orders of magnitude in time should allow the distinction to be made. This also points out one of the disadvantages of RDE studies, namely, that laminar flow is not obtained over an adequately large range of rotation rates. In Figure 2 chronoamperometric data are shown for several experiments in which pyridine was added to DPA. The measurements were made at a planar platinum electrode in acetonitrile which was 0.1 *M* in tetraethylammonium perchlorate and 8.0×10^{-4} *M* in DPA. The pyridine concentrations used were 5.8×10^{-3} *M*, 1.1×10^{-2} *M*, 2.2×10^{-2} *M*, and 4.1×10^{-2} *M*. The solid line represents the simulation for the disproportionation mechanism with $K = 4.0 \times 10^{-6}$ (calculated from the 320-mV separation between the first and second oxidation waves of DPA) and a rate constant of (4.5×10^{6}) [pyridine]. In actuality, for this particular case, the assumption of slow equilibrium was found to provide a better fit, and the simulation shown is for the case

$$K = \frac{k_f}{k_r} = \frac{4 \times 10^{3}}{1 \times 10^{9}}$$

The broken curve is the working curve for the ECE mechanism included for the purposes of comparison. The experimental data clearly favor the disproportionation mechanism. It should be borne in mind, however, that in reality these data only indicate that the first-order ECE interpretation is doubtful, and disproportionation provides a satisfactory alternative for which there exists a chemical precedent. It is also obvious that data obtained over shorter time intervals could easily fit either curve. One can only begin to distinguish between the two mechanisms when data are available over the entire range of variation for the particular working curve. This work demonstrates that at present one cannot unequivocally assign the mechanism of the DPA–pyridine reaction to the ECE pathway, and it further suggests that the disproportionation mechanism is a more likely route.

Acknowledgment. The author is indebted to the Research Corporation for a Frederick Gardner Cottrell grant-in-aid and to Drs. R. N. Adams, A. J. Bard, and H. J. Shine for helpful discussions.

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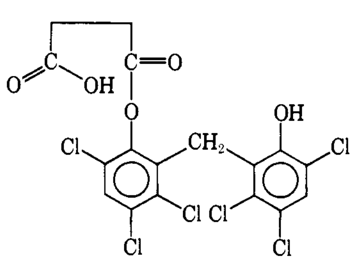
Received October 19, 1970

Intramolecular Bifunctional Facilitation in Complex Molecules. Combined Nucleophilic and General Acid Participation in Hydrolysis of Hexachlorophene Monosuccinate

Sir:

Intramolecular facilitation of the hydrolysis of carboxylic acid esters and amides has previously been shown to occur by either nucleophilic attack of a neighboring nucleophile such as a carboxylate group[1] at the ester carbon atom or by neighboring groups acting as general acids and bases.[2,3] We have now been able to show that simultaneous bifunctional twofold facilitation can be conferred on hydrolysis of a molecule as complex as hexachlorophene monosuccinate (I), where the participating structures involve formation of an 8-atom and a 5-atom ring. This appears to be the first definitively proven case of a push–pull nucleophilically assisted hydrolytic reaction, although a similar mechanism has been suggested by Morawetz[1] in the hydrolysis of succinylsalicylic acid. Unlike some of the earlier suggested systems of this nature, the present case involves participation of nonadjacent sites and a reaction in largely aqueous ($N_{H_2O} = 0.7$, $N_{CH_3OH} = 0.3$) solution.[3]



I

Intramolecular nucleophilic attack by the succinate carboxylate group at the ester carbonyl carbon atom in I followed by bond rearrangement should lead to the formation of succinic anhydride. Strong evidence that this reaction occurred has been obtained by the chromatographic isolation of succinanilic acid following addition of aniline to a reaction mixture at pH 7.85 (phosphate buffer) at a time when it was calculated that all of I has been hydrolyzed to hexachlorophene. The yield of succinanilic acid obtained in this way was 17% of the succinyl function present. A control experiment using succinic anhydride instead of I yielded 13% of the anhydride in the form of succinanilic acid. The remaining 87% probably was lost in the hydrolysis of the anhydride and in the formation of succinyl phosphate.[4] These results strongly indicated that the reaction proceeded exclusively *via* intramolecular nucleophilic catalysis.

