Bifunctional Catalysis of the Dedeuteration of Methoxyacetone-*1,1,3,3,3-d*$_5$[1]

Jack Hine* and Ashoke Sinha

Department of Chemistry, The Ohio State University, Columbus, Ohio 43210

Received January 19, 1984

The dedeuteration of methoxyacetone-*1,1,3,3,3-d*$_5$ is subject to bifunctional catalysis by 3-(dimethylamino)-propylamine (3DP) and (1*R*,2*S*,3*R*,4*R*)-3-((dimethylamino)methyl)-1,7,7-trimethyl-2-norbornamine (DTN). These catalysts act by using their primary amino groups to transform the ketone to an iminium ion and their tertiary amino groups to transfer a deuteron internally, changing the iminium ion to an enamine. Although analogous monofunctional bases favor exchange at the methyl position relative to exchange at the methylene position by factors of up to 4-fold, bifunctional catalysis by the diamines used favors the methyl group by 11- to 15-fold. Exchange at the methylene group in the presence of DTN was strongly stereoselective. The pro-*S* deuteron was removed 12–20 times as rapidly as the pro-*R* deuteron. This is the result of the steric effect of the methoxy substituent.

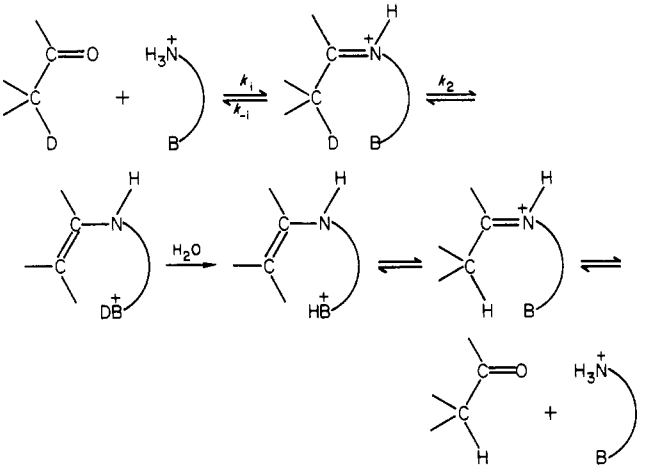
The dedeuteration of acetone-d_6,[2-5] cyclopentanone-*2,2,5,5-d*$_4$,[5-7] and 3-pentanone-*2,2,4,4-d*$_4$[8] has been found to be subject to bifunctional catalysis by monoprotonated 3-(dimethylamino)propylamine and certain other monoprotonated primary–tertiary diamines. These catalysts act by transforming the ketone into an iminium ion, which is transformed to an enamine via an internal deuteron transfer to the tertiary amino group, as shown in Scheme I.

In order to learn how regioselective these catalysts are we have now studied an unsymmetrical ketone. Methoxyacetone has been chosen, partly because the methoxy substituent provides a good model for the hydroxy substituent, which is so important in carbohydrate chemistry for example, without giving the complications that the hydroxy substituent does when the hydroxylic proton is removed. In addition, an earlier study of catalysis of the dedeuteration of methoxyacetone-*1,1,3,3,3-d*$_5$ by monofunctional catalysts[9] provides reference data for comparison purposes. We have also used a chiral bifunctional catalyst to learn how stereoselectively it acts on methoxyacetone.

