could presumably be made by using α,α-diphenylethylene in place of ethylene in **2**. If both phenyls were either above or below the square plane, two signals for the *o*-methyls should be observed. However, if the diphenylethylene were frozen out so that one phenyl was above and one phenyl below the plane, the *o*-methyls would again be magnetically equivalent and only one signal should result. Unfortunately, the compound of interest could not be prepared, but the investigation is being pursued.

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Catalysis of α-Hydrogen Exchange. IV. Deuterium Exchange of Methoxyacetone[1,1a]

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Abstract: The kinetics of loss of deuterium from methoxyacetone containing deuterium α to the carbonyl group have been studied in aqueous solution. Catalytic constants have been determined for hydrogen ions, hydroxide ions, water, phenoxide ions, *p*-nitrophenoxide ions, trimethylamine, triethylamine, N-methylpyrrolidine, and N-methylmorpholine. In the presence of N-methylmorpholine buffers the reaction is slightly subject to catalysis by methylammonium chloride, presumably because of the intermediate formation of an enamine. Exchange at the methyl position is faster (by up to sixfold) than at the methylene position for all the catalysts studied except hydroxide ions, which brought about slightly more rapid exchange at the methylene position.

Many physiologically important reactions, such as aldol condensations, epimerizations, etc., involve deprotonation of an organic molecule (*e.g.*, a sugar) at a position that is α to a carbonyl group and to a hydroxy group. As a first step in studying the mechanisms of such reactions we have investigated the deuterium exchange of methoxyacetone. The methoxy substituent should have an influence on the acidity of hydrogen atoms attached to the same carbon atom that is quite similar to that of a hydroxy substituent, but the greater difficulty of oxidizing and deprotonating the methoxy substituent should decrease the probability of complicating side reactions.

Results

The proton magnetic resonance (pmr) spectrum of methoxyacetone consists of three singlets, at τ 5.97, 6.59, and 7.87, attributed to the methylene hydrogen atoms, the methoxy hydrogen atoms, and the carbon-bound methyl (referred to hereafter simply as methyl) hydrogen atoms, respectively, on the basis of their relative intensities and chemical shifts. When solutions of the compound in deuterium oxide are heated with sodium carbonate, the absorption due to the methylene and methyl hydrogen atoms decreases in intensity. We have studied the catalytic action of hydrogen ions and various bases on the dedeuteration of the deuterated methoxyacetone prepared in this way. The reaction was followed by extracting the aqueous reaction solutions with chloroform and integrating the pmr spectra of the chloroform extracts. The methoxy group of the ketone provides an internal standard for comparison with the increasing intensities of the other two absorption peaks. First-order rate constants were determined using the equation

$$k_pt = 2.303 \log \frac{(M/R)_\infty - (M/R)_0}{(M/R)_\infty - (M/R)_t} \qquad (1)$$

where R is the integrated intensity of the reference (methoxy) peak, M is the integrated intensity of the methyl or methylene peak, and the subscripts refer to the reaction time. For $(M/R)_\infty$ the theoretical values, 1 for methyl and $^2/_3$ for methylene, were used. For each run two rate constants may be calculated, one for loss of deuterium from the methylene group ($k_p{}^{CH_2}$) and one for loss of deuterium from the methyl group ($k_p{}^{CH_3}$).

It is assumed that the reaction is subject to catalysis by all the acids and bases present in the solution, so that in the presence of the B–BH$^+$ buffer the first-order rate constant k_p may be expressed

$$k_p = k_H[H^+] + k_h[OH^-] + k_w[H_2O] + k_B[B] + k_{BH}[BH^+] \qquad (2)$$

where the k's are catalytic constants for the various possible catalysts. Superscripts will be used to show

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[1] This investigation was supported in part by Public Health Service Grant AM-10378 from the National Institute of Arthritis and Metabolic Diseases. For the preceding paper in this series see J. Hine, F. C. Kokesh, K. G. Hampton, and J. Mulders, *J. Am. Chem. Soc.*, **89**, 1205 (1967).

