

The Influence of the Solvent on Reaction Velocity

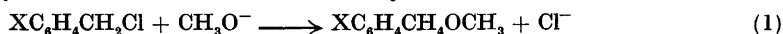
XXXI. The Reaction between Benzyl Chlorides and Methoxide Ion in Dimethyl Sulphoxide-Methanol Mixtures

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The reaction between benzyl chlorides and methoxide ion in methanol is accelerated by dimethyl sulphoxide, especially at high DMSO concentrations. The rate increase at high DMSO concentrations is attributed to an increased activity of the methoxide ion caused by reduced solvation, but probably other factors are more important at low DMSO concentrations. The activation energy decreases continuously as the DMSO concentration is increased, but the frequency factor passes through a minimum. The variation of ΔG^* , ΔH^* , and ΔS^* with solvent composition is discussed. Specific solvent effects are more important than the influence of changes in the dielectric constant of the solvent mixture. Instead of an ether *p*-nitrobenzyl chloride gives *trans*-4-4'-dinitrostilbene. The mechanism of the reaction is discussed.

The reaction between benzyl chlorides and hydroxide ion in acetone-water and dimethyl sulphoxide-water mixtures was discussed in the preceding communication of this series.¹ It was found that the reaction is retarded by acetone but, like many other reactions between a negative ion and an organic molecule, accelerated by dimethyl sulphoxide (DMSO). The present paper records a study of the reaction between benzyl chlorides and methoxide ion,



in methanol and various methanol-dimethyl sulphoxide mixtures. The progress of the reaction can be conveniently followed by titration and the reaction is well suited for solvent effect studies, because there are no solubility restrictions. Other reasons for choosing this reaction for study were that it has received little attention and that a comparison of it with the hydroxide ion reaction of benzyl chlorides could be expected to reveal facts of considerable interest. The solvent pair methanol-dimethyl sulphoxide seemed particularly attractive because the dielectric constant of dimethyl sulphoxide (*ca.* 46) is somewhat larger than that of methanol (*ca.* 34), so that addition of DMSO to the solvent causes an increase in the dielectric constant of the medium,

whereas the dielectric constant of water-DMSO mixtures decreases with increasing DMSO concentration. Thus the changes in the dielectric constant of the medium caused by DMSO are opposite in the two sets of mixtures, whereas the specific solvent effects change in the same direction.

EXPERIMENTAL

The benzyl chlorides were of the same qualities as in the two preceding investigations of this series. Before use, they were distilled at reduced pressure or recrystallized from ethanol (*p*-nitrobenzyl chloride). Dimethyl sulphoxide (Nitroglycerin AB, Gyttop, Sweden) was distilled at reduced pressure and repeatedly crystallized from the melt until its melting point was 18.50°–18.55°. Methanol (Merck AG, *pro analysi*) was dried by the method of Lund and Bjerrum.²

All the solvent mixtures employed in the kinetic experiments were prepared by pipetting the desired volume of methanol or sodium methylate solution into a volumetric flask and filling the flask with DMSO. There is a considerable evolution of heat on mixing; the flasks were left to stand until they had cooled to room temperature, after which they were refilled to the mark with DMSO. The compositions of the solvent mixtures were determined also by weighing. The sodium methylate solutions were prepared from sodium and methanol, the concentrations were determined by titration with hydrochloric acid and adjusted to the desired value by dilution with methanol.

The reactions were carried out in sealed ampoules of Pyrex glass. Equal volumes (4 ml) of 0.1 M organic chloride solution and 0.1 m sodium methylate solution were pipetted into 10-ml ampoules so that the initial concentration of both reactants was 0.05 M. The ampoules were sealed and placed in water thermostats constant to within 0.02°. At suitable time intervals an ampoule was withdrawn, cooled in ice-water and opened, and the reaction mixture was flushed with water into an erlenmeyer flask which contained an excess of 0.02 N hydrochloric acid. The excess of the acid was titrated with 0.02 N sodium hydroxide using cresol red as indicator. As the reaction times were fairly long, as the contents of the tubes were small, and as all operations could be carried out quickly, corrections for the time required for warming and analysing the mixture could be neglected. The vapour volume in the tubes was only 2–3 ml and thus also the changes in the compositions of the mixtures due to evaporation were negligible. The solutions of the reactants were always prepared immediately before the experiment. In solvents containing 80 % or more of DMSO the reactions were very fast. In these cases the reactions were carried out in reaction vessels that have been previously described.³ The data for all runs conformed well with the second-order rate equation.

Several attempts were made to determine the reaction velocity in pure DMSO. Solid sodium methylate obtained by evaporating the methanol from the solution was dissolved in DMSO. Owing to the poor solubility of sodium methylate in DMSO, the instability of the solution and the rapidity of the reaction, the results were only approximate. Satisfactory second-order rate constants were obtained already for the reaction in a mixture containing 2 % methanol.

When benzyl chloride is dissolved in dry methanol, a number of changes may occur. However, preliminary experiments showed that the rate of hydrogen chloride evolution from the solution in pure methanol is only about one fortieth of the rate of the reaction between benzyl chloride and methoxide ion. In solvents containing DMSO the ratio is still much smaller. Thus the uncatalysed solvolysis could be neglected.

All rate constants were corrected for the thermal expansion of the solvent. The expansion coefficients used were taken from a paper of Murto⁴ or calculated from density data reported by Lindberg.⁵ The parameters of the Arrhenius equation were calculated by the method of least squares from the rate constants at four temperatures, the plots of $\log k$ against $1/T$ being linear in all cases.

