



CHAPTER III

EXPERIMENTAL

Equipment

1. Melting Point Apparatus - Buchi Capillary Melting Point Apparatus
2. Infrared Spectrophotometer - Perkin-Elmer Model FTIR 1720 ^a
3. Nuclear Magnetic Resonance Spectrophotometer - Bruker FT-NMR 80 MHz ^a, Joel FX 90Q (90 MHz) ^b
4. Mass Spectrometer - Joel FX 3000 double focusing ^b

^a Department of Science Services, Ministry of Science, Technology and Energy.

^b The Scientific and Technological Research Equipment Center, Chulalongkorn University.

Chemicals

The starting materials, rhodanine, 2,6-dichloro benzaldehyde and phenylhydrazine were supplied by Fluka Chemie AG, benzaldehyde was supplied by May & Baker, p-nitrobenzaldehyde was supplied by Aldrich Chemical Co., hydroxylamine and aniline were supplied by Merck. However, aniline and phenylhydrazine were freshly redistilled before use. The solvents used were all BP. grade.

5-Benzylidenerhodanine

A 6.66 g (50 mmole) of rhodanine was dissolved in 50 ml of glacial acetic acid, then 12.3 g (150 mmole) of anhydrous sodium acetate was added. After the mixture became clear, 5.31 g (50 mmole) of benzaldehyde was added, and the reaction mixture was refluxed for 45 mins. After cooled to room temperature, yellow crystals were formed. The whole mixture was kept overnight in the refrigerator. The crystals were separated by filtration and washed several times with water to remove excess acid. The filtrate was poured into 300 ml of water and kept overnight in the refrigerator. A yellow precipitate formed was separated by filtration and washed with water. The crude product was dried in reduced pressure oven at 60 °C. Recrystallization from toluene yielded 8.8 g of the product (80 % yield), mp. 200-203 °C (lit. mp. 204-205) (49).

IR (KBr) : 3150-3440, 1720, 1601, 1197 cm^{-1}
(see figure 1)
 $^1\text{H-NMR}$: 13.48, 7.54, 7.46 ppm
(DMSO- d_6 + CDCl_3) (see figure 2)
MS : MW. 221(59.42 %) ; m/e 162(7.52 %),
134(100 %), 90(11.51 %)
(see figure 3)

5-(4-Nitrobenzylidene)rhodanine

A 13.3 g (100 mmole) of rhodanine and 24.6 g (300 mmole) of anhydrous sodium acetate were added to 100 ml glacial acetic acid. The mixture was warmed on a water bath to a clear solution, then 15.1 g (100 mmole) of p-nitrobenzaldehyde was added. The reaction mixture was refluxed for 45 mins. After cooling the mixture to room temperature, yellow crystals were formed. The mixture was kept overnight in the refrigerator and the crystals were separated by filtration and washed with water to remove excess acid. The filtrate was poured into another 200 ml of water and kept overnight in the refrigerator to obtain more crystals. The crystals were separated by filtration and washed with water. The crude product was dried in reduced pressure oven at 60 $^{\circ}\text{C}$. Recrystallization from acetone yielded 26.02 g of the product (97.7 % yield), mp. 259-260 $^{\circ}\text{C}$ (lit. mp. 273-274)(64).

IR (KBr) : 3050-3440, 1720, 1607, 1192 cm^{-1}
(see figure 4)
 $^1\text{H-NMR}$: 7.50 - 8.50 ppm
(DMSO- d_6 + CDCl_3) (see figure 5)

5-(2,6-Dichlorobenzylidene)rhodanine

A 6.66 g (50 mmole) of rhodanine and 12.3 g (150 mmole) of anhydrous sodium acetate were mixed in 50 ml glacial acetic acid. The mixture was warmed on a water bath until a clear solution was obtained. Then 8.75 g (50 mmole) of 2,6-dichlorobenzaldehyde was added to the solution. The mixture was refluxed for 60 mins and yellow needle crystals formed during the reflux. The reaction mixture was kept overnight in the refrigerator to get more crystals which were separated by filtration. The crystals were washed with water several times to remove excess acid. The filtrate was poured into another 100 ml of water and kept overnight in the refrigerator. The second crop of precipitate was filtered and washed with water. The crude product was dried in reduced pressure oven at 60 $^{\circ}\text{C}$. Recrystallization from methanol yielded 13.85 g of the product (95.4 % yield), mp. 178-179 $^{\circ}\text{C}$ (lit. mp.184-186)(3).

IR (KBr) : 3060-3440, 1706, 1610, 1190 cm^{-1}
 (see figure 6)
 $^1\text{H-NMR}$: 7.60, 7.40 ppm
 (DMSO- d_6 + CDCl_3) (see figure 7)

2-Oximino-5-benzylidene-4-thiazolidinone

A mixture of 1.1 g (5 mmole) of 5-benzylidene rhodanine, 615 mg (7.5 mmole) of anhydrous sodium acetate and 525 mg (7.5 mmole) hydroxylamine hydrochloride in 30 ml absolute ethanol was stirred at 60 °C until the evolution of H_2S ceased. Sodium chloride formed was filtered from the hot mixture. Then, the yellow clear solution was left at the room temperature. Yellow crystals were formed and separated by filtration. The total weight of the product was 452 mg (41.1 % yield). The crude product was recrystallized from ethanol which yielded yellow needle crystal, mp. 233-234 ° C.

IR (KBr) : 3300-3380, 3000-3130, 1700, 1666,
 1607 cm^{-1} (see figure 8)
 $^1\text{H-NMR}$: 10.52, 7.59, 7.54, 7.40 - 7.50 ppm
 (DMSO- d_6 + CDCl_3) (see figure 9)
 MS : MW. 220(100 %) ; m/e 204(7.29 %),
 203(4.01 %), 162(2.59 %), 134(83.12 %),
 90(10.32 %) (see figure 10)

2-Oximino-5-(4-nitrobenzylidene)-4-thiazolidinone

A 1.33 g (5 mmole) of 5-(4-nitrobenzylidene)rhodanine was dissolved in 40 ml of absolute ethanol. Then 1.4 g (20 mmole) of hydroxylamine hydrochloride and 1.64 g (20 mmole) of anhydrous sodium acetate were added. The mixture was refluxed for 4-5 hrs. After that the sodium chloride was filtered from the hot mixture. The orange filtrate was left at room temperature and then the pale yellow crystals were obtained. The crude product was recrystallized from ethanol which yielded 145 mg of yellow powder (10.9 % yield, mp. 251-252 °C).

IR (KBr) : 3300-3380, 2900-3120, 1694, 1666,
1611 cm^{-1} (see figure 11)

$^1\text{H-NMR}$: 11.89, 10.67, 7.57, 7.55 - 8.35 PPM
(DMSO- d_6 + CDCl_3) (see figure 12)

MS : MW. 265(100 %) ; m/e 249(4.87 %),
248(2.38 %), 179(50.31 %),
133(13.74 %), 90(3.46 %)
(see figure 13)

2-Oximino-5-(2,6-dichlorobenzylidene)-4-thiazolidinone

A mixture of 1.45 g (5 mmole) of 5-(2,6-dichlorobenzylidene)rhodanine, 615 mg (7.5 mmole) of anhydrous sodium acetate and 525 mg (7.5 mmole) hydroxylamine hydrochloride in 30 ml absolute ethanol was stirred at 60 °C

for 10 hrs. Then sodium chloride formed was filtered from the hot mixture and the filtrate was left at the room temperature. The pale yellow crystals were formed. The crude product was recrystallized from ethanol which yielded 413 mg pale yellow needles (28.7 % yield), mp. 240-243 °C.

IR (KBr) : 3100-3450, 3000-3400, 1694, 1621,
1602 cm^{-1} (see figure 14)

$^1\text{H-NMR}$: 11.31, 10.20, 7.49, 7.30 - 7.45 ppm
(DMSO- d_6 + CDCl_3) (see figure 15)

MS : MW. 288(20.28 %) ; m/e 272(2.37 %),
253(100 %), 202(40.25 %),
(see figure 16)

2-Phenylimino-5-benzylidene-4-thiazolidinone

The mixture of 1.1 g (5 mmole) 5-benzylidene rhodanine and 3 ml (32 mmole) aniline was heated until the evolution of H_2S ceased. The orange precipitates formed were filtered and washed with ethanol. The crude product was recrystallized from dimethylsulfoxide, which yielded 705 mg of orange powder (50.3 % yield), mp. 251-252 °C.

IR (KBr) : 3200-3300, 1679, 1640, 1602 cm^{-1}
 (see figure 17)

$^1\text{H-NMR}$: 11.19, 7.76, 7.00 - 7.70 ppm
 (DMSO- d_6 + CDCl_3) (see figure 18)

MS : MW. 280(63.0 %) ; m/e 163(20.42 %),
 135(21.09 %), 134(100 %), 90(9.39 %)
 (see figure 19)

2-Phenylhydrazino-5-benzylidene-4-thiazolidinone

The mixture of 1.1 g (5 mmole) 5-benzylidene rhodanine and 3 ml (30 mmole) phenylhydrazine was heated until the evolution of H_2S ceased. The dark syrupy mass obtained was dissolved with 10 ml of benzene, then 10 ml of dilute hydrochloric acid was added. The aqueous was discarded and the benzene solution was evaporated. Hexane was added to the syrupy mass and then the dark orange precipitates were obtained. The dried precipitates were recrystallized from ethanol which yielded 243 mg of dark orange needles (16.4 % yield), mp. 217-218 $^\circ\text{C}$.

IR (KBr) : 3100-3450, 1676, 1642, 1602 cm^{-1}
 (see figure 20)

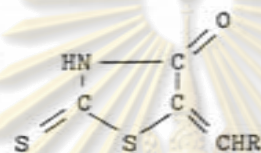
$^1\text{H-NMR}$: 8.6, 7.65, 6.80 - 7.70 ppm
 (DMSO- d_6 + CDCl_3) (see figure 21)

MS : MW. 295(100 %) ; *m/e* 163(8.43 %),
134(35.81 %), 105(5.25 %), 90(6.15 %)
(see figure 22)



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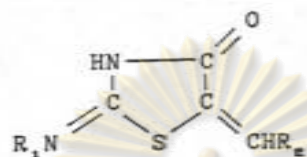
Table 1 : Physicochemical Properties of 5-Arylmethylenerrhodanines.



Compound	Appearance	mp(°C)	% Yield	Formula	MW.
I. 5-Benzylidenerhodanine R = C ₆ H ₅	Yellow needles	200-203	80.0	C ₁₀ H ₇ NOS ₂	221
II. 5-(4-Nitrobenzylidene) rhodanine R = C ₆ H ₄ NO ₂	Yellow needles	256-259	97.7	C ₁₀ H ₆ N ₂ O ₃ S ₂	266
III. 5-(2,6-Dichlorobenzylidene) rhodanine R = C ₆ H ₃ Cl ₂	Pale yellow needles	178-179	95.4	C ₁₀ H ₅ NOS ₂ Cl ₂	289

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Table 2 : Physicochemical Properties of 2-Imino-5-arylmethylene-4-thiazolidinones.



Compound	Appearance	mp (°C)	% Yield	Formula	MW.
I. 2-Oximino-5-benzylidene-4-thiazolidinone $R_1 = OH, R_2 = C_6H_5$	Yellow needles	233-234	41.1	$C_{10}H_8N_2O_2S$	220
II. 2-Oximino-5-(4-nitrobenzylidene)-4-thiazolidinone $R_1 = OH, R_2 = C_6H_4NO_2$	Yellow powder	251-252	10.9	$C_{10}H_7N_3O_4S$	265
III. 2-Oximino-5-(2,6-dichlorobenzylidene)-4-thiazolidinone $R_1 = OH, R_2 = C_6H_3Cl_2$	Pale yellow needles	240-243	28.7	$C_{10}H_6N_2O_2SCl_2$	288
IV. 2-Phenylimino-5-benzylidene-4-thiazolidinone $R_1 = C_6H_5, R_2 = C_6H_5$	Orange powder	251-252	50.3	$C_{16}H_{12}N_2OS$	280
V. 2-Phenylhydrazino-5-benzylidene-4-thiazolidinone $R_1 = NHC_6H_5, R_2 = C_6H_5$	Dark orange needles	217-218	16.4	$C_{16}H_{13}N_3OS$	295

Table 3 : Characteristic IR-Absorption of 5-Arylmethylenethioamides as Potassium Bromide Pellets.

