as those described for racemic **18**. That these crystals were the dextrorotatory enantiomorph of **18** containing a small impurity of the levorotatory isomer was demonstrated by its optical rotatory dispersion curve taken on a solution of 1.13 mg of these crystals in 5 ml of ethanol. The specific rotations of the peaks and troughs at the various wavelengths were 660 mμ (−305°), 651 (0°), 637 (+243°), 550 (+120°), 503 (+340°), 480 (0°), 393 (−182°), 387 (0°), 365 (+3000°), 348 (0°), 278 (+222°), 275 (0°), 261 (−2120°), 240 (0°), 227 (+7150°), 213 (+6450°), and 200 (0°).

Attempted Thermal Racemization of Optically Active 4-Carboxy-*trans*-15,16-dimethyldihydropyrene (18). A solution of 1.46 mg of the dextrorotatory enantiomorph of **18** in 1.0 ml of ethanol was placed in a small tube, the solution was degassed, and the tube was sealed. The tube was then totally immersed in a constant-temperature bath at 180° for 10 min. After removal from the bath, the tube was cooled and opened and its contents washed into a volumetric flask diluting in volume to exactly 5.0 ml. The absorption spectrum in the visible region showed λ_{max} at 651 mμ (ϵ 720), 593 (160), and 472 (2650) corresponding to an average of 47% of the original extinction coefficients. The optical rotatory dispersion curve in the visible showed the following specific rotations: 660 mμ (−154°), 651 (0°), 637 (+115°), 550 (+59°), and 505 (+151°). Again, within experimental error this corresponds to an average of 47% of the values of the original specific rotations.

Reduction of the Optically Active 4-Carboxy-*trans*-15,16-dimethyldihydropyrene (18) to Optically Active 4-Methyl-*trans*-15,16-dimethyldihydropyrene (21). A solution of 30 mg of the dextrorotatory enantiomorph of **18** in 50 ml of ether was added dropwise with stirring to a solution of 0.2 g of lithium aluminum hydride and 0.7 g of aluminum chloride in 50 ml of ether held at −70°. After the addition was complete, the mixture was allowed to warm to room temperature with stirring over a 12-hr period. Moist ether was then added, followed by water itself. The green ether layer was separated, dried, and concentrated. The residue was taken up in a 20:1 pentane–ether mixture and chromatographed over alumina (Woelm, activity 1). The emerald green eluate fraction was concentrated to yield 20 mg of green crystals. Recrystallization from 5% aqueous methanol gave fine, green needles: mp 110–115°; uv, λ_{max}^{hexane} 643 mμ (ϵ 354), 629 (224), 613 (198), 598 (155), 538 (80), 468 (6190), 453 (sh, 5610), 429 (sh, 3900), 379 (42,100), 353 (sh, 22,400), and 339 (86,500); nmr (CCl_4), multiplet at τ 1.50 (7 H, Ar*H*), triplet at 2.00 (2 H, Ar*H*), doublet at 6.74 (3 H, $ArCH_3$), and two singlets at 14.18 and 14.20 (3 H each, $-CH_3$); mass spectrum, M^+ − 246; ORD (hexane, *c* 1.074 mg/15 ml), 559 mμ (−160°), 485 (−1720°), 417.5 (+885°), 387 (0°), 380 (−1210°), 378 (0°), 375 (+1860°), 265 (+1670), 252.5 (0°), 234 (+27,000°), 224 (+1720), 210 (+6800), and 207 (0°).

Anal. Calcd for $C_{19}H_{18}$: C, 92.63; H, 7.37. Found: C, 92.42; H, 7.51.

4-Formyl-*trans*-15,16-dimethyldihydropyrene (22). To a solution of 200 mg of **1** in 40 ml of methylene chloride at 0°, there was added with stirring a mixture of 0.20 ml of stannic chloride and 180 mg of *n*-butyl dichloromethyl ether in 5 ml of methylene chloride. After the mixture had been allowed to stir for an additional 2 hr, it was poured onto 100 ml of ice water. The aqueous layer was separated and extracted with methylene chloride. The methylene chloride extracts were combined, washed with water, dried, and concentrated. The residue was taken up in methylene chloride and chromatographed over silica gel. The main purple eluate fraction was collected and rechromatographed twice more in the same way. This effected separation into a green band and a purple band. The purple fraction on concentration gave 162 mg (72%) of reddish purple plates, mp 129–131°, identical with the 2-formyl-*trans*-15,16-dimethyldihydropyrene described previously.[4] The green eluate, on concentration, gave 40 mg (18%) of green crystals which, after recrystallization from aqueous methanol, yielded long, green needles: mp 107–108°; uv, $\lambda_{max}^{cyclohexane}$ 679 mμ (ϵ 2130), 670 (1550), 613 (485), 559 (263), 470 (3740), 447 (7000), 429 (7250), 394 (21,800), and 369 (67,100); ir, $\nu_{max}^{CHCl_3}$ 1668 cm^{-1} (C=O); nmr ($CDCl_3$), singlet at τ −1.20 (1 H, $-CH{=}O$), doublet at 0.20 (1 H, Ar*H*), multiplet at 1.35 (7 H, Ar*H*), triplet at 1.85 (1 H, Ar*H*), and singlets at 14.00 (3 H, $-CH_3$) and 14.05 (3 H, $-CH_3$)

Anal. Calcd for $C_{19}H_{16}O$: C, 87.06; H, 6.19. Found: C, 87.76; H, 6.31.

