ปฏิกิริยาเคมีแสงของ เฟนิล-1,2,4-ไทอะไดอะโซล

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PHOTOCHEMICAL REACTIONS OF PHENY-1,2,4-THIADIAZOLES

Mr. Chuchawin Changtong

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for the Degree of Master of Science in Chemistry

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ในงานวิจัยนี้เป็นการตรวจสอบปฏิกิริยาเคมีแสงของสารกลุ่ม 1,2,4-ไทอะไดอะโซล โดยสังเคราะห์ 3- และ 5-เฟนิล-1,2,4-ไทอะไดอะโซลขึ้นเพื่อใช้เป็นสารตั้งต้น และศึกษาปฏิกิริยาเคมีแสง เนื่องจากสารกลุ่ม 1,2,4-ไทอะไดอะโซล มีโครงสร้างที่เป็นทั้งไทอะโซล และไอโซไทอะโซล จึงคาดว่าผลิตภัณฑ์ที่เกิดขึ้นจะคล้ายคลึงกัน ด้วยเหตุนี้อาจทำนายได้ว่าผลิตภัณฑ์จากปฏิกิริยาเคมีแสงของ 5-เฟนิล-1,2,4-ไทอะไดอะโซล คือ 3-เฟนิล-1,2,4-ไทอะไดอะโซล และ 2-เฟนิล-1,3,4-ไทอะไดอะโซล ในทางกลับกัน 3-เฟนิล-1,2,4-ไทอะไดอะโซล ควรจะเกิดโฟโตทรานสโพสิชันเป็น 5-เฟนิล-1,2,4-ไทอะไดอะโซล และ 2-เฟนิล-1,3,4-ไทอะไดอะโซล แต่จากผลการวิเคราะห์ และติดตามปฏิกิริยาด้วยเทคนิคแก๊สโครมาโทกราฟี โดยใช้ดีเทคเตอร์ประเภท เฟลมไอออไนเซชัน และ แมสสเปกโทรมิเทอร์ พบว่าในปฏิกิริยาเคมีแสงของ 5-เฟนิล-1,2,4-ไทอะไดอะโซลให้ผลิตภัณฑ์ 8 ชนิด ซึ่งสามารถยืนยันโครงสร้างได้ดังนี้คือ เบนโซไนไทรล์, 3-เฟนิล-1,2,4-ไทอะไดอะโซล, 3,5-ไดเฟนิล-1,2,4-ไทอะไดอะโซล, เฟนิล- และ ไดเฟนิล-ซิม-ไทรอะซีน ส่วนผลิตภัณฑ์อีกสามชนิดพบในปริมาณน้อยมาก จึงไม่สามารถตรวจสอบโครงสร้างได้ ในขณะที่ผลการวิเคราะห์แสดงให้เห็นว่ามีเพียงเบนโซไนไทรล์เท่านั้นที่เกิดขึ้นในปฏิกิริยาของ 3-เฟนิล-1,2,4-ไทอะไดอะโซล การยืนยันโครงสร้างนี้ได้จากการเปรียบเทียบข้อมูลทางโครมาโทกราฟฟี และแมสสเปกโทรเมทรี กับสารมาตรฐานที่สังเคราะห์ กลไกการเกิดปฏิกิริยานี้สามารถอธิบายได้ในแนวทางเดียวกันกับกลไกการเกิดปฏิกิริยาของระบบไทอะโซลและไอโซไทอะโซล โดยเกิดผ่านการปิดวงด้วยปฏิกิริยาอิเล็กโทรไซคลิกตามด้วยการเปลี่ยนตำแหน่งของอะตอมของซัลเฟอร์ และ/หรือ การแตกของพันธะ S-N ตามด้วยการสูญเสียอะตอมของซัลเฟอร์ และพบว่า 3,5-ไดเฟนิล-1,2,4-ไทอะไดอะโซล ที่เกิดจากปฏิกิริยาของ 5-เฟนิล-1,2,4-ไทอะไดอะโซล เกิดผ่านเบนโซไนไทรล์ ซัลไฟด์ ซึ่งสามารถพิสูจน์ได้โดยให้ทำปฏิกิริยากับ เอทิล ไซยาโนฟอร์เมต ได้ เอทิล 3-เฟนิล-1,2,4-ไทอะไดอะโซล-5-คาร์บอกซิเลตเป็นผลิตภัณฑ์.

ภาควิชา.....เคมี..... ลายมือชื่อนิสิต .....
สาขาวิชา.....เคมีอินทรีย์.....ลายมือชื่ออาจารย์ที่ปรึกษา .....
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MR. CHUCHAWIN CHANGTONG : PHOTOCHEMICAL REACTIONS OF PHENYL-1,2,4-THIADIAZOLES.

THESIS ADVISOR : ASSOC. PROF. SUPAWAN TANTAYANON

THESIS COADVISOR : PROF. JAMES W. PAVLIK

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This research involves the exploration in the photochemical reactions of phenyl substituted-1,2,4-thiadiazoles. 3- And 5-phenyl-1,2,4-thiadiazole were initially synthesized and their photochemical behaviors were investigated. Since the structure of 1,2,4-thiadiazole system could be viewed as a combination of isothiazole and thiazole, thus, the photoproduct formation could be predicted by analogy with thiazole and isothiazole. Therefore, 3-pheny-1,2,4-thiadiazole and 2-phenyl-1,3,4-thiadiaozle were anticipated to observe upon the reaction of 5-phenyl-1,2,4-thiadiazole. In contrast, 3-phenyl-1,2,4-thiadiazole should undergo phototransposition reaction to 5-phenyl-1,2,4-thiadiazole and 2-phenyl-1,3,4-thiadiazole. The photoreactions were carried out with appropriate light sources and monitored by GC-FID and GC-MS. The product identification was performed by the comparison of their chromatographic and mass spectroscopic data with the authentic samples. Upon irradiation of 5-phenyl-1,2,4-thiadiazole, the results indicated the generation of four major and four minor products while only one quantitatively detectable product was observed on the reaction of 3-phenyl-1,2,4-thiadiazole. According to the mass spectral analysis, the reaction of 5-phenyl-1,2,4-thiadiazole gave benzonitrile, 3-phenyl-1,2,4-thiadiazole, 3,5-diphenyl-1,2,4-thiadiazole, phenyl- and diphenyl-sym-triazine while the other three products were observed in trace amount and, thus, unidentifiable. Benzonitrile was observed in quantitative yield upon irradiation of 3-phenyl-1,2,4-thiadiazole while the predicted transposition product was undetectable. The formation of these photoproducts can be explained by a mechanism involving either electrocyclic ring closure followed by heteroatom migration or the cleavage of the S-N bond and loss of sulfur. Benzonitrile sulfide was suspected to serve as an intermediate for the formation of 3,5-diphenyl-1,2,4-thiadiazole. The presence of benzonitrile sulfide was proved by allowing it to react with ethyl cyanoformate to yield ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate.

Department Chemistry Student's signature .....

Field of study Organic Chemistry Advisor's signature .....

Academic year 2001 Co-advisor's signature .....

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LIST OF ABBREVIATIONS

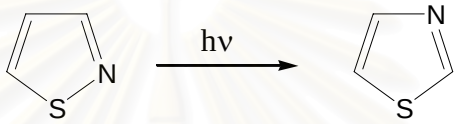
ppm	parts per million
δ	chemical shift
s	singlet (NMR)
d	doublet (NMR)
t	triplet (NMR)
q	quartet (NMR)
μL	microliter
mL	milliliter
nm	nanometer
m/z	mass to charge ratio
λ	wavelength
λ_{max}	the wave length at maximum absorption
h	planck's constant
hν	excitation energy
bp	boiling point
mp	melting point
THF	tetrahydrofuran
BC	bicyclic intermediate
TZ	tricyclic zwitterionic intermediate
CB	cyclobutadiene analogue (intermediate)
D	diradical
I	intermediate
P	permutation pattern
5PTD	5-phenyl-1,2,4-thiadiazole
3PTD	3-phenyl-1,2,4-thiadiazole
3M5PTD	3-methyl-5-phenyl-1,2,4-thiadiazole
TZ	triazines
PTZ	phenyl-sym-triazine
dPTZ	diphenyl-sym-triazine

CHAPTER 1

INTRODUCTION

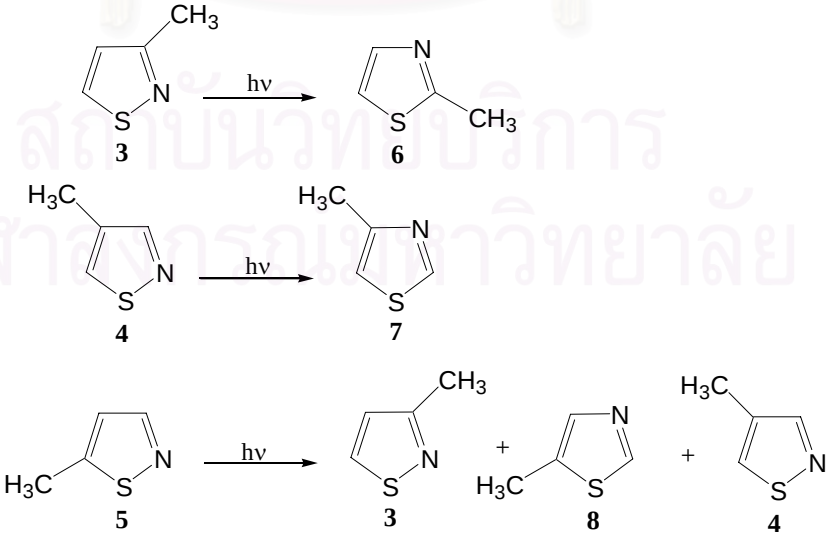
1.1 Photochemistry of isothiazoles and thiazoles

The photoisomerization of isothiazole **(1)** to thiazole **(2)** was first reported to undergo phototransposition reaction.[1] However, the reverse transposition of isothiazole was reported not to take place. ν



1 **2**

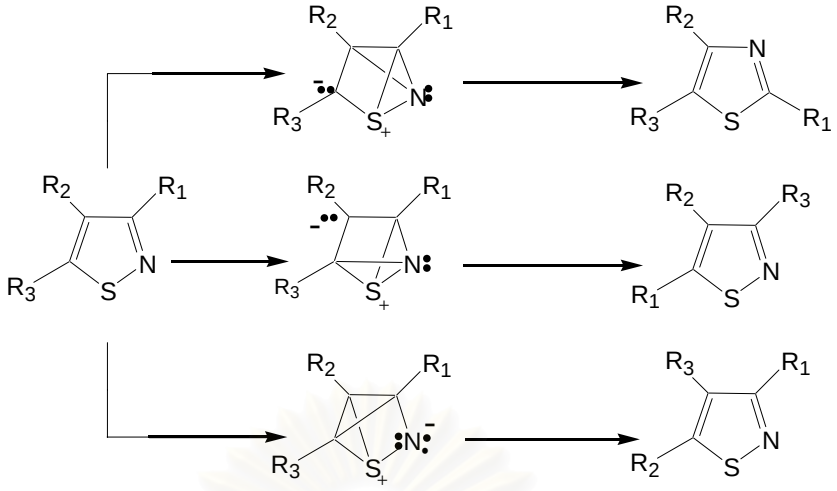
Methylisothiazoles have also been shown to undergo transposition. Lablache-Combier and co-workers[2] reported that 3- and 4-methylisothiazole **(3** and **4)** each transposes to a single N2-C3 interchanged thiazole product **(6** and **7)**. But 5-methylthiazole **(5)** transposes to the thiazole **(8)**, and isomeric isothiazoles **(3** and **4)**. These methylisothiazoles were suggested to phototranspose *via* tricyclic zwitterionic intermediates (Scheme 1) based on the known phototransposition reaction of 2-phenylthiophene.[3]



3 **6**

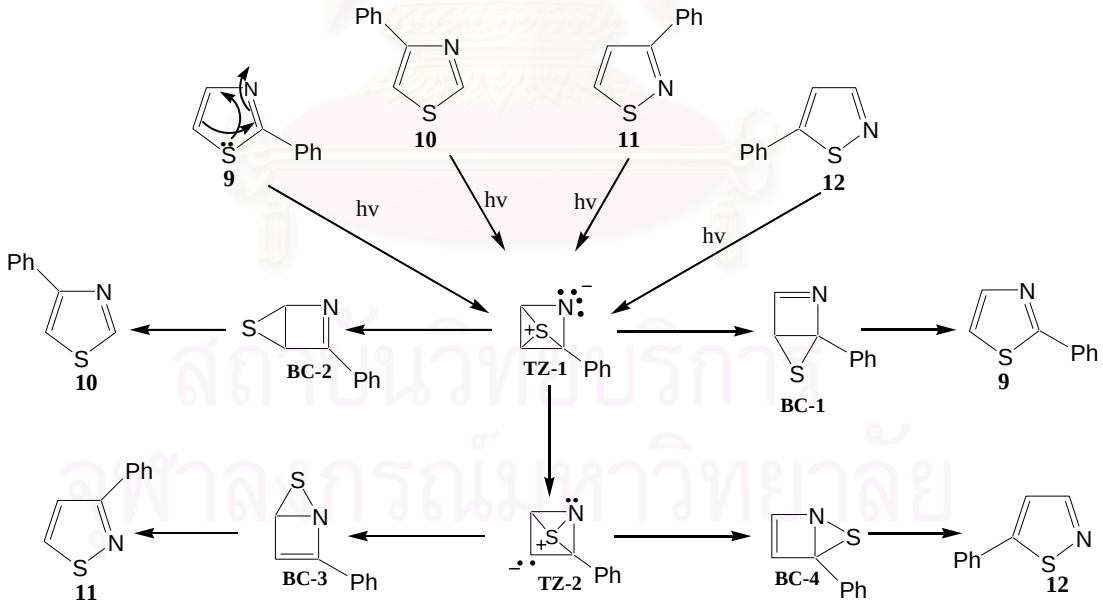
4 **7**

5 **3** **8** **4**



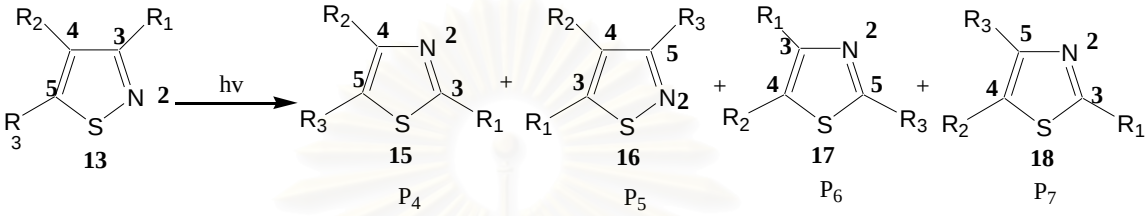
Scheme 1 The proposed phototransposition of isothiazoles *via* tricyclic zwitterionic intermediates.

A research group in France[4] and Japan[5] further extended the study to phenylisothiazoles and phenylthiazoles. Pavlik and colleagues propose that the phototransposition of phenylisothiazoles and phenylthiazoles takes place by a mechanism, which involves tricyclic zwitterionic intermediates as shown in Scheme 2.[6]

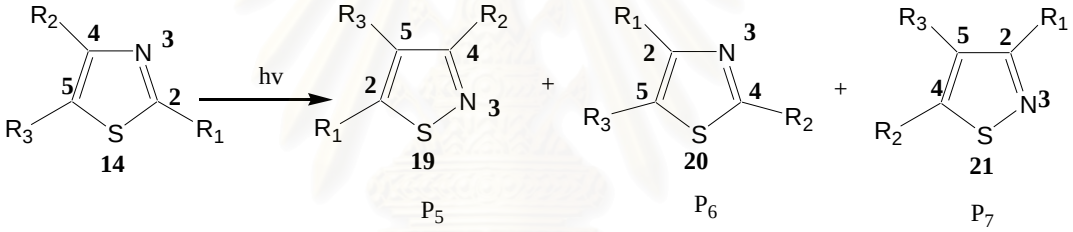


Scheme 2 The proposed phototransposition of phenylisothiazoles and phenylthiazoles *via* tricyclic zwitterionic intermediates.

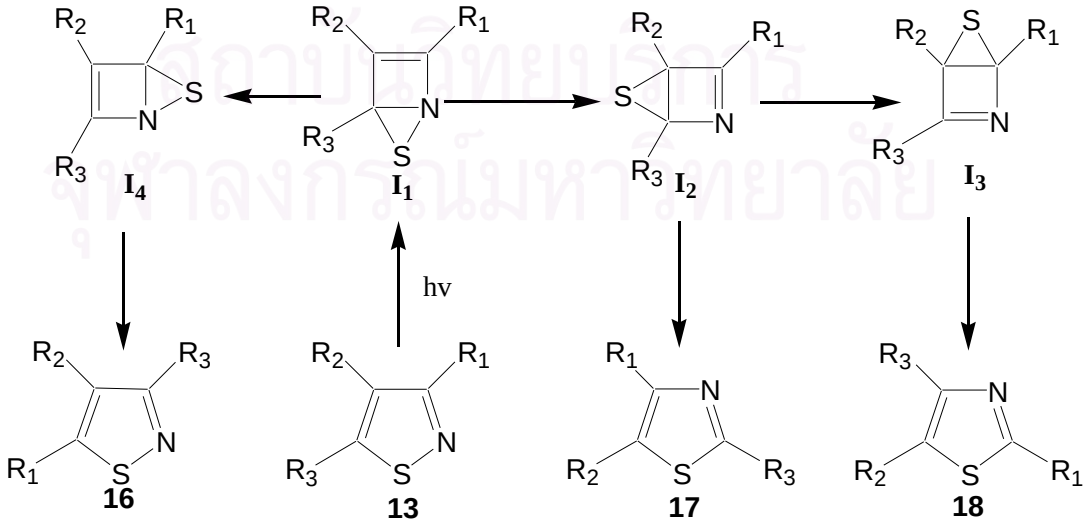
However, they found several ambiguities from those previous reports.[6] Thus, the reinvestigation of the photochemistry of phenylisothiazoles and phenylthiazoles was carried out. This study revealed that the mechanism involved tricyclic zwitterionic intermediates did not correspond to some of their results. They reported that isothiazoles transposed by four different transposition patterns, which can be labeled as P_4, P_5, P_6 and P_7, respectively leading to the isomeric thiazoles and isothiazoles.[6]



Similarly, thiazoles were observed to transpose to isomeric isothiazoles and thiazoles by the P_5, P_6 and P_7 transposition patterns.[6]



Although the P_5, P_6 and P_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,[6] as shown in Scheme 3.



Scheme 3 The electrocyclic ring closure heteroatom migration mechanism.

They suggested that sulfur migration in the initially formed 1-aza-5-thiabicyclopentane intermediate, **I_1**, occured 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]

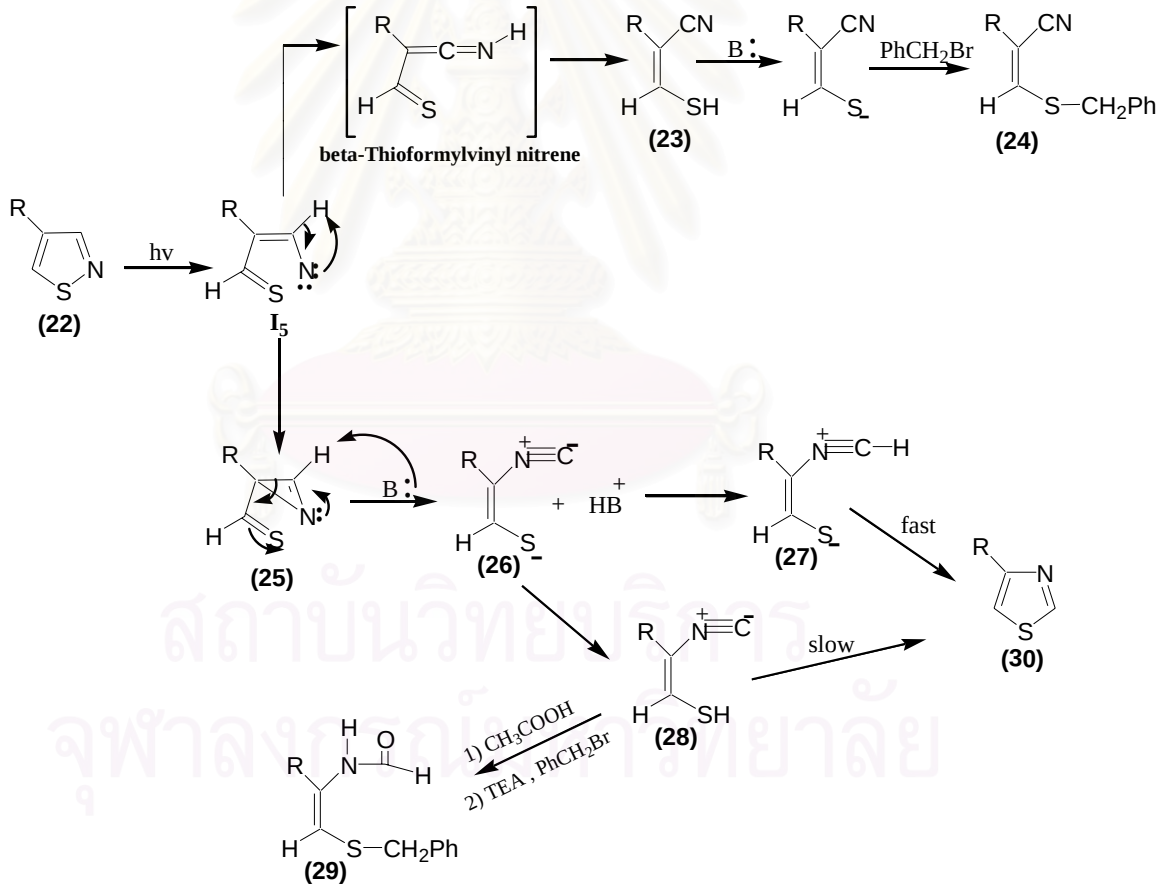
According to Pavlik and Tongcharoensirikul,[6-8] electrocyclic ring closure (the first step of the electrocyclic ring closure heteroatom migration pathway) is in competition with cleavage of the S–N bond in the isothiazole reactant, which this cleavage results in the formation of a species **I_5** (Scheme 4). It can be viewed as a β-thioformylvinyl nitrene. 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, **I_5**, 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 attacked 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 = $PhCH_2$ or CH_3**)**, 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)**.

Since the structure of 1,2,4-thiadiazole is likely a combination between thiazole and isothiazole. Thus, based on the known photochemistry of phenyl substituted isothiazoles and thiazoles discussed previously, photochemistry of phenyl substituted-1,2,4-thiadiazoles could be proposed to undergo phototransposition and photo-cleavage of the S-N bond leading to the N2-C3 interchange product.



Scheme 4 The photocleavage of the S–N bond in the isothiazole.

1.2 Objectives

There is a few published reports in the literature regarding the photochemistry of thiadiazoles. In contrast, the photochemistry of oxadiazoles, especially 1,2,4-oxadiazoles, has been received more considerable attention.[9-13] Basically, 1,2,4-oxadiazoles and 1,2,5-oxadiazoles undergo photocleavage of the O–N bond of the various isomeric oxadiazoles. 1,2,4-Thiadiazoles are particularly interesting since the ring system can be viewed as a combination of a thiazole and an isothiazole. Consequently, photochemistry of 1,2,4-thiadiazoles could be expected to undergo photochemical reactions 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, this research will be directed to 1,2,4-thiadiazole system.

The goal of this research is to investigate the primary photochemical reaction of phenyl substituted-1,2,4-thiadiazoles.

CHAPTER 2

EXPERIMENTAL

2.1 Synthesis of the starting materials and predicted photoproducts

2.1.1 General procedure

All chemicals were purchased from Aldrich Chemical Company and were used without further purification except methanol, ethanol, and acetonitrile. Methanol and ethanol were refluxed with Mg/I_2 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 Avance FT-NMR (400 and 200 MHz for ^1H and ^{13}C, respectively) with $CDCl_3$ or acetone-d_6 as internal standards. Ultraviolet absorption spectra were recorded on a Shidamazu 2110U spectrophotometer. Gas liquid chromatography (GLC) analyses were performed on a Perkin Elmer gas chromatograph PE 9000 FID instrument equipped with a 30 m × 0.25 mm i.d. fused silica column coated with 0.25μ Supelwax 10 bonded phase. Mass spectra were recorded on a Hewlett Packard HP 5970B mass selective detector (EI) interfaced to HP 5890 A 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 (254 and 300 nm) were employed as light sources.

2.1.2 Synthesis of the starting materials

2.1.2.1 Synthesis of 5-phenyl-1,2,4-thiadiazole (31)[14]

2.1.2.1.1 Synthesis of *N*-[(dimethylamino)methylene]thiobenzamide (35)

Thiobenzamide **(37)** (1.0 g, 7.3 mmol) was added to a 25 ml. three-neck flask. The flask was purged with argon for 30 minutes. *N*,*N*-Dimethylformamide dimethylacetal **(49)** (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 **(49)** was added dropwise to dissolve the un-dissolved thiobenzamide. The red reaction solution was allowed to stand at room temperature under an argon atmosphere upon stirring for 45 minutes. 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 **(35)** as red-orange crystals : **mp.**56-58°C (lit. mp.[14] 50-54°C); 1.2 g. (6.3 mmol, 87.5 %); **^{1}H–NMR** ($CDCl_3$) 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); **^{13}C–NMR** ($CDCl_3$) δ 36.8, 42.4, 128.1, 129.3, 132.3, 143.5, 159.5, 216.6; **^{1}H–^{13}C correlation** ($CDCl_3$) δ^{1H} 3.24 - δ^{13C} 36.8, δ^{1H} 3.25 - δ^{13C} 42.4, δ^{1H} 7.32-7.36 - δ^{13} 128.1, δ^{1H} 7.44-7.48 - δ^{13C} 132.3, δ^{1H} 8.39-8.42 - δ^{13C} 129.3, δ^{1H} 8.73 - δ^{13C} 159.5; **MS** *m/z* (%) 192 ($M^{+\bullet}$; 70.8), 159 (52.8), 121 (79.1), 77 (36.1), 44 (100), 42 (73.6).

2.1.2.1.2 Synthesis of 5-phenyl-1,2,4-thiadiazole (31)

N-[(dimethylamino)methylene]thiobenzamide **(35)** (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 **(36)** acid (0.61 g, 5.4 mmol) dissolved in absolute methanol (10 mL) was added to the three-neck flask resulting in a clear red-orange solution. The solution was stirred at room temperature for one hour. The reaction solution finally turned yellow with a small amount of white precipitates. 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), and 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) (lit. bp.[14] 86°C at 0 Torr), 0.70 g (4.3 mmol, 80 %); **^{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 ($M^{+\bullet}$; 95.2), 135 (100), 104 (79.3), 103 (19.0), 77 (47.6).

2.1.2.2 Synthesis of 3-phenyl-1,2,4-thiadiazole (32)[15]

2.1.2.2.1 Synthesis of 5-phenyl-1,2,4-oxadiazole-2-one (44)

Chlorocarbosulfenyl chloride **(45)** (5.0 g, 38 mmol) was added dropwise to a 100 mL round bottom flask containing benzamide **(40)** (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 (lit. mp.[15] 67°C); 5.0 g (27.0 mmol, 73.5 %); **^{1}H–NMR** ($CDCl_3$) δ 7.45-7.54 (m, 2H), δ 7.93-7.95 (m, 3H); **^{13}C–NMR** ($CDCl_3$) δ 126.1, 127.8, 129.4, 133.1, 157.8, 174.3; **^{13}C-DEPT 135** ($CDCl_3$) δ 126.1(+), 127.8(+), 129.4(+); **MS** *m/z* (%) 179 ($M^{+\bullet}$; 38), 105 (100), 103 (24), 77 (42).

2.1.2.2.2 Synthesis of ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate (43)

5-Phenyl-1,2,4-oxadiazole-2-one **(44)** (2.0 g, 11 mmol) was dissolved in dodecane (25 mL) in a 50 mL three-neck flask. Four equivalents of ethyl cyanoformate **(42)** (4.4 mL, 4.4 g, 40 mmol) were added to the solution. The resulting solution was purged with nitrogen for 30 minutes, 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 solid 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 (lit. mp.[15] 70-71°C); 2.0 g (8.0 mmol, 77.8 %); **^{1}H–NMR** ($CDCl_3$) δ 4.41 (t, 3H, *J* = 7.1 Hz), δ 4.51 (q, 2H, *J* = 7.1 Hz), δ 7.43-7.44 (m, 3H), δ 8.28-8.29 (m, 2H); **^{13}C–NMR** ($CDCl_3$) δ 14.6, 63.8, 128.9, 129.2, 131.3, 132.3, 158.9, 175.1, 179.4; **^{13}C–DEPT 135** ($CDCl_3$) δ 14.6(+), 63.8(-), 128.9(+), 129.2(+), 131.3(+); **MS** *m/z*(%) 234 ($M^{+\bullet}$;50.8), 135 (100), 103 (28.5), 77 (20).

2.1.2.2.3 Synthesis of 3-phenyl-1,2,4-thiadiazole (32)

A mixture of ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate **(43)** (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 one 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-thiadizole-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 **(32)**as a white solid : **bp.** (oven temperature) 40°C (0.02 Torr), **mp.** 34-35 °C; 0.46 g (2.8 mmol, 72 %); **^{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 ($M^{+\bullet}$;75.7), 135 (100), 103 (24.3), 77 (31.4).

2.1.2.3 Synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole (33)[14]

2.1.2.3.1 Synthesis of *N*-[(dimethylamino)ethyledine]thiobenzamide (48)

Thiobenzamide **(37)** (1.5 g, 10.95 mmol) was dissolved in *N*,*N*-dimethylacetamide dimethylacetal **(49)** (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 of *N*,*N*-dimethylacetamide dimethylacetal **(49)** was added dropwise until the thiobenzamide totally dissolved. The resulting reddish reaction mixture was allowed to stand at room temperature for 45 minutes. 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]thiobenzamide **(48)** as orange crystals : **mp.**109-111°C (lit. mp.[14] 111-113°C), 2.0g (9.8 mmol, 89.8 %); **^{1}H–NMR** ($CDCl_3$) δ 2.48 (s, 3H), δ 3.20 (s, 3H), δ 3.22 (s, 3H), δ 7.28-7.33 (m, 2H), δ 7.38-7.42 (m, 1H), δ 8.22-8.28 (m, 2H); **^{13}C–NMR** ($CDCl_3$) δ 18.4, 39.5, 39.7, 128.0, 128.8, 131.3, 142.8, 168.3, 202.76; **^{1}H–^{13}C correlation** ($CDCl_3$) δ^{1H} 2.48 - δ^{13C} 18.4, δ^{1H} 3.20 - δ^{13C} 39.5, δ^{1H} 3.22 - δ^{13C} 39.7, δ^{1H} 7.28-7.33 - δ^{13} 128.0, δ^{1H} 7.38-7.42 - δ^{13C} 131.3, δ^{1H} 8.22-8.28 - δ^{13C} 128.8; **MS** *m/z* (%) 206 ($M^{+\bullet}$;28.7), 173 (38.3), 121 (52.1), 103 (100), 77 (26.0), 44 (50.7).

2.1.2.3.2 Synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole (33)

N-[(dimethylamino)ethylidine]thiobenzamide **(48)** (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 for 30 minutes.

Hydroxylamine-*O*-sulfonic acid **(36)** (0.59 g, 5.2 mmol) dissolved in absolute methanol (10 mL) was added to the three-neck flask resulting in a clear orange 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 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 : **mp.** 52-54°C (lit. mp.[14] 54-56°C), 0.63 g (3.6 mmol, 75 %); **^{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 ($M^{+\bullet}$;37.7), 135 (100), 103 (9.8), 73 (59.1)

2.1.3 Synthesis of the Photoproducts

2.1.3.1 Synthesis of phenyl-sym-triazine and diphenyl-sym-triazine (**50** and **51**)[16]

A mixture of formamidine hydrochloride **(52)** (2.0 g, 25 mmol) and benzamidine hydrochloride **(53)** (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 phenyl- and diphenyl-s-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 phenyl-sym-triazine **(50)** : **mp.** 62-64°C (lit. mp.[16] 60-62°C); 50 mg (0.32 mmol, 1 %); **^{1}H–NMR** ($CDCl_3$) δ 7.73-7.83 (m, 3H), δ 8.77-8.79 (m, 2H), δ 9.55 (s, 2H); **^{13}C–NMR** ($CDCl_3$) δ 129.30, 129.31, 133.6, 135.3, 166.7, 171.6; **^{13}C–DEPT 135** ($CDCl_3$) δ 129.30(+), 129.31(+), 133.6(+), 166.7(+); **MS** *m/z* (%) 157 ($M^{+\bullet}$;64.1), 104 (100), 103 (20.3).

The white solid residue left in the flask was filtered and recrystallized from ethanol to yield diphenyl-s-triazine **(51)** as white needle crystals : **mp.** 80-82°C (lit. mp.[16] 87-88°C); 1.4 g (4.3 mmol, 24 %); **^{1}H–NMR** ($CDCl_3$) δ 7.56-7.63 (m, 6H), δ 8.65-8.68 (m, 4H), δ 9.28 (s, 1H); **^{13}C–NMR** ($CDCl_3$) δ 128.7, 128.9, 132.8, 135.5, 166.7, 171.3; **^{13}C–DEPT 135** ($CDCl_3$) δ 128.7(+), 128.9(+), 132.8(+), 166.7(+); **MS** *m/z* (%) 233 ($M^{+\bullet}$; 56.7), 104 (10.4), 103 (100).

2.1.3.2 Synthesis of 2,4-dimethyl-6-phenyl-1,3,5-triazine and 2-methyl-4,6-diphenyl-1,3,5-triazine (**55** and **56**)[17]

2.1.3.2.1 Synthesis of *N*-[(dimethylamino)ethylidine]benzamide (57)

N,*N*-dimethylacetamide dimethylacetal **(49)** (yellow liquid; 0.87g, 0.96 mL, 6.5 mmol) was added in a pear-shape flask containing benzamide **(40)** (0.6 g, 5 mmol). The flask was equipped with a condenser, heated, and maintained at 80°C in an oil bath for one hour. Benzamide **(40)** dissolved after 15 minutes 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, ^{1}H-NMR and GC-MS analysis of the distillate showed identical results to the analytical results before distillation. Therefore, this obtained *N*-[(dimethylamino)ethylidine]benzamide **(57)** was employed to the next step synthesis without further purification; **^{1}H–NMR** ($CDCl_3$) 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); **^{13}C–NMR** ($CDCl_3$) δ 18.7, 38.63, 38.68, 128.2, 129.7, 131.6, 137.9, 165.7, 176.4; **^{1}H–^{13}C correlation** ($CDCl_3$) δ^{1H} 2.23 - δ^{13C} 18.7, δ^{1H} 2.97- δ^{13C} 38.63, δ^{1H} 3.07 - δ^{13C} 38.68, δ^{1H} 7.31-7.39 - δ^{13} 128.2 and 131.6, δ^{1H} 8.07-8.12 - δ^{13C} 129.7; **MS** *m/z* (%) 190 ($M^{+\bullet}$;21), 105 (100), 77 (84.2), 44 (84.2).

2.1.3.2.2 Synthesis of 2,4-dimethyl-6-phenyl-1,3,5-triazine (55)

N-[(dimethylamino)ethylidine]benzamide **(57)**(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 **(58)**(0.8 mmol, 76 mg) was added into a round bottom flask containing sodium methoxide (0.8 mmol) in excess methanol. Acetamidine hydrochloride **(58)** dissolved and white solid, sodium chloride, precipitated. Acetamidine **(58)** solution was added into the three-neck flask. The reaction flask was purged with argon for 30 minutes, 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 TLC plate (hexane:ethyl acetate 1:1). A band at R_f of 0.79 was scrapped 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 **(55)** as a light yellow liquid : 54 mg (0.3 mmol, 15 %); **^{1}H–NMR** ($CDCl_3$) δ 2.67 (s, 6H), δ 7.44-7.55 (m, 3H), δ 8.47-8.52 (m, 2H); **^{13}C–NMR** ($CDCl_3$) δ 26.2, 129.1, 129.2, 132.9, 136.0, 171.4,176.8; **^{13}C–DEPT 135** ($CDCl_3$) δ 26.2(+), 129.1(+), 129.2(+), 132.9(+); **MS** *m/z* (%) 185 ($M^{+\bullet}$;46.5), 103 (100), 82 (47.3), 42 (33.3).

2.1.3.2.3 Synthesis of 2-methyl-4,6-diphenyl-1,3,5-triazine (56)

Benzamidine hydrochloride **(59)** (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 **(59)** dissolved and a white solid precipitated. The mixture was filtered. The filtrate was added to a 25 mL three-neck flask containing *N*-[(dimethylamino)ethylidine]benzamide **(57)** (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 **(56)**. Therefore, the crude product was subjected to preparative TLC plates (0.45 g on each plate). Hexane:ethyl acetate (4:1) was employed as a solvent system. The highest band at R_f of 0.85 was scrapped off and extracted by ethyl acetate. Ethyl acetate was removed by rotary evaporation to give 2-methyl-4,6-diphenyl-1,3,5-triazine **(56)** as a white solid : **mp.** 102-104°C (lit. mp.[17] 104-108°C); 25 mg (4.0 mmol, 12.5 %); **^{1}H–NMR** ($CDCl_3$) δ 2.77 (s, 3H), δ 7.50-7.57 (m, 3H), δ 8.61-8.63 (m, 2H); **^{13}C–NMR** ($CDCl_3$) δ 26.5, 129.1,

129.3, 132.9, 136.3, 171.6, 177.5; **^{13}C–DEPT 135** ($CDCl_3$) δ 26.2(+), 129.1(+), 129.3(+), 132.9(+); **MS** *m/z* (%) 247 ($M^{+\bullet}$;43.8), 103 (100).

2.2 Photochemistry study

2.2.1 Photolysis of 5-phenyl-1,2,4-thiadiazole (31)

2.2.1.1 UV scale photolysis

Solutions of 5-phenyl-1,2,4-thiadiazole **(31)** (5.0×10^{-5} M) in acetonitrile and cyclohexane were placed in quartz UV cells. Each cell was irradiated with three 300 nm lamp through a Pyrex filter and monitored by UV absorption spectroscopy at 60 second intervals.

2.2.1.2 GLC-scale photolysis.

Solutions of 5-phenyl-1,2,4-thiadiazole **(31)** (2.0×10^{-2} M, 4 mL) in acetonitrile and cyclohexane solvents were placed in Pyrex tubes (L×ID = 14×0.7 cm), sealed with rubber septa and purged with argon for 30 minutes. The solutions were irradiated with sixteen 300 nm lamps in a Rayonet photochemical reactor. The formation of photoproduct was monitored by removing aliquots for GLC analysis [140 (4 min.), 20°C/min. to 180°C (14 min.), 20°C/min to 240 (30min.); range 1; attn 16] every 30 minutes.

Quantitative GLC analysis of photoproduct formation was accomplished using calibration curves constructed for each product by plotting detector responses vs 5 standards of known concentrations.

GLC analysis of irradiated 5-phenyl-1,2,4-thiadiazole in acetonitrile and cyclohexane solvents after 120 minutes showed the consumption of the starting material **(31)** in 65.1% and 33.0 % respectively. The results showed the formation of 50 and 35 % of benzonitrile **(54)**, 2 and 0.8 % of phenyl-s-triazine **(50)**, 6.5 and 3 % of 3-phenyl-1,2,4-thiadiazole **(32)**, diphenyl-s-triazine **(51)** 0.7% in acetonitrile and trace amount in cyclohexane solvent. These photoproducts eluted with retention times of 4, 12, 17.5, 41 minutes, respectively.

The final reaction solutions were concentrated and analyzed by GC-MS [140 (5 min.), 20°C/min to 200°C (20 min.), 10°C/min to 240(20 min.)] to identify the photoproducts by comparison of their chromatographic and mass spectroscopic properties with authentic samples.

Tables 1 and 2 show the relationship between time vs. peak area of photolysis of 5-phenyl-1,2,4-thiadiazole in acetonitrile and cyclohexane respectively.

Table 1 : Photolysis of 5-phenyl-1,2,4-thiadiazole in acetonitrile.

Compounds	Time (minutes)				
	0	30	60	90	120
5PTD	2785.3±6.1	2153.3±3.2	1596.6±5.3	1277.6±5.2	970.6±10
3PTD	0	35.7±2.8	65.5±2.8	138.6±2.1	170.3±4.1
Benzonitrile	0	118.3±1.2	193.9±1.3	258.5±4.6	352.3±7.1
Phenyl-s-triazine	0	41.3±3.0	63.3±1.2	69.6±1.0	78.5±2.3
Diphenyl-s-triazine	0	24.3±1.5	29.0±0.4	41.1±1.2	52.8±2.5

Table 2 : Photolysis of 5-phenyl-1,2,4-thiadiazole in cyclohexane.

Compounds	Time (minutes)				
	0	30	60	90	120
5PTD	2393.6±5.1	-	1966±4.8	1974.3±6.3	1603±6.8
3PTD	0	-	39.6±1.0	69.2±0.8	85.1±2.0
Benzonitrile	0	-	122.3±2.6	176.9±4.9	252.8±5.1
Phenyl-s-triazine	0	-	16.8±0.7	24.1±0.6	32.2±2.6
Diphenyl-s-triazine	0	-	trace	trace	trace

2.2.2 Photolysis of 3-phenyl-1,2,4-thiadiazole (32)

2.2.2.1 UV scale photolysis

A solution of 3-phenyl-1,2,4-thiadiazole **(32)** (5.0×10^{-5} M) in cyclohexane was placed in a quartz cell and irradiated with three 300 nm lamps through a Pyrex filter. The solution was monitored by ultraviolet absorption spectroscopy at 40 second intervals. .

2.2.2.2 GLC-scale photolysis

A solution of 3-phenyl-1,2,4-thiadiazole **(32)** (2.0×10^{-2} M, 4 mL) in acetonitrile solvent was placed in a Pyrex tube (L×ID = 14×0.7 cm), sealed with rubber septum and purged with argon for 30 minutes. The solution was irradiated with sixteen 300 nm lamps in a Rayonet photochemical reactor. The formation of the photoproduct was monitored by removing aliquots for GLC analysis [140 (4 min.), 15°C/min. to 180°C (14 min.); range 1; attn 16] every 15 minutes.

Benzonitrile was identified by GC-MS [140°C (5min.), 20°C /min. to 250°C (14 min.)] as the only GLC-volatile photoproduct. Quantitative GLC analysis of benzonitrile was accomplished by using the calibration curve constructed previously.

Table 3 shows relationship between time vs. peak area of photolysis of 3-phenyl-1,2,4-thiadiazole in acetonitrile.

Table 3 : Photolysis of 3-phenyl-1,2,4-thiadiazole in acetonitrile.

Compounds	Time (minutes)				
	0	30	60	90	150
3PTD	2406.6±68.9	1568.7±20.9	1144.6±28.5	738.5±17.0	480.1±18.9
Benzonitrile	-	641.65±12.4	1249.4±23.4	1476.5±23.0	1863.5±21.2

2.2.3 Photolysis of 3-methyl-5-phenyl-1,2,4-thiadiazole (33)

2.2.3.1 UV scale photolysis

A solution of 3-methyl-5-phenyl-1,2,4-thiadiazole **(33)** (6.0×10^{-5} M) in acetonitrile was placed in a UV quartz cell and the UV-absorption spectrum recorded. The spectrum revealed a λ_{max} at 278 nm with an extinction coefficient of 14167. Thus, this solution was irradiated with three 300 nm lamps through a Pyrex filter. The solution was monitored by ultraviolet absorption spectroscopy at 40 second intervals for 400 seconds totally.

2.2.3.2 GLC-scale photolysis

Solutions of 3-methyl-5-phenyl-1,2,4-thiadiazole **(33)** (2.0×10^{-2} M, 4 mL) in acetonitrile and methanol solvents were placed in Pyrex tubes (L×ID = 14×0.7 cm), sealed with rubber septa and purged with argon for 30 minutes. The solutions were irradiated with sixteen 300 nm lamps in a Rayonet photochemical reactor. The formation of photoproduct was monitored by removing aliquots for GLC analysis [140 (4 min.), 10°C/min. to 240°C (20 min.); range 1; attn 16] every 40 minutes.

Quantitative GLC analysis of photoproduct formation was accomplished using calibration curves constructed for each products by plotting detector responses vs 5 standard known concentrations.

GLC analysis of irradiated 3-methyl-5-phenyl-1,2,4-thiadiazole **(33)** in acetonitrile and methanol solvents after 150 minutes showed the consumption of the starting material **(33)** in 76.3 and 44.6 %, respectively. The results showed the formation of 66.6 and 65.2 % benzonitrile **(54)**, 33.3 and 1.7% 2,4-dimethyl-6-phenyl-1,3,5-triazine **(55)**, 5-methyl-3-phenyl-1,2,4-thiadiazole **(60)**, 6.6% 2-methyl-4,6-diphenyl-1,3,5-triazine **(56)** in acetonitrile and trace amount in methanol solvent. These photoproducts eluted with retention times of 5, 11.5, 14, 28.5 minutes, respectively.

The final reaction solutions were concentrated and analyzed by GC-MS [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 4 and 5 show the relationship between time vs. peak area of photolysis of 5-phenyl-1,2,4-thiadiazole in acetonitrile and methanol, respectively.

Table 4 : Photolysis of 3-methyl-5-phenyl-1,2,4-thiadiazole in acetonitrile.

Compounds	Time (minutes)				
	0	30	70	110	150
3M5PTD	3895.7±13.5	2859.4±39.5	1828.8±20.9	1340.5±26.6	923.8±11.9
5M3PTD	-	83.5±2.7	168.1±6.1	428.6±8.4	347.9±13.6
Benzonitrile	-	382.4±7.9	733.05±16.3	1011.3±5.8	1181.9±31.6
2,4-Dimethyl-6-phenyl-1,3,5-triazine	-	306.25±5.4	534.55±9.8	769.5±4.6	855.8±18.3
2-Methyl-6-diphenyl-1,3,5-triazine	-	47.8±3.5	100.0±1.9	150.5±12.4	196.6±4.5

Table 5 : Photolysis of 3-methyl-5-phenyl-1,2,4-thiadiazole in methanol.

Compounds	Time (minutes)			
	0	30	90	150
3M5PTD	4022±33.9	3520.4±47.8	2797.5±10.6	2227.7±44.2
5M3PTD	-	73.7±2.7	311.5±8.3	397.4±2.5
Benzonitrile	-	108.1±3.8	398.9±8.8	694.9±5.8
2,4-Dimethyl-6-phenyl-1,3,5-triazine	-	trace	trace	25.6±4.2
2-Methyl-6-diphenyl-1,3,5-triazine	-	trace	trace	trace

2.2.4 Photolysis of 5-phenyl-1,2,4-thiadiazole (31) in the presence of ethyl cyanoformate (42)

A solution of 5-phenyl-1,2,4-thiadiazole **(31)** (2.0×10^{-2} M, 4 mL) in acetonitrile with the presence of ethyl cyanoformate **(42)** (0.1 mL, 1×10^{-1} M) was placed in a Pyrex and a quartz tube, sealed with rubber septa, purged with argon for 30 minutes. The solution in a Pyrex tube was irradiated with sixteen 300 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 minute of irradiation. Aliquots of the solution in a quartz tube at 60 minutes and 90 minutes 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 photolyzed for 150 minutes while the solution in a quartz tube was photolyzed for 90 minutes. Aliquots of the final solution in the quartz tube and Pyrex tube were removed, co-injected with ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate **(43)** 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.

