Registry No. **1a**, 4401-11-0; **1b**, 4538-50-5; **1c**, 5694-00-8; **1d**, 106-88-7; **1e**, 137946-04-4; **2a**, 137946-05-5; **2b**, 42998-10-7; **2c**, 137946-07-7; **2d**, 137946-09-9; **2e**, 137946-10-2; **3a**, 137946-06-6; **3b**, 54864-75-4; **3c**, 137946-08-8; **3d**, 76137-53-6; **3e**, 137946-11-3; $NaSCH_3$, 5188-07-8; $NaDCO_3$, 21254-75-1.

The Simplest Cyclic Polyacene. A Semiempirical (MNDO) Study of *cyclo*-Anthracene

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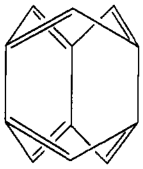
Introduction

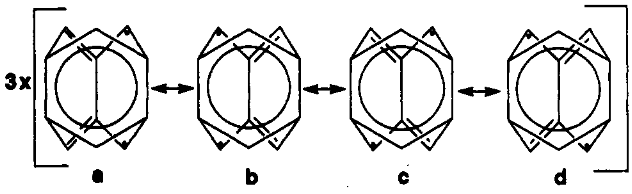
In 1983, Kivelson and Chapman[1] proposed the possibility of cyclic polyacenes in their computational study of infinite linear polyacenes as potential one-dimensional conductors. Although we find these cyclic polyacenes to be inherently interesting, they have apparently not been studied since this original report.[2]

The smallest and simplest possible cyclic polyacene contains three fused hexagonal rings, 1. Drawn as 1, the molecule does not contain any aromatic sextets[3] and is, in fact, a Hückel 4*n* system with 12 π electrons.



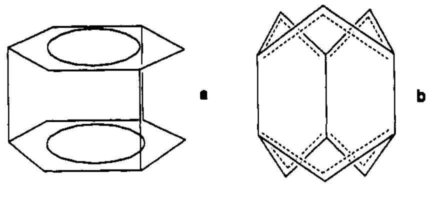
1

If the presence of an aromatic sextet is of greatest importance to the stability of this cyclic triacene (*cyclo*-anthracene), 1 could be envisioned as containing one (but only one) lateral aromatic ring. Such a structure, 2, must be a diradical with the unpaired electrons conjugated with both the aromatic system and the two alkene moieties, as in **2a** and **2b**. Other possibilities, **2c** and **2d**, place the radicals in adjacent rings. (There are two additional sets of four equivalent structures in which the aromatic system is permuted into the other two lateral hexagonal rings.) A total of 12 "resonance structures" for such a small molecule, albeit all diradicaloid, might allow the molecule some stability. However, the extremely distorted nonplanar nature of the central carbon atoms and the subsequent unfavorable orbital overlaps may make the conjugation effects unlikely and, therefore, somewhat less important.



2

There is yet a third possible representation of 1. The molecule could be described as a "1,3,5-face-fused"-cyclophane, as in **3a**. If *cyclo*-anthracene were constructed in this manner, 3 would contain two probably extremely distorted aromatic systems, but delocalized bonds might be expected on the molecular "top" and "bottom", as in **3b**. The delocalized systems would be connected by isolated single bonds.



3

We have developed an interest in moderately strained systems composed of benzene-like hexagons.[4] The cyclic polyacenes certainly meet this strain criterion, and 1 would probably be expected to exceed the term "moderately". Herein we report our computational investigation of 1 using the MNDO (modified neglect of diatomic overlap) method.[5]

Methods

The MOPAC Version 5.0 package[6] of semiempirical molecular calculational programs, which incorporates MNDO, was used. All minimization calculations were carried out on an Apollo/Hewlett-Packard DN4600 workstation under the Domain O/S operating system. For calculations involving force constant determinations, an Apollo/Hewlett-Packard DN10000 computer was employed due to the long times involved for these calculations.

