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EPR Chiral Discrimination of *R*- and *S*-Anion Radicals

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Electron paramagnetic resonance spectroscopy has been used to discriminate between the *R*- and *S*-forms of the anion radical of camphorquinone. In a chiral solvent [*SS*- or *RR*-2,3-dimethoxy-1,4-bis(dimethylamino)-butane saturated with sodium iodide], ion association between the semidione and Na$^+$ takes place. PM3 calculations suggest that the complex relationship between the solvent, anion, and cation varies sufficiently with changes in the chiral nature of the solvent or anion radical to alter the appearance of the EPR signal allowing EPR chiral discrimination.

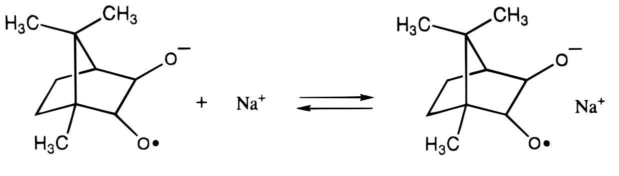
Introduction

The first recognition of chiral isomers by EPR has been recorded. Since Pirkle's earliest studies demonstrating the possibility of distinguishing enantiomers via the use of NMR with chiral shift reagents,[1] NMR has been routinely used for the determination of enantiomeric composition.[2,3] Such NMR studies cannot be extended to radical species owing to the fact that radicals are normally not amenable to NMR studies because of the large gyromagnetic ratio (γ) of an electron ($\gamma_e/\gamma_{1H} \cong 500$), which leads to exceedingly short T_2's and consequent extreme line broadening. EPR is clearly the most important tool in the study of ion radicals, and it has an analogous relationship to the electron that NMR has to the nucleus. In despite of this, spectroscopists have yet to utilize EPR techniques to investigate the chirality of ion radicals.

Chiral shift reagents perturb the NMR chemical shifts of enantiomers differently allowing for chiral resolution. The EPR parameter analogous to the chemical shift is the *g*-value, which is a function of spin−orbit coupling. Hence, an EPR chiral shift reagent that leads to a perturbation in the spin−orbit coupling should lead to EPR chiral recognition.[4] The spin density on sp^2-hybridized oxygen atoms can be altered (hence altering the spin−orbit coupling and, consequently, the *g*-value) via ion association.[5] We were motivated to see if an alteration of the chirality of an anion radical in a enantiomerically pure solvent would perturb the ion association characteristics sufficiently to lead to an observable change in the *g*-value.

Results and Discussion

EPR analysis of a 0.018 M solution of *R*-camphorquinone reduced with sodium *tert*-butoxide in *S*,*S*-(+)-2,3-dimethoxy-1,4-bis(dimethylamino)butane (*SS*-DDB) yields the well-resolved EPR spectrum previously observed in dimethyl sulfoxide.[6] The addition of the NaI to the anion radical solution results in broadening of the hyperfine components owing to the rapid formation and dissociation of ion-associated semidiones, reaction 1.



(1)

Ion association pulls charge and spin density into the oxygen atoms, where the spin−orbit coupling is greater. Hence, the ion-associated species has a smaller effective *g*-value and a slightly different set of coupling constants than does the unassociated ion radical causing the line broadening to be asymmetrical.[7] In this case (the *R*-semidione in the *SS*-solvent), the low-field lines experience more broadening owing to reaction 1 than do the high-field lines, Figure 1. However, in the case of the *S*-semidione in the same (*SS*) solvent, the reverse is true; the high-field lines are broader than the low-field lines. The differences in the broadening characteristics are due to the EPR chiral discrimination of the semidiones in a chiral solvent (solvent−ion pair chiral recognition). Consistent with this interpretation is the fact that the EPR spectrum of the *S*-semidione in the *RR*-solvent is identical to that of the *R*-semidione in the *SS*-solvent (low-field lines broader), and the spectra of the *R*-semidione in the *RR*-solvent is identical with that of the *S*-anion radical in the *SS*-solvent (high-field lines broader, Figure 1).

Analogous to Mislow and Raban's realization that the interaction of chiral solute molecules with a chiral NMR shift reagent transforms the previous enantiotropic relationships of nuclei into diastereometric ones,[8] the interaction of the chiral solvated cation with the chiral radical results in diasteriometric interactions. The differences in the *g*-values and coupling constants are generated by diasteriotopic solvated ion pairs that form and dissociate rapidly on the EPR time scale, leading to the asymmetry in the spectrum.

Simply to demonstrate a possible mechanism for these EPR observations, PM3 calculations were carried out on the Li$^+$-ion-associated camphorquinone anion radical, where the cation is solvated by a single solvent molecule. The Merck force field was used to obtain a starting geometry of the camphor semidione. The Li$^+$ was then placed equidistant in the plane between the two oxygens, and the geometry was again optimized utilizing the UHF/PM3//UHF/PM3 basis set.[9] This process yielded a structure where the cation is nearly equal distance (2.0101 and 2.0131 Å) from the two oxygens when the *S*-radical is in the *SS*-solvent. Simply moving the methyl group of the radical to the opposite side of the norbornyl moiety (thus changing the chirality of the radical) results in the cation being 0.02 Å closer to the oxygen on the methyl side (2.0221 vs 2.0019 Å).

