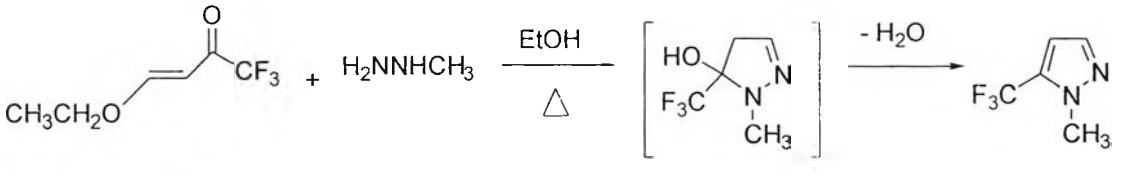
CHAPTER III

RESULTS AND DISCUSSIONS

3.1 Synthesis of photochemical reactants and expected photochemical products

3.1.1 Synthesis of 1-methyl-3-(trifluoromethyl)pyrazole [39], 4,5-dihydro-1-methyl-5-trifluoro-1H-pyrazole [40][9,10], and 1-methyl-5-(trifluoromethyl)pyrazole [42][11]

Braibante, Martins, and colleagues have reported that the reaction of 4-ethoxy-1,1,1-trifluoro-3-buten-2-one **[38]** with methylhydrazine **[41]** in refluxing ethanol leads to the formation of 1-methyl-5-(trifluoromethyl)pyrazole **[42]** in 78% yield.[9] This reaction presumably occurs, as shown in Scheme 3, *via* the intermediacy of

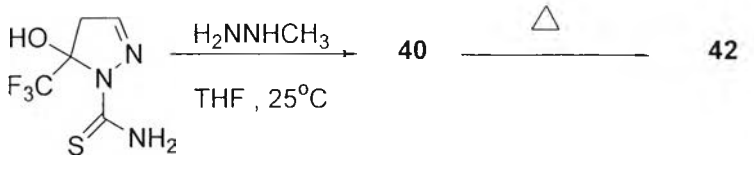


[38] **[41]** **[40]** **[42]**

Scheme 3 Formation of 1-methyl-5-(trifluoromethyl)pyrazole **[42]** from **[38]** and **[41]**

4,5-dihydro-1-methyl-5-(trifluoromethyl)pyrazole-5-ol **[40]**. Although **[40]** was reportedly not an isolable product in this reaction, Bonacorso, Martins, and colleagues subsequently reported (Scheme 4) that **[40]** could be formed in 86% yield by treating the analogous 1-pyrazolethiocaboxamide **[50]** with

methylhydrazine **[41]** in THF at 25 °C.[15] Formed in this way, **[40]** was reported to undergo dehydration when heated to 100-130 °C to provide **[42]** in unspecified yield.



[52]

Scheme 4 Formation of 1-methyl-5-(trifluoromethyl)pyrazole **[42]** from **[52]**

In an attempt to synthesize 1-methyl-5-(trifluoromethyl)pyrazole **[42]** the reaction of **[38]** and **[41]** was repeated but gave substantially different results.[8] After refluxing a solution of **[38]** and **[41]** in absolute ethanol[16] as previously described,[9] tlc examination revealed the formation of two products which could be separated by column chromatography on silica gel, or more readily, by using their greatly different volatilities.

The more volatile component of this mixture was obtained as an oil. Gas liquid partition chromatography (Glpc) of this oil showed a single volatile component. The mass spectrum of this compound (Figure 1) exhibited a molecular ion at m/z 150 as expected for a trifluoromethyl substituted 1-methylpyrazole. The ^{1}H-NMR spectrum of the oil (Figure 2) exhibited a 3H singlet at δ 3.86, a 1H doublet (J = 2.0 Hz) at δ 6.58, and a 1H broad singlet at δ 7.40 also consistent with a mono-substitued-1-methylpyrazole.[18] The ^{13}C-NMR spectrum of this compound (Figure 3) exhibited a singlet at δ 39.9 and a quartet (J = 266.6 Hz) at δ 120.7 due to the *N*-methyl and trifluoromethyl carbons, respectively. In addition, the spectrum also shows signals at δ 104.9, 131.8, and 142.7 for the three carbons of the pyrazole ring. Based on the ^{13}C-NMR spectra of other 1-methylpyrazoles these signals can be assigned to the carbons at ring positions 4, 5, and 3, respectively, since the C-4 carbon of the pyrazole ring absorbs furthest upfield whereas the C-3 carbon is generally observed furthest downfield. Interestingly, it is the signal for the

C-3 carbon at δ 142.7 that appeared as a quartet (J = 38 Hz) due to coupling with the fluorine nuclei of the trifluoromethyl group whereas the signal due to the C-5 carbon at δ 131.8 appeared as a sharp singlet. This shows that the trifluoromethyl substituent is at ring position 3 and identifies this product as 1-methyl-3-(trifluoromethyl)pyrazole **[39]**. Indeed, Bonacorso and colleagues reported that the compound they isolated from the dehydration of 4,5-dihydro-1-methyl-5-(trifluoromethyl)pyrazol-5-ol **[40]** exhibited signals in the ^{13}C-NMR spectrum at δ 107.5 (C-4), 131.9 (C-5), and 138.1 (C-3).[15] In this case, it was the signal at δ 131.9 for C-5 which exhibited the long-range coupling (J = 39 Hz). This confirms that these workers isolated 1-methyl-5-(trifluoromethyl)pyrazole **[42]** from the dehydration of **[40]**.

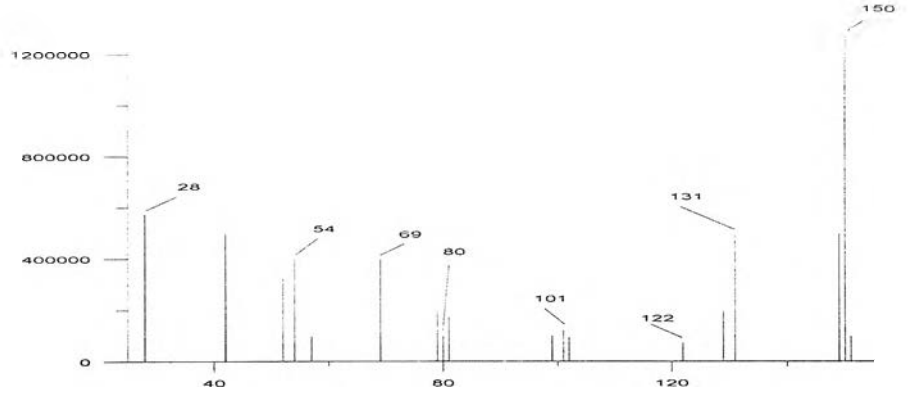


Figure 1 The mass spectrum of more volatile component, 1-methyl-3-(trifluoromethyl)pyrazole **[39]**

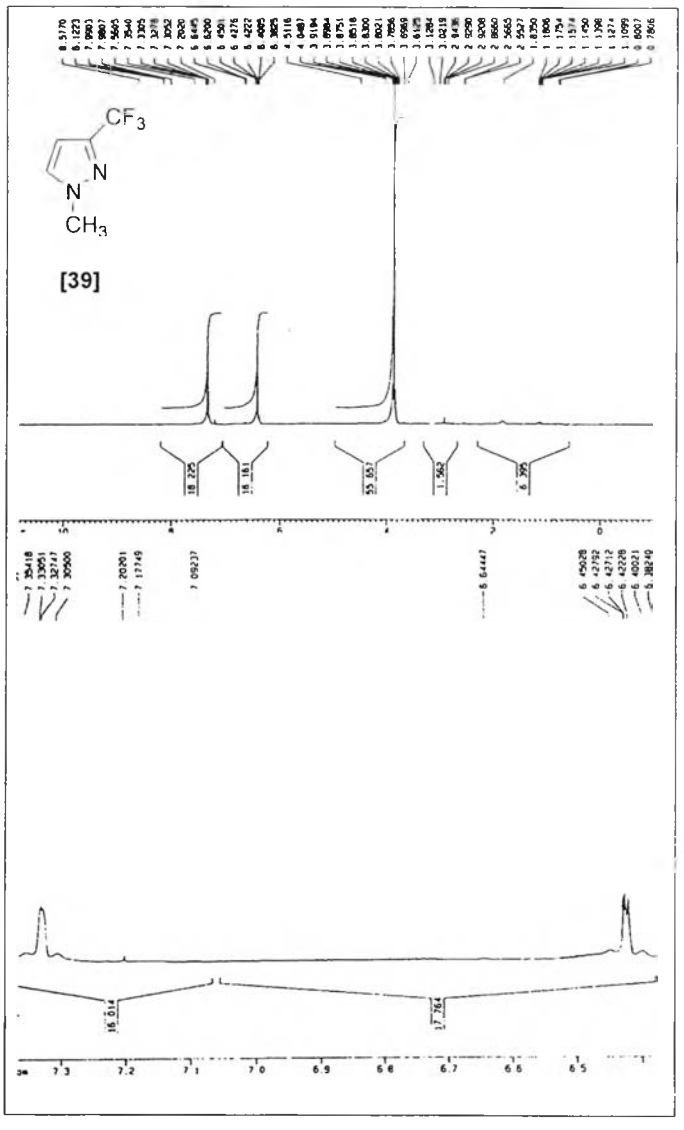


Figure 2 The ^{1}H-NMR spectrum of more volatile component, 1-methyl-3-(trifluoromethyl)pyrazole **[39]**

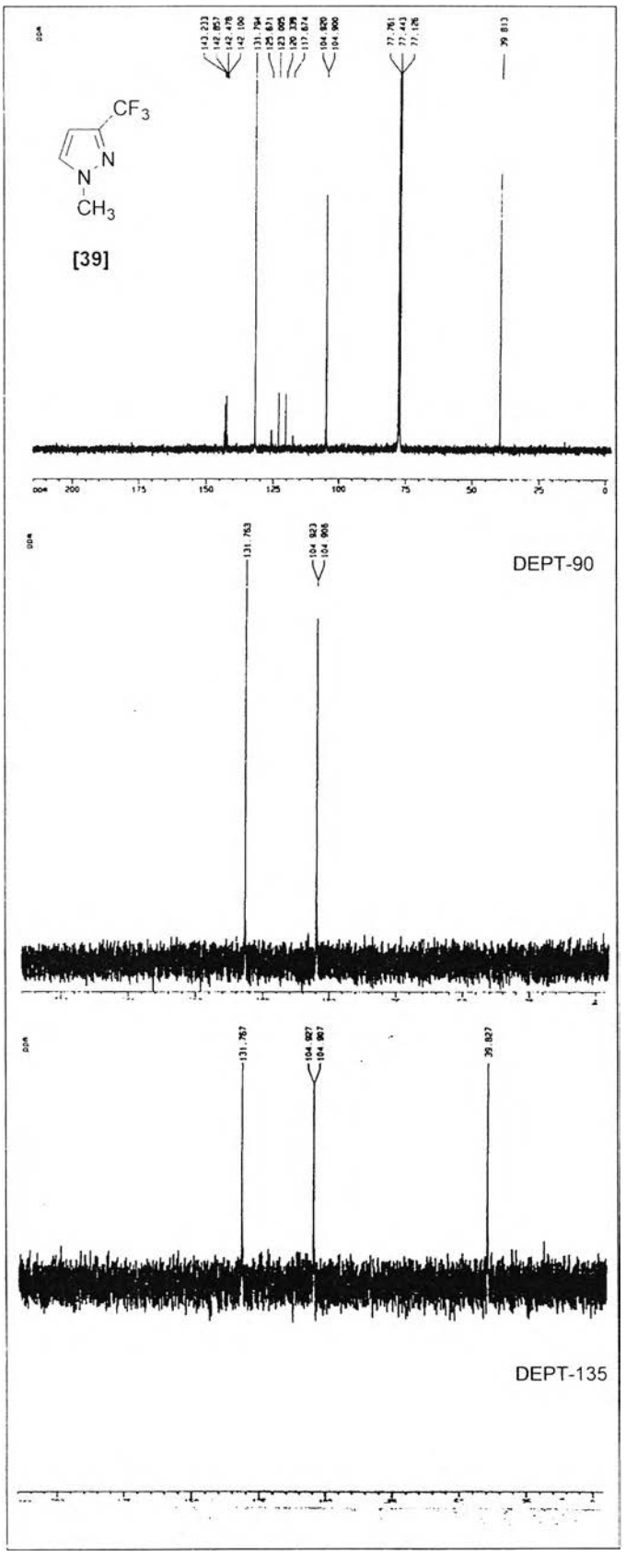


Figure 3 The ^{13}C-NMR spectrum of more volatile component, 1-methyl-3-(trifluoromethyl)pyrazole **[39]**

The less volatile component of the mixture was obtained as a white crystalline compound, which melted at 69-70 °C. Glpc-mass spectroscopic analysis with an oven temperature of 70 °C showed a single volatile compound with a retention time of 14 minutes. The mass spectrum (Figure 4) exhibited a molecular ion at m/z 168, consistent with a hydrated product, and a base peak at m/z 150, which indicates that the major fragmentation pathway involves dehydration. Interestingly, when the analysis was carried out at an oven temperature of 100 °C, Glpc showed that the compound with a retention time 14 minutes was replaced by a single peak with a retention time of 7 minutes. The mass spectrum of this compound (Figure 5) exhibited a molecular ion at m/z 150 with no sign of the signal at m/z 168. This indicates that at the higher oven temperature dehydration occurs in the column and that the hydrated compound never reaches the detector.

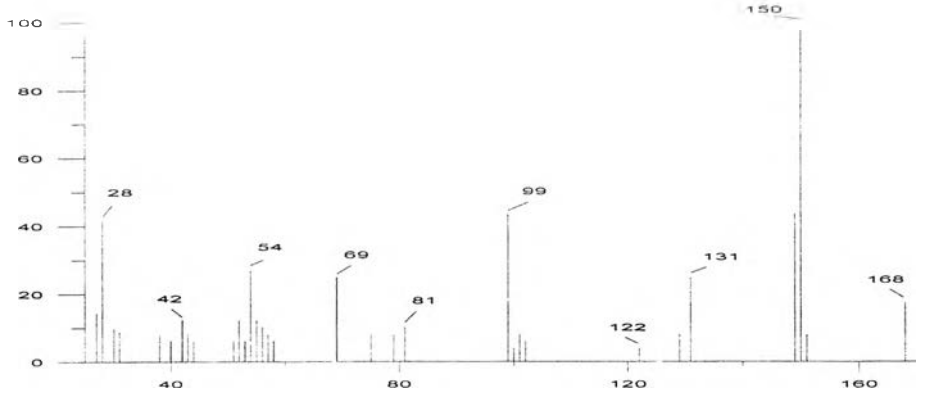


Figure 4 The mass spectrum of non-volatile component with an oven temperature of 70 °C, 4,5-dihydro-1-methyl-5-(trifluoromethyl)pyrazol-5-ol **[40]**

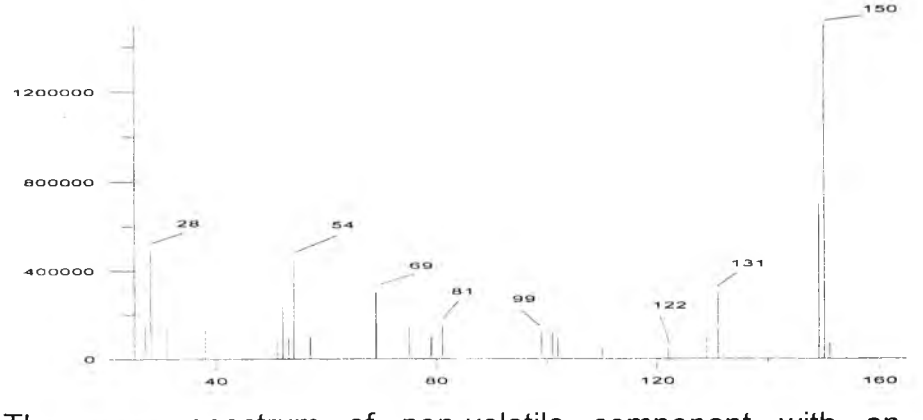


Figure 5 The mass spectrum of non-volatile component with an oven temperature of 100 °C, 1-methyl-5-(trifluoromethyl)pyrazole **[42]**

This data indicates that this product is 4,5-dihydro-1-methyl-5-(trifluoromethyl)pyrazol-5-ol **[40]**.[15] The NMR spectra are consistent with this assignment. Thus, as demanded by the structure, the ^{1}H-NMR spectrum (Figure 6) exhibited a 3H singlet at δ 2.90 for the protons of the *N*-methyl group and a 1H singlet at δ 6.67 due to the imine proton at C-3. In addition, the spectrum exhibited at δ 2.89 (J = 1.3, 18.8 Hz) due to one H-4, which should be coupling with H-3, H-4, and hydroxy proton, and at 3.22 (J = 0.8, 18.8 Hz) due to another H-4, which should be coupling with only H-3 and non-equivalent H-4. The ^{13}C-NMR spectrum (Figure 7) was also consistent with the assigned structure and showed singlet at δ 34.5 due to the N-methyl carbon, at δ 44.9 due to the C-4 ring carbon, and at δ 139.1 due to the C-3 imine carbon. As expected by these assignments only the signal at 44.9 was negative in the DEPT-135 spectrum confirming that this signal is due to a methylene carbon. In addition to these singlet, the ^{13}C-NMR spectrum also exhibited one quartet (J = 282.7 Hz) at δ 124.0 and a second quartet (J = 31.4 Hz) at δ 92.0 due to the trifluoromethyl and C-5 ring carbons respectively.

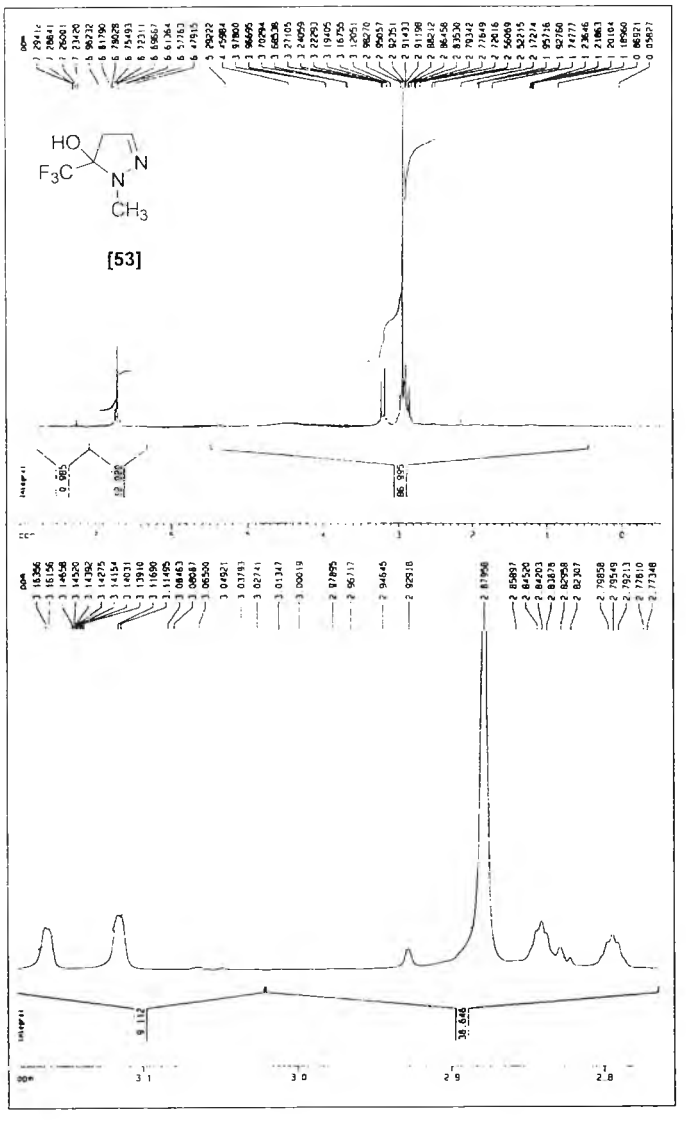


Figure 6 The ^{1}H-NMR spectrum of 4,5-dihydro-1-methyl-5-(trifluoromethyl) pyrazol-5-ol **[40]**

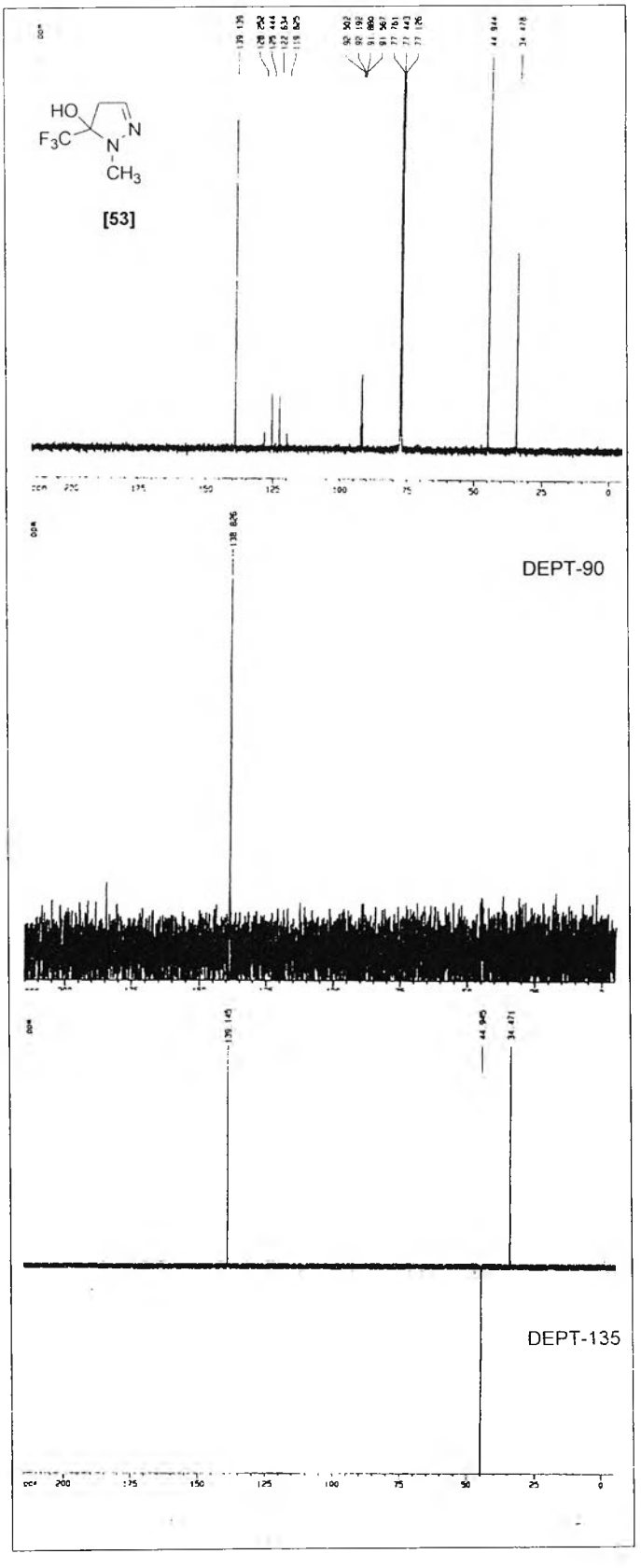


Figure 7 The ^{13}C-NMR spectrum of 4,5-dihydro-1-methyl-5-(trifluoromethyl) pyrazol-5-ol **[40]**

4,5-Dihydro-1-methyl-5-(trifluoromethyl)-1H-pyrazol-5-ol **[40]** was found to undergo smooth dehydration upon treatment with methylene chloride – conc. hydrochloric acid at room temperature.[11] The ^{1}H-NMR spectrum of the resulting oil[19] (Figure 8) exhibited a 3H singlet at δ 3.91 and a 1H doublet (J = 1.2 Hz) at δ 6.52 and a broad 1H singlet at δ 7.39, almost indistinguishable from the ^{1}H-NMR spectrum of 1-methyl-3-(trifluoromethyl)pyrazole **[39]**. The ^{13}C-NMR spectrum (Figure 9), however, clearly shows that this compound is 1-methyl-5-(trifluoromethyl)pyrazole **[42]**. Thus, in addition to singlets at δ 38.3 (N-methyl) and δ 107.9 (C-4 ring carbon) and a quartet (J = 268.3 Hz) at δ 120.5 (trifluoromethyl carbon), the ^{13}C spectrum also showed that the most downfield carbon due to the C-3 ring carbon appeared as a sharp singlet at δ 138.5 while the signal due to the C-5 ring carbon appeared upfield at δ 132.2 as a quartet (J = 39.2 Hz). This confirms that in this product the trifluoromethyl substituent is bonded to the C-5 ring carbon.

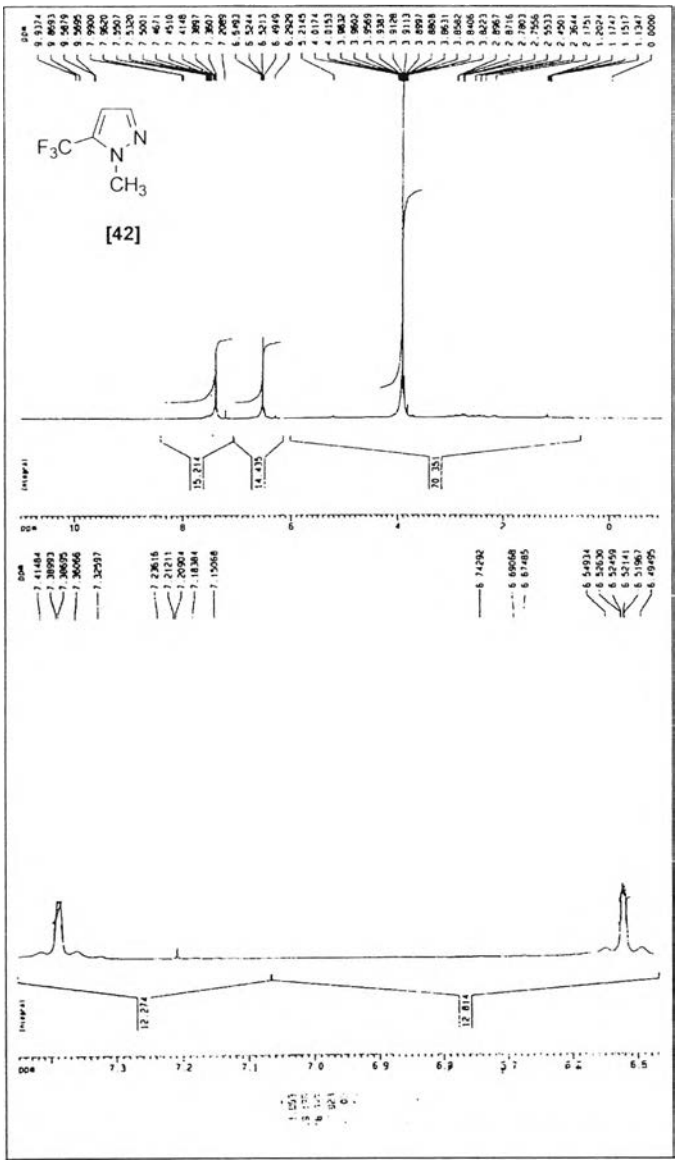


Figure 8 The ^{13}H-NMR spectrum of 1-methyl-5-(trifluoromethyl)pyrazole **[42]**

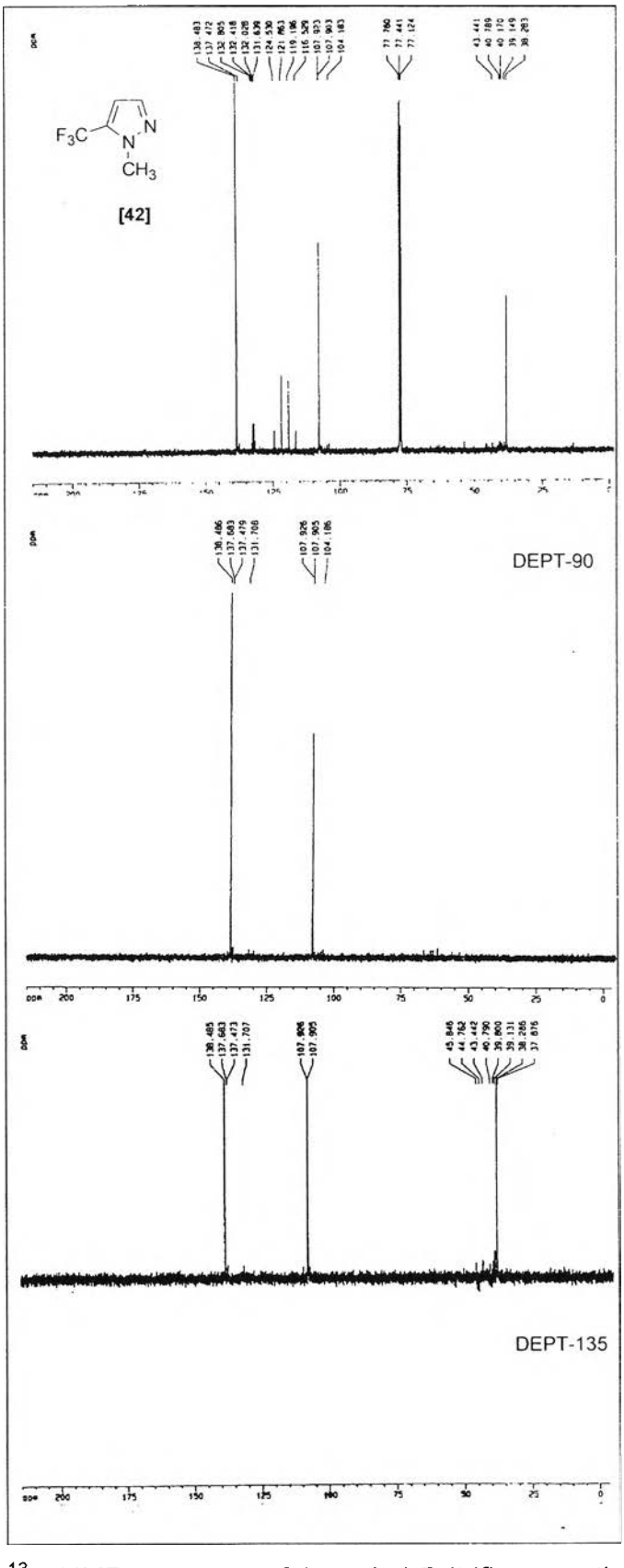
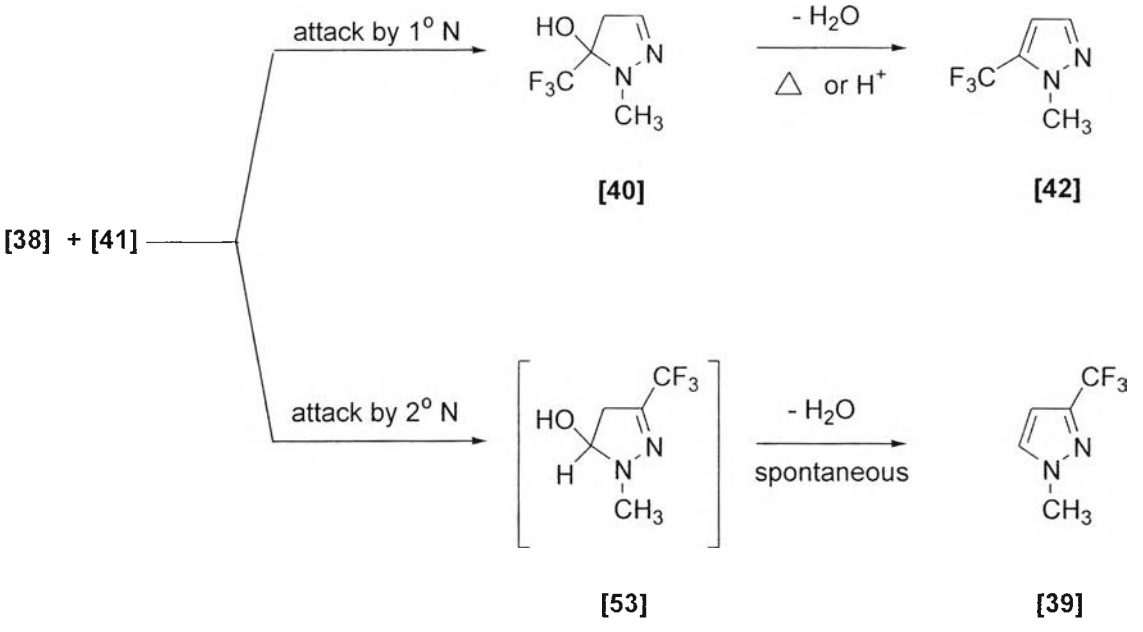


Figure 9 The ^{13}H-NMR spectrum of 1-methyl-5-(trifluoromethyl)pyrazole **[42]**

These results indicate that reaction of vinyl ketone **[38]** with methylhydrazine **[41]** involves a competition of Michael attack by both the primary and secondary nitrogen atoms of **[41]** and a subsequent cyclization, as shown in Scheme 5, to 4,5-dihydro-1-methyl-5-(trifluoromethyl)pyrazol-5-ol **[40]** and 4,5-dihydro-1-methyl-3-

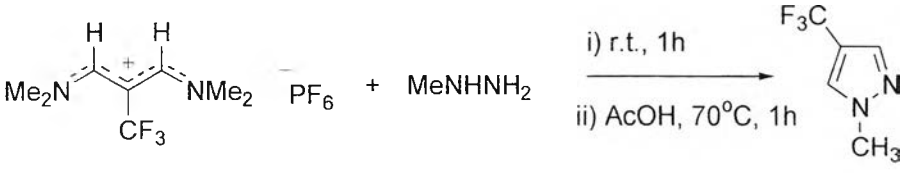


Scheme 5 Reaction of 4-ethoxy-1,1,1-trifluoro-3-buten-2-one **[38]** with methylhydrazine **[41]**

(trifluoromethyl)pyrazol-5-ol **[53]**. Dehydration of either **[40]** or **[53]** would be accompanied by development of positive charge at C-5 of the dihydropyrazole ring. In both **[40]** and **[53]** this positive charge would be stabilized by resonance interaction with the adjacent non-bonded electrons on nitrogen. In the case of **[40]**, however, the charge would be significantly destabilized by the trifluoromethyl group at C-5. This destabilization would increase the energy barrier to dehydration. As a result, **[40]** is sufficiently stable to allow its isolation. In contrast, the trifluoromethyl group at position 3 is expected to have little effect on the developing positive charge at C-5 in **[53]**, which therefore is not isolated but undergoes spontaneous dehydration to pyrazole **[39]**.

3.1.2 Synthesis of 1-methyl-4-(trifluoromethyl)pyrazole [43][12]

1-Methyl-4-(trifluoromethyl)pyrazole **[43]** was carried out according to the earlier procedure by Yamanaka, Takekawa, Morita, and Ishihara.[12]



[44] **[41]** **[43]**

Scheme 6 Reaction of 1,1,5,5-tetramethyl-1,5-diaza-3-(trifluoromethyl)-1,3-pentadienium hexafluorophosphate **[44]** with methylhydrazine **[41]**

The mass spectrum of 1-methyl-4-(trifluoromethyl)pyrazole **[43]** (Figure 10) exhibited a molecular ion at m/z 150 as expected for a trifluoromethyl substituted 1-methylpyrazole. The ^{1}H-NMR spectrum (Figure 11) exhibited singlets at δ 3.87 due to the protons of the N-methyl group and at δ 7.58 due to the proton at C-5, and at δ 7.61 due to the proton at C-3. The ^{13}C-NMR spectrum (Figure 12) shows singlets at δ 37.5 (N-methyl) and δ 127.4 (C-5 ring carbon) and a quartet (J = 266 Hz) at δ 120.7 (trifluoromethyl carbon). The ^{13}C spectrum also showed that the most downfield carbon due to the C-3 ring carbon appeared as a sharp singlet at δ 135.1 while the signal due to the C-4 ring carbon appeared upfield at δ 111.8 as a quartet (J = 38 Hz). This confirms that in this product the trifluoromethyl substituent is bonded to the C-4 ring carbon.