A solution of 25 mg of **22** in 100 ml of ether was added dropwise with stirring at −70° to a solution of 100 mg of lithium aluminum hydride and 350 mg of aluminum chloride in 20 ml of ether. After the addition was complete, the solution was allowed to warm to room temperature and stir for 5 hr. After addition of water, the ether layer was separated, dried, and concentrated. The residue was taken up in a 20:1 pentane–ether mixture and chromatographed over alumina (Woelm, activity 1). The bright green eluate fraction was concentrated to give 14 mg of crystals. Recrystallization from aqueous methanol gave long green needles, mp 80–81°. The solution spectra of these crystals were essentially identical with those described previously for the optically active sample of **21**.

Base-Catalyzed β-Elimination Reactions in Aqueous Solution. II. ElcB Elimination from β-Methoxy Ketones

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Received July 22, 1968

Abstract: β elimination of methoxide ion from 4-methoxy-2-butanone and from 4-methoxy-4-methyl-2-pentanone to give the respective α,β-unsaturated ketones is kinetically specific base catalyzed. The reactions likely proceed *via* rapid general base catalyzed enolate anion formation, as determined by α-methylene proton exchange in deuterium oxide, followed by rate-determining loss of methoxide ion from the enolate anion. Deuterium solvent kinetic isotope effects as well as Arrhenius activation parameters provide additional support for the postulated mechanism.

Previously, general base catalysis in β-elimination reactions of β-acetoxy ketones was established.[1] Similarly, general base catalysis in β-elimination reactions of β-acetoxy thiol esters as well as in β-phenoxy ketones and β-thiophenoxy ketones has been established.[2,3] Thus for these particular cases general base catalysis in elimination reactions is observed when good leaving groups are involved. It could be anticipated

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[1] L. R. Fedor, *J. Am. Chem. Soc.*, **89**, 4479 (1967).

[2] L. R. Fedor, to be published.

[3] See ref 1 for references to studies involving general base catalysis in elimination reactions of compounds structurally dissimilar to β-substituted ketones and thiol esters.

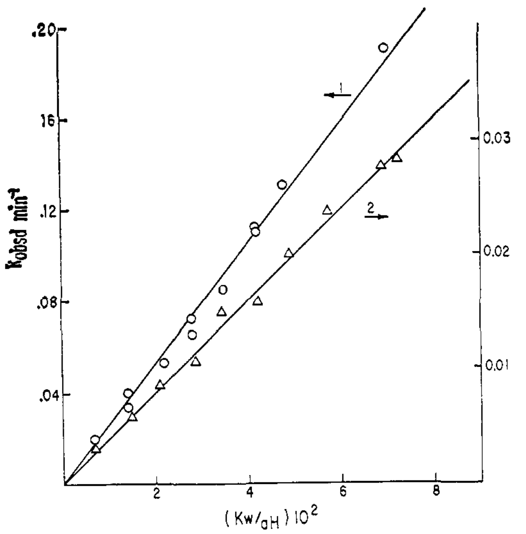

Figure 1. Plot of the pseudo-first-order rate constants, k_{obsd} *vs.* K_w/a_H for the β elimination of methoxide ion from 4-methoxy-2-butanone (**1**) and from 4-methoxy-4-methyl-2-pentanone (**2**) (solvent, H_2O; $t = 30°$; $\mu = 1.0\,M$(KCl)).

that if the general base catalyzed reactions of the above compounds proceed *via* rate-determining enolate anion formation (*vs.* a concerted process) followed by rapid elimination of the β substituent to give product, replacement of a good leaving group with a poor one such as methoxide ion could lead to a change in mechanism whereby rapid enolate anion formation precedes rate-determining loss of methoxide ion to give α,β-unsaturated ketone (ester). The present study explores this hypothesis.

Results and Discussion

β eliminations of methoxide ion from 4-methoxy-2-butanone (**1**) to give 3-buten-2-one and from 4-methoxy-4-methyl-2-pentanone (**2**) to give 4-methyl-3-penten-2-one in aqueous solution are kinetically specific base catalyzed reactions and are described by eq 1. Under

$$dP/dt = (k_2K_w/a_H)\,[\mathbf{1}] \text{ or } [\mathbf{2}] \qquad (1)$$

pseudo-first-order conditions ($K_w/a_H = a_{OH} \gg [\mathbf{1}]$ or $[\mathbf{2}]$) $k_{obsd} = k_2K_w/a_H$ and plots of k_{obsd} *vs.* K_w/a_H are linear with slope = k_2 which for **1** is 0.78 M^{-1} min^{-1} and for **2** is 0.40 M^{-1} min^{-1} (Figure 1, Table I). No catalysis of this reaction by trimethylamine or triethylamine is evident since the reaction rate in solutions of these amines can be accounted for by hydroxide ion catalysis alone (Table II). At least two reasonable mechanisms can be offered to explain the results: (1) general base catalyzed decomposition of **1** or **2** wherein the Brønsted β coefficient approaches 1; (2) rapid enolate anion formation followed by rate-determining decomposition of this anion to products (eq 2). Concerning mechanism 1 a concerted reaction or one involving a rate-determining enolate anion formation can be envisaged and a large value for β could preclude detection of catalysis by any base but hydroxide ion. Attempts to distinguish between these alternatives *via a priori* arguments are inconclusive and it is more instructive to proceed to mechanism 2 which requires that the loss of a proton from SH to give S^- be rapid relative to the rate of decomposition of S^- to products. Further, this mechanism predicts that the enolization reaction will be general base catalyzed.[4] Thus Rappe[5] and Warkentin and Cox[6] have recently shown that the enolization of 2-butanone is general base catalyzed by acetate ion, bicarbonate ion, carbonate ion, and deuterioxide ion and is characterized by a Brønsted β of *ca.* 0.4.

