Chapter II

Experiment

Synthesis of Carbamates

Reagents

1. Aniline
2. N-methylaniline
3. o-Aminobenzoic acid (Anthranilic acid)
4. p-Aminobenzoic acid (PABA)
5. p-(N-methylamino)benzoic acid (N-methyl PABA)
6. Cetyltrimethylammonium bromide (CTAB)
7. Phenylchloroformate
8. Phenylisocyanate
9. Phenol

The reagents 1 - 6 were purified by either recrystallization or distillation and then confirmed by melting points or boiling points (Table 1) before used. The reagents 7 - 9 were used without further purification.

Table 1.

Observed melting and boiling points of starting material.

substrate	observed (°C)		literature (°C)
	melting point	boiling point	
Aniline		184	184
N-methyl-aniline		197	196
Anthranilic acid	146-147		146-148
PABA	184-185		187-187.5
N-methyl PABA	160-161		160-162
CTAB	228(dec.)		>230(dec.)

Synthesis of N-methylanthranilic acid

The 27.4 g of Anthranilic acid was mixed with 150 cm^3 of 5% sodium hydroxide solution with stirring until it was completely dissolved, at which the pH of the solution was 8. The 35.48 g of methyl iodide(25% excess)was added. While the whole solution was stirring at room temperature for overnight, the flask was connected with the condenser in order to prevent the evaporation of methyl iodide from the solution. The precipitates was filtered off and washed with plenty of distilled water. Recrystallization was carried out twice from ether and then from chloroform-hexane . The crystal obtained had m.p. 170-172°C (lit., 170-172°C dec.). The structure was confirmed by IR (Figure 2) and NMR (Figure 3).

Synthesis of Phenyl N-phenylcarbamate (I)

This synthesis was followed the procedure of Hegaty , A.F. et.al.(10). The 1.19 g of phenylisocyanate and 0.94 g of phenol in 15 cm^3 of benzene with a drop of pyridine was refluxed for 1 hour . After most of the solvent was removed, the residue was recrystallized from chloroform-hexane. The compound had m.p. 122-123°C (lit., 121-124°C). The structure was confirmed by the elemental analysis (Table 2), IR (Figure 4) and NMR (Figure 5) .

Synthesis of Phenyl N-methyl-N-phenylcarbamate(II)

The synthesis of this compound was followed the procedure of Hutchins,J.E.C. et al. (11). The 2.14 g of freshly distilled N-methylaniline was added to the stirred solution of 1.56 g of phenyl chloroformate in 20 cm^3 of ether. The mixture was stirred for two hours, water was added to dissolve the hydrochloride salt, and the solution was then extracted with ether. After the ether was removed, the clear solid was obtained which was then recrystallized from hexane. The compound had m.p. 57-58°C (lit., 57-59°C). The structure was confirmed by the elemental analysis (Table 2), IR (Figure 6), and NMR (Figure 7) .

Synthesis of Phenyl N-(o-carboxyphenyl)carbamate (III)

The general procedure given by Hegarty A.F. et al.(9) was used. The solution of phenyl chloroformate (1.56g) in ether($10\ cm^3$) was added to the stirred solution of 2.74 g of anthranilic acid in $20\ cm^3$ of ether. The mixture was let to stir for two hours. The hydrochloride salt of anthranilic acid was filtered off. After the ether was removed, the residue was recrystallized from chlorofrom-hexane. The compound had m.p. 172-173°C (lit., 171-173°C). The structure was confirmed by the elemental analysis (Table 2), IR (Figure 8), and NMR (Figure 9) .

Synthesis of Phenyl N-(p-carboxyphenyl)carbamate (IV)

Phenyl N-(p-carboxyphenyl)carbamate was synthesized by the same procedure as phenyl N-(o-carboxyphenyl) carbamate. The solution of phenyl chloroformate (1.56g) in dioxan ($10\ cm^3$) was added to the stirred solution of 2.74 g of p-aminobenzoic acid in $20\ cm^3$ of dioxan. The mixture was stirred for two hours. The hydrochloride salt was filtered off. After the dioxan was removed, the residue was recrystallized from ethanol. The compound had m.p.244-235°C (lit., 244-246°C). The structure was confirmed by the elemental analysis (Table 2), IR (Figure 10), and NMR (Figure 11) .

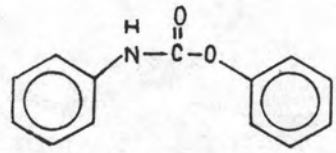
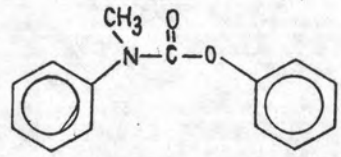
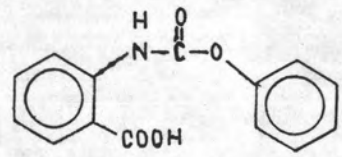
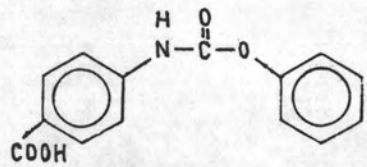
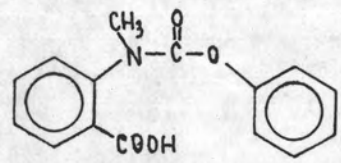
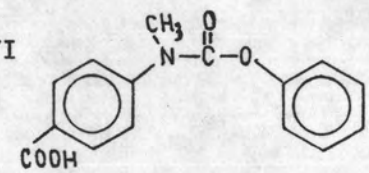
Synthesis of Phenyl N-methyl-N-(o-carboxyphenyl)carbamate(V)

The solution of phenyl chloroformate(1.56g) in dioxan (10 cm^3) was added to the stirred solution of 3.02 g of N-methylanthranilic acid in 20 cm^3 of dioxan. The mixture was stirred for two hours. The hydrochloride salt was filtered off. If the dioxan was evaporated,the residue could suddenly converted to N-methylisatoic anhydride. Hence the target carbamate could not collected in pure solid form. However, it was collected in dioxan solution, in order to decrease the rate of decomposition. Figure 12 showed IR spectrum of obtained N-methylisatoic anhydride.

Synthesis of phenyl N-methyl-N-(p-carboxyphenyl)carbamate(VI)

Phenyl N-methyl-N-(p-carboxyphenyl)carbamate was synthesized by the same procedure as carbamate No.IV . The solution of Phenyl chloroformate (1.56g) in dioxan (10 cm^3) was added to the stirred solution of 3.02 g of p-(N-Methyl) aminobenzoic acid in 20 cm^3 of dioxan. The mixture was stirred for two hours. The hydrochloride salt was filtered off. After the dioxan was removed, the residue was recrystallized from chloroform-hexane. The compound had m.p. 169-170^{o}C. The structure was confirmed by the elemental analysis (Table 2) , IR (Figure 13), and NMR (Figure 14),

Table2. Elemental analysis of various carbamates

substrate		Element(%)		
		C	N	H
I 	calc.	73.24	6.57	5.16
	found	73.18	6.47	5.11
II 	calc.	74.01	6.17	5.73
	found	73.98	6.13	5.68
III 	calc.	65.37	5.45	4.28
	found	65.19	5.35	4.3
IV 	calc.	65.37	5.45	4.28
	found	65.29	5.36	4.34
V 	calc.	66.42	5.17	4.80
	found	-	-	-
VI 	calc.	66.42	5.17	4.80
	found	66.32	5.12	4.82