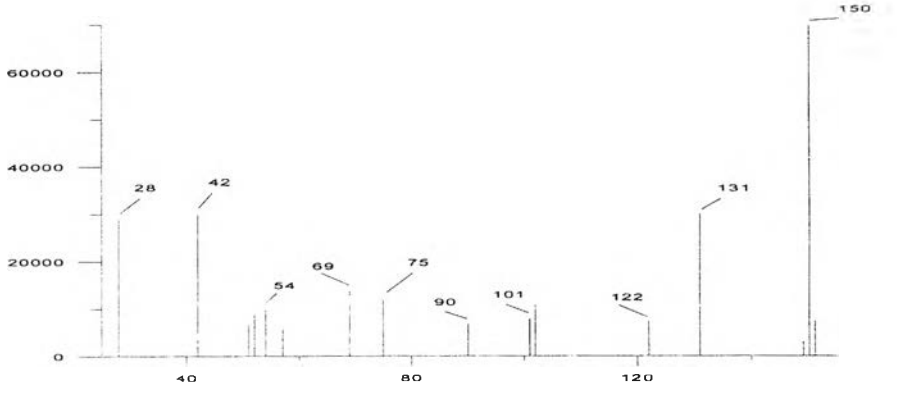


Figure 10 The mass spectrum of 1-methyl-4-(trifluoromethyl)pyrazole **[43]**

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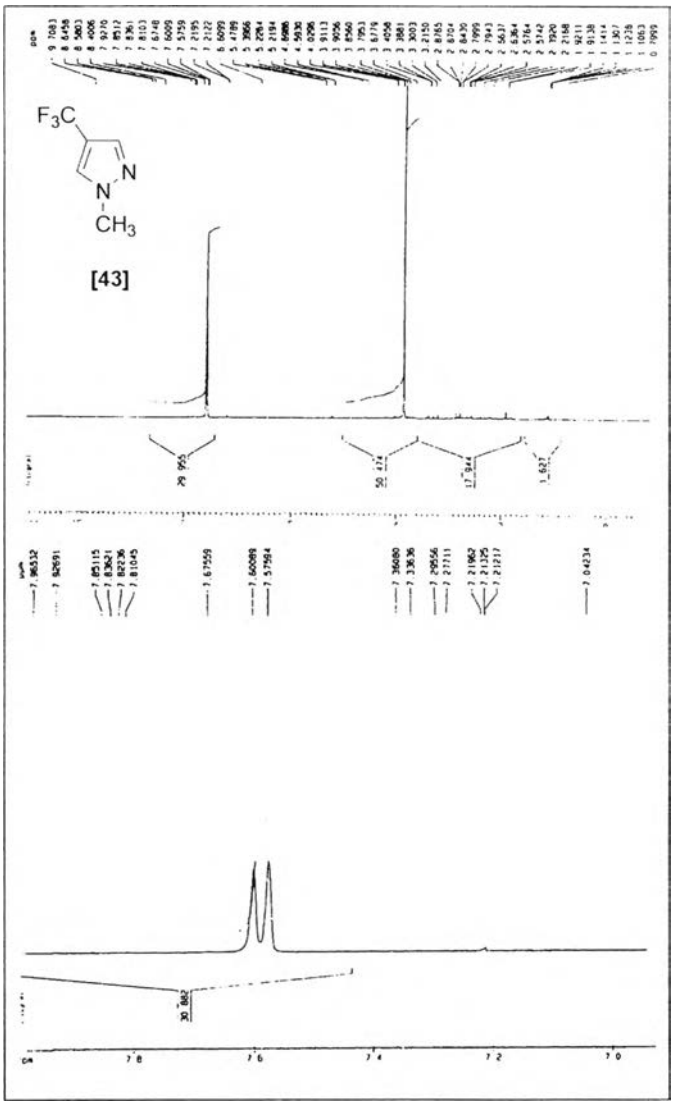


Figure 11 The ^{1}H-NMR spectrum of 1-methyl-4-(trifluoromethyl)pyrazole **[43]**

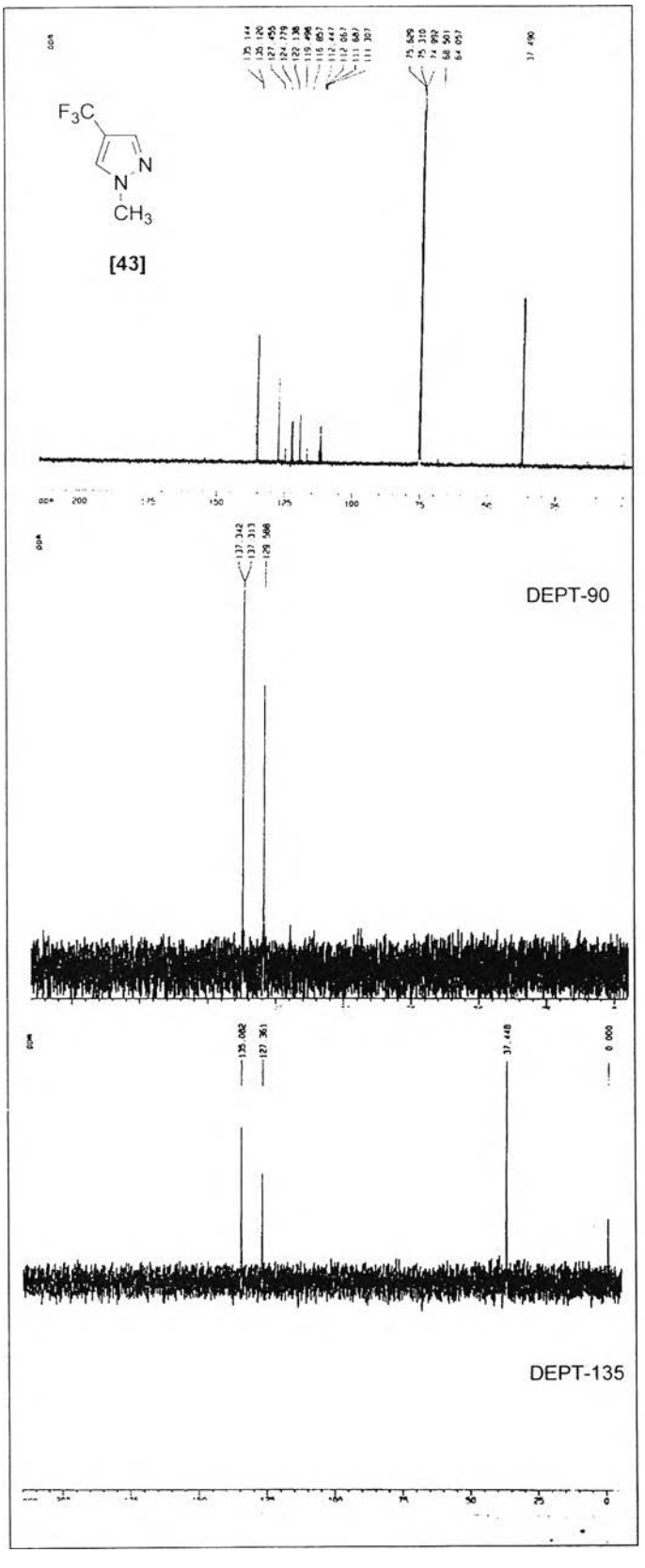
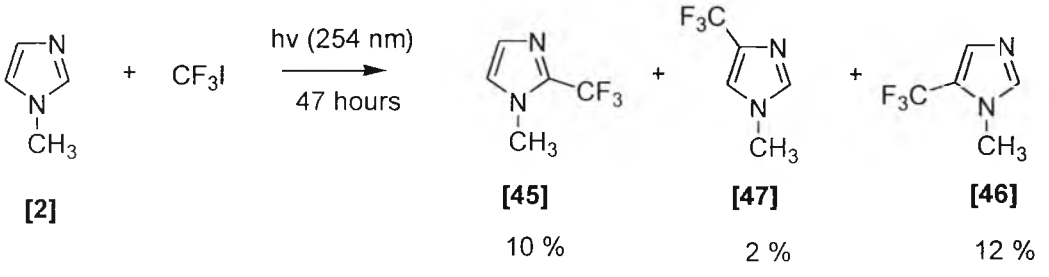


Figure 12 The ^{13}C-NMR spectrum of 1-methyl-4-(trifluoromethyl)pyrazole **[43]**

3.1.3 Synthesis of 1-methyl-2-(trifluoromethyl)imidazole [45], 1-methyl-4-(trifluoromethyl)imidazole [47], and 1-methyl-5-(trifluoromethyl)imidazole [46][13]

The synthesis of trifluoromethyl substituted imidazoles **[45-47]** was carried out according to the earlier procedure by Kimoto, Fujii, and Cohen.[13] This method involved the photochemical trifluoromethylation of 1-methylimidazole **[2]** using trifluoromethyliodide.



[2] **[45]** 10 % **[47]** 2 % **[46]** 12 %

Scheme 7 Trifluoromethylation of 1-methylimidazole **[2]**

After irradiation of a solution of 1-methylimidazole **[2]** and trifluoromethyliodide in methanol at 254 nm for 47 hours, the reaction mixture was analyzed by GC2, a Perkin Elmer Autosystem (9000) equipped with 15m x 0.53mm 50% phenyl silicone phase capillary column oven temperature 70 °C. The analysis showed that the solution contained at least three compounds at retention times of 6.3, 19.0, and 35.7 minutes. The peak at retention time 19.0 was due to 1-methylimidazole by comparison with authentic compound. The other two peaks should be trifluoromethyl substituted products **[45-47]**. The crude products were purified by flash column chromatography on siliga gel, eluting with 10% ethyl acetate in hexane, and collecting 15 ml fractions. Glpc and tlc analysis showed that fractions 17-25 contained the same compounds and that fractions 33-42 also contained the same compounds. The ^{1}H-NMR spectrum of the residue obtained from fractions 17-25 (Figure 13) exhibited a 3H singlet at δ 3.72, a 1H singlet at δ 6.91, and a 1H singlet at δ 6.99 consistent with mono-substitued-1-methylimidazole **[45]**. The ^{13}C-NMR spectrum of this compound (Figure 14) exhibited a singlet at δ 32.7 and a quartet (J = 269 Hz) at δ 118.1 due to the N-methyl and trifluoromethyl carbons, respectively. In addition, the spectrum also shows signals at δ 123.8,

127.3, and 134.7 for the three carbons of the imidazole ring. Based on the ^{13}C-NMR spectra of other 1-methylimidazoles these signals can be assigned to the carbons at ring positions 5, 4, and 2 respectively since the C-2 carbon of the imidazole ring absorbs furthest downfield whereas the C-5 carbon is generally observed furthest upfield. Interestingly, it is the signal for the C-2 carbon at δ 134.7 that appeared as a quartet (J = 39 Hz) due to long-range coupling with the fluorine nuclei of the trifluoromethyl group whereas the signals due to the C-4 and C-5 carbons at δ 127.3 and 123.8 respectively both appeared as sharp singlets. This shows that the trifluoromethyl substituent is at ring position 2 and identifies this product as 1-methyl-2-(trifluoromethyl)imidazole **[45]**. GC analysis shows that this fraction contains only one compound appearing at retention time of 6.3 minute. For fractions 33-42, analysis trace showed that these combined fractions contain two products at retention time 6.3 and 35.7 minutes. Since, these products could not be separated by column chromatography, the residue from these combined fractions were connected to a vacuum line and pumped down to 0.1-1.0 Torr. The effluent from the flask containing the residue was passed through a glass trap submerged in a dry ice-acetone bath. GC analysis of the volatile fraction showed that it contained two products, which appeared at retention times 6.3 (major) and 35.7 (minor). The mixture was kept in the freezer until a precipitate appeared. The precipitate was collected by filtration. The precipitate was then washed with cold hexane, giving the product as a white solid. The ^{1}H-NMR spectrum of the precipitate (Figure 15) exhibited a 3H singlet at δ 3.70, a 1H singlet at δ 7.36, and a 1H singlet at δ 7.46 consistent with mono-substituted-1-methylimidazole **[46]**. The ^{13}C-NMR spectrum of this compound (Figure 16) exhibited a singlet at δ 32.7 and a quartet (J = 266 Hz) at δ 121.2 due to the N-methyl and trifluoromethyl carbons, respectively. In addition, the spectrum also shows signals at δ 122.1, 131.7, and 141.6 for the three carbons of the imidazole ring. Interestingly, it is the signal for the C-5 carbon at δ 122.1 that appeared as a quartet (J = 40 Hz) due to long-range coupling with the fluorine nuclei of the trifluoromethyl group whereas the signals due to the C-4 and C-2 carbons at δ 131.7 and 141.6 respectively both appeared as sharp singlets. This shows that the trifluoromethyl substituent is at ring position 5 and identifies this product as 1-methyl-5-(trifluoromethyl)imidazole **[46]**. GC analysis shows that this precipitate contains only one product with a retention time

6.3 minute. The ^{1}H-NMR spectrum of the non-volatile fraction (Figure 17) exhibited a 3H singlet at δ 3.67, a 1H singlet at δ 7.16, and a 1H singlet at δ 7.40 consistent with a mono-substitued-1-methylimidazole **[47]**. The ^{13}C-NMR spectrum of this compound (Figure 18) exhibited a singlet at δ 34.1 and a quartet (J = 267 Hz) at δ 121.9 due to the N-methyl and trifluoromethyl carbons, respectively. In addition, the spectrum also shows signals at δ 120.4, 123.1, and 139.6 for the three carbons of the imidazole ring. Interestingly, it is the signal for the C-4 carbon at δ 123.1 that appeared as a quartet (J = 39 Hz) due to long-range coupling with the fluorine nuclei of the trifluoromethyl group whereas the signals due to the C-5 and C-2 carbons at δ 120.4 and 139.6 respectively both appeared as sharp singlets. This shows that the trifluoromethyl substituent is at ring position 4 and identifies this product as 1-methyl-4-(trifluoromethyl)imidazole **[47]**. GC analysis shows that this material contains only one product with a retention time 35.7 minute. The mass spectra of each of three compounds exhibit (Figures 14,16, and 18) a molecular ion at m/z 131, as expected for a trifluoromethyl substituted 1-methylimidazole, and a major fragment peak at m/z 131 due to loss a fluorine atom.

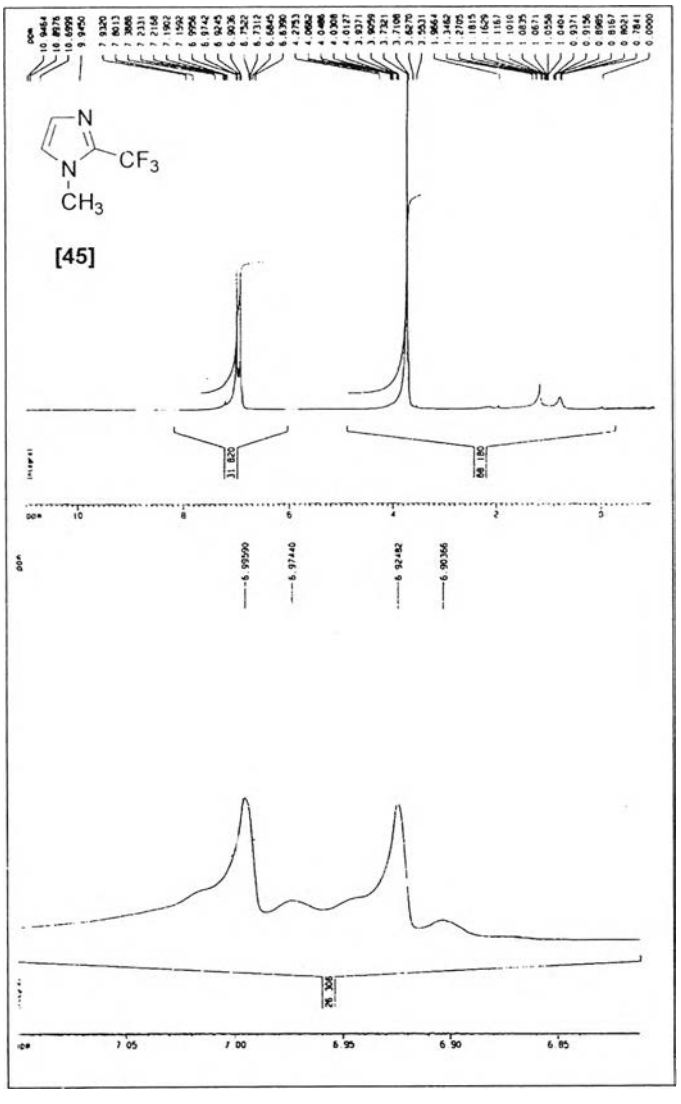


Figure 13a The ^{1}H-NMR spectrum of 1-methyl-2-(trifluoromethyl)imidazole **[45]**

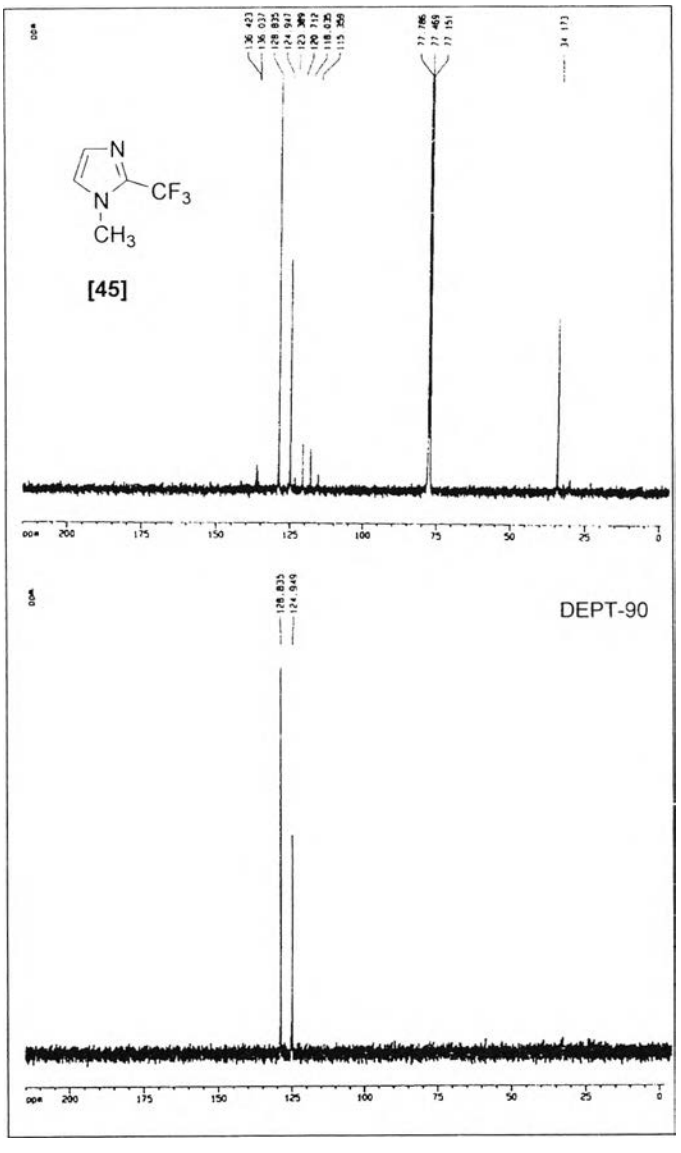


Figure 13b The ^{13}C-NMR spectrum of 1-methyl-2-(trifluoromethyl)imidazole **[45]**

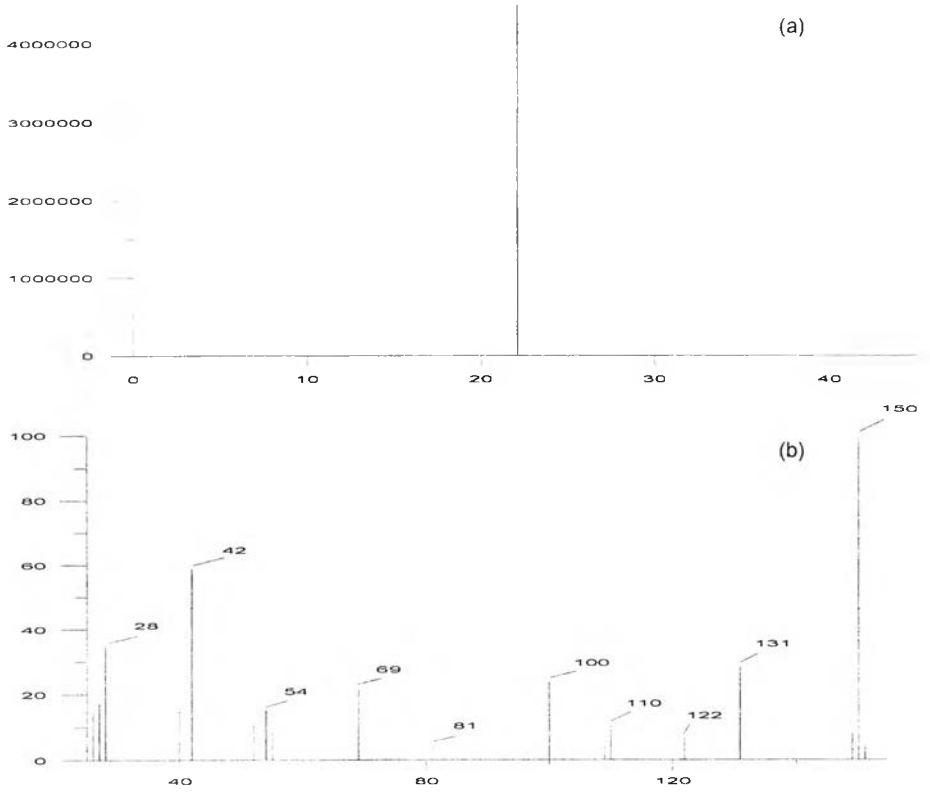


Figure 14 The GC-MS analysis of 1-methyl-2-(trifluoromethyl)imidazole **[45]** (a) GC analysis (b) mass spectrum

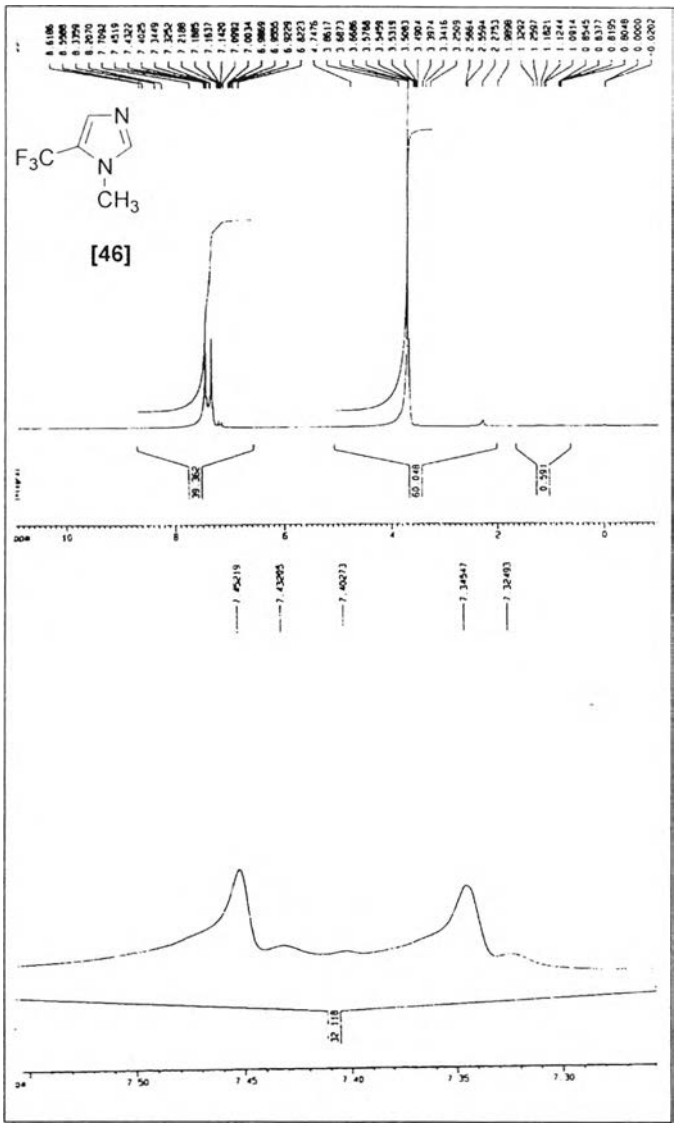


Figure 15a The ^{1}H-NMR spectrum of 1-methyl-5-(trifluoromethyl)imidazole **[46]**

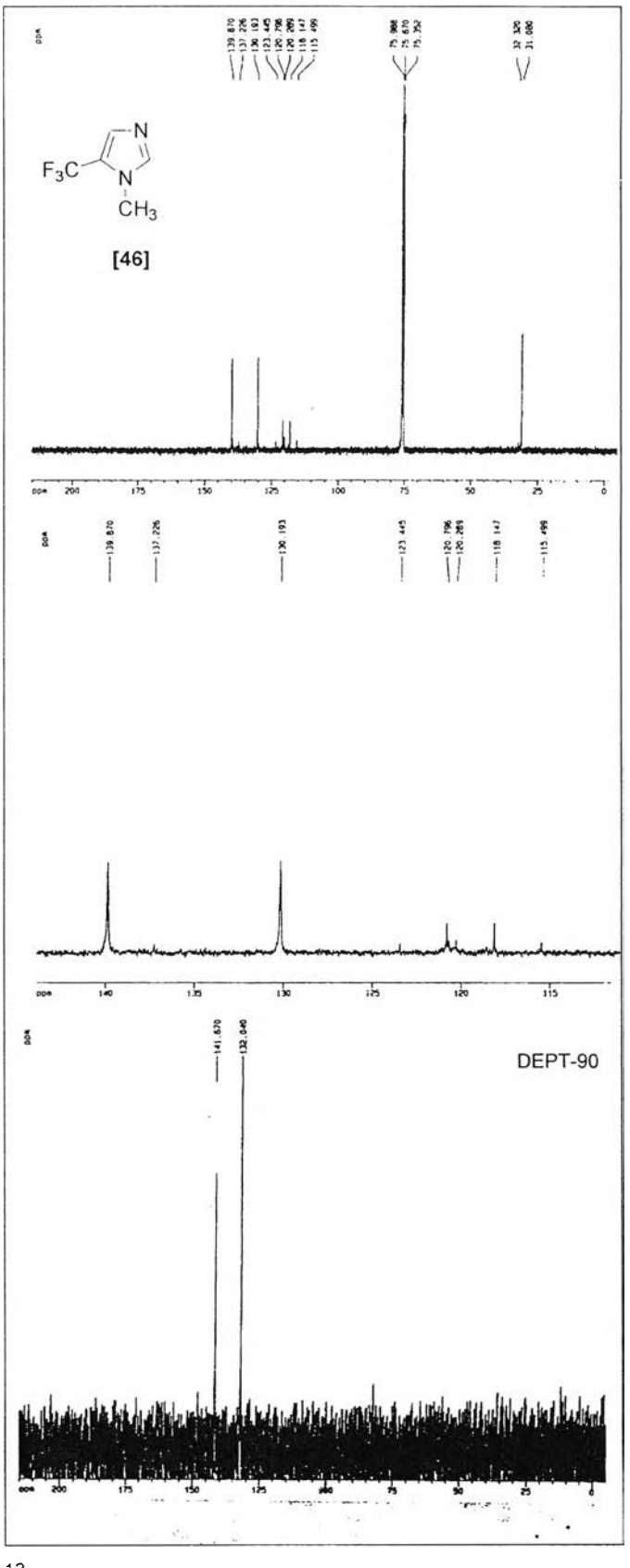


Figure 15b The ^{13}C-NMR spectrum of 1-methyl-5-(trifluoromethyl)imidazole **[46]**

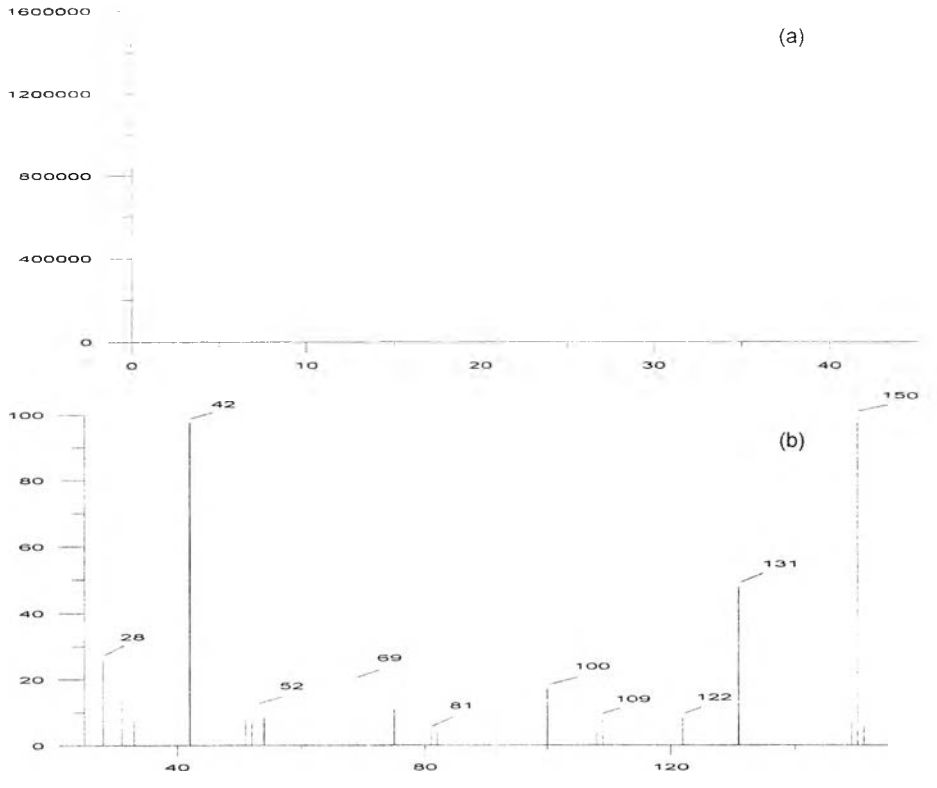


Figure 16 The GC-MS analysis (a) GC analysis of 1-methyl-5-(trifluoromethyl) imidazole **[46]** (b) mass spectrum of 1-methyl-5-(trifluoromethyl) imidazole **[46]**

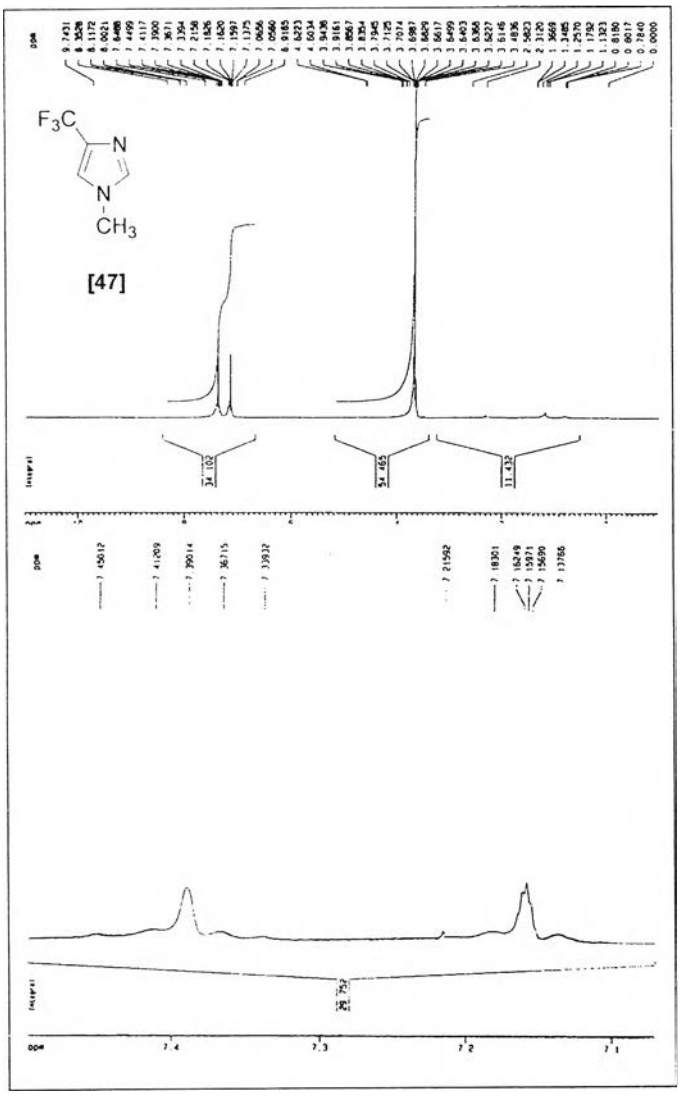


Figure 17a The ^{1}H-NMR spectrum of 1-methyl-4-(trifluoromethyl)imidazole **[47]**

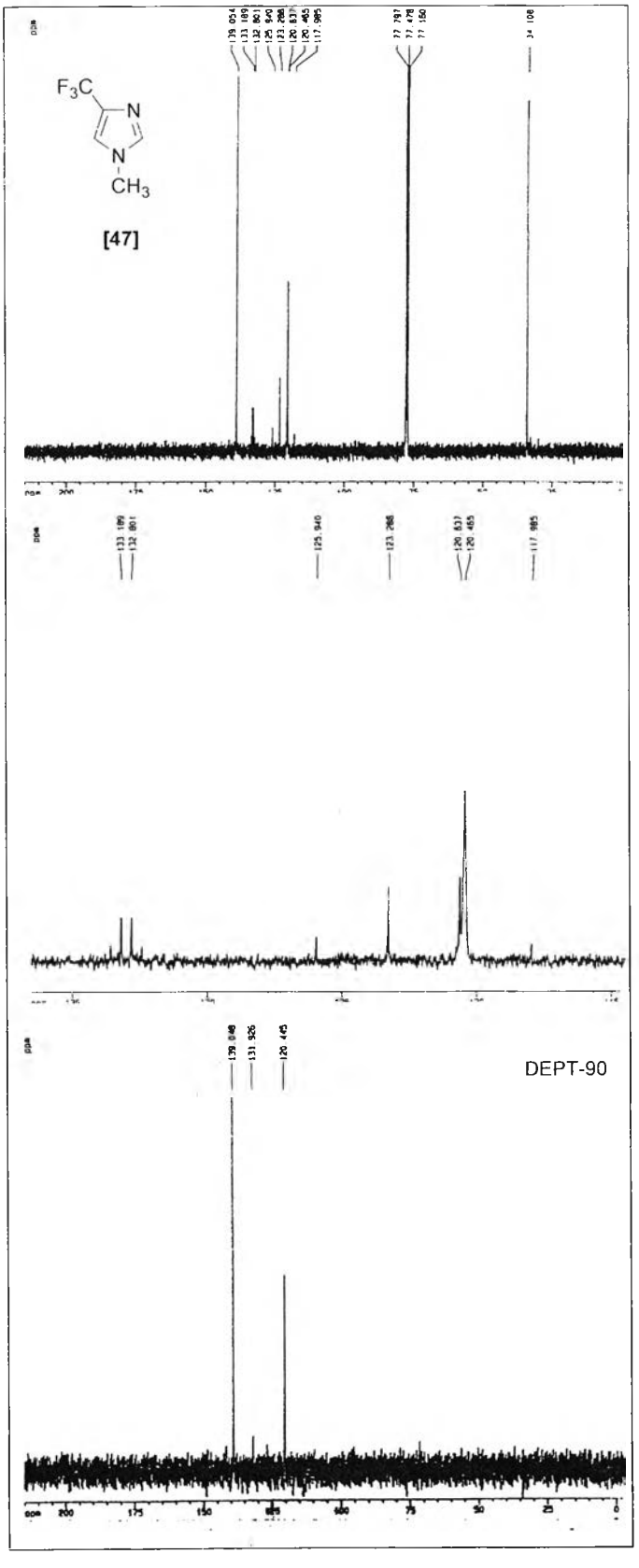


Figure 17b The ^{13}C-NMR spectrum of 1-methyl-4-(trifluoromethyl)imidazole **[47]**

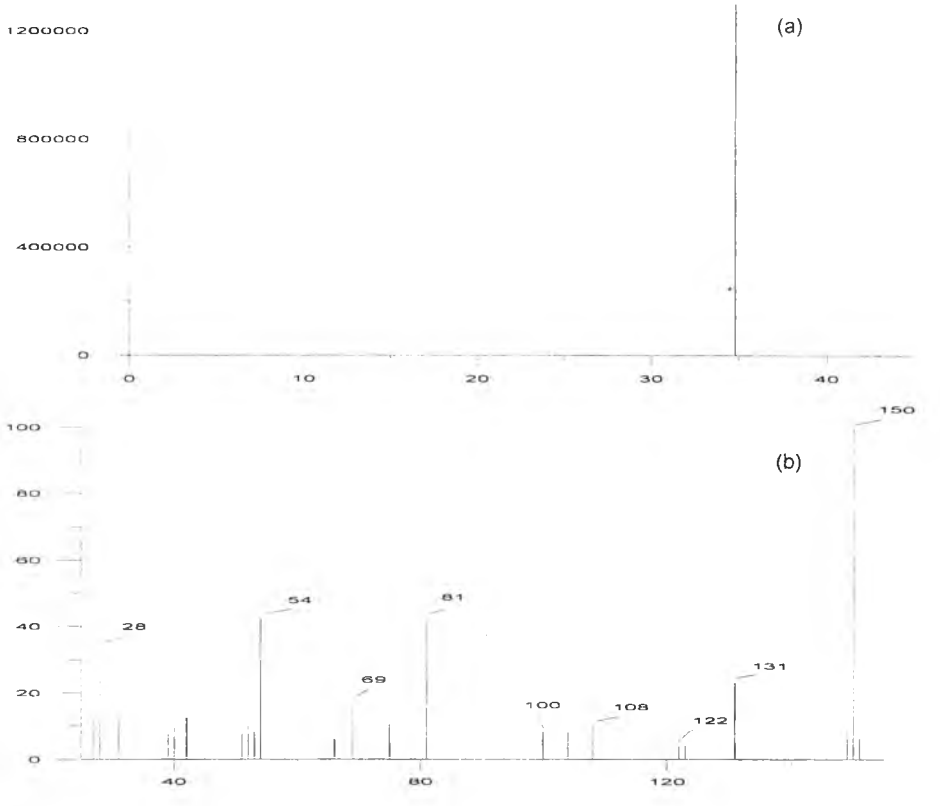


Figure 18 The GC-MS analysis of 1-methyl-4-(trifluoromethyl)imidazole **[47]** (a) GC analysis (b) mass spectrum

3.2 Photoreaction of 1-methyl-3-(trifluoromethyl)pyrazole

3.2.1 UV-Absorption analysis of 1-methyl-3-(trifluoromethyl)pyrazole [39].

The UV absorption spectra of 1-methyl-3-(trifluoromethyl)pyrazole **[39]** was recorded in acetonitrile or methanol solvent at concentrations of $5x10^{-4}$ M, $4x10^{-4}$ M, $3x10^{-4}$ M, $2x10^{-4}$ M, and $1x10^{-4}$ M. The spectra, as shown in figure 19, displayed an absorption maximum at 215 nm with an extinction coefficient, ϵ, of 3267 $M^{-1}cm^{-1}$. Because of this absorption maximum at 215 nm it was necessary to irradiate this compound with a 450 W medium pressure Hg lamp which has output at that wavelength. Other low pressure lamps have outputs at 254 nm, 300 nm, and 360 nm but no output at 215 nm.

