Electron Spin Resonance Studies. Part 62.[1] Acid-catalysed Interconversion of β-Hydroxyalkyl Radicals: Radical-cation Intermediates

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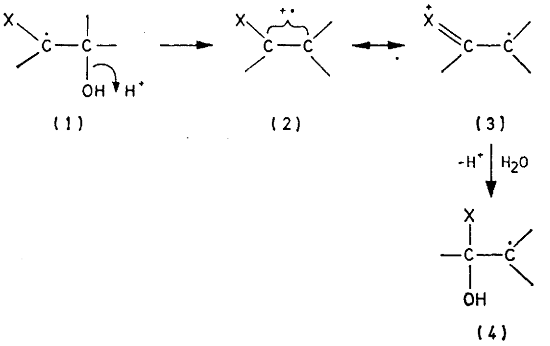
Evidence is presented that isomerism of β-hydroxyalkyl radicals (*e.g.*, the conversion of $\cdot CH_2CMe_2OH$ into $\cdot CMe_2CH_2OH$) can be brought about in acid solution and that reaction occurs *via* the formation and hydration of a radical-cation. The reaction rates for loss of OH^- (*e.g.* $\cdot CHMeCEt_2OH > \cdot CH_2CMe_2OH > \cdot CH_2CHMeOH$) are correlated with the stabilities of the radical-cations as measured by the ionization potentials of the corresponding alkenes.

RADICALS of the type (1), in which X is a group of $+M$ type such as hydroxyl, undergo the rearrangement (1) in acidic solution.[2] It has been inferred that radical-cations (2) mediate, their formation being assisted by acid-catalysed removal of OH^- and by delocalization of charge on to the group X [*cf.* structure (3)].[2]



(1)

In this paper, we report that radicals of type (1) but lacking the $+M$ group X also undergo acid-catalysed loss of hydroxide although, as anticipated, with a more stringent requirement for acid catalysis.

RESULTS AND DISCUSSION

Reactions were carried out by admixture of titanium(III) ion, hydrogen peroxide, and a (saturated) alcohol, with acid added as required, *ca.* 70 ms before passage of the combined solution into the cavity of an e.s.r. spectrometer. Under these conditions, the hydroxyl radical from the redox couple abstracts a hydrogen atom from the alcohol.

In the pH range 0.5—2.0, t-butyl alcohol yielded only the radical (5), as reported before.[3] However, when the pH was reduced to 0, the spectrum from a second species became detectable; it was identified by its e.s.r. parameters [a(6 H) 2.33, a(2 H) 1.44 mT, g 2.0026] as radical (6), which has been generated [4] previously by addition of $\cdot OH$ to isobutylene. As the pH was reduced further, the spectrum of radical (6) increased in intensity at the expense of that from radical (5), until, with $[H_2SO_4]$ 3 mol dm^{-3}, the ratio [(6)] : [(5)] was *ca.* 0.8 : 1.

$\cdot CH_2C(OH)Me_2$ (5) $\qquad$ $\cdot CMe_2CH_2OH$ (6)

3-Ethylpentan-3-ol gave four radicals in all. Three were assigned structures (7)—(9) on the basis of their e.s.r. parameters (Table); thus, each has a 'hydrocarbon-like' g-factor, and α- and β-proton splittings typical of alkyl-type radicals.[5,6] A notable point in the case of radical (9) is that only the unique set of methyl protons, of the three, shows a detectable interaction. This suggests the preference for a conformation of the type (10) in which the corresponding C–Me bond eclipses the half-filled p-orbital, so favouring hyperconjugative delocalization of the spin on to the γ-carbon atom.[7] This in turn is consistent with the magnitude of the splitting for the single β-proton shown which, assuming a $B \cos^2\theta$ dependence [6] (with B *ca.* 4.6 mT for tertiary radicals of this sort †), gives θ (average) 63° for the cor-