Note: - no experiment

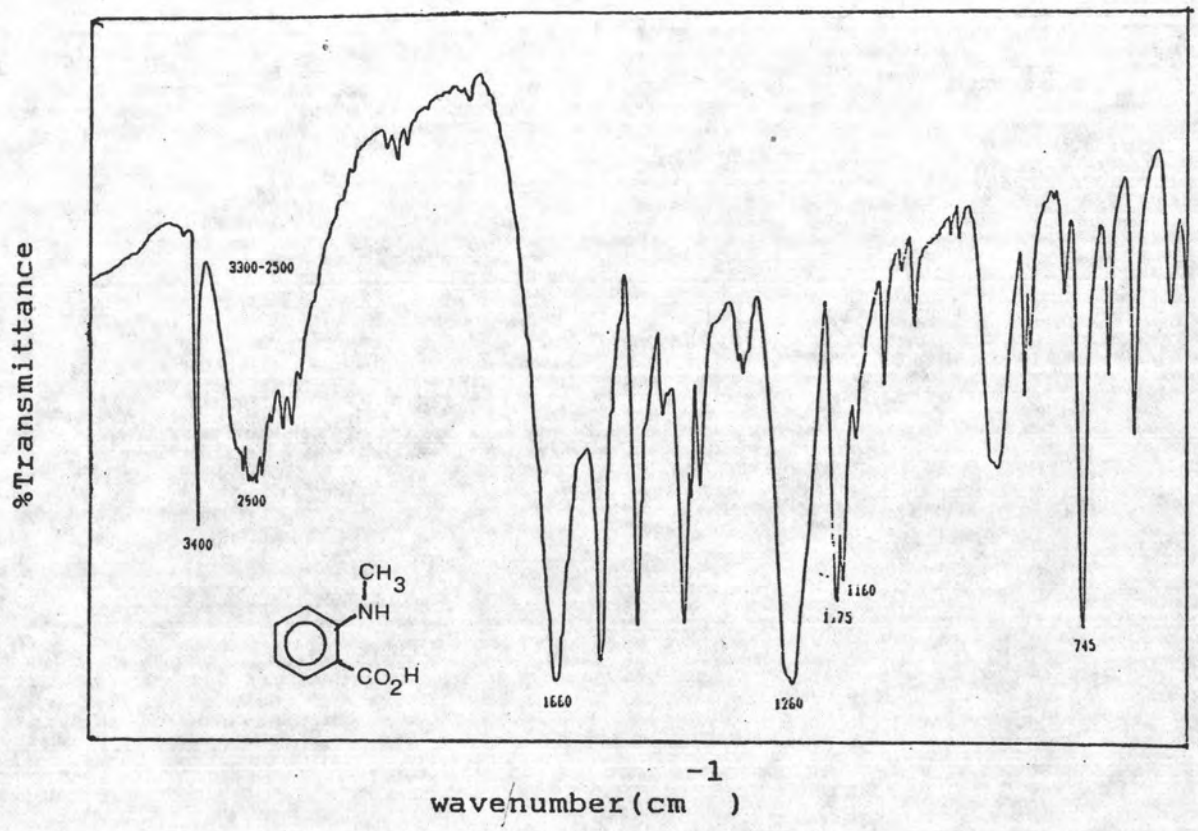


Figure 2 IR spectrum of N-methylantranilic acid in KBr pellet

Interpretation

band (cm^{-1})	Assignment
3400	N-H str. of 2-amine
3300-2500	O-H str. of acid
2900	C-H str. of CH_3-group
1660	C=O str. of acid
1260,1175,1160	C-O str. of acid, and C-N str. of aliphatic and aromatic
745	C-H out of plane bending

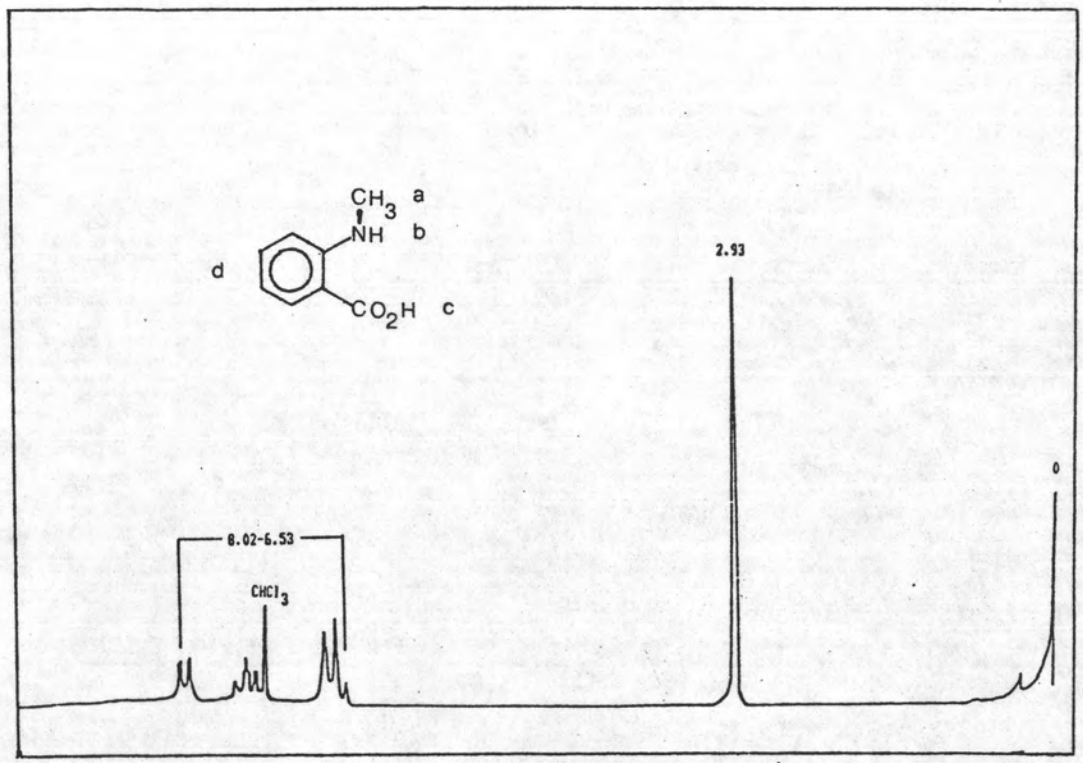


Figure 3 NMR spectrum of N-methylantranilic acid in $CDCl_3$

Interpretation

Assignment	Chemical shift(ppm)
a	2.93
b , c	can not observed
d	6.53-8.02

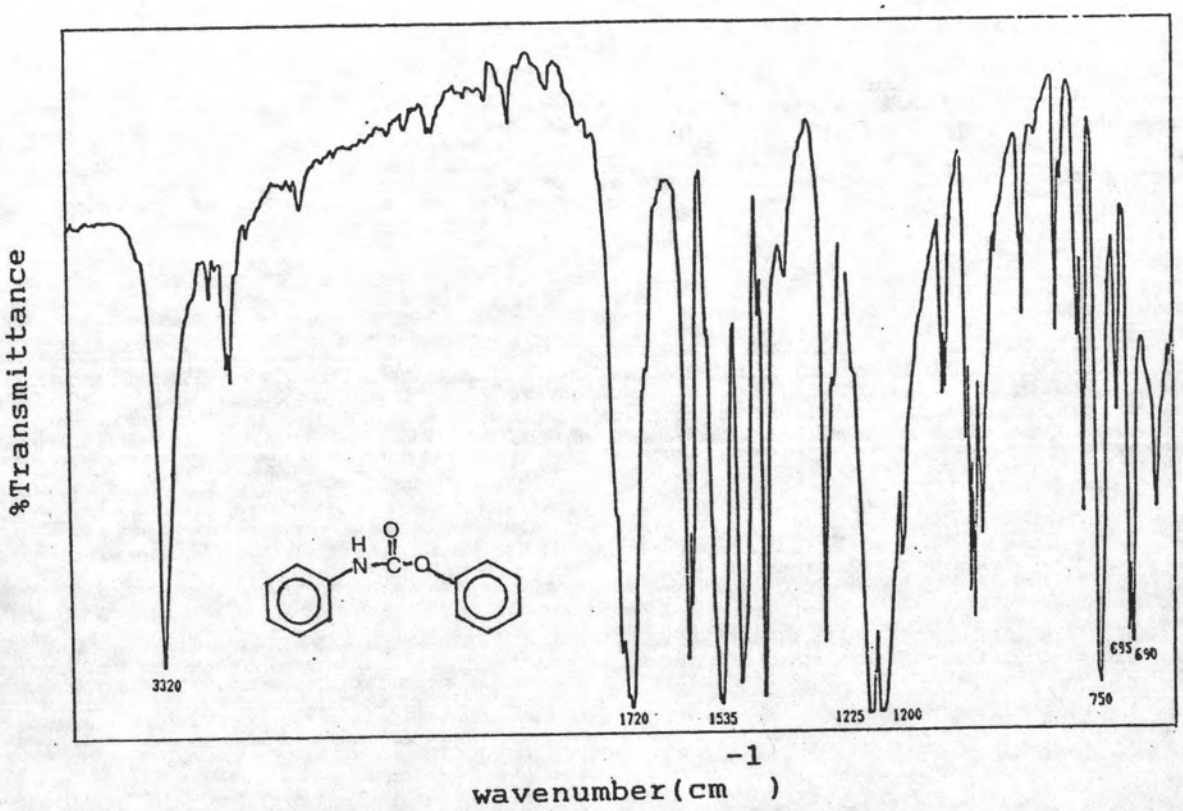
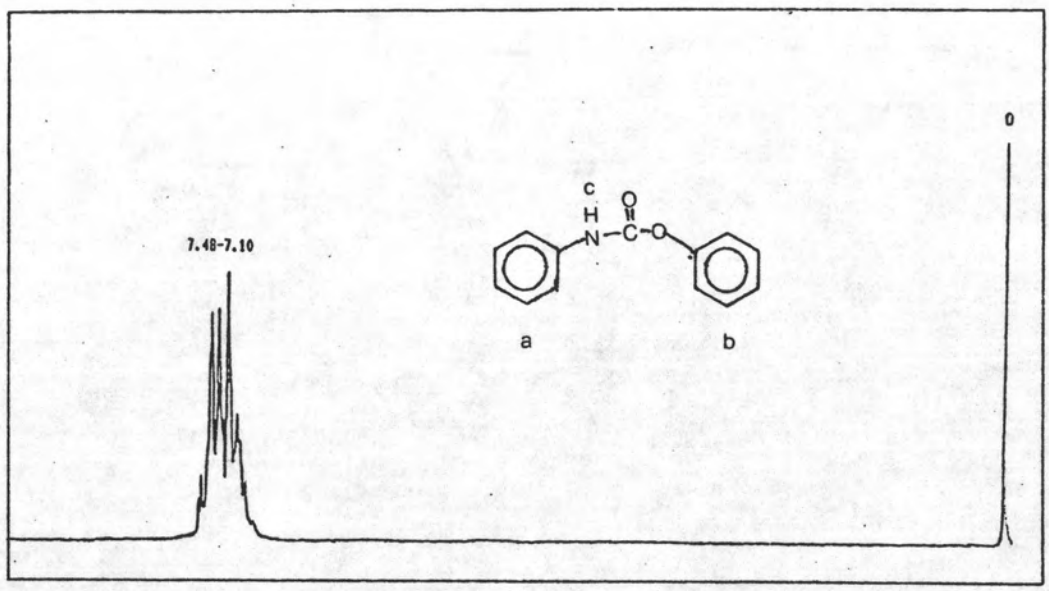


Figure 4 IR spectrum of carbamate No.I in KBr pellet

Interpretation

band (cm^{-1})	Assignment
3320	N-H str. of 2-amine
1720,1535	C=O str. of amideI and amideII
1225,1200	C-O, C-N str. of amide, ester
750,695,690	C-H out of plane bending



chemical shift(ppm)

Figure 5 NMR spectrum of carbamate No.I in $CDCl_3$.

