Kinetic and Thermodynamic Study of the Acid-Catalysed Hydrolysis of Diethylmalonate in Dioxane-Water Mixtures

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A kinetic study of the acid-hydrolysis of diethylmalonate in water and dioxane-water mixtures covering the range 0–95% (w/w) of dioxane is reported. The reaction rate is inversely proportional to the organic content of the medium up to about 80% (w/w) then, after passing through a minimum, it becomes directly proportional as the dioxane cosolvent is further added. The kinetic ratio k_1/k_2 is independent of the solvent composition. The observed activation energies, thermodynamic parameters and radii of the activated complexes along the whole range of solvent composition, for the two consecutive steps of the reaction, are computed. Electrostatic theories favour an interaction in which an ion and a molecular dipole are involved. Application of the reactivity-selectivity principle (RSP) to the present reaction in comparison with that for diethylsuccinate, under different conditions of temperature and solvent composition, is presented.

Introduction

While extensive studies of the kinetics and solvent effects in the hydrolysis of esters in general have been reported, the dicarboxylic ester hydrolyses, specially the acid-catalysed ones are little explored in literature. The scarce systems that were investigated used either pure water or an aqua-organic solvent mixture of one composition only [1–5]. In order to gather more information about the mechanism of the acid-catalysed hydrolysis of dicarboxylic esters as well as to test the various theories [6–8] pertaining to the reaction in aqua-organic binaries, the system diethylmalonate in acidic dioxane-water mixtures was chosen for study. The influence of solvent variation on the reaction rate may be examined in terms of changes in thermodynamic activation parameters with the dielectric constant of the medium, which displays large variations with solvent composition. Moreover, a comparison of the present system with that of diethylsuccinate is made on the basis of the reactivity-selectivity principle (RSP) [9, 10] in the whole range of temperature and solvent composition.

Experimental

Materials

Diethylmalonate (B. D. H.) was distilled before using; b. p. 199.3 °C at 760 mm pressure, its purity was detected by gas chromatography, IR (film): 3000, 1750 (C=O), 1350 and 1040 cm^{-1}; UV (CH_3OH): $\lambda_{\max} = 235$ nm $\log \varepsilon = 50$; ^{1}H-NMR ($CDCl_3$): $\delta = 1.0$ (t, 6H, CH_3, $J = 7.0$ Hz), 3.1 (s, 2H, CH_2), 3.95 (q, 4H, CH_2, $J = 7.0$ Hz).

1,4-Dioxane was purified using standard methods [11, 12]. The water used in the preparation of solutions and in the kinetic runs was distilled freshly from alkaline potassium permanganate. The screened indicator used in the titration technique was prepared by mixing equal volumes of 0.1% solution of methylene blue and neutral red in absolute ethanol [5].

Kinetic Procedure

Appropriate amounts of diethylmalonate (0.02 M) were mixed with hydrochloric acid solution (0.05 M) in a series of dioxane-water mixtures within the composition range 0–95% (w/w). The acid produced during the course of the reaction was titrated against standard sodium hydroxide using the indicator mentioned above. The volumes of the titres at completion of the reaction were determined by heating aliquots in sealed ampoules at 80 °C till constant reading, consistent in most cases with the calculated value, was obtained.

Results and Calculations

The acid-catalysed hydrolysis of diethylmalonate followed a consecutive first-order kinetics of the type $A \xrightarrow{k_1} B \xrightarrow{k_2} C$ to about 80% completion. The

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specific rate constants k_1 and k_2 corresponding to the two steps of the reaction were determined using the time ratio method developed by Frost and Pearson [13] and based on the earlier method of Swain [14]. The values of k_1 and k_2 and the kinetic ratio k_1/k_2 for different solvent compositions are collected in Table 1 at the indicated temperatures.

A statistical treatment of the Arrhenius equation using the least-squares method [15] led to nearly constant values for the activation energies E_1 and E_2 (76–80 kJ mol^{-1}), based on k_1 and k_2, respectively, for different solvent media. The correlation coefficients (r) of the linear plots of the Arrhenius equation are almost equal to unity.

