2754 J. Am. Chem. Soc. 1996, 118, 2754−2755

Synthesis and Characterization of the First Corannulene Cyclophane

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Received November 6, 1995

Fullerene fragments,[1] such as corannulene, inspire the design of several cyclophane motifs: [2] ansa baskets, covered baskets, and "basket balls" (Figure 1). These related structural types potentially serve as fullerene mimics with novel physical properties; for example, as fullerenoid receptors, they would be precursors to endohedral complexes.[3] Corannulene alone shows intricate redox behavior[4] and photochemistry.[5] Despite the abundance of novel molecular designs, the synthetic routes to these structures are not yet well developed. In particular, the synthetic challenge, although addressed in some elegant flash vacuum pyrolysis techniques,[6,7] does not have a general solution for the preparation of keystones suitable as cyclophane precursors. In response to this synthetic challenge, we present the first synthesis of a corannulene based cyclophane, **1**, which showcases a new route to the corannulene nucleus.

Retrosynthetic analysis of **1** shows obvious disconnections to 2,5-dimethylcorannulene (**2**) that retains bilateral symmetry (Figure 2). Disconnection of the rim bonds[8] directs the synthesis through 1,6-dimethyl-7,10-diethylfluoranthene (**3**), a molecule with readily functionalized benzylic positions. A variety of methods have been developed to couple functionalized benzylic carbons.[9] From **3** the retrosynthetic path to 2,7-dimethylnaphthalene parallels our previous work on corannulene.[10]

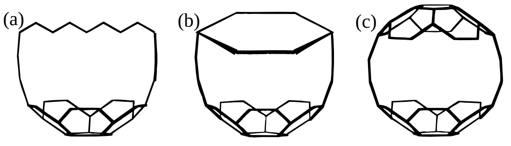


Figure 1. Corannulene-based cyclophane motifs: (a) ansa-baskets, (b) covered-baskets, (c) "basket balls".

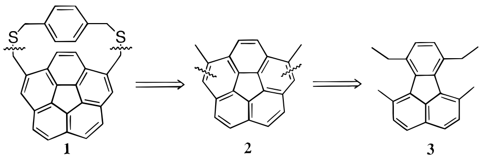
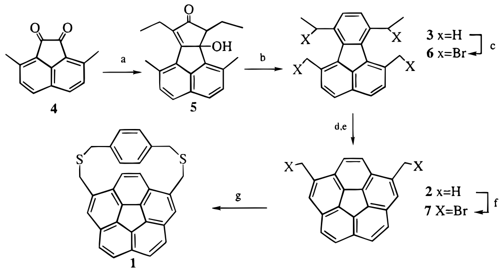


Figure 2. Retrosynthetic analysis of **1**.

Scheme 1[a]



[a] Conditions: (a) 4-heptanone, KOH; (b) norbornadiene, acetic anhydride (49%, 2 steps); (c) NBS, benzoylperoxide, *hν* (quantitative); (d) $TiCl_3$, $LiAlH_4$ (33%); (e) DDQ (55%); (f) NBS, benzoylperoxide, *hν* (quantitative); (g) potassium *tert*-butoxide, 1,4-bis(mercaptomethyl)benzene (40%).

Scheme 1 shows the synthesis of **1** initiated from the diketone (**4**),[10] which was condensed with 4-heptanone under basic conditions to yield a crude cyclopentenone carbinol (**5**). Reaction of crude **5** under dehydrating conditions (acetic anhydride) with an acetylene equivalent (2,5-norbornadiene) produced **3**.[11] Bromination with *N*-bromosuccinimide in carbon tetrachloride forms a diastereomeric mixture of 1,6-bis(bromomethyl)-7,10-bis(1-bromoethyl)fluoranthenes (**6**), which was not separated. Internal cyclization of the benzylic bromides of **6**, by reductive coupling with $TiCl_3$/$LiAlH_4$ or VCl_3/$LiAlH_4$, yielded a mixture of *cis*- and *trans*-dimethyltetrahydrocorannulene; dehydrogenation of this mixture with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) produced **2.**[12] Bromination with *N*-bromosuccinimide afforded bis(bromomethyl)corannulene (**7**),[13] which upon slow addition to 1,4-bis(mercaptomethyl)benzene in potassium *tert*-butoxide/tetrahydrofuran solution cyclized to **1**.[14]

The variable temperature ^1H NMR of **7** provided an alternative determination of the barrier to bowl-to-bowl inversion for comparison with that previously reported by Scott et al.[6a] At −100 °C, the diastereotopic methylene protons of **7** show a four-line AB pattern centered at δ 5.36 ($^2J = 10.5$ Hz; $\Delta\nu = 38.5$ Hz). With warming, the signals broaden, then coalesce, at −58 °C. Further warming, to ambient temperature affords a sharp singlet at δ 5.31, corresponding to the methylene protons under rapid exchange by the bowl-to-bowl inversion. From the NMR data,[15] the $\Delta G_c^\ddagger$ for the bowl-to-bowl inversion is calculated to be 10.5 ± 0.2 kcal/mol (10.2 ± 0.2 kcal/mol, Scott et al.).[6a]

The structure of **1** is deduced from ^1H NMR, ^{13}C NMR, and *ab initio* computations; the molecular weight was confirmed by high-resolution mass spectroscopy.[14,16,17] Three conformational isomers of the cyclophane are feasible: two C_s symmetric

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[†] UCSD.

