

TIME RESOLVED ELECTRON SPIN RESONANCE SPECTROSCOPY

BALU VENKATARAMAN

Tata Institute of Fundamental Research Homi Bhabha Road, Bombay 400 005, India

RAPID advances in electron spin resonance (ESR) instrumentation during the last ten years have enabled the observation of ESR absorption signals with time resolution of the order of 100 ns; indeed electron spin echo techniques have pushed the limits further down to 30 ns. When referring to time-resolved ESR studies one usually refers to time scales shorter than milliseconds, though strictly speaking any time-dependent investigation of the ESR signal is a time-resolved study. Two areas of time-resolved ESR studies which have attracted considerable attention are: (1) kinetic studies, especially on free radicals produced by photolysis and radiolysis and (2) relaxation studies using pulsed techniques. For brevity we confine our attention to studies in liquids and this restriction reflects the present author's interests.

KINETIC STUDIES

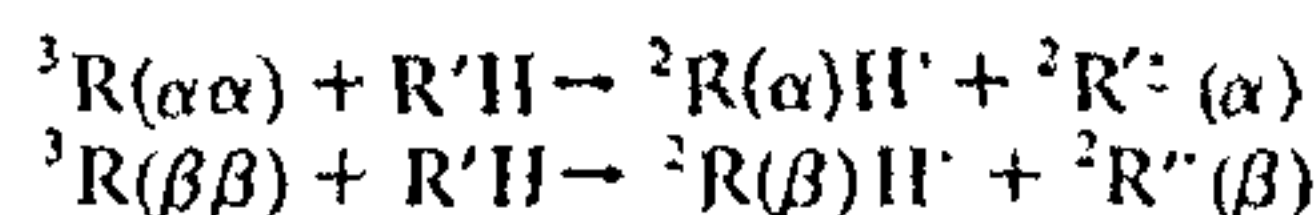
The ESR investigations in chemical kinetics are often just extensions of the well-known principle that any physical property that is a function of concentrations can be utilized to follow the progress of a chemical reaction. However, the fact that in certain reactions products are formed with electronic and nuclear spin polarizations, has heightened the interest in ESR investigations of rapid reactions. In ESR, signal heights are proportional to the population differences between the states connected by the ESR transition rather than just the concentrations of the paramagnetic species. It is known that both ESR and NMR lines with anomalous intensities are observed often in chemically reacting systems and the phenomena have been called, in general, chemically-induced dynamic magnetic polarization; in short, CIDEP for electron spin polarization and CIDNP for nuclear spin polarization. Though ESR has been utilized to follow the formation and fate of intermediate species in many reactions, we shall confine our attention to situations where spin polarization is concomitant with the chemical reaction.

Once the paramagnetic species, in the case of ESR and the diamagnetic products, in the case of NMR, are formed with non-equilibrium spin state populations, the time profile of the magnetic resonance signal, depends on the relaxation of the spin population toward thermal equilibrium and on the rate of change of the concentration of the observed species. The determination of kinetic parameters from time-resolved ESR measurements is thus not easy and requires a knowledge of the relaxation parameters. If

the chemical reaction rates and relaxation rates are well-separated in time domain, both can be determined in a single experiment as demonstrated by Atkins, McLauchlan and co-workers¹⁻⁸. In certain other cases where the separation is not sharp, judicious estimates of the relaxation times have been utilized to determine the kinetic parameters and a typical example is the study on hydrogen atoms by Fessenden and Verma⁹⁻¹². It has now been shown that it is possible to determine both relaxation and kinetic parameters from independent experiments on transient species, and T_1 s of transient species such as hydrogen atom and deuterium atom in aqueous solutions have been determined by Fessenden, Hornak and Venkataraman¹³.

The first observation of chemically-induced electron spin polarization was in hydrogen and deuterium atoms produced by the electron bombardment of liquid CH_4 and CD_4 ¹⁴. A satisfactory explanation for the low field hyperfine line being observed in emission and the high field line in enhanced absorption had to await the observation of the twin phenomenon of CIDNP in NMR and successful explanation for it in terms of radical intermediates.¹⁵⁻²⁰ It is now known that both CIDNP and CIDEP have their origin in the formation and removal reactions of free radicals. As a result it is now possible to gain from magnetic resonance studies, information not normally obtained. For example, the NMR signal of the ring protons of hydroquinone occurs in emission when a mixture of 0.02M hydroquinone, 10^{-3}M chlorophyll-a in methanol d^4 chloroform-d is irradiated at $\lambda=760\text{ nm}$ ²¹. Since hydroquinone and chlorophyll are recovered in tact after the photoexcitation the only evidence for the participation of the hydroquinone in the electron transfer reactions is the observation of a CIDNP signal for hydroquinone.