[1a] Note Added in Proof. Since this paper was submitted, a a study of the deuterium exchange of methoxyacetone in the presence of sodium acetate and potassium bisulfate has been published by A. A. Bothner-By and C. Sun [*J. Org. Chem.*, 32, 492 (1967)].

[2] U. S. Public Health Service Postdoctoral Fellow, 1965–1966.

Table I. Kinetics of the Deuterium Exchange of Methoxyacetone in Aqueous Solution[a]

Catalyst	M[c]	$10^6 k_p^{CH_2}$, sec^{-1}	$10^6 k_p^{CH_3}$, sec^{-1}	$10^6 k_B^{CH_2}$,[b] M^{-1} sec^{-1}	$10^6 k_B^{CH_3}$,[b] M^{-1} sec^{-1}
NaOH[d]	0.0050	87	58	17000	12000
NaOH	0.0050	75	63	15000	13000
NaOH[d]	0.0059	84	58	14000	10000
NaOH[d]	0.0079	136	100	17000	13000
N-Methylpyrrolidine	0.0050[e]	27	74	4400	15000
N-Methylpyrrolidine	0.0100[e]	50	160	4400	16000
Me_3N	0.0152[e]	33	116	2100	7600
Me_3N	0.0253[e]	51	194	2000	7600
Et_3N	0.0200[e]	41	82	1300	3700
Et_3N	0.0250[e]	53	117	1500	4300
C_6H_5ONa[d]	0.0496[e]	37	52	700	1000
C_6H_5ONa[d]	0.0992[e]	58	91	570	900
C_6H_5ONa[d]	0.0992[e]	69	103	680	1000
N-Methylmorpholine	0.200[e]	7.7	50	38	250
N-Methylmorpholine	0.500[e]	18.3	135	37	270
p-$O_2NC_6H_4ONa$[d]	0.0496[e]	0.50	0.85	10	17
Water[f]	50.5	2.36	4.7	0.048	0.093
Water[g]	51.9	0.184	0.43	0.0035	0.0083
Water[h]	54.0	0.00024	0.00086	0.0000045	0.000016
$HClO_4$[d]	0.500	0.111	0.148	0.22	0.30

[a] Unless otherwise noted, all runs were made at 35°, using ~0.23 M methoxyacetone and enough sodium chloride to give an ionic strength of 0.500 M. [b] Or k_h, or k_W, or k_H, if appropriate. [c] The concentrations given are titrimetric concentrations, in which no allowance for ionization has been made. [d] ~0.33 M methoxyacetone used. [e] Plus an equal concentration of the conjugate acid of this base. [f] At 133°. [g] At 100°. [h] Extrapolated from data at 100 and 133°.

whether a given catalytic constant refers to attack on the methyl or methylene side of the reactant.

The catalytic constant for hydrogen ions was determined by measurements using 0.5 M perchloric acid, with the result shown in Table I. Catalysis by other catalysts is negligible under these conditions. From the value of k_H obtained it follows that catalysis by hydrogen ions would never contribute as much as $10^{-5}\%$ to the over-all reaction rate in any case except the runs with pure water, which will be discussed separately.

The catalytic constants for hydroxide ions shown in Table I give average values of 1.6×10^{-2} and 1.2×10^{-2} M^{-1} sec^{-1} for $k_h^{CH_2}$ and $k_h^{CH_3}$, respectively. The ratio of the catalytic constants for hydroxide ions to those for hydrogen ions (7×10^4 and 4×10^4 for attack on the methylene and methyl hydrogen atoms, respectively) is larger than in the case of isobutyraldehyde,[3] where it is 1.3×10^3. Since only the acetate ions in acetate buffers were found to catalyze the dedeuteration of isobutyraldehyde-2-d significantly, it was assumed that in the present case, where the sensitivity to base catalysis relative to the sensitivity to acid catalysis is even greater and where all the buffers used contained bases much stronger than the acetate ion and acids much weaker than acetic acid, all the catalytic action of the buffers used was due to the buffer bases; *i.e.*, the k_{BH} term in eq 2 may be neglected.