Radicals detected during the oxidation of alcohols

		Hyperfine splittings (mT) [a]			
		a(α-H)	α(β-H)	a (other)	g [b]
$Me_3C(OH)$	$\cdot CH_2C(OH)Me_2$	2.23(2)		0.13(6)	2.0025
	$\cdot CMe_2CH_2OH$		2.33(6) 1.44(2)		2.0026
$Et_3C(OH)$	$\cdot CHMeC(OH)Et_2$	2.18(1)	2.53(3)	*c*	2.0027
	$\cdot CH_2CH_2C(OH)Et_2$	2.23(2)	2.45(2)	*c*	2.0028
	$\cdot CEt_2CH(OH)Me$		1.74(4) 0.94(1)	0.125(3)	2.0026
	$\cdot CHMe{-}CEt{=}CHMe$	2.6 [d]	3.4 [d]	0.20(2)	2.0028
$(Me_2CH)_2CHOH$	$\cdot C(OH)(CHMe_2)_2$		1.09(2)	0.19(1)	2.0030
	$\cdot CMe_2CH(OH)CHMe_2$		2.34(6) 0.60(1)	*c*	2.0026
	$\cdot CH_2CHMe{\cdot}CH(OH)CHMe_2$	2.18(2)	2.65(1)	*c*	2.0027

[a] ±0.01, except where stated. [b] ±0.0001. [c] Further small, unresolved splittings. [d] Sum of two splittings in each case: approximate analysis (see text).

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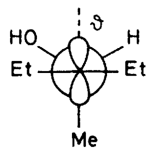
† See *e.g.* β-splittings for freely rotating methyl groups ($\langle\cos^2\theta\rangle = \frac{1}{2}$) in (6) and [5] $Bu^t\cdot$.

responding C–H bond and therefore an average dihedral angle of only 3° for the C–Me bond.

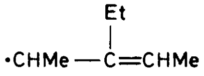
$\cdot CHMeC(OH)Et_2$
(7)

$\cdot CH_2CH_2C(OH)Et_2$
(8)

$\cdot CEt_2CH(OH)Me$
(9)



(10)


$\cdot CHMe{-}\overset{Et}{\overset{|}{C}}{=}CHMe$
(11)

An unambiguous analysis could not be achieved for the fourth radical, for many of its lines were apparently obscured by those from the other radicals. However, it is thought to be the allylic species (11) (analysis of the spectrum of which might in any case be complicated by the presence of up to three geometrical isomers), on the basis of its splittings and *g*-factor and also of the mechanistic considerations discussed in the sequel.

The relative concentrations of radicals (7)—(9) and (11) varied markedly with pH. At pH > 2.5, only the first two were detected; as the pH was lowered, the observed concentration of radical (8) remained approximately constant but that of radical (7) decreased and the spectrum of radical (9) appeared; by pH 1, the resonances from radical (7) had essentially disappeared, those from radical (9) were becoming weaker, and a weak spectrum ascribed to radical (11) had appeared; further lowering, to pH 0, resulted in the dominance of the spectrum ascribed to radical (11) over that of radical (9), with radical (7) undetectable.

The oxidation of 2,4-dimethylpentan-3-ol also gave four radicals. One is assigned the structure (12) on the basis of its *g*-factor, which is typical of those in which the tervalent carbon is attached to hydroxyl,[8] and of the fact that the doublet splitting of 0.19 mT collapsed to a singlet when the pH was lowered from 1.5 to 1, consistent with its being associated with an exchangeable proton on hydroxyl attached to the tervalent carbon atom.[9] Two others are assigned structures (13) and (14), their hyperfine splittings and *g*-factors being in the usual ranges for alkyl-type radicals. The fourth radical was evidently from an impurity since the intensity of its spectrum increased when further portions of the substrate were added to a saturated solution; no consideration was taken of this species in the mechanistic analysis below.

$\cdot C(OH)(CHMe_2)_2$
(12)

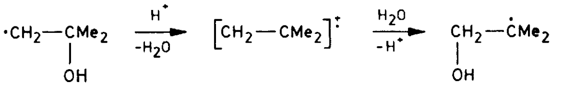
$\cdot CMe_2CH(OH)CHMe_2$
(13)

$\cdot CH_2CHMe{\cdot}CH(OH)CHMe_2$
(14)

The relative concentrations of radicals (12)—(14) remained independent of pH in the range 1—3, but as the pH was lowered below 1, the signal from radical (13) diminished in intensity relative to those of the other two until, with $[H_2SO_4]$ 1.5 mol dm^{-3}, it was no longer detectable. Its disappearance was not accompanied by the growth of signals of comparable intensity, although a number of weak, unanalysable lines were evident.