Compound ^a	Wave Number (cm ⁻¹)					
	N-H st	C=O st	C=C st	N-H st	C=S st	C-N st
I	3150-3440	1702	1601	1590	1197	1239
II	3050-3440	1720	1607	1589	1192	1238
III	3060-3440	1706	1610	1580	1190	1228

- ^a I = 5-Benzylideneethioamide,
 II = 5-(4-Nitrobenzylidene)ethioamide,
 III = 5-(2,6-Dichlorobenzylidene)ethioamide

Table 4 : Characteristic IR-Absorption of 2-Imino-5-arylmethylene-4-thiazolidinones as Potassium Bromide Pellets.

Compound*	Wave Number (cm ⁻¹)						
	O-H st	N-H st	C=O st	C=N st	C=C st	N-H δ	C-N st
I	3300-3380	3000-3130	1700	1661	1607	1493	1251
II	3300-3380	2900-3120	1694	1666	1611	1592	1249
III	3100-3450	3000-3400	1694	1621	1602	1591	1242
IV	-	3200-3300	1679	1640	1602	1573	1247
V	-	3100-3450	1676	1642	1602	1495	1257

- * I = 2-Oximino-5-benzylidene-4-thiazolidinone,
 II = 2-Oximino-5-(4-nitrobenzylidene)-4-thiazolidinone,
 III = 2-Oximino-5-(2,6-dichlorobenzylidene)-4-thiazolidinone,
 IV = 2-Phenylimino-5-benzylidene-4-thiazolidinone,
 V = 2-Phenylhydrazino-5-benzylidene-4-thiazolidinone.

Table 5 : Characteristic ¹H-NMR of 5-Arylmethylenerrhodanines.

Compound ^a	Solvent	Chemical Shift of Proton (ppm)		
		-NH	=CH	ar-H
I	DMSO-d ₆ + CDCl ₃	13.48	7.54	7.46
II	DMSO-d ₆ + CDCl ₃	-	-	7.50 - 8.50
III	DMSO-d ₆ + CDCl ₃	-	7.60	7.40

^a I = 5-Benzylidenerhodanine,

II = 5-(4-Nitrobenzylidene)rhodanine,

III = 5-(2,6-Dichlorobenzylidene)rhodanine.

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Table 6 : Characteristic ¹H-NMR of 2-Imino-5-arylmethylene-4-thiazolidinones.

Compound ^a	Solvent	Chemical Shift of Proton (ppm)			
		-NH	-NOH	=CH	ar-H
I	DMSO-d ₆ + CDCl ₃	10.52	7.59	7.54	7.40 - 7.50
II	DMSO-d ₆ + CDCl ₃	11.89	10.67	7.57	7.55 - 8.35
III	DMSO-d ₆ + CDCl ₃	11.31	10.20	7.49	7.30 - 7.45
IV	DMSO-d ₆ + CDCl ₃	11.19	-	7.76	7.00 - 7.70
V	DMSO-d ₆ + CDCl ₃	8.6	-	7.65	6.80 - 7.70

- ^a I = 2-Oximino-5-benzylidene-4-thiazolidinone,
 II = 2-Oximino-5-(4-nitrobenzylidene)-4-thiazolidinone,
 III = 2-Oximino-5-(2,6-dichlorobenzylidene)-4-thiazolidinone,
 IV = 2-Phenylimino-5-benzylidene-4-thiazolidinone,
 V = 2-Phenylhydrazino-5-benzylidene-4-thiazolidinone.

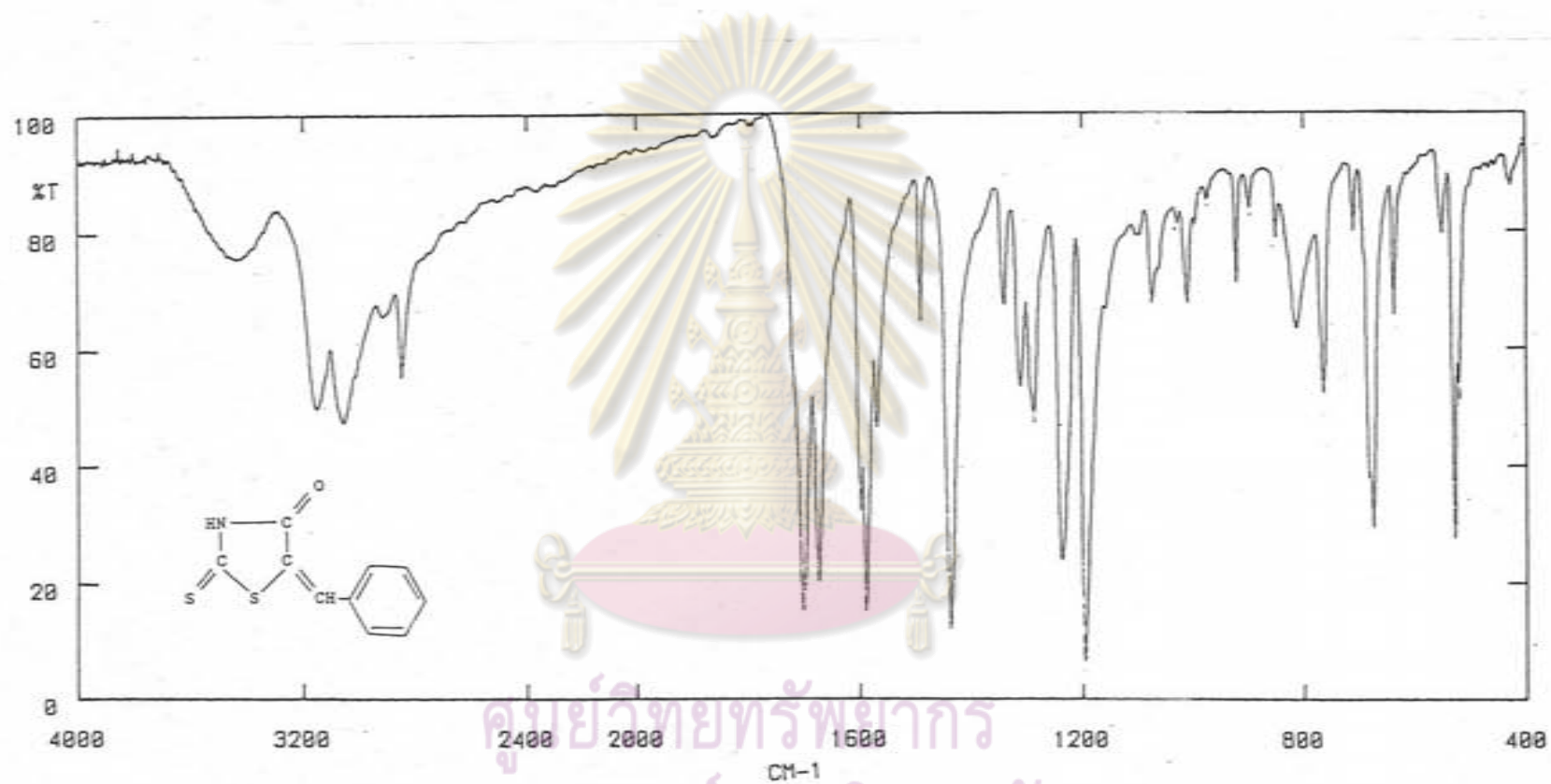


Figure 1 Infrared Absorption Spectrum of 5-Benzylidenerhodanine as a Potassium Bromide Pellet.

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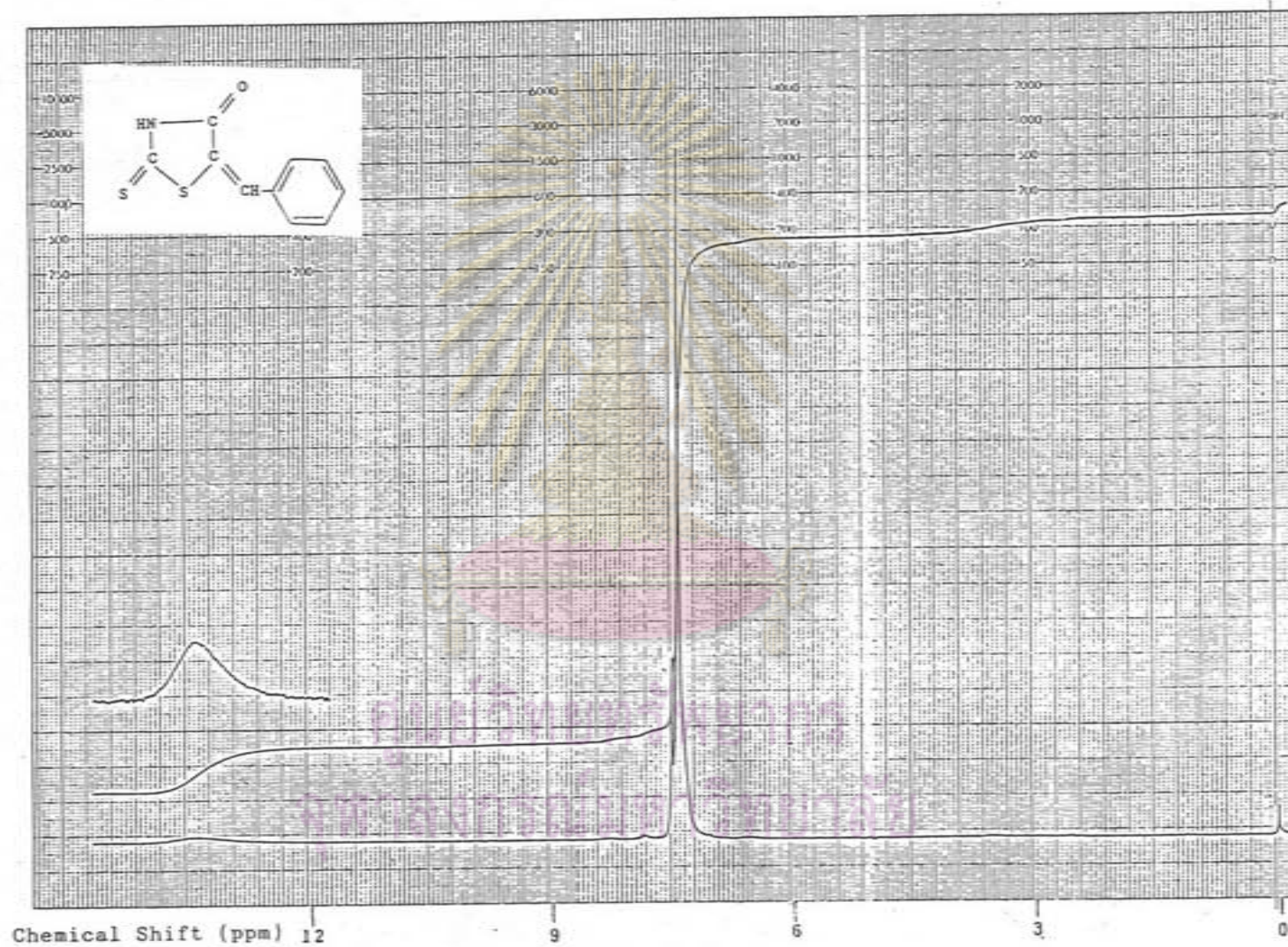


Figure 2 Proton Nuclear Magnetic Resonance Spectrum of 5-Benzylidenerhodanine in Dimethylsulfoxide-d₆ and Chloroform-d.

