

SOLVOLYSIS OF PHENYL N,N-DIMETHYLCARBAMATES IN ALKALINE AND ACID MEDIA*

T.VONTOR, V.DROBILIČ, J.SOCHA and M.VEČEŘA

Department of Organic Chemistry,

Institute of Chemical Technology, 532 10 Pardubice

Received March 20th, 1973

Basic kinetic data have been measured for hydrolysis of eleven *m*- and *p*-substituted phenyl N,N-dimethylcarbamates in aqueous 1M sodium hydroxide at 40°C and in aqueous sulphuric acid in the H_0 range 0 to -7 at 64°C. Methanolysis kinetics of phenyl N,N-dimethylcarbamates and phenyl acetate have been studied with respect to the basicity of medium. Mechanism of the hydrolysis and methanolysis of the carbamates mentioned has been suggested on the basis of the experimental data obtained.

In the first report of this series¹ it was stated that 1-naphthyl N-methylcarbamates differed considerably from 1-naphthyl N,N-dimethylcarbamates in their behaviour during hydrolysis. A series of eleven *m*- and *p*-substituted phenyl N,N-dimethylcarbamates has been chosen in this work for more detailed study of reactivity of carbamates substituted by two methyl groups at the nitrogen atom. The hydrolysis of N-methylcarbamates takes the ElcB course; N,N-dimethylcarbamates generally react more slowly in acid and alkaline media and the mechanism can be presumed to be analogous to that of ester eventually amide hydrolysis. As the cases are known where the amide hydrolysis is of fractional order² (the reaction rate expression contains the terms of both the first and second order in hydroxyl ion concentration), we decided to determine the reaction order in the case of alkaline hydrolysis of dimethylcarbamates, too. For strongly basic media the systems methanol-methanolate (H_R -function³) and dimethyl sulphoxide-methanol-sodium methanolate have been used. The kinetic measurements were carried out by discontinuous spectrophotometric method¹ at the wavelength of maximum absorption of the phenolate. *p*-Nitrophenyl N,N-dimethylcarbamate was used for study of acid hydrolysis, the measurements being analogous to those mentioned, *viz.* spectrophotometric determination of the *p*-nitrophenol concentration increase (the absorption maxima of phenol and the respective carbamate are sufficiently different). Hydrolysis of the other carbamates could not be followed spectrophotometrically with sufficient accuracy.

* Part V in the series Carbamates; Part IV: This Journal 38, 3139 (1973).

EXPERIMENTAL

The studied substances. A total of 0.2 mol dimethylcarbamoyl chloride was added to 0.1 mol of the respective substituted phenol dissolved in 80 ml pyridine. The reaction mixture was left to stand 24 hours at the room temperature. Then it was boiled under a reflux condenser 20 minutes, poured onto ice and extracted with ether. The ether layer was extracted subsequently with hydrochloric acid solution, water, 10% sodium hydrogen carbonate solution and twice with water. Then it was dried over sodium sulphate, ether was distilled off and the carbamate was recrystallized from chloroform. Phenyl N,N-dimethylcarbamates with the following substituents were prepared: 4-OCH₃ (I), m.p. 62–63°C; 4-CH₃ (II), m.p. 51–53°C; 3-CH₃ (III), b.p. 88–90°C : 0.14 Torr; H (IV), m.p. 44–45°C; 4-Cl (V), m.p. 33–34°C; 3-Cl (VI), b.p. 88–92°C/0.04 Torr; 3-NO₂ (VII), m.p. 61–62°C; 4-COCH₃ (VIII), m.p. 63–64°C, for C₁₁H₁₃NO₃ (207.2) calculated: 61.52% C, 6.71% H, 7.18% N; found: 61.58% C, 6.70% H, 7.22% N; 4-CN (IX), m.p. 119–120°C, for C₁₀H₁₀N₂O₂ (190.1) calculated: 63.15% C, 5.30% H, 14.73% N; found: 63.10% C, 5.25% H, 14.75% N; 4-SO₂CH₃ (X), m.p. 120–121°C, for C₁₀H₁₃NO₄S (243.3) calculated: 49.49% C, 5.35% H, 5.76% N; found: 49.45% C, 5.30% H, 5.80% N; 4-NO₂ (XI), m.p. 105–106°C. The melting resp. boiling points of the substances I–VIII and XI agreed with those given in ref.⁴.

Kinetic measurements. The rate constants were determined by the procedure given in our previous paper¹. The experimental error of the k_{obs} determination did not exceed 10%; the pK value was determined by the classical spectral method⁵.

