Mechanism of the Reaction of Methylene Halides with Alkali Metal Alkoxides in Alcohol Solution[1a]

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Abstract: Rate constants have been determined for the nucleophilic substitution reactions of methylene chloride, bromochloromethane, methylene bromide, and methylene iodide with sodium methoxide in methyl alcohol and methyl alcohol-*d*, with potassium isopropoxide in isopropyl alcohol and isopropyl alcohol-*d*, and with potassium *t*-butoxide in *t*-butyl alcohol and *t*-butyl alcohol-*d*. For a given methylene halide the rate constants increase by about fourfold on going from sodium methoxide to potassium isopropoxide and then decrease somewhat on going to potassium *t*-butoxide. The rate constant for chloroform, which is known to react by an α-elimination mechanism, increases by 700-fold on going from sodium methoxide to potassium isopropoxide and by another 140-fold on going to potassium *t*-butoxide. The rate constants for the alkoxide ion catalyzed deuterium exchange of the methylene halides increase by about 300-fold on going from sodium methoxide to potassium isopropoxide and by about another 20-fold on going to potassium *t*-butoxide. These reactivity data show that an α-elimination mechanism is improbable for the reaction of methylene halides with alkoxide ions in alcohol solution. The reaction mechanism is probably largely SN2, with the reactivity of the *t*-butoxide ion and to a lesser extent that of the isopropoxide ion being decreased by steric hindrance. The SN2 mechanism is further supported by the fact that 0.5 *M* sodium iodide does not decrease the rate of reaction of methylene iodide with sodium methoxide and the fact that methylal isolated from the reaction of methylene bromide with sodium methoxide in methyl alcohol-*d* contains only about that small amount of deuterium that would result from deuterium exchange of the methylene bromide before its transformation to methylal. The rate constants for reaction of a given methylene halide with a given alkali metal alkoxide are 1.66 ± 0.15 times as large in the deuterated alcohol as in the protiated alcohol.

Closs and coworkers have shown that when methylene chloride is treated with alkyllithium compounds a major fraction of the ensuing reaction involves α dehydrochlorination.[2-4] Using the more weakly basic reagent potassium *t*-butoxide, Volpin, Dulova, and Kursanov found that methylene chloride, bromide, and iodide are capable of transforming benzene to tropylium *t*-butoxide in yields ranging from 0.1 to 1.4%.[5] From these observations it is clear that alcohol-free potassium *t*-butoxide is capable of α-dehydrohalogenating methylene halides to an extent of at least 0.1–1.4%. Whether the other 98+% of the reaction involves largely α dehydrohalogenation or not cannot be told, however. With nucleophilic reagents, such as iodide ions, whose proton basicity is relatively low, reaction with methylene halides would be expected to proceed almost entirely by the SN2 mechanism, with no significant contribution of α dehydrohalogenation.

It therefore seems likely that methylene halides can react with nucleophilic reagents by either an SN2 or an α-dehydrohalogenation mechanism.[6] The extent of occurrence of the α-dehydrohalogenation mechanism might be expected to increase with increasing proton basicity and/or decreasing carbon basicity[9] of the nucleophilic reagent, although other factors should also be important. However, little is known about the point at which the predominant reaction mechanism changes from SN2 to α elimination. To shed more light on this subject we have investigated the mechanism of reaction of methylene halides with alkali metal alkoxides in alcohol solution, partly because of the evidence that at least some dehydrohalogenation occurs in the reaction of several methylene halides with an alcohol-free alkali metal alkoxide,[5] and partly in order to determine the validity of an earlier assumption that methylene halides react with methanolic sodium methoxide by the SN2 mechanism.[10]

In order to learn which mechanism is operative, we have studied the reactivities of several methylene halides toward nucleophilic displacements and deuterium exchange in the presence of three different alcoholic alkali metal alkoxide reaction mixtures, we have tried to learn whether the nucleophilic displacement could be slowed by a mass-law effect, and we have determined the deuterium content of a dialkylformal formed from a methylene halide and an alkali metal alkoxide in a deuterated alcohol.

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[1] (a) Part XXVI in the series "Methylene Derivatives as Intermediates in Polar Reactions." For part XXV see J. Hine, R. P. Bayer, and G. G. Hammer, *J. Amer. Chem. Soc.*, **84**, 1751 (1962). This investigation was supported in part by Grant DA-ARO(D)-31-124-G309 from the U. S. Army Research Office (Durham) and National Science Foundation Grant GP-7629. This manuscript was abstracted in part from the Ph.D. thesis of R. B. D. (Georgia Institute of Technology, 1967) and the M.S. thesis of E. F. G. (The Ohio State University, 1969). (b) Author to whom inquiries may be addressed at The Ohio State University.

[2] G. L. Closs and L. E. Closs, *J. Amer. Chem. Soc.*, **81**, 4996 (1959); **82**, 5723 (1960).

[3] G. L. Closs, R. A. Moss, and J. J. Coyle, *ibid.*, **84**, 4985 (1962).

[4] G. L. Closs and G. M. Schwartz, *ibid.*, **82**, 5729 (1960).

[5] M. E. Volpin, V. G. Dulova, and D. N. Kursanov, *Dokl. Akad. Nauk SSSR*, **128**, 951 (1959); *Tetrahedron*, **8**, 33 (1960).

[6] Whether reaction by the α-dehydrohalogenation mechanism involves the intermediate formation of a methylene derivative, or whether the halomethyl–metal compound reacts without passing through a methylene, is an important point,[7a,8] but not one to which attention will be given in the present paper.

[7] J. Hine, "Divalent Carbon," The Ronald Press Co., New York, N. Y., 1964: (a) pp 25–30, 66, 76–77; (b) Chapter 3.

[8] G. L. Closs and R. A. Moss, *J. Amer. Chem. Soc.*, **86**, 4042 (1964).

[9] J. Hine and R. D. Weimar, Jr., *ibid.*, **87**, 3387 (1965).

[10] J. Hine, C. H. Thomas, and S. J. Ehrenson, *ibid.*, **77**, 3886 (1955).

Table I. Rate Constants for the Reactions of Methylene Halides and Chloroform with Alkali Metal Alkoxides at 36°

Solvent	Base	10^6k, M^{-1} sec^{-1}				
		CH_2Cl_2	CH_2BrCl	CH_2Br_2	CH_2I_2	$CHCl_3$
MeOH	NaOMe	*a*	3.78 ± 0.02[b]	1.23 ± 0.01	1.88[c]	4.35 ± 0.11
MeOD	NaOMe	0.185 ± 0.005	6.89 ± 0.05	2.34 ± 0.08	2.51 ± 0.13	
i-PrOH	KOPr-*i*	0.396 ± 0.026	19.2 ± 0.2	5.49 ± 0.03	6.84 ± 0.15	3,100 ± 30
i-PrOD	KOPr-*i*	0.593 ± 0.029	31.2 ± 0.5	8.17 ± 0.10	10.2 ± 0.1	
t-BuOH	KOBu-*t*	0.241 ± 0.006	11.8 ± 0.1	2.72 ± 0.07	2.30 ± 0.03	433,000 ± 14,000
t-BuOD	KOBu-*t*	0.457 ± 0.057	19.7 ± 0.6	4.79 ± 0.12	3.97 ± 0.02	

[a] A value of (0.568 ± 0.020) × 10^{-6} M^{-1} sec^{-1} at 50° was reported in ref 10. [b] Data from ref 10. [c] Obtained by interpolation between values at 20.3 and 50.0° reported in ref 10.