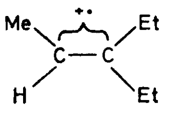
Finally, when propan-2-ol was oxidised, the radicals $\cdot CMe_2(OH)$ and $\cdot CH_2CH(OH)Me$ were observed as before,[10] but their relative concentrations did not change detectably in the acidity range pH 2.5 to $[H_2SO_4]$ 3 mol dm^{-3}.

Mechanism of Reaction.—The disappearance of the e.s.r. signals from the β-hydroxy-substituted radicals (5), (7), and (13) as the pH is lowered, and, in the case of the first two, the corresponding appearance of the signals of isomeric radicals which cannot be derived by simple hydrogen-atom abstraction from the parent compound, closely resembles the behaviour of radicals of the type (1). It may likewise be interpreted in terms of the formation of a radical-cation and its subsequent hydration, as in reaction (2) for the initial radical from t-butyl alcohol. However, an alternative interpretation is also consistent with the results, namely, that an alkene is formed by acid-catalysed elimination from the parent alcohol and this then forms the new hydroxy-substituted radical by addition. This possibility was tested for in the case of t-butyl alcohol by carrying out its oxidation with the redox couple with inclusion of acid (to give an overall acid concentration of 3 mol dm^{-3}) in each of three ways: (i) in all three streams of the flow system, (ii) in only the titanium(III) solution, and (iii) in only the t-butyl alcohol solution. The spectra obtained were identical. Further, when isobutylene (present in one stream as an acid-free saturated solution) was oxidised by the redox couple, only the radical (6) was detected, regardless of the acidity of the medium. These observations enable us to eliminate the above alternative hypothesis since this would require that the observed ratio [(6)] : [(5)] should be higher in experiment (iii), owing to the longer contact time between acid and alcohol, than in (i) or (ii), tending to the extreme represented by the behaviour of isobutylene. We therefore infer the importance of reaction (2) and corresponding reactions for the other two alcohols.

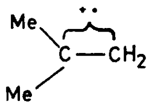

$$\underset{(5)}{\cdot CH_2{-}\underset{OH}{\underset{|}{C}}Me_2} \xrightarrow[-H_2O]{H^+} [CH_2{-}CMe_2]^{+\cdot} \xrightarrow[-H^+]{H_2O} \underset{(6)}{\underset{OH}{\underset{|}{C}}H_2{-}\dot{C}Me_2} \qquad (2)$$

The suggestion that hydration of $[CH_2{-}CMe_2]^{+\cdot}$ leads to (6) rather than (5) finds support from e.s.r. experiments on the reaction between isobutylene and $Cl_2^{-\cdot}$ (which, by analogy with the oxidation of electron-rich alkenes with $Cl_2^{-\cdot}$, would be expected to yield the radical-cation directly [2]). When this reaction was carried out both at pH < 0 and at pH 1, the only radical detected was (6). We conclude that electron-transfer has indeed taken place and that, as judged by the results at pH 1 (at which no acid-catalysed interconversion occurs), radical (6) is the kinetically controlled product of hydration; since it also predominates at very low pH, it is also evidently (as expected) the more stable of the two isomers.

Comparison of the results of the oxidation of 3-ethylpentan-3-ol and 2,4-dimethylpentan-3-ol with those for t-butyl alcohol reveals several notable features. First, the acid-catalysed elimination of hydroxide from the radical (7) from 3-ethylpentan-3-ol occurs at a rate which is detectable by the e.s.r. method at significantly higher pH than does that from radical (5). This evidently reflects the greater stabilisation of radical-cation (15), compared with (16), afforded by the larger number of alkyl substituents (*cf.* the reduction in ionisation potential on the introduction of alkyl groups into alkenes [11]).

