CHAPTER IV

DISCUSSION

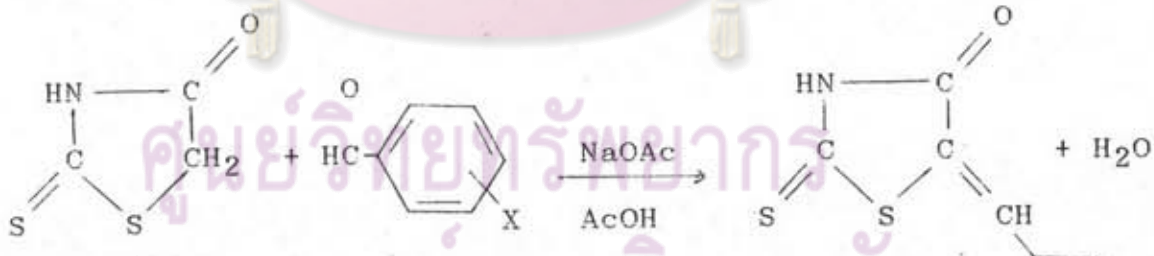
The target products can be synthesized by two steps. First, the synthesis of 5-arylmethylenerhodanines which are readily obtained from rhodanine and aromatic aldehyde, using anhydrous sodium acetate in glacial acetic acid as condensing agent. Secondly, the reactions of 5-arylmethylenerhodanines with organic bases to give the target 2-imino-5-arylmethylene-4-thiazolidinones.

Step I : Condensation of Rhodanine and Aldehyde

In the synthesis of 5-arylmethylenerhodanine derivatives reported here, only anhydrous sodium acetate with glacial acetic acid was used as a condensing agent. The procedure involved dissolving the rhodanine in glacial acetic acid by warming the mixture in a water bath, then adding anhydrous sodium acetate. After the salt had dissolved, equimolar of aldehyde was added to the solution. The mixture was refluxed for 30-60 mins. After cooling the mixture to room temperature, most preparations formed crystal products. In some preparations, crystal products were formed during refluxing which indicated the ease of condensation between rhodanine and aldehyde in

the presence of sodium acetate and acetic acid. In order to gain more crystals, the mixture must be kept in the refrigerator overnight. The crystals were isolated by filtration and washed with water to remove the excess acid. In order to maximize the yield of the product, the filtrate was combined with the washed water and poured into another amount of water which gave more crystals after cooling in the refrigerator. Purification was generally done by recrystallization, but the first crop crystallized from the reaction mixture was usually pure enough for used in subsequent reactions.

In this study, only three derivatives were selected which were 5-benzylidenerhodanine, 5-(4-nitrobenzylidene)rhodanine and 5-(2,6-dichlorobenzylidene) rhodanine.



X = H; 4-NO_2; 2,6-Cl_2

The physicochemical properties, characteristic IR-absorption and characteristic ^{1}H-NMR were shown in table 1,3 and 5 respectively.

1. IR-Absorption Spectra Analysis

The infrared spectra of 5-arylmethylene rhodanines showed the carbonyl peak between 1700-1720 cm^{-1} which confirmed the previous report that the unsaturation of 5-position carbon atom, being conjugated with the carbonyl group, produced a bathochromic shift (37). The hydrogen attached to the nitrogen atom showed absorption in the region 3050-3440 cm^{-1}, characteristic of the N-H stretching. Strong peak for thione group (C=S) and C=C stretching were found at 1200 cm^{-1} and 1600 cm^{-1} respectively.

2. ^{1}H-NMR Spectra Analysis

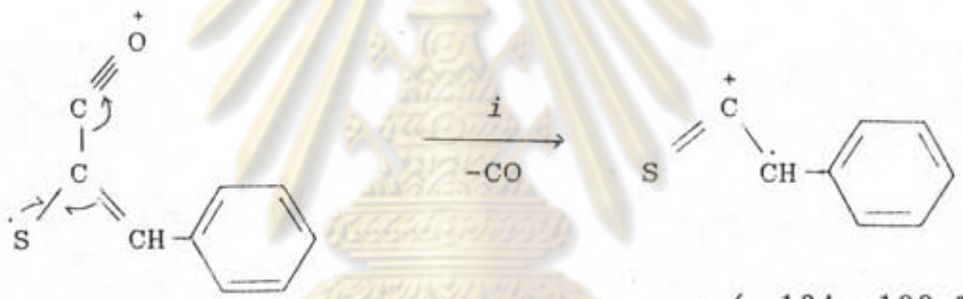
The nuclear magnetic resonance data of 5-arylmethylenerhodanines showed characteristic proton attached to the ring nitrogen at 13.48 ppm and aromatic proton in range of 7.4 - 8.5 ppm.