Results

Kinetics of Reactions with Alkali Metal Alkoxides. Second-order rate constants for the reactions of methylene halides with alkali metal alkoxides in alcohol solution were calculated from eq 1 where *a* and

$$k = \frac{2.303}{t(2a - b)} \log \frac{b(a - x)}{a(b - 2x)} \qquad (1)$$

b are the initial concentrations of methylene halide and base, respectively, and *x* is the change in concentration of methylene halide that has occurred at time *t*, *i.e.*, 2*x* is the change in base concentration at time *t*. This equation may be derived on the basis of the assumption that 2 mol of base react/mol of methylene halide and that all reaction intermediates, *e.g.*, alkyl halomethyl ethers, are much more reactive than the methylene halides from which they are formed, under the reaction conditions. In a study of the reactions of methylene halides with methanolic sodium methoxide, the constancy of rate constants calculated from eq 1 supported the validity of these assumptions for a number of methylene halides but not for those in which fluoromethyl methyl ether could be an intermediate.[10] The rate constants for the reaction of methylene iodide with sodium methoxide consistently drifted downward, by about 10% between about 15 and 70% reaction. No explanation was found for this tendency, which had been observed previously for the reaction at 20.3° (but not at 50°).[10] The rate constant reported at 20.3° had been obtained by extrapolation to zero time, with the assumption that the observed constants were drifting away from the correct constant.[10] In the current investigation we have simply averaged the values obtained between 5 and 75% reaction. A less consistent tendency for the rate constants for several of the reactions of methylene chloride to drift downward by about the same amount was treated in the same way. There also appeared to be a tendency for larger rate constants to be obtained in runs using larger concentrations of reactants, but this point was not investigated systematically.

The reactions of methylene chloride, bromochloromethane, methylene bromide, and methylene iodide were studied using most or all of the reagents: sodium methoxide in methyl alcohol and in methyl alcohol-*d*, potassium isopropoxide in isopropyl alcohol and in isopropyl alcohol-*d*, and potassium *t*-butoxide in *t*-butyl alcohol and in *t*-butyl alcohol-*d*. Rate constants and average deviations obtained at 36° are listed in Table I.

The reaction of methylene iodide with sodium methoxide in methyl alcohol-*d* was also carried out in the presence of 0.5 *M* sodium iodide and in the presence of 0.5 *M* sodium perchlorate. Rate constants of (2.36 ± 0.18) × 10^{-6} and (2.35 ± 0.18) × 10^{-6} M^{-1} sec^{-1} were obtained, respectively.

Measurements were also made on the rate of reaction of chloroform with alkali metal alkoxides in the three alcoholic solvents used. Rate constants were calculated from eq 2 where *a* is the initial concentration of

$$k = \frac{2.303}{t(3a - b)} \log \frac{b(a - x)}{a(b - 3x)} \qquad (2)$$

chloroform and *b*, *x*, and *t* have the definitions given in connection with eq 1. Equation 2 may be derived on the basis of the assumption that 3 mol of base react/mol of chloroform (which is plausible in all cases but which was checked only in the case of potassium *t*-butoxide) and that the reaction is first order in base and first order in chloroform. The results obtained are shown in Table I.

Formation of Deuterated Methylene Halides and Methylal. The kinetics of the deuterium exchange of methylene chloride, bromochloromethane, methylene bromide, and methylene iodide were studied in isopropyl alcohol-*d* and *t*-butyl alcohol-*d* in the presence of the potassium salts of the alcohols. The deuterium exchange of methylene bromide and iodide was also studied in methyl alcohol-*d* containing sodium methoxide. It was found most convenient to follow the rate of deuterium exchange of the methylene halides by measuring the extent of the concomitant increase in the protium content of the alcohol. This was done by infrared measurements on the O–H stretching band between 2.9 and 3.0 μ. In all the cases for which rate constants were determined, the deuterium-exchange reaction was faster than nucleophilic displacement on carbon. However, nucleophilic displacement on carbon was fast enough to bring about a significant decrease in the concentration of the alkali metal alkoxide used as a catalyst (sometimes in rather small concentrations in order to make the deuterium exchange slow enough to study conveniently) during the time required for exchange of a major fraction of the methylene halide used. In some cases a significant fraction of the methylene halide was also used up by nucleophilic displacements on carbon.

A rate equation for the deuterium-exchange reaction may be based on mechanism 3. Inasmuch as k_{-1} and k_2 should be of about the same order of magnitude[11] and the deuterium content of the alcohol never

$$\begin{aligned}
&RO^- + CH_2X_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ROH + CHX_2^- \\
&CHX_2^- + ROD \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} CHDX_2 + RO^- \\
&RO^- + CHDX_2 \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} CDX_2^- + ROH \\
&CDX_2^- + ROD \underset{k_{-4}}{\overset{k_4}{\rightleftharpoons}} CD_2X_2 + RO^-
\end{aligned} \qquad (3)$$

dropped below 90% in any of the runs made, it is assumed that k_2[ROD] is much larger than k_{-1}[ROH], *i.e.*, that the intermediate carbanions are always deuterated and that the deuterium exchange is irreversible. Then, if p is the increase in the protium concentration in the alcohol at a given time

$$dp/dt = k_1[RO^-][CH_2X_2] + k_3[RO^-][CHDX_2] \qquad (4)$$

It is also assumed that k_1 is equal to $2k_3$, *i.e.*, that secondary deuterium kinetic isotope effects may be neglected. It may then be shown that if the amount of methylal formed is very small compared to p, the following equation is an excellent approximation

$$p = [CHDX_2] + 2[CD_2X_2] \qquad (5)$$

and therefore that

$$dp/dt = k_1[RO^-][a - (p/2)] \qquad (6)$$

where a represents $[CH_2X_2]_0$. If the decrease in the alkoxide concentration that occurs during the reaction is a linear function of p, the extent of reaction, [RO⁻] may be replaced by $b - cp$ where b is equal to $[RO^-]_0$ and c is obtained from the slope of a plot of [RO⁻] against p. Substitution into eq 6 and integration gives

$$k = \frac{2.303}{t[ac - (b/2)]} \log \frac{b[a - (p/2)]}{a(b - cp)} \qquad (7)$$

Equation 7 was used to calculate rate constants for all the exchange reactions carried out in isopropyl alcohol-*d* and *t*-butyl alcohol-*d*. In addition to the determination of the protium content of the alcohol by infrared measurements, the concentration of alkali metal alkoxide was determined at intervals by titration. In each case the plot of [RO⁻] *vs.* p satisfactorily approximated a straight line.