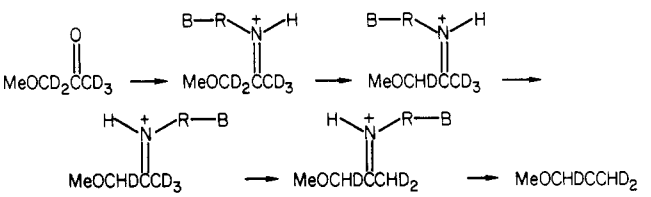
Results

The dedeuteration of methoxyacetone-d_5 in the presence of monofunctional catalysts had been followed by ^{1}H NMR measurements but this gave only the total amount of exchange at the methylene and carbon-bound methyl positions.[9] It does not tell quantitively how much of the various isotopically different species are present—pure $RCHD_2$, for example, strongly resembles an equimolar mixture of RCH_2D and RCD_3. For this reason, in the present study we have also made mass spectral measurements. The heights of the methoxymethyl peaks, the acetyl peaks, and the parent peaks were all measured. Unfortunately, there is overlap in that CHD_2CO and $MeOCH_2$ fragments both have a mass of 45 and CD_3CO and MeOCHD both have a mass of 46. From the NMR data and mass spectral fragment peaks we can calculate what fraction of the methylene groups are di-, mono-, and undeuterated and what fraction of the acetyl groups are in the various extents of deuteration. These calculations, which are described in more details in the Appendix, gave only fairly good internal consistency, perhaps because of the complications produced by the overlapping mass spectral peaks. Therefore we added the data on the mass spectral parent peaks, which could be used only if we assumed that the exchange reactions at the methyl and methylene positions are independent of each other—that is, that exchange at the methyl position does not make exchange at the methylene position any more or less likely than it would otherwise be. This involves a neglect of secondary deuterium kinetic isotope effects. It also assumes that no significant amount of exchange takes place by a process like Scheme II, in which the iminium ion gives

Scheme I



Scheme II



(1) (a) Part 24 in the series "Catalysis of α-Hydrogen Exchange". (b) For part 23 see: Hine, J.; Tsay, H.-M. *J. Org. Chem.* **1983**, *48*, 3797–3802. (c) Abstracted in part from the Ph. D. Dissertation of A. Sinha, The Ohio State University, 1983.

(2) Hine, J.; Cholod, M. S.; Jensen, J. H. *J. Am. Chem. Soc.* **1971**, *93*, 2321–2322.

(3) Hine, J.; Cholod, M. S.; King, R. A. *J. Am. Chem. Soc.* **1974**, *96*, 835–845.

(4) Hine, J.; Li, W.-S. *J. Am. Chem. Soc.* **1976**, *98*, 3287–3294.

(5) Hine, J.; Li, W.-S.; Zeigler, J. P. *J. Am. Chem. Soc.* **1980**, *102*, 4403–4409.

(6) Hine, J.; Li, W.-S. *J. Am. Chem. Soc.* **1975**, *97*, 3550–3551.

(7) Hine, J.; Miles, D. E.; Zeigler, J. P. *J. Am. Chem. Soc.* **1983**, *105*, 4374–4379.

(8) Hine, J.; Zeigler, J. P. *J. Am. Chem. Soc.* **1980**, *102*, 7524–7529.

(9) Hine, J.; Hampton, K. G.; Menon, B. C. *J. Am. Chem. Soc.* **1967**, *89*, 2664–2668.

0022-3263/84/1949-2186$01.50/0

Table I. Kinetics of the Disappearance of CD_3 and CD_2 Groups from CD_3COCD_2OMe[a]

catalyst	100[Am]$_t$, M	μ[b]	pH	$10^6k_{obsd}^{CD_3}$[c]	$10^6k_p^{CD_3}$	$10^6k_{obsd}^{CD_2}$[c]	$10^6k_p^{CD_2}$	$k_{obsd}^{CD_3}/k_{obsd}^{CD_2}$	$k_p^{CD_3}/k_p^{CD_2}$
3DP[d]	4.89	0.64	8.55	617 (41)	16	48.8 (5.2)	3.9	13	4
3DP[d]	4.87	0.19	8.53	682 (49)	17	50.0 (3.9)	4.1	14	4
3DP[d]	4.52	0.26	7.98	347 (8)	8	23.7 (1.8)	1.8	15	4
DTN[e]	0.50	0.25	10.06	1260 (230)	9	111 (12)	7	11	1.3
DTN[e]	0.50	0.25	9.17	1630 (130)	2	137 (17)	1.2	12	2

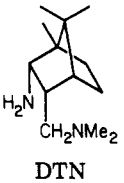
[a] In water at 35 °C. All rate constants have the units M^{-1} s^{-1}. [b] Ionic strength. [c] Parenthesized figures are standard deviations. [d] 3-(Dimethylamino)propylamine. [e] (1*R*,2*S*,3*R*,4*R*)-3-((Dimethylamino)methyl)-1,7,7-trimethylnorbornamine.

exchange on one side, undergoes geometric isomerization (without hydrolysis to ketone), and gives exchange on the other side. Exchange of this type has been observed for cyclopentanone-d_4 in the presence of 3-(dimethylamino)-propylamine[7] and for acetone-d_6 in the presence of 3-*exo*-((dimethylamino)methyl)-2-*exo*-norbornamine.[1b] We shall describe results showing that no substantial amounts of exchange occur by such a mechanism in the present case, however.

