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Alkoxycyclooctatetraene Anion Radicals: An Unusual Spin Density Perturbation Due to 1,3-Carbon/Carbon Interactions

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A series of new alkoxycyclooctatetraene ethers was synthesized and their anion radicals generated in hexamethylphosphoramide. The EPR measured spin densities can be explained in terms of the odd electron occupying MOs, $\Psi_4' = [1/2\sqrt{(n^2+1)}](n\psi_1 + \psi_2 - n\psi_3 - \psi_4 + n\psi_5 + \psi_6 - n\psi_7 - \psi_8)$ and $\Psi_5' = [1/2\sqrt{(n^2+1)}](n\psi_1 - \psi_2 - n\psi_3 + \psi_4 + n\psi_5 - \psi_6 - n\psi_7 + \psi_8)$, where n increases with the electron-releasing nature of the alkoxy group. The anion radicals of *n*-propoxycyclooctatetraene and ibuprofoxycyclooctatetraene exhibit a small (ca. 0.35 G) splitting for the γ proton on the sp^3 hybridized carbon. Further, the EPR pattern for the *tert*-butoxycyclooctatetraene anion radical is consistent with a relatively smaller value for n (in Ψ_4' and Ψ_5'). These observations are consistent with a rather unusual homohyperconjugative interaction involving overlap of the σ-bond to the γ-hydrogen and the π-system of the conjugated COT ring.

Introduction

There is only one available annulene with all external protons and $4n$ π-electrons (antiaromatic in the Huckel sense), rendering the addition and subtraction of π-electrons from this system of intense experimental and theoretical interest.[1] Consequently, one of the first[2] and most intensely studied open-shell systems is represented by the radical anion of cyclooctatetraene (COT).[3] The EPR spectrum of this system was first reported almost 40 years ago, and it reveals that the unpaired spin density is distributed equally over the eight-membered ring.[2] The eight equivalent protons have a coupling constant of −3.209 G, which is well within the range expected for a planar anion radical.[2,4] Calculation[4] and experiment[2,3,5,6] also agree that, unlike the tub-shaped neutral COT,[7] the radical anion (COT$^{-\bullet}$) is planar. The necessary Jahn-Teller distortion from D_{8h} symmetry[8] comes from a b$_{2g}$ distortion leading to a pair of rapidly interconverting D_{4h} equilibrium geometries with alternating bond lengths (Figure 1).[4]

There are three electrons in the nonbonding molecular orbitals of COT$^{-\bullet}$, which constitute Ψ_4 and Ψ_5 in eqs 1 and 2. Ψ_4 and Ψ_5 simply represent

$$\Psi_4 = (0.5/\sqrt{2})(\psi_1 + \psi_2 - \psi_3 - \psi_4 + \psi_5 + \psi_6 - \psi_7 - \psi_8) \quad (1)$$

$$\Psi_5 = (0.5/\sqrt{2})(\psi_1 - \psi_2 - \psi_3 + \psi_4 + \psi_5 - \psi_6 - \psi_7 + \psi_8) \quad (2)$$

the 1:1 linear combinations of the NBMOs for the D_{4h} equilibrium geometries with alternating bond angles (eqs 3 and 4).[4] That is, $\Psi_4 = (\Phi_4 + \Phi_5)/\sqrt{2}$ and $\Psi_5 = (\Phi_4 - \Phi_5)/\sqrt{2}$.

$$\Phi_4 = (1/2)(\psi_1 - \psi_3 + \psi_5 - \psi_7) \quad (3)$$

$$\Phi_5 = (1/2)(\psi_2 - \psi_4 + \psi_6 - \psi_8) \quad (4)$$

Although the b$_{1g}$ distortion (Figure 1) to yield the D_{4h} symmetry with alternating bond angles is allowed, CI calculations suggest that the b$_{2g}$ distortions are preferred by some 4−5 kcal/mol.[4] This theoretical suggestion is in agreement with INDO calculations carried out a dozen years ago.[9]

