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Synthesis and Properties of the 5,10,15-Trimesityltruxen-5-yl Radical

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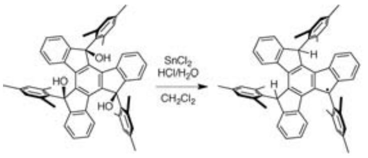
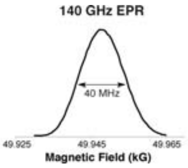
ABSTRACT





The synthesis of a long-lived, truxene-based radical that is highly delocalized and exhibits a narrow EPR absorption is reported. The radical is stable for multiple hours in a solution exposed to air and remains for months in the solid state under inert gas. Characterization and properties are discussed.

Dynamic nuclear polarization (DNP) is a promising technique to dramatically increase sensitivity in NMR experiments.[1] In a contemporary DNP experiment, the large polarization of a stable radical's unpaired electron is transferred to proximal nuclei via μ-wave electron–nuclear transitions.[2] Enhancements in nuclear polarization could theoretically reach values approaching the quotient of the gyromagnetic ratios of an electron and the nucleus of interest ($\gamma_e/\gamma_{1H} \approx 660$; $\gamma_e/\gamma_{13C} \approx 2600$).

Radicals with narrow EPR absorptions efficiently participate in the solid effect (SE)-DNP mechanism.[3] At present, derivatives of triphenylmethyl (trityl)[4] and 1,3-bisdiphenylene-2-phenylallyl (BDPA)[5] are the only readily available radicals whose EPR absorptions are sufficiently narrow to support SE-DNP. Mixtures of narrow-line radicals whose EPR signals are separated by the Larmor frequency of a nucleus are expected to induce remarkable polarization of that nucleus via the cross effect (CE)-DNP mechanism. CE is a two electron–one nucleus spin-flip process that tends to affect DNP more efficiently than SE at high magnetic fields.[6] The EPR absorptions of trityl OX063 and a sulfonated, water-soluble derivative of BDPA (SA-BDPA)[7] are roughly separated by the Larmor frequency of ^{13}C, and it was recently demonstrated that DNP with a mixture of these radicals achieved ^{13}C NMR signal enhancements of over 600.[8] The success of C-centered, delocalized radicals in promoting DNP through both SE and CE mechanisms served as motivation for investigating new structures for the generation of novel, narrow-line radicals.

We targeted 5,10-15-triaryltribenzo[*a*,*f*,*k*]trinden-5-yl (**1**) as a potentially stable radical system. This structure could feature highly delocalized spin density shared primarily by quaternary C-atoms, a condition that could offer narrow EPR line widths. Structure **1** contains an indeno-[1,2-*a*]fluorene (**2**) unit, fully π-delocalized derivatives of which have yet to be realized synthetically. A flurry of recent work by Haley, Tobe, and co-workers have yielded

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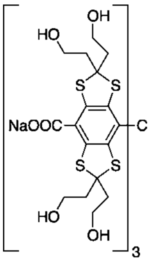
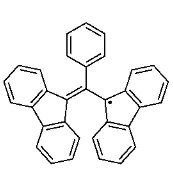
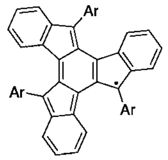
stable derivatives of the [2,1-*b*],[9] [1,2-*b*],[10] [2,1-*a*],[11] and [2,1-*c*][12] isomers, each of which have fascinating electronic and optical properties.



trityl (OX063)



BDPA



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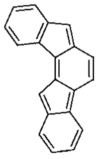