2.2.5 Photolysis of 3-phenyl-1,2,4-thiadiazole (32) in the presence of ethyl cyanoformate (42)

A solution of 3-phenyl-1,2,4-thiadiazole **(32)** (2.0×10^{-2} M, 4 mL) in acetonitrile with the presence of ethyl cyanoformate **(42)** (0.1 mL, 1×10^{-1} M) was placed in a Pyrex and a quartz tube, sealed with rubber septa, purged with argon for 30 minutes. The solution in a Pyrex tube was irradiated with sixteen 300 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 minute of irradiation. Aliquots of the solution in a quartz tube at 60 minutes and 90 minutes 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 photolyzed for 300 minutes while the solution in a quartz tube was photolyzed for 120 minutes. 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 **(43)**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.

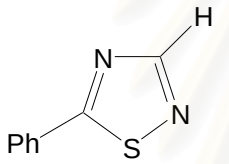
CHAPTER 3

RESULTS AND DISCUSSION

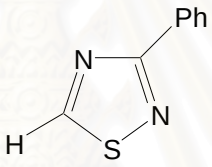
3.1 Synthesis of the starting materials and predicted photoproducts

3.1.1 Synthesis of the starting materials

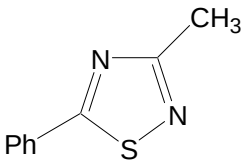
The goal of this research is to study photochemical behavior of phenyl-substituted-1,2,4-thiadiazoles. Therefore, 5-phenyl-1,2,4-thiadiazole **(31)**, 3-phenyl-1,2,4-thiadiazole **(32)**, 3-methyl-5-phenyl-1,2,4-thiadiazole**(33)** were synthesized as the starting materials.



31



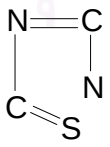
32



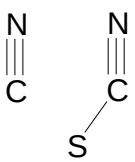
33

3.1.1.1 Synthesis of 5-phenyl-1,2,4-thiadiazole (31)

The 1,2,4-thiadiazole ring can be synthesized by several following methods:[14] 1) oxidative cyclization of an *N*-thioacyl amidine (method A); 2) cycloaddition of nitrile sulfides with a nitrile (method B); 3) oxidation of thioamides or thioureas (method C); and 4) condensation of amidines with halogenated methymercaptans (method D).



(A)



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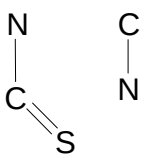
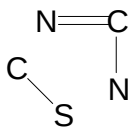


(C)

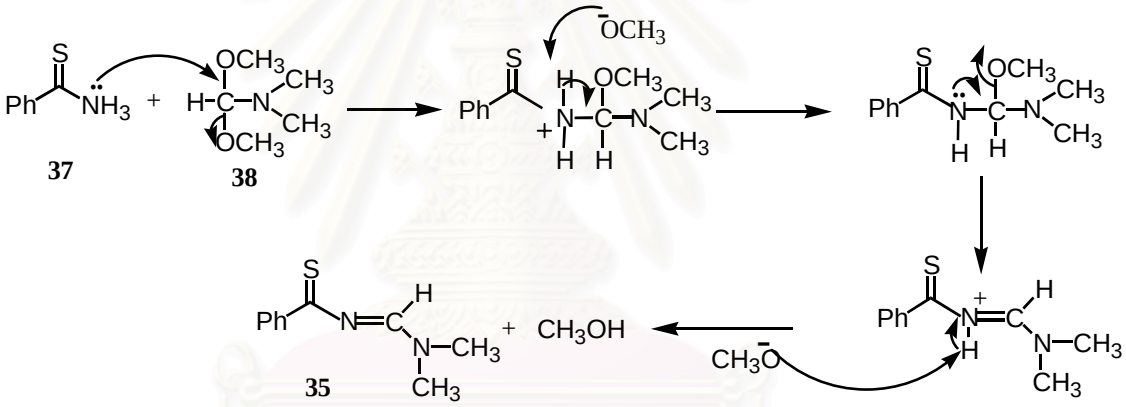


(D)

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 Lin and colleagues.[14] According to this approach, the amination cyclization of *N*-[(dimethylamino)methylene]thiobenzamide **(35)** with the aminating agent, hydroxylamine-*O*-sulfonic acid **(36)**, resulted in the formation of **31** as a colorless viscous liquid in 70 % yield.

3.1.1.1.1 Synthesis of *N*-[(dimethylamino)methylene]thiobenzamide

According to the synthetic method for **31** described by Lin and colleagues, *N*-[(dimethylamino)methylene]thiobenzamide **(35)** was required as the starting material. Therefore, **35** was synthesized in 87.5 % by the condensation between thiobenzamide **(37)** and *N*,*N*-dimethylformamide dimethylacetal **(38).**



The orange crystalline product was identified by GC-MS, ^{1}H- and ^{13}C-NMR spectroscopy. The GC-MS analysis of the sample (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 the retention time of 33.9 minutes (Figure 1b), exhibits the molecular ion at m/z 192 corresponding to the molecular weight of **35** (MW 192). It also shows a base peak at m/z 44 due to the $[(CH_3)_2N]^{+\bullet}$ fragment which is consistent with the structure of this compound.

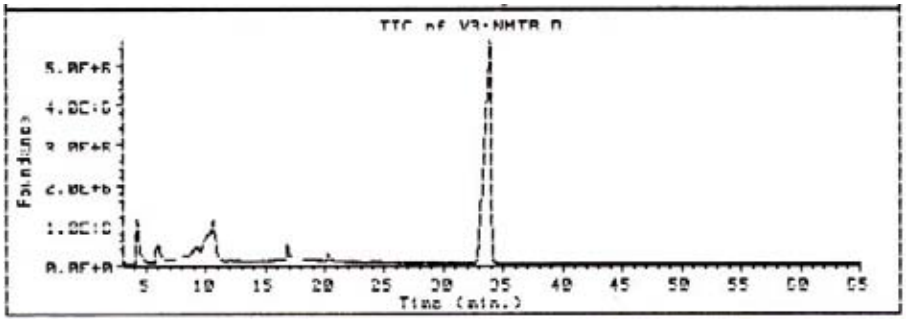


Figure 1a The GC-MS analysis of the synthesized **35**

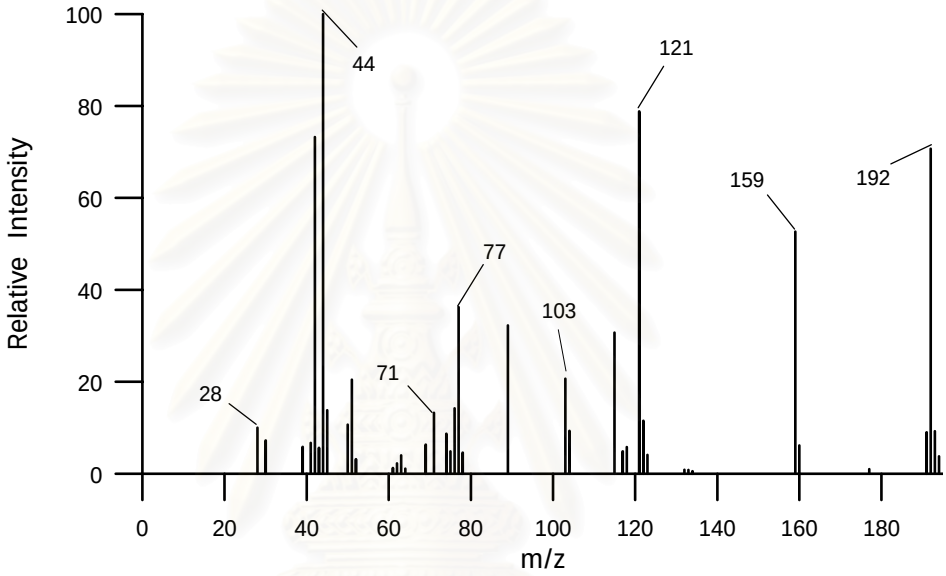


Figure 1b The mass spectrum of the compound eluted at a retention time 33.9 minutes.

The ^{1}H–NMR spectrum of this amidine (Figure 2) exhibits a singlet (1H) at δ 8.73 due to the imine proton. The two non-equivalent methyl groups are shown as two singlets (3H) at δ 3.24 and 3.25. The phenyl ring protons appear as two multiplet at δ 7.32-7.36 (3H) due to the set of meta-, and para- ring protons and 8.39-8.41 (2H) due to ortho- ring protons..

The ^{13}C–NMR spectrum (Figure 3) exhibits signals due to the two non-equivalent methyl carbons at δ 36.81 and 42.37. The four singlets at δ 128.12, 129.27, 132.33 and 143.47 are assigned to phenyl ring carbons. The imine carbon absorbs at δ 159.49. The thiocarbonyl carbon appears downfield at δ 216.66.

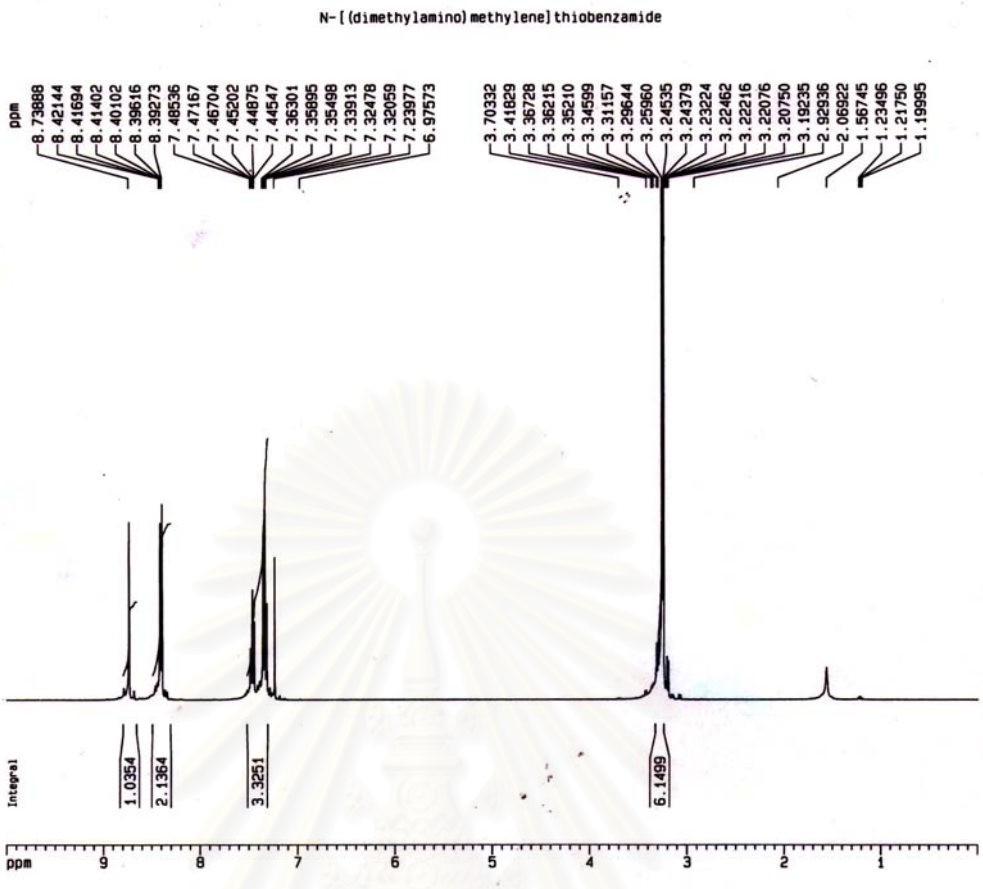


Figure 2 The ^{1}H–NMR spectrum of the synthesized **35**.

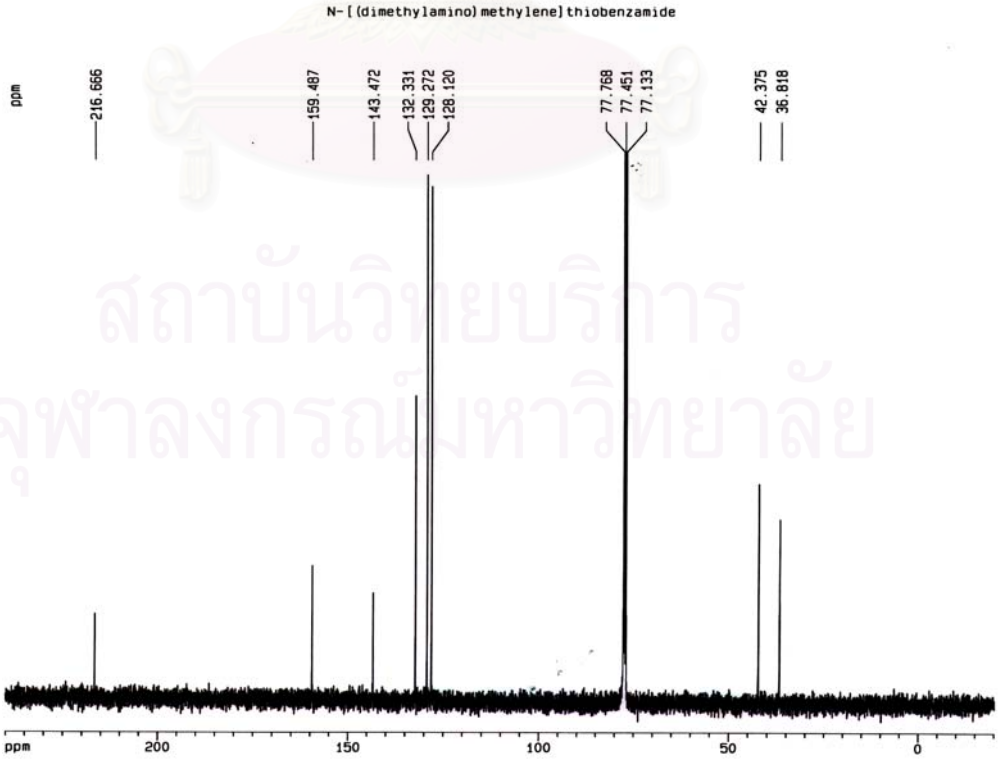


Figure 3 The ^{13}C–NMR spectrum of the synthesized **35**.

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 reveals that the two carbon signals at δ 36.81 and 42.37, that were assigned to the non-equivalent methyl carbons, correlate with the two singlets at δ 3.24 and 3.25 in the ^{1}H-NMR spectrum, that were assigned to the protons of the two non-equivalent methyl groups. In addition, the signal in the ^{13}C-NMR spectrum at δ 159.49, assigned to the imine carbon, correlates with the downfield singlet in the ^{1}H-NMR spectrum at δ 8.74, assigned to the imine proton. The signal at δ 143.47 in the ^{13}C-NMR 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-NMR spectrum due to the phenyl ring carbons still appear in the two dimensional spectrum. The signals in the ^{13}C-NMR spectrum at δ 128.12 and 132.33 can be assigned to the meta- and para- carbons of the phenyl ring respectively since they correlate with the multiplet (3H) at δ 7.32-7.36 in the ^{1}H–NMR spectrum assigned to the meta- and para- protons. Finally, the last signal at δ 129.27 in the ^{13}C–NMR spectrum can be assigned to the ortho- carbons of the phenyl ring since this signal correlates with the multiplet (2H) at δ 8.39 – 8.41 in the ^{1}H–NMR spectrum assigned to the ortho-protons.

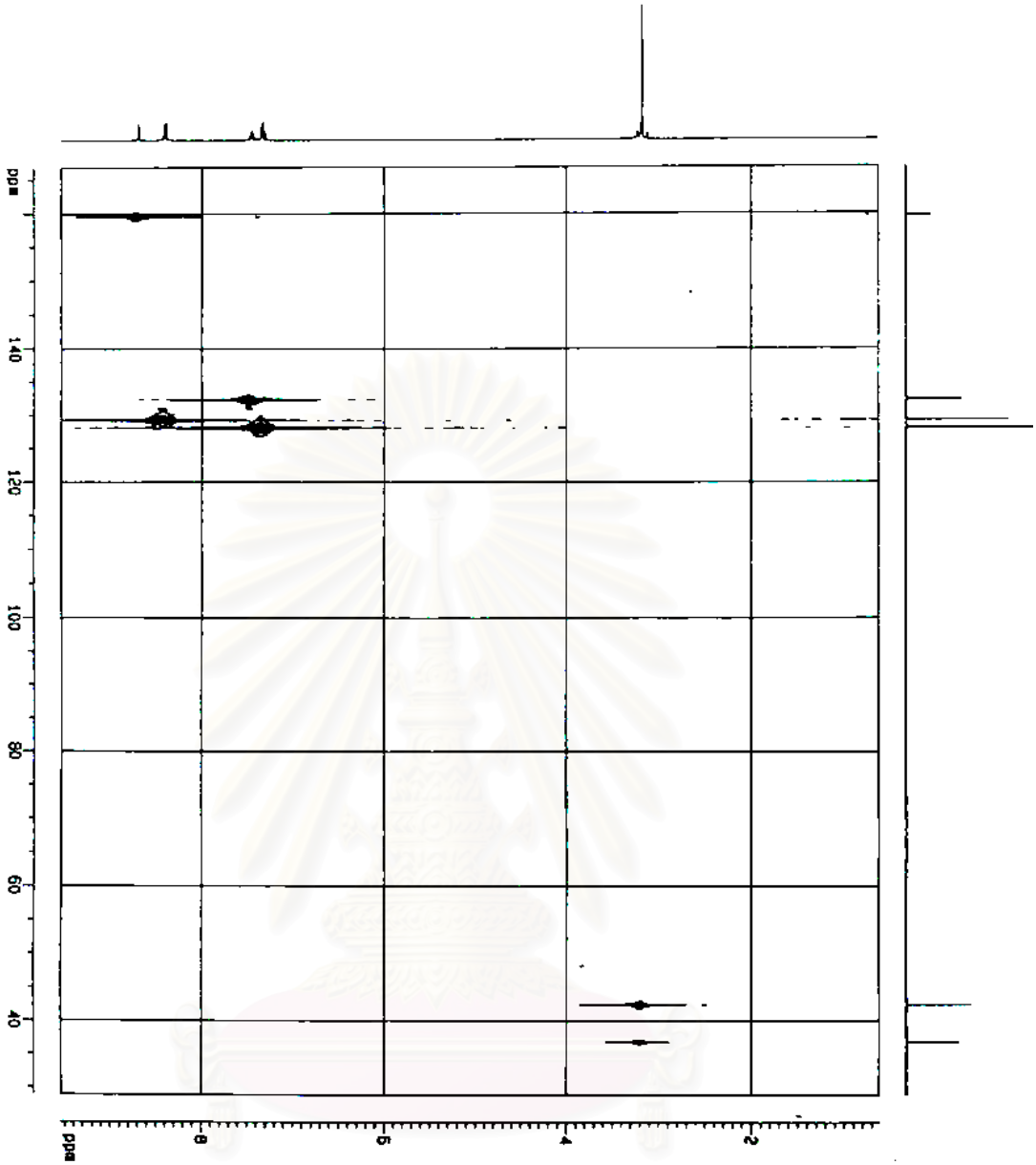
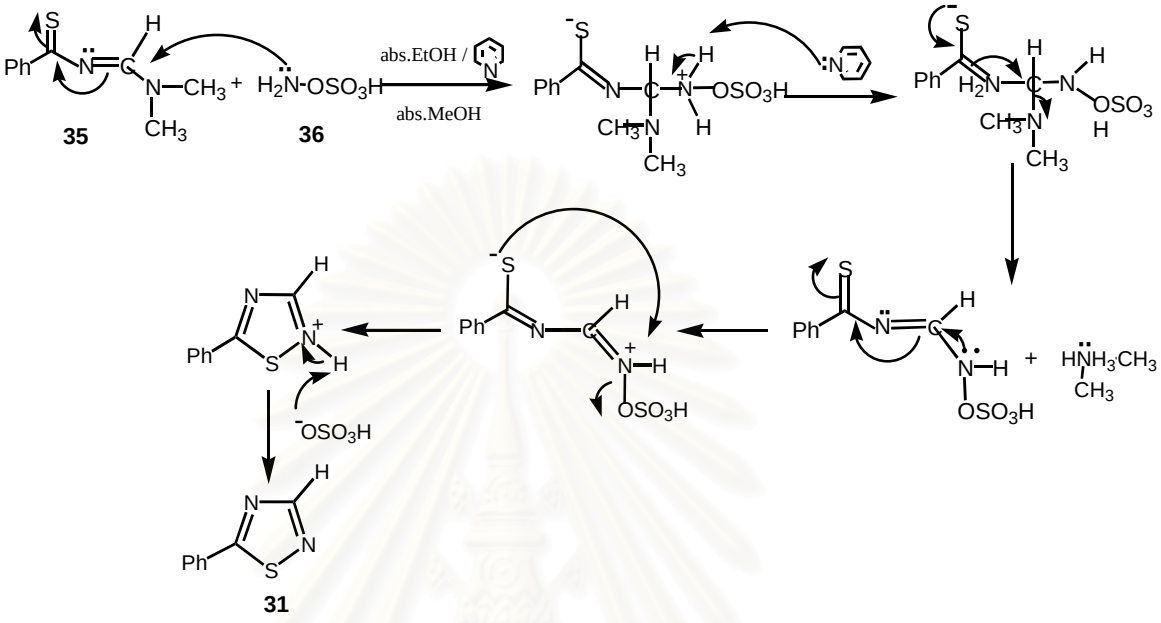


Figure 4 The ^{1}H-^{13}C NMR correlation spectrum of the synthesized **35**.

3.1.1.1.2 Synthesis of 5-phenyl-1,2,4-thiadiazole (31)

The amination cyclization of **35** using **36** and pyridine as basic catalyst led to the formation of 5-phenyl-1,2,4-thiadiazole **(31)**.



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 Lin, **31** was reported as a colorless liquid. But in this synthesis, **31** was obtained as a light yellow viscous liquid. Therefore, there might be an impurity in this product.

GC-MS analysis (Figure 5a) indicated the presence of an impurity, which eluted at a retention time of 6.6 minutes. 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 was eluted at a retention time of 10.9 minutes. The mass spectrum (Figure 5c) of this compound exhibits a molecular ion at m/z 162, corresponding to the molecular weight of **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 **31** undergoes fragmentation in the mass spectrometer to yield $[C_5H_6CNS]^{+\bullet}$ and $[C_5H_6CNH]^{+\bullet}$, respectively.

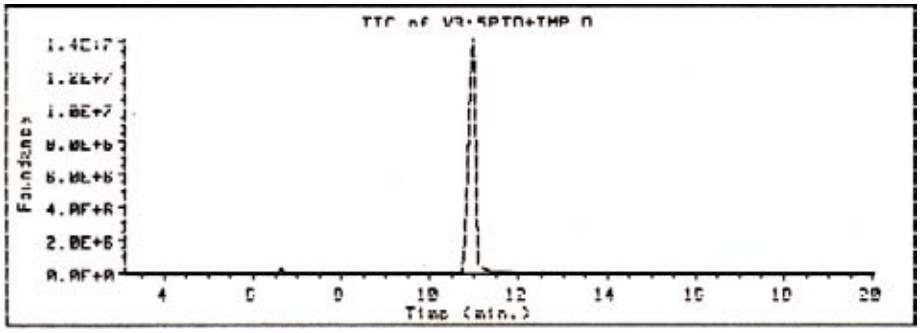
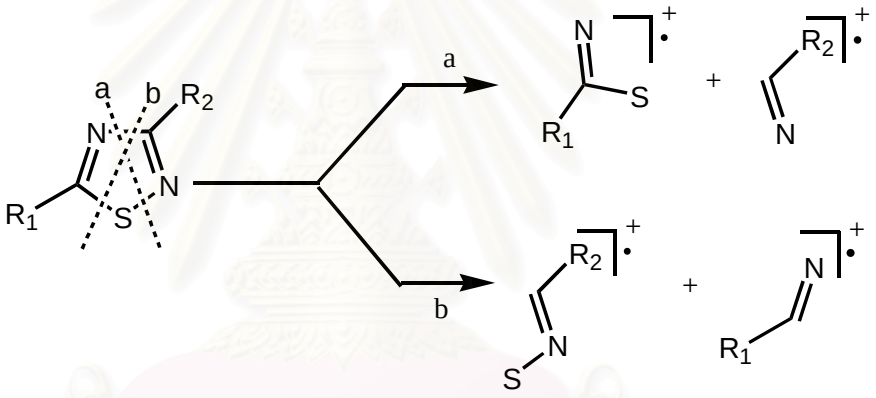


Figure 5a The GC-MS analysis of synthesized **31**.

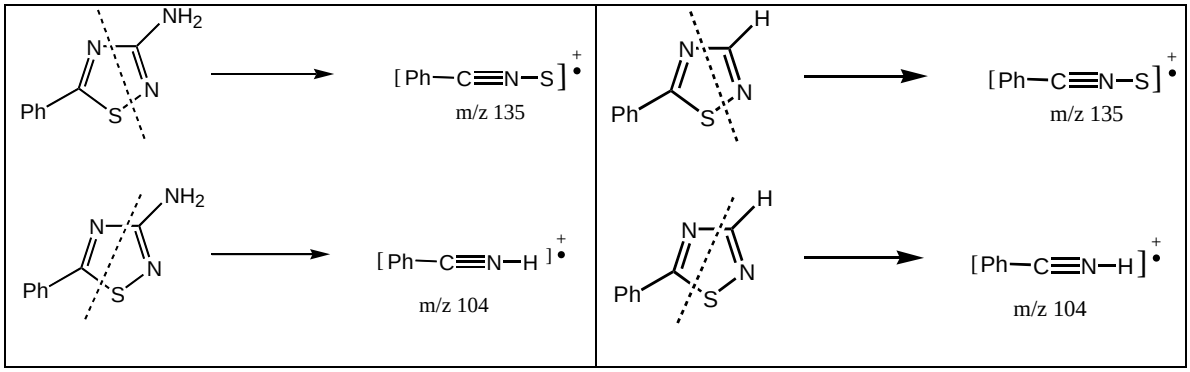
Interestingly, based on the reported fragmentation patterns of 1,2,4-thiadiazoles [18] (Scheme 5), the cleavage of $[C_5H_6CN]^{+\bullet}$ is expected to be one of major fragments. But according to the mass spectrum, shown in Figure 5c, the peak at m/z 104 is much more intense than the peak at m/z 103.



Scheme 5 The major fragmentation pathways of 1,2,4-thiadiazoles.

However, the literature also reported the mass spectrum of 3-amino-5-phenyl-1,2,4-thiadiazole with a peak at m/z 104 as one of intense peaks.[18] This was suggested to be due to the cleavage of $[C_5H_6CN]^{+\bullet}$ with a proton from the amino group at position 3 on the thiadiazole (Scheme 6).

Consequently, based on these suggestions, the intense peak at m/z 104 is due to the $[C_6H_5CNH]^{+\bullet}$ fragment and the base peak at m/z 135 is due to the $[C_6H_5CNS]^{+\bullet}$ fragment which can also be expected as a major fragmentation pathway for **31** (R_1 = Ph, R_2 = H), as shown in Scheme 6.



Scheme 6 The possible fragmentation pathways of 3-amino-5-phenyl-1,2,4-thiadiazole and 5-phenyl-1,2,4-thiadiazole.

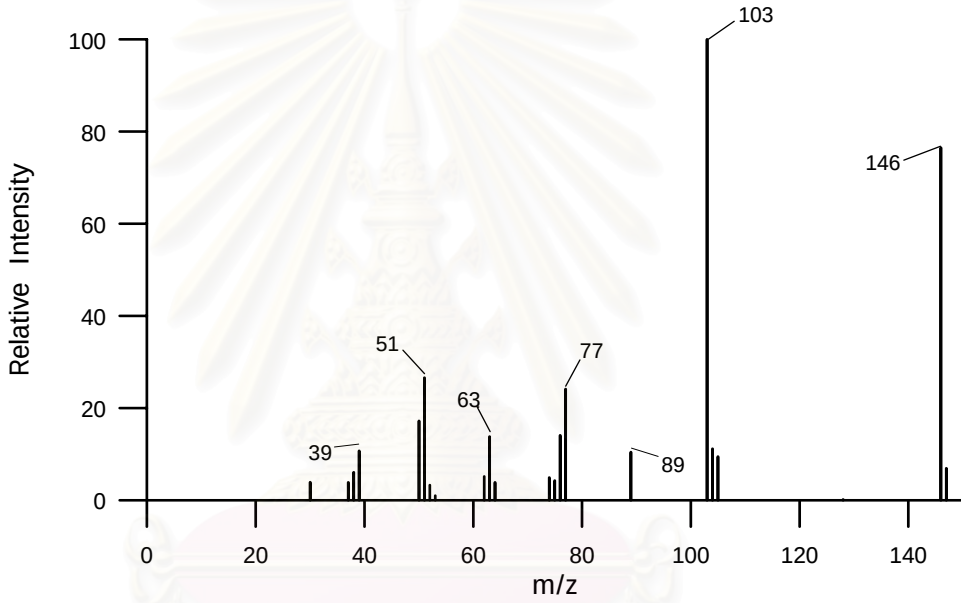


Figure 5b The mass spectrum of the compound eluted at retention time 6.6 minutes.

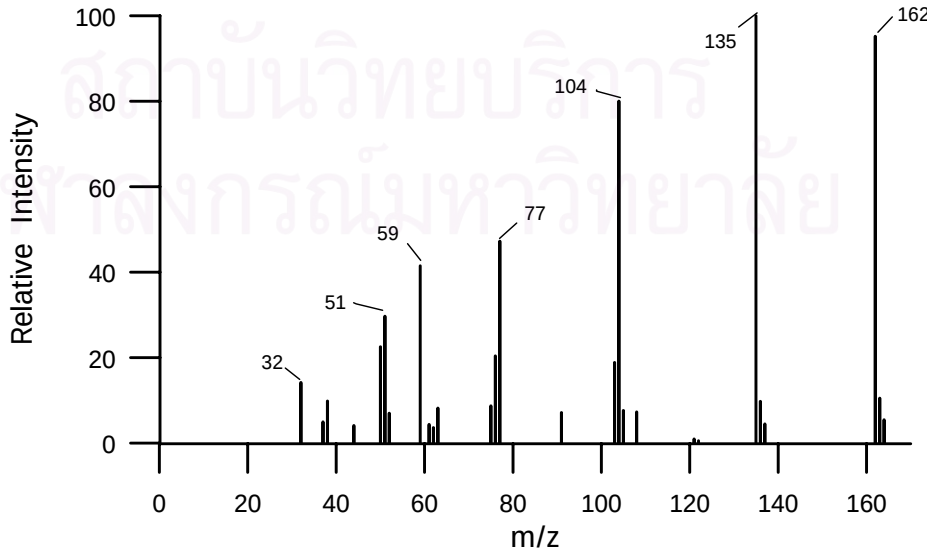


Figure 5c The mass spectrum of the compound eluted at retention time 10.9 minutes.

The ^{1}H–NMR spectrum (Figure 6) shows a singlet at δ 8.53 due to the proton at position 3 of the thiadiazole ring and 3H and 2H multiplets at δ 7.32-7.38 and δ 7.80-7.82 due to the meta-, para- protons and the ortho- protons of the phenyl ring, respectively. In addition, the spectrum also reveals a singlet of low intensity at δ 8.31 and a multiplet of low intensity in the phenyl region which must be due to the observed impurity similarly observed in the GC-MS analysis.

Based on the ^{1}H–NMR and GC-MS data, this impurity was suspected to be 5-phenyl-1,2,4-oxadiazole **(39)**. The isolation of this side product was carried out by preparative thin layer chromatography.

The synthesized 5-phenyl-1,2,4-thiadiazole **(31)** (0.1 g) was dissolved in small amount of chloroform and subjected to a preparative thin layer chromatography using hexane: ethyl acetate (4:1) as a developing system. 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 completed 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 thin layer chromatography was unsuccessful.

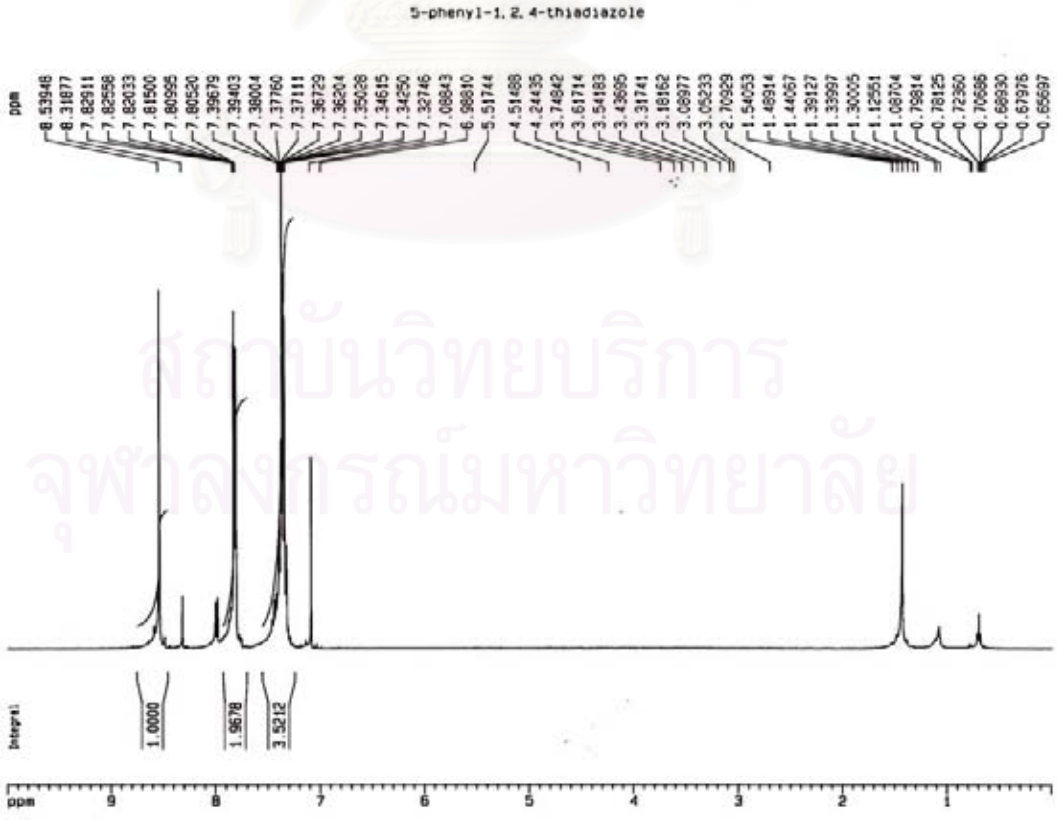


Figure 6 The ^{1}H-NMR spectrum of the synthesized **31**.

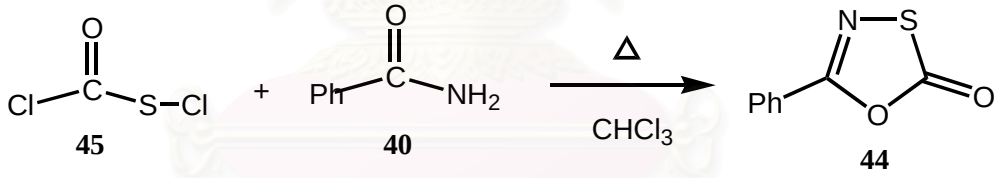
3.1.1.2 Synthesis of 3-phenyl-1,2,4-thiadiazole (32)

The 1,2,4-thiadiazole-ring system can also be prepared from the 1,3-dipolar cycloaddition of a nitrile sulfide with a nitrile as described by Howe and Franz.[15]

In the case of 3-phenyl-1,2,4-thiadiazole **(32)**, cycloaddition of benzonitrile sulfide **(41)** with ethyl cyanoformate **(42)** led to the formation of ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate **(43)**. Base catalyzed ester hydrolysis followed by decarboxylation of the acid form of **43** produced **32** in 72 % as a white solid.

3.1.1.2.1 Synthesis of 5-phenyl-1,3,4-oxathiazole-2-one (44).

According to the method described by Howe and Franz[15] to synthesize **32** by cycloaddition of **41** which can be *in situ* generated by decarboxylation of 5-phenyl-1,3,4-oxathiazole-2-one **(44)**. 5-Phenyl-1,3,4-oxathiazole-2-one **(44)** was prepared by a coupling between chlorocarbo sulfenyl chloride **(45)** and **40** in refluxed chloroform under anhydrous condition, described by Muhlbauer and Weiss [20] to yield the desired oxathiazole **(44)** in 95.5% yield as white crystals.



GC-MS analysis of the white crystals (Figure 7) exhibited two components eluted at a retention time of 4.1 and 17.2 minutes. The mass spectrum of the major peak at retention time 17.2 minutes exhibited 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 due to $[C_6H_5CNS]^{+\bullet}$ fragment caused by the loss of CO_2.

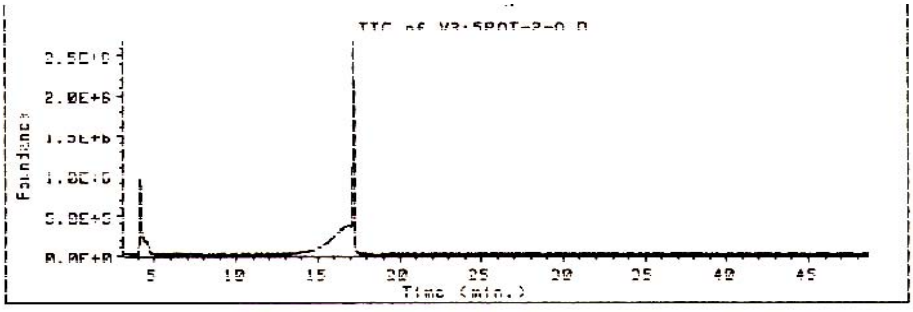


Figure 7 The GC-MS analysis of the white crystals.

The ^{1}H-NMR spectrum of this compound (Figure 8) exhibits two multiplets at δ 7.45-7.54 (2H) and δ 7.93-7.95 (3H) which are assigned to ortho-, and a set of meta- and para- phenyl-ring protons, respectively.

The ^{13}C-NMR spectrum (Figure 9) exhibited the carbon signals correspond to the structure of **44**. The carbonyl carbon on oxathiazole ring absorbs downfield at δ 174.30. The carbon at position 5 of oxathiazole ring appears at δ 157.80. The phenyl ring carbons appear as four singlets at δ 126.16, 127.81, 129.43 and 133.07. These assignments are consistent with the ^{13}C–NMR DEPT 135 spectrum (Figure 9). The two signals at δ 157.80 and 174.30 disappeared in the ^{13}C–NMR DEPT 135 spectrum, which are consistent with the assignment the two quaternary carbons on oxathiazole ring.

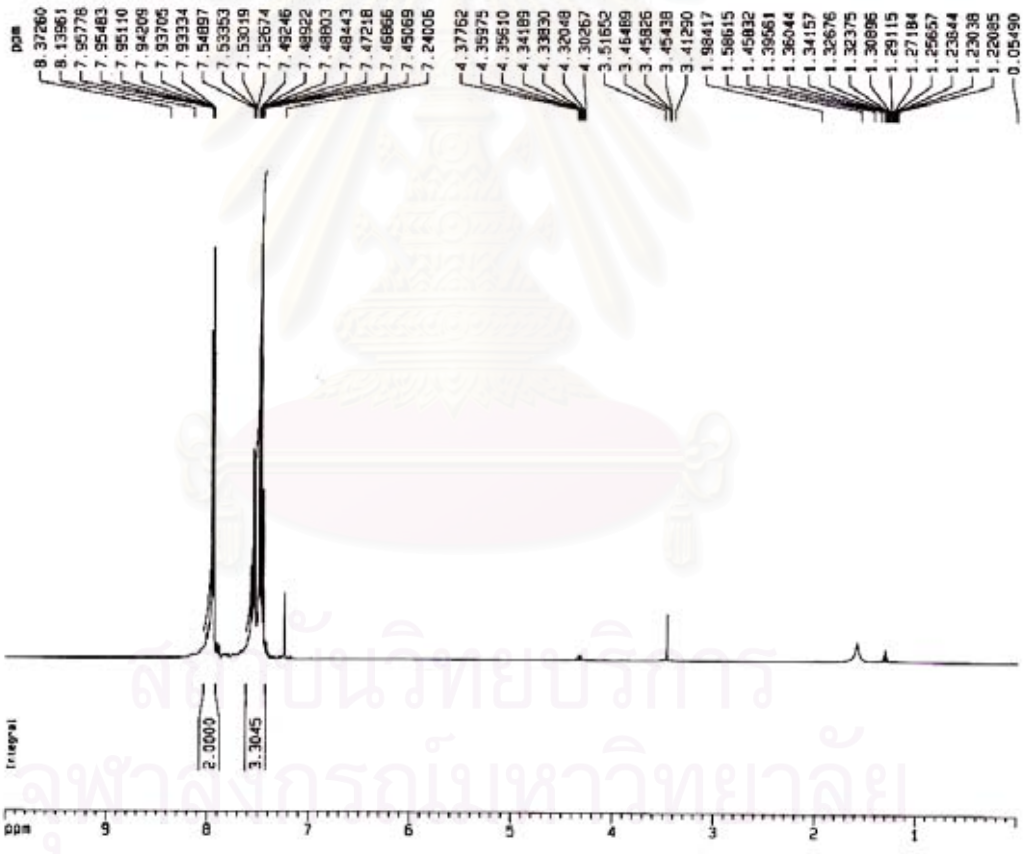


Figure 8 The ^{1}H-NMR spectrum of the white crystals.

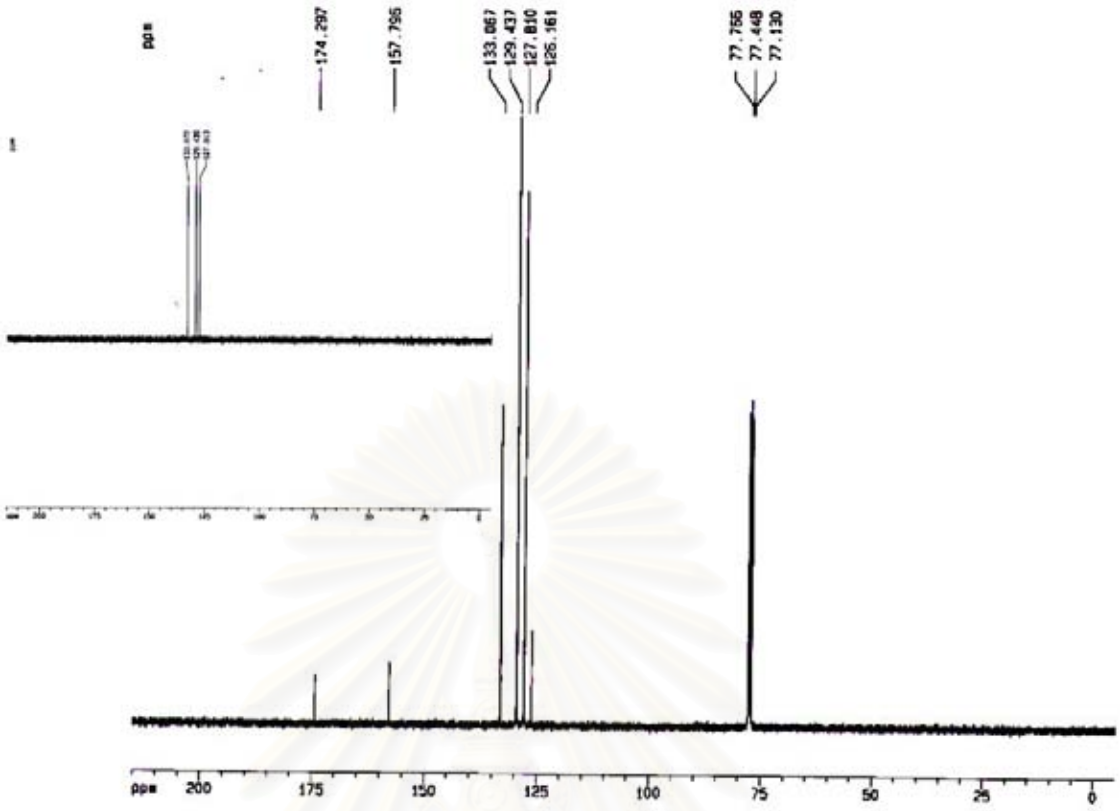
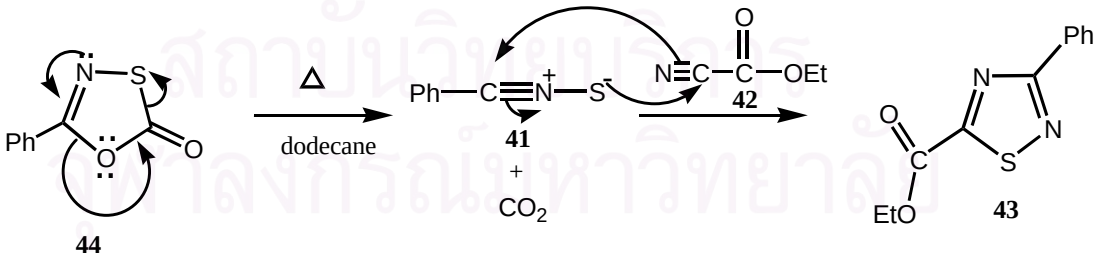


Figure 9 The ^{13}C and ^{13}C-NMR DEPT 135 spectra of the white crystals.

3.1.1.2.2 Synthesis of ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate (43)

Ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate **(43)** was prepared in 80% as light brown crystals by trapping of **41**, *in situ* generated upon decarboxylation of **44**, with **42**.



The GC-MS analysis [isothermal 220°C (30 min.)] of the cycloaddition product shows that a GC-volatile product was eluted at a retention time of 12.4 minutes (Figure 10a). The mass spectrum (Figure 10b) of this compound exhibits a molecular ion at m/z 234 which corresponds to the molecular weight of **43** (MW 234). It also shows a base peak at m/z 135 due to the $[C_6H_5CNS]^{+\bullet}$ fragment.

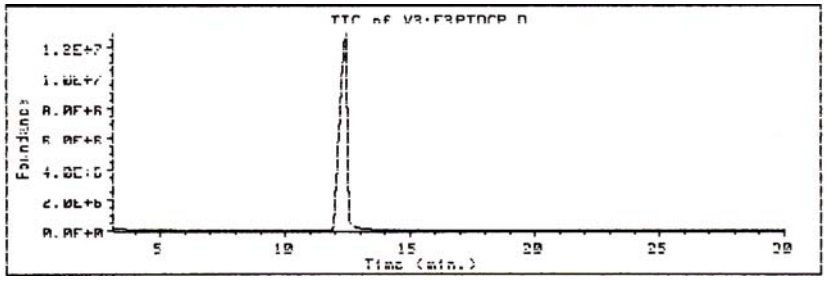


Figure 10a The GC-MS analysis of the synthesized **43**.

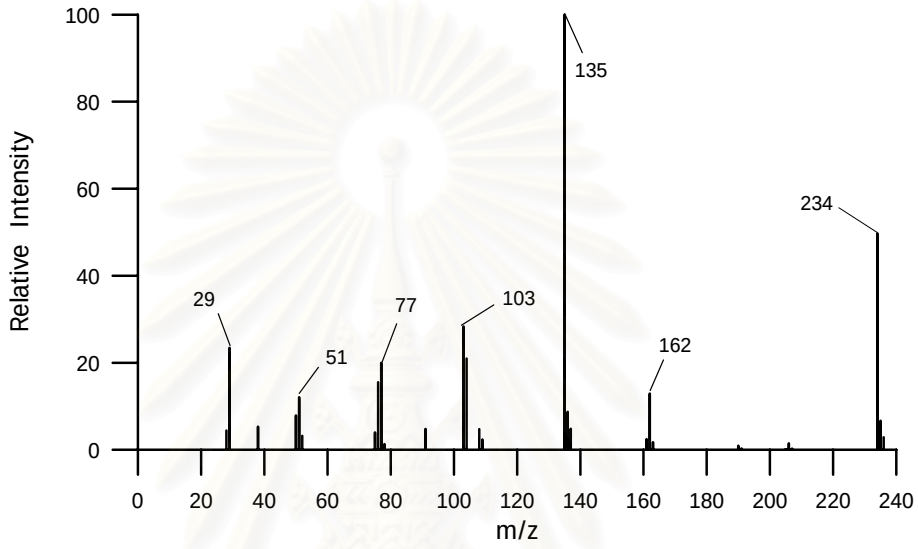


Figure 10b The mass spectrum of the compound eluted at retention time 12.4 minutes.