[‡] SDSC.

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(11) Spectral data for **3**: ^1H NMR ($CDCl_3$, 500 MHz) δ 1.30 (t, $J = 7.0$ Hz, 3H), 2.79 (s, 3H), 3.11 (q, $J = 7.0$ Hz, 2H), 7.26 (s, 2H), 7.35 (d, $J = 8.0$ Hz, 2H), 7.66 (d, $J = 8.0$, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 15.49, 24.54, 28.41, 125.98, 126.62, 128.51, 131.82, 131.93, 133.61, 135.10, 136.49, 139.19.

(12) Spectral data for **2**: ^1H NMR ($CDCl_3$, 500 MHz) δ 2.83 (s, 6H), 7.55 (s, 2H), 7.68 (d, $J = 8.5$ Hz, 2H), 7.74 (d, $J = 8$ Hz, 2H), 7.94 (s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 18.74, 124.83, 125.79, 126.31, 127.12, 129.97, 130.66, 131.56, 134.93, 135.50, 136.04, 136.66; HRMS (FAB^+) $MCs^+ = 411.0150$; expected=411.0166.

(13) Spectral data for **7**: ^1H NMR (THF-d_8, 500 MHz) δ 5.31 (s, 4H), 7.92 (d, $J = 9$Hz, 2H), 7.94 (d, $J = 8.5$ Hz, 2H), 8.05 (s, 2H), 8.30 (s, 2H).

(14) Spectral data for **1**: ^1H NMR ($CDCl_3$, 500 MHz) δ 1.89 (s, 2H, H_a), 2.64 (d, $J = 14.5$ Hz, 2H, H_d), 3.31 (d, $J = 14.5$ Hz, 2H, H_c), 4.45 (d, $J = 12.5$ Hz, 2H, H_f), 4.68 (d, $J = 12$ Hz, 2H, H_e), 6.75 (s, 2H, H_b), 7.62 (s, 2H, H_g), 7.73 (s, 2H, H_h), 7.91 (s, 4H, H_i and H_j). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 32.39, 34.05, 122.42, 125.47, 126.48, 127.32, 128.99, 129.04, 130.12, 130.40, 130.96, 134.21, 135.09, 135.22, 135.65, 137.96. HRMS (FAB^+) $MCs^+ = 577.0085$; expected = 577.0061.

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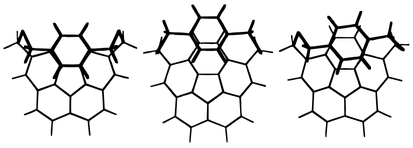

1-I (0.0 kcal/mol) **1-II** (3.7 kcal/mol) **1-III** (2.4 kcal/mol)

Figure 3. Three conformers of **1**: relative energies (RHF/6-31G(2d,p)//3-21G(2d,p)) in parentheses.

isomers (one with both sulfurs pointing out away from the bowl (**1-I**) and one with both sulfurs pointing in toward the bowl (**1-II**)) and one C_1 symmetric isomer (one sulfur in and one out (**1-III**)) (Figure 3). *Ab initio* computations at the RHF/6-31G(2d,p)//3-21G(2d,p) level of theory predict a relative ordering of these conformers, **1-I** (0.0 kcal/mol), **1-II** (3.7 kcal/mol), and **1-III** (2.4 kcal/mol). Conformation **1-I** has the benzene ring suspended above the cavity of the bowl, with two protons pointed into the cavity of the bowl, reminicent of the t-shaped dimer of benzene. Although t-shaped structures have been indicated as a structural imperative in some systems, certainly the conformational controlling effect in **1-I** is the steric strain between the juxtaposed aromatic fragments.

For a more precise comparison to the experimental data, a higher level density functional theory optimization of the lowest energy isomer (**1-I**) was performed. Hydrogen−hydrogen distances in isomer **1-I** are consistent with NOE difference intensities (Figure 4). A calculated bowl depth (hub plane to rim plane) of 0.87 Å agrees well with the experimental bowl depth found in corannulene, 0.89 Å, and suggests that the dithiol linker is not introducing a significant amount of strain into **1-I**.

