The Significance of Brønsted Plots and Deviations from Them in the Acid- and Base-Catalyzed Decomposition of Some Benzaldehyde Ethyl Hemiacetals and Hydrates

Brian G. Cox,[a] A. Jerry Kresge[b] and Poul E. Sørensen[c,*]

[a]Department of Chemistry, University of Stirling, Stirling FK9 4LA, Scotland, U.K. [b]Department of Chemistry, University of Toronto, Toronto, Ontario M5S 1A1, Canada and [c]Chemistry Department A, The Technical University of Denmark, DK-2800 Lyngby, Denmark

Cox, B. G., Kresge, A. J. and Sørensen, P. E., 1988. The Significance of Brønsted Plots and Deviations from Them in the Acid- and Base-Catalyzed Decomposition of Some Benzaldehyde Ethyl Hemiacetals and Hydrates. – Acta Chem. Scand., Ser. A 42: 202–213.
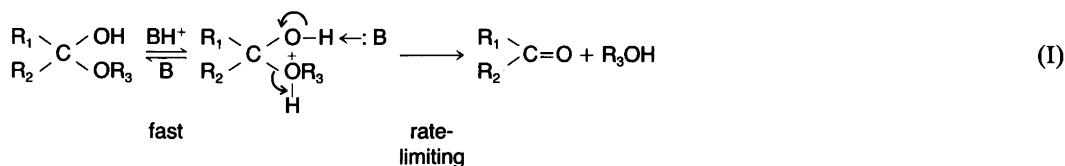
A detailed study of the general acid- and base-catalyzed decomposition of the ethyl hemiacetals and hydrates of three substituted benzaldehydes of different reactivity (2-chloro-5-nitrobenzaldehyde > 3-nitrobenzaldehyde > 3,4-dichlorobenzaldehyde) has been carried out at 298 K and an ionic strength of 1.0 M (KCl). Three main features are observed: (1) The change in Brønsted β for base catalysis by carboxylate ions from $\beta = 0.36$–0.38 for 2-chloro-5-nitrobenzaldehyde to $\beta = 0.42$–0.50 for the corresponding reactions of 3,4-dichlorobenzaldehyde is consistent with a class n mechanism characterized by a normalized value of $p_{xy} = \partial\beta/-\partial\sigma_{norm} = 0.035$. Similarly, a change in Brønsted α for acid catalysis by corresponding carboxylic acids from $\alpha = 0.33$–0.39 to $\alpha = 0.48$–0.50 for the same compounds indicates a class e mechanism for these reactions with $p_{xy-} = \partial\alpha/-\partial\sigma_{norm} = 0.069$. The correlation between α and σ_{norm} forms two separate lines of equal slope: one for aromatic and one for aliphatic aldehydes, presumably reflecting pronounced differences in acidities of the protonated forms of the two types of aldehydes. (2) A positive deviation of the point for hydroxide ion catalysis from the Brønsted plot decreases systematically with increasing Brønsted β values. The change can be attributed to a variation in the balance between two concurrent mechanisms, viz. general and specific base catalysis, respectively. (3) An upward curvature in the Brønsted plot for base catalysis of addition to the carbonyl group might be expected in cases where β is relatively small. Although we have investigated catalysis in a relatively wide pK range, we could see no sign of such a curvature in the Brønsted plot within experimental error.

Since the pioneering work by Faurholt[1] more than sixty years ago on the kinetics of the reaction of carbon dioxide with water and hydroxide ion, there have been numerous studies on the acid- and base-catalyzed decomposition/formation of hemiacetals and hydrates of aldehydes and ketones.[2-5] All these contributions have been of paramount importance to our present understanding of the general nature of acid-base catalysis. Recent investigations on the decomposition of hemiacetals and hydrates of formaldehyde[6]
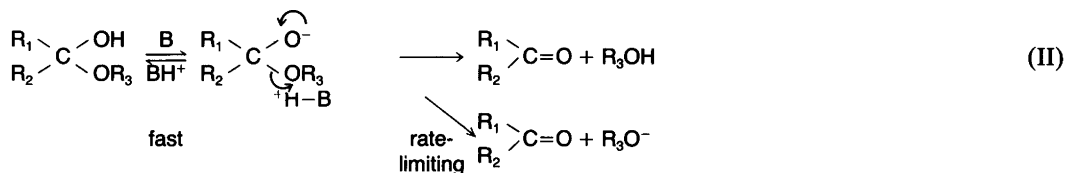
and acetaldehyde[7] have shown that the acid- and base-catalyzed reactions proceed by two different concerted mechanisms, which are reasonably well understood [eqns. (I) and (II), respectively]. However, it is also clear from these and other studies that large changes in the stability of the adducts, caused by changing the nature of either the carbonyl group (electrophile) and/or the leaving group (nucleofuge), may result in deviations from such well-established mechanisms. Thus, one extreme is represented by the formation of very stable addition compounds from carbonium ions and nucleophilic reagents[8a] or by the decom-

*To whom correspondence should be addressed.

Acid catalysis, class e, concerted:

$$\begin{array}{ccc} R_1 \diagdown \!\!\!\!\! \underset{R_2 \diagup}{\overset{}{C}} \!\! \diagdown \!\! \underset{OR_3}{\overset{OH}{}} \quad \underset{B}{\overset{BH^+}{\rightleftharpoons}} & R_1 \diagdown \!\!\!\!\! \underset{R_2 \diagup}{\overset{}{C}} \!\! \diagdown \!\! \underset{\overset{+}{O}R_3}{\overset{O\text{-}H \leftarrow : B}{}} & \longrightarrow & \underset{R_2}{\overset{R_1}{}}\!\!\!\!\!>\!\!C{=}O + R_3OH \end{array} \qquad (I)$$

fast   rate-limiting

Base catalysis, class n, concerted and non-concerted (specific):

$$\begin{array}{ccc} R_1 \diagdown \!\!\!\!\! \underset{R_2 \diagup}{\overset{}{C}} \!\! \diagdown \!\! \underset{OR_3}{\overset{OH}{}} \quad \underset{BH^+}{\overset{B}{\rightleftharpoons}} & R_1 \diagdown \!\!\!\!\! \underset{R_2 \diagup}{\overset{}{C}} \!\! \diagdown \!\! \underset{\overset{+}{H}{-}B}{\overset{O^-}{OR_3}} & \longrightarrow & \underset{R_2}{\overset{R_1}{}}\!\!\!\!\!>\!\!C{=}O + R_3OH \end{array} \qquad (II)$$

fast   rate-limiting $\searrow \underset{R_2}{\overset{R_1}{}}\!\!\!\!\!>\!\!C{=}O + R_3O^-$

position of acetals,[9] where in both cases no or only slight general base catalysis is observed (Brønsted β approaching zero). Another (contrasting) extreme is demonstrated by the decomposition of some very unstable hemiketals of acetophenone, generated from precursors, where Brønsted β values for base catalysis approach unity.[10]

The task of defining the various mechanisms and distinguishing between them e.g. by experimental means is a difficult one, especially in the transition regions.[11] It is also clear that for base catalysis (and possibly also for acid catalysis) a substantial change in the strength of the base catalyst, such as on going from weaker bases to the hydroxide ion, may result in "changes" in mechanism.[7] Thus, for the hydroxide ion as catalyst there have been numerous reports of a (large) positive deviation for this catalyst from the Brønsted plot for general base catalysis based on water and a series of carboxylate ions. It is generally accepted that this can be ascribed to a different mechanism for hydroxide ion catalysis.