It is now well established that there are two types of mechanisms that lead to nuclear and electron spin polarizations in photolysis. The first is the triplet mechanism where selectivity in the inter-system crossing from the singlet state to the three sublevels of the triplet manifold, which are non-degenerate in the presence of a magnetic field, can lead to unequal population in the three triplet sublevels. When radical pairs are formed by the reaction of the triplet, for example, with a hydrogen donor the reactions are:



where α and β are electron spin states. Unequal population of the three triplet sublevels would therefore lead to spin polarization in the doublet state of the free radicals formed from the molecule in the triplet state.

The other mechanism is the radical pair mechanism. Even if there is no triplet precursor (as might arise in radiolysis) or even if there is no polarization in the triplet state intermediate, free radicals formed in pairs, as in



can be described, when they have not separated adequately, as triplet radical pair $^3\overline{RH} \overline{R'}$ or singlet radical pair $^1\overline{RH} \overline{R'}$. This identification is appropriate when the radicals of the formation time (geminate pair) in the solvent cage or in a random encounter (random pair) in the bulk solvent. It is obvious that the probability of recombination of singlet pairs is higher than that of triplet pairs. The radical pair mechanism has been theoretically developed and correlations between the CIDNP spectral features and the reaction mechanisms have been established by Kaptein and others^{22,23}. For example, depending on whether there is a difference in the g value of the two free radicals of the pair, or when $\Delta g = 0$ and there is a difference in the hyperfine multiplicity of the two free radicals, the nature of the CIDNP spectra obtained can be understood in terms of whether the reaction leading to the diamagnetic product, whose NMR is studied, occurred in the cage or from pairs escaped out of the cage. One can also say whether the radical pair precursor was a triplet pair or a singlet pair. It is this kind of detailed knowledge on the physical aspects of the chemical reaction that has made CIDNP studies a very important tool, especially in photochemistry.

Time-resolved ESR spectroscopy has been a very valuable tool in verifying many aspects of the theory of chemically-induced magnetic polarization and many predictions of both mechanisms mentioned above have been verified. The experimental observations support in main the radical pair mechanism²⁴ but evidence for the triplet pair mechanism has also been observed²⁵.

RELAXATION STUDIES

From the time the magnetic resonance technique has been employed as a tool for physicochemical studies, information on relaxation had been obtained from line-width studies; the seminal work often quoted as BPP is an outstanding example²⁶. By the very nature of interactions, the NMR relaxation times are orders of magnitude larger than ESR relaxation times and hence have been more easily and thoroughly investigated. In fact determination of relaxation times

of protons is a standard facility available in most present generation FT-NMR spectrometers and is an invaluable tool in the studies of structure and dynamics. However, electron spin relaxation times in the liquid state, which are usually microseconds and less at room temperature, have been subjects of investigation only in the past few years. We shall focus our attention on the studies of relaxation times in organic free radicals in the liquid state.

Among spin systems one refers to two kinds of relaxation times: the spin lattice relaxation time, T_1 which governs the rate of attainment of thermal equilibrium between the spin system and the surroundings and the spin-spin relaxation time T_2 that is related to the equilibrium among the spins of the system. T_1 and T_2 can be measured for electron spins by several techniques but in general T_2 's are derived from linewidth measurements and T_1 's from pulsed techniques, though both relaxation times can be measured by either method. We shall, again reflecting the interests of the author, confine our attention to the determination of T_1 's from time-resolved studies, the topic of the present review; we shall not discuss spin echo methods. One of the methods mentioned earlier utilizes the formation of the radical in a spin-polarized state due to the phenomenon of CIDEP and the separation of relaxation and chemical reaction phenomena into two separate time domains. Atkins, McLauchlan and co-workers have measured T_1 's for several free radicals produced by pulsed photolysis and even determined indirectly the spin lattice relaxation time of the triplet precursor in a particular reaction².

A more general method available for direct determination of T_1 of relatively stable and transient free radicals is the pulsed saturation recovery technique, wherein the time evolution of a system prepared in a non-equilibrium state by a high power microwave pulse is studied to determine T_1 . The experimental literature consists of references 27-30 by the author and his colleagues and references 31-36 by the group of Hyde and reference 13 by Fessenden, Hornak and Venkataraman.

Hyde's group has contributed significantly to the analysis of time domain ESR spectra following a saturation pulse and have established benchmarks for successful exploitation of the method to measure T_1 's without interference from the free induction decay that always accompanies the relaxation recovery signal after a saturating pulse. In fact that group's efforts to measure the short relaxation times of nitroxide radicals is definite to find many applications in biological systems where the spin-labels utilized to study motions in large molecules are derived from nitroxide radicals.