The amount of base used up in the exchange of methylene chloride with isopropyl alcohol-*d* corresponded to the reaction of 1.3% of the methylene chloride. In no other case was as much as 0.3% of the methylene halide used up by reaction with base. Therefore the treatment of these exchange reactions in terms of mechanism 3, which neglects the transformation of methylene halides to formals, is a good approximation. The rate constants obtained within a given run usually agreed very well. The agreement between different runs was not as good. The principal reason for this is believed to be the fact that small concentrations of alkali metal alkoxides (as low as 7×10^{-4} *M*) were used in order to make the reactions slow enough to follow conveniently. These concentrations are difficult to measure accurately and the presence of small amounts of carbon dioxide may cause large errors. For this reason the relative rate constants reported in a given solvent are more reliable than the absolute rate constants.

In the deuterium-exchange reactions carried out in methyl alcohol-*d* around 20% of the methylene halide was used up by reaction with alkali–metal alkoxide. To take this fact into account, a more complicated kinetic treatment was used. In this treatment it is assumed that formal is produced by the SN2 attack of alkoxide ions on methylene halide followed by relatively rapid alcoholysis of the halomethyl methyl ether produced thereby. This assumption was made on the basis of the arguments to be given that the initial nucleophilic displacement of halogen from the methylene halides proceeds by the SN2 mechanism and not by α elimination under the conditions used. A treatment in which an α elimination mechanism was assumed would yield values of k_1 that differ from the ones we have obtained, but not by a large enough factor to affect any of the arguments that are to be presented. Thus k_5 is the rate constant for nucleophilic displacement of halogen from the methylene halide in question.

$$\begin{aligned}
&RO^- + CH_2X_2 \xrightarrow{k_5} ROCH_2X + X^- \\
&RO^- + ROCH_2X \xrightarrow{k_6} (RO)_2CH_2 + X^- \\
&\qquad k_6 \gg k_5
\end{aligned} \qquad (8)$$

It is assumed that deuterium kinetic isotope effects on k_5 are negligible, *i.e.*, that $CHDX_2$ and CD_2X_2 react at the same rate that CH_2X_2 does.

We now consider the simultaneous operation of mechanisms 3 and 8. The same definitions of a, b, p, t, and x are used as were used in connection with eq 1 and 4. We also define a new term d as equal to the amount of deuterium present in the formal

$$d = [CHD(OR)_2] + 2[CD_2(OR)_2] \qquad (9)$$

Inasmuch as we are now dealing with cases in which the amount of formal produced is not negligibly small in comparison to the amount of methylene halide used, eq 5 is no longer an adequate approximation for p, which is instead expressed

$$p = [CHDX_2] + 2[CD_2X_2] + [CHD(OR)_2] + 2[CD_2(OR)_2] \qquad (10)$$

A derivation analogous to that used for eq 6 gives the relation

$$dp/dt = k_1[RO^-][a - x - (p/2) + (d/2)] \qquad (11)$$

In order to integrate this expression we eliminated the variables d and x from it as follows. From mechanism 8 it follows that

$$\begin{aligned}
dd/dt &= k_5[RO^-]([CHDX_2] + 2[CD_2X_2]) \\
&= k_5[RO^-](p - d)
\end{aligned} \qquad (12)$$

Values of k_5, the rate constant for displacement of halogen from the methylene halide, are already available (Table I). Values of p and [RO⁻] were determined at intervals throughout the reaction. By use of these values eq 12 may be integrated graphically to get values of d at various times. Since x may be calculated from

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(11) Primary deuterium kinetic isotope effects in the deuterium exchange of haloforms are relatively small[12-14] and therefore may also be in the case of methylene halides.

(12) J. Hine, R. C. Peek, Jr., and B. D. Oakes, *J. Amer. Chem. Soc.*, 76, 827 (1954).

(13) J. Hine and N. W. Burske, *ibid.*, 78, 3337 (1956).

(14) J. Hine, N. W. Burske, M. Hine, and P. B. Langford, *ibid.*, 79, 1406 (1957).

[RO$^-$], which is equal to $b - 2x$, it is possible to calculate values of $a - x - (p/2) + (d/2)$ at various times. These values were then plotted against p. The average deviation of the points from the best straight line was less than 0.3%. Therefore the function $a - x - (p/2) + (d/2)$ could be adequately represented as $a - mx$, where m may be calculated from the slope of the plot. Analogously a plot of [RO$^-$] *vs.* p gave a straight line (within an average deviation of less than 1%), from which [RO$^-$] was represented as $b - cx$. Substitution into eq 11 then yields

$$\mathrm{d}p/\mathrm{d}t = k_1(b - cx)(a - mx) \tag{13}$$

which may be integrated to give

$$k_1 t = \frac{2.303}{ac - bm} \log \frac{b(a - mp)}{a(b - cp)} \tag{14}$$

Rate constants for carbanion formation by methylene halides are shown in Table II. The values in isopropyl alcohol-*d* and *t*-butyl alcohol-*d* were calculated from eq 7 and those in methyl alcohol-*d* from eq 14.

Table II. Rate Constants for the Deuterium Exchange of Methylene Halides in the Presence of Alkali Metal Alkoxides at 36°

	10^5k, M^{-1} sec^{-1}		
Halide	MeOD, NaOMe	*i*-PrOD, *i*-PrOK	*t*-BuOD, *t*-BuOK
CH_2Cl_2		2.81 ± 0.12	105 ± 3
CH_2BrCl		38 ± 4	700 ± 50
CH_2Br_2	0.63 ± 0.02	210 ± 80	3,100 ± 300
CH_2I_2	3.62 ± 0.09	1,120 ± 30	25,200 ± 800

In order to learn the deuterium content of the methylal formed from methylene bromide and sodium methoxide in methyl alcohol-*d* at a stage early enough in the reaction that the methylene bromide had not become highly deuterated, several reactions were stopped when only 9–14% of the methylene bromide had been transformed to methylal. Methylal was isolated from these reaction mixtures by preparative gas–liquid partition chromatography. The deuterium content of the first two samples was measured by integration of the proton magnetic resonance spectra and comparison with methylal containing deuterium in only the natural abundance. When this method proved to be less precise than desired, the deuterium content of these and two additional samples was determined by combustion and measurement of the density of the water produced.[15] The results of these determinations are shown in Table III.

