TILDEN LECTURE*

Applications of E.S.R. Spectroscopy to Kinetics and Mechanism in Organic Chemistry

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1 Introduction

Electron spin resonance (e.s.r.) spectroscopy is now firmly established as a technique[1] for studying both the structures of organic radicals[2] and the kinetics and mechanisms of reactions in which they take part. This review will be concerned only with applications of the technique to determining kinetics and mechanism in the liquid phase and will be confined essentially exclusively to transient radicals—*i.e.*, to those organic radicals (by far the majority) that have only a fleeting existence in solution because of the very large rate constants with which they react with each other or with other species. Details of the e.s.r. spectra and their interpretation will not be given; emphasis will be placed on the methods that are suitable for these studies and the results of interest which are derived from them. The account is not intended to be exhaustive but rather to highlight some of the major themes.

2 Methods for Radical Generation

Chemists were perhaps slow to realize the potential of e.s.r. spectroscopy for the study of free-radical reactions in solution. This doubtless stemmed from their knowledge of the transience of most radicals; with the exception of the small class of persistent radicals, almost all react bimolecularly, by dimerization and disproportionation, with rate constants of the order of 10^9 dm^3 mol^{-1}s^{-1}—close to the diffusion-controlled limit—and it was assumed that they would not reach detectable concentration. The first attempts involved generating radicals in a highly viscous medium so that their diffusion, and therefore their combination, would be very slow. For example, when a mixture of an alcohol and hydrogen peroxide is frozen to a glass which is then irradiated, the hydroxyl radical is formed by photolysis of the peroxide and abstracts a hydrogen atom from a

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[1] A rigorous account of the principles is given by A. Carrington and A. D. McLachlan, 'Introduction to Magnetic Resonance', Harper International Editions, 1967, and by N. M. Atherton, 'Electron Spin Resonance', Halsted Press, London, 1973.

[2] See *e.g.*, 'Electron Spin Resonance', Specialist Periodical Reports, The Chemical Society, London, Vols. 1—4, and H. Fischer, in 'Free Radicals', Vol. 2, ed. J. K. Kochi, Wiley-Interscience, New York, 1973.

neighbouring molecule of the alcohol; the resulting organic radicals are effectively trapped and accumulate to an observable concentration. However, this approach is limited in scope both for structural studies—since the spectrum is complicated by anisotropic effects associated with the relatively slow tumbling of the radicals—and for mechanistic studies—since reactions of interest are successfully prevented.

In retrospect, this approach was unnecessarily conservative given, on the one hand, the high sensitivity of e.s.r. (a 10^{-7} mol dm^{-3} solution of radicals gives a detectable spectrum provided that its resonances are sharp, as is usual in solution) and, on the other hand, the very large rate constants associated with many radical-forming reactions. Consider the simple reaction scheme (1) and (2), in

$$R_2 \xrightarrow{k_1} 2R\cdot \qquad (1)$$

$$2R\cdot \xrightarrow{k_2} R_2 \qquad (2)$$

which radicals are generated by homolysis of R_2 (*e.g.* thermally or photolytically) and decay by bimolecular processes. At the steady state $2k_1[R_2] = 2k_2[R\cdot]^2$. For $[R_2] = 0.1$ mol dm^{-3} and $k_2 = 10^9$ dm^3 mol^{-1} s^{-1}, $[R\cdot]$ is greater than 10^{-6} mol dm^{-3} (so that a strong spectrum can be seen) provided that $k_1 > 10^{-2}$ s^{-1}, and this value is exceeded in many radical-forming reactions. (If the radical-forming reaction is bimolecular, $X + Y \rightarrow R\cdot$, then $[R\cdot]_{s.s.} > 10^{-6}$ mol dm^{-3} provided $k > 2 \times 10^{-1}$ dm^3 mol^{-1} s^{-1} for $[X] = [Y] = 0.1$ mol dm^{-3}.)

Certainly the kinetic requirements preclude the use of a number of methods for producing radicals that are of value when more persistent species are to be studied. For example, electrochemical reduction, which is suitable for the generation of $RNO_2\cdot^-$ for e.s.r. study, is not adequate for more transient radicals. Nevertheless, three general methods have been developed and are widely applicable: radiolysis, photolysis (usually of a peroxide), and rapid redox reactions.

A. Radiolysis.—The first method to be employed was the irradiation of liquid hydrocarbons, which were contained in the cavity of the e.s.r. spectrometer, with a 2.8 MeV electron beam.[3] A wide variety of radicals can be generated in this way, including alkyl, vinyl, and allyl radicals, but complex compounds can give mixtures of radicals of which the resulting spectra are difficult to analyse.

The *in situ* radiolysis method was later adapted to aqueous solutions.[4] Radiolysis of water yields three primary radicals: the electron, e^-, $H\cdot$, and $\cdot OH$. In order to study the reactions of one of these three species with an organic solute, selective scavengers are included in the medium. Thus, the inclusion of nitrous oxide results in conversion of the electron into $\cdot OH$, acid converts

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[3] R. W. Fessenden and R. H. Schuler, *J. Chem. Phys.*, 1963, **39**, 2147.

[4] K. Eiben and R. W. Fessenden, *J. Phys. Chem.*, 1971, **75**, 1186.

it into the hydrogen atom, and t-butyl alcohol removes the hydroxyl radical (but is relatively unreactive towards the hydrogen atom):

$$e^- + N_2O + H_2O \longrightarrow \cdot OH + OH^- + N_2 \qquad (3)$$

$$e^- + H^+ \longrightarrow H\cdot \qquad (4)$$

$$\cdot OH + Bu^tOH \longrightarrow \cdot CH_2CMe_2(OH) + H_2O \qquad (5)$$

The hydrogen atom is not readily scavenged, but this is of little consequence. For example, the presence of nitrous oxide yields a mixture containing approximately 90% ·OH and 10% H·; reactions of the former can be readily distinguished from those of the latter.

The advantages of radiolysis of aqueous solutions compared with that of liquid hydrocarbons are, first, that the chemistry of a selected radical (*e.g.* e^-, H·, ·OH, or a species derived from one or other of these with a further additive) can be explored; and secondly that the effects of pH on radical reactions —which have transpired to be in many cases profound (see later)—can be studied. The chief disadvantage is that the temperature range is restricted; in particular, the kinetics of several interesting intramolecular radical reactions can only be studied by e.s.r. well below 0 °C. The requirement for water solubility is also a disadvantage, but this is of less importance since very small concentrations of organic substrates yield detectable concentrations of radicals.

B. Photolysis.—The first photolytic method involved the ultraviolet irradiation of a very dilute solution of hydrogen peroxide in an alcohol while it flowed slowly through the spectrometer cavity.[5] The hydroxyl radical is formed and reacts with the alcohol [*e.g.* reaction (7)]. The purpose of flowing the solution was to remove products which would otherwise lead to further radicals by reaction with ·OH.

$$H_2O_2 \xrightarrow{h\nu} 2\cdot OH \qquad (6)$$

$$CH_3OH + \cdot OH \longrightarrow \cdot CH_2OH + H_2O \qquad (7)$$

Later, more general methods were introduced in which di-t-butyl peroxide [reaction (8)], diacyl peroxides [reactions (9) and (10)], or peresters [reaction (11)] are irradiated in the cavity in the presence of an organic compound whose radical reactions are to be studied.[6] An organic solvent which is relatively inert to oxygen- or carbon-centred radicals is used; cyclopropane is often chosen and it has the added advantage that studies down to *ca.* – 120 °C can be carried out.

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[5] R. Livingston and H. Zeldes, *J. Chem. Phys.*, 1966, **44**, 1245.

[6] J. K. Kochi and P. J. Krusic, in 'Essays on Free-radical Chemistry', Chemical Society Special Publication No. 24, 1970, p. 147.

$$\mathrm{Me_3C{-}O{-}O{-}CMe_3} \xrightarrow{h\nu} \mathrm{2Me_3C{-}O\cdot} \tag{8}$$

$$\mathrm{RCO{-}O{-}O{-}COR} \xrightarrow{h\nu} \mathrm{2RCO_2\cdot} \tag{9}$$

$$\mathrm{RCO_2\cdot} \longrightarrow \mathrm{R\cdot + CO_2} \tag{10}$$

$$\mathrm{R^1CO{-}O{-}O{-}CR^2_3} \xrightarrow{h\nu} \mathrm{R^1\cdot + CO_2 + \cdot OCR^2_3} \tag{11}$$

The sulphate radical-anion, $SO_4\cdot^-$, can also be generated photolytically, by irradiation of an inorganic persulphate in aqueous solution:[7,8]

$$\mathrm{S_2O_8{}^{2-}} \xrightarrow{h\nu} \mathrm{2SO_4\cdot^-} \tag{12}$$

C. Redox Reactions.—Some transition-metal ions which are capable of undergoing one-electron reduction or oxidation can be used for the generation of organic radicals in one of two ways: by direct interaction with an organic compound, in some cases with photochemical activation; or, indirectly, by reaction with a third compound (often a peroxide) to give a radical which then reacts with the selected organic compound. The former method in some instances, and the latter method invariably, requires to be applied in conjunction with a continuous-flow system: the reagents are mixed shortly (typically *ca.* 50 ms) before the combined solution enters the cavity of the spectrometer; radicals are then generated continuously and can exceed the detectable limit in the cavity. The indirect method has been much the more widely used and will be described first.

The best known system is the one-electron reduction of hydrogen peroxide by titanium(III) ion, which yields the hydroxyl radical [reaction (13)].[9] The organic compound for study is included in either the titanium(III) or the peroxide stream, or, if it might react at an appreciable rate with each, in a third stream. The overall system is a complex one,[10,11] for in addition to reacting with an organic compound [*e.g.* reaction (14)], the hydroxyl radical is reduced by titanium(III) ion [reaction (15)], reacts with hydrogen peroxide [reaction (16)], and reacts with titanium(IV)–peroxide complexes to form two titanium(IV)–complexed radicals which appear as e.s.r. singlets (with weak satellite lines from the low-abundant ^{47}Ti and ^{49}Ti isotopes which can be discerned if the signal-to-noise ratio is high[12]). However, fortunately most organic compounds are of such high reactivity towards ·OH that their inclusion in moderate concentration ensures that they scavenge essentially all the ·OH radicals.