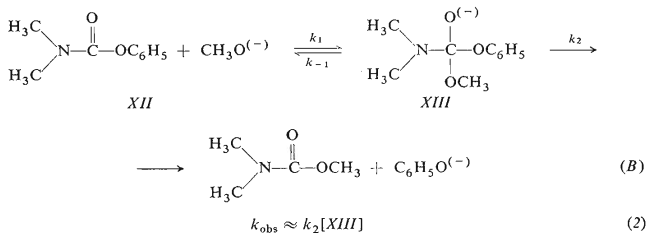
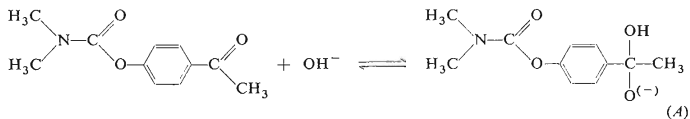
RESULTS AND DISCUSSION

The hydrolysis rate constants ($10^3 \cdot k_{\text{obs}}$, s⁻¹) of *p*-nitrophenyl N,N-dimethylcarbamate in aqueous 0.1, 0.5, 1.0 and 2.0M-NaOH at 40°C are 0.21, 1.19, 2.87 and 5.60, respectively, which means that the reaction order is unity with respect to hydroxyl ion. The medium of aqueous 1M-NaOH at 40°C was used for study of hydrolysis of substituted phenyl N,N-dimethylcarbamates I–XI, and the following values of $k \cdot 10^5$ (s⁻¹) were obtained: I 17.4, II 4.90, III 12.2, IV 21.9, V 38.3, VI 78.5, VII 98.5, VIII 9.45, IX 63.9, X 1.32, XI 295. These values of pseudomonomolecular rate constants were correlated with σ constants⁶ to give Eq. (I). The ρ value found (1.00) is close to that found for alkaline hydrolysis of the substituted phenyl acetates (0.976) (ref.⁶).

$$\log k_{\text{obs}} = 1.00\sigma - 3.62 ; \quad r = 0.98, \quad s = 0.081, \quad (I)$$

The k_{obs} values of *p*-acetylphenyl N,N-dimethylcarbamate hydrolysis were not included in the regression analysis. This compound is hydrolyzed about 8 times more slowly than it should react according to the value calculated from the regression straight line. It is presumed that, in strongly alkaline media, hydroxyl ion reacts with the *p*-acetyl group (Eq. (A)) converting it into a negatively charged substituent which decreases the reactivity of the substrate towards hydroxyl ion. It is surprising that in literature there are no data about hydrolysis of *p*-acetylbenzoic esters where a similar phenomenon should occur.

Methanolysis of phenyl N,N-dimethylcarbamates produces methyl N,N-dimethylcarbamate besides the respective phenolate ion. In accord with $\text{CH}_3\text{O}^{(-)}$ ion being a stronger nucleophilic agent than OH^- ion, methanolysis is 10–15 times faster than hydrolysis when the concentrations of the both bases are the same. Fig. 1 gives the dependence of $\log k_{\text{obs}}$ vs $H_{\text{R}-}$. The $H_{\text{R}-}$ function was constructed for addition of $\text{CH}_3\text{O}^{(-)}$ anion to an activated $\text{C}=\text{C}$ bond and can be well used for the addition of $\text{CH}_3\text{O}^{(-)}$ anion to the carbonyl carbon atom of phenyl acetates, too. The dependence of $\log k$ of phenyl acetate methanolysis on the $H_{\text{R}-}$ function is linear in the range of $H_{\text{R}-}$ 12–16, the angular coefficient being unity (Fig. 1). In the case of methanolysis of N,N-dimethylcarbamates, however, the reaction order decreases with increasing methoxide concentration, the rate being practically independent of methanolate concentration above $H_{\text{R}-}$ 17. This finding is explained by the decomposition of the tetrahedral intermediate being the rate-limiting step of the methanolysis in strongly alkaline medium (Eqs (B) and (2)). At lower concentrations of methoxide



anion the reaction order with respect to $\text{CH}_3\text{O}^{(-)}$ approaches unity, the reaction being limited by the attack of the substrate by methoxide anion. Methanolysis of *p*-nitrophenyl N,N-dimethylcarbamate with various additions of dimethyl sulphoxide at a constant sodium methoxide concentration (0.5M) showed a steep increase of the reaction rate with increasing dimethyl sulphoxide content (Fig. 1). This reaction rate increase is ascribed to the increase of activity of methoxide anion (with increasing dimethyl sulphoxide content the extent of solvation of methoxide with methanol decreases and, on the other hand, that of the sodium cation by dimethyl sulpho-

xide increases). As there has not yet been constructed any acidity function for the system 0.5M sodium methoxide-methanol-dimethyl sulphoxide, we can only state

TABLE I
Rate Constants of Acid Hydrolysis of *p*-Nitrophenyl N,N-Dimethylcarbamate at 70°C