The addition of the mass spectral parent peaks to our data sets did not greatly improve the internal consistency of the analysis, as described in more detail in the Appendix. Since the analysis is therefore not as reliable as those used in our previous studies,[2-8] it is not surprising that the agreement of our data with proposed reaction mechanisms is not as good in the present case. However, we believe that it is good enough to support the conclusions that we shall draw.

The two bifunctional catalysts that we studied were 3-(dimethylamino)propylamine (3DP) and the chiral cat-

3DP

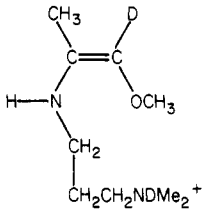


DTN

alyst (1*R*,2*S*,3*R*,4*R*)-3-((dimethylamino)methyl)-1,7,7-trimethyl-2-norbornamine (DTN). For each run the disappearance of CD_3CO and $MeOCD_2$ groups were good first-order reactions with rate constants denoted $k_{obsd}^{CD_3}$ and $k_{obsd}^{CD_2}$, respectively. The values obtained are listed in Table I along with the first-order rate constants, $k_p^{CD_3}$ and $k_p^{CC_2}$, that would be expected if the catalysts used had acted only as monofunctional catalysts. The k_p values were calculated from data on monofunctionally catalyzed dedeuteration of methoxyacetone-d_5 by using the Brønsted equation, as described in more detail in the Appendix.

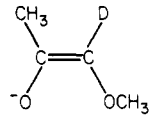
In each run the observed rate constants for CD_3 disappearance and CD_2 disappearance are at least 13 times as large as would be expected if the catalysts were acting monofunctionally. Hence the catalysts are acting largely bifunctionally. In the presence of 3DP the ratio of $k_{obsd}^{CD_2}$ to $k_p^{CD_2}$ is slightly larger than 10. This is essentially equal to the ratios of observed rate constant to k_p for the dedeuteration of acetone-d_6 in the presence of about the same concentration of the same catalyst at about the same pH.[3] The ratios of $k_{obsd}^{CD_3}$ to $k_p^{CD_3}$ found with 3DP are seen to be around 35. Thus, the susceptibility of methoxyacetone to bifunctional catalysis by 3DP (relative to its susceptibility to monofunctional catalysis) on the methylene side is about the same as that of acetone, but on the methyl side methoxyacetone is significantly more susceptible to bifunctionally catalyzed exchange. Inasmuch as the regioselectivity of monofunctional catalysis already favors the methyl group over the methylene group somewhat, it follows that the bifunctional catalyst 3DP is considerably more regio-selective. Thus the $k_{obsd}^{CD_3}/k_{obsd}^{CD_2}$ values for 3DP in Table I are about three times as large as the $k_p^{CC_3}/k_p^{CD_2}$ values.

There is probably a steric contribution to this increased regioselectivity. The transition state leading from the iminium ion to that geometric isomer of the intermediate enamine in which the methoxy group is trans to the methyl group (1) will suffer steric repulsions between the methoxy



1

group and the methylene group from the C-1 position of 3DP. (In the transition state this methylene group will be held near coplanarity by the partial double bond character in the C–N bond.) In contrast, the analogous isomer of the enolate ion formed by monofunctional catalysis (2) should be less sterically strained.



2

In the presence of the chiral catalyst DTN the observed regioselectivity is also greater than that which would be expected from monofunctional catalysis—probably for reasons that are similar to those that hold for 3DP. In this case, however, the ratio $k_{obsd}^{CD_2}/k_p^{CD_2}$ is only about one fifth as large as the values found with acetone and the same concentration of the same catalyst at about the same pH.[5] The $k_{obsd}^{CD_3}/k_p^{CD_3}$ ratios are somewhat larger than those found for acetone.