In order to be applicable to e.s.r. studies of transient radicals, redox processes

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[7] H. Zemel and R. W. Fessenden, *J. Phys. Chem.*, 1975, **79**, 1419.
[8] O. P. Chawla and R. W. Fessenden, *J. Phys. Chem.*, 1975, **79**, 2693.
[9] W. T. Dixon and R. O. C. Norman, *J. Chem. Soc.*, 1963, 3119.
[10] R. O. C. Norman, in ref. 6, p. 117.
[11] G. Czapski, *J. Phys. Chem.*, 1971, **75**, 2957.
[12] H. Fischer, *Ber. Bunsengesellschaft phys. Chem.*, 1967, **71**, 685.

$$\mathrm{Ti^{III} + H_2O_2 \longrightarrow Ti^{IV} + \cdot OH + OH^-} \quad (13)$$

$$\mathrm{\cdot OH + RH \longrightarrow H_2O + R\cdot} \quad (14)$$

$$\mathrm{\cdot OH + Ti^{III} \longrightarrow OH^- + Ti^{IV}} \quad (15)$$

$$\mathrm{\cdot OH + H_2O_2 \longrightarrow H_2O + HO_2\cdot} \quad (16)$$

$$\mathrm{2R\cdot \longrightarrow molecular\ products} \quad (17)$$

such as the Ti^{III} –H_2O_2 couple must have rate constants not only greater than a well defined minimum, but also not greater than a defined maximum, for the following reason. If the organic radical R· decays bimolecularly [reaction (17)] with a rate constant, k_t, of 10^9 dm^3 mol^{-1} s^{-1}, and if the observed concentration of R· is (as is typical) 10^{-6} mol dm^{-3}, then the half-life of R· ($= 1/2k_t[\mathrm{R}\cdot]$) is *ca.* 10^{-3} s. This is far less than the time that elapses between the mixing of the reagents and the entry of the combined solution into the spectrometer cavity (usually > 20 ms), from which it follows that essentially all radicals formed between the mixing-point and the cavity have decayed before they reach the latter; effectively, only those radicals that are generated in the cavity are observed by e.s.r.[11,13] Consider now a system described by reactions (13), (14), and (17), in which all ·OH radicals are scavenged by RH as fast as they are formed [*i.e.* reaction (13) defines the rate of formation of R·]. The steady-state approximation for R· in the cavity gives:

$$-\mathrm{d}[\mathrm{R}\cdot]/\mathrm{d}t = k_{13}[\mathrm{Ti^{III}}]_t[\mathrm{H_2O_2}]_t - 2k_t[\mathrm{R}\cdot]^2 = 0 \quad (18)$$

where subscript t refers to concentrations in the cavity, t s after mixing. If, at mixing, $[H_2O_2]_0 \gg [Ti^{III}]_0$, then $[H_2O_2]$ remains sensibly unchanged and $[Ti^{III}]$ falls exponentially, so that:

$$[\mathrm{R}\cdot]^2 = k_{13}[\mathrm{Ti^{III}}]_0[\mathrm{H_2O_2}]_0 \exp(-k_{13}[\mathrm{H_2O_2}]_0 t)/2k_t \quad (19)$$

If, for example, $[Ti^{III}]_0 = 0.01$ mol dm^{-3}, $[H_2O_2]_0 = 0.1$ mol dm^{-3}, and $t = 50$ ms, then $[\mathrm{R}\cdot] \geqslant 10^{-6}$ mol dm^{-3} for *ca.* $1 < k_{13} < 2 \times 10^3$ dm^3 mol^{-1} s^{-1}. The value of k_{13}, measured spectrophotometrically by a stopped-flow method, lies within this range; it varies slightly with conditions and is 590 dm^3 mol^{-1} s^{-1} in 0.1 M-H_2SO_4 at room temperature.[14]

The initial choice of the Ti^{III}–H_2O_2 couple for e.s.r. studies is now seen to have been a fortunate one; were k_{13} much larger, essentially all the reaction would be over by the time the reactant solution reached the cavity, whereas if it were much smaller, radicals would be generated in the cavity but would not reach a detect-

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[13] C. E. Burchill and P. W. Jones, *Canad. J. Chem.*, 1971, **49**, 4005.

[14] A. Samuni, D. Meisel, and G. Czapski, *J.C.S. Dalton*, 1972, 1273.

able level. Nevertheless, a number of redox reactions do have rate constants in the appropriate range [*e.g.* reactions (20), (21), (22),[15] (23),[16] and (24)[17]].

$$\mathrm{Fe^{II}} + \mathrm{H_2O_2} \longrightarrow \mathrm{Fe^{III}} + \cdot\mathrm{OH} + \mathrm{OH^-} \tag{20}$$

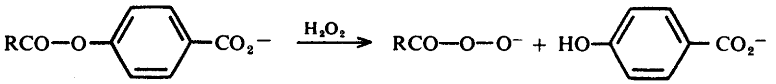
$$\mathrm{Ti^{III}} + \mathrm{Bu^tO_2H} \longrightarrow \mathrm{Ti^{IV}} + \mathrm{Bu^tO}\cdot + \mathrm{OH^-} \tag{21}$$

$$\mathrm{Ti^{III}} + \mathrm{PrO_2H} \longrightarrow \mathrm{Ti^{IV}} + \mathrm{PrO}\cdot + \mathrm{OH^-} \tag{22}$$

$$\mathrm{Ti^{III}} + \mathrm{NH_2OH} \longrightarrow \mathrm{Ti^{IV}} + \cdot\mathrm{NH_2} + \mathrm{OH^-} \tag{23}$$

$$\mathrm{Ti^{III}} + \mathrm{S_2O_8^{2-}} \longrightarrow \mathrm{Ti^{IV}} + \mathrm{SO_4}\cdot^- + \mathrm{SO_4^{2-}} \tag{24}$$

Two disadvantages attend the use of redox systems of this type: first, the organic compound whose reactions are to be studied must have at least moderate solubility in water; secondly, radicals such as ·OH are relatively unselective, and organic substrates of any complexity are likely to give mixtures of radicals and therefore spectra which can be difficult to analyse. These snags can be avoided by the use of a direct redox reaction with the strategy summarized in reactions (25) and (26): the water-soluble ester (1) is treated with hydrogen peroxide at *ca.* pH 9, at which the peroxo-acid anion is formed relatively rapidly (evidently through nucleophilic substitution by HO_2^-) but does not decompose rapidly; reaction with titanium(III) ion then gives $RCO_2\cdot$ which (unless R is unsaturated or aromatic) essentially instantaneously yields the radical R· specifically.[18]



(25)

(1)

$$\mathrm{RCO_2OH} \xrightarrow{\mathrm{Ti^{III}}} \mathrm{RCO_2}\cdot \longrightarrow \mathrm{R}\cdot + \mathrm{CO_2} \tag{26}$$

Other direct redox reactions include the oxidation of alkyl aryl ethers by cerium(IV) ion in concentrated sulphuric acid, to give aromatic radical-cations [reaction (27)],[19] the photochemically induced oxidation of compounds such as alcohols, aldehydes, and carboxylic acids by cerium(IV) ion or uranyl ion at low temperature [*e.g.* reaction (28)],[20,21] and the reduction of arenediazonium

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[15] B. C. Gilbert, R. G. G. Holmes, H. A. H. Laue, and R. O. C. Norman, *J.C.S. Perkin II*, 1976, 1047.

[16] B. C. Gilbert and P. R. Marriott, *J.C.S. Perkin II*, 1977, 987.

[17] R. O. C. Norman, P. M. Storey, and P. R. West, *J. Chem. Soc.* (*B*), 1970, 1087.

[18] B. C. Gilbert, R. G. G. Holmes, P. D. R. Marshall, and R. O. C. Norman, *J. Chem. Research*, 1977, (S) 172, (M) 1949.

[19] W. T. Dixon and D. Murphy, *J.C.S. Perkin II*, 1976, 1823.

[20] D. Greatorex and T. J. Kemp, *J.C.S. Faraday I*, 1972, **68**, 121.

[21] D. Greatorex, R. J. Hill, T. J. Kemp, and T. J. Stone, *J.C.S. Faraday I*, 1974, **70**, 216.

salts by titanium(III) ion complexed with edta in a flow system [reaction (29)].[22]

$$ArOR + Ce^{IV} \longrightarrow ArOR^{\cdot+} + Ce^{III} \qquad (27)$$

$$RCHO + Ce^{IV} \longrightarrow R\dot{C}O + Ce^{III} + H^+ \qquad (28)$$

$$ArN_2^+ + Ti^{III}(edta) \longrightarrow Ar\cdot + N_2 + Ti^{IV}(edta) \qquad (29)$$

D. Derived Radicals.—The radiolysis, photolysis, and redox methods have all been adapted to the generation of specific radicals in order to study their reactions. The following are examples.

The u.v. irradiation of a mixture of a bromo- or chloro-alkane, RX, triethylsilane, and di-t-butyl peroxide yields the radical R• by the sequence (30).[23] The generation of •OH by radiolysis[24] or redox reaction[25,26] in the presence of sulphur- or phosphorus-containing anions yields the corresponding radicals by one-electron oxidation [*e.g.* reactions (31), (32), and (33)]. The titanium(III)–H_2O_2 couple in the presence of dimethyl sulphoxide yields the methyl radical [reaction (34)].[27] Finally, the phenyl radical is formed by photochemical generation of the sulphate radical-anion in the presence of benzoate anion [reaction (35)].[7]

$$(Bu^tO)_2 \xrightarrow{h\nu} Bu^tO\cdot \xrightarrow{Et_3SiH} Et_3Si\cdot \xrightarrow{RX} Et_3SiX + R\cdot \qquad (30)$$

$$\cdot OH + HS^- \longrightarrow H_2O + S\cdot^- \qquad (31)$$

$$\cdot OH + HSO_3^- \longrightarrow H_2O + SO_3\cdot^- \qquad (32)$$

$$\cdot OH + H_2PO_2^- \longrightarrow H_2O + HPO_2\cdot^- \qquad (33)$$

$$\cdot OH + Me_2SO \longrightarrow Me\cdot + (MeSO_2H) \qquad (34)$$

$$SO_4\cdot^- + PhCO_2^- \longrightarrow SO_4^{2-} + Ph\cdot + CO_2 \qquad (35)$$

E. Spin-trapping.—Radicals which mediate in reactions may nonetheless be undetectable by e.s.r. spectroscopy for one or both of two reasons: either their concentrations do not reach the detectable level, or their e.s.r. resonances are so broad, and the amplitudes consequently so small, that they cannot be discerned. The latter applies when there is marked *g*-factor anisotropy, as for example with the hydroxyl radical.[28] In these cases it is helpful to include in the system a spin

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[22] A. L. J. Beckwith and R. O. C. Norman, *J. Chem. Soc.* (*B*), 1969, 403.