RESULTS AND DISCUSSION

In Tables 1–5 are given the experimental rate constants, the values of the parameters of the Arrhenius equation, the activation entropies (ΔS^*) and

the free enthalpies of activation (ΔG^*). The values of ΔS^* were calculated from the equation

$$A = e(kT/h) \exp(\Delta S^*/R)$$

for 25°. ΔG^* was obtained from the equation $\Delta G^* = \Delta H^* - T\Delta S^*$, where $\Delta H^* = E - RT$. The properties of the solvent mixtures are given in Tables 6 and 7.

The reaction rates. The rate constants in the tables show that irrespective of the benzyl chloride addition of DMSO to the solvent results in an increase in the reaction rate. This rate enhancement is considerable already at low DMSO concentrations and great at high DMSO concentrations (Fig. 1).

Table 1. The reaction $C_6H_5CH_2Cl + CH_3O^- \rightarrow C_6H_5CH_2OCH_3 + Cl^-$ in DMSO-methanol mixtures.

MeOH ml/l	$10^4 k, \text{l mole}^{-1} \text{sec}^{-1}$						E cal	log A	ΔS^* (25°)	ΔG^* cal
	15.00°	25.00°	32.00°	40.00°	50.00°	60.00°				
1000		0.254 ^a		1.64	4.88	14.1	22 540	11.934	- 5.92	23 715
900		0.433 ^a		2.64	7.81	20.8	21 800	11.628	- 7.31	23 490
800		0.785 ^a		4.43	12.6	32.8	21 000	11.295	- 8.84	23 050
700		1.30		6.76	18.3	48.8	20 220	10.929	-10.51	22 770
650		1.73		8.66	23.4	61.1	19 920	10.832	-10.96	22.600
600		2.54		12.5	33.2	84.2	19 530	10.730	-11.42	22 340
500		4.95		22.9	60.2	148	19 010	10.634	-11.86	21 950
400		11.0	23.0	50.4	124		18 440	10.563	-12.19	21 490
300	9.41	26.8		115	275		17 870	10.534	-12.32	20 950
200	28.9	76.5		319	765		17 380	10.633	-11.87	20 330
100	130 ^b	340	565	1350			16 780	10.844	-10.90	19 440
50	^b	1250	2410	4820			16 640	11.304	- 8.80	18 670
20		3850	7620	14300	^c		16 400	11.611	- 7.40	18 015

^a $t = 24.90^\circ$

^b $20^\circ : k = 0.0780$

^c $45^\circ : k = 2.25$

Table 2. The reaction between *p*-methylbenzyl chloride and methoxide ion in DMSO-methanol mixtures.

MeOH ml/l	$10^4 k, \text{l mole}^{-1} \text{sec}^{-1}$						E cal	log A	ΔS^* (25°)	ΔG^* cal
	20.00°	25.00°	32.00°	40.00°	50.00°	60.00°				
1000		0.487		2.88	8.00	22.2	21 300	11.313	- 8.76	23 320
800		1.15		5.93	16.8	44.4	20 420	11.029	-10.05	22 830
600		3.28		15.8	42.5	106	19 430	10.764	-11.27	22 200
400		12.3	25.6	54.3	136		18 360	10.548	-12.26	21 425
200	49.6	79.6		342	823		17 730	10.905	-10.63	20 310
70	456	716	1410	2870			16 890	11.244	- 9.07	19 005

Table 3. The reaction between *p*-chlorobenzyl chloride and methoxide ion in DMSO-methanol mixtures.

MeOH ml/l	$10^4 k, \text{l mole}^{-1} \text{sec}^{-1}$						<i>E</i> cal	log <i>A</i>	ΔS^* (25°)	ΔG^* cal
	15.00°	25.00°	32.00°	40.00°	50.00°	60.00°				
1000		0.360		2.25	6.94	19.0	22 230	11.864	- 6.24	13 500
800		1.12		6.08	17.2	45.7	20 770	11.276	- 8.92	22 840
600		4.05		19.5	51.0	127	19 240	10.717	-11.48	22 070
400		19.7	40.1	87.1	219		18 460	10.851	-10.87	21 110
200	53.7	151		615	1510		17 610	11.087	- 9.79	19 940

Table 4. The reaction between *m*-chlorobenzyl chloride and methoxide ion in DMSO-methanol mixtures.

MeOH ml/l	$10^4 k, \text{l mole}^{-1} \text{sec}^{-1}$					<i>E</i> cal	log <i>A</i>	ΔS^* (25°)	ΔG^*
	20.00°	25.00°	40.00°	50.00°	60.00°				
1000		0.266	1.59	4.88	13.8	22 110	11.638	-7.27	23 690
500	4.04	7.03	33.3	88.6		19 350	11.038	-10.02	21 750

Table 5. The reaction between *p*-nitrobenzyl chloride and methoxide ion in DMSO-methanol mixtures.

MeOH ml/l	$10^4 k, \text{l mole}^{-1} \text{sec}^{-1}$						<i>E</i> cal	log <i>A</i>	ΔS^* (25°)	ΔG^*
	20.00°	25.00°	32.00°	40.00°	50.00°	60.00°				
1000		0.482		3.15	9.93	29.4	22 980	12.532	-3.18	22 790
800		2.09		12.0	35.4	103	21 730	12.251	-4.47	21 140
600		11.2	25.4	60.2	158		20 290	11.927	-5.95	19 700
500 ^a	18.5	33.2		165			19 750	11.999	-5.62	19 160
400	233	391	477	1750			18 330	12.028	-5.49	17 740

^a 15°: *k* = 0.00106.

Table 6. The solvent mixtures.