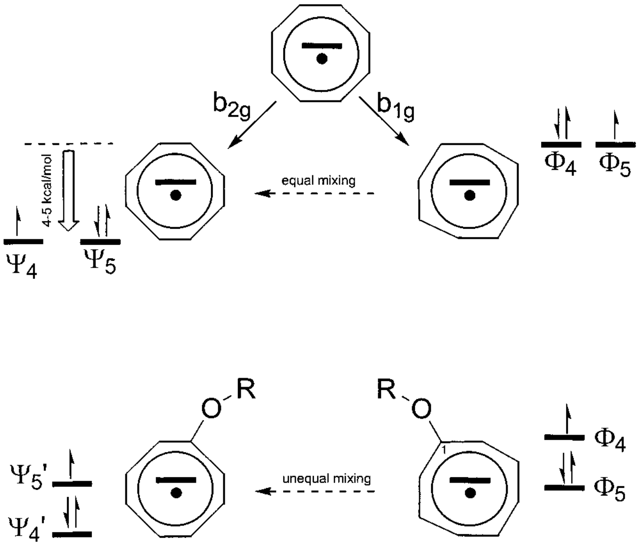

Figure 1. Pictorial representation of the Jahn-Teller distortion of D_{8h} COT anion radical to the bond length alternating and bond angle alternating D_{4h} geometries. The alternating bond length geometry is the more stable form, and its wave functions are generated via the equal mixing of the two LCAOs for the alternating bond angle geometry. Below is the analogous representation for the unequal mixing of Φ_4 and Φ_5 for an alkoxy-substituted system.

The addition of an electron-donating substituent at position 1 raises the energy of Φ_4 while not perturbing Φ_5, which has a node at position 1. This splitting of the degeneracy of Φ_4 and Φ_5 means that there is no longer equal mixing of Φ_4 and Φ_5. Thus, the resulting MOs for the substituted COT, with alternating bond lengths, have unequal coefficients. Since there are three nonbonding electrons, the odd electron resides in Ψ_4' and Ψ_5' (eqs 5 and 6 where $n > 1$). The distribution of the odd electron in Ψ_4' and Ψ_5' results in a large EPR coupling constant for the protons in positions 3, 5, and 7 ($a_{\mathrm{H(odd)}}$) and a small a_{H} for those in positions 2, 4, 6, and 8 ($a_{\mathrm{H(even)}}$). Larger values of n

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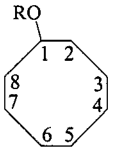
correspond to larger differences in the a_Hs.

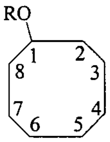
$$\Psi_4' = (n\Phi_4 + \Phi_5)/\{2\surd(n^2 + 1)\} = [1/2\surd(n^2 + 1)](n\psi_1 + \psi_2 - n\psi_3 - \psi_4 + n\psi_5 + \psi_6 - n\psi_7 - \psi_8) \quad (5)$$

$$\Psi_5' = (n\Phi_4 - \Phi_5)/\{2\%(n^2 + 1)\} = [1/2\surd(n^2 + 1)](n\psi_1 - \psi_2 - n\psi_3 + \psi_4 + n\psi_5 - \psi_6 - n\psi_7 + \psi_8) \quad (6)$$

All of this implies that the orbital in which the electron resides depends on the geometry of the system. That is, whether Ψ_4 or Ψ_5 is lower in energy depends on the geometry of the system (structures **I** and **II**). For structure **I**, Φ_4 is higher in energy than is Φ_5. Consequently, Φ_5 contributes more to the bonding MO, and $\Psi_4' = N(\Phi_4 + n\Phi_5)$, with $n > 1$. Ψ_4' is lower in energy than is Ψ_5', which is antibonding at this geometry. The antibonding orbital has a larger contribution from Φ_4, with $\Psi_5' = N(n\Phi_4 - \Phi_5)$. Three electrons occupy Ψ_4' and Ψ_5', leaving Ψ_5' singly occupied. Because Ψ_5' has a larger contribution from Φ_4, the single electron is more localized on carbons 1, 3, 5, and 7.



I



II

This theoretical model predicts that monosubstituted COTs with very strong electron-donating substituents will yield a negligible $a_{H(even)}$, and as n approaches infinity, $\Psi_5' = \Psi_4' = (1/2)(\psi_1 - \psi_3 + \psi_5 - \psi_7)$. This situation is not realized in practice, as these systems actually exhibit small negative π-electron densities at carbons 2, 4, 6, and 8. These, in turn, correspond to small positive 1s spin densities and a small positive $a_{H(even)}$.

