysis reaction to yield an amide under a strong basic condition. In order to avoid the un-desired hydrolysis to the cyano group, the base catalyzed ester hydrolysis of 115 was carried out with diluted aqueous sodium bicarbonate in tetrahydrofuran solvent at room temperature for 12 hours. Acidification of the resulting solution by hydrochloric acid (conc.) led to the formation of 3-(4′-cyano)phenyl-1,2,4-thiadiazole-5-carboxylic acid (116). Decarboxylation of 116 in refluxing toluene gave a pale yellow solid. The yellow solid was subjected to sublimation to give 3-(4′-cyano)phenyl-1,2,4-thiadiazole (106) as a white solid. Scheme 89 shows the synthetic scheme of 106.

Scheme 89: Synthesis of 3-(4′-cyano)phenyl-1,2,4-thiadiazole

Figure 216 shows the infrared spectrum (neat) of the hydrolyzed product revealing a sharp moderate absorption peak at 2232 cm⁻¹ and a strong absorption peak at 1688 cm⁻¹. These two infrared absorptions are characteristic absorptions for a molecule containing cyano and carboxylic groups, respectively. Thus, this infrared spectrum confirms that the hydrolyzed product was the acid 116 with the remaining of cyano functional group in the structure.
Figure 216: Infrared spectrum of 3-(4′-cyano)phenyl-1,2,4-thiadiazole-5-carboxylic acid

Figure 217a shows the GC analysis of the white solid obtained from sublimation. The GC trace exhibits only one component which eluted with a retention time of 14.9 min. The mass spectrum (Figure 217b) of this white solid exhibits a molecular ion at m/z 187 which corresponds to the molecular formula of C₉H₅N₃S (MW 187). The spectrum also reveals a base peak at m/z 160 corresponding with the possible [CNC₆H₅CNS]⁺⁺ fragment due to the cleavage of [HCN] from the molecular ion. This fragmentation pathway is a characteristic pathway for 3-phenyl-1,2,4-thiadiazoles, thus confirming that this white solid is 3-(4′-cyano)phenyl-1,2,4-thiadiazole (106).
Figure 217a: GC analysis of 3-(4'-cyano)phenyl-1,2,4-thiadiazole

Figure 217b: Mass spectrum of 3-(4'-cyano)phenyl-1,2,4-thiadiazole
The $^1$H-NMR spectrum (Figure 218) exhibits a clear spectrum. The proton on the thiadiazole ring at position 5 absorbs downfield at $\delta$ 9.91 as a singlet (1H). The phenyl ring protons at positions 2, 6 and 3, 5 appear as two doublets at $\delta$ 7.78 (2H; $J = 8.3$ Hz) and 8.45 (2H; $J = 8.3$ Hz), respectively.

![Figure 218: $^1$H–NMR spectrum of 3-(4′-cyano)phenyl-1,2,4-thiadiazole.](image)

The $^{13}$C–NMR spectrum (Figure 219a) shows that the two carbon atoms of the thiadiazole ring absorb at $\delta$ 172.1 and 173.4. The former signal was assigned to the carbon at ring position 3, while the latter signal was assigned to the carbon at ring position 5. These assignments are consistent with the $^{13}$C–DEPT 135 spectrum (Figure 219b) which confirms that the signal at $\delta$ 172.1 is due to a quaternary carbon. The signal at $\delta$ 173.4 still appears in the $^{13}$C–DEPT 135 spectrum and that must be due to the carbon at ring position 5 of the thiadiazole ring. The phenyl ring carbons at positions 2, 6 and 3, 5 appear at $\delta$ 128.8 and 132.6, respectively, while the carbons at positions 1 and 4 absorb at $\delta$ 118.5 and
136.1, respectively. These assignments are also consistent with the disappearance of the signals at $\delta$ 118.5 and 136.1 due to absorptions of quaternary carbons. The signal at $\delta$ 113.9 disappears in the $^{13}$C–DEPT 135 spectrum and thus can be assigned to the cyano carbon.

**Figure 219a:** $^{13}$C–NMR spectrum of 3-(4′-cyano)phenyl-1,2,4-thiadiazole

**Figure 219b:** $^{13}$C–DEPT 135 spectrum of 3-(4′-cyano)phenyl-1,2,4-thiadiazole
2.10.2.3 Photochemistry of 3-(4′-substituted)phenyl-1,2,4-thiadiazoles

The photolysis of 3-(4′-methoxy)- and 3-(4′-cyano)-phenyl-1,2,4-thiadiazoles (105 and 106) were first monitored by UV–absorption spectroscopy. Solutions of 105 (5×10⁻⁵ M) and 106 (5.1×10⁻⁵ M) in acetonitrile were placed in quartz cells and irradiated with two > 290 nm lamps through a Pyrex filter. The photoreactions were monitored by UV-absorption spectroscopy.

Figure 220a shows the UV–absorption spectrum of 105 in acetonitrile before irradiation revealing two absorption bands with $\lambda_{\text{max}}$ at 275 and 218 nm. The extinction coefficients of the absorption bands at 275 and 218 nm are 18,140 and 13,200 L mol⁻¹ cm⁻¹, respectively. The spectrum also reveals two shoulders at 298 and 245 nm which are part of the absorption band that has a $\lambda_{\text{max}}$ at 275 nm.

![Figure 220a: UV-absorption spectrum of 105 in acetonitrile (5×10⁻⁵ M) before irradiation](image)
The UV-absorption overlay spectra of the photolysis of 105 (Figure 220b) show the continuous consumption of the reactant, as indicated by the decrease in the optical density of the absorption band at $\lambda_{\text{max}}$ of 275 nm from 0.91 to 0.61 after 50 min of irradiation. Figure 220b also shows an increase in the optical density at the wavelength of 246 nm. Figure 221 shows the UV-absorption spectrum of an authentic sample of 4-methoxybenzonitrile (104) in acetonitrile revealing a maximum absorption at 246 nm. Figure 222 exhibits an overlay between the absorption spectrum of an authentic sample of 104 on the absorption spectra of photolysis of 105. This indicates that the new forming absorption at 246 nm upon irradiation of 105 was due to the formation of 4-methoxybenzonitrile (104).
Results and Discussion

Figure 221: UV-absorption of an authentic sample of 104 in acetonitrile

Figure 222: The overlay spectra between authentic 104 on the photolysis of 105 in acetonitrile

Figure 223a shows the UV–absorption spectrum of 106 in acetonitrile before irradiation. The spectrum shows a broad absorption band at \( \lambda_{\text{max}} \) of 270 nm with an extinction coefficient of 7,255 L mol\(^{-1}\) cm\(^{-1}\).
Results and Discussion

Figure 223a: UV-absorption spectrum of 106 in acetonitrile (5.1×10^{-5} M) before irradiation

Figure 223b: UV-absorption overlay spectra of photolysis of 106 in acetonitrile

Figure 223b shows the UV-absorption overlay spectra of the photolysis of 106 revealing the continuous consumption of 106, as indicated by the decrease in the optical density of the absorption band at \( \lambda_{\text{max}} \) of 270 nm from 0.76 to 0.51 after 25 min of irradiation. The overlay spectra also show an increasing in the optical densities at wavelengths of 246
and 236 nm. Figure 44 shows the UV-absorption spectrum of an authentic sample of 1,4-dicyanobenzene (103) in acetonitrile revealing two absorption bands with maximum absorptions at 245 and 235 nm. Comparison of Figure 223b and 224 confirms that the new absorptions at 246 and 236 nm observed upon irradiation of 106 was due to the formation of 1,4-dicyanobenzene (103).

![UV-absorption spectrum](image)

**Figure 224:** UV-absorption of an authentic sample of 103 in acetonitrile

The photoreactions of 105 and 106 were also monitored by gas–liquid chromatography. Solutions of 105 (1.0×10⁻² M) and 106 (1×10⁻² M) in acetonitrile in sealed Pyrex tubes were purged with argon for 15 min. These solutions were irradiated with sixteen > 290 nm lamps in a Rayonet reactor equipped with a merry-go-round apparatus. The photoreactions were monitored by GLC.

GLC analyses of the solutions of 105 and 106 before irradiation, shown in Figure 225 and 226, reveal the presence of only one component in each sample eluting with retention times of 13 and 10 min, respectively.
GLC analysis of the solution of 105 after 180 min of irradiation showed only trace quantity of one ge-volatile product which eluted with retention time of 7 min. GLC analysis of the solution of 106 after 180 min of irradiation showed the formation of one major and one minor product eluting with retention times of 7.5 and 9.5 min, respectively. The photolysates of 105 and 106 were concentrated and analyzed by the GC interfaced with a
mass spectrometer [140°C (3 min), 20 min/°C to 200°C (5 min), 20 min/°C to 260°C (25 min)].

The GC-trace of the concentrated photolysate of 105 (Figure 227a) shows the presence of two gc-volatile components. The major component, which eluted with a retention time of 15.5 min, has a base molecular ion at m/z 192 and fragmentation pattern (Figure 227c) corresponding with the starting thiadiazole, 105.

**Figure 227a:** GC-trace of concentrated photolysate of 105

**Figure 227c:** Mass spectrum of the component at RT 15.5 min
The minor component, which eluted with a retention time of 7.5 min, was the only photoproduct observed after irradiation of 105. The mass spectrum of this component (Figure 227b) shows a molecular ion peak at m/z 133 which is consistent with a molecular formula of C₈H₇NO (FW 133). This product was identified as 4-methoxybenzonitrile (104), the expected photofragmentation product, by comparison of the gas chromatographic and mass spectroscopic properties with those of an authentic sample of 104.
Figure 228a: GC-trace of concentrated photolysate of 106

The GC-trace of the concentrated photolysate of 106 (Figure 228a) shows the presence of two major components eluting with retention times of 8 and 16.2 min and one minor component eluting with retention time of 15.8 min. The mass spectrum of the major component (Figure 228d) at retention time of 16.2 min reveals a molecular ion peak at m/z 187 and fragmentation pattern corresponding with the reactant, 106.

Figure 228d: Mass spectrum of the component at RT 16.2 min
Figure 228b shows a mass spectrum of the major component at RT of 8 min revealing a molecular ion peak at m/z 128. Comparison of GC-retention time and mass spectral fragmentation pattern of this product with those of an authentic sample of 1,4-dicyanobenzene (103) confirmed that this product was 1,4-dicyanobenzene (103), the expected photofragmentation product.

Figure 228b: Mass spectrum of the component at RT 8 min
The mass spectrum of the minor component at 15.8 min (Figure 228c) reveals a molecular ion peak at m/z 146 and a base peak at m/z 130. The molecular ion at m/z 146 is consistent with a molecular formula of C₈H₆N₂O. Benzamide (38) was observed after irradiation of 3-phenyl-1,2,4-thiadiazole (46) which was expected to result from a reaction of benzonitrile sulfide (48) with water presented in the reaction media. Based on the similar analogy to the photoreaction of 46, the product observed in the photoreaction of 106 that has a molecular ion at m/z 146 was expected to be 4-cyanobenzamide (100). Comparison of GC-retention time and mass spectral fragmentation pattern of this product with those of an authentic sample of 100 confirmed that this product was 4-cyanobenzamide (100).
Diphenyl-1,2,4-thiadiazole (47) was observed by GC analysis at high oven temperature in trace quantity after irradiation of 46. Thus, the GC analysis of both concentrated photolysates of 105 and 106 were also carried out at a higher oven temperature but no sign of any other photoproduct that would correspond to the expected 3,5-diphenyl-1,2,4-thiadiazole analogues was observed.

Quantitative analysis of the solutions of 105, 106 and 46 after 120 min of irradiation in acetonitrile revealed the consumptions of the starting materials at 5 %, 18 % and 25 %, respectively. The formations of 4-methoxybenzonitrile (104), formed in the photoreaction of 105, 1,4-dicyanobenzene (103), formed in the photoreaction of 106, and benzonitrile (43), formed in the photoreaction of 46, were observed at 90%, 78% and 72%, respectively. This result indicates that introduction of a methoxy or cyano group on the $p$-position of the phenyl ring leads to the similar photochemical reactions as observed in the un-substituted compound, 3-phenyl-1,2,4-thiadiazole (46) but 105 and 106 are less reactive than the un-substituted compound, 46. Scheme 90 shows the photoreactions of 3(4′-methoxy)- and 3(4′-cyano)-phenyl-1,2,4-thiadiazole (105) and (106) in acetonitrile solvent.

![Scheme 90: Photoreaction of 3(4′-methoxy)- and 3(4′-cyano)-phenyl-1,2,4-thiadiazole](image-url)
It is of interest to note that the introduction of an electron donating or withdrawing group on $p$-position of the phenyl ring of both 3- and 5-phenyl-1,2,4-thiadiazole affect only their photoreactivities but not their photochemistries. This would, therefore, suggest that introduction of these substituents would have an effect on the photophysical process of the excited thiadiazoles. Thus, in an attempt to understand the nature of the excited states of phenyl substituted 1,2,4-thiadiazoles, it was proposed to study the absorption and luminescence spectroscopy of these compounds.
2.11 Spectroscopic Data of Phenyl Substituted-1,2,4-Thiadiazoles

In an attempt to understand the nature of the excited states of phenyl substituted 1,2,4-thiadiazoles, the absorption and luminescence spectroscopy of these compounds has been studied.

The UV-absorption spectrum of 1,2,4-thiadiazole has been reported to exhibit a $\lambda_{\text{max}}$ of 229 nm and an extinction coefficient ($\varepsilon$) of $5,012$ L mol$^{-1}$ cm$^{-1}$. Based on the magnitude of the extinction coefficient, this absorption band is expected to correspond to an absorption band due to a $S_0 \rightarrow S_1(\pi,\pi^*)$ transition.

2.11.1 5-Phenyl-1,2,4-thiadiazole

UV-absorption

The UV-absorption spectrum (Figure 229) of 5-phenyl-1,2,4-thiadiazole (31) in acetonitrile ($2.2 \times 10^{-5}$ M) exhibits a broad absorption band with a $\lambda_{\text{max}}$ at 274 nm and two small shoulders at 239 and 250 nm. The extinction coefficient at maximum absorption is observed at $20,636$ L mol$^{-1}$ cm$^{-1}$. The magnitude of this extinction coefficient suggest that this absorption band is part of the $S_0 \rightarrow S_1(\pi,\pi^*)$ absorption transition. Figure 230 shows UV-overlay spectra of 31 in acetonitrile at various concentrations. These spectra do not reveal a longer wavelength ($n,\pi^*$) absorption transition. The energy of the first excited singlet can be estimated from the onset of this absorption at $\sim 310$ nm to give the energy value of $92$ kcal/mol.
Figure 229: UV-absorption spectrum of 31 in acetonitrile (2.2×10⁻⁵ M)

Figure 230: UV-absorption overlay spectra of 31 in acetonitrile at various concentrations
Fluorescence emission

Figure 231 shows the fluorescence spectrum of 31 recorded in acetonitrile (6×10^{-5} M). Upon excitation at 285 nm, the spectrum reveals a broad fluorescence band from 290-450 nm with $\lambda_{\max}$ of 336 nm (---). The energy of the first excited singlet state estimated from the onset of this fluorescence emission spectrum at ~297 nm would give an energy value of 96 kcal/mole. This energy value corresponds with the energy of the first excited singlet estimated from the onset in the absorption spectrum (92 kcal/mol). The excitation spectrum (---: emission wavelength set at 336 nm) reveals a broad excitation band with a $\lambda_{\max}$ at 284 nm slightly longer than the $\lambda_{\max}$ observed in the absorption spectrum ($\lambda_{\max}$ 275 nm).

**Figure 231:** Fluorescence spectrum of 31 in acetonitrile (6×10^{-5} M)
It should, however, be noted that in the synthesis of 31, 5-phenyl-1,2,4-oxadiazole (37) was always observed as a very minor product ~ 1%. This oxadiazole has its chromatographic properties very close to 31 and, thus, could not be isolated. Since the fluorescence of the solution of 31 in acetonitrile exhibits low emission intensity, this may lead to an ambiguity that the observed emission results directly from the decay of the excited state of 31 or 37. In order to clarify this ambiguity, 37 was synthesized by the same procedure as for synthesis of 31, employing benzamide (38) as the starting material instead of thiobenzamide (34).

Figure 232 shows UV-absorption spectrum of 37 in acetonitrile (5.2×10⁻⁵ M) revealing a broad absorption band at λ_max of 248 nm with extinction coefficient of 19,615 L mol⁻¹ cm⁻¹. The observed λ_max of 37 is approximately 26 nm different from the observed maximum absorption in 31 (274 nm). Figure 233 exhibits fluorescence emission spectrum of 37 in aceonitrile (5.2×10⁻⁷ M). After excitation at 245 nm, the spectrum reveals the broad high intensity emission band from 280-440 nm (---) with a maximum intensity at 313 nm. Excitation spectrum (——; emission wavelength set at 314 nm) of 37 shows a broad excitation band from 210-280 nm with maximum intensity at 244 nm. This observed excitation spectrum with maximum intensity at 244 nm corresponds with the observed absorption spectrum with a λ_max of 248 nm.
Results and Discussion

Figure 232: UV-absorption spectrum of 37 in acetonitrile (5.2×10⁻⁵ M)

Figure 233: Fluorescence spectrum of 37 in acetonitrile (5.2×10⁻⁷ M)
Comparison of these spectroscopic data of 37 with 31 clearly shows that 37 fluoresces at shorter wavelength (313 nm) while the maximum absorption of 37 is also observed at shorter wavelength (248 nm). This confirms that the fluorescence emission observed in the solution of 31 in acetonitrile results directly from the relaxation of the excited state of 31 not 37. Since the magnitude of extinction coefficients of 37 at 290-300 nm are relatively very small compared with 31, thus, in the irradiation of solution of 31 (with ~ 1% un-isolable 37) at 300 nm, most portion of light will be absorbed by 31 rather than 37 at this irradiation wavelength. The observed fluorescence efficiency of 37 is also greater than 31. Thus, if 37 was able to absorb light, the excited state of 37 would rather undergo relaxation via fluorescence than undergo any photochemical reactions. Therefore, contamination of 37 in 31 would not interfere the observed photochemical reaction of 31.

**Phosphorescence emission**

After excitation at 275 nm, the phosphorescence emission of 31 in methanol/ethanol (5×10^{-5} M) at 77 K (Figure 234a) reveals a structured emission band with maximum intensities at 460, 492 and 525 nm. The very weak intensity band from 375-400 nm is due to emission from the solvent. The observed 0-0 emission band at 460 nm indicates the first excited triplet energy of 31 at 62 kcal/mol. The S_{1-}T_{1} energy gap is thus approximately 30 kcal/mol. This is typical for a S_{1}(\pi,\pi^*) - T_{1}(\pi,\pi^*) system and thus suggests that T_{1} also has a \pi,\pi^* configuration. The energy difference between the 0-0 and 0-1 phosphorescence emission bands corresponds to an energy value in wavenumber of 1414 cm\(^{-1}\). This is in the region of the infrared absorption spectrum (Figure 235) corresponding to ring vibrations of 1,2,4-thiadiazole.\(^{24}\) The vibrational progression observed in the phosphorescence spectrum is presumably due to these ring vibrations.
Figure 234a: Phosphorescence emission spectrum of 31 in methanol/ethanol (5×10⁻⁵ M)

Figure 234b exhibits an overlay of the phosphorescence excitation spectra of 31 when the emission wavelengths are set at the emission maxima at 460, 492, and 525 nm. The spectrum shows a broad excitation band from 250-300 nm with a maximum at 276 nm. This is the same as the λ_max (275 nm) observed in the absorption spectra. As shown, the excitation intensity decreases substantially when the emission wavelength is changed from 490 nm to 458 nm. This corresponds to the decrease in emission intensity at 458 nm as compared to the intensity at 490 nm.
Results and Discussion

**Figure 234b**: Phosphorescence excitation overlay spectra of 31 in methanol/ethanol ($5 \times 10^{-5}$ M)

**Figure 235**: Infrared spectrum of 31 (neat liquid)
Figure 236: State diagram of 31
2.11.2 5(4′-Methoxy)-phenyl-1,2,4-thiadiazole

**UV-absorption**

Figure 237 exhibits a UV-absorption spectrum of 5-(4′-methoxy)phenyl-1,2,4-thiadiazole (90) in acetonitrile (4×10^{-5} M). The spectrum reveals two absorption bands at 218 and 298 nm with extinction coefficients of 5,075 and 9,500 L mol^{-1} cm^{-1}, respectively. The magnitude of these extinction coefficients indicates that both absorption bands are due to π→π* absorptions. Thus, the band at 298 nm would be associated with S_0→S_1(π,π*) absorption while the band at 218 nm would be associated with the S_0→S_2(π,π*) absorption. From the onset of absorption the energies of these S_1(π,π*) and S_2(π,π*) states are estimated as 87 and 116 kcal/mol, respectively. Figure 238 shows an overlay of the absorption spectrum of 2 in acetonitrile at various concentrations. The spectra at higher concentrations do not reveal the existence of any longer wavelength transitions of lower intensity that would be associated with an n→π* transition. Comparison of Figure 237 and 229 shows that the p-methoxy group in 90 results in a red shift of 24 nm or approximately 8 kcal/mol.
Results and Discussion

Figure 237: UV-absorption spectrum of 90 in acetonitrile (4×10⁻⁵ M)

Figure 238: UV-absorption overlay spectra of 90 at various concentrations
Fluorescence emission

Excitation of 90 in acetonitrile (8×10^{-7} M; Figure 239) at 295 nm leads to the broad high intensity fluorescence band (--) from 320-450 nm with a $\lambda_{\text{max}}$ of 369 nm. The ten-fold increase in the fluorescence intensity of 90 as compared to 31 shows that a greater amount of the energy absorbed by 90 is returned as fluorescence than in the case of 31. This is consistent with the observation that 90 is less photoreactive than 31. The excitation spectrum (—; emission wavelength set at 390 nm) of 90 reveals a broad excitation band from 250-320 nm with a maximum intensity at 295 nm corresponding with the maximum absorption observed at 298 nm in the absorption spectrum (Figure 237). Figure 239 shows the near mirror image relationship expected for the $S_0 \rightarrow S_1$ absorption and the $S_0 \rightarrow S_1$ emission. The estimated $S_0 \rightarrow S_1$ transition energy from the onset of this fluorescence spectrum at ~ 331 nm would give energy for the first excited singlet state of 90 at approximately 86 kcal/mol. This energy value is consistent with the first excited singlet energy value obtained from the onset of the absorption spectrum (Figure 237).
Figure 239: Fluorescence spectrum of 90 in acetonitrile (8×10⁻⁷ M)

Figure 240 shows UV-overlay absorption spectra of 90 in acetonitrile and cyclohexane. The overlay reveals similar absorption structures of 90 in these solvents while the maximum absorptions are also observed at approximately the same wavelength. This indicates that polarities of the solvent do not affect the excitation of 90.

Figure 240: UV-absorption spectra of 90 in acetonitrile and cyclohexane
Figure 241: Fluorescence spectrum of 90 in cyclohexane (8×10⁻⁷ M)

Figure 241 exhibits fluorescence emission spectrum of 90 in cyclohexane (8×10⁻⁷ M). Upon excitation at 296 nm, the spectrum exhibits a broad emission band from 310-450 nm (-----) with a maximum intensity at 352 nm. Excitation spectrum (——; emission wavelength set at 352 nm) shows a broad excitation band at $\lambda_{\text{max}}$ of 294 nm corresponding with the observed maximum absorption in the absorption spectrum (Figure 240). The spectrum also reveals a near mirror image relationship between the excitation and emission spectrum, however, the observed maximum emission intensity in cyclohexane is blue shifted approximately 17 nm compared with the observed emission of 90 in acetonitrile.
Phosphorescence emission

Figure 242a shows the phosphorescence emission spectrum of 90 in methanol/ethanol (5×10^{-4} M) at 77 K. Upon excitation at 298 nm, the spectrum reveals a structured emission band with maximum intensities at 467, 498 and 530 nm. The energy of the first excited triplet can be determined from the observed 0-0 emission band at 467 nm to give the energy value of 61.2 kcal/mol. The S_1-T_1 energy gap is 26 kcal/mole, again suggesting that both S_1 and T_1 are π,π*. The energy difference between 0-0 and 0-1 band corresponds to 1333 cm^{-1}. The energy difference between 0-0 and 0-1 band also corresponds with an observed vibrational absorption band in the infrared spectrum of 90 (neat solid; Figure 243) in the region of 1650-1300 cm^{-1} due to the ring stretching.24

Figure 242a: Phosphorescence emission spectrum of 90 in methanol/ethanol (5×10^{-4} M)
Figure 243: Infrared spectrum of 90 (neat solid)

It should be noted that the overlay of the phosphorescence excitation spectra (Figure 242b) obtained when the emission maxima are set at 467, 498 and 530 nm exhibit excitation maxima at 316 and 270 nm. These do not correspond to the absorption spectrum shown in Figure 237.
**Results and Discussion**

\[ S_2(\pi,\pi^*) \quad 116 \text{ kcal/mol} \]

\[ S_1(\pi,\pi^*) \quad 87 \text{ kcal/mol} \]

\[ T_1(\pi,\pi^*) \quad 61.2 \text{ kcal/mol} \]

*Figure 242b:* Phosphorescence excitation overlay spectra of 90

*Figure 244:* State diagram of 90
2.11.3 5(4'-Cyano)-phenyl-1,2,4-thiadiazole

UV-absorption

The UV-absorption of 5(4'-cyano)-phenyl-1,2,4-thiadiazole (98) in acetonitrile (5.1×10⁻⁵ M) shows a broad absorption band with maximum intensity at 280 nm and a shoulder at 245 nm (Figure 245). The extinction coefficient at maximum absorption is 7,450 L mol⁻¹ cm⁻¹. Based on the magnitude of the extinction coefficient, this absorption band is expected to be due to a π→π* absorption transition. Figure 246 shows the UV-overlay absorption spectra of 98 recorded at various concentrations. The spectra at higher concentrations do not reveal the existence of any longer wavelength transitions of lower intensity that would be associated with an n→π* transition. Thus, the observed absorption band with maximum at 280 nm would be associated with S₀→S₁ absorption transition of 98. The magnitude of extinction coefficient of this band at 7,451 L mol⁻¹ cm⁻¹ suggests a π→π* transition associated with this absorption. The estimation of the S₁ (π,π*) energy from the onset of this UV-absorption spectrum at ~ 310 nm would give an energy value of 92 kcal/mol.
**Figure 245:** UV-absorption spectrum of 98 in acetonitrile (5.1×10^{-5} M)

**Figure 246:** UV-absorption overlay spectra of 98 at various concentrations
Fluorescence emission

Figure 247a shows the fluorescence spectrum of 98 in acetonitrile (5.1×10⁻⁵ M). Upon excitation at 279 nm, the spectrum exhibits a broad low emission intensity band (---) from 300-450 nm with a maximum intensity at 340 nm. The observed excitation spectrum (-----) when the emission wavelength set at 340 nm reveals a maximum excitation intensity at 238 nm and three shoulders at 279, 257 and 228 nm. This excitation spectrum does not correspond to the observed absorption spectrum of this compound, shown in Figure 245.

**Figure 247a:** Fluorescence spectrum of 98 in acetonitrile (5.1×10⁻⁵ M)
Fluorescence emission overlay spectra at excitation wavelengths set from 290-240 nm (Figure 247b) show emission spectra with emission intensities correspond to the observed excitation intensities in the excitation spectrum (Figure 247a) at these wavelengths. Theoretically, the observed fluorescence excitation and emission spectrum should exhibit mirror image relationship due to the $S_0 \rightarrow S_1$ absorption and the $S_1 \rightarrow S_0$ emission and thus the excitation spectrum should also correspond to the observed absorption spectrum. In the case of 5-(4'-cyano)phenyl-1,2,4-thiadiazole (98), the observed excitation intensities in the excitation spectrum (Figure 247a) at around 300-250 nm decreases dramatically compared with the molar absorptivities in the absorption spectrum (Figure 245) at the same region resulting in the observed maximum excitation intensity at 238 nm instead of 280 nm as expected from the absorption spectrum. This result would suggest that upon excitation at wavelengths of 290-250 nm, which are resided in the energy level of $S_0 \rightarrow S_1$ transition, the excited state of $3$ would not only return to the ground state via fluorescence relaxation but it would also be deactivated by an unknown non-radiative deactivation pathway. This unknown deactivation would occur only at the certain energy levels, in this case within the vibrational energy levels of $S_1$ above the $S_1$ origin which does not exceed 7740 cm$^{-1}$. For excitations exceed 7740 cm$^{-1}$ above the $S_1$ origin, vibrational relaxation back to the $S_1$ origin would not compete with an unknown non-radiative decay, thus, leading to a greatly increase in emission intensities compared with the emission intensities observed when excitations were carried out from 290-250 nm as observed in Figure 247b.
**Figure 247b:** Fluorescence emission overlay spectra of 3 at various excitation wavelengths

**Phosphorescence emission**

After excitation at 280 nm, the phosphorescence emission spectrum of 98 recorded in methanol/ethanol at 77 K (5×10^{-5} M: Figure 248a) shows a structured emission spectrum with maximum intensities at 479, 513 and 551 nm. The excitation spectra recorded at these wavelengths exhibit an excitation band at $\lambda_{\text{max}}$ 282 nm (Figure 248b) corresponding with the $\lambda_{\text{max}}$ observed in UV-absorption spectrum (Figure 245). The energy of the first excited triplet state can be estimated from the 0-0 band at 479 nm which equals to the energy of 59.7 kcal/mol. In this case the $S_1$-T$_1$ energy gap is 23.8 kcal/mol, which is less than in the case of 31 and 90. The very weak intensity emission band at 380-460 nm is due to the emission from the solvent. The energy difference between 0-0 and 0-1 band equals to the energy value in wavenumber of 1384 cm$^{-1}$ which corresponds to a vibrational absorption band due to ring stretching$^{24}$ between 1,300-1,000 cm$^{-1}$ in infrared spectrum of 98 (neat solid; Figure 249).
Figure 248a: Phosphorescence emission spectrum of 98 in methanol/ethanol

Figure 248b: Phosphorescence excitation spectra of 98 in methanol/ethanol
Figure 248b exhibits an overlay of the phosphorescence excitation spectra of \(98\) when the emission wavelengths are set at the emission maxima at 479, 513, and 551 nm. The spectrum shows a broad excitation band from 260-320 nm with a maximum at 282 nm. This is the same as the \(\lambda_{\text{max}}\) (280 nm) observed in the absorption spectrum. As shown, the excitation intensity decreases, when the emission wavelength is changed from 513 nm to 479 nm. This corresponds to the decrease in emission intensity at 479 nm as compared to the intensity at 513 nm.

\[\text{Figure 249: Infrared spectrum of 98 (neat solid)}\]
Figure 250: State diagram of 98

\[ S_0 \]

\[ S_1(\pi, \pi^*) \quad 92 \text{ kcal/mol} \]

\[ T_1(\pi, \pi^*) \quad 59.7 \text{ kcal/mol} \]

\[ N \]

\[ N \]

\[ S_0 \]

\[ H \]

\[ H \]

\[ N \]

\[ N \]

\[ NC \]
Results and Discussion

2.11.4 3-Methyl-5-phenyl-1,2,4-thiadiazole

UV-absorption

The UV-absorption spectrum (Figure 251) of 3-methyl-5-phenyl-1,2,4-thiadiazole (54) in acetonitrile ($5 \times 10^{-5}$ M) exhibits an absorption band at $\lambda_{\text{max}}$ of 278 nm with an extinction coefficients of 17,620 L mol$^{-1}$ cm$^{-1}$. The spectrum also reveals two absorption bands at 251 and 242 nm with extinction coefficients of 9,700 and 9,960 L mol$^{-1}$ cm$^{-1}$, respectively. The magnitude of these extinction coefficients suggest that these absorptions are due to $\pi \rightarrow \pi^*$ absorption transition. The absorption band at 251 nm is expected due to either $S_0 \rightarrow S_2(\pi,\pi^*)$ transition or part of the $S_0 \rightarrow S_1(\pi,\pi^*)$ transition while the absorption at 242 nm would be associated with the $S_0 \rightarrow S_2(\pi,\pi^*)$ transition. Figure 252 shows the UV-overlay absorption spectra of 7 in acetonitrile at various concentrations. These spectra do not reveal a longer wavelength ($n,\pi^*$) absorption transition. The energy of the first excited singlet ($\pi,\pi^*$) can be estimated from the onset of this absorption at $\sim 310$ nm to give the energy value of 92 kcal/mol. Comparison of Figure 251 and 229 shows a red shift of approximately 4 nm when methyl is substituted at position 3 of the 5-phenyl-1,2,4-thiadiazole. The methyl group substitution at position 3 of thiadiazole ring does not alter the $S_1$ energy of 7 compared with 31. The UV-absorption spectrum of 54, however, reveals a better resolution of the absorptions at around 250 and 240 nm than in the absorption spectrum of 31 under the same solvent environment (acetonitrile).
Results and Discussion

Figure 251: UV-absorption spectrum of 54 in acetonitrile (5×10⁻⁵ M)

Figure 252: UV-absorption overlay spectra of 54 at various concentrations
Fluorescence emission

Figure 253a exhibits fluorescence spectrum of 54 recorded in acetonitrile (5×10⁻⁵ M) at excitation wavelength of 277 nm. The spectrum reveals a broad structureless fluorescence emission band with a maximum intensity at 352 nm. The excitation spectrum with emission wavelength set at 352 nm exhibits a broad excitation band from 250-300 nm with a λ_max at 289 nm which does not correspond to the λ_max observed in the UV-absorption spectrum (λ_max 278 nm: Figure 251). The energy of S₀→S₁ transition can be estimated from the onset of this absorption spectrum, at ~ 305 nm, to give energy of 94 kcal/mol. The energy of the first excited singlet state obtained from this fluorescence emission spectrum corresponds to the energy estimated from the absorption spectrum (Figure 251; 92 kcal/mol).

![Fluorescence spectrum of 54 in acetonitrile (5×10⁻⁵ M)](image_url)

**Figure 253a:** Fluorescence spectrum of 54 in acetonitrile (5×10⁻⁵ M)
Figure 253b shows emission spectra of 54 at various excitation wavelengths. The spectra exhibits well-behaved emission intensities corresponding with molar absorptivities observed in the absorption spectrum at each excitation wavelength. These spectra, however, also reveal that the observed maximum emission intensity results from excitation wavelength at 290 nm which does not correspond to the maximum absorptivity observed at 277 nm in the absorption spectrum. It should, however, also be noted that at short excitation wavelengths (< 265 nm), the spectra exhibits the formation of a new emission band with maximum intensity (at excitation wavelength 255 nm) approximately at 318 nm.