For the successful[7] initial trial geometries (ITGs), and the Z matrices, all carbon–carbon distances were set at either 1.3, 1.4, or 1.5 Å, while carbon–hydrogen distances were set at either 1.1 or 1.0 Å. All hexagons were considered to be regular, with angles of 120°. Each hexagon was considered to be individually planar, and the plane torsion angle between two adjacent hexagons was set to 60° so as to produce an overall system with a triangular cross-section. All $3n-6$ degrees of freedom were allowed to minimize fully under the MNDO conditions. The keyword PRECISE was used to automatically increase the gradient norm and self consistent field criteria by a factor of 100. This increase resulted in individual distance, angle, and torsion gradients of less than 0.01 kcal/Å or kcal/radian.

Results and Discussion

The simplest cyclic polyacene, *cyclo*-anthracene, is formally constructed from three cyclically fused hexagons. This molecule minimizes on the MNDO potential energy

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(1) Kivelson, S.; Chapman, O. L. *Phys. Rev. B* **1983**, *28*, 7236.

(2) Some partially hydrogenated, nonconjugated relatives of the cyclic polyacenes have been studied using the MM2 method. Alder, R. W.; Sessions, R. B. *J. Chem. Soc., Perkin Trans. 2* **1985**, 1849.

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(7) Only ITGs in which all hexagons were regular and planar, producing a molecule with a triangular cross-section, resulted in an output optimized molecule which exhibited real vibrational, rotational, and translational frequencies after a force constant calculation. Other ITGs, in which the input geometry appeared to be a better approximation of the successfully minimized geometry, resulted in molecules with imaginary translational frequencies after force constant calculations, and were, therefore, not considered further. The input geometry with carbon–carbon distances of 1.4 Å and carbon–hydrogen distances of 1.0 Å resulted in the optimized molecule with the least positive (most stable) heat of formation.

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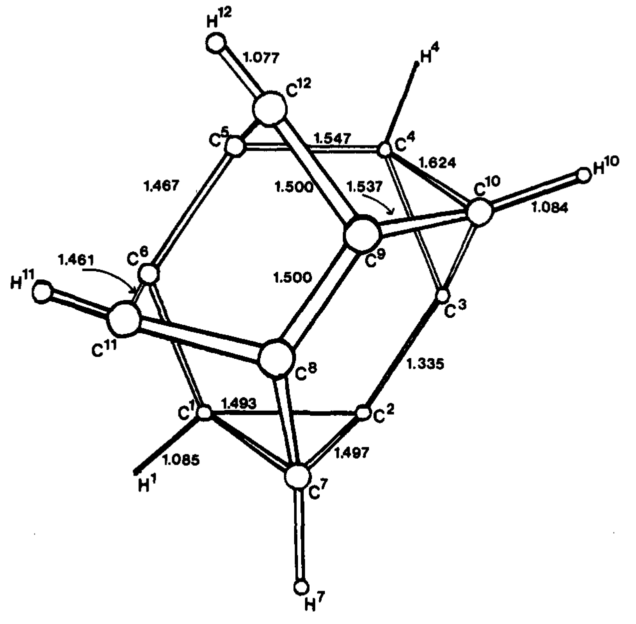


Figure 1. Bond distances in MNDO-optimized *cyclo*-anthracene. Bond distances are symmetrical about the plane which bisects bonds $C^2–C^3$, $C^5–C^6$, and $C^8–C^9$.

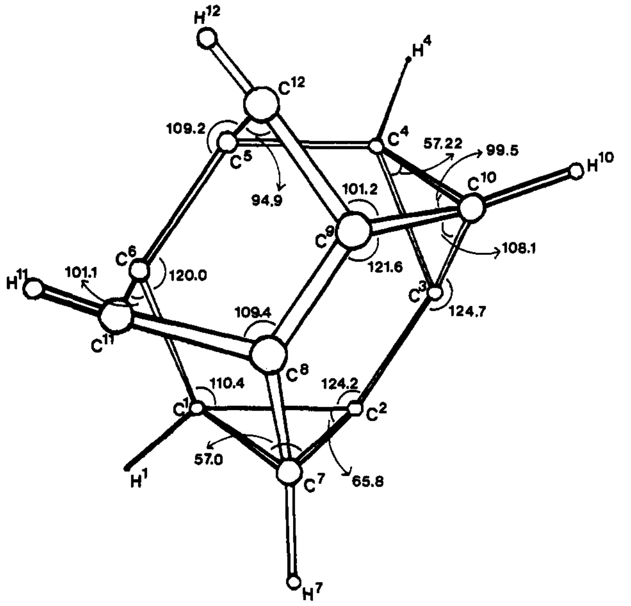


Figure 2. Selected nontrivial bond angles (∠C–C–C only) in MNDO-optimized *cyclo*-anthracene. Bond angles are symmetrical about the plane which bisects bonds $C^2–C^3$, $C^5–C^6$, and $C^8–C^9$.