$$\begin{gathered} SH \overset{K_s}{\rightleftarrows} S^- + H^+ \\ S^- \xrightarrow{k_{rate}} CH_3O^- + \alpha,\beta\text{-unsaturated ketone} \end{gathered} \qquad (2)$$

Table I. Rate Data for the Elimination of Methoxide Ion from 4-Methoxy-2-butanone (**1**) and from 4-Methoxy-4-methyl-2-pentanone (**2**) by Lyoxide Species[a]

Ketone	Solvent	pH (pD) range	No. of k_{obsd} values	k_2, M^{-1} min^{-1}	k_2^D/k_2^H
1	H_2O	11.98–12.68	12	0.78	
1	D_2O	12.86–13.50	5	0.90	1.15
1	*b*	12.75–13.29	3	0.78	
2	H_2O	11.99–12.69	10	0.40	
2	D_2O	12.82–13.48	5	0.52	1.3

[a] Temperature, 30°; μ = 1.0 *M* (KCl). [b] 9.1% v/v isopropyl alcohol-D_2O, pD values are given and $-\log K_{D_2O}$ = 14.65 was assumed.

Table II. Rate Data for the Reaction of 4-Methoxy-4-methyl-2-pentanone (**2**) in Aqueous Trimethylamine (A) Solution and in Aqueous Triethylamine (B) Solution[a]

Amine	Concn, *M*	pH	k_{obsd}, min^{-1} [b]	k_{obsd}, min^{-1} [c]
A	0.024	11.97	0.0058	0.0055
	0.048	12.28	0.0113	0.0113
	0.072	12.46	0.0161	0.0170
	0.096	12.58	0.0240	0.0224
	0.120	12.69	0.0289	0.0290
B	0.04	11.05	0.000718	0.000665
B	0.08	11.09	0.000645	0.000728
B	0.12	11.09	0.000566	0.000728

[a] Temperature, 30°; μ = 1.0 *M* (KCl). [b] Rate constant determined in the presence of amine. [c] Rate constant calculated on the basis of the hydroxide rate alone ($k_{obsd} = k_2K_w/a_H$).

In the present study the rate of exchange of the α-methylene protons of **1** with deuterium in deuterium oxide solution was determined *via* nmr spectrometry (Figure 2, Table III) and was compared to the rate of elimination determined by ultraviolet spectrophotometry (Figure 2, Table I). The rate of exchange, on a per proton basis, is 176 M^{-1} min^{-1} which may be compared with the rate of elimination, determined under comparable conditions, which is 0.78 M^{-1} min^{-1}.[7] Clearly, the rate of exchange exceeds the rate of elimination. Further, as predicted (*vide supra*) the exchange

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(4) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., p 144 ff, and references therein.

(5) C. Rappe, *Acta Chem. Scand.*, **20**, 2236 (1966).

(6) J. Warkentin and R. A. Cox, *J. Org. Chem.*, **33**, 1301 (1968).

(7) The rate of elimination of methoxide ion from **1** was followed in 9.1% v/v isopropyl alcohol–deuterium oxide, isopropyl alcohol having approximately the same dielectric constant as butanone, as well as possessing the requisite miscibility with deuterium oxide.

Table III. Rate Data for the Base-Catalyzed Exchange of the α-Methylene Protons of 4-Methoxy-2-butanone (**1**) in Deuterium Oxide[a]

Base	Concn, M	pD	pK_D	K_{D_2O}/a_D [e]	k_{obsd}, min^{-1}	k_2, M^{-1} min^{-1} [f]
A[b]	0.0364	10.71	11.03	1.15×10^{-4}	0.069	5.57
A	0.0545	10.71		1.15×10^{-4}	0.094	
A	0.0727	10.71		1.15×10^{-4}	0.128	
A	0.0910	10.71		1.15×10^{-4}	0.147	
D[c]		11.03	16.42[d]	0.24×10^{-3}	0.021	88.0
D		11.62		0.98×10^{-3}	0.088	
D		12.05		2.52×10^{-3}	0.227	
D		12.30		4.46×10^{-3}	0.380	

[a] 0.05 ml of **1** was added to 0.5 ml of base in D_2O in an nmr tube. Temperature, 29 ± 1°; $\mu = 0.05\ M$ (KCl). [b] Dimethylethylamine. [c] Deuterioxide ion. [d] Negative log of autoprotolysis constant for D_2O divided by 58.2. [e] a_{OD}. [f] Second-order rate constant for exchange of H on a per methylene basis. These rate constants should be multiplied by 2 for the exchange constant per hydrogen atom.[5]