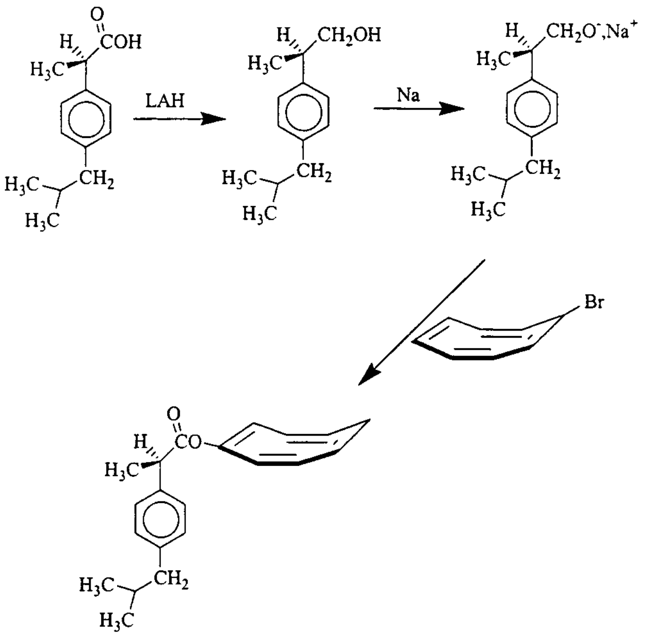
The model outlined above contrasts significantly with another model (previously used by us and others)[10] wherein the alternating small and large couplings observed in substituted COTs are explained in terms of a Boltzmann distribution of the odd electron in Φ_4 and Φ_5. In our course of studying physiologically active drugs connected to COT anion radicals via an ether linkage, we found an interesting 1,3 carbon/carbon interaction between the sp^3 hybridized carbon next to the oxygen (the alkoxy carbon) and the COT ring system. This nonclassical interaction perturbs spin distribution and solution electron affinity of the alkoxy−COT$^{\bullet-}$, and it clearly supports the quantum mechanical model put forth by Borden and coworkers,[4] detailed above.

Results and Discussion

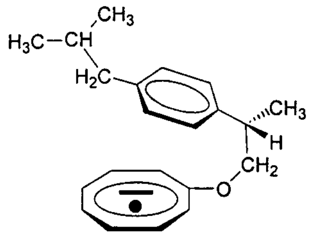
Ibuprofen was reduced to the alcohol (ibuprofenol) with lithium aluminum hydride. The corresponding sodium alkoxide was then reacted with monobromocyclooctatetraene to yield the ibuprofoxycyclooctatetraene (ibu-O-COT) system (Scheme 1). The only previously reported alkoxycyclooctatetrene system is *tert*-butoxycyclooctatetraene (*t*-but-O-COT).[10a−c]

The anion radicals of ibu-O-COT and of *n*-propoxycyclooctatetraene (*n*-prop-O-COT) exhibit nearly (but not quite) identical EPR signals. Lithium reduction of *n*-prop-O-COT in HMPA yields the corresponding anion radical, free of ion association,[11] and EPR analysis exhibits a quartet ($a_{H(odd)} = 5.64$ G, 3 Hs) of pentets ($a_{H(even)} = 0.68$ G, 4 Hs), consistent with the quantum mechanical model. Surprisingly, there is an additional splitting of 0.35 G from two equivalent γ-protons on the sp^3 hybridized carbon connected to the oxygen atom (the alkoxy carbon). Identical spectra are recorded whether the reduction is carried out with ^{7}Li or with ^{6}Li, and replacing the two γ protons with deuteriums results in the loss of the 0.35 G splitting (Figure 2).

SCHEME 1



The anion radical of ibu-O-COT, generated in an analogous manner, is described by a quartet of pentets with a_Hs of 5.71 and 0.68 G, respectively (Figure 2). Like the anion radical of *n*-prop-O-COT, ibu-O-COT$^{\bullet-}$ exhibits a splitting of 0.33 G for the γ protons. The EPR patterns for ibu-O-COT$^{\bullet-}$ and *n*-prop-O-COT$^{\bullet-}$ are strikingly similar, differing mainly in the magnitude of a_H for the pentet. UPM3 calculations suggest that this 0.07 G difference is due to a weak interaction between the π systems of the benzene ring and the COT$^{\bullet-}$ ring as in structure **II**.