Table III. Deuterium Content of Methylal Formed from CH_2Br_2 and NaOMe in MeOD

			Atoms of D/molecule		
$[CH_2Br_2]_0$, M	$[NaOMe]_0$, M	% reaction[a]	Combustion anal.	Pmr anal.	Calcd[b]
1.305	1.052	9.9	0.12, 0.12	0.19 ± 0.10	0.12[c]
1.305	1.052	13.1	0.18, 0.18	0.21 ± 0.05	0.17[c]
0.747	0.562	10.0	0.08,[d] 0.07		0.13[e]
0.747	0.562	13.3	0.11, 0.11		0.17[e]

[a] % methylene bromide transformed to methylal. [b] From eq 20. [c] Using $k_1 = 6.36 \times 10^{-6}$ M^{-1} sec^{-1} and $k_5 = 3.06 \times 10^{-6}$ M^{-1} sec^{-1} [d] An explosion occurring during the analysis makes this value suspect. [e] Using $k_1 = 6.36 \times 10^{-6}$ M^{-1} sec^{-1} and $k_5 = 2.43 \times 10^{-6}$ M^{-1} sec.$^{-1}$.

Mechanisms 3 and 8 may be used in calculating how much deuterium would be present in the methylal because of deuterium exchange of the methylene bromide before its transformation to methylal. In this calculation $p - d$ is treated as a variable.

$$\mathrm{d}(p - d)/\mathrm{d}t = \left[k_1\left(a - x - \frac{p - d}{2}\right) - k_5(p - d)\right][\mathrm{RO}^-] \tag{15}$$

$$\mathrm{d}x/\mathrm{d}t = k_5(a - x)[\mathrm{RO}^-] \tag{16}$$

Dividing eq 15 by eq 16

$$\frac{\mathrm{d}(p - d)}{\mathrm{d}x} = \frac{k_1}{k_5} - \left(\frac{k_1}{2k_5} + 1\right)\left(\frac{p - d}{a - x}\right) \tag{17}$$

Integration of eq 17 gives

$$p - d = 2(a - x)\left[1 - \left(1 - \frac{x}{a}\right)^q\right] \tag{18}$$

where $q = k_1/(2k_5)$. Combination of eq 12 and 16 gives

$$\mathrm{d}d/\mathrm{d}x = (p - d)/(a - x) \tag{19}$$

Combination of eq 18 and 19, and integration, give

$$d = 2x + \left(\frac{2a}{q + 1}\right)\left[\left(1 - \frac{x}{a}\right)^{q+1} - 1\right] \tag{20}$$

The values of the nucleophilic substitution rate constant k_5 used with eq 20 in calculating the last column of Table III were those determined at about the reactant concentrations used. Values of k_1 were not determined at various reactant concentrations and the calculations using eq 20 were carried out with the k_1 value from Table II, which was determined at reactant concentrations near those used for the last two samples of Table III.

Discussion

The change in the reactivities of the four methylene halides studied that occurs on going from sodium methoxide to potassium isopropoxide to potassium *t*-butoxide (each in the corresponding alcohol) shows a similar pattern (Table I). In each case the reactivity reaches a maximum in isopropyl alcohol, where the reactivity is from 3.2 to 5.1 times that in methyl alcohol, and then decreases on going to *t*-butyl alcohol, where the reactivity is 1.2 to 3.1 times that in methyl alcohol.

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(15) The deuterium determinations by combustion analysis were carried out by Josef Nemeth, Urbana, Ill.

This behavior is in striking contrast to that of chloroform, which is about 700 times as reactive toward potassium isopropoxide and about 100,000 times as reactive toward potassium *t*-butoxide as toward sodium methoxide. We assume that in each of the three solvents the reaction of chloroform involves its transformation to a trichloromethyl anion which then decomposes to give dichloromethylene.[7b] The increase in reactivity of chloroform that occurs on going from methyl alcohol to isopropyl alcohol to *t*-butyl alcohol we attribute largely to the increase in basicity that occurs in the series MeO^-, *i*-PrO^-, *t*-BuO^-. The 53-fold greater basicity of isopropoxide ions compared with methoxide ions (*i.e.*, greater acidity of methyl alcohol compared with isopropyl alcohol[16]) combined with the almost doubled concentration of alcohol in pure methyl alcohol compared to isopropyl alcohol should make the equilibrium constant for the formation of trichloromethyl anions

$$K = \frac{[CCl_3^-]}{[CHCl_3][RO^-]}$$

about 100 times as large in isopropyl alcohol solution as in methyl alcohol, even if there were no solvent effects (*i.e.*, if activity coefficients had the same value in isopropyl alcohol as in methyl alcohol).

If the methylene halides were reacting by an α-elimination mechanism, either the formation of a dihalomethyl anion (or dihalomethyl–alkali metal compound) or the subsequent reaction of such a carbanion would be the rate-controlling step. In either case the reaction rate would be expected to be increased when a more strongly basic alkoxide ion was used as a reactant. If as much as 0.1% of the reaction of sodium methoxide with any of the methylene halides studied proceeded by an α-elimination mechanism and if the rate constant for α elimination increased by 10^5-fold on going to potassium *t*-butoxide (as it does in the case of chloroform) then the reaction of that methylene halide with potassium *t*-butoxide would have a rate constant 100 times larger than its rate constant for reaction with sodium methoxide. The fact that no such increases in reactivity are seen on going from sodium methoxide to potassium *t*-butoxide provides strong evidence that no significant fraction of the reactions of sodium methoxide with the methylene halides studied consists of α elimination. It does not rule out the possibility that significant fractions of some of the reactions of methylene halides with potassium *t*-butoxide are α eliminations.

The rates of base-catalyzed deuterium exchange of the methylene halides were studied to test the possibility that, for some unforeseen reason, the three alkali-metal alkoxides used differ very little in their rates of removal of protons from methylene halides. It was found (Table II) that the three catalysts stand in the order *t*-BuOK > *i*-PrOK ≫ MeONa with regard to their rates of deprotonation of methylene halides. The relative rates of deprotonation of methylene halides depend on the relative stabilities of the transition states for deprotonation, in which the alkoxide ion has partially coordinated with a proton. The relative reactivity of chloroform with the various alkoxide ions presumably depends on the relative concentrations of trichloromethyl anions, which are formed by the complete coordination of the alkoxide ion with a proton. Therefore the greater basicity of *t*-butoxide ions would be expected to be more fully reflected in the rate of decomposition of chloroform than in the rate of deuterium exchange of methylene halides. Hence it is not surprising that the increase in reactivity in the deuterium exchange of methylene halides found on going from sodium methoxide to potassium *t*-butoxide (about 6000-fold) is smaller than the corresponding increase in the rate constant for the decomposition of chloroform (100,000-fold).

