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Efficient Synthesis of Benzene and Planar Cyclooctatetraene Fully Annelated with Bicyclo[2.1.1]hex-2-ene

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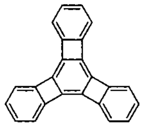
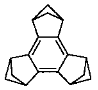
Recently, the phenomenon of bond alternation (or localization) in benzene, which is associated with the Mills−Nixon effect,[1] has become the focus of revisited attention, and such a bond-alternated benzene, that is, 1,3,5-cyclohexatriene, has been not only a subject of considerable theoretical investigation[2] but also a synthetic target for organic chemists.

For examples of the compounds that possess cyclohexatriene motifs, several "phenylenes" such as **1** have been synthesized,[3] and X-ray analysis has revealed the manifestation of a pronounced bond alternation ($\Delta R = R_{\rm endo} - R_{\rm exo} = 0.1\sim0.18$ Å) in the central benzene ring. On the other hand, Siegel et al. have reported the synthesis of tris(bicyclo[2.1.1]hexeno)benzene (**2**),[4] as the first example of *mononuclear benzenoid hydrocarbon* with a cyclohexatriene-like geometry ($\Delta R = 0.089$ Å).[5] Compared with such phenylenes as **1**, in which the central benzene ring is embedded within extensively delocalized π-systems, electronic perturbation of the central benzene ring would be much less significant in **2** with no annelation of π-systems. Thus, compound **2** may be considered to be a more appropriate model for probing the nature of the "cyclohexatriene" itself. However, its yield is extremely low (<1% in the final step), which hampers further scrutiny of this fascinating molecule. Here we report an efficient synthesis of **2**, as well as the first synthesis of a novel cyclooctatetraene (COT) derivative **3** with a completely planar cyclic 8π-system.



1



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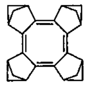
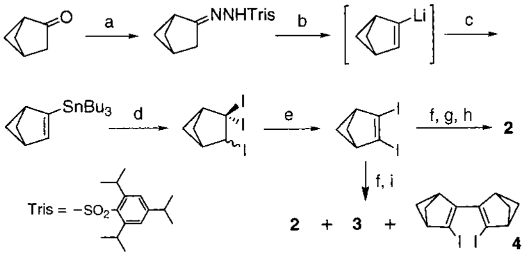


3

An efficient route to **2** was established by cyclotrimerization of the organometals derived from 2,3-diiodobicyclo[2.1.1]hex-2-ene, which was synthesized from bicyclo[2.1.1]hexan-2-one[6] (Scheme 1). Treatment of the diiodoolefin with *n*-butyllithium in THF followed by the sequential addition of CuI and CuCl$_2$ successfully afforded benzene **2** in 43% yield.[7] The overall yield of **2** from the starting ketone was 21%, and the availability of **2** in a larger quantity should allow thorough exploration of the chemistry of this bond-alternated benzene **2**.

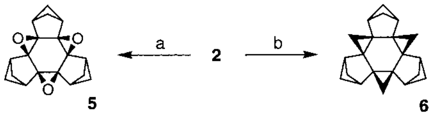
Scheme 1[a]



[a] (a) 2,4,6-triisopropylbenzenesulfonylhydrazide, Et$_2$O, rt, 77%. (b) *t*-BuLi, THF, −78 → 0 °C. (c) *n*-Bu$_3$SnCl, −78 °C, 88%. (d) I$_2$, CCl$_4$, rt, 78%. (e) *t*-BuOK, THF, rt, 94%. (f) *n*-BuLi, THF, −78 °C. (g) CuI, −78 → −45 °C. (h) CuCl$_2$, −78 °C → rt. (i) CuI, −78 °C → rt.

Star-phenylene **1** has been reported to undergo reactions characteristic of olefin rather than of benzene, that is, hydrogenation,[8] epoxidation,[9] and cyclopropanation,[9] which could be ascribable to significant bond localization. Although the degree of bond alternation in **2** is much smaller than in **1** ($\Delta R = 0.159$ Å),[3a] both epoxidation and cyclopropanation of **2** do, in fact, take place readily. As shown in Scheme 2, reaction of **2** with *m*-chloroperbenzoic acid afforded all-*cis*-trisepoxide **5** in a quantitative yield, and a modified Simmons−Smith reaction gave all-*cis*-triscyclopropane **6** in 75% yield. However, **2** is inert to catalytic hydrogenation and diimide reduction, presumably for steric reasons.[10]

Scheme 2[a]



[a] (a) *m*-CPBA, CH$_2$Cl$_2$, rt. (b) ZnEt$_2$/CH$_2$I$_2$, ClCH$_2$CH$_2$Cl, rt.