![Figure 253b: Fluorescence spectrum of 54 at various excitation wavelengths](image)

**Figure 253b**: Fluorescence spectrum of 54 at various excitation wavelengths
2.11.5 3-Cyano-5-phenyl-1,2,4-thiadiazole

UV-absorption

Figure 254 exhibits a UV-absorption of 3-cyano-5-phenyl-1,2,4-thiadiazole (117) recorded in acetonitrile (5.2×10⁻⁵ M). The spectrum reveals three absorption bands at 283, 232 and 202 nm with extinction coefficients of 13,654, 18,462 and 27,115 L mol⁻¹ cm⁻¹, respectively. Base on the magnitude of these extinction coefficients, these absorption bands are due to π→π* absorption transitions. The band at 283 nm would be associated with the S₀→S₁(π,π*) absorption while the band at 232 and 202 nm would be associated with the S₀→S₂(π,π*). Figure 255 shows an overlay of the absorption spectra of 117 in acetonitrile at various concentrations. The overlay spectra of 117 at higher solute concentrations do not reveal the existence of any longer wavelength transitions of lower intensity that would be associated with an n→π* transition. Thus, the estimation of 0-0 transition energy from the onset of these absorption bands at ~ 308 and 250 nm would represent the energies of S₁(π,π*) and S₂(π,π*) states at 93 and 114 kcal/mol, respectively. Comparison of Figure 254 and 229 shows a red shift of the S₀→S₁ absorption maxima at approximately 9 nm when cyano group is substituted at ring position 3 of the thiadiazole. The cyano substitution at ring position 3 of the thiadiazole does, however, not affect the S₁ energy of 117 (93 kcal/mol) compared with 31 (92 kcal/mol).
**Results and Discussion**

**Figure 254:** UV-absorption spectrum of 117 in acetonitrile (5.2×10⁻⁵ M)

**Figure 255:** UV-absorption overlay spectra of 117 at various concentrations
Fluorescence emission

Fluorescence spectrum (Figure 256) of 117 recorded in acetonitrile (5.2×10^{-5} M), with excitation wavelength at 283 nm, exhibits a broad emission spectrum (……) from 300-450 nm with a maximum intensity at 349 nm. The excitation spectrum (——; emission wavelength set at 349 nm) of 117 reveals two broad excitation bands with maximum intensities at 285 and 227 nm corresponding with the maximum absorptions observed in the absorption spectrum (Figure 254). Figure 256 shows the near mirror image relationship between the emission spectrum and the excitation spectrum (from 250-325 nm) expected for the S_0→S_1 absorption and the S_0→S_1 emission. Thus, this result confirms that the absorption band at 283 nm is associated with the S_0→S_1 transition. The estimated S_0→S_1 transition energy from the onset of this fluorescence spectrum at ~310 nm would give energy for the first excited singlet state of 117 at approximately 92 kcal/mol which is consistent with the observed S_1 energy obtained from the absorption spectrum (Figure 254; 93 kcal/mol). The observed fluorescence intensity of 117 is approximately fifteen-fold higher than the observed fluorescence of 31. This shows that the excited state of 117 is deactivated via fluorescence emission with greater efficiency than excited state of 31. This is consistent with the observed lack of photoreactivity of 117 compared with 31.
Figure 256: Fluorescence spectrum of 117 in acetonitrile (5.2×10⁻⁵ M)
2.11.6 3-Amino-5-phenyl-1,2,4-thiadiazole

UV-absorption

The UV-absorption (Figure 257) of 3-amino-5-phenyl-1,2,4-thiadiazole (118) exhibits two absorption bands at 315 and 250 nm with extinction coefficients of 6,466 and 18,633 L mol\(^{-1}\) cm\(^{-1}\). The magnitude of these absorption bands suggests that these bands are due to \(\pi \rightarrow \pi^*\) absorption transitions. The UV-overlay absorption spectra of 118 at various concentrations (Figure 258) do not reveal an existence of lower intensity absorption transitions at longer wavelengths and higher solute concentrations expecting due to \(n \rightarrow \pi^*\) absorption transitions. Thus, the absorption band at 315 nm would be associated with the \(S_0 \rightarrow S_1(\pi, \pi^*)\) transition while the absorption band at 250 nm would be associated with \(S_0 \rightarrow S_2(\pi, \pi^*)\) transition. The energies of these excited singlet states can be estimated from the onset of these absorption bands at \(\sim 354\) and 274 nm to give the energies of 81 and 104 kcal/mol, respectively. Amino group substitution at ring position 3 of the thiadiazole results in a red shift of the observed \(S_0 \rightarrow S_1\) maximum absorption approximately 41 nm. This substitution also lowers the \(S_1\) state energy of 118 (-12 kcal/mol) compared with \(S_1\) energy of 31.
Figure 257: UV-absorption spectrum of 118 in acetonitrile ($6 \times 10^{-5}$ M)

Figure 258: UV-absorption overlay spectra of 118 at various concentrations
**Fluorescence emission**

Excitation of 118 in acetonitrile (1.6×10⁻⁷ M: Figure 259) at 315 nm leads to the broad fluorescence emission band (--) from 370-550 nm with a maximum intensity at 435 nm. The excitation spectrum (— ; emission wavelength set at 435 nm) of 118 reveals two excitation bands with maximum intensities at 317 and 246 nm corresponding with the maximum absorptions observed at 315 and 250 nm in the absorption spectrum (Figure 257). Figure 259 shows the mirror image relationship between the emission spectrum and the excitation spectrum (from 270-370 nm) expected for the S₀→S₁ absorption and the S₀→S₁ emission. Excitation of 118 at 250 nm also results in the broad fluorescence emission spectrum with maximum intensity at 435 nm. This emission intensity is approximately three-fold higher than the emission observed at excitation wavelength of 315 nm. This observed high emission intensity corresponds to the observed molar absorptivity in the absorption spectrum at 250 nm. Thus, this result confirms that the absorption band at 315 nm is associated with the S₀→S₁ transition. If the molecule is excited to the second excited singlet state (S₂), a typical rapidly decay due to internal conversion will relax the excited molecule from S₂ to the S₁ state (in 10⁻¹² s). Thus, the fluorescence emission typically results from S₁→S₀ transition. This result, therefore, confirms that the absorption at 250 nm is associated with S₀→S₂ transition, internal conversion resulting in the rapid decay of S₂ to S₁ state and thus relaxation of the S₁ to S₀ results in the observed emission at 375 nm. Figure 38 also reveals a large stoke shift of 118 nm. The estimated S₀→S₁ transition energy from the onset of this fluorescence spectrum at ~ 390 nm would give energy of the first excited singlet state of 118 at approximately 73 kcal/mol. This energy value does not correspond to the first excited singlet energy value obtained from the onset of the absorption spectrum (81 kcal/mol: Figure 257) due to a large stoke shift. Thus, the first excited singlet
state energy of 118 could be estimated by taking an average of the energies value obtained from absorption (81 kcal/mol) and fluorescence emission spectrum (73 kcal/mol) to give an average value of 77 kcal/mol. This result also shows that excitation of 118 in acetonitrile results in more fluorescence efficiency than excitation of 31 in acetonitrile (relatively at the same concentrations). This is again consistent with the observed lack of photoreactivity of 118 in acetonitrile compared with 31.

**Figure 259:** Fluorescence spectrum of 118 in acetonitrile (1.6×10⁻⁷ M)
2.11.7 Diphenyl-1,2,4-thiadiazole

UV-absorption

The UV-absorption (Figure 260) of diphenyl-1,2,4-thiadiazole (47) in acetonitrile (2.2×10⁻⁵ M) exhibits two broad absorption bands at λ<sub>max</sub> of 280 and 254 nm with extinction coefficients of 6,818 and 30,454 L mol⁻¹ cm⁻¹, respectively. The magnitude of these extinction coefficients indicates that these absorption bands are part of π→π* absorption transitions. The UV-absorption overlay spectra of 47 in acetonitrile at various solute concentrations (Figure 261) do not reveal any existence of a longer wavelength absorption with lower intensity expecting due to an n→π* absorption transition. Thus, the absorption band at 280 nm would be associated with S₀→S₁(π,π*) transition while the absorption band at 254 nm would be associated with S₀→S₂(π,π*) transition. The energy of the S₁ and S₂ state of 47 can be estimated from the onset of this absorption spectrum at ~ 305 and 285 nm to give energies of 94 and 100 kcal/mol, respectively. Comparison between Figure 260 and 229 shows that phenyl substitution at ring position 3 of 5-phenyl-1,2,4-thiadiazole results in approximately three-fold decrease in the molar absorptivity of the S₀→S₁(π,π*) transition. But the S₁ energy of 47 (94 kcal/mol), however, still lies above its ground state at approximately the same energy level as observed in 5-phenyl-1,2,4-thiadiazole (31; 92 kcal/mol). Figure 262 shows UV-absorption spectra of 47 in acetonitrile and cyclohexane exhibiting no spectral shift. This reveals that solvent polarities do not have an effect on the excitation of 47.
**Figure 260:** UV-absorption spectrum of 47 in acetonitrile (2.2×10^{-5} M)

**Figure 261:** UV-absorption overlay spectra of 47 at various concentrations
Fluorescence emission

Excitation of 47 in acetonitrile (2.75×10⁻⁶ M) at 280 nm leads to the broad fluorescence spectrum (----) with a maximum intensity at 375 nm (Figure 263). The excitation spectrum (-----; emission wavelength set at 375 nm) of 47 reveals two broad excitation bands with maximum intensities at 280 and 255 nm corresponding with the maximum absorptions observed in the absorption spectrum (Figure 260). Excitation of 47 at 255 nm (-----) results in the higher emission intensity at 375 nm corresponding with the observed intensity at 255 nm in the excitation spectrum. This result again confirms that the absorptions at 280 and 255 nm are due to the $S_0\rightarrow S_1(\pi,\pi^*)$ and $S_0\rightarrow S_2(\pi,\pi^*)$ transitions. The estimation of the $S_1$ energy of 47 from the onset of this emission spectrum at ~ 340 nm would give an energy value of 84 kcal/mol. This $S_1$ energy is not consistent with the $S_1$ energy obtained from the absorption spectrum (94 kcal/mol) due large stoke shift observed in this fluorescence spectrum.
Figure 263: Fluorescence spectrum of 12 in acetonitrile (2.75×10^{-6} M)

Figure 264 exhibits the fluorescence emission spectra of 47 in cyclohexane (5.2×10^{-5} M) at excitation wavelengths of 285 and 255 nm. The spectra exhibit broad emission bands with maximum intensity at 365 nm revealing a blue shift of 10 nm compared with the emission spectrum observed in acetonitrile (Figure 263). Excitation spectrum of 47 in cyclohexane (---; emission wavelength set at 365 nm) exhibits more structured excitation band compared with the excitation spectrum observed in acetonitrile with maximum intensities at 305, 286 and 240 nm. The observed emission intensities at excitation wavelengths of 285 and 255 nm in cyclohexane do not correspond to the observed molar absorptivities at these wavelengths in the absorption spectrum but these observed emission, however, correspond to the observed intensities in the excitation spectrum. The observed excitation spectrum of 47 in cyclohexane does not correspond to the absorption spectrum observed in this same solvent environment (Figure 262). The estimation of the S1 energy from the onset of this emission spectrum at ~ 330 would give the energy value of 87 kcal/mol.
Results and Discussion

DPTD (Cyh: $5.2 \times 10^{-5}$ M)

Figure 264: Fluorescence spectrum of 47 in cyclohexane ($5.2 \times 10^{-5}$ M)
2.11.8 3-Phenyl-1,2,4-thiadiazole

UV-absorption

The UV-absorption spectrum (Figure 265) of 3-phenyl-1,2,4-thiadiazole (46) in acetonitrile (6.9×10⁻⁵ M) exhibits an absorption band with a λ<sub>max</sub> at 261 nm and two shoulders at 286 and 245 nm with extinction coefficients of 13,768, 3,043 and 10,580 L mol⁻¹ cm⁻¹, respectively. The magnitude of these extinction coefficients suggest that this absorption is part of π→π* absorption transition. Figure 266 shows the UV-overlay absorption spectra of 46 in acetonitrile at various concentrations. These spectra do not reveal a longer wavelength (n,π*) absorption transition. The energy of the first excited singlet (π,π*) can be estimated from the onset of this absorption at ~ 294 nm to give the energy value of 97 kcal/mol.

![Figure 265: UV-absorption spectrum of 46 in acetonitrile (6.9×10⁻⁵ M)](image-url)
According to the UV-absorption of 46 in Figure 265, the shoulder absorption at 286 nm might be due to impurities in the sample. In order to clarify this ambiguity, further purification of 46 was performed by Kugelrohr distillation (oven temp 55°C, 0.3 torr). A white solid was collected in a bulb cooled in a dry ice bath. The solid melted at room temperature to give a colorless clear viscous liquid. This liquid was analyzed by $^1$H-NMR and TLC. The $^1$H-NMR analysis of this liquid showed a singlet at $\delta$ 9.81 (1H) and two multiplets at $\delta$ 7.37-7.51 (3H) and 8.32-8.43 (2H) with no significant signals due to an impurity. These observed signals were consistent with the structure of 46 as previously discussed in the synthesis section. TLC analysis of this liquid (100% hexane; 5 runs) showed the presence of only one component with an R$_f$ of 0.5. Both TLC and $^1$H-NMR analysis indicate more than 99% purity of this re-purified 46.
Figure 267 shows UV-absorption overlay spectra of 46 after re-purification recorded in cyclohexane, methanol and acetonitrile. These spectra show identical absorption structures as observed before re-purification (Figure 265). The spectrum in cyclohexane exhibits a maximum absorption at 264 nm which is 3 nm red shifted from the maximum absorption observed in acetonitrile (261 nm). The spectrum in cyclohexane also exhibits better resolution of the absorptions around 275-300 nm, compared with the spectrum recorded in acetonitrile, revealing two shoulders at 288 and 281 nm.

Spectroscopic and chromatographic analyses of 46 before and after re-purification reveal identical results indicating no contamination in 46. Thus, the shoulder absorption band at 286 nm observed in Figure 265 should be part of the absorption of 46, not from any contaminations.

**Figure 267:** UV-absorption spectra of 46 after re-purification in various solvents
Fluorescence emission

Excitation of 46 in acetonitrile (5×10⁻⁵ M) at the maximum absorption (260 nm; Figure 268a) leads to the very weak intensity broad fluorescence band (——) from 290-400 nm with a λ_max of 310 nm. The excitation spectrum of 46 (--; emission wavelength set at 310 nm) reveals two excitation bands with maximum intensities at 275 and 220 nm indicating that the species emitting with λ_max of 310 nm has an absorption maximum at 220 nm. This would indicate that the species that absorb light has a maximum absorption at 220 nm. This is, however, not consistent with the observed absorption spectrum of 46. The previous spectroscopic and chromatographic analyses have, however, indicated more than 99% purity of 46. Therefore, the observed absorption and emission should result only from the molecule of 46. According to the absorption spectrum of 46, the emission intensity should have a maximum at the excitation wavelength of 260 nm (maximum absorptivity). Figure 268b shows the fluorescence emission spectra of 46 at various excitation wavelengths over the range of 285-250 nm. It should be noted that although 46 has a lower extinction coefficient at 285 nm than at 260 nm, excitation at 285 nm leads to a greater intensity of fluorescence emission than observed when the compound is excited at 260 nm. These overlay spectra clearly indicate the decrease in fluorescence intensity when the molecule is excited at excitation wavelengths shorter than 285 nm. Thus, this result suggests that there may be an alternate pathway for the deactivation of the excited state of 46 when the excitation energy reaches > 1070 cm⁻¹ above the S₁ origin.
Results and Discussion

**Figure 268a:** Fluorescence spectrum of 46 in acetonitrile ($5 \times 10^{-5}$ M)

**Figure 268b:** Fluorescence emission overlay spectra of 46 in acetonitrile ($5 \times 10^{-5}$ M)
Figure 268c: Fluorescence spectrum of 46 in methanol at various excitation wavelengths

Figure 268c shows the fluorescence emission spectra of 46 at various excitation wavelengths over the range of 255-220 nm. These overlay spectra reveal that the emission intensities greatly increase when excitation wavelength is set at a wavelength shorter than 240 nm. The observed emission intensities at short excitation wavelengths (235-220 nm) correspond to the excitation intensities observed in the excitation spectrum at these wavelengths (240-220 nm; Figure 268a). This also corresponds to an increase in the molar absorptivities observed from 240-220 nm in the absorption spectrum (Figure 265). The inconsistency between excitation spectrum (Figure 268a) and absorption spectrum (Figure 265) would be due to the decrease of the fluorescence quantum yield at vibrational energy levels > 1070 cm\(^{-1}\) above the S\(_1\) origin, via an unknown non-radiative deactivation process. In the case of benzene, Kaplan and Wilzbach observed a decrease in the fluorescence quantum yield upon irradiation of benzene in the gas phase from 0.18 at 253 nm, 0.10 at 248 nm and 0 at < 242 nm.\(^{26}\) All observed fluorescence from the S\(_1\) benzene excited state vanished when the excitation wavelengths exceeded 3000 cm\(^{-1}\) above the S\(_1\) origin. It was suggested that the loss of fluorescence occurred via an unconventional non-radiative decay, which was named channel 3, leading to the formation of benzvalene. Villa
and co-workers also report the existence of this unconventional non-radiative decay, channel 3, in jet-cooled S1 pyridine.\(^{27}\) It occurs at 1600 cm\(^{-1}\) above the S1 origin of pyridine. Therefore, the observed decrease in fluorescence quantum yield of 46, within the vibrational energy level of > 1070-7650 cm\(^{-1}\) above the S1 origin, would indicate the existence of a channel 3 type non-radiative deactivation pathway upon irradiation of 46. The absorption band observed in the region of 230-200 nm in the absorption spectrum (Figure 265) could be expected due to the S0 $\rightarrow$ S2 absorption transition. Thus, when the molecule is excited at the wavelengths in the region of 235-220 nm, which are resided in the energy level of S0 $\rightarrow$ S2 transition, fast internal conversion process would relax the excited molecule to the S1 state and then return to the ground state via fluorescence decay. Thus, the fluorescence quantum yield in this case would not be interfered by the unknown deactivation pathway resulting in the observed high fluorescence intensities when excited at short excitation wavelengths (235-220 nm).

**Phosphorescence emission**

After excitation at 261 nm, the phosphorescence emission spectrum of 46 recorded in methanol/ethanol at 77 K (5\times10^{-5} M: Figure 269a) shows a broad emission spectrum with a $\lambda_{\text{max}}$ at 465 nm and two shoulders at 445 and 493 nm. The excitation spectra recorded at these wavelengths exhibit an excitation band with a $\lambda_{\text{max}}$ at 262 nm (Figure 269b) corresponding with the $\lambda_{\text{max}}$ observed in UV-absorption spectrum (Figure 265). The energy of the first excited triplet state can be estimated from the onset of this phosphorescence emission spectrum at ~ 418 nm, which corresponds to the energy of 68 kcal/mol. The S1-T1 energy gap is approximately 29 kcal/mol which corresponds to the typical S1(\(\pi,\pi^*\)) - T1(\(\pi,\pi^*\)) energy difference and thus suggests that the T1 state of 46 also has a \(\pi,\pi^*\) configuration.
**Figure 269a:** Phosphorescence emission spectrum of 46 in methanol/ethanol

**Figure 269b:** Phosphorescence excitation spectra of 46 at various emission wavelengths

Excitation of 46 in methanol/ethanol glass at various excitation wavelengths (Figure 269c) exhibits phosphorescence emission spectra with their intensities proportional to the molar absorptivity of 46 at each excitation wavelength.
Figure 269c: Phosphorescence emission spectra of 46 at various excitation wavelengths

\[ S_{1}(\pi,\pi^*) \quad 97 \text{ kcal/mol} \]

\[ T_{1}(\pi,\pi^*) \quad 68 \text{ kcal/mol} \]

Figure 270: State diagram of 46
Results and Discussion

2.11.9 3-(4′-Methoxy)phenyl-1-2,4-thiadiazole

**UV-absorption**

The UV-absorption spectrum of 3-(4-methoxy)phenyl-1,2,4-thiadiazole (105) in acetonitrile ($5 \times 10^{-5}$ M; Figure 271) exhibits two absorption bands with $\lambda_{\text{max}}$ at 275 and 218 nm. The spectrum also reveals two shoulders at 298 and 245 nm which are part of the absorption band that has a $\lambda_{\text{max}}$ at 275 nm. The extinction coefficients of the absorption bands at 275 and 218 nm are 18,140 and 13,200 L mol$^{-1}$ cm$^{-1}$, respectively. The magnitude of these extinction coefficients indicates that these absorptions are due to $\pi \rightarrow \pi^*$ absorptions. Thus, the band at 275 nm would be associated with the $S_0 \rightarrow S_1(\pi,\pi^*)$ absorption while the band at 218 nm would be associated with the $S_0 \rightarrow S_2(\pi,\pi^*)$ absorption.

Figure 272 shows an overlay of the absorption spectra of 105 in acetonitrile at various concentrations. The spectra at higher concentrations do not reveal the existence of any longer wavelength transitions of lower intensity that would be associated with $n \rightarrow \pi^*$ transition. The energies of these $S_1(\pi,\pi^*)$ and $S_2(\pi,\pi^*)$ states can be estimated from the onset of the absorption at $\sim$ 305 and 238 nm resulting in energies of 94 and 120 kcal/mol, respectively. Comparison of Figure 271 and 266 shows that the $p$-methoxy group in 105 results in a red shift of 14 nm or approximately 6 kcal/mol.
Figure 271: UV-absorption spectrum of 105 in acetonitrile (5×10⁻⁵ M)

Figure 272: UV-absorption overlay spectra of 105 at various concentrations
Florescence emission

Excitation of $105$ in acetonitrile ($5.5 \times 10^{-6}$ M: Figure 273) at 275 nm leads to the broad high intensity fluorescence band (-----) from 300-500 nm with a $\lambda_{\text{max}}$ of 377 nm. The excitation spectrum (---; emission wavelength set at 377 nm) of $105$ reveals a broad excitation band from 230-330 nm with a maximum intensity at 273 nm corresponding with the maximum absorption observed at 275 nm in the absorption spectrum (Figure 271). The spectrum also reveals a shoulder in this excitation spectrum at 245 nm corresponding with the shoulder observed in the absorption spectrum at 245 nm. Figure 273 reveals a large stoke shift of 9,838 cm$^{-1}$. The estimated $S_0 \rightarrow S_1$ transition energy from the onset of this fluorescence spectrum at ~309 nm would give energy of the first excited singlet state of $105$ at approximately 93 kcal/mol. This energy value is consistent with the first excited singlet energy value obtained from the onset of the absorption spectrum (Figure 271).

![34MPTD (AcCN: 5.5x10^{-6} M)](image)

**Figure 273:** Fluorescence spectrum of $105$ in acetonitrile ($5.5 \times 10^{-6}$ M)
Results and Discussion

Figure 274: UV-absorption overlay spectra of 105 in acetonitrile and cyclohexane

Figure 274 exhibits UV-absorption overlay spectra of 105 in acetonitrile and cyclohexane. The overlay reveals a 3 nm red shift of the maximum absorption and better resolution of the absorption at ~ 245 nm in cyclohexane compared with the absorption in acetonitrile. Estimation of the S1 (π,π*) energy of 105 from the onset of the absorption in cyclohexane at ~ 305 nm would give an energy value at the same energy level as observed in acetonitrile.

Figure 275: Fluorescence spectrum of 105 in cyclohexane (5.6×10⁻⁶ M)
Results and Discussion

After excitation at 278 nm, fluorescence emission spectrum (Figure 275) of 105 in cyclohexane (---; 5.6×10⁻⁶ M) exhibits a broad emission band from 295-425 nm with a maximum intensity at 325 nm. The observed emission maximum in cyclohexane (325 nm) is 52 nm blue shifted and the observed intensity at maximum is approximately six-fold lower than the maximum emission in acetonitrile (377 nm). Excitation spectrum of 105 in cyclohexane (----; emission wavelength set at 325 nm) shows two excitation bands with maxima at 289 and 243 nm. The maximum excitation intensity of the former band (289 nm) does not correspond to the observed absorption maximum at 278 nm in the UV absorption spectrum in cyclohexane.

Phosphorescence emission

Upon excitation at 275 nm, the phosphorescence emission spectrum of 105 recorded in methanol/ethanol at 77 K (5.5×10⁻⁶ M: Figure 276a) shows a broad phosphorescence emission spectrum with a λ_max at 474 nm. The spectrum also reveals two shoulders at approximately 450 and 504 nm. The excitation spectra recorded at these wavelengths (Figure 276b) exhibit an excitation band with maximum intensities at 276 and 244 nm corresponding with the maximum absorptions observed in the UV-absorption spectrum (Figure 271). The energy of the first excited triplet state can be estimated from the onset of this phosphorescence emission spectrum at ~ 425 nm which equals to the energy of 67 kcal/mol. The S₁-T₁ energy gap is 27 kcal/mol, again suggesting that both S₁ and T₁ are π,π*.
Figure 276a: Phosphorescence emission spectrum of 105 in methanol/ethanol

Figure 276b: Phosphorescence excitation spectra of 105 in methanol/ethanol
Figure 277: State diagram of 105
2.11.10 3-(4′-Cyano)phenyl-1,2,4-thiadiazole

UV-absorption

The UV-absorption of 3(4-cyano)-phenyl-1,2,4-thiadiazole (106) in acetonitrile (5.1×10⁻⁵ M: Figure 281) shows a broad absorption band at \( \lambda_{\text{max}} \) of 270 nm with an extinction coefficient of 7,255 L mol⁻¹ cm⁻¹. Based on the magnitude of extinction coefficient, this absorption band would be due to a \( \pi \rightarrow \pi^* \) absorption transition. Figure 282 shows the UV-overlay absorption spectra of 106 recorded at various concentrations which reveals a low intensity absorption band with a maximum intensity at ~ 308 nm at high solute concentration (\( \geq 1.6 \times 10^{-2} \) M). This absorption has been identified due to absorption of an impurity. Since the absorption at ~ 308 nm is due to an impurity not due to a \( n \rightarrow \pi^* \) absorption transition, therefore, the absorption band at 270 nm would be associated with \( S_0 \rightarrow S_1(\pi, \pi^*) \) absorption transition. The energy of \( S_1(\pi, \pi^*) \) can be estimated from the onset of this absorption spectrum after sublimation at ~ 295 nm to give an energy value of 97 kcal/mol.
Figure 281: UV-absorption overlay spectra of 106 before and after purification in acetonitrile

Figure 282: UV-absorption overlay spectra of 106 at various concentrations
Figure 283: Fluorescence spectrum of 106 in acetonitrile (5.1×10^{-5} M) after purification.

Figure 283 exhibits fluorescence spectrum of 106 in acetonitrile after purification. The spectrum shows the broad emission band (-----) from 280-400 nm with maximum intensity at 315 nm similar to the maximum emission wavelength observed before sublimation (Figure 280). The excitation spectrum (-----; emission wavelength set at 315 nm) of 106 after sublimation shows the broad excitation band with maximum intensity at 268 and a small shoulder at 247 nm. This observed excitation spectrum after purification corresponds to the observed absorption spectrum shown in Figure 281. Estimation of the S_1 energy from the onset of this fluorescence emission spectrum at ~ 295 nm would give an energy value of 97 kcal/mol. This energy value is consistent with the S_1 energy value estimated from the onset of absorption spectrum after sublimation. The observed high fluorescence emission intensity of 106 is consistent with the observed lack of photoreactivity of 106 compared with 46 in acetonitrile.
Phosphorescence emission

After excitation at 270 nm, the phosphorescence emission spectrum of 106 recorded in methanol/ethanol at 77 K (6.7×10⁻⁵ M: Figure 284a) shows a structured emission spectrum with maximum intensities at 458, 486 and 520 nm. The excitation spectra recorded at these wavelengths exhibit a broad excitation band with a $\lambda_{\text{max}}$ 270 nm (Figure 284b) corresponding with the $\lambda_{\text{max}}$ observed in UV-absorption spectrum (Figure 281). The energy of the first excited triplet state can be estimated from the 0-0 band at 458 nm which equals to the energy of 62 kcal/mol. The $S_1$-$T_1$ energy gap is approximately 35 kcal/mol, which would correspond to the typical energy difference of $S_1(\pi,\pi^*)$ - $T_1(\pi,\pi^*)$ system. Thus, this suggests that $T_1$ of 106 also has $\pi,\pi^*$ configuration.

![Figure 284a: Phosphorescence emission spectrum of 106 in methanol/ethanol](image-url)
Results and Discussion

Figure 284b: Phosphorescence emission overlay spectra of 106 in methanol/ethanol

![Graph showing phosphorescence emission spectra](image)

Figure 285: State diagram of 106

\[ S_1(\pi,\pi^*) \quad 97 \text{ kcal/mol} \]

\[ T_1(\pi,\pi^*) \quad 62 \text{ kcal/mol} \]
2.11.11 5-Cyano-3-phenyl-1,2,4-thiadiazole

UV-absorption

The UV-absorption spectrum of 5-cyano-3-phenyl-1,2,4-thiadiazole (119) in acetonitrile (6.8×10⁻⁵ M; Figure 286) exhibits two absorption bands with maximum intensities at 296 and 241 nm. The extinction coefficients of these maxima are observed at 1471 and 8824 L mol⁻¹ cm⁻¹, respectively. The magnitude of these extinction coefficients suggests π→π* absorption transitions associated with these absorption bands. The UV-overlay absorption spectra of 119 at various concentrations (Figure 287) do not reveal an existence of any weak intensity absorptions at longer wavelengths. Thus, the absorption band at 296 and 241 nm would be associated with S₀→S₁(π,π*) and S₀→S₂(π,π*), respectively. The energies of the first and second excited singlet states of 119 can be estimated from the onset of these absorptions at ~ 320 and 275 nm to give energy values of 89 and 104 kcal/mol, respectively. The energy of the first excited singlet state of 119 is located at 8 kcal/mol lower than the excited singlet state of unsubstituted 3-phenyl-1,2,4-thiadiazole (46; 97 kcal/mol). This cyano substitution also results in the decrease of extinction coefficients of S₀→S₁(π,π*) and S₀→S₂(π,π*) absorption transitions compared with absorption of 46.
Results and Discussion

Figure 286: UV-absorption spectrum of 119 in acetonitrile (6.8×10⁻⁵ M)

Figure 287: UV-absorption spectra of 119 in acetonitrile at various concentrations
Results and Discussion

Fluorescence emission

Excitation of 119 in acetonitrile (6.8×10⁻⁵ M; Figure 288) at 298 nm results in a broad emission spectrum with maximum intensity at 399 nm (—···) while excitation at 240 nm results in approximately two-fold emission intensity (—·) higher than the emission observed at excitation wavelength of 298 nm. The excitation spectrum (—; emission wavelength set at 399 nm) shows two excitation bands with maxima at 291 and 243 nm. The structure of this excitation spectrum corresponds to the observed absorption spectrum (Figure 286). It should, however, be noted that the observed molar absorptivity of S₀→S₂(π,π*) absorption (241 nm; ε 8824 L mol⁻¹ cm⁻¹) is approximately eight-fold higher than the molar absorptivity of S₀→S₁(π,π*) absorption (296 nm; ε 1471 L mol⁻¹ cm⁻¹) while the excitation intensity at 240 nm, associated with S₀→S₂(π,π*) transition, is approximately only two-fold higher than the excitation intensity at 298 nm, associated with S₀→S₁(π,π*) transition. This result would be due to the loss of internal conversion quantum yield via an unknown non-radiative deactivation process which is in competition with fast internal conversion of S₂ to S₁.

Figure 288: Fluorescence spectrum of 119 in acetonitrile (6.8×10⁻⁵ M)
Estimation of the $S_1$ energy from the onset of this fluorescence emission spectrum at \( \sim 360 \) nm would give an energy value of 79 kcal/mol. This energy value is not consistent with the $S_1$ energy estimated from the onset of the absorption spectrum (89 kcal/mol) due to large stoke shift of 108 nm. Thus, the $S_1$ energy of 119 can be represented by an average value between the energies obtained from absorption (79 kcal/mol) and fluorescence spectrum (89 kcal/mol) to be 84 kcal/mol.
2.11.12 5-Amino-3-phenyl-1-2,4-thiadiazole

UV-absorption

The UV-absorption spectrum of 5-amino-3-phenyl-1,2,4-thiadiazole (120) in acetonitrile (5.5×10⁻⁵ M: Figure 289) exhibits two absorption bands with λ_{max} at 272 and 233 nm. The extinction coefficients of absorption bands at 272 and 233 nm are observed at 7,373 and 27,636 L mol⁻¹ cm⁻¹, respectively. The magnitude of these extinction coefficients indicates that these absorptions are due to π→π* absorptions. Figure 290 shows an overlay of the absorption spectra of 120 in acetonitrile at various concentrations. The spectra at higher concentrations do not reveal the existence of any longer wavelength transitions of lower intensity that would be associated with n→π* transition. Thus, the band at 272 nm would be associated with the S₀→S₁(π,π*) absorption while the band at 233 nm would be associated with the S₀→S₂(π,π*) absorption. The energies of these S₁(π,π*) and S₂(π,π*) states can be estimated from the onset of the absorption at ~ 300 and 260 nm resulting in energies of 95 and 110 kcal/mol, respectively. Comparison of Figure 265 and 289 shows that amino substitution at ring position 5 of 3-phenyl-1,2,4-thiadiazole results in blue shifts of 24 and 8 nm for both S₀→S₁(π,π*) and S₀→S₂(π,π*) absorption transitions, respectively, compared with cyano substitution in 119 (Figure 289).
Results and Discussion

Figure 289: UV-absorption spectrum of 120 in acetonitrile (5.5×10⁻⁵ M)

Figure 290: UV-absorption spectrum of 120 in acetonitrile at various concentrations
Figure 291a: Fluorescence spectrum of 120 in acetonitrile (5.5×10⁻⁵ M)

Figure 291b: Scale expansion of fluorescence spectrum of 120 in acetonitrile (5.5×10⁻⁵ M)
After excitation of 120 in acetonitrile (5.5×10⁻⁵ M) at 271 nm, Figure 291a exhibits a very weak intensity emission band (—) with an observed maximum intensity at 307 nm. Excitation of 120 in acetonitrile at 233 nm (---) results in a lower emission intensity with maximum at 313 nm while the molar absorptivity at this excitation wavelength (233 nm) is observed at approximately four-fold higher than the molar absorptivity at 271 nm. Excitation spectrum of 120 in acetonitrile (-----; emission wavelength set at 304 nm) exhibits two excitation bands at 269 and 212 nm (Figure 291b). The short excitation band (212 nm) is observed with approximately eleven-fold higher intensity than the excitation band at longer wavelength (269 nm). In this case, loosing of fluorescence quantum yield in the excitation region of 220-280 nm would explain these observations, however, when the observed fluorescence intensity is very weak, it will be very difficult to distinguish or justify whether the observed emission results directly from the excited state of the molecule of interest or from an unknown impurity. Thus, this observed fluorescence emission of 120 in acetonitrile is still unclear.
2.11.13 Summary on Spectroscopic Properties of Phenyl Substituted-1,2,4-Thiadiazoles

5-Phenyl-1,2,4-thiadiazoles

The $S_1(\pi,\pi^*)$ energy of 5-phenyl-1,2,4-thiadiazole (31) is approximately 92 kcal/mol above the ground state as estimated from the onset of its absorption spectrum in acetonitrile. Table 1 shows that substitution of a methoxy group at the $p$-position on the phenyl ring results in a red shift of the $S_1(\pi,\pi^*)$ energy while replacing with a cyano group at this position did not alter the energy of the $S_1(\pi,\pi^*)$ compared with the $S_1(\pi,\pi^*)$ energy of the parent compound, 31. The observed $\lambda_{\text{max}}$ for both $p$-substituted compounds were, however, red shifted from the observed $\lambda_{\text{max}}$ of 31. Table 2 also reveals that substitution of cyano or an amino group at ring position 3 of the thiadiazole ring resulted in red shifts of the $\lambda_{\text{max}}$ in $S_0 \rightarrow S_1(\pi,\pi^*)$ absorption transitions and the decrease in the $\varepsilon_{\text{max}}$ of these $S_0 \rightarrow S_1(\pi,\pi^*)$ absorption transitions. While cyano substitution at ring position 3 of the thiadiazole ring does not alter the $S_1(\pi,\pi^*)$ energy, the amino substitution at this position resulted in a 11 kcal/mol red shift of the $S_1(\pi,\pi^*)$ energy relative to the $S_1(\pi,\pi^*)$ energy of the un-substituted compound. The $n \rightarrow \pi^*$ absorption transitions could not be detected at longer wavelengths and high solute concentrations for any of the 5-phenyl-1,2,4-thiadiazoles. This confirms that the $S_1$ states of these 5-phenyl-1,2,4-thiadiazoles are $\pi,\pi^*$ in configuration.
Table 2: UV-absorption properties of 5-phenyl-1,2,4-thiadiazoles in acetonitrile

<table>
<thead>
<tr>
<th>Compound</th>
<th>S&lt;sub&gt;0&lt;/sub&gt;→S&lt;sub&gt;1&lt;/sub&gt;(π,π*)</th>
<th>S&lt;sub&gt;0&lt;/sub&gt;→S&lt;sub&gt;2&lt;/sub&gt;(π,π*)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Onset (nm)</td>
<td>Energy (kcal/mol)</td>
</tr>
<tr>
<td>31</td>
<td>310</td>
<td>92</td>
</tr>
<tr>
<td>90</td>
<td>330</td>
<td>87</td>
</tr>
<tr>
<td>98</td>
<td>310</td>
<td>92</td>
</tr>
<tr>
<td>54</td>
<td>310</td>
<td>92</td>
</tr>
<tr>
<td>117</td>
<td>308</td>
<td>93</td>
</tr>
<tr>
<td>118</td>
<td>354</td>
<td>81</td>
</tr>
<tr>
<td>47</td>
<td>305</td>
<td>94</td>
</tr>
</tbody>
</table>

It is clearly seen from the Table 2 and Figure 292 that an electron withdrawing group on either the phenyl or the thiadiazole ring does not affect the energy of the first excited singlet, compared with the parent compound, but results in an approximately 7 nm red shift of the λ<sub>max</sub> of S<sub>0</sub>→S<sub>1</sub>(π,π*) absorption transitions. In contrast, an electron donating group on either the phenyl ring at the <i>p</i>-position or at the 3-position of the thiadiazole ring results in red shifts of the first excited singlet state energies and the observed λ<sub>max</sub> of S<sub>0</sub>→S<sub>1</sub>(π,π*) absorption transitions relative to the values observed in the parent compound.
Results and Discussion

The fluorescence emission spectra of 5-phenyl-1,2,4-thiadiazoles exhibited broad structureless emission bands with large Stokes’ shift, especially when either the phenyl ring or the thiadiazole ring was substituted with an electron donating group. Table 3 shows that the Stokes’ shifts decrease when the spectra were recorded in cyclohexane. This result suggests that the excited states of these thiadiazoles are associated with charge transfer character. Thus, the charge transfer excited states would be more stable in acetonitrile (polar solvent) resulting in the observed larger Stokes’ shifts than in cyclohexane.
Results and Discussion

Table 3: Fluorescence properties of 5-phenyl-1,2,4-thiadiazoles in acetonitrile

<table>
<thead>
<tr>
<th>Compound</th>
<th>Emission spectrum (S₁→S₀)</th>
<th>Excitation spectrum</th>
<th>Stokes' Shift (cm⁻¹)</th>
<th>Absorption maximum (λ_max; nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Onset (nm)</td>
<td>Energy (kcal/mol)</td>
<td>λ_max (nm)</td>
<td>λ_max (nm)</td>
</tr>
<tr>
<td>31</td>
<td>297</td>
<td>96</td>
<td>336</td>
<td>284</td>
</tr>
<tr>
<td>90</td>
<td>331</td>
<td>86</td>
<td>369</td>
<td>295</td>
</tr>
<tr>
<td></td>
<td>318&lt;sup&gt;a&lt;/sup&gt;</td>
<td>90&lt;sup&gt;a&lt;/sup&gt;</td>
<td>352&lt;sup&gt;a&lt;/sup&gt;</td>
<td>294&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>98</td>
<td>308</td>
<td>93</td>
<td>320</td>
<td>279</td>
</tr>
<tr>
<td>54</td>
<td>305</td>
<td>94</td>
<td>352</td>
<td>289</td>
</tr>
<tr>
<td>117</td>
<td>310</td>
<td>92</td>
<td>349</td>
<td>285 (S₁)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>227 (S₂)</td>
</tr>
<tr>
<td>118</td>
<td>390</td>
<td>73</td>
<td>435</td>
<td>317 (S₁)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>246 (S₂)</td>
</tr>
<tr>
<td>47</td>
<td>340</td>
<td>84</td>
<td>375</td>
<td>280 (S₁)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>255 (S₂)</td>
</tr>
<tr>
<td></td>
<td>330&lt;sup&gt;a&lt;/sup&gt;</td>
<td>87&lt;sup&gt;a&lt;/sup&gt;</td>
<td>365&lt;sup&gt;a&lt;/sup&gt;</td>
<td>286 (S₁)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>240 (S₂)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Data are recorded in cyclohexane solution
The phosphorescence emission spectra of 5-(4-substituted)phenyl-1,2,4-thiadiazoles exhibited well-resolved structured phosphorescence bands. The first excited triplet state of these thiadiazoles could be determined from the observed 0-0 bands as shown in Table 4. Substitution of an electron donating or withdrawing group at the \( p \)-position of the phenyl ring did not affect the first excited triplet state energy relative to the energy of the un-substituted compound. The energy differences between \( S_1 \) states and \( T_1 \) states were approximately 30 kcal/mole which is the typical energy difference of \( S_1(\pi,\pi^*) - T_1(\pi,\pi^*) \) system. Thus, the \( T_1 \) states of these thiadiazoles were expected to have \( \pi,\pi^* \) configurations. The energy differences between 0-0 and 0-1 band were in the range of 1,300-1,400 cm\(^{-1} \) which corresponded to the observed vibrational absorption bands in their infrared spectra in the region of 1650-1300 cm\(^{-1} \) due to the ring stretching.