Further evidence for bifunctional catalysis is found in the fact that the data on exchange on the methyl side cannot be fit satisfactorily by the assumption of one-at-a-time exchange, as in Scheme III. However, the bi-

Scheme III

$$RCOCD_3 \xrightarrow{k} RCOCHD_2 \xrightarrow{2k/3} RCOCH_2D \xrightarrow{k/3} RCOCH_3$$

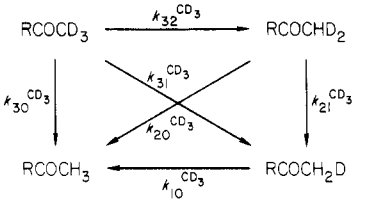
functional catalysis mechanism shown in Scheme IV, in which k_{im}, k_x, and k_h are the rate constants for iminium ion formation, exchange by the iminium ion, and hydrolyses of the iminium ion does operate. Figure 1 covers the dedeuteration of methoxyacetone in the presence of 3DP at pH 7.98. Scheme IV is seen to fit the data satisfactorily, but Scheme III does not. The least-squares best values of k_{im} and r are listed in Table II. The standard deviations observed with Scheme IV were about 2.4%,

Table II. Dedeuteration of Methoxyacetone[a]

catalyst	pH	$10^4 k_{im}$,[b] M^{-1} s^{-1}	r[b]	$10^6 k_d$,[b] M^{-1} s^{-1}	$10^4 k_l$,[b] M^{-1} s^{-1}
3DP	8.55	9.4 (1.2)	0.52 (0.09)		
3DP	8.53	12.8 (1.6)	0.35 (0.05)		
3DP	7.98	6.4 (0.6)	0.35 (0.04)		
DTN	10.06	14.1 (2.5)	0.54 (0.13)	8.8 (1.2)	1.03 (0.08)
DTN	9.17	20.5 (4.3)	0.37 (0.14)	6.4 (0.8)	1.26 (0.11)

[a] In water at 35 °C. [b] The figures in parentheses are standard deviations.

Scheme IV



$$k_{32} = k_{im}\left(\frac{3r}{3r+1}\right)\left(\frac{1}{2r+1}\right) + k_p^{CD_3}$$

$$k_{31} = k_{im}\left(\frac{3r}{3r+1}\right)\left(\frac{2r}{2r+1}\right)\left(\frac{1}{r+1}\right)$$

$$k_{30} = k_{im}\left(\frac{3r}{3r+1}\right)\left(\frac{2r}{2r+1}\right)\left(\frac{r}{r+1}\right)$$

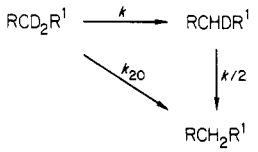
$$k_{21} = k_{im}\left(\frac{2r}{2r+1}\right)\left(\frac{1}{r+1}\right) + 2k_p^{CD_3}/3$$

$$k_{20} = k_{im}\left(\frac{2r}{2r+1}\right)\left(\frac{r}{r+1}\right)$$

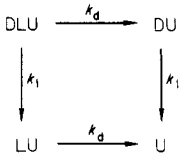
$$k_{10} = k_{im}\left(\frac{r}{r+1}\right) + k_p^{CD_3}/3$$

$$r = k_x/k_h$$

Scheme V



Scheme VI



those obtained assuming Scheme III are about twice this large.

For exchange on the methylene side the data were fit to Scheme V, with k_{20} set equal to zero. For the runs carried out in the presence of 3DP, the agreement between observed and calculated deuterium contents was excellent. When values of k_{20} were sought, using least-squares techniques, the resulting values were negligible ($<0.001k$).

The runs carried out in the presence of the chiral diamine DTN, however, did not follow Scheme V. They fit Scheme VI, which allows for stereoselectivity. In this scheme DLU is $MeOCD_2Ac$, DU is (*R*)-MeOCHDAc, LU is (*S*)-MeOCHDAc, and U is $MeOCH_2Ac$. The results are summarized in Table II and Figure 2, where the solid line is based on Scheme V, with the k_d and k_l values shown in Table II and the k_p values shown in Table I. The k_l/k_d ratios of 12 and 20 show that the steroselectivity is marked

