Why can Transient Free Radicals be observed in Solution using ESR Techniques?

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1 Introduction

Initial studies of the ESR spectra of free radicals were in the solid state, in which the radicals were isolated by the matrix and unable to annihilate each other by reaction. This limited the range of radicals which could be studied and inhibited studies of their essential characteristic, their reactivity. In consequence, methods were devised by which reactive free radicals could be studied directly. These have involved photolysis of samples with continuous wave light, preparation of radicals in rapid flow systems, electrolysis, and, more recently, flash photolysis and pulse radiolysis. It is the object of this paper to examine the processes for radical production, and to see why these particular experimental methods have arisen. It is hoped that this may provide insight to improving technique, and extending the range of the radicals which may be observed routinely. No systematic consideration of this problem seems to have been made previously.

2 How Free Radicals are Created

Whether primary or secondary free radicals are observed in experiments, they result from a seminal event in which a pair of doublet entities is produced. In normal chemistry and photochemistry this is a pair of radicals, whereas in radiation chemistry one member may be an electron. The primary process in the former cases is the breaking of a chemical bond. This has not received the attention it deserves from chemists, particularly ESR scientists, who have by-and-large simply accepted that the bond does break, under the correct conditions, without enquiring into the consequences and implications. It has been known for 70 years that to form a chemical bond requires the two electrons which comprise it to have antiparallel spins, but only comparatively recently was the question asked as to what happens to the spin orientations when the bond is broken, and the electrons find themselves on different radicals. It was first asked in the abstract in radiation chemistry[1] but then became a prerequisite to the understanding of the magnetic resonance phenomena Chemically Induced Dynamic Nuclear Polarization (CIDNP),[2,3] and Chemically Induced Dynamic Electron Polarization (CIDEP).[4] In fact, electron spin orientation is normally conserved on chemical reaction, and the radicals are formed in a pair which, at the time of its creation, possesses the same electron spin multiplicity as did its molecular precursor. This, together with the existence of rigid spin selection rules for chemical reaction (normally the radical pair must be in the singlet state, with antiparallel electron spins on the radicals for reaction to occur), forms the entire basis of the new research field, 'spin chemistry'. It underlies why magnetic fields affect radical reactions[5] and why the techniques of Stimulated Nuclear Polarization (SNP),[6] Optically Detected Magnetic Resonance (ODMR),[7] and Reaction Yield Detected Magnetic Resonance (RYDMR)[8] exist. The effects may have wide technical application in industrial processes[9] involving free radicals, and may be the source of environmental field effects on man.[10]

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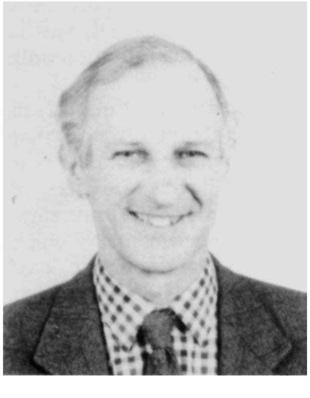

The implications to ESR observations of transient radicals seem not to have been appreciated save for the causation of electron spin polarization in reactive systems. In normal chemistry, most free radicals result from bond-breaking in the ground (normally singlet state) molecule and this produces a pair of free radicals with antiparallel electron spins, as shown for the molecule R_1R_2 below:

$$R_1{\uparrow}{\downarrow}R_2 \rightarrow R_1{\uparrow} + R_2{\downarrow}$$

Since two radicals which may recombine with small activation energies appear to be formed side-by-side with their electron spins correctly aligned for reaction, it might be expected that they would immediately back-react to re-form the reactant, and no radicals would be observed in experiments performed on a timescale greater than the reaction lifetime (*i.e.* all experiments). Luckily, however, the energy of the reaction causes some spatial separation of the radicals and not all vanish immediately, but even so some 90% of the radicals re-combine in the first few hundred pico-seconds after they have been created, as a result of re-encounters during short-term diffusion. This has been demonstrated by direct observation using pico-second flash photolysis with optical detection techniques,[11] and predicted theoretically.[12] It is only those radicals which survive this very rapid, geminate, period of the reaction which later became the free radicals in the system and are observed, and it is a sobering thought that this represents only a small fraction of those originally produced. The object of the ESR scientist is to maximize this fraction.