In addition to the preceding argument that the change in relative reaction rates that accompanies a change in the nature of the alkoxide ion is not a plausible one for an α-elimination mechanism, it is worthwhile to consider whether this change is plausible for reaction by the SN2 mechanism. Although we have found no reported kinetic studies of the reactions of a given substrate with the three nucleophilic reagents we have investigated, the following observations give a fairly good indication of how the SN2 reactivity of methylene halides would be expected to vary with the different nucleophilic reagents (and solvents) used. Ethyl bromide is about twice as reactive toward sodium ethoxide in ethyl alcohol[17] and about 3.6 times as reactive toward potassium isopropoxide in isopropyl alcohol[18] as toward sodium methoxide in methanol.[10] All three of these reactions are probably largely SN2. The rate constant for the SN2 attack of sodium ethoxide on isopropyl bromide in ethyl alcohol is $1.06 \times 10^{-6}\ M^{-1}$ at 25°.[19] The reaction of isopropyl bromide with potassium *t*-butoxide in *t*-butyl alcohol is so largely an elimination reaction that the rate constant for substitution has not been determined, but from the report that the reaction is more than 90% elimination an upper limit of $0.23 \times 10^{-6}\ M^{-1}\ \text{sec}^{-1}$ is established for the substitution reaction.[20] The rate constant for the reaction of methyl iodide with potassium *t*-butoxide in *t*-butyl alcohol[21] is about 13 times as large as that for its reaction with sodium methoxide in methyl alcohol.[10] These data may be rationalized by the generalization that the increasing basicity that accompanies α methylation of an alkoxide ion may increase its reactivity toward an alkyl halide if that halide is relatively unhindered but it may decrease the reactivity if hindrance is too great. Since a methyl group is about the same size as a bromine atom, SN2 attack on ethyl bromide should be sterically similar to SN2 attack on methylene bromide. It may be noted that the increase in reactivity on going from sodium methoxide to potassium isopropoxide is about the same for these two compounds. The increases in reactivity on going from sodium methoxide to potassium *t*-butoxide are smaller for the methylene halides than for the less hindered methyl iodide but probably larger than for the more hindered isopropyl bromide. We suggest that the increased SN2 reactivity that occurs on going from methoxide to isopropoxide, indicating that increased basicity is more important than increased steric hindrance, is related

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[17] E. D. Hughes, C. K. Ingold, S. Masterman, and B. J. McNulty, *J. Chem. Soc.*, 899 (1940).

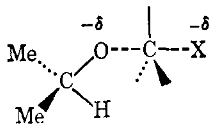
[18] J. Hine and K. Tanabe, *J. Amer. Chem. Soc.*, **80**, 3002 (1958).

[19] V. J. Shiner, *ibid.*, 74, 5285 (1952).

[20] H. C. Brown, I. Moritani, and Y. Okamoto, *ibid.*, 78, 2193 (1956).

[21] J. O. Schreck, *J. Chem. Educ.*, **43**, 149 (1966).

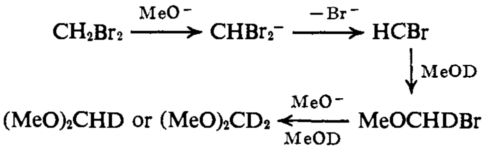
to the ability of an isopropoxide anion in an SN2 transition state to orient itself with its α-hydrogen atom toward the plane of the three "nonreacting" substituents of the carbon atom at which displacement is occurring.



In the transition state for attack by a *t*-butoxide ion any conformation around the carbon–oxygen bond orients at least one of the methyl groups toward the plane of the nonreacting substituents. Thus on going from isopropoxide to *t*-butoxide the increased steric hindrance is a larger factor than the increased basicity (in the case of methylene halides, at least) and a decrease in reactivity is observed. In addition to basicity and steric hindrance the relative reactivities observed in the different solvents must also be affected by differences in solvation and ionic association.

In the preparation of methylene-d_2 iodide by the base-catalyzed deuterium exchange of methylene iodide, Blanchard and Simmons added sodium iodide to the reaction mixture "to suppress carbene hydrolysis," but did not describe evidence indicating the necessity for this precaution.[22] We have found that the reaction of methylene iodide with sodium methoxide in methyl alcohol-*d* proceeds at the same rate, within the experimental uncertainty, in the presence of 0.5 *M* sodium iodide as in its absence. To test the possibility that a mass-law effect by the iodide ions was being masked by a compensating ionic strength effect, the reaction kinetics were also studied in the presence of 0.5 *M* sodium perchlorate, which was also found to have no significant effect on the reaction rate. According to the competition factors determined for dichloromethylene,[23] 0.5 *M* iodide ions in water should decrease the initial rate of reaction of chloroform with hydroxide ions to one-sixth of that in the absence of iodide ions. The absence of any significant effect of iodide ions on the rate of reaction of methylene iodide with sodium methoxide is demanded by the SN2 mechanism, but it provides little direct evidence against an α-elimination mechanism since even if iodomethylene were a reaction intermediate there is no guarantee that it would react to a significant extent with 0.5 *M* iodide ions in the presence of about 20 *M* methyl alcohol.

In the case of the reaction of methylene bromide with sodium methoxide in methyl alcohol-*d* the reaction mechanism was investigated by determination of the deuterium content of the reaction product. If the reaction proceeds by an α-elimination mechanism, *e.g.*



$$\begin{tikzcd}
CH_2Br_2 \arrow[r, "MeO^-"] & CHBr_2^- \arrow[r, "-Br^-"] & HCBr \arrow[d, "MeOD"] \\
(MeO)_2CHD \text{ or } (MeO)_2CD_2 & & MeOCHDBr \arrow[ll, "MeO^-", "MeOD"']
\end{tikzcd}$$

the methylene group of the methylal produced would contain at least one deuterium atom per molecule. (The same result would be obtained from an α-elimination mechanism in which bromomethylene is not an intermediate, *e.g.*, one in which bromomethyl methyl ether is formed by attack of methanol on bromomethylsodium.) If the reaction of methylene bromide with sodium methoxide consists of two consecutive SN2 reactions, or of an SN2 reaction followed by an SN1 reaction, the methylal produced will contain no

$$CH_2Br_2 \xrightarrow{MeO^-} MeOCH_2Br \xrightarrow{MeO^-} (MeO)_2CH_2$$

more deuterium than the methylene bromide (neglecting complications due to secondary deuterium kinetic isotope effects). This method of distinguishing between the two possible reaction mechanisms will not be experimentally feasible if the base-catalyzed deuterium exchange is too much faster than the basic alcoholysis, because in such a case the methylene halide would become highly deuterated so early in the reaction that any methylal that could be isolated would also be highly deuterated, regardless of the mechanism of its formation. In the case of the reaction of methylene bromide with sodium methoxide in methyl alcohol, the rate constant for deuterium exchange is less than three times as large as that for nucleophilic substitution. Therefore the amount of deuterium introduced into the methylal *via* exchange of methylene bromide before alcoholysis would be relatively small for the methylal formed early in the reaction.