Interpretation

Assignment	Chemical shift(ppm)
a + b	7.10-7.48
c	can not observed

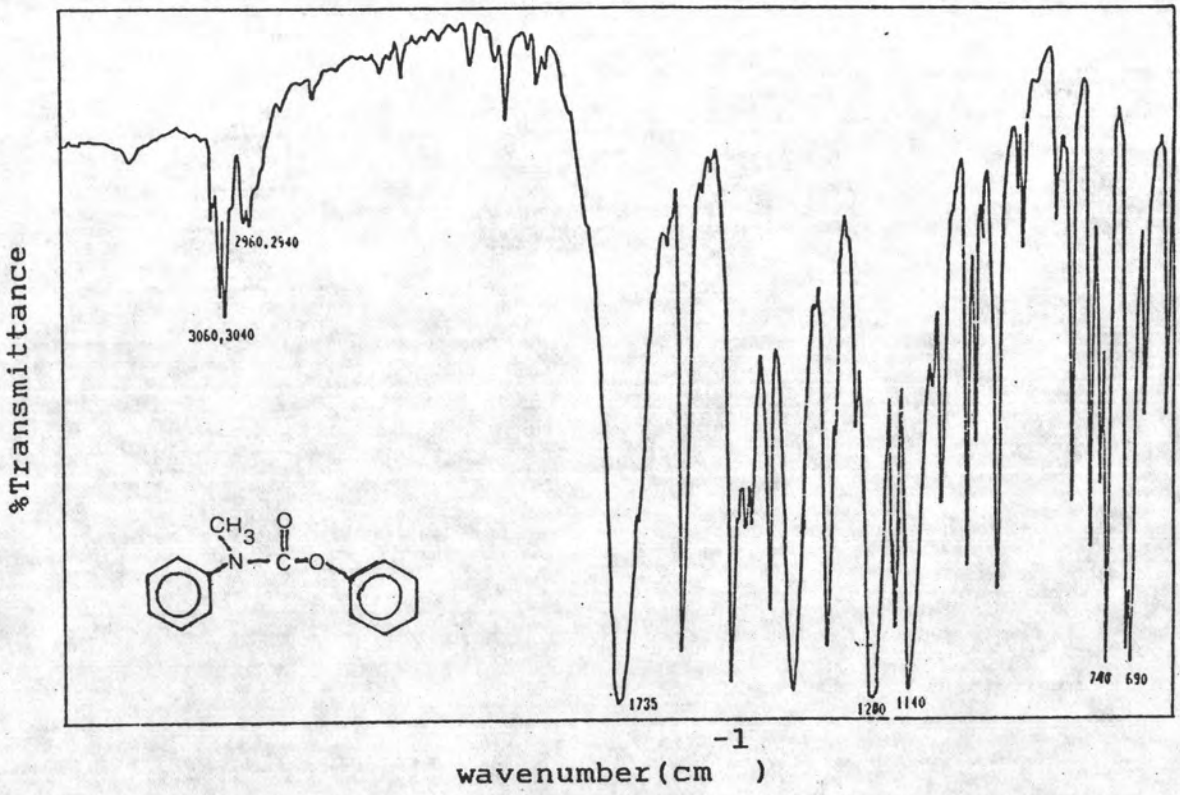


Figure 6 IR spectrum of carbamate No.II in KBr pellet

Interpretation

band (cm^{-1})	Assignment
2960,2940	C-H str. of CH_3-group
1735	C=O str. of carbonyl
1200,1140	C-O, C-N str. of amide, ester
740,690	C-H out of plane bending

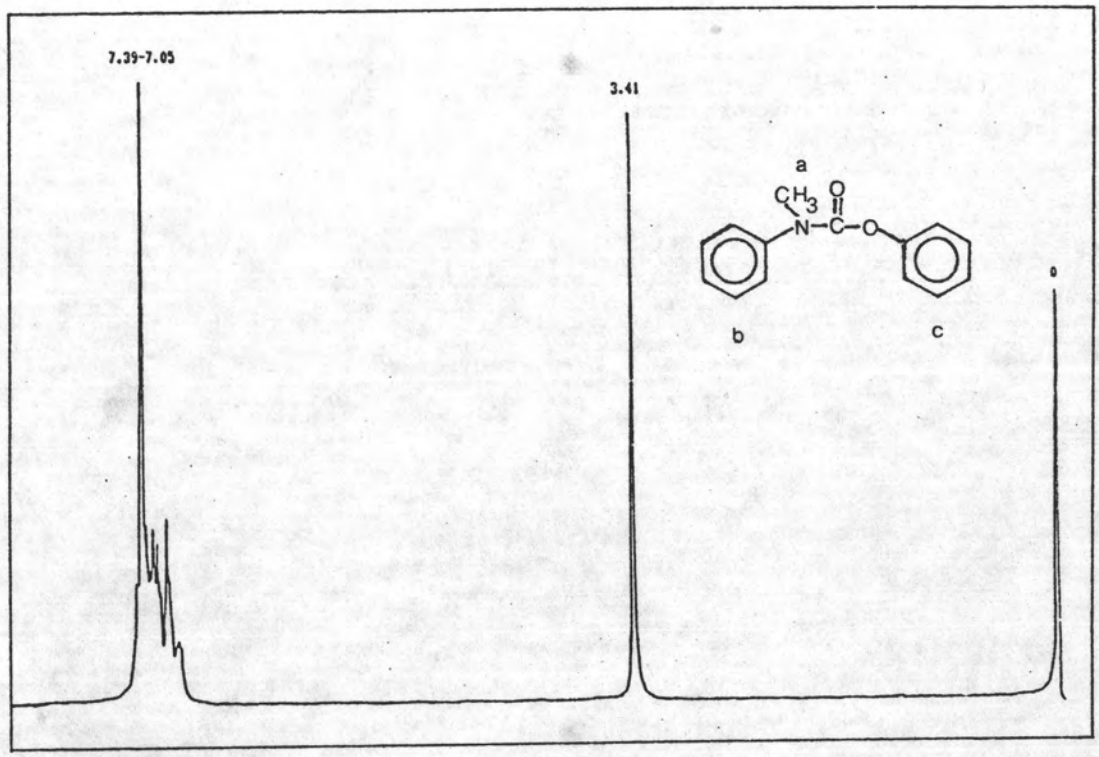


Figure 7 NMR spectrum of carbamate No.II in $CDCl_3$.

