opening, respectively, which are in turn involved in polymerization. In the case of b_2, the ring closure path may lead to the product disilacyclohexane. All other products from pyrolysis of the polymers are verified experimentally. Path c represents the other possible pathway, the link of the two different radicals from ring opening of the silirane. This path leads to the formation of $(CH_2{=}CH)_2SiF_2$. Although it seems conceivable to obtain $CH_2{=}CHSiF_2SiF_3$ from the polymer pyrolysis, the observation of this compound in the cocondensation reaction can not be explained without raising more skeptical assumptions in this reaction scheme based solely on the silirane intermediate. On the other hand, if the $\cdot SiF_2SiF_2\cdot$ diradical is involved, the formation of $CH_2{=}CHSiF_2SiF_3$ becomes straightforward.

On the basis of argument of the different types of products of each reaction under various experimental conditions (Table I), and the fact that the configuration retentions increase with n in $CHF{=}CH(SiF_2)_nF$ (Table II), the involvement of $\cdot SiF_2SiF_2\cdot$ diradical in the cocondensation reactions is evident. Besides, there have been a number of physical evidences for the existence of $\cdot(SiF_2)_n\cdot$ demonstrated spectroscopically by Margrave's earlier works.[3,4] We therefore add the reaction paths inside the dashed lines into the scheme.

Since our "alternate layer" experiments clearly confirm that some SiF_2 remain monomeric at −196 °C, the silirane mechanism can not be ruled out. The observation of $(CH_2{=}CH)_2SiF_2$ in the vinyl fluoride reaction further augments its plausibility. The silirane mechanism may account for most of the experimental results so far obtained; however, it seems insufficient. In fact, the silirane intermediate may be considered as a special case in the $\cdot(SiF_2)_n\cdot$ homologues with $n = 1$. At this point, we feel that the "difference" between these two mechanisms has been taken too literally and overemphasized. While the detailed reaction mechanism (such as to what extent each mechanism contributes) may vary from reaction to reaction, we tend to conclude that both are involved in the cocondensation experiments in general.[18]

If so, one most important question yet to be answered in the chemistry of SiF_2 is the spin state of the monomeric SiF_2 generated by the thermal reduction method. The formation of silirane as an initial step in these reactions is consistent with the chemistry of singlet SiF_2, which is in agreement with the absence of ESR signal in Margrave's earlier work.[19] Besides, an ab initio calculation also showed that SiF_2 had a singlet ground state.[20] On the other hand, a number of chemical observations have suggested the participation of triplet SiF_2 in some reactions.[21] It is obvious that more work on this point is required to clarify this basic confusion in the chemistry of difluorosilylene.

Acknowledgment. The financial support to this work by the Chinese National Science Council is gratefully acknowledged. T.L.H. thanks the Institute of Nuclear Energy Research for a research fellowship. Y.M.P. thanks the Ministry of Education for a post graduate fellowship.

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(18) A mechanism involving the direct attack of $\cdot(SiF_2)_n\cdot$ to the CF bonds is seldomly discussed but not ruled out experimentally.

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(21) Chernyshev, E. A.; Komalenkova, N. G.; Bashkirova, S. A. *Russ. Chem. Rev.* **1976**, *45*, 913–930. We also observed that in the study of SiF_2-induced polymerization of isonitriles, trace amounts of oxygen would greatly inhibit the polymerization reactions.

Stereoselective Bifunctional Catalysis of the Dedeuteration of 3-Pentanone-*2,2,4,4-d*$_4$[1]

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Contribution from the Department of Chemistry,
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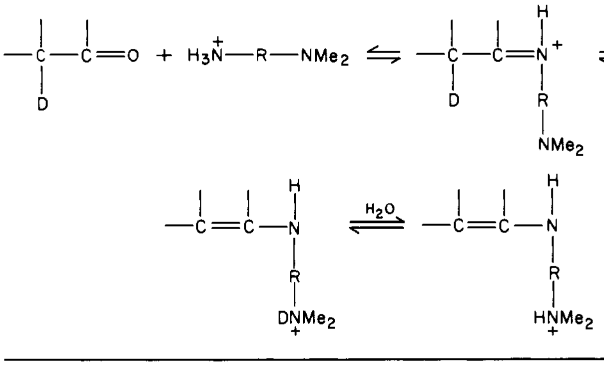
Abstract: The dedeuteration of 3-pentanone-*2,2,4,4-d*$_4$ was studied in the presence of perchloric acid, sodium hydroxide, and four amines of the type RCH_2NMe_2. The Brønsted β for the amines is 0.56. The monoprotonated forms of both *N,N*-dimethyl-1,3-propanediamine and *N,N*,2,2-tetramethyl-1,3-propanediamine are bifunctional catalysts for the dedeuteration. Their primary amino group transforms the ketone to an iminium ion from which the tertiary amino group removes a deuteron internally. The monoprotonated form of the chiral catalyst **1** is a very effective bifunctional catalyst and it acts stereoselectively. The pro-*S* deuterons of the ketone are removed more rapidly than the pro-*S* deuterons, by as much as 70-fold. Partially dedeuterated ketone containing more than 80% of the dideuterio species was isolated and found to be optically active, with a positive Cotton effect. Unlike cyclopentanone, which was studied previously, 3-pentanone is dedeuterated less stereoselectively below pH 7 than between pH 8 and 9. The reasons for this are discussed.