3. Mass Spectra Analysis

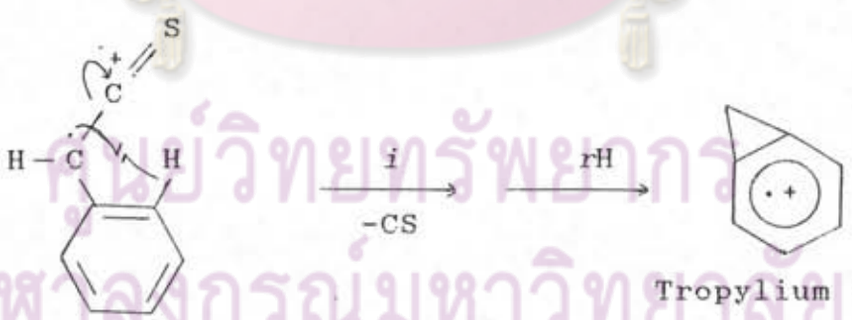
The EI mass spectra of 5-benzylidenerhodanine ($C_{10}H_7NOS_2$, MW.221) showed isotopic abundances M+1 at 13.46 %(calcd. 12.94 %) and M+2 at 10.29 %(calcd.

9.58 %). The characteristic peaks were found at *m/e* 134, 90 and 162 with abundances decreasing respectively. Ion fragmentation was proposed as following :

m/e 221, 59.42 % *m/e* 162, 7.52 %



m/e 134, 100 %



Tropylium ion

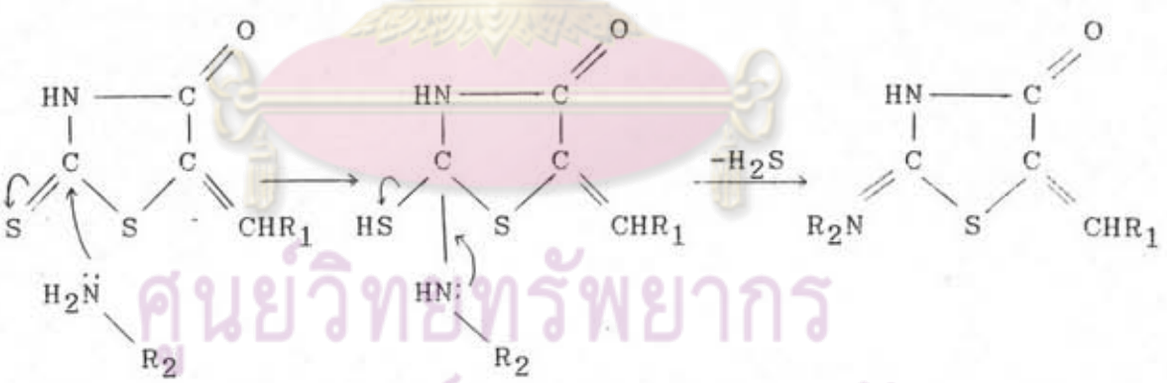
m/e 90, 11.51 %

The loss of CO group (mass=28) from *m/e* 162 gave the base peak at *m/e* 134. The loss of CS group

(mass=44) from the base peak exhibited an abundant benzyl ion and gave stabilized tropylium ion (67).