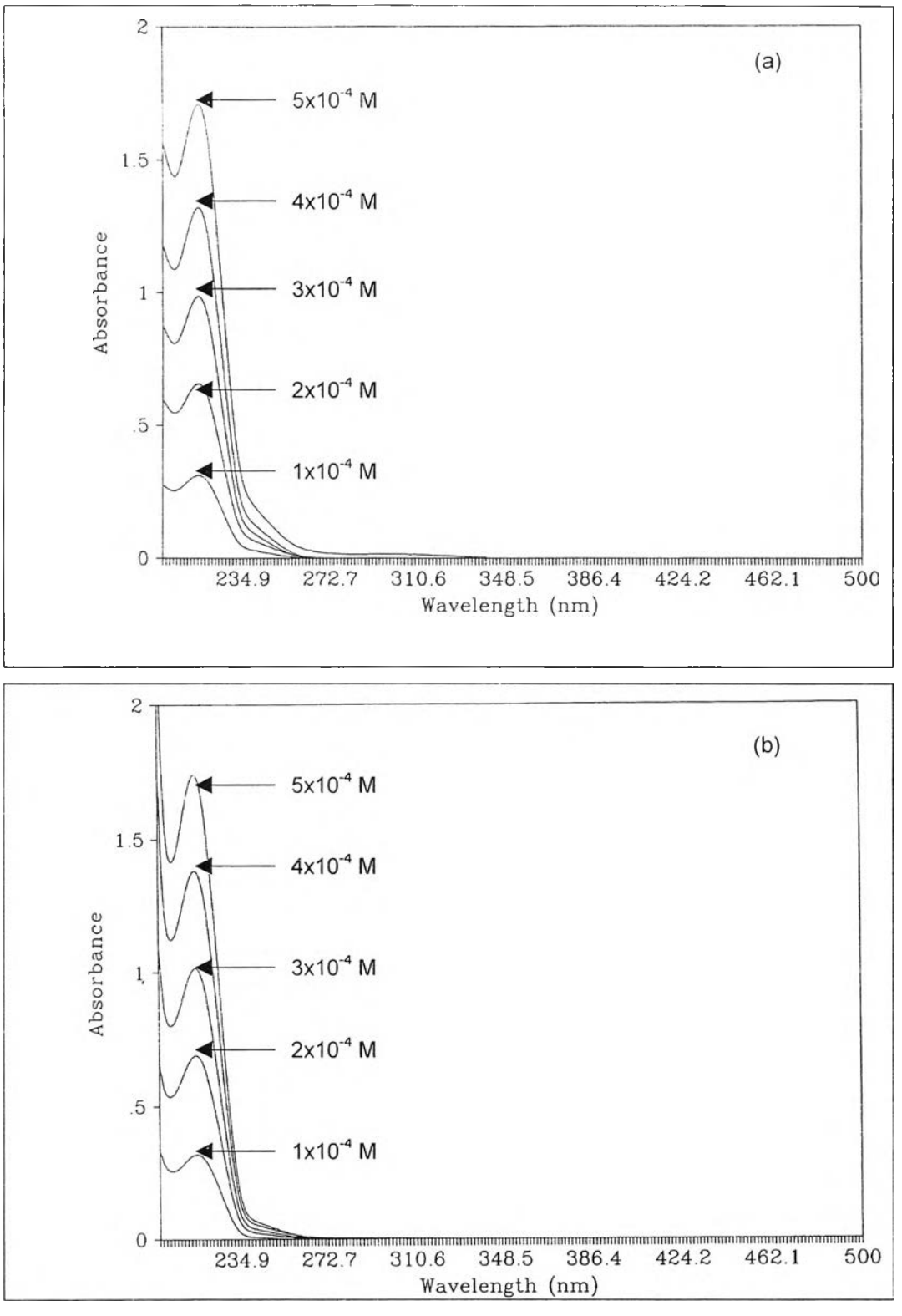
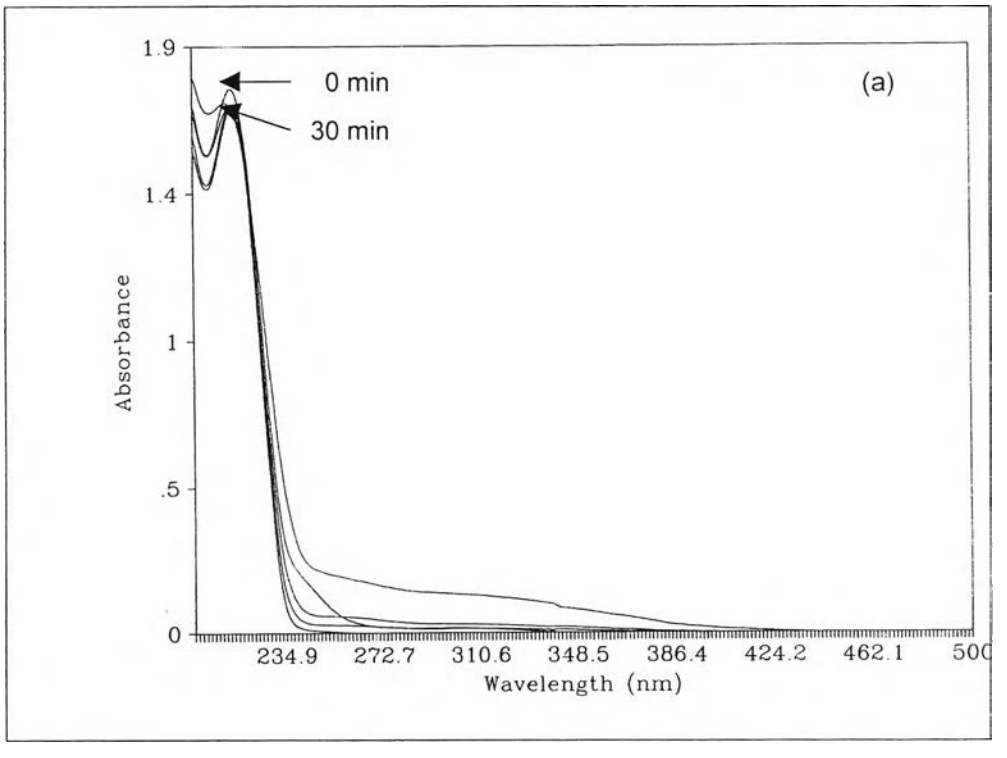


Figure 19 UV absorption spectra of **[39]** (a) in acetonitrile (b) in methanol

3.2.2 Investigation of the photoreaction by UV spectrophotometer.

The solution of 1-methyl-3-(trifluoromethyl)pyrazole **[39]** in acetonitrile or methanol (3.0 ml, $1.5x10^{-2}$ M) was placed in a quartz tube (diameter = 7 mm and length = 12 cm), sealed with a rubber septum, purged with a fine stream of nitrogen for 5 minutes and then irradiated with the Hanovia lamp under a nitrogen atmosphere. The reaction was monitored by UV spectroscopy. After each period of irradiation an aliquot of the solution was removed and diluted (1:30). Figure 20a shows the UV absorption spectrum of **[39]** in acetonitrile solution before irradiation and after irradiation times of 5, 10, 15, and 30 minutes. As the spectra show, irradiation is accompanied by a shift in the absorption maximum from 215 nm to 212 nm. Figure 20b shows that irradiation is also accompanied by a shift in the absorption maximum from 215 to 212 nm. In this case, however, the figure shows that irradiation is also accompanied by an increase in the optical density at 299 nm. From these results it appears that 1-methyl-3-(trifluoromethyl)pyrazole is photochemically converted to a compound absorbing at 212 nm in either acetonitrile or methanol solvent but in methanol a second product absorbing at 299 nm is also formed.



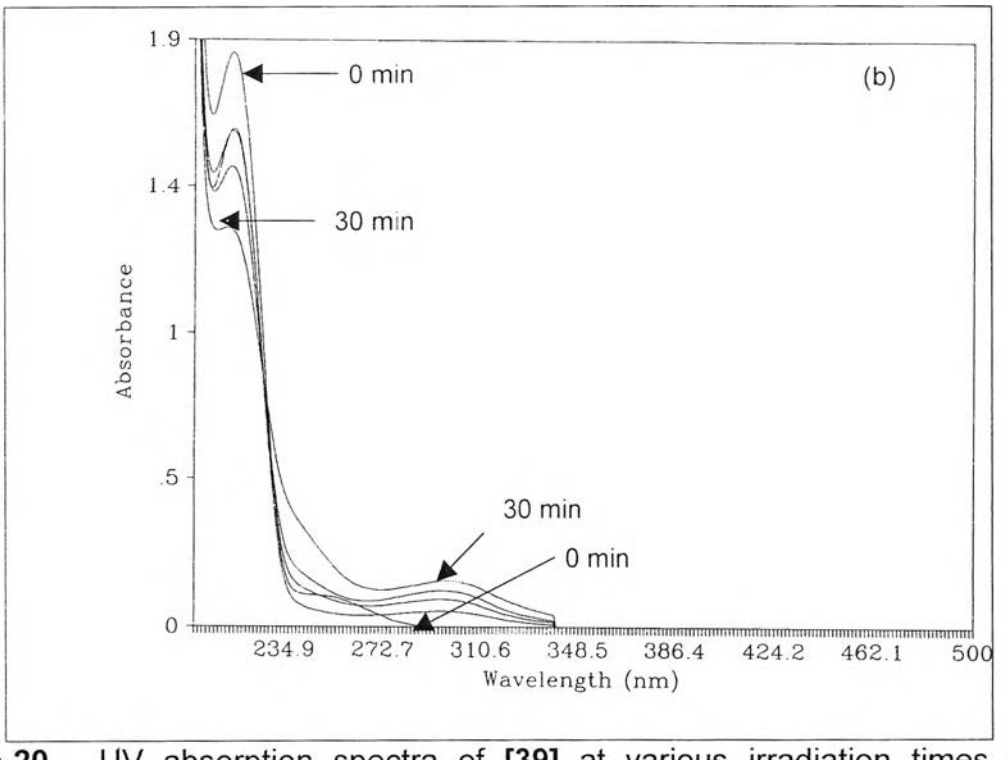
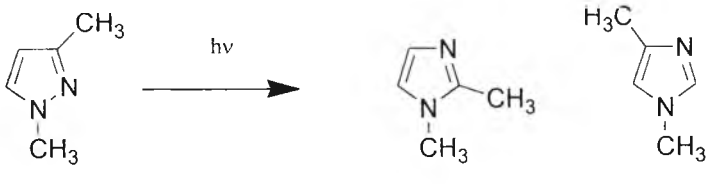
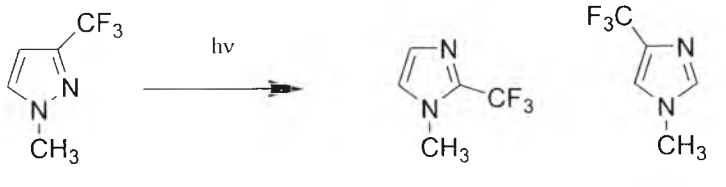


Figure 20 UV absorption spectra of **[39]** at various irradiation times (a) in acetonitrile (b) in methanol

1,3-Dimethylpyrazole **[7]** is known to phototranspose to 1,2-dimethylimidazole **[8]** and 1,4-dimethylimidazole **[10]**. Based on this it could be



[7] **[8]** **[10]**



[39] **[45]** **[47]**

predicted that 1-methyl-3-(trifluoromethyl)pyrazole **[39]** would transpose to 1-methyl-2-(trifluoromethyl)imidazole **[45]** and/or 1-methyl-4-(trifluoromethyl) imidazole **[47]**. Figure 21 shows the UV absorption spectra of the three isomeric 1-methyltrifluoromethylimidazoles **[45-47]** in acetonitrile solvent and shows that the 1-methyl-2-(trifluoromethyl)imidazole **[45]**, 1-methyl-4-(trifluoromethyl)imidazole **[47]**, and 1-methyl-5-(trifluoromethyl)imidazole **[46]**, absorb at 221 nm (ϵ = 4200 $M^{-1}cm^{-}$

^{1}), 203 nm (ϵ = 6080 $M^{-1}cm^{-1}$), and 200 nm (ϵ = 5120 $M^{-1}cm^{-1}$) respectively. None of these absorption maxima corresponds to the absorption maxima observed at 212 nm for the photoproduct.

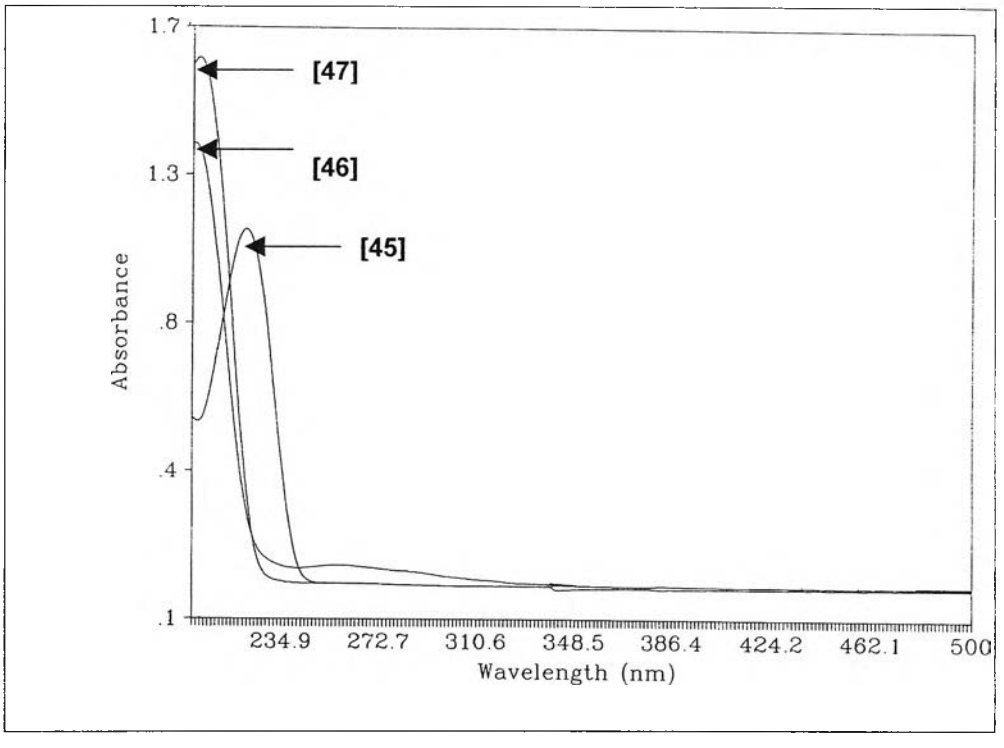


Figure 21 UV absorption spectra of 1-methyl-2-(trifluoromethyl)imidazole **[45]** (2.5 x 10^{-4} M), 1-methyl-4-(trifluoromethyl)imidazole **[47]** (2.5 x 10^{-4} M), and 1-methyl-5-(trifluoromethyl)imidazole **[46]** (2.5 x 10^{-4} M) in acetonitrile

3.2.3 Investigation of the photoreaction by gas-liquid chromatography.

To monitor the photoreaction of 1-methyl-3-(trifluoromethyl)pyrazole **[39]** in acetonitrile, aliquots of 1μl of the solution were taken after 5, 10, 15, 20, and 30 minutes of irradiation for analysis by gas chromatography, using GC1 (Perkin Elmer Autosystem (9000) equipped with 15m x 0.53mm 50% phenyl silicone phase capillary column using temperature program (40 °C for 25 minutes, 100 °C for 10 minutes, and 140 °C for 5 minutes with temperature changing rate of 20 °C per minute)). As shown in Figure 22, before irradiation, the gas chromatogram shows a single peak at a retention time of 19.6 minutes. Figures 23-27 show the continuous decrease in the area of the peak at 19.6 minutes due to the consumption of 1-

methyl-3-(trifluoromethyl)pyrazole **[39]** and the appearance of two new peaks with retention times of 26.5 and 34.2 minutes which continued to increase in area throughout the irradiation.

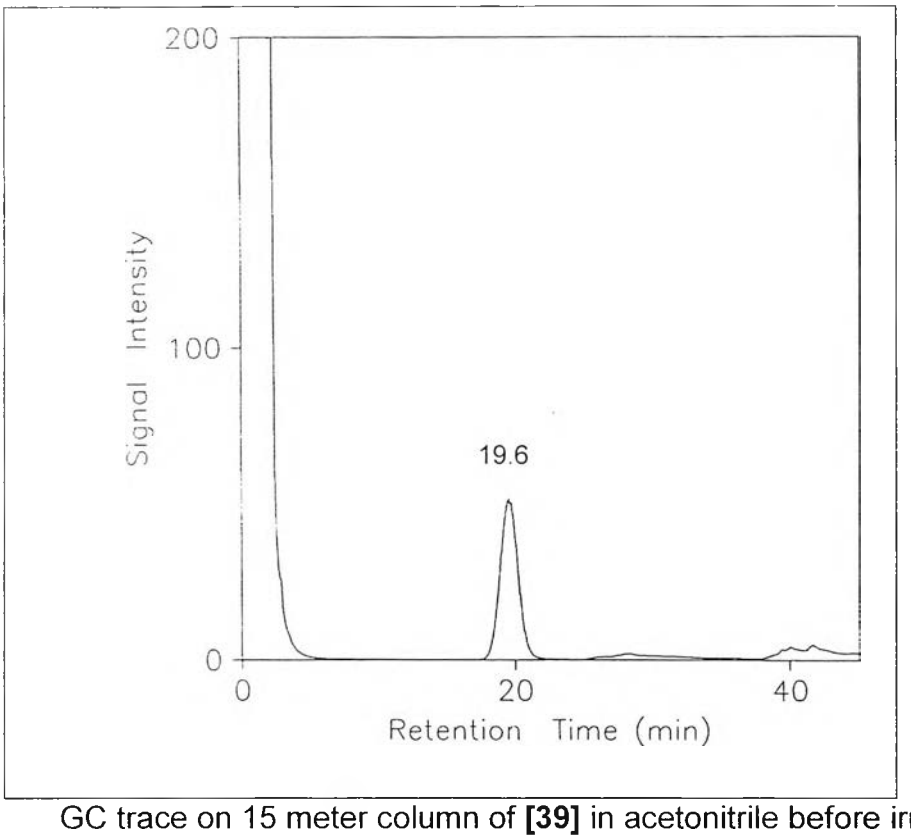


Figure 22 GC trace on 15 meter column of **[39]** in acetonitrile before irradiation

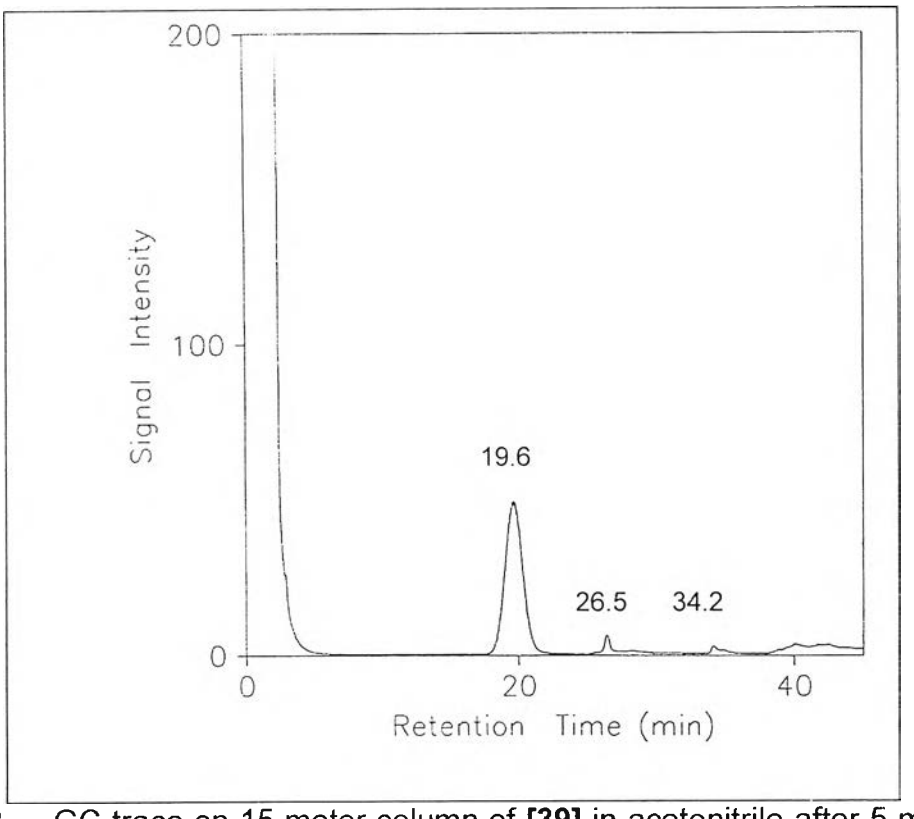


Figure 23 GC trace on 15 meter column of **[39]** in acetonitrile after 5 minutes of irradiation

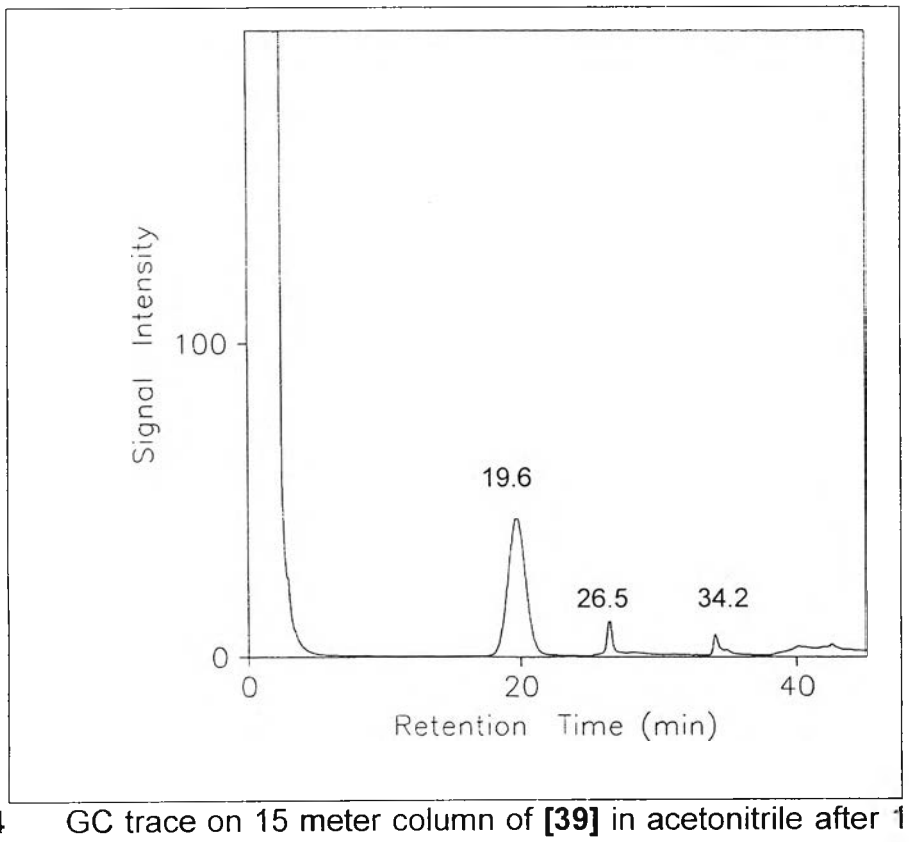


Figure 24 GC trace on 15 meter column of **[39]** in acetonitrile after 10 minutes of irradiation

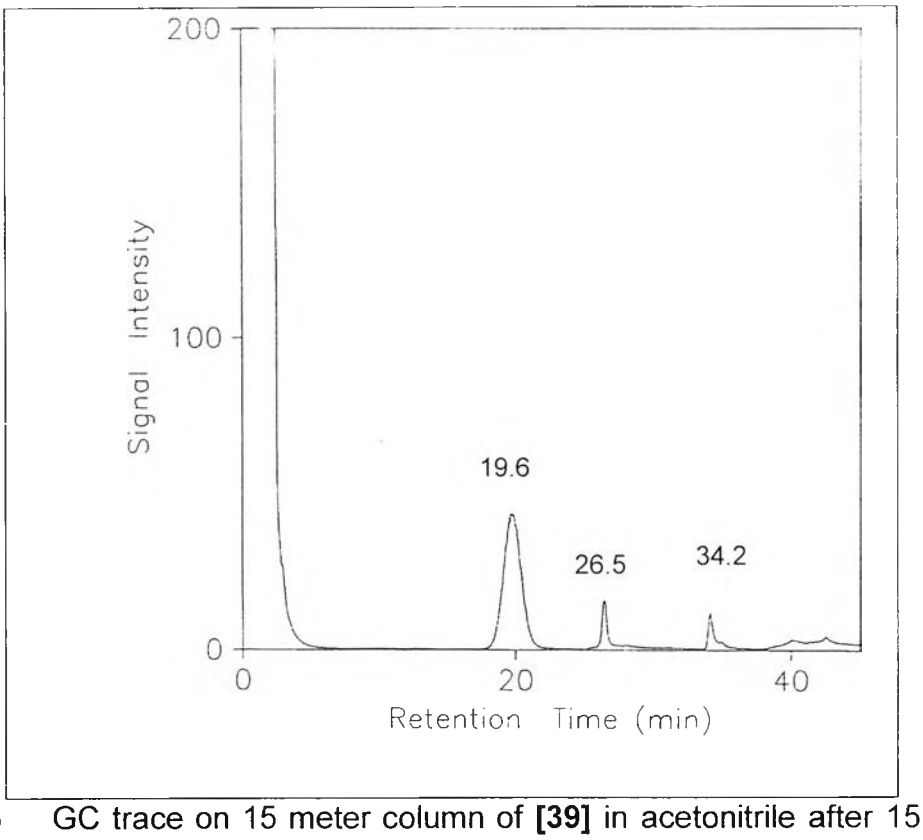


Figure 25 GC trace on 15 meter column of **[39]** in acetonitrile after 15 minutes of irradiation

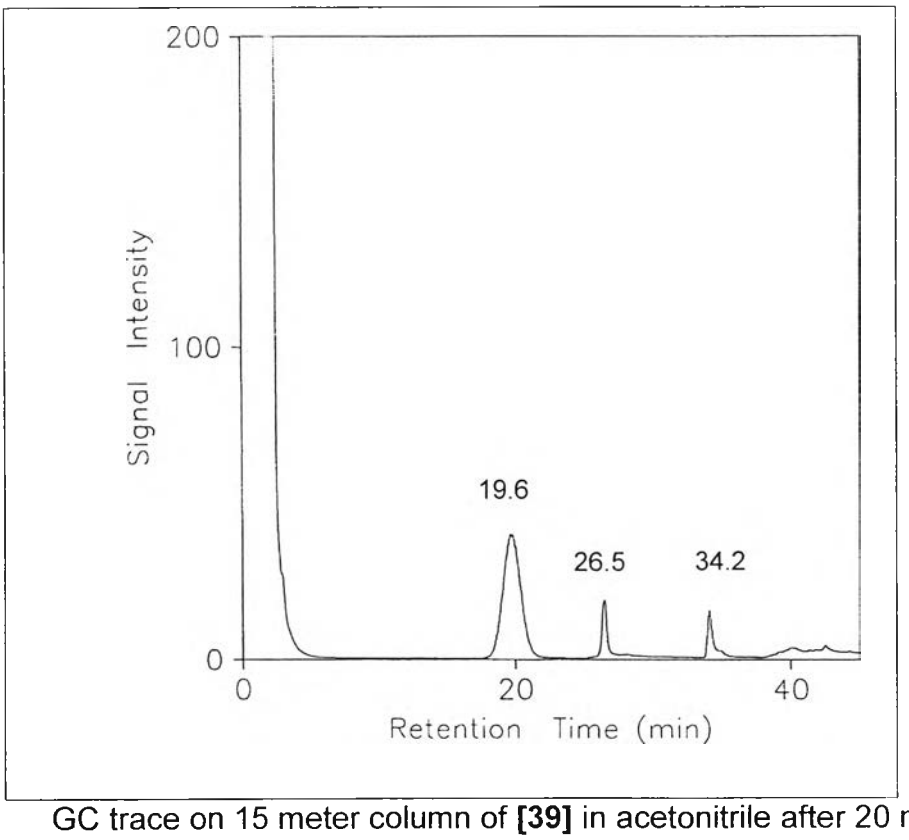


Figure 26 GC trace on 15 meter column of **[39]** in acetonitrile after 20 minutes of irradiation

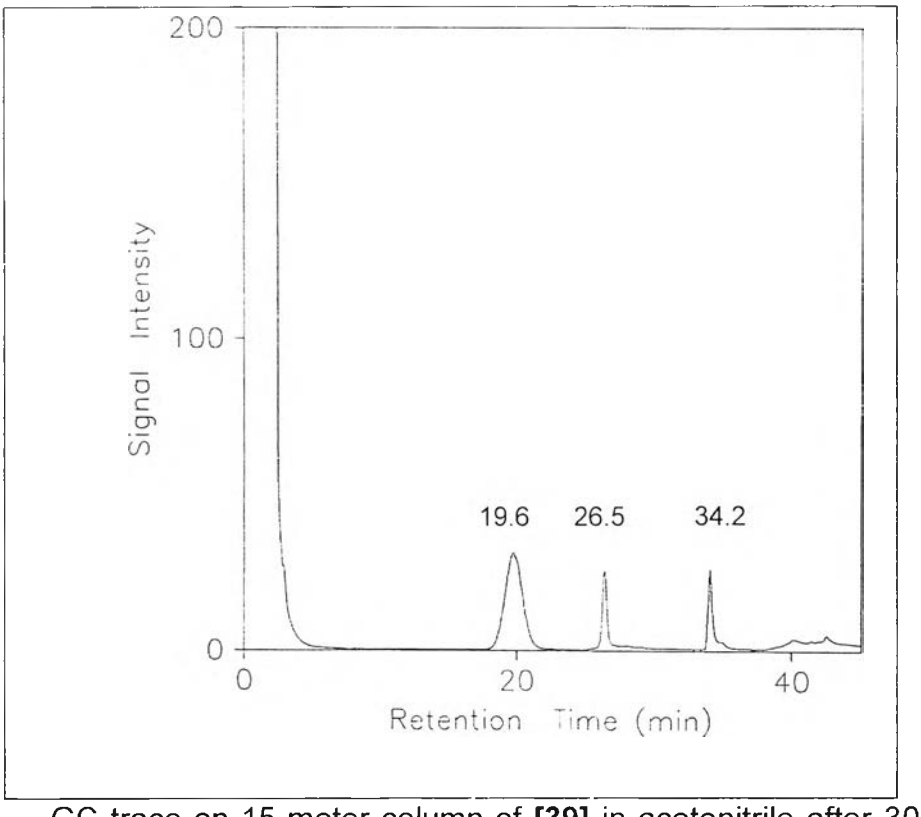


Figure 27 GC trace on 15 meter column of **[39]** in acetonitrile after 30 minutes of irradiation

It is possible that these product peaks are due to the formation of two of the three possible 1-methyltrifluoromethylimidazole phototransposition products **[45-47]**. In order to investigate this possibility the gas chromatographic retention times of the three isomeric imidazoles were measured by GC1 to be 26.5 minutes for both 1-methyl-2-(trifluoromethyl)imidazole **[45]** and 1-methyl-5-(trifluoromethyl) imidazole **[46]** and 34.2 minutes for 1-methyl-4-(trifluoromethyl)imidazole **[47]** (Figure 20). Thus, under these conditions, 1-methyl-2-(trifluoromethyl) **[45]** and 1-methyl-5-(trifluoromethyl)imidazole **[46]** cannot be resolved on the 15 meter column. Figure 29, however, shows that the three isomeric trifluoromethylimidazoles **[45-47]** can be resolved when they are chromatographed on the PE-8500 FID instrument equipped with a 30m x 0.25mm i.d. fused silica column coated with 0.25μ Supelwax 10 bonded phase using temperature program (35 °C for 5 minutes, 40 °C for 7 minutes, 60 °C for 15 minutes, 100 °C for 10 minutes, and 140 °C for 13 minutes with temperature changing rate of 20 °C per minute). Thus, on this column the retention times for the three isomers **[45]**, **[46]**, and **[47]** are 28.2, 27.6, and 46.3 minutes, respectively.

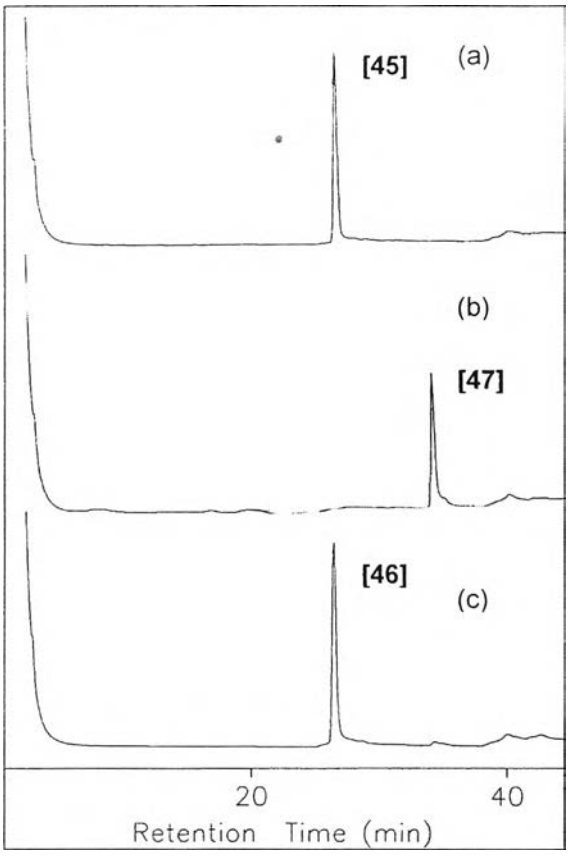


Figure 28 GC trace on 30 meter column of authentic (a) 1-methyl-2-(trifluoromethyl)imidazole **[45]** (b) 1-methyl-4-(trifluoromethyl) imidazole **[47]** (c) 1-methyl-5-(trifluoromethyl)imidazole **[46]**. Analysis on 15 meters column.

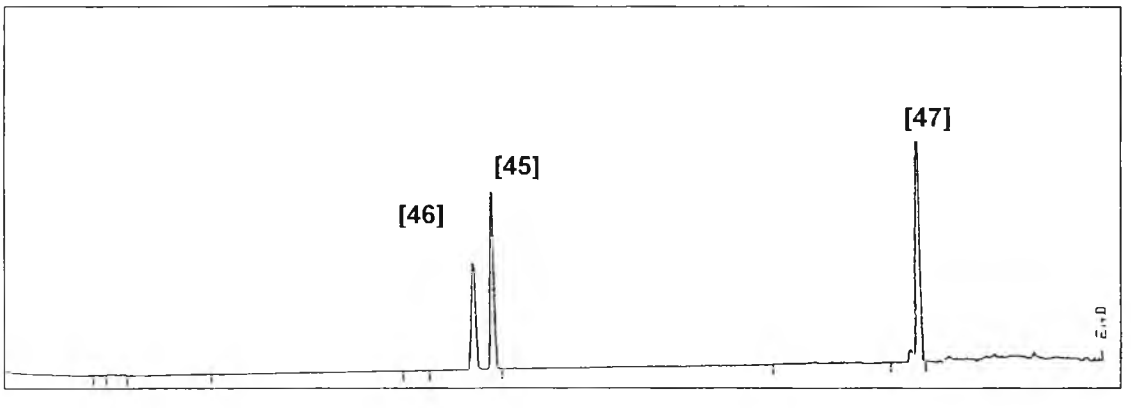


Figure 29 GC trace on 30 meter column of the mixture of 1-methyl-2-(trifluoromethyl)imidazole **[45]**, 1-methyl-4-(trifluoromethyl)imidazole **[47]**, and 1-methyl-5-(trifluoromethyl)imidazole **[46]**

Figure 30a shows the GC trace on the 30 metre column of the solution of 1-methyl-3-(trifluoromethyl)pyrazole **[39]** in acetonitrile after 30 minutes of irradiation and shows a large peak for the starting material at 23.3 minutes and peaks at 28.2 and 46.3 minutes for **[45]** and **[47]**. In order to confirm that the peak at retention time of 28.2 minutes is 1-methyl-2-(trifluoromethyl)imidazole **[45]**, authentic 1-methyl-2-(trifluoromethyl)imidazole **[45]** was added to the solution of the photolysate. The GC trace of the resulting solution (Figure 90b) shows that the peak area increases at the retention time of 28.2 minutes but that no new peak is observed. This clearly indicated that the GC peak at retention time 28.2 minutes is 1-methyl-2-(trifluoromethyl)imidazole **[45]**.

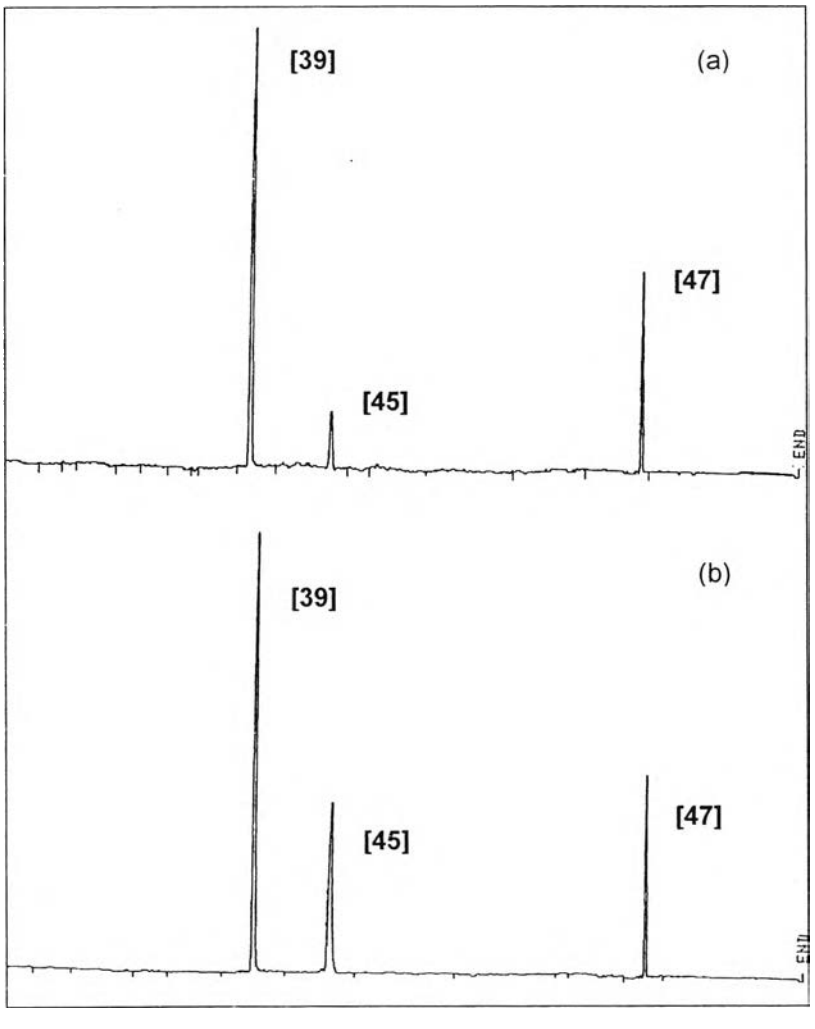
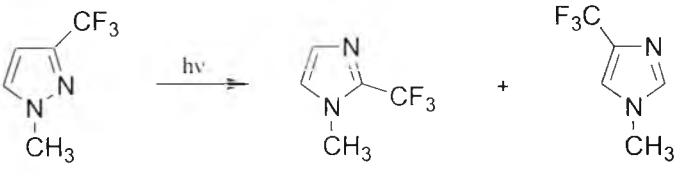


Figure 30 (a) GC trace on 30 meter column of **[39]** after 30 minutes of irradiation (b) spiked with authentic 1-methyl-2-(trifluoromethyl) imidazole **[45]**

The photoreaction of 1-methyl-3-(trifluoromethyl)pyrazole **[39]** in acetonitrile after 10 minutes of irradiation showed that 15% ($7x10^{-6}$ mol) of **[39]** was consumed to generate two photoproducts, 64% yield of 1-methyl-2-(trifluoromethyl)imidazole **[45]** and 31% yield of 1-methyl-4-(trifluoromethyl)pyrazole **[47]**. After 15 minutes



	[39]	[45]	[47]
10 minutes	-15%	64%	31%
15 minutes	-17%	58%	40%

of irradiation the ratio of the photoproducts was changed from 64:31 to 58:40. These results suggest that **[45]** transposes to **[47]** in a secondary photoreaction. To confirm this 1-methyl-2-(trifluoromethyl)imidazole **[45]** in acetonitrile (1.0 ml, 2.0x10-2 M) was placed in a quartz tube (diameter = 7 mm and length = 12 cm), sealed with a rubber septum, purged with a fine stream of nitrogen for 5 minutes and then irradiated with the Hanovia lamp under a nitrogen atmosphere. An aliquot of 1μl of the solution was taken after 30 minutes of irradiation for analysis by gas chromatograph using the 15 meters column. As shown in Figure 31, before irradiation the gas chromatogram shows a single peak at a retention time of 26.5 minutes. Figure 32 shows the decrease in the area of the peak at 26.5 minutes due to the consumption of 1-methyl-2-(trifluoromethyl)imidazole **[45]** and the appearance of a new peak with retention times of 34.2 minutes due to the formaton of 1-methyl-4-(trifluoromethyl)imidazole **[47]**. These results showed that 20% ($1.2x10^{-5}$ mol) of **[45]** was consumed to generate a 46% yield of 1-methyl-4-(trifluoromethyl)imidazole **[47]**.

