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A NEW INTERPRETATION OF THE KINETICS OF THE REACTION BETWEEN CARBOXYLIC ACIDS AND DIAZODIPHENYLMETHANE IN TOLUENE.

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The reaction between diazodiphenylmethane and carboxylic acids in ethanol or other alcohols as solvent has been much studied (see references 2 to 14 in reference (1) of this note and references 2 to 8) and the main features of the mechanism have now been established (1,2). The rate-limiting step involves the transfer of a proton from the carboxylic acid to diazodiphenylmethane, thus forming an ion-pair.

The reaction, in non-hydroxylic solvents, most commonly toluene (see reference (2) and references therein) has also been studied (9). Until recently, however, (2) little attention has been paid to the mechanism of the reaction in toluene and in particular to the possible roles of carboxylic acid monomer and dimer, although the reaction between diazodiphenylmethane and carboxylic acids, in benzene and similar solvents, is known not to be of integral order with respect to acid (10). Hoefelmeyer and Hancock (11) nevertheless applied a rate expression to the reaction in toluene in which the order with respect to acid was assumed to be unity. Bowden, Chapman, and Shorter (9) found that the second-order rate coefficients for the reactions of various arylaliphatic carboxylic acids with diazodiphenylmethane in toluene varied with initial concentration of acid, but found a good linear free-energy relationship between the results obtained with toluene as solvent (the acids being at a standard concentration) and those obtained with 2-butoxyethanol as solvent, where the complication of dimerisation does not arise. They argued in favour of the dimer as the reactive species at the acid concentration used (0.03*M*).

The observed rate coefficient for the reaction of a carboxylic acid with diazodiphenylmethane in toluene usually increases with increase in the concentration of the acid (2): this is most easily explained by supposing that the dimer is more reactive than the monomer. The supposed high reactivity of the dimer would also explain the surprisingly high rate coefficients for the reactions of carboxylic acids with diazodiphenylmethane in toluene. For a series of solvents in which dimerisation of carboxylic acids does not occur, the rate coefficient decreases as the polarity of the medium falls. Thus the reaction is very slow in a medium of low dielectric constant such as dioxan (ε = 2.2) (12, 13). However the reactivity in toluene (ε = 2.4) is comparable with the reactivity in ethanol. O'Ferrall, Kwok, and Miller (2), and Buckley (13), account for the enhanced reactivity of dimer relative to monomer in terms of the dimer providing a 'built-in' solvation of the transition state.

The situation is, however, more complicated that the above discussion implies. At very low concentrations of acid the rate coefficient does not fall off as rapidly as implied by dimer being much more reactive than monomer, and at high concentrations the rate coefficient continues to rise beyond the concentration at which the acid should effectively be entirely dimeric (2). O'Ferrall, Kwok, and Miller (2) interpret these facts in terms of a 'substantial medium effect in toluene'. Further, we point out that kinetic orders considerably greater than unity with respect to acid characterise a number of reactions of carboxylic acids in aprotic solvents (14, 15, 16), and this has usually been interpreted in terms of 'acid catalysis', with the monomer more reactive than the dimer.

We now put forward tentatively a re-interpretation of the reaction between diazodiphenylmethane and carboxylic acids in toluene, on the basis of what has previously been observed and suggested for related systems (14, 15, 16). There is one important feature of the reaction which O'Ferrall, Kwok, and Miller (2) could not explain, *viz*,, for the reaction of diazodiphenylmethane with $Ph.CO_2D$ in toluene, the observed second-order rate coefficient *falls* with increase in the concentration of carboxylic acid (2). This observation has recently been confirmed by Mr. M.R.J. Dack in our laboratory. The difference in the behaviour of the protio- and deuterio-acid in this respect may be explained by supposing that (*a*) increase in concentration leads to the replacement of *highly reactive* monomer by *less reactive* dimer, and (b) acid-catalysis of the type observed for related systems becomes more pronounced as the concentration of the acid is increased. The first of these factors will tend to decrease the observed second-order rate coefficient as the concentration of the acid is increased, and the second will produce the opposite effect. We suggest that factor (*b*) is dominant for the protio-acid and factor (*a*) for the deuterio-acid. These ideas are now elaborated quantitatively.

We suggest that the following processes occur:

$$A_2 \overset{K}{\rightleftharpoons} 2A \qquad \text{......(i)}$$

$$A + B \overset{K'}{\rightleftharpoons} AB \qquad \text{.....(ii)}$$

$$AB \xrightarrow{k_1} P \qquad \text{....(iii)}$$

$$AB + A \xrightarrow{k_2} P + A \qquad \text{.....(iv)}$$

$$AB + A_2 \xrightarrow{k_3} P + A_2 \qquad \text{......(v)}$$

A represents monomeric acid, A_2 the dimer, B diazodiphenylmethane, and P the products (ester and nitrogen). The reversible dissociation of the dimer [(i)] has the equilibrium constant K, and we assume $K = [A]^2/[A_2]$. (In this discussion it is assumed that we are dealing with ideal solutions and therefore concentrations rather than activities may legitimately be used. This assumption is unlikely to be strictly correct but unless it is made no progress is possible.) Diazodiphenylmethane is considered to react reversibly with monomeric acid [(ii)] to form an intermediate complex AB (equilibrium constant K'). Reactions (iii), (iv), and (v) are the rate-limiting processes. Reaction (iii) is the uncatalysed breakdown of the intermediate complex; (iv) and (v) involve the breakdown of the complex catalysed by monomer and dimer respectively.