The entropies, enthalpies and free energies of activation, $\Delta S^{\neq}$, $\Delta H^{\neq}$ and $\Delta G^{\neq}$, respectively, were obtained from the expressions [16, 17]

$$\log k/T = 10.3187 + \frac{\Delta S^{\neq}}{19.147} - \frac{\Delta H^{\neq}}{19.147\,T},$$

$$\Delta G^{\neq} = \Delta H^{\neq} - T\,\Delta S^{\neq}$$

with the rate constants k in s^{-1}. These thermodynamic parameters, calculated at 35 °C, are collected in Table 2.

Discussion

Figure 1 shows a plot of the rate constants k_1 and k_2 against the weight percentages of dioxane. The rates of the two steps decrease until they reach a minimum at about 80% dioxane (w/w) and then increase again. This minimum is due to the maximum in the acidity function of the mixed solvent near this composition [18–20], where the catalytic effect of the medium on both sides of the minimum

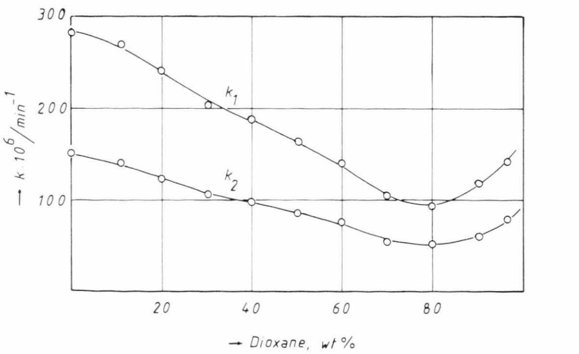

Fig. 1. Variation of the specific reaction rates with dioxane content of the medium at 35 °C.

Table 1. Rate constants k_1, k_2 and the kinetic factor k_1/k_2 for the consecutive acid-catalysed hydrolysis of diethylmalonate in dioxane-water mixtures.

t [°C]	$k \cdot 10^6$ [min^{-1}]	dioxane [wt%]									
		0.000	10.201	20.318	30.335	40.147	50.071	59.763	69.681	79.539	89.720	94.673
35	k_1	285.1	271.5	241.3	203.4	190.4	163.8	143.9	105.5	96.9	117.7	146.8
	k_2	149.4	142.4	126.6	107.2	99.6	85.9	75.5	55.4	50.8	61.8	77.0
	k_1/k_2	1.908	1.906	1.906	1.897	1.991	1.906	1.906	1.904	1.907	1.904	1.906
45	k_1	745.6	710.7	613.8	519.3	473.2	462.8	363.4	276.7	253.9	306.3	377.9
	k_2	389.9	376.8	322.3	272.8	248.5	242.5	188.6	135.2	133.0	160.5	198.0
	k_1/k_2	1.912	1.886	1.904	1.904	1.904	1.908	1.926	1.906	1.908	1.908	1.908
55	k_1	1820.1	1641.3	1462.1	1236.1	1086.1	962.7	871.0	692.0	619.3	731.8	874.4
	k_2	947.9	860.6	767.9	642.8	569.5	504.8	456.7	362.8	324.7	382.7	458.5
	k_1/k_2	1.920	1.907	1.904	1.923	1.907	1.907	1.907	1.907	1.907	1.912	1.907
65	k_1	3389.2	3160.7	2977.0	2342.2	2026.1	1784.5	1680.9	1372.2	1212.5	1444.1	1696.0
	k_2	1787.1	1659.4	1540.9	1213.9	1052.1	929.0	882.4	732.3	636.6	758.6	879.2
	k_1/k_2	1.896	1.904	1.932	1.929	1.925	1.920	1.904	1.876	1.904	1.903	1.929
E_1 [kJ mol^{-1}]		76.90 ± 0.01	75.73 ± 2.41	80.92 ± 4.32	75.71 ± 0.50	73.18 ± 0.87	73.08 ± 1.10	76.13 ± 1.02	79.51 ± 1.11	78.65 ± 1.41	77.44 ± 1.69	75.50 ± 2.05
E_2 [kJ mol^{-1}]		76.99 ± 1.26	75.66 ± 3.15	80.58 ± 4.44	75.12 ± 0.99	72.98 ± 1.16	72.89 ± 1.10	76.23 ± 1.46	80.48 ± 2.70	78.26 ± 0.80	77.43 ± 1.93	75.20 ± 1.78

Table 2. Thermodynamic parameters of activation for the reaction at 35 °C.