[23] A. J. Bowles, A. Hudson, and R. A. Jackson, *J. Chem Soc.* (*B*), 1971, 1947.

[24] D. Behar and R. W. Fessenden, *J. Phys. Chem.*, 1972, **76**, 1706.

[25] R. O. C. Norman and P. M. Storey, *J. Chem. Soc.* (*B*), 1971, 1009.

[26] B. C. Gilbert, J. P. Larkin, R. O. C. Norman, and P. M. Storey, *J.C.S. Perkin II*, 1972, 1508.

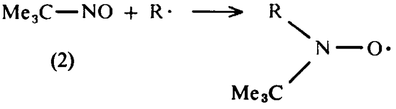
[27] B. C. Gilbert, R. O. C. Norman, and R. C. Sealy, *J.C.S. Perkin II*, 1975, 303.

[28] M. C. R. Symons, *J. Amer. Chem. Soc.*, 1969, **91**, 5924.

trap, *i.e.* a species which reacts with the undetectable radical to give a new radical which is e.s.r.-detectable.

The main criteria which should be met for a good spin trap are that it should react rapidly with a range of radicals of different types, that the resulting radicals should be relatively stable so that they reach detectable concentration, and that the e.s.r. parameters of the new radicals should be such that the original radical can be identified.

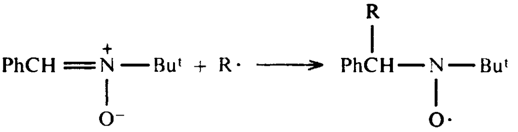
For non-aqueous studies, by far the most widely employed approach is to make use of the relative stability of the nitroxide function, $>N{-}O\cdot$, and the associated reactivity of compounds which react with radicals to form this function. These are of two types, *C*-nitroso-compounds such as (2)[29] and nitrones such as (4).[30] Aromatic nitroso-compounds such as nitrosodurene[31] are also suitable.



(2)

(3)

(36)



$$PhCH{=}\overset{+}{N}(O^-){-}Bu^t + R\cdot \longrightarrow PhCH(R){-}N(O\cdot){-}Bu^t$$

(4) (5)

(37)

Nitroso-compounds have the advantage over nitrones that one is more likely to be able to identify the radical R·: the nitrogen hyperfine splitting in the resulting nitroxide (3) is sensitive to the nature of the atom (*e.g.* C or O) through which R· attaches to nitrogen, and hyperfine splittings can usually be detected from protons attached to the atom which bonds to nitrogen, so that $RCH_2\cdot$, $R_2CH\cdot$, and $R_3C\cdot$ can be distinguished. In the adducts (5), on the other hand, R is further away from the radical centre and the e.s.r. parameters are much less sensitive to its nature.

It is notable that metal-centred radicals can also be trapped. For example, when an alkylpentacarbonyl manganese $RMn(CO)_5$ is irradiated in the presence of nitrosodurene both R· and $\cdot Mn(CO)_5$ are trapped.[32]

For studies in aqueous basic solution, both the fumarate ion[33] and the *aci*-

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[29] M. J. Perkins, in ref. 6, p. 97.

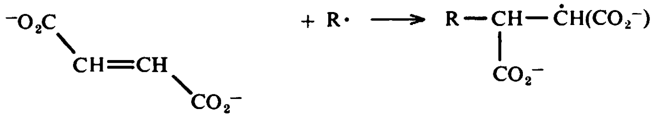
[30] E. G. Janzen, *Accounts Chem. Res.*, 1971, **4**, 31.

[31] S. Terabe, K. Kuruma, and R. Konaka, *J.C.S. Perkin II*, 1973, 1252.

[32] A. Hudson, M. F. Lappert, P. W. Lednor, and B. K. Nicholson, *J.C.S. Chem. Comm.*, 1974, 966.

[33] P. Neta, *J. Phys. Chem.*, 1971, **75**, 2570.

anion from nitromethane[34,35] are suitable as traps. The success of the former stems from the fact that the adducts (6), though carbon-centred radicals, decay bimolecularly much less rapidly than uncharged or singly charged species, presumably owing to charge repulsion. In the latter case, nitro radical-anions are formed which, compared with most carbon-centred radicals, are relatively long-lived. The nitromethane *aci*-anion has the advantage that the hyperfine splittings of its adducts (7) are sensitive to the nature of the radical centre in R· and to the presence of protons on this atom.

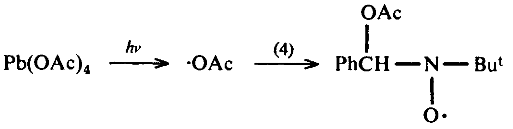


$$ {}^{-}O_2C\text{—}CH{=}CH\text{—}CO_2^{-} + R\cdot \longrightarrow R\text{—}\underset{CO_2^{-}}{CH}\text{—}\dot{C}H(CO_2^{-}) \qquad (38)$$

(6)

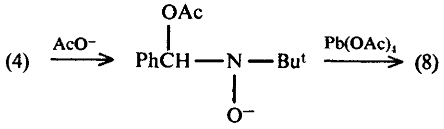
$$CH_2{=}NO_2^{-} + R\cdot \longrightarrow \underset{(7)}{RCH_2NO_2\cdot^{-}} \qquad (39)$$

An inherent danger in the use of a spin trap is that it may play a part in the reaction sequence other than trapping the suspected radical, and it is important to guard against this. For example, irradiation of lead tetra-acetate in the presence of the nitrone (4) gave a radical identified as (8), from which reaction (40) was inferred. However, it was shown later that (8) is formed by the heterolytic addition of acetate to the nitrone followed by one-electron oxidation of the adduct by Pb^{IV}; there was no evidence for the presence of the acetoxyl radical.[36]



$$Pb(OAc)_4 \xrightarrow{h\nu} \cdot OAc \xrightarrow{(4)} Ph\overset{OAc}{CH}\text{—}\underset{O\cdot}{N}\text{—}Bu^{t} \qquad (40)$$

(8)



$$(4) \xrightarrow{AcO^{-}} Ph\overset{OAc}{CH}\text{—}\underset{O^{-}}{N}\text{—}Bu^{t} \xrightarrow{Pb(OAc)_4} (8) \qquad (41)$$

3 Kinetics of Radical Reactions

E.s.r. spectroscopy can be applied to the determination of reaction rate constants in each of two ways: by measurement of the concentration of radicals as a function of time (or, as we shall show, of an equivalent parameter), and from the linewidths of the e.s.r. resonances.

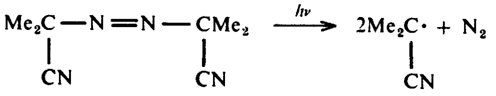
[34] B. C. Gilbert, J. P. Larkin, and R. O. C. Norman, *J.C.S. Perkin II*, 1972, 1272.
[35] D. Behar and R. W. Fessenden, *J. Phys. Chem.*, 1972, **76**, 1710.
[36] A. R. Forrester and S. P. Hepburn, *J. Chem. Soc. (C)*, 1971, 701.

The latter method, which depends on the relationship between the lifetime of a radical (or of a particular state of a radical such as a conformation) and the linewidths of its resonances, is not generally applicable; it can be applied only when the rate lies within a relatively narrow range. The former method is of more general use; rate constants close to the diffusion-controlled limit have been measured.

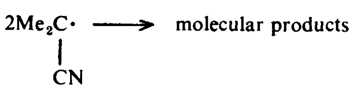
The commonest alternative to e.s.r. for determining the kinetics of radical reactions in solution combines pulse radiolysis for the generation of radicals with u.v. or visible spectrophotometry for their estimation. This method, which pre-dates the e.s.r. one, has the disadvantage that optical spectroscopy provides much less detailed evidence about the structure of the radical which is being monitored than does the e.s.r. spectrum. On the other hand, it can sometimes be applied when the e.s.r. method is unsuitable, for reasons that will be discussed subsequently.

A. Radical Concentration as a Function of Time.—(i) *Bimolecular Radical Termination.* The rotating sector technique, with photochemical generation of radicals, has become the standard method for determining the rate constants for the destruction of radicals which can occur when they collide with each other (*e.g.* dimerization or disproportionation; in general, 'bimolecular termination').

The first case studied is illustrative. Weiner and Hammond irradiated a solution of azobisisobutyronitrile in benzene at room temperature through a rotating sector which provided equal light and dark periods of *ca.* 2 × 10^{-3} s. During the light periods, a steady-state concentration of 2-cyanopropyl radicals was established [reactions (42) and (43)] and decay curves for these radicals were accumulated during the dark periods by a computer which was triggered off by the rotating sector.[37] The rate constant so derived for reaction (43) was $(2.2 \pm 1.0) \times 10^9$ dm^3 mol^{-1} s^{-1}.



$$\underset{\displaystyle\mathrm{CN}}{\mathrm{Me_2C}}-\mathrm{N}=\mathrm{N}-\underset{\displaystyle\mathrm{CN}}{\mathrm{CMe_2}} \xrightarrow{h\nu} 2\underset{\displaystyle\mathrm{CN}}{\mathrm{Me_2C\cdot}} + \mathrm{N_2} \tag{42}$$



$$2\underset{\displaystyle\mathrm{CN}}{\mathrm{Me_2C\cdot}} \longrightarrow \text{molecular products} \tag{43}$$

More generally, the radicals R· whose decay is to be studied are generated by photolysis of a peroxide in the presence of the parent compound RH; the oxy-radical from the peroxide abstracts a hydrogen atom to yield R·. The results in the Table were obtained by use of di-t-butyl peroxide.[38] It was noted that log k_t is correlated surprisingly well with the molecular weight of the

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[37] S. Weiner and G. S. Hammond, *J. Amer. Chem. Soc.*, 1968, **90**, 1659.