II

Alkylation of two of the positions on the alkoxy carbon (as in the cases of isoprop-O-COT$^{\bullet-}$ and methylcyclohexoxy−COT$^{\bullet-}$) causes a loss of the splitting from the γ-proton, a small increase in $a_{H(even)}$ and a small decrease in $a_{H(odd)}$. When the third position is alkylated (as in the case of *t*-but-O-COT$^{\bullet-}$), a rather dramatic decrease in the large splitting and increase in the small splitting is observed (Figure 3).

The presence of the third alkyl group on the sp^3 alkoxy carbon blocks the 1,3-homohyperconjugative carbon/carbon interaction between the alkoxy carbon and carbon 1 on the COT ring (Figure 4). Also, the bulky *tert*-butyl group makes it more difficult for the carbon−oxygen bond to lie in the plane of the ring, thus causing the 2p atomic orbital on the oxygen to twist further out of alignment with the p-π atomic orbital of C$_1$. Hence, the bulky *tert*-butoxy group is a less efficient electron donor.

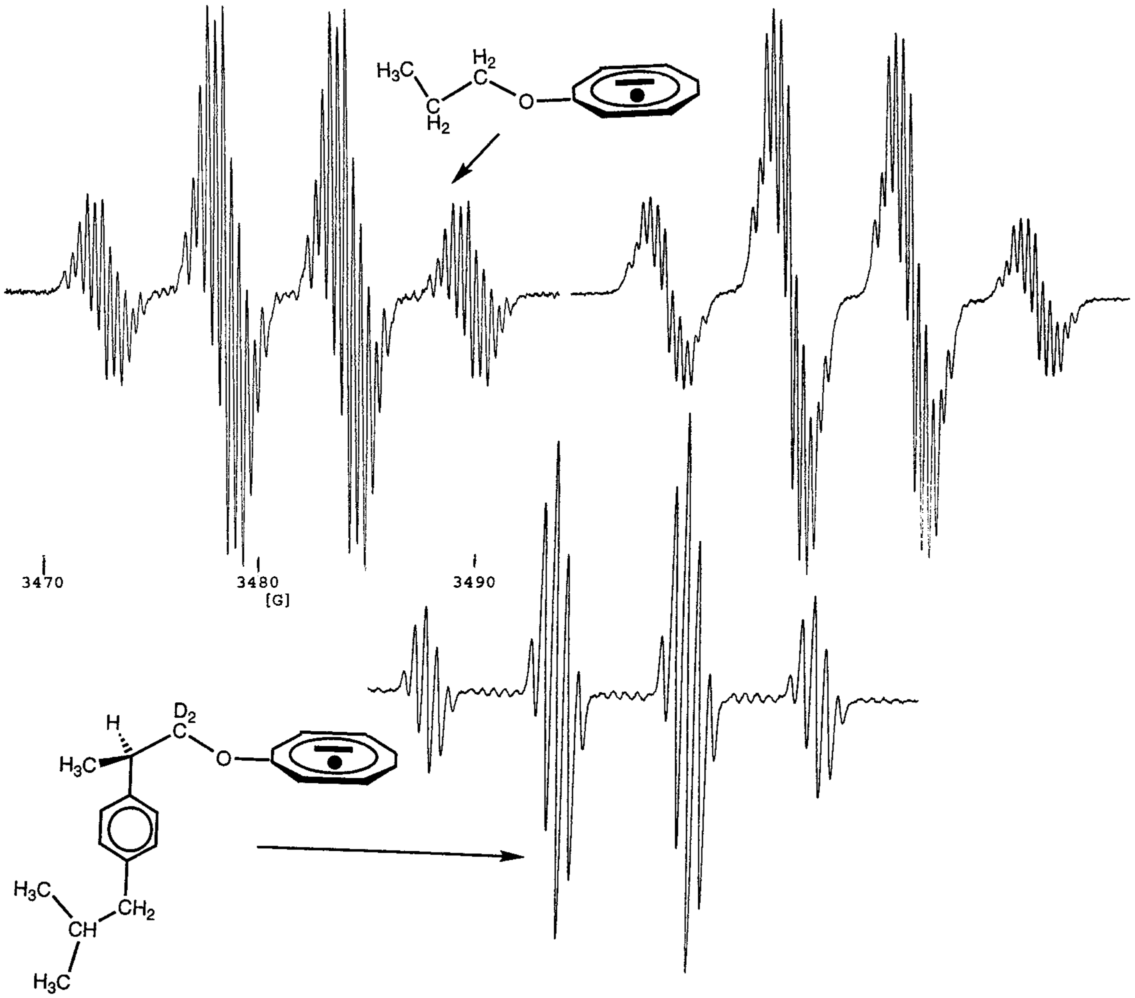


Figure 2. (upper left) EPR spectrum of the *n*-propoxycyclooctatetraene anion radical recorded in HMPA at 298 K. Note the splitting due to the γ protons. (upper right) The ibuprofoxycyclooctatetraene anion radical yields a very similar spectrum. Below is the spectrum recorded for the ibuprofoxycyclooctatetraene-d_2 system. The γ splitting is now absent, as the γ protons are replaced by two deuteriums.