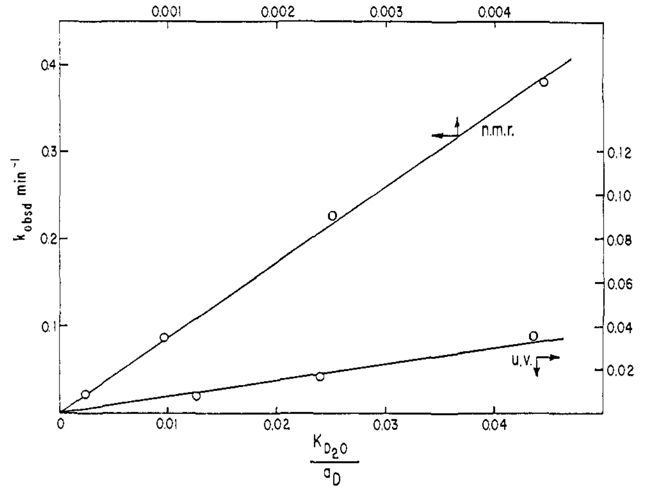

Figure 2. Plot of the pseudo-first-order rate constants, k_{obsd}, *vs.* K_{D_2O}/a_D for the exchange of the α-methylene protons of 4-methoxy-2-butanone (**1**) *via* nmr (top line, solvent 9.1% v/v **1**-D_2O, t = 29 ± 1°, $\mu = 0.05\ M$ (KCl)) and for elimination of methoxide from **1** *via* spectrophotometry (bottom line, solvent 9.1% v/v isopropyl alcohol-D_2O, t = 30 ± 0.1°, $\mu = 0.05\ M$(KCl)).

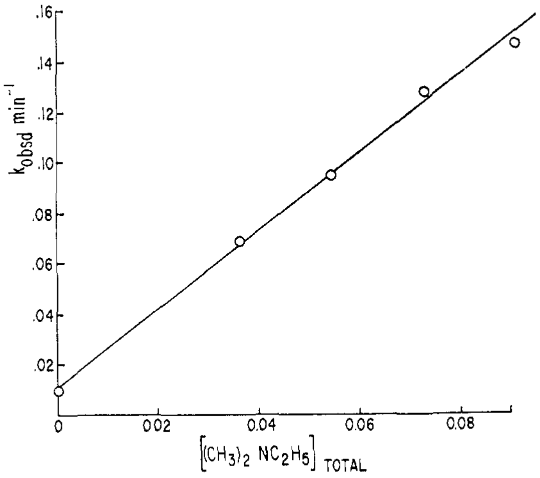

Figure 3. Plot of the pseudo-first-order rate constants, k_{obsd}, *vs.* the total concentration of dimethylethylamine for exchange of the α-methylene protons of **1** (pD = 10.71, pK_D = 11.03; solvent, 9.1% v/v **1**-D_2O; t = 29 ± 1°; $\mu = 0.05\ M$ (KCl)). The slope of the line multiplied by $(K_D + a_D)/K_D = k_2$ (Table III).

reaction is catalyzed by dimethylethylamine (Figure 3, Table III) as well as by deuterioxide ion. It may be of mechanistic significance that the Brønsted β value (calculated from the two rate constants) for the exchange reaction is *ca.* 0.21 which is close to the value of 0.25 determined for the general base catalyzed elimination of acetate from 4-acetoxy-2-butanone and from t-butyl 3-acetoxy-thiolpropionate,[1,2] reactions which could proceed *via* rate-determining enolization.

The deuterium solvent isotope effects (Table I, Figure 4) for the reactions of **1** and **2** with lyoxide species provide additional support for the postulated ElcB mechanism. According to eq 2, $dP/dt = k_{rate}\cdot(S^-)$ and assuming SH and S^- to be in equilibrium and assuming (S^-) to be low relative to (SH) then

$$dP/dt = \frac{k_{rate}K_s a_{OH}(SH)}{K_w} \tag{3}$$

From eq 3 and 1, $k_2 = k_{rate}K_s/K_w$ and the theoretical deuterium solvent kinetic isotope effect for the mechanism can be calculated from

$$\frac{k_2^D}{k_2^H} = \left(\frac{k_{rate}^D}{k_{rate}^H}\right)\left(\frac{K_s^D}{K_s^H}\right)\left(\frac{K_w}{K_D}\right)$$

Assuming little or no medium effect for the decomposition of S^- *via* k_{rate},[8] $k_{rate}^D/k_{rate}^H = 1$. The ratio of the ion products K_w/K_{D_2O} for water and deuterium oxide at 30° is 6.6 (experimental). The ratio K_s^D/K_s^H is dependent on the acidity of the acids **1** and **2** and for known acids varies from 1 for lyoxonium ion (pK_H = −1.74) to 0.154 for water (pK_H = 15.74). These values of K_s^D/K_s^H are related to pK_s^H by the equation $\log K_s^D/K_s^H = -0.02\text{p}K_s^H - 0.416$.[9] Although no values were found for the ratio K_s^D/K_s^H for a carbon acid, or for the pK_s^H for a β-methoxy ketone, a reasonable value for this ratio is between 0.17 and 0.20 which corresponds to pK_s^H = 17.7 and 14.2. Accordingly, the calculated deuterium solvent kinetic isotope effect for the ElcB mechanism is between 1.12 and 1.32. The experimentally determined values are 1.15 for **1** and 1.30 for **2** (Table I).[10]

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(8) L. Pentz and E. R. Thornton, *J. Am. Chem. Soc.*, **89**, 6931 (1967).

(9) Reference 4, p 188.

(10) For the general base catalyzed elimination of acetate from t-butyl 3-acetoxythiolpropionate and t-butyl 3-acetoxy-3-methylthiolbutyrate,[2] structural analogs of the methoxy ketones, k_2^D/k_2^H for lyoxide species is 1.65 and 1.50, respectively, and for dimethylethylamine k_2^D/k_2^H is 1.08 and 0.96, respectively. These ratios are as anticipated for rate-determining proton abstraction by lyoxide ion, as well as by the amine, the former calculated ratios being 1.4:2.[11]

(11) F. A. Long, *Ann. N. Y. Acad. Sci.*, **84**, 596 (1960).