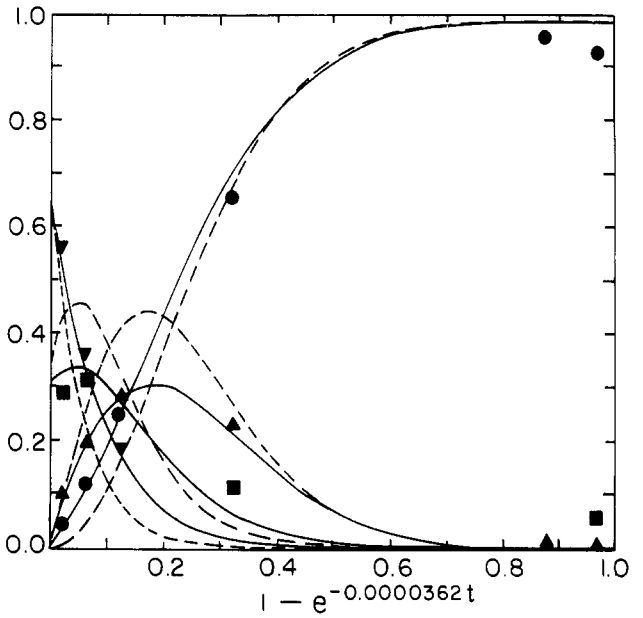


Figure 1. Dedeuteration of the methyl group of methoxyacetone-*1,1,3,3,3-d*$_5$ in the presence of 0.0452 M 3-(dimethylamino)propylamine at pH 7.98 (▼, CD_3; ■, CD_2H; ▲, CD_2H; ●, CH_3).

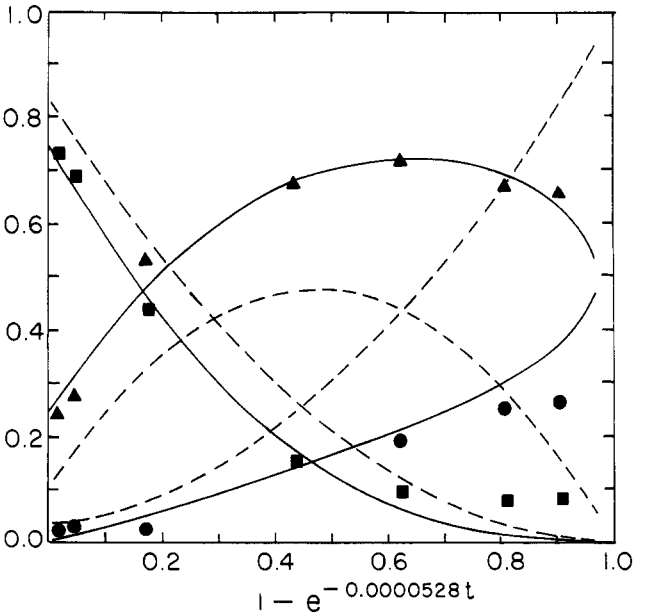
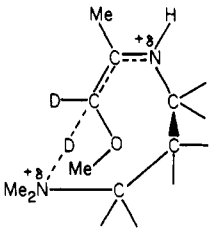


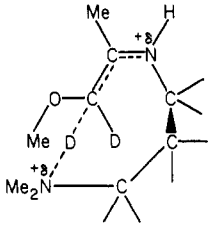
Figure 2. Dedeuteration of the methylene group of methoxyacetone-*1,1,3,3,3-d*$_5$ in the presence of 0.0050 M (1*R*,2*S*,3*R*,4*R*)-3-((dimethylamino)methyl)-1,7,7-trimethylnorbornamine at pH 9.17 (■, CD_2; ▲, CDH; ●, CH_2).

but not as large as that observed with cyclopentanone-d_4 or 3-pentanone-d_4. This is not surprising because the methoxy substituent, when properly oriented, is smaller than a methyl substituent. As shown in transition state **3**, it is the repulsion between this methoxy group and the carbon atom from the catalyst to which the primary amino group was attached that is responsible for the stereose-



3

lectivity. The transition state for the principal part of the reaction (4) has only a deuterium atom to interact with



4

the carbon atom. The dashed line in Figure 2 is the result of the least-squares best fit to Scheme V with k_{20} set equal to zero. (Positive values of k_{20} give even poorer agreement.)

