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Paramagnetic Interactions of Triplet Radical Pairs with Nitroxide Radicals: An "Antiscavenging" Effect

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Abstract: The recombination probability, P_r, of triplet *sec*-phenethyl/*sec*-phenethylacyl radical pairs (RP) generated in the photolysis of *d,l*-2,4-diphenylpentan-3-one (*d,l*-DPP) in benzene increases from 0.033 to 0.098 as the concentration of the stable free radical, TEMPO, increases from 0 m to 0.146 M. The unusual effect of a putative free radical scavenger is explained in terms of a competition between two processes: chemical scavenging of geminate radicals by nitroxide, and spin exchange between geminate radicals and nitroxide. The second process is evidently faster and enhances triplet to singlet intersystem crossing of the geminate triplet RP. As a result, P_r increases as the concentration of the free radical scavenger, TEMPO, increases. These results reveal a peculiar situation for which a paramagnetic scavenger, by physically accelerating intersystem crossing faster than it scavenges, enhances the reactivity of a triplet geminate pair as it approaches. The new result is an increase in the "cage effect", or recombination efficiency of geminate radical pairs. These results allow a novel view of the cage effect of geminate pairs in homogeneous, non-viscous solutions.

Introduction

Nitroxides have proven to be both outstanding scavengers of carbon centered free radicals[1] and probes of electron spin exchange processes.[2,3] The second-order rate constants for spin exchange between doublet free radicals are typically of the order of diffusion controlled in ordinary, non-viscous solvents.[2,3] The second-order rate constants for reaction of nitroxides with carbon centered reactive free radicals are somewhat slower than diffusion controlled. For example, a range of alkyl and benzyl carbon centered radicals are typically of the order of 10^8 M^{-1} s^{-1} or higher.[1] Thus, when a nitroxide approaches an ordinary (doublet) carbon centered free radical, both spin exchange and bond formation are expected to be possible and competitive processes (eqs 1 and 2), with spin exchange being generally faster. The competition between bond formation and spin exchange between two doublets has only been investigated in a limited number of systems.[3,4] The main conclusion of these investigations is that a spin exchange process is generally faster then the chemical interaction.[3,4] The competition between the spin exchange and chemical interaction for doublet–doublet systems has interesting consequences in the very fundamental process of geminate cage reactions and the scavenging of geminate radical pairs produced by photochemical reactions in non-viscous solvents.

When the nitroxide approaches the free radical, it is not expected that the reactivity of the free radical toward scavenging by nitroxide will be influenced measurably by spin exchange, because the total spin of a system of two interacting doublets (S = 1 or 0) is not affected by the exchange interaction. However, if a nitroxide approaches a triplet geminate pair, the exchange interaction could cause an intersystem crossing in the pair, i.e., the exchange interaction of a doublet and a triplet may lead to a *reactive* singlet and a doublet. Should this be the case, the possibility exists that, if spin exchange induced intersystem crossing is faster than scavenging, as a nitroxide approaches a triplet geminate radical pair, it may make the pair more reactive toward recombination (by inducing singlet formation) and thereby reduce the efficiency of scavenging, i.e., a free radical scavenger becomes an *antiscavenger* when it attempts to scavenge a radical in a triplet geminate pair.

$$\overset{\uparrow}{R} + R_2\overset{\downarrow}{NO} \longrightarrow \overset{\downarrow}{R} + R_2\overset{\uparrow}{NO} \qquad \text{spin exchange} \qquad (1)$$

$$\overset{\uparrow}{R} + R_2\overset{\downarrow}{NO} \longrightarrow R\text{-}ONR_2 \qquad \text{bond formation} \qquad (2)$$

Noyes has provided a physical model of the reactions of geminate radical pairs produced by, say, a photochemical cleavage of a ketone.[5] According to the model, which assumes a random walk of the geminate pair that leads to a competition of reencounters and separation of the pair into the solvent bulk, there should be three possible stages of scavenging:[5–8] (1) scavenging of **primary** geminate radical pairs directly produced by the cleavage, before the primary geminate pair has had an opportunity to move far enough apart for a solvent molecule to come between them; (2) scavenging of solvent separated **secondary** geminate radical pairs which have left the primary cage and are in the process of undergoing reencounters; and (3) scavenging of **random** radicals which have separated from their geminate partner and have become statistically distributed in the bulk solvent. The

