A Kinetic and Thermodynamic Study of the Addition of Methoxide Ion to Substituted Benzaldehydes

By **Mohini Arora** and **Brian G. Cox**, Department of Chemistry, University of Stirling, Stirling FK9 4LA, Scotland
Poul E. Sørensen,* Chemistry Department A, The Technical University of Denmark, DK-2800 Lyngby, Denmark

Reaction rates have been investigated for the addition of methoxide ion to eleven substituted benzaldehydes in methanol at 25 °C. Thermodynamic parameters for the addition of both methanol and methoxide have also been determined, using a combination of n.m.r. and calorimetric data. The reaction rates are somewhat higher, and the adducts more stable than those of the corresponding reactions in water. The forward rates for the addition reaction are again considerably more sensitive to the effect of substituents than the reverse rates. The results are discussed in terms of a two step process, (1) formation or breaking of the C–O bond (sensitive to substitution) and (2) reorganization of the solvent (insensitive to substitution). It is concluded that the transition state for the reaction resembles the final products with respect to C–O bond formation, but that the state of solvation of the transition state corresponds to that of the reactants.

RECENT kinetic and thermodynamic experiments on the addition of hydroxide ions to a series of substituted benzaldehydes [1] gave interesting results concerning the role of the solvent (water) for such reactions. It was suggested that the reaction can be described essentially as a two step process, C–O bond formation and reorganization of the solvent, with the state of the C–O bonds in the transition state closely resembling those of the product, but the state of solvation of the transition state resembling that of the reactants.

In order to investigate this mechanism further, we have studied the kinetic and thermodynamic behaviour of a closely related reaction, the addition of methoxide to substituted benzaldehydes in methanol. Kinetic measurements have been made using a conventional temperature-jump technique with optical detection. Equilibrium constants and reaction enthalpies for the addition of both methanol and methoxide to the benzaldehydes have been determined using a combination of n.m.r. and calorimetric measurements. Equilibrium data for some of the compounds studied have recently been reported by Crampton.[2]

EXPERIMENTAL

Benzaldehydes.—The compounds used were all commercial samples, and their characteristics are given in Table 1.

TABLE 1

Compounds investigated

Benzaldehyde	Purification	$\lambda_{max.}$nm
H	*a*	245
4-Cl	*b*	255
4-Br	*b*	258
3-Cl	*a*	244
3,4-Cl_2	*b*	255
2-Cl	*a*	248
2,4-Cl_2	*b*	260
3-NO_2	*c*	261
3-NO_2-4-Cl	*c*	245
4-NO_2	*c*	265
2-Cl-5-NO_2	*c*	270

[a] Distilled *in vacuo*. [b] Sublimed. [c] Recrystallized from water.

The $\lambda_{max.}$ values given refer to $\pi \longrightarrow \pi^*$ transitions in the benzaldehyde molecules, and are for neutral solutions in methanol at 25 °C.

Methanol was purified by distillation from $Mg(OMe)_2$ as described by Lund and Bjerrum,[3] and a stock solution of sodium methoxide in methanol was obtained by dissolution of AnalaR grade sodium. Methoxide concentrations were established by titration against standard acid.

As methoxide is a strong base and dry methanol is hygroscopic, the possibility of contact between solutions and the atmosphere (H_2O, CO_2) was reduced considerably by using burettes fitted with drying tubes, containing H_2O- and CO_2-absorbing material, and standard flasks flushed with dry nitrogen before use. Dried AnalaR sodium bromide was used to adjust the ionic strength (and hence the cell resistance) in the temperature-jump experiments.

Methan[^{2}H]ol (Merck, >99% D) and spectroscopic grade deuteriochloroform were used without further purification.

Equilibrium Measurements.—It has recently been demonstrated that n.m.r. can be used to obtain formation constants for the addition of methanol and methoxide ion to benzaldehydes.[2] The results are obtained from integrated peak areas, combined with the effect of methoxide ion on the observed chemical shifts. In principle, this method can also be used to obtain enthalpies of reaction if the measurements are carried out at a range of temperatures. In practice, however, we have found it considerably more convenient to use a combination of n.m.r. and calorimetric measurements as described below to determine the equilibrium constants and enthalpies of reaction.