Interpretation

Assignment	Chemical shift(ppm)
a	3.41
b + c	7.05-7.39

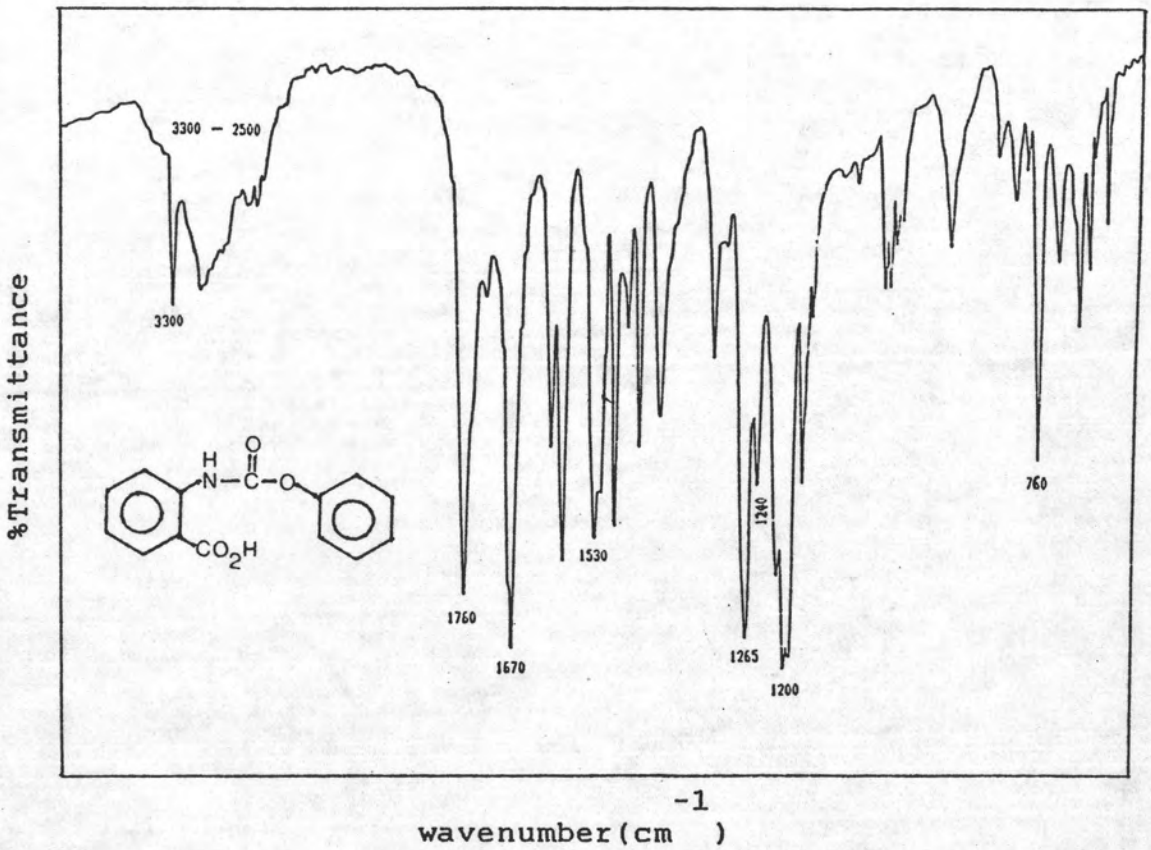


Figure 8 IR spectrum of carbamate No.III in KBr pellet

Interpretation

band (cm^{-1})	Assignment
3300	N-H str. of 2-amine
3300-2500	O-H str. of acid
1760,1670,1530	C=O str. of acid amideI and amideII
1265,1240,1200	C-O, C-N str. of amide, ester
760	C-H out of plane bending

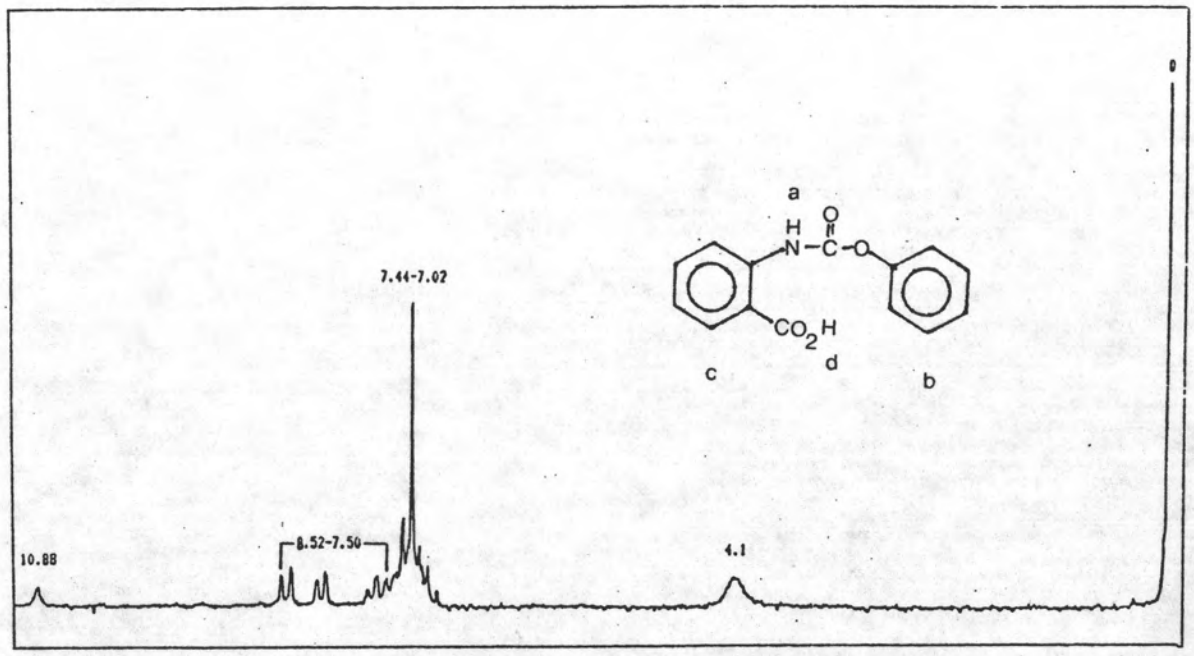


Figure 9 NMR spectrum of carbamate No. III in $CDCl_3$.

Interpretation

Assignment	Chemical shift(ppm)
a	4.10
b	7.02-7.44
c	7.50-8.52
d	10.88

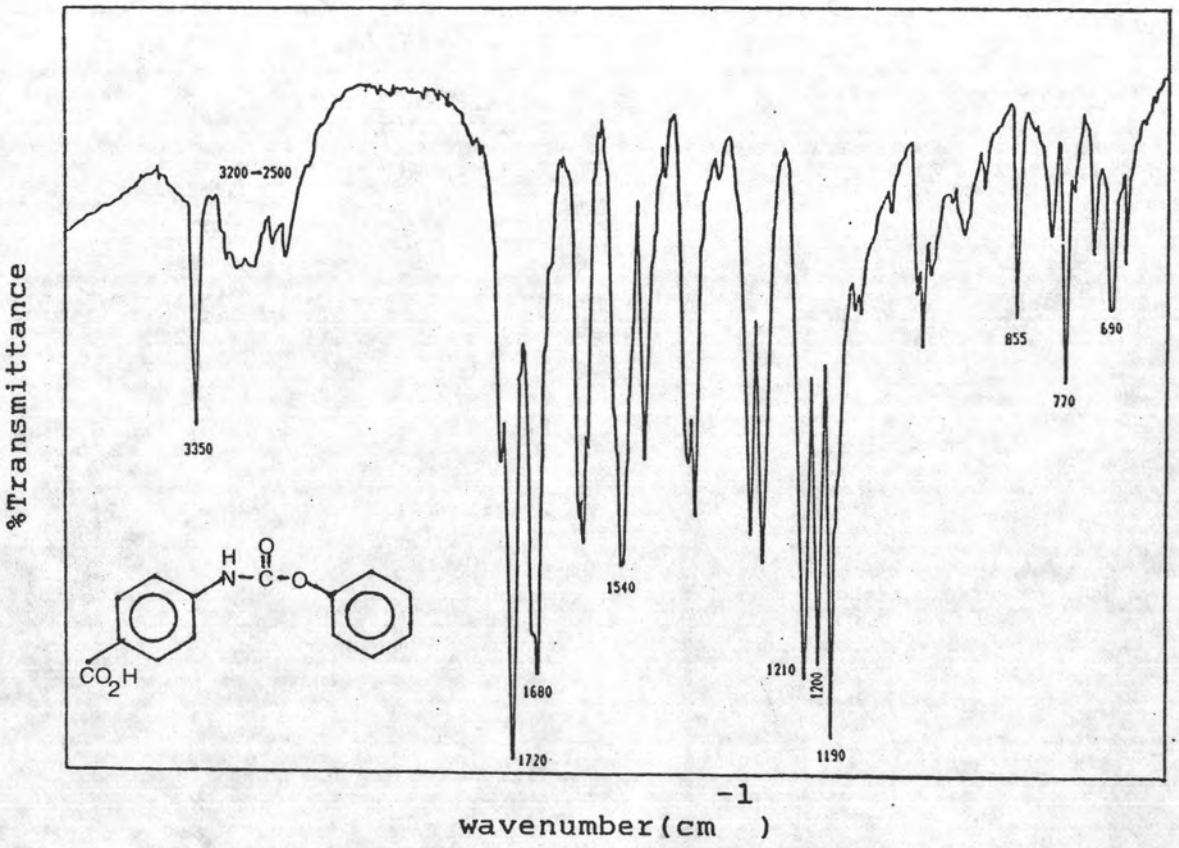


Figure 10 IR spectrum of carbamate No. IV in KBr pellet

Interpretation

band (cm^{-1})	Assignment
3350	N-H str. of 2-amine
3200-2500	O-H str. of acid
1720,1680,1540	C=O str. of acid amideI and amideII
1210,1200,1190	C-O, C-N str. of amide, ester
855,770,690	C-H out of plane bending

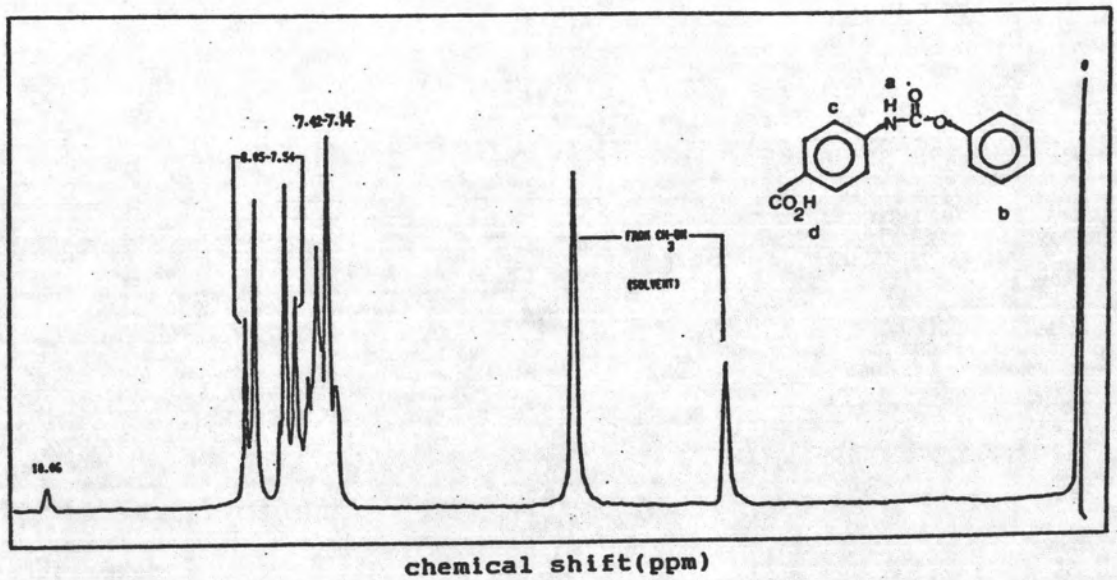


Figure 11 NMR spectrum of carbamate No.IV in CD_3OD.