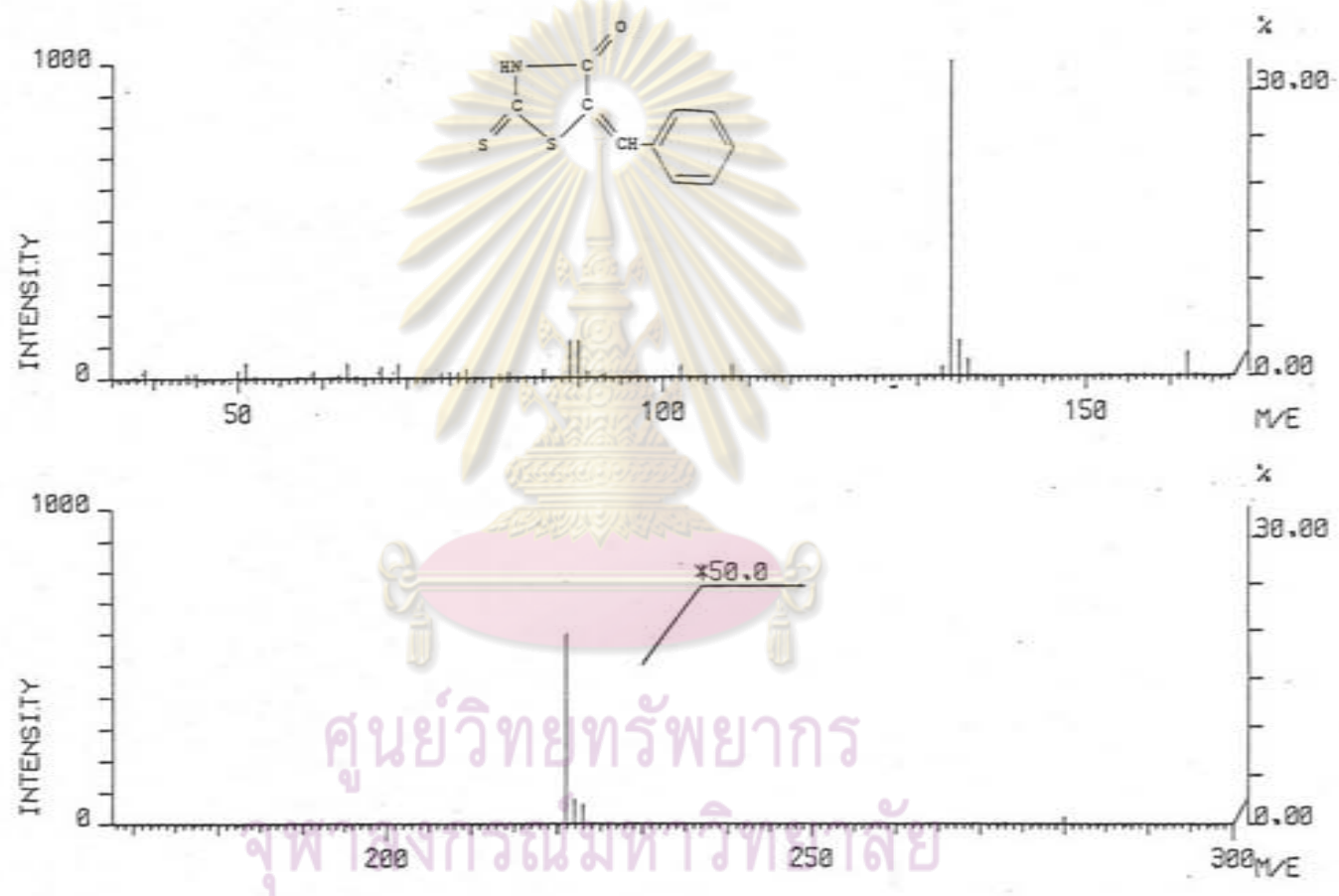


Figure 3 Mass Spectrum of 5-Benzylidenerhodanine.

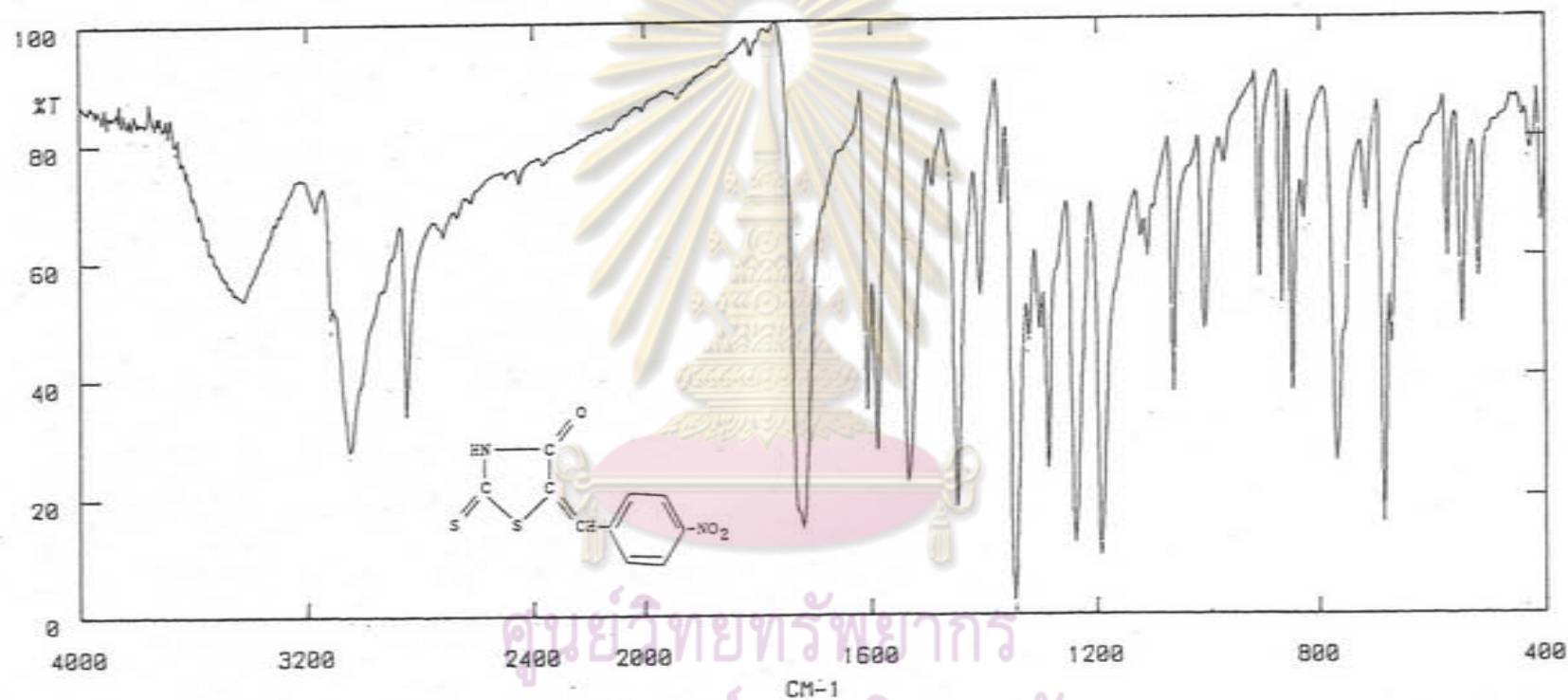


Figure 4 Infrared Absorption Spectrum of 5-(4-Nitrobenzylidene) rhodanine as a Potassium Bromide Pellet.

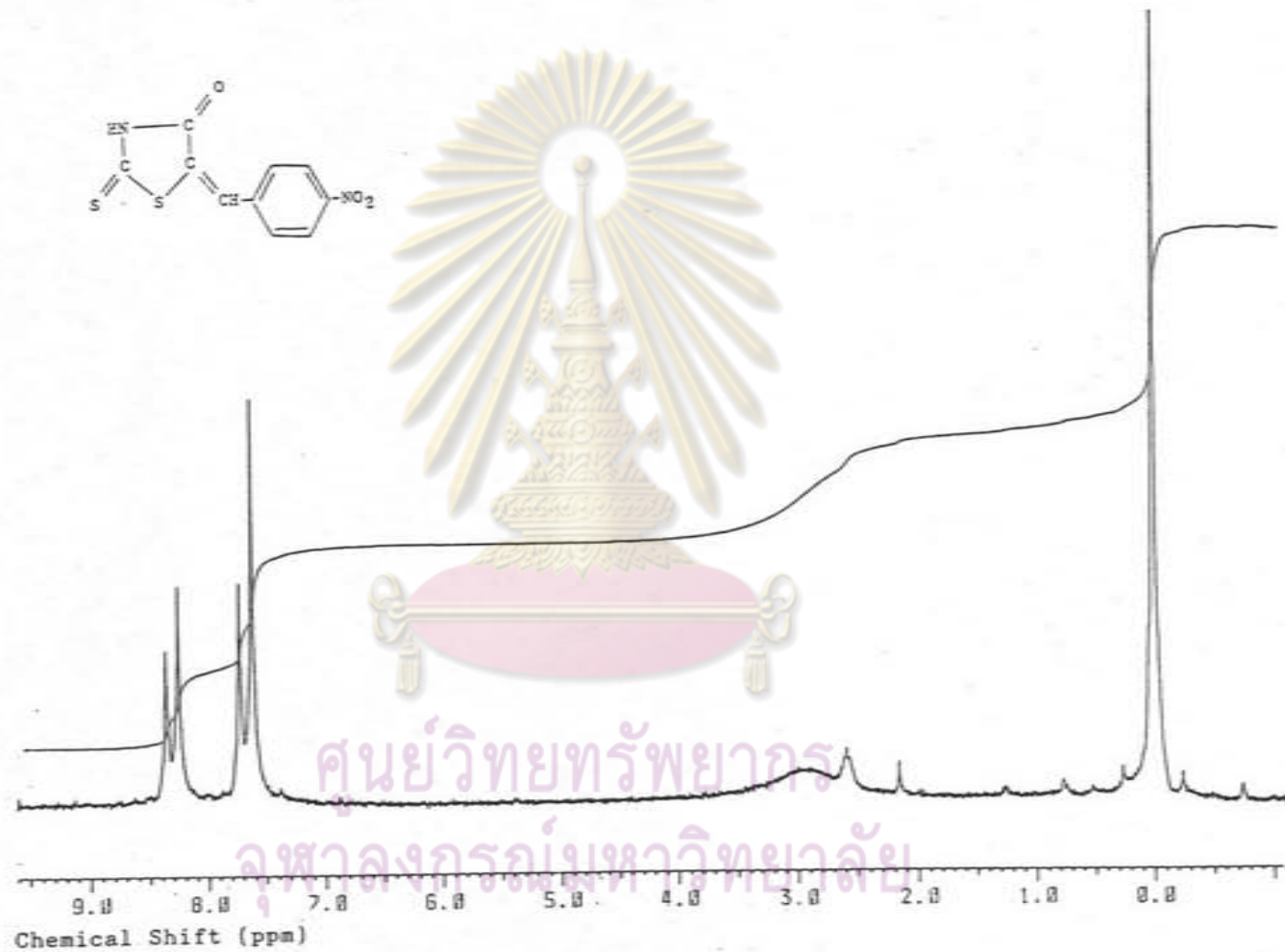


Figure 5 Proton Nuclear Magnetic Resonance Spectrum of
5-(4-Nitrobenzylidene)rhodanine in
Dimethylsulfoxide-d₆ and Chloroform-d.

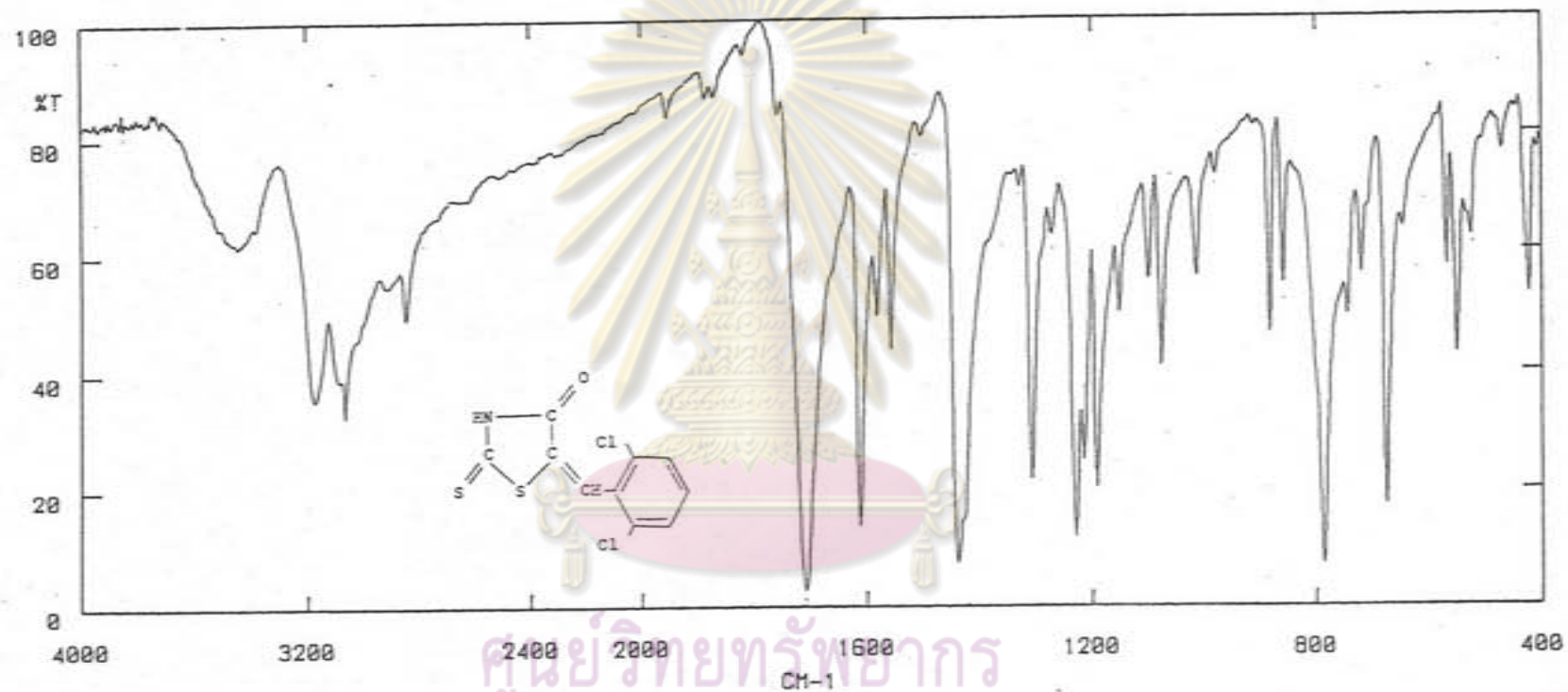


Figure 6 Infrared Absorption Spectrum of 5-(2,6-dichlorobenzylidene)rhodanine as a Potassium Bromide Pellet.

