969. *Reactions in Strongly Basic Media. Part II.* The Kinetic Dependence of some Base-catalysed Reactions on the Concentration of Sodium Methoxide.*

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The rates of reaction of sodium methoxide with chloroform, phenethyl chloride, and 1-chloro-3,3-dimethylbutane in methanol have been studied. In the methanolysis of chloroform, the order (n) with respect to methoxide ion increases rapidly at high concentrations of sodium methoxide; a logarithmic plot of the first-order rate coefficient against H_- has a mean slope of about 0·8 over the range $[OMe^-] = 1$—3M. A smaller variation of n is observed in elimination from phenethyl chloride, but there is almost no variation in elimination and substitution involving 1-chloro-3,3-dimethylbutane. These differences are discussed with reference to the solvation of the methoxide ion in the transition state.

This paper is concerned with the order with respect to methoxide ion in the two reaction paths below:

$$\left.\begin{array}{l} \mathrm{SH} + \mathrm{MeO}^- \rightleftharpoons \mathrm{S}^- + \mathrm{MeOH} \\ \mathrm{S}^- \longrightarrow \text{Products} \\ \text{Slow (unimolecular)} \end{array}\right\} \quad . \; . \; . \; . \; . \; . \; . \; . \; . \; . \quad (1)$$

$$\mathrm{SH} + \mathrm{MeO}^- \xrightarrow[\text{Slow (bimolecular)}]{} \text{Products} \quad . \; . \; . \; . \; . \; . \; . \; . \; . \; . \quad (2)$$

Reactions of the first type can be classified as $B1$ by analogy with the $A1$ reactions studied in acidic media [reaction (3)]:

$$\left.\begin{array}{l} \mathrm{S} + \mathrm{H}^+ \underset{\text{Fast}}{\rightleftharpoons} \mathrm{SH}^+ \\ \mathrm{SH}^+ \longrightarrow \text{Products} \\ \text{Slow (unimolecular)} \end{array}\right\} \quad . \; . \; . \; . \; . \; . \; . \; . \; . \; . \quad (3)$$

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* Part I, preceding paper.

The *B*1 class is illustrated by those *E*1*cb* reactions involving a pre-equilibrium proton transfer. Reactions of the second type include *E*2 eliminations and S_N2 substitutions. Both the reaction paths (1) and (2) above should be of the first-order with respect to methoxide ion when the concentration of sodium methoxide is low; however, for the reasons given below, the order may deviate from unity when this concentration is high.

The rates of many *A*1 reactions are proportional to the H_0 function to a good approximation;[1] this suggests that medium effects on the second step of reaction (3) are small in comparison with the extent of acid catalysis. A similar result might be expected for the *B*1 reactions of neutral substrates since these differ from *A*1 reactions only in the direction of the initial proton transfer and in the sign of the charge on the transition state. This argument gains support from the absence of specific salt effects in the rate of heterolysis of t-butyl chloride; the specific salt effects on the initial and the transition state cancel.[2] A similar cancellation in specific salt effects on the heterolysis of a negative ion (as in an *E*1*cb* reaction of a neutral substrate) would lead to a very small medium effect. Thus, for *B*1 reactions, a logarithmic plot of the first-order rate coefficient against the H_- function should be linear with a slope of unity. The main uncertainty is whether the H_- function as defined in Part I is applicable to substrates that are structurally very different from the indicators used. Recent studies in acidic media have demonstrated that the protonation of some neutral substrates deviates markedly from the conventional H_0 scale.[3]

The rate of S_N2 and *E*2 reactions should, to a first approximation, be proportional to the concentration of methoxide ion. However, the definition of an *E*2 reaction covers a wide range of transition states depending on the timing of the stages involved.[4,5] In the *E*2 elimination of the molecule HX, one extreme type of transition state could involve almost complete proton transfer before significant weakening of the C–X bond or development of the C–C double bond. The neutralisation of the methoxide ion could thus be almost complete in the transition state, and the medium effect might therefore be almost equal to that of a *B*1 reaction.* In the same way, it is possible to visualise a range of transition states for S_N2 substitution, differing in the charge distribution between the methoxide ion and the displaced group.