The ^{1}H–NMR spectrum of **43** (Figure 11) exhibits phenyl ring protons as two set of multiplets at δ 7.43-7.44 (3H) and δ 8.28-8.29 (2H) due to the set of meta-, para- and set of ortho- ring proton, respectively. The ethyl ester protons are shown at δ 4.51 as a quartet (2H; J = 7.07 Hz) and at δ 1.41 as a triplet (3H; J = 7.07 Hz).

The ^{13}C–NMR spectrum (Figure 12) exhibits the two carbons of ethyl ester group at δ 14.59 (-CH_2-) and 63.77 (CH_3-). The ring phenyl carbons appear as four singlets at δ 128.90, 129.21, 131.34 and 132.38. The signal at δ 179.37 is assigned to the ester carbonyl carbon. The two carbons of the thiadiazole ring at position 3 and 5 appear at δ 158.95 and at δ 175.12, respectively. These assignments can be supported by the ^{13}C-NMR DEPT 135 spectrum, shown in Figure 13. The signals at δ 14.59 and 63.77 absorb in positive and negative directions in the ^{13}C–NMR DEPT 135 spectrum, respectively, which are consistent with their assignments as methylene and methyl carbons, respectively. Three signals at δ 158.95, 175.12 and 179.37 disappear in the ^{13}C–NMR DEPT 135 spectrum confirming that they are all quaternary carbons.

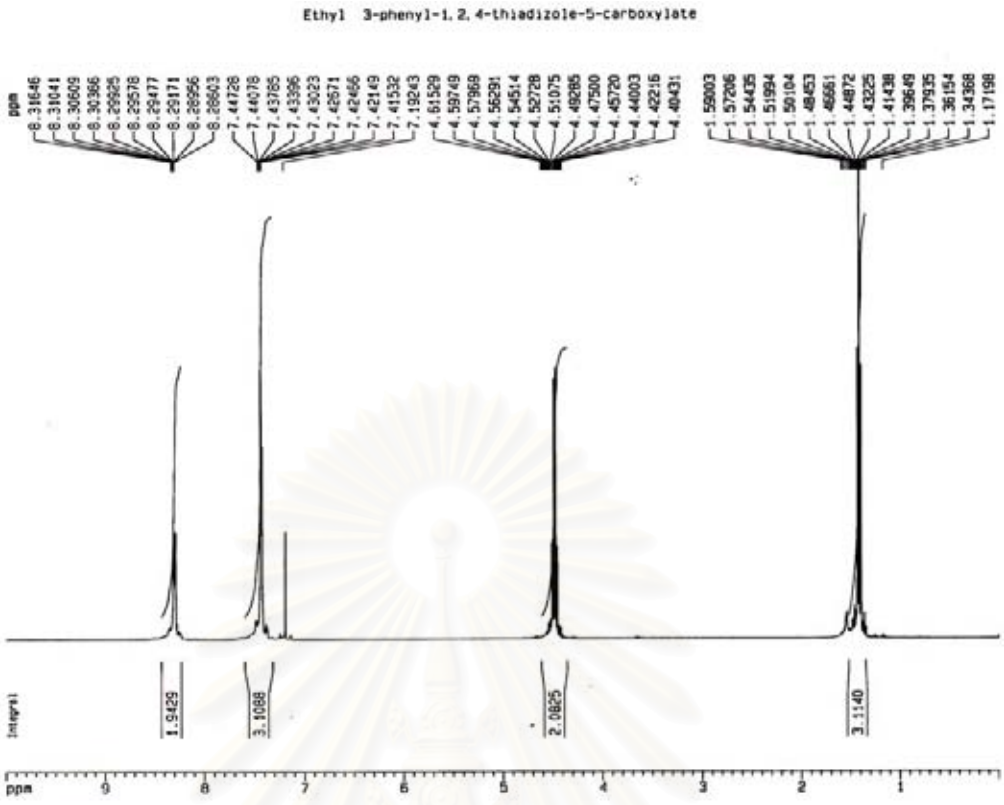


Figure 11 The ^{1}H–NMR spectrum of **43**.

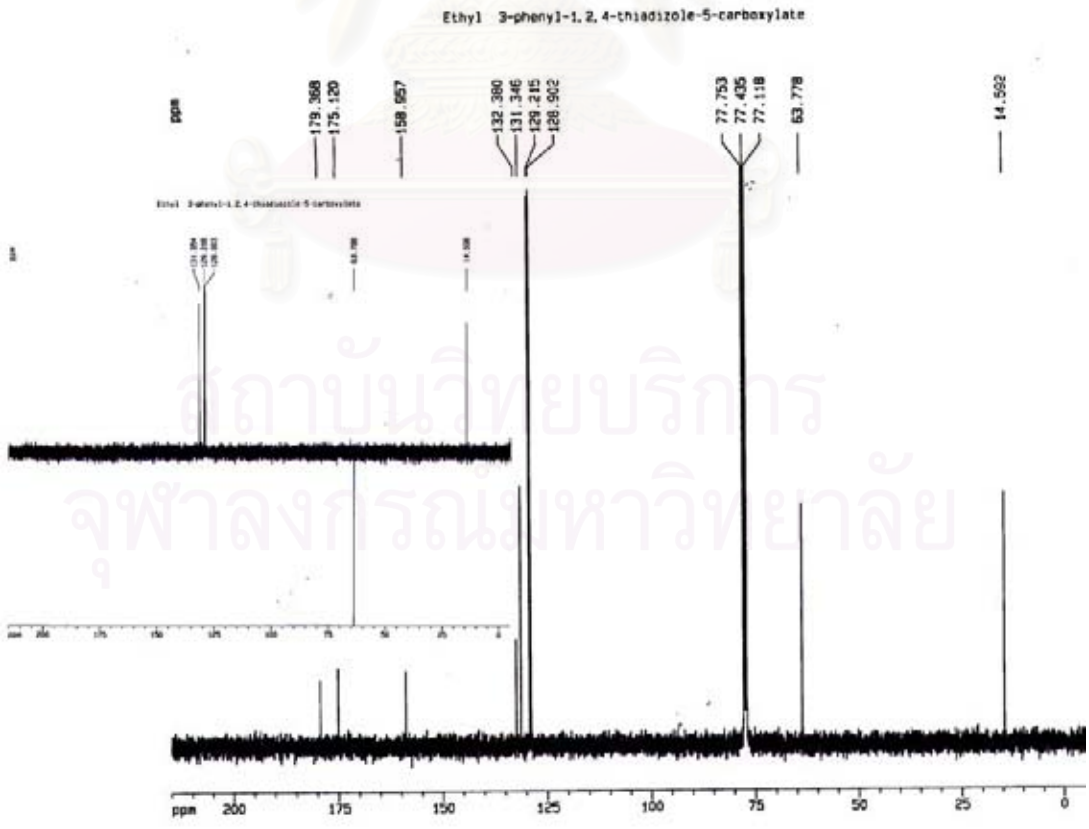
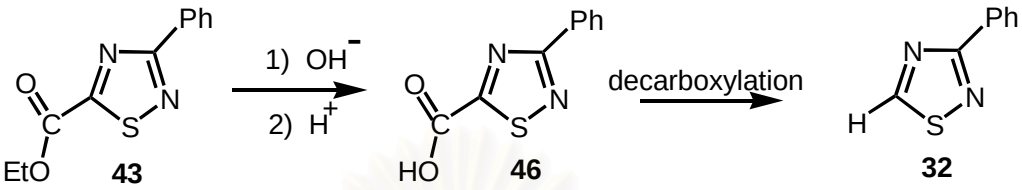


Figure 12 The ^{13}C and ^{13}C–NMR DEPT 135 spectra of **43**.

3.1.1.2.3 Synthesis of 3-phenyl-1,2,4-thiadiazole (32)

Base catalyzed ester hydrolysis of **43** led to the formation of 3-phenyl-1,2,4-thiadiazole-5-carboxylic acid **(46)**. Decarboxylation of **46** produced 3-phenyl-1,2,4-thiadiazole **(32)** as a white solid in 72 % yield.



The GC-MS analysis [150°C (5 min.), 30°C/min. to 180°C (17 min.)] (Figure 13a) shows only one component, which was eluted with a retention time of 13.2 minutes. The mass spectrum (Figure 13b) of this product exhibits a molecular ion at m/z 162 and the base peak at m/z 135 which corresponds to its molecular weight (MW 162) and to the possible fragment $[C_6H_5CNS]^{+\bullet}$. The mass spectrum also corresponds with the reported molecular ion of this compound.[15]

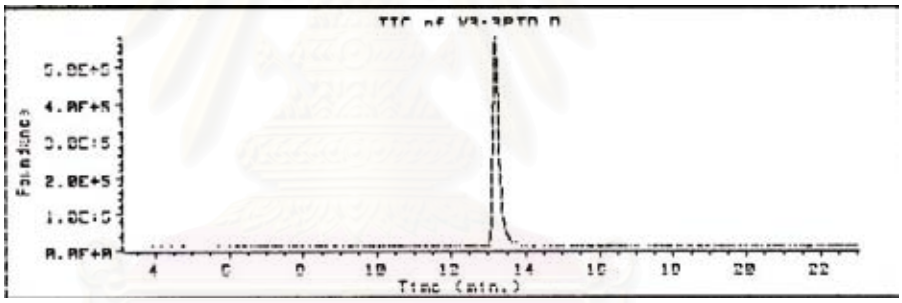


Figure 13a The GC-MS analysis of **32**.

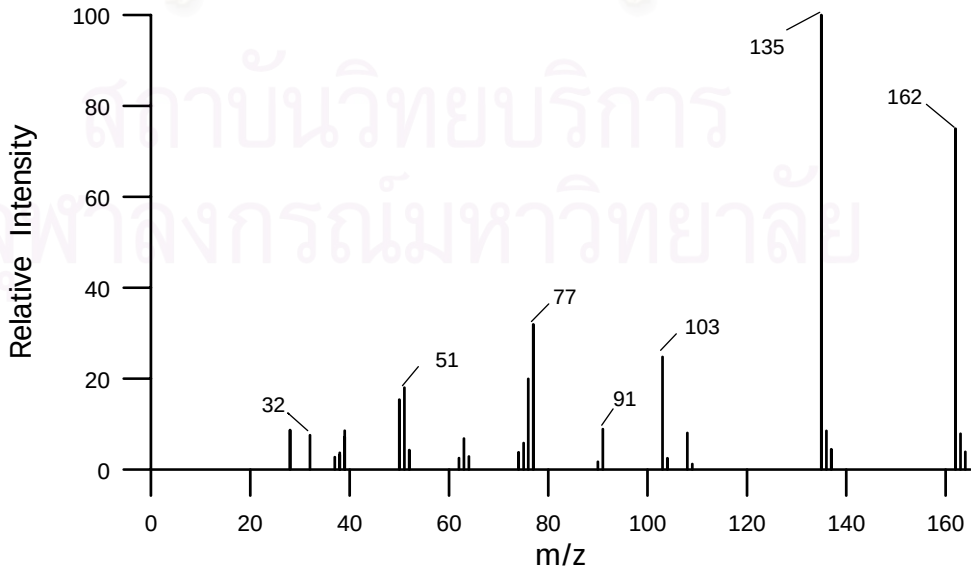


Figure 13b The mass spectrum of the compound eluted at a retention time of 13.2 minutes.

The ^{1}H–NMR spectrum (Figure 14) exhibits a very clear spectrum. The proton at ring position 5 absorbs downfield at δ 10.27 as a singlet (1H). The phenyl ring protons appear as two set of multiplets at δ 7.49-7.55 (3H) assigned to the meta- and para- ring protons and δ 8.33-8.36 (2H) assigned to the ortho- ring protons.

The ^{13}C–NMR spectrum (Figure 15) shows the two carbon atoms of the thiadiazole ring at δ 174.91 and 75.99. 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–NMR DEPT 135 spectrum (Figure 15) which confirms that the signal at δ 174.91 is due to a quaternary carbon. The signal at δ 175.99 still appears in the ^{13}C–NMR DEPT 135 spectrum and that must be due to the carbon at ring position 5 of the thiadiazole ring.

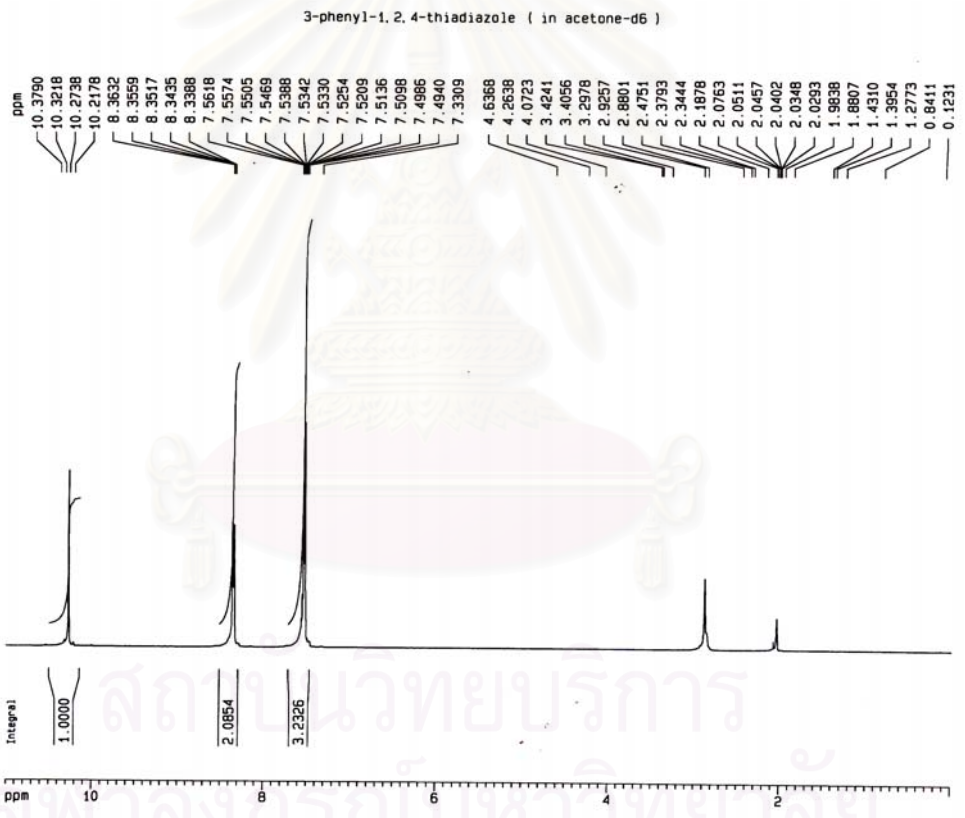


Figure 14 The ^{1}H–NMR spectrum of **32**.

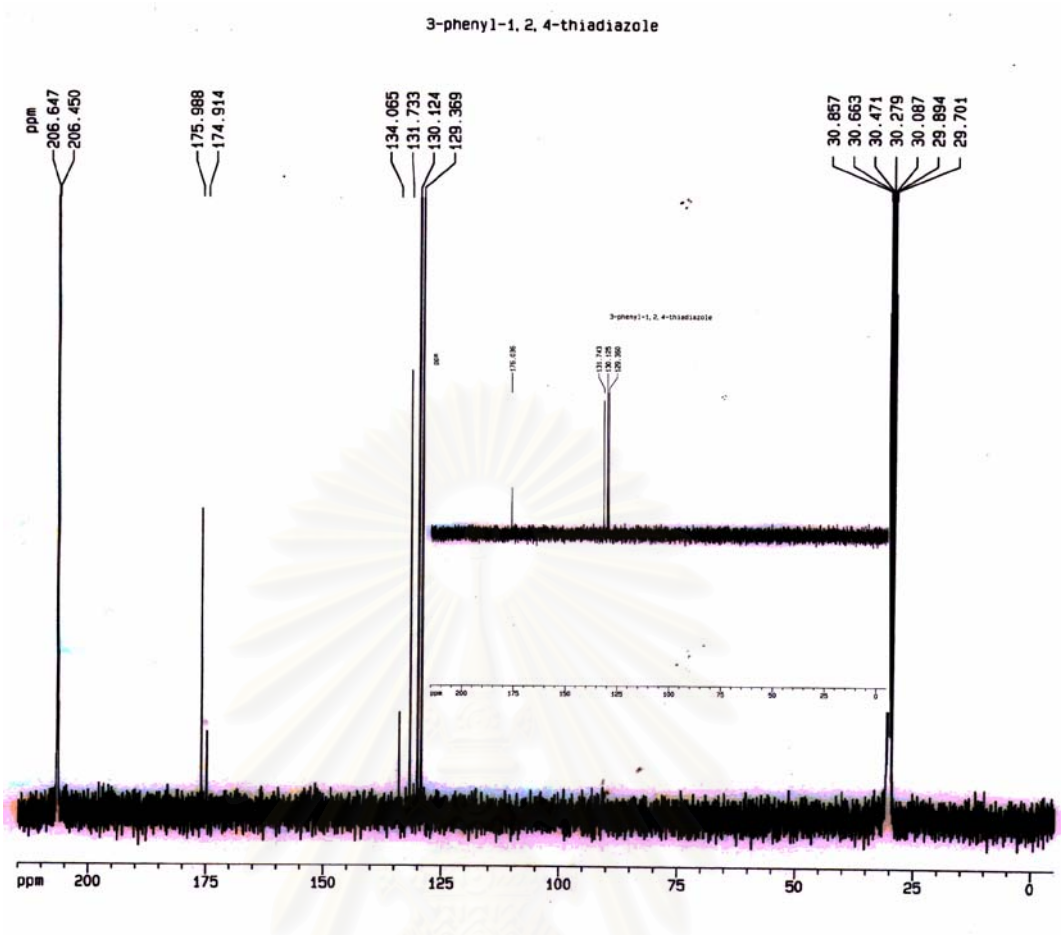
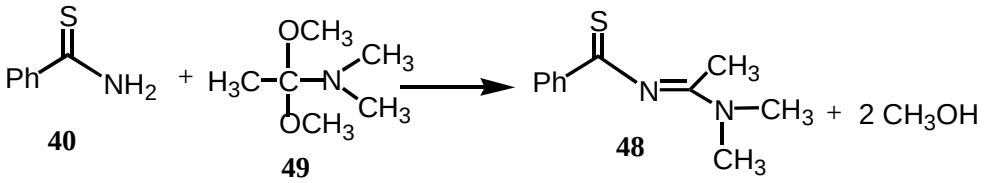


Figure 15 The ^{13}C and ^{13}C-DEPT 135 NMR spectra of **32**.

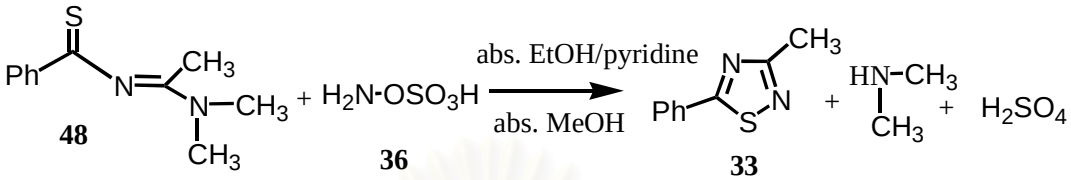
3.1.1.3 Synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole (33)

As mentioned in section 1.1.2, 5-phenyl-1,2,4-thiadiazole **(31)** can be synthesized by the amination cyclization of **35** with **36**. The reaction not only allows the formation of 5-monosubstituted-1,2,4-thiadiazole but also allows 3,5-disubstituted-1,2,4-thiadiazoles.

Therefore, 3-methyl-5-phenyl-1,2,4-thiadiazole **(33)** was synthesized by the amination cyclization of the corresponding amidine, *N*-[(dimethylamino)ethylidine]thiobenzamide **(48)**.[14]



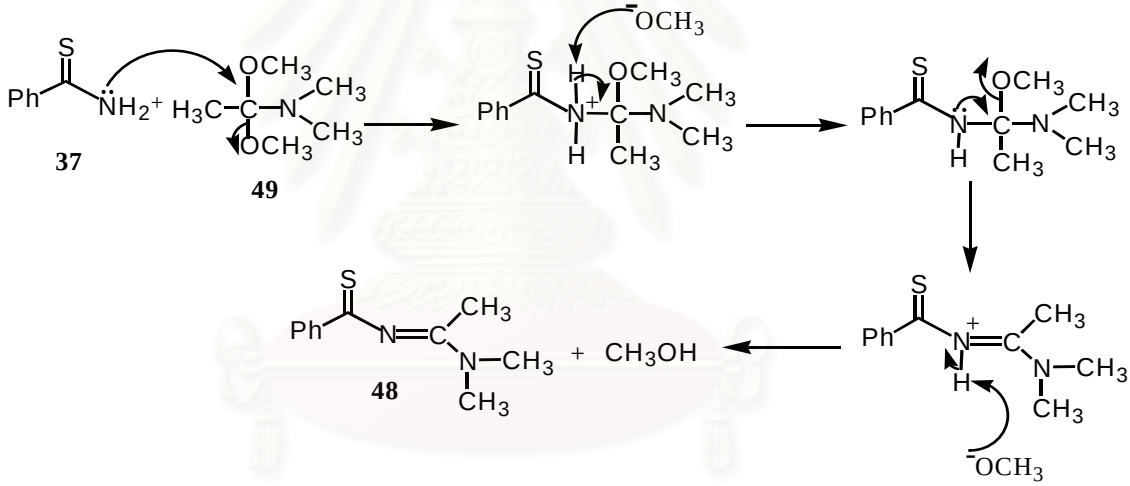
40 **49** **48**



48 **36** **33**

3.1.1.3.1 Synthesis of *N*-[(dimethylamino)ethylidine]thiobenzamide (48)

N-[(dimethylamino)ethylidine]thiobenzamide **(48)** was prepared in 89.8 % by the condensation between **37** and *N*,*N*-dimethylacetamide dimetylacetal **(49)**.



37 **49** **48**

The orange crystalline 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.)]. The mass spectrum of the compound eluted at the retention time of 23.9 minutes (Figure 16b) exhibited a molecular ion at m/z 206 which corresponds to the molecular weight of the desired product, *N*-[(dimethylamino)ethylidine]thiobenzamide **(48)**. It should be noted the presence of some impurities in the GC trace (Figure 16a).

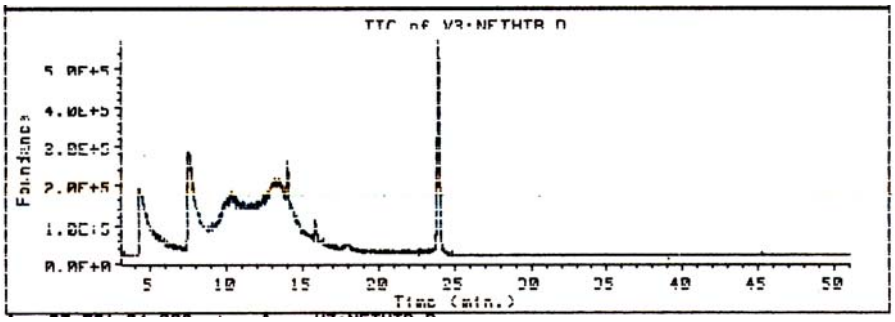


Figure 16a GC-MS analysis of **48**.

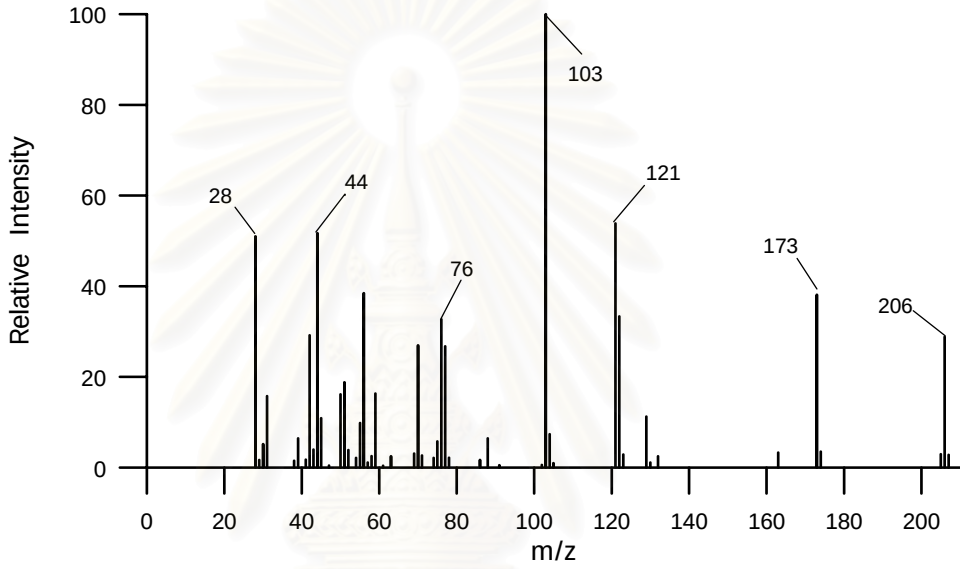


Figure 16b The mass spectrum of the compound eluted at a retention time of 23.9 minutes.

This orange crystalline solid is different from *N*-[(dimethylamino)methylene]thiobenzamide **(35)**, and expected to be **48**, since the substituent at the imine carbon in this case is methyl group instead of hydrogen. Indeed, the ^{1}H–NMR spectrum of this orange solid (Figure 17) exhibits a 3H singlet at δ 2.45 which can be assigned to the methyl protons of the methyl group attached to the imine carbon. The two singlets (3H) at δ 3.20 and 3.22 are the absorptions due to the two sets of the non-equivalent methyl protons bonded to the amino group. The two sets of multiplet at δ 7.31-7.41 (3H) and δ 8.22-8.28 (2H) are assigned to the set of para-, and meta- and the set of ortho- phenyl protons, respectively.

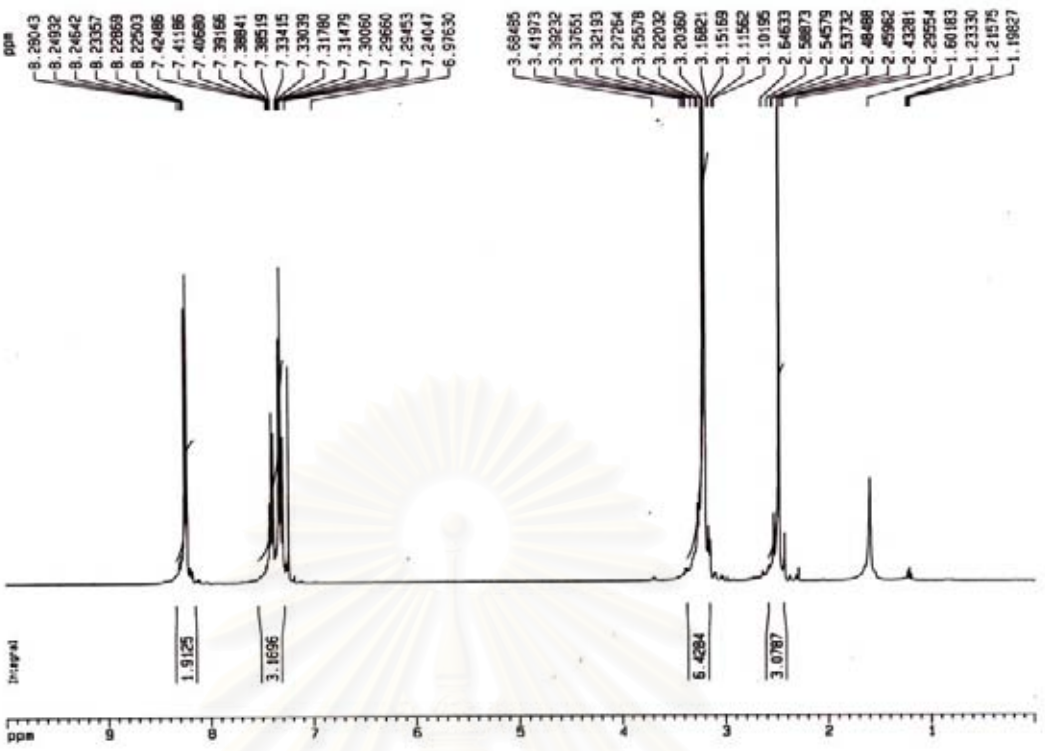


Figure 17 The ^{1}H–NMR spectrum of **48**.

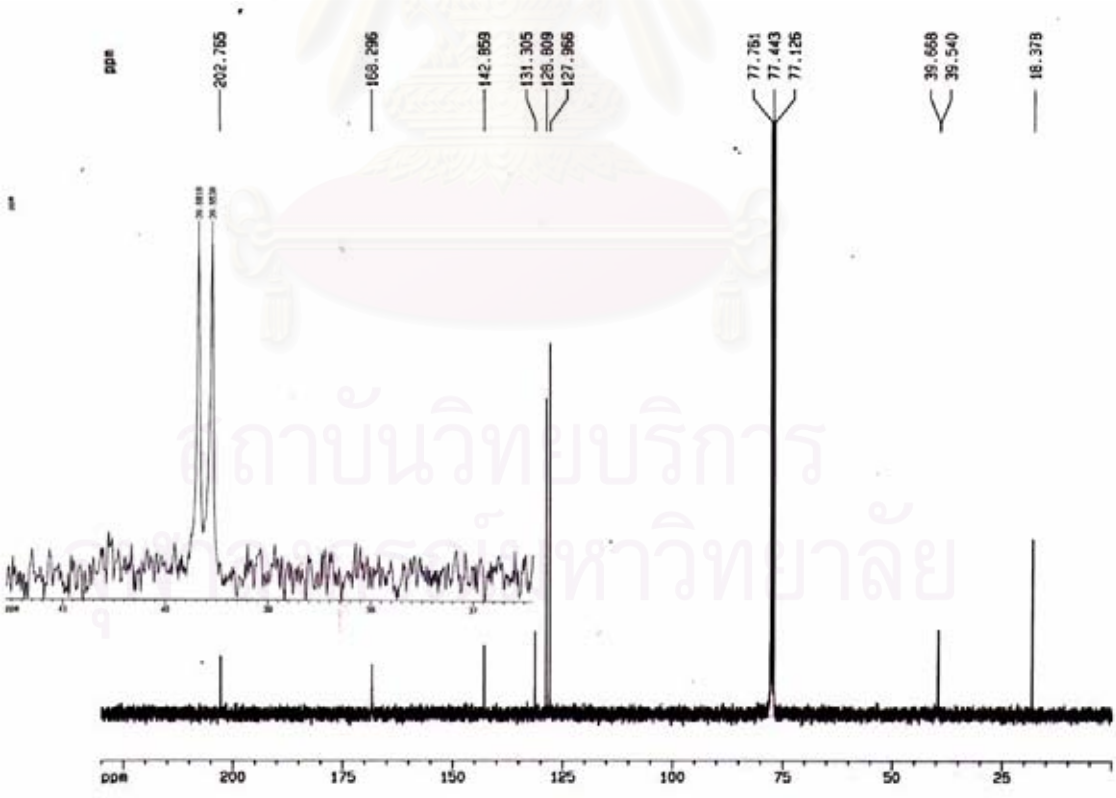


Figure 18 The ^{13}C – NMR spectrum of **48**.

In the ^{13}C–NMR spectrum (Figure 18), the most down field signal at δ 202.76 is assigned to the thiocarbonyl carbon. The imine carbon absorbs at δ 168.29. The four signals at δ 127.97, 128.81, 131.30 and 142.86 are assigned to the ring phenyl carbons. The spectrum reveals the two non-equivalent methyl carbons of the amino group as two singlets at δ 39.54 and 39.67. The methyl carbon attached to the imine carbon appears at δ 18.38.

The above ^{13}C–spectral assignments are consistent with the ^{1}H–^{13}C correlation spectrum (Figure 19). The carbon signal at δ 18.38, which was assigned to the methyl carbon attached to the imine carbon, correlates with 3H-singlet proton signal at δ 2.48, which was assigned to the protons of the methyl group attached to the imine carbon. The two singlet carbons at δ 39.54 and 39.67, 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, in the GC-MS analysis exhibited the presence of some impurities, all NMR results are consistent with the structure of the desired product **(48)**.

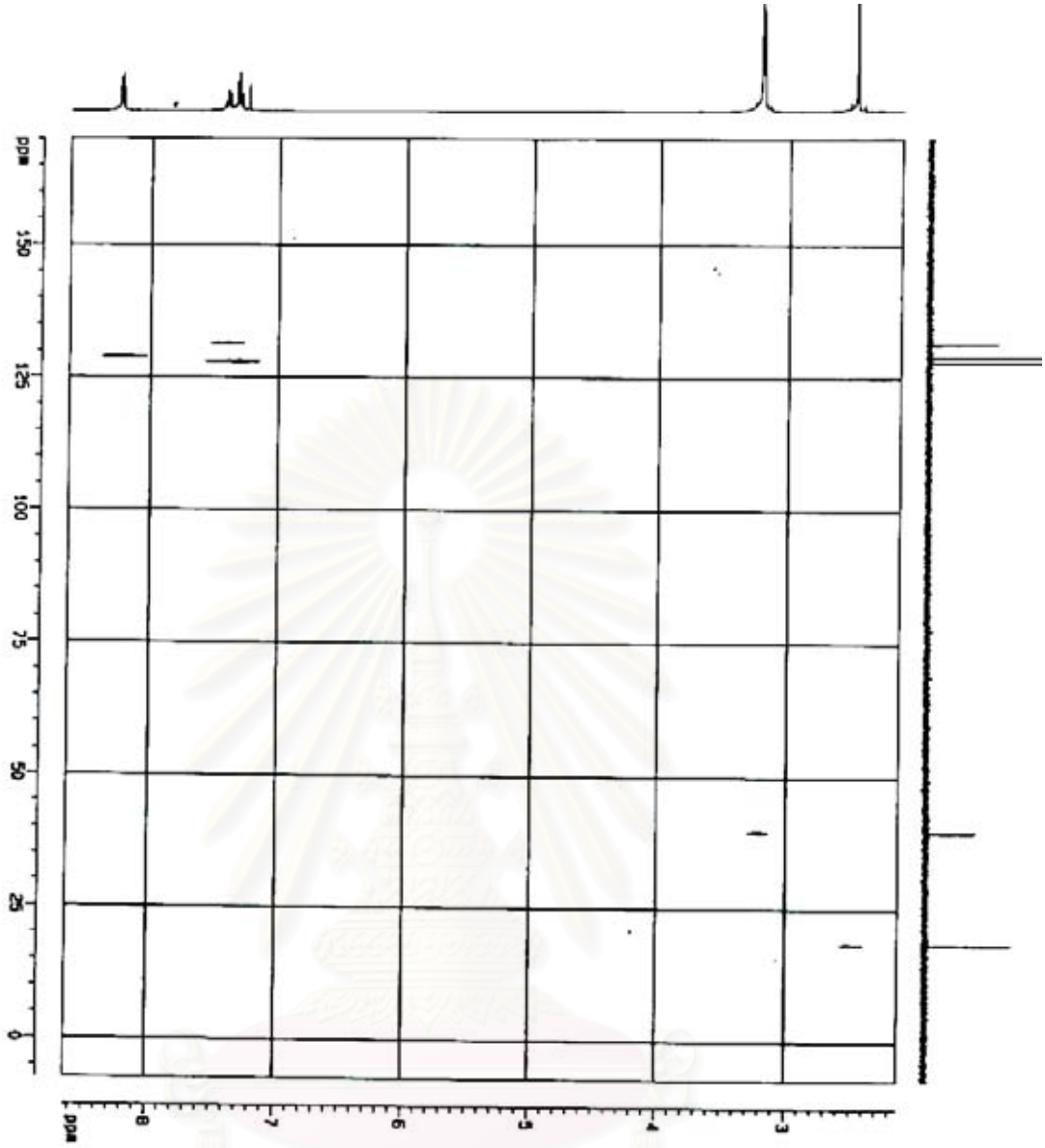
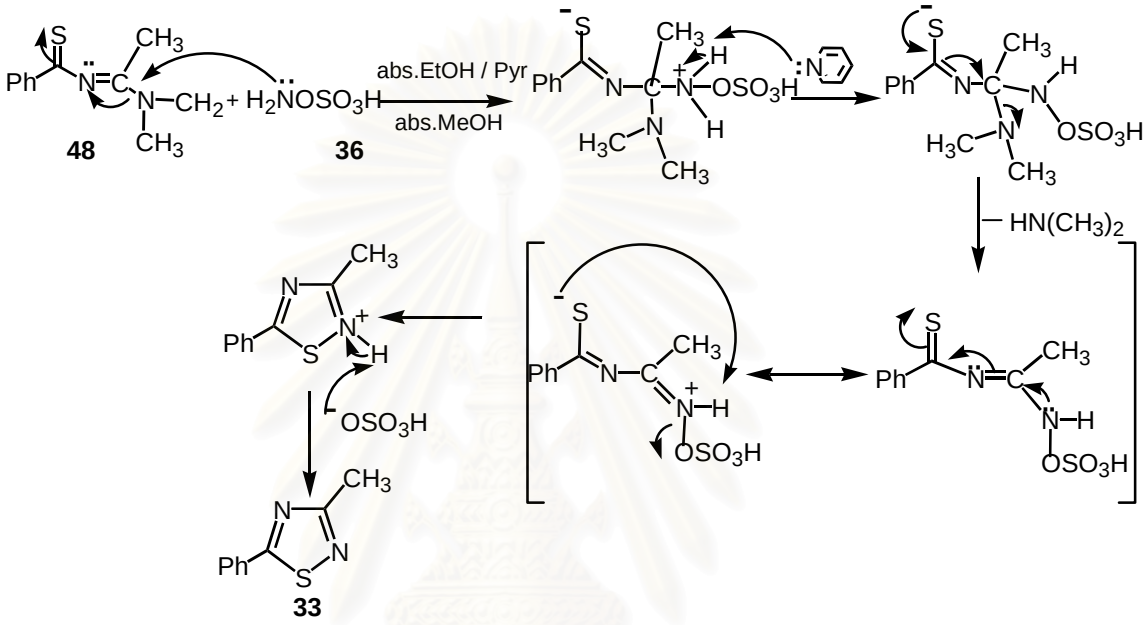


Figure 19 The ^{1}H–^{13}C NMR correlation spectrum of **48**.

3.1.1.3.2 Synthesis of 3-methyl-5-phenyl-1,2,4-thiadiazole (33)

3-Methyl-5-phenyl-1,2,4-thiadiazole **(33)** can be synthesized by the same method as described by Yang-i Lin[14] and colleagues for the synthesis of **31**. But in the case of **33**, the amination cyclization will employ **48** as the starting material instead of **35**.



3-Methyl-5-phenyl-1,2,4-thiadiazole **(33)** was obtained in 75% as white colorless crystal. Its GC-MS analysis (isothermal 170°C) exhibits a major peak at a retention time of 15.6 minutes (Figure 20a) and shows a molecular ion at m/z 176 (Figure 20b) which is consistent with the molecular weight of **33** (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 fragments of $[C_6H_5CNS]^{+\bullet}$ and $[CH_3CNS]^{+\bullet}$, respectively.

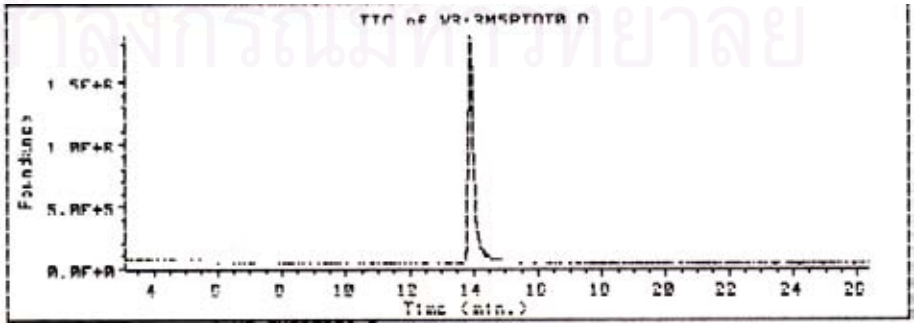


Figure 20a The GC-MS analysis of **33**.

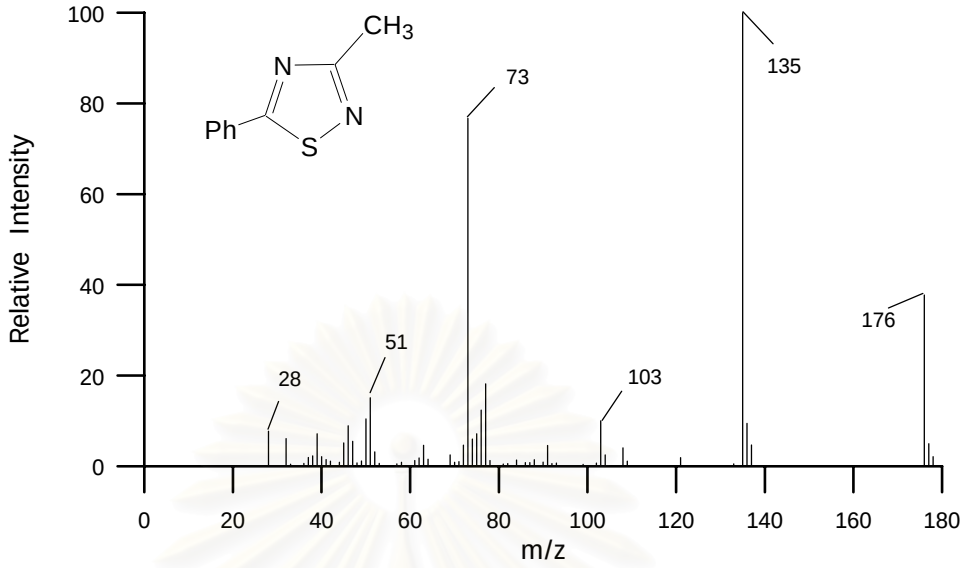


Figure 20b The mass spectrum of the compound eluted at a retention time of 15.6 minutes.

The ^{1}H-NMR spectrum (Figure 21) shows the methyl group as a 3H singlet at δ 2.70. The phenyl ring protons appear as two multiplets at δ 7.46-7.51 (3H) assigned to para-, and meta- phenyl ring protons and δ 7.90-7.93 (2H) assigned to ortho- phenyl ring protons.

The ^{13}C–NMR spectrum (Figure 22) reveals the methyl carbon at δ 19.45. The two ring carbons at positions 3 and 5 on thiadiazole ring absorb at δ 174.55 and 188.47, respectively. The four signals at δ 127.78, 129.69, 130.93 and 132.27 are assigned to the phenyl ring carbons. These spectral assignments were confirmed by the ^{13}C–NMR DEPT 135 spectrum (Figure 22). The signal at δ 19.45 still appears in the ^{13}C–NMR DEPT 135 spectrum, which is consistent with the assignment to the methyl carbon. The two signals at δ 174.55 and 188.4, which were assigned to the two carbons positions 3 and 5 of thiadiazole ring, are not observed in the ^{13}C–NMR 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–NMR DEPT 135 spectrum. Thus, these signals can be assigned to the ortho-, meta- and para- phenyl ring carbons. The signal at δ 130.93, which, however, was not observed in the ^{13}C–NMR DEPT 135 spectrum, and therefore can be assigned to the phenyl carbon at ring position 1.

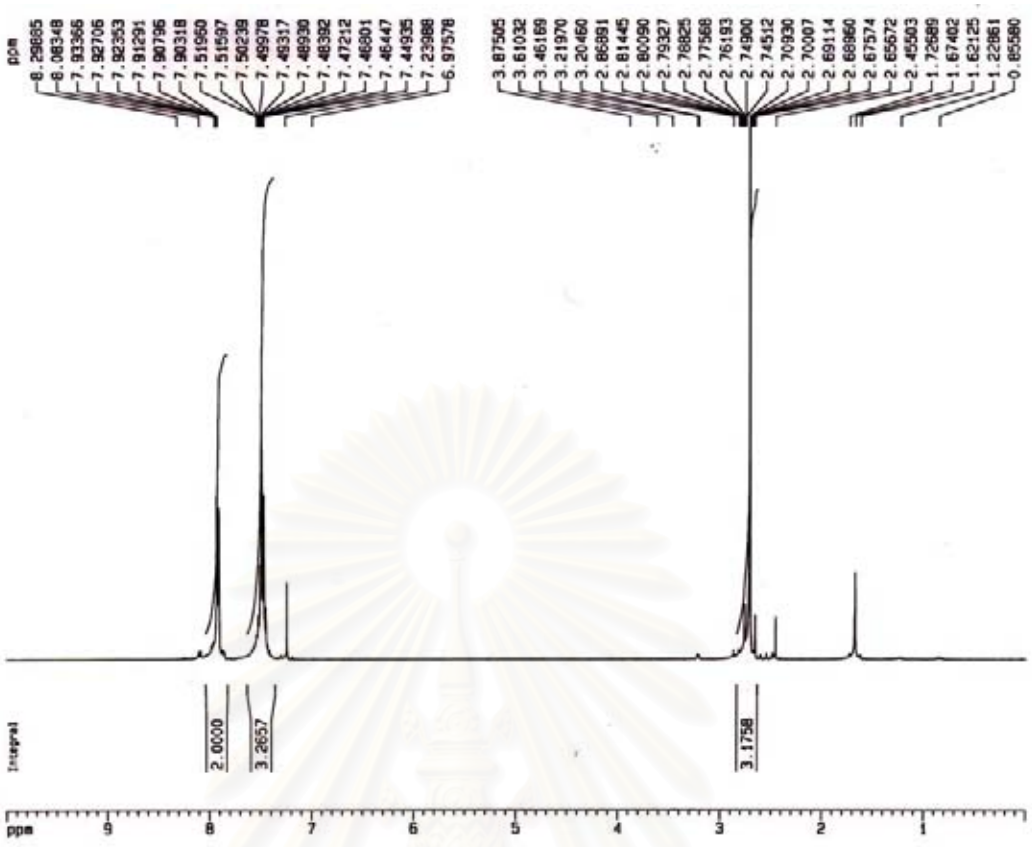


Figure 21 The ^{1}H–NMR spectrum of **33**.

