the result of different sample conditions; the FTIR data were taken on hydrated films or pellets which may trap nonnative protein conformations. Another possibility is that the FTIR studies are detecting *tyrosine* environmental changes[17] as opposed to full protonation/deprotonation events. One implication of this study is that if tyrosinate is not involved in the $BR_{568} \rightarrow BR_{555}$ transition, then tyrosinate is not involved in the photocycle. This implication is supported by the absence of a shoulder at 1600 cm^{-1} with sufficient intensity to justify the presence of a tyrosinate in BR_{568} (Figure 1B). We have recently proposed a detailed molecular mechanism (the C-T model) for proton pumping which is consistent with these results on the role of tyrosine in the photocycle.[18-20]

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Electron Spin Polarization Transfer between Radicals

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Electron spin exchange between paramagnetic particles is an elementary bimolecular process that is accessible to both detailed experimental investigation and probing theoretical analysis, allowing study of the elementary processes of collisions and interactions of molecules in fluid media.[1,2] An important parameter for experimentally characterizing the strength of such interactions is the rate constant of spin exchange, k_e, which is commonly obtained indirectly from the dependence of the line broadening of ESR spectra on the concentration of paramagnetic particles. Since exchange involves the overlap of electron orbitals, k_e is expected to be influenced by the same factors that usually affect other important chemical interactions between molecules, such as energy transfer, electron transfer, and frontier orbital interactions that initiate bond formation and bond breaking.[3] Measurements of k_e have been employed to investigate how collisions are influenced by microscopic properties of homogeneous liquids and more recently by inclusion of reactants in microheterogeneous systems, such as micelles.[4]

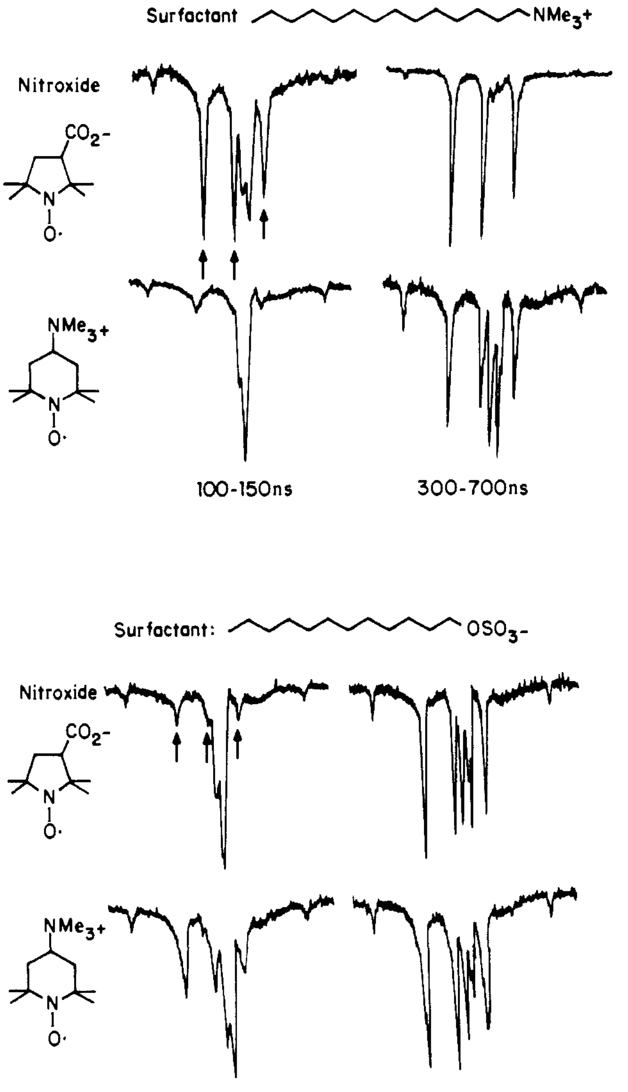

Figure 1. Time-resolved EPR spectra of micellar solutions containing 100 mM surfactant, 3 mM **1**, 20 mM NaOAc, and 3 mM **2** or **4**, titrated to pH 7.0. The three lines of the nitroxide are noted by arrows in the upper left spectrum of each set. The rest of the lines are attributable to the benzoyl and hydroxycyclohexyl radicals.