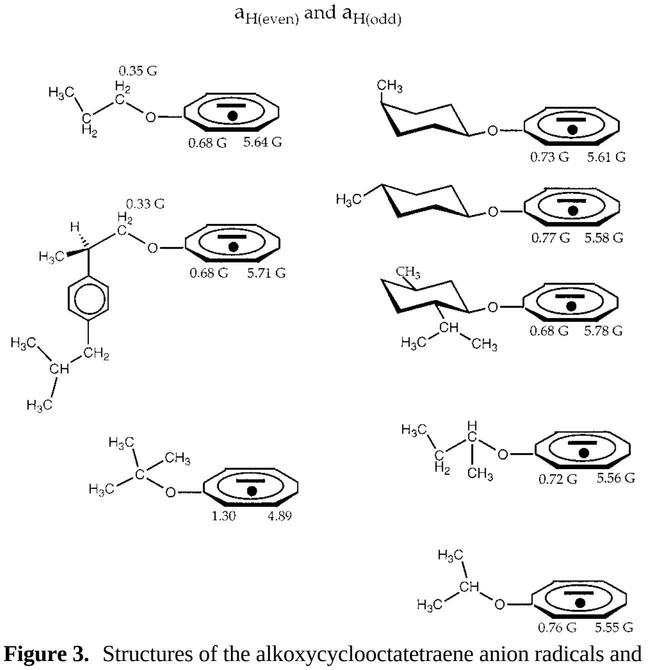


Figure 3. Structures of the alkoxycyclooctatetraene anion radicals and the respective EPR coupling constants ($a_{H(even)}$ and $a_{H(odd)}$) observed in HMPA at 298 K.

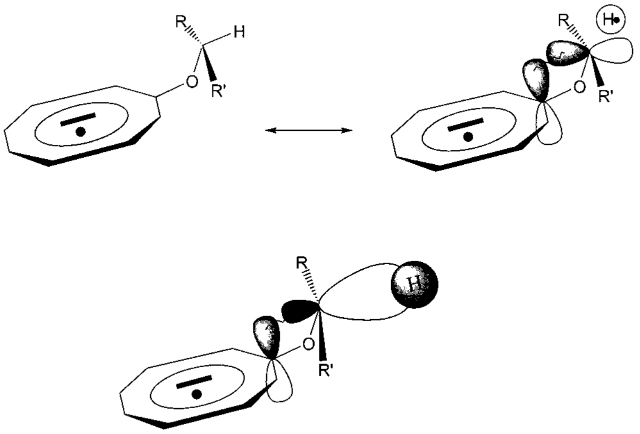


Figure 4. (upper) Valence bond type representation of the homohyperconjugative interaction whereby spin is transmitted to a γ proton. (lower) MO model depicting the overlap of the back lobe of the σ bond (with a little sp^2 character) with the ring π-system. This describes the transmission of spin in terms of an MO approach.

The 1,3-homohyperconjugative carbon/carbon interaction was first described by Bauld and Cessac,[12] wherein they pointed out how it can perturb spin densities as measured by EPR hyperfine couplings. The γ-proton a_H is proportional to the spin density on C_1 (ρ_1). The hyperconjugative interaction between the eight-membered ring and the alkoxy carbon results in augmentation of the mixing bias (Φ_5 over Φ_4) and an increase in *n* (eqs 5 and 6). This may also, along with the steric consideration (mentioned above), contribute to a larger difference between