**Table 4**: Phosphorescence properties of 5-phenyl-1,2,4-thiadiazoles in ethanol/methanol (4:1) at 77 K

<table>
<thead>
<tr>
<th>Compound</th>
<th>0-0 band (nm)</th>
<th>0-1 band (nm)</th>
<th>( \Delta E ) 0-0 and 0-1 (cm(^{-1} ))</th>
<th>( T_1 ) Energy (kcal/mol)</th>
<th>( S_1-T_1 ) (kcal/mol)</th>
<th>( T_1 ) Configuration</th>
</tr>
</thead>
<tbody>
<tr>
<td>31</td>
<td>460</td>
<td>492</td>
<td>1,414</td>
<td>62</td>
<td>30</td>
<td>( \pi,\pi^* )</td>
</tr>
<tr>
<td>90</td>
<td>467</td>
<td>498</td>
<td>1,333</td>
<td>61.2</td>
<td>26</td>
<td>( \pi,\pi^* )</td>
</tr>
<tr>
<td>98</td>
<td>479</td>
<td>513</td>
<td>1,384</td>
<td>60</td>
<td>32</td>
<td>( \pi,\pi^* )</td>
</tr>
</tbody>
</table>
3-Phenyl-1,2,4-thiadiazoles

The $S_1(\pi,\pi^*)$ energy of 3-phenyl-1,2,4-thiadiazole was observed approximately at 97 kcal/mol from the onset of the absorption spectrum in acetonitrile. The phenyl group substituted on the thiadiazole ring at position 3 or 5 resulted in an energy difference between their first excited singlet states of approximately 5 kcal/mole. Substitution of a methoxy group at the $p$-position on the phenyl ring resulted in a red shift of the $S_1(\pi,\pi^*)$ energy (3 kcal/mol) while cyano group at this position did not alter the energy of the $S_1(\pi,\pi^*)$ relative to the parent compound as shown in Table 5. The observed $\lambda_{\text{max}}$ for electron donating or electron withdrawing $p$-phenylsubstituted compounds were, however, red shifted from the observed $\lambda_{\text{max}}$ of 3-phenyl-1,2,4-thiadiazole by 14 and 9 nm, respectively. Substitution of a cyano or an amino group at ring position 5 of the thiadiazole ring resulted in red shifts of the $S_1(\pi,\pi^*)$ energies and the observed $\lambda_{\text{max}}$ of the $S_0\rightarrow S_1(\pi,\pi^*)$ absorption transitions. The decrease in the $\varepsilon_{\text{max}}$ of the $S_0\rightarrow S_1(\pi,\pi^*)$ absorption transitions were also observed relative to the parent compound with cyano substitution leading to a larger decrease. The $n\rightarrow\pi^*$ absorption transitions could not be detected at longer wavelengths and high solute concentrations for all of the 3-phenyl-1,2,4-thiadsazoles. This confirms that the $S_1$ states of these 3-phenyl-1,2,4-thiadsazoles are $\pi,\pi^*$ in configurations. Figure 293 shows UV-absorption spectra of 3-phenyl-1,2,4-thiadiazoles in acetonitrile.
Table 5: UV-absorption properties of 3-phenyl-1,2,4-thiadiazoles in acetonitrile

<table>
<thead>
<tr>
<th>Compound</th>
<th>$S_0 \rightarrow S_1(\pi,\pi^*)$</th>
<th>$S_0 \rightarrow S_2(\pi,\pi^*)$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Onset (nm)</td>
<td>Energy (kcal/mol)</td>
</tr>
<tr>
<td>46</td>
<td>294</td>
<td>97</td>
</tr>
<tr>
<td>105</td>
<td>305</td>
<td>94</td>
</tr>
<tr>
<td>106</td>
<td>295</td>
<td>97</td>
</tr>
<tr>
<td>119</td>
<td>320</td>
<td>89</td>
</tr>
<tr>
<td>120</td>
<td>300</td>
<td>95</td>
</tr>
</tbody>
</table>

Figure 293: UV-absorption overlay spectra of 3-phenyl-1,2,4-thiadiazoles in acetonitrile
Excitation of 3-phenyl-1,2,4-thiadiazole (46) in acetonitrile with the excitation wavelengths in the range of 220-285 nm resulted in unusual fluorescence intensities inconsistent with the observed absorptivities over this region. Excitation at short excitation wavelength region (220-240 nm) resulted in broad emission bands of moderate intensities with the maximum emission intensities at 300 nm. Excitation at longer excitation wavelengths in the range of 250-285 nm resulted in weak intensities fluorescence bands. The fluorescence at excitation wavelength of 260 nm, where the thiadiazole absorbs most light, was observed with the least intensity in this region (250-285 nm). The maximum emission intensity, in this excitation region (250-285nm), was observed when the molecule was excited at 285 nm, where the thiadiazole absorbs less light. This unusual fluorescence behavior observed from 46 is similar to the fluorescence behavior of benzene and pyridine. In both of these aromatic molecules the fluorescence quantum yields have been observed to decrease when the excitation energy is increased above the $S_0$-$S_1$ origin due to the onset of a new radiationless decay pathway that is accessible from higher vibrational energy states within the $S_1$ excited molecule. This pathway has been termed the channel 3. The observed $λ_{\text{max}}$ in the UV-absorption spectra of these 3-phenyl-1,2,4-thiadiazoles are mostly consistent with the observed $λ_{\text{max}}$ in excitation spectra except in the case of the absorption spectrum of 3-(4′-methoxy)phenyl-1,2,4-thiadiazole (105) recorded in cyclohexane as shown in Table 6. Table 6 also reveals that the magnitude of the Stokes’ shift of this compound greatly decreases in cyclohexane relative to the Stokes’ shift observed in acetonitrile. Substitution of methoxy group at the $p$-position on the phenyl ring resulted in a large Stokes’ shift in acetonitrile solvent of approximately the same magnitude as observed for cyano substitution at position 5 of the thiadiazole ring in acetonitrile solvent.
In contrast, cyano substitution at the \( p \)-position of the phenyl ring caused a moderate Stokes' shift while fluorescence was not observed when amino substitution was at position 5 of the thiadiazole ring.

### Table 6: Fluorescence properties of 3-phenyl-1,2,4-thiadiazoles in acetonitrile

| Compound | Emission spectrum 
\((S_1 \rightarrow S_0)\) | Excitation spectrum | Stokes’ Shift \( (\text{cm}^{-1}) \) | Absorption maximum; \( \lambda_{\text{max}} \) (nm) |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Onset ( (\text{nm}) )</td>
<td>Energy ( (\text{kcal/mol}) )</td>
<td>( \lambda_{\text{max}} ) (nm)</td>
<td>( \lambda_{\text{max}} ) (nm)</td>
</tr>
<tr>
<td>46</td>
<td>295</td>
<td>97</td>
<td>310</td>
<td>272 ( (S_1) )</td>
</tr>
<tr>
<td>105</td>
<td>309</td>
<td>93</td>
<td>377</td>
<td>273</td>
</tr>
<tr>
<td></td>
<td>305(^a)</td>
<td>94(^a)</td>
<td>325(^a)</td>
<td>289 ( (S_1) )(^a)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>243 ( (S_2) )(^a)</td>
</tr>
<tr>
<td>106</td>
<td>295</td>
<td>97</td>
<td>315</td>
<td>268</td>
</tr>
<tr>
<td>119</td>
<td>360</td>
<td>79</td>
<td>399</td>
<td>291 ( (S_1) )</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>243 ( S_2 )</td>
</tr>
<tr>
<td>120</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

\(^a\)Data are obtained from cyclohexane solution
The phosphorescence emission spectra of 3-(4'-substituted)phenyl-1,2,4-thiadiazoles appeared as broad phosphorescence bands with two small shoulders. The first excited triplet state of these thiadiazoles could be determined from the onset of these bands as shown in Table 7. Substitution of a cyano group at the \( p \)-position of the phenyl ring reduced the energy of the first excited triplet while methoxy substitution did not affect the first excited triplet state energy relative to the unsubstituted compound. The energy differences between \( S_1 \) states and \( T_1 \) states were approximately 30 kcal/mole which is the typical energy difference of \( S_1(\pi,\pi^*) - T_1(\pi,\pi^*) \) system. Thus, the \( T_1 \) states of these thiadiazoles were expected to have \( \pi,\pi^* \) configurations.

**Table 7: Phosphorescence properties of 3-phenyl-1,2,4-thiadiazoles in ethanol/methanol (4:1) at 77 K**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Onset (nm)</th>
<th>( T_1 ) Energy (kcal/mol)</th>
<th>( S_1-T_1 ) (kcal/mol)</th>
<th>( T_1 ) Configuration</th>
</tr>
</thead>
<tbody>
<tr>
<td>46</td>
<td>418</td>
<td>68</td>
<td>29</td>
<td>( \pi,\pi^* )</td>
</tr>
<tr>
<td>105</td>
<td>425</td>
<td>67</td>
<td>27</td>
<td>( \pi,\pi^* )</td>
</tr>
<tr>
<td>106</td>
<td>458</td>
<td>62</td>
<td>35</td>
<td>( \pi,\pi^* )</td>
</tr>
</tbody>
</table>

The fluorescence emission spectra of both 5- and 3-phenyl-1,2,4-thiadiazoles exhibit moderate - large Stokes’ shifts in acetonitrile. The magnitude of these Stokes’ shifts decrease in cyclohexane. This suggests a difference between the dipole moments in the excited states and ground states of these thiadiazoles. Polar solvents can stabilize the high dipole moment excited states resulting in solvent reorganized excited states with lower energy levels relative to the Frank-Condon excited states. Thus, this would cause the observed fluorescence with Stokes’ shifts as shown in Scheme 91.
The difference in the geometries of the absorbing and emitting species can also lead to large Stokes’ shifts. A possible explanation for this would be if in the ground state ($S_0$) the two rings of the phenylthiadiazole are coplanar but are perpendicular in the energy minimized singlet state ($S_1$)$_{V0}$. Scheme 92 shows the consequences of this change in geometry. As shown, absorption of light $h\nu_{abs}$ by the coplanar $S_0$ molecule leads to the Franck-Condon coplanar $S_1$(vib) state. According to this example, vibrational relaxation of $S_1$(vib) to $S_1$(v0) is accompanied by twisting of the two rings leading to the energy minimized twisted $S_1$(v0) state. Fluorescence is also a Franck-Condon transition and thus emission of $h\nu_{flu}$ would lead to the vibrationally excited twisted ground state $S_0$(vib). This would be followed by rapid vibrational relaxation back to the coplanar $S_0$ state. The net result is that the geometry change is accompanied by a large change in the energy gap between $S_0 \rightarrow S_1$(vib) and $S_1$(v0) $\rightarrow S_0$(vib). Accordingly, there would be a large difference in the wavelengths of $h\nu_{abs}$ and $h\nu_{flu}$, i.e., a large Stokes’ shift would be observed.

**Scheme 91:** Solvent reorganization resulting in lowering of the excited state energy level

[Diagram of energy levels and transitions]
Tinuvin P [2-(2-hydroxy-5-methylphenyl)benzotriazole], a commercial UV-absorber, has been reported to undergo excited state intramolecular proton transfer (ESIPT) upon irradiation and subsequently fast internal conversion back to ground state resulting in the observed photostability of this compound. Hence, it is essentially non-fluorescent. In order to have an effective ESIPT deactivation, it is important that the molecule remain planar. In the case of Tinuvin P, intramolecular hydrogen bonding plays an important role to retain the planarity of Tinuvin P. The photostability of this compound, however, suffers in basic or good hydrogen bond acceptor solvents, for instance DMSO, resulting in the observed fluorescence with a moderate stokes’ shift. It has been suggested that the observed fluorescence in such basic solvents is an indicator for loss of photostability of this compound due to the loss of planarity of the molecule leading to elimination of the effective ESIPT.

**Scheme 92:** Energy difference between absorbing and emitting states due to geometry change upon excitation
deactivation pathway. Scheme 93 shows the effective deactivation pathway and the loss of photostability in DMSO of Tinuvin P.

Maliakal and co-workers reported that 6′-methyl substituted Tinuvin P (b) undergoes deactivation in DMSO by an alternative pathway involving a twisted intramolecular charge transfer excited state (TICT).28 Thus, compound b remains photostable in DMSO because the 6′-methyl group interferes with the planarity of the Tinuvin P molecule. This enhances the twist angle of the relaxed excited state and, thus, enhances the charge transfer character which results in a high dipole moment of the excited state. The TICT excited state is well-stabilized in a polar solvent such as DMSO. Therefore, the Frank-Condon excited state is at higher energy than the TICT excited state. This causes a large Stokes’ shift (Δ or Δ’; Scheme 94). Moreover, the energy level of the twisted ground state is higher than that of
the stable ground state. Thus, relaxation from the TICT state to the twisted ground state will further increase the magnitude of the Stokes’ shift (B; Scheme 94). Therefore, the observed stokes’ shift in this case is a summation of A+B, which can be envisioned in Scheme 94.

In some cases, energy levels of twisted ground states are very high relative to the stable ground states resulting in a small energy gap between TICT states and twisted ground states. Thus, in these cases non-radiative deactivation through a conical intersection\cite{29} would be favorable leading to quenching of the fluorescence quantum yields in polar solvents.

**Scheme 94:** A large Stokes’ shift due to emission from a TICT excited state
The Stokes’ shifts of compounds d and e in DMSO were observed at 10,617 cm\(^{-1}\) and 6,374 cm\(^{-1}\), respectively. In the compound d, methyl substitution at the 6’-position enhances twisting between the two ring units thus enhancing the TICT character of the excited state in this compound. The large Stokes’ shift in the compound d is associated with two effects; geometry change and dipole moment change during relaxation (TICT excited state) relative to the ground state, whereas the smaller Stokes’ shift in the compound e is due mostly to the internal charge transfer character of the molecule (dipole moment change; CT excited state). The magnitude of the Stokes’ shifts decreases for both compounds in cyclohexane solvent. This confirms the charge transfer character for both compounds.

By analogy with 2-arybenzotriazoles, the observed fluorescence Stokes’ shifts of 1,2,4-thiadiazoles in acetonitrile could also be explained by emission from TICT states. Thus, the observed large Stokes’ shift would be governed by two factors; the geometry between the donor and acceptor and donor/acceptor character.
Michael Maus studied photoinduced intramolecular charge transfer in three different twisted donor-acceptor biphenyl systems (BA1-3). The AM1 calculations were first performed on geometry optimization of BA1-3 resulting in the twist angles of 0°, 39° and 78°, respectively.

The observed fluorescence emissions of these compounds were suggested to occur from the charge transfer excited states where their excited state geometries were greatly different from the ground states. The photoinduced charge transfer and structural relaxation process in these biaryl compounds leading to large Stokes’ shifts were summarized by Maus as shown in Scheme 95. After excitation of these compounds, the following transitions were suggested to occur:

1) Vibrational relaxation
2) Initial solvation and geometry relaxation towards a more planar geometry than in S₀
3) Electron transfer
4) Fluorescence relaxation from the TICT excited state
5) Addition structural relaxation to a more twisted conformation (CTR) than in S₀ occurring only in BA-3
In the case of 2-arybenzotriazoles, shown above, the triazole rings which contain three electronegative nitrogen atoms are generally considered as the acceptor groups except the compound C. Therefore, in the case of phenylthiadiazoles, the thiadiazole rings, containing two electronegative nitrogen atoms and one moderately electronegative sulfur atom, could also be generally considered as acceptor groups.

The energy minimized ground states of 5-phenyl-1,2,4-thiadiazole (31) and 5-(4′-methoxy)phenyl-1,2,4-thiadiazole (90) were determined by AM1 calculations in acetonitrile solvent leading to the twist angles between the thiadiazole ring and the phenyl ring of 7° and 1°, respectively. The AM1 calculations of 31 and 90 revealed the dipole moments of 2.29 and 3.17 debye, respectively, with direction as shown below. This also corresponds to the prediction that the thiadiazole rings would behave as the acceptor group.
Based on the discussions of Maliakal and co-workers\textsuperscript{28} and Maus\textsuperscript{30}, a diagram, shown in Scheme 96, could be constructed to explain the excited state transitions that would lead to the observed large Stokes’ shifts in phenyl substituted-1,2,4-thiadiazoles in acetonitrile.

\textbf{Scheme 96:} Possible energy diagram of phenythiadiazoles in acetonitrile or cyclohexane solvent
According to Scheme 96, after excitation, vibrational relaxation ($V$) of $S_{1(v)n}$ to $S_{1(v)0}$, Franck-Condon excited state, would occur followed by solvent relaxation leading to a solvent reorganized excited state, which has a geometry different from the Franck-Condon excited state. In the case of unsubstituted phenyl-1,2,4-thiadiazole (31 and 46), solvent relaxation of the Franck-Condon excited states to more twisted excited states followed by fluorescence decay would result in the observed moderate Stokes’ shifts. When the $p$-position of the phenyl ring is substituted with an electron donating (compound 90 and 105; $p$-OMe) or electron withdrawing group (compound 98 and 106; $p$-CN), fluorescence emission of these thiadiazoles exhibited large Stoke’ shifts in acetonitrile and the Stokes’ shift magnitudes decreased in cyclohexane solvent. The experimental results also revealed that these thiadiazoles (90, 98, 105 and 106) were not photoreactive in acetonitrile but became more reactive in cyclohexane. Changing polarity of the solvent from cyclohexane to acetonitrile would result in the different lowest energy excited state. As shown in Scheme 96, in acetonitrile solvent the high polar TICT excited state would be stabilized by acetonitrile solvent and, thus, the transition via pathway A’ would be thermodynamically favorable resulting in the TICT state as the lowest energy excited state. The TICT state would not be a photoreactive excited state, therefore, it would return to the ground state mainly via fluorescence or internal conversion relaxation. In cyclohexane solvent, the TICT excited state would become a high energy excited state and, thus, transition via pathway C would be energetically unfavorable. The relaxed $S_{1(v=0)}(\pi,\pi^*)$ would, then, become the lowest excited state. Thus, the relaxed $S_{1(v=0)}(\pi,\pi^*)$ would be the state from which the observed photoproducts originates and the observed fluorescence with the smaller Stokes’ shifts compared with the Stokes’ shifts observed in acetonitrile.
In the quantum mechanic view, a lowest molecular wavefunction of donor-acceptor type excited sate, \([\Psi_{(D-A)^*}]\), would be represented as a linear combination between wavefunctions of each atomic orbital as shown below;

\[
[\Psi_{(D-A)^*}] = a\psi(D^*A) + b\psi(DA^*) + c\psi(D^+A^-) + d\psi(D^-A^+)
\]

The \(\psi(D^*A)\) or \(\psi(DA^*)\) represents the wavefunction of the excited state in which the electron is localized in the D-unit or A-unit, respectively. The charge transfer character of this excited state is represented by \(c\psi(D^+A^-)\) and \(d\psi(D^-A^+)\) wavefunctions. The direction of electron transfer will depend on redox properties between donor and acceptor pair. The magnitudes of the mixing coefficients \(a\), \(b\), \(c\) and \(d\) will determine the lowest energy excited state. In the case of phenyl substituted-1,2,4-thiadiazoles, as previously discussed, the phenyl ring would act as a donor while the thiadiazole ring would be an acceptor. In cyclohexane solvent, the magnitudes of the mixing coefficients \(c\) and \(d\) would be less than the magnitudes of the mixing coefficients \(a\) and \(b\). Thus, in this case, the lowest excited state molecular wavefunctions, \([\Psi_{(D-A)^*}]\), would be viewed as a LCAO of \(a\psi(D^*A) + b\psi(DA^*)\) which would be referred as a locally excited state (LE). The LE state in cyclohexane would be a reactive excited state leading to the observed photochemical reaction of these thia diazoles. In contrast, if the magnitudes of the mixing coefficients \(c\) and \(d\) become larger than the magnitudes of the mixing coefficients \(a\) and \(b\), the \(c\psi(D^+A^-) + d\psi(D^-A^+)\) wavefunctions would be the major contribution in the \([\Psi_{(D-A)^*}]\) leading to a charge transfer character of the excited state. This high polar excited state would be stabilized in acetonitrile solvent leading to the CT excited state as the lowest energy excited state. This CT excited state would be un-reactive and deactivated mainly via radiative and non-radiative decays.
2.12 Triplet Sensitizations

Triplet sensitization of a molecule, IM, can take place if 1) the $S_1$ energy level of IM is higher than the $S_1$ energy level of the sensitizer, 2) the $T_1$ state of the sensitizer is of lower energy than the $T_1$ state of acceptor IM, 3) the energy gap between the $T_1$ state of the sensitizer and the $T_1$ state of IM does not exceed approximately 5-6 kcal/mole in order to have an effective energy transfer, and 4) IM should have no or weak absorption at irradiation wavelengths for excitation of the sensitizer.

2.12.1 Triplet sensitization of 5-phenyl-1,2,4-thiadiazole

The previous spectroscopic studies, presented in the spectroscopic section of this thesis, have shown that energy of the first excited triplet state of 5-phenyl-1,2,4-thiadiazole (31) can be determined from the 0-0 band in the phosphorescence spectrum, recorded in ethanol/methanol glass, to lie 62 kcal/mol above its ground state. Thus, the excited triplet state of 31 could be sensitized by energy transfer from excited triplet states of phenones which have their first excited triplet state energies in the range of 68 - 72 kcal/mol. The
Results and Discussion

The triplet state energy of butyrophenone has been reported at 69 kcal/mol.\textsuperscript{31} Figure 294 shows UV-absorption spectra of butyrophenone in acetonitrile at various concentrations. The spectra reveal an absorption band at $\lambda_{\text{max}}$ of 316 nm at high solute concentration ($2 \times 10^{-2}$ M) due to $S_0 \rightarrow S_1(n,\pi^*)$ absorption transition. Comparison between the butyrophenone absorption spectrum (Figure 294) and the absorption spectrum of 31 (Figure 295) clearly indicates that the $S_1(\pi,\pi^*)$ energy level of 31 is higher than $S_1(n,\pi^*)$ of butyrophenone and that 31 has no absorption in the wavelength region corresponding with $S_0 \rightarrow S_1(n,\pi^*)$ absorption transition of butyrophenone. The black mercury lamps, with light emitting in a range of 325-400 nm, can be employed as light sources. This will allow the excitation energies delivered directly to the sensitizer rather than 31. Moreover, utilization of a Pyrex filter, which has a cut off at $\sim$ 290 nm will also eliminate the possibility of light absorption by 31. Thus, sensitization of the excited triplet state of 31 is expected to occur upon irradiation of a solution in a Pyrex tube containing a mixture of 31 and butyrophenone at excitation wavelengths corresponding with $S_0 \rightarrow S_1(n,\pi^*)$ absorption of butyrophenone.
Results and Discussion

Figure 294: UV-absorption spectra of butyrophenone in acetonitrile at various concentrations

1: $2 \times 10^{-2} \text{ M}$
2: $2 \times 10^{-3} \text{ M}$
3: $2 \times 10^{-4} \text{ M}$

Figure 295: UV-absorption spectrum of 31 in acetonitrile ($2.2 \times 10^{-5} \text{ M}$)
Upon irradiation, butyrophenone is known to undergo a Norrish Type II reaction as the major photochemical reaction. This reaction occurs from the first excited triplet state of butyrophenone as shown in Scheme 97.

\[
\begin{align*}
\text{O} & \xrightarrow{1) \text{hv}} \text{O}^* \xrightarrow{2) \text{ISC}} \text{O} \\
& \text{H-atom transfer} \\
\text{OH} & \rightarrow \text{Product 1} \\
\text{OH} & \rightarrow \text{Product 2}
\end{align*}
\]

Scheme 97: Major photochemical reaction of butyrophenone

Sensitization of 31 was studied in acetonitrile employing butyrophenone as a triplet photosensitizer. The acetonitrile solutions (3.5 mL) of 31 (8×10^{-3} M), butyrophenone (1.6×10^{-1} M), and 31+butyrophenone (8×10^{-3} and 1.6×10^{-1} M) in sealed Pyrex tubes were simultaneously irradiated with sixteen > 325 nm lamps for a total 90 min. The photoreactions were monitored by GLC at 30 and 90 min of irradiation. Figure 296a-b show GLC chromatograms of the butyrophenone solution before and after 90 min of irradiation. Figure 296b reveals 38% consumption of butyrophenone and formation of product 1 and product 2 as two major photoproducts after irradiation.
Figure 296a: GLC analysis of butyrophenone solution (acetonitrile; 1.6×10⁻¹ M) before irradiation

Figure 296b: GLC analysis of butyrophenone solution (acetonitrile; 1.6×10⁻¹ M) after 90 min of irradiation

Figure 297a-b show GLC analysis of the solution of 31 before and after 90 min of irradiation. Figure 4b indicates that no consumption of 31 is observed after 90 min of irradiation at > 325 nm. This confirms that no significant amount of light was absorbed by 31. This is consistent with the observed molar absorptivity of 31 in the UV-absorption spectrum in the region where the lamps emit (Figure 295).
Results and Discussion

Figure 297a: GLC analysis of solution of 31 (acetonitrile; $8 \times 10^{-3}$ M) before irradiation

Figure 297b: GLC analysis of solution of 31 (acetonitrile; $8 \times 10^{-3}$ M) after 90 min of irradiation

Figure 298a-b exhibit GLC chromatograms of the solution mixture of 31+butyrophenone before and after 90 min of irradiation.
**Results and Discussion**

**Figure 298a:** GLC analysis of solution of 31+Butyrophenone (acetonitrile; $8 \times 10^{-3}$ and $1.6 \times 10^{-1}$ M) before irradiation

**Figure 298b:** GLC analysis of solution of 31+Butyrophenone (acetonitrile; $8 \times 10^{-3}$ and $1.6 \times 10^{-1}$ M) after 90 min of irradiation
Results and Discussion

Comparison of the GLC analyses of the butyrophenone photoreaction in the presence (Figure 298b) and absence (Figure 296b) of 31 after 90 min of irradiation shows that both the consumption of butyrophenone and the formation of product 1 and product 2 are quenched by the presence of 31 in the solution. Quantitative analysis (Table 8) reveals only 13.3% consumption of butyrophenone in the presence of 31 while 38.3% consumption of butyrophenone was observed in the absence of 31 after the same period (90 min) of irradiation.

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Butyrophenone reaction</th>
<th>31+Butyrophenone reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BP (% cons)</td>
<td>P1 (peak area)</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30</td>
<td>-14.8 %</td>
<td>62.1</td>
</tr>
<tr>
<td>90</td>
<td>-38.3 %</td>
<td>92</td>
</tr>
</tbody>
</table>

BP = butyrophenone; P1 = Product 1; P2 = Product 2

Table 8: Quantitative analysis of triplet sensitization reaction of 1

Since the first excited triplet state of butyrophenone is the reactive excited state responsible for the consumption of butyrophenone and the formation of product 1 and product 2, these results indicate that the T1 of butyrophenone has been quenched by the presence of 31 in the reaction mixture. This confirms that energy transfer has occurred from the T1 state of butyrophenone to the T1 state of 31. This energy transfer, thus, results in the population of the T1 state of 31 without passing through the S1 state of 31. GLC analysis of this reaction mixture (Figure 298b), however, does not reveal the consumption of 31 or the formation of any of the known photoproducts formed upon direct irradiation of 31. Thus, this result indicates that the first excited triplet state of 31 is not reactive but decays to S0 by radiative and non-radiative pathways. This would also indicate that the reactive excited state
of 31 is the first excited singlet state, which would be responsible for the formation of the phototransposition, photo ring-expansion, and photofragmentation products upon irradiation of 31.

![Scheme 98](image)

**Scheme 98**: Triplet sensitization of 31 by butyrophenone photosensitizer

### 2.12.2 Triplet sensitization of 3-phenyl-1,2,4-thiadiazole

In the case of 3-phenyl-1,2,4-thiadiazole (46), the previous spectroscopic studies have shown that the energy of the first excited triplet state of 46, as determined from the onset of the phosphorescence spectrum recorded in ethanol/methanol glass lies 68 kcal/mole above its ground state, which is very close to $T_1$ of butyrophenone. Comparison between Figure 294 and 299 shows that 46 has no absorption in the $S_0 \rightarrow S_1(n,\pi^*)$ excitation region of butyrophenone. Therefore, butyrophenone can also be used as a triplet photosensitizer to generate excited triplet states of 46.
Sensitization of 46 was studied in acetonitrile employing butyrophenone as a triplet photosensitizer. The acetonitrile solutions (3.5 mL) of 46 (8×10⁻³ M), butyrophenone (1.6×10⁻¹ M), and 46+butyrophenone (8×10⁻³ and 1.6×10⁻¹ M) in sealed Pyrex tubes were simultaneously irradiated with sixteen 350 nm lamps for a total 120 min. The photoreactions were monitored by GLC at 30 and 120 min of irradiation.

Figure 300a-b exhibit GLC analysis of the solution of 46 before and after irradiation. The GC-trace, after 120 min of irradiation (Figure 300b), reveals no consumption of 46. This confirms that 46 did not undergo any photochemical reactions at this irradiation wavelength. This is consistent with the observed molar absorptivity of 46 in its UV-absorption spectrum (Figure 299).
Results and Discussion

**Figure 300a:** GLC analysis of solution of 46 (acetonitrile; $8 \times 10^{-3}$ M) before irradiation

**Figure 300b:** GLC analysis of solution of 46 (acetonitrile; $8 \times 10^{-3}$ M) after 120 min of irradiation

Figure 301a-b shows the GLC analysis of butyrophenone solution before and after 120 min of irradiation. Figure 301b reveals 73.8% consumption of butyrophenone and the formation of **product 1** and **product 2** as the major photoproducts upon irradiation.
Results and Discussion

Figure 301a: GLC analysis of butyrophenone solution (acetonitrile; $1.6 \times 10^{-1}$ M) before irradiation

Figure 301b: GLC analysis of butyrophenone solution (acetonitrile; $1.6 \times 10^{-1}$ M) after 120 min of irradiation

Figure 302a-b show GLC analysis of solution mixture of 46+butyrophenone before and after 120 min of irradiation. Figure 302b shows that 46 had not been consumed and the consumption of butyrophenone and the formation of product 1 and product 2 were quenched during photolysis.
Results and Discussion

Figure 302a: GLC analysis of solution of 46+BP (acetonitrile; 8×10^{-3} and 1.6×10^{-1} M) at T 0 min

Figure 302b: GLC analysis of solution of 46+BP (acetonitrile; 8×10^{-3} and 1.6×10^{-1} M) after 120 min irradiation
Table 9: Quantitative analysis of triplet sensitization reaction of 46

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Butyrophenone reaction</th>
<th>46+Butyrophenone reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BP (% cons) P1 (peak area) P2 (peak area)</td>
<td>BP (% cons) P1 (peak area) P2 (peak area)</td>
</tr>
<tr>
<td>0</td>
<td>0 0 0</td>
<td>0 0 0</td>
</tr>
<tr>
<td>30</td>
<td>-18.3 % 64.1 17.5</td>
<td>-9.3 % 49.1 11.3</td>
</tr>
<tr>
<td>120</td>
<td>-73.8 % 86.3 55.8</td>
<td>-29 % 77.4 34</td>
</tr>
</tbody>
</table>

BP = butyrophenone; P1 = Product 1; P2 = Product 2

Table 9 shows the consumption of butyrophenone decreases from 73.8% in the absence of 46 to 29% in the presence of 46 after 120 min of irradiation. GLC analysis of the mixture shown in Table 9 confirms that the consumption of butyrophenone and formation of product 1 and product 2 had been quenched during irradiation at > 325 nm. This result again confirms that energy transfer from the first excited triplet state of butyrophenone to the T1 state of 46 had occurred. Relaxation of the first excited triplet state of butyrophenone to its ground state via energy transfer to 46 is consistent with the observed decrease in the consumption of butyrophenone and quenching in the formation of product 1 and product 2 in the presence of 46. Benzonitrile (43), the only photoproducing observed upon direct irradiation of 46, was not detected in the mixture after this sensitized irradiation. Thus, this result indicates that the first excited triplet state of 46 is not reactive but it will relax back to the ground state. This also shows that the reactive excited state of 46 is the first excited singlet state, which is responsible for the formation of 43, the observed photofragmentation products upon direct irradiation of 46.
Scheme 99: Triplet sensitization of 46 by butyrophenone photosensitizer
2.13 Photochemistry of phenyl substituted-1,2,4-thiadiazoles in the presence of tri-n-butylphosphine

Hiroshi Kato and colleagues\textsuperscript{35} studied the photochemistry of 4-amino-3-methyl-2,5-diphenylthiazolium picrate (121) in the presence of phosphines. Experimental result showed that irradiation of thiazolium salt 121 in dichloromethane solvent with the presence of tri-n-butylphosphine (127) led to the formation of a mixture of E- and Z-isomers of β-(methylamino)-α-phenylcinnamonic acid (126) in 56% yield. Upon irradiation, this thiazolium salt was expected to undergo electrocyclic ring closure to the formation of the bicyclic intermediate (122).\textsuperscript{35} The formation of 126 was suggested to result from a desulphurization of the bicyclic intermediate 122 with 127 to give an aminoazetium intermediate (123), deprotonation of 123 to a iminodihydroazetene intermediate (124) followed by ring opening could give a imino ketenimine intermediate (125) and finally isomerization of 125 could result in the formation of the observed cinnamonic acid, 126, as shown in Scheme 100.

\textbf{Scheme 100:} Possible pathway for the formation of 126 upon irradiation of 121 in the presence of 127
In the case of 5-phenyl-1,2,4-thiadiazole (31), a photochemically generated 1,3-diaza-5-thiabicyclo[2.1.0]pentene (BC-31) have been suggested as the key intermediate in this photoreaction.

![Scheme 101: BC-1 intermediate – the key intermediate in the photoreaction of 31](image)

By analogy with the results reported by Hiroshi Kato and colleagues, irradiation of 31 in the presence of tri-n-butylphosphine (127) would lead to a desulphurization of the photochemically generated BC-31 which would result in the formation of the phenyldiazacyclobutadiene intermediate (CB). Previous results presented in this thesis have also suggested that phenyldiazacyclobutadiene intermediate (CB) is a precursor for the formation of benzonitrile (43), the photofragmentation product, and phenyl-triazines (39) and (40), the photo-ring expansion products (Scheme 101). Therefore, upon irradiation of 31 in the presence of 127, the photochemically generated BC-31 would be expected to undergo desulphurization with 127 leading to the formation of the CB intermediate. Direct cleavage of the CB intermediate would give benzonitrile (43) or [4+2] cycloaddition self-coupling of CB followed by elimination of nitriles would lead to the formation phenyl-triazines (39) and (40). In this case, the formation of 3-phenyl-1,2,4-thiadiazole (46), the known phototransposition product, was expected to be quenched since this product has been suggested to arise from the BC-1 intermediate. Although, Hiroshi Kato and colleagues did not report an observation on the desulphurization product of tri-n-butylphosphine (90), it
would be possible to assume that desulphurization would transform 127 to tri-n-butylphosphine sulfide (128). Thus, 128 was expected to be observed upon irradiation of 31 in the presence of 127.

