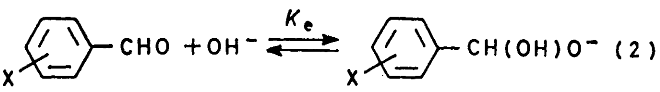
Intramolecular Catalysis. Part 3.[1] The Hydration and Ionisation of *o*-Phthalaldehyde

By **Keith Bowden,* Faiq A. El-Kaissi,** and **Nighat S. Nadvi,** Department of Chemistry, University of Essex, Colchester, Essex CO4 3SQ

o-Phthalaldehyde hydrates to form a bridged (cyclic) monohydrate. The hydrate exists as a *cis–trans* mixture, with the equilibrium constant for hydration, K_H, at 20 °C in water being 9.39. The pK_a value of *o*-phthalaldehyde hydrate at 20 °C in water is 12.08. The hydration and ionisation have been investigated at several temperatures, as has the rate of the uncatalysed hydration. A mechanism for the uncatalysed hydration is suggested.

ALDEHYDES are known to hydrate in aqueous solution and the degree of hydration has been measured for several aldehydes.[2] The simple hydration of a carbonyl compound RR^1CO to give a monohydrate $RR^1C(OH)_2$ is illustrated in (1); K_H is the equilibrium constant for hydration. These aldehyde hydrates, which are *gem*-diols, are considerably stronger acids than simple glycols or alcohols.[2] Both the pK_a values of the hydrates and the equilibrium constants for hydration have been correlated with substituent constants,[2,3] as have the equilibrium constants K_e for the addition of hydroxide anions to substituted benzaldehydes [4,5] [see (2)].

$$RR^1CO + H_2O \overset{K_H}{\rightleftharpoons} RR^1C(OH)_2 \qquad (1)$$

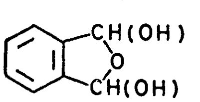


(2)

In the present study we have investigated the hydration of *o*-phthalaldehyde by determining the structure and pK_a value of the hydrate, the hydration equilibrium constants, and the rates of the uncatalysed hydration.

RESULTS AND DISCUSSION

Hydration of o-*Phthalaldehyde*.—Hydrates of dialdehydes can exist as simple monohydrates or dihydrates or as bridged (cyclic) monohydrates. ^1H and ^{13}C n.m.r. studies have shown that the structure of the hydrate of *o*-phthalaldehyde is a bridged (cyclic) monohydrate (1) which occurs as a *ca.* 1 : 1 *cis–trans* mixture. The equilibrium constant for hydration, K_H, for *o*-phthalaldehyde is defined by the relationship (3); a series of values are given in Table 1, they were measured by both ^1H n.m.r. and u.v. spectroscopic methods which give identical results within the limits of experimental accuracy. Studies [6,7] of glutaraldehyde hydrate have also indicated a cyclic monohydrate for this dialdehyde. Both 1,8-diformylnaphthalene and 4,5-diformylphenanthrene appear to be extensively hydrated and there is evidence for bridged monohydrate structures.[8,9]



(1)

$$K_H = [\text{Hydrate}]/[\text{Aldehyde}] \qquad (3)$$

As shown in Tables 1 and 2 the K_H values in aqueous 1.0M-sodium chloride are less than those in water at the same temperatures and those in aqueous dioxan fall with decreasing water content of the medium. Both these results arise from the decreased ' free ' water available which causes the equilibrium to favour the aldehyde. A plot of log K_H *vs.* log $[H_2O]$, as used by others,[10] gives a linear plot for aqueous dioxan with a slope of *ca.* 2.0. One molecule of water is used in forming the bridged (cyclic) hydrate and the second water molecule would appear to be the excess solvation requirement of the hydrate compared with the dialdehyde.

TABLE 1

Equilibrium constants for the hydration, K_H, of *o*-phthalaldehyde in water and in aqueous 1.0M-sodium chloride *

Temp. (°C)	K_H In water	K_H In aqueous 1.0 M-sodium chloride
20	9.39 †	7.05 †
25	7.9 ‡	
30	5.50 †	4.15 †
36	4.8 ‡	
40	3.46 †	2.45 †
48	2.8 ‡	
50	2.17 †	1.60 †
60	1.8 ‡	

* The K_H values were reproducible to ±4% (u.v. method) and ±10% (^1H n.m.r. method). † U.v. method. ‡ ^1H n.m.r. method.