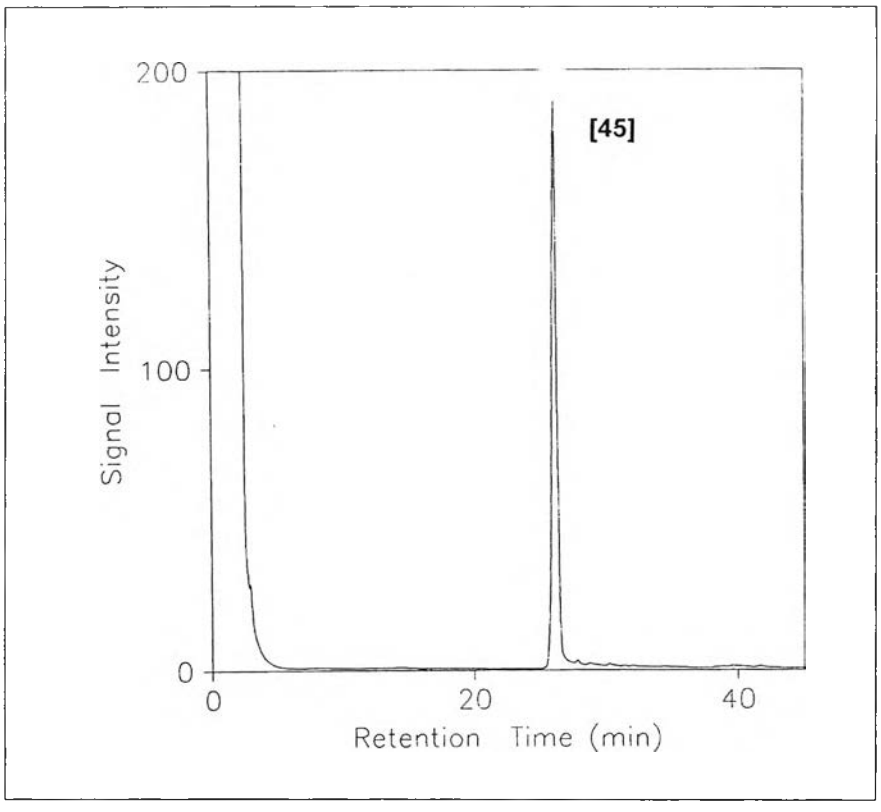


Figure 31 GC trace on 15 meter column of **[45]** in acetronitrile before irradiation.

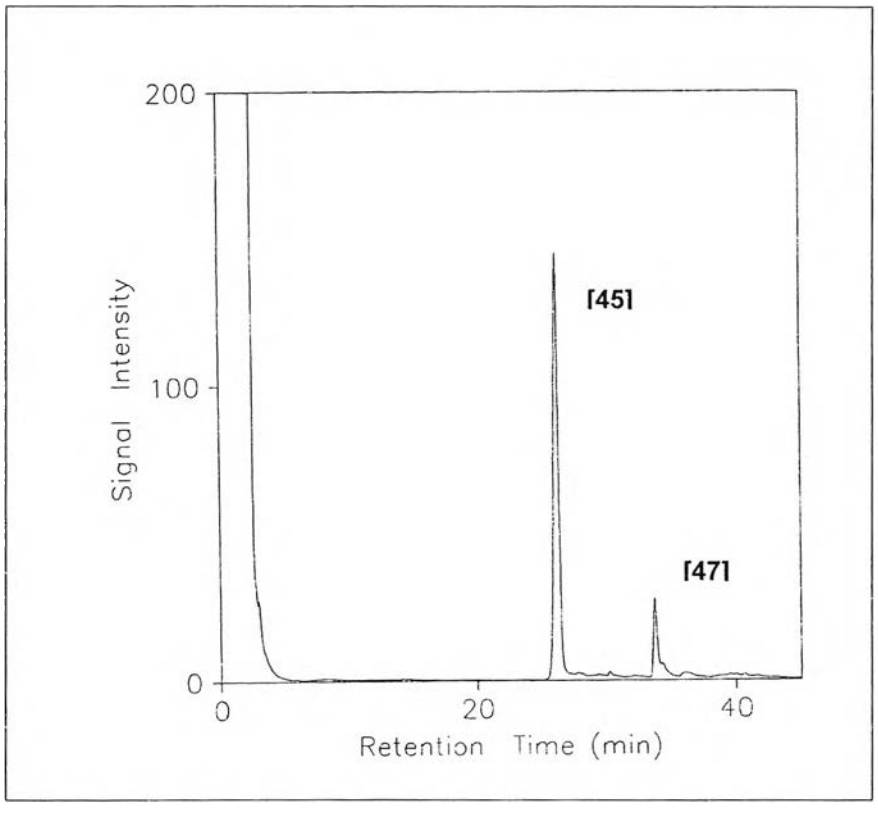


Figure 32 GC trace on 15 meter column of **[45]** in acetronitrile after 30 minutes of irradiation

3.2.4 Identification of phototransposition product by GC-MS.

To further identify the phototransposition products, the concentrated photolysate in acetonitrile after 30 minutes of irradiation was analyzed by GC-MS (Hewlett Packard HP 5890A GC coupled HP 5970B mass spectrometer on 30m x 0.25 mm Supelcowax^{TM} 10 column using temperature program (40 °C for 11 minutes, 60 °C for 10 minutes, 100 °C for 10 minutes, 140 °C for 9 minutes with temperature changing rate of 20 °C per minute)). As shown in Figures 33b –33d, the mass spectrum of each of the three photoproducts exhibits a molecular ion at m/z 150, as expected for a trifluoromethyl substituted 1-methylimidazole, and a major fragment peak at m/z 131 due to loss of a fluorine atom. In addition, the fragmentation patterns are all very similar and very similar to the mass spectra of the three authentic trifluoromethyl substituted 1-methylimidazoles shown in Figures 14, 16 , and 18. Although the mass spectra indicate that these two photoproducts are both trifluoromethyl substituted 1-methylimidazoles, the mass spectra are all too similar to allow distinction among the three isomers. As a result, the three isomers were distinguished by their gas chromatographic retention times. Compared with the gas chromatograph and MS of authentic compounds, the peak at retention time of 17.6 minutes was identified as the photoreactant (Figure 33b). The other two peaks at retention times of 22.6 and 35.3 minutes were identified as 1-methyl-2-(trifluoromethyl)imidazole **[45]** and 1-methyl-4-(trifluoromethyl)imidazole **[47]** respectively (Figure 33c and 33d) .

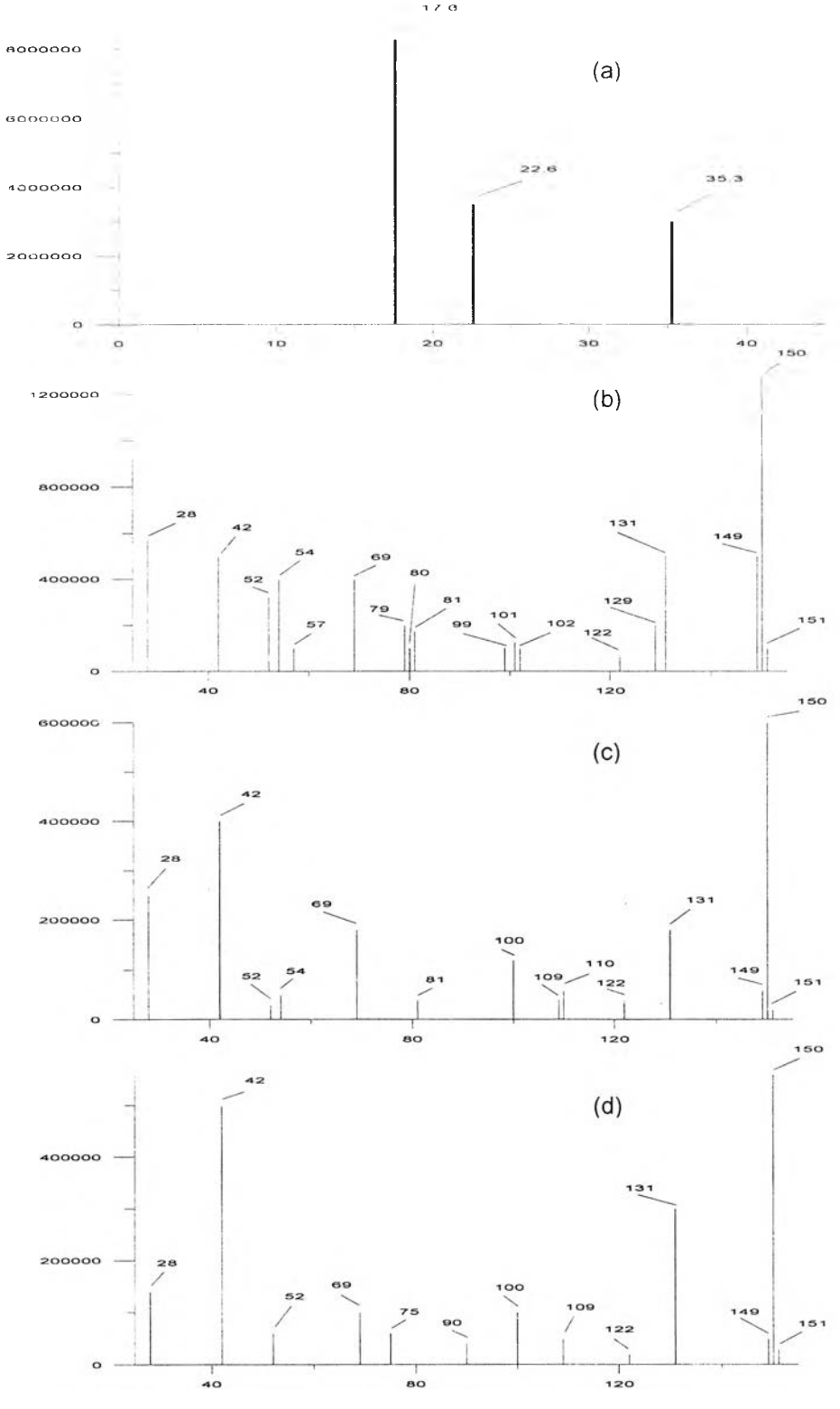
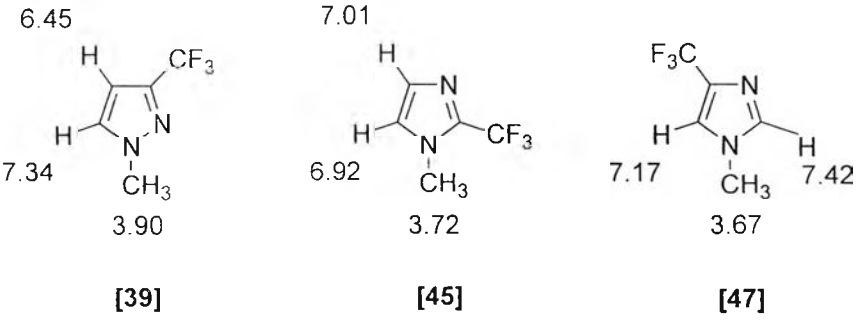


Figure 33 (a) The GC trace of **[39]** after 30 minutes of irradiation (from GC-MS) (b) The mass spectrum of peak at retention time 17.6 minutes (c) 22.6 minutes (d) 35.3 minutes

3.2.5 ^{1}H-NMR spectrum of the photolysate of 1-methyl-3-(trifluoromethyl)pyrazole

After 30 minutes of irradiation in acetonitrile (3.0 ml, $1.5x10^{-2}$ M) the resulting solution was concentrated and the residue was dissolved in $CDCl_3$ and analyzed by ^{1}H-NMR. The full spectrum is shown in Figure 34 with scale expansions shown in Figures 35a and 35b. ^{1}H-NMR spectrum of product mixture was compared with the spectra of the authentic compounds synthesized in this work. Figure 35a shows the ^{1}H-NMR spectrum from δ 3.3-5.0 ppm where the *N*-methyl protons of *N*-methylpyrazoles and *N*-methylimidazoles are known to absorb. As shown, the spectrum exhibits a signal at δ 3.90 due to the *N*-methyl group of the reactant, 1-methyl-3-(trifluoromethyl)pyrazole **[39]**, and signals at δ 3.72 and 3.67 for the *N*-methyl protons of **[45]** and **[47]** respectively, but no signal at δ 3.70 where the *N*-methyl protons of 1-methyl-5-(trifluoromethyl)imidazole **[46]** are known to absorb. Figure 35b shows the ^{1}H-NMR spectrum from δ 6.2-7.6 ppm where the ring protons of *N*-methylpyrazoles and *N*-methylimidazoles are known to absorb. As shown, the spectrum exhibits signals at δ 6.46 and 7.34 due to a proton on C-4 and a proton on C-5 respectively of the reactant 1-methyl-3-(trifluoromethyl) pyrazole **[39]**, signals at δ 7.01 and 6.92 due to a proton on C-4 and a proton on C-5 respectively of **[45]**, and signals at δ 7.42 and 7.17 due to a proton on C-2 and a proton on C-5 respectively of **[47]**, but no signal at δ 7.46 and 7.36 where the proton on C-2 and C-4 respectively of 1-methyl-5-(trifluoromethyl)imidazole **[46]** are known to absorb.



Scheme 8 Assignment of the chemical shifts for the protons of components in the photolysate **[39]** in acetonitrile after 30 minutes of irradiation

-0.0802
-0.0406
0.0000
0.0097
1.1014
1.5404
1.6924
1.7856
1.7876
1.7957
1.8011
1.8236
1.8408
1.8517
1.8642
1.9055
1.9361
1.9391
1.9453
2.0320
3.3390
3.5958
3.6427
3.6641
3.7808
3.8212
3.8622
3.9948
5.1546
6.3629
6.3681
6.8460
7.0772
7.0903
7.1177
7.1588
7.1816
7.2224
7.2625
7.3032
7.3343
7.3764
7.9163
7.9298
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8.6227
8.6368
9.5695
87.852
12.148
0
2
4
6
8
10

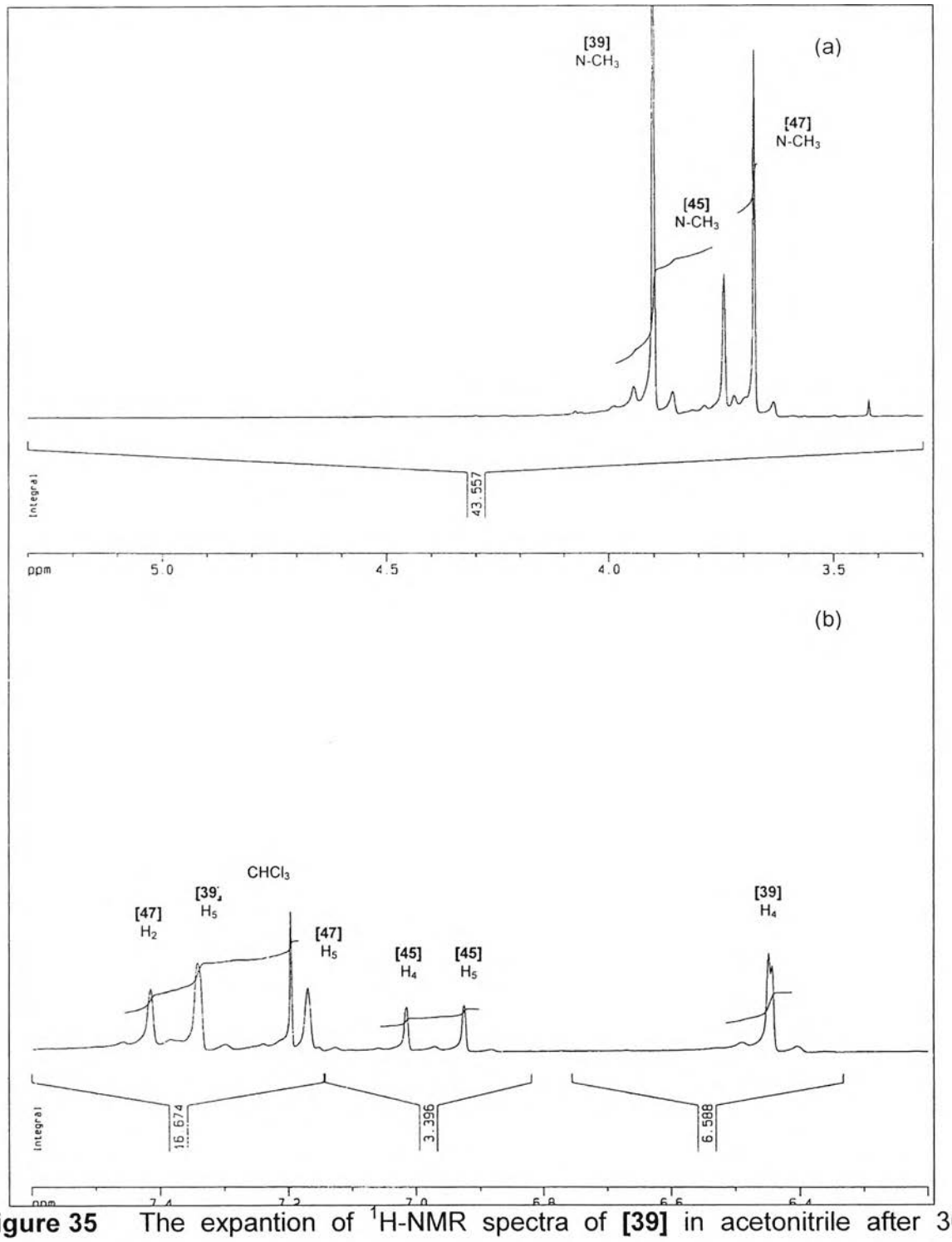
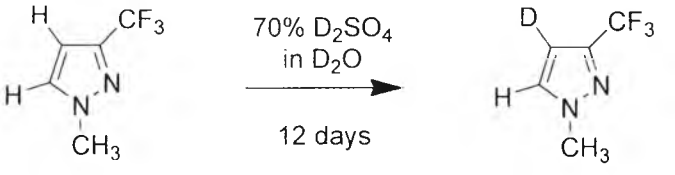


Figure 35 The expantion of ^{1}H-NMR spectra of **[39]** in acetonitrile after 30 minutes of irradiation (a) 3.3-5.3 ppm and (b) 6.2-7.6 ppm

3.2.6 Permutation pattern study for 1-methyl-3-(trifluoromethyl) pyrazole.

The permutation patterns for these products were confirmed by studying the phototransposition chemistry of 4-deuterio-1-methyl-3-(trifluoromethyl)pyrazole **[39-4d$_1$]** prepared by the acid catalyzed deuterium exchange of **[39]** (Scheme 9).



[39] **[39-4d$_1$]**

Scheme 9 Deuterium labeling reaction on 1-methyl-3-(trifluoromethyl)pyrazole **[39]**

The mass spectrum of the deuterated product shown in Figure 36 exhibits a base peak for the molecular ion at m/z 151, indicating that one proton was exchanged by one deuterium atom. As shown, the spectrum also exhibits a prominent signal at m/z 150 which is 50% of the intensity of the M^+ peak. This is due either to a M^+-1 peak formed by loss of one H-atom from the molecular ion or from a large amount of undeuterated 1-methyl-3-(trifluoromethyl)pyrazole **[39]** in the sample. The mass spectrum of undeuterated **[39]**, shown in Figure 1, exhibits a base peak for the molecular ion at m/z 150 and a prominent signal at m/z 149 which is 50% of the intensity of the M^+ peak. This is due to a M^+-1 peak formed by loss of one H-atom from the molecular ion. These results show that the prominent signal at m/z 150 in the mass spectrum of the deuterated product is also due to a M^+-1 peak formed by loss of one H-atom from the molecular ion and is not due to undeuterated **[39]** in the sample. The ^{1}H-NMR spectrum of **[39-4d$_1$]** exhibited signals at δ 3.89 (s, 3H) and 7.34 (s, 1H) which are due to the N-methyl protons and a proton on C-5 respectively, and a signal of very low intensity at δ 6.58 for the small amount of residual hydrogen at the C-4 position(Figure 37).

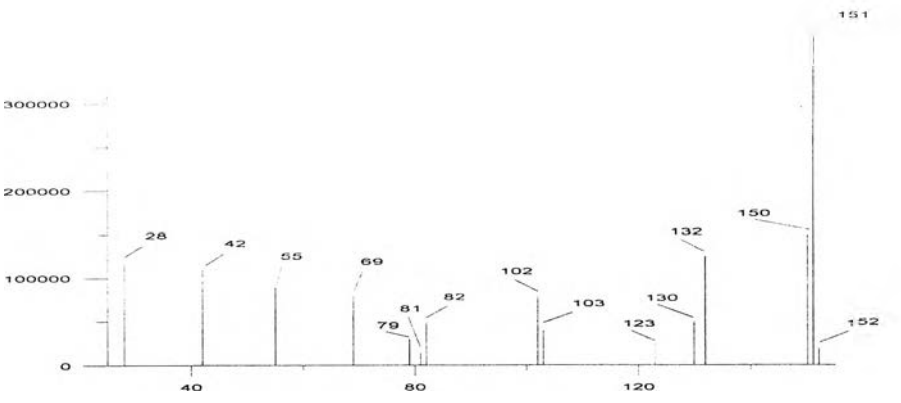


Figure 36 The mass spectrum of 4-deuterio-1-methyl-3-(trifluoromethyl)pyrazole **[39-4d$_1$]**

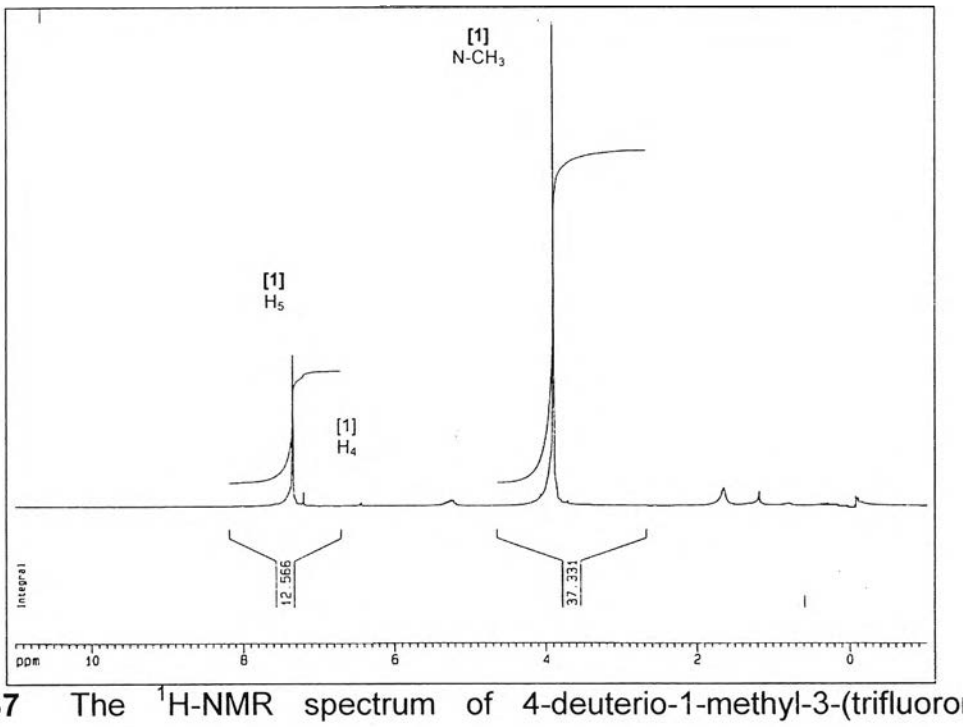
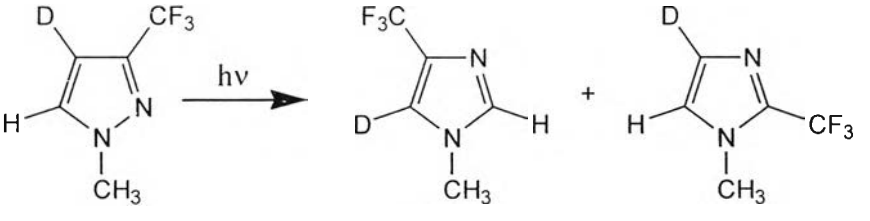


Figure 37 The ^{1}H-NMR spectrum of 4-deuterio-1-methyl-3-(trifluoromethyl) pyrazole **[39-4d$_1$]**

A solution of 4-deuterio-1-methyl-3-(trifluoromethyl)pyrazole **[39-4d$_1$]** in acetonitrile (3.0ml, 1.5x10^{-2} M) was irradiated for 10 minutes under the conditions used for the irradiation of undeuterated 1-methyl-3-(trifluoromethyl)pyrazole **[39]**. The residue left after removal of the solvent was dissolved in $CDCl_3$ and analyzed by ^{1}H-NMR (Figure 38 and Figure 39). Figure 39a shows the ^{1}H-NMR spectrum from δ 3.3-5.0 ppm where the N-methyl protons of N-methylpyrazoles and N-methylimidazoles are known to absorb. As shown, the spectrum exhibits a signal at δ 3.83 due to the N-methyl group of the reactant, 4-deuterio-1-methyl-3-

(trifluoromethyl)pyrazole **[39-4d$_1$]**, and signals at δ 3.66 and 3.59 for the N-methyl protons of 4-deuterio-1-methyl-2-(trifluoromethyl)imidazole **[45-4d$_1$]** and 5-deuterio-1-methyl-4-(trifluoromethyl)imidazole **[47-5d$_1$]** respectively, but no signal at δ 3.70 where the N-methyl protons of 1-methyl-5-(trifluoromethyl)imidazole **[46]** are known to absorb. This clearly indicated that **[46]** is not a photoproduct from irradiation of **[39]**. Figure 39b shows the ^{1}H-NMR spectrum from δ 6.2-7.6 ppm where the ring protons of N-methylpyrazoles and N-methylimidazoles are known to absorb. As shown, the spectrum exhibits a signal at δ 7.26 due to a proton on C-5 of the reactant, 4-deuterio-1-methyl-3-(trifluoromethyl)pyrazole **[39-4d$_1$]**, a signal at δ 6.84 due to a proton on C-5 of **[45-4d$_1$]**, and a signal at δ 7.33 due to a proton on C-2 of **[47-5d$_1$]**, but no signal at δ 6.99 where the proton on C-4 of 1-methyl-2-(trifluoromethyl)imidazole **[45]** is known to absorb. This showed that a proton on C-3 of the reactant had transposed to only position 4 in **[39-4d$_1$]** and to position 5 in **[47-5d$_1$]** confirming that the transpositions had occurred *via* the P_6 and P_7 permutation pathway.



[39-4d$_1$] **[47-5d$_1$]** **[45-4d$_1$]**

Scheme 10 Photoreaction for irradiation of 4-deuterio-1-methyl-3-(trifluoromethyl) pyrazole **[39-4d$_1$]**

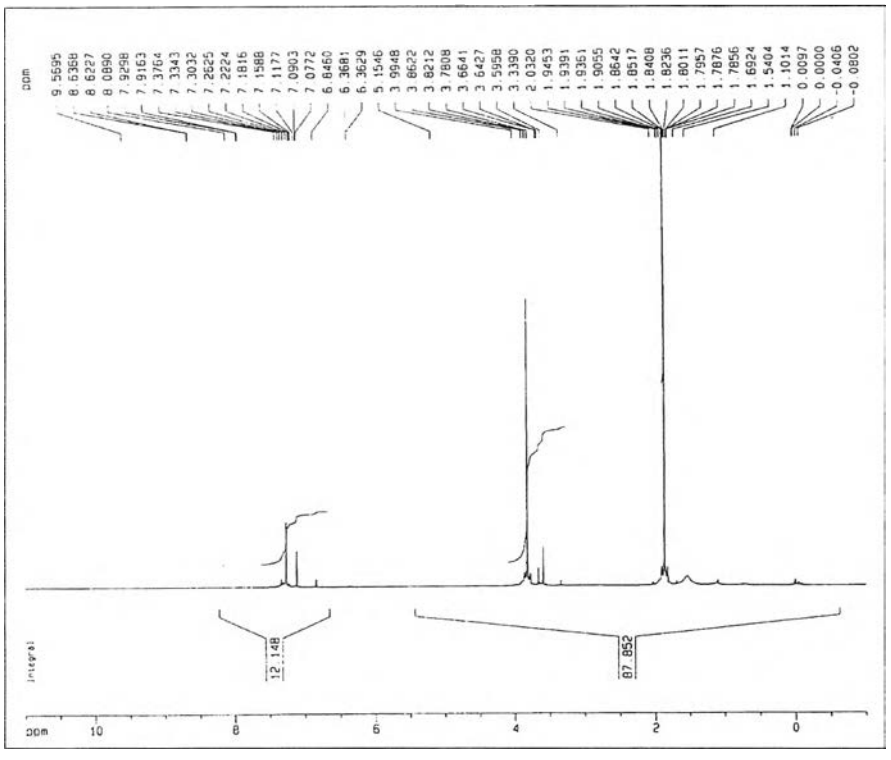


Figure 38 The ^{1}H-NMR spectrum of 4-deuterio-1-methyl-3-(trifluoromethyl) pyrazole **[39-4d$_1$]** in acetonitrile after 10 minutes of irradiation

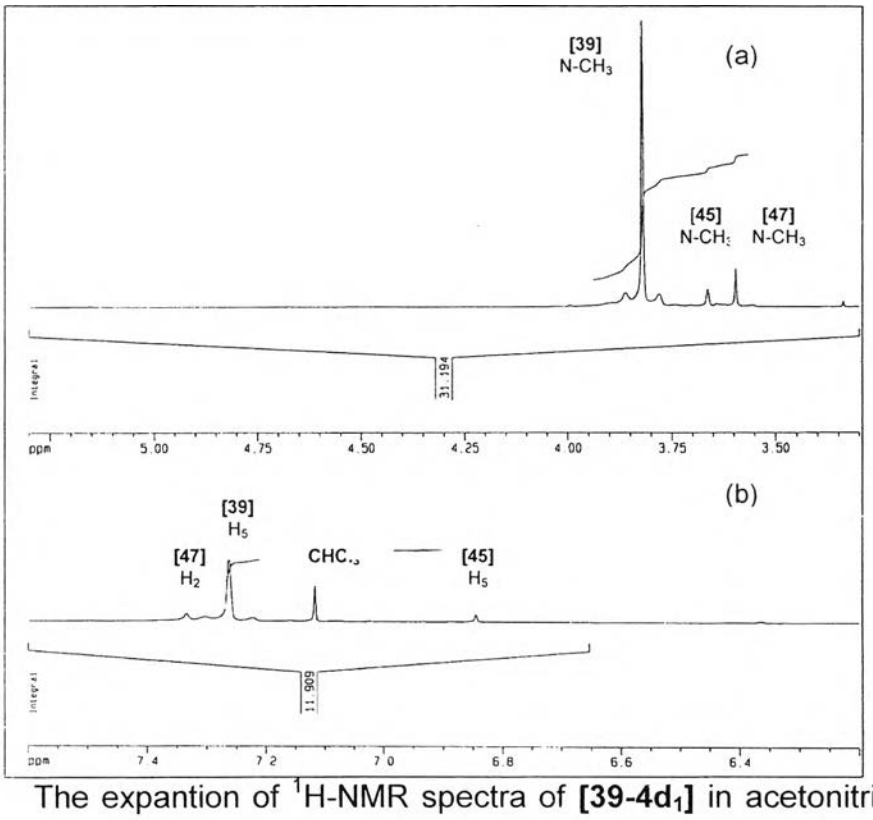


Figure 39 The expantion of ^{1}H-NMR spectra of **[39-4d$_1$]** in acetonitrile after 10 minutes of irradiation (a) 3.3-5.3 ppm and (b) 6.2-7.6 ppm

Pyrazoles with H at C-3 are known to undergo photocleavage to enaminonitriles and enaminoisocyanide. In the case of 1-methyl-3-(trifluoromethyl) pyrazole **[39]**, there is no H on C-3, so it should undergo only phototransposition. To confirm that no enaminonitrile and isocyanide was present in the photolysate, the concentrated photolysate after 30 minutes of irradiation was analyzed by IR spectrometer. Normally, cyano and isocyano groups would be detected by Infared spectroscopy to show symmetric stretching at 2300 cm^{-1} and 2200 cm^{-1} respectively. Figure 40, shows that the IR spectrum of the 1-methyl-3-(trifluoromethyl)pyrazole **[39]**, photolysate in acetonitrile, and the photolysate in methanol does not have absorption around 2200-2300 cm^{-1}. This shows that 1-methyl-3-(trifluoromethyl)pyrazole **[39]** transposed to 1-methyltrifluoromethyl photoproducts but does not lead to the formation of an enaminonitrile and/or an isocyanide intermediate.

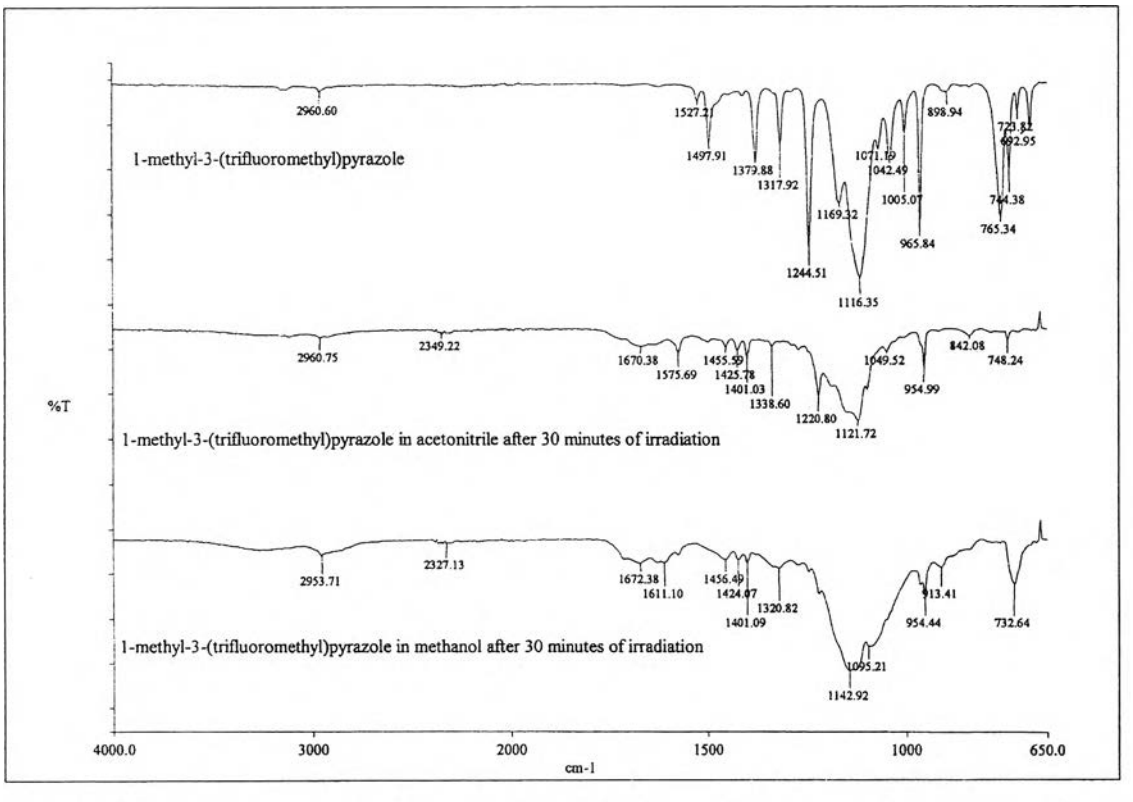
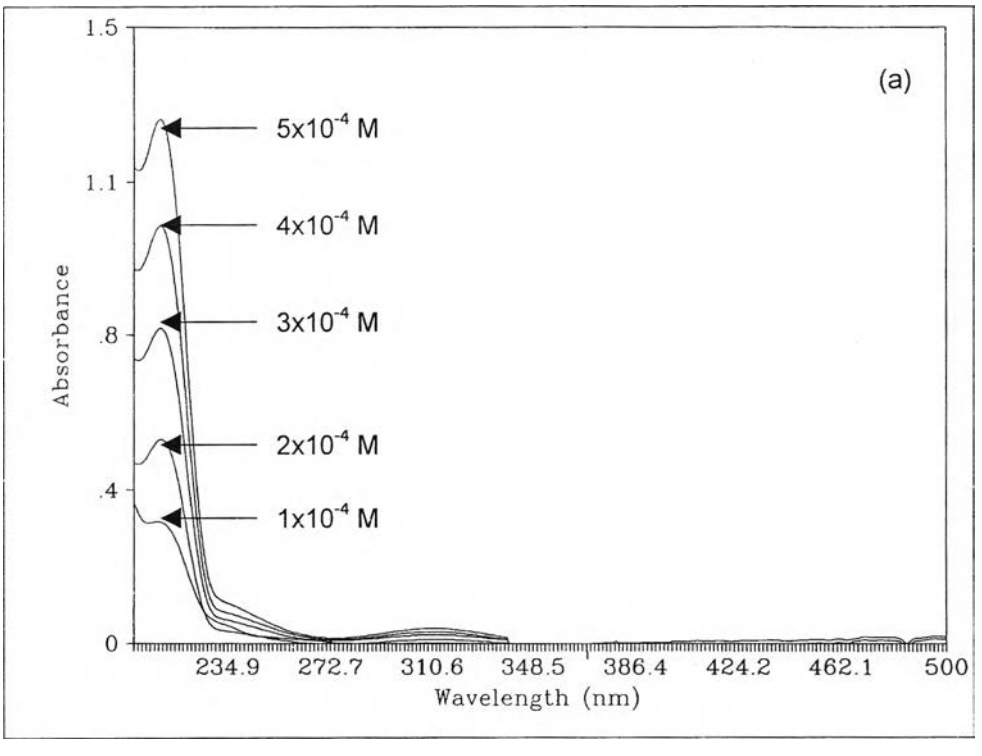


Figure 40 IR speatra of 1-methyl-3-(trifluoromethyl)pyrazole **[39]**, photolysate in acetonitrile after 30 minutes of irradiation, and photolysate in methanol after 30 minutes of irradiation

3.3 Photoreaction of 1-methyl-4-(trifluoromethyl)pyrazole

3.3.1 UV-Absorption analysis of 1-methyl-4-(trifluoromethyl)pyrazole.

The UV absorption spectrum of 1-methyl-4-(trifluoromethyl)pyrazole **[43]** was recorded in acetonitrile or methanol solvent at concentrations of $5x10^{-4}$ M, $4x10^{-4}$ M, $3x10^{-4}$ M, $2x10^{-4}$ M, and $1x10^{-4}$ M. The spectra, as shown in figure 41, displayed an absorption maximum at 210 nm with an extinction coefficient, ϵ, of 2605 $M^{-1}cm^{-1}$. Because of this absorption maximum at 210 nm it was necessary to irradiate this compound with a 450 W medium pressure Hg lamp which has output at that wavelenght. Other low pressure lamps have outputs at 254 nm, 300 nm, and 360 nm but no output at 210 nm.