The small value of k_{20} obtained for exchange on the methylene side in the presence of 3DP shows that only a negligible amount of exchange takes place as shown in Scheme II. This small value shows that the iminium ions hydrolyze a lot faster than they exchange on the methylene side. Hence, even if the iminium ion that is trans to this side underwent geometric isomerization it would be unlikely to exchange. Similarly, any iminium ion that is cis to the methylene group and isomerizes is quite unlikely to have exchanged before doing so. The fact that r for exchange vs. hydrolysis on the methyl side is of about the same magnitude for DTN as for 3DP shows that similar arguments are very probably applicable in the case of DTN also. As in the cases of cyclopentanone-2,2,5,5-d_4[5-7] and 3-pentanone-2,2,4,4-d_4,[8] three-dimensional molecular models of the transition state (4) were used to show that the more rapidly formed monodeuterio product has the *S* configuration. This conclusion for cyclopentanone was later supported by the results of Kergomard et al., who obtained cyclopentanone-2-*d* by enzymatic reduction of 2-cyclopentenone-2-*d* and made the plausible assumption that the stereochemistry of the reduction was the same as in the case of 2-cyclohexenone.[10] Partly dedeuterated cyclopentanone-d_4 and 3-pentanone-d_4 both gave optical rotatory dispersion spectra that showed positive Cotton effects.[5-8] In the case of 3-pentanone this further supported the *S* configuration because (*S*)-succinic-2-*d* acid, the only other acyclic compound of the type $-CH_2CHDCO-$ that we knew of whose ORD curve had been determined, also gave a positive Cotton effect.[11] On the basis of the octant rule[12] in its simplest form (*S*)-cyclopentanone-2-*d* should have a negative Cotton effect. For this reason, the *S* configuration was originally doubted by Sundaraman, Barth, and Djerassi[13] but they later showed that it was correct.[14]

(10) Dauphin, G.; Gramain, J. C.; Kergomard, A.; Renard, M. F.; Veschambre, H. *Tetrahedron Lett.* **1980**, *21*, 4275–4279.
(11) Englard, S.; Britten, J. S.; Listowsky, I. *J. Biol. Chem.* **1967**, *242*, 2255–2259.
(12) Moffitt, W.; Woodward, R. B.; Moscowitz, A.; Klyne, W.; Djerassi, C. *J. Am. Chem. Soc.* **1961**, *83*, 4013–4018.
(13) Sundaraman, P.; Barth, G.; Djerassi, C. *J. Org. Chem.* **1980**, *45*, 5231–5236.
(14) Sundaraman, P.; Barth, G.; Djerassi, C. *J. Am. Chem. Soc.* **1981**, *103*, 5004–5007.

Experimental Section

Reagents. Methoxyacetone-1,1,3,3,3-d_5,[9] which was at least 99% pure by GLC and at least 90% deuterated at its exchangeable positions, 3-(dimethylamino)propylamine,[8] and (1*R*,2*S*,3*R*,4*R*)-3-((dimethylamino)methyl)-1,7,7-trimethyl-2-norbornamine dihydrochloride,[5] which melted at 243–245 °C instead of the previously reported 269–271 °C, but whose 200-MHz ^{1}H NMR and mass spectra were identical with those reported previously, were all obtained as described previously.

Kinetics. In a typical run, 3.00 mL of buffer solution of known pH was added to each of nine 10-mL ampules, which were then placed in a 35 °C constant-temperature bath. At a recorded time 3.00 mL of aqueous 0.246 M methoxyacetone-d_5 was added to each ampule, which was shaken and returned to the bath. At a second recorded time a calculated excess of standard hydrochloric acid was added to quench the reaction. The quenched solution was immediately cooled in an ice–water bath and divided into two equal portions. One portion was extracted three times with 3-mL portions of methyl iodide and the other five times with 3-mL portions of chloroform. The solutions were dried ($MgSO_4$), filtered, and concentrated to 1–2 mL. The methyl iodide solutions were analyzed by mass spectral measurements using an AEI-MS9 Mass Spectrometer. The areas under the three peaks in the chloroform solutions were measured by using a Perkin-Elmer 60-MHz ^{1}H NMR spectrophotometer model 390. In the run at pH 7.98, the mass spectral measurements were also made on the chloroform extracts.

