

The Kinetics and Mechanism of Alkaline Hydrolysis of Acryl Substituted Benzoate Esters

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Summary: The reaction rates of alkaline hydrolyses of methyl-, phenyl-, p-nitrophenyl-p-methoxybenzoate esters have been studied at 32°C. The plot of the logarithmic of bimolecular nucleophilic rate constants against pK_a of leaving groups has resulted in Bronsted coefficient (β_{lg}) of -0.2 ± 0.1 which indicates an insignificant amount of bond cleavage between carbonyl carbon and leaving group in the rate-determining step.

Introduction

It has been well established that the alkaline hydrolysis of esters follow a stepwise mechanism involving an oxymonoanionic tetrahedral intermediate [1]. Recently, we have observed kinetically the existence of an oxydianionic tetrahedral intermediate in the alkaline hydrolysis of methyl-o-methoxybenzoate [2]. Kirsch et al. [3] studied the aqueous cleavages of several acyl and aryl substituted benzoate esters in a considerably low alkaline medium where the existence of oxydianionic tetrahedral intermediate could not be expected to occur. A search of literature reveals that the existence of an oxydianionic tetrahedral intermediate in methylbenzoate ester. The results and probable mechanistic conclusions are described in this paper.

Experimental

Materials:

Methyl-p-methoxybenzoate (1), phenyl-p-methoxybenzoate (4), were prepared by the reaction of p-methoxybenzoyl chloride (anisoyl chloride) with the appropriate phenols or methanol in the presence of traces amount of pyridine according to a standard procedure [5] to afford the desired products as white crystalline solids: (1), 65% yield, mp 48-49°C (lit [6] mp 49°C); (2), 73%

yield, mp 71-72°C, IR (Nujol) 1725, 1608, 1450, 1275, 1200, 1090 cm⁻¹, ¹H-NMR (DMSO) 6.9-7.9 (m, 9H) aromatic, 1.4 (s, H, CH₃); (3), 84% yield, mp 152-154°C, IR (Nujol) 1725, 1608, 1450, 1275, 1200, 1090, cm⁻¹, ¹H NMR (DMSO) 6.9-7.9 (m, 9H) aromatic, 1.4 (s, 3H, CH₃), 84% yield, mp 152-154°C, IR (Nujol) 1725, 1608, 1480, 1475, 1455, 1350, 1290, 1220, 1060 cm⁻¹.

All other chemicals used were reagent grade. Glass distilled water was used throughout the kinetic studies.

Kinetic Measurements

The rates of alkaline hydrolyses of (1) and (2) were studied by monitoring spectrophotometrically the disappearance of substrate at 268 nm and 298 nm, respectively. The rate of alkaline hydrolysis of (3) was studied by monitoring the appearance of p-nitrophenolate ion at 400 nm. The Beckman Model 3500 UV-visible spectrophotometer was used throughout the kinetic studies. In a typical kinetic run, all reaction ingredients except substrate were taken in a hundred ml round bottom flask and the total volume of the reaction mixture was adjusted to 49 ml. This reaction mixture was incubated at 32°C in a thermostatic water bath for about 10-15 mins. The reaction was then started by adding either 1 ml

or 0.5 ml of concentrated solution of appropriate substrate prepared in either absolute ethanol or acetonitrile. This procedure thus added a maximum 2% organic solvent and produced initial concentration of (1), (2), and (3) as $1.0 \times 10^{-3} \text{M}$, $4.0 \times 10^{-5} \text{M}$ and $1.0 \times 10^{-3} \text{M}$, respectively, into the aqueous reaction mixture. An aliquote of $\sim 2.5 \text{ ml}$ was withdrawn from the reaction mixture and was transferred quickly to the 3 ml quartz cuvette kept in preincubated at 32°C thermostatic cell holder of spectrophotometer. The constant temperature of cell holder was maintained electronically by the use of the temperature control unit of the spectrophotometer. The observed pseudo first-order rate constants, k_{obs} , were calculated from eqn (1) or (2) depending upon whether the reaction rates were studied by monitoring the disappearance of substrate or appearance of product.