The catalytic constant for water is too small to be determined conveniently at 35°. Therefore the runs in which no catalyst (other than the solvent water) was added were carried out at 100 and 133°. From the results, shown in Table I, Arrhenius activation energies of 23.3 and 21.8 kcal/mole were calculated for reaction at the methylene and methyl positions, respectively. These activation energies were used to calculate the rate constants at 35°, which are also listed in Table I. Because of a small amount of impurity in the deuterated methoxyacetone used, the reaction solutions used for determining k_w had a pH of about 4.6. After 240 hr at 133° the pH had dropped to about 3.5. It is, therefore, possible that some of the deuterium exchange observed is due to catalysis by acid or some other catalyst other than water. Hence the catalytic constants determined for water should be regarded as maximum values. Although the k_w's may thus be the least reliable of the catalytic constants that we have determined, the values obtained do show that the k_w terms will not contribute more than 0.2% to the rate of reaction in any of the other runs made except the one in which perchloric acid was used, where a contribution as large as 1% is possible. Hence for the runs made using buffers, the k_w terms may also be neglected and eq 2 may be written in the form

$$k_B[B] = k_p - k_h[OH^-] \qquad (3)$$

In order to use eq 3 to determine values of k_B, the basicity constants of the buffer bases (or the acidity constants of the buffer acids and the ion-product constant of water) are needed under the conditions of the kinetic experiments, so that the concentrations of hydroxide ions present in the various runs may be calculated. The thermodynamic pK_a at 35° may be interpolated from the data of Everett and Wynne-Jones[4] for trimethylammonium ions (9.58). The value for triethylammonium ions (10.45) was reported by Fyfe;[5] the values for phenol (9.86) and p-nitrophenol (7.03) were calculated from the values at 25° and the enthalpies of ionization determined by Fernandez and Hepler;[6] the values for N-methylmorpholine (7.17) and n-methylpyrrolidinium ions (10.14) were calculated from the values at 25°[7,8] and Perrin's method of mak-

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[3] J. Hine, J. G. Houston, J. H. Jensen, and J. Mulders, *J. Am. Chem. Soc.*, **87**, 5050 (1965).

[4] D. H. Everett and W. F. K. Wynne-Jones, *Proc. Roy. Soc.* (London), **A177**, 499 (1941).

[5] W. S. Fyfe, *J. Chem. Soc.*, 1347 (1955).

[6] L. P. Fernandez and L. G. Hepler, *J. Am. Chem. Soc.*, **81**, 1783 (1959).

[7] H. K. Hall, *J. Phys. Chem.*, **60**, 63 (1956).

[8] S. Searles, M. Tamres, F. Block, and L. A. Quarterman, *J. Am. Chem. Soc.*, **78**, 4917 (1956).

ing temperature corrections.[9] According to the simplest form of the Debye–Hückel equation the acidity constant of an acid of charge type plus one should not change with changing ionic strength. Because of the difficulty in determining all the appropriate salt effects we have assumed that the acidity constants of all the substituted ammonium ions in our reaction solutions are the same as they are at infinite dilution, in spite of the fact that we have found that the acidity constant of 2,6-lutidinium ions changes when salts are added, in one direction when the salt is sodium chloride or methylammonium chloride and in the opposite direction when it is 2,6-lutidinium chloride.[1b] We have assumed that the ion-product constant of water is 4.06×10^{-14} in all our runs at ionic strength 0.50 *M*, although this figure refers to measurements at 35° in which essentially all the 0.50 *M* ionic strength was due to sodium chloride.[10] We have also assumed that the ionization constants of all electrically neutral acids change with added salt in the same way that the ion-product constant of water does. With these assumptions it was possible to calculate the hydroxide ion concentrations needed for use in eq 3. In the two runs with triethylamine the calculated value of $k_h^{CH_2}[OH^-]$ was 32–41% of $k_p^{CH_2}$ and $k_h^{CH_3}[OH^-]$ was 11–15% of $k_p^{CH_3}$. With the other weak bases the extent of hydroxide ion catalysis is less, falling below 0.1% for N-methylmorpholine and sodium *p*-nitrophenoxide. Therefore, uncertainties in the ionization constants from which the hydroxide ion concentrations were calculated may result in errors in k_B. There are some compensating effects, however. If the ionization constant of a base is increased, then $[OH^-]$ is increased and $k_p - k_h[OH^-]$ decreased, tending to decrease k_B. However, since the value of [B] to be used in eq 3 is not the titrimetric value listed in Table I but the actual value present at equilibrium in solution ($[B]_{titrimetric} - [OH^-]$), an increase in $[OH^-]$ will also tend to increase k_B. In a case like that of $k_B^{CH_3}$ for N-methylpyrrolidine, which is of almost the same size as $k_h^{CH_3}$, the two effects nearly cancel and very little uncertainty in k_B results from uncertainty in the ionization constant of the base; that is, the reaction rate is very little affected by the amount of pyrrolidine that deprotonates water to give hydroxide ions since the reactivity of the hydroxide ions is about the same as that of the pyrrolidine.