[38] G. B. Watts and K. U. Ingold, *J. Amer. Chem. Soc.*, 1972, **94**, 491.

Table *Some values of* $2k_t$ *from the rotating sector method*

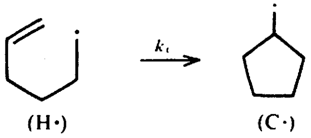
R·	$10^{-9} \times 2k_t$/dm^3 mol^{-1} s^{-1}	T/°C
$\cdot CH_3$	11 ± 1.0	-18
$\cdot CMe_3$	8.1 ± 0.3	25
$\cdot SiMe_3$	5.5 ± 0.2	25
$\cdot GeMe_3$	3.6 ± 0.2	-65
$\cdot SnMe_3$	2.8 ± 0.3	-65

radical, suggesting that, as the molecular weight increases, the radius for diffusion increases whereas that for reaction is almost unchanged.

The *in situ* radiolysis procedure has also been adapted for the equivalent of the rotating sector experiment: liquid ethane was irradiated with 2.8 MeV electrons from a Van de Graaff generator which was equipped with electronically controlled pulsing circuits.[39] The rate constant obtained for decay of the ethyl radical was $(1.7 \pm 0.4) \times 10^8$ dm^3 mol^{-1} s^{-1} at -177 °C, with an activation energy of 0.83 kcal mol^{-1} and a pre-exponential factor of 1.3×10^{10} s^{-1}.

(ii) *Intermolecular Radical Reactions.* In the determination of reaction rates, there is an alternative to monitoring the concentration of radicals as a function of time, namely to measure their concentration as a function of another variable whose time-dependence is already known or can be measured independently.

This approach has been especially fruitful in determining the rates of some intramolecular radical reactions; the following example is illustrative.[40] The unsaturated radical (H·) was generated from tris(hex-5-enyl)phosphine with Bu^{t}O· (from photolysis of the peroxide) in isopentane, and it proved possible to observe the e.s.r. spectra of both it and the radical to which it cyclizes (C·), in the range 188—228 K [reaction (44)].



(44)

At the steady state, $d[(C\cdot)]/dt = k_c[(H\cdot)] - 2k_t[(C\cdot)]^2 - 2k'_t[(H\cdot)][(C\cdot)] = 0$, where k_t and k'_t are the bimolecular rate constants for (C·) + (C·) and (H·) + (C·), respectively. Since both (H·) and (C·) are primary radicals of the same molecular weight, it may be assumed that $k_t = k'_t$, from which it follows that

$$k_c/2k_t = \{[(C\cdot)]^2/[(H\cdot)]\} + [(C\cdot)] \qquad (45)$$

The ratio $k_c/2k_t$ was determined by measuring [(H·)] and [(C·)], and $2k_t$ was determined by generating (C·) in the same solvent from tris(cyclopentylmethyl)-

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[39] R. W. Fessenden, *J. Phys. Chem.*, 1964, **68**, 1508.

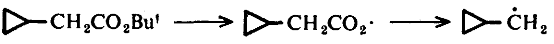
[40] D. Lal, D. Griller, S. Husband, and K. U. Ingold, *J. Amer. Chem. Soc.*, 1974, **96**, 6355.

borane with $\mathrm{Bu^tO\cdot}$. This yielded k_c at several temperatures in the range 188—228 K and the Arrhenius parameters

$$\log(k_c/\mathrm{s}^{-1}) = (10.7 \pm 1.0) - (7.8 \pm 1.0)/2.3\,RT \qquad (46)$$

Extrapolation gives $k_c = 1 \times 10^5\ \mathrm{s}^{-1}$ at 25 °C.

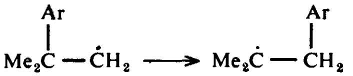
Similar methods have been used to determine the rates of ring-opening of the cyclopropylmethyl radical (9) in the range 128—153 K [k (extrapolated) = $1.3 \times 10^8\ \mathrm{s}^{-1}$ at 25 °C],[41] of the aryl-shift in reaction (49) (*e.g.* $k = 59\ \mathrm{s}^{-1}$ at 25 °C for Ar = phenyl),[42] and of the intramolecular hydrogen-atom transfer in reaction (50).[43]



(9)

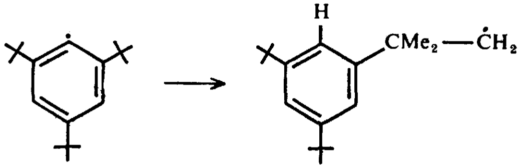
(47)

(48)



$$\mathrm{Me_2}\overset{\mathrm{Ar}}{\underset{}{\mathrm{C}}}-\dot{\mathrm{C}}\mathrm{H_2} \longrightarrow \mathrm{Me_2}\dot{\mathrm{C}}-\overset{\mathrm{Ar}}{\mathrm{C}\mathrm{H_2}}$$

(49)



(50)

Reaction (50) is of especial note. Kinetic data were obtained over a wide temperature range both in this case and for the perdeuterio-t-butyl analogue, and the results provide most convincing evidence for the occurrence of quantum-mechanical tunnelling in the hydrogen-atom transfer: in particular, the Arrhenius plots show the expected marked curvature, and the kinetic isotope effect is far higher than is theoretically possible for a classical hydrogen shift (*e.g.* $k_\mathrm{H}/k_\mathrm{D}$ = 13 000 at −150 °C, compared with a calculated maximum of 260).[43]

(iii) *Intermolecular Radical Reaction.* The combination of a redox reaction with a flow system has been used to determine the rate constants of a variety of radical reactions. Consider the system described by reactions (51)—(53) in which $[\mathrm{XO_2H}] \gg [\mathrm{Ti^{III}}]$ and $\mathrm{XO\cdot}$ reacts with RH as fast as it is formed, so that reaction (51) determines the rate of formation of $\mathrm{R\cdot}$. The quasi-steady-state in the

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[41] B. Maillard, D. Forrest, and K. U. Ingold, *J. Amer. Chem. Soc.*, 1976, **98**, 7024.

[42] B. Maillard and K. U. Ingold, *J. Amer. Chem. Soc.*, 1976, **98**, 1224.

[43] G. Brunton, D. Griller, L. R. C. Barclay, and K. U. Ingold, *J. Amer. Chem. Soc.*, 1976, **98**, 6803.

$$\mathrm{Ti^{III}} + \mathrm{XO_2H} \longrightarrow \mathrm{Ti^{IV}} + \mathrm{XO}\cdot + \mathrm{OH^-} \qquad (51)$$

$$\mathrm{XO}\cdot + \mathrm{RH} \longrightarrow \mathrm{XOH} + \mathrm{R}\cdot \qquad (52)$$

$$2\mathrm{R}\cdot \xrightarrow{k_t} \text{molecular products} \qquad (53)$$

e.s.r. cavity is given (see earlier) by

$$[\mathrm{R}\cdot]^2 = k_{51}[\mathrm{Ti^{III}}]_0[\mathrm{XO_2H}]_0 \exp(-k_{51}[\mathrm{XO_2H}]_0 t)/2k_t \qquad (54)$$

Equation (54) has been found to hold (*i.e.* $[\mathrm{R}\cdot] \propto [\mathrm{Ti^{III}}]_0^{\frac{1}{2}}$) in a number of cases (*e.g.*[44] for X = H, R· = ·CH_2COMe, pH 1).

It follows, first, that, if k_t is known, k_{51} can be determined; a simple method is to find the value of $[\mathrm{XO_2H}]_0$ for which [R·] is maximal, for differentiation of equation (54) shows that this occurs when $[\mathrm{XO_2H}]_0 = 1/k_{51}t$. For example, application of this method gives $k_{51} = 280\ \mathrm{dm^3\ mol^{-1}\ s^{-1}}$ for X = Pr at pH 1 and room temperature.[15]

Secondly, deviations from linearity of the plot of [R·] against $[\mathrm{Ti^{III}}]_0^{\frac{1}{2}}$ are indicative of there being a significant contribution to radical termination from processes other than the bimolecular one. Analysis of the plot can yield kinetic information. In one example,[44] the $\mathrm{Ti^{III}}$–H_2O_2 couple has been used to generate the radical ·CH_2COMe from acetone; in acid solution (pH 1), R· is related linearly to $[\mathrm{Ti^{III}}]_0^{\frac{1}{2}}$ as we have seen, whereas at pH 7 in the presence of edta the plot shows curvature (convex upwards) consistent with the occurrence of reaction (55), the rate constant for which was evaluated as $1.4 \times 10^7\ \mathrm{dm^3\ mol^{-1}\ s^{-1}}$. It is evident that the $\mathrm{Ti^{III}}$–edta complexes present at pH 7 are more effective reducing agents than aqueous $\mathrm{Ti^{III}}$.

$$\cdot\mathrm{CH_2COMe} + \mathrm{Ti^{III}\,edta} \longrightarrow {}^-\mathrm{CH_2COMe} + \mathrm{Ti^{IV}\,edta} \qquad (55)$$

Under the same conditions (pH 7), ·CHMeCOEt (from diethyl ketone with ·OH) gave a linear plot with $[\mathrm{Ti^{III}}]_0^{\frac{1}{2}}$—*i.e.* its reduction does not contribute significantly to its decay—whereas the radical ·CH_2CHO could not be detected, implying that it is reduced so rapidly that an observable concentration is not achieved. These results not only show an order for the ease of reduction (·CH_2-CHO > ·CH_2COMe > ·CHMeCOEt) consistent with the electron-releasing (and therefore deactivating) effect of a methyl substituent, but also reveal one of the limitations of the e.s.r. method for kinetic measurements of this kind: if the reaction which competes with bimolecular termination is not fast enough, it does not compete effectively enough to be detected, whereas if it is too fast the radical concentration is too small to be estimated.