Table IV. Arrhenius Activation Parameters for β Elimination of Methoxide Ion from 4-Methoxy-2-butanone (**1**) and from 4-Methoxy-4-methyl-2-pentanone (**2**)[a]

Ketone	Temp, °C	pH (range)	No. of k_{obsd} values	k_{obsd},[b] min^{-1}	k_2, M^{-1} min^{-1} [d]	$\Delta F^{\ddagger}$, kcal/mole	$\Delta H^{\ddagger}$, kcal/mole	$\Delta S^{\ddagger}$, eu
1	15	24.61	3	9.87×10^{-3}	0.160	20.3	17.6	−9.2
1	20	12.38	3	1.49×10^{-2}	0.273			
1	25	12.20	3	2.37×10^{-2}	0.445			
1	30	11.98–12.68	12		0.777[c]			
2	20	13.07	3	1.19×10^{-2}	0.149	20.7	17.3	−11.5
2	25	12.60	3	1.03×10^{-2}	0.258			
2	30	11.99–12.69	10		0.40[c]			
2	35	12.07	3	1.68×10^{-2}	0.683			

[a] Solvent, water; $\mu = 1.0\ M$ (KCl). $E_a = \Delta H^{\ddagger} + RT$, $\Delta F^{\ddagger} = -2.303RT \log (k_2h/kT)$, $\Delta S^{\ddagger} = (\Delta H^{\ddagger} - \Delta F^{\ddagger})/T$, concentrations in M and time in sec, calculated for 25° by the least-squares method. [b] Average of three rate constants ±3%. [c] Determined from the slope of a plot of k_{obsd} *vs.* K_w/a_H. [d] Rate constants for **1** corrected for 30% elimination of methanol from **1** (*cf.* Experimental Section).

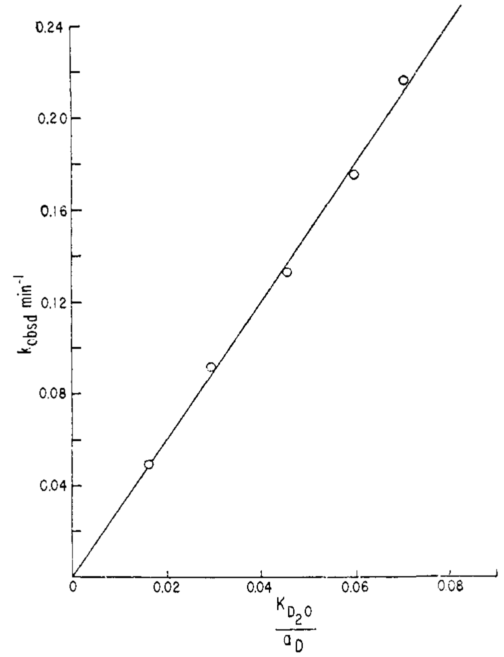

Figure 4. Plot of the pseudo-first-order rate constants, k_{obsd}, *vs.* K_{D_2O}/a_D for the elimination of methoxide ion from 4-methoxy-2-butanone (**1**) (solvent, D_2O; $t = 30°$; $\mu = 1.0\ M$ (KCl)).

Since the rate of an ElcB reaction is dependent on the equilibrium concentration of S^-, the rate should be greater for the stronger acid **1** (k_2(**1**) = 0.78 M^{-1} min^{-1}, k_2(**2**) = 0.40 M^{-1} min^{-1}); the methyl substituents of **2** are acid weakening by inductive effects and also the steric bulk of these substituents should hinder solvation of the anion S^-.[12] For the ElcB mechanism the overall entropy of activation, $\Delta S^{\ddagger}$, could be reflected primarily in K_s and it should be more unfavorable for **2** than for **1**.[13] This is by analogy to the dissociation entropies of such hindered acids as trimethylammonium ion, pK_a = 9.800, ΔH = 8.83 kcal/mol, ΔS = −15.2 eu *vs.* NH_4^+, pK_a = 9.245, ΔH = 12.40 kcal/mol, ΔS = −0.6 eu, and 2,6-lutidinium ion, pK_a = 6.72, ΔH = 6.15 kcal/mol, ΔS = −10.1 eu *vs.* 2-picolinium ion, pK_a = 5.96, ΔH = 6.95 kcal/mol, ΔS = −4.0 eu.[14] Such large decreases in entropy for the dissociation of hindered acids have been rationalized on the basis of steric hindrance to solvation.[4,15] The Arrhenius activation parameters were determined for the elimination reaction of **1** and **2**. Examination of these parameters (Table IV) reveals that the decomposition of **2** is accompanied by $\Delta S^{\ddagger}$ = −11.5 eu *vs.* the decomposition of **1** for which $\Delta S^{\ddagger}$ = −9.2 eu.

The data support an ElcB mechanism for the base-catalyzed decomposition of **1** and **2**, the most convincing evidence being the value for $k_{exchange}/k_{elimination}$ = 226. However it may be that these reactions lie on different paths and are independent of each other.[16] Certainly the compounds **1** and **2** satisfy the classical structural requirements[16] for the ElcB mechanism, *i.e.*, the compounds possess acidic hydrogen atoms, potential for stabilizing negative charge and poor leaving groups.

Experimental Section

Reagents. Fisher Certified ACS, inorganic reagents were used without further purification. Deuterium oxide, 99.8%, and DCl in D_2O were supplied by Ciba Co. Sodium deuterioxide in deuterium oxide was prepared from deuterium oxide and sodium. The organic reagents triethylamine (Eastman), dimethylethylamine (Ames Labs., Inc.), and 4-methoxy-4-methyl-2-pentanone (K & K Laboratories, Inc.) were distilled prior to use. Aqueous trimethylamine (25%) (Eastman) was used as supplied. 4-Methoxy-2-butanone was prepared by heating 3-buten-2-one and a few crystals of *p*-toluenesulfonic acid in excess methanol at reflux for 24 hr. Removal of the excess methanol gave the product, bp 55–56° (30 mm) (lit.[17] 52–53° (22 mm)).