The marked deviation of the H_- function from ideality in methanolic sodium methoxide (cf. Part I) provides a hint that medium effects in this system may be unusually sensitive to the degree of neutralisation of the lyate ion in the transition state. Medium effects on three reactions of known mechanism have therefore been studied under these conditions.

B1 *Reactions: the Methanolysis of Chloroform.*—The reaction of chloroform with sodium methoxide in methanol has not been studied in detail; its classification as a *B*1 reaction is based on the extensive work of Hine and his co-workers[6,7] on the decomposition of chloroform in aqueous solution. In these solutions the slow step is the heterolysis of the conjugate base (CCl_3^-) to give dichlorocarbene (CCl_2); this species then reacts with the solvent to form carbon monoxide and formic acid. In alcoholic media, at low concentrations of alkoxide ion, the kinetic form is unchanged[8] but the products are much more complex,[9] including olefins, alkyl orthoformates, and ethers. The results suggest the slow

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* This limiting medium effect on an *E*2 reaction should still be a little less than that on a *B*1 reaction because one methanol molecule (derived from the neutralised methoxide ion) is necessarily present in the *E*2 transition state.

[1] Long and Paul, *Chem. Rev.*, 1957, **57**, 935.
[2] Clarke and Taft, *J. Amer. Chem. Soc.*, 1962, **84**, 2295.
[3] Cf. *Ann. Reports*, 1961, **58**, 153.
[4] Cram, Greene, and De Puy, *J. Amer. Chem. Soc.*, 1956, **78**, 790; Bunnett, *Angew. Chem.* (*Internat. Edn.*), 1962, **1**, 225.
[5] Ingold, *Proc. Chem. Soc.*, 1962, 265.
[6] Hine, *J. Amer. Chem. Soc.*, 1950, **72**, 2438.
[7] Hine, Peek, and Oakes, *J. Amer. Chem. Soc.*, 1954, **76**, 827.
[8] Bose, *J. Indian Chem. Soc.*, 1960, **37**, 325.
[9] Skell and Starer, *J. Amer. Chem. Soc.*, 1959, **81**, 4117; Hine, Ketley, and Tanabe, *ibid.*, 1960, **82**, 1398.

formation of dichlorocarbene which then reacts in a number of ways with the medium.[9] The reaction path in methanolic sodium methoxide should therefore be:

$$CHCl_3 + OMe^- \underset{\text{Fast}}{\rightleftharpoons} CCl_3^- + MeOH \quad . \quad . \quad . \quad . \quad . \quad (4)$$

$$CCl_3^- \xrightarrow[\text{Slow}]{} CCl_2 + Cl^- \quad . \quad . \quad . \quad . \quad . \quad (5)$$

$$CCl_2 \xrightarrow[\text{Fast}]{} \text{Products} \quad . \quad . \quad . \quad . \quad . \quad (6)$$

Our kinetic results are consistent with this reaction path. At low concentrations of sodium methoxide, the order with respect to methoxide ions approaches unity (Table 1) and the value of the second-order rate coefficient (k_2, eqn. 7) at 59·7° is about equal to that in water[10] at 35°; the ratio $k_2^{H_2O}/k_2^{MeOH}$ should be about 46 at 35°. The corresponding ratio for deuterium exchange[11] is about 11, so the large rate ratio observed[7] in aqueous media between deuterium exchange and solvolysis (a factor of 2000) is more than maintained in methanol. In the presence of a large excess of sodium methoxide, the concentration of chloride ion increases steadily to the expected limit according to a first-order law; this indicates that the loss of the first chloride ion is rate-determining. These results therefore support the fast equilibrium of equation (4), followed by the slow and effectively irreversible stage of equation (5). The final products have not been investigated, but results with other haloforms suggest that methyl orthoformate would be formed;[12] any dichloromethyl methyl ether would be rapidly hydrolysed under the reaction conditions.

$$\text{Rate} = k_2[SH][OR^-] \quad . \quad . \quad . \quad . \quad . \quad (7)$$

$$SH = CHCl_3,\ Ph{\cdot}CH_2{\cdot}CH_2Cl,\ Me_3C{\cdot}CH_2{\cdot}CH_2Cl;\ \ OR = OH,\ OMe$$

The kinetic runs in Table 1 were carried out in the presence of a large excess of sodium methoxide so that first-order kinetics were obtained. The values of log k_1 are plotted against H_- (Part I) in Fig. 1; the graph is curved * and the mean slope between 1M and 3M sodium methoxide is about 0·8. The medium effect is therefore less than that expected from the simple relation between rate coefficients and acidity functions (see above).