In a second example, the one-electron oxidation of organic radicals by hydrogen peroxide was studied. The procedure was to generate simultanously two radicals, R· and R′·, by use of the $\mathrm{Ti^{III}}$–H_2O_2 couple, of which R′· was known not to terminate to a significant extent by oxidation, compared with the bi-

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[44] B. C. Gilbert, R. O. C. Norman, and R. C. Sealy, *J.C.S. Perkin II*, 1973, 2174.

molecular pathway. It can be shown that, under these conditions, $[\text{R}'\cdot]/[\text{R}\cdot]$ should vary linearly with $[\text{Ti}^{\text{III}}]_0^{-\frac{1}{2}}$ with a gradient related to the rate constant for reaction (56). The rate constants so derived show in particular that a hydroxy- or alkoxy-substituent attached to tervalent carbon strongly activates the radical to one-electron loss, and that alkyl groups have a smaller activating effect (*e.g.* k_{56} for $\cdot\text{CH}_2\text{OH}$, $\cdot\text{CMe}_2\text{OH}$, and $\cdot\text{CH(OMe)}_2$ = 2.3×10^4, 5×10^5, and 1.1×10^6 dm^3 mol^{-1} s^{-1}, respectively, at room temperature).[45]

$$\text{R}\cdot + \text{H}_2\text{O}_2 \longrightarrow (\text{R}^+\text{OH}^-) + \cdot\text{OH} \tag{56}$$

The occurrence of these one-electron transfer processes, with large rate constants in some instances, serves to warn investigators to test for the possibility of their significance before drawing conclusions from e.s.r. observations. For example, when ethanol is oxidized with the Fe^{II}–H_2O_2 couple, the predominant radical is $\cdot\text{CH}_2\text{CH}_2\text{OH}$, whereas with the Ti^{III}–H_2O_2 system it is $\cdot\text{CHMe(OH)}$. This has been taken as indicating that the hydroxyl radical is not 'free' in the former case, but in fact it is almost certainly the result of the more rapid oxidation of $\cdot\text{CHMe(OH)}$ than of $\cdot\text{CH}_2\text{CH}_2\text{OH}$ by Fe^{III}; in contrast, Ti^{IV} is a weak oxidant. On the other hand, when kinetic analysis reveals that such one-electron and other processes are insignificant compared with bimolecular decay, then competitive experiments can be used to determine relative reactivities; if a compound yields radicals R· and R′·, with rate constants k and k', then, providing that it can reasonably be assumed that the three bimolecular termination constants are the same, $[\text{R}\cdot]/[\text{R}'\cdot] = k/k'$.

The Ti^{III}–H_2O_2 couple has also been used in determining the rates of abstraction reactions by carbon-centred radicals. Examples include both hydrogen-atom abstraction (by $\cdot\text{CH}_3$[46] and by Ph·[47]) and iodine-atom abstraction (by *e.g.* $\cdot\text{CH}_2\text{OH}$[48]), and the effect on the rates of changes in the structure of the substrate reveal the nucleophilic character of $\cdot\text{CH}_2\text{OH}$, $\cdot\text{CH}_3$, and, to a lesser extent, Ph·. Typical results (for room temperature) are given in reactions (57) and (58).

$$\text{CH}_3\text{CH}_2\text{CO}_2\text{Me} \xrightarrow[2.9\,\times\,10^3\ \text{dm}^3\ \text{mol}^{-1}\ \text{s}^{-1}]{\cdot\text{CH}_3} \text{CH}_3\dot{\text{C}}\text{HCO}_2\text{Me} \tag{57}$$

$$\text{ICH}_2\text{CO}_2\text{H} \xrightarrow[2.1\,\times\,10^8\ \text{dm}^3\ \text{mol}^{-1}\ \text{s}^{-1}]{\cdot\text{CH}_2\text{OH}} \cdot\text{CH}_2\text{CO}_2\text{H} \tag{58}$$

Photochemical radical generation has also been used in determining the kinetics of intermolecular radical reactions. A particularly elegant method was used in determining the rates of addition of a primary alkyl radical [the radical

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[45] B. C. Gilbert, R. O. C. Norman, and R. C. Sealy, *J.C.S. Perkin II*, 1974, 824.

[46] B. C. Gilbert, R. O. C. Norman, G. Placucci, and R. C. Sealy, *J.C.S. Perkin II*, 1975, 885.

[47] B. Ashworth, B. C. Gilbert, and R. O. C. Norman, *J. Chem. Research*, 1977, (S) 94, (M) 1101.

[48] B. C. Gilbert, R. O. C. Norman, and R. C. Sealy, *J.C.S. Perkin II*, 1974, 1435.

(H·); see reaction (44)] to a series of spin traps.[49]. Both (H·) and the radical to which it cyclizes, (C·), added to the trap (T), and by labelling (H·) with ^{13}C at the radical centre it was possible to distinguish between the adducts (HT·) and (CT·) by their spectra (since ^{13}C in the former, but not in the latter, is close enough to the unpaired electron in the adduct to yield a splitting). The relative concentrations of (HT·) and (CT·), together with the known rate for the cyclization of (H·) to (C·), enabled the rate constant for (H·) + (T) → (HT·) to be determined. Some results (at 40 °C) were: $Me_3C{-}NO$, 90×10^5; $PhCH{=}\overset{+}{N}(O^-)Bu^t$, 1.3×10^5; nitrosodurene, 394×10^5 dm^3 mol^{-1} s^{-1}.

The photochemical decomposition of di-t-butyl peroxide in the presence of organoboranes and organophosphorus compounds has been used to measure rate constants for reactions such as (59) (*e.g.* 3×10^7 dm^3 mol^{-1} s^{-1} at 30 °C for R = Bu)[50] and (60) (*e.g.* 1.6×10^8 dm^3 mol^{-1} s^{-1} at 30 °C for R = Et).[51]

$$Bu^tO\cdot + BR_3 \longrightarrow Bu^tOBR_2 + R\cdot \qquad (59)$$

$$Bu^tO\cdot + P(OR)_3 \longrightarrow Bu^t\cdot + OP(OR)_3 \qquad (60)$$

Finally, the *in situ* radiolysis method has been used to generate hydrogen atoms for studying their rates of reaction with both aliphatic[52] and aromatic[53] compounds. The rate constants are large (*e.g.* MeOH, 1.6×10^6; PhOMe, 1.2×10^9 dm^3 mol^{-1} s^{-1}) and their variation with structure reveals the electrophilicity of the hydrogen atom.

B. Linewidths.—The linewidths of e.s.r. resonances depend on the lifetimes of the corresponding spin-states. This is a result of the Uncertainty Principle, through which energy and time are correlated (($\delta E . \delta t \sim h/2\pi$); the shorter the lifetime, the larger is the uncertainty in the energy of the spin-state and the broader is the resonance. For radicals in fluid solution, the linewidth is usually fairly narrow (*ca.* 0.01 mT); it is determined largely by spin–lattice relaxation (energy exchange between the spin system and surrounding molecules)—a phenomenon which serves to maintain the Boltzmann distribution between the upper- and lower-energy spin-states and which therefore allows continuous e.s.r. absorption to be observed. However, if a radical takes part in a process which further shortens its lifetime, the resonances can be broadened to a greater extent; in return, the extra broadening can give information about radical lifetime and can therefore provide kinetic data.

For example, naphthalene reacts with sodium in an inert solvent to form the naphthalene radical-anion, $NpH^{\cdot -}$. In the absence of an excess of naphthalene, the e.s.r. spectrum consists of 25 sharp lines (a quintet of quintets, from the four 'α'-type protons and the four 'β'-type protons). As more naphthalene is added,

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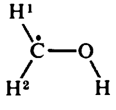
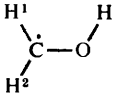
[49] P. Schmid and K. U. Ingold, *J. Amer. Chem. Soc.*, 1978, **100**, 2493.
[50] A. G. Davies, D. Griller, and B. P. Roberts, *J. Chem. Soc.* (*B*), 1971, 1823.
[51] A. G. Davies, D. Griller, and B. P. Roberts, *J.C.S. Perkin II*, 1972, 993.
[52] P. Neta, R. W. Fessenden, and R. H. Schuler, *J. Phys. Chem.*, 1971, **75**, 1654.
[53] P. Neta and R. H. Schuler, *J. Amer. Chem Soc.*, 1972, **94**, 1056.

the radical-anion and naphthalene undergo electron exchange at an increasing rate ($\text{NpH}^{\cdot -} + \text{NpH} \rightarrow \text{NpH} + \text{NpH}^{\cdot -}$), the average lifetime of each $\text{NpH}^{\cdot -}$ decreases, and the lines broaden. Further addition of naphthalene causes the broadened lines to coalesce and eventually the single absorption narrows to a sharp line. The rate constant for the exchange can be obtained from the line-broadened spectra; its value lies in the range 10^7—10^9 dm^3 mol^{-1} s^{-1}, depending on solvent and temperature.[54]

Intramolecular processes such as configurational and conformational changes can also be examined in this way, and attention will be focused on these. Here, a further aspect—the *alternating* linewidth effect—applies. It is best introduced by an example. At −125 °C the spectrum of the radical $\cdot CH_2OH$ shows two doublet splittings for the C—H protons; that is, they interact to different extents with the unpaired electron. This is consistent with the occurrence of the radical in the coplanar conformations (10) and (11) in which H^1 and H^2 are inequivalent with respect to the spin and which interconvert slowly relative to the 'e.s.r. time-scale' (see later). As the temperature is raised the two inner lines of the four broaden, they then coalesce to a single broad line, and eventually (*ca.* −60 °C) this sharpens to give overall a 1:2:1 triplet.[55] The reason for the broadening only of the inner lines is as follows. The outer lines correspond to radicals in which both H^1 and H^2 have either the same spin (α), the associated magnetic moments of which augment the applied field so that resonance occurs at a low value of the field, or the same spin (β), with the opposite effect, so that resonance is at high field; when interconversion occurs, the unpaired electron remains in the same magnetic environment. In contrast, the inner lines correspond to radicals in which H^1 and H^2 have opposite spins, so that their magnetic effects are in opposition; since these effects are different, interconversion alters the total magnetic environment of the odd electron. It transpires that, when interconversion occurs with a frequency which is of the same order as the hyperfine splitting interval between H^1 and H^2, the inner lines are broadened. On the other hand, when interconversion is much slower the unpaired electron in effect 'feels' the individual protons so that two sharp inner lines are recorded, and when it is much faster the electron 'feels' the average magnetic effect of the two possible situations so that one sharp central line is recorded. In this case, the hyperfine splitting interval between H^1 and H^2 is 0.088 mT (equivalent to 1.6×10^6 Hz), and the rate constant for (10) $\rightleftharpoons$ (11) has been obtained at various temperatures by lineshape analysis, to give[55] the activation energy as 19 kJ mol^{-1}.