In this paper we present some new conclusions concerning the mechanisms of acid-base catalysis.

(1) In general *acid catalysis* there is a "jump" in the structure−reactivity data in going from aliphatic to aromatic carbonyl compounds. Thus, if adducts of aliphatic and aromatic aldehydes of equal thermodynamic stability are compared, the observed Brønsted α values for the aliphatic aldehydes are generally higher than those for the

aromatic aldehydes by 0.15 units. Although this difference is hard to explain quantitatively due to the large structural differences between aliphatic and aromatic compounds, one rationalization might lie in the pronounced differences in acidities of the protonated forms of the two types of aldehyde. It is interesting that our corresponding data for general *base catalysis* show no such difference in the behaviour of aliphatic and aromatic compounds.

(2) The different mechanism for the *hydroxide ion* does not always lead to the deviations described above. The positive deviation for the hydroxide point seems to vary in a systematic way, at least qualitatively, with the observed Brønsted β value based on a series of carboxylates. Thus, we have found that the positive deviation of almost three log-units in the case of decomposition of 2-chloro-5-nitrobenzaldehyde ethyl hemiacetal and hydrate (β relatively small) has almost disappeared for the corresponding compounds of 3,4-dichlorobenzaldehyde (β relatively large). The results for 3-nitrobenzaldehyde are intermediate between the two, and literature data for a number of carbonyl reactions imply that the trend may be generalized. In a solution containing a general base catalyst catalysis will take place via two different, parallel (concurrent) mechanisms: (a) via a concerted, general-base-catalyzed reaction and (b) via a non-concerted, specific-base-catalyzed route (catalysis by the hydroxide ion).

(3) A reported *convex* curvature attributed to "perpendicular" or "anti-Hammond" effects in the extended Brønsted plot for the base-catalyzed mutarotation of glucose[12] might also be detected for the hemiacetals and hydrates studied here, since the mechanisms are expected to be closely related. We found that the assessment of catalytic data in the basic region is much more difficult in our case than with glucose, due to a much stronger catalytic competition from the hydroxide ion, and we could see no evidence for such an effect.

Experimental

Materials. The benzaldehydes, Ar−CHO (Ar = 2-Cl-5-NO$_2$-C$_6$H$_3$, 3-NO$_3$-C$_6$H$_4$ and 3,4-Cl$_2$C$_6$H$_3$), were all commercially available (Aldrich) and were purified by sublimation under reduced pressure before use. The ethyl hemiacetals were formed readily for all three compounds by dissolving small samples of the aldehydes in anhydrous ethanol (15 mg in 1 ml) and leaving these stock solutions to react for a couple of hours. The solutions were stable for several days when kept at 4 °C. Alkaline aqueous solutions of the benzaldehydes for hydration/dehydration experiments (*vide infra*) were prepared just before use by injecting suitable amounts of the hemiacetal stock solutions described above into 0.1 M KOH. This results in instantaneous breakdown of the hemiacetal and formation of the anion of the aldehyde hydrate, and is an easy way of obtaining a well-defined aqueous solution of the very sparingly soluble benzaldehydes.

Methyl, mono- and dichloromethyl, and t-butyl phosphonic acid were synthesized and handled according to Kresge and Tang.[13] Cyanoacetic and 3-chloropropionic acids were purified by sublimation under reduced pressure. Methoxyacetic and dichloroacetic acids were distilled before use. All other buffer substances and reagents were of analytical grade. Purified water from a Milli-Q apparatus was used throughout.

Kinetics. In the pH range 3–7 all reactions are slow enough to be studied by conventional spectrophotometry.

Hemiacetal breakdown was initiated by injecting approximately 1 µl of hemiacetal stock solution into 1 ml of buffer in the thermostatted spectro-photometer cell. The appearance of free aldehyde was followed at 248 nm for 2-chloro-5-nitro- and 3-nitrobenzaldehyde, and at 260 nm for 3,4-dichlorobenzaldehyde.

Hydration/dehydration studies were performed by the procedure suggested by McClelland and Coe:[14] the equilibrium constants for addition of hydroxide ion to the aldehydes are approximately 50–100 times larger than the corresponding values for K_{hydr}.[14a,15] Thus, a perturbation of the hydration equilibrium is possible in alkaline solution. When a solution of the aldehyde in aqueous sodium hydroxide of known concentration is neutralized in a stopped-flow apparatus with a buffer containing an equivalent concentration of HCl, a relaxation to the equilibrium position in "neutral" buffer will take place.[14a]

In the pH range above 7 and below 3, catalysis by hydroxide and hydronium ion, respectively, is dominant, and fast recording techniques are required to measure reaction rates. For the hemiacetal decomposition reactions it was possible to prepare an aqueous solution of the hemiacetal by injection of a suitable amount of the alcoholic stock solution into prethermostatted water (aqueous potassium chloride) of pH around the minimum on the pH profile (pH ≃ 5, adjusted by addition of minimal amounts of acetate buffer). The half-life of the hemiacetal decomposition under such conditions is slightly less than one minute for all three substances. This is time enough for filling the drive-syringe of the stopped-flow apparatus and mixing the solution with an appropriate buffer from the other syringe. Depending on the rate of reaction in the mixture, two or three runs could usually be carried out starting from the same aqueous hemiacetal solution.

A Messanlagen temperature-jump instrument was also used to study some of the faster hydration/dehydration reactions. This method is particularly useful for 2-chloro-5-nitrobenzaldehyde since the hydration equilibrium constant for this substance (K_{hydr} = 0.64)[15] is ideal for this relaxation method.

Finally it should also be mentioned that a more simple temperature-jump technique was also applied in some cases for the slower hydration/dehydration experiments: if an ice-cooled solution of the compound in buffer is quickly transferred to, and stirred (or shaken) in, a thermostatted (water-jacketed) spectrophotometer cell, the

temperature of the solution reaches 25 °C within 20–30 s. The relaxation to equilibrium at this temperature can then be monitored at appropriate wavelengths. Similarly, in the transition area between slow and fast reactions we were also able to take advantage of a spectrophotometer (Beckman DU) equipped with a magnetic micro-stirrer in connection with the cell holder. The liquid in the 1 cm cuvette was kept moving by the stirrer, and the substrate (hemiacetal or hydrate) was injected by a spring-loaded micro-syringe. Complete mixing takes place within 1–2 s by this method.