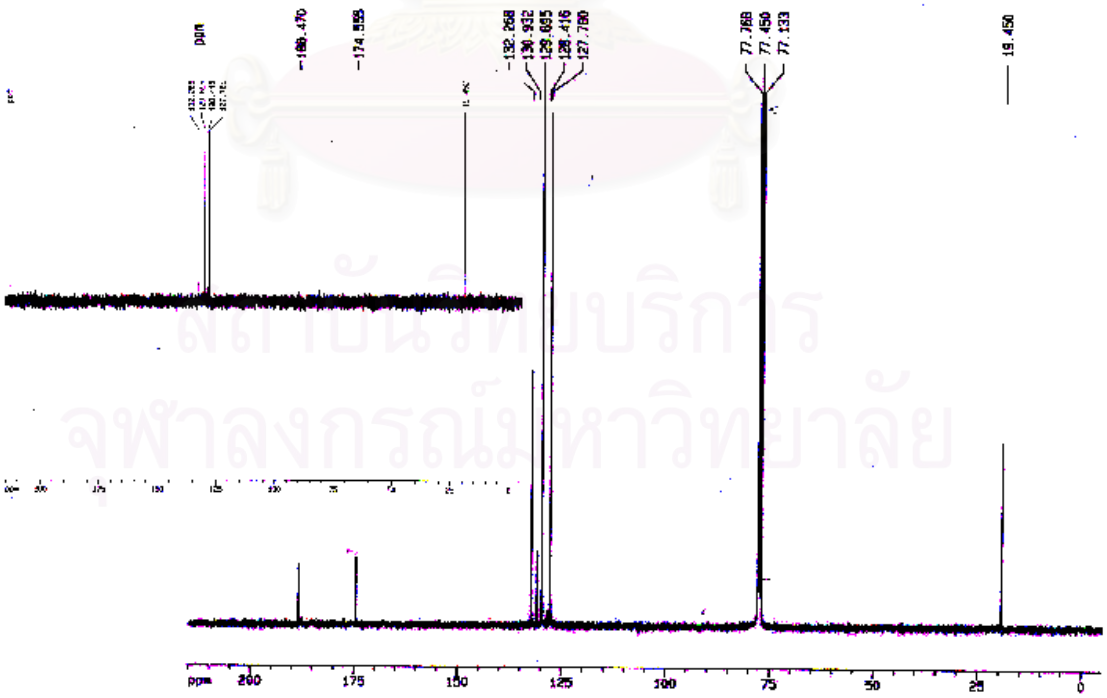


Figure 22 The ^{13}C- and ^{13}C-NMR DEPT 135 spectra of **33**.

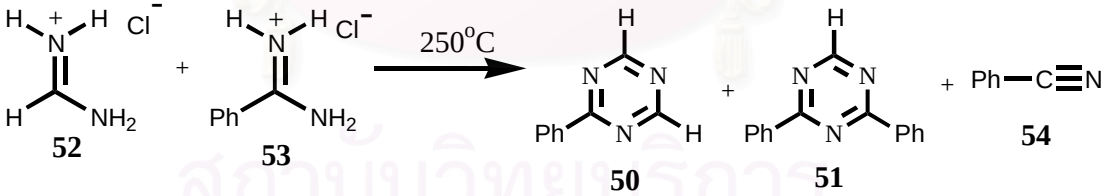
3.1.2 Synthesis of the predicted photoproducts

3.1.2.1 Synthesis of phenyl- and diphenyl-s-triazine

Since phenyl-s-triazine **(50)** and diphenyl-s-triazine **(51)** were suspected to form in the photolysis of 5-phenyl-1,2,4-thiadiazole **(31)**, thus, **50** and **51** were synthesized as authentic samples.

It has been reported that 1,3,5–triazines can be prepared *via* cyclotrimerization of nitriles,[16] 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.

F.C Schaefer and I.Hechenbleiner reported[16] the synthesis of sym-triazines with different substituent groups by trimerization and cotrimerization of amidines. According to their report, **50** and **51** can be prepared in 20% and 50%, respectively, by the cotrimerization of formamidine hydrochloride **(52)** and benzamidine hydrochloride **(53)**.



By employing their procedure, both triazines were obtained as a mixture and separated by steam distillation. Both isolated triazines, A and B, were obtained as white solids with melting points of 62-64 °C and 80-82°C, respectively.

GC-MS analysis of the white solid A [isothermal 170 °C (30 min.)] (Figure 23a) shows only one component, eluted at a retention time of 8.5 minutes. Its mass spectrum (Figure 23b) exhibits a molecular ion at m/z 157 corresponding to the molecular weight of **50** (MW 157). The base peak at m/z 104 due to the $[C_6H_5CNH]^{+\bullet}$ fragment further confirms the major fragmentation pathway of **50** rather than the cleavage of benzonitrile fragment (m/z 103).

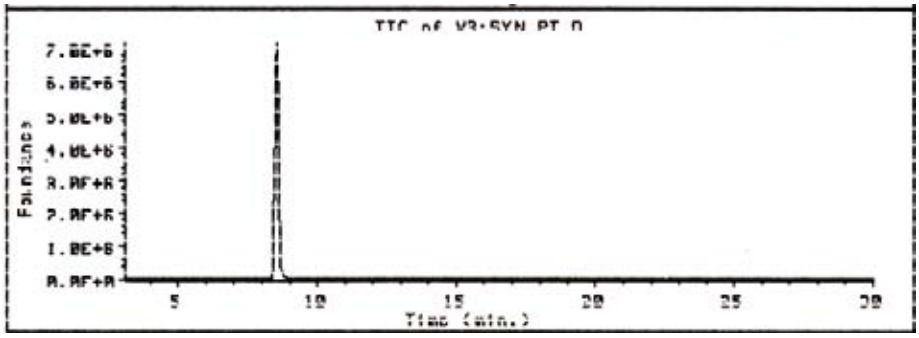


Figure 23a The GC-MS analysis of the white solid A.

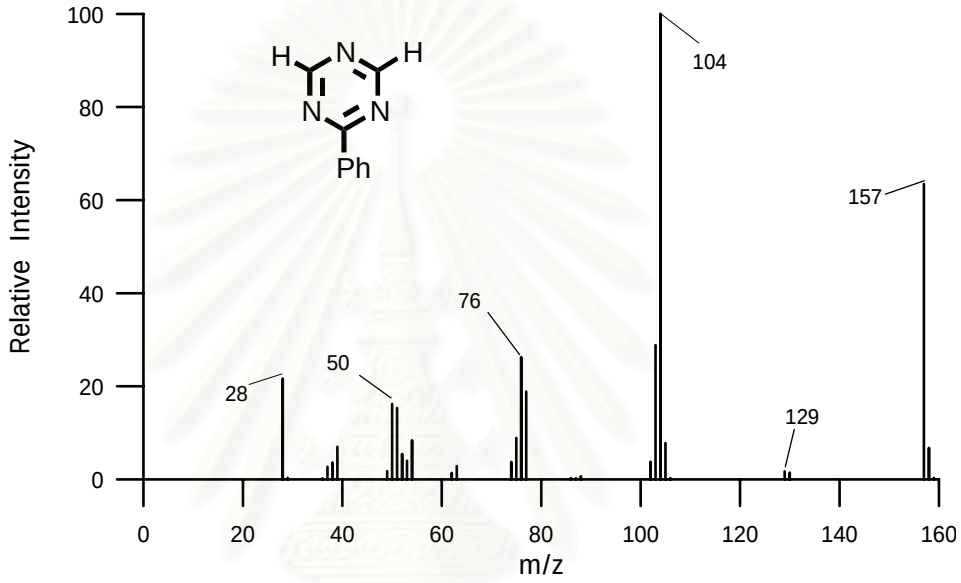


Figure 23b The mass spectrum of the white solid A.

GC-MS analysis of the white solid B [isothermal 240°C (30 min.)] (Figure 24a) also shows only one GC-volatile component eluted at a retention time of 16.2 minutes. As expected, its mass spectrum (Figure 24b) exhibits a molecular ion at m/z 233, which is consistent with the molecular weight of **51** (MW 233). In this case the base peak is observed at m/z 103 instead, which probably due to the cleavage of $[C_6H_5CN]^{+\bullet}$.

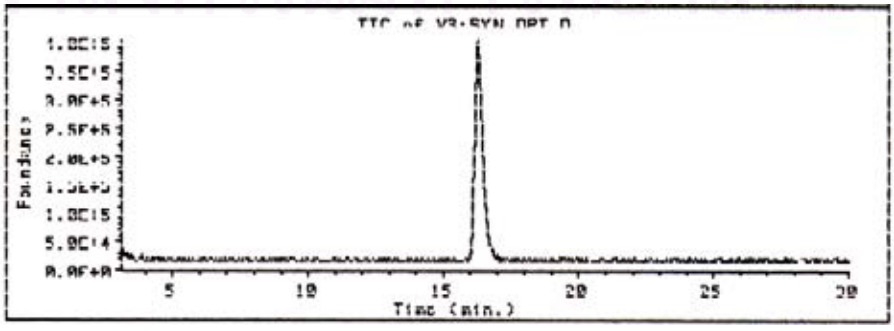


Figure 24a GC-MS analysis of the white solid B.

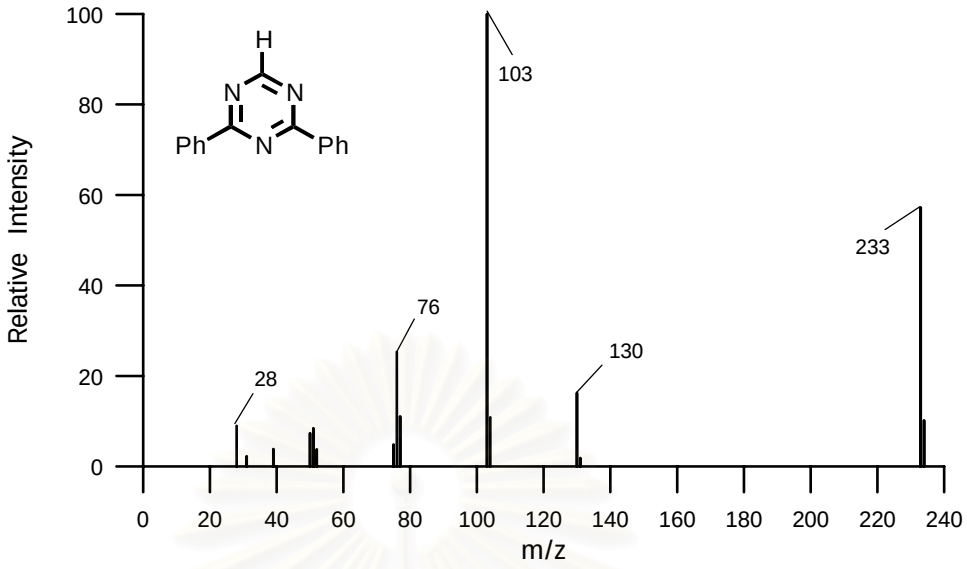


Figure 24b The mass spectrum of the white solid B.

The ^{1}H–NMR spectrum of the white solid A (Figure 25) exhibits a downfield singlet (2H) at δ 9.14 and two multiplets at δ 7.43-7.54 (3H) and δ 8.43-8.45 (2H). In the case of the white solid B, the ^{1}H–NMR spectrum exhibits a singlet (1H) at δ 9.28 and two multiplets at δ 7.56-7.63 (6H) and δ 8.66-8.68 (4H). The ^{1}H–NMR spectrum of white solid A is consistent with the assignment of **50**, 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 the set of meta- protons and 3H due to the set of ortho-, and para- protons). The ^{1}H–NMR spectrum of the white solid B (Figure 26) is also consistent with the assignment of **51**, in which the triazine ring proton absorb at δ 9.28 as a singlet (1H) and the two multiplets at δ 7.56-7.63 (6H) and δ 8.66-8.68 (4H) assigned to the two sets of equivalent phenyl ring protons of **51**. According to the above mass spectra and ^{1}H–NMR spectra, the white solid A can be identified as **50** and the white solid B can be identified as **51**.

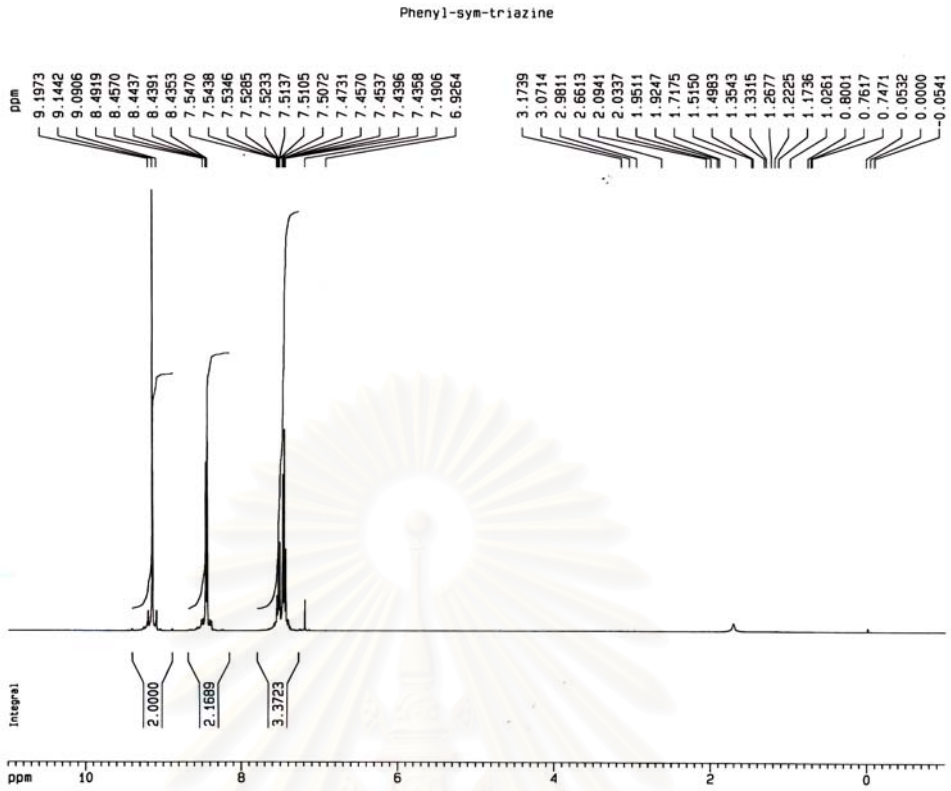


Figure 25 The ^{1}H–NMR spectrum of the white solid A.

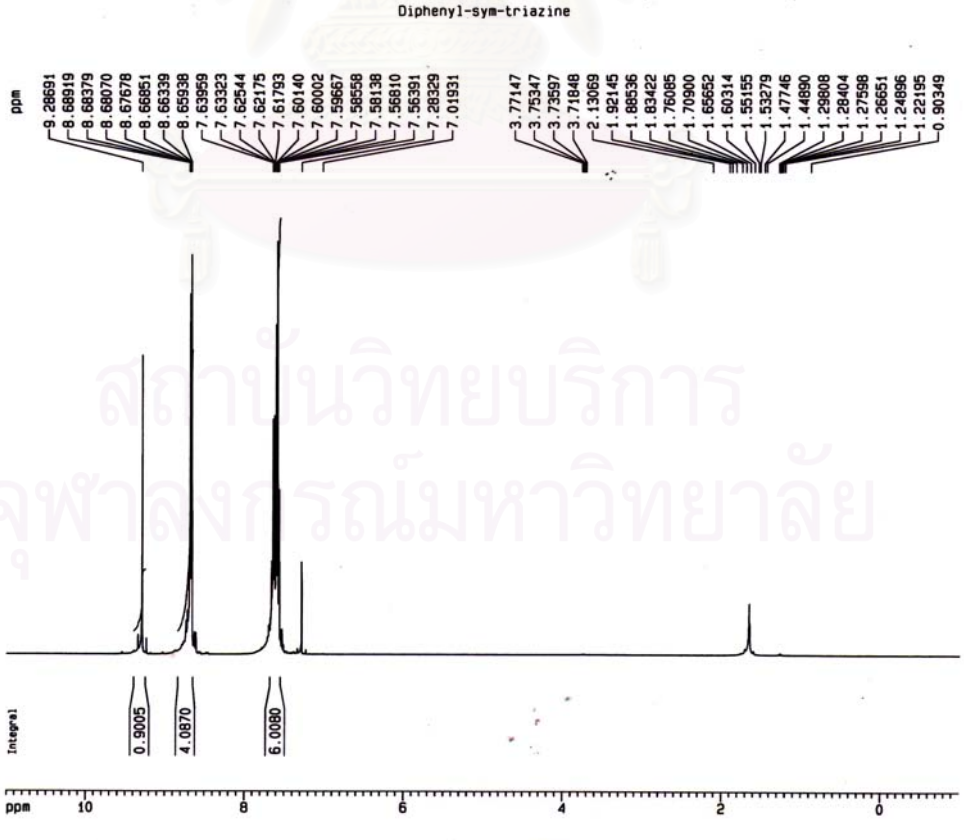
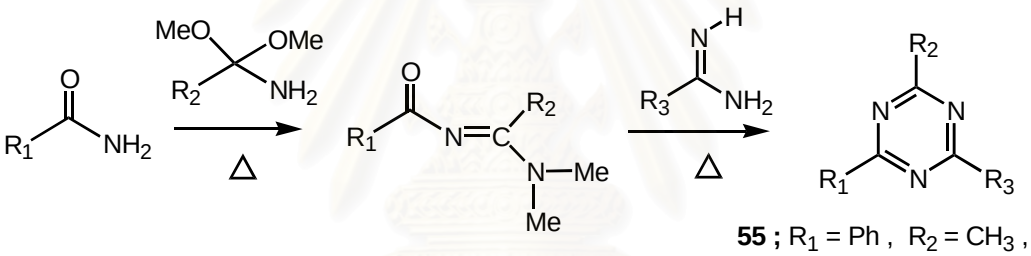


Figure 26 The ^{1}H–NMR spectrum of the white solid B.

3.1.2.2 Synthesis of 2,4-dimethyl-6-phenyl-1,3,5-triazine (55) and 2-methyl-4,6-diphenyl-1,3,5-triazine (56)

2,4-Dimethyl-6-phenyl-1,3,5-triazine **(55)** and 2-methyl-4,6-diphenyl-1,3,5-triazine **(56)** were also anticipated to occur in the photolysis of 3-methyl-5-phenyl-1,2,4-thiadiazole **(33)**. These expected photoproducts, were thus synthesized as authentic samples.

The cotrimerization of amidines described by Schaefer and colleagues[16] afforded to the formation of monosubstituted-sym-triazines as well as the unsymmtrically substituted-sym-triazines. Therefore, this procedure can lead to the mixture of sym-triazines products. More recently, a new synthesis of unsymmetrically substituted-sym-triazines was reported. This method involves the condensation of *N*-acylamidines and amidines or guanidines in aprotic solvent.[17] Therefore, both **55** and **56** were synthesized by the latter method.

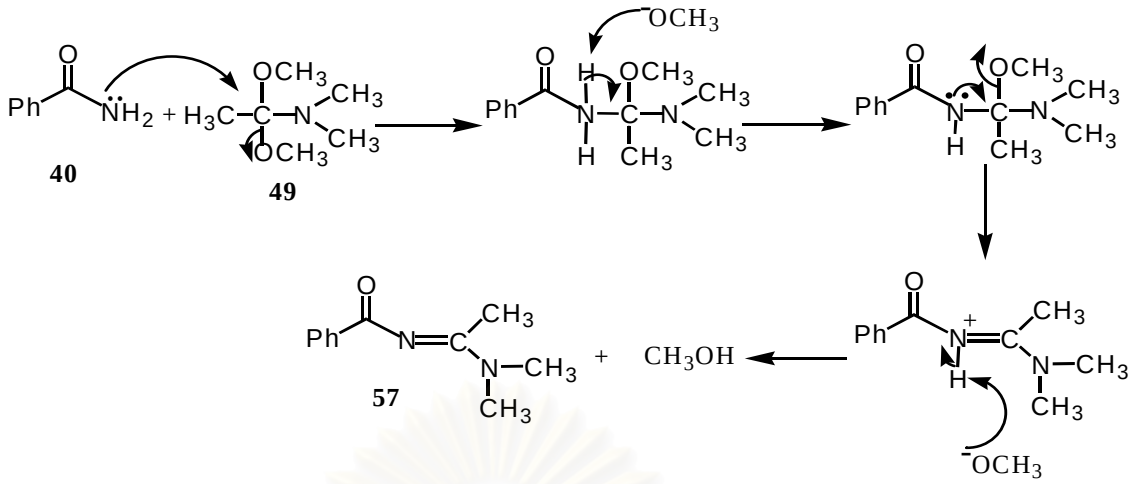


55 ; R_1 = Ph , R_2 = CH_3 , R_3 = CH_3

56; R_1 = Ph , R_2 = CH_3 , R_3 = Ph

3.1.2.2.1 Synthesis of *N*-[(dimethylamino)ethylidine]benzamide (57)

To synthesize **55** and **56** by the method described by Dengino and colleagues, it requires the acylamidine, *N*-[(dimethylamino)ethylidine]benzamide **(57)**. This amidine **57** was prepared in 90% as a dark viscous liquid by the condensation of benzamide **(40)** and *N*,*N*-dimethylacetamide dimethylacetal **(49)**.



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GC-MS analysis of this dark liquid [180°C(5min.), 10°C/min. to 240°C (30 min.)] (Figure 27a) shows the presence of only one component at a retention time of 17.4 minutes. The mass spectrum (Figure 27b) 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 *N*-[(dimethylamino)ethylidine]benzamide **(57)** (MW190). Furthermore the base peak at m/z 105 corresponds to the cleavage of $[C_6H_5CO]^{+\bullet}$ and the two strong intensity peaks at m/z 44 and 77 correspond to the cleavage of $[C_2H_6N]^{+\bullet}$ and $[C_6H_5]^{+\bullet}$, respectively.

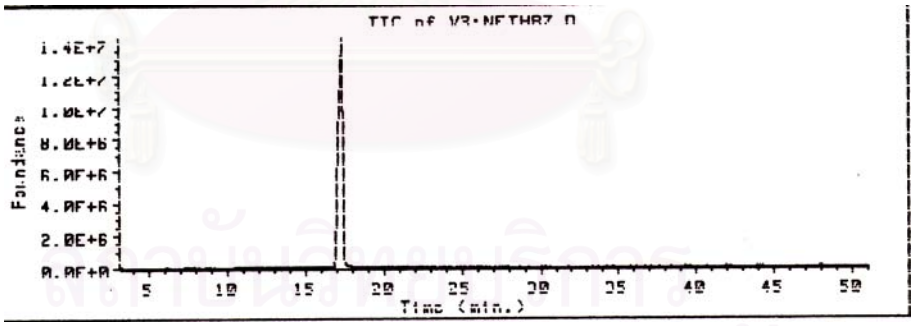


Figure 27a The GC-MS analysis of the dark viscous liquid

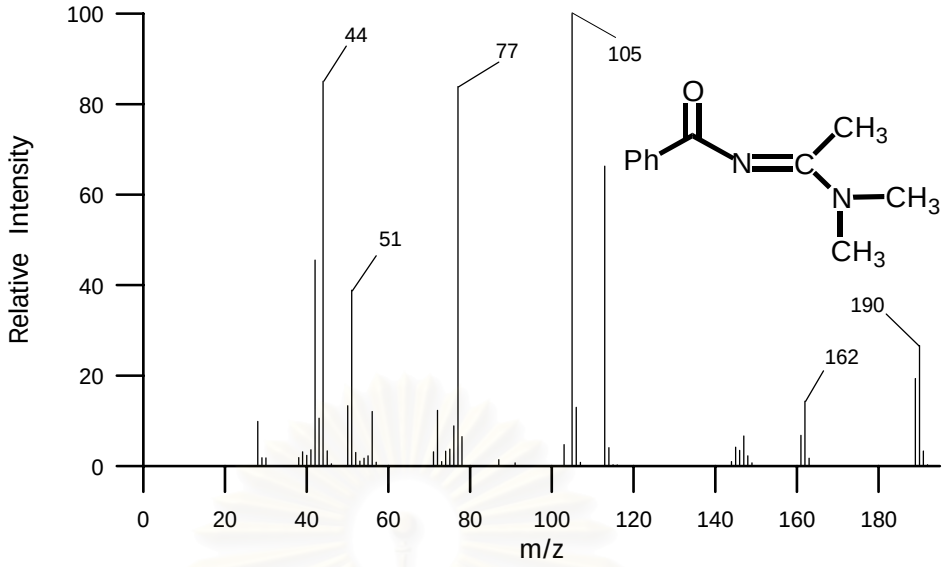


Figure 27b The mass spectrum of the compound eluted at a retention time of 17.4 minutes.

The ^{1}H-NMR spectrum of this liquid (Figure 28) exhibits two multiplets at δ 7.31-7.39 (3H) and δ 8.07-8.12 (2H) and three singlets at δ 2.23 (3H), 2.97 (3H) and 3.07 (3H). This spectrum is consistent with the structure of **57**. The multiplet at δ 7.31-7.39 is assigned to the meta-, and para- phenyl ring protons and the multiplet at δ 8.07-8.12 is assigned to the ortho- ones. The 3H-singlet at δ 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.

The ^{13}C–NMR spectrum of this liquid (Figure 29) also reveals signals consistent with the structure of **57**. The methyl carbon bonded to the imine carbon appears at δ 18.74. The two non-equivalent N-methyl carbons were observed at δ 38.63 and 38.68. In the normal scale spectrum, these two absorptions appear as only one signal. But upon scale expansion (Figure 29), this signal is resolved into two peaks. The signals at δ 128.22, 129.72, 131.66 and 137.93 were assigned to the phenyl ring carbons. Also the signals at δ 165.72 and 176.38 were assigned to the imine carbon and the carbonyl carbon, respectively.

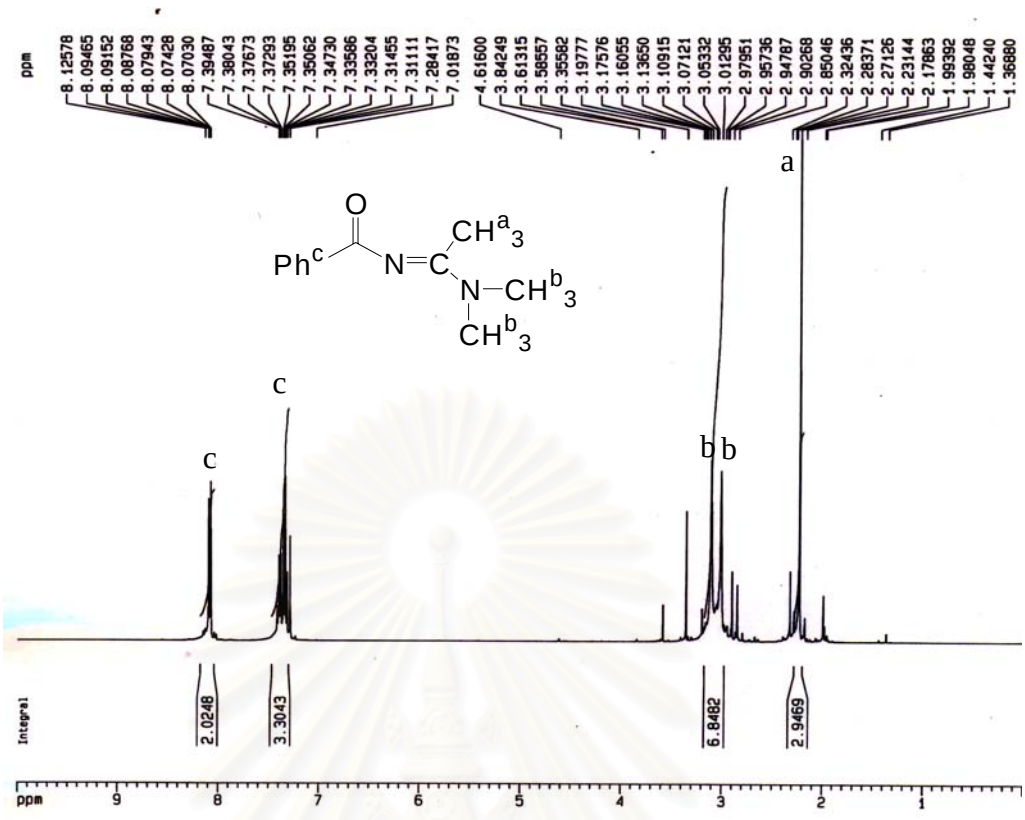


Figure 28 The ^{1}H-NMR spectrum of the dark liquid.

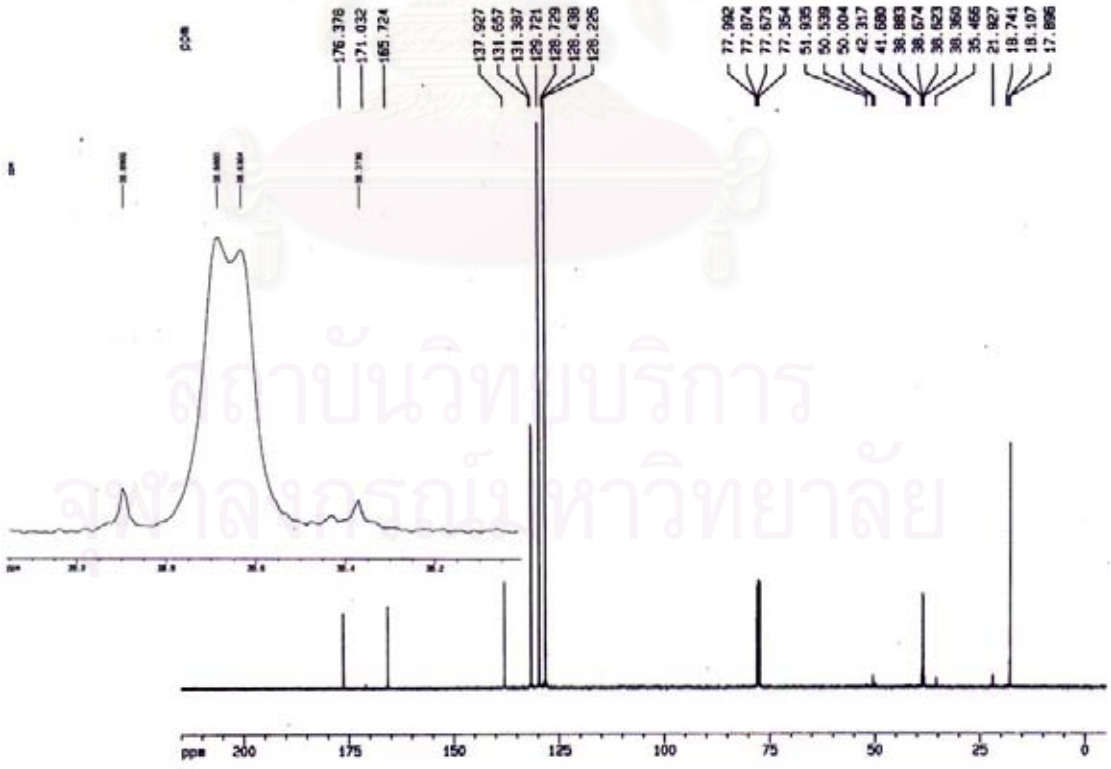


Figure 29 The ^{13}C–NMR spectra of the dark liquid .

In order to confirm the above spectral assignments, the $^{1}H–^{13}C$ NMR correlation spectrum was recorded. This spectrum (Figure 30) reveals that the signal at δ 18.74 in the ^{13}C-NMR spectrum assigned to the methyl carbon bonded to the imine carbon, correlates with the singlet (3H) at δ 2.23 in the ^{1}H–NMR spectrum assigned to the protons of the methyl group bonded to the imine carbon. The signals at δ 38.63 and 38.68 in the ^{13}C-NMR spectrum assigned to the two non-equivalent methyl carbons of the amino group, correlate with the two singlets (3H) at δ 2.97 and 3.07 in the ^{1}H-NMR 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 δ 128.22, 129.72 and 131.66 in ^{13}C–NMR spectrum correlate with the two multiplets at δ 7.31-7.39 and δ 8.07-8.12 in the ^{1}H-NMR spectrum, which were assigned to the protons of the phenyl group. The spectrum also shows the signals of para- and meta-phenyl ring carbons at δ 128.22 and 131.66, respectively, in the ^{13}C-NMR spectrum. Thus, the signal at δ 129.72 can be assigned to the ortho phenyl ring carbons. The signal at δ 137.93 in the ^{13}C–NMR spectrum, which disappear in the $^{1}H–^{13}C$ NMR spectrum, indicated the presence of the phenyl carbon at ring position 1. The signals at δ 165.72 and 176.73 in the ^{13}C–NMR spectrum also disappear in the $^{1}H–^{13}C$ NMR spectrum, is consistent with the assignment of these two quaternary carbons to the imine carbon and the carbonyl carbon.

According to the literature,[18] the melting point of this compound was 47°C, thus, the synthesis of this compound 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 result are consistent with the assignment of this product to be *N*-[(dimethylamino)ethylidine]benzamide **(57)**.

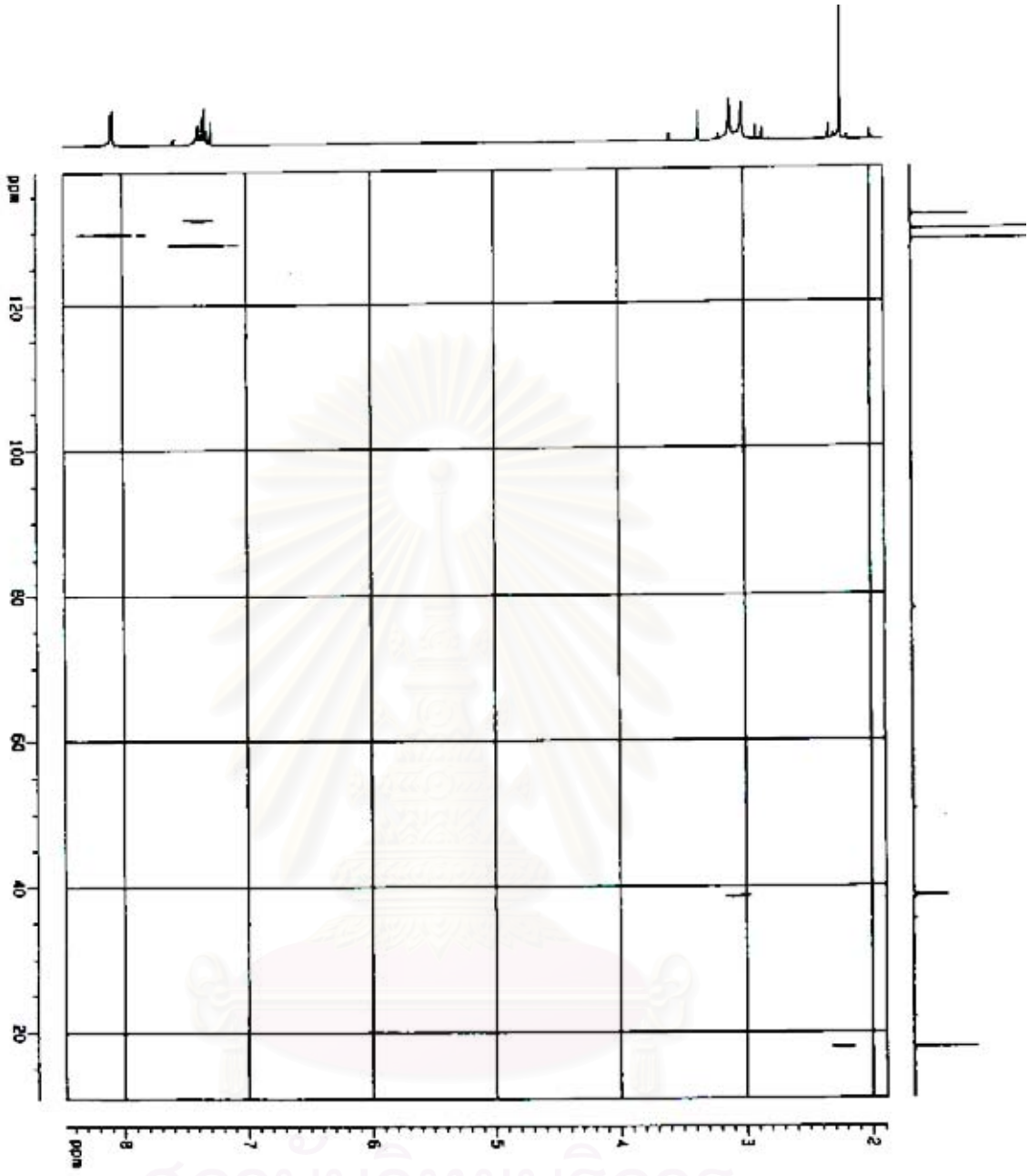
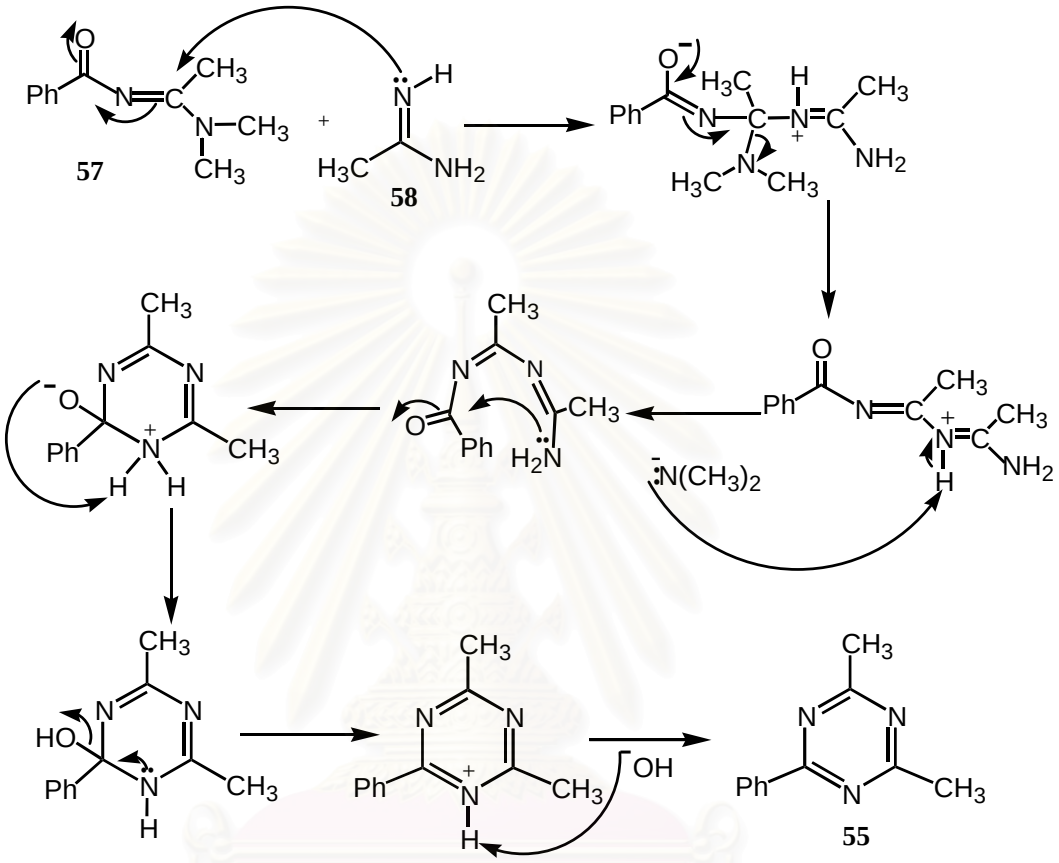


Figure 30 The $^{1}H–^{13}C$ NMR correlation spectrum of the dark liquid.

3.1.2.2.2 Synthesis of 2,4-dimethyl-6-phenyl-1,3,5-triazine (55)

The condensation between **57** and acetamidine **(58)** in refluxing anhydrous tetrahydrofuran led to the formation of 2,4-dimethyl-6-phenyl-1,3,5-triazine **(55)** in 14.6% as a light yellow liquid.



GC-MS analysis [110°C(10 min.), 10°C/min. to 240°C (30 min.)] of the crude product (Figure 31a) indicates the presence of more than one product. The mass spectrum of the compound eluted at a retention time of 16.3 minutes (Figure 31b) exhibits a molecular ion at m/z 185, thus, this compound was expected to be the desired triazine **(55)** (M^+ 185).

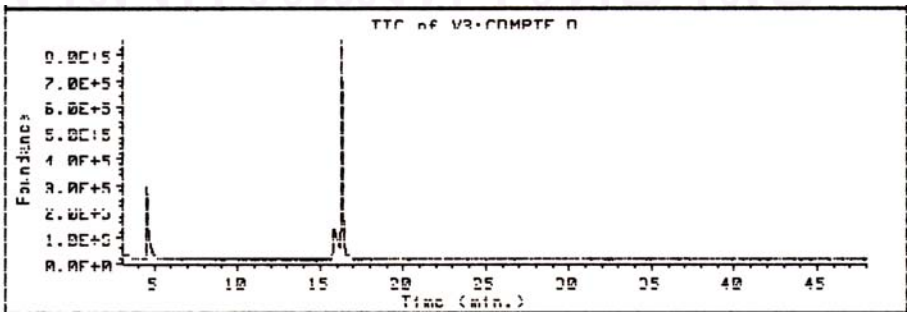


Figure 31a GC-MS analysis of the crude product from the synthesis of **55**.

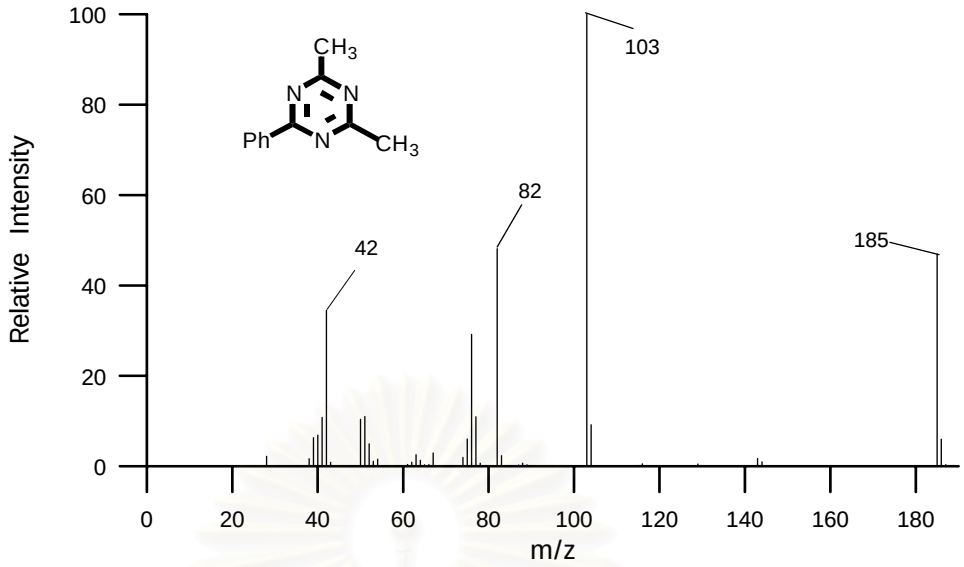


Figure 31b The mass spectrum of the compound eluted with a retention time of 16.3 minutes.

This crude product was purified by preparative thin-layer chromatography. The GC-MS analysis (at the same temperature program) of the highest band (Figure 32a) with an R_f of 0.79, light yellow liquid, exhibits a major component with a retention time of 16.3 minutes. The mass spectrum of this peak (Figure 32b) exhibits a molecular ion at m/z 185 which is consistent with the molecular weight of **55**. The spectrum also shows a base peak at m/z 103 and a peak at m/z 82 which correspond to the fragment of $C_6H_5CN^{+\bullet}$ and $C_4H_6N_2^{+\bullet}$, respectively, from **55**.

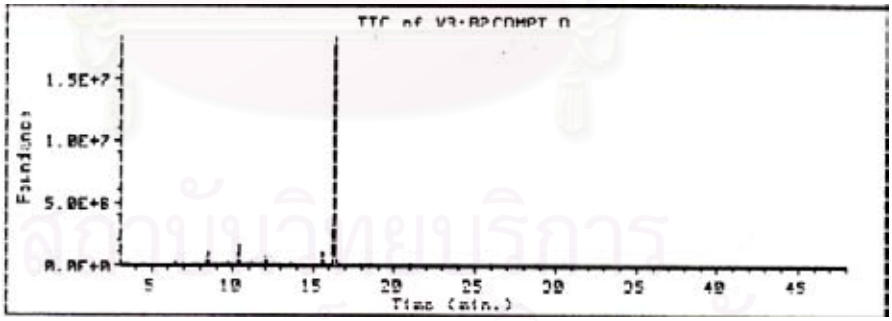


Figure 32a GC-MS analysis of the highest band, yellow liquid.

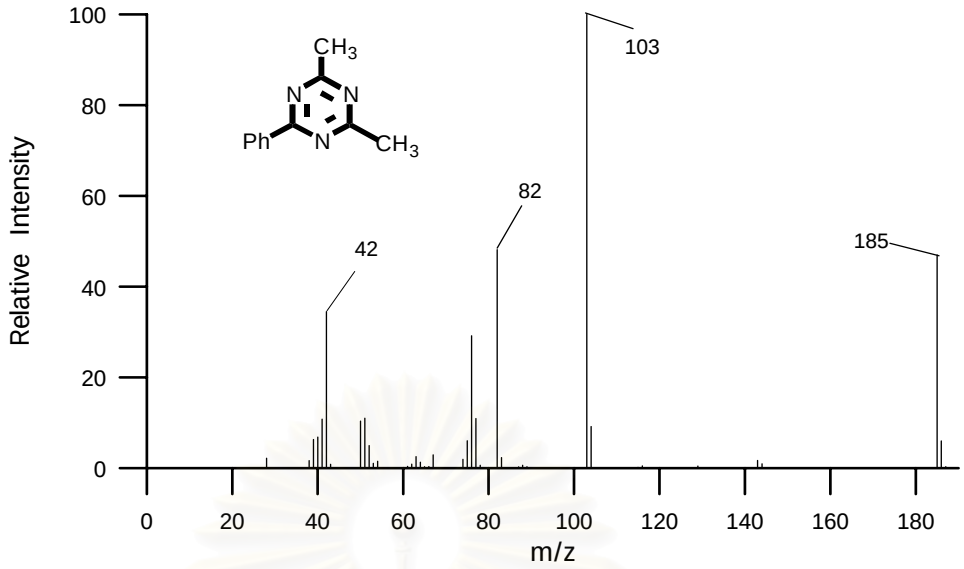


Figure 32b The mass spectrum of the major component at a retention time of 16.3 minutes.

The ^{1}H–NMR spectrum of this yellow liquid (Figure 33) exhibits a singlet at δ 2.67 which is expected to be the absorption of the protons of the two equivalent methyl group substituted on triazine ring. The two set of multiplets at δ 7.44-7.55 (3 H) and δ 8.47-8.49 (2H) were assigned to the set of para-, and meta- and the set of ortho- phenyl ring protons, respectively.