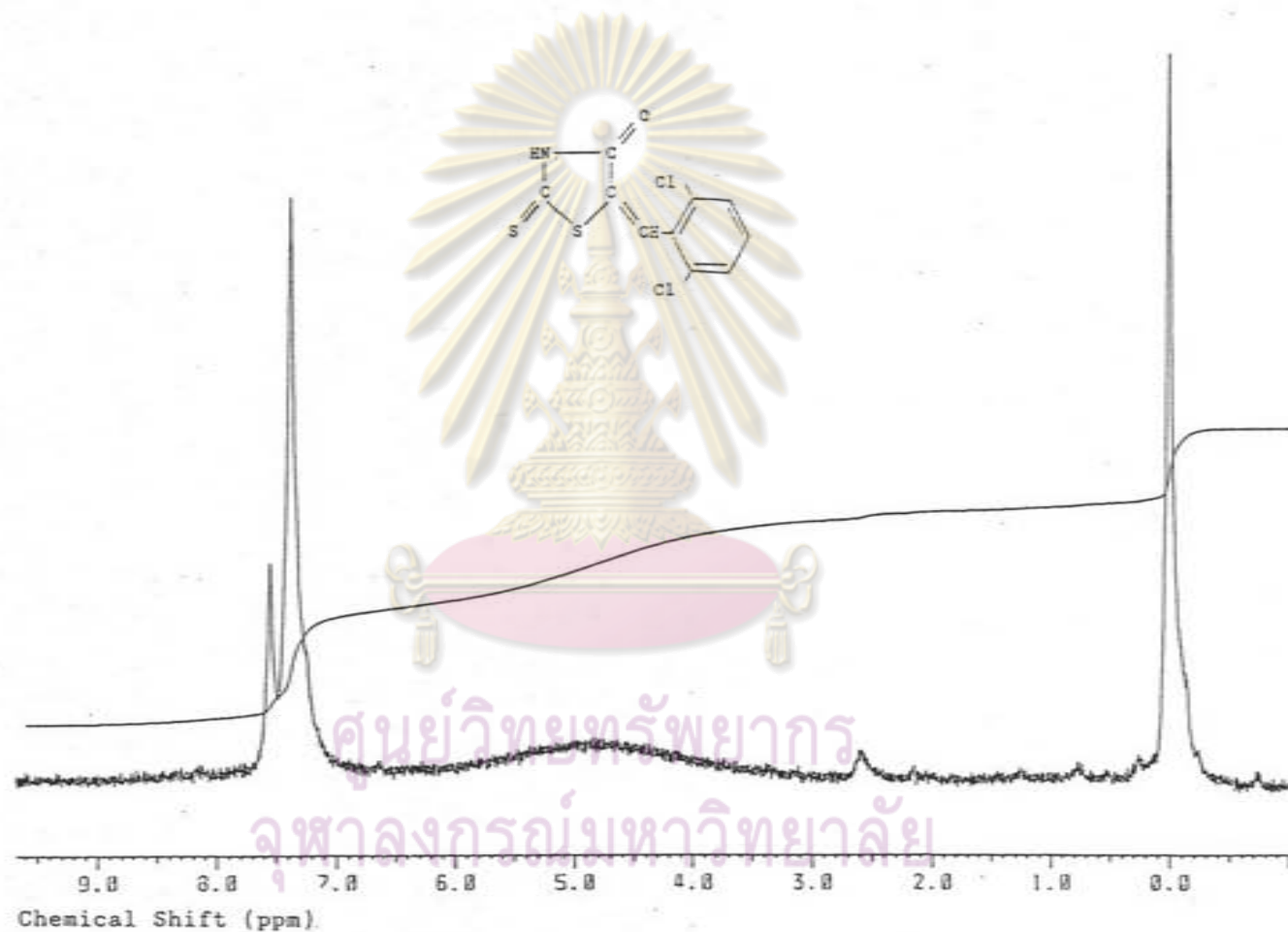


Figure 7 Proton Nuclear Magnetic Resonance Spectrum of 5-(2,6-dichlorobenzylidene)rhodanine in Dimethylsulfoxide- d_6 and Chloroform- d .

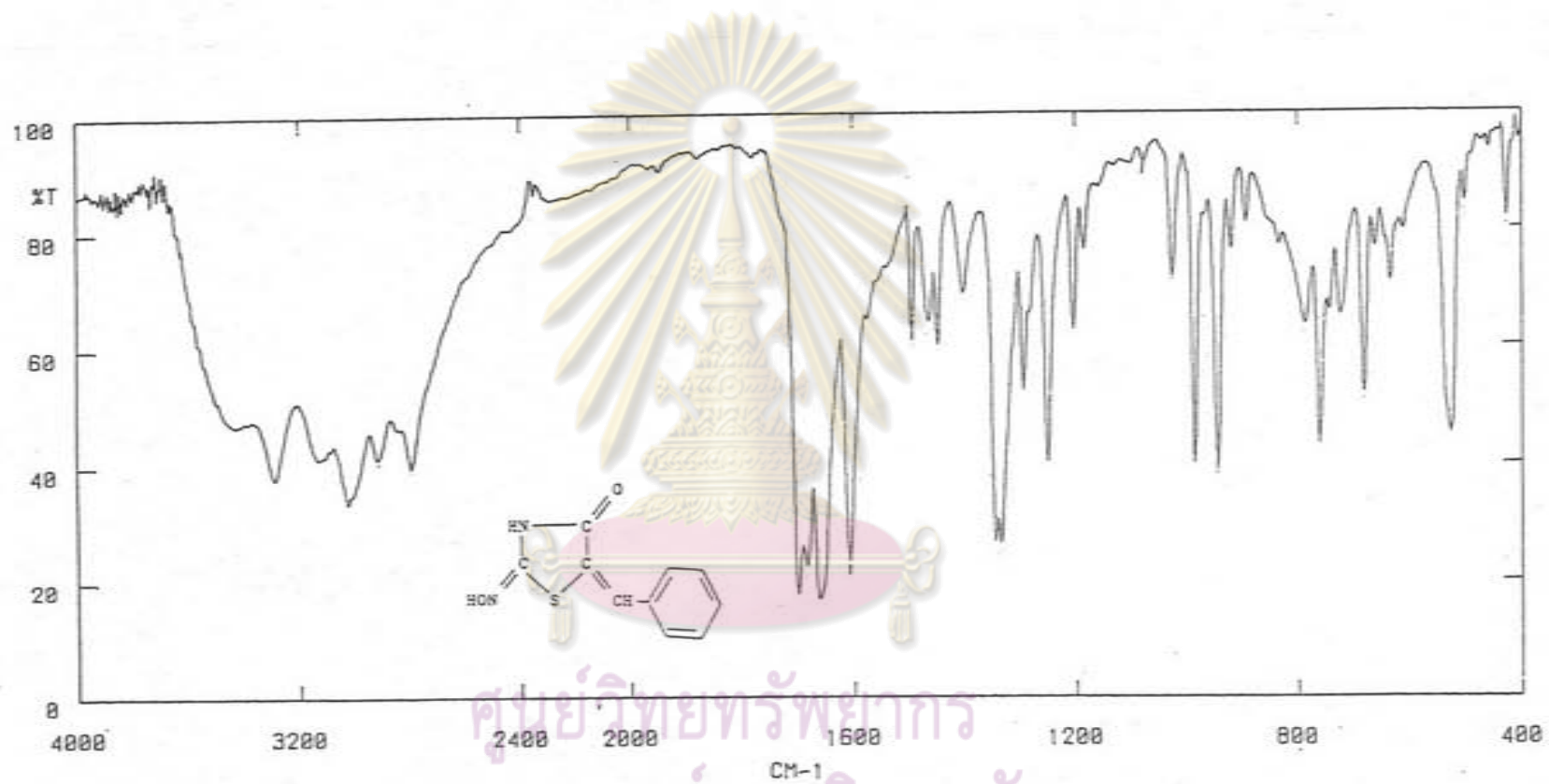


Figure 8 Infrared Absorption Spectrum of 2-Oximino-5-benzylidene-4-thiazolidinone as a Potassium Bromide Pellet.

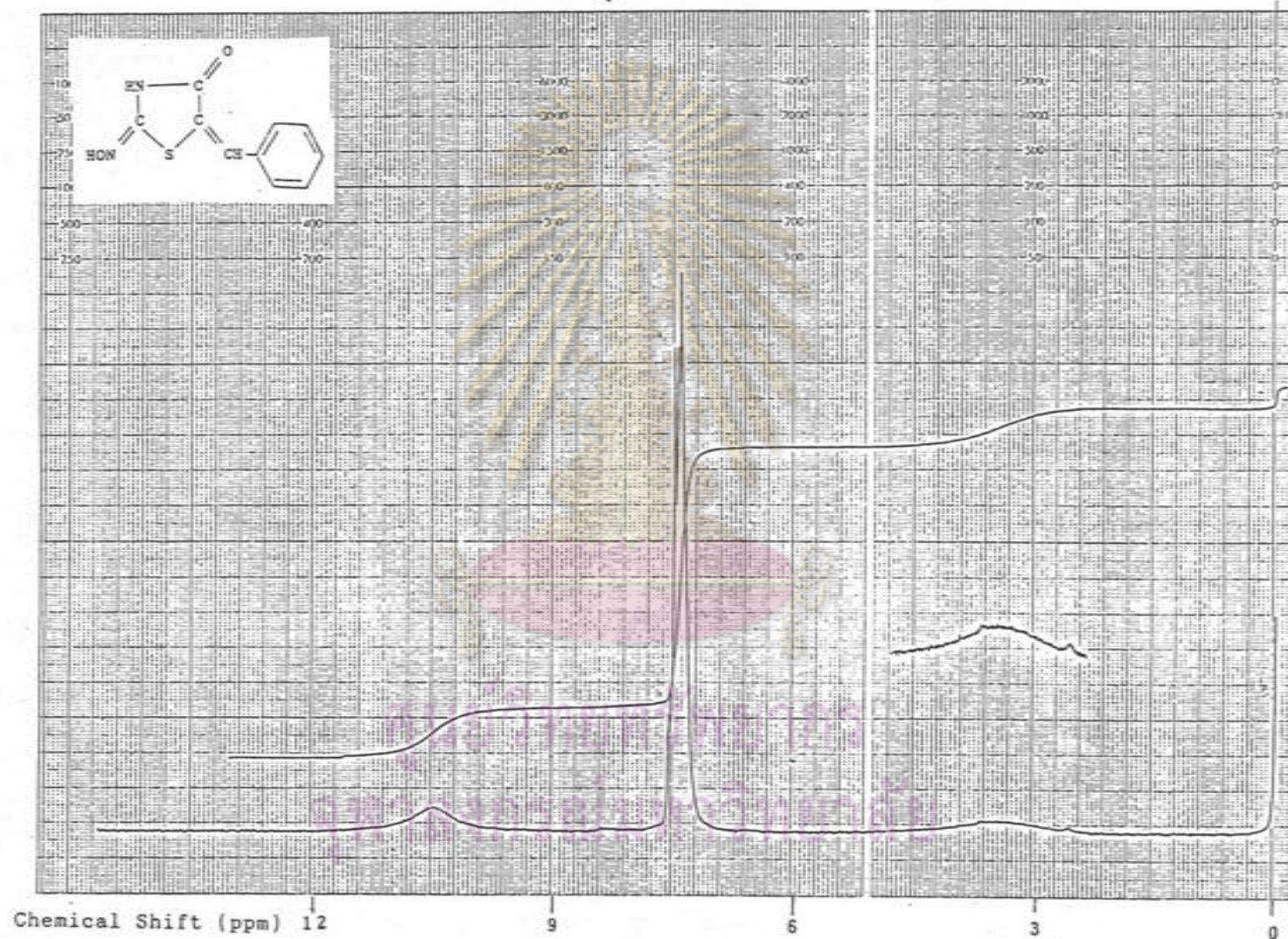


Figure 9 Proton Nuclear Magnetic Resonance Spectrum of
 2-Oximino-5-benzylidene-4-thiazolidinone in
 Dimethylsulfoxide-d₆ and Chloroform-d.