In order to explore the photochemistry of phenyl substituted-1,2,4-thiadiazoles in the presence of tri-n-butylphosphine (127), irradiations of 5-phenyl- (31) and 3-phenyl-1,2,4-thiadiazole (46) in acetonitrile containing 127 were carried out. Tri-n-butylphosphine sulfide (128) was also synthesized as an authentic sample.

### 2.13.1 Synthesis of tri-n-butylphosphine sulfide

Tri-n-butylphosphine sulfide (128) is not commercially available. Thus, it was synthesized by a reaction of tri-n-butylphosphine (127) with elemental sulfur in refluxing toluene instead of benzene as described by Samuel and co-workers. The crude tri-n-butylphosphine sulfide (128) was purified by Kugelrohr distillation (0.3 mm Hg; 120°C) to give the desired phosphine sulfide 128 as a colorless viscous liquid. The product was characterized by $^1$H-, $^{13}$C-NMR and mass spectroscopy.

![Scheme 102: Synthesis of tri-n-butylphosphine sulfide](image)
Figure 303a: GC-trace of the viscous liquid product

Figure 303b: Mass spectrum of the viscous liquid product
Figure 303a shows the GC-trace of the viscous colorless liquid revealing the presence of one gc-volatile component eluting with a retention time of 26.8 min. The mass spectrum of this component (Figure 303b) exhibits a molecular ion peak at m/z 234 and a base peak at m/z 122. The molecular ion at m/z 234 is consistent with a molecular formula of C_{12}H_{27}PS which corresponds to a molecular weight of the desired phosphine sulfide 128 (MW 234). The peak at m/z 178 and the base peak at m/z 122 correspond to the cleavage of one and two [C_{4}H_{8}] fragments from the molecular ion, respectively. These cleavages would involve a McLafferty rearrangement followed by elimination of [CH3] fragment. The first cleavage gives a peak at m/z 178 and the second cleavage gives the base peak at m/z 122 as shown in Scheme 103. The molecular ion and fragmentation pattern of this product are consistent with the structure of tri-n-butylphosphine sulfide (128).

Scheme 103: Possible fragmentation pathway of tri-n-butylphosphine sulfide
Figure 304: $^1$H-NMR spectrum of the viscous colorless liquid

Figure 304 shows the $^1$H-NMR spectrum of the viscous colorless liquid corresponding with the structure of 128 reported in the literature.$^{37}$ The spectrum shows a 3H triplet at $\delta$ 0.94 (J = 7.58 Hz) due to absorption of the methyl protons. The $\gamma$-protons appears at $\delta$ 1.43 as a septet (2H; J = 7.33 Hz). The two multiplets at $\delta$ 1.51-1.61 (2H) and 1.77-1.84 (2H) were assigned to the $\beta$- and $\alpha$-protons, respectively. This assignment is consistent with integration of each multiplet due to absorption of two protons. The $\gamma$-proton appears as a mutiplet due to a coupling with the $\beta$-protons and with $^{31}$P.$^{37}$
Figure 305a: $^{13}$C-NMR spectrum of the viscous colorless liquid

Figure 305a shows the $^{13}$C-NMR spectrum of the viscous colorless liquid revealing the $^{13}$C-absorptions of this compound in the region of $\delta$ 13.9-31.2. The scale expansion within this region, shown in Figure 305b, shows the methyl carbon at $\delta$ 14.1 as a singlet. The scale expansion spectrum, however, reveals the $\alpha$-, $\beta$- and $\gamma$-carbons as three doublets due to couplings between $^{13}$C and $^{31}$P at $\delta$ 30.9 ($J_{^{13}C^{31}P} = 50.1$ Hz), 24.8 ($J_{^{13}C^{31}P} = 3.8$ Hz) and 24.4 ($J_{^{13}C^{31}P} = 16.1$ Hz), respectively.
Figure 305b: $^{13}$C-NMR spectrum of the viscous colorless liquid; scale expansion

This assignment is consistent with the $^{13}$C-DEPT 135 spectrum, shown in Figure 305c. The three doublets at δ 30.9, 24.8 and 24.4 which were assigned to absorptions of secondary carbons of the α-, β- and γ-carbons appears in the negative directions in the $^{13}$C-DEPT 135 spectrum. The singlet at δ 14.1 is present in the positive direction in the $^{13}$C-DEPT 135 spectrum which corresponds to the assignment to the methyl carbons.
Results and Discussion

2.13.2 Photochemistry of 5-phenyl-1,2,4-thiadiazole in the presence of tri-n-butylphosphine

Solution of 5-phenyl-1,2,4-thiadiazole (31) in acetonitrile (2×10⁻² M, 3.5 mL) + 40 µL of neat tri-n-butylphosphine (127) in a sealed Pyrex tube was purged with argon gas for 15 min. The resulting solution was analyzed by the GC interfaced with a mass spectrometer.
Results and Discussion

Figure 306: GC-trace of $31+127$ mixture in acetonitrile before irradiation

The GC-trace of the mixture of $31+127$ before irradiation (Figure 306) shows the presence of two major component eluting with retention times of 12.3 and 22.5 min. The mass spectra of these two components exhibited molecular ion peaks at m/z 202 and m/z 162, respectively. The component which had a molecular ion at m/z 202 corresponded to 127 while the component which had a molecular ion at m/z 162 was due to the reactant, 31.

Since 127 has also been reported as a desulphurizing agent$^{39}$, it is possible that the formation of 128 could result from a thermal reaction of 31 with 127. In order to clarify this ambiguity, a mixture of 31 ($2\times10^{-2}$ M) + 127 (40 µL) in acetonitrile in a sealed Pyrex tube was allowed to stand at room temperature in the dark for three hours and at 80°C in a water bath in the dark for three hours. The resulting solution was analyzed by the GC interfaced with a mass spectrometer. The GC-analysis of the solution before and after heating in the dark clearly showed no consumption of both 31 and 127. The GC-trace did also not show an increase of the component that has a molecular ion at m/z 234 nor the formation of any new product. Thus, this confirms that 31 and 127 did not undergo a thermal reaction that would lead to the formation of 128.
Results and Discussion

However, 31 could also be assumed to have an interaction with tri-n-butylphosphine (127) in the ground state resulting in the formation of a 31--127 ground state complex, which would be envisioned in Scheme 104. In this case, irradiation of a mixture of 31+127 would give an excited state complex, [31--127]*, desulphurization of this excited state complex would give 128 and a fragmentation product(s). Since the BC-31 intermediate (Scheme 101) is suggested to result from excitation of 31, desulphurization of the excited state complex, [31--127]*, would lead to the quenching of all known photoproducts upon irradiation of 31 as shown in Scheme 104.

![Scheme 104: A possible ground state interaction between 31 and 127](image)

In order to investigate this assumption, a UV-absorption spectrum of a mixture of 31+127 in acetonitrile solvent was recorded. If 31 had an interaction with 127 in the ground state, the UV-absorption spectrum of 31 in the presence of 127 would be different from the UV-absorption 31 in an absence of 127.
Results and Discussion

Figure 307: UV-absorption spectrum of 31 in acetonitrile (6.4 × 10⁻⁵ M)

Figure 307 shows a broad absorption band of 5-phenyl-1,2,4-thiadiazole (31) in acetonitrile with a maximum absorption at λ_max of 274 nm. Figure 308 shows a UV-absorption spectrum of tri-n-butylphosphine (127) in acetonitrile solvent (4 × 10⁻³ M). The spectrum shows no absorption from 700-250 nm and strong absorption with OD > 1 form 250-200 nm. Figure 309 shows the UV-absorption spectrum of 31+127 mixture in acetonitrile solvent revealing a broad absorption band with a maximum absorption at 274 nm (OD 0.48) and strong absorption with OD > 1 from 250-200 nm. Figure 5 reveals the UV-absorption spectrum of 1+70 mixture as a combination between individual absorption spectrum of each compound (Figure 307 and 308) indicating that the UV-absorption spectrum of 31 in the presence of 127 did not change compared with the UV-absorption spectrum of 31 in the absence of 127 (Figure 307).
Results and Discussion

Figure 308: UV-absorption spectrum of 127 in acetonitrile (4×10⁻³ M)

Figure 309: UV-absorption spectrum of a mixture of 31+127 in acetonitrile
This result suggests that 31 has no interaction with 127 in the ground state. This UV-absorption of 31+127 mixture also corresponds to the result observed from the analysis of mixture of 31+127 upon heating in the dark confirming that 31 did not undergo any thermal reaction or forming any ground state complex with 127.

The mixture of 31+127 (2×10^{-2} M + 40 \mu L) was irradiated with sixteen > 290 nm lamps for a total of 180 min. The irradiated solution was analyzed by the GC interfaced with a mass spectrometer.

**Figure 310a:** GC-trace of 31+127 mixture after 180 min of irradiation

Figure 310a shows the GC-trace of the 31+127 mixture after 180 min of irradiation. The trace reveals the consumption of 31 and 127 and the increase of the component that eluted with a retention time of 26.7 min. Figure 310b shows the mass spectrum of the component with RT of 26.7 min revealing a molecular ion peak at m/z 234 and a base peak at m/z 122. Comparison of gc-retention times and mass spectral fragmentation pattern of this product with those of an authentic sample of 128 (Figure 303b) confirming that this product was tri-n-butylphosphine sulfide (128).
It should be noted that the GC-analysis of the mixture after irradiation, shown in Figure 310a, did not show the formation of the known photoproducts which have been observed upon irradiation of 31. Quantitative analysis of the photoreaction of 31 in the presence of 127 was performed on a PE-9000 gas chromatograph. All formation yields were determined relative to the consumption of 31. The result showed 75 % consumption of 31 and 33.1 % consumption of 127 and the formation of 128 in 55 %. The analysis also showed the formation of benzonitrile (43), 3-phenyl-1,2,4-thiadiazole (46), 2-phenyl-1,3,5-triazine (39) and 2,4-diphenyl-1,3,5-triazine (40) in 3.5 %, trace, 1.3 % and 1.8 %, respectively. Comparison of a quantitative analysis of photolysis of 31 in an absence of 127 with this result clearly showed that all known photoproducts observed after photolysis of 31 in the presence of 127 were quenched. The previous results from the irradiation of 31
have suggested that a photochemically generated 1,3-diaza-5-thiabicyclo[2.1.0]pentene (BC-31) is the key intermediate in this photoreaction (Scheme 101). Thus, the observed quenching of all photoproducts suggest that the quencher may be reacting with 1,3-diaza-5-thiabicyclo[2.1.0]pentene (BC-31) which is a precursor of these products.

If 127 did react with BC-31, it would lead to the formation of 128 and phenyldiazacyclobutadiene (CB). According to Scheme 101, phenyldiazacyclobutadiene (CB) is a precursor for the formation of benzonitrile (43) and the triazines 39 and 40. Thus, photolysis of 1 in the presence of 90 would reveal a profound quenching effect on the yield of 3-phenyl-1,2,4-thiadiazole (46) but not benzonitrile (43), 2-phenyl-1,3,5-triazine (39) and 2,4-diphenyl-1,3,5-triazine (40). Quantitative analysis of the photolysate of 31+127 mixture after 180 min showed that 43, 39 and 40 were approximately 50% quenched while 46, the transposition product, was approximately 90% quenched. A possible explanation to this observation would be that 127 would not only react with BC-31 but also react with the excited state of 31. Desulphurization of BC-31 would lead to a complete quenching of the transposition product, 4, but not to the formation of 50, 51 and 52 while reaction between the excited state of 31 with 127 would lead to quenching of all photoproducts. Tri-n-butylphosphine (127) is a powerful nucleophile but is not strongly basic. It can also act as a good reducing agent. Therefore, it would be possible that upon excitation of 31 in the presence of 127, an electron transfer from the ground state of 127 to the excited state of 31 would occur leading to desulfurization of the excited state of 31 to give 128 and ring fragmentation. If this electron transfer process occurred, upon excitation of a mixture of 31+127 it would result in a quenching of fluorescence emission of the excited state of 31. However, 31 exhibited a weak fluorescence emission intensity in acetonitrile. Therefore, 5-(4′-methoxy)phenyl-1,2,4-thiadiazole (90) was employed as a model compound instead of 1 in the fluorescence quenching study in the presence of 127 since 90 exhibited a
strong fluorescence emission with maximum emission at wavelength of 369 nm in acetonitrile. Photochemistry of 90 in the presence of 127 was also studied in the GC-scale.

2.13.3 Photochemistry of 5-(4'-methoxy)phenyl-1,2,4-thiadiazole in the presence of tri-n-butylphosphine

Irradiation of 90 in acetonitrile containing 127 was first studied in the GC-scale. Solution of 90 in acetonitrile (2×10^{-2} M, 3.5 mL) + 40 µL of neat tri-n-butylphosphine (127) in a sealed Pyrex tube was purged with argon gas for 15 min and irradiated with sixteen > 290 nm lamps for a total of 180 min. The photolysate was analyzed by the GLC.

Figure 311: GC-trace of 90+127 mixture before irradiation
The GC-chromatogram of the 90+127 mixture before irradiation (Figure 311) reveals the presence of two components eluting with retention times of 5.7 and 21 min. The two major components eluting with retention times of 5.7 and 21 min were due to 127 and 90, respectively.

After 180 min of irradiation, the trace (Figure 312) reveals the formation of new product with retention time of 20.4 min and consumptions of the reactant, 90. The trace also reveals the formation of a trace quantity of 4-methoxybenzonitrile (104), which eluted with a retention time of 8.4 min. The new product was identified to be 128 by comparison gc-retention time with an authentic sample of 128. Quantitative analysis of the photolysis of 90 in the presence of 127 after 180 min of irradiation showed 49% consumption of the reactant, 90 and 4% consumption of 127 while the reactant 90 was 15% consumed in the reaction without 127. The analysis also showed 14% formation of 128. All formation yields were determined relative to the consumption of 90. This result shows that the presence of 127 enhances the consumption of 90 approximately three-fold greater than the consumption of 90 observed in an absence of 127 while the formation of 104 was quenched in the reaction.
containing 127. In this case, if 127 did react with only the corresponding BC intermediate, the result should not show quenching of 4-methoxybenzonitrile (104) and (4′-methoxy)phrenyltriazines (94) and (95) formations. However, the formation of 104 in the photoreaction of 90 containing 127 was observed in trace quantity and no other new gc-volatile product was observed beside 128. This result would again suggest that upon irradiation of 90 in the presence of 127, 127 would possibly react with both the excited state of 90 and the corresponding BC intermediate. The reaction of 127 with the excited state of 90 would lead to the quenching of all photoproducts while the reaction of 127 with the BC intermediate would quench the formation of the phototransposition product but not the photofragmentation and photo-ring expansion products.

Fluorescence quenching of 90 in the presence of 127 was further studied. Fluorescence emission of 90 in acetonitrile solutions (1.6×10^{-2} M) containing various concentrations of 127 (1.1×10^{-2} – 2.4×10^{-2} M) were recorded.

![Figure 313: Fluorescence quenching of the excited state of 90 by 127](image-url)
Figure 313 shows a plot that reveals the effect of increasing concentration of 127 on the fluorescence of 90 in the absence of 127 divided by the fluorescence of 90 observed at the various concentrations of 127. This plot shows a linear decrease in fluorescence of 90 with increasing concentrations of 127. This indicates that 127 quenches the fluorescence of 90. This observed fluorescence quenching at various concentrations of 127 would support an assumption that photo-induced electron transfer from the ground state of 127 to the excited state of 90 has occurred during photolysis.

In order to confirm this result, thermodynamic feasibility of this electron transfer process was considered. Cyclic voltametry measurement of 90, presented in the previous section, has revealed an irreversible reductive process of 90 with a reduction potential of -2.13 V. Redox potential of 127 was attempted to determine by a cyclic voltametry under the similar condition as carried out for 90. (0.1 M; acetonitrile, employing 0.1 M tetrabutylammonium bromide as a supporting electrolyte). In the case of 127, applying voltages in both positive and negative directions did not result in any reductive or oxidative curves. This would suggest that 127 decomposed during the measurement which may be the reason why the redox potential of 127 cannot be found in the literature.

Although, thermodynamic feasibility of the electron transfer process between 90 and 127 could not be determined due to the lack of information on redox potential of 127, it could, however, be assumed that the observed fluorescence quenching of 90 in the presence of 127 was probably due to an electron transfer from the ground state of 127 to the excited state of 90. This electron transfer process would result in the formation of 128 and the thiadiazole ring cleavage followed by polymerization of the resulting species leading to formation of non-ge-volatile products which could not be detected by a gas-liquid chromatography analysis.
2.13.4 Photochemistry of 3-phenyl-1,2,4-thiadiazole in the presence of tri-n-butylphosphine

The photochemistry of 3-phenyl-1,2,4-thiadiazole (46) in the presence of tri-n-butylphosphine (127) was also studied. Previous results carried out in this laboratory on photochemistry of 3-phenyl-1,2,4-thiadiazole-2-15N (46-2-15N) have shown that excitation of this thiadiazole does not lead to the formation of the bicyclic intermediate but exclusively result in the formation of only benzonitrile-15N (43-15N). Previous result on irradiation of 5-phenyl-1,2,4-thiadiazole (31) in the presence of tri-n-butylphosphine (127) has suggested that 127 reacted with both the bicyclic intermediate and the excited state of 31. In the case of irradiation of 46, the formation of benzonitrile is suggested to arise from direct fragmentation of the excited thiadiazole, therefore, it would be expected that irradiation of a mixture of 46+127 would result in the quenching of benzonitrile formation which would be due to the reaction between the ground state of 127 with the excited state of 46. Tri-n-butylphosphine sulfide (128) was also expected to observe in the photoreaction of 46 containing 127.

Solution of 3-phenyl-1,2,4-thiadiazole (46) in acetonitrile (2.1×10^{-2} M, 3.5 mL) with additional of 40 µL of 127 in sealed Pyrex tubes was purged with argon gas for 15 min and irradiated with sixteen > 290 nm lamps for 120 minutes. The irradiated solution was analyzed by the GC interfaced with a mass spectrometer.

The GC-trace of 46+127 mixture before irradiation (Figure 314) shows two components eluting with retention times of 12 and 24 min. The mass spectra of the two components exhibited molecular ion peaks at m/z 202 and 162 which corresponded to 127 and 46, respectively.
In order to investigate the possibility that 46 might undergo a thermal reaction with 127 to yield 128, a mixture of 46+127 in acetonitrile solvent in a sealed Pyrex tube in the dark was heated at 80°C in a water bath. After three hours of heating, the mixture was analyzed by the GC interfaced with a mass spectrometer. The GC-trace showed no consumption of either 46 or 127. The trace did also not show any new product formation. This result confirmed that no thermal reaction between 46 and 127 was observed.

**Figure 314:** GC-trace of a mixture of 46+127 before irradiation

Figure 315a shows the GC-trace of mixture of 46+127 after 120 min of irradiation. The trace shows the major component eluting with a retention time of 26.7 min. Figure 315b shows the mass spectrum of this component revealing a molecular ion peak at m/z 234 and a base peak at m/z 122. This component was identified as 128 by comparison its fragmentation pattern and gc-retention time with those of an authentic sample of 128. Comparison between Figure 314 and 315 clearly reveals an increase of the component at RT of 26.7. The trace also shows four minor components eluting with retention times of 9, 12 and 24 min. The mass spectra of the component with RTs of 9 and 12 min revealed molecular ion peaks at m/z 103 and m/z 202. The component that had a molecular ion at m/z 103 was identified as benzonitrile (43), the known photofragmentation product in the photoreaction of 46. The component that had a molecular ion at m/z 202 was due to the
unconsumed 127. The component eluting with a retention time of 24 min had a molecular ion at m/z 162 corresponding with the unconsumed reactant, 46.

**Figure 315a:** GC-trace of a mixture of 46+127 after 120 min of irradiation

**Figure 315b:** Mass spectrum of the component at RT of 26.7 min
Quantitative analysis of the photolysis of the \(46+127\) mixture was performed on the GC-PE9000 gas chromatograph. After 120 min of irradiation, the result showed 80% consumption of \(46\) in the reaction containing \(127\) and 50% consumption in the reaction without \(127\). The formation of \(128\) was observed at 71% after this irradiation period. The formation of benzonitrile (43) was observed in the photoreaction with the presence and absence of \(127\) at 51% and 76%, respectively. This result indicates that the presence of \(127\) in this reaction quenches the formation of 43 and no new gc-volatile product was observed. The observed quenching of the formation of 43 in this case was also expected to occur via an electron transfer process from the ground state of \(127\) to the excited state of \(46\) leading to the thiazole ring cleavage followed by polymerization of the resulting species to yield a non-gc-volatile material(s).
2.14 Photochemistry of phenyl substituted-1,2,4-thiadiazoles in the presence of triethylamine or propylamine

Spectroscopic data of phenyl substituted-1,2,4-thiadiazoles presented in this thesis have revealed that introduction of electron donating or withdrawing groups on the phenyl or thiadiazole ring enhances the formation of charge transfer excited states of these compounds and, thus, fluorescence emission becomes an effective deactivation process. This also implies that the thiadiazole ring behaves as an electron acceptor group. The previous results on the photochemistry of 5-phenyl- (31), 5-(4′-methoxy)phenyl- (90) and 3-phenyl-1,2,4-thiadiazole (46) in the presence of tri-n-butylphosphine (127) indicated that an electron transfer occurs from the ground state of 127 to the excited states of the thiadiazoles. Therefore, it was of interest to explore the nature of the electron transfer process. In this thesis, sensitization by photoinduced electron transfer from ground state electron donors (triethylamine; TEA or propylamine; PA) to excited states of the 5- or 3-phenyl-1,2,4-thiadiazole (31 or 46) has been studied.

Reduction potentials of some phenyl-1,2,4-thiadiazoles were obtained from their cyclic voltagrams (Figure 316-319). These cyclic voltametries were performed in acetonitrile employing 0.1 M tetrabutylammonium bromide as a supporting electrolyte. Three glass cells, equipped with a graphite disk working electrode, platinum counter electrode, and saturated calomel electrode (SCE) as a reference electrode, were employed in this measurement.
Figure 316: Cyclic voltametry of 31 in acetonitrile

Figure 316 shows the cyclic voltogram of 5-phenyl-1,2,4-thiadiazole (31) (0.1 M; acetonitrile). This cyclic voltogram reveals that electrochemical reduction of 1 is a reversible process. The reduction potential can be determined from the half wave potential at -1.86 V.

Figure 317: Cyclic voltametry of 46 in acetonitrile

Figure 317 exhibits cyclic voltogram of 3-phenyl-1,2,4-thiadiazole (46) (0.1 M; acetonitrile) revealing two reductive signals at -2.06 and -2.22 V. Figure 317 also indicates that electrochemical reduction of 46 is an irreversible process.
Figure 318: Cyclic voltametry of 2 in acetonitrile

Figure 318 exhibits cyclic voltogram of 5-(4′-methoxy)phenyl-1,2,4-thiadiazole (90) (0.1 M; acetonitrile) revealing an irreversible reductive process with a reduction potential of -2.13 V. This cyclic voltogram also reveals that substitution of a methoxy group at the para-position of the phenyl ring increases the reduction potential of this thiadiazole relative to the unsubstituted compound. This indicates that there is more intramolecular charge transfer character in the ground state of 90 compared with 31 leading to the higher energy required for a reductive process in 90.

Figure 319: Cyclic voltametry of 47 in acetonitrile
Figure 319 shows the cyclic voltagram of diphenyl-1,2,4-thiadiazole (47) (0.1 M; acetonitrile) revealing a reversible electrochemical reductive process. The reduction potential can be determined from the half wave potential at -1.83 V. This cyclic voltagram also reveals that the electrochemical behavior of 47 is more similar to 31 than 46.

**Table 10:** Reduction potentials and $E_{00}$ (eV) of some phenyl-1,2,4-thiadiazoles in acetonitrile

<table>
<thead>
<tr>
<th>Compounds</th>
<th>$E_{\text{red}}$ (V; SCE)</th>
<th>$E_{00}$ (eV)</th>
<th>$E_s$ (kcal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>31</td>
<td>-1.86</td>
<td>3.99</td>
<td>92</td>
</tr>
<tr>
<td>90</td>
<td>-2.13</td>
<td>3.77</td>
<td>87</td>
</tr>
<tr>
<td>47</td>
<td>-1.83</td>
<td>4.07</td>
<td>94</td>
</tr>
<tr>
<td>46</td>
<td>-2.06 &amp; -2.22</td>
<td>4.21</td>
<td>97</td>
</tr>
</tbody>
</table>

The feasibility of photoinduced electron transfer between a ground state donor to an excited state acceptor is dictated by the overall change in free energy, $\Delta G$, which accompanies the reaction. The condition of exothermicity, $\Delta G < 0$, is a major requirement for an electron transfer process (eq 1).  

$$
\Delta G \text{ (kcal/mol)} = 23.06 \left[ E_{\text{ox}} - E_{\text{red}}^* \right] - wp 
$$  

$$
E_{\text{red}}^* = E_{\text{red}} + E_{00} 
$$

$$
w_p = \text{Coulombic work} \\
Z_{D^+} \text{ and } Z_{A^-} = \text{charges on the molecules} \\
d_{cc} = \text{center to center distance between the two ions} \\
\varepsilon_s = \text{dielectric constant of the solvent}
$$

$$
w_p = \frac{332(Z_{D^+} Z_{A^-})}{d_{cc} \varepsilon_s} 
$$
In general cases where $Z_{D+} = +1$ and $Z_{A-} = -1$ and $d_{cc} \sim 7 \text{ Å}$ in acetonitrile ($\varepsilon_s = 37$), the result of $w_p$ from eq. 2 is approximately -1.3 kcal/mole. Thus, in these cases, the coulombic work may be disregarded when considering the thermodynamic feasibility of these electron transfer processes.

Scheme 105 shows the thermodynamic feasibility of electron transfer between TEA and some phenyl-1,2,4-thiadiazoles. This scheme reveals that electron transfer from TEA (donor) to each excited thiadiazoles (acceptor) is energetically feasible.

![Diagram of electron transfer](attachment:diagram.png)

**TEA**: $E_{ox} = 0.76 \text{ V vs SCE}$

31; $E_{red} = -1.92 \text{ V vs SCE}$; $E_{00} = 3.99 \text{ eV}$

46; $E_{red} = -2.02 \text{ V vs SCE}$; $E_{00} = 4.21 \text{ eV}$

90; $E_{red} = -2.13 \text{ V vs SCE}$; $E_{00} = 3.77 \text{ eV}$

47; $E_{red} = -1.83 \text{ V vs SCE}$; $E_{00} = 4.07 \text{ eV}$

Electron transfer in 31

\[ \Delta G (\text{kcal/mol}) = 23.06 \left[ E_{ox} - E_{red}^* - E_{00} \right] \]

\[ = 23.06 \left[ 0.76 \text{ V} - (-1.94 \text{ V}) - 3.99 \text{ eV} \right] \]

\[ = -1.29 \text{ V} \times 23.06 \text{ kcal/eV} \]

\[ = -29.75 \text{ kcal/mol} \] feasible process

Electron transfer in 46

\[ \Delta G (\text{kcal/mol}) = 23.06 \left[ E_{ox} - E_{red}^* - E_{00} \right] \]

\[ = 23.06 \left[ 0.76 \text{ V} - (-2.02 \text{ V}) - 4.21 \text{ eV} \right] \]

\[ = -1.43 \text{ V} \times 23.06 \text{ kcal/eV} \]

\[ = -32.97 \text{ kcal/mol} \] feasible process
Electron transfer in 90

\[ \Delta G (\text{kcal/mol}) = 23.06 \left[ E_{\text{ox}} - E_{\text{red}}^* - E_{\text{00}} \right] \]
\[ = 23.06 \left[ 0.76 \text{ V} - (-2.13 \text{ V}) - 3.77 \text{ eV} \right] \]
\[ = - 0.88 \text{ V} \times 23.06 \text{ kcal/eV} \]
\[ = - 20.3 \text{ kcal/mol} \] feasible process

Electron transfer in 47

\[ \Delta G (\text{kcal/mol}) = 23.06 \left[ E_{\text{ox}} - E_{\text{red}}^* - E_{\text{00}} \right] \]
\[ = 23.06 \left[ 0.76 \text{ V} - (-1.83 \text{ V}) - 4.07 \text{ eV} \right] \]
\[ = - 1.48 \text{ V} \times 23.06 \text{ kcal/eV} \]
\[ = - 34.13 \text{ kcal/mol} \] feasible process

Scheme 105: Thermodynamic feasibilities of electron transfer between TEA and some thiadiazoles

The redox potential of n-propylamine (PA) is not available in the literatures. However, the redox potentials of n-butylamine and isopropylamine have been reported at 1.88 V and 1.89 V, respectively, Vs SCE in acetonitrile.\textsuperscript{34} Based on this information, the oxidation potential of n-propylamine (PA) could, therefore, be estimated at approximately 1.88 V. Scheme 106 shows the thermodynamic feasibility consideration of electron transfer between PA and some phenyl-1,2,4-thiadiazoles. This scheme reveals that electron transfer from PA (donor) to each excited thiadiazoles (acceptor) is energetically feasible except for 5-(4′-methoxy)phenyl-1,2,4-thiadiazole (90).
Results and Discussion

\[ \text{TD} \xrightarrow{\text{hv}} \text{TD}^* \xrightarrow{\text{PA}^*} \text{PA}^* + \text{TD}^- \]

**Scheme 106:** Thermodynamic feasibilities of electron transfer between PA and some thiadiazoles

**PA:**
- \( E_{\text{ox}} = 1.88 \text{ V} \) vs SCE,
- \( E_{\text{red}} = -1.92 \text{ V} \) vs SCE; \( E_{00} = 3.99 \text{ eV} \)
- \( E_{\text{red}} = -2.02 \text{ V} \) vs SCE; \( E_{00} = 4.21 \text{ eV} \)
- \( E_{\text{red}} = -2.13 \text{ V} \) vs SCE; \( E_{00} = 3.77 \text{ eV} \)
- \( E_{\text{red}} = -1.83 \text{ V} \) vs SCE; \( E_{00} = 4.07 \text{ eV} \)

**Electron transfer in 31**

\[ \Delta G \text{ (kcal/mol)} = 23.06 \left[ E_{\text{ox}} - E_{\text{red}}^* - E_{00} \right] \]
\[ = 23.06 \left[ 1.88 \text{ V} - (-1.94 \text{ V}) - 3.99 \text{ eV} \right] \]
\[ = -0.17 \text{ V} \times 23.06 \text{ kcal/eV} \]
\[ = -3.92 \text{ kcal/mol} \quad \text{feasible process} \]

**Electron transfer in 46**

\[ \Delta G \text{ (kcal/mol)} = 23.06 \left[ E_{\text{ox}} - E_{\text{red}}^* - E_{00} \right] \]
\[ = 23.06 \left[ 1.88 \text{ V} - (-2.02 \text{ V}) - 4.21 \text{ eV} \right] \]
\[ = -0.31 \text{ V} \times 23.06 \text{ kcal/eV} \]
\[ = -7.15 \text{ kcal/mol} \quad \text{feasible process} \]

**Electron transfer in 90**

\[ \Delta G \text{ (kcal/mol)} = 23.06 \left[ E_{\text{ox}} - E_{\text{red}}^* - E_{00} \right] \]
\[ = 23.06 \left[ 1.88 \text{ V} - (-2.13 \text{ V}) - 3.77 \text{ eV} \right] \]
\[ = 0.24 \text{ V} \times 23.06 \text{ kcal/eV} \]
\[ = 5.53 \text{ kcal/mol} \quad \text{not feasible process} \]

**Electron transfer in 47**

\[ \Delta G \text{ (kcal/mol)} = 23.06 \left[ E_{\text{ox}} - E_{\text{red}}^* - E_{00} \right] \]
\[ = 23.06 \left[ 1.88 \text{ V} - (-1.83 \text{ V}) - 4.07 \text{ eV} \right] \]
\[ = -0.06 \text{ V} \times 23.06 \text{ kcal/eV} \]
\[ = -1.38 \text{ kcal/mol} \quad \text{feasible process} \]
2.14.1 Irradiation of 5-phenyl-1,2,4-thiadiazole in the presence of triethylamine or propylamine

Solutions of 5-phenyl-1,2,4-thiadiazoles (31) (0.01 M), 1+TEA (0.01 M + 0.4 M), and 31+PA (0.01 M + 0.4 M) in acetonitrile solvent in sealed Pyrex tubes were purged with argon gas for 15 min and simultaneously irradiated with sixteen >290 nm lamps in a Rayonet photochemical reactor. These solutions were irradiated for a total of 120 min and analyzed by GLC. After irradiation, the solution of 31 without amines still remained clear colorless while the 31+TEA mixture became brown yellow. The 31+PA mixture became green with the formation of white precipitate. The green color of the 31+PA mixture vanished upon sitting at room temperature in the dark and the solutions became colorless.

GC-trace of the mixture of 31+TEA in acetonitrile before irradiation showed the presence of only one component eluting with a retention time of 13 min which was due to the reactant, 31. This showed that no ground state reaction between 31 and TEA was observed. Figure 320 shows the GC-chromatogram of this mixture after 30 min of irradiation. The trace reveals 28% consumption of 31 and the formation of trace quantities of the known photoproducts after irradiation.
Results and Discussion

Figure 320: GC-trace of the Solution 31+TEA after 30 min of irradiation

Figure 321: GC-trace of Solution 31+PA after 30 min of irradiation
The GC-chromatogram of a mixture of 31+PA before irradiation showed only one component eluting with a retention time of 13 min which was due to the reactant, 31. This also indicated that no ground state reaction between 31 and PA was observed. Figure 321 shows the GLC analysis of 31+PA mixture after 30 min of irradiation revealing 46.5% consumption of 1 and the formation of benzonitrile (43) as the only one major product.

Table 11 reveals the quantitative analysis of the photoreaction of 5-phenyl-1,2,4-thiadiazole (31) in acetonitrile containing TEA or PA. Table 11 shows 18% and 28% consumptions of 31 in the reaction without amines and in the reaction containing TEA (31+TEA) respectively, after 30 min of irradiation. The known photoproducts formed in these two reactions were also observed in trace quantities. These results show that the presence of triethylamine (TEA) does not greatly affect the photochemistry of 31. In contrast, Table 11 shows 47% consumption of 31 after 30 min of irradiation in the reaction containing PA (31+PA), which is approximately two-fold greater than the consumption of 31 observed in absence of amines, and 10% formation of benzonitrile (43) which is approximately ten-fold greater than the formation of 43 observed in the reaction without amines and the reaction with the presence of TEA (31+TEA). Table 11 also shows that the presence of propylamine (31+PA) leads to the quenching of phototransposition and photoring expansion product formations in this reaction. This indicates that propylamine (PA) has a greater effect on the photochemistry of 31 than triethylamine (TEA).
Table 11: Quantitative analysis of the photoreaction of 31 in AcCN with the presence of TEA or PA

<table>
<thead>
<tr>
<th></th>
<th>Time</th>
<th>31</th>
<th>46</th>
<th>43</th>
</tr>
</thead>
<tbody>
<tr>
<td>31 in AcCN</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>-18%</td>
<td>trace</td>
<td>1%</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>-70%</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>31+TEA in AcCN</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>-28%</td>
<td>trace</td>
<td>1%</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>-70%</td>
<td>1%</td>
<td>3%</td>
</tr>
<tr>
<td>31+PA in AcCN</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
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<td></td>
<td>30</td>
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<td>0</td>
<td>10%</td>
</tr>
<tr>
<td></td>
<td>120</td>
<td>-93%</td>
<td>trace</td>
<td>18%</td>
</tr>
</tbody>
</table>

Solutions of 31 (0.01 M), 31+TEA (0.01 M + 0.4 M), 31+TEA, and 31+PA (0.01 M + 0.4 M) in methanol solvent in sealed Pyrex tubes were purged with argon gas for 15 min and simultaneously irradiated with sixteen > 290 nm lamps in a Rayonet photochemical reactor. These solutions were irradiated for a total of 120 min and analyzed by GLC. After photolysis, all solutions became clear yellow, no precipitate was observed in the solutions containing propylamine (PA) as was observed after photolysis in acetonitrile solvent.

The GC trace of the photolysate of 31+TEA in methanol (Figure 322) shows 25% consumption of 31 after 30 min of irradiation and the formation of trace quantities of benzonitrile (43) and 3-phenyl-1,2,4-thiadiazole (46) which eluted with retentions of 7.4 and 13.5 min, respectively.
Figure 323 shows GLC analysis of the photolysate of $31+PA$ in methanol solvent after 30 min of irradiation. The trace shows 33% consumption of $31$ and the formation of benzonitile ($43$) as the only major photoprodut.