TABLE 2

Equilibrium constants for the hydration, K_H, of *o*-phthalaldehyde in aqueous dioxan at 60 °C using u.v. method *

Mol % dioxan	K_H
0	1.25
8.3	0.553
17.4	0.300
33.0	0.124

* See Table 1.

Benzaldehydes are not normally significantly hydrated, except for *o*- and *p*-nitrobenzaldehyde which have K_H values of 0.43 and 0.25, respectively.[11,12] It is possible to estimate K_H at 25 °C for the formation of a ' normal ' monohydrate of *o*-phthalaldehyde, after allowing for the statistical advantage of two formyl groups, as *ca.* 0.1 from the values above and the cycle of equilibria given by Greenzaid.[4] The hydration of *o*-phthalaldehyde to form a bridged (cyclic) hydrate is *ca.* 50 times greater than this. The advantage of the bridged (cyclic) monohydrate appears to arise from the five-membered ring and the reduction in steric interactions in this ring tautomer, compared to the ' normal ' monohydrate which is the chain tautomer.

The enthalpy and entropy of hydration for *o*-phthalaldehyde at 30.0 °C both in water and aqueous 1.0M-sodium chloride are shown in Table 3. The ΔS^0 values of -24 to -28 J K^{-1} mol^{-1} are well within the range of -16 to -31 J K^{-1} mol^{-1} are found for a series of aldehydes.[13,14] This arises mainly from the loss of freedom and motions of one molecule of water ' destroyed ' in forming the hydrate.

TABLE 3

Reaction parameters for the equilibrium and uncatalysed hydration of *o*-phthalaldehyde and the ionisation of *o*-phthalaldehyde hydrate at 30.0 °C

	ΔH^0/ kcal mol^{-1}	ΔS^0/ cal mol^{-1} K^{-1}
Hydration in water (u.v. method)	9.2 ($\pm$0.1)	-27 ($\pm$1)
In water (^1H n.m.r. method)	8.4 ($\pm$0.3)	-24 ($\pm$2)
In aqueous 1.0M-sodium chloride (u.v. method)	9.4 ($\pm$0.2)	-28 ($\pm$1)
Ionisation in water	11.5 ($\pm$0.4)	-16 ($\pm$2)
In water at constant ionic strength (1.0μ)	10.9 ($\pm$0.3)	-18 ($\pm$2)
	$\Delta H^‡$/ kcal mol^{-1}	$\Delta S^‡$/ cal mol^{-1} K^{-1}
Uncatalysed hydration in water	9.8 ($\pm$0.5)	-37 ($\pm$2)
In aqueous 1.0M-sodium chloride	8.9 ($\pm$0.2)	-39 ($\pm$1)
Uncatalysed dehydration in water	18.9 ($\pm$0.6)	-10 ($\pm$2)
In aqueous 1.0M-sodium chloride	18.2 ($\pm$0.2)	-11 ($\pm$1)

Ionisation of the Hydrate.—The pK_a values of the hydrate of *o*-phthalaldehyde have been measured both in water and in water at constant ionic strength (1.0 μ) at various temperatures. The results of these determinations are shown in Table 4. The values in water at constant ionic strength are almost the same, as would be expected. The acidity of the cyclic hydrate can be estimated as 11.9 at 25 °C from the relation of Barlin and Perrin [3] for simple alcohols, shown as (4) below, together

$$pK_a = 15.9 - 1.42\ \sigma^* \qquad (4)$$

with a statistical correction of 0.30 for the two identical acidic centres. This is in good agreement with the value found. The enthalpies and entropies of ionisation are shown in Table 3. The entropy factor for such ionisation processes appears mainly to be dependent on interactions of the species with the solvent.[15] Thus the value observed here is comparable to those observed for benzoic acid [16] and phenol.[15]

TABLE 4

pK_a Values of *o*-phthalaldehyde hydrate *

	pK_a	
Temp. (°C)	In water	In water at constant ionic strength (1.0μ)
20	12.08	12.09
30	11.77	11.83
40	11.54	11.59
50	11.27	11.33

* pK_a values were reproducible to $\pm$0.03.

