

Kinetics of the Hydrolysis and Formation of Dimethylmaleic Anhydride in Solvent Mixtures

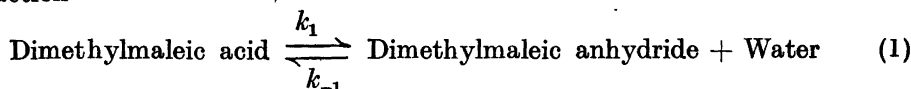
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In a study of the rate of attainment of the equilibrium between dimethylmaleic anhydride and the acid in various acetone-water mixtures it has been established that the molecularity with respect to water is about three for the hydrolysis of the anhydride and about two for the reverse reaction. The rate of anhydride formation from dimethyl maleic acid has been investigated also in non-aqueous solvents as in acetone, dioxan and various diethyl ether-benzene mixtures. In benzene the rate was more than a thousand times as fast as in pure ether. The reaction was kinetically of second order and the rate constant was found to vary approximately as $1/c_{\text{ox}}^2$, where c_{ox} is the molar concentration of the solvent component which contains oxygen. The value of the rate constant obtained in dioxan fulfils the same relation fairly well if c_{ox} is taken to be equal to half the molar concentration of dioxan.

The activation energy for the hydrolysis reaction 13.4 kcal in 50 vol. % acetone-water is smaller than that for the reverse reaction, 16 kcal, and the hydrolysis reaction is exothermic by 2.6 kcal. The entropies of activation are for the hydrolysis -30.2 cal/degree and for the anhydride formation -18.7 cal/degree. These large differences in the entropies more than counterbalances the difference in the activation energies, and hence the rate of hydrolysis is smaller than the rate of the reverse reaction, and the equilibrium lies more on the side of the anhydride.

In a previous paper¹ are given data of the equilibrium constant for the reaction



in various acetone-water mixtures. The composition of the solvent was found to influence the equilibrium only slightly. On the other hand, previous work² had shown that the rates of hydrolysis of acetic, succinic, and glutaric anhydrides decrease considerably when acetone is added to water. For com-

parison, kinetic measurements on the formation and hydrolysis of dimethylmaleic anhydride have been performed in acetone-water and diethyl ether-benzene mixtures and in dioxan.

EXPERIMENTAL

The dimethylmaleic anhydride was prepared as described previously¹. The disodium-salt of dimethylmaleic acid was obtained by shaking a concentrated acetone solution of the anhydride with an approximately 20 % aqueous sodium hydroxide solution. The precipitated salt was washed with acetone and dried *in vacuo*.

For the kinetic experiments, a weighed quantity of the disodium salt was dissolved in a small volume of water, the solution cooled to 0°, and slightly less than the calculated amount of 30 % hydrochloric acid added. The liberated dimethylmaleic acid was dissolved in a small volume of one of the solvent components used in the kinetic experiments. After shaking with anhydrous sodium sulphate, the nearly anhydrous solution was warmed to 20° and pipetted to the solvent mixture previously tempered to 20° to make the mixture desired. The disadvantage of the method was that, in spite of the drying with sodium sulphate, small amounts of water were still present in the reaction mixture (especially when acetone and dioxan were used). Experiments made with diethyl ether saturated with water showed an about 5 % increase in the rate at 60° as compared with experiments made in previously dried ether solution. The values of the rate constants given in Table 5 are therefore probably all higher than the values for the corresponding dry solvents, but in no case more than about 1–2 %.

In all the organic solvents and their mixtures the conversion of dimethylmaleic acid into anhydride went to completion. Samples were titrated with 0.05 N sodium methylate, the consumption of which decreases as the acid is converted into anhydride because the anhydride consumes only one equivalent of methylate (anhydride + MeONa → mono-ester salt), whereas the acid consumes two equivalents. When titrated with baryta, both the acid and the anhydride consume two equivalents of base, and at the end of the reaction the consumption should be twice the methylate value if the reaction goes to completion. This was found to be the case in the dry organic solvents. Second-order kinetics were obeyed, and the rate constants were calculated from the following equation

$$k_2 = \frac{100}{at} \left(\frac{1}{100-p} - \frac{1}{100} \right) \quad (2)$$

where a is the initial concentration of the acid, t time in seconds and p the percentage of the acid changed into anhydride. Table 1 shows an example of a typical kinetic run.