N.m.r. spectra of equilibrated solutions of the benzaldehydes in methanol (*ca.* 0.2M) were recorded at 10° intervals from 0 to 50 °C, using a Perkin-Elmer R32 spectrometer, fitted with a thermostatted probe. Temperature control was to ±0.5 °C. N.m.r. spectra of the aldehydes in deuteriochloroform were used as an aid to the interpretation of the spectra.

Heats of solution of the aldehydes in pure methanol and methanol containing various methoxide concentrations were determined calorimetrically with a Tronac 450 solution calorimeter. Aldehyde concentrations were *ca.* 5×10^{-3}—10^{-2}M. As equilibration of the benzaldehydes in pure methanol was relatively slow, catalytic traces of methoxide ($< 10^{-5}$M) were usually added to these solutions and it was checked that the concentration of methoxide was small enough to have no observable effect on the measured heats of solution.

Kinetic Measurements.—These were made with a Durrum-Gibson temperature-jump spectrophotomer or a Garsching temperature-jump instrument (at the Max-Planck-Institut, Göttingen), the latter instrument being used primarily for the more reactive aldehydes. Methoxide concentrations varied between 5×10^{-3} and 10^{-1}M. Benzaldehyde concentrations were *ca.* 10^{-5}—10^{-4}M. The solutions were prepared immediately prior to use, to avoid complications that may arise from slow side reactions between methoxide and the aldehydes. The ionic strength was maintained at *0.1* or *0.2* by addition of NaBr to keep the cell resistance sufficiently low and to ensure a known temperature jump. Measured relaxation times refer to a final solution temperature of 25 (±0.5) °C.

RESULTS

Equilibria and Enthalpies of Reaction.—If it is assumed that acetal formation in the neutral and alkaline solutions is negligible, the system may be described stoicheiometrically by equations (1) and (2). In all cases. K_2 values were

$$\underset{\text{(A)}}{\text{RCHO}} + \text{MeO}^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{\text{(B)}}{\text{RCH(OMe)O}^-},$$

$$K_1 = \frac{k_1}{k_{-1}} = \frac{[\text{B}]}{[\text{A}][\text{OMe}^-]},\ \Delta H_1 \quad (1)$$

$$\underset{\text{(A)}}{\text{RCHO}}(+\text{MeOH}) \underset{\text{slow}}{\rightleftharpoons} \underset{\text{(C)}}{\text{RCH(OMe)OH}},$$

$$K_2 = \frac{[\text{C}]}{[\text{A}]},\ \Delta H_2 \quad (2)$$

obtained from n.m.r. measurements, and ΔH_2 from the temperature dependence of K_2. The general procedure is illustrated for 4-nitrobenzaldehyde, the n.m.r. spectrum of an equilibrated solution of 4-nitrobenzaldehyde in CH_3OD at 10 °C being shown in Figure 1. The singlet at δ 10.1 derives from the aldehyde proton of the free aldehyde and that at δ 5.6 from the corresponding proton of the hemiacetal. The signals in the range δ *ca.* 7.5—8.5 correspond to the four aromatic protons of the free aldehyde and the hemiacetal. These are seen to consist of two partially overlapping quartets, with the right half of the hemiacetal quartet (δ 7.7 being sufficiently clear to be useful in determining K_2). Three different methods were used to estimate K_2: (i) the ratio of the areas of the two singlet peaks; (ii) comparison of the area of the formyl proton peak of the free aldehyde at δ 10.1 with the separated half area of the hemiacetal aromatic peaks; and (iii) comparison of the formyl proton peak of the free aldehyde with the total aromatic signal (free aldehyde and hemiacetal). The three methods give values of 6.9, 6.0, and 6.0 respectively for K_2. Generally, however, when the spectra were run in CH_3OH, it was not possible to use the hemiacetal singlet for quantitative measurements as it overlaps with the OH signal for methanol itself.