The catalytic activity of methylammonium chloride was investigated for the reaction carried out in the presence of N-methylmorpholine buffers with the results shown in Table II. Inasmuch as the catalytic activity of water, hydrogen ions, and hydroxide ions are all negligible in the presence of N-methylmorpholine (Nmm) buffers, the first-order rate constant for the reaction would be expected to be equal to $k_{Nmm}[Nmm]$ if there were no catalysis by the methylammonium ions. Hence the quantity $k_p - k_{Nmm}[Nmm]$ is a measure of the extent of catalysis by methylammonium ions. The amount of catalysis observed in the runs with 0.100 *M* methylammonium chloride is too small to be clearly significant. With 0.300 *M* methylammonium chloride it seems clear that there is catalysis by methylammonium ions (or by some species derived from methylammonium ions).

Table II. Kinetics of the Deuterium Exchange of Methoxyacetone in the Presence of $MeNH_3Cl$ and N-Methylmorpholine Buffers in Aqueous Solution at 35°[a]

		Sec⁻¹			
$[Nmm]^b$	[MeN-H$_3$Cl]	$10^6 \cdot k_p^{CH_2}$	$10^6 \cdot k_p^{CH_3}$	$10^6 \cdot (k_p^{CH_2} - k_{Nmm}^{CH_2} \cdot [Nmm])$	$10^6 \cdot (k_p^{CH_3} - k_{Nmm}^{CH_3} \cdot [Nmm])$
0.400	0.100	16.2	108	1.2	4
0.200^c	0.100	8.9	54	1.4	2
0.200	0.300	11.4	86	3.9	34

[a] In all runs methoxyacetone concentrations of about 0.22 *M* were used. [b] An equal concentration of N-methylmorpholine hydrochloride was also present. [c] 0.200 *M* sodium chloride added to bring the ionic strength to 0.500 *M*.

Discussion

If k_1 is the rate constant per deuterium for the removal of a deuterium from the methylene group of methoxyacetone and if there is no secondary deuterium kinetic isotope effect, we may write

$$AcCD_2OMe + B \xrightarrow{2k_1} AcCDOMe^- + BD^+$$

$$AcCDOMe^- + BH^+ \longrightarrow AcCHDOMe + B$$

$$AcCHDOMe + B \xrightarrow{k_1} AcCHOMe^- + BD^+$$

$$AcCHOMe^- + BH^+ \longrightarrow AcCH_2OMe + B$$

Let [D] be the total concentration, in equivalents, of deuterium in the methylene group.