Parameter	dioxane [wt%]										
	00.000	10.201	20.318	30.335	40.147	50.071	59.763	69.681	79.539	89.720	94.673
$\Delta G_1^{\ddagger}$ [kJ mol^{-1}]	106.97	107.09	107.70	110.09	107.96	108.39	108.72	109.53	110.57	109.24	108.69
$\Delta H_1^{\ddagger}$ [kJ mol^{-1}]	74.34	73.17	78.36	75.40	70.62	70.52	73.57	76.95	76.09	74.88	72.94
$-\Delta S_1^{\ddagger}$ [J mol^{-1} deg^{-1}]	105.91	110.11	95.24	112.58	121.18	122.91	114.09	105.70	111.92	111.51	116.01
$\Delta G_2^{\ddagger}$ [kJ mol^{-1}]	108.63	108.75	109.36	109.48	109.67	110.05	110.38	111.17	111.39	110.89	110.33
$\Delta H_2^{\ddagger}$ [kJ mol^{-1}]	74.43	73.09	78.02	73.15	70.42	70.33	73.67	77.92	75.70	74.87	72.64
$-\Delta S^{\ddagger}$ [J mol^{-1} deg^{-1}]	110.99	115.70	101.70	117.90	127.37	128.89	119.13	107.91	115.84	116.90	123.31

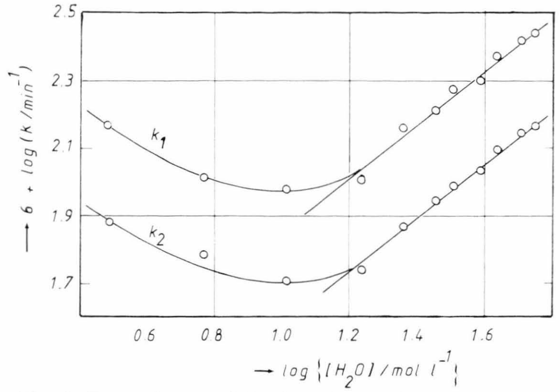

Fig. 2. Dependence of the logarithm of the specific reaction rates on the water concentration at 35 °C.

is different. The value of the ratio k_1/k_2 (Table 1) is almost equal to 2.0, which is expected from the statistical calculations of symmetric dicarboxylic esters [2, 5]. However, it is to be noted that this is not always the case, as exemplified by the ditert.-butyl dicarboxylic esters* which have lower values of k_1/k_2.

The activation energies E_1 and E_2 lie within the range characteristic for most esters hydrolysing via A_{Ac^2} mechanism. The independence of these energies of activation on solvent composition can be rationalised if one assumes that the solvent effects on both reactants and the transition state in each step of the reaction are more or less the same.

Figure 2 illustrates the dependence of the rate constants on water concentration, in which a linear relationship between log k and log [H_2O] is obtained at higher water concentrations above 30% (w/w). The slope of these linear portions is unity at all temperatures investigated, indicating that the rate is of first order with respect to water. This confirms the A_{Ac^2} mechanism, where one water molecule is involved in the transition state structure [21, 22]. Deviations from linearity observed in media of low water contents can well be attributed to the rapid increase in the acidity function of the reaction mixture in this range of composition [23].

Figure 3 represents the variation of the calculated concentrations of diethylmalonate, the half-ester ethylhydrogenmalonate and the produced malonic

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* Details on acid-catalysed hydrolysis of ditert.-butyl dicarboxylic esters in general will be dealt with in a subsequent communication.