In water, the hydrolysis of dimethylmaleic anhydride was followed conductometrically. In order to calculate the concentration of the acid, the conductances of the acid at various dilutions had to be measured separately. In aqueous solution the anhydride is

Table 1. Conversion of dimethylmaleic acid into anhydride in diethyl ether solution at 20°.

Time in seconds	Canhydride mole/l	Acid mole/l	% reacted	$10^3 \times k_2$ l · mole ⁻¹ sec ⁻¹
0	0.0254	0.0309	0	
6 060	0.0318	0.0245	20.7	1.40
9 120	0.0344	0.0219	29.1	1.46
13 680	0.0370	0.0193	37.5	1.42
25 020	0.0414	0.0149	51.8	1.39
70 200	0.0488	0.0075	75.7	1.43
96 780	0.0504	0.0059	80.9	1.37

Table 2. Hydrolysis of dimethylmaleic anhydride in water at 0°.

Conductance data		Kinetic experiment				
$10^4 \times c_{\text{acid}}$ mole/l	$10^4 \times 1/R$ ohm ⁻¹	Time in sec.	$10^4 \times 1/R$ ohm ⁻¹	$10^4 \times c_{\text{acid}}$ mole/l	% reacted	$10^4 \times (k_1 + k_{-1})$ sec ⁻¹
19.8	16.62	0	7.24	7.1	0	
14.9	13.40	61	8.52	8.5	9.4	16.2
9.9	9.71	92	9.23	9.3	14.8	17.5
3.96	4.33	137	10.00	10.2	20.8	17.0
2.97	3.14	192	10.83	11.3	28.2	17.0
1.98	2.09	261	11.74	12.3	34.9	16.6
		351	12.73	13.8	45.0	17.0
		477	13.81	15.3	55.0	16.7
		688	15.00	17.3	68.5	17.3
		7 200	17.62	22.0	100	

in equilibrium with the acid. This equilibrium is disturbed on dilution since the concentration of unionized acid is changed, and hence the values of conductances had to be extrapolated to zero mixing time. The conductances thus obtained are proportional to the acid concentrations, and the concentrations required in calculating the rate constants may be obtained with the aid of a graph. Because of the acid-anhydride equilibrium, rate constants were calculated using the following equations

$$k_1 + k_{-1} = \frac{2.303}{t} \log \frac{c_0 - c_{\text{eq}}}{c_t - c_{\text{eq}}} \quad (3)$$

$$K = \frac{k_1}{k_{-1}} = \frac{c_0 - c_{\text{eq}}}{c_{\text{eq}}} \quad (4)$$

where k_1 and k_{-1} are the first-order rate constants (see eqn. 1), t the time and c_0 , c_t , c_{eq} the concentrations of acid at the beginning of the experiment, at time t , and at equilibrium, respectively. The conductances of different dilutions of a stock solution con-

Table 3. Conversion of dimethylmaleic acid into anhydride in 90 % acetone-water at 20°. 5-ml samples were analysed by adding 5 ml of 0.0508 M MeONa and titrating with 0.0202 N HCl. A sample titrated with 0.0205 N baryta consumed 11.1 ml which corresponds to 0.0114 mequiv.