Kinetics of the Uncatalysed Hydration.—A number of studies have been made of the mechanism of uncatalysed hydration of aldehydes and ketones.[2,10,13,17] The observed rate coefficients of *o*-phthalaldehyde in water, together with those for hydration and dehydration, are shown in Table 5. Previous studies [2] show that the rates of uncatalysed hydration of carbonyl compounds are retarded by electron-releasing and ' bulky ' substituents, as well as by resonance interactions, between the carbonyl and aromatic groups, and accelerated by electron-withdrawing substituents. Even allowing for the statistical advantage of being a diformyl compound, the rates of hydration of *o*-phthalaldehyde appear to be very rapid. Thus acetaldehyde at 25 °C has a rate coefficient for the uncatalysed hydration in water of 0.75 s^{-1}. Neighbouring-group participation by the second formyl group appears to be the cause of this facilitation. The activation parameters for the forward and reverse uncatalysed hydration at 30.0 °C are shown in Table 3. The very large negative $\Delta S^‡$ value for the hydration contrasts with the much smaller value for dehydration. The hydration is characterised by the significant orientation requirements in going to the transition state; these involve loss of freedom and motion which are frozen-out. A major re-organisation of ' solvation ' in the transition state avoids excessive enthalpy requirements for hydration; whereas, in dehydration, the ' solvation ' is ' built-in ', the enthalpy requirement is high because of the ' destruction ' of the stable ring structure. The decrease in the rates of hydration and dehydration with increasing dioxan content and the increase with increasing ionic strength indicate dispersal and/or creation of charge in forming the transition state. A suggested path is shown below which is in general agreement with related mechanisms.[10,13,17] This is shown as a concerted process in (2) which involves the dialdehyde and two water molecules (neglecting further solvation). One water molecule attacks the first carbonyl group, this group then attacking the second carbonyl group intramole-

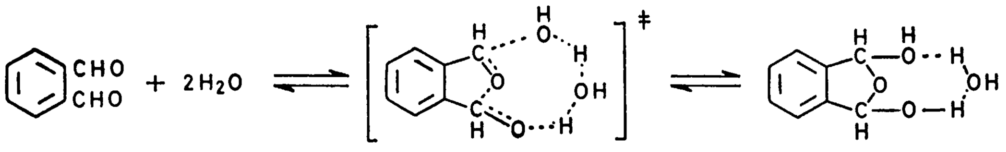
TABLE 5

Observed rate coefficients, k_{obs}, together with those for hydration, k_{hyd}, and dehydration, k_{dehyd}, for the uncatalysed hydration of *o*-phthalaldehyde in water

Temp. (°)	$10^3k_{obs}/s^{-1}$	$10^3k_{hyd}/s^{-1}$	$10^3k_{dehyd}/s^{-1}$
25	4.52 (6.91)	3.97 (5.82)	0.55 (1.09)
30	6.98 (9.72)	5.90 (7.83)	1.07 (1.89)
35	9.61 (13.2)	7.82 (10.1)	1.79 (3.15)
40	12.7 (17.6)	9.85 (12.5)	2.85 (5.1)
50	23.3 (33.2)	15.9 (20.4)	7.35 (12.8)

* k_{obs} Values were reproducible to 3%. The values in parentheses are for aqueous 1.0M-sodium chloride.

cularly. The nucleophilic process is assisted by a second water molecule acting as a general acid-base in transferring a proton. Alternatively the pathway could be shown as proceeding *via* tetrahedral immediates.

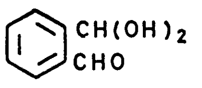


(2)

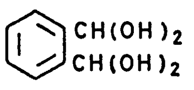
EXPERIMENTAL

Materials.—*o*-Phthalaldehyde (B.D.H.), was dissolved in warm (< 60 °C) light petroleum (b.p. 80—100 °C) and the clear solution was decanted. On cooling, colourless crystals were produced and these were filtered off and dried in a desiccator under reduced pressure; the compound had m.p. 54—55 °C (lit.,[18] 53.2 °C). The purified compound tended to decompose with time, the resulting sample giving a product with $\lambda_{max.}$ 348 nm when treated with aqueous sodium hydroxide. The impurity could not be detected by any of the standard physical methods. Solvents were purified as described previously.[19] Inorganic salts were of analytical grade and were used without further purification.