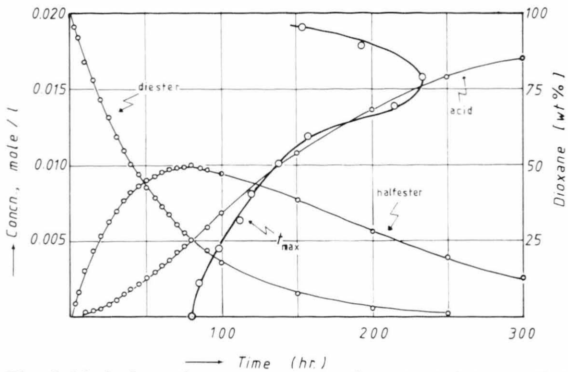

Fig. 3. Variation of concentrations of reactant, intermediate and product with time during the course of the reaction; and of t_{max} with dioxane content of the medium.

acid with time during the course of the reaction in a purely aqueous medium. The figure shows also the dependence of the time t_{max} at which the half-ester concentration is maximum, on the solvent composition. The general features of the figure confirm the picture expected for the acid hydrolysis of simple dicarboxylic esters, while the minimum in the t_{max} curve is consistent with the minimum exerted by k_1 and k_2 at 80% (w/w) dioxane.

It is worthy to mention here that the rate of the acid hydrolysis of diethylmalonate is slower than that of the diethylsuccinate [17] up to 80% (w/w) dioxane-water mixtures, while the reverse is true in media of higher dioxane contents. This may be due to a difference in the effect of preferential solvation (or solvent sorting) in both cases ($t_{max} = 4762$ and 3690 min in purely aqueous media, respectively). This observation indicates that the rate of the reaction depends on the distance between the two carbethoxy groups, such that the larger the distance the more facile the reaction is. This trend is reversed in the alkaline hydrolysis of dicarboxylic esters [1–3, 24], as will be seen later on when discussing the reactivity-selectivity principle (RSP).

The reaction rates of the two consecutive steps are enhanced with increase of the dielectric constant of the medium. The latter is taken or interpolated from the data of Åkerlof [25] for different solvent mixtures. Application of the electrostatic ion-molecular dipole interaction theory of Laidler and Landskroener [21], and also Heromi [26], to the present data gives a linear plot of log k_1 and log k_2 against $1/D$ in the high range of dielectric constant. The values of the radii of the activated complexes for the two steps, calculated using this theory, are 4.2 and 4.3 Å, respectively; they are in good agreement with those calculated before for other esters [27].

On the other hand, according to the Laidler-Eyring treatment [28] of molecular dipole-molecular dipole types of interaction, the plot of log k against $(D-1)/(2D+1)$ gave a relatively poor linear relationship and the linear portion is also confined to the higher D values only. These and other relationships, illustrating the variation of the rate with the dielectric constant [29–31], are represented in Fig. 4 for the two rate constants k_1 and k_2, from which it can be deduced that the reaction is an ion-molecular dipole rather than molecular dipole-molecular dipole interaction. Deviation from linearity at low dielectric constants is probably due to preferential solvation effects [31], in which the concentration of the potential nucleophile, the water

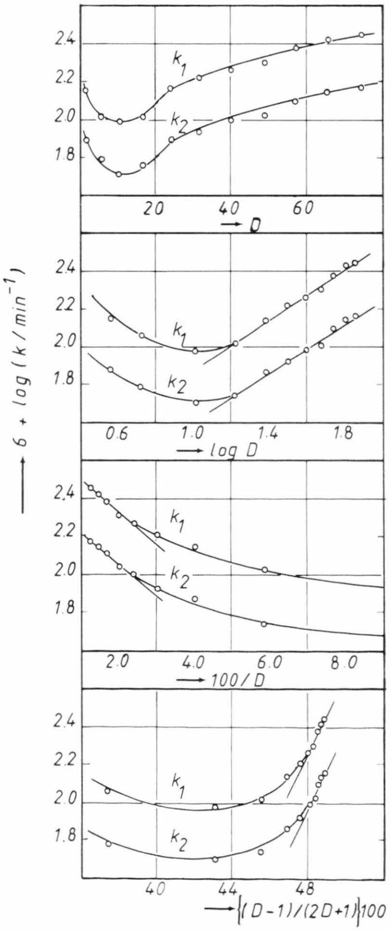

Fig. 4. Dependence of the rates of the two steps of the reaction on the dielectric constant of the medium.

molecules, around the transition state differs from that in the bulk of the solution.