$$[D] = 2[AcCD_2OMe] + [AcCHDOMe]$$

Then the rate of loss of deuterium from the methylene group may be expressed

$$d[D]/dt = [B](2k_1[AcCD_2OMe] + k_1[AcCHDOMe])$$

$$d[D]/dt = k_1[B][D]$$

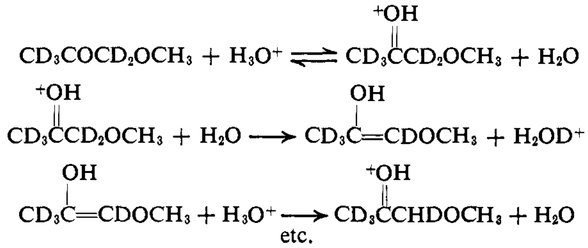
Thus, if only one base is catalytically important, the reaction is expected to follow the first-order eq 1 in which k_p is equal to $k_1[B]$ ([B] does not change during a given run), where k_1 is the rate constant *per* deuterium. Analogous derivations may be made for methyl exchange and for exchange due to the simultaneous action of several catalysts to show that the catalytic constants we have listed in Table I are statistically corrected rate constants.

Although we observed no consistent tendency for our rate constants to drift either up or down, secondary kinetic isotope effects, which we have neglected, could cause such a tendency. This fact added somewhat to the uncertainty in the rate constants calculated from our data.

Our results show that the methyl hydrogens are removed more rapidly than the methylene hydrogens by every catalyst except hydroxide ions. This is certainly not the result to be expected from the inductive effect of the methoxy substituent. Discussion of the rate effect in terms of the relative stabilities of the two possible carbanions is hampered by our ignorance of which of the two is really the more stable. If the mechanism of the acid-catalyzed deuterium exchange is the following

(9) D. D. Perrin, *Australian J. Chem.*, 17, 484 (1964).

(10) H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions," 3rd ed, Reinhold Publishing Corp., New York, N. Y., 1958, pp 752 and 754.



$$CD_3COCD_2OCH_3 + H_3O^+ \rightleftharpoons CD_3\overset{^{+}OH}{\overset{\|}{C}}CD_2OCH_3 + H_2O$$

$$CD_3\overset{^{+}OH}{\overset{\|}{C}}CD_2OCH_3 + H_2O \longrightarrow CD_3\overset{OH}{\overset{|}{C}}{=}CDOCH_3 + H_2OD^+$$

$$CD_3\overset{OH}{\overset{|}{C}}{=}CDOCH_3 + H_3O^+ \longrightarrow CD_3\overset{^{+}OH}{\overset{\|}{C}}CHDOCH_3 + H_2O$$

etc.

with the second step (and an analogous step for exchange at the methyl position) being rate controlling, then a compound with a methoxy group attached to a double bond is being formed in the rate-controlling step of the reaction. In view of the known ability of alkoxy substituents to stabilize double bonds,[11–15] it might be assumed that the enol resulting from reaction at the methylene side would be more stable than the one resulting from reaction at the methyl side. This assumption is supported by the report that methoxyacetone contains 1.1% enol,[16] a much larger enol content than that of acetone.[17,18] Thus, it appears that the more rapid acid-catalyzed deuterium exchange at the methyl position of methoxyacetone is an example of a proton transfer reaction in which the less stable product is formed more rapidly. A number of rate-equilibrium disparities of this type have been observed and some have been rationalized in terms of the principle of least motion.[19] According to the principle of least motion the shortening of the carbon–oxygen bond that would accompany the formation of 1-methoxy-2-hydroxypropene should tend to cause this enol to be formed more slowly than 3-methoxy-2-hydroxypropene, the alternative possibility. However, the magnitude of the change in bond length to be expected is so small (compared to the changes in bond lengths in the cases previously considered[19]) that only a very small effect would be anticipated.

It has been suggested that the increased electronegativity of sp^2 carbon may tend to slow reactions in which a carbon whose hybridization changes from sp^3 to sp^2 bears a highly electronegative substitutent. This point is discussed in more detail in connection with a study of the effect of α-methoxy and α-fluoro substituents on the ease of carbanion formation by esters.[20] In any attempt to rationalize the present data it should be noted that the relative rates of exchange at the methyl and methylene positions do not constitute a simple comparison of the methoxy substituent with hydrogen. The comparison is of a methoxy and an acetyl substituent with a hydrogen and a methoxyacetyl substituent.