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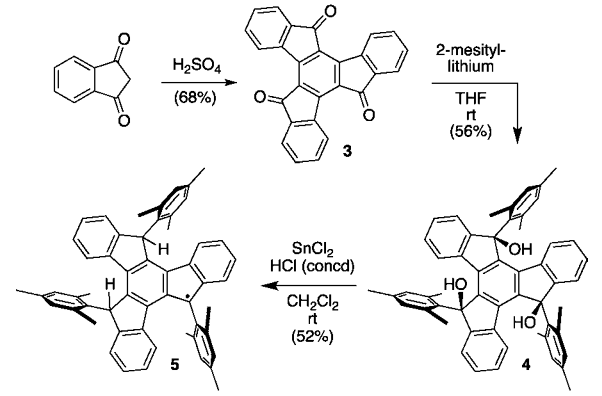
Truxene-5,10,15-trione (**3**), envisioned as a synthetic intermediate to **1**, was prepared by aldol trimerization[13] of 1,3-indanedone following a literature procedure[14] (Scheme 1). Addition of mesityllithium to trione **3** afforded triol **4**, which was isolated entirely as the *syn*, C_3-symmetric stereoisomer. Though it is unclear if the *anti* diastereomer is formed and removed in purification, it is noteworthy that Echavarren and co-workers also observe the C_3 tris-adduct exclusively after addition of 9-fluorenyllithium to **3**.[15] In an attempt to form either radical **1** or a tribenzotrindene derivative that could be synthetically transformed to **1**, triol **4** was treated with $SnCl_2$ and HCl in CH_2Cl_2, conditions for reductive aromatization reactions.[16] The result was the formation of a bright green material that could be purified by silica column chromatography.

Solution-phase EPR revealed that the green material is a radical with a narrow absorbance and no clear hyperfine couplings.[17] High resolution ESI-MS (positive mode) spectra of the radical showed a cation with the formula $C_{54}H_{47}^+$, corresponding to the ionized form of 5,10,15-trimesityltruxen-5-yl (**5**). The radical's IR spectrum shows no discernible O−H vibrations, which are clearly observable in the IR spectrum of triol **4**, suggesting that no alcohol groups remain in the radical. This conclusion is corroborated by the radical's high R_f value (0.83) on a silica TLC plate with 1:1 CH_2Cl_2−hexane as the eluent. Triol **4**, like many organic alcohols, remains on the baseline of a TLC plate eluted with this solvent system.

Scheme 1. Synthesis of Radical **5** from Truxenetrione **3** via Triol Intermediate **4**



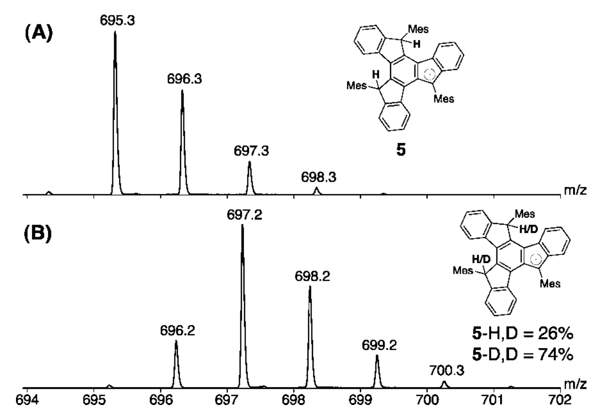


Figure 1. (A) ESI-TOF-MS (+ mode) spectrum of radical **5**. (B) Spectrum of deuterated products formed by reaction of **4** with DCl/D_2O and $SnCl_2$.

The acidic reduction of **4** must introduce two C−H bonds at the 10- and 15-positions for **5** to be the correct structure of the radical. Accordingly, substituting DCl/D_2O for HCl/H_2O should yield doubly deuterated radical **5**-D,D. This reaction was carried out, and ESI-MS (positive mode) analysis of the products showed peaks corresponding to doubly and singly deuterated derivatives of 5^+ in a 74:26 (D,D to H,D) ratio, indicating 87% total deuteration of the 10- and 15-positions (Figure 1).[18] The prevalence of **5**-D,D and the absence of species with more than two deuteriums confirm that two C−H/D bonds are formed in the reaction and strongly suggest that **5** is the structure of the nondeuterated radical. The compound may exist as *syn* and *anti* diastereomers, depending on the relative configurations of the newly introduced H-atoms.