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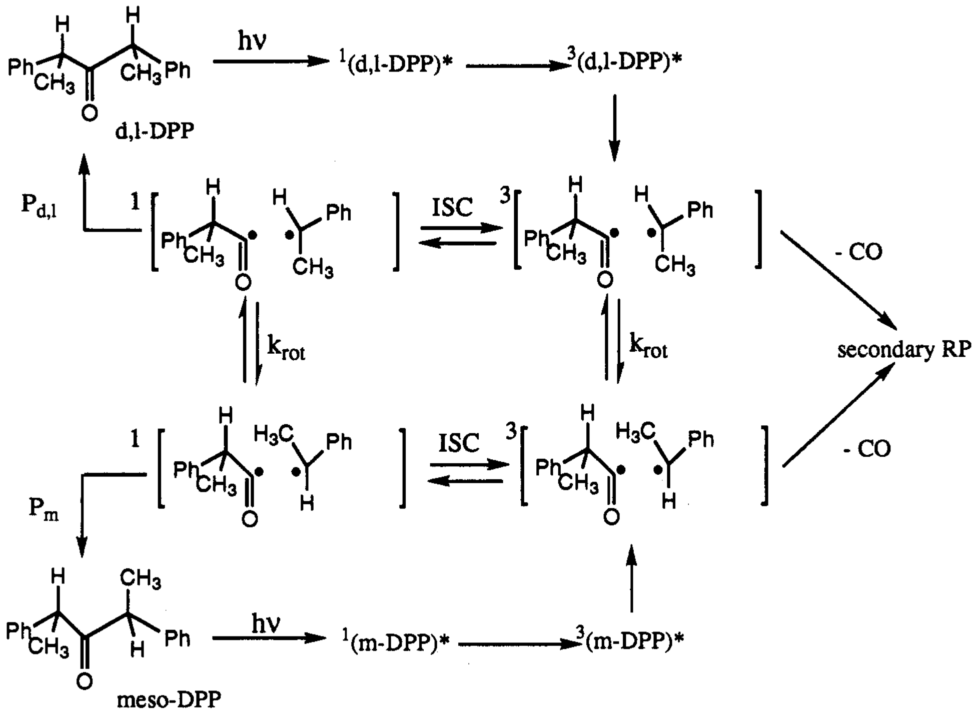
Scheme 1



original meaning of a solvent "cage" in solution is usually taken to mean a structure produced by a wall of solvent molecules surrounding two potential reactants which are held together in direct contact. From the Noyes model the concept of the cage is extended so that two potential reactants, such as a radical pair, may be considered to be in an "effective cage" not only at the moment of direct contact but also between reencounters. In this sense, a "cage" is interpreted as a certain region of space in a solution in which the radical pair has a much higher probability of geminate recombination, P_r, than the probability of one of the partners of the geminate pair reacting with a partner from another pair. In other words, as long as the geminate pair is in this extended cage, the probability of their reaction with other pairs and with scavengers is low compared to the probability that they will undergo recombination reactions with each other.

The complete scavenging of random free radicals by scavengers which intercept radicals at high rate ($k_{sc} = 10^7–10^9\ M^{-1}\ s^{-1}$) is well established.[6–8] Thus, for the interception of such radicals, the use of such a scavenger in a conventional non-viscous solvent requires scavenger concentrations of ca 0.0001 to 0.01 M for efficient scavenging of the random or free radicals produced by photodissociation of a ketone yielding a triplet geminate radical pair. However, experimental attempts to observe the scavenging of primary or secondary geminate radical pairs in non-viscous solutions have proven difficult.[6,7] In the absence of scavenger, the maximum lifetime of a triplet geminate pair (time beyond which reencounters are negligible) in a conventional nonviscous solvent has been estimated to be ca. 1 ns.[5,9] Even if a scavenger possesses a scavenging rate constant of ca. $10^9\ M^{-1}\ s^{-1}$, i.e., close to diffusion controlled, a scavenger concentration of ca. 0.1 M is required for geminate scavenging to become at least partially competitive with the formation of random radicals from the triplet geminate radical pair.