All kinetic measurements were carried out at 25 °C and at an ionic strength of 1.0 M (KCl).

Results

The hemiacetal decomposition reactions were assumed to be virtually irreversible in aqueous buffers under the present conditions, and pseudo-first-order kinetics were observed for the appearance of both 3,4-dichloro- and 3-nitro-benzaldehyde. We did, however, notice deviations from first-order kinetics for the hemiacetal of 2-chloro-5-nitrobenzaldehyde in some cases. This is because the aldehyde, which is the primary product of the decomposition reaction, undergoes partial hydration (cf. $K_{hydr} = 0.64$ as mentioned above) in a subsequent step according to the reaction scheme in (III).

$$A \xrightarrow{k_1} B \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} C \qquad \text{(III)}$$

This complication would cause no problem if reaction rates were measured by monitoring the disappearance of the hemiacetal A in (III). However, since the appearance of aldehyde B in (III) is monitored, and because the sum of the two rate constants, $k_2 + k_{-2}$ for the hydration equilibration, is not always considerably larger than the hemiacetal decomposition rate constant k_1, the evaluation of k_1 from the kinetic data requires a mathematical (statistical) analysis based on the integrated rate expression for (III).

Such a reaction scheme is not unusual in chemical kinetics and was treated long ago by Lowry

and John.[16] If A_0, B_0 and B_∞ indicate initial and final concentrations of A and B, the integrated rate expression for changes in concentration of B with time is given by eqn. (IV), which allows for the fact that the hemiacetal may have undergone partial breakdown ($B_0 \neq 0$) before spectrophotometric detection can commence. The rate constants k_1 and $(k_2 + k_{-2})$ were then computed (IBM 3081D) from the absorbance–time data using eqn. (IV) and a least-squares procedure. In most cases this led to rate constants of satisfactory accuracy for k_1 only, because the change in absorbance due to hydration is relatively small. However, the hydration reaction was studied separately and the relevant rate constants inserted in eqn. (IV), leading to improved accuracy of the calculated value for k_1. Hydration kinetics were found to be simple first-order throughout, and rate constants were determined by plotting $\ln (A_\infty - A)$ vs. time or by using the Swinbourne-Kezdy procedure.

The accelerating effects of acids and bases on the hemiacetal decomposition and hydration equilibration were evaluated from rate–buffer plots in the normal fashion.[6,7,12,14a] Catalytic constants for all the substances investigated are collected in Table 1. Weaker acids are not included in Table 1 since their catalytic constants are too small to be detected. The values for H^+, OH^- and water catalysis in Table 1 are calculated from the rate–pH profiles shown in Fig. 1. The accuracy of the catalytic constants for the stronger general bases is seen to be poor. This is due to strong background catalysis by hydroxide.

Discussion

Two preliminary qualitative observations may be made from Fig. 1 (Table 1): (i) rate constants for the hydrates are generally larger than those for the hemiacetals, but these constants are not directly comparable since both forward and reverse rate constants are involved for the hydrates (vide infra); (ii) it is immediately obvious that considerable aromatic substituent effects are operative for the H^+-catalyzed decomposition of both types of adducts. These effects are consistent with the large negative Hammett ϱ values ($\varrho \approx -2.0$) observed in earlier studies of the H^+-catalyzed

$$B = B_\infty + ((k_1 - k_{-2})A_0/(k_2 + k_{-2} - k_1))e^{-k_1 t} + [B_0 - B_\infty - \{(k_1 - k_{-2})A_0/(k_2 + k_{-2} - k_{-1})\}]e^{-(k_2 + k_{-2})t} \qquad \text{(IV)}$$

Table 1. Catalytic constants for the breakdown of some benzaldehyde ethyl hemiacetals and hydrates at 298 K and ionic strength 1.0 (KCl).

Catalyst	pK_a	p,q	$k_{cat}/M^{-1}\,s^{-1}$ Hydration			Ethyl hemiacetal decomposition		
			2-Cl-5-NO$_2$	3-NO$_2$	3,4-Cl$_2$	2-Cl-5-NO$_2$	3-NO$_2$	3,4-Cl$_2$
Acids								
H$_3$O$^+$	−1.74	3,1	48(2)	107(5)	270(15)	6(1)	40(2)	89(2)
Cl$_2$CHCO$_2$H	1.26[c]	1,2	−[f]	−[f]	−[f]	0.75(10)	−[f]	−[f]
NCCH$_2$CO$_2$H	2.23[a]	1,2	0.78(4)	1.7(1)	3.5(5)	0.15(2)	0.44(3)	0.66(6)
ClCH$_2$CO$_2$H	2.70[a]	1,2	0.8(1)	1.4(1)	2.2(4)	0.20(1)	0.20(5)	0.50(10)
MeOCH$_2$CO$_2$H	3.40[a]	1,2	0.27(2)	0.41(2)	0.70(8)	0.05(1)	0.17(1)	0.20(1)
HCO$_2$H	3.62[c]	1,2	−[f]	−[f]	−[f]	−[f]	−[f]	0.142(4)
ClCH$_2$CH$_2$CO$_2$H	3.93[a]	1,2	0.20(3)	0.26(2)	0.34(5)	0.020(4)	0.054(6)	0.152(9)
CH$_3$CO$_2$H	4.65[a]	1,2	0.11(2)	0.20(1)	0.23(3)	0.06(1)	−[e]	0.04(1)
Cl$_2$CHPO$_3$H$^-$	5.20[d]	1,3	−[f]	−[f]	−[f]	0.08(1)	−[f]	−[f]
ClCH$_2$PO$_3$H$^-$	6.12[d]	1,3	−[f]	−[f]	−[f]	0.050(5)	−[f]	−[f]
(CH$_3$)$_2$AsO$_2$H	6.16[b]	1,2	0.35(5)	0.15(2)	0.35(5)	0.10(2)	0.10(2)	0.06(1)
H$_2$PO$_4$$^-$	6.49[b]	2,3	0.6(1)	0.6(1)	0.6(1)	0.07(2)	0.10(5)	0.15(5)
Bases								
H$_2$O	−1.74	3,1	1.2(1)×10^{-3}	5(2)×10^{-4}	5(2)×10^{-4}	2.9(3)×10^{-4}	1.8(2)×10^{-4}	2.0(4)×10^{-4}
Cl$_2$CHCO$_2$$^-$	1.26[c]	1,2	−[f]	−[f]	−[f]	−[e]	−[f]	−[f]
NCCH$_2$CO$_2$$^-$	2.23	1,2	0.15(1)	0.10(3)	−[e]	0.021	0.013(2)	0.015(2)
ClCH$_2$O$_2$$^-$	2.70	1,2	0.08(2)	0.08(2)	0.10(4)	0.035(2)	0.023(2)	0.03(1)
MeOCH$_2$CO$_2$$^-$	3.40	1,2	0.27(2)	0.18(1)	0.14(4)	0.06(1)	0.07(1)	0.062(3)
HCO$_2$$^-$	3.62	1,2	−[f]	−[f]	−[f]	−[f]	−[f]	0.101(3)
ClCH$_2$CH$_2$CO$_2$$^-$	3.93	1,2	0.34(3)	0.26(2)	0.23(3)	0.11(1)	0.172(7)	0.122(7)
CH$_2$CO$_2$$^-$	4.65	1,2	0.67(2)	0.44(1)	0.50(3)	0.175(4)	0.24(1)	0.25(1)
Cl$_2$CHPO$_3$$^{2-}$	5.20[d]	1,3	−[f]	−[f]	−[f]	0.26(4)	−[f]	−[f]
ClCH$_2$PO$_3$$^{2-}$	6.12	1,3	−[f]	−[f]	−[f]	0.61(8)	−[f]	−[f]
(CH$_3$)$_2$AsO$_2$$^-$	6.16	1,2	2.75(10)	2.6(1)	2.6(2)	0.65(3)	1.55(15)	1.45(5)
HPO$_4$$^{2-}$	6.49	2,3	4.5(1)	5.10(4)	4.3(3)	0.95(5)	2.2(2)	2.3(2)
CH$_3$PO$_3$$^{2-}$	7.3	1,3	4.8(2)	5.0(2)	5.8(1)	1.22(4)	2.7(1)	2.84(12)
(CH$_3$)$_3$CPO$_3$$^{2-}$	8.05	1,3	−[f]	−[f]	−[f]	−[f]	2.2(1.4)	2.3(1.5)
(CH$_2$OH)$_3$CNH$_2$	9.05	3,1	3.0(8)	2.7(8)	8(2)	5.5(5)	6(2)	6(2)
H$_2$BO$_3$$^-$	9.4	3,4	49(6)	28(6)	64(6)	−[f]	−[f]	11.2(1.6)
NH$_3$	9.48	4,1	13(5)	−[f]	48(3)	40(5)	58(12)	64(9)
HO$^-$	15.74	2,1	6.0(3)×10^5	6.0(4)×10^5	4.7(6)×10^5	4.9(6)×10^5	7.5(5)×10^5	7.8(5)×10^5