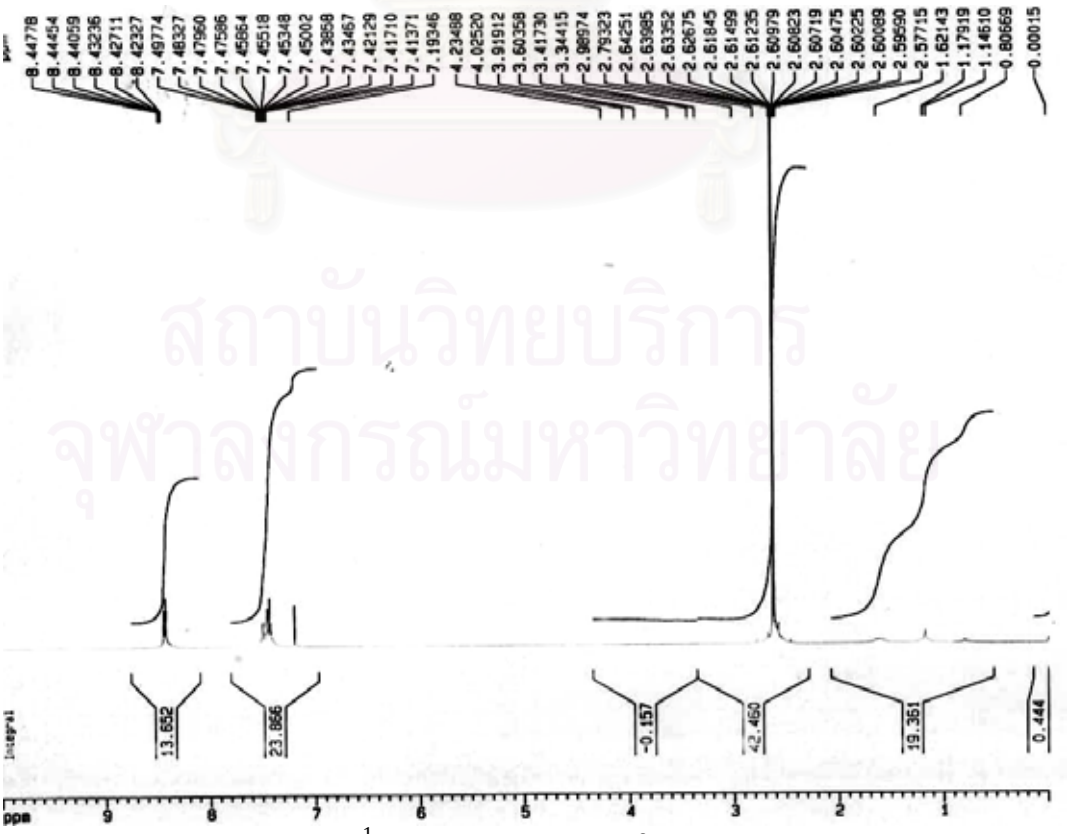


Figure 33 The ^{1}H–NMR spectrum of the yellow liquid.

The ^{13}C–NMR spectrum of this yellow liquid (Figure 34) also reveals the signals corresponding to the structure of **55**. The signal at δ 25.7 is assigned to the two equivalent methyl carbons on triazine ring. The signal at δ 171.2 is assigned to the triazine ring carbon position 6. The two equivalent triazine ring carbons position 2 and 4 absorb at the same chemical shift of δ 176.3. The four signals at δ 128.6, 128.8, 132.5 and 135.5 are assigned to the phenyl ring carbons. This assignment also corresponds to the signals appear in the ^{13}C–DEPT 135 spectrum (Figure 34). The signal at δ 25.7 still appears in the ^{13}C–DEPT 135 spectrum, which belongs to the two equivalent methyl carbons. The two signals at δ 171.2 and 176.4 disappear in the ^{13}C–DEPT 135 spectrum corresponding to the assignment of the three quaternary triazine ring carbons.

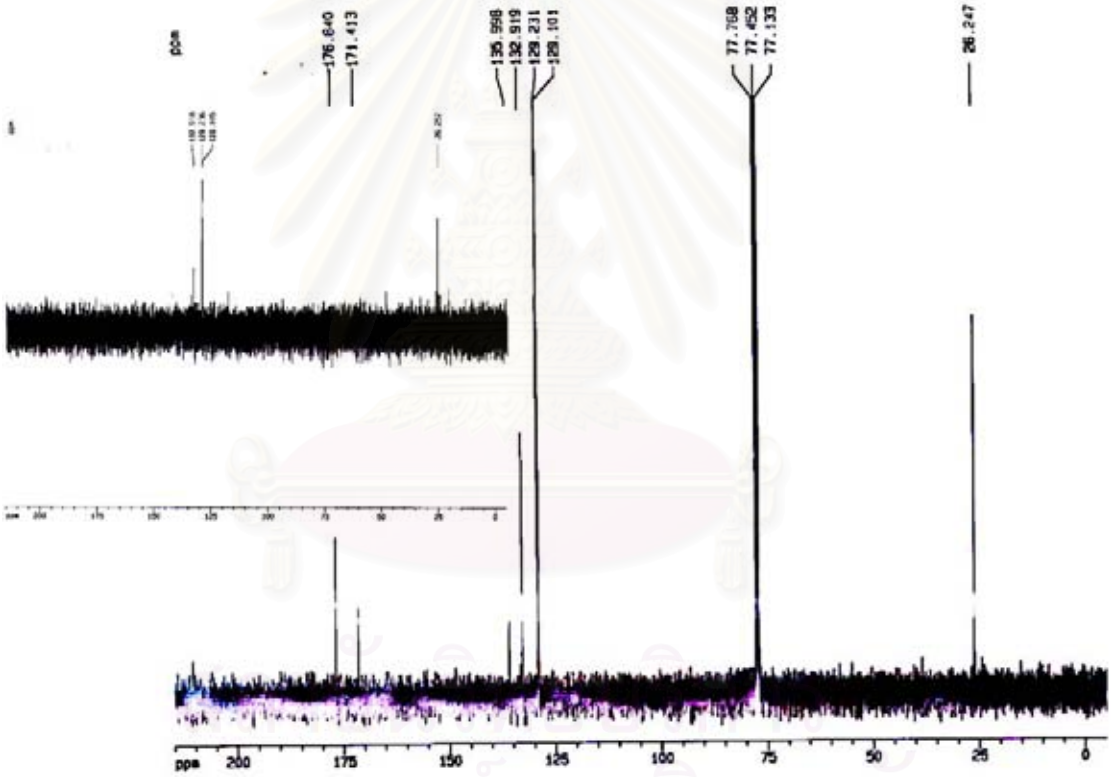
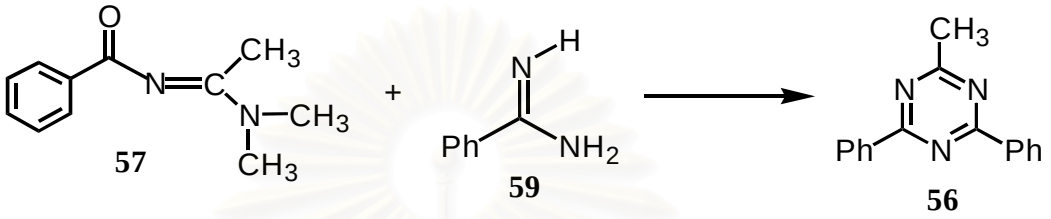


Figure 34 The ^{13}C- and ^{13}C–NMR DEPT 135 spectrum of the yellow liquid.

3.1.2.2.3 Synthesis of 2-methyl-4,6-diphenyl-1,3,5-triazine (56)

Raymond Dengino and colleagues did not report the synthesis of 2-methyl-4,6-diphenyl-1,3,5-triazine **(56)**. However, by analogy with the synthesis of **55**, it should be possible to synthesize **56** by the reaction of **57** with benzamidine **(59)** instead of acetamidine **(58)**.



GC-MS analysis [110°C (5 min.), 10°C/min. to 240°C (30 min.)] of the white solid (Figure 35a) shows the presence of two components. The mass spectrum of the major component (Figure 35b) eluted with a retention time of 32.4 minutes exhibits a molecular ion at m/z 247 which corresponds to the molecular weight of **56** (MW 247). The spectrum also exhibits a base peak at m/z 103, which is consistent with $[C_6H_5CN]^{+\bullet}$ fragment.

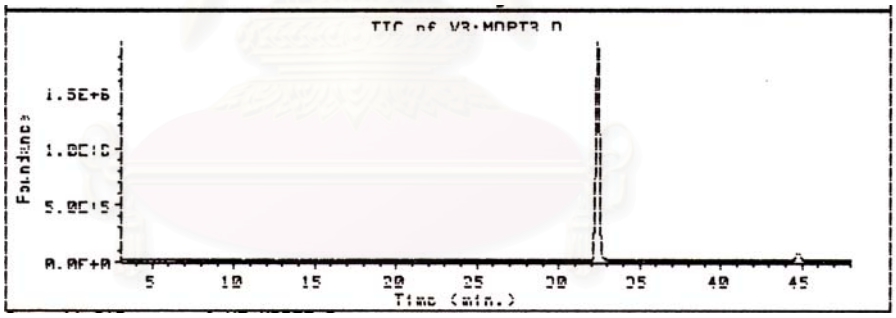


Figure 35a GC-MS analysis of the white solid expected to be **56**.

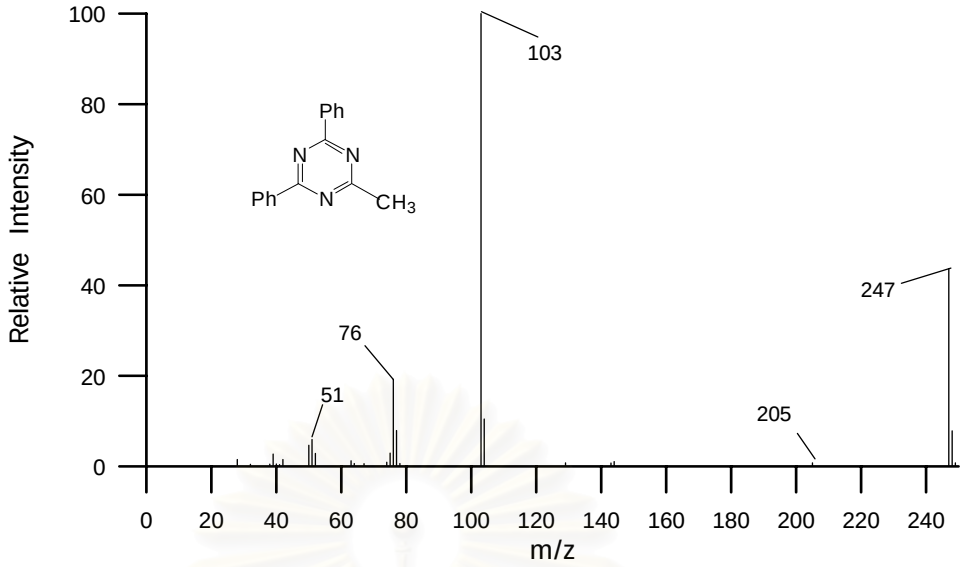


Figure 35b The mass spectrum of the compound eluted with a retention time of 32.4 minutes.

The ^{1}H–NMR spectrum of this white solid (Figure 36) exhibits a 3H-singlet at δ 2.77 which was assigned to the protons of the methyl group substituted on triazine ring. The two multiplets at δ 7.46-7.57 (6H) and δ 8.61-8.64 (4H) were assigned to the set of meta- and para- and the set of ortho- phenyl ring protons, respectively.

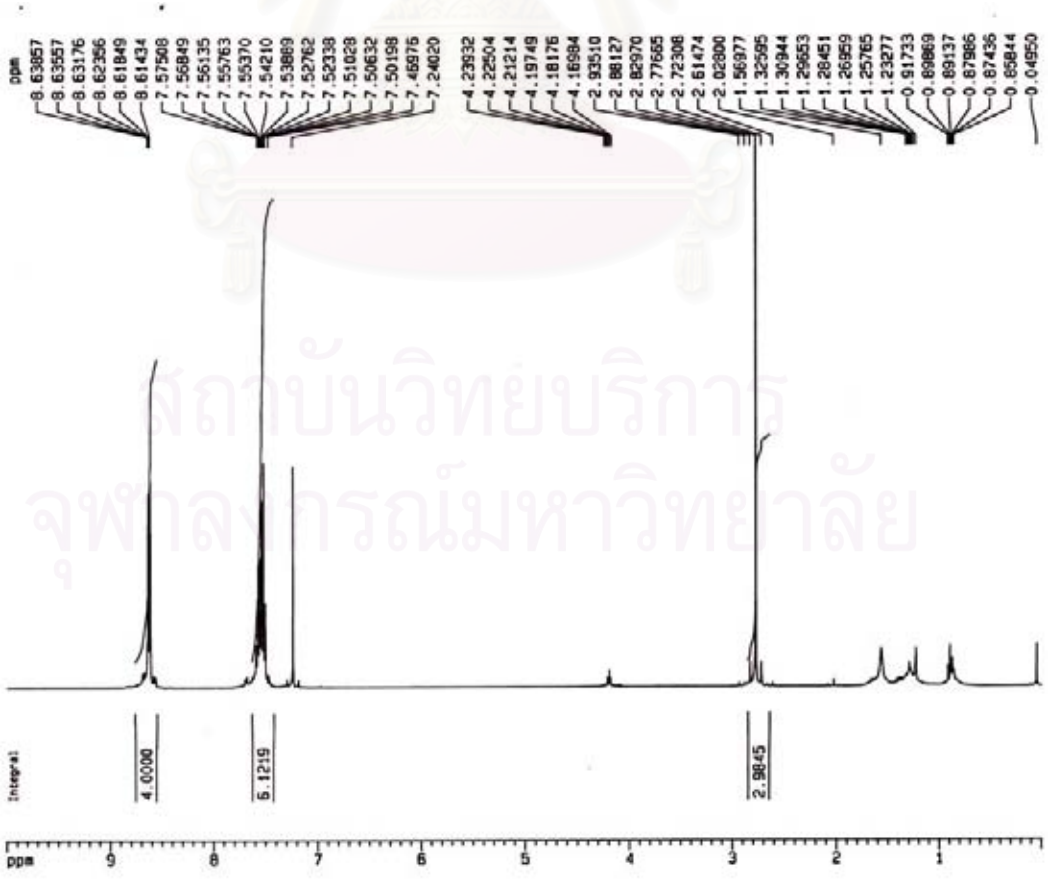


Figure 36 The ^{1}H–NMR spectrum of the white solid.

The ^{13}C–NMR spectrum (Figure 37) reveals the methyl signal at δ 26.5. The two equivalent phenyl ring carbons absorb at δ 129.1, 129.3, 132.9 and 136.3. The triazine ring carbon at position 2 appears at δ 177.5 while the two equivalent triazine ring carbons at positions 4 and 6 absorb at δ 171.6. The 13C–NMR DEPT 135 spectrum, can confirm these 13C-NMR spectral assignments. The spectrum (Figure 37) still reveals the signal at δ 26.5 as expected for a signal due to a methyl carbon. The two signals at δ 171.6 and 177.5, however, disappear in the ^{13}C–NMR DEPT 135 spectrum. This is consistent with the assignment to the three quaternary carbons of the triazine ring. In the phenyl region, the signal at δ 36.3 disappears in the ^{13}C–DEPT 135 spectrum and can, therefore, be assigned to the carbon at position 1 of the phenyl ring.

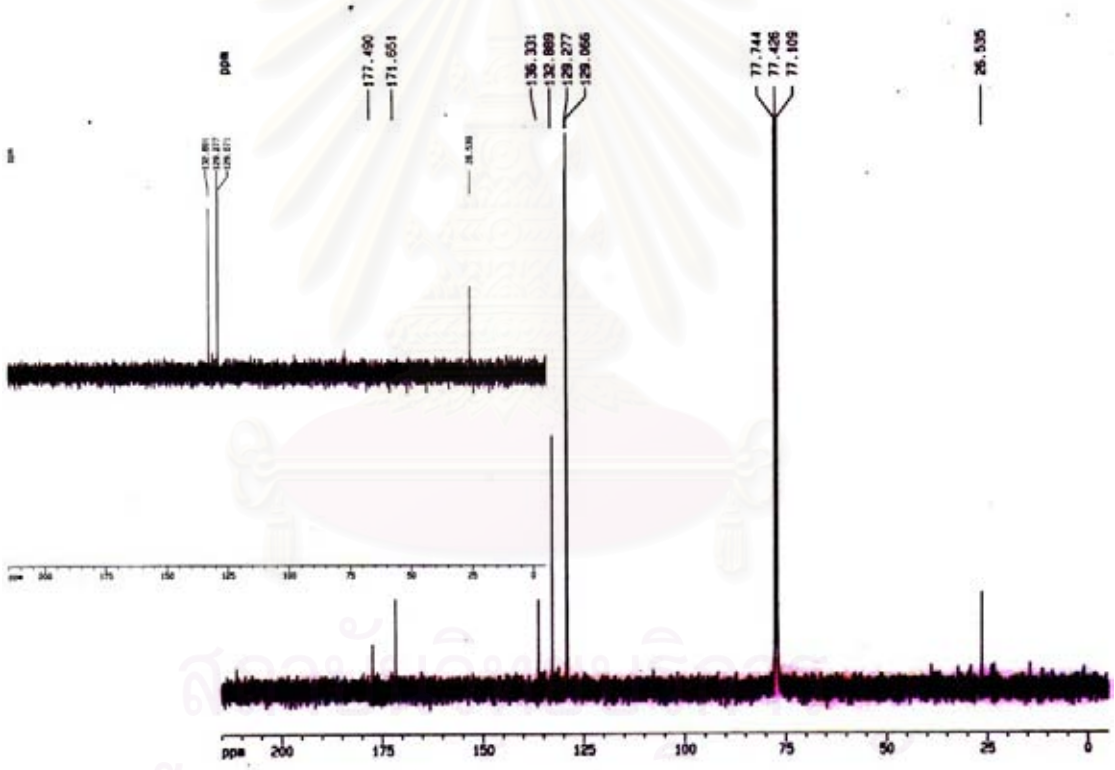
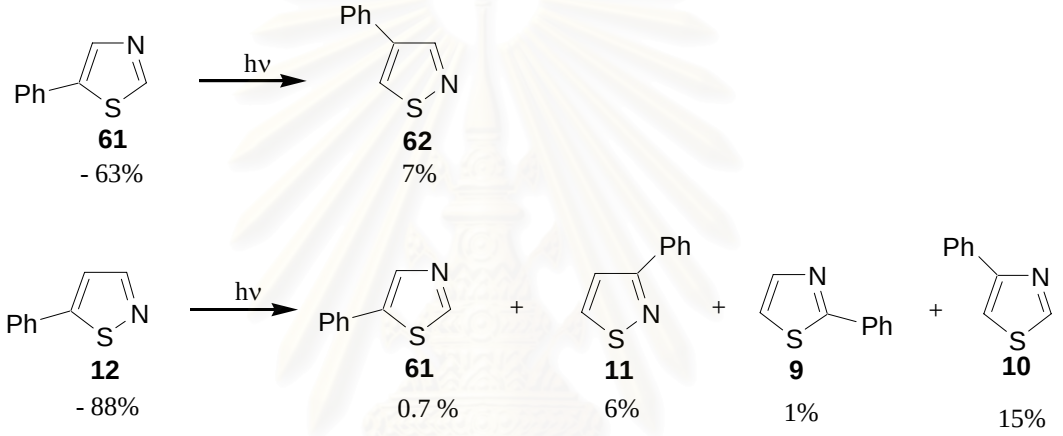


Figure 37 The ^{13}C- and ^{13}C–NMR DEPT 135 spectra of the white solid.

3.2 Photochemistry study of phenyl-substituted-1,2,4-thiadiazoles.

3.2.1 Photochemistry of 5-phenyl-1,2,4-thiadiazole.

5-Phenyl-1,2,4-thiadiazole **(31)** can be viewed as a combination of 5-phenylthiazole **(61)** and 5-phenylisothiazole **(12)**, which have been reported to undergo the phototransposition reactions.[6-8] Therefore, the photochemistry of **31** might be expected to exhibit the same type of photochemistry.



The photolysis of **31** [(5×10^{-5} M) in acetonitrile and cyclohexane] was first monitored by ultraviolet absorption spectroscopy at 60 seconds intervals. Figure 38a and 39a show the UV–absorption spectra of **31** in acetonitrile and cyclohexane before irradiation, respectively. The λ_{max} is shown at the same wavelength of 273.2 nm. in both solvents with an extinction coefficient of 13880 in cyclohexane and 13873 in acetonitrile.

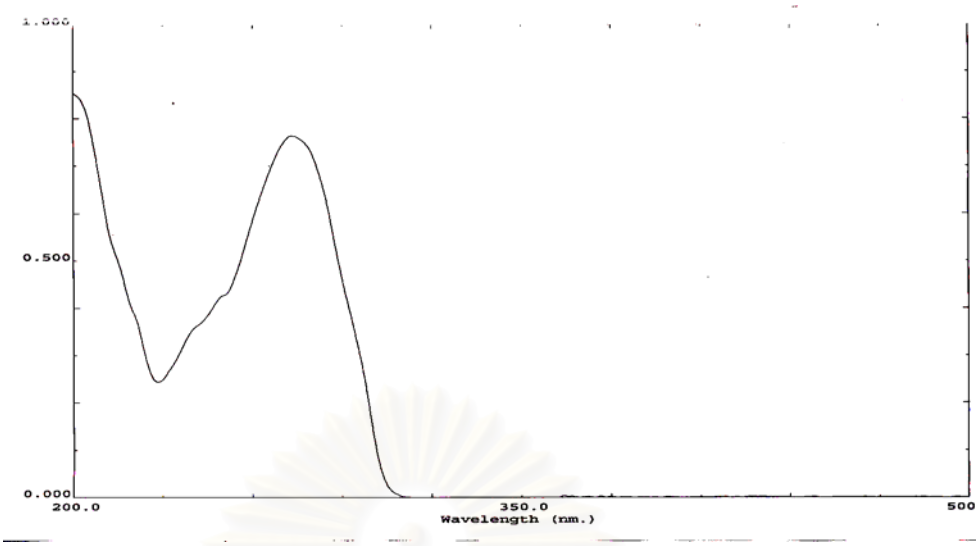


Figure 38a The UV–absorption spectrum of **31** in acetonitrile.

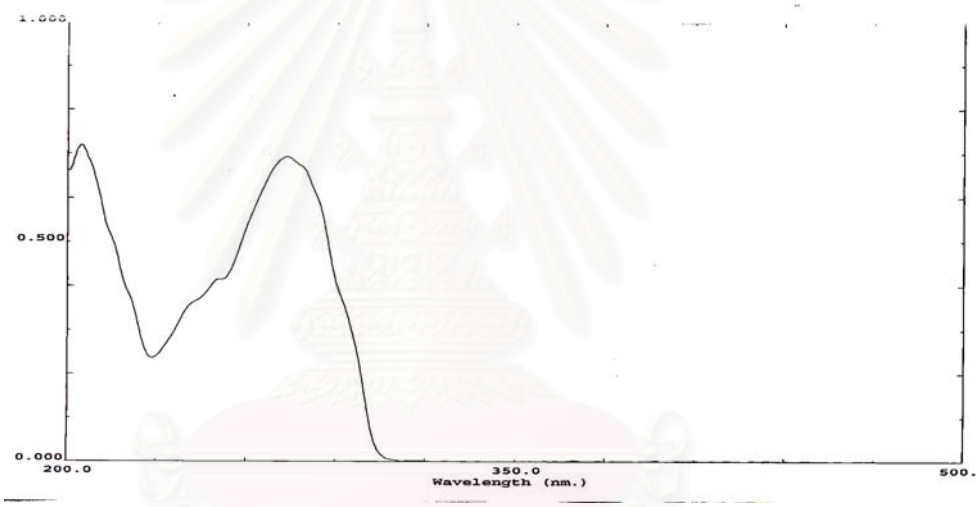


Figure 39a The UV–absorption spectrum of **31** in cyclohexane.

The UV overlay spectrum of the photolysis in acetonitrile (Figure 38b) exhibits the decreasing in the absorption band at the λ_{max} 273.2 nm from 0.76 to 0.68 after 240 seconds. After 1560 seconds of irradiation time, the spectrum reveals the absorption band at the λ_{max} 273.2 nm shifted to λ_{max} 260.2 nm. The spectrum also reveals the increasing in the absorption band at λ 230 nm.

The UV overlay spectrum of the photolysis in cyclohexane exhibits (Figure 39b) the same spectral pattern. But the shift of the absorption band at λ_{max} 273.2 nm to λ_{max} 264.4 nm was being formed more slower than the photolysis in acetonitrile as well as the increasing of the absorption band at λ 230 nm.

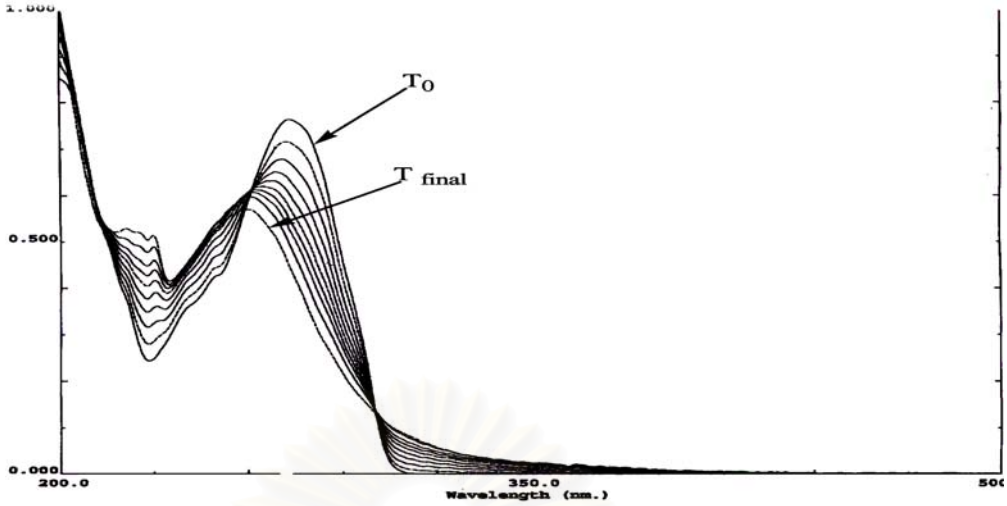


Figure 38b The UV overlay spectrum of the photolysis in acetonitrile.

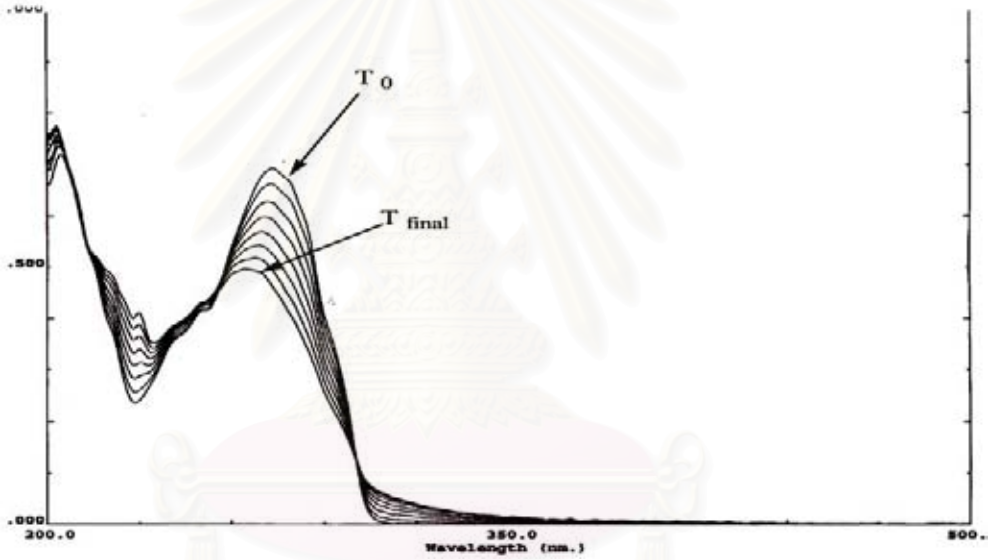


Figure 39b The UV overlay spectrum of the photolysis in cyclohexane.

The photochemical reaction of **31** was also monitored by gas chromatography. The GLC analysis of **31**, before irradiation, (Figure 40a) [140°C (4 min.), 20°C/min. to 180°C (14 min.), 20°C/min to 240(30min.)] shows the major component at a retention time of 12 minutes and a small peak at a retention time of 8 minutes. This component at 8 minutes is probably due to the presence of an impurity. The solution of **31** was irradiated with sixteen 300 nm lamps for 210 minutes. The GLC analysis of the resulting solution (Figure 40b) shows the consumption of 33.4% of the reactant and the appearance of six new photoproducts with retention times of 4, 11, 18, 39 and 40 minutes.

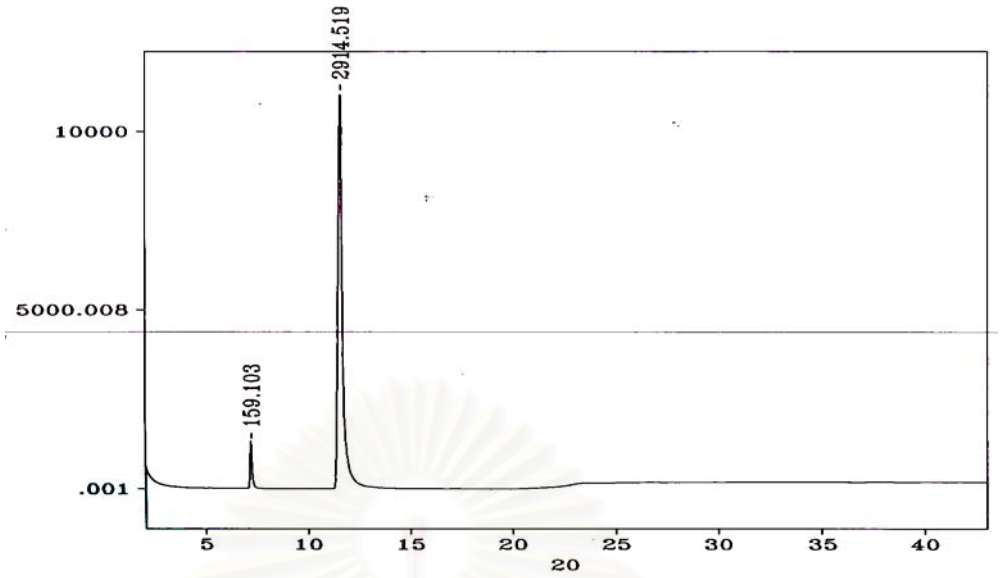


Figure 40a The GLC analysis of the reactant (in acetonitrile) before irradiation.

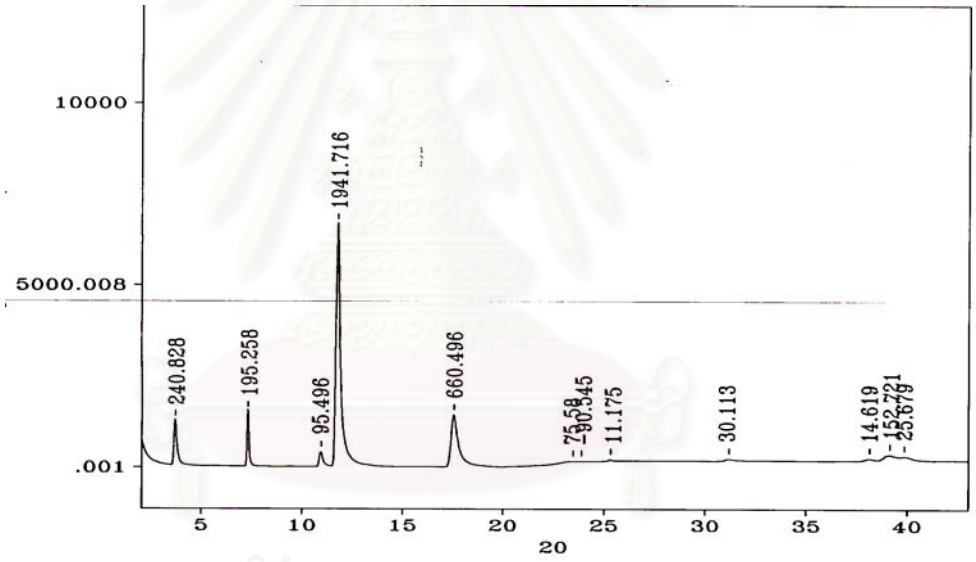


Figure 40b The GLC analysis of the photolysis (in acetonitrile) after 210 minutes

After removal of acetonitrile, the GC-MS analysis of the concentrated reaction mixture (Figure 41a) [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 minutes.

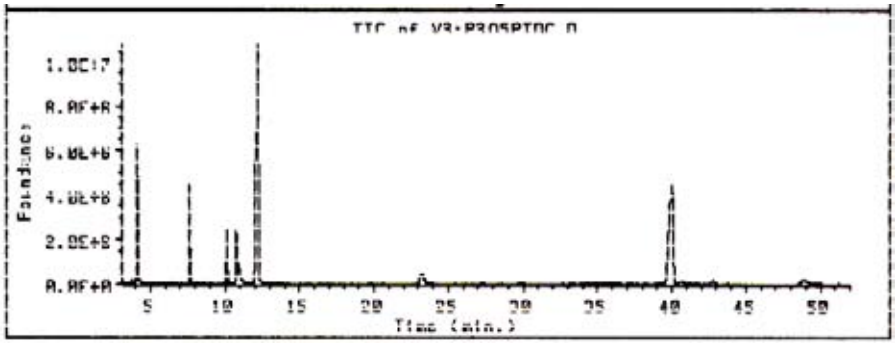


Figure 41a The GC-MS analysis of the concentrated photolyzed solution of **31** (in acetonitrile) after 210 minutes of irradiation.

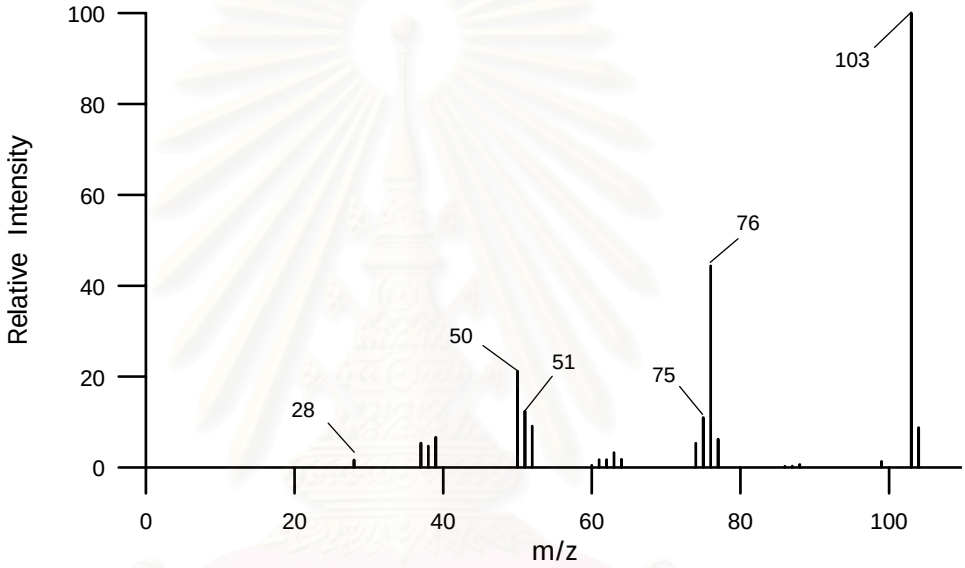


Figure 41b The mass spectrum of the first eluted photoproduct at a retention time of 4 minutes.

The mass spectrum of the first eluted photoproduct at a retention time of 4 minutes (Figure 41b) shows a base molecular ion peak at m/z 103. This product was assumed to be benzonitrile **(54)**.

In order to prove this assumption, GC-MS analysis of the authentic of **54** was carried out at the same GC-MS conditions (Figure 42). The result revealed that the authentic of **54** was eluted at the same retention time as the first eluted photoproduct. Furthermore, Figure 41b and 42 show that the fragmentation pattern and molecular ion from both the photoproduct and the authentic of **54** are also identical. Therefore, based on these chromatographic and mass spectroscopic results, the first eluted photoproduct was identified as benzonitrile **(54)**, a photofragmentation product.

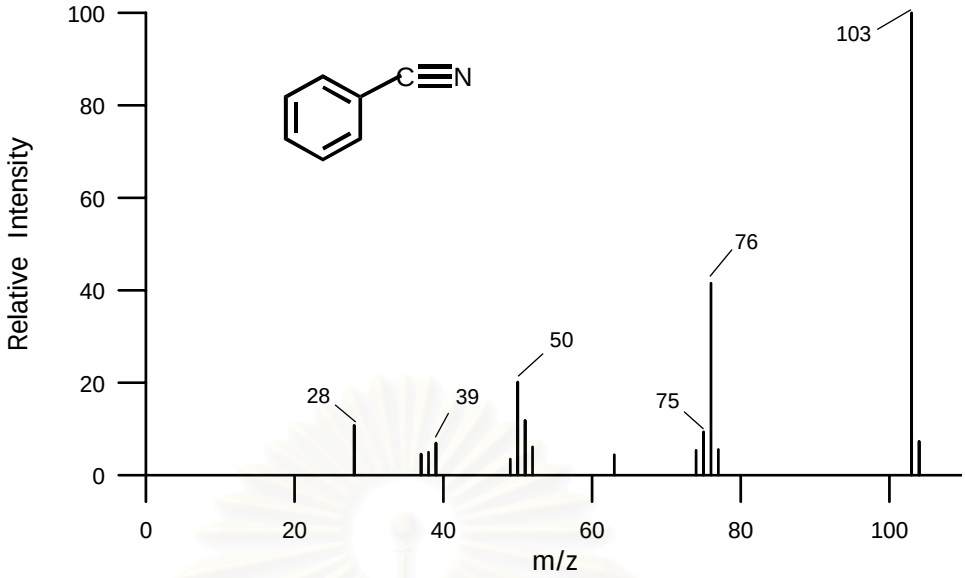


Figure 42 The mass spectrum of the authentic of benzonitrile eluted at a retention time of 4 minutes..

The peak at retention time of 7.5 minutes was identified as 5-phenyl-1,2,4-oxadiazole **(39)**, which was formed as a minor product during the synthesis of **31** (as discussed in the synthesis section of **31**). 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 the reaction of this compound.

The mass spectrum of the product eluted at a retention time of 10.0 minutes (Figure 41c) exhibits a molecular ion at m/z 157, consistent with the molecular formula of $C_9H_7N_3$ and a base peak at m/z 104, consistent with $[C_6H_5CNH]^{+\bullet}$ as the major fragment. Accordingly, this photoproduct was suggested to be phenyl-sym-triazine **(50)**, a unique ring expansion product, which was confirmed by a direct comparison with the retention time and mass spectrum of the authentic of phenyl-sym-triazine (Figure 43).

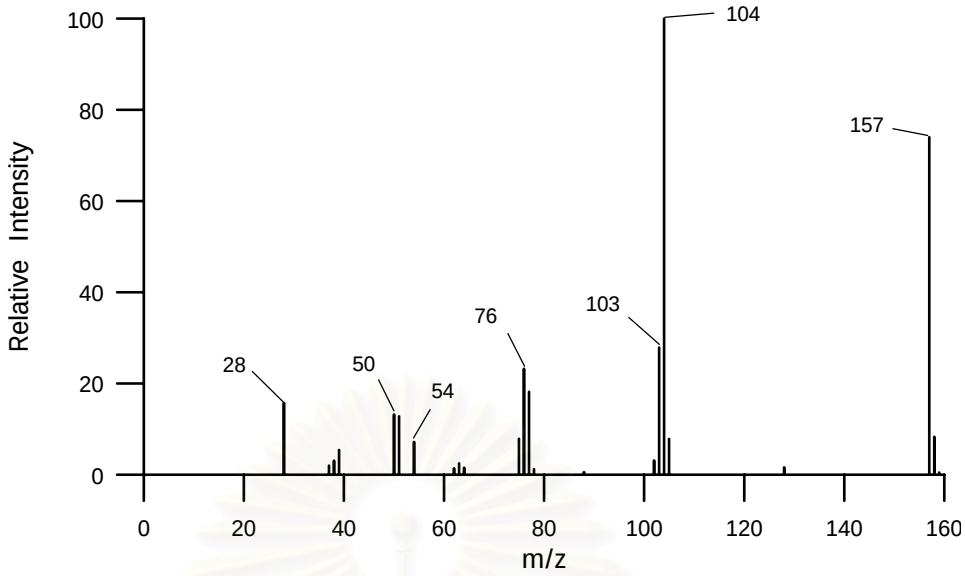


Figure 41c The mass spectrum of the second eluted phtoproduct at a retention time of 10.0 minutes.

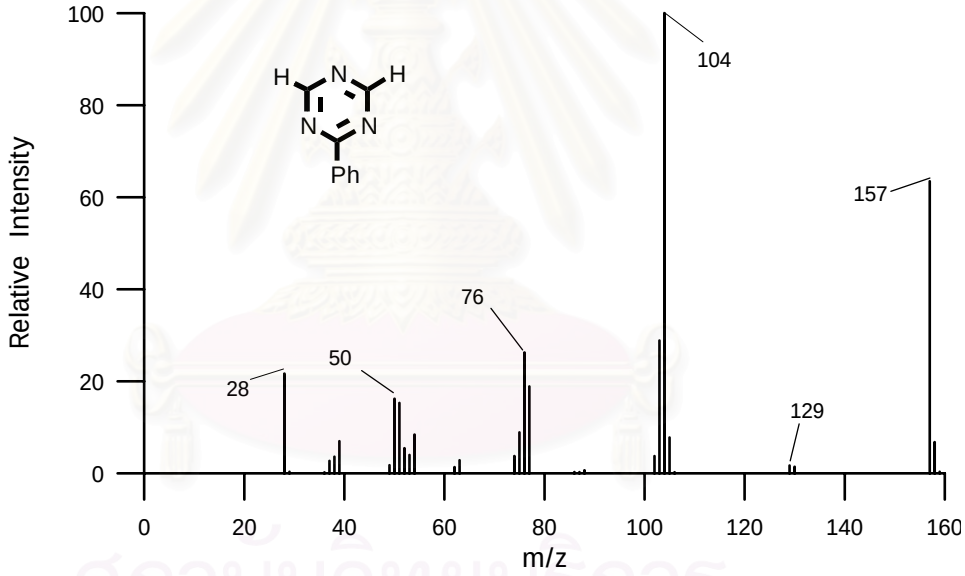


Figure 43 The mass spectrum of the authentic of **50** eluted at a retention time of 10 minutes.

The compound eluted at a retention time of 10.6 minutes is the starting material since it has a retention time and a mass spectrum (Figure 41d) identical to the reactant (Figure 5c).

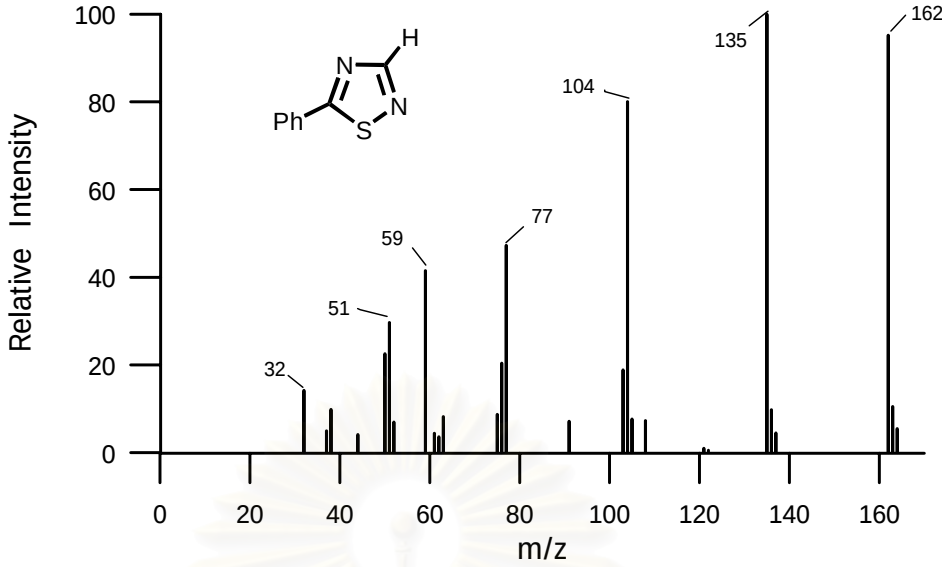


Figure 41d The mass spectrum of the compound eluted at a retention time of 10.6 minutes.

The mass spectrum of the second photoproduct eluted at a retention time of 12.1 minutes also exhibits a molecular ion at m/z 162 (Figure 41e). It is also consistent with the molecular formula of $C_8H_6N_2S$, identical to the formula of the reactant **(31)**. The comparison of these mass spectra clearly shows that, although the mass spectrum of this photoproduct is different from the mass spectrum of **31** (Figure 41d), but it is exactly identical to the mass spectrum of 3-phenyl-1,2,4-thiadiazole **(32)** (Figure 44). This photoproduct is thus identified as the phototransposition product, 3-phenyl-1,2,4-thiadiazole **(32)**.

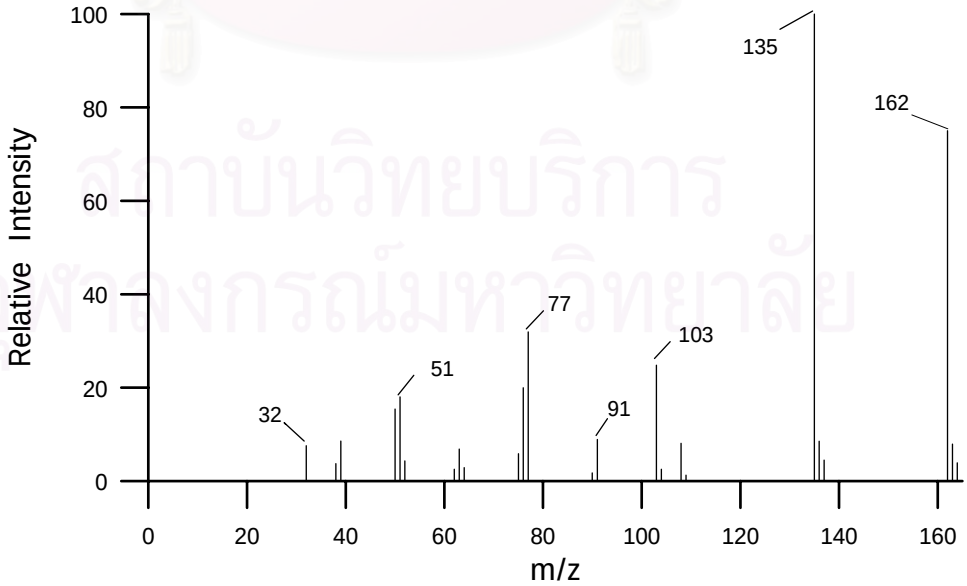


Figure 41e The mass spectrum of the product eluted at a retention time 12.1 minutes.

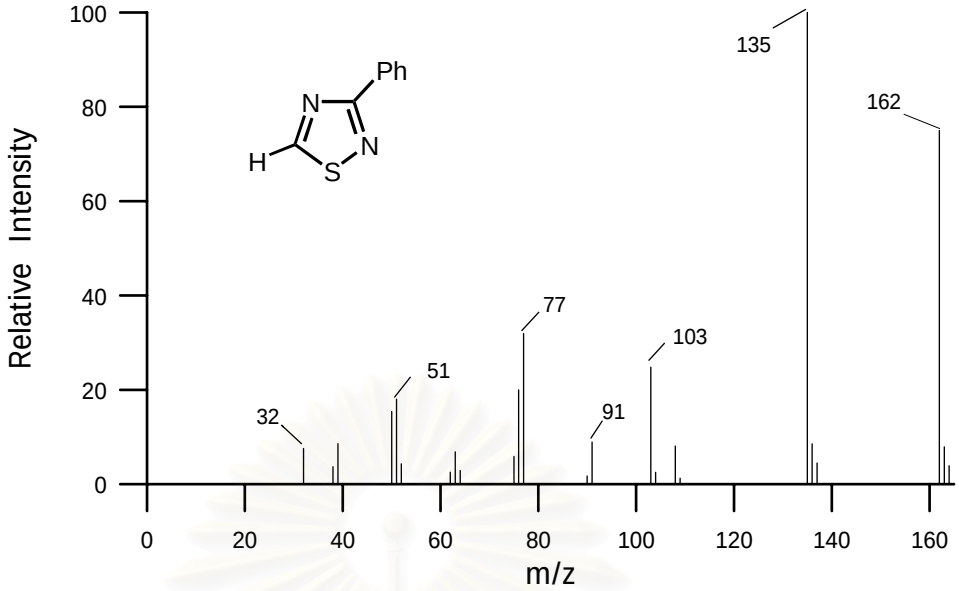


Figure 44 The mass spectrum of the authentic of **32**.