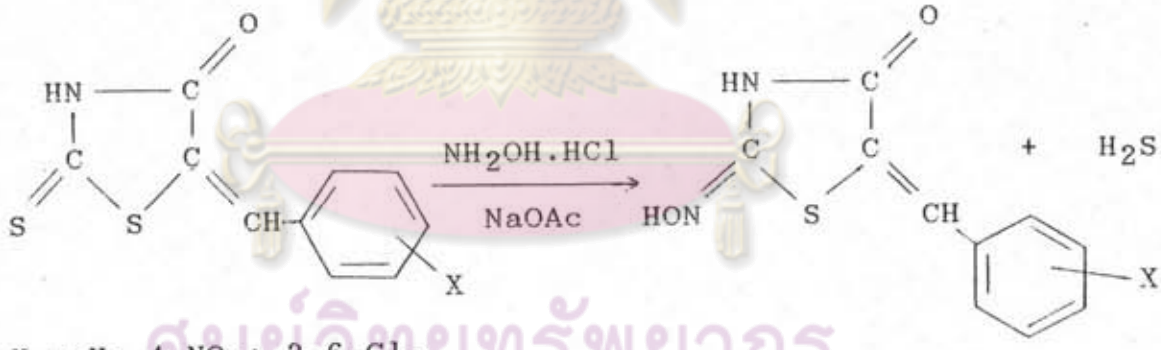
Step II : Reaction of 5-Arylmethylenerhodanines with Organic Bases

The target 2-imino-5-arylmethylene-4-thiazolidinones were synthesized by reacting 5-arylmethylene rhodanines with hydroxylamine, aniline and phenylhydrazine. The organic bases attached the carbon atom at 2-position of thiazolidine ring and lost hydrogen sulfide by conversion sulfur atom of thione group to imino group (24,60-62). This was confirmed by the evolution of H_2S during reaction and the presence of substituents in the 5-position stabilised the thiazolidine ring.



1. Reaction of 5-arylmethylenerhodanines with hydroxylamine hydrochloride

The reaction of 5-arylmethylenerhodanines, hydroxylamine hydrochloride and anhydrous sodium acetate in ethanol gave 2-oximino-5-arylmethylene-4-thiazolidinones. The 5-benzylidenerhodanine reaction with hydroxylamine was carried by stirring at 60 °C until the evolution of H_2S ceased and gave 41.1 % yield. In comparison, the condition for 5-(2,6-dichlorobenzylidene) rhodanine needed longer time for stirring at 60 °C (10 hrs) and gave 28.7 % yield. The condition for 5-(4-nitro benzylidene)rhodanine needed refluxing for 4-5 hrs and gave only 10.9 % yield.



X = H; 4-NO_2; 2,6-Cl_2

a. IR-Absorption Spectra Analysis

The infrared absorption spectra showed the characteristic carbonyl peak in the region 1690-1700 cm^{-1} according to the bathochromic shift (37). This indicated that the 4 position in the rhodanine nucleus did not

involved in the reaction. The characteristic peak for thione group at 1200 cm^{-1} was not observed which also indicated that the reaction was taken place at the 2 position. In addition, strong peak in region 1620-1660 cm^{-1} was observed which can be assigned as of C=N stretching vibration (65,66). In general, The characteristic unbonded or " free " hydroxyl group of alcohols and phenols usually absorbs strongly in the 3650-3584 cm^{-1} region. Sharp, " free " hydroxyl bands are observed only in the vapor phase in very dilute solution in nonpolar solvents. Intermolecular hydrogen bonding increases as the concentration of the solution increase, and addition bands start to appear at lower frequencies, 3550-3200 cm^{-1}, at the expense of the " free " hydroxyl band (65). Therefore, the absorption in the region 3250-3400 cm^{-1} confirmed the characteristic O-H stretching found in the 2-oximino-5-arylmethylene-4-thiazolidinones.