[a] Ref. 6. [b] Ref. 19. [c] Ref. 20. [d] Taken as the pH of equimolar solutions of acid and base component of buffer ($I=1.0$). [e] Not detectable or assumed not detectable. [f] No attempts made to determine this constant.

decomposition of a series of *meta*- and *para*-substituted benzaldehyde hydrates,[14a] ethyl hemiacetals,[14b] and recently also for some hemiketals of α-bromoacetophenone.[10b] Similar effects are observed for the general-acid-catalyzed reactions (Table 1) but to a lesser extent, which is a result of the observed change in Brønsted α with aromatic substitution, i.e. $p_{xy-} > 0$ (*vide infra*). The corresponding aromatic substituent effects in the water- and base-catalyzed reactions are seen to be much smaller: (a) small positive ϱ values are observed for the water-catalyzed reactions (Table 1) in accordance with earlier observations;[14,10 b] (b) Our data for catalysis by the hydroxide ion (Table 1) are consistent with a reported change in sign of ϱ from ϱ = −0.3 for the decomposition of benzaldehyde ethyl hemiacetals catalyzed by the hydroxide ion[14b] to ϱ = +0.5 for the correspond-
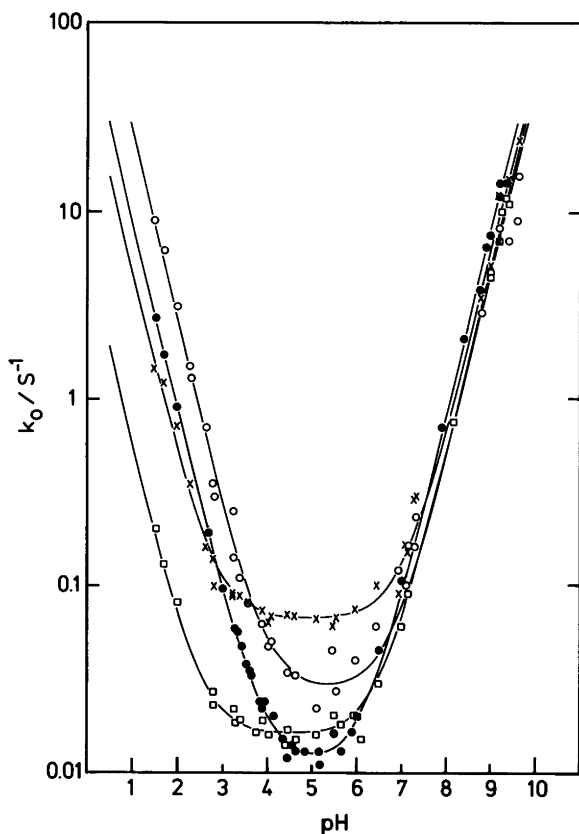
Fig. 1. Buffer-independent rate constants as a function of pH for decomposition of 2-chloro-5-nitrobenzaldehyde hydrate ($\times$), 2-chloro-5-nitrobenzaldehyde ethyl hemiacetal ($\square$), 3,4-dichlorobenzaldehyde hydrate ($\bigcirc$) and 3,4-dichlorobenzaldehyde ethyl hemiacetal ($\bullet$) at ionic strength 1.0 M (KCl) and 25 °C. The curves are drawn from $k_0 = k_{H_2O} + k_H a_{H^+} + k_{HO} a_{HO^-}$ (Table 1).

ing reaction for the hydrates.[14a] The difference has been interpreted in terms of a solvation effect.[10b,15]