Interpretation

Assignment	Chemical shift(ppm)
a	can not observed
b	7.14-7.42
c	7.54-8.05
d	10.06

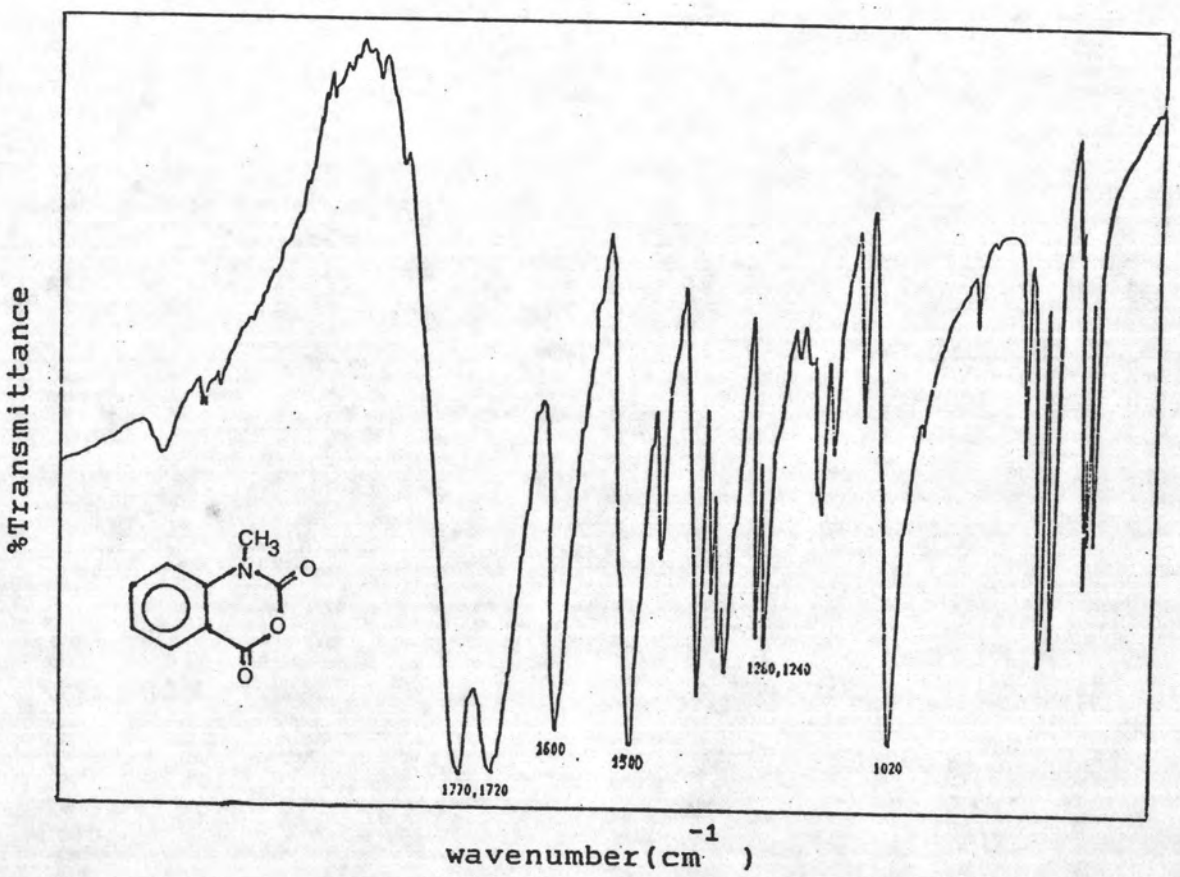


Figure 12 IR spectrum of methylisatoic anhydride in KBr pellet

Interpretation

band (cm^{-1})	Assignment
1170,1720	split of C=O str. cyclic anhydride
1600,1500	aromatic sumation band
1260,1240	C-O-C str. of anhydride
1020	charactor of 6-memberred ring anhydride

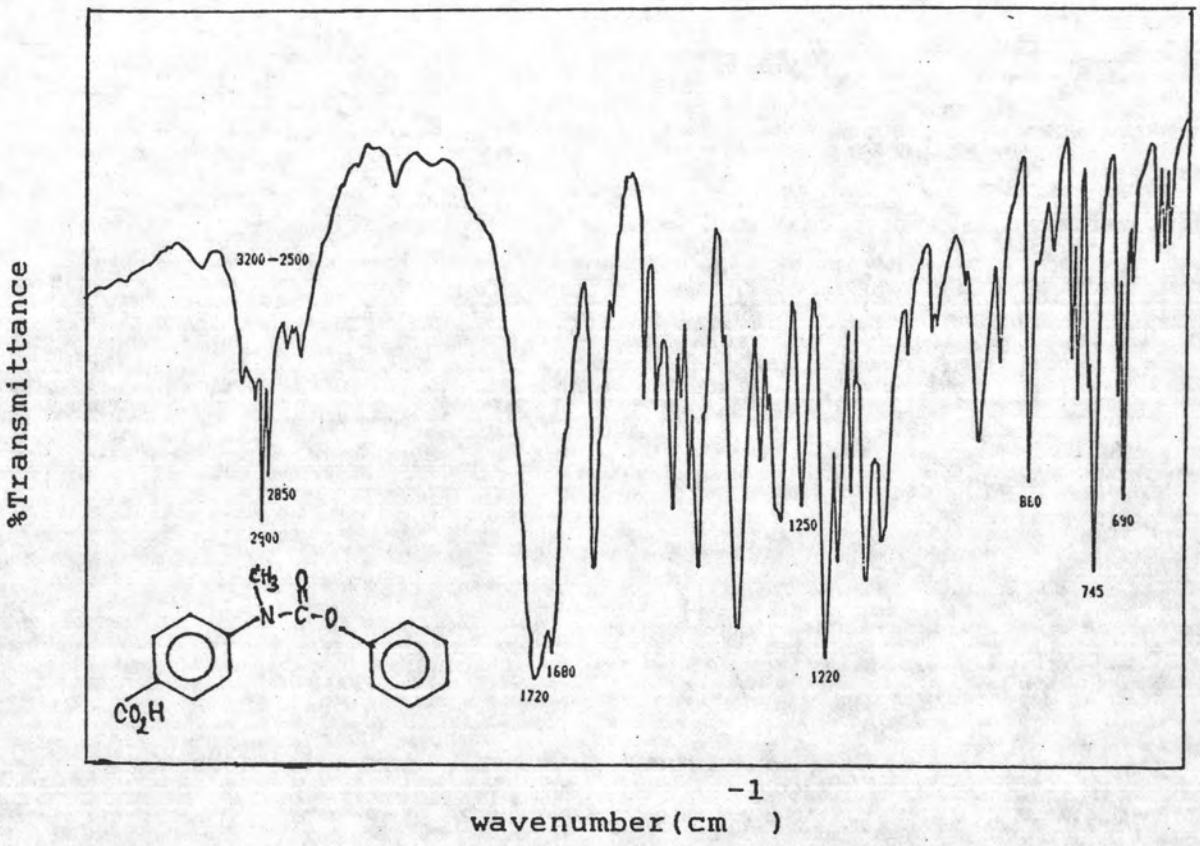


Figure 13. IR spectrum of carbamate No.VI in KBr pellet

Interpretation

band (cm^{-1})	Assignment
3200-2500	O-H str. of acid
2900,2850	C-H str. of CH_3-group
1720,1680	C=O str. of acid and amide or ester
1250,1220	C-O, C-N str. of amide, ester
860,745,690	C-H out of plane bending