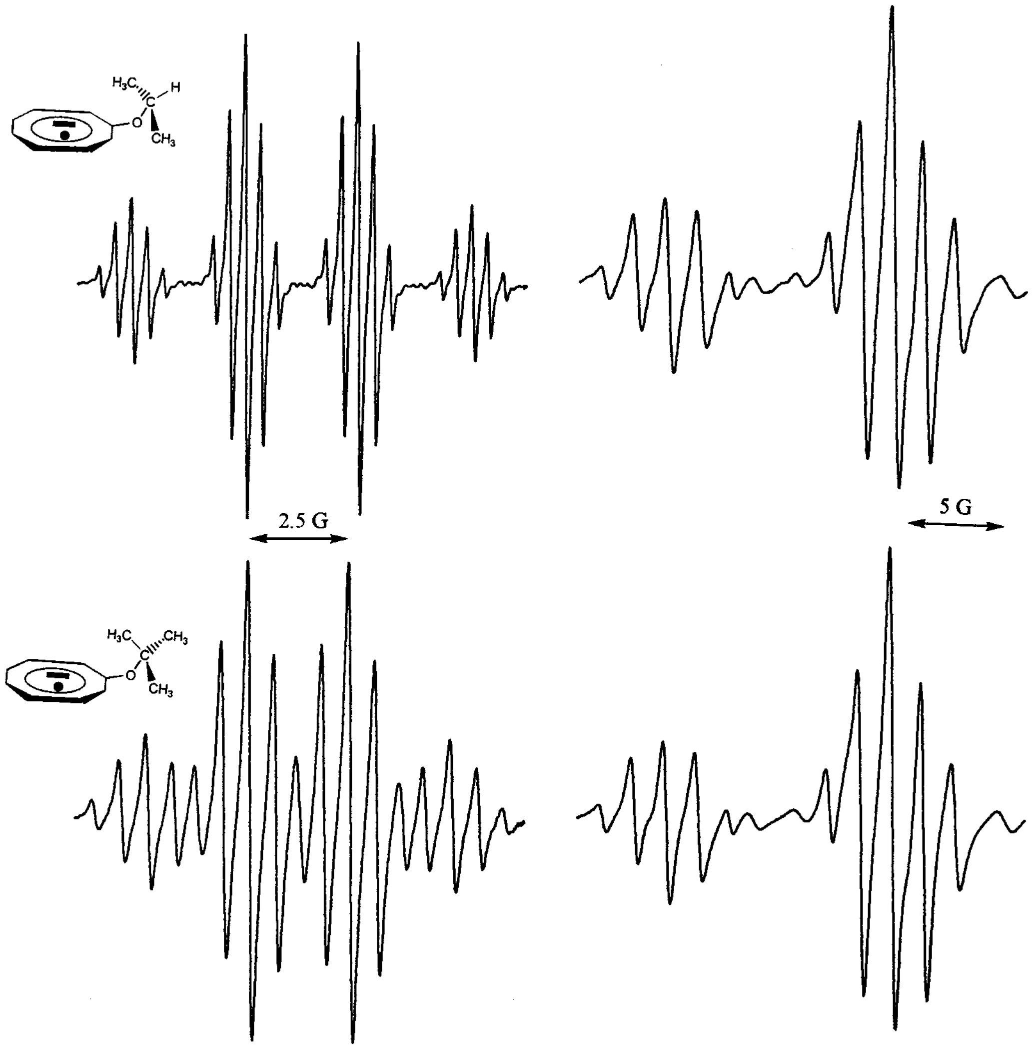
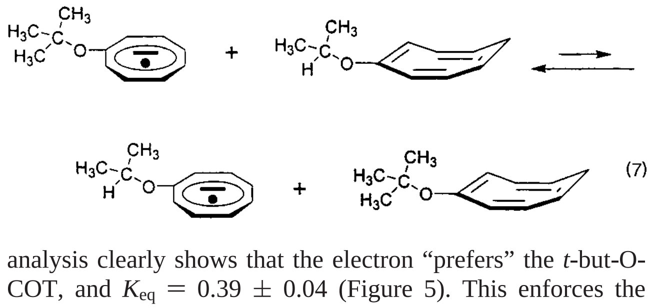


Figure 5. (upper right) Low-field portion of the EPR spectrum recorded from an HMPA solution of a 5.17:1 molar mixture of isopropoxycyclooctatetraene and *tert*-butoxycyclooctatetraene reduced by a very deficient amount of lithium metal. (lower right) Computer simulation generated using a ratio of anion radical equal to 2.0:1. This implies K_{eq} for reaction 8 is 0.39. On the left are shown the EPR spectra for isoprop-O−COT$^{\bullet -}$ (upper) and *t*-but-O−COT$^{\bullet -}$ (lower).