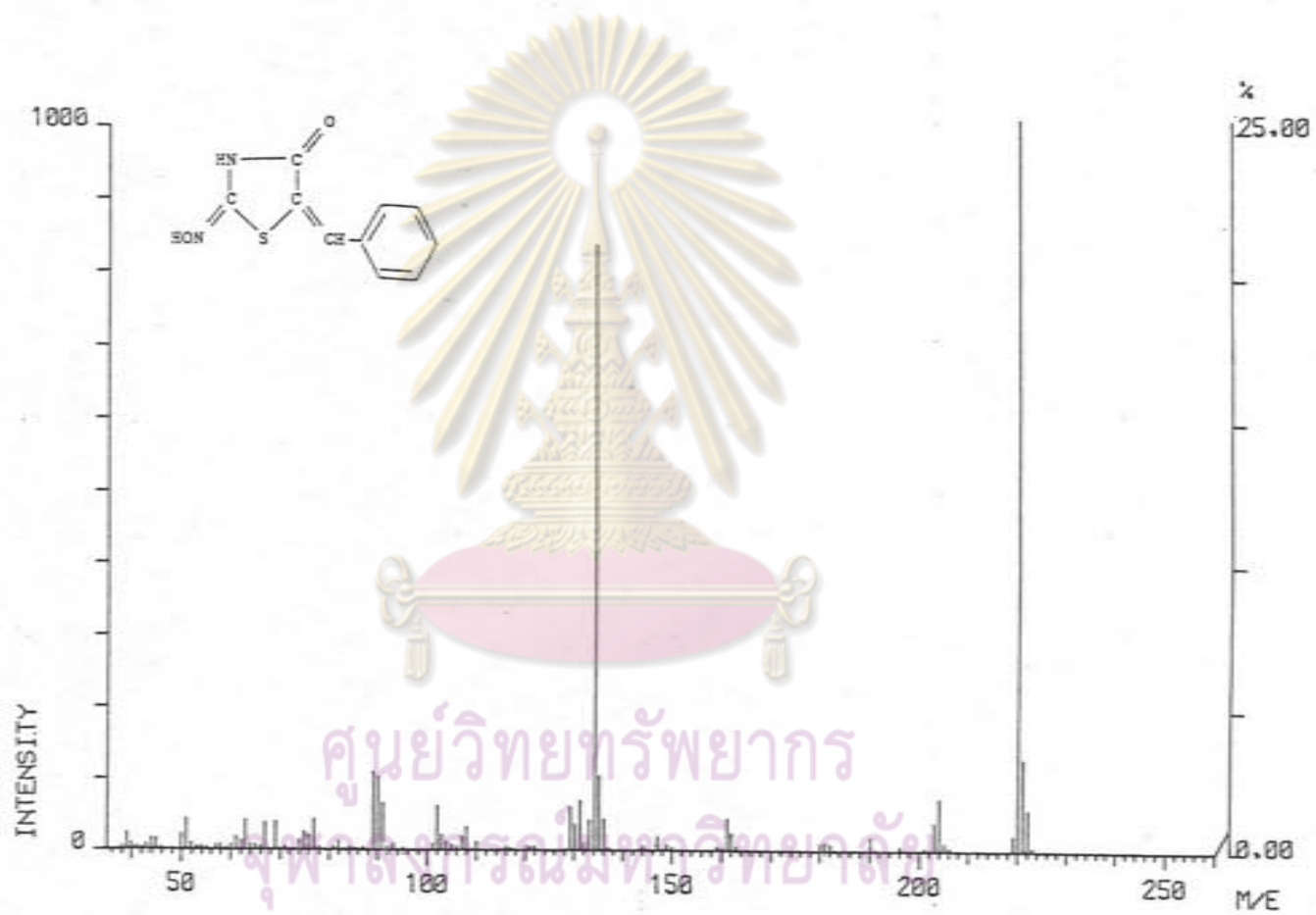


Figure 10 Mass Spectrum of 2-Oximino-5-benzylidene-4-thiazolidinone.

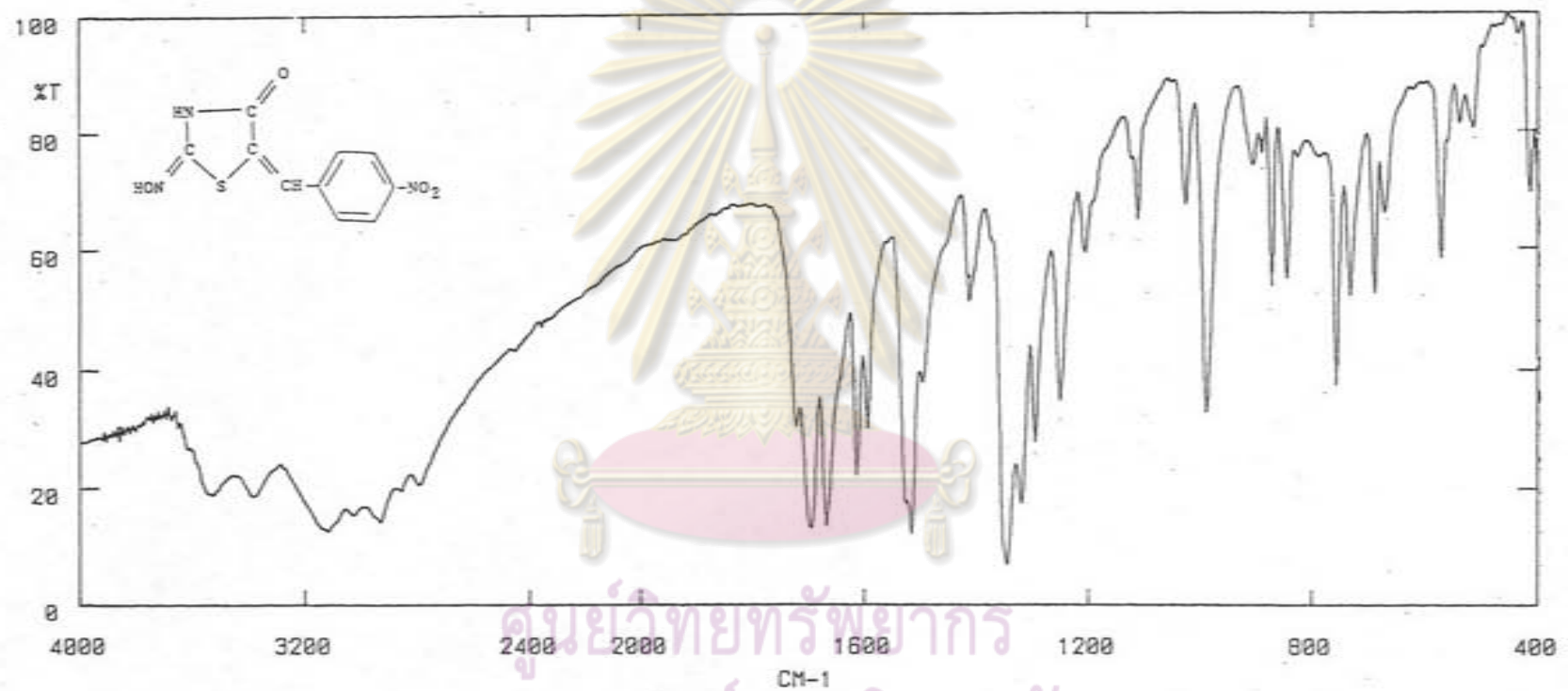


Figure 11 Infrared Absorption Spectrum of 2-Oximino-5-(4-nitrobenzylidene)-4-thiazolidinone as a Potassium Bromide Pellet.

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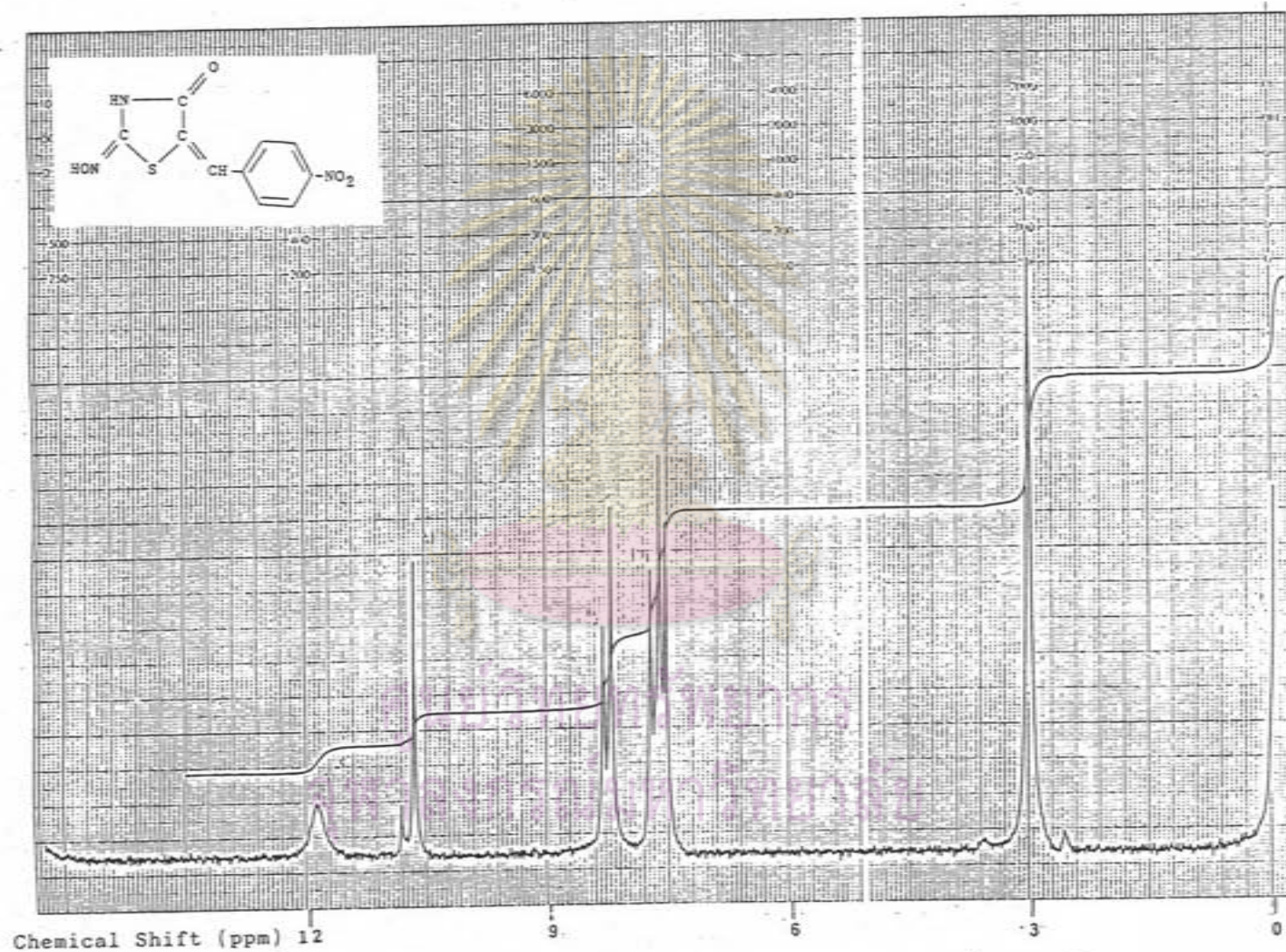


Figure 12 Proton Nuclear Magnetic Resonance Spectrum of
 2-Oximino-5-(4-nitrobenzylidene)-4-thiazolidinone
 in Dimethylsulfoxide- d_6 and Chloroform- d .