Time in min.	HCl 0.0202 N ml	An- hydride mequiv.	Acid mequiv.	% reacted	$10^5 \times k_1$ sec ⁻¹	$10^5 \times$ $(k_1 + k_{-1})$	$10^5 \times k_2$ l. mole ⁻¹ sec ⁻¹	$10^5 \times k_1$ sec ⁻¹ $\beta = 0.5$
0	1.90	0.012	0.102	0				
25	2.45	23	91	10.8	7.54	8.15	4.23	4.91
71	3.10	37	77	24.5	6.60	7.15	4.03	3.78
117	3.65	48	66	35.3	6.19	6.70	4.20	4.00
182	4.25	60	54	47.1	5.82	6.39	4.50	3.77
250	4.75	70	44	56.9	5.63	6.19	4.96	3.78
326	5.20	79	35	65.7	5.46	6.13	5.78	3.92
358	5.30	81	33	67.6	5.26	5.92	5.81	3.83
1 270	6.50	105	9	91.2	3.18	4.54	20.0	3.68
4 000		108	6	94				

taining 19.8×10^{-4} mole/l of acid and anhydride are given in Table 2. With aid of these values, using a graph, the conductances obtained in a kinetic run may be converted into concentrations, and values for the sum of rate constants are obtained. An example of a typical kinetic run is given in Table 2. The mean of the sum of rate constants is 16.9×10^{-4} sec $^{-1}$ and when the value $K = 2.6$ taken from the previous paper¹ is used, it is found that $k_{-1} = 12.2 \times 10^{-4}$ and $k_1 = 4.7 \times 10^{-4}$ sec $^{-1}$. As already mentioned the acid concentrations and conductances given in Table 2 are only values proportional to the true values. The constancy of the sum $k_1 + k_{-1}$ in this typical run indicates that first-order kinetics are well obeyed.

In the case of all acetone-water mixtures, the samples were analysed as in the previous work¹ by titrating with 0.05 N sodium methylate and 0.02 N baryta. The experimental data for acetone-water mixture containing 90 vol. % acetone were not found to fit either first-order or the second-order rate equation. The reaction does not proceed to completion and at equilibrium at 20° 95 % of acid has been converted into anhydride. In order to simplify the calculations, the reverse reaction was disregarded and the constants were calculated by assuming two reactions, one of first-order and one of second-order to occur simultaneously:

$$-\frac{dx}{dt} = k_1(a-x) + k_2(a-x)^2 \quad (5)$$

which gives on integration

$$k_1 = \frac{2.303}{t} \log \frac{a-\beta x}{a-x}; \beta = \frac{k_1 + ak_2}{ak_2} \quad (6)$$

where a is the initial acid concentration, x the reacted amount of acid, t time in seconds and β a constant.

Rate constants calculated in different ways, from the rate equation for an overall first-order reaction disregarding the equilibrium (Table 3, column 6), from the first-order rate equation taking into account the equilibrium (Table 3, column 7, eqn. 3), from the second-order rate equation disregarding the equilibrium (column 8, eqn. 2) and from the rate equation for simultaneous first-order and second-order reactions assuming the value 0.5 for β (column 9, eqn. 6). Only in this last case are fairly good constants obtained. In pure acetone, the reaction is solely of the second-order, and thus a transition from first-order into second-order kinetics occurs in the acetone-water mixture containing about 90 % acetone.

RESULTS AND DISCUSSION

The rate constants obtained are summarized in Tables 4 and 5. The hydrolysis of dimethylmaleic anhydride in aqueous solution is considerably slower than the hydrolysis of maleic anhydride², the respective first-order rate constants at 0° being 4.7×10^{-4} and 34.3×10^{-4} sec $^{-1}$, but somewhat faster than the hydrolysis of succinic anhydride² for which the first-order rate constant at 0° is 3.34×10^{-4} . The hydrolysis of maleic anhydride is only slightly faster than the hydrolysis of methylmaleic anhydride³: the rate constants at 25° are 26.6×10^{-4} and 17.6×10^{-4} sec $^{-1}$, respectively. These differences in the rates are in the direction predicted by steric and inductive effects⁶.