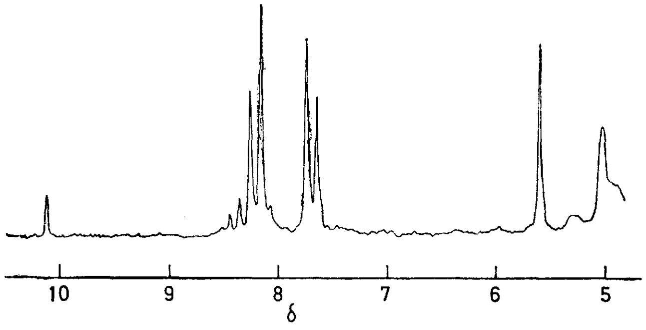

FIGURE 1 N.m.r. spectrum of 0.02M-4-nitrobenzaldehyde in deuteriated methanol at 10 °C

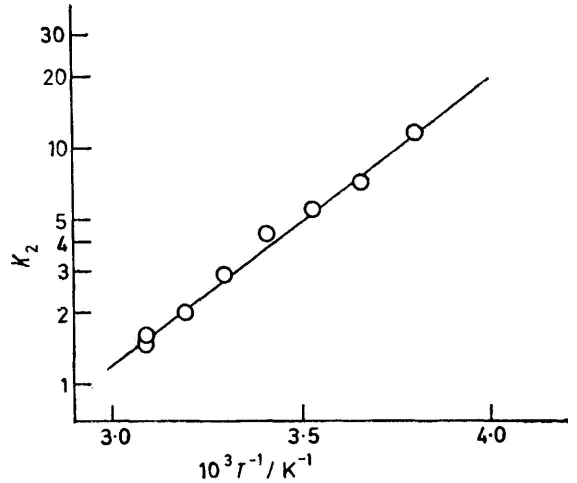

FIGURE 2 K_2 plotted against T^{-1} for 4-nitrobenzaldehyde in methanol

Analogous methods were used for all the benzaldehydes, although the spectra of the aromatic protons varied considerably depending upon the substituents present. From spectra in CH_3OD, the consistency of at least two methods, including the direct method using the two singlets could be checked. For all compounds, except the 2-chloro and 3-nitro-4-chloro derivatives, the different methods were internally consistent to within ±10%. For these two compounds, comparison of the singlet for the aldehydic proton with the total aromatic signal gave results significantly higher than those obtained from the direct comparison of the singlet areas. It was found also that for these compounds, the relative areas of the formyl and the aromatic proton signals in deuteriochloroform (where, of course, no hemiacetal formation takes place) differed from the expected value. This presumably results from selective saturation effects.[4] We have assumed the values obtained from the direct comparison of the singlet areas to be correct, and have applied an appropriate correction factor to the values obtained in CH_3OH, based on a comparison of the formyl singlet with the total aromatic signal.

Values of K_2 and ΔH_2 obtained from the n.m.r. measurements for the various benzaldehydes are listed in Table 2. Figure 2 shows a plot of K_2 against T^{-1} for 4-nitrobenzaldehyde.

The equilibrium constants, K_1, and enthalpies of reaction, ΔH_1, for formation of the methoxide adduct [equation (1)] were obtained from calorimetric measurements. It can be readily shown that the observed enthalpies of solution of the benzaldehyde in a methoxide solution [ΔH_{obs} (1)] and in pure methanol [ΔH_{obs} (2)] are given by equations (3) and

$$\Delta H_{\text{obs}}(1) = \Delta H_s + \frac{K_2}{1 + K_2 + K_1[\text{MeO}^-]} \cdot \Delta H_2 + \frac{K_1[\text{MeO}^-]}{1 + K_2 + K_1[\text{MeO}^-]} \cdot \Delta H_1 \quad (3)$$

$$\Delta H_{\text{obs}}(2) = \Delta H_s + \frac{K_2}{1 + K_2} \cdot \Delta H_2 \quad (4)$$