From these considerations it is reasonable to expect that when a nitroxide is employed as scavenger at concentrations of ca. 0.1 M, the paramagnetism of the nitroxide might influence the magnetic properties of the triplet geminate pair, i.e., influence the rate of triplet–singlet intersystem crossing of the triplet geminate pair by spin exchange with one of the radicals of the geminate RP in a "cage" but between reencounters. If this happens, the probability, P_r, of cage recombination of a triplet geminate RP might increase, since spin exchange between two radicals (a radical from RP and nitroxide) is known to be faster than a chemical reaction[3b,4] (scavenging).

In the present investigation a nitroxide was employed as scavenger of the radicals produced by α-cleavage of 2,4-diphenypentan-3-one (DPP) in benzene. It was expected that the nitroxide would behave as an efficient scavenger of the random radicals produced by separation of the geminate pairs. The maximum extent of geminate recombination of the primary pair, although expected to be only of the order of a few percent at best, may be evaluated by measuring the probability of recombination, P_r, of primary radicals to regenerate the starting ketone. The extent of the latter may be evaluated accurately by determining the extent of photodiastereomerization[10,11] of *d,l*- or *meso*-DPP. On the basis of previous results,[8] it was anticipated that, since combination products normally result from combination of random radical pairs and not from recombination of geminate pairs, all radical recombination products would be "quenched" as the result of efficient scavenging by nitroxide. However, we shall show that the actual experiments led to the surprising result that **the probability of recombination, P_r, as measured by photodiastereomerization, increased as the concentration of the scavenger increased**. This unusual finding represents an example of an effect by which a (paramagnetic) scavenger interacts with radicals of a triplet geminate radical pair and catalyzes intersystem crossing in the geminate pair; the net result is that the geminate pair suddenly becomes reactive toward recombination and thereby avoids scavenging. The paramagnetic scavenger thus effectively thwarts the scavenging reaction by catalyzing intersystem crossing and causing the formation of a stable, unscavengeable molecule. In such a situation, the putative scavenger may be more appropriately termed an "antiscavenger".

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Experimental Section

2,4-Diphenylpentan-3-one (DPP) was prepared by methylating dibenzyl ketone similar to a literature procedure.[10] The separation of *meso* and *d,l* forms of DPP was achieved by HPLC on a 25 × 1.0 cm silica column (Rainin) with 1.75% ethylacetate in hexane as an eluent. Isolated *d,l*-DPP contained 1.3% *meso*-DPP according to gas chromatographic data. TEMPO, 2,2,6,6-tetramethylpiperidinoxyl (Aldrich), was purified by sublimation under reduced pressure. Benzene (Aldrich, spectrophotometric grade) was used as received. The concentration of *d,l*-DPP used for photolysis was 5.1×10^{-3} M. Solutions were bubbled with Ar before and during photolysis. Photolysis of *d,l*-DPP in benzene was carried out at room temperature in a Rayonet photochemical reactor equipped with a set of lamps, emitting at 300 nm, in a quartz cell. Diphenylmethane (Aldrich), used as internal standard for GC analysis, was added to the solution before the photolysis.

Gas chromatographic analysis was performed on a Hewlett-Packard 5890 capillary gas chromatograph interfaced to a Hewlett-Packard 3996 electronic integrator on a 25-m Carbowax 20M column.

Results

The conventional paradigm for the photochemistry of DPP is given in Scheme 1. Photoexcited DPP undergoes efficient $S_1 \rightarrow T_1$ intersystem crossing, followed by rapid and efficient α-cleavage to form a geminate primary triplet radical pair (^{3}RP) consisting of a *sec*-phenethylacyl and *sec*-phenethyl radical in a primary solvent cage. The primary geminate ^{3}RP undergoes long diffusional trajectories which rapidly lead to random radicals or, after intersystem crossing, (ISC) to singlet RP (^{1}RP) which recombine after short trajectories during reencounters (geminate recombination). In non-viscous solvents there is very little, if any, geminate recombination and almost all of the geminate pairs become random radicals which lead to the observed products.[8] Most if not all of the small amount of recombination product formed (determinated by the extent of photodiastereomerization, *vide infra*) is believed to arise from recombination of random radicals, not from recombination of geminate radical pairs.[8]