Appendix

In treating the mass spectral data none of the processes whose relative extents were being measured involved primary deuterium kinetic isotope effects. Secondary deuterium kinetic isotope effects were neglected.[15,16]

If we let M_{xy} be the mole fraction of material with x deuterium atoms in the methylene group and y deuterium atoms in the methyl group, M_{23} becomes the mole fraction of methoxyacetone-1,1,1,2,2-d_5, and M_{x2} is the sum of M_{02}, M_{12}, and M_{22}. The ^{1}H NMR data give eq 1 and 2, where

$$2M_{0y} + M_{1y} = 3N_2/N_1 \quad (1)$$

$$3M_{x0} + 2M_{x1} + M_{x2} = 3N_3/N_1 \quad (2)$$

N_1, N_2, and N_3 are the integrated areas of the methoxy peak, the methylene peak, and the carbon-bound methyl peak. The mass spectral peaks for the acetyl and methoxymethyl peaks give eq 3–7, where $\sum_A$ and $\sum_M$ are the

$$M_{x0} = P_{43}/\sum_A \quad (3)$$

$$M_{x1} = P_{44}/\sum_A \quad (4)$$

$$M_{0y} + M_{x2}\sum_A/\sum_M = P_{45}/\sum_M \quad (5)$$

$$M_{1y} + M_{x3}\sum_A/\sum_M = P_{46}/\sum_M \quad (6)$$

$$M_{2y} = P_{47}/\sum_M \quad (7)$$

sums of the areas of the acetyl and methoxymethyl peaks, respectively. The ratio of $\sum_A$ to $\sum_M$ was assumed to be the same as it is observed to be (0.667) for methoxyacetone-d_0. Equations 8 and 9 then provided nine equations that were resolved for the seven unknowns by use of a linear least-squares treatment.[17] If a negative value was obtained that parameter was set equal to zero and the

$$M_{x0} + M_{x1} + M_{x3} = 1.00 \quad (8)$$

$$M_{0y} + M_{1y} + M_{2y} = 1.00 \quad (9)$$

(15) Williams, D. H.; Budzikiewicz, H.; Djerassi, C. *J. Am. Chem. Soc.* **1964**, *86*, 284–288.
(16) Biemann, K. "Mass Spectrometry, Organic Chemical Applications"; McGraw-Hill, Inc.: New York, 1962; Chapter 5.
(17) Hamilton, W. C. "Statistics in Physical Sciences"; Ronald Press: New York, 1964; Sections 4.1 and 5.3.

least-squares treatment was repeated until no negative values were obtained.

Later the mass spectral parent peaks were added to the data base to obtain eq 10–15 in which the P's are peak

$$M_{0y}M_{x0} = P_{88}/\sum_P \quad (10)$$

$$M_{0y}M_{x1} + M_{1y}M_{x0} = P_{89}/\sum_P \quad (11)$$

$$M_{0y}M_{x2} + M_{1y}M_{x1} + M_{2y}M_{x0} = P_{90}/\sum_P \quad (12)$$

$$M_{0y}M_{x3} + M_{1y}M_{x2} + M_{2y}M_{x1} = P_{91}/\sum_P \quad (13)$$

$$M_{1y}M_{x3} + M_{2y}M_{x2} = P_{92}/\sum_P \quad (14)$$

$$M_{2y}M_{x3} = P_{93}/\sum_P \quad (15)$$

heights and $\sum_P$ is the sum of the corrected (for ^{18}O and ^{13}C) heights of the parent peaks. In this case the results obtained using nine equations were the first approximation used in the nonlinear least-squares treatment involving 19 equations.

The deuterium contents at various times throughout the reaction that were thus obtained were then fit to a given mechanistic scheme. The methods of Rodaguin and Rodaquina[18] were used to obtain eq 16–22 from Scheme III and eq 23–27 from Scheme V with k_{20} set equal to zero.

$$M_{x3} = M_{x3}^{\circ}E_3 \quad (16)$$

$$M_{x2} = 3M_{x3}^{\circ}(E_2 - E_3) + M_{x2}^{\circ}E_2 \quad (17)$$

$$M_{x1} = 3M_{x}^{\circ}(E_1 - E_2 + E_3) + 2M_{x2}^{\circ}(E_1 - E_2) + M_{x1}^{\circ}E_1 \quad (18)$$

$$M_{x0} = 1 - M_{x3} - M_{x2} - M_{x1} \quad (19)$$

$$E_3 = \exp(-3kt) \quad (20)$$

$$E_2 = \exp(-2kt) \quad (21)$$

$$E_1 = \exp(-kt) \quad (22)$$

$$M_{2x} = M_{2x}^{\circ}F_2 \quad (23)$$

$$M_{1x} = 2M_{2x}^{\circ}(F_1 - F_2) + M_{1x}^{\circ}F_1 \quad (24)$$

$$M_{0x} = 1 - M_{2x} - M_{1x} \quad (25)$$

$$F_2 = \exp(-kt) \quad (26)$$

$$F_1 = \exp(-kt/2) \quad (27)$$

(18) Rodaguin, N. M.; Rodaguina, E. N. "Consecutive Chemical Reactions"; English Translation, Schneider, R. F., Ed.; D. van Nostrand: Princeton, NJ, 1964.