$$A_{\text{obs}} = E_{\text{app}}X_0\exp(-k_{\text{obs}}t) + A\alpha \quad (1)$$

$$A_{\text{obs}} = E_{\text{app}}X_0(1-\exp(-k_{\text{obs}}t)) + A_0 \quad (2)$$

In eqn (1) and (2), X_0 is the initial concentration of substrate, A_{obs} , $A\alpha$ and A_0 are the absorbance values at any time, t , $t = \alpha$ and $t = 0$, respectively, and E_{app} represents the apparent molar extinction coefficient. The three unknown parameters, k_{obs} , E_{app} and $A\alpha$ or A_0 were calculated from appropriate eqn (1) or (2) by means of nonlinear least squares technique. Most of the kinetic runs were carried out for more than 6 half-lives of the reactions. The fitting of observed data to the appropriate eqn (1) or (2) was reasonably good for all kinetic runs.

Results and Discussion

The alkaline hydrolyses of (1), (2) and (3) have been carried out within the $[\text{OH}^-]$ range that could be covered with conventional spectrophotometric technique. The ionic strength of the reaction medium was kept constant at either 2.0 M for (1) or 1.0 M for (2) and (3). The observed pseudo first-order rate constants, k_{obs} , as shown graphically in Figure 1, obeyed equation (3).

$$k_{\text{obs}} = k_{\text{OH}}[\text{OH}^-] \quad (3)$$

The second-order hydroxide ion-catalysed rate constants, k_{OH} , were calculated from equation (3) with linear least squares technique for (1), (2),

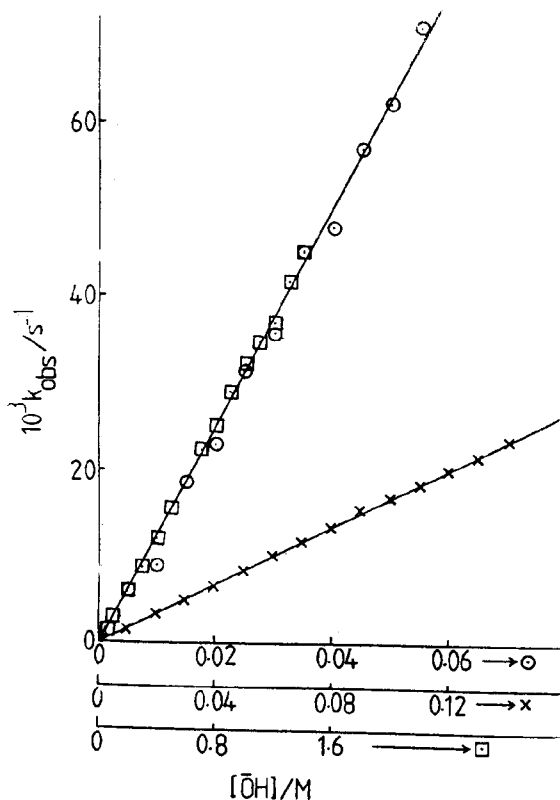


Fig. 1: Plots showing the dependence of k_{obs} vs. $[\text{OH}^-]$ for hydrolyses of (1) (O), (2) (X) and (3) (□). Solid lines are drawn through the least squares calculated points as described in the text.

and (3) and the results thus obtained are summarized in Table 1. The fitting of the observed data to equation (3) is evident from the plots shown in Figure 1 where solid lines are drawn through the least square calculated points. The linear least square treatment of the observed data to equation: $k_{\text{obs}} = C + D [\text{OH}^-]$ resulted in the values of C either negative or positive with standard deviations of more than 100% which revealed that the water-catalysed term (C) could be neglected compared to the k_{OH} term within the experimental conditions employed. Consistent with this conclusion is the fact that the observed value of k_{obs} of ca. $2 \times 10^{-7} \text{ s}^{-1}$ obtained for neutral hydrolysis of *p*-nitrophenyl-*p*-nitrobenzoate [3] at 25°C and 33% MeCN is nearly 175 times smaller than the k_{obs} obtained for aqueous cleavage of methyl-*p*-hydroxybenzoate at 0.02 M NaOH and 32°C .

Table 1: Apparent hydroxide ion-catalyzed second-order rate constants (k_{OH}) for aqueous cleavages of (1), (2) and (3).