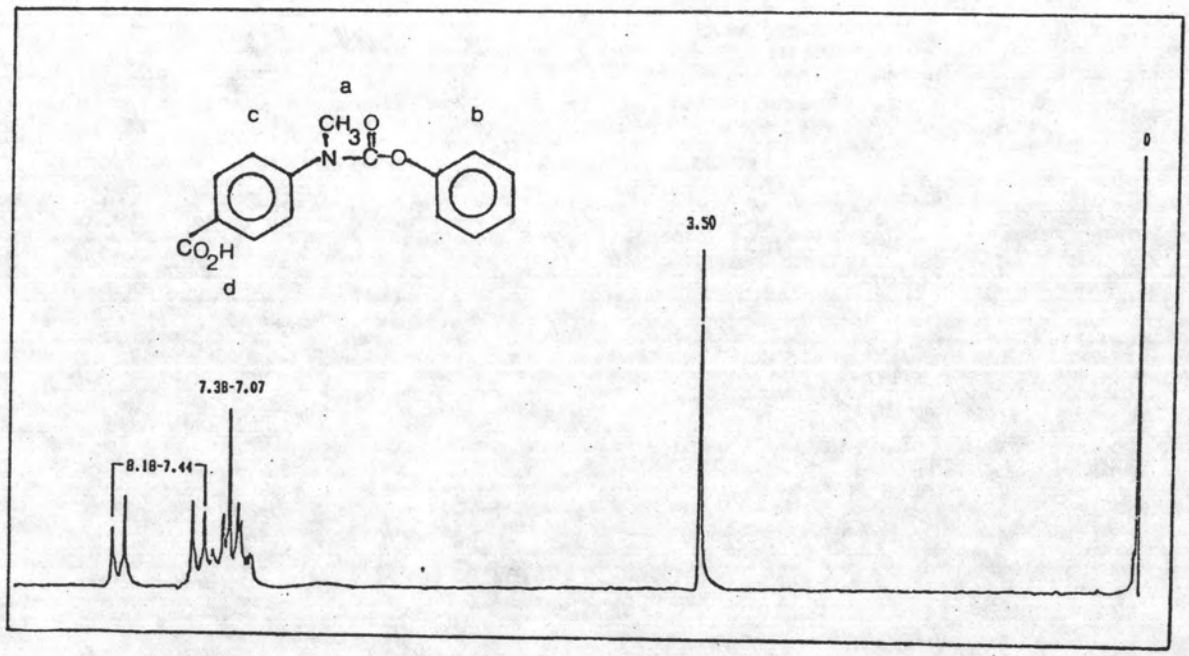


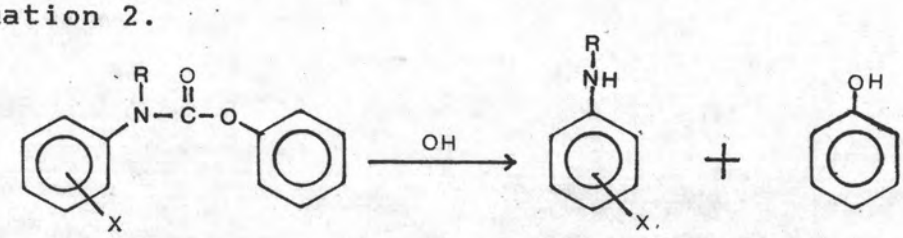
Figure 14. NMR spectrum of carbamate No.VI in $CDCl_3$.

Interpretation

Assignment	Chemical shift(ppm)
a	3.50
b	7.07-7.38
c	7.44-8.18
d	can not observed

Kinetic Experiment

The basic hydrolysis of carbamates will lead to the formation of phenol and substituted aniline as shown in equation 2.



(2)

This reaction is pseudo first—order since the hydroxyl ion concentration is in large excess compared with the carbamate concentration. Consequently, the rate constant (k) were determined by the equation 3 .

$$\log \frac{C_t}{C_o} = \frac{-kt}{2.303} \qquad (3)$$

Where C_o and C_t are concentration of the substrate at initial time (t=0) and at time t . However, the reaction was followed by measuring the increasing of product concentration(Cp).

then

$$C_t = C_o - Cp_t \quad \text{and} \quad C_o = Cp_\infty$$

$$C_t = Cp_\infty - Cp_t$$

hence

$$\log \frac{C_t}{C_o} = \log \frac{(Cp_\infty - Cp_t)}{Cp_\infty}$$

Since the concentration of compound is function to its absorption. By using the UV spectrophotometer, the reaction was followed by measuring the increasing of absorbance(A) of product at appropriate wavelength(λ). then

$$\log \frac{(Cp_\infty - Cp_t)}{Cp_\infty} = \log \frac{(A_\infty - A_t)}{A_\infty}$$

and

$$\log(A_\infty - A_t) = \frac{-kt}{2.303} + \log A_\infty \qquad (4)$$

A plot of $\log(A_\infty - A_t)$ versus time(t) yields a slope of $k_{obs}/2.303$. The k_{obs} was precisly obtained from least square treatment.

Kinetic experiment was done by using Jasco Uvidex 650 UV-VIS spectrophotometer with 10.0 mm quartz cells, and equipped with a thermostatic cell compartment.

Preliminary study of kinetic experiments

The appropriate condition for the reaction has to be obtained in order to carry out the reaction in reasonable time and be manipulated with convenience for the whole experiment. The kinetic experiment was done in constant temperature at 20°C, but the pH of the solution was varied with basic pH buffer(12) to give different pH. Data of rate constant of various carbamate derivatives at different pH were obtained from equation 3 (Table 3). The plot of $\log k_{obs}$ versus pH was shown in Figure 15, and pH 11.2 was choosen as the appropiate pH.

Under the appropriate pH(11.2) and temperature was kept constant at 20°C, rate of the reaction without micelle was too fast (reaction period about 1-20 min). It is believed that the reaction with micelle would be much faster than that without micelle. Then the temperature must be below 20°C to increase the reaction period and have enough time to measure by ordinary instrument. The suitable temperature for the kinetic study is at 10°C .

Consequently, all kinetic experiments in this research work were run at pH 11.2 and temperature at 10°C.

Table 3. data of average k_{obs} at various pH, at 20°C

pH	average k_{obs} ($\times 10^{-3}$) of carbamate No.					
	I	II	III	IV	V	VI
8.0	-	Can not observed	1.861	-	20.511	Can not observed
9.0	-		1.918	-	22.182	
10.0	1.519		2.030	0.922	20.828	
11.0	20.217		6.394	18.174	28.384	
11.5	125.350		18.272	101.898	51.918	
12.0	-		62.783	-	125.201	

Note. In the same condition, rates of reactions of carbamate No. II and VI were very slow, thus we could not observe their reactions(Appendix I).

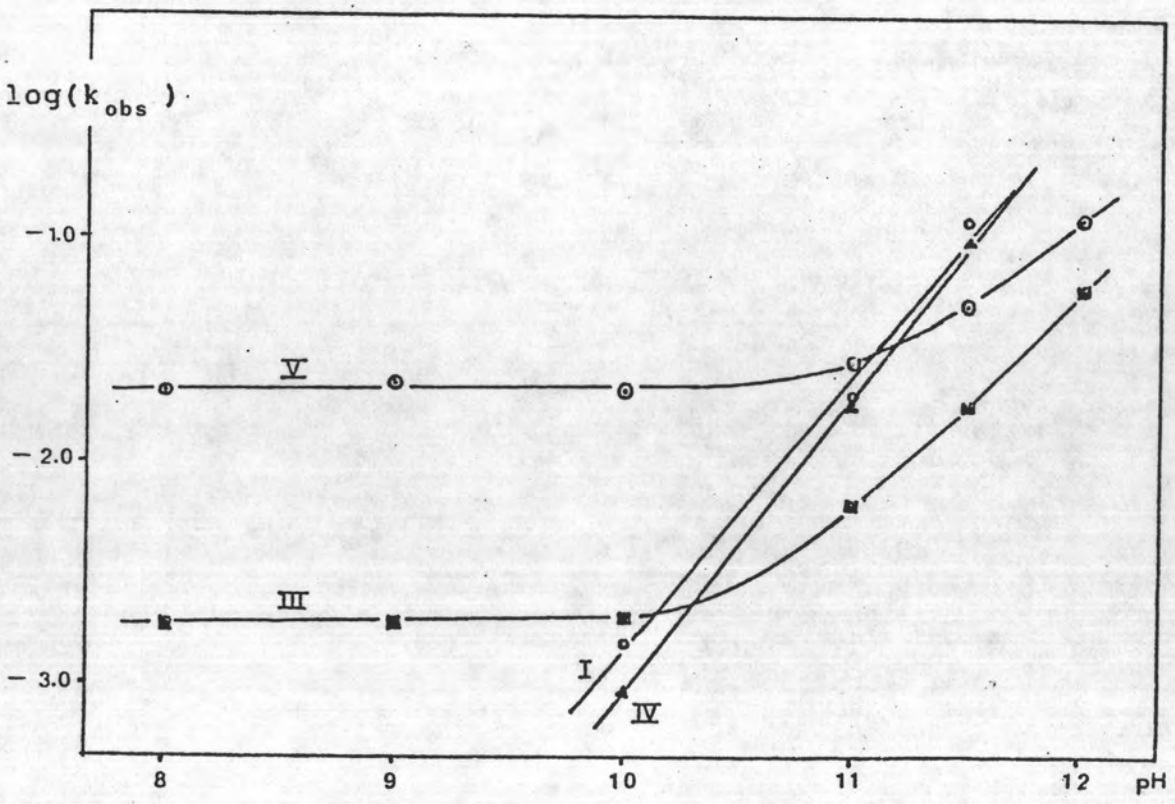


Figure 15. A plot of logk_{obs} vs pH of various carbamates.

Preparation of the stock solution

Preparation of stock 0.1M sodium hydroxide solution

This solution was prepared by using double distilled water. It was then standardized by titrating with 0.1M potassium hydrogen phthalate(KHP) and phenolphthalein as an indicator. The result of standardization was in Table 4 .

Table 4. Standardization of NaOH against 0.100 M KHP

Trial	cm^3 of 0.100M KHP	cm^3 of NaOH	average of 3 NaOH (cm^3)	M NaOH
1	25.0	25.95		
2	25.0	25.85	25.88	0.0966
3	25.0	25.85		

Test of the surfactant

The surfactant, CTAB, was purified(13) by recrystalization from methanol-ether and stored in desiccator with silica gel as drying agent.