Our group has been utilising the T_1 's measured by saturation recovery technique to delineate radical-

radical interactions and radical-solvent interactions in semiquinones in hydrogen bonding and non-hydrogen bonding solvents and the methodology of analysis is similar to the BPP approach. It has been established that the semiquinone radicals in alcoholic solvents sit inside a cage of solvent, minimising radical-radical interactions and hence have a T_1 that is independent of concentration of semiquinone. The T_1 relaxation times in hydrogen bonding solvents are shown to be having a viscosity-dependent part that is dominated by spin-rotation interaction while the viscosity independent part is attributed to a hindered rotation within the cage. The viscosity independent part persists in such cases even below the glassy point of the solvent. The same semiquinones in non-hydrogen bonding solvents such as acetonitrile and tetrahydrofuran have T_1 's strongly dependent on concentration of the semiquinone and the expression for T_1 as a function of temperature does not have a viscosity-independent term which was attributed to the motion within a cage formed due to hydrogen bonding in alcoholic solvents. For further studies on the system, a magnetic field pulsed electron-electron double resonance spectroscopy method has been developed.³⁷ The method relies on the time domain studies of a particular hyperfine transition, to determine the saturation transfer to this transition, following the saturation of a neighbouring hyperfine transition with a high power pulse. Such studies, when carried out on dilute solutions where overlap between hyperfine lines due to line broadening is negligible, can throw light on cross relaxation mechanisms in such systems.

Our earlier work on semiquinones was restricted to reasonably concentrated solutions ($>10^{-3}$ M) on account of the signal-to-noise ratio problems in ESR signal detection with no field modulation. This drawback has been overcome by employing signal averaging techniques, as described by Hyde and co-workers³⁶ and Fessenden. Hornak and Venkataraman¹³. Using extensive computer control of the spectrometer, and with signal-averaging techniques, the limit of detection has been pushed down to 10^{-6} M for aqueous solutions (even lower if electron spin polarization is present) and such techniques have yielded T_1 's of transient species such as H-atom, D-atom, etc. The observation of a temperature independent T_1 for H-atom and D-atom between 25°C and 3°C and the fact that D-atoms have smaller T_1 's await a theoretical explanation.

It was mentioned earlier that in pulsed radiolysis or photolysis, the time profile of the ESR signal conveys information on relaxation parameters and chemical kinetic parameters. By using CW perturbation techniques (such as a CW vande Graff or continuous radiation with light) one can determine T_1 's of transient species independently from time domain

studies after a saturating microwave pulse, because the chemistry is in a steady state. Therefore such a reliable determination of T_1 and T_2 of the transient species in an independent experiment allows a more unambiguous determination of chemical kinetic parameters from a time domain ESR study after pulsed radiolysis or photolysis.

Time domain ESR studies have reached a point where they are expected to contribute significantly to identification of photoexcited states such as encountered in photosynthesis. Such investigations are bound to play a very significant role in the area of chemical dynamics.

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STRATEGIES OF SYNTHESIS OF AROMATIC POLYKETIDES USING CYCLOHEXA-1, 4- AND -1, 3-DIENES IN ALDER-RICKERT REACTIONS

CHARLES C. KANAKAM, HALASYA RAMANATHAN, G. S. R. SUBBA RAO
AND ARTHUR J. BIRCH

Department of Organic Chemistry, Indian Institute of Science, Bangalore 560 012, India

ABSTRACT

Cyclohexa-1, 4-dienes with appropriate substituents, obtained by Birch reduction of the substituted benzene, react directly with derivatives of propiolic ester or aldehyde to yield aromatic polyketides. The following compounds have been synthesised: mycophenolic acid, nidulol methyl ether, the root growth hormone 3, 5-dihydroxy-2-formyl-4-methyl-benzoic acid, antibiotic DB 2073, the macrocyclic lactones lasiodiplodin and dihydrozearalenone and the biphenyl derivatives alternariol and altenusin. Polyketide anthraquinones can be made from naphthoquinone precursors.

DIFFICULTIES in the syntheses of polyketides are due to the relative positions of the variety of OR, alkyl, CO₂H, CHO, COR substituents resulting from the mode of biosynthesis¹. In particular the relative orientations of substituents to each other and to positions of ring-closure often make classical aromatic substitution procedures awkward to apply²⁻⁴.

An alternative is to build up an appropriately substituted aromatic system *de novo* using the Alder-Rickert reaction⁵. This employs a Diels-Alder addition to cyclohexa-1, 3-dienes with a dienophile of such a nature that there can be obtained, directly or

indirectly, a cyclohexa-1, 4-diene with a 2, 5-bridge. Appropriate dienophiles for the direct process are acetylenes activated by an electron-sink such as CO₂Me or CHO, most reactions having previously been carried out with dimethyl acetylenedicarboxylate⁶⁻⁸. Indirect precursors are quinones followed by oxidation of the adduct to regenerate the necessary unsaturation. Thermal removal of the bridge as an olefin occurs readily to form the substituted benzene.

The advantages for polyketide synthesis are: (1) The 1-OMe; 1, 3-diOMe, 3-Me etc. cyclohexa-1,4-dienes needed as precursors are readily available by Birch