Acid Catalysis. Data for the acid-catalyzed decomposition of the three benzaldehyde ethyl hemiacetals and hydrates (taken from Table 1) are shown in Brønsted plots in Fig. 2. Since the data for hydration in Table 1 represent the approach to an equilibrium, i.e. $k = k_{HB}^d + k_{HB}^h$ where $k_{HB}^h/k_{HB}^d = K_{hydr}$ (K_{hydr} taken from Table 3), k_{HB}^d is obtained from $k_{HB}^d = \frac{1}{2}xk/(1 + K_{hydr})$. The factor one-half is applied as a statistical correction accounting for the presence of two hydroxy groups in the hydrates compared with only one in the hemiacetals. The plots in Fig. 2 are separated conveniently by adjusting the parameter A. The similarities between the locations of the points for hemiacetal decomposition and dehydration for each benzaldehyde are striking, and suggest very similar mechanisms for the two reactions.
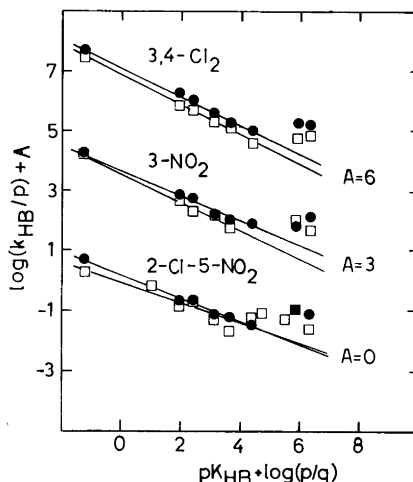

Fig. 2. Brønsted plots for general acid catalysis of the breakdown of ethyl hemiacetals ($\square$) and hydrates ($\bullet$) of three benzaldehydes. The lines are least-squares fits to the data, including H_3O^+ but omitting the points for cacodylic acid, dihydrogen phosphate and phosphonic acids (Table 1).

Table 2. Observed Brønsted coefficients for the general-acid and base-catalyzed decomposition of some benzaldehyde ethyl hemiacetals and hydrates at $I = 1.0$ M and 25 °C.

	Ethyl Hemiacetal		Hydrate	
	α	β	α	β
3,4-Dichloro	0.50(1)	0.50(2)	0.48(1)	0.42(2)
3-Nitro	0.47(1)	0.52(2)	0.42(1)	0.38(4)
2-Chloro-5-nitro	0.33(2)	0.38(1)	0.39(1)	0.36(2)

There is a slight, positive deviation for the points for dehydration which leads to a negative value of $\beta_{lg} = \partial \log k_{HB}^d / \partial pK_{HB}$. Such an effect was also observed for formaldehyde[6] and acetaldehyde,[7] but more extensive work covering a much wider pK range for the leaving group demonstrates that β_{lg} should be positive for this type of reaction.[6,7] The positive deviation for water as a leaving group probably reflects a small steric effect.

The Brønsted lines in Fig. 2 have been drawn as least-squares fits to all the points in each set, omitting data for cacodylic acid, dihydrogen phosphate and the phosphonic acid monoanions, which all show considerable, positive deviations. A similar positive deviation has been observed recently for cacodylic acid in the catalyzed decompostion of acetaldehyde hemiacetals and hy-

drate, and was attributed to bifunctional catalysis.[7] A positive deviation for catalysis by hydrogen phosphate and by phosphonic acid monoanion was also noticed by McClelland and Coe[14a] in their studies of the hydration of a series of benzaldehydes. They ascribed the effect to the difference in charge type compared with carboxylic acids for these catalysts.

Considering each of the three benzaldehydes separately, the two α values for decomposition of hemiacetal and hydrate, respectively, may be indistinguishable within experimental error (Table 2). However, a significant decrease in α is observed on changing the electrophile from 3,4-dichloro-, via 3-nitro-, to 2-chloro-5-nitrobenzaldehyde. Such a substituent effect is expected for this type of reaction and is indicative of a class e
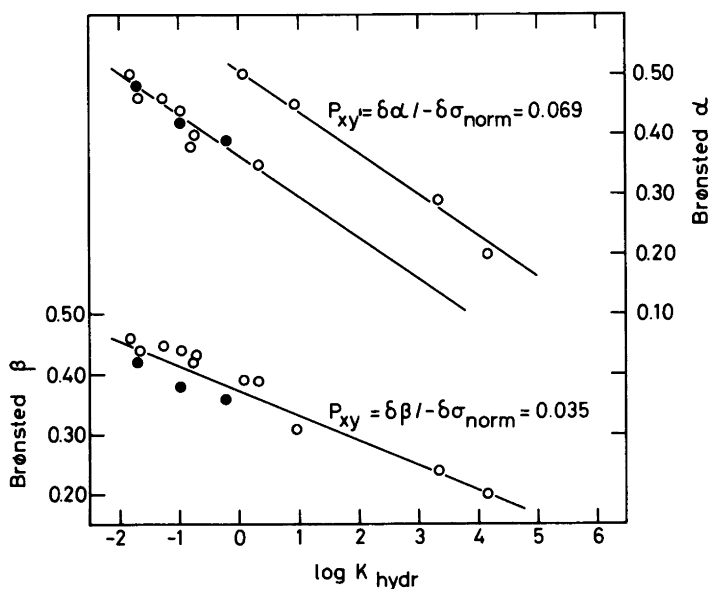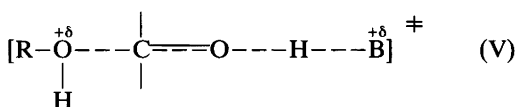

Fig. 3. Correlations between Brønsted coefficients and the stability of the carbonyl compound for acid- and base-catalyzed breakdown of some aldehyde hydrates. ● This work; ○ Taken from Table 3.

Table 3. Dependence of Brønsted α and β values on carbonyl reactivity in the hydration of various aldehydes.

Aldehyde	K_{hydr}[a]	$\log K_{hydr}$	α	β
Chloral	1.5×10^4 [b,c]	4.17	0.2[b,d,e]	0.2[b,d]
Formaldehyde	2.27×10^3 [f]	3.356	0.29[f]	0.24[f]
Glycolaldehyde	9[g]	0.95	0.45[g]	0.31[g]
3,5-Dinitrobenzaldehyde	2.1[h]	0.322	0.35[h]	0.39[h]
Acetaldehyde	1.2[i]	0.079	0.50[i]	0.39[i]
2-Chloro-5-nitrobenzaldehyde	0.64[k]	−0.194	0.39[j]	0.36[j]
3-Nitro-4-chlorobenzaldehyde	0.18[h]	−0.745	0.40[h]	0.43[h]
4-Nitrobenzaldehyde	0.17[h]	−0.769	0.38[h]	0.42[h]
3-Nitrobenzaldehyde	0.11[h]	−0.959	0.44[h], 0.38[j]	0.44[h], 0.42[j]
4-Trifluoromethylbenzaldehyde	0.055[h]	−1.259	0.46[h]	0.45[h]
3-Chlorobenzaldehyde	0.022[h]	−1.658	0.46[h]	0.44[h]
3,4-Dichlorobenzaldehyde	0.02[k]	−1.699	0.48[j]	0.42[j]
4-Chlorobenzaldehyde	0.016[h]	−1.796	0.50[h]	0.46[h]