From Table III it may be seen that none of the samples of methylal isolated after about 10–13% reaction contained significantly more deuterium than would be expected from SN2 attack on the increasingly deuterated methylene bromide present in the reaction mixture. In fact the last two samples contain an unexpectedly small amount of deuterium. We feel that this probably results from some combination of a secondary deuterium kinetic isotope effect on k_5, variations in k_1 and k_5 due to changes in reactant concentrations, and experimental error in the determination of the deuterium content and of k_1 and k_5.

The results shown in Table III show not only that methylene bromide does not react to a significant extent by an α-elimination mechanism, but also that the intermediate bromomethyl methyl ether neither undergoes deuterium exchange under the reaction conditions nor reacts by an α-elimination mechanism. Thus there is a change in mechanism between the reaction of bromomethyl methyl ether with methanolic sodium methoxide and the reaction of dichloromethyl methyl ether with potassium isopropoxide in isopropyl alcohol, which proceeds by an α-elimination mechanism.[24] Increased basicity of the alkoxide ion, increased acidity of the proton that must be removed, increased stability of the intermediate methylene, and decreased reactivity by alternative (SN1 and SN2) mechanisms should all contribute to such a change in mechanism.

In contrast to the alkali metal alkoxides in alcohol, which displace halogen from each of the four methylene halides studied largely or almost entirely by the SN2 mechanism, methyllithium and *n*-butyllithium in diethyl ether displace chlorine from methylene chloride very largely by an α-dehydrochlorination mechanism.[2-4] Thus it is clear that with the alkyllithium compounds

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(22) E. P. Blanchard and H. E. Simmons, *J. Amer. Chem. Soc.*, **86**, 1337 (1964).

(23) J. Hine and A. M. Dowell, Jr., *ibid.*, **76**, 2688 (1954).

(24) J. Hine, R. J. Rosscup, and D. C. Duffey, *ibid.*, **82**, 6120 (1960).

nucleophilic attack on the hydrogen atoms of methylene chloride is faster than nucleophilic attack on the carbon atom. This alone is not enough to make the α-elimination mechanism predominant, however. In all the cases studied in the present investigation the alkoxide ion deprotonates the methylene halide more rapidly than it attacks the carbon atom. The important difference in the case of alkyllithium compounds is the fact that the very low level of acidity of alkanes makes the deprotonation of methylene chloride essentially irreversible.

In studies of the kinetics of the deuterium exchange of haloforms it was found that α-iodine and -bromine substituents both increase the ease of carbanion formation more than does α-chlorine, which in turn is much more effective than α-fluorine.[25] In some cases (compare iodoform and bromoform or dichloroiodomethane and bromodichloromethane) α-iodine and α-bromine were found to have about the same effect, but in one case (compare diiodofluoromethane and dibromofluoromethane) α-iodine facilitated carbanion formation somewhat, compared to α-bromine, as it has also been found to in the present experiments on methylene halides. In a closely related series of compounds, the 1,1-dihalo-2,2,2-trifluoroethanes, α-bromine was found to facilitate carbanion formation somewhat, compared to α-iodine.[26] Comparison of the data on methylene halides with those on haloforms seems to show clearly that any α-halogen substituent, even fluorine, increases the ease of carbanion formation in this series of compounds. The rate constant for the dedeuteration of diiodofluoromethane-*d* by hydroxide ions in water at 36.0° is $590{,}000 \times 10^{-5}\ M^{-1}\ \text{sec}^{-1}$ (extrapolated from data at 0 and 20°).[27] Even after allowing for a deuterium kinetic isotope effect[25] and the fact that hydroxide ion catalyzed deuterium exchange in water may be somewhat faster than methoxide ion catalyzed exchange in methyl alcohol,[26] this rate constant is thousands of times larger than the rate constant for the methoxide ion catalyzed deuterium exchange of methylene iodide in methyl alcohol-*d*.

As a by-product of our mechanistic investigation we have observed a fairly large solvent kinetic isotope effect. In every case studied the S_N2 reaction of a given methylene halide with a given alkali metal alkoxide is faster in the deuterated alcohol than in the protiated alcohol. In the 11 cases for which data are listed in Table I, $k_{\text{ROD}}/k_{\text{ROH}}$ ranges from 1.34 to 1.90, averaging 1.66 with an average deviation of 0.15. In the ten cases that were studied, the deuterium exchange was faster, usually much faster, than the nucleophilic substitution reaction. Hence over most of the course of the nucleophilic substitution reaction the organic halide that is reacting is largely a methylene-d_2 halide. It follows that the $k_{\text{ROD}}/k_{\text{ROH}}$ values, which average 1.66 ± 0.15, are due to solvent deuterium kinetic isotope effects *and* to substrate secondary deuterium isotope effects on S_N2 reactivity. Both positive and negative α-deuterium isotope effects have been reported for nucleophilic substitution reactions.[28] In no case where the mechanism seems clearly to be S_N2 has an absolute magnitude greater than 4% per deuterium been reported for such an effect, however. Therefore, unless the reactions of the methylene-d_2 halides are being accelerated by α-deuterium kinetic isotope effects of unprecedented magnitude, the S_N2 reactivity of alkoxide ions toward methylene halides must be considerably larger in deuterio alcohol solutions than in protio alcohol solutions.

It is known that nucleophilic displacements on the acidic protons of nitromethane and certain carbonyl compounds by acetate and chloroacetate ions are 20–40% faster in protium oxide than in deuterium oxide solution.[29] This contrasts with the fact that deuterioxide ions in deuterium oxide solution perform similar nucleophilic displacements on protons 20–40% faster and nucleophilic attacks on the carbon atoms of epoxides[30] and alkyl sulfonates[31] 4–16% faster than protioxide ions in protium oxide solution. The difference in direction between these two deuterium solvent isotope effects could have been rationalized by noting that acetate and chloroacetate ions are isotopically the same in heavy water as in light water whereas hydroxide ions are isotopically different in these two solvents. This rationalization is rendered much less plausible by the observation that alkoxide ions, which are isotopically the same in a deuterated as in a protiated solvent, behave like hydroxide ions, showing greater reactivity in a deuterated solvent. The greater reactivity in deuterio alcohol solution is in agreement with Bunton and Shiner's generalization that centers of high local acidity or basicity are stabilized more by a protioxylic solvent than by a deuterioxylic solvent.[32]

Experimental Section[33]

Deuterio Alcohols. Some of the methyl alcohol-*d* used was prepared from trimethyl borate, deuterium oxide, and sodium carbonate[34] and some from dimethyl carbonate, deuterium oxide, and deuterium sulfate.[35] Isopropyl alcohol-*d* and *t*-butyl alcohol-*d* were prepared by mixing the alcohol with deuterium oxide, adding potassium carbonate to remove the exchanged water, repeating the process several times, and then thoroughly drying and purifying the alcohol. The deuterio alcohols thus prepared were found by pmr spectroscopy to be 0.1 to 0.4 *M* in their protio counterparts.