(4) respectively. In equations (3) and (4), ΔH_s represents the enthalpy of solution in the absence of any reaction with methanol and methoxide, and the remaining terms represent the heat changes resulting from the subsequent reactions [equations (1) and (2)]. ΔH_s is assumed to be independent of the methoxide concentration in the range studied ($\leqslant$0.4M). Subtracting equation (4) from (3) and taking reciprocals gives equations (5) and (6). Thus a plot of $(\Delta\Delta H_{obs})^{-1}$ against $[\text{MeO}^-]^{-1}$ should be linear, with slope $A(1 + K_2)$ and intercept AK_1, and hence, using K_2 from

$$\frac{1}{\Delta\Delta H_{obs}} = \frac{1}{\Delta H_{obs}(1) - \Delta H_{obs}(2)} = AK_1 + \frac{A(1 + K_2)}{[\text{MeO}^-]} \quad (5)$$

$$A = (1 + K_2)/[K_1K_2(\Delta H_1 - \Delta H_2) + K_1\Delta H_1] \quad (6)$$

Table 2, $K_1 = (1 + K_2) \cdot (\text{intercept})/(\text{slope})$. It is also seen that $\Delta H_1 = (\text{intercept})^{-1} + K_2\Delta H_2/(1 + K_2)$.

TABLE 2

Equilibrium constants, K_2, and enthalpies, ΔH_2, for hemiacetal formation of substituted benzaldehydes in methanol

	K_2[a] at temperature (°C)						
Aldehyde	0	10	20	30	40	50	ΔH_2/kJ mol^{-1}
4-Cl	0.40	0.34	0.28	0.26	0.23	0.16	-12 ± 2
3,4-Cl_2	1.3	1.4	0.98	0.63	0.51	0.44	-19 ± 3
2-Cl	1.7	1.3	1.1	0.62	0.65	0.50	-18 ± 2
2,4-Cl_2	5.1	3.2	2.3	1.6	1.2	0.93	-25 ± 1
3-NO_2	—	3.6	3.2	2.7	1.4	1.2	-23 ± 4
3-NO_2-4-Cl	8.0	4.5	3.5	2.3	1.7	1.2	-27 ± 1
4-NO_2 [b]	7.1	5.5	4.3	2.9	2.0	1.5	-24 ± 1
2-Cl-5-NO_2			16 [c]				-27 [d]

[a] Estimated uncertainty ±10%. [b] $K_2 = 12$ at -10 °C. [c] At 25 °C. [d] Estimated value.

Calorimetric results for 4-nitrobenzaldehyde, plotted according to equation (5) are shown in Figure 3. From the slope and intercept, values of $K_1 = 55$ dm^3 mol^{-1} and $\Delta H_1 = -27$ kJ mol^{-1} are obtained. The value of K_1 may be compared with a value of $K_1 = 50(\pm 10)$ dm^3 mol^{-1} reported by Crampton [2] from n.m.r. measurements in methoxide solutions. Similar agreement between the two methods was obtained for the 3-nitro (K_1 21 and 23 dm^3 mol^{-1} [2]) and the 4-chloro derivatives (K_1 0.8 and 0.80 dm^3 mol^{-1} [2]) which have also been studied by Crampton. The results for the various benzaldehydes are summarized in Table 3.