Compound	$k_{OH} 10^3 k^a_{OH}$ $M^{-1} s^{-1}$
(1)	$115.14^{b} 31.64 \pm 0.19$
(2)	$29.76^c 166.9 \pm 0.7$
(3)	$37.02^c 1257 \pm 14$

^aError limits are standard deviations; ^bp. Balinger, and F.A. Long, J. Am. Chem. Soc., **82**, 795, (1960); ^cJ. F. Kirsch, and W.P. Jencks, *Ibid.*, **86**, 837, (1964).

The value of k_{OH} for (1) is similar to the k_{OH} ($0.031 m^{-1} s^{-1}$ at $35^{\circ}C$) for methyl-*o*-methoxybenzoate [2]. This similarity cannot be explained by assuming that electronic effects exhibited by OMe group from *p*- and *o*-positions are same because *o*-OMe is expected to display a significant steric effect. Nearly 7-fold decrease in the rate of alkaline hydrolysis of methyl-*o*-methylbenzoate compared to methylbenzoate in 80% methanol solvent [7] is presumably due to the combined effects of electronic, steric and solvation effects. Considering the value of ρ as 2.54 (obtained for alkaline hydrolyses of 3- substituted ethyl-benzoate in 85% ethanol solvent [8]) and σ_{m-Me} as -0.07 [9], the decrease in rate due to electronic effect could be estimated to be 1.5-fold. Thus, 4.5-fold decrease in rate could be due to solvation changes and steric factor. The estimated 1.5-fold rate retarding effect of *o*-Me groups is based on the assumption that both the substituent (*o*-Me) and reaction center ($-CO_2Et$) maintain the coplanarity with the benzene ring. But in actual fact the *o*-Me substituent has been observed to be acting as an electron withdrawer [10] rather than an electron donor to the reaction center. This could be explained by assuming that the interaction between adjacent methyl and carboxy groups causes carboxy group to be noncoplanar with the benzene ring and thus it

reduces the electron donating resonance effect of the ring to the carboxy group [14]. The steric requirements of *o*-OMe group may also be expected to cause CO_2Me group in methyl-*o*-methoxybenzoate to be off from being coplanar with the benzene ring and consequently resonance electron donating effect of *o*-OMe towards the reaction centre is no more effective. Thus, the polar effect (inductive) of *o*-OMe which is electron withdrawing in nature is only effective. In the alkaline hydrolysis of methyl-*o*-methoxybenzoate, the polar effect of *o*-OMe is therefore expected to increase the rate by a factor of at least $10^{0.24}$ compared to an unsubstituted compound (considering ρ as 2.0^3 and σ_{OMe} as 0.12^9). Nearly 5-fold decrease in rate of alkaline hydrolysis of methyl-*o*-methoxybenzoate compared to that of methylbenzoate [15] reveals 9-fold rate retarding due to solvation changes and steric requirements of *o*-OMe group which is not an unreasonable number. In the alkaline hydrolysis of many *o*-substituted benzoate esters, the rate retarding effect of substituents (steric and other effects) has been found to be nearly counterbalanced by their rate increasing polar effect [16].

In contrast with the kinetically observed existence of an oxydianionic tetrahedral intermediate in the alkaline hydrolysis of methyl-*o*-methoxybenzoate, we could not kinetically observe such an intermediate in the alkaline hydrolysis of (1). The reasons for it may be given as follows: (1) The *o*-OMe substituent is apparently acting as an electron withdrawer by which it increases the acidity of hydroxyl proton of oxymonoanionic tetrahedral intermediate while the reverse is true with *p*-OMe substituent. (ii) A steric repulsion between hindering group and ionizable proton would increase the acidity of oxymonoanionic tetrahedral intermediate in methyl-*o*-methoxybenzoate compared to that in (1) [17]. However, this effect would be partially offset or dominated by steric hindrance to the solvation of oxydianionic tetrahedral intermediate. An alternative explanation might be that the "push" derived from resonance interaction with the phenyl ring and the *p*-OMe group provides adequate driving force for leaving group expulsion from a monoanionic intermediate, whereas in the *o*-OMe compound, the incipient carbonyl group cannot be aligned to take advantage of such a "push", and thus reaction via a dianionic, where more "push" is provided by an additional negative charge, becomes important.

