An EPR and NMR Study of Supramolecular Effects on Paramagnetic Interaction between a Nitroxide Incarcerated within a Nanocapsule with a Nitroxide in Bulk Aqueous Media

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Cram introduced the concept of guest incorporation within a carcerand (guest@carcerand) as a means of taming a guest-reactive ground-state intermediate, such as cyclobutadiene in a host carcerand.[1] Guest@carcerand complexes provide an opportunity to investigate the behavior of both incarcerated ground-state and excited-state guest molecules in a distinct, stable, well-characterized molecular environment that is analogous to a fleeting solvent cage of nonviscous solvents. In pioneering studies involving energy and electron transfer processes, it has been demonstrated that incarcerated molecules in their electronically excited states can communicate through the walls of a carcerand with molecules in external bulk solvent.[2] The incarcerated guests were found to be able to interact with molecules outside the complex with rate constants considerably smaller than those found for free guest in solution. That such interactions occur at all is the result of the overlap of the orbitals of the incarcerated guest with the orbitals of molecules present outside (through the carcerand's orbitals). Such electronic communication through orbitals is termed "superexchange". The superexchange phenomenon is also well-known in nuclear and electronic spin spectroscopy.[3] Enabled by employing a ^{15}N-labeled incarcerated nitroxide and a ^{14}N-labeled free nitroxide in the external aqueous phase, we report here an example of the simultaneous observation, by EPR spectroscopy, of the electron spin−spin superexchange between an incarcerated paramagnetic nitroxide molecule and a nitroxide molecule present in the external aqueous phase. In addition to observation of electron spin−spin interactions, the EPR data provide direct information on the motion and the polarity of a ^{15}N-labeled incarcerated guest and ^{14}N-labeled free molecule in the bulk solvent. We also show how this communication between an incarcerated guest and molecules in the bulk solvent can be controlled by supramolecular factors such as Coulombic attraction and repulsion between a charged guest@host complex and charged molecules in the bulk aqueous phase. Finally, we present evidence for complex formation through paramagnetic NMR relaxation experiments that involve electron spin−nuclear spin interactions.

Chart 1 provides the structures of the guests and host investigated in this report. The host, termed "octa acid" (OA), is well-known to incarcerate nonpolar guest molecules under basic conditions in water (borate buffer, pH = 9).[4] Addition of 0.5 equiv of BP-[14]T to OA (1 mM in 10 mM buffered D_2O) leads to paramagnetic NMR broadening of all host inner proton signals but leaves the external methylene signals of the propanoic chains unaffected (Figure 1a; for peak assignments, see Supporting Information, Figures S4 and

Chart 1. Structures of Guest Molecules and Host
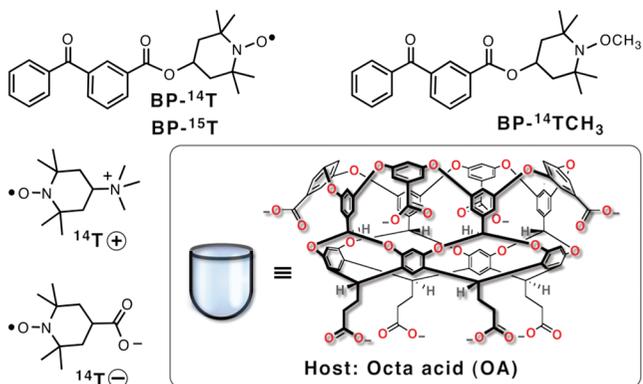
S8), a signature of the formation of a BP-[14]T@OA complex. Complexation was confirmed by the NMR of the diamagnetic BP-[14]TCH₃, a molecule similar in size and shape to that of BP-[14]T (Chart 1). In the latter case, all methyl signals of BP-[14]TCH₃ appeared at negative δ, characteristic of guest inclusion within an aromatically rich cavity and only a small broadening (expected from the larger molecular weight of the complex) of the proton signals of OA was observed. The stoichiometry of the complexes was found to be 1:2 (guest:host) by ^{1}H NMR titrations [BP-[14]T@(OA)₂ and BP-[14]TCH₃@(OA)₂].