Why then, do not all the radicals recombine in this very early period of reaction? To some extent this is because not all diffusion paths lead to re-encounters in the geminate phase of the reaction. More importantly, however, a mechanism exists for making a proportion of those encounters that do occur unproductive in leading to reaction. This happens by the radicals becoming unable to react by virtue of their spin state having changed in the brief period after they were formed, the radical pair having converted into a triplet configuration by the time the encounter occurs. It is precisely those radicals which fail to react at re-encounter as a result of then being triplet-correlated which exhibit radical pair mechanism CIDEP in experiments. This phenomenon provides direct evidence for the detailed history of the radicals being described. The essential feature needed for the highest possible concentration of radicals to survive the initial geminate period and be observed as free radicals in an experiment is consequently singlet–triplet interconversion in the pair. Since the re-encounter probability of two radicals formed together diminishes rapidly in time afterwards, the faster the singlet–triplet mixing, the greater the concentration of radicals which escape initial recombination.

The overall process following dissociation of the precursor molecule may be represented

$$^{1}\mathrm{M} \rightarrow \{^{1}\{\mathrm{R}_1^{\bullet} + \mathrm{R}_2^{\bullet}\} \rightarrow {}^{3}\{\mathrm{R}_1^{\bullet} + \mathrm{R}_2^{\bullet}\}\} \rightarrow \mathrm{R}_1^{*\bullet} + \mathrm{R}_2^{*\bullet}$$

where M is the precursor molecule, and the asterisk denotes that the radicals are electron spin polarized, and exhibit CIDEP in their ESR spectrum. The outer brackets enclose what is now known as the 'spin correlated radical pair', a species which exists throughout the geminate period of the reaction. It is a true, if unusual, reaction intermediate which occurs in all radical combination reactions.

Singlet–triplet interconversion can be caused in several different coherent and incoherent (spin relaxation) ways. In the coherent sense, it happens as a result of the spin state of the radical pair developing under the action of the spin Hamiltonian ($\mathscr{H}_{\mathrm{M}}$) which, for the majority of the lifetime of the pair is time-independent. That is, it can be written in the form familiar to ESR scientists in terms of interactions at the two radicals considered separately, with simply the Zeeman interactions and their hyperfine coupling terms included. This is equivalent to saying that the coupled spin state of the radical pair evolves in time with the two electrons independent of each other. This is normally a good approximation since the electron exchange interaction between the electrons in the pair falls off rapidly with distance, and therefore time, as the radicals separate, and it is assumed that any anisotropic interactions are rotationally averaged to zero. For a radical pair created in a pure spin state (and it is always formed either in the singlet or one or more of the triplet states), the wavefunction at a later time, t, can be written.[13]

$$|\psi(t)\rangle = c_S(t)|S\rangle + \sum_i c_{T_i}(t)|T_i\rangle$$

where $|S\rangle$ and $|T_i\rangle$ are the pure singlet and triplet functions and $c(t)$ is a time-dependent coefficient, whose product with its complex conjugate yields the fractional contribution of the state to the overall wave function at a given time. There are three independent triplet functions which in the high-field limit are the Zeeman states T_0 and $T_{\pm 1}$. Here we have chosen to write the wavefunction of the radical pair in the coupled representation, rather than to talk of the spins of the individual electrons, because it is the spin multiplicity of the pair considered together which determines the reaction probability. The wavefunction is obtained by solution of the time-dependent Schrodinger equation,

$$\mathscr{H}_{\mathrm{M}}|\psi(t) = i\hbar[\frac{\mathrm{d}}{\mathrm{d}t}|\psi(t)\rangle$$

The three different triplet states may mix with the singlet one if the radicals are produced in low, or zero, magnetic fields. This implies that the singlet has three accessible non-reactive triplet states. If, on the other hand, they are created inside the magnetic field of an ESR spectrometer, the Zeeman interaction lifts the degeneracies of the magnetic $T_{\pm 1}$ states sufficiently to prevent their mixing with the others, and only the S and T_0 states are left to evolve in time. Now the singlet can turn into only one triplet state, and the reaction probability has increased. In this situation, solution of the equation gives

$$c_S(t) = c_S(0)\cos Qt - ic_{T_0}(0)\sin Qt$$

and

$$c_{T_0}(t) = c_{T_0}(0)\cos Qt - ic_S(0)\sin Qt$$

where,

$$Q = \langle S|\mathscr{H}_{\mathrm{M}}|T_0\rangle$$
$$= \tfrac{1}{2}\{(g_1 - g_2)\mu_B B + \sum_n a_{1n}m_{1n}^{(\mathrm{a})} + \sum_m a_{2m}m_{2m}^{(\mathrm{b})}\}$$

Here the symbols have their usual significance, with, for example, $m_{1n}^{(a)}$ representing the magnetic quantum number of the n^{th} nucleus in radical 1, which exists in the overall nuclear spin state (a).