CTAB was tested for resistance to basic hydrolysis by reflux with 0.1 M sodium hydroxide solution for 10 hr, the CTAB was extracted by amyl alcohol. The amyl alcohol was distilled off gave a CTAB residue. the IR and NMR spectra were obtained for the residue. The spectra were identical to those of the starting CTAB.

Preparation of 0.1M CTAB

The 3.639g of CTAB was tranferred into 100.0 cm^3 volumetric flask, then added 50 cm^3 of double distilled water, kept it until completely dissolved (without shake) and made volume to the mark with double distilled water. Then the solutiion was shaked well before used.

Preparation of 0.05M Carbamates

Each of carbamate derivatives was prepared by weighing the required amount of each of carbamates and dissolved in dioxan.

Preparation of the kinetic stock solution

The 4.1 cm^3 of 0.0966 M NaOH was pipetted into the 250.0 cm^3 volumetric flask and a certain volume of 0.1 M CTAB was then added as shown in Table 5 . Finally, the mixtured was made up to the mark with double distilled water.

This solution would be used as the stock solution for the kinetic run.

Table 5. amount of 0.1M CTAB for desired concentration

Required cm^3 of 0.1M CTAB	Final concentration of CTAB(C_D) in 1.585×10^{-3} M NaOH (pH 11.2)
0.00	0.0
0.25	0.1
0.50	0.2
0.75	0.3
1.00	0.4
1.25	0.5
1.50	0.6
1.75	0.7
2.00	0.8
2.25	0.9
2.50	1.0
3.00	1.2
3.75	1.5
5.00	2.0
7.50	3.0
10.00	4.0
12.50	5.0
15.00	6.0

Kinetic procedures

The 3.0 cm^3 of the kinetic stock solution was pipetted into the two 10.0 mm cuvette cells which were the sample and the reference cells. Both cells were inserted into the cell compartments which was equipped with the temperature controller. The solution was allowed to stand at 10 ^oC for 10-20 minutes. The UV-spectrophotometer was then set zero at the certain wavelength where the carbamate absorped and least interference from other components were observed. The reaction was initiated by adding the 10 μl of 0.05 M carbamate solution into the sample cell. The absorbance (A) at different time (t) was measured until the constant value was obtained (normally about ten half-lives).

The k_{obs} of the reaction was determined by plotting of $\log(A_\infty - A_t)$ versus time as in equation 4 (Figure 17). The above experiment was repeated at least twice for each carbamate . Then the average k_{obs} were calculated.

Consequently, each carbamate in the presence of certain concentration of CTAB had one value of k_{obs} . These values was summarised in Table 6. In order to obtain cmc, a plot of k_{obs} wersus C_D of!one carbamate was performed. Figure 18 exhibits the typical feature of such a plot. It was found that cmc evaluated from every plot was approximately the same vlue .

Finally, $1/(k_w - k_{obs})$ was plotted against $1/(C_D$ - cmc) which yielded the straight line. Thus k_m and K/N were determined from the straight line. By tiis way k_m and K/N for each carbamate were obtained (Table 8).

Carbamate No. : III

CTAB concentration (C_D) : 0

Temperature : $10^{\circ}C$

pH : 11.2

Wave length : 318 nm

time(sec)	Absorbance (A_t) 1	2
0	0.035	0.064
120	0.086	0.117
240	0.116	0.158
360	0.142	0.194
480	0.167	0.224
600	0.186	0.250
720	0.200	0.272
840	0.212	0.289
960	0.222	0.305
1080	0.230	0.318
infinity(A_∞)	0.280	0.382
Slope :	6.36×10^{-4}	6.17×10^{-4}
Intercept :	0.6461	0.4965
Correlation :	0.9995	0.9999
k_{obs} = Slopex2.303 :	1.464×10^{-3}	1.479×10^{-3}

average k_{obs} : 1.472×10^{-3} sec^{-1}

Figure 16. The typical raw data of carbamate No.III

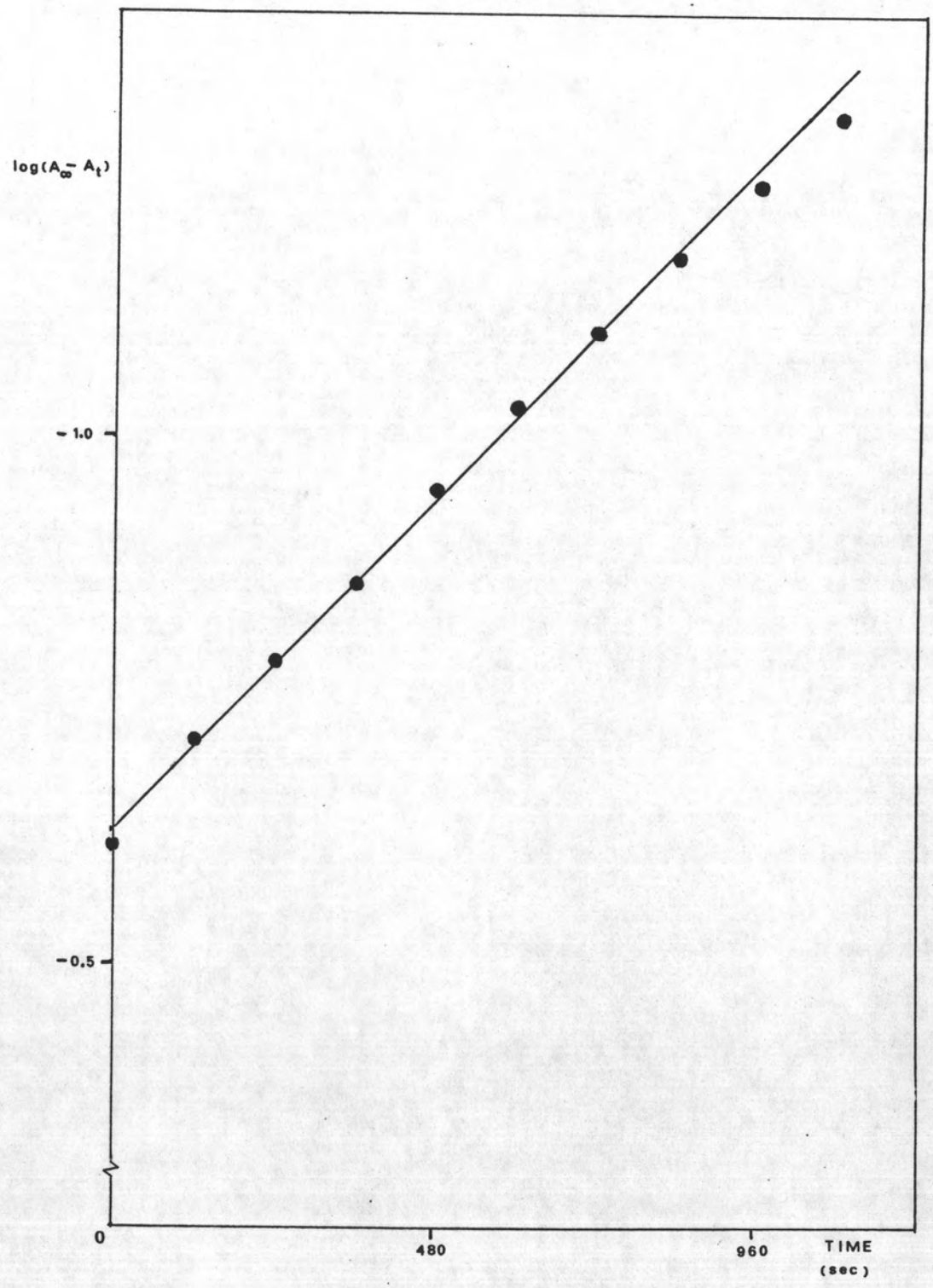


Figure 17. A plot of $\log(A_\infty - A_t)$ vs time(t) of carbamate No.III

Determination of cmc of the CTAB

The cmc of the CTAB is the concentration at which the rate of reaction begins to be markedly changed by increasing surfactant concentration. By graphical extraporation of the graph of k_{obs} versus C_D, cmc was obtained. A typical graphic was shown in Figure 18. The cmc was found to be 0.1×10^{-3} M. Data of k_{obs} of various C_D of various carbamate derivatives are summarized in Table 6.

Table 6.

Data of average k_{obs} VS C_D of various carbamate derivatives at the appropriate condition.

C_D (mM)	k_{obs} ($\times 10^{-3}$) (sec^{-1}) of carbamate derivatives					
	I	II	III	IV	V	VI
0.0	5.447	Can not observed	1.472	4.211	9.172	Can not observed
0.1	3.161		1.494	3.735	9.114	
0.2	-		1.898	-	-	
0.3	3.803		2.188	5.639	-	
0.5	6.820		4.190	18.214	10.700	
0.7	7.084		6.735	39.284	-	
0.8	-		9.526	-	-	
1.0	14.197		11.509	59.334	12.530	
1.2	-		14.184	-	-	
1.5	69.915		11.530	-	-	
2.0	182.112		8.406	123.757	15.877	
3.0	202.400		-	144.530	-	
4.0	219.985		-	159.461	22.622	
5.0	228.368		-	-	-	
6.0	-		-	-	23.199	

Note: - no experiment

The reaction of carbamate No.II and IV cannot be observed because of very slow reaction at this condition.