Figure 1 (left) shows the NMR spectra of (a) BP-[14]T@(OA)₂, (b) [14]T⊕ + BP-[14]TCH₃@(OA)₂, and (c) [14]T⊖ + BP-[14]TCH₃@(OA)₂, in aqueous solution (for peak assignments, see Supporting Information, Figures S8 and S9). The decrease in the line broadening in going from (a) to (b) to (c) is a signature of changes in the effective nitroxide paramagnetic relaxation of the protons of OA in the complex as a result of the supramolecular structures and Coulombic interactions of the system. The least broadening occurs for (c), where Coulombic repulsions inhibit approach of the external negatively charged nitroxide and the complex; greater broadening occurs for (b), where Coulombic attractions encourage the approach of the external nitroxide and the complex; and the greatest broadening occurs for (a), for which the nitroxide is the guest in the complex.

Figure 1 (right) shows the EPR spectra of (d) BP-[14]T@(OA)₂, (e) the diamagnetic complex BP-[14]TCH₃@(OA)₂ + [14]T⊕, and (f) the diamagnetic complex BP-[14]TCH₃@(OA)₂ + [14]T⊖. The rotational correlation times, τ_c, are a measure of the rotational mobility of the nitroxide probe, and the hyperfine coupling, a_N, measures the environmental polarity.[5] These parameters were obtained by computer simulation of the experimental spectra (Supporting Information, Figure S12 and Table S1). For BP-[14]T@(OA)₂, an

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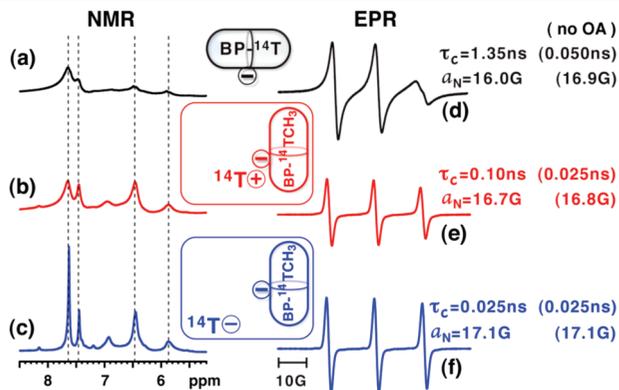
Figure 1. ^{1}H NMR (left) and EPR (right) spectra of guest@host systems in the absence (a,d) and presence of a positively charged (b,e) or negatively charged (c,f) external guest in aqueous buffer solution (pH = 9) at 22 °C. [OA] = 2 mM; [guest] = 1 mM. The correlation times (τ_c) and hyperfine coupling constants (a_N) are given for the EPR spectra (values in brackets are in the absence of OA).

increase in correlation time, τ_c, from 0.050 to 1.35 ns was observed after addition of OA (Figure 1d), which is consistent with the reduced mobility of BP-^{14}T inside the OA cavity. In addition, the coupling constant, a_N, decreased from 16.9 to 16.0 G upon inclusion within OA. Such a change is consistent with the interior of the cavity being nonpolar,[5] an observation recently reported with pyrene as a probe.[4d] The differences in the above two parameters, τ_c and a_N, in the presence and absence of OA confirm that the probe BP-^{14}T is present within the OA capsule. The correlation times and the hyperfine coupling for ^{14}T⊕ and ^{14}T⊖ in water are identical (~0.025 ns and ~17 G) within the experimental error and correspond to essentially free rotation in a polar aqueous environment. The correlation time of ^{14}T⊕ shows a significant increase by a factor of ~4 after addition of BP-^{14}TCH$_3$@(OA)$_2$ (Figure 1e), indicating an interaction between the complex [BP-^{14}TCH$_3$@(OA)$_2$] and ^{14}T⊕. In contrast, the value of τ_c for the system BP-^{14}TCH$_3$@(OA)$_2$ + ^{14}T⊖ (Figure 1f) shows no significant variation in correlation time from the free ^{14}T⊖, indicating no significant interaction between the two.