In Figure 1 is a Brønsted plot for the buffer bases studied. The points for water and hydroxide ions were omitted to permit the use of a scale that would make it easier to see the relationship between the points for the other bases. The points plotted certainly do not describe a good straight line for either the methyl or methylene exchange reaction, but they fall nearer straight lines than the points for the same bases in the exchange of isobutyraldehyde.[3] This is probably at least partly due to a decrease in steric effects. Triethylamine, which is more than seven times as basic as trimethylamine, was only $^1/_{20}$ as reactive as trimethylamine toward isobutyraldehyde;[3] it is more than one-half as reactive as trimethylamine toward either the methyl or the methylene hydrogen atoms of methoxyacetone. The points for the two phenoxides used may be considered to describe Brønsted lines with slopes of about 0.62. This is somewhat larger than the slope (0.53) obtained from data on eight phenoxide ions in the case of isobutyraldehyde. The points for trimethylamine do not lie as far above these lines as the point for trimethylamine lay above the Brønsted line for phenoxide ions in the exchange of isobutyraldehyde. Instead it is roughly collinear with the points for N-methylpyrrolidine and N-methylmorpholine. This suggests that attack of the two cyclic amines on isobutyraldehyde was slowed by steric hindrance but that their attack on methoxyacetone is not. The fact that tertiary amines often remove hydrogen more rapidly than do primary or secondary amines of equal basicity[21,22] cannot be explained in terms of steric hindrance, however.

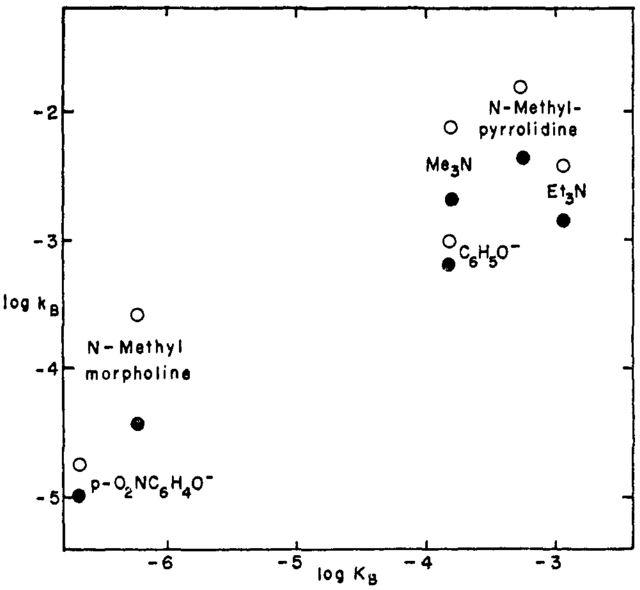


Figure 1. Bronsted plot for dedeuteration of methoxyacetone at the methyl, ○, and methylene, ●, positions.

A Brønsted plot on a scale that permits inclusion of the points for water and hydroxide ions shows that water is somewhat less reactive than would be expected from the Brønsted line for phenoxide ions or a Brønsted line that could be drawn through the points for trimethylamine, N-methylpyrrolidine, and N-methylmorpholine. This type of behavior has been observed in several (but not all) other general-base-catalyzed reactions[3,23,24]

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(11) A. J. Birch, *J. Chem. Soc.*, 1642 (1947).

(12) R. Paul, M. Fluchaire, and G. Collardeau, *Bull. Soc. Chim. France*, 668 (1950).

(13) W. H. Watanabe and L. E. Conlon, *J. Am. Chem. Soc.*, **79**, 2828 (1957).

(14) T. J. Prosser, *ibid.*, **83**, 1701 (1961).

(15) C. C. Price and W. H. Snyder, *ibid.*, **83**, 1773 (1961).

(16) J. Kenner and G. N. Richards, *J. Chem. Soc.*, 2240 (1953).

(17) R. P. Bell and P. W. Smith, *ibid.*, *Phys. Org.*, 241 (1966).

(18) It should be noted, however, that the determination of the enol content of ketones that are not highly enolized is subject to errors resulting from the presence of small amounts of impurities.[17]

(19) J. Hine, *J. Org. Chem.*, **31**, 1236 (1966).