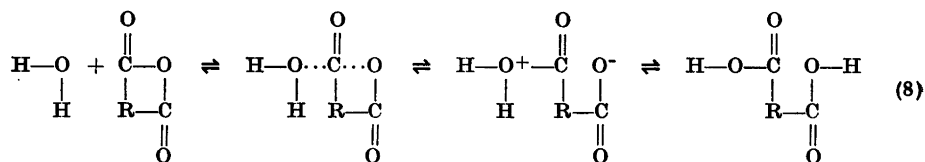
In acetone-water mixtures, the hydrolyses of all anhydrides studied previously² and the conversion of dimethylmaleic acid into anhydride are greatly retarded as the acetone content of the aqueous solvent is increased (Table 4). When $\log k$ is plotted against $\log c_{\text{H}_2\text{O}}$, fairly constant slopes are obtained for the cyclic anhydrides, but not for acetic anhydride² (Table 6). For succinic, glutaric and dimethylmaleic anhydrides, the slope is about three, while for acetic anhydride the slope decreases continuously from about four to one.

In 99.93 wt. % dioxan-water the hydrolysis of acetic anhydride is of the first-order with respect to water². The rate of conversion of dimethylmaleic acid into anhydride is approximately proportional to the second power of the water concentration, while the rate of hydrolysis varies as the third power of the water concentration. Similar solvent effects are found for reactions occurring by the S_N2 mechanism⁴.

It is interesting to note that the equilibrium constant

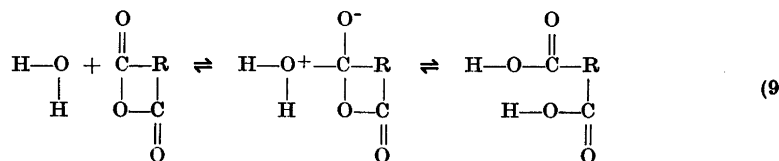
$$K = \frac{[\text{dimethylmaleic anhydride}] [\text{water}]}{[\text{dimethylmaleic acid}]} = \frac{k_1}{k_{-1}} \quad (7)$$

remains fairly constant in acetone-water mixtures, at least up to the 90 vol. % acetone-water mixture¹. Thus both k_1 and k_1/c_{H_2O} should decrease to about the same extent in acetone-water mixtures as is also obtained. Consequently the reactants and products should be similar, and in this case neutral molecules. The S_N2 mechanism usually written for the hydrolysis of anhydrides gives as the primary reaction products two ions of opposite charge which are formed from the anhydride and water^{6,2}. Thus the hydrolysis of the anhydride should be retarded when acetone is added to water, but the reverse reaction should simultaneously be greatly accelerated.



In this equation R denotes the group $\text{CH}_3\dot{\text{C}}=\dot{\text{C}}\text{CH}_3$, while for monocarboxylic acids and their anhydrides R denotes two alkyl groups, *e. g.* two methyl groups in the case of acetic anhydride.

A mechanism analogous to the Lowry mechanism for the ester hydrolysis would give better agreement with the solvent effects observed in the reversible hydrolysis of dimethylmaleic anhydride:



The main difference between these mechanism is that in eqn. (8) the proton shift does not occur simultaneously as the C—O bond is broken, whereas in eqn. (9) the proton shift occurs at the same time as the C—O bond is broken, *i. e.* in the rate-determining slow step. The addition of a water molecule to the carbonyl carbon involves a loosening of the O—H bonds in the water molecule, and it can be assumed that a kind of hydrogen bond is developed between one of the protons of the water and the "etheral oxygen" atom of the an-

Table 4. Conversion of dimethylmaleic acid into anhydride in acetone-water mixtures. The equilibrium values are from a previous paper¹.

H ₂ O vol. %	CH ₃ O mole/l	t°	10 ⁴ × k ₁ sec ⁻¹	10 ⁴ × k ₋₁ sec ⁻¹	10 ⁴ × k ₂ l · mole ⁻¹ sec ⁻¹	Equi- librium C _{anh} /C _{acid}
100	55.4	0	12.2	4.7		2.6
50	29.1	0	2.03	0.70		2.9
50		20	15.2	3.8		4.0
10	11.2	20	0.38	0.020	17.7	18
1		20			6.52	

hydride. The breaking of the C—O bond will thus occur more easily and the reaction products will not carry any charges. The acid formed may of course ionize later. About the transition state between reactants and products, it can only be said that it is more polar than either the reactants or products because both the hydrolysis and the reverse reaction are retarded in solvents of low ionizing power (acetone).

