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Kinetics of the Hydrolysis of Some Acid Phthalic and Acid Terephthalic Esters

By R. Anantaraman,* T. D. Radhakrishnan Nair, and (Miss) K. Saramma, Department of Chemistry, University of Kerala, Trivandrum, India

The kinetics of the hydrolysis of the acid phthalic and acid terephthalic esters of some para-substituted derivatives of 1-phenylethanol and of p-methoxybenzyl alcohol are reported. The results are interpreted in terms of intramolecular electrophilic catalysis by the free ortho-carboxy-group in the phthalate series.

INTRAMOLECULAR catalysis by a neighbouring carboxygroup has been much studied.¹⁻³ Generally however investigations have been restricted to substrates which do not react appreciably in the absence of such catalysis and it was of interest to ascertain whether the hydrolysis of more reactive esters was also similarly catalysed. We report here the kinetics of the hydrolysis, in aqueous acetone, of the following compounds: (a) acid phthalic esters of 1-phenylethanol (I) and its p-methyl (II), -ethyl (III), -isopropyl (IV), -t-butyl (V), and -methoxyderivatives (VI), and of p-methoxybenzyl alcohol (VII); and (b) acid terephthalate esters of 1-phenylethanol (VIII), and its p-methyl (IX), -ethyl (X), -t-butyl (XI), and -methoxy-derivatives (XII). (The figures in parentheses are used to identify the compound in the Table). The terephthalate esters were included in the study since one method of judging the catalytic effect of the o-carboxy-group is to compare the rates of the o- and p-carboxy-derivatives.¹

EXPERIMENTAL

Materials.—The alcohols were prepared by conventional methods and converted to the acid phthalic esters by heating with phthalic anhydride in pyridine. The acid terephthalates were prepared by use of p-chloroformylbenzoic acid 4 in place of phthalic anhydride. The terephthaloyl chloride used for the preparation was conveniently obtained by reaction of disodium terephthalate with thionyl chloride. This is better than the usual method using pyridine as solvent. Acetone was purified by the method of Conant and Kirner⁵ and dioxan by the standard method. Optically active 1-(p-t-butylphenyl)ethyl hydrogen phthalate was prepared by a method similar to that used by Downer and Kenyon for resolving the acid phthalate of 1-phenylethanol.⁶ [x% aq. acetone signifies solvent made up at room temp. of x vol. of acetone and (100 - x) vol. of water.]

Kinetic Technique.-The rate of hydrolysis was followed by titration of the liberated phthalic/terephthalic acid with standard alkali with o-cresolphthalein as indicator. The weight of acid calculated on the basis of weight of ester taken closely agreed with the value calculated from the infinity titre. The first-order rate constants were calculated as usual. The activation parameters were obtained by the least-squares method for rate measurements at four temperature, each run being carried out in triplicate. The probable errors were calculated by the usual method? as $\Delta H = 0.8$ kJ mol⁻¹ and $\Delta S = 4$ J mol⁻¹ K⁻¹.

The influence of pH on rate was studied for 1-phenylethyl hydrogen phthalate by following the rate of formation of phthalic acid under conditions of constant ionic strength (0.895) with a citrate buffer to control the pH; dioxanwater was used as solvent because of the high light absorption by aqueous acetone at the wavelength used (295 nm).

RESULTS AND DISCUSSION

The kinetic data are given in the Table. The firstorder rate coefficients at 25° have been given to facilitate

Rate constants and activation parameters at 25° for the hydrolysis of the acid phthalic and terephthalic esters

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		ΔH ‡	ΔS^{\ddagger}
Compound	10 ¹⁰ k ₁ /s ⁻¹	kJ mole ⁻¹	J K ⁻¹ mol ⁻¹
Solvent 75% aq. acetone			
(I)	1.25	120	32
(ÎI)	21.8	120	-9.5
(III)	17.6	120	8.6
(IV)	13.7	122	-5.7
(V)	9.89	123	-6.1
(VI)	11,600	107	-0.8
(VII)	50.6	113	-25
(VIII)	0.0346	118	-70
(IX)	1.12	112	-58
(X)	0.990	112	-59
(XI)	0.540	114	60
(XII)	0.498	106	29
Solvent 65% aq. acetone			
(I)	4.37	117	38
(ÌI)	57.9	116	-14
(V)	25.4	120	-7.5
Solvent 55% aq. acetone			
(I)	8.11	115	-32
(ÌI)	129	116	- 5.8
(ÌII)	107	115	10
(IV)	79·3	118	4.5
`(V)	50.2	120	-2.0

convenient comparison of the results, although the actual measurements were done at higher temperatures.