Two diastereomeric forms of DPP (*d,l* and *meso*) are easily separable by GC and HPLC, which allows for accurate quantitative analysis. The geminate photodiastereomerization which interconverts *meso*-DPP and *d,l*-DPP is a result of rotation (or inversion) of a *sec*-phenethyl radical within a geminate RP. Photodiasteromerization has been employed to determine directly the probability of recombination, P_r, of geminate RP in solution.[11] Briefly, if Z_0 is the initial diastereomeric purity of DPP, $Z_0 = (r - m)/(r + m)$, where r is the concentration of *d,l*-DPP and m is the concentration of *mezo*-DPP, and Z is diastereometric purity of DPP after photolysis with conversion f, then eq 3 applies,

$$\log(Z/Z_0) = S \log(1 - f) \quad (3)$$

In eq 3, the value of S, the slope of the experimental plot of $\log(Z/Z_0)$ *vs* $\log(1 - f)$, characterizes the maximum efficiency of isomerization of geminate RP. The ratio of Z/Z_0 as well as conversion of photolysis, f, is accurately determined by GC analysis after photolysis and does not require the isolation of the diastereomers. The measured efficiency of isomerization S is related to the recombination probability, P_r, of geminate RP by eq 4:

$$P_r = S/(1 + S) \quad (4)$$

The probability of geminate recombination is overestimated if there is a random radical recombination contribution to the measured photodiastereoisomerization.

Figure 1 shows data, plotted in terms of eq 3, for photodiastereomerization of *d,l*-DPP in benzene with and without 0.146 M of TEMPO. Figure 2 shows the TEMPO concentration dependence of P_r (derived from the data which are analyzed as in Figure 1) for the photolysis of *d,l*-DPP in benzene. The salient feature of the results is that P_r is gradually **increased** from a value of 0.033 in the absence of TEMPO to a value of 0.098 as the TEMPO concentration is increased to ca. 0.15 M.

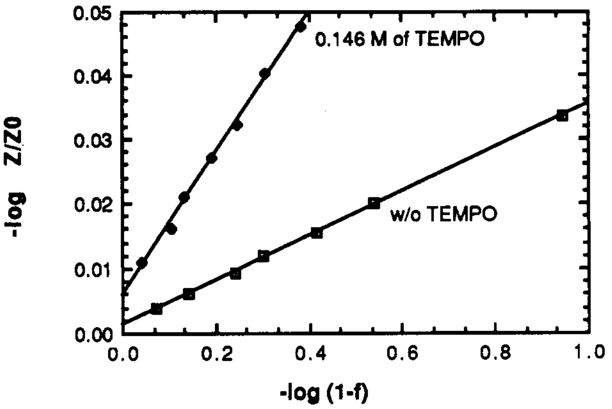


Figure 1. Photodiastereomerization of *d,l*-DPP in benzene in the presence of 0.146 M TEMPO and without TEMPO *vs* conversion of photolysis in the variables of eq 3.