Measurements.—The ^{1}H n.m.r. spectra were measured using Varian A60-A and Anaspect EM 360 spectrometers. Tetramethylsilane was used as an internal standard, except in aqueous solutions where it was used externally. The spectra of *o*-phthalaldehyde in carbon tetrachloride indicated the expected structure with formyl [τ −0.6 (s, 2 H)] and aromatic [τ 2.1 (m, 2 H)] protons. The spectra of 0.5M-*o*-phthalaldehyde in water showed a diminished formyl proton absorption (τ −0.6) in relative intensity to that of the aromatic protons, whereas two new absorptions (τ 4.0 and 3.7) of approximately equal intensities were present. The possible structures for a hydrate are the monohydrate (3), dihydrate (4), and bridged (cyclic) monohydrate (1). An early study [20] gave evidence for a monohydrate of *o*-phthalaldehyde. Only (1), in combination with the dialdehyde itself, would give rise to the observed spectra. The chemical shifts of the methine protons in (1) can be predicted to appear at τ *ca*. 2.8 in deuteriochloroform using the relation given by Williams and Fleming; [21] but those for the *cis*- and *trans*-isomers would be expected to have different chemical shifts. Fay *et al*.[22] have shown that a general relation for such stereochemically related systems exists. It can be predicted that the hemiacetal protons of the *cis*-isomer will appear at 0.2 to 0.3 p.p.m. towards low field relative to those of the *trans*-isomer; this is as observed. The ^{13}C n.m.r. spectra were measured using a Bruchker HFX 90 spectrometer. The spectra of *o*-phthalaldehyde in dioxan showed the aromatic (multiplet, centred at 66.5 p.p.m.) and formyl carbons (singlet, 191.8 p.p.m.). The spectra of 0.5M-*o*-phthalaldehyde diminished in relative intensity and two new absorptions appeared (singlets; 99.3 and 100.3 p.p.m.). Thus these results all clearly indicate that *o*-phthalaldehyde forms the bridged (cyclic) monohydrate (1), which occurs as *cis*- and *trans*-isomers in approximately equal amounts.



(3)



(4)

A ^{1}H n.m.r. spectroscopic method was used to measure the equilibrium constant for hydration using the Varian A60-A and variable-temperature controller by integrating the signals for the formyl and hemiacetal protons at various temperatures (±1 °C). A u.v. spectrophotometric method was used to measure the equilibrium constants for hydration, the pK_a values of the hydrate and the rate coefficients for the uncatalysed hydration. A Unicam SP 8000 was used and the cell temperature was controlled to ±0.05 °C by means of a Churchill thermocirculator. Dioxan or aqueous solutions (2.5 ml) were pipetted into 1-cm spectrophotometric cells. After the cells had been in the thermostatted cell holder to enable thermal equilibration, *ca*. 5 µl of a solution of the dialdehyde in dioxan was added from a Hamilton microsyringe, such that the final substrate concentration in the cell was *ca*. 5 × 10^{-5}M. The optical density was then measured at 297 nm, where the hydrate does not absorb, to give in dioxan, O.D.$_D$, and in water, O.D.$_W$. K_H can then be calculated as shown in equation (5) below, which assumes that the optical density of the

$$K_H = \frac{\text{O.D.}_D - \text{O.D.}_W}{\text{O.D.}_W} \qquad (5)$$

dialdehyde is identical in dioxan and water.[2] The hydration of the dialdehyde in water was rapid, but it could be followed spectrophotometrically. The O.D.$_W$ extrapolated back to mixing time was consistent with O.D.$_D$. The uncatalysed hydration was followed by monitoring the O.D. at 297 nm. The rate coefficients, k_{obs}, were obtained using equations (6) and (7) below. The hydrate of *o*-

$$k_{obs} = k_h + k_d \qquad (6)$$

$$K_H = k_h/k_d \qquad (7)$$

phthalaldehyde can ionise in base as shown below (neglecting solvation and assuming second ionisation is negligible under the conditions) in equation (8). Equations (9) and

