

EFFECT OF SOLVENTS ON KINETICS OF ESTER AMINOLYSIS.

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n-Butylamine reacts with phenyl dichloroacetate in cyclohexane following third order kinetics only. When the same reaction was carried in cyclohexane-dioxan mixture, the rate of the reaction was found to increase as the percent of dioxan in the mixture is increased. These results suggest that the second order term in the aminolysis of esters in dioxan, reported previously,¹ represents a solvent catalyzed process. The possible mechanisms of such processes are discussed.

Introduction

Satchell and Secomski² have claimed that the aminolysis of esters by 1^{ary} or 2^{ary} amines in diethyl ether obeys the rate equation (1) :

$$-d[\text{ester}]/dt = k_2 [\text{ester}][\text{amine}] + k_3 [\text{ester}][\text{amine}]^2 \dots (1)$$

and that added tertiary amines do not accelerate the reaction. It was further argued that these observations rigorously exclude the

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possibility of the participation of the solvent in a path involving only one amine molecule.

Previously reported results¹ have shown that only 1^{ary}, and not 2^{ary}, amines lead to rate equation (1); 2^{ary} amines have been found to lead exclusively, to an expression first order in amine, as shown in equation (2)^{1,3}:

$$-d[\text{ester}]/dt = k_2 [\text{ester}][\text{amine}] \dots\dots\dots(2)$$

It was shown in several reports that ester aminolysis is subject to both inter- and intramolecular base catalysis.^{1,3,4}

It has been our experience that for the experimental conditions carried for the n-butylaminolysis of p-nitrophenylacetate investigated by Satchell and Secomski², third order kinetics may very easily escape detection.^{1,5} This sheds doubts on Satchell's conclusions, and we thought it is interesting to investigate the aminolysis of esters in different solvents. The systems investigated in this work include the reaction of phenyl dichloroacetate with n-butylamine in cyclohexane and in cyclohexane-dioxan mixtures. The same aminolysis reaction was reported before in dioxan.¹ Cyclohexane and dioxan were chosen because they have almost similar dielectric constants, but differ in their ability to interact with the solute molecules. If the solvent plays a role, the kinetics of aminolysis in either solvent or in their mixture would be expected to be the same.

Experimental

Materials: Cyclohexane and dioxan were Matheson, Coleman and Bell Spectroquality reagents grade solvents. Their purity was checked by uv and vapor phase chromatographic analysis.

n-Butylamine was purchased from Matheson, Coleman and Bell. It was purified by storing overnight over sodium hydroxide pellets, then distilled from fresh sodium hydroxide pellets using a 15-in. Vigreux column. The fraction having constant b.p. was collected and stored in an amber glass bottle over fresh sodium hydroxide pellets. Its degree of purity was determined by acid-base titration and checked by vapor phase chromatographic analysis. A clean single peak was obtained, indicating almost 100% purity. Its physical constants agreed with those in the literature.⁶

Phenyl dichloroacetate was prepared from dichloroacetyl chloride⁷ and phenol as described previously.¹ Its physical constants also agreed with literature values.^{6,8}

Kinetics: A Bausch and Lomb Spectronic 505 uv spectrophotometer with jacketed cell compartment maintained at $25.5 \pm 0.1^\circ$ was used for the kinetic measurements. The reactions were carried out in 1-cm pressureless-stoppered fused silica absorption cells. The procedure of following the kinetics of the reactions, and the methods of treating the data are similar to those described previously.¹

Stoichiometry and Isolation of Product: Authentic samples of n-butyl dichloroacetamide was prepared by independent methods. When the reaction of phenyl dichloroacetate with n-butylamine was carried out on laboratory scale, the expected amide was obtained in about 85% yield and was identical with the authentic sample.

Results

In all kinetic runs the ester concentration was maintained at 1.0×10^{-4} M, whereas amine concentration was varied in the range 0.01 to 0.1 M. This excess concentration of amine led to pseudo-

first order disappearance of ester. The reactions were followed by rate of appearance of the phenol peak at 274 μ . The observed first order rate constants, k_{obs} , were calculated from plots of $\log (D_{\infty} - D_t)$ vs. time, where D_{∞} and D_t represent the optical densities, at the chosen wave length, at infinite time and at any interval 't', respectively, as explained previously.¹ Values of k_{obs} were normally reproducible to $\pm 3\%$ or better.