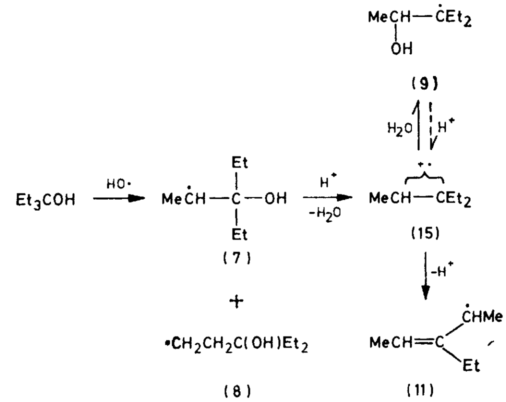


(15)



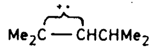
(16)

Secondly, there is clear evidence that (15) has, unlike (16), a further mode of reaction besides its hydration to yield $\cdot\mathrm{CEt_2CHMeOH}$. Thus at pH < 1.4 the signal from $\cdot\mathrm{CEt_2CHMeOH}$ (9) is replaced by that ascribed to the allylic species (11). The disappearance of (9) indicates that at very low pH the route to its formation (see Scheme) essentially becomes reversible [*i.e.* the acid-catalysed loss of $\mathrm{OH^-}$ to regenerate (15) becomes important]; the appearance of (11) is then attributed to the deprotonation of the radical-cation. It follows that hydration is kinetically preferred over deprotonation, but that when conditions of reversibility are established the formation of the allylic species is preferred. The fact that $\cdot\mathrm{CEt_2CHMeOH}$ (9) undergoes loss of $\mathrm{OH^-}$ less readily (*i.e.* at a lower pH) than its isomer $\cdot\mathrm{CHMeCEt_2OH}$ (7) implies that, as expected on the basis of structural considerations, the former is the more stable.

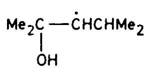


SCHEME

Thirdly, although the formation of the radical-cation (17) is suggested by the disappearance of (13) as the pH was lowered in the reaction of 2,4-dimethylpentan-3-ol with ·OH, no new radicals were detected. We believe that signals from the isomeric radical (18) would have been detectable if this had been formed to any significant extent in the hydration of the radical-cation (17). We suggest that hydration leads instead to the regeneration of the more stable isomer (13) and that the depletion of the latter reflects an alternative fate for the cation-radical (17) [*e.g.* reduction by $\mathrm{Ti^{III}}$ or, more likely, deprotonation to give an allyl radical (19) which cannot be unambiguously detected because of the multiplicity of its resonances (98 lines are expected in all)].

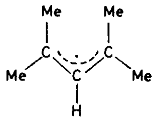


(17)



$\mathrm{Me_2C(OH)}$—$\dot{\mathrm{C}}\mathrm{HCHMe_2}$

(18)



(19)

The failure to observe any changes in the relative proportion of the radicals $\cdot\mathrm{CH_2CHMeOH}$ and $\cdot\mathrm{CMe_2OH}$ derived from propan-2-ol suggests that, within the accessible range of acidity, acid-catalysed loss of $\mathrm{HO^-}$ from $\cdot\mathrm{CH_2CHMeOH}$ does not take place at a significant rate. This no doubt reflects the fact that in the transition state leading to the radical-cation only one alkyl substituent is available for conjugation with the developing one-electron π-bond.

Finally, it was decided to examine more closely the relationship between the ease of formation of particular radical-cations and the substituents present, not only for the alkene radical-cations discussed here but also for those from vinyl ethers whose reactions have been described previously.[2]

For the reaction of ·OH with a substrate RH to give radicals $\mathrm{R_1\cdot}$, $\mathrm{R_2\cdot}$, *etc.*, of which only one ($\mathrm{R_i\cdot}$) undergoes acid-catalysed rearrangement, to give S·, the system is described by reactions (3)—(8) and the steady-state analysis

$$\mathrm{Ti^{III}} + \mathrm{H_2O_2} \longrightarrow \mathrm{Ti^{IV}} + \mathrm{OH^-} + \cdot\mathrm{OH} \tag{3}$$

$$\cdot\mathrm{OH} + \mathrm{RH} \longrightarrow \mathrm{R_1\cdot} + \mathrm{R_2\cdot} + \ldots \tag{4}$$

$$2\mathrm{R_i\cdot} \longrightarrow \text{molecular products} \tag{5}$$

$$\mathrm{R_i\cdot} + \mathrm{R_j\cdot} \longrightarrow \text{molecular products} \tag{6}$$