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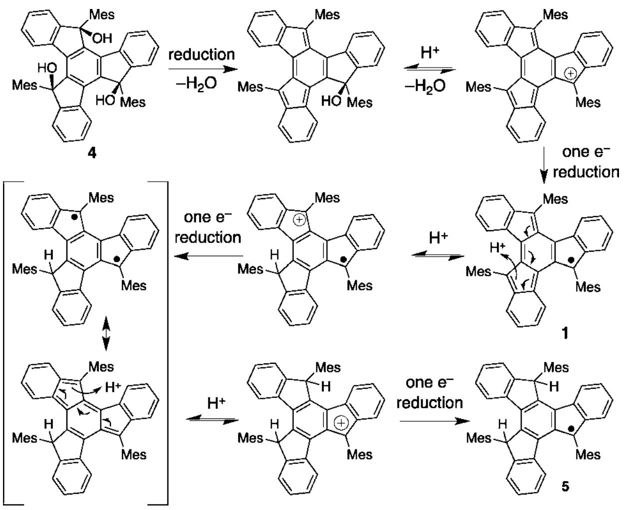
(17) See Figure S6 in the Supporting Information for a solution-phase EPR spectrum of **5**.

(18) We assume here that ionization is equally efficient for the doubly, singly, and nondeuterated products and that analysis of peak heights gives an accurate value for their relative ratio.

We propose that the mechanism of the reaction from **4** to **5** may involve a series of cation formation/reduction steps through short-lived indeno[1,2-*a*]fluorene-containing intermediates, including radical **1** (Scheme 2). These quinoidal species are likely basic[19] and may be protonated by HCl to form cations that are stabilized by conjugation to localized benzene rings. The cations then undergo single-electron reduction to radical species, and the process repeats until **5** is formed. This mechanistic proposal accounts for yields above 50% for radical **5**, whereas a sequence of cation formation−reduction−protonation steps at each methanetriyl group would be expected to afford the diamagnetic trihydride as the major product.

Scheme 2. Proposed Mechanism for Formation of Radical **5** from Triol **4** in the Presence of HCl and $SnCl_2$



DFT calculations (B3LYP/6-31G*) of radical **5** reveal that spin density is delocalized throughout the truxene core (Figure 2). A large proportion of the radical's spin density (31%) is located at C(5), and significant spin is shared by alternating sp^2-hybridized C atoms extending from C(5). The aromatic ring of the mesityl group lies roughly perpendicular to the truxene system and bears only a small amount of spin density (0.9%). The structure shown is the *anti* diastereomer, which was found to be less than 0.3 kcal/mol lower in energy than the *syn* diastereomer. Distribution of spin density is almost identical in both configurations (see Supporting Information (SI) for additional information).

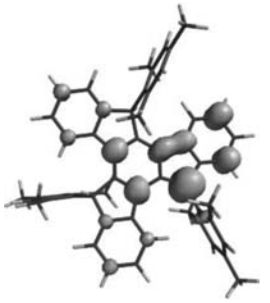


Figure 2. Calculated (B3LYP/6-31G*) spin density map of **5**.

The high-field (140 GHz) EPR spectrum of radical **5** exhibits a narrow absorbance at roughly the same frequency as SA-BDPA (Figure 3). The line width at half-height of the radical's maximum 140 GHz EPR absorption is 1.37 mT, broader than that of SA-BDPA (1.03 mT) and narrower than that of trityl OX063 (1.77 mT). The electron T_1 relaxation time of **5**, measured through a saturation recovery experiment at 4994.75 mT, was determined to be 7.3 ms (see Figure S7 in SI), an intermediate value compared to BDPA (55.9 ms) and Trityl OX063 (1.28 ms).[8]