MeOH, ml/l	1000	900	800	700	650	600	500
MeOH, wt. %	100	85.5	73.3	61.6	56.3	51.0	41.1
MeOH, mole/l	24.7	22.1	19.7	17.2	16.0	14.7	12.3
<i>x</i> _{DMSO}	0.000	0.065	0.130	0.204	0.242	0.282	0.370
MeOH, ml/l	400	300	200	100	50	20	
MeOH, wt. %	31.9	23.3	15.1	7.3	3.62	1.43	
MeOH, mole/l	9.9	7.4	4.9	2.44	1.22	0.49	
<i>x</i> _{DMSO}	0.467	0.574	0.697	0.838	0.923	0.966	

Table 7. Temperature expansion coefficients of methanol-DMSO mixtures.

MeOH, ml/l	15°	20°	25°	32°	40°	50°	60°	75°
1000	0.994	1.000	1.006	1.015	1.024	1.037	1.051	1.074
900	0.994	1.000	1.006	1.015	1.024	1.037	1.050	1.070
800	0.994	1.000	1.006	1.014	1.024	1.036	1.048	1.068
700	0.994	1.000	1.006	1.014	1.023	1.035	1.047	1.065
600	0.995	1.000	1.005	1.013	1.022	1.034	1.045	1.063
500	0.995	1.000	1.005	1.013	1.021	1.033	1.044	1.061
400	0.995	1.000	1.005	1.012	1.021	1.032	1.043	1.060
300	0.995	1.000	1.005	1.012	1.020	1.031	1.042	1.058
200	0.995	1.000	1.005	1.012	1.020	1.030	1.041	1.056
100	0.995	1.000	1.005	1.011	1.019	1.028	1.040	1.055
0	0.996	1.000	1.005	1.011	1.018	1.024	1.038	1.053

A comparison of data in Tables 1—4 reveals further that the rate of reaction, as also the rates of reaction of benzyl chlorides with hydroxide ion,¹ is a minimum for the unsubstituted compound, a common feature of the reactions of benzyl halides with negative ions.⁶

The activation parameters. An attack of a methoxide ion upon a benzyl chloride molecule results in a dispersal of charge in the transition state. When the relative amounts of the components in a binary solvent mixture are continuously varied, the activation parameters of such reactions pass in general through a maximum in water-rich solvents.^{1,7-9} (In contrast, the activation parameters of many other reactions often show minima for certain solvent compositions). Consequently, it could be expected that the curves plotting

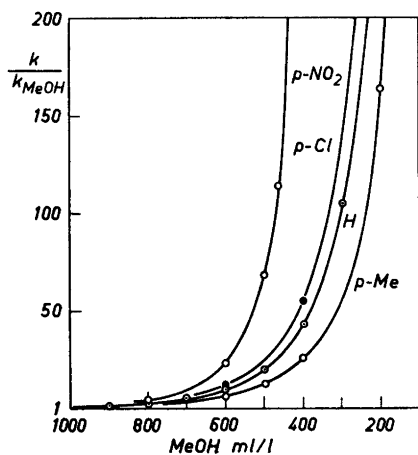


Fig. 1. Variation of k/k_{MeOH} with solvent composition, 25°.

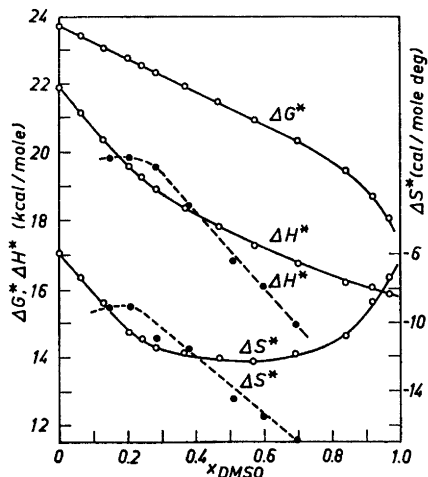


Fig. 2. Benzyl chloride; variation of activation parameters with solvent composition. The dotted lines refer to the reaction between benzyl chloride and hydroxide ion in DMSO-water mixtures.

the parameters of the Arrhenius equation as functions of solvent composition should pass through a maximum. This is not the case, however. Tables 1–4 show that the activation energy decreases continuously with increasing DMSO concentration and that the frequency factor passes through a minimum. The site of this minimum varies somewhat between methanol concentrations of 600 ml and 400 ml per litre, depending on the halide.

Fig. 2 shows the variation of the quantities ΔH^* , ΔS^* , and ΔG^* with solvent composition in the case of benzyl chloride. The curves for the other compounds are very similar in form. Especially conspicuous is the smooth course of the ΔH^* curve. In the range of 0–50 mole % of DMSO, the rate changes are due mainly to changes in ΔH^* , changes in ΔS^* having an opposite effect. When the mole percentage of DMSO is greater than 60, changes in ΔH^* and ΔS^* operate in the same direction, and thus the increase in the reaction rate is particularly strong in this range. The dependence of the activation parameters on solvent composition is discussed in detail later in this paper.

When the composition of the solvent is varied, there is often a general tendency for $\log A$ to a linear increase with E or for ΔS^* to increase linearly with ΔH^* . Cases in which both E and A pass through extrema as the composition of the solvent mixture is gradually changed are, as mentioned above, not uncommon, and in such cases the plot of $\log A$ vs. E usually has two linear parts, one on each side of the extremum. In the present case E decreases continuously with increasing proportion of DMSO in the solvent, but $\log A$ passes through a minimum, and thus no linearity can exist between ΔH^* and ΔS^* over large ranges of solvent mixtures. Yet the plot is linear over the range from pure methanol to a methanol concentration of about 650 ml/l. The form of the plot is seen from Fig. 3.

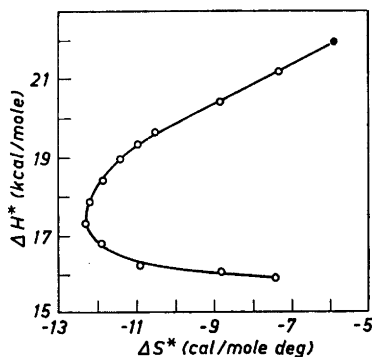


Fig. 3. Benzyl chloride, variation of ΔH^* with ΔS^* with the solvent composition.
● Methanol.