In carbon-centred radicals, with similar g-values, in the 0.33 T field of an X-band spectrometer, the dominant interaction is almost always the hyperfine coupling and even in a pair of chemically identical radicals, the overall nuclear hyperfine state of the two radicals usually differs. With couplings typical of these radicals, complete state interconversion takes 1—10 nanoseconds, and so it is those re-encounters which occur at about this time that are ineffective in leading to reaction. A more strict description would say that immediately after the radical pair is formed in the pure singlet state, the states start to mix, and the probability of reaction at a subsequent re-encounter depends upon the singlet character of the radical pair at that time. Nevertheless, the implication is that the process is not very efficient for producing observable free radicals, since most re-encounters occur before the triplet character is appreciable, 10 nanoseconds being a long time on the timescale of molecular diffusion. This has unfortunate implications for the observation of free radicals produced in thermal reactions and, in particular, due to the low concentrations which might anyway be expected, in enzyme reactions.

This theory now may be extended to obtain an expression for the overall reaction probability inside the geminate period of the reaction. We again use the model in which the exchange interaction can be neglected, and in which the spin and molecular dynamics (diffusion) are assumed to occur on different timescales, so that the effects of the two are separable. In this case, the total reaction probability of geminately created radicals is given by[13]

$$P_{\mathrm{R}} = \lambda\int_0^{\infty} P_{\mathrm{S}}(t)P_{\mathrm{E}}(t)\mathrm{d}t$$

where λ is the probability that two radicals which encounter in the singlet state actually react, $P_{\mathrm{S}}(t)$ is the probability that the system is in the singlet state at the time of the re-encounter, and $P_{\mathrm{E}}(t)\mathrm{d}t$ is the probability of a re-encounter in the time-interval $\mathrm{d}t$ at that time. The probability of free radicals escaping reaction, and being observable in the ESR experiment, is simply $(1 - P_{\mathrm{R}})$. This formulation is useful, for it reminds us very directly that diffusion is another factor in the whole process, and that it can be adjusted empirically in experiment either to enhance reaction probability in the geminate period, or to decrease it so as to optimize the number of free radicals in the system. This can be accomplished in several ways, such as change in solution viscosity and encapsulation of the radicals inside micelles. The description is, however, an approximate one, for in most cases spin evolution and molecular diffusion occur simultaneously. This situation can be analysed using the stochastic Liouville equation which is, however, capable of analytical solution only in some simple cases.[14]

The coherent processes drive the spin mixing continuously in time under the influence of a constant interaction, provided that the hyperfine states are not changed during the geminate pair lifetime as a result, for example, of fast degenerate electron hopping processes. These have been observed to affect spin state evolution in CIDEP[15] and RYDMR experiments[16] which therefore provide the means to study them on the timescale of the geminate pair lifetime. A similar result has been reported from fast energy transfer processes in a study of the RYDMR and magnetic field effect (MFE) behaviour of electronically excited radicals.[17] These are specific examples of relaxation processes which, by contrast with the coherent ones, cause random changes in the local fields, leading to spin flips and a stochastic generation of spin mixing It happens, however, that for small carbon-centred radicals in solutions of normal viscosity at room temperature, and with no such very fast reactions occurring, the relaxation times are typically of the order of 1—2 μs, so that the coherent process is faster, and dominates Relaxation effects on spin mixing are, however, well known in MFE experiments conducted in viscous or micellar solutions where the geminate lifetime is extended sufficiently long for them to be observed [5] If the electron is centred on an atom different from carbon, relaxation may be sufficiently fast to compete successfully with the hyperfine-driven spin mixing We shall return to the beneficial effects of relaxation in some instances below