In acetone, diethyl ether and dioxan and their mixtures with benzene, dimethylmaleic acid is, as far as can be determined, spontaneously and completely changed into its anhydride, and it is not possible to measure the position of the equilibrium. The rate of reaction is slow in all solvents but benzene which, when added to ether, increases the rate more than a thousand times. The reaction is of second order with respect to the acid in all the nonaqueous solvents studied, but of first order with respect to the acid in acetone-water mixtures containing less than 90 vol. % acetone. The conversion of dimethylmaleic acid into anhydride is thus probably acid-catalysed in solvents containing no, or only small amounts of, hydroxylic solvents. The hydrolysis of succinic anhydride is catalysed by acids in acetone-water mixtures containing

Table 5. Conversion of dimethylmaleic acid into anhydride in acetone, dioxan and diethyl ether-benzene mixtures.

Solvent	Benzene	Cox. mole/l	10 ² × k ₂ l · mole ⁻¹ sec ⁻¹				E kcal.	log A
			0°	20°	40°	60°		
Ether-benzene	0	9.63	0.0180	0.141	0.82	4.35	16.49	9.44
	50	4.85	0.0566	0.386	0.232	1.09	16.17	9.67
	75	2.41		1.12				
	90	0.964		4.95	27.7		15.7	10.42
	95	0.482		16.05	66.3		12.9	8.85
	98.5	0.144		48.3	168		11.4	8.17
	99.6	0.0385		113	324		10.1	7.35
	99.9	0.0096		200				
Dioxan-benzene	0	23.5		0.0242				
	98.8	0.247		30.4				
Acetone	0	13.55		0.065				

Table 6. The order of the hydrolysis reaction with respect to water in acetone-water mixtures at 20°.

Acetone wt. %	Order of reaction with respect to water = $\Delta \log k / \Delta \log c_{H_2O}$				
	in hydrolysis of				conversion of DiMe-maleic acid into anhydride
	Acetic anhydride	Succinic anhydride	Glutaric anhydride	DiMe-maleic anhydride	
0 — 40		3.47			
0 — 43.9				2.46	2.32
0 — 50	4.04		3.12		
40 — 70		3.17			
43.9 — 87.8				3.04	2.18
50 — 70	3.06		3.12		
70 — 90	2.30	3.22	3.25		
90 — 99	1.40				

small amounts of water, as is also the case for the ethanolysis in ethanol-benzene mixtures containing small amounts of ethanol². The hydrolysis and alcoholysis of acetic anhydride was found to be slow in acetone, dioxan and ether, but fast in benzene². Thus the solvent effects are very similar to those found in the present study (Table 5).

In Fig. 1, $\log k_2$ (second order rate constant for the conversion of dimethyl-maleic acid into anhydride) is plotted against $\log c_{ox}$ the molar concentration of the oxygen-containing solvent component, (in the case of dioxan the molar concentration divided by two). A linear relationship is found in mixtures containing less than 90 % benzene. The values for the pure solvents acetone, ether and dioxan fit the same curve too, but in case of dioxan only when the molar concentration is divided by two in order to take into account the two oxygen atoms in the molecule. The slope of the linear part of the curve is slightly less than two. All these effects suggest that the reactant, the acid molecule, forms an addition product with the oxygen-containing solvent molecules by hydrogen bond formation⁵, which retards the rate of reaction:



$$c_{\text{free acid}} = K' \frac{c_{\text{add. prod.}}}{c_{\text{solvent}}} \quad (11)$$

$$-\frac{dc}{dt} = k_2 \cdot c_{\text{free acid}}^2 = k_2 K'^2 \frac{c_{\text{add. prod.}}^2}{c_{\text{solvent}}^2} \quad (12)$$

In solvent mixtures containing a high proportion of the oxygen-containing solvent the addition of solvent to acid molecules may be regarded as complete and $c_{\text{add. prod.}}$ equals the total acid concentration (in curve 1 the linear part up to 90 vol. % benzene). In pure benzene the association between acid molecules and the solvent can be neglected, and hence a limiting value will be obtained.