TABLE 1.

First- and second-order rate coefficients for the methanolysis of chloroform.

Temp. 45·1°			Temp. 45·1°			Temp. 59·7°		
[NaOMe]	10^5k_1	10^5k_2	[NaOMe]	10^5k_1	10^5k_2	[NaOMe]	10^5k_1	10^5k_2
1·04	3·11	2·99	2·74	42·2	15·4	0·145	2·58	17·8
1·36	6·15	4·52	3·12	78·5	25·2	0·209	2·95	14·1
1·79	11·2	6·28	3·40	112	32·9	0·306	7·25	23·7
2·13	18·1	8·48	3·99	283	70·8	0·379	7·91	20·9
2·34	24·6	10·5				0·578	14·5	25·2
						0·842	25·3	30·1
						1·10	39·4	35·8

In this and other Tables, units of k_1 are sec.$^{-1}$; units of k_2 are mole^{-1} sec.$^{-1}$ l.

This direction of curvature could be explained by assuming that a significant fraction

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* The first results[13] were restricted to lower concentrations of sodium methoxide and the curvature of the graph was not then appreciated. The values of H_- in ref. 13 differ by being calculated on the aqueous scale (cf. Part I).

[10] Hine and Dowell, *J. Amer. Chem. Soc.*, 1954, **76**, 2688.
[11] Hine, Wiesboeck, and Ghirardelli, *J. Amer. Chem. Soc.*, 1961, **83**, 1219.
[12] Hine and Tanabe, *J. Amer. Chem. Soc.*, 1957, **79**, 2654.
[13] Allison, Bamford, and Ridd, *Chem. and Ind.*, 1958, 718; cf. Ridd, *ibid.*, 1957, 1268.

of the chloroform is ionised in the more basic solutions, but some indirect evidence on the acidity of chloroform makes this unlikely. The rate of deuterium exchange of chloroform in aqueous alkali is similar to that of acetone,[7] and so the acidities are also probably similar. The pK_a of acetone in aqueous solutions has been estimated [14] at 20, a value too high for extensive ionisation in these solutions of sodium methoxide. The curvature is therefore more probably derived from the difference in temperature between the kinetic studies and the indicator measurements or from the difference in structure between chloroform and the indicators used.

Although the medium effect is less than expected, it is still very large and leads to a marked dependence of k_2 on the concentration of sodium methoxide (Table 1). A similar increase in k_2 in ethanolic potassium hydroxide has been observed and has recently been ascribed [8] to the incursion of the new reaction path (8); this involves two hydroxide ions before the rate-determining step. This explanation of the catalysis is improbable because

$$\left.\begin{aligned} \mathrm{CHCl_3 + 2HO^-} &\underset{\text{Fast}}{\rightleftharpoons} \mathrm{HO{\cdot}CCl_2^- + H_2O + Cl^-} \\ \mathrm{HO{\cdot}CCl_2^-} &\xrightarrow[\text{Slow}]{} \mathrm{HO{\cdot}CCl} \\ \mathrm{HO{\cdot}CCl} &\xrightarrow[\text{Fast}]{} \text{Products} \end{aligned}\right\} \quad \cdots\cdots \quad (8)$$

the pre-equilibrium step requires that the species $HO{\cdot}CCl_2^-$ should readily undergo replacement of hydroxyl by chlorine in alkaline solution. The explanation also fails to account for the magnitude of the medium effect observed in methanolic sodium methoxide: a plot of log k_1 against log c_{NaOMe} shows that the order with respect to methoxide ion reaches 2 in 1M-sodium methoxide and increases steadily to a value of about 6 in 4M-sodium methoxide. In both methanol and ethanol, the high order with respect to the base is probably best understood as the expected medium effect on a *B*1 reaction.