**Figure 322**: GC-trace of the $31+TEA$ mixture after 30 min of irradiation

**Figure 323**: GC-trace of $31+PA$ mixture after 30 min of irradiation
Table 12 shows quantitative analysis of irradiation of 31 in the presence of TEA or PA in methanol and acetonitrile solvent. Table 12 reveals that the presence of TEA in the photoreaction of 31 in acetonitrile or methanol solvent leads to the consumption of 31 approximately in the same quantities after 30 min of irradiation. The formations of 46 and 43 were quenched in both solvents after the period of irradiation but formation of 46 was, however, less effectively quenched in methanol than in acetonitrile. After photolysis of 31+PA mixture in acetonitrile for 30 min, Table 12 shows 47 % consumption of 31 and 10% formation of 43 while 46 was observed in trace quantity. Table 12 also shows the quantitative results of the photoreaction of 31 with the presence of PA in methanol similar to the results observed in acetonitrile except the consumption of 31 in methanol was approximately 30 % less than the consumption of 31 observed in acetonitrile solvent. This indicates that the photoreaction of 31 in the presence of PA is less effective in methanol than acetonitrile solvent. Comparison between the quantitative results of the photoreactions of 31 in acetonitrile and methanol solvent with the photoreactions of 31 containing propylamine (PA) in both solvents shows that the presence of PA in either acetonitrile or methanol solvent leads to two-fold greater consumption of 31 compared to the consumption of 31 observed in the photoreaction without PA in both solvents and to the formation of 43 ten-fold greater than the formation of 43 observed in the reaction without PA. The other known photoproduts were quenched in both solvents.
Table 12: Quantitative analysis of the photoreaction of 31 in acetonitrile and methanol with the presence of TEA or PA

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>31 in AcCN</th>
<th></th>
<th>31 in MeOH</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>31</td>
<td>46</td>
<td>43</td>
<td>31</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30</td>
<td>-18%</td>
<td>0.5%</td>
<td>1%</td>
<td>-17%</td>
</tr>
<tr>
<td>120</td>
<td>-70%</td>
<td>2%</td>
<td>2%</td>
<td>-72%</td>
</tr>
<tr>
<td>31+TEA in AcCN</td>
<td></td>
<td></td>
<td></td>
<td>31+TEA in MeOH</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30</td>
<td>-28%</td>
<td>0.4%</td>
<td>1%</td>
<td>-25%</td>
</tr>
<tr>
<td>120</td>
<td>-70%</td>
<td>1%</td>
<td>3%</td>
<td>-68%</td>
</tr>
<tr>
<td>31+PA in AcCN</td>
<td></td>
<td></td>
<td></td>
<td>31+PA in MeOH</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30</td>
<td>-47%</td>
<td>trace</td>
<td>10%</td>
<td>-33%</td>
</tr>
<tr>
<td>120</td>
<td>-93%</td>
<td>0.4%</td>
<td>18%</td>
<td>-85%</td>
</tr>
</tbody>
</table>
2.14.2 Irradiation of 3-phenyl-1,2,4-thiadiazole in the presence of triethylamine or propylamine

Solutions of 3-phenyl-1,2,4-thiadiazole \((46)\) (0.008 M), \(46+\text{TEA}\) (0.008 M + 0.4 M), and \(46+\text{PA}\) (0.008 M + 0.4 M) in acetonitrile solvent in sealed Pyrex tubes were purged with argon gas for 15 min and simultaneously irradiated with sixteen > 290 nm lamps in a Rayonet photochemical reactor. These solutions were irradiated for a total of 120 min and analyzed by GLC. After irradiation, the reaction solution containing \(\text{PA}\) became blue green with the formation of white precipitate. The light green color in this solution again vanished upon sitting at room temperature in dark and became colorless. GLC analysis of solutions of \(46\) in the presence of \(\text{TEA}\) or \(\text{PA}\) in acetonitrile before irradiation showed only one gc-volatile component in each solution, which was due to the reactant, \(46\), indicating that no ground state reaction between \(46\) and amines was observed.

The GC-traces of the \(46+\text{TEA}\) mixture (Figure 324) and \(46+\text{PA}\) mixture (Figure 325) in acetonitrile after 120 min of irradiation show the formation of benzonitrile \((43)\) as the major product. This indicates that photolysis of \(46\) in acetonitrile containing \(\text{TEA}\) or \(\text{PA}\) leads mainly to the formation of \(43\) with trace quantities of unknown products.
Results and Discussion

Figure 324: GLC analysis of the 46+TEA mixture after 120 min of irradiation

Figure 325: GLC analysis of the 46+PA mixture after 120 min of irradiation
Photolysis of 46 in the presence of TEA or PA was also carried out in methanol solvent. Solutions of 46 (0.0086 M), 46+TEA (0.0086 M + 0.4 M), and 46+PA (0.0086 M + 0.4 M) in methanol solvent in sealed Pyrex tubes were purged with argon gas for 15 min and simultaneously irradiated with sixteen > 290 nm lamps in a Rayonet photochemical reactor. These solutions were irradiated for a total of 120 min and analyzed by GLC. After photolysis, the photoreaction of 46 without amines became cloudy while the reactions with amines remained clear and no precipitate was observed in the solution containing propylamine as was observed in the photolysis in acetonitrile solvent.

The GC-chromatograms of the mixture of 46+TEA and 46+PA in methanol before irradiation showed only one gc-volatile component in each solution which was due to the starting thia diazole, 46. Figure 326 and 327 reveal the formation of 43 as the only major photoproduct observed after 30 min of irradiation of 46 in the presence of TEA or PA in methanol solvent, respectively.
Results and Discussion

Figure 326: GC-trace of the 46+TEA mixture after 120 min of irradiation

Figure 327: GLC analysis of the 46+PA mixture after 120 min of irradiation
Table 13: Quantitative analysis of irradiation of 46 in the presence of TEA or PA in acetonitrile or methanol solvent

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>46 in AcCN</th>
<th>46 in MeOH</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>46</td>
<td>43</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30</td>
<td>-36%</td>
<td>57%</td>
</tr>
<tr>
<td>120</td>
<td>-86%</td>
<td>60%</td>
</tr>
<tr>
<td></td>
<td>46+TEA in AcCN</td>
<td>46+TEA in MeOH</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30</td>
<td>-34%</td>
<td>66%</td>
</tr>
<tr>
<td>120</td>
<td>-78%</td>
<td>65%</td>
</tr>
<tr>
<td></td>
<td>46+PA in AcCN</td>
<td>46+PA in MeOH</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30</td>
<td>-63%</td>
<td>65%</td>
</tr>
<tr>
<td>120</td>
<td>-93%</td>
<td>73%</td>
</tr>
</tbody>
</table>

Quantitative analysis of the photoreactions of 46 in the presence of amines in acetonitrile (Table 13) shows 34% and 63% consumptions of 46 in the reactions containing TEA and PA, respectively, while 46 was 36% consumed in the reaction in acetonitrile without amines after 30 min of irradiation. After 30 min of irradiation, Table 13 also shows the formation of benzonitrile (43) at 57%, 66% and 65% in the reaction without amines, the reaction containing TEA and the reaction containing PA, respectively. These results show that the presence of TEA does not greatly affect the photoreaction of 46 while the presence of PA leads to the consumption of 46 approximately two-fold greater than the consumption
of 46 observed in the reaction without amines or the reaction containing TEA but it does not greatly affect the formation of 43 after 30 min of irradiation.

Quantitative analysis of the photoreaction of 46 with the presence of amines in methanol (Table 13) shows 26% and 39% consumptions of 46 in the reaction containing TEA and PA, respectively, while 46 was 25% consumed in the reaction without amines after 30 min of irradiation. After 30 min of irradiation, Table 13 also shows the formation of benzonitrile (43) at 79%, 82% and 86% in the reaction without amines, the reaction containing TEA and the reaction containing PA, respectively. These results show again that the presence of triethylamine does not affect the photoreaction of 46. The presence of propylamine in methanol shows no great effect on the formation of 43 but affects the consumption of 46, however, in a less magnitude than the consumptions of 46 observed in the reaction containing propylamine in acetonitrile.

Thermodynamic feasibility considerations of electron transfer, as shown in Scheme 106 and 107, predicted that electron transfer processes between triethylamine or propylamine to the excited thiadiazoles would be energetically favorable. Scheme 106 and 107 also showed that an electron transfer that involves triethylamine as an electron donor would be more favorable than the process involving propylamine. However, the photolysis of 31 or 46 in the presence of these amines showed the results in the opposite direction to this prediction. The results showed that propylamine had profound effect on the photochemistry of 31 and 46 while triethylamine only slightly affected the photochemistry of 31 and 46. Although, the thermodynamic feasibilities of the electron transfer from TEA or PA to 31 or 46 are energetically feasible, it is also necessary to consider the kinetic feasibility of these electron transfer processes. Thus, diffusion controlled bimolecular electron transfer from an amine to the excited singlet of the thiadiazoles would be in competition with unimolecular
decay of the excited thiadiazoles. The ratio of the rates of these two processes is given by the equation shown below:

\[
\frac{\text{Rate of singlet unimolecular decay}}{\text{Rate of bimolecular electron transfer}} = \frac{k_{\text{decay}} \times [\text{TDZ}]^1}{k_{\text{diffusion}} \times [\text{TDZ}]^1 \times [\text{amine}]^1} = \frac{k_{\text{decay}}}{k_{\text{diffusion}} \times [\text{amine}]}
\]

Work carried out in this laboratory on the photochemistry of isothiazoles has shown the excited singlet life time of 4-phenylisothiazole at $1.2 \times 10^{-12}$ sec; $k_{\text{decay}} = 8.3 \times 10^{11}$ sec$^{-1}$. The excited singlet life times of 5-phenyl- or 3-phenyl-1,2,4-thiadiazole has not experimentally been determined but it could be estimated approximately at $1 \times 10^{-12}$ sec; $k_{\text{decay}} \sim 1 \times 10^{12}$ sec$^{-1}$ based on the observed life time of 4-phenylisothiazole. The diffusion controlled rate constant for acetonitrile is given at $1 \times 10^{10}$ M$^{-1}$ sec$^{-1}$. At the TEA or PA concentration of $4 \times 10^{-1}$ M, the ratio of the rates can be calculated as follows:

\[
\frac{\text{Rate of singlet unimolecular decay}}{\text{Rate of bimolecular electron transfer}} = \frac{1 \times 10^{12} \text{ sec}^{-1}}{10^{10} \text{ M}^{-1} \text{ sec}^{-1} \times 0.4 \text{ M}} = 250
\]

Thus, the unimolecular decay rate of the thiadiazole 31 or 46 is calculated to be 250 times faster than the rate of bimolecular diffusion controlled electron transfer. This clearly shows that under these conditions electron transfer from ground state of TEA or PA to excited states of 31 or 46 would not be expected to compete with unimolecular decay of the thiadiazole singlet states. Thus, this analysis indicates that electron transfer from TEA or PA to the excited states of 5-phenyl- (31) or 3-phenyl-1,2,4-thiadiazole (46) does not likely occur.

The effect of propylamine on the photochemistry of 5-phenyl- (31) or 3-phenyl-1,2,4-thiadiazole (46) is, however, still unclear.
CHAPTER 3

Experimental

3.1 Synthesis of the phenyl-1,2,4-thiadiazoles and some expected photoproducts

3.1.1 General procedure

All chemicals were used without further purification except methanol, ethanol, and acetonitrile. Methanol and ethanol were refluxed with Mg/I₂ overnight and distilled before used. Acetonitrile was redistilled before used. Melting points were determined using a Fisher-John melting point apparatus. NMR spectra were recorded on a Bruker FT-NMR (400.1, 100.6, 40.5 MHz for ¹H, ¹³C and ¹⁵N, respectively) with CDCl₃, Acetone-d₆, and DMSO-d₆ as internal standards and Na¹⁵NO₃(aq) as an external standard for ¹⁵N-experiments. Ultraviolet absorption spectra were recorded on a Shimadzu 2110U spectrophotometer. Fluorescence and phosphorescence spectra were recorded on a luminescence spectrometer (PE LS50B). Gas liquid chromatography (GLC) analyses were performed on a Perkin Elmer gas chromatograph PE 9000 FID instrument equipped with a 15 m × 3 μm i.d. fused silica column coated with Carbowax 20M bonded phase. Mass spectra were recorded on a Hewlett Packard HP 5970B mass selective detector (EI) interfaced to HP 588 GC coupled with a 20 m × 0.18 mm 50% phenyl silicone phase capillary column. Photochemical reactions were carried out in three scales (UV, GLC, and Preparative scale) in a Rayonet merry-go-round reactor and will be described in details later. Low pressure Hg-arc lamps
3-Cyano- and 3-amino-5-phenyl-1,2,4-thiadiazole and 5-cyano- and 5-amino-3-phenyl-1,2,4-thiadiazole were previously synthesized in this laboratory.

### 3.1.2 Synthesis of 5-phenyl-1,2,4-thiadiazole

#### 3.1.2.1 Synthesis of N-[(dimethylamino)methylene]thiobenzamide

Thiobenzamide (1.0 g, 7.3 mmol) was added to a 25 mL three-neck flask. The flask was purged with argon for 30 min. N,N-Dimethylformamide dimethylacetal (0.90 g, 1.0 mL, 7.5 mmol) was added to the flask through a rubber septum by a 1 mL syringe. The red reaction mixture was stirred while a couple drops of additional N,N-dimethylformamide dimethylacetal was added dropwise to dissolve the un-dissolved thiobenzamide. The red reaction solution was allowed to stand at room temperature under an argon atmosphere for 45 min. The volatile materials were removed by rotary evaporation to yield a reddish solid residue (1.7 g). The reddish residue was dissolved in warm ethanol, cooled to room temperature and cooled in an ice bath to crystallize. The obtained red crystals were filtered by suction filtration. The crystals (1.54 g) were recrystallized from ethanol to yield N-[(dimethylamino)methylene]thiobenzamide as red-orange crystals:

- **mp** 56-58°C (lit mp 50-54°C); 1.2 g (6.3 mmol, 87.5 %yield);
- **¹H–NMR** (CDCl₃) δ 3.24 (s, 3H), δ 3.25 (s, 3H), δ 7.32-7.36 (m, 2H), δ 7.44-7.48 (m, 1H), δ 8.39-8.42 (m, 2H), δ 8.73 (s, 1H);
- **¹³C–NMR** (CDCl₃) δ 36.8, 42.4, 128.1, 129.3, 132.3, 143.5, 159.5, 216.6;
- **¹H–¹³C correlation** (CDCl₃) δ¹H 3.24 - δ¹³C 36.8, δ¹H 3.25 - δ¹³C 42.4, δ¹H 7.32-7.36 - δ¹³C 128.1, δ¹H 7.44-7.48 - δ¹³C 132.3, δ¹H 8.39-8.42 - δ¹³C 129.3, δ¹H 8.73 - δ¹³C 159.5;
- **MS** m/z (%) 192 (M⁺; 70.8), 159 (52.8), 121 (79.1), 77 (36.1), 44 (100), 42 (73.6).
3.1.2.2 Synthesis of 5-phenyl-1,2,4-thiadiazole

N-[(dimethylamino)methylene]thiobenzamide (1.0 g., 5.2 mmol) was dissolved in absolute ethanol (15 ml.) in a 50 ml. three-neck flask containing pyridine (0.8 ml., 10 mmol). The solution was purged with argon for 30 minutes.

Hydroxylamine-O-sulfonic acid (0.61 g., 5.4 mmol) dissolved in absolute methanol (10 mL) was added to the three-neck flask resulting in a red-orange clear solution. The solution was stirred at room temperature for one hour. The reaction solution finally turned to yellow with a small amount of white precipitate. The volatile materials were removed by rotary evaporation to give a light yellow viscous residue. Dichloromethane (40 mL) was added to dissolve the residue. The solution was washed with water (20 mL), 0.1 N NaOH (20 mL), water (20 mL). The organic phase was dried over sodium sulfate and concentrated by rotary evaporation to give a light yellow liquid residue (0.93 g). Distillation (Kugelrohr) of the residue oil gave 5-phenyl-1,2,4-thiadiazole as a light yellow viscous oil: bp (oven temperature) 35-40°C (0.3 Torr), 0.70 g (4.3 mmol, 80 %yield);

$^1$H–NMR (CDCl$_3$) δ 7.32-7.39 (m,3H), δ 7.80-7.82 (m,2H), δ 8.54 (s,1H); $^{13}$C–NMR (CDCl$_3$) δ 127.9, 129.5, 132.4, 163.8, 188.6; MS m/z (%) 162 (M$^+$; 95.2), 135 (100), 104 (79.3), 103 (19.0), 77 (47.6).
5-Phenyl-1,2,4-oxadiazole was suspected to be a minor component in the synthetic 5-phenyl-1,2,4-thiadiazole. The isolation of this side product was attempted by preparative thin layer chromatography.

- Preparative layer chromatography: attempt to isolate 5-phenyl-1,2,4-oxadiazole

The synthesized 5-phenyl-1,2,4-thiadiazole (0.1 g) was dissolved in small amount of chloroform and subjected to a preparative layer chromatography by using hexane : ethyl acetate (4:1) as a eluent. The isolation was also carried out in different solvent systems (100% hexane, 20% ethyl acetate in hexane, 1% ethyl acetate in hexane, hexane : dichloromethane : ethyl acetate (29.7:0.2:0.1)). Although, analytical TLC [hexane : ethyl acetate (4:1)] indicated a complete separation between 5-phenyl-1,2,4-oxadiazole and 5-phenyl-1,2,4-thiadiazole with R_f of 0.6 and 0.53, respectively, separation by preparative layer chromatography was unsuccessful.

5-Phenyl-1,2,4-oxadiazole was expected to be formed due to the presence of benzamide in the thiobenzamide used. In order to prove this assumption, 5-phenyl-1,2,4-oxadiazole was synthesized by the similar method as 5-phenyl-1,2,4-thiadiazole but using benzamide instead of thiobenzamide.
- Synthesis of 5-phenyl-1,2,4-oxadiazole

N,N-dimethylformamide dimethyacetal (0.55 mL, 5.2 mmol) was added to a pear-shape flask containing benzamide (0.5 g, 4.1 mmol). The reaction mixture was allowed to stand in a warm water bath and stirred until benzamide totally dissolved. The light yellow reaction solution was allowed to stand at room temperature for one hour. The volatile materials were removed by rotary evaporation to give light yellow viscous residue. The residue was allowed to cool at -10°C for a couple minutes and scratched to yield white solid (0.78 g). This solid was recrystallized from ethanol to yield N-[(dimethylamino)methylene]benzamide as white crystals: 52-56°C; 0.65 g (3.7 mmol; 89 % yield); $^1$H–NMR (CDCl$_3$) δ 3.20 (s,1H), δ 3.21 (s, 1H), δ 7.40-7.51 (m, 3H), δ 8.27-8.30 (m, 2H), δ 8.65 (s, 1H).

- Synthesis of 5-phenyl-1,2,4-oxadiazole

N-[(dimethylamino)methylene]benzamide was dissolved in a mixture of pyridine (0.5 mL, 6.2 mmol) and absolute ethanol (10 mL). Hydroxylamine-O-sulfonic acid (0.45 g, 4.0 mmol) dissolved in absolute methanol (6 mL) was immediately added to the first solution to give a light yellow solution. The solution was stirred at room temperature for one hour. The volatile materials were removed by rotary evaporation to give a light yellow viscous residue. Dichloromethane (35 mL) was added to the residue. The solution was washed with water (10 mL), 0.1 N NaOH (10 mL), water (10 mL). The organic phase was dried over sodium sulfate and filtered by suction filtration. The filtrate was
concentrated to give a slurry mixture of white solid and a light yellow liquid. Hexane (20 mL) was added to the mixture. The mixture was filtrated by suction filtration. The filtrate was concentrated to yield a light green oil. This concentrated filtrate was analysed by GC-MS. The GC-MS result revealed the presence of only one component with a retention time of 5.9 min, which exhibited a molecular ion at m/z 146 consistent with the molecular weight of 5-phenyl-1,2,4-oxadiazole. Both chromatographic and mass spectroscopic properties of this synthesized compound also corresponded to the properties of the minor product present in the synthesized 5-phenyl-1,2,4-thiadiazole.

3.1.3 Synthesis of 3-phenyl-1,2,4-thiadiazole

3.1.3.1 Synthesis of 5-phenyl-1,3,4-oxadiazole-2-one

Chlorocarbosulfenyl chloride (5.0 g, 38 mmol) was added dropwise to a 100 mL round bottom flask containing benzamide (4.6 g, 38 mmol) in stirred chloroform (30 mL) at 50°C. The white cloudy reaction mixture was refluxed for 4 hours.

The reaction mixture was allowed to cool to room temperature. The volatile materials were removed by rotary evaporation at room temperature to give a white solid residue (6.5 g). This residue was recrystallized from methanol to yield 5-phenyl-1,2,4-oxadiazole-2-one as colorless crystals: mp 61-64°C; 5.0 g (27.0 mmol, 73.5 %yield); $^1$H–NMR (CDCl$_3$) $\delta$ 7.45-7.54 (m,2H), $\delta$ 7.93-7.95 (m,3H); $^{13}$C–NMR (CDCl$_3$) $\delta$ 126.1, 127.8, 129.4, 133.1, 157.8, 174.3; $^{13}$C-DEPT 135 (CDCl$_3$) $\delta$ 126.1(+), 127.8(+), 129.4(+); MS m/z (%) 179 (M$^{**}$; 38), 105 (100), 103 (24), 77 (42).
3.1.3.2 Synthesis of ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate

5-phenyl-1,2,4-oxadiazole-2-one (2.0 g, 11 mmol) was dissolved in dodecane (25 mL) in a 50 mL three-neck flask. Four equivalents of ethyl cyanoformate (4.4 mL, 4.4 g, 40 mmol) was added to the solution. The resulting solution was purged with nitrogen gas for 15 min, then refluxed under a nitrogen atmosphere for 13 hours. The reaction flask was allowed to cool to room temperature and placed in an ice-water bath to allow the light brown solid to precipitate.

The light brown precipitate was filtered by suction filtration and washed by cold ethanol and recrystallized from ethanol to yield the ester as light brown crystals: mp 64-66°C; 2.0 g (8.0 mmol, 77.8 % yield); ¹H–NMR (CDCl₃) δ 4.41 (t, 3H, J = 7.07 Hz), δ 4.51 (q, 2H, J = 7.07 Hz), δ 7.43-7.44 (m, 3H), δ 8.328-8.29 (m, 2H); ¹³C–NMR (CDCl₃) δ 14.6, 63.8, 128.9, 129.2, 131.3, 132.3, 158.9, 175.1, 179.4; ¹³C–DEPT135 (CDCl₃) δ 14.6(+), 63.8(-), 128.9(+), 129.2(+), 131.3(+); MS m/z (%) 234 (M⁺,50.8), 135 (100), 103 (28.5), 77 (20).

3.1.3.3 Synthesis of 3-phenyl-1,2,4-thiadiazole

A mixture of ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate (1.0 g, 4.3 mmol), sodium hydroxide (0.1 g, 4.75 mmol), ethanol (1.5 mL), water (7.5 mL) in a 25 mL Erlenmeyer flask was heated and stirred. The temperature was slightly increased until the ester completely dissolved and maintained at this temperature for 1 hour. The reaction solution was cooled to room temperature and acidified with concentrated hydrochloric acid. The acidification resulted in the formation of 3-phenyl-1,2,4-thiadiazole-5-carboxylic acid as
a white precipitate. The reaction mixture was reheated and stirred until decarboxylation was complete. Upon complete decarboxylation, a brownish secondary phase separated from the aqueous phase. The mixture was extracted with ether (5×5 mL). The ethereal extract was dried over sodium sulfate and concentrated by rotary evaporation to give light brownish residue (0.63 g). Distillation (Kugelrohr) of this residue gave 3-phenyl-1,2,4-thiadiazole as a white solid: bp (oven temperature) 40°C (0.02 Torr), mp 34-35 °C; 0.46 g. (2.8 mmol, 72 % yield); $^1$H–NMR (acetone-d$_6$) δ 7.49-7.55 (m,3H), δ 8.33-8.36 (m,2H), δ 10.3 (s,1H); $^{13}$C–NMR (acetone-d$_6$) δ 129.4, 130.1, 131.7, 134.1, 174.9, 175.9; $^{13}$C–DEPT 135 (acetone-d$_6$) δ 129.4(+), 130.1(+), 131.7(+), 176.0(+); MS m/z (%) 162 (M$^+$; 75.7), 135 (100), 103 (24.3), 77 (31.4).

3.1.4 Synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole

3.1.4.1 Synthesis of N-[(dimethylamino)ethyledine]thiobenzamide

Thiobenzamide (1.5 g, 10.95 mmol) was dissolved in N,N-dimethylacetamide dimethylacetal (1.45 g, 1.5 mL, 10.95 mmol) in a 25 mL three-neck flask under an argon atmosphere. The mixture was heated in a warm water bath while additional N,N-dimethylacetamide dimethylacetal was added dropwise until thiobenzamide totally dissolved. The resulting reddish reaction mixture was allowed to stand at room temperature for 45 min. The volatile materials were removed by rotary evaporation to give a reddish viscous residue. The residue was scratched to give fine dark orange crystals (2.37 g), which were recrystallized from ethanol to yield N-[(dimethylamino)ethyledine]
Experimental

thiobenzamide as orange crystals: mp 109-111°C, 2.0g. (9.8 mmol, 89.8 % yield); \(^1^H\text{-NMR}\) (CDCl\(_3\)) \(\delta\) 2.48 (s,3H), \(\delta\) 3.20 (s,3H), \(\delta\) 3.22 (s,3H), \(\delta\) 7.28-7.33 (m,2H), \(\delta\) 7.38-7.42 (m,1H), \(\delta\) 8.22-8.28 (m,2H); \(^{13}C\text{-NMR}\) (CDCl\(_3\)) \(\delta\) 18.4, 39.5, 39.7, 128.0, 128.8, 131.3, 142.8, 168.3, 202.76; \(^1^H\text{-}^{13}C\) correlation (CDCl\(_3\)) \(\delta\)\(^{1}H\) 2.48 - \(\delta\)\(^{13}C\) 18.4, \(\delta\)\(^{1}H\) 3.20 - \(\delta\)\(^{13}C\) 39.5, \(\delta\)\(^{1}H\) 3.22 - \(\delta\)\(^{13}C\) 39.7, \(\delta\)\(^{1}H\) 7.28-7.33 - \(\delta\)\(^{13}C\) 128.0, \(\delta\)\(^{1}H\) 7.38-7.42 - \(\delta\)\(^{13}C\) 131.3, \(\delta\)\(^{1}H\) 8.22-8.28 - \(\delta\)\(^{13}C\) 128.8; MS\( m/z \) (%) 206 (M\(^{+}\);28.7), 173 (38.3), 121 (52.1), 103 (100), 77 (26.0), 44 (50.7).

3.1.4.2 Synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole

N-[(dimethylamino)ethylidine]thiobenzamide (1.0 g, 4.8 mmol) was dissolved in absolute ethanol (15 mL) in a 50 mL three-neck flask containing pyridine (0.8 mL, 10 mmol). The solution was purged with argon gas for 30 min.

Hydroxylamine-O-sulfonic acid (0.59 g, 5.2 mmol) dissolved in absolute methanol (10 mL) was added to the three-neck flask resulting in an orange clear solution. The solution was stirred at room temperature for 1 hour. The reaction solution finally turned to light yellow with a small amount of white precipitate. The volatile materials were removed by rotary evaporation to give an orange viscous residue. Dichloromethane (40 mL) was added to dissolve the residue. The solution was washed with water (20 mL), 0.1 N NaOH (20 mL), water (20 mL). The organic phase was dried over sodium sulfate and concentrated by rotary evaporation to yield light clear yellow solid residue (0.68 g). The residue was recrystallized from hexane to give a light yellow crystals, which were sublimed (45-50°C, 15 Torr) to give 3-methyl-5-phenyl-1,2,4-thiadiazole as white crystals:
Experimental

mp 52-54°C, 0.63 g (3.6 mmol, 75 % yield); $^1$H–NMR (CDCl$_3$) δ 2.70 (s, 3H), δ 7.46-7.51 (m, 3H), δ 7.90-7.93 (m, 2H); $^{13}$C–NMR (CDCl$_3$) δ 19.4, 127.8, 129.7, 130.9, 132.3, 174.5, 188.5; $^{13}$C–DEPT 135 (CDCl$_3$) δ 19.4(+), 127.8(+), 129.7(+), 132.3(+); MS m/z (%) 176 (M$^+$; 37.7), 135 (100), 103 (9.8), 73 (59.1).

3.1.5 Synthesis of diphenyl-1,2,4-thiadiazole

Dimethyl sulfoxide (5.0 mL) was added to a 25 mL round bottom flask containing thiobenzamide (0.5 g, 3.6 mmol). The mixture was stirred vigorously to give a yellow solution. Aqueous hydrochloric acid (36 %, 0.06 mL, 2.2 mmol) was added to the solution to give an orange solution. The reaction solution was heated and maintained at 35-40°C. After 30 min, a cloudy solid precipitated. After 2.5 hours, the reaction mixture color turned from orange to pale pink and finally white cloudy. TLC analyses of the white cloudy mixture indicated that thiobenzamide was completely consumed. The reaction mixture was cooled to room temperature and filtered by suction filtration. A pale yellow precipitate was collected. Water (20 mL) was added to the filtrate to yield a pale pink precipitate. This precipitate was collected by suction filtration and recrystallized from hot ethanol to give diphenyl-1,2,4-thiadiazole as white crystals: mp 84-86°C, 0.34 g (1.4 mmol, 79 % yield); $^1$H–NMR (CDCl$_3$) δ 7.46-7.53 (m, 6H), δ 8.02-8.05 (m, 2H), δ 8.36-8.38 (m, 2H); MS m/z (%) 238 (M$^+$; 35.4), 135 (100), 103 (20.8), 77 (25).
3.1.6 Synthesis of 5-phenyl-1,2,4-thiadiazole-4-\(^{15}\)N

3.1.6.1 Synthesis of thiobenzamide-\(^{15}\)N

Benzamide-\(^{15}\)N (1.0 g, 8.2 mmol), phosphorus pentasulfide (0.36g, 1.6 mmol) and benzene (6 mL) were placed in a 25 mL round bottom flask. The mixture was refluxed and stirred vigorously for 50 min. The yellow benzene solution was decanted to a 25 mL Erlenmeyer flask from the red solid residue. A yellow solid formed immediately. This solid was filtered by suction filtration. Benzene (3 mL) was added to the reaction flask containing the red solid residue and refluxed for several min. The benzene solution was decanted to another clean 25 mL Erlenmeyer flask. The benzene extraction was repeated 4 times. All benzene extracts were collected in a 25 mL Erlenmeyer flask. The first filtrate was added to this benzene extracted solution. The combined solution was concentrated on a heating mantle and then allowed to cool to room temperature to crystallize. The obtained yellow crystals were dissolved in a small amount of dichloromethane and subjected to a column chromatography (diameter: 3.5 cm, silica gel: 40 g, height: 22 cm). Dichloromethane was employed as an eluent. The column was eluted with dichloromethane (75 mL) to move the yellow band of thiobenzamide down the column. Then, 10 mL fractions were collected. Based on TLC analyses, fractions 2-20 were combined. Dichloromethane was removed by rotary evaporation to give a yellow solid. The solid was dissolved in hot chloroform, cooled to room temperature and finally in an ice bath. A couple drops of hexane were added to the solution to induce the crystallization. Thiobenzamide-\(^{15}\)N was obtained as yellow crystals: mp 113-115°C, 0.6 g (4.3 mmol, 60 %yield); \(^1\)H–NMR (CDCl\(_3\)) \(\delta\) 7.06-7.30 (dd, 1H, \(J_{HH} = 4.29\) Hz, \(J_{H15N} = 89.18\) Hz), \(\delta\) 7.70-7.94 (dd, 1H, \(J_{HH} = 4.29\) Hz, \(J_{H15N} = 92.71\) Hz), \(\delta\) 7.35-7.40 (m, 2H),
δ 7.47-7.52 (m, 2H), δ 7.83-7.90 (m, 2H); $^{13}$C–NMR (CDCl$_3$) δ 126.8, 128.5, 133.2, 138.2, 202.8 (d, J$_{C15N}$ = 13.80 Hz); $^{15}$N–NMR [CDCl$_3$-$^{15}$NO$_3$ (ext. ref.)] δ 132.8 (t, J$_{15NH}$ = 91.20 Hz); MS m/z (%) 138 (M$^+$; 100), 121 (31.7), 105 (58.8), 77 (43.5).

3.1.6.2 Synthesis of N-[(dimethylamino)methylene]thiobenzamide-$^{15}$N

Thiobenzamide-$^{15}$N (0.5 g, 3.6 mmol) was added to a 25 mL three-neck flask. The flask was purged with argon for 30 min. N,N-dimethylformamide dimethylacetal (0.5 g, 0.6 mL, 4.2 mmol) was added to the flask through a rubber septum by a 1 mL syringe. The red reaction mixture was stirred while a couple drops of additional N,N-dimethylformamide dimethylacetal was added dropwise to dissolve the un-dissolved thiobenzamide-$^{15}$N. The red reaction solution was allowed to stand at room temperature under an argon gas atmosphere for 30 min. The volatile materials were removed by rotary evaporation. The residue was cooled for 2-3 min and then scratched to yield a reddish orange solid (0.7 g). The residue was dissolved in warm ethanol, cooled to room temperature and in an ice bath to crystallize. The obtained red crystals were filtered by suction filtration. The crystals (0.61 g) were recrystallized from ethanol to yield N-[(dimethylamino)methylene]thiobenzamide-$^{15}$N as orange crystals: mp 52-54°C; 0.58 (3.0 mmol, 83 % yield); $^1$H–NMR (CDCl$_3$) δ 3.24 (s,3H), δ 3.25 (s,3H), δ 7.29-7.42 (m,2H), δ 7.44-7.51 (m,1H), δ 8.36-8.45 (m,2H), δ 8.78 (s,1H); $^{13}$C–NMR (CDCl$_3$) δ 36.3 (d, J$_{C15N}$ = 2.3 Hz), 41.9, 127.0, 128.8 (d, J$_{C15N}$ = 3.1 Hz), 131.8, 143.0 (d, J$_{C15N}$ = 8.4 Hz), 159.0 (d, J$_{C15N}$ = 10.0 Hz), 216.1; $^{15}$N–NMR (CDCl$_3$-$^{15}$NO$_3$ (ext. ref.) δ 266.8 (d, J$_{15NH}$ = 2 Hz); $^1$H–$^{13}$C correlation (CDCl$_3$) δ$^1$H 3.24 - δ$^{13}$C 36.3, δ$^1$H 3.25 - δ$^{13}$C 41.9, δ$^1$H 7.29-7.42 -
δ^{13}C 128.8, δ^{1H} 7.44-7.51 - δ^{13C} 143.0, δ^{1H} 8.36-8.45 - δ^{13C} 131.8, δ^{1H} 8.78 - δ^{13C} 159.0;  

**MS** m/z (%) 193 (M^{+*}; 70.8), 159 (52.8), 121 (79.1), 77 (36.1), 44 (100), 42 (73.6).

### 3.1.6.3 Synthesis of 5-phenyl-1,2,4-thiadiazole-4\(^{15}\)N

N-[(dimethylamino)methylene]thiobenzamide-\(^{15}\)N (0.48 g, 2.5 mmol) was dissolved in absolute ethanol (10 mL) in a 50 mL three-neck flask containing pyridine (0.5 mL, 6.2 mmol). The solution was purged with argon for 30 min.

Hydroxylamine-O-sulfonic acid (0.34 g, 3.0 mmol) dissolved in absolute methanol (8 mL) was added to the three-neck flask resulting in a red-orange clear solution. The solution was stirred at room temperature for 10 hour. The reaction solution finally turned to pale clear yellow with a small amount of white precipitate. The volatile materials were removed by rotary evaporation to give a light yellow viscous residue. Dichloromethane (30 mL) was added to dissolve the residue. The solution was washed with water (15 mL), 0.1 N NaOH (15 mL), water (15 mL). The organic phase was dried over sodium sulfate and concentrated by rotary evaporation to give a light yellow liquid residue (0.48 g). Distillation (Kugelrohr) of the residue oil gave 5-phenyl-1,2,4-thiadiazole-4\(^{15}\)N as a light yellow viscous oil: bp (oven temperature) 40-45°C (0.4 Torr), 0.34 g (2.1 mmol, 84 % yield). Some of 5-phenyl-1,2,4-thiadiazole-4\(^{15}\)N was finally purified by preparative gas chromatography to record \(^1\)H-, \(^{13}\)C- and \(^{15}\)N–NMR spectrum; \(^1\)H–NMR (acetone-d<sub>6</sub>) δ 7.58-7.61 (m,3H), δ 8.06-8.08 (m,2H), δ 8.84 (d, 1H, J<sub>H15N</sub> = 13.9 Hz); \(^{13}\)C–NMR (acetone-d<sub>6</sub>) δ 128.2, 130.3, 131.12 (d, J<sub>C15N</sub> = 6.3 Hz), 133.0, 164.6 (d, J<sub>C15N</sub> = 3.8 Hz), 188.6; \(^{15}\)N–NMR (acetone-d<sub>6</sub> - Na\(^{15}\)NO<sub>3</sub>(ext. ref.) δ 302.20 (d, J<sub>15NH</sub> = 13.9 Hz);
3.1.7 Experimental

**1H–13C correlation** (acetone-\(d_6\)) \(\delta^{1H} 7.58-7.61 - \delta^{13C} 130.3\) and 133.0, \(\delta^{1H} 8.06-8.08 - \delta^{13C} 128.2\), \(\delta^{1H} 8.84 - \delta^{13C} 164.6\); **MS** \(m/z\) (%) 163 (M\(^+\); 88), 136 (100), 105 (92), 104 (24), 77 (58.6), 59 (62.6).