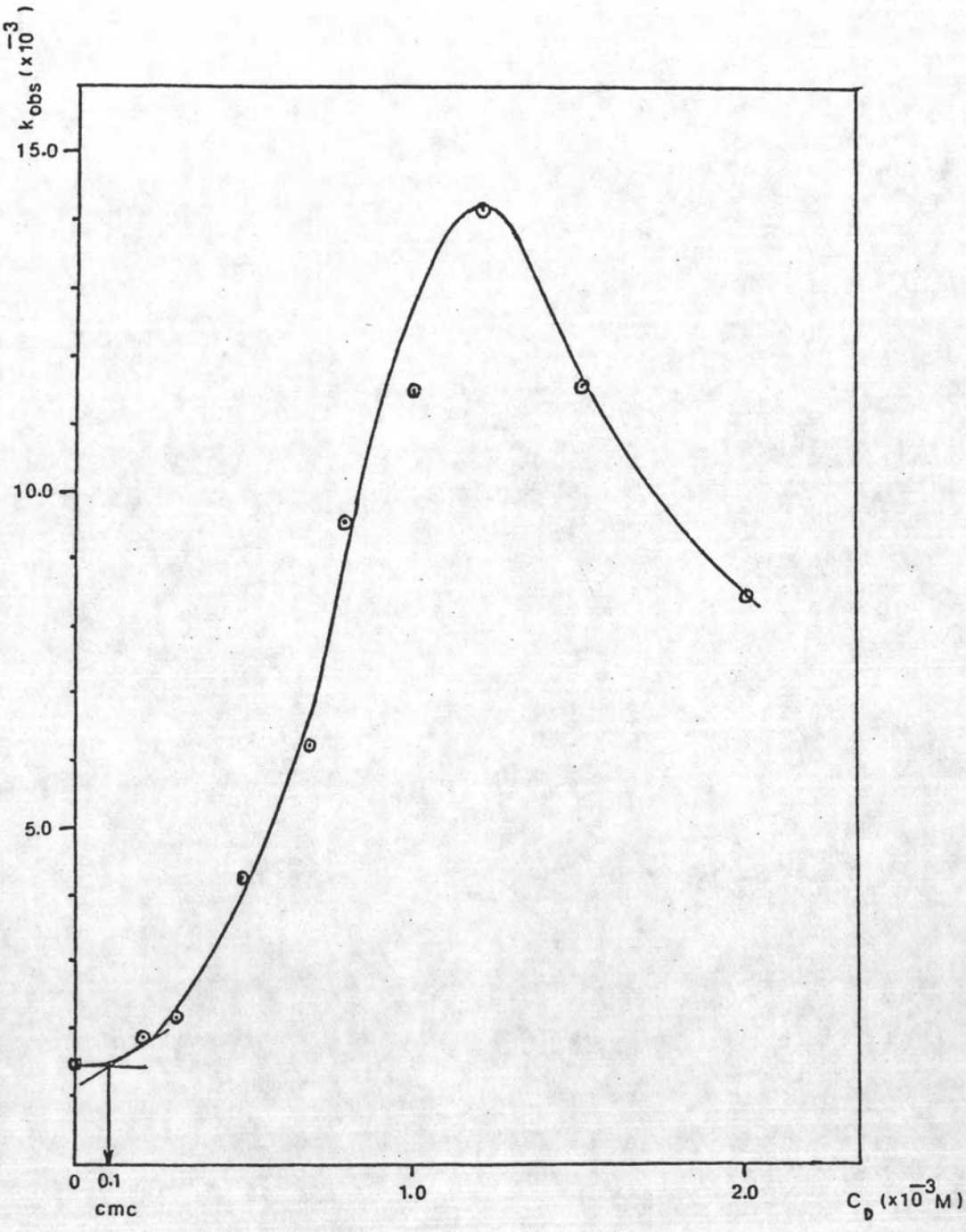


Figure 18. The typical plot of k_{obs} VS C_D of carbamate No.III

k_m and K/N can be calculated using equation 1. An example calculation by equation 1 of carbamate No.III is given in Table 7 and was plotted in Figure 19 . The result for all derivatives were summarized in Table 8.

Table 7.

Typical calculation of parameters for equation 1.

C_D (M)	$1/(C_D - cmc)$	k_{obs} (sec^{-1})	$1/(k_w - k_{obs})$
0.0008	1428.571	0.009526	-124.162
0.0010	1111.111	0.011509	-99.631
0.0012	909.091	0.014184	-78.666

Note : compound is carbamate No.III

: cmc = 0.1×10^{-3} M or 0.0001M

: k_w = 0.001472 sec^{-1}

From least squares :

correlation coefficient, r, is -0.9966

intercept or $1/(k_w - k_m)$ is -1.1991

slope or $[1/(k_w - k_m)](N/K)$ is -0.08666

So

K/N = 13.7789

k_m = 0.8389 sec^{-1}

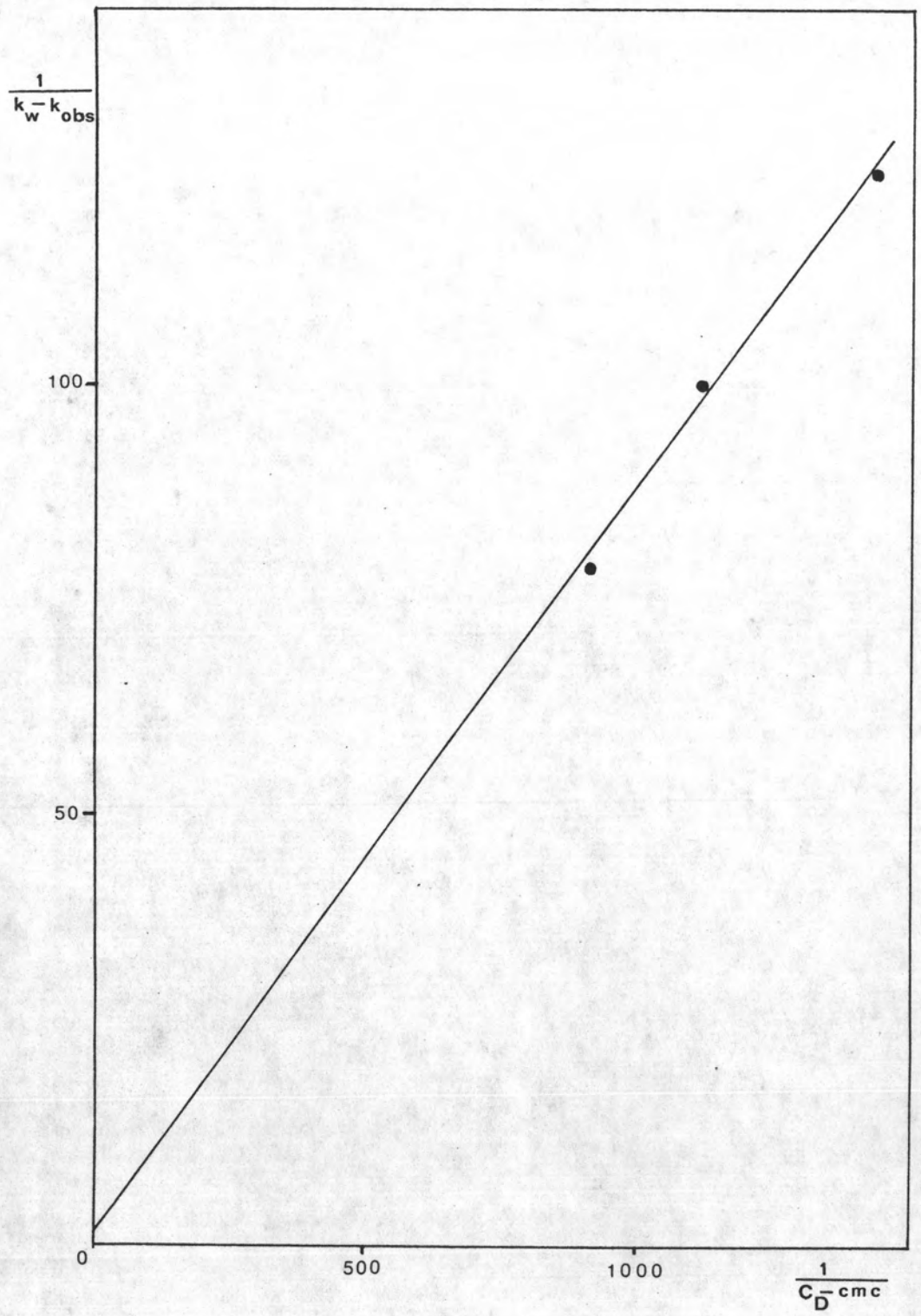


Figure 19. The plot of $1/(k_w - k_{obs})$ VS $1/(C_D - cmc)$ of carbamate No.III

Table 8.

Data from plot of $1/(k_w - k_{obs})$ VS $1/(C_D - cmc)$ from equation 1.

Carbamate	k_w (sec^{-1})	k_m (sec^{-1})	K/N	k_m/k_w	C_D range
I	0.005447	0.2724	1017.8680	50.0092	2.0-5.0
III	0.001472	0.8389	13.7789	569.9049	0.8-1.2
IV	0.004211	0.7686	82.3475	182.5220	0.7-4.0
V	0.009172	0.0599	79.2296	6.5307	1.0-6.0