$$\mathrm{R_i} + \mathrm{H^+} \longrightarrow \mathrm{S\cdot} \tag{7}$$

$$\mathrm{S\cdot} + \mathrm{R_i\cdot} \longrightarrow \text{molecular products} \tag{8}$$

$$0 = \mathrm{d}[\mathrm{R_i\cdot}]/\mathrm{d}t = rk_3[\mathrm{Ti^{III}}]_t[\mathrm{H_2O_2}]_t - k_7[\mathrm{R_i\cdot}][\mathrm{H^+}] - 2k_5[\mathrm{R_i\cdot}]^2 - [\mathrm{R_i\cdot}]k_6\Sigma[\mathrm{R_j\cdot}] - [R_i]k_8[\mathrm{S\cdot}] \tag{9}$$

(9),[12] where r is the fraction of ·OH radicals which react to give $\mathrm{R_i}$, rather than any other species, and t is the time between mixing and observation. On the assumption that all radicals ($\mathrm{R_i\cdot}$, $\mathrm{R_j\cdot}$, and S·) terminate at comparable rates (*i.e.* that $2k_5 = k_6 = k_8 = k$), equation (9) can be simplified to give (10), where $[\mathrm{R\cdot}]_\mathrm{T}$ is the total radical

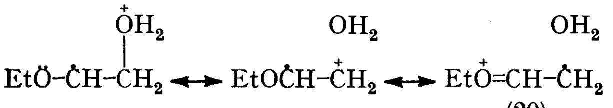
$$rk_3[\mathrm{Ti^{III}}]_t[\mathrm{H_2O_2}]_t = k_7[\mathrm{R_i\cdot}][\mathrm{H^+}] + k[\mathrm{R_i\cdot}][\mathrm{R\cdot}]_\mathrm{T} \tag{10}$$

$$[\mathrm{R_i\cdot}] = \frac{r\,k_3[\mathrm{Ti^{III}}]_t\,[\mathrm{H_2O_2}]_t}{k_7[\mathrm{H^+}] + k[\mathrm{R\cdot}]_\mathrm{T}} \tag{11}$$

concentration, and hence (11). It follows that for a series of experiments in which the concentrations of

Ti^{III} and H_2O_2 and the dead time of the mixing chamber and flow cell are unchanged, then for aliphatic radicals of similar size and charge (and hence termination rates) the total radical concentration is approximately the same. Then, the pH for 50% conversion of $R_i\cdot$ into $S\cdot$ (when $k_7[H^+] = k[R\cdot]_T$) is a direct measure of the rate constant for the acid-catalysed process. This analysis is employed below.

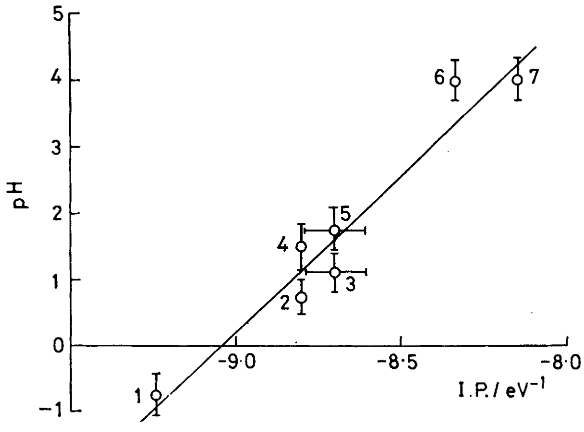
We have suggested above that the role of alkyl substituents in increasing the rate of acid-catalysed loss of hydroxide ion is to stabilize, presumably *via* a hyperconjugative mechanism, the incipient radical-cation. Similarly, we have argued[2] that the role of the $+M$ substituent in assisting the departure of the β-leaving group in the acid-catalysed rearrangement of, *e.g.* $\cdot CH(OEt)CH_2OH$, is to stabilize the developing positive charge in the transition state, *via* the contribution of structure (20). This type of interaction is presumably also that which is responsible for the stabilization of, for example, $[Et\dot{O}CH - CH_2]^{+\cdot}$ relative to the unsubstituted radical cation $[CH_2 - CH_2]^{+\cdot}$ (as judged by the ionization potentials of ethyl vinyl ether[13] and ethene,[14] 8.80 and 10.51 eV, respectively).