Previous studies showed that, in the presence of certain primary–tertiary diamines, α-hydrogen atoms of aldehydes and ketones are exchanged with those of the solvent (water) by a mechanism shown in part in eq 1.[2-5] In the presence of the chiral catalyst (1*R*,2*S*,3*R*,4*R*)-3-[(dimethylamino)methyl]-1,7,7-trimethyl-2-norbornanamine (**1**) the dedeuteration of cyclopentanone-*2,2,5,5-d*$_4$ is highly stereoselective.[1b,5,6]


$$\underset{D}{\overset{|}{-C}}-\overset{|}{C}{=}O + H_3\overset{+}{N}-R-NMe_2 \rightleftharpoons \underset{D}{\overset{|}{-C}}-\overset{|}{C}{=}\overset{H}{\overset{|}{N^+}}-R-NMe_2 \rightleftharpoons \overset{|}{-C}{=}\overset{|}{C}-\overset{H}{\overset{|}{N}}-R-D\overset{+}{N}Me_2 \xrightleftharpoons{H_2O} \overset{|}{-C}{=}\overset{|}{C}-\overset{H}{\overset{|}{N}}-R-H\overset{+}{N}Me_2$$
(1)

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(1) (a) Research supported in part by Grant GM 18593 from the National Institute of General Medical Sciences, Part 21 in the series "Catalysis of α-Hydrogen Exchange". (b) For part 20 see Hine, J.; Li, W.-S.; Zeigler, J. P. *J. Am. Chem. Soc.* **1980**, *102*, 4403–9. (c) Abstracted in part from the Ph.D. Dissertation of James P. Zeigler, The Ohio State University, Columbus, OH, 1978.

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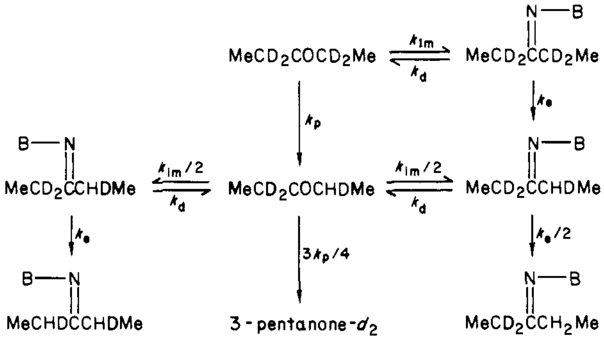
Scheme I

$$d_4 \xrightarrow{k_4} d_3 \xrightarrow{k_3} d_2 \xrightarrow{k_2} d_1 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} d_0$$

Scheme II



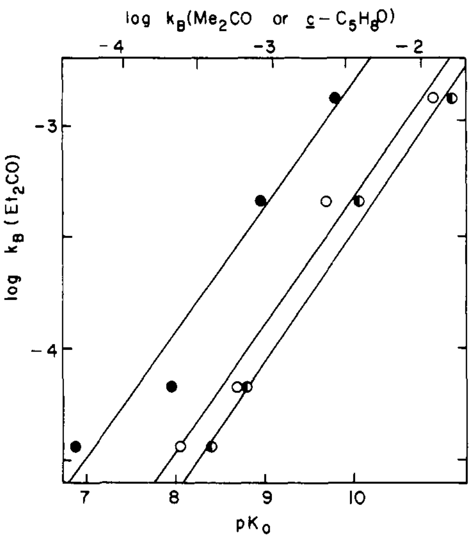
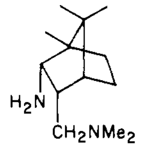


Figure 1. Plot of log k_B for dedeuteration of 3-pentanone-*2,2,5,5*-d_4 by amines of the type RCH_2NMe_2 in water at 35 °C vs. (●) pK_a for the conjugate acids of the amines (legend at the bottom of the figure), (○) log k_B for dedeuteration of acetone-d_6 under the same conditions (legend at the top of the figure), and (◐) log k_B for dedeuteration of cyclopentanone-*2,2,5,5*-d_4 under the same conditions (legend at the top of the figure).

Table I. Kinetics of Dedeuteration of 3-Pentanone-*2,2,4,4*-d_4[a]

catalyst	10^5k_B,[b] M^{-1} s^{-1}	pK_a[c]
$HClO_4$	1.44	
NaOH	1760	
n-$BuNMe_2$	131	9.80
$MeOCH_2CH_2NMe_2$	45.9	8.96
$(EtO)_2CHCH_2NNe_2$	6.74	7.96
$NCCH_2CH_2NMe_2$	3.64	6.89

[a] In water at 35 °C, using 0.17 M ketone. [b] For transformation of the d_4 to the d_3 ketone. [c] For the conjugate acid of the amine.



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This stereoselectivity can be attributed in part to the impossibility of rotation around the carbon–carbon bonds of cyclopentanone. Hence it was of interest to study an acyclic substrate. Also of interest was a type of transition-state steric hindrance that had been blamed for the absence of bifunctional catalysis in the dedeuteration of isobutyraldehyde-*2*-*d* by monoprotonated *N*,*N*-dimethyl-1,3-propanediamine ($Me_2NCH_2CH_2CH_2NH_2$, **2**), a catalyst that clearly dedeuterates acetone-d_6 by a bifunctional mechanism.[5] This type of hindrance should help make possible the stereoselective bifunctionally catalyzed α-hydrogen exchange of aldehydes and ketones of the type RCH_2CO–. For this reason we have studied the dedeuteration of 3-pentanone-*2,2,4,4*-d_4.