On the other hand, when the cyclotrimerization reaction was conducted without CuCl$_2$ (Scheme 1), COT **3** was obtained as an orange solid in 21% yield, together with a mixture of benzene **2** and the dimer **4** (34 and 5%, respectively). Considering the observed effect of the annelation with bicyclo[2.1.1]hexene in **2** to localize the double bond to the position exo with respect to the annelation, the COT **3** was expected to possess a planar eight-membered ring instead of the usual tub-shaped one.[11,12] The anticipated D_{4h} symmetric structure is reflected in the simplicity of the ^{1}H and ^{13}C NMR (CDCl$_3$) spectra:[13] ^{1}H NMR (Figure 1)

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(8) Mohler, D. L.; Vollhardt, K. P. C.; Wolff, S. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1151.

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(10) The 2,3,6,7,10,11-hexakis(trimethylsilyl) substitution of **1** also makes the central ring inert to catalytic hydrogenation even under forcing conditions. See ref 8.

(11) Computational prediction for the planar structure of **3** has been recently performed by Baldridge and Siegel, see: Baldridge, K. K.; Siegel, J. S. *J. Am. Chem. Soc.* **2001**, *123*, 1755−1759.

(12) As to the COT derivative with a planar π-system, only perfluorocyclobutene-annelated derivative has been reported, see: Einstein, F. W. B.; Willis, A. C. *J. Chem. Soc., Chem. Commun.* **1981**, 526.

10.1021/ja003512m CCC: $20.00

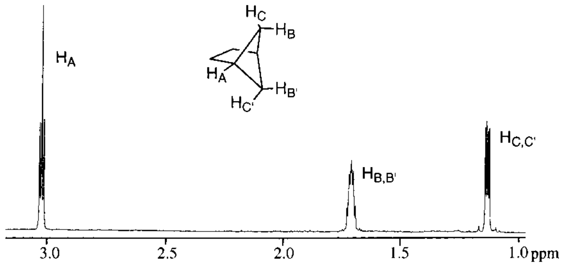

Figure 1. ^{1}H NMR (300 MHz) spectrum of **3** in $CDCl_3$.

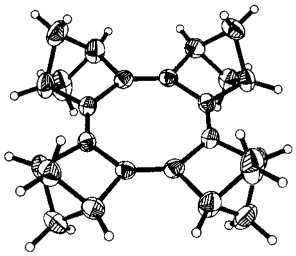

Figure 2. ORTEP drawing of **3** (50% probability).

δ 3.03 (t, $J^3_{AB} = 2.7$ Hz, 8H, H_A), 1.71 (m, 8H, H_B), 1.13 (dd, $J^3_{CC'} = 3.6$ Hz, $J^3_{BC} = 1.5$ Hz, 8H, H_C); ^{13}C NMR δ 132.25 (olefinic), 47.19 (bridgehead), 37.11 (methylene).

The molecular structure of **3** was determined by X-ray crystallography (Figure 2).[14] As expected, the central eight-membered ring is planar, and all internal bond angles of the COT ring are almost 135° (134.8−135.2°, average 135.0(1)°). The bond lengths are alternately shorter (average 1.331(1) Å) and longer (average 1.500(1) Å) with the shorter bonds exocyclic to bicycloannelation. Thus, compound **3** is proven to be the first non-benzoannelated hydrocarbon with a completely planar COT ring.

The UV−vis spectrum of **3** in CH_2Cl_2 exhibited the longest wavelength absorption at 459 nm (ϵ 130). This value is red-shifted by 177 nm compared with that of tetrakis(bicyclo[2.2.2]octeno)-COT (**7**)[15] ($\lambda_{max} = 282$ nm, ϵ 800) with the tub-shaped COT ring, indicating that planarization of the COT ring in **3** causes a substantial decrease in the HOMO−LUMO gap.

The remarkable influence of planarization on the electronic structure of COT was also manifested by the oxidation potential of **3** as measured by cyclic voltammetry in CH_2Cl_2. COT **3** exhibited a well-defined reversible oxidation wave at +0.07 V versus Fc/Fc$^+$ and an irreversible one at +0.76 V. These potentials are lower by ~0.4 V than corresponding values in **7**, which is evidently due to planarization that raises the HOMO of COT.