Apparatus. Spectrophotometric rates were monitored using a Gilford Model 2000 spectrophotometer equipped with thermospacers through which water from a Tamson Model T9 water bath was circulated. pH was determined using a Radiometer Model 22 pH meter with a PHA scale expander fitted with a Radiometer GK2021 B combination glass-calomel electrode. Proton-exchange rates were determined with the use of a Varian A-60 nuclear magnetic resonance spectrometer.

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(12) With respect to the relative acidity of **1** and **2** it has been determined that the Brønsted β coefficients for the general base catalyzed elimination of acetate from *t*-butyl 3-acetoxythiolpropionate, 3-acetoxythiolbutyrate, and 3-acetoxy-3-methylthiolbutyrate are 0.25, 0.37, and 0.47, respectively.[2] A possible interpretation of these results is that the acidity of these compounds decreases in the order given for the above reasons.

(13) It is reasonably assumed that the inrease in entropy accompanying the decomposition of **1** and **2** to products parallel one another.

(14) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley & Sons, Inc., New York, N. Y., 1963, p 371, and references therein.

(15) A. G. Evans and S. D. Hamann, *Trans. Faraday Soc.*, **47**, 34 (1952).

(16) For a discussion of this possibility see J. Hine, R. Wiesboeck, and O. B. Ramsay, *J. Am. Chem. Soc.*, **83**, 1222 (1961).

(17) I. N. Nazarov, S. A. Vartanyan, and S. G. Matsoyan, *Zh. Obshch. Khim.*, **25**, 1111 (1955).

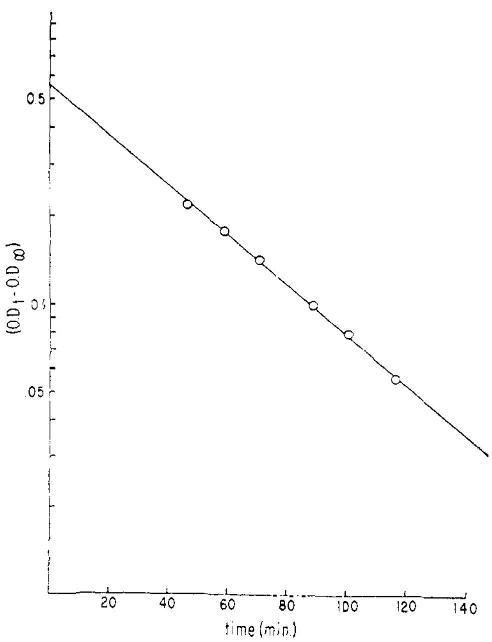


Figure 5. Plot of log (OD_{time} − OD_∞) *vs.* time for the reaction of 4-methoxy-2-butanone (**1**) with hydroxyl ion (pH 12.20; t = 25°; μ = 1.0 M(KCl)).

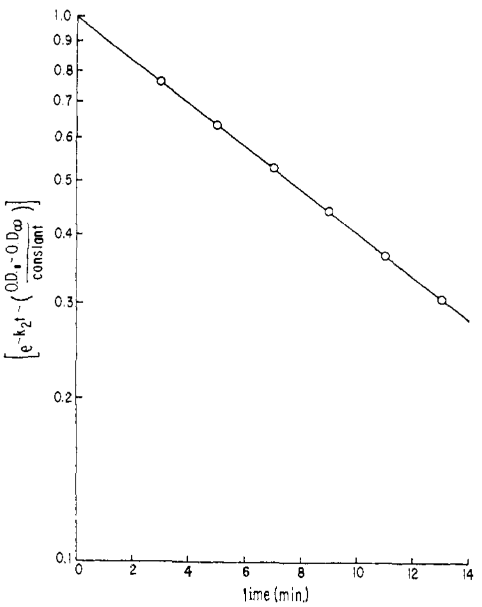
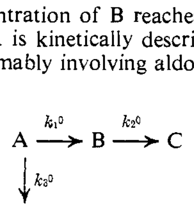


Figure 6. Plot of log $\{e^{-k_2't}$ − [(OD_{time} − OD_∞)/constant]} *vs.* time for the reaction of 4-methoxy-2-butanone (**1**) with hydroxyl ion (pH 12.20; t = 25°; μ = 1.0 M(KCl)).

Kinetics. Spectrophotometric Method. The courses of the reactions of 4-methoxy-2-butanone (**1**) and of 4-methoxy-4-methyl-2-pentanone (**2**) were monitored at 225 and 244 mμ, respectively, as previously described.[1] All reactions except where noted were carried out in water at 30 ± 0.1° and at a calculated ionic strength of 1.0 M(KCl). pK_a was determined by the method of half-neutralization and for dimethylethylamine had the value 10.35 in water and 11.03 in deuterium oxide. pD was determined from pH by the method of Fife and Bruice.[18] The hydroxide ion activity, a_{OH}, was determined from K_w/a_H where a_H is the activity of the hydrogen ion measured with the glass electrode and K_w is the autoprotolysis constant for water, $-\log K_w$ = 14.346 (15°), 14.167 (20°), 13.997 (25°), 13.833 (30°).[19] K_{D_2O}, the autoprotolysis constant for deuterium oxide has the value 2.24 × 10^{-15} (30°).[20] Pseudo-first-order rate constants for reactions of 4-methoxy-4-methyl-2-pentanone were determined by multiplying the slopes of plots of log (OD_∞ − $OD_{initial}$)/(OD_∞ − OD_{time}) *vs.* time by 2.303. All reactions were followed to completion and the pseudo-first-order plots were generally linear to at least two half-lives. Spectrally, the reactions of 4-methoxy-2-butanone are characterized by a rapid increase in optical density to some maximum value followed by a slower decrease in optical density showing that the reaction product is unstable under the conditions of the elimination reaction. Accordingly, the kinetics of the reaction were treated assuming an A → B (k_1') → C (k_2') reaction. The concentration of B is related[21] to its rate of formation and loss by the expression