Treatment of the above reaction scheme by the method of stationary states involves the assumption that $[A] \sim \sqrt{Kc/2}$ and $[A_2] \sim c/2$, where c is the concentration of the acid in mole l.$^{-1}$, calculated as monomer. This assumption will not be valid at low concentrations where the dissociation of the dimer is considerable. The concentration of the intermediate complex is assumed to be small compared with those of monomer and diazodiphenylmethane. The observed second-order rate coefficient k (l.mole^{-1} min.$^{-1}$) is given by the following expression:

$$k = k_1K'\sqrt{K/2c} + k_2K'K/2 + k_3K'\sqrt{Kc/8} \qquad \ldots\ldots\ldots\ldots(1)$$

This expression is conveniently used in the form:

$$k\sqrt{c} = k_1K'\sqrt{K/2} + k_2K'K\sqrt{c/4} + k_3K'c\sqrt{K/8} \qquad \ldots\ldots\ldots\ldots(2)$$

We have tested expression (2) by using the results of O'Ferrall, Kwok, and Miller (2) for protio- and deuterio-benzoic acid at 26.9° and 35.5° in a multiple correlation (17) of $k\sqrt{c}$ with $\sqrt{c}$ and c, i.e. we have examined the validity of an expression of the form:

$$k\sqrt{c} = \alpha + \beta\sqrt{c} + \gamma c \qquad \ldots\ldots\ldots\ldots(3)$$

where α, β, and γ are constants.

In three of the four cases examined expression (3) gives a correlation coefficient greater than 0.999; in the fourth case (deuterio-benzoic acid at 26.9°) the correlation coefficient is 0.969. The experimental results involved in the latter show irregularities: when $k\sqrt{c}$ is plotted against c there is a wide scatter of points, whereas the experimental results in the three other cases conform closely to a smooth curve.

The ratio of the values of β (corresponding to $k_2K'K/2$) as between protio- and deuterio-acid at a given temperature is about 4. This may well reflect largely the isotope effect on the rate of the monomer-catalysed decomposition of the intermediate, (iv). The ratio for γ (corresponding to $k_3K'\sqrt{K/8}$) is about 3.5 at 35.5° and this is probably due mainly to the isotope effect in the dimer-catalysed step (v). Unfortunately the limitations of the results for deuteriobenzoic acid at 26.9° have the effect of imparting a small *negative* value to γ.

The value of α (the constant term in (3), corresponding to $k_1K'\sqrt{K/2}$)is seriously affected by the assumption that $[A] \sim \sqrt{Kc/2}$ and $[A_2] \sim c/2$ (see above). This will hold only very approximately at the lower concentrations employed by O'Ferrall, Kwok and Miller (2). This limitation of our treatment leads to α having a small negative value for protio-benzoic acid, both at 26.9° and at 35.5°. For deuterio-benzoic acid the value of α remains positive, and this seems likely to be due to $k_1K'\ \sqrt{K/2}$ having a larger value for deuterio-benzoic than for protio-benzoic acid. This implies that in the formation and uncatalysed decomposition of the intermediate AB, the proton transfer occurs in the non-rate-limiting formation, the equilibrium constant K' being greater for deuterio- than for protio-benzoic acid, and k_1 being insensitive to isotopic substitution.

The intervention of a reactive complex was suggested by Hartman, Hochanadel, and Bobalek (15) for the reaction of ethyl diazoacetate with halogenoacetic acids in aprotic solvents. The occurrence of processes in addition to those suggested in (i) to (v) is not excluded. For instance the formation of a complex between dimer and diazodiphenylmethane A_2B, and its subsequent uncatalysed or catalysed decomposition would lead to the appearance of further terms involving $\sqrt{c}$ and c, and a new term in $c^{3/2}$ in expression (2). The results at our disposal do not appear to require a term in $c^{3/2}$ for their correlation, but it is possible that β and γ have a more complex significance than in the analysis we have given.

Encouraged by the limited success of the above treatment we have begun further work on the isotope effect in the reaction of diazodiphenylmethane with carboxylic acids in toluene and other aprotic solvents. On the basis of a much greater body of results than is at present available we shall give a detailed account of the reaction mechanism which involves less assumptions and limitations than that given above, but a tentative statement of our present views is now appropriate. O'Ferrall, Kwok, and Miller's paper (2) appeared in 1964, and our views on the mechanism date in part from 1965 (18). Publications using the reaction in toluene as a means of investigating the relationship between structure and reactivity continue to appear (19, 20).

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