Bromination of Saturated Aliphatic Ketones in an Acidic Medium: Effects of Structure on Apparent Rate Constants for Enolization and for Bromination of the Enol

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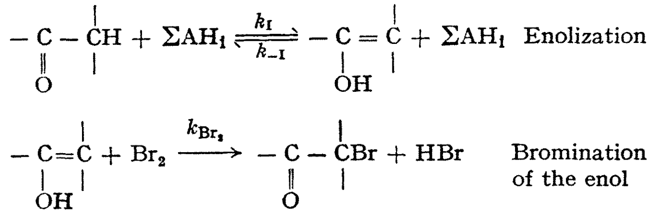
IN a study of the effects of structure on keto-enol tautomerism of saturated aliphatic ketones, with particular reference to rate of ketonization of the enol,[1] we have developed a kinetic analysis of the bromination under such conditions that the two successive steps, enolization† and addition of halogen‡ to the enol, proceed at comparable rates.



$$-\underset{\substack{\| \\ \mathrm{O}}}{\mathrm{C}}-\overset{|}{\underset{|}{\mathrm{C}}}\mathrm{H} + \Sigma\mathrm{AH_i} \underset{k_{-\mathrm{I}}}{\overset{k_{\mathrm{I}}}{\rightleftharpoons}} -\underset{\substack{| \\ \mathrm{OH}}}{\mathrm{C}}=\overset{|}{\underset{|}{\mathrm{C}}} + \Sigma\mathrm{AH_i} \quad \text{Enolization}$$

$$-\underset{\substack{| \\ \mathrm{OH}}}{\mathrm{C}}=\overset{|}{\underset{|}{\mathrm{C}}} + \mathrm{Br_2} \xrightarrow{k_{\mathrm{Br_2}}} -\underset{\substack{\| \\ \mathrm{O}}}{\mathrm{C}}-\overset{|}{\underset{|}{\mathrm{C}}}\mathrm{Br} + \mathrm{HBr} \quad \text{Bromination of the enol}$$

($\mathrm{AH_i}$ = any acid species in the medium)

Two constants are calculated simultaneously from the rate data:[2]

$$k_{\mathrm{I}} = \Sigma(k_{\mathrm{HA_i}} \times [\mathrm{HA_i}]) = \text{Overall enolization rate constant,}$$

and

$$k_{\mathrm{II}} = \frac{k_{-\mathrm{I}}}{k_{\mathrm{I}}}k_{\mathrm{Br_2}} = \text{Apparent enol bromination rate constant,}$$

by means of equation (1):

$$\frac{t'-t}{[\mathrm{Br_2}]-[\mathrm{Br_2}]'} = \frac{1}{k_{\mathrm{II}}[\text{ketone}]}\,\frac{\ln[\mathrm{Br_2}]-\ln[\mathrm{Br_2}]'}{[\mathrm{Br_2}]-[\mathrm{Br_2}]'} + \frac{1}{k_{\mathrm{I}}[\text{ketone}]} \qquad (1)$$

which is only valid in very acidic media and at very low bromine concentration[2,3] ($[\mathrm{Br_2}]$ and $[\mathrm{Br_2}]'$ are the analytical bromine concentrations at times t and t': $[\text{ketone}] \gg [\mathrm{Br_2}]$).

The ratio of the experimental rate constants is, in fact, that of the rates of the two competitive reactions of the enol, its bromination and its protonation:

$$k_{\mathrm{I}}/k_{\mathrm{II}} = k_{-\mathrm{I}}/k_{\mathrm{Br_2}} \qquad (2)$$

The introduction of a α-2 methyl group [*cf.* (Ia) and (Ib)] diminishes[4] k_{I} by a factor of 3 and increases k_{II} by a factor of 5·5. The preferred enol[5] of an unsymmetrical aliphatic ketone is that stabilized by the hyperconjugative effect of an alkyl group, which also decreases the rate of ketonization. The large change in the value of $k_{\mathrm{I}}/k_{\mathrm{II}}$ is, therefore, largely attributable to a decrease in the ketonization rate by hyperconjugation.

For R ≠ H, $k_{\mathrm{I}}/k_{\mathrm{II}}$ ($= k_{-\mathrm{II}}/k_{\mathrm{Br_2}}$) is roughly constant. The energies of the transition states for the attack by bromine and acids on the enol must therefore have similar dependence on structure. The small increase in $k_{\mathrm{I}}/k_{\mathrm{II}}$ for R = Me < Et < Pr$^{\mathrm{i}}$ < Bu$^{\mathrm{t}}$ can be associated with the different dependence of bromination and protonation rates on the energy of the hyperconjugation-stabilized enol. Since the transition state for the former reaction is closer to the initial state, destabilization of the enol accelerates protonation more than bromination. However, the change is very small and steric differences between the two electrophiles may also be significant.