$$[B] = [A_0k_1'/(k_2' - k_1')](e^{-k_1't} - e^{-k_2't}) \qquad (4)$$

At large values of t, log [B] = log (OD_{time} − OD_∞) = $(k_2'/2.303)t$ + log constant and plots of log (OD_{time} − OD_∞) *vs.* time are linear with slope equal to $k_2'/2.303$ and intercept equal to log constant (Figure 5). Given k_2' and constant, k_1' can be evaluated by multiplying the slope of a plot of log $\{e^{-k_2't}$ − [(OD_{time} − OD_∞)/constant]} *vs.* time by −2.303 (Figure 6). From the determined rate constants k_1 = 2.6 M^{-1} $\min^{-1}$ (Figure 1) and k_2 = 0.52 M^{-1} $\min^{-1}$ (t = 30°), which are proportional to k_1' and k_2' (eq 4), it can be shown that the maximum concentration of B at t_{max} is 0.67A_0 where A_0 is the initialcon centration of **1**.[21] Experimentally the concentration of B reaches 0.20A_0 and therefore the decomposition of **1** is kinetically described by eq 5, the pathway A → D (k_3) presumably involving aldol-type condensation reactions.



$$\begin{tikzcd} A \arrow[r, "k_1^0"] \arrow[d, "k_3^0"] & B \arrow[r, "k_2^0"] & C \\ D \end{tikzcd} \qquad (5)$$

For (5), the concentration of B at anytime is given by eq 6 where $a = (k_1^0 + k_3^0)$. Comparison of eq 4 and 6 shows that they are

$$[B] = \frac{A_0k_1^0}{k_2^0 - a}(e^{-at} - e^{-k_2^0t}) \qquad (6)$$

of the same form, a of eq 6 replacing k_1' of eq 4. From the condition d([B]/A_0)/dt = 0, the time at which the concentration of B is maximal is given by $t_{max} = (a - k_2^0)^{-1} \ln (a/k_2^0)$ and t_{max} maybe be determined from the experimental values for a = 2.6 M^{-1} $\min^{-1}$ and k_2^0 = 0.52 M^{-1} $\min^{-1}$. Substitution of t_{max} and the experimentally obtained value for [B]/A_0 = 0.20 allows calculation of k_1^0 = 0.78 M^{-1} $\min^{-1}$ (30°, Table I).

Nmr Method. The rates of exchange of the α-methylene protons of 4-methoxy-2-butanone by deuterium in deuterium oxide solutions were monitored at 29 ± 1°. The temperature in the probe was determined by measuring the difference between the temperature-dependent chemical shifts of the protons in ethylene glycol at the time of the kinetic runs and reading temperature from a plot of Δ(chemical) shift *vs.* temperature.[22] The spectrum of 4-methoxy-2-butanone shows a singlet at 135 cps (α-CH_3), a triplet centered at 170 cps (α-CH_2), a singlet at 202 cps (CH_3O–), and a triplet centered at 224 cps (β-CH_2) relative to TMS. These chemical shifts from TMS were determined from the chemical shifts measured from *t*-butyl alcohol in deuterium oxide and the chemical shifts of *t*-butyl alcohol from TMS in deuteriochloroform. Repetitive scans of the nmr spectrum of 4-methoxy-2-butanone in sodium deuterioxide–deuterium oxide solutions and in deuterium oxide solutions of dimethylethylamine show the loss of the triplet at 170 cps (α-CH_2) with conversion of the triplet at 224 cps (β-CH_2) to a singlet. The rate of loss of the methylene proton signal is *ca.* sevenfold greater than the rate of loss of the methyl signal at 135 cps.[5,6,23] Rates

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(18) T. H. Fife and T. C. Bruice, *J. Phys. Chem.*, **65**, 1079 (1961).

(19) R. A. Robinson and R. H. Stokes, "Electrolyte Solutions," 2nd ed, Butterworth and Co. (Publishers), Ltd., London, 1959.

(20) T. C. Bruice and J. J. Bruno, *J. Am. Chem. Soc.*, **83**, 3494 (1961).

(21) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley & Sons, Inc., New York, N. Y., 1962, p 166.

(22) Preliminary Instruction Manual V-6057, Variable Temperature System for A-60 Analytical Spectrometers, Publication No. 87-100-110, Varian Associates, Palo Alto, Calif., p 29.

(23) J. Hine, K. G. Hampton, and B. C. Menon, *J. Am. Chem. Soc.*, **89**, 2664 (1967).

of exchange of the α-methylene protons were followed by integrating the signals at 170 and 202 cps using the latter methoxy signal as internal standard. The methoxy group integral, divided by three, gave the value of the integral for one proton and from this the number of α-methylene protons as a function of time was determined. Pseudo-first-order rate constants were determined by multiplying the slopes of plots of log (hydrogen atoms remaining) *vs.* time by -2.303 (Table III).