$a_{H(even)}$ and $a_{H(odd)}$. The steric factor, and possibly the inhibited 1,3-interaction, imply a larger value for n in eqs 5 and 6. The a_Hs listed in Figure 3 suggest that n is 1.95 and 2.70 for the *t*-but-O-COT and isoprop-O-COT systems, respectively, if all of the coupling constants are negative. We do not, however, have a way to establish the sign of a_H.

There is some modification of the angle between the γ C−H σ bond and the ring p orbital (θ) due to alkylation of the alkoxy carbon (Figure 4). Since the γ-splitting is small and is proportional to $\cos^2 \theta$,[12] a relatively small increase in this angle can result in this splitting being lost in the line width.The anion radicals of *cis*-4-methylcyclohexoxycyclooctatetraene and of *trans*-4-methylcyclohexoxycyclooctatetraene are nearly identical but differ slightly (Figure 3). It is clear that even this small alteration of structure, far from the COT moiety, can yield some changes in the a_Hs. This is probably just a result of some solvent reorganization, as a PM3 calculation carried out on the *cis*- and *trans*-4-methylcyclohexoxycyclooctatetraene predicts no intrinsic difference in the a_Hs. However, a larger alkyl group placed in the 2 position of the cyclohexyl moiety creates some steric interaction with the COT ring system, and a much larger perturbation in the COT ring a_Hs is observed. The difference between $a_{H(even)}$ and $a_{H(odd)}$ is considerably larger for the menthoxycyclooctatetraene system (Figure 3).

If, indeed, the homohyperconjugative carbon/carbon interaction is present in the dialkylated alkoxy carbon systems, the normal σ-electron-donating character of the alkoxy group would gain some π-electron-donating character. Since it has been established that increased electron-donating character of a substituent on COT does, indeed, lower the respective solution EA,[10d] the solution EA of isoprop-O-COT should be lower than that of *t*-but-O-COT. Mixtures of isoprop-O-COT and *t*-but-O-COT were reduced with deficient amounts of lithium metal setting up the following electron competition reaction. EPR analysis clearly shows that the electron “prefers” the *t*-but-O-COT, and K_{eq} = 0.39 ± 0.04 (Figure 5). This enforces the suggestion that the isoprop-O-COT has some extended conjugation (homohyperconjugation) relative to that for the *t*-but-O-COT system.



(7)

Experimental Section

Alkoxycyclooctatetraenes. The syntheses of the alkoxy−COTs were based on Kreb's preparation of *tert*-butoxycyclooctatetraene.[15] COT was brominated, to yield [4,2,0]-bicyclo-5,6-dibromo-1,3-octadiene, which was then dehydrohalogenated with potassium *tert*-butoxide to yield monobromocyclooctatetraene.

The alkoxycyclooctatetraenes were all prepared by adding the appropriate potassium alkoxide to monobromocyclooctatetraene as previously described.[15] The potassium alkoxide was prepared by dropwise addition of the alcohol to a stirred solution of an excess of potassium metal in THF. The mixture was subsequently refluxed for 6 h in a nitrogen atmosphere. The resulting alkoxide solution was then added dropwise to a stirred solution consisting of 0.9 equiv of bromocyclooctatetraene in THF at −79 °C under a nitrogen atmosphere. After the addition was complete, the solution was allowed to warm to room temperature and the THF was removed under reduced pressure. The resulting alkoxy−COT was purified via vacuum distillation (1 Torr and 45−50 °C for isopropoxy−COT). NMR and mass spectral analysis are consistent with C_8H_7−alkoxide in all cases. In each case, the parent mass spectral peak represents the molecular ion of the alkoxy−COT (e.g., $m/e = 162$ for isoprop-O-COT), and the base peak is $m/e = 120$ (from $COT-OH^+$).

General. The reductions were carried out by allowing HMPA solutions of the alkoxycyclooctatetraene to come into contact with lithium metal in vacuo as previously described.[15] The EPR spectra were recorded with an Bruker EMX-080 spectrometer equipped with a variable-temperature unit.

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