(20) L. G. Mahone, Ph.D. Thesis, School of Chemistry, Georgia Institute of Technology, Atlanta, Ga., 1966.

(21) R. G. Pearson, *J. Am. Chem. Soc.*, **70**, 204 (1948).

(22) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, pp 175–176.

(23) R. P. Bell, "Acid-Base Catalysis," Oxford University Press, London, 1941, pp 91–95.

(24) J. Hine and L. A. Kaplan, *J. Am. Chem. Soc.*, **82**, 2915 (1960).

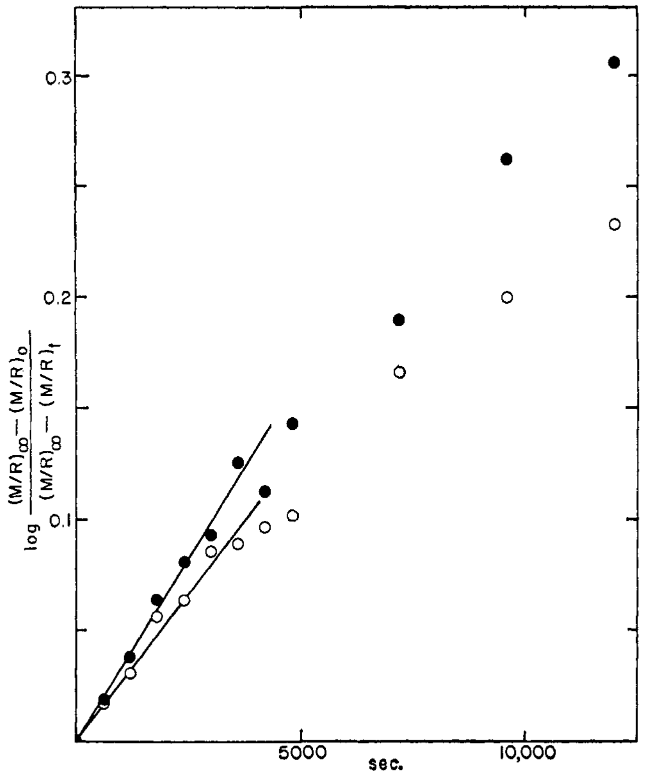

Figure 2. Kinetic plot for the dedeuteration of deuterated methoxyacetone in the presence of sodium hydroxide at the methyl, ○, and methylene, ●, positions.

and is in agreement with an expected tendency for the slope of the Brønsted line (β) to decrease with increasing strength of the bases studied.[25]

The hydroxide ion is much less reactive than would be expected from the Brønsted line for phenoxide ions or the Brønsted line for unhindered tertiary amines. Toward the methyl group of methoxyacetone it is even somewhat less reactive than N-methylpyrrolidine, although it is about 100,000 times as strong a base as the amine. Bell has pointed out that this anomolously low reactivity of hydroxide ions occurs rather commonly;[23] it was observed in the deuterium exchange of isobutyraldehyde.[3]

The effect of methylammonium chloride on the reaction rate shows that the deuterium exchange of methoxyacetone is catalyzed by methylammonium ions but that it is much less susceptible to such catalysis than is the deuterium exchange of isobutyraldehyde. From the data in Table II and related data in Table I it may be seen that the addition of 0.300 M methylammonium chloride to a 0.200 M N-methylmorpholine-0.200 M N-methylmorpholinium buffer increases the reaction rate by about 50-70%. In the case of isobutyraldehyde, the rate of exchange in the presence of a 0.21 M N-methylmorpholine-0.21 M N-methylmorpholinium buffer is more than doubled by addition of 0.176 M methylammonium chloride.[26] The catalysis by methylammonium ions is probably due to the reversible formation of a deuterated imine and then a deuterated iminium ion, which is rate controllingly transformed to an enamine.[1b,27] The greater susceptibility of isobutyraldehyde to such catalysis may be due in part, at least, to a larger equilibrium constant for imine formation. In view of the larger equilibrium constants for semicarbazone formation that have been observed for aldehydes (compared to the constants for related ketones)[28,29] the aldehyde would be expected to have a larger equilibrium constant for imine formation.