Figure 2 (top) shows the spectrum of BP-^{15}T@(OA)$_2$ in the presence of ^{14}T⊕ (red spectrum) and the sum of the individual spectra (black dashed spectra) of BP-^{15}T@(OA)$_2$ and ^{14}T⊕ [in the presence of the diamagnetic complex BP-^{14}TCH$_3$@(OA)$_2$]. By visual inspection, it can be seen that the spectrum of the BP-^{15}T@(OA)$_2$ + ^{14}T⊕ system has significantly more broadening than the sum of the individual spectra, which is indicative of electron spin−electron spin interaction. In addition to the broadening, about 20% reduction in EPR signal intensity of BP-^{15}T@(OA)$_2$ + ^{14}T⊕ was observed, which indicates strong spin−spin interaction. This result contrasts with the spectra in Figure 2 (bottom), which show the system with the negatively charged external guest (^{14}T⊖). In this case, both spectra are superimposible on the sum of the individual spectra, indicating no significant spin−spin interaction occurs.

At pH = 9, the OA complex is negatively charged as a result of the ionization of its carboxylic acid groups. Thus, for the system BP-^{15}T@(OA)$_2$ + ^{14}T⊕, there will be an attractive interaction between BP-^{15}T@(OA)$_2$ and the external ^{14}T⊕ nitroxide molecule in the bulk aqueous phase. On the other hand, for the system BP-^{15}T@(OA)$_2$ + ^{14}T⊖, there will be a repulsive interaction between
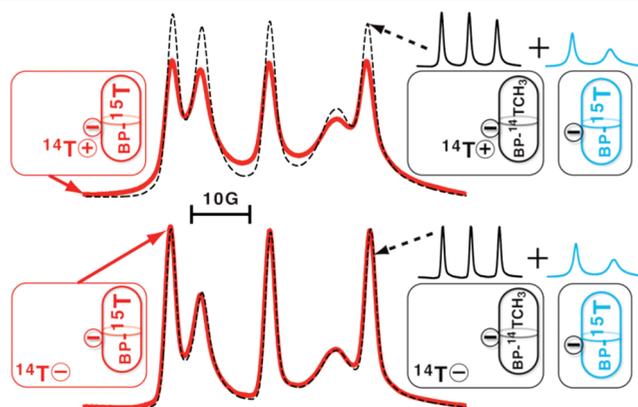
Figure 2. Integrated EPR spectra of BP-^{15}T@(OA)$_2$ in the presence (red lines) of positively charged external guest (top) and negatively charged external guest (bottom). The dashed black lines represent the sum of the integrated EPR spectra (insets) of BP-^{15}T@(OA)$_2$ in the absence of external guest and the integrated EPR spectrum of the external guest (top ^{14}T⊕, or bottom ^{14}T⊖) and diamagnetic complex BP-^{14}TCH$_3$@(OA)$_2$. [guest] = 1 mM; [OA] = 2 mM.

the BP-^{15}T@(OA)$_2$ and the external ^{14}T⊖ nitroxide molecule present in the bulk aqueous phase. As a result, we would expect greater and more effective spin−spin interactions for the BP-^{15}T@(OA)$_2$ + ^{14}T⊕ system than for the BP-^{15}T@(OA)$_2$ + ^{14}T⊖. Results presented in Figure 2 are consistent with this expectation.

In conclusion, several important supramolecular and electron spin effects are demonstrated clearly in this report: (1) spin−spin interactions can be significant between two nitroxides, even when one is protected by the walls of a host cage; (2) spin−spin interactions can be enhanced by supramolecular binding resulting from Coulombic attractions or inhibited via Coulombic repulsions; and (3) paramagnetic nuclear relaxation of guest and internal relaxants can be employed to elucidate supramolecular interactions and structures.

Supporting Information Available: Experimental details, NMR analysis of complexes, and EPR simulations. This material is available free of charge via the Internet at http://pubs.acs.org.

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