A significant difference in the EPR experiments described here and the use of NMR chiral shift reagents comes from the

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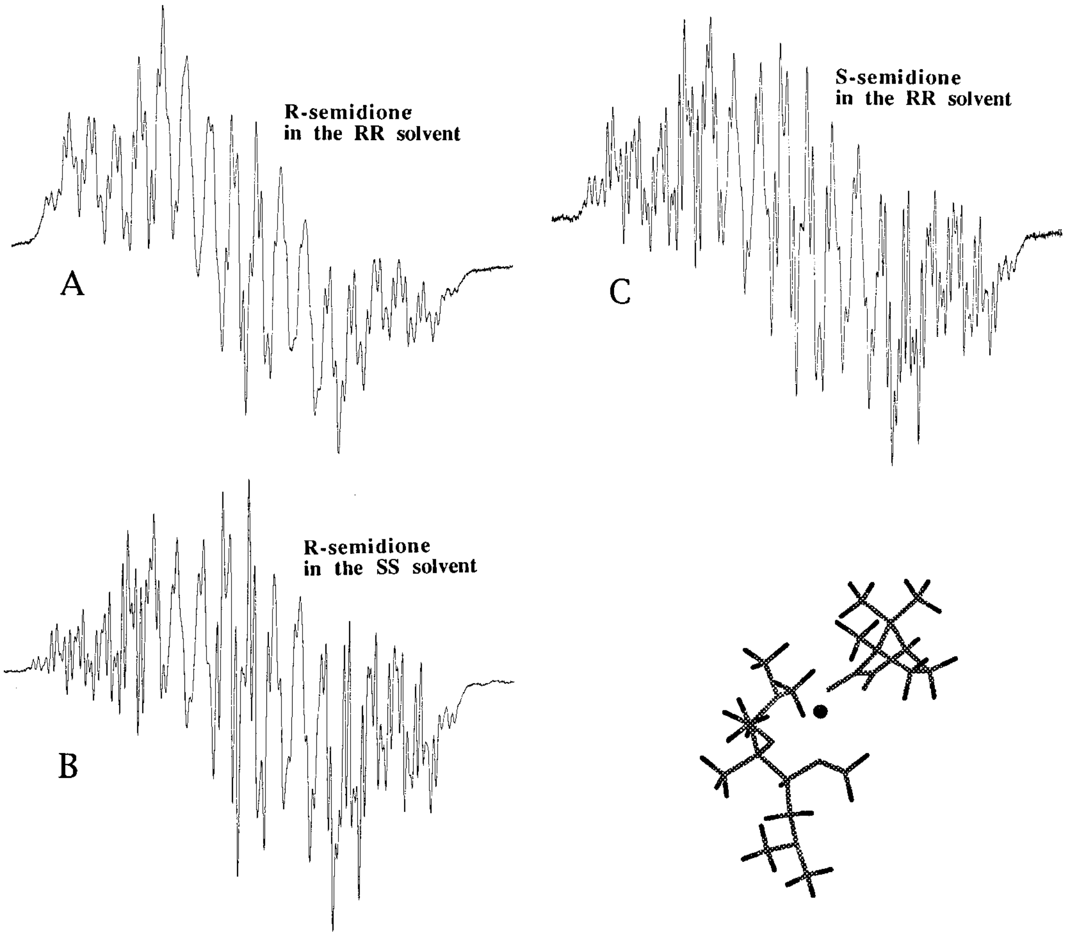

Figure 1. EPR spectra of the *R*- and *S*-chiral isomers of the camphorquinone anion radical in the *RR*- and *SS*-isomers of DDB saturated with sodium iodide. Note that the low-field lines experience less line broadening than do the high-field lines in spectrum A, while the reverse is the case in spectra B and C. This asymmetry in the spectra arises from the differing *g*-values and coupling constants of the ion-associated and fully solvated species. In spectrum A, the differences in line positions are additive in the high-field region and subtractive in the low-field portion of the spectrum. The reverse is true in spectra B and C. Spectrum A has a total spectral width of 13.0 G. (Lower right) Structure for the *R*-camphorsemidione interacting with a lithium ion in the presence of one molecule of *SS*-DDB predicted by a UHF/PM3 calculation.

fact that the EPR chiral shift reagent is the solvent itself. However, only enough solvent to fill a 3 mm EPR tube to about 2 cm (100 μL) is required for a chirality determination. Interestingly, the EPR spectrum of the *R*-semidione appears as the phase-reversed mirror image of the EPR spectrum of the *S*-semidione in the same chiral solvent, and we foresee that similar effects will be observable for a host of other ion radicals and chiral solvents. We are currently involved in experiments to test these predictions.

Experimental Section

EPR samples were prepared by adding 0.018 mmol of camphorquinone, 0.50 mmol of NaI, and 0.094 mmol of sodium *tert*-butoxide to a small bulb with an attached 3 mm EPR sample tube. This bulb was subsequently evacuated. One milliliter of *SS*-DDB or *RR*-DDB was then distilled from a vessel containing potassium metal directly onto this mixture while maintaining high vacuum. The resulting solution was then poured into the attached EPR sample tube and submitted to EPR analysis. All EPR spectra were recorded on a Bruker EMX 6/1 x-band EPR spectrometer with the following settings: modulation amplitude = 0.05 G, power = 0.20 mW, and a 16 G sweep width.

Conclusions

Perturbations in the EPR observed *g*-value of anion radicals owing to the chirality of the ion radicals have been observed in chiral environments. This is analogous to the observed perturbations in NMR chemical shifts in the presence of chiral shift reagents. These preliminary results suggest that, with future developments, EPR can become a valuable tool for the recognition of ion radical chirality as NMR presently is for diamagnetic materials.

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