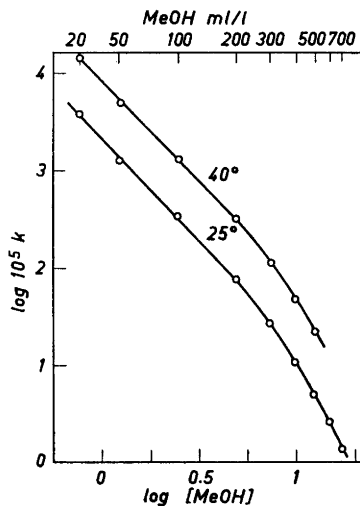


Fig. 4. Benzyl chloride, plot of $\log k$ against $\log [\text{MeOH}]$.

The role of dimethyl sulphoxide. The rate enhancement of reactions involving negative ions caused by DMSO has in general been ascribed to an increased reactivity of the ions as a result of their reduced solvation.^{4,11,12} In pure DMSO anions apparently are poorly solvated,^{10,11,13-15} and one can assume that this might well be true also in solvents rich in DMSO.

The large evolution of heat on mixing DMSO with water¹⁶ and methanol¹⁷ and other facts¹⁸⁻²³ indicate that DMSO has a powerful attraction for these compounds. However, up to rather high DMSO concentrations there is sufficient water or alcohol present to form adducts with DMSO and to completely solvate the hydroxide or methoxide ions in 0.1 M solution as well. Accordingly, if only the decrease in the solvation of the negative ions were operative, the reaction rate should remain nearly unchanged until the concentration of DMSO is rather high. This is, in fact, the case in the alkaline hydrolysis of ethyl benzoate²⁴ and probably also in the reaction between hydroxide ion and benzyl chloride¹ in aqueous DMSO. The rate of alkaline hydrolysis of ethyl benzoate even decreases slightly at first. In both cases as well as in the alkaline hydrolysis of ethyl acetate,¹² the reaction rate increases rapidly when the mole fraction of DMSO exceeds about 0.30, *i.e.* when the ratio of the number of water molecules to the number of DMSO molecules is smaller than 2:1. Already at the said mole fraction, most of the water molecules are probably bound to DMSO as 2:1 complexes and on further addition of DMSO the number of "free" water molecules decreases rapidly and simultaneously the hydroxide ions are deprived of their solvate water. In DMSO-MeOH mixtures the sharp rise in the curve begins when the mole fraction of DMSO is about 0.5 (Fig. 1), after which, practically all the methanol is united with DMSO to 1:1 adducts.

Fig. 4 shows that a very good straight line of slope -2.0 is obtained when $\log k$ is plotted against $\log [\text{MeOH}]$ at high DMSO concentrations, *i.e.* when the concentration of methanol is less than 200 ml per litre. The result is practically similar for the reaction of benzyl chloride with hydroxide ion in aqueous DMSO,¹ where the plot of $\log k$ *vs.* $\log [\text{H}_2\text{O}]$ is a straight line of slope approximately -3 at water concentrations less than 400 ml/l. And the same is true for the reaction between benzyl chloride and thiosulphate ion²⁵ and for alkaline ester hydrolysis^{12,24} in aqueous DMSO. It is likely that the solvation water or methanol molecules are lost, one after the other with increasing DMSO concentration, and so for each solvent composition there is a certain average number of ROH molecules in the solvation shell of the anion. When this number decreases, the activity of the negative ions increases. The log-log relationship shows that their reactivity is proportional to $1/[\text{ROH}]^n$ at high DMSO concentrations, n varying between 1 and 3. The reduction in the number of solvation molecules of a definite ion RO^- is of course always the same if the solvent system is the same, and also the increase in the activity of the anion is the same, but this increase may in different cases cause changes in the rate constant which differ in magnitude, as shown by the above examples. As further examples may be mentioned the reactions of methyl iodide with hydroxide ion in aqueous DMSO and with methoxide ion in DMSO-MeOH mixtures.⁴ The mathematical treatment of the problem is difficult, and for the present we must content ourselves with experimental results.

Table 8. Relative rates, k/k_{MeOH} .

Temp. °C	MeOH in the solvent, ml/l.											
	1000	900	800	700	600	500	400	300	200	100	50	20
Benzyl chloride												
25	1	1.72	3.09	5.10	10.0	19.5	43.1	105	300	1330	4900	14800
40	1	1.62	2.70	4.12	7.62	14.0	30.7	70.1	195	823	2940	8700
50	1	1.57	2.58	3.75	6.80	12.3	24.4	56.3	157	786		
60	1	1.51	2.33	3.46	5.97	10.5	20.9	46.3	116	490		
<i>p</i> -Methylbenzyl chloride												
25	1		2.36		6.74		25.3		163			
40	1		2.13		5.68		18.9		119			
50	1		2.10		5.31		17.0		103			
60	1		2.00		4.74		14.5		86.6			
<i>p</i> -Chlorobenzyl chloride												
25	1		3.11		11.3		54.7		419			
40	1		2.70		8.67		38.7		273			
50	1		2.48		7.35		31.6		218			
60	1		2.40		6.68		28.7		179			
<i>m</i> -Chlorobenzyl chloride												
25	1						26.4					
40	1						20.9					
50	1						18.2					
<i>m</i> -Nitrobenzyl chloride												
25	1		4.34		23.2	68.9	811					
40	1		3.81		19.1	52.4	556					
50	1		3.56		15.9	43.7						
60	1		3.50		13.9	37.0						

As is seen from Tables 1–4, the rates of the reactions of benzyl chlorides with methoxide ion increase considerably already at low DMSO concentrations. The relative rates, k/k_{MeOH} , are given in Table 8. An increased activity of the methoxide ions caused by their reduced solvation can hardly be the only reason for the rate increase in this range of the solvent mixtures, because, as pointed out above, significant changes in solvation are very unlikely in these mixtures. Thus we must search for other explanations for the rate enhancement. Such are in the first instances (1) the solvation of the transition state and (2) catalysis.