The thermodynamic data of activation, i.e., the free energies $\Delta G^{\neq}$, the enthalpies $\Delta H^{\neq}$ and the entropies $\Delta S^{\neq}$ are calculated for the whole range of solvent composition and are compiled in Table 2. The values of $\Delta G_1^{\neq}$ and $\Delta G_2^{\neq}$ show in general a very slight increase as the dioxane content is increased, which is attributed to a large compensation between $\Delta H^{\neq}$ and $\Delta S^{\neq}$. The highly negative values of $\Delta S^{\neq}$ are in concordance with the A_{Ac2} mechanism involved [32–34]. These values show in general a slight non-linear lowering as the dioxane content of the solvent mixture increases, indicating the preferential solvation of the activated complex, and, consequently, the non-random distribution of the solvent molecules in the medium. Furthermore, $\Delta S_2^{\neq}$ has lower values than $\Delta S_1^{\neq}$ due to the higher polarity of the activated complex produced during the half-ester hydrolysis. The free carboxylic group of the half-ester renders the activated complex more fit to solvation through hydrogen bonding with water than the ester group.

The RSP is one of the most advanced tools to give information about the reaction mechanism [9, 10] and the effect of solvent on the transition states [35]. An explanation for the unexpected behaviour of diethylcarboxylic esters towards acid hydrolysis can be given using this principle. The rate of the acid hydrolysis of diethylmalonate should be greater than that of diethylsuccinate, since the carbethoxy group has an electron-withdrawing effect, thereby enhancing the rate of acid hydrolysis of the first step in the malonate more than in the succinate ester, as in the former the two carbethoxy groups are separated by one methylene group only, while in the latter by two. The second step is similar in both cases, since one carbethoxy group is now replaced by a carboxylic group. This can be visualized by comparing their properties; the IR spectra show a $\nu(C{=}O)$ for malonate and succinate of 1750 and 1760 cm^{-1}, respectively, the methylene group of succinate appears, in NMR spectra, at a higher field ($\delta = 2.5$) [17] than that of malonate ($\delta = 3.1$). Moreover, the first dissociation constant k_{a1} for malonic acid is 14×10^{-4} while that for succinic acid [36] is 0.641×10^{-4}. However, it was found experimentally in our present and previous [17] work that the specific rate constants k_1 and k_2 are larger for succinate than for malonate.

This can be rationalised on the basis of the first step of the reaction, which is the attack of the water molecule, as a nucleophile, on the carbonyl group of the oxonium ion (SH^+) of the ester. This step is definitely faster in the case of malonate than in succinate:

$$S + H^+ \overset{\text{fast}}{\rightleftharpoons} SH^+ ,$$

$$HS^+ + H_2O \xrightarrow{\text{slow}} S^{\neq} \rightarrow \text{products} .$$

The behaviour of the A_{Ac2} transition state ($S^{\neq}$) can be explained by postulating a structure which closely resembles the tetrahedral intermediate [37–39]. The bond between the acyl carbon and the oxygen of the attacking water is almost fully formed, and most of the positive charge residues on the incoming water molecule. These intermediates can be represented as:


(a) malonate ($Z_1 = CH_2CO_2Et$)
(b) succinate ($Z_2 = (CH_2)_2CO_2Et$)

It is obvious that the positive charge ($\delta+$) on the carbon of the carbonyl group, due to the electron-withdrawing effect of the carbethoxy group is greater for malonate than that ($\delta\delta+$) for succinate.

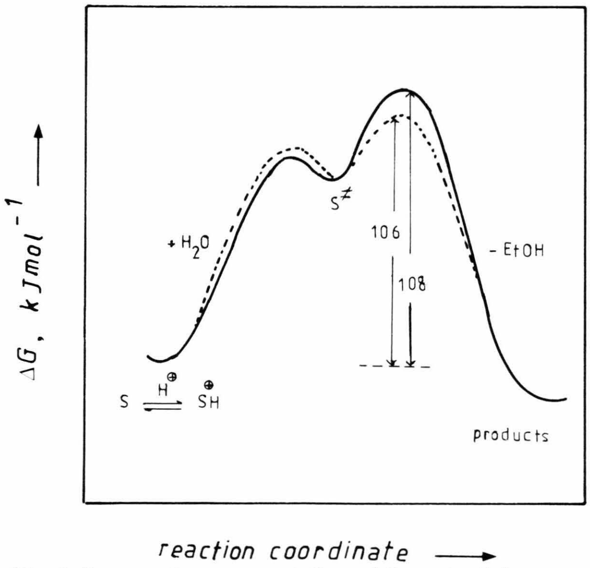

Fig. 5. Comparative representation of the potential energy profiles for the acid-catalysed hydrolyses of diethylmalonate (——) and succinate (…).