TABLE 3

Thermodynamic data for the addition of methoxide (K_1,ΔH_1) and methanol (K_2,ΔH_2) to substituted benzaldehydes at 25 °C

Aldehyde	−Intercept [a]/ kJ^{-1} mol	−Slope [a]/ kJ^{-1} mol^2 dm^{-3}	K_2 [b]	K_1 [b]/ mol^{-1} dm^3	$-\Delta H_2$/kJ mol^{-1}	$-\Delta H_1$/kJ mol^{-1}
H			(0.090)	(0.14)		
4-Cl	0.048	0.074	0.26 (0.24)	0.8 (0.80)	12 ± 2	23
4-Br			(0.27)	(0.93)		
3-Cl			(0.45)	(2.2)		
3,4-Cl_2	0.048	0.023	0.8	3.7	19 ± 3	29
2-Cl	0.060	0.024	0.9	4.7	18 ± 2	25
2,4-Cl_2	0.062	0.016	2.0	12	25 ± 1	33
3-NO_2	0.103	0.017	2.5 (2.1)	21 (23)	23 ± 4	26
3-NO_2-4-Cl	0.096	0.013	2.8	27	27 ± 1	30
4-NO_2	0.109	0.0082	3.2 (3.0)	55 (50)	24 ± 1	27
2-Cl-5-NO_2	0.150	0.0087	16	280	27 [c]	32

[a] Equations (5) and (6). [b] Values in parentheses from ref. 2. [c] Estimated value.

Kinetic Measurements.—The direct formation of the hemiacetal *via* reaction (2) is too slow to contribute to the observed reaction rate. However, it is formed indirectly *via* the hemiacetal anion, with which it may be assumed to be in rapid equilibrium. The standard relaxation treatment applied to this system,[1] yields equation (7), where τ

$$k_1 = \frac{\tau^{-1}(K_2 + K_1[\text{MeO}^-])}{[\text{MeO}^-](1 + K_2 + K_1[\text{MeO}^-])} \quad (7)$$

is the observed relaxation time, and k_1 the rate constant for the forward reaction in equation (1). The corresponding rate constant for the reverse reaction, k_{-1}, may be determined from $k_{-1} = k_1/K_1$. The validity of equation (7) was tested for each of the aldehydes (except 2-chloro-5-nitro) by measuring τ^{-1} at several different methoxide concentrations. k_1 Values calculated from equation (7) showed no trends with methoxide concentration, and were constant to within ±10%. The results are summarized in Table 4.

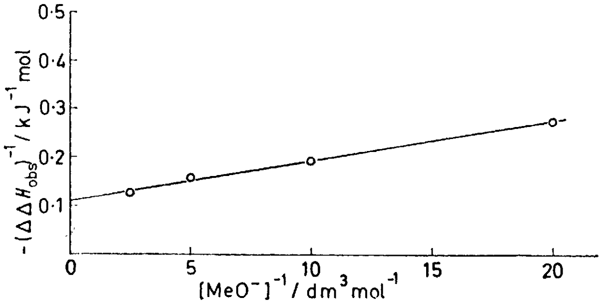

FIGURE 3 Plot of $-(\Delta\Delta H_{obs})^{-1}$ against $[\text{MeO}^-]^{-1}$ [equation (3)] for 4-nitrobenzaldehyde in methanol at 25 °C

DISCUSSION

Equilibria.—Thermodynamic data for the addition of methoxide and methanol to the benzaldehydes, calculated from the various K_1, K_2, and enthalpies of reaction, are given in Table 5. The reactions are in all cases exothermic, with ΔH becoming more negative as the stability of the adduct increases. Although a considerable amount of scatter is found, there is a general tendency towards increasingly more negative entropies for the addition of methanol as the electron-withdrawing power of the substituents increases, and *vice versa* for methoxide addition. This is not unexpected, if the changes in the entropy terms reflect the changes in the interactions of the hemiacetal and hemiacetal anion respectively with the solvent methanol. Thus increasing electron withdrawal increases the acidity and hence the hydrogen bonding ability of the hemiacetal, causing an increased interaction with the solvent, and correspondingly decreases the basicity and hydrogen bond acceptor ability of the hemiacetal anion.