Apparent rate constants for enolization and bromination of* $\mathrm{Bu^tCO{\cdot}CH_2R}$ *at 25°, in aqueous acetic acid* (75% *v*/*v*; [HBr] = 0·5M)

Ketone	R	$10^5 \times k_{\mathrm{I}}$ (sec.$^{-1}$)	k_{II} (l.mole^{-1}sec.$^{-1}$)	$10^5 \times k_{\mathrm{I}}/k_{\mathrm{II}}$ (mole l.$^{-1}$)
(Ia)	H	2·10	0·49	4·30
(Ib)	Me	0·72	$2{\cdot}7_5$	0·26
(Ic)	Et	0·49	1·67	0·29
(Id)	Pr$^{\mathrm{i}}$	$0{\cdot}26_7$	0·82	0·33
(Ie)	Bu$^{\mathrm{t}}$	$0{\cdot}06_3$	0·13	$0{\cdot}4_8$
(If)	Pr$^{\mathrm{n}}$	0·59	$2{\cdot}2_5$	0·26
(Ig)	Bu$^{\mathrm{n}}$	0·58	$2{\cdot}2_2$	0·26
(Ih)	$n\text{-}\mathrm{C_5H_{11}}$	0·58	$2{\cdot}1_5$	0·27

* Rates were determined by couloamperometry (J. E. Dubois, P. Alcais, and G. Barbier, *J. Electroanalyt. Chem.*, 1964, **8**, 359) for ketone concentrations between 10^{-2} and $5{\cdot}10^{-2}$ M, and bromine concentrations of *ca.* 10^{-4} to 10^{-7} M. Values of k_{I} and k_{II}, computer calculated from Equation (1), agree to within ± 5%, except that for (Ie) (±20%).

The linear correlation with Taft's values[6] (Figure) shows

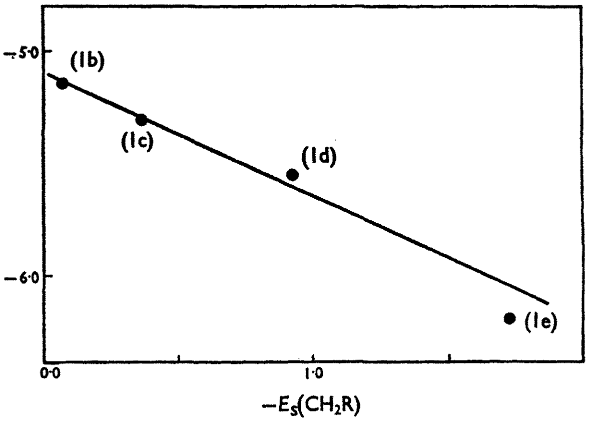


FIGURE. *Correlation of* E_s *with* log k_{I} *for β-2-methyl derivatives*

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† The first step is assumed to involve the rapid pre-equilibrium formation of an intermediate hydroxycarbonium ion.

‡ Enol bromination involves both free bromine and the tribromide ion. The constant $k_{\mathrm{Br_2}}$, defined in terms of the analytical bromine concentration, is, in fact, a combination of constants for $\mathrm{Br_2}$ and $\mathrm{Br_3^-}$.

that the enolization rate has a dependence on progressive β-2-methyl, characteristic of the operation of a predominantly steric effect. However, it is not obvious whether this effect is one of interference with the protonation of the ketone or of destabilization of the enol. In fact, the behaviour of the n-alkyl compounds, where the ethyl-substituted compound has a particularly low k_1 value (Me > $Pr^n = Bu^n$ = n-C_5H_{11} > Et) supports a special interpretation involving participation of *terminal methyl groups*. Such a minimum, already observed in phenyl alkyl ketones[4] can be considered to arise from an interaction between the terminal methyl group of the chain and the carbonyl function.

Our preliminary results and discussion show that this system is of considerable potential interest for the study of the various structural effects associated with alkyl groups. Further work on the direct determination of the enol bromination rate, which has as yet been little studied,[7] and on the reactivity of stable derivatives, *i.e.* ethers and esters of enols, is in hand.

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[1] Little information on the enolization equilibrium constant is available for saturated aliphatic ketones. Direct enol determination in the pure ketone or its concentrated aqueous solutions gives imprecise results: R. P. Bell and P. W. Smith, *J. Chem. Soc.* (*B*), 1966, 241.

[2] J. E. Dubois and J. Toullec, *J. Chim. phys.*, 1968, **65**, 2166.

[3] R. P. Bell and G. G. Davis, *J. Chem. Soc.*, 1964, 902.

[4] A similar decrease in k_I caused by an α-2-methyl group has been observed for the same ketones (D. P. Evans and J. R. Young, *J. Chem. Soc.*, 1954, 1314) as well as for the phenyl alkyl ketones (D. P. Evans, V. G. Morgan, and H. B. Watson, *J. Chem. Soc.*, 1935, 1167).

[5] C. Rappe and W. H. Sachs, *J. Org. Chem.*, 1967, **32**, 3700.

[6] R. W Taft, "Steric Effects in Organic Chemistry," ed. M. S. Newman, Wiley, New York, 1956, p. 601.

[7] J. E. Dubois and G. Barbier, *Bull. Soc. chim., France*, 1965, 682.