3.1.7 Synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole-4-\(^{15}\)N

3.1.7.1 Synthesis of \(N-[(\text{dimethylamino})\text{ethyledine}]\text{thiobenzamide-}^{15}\)N

Thiobenzamide-\(^{15}\)N (0.46 g, 3.3 mmol) was dissolved in \(N,N\)-dimethylacetamide dimethylacetal (0.44 g, 0.6 mL, 3.3 mmol) in a 25 mL three neck flask under an argon atmosphere. The mixture was heated in a warm water bath while additional \(N,N\)-dimethylacetamide dimethylacetal was added dropwise until thiobenzamide-\(^{15}\)N totally dissolved. The resulting reddish reaction mixture was allowed to stand at room temperature for 30 min. The volatile materials were removed by rotary evaporation to give a reddish viscous residue. The residue was cooled and scratched to give fine dark orange solid (0.7 g.), which was recrystallized from warm ethanol to yield \(N-[(\text{dimethylamino})\text{ethyledine}]\text{thiobenzamide-}^{15}\)N as orange crystals: mp 110-113°C, 0.56 g (2.8 mmol, 82.3 % yield); **1H–NMR** (CDCl\(_3\)) \(\delta 2.48\) (s,3H), \(\delta 3.20\) (s,3H), \(\delta 3.21\) (s,3H), \(\delta 7.29-7.33\) (m,2H), \(\delta 7.38-7.42\) (m,1H), \(\delta 8.22-8.24\) (m,2H); **13C–NMR** (CDCl\(_3\)) \(\delta 18.4, 39.5, 39.7, 128.0, 128.8\) (d, \(J_{C15N} = 2.3\) Hz), 131.3, 142.7 (d, \(J_{C15N} = 8.4\) Hz), 168.3 (d, \(J_{C15N} = 12.3\) Hz), 202.7 (d, \(J_{C15N} = 6.9\) Hz); **1H–13C correlation** (CDCl\(_3\)) \(\delta^{1H} 2.48 - \delta^{13C} 18.4, \delta^{1H} 3.20 - \delta^{13C} 39.5, \delta^{1H} 3.21 - \delta^{13C} 39.7, \delta^{1H} 7.29-7.33 - \delta^{13C} 128.0, \delta^{1H} 7.38-7.42 - \delta^{13C} 131.3, \delta^{1H} 8.22-8.24 - \delta^{13C} 164.6\).
\[ \delta^{13C} 128.82; \quad ^{15}N-NMR \text{ (CDCl}_3-\text{Na}^{15}\text{NO}_3\text{ (ext. ref.) } \delta 289.5; \quad \text{MS } m/z (\%) \ 207 (M^+; 50.7), 174 (65.2), 121 (100), 104 (79.7), 77 (42), 56 (62.3). \]

3.1.7.2 Synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole-4-\(^{15}\)N

N-[(dimethylamino)ethylidene]thiobenzamide-\(^{15}\)N (0.52 g, 2.5 mmol) was dissolved in absolute ethanol (15 mL) in a 50 mL three neck flask containing pyridine (0.6 mL, 6.2 mmol). The solution was purged with argon gas for 30 min.

Hydroxylamine-O-sulfonic acid (0.34 g, 3.0 mmol) dissolved in absolute methanol (10 mL) was added to the three neck flask resulting in a light orange clear solution. The solution was stirred at room temperature for one hour. The reaction solution finally turned to light yellow with a small amount of white precipitate. The volatile materials were removed by rotary evaporation to give a light yellow viscous residue. Dichloromethane (40 mL) was added to dissolve the residue. The solution was washed with water (20 mL), 0.1 N NaOH (20 mL), water (20 mL). The organic phase was dried over sodium sulfate and concentrated by rotary evaporation to yield a light yellow solid residue (0.42 g). The yellow residue was recrystallized from hexane to give a yellow solid, which was sublimed (64°C, 20 Torr) to give 3-methyl-5-phenyl-1,2,4-thiadiazole as white crystals: mp 50-52°C, 0.35 g (2.0 mmol, 80 % yield); \(^1H-NMR\text{ (CDCl}_3\) \(\delta 2.71\text{ (d, 3H, } J_{15N} = 2.27\text{),}\)
\(\delta 7.46-7.48\text{ (m,3H), } \delta 7.90-7.92\text{ (m,2H); }^{13}C-NMR\text{ (CDCl}_3\) \(\delta 19.5\text{ (d, } J_{15N} = 8.4\text{ Hz),}\)
\(127.8\text{ (d, } J_{15N} = 2.3\text{ Hz), 129.7, 130.9\text{ (d, } J_{15N} = 6.16\text{ Hz), 132.3, 174.5\text{ (d, } J_{15N} = 2.3\text{ Hz), 188.4; }^{13}C-DEPT 135\text{ (CDCl}_3\) \(\delta 19.4(+)\), 127.8(+$), 129.7(+$), 132.3(+$); }^{15}N-NMR\text{ (CDCl}_3-\)
\[ \text{Na}^{15}\text{NO}_3(\text{ext. ref.}) \; \delta 301.7 \; (d, \; J_{\text{15NH}} = 2.0 \; \text{Hz}); \quad \textbf{MS} \; m/z \; (\%) \; 177 \; (M^+; \; 33), \; 136 \; (100), \; 104 \; (12.5), \; 73 \; (76.8). \]

3.1.8 Synthesis of 5-(4'-methoxy)phenyl-1,2,4-thiadiazole

3.1.8.1 Synthesis of 4-methoxythiobenzamide

A yellow solution of 4-methoxybenzamide (1.0 g; 6.6 mmol), Lawesson reagent (2.7 g; 6.6 mmol) in tetrahydrofuran (8 mL) was refluxed and stirred in a 50 mL round bottom flask. The reaction was monitored by TLC (hexane-ethyl acetate 4:1). After 1 hour, TLC analysis indicated the formation of the product as a yellow spot. The TLC also showed the remaining of 4-methoxybenzamide. At prolong reaction time, the solution turned to a reddish orange solution, thus, the reaction was stopped at 1.5 hours. The reaction mixture was concentrated to give an orange viscous liquid (1.05 g). A small portion of dichloromethane was added to the crude orange liquid. Silica gel (2 g) was added to the crude solution to give a slurry crude-mixture. The slurry silica-crude mixture was stirred and left at room temperature to dryness. The dried silica-crude mixture was subjected to a column chromatography (3.5 \times 17 \text{ cm}; silica gel 40 g). The column was eluted with hexane-ethyl acetate 4:1 and 25 mL fractions were collected. The yellow fractions 8-25 were combined. The solvent was removed by rotary evaporation in a warm water bath to give 4-methoxythiobenzamide as a yellow solid: mp 138-140°C; 0.6 g (3.6 mmol, 54.5 % yield); \[^1\text{H–NMR} \; (\text{CDCl}_3) \; \delta 3.84 \; (s,3H), \; \delta 6.90 \; (d, \; 2H; \; J = 8.8 \; \text{Hz}), \; 7.92 \; (d, \; 2H; \; J = 8.8 \; \text{Hz}), \; \delta 7.9-8.3 \; (\text{two broad singlets}); \; ^{13}\text{C–NMR} \; (\text{CDCl}_3) ; \; \delta 55.5 \; (+), \; 113.6 \; (+), \; 129.1 \; (+), \; 130.9 \; (0), \; 163.1 \; (0), \; 202.8 \; (0); \quad \textbf{MS} \; m/z \; (\%) \; 167 \; (M^+; \; 100), \; 151 \; (35.2), \; 134 \; (84), \; 133 \; (38.4), \; 103 \; (16.6), \; 90 \; (18.3), \; 63\; (16.3). \]
3.1.8.2 Synthesis of N-[(dimethylamino)methylene]4-methoxythiobenzamide

N,N-dimethylformamide dimethylacetal (0.5 mL; 4.2 mmol) was added to a pear-
shape flask containing 4-methoxythiobenzamide (0.6 g; 3.6 mmol). An additional small
portion of N,N-dimethylformamide dimethylacetal was added dropwise to dissolve the
thiobenzamide. The reaction mixture was allowed to sit at room temperature to yield a
reddish orange solid after 15 minutes. The volatile materials in the crude mixture were
removed by rotary evaporation at room temperature. The crude orange solid was
recrystallized from hot ethanol to give N-[(dimethylamino)methylene]4-methoxythiobenzamide as reddish orange fine crystals: mp 104-106°C; 0.76 g (3.4 mmol;
94 % yield); $^1$H–NMR (CDCl$_3$) $\delta$ 3.83 (s, 3H), $\delta$ 3.27 (s, 3H), 3.29 (s, 3H), $\delta$ 6.84 (d, 2H;
J = 9.1 Hz), $\delta$ 8.44 (d, 2H; J = 9.1 Hz), $\delta$ 9.45 (s, 1H); $^{13}$C–NMR (CDCl$_3$) $\delta$ 36.3 (+),
41.8 (+), 55.4 (+), 112.8 (+), 131.1 (+), 136.3 (0), 159.1 (+), 163.3 (0), 214.7 (0).

3.1.8.3 Synthesis of 5-(4′-methoxy)phenyl-1,2,4-thiadiazole

N-[(dimethylamino)methylene]4-methoxythiobenzamide (0.65 g; 3 mmol) was
slightly dissolved in absolute ethanol (20 mL) in a 50 mL three-neck flask containing
pyridine (0.8 mL). The mixture was stirred and purged with argon for 30 min.
Hydroxylamine-O-sulfonic acid (0.5 g; 4.4 mmol) dissolved in absolute methanol (10 mL)
was added to the three-neck flask via a dropping funnel resulting an orange solution.
The reaction mixture was allowed to stir at room temperature under an argon atmosphere
until the solution colour changed from orange to very light yellow within 2-3 hours.
The yellow solution was concentrated to give a crude yellow viscous liquid. The yellow
viscous liquid was dissolved in dichloromethane (30 mL). The organic solution was washed by water (20 mL), 1N NaOH (20 mL) and water (20 mL). The organic layer was collected and dried over anhydrous sodium sulphate. The solvent was removed to give light yellow solid (0.62 g). The yellow solid was recrystallized from hot ethanol to give 5-(4′-methoxy)phenyl-1,2,4-thiadiazole as white crystals: mp 55-57 °C; 0.4 g (2.1 mmol; 70 % yield); \(^1\text{H–NMR} \text{(CDCl}_3\text{)} \delta 3.87 \text{ (s, 3H)}, \delta 6.99 \text{ (d, 2H; } J = 8.6 \text{ Hz)}, \delta 7.92 \text{ (d, 2H; } J = 8.6 \text{ Hz)}, 8.87 \text{ (s, 1H)}; \(^{13}\text{C–NMR} \text{(CDCl}_3\text{)} \delta 55.5 \text{ (+),114.7 \text{ (+),123.1 \text{ (0), 129.3 \text{ (+), 162.7 \text{ (0), 163.2 \text{ (+),187.8 \text{ (0); MS m/z (}) 192 \text{ (M}^+\text{; 100), 165 \text{ (25.8), 134 \text{ (87.3), 133 \text{ (48.4), 103 \text{ (12.8), 90 \text{ (16.4).}}}}}

### 3.1.9 Synthesis of 5-(4′-cyano)phenyl-1,2,4-thiadiazole

#### 3.1.9.1 Synthesis of 4-cyanobenzamide

Thionyl chloride (3 mL; 41 mmol) was added to a 50 mL round bottom flask containing 4-cyanobenzoic acid (1 g; 6.8 mmol). The reaction mixture was refluxed at 80°C until all acid completely dissolved within two hours to give a brown solution. The reaction was allowed to cool to room temperature and placed in an ice bath. Ammonium hydroxide solution (conc.) was added dropwise to the reaction mixture resulting in white cloudy smoke and a brown precipitate. Ammonium hydroxide (> 5 mL) was added to the reaction mixture until no further gas evolution was observed. Water (5 mL) was added to the reaction mixture. The mixture was filtered by suction filtration. The brown solid (0.98 g) was collected and washed with sodium bicarbonate solution. The brown solid was recrystallized
Experimental

from hot acetonitrile to give 4-cyanobenzamide as light brown crystals: mp 217-220°C; 0.91 g (6.2 mmol; 91 % yield); \textsuperscript{1}H–NMR (DMSO-d\textsubscript{6}) δ 7.94 (d, 2H; J = 7.3 Hz), 8.00 (d, 2H; J = 7.3 Hz), 9.6 (s, 1H), 10.18 (s, 1H); \textsuperscript{13}C–NMR (DMSO-d\textsubscript{6}) δ 119.3 (0), 129.1 (+), 133.3 (+), 139.1 (0), 167.3 (0); MS m/z (%) 146 (M\textsuperscript{+}; 59.8), 130 (100), 102 (60.6), 76 (21.4), 75 (20.7), 51 (16.9), 50 (19.9).

3.1.9.2 Synthesis of 4-cyanothiobenzamide

A mixture of 4-cyanobenzamide (0.8 g; 5.5 mmol), Lawesson reagent (2.7 g; 6.6 mmol) in tetrahydrofuran (10 mL) was refluxed and stirred in a 50 mL round bottom flask. The reaction was monitored by TLC (hexane-ethyl acetate 4:1). TLC analysis indicated complete consumption of the reactant after 4 hours with the formation of the product as a yellow spot. The reaction mixture was concentrated to give a yellow-orange viscous liquid. Dichloromethane (20 mL) was added to the crude yellow-orange liquid. Hexane (10 mL) was added to this solution resulting in the formation of a yellow precipitate. The mixture was filtered and yellow precipitate was collected. The yellow precipitate (0.64 g) was recrystallized from hot dichloromethane and addition of a small portion of hexane to give 4-cyanothiobenzamide as a fine yellow solid: mp 220-223 °C; 0.51 g (3.1 mmol, 56 % yield); \textsuperscript{1}H–NMR (DMSO-d\textsubscript{6}) δ 7.90 (d, 2H; J = 8.1 Hz), 7.96 (d, 2H; J = 8.1 Hz), 9.75 (s, 1H), 10.18 (s, 1H); \textsuperscript{13}C–NMR (DMSO-d\textsubscript{6}) δ 113.9 (0), 119.2 (0), 128.6 (+), 132.8 (+), 144.2 (0), 199.3 (0); MS m/z (%) 162 (M\textsuperscript{+}; 100), 146 (37.2), 129 (70.3), 128 (39.9), 103 (19.9), 102 (32.6), 60 (48.7).
3.1.9.3 Synthesis of N-[(dimethylamino)methylene]4-cyanothiobenzamide

4-Cyanothiobenzamide (0.4 g; 2.5 mmol) was dissolved in tetrahydrofuran (10 mL) in a 50 mL round bottom flask. N,N-dimethylformamide dimethylacetal (0.5 mL; 4.2 mmol) was added to the reaction flask to yield a reddish mixture. The reaction mixture was stirred in a warm water bath for 2 hours. Volatile materials were removed by rotary evaporation at room temperature to give a reddish solid residue (0.38 g). The residue was recrystallized from warm dichloromethane with addition of hexane to give N-[(dimethylamino)methylene]4-cyanothiobenzamide as reddish fine crystals: mp 105-108°C; 0.3 g (1.4 mmol; 56 % yield);

\[ ^1H–NMR\ (CDCl_3) \delta 3.31-3.32\ (2s, 6H), 7.63\ (d, 2H; J = 8.6 Hz), 8.43\ (d, 2H; J = 8.6 Hz), 8.75\ (s, 1H);\]

\[ ^13C–NMR\ (CDCl_3) \delta 37.0\ (+), 42.6\ (+), 114.8\ (0), 119.4\ (0), 129.5\ (+), 132.0\ (+), 146.5\ (0), 159.9\ (+), 213.9\ (0);\]

\[ MS\ m/z\ (\%)\ 217\ (M^{+}\); 51.7), 184\ (41.8), 146\ (52.7), 128\ (52.4), 89\ (37), 44\ (100).\]

3.1.9.4 Synthesis of 5-(4′-cyano)phenyl-1,2,4-thiadiazole

A mixture of N-[(dimethylamino)methylene]4-cyanothiobenzamide (0.45 g; 2.1 mmol), pyridine (0.5 mL) in absolute ethanol (20 mL) was stirred in a 50 mL three-neck flask under an argon atmosphere for 30 min. Hydroxylamine-O-sulfonic acid (0.4 g; 3.5 mmol) dissolved in absolute methanol (10 mL) was added to the three-neck flask via a dropping funnel resulting an orange solution mixture. The reaction mixture was allowed to stir at room temperature under an argon atmosphere until the solution colour changed from orange to very light clear yellow after 4 hours. The yellow solution was concentrated to give light yellow semi-solid residue. The yellow residue was dissolved in dichloromethane
Experimental

(20 mL). The organic solution was washed by water (15 mL), 1N NaOH (15 mL) and water (15 mL). The organic layer was collected and dried over anhydrous sodium sulphate. The solvent was removed to give light yellow solid (0.42 g). The yellow solid was washed by cold ethanol to give light yellow solid (0.1 g) and colourless filtrate. The colourless filtrate was concentrated to give light yellow fine solid. The light yellow solid was subjected to sublimation (120 °C; 0.3 torr) to yield 5-(4'-cyano)phenyl-1,2,4-thiadiazole as a white solid: mp 125-128 °C; 0.25 g (1.3 mmol; 62 % yield); \(^1\)H–NMR (CDCl\(_3\)) \(\delta\) 7.8 (d, 2H; \(J = 8.3\) Hz), 8.1 (d, 2H; \(J = 8.3\) Hz), 8.83 (s, 1H); \(^1\)C–NMR (CDCl\(_3\)) \(\delta\) 115.8 (0), 118.3 (0), 128.5 (+), 133.6 (+), 134.4 (0), 164.3 (+), 186.4 (0); MS \(m/z\) (%) 187 (M⁺; 55.9), 160 (100), 129 (26), 102 (16.6), 75 (13.7), 59 (67.2).

3.1.10 Synthesis of 3-(4'-methoxy)phenyl-1,2,4-thiadiazole

3.1.10.1 Synthesis of 5-(4'-methoxy)phenyl-1,3,4-oxathiazole-2-one

A solution of chlorocarbosulphenyl chloride (0.6 mL, 0.87 g, 6.6 mmol) in chloroform (3 mL) was added dropwise to a 100 mL round bottom flask containing 4-methoxybenzamide (1.0 g, 6.6 mmol) in stirred chloroform (20 mL) at 50°C. The white cloudy reaction mixture was refluxed for 4 hours. The reaction mixture was allowed to cool to room temperature. The volatile materials were removed by rotary evaporation to give a white solid residue (1.25 g). This solid residue was recrystallized from hot methanol to yield 5-(4'-methoxy)phenyl-1,3,4-oxathiazole-2-one as colourless clear crystals: mp 114-116°C.
Experimental

(lit mpref 108-110°C); 1.1 g (5.2 mmol, 80 % yield); \(^{1}H\text{--NMR}\) (CDCl\(_3\)) \(\delta\) 3.86 (s, 3H), 6.99 (d, 2H; \(J = 8.8\) Hz), 7.89 (d, 2H; \(J = 8.8\) Hz); \(^{13}C\text{--NMR}\) (CDCl\(_3\)) \(\delta\) 56.0 (+), 114.8 (+), 118.8 (0), 129.7 (+), 157.7 (0), 163.4 (0), 174.7 (0).

3.1.10.2 Synthesis of ethyl 3-(4′-methoxy)phenyl-1,2,4-thiadiazole-5-carboxylate

Ethyl cyanoformate (1.9 mL, 0.46 g, 19 mmol) was added to a three neck flask containing a mixture of 5-(4′-methoxy)phenyl-1,3,4-oxathiazole-2-one (0.98 g, 4.7 mmol) and dodecane (20 mL). The resulting mixture was purged with nitrogen for 30 minutes, then refluxed under nitrogen atmosphere (with sand bath temperature of 220°C) for 13 hours. The reaction flask was allowed to cool to room temperature and placed in an ice bath to allow the brown solid to precipitate. The brown solid was collected by suction filtration (1.1 g) and recrystallized from hot ethanol to give ethyl 3-(4′-methoxy)phenyl-1,2,4-thiadiazole-5-carboxylate as light brown crystal: mp 72-74 °C; 0.82 g (3.1 mmol, 66% yield); \(^{1}H\text{--NMR}\) (CDCl\(_3\)) \(\delta\) 3.86 (s, 3H), 1.45 (t, 3H; \(J = 7.1\) Hz), 4.51 (q, 2H; \(J = 7.1\) Hz), 6.97 (d, 2H; \(J = 8.6\) Hz), 8.28 (d, 2H; \(J = 8.6\) Hz); \(^{13}C\text{--NMR}\) (CDCl\(_3\)) \(\delta\) 14.6 (+), 63.7 (-), 114.5 (+),130.6 (+),125.4 (0), 159.0 (0), 179.1 (0), 162.2 (0), 175.0 (0); MS m/z(%) 264 (M\(^+\); 100), 165 (70.9), 150 (19.1), 133 (50.1), 90 (12.2).

3.1.10.3 Synthesis of 3-(4′-methoxy)phenyl-1,2,4-thiadiazole

A mixture of ethyl 3-(4′-methoxy)phenyl-1,2,4-thiadiazole-5-carboxylate (0.72 g, 2.7 mmol), sodium hydroxide (0.13 g, 3.3 mmol), ethanol (1.5 mL) and water (10 mL) in a
100 mL Erlenmeyer flask was heated with stirring until the ester completely dissolved and maintained at this temperature (60°C) for 1 hour. The reaction solution was cooled to room temperature resulting in the formation of clear crystals. The mixture was acidified by conc. hydrochloric acid to yield 3-(4′-methoxy)phenyl-1,2,4-thiadiazole-5-carboxylic as a white cloudy precipitate. The mixture was reheated and stirred until decarboxylation was complete and a brownish secondary phase was formed. The mixture was extracted with ether (3×10 mL). The ethereal extract was collected and dried over anhydrous sodium sulphate. Ether solvent was removed by rotary evaporation to give a light brown solid residue (0.62 g). The solid residue was recrystallized from warm methanol with addition of water to give 3-(4′-methoxy)phenyl-1,2,4-thiadiazole as a clear colourless crystals: mp 76-78°C; 0.46 g (2.4 mmol; 88 % yield); $^1{\text{H}}$–NMR (CDCl$_3$) $\delta$ 3.86 (s, 3H), 6.99 (d, 2H; J = 8.8 Hz), 8.27 (d, 2H; J = 8.8 Hz), 9.83 (s, 1H); $^{13}{\text{C}}$–NMR (CDCl$_3$) $\delta$ 55.8 (+), 114.5 (+), 125.9 (0), 130.3 (+), 161.9 (0), 172.8 (+), 174.3 (0); MS m/z (%) 192 (M+;100), 165 (71.9), 150 (28.9), 133 (38.7), 90 (14.2).

3.1.11 Synthesis of 3-(4′-cyano)phenyl-1,2,4-thiadiazole

3.1.11.1 Synthesis of 5-(4′-cyano)phenyl-1,3,4-oxathiazole-2-one

A solution of chlorocarbosulphenyl chloride (0.6 ml, 0.87 g, 6.6 mmol) in toluene (3 mL) was added dropwise to a 100 mL round bottom flask containing 4-cyanobenzamide (0.2 g, 1.3 mmol) in toluene (20 mL) with stirring at 50°C. The brown
cloudy reaction mixture was refluxed for 8 hours. The reaction mixture was allowed to cool to room temperature. The volatile materials were removed by rotary evaporation to dryness to give a brown solid residue (0.25 g). This solid residue was recrystallized from dichloromethane-hexane to yield 5-(4′-cyano)phenyl-1,3,4-oxathiazole-2-one as brown clear crystals: mp 173-175°C (lit mp ref 173°C); 0.2 g (71 % yield); \(^1\)H–NMR (CDCl\(_3\)) \(\delta\) 7.79 (d; 2H; \(J = 8.3\) Hz), 8.07 (d, 2H; \(J = 8.3\) Hz); \(^{13}\)C–NMR (CDCl\(_3\)) \(\delta\) 116.1 (0), 117.7 (0), 127.9 (+), 129.3 (0), 132.8 (+), 155.6 (0), 172.8 (0).

3.1.11.2 Synthesis of ethyl 3-(4′-cyano)phenyl-1,2,4-thiaidazole-5-carboxylate

Ethyl cyanoformate (0.5 mL, 5 mmol) was added to a three neck flask containing a mixture of 5-(4′-cyano)phenyl-1,3,4-oxathiazole-2-one (0.2 g, 1 mmol) and dodecane (10 mL). The resulting mixture was purged with nitrogen for 30 min, heated and maintained at sand bath temperature of 180°C under nitrogen atmosphere for 13 hours. The reaction mixture was allowed to cool to room temperature and placed in an ice bath to allow a brown solid to precipitate. The brown solid was collected by suction filtration (0.13 g) and recrystallized from warm dichloromethane with addition of hexane to give ethyl 3-(4′-cyano)phenyl-1,2,4-thiaidazole as light brown crystals: mp 75-78 °C; 0.1 g (0.4 mmol, 40 % yield); \(^1\)H–NMR (CDCl\(_3\)) \(\delta\) 7.78 (d, 2H; \(J = 8.3\) Hz), \(\delta\) 8.47 (d, 2H; \(J = 8.3\) Hz), 4.54 (q, 2H; \(J = 7.1\) Hz), \(\delta\) 1.47 (t, 3H; \(J = 7.1\) Hz); \(^{13}\)C–NMR (CDCl\(_3\)) \(\delta\) 14.6 (+), 64.0 (-), 114.7 (0), 118.8 (0), 129.4 (+), 133.1 (+), 136.0 (0), 158.6 (0), 173.0 (0), 180.1 (0); MS \(m/\epsilon(\%)\) 259 (M\(^+\); 45.8), 187 (13.9), 160 (100), 129 (21.5), 128 (20.8), 102 (9.8).
3.11.13 Synthesis of 3-(4'-cyano)phenyl-1,2,4-thiadiazole

Ethyl 3-(4'-cyano)phenyl-1,2,4-thiadiazole-5-carboxlylate (0.5 g; 2.6 mmol) was stirred in a solution of aqueous sodium bicarbonate (20 mL) and teterhydrofuran (10 mL) at room temperature. TLC analysis (1:1 EtOAc:CH₂Cl₂) showed an absence of the ester after 24 hours. The mixture was acidified by conc. HCl and extracted by chloroform (3×15 mL). The combined organic extract was dried over anhydrous sodium sulphate and concentrated to dryness to give a light yellow solid (420 mg). The yellow solid was analyzed by infrared spectroscopy (neat). The infrared spectrum of this sample revealed a sharp absorption of moderate intensity at 2232 cm⁻¹ and a strong absorption at 1688 cm⁻¹. These are characteristic absorptions for a molecule containing cyano and carbonyl of carboxylic functional groups, respectively. Thus, this infrared spectrum confirmed that hydrolysis of ethyl 3-(4-cyano)phenyl-1,2,4-thiadiazole-5-carboxlylate yielded the desired acid without over-hydrolysis of the cyano functional group. Toluene (20 mL) was added to the yellow solid. The mixture was refluxed and became a homogeneous brown solution after 1 hour. The brown solution was allowed to cool in an ice bath to give brown precipitate (100 mg). The mixture was filtered and the filtrate was concentrated to dryness to give a brown solid residue (250 mg). This solid residue was dissolved in small portion of dichloromethane and subjected to preparative layer chromatography (DCM:EtOAc 4:1). A band with Rf of 0.6 was removed and extracted by ethyl acetate. Ethyl acetate was removed to give a light yellow solid (95 mg). This solid was subjected to sublimation (0.3 torr; 120°C) to give 3-(4'-cyano)phenyl-1,2,4-thiadiazole as a white solid: mp 138-140°C; 0.078 g (0.42 mmol; 16 % yield); $^1$H–NMR (CDCl₃) δ 7.78 (d; 2H; J = 8.3 Hz), 8.45 (d, 2H; J = 8.3 Hz),
Experimental

9.91 (s, 1H); $^{13}$C–NMR (CDCl$_3$) $\delta$ 113.9 (0), 118.5 (0), 128.8 (+), 136.1 (0), 132.6 (+), 172.1 (0), 173.4 (+); MS m/z (%) 187 (M$^+$; 71), 160 (100), 128 (17.2), 102 (11.8), 40 (20).

3.1.12 Synthesis of 5-methyl-3-phenyl-1,2,4-thiadiazole

3.1.12.1 Synthesis of 5-chloro-3-phenyl-1,2,4-thiadiazole

Sodium hydroxide solution (0.7 N, 50 mL) was slowly added, through a dropping funnel, to a 125 mL Erlenmeyer flask containing a solution of benzamidine hydrochloride (1.4 g; 8.9 mmol) in water (10 mL) resulting in a clear solution. Sodium dodecanesulfonate (saturated in water) was added to the clear solution to give a white cloudy mixture. This mixture was stirred in an ice-water bath maintained at 10°C. Perchlomethyl mercaptan (1.2 g; 0.7 mL; 6.4 mmol) was added dropwise to the mixture via a pasture pipette resulting in a pale yellow mixture. The mixture was stirred vigorously at 10°C until the reaction mixture turned to complete yellow cloudy mixture within 2 hours. The cloudy reaction mixture was extracted by ether (2×40 mL). The yellow cloudy ethereal extract was collected, filtered and dried over anhydrous sodium sulfate. This yellow ethereal layer was analyzed by TLC (hexane) revealing the presence of three components with $R_f$ of 0, 0.05 and 0.25 and no perchlomethyl mercaptan residue was observed. Ether was removed by rotary evaporation to give orange viscous liquid (1.2 g). The crude viscous liquid was subjected to a column chromatography (100% hexane). The eluent was collected at 100 mL in the first fraction. Then, 30 mL fractions were collected. Fractions 2-18 were combined. TLC analysis of the combined fractions showed only single spot with $R_f$ of 0.25. Thus, the solvent was removed to give a white solid residue (0.6 g). The solid was recrystallized from
ethanol-water to give 5-chloro-3-phenyl-1,2,4-thiadiazole as white crystals: mp 40-43 °C;
0.52 g (2.6 mmol; 41 % yield); $^1$H–NMR (CDCl$_3$) $\delta$ 7.36-7.43 (m; 3H), 8.15-8.22 (m, 2H);
$^{13}$C–NMR (CDCl$_3$) $\delta$ 128.4 (+), 129.2 (+), 131.3 (+), 132.3 (0), 172.5 (0), 173.4 (0);
MS m/z (%) 196 (M$^+$; 80.3), 197 (p+2; 27.6), 135 (100), 103 (22.6), 77 (16.9).

3.1.12.2 Synthesis of diethyl 3-phenyl-1,2,4-thiadiazole-5-malonate

Small pieces of sodium metal (0.5 g; 21 mmol) were added to a 50 mL round bottom flask containing toluene (10 mL). Diethyl malonate (4 mL; 26 mmol) was added dropwise to the flask resulting in gas evolution and the consumption of sodium metal. 5-Chloro-3-phenyl-1,2,4-thiadiazole (1 g; 5.1 mmol) was added to a clear solution of malonate ester anion to give a yellow solution. The reaction mixture was refluxed for 8 hours. The yellow cloudy mixture was cooled to room temperature and extracted by water (50 mL) and 2N NaOH (50 mL). The aqueous yellow layer was acidified by conc. HCl to give light yellow precipitate (0.45 g). The yellow precipitate was recrystallized from warm methanol to give diethyl 3-phenyl-1,2,4-thiadiazole-5-malonate as light yellow crystals: mp 130-133 °C; 0.4 g (1.2 mmol; 20 % yield); $^1$H–NMR (CDCl$_3$) $\delta$ 1.32-71.41 (m; 6H), 4.25-4.40 (m, 4H), 7.46-7.52 (m, 3H), 7.89-7.92 (m, 2H), 13.74 (s, 1H); $^{13}$C–NMR (CDCl$_3$) $\delta$ 14.3 (+), 14.4 (+), 60.7 (-), 61.1 (-), 85.7 (0), 126.8 (+), 127.5 (0), 129.3 (+), 131.7 (+), 155.2 (0), 167.8 (0), 178.9 (0); $^1$H–$^{13}$C correlation (CDCl$_3$) $\delta^{1H}$ 1.32-71.41 - $\delta^{13C}$ 14.3 and 14.4, $\delta^{1H}$ 4.25-4.40 - $\delta^{13C}$ 60.7 and 61.1, $\delta^{1H}$ 7.46-7.52 - $\delta^{13C}$ 129.3 and 131.7, $\delta^{1H}$ 7.89-7.92 - $\delta^{13C}$ 126.8.
3.12.1.3 Synthesis of 5-methyl-3-phenyl-1,2,4-thiadiazole

Diethyl-3-phenyl-1,2,4-thiadiazole-5-malonate (0.35 g; 1.1 mmol) was added to an aqueous acidic solution (30 mL water acidified by conc. H$_2$SO$_4$). The reaction flask was saturated with nitrogen gas. The mixture was heated under nitrogen atmosphere at 120 °C for 2 hours. The reaction mixture was poured on ice, no white precipitate of the acid product was obtained as expected. Additional conc. H$_2$SO$_4$ was added to the filtrate resulting in the precipitation of a pale yellow solid (0.2 g). The yellow solid was heated in refluxed toluene for 1 hour. Toluene was removed to give a light brown viscous residue. The residue was subjected to preparative chromatography employing 30 % dichloromethane in hexane as an eluent (4 runs). The band at an R$_f$ of 0.33 was removed and extracted with ethyl acetate. The solvent was removed to give 5-methyl-3-phenyl-1,2,4-thiadiazole as a white solid (8 mg); mp 83-85°C; $^1$H–NMR (CDCl$_3$) δ 2.84 (s, 3H), 7.34-7.48 (m; 3H), 8.17-8.27 (m, 2H); $^{13}$C–NMR (CDCl$_3$) δ 17.0, 128.1, 128.7, 130.2, 132.7, 173.1, 186.5; MS m/z (%) 176 (M$^+$; 33.4), 135 (100), 103 (15.4), 77 (19.9).

3.1.13 Synthesis of 2-phenyl-1,3,5-triazine and 2,4-diphenyl-1,3,5-triazine

A mixture of formamidine hydrochloride (2.0 g., 25 mmol) and benzamidine hydrochloride (3.91 g, 25 mmol) was placed in a 25 ml Erlenmeyer flask and stirred vigorously to obtain an intimate mixture. The flask was connected to two glass bulbs. The flask was heated and maintained at 145°C under reduced pressure (20 Torr) in a Kugelrohr oven while the two bulbs were left outside
the oven. The second bulb was placed in a dry-ice bath as a collecting container. A white solid sublimed on the first bulb. The reaction flask was heated until no additional white solid sublimed on the first bulb. The flask was allowed to cool to room temperature. The white solid mixture in the first bulb was transferred to a 500 mL round bottom flask. Water (250 mL) was added to the mixture. The mixture of 2-phenyl- and 2,4-diphenyl-1,3,5-triazine (4.68 g.) was separated by steam distillation. A white solid was distilled out with water and solidified on the condenser. This solid was washed from the condenser by water, filtered and dried over a suction filtration. This white solid was identified as 2-phenyl-1,3,5-triazine: mp 62-64°C; 50 mg. (0.32 mmol, 1 % yield);

\(^1\)H–NMR (CDCl\(_3\)) \(\delta\) 7.73-7.83 (m, 3H), \(\delta\) 8.77-8.79 (m, 2H), \(\delta\) 9.55 (s, 2H); \(^{13}\)C–NMR (CDCl\(_3\)) \(\delta\) 129.30, 129.31, 133.6, 135.3, 166.7, 171.6; \(^{13}\)C–DEPT135 (CDCl\(_3\)) \(\delta\) 129.30(+), 129.31(+), 133.6(+), 166.7(+); MS m/z (%) 157 (M\(^+\); 64.1), 104 (100), 103 (20.3).

The white solid residue left in the flask was filtered and recrystallized from ethanol to yield 2,4-diphenyl-1,3,5-triazine as white needle crystals: mp 80-82°C; 1.4 g. (4.3 mmol, 24 % yield); \(^1\)H–NMR (CDCl\(_3\)) \(\delta\) 7.56-7.63 (m, 6H), \(\delta\) 8.65-8.68 (m, 4H), \(\delta\) 9.28 (s, 1H); \(^{13}\)C–NMR (CDCl\(_3\)) \(\delta\) 128.7, 128.9, 132.8, 135.5, 166.7, 171.3; \(^{13}\)C–DEPT135 (CDCl\(_3\)) \(\delta\) 128.7(+), 128.9(+), 132.8(+), 166.7(+); MS m/z (%) 233 (M\(^+\); 56.7), 104 (10.4), 103 (100).
3.1.14 Synthesis of 2,4-dimethyl-6-phenyl-1,3,5-triazine and 2-methyl-4,6-diphenyl-1,3,5-triazine

3.1.14.1 Synthesis of N-[(dimethylamino)ethylidine]benzamide

N,N-dimethylacetamide dimethylacetal (yellow liquid; 0.87 g., 0.96 mL, 6.5 mmol) was added in a pear-shape flask containing benzamide (0.6 g., 5 mmol). The flask was equipped with a condenser, heated, and maintained at 80°C in an oil bath for 1 hour. Benzamide dissolved after 15 min of heating, the reaction solution turned to dark red and dark solution. The volatile materials were removed by rotary evaporation at room temperature resulting in a viscous dark liquid (0.85 g.). This dark liquid (0.1 g) was attempted to purified by Kugelrohr distillation (100°C, 22 Torr). However, 1H-NMR and GC-MS analysis of the distillate showed identical results to the analytical results before distillation. Therefore, this obtained N-[(dimethylamino)ethylidine]benzamide was employed to the next step synthesis without further purification; 1H–NMR (CDCl3) δ 2.23 (s, 3H), δ 2.97 (s, 3H), δ 3.07 (s, 3H), δ 7.31-7.39 (m, 3H), δ 8.07-8.12 (m, 2H); 13C–NMR (CDCl3) δ 18.7, 38.63, 38.68, 128.2, 129.7, 131.6, 137.9, 165.7, 176.4; 1H–13C correlation (CDCl3) δ1H 2.23 - δ13C 18.7, δ1H 2.97 - δ13C 38.63, δ1H 3.07 - δ13C 38.68, δ1H 7.31-7.39 - δ13C 128.2 and 131.6, δ1H 8.07-8.12 - δ13C 129.7; MS m/z (%) 190 (M+•, 21), 105 (100), 77 (84.2), 44 (84.2).
3.1.14.2 Synthesis of 2,4-dimethyl-6-phenyl-1,3,5-triazine

N-[(dimethylamino)ethylidine]benzamide (dark liquid; 2 mmol, 0.4 g) was placed into three-neck flask containing anhydrous tetrahydrofuran (10 mL) and equipped with a condenser.