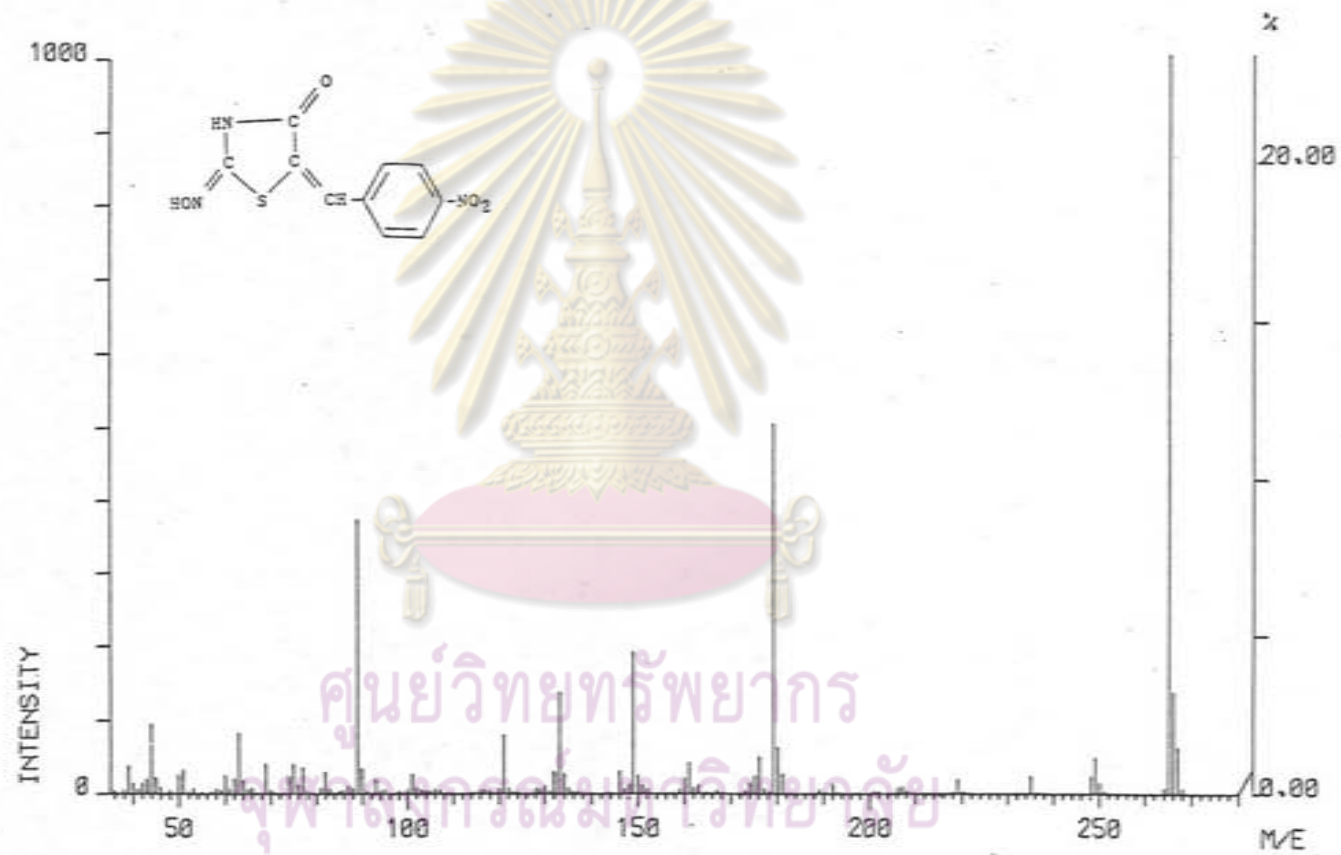


Figure 13 Mass Spectrum of 2-Oximino-5-(4-nitrobenzylidene)-4-thiazolidinone.

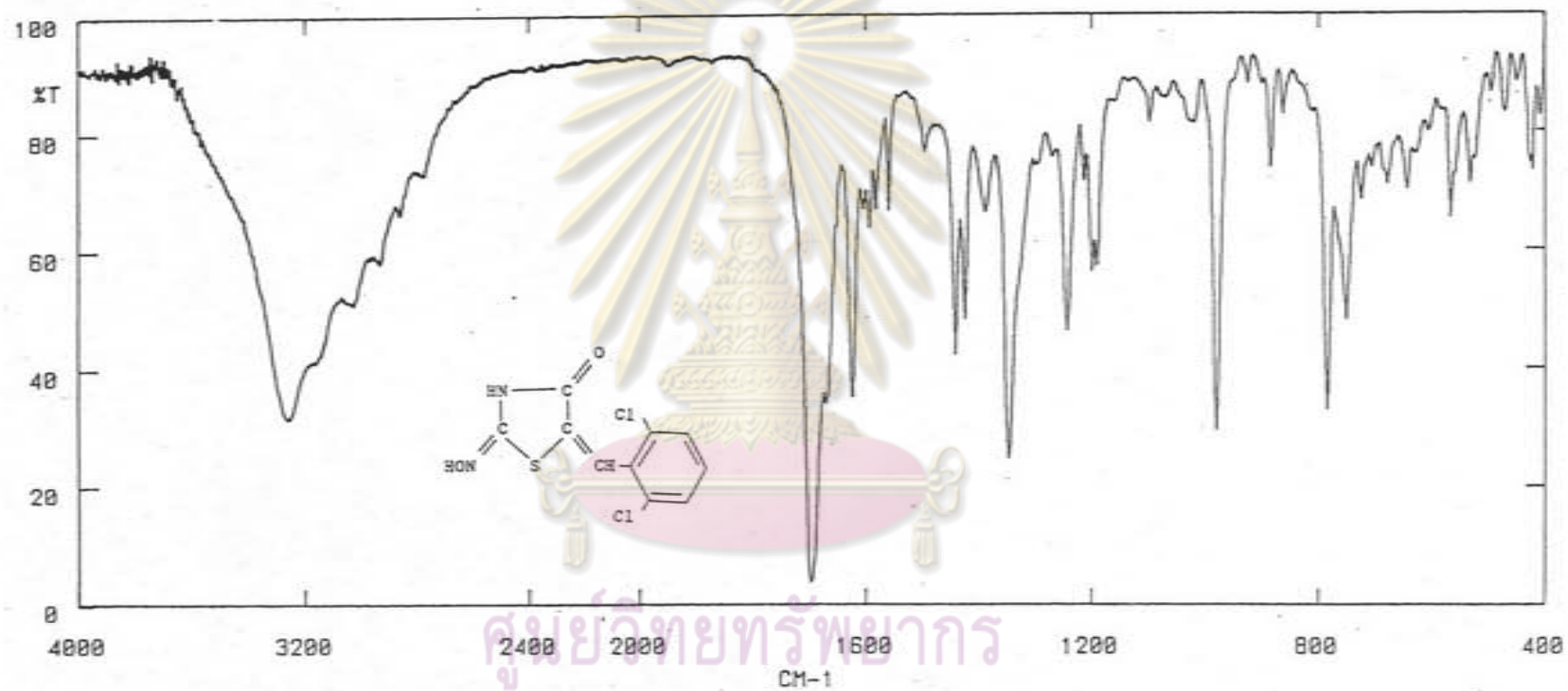


Figure 14 Infrared Absorption Spectrum of 2-Oximino-5-(2,6-dichlorobenzylidene)-4-thiazolidinone as a Potassium Bromide Pellet.

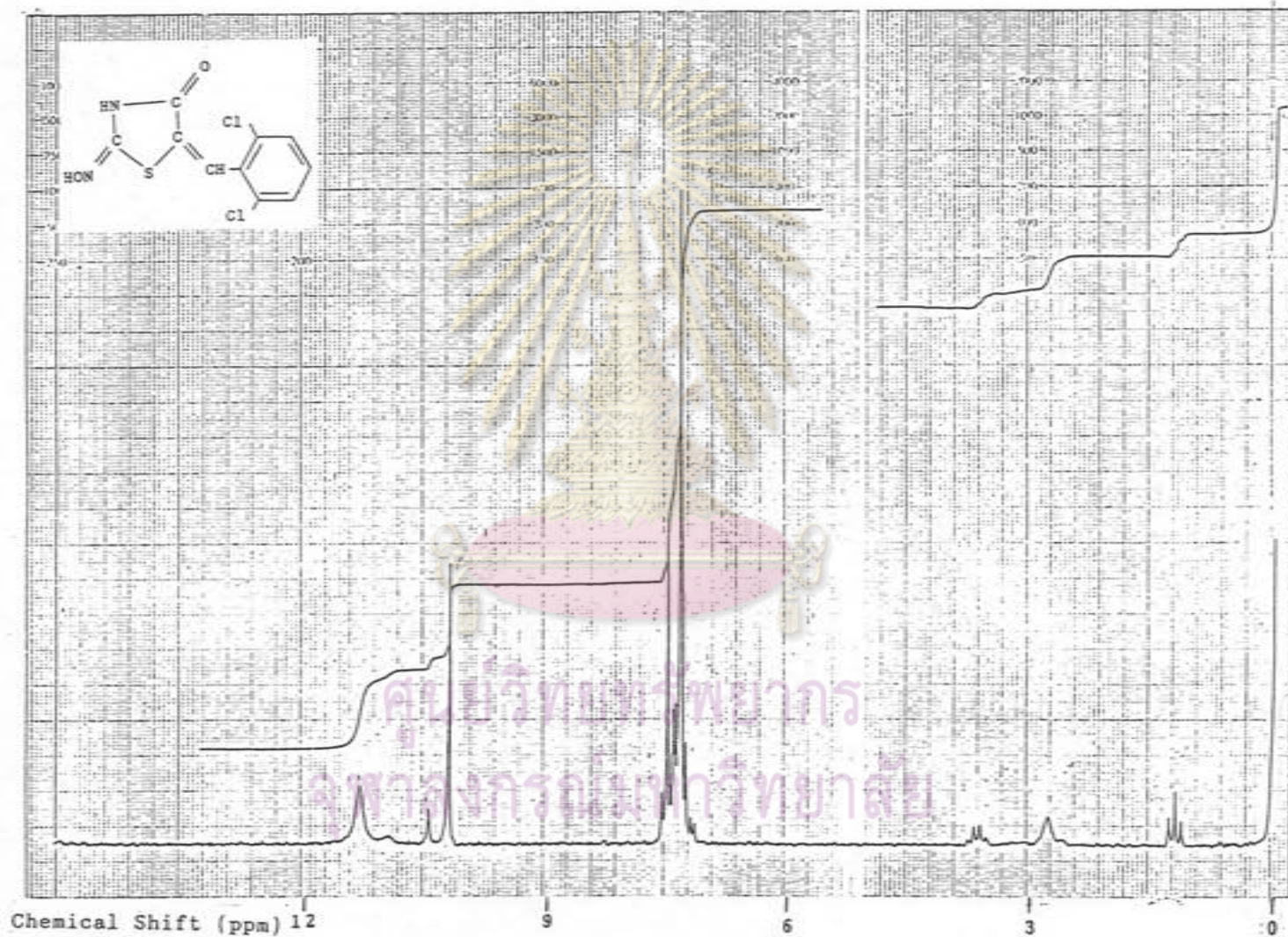


Figure 15 Proton Nuclear Magnetic Resonance Spectrum of
 2-Oximino-5-(2,6-dichlorobenzylidene)-4-thiazolidinone
 in Dimethylsulfoxide-d₆ and Chloroform-d.