(10)



(11)

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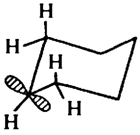
[54] R. L. Ward and S. I. Weissman, *J. Amer. Chem. Soc.*, 1957, **79**, 2086.

[55] A. Hudson, *J. Chem. Soc.* (*A*), 1969, 2513; P. J. Krusic, P. Meakin, and J. P. Jesson, *J. Phys. Chem.*, 1971, **75**, 3438.

Corresponding effects have been observed for a number of other acyclic radicals.[56] An interesting example is the radical (12) which shows alternating linewidths for both sets of methylene protons; it has been concluded that rotation is restricted about both the $\cdot CH_2$—O and the O—CH_3 bonds, with barriers of *ca.* 17 and 19 kJ mol^{-1}, respectively.[57]

$\cdot CH_2OCH_2OCH_3$

(12)



(13)

Amongst cyclic radicals, the interconversion of cyclohexyl (13) and the alternative chair-like conformation is illustrative.[58] The axial protons shown interact with the unpaired electrons more strongly than the equatorial protons (the splitting constant is approximately proportional to $\cos^2\theta$ where θ is the dihedral angle made by the C—H bond and the half-filled orbital). At − 80 °C, these four protons couple as two non-equivalent pairs, showing that interconversion occurs much more slowly than the hyperfine splitting interval (*ca.* 10^8 Hz). As the temperature is raised, the appropriate resonances broaden, and kinetic analysis has given the activation energy as *ca.* 20 kJ mol^{-1} (*cf.* 46 kJ mol^{-1} for cyclohexane, from n.m.r. data).

The absence of line-broadening can also be of value. For example, it is absent in the spectrum of the radical (14), showing that internal electron exchange to give (15) is slow relative to the hyperfine splitting interval for the two sets of methylene protons (*ca.* 30 MHz).[59]

$O_2NCH_2CH_2NO_2\cdot^-$ (14)

$\cdot^-O_2NCH_2CH_2NO_2$ (15)

4 Elucidation of Mechanism

The e.s.r. method is an especially valuable one for elucidating the mechanisms of free-radical reactions; its sensitivity allows radicals to be detected which, because of their rapid reactions, reach only very low concentrations, and their hyperfine splittings and *g*-factors can provide unambiguous evidence of their structures. However, its high sensitivity can also be a source of ambiguity, which must be guarded against. That is, e.s.r. evidence that a particular radical is present during a reaction does not necessarily mean that it lies in the main reaction pathway; it could represent a comparatively unimportant pathway, with the main one involving other (undetectable) radicals or even being of ionic type. Other techniques must therefore be used to complement the e.s.r. information. For

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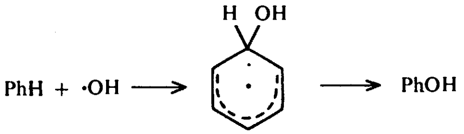
[56] J. K Kochi, *Adv. Free-Radical Chem.*, 1975, **5**, 189.

[57] C. Gaze and B. C. Gilbert, *J.C.S. Perkin II*, 1977, 116.

[58] S. Ogawa and R. W. Fessenden, *J. Chem. Phys.*, 1964, **41**, 994.

[59] D. J. Edge, R. O. C. Norman, and P. M. Storey, *J. Chem. Soc.* (*B*), 1970, 1096.

example, when benzene reacts with the hydroxyl radical, the spectrum of the radical (16) is observed,[60] suggesting that this mediates in the formation of the product, phenol, as in reaction (61). Nevertheless, alternative possibilities, such as mediation of the phenyl radical, cannot be ruled out. However, in this case, other methods (*e.g.* variation of products with conditions, and kinetic studies) have provided support for reaction (61).[61]



(16) (61)

On the other hand, there is less ambiguity in employing e.s.r. to trace the conversion of one radical into another radical, and the majority of the following examples are concerned with this.

Applications of e.s.r. to the study of the most frequently encountered types of radical reaction—abstraction of hydrogen from C—H bonds, addition to C=C bonds (including polymerization), and homolytic aromatic substitution—have been reviewed,[10] and attention is focused here principally on two less commonly met classes of reaction, chosen because e.s.r. has been particularly fruitful in characterizing them.

A. Electron- and Atom-transfer.—The reactions of different types of oxygen-centred radicals have been found to differ significantly. First, the t-butoxyl radical differs from hydroxyl in the relative ease with which the two add to C=C as compared with abstracting a hydrogen atom from C—H. For example, ·OH adds to propylene (at each end of the double bond) whereas $Bu^tO\cdot$ abstracts $H\cdot$ to form the allyl radical,[62] and in general the abstraction/addition ratio is much higher for $Bu^tO\cdot$ than for ·OH.[63] Secondly, the properties of a radical can differ appreciably from those of its conjugate acid or base. For example, $Bu^tOH^{\cdot +}$ (from photolysis of di-t-butyl peroxide in trifluoroacetic acid) is more prone to add to C=C than is $Bu^tO\cdot$,[64] and whereas ·OH preferentially adds to the olefinic bond in allylic alcohols, $O^{\cdot -}$ preferentially abstracts a hydrogen atom;[65] pulse-radiolysis studies have shown that $O^{\cdot -}$ abstracts $H\cdot$ from saturated alcohols and acids at about half the rate for ·OH, whereas the rate at which it adds to C=C is relatively low.[66]

[60] W. T. Dixon and R. O. C. Norman, *J. Chem. Soc.*, 1964, 4857.

[61] J. R. Lindsay Smith and R. O. C. Norman, *J. Chem. Soc.*, 1963, 2897.

[62] H. J. Hefter, T. A. Hecht, and G. S. Hammond, *J. Amer. Chem. Soc.*, 1972, **94**, 2793.

[63] I. H. Elson, S. W. Mao, and J. K. Kochi, *J. Amer. Chem. Soc.*, 1975, **97**, 335.

[64] P. G. Cookson, A. G. Davies, B. P. Roberts, and M.-W. Tse, *J.C.S. Chem. Comm.*, 1976, 937.

[65] M. Simic, P. Neta, and E. Hayon, *J. Phys. Chem.*, 1973, **77**, 2662.

[66] P. Neta and R. H. Schuler, *J. Phys. Chem.*, 1975, **79**, 1.

Thirdly, an even more marked contrast is displayed between ·OH and $SO_4^{\cdot-}$. In general, the latter frequently removes an electron from an organic molecule whereas the former adds to C=C or abstracts from C—H. The following are examples.

(i) Carboxylate ions from saturated acids react with $SO_4\cdot$ to give alkyl radicals; electron abstraction followed by decarboxylation [*e.g.* reaction (62)] has been inferred.[17] On the other hand ·OH reacts mainly at C—H [*e.g.* reaction (63)].

$$\mathrm{CH_3CO_2^-} \xrightarrow{SO_4^{\cdot-}} \mathrm{CH_3CO_2\cdot} \longrightarrow \mathrm{\cdot CH_3 + CO_2} \qquad (62)$$

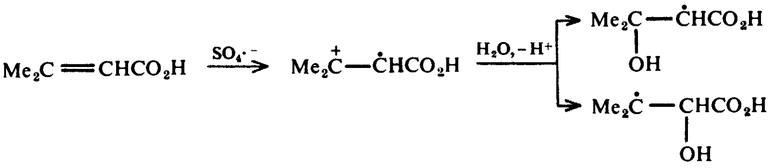
$$\mathrm{CH_3CO_2^-} \xrightarrow{\cdot OH} \mathrm{\cdot CH_2CO_2^-} \qquad (63)$$

(ii) The *aci*-anion from nitromethane reacts with $SO_4^{\cdot-}$ to yield the dimeric species (14), evidently *via* electron transfer followed by the trapping of $\cdot CH_2NO_2$.[59] In contrast, ·OH reacts principally by addition.

$$\mathrm{CH_2{=}NO_2^-} \xrightarrow{SO_4^{\cdot-}} \mathrm{\cdot CH_2NO_2} \xrightarrow{CH_2=NO_2^-} \underset{(14)}{\mathrm{O_2NCH_2CH_2NO_2^{\cdot-}}} \qquad (64)$$

$$\mathrm{CH_2{=}NO_2^-} \xrightarrow{\cdot OH} \mathrm{HOCH_2NO_2^{\cdot-}} \qquad (65)$$

(iii) Olefinic compounds which would be expected to yield relatively stable radical-cations (*e.g.* with spin or charge associated with tertiary carbon) react with $SO_4^{\cdot-}$ in water to yield hydroxy-adducts; reactions such as (66) have been inferred.[17] However, $SO_4^{\cdot-}$ adds directly to other olefins.



$$\mathrm{Me_2C{=}CHCO_2H} \xrightarrow{SO_4^{\cdot-}} \mathrm{Me_2\overset{+}{C}{-}\dot{C}HCO_2H} \xrightarrow{H_2O,\,-H^+} \begin{cases} \mathrm{Me_2\underset{OH}{C}{-}\dot{C}HCO_2H} \\ \mathrm{Me_2\dot{C}{-}\underset{OH}{C}HCO_2H} \end{cases} \qquad (66)$$

(iv) Anisole and dimethoxybenzenes yield detectable radical-cations with $SO_4^{\cdot-}$ in water.[67] Benzene does not, but gives the adduct (16); mediation of $PhH^{\cdot+}$ is implied.[8,17] Evidently species such as (17) from anisole, in which the charge is stabilized by the +M effect of oxygen, are less readily attacked by water than is $PhH^{\cdot+}$.

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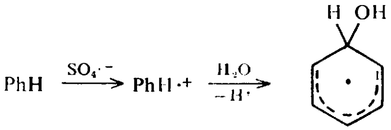
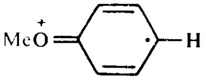
[67] P. O'Neill, S. Steenken, and D. Schulte-Frohlinde, *J. Phys. Chem.*, 1975, **79**, 2773.