The kinetic data are included in Table 1. For the reaction of phenyl dichloroacetate with n-butylamine in cyclohexane, the following relation was obtained:

$$k_{obs}/[\text{amine}] = k_3 [\text{amine}] \dots\dots\dots(3)$$

This is illustrated in Fig. 1, where a plot of $k_{obs}/[\text{amine}]$ vs. $[\text{amine}]$ gives a straight line, whose slope is equal to k_3 .

Results for a series of experiments for the reaction of phenyl dichloroacetate and n-butylamine in cyclohexane-dioxan mixtures are represented in Table 1. In this series, both ester and amine concentrations were held constant and the solvent composition was varied. The data indicate that at constant amine concentration, there is a gradual increase in the rate of the reaction as the ratio of dioxan to cyclohexane in the reaction mixture is increased, then the rate eventually levels off at high concentrations of dioxan, as can be observed in Fig. 2.

Discussion

In a reaction system containing the ester and n-butylamine there are three possible pathways that may be considered: (a) the uncatalyzed reaction, (b) base-catalyzed reaction and (c) solvent-catalyzed reaction.

If all three pathways were operating simultaneously, the overall rate expression could be given by:

$$\text{rate} = k_2[E][A] + k_3[E][A]^2 + k_2[E][A][S] \dots\dots\dots(1)$$

where E, A and S refer to the ester, amine and solvent respectively.

In cyclohexane, the catalytic contribution of the solvent molecules is absent. Accordingly, the rate equation (1) would be reduced to:

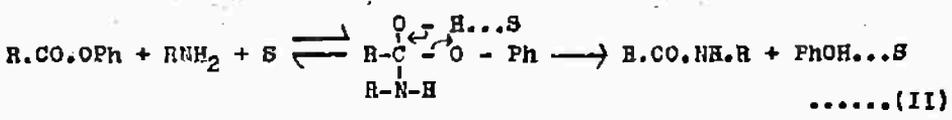
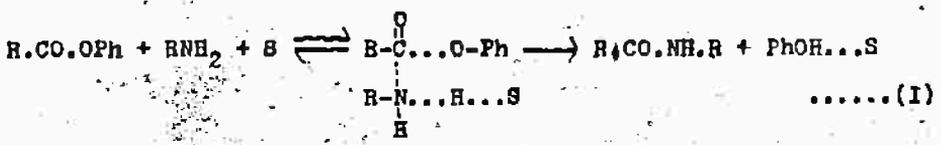
$$\text{rate} = k_2[E][A] + k_3[E][A]^2 \dots\dots\dots(2)$$

The available data indicate, however, that only the third order pathway is operating for the aminolysis in cyclohexane. This conclusion is in accordance with Menger's results⁹ for the aminolysis of p-nitro phenylacetate in chlorobenzene, where the second order term in amine, is the only term observed. The absence of the second order term when cyclohexane is the solvent suggests that the second order term obtained for the n-butylaminolysis of phenyl esters in dioxan¹ represents a solvent catalyzed reaction. Also, the fact that the overall rate of the reaction of phenyl chloroacetate with n-butylamine increases as the percentage of dioxan increases when the reaction is carried out in cyclohexane-dioxan mixture, substantiates this conclusion.

An alternate explanation for the disappearance of the overall second order term is that in hydrocarbon solvents, such as cyclohexane, the amine exists predominantly in the dimerized form. This is because hydrogen bonding to the solvent itself will be less prominent. Under such conditions, the amine catalyzed pathway becomes the predominant one. This explanation, although seems reasonable, is considered unlikely because the linear relationship of $k_{obs}/[\text{amine}]$ vs. $[\text{amine}]$ (Fig. 1), means that n-butylamine must exist essentially either all

in the monomeric form or in the dimeric form, in the concentration range used. If both monomers and dimers were present in appreciable amounts in the concentration range used in this study, then a plot $k_{obs}/[amine]$ vs. $[amine]$ would be curved. At lower concentration there would be a lower percentage of reactive dimers in solution than at higher concentration. Nevertheless, the data do not exclude a situation in which there is, for example, 1% monomers and 99% dimers. This is considered unlikely since it would mean that the true third order rate constant for the reaction of n-butylamine dimer with the phenyl ester in cyclohexane would be larger than that observed in dioxan. The values of k_3 obtained in cyclohexane and dioxan¹ were found to be 1.30 and 1.65 molar⁻².sec⁻¹, respectively.