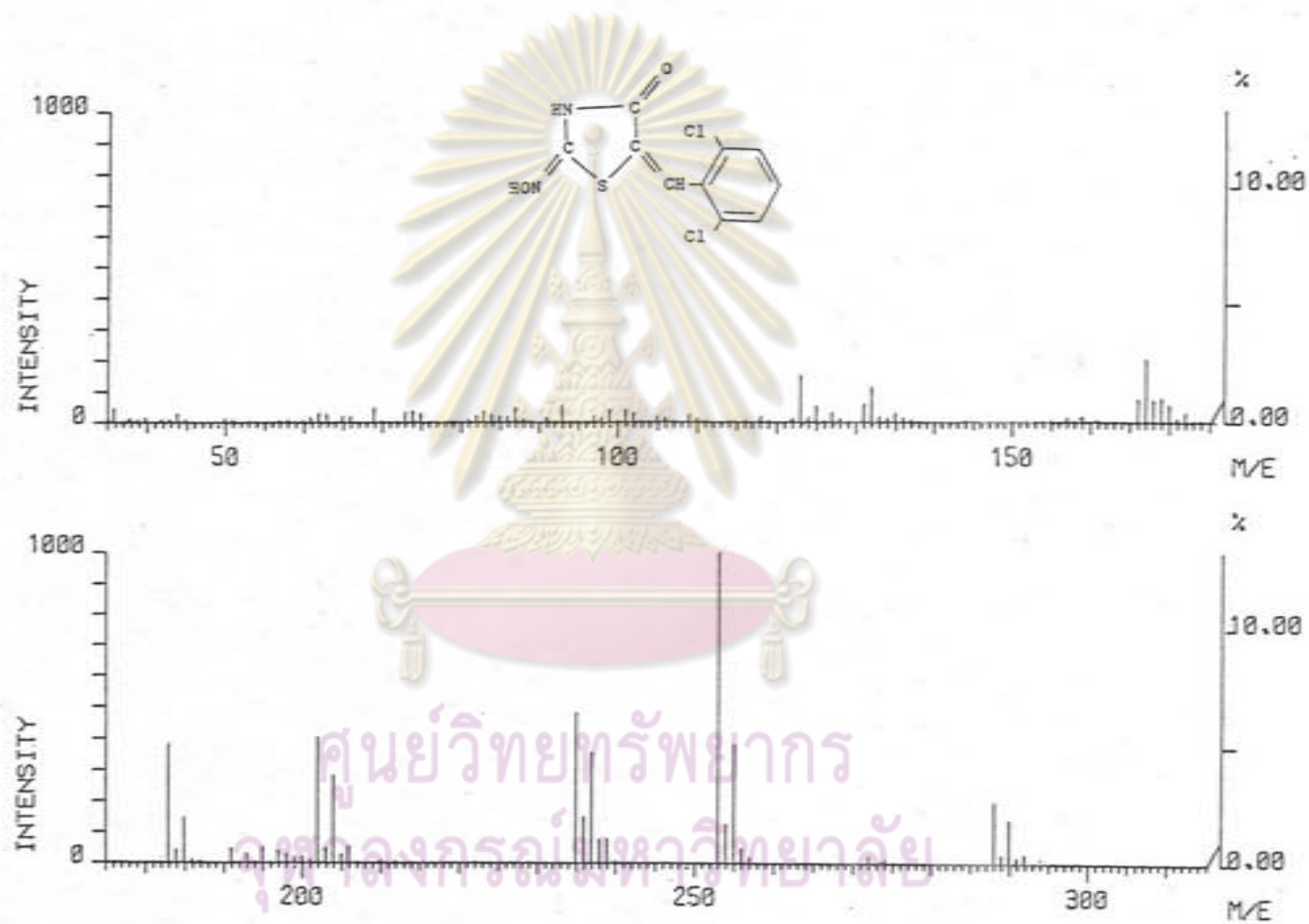


Figure 16 Mass Spectrum of 2-Oximino-5-(2,6-dichloro-benzylidene)-4-thiazolidinone.

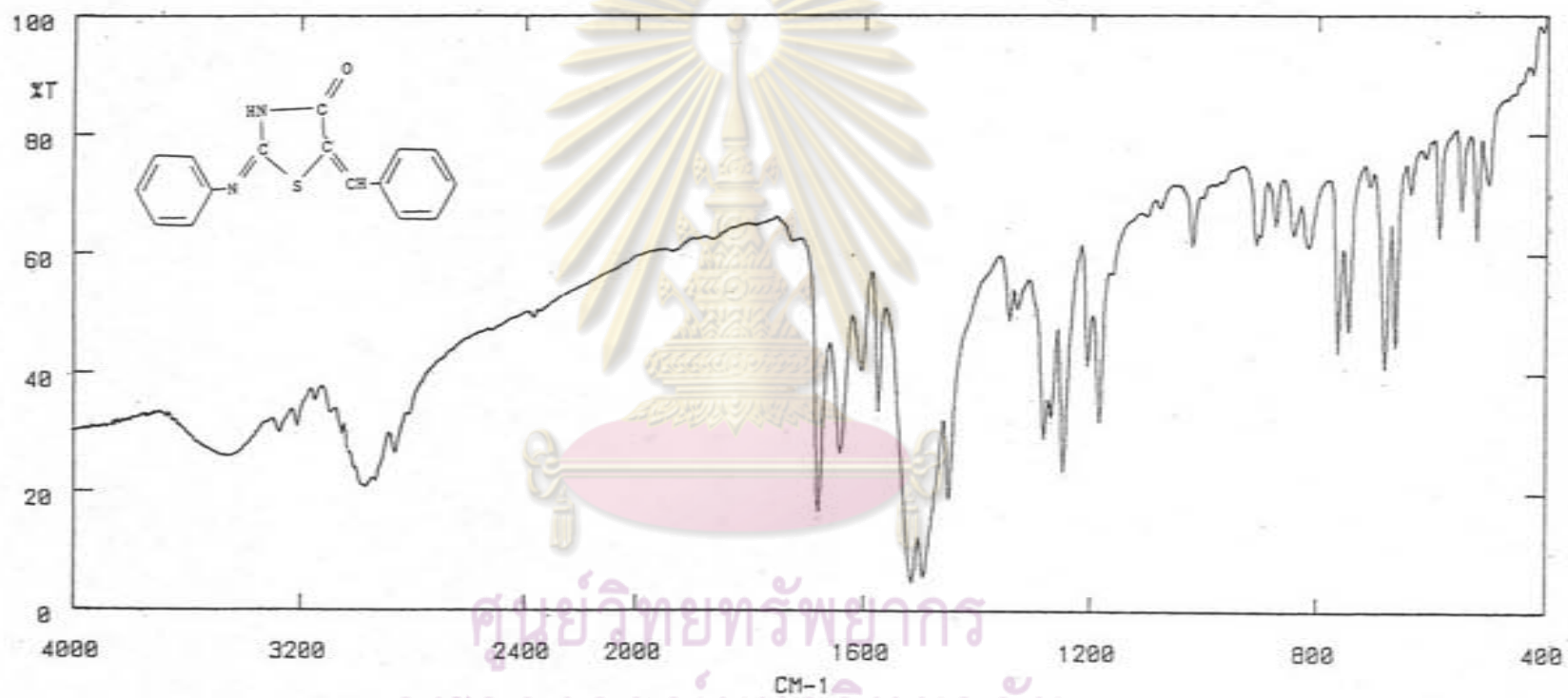


Figure 17 Infrared Absorption Spectrum of 2-Phenylimino-5-benzylidene-4-thiazolidinone as a Potassium Bromide Pellet.

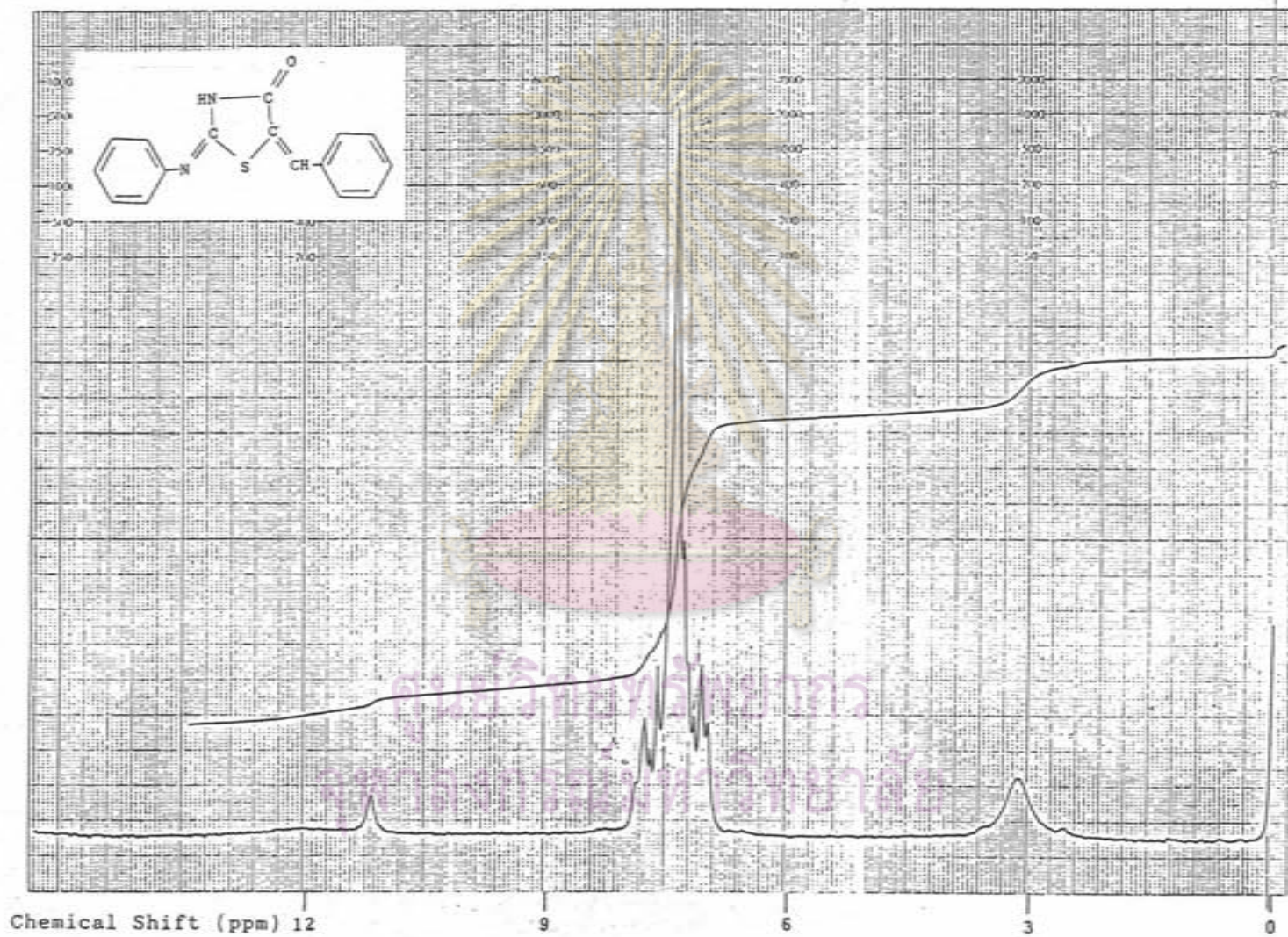


Figure 18 Proton Nuclear Magnetic Resonance Spectrum of
2-Phenylimino-5-benzylidene-4-thiazolidinone in
Dimethylsulfoxide- d_6 and Chloroform- d .

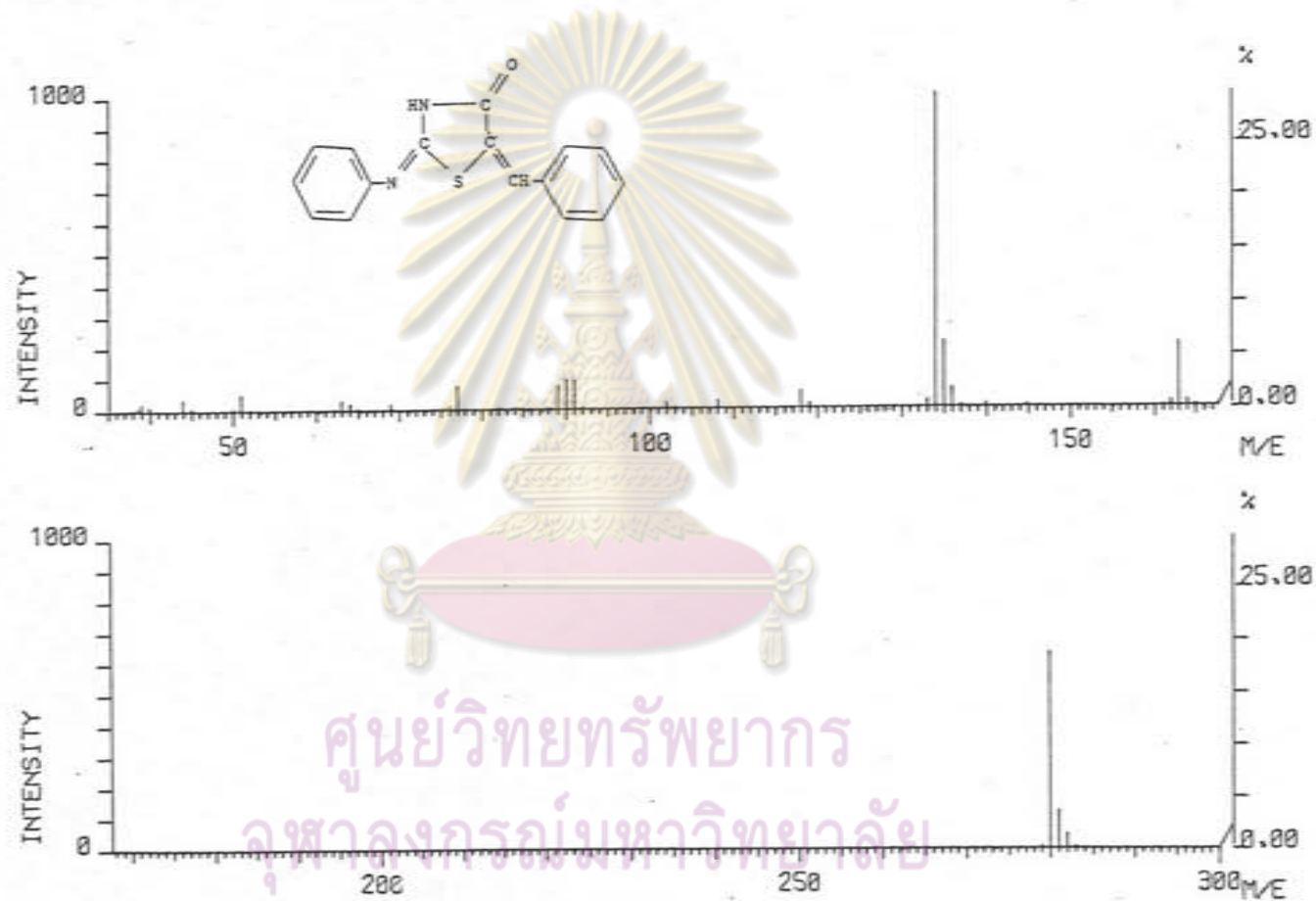


Figure 19 Mass Spectrum of 2-Phenylimino-5-benzylidene-4-thiazolidinone.