$$H_2A \rightleftharpoons H^+ + HA^- \qquad (8)$$

(10) are obeyed up to a pOH of *ca*. 10, when equation (11) is

$$pK_a = pH + \log [H_2A]/[HA^-] \qquad (9)$$

$$pH = pK_W - pOH \qquad (10)$$

$$pH = pK_W - pOH + \log f_\pm \qquad (11)$$

required using the activity coefficient $f_\pm$.[23] The ionisation ratio of the acid, [H$_2$A]/[HA$^-$], can be obtained from the O.D. at 297 nm in presence of base, O.D.$_B$, and the measurements of hydration already made as shown in equation (12)

$$[H_2A]/[HA^-] = K_H\text{O.D.}_B/(\text{O.D.}_D - \text{O.D.}_B - K_H\text{O.D.}_B) \qquad (12)$$

below. The equilibrium constants for hydration, K_H, measured by both methods water, aqueous 1.0M-sodium chloride, and aqueous dioxan are shown in Tables 1 and 2 and are the result of at least two independent measurements. The rate coefficients for the uncatalysed hydration of the dialdehyde both in water and in aqueous 1.0M-sodium chloride are shown in Table 5. The pK_a values of *o*-phthalaldehyde hydrate are shown in Table 4. The reaction parameters for the equilibrium and uncatalysed hydration of *o*-phthalaldehyde and the ionisation of *o*-phthalaldehyde hydrate are shown in Table 3. The intramolecular Cannizzaro reaction of *o*-phthalaldehyde is comparatively slow at the temperatures studied here and this reaction will be discussed in a subsequent report.[24]

[8/1259 *Received*, *7th July*, 1978]

REFERENCES

[1] Part 2, K. Bowden, D. Law, and R. J. Ranson, *J.C.S. Perkin II*, 1977, 1799.

[2] R. P. Bell, *Adv. Phys. Org. Chem.*, 1966, **4**, 1.

[3] G. B. Barlin and D. D. Perrin, *Quart. Rev.*, 1966, **20**, 75.

[4] P. Greenzaid, *J. Org. Chem.*, 1973, **38**, 3164.

[5] W. J. Bover and P. Zuman, *J.C.S. Perkin II*, 1973, 786.

[6] E. B. Whipple and M. Ruta, *J. Org. Chem.*, 1974, **39**, 1666.

[7] P. M. Hardy, A. C. Nichollas, and H. N. Rydon, *J.C.S. Perkin II*, 1972, 2270.

[8] R. Criegee, L. Kraft, and B. Bank, *Annalen*, 1933, **507**, 194.

[9] M. G. Sturock and R. A. Duncan, *J. Org. Chem.*, 1968, **33**, 2149.

[10] R. P. Bell and P. E. Sorenson, *J.C.S. Perkin II*, 1972, 1740.

[11] E. Laviron, H. Troncin, and J. Tirouflet, *Bull. Soc. chim. France*, 1962, 524.

[12] J. M. Sayer, *J. Org. Chem.*, 1975, **40**, 2545.

[13] Y. Pocker, J. E. Meany, and C. Zadorojny, *J. Phys. Chem.*, 1971, **75**, 792.

[14] Y. Pocker and D. G. Dickerson, *J. Phys. Chem.*, 1969, **73**, 4005.

[15] P. D. Bolton and L. G. Hepler, *Quart. Rev.*, 1971, **25**, 521.

[16] T. Matsui, *Canad. J. Chem.*, 1974, **52**, 2906.

[17] J. L. Kurz and J. I. Coburn, *J. Amer. Chem. Soc.*, 1967, **89**, 3524, 3528.

[18] S. Wawzonek and R. E. Karll, *J. Amer. Chem. Soc.*, 1948, **70**, 16666.

[19] K. Bowden, M. J. Hanson, and G. R. Taylor, *J. Chem. Soc.*, 1968, 174.

[20] L. Seekles, *Rec. Trav. chim.*, 1923, **42**, 706.

[21] D. H. Williams and I. Fleming, 'Spectroscopic Methods in Organic Chemistry,' McGraw-Hill, London, 1973.

[22] C. K. Fay, J. B. Grutzner, L. F. Johnson, S. Sternhell, and P. W. Westerman, *J. Org. Chem.*, 1973, **38**, 3122.

[23] A. Albert and E. B. Serjeant, 'Ionization Constants of Acids and Bases,' Methuen, London, 1962.

[24] K. Bowden and F. A. El-Kaissi, unpublished work.