The mass spectrum of the component eluted at a retention time of 23.3 minutes (Figure 41f) exhibits a base molecular ion at m/z 172 and two medium intensity peaks at m/z 103 and 104. The structure of this product can thus be suggested to contain a system similar to **31**, which can cleave to give two fragments $[C_6H_5CN]^{+\bullet}$ and $[C_6H_5CNH]^{+\bullet}$, as discussed previously. However, the absolute structure of this product has not been identified.

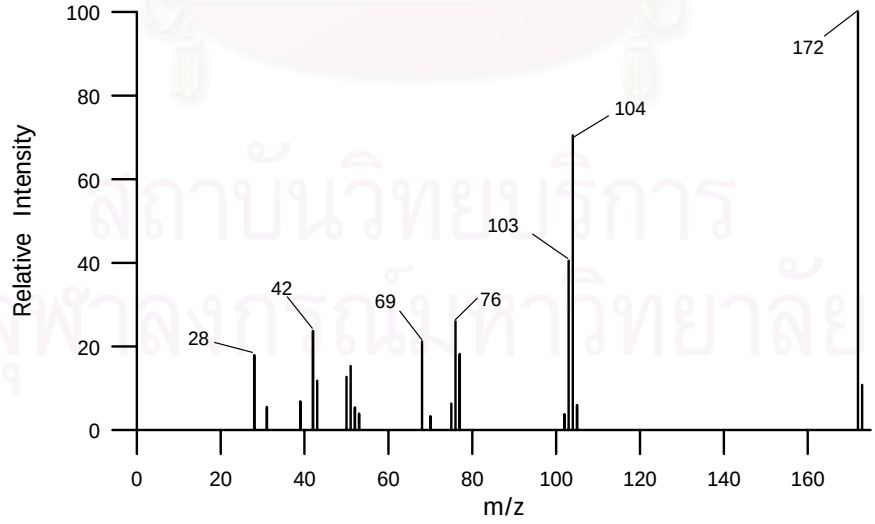


Figure 41f The mass spectrum of the compound eluted with a retention time of 23.3 minutes.

The mass spectrum of the photoproduct eluted at a retention time of 40 minutes (Figure 41g) 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 ion peak at m/z 103, consistent with the formation of $[C_6H_5CN]^{+\bullet}$ as the major fragment. Based on this information the photoproduct was thus suggested to be diphenyl-sym-triazine **(51)**, a photo ring expansion product. This was confirmed by a direct comparison with the retention time and the mass spectrum of the authentic of **51** (Figure 45).

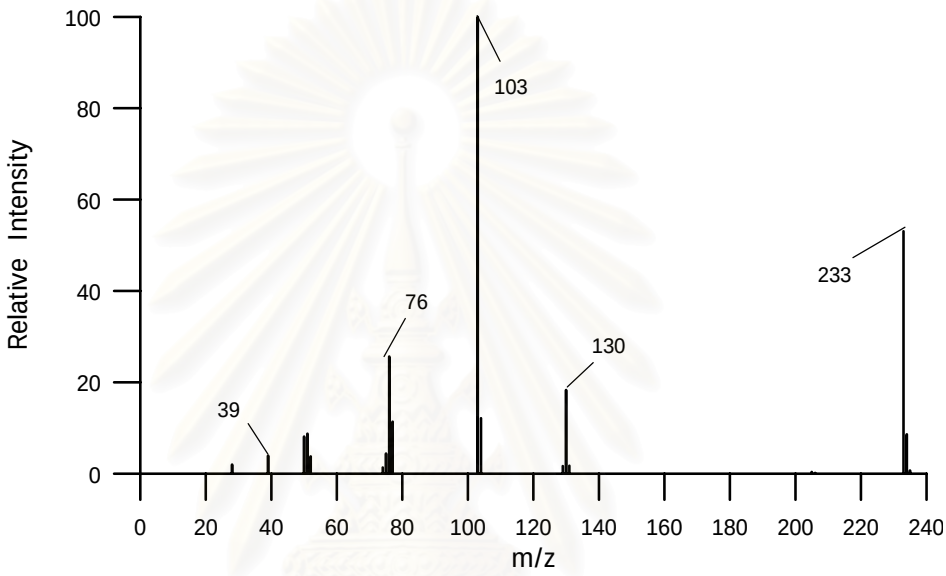


Figure 41g The mass spectrum of the compound eluted at a retention time 40 minutes.

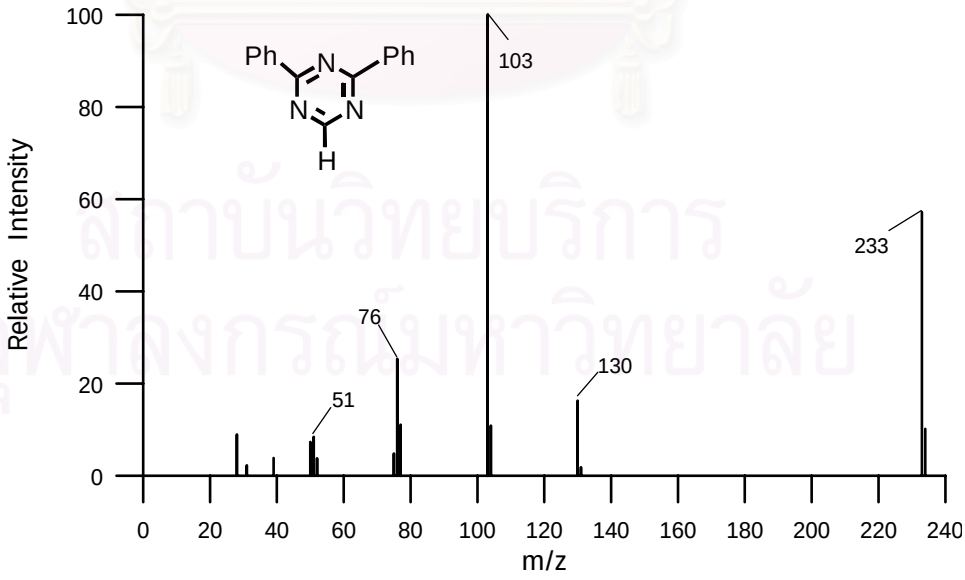


Figure 45 The mass spectrum of the authentic of **51** eluted at a retention time 40 minutes.

Besides the four major photoproducts shown in the Figure 41a, the GC-trace also shows three minor peaks eluted at retention times of 40.6, 42.7 and 48.9 minutes. Their mass spectra (Figure 41h, i, j) exhibit the molecular ions at m/z 187, 238, 205, respectively. These minor 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 $[C_6H_5]^{+\bullet}$, $[C_6H_5CN]^{+\bullet}$ and $[C_6H_5CNH]^{+\bullet}$ fragment, respectively, as previously discussed. Especially, the mass spectra of the compounds eluted at retention times of 42.7 and 48.9 minutes also exhibit a peak at m/z 135 as a base peak. This peak has been previously assigned to $[C_6H_5CNS]^{+\bullet}$. Therefore, these three minor peaks could also be expected as photoproducts formed upon irradiation of **31** (in acetonitrile).

The mass spectrum of the compound eluted at a retention time of 42.7 minutes (Figure 41i) exhibits a molecular ion at m/z 238 corresponding to the molecular weight of 3,5-diphenyl-1,2,4-thiadiazole **(34)** (MW 238). By a direct comparison of the chromatographic and mass spectroscopic properties of this product with the authentic of **34** (previously synthesized in this laboratory) (Figure 46), this photoproduct was therefore identified as 3,5-diphenyl-1,2,4-thiadiazole **(34)**.

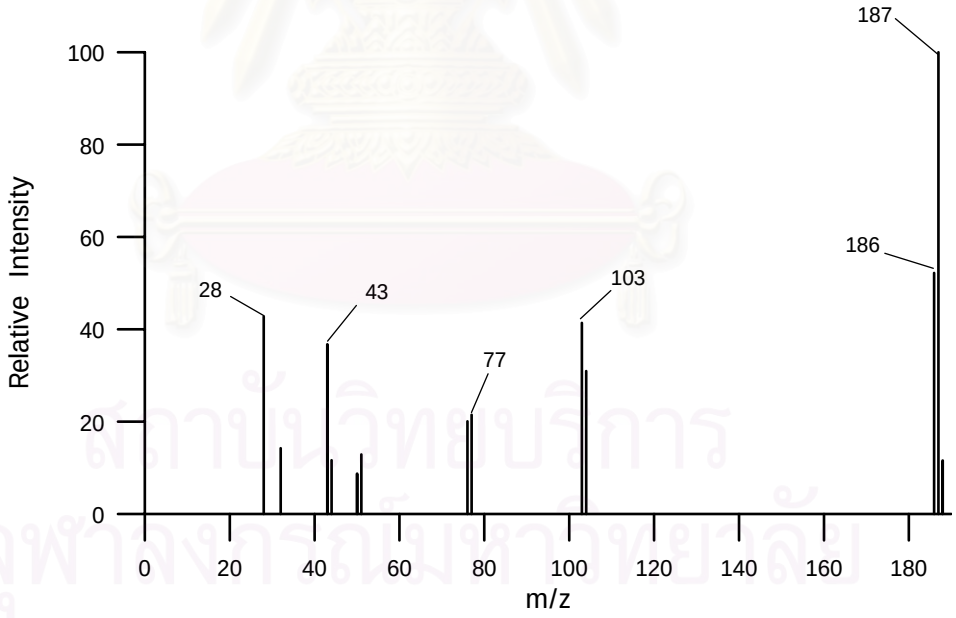


Figure 41h The mass spectrum of the compound eluted at a retention time of 40.6 minutes.

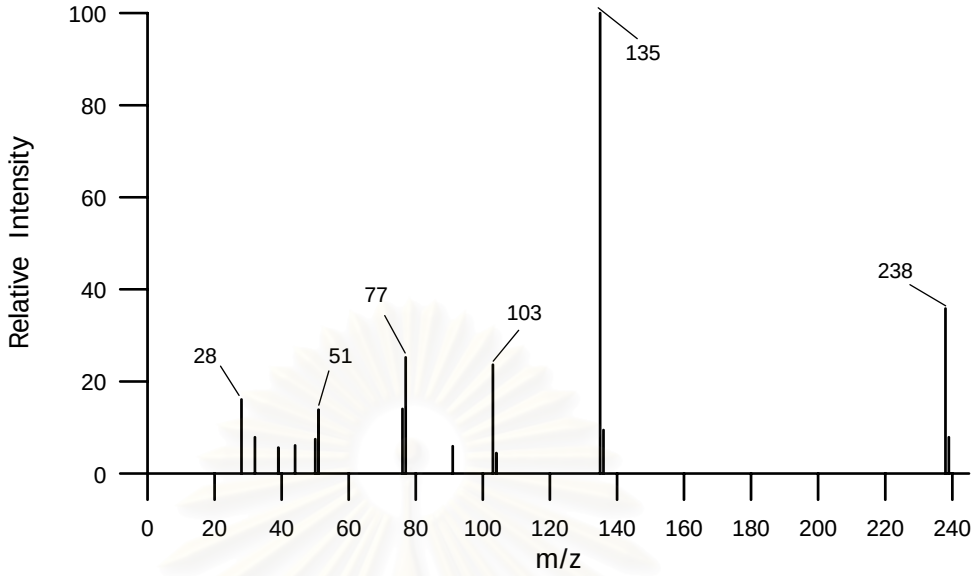


Figure 41i The mass spectrum of the compound eluted at a retention time of 42.7 minutes.

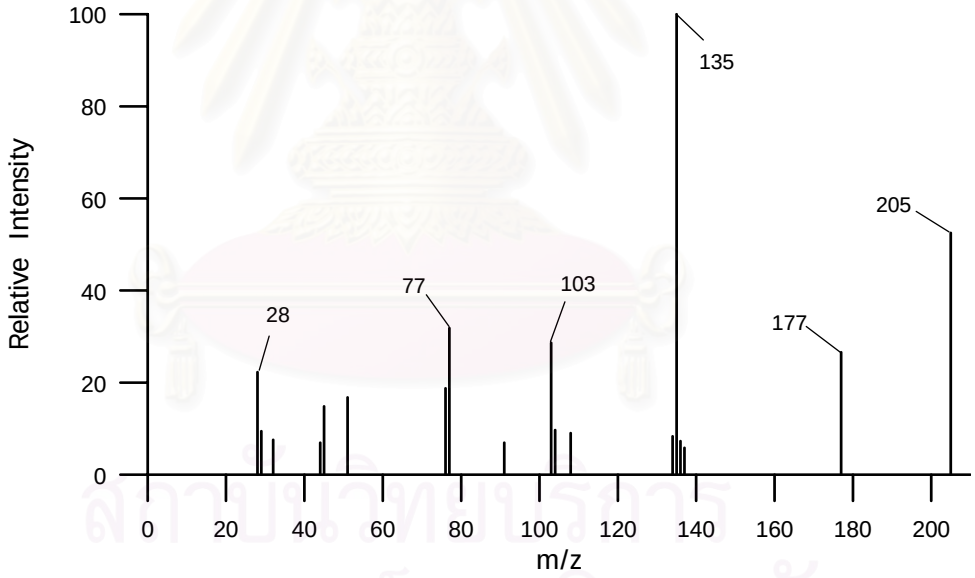


Figure 41j The mass spectrum of the compound eluted at a retention time of 48.9 minutes.

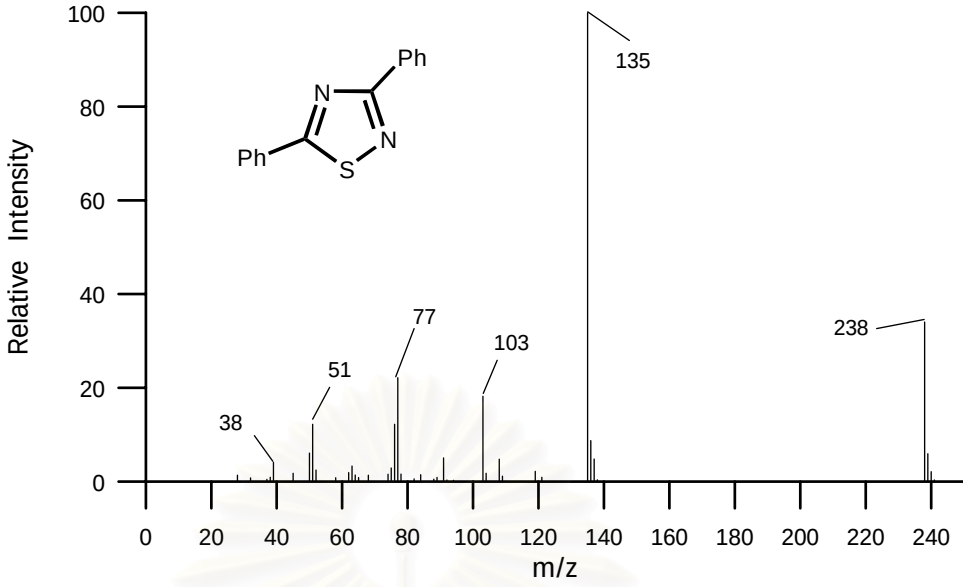


Figure 46 The mass spectrum of the authentic of **34** eluted at a retention time of 42.7 minutes.

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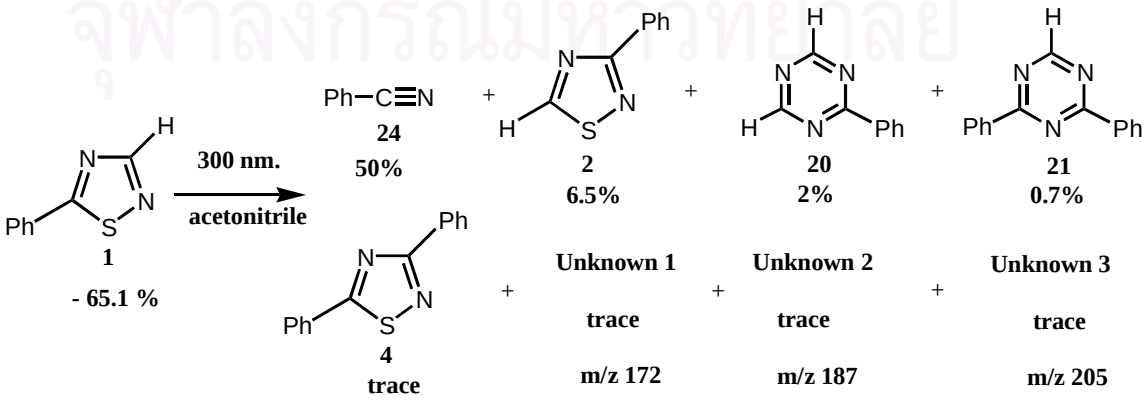
These results conclusively show that irradiation of **31** in acetonitrile at 300 nm leads to the formation of eight GLC-volatile products. Five of these products have been identified as benzonitrile **(54)** (the photofragmentation product), phenyl- and diphenyl-sym-triazine **(50 and 51**; the photo ring expansion products), 3-phenyl-1,2,4-thiadiazole **(32)** (the phototransposition product) and 3,5-diphenyl-1,2,4-thiadiazole **(34)**. 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 300 nm lamps and monitored by gas–liquid chromatography every 30 minutes for 150 minutes. The GLC-calibration curves for the four identified photoproducts were constructed by plotting concentration versus peak area. Scheme 7 shows the overall photoreaction of **31**.

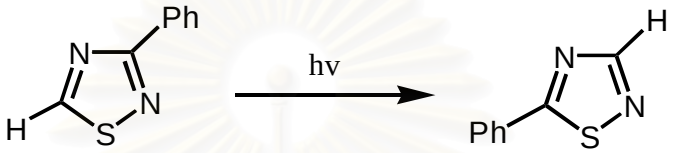


Scheme 7 The photoreaction of 5-phenyl-1,2,4-thiadiazole.

3-Phenyl-1,2,4-thiadiazole **(32)**, the phototransposition product, was found in 10 % yield. Benzonitrile **(54)**, the photofragmentation product, was formed in 22.4 % yield. The two unique ring expansion photoproducts, phenyl- and diphenyl-sym-triazine (**50** and **51**), were observed in 3 and 1 % yield, respectively. GC-MS analysis of the concentrated solution revealed the presence of trace amount of three unidentified photoproducts, which were not observed in GLC analysis of the reaction mixture before concentration.

3.2.2 Photochemistry of 3-phenyl-1,2,4-thiadiazole

This study has shown that **31** undergoes phototransposition to **32** in 10% yield and to the formation of 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 **32** has also been studied. By the transposition analogy in the reaction of **31**, it could be predicted to observe **31** as the transposition product upon a photolysis of **32**.



32 **31**

The photolysis of **32** in cyclohexane with three 300 nm lamps was first monitored by UV–absorption spectroscopy at 40 seconds of intervals.

Figure 47a shows the UV–absorption spectrum of **32** in cyclohexane before irradiation. The UV-overlay spectrum (Figure 47b) 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 seconds 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 **54** in this reaction since the latter is known to absorb at λ_{max} 224 nm in acetonitrile (from previous results).

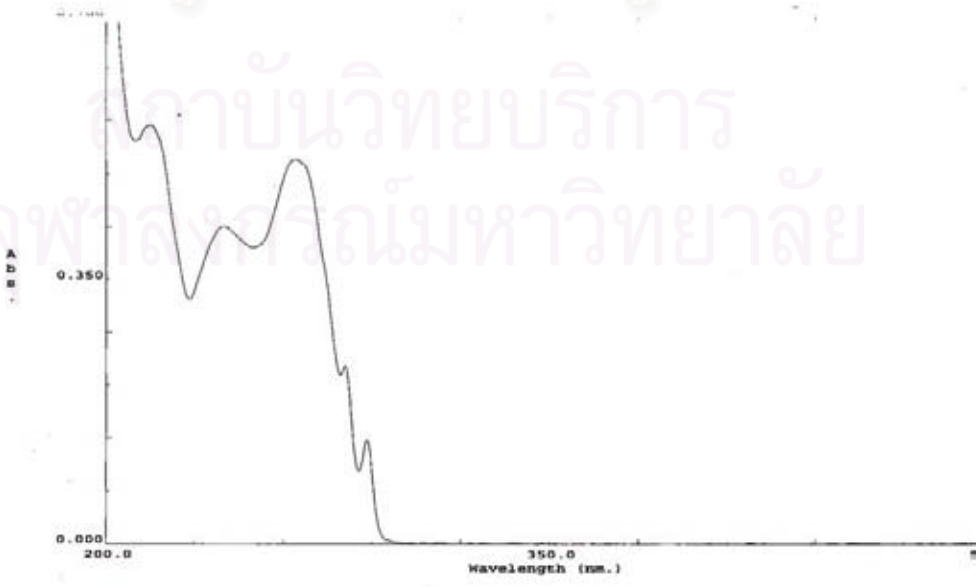


Figure 47a The UV–absorption spectrum of the reactant in cyclohexane before irradiation.

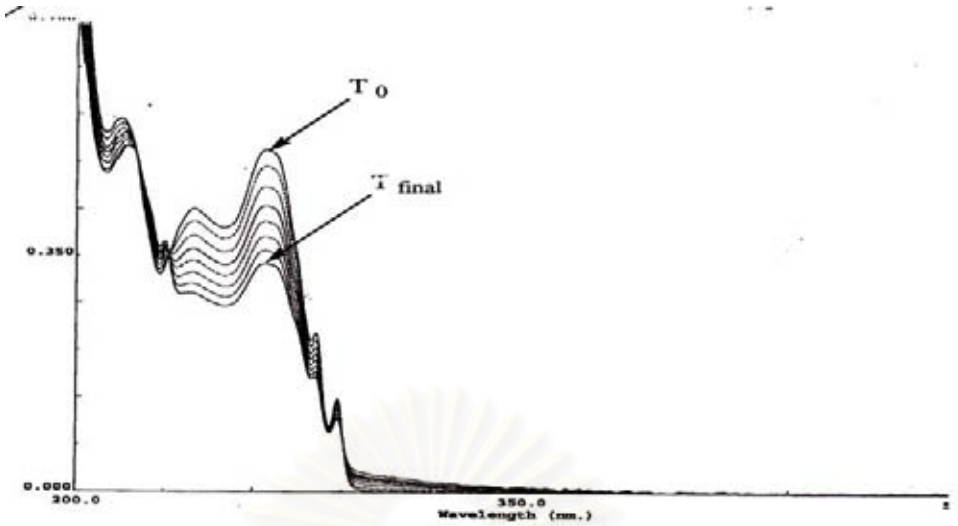


Figure 47b The UV overlay spectrum of the photolysis of **32**.

The photoreaction of **32** in acetonitrile was also monitored by gas–liquid chromatography. The GLC trace of the solution before irradiation [140°C (4 min.), 15 min./°C to 180°C (14 min.)] (Figure 48) indicates the presence of only one component, which was eluted at a retention time of 18 minutes. The solution was irradiated with sixteen 300 nm lamps and monitored by gas–liquid chromatography every 15 minutes. The GLC analyses showed the consumption of the reactant and the formation of a product at a retention time of 4 and 18 minutes, respectively. Figure 49 shows the GLC analysis of the reaction after 120 minutes of irradiation. The trace exhibits only two volatile components in this reaction mixture. The compound eluted at a retention time of 18 minutes is the reactant. The GLC analysis was carried out at a higher oven temperature but no sign of any other photoproduct was observed.

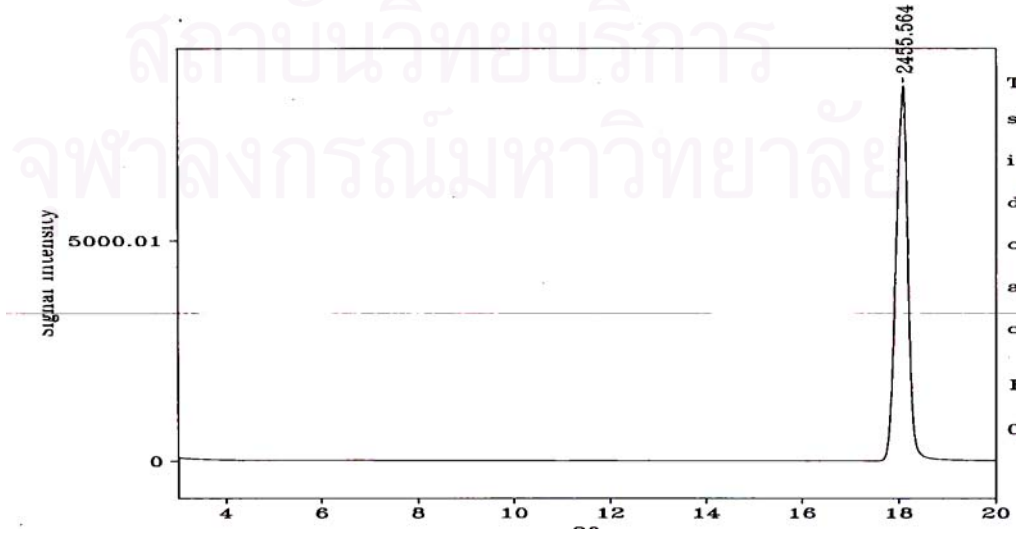


Figure 48 The GLC analysis of **32** in acetonitrile before irradiation.

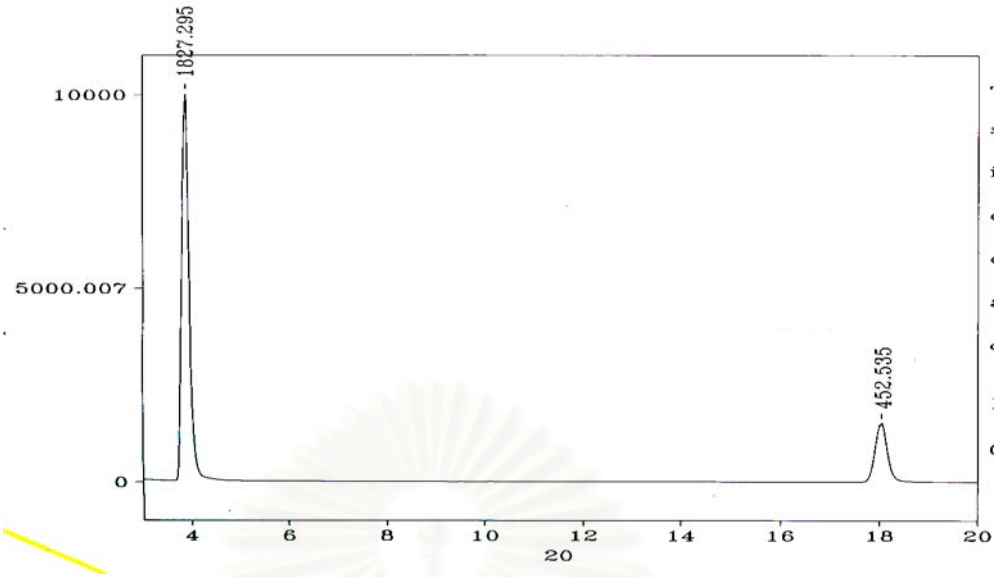


Figure 49 The GLC analysis of **32** in acetonitrile after 120 minutes of irradiation.

The solution after 120 minutes of irradiation time was concentrated by rotary evaporation at room temperature and analyzed by GC-MS [140°C (5min.), 20°C /min. to 250°C (14 min.)]. The GC trace (Figure 50a) again exhibits two components in the reaction mixture. The mass spectrum of the compound eluted at a retention time of 14.3 minutes (Figure 50b) reveals a molecular ion at m/z 162 and a fragmentation pattern identical to the mass spectrum of the reactant **(32)**. Therefore, this compound is due to the reactant. The mass spectrum of the product eluted at a retention time of 4.1 minutes (Figure 50c) reveals a molecular ion at m/z 103.

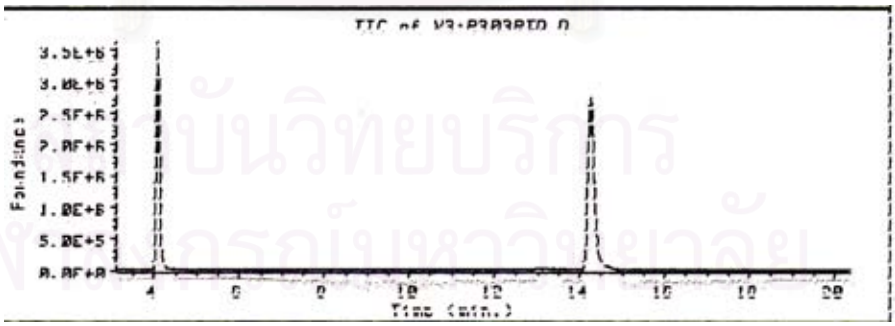


Figure 50a The GC-MS analysis of **32** after 120 minutes of irradiation.

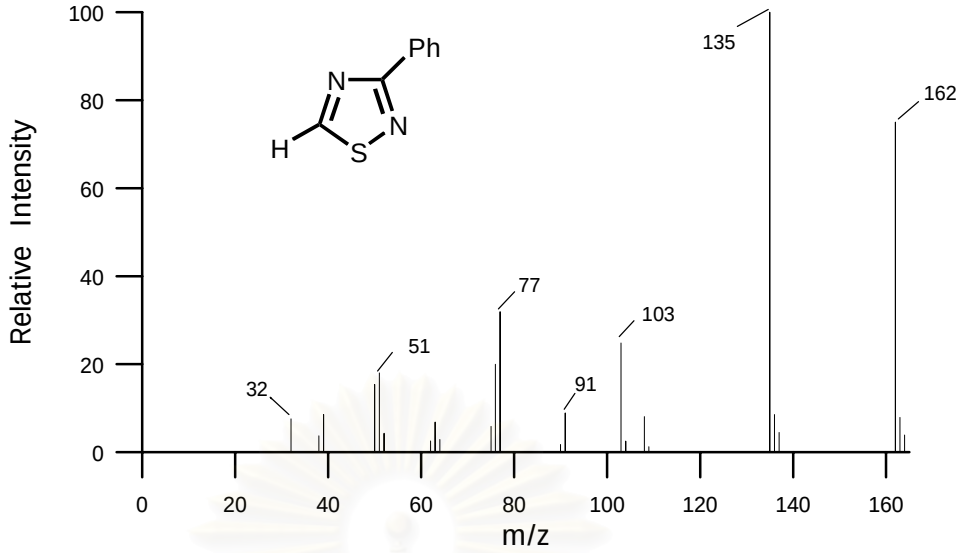


Figure 50b The mass spectrum of the compound eluted at a retention time of 14.3 minutes.

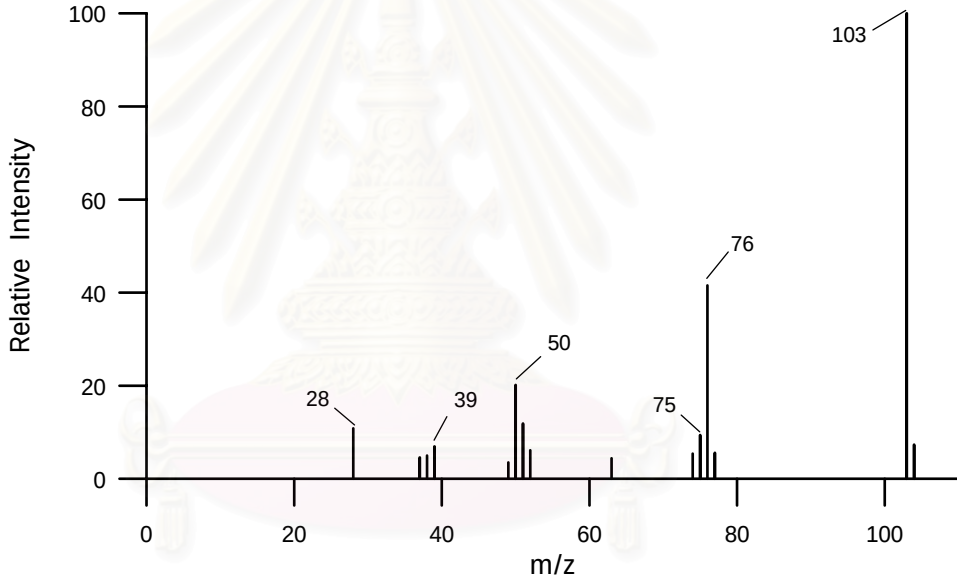


Figure 50c The mass spectrum of the product eluted at a retention time of 4.1 minutes.

By direct comparison of the mass spectroscopic and gas chromatographic properties of this product with these properties of the authentic of **54** (Figure 51), it indicates that the only photoproduct observed upon irradiation of **32** is benzonitrile **(54)**. This result also indicates that 5-phenyl-1,2,4-thiadiazole **(31)** is not formed as a phototransposition product upon irradiation of **32** expected by photochemical reaction analogy of **31**.

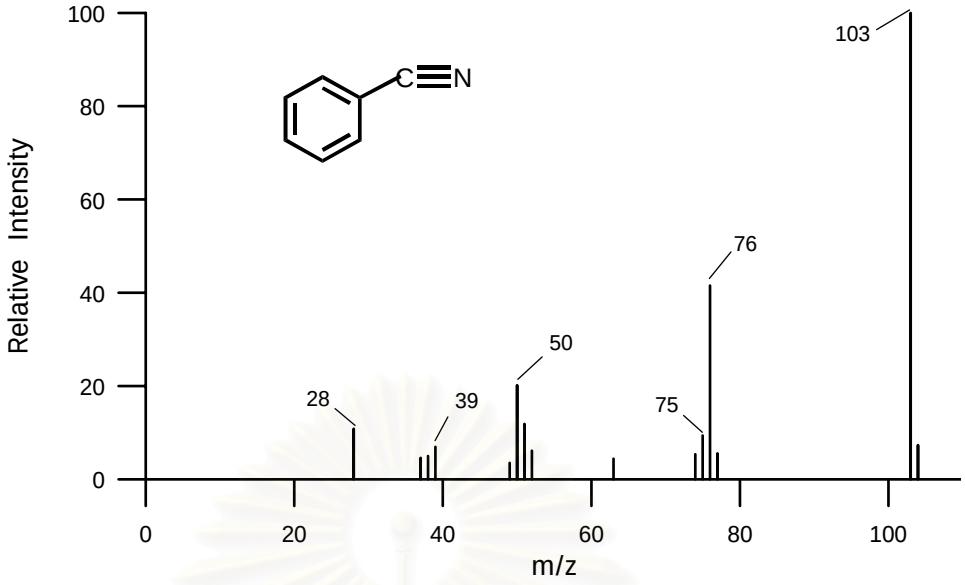


Figure 51 The mass spectrum of the authentic of benzonitrile eluted at a retention time of 4.1 minutes.

The percent yield of **54** was determined by using the same benzonitrile calibration curve previously constructed. After 120 minutes of irradiation, the trace (Figure 49) shows the reactant consumption of 81.6 % and the formation of **54** in 74.1 % yield.

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

As shown in section 3.2.1, **31** undergoes phototransposition leading to the formation of **32**. It also undergoes photofragmentation leading to the formation of **54** and photo ring expansion to yield **50** and **51**. However, upon irradiation of **32**, only **54** was observed in quantitative yield. There is no evidence indicating the formation of **(31)**, the expected phototransposition product upon irradiation of **32.**

This work was also extended to study the photochemistry of a disubstituted-1,2,4-thiadiazole, 3-methyl-5-phenyl-1,2,4-thiadiazole **(33)**. Based on the observed photochemistry of **31**, the expected photoproducts upon irradiation of **33** would be benzonitrile **(54)**, 5-methyl-3-phenyl-1,2,4-thiadiazole **(60)**, 2,4-dimethyl-6-phenyl-1,3,5-triazine **(55)** and 2-methyl-4,6-diphenyl-1,3,5-triazine **(56)**.

The photochemistry of **33** was first studied in acetonitrile. Figure 52a shows the UV-absorption spectrum of the solution before irradiation (6.0×10^{-5} M, 10 mL). The spectrum reveals the λ_{max} at 278 nm with an extinction coefficient of 14,100. Figure 52b exhibits the UV–overlay spectrum of the photolysis of this compound (with three 300 nm lamps) recorded at 40 seconds of intervals. The spectrum reveals the decrease in the absorption at λ 278 nm from 0.85 to 0.7, which is due to the reactant consumption. It also reveals the increase in the absorption at λ 261 nm from 0.56 to 0.65.

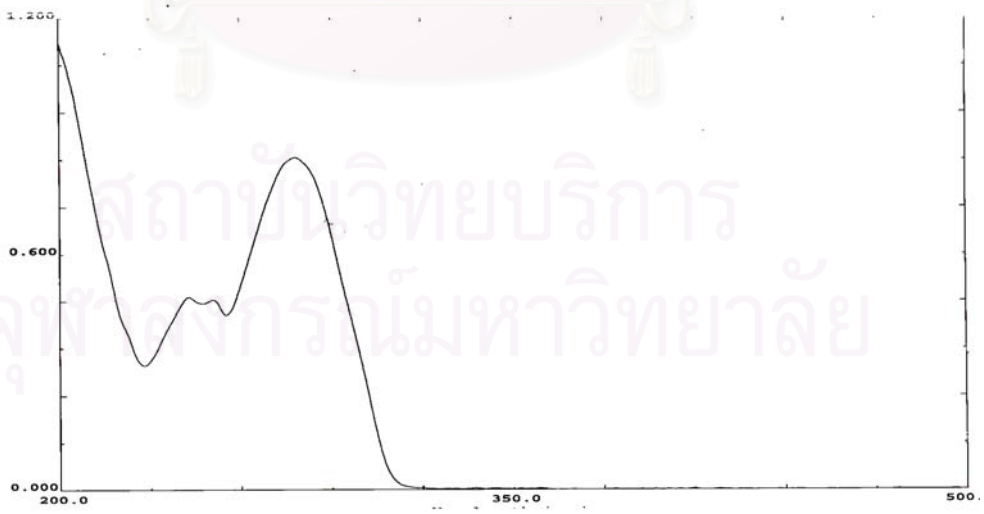


Figure 52a The UV-absorption spectrum **33** in acetonitrile before irradiation.

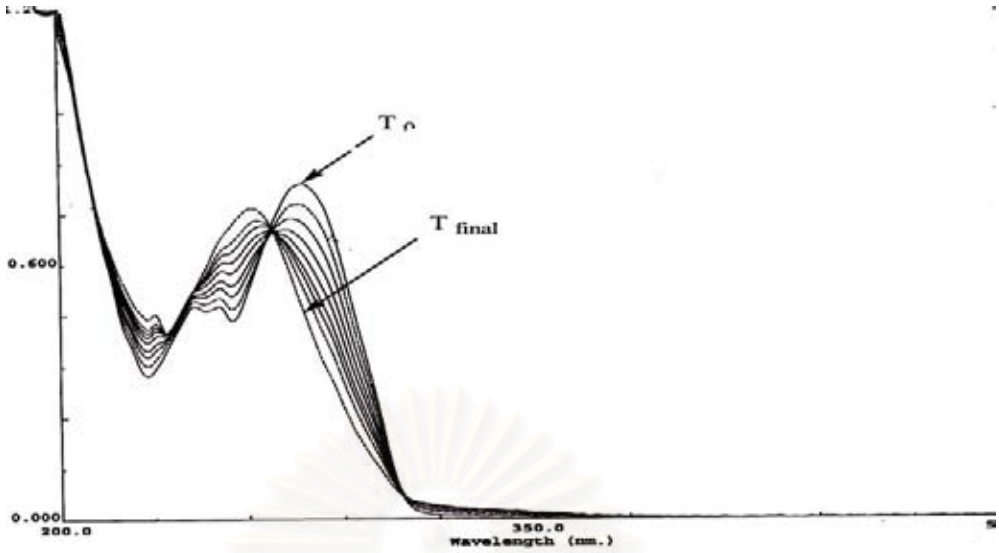


Figure 52b The UV-overlay spectrum of the photolysis of **33** in acetonitrile.

It is of interest to compare the UV-overlay spectrum of **33** (Figure 52b) with the analogous overlay spectrum of **31** (Figure 53). In both cases irradiation is accompanied by the decrease of the absorption band at λ_{max} 278 or 275 nm due to **33** or **31** and the increase of an absorption band at 230 or 224 nm due to the formation of the photoproducts from each compound, respectively.

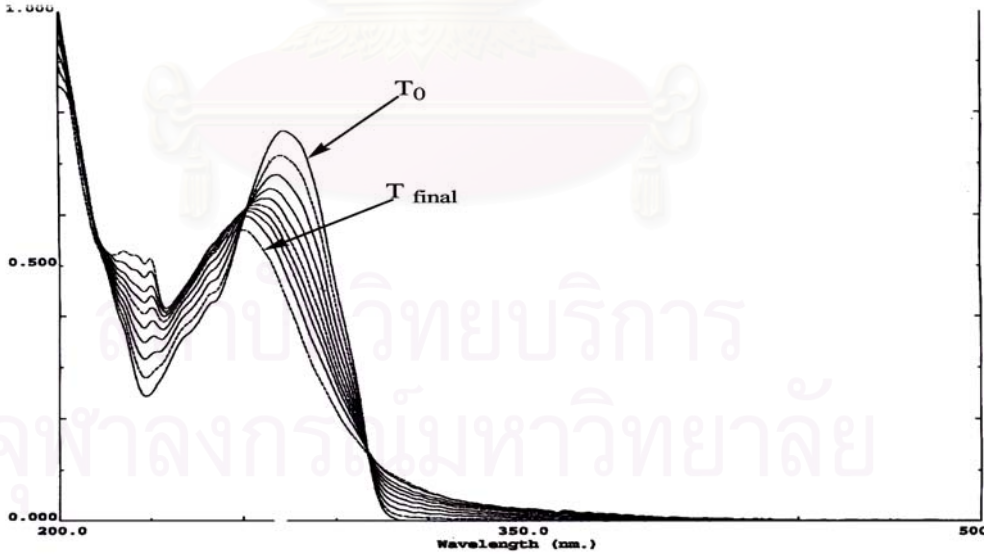


Figure 53 The UV overlay spectrum of the photolysis of **31** in acetonitrile.

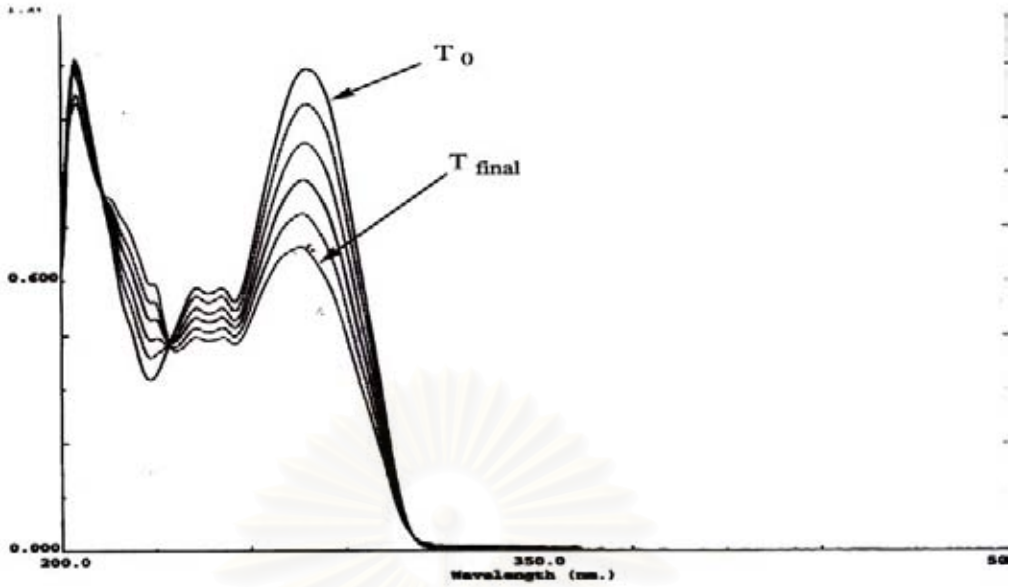


Figure 52c The UV–overlay spectrum of the photolysis of **33** (in methanol).

Figure 52c shows a time lapse photolysis UV–absorption spectrum of **33** in methanol photolyzed for 1,000 seconds at 100 seconds intervals. This spectrum reveals the dramatically decrease in the formation of the absorption band at λ 261 compared to the reaction in acetonitrile (Figure 52b).

The photolysis was also monitored by GLC. Figure 54a shows the GLC analysis [140°C(4 min.), 10°C/min. to 240°C (20 min.)] of the solution (acetonitrile; 2.0×10^{-2} M, 4 ml.) before irradiation. The trace exhibits the eluted reactant at a retention time of 12 minutes. The solution was irradiated with sixteen 300 nm lamps and monitored by gas-liquid chromatography at 40 minutes of intervals. Figure 54b shows the GLC-trace of the reaction mixture after 150 minutes of irradiation. The trace reveals the consumption of 76.4 % of the reactant and the formation of four new products at retention times of 5, 11.5, 13.5 and 28 minutes.

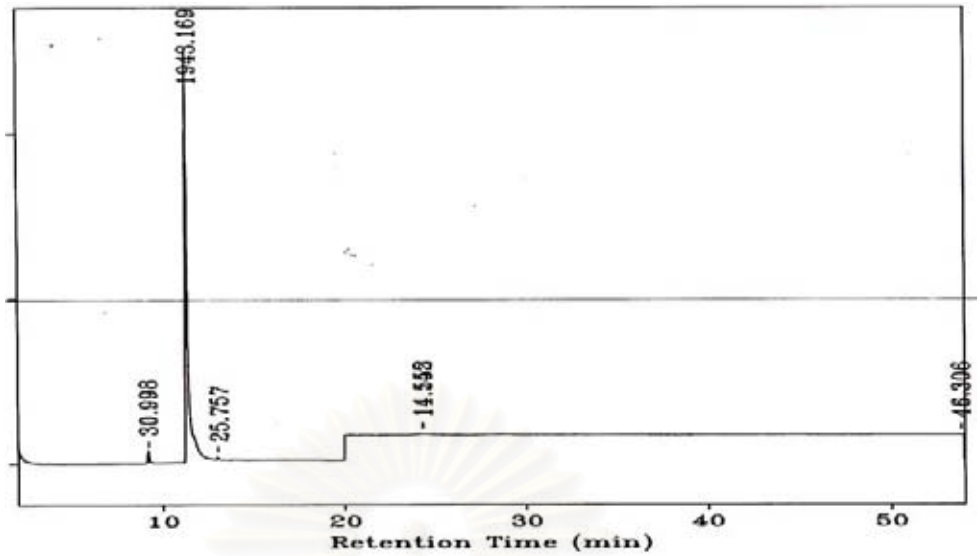


Figure 54a The GLC analysis of the reactant (in acetonitrile) before irradiation.

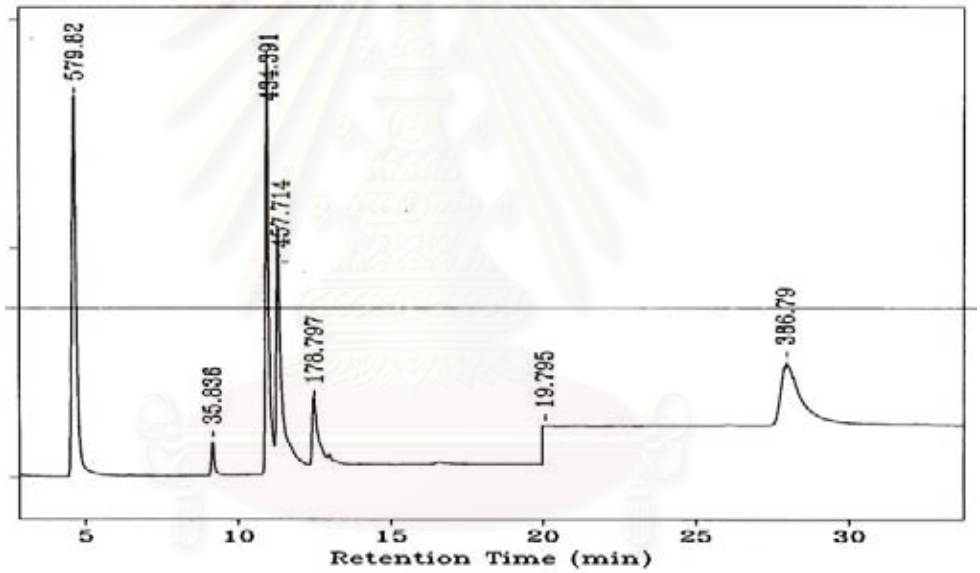


Figure 54b The GLC analysis of the reaction mixture after 150 minutes of irradiation.