Experimental Section

Deuterated Methoxyacetone. Methoxyacetone was prepared by oxidizing 1-methoxy-2-propanol with aqueous sodium dichromate and sulfuric acid.[30] The material thus obtained contained up to 10% unoxidized starting alcohol. Except in one run in which only 2% alcohol was present, the methoxyacetone was purified by preparative gas-liquid partition chromatography using a stationary phase of silicone fluid XF-1150 to give material containing 1% alcohol or less. The pmr spectrum of the product in deuteriochloroform showed singlets at τ 5.97, 6.59, and 7.87 with relative areas of 2:3:3.

A solution of 33 g (0.375 mole) of methoxyacetone and 0.5 g of anhydrous sodium carbonate in 37.5 g (1.87 moles) of deuterium oxide was heated at reflux for 7 hr, then cooled and extracted with several 25-ml portions of ether. The ether solution was dried over anhydrous sodium sulfate and filtered, and the ether evaporated to give a residue that was passed through the deuteration procedure again. The residue from the second deuteration was distilled through a spinning-band column to give 12 g of deuterated methoxyacetone, bp 109-112°. The pmr spectrum of the product showed peaks at τ 5.97, 6.59, and 7.87 with relative areas of 0.24:3.0:0.36. The τ 5.97 and 7.87 peaks were significantly broader than the corresponding peaks in undeuterated methoxyacetone.

Kinetic Runs. In a typical run 2.0855 g of deuterated methoxyacetone and 16.5 ml of 3.0 M aqueous sodium chloride solution were diluted to volume in a 50-ml volumetric flask at 35.0°. From this flask 3-ml samples were transferred by pipet to each of a number of 10-ml volumetric flasks that already contained 3 ml of 0.01 M aqueous sodium hydroxide. At a recorded time the reaction in each flask was stopped by the addition of a small excess of acetic acid, and then the solution was extracted with chloroform. The pmr spectrum of the chloroform extract was integrated several times. Rate constants were determined by plotting the right-hand side of eq 1 against time. In this run, as in the others in which sodium hydroxide was used as the catalyst, the plot (Figure 2) showed curvature (corresponding to a decrease in the first-order rate constant) after about 20% reaction, and therefore only the data for the first 20% of the reaction were used. No such curvature was noticed in the other runs, which were usually followed to 50-75% completion. In the cases of some catalysts, where there was a rather large difference between the rates of exchange at the methyl and methylene positions, the rate constant for exchange at the methyl position was determined from a series of points taken before very much exchange had taken place at the methylene position, and the rate constant for exchange at the methylene position was determined from a series of points taken after exchange at the methyl position was almost complete.

The methoxyacetone used contained a small amount of an unidentified acidic impurity that gave the initial reaction solution a pH of about 4 due to an acid content around 0.001 M. In the most vigorous conditions used for any of the reactions (133°) the pH dropped to 3.5 and the acid content rose to 0.004 M after a time four times as long as that used for the last kinetic point taken. Because of the presence of these small amounts of acidic impurities, the catalytic constants we have reported for basic catalysts will tend to be too low. This will be significant only in cases where the concentrations of basic catalysts are relatively small. The errors resulting from these impurities must not be very large, because if they were we would not get about the same catalytic constant using significantly different concentrations of catalysts.

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(25) J. Hine, "Physical Organic Chemistry," 2nd ed, McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 119.

(26) J. G. Houston, Ph.D. Thesis, School of Chemistry, Georgia Institute of Technology, Atlanta, Ga., 1964.

(27) J. Hine, B. C. Menon, J. H. Jensen, and J. Mulders, *J. Am. Chem. Soc.*, **88**, 3367 (1966).

(28) J. B. Conant and P. D. Bartlett, *ibid.*, **54**, 2881 (1932).

(29) F. H. Westheimer, *ibid.*, **56**, 1962 (1934).

(30) R. P. Mariella and J. L. Leech, *ibid.*, **71**, 3558 (1949).