% H ₂ SO ₄	-H ₀	<i>k</i> · 10 ⁵ , s ⁻¹
9.5	0.30	1.51
20	1.00	3.37
30	1.70	6.77
40	2.45	13.2
50	3.30	27.4
60	4.45	43.7
70	5.75	99.8
79.5	7.30	207

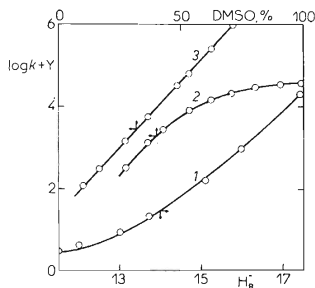


FIG. 1
Dependence of Methanolysis Rate Constants of *p*-Nitrophenyl N,N-Dimethylcarbamate (3, Y = 4) and Phenyl Acetate (2, Y = 7) on H_R. Function and Dependence of Methanolysis Rate Constants of *p*-Nitrophenyl N,N-Dimethylcarbamate on Dimethyl Sulphoxide Concentration (% DMSO) in 0.5M Methanolic Sodium Methoxide (1, Y = 0) at 20°C

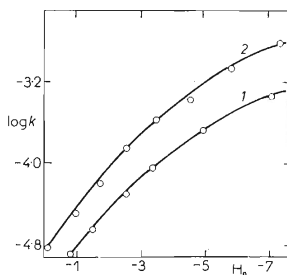
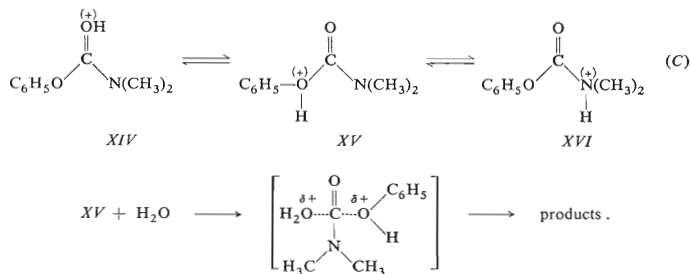


FIG. 2
Dependence of Acid Hydrolysis Rate Constants of Phenyl N,N-Dimethylcarbamate (1) and *p*-Nitrophenyl N,N-Dimethylcarbamate (2) on H₀ Function at 64°C

that the difference between the hydrolysis rate in methanol and that in 95% dimethyl sulphoxide containing 5% methanol is almost 4 orders of magnitude for the same molar concentration of methoxide.



The hydrolysis of *p*-nitrophenyl N,N-dimethylcarbamate was studied in aqueous acid medium. Results of the kinetic measurements in the range of H_0 0 to -7 at 64°C are given in Fig. 2 (Table I). It is obvious that increasing acidity results in steady increase of the hydrolysis velocity which does not reach its maximum value even in 70% perchloric acid in contrast to *p*-nitrophenyl N-methylcarbamate hydrolysis. Fig. 2 also gives the experimental points of phenyl N,N-dimethylcarbamate hydrolysis obtained by Armstrong⁷. The shape of the both curves shows that the respective measurements stand in accord to each other. The negative substituents increase the hydrolysis rate in a similar way as in the series of N-methylcarbamates. The difference of acidity-dependences between the N-methyl and N,N-dimethyl series suggests a difference in the hydrolysis mechanism of the both series, and it is interesting that in the case of the N,N-dimethyl derivative the hydrolysis rate is increasing even in the range of more than three H_0 units above the determined value of half-neutralization (-3.781). Armstrong⁷ supposes that the hydrolysis of N,N-dimethylcarbamate does not go through the tetrahedral intermediate, but a simultaneous formation of one C—O bond and splitting of another one take place in the activated complex. Our experiments do not enable any decision as to whether the tetrahedral intermediate is formed during hydrolysis or a single-step process takes place. In the case of the both possible mechanisms, the velocity increase in the ranges above the determined pK value could be ascribed to that the medium changes the position of tautomeric equilibria of the monoprotonated form in favour of the tautomer XV which is the main form for the reaction with nucleophile.

REFERENCES

1. Vontor T., Socha J., Večeřa M.: *This Journal* 37, 2183 (1972).
2. Biechler S. S., Taft R. W.: *J. Am. Chem. Soc.* 79, 4927 (1957).
3. Kroeger D. J., Stewart R.: *Can. J. Chem.* 45, 2163 (1967).
4. Valega T. M.: *J. Org. Chem.* 31, 1150 (1966).
5. Albert A., Serjeant E. P.: *Ionization Constants*. Wiley, London 1962.
6. Ritchie C. D., Sager W. F. in the book: *Progress in Physical Organic Chemistry* (W. R. Taft, A. Streitwieser, S. G. Cohen, Eds), Vol. 2, p. 323. Wiley, New York 1964.
7. Armstrong V. C., Moodie R. B.: *J. Chem. Soc. (B)* 1969, 934.

Translated by J. Panchartek.