Electron spin polarization, detected by time-resolved EPR spectroscopy (TREPR), has opened the possibility of direct determination of k_e by polarization transfer. Transfer of triplet mechanism polarization has been demonstrated in triplet to doublet,[5] triplet to singlet,[6] doublet to singlet,[7] and doublet to

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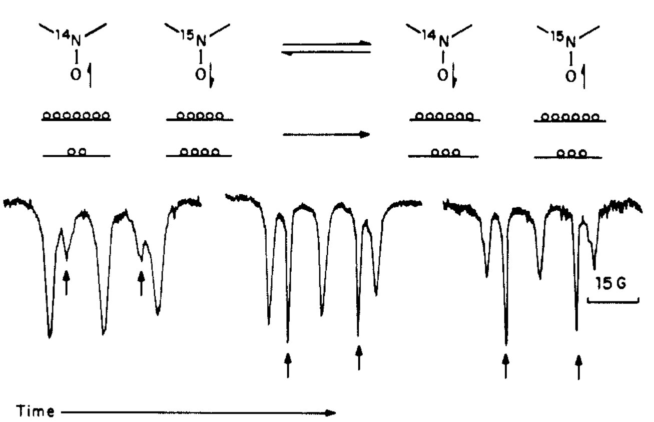
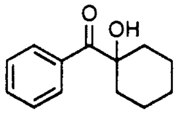


Figure 2. Time-resolved EPR spectra of *tert*-amyl alcohol solutions containing 2 mM each **5** and **6** which show polarization transfer by spin exchange from **5** to **6**. Detection gates are nominally 50–100 ns, 400–600 ns, and 900–1100 ns. The lines attributable to **6** are marked with arrows.

doublet[8] systems. We report here an investigation of doublet to doublet spin exchange in micellar systems measured directly by spin polarization transfer, and we provide evidence that, under specific conditions, spin exchange can be unambiguously isolated as the polarization transfer mechanism.

Phenyl 1-hydroxycyclohexyl ketone (**1**) was solubilized in aqueous solutions containing sodium dodecyl sulfate or tetradecyltrimethylammonium bromide micelles and one of the nitroxides **2–4**. Micellized, polarized 1-hydroxycyclohex-1-yl and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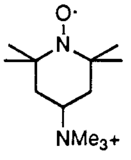
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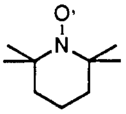
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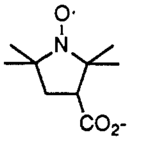
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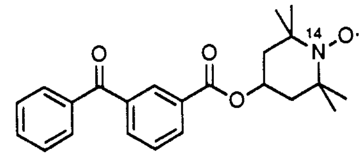
benzoyl radicals were produced on photolysis. Polarization transfer to the nitroxides was monitored by TREPR. The results of manipulating the charge of the micelle and the charge of the nitroxide polarization acceptor are shown in Figure 1. The qualitative but clear result is that at the earliest acquisition times the nitroxide spin acceptors show only weak polarization (indicated by arrows in Figure 1) for the "same charge" system $\{+_{M}/+_{NO}\}$ and $\{-_{M}/-_{NO}\}$, while substantial polarization transfer has occurred in the "opposite charge" systems, $\{-_{M}/+_{NO}\}$ and $\{+_{M}/-_{NO}\}$, even at the earliest acquisition time. The results for neutral nitroxide systems, $\{-_{M}/0_{NO}\}$ and $\{-_{M}/0_{NO}\}$, are very similar to those for oppositely charge micelle/nitroxide systems. These experiments demonstrate that the charge on the micelle surface serves to enhance collisions between polarized radicals produced by photolysis and nitroxides possessing opposite charge (or no charge) and to inhibit collisions between polarized radicals produced by photolysis and nitroxides possessing the same charge.[9] The more recent results are consistent with escape rates of the order of 10^{6}–10^{7} s^{-1} for the radicals from micelles of either charge.[10]

Collisions between reactive radicals can result in either reaction or polarization transfer. Three mechanisms for spin polarization transfer between radicals can be envisioned: (a) dipole–dipole, (b) exchange, and (c) spin-selective reaction. The latter could result from the fact that only singlet radical pairs are reactive upon collision, so that spin polarization might result from the selective depletion of certain spin states of the acceptor.

These mechanisms can be distinguished by a direct experiment that takes advantage of the specific initial generation of electron spin polarization in a ^{14}N-labeled nitroxide spin polarization donor followed by times-resolved observation of spin polarization transfer to a ^{15}N-labeled nitroxide acceptor. The ^{14}N-labelled nitroxide **5** was employed as the polarization donor, and the ^{15}N-labelled nitroxide **6** was employed as the polarization acceptor; the two have readily distinguishable EPR spectra. Because collisions between nitroxides do not lead to reaction, the selective reaction mechanism (c) for polarization transfer can be excluded. The dipole–dipole mechanism (a) can be minimized by running the experiment in solvents of low viscosity, because dipole–dipole interactions average to zero in the limit of rapid rotations.[11] Since an ambiguity concerning the magnitude (and even the meaning) of viscosity in micellar systems exists, the polarization transfer between **5** and **6** was investigated in homogeneous solution of clearly defined viscosity.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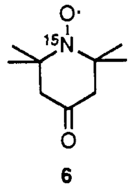
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TREPR spectra obtained from dilute (ca. 1 mM) solutions of **5** showed a strong emissive typical nitroxide triplet, providing a unimolecular source of polarized, unreactive radicals that could be produced by flash laser excitation. Conventional steady-state EPR spectra of solutions containing equimolar amounts of both **5** and **6** showed five distinct lines, corresponding to the triplet of **5** and a doublet of **6**.[1b]