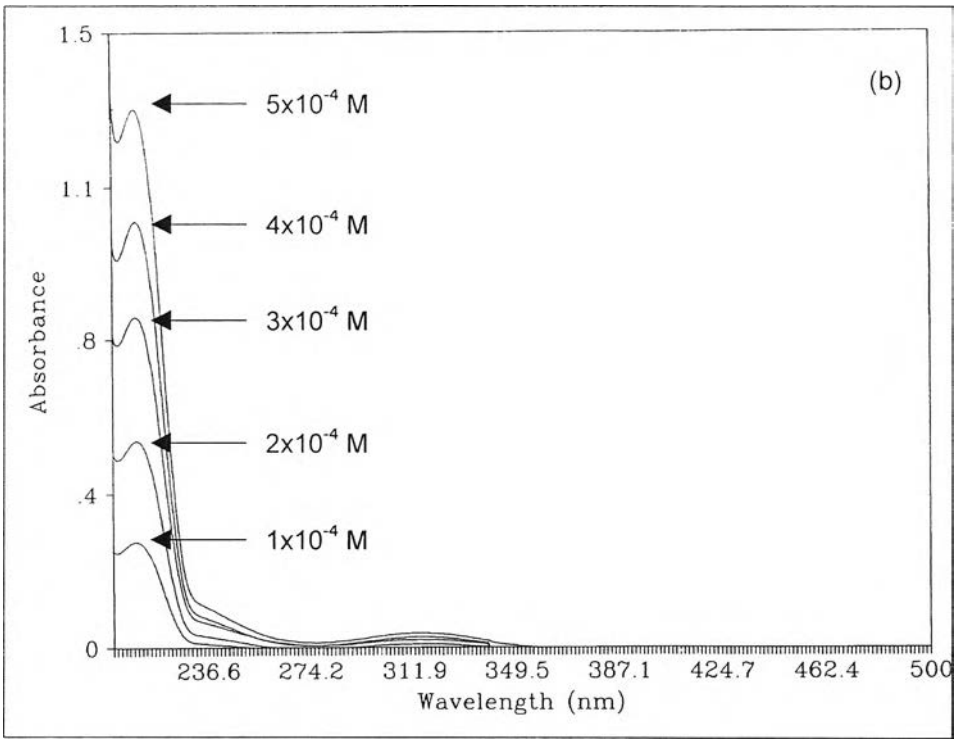


Figure 41 UV absorption spectra of **[43]** (a) in acetonitrile (b) in methanol

3.3.2 Investigation of the photoreaction by UV spectrophotometer.

The solution of 1-methyl-4-(trifluoromethyl)pyrazole **[43]** in acetonitrile or methanol (3.0ml, $1.5x10^{-2}$ M) was placed in a quartz tube (diameter = 7 mm and length = 12 cm), sealed with a rubber septum, purged with a fine stream of nitrogen for 5 minutes and then irradiated with the Hanovia lamp under a nitrogen atmosphere. The reaction was monitored by UV spectroscopy. After each period of irradiation an aliquot of the solution was remove and diluted (1:30). Figure 42a shows the UV absorption spectrum of **[43]** in acetronitrile solution before irradiation and after irradiation times of 5, 10, 15, 20, and 30 minutes. As the spectra shows, irradiation in acetonitrile is accompanied by a shift in the absorption maximum from 210 nm to 200 and the formation of a new absorption band at 260 nm. Figure 42b also shows that irradiation in methanol is accompanied by similar changes in the absorption spectrum. From these results it appears that 1-methyl-4-(trifluoromethyl) pyrazole **[43]** is photochemically converted to a compound absorbing at 200 and 260 nm. These spectral changes are quite different than those abservated (Figure 41a and 41b) upon irradiation of 1-methyl-3-(trifluoromethyl)pyrazole **[39]**. In the latter case, no intense absorption at 260 nm was observed after irradiation.

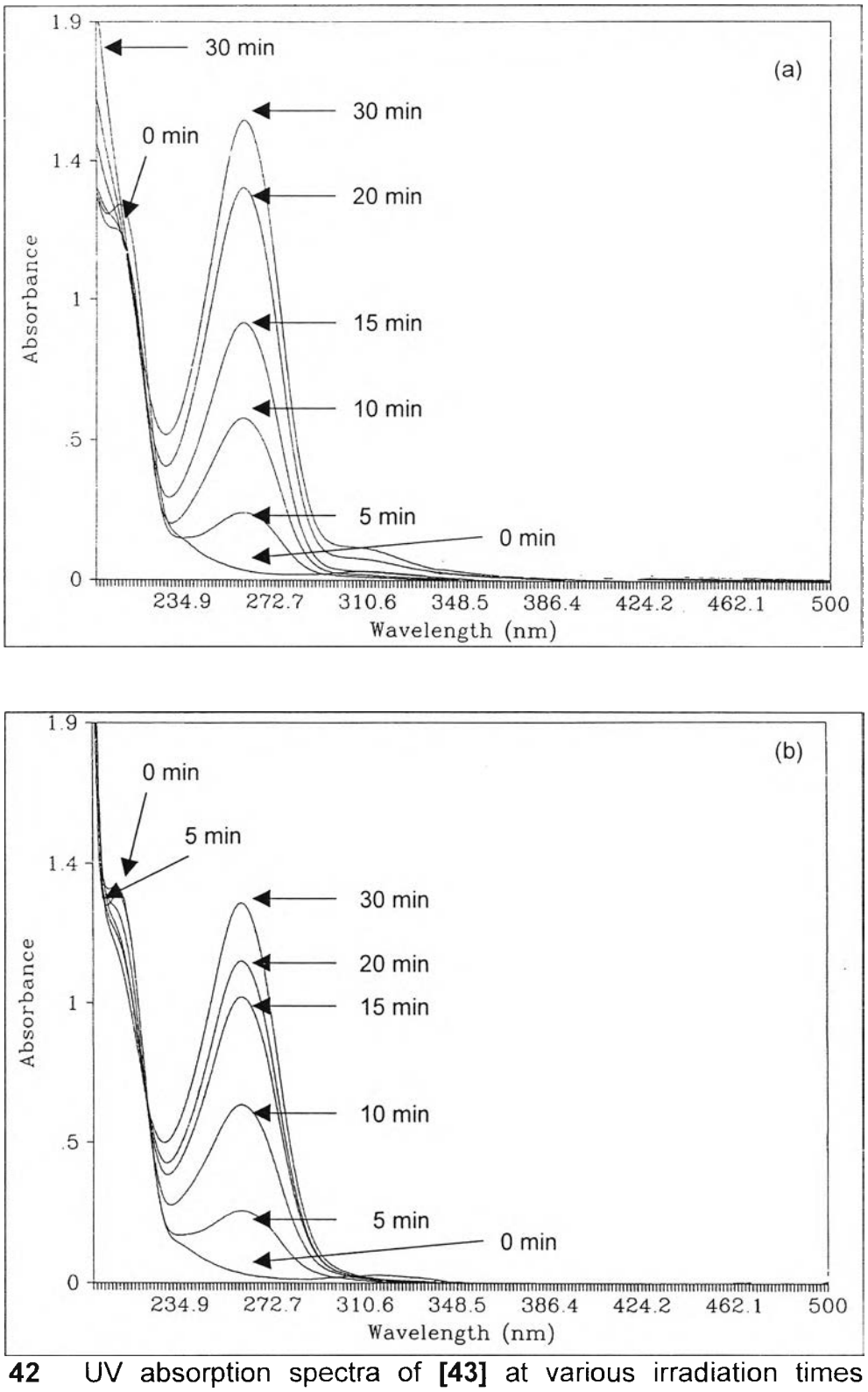
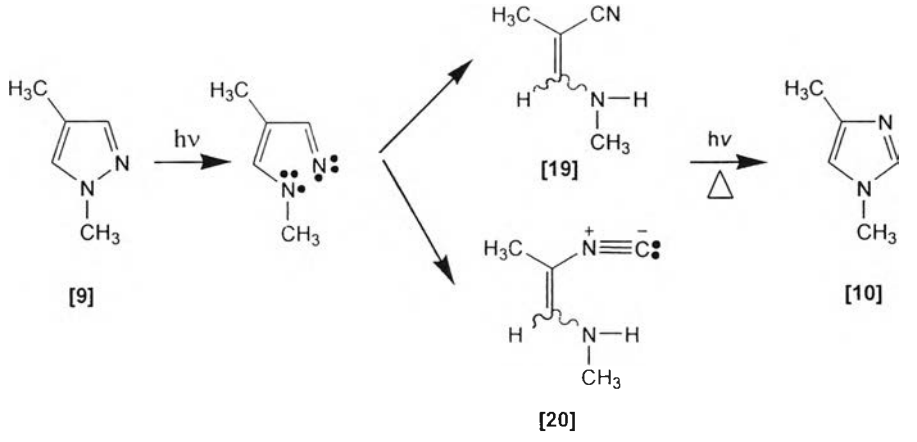


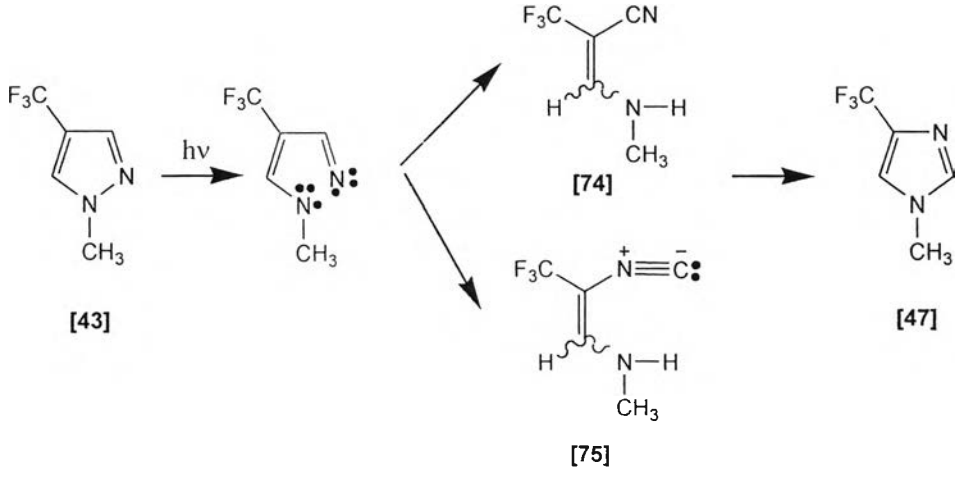
Figure 42 UV absorption spectra of **[43]** at various irradiation times (a) in acetonitrile (b) in methanol

1,4-Dimethylpyrazole **[9]** is known to undergo photocleavage to 3-(N-methylamino)-2-methylpropenenitrile **[19]** and 2-(N-methylamino)-1-

methylethenylisocyanide **[20]**, which are thermally and/or photochemically converted to the observed transposition product, 1,4-dimethylimidazole **[10]**.



Based on this, it can be assumed that 1-methyl-4-(trifluoromethyl)pyrazole **[43]** will transpose to 1-methyl-4-(trifluoromethyl)imidazole **[47]** via the two photocleavage



products 3-(*N*-methylamino)-2-(trifluoromethyl)propenenitrile **[75]** and 2-(*N*-methylamino)-1-(trifluoromethyl)ethenylisocyanide **[76]** intermediates.

Figure 21 shows that 1-methyl-4-(trifluoromethyl)imidazole **[43]** has an absorption maximum at 203 nm but does not absorb at 260 nm. This indicates that the absorption maximum observed near 200 nm after irradiation (Figure2) might be due to the formation of 1-methyl-4-(trifluoromethyl)imidazole **[43]**. This also clearly shows that the new absorption formed at 260 nm cannot be due to the formation of this transposition product.

Both enaminonitrile and enaminoisocyanide photocleavage products are known to absorb in the 260 nm region of the spectrum. These two types of

compounds have previously been distinguished on the basis of their stability in acidic medium. Thus, although enaminonitriles are generally stable upon addition of a small quantity of acid, enaminoisocyanides are immediately destroyed.

In order to determine the effects of added acid on the compound or compounds absorbing at 260 nm, a solution of pyrazole **[43]** in acetonitrile was irradiated for 30 minutes. The UV spectrum (Figure 43a) shows that the absorbance of 260 nm increased to 1.7 after this irradiation time. The figure also shows that addition of 1 microdrop of conc. HCl leads to a decrease in the absorbance from 1.7 to 1.1. Interestingly, addition of a second microdrop of HCl caused no further change in the absorbance at 260 nm. Figure 43b shows very similar results in methanol solvent. Thus, after 30 minutes of irradiation the absorbance at 260 nm increased to 1.5. This decreased to 1.05 after addition of 1 microdrop of acid but did not change after the addition of a second drop. These results indicate that the absorbance at 260 nm is due to two compounds. One compound is very sensitive to acid while the other is not. This suggests that the absorption at 260 nm is due to the two photocleavage products, 3-(N-methylamino)-2-(trifluoromethyl)propenenitrile **[48]** and 2-(N-methylamino)-1-(trifluromethyl)ethenylisocyanide **[49]**.

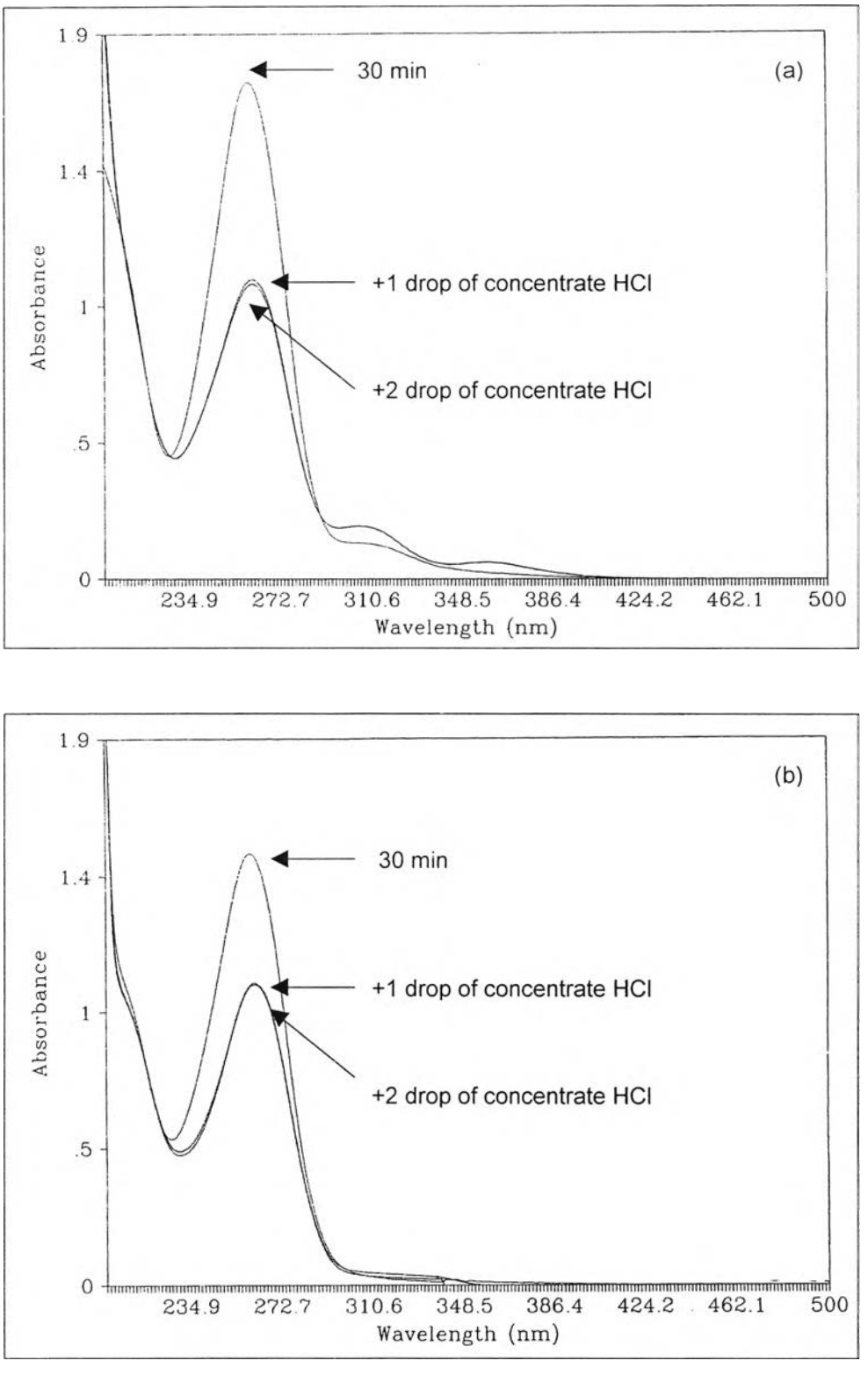


Figure 43 (a) UV absorption spectra of **[43]** in acetonitrile after 30 minutes of irradiation and the addition of one drop of acid (b) UV absorption spectra of **[43]** in methanol after 30 minutes of irradiation and the addition of one drop of acid

3.3.3 Investigation of the photoreaction by gas-liquid chromatography.

To monitor the photoreaction of 1-methyl-4-(trifluoromethyl)pyrazole **[43]** in acetonitrile, aliquots of 1μl of the solution were taken after 5, 10, 15, 20, and 30 minutes of irradiation for analysis by gas chromatography, using GC1 (Perkin Elmer Autosystem (9000) equipped with 15m x 0.53mm 50% phenyl silicone phase capillary column using temperature program (40 °C for 25 minutes, 100 °C for 10 minutes, and 140 °C for 5 minutes with temperature changing rate of 20 °C per minute)). As shown in Figure 4, before irradiation the gas chromatogram shows a single peak at a retention time of 13.8 minutes. Figures 44-49 show the continuous decrease in the area of the peak at 13.8 minutes due to the consumption of 1-methyl-4-(trifluoromethyl)pyrazole **[43]** and the appearance of four new peaks with retention times of 26.9, 28.2, 34.2, and 36.7 minutes which continued to increase in area throughout the irradiation.

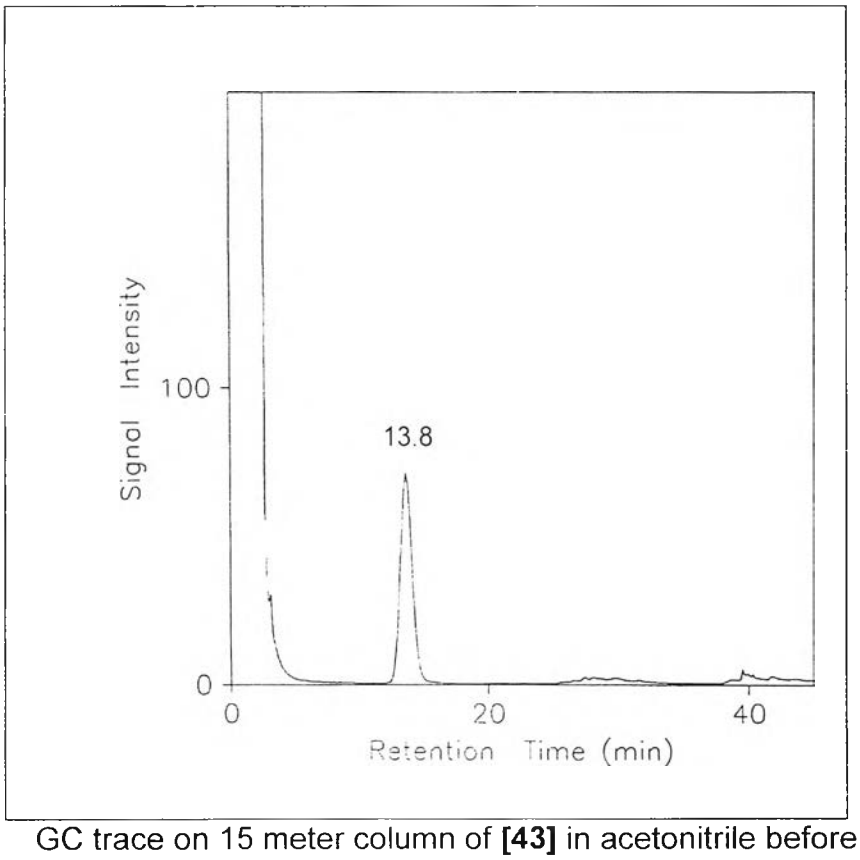


Figure 44 GC trace on 15 meter column of **[43]** in acetonitrile before irradiation

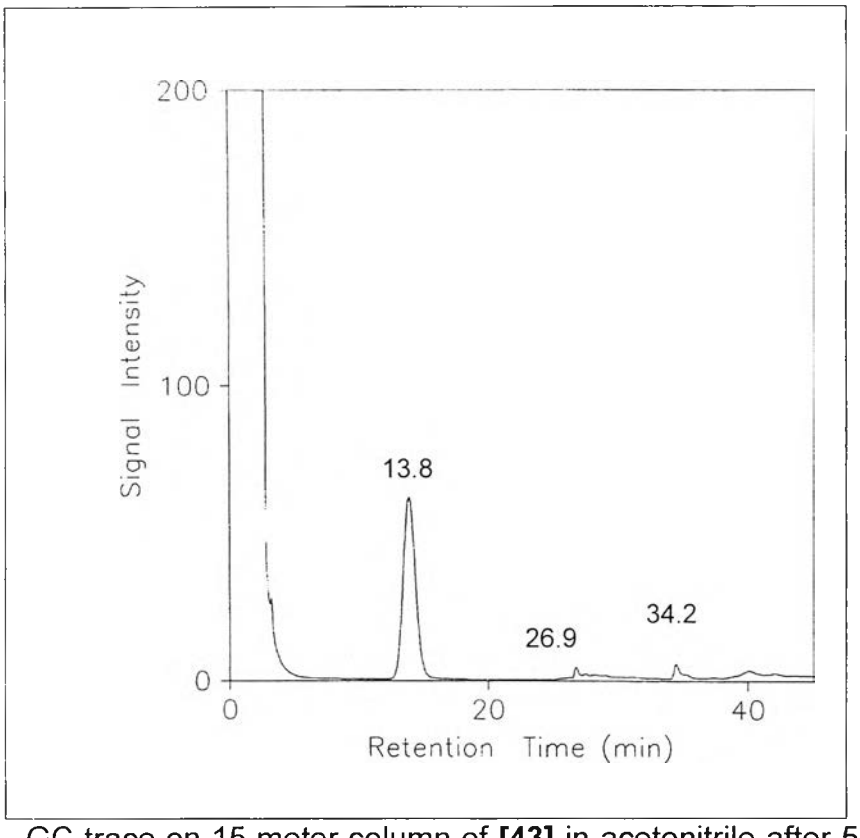


Figure 45 GC trace on 15 meter column of **[43]** in acetonitrile after 5 minutes of irradiation

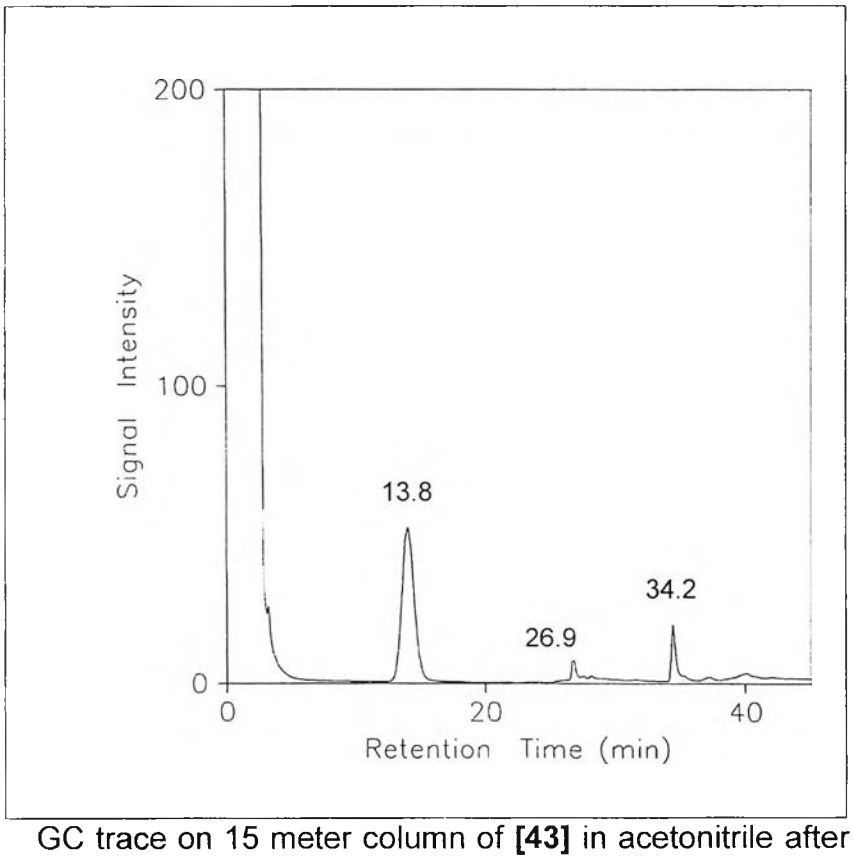


Figure 46 GC trace on 15 meter column of **[43]** in acetonitrile after 10 minutes of irradiation

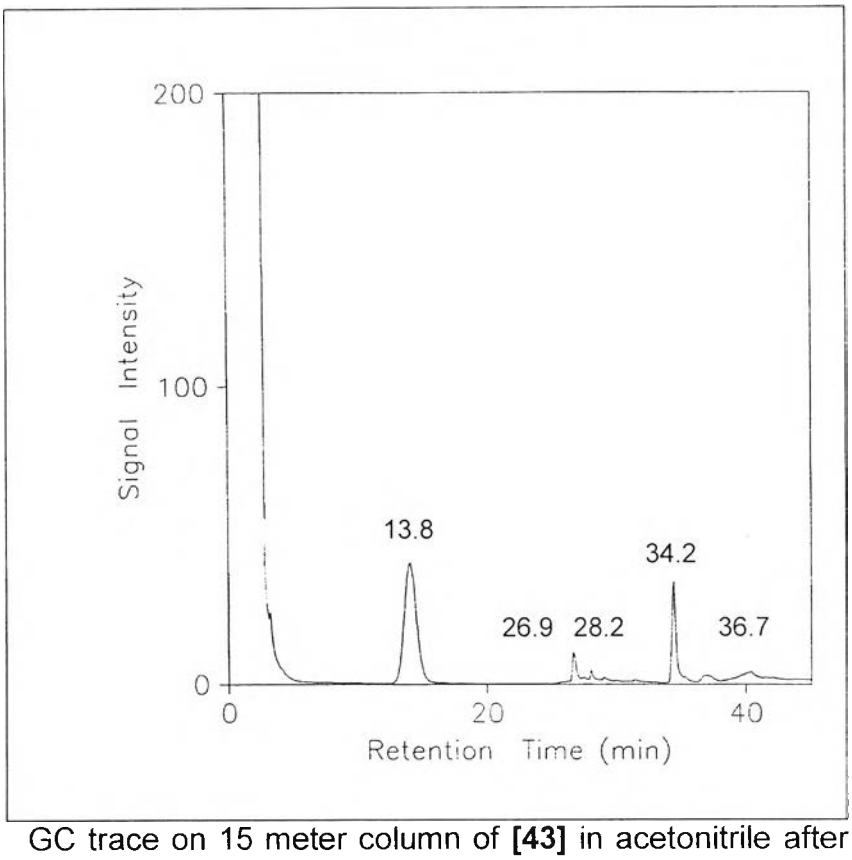


Figure 47 GC trace on 15 meter column of **[43]** in acetonitrile after 15 minutes of irradiation

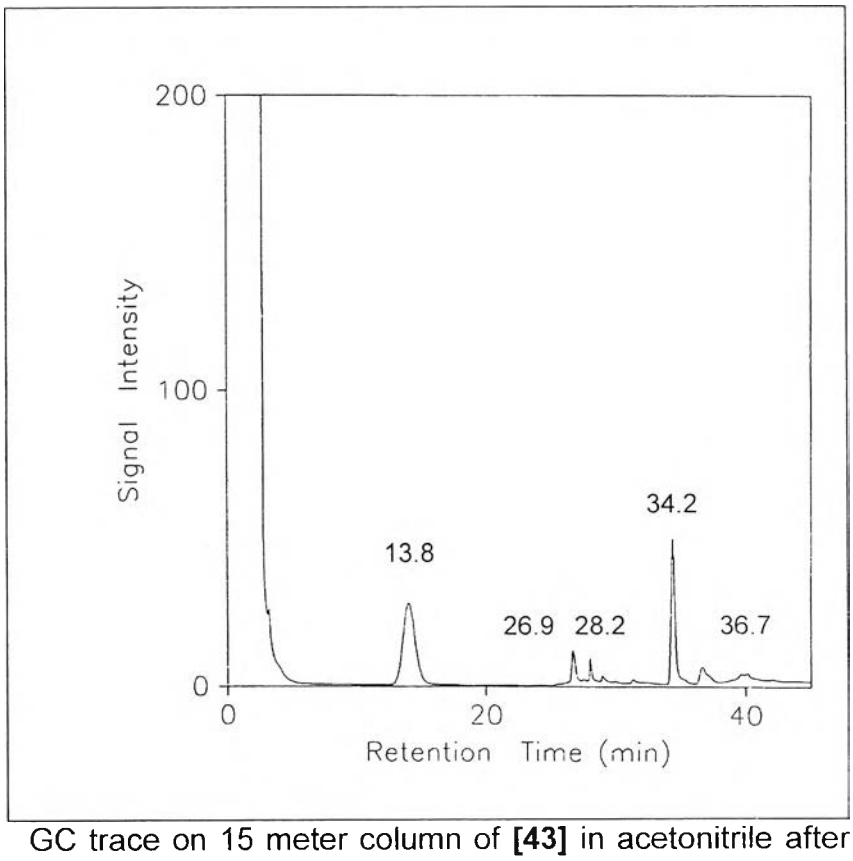


Figure 48 GC trace on 15 meter column of **[43]** in acetonitrile after 20 minutes of irradiation

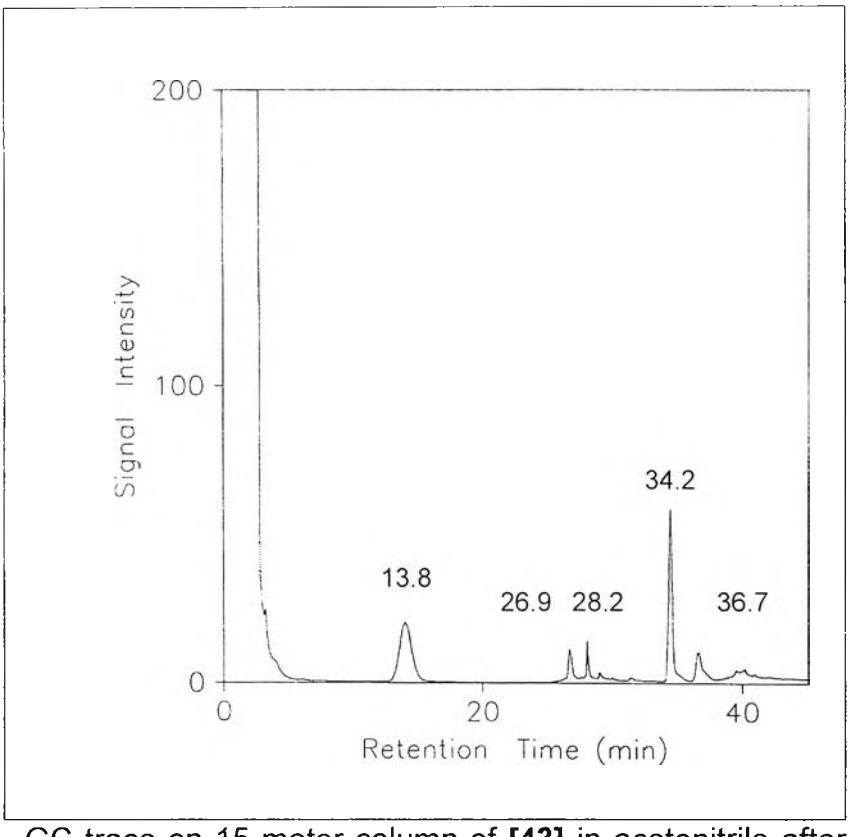


Figure 49 GC trace on 15 meter column of **[43]** in acetonitrile after 30 minutes of irradiation

It is possible the one of these observed product peaks is due to the formation of one of the three possible 1-methyltrifluoromethyl phototransposition products **[45-47]**. By comparison with the retention times of the known compounds on the 15 meter column, the peak at 34.2 minutes can be identified as 1-methyl-4-(trifluoromethyl)imidazole **[47]**. The peak observed at 26.9 minutes, however, is close to the retention time of 1-methyl-2-(trifluoromethyl)imidazole **[45]** and 1-methyl-5-(trifluoromethyl)-imidazole **[46]** which both elute at 26.5 minutes on the 15 meter column. Accordingly, the solution was also analyzed on the 30 meter column using the temperature program (35 °C for 5 minutes, 40 °C for 7 minutes, 60 °C for 15 minutes, 100 °C for 10 minutes, and 140 °C for 13 minutes with temperature changing rate of 20 °C per minute). Figure 50a shows that this substance elutes with a retention time of 27.9 minutes which does not correspond with the known retention times for either 1-methyl-2-(trifluoromethyl)imidazole **[45]** or 1-methyl-5-(trifluoromethyl)imidazole **[46]**. To confirm this, a portion of the photolysate was first spiked with authentic **[45]**. Figure 50b shows that authentic **[45]** eluted with a retention time of 28.2 minutes and is clearly resolvable with the

peak at 27.9 minutes. A second portion of the photolysate was then spiked with authentic **[46]**. Figure 50c shows that this compound eluted with a retention time of 27.6 minutes and was also resolvable with the product, which elutes at 27.9 minutes. This confirms that the observed product is neither **[45]** nor **[46]**.

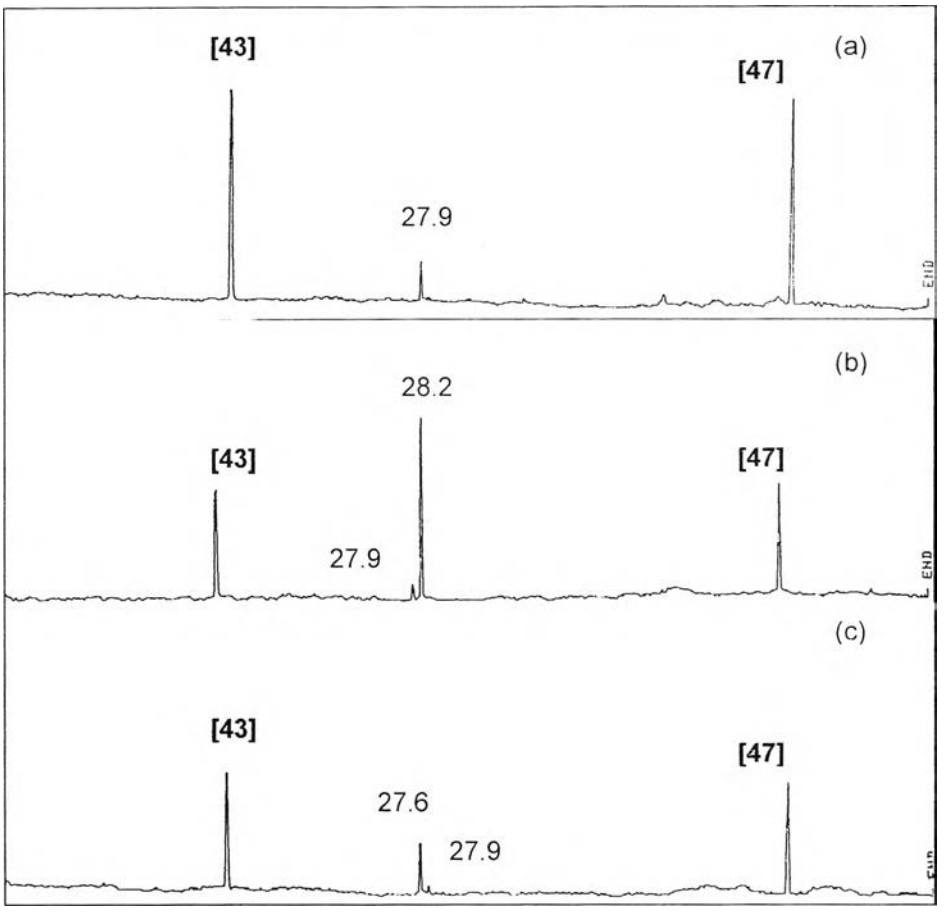


Figure 50 (a) GC on 30 meter column trace of **[43]** after 30 minutes of irradiation (b) GC trace on 30 meters column of **[43]** after 30 minutes of irradiation added authentic 1-methyl-2-(trifluoromethyl)imidazole **[45]** (c) GC trace on 30 meters column of **[43]** after 30 minutes of irradiation added authentic 1-methyl-5-(trifluoromethyl)imidazole **[46]**

The photoreaction of 1-methyl-4-(trifluoromethyl)pyrazole **[43]** in acetonitrile after 5 minutes of irradiation showed that 11% ($5x10^{-6}$ mol) of **[43]** was consumed to generate an 83% yield of 1-methyl-4-(trifluoromethyl)imidazole **[47]** and the unidentified product at retention time 26.9 minutes. After 10 and 15 minutes of irradiation the products at retention times of 28.2 and 36.7 were also detected.

From these results it appears that only the product at retention time 34.2 due to 1-methyl-4-(trifluoromethyl)imidazole **[47]** is the primary photoproduct.

3.3.4 Analysis of irradiation solution by GC-MS.

Figure 51 shows the GC-MS analysis of 1-methyl-4-(trifluromethyl)pyrizole **[43]** before irradiation. This shows that **[43]** has a retention time of 13.9 minutes on the GC-MS column. The mass spectrum of this material shows a molecular ion at m/z 150, as expected for the reactant, and major fragmentation peaks at m/z 149, due to loss of one hydrogen atom from the molecular ion, and m/z 131, due to loss of one fluorine atom. Figure 52 a shows the GC trace on the GC-MS after 30 minutes of irradiation. This shows a small peak at 13.9 minutes due to a small amount of unconverted 1-methyl-4-(trifluoromethyl)pyrazole **[43]** reactant and peaks at retention times of 35.3 minutes and 36.7 minutes due to the major and minor photoproducts respectively. The mass spectra of these two photoproducts are shown in Figures 52c and 52d. Both mass spectra exhibit molecular ions at m/z 150 showing that the two products are isomeric with each other and isomeric with the reactant. The mass spectrum of the major product also exhibits fragment peaks at m/z 149 and 131 characteristic of trifluorosubstituted-1-methylpyrazoles and imidazoles. Based on this and the gas chromatographic retention time this product was identified as minor product shown in Figure 52c is isomeric with **[43]** and **[47]**, the mass spectrum does not exhibit peaks at M^+-1 and M^+-19 that are characteristic of trifluoromethyl-1-methylpyrazole or trifluoromethyl-1-methyl-imidazole. Instead, the spectrum shows a fragment peaks at m/z 81 and m/z 69 which are likely due to the M^+-CF_3 and CF_3 fragments. This product is not identified at this time but might be due to the enaminonitrile **[48]**.