Results and Discussion

Dedeuteration by Monofunctional Catalysts. To estimate how active our bifunctional compounds would be if they acted only as monofunctional catalysts, we studied several catalysts whose structures permit only a monofunctional mechanism. The dedeuteration of 0.17 M 3-pentanone-*2,2,4,4*-d_4 was studied in the presence of perchloric acid, sodium hydroxide, and four amines of the type RCH_2NMe_2 in water at 35 °C. These reactions follow Scheme I, in which reversibility needs to be allowed for only in the last step. The forward rate constants differ largely by statistical factors resulting from the differing number of deuterium atoms in the d_4, d_3, d_2, and d_1 species. In addition there are small secondary deuterium kinetic isotope effects. If the γ isotope effect is independent of the stereochemistry and if it and the α isotope effect are multiplicative, we obtain eq 2, in which z is equal to

$$k_1 = k_2z/2 = k_3z^2/3 = k_4z^3/4 \qquad (2)$$

$(a + 2g)/3$, where a is the k^H/k^D α secondary isotope effect and g is the γ effect. The k_4 and z values, which define all the constants in eq 2, for each run are listed in the Experimental Section. From the k_4 values, second-order rate constants were calculated for each catalyst, with the amount of catalysis by hydrogen and hydroxide ions being allowed for in obtaining the rate constants for the amine catalysts. The z values were in the range 1.01–1.07, but in almost half of the runs the values were within the estimated standard deviation of 1.00.

The second-order rate constants (Table I) for the amines give a Brønsted plot (solid circles in Figure 1) with a slope of 0.56. Plots against log k_B for the same amines in the deprotonation of acetone-d_6 (open circles) and cyclopentanone-*2,2,5,5*-d_4 (half-filled circle) are somewhat better and have slopes of 0.96 and 0.98, respectively.

Dedeuteration by Achiral Bifunctional Catalysts. The dedeuteration of 3-pentanone-*2,2,4,4*-d_4 was also studied in the presence of two achiral diamines, **2** and *N*,*N*,2,2-tetramethyl-1,3-propanediamine ($Me_2NCH_2CMe_2CH_2NH_2$, **3**), whose monoprotonated forms have already been found to be bifunctional catalysts for the dedeuteration of acetone-d_6.[2,4,7] If the catalyst

Table II. 3-Pentanone-*2,2,4,4*-d_4 Exchange in the Presence of *N*,*N*-Dimethyl-1,3-propanediamine (**2**)[a]

pH	100[Cat]$_t$,[b] M	100μ[c]	10^5k_4, s^{-1}	10^5k_p, s^{-1}	q	r	10^5k_{im}, s^{-1}	$10^5k_{im}^{calcd}$, s^{-1}
8.05	2.07	3.00	2.05	0.27	0.83	0.49	5.4	7.7
8.33	2.15	2.69	3.06	0.36	0.82	0.52	7.8	10
8.97	1.97	1.97	3.50	0.52	0.83	0.49	9.0	12
9.50	2.15	1.16	4.23	0.87	0.86	0.44	11	14
9.94	1.99	1.13	4.18	1.3	0.94	0.18	19	13
10.03	2.02	0.98	4.16	1.4	0.94	0.21	16	14

[a] Using 0.17 M ketone in aqueous solution at 35 °C. [b] Total concentration of **2** + $2H^+$ + $2H_2^{2+}$. [c] Ionic strength.

Table III. 3-Pentanone-*2,2,4,4-*d_4 Exchange in the Presence of *N*,*N*,2,2-Tetramethyl-1,3-propanediamine (3)[a]

pH	100[Cat]$_t$,[b] M	100μ[c]	10^5k_4, s^{-1}	10^5k_p, s^{-1}	q	r	10^5k_{im}, s^{-1}	$10^5k_{im}^{calcd}$, s^{-1}
6.86	1.03	2.06	1.24	0.03	0.66	1.1	1.6	1.3
7.40	2.77	5.55	5.13	0.11	0.69	1.0	6.4	5.2
8.68	10.0	20.1	25.6	0.8	0.58	1.5	27	26
8.70	9.83	19.7	15.8	0.5	0.61	1.4	26	25
9.43	2.77	5.55	4.09	0.4	0.73	0.9	8.0	7.3
9.86	1.03	2.06	2.87	0.9	0.82	1.5	1.2	2.7

[a] Using 0.17 M ketone in aqueous solution at 35 °C. [b] Total concentration of 3 + $3H^+$ + $3H_2^{2+}$. [c] Ionic strength.

is denoted B–NH$_2$ and the rate constants are k_p for simple monofunctionally catalyzed dedeuteration, k_{im} for imine formation, k_d for imine hydrolysis, and k_e for imine exchange and if secondary deuterium kinetic isotope effects are neglected, we obtain Scheme II. Values of k_4, the first-order rate constant for disappearance of 3-pentanone-d_4 at various pHs, are listed for **2** in Table II and for **3** in Table III. Values of k_p were estimated from the Brønsted equation, the pK_1 and pK_2 values of the catalysts, and the difference in basic catalysis ability of primary and tertiary amino groups as described previously.[4,7] From data on dedeuteration of acetone-d_6 by attack of base on the intermediate *N*-methyliminium ion[8] the amount of attack by external bases on the intermediate iminium ion in the present case should be considerably smaller than k_p, unless 3-pentanone is relatively more susceptible to exchange via iminium ion formation than acetone is. However, in reaction with **2**, values of k_6/[Am] for acetone[4] at a given pH are about 11 times as large as the corresponding k_4/[Am] values for 3-pentanone (Table II), whereas k_B values for simple amines are only 5–9 times as large for acetone[4] as the values in Table I. This suggests that 3-pentanone may be relatively less susceptible to exchange via iminium ions than acetone is.