[a]$K_{hydr} = [RCH(OH)_2]/[RCHO]$. [b]Ref. 21. [c]Ref. 22. [d]2.73 M water in dioxane. [e]A value of $\alpha = 0.13$ reported here is probably too low. We prefer a value of $\alpha = 0.2$ estimated from the same data but omitting a point for acid catalysis by water, which almost certainly proceeds by another mechanism (general base catalysis). [f]Ref. 6. [g]Ref. 23. [h]Ref. 14a. [i]Ref. 7. [j]This work. [k]Ref. 15.

mechanism, in which the rate-determining step involves proton transfer to or from the electrophile in the transition state, as shown in (V).[7,14]

$$[\text{R}-\overset{+\delta}{\underset{\underset{\text{H}}{|}}{\text{O}}}---\overset{|}{\text{C}}=\!=\!=\text{O}---\text{H}---\overset{+\delta}{\text{B}}]^{\ddagger} \qquad (V)$$

The substituent effect observed can be quantified by the cross correlation coefficient $p_{xy-} = \partial\alpha/-\partial\sigma_{norm}$, which is equivalent to the term $\partial\alpha/-\partial\log K_{hydr}$ if $\partial\sigma_{norm}$ is defined as $\partial\sigma_{norm} = \partial\sigma\varrho_{eq}$, where $\varrho_{eq} = \partial\log K_{hydr}/\partial\sigma$.[7] A value of $p_{xy-} = 0.069$ is obtained from the slopes of the plots in Fig. 3, based on data for a number of carbonyl hydration reactions (Table 3). Our data (filled circles) are seen to fit in well with those for other benzaldehydes.

It is interesting to notice that aliphatic and aromatic aldehydes give rise to two different correlations for acid catalysis. Despite the large structural differences between the two classes of compounds, a (speculative) explanation for this might result from comparing the energy contour diagrams for the general-acid-catalyzed dehydration (class e mechanism) of a substrate from each class and of similar thermodynamic stability. An energy diagram is shown in Fig. 4, in which the

location of the transition state for acetaldehyde hydrate is based on data from the literature.[7] The corresponding location of the transition state for the hydrate of 2-chloro-5-nitrobenzaldehyde is also shown, although the exact position along the vertical axis is not known, no value being available for β_{lg} of this compound.

The shift in location of the two transition states shown is consistent with a decrease in α as observed experimentally, and with an increase in β_{lg} when acetaldehyde is replaced with 2-chloro-5-nitrobenzaldehyde. Such a shift can be rationalized as being the result of a movement parallel to the reaction coordinate toward the upper right corner R_+ (a Hammond effect) and a movement perpendicular to the reaction coordinate toward the upper left corner R_r (an anti-Hammond effect). These effects are indicated by the small arrows and result from raising the energy of the species on the right-hand side relative to the left-hand side of the diagram. Although the two aldehydes considered exhibit very similar values of K_{hydr}, there is a large difference between the acidity constants of the protonated species which can cause the effects described above: a value of $pK_{BH^+} = -3.8$ was estimated for protonated acetaldehyde[7] and this constant is probably 2–3 pK units more negative for protonated 2-chloro-5-nitrobenzaldehyde, based on a value of pK_{BH^+}
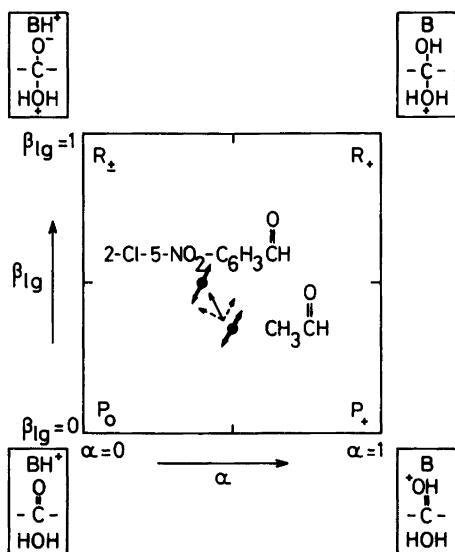
Fig. 4. Reaction coordinate–energy contour diagram (contour curves not shown) for the concerted, general-acid-catalyzed hydration of 2-chloro-5-nitrobenzaldehyde compared with that of acetaldehyde, the two compounds having similar values of K_{hydr}. An increase in the acidity of the protonated aldehyde and its hydrate can be visualized as raising the right hand side of the diagram (R_+ and P_+) compared to the left hand side (R_+ and P_0). If the reaction coordinates (via saddle points) as shown by the heavy arrows are relatively vertical, the position of the transition state may shift as indicated by the small arrows in the middle of the diagram.

Fig. 5. Brønsted plots for general base catalysis of the decomposition of ethyl hemiacetals (□) and hydrates (×) of three benzaldehydes. The rate constants for dehydration have been multiplied by a factor of $^1/_2(1 + K_{hydr})$ before being plotted (see text). The parameter A is chosen arbitrarily so as to arrange the plots conveniently; observed positions are shown in the inset. The lines are least-squares fits to the data for carboxylate ions and cacodylate only.

$= -4.2$ reported by Modena *et al.*[17] for acetophenone and subtracting 0.9 for substituting H for CH_3.[7] The presence of 2-chloro- and 5-nitro-substituents in the benzene ring will further increase the acidity. Similar differences in acidity of the protonated hydrates of the two aldehydes (corner R_+ in Fig. 4) are expected.

Base catalysis. Brønsted plots for base catalysis (data from Table 1) are shown in Fig. 5. According to the arguments presented in the previous section, the values for hydration in Table 1 are lowered by a factor of $^1/_2(1 + K_{hydr})$ to make them comparable with the corresponding points for hemiacetal decomposition. The closely related mechanisms expected for expulsion of the two groups may be confirmed by the two almost
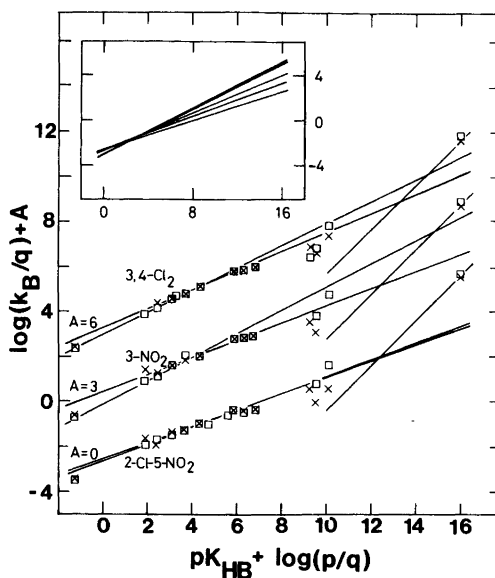
indistinguishable (within experimental error) sets of points for each benzaldehyde. The Brønsted lines are drawn by the method of least squares and are based on carboxylate ions and the cacodylate ion only (β values are given in Table 2). The substantial difference between the two β values for 3-nitrobenzaldehyde is mainly due to uncertain data for catalysis by cyanoacetate. There is a clear tendency for β to decrease with increasing electronegativity of the substituents in the benzaldehyde, as is to be expected in a class n, concerted mechanism for general base catalysis [transition state shown in (VI)]:[7,14]

$$[\overset{-\delta}{O}---\overset{|}{\underset{|}{\underset{R}{C}}}--O---\overset{+}{H}---\overset{-\delta}{B}]^{\ddagger} \qquad \text{(VI)}$$
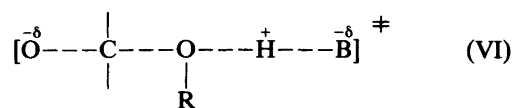
This effect is conveniently described by the corre-