b. ^{1}H-NMR Spectra Analysis

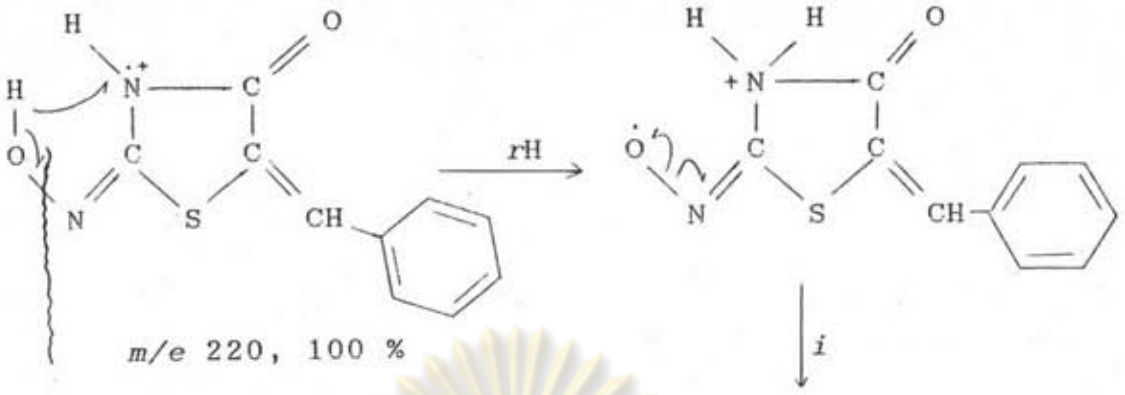
The nuclear magnetic resonance spectra of 2-oximino-5-arylmethylene-4-thiazolidinones exhibited a broad peak at 10.5-11.3 ppm, which was assigned as the -NH group at position 3 of the thiazolidene ring (65,66). The proton chemical shift of oximino group (-NOH) presented at range 7-10 ppm (66). The aromatic hydrogen atoms of benzylidene ring were found at range 7.30-8.35 ppm. The

strong electron-withdrawing effect of substituent nitro group in 2-oximino-5(4-nitrobenzylidene)-4-thiazolidinone (figure 12) deshielded the aromatic ring proton(66), hence downfield peaks were observed. With the chloro substituent in 2-oximino-5(2,6-dichlorobenzylidene)-4-thiazolidinone (figure15), the deshielding effect was observed to the lesser extent than from the nitro group.

c. Mass Spectra Analysis

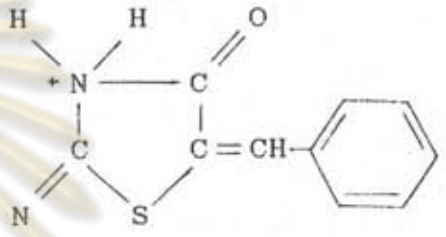
The EI mass spectra of 2-oximino-5-aryl methylene-4-thiazolidinones were analysed as following.

2-Oximino-5-benzylidene-4-thiazolidinone ($C_{10}H_6N_2O_2S$, MW.220) showed isotopic abundances M+1 at 12.94 %(calcd. 12.58 %) and M+2 at 5.81 %(calcd. 5.43 %). The characteristic peaks were found at *m/e* 134, 90, 204 and 162 with abundances decreasing respectively. The presence of characteristic peaks at *m/e* 134, 90 and 162 indicated that 1-, 4- and 5-positions of the thiazolidine ring had not been involved in the reaction. The characteristic peaks at *m/e* 204 and 203, which exhibited the loss of O atom (mass=16) and -OH group (mass=17) respectively, indicated the free -OH group presence.



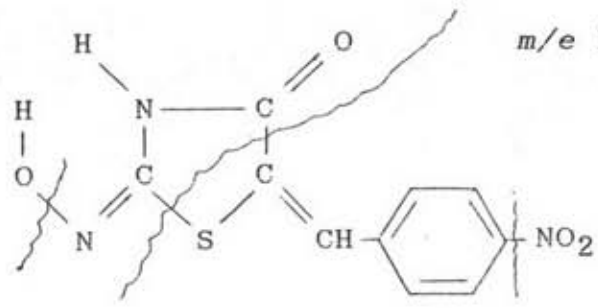
m/e 220, 100 %

(-17) *m/e* 203, 4.01 %



m/e 204, 7.29 %

2-Oximino-5-(4-nitrobenzylidene)-4-thiazolidinone ($C_{10}H_7N_3O_4S$, MW.265) showed isotopic abundances M+1 at 13.88 %(calcd. 13.02 %) and M+2 at 6.32 %(calcd. 5.87 %). The characteristic peaks were found at *m/e* 179, 90, 133, 248 and 249 with abundances decreasing respectively. The presence of characteristic peaks at *m/e* 179, 133 and 90 indicated that 1- and 5-positions of the thiazolidine ring had not been involved in the reaction. The characteristic peaks at *m/e* 248 and 249, which exhibited the loss of O atom (mass=16) and -OH group (mass=17) respectively, indicated the free -OH group presence.