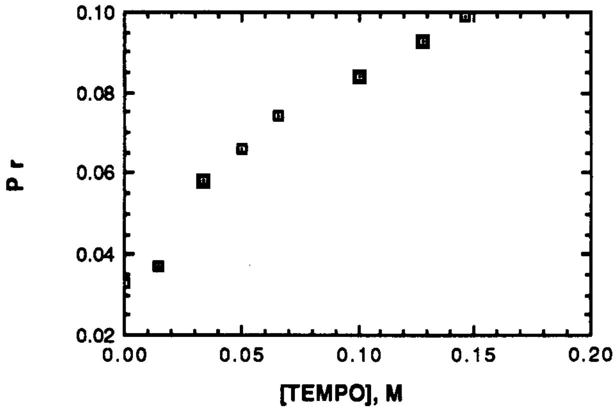


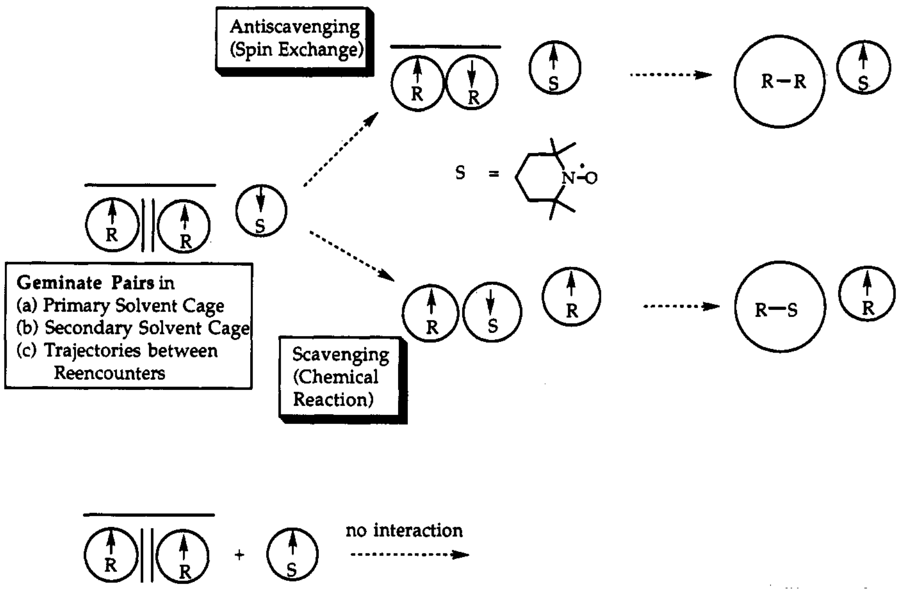
Figure 2. The dependence of recombination probability, P_r, of the triplet *sec*-phenethyl/*sec*-phenethylacyl radical pair generated in the photolysis of *d,l*-DPP in benzene in the presence of TEMPO *vs* concentration of TEMPO.

Discussion

The most important experimental result obtained in this report is summarized in Figure 2, which shows that the probability, P_r, of formation of recombination products increases as the concentration of the paramagnetic scavenger TEMPO increases. This result contrasts with the observation that the addition of the diamagnetic scavenger, dodecanethiol, on P_r of benzoyl/*sec*-phenethyl RP decreased, *as expected for a scavenger that only chemically reacts with the radicals produced by photolysis.*[8]

As mentioned in the Introduction, according to the Noyes model of a dynamic radical pair, recombination products can be produced in three distinct stages: in the primary cage before a solvent molecule has come between the geminate pair, in a secondary cage after the primary pair has been separated by one or more solvent molecules and then reencountered, and in random cages formed by the encounter of random radicals produced by independent α-cleavages. At sufficiently high concentration (ca. 0.1 M), paramagnetic TEMPO molecules may be able to interact both magnetically (spin exchange, eq 1) and chemically (scavenging, eq 2) with geminate triplet radical pairs. The chemical interaction irreversibly removes radicals from the system and will result in a decrease in the fraction of recombination products produced by photodissociation of ketone molecules by either random or geminate processes. The exchange interaction between a triplet radical pair and a nitroxide, however, can cause

Scheme 2



intersystem crossing of the triplet geminate pair to a singlet geminate pair. Since the latter pair is exceedingly reactive toward recombination, an increase in P_r in the fraction of recombination product formed by photodissociation of a ketone molecule would be expected if the exchange interaction which causes intersystem crossing competes with the chemical reaction. The average exchange distance between two reactive radicals was experimentally found to be 2–3 times larger than the hard-sphere encounter distance.[4] Thus, spin exchange may occur even when a nitroxide and radical are separated by one or more solvent molecules, but still in the region of space classifiable as the "cage". It is even possible that intersystem crossing may be induced by the paramagnetic scavenger, under the conditions when chemical scavenging is negligible.