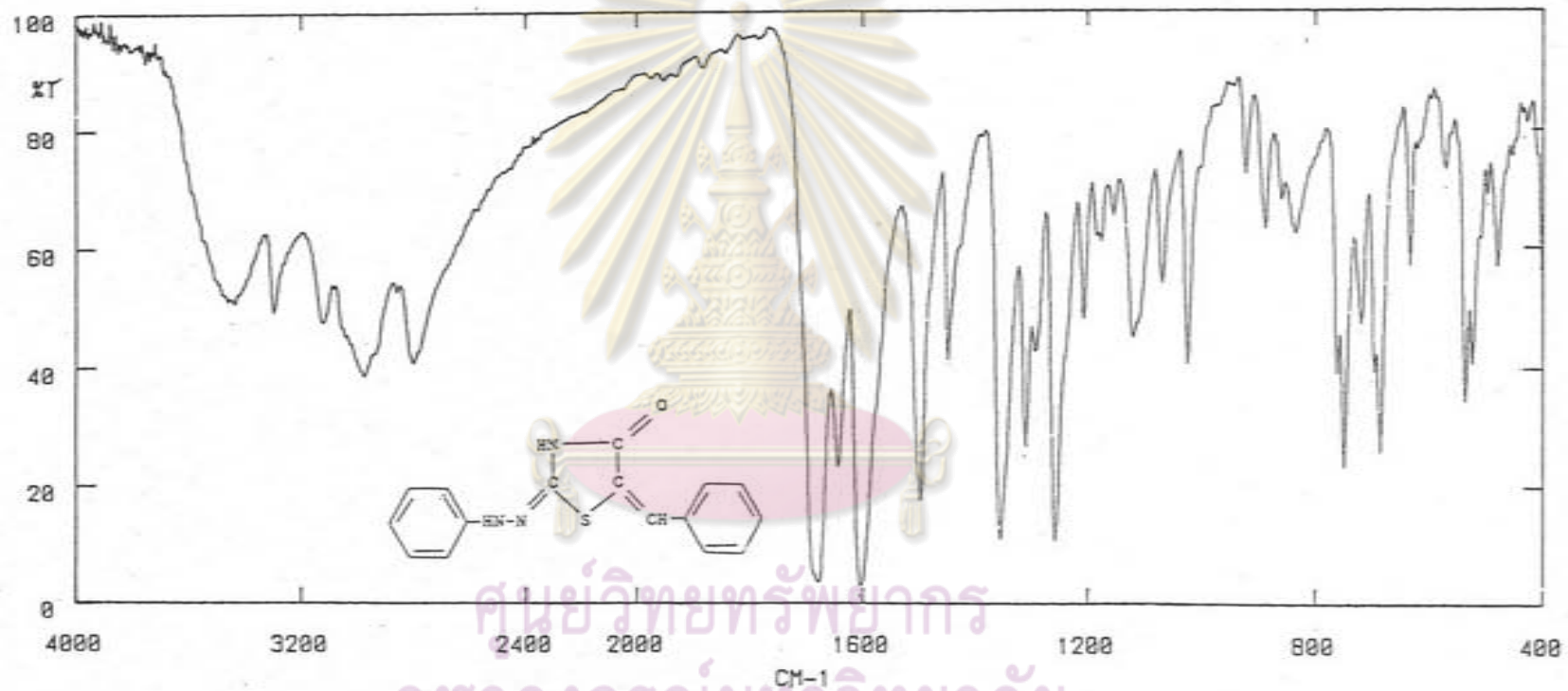


Figure 20 Infrared Absorption Spectrum of 2-Phenyldiazono-5-benzylidene-4-thiazolidinone as a Potassium Bromide Pellet.

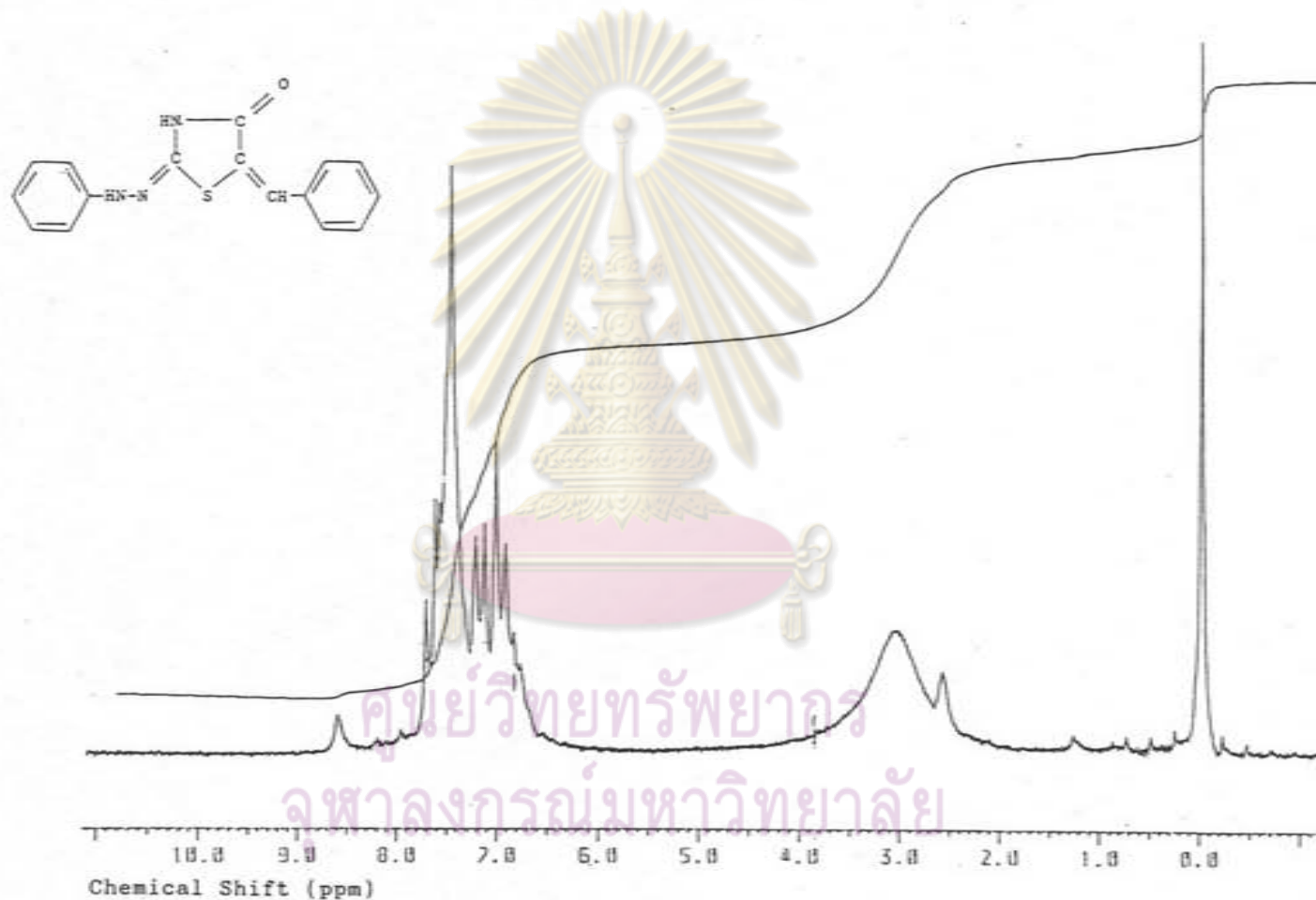


Figure 21 Proton Nuclear Magnetic Resonance Spectrum of 2-Phenylhydrazino-5-benzylidene-4-thiazolidinone in Dimethylsulfoxide-d₆ and Chloroform-d.

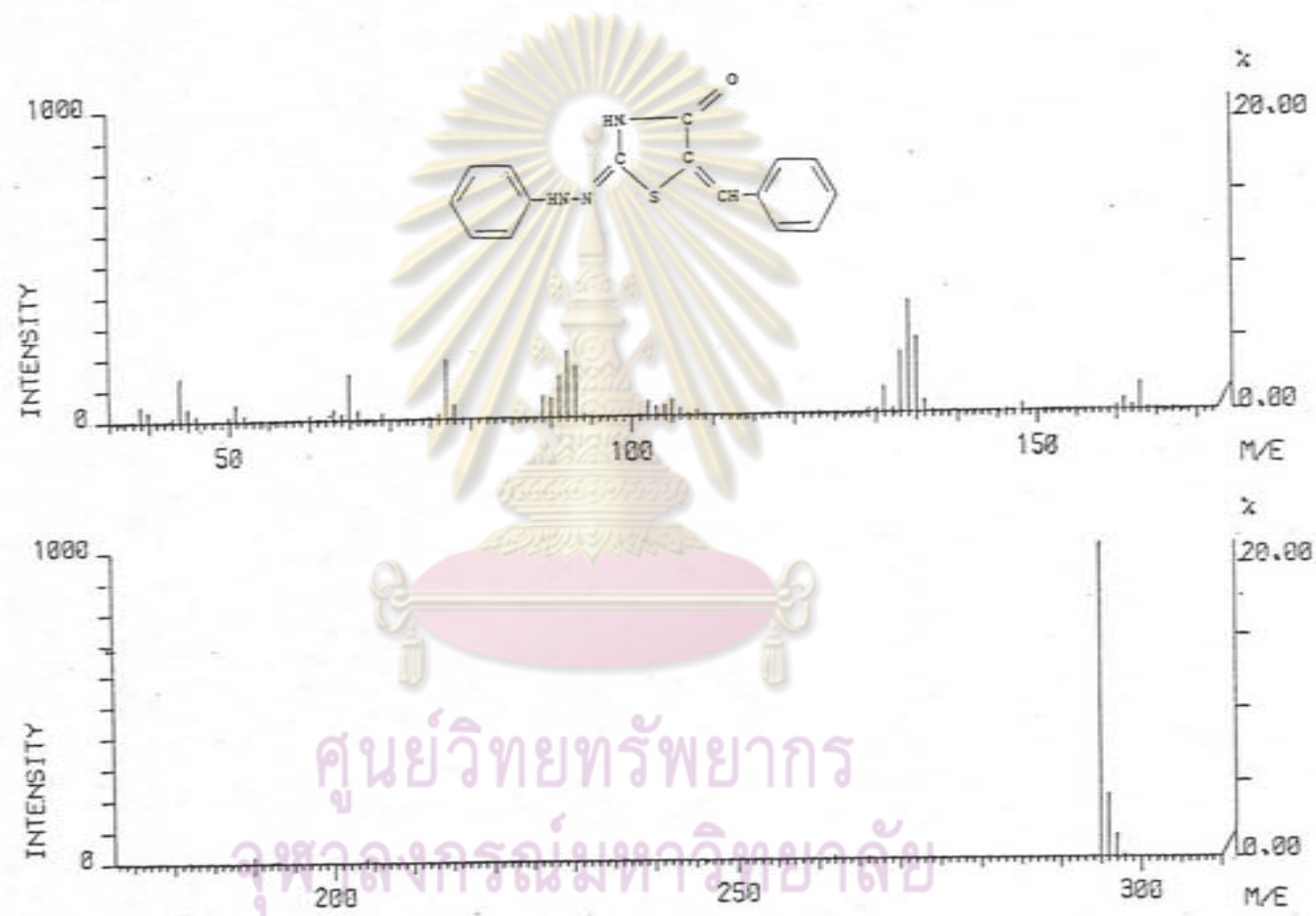


Figure 22 Mass Spectrum of 2-Phenylhydrazino-5-benzylidene-4-thiazolidinone.