In view of the cyclohexatriene-like geometry of the benzene ring in **2** and the planar geometry of the COT ring in **3**, the most interesting aspect of these molecules appears to be their aromaticity and antiaromaticity. Since the bridgehead hydrogens in **2** and **3** are rigidly fixed in the same plane of π-systems, they are most susceptible to the effect of the ring current, and their ^{1}H NMR chemical shift is the most useful indicator for characterizing aromaticity/antiaromaticity. Surprisingly, the difference in ^{1}H NMR chemical shifts of bridgehead protons between **2** and **3** was found to be *only 0.18 ppm* (δ 3.21 for **2** in $CDCl_3$), despite the change in the π-system from formally aromatic 6π to formally antiaromatic 8π.

Table 1. Calculated Aromatic Stabilization Energies (ASE, kcal/mol), Magnetic Susceptibility Exaltations (Λ, ppm cgs), and the Nucleus Independent Chemical Shifts (NICS, ppm) at the Ring Centers[a]

compd	ASE[b]	Λ[c]	NICS[d]
benzene	−34.1	−16.2	−9.7
2	−34.0	−8.4	−8.0
planar COT (D_{4h})	2.9	61.1	27.2
3	4.1	17.2	10.6

[a] B3LYP/6-31G* geometries were employed. [b] B3LYP/6-311+G**.[17] [c] CSGT-HF/6-31+G**.[17] [d] GIAO−HF/6-31+G**.

To evaluate the aromaticity of **2** and the antiaromaticity of **3**, the nucleus independent chemical shifts (NICS),[16] the magnetic susceptibility exaltations (Λ), and the aromatic stabilization energies (ASE) were calculated for **2** and **3** as well as for benzene and the D_{4h} planar COT (Table 1).[17] To compensate for the strain, reference molecules used to estimate the ASE were optimized under appropriate constraints.[18]

The large negative NICS value of **2** (−8.0), comparable to that of D_{6h} benzene itself (−9.7), indicates that **2** retains a substantial degree of aromaticity, which is consistent with the previous results of theoretical calculations for hypothetical cyclohexatriene.[16,19] The considerable aromatic character of **2** was also confirmed by the negative Λ value (−8.4) and the large ASE (34.0 kcal/mol).

On the other hand, although the destabilization energy of **3** slightly exceeds that of the D_{4h} planar COT, the NICS value (10.2) as well as the Λ value (17.2) is considerably reduced, compared with those of the D_{4h} planar COT. Such a reduction of antiaromaticity of **3** might appear to be attributed to an enhanced bond alternation ($\Delta R = 0.161$ Å) relative to that in the D_{4h} planar COT ($\Delta R = 0.132$ Å). However, the NICS value of the hypothetical molecule, tetrakis(cyclobuteno)COT, which has the same degree of bond alternation ($\Delta R = 1.491$ Å − 1.336 Å = 0.155 Å) as **3**, reveals the considerable retention of antiaromaticity (NICS: 20.9). Thus, electronic interaction between 1,3-bridged cyclobutane subunits in the bicyclohexene frameworks and the planar COT ring must be responsible for the change in the inherent magnetic properties and the reduced antiaromaticity of the present 8π electronic system **3**.

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Supporting Information Available: Experimental and calculation details and X-ray crystallographic data of **3** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(13) The ^{1}H and ^{13}C NMR signals of **3** were assigned on the basis of the DEPT experiment, the CH-COSY spectrum, and the ^{1}H coupling patterns.

(14) Crystallographic data for $C_{24}H_{24}$ (**3**): The space group is $P2_1/n$, monoclinic, with unit-cell demensions $a = 9.9040(10)$ Å, $b = 8.7204(9)$ Å, $c = 10.5525(11)$ Å, $\beta = 114.719(2)°$, $V = 827.87(15)$ Å^3, $Z = 2$, $D_{calc} = 1.253$ Mg/m^3. Intensity data were collected at 300 K on a Bruker SMART APEX diffractometer with Mo Kα radiation and graphite monochromator. The structure was solved by direct methods and refined by the full-matrix least-squares on F^2 (SHELXTL). A total of 6948 reflections were measured and 2574 were independent. Final $R_1 = 0.0588$, $wR_2 = 0.1356$ ($I > 2\sigma(I)$), and GOF = 0.908 (for all data, $R_1 = 0.0886$, $wR_2 = 0.1451$). Full details are described in the Supporting Information.

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