The acidity of the hemiacetals, K_a, may be readily obtained from equation (8), where K_{MeOH} ($= 10^{-16.7}$ mol^2 dm^{-6})[5] is the ionic product of methanol. pK_a

$$K_a = K_1 K_{MeOH}/K_2 \qquad (8)$$

Values for the various hemiacetals are also included in Table 5. Where comparison is possible, they are 3—4 log units larger than the corresponding values for the benzaldehyde hydrates in water,[1] this difference being fairly typical for species such as carboxylic acids and phenols in water and methanol.[6] The substituent effects on the ionization of the hemiacetals parallel those for benzoic acids in methanol,[7] the p-NO$_2$ derivatives, for example, of both compounds being one log unit more acidic than the corresponding unsubstituted acid.

Values of $(\Delta H_1^0 - \Delta H_2^0)$ and $T(\Delta S_1^0 - \Delta S_2^0)$, also included in Table 5, differ from ΔH^0 and $T\Delta S^0$ for the acid dissociation reaction of the hemiacetals by the (constant) thermodynamic parameters for the ionization of methanol. Their variation with substituents may also be compared with corresponding changes for similar reactions such as the dissociation of substituted benzoic acids. The change in pK_a with substituent for a series of benzoic acids in water is found to be due mainly to entropy effects,[8] which means that the variation in the enthalpy of breaking of the O–H bond is effectively compensated for by the variation in the enthalpy of hydrogen bond formation between the anions and the solvent.[9] For our system a similar effect is observed although the influence of the entropy changes seems to be smaller. This may be the result of the lower hydrogen bond capacity of methanol compared with water.

TABLE 4

Rates of addition of methoxide to substituted benzaldehydes at 25 °C

Aldehyde	H	4-Cl	4-Br	3-Cl	3,4-Cl$_2$	2-Cl	2,4-Cl$_2$	3-NO$_2$	3-NO$_2$,4-Cl	4-NO$_2$	2-Cl, 5-NO$_2$
$10^{-3}\ k_1$/mol^{-1} dm^3 s^{-1}	6.1	30	35	58	118	152	223	327	595	430	1 550
$10^{-3}\ k_{-1}$/s^{-1}	44	38	38	26	32	32	19	16	22	7.8	5.5
K_1/mol^{-1} dm^3	0.14	0.80	0.93	2.2	3.7	4.7	12	21	27	55	280

TABLE 5

Thermodynamic parameters for the addition of methanol and methoxide ions to benzaldehydes at 25 °C

Compound	$\Delta G_1°$ [a]/ kJ mol^{-1}	$\Delta H_1°$ [a]/ kJ mol^{-1}	$T\Delta S_1°$ [a]/ kJ mol^{-1}	$\Delta G_2°$ [b,c]/ kJ mol^{-1}	$\Delta H_2°$ [b]/ kJ mol^{-1}	$T\Delta S_2°$ [b,c]/ kJ mol^{-1}	pK_a [d]	$\Delta H_1° - \Delta H_2°$/ kJ mol^{-1}	$T(\Delta S_1° - \Delta S_2°)$/ kJ mol^{-1}
H	4.8_7			13.9			16.5		
4-Cl	0.5_5	−23	−24	11.3	−12	−23	16.2	−11	−1
4-Br	0.1_8			11.2			16.2		
3-Cl	-1.9_6			9.9_3			16.0		
3,4-Cl$_2$	-3.2_4	−29	−26	8.5_0	−19	−28	16.0	−10	2
2-Cl	-3.8_4	−25	−21	8.2_1	−18	−26	16.0	−7	5
2,4-Cl$_2$	-6.1_6	−33	−27	6.2_3	−25	−31	15.9	−8	4
3-NO$_2$	-7.5_5	−26	−18	5.6_8	−23	−29	15.8	−3	11
3-NO$_2$,4-Cl	-8.1_7	−30	−22	5.4_0	−27	−32	15.7	−3	10
4-NO$_2$	-9.9_4	−27	−17	5.0_7	−24	−29	15.5	−3	12
2-Cl, 5-NO$_2$	-13.9_7	−32	−18	1.0_8	−27	−28	15.5	−5	10

[a] Addition of MeO$^-$ [equation (1)]. [b] Addition of MeOH [equation (2)]. [c] Corrected to a standard state of 1 mol dm^{-3}. [d] pK_a of the hemiacetal [equation (8)].