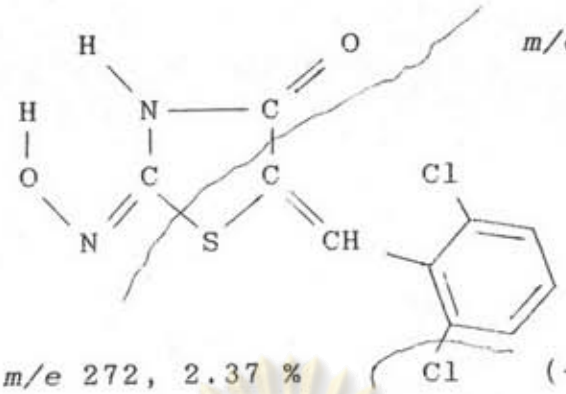


m/e 179, 50.31 %

(-17) *m/e* 248, 2.38 %

(-46) *m/e* 133, 13.74 %

2-Oximino-5-(2,6-dichlorobenzylidene)-4-thiazolidinone ($C_{10}H_6N_2O_2SCl_2$, MW.288) showed isotopic abundances M+1 at 13.51 %(calcd. 12.54 %) and M+2 at 69.52 %(calcd. 70.43 %). The characteristic peaks were found at *m/e* 253, 202 and 272 with abundances decreasing respectively. The loss of Cl atom (mass=35) gave the base peak at *m/e* 253. The presence of characteristic peaks at *m/e* 202 indicated that 1- and 5-positions of the thiazolidine ring had not been involved in the reaction. It was noted that the tropylium ion (*m/e* 90) could not be found due to the substitution of chlorine atom at ortho positions of benzyl structure. The characteristic peak at *m/e* 272, which exhibited the loss of O atom (mass=16), indicated the free -OH group presence.



m/e 202, 40.25 %

(-16) *m/e* 272, 2.37 %

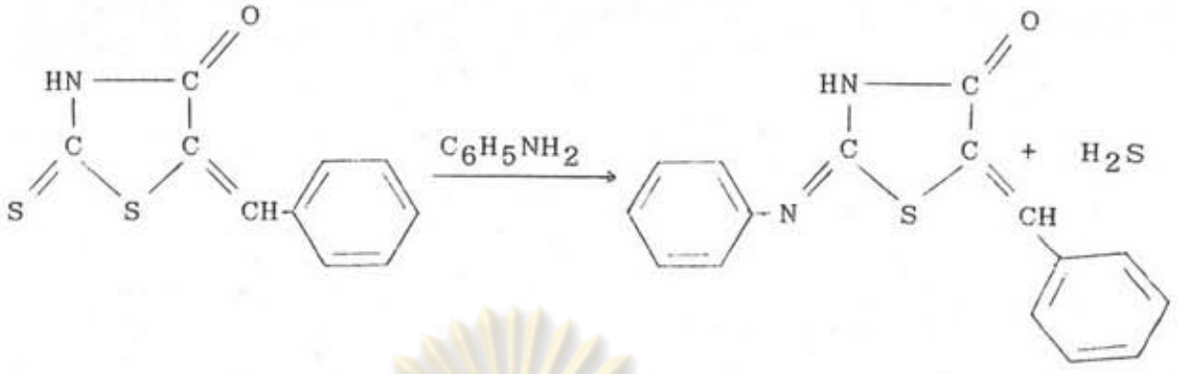
(-35) *m/e* 253, 100 %

m/e 288, 20.28 %

With the above evidences, confirmed that hydroxylamine reacted with 5-arylmethylenerhodanines at position 2 of the thiazolidine ring and gave the corresponding oximes.

2. Reaction of 5-arylmethylenerhodanines with aniline

The mixture of 5-benzylidenerhodanine and freshly redistilled aniline was heated until the evolution of H_2S ceased and gave 2-phenylimino-5-benzylidene-4-thiazolidinone, yield 50.3 %. However, when 5-(4-nitrobenzylidene)rhodanine or 5-(2,6-dichlorobenzylidene)rhodanine reacted with aniline under the above condition, more than ten products were observed on TLC plate. Seperation for pure product was unsuccessful.