Acetamidine hydrochloride (0.8 mmol, 76 mg) was added into a round bottom flask containing sodium methoxide (0.8 mmol) in excess methanol. Acetamidine hydrochloride dissolved and white solid, sodium chloride, precipitated.

Acetamidine solution was added into the three-neck flask. The reaction flask was purged with argon for 30 min, then heated and maintained at 70°C under an argon atmosphere for 16 hours.

The light brown reaction mixture was filtered by suction filtration. The brown filtrate was evaporated to dryness by rotary evaporation at room temperature to give brown solid residue (0.15 g). This crude product (0.15 g) was dissolved in methanol and subjected on a preparative LC plate (hexane : ethyl acetate 1:1). A band at R_t of 0.79 was removed of and extracted from silica gel by ethyl acetate. Ethyl acetate was removed by rotary evaporation to give 2,4-dimethyl-6-phenyl-1,3,5-triazine as a light yellow liquid: 54 mg (0.3 mmol, 15 % yield);

^1H–NMR (CDCl_3) δ 2.67 (s, 6H), δ 7.44-7.55 (m, 3H), δ 8.47-8.52 (m, 2H); ^13C–NMR (CDCl_3) δ 26.2, 129.1, 129.2, 132.9, 136.0, 171.4,176.8 ; ^13C–DEPT135 (CDCl_3) δ 26.2(+), 129.1(+), 129.2(+), 132.9(+); MS m/z (%) 185 (M^{*}; 46.5), 103 (100), 82 (47.3), 42 (33.3).
3.1.14.3 Synthesis of 2-methyl-4,6-diphenyl-1,3,5-triazine

Benzamidine hydrochloride (0.8 mmol, 0.12 g) was added to a round bottom flask containing 0.8 mmol of sodium ethoxide in excess ethanol. Benzamidine hydrochloride dissolved and a white solid precipitated. The mixture was filtered. The filtrate was added to a 25 mL three-neck flask containing N-[(dimethylamino)ethylidene]benzamide (dark liquid; 2 mmol, 0.4 g) and anhydrous tetrahydrofuran (10 mL). The reaction mixture was heated and maintained at 70°C under an argon atmosphere for 16 hours.

The reaction mixture was filtered by suction filtration. The brown filtrate was concentrated by rotary evaporation to give a dark brown residue. A TLC analysis of this residue showed at least three components. The highest spot was presumed to be 2-methyl-4,6-diphenyl-1,3,5-triazine. Therefore, the crude product was subjected to preparative LC plates (0.45 g on each plat). Hexane : Ethyl acetate (4:1) was employed as a solvent system. The highest band at Rf of 0.85 was removed and extracted by ethyl acetate. Ethyl acetate was removed by rotary evaporation to give 2-methyl-4,6-diphenyl-1,3,5-triazine as a white solid: mp 102-104°C; 25 mg (4.0 mmol, 12.5 % yield); $^1$H–NMR (CDCl₃) δ 2.77 (s, 3H), δ 7.50-7.57 (m, 3H), δ 8.61-8.63 (m, 2H); $^{13}$C–NMR (CDCl₃) δ 26.5, 129.1, 129.3, 132.9, 136.3, 171.6, 177.5; $^{13}$C–DEPT135 (CDCl₃) δ 26.2(+), 129.1(+), 129.3(+), 132.9(+); MS m/z (%): 247 (M⁺; 43.8), 103 (100).
3.1.15 Synthesis of 2-(4′-methoxy)phenyl-1,3,5-triazine

3.1.15.1 N,N-[dimethylamino(methylene)]4-methoxybenzamide

N,N-dimethylformamide dimethylacetal (0.6 mL; 5 mmol) was added to a 25 mL round bottom flask containing 4-methoxybenzamide (0.5 g; 3.3 mmol) in tetrahydrofuran (5 mL). The mixture was heated until 4-methoxybenzamide completely dissolved and was maintained at this temperature (~ 70°C) for 2 hours resulting in an orange-brown solution. The volatile materials were removed by rotary evaporation over a warm water bath to give an orange-brown viscous residue. The viscous residue was cooled in an ice bath to solidify as give an orange-brown solid (0.7 g). The orange-brown solid was recrystallized from warm 1-butanol to give N,N-[dimethylamino(methylene)]4-methoxybenzamide as colorless crystals: mp 80-82 °C; 0.58 g (2.8 mmol; 86 % yield); \(^1\)H–NMR (CDCl\(_3\)) \(\delta\) 3.19 (s, 3H), 3.23 (s, 3H), 3.84 (s, 3H), 6.89 (d, 2H; \(J = 8.59\) Hz), 8.23 (d, 2H; \(J = 8.59\) Hz), 8.82 (s, 1H); \(^1\)C–NMR (CDCl\(_3\)) \(\delta\) 35.7 (+), 41.8 (+), 55.8 (+), 113.6 (+), 129.9 (0), 132.2 (+), 160.6 (+), 163.1 (0), 177.6 (0); MS \(m/z\) (%) 206 (M\(^+\); 36.5), 135 (100), 99 (16.5), 77 (20.7).

3.1.15.2 Synthesis of 2-(4′-methoxy)phenyl-1,3,5-triazine

A freshly prepared sodium ethoxide solution (0.05 g Na in 10 mL abs. ethanol) was added to a 25 mL round bottom flask containing formimidine hydrochloride (0.058 g; 0.73 mmol) to give a white cloudy precipitate (NaCl). N,N-[dimethylamino(methylene)](4-methoxy)benzamide (0.15g; 0.73 mmol) in abs. ethanol (10 mL) was added to the reaction flask. The resulting mixture was refluxed and stirred under nitrogen atmosphere for 8 hours.
The reaction mixture was cooled to room temperature and filtered. The yellow filtrate (F1) was concentrated to dryness to give a yellow solid residue (0.11 g). Dichloromethane (10 mL) was added to the residue to give a mixture of colourless crystals in a yellow solution. The crystals were collected by filtration (20 mg) and analyzed by GC-MS and \(^1\)H-NMR while the yellow filtrate (F2) was analyzed by GC-MS. Based on the \(^1\)H-NMR and mass spectroscopic analyses, the colorless crystals were identified as 4-methoxybenzamide.

GC-MS analysis of the yellow filtrate (F2) showed that this solution contained the desired triazine product. The filtrate (F2) was concentrated to give a yellow viscous liquid (80 mg), which was subjected to preparative layer chromatography (EtOAc:Hexane 4:1) resulting in four separated bands with R\(_f\)s of 0, 0.5, 0.85 and 0.96. The band with R\(_f\) of 0.85 was removed and extracted by EtOAc. The solvent was removed to give 2-(4'-methoxy)phenyl-1,3,5-triazine as colorless crystals: mp 115-120 °C; 58 mg (0.31 mmol; 42 % yield); \(^1\)H–NMR (CDCl\(_3\)) \(\delta\) 3.87 (s, 3H), 6.99 (d, 2H; J = 8.84 Hz), 8.46 (d, 2H; J = 8.84 Hz), 9.11 (s, 2H); MS m/z(%) 187 (M\(^+\); 100), 134 (75.9), 133 (18.5), 90 (16.1), 63 (9.9).
3.2 Photochemistry

3.2.1 Photolysis of 5-phenyl-1,2,4-thiadiazole

- **UV-scale photolysis**

Solutions of 5-phenyl-1,2,4-thiadiazole (5.0×10⁻⁵ M) in acetonitrile and cyclohexane were placed in quartz UV cells. Each cell was irradiated with three > 290 nm lamp through a Pyrex filter and monitored by UV-absorption spectroscopy at 60 sec intervals.

- **GC-scale photolysis**

Solutions of 5-phenyl-1,2,4-thiadiazole (2.0×10⁻² M, 4 mL) in acetonitrile and cyclohexane solvents were placed in Pyrex tubes (14 cm × 0.7 cm), sealed with rubber septa and purged with argon gas for 15 min. The solutions were irradiated with sixteen > 290 nm lamps in a Rayonet photochemical reactor. The formation of photoproducts was monitored by removing aliquots for GLC (PE9000) analysis [140 (4 min), 20°C/min to 180°C (14 min), 20°C/min to 240°C (30 min); range 1; attn 16] every 30 min.

Quantitative GLC analysis of photoproducts formation was accomplished using calibration curves constructed for each product by plotting detector responses Vs five standards of known concentrations.

The final reaction solutions were concentrated and analyzed by the GC (HP588) interfaced with a mass spectrometer [140(5 min), 20°C/min to 200°C (20 min), 10°C/min to 240°C (20 min)] to identify the photoproducts formation by comparison of their chromatographic and mass spectroscopic properties with authentic samples.
Table 14 and 15 show the relationship between time Vs peak area of component found in the photolysate of 5-phenyl-1,2,4-thiadiazole in acetonitrile and cyclohexane, respectively.

**Table 14:** Photolysis of 5-phenyl-1,2,4-thiadiazole in acetonitrile

<table>
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<th>Compounds</th>
<th>Time (min)</th>
<th>0</th>
<th>30</th>
<th>60</th>
<th>90</th>
<th>150</th>
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<tr>
<td>1</td>
<td></td>
<td>2785.3±6.1</td>
<td>2153.3±36.2</td>
<td>1596.6±15.3</td>
<td>1277.6±35.6</td>
<td>970.6±10</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td>35.7±2.8</td>
<td>65.5±2.8</td>
<td>138.6±2.1</td>
<td>170.3±4.1</td>
</tr>
<tr>
<td>50</td>
<td></td>
<td></td>
<td>118.3±1.2</td>
<td>193.9±1.3</td>
<td>258.5±4.6</td>
<td>352.3±7.1</td>
</tr>
<tr>
<td>51</td>
<td></td>
<td></td>
<td>41.3±3.0</td>
<td>63.3±1.15</td>
<td>69.6±0.81</td>
<td>78.5±2.3</td>
</tr>
<tr>
<td>52</td>
<td></td>
<td></td>
<td>24.3±1.5</td>
<td>29±0.36</td>
<td>41.1±1.2</td>
<td>52.8±2.5</td>
</tr>
</tbody>
</table>
Table 15: Photolysis of 5-phenyl-1,2,4-thiadiazole in cyclohexane

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Time (min)</th>
<th>0</th>
<th>30</th>
<th>60</th>
<th>90</th>
<th>150</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2393±60.3</td>
<td>2019.9±75.5</td>
<td>1596.6±15.3</td>
<td>1974.3±17.0</td>
<td>1603±20.8</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>-</td>
<td>-</td>
<td>39.6±0.9</td>
<td>69.2±0.75</td>
<td>85.1±2.8</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>-</td>
<td>73.1±2.7</td>
<td>122.3±2.6</td>
<td>176.9±4.9</td>
<td>252.8±8.4</td>
<td></td>
</tr>
<tr>
<td>51</td>
<td>-</td>
<td>-</td>
<td>16.8±0.7</td>
<td>24.1±0.6</td>
<td>32.2±2.6</td>
<td></td>
</tr>
<tr>
<td>52</td>
<td>-</td>
<td>-</td>
<td>trace</td>
<td>trace</td>
<td>trace</td>
<td></td>
</tr>
</tbody>
</table>

3.2.2 Photolysis of 3-phenyl-1,2,4-thiadiazole

- UV-scale photolysis

A solution of 3-phenyl-1,2,4-thiadiazole (5.0×10⁻⁵ M) in cyclohexane was placed in a quartz cell and irradiated with three > 290 nm lamps through a Pyrex filter. The solution was monitored by ultraviolet absorption spectroscopy at 40 seconds intervals.
• **GC-scale photolysis**

A solution of 3-phenyl-1,2,4-thiadiazole (2.0×10⁻² M, 4 mL) in acetonitrile solvent was placed in a Pyrex tube (14 cm × 0.7 cm), sealed with rubber septum and purged with argon gas for 15 min. The solution was irradiated with sixteen > 290 nm lamps in a Rayonet photochemical reactor. The formation of photoproduct was monitored by removing aliquots for GLC (PE9000) analysis [140 (4 min), 15°C/min to 180°C (14 min); range 1; attn 16] every 15 min.

Benzonitrile was identified by GC (HP588) interfaced with a mass spectrometer [140°C (5 min), 20°C/min to 250°C (14 min)] as the only gc-volatile photoproduct. Quantitative GLC (PE9000) analysis of benzonitrile was accomplished by using the calibration curve previously constructed.

Table 16 shows relationship between time Vs peak area of photolysis of 3-phenyl-1,2,4-thiadiazole in acetonitrile.

**Table 16: Photolysis of 3-phenyl-1,2,4-thiadiazole in acetonitrile**

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>2406.6±68.9</td>
</tr>
<tr>
<td>50</td>
<td>-</td>
</tr>
</tbody>
</table>
3.2.3 Photolysis of 3-methyl-5-phenyl-1,2,4-thiadiazole

- **UV scale photolysis**

A solution of 3-methyl-5-phenyl-1,2,4-thiadiazole (6.0×10⁻⁵ M) in acetonitrile was placed in a UV quartz cell and the UV absorption spectrum recorded. The solution was irradiated with three > 290 nm lamps through a Pyrex filter. The reaction was monitored by ultraviolet absorption spectroscopy at 40 sec intervals for a total of 400 sec.

- **GC-scale photolysis**

Solutions of 3-methyl-5-phenyl-1,2,4-thiadiazole (2.0×10⁻² M, 4 mL) in acetonitrile and methanol solvents were placed in Pyrex tubes (14 cm × 0.7 cm), sealed with rubber septa and purged with argon gas for 15 min. The solutions were irradiated with sixteen > 290 nm lamps in a Rayonet photochemical reactor. The formation of photoproducts was monitored by removing aliquots for GLC (PE9000) analysis [140 (4 min), 10°C/min to 240°C (20 min); range 1; attn 16] every 40 min.

Quantitative GLC (PE9000) analysis of the photoproducts formation was accomplished by using calibration curves constructed for each product by plotting detector responses Vs five standard known concentrations.

The final reaction solutions were concentrated and analyzed by the GC (HP588) interfaced with GC [140°C (5 min), 20°C/min to 200°C (20 min), 10°C/min to 240 (20 min)] to identify the formation of photoproducts by comparison of chromatographic and mass spectroscopic properties with authentic samples.

Tables 17 and 18 show the relationship between time Vs peak area of photolysis of 3-methyl-5-phenyl-1,2,4-thiadiazole in acetonitrile and methanol, respectively.
Table 17: Photolysis of 3-methyl-5-phenyl-1,2,4-thiadiazole in acetonitrile

<table>
<thead>
<tr>
<th>Compounds</th>
<th>0</th>
<th>30</th>
<th>70</th>
<th>110</th>
<th>150</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>3895.7±13.5</td>
<td>2859.4±39.5</td>
<td>1828.8±20.9</td>
<td>1340.5±26.6</td>
<td>923.8±11.9</td>
</tr>
<tr>
<td>53</td>
<td>-</td>
<td>83.5±2.7</td>
<td>168.1±6.1</td>
<td>428.6±8.4</td>
<td>347.9±13.6</td>
</tr>
<tr>
<td>50</td>
<td>-</td>
<td>382.4±7.9</td>
<td>733.0±16.3</td>
<td>1011.3±5.8</td>
<td>1181.9±31.6</td>
</tr>
<tr>
<td>54</td>
<td>-</td>
<td>306.25±5.4</td>
<td>534.55±9.8</td>
<td>769.5±4.6</td>
<td>855.8±18.3</td>
</tr>
<tr>
<td>55</td>
<td>-</td>
<td>47.8±3.5</td>
<td>100.0±1.9</td>
<td>150.5±12.4</td>
<td>196.6±4.5</td>
</tr>
</tbody>
</table>

Table 18: Photolysis of 3-methyl-5-phenyl-1,2,4-thiadiazole in methanol

<table>
<thead>
<tr>
<th>Compounds</th>
<th>0</th>
<th>30</th>
<th>90</th>
<th>150</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>4022±33.9</td>
<td>3520.4±47.8</td>
<td>2797.5±10.6</td>
<td>2227.7±44.2</td>
</tr>
<tr>
<td>53</td>
<td>-</td>
<td>73.7±2.7</td>
<td>311.5±8.3</td>
<td>397.4±2.5</td>
</tr>
<tr>
<td>50</td>
<td>-</td>
<td>108.1±3.8</td>
<td>398.9±8.8</td>
<td>694.9±5.8</td>
</tr>
<tr>
<td>54</td>
<td>-</td>
<td>trace</td>
<td>trace</td>
<td>25.6±4.2</td>
</tr>
<tr>
<td>55</td>
<td>-</td>
<td>trace</td>
<td>trace</td>
<td>trace</td>
</tr>
</tbody>
</table>
3.2.4 Photolysis of 5-phenyl-1,2,4-thiadiazole-4-$^{15}$N

A solution of 5-phenyl-1,2,4-thiadiazole–$^{15}$N (4 mL, $3\times10^{-2}$ M) was placed in a Pyrex tube (14 cm × 0.7 cm), sealed with a septum and purged with argon gas for 15 min. The solution was irradiated by sixteen > 290 nm lamps and monitored by GLC (PE9000) every 30 min for 180 min. The final reaction solution was concentrated and analyzed by GC-MS [140°C (5 min), 20°C/min to 240°C (20 min)].

The reaction was also carried out at a shorter period of irradiation. A solution of 5-phenyl-1,2,4-thiadiazole–$^{15}$N (4 mL, $3\times10^{-2}$ M) was placed in a Pyrex tube (14 cm × 0.7 cm), sealed with a septum and purged with argon gas for 15 min. The solution was irradiated by sixteen > 290 nm lamps and monitored by GLC (PE9000) every 4 min for a total of 16 min. Aliquots of the reaction solution were removed after every 4 min of irradiation, concentrated, and analyzed by GC-MS [140°C (5 min), 20°C/min to 240°C (20 min)].

Table 19: Time (min) $V_s$ ratio of 103/104 peaks of benzonitrile-photoproduct

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Inj.no.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Average</th>
<th>STDEV</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>0.15</td>
<td>0.2</td>
<td>0.1</td>
<td>0.17</td>
<td>0.23</td>
<td>0.17</td>
<td>0.17</td>
<td>±0.05</td>
</tr>
<tr>
<td>4</td>
<td>0.25</td>
<td>0.25</td>
<td>0.23</td>
<td>0.25</td>
<td>-</td>
<td>0.245</td>
<td>±0.01</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>0.30</td>
<td>0.27</td>
<td>0.27</td>
<td>0.27</td>
<td>0.30</td>
<td>0.28</td>
<td>±0.02</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>-</td>
<td>0.30</td>
<td>0.33</td>
<td>0.30</td>
<td>0.31</td>
<td>0.31</td>
<td>±0.01</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>0.31</td>
<td>0.38</td>
<td>(0.5)</td>
<td>0.31</td>
<td>-</td>
<td>0.33</td>
<td>±0.04</td>
<td></td>
</tr>
</tbody>
</table>
**Table 20:** Time (min) Vs ratio of 158/159 peaks of 2-phenyl-1,3,5-triazine-photoprodct

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Average</th>
<th>STDEV</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>-</td>
<td>0.64</td>
<td>0.62</td>
<td>0.78</td>
<td>-</td>
<td>0.68</td>
<td>±0.09</td>
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<tr>
<td>8</td>
<td>0.79</td>
<td>0.76</td>
<td>0.75</td>
<td>0.76</td>
<td>0.74</td>
<td>0.76</td>
<td>±0.02</td>
</tr>
<tr>
<td>12</td>
<td>0.68</td>
<td>0.71</td>
<td>0.78</td>
<td>0.75</td>
<td>0.75</td>
<td>0.73</td>
<td>±0.04</td>
</tr>
<tr>
<td>16</td>
<td>0.76</td>
<td>0.76</td>
<td>0.79</td>
<td>0.76</td>
<td>-</td>
<td>0.77</td>
<td>±0.01</td>
</tr>
</tbody>
</table>

**Table 21:** Time (min) Vs ratio of 135/136 peaks of un-consumed 5-phenyl-1,2,4-thiadiazole-4\textsuperscript{15}N

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Average</th>
<th>STDEV</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.01</td>
<td>0.01</td>
<td>0.02</td>
<td>0.02</td>
<td>-</td>
<td>0.015</td>
<td>±0.005</td>
</tr>
<tr>
<td>2</td>
<td>-</td>
<td>-</td>
<td>0.02</td>
<td>-</td>
<td>-</td>
<td>0.02</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>-</td>
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<td>0</td>
</tr>
<tr>
<td>8</td>
<td>0.02</td>
<td>0.02</td>
<td>0.02</td>
<td>(0.04)</td>
<td>0.02</td>
<td>0.02</td>
<td>0</td>
</tr>
<tr>
<td>12</td>
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<td>0.08</td>
<td>0.08</td>
<td>-</td>
<td>0.08</td>
<td>0</td>
</tr>
</tbody>
</table>
### Table 22: Time (min) Vs ratio of 135/136 peaks of 3-phenyl-1,2,4-thiadiazole-photoproduct

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Inj.no.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Average</th>
<th>STDEV</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>0.91</td>
<td>0.82</td>
<td>0.88</td>
<td>1.03</td>
<td>0.86</td>
<td>0.9</td>
<td>± 0.08</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>0.84</td>
<td>0.89</td>
<td>1.03</td>
<td>0.9</td>
<td>-</td>
<td>0.91</td>
<td>± 0.08</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>0.97</td>
<td>0.94</td>
<td>0.97</td>
<td>0.94</td>
<td>-</td>
<td>0.95</td>
<td>± 0.02</td>
<td></td>
</tr>
</tbody>
</table>

### Table 23: Time (min) Vs ratio of 234/235 peaks of 2,4-diphenyl-1,3,5-triazine-photoproduct

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Inj.no.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Average</th>
<th>STDEV</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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</tr>
<tr>
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<td>-</td>
<td>-</td>
<td>-</td>
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<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>8</td>
<td>-</td>
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<td>-</td>
<td>-</td>
</tr>
<tr>
<td>12</td>
<td>-</td>
<td>1.18</td>
<td>0.95</td>
<td>1.19</td>
<td>0.92</td>
<td>1.06</td>
<td>± 0.14</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>0.96</td>
<td>0.91</td>
<td>0.91</td>
<td>0.91</td>
<td>-</td>
<td>0.92</td>
<td>± 0.03</td>
<td></td>
</tr>
</tbody>
</table>
Experimental

- **Preparative scale photolysis**

5-Phenyl-1,2,4-oxadiazole-4-$^{15}$N was identified as a minor component in the synthesized 5-phenyl-1,2,4-thiadiazole-4-$^{15}$N. Thus, this sample (0.5 g) was further purified by preparative gas chromatography (isothermal 170°C) by using Carbowax 20 M as a stationary phase. The purified 5-phenyl-1,2,4-thiadiazole-4-$^{15}$N was collected as a white clear viscous liquid (0.38 g). This $^{15}$N labeled–thiadiazole was employed as a starting material in the preparative scale photolysis.

- **Preparative gas chromatography: packing material preparation**

Chloroform (100 mL) was added to Carbowax 20 M (1.5 g). The mixture was stirred at room temperature for 3 hours. Carbowax 20 M solution was poured on to the chromosorb G powder (48.5 g). The mixture was continuously stirred while the temperature was slightly increased to evaporate chloroform to a dry mixture. The resulted powder was dried overnight in an oven at 60°C.

- **Preparative gas chromatography: isolation of 5-phenyl-1,2,4-oxadiazole-4-$^{15}$N**

The isolation was performed on Perkin Elmer 3920 gas chromatography at 170°C oven temperature. 5-Phenyl-1,2,4-oxadiazole-4-$^{15}$N eluted with a retention time of 6 min. 5-Phenyl-1,2,4-thiadiazole-4-$^{15}$N had a retention time of 9.5 min and was collected in a tube, which was placed in an ice-water bath, as a white solid. This solid melted at room temperature to give a clear viscous liquid.
Preparative scale photolysis

A solution of un-purified 5-phenyl-1,2,4-thiadiazole-4-\textsuperscript{15}N (1.8×10\textsuperscript{-2} M, 25 mL) was placed in a Pyrex tube (30 cm × 1.0 cm), sealed with a septum and purged with argon for 60 min, and irradiated with sixteen > 290 nm lamps for 180 min with 58 % consumption of the reactant in order to maximize the formation of 3-phenyl-1,2,4-thiadiazole-photoproduct which was identified with 20 % formation. The solution was purged with fine steam argon during the photolysis. The final reaction solution turned to light brown clear solution. The solution was concentrated to give a dark brown viscous liquid. The un-consumed reactant and the phototransposition product, 3-phenyl-1,2,4-thiadiazole-\textsuperscript{15}N, were isolated from the crude reaction by preparative gas chromatography at 170°C oven temperature with retention times of 17 and 9.5 min, respectively. These two eluted compounds were analyzed by \textsuperscript{1}H-, \textsuperscript{13}C-, \textsuperscript{15}N-NMR spectroscopy (acetone-d\textsubscript{6}) and GC-MS. The results indicated that the eluted un-consumed reactant was containing phenyl-s-triazine-\textsuperscript{15}N, thus, this sample was further purified by preparative thin layer chromatography.

Thin layer chromatography: purification of the isolated un-consumed reactant

The collected un-consumed reactant was removed from a collection tube by washing with acetone. The solution was concentrated (34 mg) and subjected on a preparative layer chromatographic plate. Hexane:chloroform (3:2) was employed as a mobile phase. The higher band with a R\textsubscript{f} of 0.8 (10 runs) was removed and extracted with ethyl acetate. Ethyl acetate was removed by rotary evaporation to give the un-consumed reactant as a white solid (8 mg). This sample was analysed by \textsuperscript{1}H-, \textsuperscript{15}N-NMR spectroscopy (acetone-d\textsubscript{6}) and GC-MS.
Isolation of the phototransposition product and the un-consumed reactant was also performed by preparative layer chromatography. A solution of purified 5-phenyl-1,2,4-thiadiazole-4-$^{15}$N ($2 \times 10^{-2}$ M, 8 mL) was photolysed to 40% consumption of the reactant. The reaction solution was concentrated to dryness (42 mg). Small amount of dichloromethane was added to dissolve the residue. The residue was subjected to preparative scale chromatography using hexane:dichloromethane (1:4). The phototransposition product, 3-phenyl-1,2,4-thiadiazole-$^{15}$N, and the un-consumed reactant were removed with a $R_f$ of 0.7 (4 runs) and 0.4 (4 runs), respectively, and extracted by ethyl acetate. Ethyl acetate was removed from both sample by rotary evaporation to yield both compounds as white solids. These two samples were analyzed by $^1$H-, $^{15}$N-NMR spectroscopy (acetone-$d_6$).

### 3.2.5 Photolysis of 3-methyl-5-phenyl-1,2,4-thiadiazole-4-$^{15}$N

A solution of 3-methyl-5-phenyl-1,2,4-thiadiazole-4$^{15}$N (4 mL, $2.5 \times 10^{-2}$ M) was placed in a Pyrex tube (12 cm $\times$ 0.7 cm), sealed with a septum and purged with argon gas for 15 min. The solution was irradiated by sixteen $> 290$ nm lamps, monitored by GLC (PE9000) and GC-MS every 2 min for a total of 18 min. In order to monitor the reaction by GC-MS, aliquots of the reaction solution were removed after every 4 min of irradiation, concentrated, and analyzed by GC-MS [140°C (5 min), 20°C/min to 240°C (20 min)].
Table 24: Time (min) Vs. ratio of 103/104 peaks of benzonitrile-photoproduct

<table>
<thead>
<tr>
<th>Time</th>
<th>Inj.no.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Average</th>
<th>STDEV</th>
</tr>
</thead>
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<td>-</td>
<td>-</td>
<td>-</td>
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<td>-</td>
<td>-</td>
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<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>-</td>
<td>0.81</td>
<td>0.83</td>
<td>0.83</td>
<td>0.85</td>
<td>0.83</td>
<td>±0.02</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>0.89</td>
<td>0.83</td>
<td>0.81</td>
<td>0.83</td>
<td>0.85</td>
<td>0.84</td>
<td>±0.03</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>0.85</td>
<td>(0.92)</td>
<td>0.88</td>
<td>0.88</td>
<td>0.83</td>
<td>0.86</td>
<td>±0.02</td>
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<tr>
<td>18</td>
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<td>0.79</td>
<td>0.83</td>
<td>0.77</td>
<td>0.79</td>
<td>0.80</td>
<td>±0.02</td>
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Table 25: Time (min) Vs. of 186/187 ratio of 2,4-dimethyl-6-phenyl-1,3,5-triazine-photoproduct

<table>
<thead>
<tr>
<th>Time</th>
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<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Average</th>
<th>STDEV</th>
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<td>0</td>
<td>0</td>
<td>0</td>
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<td>0</td>
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<td>0</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>-</td>
<td>0.64</td>
<td>0.62</td>
<td>0.78</td>
<td>-</td>
<td>0.68</td>
<td>±0.09</td>
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</tr>
<tr>
<td>8</td>
<td>0.79</td>
<td>0.76</td>
<td>0.75</td>
<td>0.76</td>
<td>0.74</td>
<td>0.76</td>
<td>±0.02</td>
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<tr>
<td>12</td>
<td>0.68</td>
<td>0.71</td>
<td>0.78</td>
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<td>0.75</td>
<td>0.73</td>
<td>±0.04</td>
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<tr>
<td>16</td>
<td>0.76</td>
<td>0.76</td>
<td>0.79</td>
<td>0.76</td>
<td>-</td>
<td>0.77</td>
<td>±0.01</td>
<td></td>
</tr>
</tbody>
</table>
Table 26: Time (min) $Vs$ of 135/136 ratio of un-consumed 3-methyl-5-phenyl-1,2,4-thiadiazole-4$^{15}$N

<table>
<thead>
<tr>
<th>Time</th>
<th>Inj.no.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Average</th>
<th>STDEV</th>
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<td>0</td>
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<td>0.021</td>
<td>0</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
<td>0.006</td>
<td></td>
</tr>
<tr>
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<td>0.05</td>
<td>0.63</td>
<td>0.063</td>
<td>0.063</td>
<td>0.063</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
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<td></td>
<td>0.083</td>
<td>0.83</td>
<td>0.083</td>
<td>0.083</td>
<td>0.083</td>
<td>0.006</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td></td>
<td>0.083</td>
<td>0.83</td>
<td>0.083</td>
<td>0.083</td>
<td>0.083</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td></td>
<td>0.11</td>
<td>0.11</td>
<td>0.11</td>
<td>0.11</td>
<td>0.11</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td></td>
<td>0.11</td>
<td>0.11</td>
<td>0.11</td>
<td>0.11</td>
<td>0.11</td>
<td>0.000</td>
<td></td>
</tr>
</tbody>
</table>

Table 27: Time (min) $Vs$ of 135/136 ratio of 5-methyl-3-phenyl-1,2,4-thiadiazole-photoproduct

<table>
<thead>
<tr>
<th>Time</th>
<th>Inj.no.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Average</th>
<th>STDEV</th>
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<td>-</td>
<td>-</td>
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<td>-</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>0.94</td>
<td>0.94</td>
<td>0.91</td>
<td>(0.85)</td>
<td>-</td>
<td>0.93</td>
<td>±0.01</td>
</tr>
<tr>
<td>10</td>
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<td>0.94</td>
<td>(0.79)</td>
<td>0.98</td>
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</tr>
<tr>
<td>14</td>
<td></td>
<td>0.94</td>
<td>0.92</td>
<td>0.89</td>
<td>0.92</td>
<td>-</td>
<td>0.92</td>
<td>±0.02</td>
</tr>
<tr>
<td>18</td>
<td></td>
<td>0.94</td>
<td>0.95</td>
<td>0.95</td>
<td>0.98</td>
<td>-</td>
<td>0.96</td>
<td>±0.02</td>
</tr>
</tbody>
</table>
Table 28: Time (min) Vs of 248/249 ratio of 2-methyl-4,6-diphenyl-1,3,5-triazine-photoproduct

<table>
<thead>
<tr>
<th>Time</th>
<th>Inj.no.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Average</th>
<th>STDEV</th>
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<tbody>
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<td>0</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<td>-</td>
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<td>-</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>-</td>
<td>0.68</td>
<td>(0.63)</td>
<td>0.75</td>
<td>0.8</td>
<td>0.74</td>
<td>±0.06</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>0.79</td>
<td>0.79</td>
<td>0.79</td>
<td>0.79</td>
<td>0.79</td>
<td>0.79</td>
<td>±0.00</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>0.81</td>
<td>0.82</td>
<td>0.79</td>
<td>0.83</td>
<td>0.81</td>
<td>0.81</td>
<td>±0.01</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>0.81</td>
<td>0.81</td>
<td>0.81</td>
<td>0.81</td>
<td>0.81</td>
<td>0.81</td>
<td>±0.00</td>
<td></td>
</tr>
</tbody>
</table>

- **Preparative scale photolysis**

A solution of 3-methyl-5-phenyl-1,2,4-thiadiazole-4\(^{15}\)N in methanol (2.06×10\(^{-2}\) M; 25 mL) was placed in a Pyrex tube (30 cm × 1.0 cm), sealed with a septum and purged with argon gas for 60 min, and irradiated with sixteen > 290 nm lamps for 640 min with 50 % consumption of the reactant. The final reaction solution turned to light brown clear solution. The solution was purged with low pressure steam argon gas during the reaction.

Fifty percent of the solvent was removed from the reaction solution. Fine yellow solid precipitated and was filtered out of the solution. The filtrate was concentrated by rotary evaporation to give dark brown residue (0.1 g). Small amount of dichloromethane was added to the residue. The sample was subjected to column chromatography (diameter : 1.5 cm) packed with 8.0 g of silica gel (12 cm) in hexane:dichloromethane (3:2). The first fraction was collected for 40 mL followed by 10 mL fraction collection. The polarity of solvent system was increased from hexane:dichloromethane→100%
dichloromethane → dichloromethane:ethyl acetate → 100% ethyl acetate. Finally, 100% ethanol was employed to elute a yellow band at the base line.

The first to fifth fractions were combined according to the TLC results, which showed only one spot. The sixteenth to eighteen fractions were combined due to the TLC results indicating the presence of the starting material. The nineteenth and twentieth fractions were combined since these fractions contained the same yellow solution and the TLC results also showed the presence of same components. The yellow band at the base line was eluted by 100% ethanol and collected as the fortieth fraction.

The solvents from every combinational fractions were removed on a rotary evaporation. The sample in each fraction was dissolved in CDCl₃ and analyzed by ¹H-, ¹³C-, ¹⁵N-NMR spectroscopy and GC-MS.

### 3.2.6 Photolysis of 5-phenyl-1,2,4-thiadiazole in the presence of ethyl cyanoformate

A solution of 5-phenyl-1,2,4-thiadiazole (2.0×10⁻² M, 4 mL) and ethyl cyanoformate (0.1 mL, 1×10⁻¹ M) in acetonitrile was placed in a Pyrex tube and a quartz tube, sealed with rubber septa, purged with argon gas for 30 min. The solution in a Pyrex tube was irradiated with sixteen > 290 nm lamps and the solution in a quartz tube was irradiated with eight 254 nm lamps. The reactions were monitored by GLC [120°C (5 min), 20°C/min to 160°C (8 min), 20°C/min to 240°C (20 min)] every 30 min of irradiation. Aliquots of the solution in a quartz tube at 60 min and 90 min for the solution in a Pyrex tube were removed, concentrated, and analyzed by GC-MS [(140°C (5 min), 20°C/min to 240°C (20 min)]. The solution in a Pyrex tube was photolysed for 150 min while the solution in a quartz tube was photolysed for 90 min. Aliquots of the final solution in the quartz tube and Pyrex tube
were removed, spiked with an authentic ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate solution and analyzed by GLC. The final clear yellow solutions were concentrated by rotary evaporation and analyzed by GC-MS and co-injection GC-MS analysis.