*E*2 *and* S_N2 *Reactions*.—The reactions of phenethyl chloride and of 1-chloro-3,3-dimethylbutane have been studied in concentrated sodium methoxide. The former reaction leads almost completely to the elimination product (styrene), and the second-order kinetics observed [15] with the corresponding bromide together with the absence of deuterium exchange [16] indicate an *E*2 elimination. The reaction of 1-chloro-3,3-dimethylbutane leads mainly to elimination with about 30—40% of substitution. Since this substrate is a primary halide with γ-methyl groups, both substitution and elimination should be entirely bimolecular.

The values of k_2 (eqn. 7) for the *E*2 reaction of phenethyl chloride are given in Table 2; the variation with the concentration of sodium methoxide is much less than that with chloroform but still significant. A logarithmic plot of the corresponding first-order rate coefficients against log c_{OMe^-} shows that the order with respect to methoxide ion reaches a value of about 3 in 4M-solutions.

TABLE 2.

Second-order rate coefficients for the *E*2 elimination reaction of phenethyl chloride.

Temp. 45·12°		Temp. 59·70°			
[NaOMe]	10^5k_2	[NaOMe]	10^5k_2	[NaOMe]	10^5k_2
2·57	1·60	0·235	3·26	2·88	9·05
3·23	2·02	0·840	3·60	3·12	10·10
4·37	3·47	1·71	5·14	3·71	13·30
		2·38	7·02	4·28	18·57

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[14] Bell, *Trans. Faraday Soc.*, 1943, **39**, 253.

[15] Hughes, Ingold, Masterman, and McNulty, *J.*, 1940, 899.

[16] Skell and Hauser, *J. Amer. Chem. Soc.*, 1945, **67**, 1661.

The values of k_2 (eqn. 7) for the combined substitution and elimination reactions of 1-chloro-3,3-dimethylbutane are given in Table 3; the constancy is remarkable. This constancy should apply to the rate coefficients of the two component reactions for the percentage elimination is not usually a marked function of the concentration of alkoxide ion.[15]

TABLE 3.

Second-order rate coefficients at 84·90° for the loss of chloride ion from 1-chloro-3,3-dimethylbutane by substitution plus elimination.

[NaOMe] (M)	0·605	1·63	2·85	3·12	4·07
10^5k_2	1·82	1·55	1·75	1·84	1·79

Olefin (in M-NaOMe) = 68%.

Comparison of the Medium Effects.—The differences is these medium effects are most clearly seen when the results are plotted as in Fig. 2, where the value of k_2 in M-sodium methoxide is taken as unity for all substrates. The large difference between the medium effect involving chloroform and that involving the other two substrates is then clearly apparent. Another large medium effect on what appears to be a *B*1 reaction has been reported[17] for the mixed solvent methanol–dimethyl sulphoxide, but this result has not been compared with medium effects on related reaction paths.

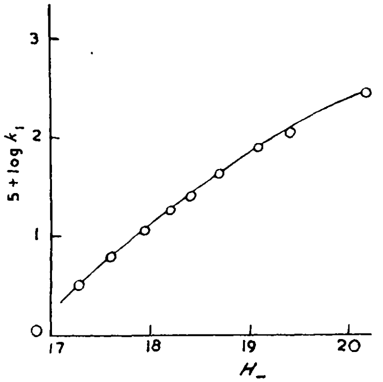

FIG. 1. The first-order rate coefficient for the methanolysis of chloroform plotted logarithmically against the H_- function.

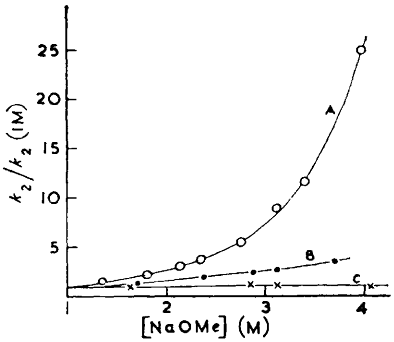

FIG. 2. Medium effects on (A) methanolysis of chloroform, (B) elimination from phenethyl chloride, and (C) combined elimination and substitution of 1-chloro-3,3-dimethylbutane.