The estimated values of k_p may well be in error by a factor of 2, but the k_4 values are so much larger that most of the exchange must arise from bifunctional catalysis (below pH 9.5, at least).

By a derivation analogous to that used earlier for acetone-d_6,[4] (in which secondary deuterium kinetic isotope effects are neglected) the 3-pentanone-d_3 concentration may be shown to follow eq 3, in which q is defined in eq 4 and 5. Least-squares values

$$d_3 = (4d_{4_0} + d_{3_0})e^{-(1-q/4)k_4t} - 4d_{4_0}e^{-k_4t} \tag{3}$$

$$q = [r(k_p/k_4) + 2]/(r + 2) \tag{4}$$

$$r = k_e/k_d \tag{5}$$

of q and values of r calculated from them by use of the estimated k_p values are shown in Tables II and III. The values of k_{im} were obtained from eq 6. These values are compared, in Tables II

$$k_{im} = (k_4 - k_p)(1 + r)/r \tag{6}$$

and III, with the values calculated from eq 7, using the k_a values

$$k_{im}^{calcd} = k_a[Am] + k_{ah}[AmH^+] \tag{7}$$

for imine formation from unprotonated diamine and the k_{ah} values for imine formation by monoprotonated diamine obtained from hydroxylamine capturing experiments.[9] The agreement obtained with **2** is only fair. With q values near 1.0, r is small or k_p/k_4 is large or both, and experimental errors make it difficult to obtain k_{im} precisely. The agreement is good enough to support the proposed mechanism, however. Better agreement is seen with k_{im} values for **3**, except at the highest pH where q is nearer 1.0 and k_p is almost one-third of k_4.

The catalytic abilities of **2** and **3** do not differ greatly. The rate constants for imine formation (k_a and k_{ah}) are larger for **2**, but r values are larger for **3**.

Stereoselective Bifunctional Catalysis. The results obtained when 3-pentanone-*2,2,4,4-*d_4 was dedeuterated at various pHs in the presence of **1** are summarized in Table IV. The rate constants for disappearance of 3-pentanone-d_4 (k_4) exceed the values that would be expected from monofunctional catalysis (k_p) by considerably larger factors than were observed for **2** and **3** at similar pHs. This shows that **1** is a more effective bifunctional catalyst.

Table IV. Dedeuteration of 3-Pentanone-*2,2,4,4-*d_4 in the Presence of 1[a]

pH	10^6k_4, s^{-1}	10^6k_p, s^{-1}	$10^3k_{ah}r/(1 + r)$, M^{-1} s^{-1}	10^6k_+, s^{-1}	10^6k_-, s^{-1}	k_-/k_+
6.48	6.04	0.06	3.3	0.18	2.84	15
6.82	8.76	0.09	3.1	0.25	4.13	16
7.66	41.9	0.2	9.4	0.47	20.5	44
8.18	104	0.3	22	0.65	51.4	79
9.72	195	3	64	1.70	95.7	56
9.90	180	5	70	2.12	87.7	41
10.03[b]	72	5	65	2.95	32.9	11

[a] Using 0.17 M ketone and 0.0050 M total 1 and an ionic strength of 0.012 ± 0.002 in aqueous solution at 35 °C unless otherwise noted. [b] Total concentration of 1 was 0.0025 M and the ionic strength was 0.0025.

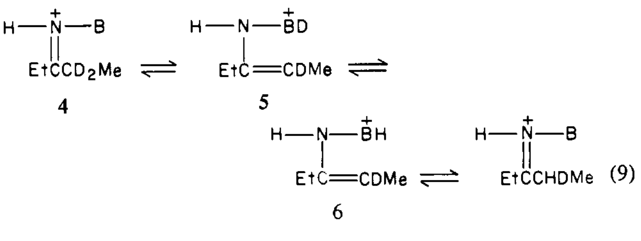
Scheme III

$$\begin{tikzcd}
d_4 \arrow[r, "2k_+"] \arrow[d, "2k_-"'] & d\text{-}d_3 \arrow[r, "k_+"] \arrow[d, "2k_-"'] & d\text{-}d_2 \arrow[d, "2k_-"'] \\
i\text{-}d_3 \arrow[r, "2k_+"] \arrow[d, "k_-"'] & i\text{-}d_2 \arrow[r, "k_+"] \arrow[d, "k_-"'] & d\text{-}d_1 \arrow[d, "k_-"'] \\
i\text{-}d_2 \arrow[r, "2k_+"] & i\text{-}d_1 \arrow[r, "k_+"] & d_0
\end{tikzcd}$$

The exchange rate is so much faster than is reasonable for k_a, the rate constant for imine formation by unprotonated **1**, that almost all the imine formation must come from **1**H$^+$, where internal acidic dehydration of the intermediate carbinolamine is possible. Hence the first-order rate constant for imine formation (k_{im}) is essentially equal to $k_{ah}[1H^+]$. Substitution into eq 6 and rearrangement gives eq 8, from which the values of $k_{ah}r/(1 + r)$

$$(k_4 - k_p)/[1H^+] = k_{ah}r/(1 + r) \tag{8}$$

listed in Table IV were calculated. The decreases that accompany decreases in pH show that r decreases with decreasing pH. This was not seen with **2** or **3** (Tables II and III) but has been seen in previous dedeuterations by **1** and other highly effective catalysts.[1b,4,5,7] The barrier between iminium ion and enamine has become so low that when the pH is lowered, the base-catalyzed transformation of unexchanged enamine (**5**) to exchanged enamine (**6**) (eq 9) no longer takes place essentially every time the iminium ion (**4**) is transformed to the unexchanged enamine. Hence the rate-controlling step becomes the transformation of **5** to **6** at lower pH.