Considering the mechanism of the solvent-catalyzed pathway, it may follow either a concerted mechanism as in scheme I, or a stepwise mechanism according to scheme II



Although the present kinetic data do not provide a direct evidence to exclude completely any of these two possible mechanisms, it is felt that the concerted mechanism (I) is very unlikely, since it ignores the most important addition property of the carbonyl group. The following facts seem also in favor of the stepwise mechanism (II)

(1) If the direct displacement mechanism (I) were operative, it

might be anticipated that as the reactivity of the ester increases, the reaction would proceed more through this pathway, since in this way it avoids going through the other multiple equilibrium steps of the base-catalyzed reaction sequence. As a result, the contribution of the latter would be expected to be small for the very reactive esters such as phenyl trichloroacetate and difluoroacetate. Contrary to this, previous kinetic data¹ of the same reaction system in dioxan indicate that the contribution of the third order process to the overall reaction generally increases as the reactivity of the ester increases. (ii) The observed applicability of Taft's relation for the observed second order rate constants for the aminolysis of esters previously reported¹, suggests the possible existence of an addition intermediate by analogy to other reaction series where such a linear free energy relationship holds.¹⁰

(iii) If the transition state (I) is the only one between the reactants (ester and amine) and the products (amide and phenol), it would be difficult to perceive why this transition state would form so much more readily in nucleophilic substitution reactions at the carbonyl-carbon than the corresponding transition state of the displacement of the alkoxy group in an ether molecule.⁴

(iv) A survey of the literature reveals that a direct displacement mechanism has not yet been reported in any nucleophilic substitution reaction at sp^2 -hybridized carbon atom.

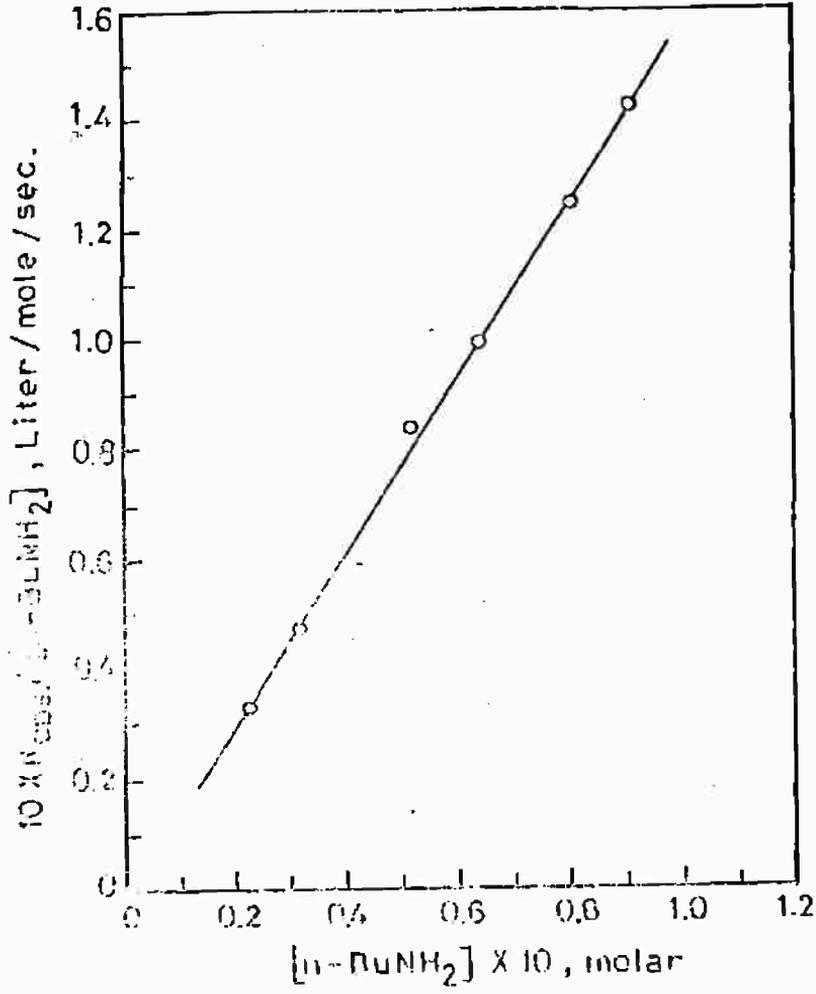
Based on the foregoing arguments, it is felt that a stepwise mechanism (II), for the second order aminolysis reaction, is more likely than the direct displacement mechanism (I).