### 3.2.7 Photolysis of 3-phenyl-1,2,4-thiadiazole in the presence of ethyl cyanoformate

A solution of 3-phenyl-1,2,4-thiadiazole (2.0×10⁻² M, 4 mL) in acetonitrile containing ethyl cyanoformate (0.1 mL, 1×10⁻¹ M) was placed in a Pyrex tube and a quartz tube, sealed with rubber septa, purged with argon for 30 min. The solution in a Pyrex tube was irradiated with sixteen > 290 nm lamps and the solution in a quartz tube was irradiated with eight 254 nm lamps. The reactions were monitored by GLC [120°C (5 min), 20°C/min to 240°C (20 min)] every 30 min of irradiation. Aliquots of the solution in a quartz tube at 60 min and 90 min for the solution in a Pyrex tube were removed, concentrated, and analyzed by GC-MS [(140°C (5 min), 20°C/min to 240°C (20 min)]. The solution in a Pyrex tube was photolysed for 300 min while the solution in a quartz tube was photolysed for 120 min. Aliquots of the final solution in a quartz tube and Pyrex tube were removed, spiked with ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate solution and performed co-injection GLC analysis. The final white cloudy solutions were concentrated by rotary evaporation and analyzed by GC-MS and co-injection GC-MS analysis.
3.2.8 Photolysis of a mixture of 3methyl-5-phenyl-1,2,4-thiadiazole and 5-phenyl-1,2,4-thiadiazole

- **Synthesis of 2-methyl-4-phenyl-1,3,5-triazine**

The triazine, 2-methyl-4-phenyl-1,3,5-triazine, was expected to form in this cross coupling experiment. Thus, it was synthesized as an authentic sample.

A freshly prepared sodium methoxide solution (0.2 g Na / 10 mL abs. methanol) was slowly added through a dropping funnel to a three neck flask containing an acetamidine hydrochloride (0.2 g; 2.4 mmol) in 5 mL abs. methanol to give a white cloudy mixture. N-[(dimethylamino)methylene]benzamide solution (0.5 g; 2.4 mmol) in 10 mL abs. methanol was added to the mixture through a septum. The mixture was refluxed under a nitrogen atmosphere for 16 hours. The white cloudy mixture was filtered. The filtrate was concentrated to give a pale red-orange solid (0.32 g). TLC analysis (EtOAc:hexane 1:1) showed three spots with Rfs of 0.76, 0.4 and 0. The crude red-orange solid (0.32 g) was dissolved in methanol and subjected on preparative layer chromatography (10% hexane in EtOAc; 2 runs). The band with Rf of 0.6 was removed and extracted by ethyl acetate. Ethyl acetate was removed to give 2-methyl-4-phenyl-1,3,5-triazine as a colorless viscous liquid: 0.14 g (0.82 mmol; 34.1 % yield); **¹H–NMR** (CDCl₃) δ 2.71 (s, 3H), δ 7.47-7.57 (m, 3H), 8.47-8.51 (m, 2H), 9.17 (s, 1H); **MS m/z(%)** 171 (M⁺; 99.2), 130 (13.2), 104 (39.3), 103 (100), 76 (36.4), 68 (75.9).
Experimental

- **Irradiation of the mixture**

The mixture of 5-phenyl-1,2,4-thiadiazole and 3-methyl-5-phenyl-1,2,4-thiadiazole (3.5 mL), the solution of 5-phenyl-1,2,4-thiadiazole (3.5 mL), and the solution of 3-methyl-5-phenyl-1,2,4-thiadiazole (3.5 mL) in acetonitrile each in sealed Pyrex tubes were purged with argon for 15 min. These solutions were then irradiated simultaneously with fifteen > 290 nm lamps for a total of 650 min. The reactions were monitored by GLC (PE9000) analysis after every 120 min of irradiation. The photolysate of the mixed thiadiazole was also analyzed by GC (HP588) interfaced with a mass spectrometer. An authentic sample of 2-methyl-4-phenyl-1,3,5-triazine was also analyzed by GLC (PE9000) and GC (HP588) interfaced with a mass spectrometer under the same analytical conditions. Aliquots of the final solution after 650 min of irradiation were removed, spiked with an authentic sample of 2-methyl-4-phenyl-1,3,5-triazine and analyzed employing GLC (PE9000) and GC (HP588) interfaced with a mass spectrometer.

### 3.2.9 Photochemistry of phenyl substituted-1,2,4-thiadiazoles in furan solvent

- **Analytical scale photolysis; irradiation of 5-phenyl-, 3-methyl-5-phenyl- and diphenyl-1,2,4-thiadiazole in neat furan**

Solutions of each thiadiazole in furan (\( \sim 2 \times 10^{-2} \) M; 3.5 mL) and in acetonitrile (\( \sim 2 \times 10^{-2} \) M; 3.5 mL) in sealed Pyrex tubes were purged with argon gas for 20 min. These solutions were simultaneously irradiated with sixteen > 290 nm lamps in a Rayonet reactor for a total of 120 min. All photolysates were analyzed by GLC (PE9000) and GC...
Experimental

(HP588) interfaced with a mass spectrometer. The photolysates were concentrated by rotary evaporation at room temperature and analyzed by GC (HP588) interfaced with a mass spectrometer.

- **Analytical scale photolysis; irradiation of 5-phenyl-1,2,4-thiadiazole in acetonitrile at various furan concentrations**

  Solutions of 5-phenyl-1,2,4-thiadiazole (1.7×10\(^{-2}\) M; 5 mL) in acetonitrile with the presence of furan from 0-90% were sealed in Pyrex tubes, purged with a fine steam argon gas for 15 min and simultaneously irradiated with sixteen > 290 nm lamps in a Rayonet reactor. The photoreactions were monitored by GLC (PE9000) at 60 min intervals. The plots between the peak area of the product in the absence of furan divided by the peak area of the product observed at the various furan concentrations were constructed.

- **Preparative scale photolysis of diphenyl-1,2,4-thiadiazole in furan solvent**

  Solution of 3,5-diphenyl-1,2,4-thiadiazole in neat furan (2×10\(^{-2}\) M; 25 mL) in a sealed Pyrex tube was irradiated with sixteen > 290 nm lamps for a total of 360 min. The reaction solution was concentrated by rotary evaporation to give a dark brownish residue. The brown residue (120 mg) was subjected to a column chromatography (column; 0.5 × 30 cm, silica gel 12 g). The column was eluted with ethyl acetate-hexane 3:7. Each fraction was analyzed by the GC (HP588) interfaced with a mass spectrometer. Mass spectra analysis indicated that that component in fraction 7 had a molecular ion at m/z 274 corresponded to the molecular ion of the 1:1 adduct of diphenyl-1,2,4-thiadiazole and furan minus the sulfur atom. Thus, fraction 7 was concentrated to give a yellow viscous liquid. This sample was
Experimental

Dissolved in CDCl₃ and analyzed by ¹H-, ¹³C-NMR, and the GC (HP588) interfaced with a mass spectrometer.

- **Analytical scale photolysis; irradiation of 3-phenyl-1,2,4-thiadiazole in neat furan**

Solutions of 3-phenyl-1,2,4-thiadiazole in furan (1.1×10⁻² M; 4 mL) and in acetonitrile (1.1×10⁻² M; 4 mL) in sealed Pyrex tubes were purged with argon gas for 15 min. These solutions were simultaneously irradiated with sixteen > 290 nm lamps in a Rayonet reactor for a total of 120 min. The photolysates after 120 min of irradiation were analyzed by the GC (HP588) interfaced with a mass spectrometer. The photolysates were concentrated by rotary evaporation at room temperature and analyzed by the GC (HP588) interfaced with a mass spectrometer.

- **Analytical scale photolysis; irradiation of 3-phenyl-1,2,4-thiadiazole in acetonitrile at various furan concentrations**

Solutions of 3-phenyl-1,2,4-thiadiazole in acetonitrile (1.1×10⁻² M; 4 mL) with the presence of furan from 0%-90% were placed in Pyrex tubes, sealed with rubber septa and purged with argon gas for 15 min. The solutions were simultaneously irradiated by sixteen > 290 nm lamps in a Rayonet reactor. The photoreactions were monitored by GLC (PE9000) at 30 min of intervals. Plot of the furan concentrations Vs the peak area of benzonitrile in the absence of furan divided by the peak area of benzonitrile observed at the various furan concentrations after 60 min of irradiation was constructed.
Experimental

- **Analytical scale photolysis; irradiation of 3-phenyl-1,2,4-thiadiazole in tetrahydrofuran solvent**

Solutions of 3-phenyl-1,2,4-thiadiazole in tetrahydrofuran (1×10^{-2} M; 3.5 mL) and in acetonitrile (1×10^{-2} M; 3.5 mL) in sealed Pyrex tubes were purged with argon gas for 20 min. These solutions were simultaneously irradiated with sixteen > 290 nm lamps in a Rayonet reactor for a total of 90 min. The reactions were analyzed by GLC (PE9000) and GC (HP588) interfaced with a mass spectrometer. The photolysates after 90 min of irradiation were concentrated by rotary evaporation at room temperature and analyzed by the GC interfaced with a mass spectrometer.

- **Analytical scale photolysis; irradiation of 3-phenyl-1,2,4-thiadiazole in acetonitrile at various tetrahydrofuran concentrations**

Solutions of 3-phenyl-1,2,4-thiadiazole in acetonitrile (1.1×10^{-2} M; 4 mL) containing tetrahydrofuran from 0%-90% were placed in Pyrex tubes, sealed with rubber septa and purged with argon gas for 15 min. The solutions were simultaneously irradiated by sixteen > 290 nm lamps in a Rayonet reactor equipped with a merry-go-round apparatus. The photoreactions were monitored by GLC at 30 min of intervals. Plots between tetrahydrofuran concentrations Vs the peak area of benzonitrile in an absence of tetrahydrofuran divided by the peak area of benzonitrile observed at various tetrahydrofuran concentrations after 30 min of irradiation was constructed. A similar plot for the consumption of starting material at various tetrahydrofuran concentrations was also constructed.
3.2.10 Photochemistry of 5-(4′-substituted)phenyl- and 3-(4′-substituted)phenyl-1,2,4-thiadiazoles

- **UV scale photolysis**

  UV-absorption spectra of each thiadiazole solution (~ $10^{-5}$ M) in acetonitrile and cyclohexane in a quartz cell were recorded. These solutions were irradiated with three > 290 nm lamps through a Pyrex filter. The reactions were monitored by UV-absorption spectroscopy.

- **GC-scale photolysis**

  Solutions of each thiadiazole (~ $10^{-2}$ M, 4 mL) in acetonitrile solvents were placed in Pyrex tubes (4 cm × 0.4 cm), sealed with rubber septa and purged with argon for 15 min. The solutions were irradiated with sixteen > 290 nm lamps in a Rayonet photochemical reactor. The formation of photoproducts was monitored by removing aliquots for GLC (PE9000) analysis. The final reaction solutions were concentrated and analyzed by the GC (HP588) interfaced with a mass spectrometer to identify the formation of photoproducts by comparison of chromatographic and mass spectroscopic properties with authentic samples.
3.2.11 Spectroscopic data of phenyl-1,2,4-thiadiazoles

UV-absorption spectra of phenyl-1,2,4-thiadiazoles in acetonitrile were recorded with the ODs in the range of 0.5-1. UV-absorption spectra of each thia diazole at various concentrations were recorded in order to determine the configurations of the first excited singlet states. Fluorescence emission spectra of phenyl-1,2,4-thiadiazoles in acetonitrile (degassed; concentrations range from $10^{-5}$-$10^{-7}$ M) were recorded by setting excitation wavelengths at maximum absorptions. Fluorescence emission spectra of each thia diazole at various excitation wavelengths were also recorded. These thiadiazoles exhibited fluorescence with moderate to large Stokes’ shifts. Thus, fluorescence of some phenyl-1,2,4-thiadiazoles in cyclohexane were recorded. Phosphorescence emission spectra of each thia diazole in ethanol-methanol (degassed; 4:1) glass were recorded by setting excitation wavelengths at maximum absorptions.

The first excited singlet state energies of each phenylthiadiazole were determined from the onsets of their UV-absorption and/or fluorescence emission spectra. The first excited triplet state energies of these thiadiazoles were determined from the onsets of their phosphorescence spectra. The configurations of the first excited triplet states were estimated from the $S_1$-$T_1$ energy gaps.

The observed Stokes’s shifts of these phenylthiadiazoles were suggested to be due to combination of effects between the change in geometries of the solvent relaxed excited states relative to the Frank-Condon excited states and charge transfer character. In order to support this suggestion, ground state geometry optimization and estimated ground state dipole moments of these thiadiazoles in acetonitrile were determined by AM1 calculations.
3.2.12 Triplet sensitization of 5-phenyl- and 3-phenyl-1,2,4-thiadiazole

The excited triplet state energies of 5-phenyl- and 3-phenyl-1,2,4-thiadiazole were determined at 62 and 68 kcal/mol, respectively. Thus, the excited triplet states of these thiadiazoles could be sensitized by energy transfer from excited triplet states of butyrophenone which has its first excited triplet state energy of 69 kcal/mol. UV-absorption spectra of butyrophenone in acetonitrile at various concentrations (2×10⁻⁴ - 2×10⁻² M) were recorded in order to confirm the $S_1(\pi,\pi^*)$ energy levels of 5-phenyl- and 3-phenyl-1,2,4-thiadiazole are higher than $S_1(n,\pi^*)$ of butyrophenone and that 5-phenyl- and 3-phenyl-1,2,4-thiadiazole have no absorption in the wavelength region corresponding with $S_0 \rightarrow S_1(n,\pi^*)$ absorption transition of butyrophenone. The $S_0 \rightarrow S_1(n,\pi^*)$ absorption transition of butyrophenone had a maxima at 316 nm. Thus, the black mercury lamps, with light emitting in a range of 325-400 nm, were employed as light sources. Pyrex glass reactors were employed since Pyrex has a cut off at ~ 290 nm which will eliminate the possibility of light absorption by the thiadiazoles. The degassed acetonitrile solutions (3.5 mL) of 5-phenyl- or 3-phenyl-1,2,4-thiadiazole (8×10⁻³ M), butyrophenone (1.6×10⁻¹ M), and mixture of 5-phenyl- or 3-phenyl-1,2,4-thiadiazole + butyrophenone (8×10⁻³ and 1.6×10⁻¹ M) in sealed Pyrex tubes were simultaneously irradiated with sixteen > 325 nm lamps for a total 90 min, for 5-phenyl-1,2,4-thiadiazole, or 120 min, for 3-phenyl-1,2,4-thiadiazole. The photoreactions were monitored by GLC.
3.2.13 Photochemistry of phenyl substituted-1,2,4-thiadiazoles in the presence of triethylamine or propylamine

- **Cyclic voltametry**

  Reduction potentials of some phenyl-1,2,4-thiadiazoles were obtained by cyclic voltametry. The cyclic voltametry of these thiadiazoles (0.1 M; degassed) were performed in acetonitrile employing 0.1 M tetrabutylammonium bromide as a supporting electrolyte. Three glass cells, equipped with a graphite disk working electrode, platinum counter electrode, and saturated calomel electrode (SCE) as a reference electrode, were employed in this measurement.

- **Irradiation of 5-phenyl- and 3-phenyl-1,2,4-thiadiazole in the presence of triethylamine or n-propylamine**

  Solutions of each thiadiazole (0.01 M), each thiadiazole + triethylamine (0.01 M + 0.4 M), and each thiadiazole + n-propylamine (0.01 M + 0.4 M) in acetonitrile or methanol solvent in sealed Pyrex tubes were purged with argon gas for 15 min and simultaneously irradiated with sixteen > 290 nm lamps in a Rayonet photochemical reactor. These solutions were irradiated for a total of 120 min and analyzed by GLC. Quantitative data of these reactions were determined employing previously constructed calibration curves.

  Thermodynamic feasibility of electron transfer between triethylamine or n-propylamine and some thiadiazoles were considered by using reported oxidation potentials of the amines and reduction potentials of the thiadiazoles obtained from cyclic voltametry.
3.2.14 Photochemistry of phenyl substituted-1,2,4-thiadiazoles in the presence of tri-n-butylphosphine

- **Synthesis of tri-n-butylphosphine sulfide**

Tri-n-butylphosphine sulfide was an expected product from the irradiation of phenyl substituted-1,2,4-thiadiazole in the presence of tri-n-butylphosphine. Thus, it was synthesized to be used as an authentic sample.

Tri-n-butylphosphine (5 mL; 4.1 g; 0.02 mol) was added to a 100 mL round bottom flask containing a yellow cloudy mixture of toluene (15 mL) and elemental sulfur (0.6 g; 0.02 mol). The mixture was refluxed and stirred for one hour. The reaction mixture was monitored by TLC. The crude reaction mixture was concentrated by rotary evaporation to give a crude clear viscous liquid (3.7 g). The crude colorless viscous liquid (1.8 g) was purified by Kugelrohr distillation at 120-123°C (0.3 mm. Hg) to give a colorless viscous liquid (1.4 g). The light yellow residue (0.22 g) remained in the flask. The liquid was characterized by GC-MS and NMR spectroscopy; \(^{1}H\text{-NMR}\) (CDCl\(_3\)) \(\delta\) 0.94 (t, 3H; \(J = 7.58\) Hz), 1.43 (septet, 2H; \(J = 7.33\) Hz), 1.51-1.61 (m, 2H), 1.77-1.84 (m, 2H); \(^{13}C\text{-NMR}\) (CDCl\(_3\)) \(\delta\) 14.1, 24.4 (d; \(J_{C-P} = 16.1\) Hz), 24.8 (d; \(J_{C-P} = 3.8\) Hz), \(\delta\) 30.9 (d \(J_{C-P} = 50.1\) Hz); MS \(m/z\) (%) 234 (M\(^{+}\); 19), 178 (28.3), 122 (100), 41 (16.6).
• **Photochemistry of 5-phenyl-, 5-(4′-methoxy)phenyl- and 3-phenyl-1,2,4-thiadiazole in the presence of tri-n-butylphosphine**

Tri-n-butylphosphine was purified by Kugelrohr distillation prior used. UV-absorption spectra of 5-phenyl-1,2,4-thiadiazole (6.4×10⁻⁵ M) and tri-n-butylphosphine (4×10⁻³ M) in acetonitrile solvent were recorded. The solutions of 5-phenyl-1,2,4-thiadiazole and tri-n-butylphosphine were mixed with a ratio of 1:1. The resulting solution was analyzed by UV-absorption spectroscopy.

Solutions of 5-phenyl-1,2,4-thiadiazole (2×10⁻² M), 5-phenyl-1,2,4-thiadiazole + tri-n-butylphosphine (2×10⁻² M + 40 µL), 5-(4′-methoxy)phenyl-1,2,4-thiadiazole (2×10⁻² M), 5-(4′-methoxy)phenyl-1,2,4-thiadiazole + tri-n-butylphosphine (2×10⁻² M + 40 µL) and 3-phenyl-1,2,4-thiadiazole (2×10⁻² M) and 3-phenyl-1,2,4-thiadiazole + tri-n-butylphosphine (2×10⁻² M + 40 µL) in acetonitrile in sealed Pyrex tubes were purged with argon gas for 15 min and irradiated with sixteen > 290 nm lamps for a total of 180 min. The irradiated solutions were analyzed by GLC (PE9000) and the GC (HP588) interfaced with a mass spectrometer. The yield of tri-n-butylphosphine sulphide was determined from a calibration curve of an authentic sample of this compound constructed by plotting detector respond Vs concentrations.

In order to investigate the possibility that these thiadiazoles might undergo a thermal reaction with tri-n-butylphosphine to yield tri-n-butylphosphine sulphide, mixtures of each thiadiazole + tri-n-butylphosphine in acetonitrile solvent in a sealed Pyrex tubes in the dark were heated at 80°C in a water bath. After three hours of heating, the mixtures were analyzed by the GC (HP588) interfaced with a mass spectrometer.
- Fluorescence quenching of 5-(4′-methoxy)phenyl-1,2,4-thiadiazole in acetonitrile the presence of tri-n-butylphosphine

Fluorescence emission of 5-(4′-methoxy)phenyl-1,2,4-thiadiazole in acetonitrile degassed solutions (1.6×10^{-2} M) containing various concentrations of tri-n-butylphosphine (1.1×10^{-2} – 2.4×10^{-2} M) were recorded. A plot between tri-n-butylphosphine concentrations Vs the fluorescence intensity of 5-(4′-methoxy)phenyl-1,2,4-thiadiazole in an absence of tri-n-butylphosphine divided by the fluorescence intensity of 5-(4′-methoxy)phenyl-1,2,4-thiadiazole observed at various tri-n-butylphosphine concentrations was constructed. This plot showed a linear decrease in fluorescence of 5-(4′-methoxy)phenyl-1,2,4-thiadiazole with increasing concentrations of tri-n-butylphosphine indicating that tri-n-butylphosphine quenched fluorescence of 5-(4′-methoxy)phenyl-1,2,4-thiadiazole. This would support an assumption that photo-induced electron transfer from the ground state of tri-n-butylphosphine to the excited state of 5-(4′-methoxy)phenyl-1,2,4-thiadiazole had occurred during photolysis. In order to confirm this result, thermodynamic feasibility of this electron transfer process was considered. Redox potential of tri-n-butylphosphine was attempted to determine by a cyclic voltametry (0.1 M; acetonitrile, employing 0.1 M tetrabutylammonium bromide as a supporting electrolyte). Three glass cells, equipped with a graphite disk working electrode, platinum counter electrode, and saturated calomel electrode (SCE) as a reference electrode, were employed in this measurement. In this measurement, however, applying voltages in both positive and negative directions did not result in any reductive or oxidative curves.
CHAPTER 4

CONCLUSION

Benzonitrile (43), the major photoproduct formed by irradiation of 5-phenyl-1,2,4-thiadiazole (31; R = H) or 3-methyl-5-phenyl-1,2,4-thiadiazole (54; R = CH₃), could be formed by direct photofragmentation of the reactant to yield 43 and either hydrogen cyanide sulfide (R = H) or acetonitrile (R = CH₃), which would be expected to undergo a rapid decomposition to HCN (R = H) or CH₃CN (R = CH₃) and sulfur. If this was the only route to the formation of 43, the ratio of benzonitrile-¹⁵N (43-¹⁵N) to benzonitrile-¹⁴N (43-¹⁴N) should be the same as the ratio of 5-phenyl-1,2,4-thiadiazole-4-¹⁵N (31-4¹⁵N) to 5-phenyl-1,2,4-thiadiazole-2-¹⁵N (31-2¹⁵N) or as the ratio of 3-methyl-5-phenyl-1,2,4-thiadiazole-4-¹⁵N (54-4¹⁵N) to 3-methyl-5-phenyl-1,2,4-thiadiazole-2-¹⁵N (54-2¹⁵N). This, however, was not observed. Thus, whereas after 16 min of irradiation, the un-consumed reactant composition was 93% of 31-4¹⁵N and 7% of 31-2¹⁵N, the composition of the benzonitrile formed at this irradiation time from the reactant was 24% 43-¹⁴N and 76% 43-¹⁵N. In the case of 3-methyl-5-phenyl-1,2,4-thiadiazole (54), after irradiation for 18 min the composition of the un-consumed reactant was 90% of 54-4¹⁵N and 10% of 54-2¹⁵N whereas the composition of the benzonitrile formed was 45% 43-¹⁴N and 55% 43-¹⁵N. Thus, in both cases, after short duration irradiation, more ¹⁵N-scrambling had occurred in
benzonitrile photoproduct than had occurred in the thiadiazole reactant. Furthermore, in the case of 31-4\(^{15}\)N, whereas after 180 min of irradiation the unconsumed reactant composition had changed to 71 % \(31-4\(^{15}\)N\) and 29 % \(31-2\(^{15}\)N\), the composition of benzonitrile had changed to 62 % \(43-\)\(^{15}\)N and 38 % \(43-\)\(^{14}\)N.

These different scrambling ratios require an additional pathway by which some or all of benzonitrile (43) is being formed. Although, 3-phenyl-1,2,4-thiadiazole (46), the phototransposition product of 5-phenyl-1,2,4-thiadiazole (31), is known to undergo quantitative photofragmentation to 43, this reaction cannot account for a significant quantity of 50 formed, especially in the early stage of the reaction when the concentration of 46 would be too low to absorb any significant amount of incident light.

In addition to these scrambling ratios, the reaction mechanism must also account for two additional experimental observations. First, 3-phenyl-1,2,4-thiadiazole-\(^{15}\)N and 5-methyl-3-phenyl-1,2,4-thiadiazole-\(^{15}\)N are both formed over the entire range of irradiation times with complete scrambling of \(^{15}\)N between ring position 2 and 4 of the thiadiazole ring. Second, 2-phenyl-1,3,5-triazine-\(^{15}\)N (39-\(^{15}\)N) and 2,4-diphenyl-1,3,5-triazine-\(^{15}\)N (40-\(^{15}\)N) formed from 5-phenyl-1,2,4-thiadiazole-4-\(^{15}\)N (31-4\(^{15}\)N) and 2,4-dimethyl-6-phenyl-1,3,5-triazine-\(^{15}\)N (65-\(^{15}\)N) and 2-methyl-4,6-diphenyl-1,3,5-triazine-\(^{15}\)N (66-\(^{15}\)N) formed from 3-methyl-5-phenyl-1,2,4-thiadiazole-4-\(^{15}\)N (54-4\(^{15}\)N) each consisted of essentially equal quantities of molecules containing one or two \(^{15}\)N atoms per molecule.

A plausible mechanism which accounts for these experimental observations begins with electrocyclic ring closure to yield bicyclic species, BC-31 (R = H or R = CH\(_3\)) (Scheme 107). As previously discussed, this bicyclic species is considered to be the starting point for phototransposition. Thus, one or two sigmatropic shifts of sulfur would lead to BC-46 and BC-46'. Since these two bicyclic species are of equal energy, they would be formed as an equilibrium mixture of equal quantities of each intermediate. Rearomatization
of this equimolar mixture of BC-46 and BC-46' would lead to a mixture of equal quantities of 3-phenyl-1,2,4-thiadiazole-4-$^{15}$N (46-4-$^{15}$N) and 3-phenyl-1,2,4-thiadiazole-2-$^{15}$N (46-2-$^{15}$N) from 5-phenyl-1,2,4-thiadiazole-4-$^{15}$N (31-4-$^{15}$N) or to a mixture of equal quantities of 5-methyl-3-phenyl-1,2,4-thiadiazole-2-$^{15}$N (57-2-$^{15}$N) and 5-methyl-3-phenyl-1,2,4-thiadiazole-4-$^{15}$N (57-4-$^{15}$N) from 3-methyl-5-phenyl-1,2,4-thiadiazole-4-$^{15}$N (54-4-$^{15}$N).

This accounts for the observed complete scrambling of $^{15}$N between positions 2 and 4 of the thiadiazole ring over the entire photochemical reaction. Furthermore, BC-31 would also be expected to be in equilibrium with BC-31' by sigmatropic migration of sulfur in the opposite direction. Rearomatization of BC-31' would lead to scrambling of $^{15}$N from position 4 to position 2 of the thiadiazole ring. This correctly predicts that irradiation of 31-4-$^{15}$N should result in an increasing amount of $^{15}$N scrambling throughout the irradiation period.

Scheme 107: Possible mechanism for the formation of the phototransposition product
In an attempt to trap the photochemically generated 1,3-diaza-5-thiabicyclo[2.1.0]pentenes with furan via a [4+2] cycloaddition reaction, the results revealed the formation of new products after irradiation of 5-phenyl-1,2,4-thiadiazole (31), 3-methyl-5-phenyl-1,2,4-thiadiazole (54), and diphenyl-1,2,4-thiadiazole (47) in furan solvent. The mass spectral analyses of these new products strongly indicated their molecular ions corresponding with 1:1 adducts of the thiadiazole and furan with loss of sulfur. These adducts could be formed by furan trapping of the initially formed diazathiabicyclo[2.1.0]pentene (BC) to form a sulfur-containing adduct (87-89) which eliminates sulfur, possibly under the condition of GC-MS analysis, or by furan trapping of the phenyldiazaaclobutadiene (CB) after the initial adduct eliminates sulfur as shown in Scheme 108. The trapping of BC with furan by these two possible pathways (Scheme 108) also corresponded with the observed quenching of all the known photoproducts formation after irradiation of 5-phenyl-1,2,4-thiadiazole in acetonitrile at various furan concentrations.

Scheme 108: Possible formation of the observed adducts
In addition to sulfur migration leading to phototransposition, it is also plausible that **BC** could also undergo loss of sulfur resulting in a species that could be viewed as an equilibrating mixture of phenyldiazacyclobutadiene **CB-1** and **CB-2** shown in Scheme 109. This species is expected to be very reactive and can be envisioned to react by several different pathways. First, such a species would be expected to undergo cleavage leading to the formation of benzonitrile and R-CN. As shown in Scheme 109, benzonitrile formed by this pathway would consist of equal quantities of benzonitrile-$^{15}$N and benzonitrile-$^{14}$N. This would result in a faster rate of $^{15}$N scrambling in the benzonitrile as compared to the scrambling predicted only by direct photocleavage of 5-phenyl-1,2,4-thiadiazole-$^{15}$N.

\[
\begin{align*}
\text{BC} & \quad \xrightarrow{S} \quad \text{CB-1} \quad \xleftrightarrow{\text{CB-2}} \quad \text{Ph-CN} + \text{Ph-CN}^* \\
\text{R = H or CH}_3
\end{align*}
\]

**Scheme 109:** Phenyldiazacyclobutadiene formation

In addition to the ring cleavage, by analogy with the known chemistry of cyclobutadiene, phenyldiazacyclobutadiene **CB-1** could also be expected to undergo a [4+2] cycloaddition followed by ring cleavage of the tricyclic adducts. Scheme 110, which shows two of the possible orientations for this cycloaddition-cleavage pathway, reveals that the sequence leads to the formation of benzonitrile (43) and 2-phenyl-1,3,5-triazine (39) and 2,4-diphenyl-1,3,5-triazine (40) or 2,4-dimethyl-6-phenyl-1,3,5-triazine (65) and 2-methyl-4,6-diphenyl-1,3,5-triazine (66) with complete $^{15}$N scrambling. Thus, this pathway correctly predicts that each triazine is formed as an equi-molar mixture of molecules containing one or two $^{15}$N atoms per molecule. Since the yields of the triazines are much smaller than the yield of benzonitrile, diazacyclobutadiene **CB-1** must have a greater tendency for direct cleavage rather than to undergo the cycloaddition-cleavage pathway.
The proposed formation of triazines via a [4+2] cycloaddition reaction of phenyldiazacyclobutadienes is also consistent with the result from photolysis of 3-methyl-5-phenyl-1,2,4-thiadiazole (54) and 5-phenyl-1,2,4-thiadiazole (31) mixture in acetonitrile. The result revealed the formation of 2-methyl-4-phenyl-1,3,5-triazine (72), the expected cross coupling product from a [4+2] cycloaddition reaction of the two different phenyldiazacyclobutadiene intermediates existed in the reaction as shown in Scheme 111.
Scheme 111: [4+2] cycloaddition cross-coupling of phenyldiazacyclobutadiene intermediates

Irradiation of 3-phenyl-1,2,4-thiadiazole (46) led almost exclusively to the formation of benzonitrile (43) while diphenyl-1,2,4-thiadiazole (47) was observed as a minor product. Work in this laboratory has also shown that irradiation of 3-phenyl-1,2,4-thiadiazole-2-$^{15}$N (46-$^{15}$N) did not lead to $^{15}$N-scrambling in the 3-phenyl-1,2,4-thiadiazole ring$^{ref}$. Irradiation of this compound led only to the formation of benzonitrile-$^{15}$N (43-$^{15}$N), the photofragmentation product. This indicates that 46-$^{15}$N does not undergo electrocyclic ring closure. When electrocyclic ring closure did not occur, irradiation of 46 in neat furan led also only to the formation of 43, no reaction occurred with furan. Therefore, it can be concluded that 3-phenyl-1,2,4-thiadiazole (46) does not undergo electrocyclic ring closure and neither the bicyclic intermediate, 2-phenyl-1,3-diaza-5-thiabicyclo[2.1.0]pentene nor 2-phenyl-1,3-diazacyclobutadiene is formed upon irradiation of 3-phenyl-1,2,4-thiadiazole (46).
The formation of the photofragmentation product, 43, upon irradiation of 46, could result from direct fragmentation of the thiadiazole ring via pathway A or B as shown in Scheme 112a. The direct fragmentation via pathway A would result in the formation of hydrogen cyanide and benzonitrile sulfide (48), which is known to eliminate sulfur to give benzonitrile\textsuperscript{ref}. Alternatively, by analogy with isothiazole photochemistry,\textsuperscript{ref} photocleavage of the S-N bond via pathway B would lead to a diradical D-1, which would undergo cleavage to yield 43, sulfur and hydrogen cyanide. When the nitrogen at ring position 2 is labeled with \textsuperscript{15}N, Scheme 112b shows that either pathway A or B is consistent with the observation that photofragmentation of 3-phenyl-1,2,4-thiadiazole-2-\textsuperscript{15}N (46-2\textsuperscript{15}N) gave only benzonitrile-\textsuperscript{15}N (43-\textsuperscript{15}N).

**Scheme 112a:** Possible photofragmentation pathways of 3-phenyl-1,2,4-thiadiazole

**Scheme 112b:** Possible photofragmentation pathways of 3-phenyl-1,2,4-thiadiazole-2-\textsuperscript{15}N
The intermediacy of benzonitrile sulfide (48) was supported by three experimental results as shown in Scheme 113; 1) The formation of diphenyl-1,2,4-thiadiazole (47) after irradiation of 46 would result from a 1,3-dipolar cycloaddition reaction of 48 with 43, 2) Irradiation of 46 in the presence of ethyl cyanoformate (49) revealed the trace quantity formation of ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate (50). The thermally generated benzonitrile sulfide has been reported to undergo effective trapping with acetylenes by 1,3-dipolar cycloadditions\textsuperscript{ref}. Thus, the formation of 50 is the evidence that irradiation of 46 resulted in the formation of 48, which was captured by cycloaddition with ethyl cyanoformate (49), 3) The formation of benzamide (38) after irradiation of 46 was also expected due to a reaction of 48 with water present in the reaction solution.

\textbf{Scheme 113:} Evidences for the intermediacy of benzonitrile sulfide upon irradiation of 46
The study of the effect of electron donating and electron withdrawing substituents in the phenyl ring on the photochemistry of 1,2,4-thiadiazoles revealed that these (4′-substituted)phenyl-1,2,4-thiadiazoles exhibited similar photochemistry to the un-substituted compounds, except for their reaction efficiency. These (4′-substituted)phenyl-1,2,4-thiadiazoles were not photoreactive in acetonitrile solvent but were more reactive in cyclohexane solvent. The fluorescence emission spectra of these (4′-substituted)phenyl-1,2,4-thiadiazoles exhibited moderate to large Stokes’ shifts in acetonitrile. The magnitude of these Stokes’ shifts decrease in cyclohexane. Spectroscopic data of these compounds suggested that introduction of electron donating or withdrawing groups on the phenyl or thiadiazole ring enhances the formation of charge transfer excited states of these compounds. In acetonitrile, these charge transfer excited states would be stabilized and become the lowest energy excited state. These charge transfer excited states would not be photoreactive and, thus, fluorescence emission became an effective deactivation process. In cyclohexane solvent, the charge transfer excited states would be less stabilized and, thus, the relaxed $S_{1(v0)}(\pi,\pi^*)$ would, then, become the lowest excited state. The relaxed $S_{1(v0)}(\pi,\pi^*)$ would be the state from which the observed photoproducts originate and the observed fluorescence with the smaller Stokes’ shifts compared with the Stokes’ shifts observed in acetonitrile.
REFERENCES


34. Encinas, M. V.; Bertolotti, S. G. and Previtali, C. M. Helvetica Chimica Acta 2005, 82, 1427.


APPENDIX A

Benzonitrile – Calibration curve

\[ y = 2853.4x \]
\[ R^2 = 0.9979 \]

4-Methoxybenzonitrile – Calibration curve

\[ y = 1665.8x \]
\[ R^2 = 0.9942 \]
3-Phenyl-1,2,4-thiadiazole – Calibration curve

![3PTD- Calibration curve](image)

\[ y = 1474.2x \]
\[ R^2 = 0.9994 \]

2,4-Dimethyl-6-phenyl-1,3,5-triazine

![dMPT- Calibration curve](image)

\[ y = 12415x \]
\[ R^2 = 0.9962 \]
2-Methyl-4,6-diphenyl-1,3,5-triazine

MdPT - Calibration curve

\[ y = 9734.1x \]

\[ R^2 = 0.9916 \]

Tri-n-butylphosphine sulfide

TnBPS - Calibration curve

\[ y = 3819.4x \]

\[ R^2 = 0.9968 \]
# APPENDIX B

Ground State Geometry Optimization of Phenyl Substituted-1,2,4-Thiadiazoles by AM1

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<thead>
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<th>Twist angle</th>
<th>Dipole moment (debye)</th>
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<td>-----</td>
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<tr>
<td>118</td>
<td>C5 = 27°, C3 = 3°</td>
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<tr>
<td>47</td>
<td>C5 = 33°, C2 = 5°</td>
<td><img src="image3.png" alt="Diagram" /></td>
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| 120 | C3 = 30°  
     | C5 = 11°  | 2.45|
APPENDIX C

List of Structures