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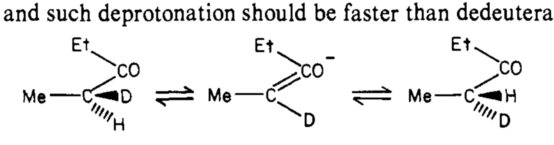
[9] Hine, J.; Zeigler, J. P.; Johnston, M. *J. Org. Chem.* **1979**, *44*, 3540–5.

When dedeuteration follows Scheme I and eq 2, with $z = 1$, the maximum concentration of 3-pentanone-d_2 that is ever present is 37.5%.[10] These were essentially the results we observed with the monofunctional catalysts (and also with **2** and **3**). With **1** as the catalyst, however, d_2 concentrations above 80% were obtained. This is explained in terms of Scheme III, in which the two types of α-deuterium atoms in 3-pentanone-d_4 (pro-*R* and pro-*S*) are assigned different rate constants for exchange. Least-squares values of these two rate coonstants were calculated from Scheme III for each run and are listed in Table IV. The quotient is a measure of the stereoselectivity, which is seen to be largest at intermediate pH and to be smaller above pH 10 and below pH 7. The maximum stereoselectivity is slightly (perhaps not significantly) higher than found for cyclopentanone-d_4.[1b] By analogy it is assumed that the more rapidly removed deuterons are of the pro-*S* type, just as in the case of cyclopentanone. With cyclopentanone the stereoselectivity also decreased above pH 10, but at lower pH it increased slightly (down to pH 6.57, the lowest pH at which measurements were made).

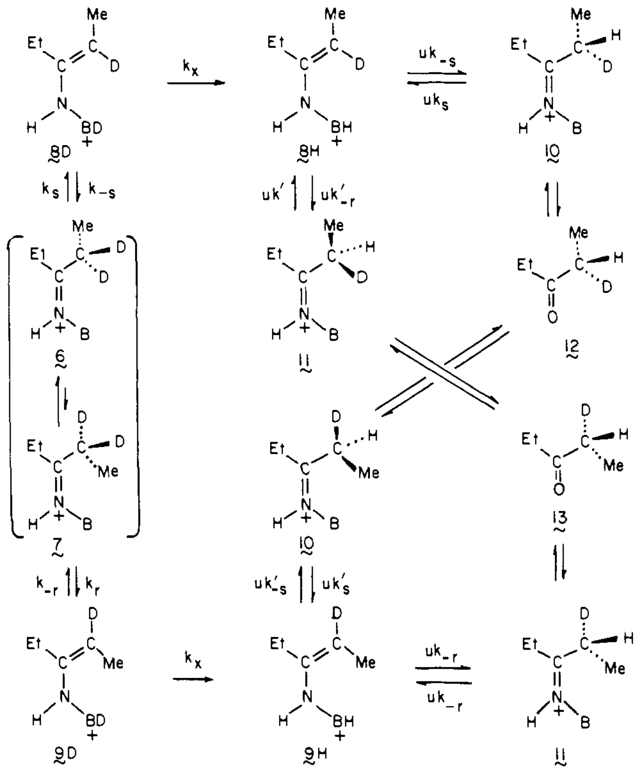
In order to explain this difference in the pH dependence of stereoselectivity, we need to consider the mechanisms of both the k_+ and k_- parts of the reactions. The k_-/k_+ ratio is particularly sensitive to k_+ because small changes in the overall reaction, if they primarily affect k_+, can change the ratio markedly. Simple (monofunctional) base catalysis must remove pro-*R* and pro-*S* deuterium at equal rates if the base is achiral, as hydroxide ions are. Such stereorandom reaction would give a k_+ value equal to $k_p/4$. Simple base catalysis by **1** or **1**H$^+$ could remove either pro-*R* or pro-*S* deuterium preferably, but we think that great stereoselectivity in this reaction is unlikely. As the preference for pro-*R* deuterons varies from zero to infinity, the contribution to k_+ will vary from zero to $k_p/2$. Another contribution to k_+ results from the fact that Scheme II is incomplete. Any species with a chiral α-carbon atom can be racemized by removal of an α-proton (eq 10), and such deprotonation should be faster than dedeuteration because of a primary deuterium kinetic isotope effect. This provides a path from *l*-d_3 to *i*-d_2, for example, that is not shown in the scheme. Reaction via eq 10 would transform *l*-d_3 to *d*-d_3, which would then give *i*-d_2 by the relatively rapid k_- path. A scheme that would allow fully for such processes would be too difficult to treat. These processes show up as increased k_+ values when Scheme III is the basis of the treatment.