TREPR spectra of a *tert*-amyl alcohol solution of 2 mM **5** and **6** were recorded (Figure 2). The earliest spectra show that most of the initial polarization is localized on **5**, as expected from the selective excitation of the benzophenone chromophore with the 355-nm line of the YAG laser.[4] The ratio of the integrated intensities varied with time and approached a value of 1 at times longer than 1000 ns. We interpret the results of Figure 2 to be a demonstration of a "degenerate" spin transfer between nonreacting radicals. As confirmation of this interpretation, an estimation of the rate of polarization transfer was made by analyzing the data in terms of an equilibrium displacement. A polarization transfer rate constant of $(6.5 \pm 1) \times 10^{8}$ M^{-1} s^{-1} was obtained for solutions of two different concentrations.[12] The spin exchange rate constant for **3** in the same solvent, determined by the steady-state line-width method,[1] is $(8.1 \pm 0.4) \times 10^{8}$ M^{-1} s^{-1}. An upper limit on dipole exchange rate can be placed at 1×10^{8} M^{-1} s^{-1}, on the basis of solvent viscosity.[11] Polarization transfer was found to be faster in less viscous solvents. These latter two observations eliminate dipole–dipole transfer as an important mechanism.[11] We can thus unambiguously conclude that polarization transfer between doublets can occur through spin exchange in the absence of other mechanisms.

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Ciba-Geigy corporation for providing **6**. W.S.J. thanks the NSF for a predoctoral fellowship, 1986–1989, and the Division of Organic Chemistry of the American Chemical Society and the Monsanto Corporation for fellowship support, 1989–1990.

Unprecedented Stereochemical Control in the Organoaluminum-Promoted Intramolecular Ene Reactions of δ,ε-Unsaturated Aldehydes

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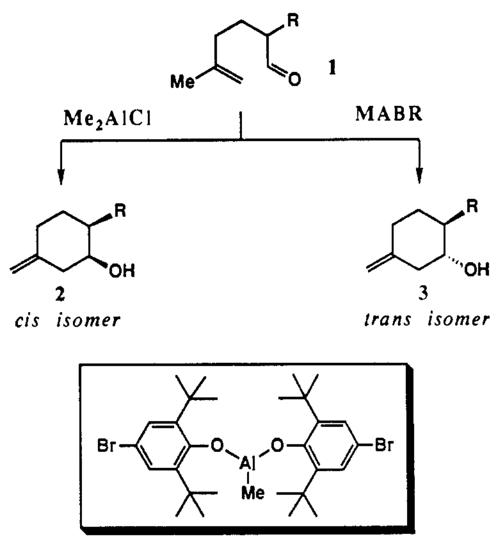
The Lewis acid promoted ene reactions of unsaturated carbonyl compounds are a valuable route to the stereoselective synthesis of highly functionalized cyclic compounds.[1] Among these, type II intramolecular ene reactions of δ,ε-unsaturated aldehydes **1** with α-substituents were reported to furnish *cis*-methylenecyclohexanols **2** with high selectivity (Scheme I).[2] The opposite, trans selectivity, however, has not yet been achieved. Here we disclose new, stereocontrolled ene reactions of δ,ε-unsaturated aldehydes **1** with α-substituents leading to *trans*-cyclohexanols **3** with exceptionally bulky methylaluminum bis(4-bromo-2,6-di-*tert*-butylphenoxide) (MABR).[3] Our results are summarized in Table I.

Scheme I



(MABR)