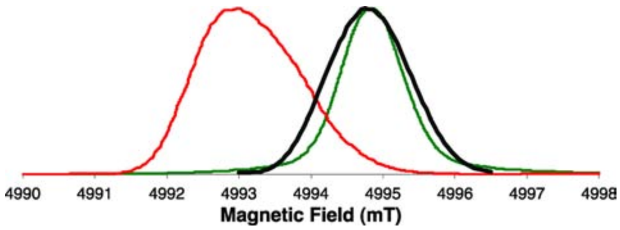


Figure 3. 140 GHz EPR spectrum of radical **5** (bold black, 1 mM in toluene, 80 K), compared to trityl OX063 (red, 1 mM in 60/40 (v/v) glycerol/D_2O, 80 K) and SA-BDPA (green, 1 mM in 60:40 (v/v) glycerol/D_2O, 80 K). Peak heights are scaled for equal intensity. The SA-BDPA and trityl data shown here are from ref 8 (see comment in SI).

Cyclic voltammetry (CV, all values reported vs Ag/$AgNO_3$) reveals that **5** undergoes one reversible oxidation ($E_{1/2}$ = 0.27 V) and one reversible reduction ($E_{1/2}$ = −1.01 V) (Figure 4A). Using the Fc/Fc^+ couple ($E_{1/2}$ = 0.21 V) as a standard,[20] the SOMO energy was found to lie at −4.81 eV compared to the vacuum level. Filling the SOMO requires 1.00 eV based on the difference in onset potentials of the oxidation and reduction peaks. The absorption spectrum of **5** is complicated and exhibits nonzero absorbance at all visible wavelengths, with the weakest visible absorbance appearing in the green region, spanning 515−550 nm (Figure 4B). No absorbance is observed in the range 900−1100 nm. The large number of peaks in the spectrum may be attributable to vibronic structure as a result of structural rigidity and/or the presence of two diastereomers. The broad absorption band over the range 550−880 nm likely corresponds to the $D_0 \rightarrow D_1$ transition. If this is the case, the $D_0 \rightarrow D_1$ transition in **5** (λ_{max} = 626 nm, ε = 2,720) is

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(19) Extended π-systems containing quinoidal rings are known or expected to be highly basic in some cases. See: (a) Aitken, I. M.; Reid, D. H. *J. Chem. Soc.* **1956**, 3487. (b) Kemp, W.; Storie, I. T.; Tulloch, C. D. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2812. (c) Knežević, A.; Maksić, Z. B. *New J. Chem.* **2005**, *30*, 215.

(20) The peak of the Fc/Fc+ couple, which overlaps with the oxidation peak of **5**, was used as an internal standard vs the reduction peak of **5**. See Supporting Information for details.

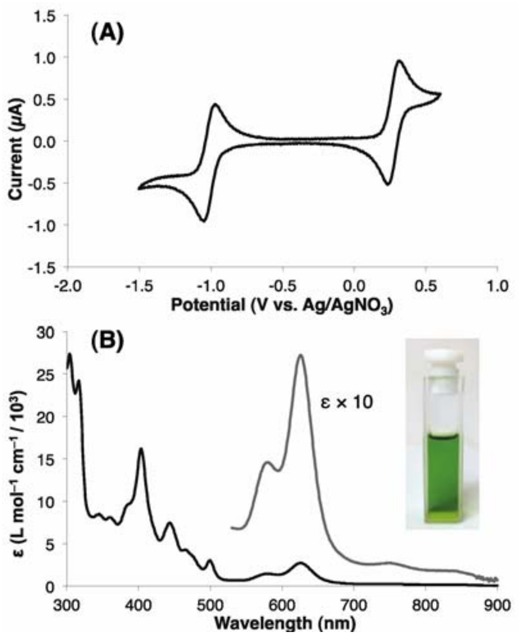

Figure 4. (A) Cyclic voltammogram of **5** (under N_2 in glovebox, 0.1 M Bu_4NPF_6 in CH_2Cl_2, Pt button (WE), Pt wire (CE), Ag/AgNO$_3$ (RE), scan rate 0.05 V/s). (B) Absorbance spectrum of **5** in CH_2Cl_2; gray spectrum shows higher wavelength absorption multiplied by a factor of 10.