(10)

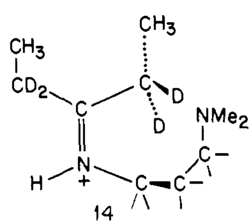
Other ways in which pro-*R* deuterium is replaced by protium involve the intermediate iminium ion formed from **1**H$^+$ and ketone. Removal of pro-*R* deuterons from a CD$_2$ group by external bases will not affect the k_-/k_+ ratio if the intermediate enamine is protonated internally. However, protonation of the intermediate enamine by an external acid can give the *R* configuration, perhaps predominantly.

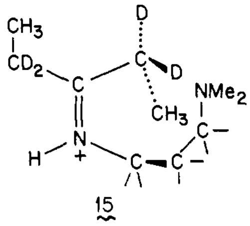
Replacement of pro-*R* deuterons by protons in the preceding ways must occur, but it does not explain the difference in the effect of pH on stereoselectivity for the two ketones. Two possible explanations for this difference are suggested by Scheme IV, in which the primary kinetic isotope effect (u) is assumed to be independent of the stereochemistry. A ketone molecule containing a CD$_2$ group can yield an iminium ion whose conformations include **6** and **7**. The previous study of cyclopentanone[1b] shows that when iminium ions derived from **1** are written with the iminium nitrogen below the iminium carbon atom and the basic substituent in **1** to the right, as in Scheme IV, deuteron (or proton) transfer will usually take place from above the plane of the double bond. Thus the more abundant conformer **6** is ordinarily transformed to the *E* enamine **8D** and **7** to the *Z* enamine **9D**. The more likely explanation[11] for the effect of low pH on k_-/k_+ reminds us that at high pH these enamines will undergo exchange a lot faster than they will be transformed back to iminium ions ($k_x >> k_{-s} >> k_{-r}$). The **8H** and **9H** formed thereby will usually be transformed by top-side proton transfer to the iminium ions **10** and **11**, respectively ($k_{-s} >> k'_{-r}$ and $k_{-r} >> k'_{-s}$), and these will be hydrolyzed to the *S* ketone **12** and the *R* ketone **13**, whose relative rates of formation will be essentially equal to the ratio k_s/k_r. As the pH is lowered, the base-catalyzed exchange of **8D** and **9D** is slowed and we move toward (but perhaps do not reach) conditions where exchange is much slower than reversion of the unexchanged enamines to unexchanged iminium ions ($k_{-s} >> k_{-r} >> k_x$). Under these conditions equilibrium is established between **8D** and **9D**. Since k_x should be about the same for **8D** as for **9D**, **12** and **13** will be formed in a ratio about equal to the equilibrium ratio of **8D** to **9D**. If this ratio is smaller than the ratio k_s/k_r, the ratio k_-/k_+ will decrease at lower pH, as observed.

Scheme IV



To estimate the relative magnitudes of the equilibrium ratio **8D**/**9D** and the rate-constant ratio k_s/k_r, let us examine structures **14** and **15**, which are more detailed pictures of **6** and **7**, respectively. The dimethylamino group from the catalyst can easily


14


15

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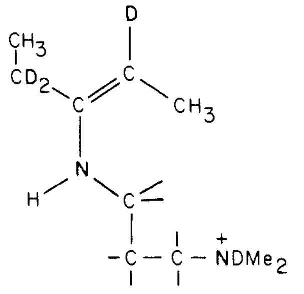
[10] Neglecting reversibility and assuming that the starting material is 100% 3-pentanone-d_4. The results are not much different with ~90% -d_4 starting material, such as we used.

[11] This is essentially the explanation suggested to us by a reviewer, to whom we are grateful.

approach α-deuterons only from above the plane of the double bond. The transition state resulting from **15** is less stable than the one from **14** because of repulsion between the methyl group from the ketone, which is moving into the plane as the enamine is formed, and parts of the three-carbon chain between the dimethylamino group and the iminium nitrogen atom.[12] This strain causes k_r to be much smaller than k_s. The equilibrium ratio **8D**/**9D** is presumably determined largely by the strain present in the Z enamine **9D**, whose structure is shown in more detail in **16**. This enamine should show increased strain, relative to the transition state via which it was formed, because the hindered methyl group is now fully in the plane of the double bond. However, it should simultaneously show reduced strain because the enamine nitrogen may not be coplanar and, especially, because most the three-carbon chain leading to the dimethylamino group can be rotated away from the hindered methyl group. We suggest that these latter two factors are more important and that the equilibrium ratio is smaller than the rate constant ratio. The enamine derived from cyclopentanone can exist only in the E form, of course, and so k_-/k_+ for cyclopentane does not decrease at lower pHs, as it does for 3-pentanone.



16

The preceding explanation does not demand any removal of deuterons from below the plane of the double bond (k'_r, k'_{-r}, k'_s, and k'_{-s} may all be zero), but an alternative (or additional) explanation does. If k'_{-r} is considerably smaller than k_{-s}, but not negligible in comparison to it, reaction of **8H** (the principal enamine intermediate) will give mostly the S ketone **12** (via **10**) and a little R ketone **13** (via **11**). At high pH, ketone **12**, which has the stereochemistry that tends to accumulate in the system, will slowly lose its remaining deuterium atom via two paths, both proceeding through iminium ion **10**. In one path **10** will undergo top-side deuteron transfer to give a Z enamine (not shown) that will exchange and hydrolyze. In the other path **10** will give **8H$^+$**, which will ordinarily revert to **10** but may occasionally give **11** by under-the-plane proton transfer. When the pH decreases and k_x decreases, the rate of formation of **12** and its rate of disappearance via a Z enamine will both decrease. However, the decrease in k_x will not decrease the rate of transformation of **12** to **11**, which will ordinarily be hydrolyzed to **13**, which, being R, will be relatively rapidly dedeuterated. This will decrease the extent of buildup of partly dedeuterated species that is characteristic of large k_-/k_+ ratios. Below-the-plane deuteration can be aided by twisting the double bond of the enamine (or more properly the $1^1/_2$ bond of the transition state) and should be more difficult when this bond is in a five-membered ring, as it would be in the case of cyclopentanone.