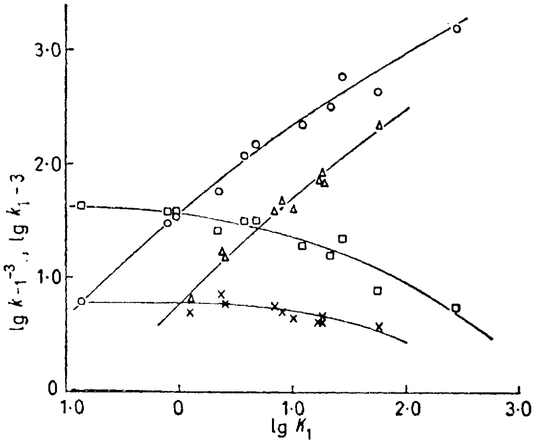

FIGURE 4 Free energy relationships for the addition of MeO$^-$ and HO$^-$, respectively, to substituted benzaldehydes: ○, k_1 (MeO$^-$); △, k_1 (HO$^-$); □, k_{-1} (MeO$^-$); ×, k_{-1} (HO$^-$). Values taken from Table 6 and from ref. 1.

Kinetics.—A plot of lg k_1 and lg k_{-1} against lg K_1 (using values from Table 4) is shown in Figure 4. For comparison, the corresponding points for the addition of hydroxide ions in water[1] are also shown. It can be seen from Figure 4 that the slopes of the curves, which correspond to the Brønsted α or β values for proton transfer reactions, approach 1 and 0 for the forward and reverse reactions respectively for both reactions, *i.e.* the forward rate is considerably more sensitive to the effects of substitution than the reverse reaction. The rate constants for formation (k_1) and dissociation (k_{-1}) are, however, somewhat higher for the addition of methoxide. The plots are also noticeably more curved for the addition of methoxide, but this may only reflect the larger range of K_1 values and substituents studied.

The much greater sensitivity of the forward reaction to the effects of substitution suggests that the transition state is very product like. The forward reactions are, however, in all cases quite strongly exothermic, suggesting a reactant like transition state. Bell and Sørensen [1] pointed out that this apparent contradiction could be resolved if the reaction proceeds by what is essentially a two step mechanism, the first step consisting of C–O bond formation (sensitive to substitution), and the second step reorganization of the solvent (relatively insensitive to substitution). The present results in methanol are clearly in accord with this suggestion. The reaction co-ordinate for such a system is represented in Figure 5, in which the reaction is shown as a two step reaction with a genuine intermediate being formed. This diagram is a simplified picture of the square potential energy diagram applied by Jencks [10] to a number of carbonyl group addition reactions, which may be described essentially by two parameters [*e.g.* the C–N and H–A bond orders for the acid (HA) catalysed addition of N to a carbonyl group]. In Figure 5, parabolae I and III represent potential energy curves for the reactants ($\mathrm{RCHO + MeO^-}$) and products [$\mathrm{RCH(OMe)O^-}$] respectively, and curve II that of the intermediate [$\mathrm{RCH(OMe)O^-}$] which differs from the product by having a solvation structure similar to that of the reactants.[1] When curve I is displaced vertically relative to curve II as a result of substitution, the endothermicity of reaction I ⟶ II should give rise to free energy relation coefficients (Figure 4) close to 1.[11] The overall energy change during the reaction, however, depends upon the relative positions of curves I and III.