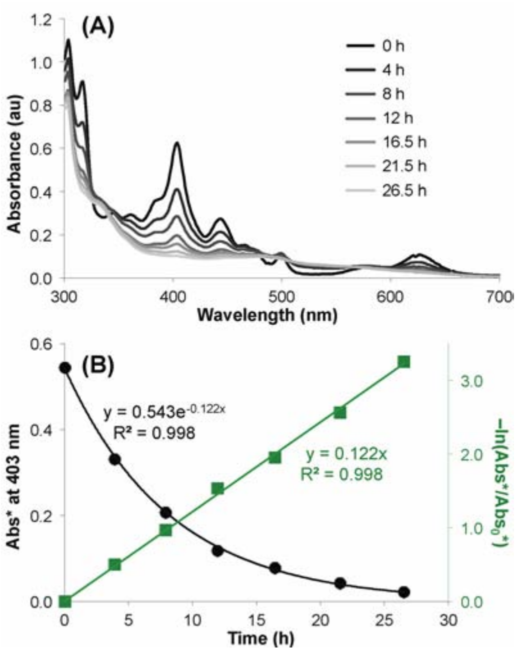

Figure 5. (A) Absorbance spectra of **5** in CH_2Cl_2 after exposure to air over specified times. (B) Plots of Abs* (see text) (black circles) and −ln(Abs*/Abs$_0$*) (green squares) over time, indicating that $k_{obs} \approx 1.2$ h and $t_{1/2} \approx 5.8$ h.

blue-shifted and more strongly absorbing than the same transition in BDPA (λ_{max} = 859 nm, ε = 1,580).[21]

A kinetic experiment provided insight into the stability of radical **5** in a solution exposed to ambient oxygen. A solution of **5** in CH_2Cl_2 (4×10^{-5} mol/L) was exposed to air, and absorption spectra were measured every several hours until only a negligible amount of **5** remained (Figure 5A). Before each measurement, CH_2Cl_2 was added to a mark on the cuvette to replace the solvent lost by evaporation and to keep the total concentration of the solute roughly consistent. The value for absorbance (Abs) at the peak at 403 nm was used to monitor the disappearance of **5** over time; however, the value does not reach zero, as the oxidized product(s) continue to absorb at this wavelength. The value Abs*, which is equal to Abs −0.080 (0.080 being the extrapolated value for Abs after complete oxidation of **5**), clearly follows *pseudo*-first-order exponential decay kinetics. It is assumed that the rate of diffusion of oxygen into the solution is much faster than the rate of reaction between oxygen and the radical. From the kinetic plots, we determine the k_{obs} of the reaction to be roughly ~0.12 h^{-1} and the half-life ($t_{1/2}$) of the radical under these conditions to be roughly ~5.8 h. The ESI-TOF-MS spectrum of the oxidized material after 26.5 h showed a major peak at 711 *m*/*z*, which corresponds to $[\mathbf{5} + O]^+$ and confirms that oxygen is incorporated into the structure. It is noteworthy that **5** remains for months when properly stored under inert conditions in the solid state.

In conclusion, we have synthesized a long-lived, truxene-based radical that exhibits an EPR resonance that should be sufficiently narrow to enable DNP by the SE mechanism. Current work is focused on developing derivatives that are both stable in the presence of oxygen and soluble in water/glycerol mixtures amenable to DNP experiments.

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Supporting Information Available. Experimental procedures, full characterization and spectral data for new compounds, Cartesian coordinates for calculated structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.