(67)

(16)

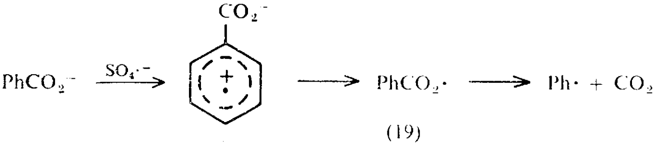


(17)

Pulse-radiolysis studies (with optical detection) have shown that the formation of aromatic radical-cations in this way occurs very rapidly; *e.g.* the first step in reaction (67) has[68] $k = 3 \times 10^9$ dm^3 mol^{-1} s^{-1}. Moreover, the Hammett ρ-value for reactions of a series of substituted benzenes with $SO_4{\cdot}^-$, -2.4, is consistent with a rate-determining electron-transfer.[68]

Reactions of this type can also have synthetic utility. For example, phenol is formed in 64% yield from benzene with $SO_4{\cdot}^-$ in water containing Cu^{II};[69] it is inferred that reaction (67) is followed by the one-electron oxidation of (16) to phenol by Cu^{II}.

Aromatic carboxylates yield aryl radicals with $SO_4{\cdot}^-$,[7] and this poses the problem of whether the radical-zwitterion such as (18), formed first, is subsequently converted into the aroyloxyl radical (19) (and thence the aryl radical) or whether structures (18) and (19) are canonical forms of the same species, so that in effect the aroyloxyl radical is formed directly. The e.s.r. evidence points to (18) and (19) being different species.[70] It has been derived by comparing the behaviour of the carboxylate–$SO_4{\cdot}^-$ system with that of the corresponding peroxo-acid with Ti^{III}, which yields the aroyloxyl radical directly [*cf.* reaction (26)], and the study has also revealed other reactions of aromatic radical-zwitterions; for example, (20) partitions between rearrangement to the aroyloxyl radical (21) and formation of the benzylic radical (22).[70]



(68)

(18)

(19)

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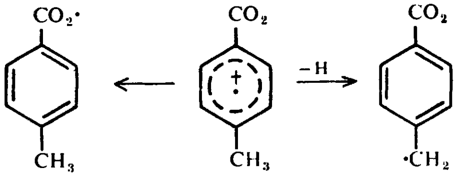
[68] P. Neta, V. Madhavan, H. Zemel, and R. W. Fessenden, *J. Amer. Chem. Soc.*, 1977, **99**, 163.

[69] C. Walling and D. M. Camaioni, *J. Amer. Chem. Soc.*, 1975, **97**, 1603.

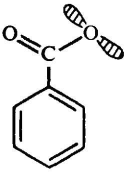
[70] B. Ashworth, B. C. Gilbert, R. G. G. Holmes, and R. O. C. Norman, *J.C.S. Perkin II*, 1978, 951.



(21) (20) (22)

(69)

That (18) and (19) are different species might not have been expected. It suggests that aroyloxyl radicals are of σ-type, with the unpaired electron in an orbital perpendicular to the plane of the carboxylate group as in (23), and not in conjugation with the π-system. This would still allow delocalization of an electron *pair* on the univalent oxygen into the carbonyl π-system.



(23)

Aromatic carboxylates which contain methoxy substituents yield detectable radical-zwitterions with $SO_4{}^{\cdot -}$,[71] no doubt because the methoxy-groups stabilize them by delocalizing positive charge [*cf.* (17)].

Certain high-valence metal ions, too, oxidize aromatic compounds by one-electron transfer. For example, Tl^{II} and Ag^{II}, formed as in reactions (70)[72] and (71),[67] yield detectable radical-cations with methoxybenzenes.[67] Other studies have shown that Ag^{II} oxidizes alcohols to give alkoxyl radicals, presumably *via* radical-cations [reaction (72)]; in this case, this is in contrast to the behaviour of $SO_4{}^{\cdot -}$ which (like $\cdot OH$) reacts by abstraction of $H\cdot$ from C—H.[73]

$$Tl^{I} + \cdot OH \longrightarrow Tl^{II} + OH^- \qquad (70)$$

$$Ag^{I} + \cdot OH \longrightarrow Ag^{II} + OH^- \qquad (71)$$

$$ROH + Ag^{II} \longrightarrow Ag^{I} + \overset{+\cdot}{R\text{O}H} \longrightarrow RO\cdot + H^+ \qquad (72)$$

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[71] S. Steenken, P. O'Neill, and D. Schulte-Frohlinde, *J. Phys. Chem.*, 1977, **81**, 26.

[72] P. O'Neill, S. Steenken, and D. Schulte-Frohlinde, *Angew. Chem. Internat. Edn.*, 1975, **14**, 430.

[73] T. Caronna, A. Citterio, L. Grossi, F. Minisci, and K. Ogawa, *Tetrahedron*, 1976, **32**, 2741; H. Elbenberger, S. Steenken, P. O'Neill, and D. Schulte-Frohlinde, *J. Phys. Chem.*, 1978, **82**, 749.

B. Heterolytic Reactions of Radicals.—The rapidity of one-electron oxidations of hydroxy- or alkoxy-conjugated radicals by hydrogen peroxide has already been mentioned. Organic compounds, too, can be effective oxidants; for example, the radical $\cdot CMe_2(OH)$ is rapidly oxidized by bromoacetic acid which as a result forms the radical $\cdot CH_2CO_2H$ [reaction (73)].[74]

$$BrCH_2CO_2H + \cdot CMe_2(OH) \longrightarrow \cdot CH_2CO_2H\ (+HBr + Me_2CO) \qquad (73)$$

When the reducing function (*e.g.* hydroxy-conjugated tervalent carbon) and the oxidizing function (*e.g.* a C—halogen bond) are built into the same compound in a 1,2-relationship, rapid reactions can occur which, overall, constitute heterolytic reactions of the organic radical. The process can be illustrated generally by reaction (74), but it should be recognized that the representation of a one-electron transfer is an oversimplification; the spin is delocalized on to oxygen in (24) and spin and charge are delocalized in (25). Some examples will be considered in more detail.

$$R\ddot{O}{-}\dot{C}H{-}CH_2{-}X \longrightarrow R\overset{+}{O}{=}CH{-}\dot{C}H_2 \qquad (74)$$

(24) (25)

When 2-chloroethanol is oxidized by ·OH in aqueous solution at *ca.* pH 4, the radicals detected are (26), (29), and (30), but not (27). Since alcohols react readily with ·OH at the hydroxy-substituted carbon, it is inferred that (27) is formed and that it reacts rapidly to give the radical-cation (28) as in reaction (76); hydration of (28) then yields (29) and (30).[75] At lower pH (*ca.* 2), radical (26) is again observed, but radicals (29) and (30) are replaced by (31) and one derived from it. From this and other observations it has been inferred that, as the pH is lowered, the rate at which (29) and (30) revert to the radical-cation (28) increases [*e.g.* reaction (77)], loss of a proton then yielding (31).[75]

Other good leaving groups can replace Cl in reactions such as (76); an example is $P(O)(OH)_2$.[76] However, OH is not of itself a good enough leaving group; thus, the oxidation of ethylene glycol with ·OH at pH 4 gives only radical (30). However, acid catalyses the departure of hydroxide, for the radical (31) is observed in a more acidic medium [reaction (77)].[75]

Reactions such as (74) can be initiated by addition of ·OH to C C as well as by abstraction of hydrogen from C—H, and this is important in the chemistry of enols and enol ethers.[77] For example, methyl vinyl ether forms both the adducts (32) and (33) with ·OH at *ca.* pH 2.5, the former in preponderance, but

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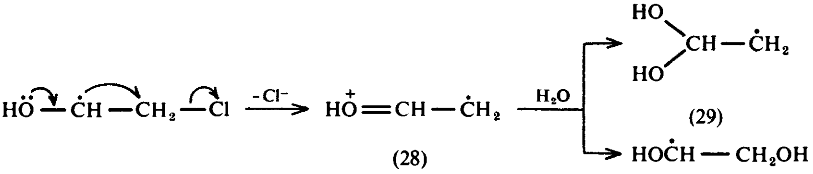
[74] A. L. J. Beckwith and R. O. C. Norman, *J. Chem. Soc. (B)*, 1969, 400.

[75] B. C. Gilbert, J. P. Larkin, and R. O. C. Norman, *J.C.S. Perkin II*, 1972, 794.

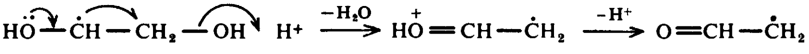
[76] A. Samuni and P. Neta, *J. Phys. Chem.*, 1973, **77**, 2425.

[77] D. J. Edge, B. C. Gilbert, R. O. C. Norman, and P. R. West, *J. Chem. Soc. (B)*, 1971, 189.

$$\mathrm{HOCH_2CH_2Cl} \xrightarrow{\cdot\mathrm{OH}} \underset{(26)}{\mathrm{HOCH_2\dot{C}HCl}} + \underset{(27)}{\mathrm{HO\dot{C}HCH_2Cl}} \qquad (75)$$

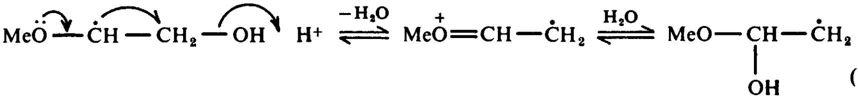


(28) (29) (30) (76)



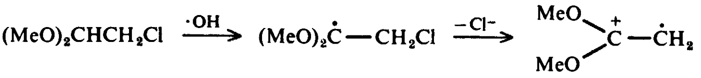
(31) (77)

at pH 1 the latter predominates. Evidence has been obtained that (32) is formed the faster by addition but that (33) is thermodynamically the more stable; (33) is formed increasingly rapidly from (32) as [H$^+$] is increased, through reaction (78). The basis for the greater stability of (33) has been discussed.[77]



(32) (34) (33) (78)

Mediation of radical-cations such as (34) has usually been inferred in these experiments; it is assumed that their hydration is so rapid that they do not reach detectable concentration. However, in one case such a radical-cation has been observed directly, namely (35) formed as in reaction (79).[78] The hydration of this species may occur relatively slowly because it is stabilized by the +M effects of two OMe groups.



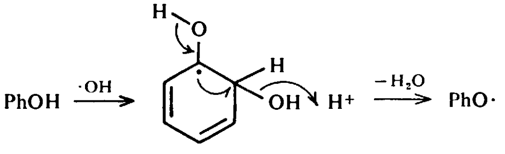
(79)

(35)

Reactions analogous to those of enols and enol ethers occur with aromatic compounds. For example, although at first sight one would have expected that the reaction of phenol with ·OH to give PhO· would occur by hydrogen-atom

[78] G. Behrens, E. Bothe, J. Eibenberger, G. Koltzenburg, and D. Schulte-Frohlinde, *Angew. Chem. Internat. Edn.*, 1978, **17**, 604.