The observed value of k_{OH} for (1), (2) and (3) were used to calculate the slope (Bronsted coefficient, β_{1g}) and intercept of the plot of $\log k_{OH}$ vs. pK of leaving group (pK_{1g}) and the respective values thus obtained are -0.2 ± 0.1 and $1.28 \pm 0.52 M^{-1} s^{-1}$. Although the value of β_{1g} of -0.2 is derived from a rather limited number of observed points (3 only) and also MeO leaving group is not structurally similar to ArO group, it is comparable with β_{1g} of -0.32 obtained in the alkaline hydrolyses of aryl acetate ester [18]. It is however, significantly different from β_{1g} of 0.46 [19] or 0.56 [20] obtained in the alkaline hydrolyses aryl benzoate ester where the pK_a range of leaving groups covered 3 pK units. The significantly small value of β_{1g} of -0.2 indicates that the nucleophilic attack is most likely the rate-determining step in a stepwise process.

References

1. A.C. Satterthwait and W.P. Jencks, *J. Am. Chem. Soc.*, **96**, 7018, (1974). P.Y. Bruice and T.C. Bruice, *J. Am. Chem. Soc.*, **96**, 5523, (1974).
2. M.N. Khan and T.O. Olagbemi, *J. Org. Chem.*, **47**, 3695 (1982).
3. J.F.Kirsch, H. Clewell and A.Simon, *J.Org.Chem.*, **33**, 127, (1968).
4. M. N. Khan, R. Ahamd, A. A. Khan, *Indian J. Chem.*, **14A**, 961, (1976).
5. D.L.Pavia, G.M.Lampman and G.S.Kriz, "Introduction to Organic Laboratory Technique"; Saunders: Philadelphia, 97, (1976).
6. Z. Rappoport, "CRC Handbook of Tables for Organic Compounds", 1980, 3rd Ed.
7. N.B. Chapman, J. Shorter, and J.B.Utley, *J.Chem.Soc.*, 1291, (1963).
8. B.Jones and J. Robinson, *J.Chem.Soc.*, 3845, (1955).
9. J.Hine, "Structural Effects on Equilibria in Organic Chemistry"; John Wiley & Sons, p. 66, 1975.
10. The values of pK_a of o-methyl-, p-methyl-, and unsubstituted benzoic acids have been found to be 3.98 [11], (3.90 [12]), 4.37 [12], and 4.22 [12], respectively at $25^\circ C$. Similarly, the observed values of pK_a at $20^\circ C$ for o-methoxy-, and p-methoxy benzoic acids are 4.09 [13] (4.13 [11] at $25^\circ C$) and 4.47 [13], respectively.
11. O.Lukkan, and E.Hakoila, *Finn.Chem.Lett.*, **2-3**, 93 (1978).
12. L.H. Bykova, and S.I. Petrov, *Usp.Khim.*, **39**, 1631, (1970).
13. J.C.Halle, R.Schaal, and A.diNallo, *Analyt.Chim.Acta*, **60**, 197 (1972).
14. ref.9, p. 85.
15. A.F.Hegarty, and T.C. Bruice, *J.Am.Chem.Soc.*, **92**, 6575 (1970).
16. M.N.Khan, *Indian J.Chem.*, **25A**, 831 (1986).
17. ref. 9, p. 168.
18. J.F.Kirsch, and W.P.Jencks, *J. Am. Chem. Soc.*, **86**, 837 (1964).
19. This value of β_{1g} was obtained by plotting the logarithm of k_{OH} (obtained from reported data [3]) vs. pK_a of leaving group (obtained in 100% water) assuming that 33% acetonitrile in the solvent would have same amount of effect on pK_a of all leaving substituted phenols.
20. It can be shown by combining Hammett and Bronsted equation that $\beta_{1g} = \rho/\rho^1$ where ρ and ρ^1 are the reaction constants with Hammett substituent constants for a given series of homologous acids. The average value of $\rho = 1.2$ was obtained by Kirsch et al. [3] and the value of $\rho^1 = 2.2$ at $25^\circ C$ was obtained from literature [21]. The value of $\beta_{1g} = 0.56$ was calculated from these known values of ρ and ρ^1 .
21. G.R. Parsons, and C.H. Rochester, *J. Chem. Soc., Faraday I*, **71**, 1058, (1975).