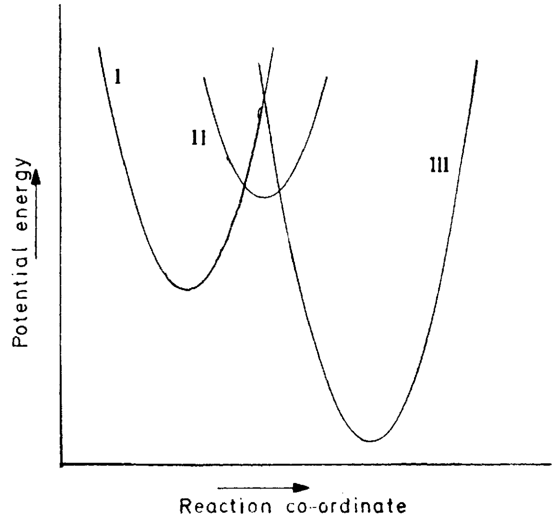

FIGURE 5 Potential energy diagrams symbolizing qualitatively the suggested mechanism for the addition of a strong nuclophile to benzaldehydes: I, reactants; II, intermediate; III, products

The above explanation relies upon the assumption that the solvent reorganization step should be relatively insensitive to substitution, *i.e.* curve II is not appreciably displaced vertically relative to III as a result of substitution. This assumption is not unreasonable, as the free energy of solvent reorganization should be mainly dependent upon the basicity of the hemiacetal anion. As the negatively charged oxygen atom in $\mathrm{R{-}\overset{|}{\underset{|}{C}}{-}O^-}$ is one atom further removed from the substituent than the carbonyl carbon atom which determines the reactivity of the nucleophiles towards the carbonyl group, this is expected to be less effected by substituents. This difference is reflected in the results in Table 5, which show that over the range of substituents studied, K_A for the hemiacetals varies only 10 fold, while K_1 varies by a factor of 2 000.

It is difficult to attribute the greater reactivity of the system in methanol as reflected in the larger K_1 and K_2 and faster rates of addition and dissociation of the methoxide ion compared with the hydroxide ion to any single factor. The effects of the solvent are clearly of some importance, as, for example, the benzaldehydes are considerably more soluble in methanol than in water. The greater curvature of the free energy plots and the greater sensitivity of the dissociation reaction (k_{-1}) to substitution (Figure 4) in methanol are, however, not inconsistent with the fact that the products are more stable in methanol.

In conclusion, the results of the present study are consistent with, and tend to confirm the conclusion reached by Bell and Sørensen [1] in their study of the addition of hydroxide ions to benzaldehydes, namely that the development of the carbon oxygen bonds, and the reorganization of the solvent develop at different rates as the reactions proceed. Experiments are at present in progress to study the kinetics of the addition of the weaker uncharged nucleophiles methanol and water, which might be expected to show different behaviour with respect to the involvement of the solvent.

We thank the Max-Planck-Institut für biophysik. Chemie, Göttingen, for the use of their temperature-jump equipment and Statens naturvidenskabelige Forskningsraad for a travel grant for P. E. S.

[8/420 *Received, 8th March*, 1978]

REFERENCES

[1] R. P. Bell and P. E. Sørensen, *J.C.S. Perkin II*, 1976, 1594.
[2] M. R. Crampton, *J.C.S. Perkin II*, 1975, 185.
[3] H. Lund and J. Bjerrum, *Ber.*, 1931, **64B**, 210.
[4] W. A. Anderson, *Phys. Rev.*, 1965, **104**, 850.
[5] G. Brière, B. Crochon, and N. Felici, *Compt. rend.*, 1962, **254**, 4458.
[6] B. W. Clare, D. Cook, E. F. C. Ko, Y. C. Mac, and A. J. Parker, *J. Amer. Chem. Soc.*, 1966, **88**, 1911.
[7] M. Kilpatric and J. H. Elliott, *J. Phys. Chem.*, 1941, **45**, 454, 466, 473.
[8] G. Briegleb and A. Bieber, *Z. Elektrochem.*, 1951, **55**, 250.
[9] W. P. Jencks, 'Catalysis in Chemistry and Enzymology', McGraw-Hill, New York, 1969, p. 313.
[10] W. P. Jencks, *Chem. Rev.*, 1972, **72**, 705.
[11] G. S. Hammond, *J. Amer. Chem. Soc.*, 1955, **77**, 334.