Evidence for additional intramolecular general acid catalysis of this reaction comes from the pH–rate profile for the hydrolysis of I in 50% aqueous methanol at 25° shown in Figure 1. The bell-shaped curve with a maximum around pH 6.8[5] indicated that the monoanion of I is much more unstable with respect to hydrolysis than either the neutral molecule or the dianion. In 50% aqueous methanol, hexachlorophene monosuccinate is estimated to have pK_a values of 5.20 and 8.14 for the carboxylic and phenolic groups, respectively.

This pH–rate profile could be accounted for either on the basis that the phenolic proton in the monoanion of I acts as an intramolecular general acid catalyst by hydrogen bonding with an oxygen atom at the reaction center in a transition state such as II or that the negatively charged oxygen atom in the dianion of I exerts an electrostatic inhibition on the reaction. Although this second possibility cannot be ruled out, we believe

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(1) (a) H. Morawetz and J. Oreskes, *J. Amer. Chem. Soc.*, **80**, 2591 (1958); (b) H. Morawetz and J. Shafer, *ibid.*, **84**, 3783 (1962).

(2) F. L. Killian and M. L. Bender, *Tetrahedron Lett.*, 1255 (1969).

(3) (a) S. M. Kupchan, S. P. Eriksen, and M. Friedman, *J. Amer. Chem. Soc.*, **88**, 343 (1966); (b) S. M. Kupchan, S. P. Eriksen, and Y. T. S. Liang, *ibid.*, **88**, 347 (1966).

(4) T. Higuchi, G. L. Flynn, and A. C. Shah, *ibid.*, **89**, 616 (1967).

(5) Between pH 5.6 and 8, the reaction is too fast to be accurately measured. The optimal pH for the reaction is therefore obtained from extrapolation.

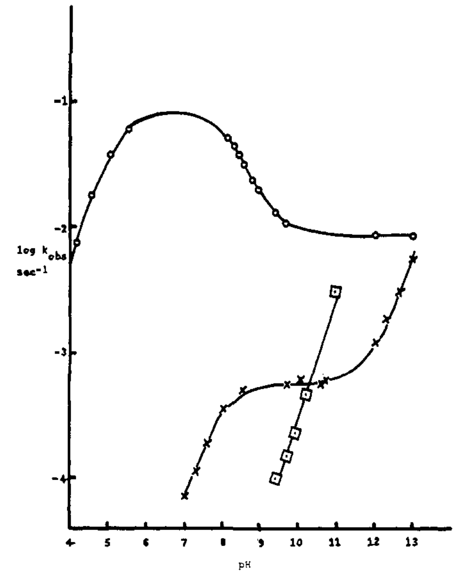
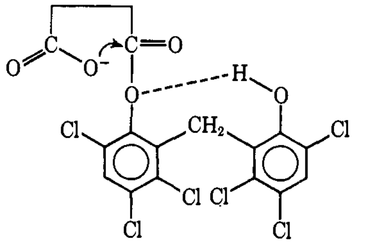


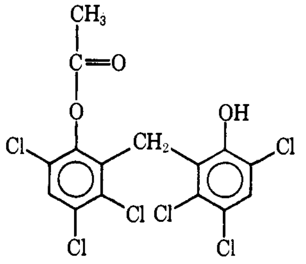
Figure 1. pH-rate profile for hexachlorophene monoacetate (×), diacetate (⊡), and monosuccinate (○).

that considerations based on the pK_a values of the reactant (monoanion of I, pK_a 8.14) and product (monoanion of hexachlorophene, pK_a 11.54) suggest that an intramolecular hydrogen bond such as that in structure II is formed during the reaction and leads to general acid catalysis.[6] The absence of strong intramolecular hydrogen bonding in the reactant is indicated by the similarity of its pK_a value to that of *O*-methylhexachlorophene (pK_a 8.22) in which the substituted phenolic oxygen would be considerably more basic. By comparison, the high value of the pK_a value of the product as well as its low basisity (pK_B 8.54) suggest that its acidic proton is strongly intramolecularly hydrogen bonded in a cyclic structure such as in II.