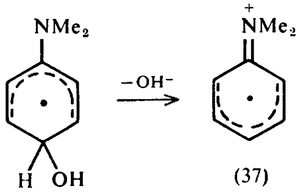
abstraction, e.s.r. observations show that it occurs by addition to give the radical (36) and its isomers, followed by acid-catalysed dehydration as in reaction (80).[79] Other phenols behave similarly.[80]



(80)

(36)

Pulse-radiolysis studies have shown that the acid-catalysed removal of hydroxide ion from hydroxycyclohexadienyl radicals can be very fast; for example, for those from methylated benzenes,[81] k is *ca.* 10^9 dm^3 mol^{-1} s^{-1}. The adducts from dimethylaniline even release hydroxide ion itself rapidly ($k = 7 \times 10^6$ s^{-1}),[82] presumably because the +M effect of NMe_2 significantly stabilizes the resulting radical-cation (37).



(81)

(37)

The related sequence (82) has been established for phenylacetic acid.[83] The adduct (38) and its isomers are observed above *ca.* pH 2, whereas the benzyl radical is formed in more acidic conditions. The radical-cation (39) cannot be detected, and it was originally thought that (38) and its isomers give benzyl directly in a concerted reaction.[83] However, the mediation of (39) has now been inferred from independent kinetic evidence.[84] The sulphate radical-anion also effects the conversion of phenylacetic acid into the benzyl radical.[17] In this case, adducts corresponding to (38) have not been detected in the pH range 1—9; either they are formed but eliminate SO_4^{2-} too fast to reach detectable level, or direct electron-transfer occurs. The balance of evidence favours the latter.[68]

Hydrocinnamic acid behaves similarly: adducts such as (40) are observed in weakly acidic media but yield the phenethyl radical in a more acidic one.[83] One possible mechanism is shown in reaction (83) but this can be ruled out on the

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[79] C. R. E. Jefcoate and R. O. C. Norman, *J. Chem. Soc.* (*B*), 1968, 48.

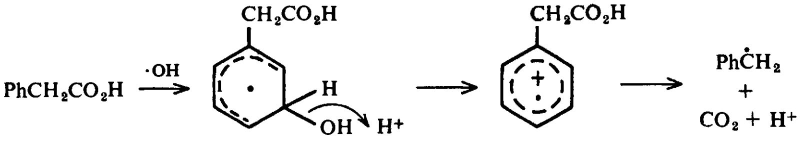
[80] P. Neta and R. W. Fessenden, *J. Phys. Chem.*, 1974, **78**, 523.

[81] K. Sehested, J. Holcman, and E. J. Hart, *J. Phys. Chem.*, 1977, **81**, 1363.

[82] J. Holcman and K. Sehested, *J. Phys. Chem.*, 1977, **81**, 1963.

[83] R. O. C. Norman and R. J. Pritchett, *J. Chem. Soc.* (*B*), 1967, 926.

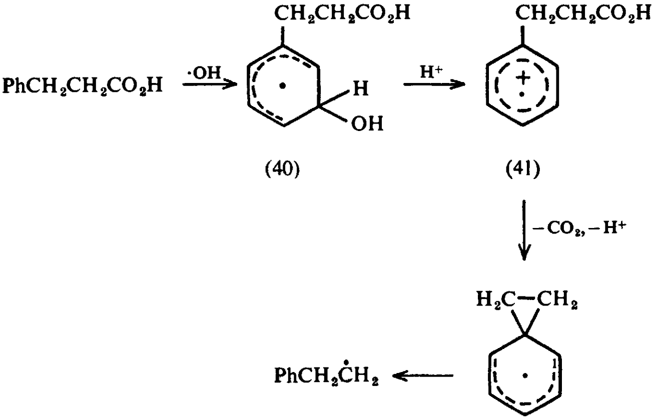
[84] C. Walling and R. A. Johnson, *J. Amer. Chem. Soc.*, 1975, **97**, 363.



(38) (39)

(82)

basis that the isomeric acids PhCH$_2$CHMeCO$_2$H and PhCHMeCH$_2$CO$_2$H would then yield the same intermediate spiran radical and so would form the same benzylic radical or mixture of radicals; in practice, they form PhCH$_2$ ·CHMe and PhCHMeCH$_2$·, respectively. It appears, therefore, that radical-cations such as (41) undergo an intramolecular electron-transfer from side-chain to ring 'across space'.



(40) (41)

(83)

C. Radical Rearrangement.—The occurrence of several radical rearrangements has been revealed by the e.s.r. method.

1,5-Shifts of hydrogen from carbon to oxygen of the type generalized by reaction (84) have been known for some time; they form the basis, for example, of the Barton reaction. E.s.r. studies of the reactions of alkynes have shown that they occur also with vinyl radicals; in the example given in reaction (85), the hydrogen-shift is followed by fragmentation.[85]

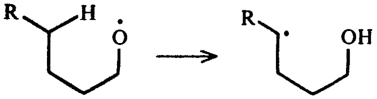
Shifts in the reverse direction—from oxygen to carbon—can occur when the resulting oxy-radical is stabilized. In reaction (86)[86] the rearrangement step yields an enolic radical and in reaction (87)[85] it yields an allylic radical.

In aqueous solution, primary and secondary alkoxyl radicals have been found to undergo a 1,2-hydrogen shift [reaction (88)].[15,87] It is not yet known whether

[85] W. T. Dixon, J. Foxall, G. H. Williams, D. J. Edge, B. C. Gilbert, H. Kazarians-Moghaddam, and R. O. C. Norman, *J.C.S. Perkin II*, 1977, 827.

[86] H. Itzel and H. Fischer, *Tetrahedron Letters*, 1975, 563.

[87] B. C. Gilbert, R. G. G. Holmes, and R. O. C. Norman, *J. Chem Research*, 1977 (S) 1, (M) 0101.



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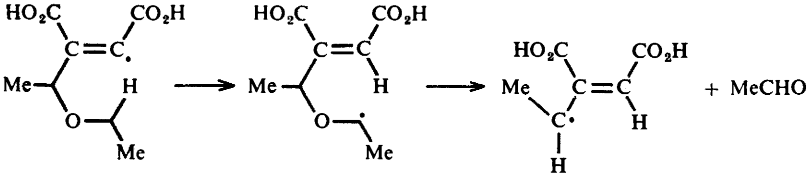

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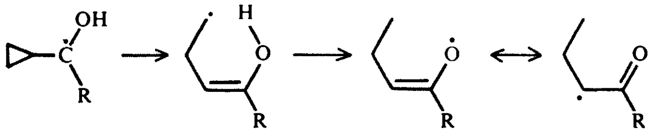

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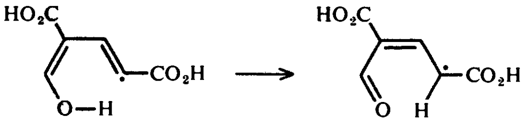

(87)

this is an intra- or an inter-molecular rearrangement; the latter seems more probable. However, it is known that the shifts occur very rapidly; for example, the rate constant for the 1,2-shift for the propoxyl radical at room temperature has been estimated[15] as *ca.* 10^7 s^{-1}, and for the butoxyl radical the 1,2- and 1,5-shifts [reaction (84); R = H] occur at approximately equal rates.[15] Alkylamino-radicals also undergo ready 1,2-shifts in aqueous solution [reaction (89)].[88]

$$R^1R^2CH{-}\dot{O} \longrightarrow R^1R^2\dot{C}{-}OH \qquad (88)$$

$$R^1R^2CH{-}\dot{N}H \longrightarrow R^1R^2\dot{C}{-}NH_2 \qquad (89)$$

The occurrence of reaction (88) has helped to account for reactions of radicals derived from oxirans.[89] For example, reaction of propylene oxide with the hydroxyl radical gives the 1-hydroxyallyl radical (42); the mechanism shown in reaction (90) is inferred.

Finally, during the reaction of t-butyl acetate with •OH the spectra of both radicals (43) and (44) are observed. The latter is evidently formed by rearrangement of the former, and the question arises whether the acetoxy-shift occurs by way of the cyclic radical (45). E.s.r. studies have shown that it does not, for

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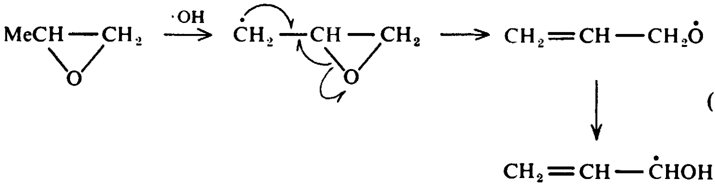
[88] N. H. Anderson and R. O. C. Norman, *J. Chem. Soc.* (*B*), 1971, 993.

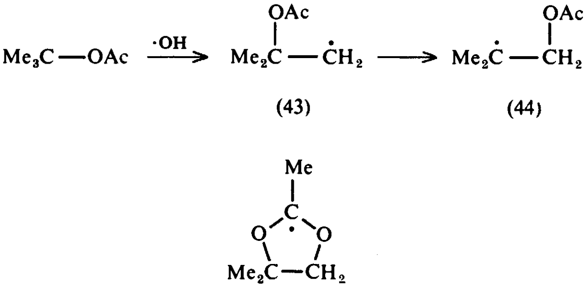
[89] A. J. Dobbs, B. C. Gilbert, H. A. H. Laue, and R. O. C. Norman, *J.C.S. Perkin II*, 1976, 1044.



(42)

(90)

under the same conditions radical (45), when generated from the parent dioxolan, gives neither (43) nor (44).[90]



$$\mathrm{Me_3C{-}OAc} \xrightarrow{\cdot\mathrm{OH}} \mathrm{Me_2C(OAc){-}\dot{C}H_2} \longrightarrow \mathrm{Me_2\dot{C}{-}CH_2OAc}$$

(43) (44)

(45)

(91)

I wish to express my gratitude to my colleague, Dr. Bruce C. Gilbert, both for his contribution to much of the work described here and for helping with the preparation of this Review.

[90] A. L. J. Beckwith and P. K. Tindal. *Austral. J. Chem.*, 1971. **24**, 2099.