(1) The ability of DMSO to solvate extended charged structures such as transition states has been discussed by several authors.^{13,14} If n molecules of DMSO are directly involved in the transition state, the kinetic equation will be

$$dx/dt = k_0(a-x)^2 + k_1[\text{DMSO}]^n(a-x)^2 = k(a-x)^2$$

where k is the experimental rate constant and k_0 the rate constant in 100 % methanol. Thus $k = k_0 + k_1[\text{DMSO}]^n$ or

$$\log(k - k_0) = n \log[\text{DMSO}] + \text{const.} \quad (2)$$

Consequently, the plot of $\log(k - k_0)$ against $\log[\text{DMSO}]$ should be a straight line of slope n . Fig. 5 shows that this is not the case and that at high DMSO

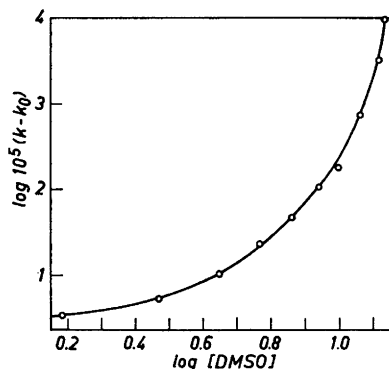


Fig. 5. Benzyl chloride, plot of $\log (k - k_0)$ against $\log [\text{DMSO}]$, 25°.

concentrations n has values which are unrealistic. This indicates that the interaction of DMSO with the transition state is not in accord with the above equation. As we shall see later, the solvation of the transition state by DMSO in the presence of methanol is probably weak.

(2) Kingsbury²⁷ found that the following relationship is valid for several nucleophilic displacement reactions of 4-fluoronitrobenzene and 2,4-dinitrochlorobenzene in methanol-DMSO, ethanol-DMSO, and isopropanol-DMSO mixtures, when the corresponding alkoxide ions, benzyl thioalkoxide ion, or benzylamine are the nucleophiles:

$$\log (k - k_0) = r[\text{DMSO}] + \text{const.} \quad (3)$$

For five of the six systems studied, r varied between 0.238 and 0.282, *i.e.* surprisingly little even though the character of the anion and the solvent varied considerably. According to Kingsbury, r is a measure of the sensitivity of a given system to catalysis by DMSO. From his results it would seem that the DMSO catalysis is relatively independent of the system involved.

Fig. 6 shows that the rate constants given in Tables 1–3 obey eqn. (3) in the range from pure methanol to a mole fraction of about 0.5 of DMSO (methanol about 350 ml/l). Furthermore, the values of r , 0.258 for benzyl chloride, 0.220 for *p*-methylbenzyl chloride, and 0.263 for *p*-chlorobenzyl chloride at 25°, are about the same as those found by Kingsbury.

The above discussion reveals that at least two, probably three effects determine the reaction rate; one of these is important only at high DMSO concentrations where it practically solely governs the situation. Their co-operation probably explains the observation that the plot of $\log k$ against the mole fraction of DMSO is linear over the range from pure methanol to a methanol concentration of about 170 ml/l (Fig. 7), *i.e.* over 75 % of the total range of mixtures. A similar linear relationship exists also for the reaction between benzyl chloride and hydroxide ion in aqueous DMSO, but at high DMSO concentrations only.¹

Further insight in the solvent effect problem is provided by the changes occurring in the activation parameters as the compositions of the solvent is varied; (*cf.* Refs. 28–30) and it is very instructive in this connection to compare the results with those obtained for the alkaline hydrolysis of benzyl chloride in DMSO-water mixtures.¹

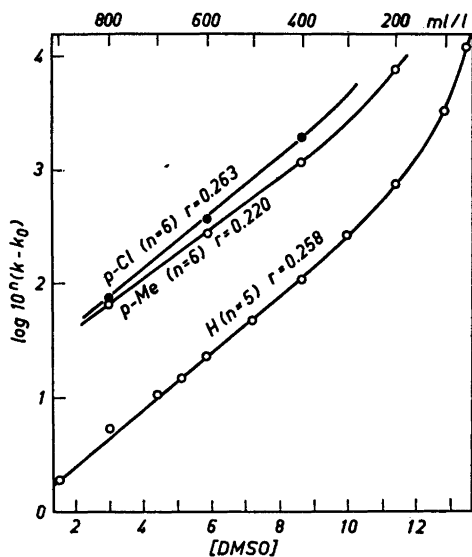


Fig. 6. Plot of $\log (k - k_0)$ against $[\text{DMSO}]$, 25° .

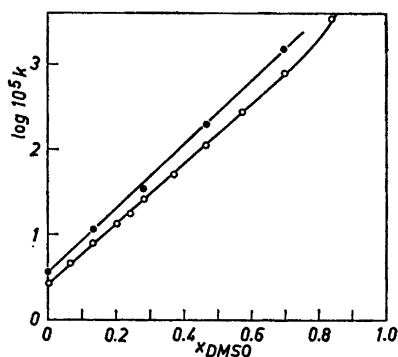


Fig. 7. Plot of $\log k$ against the mole fraction of DMSO, 25° . Benzyl chloride open circles, *p*-chlorobenzyl chloride solid circles.