a. IR-Absorption Spectra Analysis

The infrared absorption spectra of 2-phenylimino-5-benzylidene-4-thiazolidinone (figure 17) showed the characteristic carbonyl peak at 1679 cm^{-1} according to the bathochromic shift (37). This indicated that the 4 position in the rhodanine nucleus did not involved in the reaction. The characteristic peak for thione group at 1200 cm^{-1} was not observed which also indicated that the reaction was taken place at the 2 position. In addition, strong peak at 1640 cm^{-1} was observed which could be assigned as of C=N stretching vibration (65,66). And the N-H stretching was found at 3200-3300 cm^{-1}.

b. ^{1}H-NMR Spectra Analysis

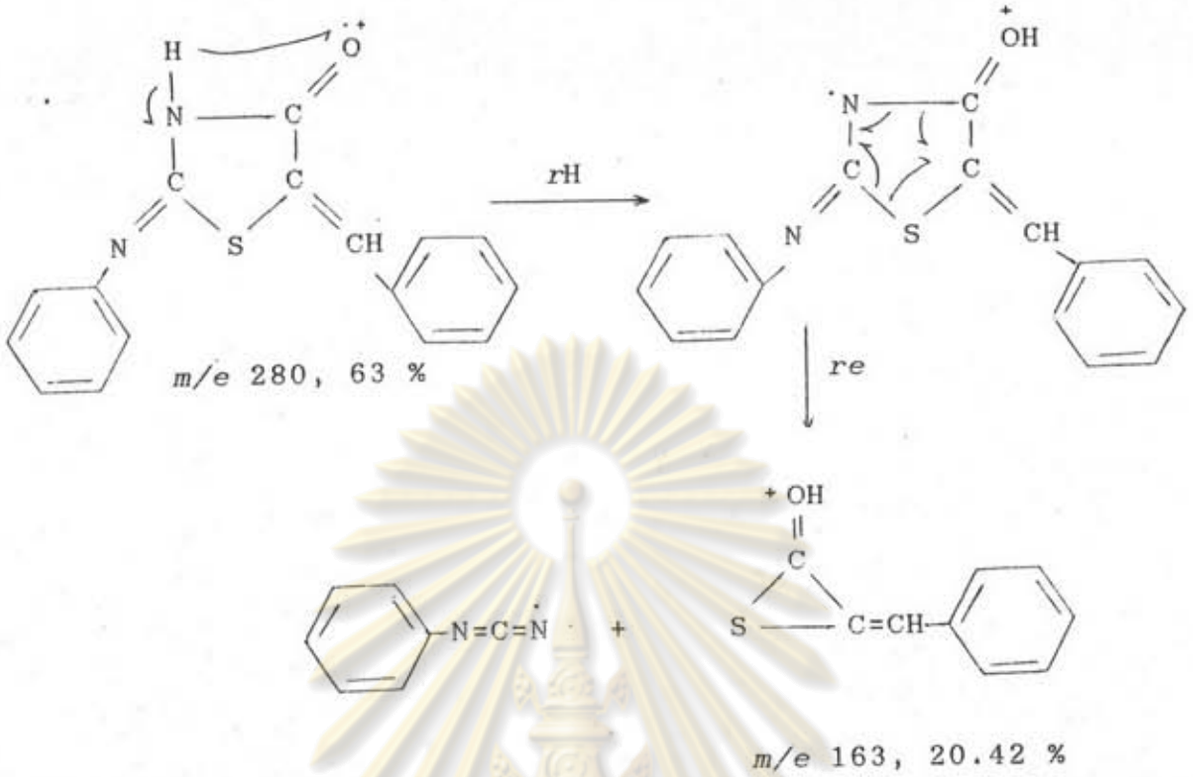
The nuclear magnetic resonance spectra of 2-phenylimino-5-benzylidene-4-thiazolidinone (figure 18) showed the broad spectrum at 11.2 ppm of -NH group. The aromatic hydrogen atoms of benzylidene ring and phenyl ring showed the chemical shift at range 7.0-7.8 ppm.