Kinetics of Reactions with Alkali Metal Alkoxides. A typical run was begun by preparing a solution of a weighed amount of methylene halide in the alcohol to be used in a dry 25- or 50-ml volumetric flask under nitrogen. A standard solution of alkali metal alkoxide in alcohol was added to the flask, which was then filled to the mark with alcohol. The flask was shaken and a sample of known volume (usually 4.00 ml) was withdrawn and added to a beaker containing 20 ml of distilled water. The contents of this beaker, in which reaction occurred at a negligible rate because of the separation of the methylene halide from the solution, were

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(25) J. Hine, "Physical Organic Chemistry," 2nd ed, McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 487.

(26) J. Hine, R. Wiesboeck, and R. G. Ghirardelli, *J. Amer. Chem. Soc.*, **83**, 1219 (1961).

(27) J. Hine, R. Butterworth, and P. B. Langford, *ibid.*, **80**, 819 (1958).

(28) *Cf.* S. Seltzer and A. A. Zavitsas, *Can. J. Chem.*, **45**, 2023 (1967).

(29) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, p 199.

(30) J. G. Pritchard and F. A. Long, *J. Amer. Chem. Soc.*, **78**, 6008 (1956).

(31) S. Hartman and R. E. Robertson, private communication to Bunton and Shiner.[32]

(32) C. A. Bunton and V. J. Shiner, Jr., *J. Amer. Chem. Soc.*, **83**, 3207 (1961).

(33) Infrared spectra were recorded using a Perkin-Elmer Model 21 spectrophotometer. For proton magnetic resonance spectra a Varian A-60 spectrometer was used with external tetramethylsilane as a reference. All boiling points were determined at atmospheric pressure in Atlanta, where the barometer was not read but where the altitude is 1000 ft.

(34) *Cf.* J. F. Bunnett and J. D. Reinheimer, *J. Amer. Chem. Soc.*, **84**, 3285 (1962).

(35) *Cf.* A. Streitwieser, J. Verbit, and P. Stang, *J. Org. Chem.*, **29**, 3706 (1964).

titrated with standard perchloric acid to the phenolphthalein end point as soon as feasible. The remainder of the contents of the volumetric flask was transferred to a dry serum bottle under nitrogen. The bottle was sealed with a serum cap that had been extracted with methylene chloride and then dried thoroughly. The serum bottle was then placed in a 36.0° constant-temperature bath, with about 3 min having elapsed since the addition of the alkali metal alkoxide solution to the methylene halide solution. At recorded times samples were withdrawn from the reaction mixture by means of a nitrogen-flushed syringe, added to water, and titrated with standard acid. Only in the runs in which methanol was the solvent did the reaction solution remain homogeneous throughout the reaction. In the runs carried out in isopropyl alcohol and *t*-butyl alcohol, alkali metal halide began precipitating from the reaction solution before 1% reaction. The samples analyzed were taken from the clear supernatant liquid in these cases. The initial time for the reaction was taken as that when the bottle was placed in the constant-temperature bath. The fact that the reaction in the constant-temperature bath proceeded relatively slowly until the contents of the bottle warmed to 36° tended to compensate for the small amount of reaction that took place before the bottle was placed in the bath. More important is the fact that all the reactions studied in this way were followed for periods of 1 to 11 days, so that a 3-min uncertainty in the reaction time does not introduce a major error in the rate constants obtained. As a sample, the data obtained in one run on the reaction of methylene iodide with sodium methoxide in methyl alcohol-*d*, the only reaction in which there seemed to be a consistent and significant trend in the rate constants, are listed in Table IV.

Table IV. Kinetics of the Reaction of Methylene Iodide with Sodium Methoxide in Methyl Alcohol-*d* at 36.0° [a]

Time, sec	[MeONa], *M*		10^6k, M^{-1} sec^{-1}
0	0.5596		
88,380	0.4593		2.53
150,840	0.4073		2.47
181,140	0.3836		2.49
255,300	0.3390		2.42
268,020	0.3326		2.41
317,820	0.3076		2.39
424,080	0.2629		2.35
512,700	0.2332		2.32
596,040	0.2093		2.30
663,060	0.1913		2.30
		Av	2.40 ± 0.07

[a] The initial concentration of methylene iodide was 0.4672 *M*.

For the reactions of chloroform with potassium isopropoxide and *t*-butoxide, which were relatively rapid, more dilute solutions of reactants were used, the reaction was started at 36°, and the technique was modified in certain other ways so as to permit samples to be taken after short but accurately known times.

Products and Stoichiometry of Reactions with Alkali Metal Alkoxides. It is known that sodium methoxide in methanol and sodium isopropoxide in isopropyl alcohol react with methylene halides to give dimethylformal(methylal) and diisopropylformal, respectively.[36] We found only these products in reactions with methylene bromide and bromochloromethane, for which we have made product studies. The only product we could isolate from the reaction of potassium *t*-butoxide with methylene bromide was di-*t*-butylformal: bp 145° (lit.[37] 50–52° (18 mm)); ir (neat, in order of decreasing intensity) 1050, 1010, 3010, 1195, 1370, and 1090 cm^{-1}; pmr (neat) τ 5.21 (s, 1, CH_2) and 9.02 (s, 9, CH_3).

The stoichiometry of the reaction of potassium *t*-butoxide with methylene bromide and of potassium isopropoxide with bromochloromethane was studied by potentiometric titration of the amount of halide ions formed after a measured amount of base had been used up. The ratios $\Delta[RO^-]/[X^-]$ were 0.99 ± 0.04. Measurements on the reaction of potassium *t*-butoxide with chloroform showed that $\Delta[RO^-]/\Delta[CHCl_3]$ was equal to 3.02 ± 0.03.

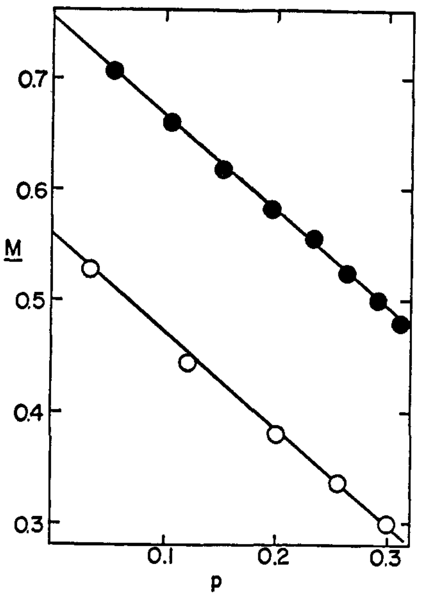

Figure 1. Plot of $a - x - (p/2) + (d/2)$ *vs.* *p*, ●; plot of [NaOMe] *vs.* *p*, ○.

Kinetics of the Deuterium Exchange of Methylene Halides. These kinetic runs were made in much the same way as the corresponding alcoholysis reactions, except that samples were taken both for acidimetric titration and for determination of the concentration of protio alcohol by the method described in the next section. Kinetic data on a run using methylene bromide and sodium methoxide in methanol-*d* are shown in Table V. The plots of $a - x - (p/2) + (d/2)$ and $[MeO^-]$ *vs.* *p* required for the determination of *m* and *c* for use in eq 14 are shown in Figure 1.