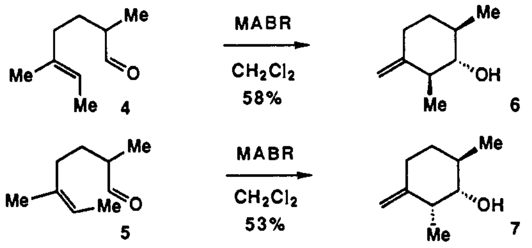
Table I. Stereocontrolled Ene Reactions of δ,ε-Unsaturated Aldehydes[a]

entry	aldehyde **1**	Lewis acid (equiv)	conditns: temp (°C), time (h)	yield, % (ratio of **2**:**3**)[b]
1	R = Me	Me_2AlCl (1.2)	−78, 0.3	65 (9:1)[c]
2		$BF_3{\cdot}OEt_2$ (2)	−78, 0.3	58 (19:1)
3		$SnCl_4$ (2)	−78, 0.3	47 (9:1)
4		MABR (1.2)	−78, 2; −40.1	85 (1:32)
5		MABR (2)	−78, 5; −40, 0.3	82 (1:32)
6	R = Et	Me_2AlCl (1.2)	−78, 0.3	60 (19:1)
7		MABR (2)	−78, 2.5; −40, 0.5	89 (1:30)
8	R = *i*-Pr	Me_2AlCl (1.2)	−78, 0.3	70 (33:1)[d]
9		MABR (2)	−78, 0.5; −40, 2	85 (1:17)[d]
10	R = allyl	Me_2AlCl (1.2)	−78, 0.7	59 (17:1)
11		MABR (2)	−78, 0.5; −40, 1	82 (1:62)
12	R = Ph	Me_2AlCl (1.2)	−78, 0.5	95 (26:1)[e]
13		MABR (2)	−78, 0.5; −40, 2	98 (1:62)[e]
14	R = SPh	Me_2AlCl (1.2)	−78, 0.3	95 (1:3)[e,f]
15		$BF_3{\cdot}OEt_2$ (2)	−78, 0.2	86 (1:2)[e,f]
16		$SnCl_4$ (2)	−78, 0.5	66 (1:3)[e,f]
17		MABR (2)	−78, 1.5	75 (1:200)[e]

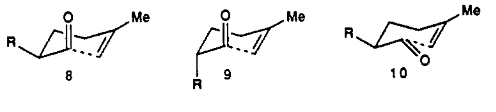
[a] The reaction was carried out in CH_2Cl_2 with 1.2-2 equiv of Lewis acids under the indicated conditions. [b] Determined by GLC analysis. [c] See ref 2. [d] The stereochemistry of **3** (R = *i*-Pr) was confirmed by correlation to menthol after hydrogenation of **3** with 10% Pd/C. [e] The authentic hydrogenated samples of **3** (R = Ph or SPh) were independently synthesized. [f] The trans selectivity with normal Lewis acids is ascribed to the effect of the electron-withdrawing phenylthio substituent. See also: Snider, B. B.; Deutsch, E. A. *J. Org. Chem.* **1983**, *48*, 1822.

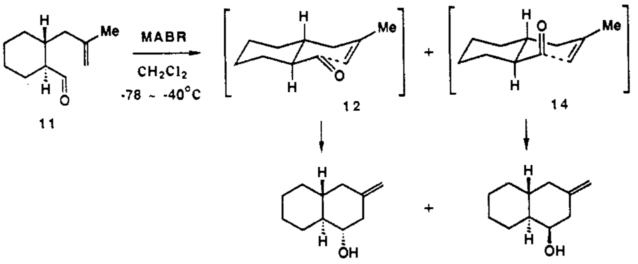
The Lewis acid promoted cyclizations of 2,5-dimethyl-5-hexenal (**1**, R = Me) are known to generally afford *cis*-6-methyl-3-methylenecyclohexanol (**2**, R = Me) predominantly (entries 1–3).[2] In marked contrast, however, treatment of **1** (R = Me) in CH_2Cl_2 with exceptionally bulky MABR (1.2–2 equiv) at −78 to −40 °C gave rise to *trans*-6-methyl-3-methylenecyclohexanol (**3**, R = Me) with excellent stereoselectivity (entries 4 and 5). The trans selectivity is markedly decreased with less bulky dimethylaluminum 4-bromo-2,6-di-*tert*-butylphenoxide or methylaluminum bis(2,6-diphenylphenoxide) (ratios of **2**:**3** (R = Me) = 3:2 and 2:1, respectively).

In a similar manner, the type II intramolecular ene reactions of α-substituted aldehydes, **4** and **5**, possessing trisubstituted double bonds under the influence of MABR gave rise exclusively to the desired alcohols, **6** and **7**, respectively, with excellent stereoselectivity.[4]



The stereochemical outcome in the present intramolecular ene reactions can be explained by the work of Snider,[2] in which the α-alkyl substituent of **1** selectively adopts the equatorial and axial conformations, **8** and **9**, in the transition states leading to the cis and trans alcohols, **2** and **3**, respectively. Here the carbonyl groups of **8** and **9** always occupy the axial conformations. However, the stereochemistry of **6** and **7** cannot be interpreted by the transition





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(4) The stereochemistry of **6** and **7** was tentatively assigned by 500-MHz ^1H NMR analysis. Furthermore, the authentic samples of the hydrogenated **6** and **7** were independently synthesized.

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