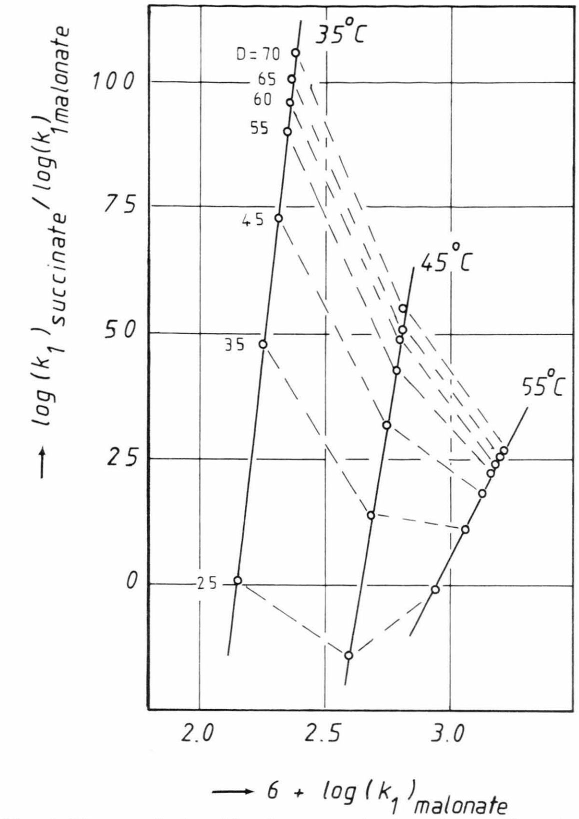

Fig. 6. Linear relationships between the logarithm of partition constant $(k_1)_{\text{succinate}}/(k_1)_{\text{malonate}}$ and the logarithm of $(k_1)_{\text{malonate}}$.

Since the ease of removal of the ethanol molecule from these intermediates is governed mainly by the magnitude of the positive charge existing on the carbonyl group, and is inversely proportional to the latter, the rate of this step will be slower for malonate than succinate. This will affect the overall rate of the reaction and the $\Delta G^{\ddagger}$ values as represented simply in Fig. 5, in which we assume that both intermediates ($S^{\ddagger}$) have the same potential energy value.

Generally, the value of $\Delta G^{\ddagger}$ is the sum of $\Delta G^{\ddagger}_{m}$ of bond making ($C-OH_2^+$) and $\Delta G^{\ddagger}$ of bond breaking ($C-\overset{+}{O}HEt$). According to the RSP, the ratio $\Delta G^{\ddagger}_{m}/\Delta G^{\ddagger}_{b}$ must be constant [9]. If this ratio is variable an anti-RSP relationship is expected, i.e., the reactivity will be directly proportional to the selectivity, and the reaction is still obeying the Hammond postulate [40]. This relationship is represented graphically in Fig. 6 for different dielectric constants and different temperatures. Inspection of this Figure reveals that the selectivity decreases with increasing temperature, but increases at higher temperatures for water-rich media. The slope m of the linear equation:

$$\log (k_1)_{\text{succinate}}/(k_1)_{\text{malonate}} = n + m \log (k_1)_{\text{malonate}}$$

varies with temperature from 0.45 at 35 °C to 0.11 at 55 °C, and the correlation coefficient is nearly unity at all temperatures investigated.

It can be concluded, therefore, that in acid-catalysed hydrolysis of dicarboxylic esters via the A_{Ac^2} mechanism, the bond-making ($C-\overset{+}{O}H_2$) between the carbonyl carbon atom and the oxygen of the incoming water becomes more intensive than the bond-breaking ($C-\overset{+}{O}HEt$), involving the removal of the ethanol molecule, on going from malonate to succinate. These observations can likewise be extended to gluterate and adipate.

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