Many of the methods that ESR spectroscopists use to produce radicals do not involve observation of the primary radicals in the system, but rather secondary ones produced from their reaction Nevertheless, the concentrations of the radicals which are observed are determined by the primary processes that have been discussed above But if a sufficient concentration of primaries is obtained, the production of secondary radicals is not a spin selective reaction, but typically proceeds through H-abstraction, addition *etc* The same principles of spin selectivity and conservation no longer apply (although the secondaries are formed with the electron spin state of their progenitor[18]), and so it is the detailed understanding of the primary processes which are the basis for optimizing radical production, even when it is secondary radicals that are of interest

The methods used in the laboratory are the results of empirical experiments, it has simply been found how to produce sufficiently high concentrations of radicals for observation We now turn to the understanding of these methods using the principles outlined above

3 The Methods for Radical Production used in ESR

3.1 Photochemistry

Whether using flash-photolysis in time-resolved experiments, or continuous wave methods to produce radicals for spectroscopic study, the majority of experiments have involved classical photochemical processes A typical reaction involves the absorption of radiation by a singlet ground state molecule leading, by an electronic transition with spin conservation, to an excited singlet state Here the radiative lifetime is short, and the excitation energy would be lost if the molecule did not undergo rapid intersystem crossing into a triplet state, whose phosphorescence is spin-forbidden The molecule therefore persists for a comparatively long time in this state, and it is the one which is normally the source of the ensuing photochemistry Its common fate is to react with a suitable substrate to form a pair of radicals In contrast to the situation discussed above in which the ground state molecule dissociated to form radicals, the radical pair is now formed, with electron spin conservation, in a triplet-correlated state For example,

$$^1Me_2CO \rightarrow {}^1Me_2CO^* \rightarrow {}^3Me_2CO^*$$

followed by

$$^3Me_2CO + Me_2CHOH \rightarrow {}^3\{Me_2COH \ + Me_2COH \ \}$$

The radicals cannot react immediately, and although a small proportion re-encounter after triplet–singlet interconversion has occurred and form product, most survive the geminate period and lead to high, and observable, free radical concentrations It is no coincidence that the triplet reaction route has been found to yield high concentrations of radicals If, on the other hand, the geminate product was the desired result of the chemical reaction, the dissociation through the singlet state would be more effective Such considerations have possible wider implications to the use of radicals in chemistry, for example in radical-initiated polymerizations, where clearly the triplet state dissociation would be best Control of the spin state of the spin-correlated radical pair at the moment of its formation should be an important part of the design of chemical reactions, and physical observations, which involve radicals

Despite the argument for triplet state reactivity given above, and which can be found in any photochemistry text-book, it is often possible to push the reaction through the singlet route simply by arranging for the reaction rate to form radicals to compete with that of the intersystem-crossing stage in the precursor molecule This has been demonstrated in a number of CIDEP experiments, where radicals produced from singlet precursors have been detected in observations on transient species It happens facilely if the triplet state is not reactive (usually a $\pi\pi^*$ state[19]) or if the excited singlet is able to react with the solvent or by fast electron transfer, as in radical ion pair systems [20] Usually, however, the signal strengths are low when compared with triplet-generated species

Not all photochemical processes involving free radical production for ESR study do proceed through triplet reaction pathways, an exception being the dissociation of a peroxide to form an initial pair of oxygen-centred radicals Why this is possible is discussed below

3.2 All Other Methods

The photochemical method involving triplet state reaction appears unique in controlling the proportion of radicals which fail to undergo recombination in the geminate period by taking advantage of the adverse initial spin state of the radical pair All the others, entirely serendipitously, appear to work by causing extremely rapid spin state interconversion, for they typically involve reactions of ground state molecules or singlet excited states The most successful method for producing transient radicals for study in steady state concentrations in flow systems has undoubtedly been that where the radicals are produced by use of a transition metal/peroxide couple [21] Here the primary process in radical production involves either the transition metal ion itself, or a hydroxyl radical produced extremely quickly after the reaction is initiated Both of these species have extremely short relaxation times as a result of orbital degeneracy, and in a singlet-correlated radical pair the system attains triplet character on a timescale which competes with, or is faster than, the coherent mixing process described above This inhibits reaction during the crucial early period after radical pair formation when re-encounters are at their most probable The result is that although the inital bond-breaking produces a singlet-correlated primary pair (whatever its nature) many of the radicals survive the geminate period and can be used to produce secondary radicals for subsequent study In addition, the mixing of the solutions in the flow system usually occurs outside of the main magnetic field of the spectrometer, in a low ambient field in which coherent spin mixing might convert the singlet radical pair into any of the triplet sub-states, which would also lead to a decrease in reaction probability in the initial phase of the reaction Nevertheless, it is the incoherent contribution to the spin mixing which is usually the most significant