As in the discussion in Part I, these medium effects can be rationalised by considering the difference in the solvation of the initial and the transition states. The less the solvation of the transition state relative to the initial state, the greater the dependence of the reaction rate on the activity of the solvent and the greater the acceleration observed when the activity of the solvent is reduced by the added sodium methoxide. If the solvation of the methoxide ion by hydrogen bonding is considered to be the most important factor, then the greater medium effect on *B*1 than on *E*2 reactions follows naturally since in the former reactions the methoxide ion has been completely neutralised before the rate-determining stage.

The difference in the medium effects on the reactions of phenethyl chloride and 1-chloro-3,3-dimethylbutane can also be explained in the same way since the β-phenyl substituent should increase the carbanion character of the transition state[4] and hence

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[17] Stewart, O'Donnell, Cram, and Rickborn, *Tetrahedron*, 1962, **18**, 917.

increase the transfer of charge from the methoxide ion. However, these smaller differences may not be significant since other factors must contribute to the medium effect. The large difference in the medium effects involving chloroform and phenethyl chloride does suggest that the proton transfer is far from complete in the *E*2 transition state of the latter; this conclusion accords with the large hydrogen isotope effect[18] observed with the corresponding bromide.

The mechanistic difference between the reactions of chloroform and phenethyl chloride is also reflected in the entropies of activation (Table 4). The relative solvation of the initial and the final state should be an important factor in determining the entropy of activation, and so a rough correlation between this quantity and the medium effect is reasonable.

TABLE 4.

Energies and entropies of activation.

Substrate	[NaOMe] (M)	10^5k_2 45·1°	59·7°	$\Delta H\ddagger$ (kcal. mole^{-1})	$\Delta S\ddagger$ (e.u.)
Chloroform	1	2·84	33·4	35·5	+30·2
$Ph{\cdot}CH_2{\cdot}CH_2Cl$	2·5	1·55	7·40	22·7	−10·7

The difference between the medium effect on *B*1 reactions and that on *E*2 reactions is less than was originally expected,[13] for the rates of both reactions can apparently fall between a linear dependence on the H_- function and a linear dependence on the base concentration. However, from the results in this paper, the difference may still be large enough to be mechanistically significant; this point is being checked by studies on other substrates. Recent work[19] suggests that methanol may be a more suitable solvent than water for such mechanistic distinctions since, in aqueous media, both nucleophilic displacement by hydroxide ion and rate-determining proton abstraction by hydroxide ion can apparently show medium effects similar to that of a prototropic equilibrium.

EXPERIMENTAL

Materials.—The preparation of methanolic sodium methoxide has been described in Part I. " AnalaR " chloroform was washed with water, dried ($CaCl_2$), and distilled. Phenethyl chloride was prepared by Gerrard and French's method[20] and distilled twice before use. 1-Chloro-3,3-dimethylbutane was prepared by Schmerling's method[21] A and fractionated under reduced pressure (b. p. 51—52°/70 mm.).

Kinetic Runs.—The methanolyses of chloroform and 1-chloro-3,3-dimethylbutane were studied by using aliquot parts of the reaction mixture in sealed tubes in a thermostat-bath. The tubes were withdrawn at suitable intervals, cooled to −80°, and then broken in a reagent bottle containing a known quantity of nitric acid. The molarity of the sodium methoxide was determined by an acid–base titration of the excess of acid, and the chloride ion was titrated potentiometrically with silver nitrate. Details of a typical kinetic run are given in Table 5(*a*). The concentrations of the reactants were adjusted so that the methoxide ion was present in large excess; first-order kinetics were therefore obtained. Second-order rate coefficients were calculated by dividing the first-order rate coefficients by the mean concentration of sodium methoxide for that kinetic run. At one concentration of sodium methoxide, the initial concentration of the substrate was varied by a factor of ten (chloroform, 0·00495—0·0497M; 1-chloro-3,3-dimethylbutane 0·0137—0·137M); no significant variation in the second-order rate coefficient was observed. With chloroform, these results show that the heterolysis of the conjugate

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[18] Saunders and Edison, *J. Amer. Chem. Soc.*, 1960, **82**, 138.