210

lation coefficient $p_{xy} = \partial\beta/-\partial\sigma_{norm} = \partial\beta/\partial\log K_{hydr}$. Fig. 3 shows that our data for hydration (filled circles) fit in reasonably well with literature data for a number of aromatic and aliphatic aldehydes. Contrary to the situation for acid catalysis all the data can now be represented by a single line, the slope of which indicates a value of $p_{xy} = 0.035$. This difference in behaviour between acid and base catalysis seen in Fig. 3 may be another indication that two entirely different mechanisms are involved.

Positive p_{xy} values have also been observed for other reactions following a class n mechanism, such as the addition of hydroxylic reagents to unstable carbocations,[8a] and in the breakdown of Meisenheimer complexes.[8b]

Fig. 5 also provides information on catalysis by solvent water and by the hydroxide ion. It is seen that the rate constants for the water reaction are close to those expected from the Brønsted plot for general base catalysis by a class n mechanism, possibly with a slight negative deviation, and suggest that the water reaction follows this mechanism. The hydroxide ion, however, gives rise to quite substantial, positive deviations from the same extrapolated Brønsted plots for general base catalysis. This indicates that the points for hydroxide may belong to Brønsted plots referring to a different mechanism for this catalyst, e.g. an uncoupled mechanism, where the expulsion of the leaving group [R_3O^- in (II)] involves no assistance from protonation by BH^+ in the transition state. Brønsted plots for such a mechanism should appear with slopes equal to unity and are drawn through the points for hydroxide ion catalysis in Fig. 5. Furthermore, the degree of positive deviation seems to decrease systematically with decreasing stability of the aldehyde addition compound. This behaviour is clearly quite incidental and would be difficult (if not impossible) to explain rigorously since it depends not only on changes in Hammett ϱ value, caused by the difference in mechanism for weaker base catalysts and the hydroxide ion,[14a] but also on changes in β with substitution in the benzaldehyde (i.e. on p_{xy}). Nevertheless, we have demonstrated the relationship in Fig. 6 by plotting β'/β vs. β for a number of carbonyl addition reactions where sufficient data are available: β is the reported value for general base catalysis of the reaction, and β' is the equivalent value based on only two points, i.e. for water and for the hydroxide ion. If no specific solvation effects are involved for stronger bases,[18] it is most likely that the points in Fig. 6 converge towards $\beta'/\beta = 1$ for $\beta = 1$, since $\beta = 1$ represents the limit where concerted catalysis has ceased and has been replaced by specific base catalysis by the hydroxide ion.

The considerations above are based on the assumption that Brønsted plots for general base catalysis are linear in the pK range -2 to 16. There are, however, indications from energy contour diagrams that this may not always be the case. Three reaction coordinates, a, b and c for a concerted class n mechanism are shown in Fig. 7: a represents a stable carbonyl addition compound characterized by a small β and a positive value for β_{lg}; b represents an addition compound of intermediate stability ($\beta \simeq 0.5$, $\beta_{lg} \simeq 0$); c represents an unstable addition compound ($\beta > 0.5$, $\beta_{lg} < 0$).[7] The introduction of stronger base catalysts (B in Fig. 7) will raise (destabilize) the left-hand side of the figure compared with the right-hand side, thus causing a movement of the transition state (saddle point) towards the lower left corner, parallel to the reaction coordinate (a Hammond effect). Simultaneously, a perpendicular effect (an anti-Hammond effect) will tend to slide the transition state downhill towards the lower right
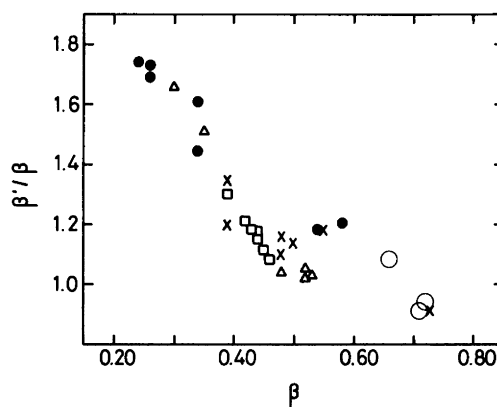

Fig. 6. Plots showing the variation in positive deviation of points for hydroxide catalysis from Brønsted plots for general base catalysis, as indicated by β'/β versus β (see text).
● Decomposition of formaldehyde hydrate and hemiacetals.[6] × Decomposition of acetaldehyde hydrate and hemiacetals.[7] △ Data from this work. □ Dehydration of benzaldehydes.[14] ○ Decomposition of hemiacetals of α-bromoacetophenones.[10]
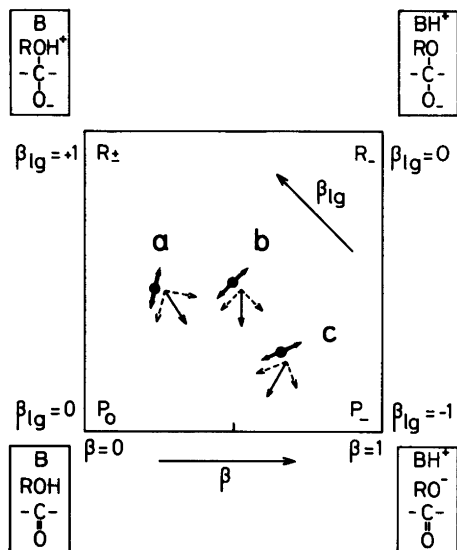
Fig. 7. Reaction coordinate—energy contour diagram for the general-base-catalyzed reactions of alcohols and water with carbonyl compounds (class n mechanism). The x and y axes represent proton transfer and C—O bond formation/breaking as measured by β and ϱ, respectively. A diagonal axis y' represents charge development on the central oxygen atom, as measured by β_{lg}.

corner. The resulting movements of the transition states are shown by the small arrows in the figure. It is now seen from Fig. 7 that only little change in β is expected for carbonyl adducts of intermediate stability (situation *b*), due to almost complete compensation of the parallel and perpendicular effects on the transition state in this situation. This could explain the fact that good linearity has been observed experimentally for many base-catalysed carbonyl addition reactions over relatively wide pK ranges.[12] However, according to Fig. 7, upward curvature might be expected in Brønsted plots for stable adducts (situation *a*), whereas downward curvature will occur for very unstable species (situation *c*).