The stereoselectivity of the dedeuteration of 3-pentanone-d_4 in the presence of **1H$^+$** was further substantiated by the optical activity of ketone isolated after the dedeuteration was only about half-completed. The ORD spectrum of this material (curve I in Figure 2) shows a positive Cotton effect, just as cyclopentanone-d_4 about half-dedeuterated by **1H$^+$** had.[1b] The fact that **14** is much more analogous than **15** to the precursor of the predominant transition state in the dedeuteration of cyclopentanone-d_4 is evidence that the chiral centers in our 3-pentanone-d_2 are largely S in configuration. Additional evidence is the positive Cotton effect found for (S)-succinic-2-d acid,[13] the only other acyclic compound of the type $-CH_2CHDCO-$ that we know of whose ORD curve has been determined. The maximum absolute specific rotation is at 252 nm where $[\alpha]^{25} = -415$ (deg mL)/(dm g). If all the chiral centers have the same configuration and the specific rotation of the d_3 and d_1 species are half that of d_2, pure d_2 has a rotation of $-460°$. Since not all the chiral centers do have the same configuration the absolute value of the rotation must be larger. The minimum value is almost twice that ($-250°$) obtained analogously for cyclopentanone. Racemization experiments (cf. curves II–IV of Figure 2) show that the observed optical rotation is due to the partly deuterated ketone. In the presence of 0.250 M protonated and 0.199 free 3-(dimethylamino)propionitrile the rate constant for racemization is 1.34×10^{-5} s^{-1} in water at 35 °C. The second-order rate constant is 6.73×10^{-5} M^{-1} s^{-1} for attack of the amine on a protium or deuterium atom at a chiral center. (Either deprotonation or dedeuteration will racemize.) Division of the rate constant in Table I by 4 gives 0.91×10^{-5} M^{-1} s^{-1} for attack of the amine on a deuterium atom. This gives $(6.73 - 0.91) \times 10^{-5}$ or 5.82×10^{-5} M^{-1} s^{-1} for attack on protium and hence a primary-plus-secondary deuterium kinetic isotope effect of 6.4, which is a perfectly plausible value.

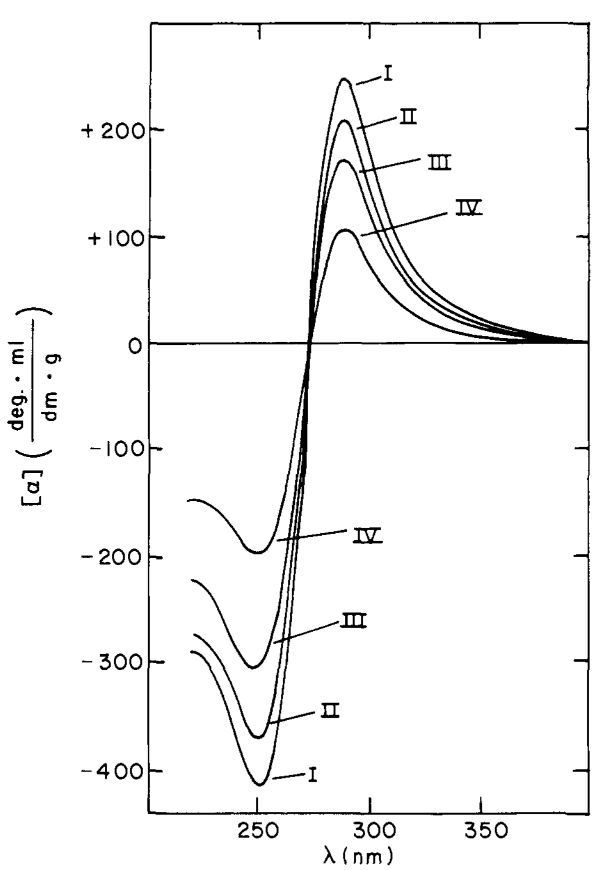


Figure 2. Optical rotatory dispersion curves for partly deuterated 3-pentanone. Curve I is for material after partial dedeuteration of 3-pentanone-2,2,4,4-d_4 by **1H$^+$**. Curves II, III, and IV are for the same material after further dedeuteration in the presence of a 3-(dimethylamino)propionitrile buffer also in water at 35 °C.

Experimental Section

Reagents. The synthesis and structure for **1** were described earlier.[1b,c] Repeated treatment of 3-pentanone with about 0.3 M sodium deuteroxide in deuterium oxide followed by salting out with sodium chloride gave the 3-pentanone-2,2,4,4-d_4, which ordinarily contained less than 2% of less highly deuterated species.

Dedeuteration Kinetics. The kinetics were followed, as they had been in the case of cyclopentanone-d_4,[1b] by injecting 0.075 mL of ketone

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[12] This is closely analogous to the repulsion that has been blamed for the absence of bifunctional catalysis in the reaction of isobutyraldehyde-2-d with **2** (ref 5).

[13] Englard, S.; Britten, J. S.; Listowsky, I. *J. Biol. Chem.* **1967**, *242*, 2255–9.