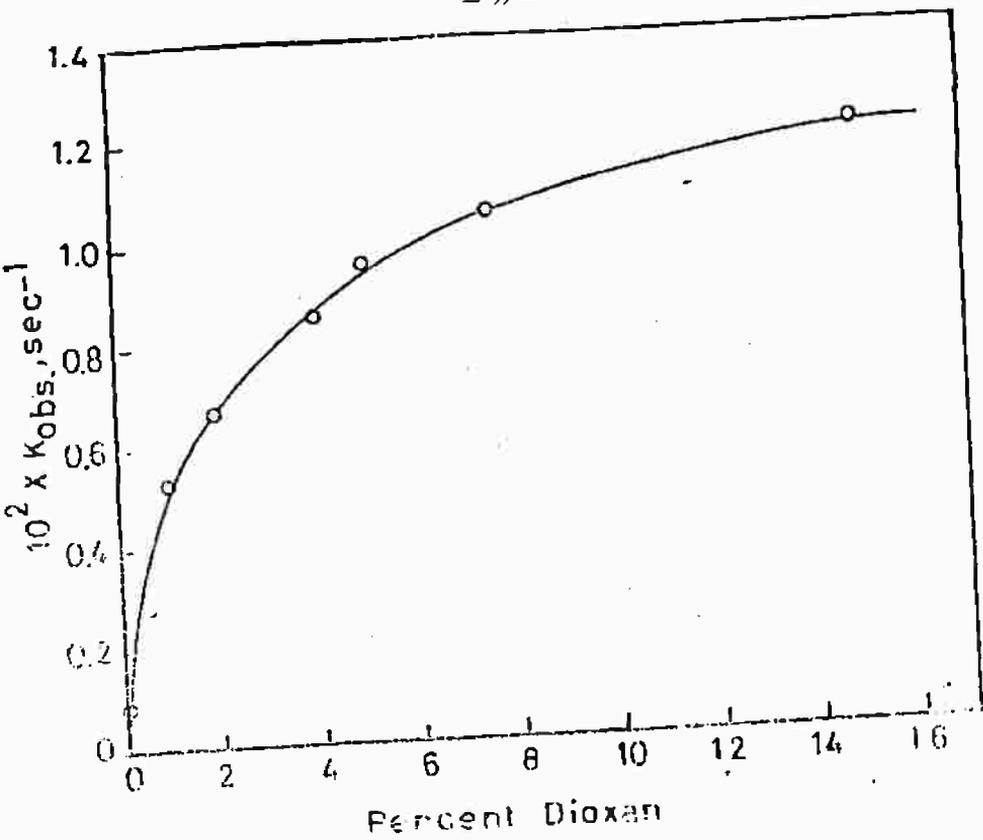
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Fig. 1. Linear Plot of $k_{obs}/[amine]$ vs. $[amine]$ for the reaction of Phenyl dichloroacetate with n-Butylamine in Cyclohexane at 25.5°.

Fig. 2. Dependence of k_{obs} on percent Dioxan for n-Butylaminolysis of Phenyl dichloroacetate in Cyclohexane-Dioxan mixtures.





تأثير المذيبات على كينيتيكية التحلل الايوني للأسترات

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تم التوصل الى ان كينيتيكية تفاعل هـ - بيوتول امين مع فيثيل ثنائي كلورو الخلات في
المكان الطبقى هي من النوع الثالثى الرتبة فقط . وعندما اجروا التفاعل نفسه في خليط
من الميثان الطبقى والديوكسان هـ وجد ان معدل التفاعل يزداد بازداد انصبابه
المثوية للديوكسان في خليط المذيب .

وبناء على هذه النتائج فقد امكن تفسير ا. الرتبة الثمانية التي تم التوصل اليها
مسبقا لكينيتيكية التحلل الايوني للأسترات من الديوكسان بفرده . تمثل تفاعل يدعى نفس
المذيب كعامل حافظ .

وتتضمن هذا البحث مناقشة طريق السير (الميكانيزم) المقترحة التي قد تتم بها
هذه التفاعلات .