The peroxide case referred to above is a simple example of this, and it occurs whether the radicals are produced by thermolysis of the ground state, or photolysis involving an electronically excited singlet state The result of a symmetrical bond scission is to create a singlet-correlated pair of radicals in which the electron is centred upon the oxygen atom, and is consequently liable to fast relaxation so as to form the unreactive triplet state It is quite common in our experience for the radical concentrations from peroxide-initiated reactions to be low, and this can be understood by an extension of the arguments given above There it was not pointed out specifically that the singlet triplet mixing process interconverts these two states, with the radical pair wavefunction continuously changing between the two pure states Damping occurs only if the radicals diffuse apart and never re-encounter, or if they re-encounter in the singlet state and react In consequence, with very fast relaxation inside the field of the spectrometer, and with the radical system prepared in the singlet state, the system thereafter jumps randomly between the triplet and singlet states Converting from the initial singlet to the triplet is effective in eventual free radical production only if a substrate which reacts to form the observed secondary radical encounters the radicals when they are triplet-correlated, for as soon as they re-attain the singlet state and encounter, they react This implies that a further criterion must be satisfied the substrate must react with the radicals on a timescale that is not dissimilar to the singlet–triplet interconversion rate driven by the random relaxation process In turn this implies employing a diffusion-controlled reaction, with the substrate in high concentration Typical examples of this in action are the production of phosphorus-[22] or silicon-centred[23] radicals by reaction with substrates with easily abstracted hydrogen atoms These can then be used to create further generations of radicals in the system The substantive point is that the secondary radical in these situations normally has a comparatively long relaxation time, and so radical pairs consisting of two such radicals do not convert to the singlet and react on this same very fast timescale

Although this last aspect has been discussed specifically in the context of peroxyl radicals, the principle is general and applies to all the other situations, including that of the metal/peroxide couple It is less important in the photochemical generation of carbon-centred free radicals from a triplet state reaction since the spin state interconversion is much slower, and diffusion controlled rate processes in the classical sense are able to compete with the rate of coherently driven return to the singlet state

Similar principles to those described in this whole section apply to radiolytic production of free radicals where one of the initial species may be either the solvated electron or, in aqueous solution, the hydroxyl radical once more, and also to the electrolytic production of radical ions

4 Conclusions

Although it has long been accepted that free radicals can be produced in suitable concentrations for direct observation, this is in fact a cause for wonder, since it is not what would be expected from a detailed consideration of the processes that occur immediately after radicals are first formed in solution The methods that have been evolved to produce them for ESR study can be understood by consideration of these fundamentals, and unknowingly, we have made use of spin selectivity on reaction on the one hand, and relaxation effects on the other Now that these principles are understood it should be possible to invent new methods, and to appreciate how to create radicals in sufficient concentration for study by ESR One of the driving forces for the study of free radicals has been their importance as reaction intermediates, and yet our methods have evolved to observe them in high concentrations It may now be possible to move smoothly between one situation and the other, by small changes in reaction conditions, so as to be sure that the radicals which are observed are indeed relevant to the reaction proceeding under its usual conditions

Radical combination rate constants are often obtained from kinetic ESR studies They have been treated in the past as empirical constants which can be interpreted in terms of the activation energy of the reaction on the one hand, and diffusion on the other This is largely adequate for the slower diffusion-controlled reactions which occur in solution By this is meant those reactions which result from radicals which are formed in different regions of the solution and later encounter There is, however, a much more fundamental very fast process which occurs between radicals created together in the geminate period of the reaction The rate constants of radical combination reactions are actually time-dependent, with these two different processes happening on very different timescales Where the geminate reactions are concerned, a detailed interpretation of the rate constants is possible, in terms of spin-mixing on the one hand, and very short-term diffusion on the other With organic radicals hyperfine-driven coherent spin mixing occurs at a very definite and calculable rate and observations of geminate kinetics can consequently be used to explore the nature of diffusion in solution on the nanosecond timescale[24] Spin considerations apply to the classical diffusion-controlled radical combinations too, but here the long-range diffusion is the rate-controlling step

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