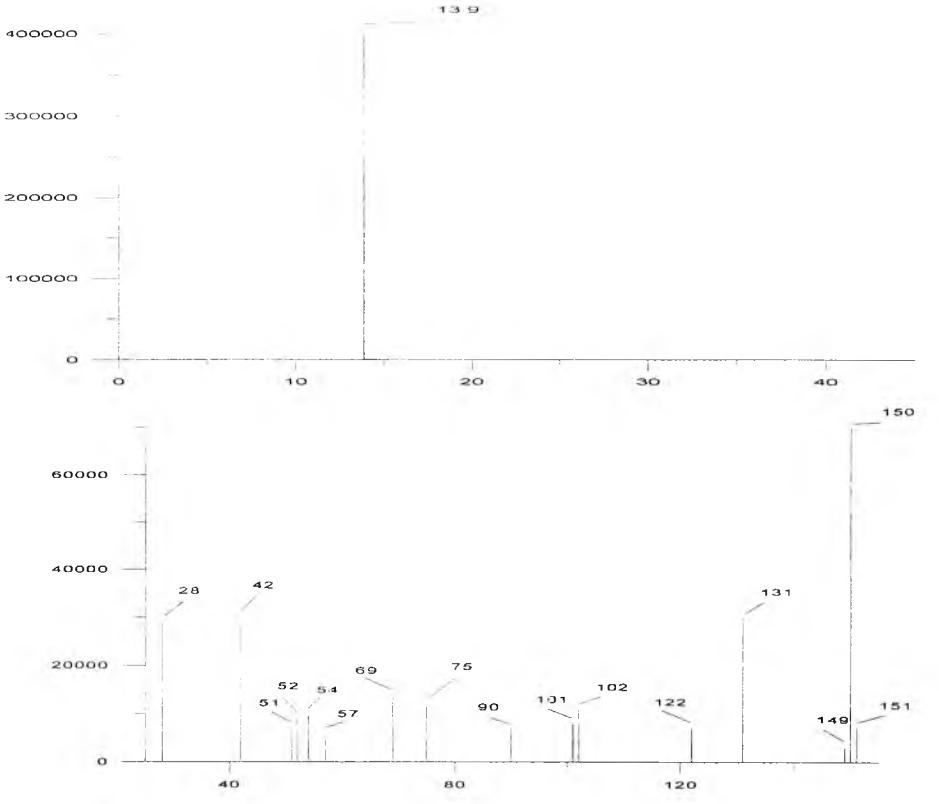


Figure 51 The GC-MS of 1-methyl-4-(trifluoromethyl)pyrazole **[43]**

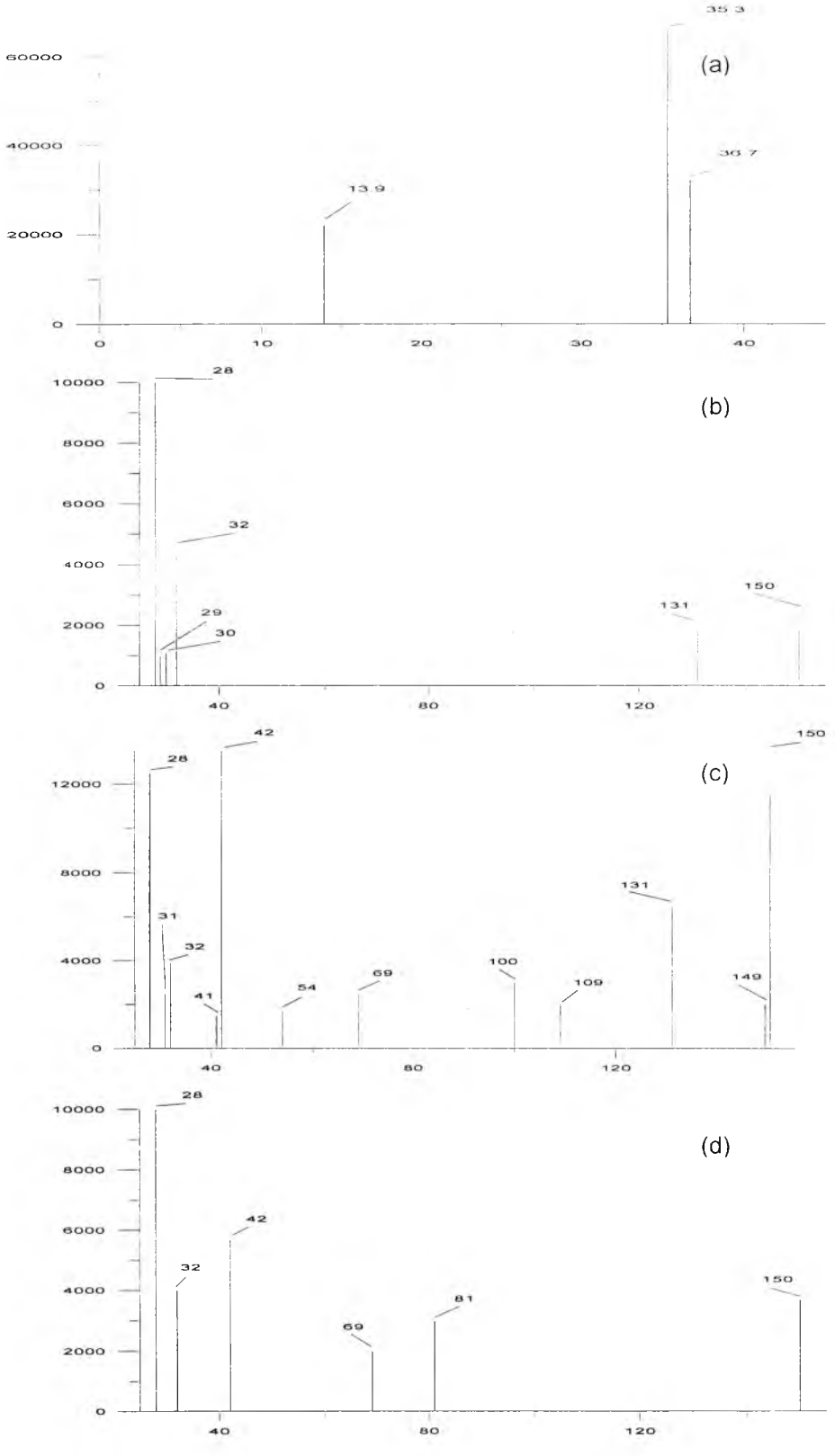
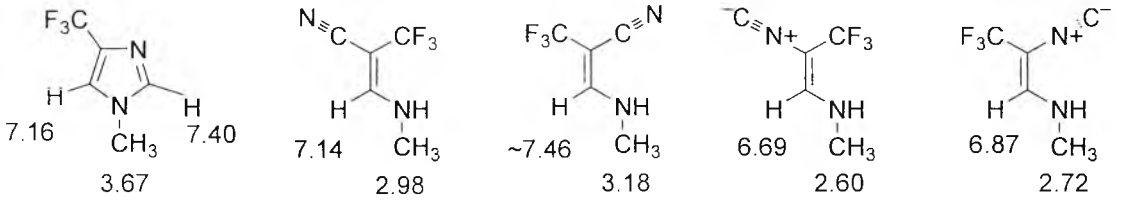


Figure 52 (a) The GC trace of **[43]** after 30 minutes of irradiation (from GC-MS) (b) The mass spectrum of peak at retention time 13.9 minutes (c) 35.3 minutes (d) 36.7 minutes

3.3.5 ^{1}H-NMR spectrum of the photolysate of 1-methyl-4-(trifluoromethyl)pyrazole

After 30 minutes of irradiation in acetonitrile (3.0 ml, $1.5x10^{-2}$ M) the resulting solution was concentrated and the residue was dissolved in $CDCl_3$ and analyzed by ^{1}H-NMR. The full spectrum is shown in Figure 53 with scale expansions shown in Figures 54a, 54b, and 54c. ^{1}H-NMR spectrum of product mixture was compared with the spectra of the authentic compounds synthesized in this work. Figure 54a shows the ^{1}H-NMR spectrum from δ 2.3-3.3 ppm. The spectrum exhibits a singlet at δ 2.98 (d, 3H, J = 4.6 Hz) due to the *N*-methyl protons of (Z)-3-(*N*-methylamino)-2-(trifluoromethyl)propenenitrile **[(Z)-48]**, a singlet at δ 3.18 (d, 3H, J = 5.3 Hz) due to the *N*-methyl protons of (E)-3-(*N*-methylamino)-2-(trifluoromethyl)propenenitrile **[(E)-49]**, a singlet at δ 2.72 (d, 3H, J = 5.0 Hz) due to the *N*-methyl protons of (Z)-2-(*N*-methylamino)-1-(trifluoromethyl)ethenylisocyanide **[(Z)-48]**, and a singlet at δ 2.60 (d, 3H, J = 5.2 Hz) due to the *N*-methyl protons of (E)-2-(*N*-methylamino)-1-(trifluoromethyl)ethenylisocyanide **[(E)-49]** Figure 54b shows the ^{1}H-NMR spectrum from δ 3.3-5.3 ppm where the N-methyl protons of *N*-methylpyrazoles and *N*-methylimidazoles are known to absorb. As shown, the spectrum exhibits a singlet at δ 3.87 due to the *N*-methyl group of the reactant 1-methyl-4-(trifluoromethyl) pyrazole **[43]**, and a singlet at δ 3.67 for the *N*-methyl protons of **[47]**, but no signal at δ 3.70 and 3.72 where the *N*-methyl protons of 1-methyl-2-(trifluoromethyl) imidazole **[45]** and 1-methyl-5-(trifluoromethyl)imidazole **[46]** respectively are known to absorb. Figure 54c shows the ^{1}H-NMR spectrum from δ 6.5-8.0 ppm where the ring protons of *N*-methylpyrazoles and *N*-methylimidazoles are known to absorb. As shown, the spectrum exhibits signals at δ 7.58 and 7.61 due to a proton on C-5 and a proton on C-3 respectively of the reactant 1-methyl-4-(trifluoromethyl) pyrazole **[43]**, signals at δ 7.42 and 7.16 due to a proton on C-2 and a proton on C-5 respectively of **[47]**, but no signal at δ 6.99 and 6.91 where the proton on C-4 and C-5 respectively of 1-methyl-2-(trifluoromethyl)imidazole **[45]** or at δ 7.46 and 7.36 where the proton on C-2 and C-4 respectively of 1-methyl-5-(trifluoromethyl) imidazole **[46]** are known to absorb. Furthermore, the spectrum also shows a doublet at δ 7.14 (d, 1H, J = 14.4 Hz) due to a proton on C-3 of (Z)-3-(*N*-methylamino)-2-(trifluoromethyl)propenenitrile **[(Z)-48]**, and a signal at δ ~7.46 due

to a proton on C-3 of (E)-3-(*N*-methylamino)-2-(trifluoromethyl)propenenitrile **[(E)-48]**. Unfortunately, the signal for the proton on C-3 of **[(E)-48]** appears near the signal of the C-2 proton of **[3]**, so one of doublet peak of the product overlap with the signal for the proton of **[3]**. In addition, the spectrum exhibits a signal at δ 6.87 (d, 1H, J = 14.9 Hz) due to the proton on C-2 of (Z)-2-(*N*-methylamino)-1-(trifluoromethyl)ethenylisocyanide **[(Z)-49]**, and the signal at δ 6.69 (d, 1H, J = 13.6 Hz) due to the proton on C-2 of (E)-2-(*N*-methylamino)-1-(trifluoromethyl) ethenylisocyanide **[(E)-49]**.



[47] **[(Z)-48]** **[(E)-48]** **[(E)-49]** **[(Z)-49]**

Scheme 11 Assignment of the chemical shifts for the protons of components in the photolysate **[43]** in acetonitrile after 30 minutes of irradiation

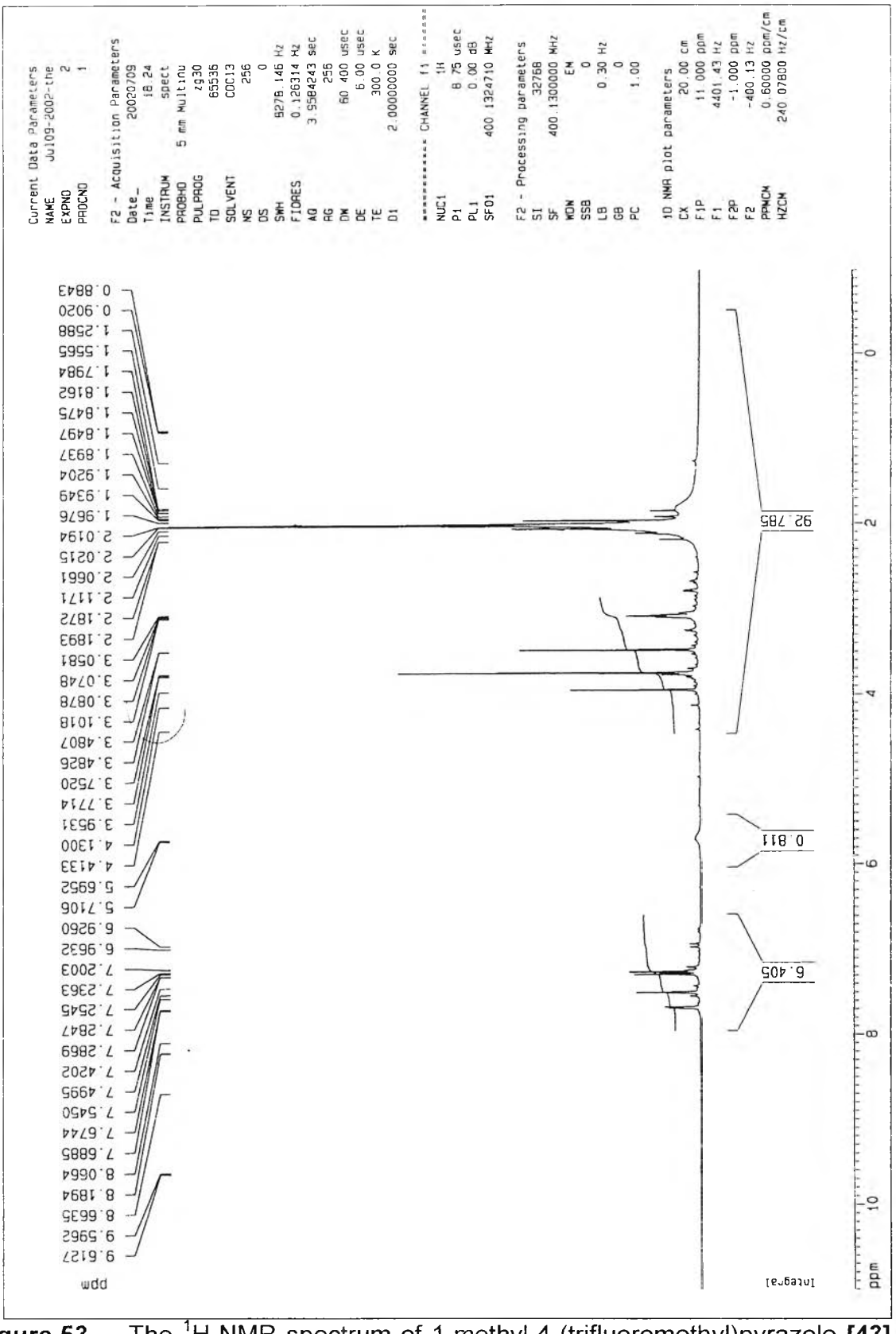


Figure 53 The ^{1}H-NMR spectrum of 1-methyl-4-(trifluoromethyl)pyrazole **[43]** in acetonitrile after 30 minutes of irradiation

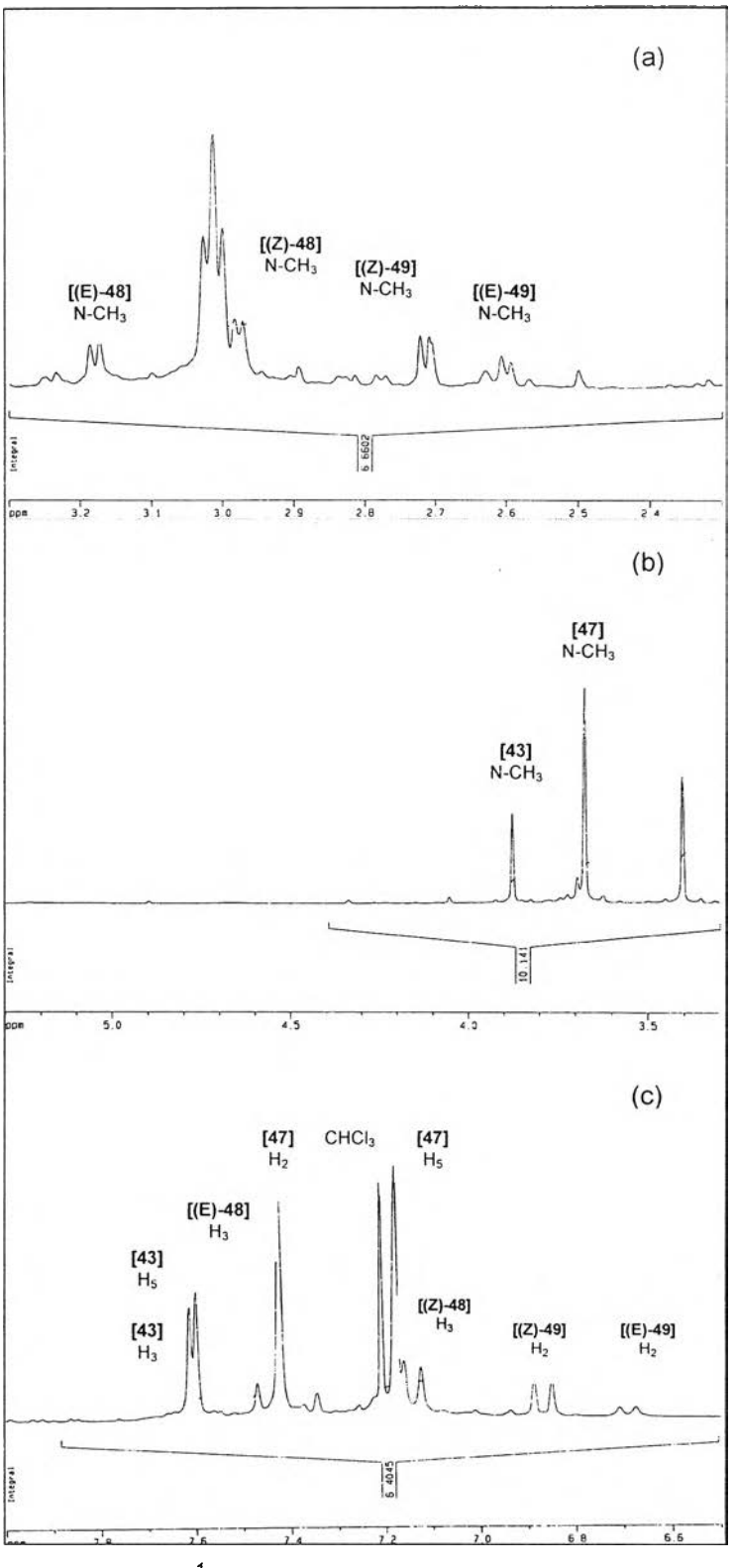


Figure 54 The expantion of ^{1}H-NMR spectra of **[43]** in acetonitrile after 30 minutes of irradiation (a) 2.3-3.3 ppm (b) 3.3-5.3 ppm (c) 6.5-8.0 ppm

Pyrazoles with hydrogen at C-3 are known to undergo photocleavage to enaminonitriles and enaminoisocyanide. To confirm the formation of enaminonitrile and isocyanide in the photolysate, the concentrated photolysate after 30 minutes of

irradiation was analyzed by IR spectrometer. Normally, cyano and isocyano groups would show symmetric stretching at 2300 cm^{-1} and 2200 cm^{-1} respectively. Figure 55, shows the IR spectra of 1-methyl-4-(trifluoromethyl)pyrazole **[43]**, the photolysate in the acetonitrile, and photolysate in methanol. These spectra reveal that the residues have absorption at 2210 and 2306 cm^{-1}. These results are consistent with the formation of enaminonitrile **[48]** and enaminoisocyanide **[49]** in these reactions.

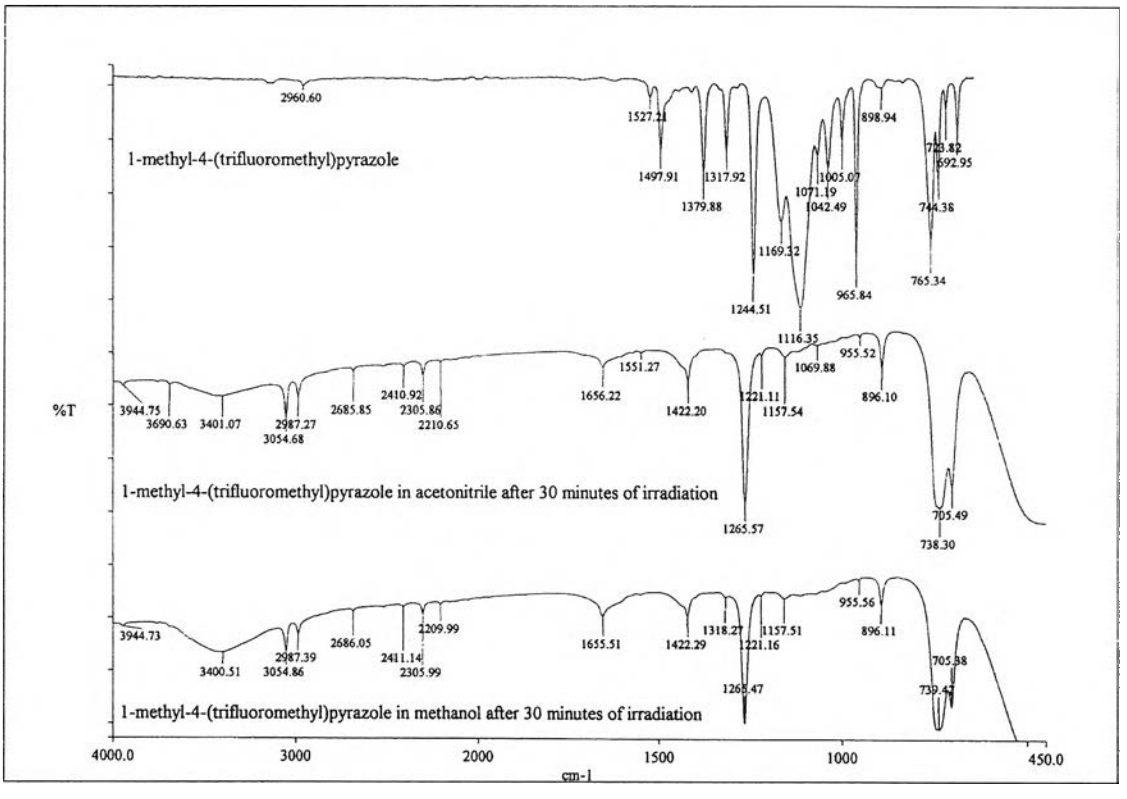


Figure 55 IR speatra of 1-methyl-4-(trifluoromethyl)pyrazole **[43]**, photolysate in acetonitrile after 30 minutes of irradiation, and photolysate in methanol after 30 minutes of irradiation

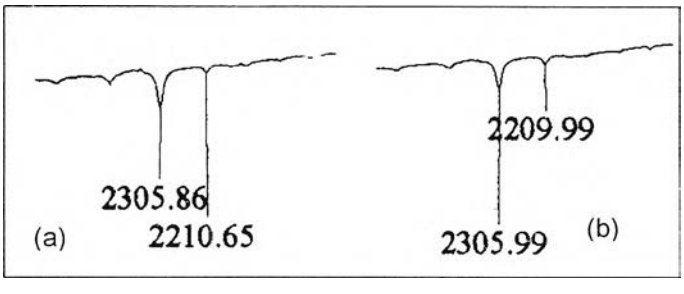
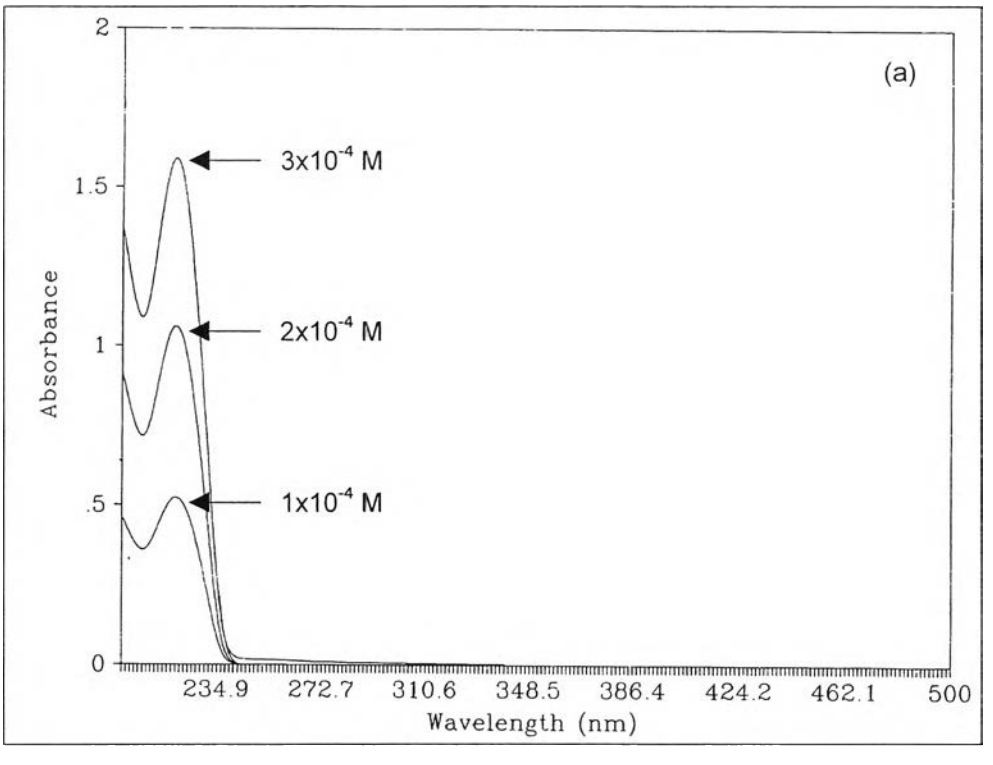


Figure 56 (a) Expansion IR spectra of 1-methyl-4-(trifluoromethyl)pyrazole **[43]**, photolysate in acetonitrile after 30 minutes of irradiation (b) photolysate in methanol after 30 minutes of irradiation

3.4 Photoreaction of 1-methyl-5-(trifluoromethyl)pyrazole

3.4.1 UV-Absorption analysis of 1-methyl-5-(trifluoromethyl)pyrazole.

The UV absorption spectrum of 1-methyl-5-(trifluoromethyl)pyrazole **[42]** was recorded in acetonitrile or methanol solvent at concentrations of $3x10^{-4}$ M, $2x10^{-4}$ M, and $1x10^{-4}$ M. The spectra, as shown in Figure 57, displayed an absorption maximum at 220 nm with an extinction coefficient, $\in$, of 5300 $M^{-1}cm^{-1}$. Because of this absorption maximum at 220 nm it was necessary to irradiate this compound with a 450 W medium pressure Hg lamp which has output at that wavelength. Other low pressure lamps have outputs at 254 nm, 300 nm, and 360 nm but no output at 220 nm.



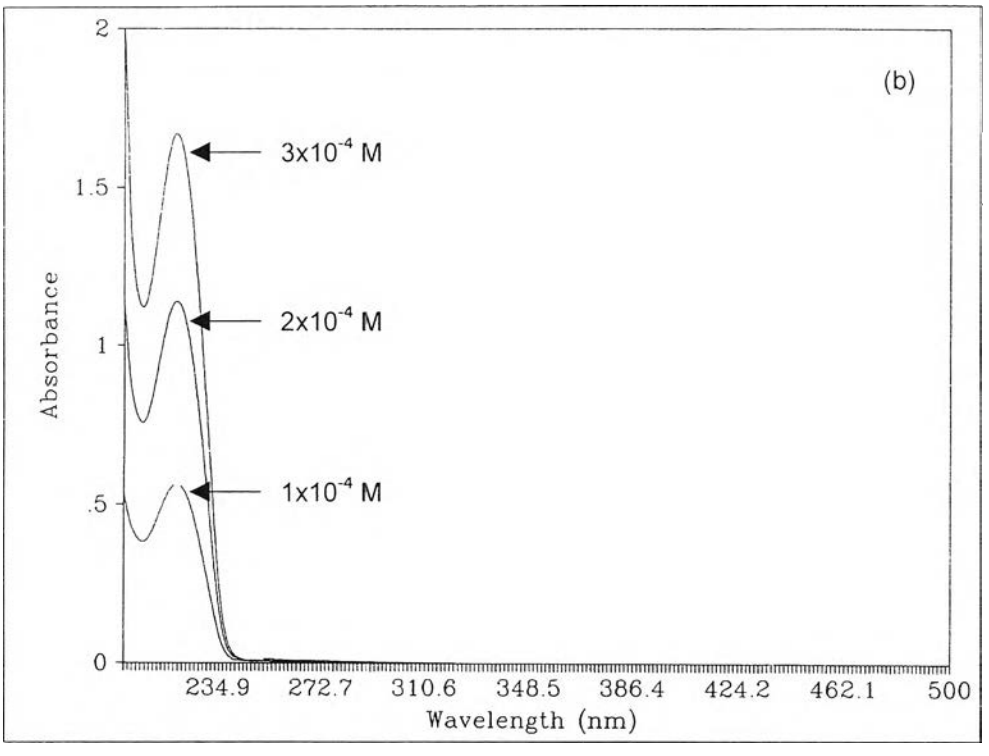


Figure 57 UV absorption spectra of **[42]** (a) in acetonitrile (b) in methanol

3.4.2 Investigation of the photoreaction by UV spectrophotometer.

The solution of 1-methyl-5-(trifluoromethyl)pyrazole **[42]** in acetonitrile or methanol (3.0ml, $1.5x10^{-2}$ M) was placed in a quartz tube (diameter = 7 mm and length = 12 cm), sealed with a rubber septum, purged with a fine stream of nitrogen for 5 minutes and then irradiated with the Hanovia lamp under a nitrogen atmosphere. The reaction was monitored by UV spectroscopy. After each period of irradiation an aliquot of the solution was removed and diluted (1:75). Figure 58a shows the UV absorption spectrum of **[42]** in acetonitrile solution before irradiation and after irradiation times of 5, 10, 15, and 30 minutes. As the spectra show, irradiation is accompanied by a decrease in the absorption maximum at 220 nm and to formation of a new absorption band at 261 nm. Figure 58b also shows that irradiation is accompanied by similar changes upon irradiation in methanol solvent. From these results it appears that 1-methyl-5-(trifluoromethyl)pyrazole **[42]** is photochemically converted to a compound absorbing at 261 nm. These results are very similar to the results observed upon irradiation of 1-methyl-4-(trifluoromethyl) pyrazole **[47]** but quite different from those observed upon irradiation of 1-methyl-3-(trifluoromethyl)pyrazole **[39]**.

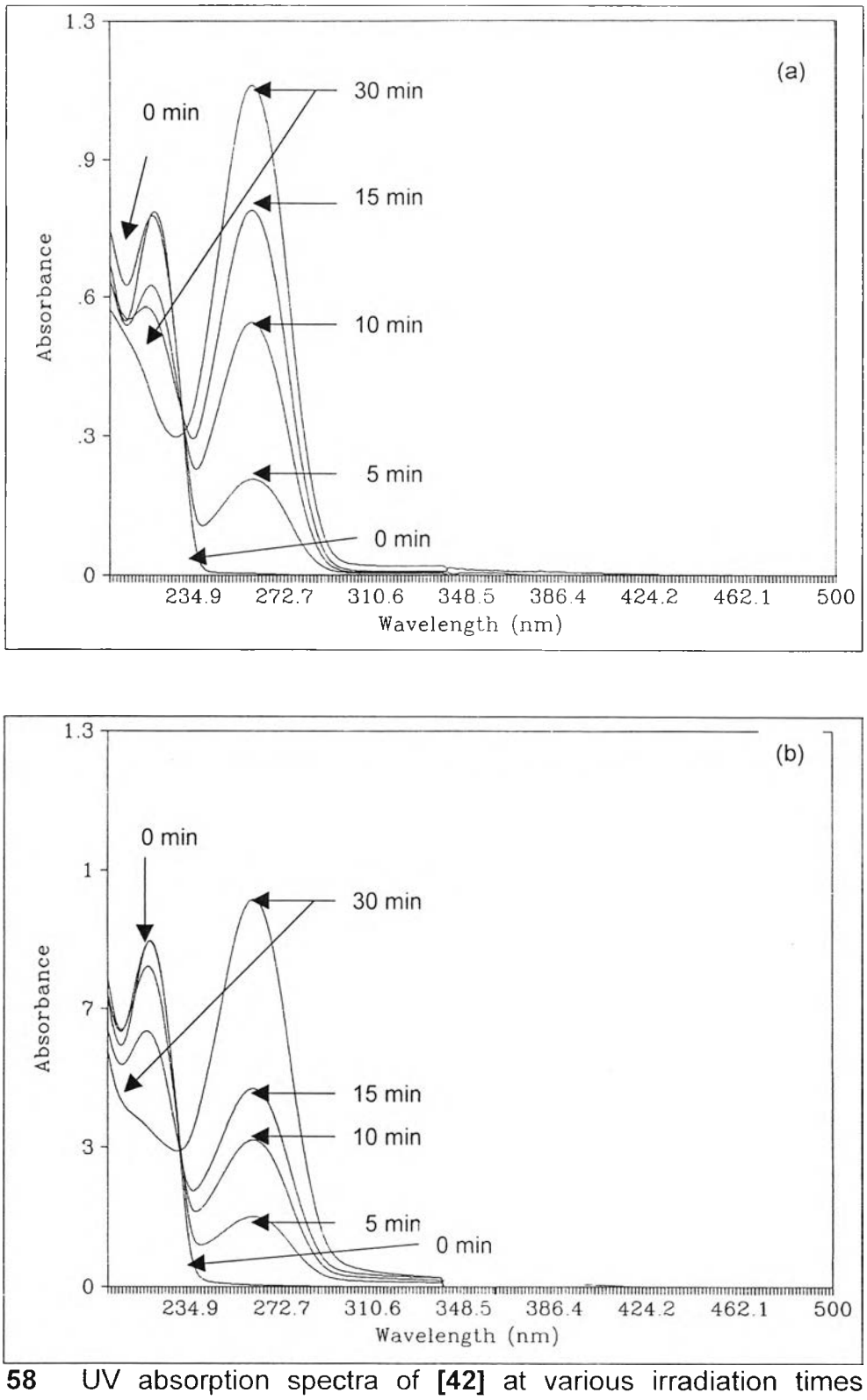
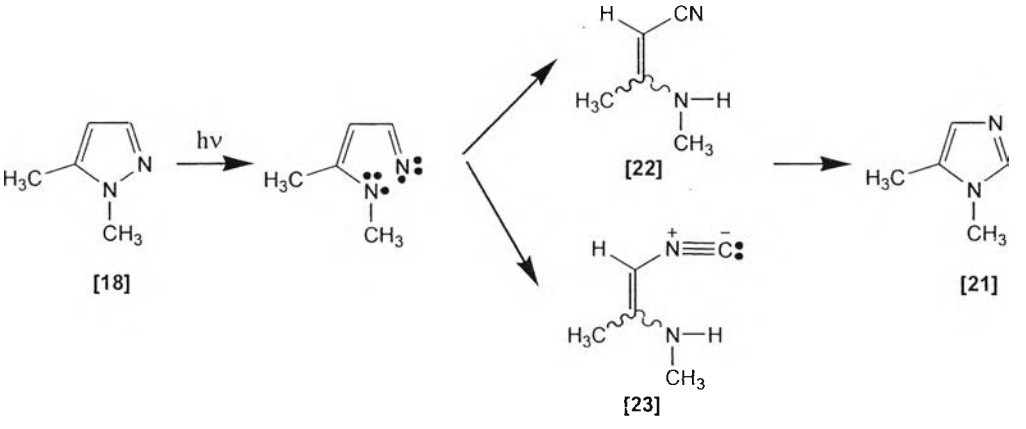


Figure 58 UV absorption spectra of **[42]** at various irradiation times (a) in acetonitrile (b) in methanol

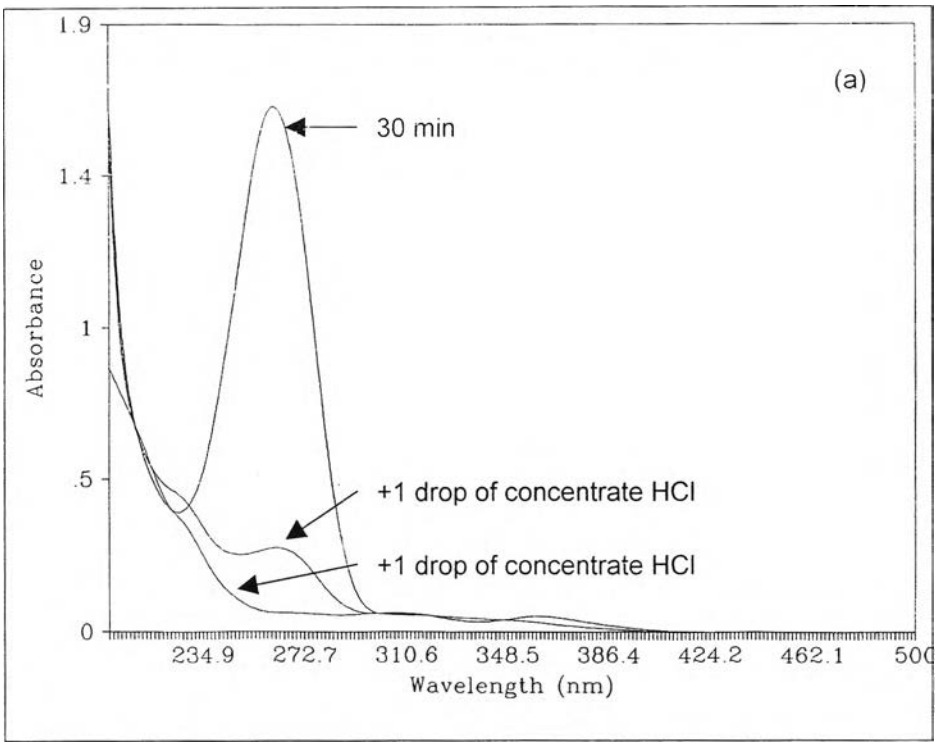
1,5-Dimethylpyrazole **[18]** is known to phototranspose to 1,5-dimethylimidazole **[21]**, 1,2-dimethylimidazole **[8]**, and 1,4-dimethylimidazole **[10]**. The two photocleavage products 3-(*N*-methylamino)-3-methyl propenenitrile **[22]**



and 2-(*N*-methylamino)-2-methylethylisocyanide **[23]** were also formed and observed to undergo subsequent photocyclization to 1,5-dimethylimidazole **[21]**.

The changes in the UV-absorption spectrum upon irradiation of 1-methyl-5-(trifluoromethyl)pyrazole **[42]** shown in Figure 58 do not indicate the formation of imidazole phototransposition products but the new absorption band at 260 nm is consistent with the formation of an enaminonitrile and/or an enaminoisocyanide.

In order to distinguish between these two possible photocleavage products, the solutions of 1-methyl-5-(trifluoromethyl)imidazole **[46]** in acetonitrile or methanol were irradiated for 30 minutes after which the absorbance at 260 nm increased to 1.6 in acetonitrile or 1.35 in methanol. After addition of one microdrop of hydrochloric acid the absorbance at 260 nm decreased from 1.6 unit to 0.3 unit in acetonitrile and from 1.35 to 0.4 in methanol (Figures 59a and 59b). After addition of another microdrop of acid the remaining absorption band at 260 nm completely disappeared. Since all of the material absorbing at 260 nm is sensitive to acid, it appears that the absorption band is due only to the presence of the enaminoisocyanide photocleavage product. ^{1}H-NMR and IR experiments, however, show that both enaminonitrile and enaminoisocyanide photocleavage products are formed in the reaction. Thus, it appears that in this case both photoclevage products react with hydrochloric acid.