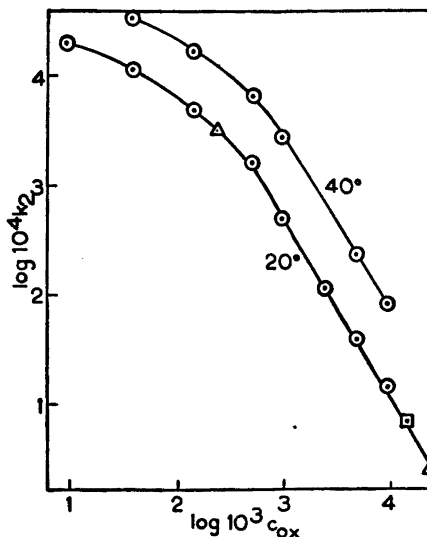


Fig. 1. Graphs showing the correlation between $\log k_2$ (the second-order rate constant of anhydride formation from dimethylmaleic acid) and $\log c_{ox}$ (the concentration of the oxygen-containing solvent component in moles per liter). Circles: diethyl ether-benzene mixtures; triangles: dioxan-benzene mixtures and square: pure acetone.

ned for the rate constant. According to eqn. (12), the rate constant k_2 should vary inversely as the square of the concentration of the oxygen-containing solvent component; this is approximate true for the different solvents studied.

The high activation energy found in ether (16.5 kcal, Table 5) is partly due to the heat of addition or to the variation of K' in eqn. (10) with temperature. The activation energy, 10.1 kcal, found in 99.6 vol % benzene-ether, should be fairly close to the true activation energy. The reaction mechanism for the acid catalysed hydrolysis and the reverse reaction can be written in the same manner as for the uncatalysed reaction (eqn. (9)) with the difference that an additional proton is attached to the "etheral oxygen" of the anhydride before reacting. That the reaction is not acid catalysed in hydroxylic solvents may be due to hydrogen bonding at the "etheral oxygen" of the anhydride which has a similar catalysing effect as a proton addition.

From the differences in the activation energies for the hydrolysis and the reverse reaction in 50 vol. % acetone-water (13.4 and 16 kcal, respectively, calculated from the values in Table 4) and also from the equilibrium data published previously¹, it is seen that the hydrolysis is an exothermic reaction. In spite of this, the anhydride form is favoured because of the greater effect of the entropy factor. The first-order frequency factors of the hydrolysis and the reverse reaction in the same solvent mixture are $\log A_{-1} = 6.61$ and $\log A_1 = 9.12$. The activation entropies calculated⁷ from frequency factors by means of the following eqn. (13)

$$A = e \frac{kT}{h} e^{\Delta S^*/R} \quad (13)$$

are $\Delta S_{-1} = -30.2$ and $\Delta S^*_{-1} = -18.7$ e.u. The hydrolysis reaction is probably bimolecular, and by writing $k_{-2} = k_{-1}/c_{H_2O}$ an even more negative value is obtained for the entropy of activation, *viz.* $\Delta S^*_{-2} = -37.4$ e.u. In the for-

mation of anhydride from dimethylmaleic acid, the entropy increases by 18.7 e.u., and therefore the equilibrium lies more on the side of the anhydride in spite of the fact that this reaction is endothermic. From the difference in the activation entropies, it can be deduced that the geometry of the transition state between reactants and products is closer to that of the acid than of the anhydride form. From the great differences between both ionization constants of maleic and methylmaleic acids and from other facts, it is deduced that the two carboxyl groups are situated close to each other. The additional methyl group in dimethylmaleic acid should still effect a decrease of the distance between carboxyl groups. The high rate of conversion of dimethylmaleic acid into anhydride is due to the closely situated carboxyl groups and the resulting greater entropy of activation, which makes the anhydride form unusually stable against hydroxylic reagents. The rates and the energies and entropies of activation of the hydrolysis reaction are, however, of the same order as those found for other anhydrides ².

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