Addition of DMSO to the aqueous solvent increases the solubility of benzyl chloride and thus also its solvation, and consequently lowers its energy. Thus in the water-rich range where the solvation of the hydroxide ions remains practically unchanged, the energy of the initial state (benzyl chloride + hydroxide ion + the surrounding solvent molecules) decreases somewhat at first with increasing DMSO concentration, but then it rises very markedly at high DMSO concentrations owing to the reduced solvation of the hydroxide ions. The entropy of the initial state varies similarly. It is reasonable to assume that the negatively charged transition state is preferentially solvated by water molecules and that there will be an initial fairly large range of mixtures over which its solvation remains practically unchanged, but then the solvation will decrease continuously because increasing amounts of water will be firmly bound to DMSO and not be available for solvation and because the pyramidal DMSO molecules³¹ cannot fit well around the transition state. Thus the enthalpy and entropy of the transition state will remain almost constant over a large range of mixtures, but will rise slowly at high DMSO concentrations. The enthalpy and entropy of activation are equal to the differences between the enthalpies and entropies of the transition state and the initial state. The net effect of the changes in solvation will be that the enthalpy and entropy of activation are a maximum at a certain solvent composition (*cf.* also Refs. 7 and 8) and thereafter they will decrease strongly. The situation is visualised in Fig. 8a. H' and S' refer to the initial state, H'' and S'' to the transition state. (Because the transition state is a state of greater order than

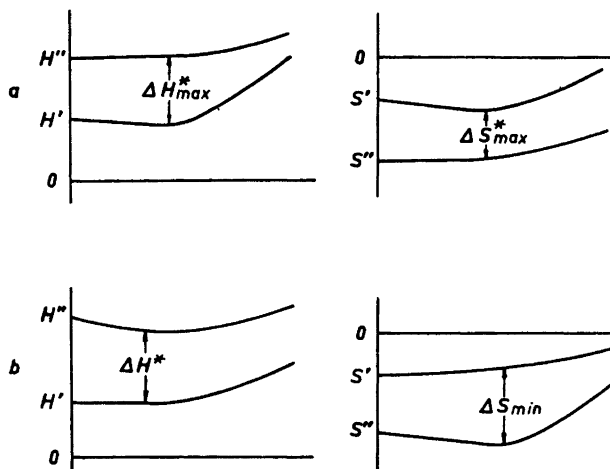
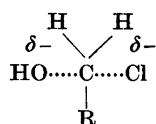


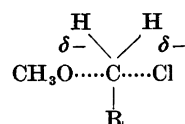
Fig. 8. Schematic representation of solvation effects. (a) Reaction $\text{OH}^- + \text{BzCl}$ in DMSO-water mixtures. ΔH^* and ΔS^* pass through a maximum and decrease steeply at high DMSO concentrations. (b) Reaction $\text{MeO}^- + \text{BzCl}$ in DMSO-methanol mixtures. ΔH^* decreases smoothly, ΔS^* passes through a minimum.

the initial state where the reactants are apart, its entropy is lower than that of the initial state.)

The situation is somewhat different in methanol-DMSO mixtures. The attraction of DMSO for methanol is weaker than for water, as is indicated by the heat of mixing, which is much less exothermic for the pair DMSO-methanol than for the pair DMSO-water.^{16,17} Both methanol and DMSO are good solvents for benzyl chloride, the latter better than the former (unpublished results); for example, the solubility of benzyl chloride in aqueous methanol containing 100 ml of water per litre ($x_{\text{MeOH}} = 0.80$) is 2.64 mole/l, and in aqueous DMSO containing the same amount of water per litre ($x_{\text{DMSO}} = 0.70$) 5.90 mole/l. The mole fractions in the former mixture are: benzyl chloride 0.12, methanol 0.70, water 0.17, and in the latter: benzyl chloride 0.47, DMSO 0.37, water 0.16. These figures show that benzyl chloride has a greater attraction for DMSO than for methanol. Consequently, the methanol molecules in the solvation shell of benzyl chloride will readily be replaced by DMSO molecules, and the energy of the benzyl chloride molecules decreases with increasing DMSO concentration. As already pointed out above, even rather large additions of DMSO do not reduce the solvation of methoxide ions in any significant degree, but a large reduction occurs at high DMSO concentrations. Thus on addition of DMSO the energy of the initial state (benzyl chloride + methoxide ion + the surrounding solvent) remains at first almost constant or probably decreases slightly and then rises at high DMSO concentrations. Since the methanol molecules are less firmly attached to methoxide ions than water molecules to hydroxide ions and the forces between DMSO and methanol are weaker than the forces between DMSO and water, the rise in the energy



Transition state for the hydroxide ion reaction



Transition state for the methoxide ion reaction

is less pronounced than in the hydroxide ion reaction. The entropy of the initial state varies in a corresponding manner. The high values of ΔH^* and ΔS^* for pure methanol indicate that the transition state in this case probably is less solvated than the transition state of the hydroxide ion reaction in water. The transition state contains a methoxyl group instead of a hydroxyl group. It is likely that water molecules have a stronger attraction for the charged points of the former transition state than methanol molecules for those of the latter. DMSO molecules have a specific attraction for the methoxyl group and also for R but not for the Cl atom. On the other hand, methanol molecules have an attraction for the chlorine atom. Thus when methanol in the solvent is gradually replaced by DMSO, the solvation of the transition state increases at first but above this range it will decrease continuously because increasing amounts of methanol will be bound to DMSO and are not available for solvation. The net effect of the changes in the solvation of the initial state and the transition state is that the activation enthalpy has no maximum or minimum and that its decrease in the DMSO-rich range is less pronounced than for the hydroxide ion reaction (Figs. 2 and 8b). Fig. 8b also explains the minimum in the activation entropy. However, the strong decrease in activation enthalpy in the methanol-rich range is difficult to explain solely by solvation phenomena, but can probably be attributed partly to the catalytic activity of DMSO discussed above. Thus we have here further evidence of catalysis by DMSO. Also the decrease in activation entropy at small DMSO concentrations may partly be a consequence of the catalysis.