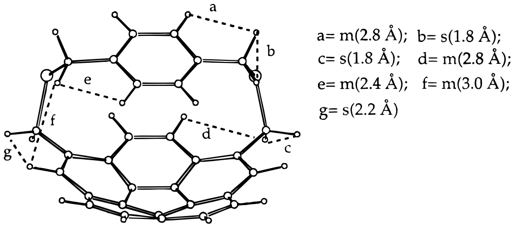

Figure 4. Comparison of calculated distances (DFT/BPW91/6-31G-(d))[16] and NOE intensities between protons of **1** (intensities: s = strong, m = medium; distance between hydrogens in parentheses).

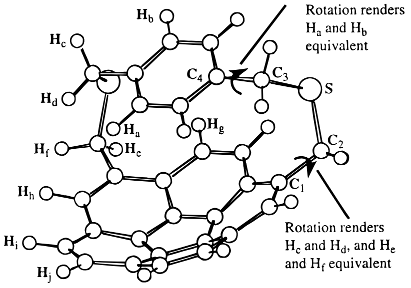

Figure 5. Dynamic processes for **1**.

The number of signals in the ^{13}C NMR of **1** are consistent with a C_s symmetric isomer; however, several novel shifts appear in the ^{1}H NMR spectrum. One anomaly in the spectrum is that the endo aromatic protons of the para-substituted benzene ring, H$_a$ (δ 1.89), appear far upfield from the usual protons of an aromatic ring (Figure 5). This upfield shift can be explained by the magnetic anisotropy of the corannulene bowl. The concave face of corannulene should be similar to the endohedral surface of a fullerene. Significant upfield shifts in ^{3}He NMR have been observed for the endohedral complexes: He@C$_{60}$ (δ −6.3) and He@C$_{70}$ (δ −28.8).[18] Alternatively, corannulene can be thought of as an annulus inside an annulus. A zwitterionic resonance form ascribes a 14-electron aromatic cationic ring to the outer 15 carbons and a six-electron aromatic cyclopentadienyl-like ring to the inner five-membered ring. Comparison of δ shifts in **1** and dimethyldihydropyrene,[19] a 14-electron annulene with protons in a shielding environment similar to those of **1**, affords a quantitative explanation of the upfield shift. The aromatic protons, H$_a$ of **1-I** (DFT/6-31G-(D)), lie 2.5 Å above the best plane of the rim carbons and 3.4 Å above the plane of the five-membered ring, and the observed shift is 5.4 ppm upfield. The methyl protons of dimethyldihydropyrene lie 2.3 Å above the plane of the annulene and experience a 5.2 ppm upfield shift. Another anomaly in the spectrum is that the signal (δ 7.91) corresponding to four protons, H$_i$ and H$_j$, appears as a singlet and not as the two doublets predicted by symmetry arguments. The assumption that this singlet is due to accidental isochrony is not unreasonable; these same protons in dimethylcorannulene and bis(bromomethyl)corannulene appear as four-line AB patterns separated by only 0.059 and 0.027 ppm, respectively.

Two different dynamic processes can be envisioned for **1** (Figure 5). The first is rotation around the C$_3$−C$_4$ bonds, which renders the endo and exo aromatic protons equivalent. The second is a rotation around the C$_1$−C$_2$ bond, forcing the entire chain around the outside of the bowl and concomitant bowl inversion, which renders both H$_c$ and H$_d$, and H$_e$ and H$_f$ equivalent. While observing the ^{1}H NMR spectrum at 300 MHz, the sample was heated to 148 °C and no coalescence or peak broadening was observed. This observation sets a minimum limit for the barrier of both processes at 18 ± 1 kcal/mol. Thus, construction of the cyclophane effectively locks the structure into only one bowl.

Acknowledgment. Support was provided by the National Science Foundation (CHE9307582; ASC-9212619 and VPW award). A grant of supercomputing time was provided by the San Diego Supercomputing Center.

Supporting Information Available: Experimental details for the preparation of **1** (1 page). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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(16) Computational details: The molecular structures of isomers of **1** were determined at a variety of theoretical methods to determine self-consistency. Reported optimized structures have been calculated using the split valence 3-21G(2d,p) basis set[17a] at the restricted Hartree−Fock (RHF) self-consistent field (SCF) level of theory. Higher level single-point energies were perfomed using the 6-31G(2d,p) basis set. Both basis sets include two sets of six d polarization functions on all non-hydrogen atoms and one set of p functions on all hydrogen atoms. These calculations were performed with the aid of the analytically determined gradient and search algorithms in GAMESS.[17b] Additional calculations were performed on the lowest energy isomer of **1**, using density functional theory (DFT), which inherently incorporates dynamical correlation, giving a more refined structure. These latter calculations were performed with the Becke88 nonlocal exchange correction,[17c] and Perdew and Wangs 1991 gradient-corrected correlation function:[17d] BPW91/6−31G(d), using the GAUSSIAN94 suite of programs.[17e]

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