$$\mathrm{Et\ddot{O}{-}\dot{C}H{-}\overset{\overset{+}{O}H_2}{C}H_2} \longleftrightarrow \mathrm{EtO\dot{C}H{-}\overset{OH_2}{\overset{+}{C}}H_2} \longleftrightarrow \mathrm{Et\overset{+}{O}{=}CH{-}\overset{OH_2}{\dot{C}}H_2}$$

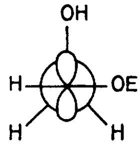
(20)

The Figure shows that, as expected on this basis, a correlation does exist between the rate of rearrangement *via* acid-catalysed loss of OH^- (as measured by the pH for 50% depletion of the initial radical) and the stability of the intermediate radical-cation (as measured by the ionization potential of the appropriate alkene); this suggests that the major factor governing the ease of formation of a radical-cation is indeed its thermodynamic stability.



Plot of pH required for 50% depletion of the observed β-hydroxy-substituted radicals against the ionization potential of the appropriate alkene: 1, $\cdot CH_2CMe_2OH$ (I.P. from ref. 14); 2, $\cdot CH_2CH(OH)OEt$ (I.P. from ref. 13, pH from ref. 2); 3, $\cdot CEt_2CHMeOH$ (I.P. estimated from data in ref. 11); 4, $\cdot CH(OEt)CH_2OH$ (I.P. from ref. 13, pH from ref. 2); 5, $\cdot CHMeCEt_2OH$ (I.P. estimated from data in ref. 11); 6, 3-hydroxytetrahydropyran-2-yl (I.P. from ref. 14, pH from ref. 2); 7, $\cdot CMe(OH)CH_2OH$ (I.P. from ref. 14, pH from ref. 15*b*)

Several further points relating to the Figure should be noted. Although the dominant influence appears to be the relative energies of the radical-cations, significant trends are also apparent in the behaviour of the different precursors of a given radical-cation. Thus, as noted previously,[2,15] $\cdot CH_2CH(OH)OEt$ undergoes loss of OH^- less readily than its isomer $\cdot CH(OEt)CH_2OH$, though both yield the same radical-cation. There are at least two likely contributing factors for this observation. First, there is evidence[15a] that a 1,1-dioxygen-substituted structure is in any case more stable than a 1,2-dioxygen-substituted structure due to interactions involving the oxygen substituents (thus, for example, ethane-1,1-diol is more stable than ethane-1,2-diol). Since such interactions are presumably lost as the reaction proceeds, the 1,1-disubstituted radical would be expected to react more slowly. Secondly, it is known that an α-alkoxy-substituent in a radical of this type induces a marked preference for a conformation in which the OH group eclipses the half-filled $p(\pi)$-orbital (21).[16] This is precisely the conformation which is expected to be achieved in the transition-state leading to the radical-cation, and a preference for it in the ground-state may well facilitate the elimination reaction.



(21)

EXPERIMENTAL

Details of the e.s.r. spectrometer, the flow system, and the procedures for measuring and calibrating spectra were as described previously.[2] Typical conditions were as follows. For reactions of $\cdot OH$, stream (i) contained 0.01 mol dm^{-3} titanium(III) [added as 12.5% (w/v) titanium(III) chloride solution (Fisons technical grade)], stream (ii) contained *ca.* 0.06 mol dm^{-3} hydrogen peroxide [added as 100-volume hydrogen peroxide (B.D.H. Ltd.)], and stream (iii) contained the substrate (0.1—1 mol dm^{-3}, depending on availability and solubility). Concentrated sulphuric acid was added usually only to the first stream to bring the final pH (on mixing) to the required value. For experiments with $Cl_2^{-\cdot}$, sodium chloride was added, usually to stream (i) alone, to give a concentration after mixing of at least 1 mol dm^{-3}. All solutions were made up in water which had been deoxygenated with a nitrogen purge, and nitrogen was bubbled through the solutions prior to mixing.

All materials were commercial samples which were used without further purification.

We thank the British Petroleum Company Ltd. for the award of a Studentship (to P. S. W.).

[1/683 *Received*, 29*th April*, 1981]

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