The concentrated reaction mixture was analyzed again by GC-MS [140°C (5 min.), 10°C/min. to 240°C (30 min.)]. Figure 55a shows four major GC-volatile components at retention times of 4.1, 13.0, 14 and 29.2 minutes. The mass spectrum of the first eluted component (Figure 55b) exhibits a base molecular ion peak at m/z 103, which could be due to **54**. This was confirmed by comparing of its chromatographic and mass spectroscopic data to the authentic of **54** (Figure 56).

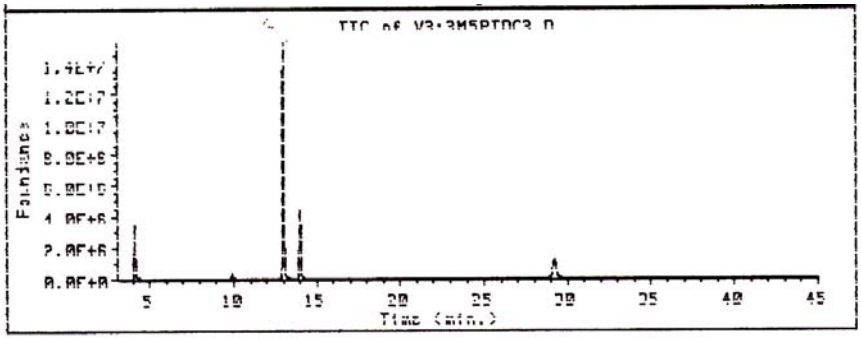


Figure 55a The GC-MS analysis of the concentrated reaction mixture.

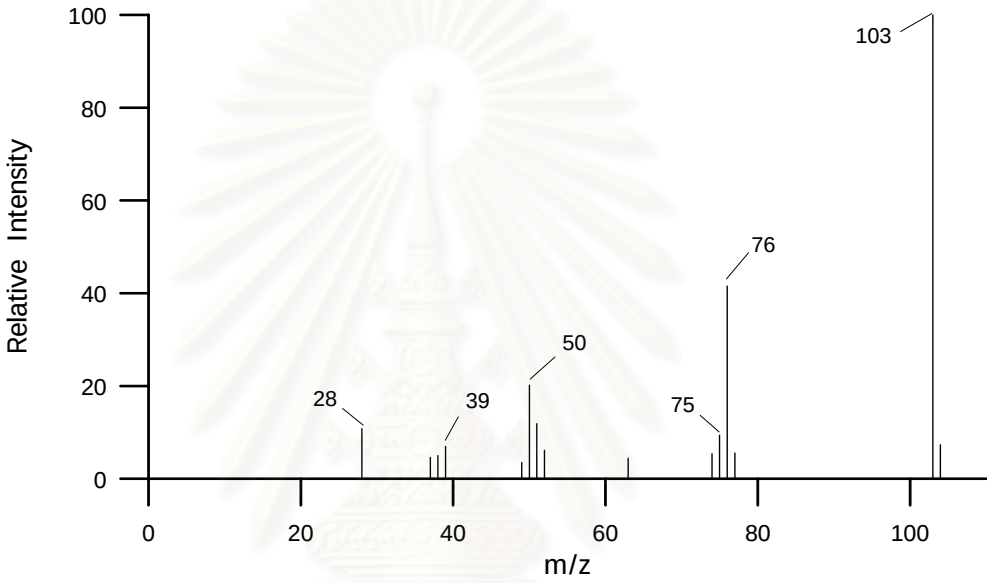


Figure 55b The mass spectrum of the product eluted at a retention time of 4.1 minutes.

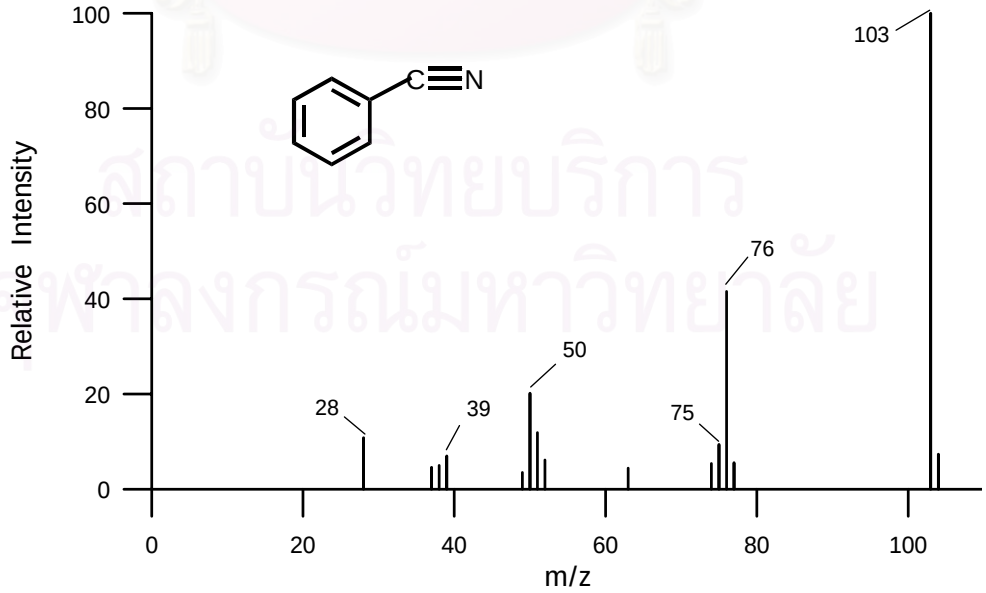


Figure 56 The mass spectrum of the authentic of benzonitrile eluted at a retention time of 4.1 minutes.

The mass spectrum of the second component eluted at a retention time of 29.2 minutes (Figure 55c) exhibits a molecular ion at m/z 247. This photoproduct was expected, by analogy with the results from the photolysis of **31**, to be 2-methyl-4,6-diphenyl-1,3,5-triazine **(56)**. The molecular ion at m/z 247 also corresponds to the molecular weight of **56** (MW 247).

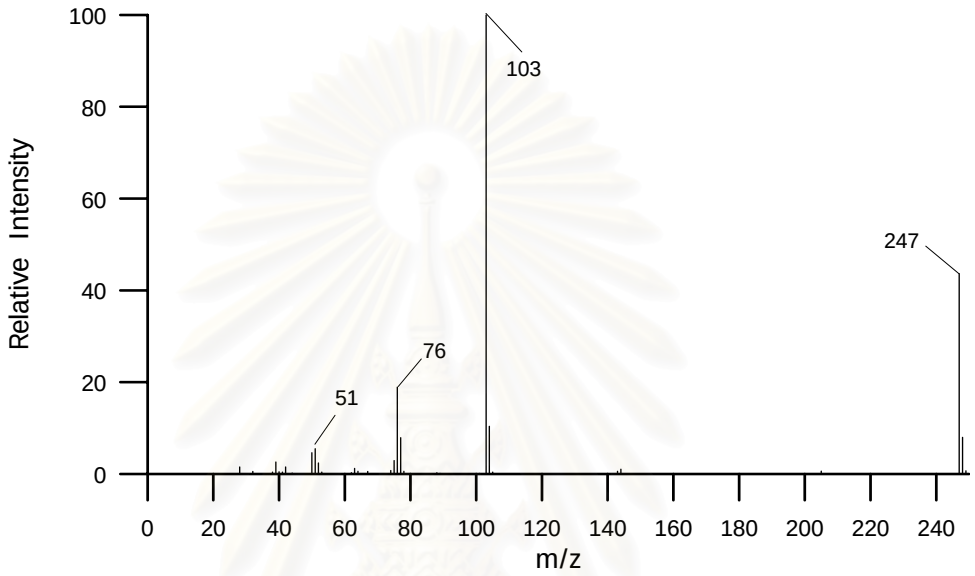


Figure 55c The mass spectrum of the compound eluted at a retention time of 29.2 minutes.

In order to confirm the formation of this photoproduct, the authentic of **56** was analyzed by GC-MS. This sample was eluted at the same retention time as of this product. The mass spectrum of this authentic sample (Figure 57) also exhibits a molecular ion at m/z 247 and a base peak at m/z 103. The fragmentation pattern of this authentic sample is identical to the fragmentation pattern of the photoproduct. (Figure 55c). Thus, the product eluted at a retention time of 29.2 minutes can be identified as **56**.

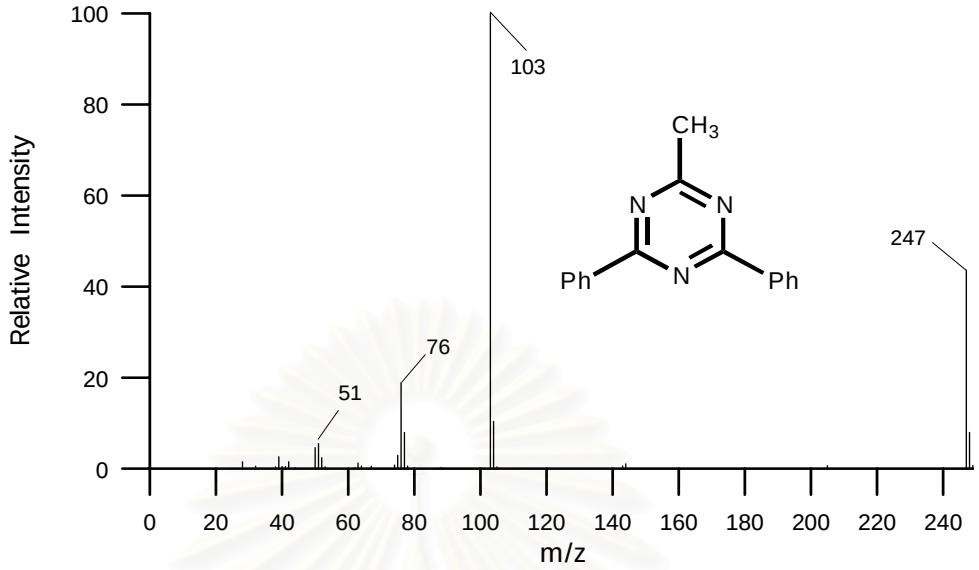


Figure 57 The mass spectrum of an authentic of **56**.

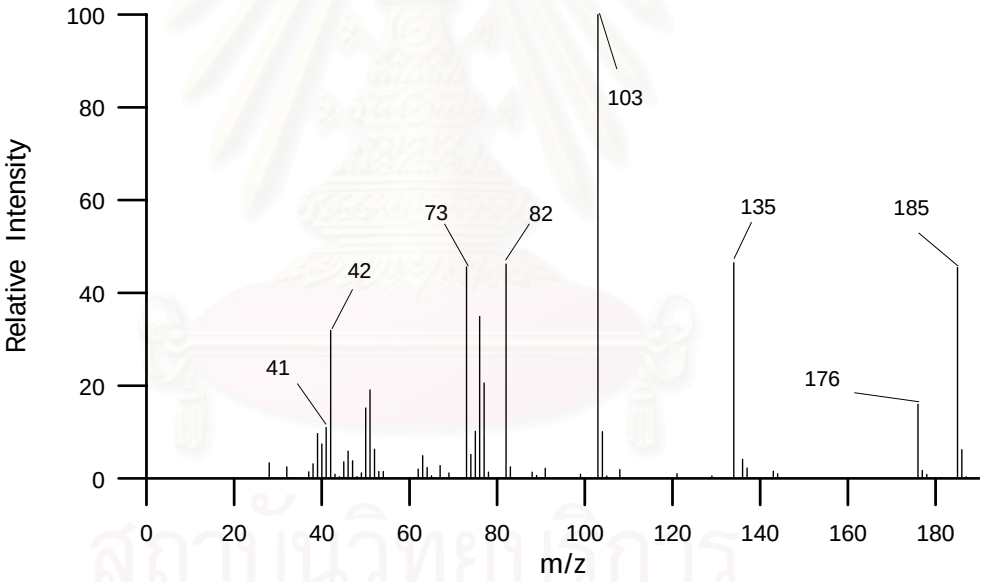


Figure 55d The mass spectrum of the compound eluted at a retention time of 13 minutes.

The mass spectrum of the compound eluted at a retention time of 13 minutes (Figure 55d) exhibits a molecular ion at m/z 185 and a base peak at m/z 103. Accordingly, this compound was suspected to be 2,4-dimethyl-6-phenyl-1,3,5-triazine **(55)**, another possible photoproduct. The fragmentation pattern of the authentic of **55** (Figure 58) is identical to the pattern of this product as well as the chromatographic property.

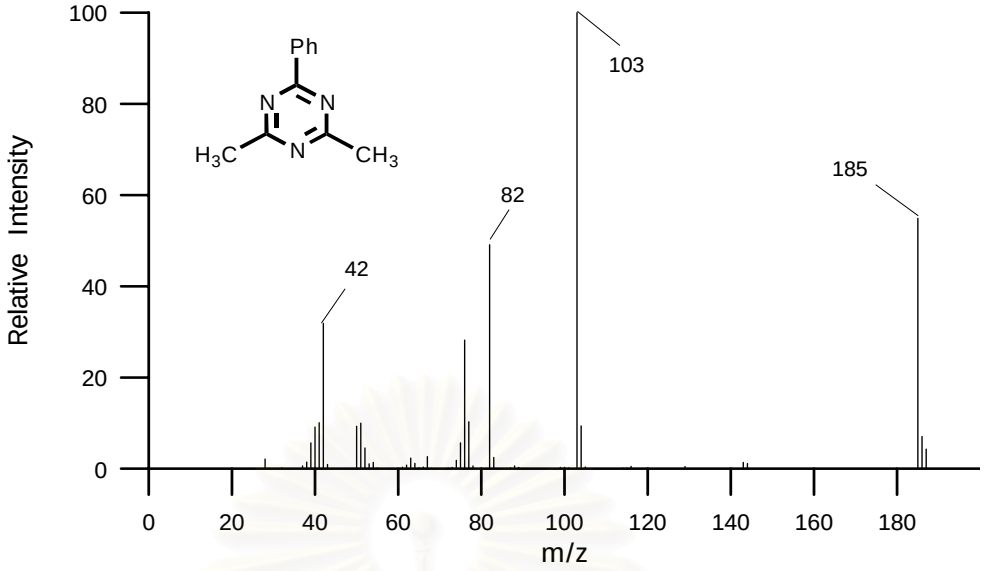


Figure 58 The mass spectrum of the authentic of **55**.

A comparison of Figure 55d and 58, the mass spectrum of the authentic sample of **55**, it is not totally identical with the mass spectrum of the photoproduct. Although, the mass spectrum of the photoproduct (Figure 55d) exhibits a molecular ion at m/z 185, a base peak at m/z 103, a peak at m/z 82, it also reveals peaks at m/z 135 and m/z 73. These two peaks are certainly not due to **55**. However, it was suspected that these peaks may be due to an overlap of **55** and the reactant **(33)**. Since GC-MS analysis of **33** before irradiation (Figure 59a, b) shows that this compound also has a retention time of 13 minutes. Furthermore, the mass spectrum (Figure 59b) exhibits a molecular ion at m/z 176, a base peak at m/z 135, which is due to $[C_6H_5CNS]^{+\bullet}$, a peak at m/z 73, which is due to $[C_2H_3NS]^{+\bullet}$. All of these major fragments are observed in the mass spectrum of the component eluted at a retention of 13 minutes indicating the overlap of the photoproduct **(55)** with the reactant **(33).**

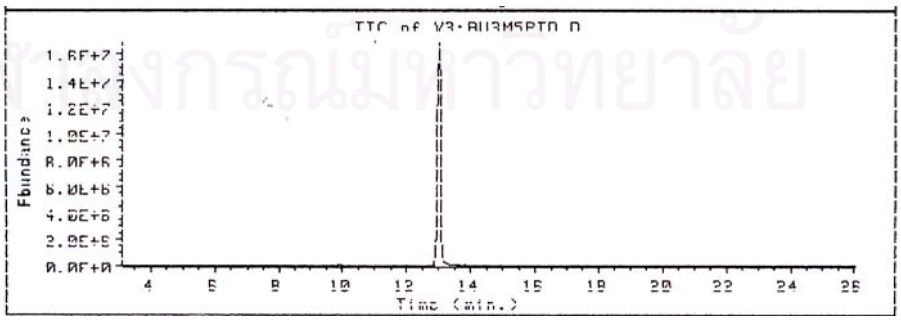


Figure 59a The GC-MS analysis of **33** before irradiation.

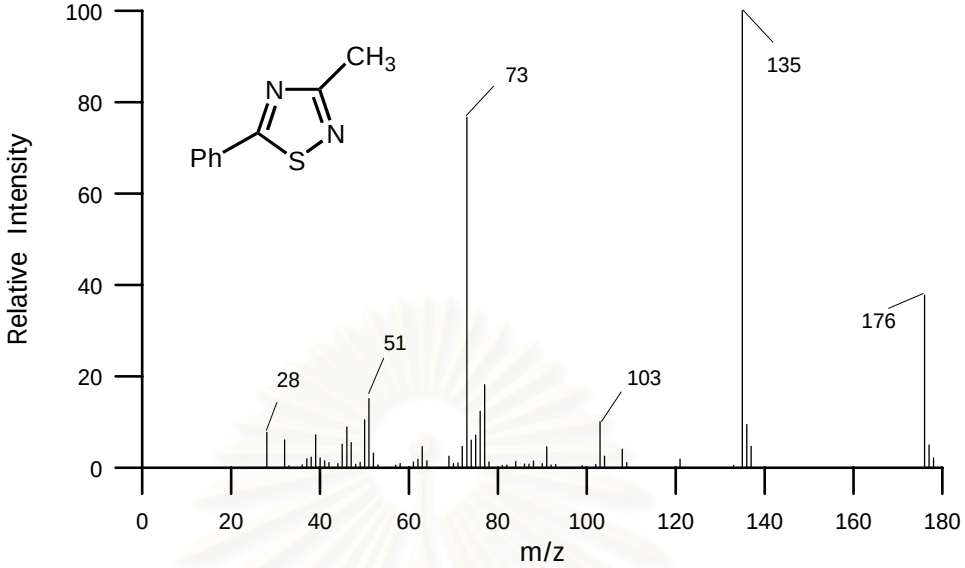


Figure 59b The mass spectrum of **(33)** before irradiation.

Moreover, the GLC-trace of the reaction mixture after 150 minutes of irradiation (Figure 54b) reveals two partially resolved peaks at a retention time of approximately 13 minutes. One of these peaks is due to the reactant **(33)**, and one is due to a photoproduct. Although these two compounds are resolved in the PE-9000 GLC, they are not resolved on the gas chromatograph interfaced to the mass detector. Thus, the mass spectrum shown in Figure 55d is the mass spectrum of a mixture of **55** and **33**.

The mass spectrum of the product eluted at a retention time of 14 minutes (Figure 55e) exhibits a molecular ion at m/z 176, and is therefore isomeric with **33**. This product has been tentatively identified as the phototransposition product, 5-methyl-3-phenyl-1,2,4-thiadiazole **(60)** .

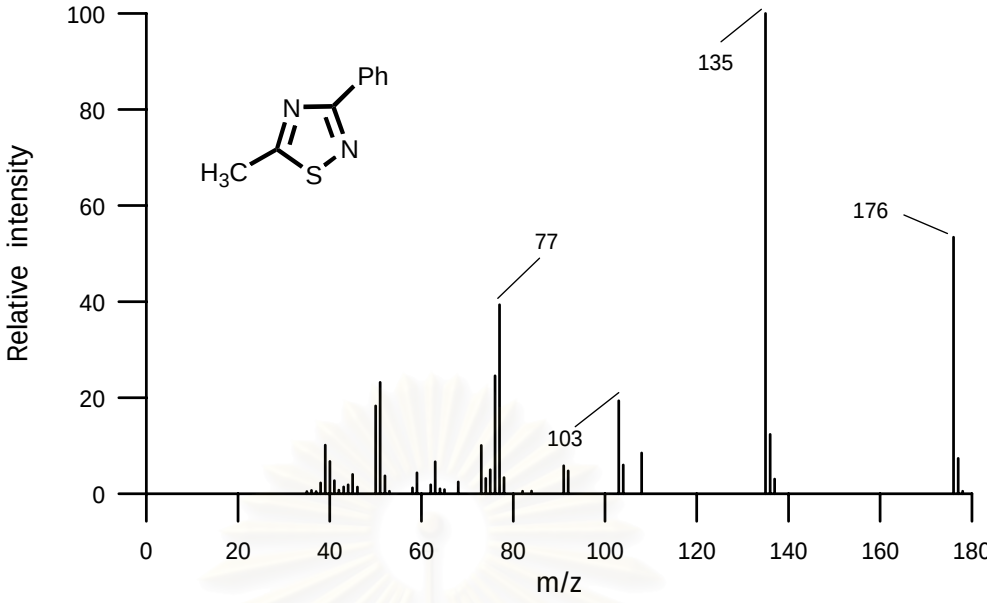
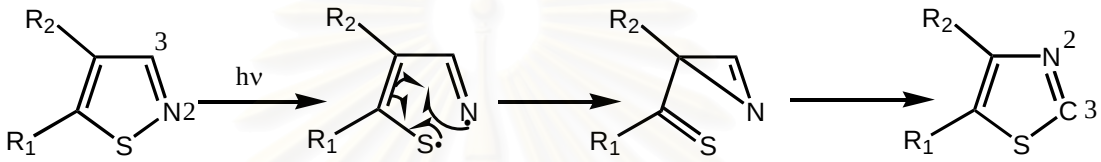


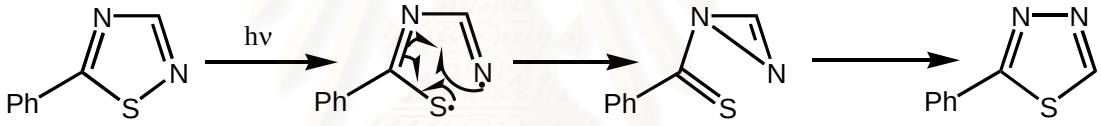
Figure 55e The mass spectrum of the product eluted with a retention time of 14 minutes.

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

According to the photochemistry of substituted isothiazoles, cleavage of the S-N bond resulting in the formation of azirine intermediates and eventually to the formation of substituted thiazole products (the N-2 and C-3 interchange product), (Scheme 8) has been reported as the major photochemical pathway of 4-substituted isothiazoles[9]. 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 9).

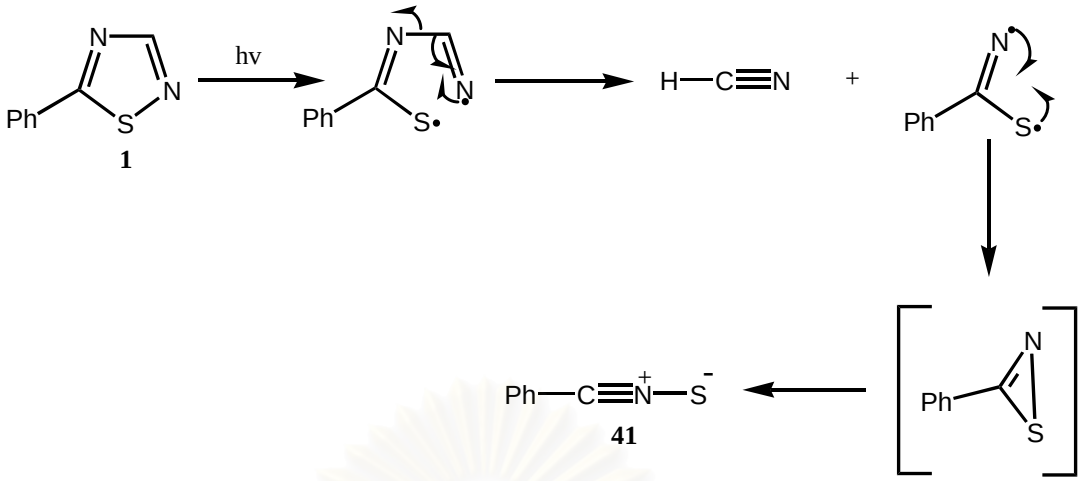


Scheme 8 The N-2 and C-3 interchange photochemical pathway of isothiazoles.



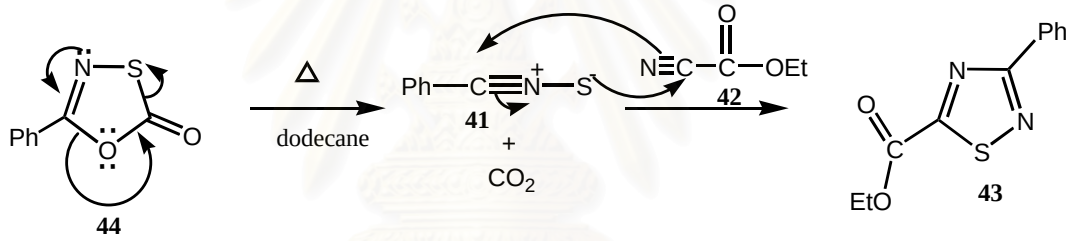
Scheme 9 The N-2 and C-3 interchange photochemical pathway of **31**.

According to the results of the photolysis of 5-phenyl-1,2,4-thiadiazole **(31)**, GLC and GC-MS analysis of the reaction solution showed no sign corresponding to the formation of 5-phenyl-1,3,4-thiadiazole, the N-2 and C-3 interchange product. According to Scheme 9, **31** could undergo the photocleavage of the S-N bond leading to the formation of a 1,5-diradical. In phenyl substituted isothiazole, cyclization of the 1,5-diradical would lead to the formation of a substituted azirine (Scheme 8). In this case of phenyl substituted-1,2,4-thiadiazoles, cyclization of the 1,5-diradical would not give an azirine but a diazirine intermediate instead, 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 the loss of HCN to yield a 1,3-diradical. This diradical could then cyclize to the formation of phenyl substituted thiazirine and eventually rearrange to yield benzonitrile sulfide **(41)**, as shown in Scheme 10.



Scheme 10 The possible mechanism for the formation of **41**.

The trapping of thermally generated **41** has been successfully carried out by a 1,3-dipolar cycloaddition reaction using **42** as a dipolarophile to yield **43**[5], as discussed in the synthesis of 3-phenyl-1,2,4-thiadiazole section (Scheme 11).



Scheme 11 The trapping of thermally generated benzonitrile sulfide by 1,3-dipolar cycloaddition reaction.

In order to investigate the possible formation of **41,** the photolysis of **31** in acetonitrile with the presence of ethyl cyanoformate **(42)** was carried out.

Two solutions of **31** (2.0×10^{-2} M, 4 mL) with the presence of **42** (0.1 mL, 1×10^{-1} M) in acetonitrile were irradiated with sixteen 300 nm lamps and eight 254 nm lamps. The reactions were monitored by GC [120 °C (5 min.), 20°C/min. to 160°C (8 min.), 20°C/min. to 240°C (20 min.)] every 30 minutes of irradiation.

Figure 60a exhibits GLC analysis of the reaction solution before irradiation. After 210 minutes of irradiation (300 nm), GLC analysis (Figure 60b) reveals the formation of **54**, **50**, **32** and **51**, the known photoproducts with retention times of 3, 9, 13 and 23.5 minutes, respectively, while the unconsumed reactant eluted at a retention

time of 11 minutes. The trace also reveals an extra peak at a retention time of 19 minutes, which was not observed upon irradiation of **31** in an absence of **42**.

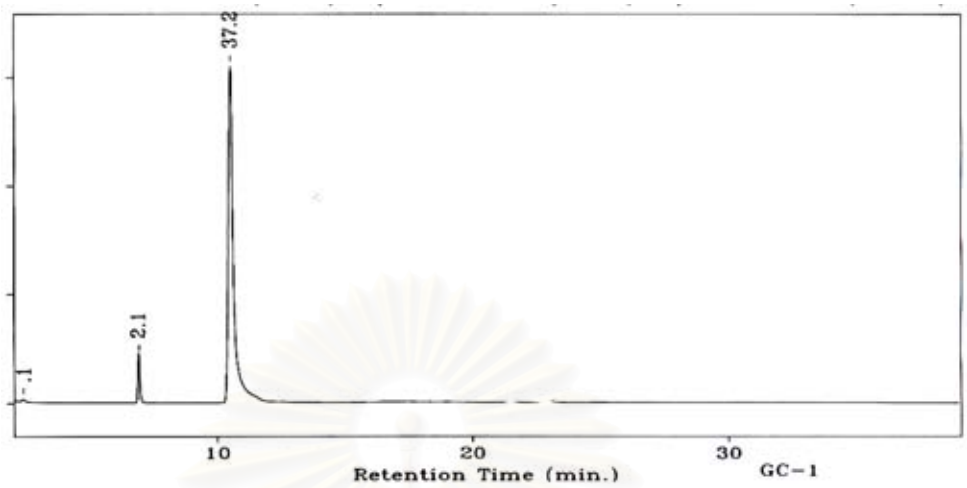


Figure 60a The GLC analysis of **31** in the presence of **42** before irradiation.

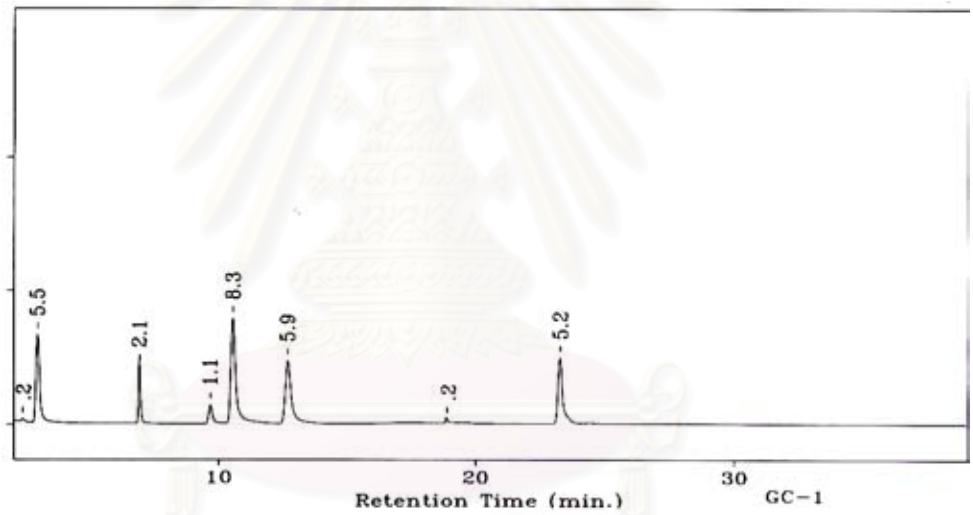


Figure 60b The GLC analysis of **31** in the presence of **42** at 210 minutes of irradiation.

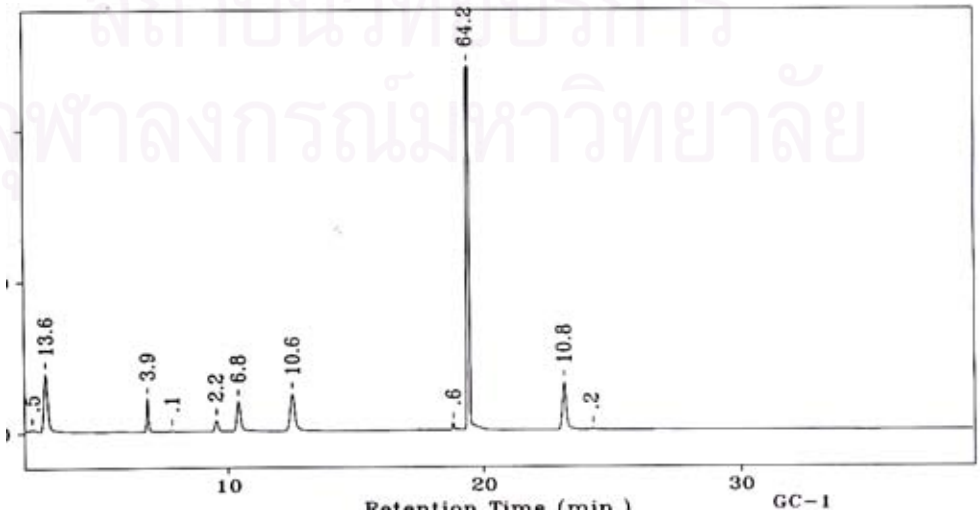


Figure 60c The GLC analysis of the reaction mixture spiked with the authentic of **43**.

A small amount of the reaction solution was removed and spiked with the authentic of **(43)** and analyzed by GLC (Figure 60c). This result reveals that the new photoproduct eluted at a retention time of 19 minutes was not due to the expected cycloaddition product **(43)**.

GC-MS analysis [140°C (5 min.), 20°C/min. to 240°C (20 min.)] of the concentrated reaction solution (Figure 61a) exhibits the formation of the known photoproducts and the unconsumed reactant with retention times of 4, 9, 11, 25 and 10.5 minutes, respectively. The trace also reveals a very small peak at a retention time of 16.4 minutes. The mass spectrum of this compound (Figure 61b) exhibits a molecular ion at m/z 234 which corresponds to the molecular weight of the expected trapping product, ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate **(43)** (MW 234). The authentic of **43** was also eluted at a retention time of 16.4 minutes under the same GC-MS analytical condition.

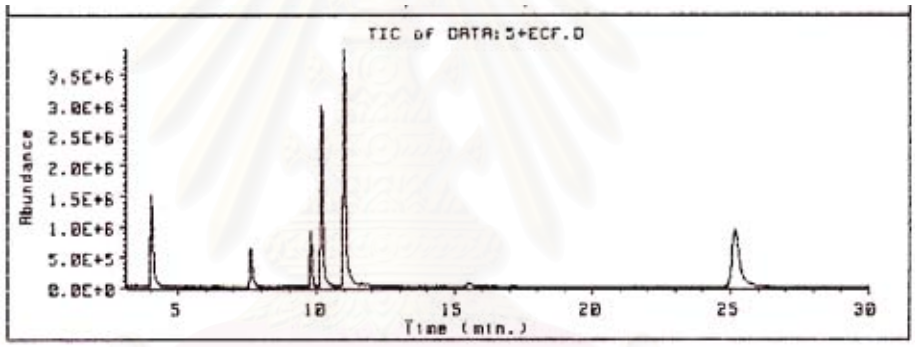


Figure 61a The GC-MS analysis of the concentrated solution after 210 minutes of irradiation.

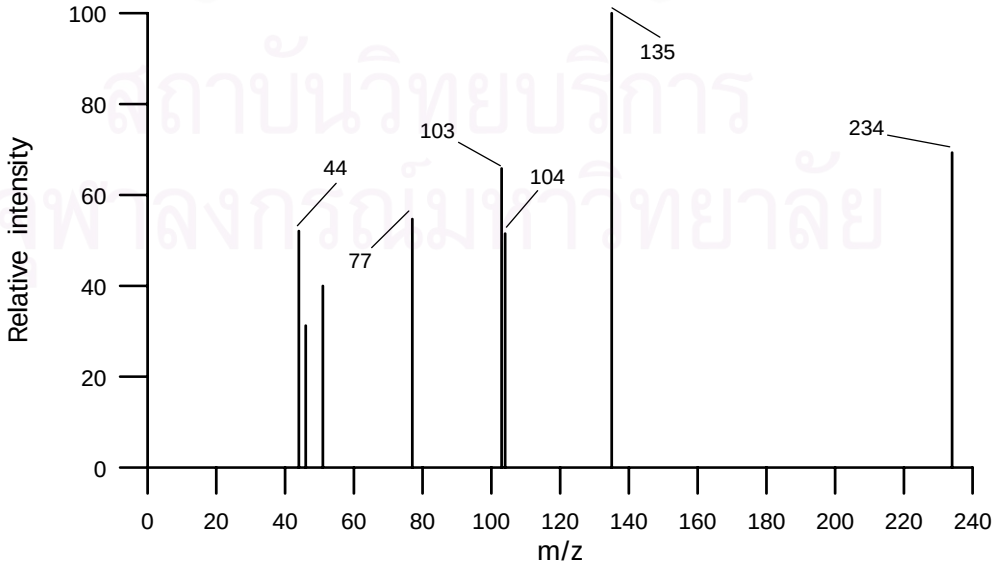


Figure 61b The mass spectrum of a suspected peak to be **43**.

The mass spectrum of the compound, which is suspected to be **43** (Figure 61b) 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 the authentic of **43** (Figure 61c) exhibits a molecular ion at m/z 234, a base peak at m/z 135, which is due $[C_6H_5CNS]^{+\bullet}$ fragment.

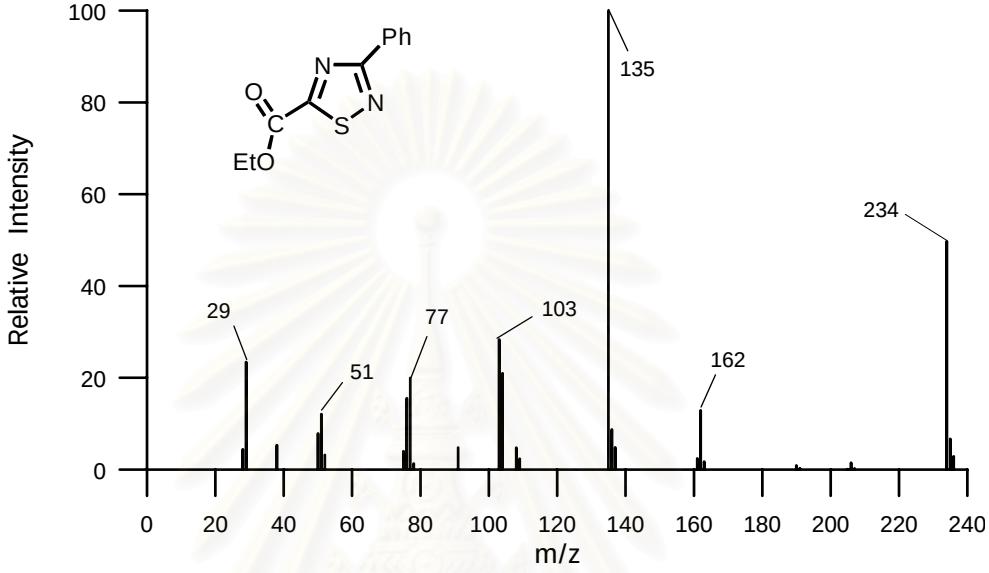


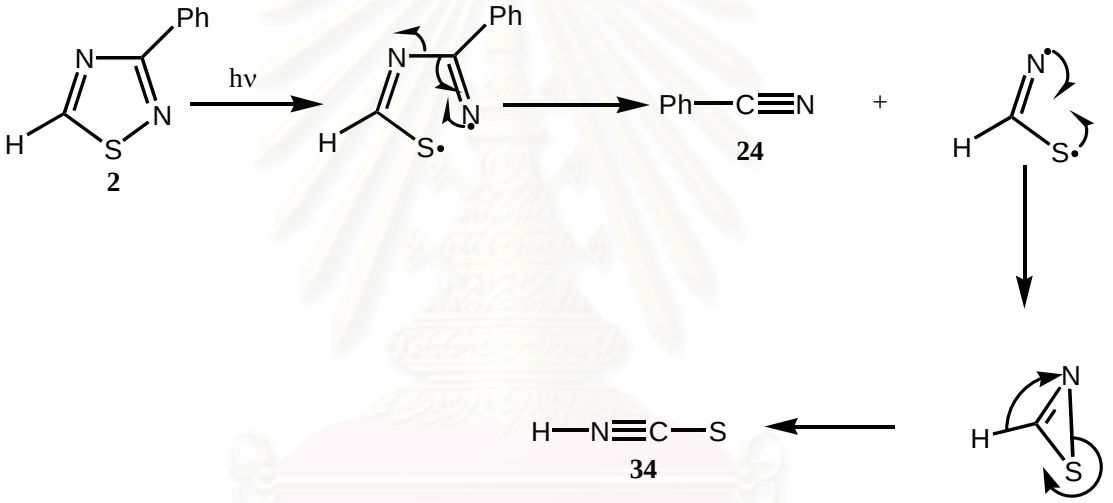
Figure 61c The mass spectrum of the authentic of **43**.

By comparison the mass spectroscopic properties of the suspected product with the authentic of **43**, it indicates that this suspected product is ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate **(43)**. However, since the presence of this product can not be detected by GLC analysis without concentration of the reaction solution, this indicates that the formation of **41** can only be a very minor pathway upon photolysis of **31**. This result is consistent with the proposed mechanism of the formation of benzonitrile sulfide upon irradiation of **31** as shown in Scheme 25.

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.

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

In an attempt to trap the expected intermediate, **41**, upon the irradiation of **31**, the results indicated the formation of very trace amount the expected cycloaddition product. However, in the case of **32**, cleavage of the 1,5-diradical would not finally produce **41**. According to Scheme 12, cleavage of the 1,5-diradical would finally lead to the formation of isothiocyanic acid **61**, which could be an unidentified photoproduct formed upon irradiation of **32**. Therefore, the formation of the cycloaddition product **(43)** could be predicted unobservable upon irradiation of **32** in the presence of **42.**.



Scheme 12 The predicted mechanism for the formation of isothiocyanic acid.

Two solutions of **32** (2.0×10^{-2} M, 4 mL) in acetonitrile containing **42** (0.1 mL, 1×10^{-1} M). Each of these solutions was irradiated with sixteen 300 nm lamps or eight 254 nm lamps. The reactions were monitored by GC [120°C (5 min.), 20°C/min. to 240°C (20 min.)] every 30 minute of irradiation. The 300 nm photolyzed solution was irradiated for 300 minutes while the 254 nm photolyzed solution was irradiated for 120 minutes.

Figure 62a exhibits GLC analysis of the solution before irradiation. After 300 minutes of irradiation (300 nm), the trace (Figure 62b) exhibits the formation of two peaks at retention times of 3 and 12 minutes and the unconsumed reactant at a retention time of 9 minutes. The compound eluted at a retention time of 3 minutes is **54**, the known major photoproduct upon irradiation of **32**. The compound eluted at a retention time of 12 minutes was not observed upon irradiation of **32** in an absence of **42.**

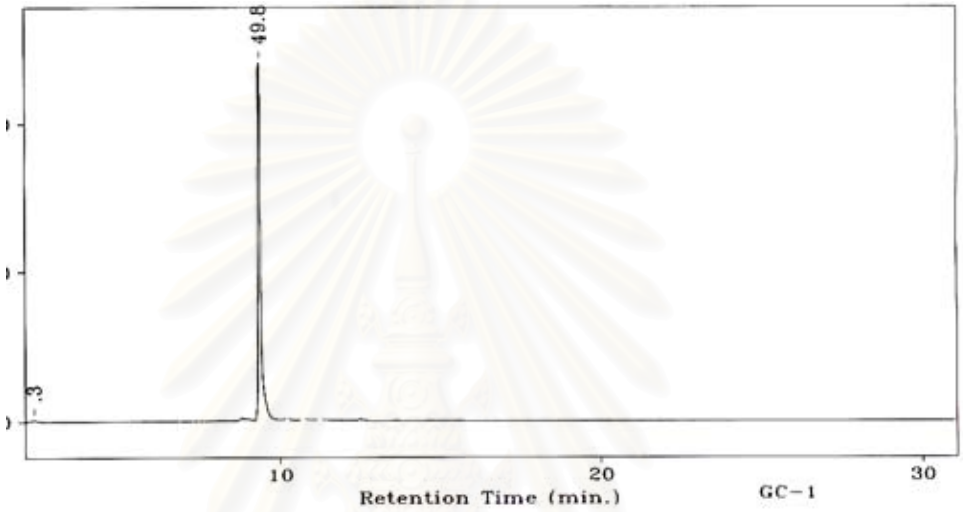


Figure 62a The GLC analysis of the solution before irradiation.

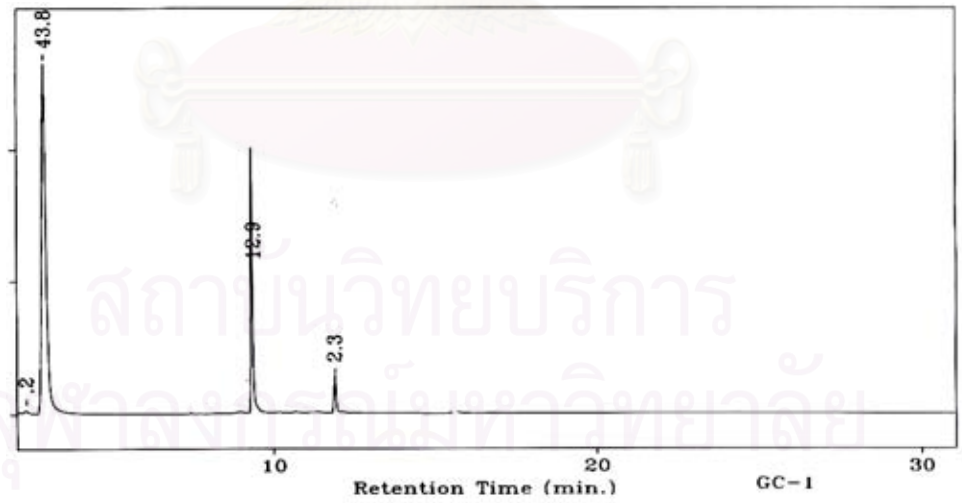


Figure 62b The GLC analysis of the reaction solution after 300 minutes of irradiation.

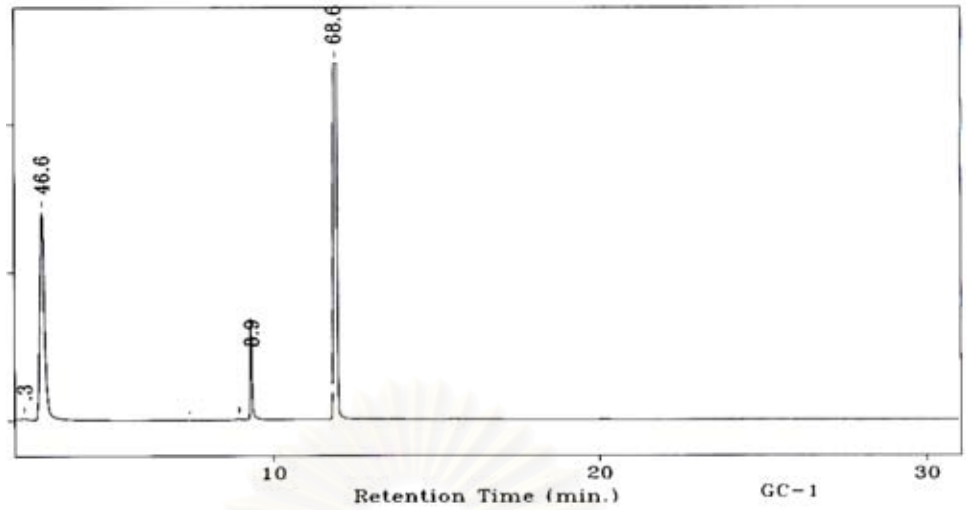


Figure 62c The GLC co-injection analysis of the reaction solution with the authentic of **43** after 300 minutes.