Before discussing the results, it is necessary to ensure that comparisons of rates are not invalidated by gross differences in mechanism. This was done by hydrolysing optically active acid phthalates of 1-phenylethyl alcohol and 1-(p-t-butylphenyl)ethyl alcohol and the acidterephthalate of 1-phenylethyl alcohol under conditions similar to those used in the kinetic study. In every case the resulting alcohol was essentially racemic showing

¹ B. Capon, Quart. Rev. 1964, 18, 48.

² S. L. Johnson in 'Advances in Physical Organic Chemistry,' ed. V. Gold, Academic Press, New York, 1967, vol. 5 p. 237.
³ W. P. Jencks, 'Catalysis in Chemistry and Enzymology,' McGraw-Hill, New York, 1969, p. 463.

⁴ C. S. Marvel and E. A. Kraiman, J. Amer. Chem. Soc., 1953,

^{18, 1664.} J. B. Conant and W. R. Kimer, J. Amer. Chem .Soc., 1924, **46**, 246.

 ⁶ E. Downer and J. Kenyon, J. Chem. Soc., 1939, 1156.
 ⁷ H. Margenau and G. M. Murphy, 'The Mathematics of Physics Chemistry,' Van Nostrand, Princeton, 1956, p. 519.

that a carbonium ion intermediate is involved in these cases, and by implication, in all the other cases as well.

The fairly high values for the rate ratio phthalate: terephthalate appears to suggest that the o-carboxygroup in the phthalate is exerting an influence other than a purely polar effect. Since the bond fission must be alkyl-oxygen, any steric effect of the o-carboxy-group should be negligible. This is also in accord with the values of the activation parameters. The values of enthalpies of activation are slightly higher, and the entropies much higher, in the phthalate than in the terephthalate series, probably because in the phthalate series, the free o-carboxy-group acts as an intramolecular electrophilic (general acid) catalyst. Practically all the acceleration in the phthalate series over the terephthalate series appears to derive from differences in the entropy factor. This change in ΔS probably stems from less solvation of the phthalate transition state. This is because intramolecular hydrogen bonding would diminish the need for solvation of the developing negative charge on the oxygen atom, and thereby make the entropy of the transition state greater than it would be if solvated to the extent required for the terephthalate ester. Further, this would also account for the fact that ΔH values are somewhat higher in the phthalate series. Evidently the decrease in solvation of the phthalate transition states (and resulting increase in entropy) is achieved at the expense of an increase in enthalpy which is only partially offset by intramolecular hydrogen bonding.

The extent of negative charge on the oxygen atom should be related to the nature of the p-R group, in the sense that a carbonium-stabilizing R group should enable the transition state to be attained earlier in the reaction co-ordinate at a point where less negative charge had

To confirm the interpretation given above, the effect of pH on the rate of hydrolysis of 1-phenylethyl hydrogen phthalate was studied spectrophotometrically, under conditions of constant ionic strength. The pH-rate profile is qualitatively similar to that obtained by Bender for the hydrolysis of methyl hydrogen phthalate. As the pH is increased from 0.2, the rate decreases, passes through a minimum at ca. 1.5, and then increases to a value which is constant over the pH range 2-4.5. Bender has interpreted his results as being due to intramolecular carboxylate ion (nucleophilic) catalysis.⁸ In a reinvestigation of the problem, Bruice obtained the same type of results as Bender, but interpreted them as being consistent with intramolecular electrophilic catalysis by the carboxy-group.⁹ This is in accord with his earlier conclusion that if the pK_a value of the leaving alcohol is above ca. 13.5, then electrophilic catalysis is involved.¹⁰ This conclusion agrees with previous data.¹¹ Since the pK_a values of the alcohols used in this study are all much greater than 13.5, the interpretation given here agrees with that of Bruice and others.9-11

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- 86, 418.
 ¹¹ A. Agren, U. Hedston, and B. Janssen, Acta Chem. Scand., 1961, 15, 1532; L. Eberson, *ibid.*, 1964, 18, 2015.

⁸ M. L. Bender, F. Chloupek, and M. C. Neven, J. Amer. Chem. Soc., 1953, 80, 5384. ⁹ J. W. Thanassi and T. C. Bruice, J. Amer. Chem. Soc., 1966,

^{88, 747.}