There is not much experimental evidence so far to show curvature in Brønsted plots according to Fig. 7. Since the effects will probably be small for most common carbonyl reactions, this will require very accurate data and studies over a relatively wide pK range. The general-base-catalyzed mutarotation of glucose[12] and possibly also the general-base-catalyzed dehydration of formalde-

hyde[6] are examples which have been claimed to exhibit Brønsted plots with slight upward curvature, as expected from Fig. 7.

Although we have investigated a pK range beyond the pK corresponding to carboxylate ions (Fig. 5), our data for base-catalyzed breakdown of ethyl hemiacetals and hydrates of three benzaldehydes fail to show significant sign of curvature. An explanation for this might be that substances of more extreme (high or low) stability than studied here are needed to observe such effects.

It is interesting, however, that relatively large changes in β_{lg}, resulting mainly from vertical movement of the transition state in Fig. 7 as the catalyst is varied, have been observed for the addition of water and alcohols to formaldehyde[6] and acetaldehyde.[7] The changes in β_{lg} follow closely the direction indicated by the resultant arrow in Fig. 7 and may illustrate the usefulness of this type of diagram in describing variations in transition state structure.

Since the Brønsted plots for base catalysis of the reactions studied here seem to be linear within experimental error, there is no doubt that the points for hydroxide catalysis do not belong to these plots but fall on separate plots as shown in Fig. 5, indicating a mechanism in which the leaving group (HO$^-$, RO$^-$) is expelled without being partially protonated in a concerted mechanism. This means that large and negative β_{lg} values are expected for such leaving groups, and this has been confirmed experimentally.[6,7] This reaction can be described by a vertical reaction coordinate on the right-hand side of Fig. 7 (not shown), and it takes place because there is no thermodynamic advantage in protonation of the leaving group by water acting as a general acid catalyst.[7] Since the non-concerted specific base pathway exists in these reactions and is by far the most dominant mechanism at high pH, the concerted mechanism is not enforced by too short lifetimes of the intermediates at corner P$_-$ in Fig. 7.

We presume that we are dealing here with systems for which general and specific base catalysis occur as separate, but parallel (concurrent) reaction paths. Since the hydroxide ion is such an overwhelmingly strong base compared with other (general) bases, this ion will dominate specific catalysis completely even at very low concentrations, although it cannot be excluded that a small

fraction of the protons could be transferred directly from the adduct to the general base, still with no assistance from the conjugate acid of the general base in the breakdown of the adduct anion. The general base would thereby also act as a specific base catalyst.

To summarize, in a solution containing a general base catalyst the relative importance of the two possible pathways will depend in a relatively simple manner upon a strength of the general base and the pH of the solution, i.e. according to and depending upon the relative positions of the two types of Brønsted plots in Fig. 5. It is interesting to notice from Fig. 5 the enormous enhancements in reaction rates caused by concerted, general base catalysis at pH values lower than 10–12. Thus, for the decomposition of 3,4-dichlorobenzaldehyde ethyl hemiacetal, for example, the observed rate constant due to concerted, general base catalysis by the acetate ion in a 1 M 1:1 acetate buffer is ca. 0.1 s^{-1}. Had there been no concerted pathway, the observed rate constant due to specific catalysis by the hydroxide ion, now being the only pathway, would have been as low as $\simeq 10^{-6}$ s^{-1}, a 10^5-fold difference.

References

1. Faurholt, C. *J. Chim. Phys. 21* (1924) 499; *Ibid. 22* (1925) 1.
2. Bell, R. P. *The Proton in Chemistry,* 2nd ed., Chapman and Hall, London 1973.
3. Bender, M. L. *Mechanism of Homogeneous Catalysis from Protons to Proteins,* Wiley, New York 1971.
4. Jencks, W. P. *Catalysis in Chemistry and Enzymology,* McGraw-Hill, New York 1969.
5. Stewart, R. *The Proton: Applications to Organic Chemistry, Organic Chemistry, a Series of Monographs,* Academic Press, London 1985, Vol. 46.
6. Funderburk, L. H., Aldwin, L. and Jencks, W. P. *J. Am. Chem. Soc. 100* (1978) 5444.
7. Sørensen, P. E. and Jencks, W. P. *J. Am. Chem. Soc. 109* (1987) 4675.
8. (a) Richard, J. P. and Jencks, W. P. *J. Am. Chem. Soc. 106* (1984) 1396; (b) Bernasconi, C. F. and Gandler, J. R. *J. Am. Chem. Soc. 100* (1978) 8117.
9. Cordes, E. H. and Bull, H. G. *Chem. Rev. 74* (1974) 581.
10. (a) Sørensen, P. E., Pedersen, K. J., Pedersen, P. R., Kanagasabapathy, V. M. and McClelland, R. A. *J. Am. Chem. Soc. In press*; (b) Sørensen, P. E., Løgager, T., Kanagasabapathy, V. M. and McClelland, R. A. *Bull. Soc. Chim. France.* In press.
11. Jencks, W. P. *Chem. Rev. 85* (1985) 511.
12. Nielsen, H. and Sørensen, P. E. *Acta Chem. Scand., Ser. A 38* (1984) 309.
13. Kresge, A. J. and Tang, Y. C. *J. Org. Chem. 42* (1977) 757.
14. (a) McClelland, R. A. and Coe, M. *J. Am. Chem. Soc. 105* (1983) 2718; (b) Przystas, T. J. and Fife, T. H. *J. Am. Chem. Soc. 103* (1981) 4884.
15. Bell, R. P. and Sørensen, P. E. *J. Chem. Soc., Perkin Trans. 2* (1976) 1594.
16. Lowry, T. M. and John, W. T. *J. Chem. Soc. 97* (1910) 2634.
17. Levi, A., Modena, G. and Scorrano, G. *J. Am. Chem. Soc. 96* (1974) 6885.
18. Jencks, W. P., Brant, S. R., Gandler, J. R., Fendrich, G. and Nakamura, C. *J. Am. Chem. Soc. 104* (1982) 7045.
19. Fox, J. P. and Jencks, W. P. *J. Am. Chem. Soc. 96* (1974) 1436.
20. Sander, E. G. and Jencks, W. P. *J. Am. Chem. Soc. 90* (1968) 4377.
21. Sørensen, P. E. *Acta Chem. Scand., Ser. A 28* (1976) 673.
22. Harder, P., Sørensen, P. E. and Ulstrup, J. *J. Electroanal. Chem. 77* (1977) 109.
23. Sørensen, P. E. *Acta Chem. Scand. 26* (1972) 3357.