Determination of the Concentration of ROH Present in ROD. The extinction coefficients of methyl alcohol in methyl alcohol-*d*, isopropyl alcohol in isopropyl alcohol-*d*, and *t*-butyl alcohol in *t*-butyl alcohol-*d* were determined at the O–H stretching maxima between 2.9 and 3.0 μ by recording the spectra of solution of known amounts of the ROH compound in the corresponding ROD compound over the range 2.4–3.2 μ. The absorbance at the absorption maximum was taken as equal to the difference between the absorbance reading at the maximum and the reading at the absorption minimum between 2.65 and 2.75 μ. The solutions studied attacked the sodium chloride windows of the cell with a resultant slow decrease in the transparency of the cell and increase in the length of the light path. The change in transparency of the cell was essentially independent of the wavelength over the range 2.6–3.0 μ, so that the *differences* in absorbance being measured were not affected. When the loss of transparency became excessive, the cell was dismantled and its windows were repolished. At frequent intervals the length of the light path was measured by determining the absorbance of the cell filled with benzene at 5.1 μ.[38] The light path was kept in the range 0.045–0.072 mm. The molar absorbancies determined were found to decrease when increasing concentrations of alkali metal alkoxides were in the solution. This effect was negligible at the concentrations (<0.02 *M*) of alkoxide used in the runs in isopropyl alcohol-*d* and *t*-butyl alcohol-*d*. The molar absorbancies used for ROH in these solvents were 170 and 148 M^{-1} cm^{-1}, respectively. For methyl alcohol-*d* the molar absorbancy of ROH decreased from 135 M^{-1} cm^{-1} in the absence of base to 102 M^{-1} cm^{-1} in the presence of 1.434 *M* sodium methoxide. In practice the molar absorbancy to be used in the presence of a given concentration of sodium methoxide was read off a plot of molar absorbancy *vs.* sodium methoxide concentration.

Deuterium Content of the Methylal Formed from Methylene Bromide and Sodium Methoxide in Methyl Alcohol-*d*. In one run 5.0 ml of methylene bromide was added to a mixture of 25.0 ml of methyl alcohol-*d* and 25.0 ml of 2.134 *M* sodium methoxide in methyl alcohol-*d* in a 60-ml serum bottle. The bottle was stoppered, shaken, and placed in a constant temperature bath at 36.0°. After 740 min the serum bottle was removed from the bath

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[36] *Cf.* M. Arnhold, *Ann.*, **240**, 192 (1887).

[37] R. Leimu, *Suomen Kemistilehti*, *B*, **19**, 66 (1946).

[38] "Instruction Manual for Infrared Sampling Accessories," Connecticut Instrument Co., Wilton, Conn., p 17.

Table V. Deuterium Exchange of Methylene Bromide with Methyl Alcohol-*d* in the Presence of Sodium Methoxide at 36°

Time, sec	Absorb.	10^3 × cell path, cm	[MeOH], *M*	[NaOMe], *M*	10^6k,[a] M^{-1} sec^{-1}
0				0.562[b]	
180	0.189[c]	6.24	0.229		
3,600				0.554	
15,780	0.220[c]	6.26	0.266		6.31[d]
18,600				0.524	
63,060	0.300[e]	6.39	0.353		5.86[f]
65,760				0.442	
100,680				0.394	
103,000	0.375[e]	6.51	0.433		6.56
148,440	0.426[g]	6.56	0.485		6.31
150,720				0.335	
184,860				0.301	
185,880	0.465[g]	6.57	0.528		6.49
237,600	0.495[g]	6.52	0.567		6.29
240,720				0.257	
271,920	0.531[g]	6.58	0.602		6.22
274,860				0.237	
				Av	6.37 ± 0.12

[a] Calculated from eq 14, using $a = 0.754$, $b = 0.562$, $c = 0.888$, and $m = 0.874$. [b] Extrapolated. [c] ϵ 132 M^{-1} cm^{-1}. [d] This value, like all those for points taken before 5% reaction, was neglected. [e] ϵ 133 M^{-1} cm^{-1}. [f] Inasmuch as this value for *k* deviated from the average of the others by more than four times the average deviation, it was neglected. [g] ϵ 134 M^{-1} cm^{-1}.

and cooled to 0°. Its contents were poured into a separatory funnel containing a water–ice slurry. The resultant mixture was extracted four times with four 5-ml portions of carbon tetrachloride. The combined extracts were dried over calcium chloride for several days in a refrigerator. Samples of from 0.25 to 0.50 ml were injected into a gas–liquid partition chromatography apparatus (Wilkins "Autoprep," Model A-700) fitted with an Apiezon column. The apparatus was at 30–40°, and its exit port was attached to a two-way valve leading to a small bottle and to a 10-in. syringe needle inserted in a small-bore nmr tube, which was surrounded by a Dry Ice bath. The two-way valve was turned so as to lead the effluent gases into the nmr tube during the time when methylal was being eluted from the column, after which the valve was turned and the apparatus programmed to 120° to remove the carbon tetrachloride and methylene bromide rapidly. After the removal of these two fractions the apparatus was cooled and another sample injected. When the carbon tetrachloride extract had been completely processed, the tube containing methylal was sealed and the nmr spectrum of its contents determined. The ratio of the area of the methylene peak to the area of the methyl peak was determined by use of the electronic integrator. Sixteen determinations gave a value 0.295 with a probable error of 0.015. Sixteen determinations carried out immediately thereafter using methylal containing only the natural abundance of deuterium gave the value 0.328 ± 0.012. The correct ratio of methylene to methyl hydrogen atoms in methylal is 0.333, of course. Therefore the value 0.295 was multiplied by 333/328 to give 0.300 with a probable error of 0.024. Combustion analysis[15] of this sample gave 1.56 and 1.56 atom % excess deuterium. In a similar run in which the reaction was stopped after 11,820 min, the corrected ratio of methylene to methyl protium atom was 0.299 ± 0.012. Combustion analysis showed 2.27 and 2.26 atom % excess deuterium.

Two other samples were obtained from more dilute reactants using similar techniques except that the extracted aqueous layer was titrated acidimetrically to determine how much reaction had taken place, and the glpc-separated methylal was collected in an evacuated Pyrex bulb cooled in liquid nitrogen. Duplicate combustion analysis[15] of samples taken after 10.0 and 13.3% reaction showed 1.00[39] and 0.86 atom % and 1.42 and 1.40 atom % excess deuterium.

Acknowledgment. We acknowledge our indebtedness to the National Science Foundation for a grant that made possible the purchase of the nmr spectrometer used in this investigation.

(39) Because of an explosion in this analysis it is not clear that combustion was complete.