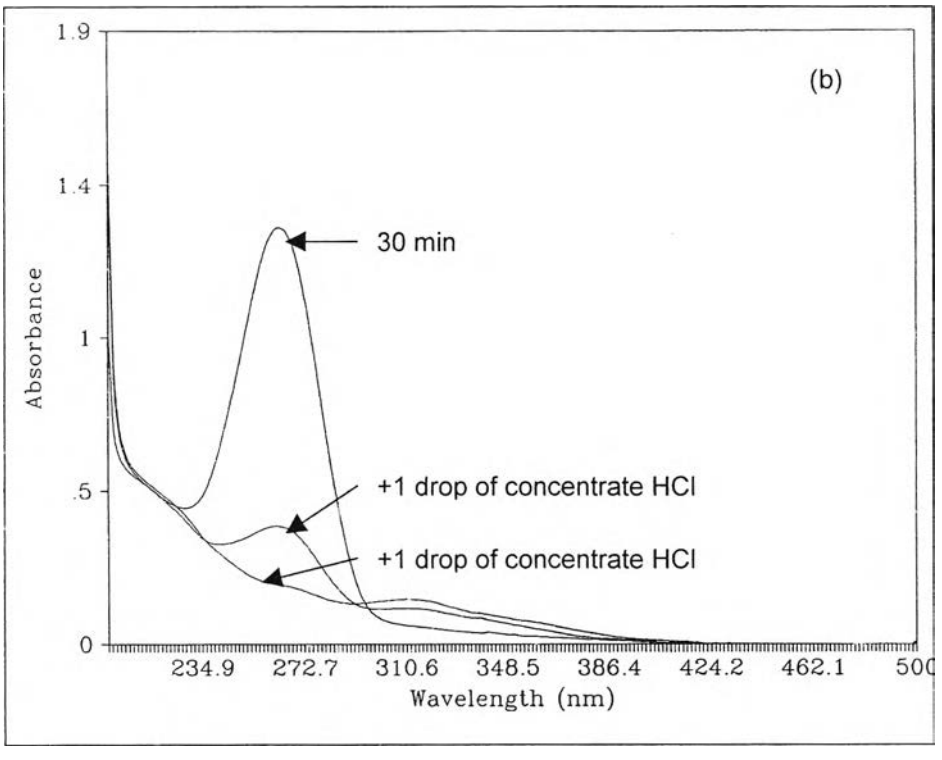


Figure 59 (a) UV absorption spectra of **[42]** in acetonitrile after 30 minutes of irradiation and added drop of acid (b) UV absorption spectra of **[42]** in methanol after 30 minutes of irradiation and added drop of acid

3.4.3 Investigation of the photoreaction by gas-liquid chromatography.

To monitor the photoreaction of 1-methyl-5-(trifluoromethyl)pyrazole **[42]** in acetonitrile, aliquots of 1μl of the solution were taken after 5, 10, 15, 20, and 30 minutes of irradiation for analysis by gas chromatography using GC1 (Perkin Elmer Autosystem (9000) equipped with 15m x 0.53mm 50% phenyl silicone phase capillary column using temperature program (40 °C for 25 minutes, 100 °C for 10 minutes, and 140 °C for 5 minutes with temperature changing rate of 20 °C per minute)) for the consumption of **[42]** and GC2 (PE-8500 FID instument equipped with a 30m x 0.25mm i.d. fused silica column coated with 0.25μ Supelwax 10 bonded phase using temperature program (35 °C for 5 minutes, 40 °C for 7 minutes, 60 °C for 15 minutes, 100 °C for 10 minutes, and 140 °C for 13 minutes with temperature changing rate of 20 °C per minute)) for the formation of photoproducts. As shown in Figure 60a, before irradiation the gas chromatogram obtained on the 15 meters column shows the peak at a retention time of 3.1 minutes. Figure 60a-65a show the continuous decrease in the area of the peak at 3.1 minutes due to the consumption of 1-methyl-5-(trifluoromethyl)pyrazole **[42]** and the appearance of six new peaks which were separated on the 30 meters column with retention times of 12.7, 23.0, 27.6, 28.2, 46.3 and 47.3 minutes which continued to increase in area throughout the irradiation (Figure 60b-65b).

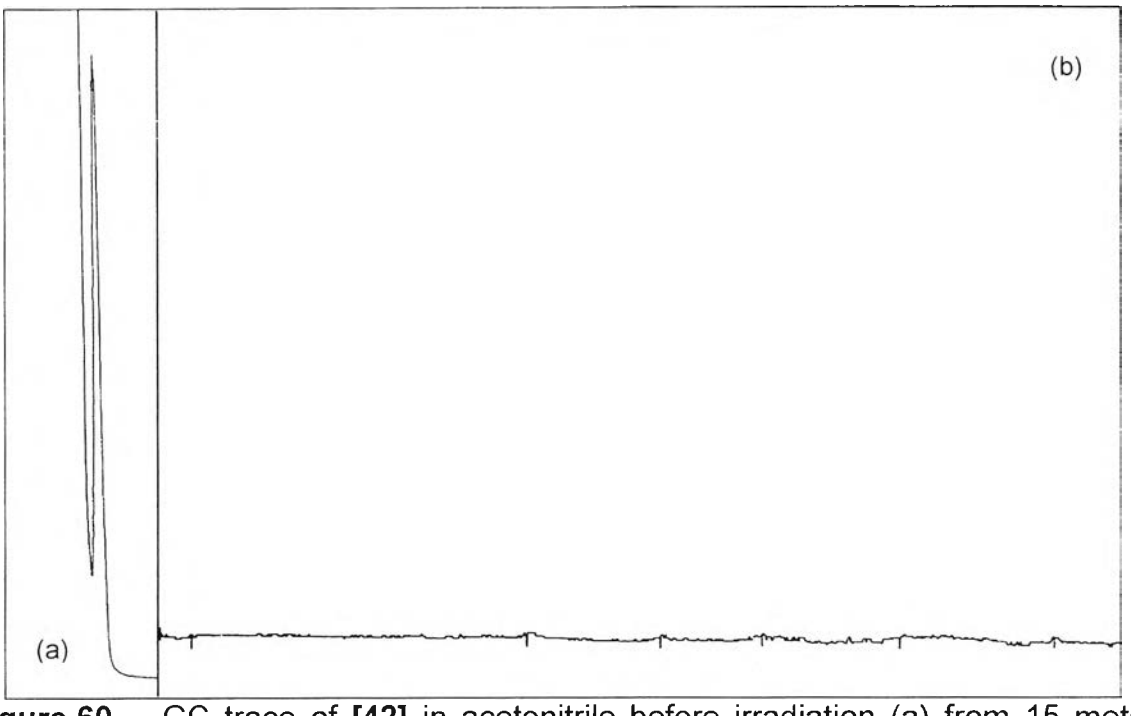


Figure 60 GC trace of **[42]** in acetonitrile before irradiation (a) from 15 meter column (b) from 30 meter column

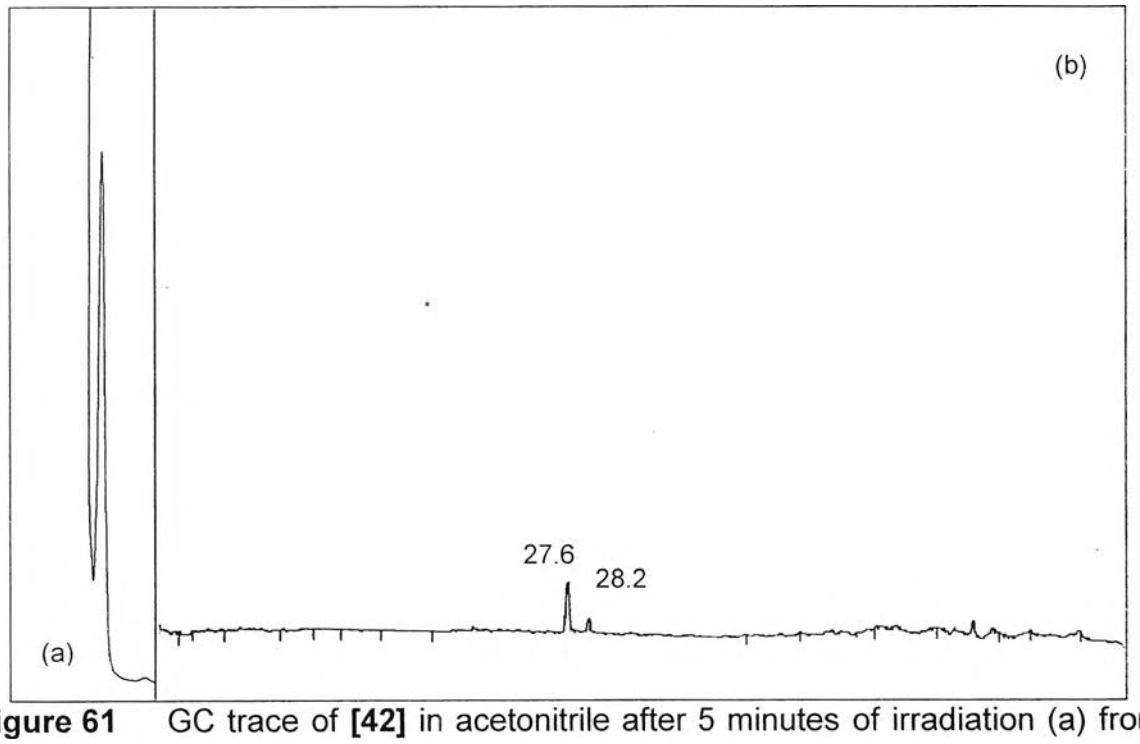


Figure 61 GC trace of **[42]** in acetonitrile after 5 minutes of irradiation (a) from 15 meter column (b) from 30 meter column

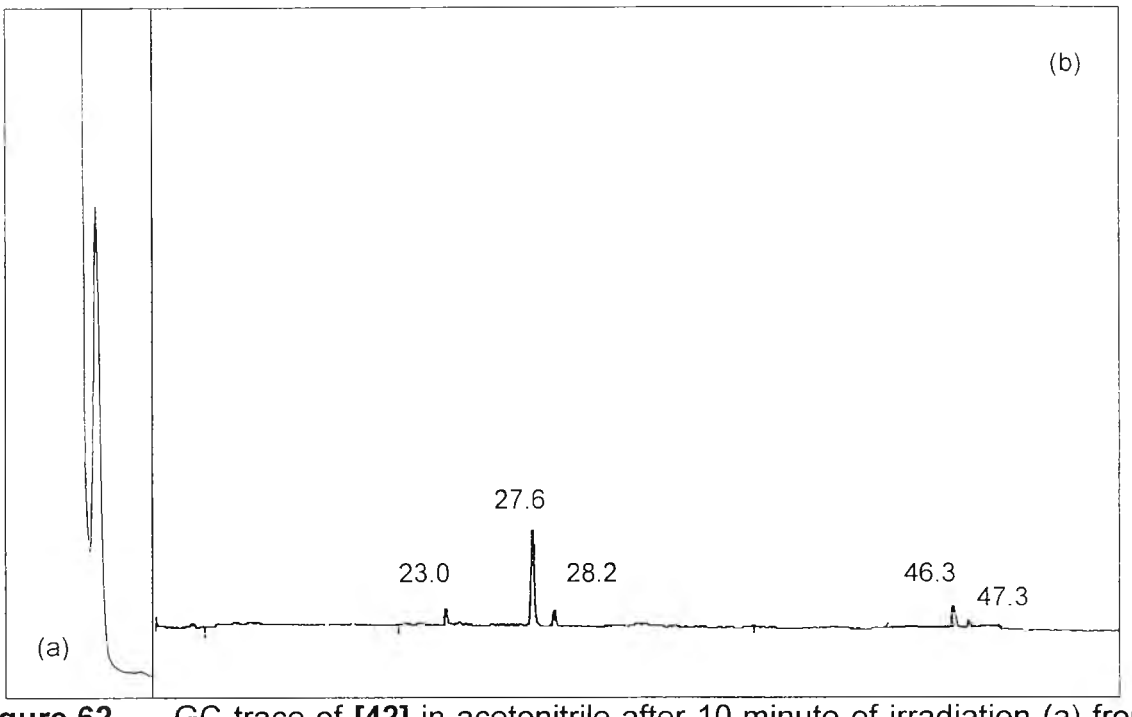


Figure 62 GC trace of **[42]** in acetonitrile after 10 minute of irradiation (a) from 15 meters column (b) from 30 meter column

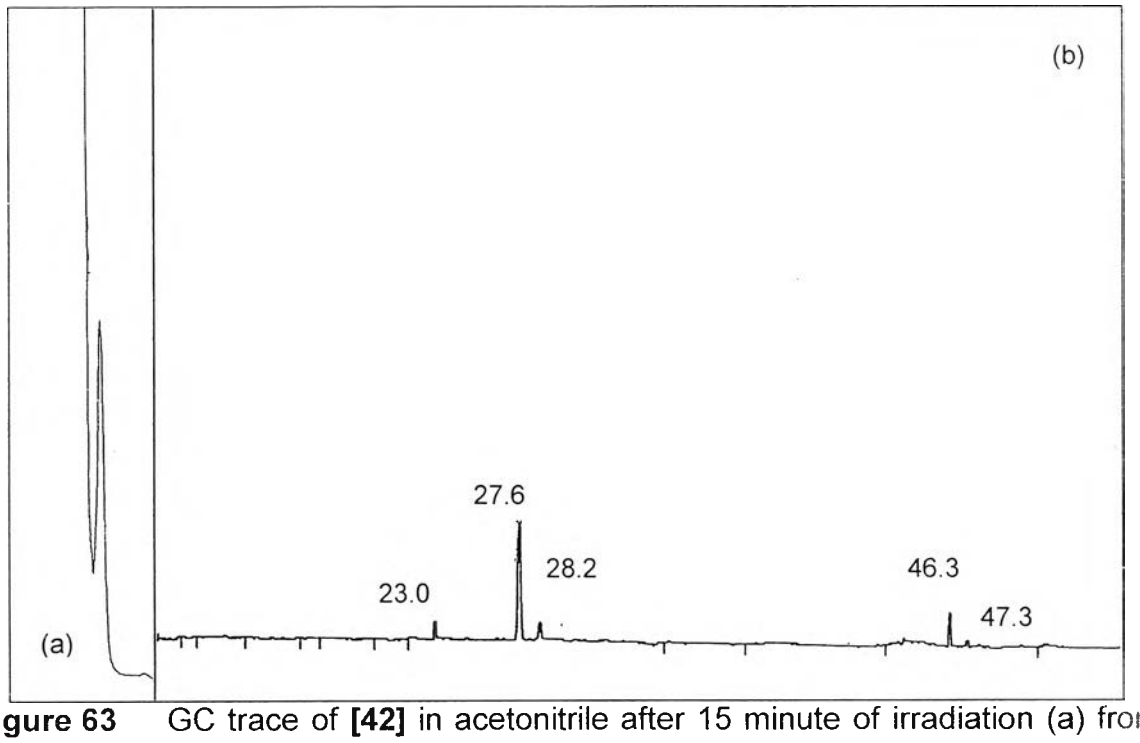


Figure 63 GC trace of **[42]** in acetonitrile after 15 minute of irradiation (a) from 15 meters column (b) from 30 meter column

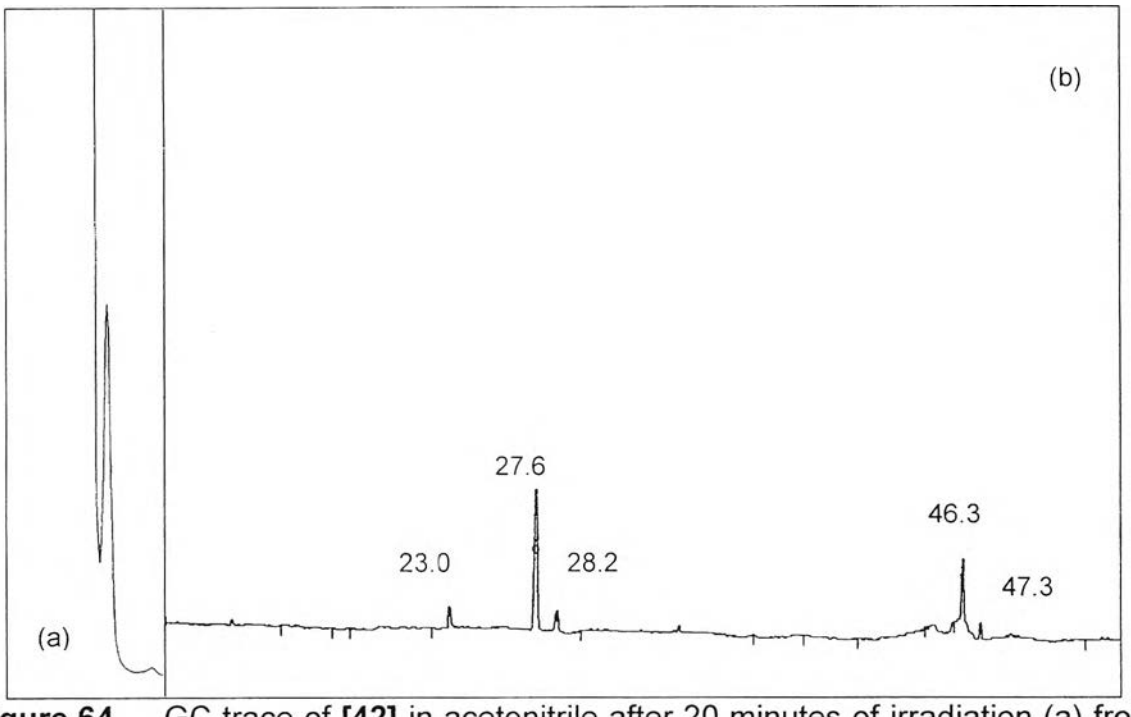


Figure 64 GC trace of **[42]** in acetonitrile after 20 minutes of irradiation (a) from 15 meter column (b) from 30 meter column

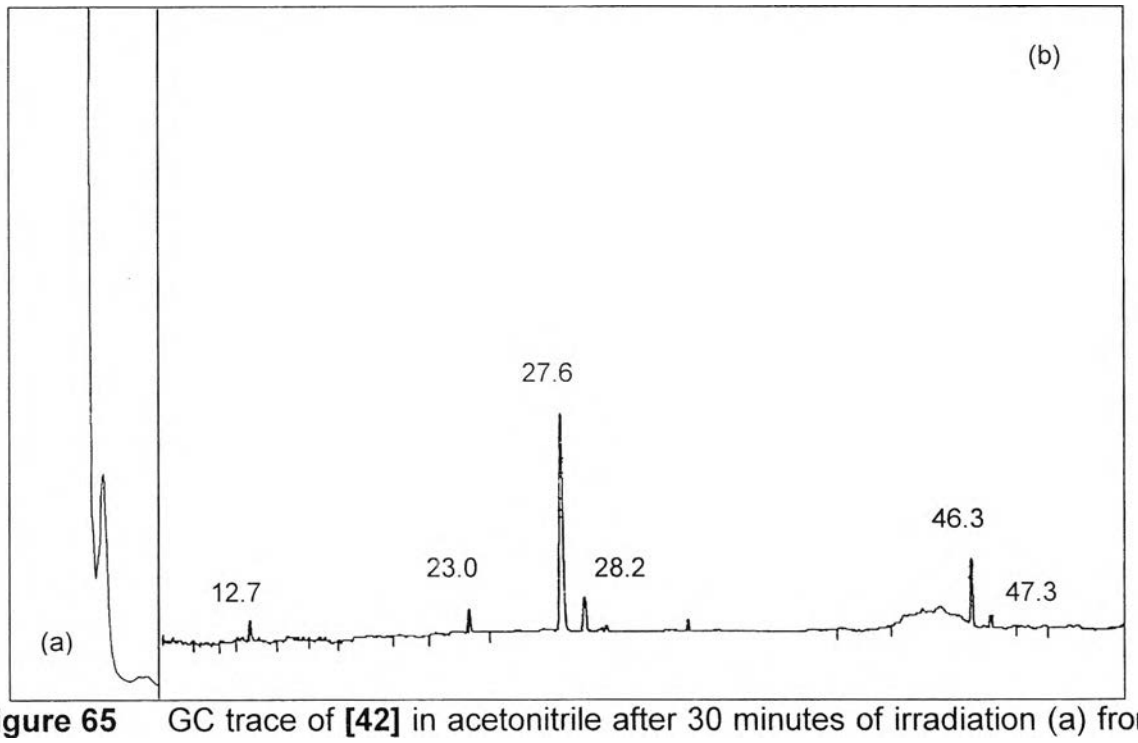


Figure 65 GC trace of **[42]** in acetonitrile after 30 minutes of irradiation (a) from 15 meter column (b) from 30 meter column

It is possible that three of product peaks are due to the formation of the three possible 1-methyltrifluoromethylimidazole phototransposition products. By comparison with the known retention times of the imidazoles, the peaks with the gas chromatographic retention times at 27.6, 28.2, and 46.3 minutes are due to 1-

methyl-5-(trifluoromethyl)imidazole **[46]**, 1-methyl-2-(trifluoromethyl)imidazole **[45]**, and 1-methyl-4-(trifluoromethyl)imidazole **[47]**.

The photoreaction of 1-methyl-5-(trifluoromethyl)pyrazole **[42]** in acetonitrile at 5 minutes of irradiation showed that 19% ($9x10^{-6}$ mol) of **[42]** was consumed to generate only three photoproducts, 19% yield of 1-methyl-2-(trifluoromethyl) imidazole **[45]**, 12% yield of 1-methyl-4-(trifluoromethyl)imidazole **[47]**, and 65% yield of 1-methyl-5-(trifluoromethyl)imidazole **[46]**. From these results it appears that only the product at retention time 27.6, 28.2, and 46.3 minutes due to 5-, 2-, and 4-trifluoromethyl-1-methylpyrazoles respectively are the primary photoproducts.

3.4.4 Identification of photocleavage product by GC-MS.

To further identify the photocleavage products, the concentrated photolysate in acetonitrile after 30 minutes of irradiation was analyzed by GC-MS (Hewlett Packard HP 5890A GC coupled HP 5970B mass spectrometer on 30m x 0.25 mm Supelcowax^{TM} 10 column using temperature program (40 °C for 11 minutes, 60 °C for 10 minutes, 100 °C for 10 minutes, 140 °C for 9 minutes with temperature changing rate of 20 °C per minute)). Figure 66 shows the GC-MS analysis of 1-methyl-5-(trifluoromethyl)pyrazole **[42]** appearing at retention time of 4.8, and Figure 67a, show the GC-MS of the photolysate which exhibits seven peaks at retention time of 12.5, 20.2, 21.0, 24.0, 29.1, 34.4, and 37.5 minutes. As shown in Figures 67b –67h, the mass spectrum of six of the photoproducts each exhibit a molecular ion at m/z 150, and a major fragment peak at m/z 131 due to loss of a fluorine atom, as expected for a trifluoromethyl substituted 1-methylimidazole. In addition, the fragmentation patterns are all very similar to each other and are very similar to the mass spectra of the three authentic trifluoromethyl substituted 1-methylimidazoles shown in Figures 14, 16, and 18. Although these mass spectra indicate that these six photoproducts are isomeric trifluoromethyl substituted compounds, the mass spectra are all too similar to allow distinction among the trifluoromethyl substituted imidazoles. As a result the three isomers were distinguished by their gas chromatographic retention times. Compared with the gas chromatograph retention times and the MS of authentic compounds, the peak at

retention time 20.2, 21.0, and 34.4 minutes were identified as 1-methyl-5-(trifluoromethyl)imidazole **[46]**, as 1-methyl-2-(trifluoromethyl)imidazole **[45]**, and as 1-methyl-4-(trifluoromethyl)imidazole **[47]** respectively (Figure 67c, 67d, and 67g). The peak at retention time 12.5, 24.0, and 29.1 should be other geometrical isomer photoproducts,for example, enaminonotrile or enaminoisocyanide, and the peak at retention time 37.4 which have fragmentation peak at m/z 130 as same as the other three products. Thus, its structure should be close to others structure, but it wasn't identified at this time.

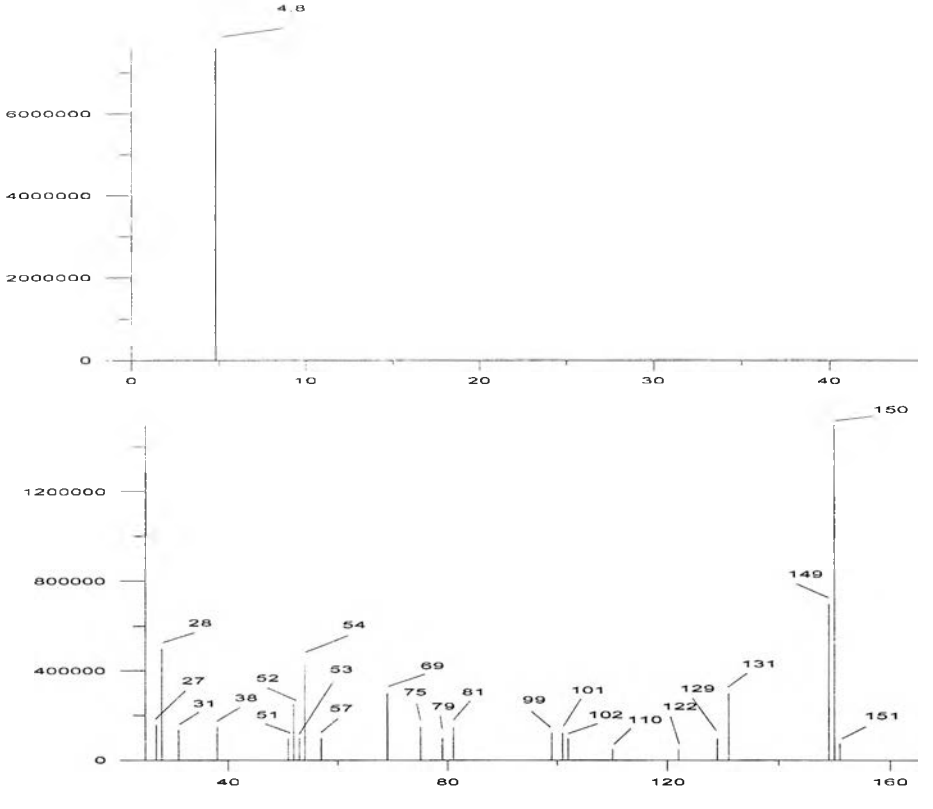


Figure 66 The GC-MS of 1-methyl-5-(trifluoromethyl)pyrazole **[42]**

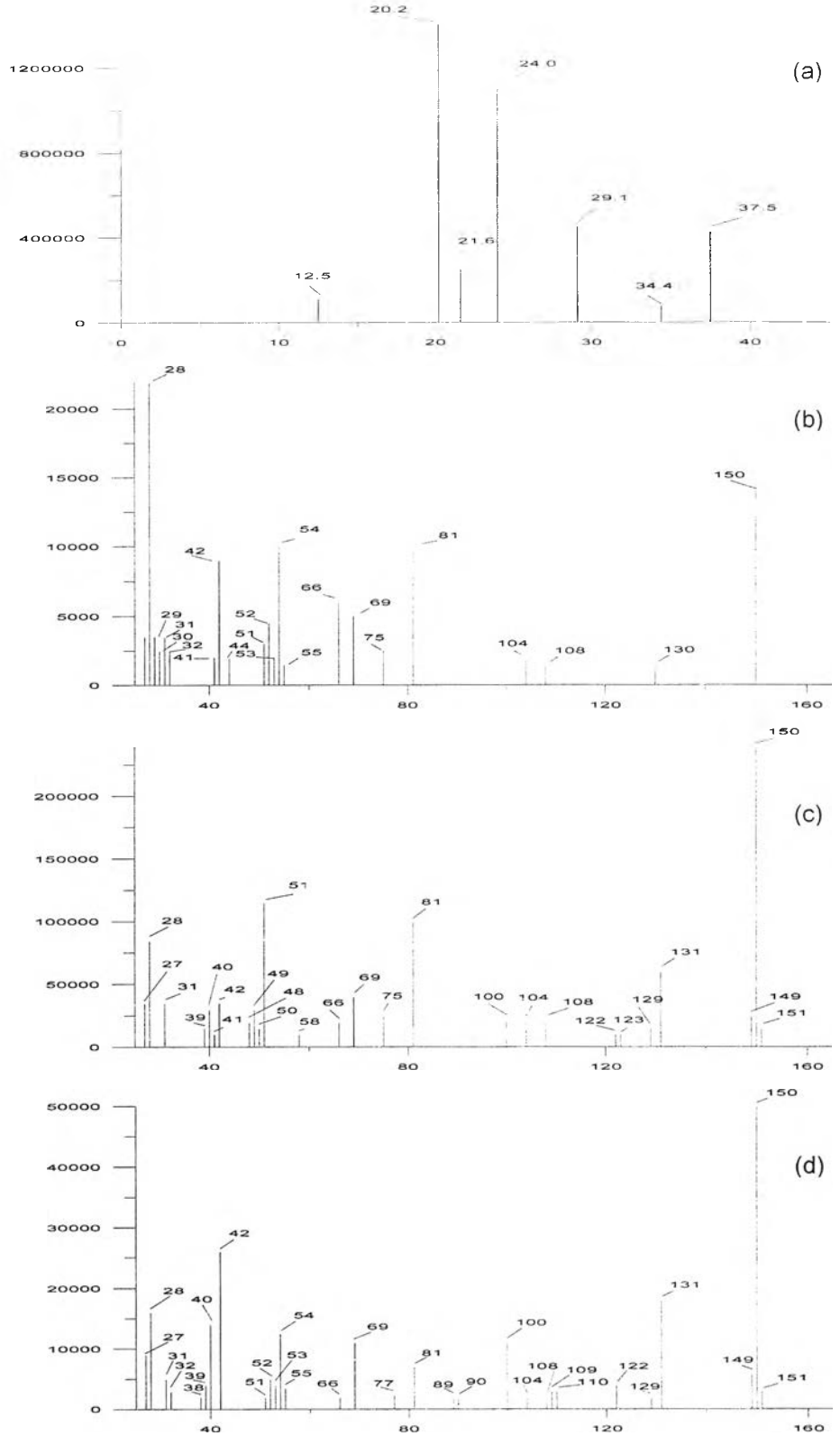


Figure 67 (a) The GC trace of **[42]** after 30 minutes of irradiation (from GC-MS) (b) The mass spectrum of peak at retention time 12.5 minutes (c) 20.2 minutes (d) 21.0 minutes

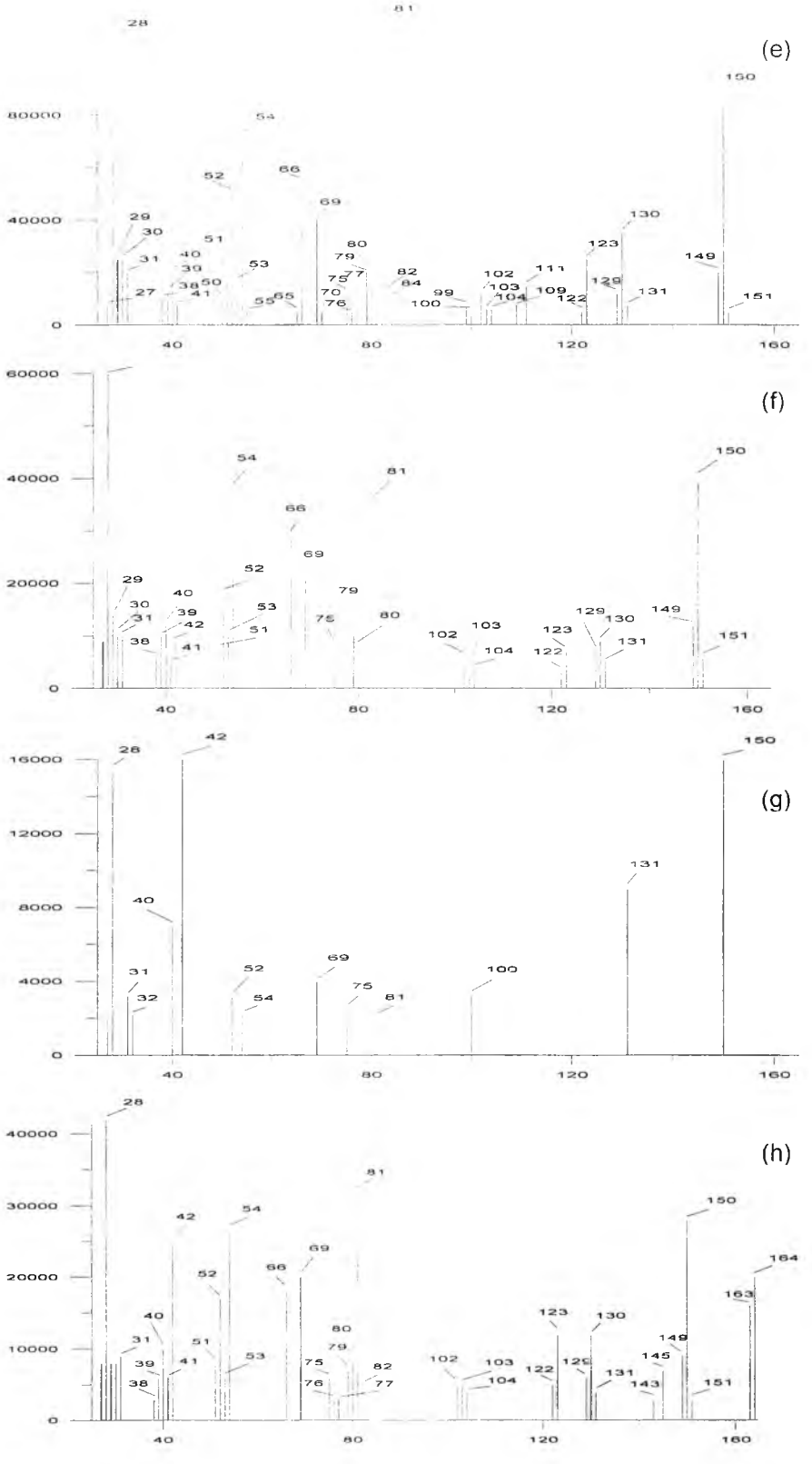
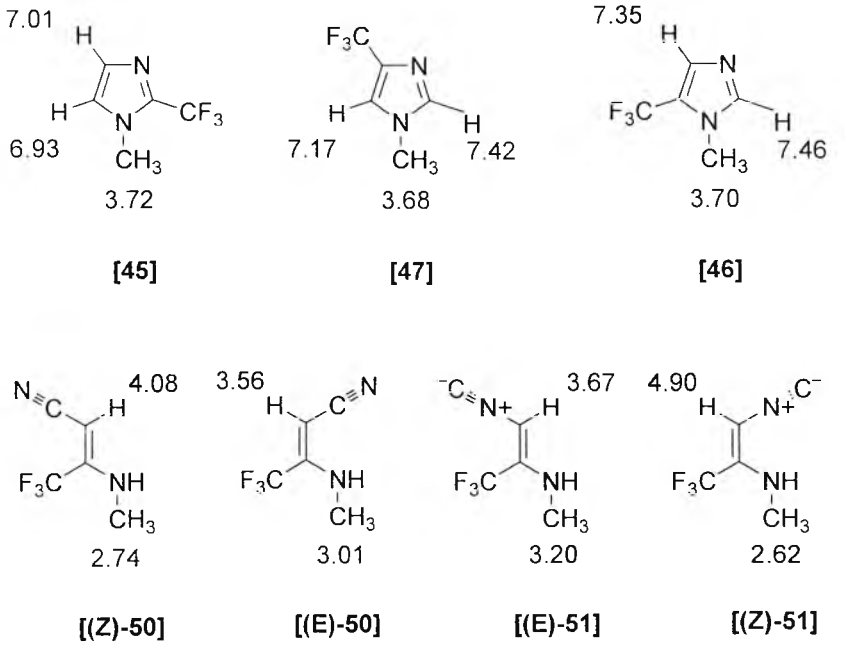


Figure 67 (e) The mass spectrum of peak at retention time 24.0 minutes (f) 29.1 minutes (g) 34.4 minutes (h) 37.5 minutes

3.4.5 ^{1}H-NMR spectrum of the photolysate of 1-methyl-5-(trifluoromethyl)pyrazole

After 30 minutes of irradiation in acetonitrile the resulting solution was concentrated and the residue was dissolved in $CDCl_3$ and analyzed by ^{1}H-NMR. The full spectrum is shown in Figure 68 with scale expansions shown in Figures 69a-69c, and the 2D-NMR is shown in Figure 70. The ^{1}H-NMR spectrum of the product mixture was compared with the spectra of the authentic compounds synthesized in this work. The spectrum showed that no signal was observed at δ 3.91 (s, 3H), 6.52 (d, 1H, J = 1.2 Hz), 7.39 (br. s, 1H) due to the N-methyl protons, the proton on C-5, and the proton on C-3 respectively of the photoreactant, 1-methyl-5-(trifluoromethyl)pyrazole **[42]** because all of it evaporated from the sample during concentration. Figure 69a shows the ^{1}H-NMR spectrum from δ 2.0-3.3 ppm, which exhibits a doublet at 2.62 (d, 3H, J = 5.2 Hz) due to the N-methyl protons of (Z)-2-(N-methylamino)-2-(trifluoromethyl)ethenyl isocyanide **[(Z)-51]**, a doublet at 2.74 (d, 3H, J = 5.1 Hz) due to the N-methyl protons of (Z)-3-(N-methylamino)-3-(trifluoromethyl)propene nitrile **[(Z)-50]**, a doublet at δ 3.01 (d, 3H, J = 5.4 Hz due to the N-methyl protons of (E)-3-(N-methylamino)-3-(trifluoromethyl)propene nitrile **[(E)-50]**, and a doublet at δ 3.20 (d, 3H, J = 5.4 Hz) due to the N-methyl protons of (E)-2-(N-methylamino)-2-(trifluoromethyl)ethenyl isocyanide **[(E)-51]**. Figure 69b shows the ^{1}H-NMR spectrum from δ 3.3-5.3 ppm where the N-methyl protons of N-methylpyrazoles and N-methylimidazoles are known to absorb. As shown, the spectrum exhibits a singlet at δ 3.68 due to the N-methyl protons of **[47]**, a singlet at δ 3.70 due to the N-methyl protons of **[46]**, and a singlet at δ 3.75 due to the N-methyl protons of **[45]**. Furthermore, the spectrum also shows a signal at δ 3.56 due the C-2 proton of (E)-3-(N-methylamino)-3-(trifluoromethyl)propene nitrile **[(E)-50]**, a signal at δ 4.08 due the C-2 proton of (Z)-3-(N-methylamino)-3-(trifluoromethyl)propene nitrile **[(Z)-50]**, a signal at δ 3.67 (s, 1H) due to the C-1 proton of (E)-2-(N-methylamino)-2-(trifluoromethyl)ethenyl isocyanide **[(E)-51]**, and a signal at δ 4.91 due to the C-1 proton of (Z)-2-(N-methylamino)-2-(trifluoromethyl)ethenyl isocyanide **[(Z)-51]**. Figure 69c shows the ^{1}H-NMR spectrum from δ 6.7-7.6 ppm where the ring protons of N-methylpyrazoles and N-methylimidazoles are known to absorb. As shown, the spectrum exhibits signals at

δ 6.93 and 7.01 due to the proton on C-5 and the proton on C-4 respectively of **[45]**, signals at δ 7.17 and 7.42 due to the proton on C-5 and the proton on C-2 respectively of **[47]**, signals at δ 7.35 and 7.46 due to a proton at C-4 and a proton at C-2 respectively of **[46]**, but no signal at δ 6.52 and 7.39 where the protons on C-5 and C-3 respectively of 1-methyl-5-(trifluoromethyl)pyrazole **[42]** are known to absorb.