We now show that such a situation is plausible for the system reported here and that TEMPO and presumably other nitroxides may behave as "antiscavengers" of triplet geminate radical pairs, i.e., theses radical scavengers may generally enhance cage combination rather than interfere with it. The arguments for the antiscavenging effect fall into two catagories: (1) demonstration that the measurements of P_r are still valid when TEMPO is employed as a scavenger, and (2) demonstration that the times and distance scales required for the antiscavenging effect are plausible.

First we consider possible reasons that might invalidate the mechanistic interpretation of the measurement of P_r in the presence of high concentrations of TEMPO. The analytical method for the evaluation of P_r measures the formation of recombination product by determining the extent of loss of diastereomeric purity (eqs 3 and 4). The mechanistic interpretation of P_r which leads to the conclusion of an antiscavenging effect requires that the only pathway for loss of diastereomeric purity is α C–C bond cleavage followed by rotation and recombination of radicals, through either random or geminate pairs (Scheme 1, the snip and knit processes[11a]). This assumption requires that only cleavage of the α C–C bond followed by random or geminate recombination induces the loss of the diastereomeric purity under the reaction conditions. There are several pathways other than the latter which could result in photodiastereoisomerization. The most plausible mechanism which could lead to loss of diastereomeric purity without cleavage of the C–C bond is probably an enolization–ketonization process involving ground or excited states of DPP. However, deuterium labeling experiments in a related deoxybenzoin system show that such a mechanism is not operative,[12] so we consider it unlikely for DPP. Control experiments show that TEMPO does not induce loss of diastereoisomerization of the ground state DPP molecule. Furthermore, the extremely short lifetime of the excited state of DPP makes it very unlikely that TEMPO can assist in promoting enolization of the excited molecule. We conclude that enolization is unlikely to be a mechanism for the observed loss of diastereoisomerization and are of the opinion that other possible mechanisms that could cause diastereoisomerization are even less likely under the reaction conditions.

It is possible that the presence of TEMPO at high concentrations could lead to experimental complications due to competitive light absorption. However, the applications of eqs 3 and 4 are completely independent of light absorption, since the *fraction of converted product which leads to diastereoisomerization is being measured not the quantum yield for diastereoisomerization.* Finally, it is possible that the absorption of light by TEMPO could produce a photoexcited TEMPO molecule that abstracts hydrogen from solvent or DPP. However, radicals formed during hydrogen abstraction from DPP are expected to be efficiently scavenged by TEMPO and should not lead to racemization through a hydrogen abstraction mechanism.

Scheme 2 summarizes the mechanism of the antiscavenging effect. As a paramagnetic scavenger S (a nitroxide radical) approaches a triplet geminate RP (which may be in a primary cage, a secondary cage, or trajectory between reencounters, i.e., in the extended dynamic cage) the scavenger may induce ISC (if spin orientation is incorrect for intersystem crossing by a spin exchange mechanism) and cause the geminate pair to become reactive toward recombination (antiscavenging effect) or "displace" one of the partners of the geminate pair (if the spin orientation is correct for intersystem crossing by a spin exchange mechanism) and form a bond with its geminate partner (scavenging effect). The average distance between the partners of a geminate RP should be an important factor in determining the efficiency of antiscavenging. When the distance between radicals in a geminate RP is too small, i.e., the trajectories of the radicals are small, the exchange interaction within the RP is large and will tend to inhibit an external spin exchange with nitroxide. At the same time when the distance between radicals in a RP is large, i.e., the radical trajectories are relatively long, spin exchange with nitroxide might be effective, although the probability of returns of long trajectories is very low.[5] Thus, the conditions for

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the antiscavenging effect are somewhat specific and may not be generally achieved.

It is worth mentioning that the proposed mechanism of antiscavenging might be operative also in the case of random RPs. Formally random RP consists of 3/4 of T and 1/4 of S and, consequently, only 1/4 of the collisions of random RPs lead to combination (upper estimation, assuming no steric or any other restrictions). Mechanisms may exist by which the nitroxide perturbs the ratio of T and S, as the random pair encounter, but we are unable to come up with one that we consider plausible. Furthermore, the contribution of random combination is very low to begin with and is expected to be negligible in the presence of a high concentration (paramagnetic) scavenger.

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