Product Analysis. The courses of the reactions of 4-methoxy-2-butanone and of 4-methoxy-4-methyl-2-pentanone were scanned using a Beckman Model DBG spectrophotometer. Only increases in absorbance with time were observed at λ_{max} for 3-buten-2-one (213 mμ) and λ_{max} for 4-methyl-3-penten-2-one (244 mμ) for the respective reactions of the β-methoxy ketones.

To 3 ml of 0.1 N aqueous KOH solution contained in a cuvette was added 1.96×10^{-5} g (5×10^{-6} M) of 4-methoxy-4-methyl-2-pentanone in $^1/_{300}$ ml of methanol. After reaction the solution (5×10^{-5} M in product, mesityl oxide) had an absorbance of 0.553 OD. From the molar extinction coefficient for mesityl oxide, 1.11×10^{-4},[24] and the absorbance value 0.553, the concentration of mesityl oxide produced was 4.98×10^{-5} M, representing essentially quantitative conversion of 4-methoxy-4-methyl-2-pentanone to mesityl oxide.

For the reactions of **1** (9.4×10^{-5} M) in 0.02–0.10 M potassium hydroxide solutions (30°), the absorbance at 221 mμ at $t_{max} = 0.145 \pm 0.002$ for five KOH concentrations. This absorbance corresponds to a 20% conversion of **1** to 3-buten-2-one ($\epsilon_{221} = 7.87 \times 10^3$) at t_{max}. Conversion of **1** to 3-buten-2-one *via* an A → B → C process alone requires 67% conversion to the α,β-unsaturated ketone at t_{max} (*vide supra*). Thus the elimination reaction of **1** proceeds to the extent of 30% and presumably most of **1** undergoes aldol-type condensation reactions. In an attempted product isolation experiment reaction of 0.5 g of **1** with potassium hydroxide solution yielded yellow, gumlike material which could not be characterized. This reaction is accompanied initially and transiently by the formation of the pungent, characteristic odor of 3-buten-2-one.

Acknowledgment. This work was supported by a research grant (AM-11403) from the National Institute of Arthritis and Metabolic Diseases and by a training grant (5-Tl-GM-555) from the Division of Medical Sciences, U. S. Public Health Services, Bethesda, Maryland.

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Base-Catalyzed β-Elimination Reactions in Aqueous Solution. III. Elimination from *t*-Butyl 3-Acetoxythiol Esters[1]

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Received August 27, 1968

Abstract: The β elimination of acetate from *t*-butyl 3-acetoxyethiolpropionate (**1**), *t*-butyl 3-acetoxythiolbutyrate (**2**), and *t*-butyl 3-acetoxy-3-methylthiolbutyrate (**3**) to give the respective α,β-unsaturated thiol esters is general base catalyzed by tertiary amines and hydroxyl ion. The reactivities of the thiol esters are reasonably correlated by the Brønsted-type equations: $\log k_2(\mathbf{1}) = 0.25\mathrm{p}K_a - 1.87$, $\log k_2(\mathbf{2}) = 0.37\mathrm{p}K_a - 4.01$, and $\log k_2(\mathbf{3}) = 0.47\mathrm{p}K_a - 6.10$.

The greater reactivity of thiol esters *vs.* oxygen esters in condensation reactions at the α-carbon atom is likely related to the stronger acidity of thiol esters as carbon acids.[2] This biologically important class of compounds possesses acidities comparable to ketones rather than to oxygen esters and accordingly thiol esters and ketones should possess similar reactivities with regard to reactions occurring at the α-methylene carbon atom. This investigation provides the basis for a comparison between the general base catalyzed elimination of acetate from *t*-butyl β-acetoxythiolcarboxylates (eq 1) and from β-acetoxy ketones.[3]

$$R_1R_2C(OAc)CH_2COSC(CH_3)_3 + B \longrightarrow R_1R_2C{=}CHCOSC(CH_3)_3 + BH^+ + AcO^- \quad (1)$$

Results

The reactions of *t*-butyl 3-acetoxythiolpropionate (**1**), *t*-butyl 3-acetoxythiolbutyrate (**2**), and *t*-butyl 3-acetoxy-3-methylthiolbutyrate (**3**) in aqueous solutions of tertiary amine buffers to give the appropriate α,β-unsaturated thiol esters (eq 1) are kinetically described by

$$dP/dt = (k_2[\text{amine}] + k_{OH}K_w/a_H)[\text{thiol ester}] \quad (2)$$

eq 2. Under pseudo-first-order conditions at constant pH, $k_{obsd} = k_2'[\text{amine}]_{total} + k_{OH} + K_w/a_H$ and plots of k_{obsd} *vs.* $[\text{amine}]_{total}$ are linear with slope, k_2', and intercept, $k_{OH}K_w/a_H$ (Figure 1). The second-order rate constant k_2' may be evaluated by dividing k_2' by $K_a/(K_a + a_H)$, the mole fraction of total amine present as free amine at a given pH (Table I). The value for k_2 was invariant within the limit of the experimental error for reactions carried out at several pH values for selected amines. No general acid catalysis was detected under the conditions of these experiments. The constant k_{OH} was evaluated from the slope of plots

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[1] Support for this investigation by the National Institutes of Health is gratefully acknowledged.

[2] T. C. Bruice and S. J. Benkovic, "Bioorganic Mechanisms," Vol. 1, W. A. Benjamin, Inc., New York, N. Y., 1966, Chapter 3 and references therein.

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