c. Mass Spectra Analysis

The EI mass spectra of 2-phenylimino-5-benzylidene-4-thiazolidinone ($C_{16}H_{12}N_2OS_2$, MW.280) showed isotopic abundances M+1 at 19.68 %(calcd. 19.08 %) and M+2 at 7.63 %(calcd. 6.18 %). The characteristic peaks were found at *m/e* 134, 135, 163 and 90 with abundances decreasing respectively. The presence of characteristic peaks at *m/e* 134 and 90 indicated that 1- and 5-positions of the thiazolidine ring had not been involved in the reaction. The characteristic peaks at *m/e* 135 and 163, exhibited the ion fragmentation as proposed as following :

m/e 280, 63 %

m/e 135, 21.09 %

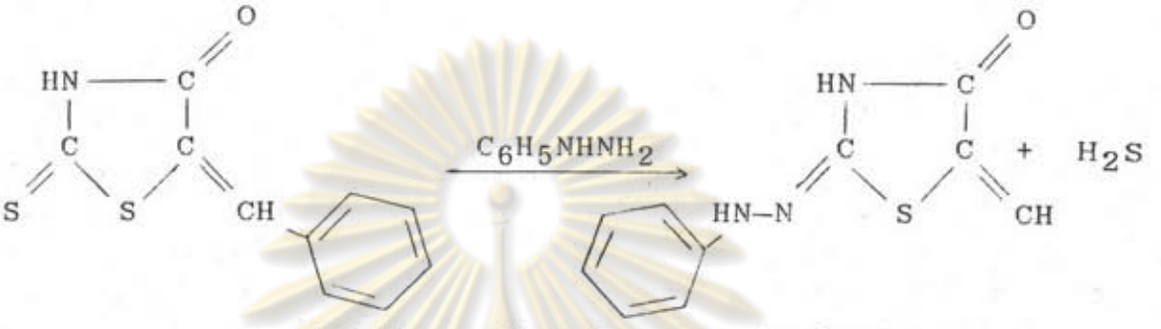


With the above data, it could be concluded that aniline reacted with 5-benzylidenerhodanine at position 2 of the thiazolidine ring and gave the phenylimino derivative.

3. Reaction of 5-arylmethylenerhodanines with phenylhydrazine

The mixture of 5-benzylidenerhodanine and phenylhydrazine was heated until the evolution of H_2S ceased and gave 2-phenylhydrazino-5-benzylidene-4-thiazolidinone. Phenylhydrazine was very sensitive to light, so the colour of the mixture was rapidly changed. The dark syrupy mass obtained made the difficulty of seperation the

target product. Therefore under this condition, the reaction failed with 5-(4-nitrobenzylidene)rhodanine and 5-(2,6-dichlorobenzylidene)rhodanine.



a. IR-Absorption Spectra Analysis

The infrared absorption spectra of 2-phenylhydrazino-5-benzylidene-4-thiazolidinone (figure 20) showed the characteristic carbonyl peak at 1676 cm^{-1} according to the bathochromic shift (37). This indicated that the 4 position in the rhodanine nucleus did not involved in the reaction. The characteristic peak for thione group at 1200 cm^{-1} was not observed which also indicated that the reaction was taken place at the 2 position. In addition, strong peak at 1642 cm^{-1} was observed which could be assigned as of C=N stretching vibration (65,66). And the N-H stretching was found at 3100-3450 cm^{-1}.