[19] Anbar and Yagil, *J. Amer. Chem. Soc.*, 1962, **84**, 1790; Samuel and Silver, *J.*, 1963, 289.

[20] Gerrard and French, *Nature*, 1949, **159**, 263.

[21] Schmerling, *J. Amer. Chem. Soc.*, 1945, **67**, 1152.

base (eqn. 5) is not retarded by a mass-action effect from the chloride ions formed. With solutions containing the higher chloroform concentrations there was some precipitation of sodium chloride during the reaction, but this did not appear to affect the reaction rate. The quoted concentrations of sodium methoxide have been corrected to allow for the temperature-dependence of the density of methanol.[22]

TABLE 5.

Typical kinetic runs: (*a*) the methanolysis of chloroform followed by potentiometic titration of chloride ion with 0·01M-silver nitrate; (*b*) elimination from phenethyl chloride followed by spectrophotometric estimation of the styrene formed. Both reactions at 59·7°.

(*a*)
Initial [$CHCl_3$] = $9{\cdot}95 \times 10^{-3}$M.

Volume of ampoule, 5·35 ml.

Time (min.)	[NaOMe] (M)	$AgNO_3$ (ml.)	10^4k_1 (sec.$^{-1}$)
0	1·11	1·71	—
4	1·11	3·03	4·04
9	1·10	4·49	4·01
15	1·10	5·97	3·94
22	1·10	7·39	3·84
30	1·09	8·87	3·86
41	1·09	10·48	3·88
50	1·08	11·7	4·00
∞	—	15·98 (calc.)	—

Mean $k_1 = 3{\cdot}94 \times 10^{-4}$ sec.$^{-1}$.
Mean [NaOMe] = 1·10M.
∴ $k_2 = 3{\cdot}58 \times 10^{-4}$ mole^{-1} sec.$^{-1}$ l.

(*b*)
Initial [$Ph{\cdot}CH_2{\cdot}CH_2Cl$] = $3{\cdot}33 \times 10^{-3}$M.

Time (min.)	Optical density (2480 Å)	10^4k_1 (sec.$^{-1}$)
0	0·070	—
3	0·152	—
6	0·208	4·86
10	0·283	4·95
15	0·370	4·99
20	0·450	5·13
26	0·510	4·98
33	0·582	4·79
∞	0·900 (calc.)	—

Mean $k_1 = 4{\cdot}95 \times 10^{-4}$ sec.$^{-1}$.
Mean [NaOMe] = 3·71M.
∴ $k_2 = 1{\cdot}33 \times 10^{-4}$ mole^{-1} sec.$^{-1}$ l.

In the reactions of 1-chloro-3,3-dimethylbutane, the percentage of olefin formed was determined by adding bromine and then determining the excess of bromine by the addition of potassium iodide and titration with sodium thiosulphate.

The *E*2 reaction of phenethyl chloride was carried out in a stoppered flask. Samples (~2 ml.) were extracted at intervals, diluted, and examined in a spectrophotometer. The reaction was followed from the absorption maximum of styrene at 2480 Å. From a product analysis, the formation of styrene appeared to be quantitative and the percentage reaction was calculated on this assumption, with $\varepsilon_{2480} = 1{\cdot}35 \times 10^4$ (ref. 23). Details of a typical kinetic run are given in Table 5(*b*). Good first-order kinetics were obtained and the second-order rate coefficients were calculated as described above. The concentration of sodium methoxide was determined from acid–base titration of samples extracted at the beginning and the end of each kinetic run.

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[22] " International Critical Tables," McGraw-Hill, New York, 1926, Vol. III, p. 27.

[23] Saunders and Ašperger, *J. Amer. Chem. Soc.*, 1957, **79**, 1612.