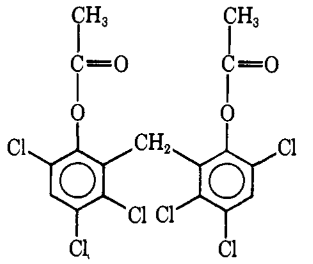


II

Further kinetic evidence for the formation of such an eight-membered ring is obtained when the pH-rate profiles of the monoacetate ester (III) and diacetate ester (IV) of hexachlorophene are examined[7] (Figure 1). On statistical grounds, the conversion of the diacetate to monoacetate would be expected to be twice as fast as that of the monoacetate to hexachlorophene, if the same mechanisms of hydrolysis occurred. However, it is evident from Figure 1 that below pH 8, the monoacetate undergoes hydrolysis at much greater rate, approximately 500 times faster. The facilitated hydrolysis of III can be explained by the two possible isokinetic mechanisms, V and VI, both of which involve the formation of an eight-membered ring in the transition state.

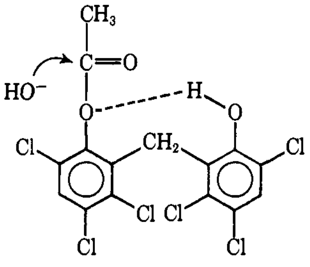


III

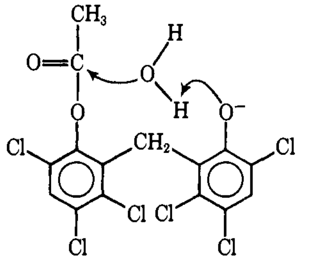


IV

Thus, the 500-fold enhancement of rate of hydrolysis, below pH 8, of the monoacetate over that of the diacetate represents an intramolecular general acid monofunctional facilitation, whereas the approximately 3 × 10^4-fold increase in rate of hydrolysis of the monosuccinate over that of the monoacetate, below pH 5, represents additional intramolecular nucleophilic monofunctional facilitation. The approximately 1.5 × 10^7-fold increase in hydrolysis rate of the monosuccinate over that of the diacetate, therefore, represents an intramolecular bifunctional facilitation in the monosuccinate.



V



VI

Acknowledgment. This work was supported in part by Vick Divisions Research and Development, Richardson-Merrell, Inc.

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Received May 22, 1970

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[6] A referee suggested that the extent of intramolecular general acid catalysis in this reaction may be better appreciated if rates of hydrolysis of the succinate of *O*-methylhexachlorophene were known. Unfortunately repeated attempts to synthesize this compound were unsuccessful.

[7] T. Higuchi and H. Takechi, to be published.

Low-Temperature Photochemistry of *p*-Diazidobenzene and 4,4′-Diazidoazobenzene

Sir:

Recent esr studies by Trozzolo, *et al.*,[1] have shown that photolysis of *p*-diazidobenzene (I) in rigid matrices at 77°K produces a triplet ground-state species A with absorptions at 1578, 2500, 2852, 3566, and 3972 G which may be described by the spin Hamiltonian

$$H = g\beta HS + DS_z^2 + E(S_x^2 - S_y^2)$$

with $|D| = 0.067\ \text{cm}^{-1}$ and $E \approx 0$. On the basis of the close similarity of its esr spectrum and the

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[1] A. M. Trozzolo, R. W. Murray, G. Smolinsky, W. A. Yager, and E. Wasserman, *J. Amer. Chem. Soc.*, **85**, 2526 (1963).