[45] **[47]** **[46]**

[(Z)-50] **[(E)-50]** **[(E)-51]** **[(Z)-51]**

Scheme 12 Assignment of the chemical shifts for the protons of components in the photolysate **[42]** in acetonitrile after 30 minutes of irradiation

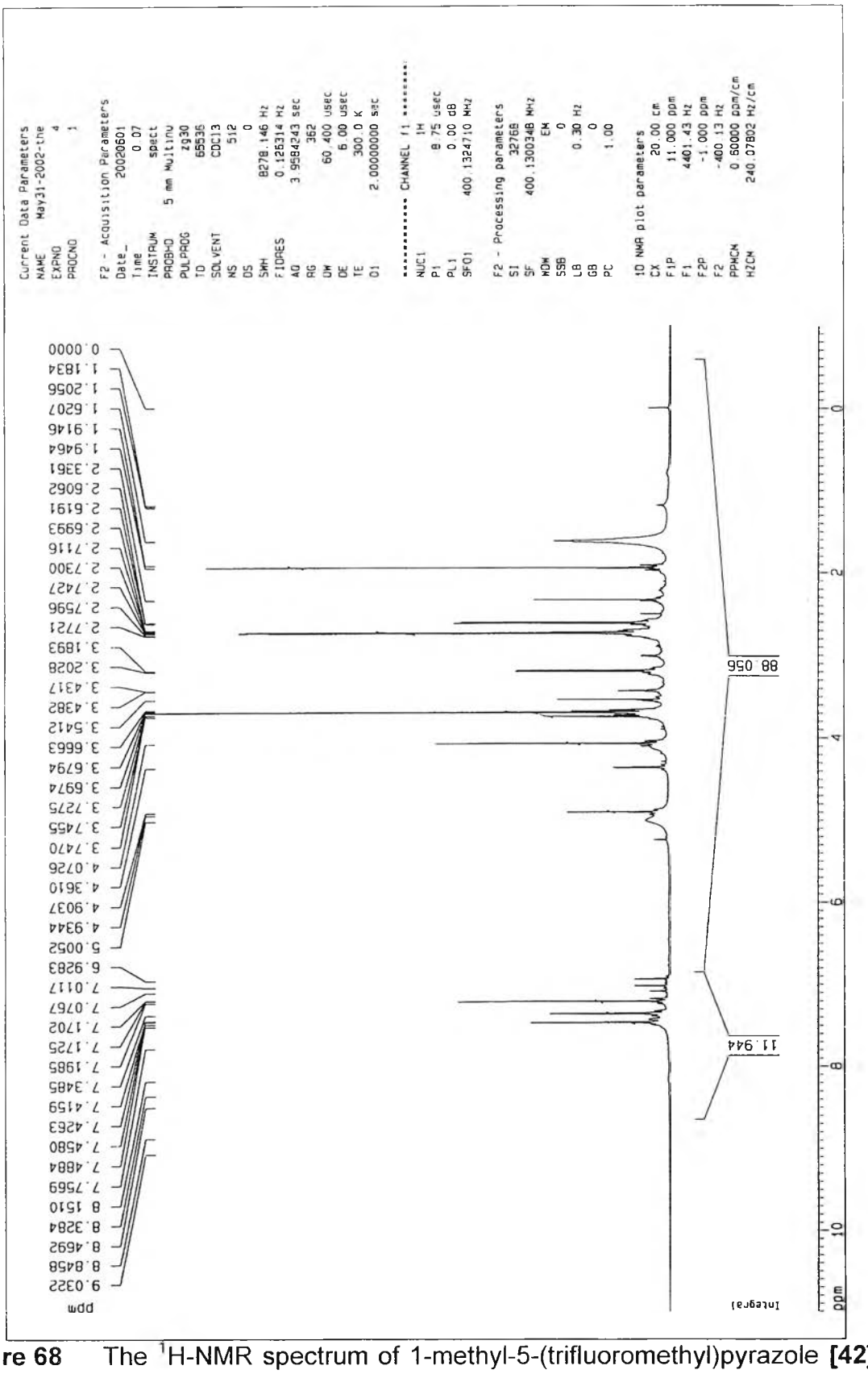


Figure 68 The ^{1}H-NMR spectrum of 1-methyl-5-(trifluoromethyl)pyrazole **[42]** in acetonitrile after 30 minutes of irradiation

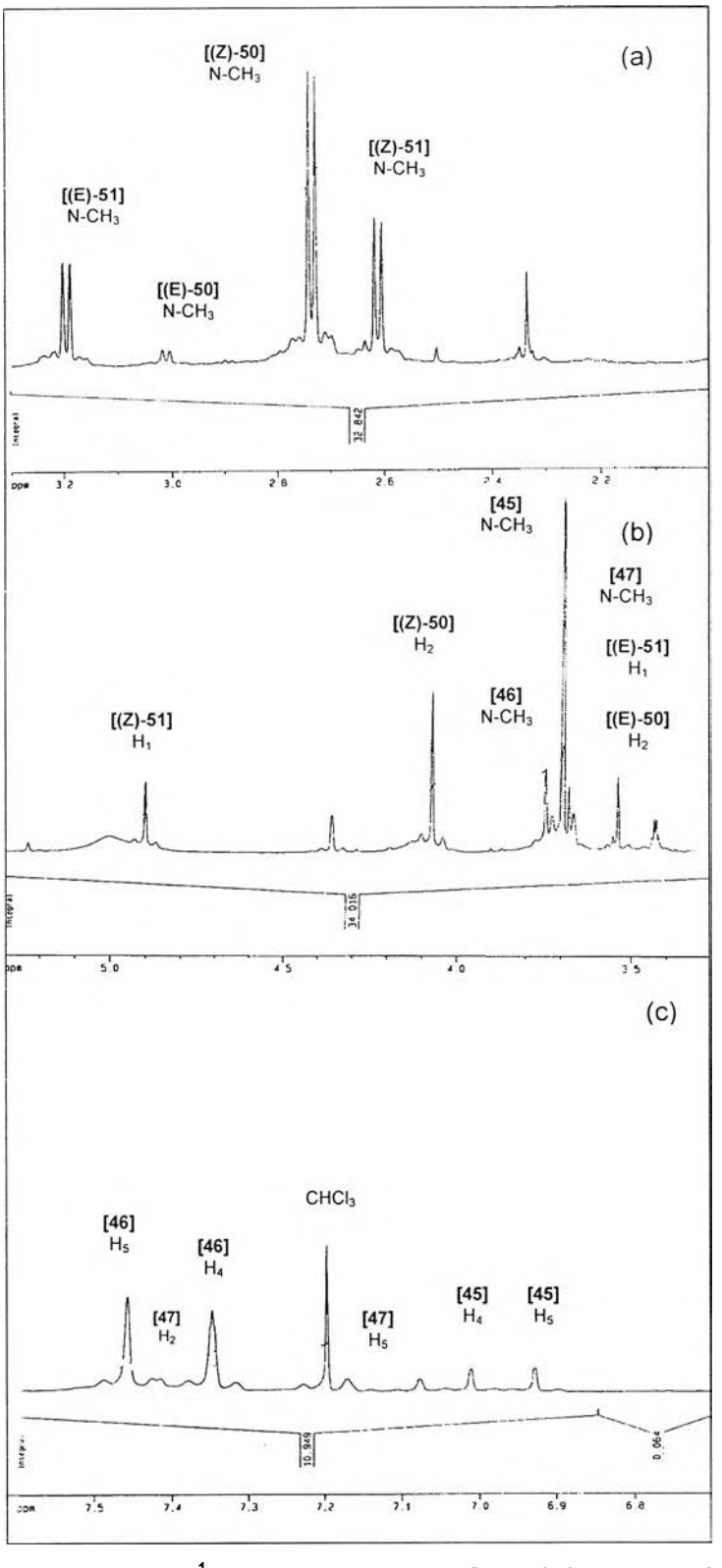


Figure 69 The expansion of ^{1}H-NMR spectra of **[42]** in acetonitrile after 30 minutes of irradiation (a) 2.0-3.3 ppm (b) 3.3-5.3 ppm and (c) 6.7-7.6 ppm

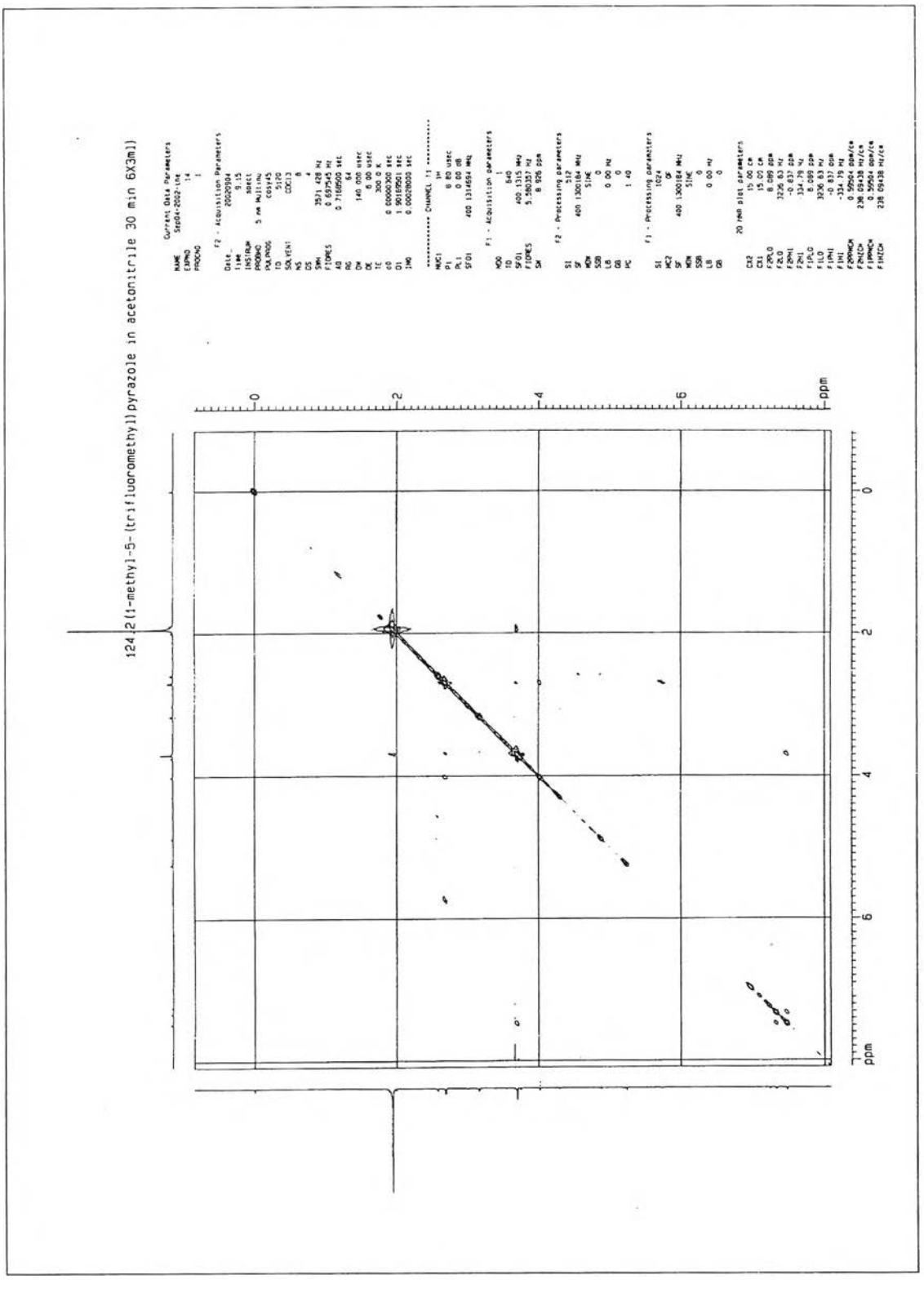


Figure 70 The 2D-NMR spectra of **[42]** in acetonitrile after 30 minutes of irradiation

Nitrile and isocyanide functional groups are known to have characteristic absorptions in the infrared at around 2300 cm^{-1} and 2200 cm^{-1} respectively, which is a region where few other absorptions occur. Accordingly, to further investigate the formation of an enaminonitrile and/or enaminoisocyanide photocleavage product or products in this reaction, the reaction was also monitored by infrared spectroscopy.

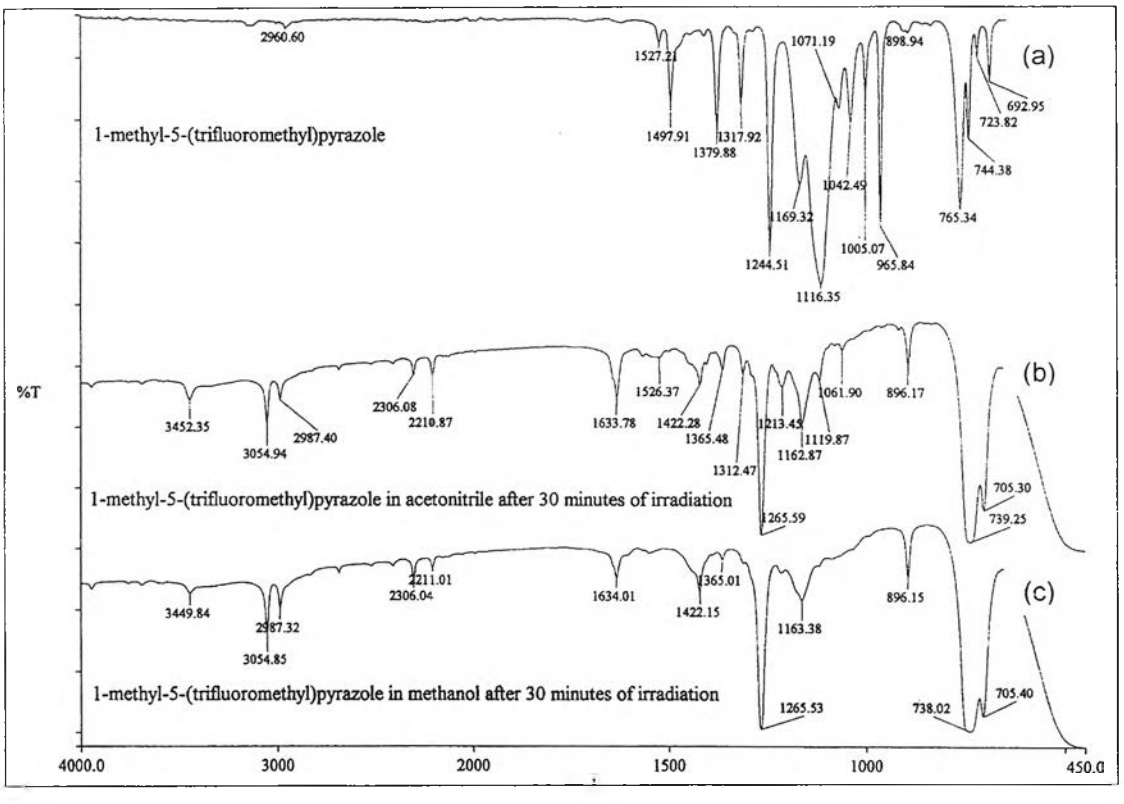


Figure 71 (a) IR spectra of 1-methyl-5-(trifluoromethyl)pyrazole **[42]** (b) photolysate in acetonitrile after 30 minutes of irradiation (c) photolysate in methanol after 30 minutes of irradiation

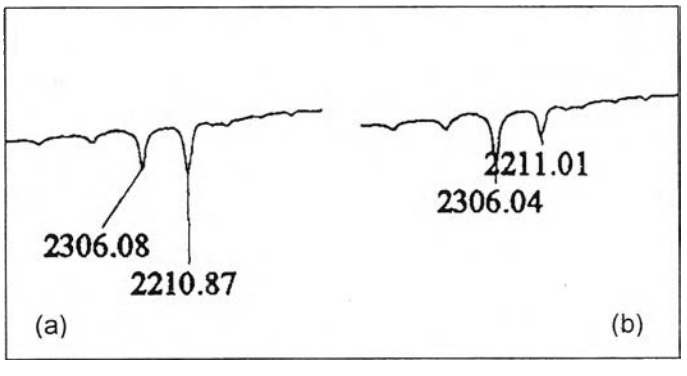


Figure 72 (a) IR spectra of 1-methyl-5-(trifluoromethyl)pyrazole **[42]**, photolysate in acetonitrile after 30 minutes of irradiation (b) photolysate in methanol after 30 minutes of irradiation

Figure 71a shows the infrared spectrum of 1-methyl-5-(trifluoromethyl) pyrazole **[42]** before irradiation. As expected by the spectrum exhibits no absorption bands in the nitrile-isocyanide region from 2100-2400 cm^{-1}. Figure 71b shows the infrared spectrum of the residue obtained after the acetonitrile solution of 1-methyl-5-(trifluoromethyl)pyrazole **[42]** was irradiated for 30 minutes and then concentrated. As shown, the infrared spectrum exhibits absorption bands at 2306 cm^{-1} and 2210 cm^{-1}, which indicate the presence of a cyano and isocyano functional group respectively. Figure 71c shows the infrared spectrum of the residue obtained after irradiation of the pyrazole in methanol solvent. Again, the spectrum shows new absorption bands at 2306 cm^{-1} and 2211 cm^{-1}, which are consistent with the formation of products cantaining cyano and an isocyano functional groups.

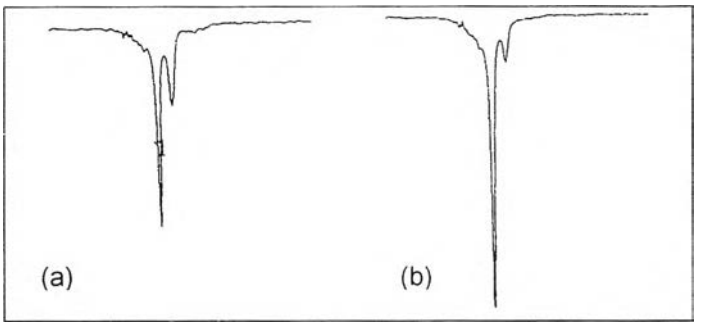


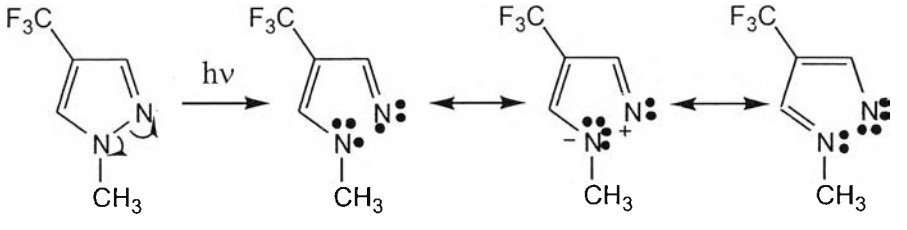
Figure 73 (a) IR speatra of 1-methyl-5-(trifluoromethyl)pyrazole **[42]**, photolysate in acetonitrile after 15 minutes of irradiation (b) IR speatra of 1-methyl-5-(trifluoromethyl)pyrazole **[42]**, photolysate in acetonitrile after 15 minutes of irradiation added one drop of concentrate acetic acid

In a second experiment a solution of 1-methyl-5-(trifluoromethyl)pyrazole **[42]** was irradiated for 15 minutes and the resulting solution was divided into two equal portions. The first portion was immediately concentrated and analyzed by infrared spectroscopy. The spectrum in Figure 73a shows absorption bands at 2306 cm^{-1} and 2211 cm^{-1} due to the formation of cyano and isocyano products in a ratio of approximately 2.5 to 1. the second fraction was treated with one drop of glacial acetic acid and one drop of water and allowed to stand for three hours. The resulting solution was neutralized with $NaHCO_3$ dried ($NaSO_4$), and concentrated. Figure 73b shows the infrared spectrum of the residue, which reveals that the 2306

cm^{-1} to 2211 cm^{-1} ration has now changed to 7:1. Thus, it appears that the band at 2211 cm^{-1} is sensitive to acid. This is consistent with it being due to a compound containing a isocyano functional group.

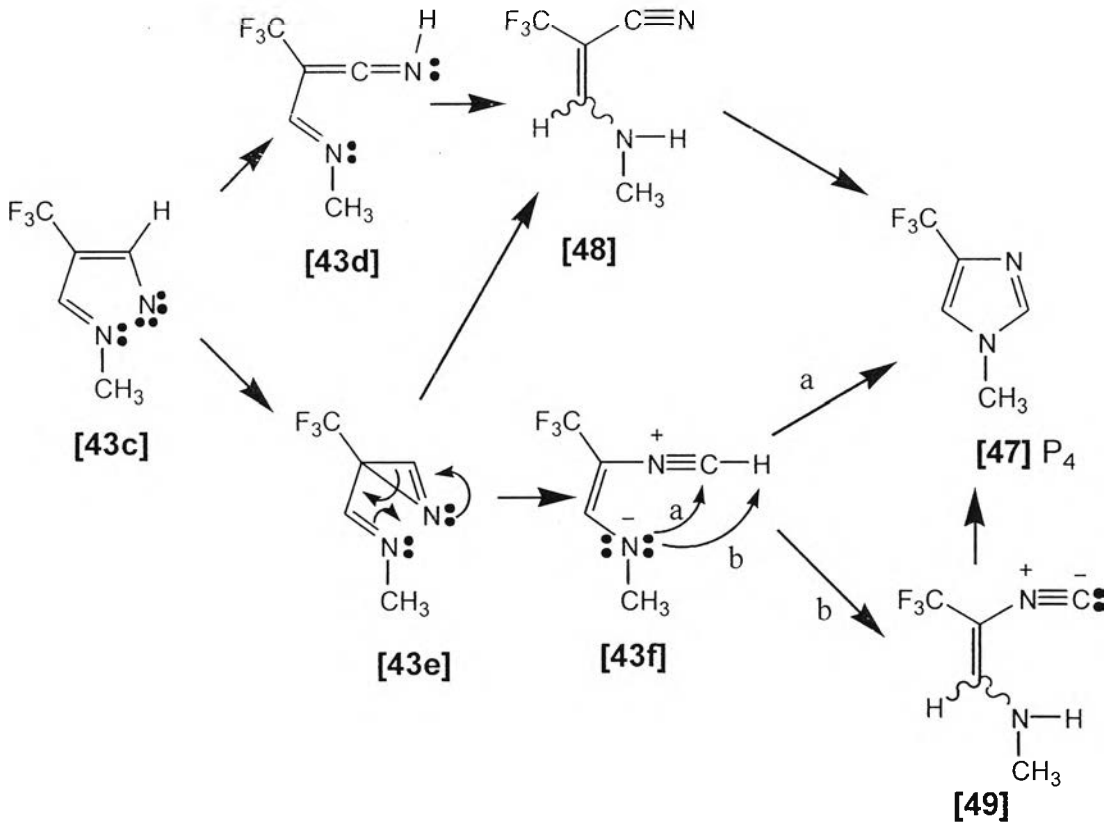
3.5 Mechanistic Discussion

The photochemistry of pyrazoles has been suggested to involve a competition between electrocyclic ring closure leading to P_6 and P_7 transpositions and cleavage of the N-N bond resulting in the formation of the precursor of the P_4 transposition product.[3] 1-Methyl-4-(trifluoromethyl)pyrazole **[43]** transposes regiospecifically *via* the latter pathway. Thus, excitation of **[43]** is suggested to result in cleavage of the N-N bond resulting in the formation of species that can be viewed as diradical **[43a]** or zwitterions **[43b]**, which are resonance forms of β-iminovinylnitrene **[43c]**.



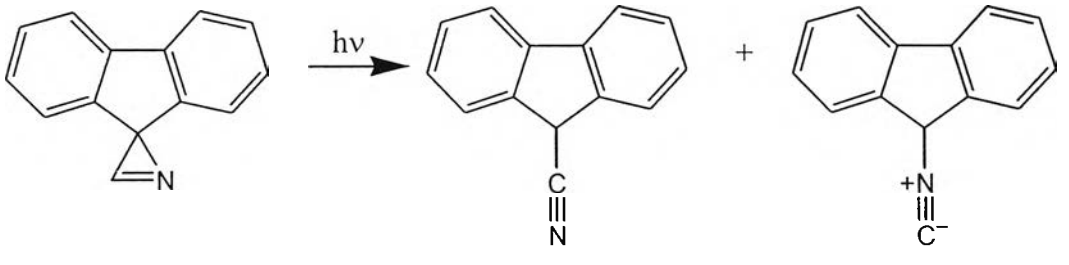
Scheme 13 Primary steps in the P_4 pathway for 1-methyl-4-(trifluoromethyl) pyrazole **[43]**

In addition to recyclizing to the pyrazole reactant, rearrangement of β-iminovinylnitrene **[43c]** to 3-(N-methylamino)-2-(trifluoromethyl)propenenitrile **[75]**, either by direct transfer of hydrogen from C-3 of the original pyrazole to nitrogen, or possible by way of ketenimine **[43d]**, is an expected pathway for a terminal vinylnitrene.[19]

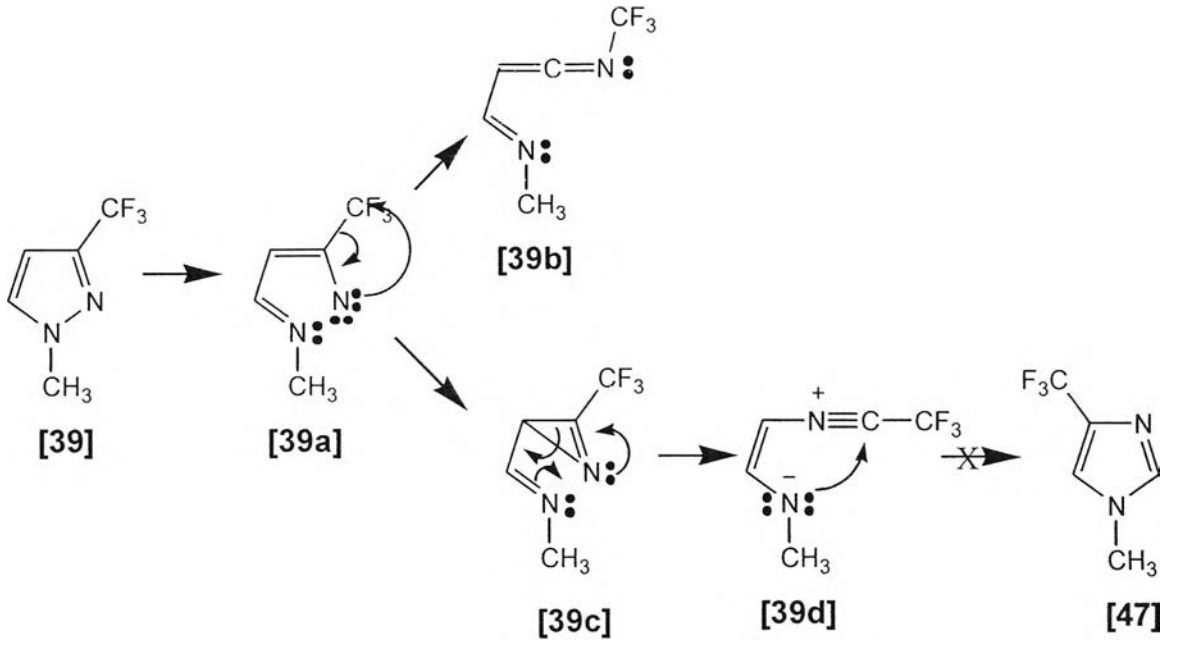


Scheme 14 Mechanism proposed in the P_4 and photocleavage pathways for 1-methyl-4-(trifluoromethyl)pyrazole

Alternatively, **[43c]** would also be expected to undergo intramolecular cyclization to yield iminoazirine **[43e]**,[4] a plausible precursor of nitrile **[48]**, isocyanide **[49]**, and imidazole **[47]**. Although azirine unsubstituted at C-2 are generally not thermally stable, one such azirine has been found to rearrange photochemically to both a nitrile and an isonitrile as shown below.[20]

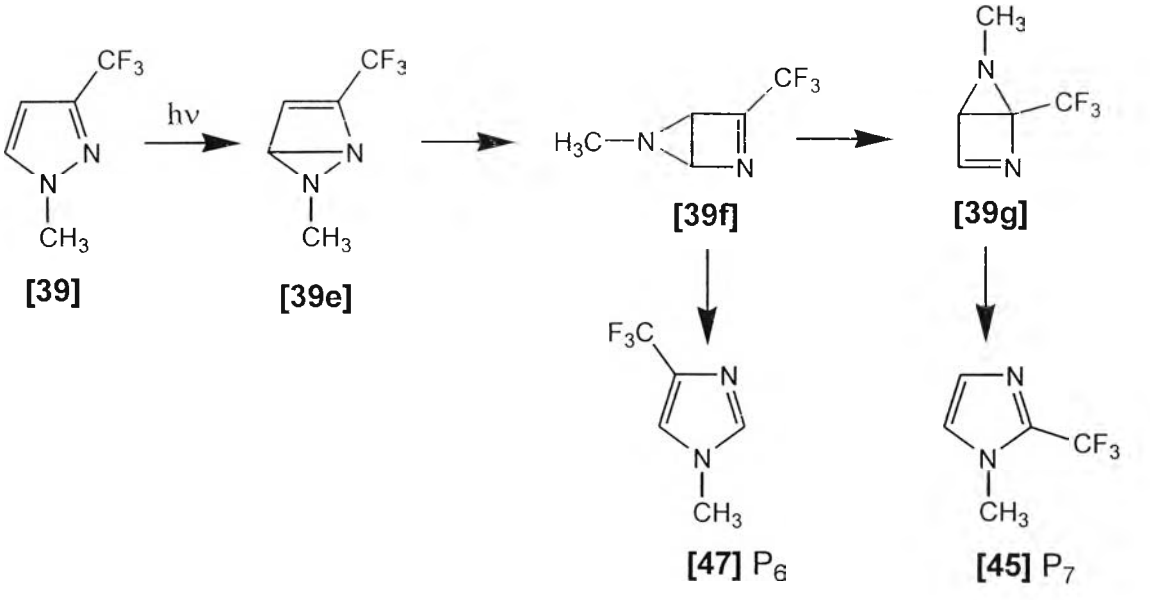


Although it is also possible that formation of nitrile may involve the vinylnitrene formed by C-N bond fission, azirines are known to undergo photochemical ring opening of the C-C bond, which in the present case would yield nitrile ylide **[43f]**, a likely precursor of imidazole **[47]** and isocyanide **[49]**.



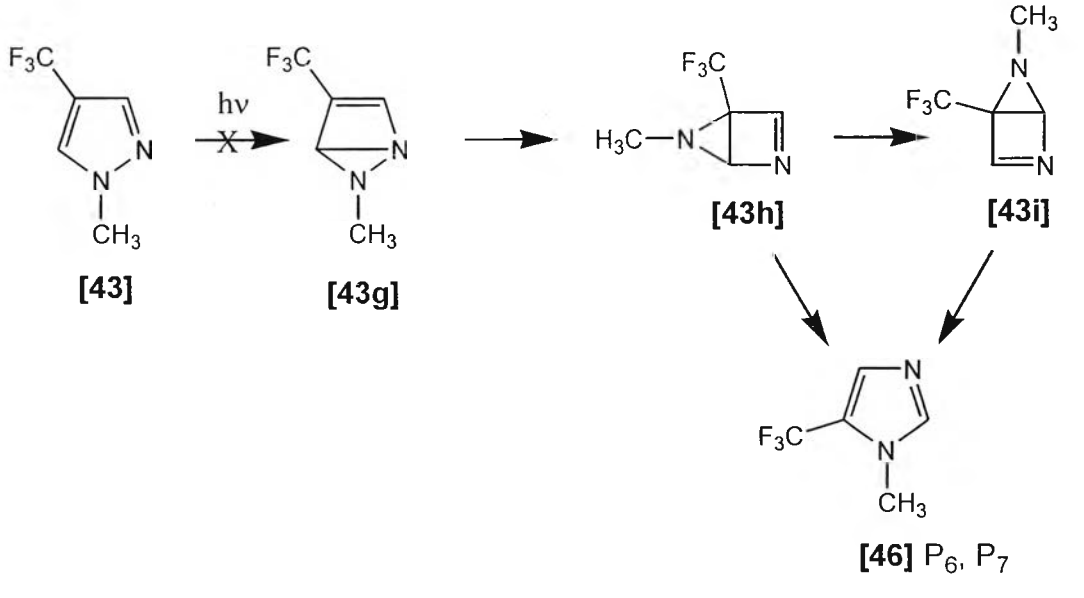
Scheme 15 Reaction mechanism of P_4 pathway for 1-methyl-3-(trifluoromethyl) pyrazole **[39]**

In case of 1-methyl-3-(trifluoromethyl)pyrazole **[39]**, **[39]** would undergo photocleavage to vinylnitrene **[39a]**, which could rearrange to an unstable N-methylketenimine **[39b]** or undergo ring closure to azirine **[39c]** which bears a C-2 methyl substituent. Photochemical ring opening of **[39c]** would yield nitrile ylide **[39d]**, and then could cyclize to imidazole **[47]** but could not yield nitrile and isocyanide. This is consistent with an observation that **[39]** transposes to **[47]** without the formation of nitrile or isocyanide photocleavage products, so the phototransposition of pyrazoles **[39]** should involve an electrocyclic ring closure leading to P_6 and P_7 transpositions. 1-Methyl-3-(trifluoromethyl)pyrazole **[39]** should undergo electrocyclic ring closure yielding 1,5-diazabicyclopentene **[39e]**, which can undergo one or two consecutive 1,3-sigmatropic shifts of nitrogen.[3] Rearomatization of the isomeric 2,5-diazabicyclopentene intermediates **[39f]** and **[39g]** would thus provide the P_6 and P_7 imidazole **[45]** and **[47]**.



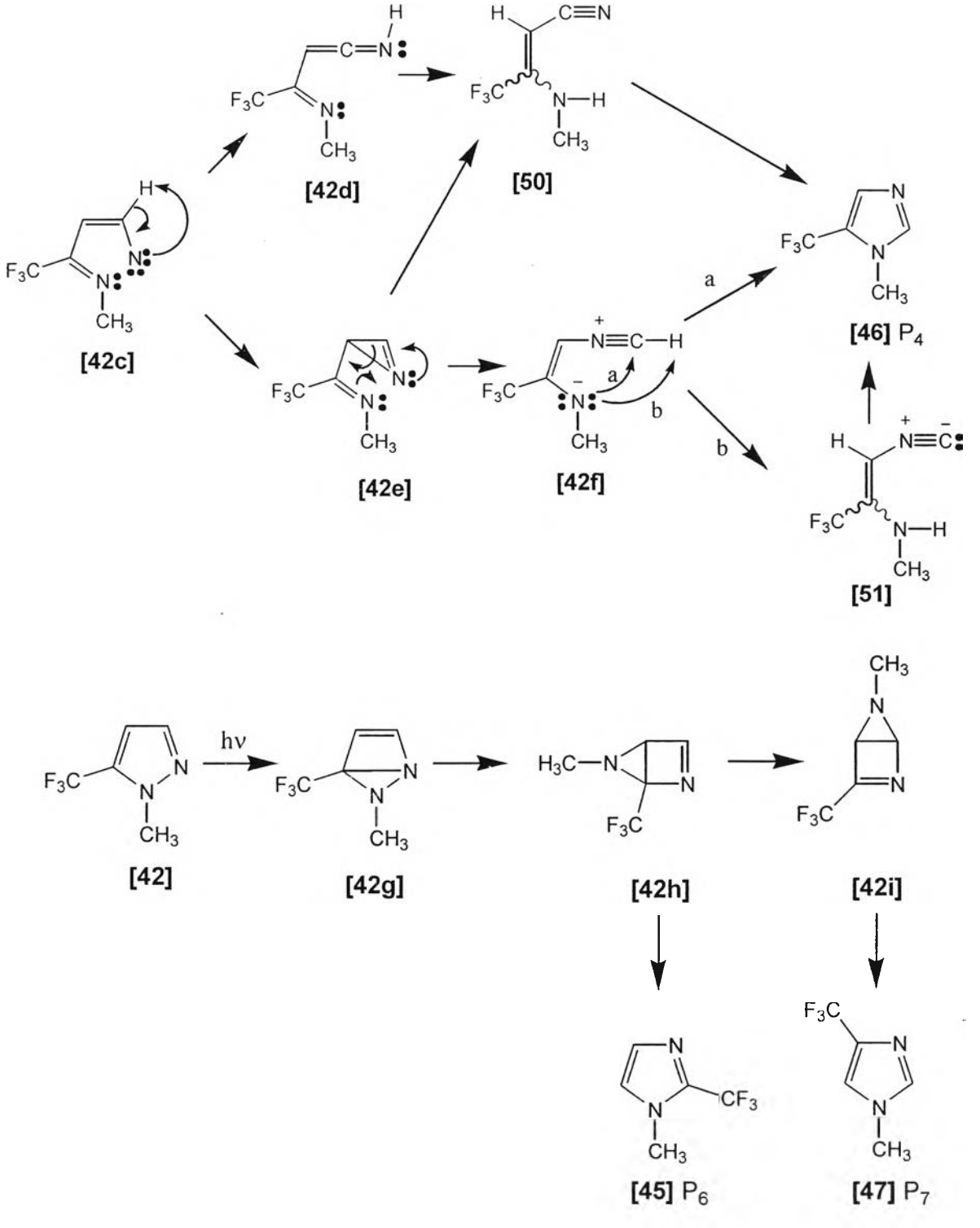
Scheme 16 Reaction mechanism of the P_6 and P_7 pathways for 1-methyl-3-(trifluoromethyl)pyrazole **[39]**

In case of 1-methyl-4-(trifluoromethyl)pyrazole **[43]**, **[43]** would undergo electrocyclic ring closure yield 1,5-diazabicyclopentene **[43g]**, which could not undergo one or two consecutive 1,3-sigmatropic shifts of nitrogen to unstable isomeric 2,5-diazabicyclopentene intermediates **[43h]** and **[43i]**, respectively.[3] This is consistent with an observation that **[43]** transposes to only imidazole **[47]** without the formation of imidazole **[46]**.



Scheme 17 Reaction mechanism of P_6 and P_7 pathways for 1-methyl-4-(trifluoromethyl)pyrazole **[43]**

In case of 1-methyl-5-(trifluoromethyl)pyrazole **[42]**, **[42]** can undergo photocleavage of the N-N bond, the initial step on the P_4 reaction pathway giving imidazole **[46]**, which competes with electrocyclic ring closure leading to P_6 and P_7 transpositions giving imidazole **[45]** and **[47]**, respectively.



Scheme 18 Reaction mechanism of P_4, P_6, and P_7 pathways for 1-methyl-5-(trifluoromethyl)pyrazole **[42]**