The GLC co-injection analysis of the reaction solution after 300 minutes with the authentic of **43** (Figure 62c) reveals that the peak at a retention time of 12 minutes has been dramatically increased. This would indicate that this new observed product eluted at a retention time of 12 minutes is ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate **(43)**.

GC-MS analysis of the same unconcentrated reaction solution after 300 minutes of irradiation (Figure 63a) exhibits three components in this reaction mixture with retention times of 4, 11.5 and 17 minutes. The mass spectrum of the first eluted component with a retention time of 4 minutes exhibited a molecular ion at m/z 103 and fragmentation pattern consistent with that of **54**, the known photoproduct. The second eluted component is the unconsumed reactant. The mass spectrum of the third eluted component (Figure 63b), which is strongly suspected to be **43**, exhibits a molecular ion at m/z 234 and a base peak at m/z 135.

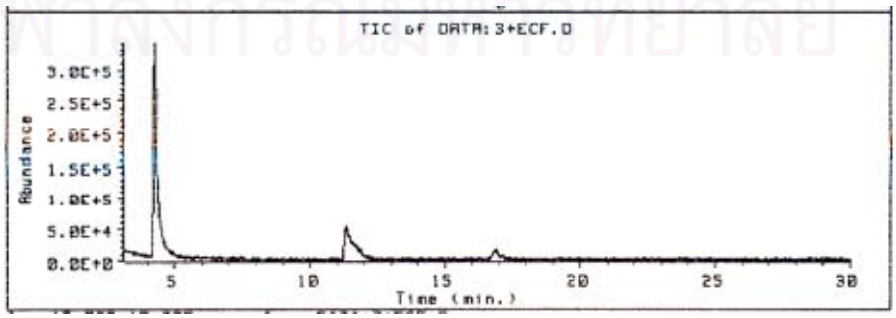


Figure 63a The GC-MS analysis of the unconcentrated reaction solution after 300 minutes of irradiation.

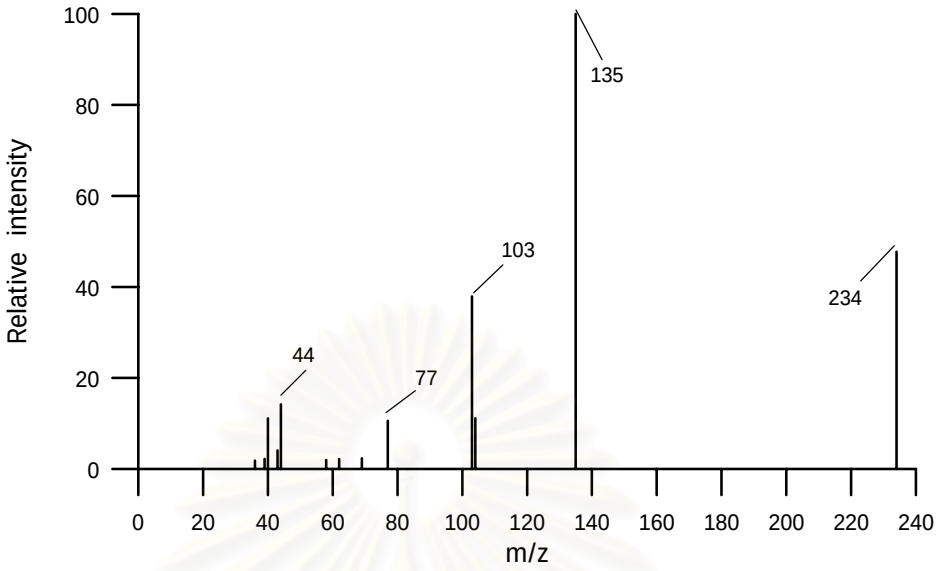


Figure 63b The mass spectrum of the suspected product.

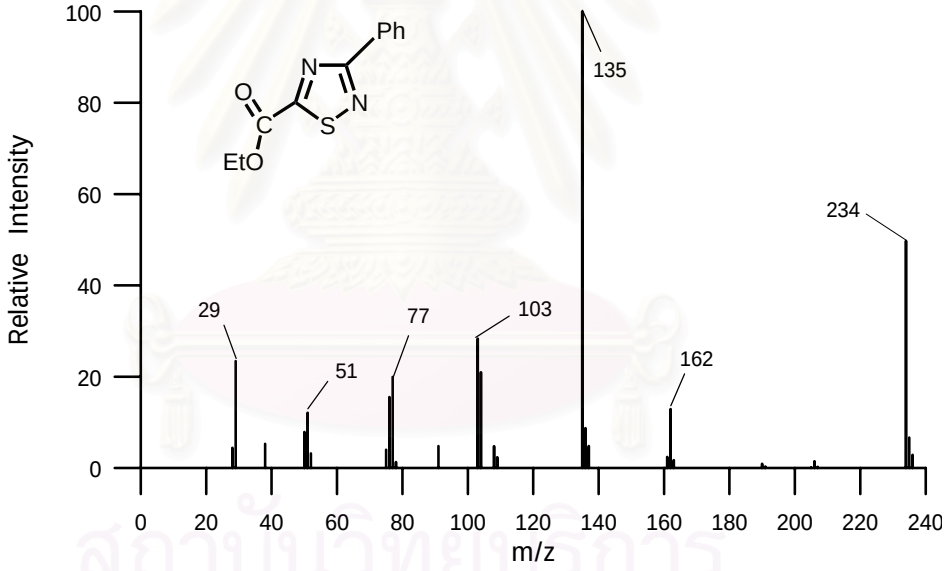
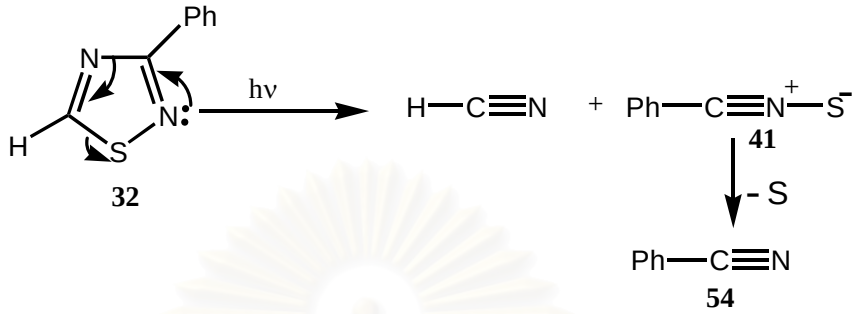


Figure 64 The mass spectrum of the authentic of **43**.

By comparison of the chromatographic and mass spectroscopic properties of the suspected product with the authentic of **43**, it can be concluded that the suspected product is ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate **(43)**. This result indicates the formation of **41**. The mechanism of the formation of **41** upon irradiation of **32** is still an ambiguity.

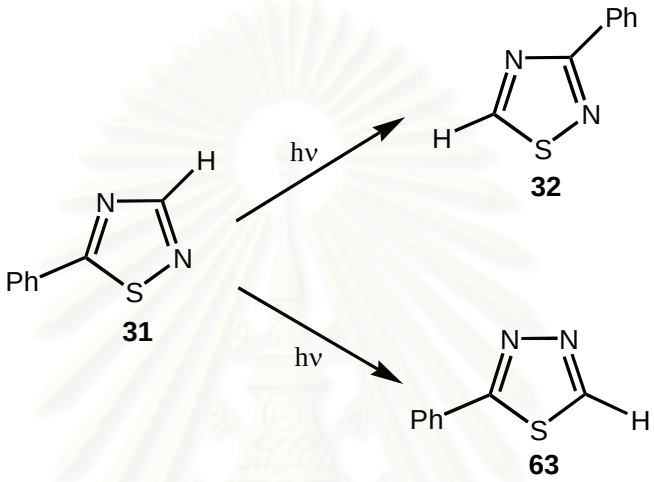
The detection of **41** would suggest a direct photocleavage of the thiadiazole ring with the formation of H-CN and **41**. The latter species can undergo cycloaddition reaction with **42** to yield **43**. In the absence of the trapping agent, **41** could split out the sulfur atom resulting in the formation of **54**, as shown in Scheme 13.



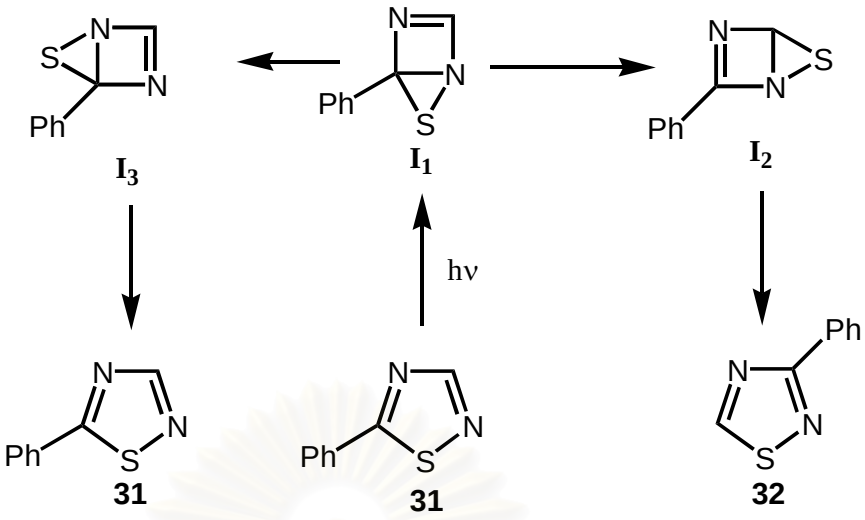
Scheme 13 The proposed mechanism for the formation of **54** upon irradiation of **32**.

3.3 Mechanistic Discussion

According to the two possible mechanisms based on the photochemistry of phenyl substituted isothiazoles and thiazoles, 5-phenyl-1,2,4-thiadiazole **(31)** could be expected to undergo phototransposition reaction lead to 3-phenyl-1,2,4-thiadiazole **(32)** and/or the N2-C3 interchange reaction lead to 5-phenyl-1,3,4-thiadiazole **(63)**.

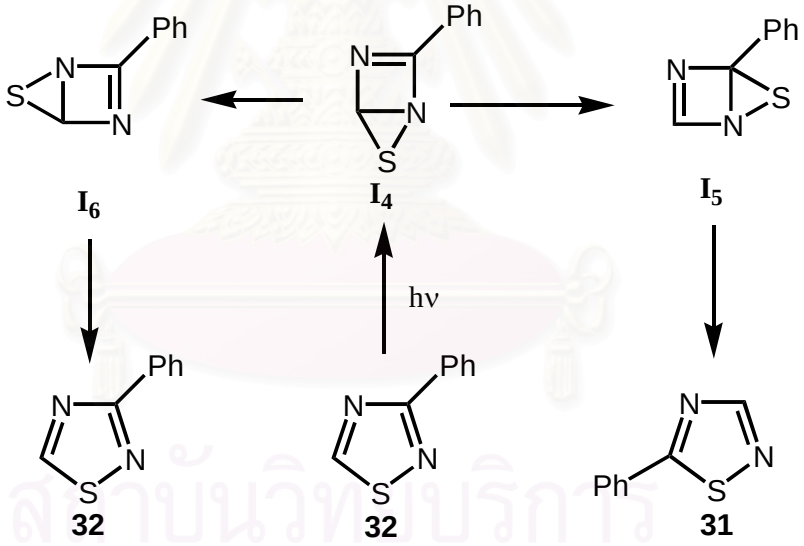


Upon irradiation of **31** in acetonitrile and cyclohexane solvent, the GLC and GC-MS results revealed the formation of **32**, one of the expected photoproducts. No signal indicated the formation of the N2-C3 interchange product **(63)**. The results also indicated the formation of benzonitrile, the photocleavage product, as a major product, phenyl- and diphenyl-sym-triazine **(50** and **51)**, the unusual photo ring-expansion products, and trace amount of 3,5-diphenyl-1,2,4-thiadiazole **(34)**. The formation of **32** from photolysis of **31** could be expected, analogous to the photochemistry of phenylisothiazoles,[6-8] due to the electrocyclic ring closure lead to the formation of the bicyclic intermediate, $\mathbf{I_1}$, which could undergo 1,3-sigmatropic shift of the heteroatom in counter clockwise direction to the more stable bicyclic intermediate, $\mathbf{I_2}$, and rearomatization to the formation of **32** (Scheme 14). 1,3-Sigmatropic shift in an opposite direction would lead to the lees stable bicyclic intermediate, $\mathbf{I_3}$, which, however, rearaomatization of this bicyclic intermediate could lead to the recovering of **31**.



Scheme 14 The proposed mechanism for the formation of **32**.

By analogous to the mechanism shown in Scheme 14, 5-phenyl-1,2,4-thiadiazole **(31)** could also be predicted to observe upon irradiation of 3-phenyl-1,2,4-thiadiazole **(32)** (Scheme 15).

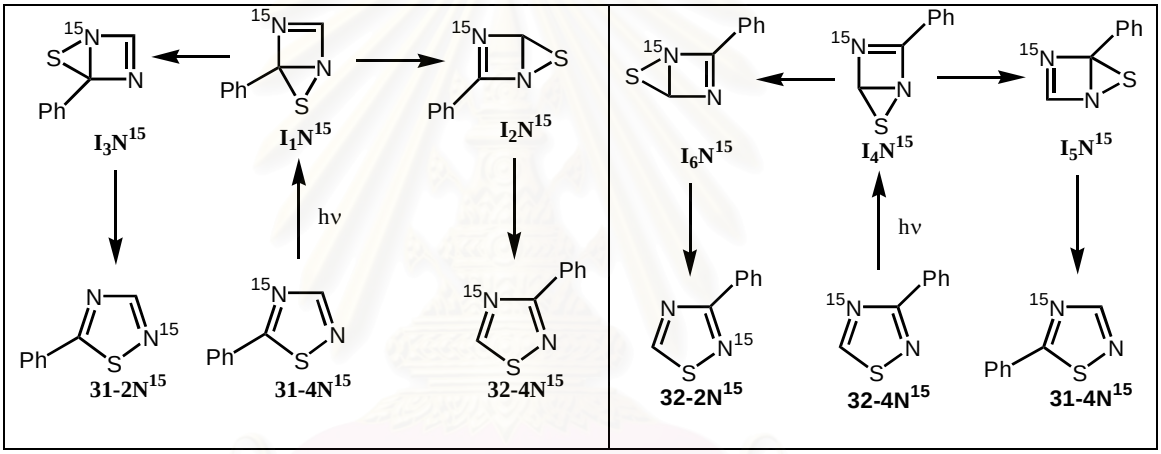


Scheme 15 The predicted mechanism for the formation of **31**.

However, upon irradiation of **32**, benzonitrile **(54)** was identified as the only one major photoproduct in quantitative yield. According to the proposed mechanism shown in Scheme 15, electrocyclic ring closure of **32** would lead to the formation of the bicyclic intermediate, $\mathbf{I_4}$, 1,3-sigmatropic shift of the heteroatom in counter clockwise direction would give the less stable bicyclic intermediate, $\mathbf{I_5}$. Rearomatization, if possible, of this bicyclic intermediate, would lead to the formation of **31**. However, GLC and GC-MS analysis of the reaction solution indicated no

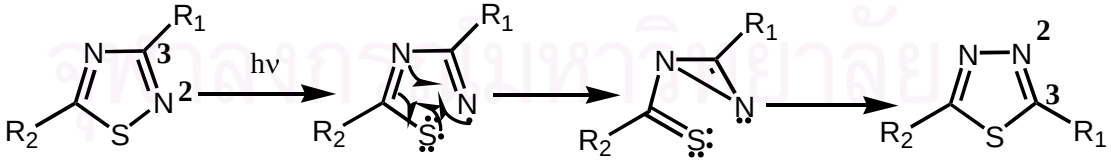
signal of the formation of **31** which these results are consistent with this mechanism revealing no formation of the phototransposition product. The analytical results also indicated no signal of the formation of 3-phenyl-1,3,4-thiadiazole **(64)**, the predicted N2-C3 interchange.

It is of interest to note that this possible mechanism for the formation of the phototransposition product in both **31** and **32** also proposes the recovering of the reactant. But upon this scale of labeling, it is impossible to distinguish between the reactant and recovering reactant formed by this pathway. However, if one of nitrogen atom in **31** or **32** was labeled with ^{15}N, in both mechanisms would reveal the recovering of the starting material with the difference of ^{15}N position from the starting material (Scheme 16).



Scheme 16 The scrambling of ^{15}N-labeling mechanism.

According to the results from photolysis of both **31** and **32**, no signal indicated the formation of the predicted photoproduct by N2-C3 interchange reaction which could be expected to observe as shown in Scheme 17.

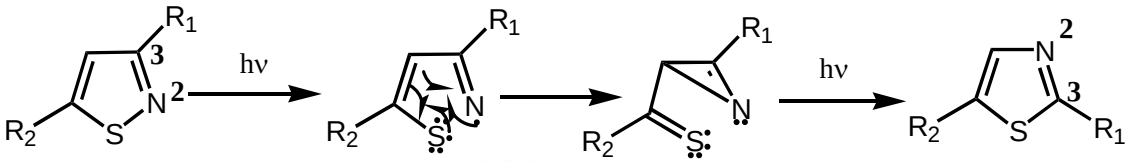


31; R_1 = H, R_2 = Ph

32; R_1 = Ph, R_2 = H

Scheme 17 The predicted photocleavage via N-2 and C-3 interchange mechanism.

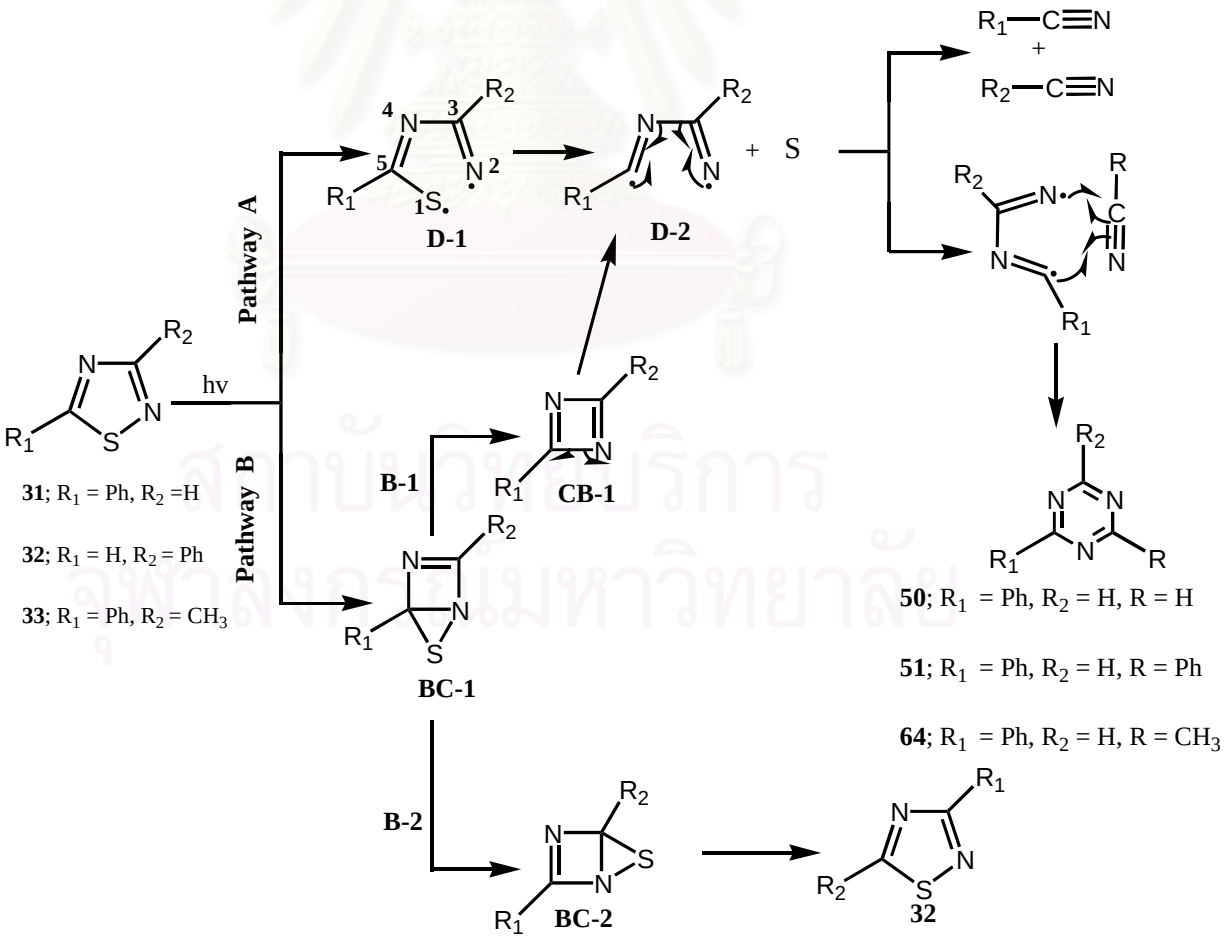
This N2-C3 interchange pathway was reported as a major photochemical pathway in the case of isothiazole. It is thought to involve initial photochemical cleavage of the bond between the two heteroatoms followed by cyclization to a substituted azirine, as shown in Scheme 18.



Scheme 18 The N2-C3 interchange mechanism in isothiazoles.

In the case of 1,2,4-thiadiazoles, bond cleavage and cyclization would result in the very high energy, anti-aromatic diazirine (Scheme 17). Therefore, this pathway may be precluded.

The primary photoreactions which have occurred in this study lead mainly to the formation of **54**, **50** and **51**. The formation of these photoproducts would be explained by mechanistic Scheme 19.

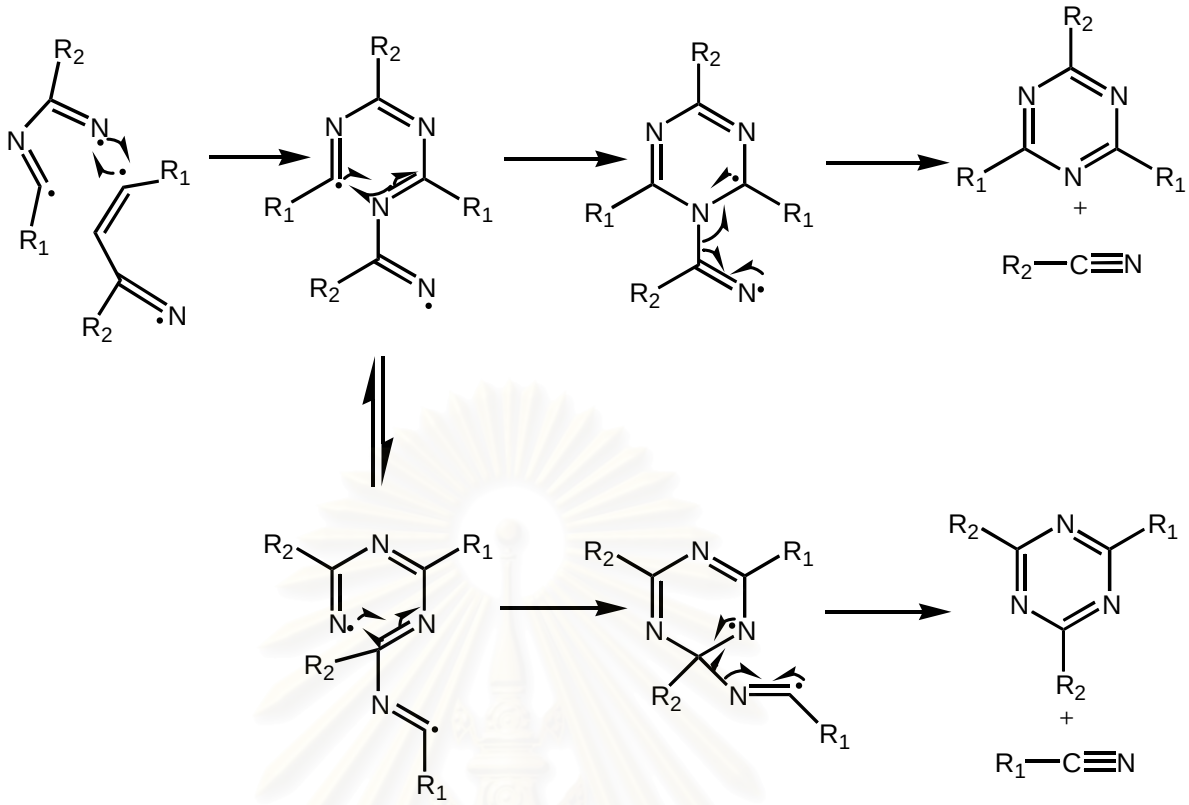


Scheme 19 The proposed mechanism for the formation of **54** and **50** and **51**.

According to this mechanistic scheme (scheme 19), phenyl substituted 1,2,4-thiadiazoles would be expected to undergo two photochemical pathways. In the pathway A, the photo-cleavage of the S-N bond leads to a 1,5-diradical, **D-1**. In the case of isothiazoles, the diradical would undergo cyclization to the formation of azirines but cyclization of **D-1** would lead to the anti-aromatic diazirines as previously discussed in the case of 1,2,4-thiadiazoles. Thus, this **D-1** would eliminate sulfur element to form a 1,4-diradical, **D-2**. The cleavage of **D-2** would result in the formation of nitriles. In this scheme, the formation of triazines is also proposed by the reaction of **D-2** with a nitrile. However, if this mechanistic pathway was possible, phenyl-sym-triazine **(50)**, diphenyl-sym-triazine **(51)** and 2-methyl-4-phenyl-1,3,5-triazine **(64)** would be observed upon irradiation of 5-phenyl-1,2,4-thiadiazole **(31)** in acetonitrile. The phenyl-, methyl-substituted triazine **(64)** could be predicted, according to the pathway A, to observe by trapping of the 1,4-diradical **(D-2)** with acetonitrile (solvent). Although acetonitrile may not be as reactive as benzonitrile in capturing the 1,4-diradical but its presence as the solvent should offset this decreased reactivity. However, the results did not indicate any sign of the formation of this expected triazine. This indicates that a reaction mechanism involving capture of the 1,4-diradical by nitrile in solution is impossible or could at most be very minor pathway for the formation of the observed triazines.

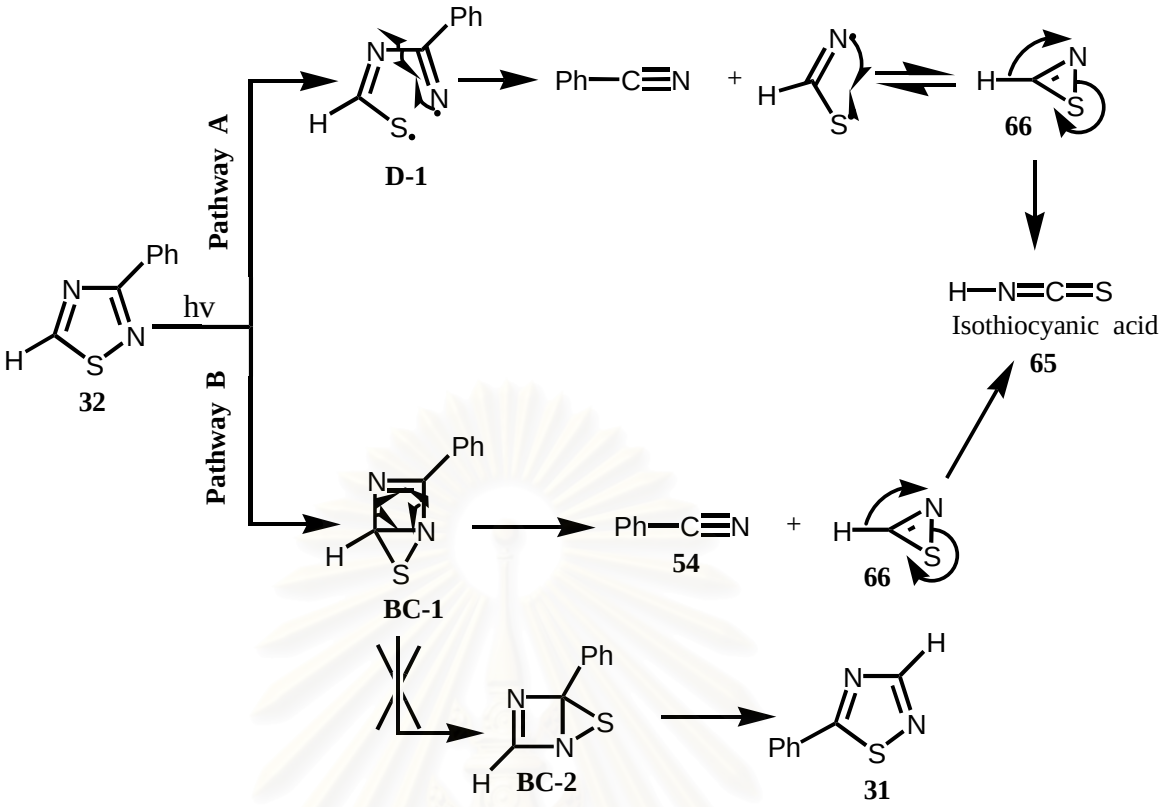
In pathway B, it is likely to occur and it is consistent with the results indicated the formation of **32**, the phototransposition products, upon irradiation of **31** . Although, in the case of 3-phenyl-1,2,4-thiadiazole, the results did not reveal the formation of the phototransposition product which is consistent with the above discussion due to this pathway lead to the less stable bicyclic intermediate.

An alternate mechanism, not involving nitrile trapping, is shown in Scheme 20. Dimerization of the 1,4-diradicals **(D-2)** would result in a conjugated eight-membered chain of alternating carbon and nitrogen atoms. Cyclization followed by elimination of R_1-CN or R_2-CN would account for the formation of both benzonitrile and triazines, which this would also be consistent with the lack of trapping of the 1,4-diradical by acetonitrile.



Scheme 20 The mechanism for the formation of phenyl substituted 1,3,5-triazine.

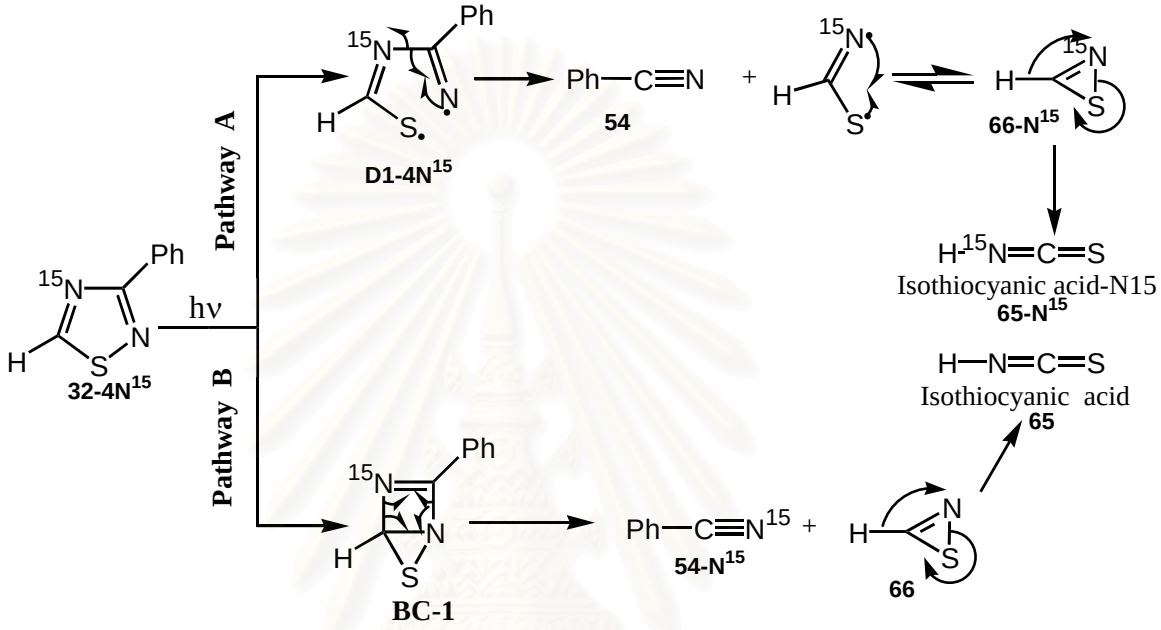
Irradiation of **32** neither gives triazines nor does it gives products as a result of phototransposition, only benzonitrile was capable to be detected upon GLC and GC-MS analysis in quantitative yield. However, benzonitrile can not be the only one photoproduct produced upon irradiation of **32**. Isothiocyanic acid **(65)** would be another spices produced upon irradiation of this thiadiazole as shown in Scheme 21.



Scheme 21 The possible mechanism for the formation of isothiocyanic acid upon irradiation of 3-phenyl-1,2,4-thiadiazole.

3-Phenyl-1,2,4-thiadiazole **(32)** could either undergo the photo-cleavage of the S-N bond lead to 1,5-diradical **(D-1)**. The cleavage of this 1,5-diradical **(D-1)** would result in the formation of benzonitrile and a new 1,3-diradical, which could then cyclize to thiazirine and rearrange to finally give isothiocyanic acid **(65)** as in pathway A. Alternatively, **32** could undergo electrocyclic ring closure to the formation of the bicyclic intermediate, **BC-1**, the cleavage of **BC-1** would result in the formation of **54** and thiazirine **(66)**. Rearrangement of **66** would yield **65** as in pathway B. According to these possible pathways, the formation of **66** is proposed as a transient intermediate for the formation of **65**. Thiazirine **(66)** is an unstable compound but it is a known compound. Therefore, it can serve as a reasonable intermediate for isothiocyanic acid formation. Isothiocyanic acid **(65)** is a known compound, which is a gas at room temperature and is known to undergo polymerization. Thus, this could be consistent with no GLC results supported the formation of isothiocyanic acid **(65)**.

However, determination of the prominent pathway can not again be clear with out the use of nitrogen labeling. For example, if the N-4 nitrogen was labeled and appeared totally in the benzonitrile product, then pathway B would be in operation. Furthermore, if the nitrogen in the benzonitrile product was identified as the labeled and unlabeled nitrogen, then the photochemical of **32** would be concluded to occur in competition between pathway A and B as summarized in Scheme 22.



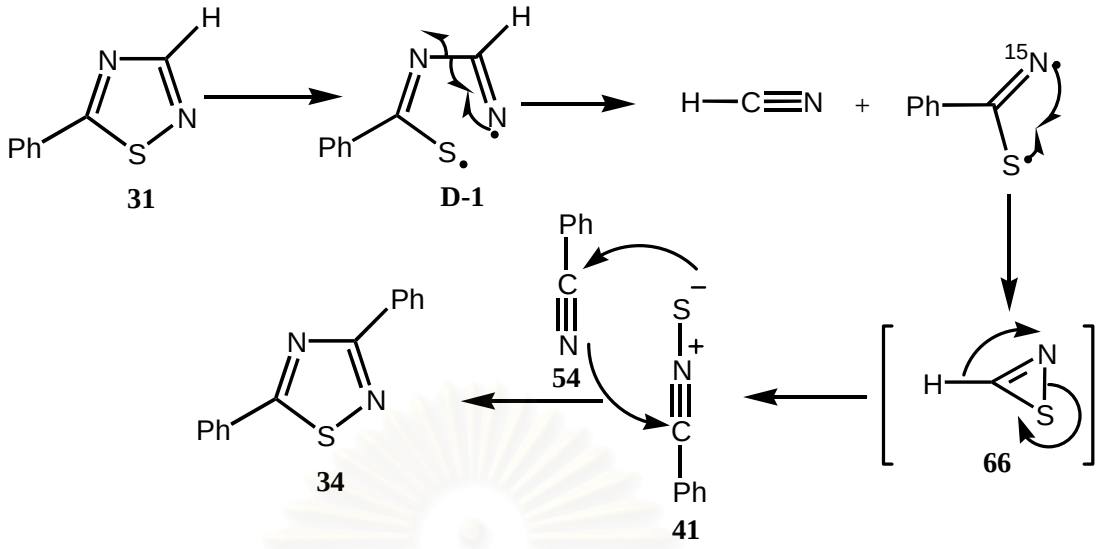
Scheme 22 The possible photochemical pathway of 3-phenyl-1,2,4-thiadiazole-4-^{15}N.

A reasonable explanation as to why irradiation of **32** does not produce the triazines may be argued on the basis of the carbon radical. According to pathway A (Scheme 19), elimination of sulfur element from the 1,5-diradiacl **(D-1)** (R_1 = H, R_2 = Ph) would lead to the 1,4-diradical **(D-2)** with no substitutent at C-5 radical which this would destabilize the 1,4-diradical **(D-2)**. Therefore, the formation of this unsubstituted carbon radical is very unfavorable process and not likely to occur. When compared with **31**, there is phenyl substitutent connected to C-5 to stabilize this 1,4-diradical **(D-2)**.

As previously discussed, in pathway B, the bicyclic **BC-1** would also not undergo 1,3-sigmatropic shift to the less stable bicyclic, **BC-2**. Thus, it would undergo ring-contraction lead to the formation of benzonitrile and thiazirine, which finally would rearrange to isothiocyanic acid.

This work was also extended to study photochemistry of 3-methyl-5-phenyl-1,2,4-thiaidazole **(33)**. This thiadiazole system is a 5-phenyl-1,2,4-thiadiazole analogue. Therefore, the photochemistry of **33** could be predicted in the same manner as **31**. The predicted photoproducts formed upon irradiation of **33** would be benzonitrile **(54)**, 2,4-dimethyl-6-phenyl-1,3-5-triazine **(55)**, 2-methyl-4,6-diphenyl-1,3,5-triazine **(56)**, 5-methyl-3-phenyl-1,2,4-thidiazole **(60)**. The results consistently revealed the formation of all those predicted photoproducts. This result supports the possibility of the proposed mechanism, which is shown in Scheme 19. However, in this experiment, it was accidentally found that the change of solvent from acetonitrile to methanol affected dramatically decrease in the yield of **55** and **56** (Figure 52b,c).

The formation of **34** upon irradiation of **31** could be accounted based on the cleavage of the 1,5-diradical **(D-1)** (Scheme 19). Since cyclization of the 1,5-diradical **(D-1)** would result a diazirine intermediate, which would be a high energy pathway as previously discussed, the experimental results strongly suggested that this 1,5-diradical would eliminate sulfur element to yield a 1,4-diradical. However, from this 1,5-diradical, it could undergo another cleavage pathway to give a 1,3-diradical. This 1,3-diradical could cyclize to the formation of phenyl substituted thiazirine which could eventually rearrange to yield benzonitrile sulfide **(41)**. 1,3-Dipolar cycloaddition reaction of **41** with **54** could yield **34** as a cycloaddition product, shown in Scheme 23.



Scheme 23 The possible formation of 3,5-diphenyl-1,2,4-thiadiazole.

This assumption was confirmed by the trapping experiment of **41**. However, thermally capturing of **41** has been successful in many cases for example in the synthesis of **32** appeared in this thesis, photochemical capturing of **41** has not been reported. Therefore, identification of the formation of **41** upon irradiation of **31** was attempted to capture this dipolar spices by a 1,3-dipolar cycloaddition with a stronger dipolarophile, ethyl cyanoformate **(42)**. The results indicated the formation of the expected cycloaddition product, ethyl 3-phenyl-1,2,4-thiadiazole-5-carboxylate **(43)**. However, the formation of **34** in normal experiment and **43** in trapping experiment were observed in only trace amounts while the fine yellow precipitates, assumed to be sulfur element, were observed in much higher yield compare with the both cycloaddition products. Thus, this implies that the reaction would favor to undergo the elimination of sulfur element from the 1,5-diradical **(D-1)** to yield the more stable 1,4-diradical rather than undergo the cleavage to give the unstable thiazirine **(66)**.

3.4 Future works

By the same cleavage analogy with 5-phenyl-1,2,4-thiadiazole **(31)**, benzonitrile sulfide **(41)** should not be observed upon photolysis of 3-phenyl-1,2,4-thiadiazole **(32)**. However, the trapping experimental results revealed the unexpected formation of the cycloaddition product indicated the formation of benzonitrile sulfide **(41)**. Considering the previous photolysis results of 3-phenyl-1,2,4-thiadiazole **(32)**, this trapping experiment also revealed the results in the same unexpected direction compared with 5-phenyl-1,2,4-thiadiazole **(31)**. This could lead to an assumption that the photochemistry of 3- and 5-phenyl-1,2,4-thiadiazole **(31** and **32)** are absolutely different. Based on the nitrogen scrambling mechanism of 3-phenyl-1,2,4-thiadiazole **(32)** (Scheme 16), the transposition product should not be observed due to formation of a less stable bicyclic intermediate but, however, this mechanism still reveals an intramolecular nitrogen scrambling which could be observed by N-15 labeling (Scheme 16). Consequently, in order to explore more consistent photochemical reaction mechanism of 1,2,4-thiadiazole system, the future work will be conducted on the photochemistry of 3- and 5-phenyl-1,2,4-thiadiazole-^{15}N to determine the primary photochemical pathways of this heterocyclic system. Additionally, permutations of 3,5-diphenyl-1,2,4-thiadiazole **(34)** could be studied by synthesizing 3-(o-methyl)phenyl-5phenyl-1,2,4-thiadiazole and carrying out irradiation experiments to determine the permutation pattern which should be expected by analogous manner of 3- and 5-phenyl-1,2,4-thiadiazole **(31** and **32)**.

CHAPTER 4

CONCLUSION

This photochemistry study of phenyl substituted-1,2,4-thiadiazoles has revealed that the photoreactions of both 3- and 5-phenyl-1,2,4-thiadiazole **(32** and **31)** lead mainly to the formation of benzonitrile **(54)**. However, these substrates did not undergo photochemical reaction in the same direction. Beside benzonitrile **(54)**, irradiation of 5-phenyl-1,2,4-thiadiazole **(31)** also leads to the formation of phototransposition product, 3-phenyl-1,2,4-thiadiazole **(32)** and photofragmentation products, phenyl-sym-triazine and diphenyl-sym-triazine **(50** and **51)**. In contrast, irradiation of 3-phenyl-1,2,4-thiadiazole **(32)** resulted quantitatively in the formation of benzonitrile **(54)**, the only one detectable photoproduct. The possible minor product in this reaction would be isothiocyanic acid **(66)**. There was no signal indicated the formation of the predicted transposition product in the same transposition manner of 5-phenyl-1,2,4-thiadiazole **(31)**.

The formation of those two triazines was proposed via radical dimerization followed by ring closure and subsequent loss of nitriles. The absence of triazines formation in irradiation of 3-phenyl-1,2,4-thiadiazole **(32)** would be expected due to the formation of the unstable 1,4-diradical intermediate. The transposition product upon irradiation of 5-phenyl-1,2,4-thiadiazole **(31)** may achieve via electrocyclic ring closure followed by 1,3-sigmatropic shift of the sulfur atom. When this mechanistic proposal was applied to 3-phenyl-1,2,4-thiadiazole **(32)**, it revealed the formation of an unstable bicyclic intermediate. The unobservable transposition product upon irradiation of 3-phenyl-1,2,4-thiadiazole **(32)** supports this proposed mechanism.

However, it is still early to indicate no transposition in the reaction of 3-phenyl-1,2,4-thiadiazole **(32)** since the mechanistic proposal involved the walk of sulfur atom also proposes the recovering of the reactant. This assumption cannot be clear without the aid of a labeled nitrogen atom.

References.

1. Catteau, J. P.; LaBlache-Combier, A.; Pollet, A. “Photoisomeriazation of Isothiazoles” *J. Chem. Soc., Chem . Commun.* **1969**, 1018.

2. LaBlache-Combier, A.; Pollet, A. “Etudes Photochimiques – XII. Photoreactions Des Methylisothiazoles.” *Tetrahedron* **1972**, *28*, 3141.

3. Wynberg, H.; van Driel, H.; Kellogg, R. M.; Buter, J. “Phototransposition reaction of 2-phenylthiophene” *J. Am. Chem. Soc*. **1967**, *89*, 3487.

4. Riou, C.; Vernin, G.; Dou, H. J. M.; Metzger, J. “Photoisomerization du phenyl-dueterio-5-thiazole et du phenyl-2-methyl-4-thiadiazole” *Bull. Soc. Chim. Fr.* **1972**, 2673.

5. Maeda, M.; Kojima, M. “Mechanism on the Photorearrangements of Phenylthiazoles” *J. Chem. Soc., Perkin Transanction 1* **1978**, 685.

6. Pavlik, J. W.; Tongcharoensirikul, P. “Phototransposition Chemistry of Phenylisothiazoles and Phenylthiazoles. 1. Interconversions in Benzene Solution.” *J. Am. Chem. Soc.* **1994**, *116*, 2292.

7. Pavlik, J. W.; Tongcharoensirikul, P.; French, K. M. “Phototransposition Chemistry of 4-Substituted Isothiazoles. The P_4 Permutation Pathway.” *J. Org. Chem.* **1998**, *63*, 5592.

8. Pavlik, J. W.; Tongcharoensirikul, P. “Photochemistry of 3- and 5-Phenylisothiazoles. Competing Phototransposition Pathways” *J. Org. Chem.* **2000**, *65*, 3626.

9. Buscemi, S.; Cicero, M. G.; Vivona, N. “Heterocyclic Photorearrangements. Photochemical Behavior of Some 3,5-Disubstituted-1,2,4-oxadiazoles in Methanol” *J. Heterocyclic Chem.* **1988**, *25*, 931.

10. Vivona , N. ; Silvestre, B. “Photoinduced Molecular Rearrangements of O-N Bond Containing Five-membered Heterocycles. An Assay for 1,2,4- and 1,2,5-Oxadiazoles.” *Heterocycles* **1995,** *41*, 2095.

11. Caronna, T.; Silvestre, B.; Vivona , N. “A Generalized and Efficient Synthesis of 3-Amino, 3-(*N*-Alkylamino)-, 3-(*N*,*N*-Dialkylamino)-5-alkyl-1,2,4-oxadiazoles by Irradiation of 3-Alkanoylamino-4-phenyl-1,2,5-oxadiazoles (Furazans)” *Synthesis* **1995**, 917.

12. Vivona , N. ; Silvestre, B. “Photoinduced Molecular Rearrangements. The Photochemistry of Some 1,2,4-oxadiazoles in the Presence of Nitrogen Nucleophiles. Formation of 1,2,4-Triazoles, Indazoles, and Benzimidazoles.” *J. Org. Chem.* **1996**, *61*, 8397.

13. Pace, A.; Vivona , N. ; Silvestre, B. “Fluoroheterocycles. A Photochemical Methodology in the Synthesis of 3-Amino- and 3-(*N*-alkylamino)-5-perfluoroalkyl-1,2,4-oxadiazoles” *Tetrahedron Lett.* **2000**, *41*, 7997.

14. Yang-I, L.; Lang, S. A. Jr.; Petty , Sharon R. “New Synthesis of 1,2,4-thiadiazoles.” *J. Org. Chem.* **1980**, *45*, 3750.

15. Howe, Robert K.; Franz, John E. “Nitrile Sulfides. Synthesis of 1,2,4-Thiadiazoles.” *J. Org. Chem.* **1974**, *39* , 962.

16. Schaefer, F.C.; Hechenblkner, I.; Peters, G.A.; Wystrach, V. P. “Synthesis of the *sym*-Triazines System. **I.** Trimerization and Cotrimerization of Amidines.” *J. Am. Chem. Soc.* **1959**, *81*, 1466.

17. Chen, C.; Raymond, D. Jr.; McCarthy, J. R. “A convenient Synthetic Method for Tri-substituted-s-Triazine” *J. Org. Chem.* **1995**, *60*, 8428.

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