Also the plots for the hydroxide ion reactions are included in Fig. 2. The values of ΔH^* and ΔS^* for the two reactions differ greatly from each other, especially in DMSO-rich mixtures, but they compensate each another so that the reaction rates are always nearly equal; at 25°, the ratio $k_{\text{OH}}/k_{\text{MeO}}$ is 1.05 when x_{DMSO} is 0.38, and 1.2 when x_{DMSO} is 0.70.

Solvent effect and temperature. The figures of Table 8 demonstrate a very remarkable dependence of the solvent effect on temperature. In all cases the relative reaction rate, k/k_{MeO} , decreases with rise in temperature. Thus also the factor r in eqn. (2) is temperature dependent; its value is 0.220 for benzyl chloride at 50° and 0.258 at 25°. Temperature-dependent solvent effects have been observed also in the alkaline hydrolysis¹ and solvolysis³² of benzyl chlorides in DMSO-water mixtures.

Reaction rate and the dielectric constant of the solvent. According to Ingold,³³ reactions in which an existing charge is dispersed should experience a slight rate decrease on going to more polar solvents. This is in agreement with the theory of Laidler,³⁴ which predicts that an ion-dipole reaction should in general be retarded when the dielectric constant of the medium increases. This is in

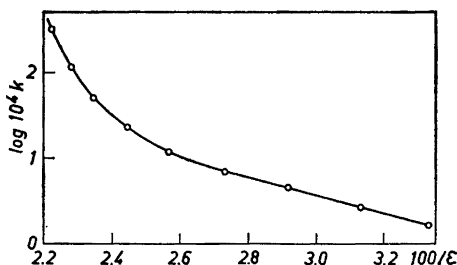


Fig. 9. Plot of $\log k$ against $1/\epsilon$. Benzyl chloride, 40° .

fact true for the reaction between benzyl chloride and hydroxide ion in DMSO-water mixtures. The results for the reaction of benzyl chloride with methoxide ion in DMSO-methanol mixtures are interesting, as the dielectric constant of the solvent increases on adding DMSO to methanol, but decreases on adding DMSO to water. Consequently, addition of DMSO to the solvent causes reaction rate changes in the two systems which are in the same direction, but in the dielectric constants changes which are opposite in sign. The experimental rate constants show that of these two effects the dielectric effect is of minor importance. One must, however, take into account that the changes in the dielectric constants of the DMSO-methanol mixtures are rather small.

According to the theory, the plot $\log k$ against the reciprocal of the dielectric constant should be a straight line. Fig. 9 shows that this holds good only in the range where the methanol content is greater than about 650 ml/l, *i.e.* where the mole fraction of DMSO is less than 0.75. The slope of the plot is opposite in sign to that predicted by the theory. In the consideration of the relationship between the rate constant and the dielectric constant, one must, however, bear in mind that the reactivity of the negative ion is dependent on the DMSO concentration. The values of the dielectric constants of the DMSO-methanol mixtures were taken from an unpublished paper of Tommila and Autio.

The substituent effects. Substituents influence reaction in two ways. An electron-attracting substituent makes the seat of the reaction, *i.e.* the carbon atom of the group $\text{—CH}_2\text{Cl}$ more positive, which, on one hand, makes the bond C—Cl stronger, but, on the other, weakens the repulsion between this carbon atom and the attacking negative ion. An electron-repelling substituent exerts opposite influences. The experimental results show that the net result of these two effects is that in reaction (1), as in the alkaline hydrolysis of benzyl chlorides,¹ both electron-attracting (Cl) and electron-repelling (CH_3) substituents accelerate the reaction. The question has already been discussed in a previous paper.³⁵ These substituent effects and also the fact that the substituent effect is clearly temperature dependent (Table 9) will be discussed in the next paper of this series. In this connection attention is drawn to the fact that additions of DMSO to methanol change the substituent effects in the same direction as additions of DMSO to water,¹ although the dielectric constants change in opposite directions.

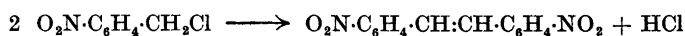
p-Nitrobenzyl chloride. The reaction of a benzyl chloride (or bromide) with an alcoholate ion yields the corresponding alkyl ether; with *o*- and *p*-nitrobenzyl chlorides, however, the reaction proceeds partially with the

Table 9. Values of k_X/k_H for $\text{XC}_6\text{H}_4\text{Cl}$.

MeOH ml/l	X = <i>p</i> -Me				MeOH ml/l	X = <i>p</i> -Cl			
	25°	40°	50°	60°		25°	40°	50°	60°
1000	1.91	1.76	1.64	1.54	1000	1.41	1.42	1.42	1.37
800	1.46	1.37	1.33	1.30	800	1.42	1.37	1.37	1.39
600	1.29	1.27	1.26	1.25	600	1.59	1.56	1.54	1.51
400	1.12	1.10	1.09	1.08	400	1.79	1.73	1.78	1.87
200	1.04	1.07	1.08	1.17	200	1.93	1.97	1.95	2.01

MeOH ml/l	X = <i>m</i> -Cl				MeOH ml/l	X = <i>p</i> -NO ₂			
	25°	40°	50°	60°		25°	40°	50°	60°
1000	1.04	1.01	1.00	0.979	1000	1.89	1.92	2.03	2.09
500	1.42	1.45	1.47	1.48	800	2.65	2.71	2.81	3.14
					600	4.41	4.81	4.76	
					500	6.70	7.28		
					400	35.5	34.7		

formation of dinitrostilbene.^{36,37} Thus *p*-nitrobenzyl chloride gives *trans*-4,4'-dinitrostilbene:



Besides, small amounts of *cis*-4,4'-dinitrostilbene are formed. Also the reaction with an alkali hydroxide in aqueous acetone or in aqueous dioxan yields *trans*-4,4'-dinitrostilbene.³⁸ The second-order kinetics are, at least approximately, obeyed also in these cases,^{35,38} but the reaction rate is much greater than what would be expected. In 50 % aqueous dioxan and in 50 % aqueous acetone *p*-nitrobenzyl chloride reacts 35–100 times faster than benzyl chloride, whereas according to the results of Olivier,³⁹ and Simonetta and Favini,⁴⁰ even quite powerful electron-withdrawing substituents have only a weak effect on the reaction rate: *e.g.* the reaction of *p*-cyanobenzyl chloride with hydroxide ion is only 1.47 times that of benzyl chloride in 50 % aqueous acetone at 30°. The kinetics of the reaction have recently been studied in aqueous acetone^{35,38} and in aqueous dioxan.³⁸

In methanol and methanol-DMSO mixtures, the reaction between *p*-nitrobenzyl chloride and the methoxide ion is, at least approximately, of the second order. Depending on the temperature the rate constant is 1.9–2.1 times that of the unsubstituted compound in 100 % methanol (Table 5). These values are quite normal and also the activation energies and frequency factors do not differ greatly from those found for the other compounds. These results suggest that in pure methanol the reaction proceeds as a normal displacement producing *p*-nitrobenzylmethyl ether. It was, in fact, ascertained that, when the concentration of the reactants is small, the main product in 100 % methanol at the temperatures used in the kinetic experiments is *p*-nitrobenzyl methyl ether. The substance obtained had the b.p. 145°/12 mm and m.p. 26–27°, the values recorded in the literature^{41a} being b.p. 150°/18 mm, m.p. 26–27°.

Only small amounts of dinitrostilbene were formed. It has been found that when *p*-nitrobenzyl chloride is heated with potassium carbonate in methanol on a water bath, *p,p'*-dinitrostilbene and *p*-nitrobenzyl methyl ether are formed.⁴¹ Also *o*-nitrobenzyl chloride, when hydrolysed by alkali in water gives the normal product, *o*-nitrobenzyl alcohol.⁴² However, when higher concentrations are used, the stilbene proved to be the main product in pure methanol and also in ethanol. Addition of DMSO to the solvent favours the stilbene formation, as shown by the fact that the ratio k_x/k_H increases more rapidly than in the other cases (Table 9). There is an abrupt strong increase in the rate ratio when the mole fraction of DMSO is increased from 0.4 to 0.5 (methanol concentration decreases from 500 to 400 ml/l), and 4,4'-dinitrostilbene is the main product. At the same time, the kinetic investigation becomes difficult owing to the deep red colour of the reaction mixture. We have isolated from the reaction mixture in the '50 %' methanol a pale yellow crystalline solid melting at 286–288° which according to the literature is the melting point of *trans*-4,4'-dinitrostilbene. In addition, a little of *cis*-isomer, m.p. 185°, was obtained.

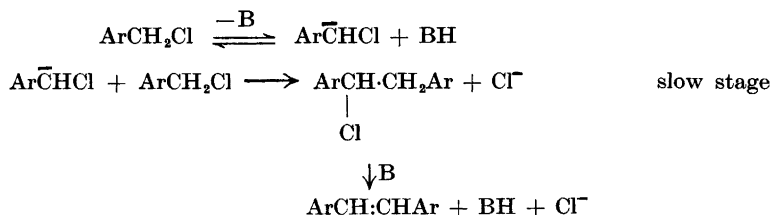
Table 5 shows that the activation entropy for *p*-nitrobenzyl chloride remains nearly constant, and is only very slightly negative, when the DMSO concentration is decreased, whereas that for benzyl chloride decreases (Table 1). As the activation energy for *p*-nitrobenzyl chloride is greater than or equal to that of the unsubstituted compound, the high velocity of dinitrostilbene formation is due to a large activation entropy. The large (only slightly negative) activation entropy shows that the transition state of the slow stage of the reaction must have a loose structure.

The mechanism of the reaction has often been discussed. The reaction has been supposed to proceed *via* formation and dimerization of an aryl-methylene:^{36,43}



The transient formation of the radical ArCH·, however, is unlikely, as one could expect that this very reactive species would react with the ambient water or alcohol with the formation of benzyl alcohol or ether.^{41a}

It has also been suggested^{41,44} that the reaction might consist of a reversible³⁸ carbanion formation, followed by alkylation and dehydrohalogenation:^{cf.45}



The carbanion formation is supported by the fact the intermediate chloride ArCH(Cl)·CH₂Ar has been isolated in the reaction of several benzyl chlorides with alkali amides in liquid ammonia,⁴⁶ and that *o*-nitrobenzyl chloride reacts

also with cyanide ion in DMSO and in ethanol to give dinitrostilbene.⁴⁷ Also addition of ArCH: to ArCH₂X has been proposed.⁴⁸ However, the attempts to trap the hypothetical carbene intermediate have not been fruitful.⁴⁹

It is also known that *p*-nitrobenzyl dimethylsulphonium tosylate^{48a} in alkaline aqueous solution and *p*-nitrobenzyl dimethylsulphonium bromide with sodium hydroxide in 50 % aqueous pyridine⁵⁰ give quantitatively 4,4'-dinitrostilbene, but it is not clear why the latter is formed only when halide or dimethyl sulphide are the leaving groups.

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