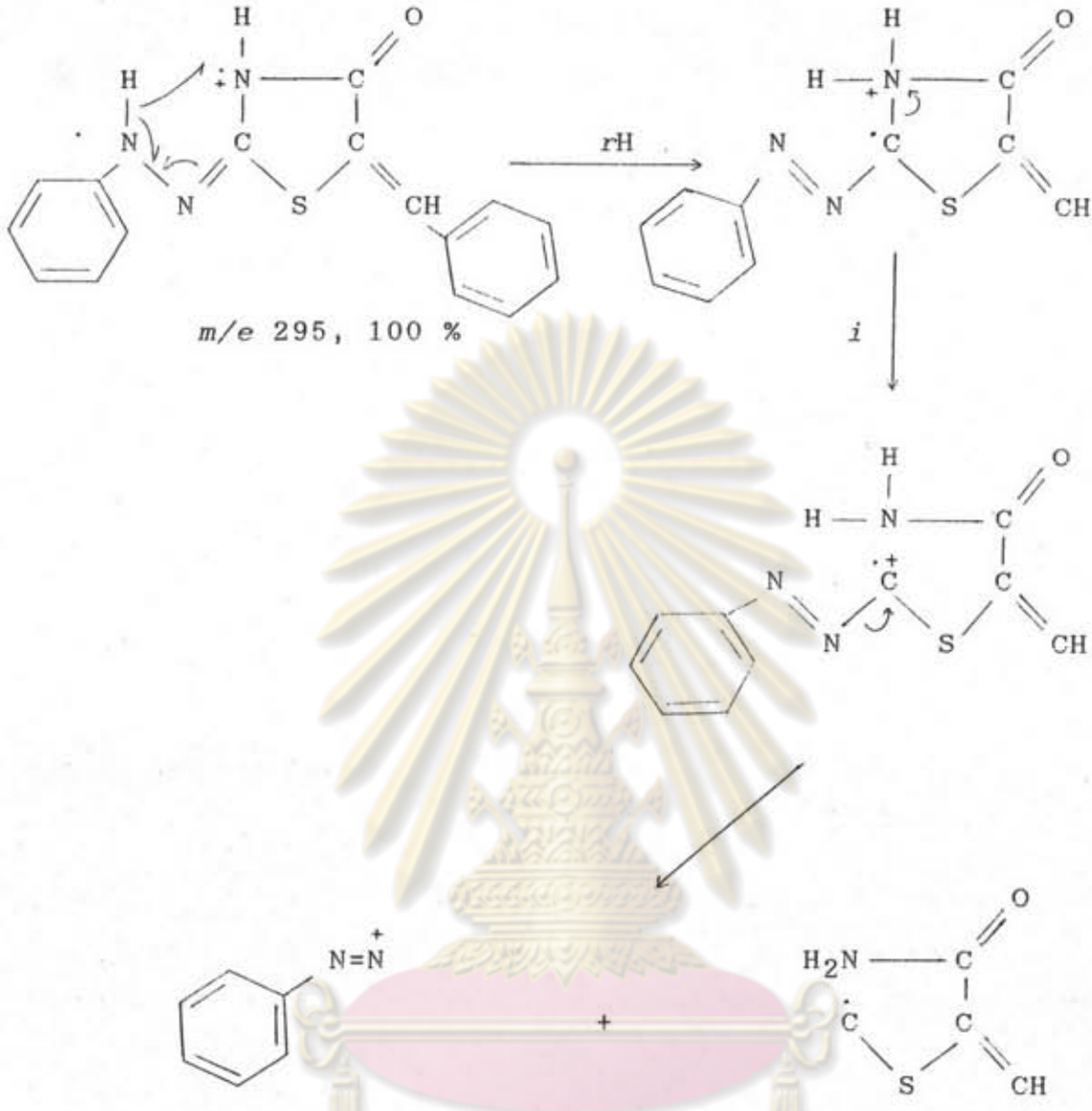
b. ^{1}H-NMR Spectra Analysis

The nuclear magnetic resonance spectra of 2-phenylhydrazino-5-benzylidene-4-thiazolidinone(figure 21)

exhibited a broad peak at 8.6 ppm, which was assigned as the -NH group at position 3 of the thiazolidine ring (65,66). The proton chemical shift was shifted further upfield, possibly, because of shielding effect of the benzene ring. The proton chemical shift of hydrazino group and benzylidene group were found at range 6.8-7.7 ppm.

c. Mass Spectra Analysis

The EI mass spectra of 2-phenyhydrazino -5-benzylidene-4-thiazolidinone ($C_{16}H_{13}N_3OS$, MW.295)showed isotopic abundances M+1 at 19.68 %(calcd. 19.48 %) and M+2 at 7.03 %(calcd. 6.24 %). The characteristic peaks were found at *m/e* 134, 163, 90 and 105 with abundances decreasing respectively. The presence of characteristic peaks at *m/e* 134 and 90 indicated that 1- and 5-positions of the thiazolidine ring had not been involved in the reaction. The characteristic peak at *m/e* 163 exhibited the ion fragmentation as 2-phenylimino-5-benzylidene-4-thiazolidinone. The characteristic peak at *m/e* 105 exhibited the ion fragmentation as proposed as following :



m/e 295, 100 %

m/e 105, 5.25 %

With the above data, it could be concluded that phenylhydrazine reacted with 5-benzylidenerhodanine at position 2 of the thiazolidine ring and gave the phenylhydrazino derivative.