For Schemes IV, VI, and V when k_{20} was one parameter to be determined, the differential reaction method was used in which the total reaction time was divided into increments and the changes in concentration calculated for each separate increment.[1b] The time increments were shortened by factors of 2 until the values of the parameter obtained changed by less than 0.1%.

The k_P values were estimated essentially by the methods used before for other ketones.[3,5,7,8] Catalysis constants were determined for hydrogen ions (always negligible under the conditions of the present study), hydroxide ions, and four tertiary amines.[9] The points for three of these amines, trimethylamine, *N*-methylpyrrolidine, and *N*-methylmorpholine, give good Brøsted plots for both methylene and methyl exchange. The point for triethylamine lies below these lines, presumably because of steric hindrance. The methylene plot has a slope of 0.68 and the methyl plot a slope of 0.59. Simple basic catalysis by the tertiary amino group of 3DP was assumed to take place at a rate that agreed with these lines. As previously, the primary amino group was assumed to be only one-seventh as reactive. These assumptions and the micro pK_a values determined earlier for 3DP give k values of 5.01×10^{-3} M^{-1} s^{-1} and 1.26×10^{-3} M^{-1} s^{-1} for removal of deuterons from the CD_3 and CD_2 groups, respectively, by the tertiary amino group of 3DP. The molecule as a whole would then be $^8/_7$ this reactive. It was assumed that the Brønsted line for monocationic amines lies 0.44 log units above the one for uncharged amines. On this basis, $Me_2NCH_2CH_2CH_2NH_3^+$ was estimated to have rate constants of 1.51×10^{-3} M^{-1} s^{-1} and 3.19×10^{-5} M^{-1} s^{-1} for dedeuteration of the CD_3 and CD_2 groups, respectively.

For DTN a pK_{HTP} value of 9.32 was assumed, since this is the value estimated earlier for 3-*endo*-((dimethylamino)methyl)-2-*endo*-norbornamine,[19] whose structure merely lacks the carbon-bound methyl groups of DTN and whose pK values (6.82 and 9.78) are near those of DTN (6.59 and 9.84). This assumption leads to estimates of 30%, 38%, and 32% for the percent of monoprotonated diamine that is tertiary protonated, primary protonated, and internally hydrogen bonded. Rate constants of 5.25×10^{-3} M^{-1} s^{-1} and 1.28×10^{-3} M^{-1} s^{-1} for attack on the CD_3 and CD_2 groups by DTN and 6.28×10^{-4} and 9.14×10^{-5} M^{-1} s^{-1} for monoprotonated DTN were then calculated.

Registry No. $MeOCD_2C(O)CD_3$, 89922-02-1; 3DP, 109-55-7; DTN, 56310-23-7.

(19) Hine, J.; Li, W.-S. *J. Org. Chem.* **1975**, *40*, 1795–1800.

Chlorocyanoketene. Synthesis and Cycloadditions to Alkenes

Paul L. Fishbein and Harold W. Moore*

Department of Chemistry, University of California, Irvine, California 92717

Received November 14, 1983

Details for two syntheses of chlorocyanoketene (CCK) are provided. These involve the thermolysis (103 °C) of 4-azido-3-chloro-5-methoxy-2(5*H*)-furanone as well as generation of the ketene at ambient temperature upon treatment of 3,4-dichlorocyclobutenedione with sodium azide in acetonitrile. In addition, the previously unreported cycloadditions of CCK to alkenes are described. These give good yields of the corresponding cyclobutanones and include additions to di-, tri-, and tetrasubstituted alkenes.

In preliminary accounts, we have shown that chloro-, bromo-, and iodocyanoketene can be conveniently generated from the corresponding 4-azido-3-halo-2(5H)-furanones (**2a–c**) upon thermolysis in refluxing benzene.[1,2]

0022-3263/84/1949-2190$01.50/0