(giving a 0.17 M solution in the case of 3-pentanone) into an ampule containing 4 mL of catalyst solution, quenching with acid, and extracting with ethyl bromide. The extent of exchange was determined by mass spectral measurements on the extracts.

Rate constants and other parameters were calculated by nonlinear least-squares treatments, as described for cyclopentanone.[1b] If the initial concentrations of d_0, d_1, and d_2 are taken as zero (although up to 2% d_2 was present initially, but essentially no d_1 or d_0) and reversibility is negected, Scheme III leads to eq 11–15, in which d_{4_0} is the initial fraction of d_4 and the A's and E's are defined in eq 16–22. To allow for reversibility, we replaced eq 14 by eq 23.

$$d_4 = d_{4_0}E_8 \tag{11}$$

$$d_3 = A_3E_7 - 4d_{4_0}E_8 \tag{12}$$

$$d_2 = A_2E_6 - 3A_3E_7 + 6d_{4_0}E_8 \tag{13}$$

$$d_1 = A_1E_5 - 2A_2E_6 + 3A_3E_7 - 4d_{4_0}E_8 \tag{14}$$

$$d_0 = 1 - d_1 - d_2 - d_3 - d_4 \tag{15}$$

$$A_1 = (d_{4_0} + 3)/2 \tag{16}$$

$$A_2 = (d_{4_0} + 1)/2 \tag{17}$$

$$A_3 = (3d_{4_0} + 1)/2 \tag{18}$$

$$E_5 = \exp(-k_+t) + \exp(-k_-t) \tag{19}$$

$$E_6 = \exp(-2k_+t) + 4\exp[-(k_+ + k_-)t] + \exp(-2k_-t) \tag{20}$$

$$E_7 = \exp[-(2k_+ + k_-)t] + \exp[-(k_+ + 2k_-)t] \tag{21}$$

$$E_8 = \exp[-(2k_+ + 2k_-)t] \tag{22}$$

$$d_1 = [A_1E_5 - 2A_2E_6 + 3A_3E_7 - 4d_{4_0}E_8 + (d_1/d_0)_{\mathrm{eq}}(1 - d_4 - d_3 - \mathrm{d}_2)]/(d_1/d_0)_{\mathrm{eq}} \tag{23}$$

The standard deviations of the calculated percent compositions of d_4, d_3, d_2, d_1, and d_0 from the observed values were less than 3% in more than 90% of the runs. The runs using monofunctional catalysts, **1**, **2**, and **3**, all gave about the same range of standard deviations. The data obtained in individual runs using monofunctional catalysts are summarized in Table V.

Table V. Rate Constants and Secondary Deuterium Kinetic Isotope Effects in 3-Pentanone-*2,2,4,4*-d_4 Exchange[a]

catalyst	100 $[\mathrm{Cat}]_t$,[b] M	pH	10^6k_4,[c] s^{-1}	z[c]
$HClO_4$	30.7		4.41 ± 0.40	1.01 ± 0.03
NaOH	7.25		1300 ± 450	1.05 ± 0.13
	3.90		680 ± 23	1.03 ± 0.01
n-$BuNMe_2$	21.1	10.13	142 ± 13	1.02 ± 0.05
	19.8	9.94	158 ± 3	1.03 ± 0.01
	1.51	9.76	10.7 ± 0.6	1.02 ± 0.02
$MeOCH_2CH_2$-NMe_2	9.55	8.93	18.5 ± 2.4	1.06 ± 0.05
	9.70	8.78	16.4 ± 0.3	1.02 ± 0.01
$(EtO)_2CHCH_2$-NMe_2	9.91	8.22	4.22 ± 0.4	1.05 ± 0.03
	30.1	8.20	10.9 ± 0.5	1.05 ± 0.02
$NCCH_2CH_2$-NMe_2	19.6	7.02	3.80 ± 0.11	1.01 ± 0.01
	20.2	7.02	3.58 ± 0.20	1.07 ± 0.02

[a] In water at 35 °C. [b] Total catalyst concentration (regardless of the state of protonation of the amine catalyst). The ionic strength was equal to twice the total catalyst concentration. [c] The ± figures are estimated standard deviations.

Optically Active Deuterated 3-Pentanone. Preliminary runs using six 4-mL samples of 0.005 17 M total **1** and 0.20 M 3-pentanone-d_4 at pH 8.42 in water at 35 °C showed that the concentration of the d_2 species should reach a maximum in about 19 h. A 238-mL sample containing the same concentration of reagents was allowed to react for 18 h 53 min, then quenched with 13 mL of 0.1 M hydrochloric acid, and extracted with three 15-mL portions of ethyl bromide. Drying over calcium sulfate, removal of ethyl bromide, and vacuum distillation gave 0.58 g of partly deuterated ketone of greater than 99.5% purity. Mass spectral analysis showed 0.8% d_4, 6.9% d_3, 83.3% d_2, 7.9% d_1, and 1.0% d_0 present. The ORD spectrum of the material is shown in Figure 2.

The racemization of this material was followed by using 0.112 M ketone and 0.250 M protonated and 0.199 M unprotonated 3-(dimethylamino)propionitrile. At recorded times, 5 mL samples were quenched with 1.25 mL of 1.0 M hydrochloric acid and diluted to 10 mL. Spectra are shown in Figure 2. Curves I–IV are samples taken after 0, 10485, 24945, and 60165 s, respectively.