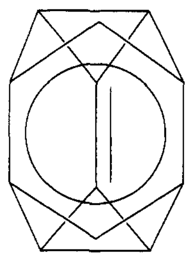
surface with a heat of formation of +451.1 kcal/mol, an ionization potential of 7.879 eV (calculated from the energy of the highest occupied molecular orbital), and a dipole moment of 1.533 debye. Force constant calculations indicate that all vibrational frequencies are real, as are the rotational and translational modes.

An examination of bond distances (Figure 1) and bond angles (Figure 2) indicates that the molecule is symmetrical about a plane bisecting the bonds connecting $C^2–C^3$, $C^5–C^6$, and $C^8–C^9$. However, there is no resemblance apparent between this MNDO-optimized molecule and the cyclic polyacene structure, 1, proposed by Kivelson and Chapman,[1] or to a face-fused cyclophane, 3. Rather, the minimized structure contains two cyclopropano groups opposed to each other on the top and bottom portions of the molecule, connected by a short double bond. The remaining hexagonal ring is symmetrical and boatlike, containing three bonds of 1.500 Å, two of 1.461 Å, and a final bond of 1.467 Å. Such a structure resembles 2 if two cyclopropano groups are added so as to eliminate the need for a diradicaloid system (as in 4).

Table I. MNDO-Optimized Bond Indices[a] for *cyclo*-Anthracene

bond[b]	bond index	bond[b]	bond index
$C^1–C^2$, $C^3–C^4$	0.967	$C^1–C^6$, $C^4–C^5$	0.932
$C^1–C^7$, $C^4–C^{10}$	0.914	$C^2–C^3$	1.803
$C^2–C^7$, $C^3–C^{10}$	0.963	$C^5–C^6$	1.286
$C^5–C^{12}$, $C^6–C^{11}$	1.473	$C^7–C^8$, $C^9–C^{10}$	0.933
$C^8–C^9$	1.643	$C^8–C^{11}$, $C^9–C^{12}$	1.117
C–H[c]	0.950		

[a] Total of σ and π bond order components. [b] For atom numbers, see Figures 1 and 2. [c] Average of all six C–H bond indices.



4

Is the ring formed by $\overline{C^5–C^6–C^{11}–C^8–C^9–C^{12}}$ aromatic (or at least delocalized) as implied by the structures comprising 2? The boatlike conformation and the relatively long bond lengths imply that the ring is not delocalized. However, without multiple-bond character, the valence of each of these six carbon atoms is less than the four expected for carbon atoms.

An examination of bond indices for the molecule (Table I) solves the problem of aromaticity or delocalization in the unique ring formed by $\overline{C^5–C^6–C^{11}–C^8–C^9–C^{12}}$. Even though the bonds in this ring exhibit no significant alteration in length, bond index data indicates that the actual bonding in this ring alternates between relatively strong bonds ($C^5–C^{12}$, $C^6–C^{11}$, and $C^8–C^9$) and relatively weak bonds ($C^5–C^6$, $C^8–C^9$, and $C^9–C^{12}$). Thus, bond lengths notwithstanding, this ring of the molecule is best described as a boatlike cyclohexatriene moiety, frozen in one benzene-like Kēkulē structure by the overall geometry adopted by the molecule.

Such a boatlike benzenoid structure is not without precedent. Regitz and co-workers[8] have reported the crystal and molecular structure of a highly substituted benzene ring which is strongly distorted due solely to steric strain factors. Their substituted benzene, which contains three adjacent 4,5,6-*tert*-butyl groups which are also adjacent to three alkoxycarbonyl groups (1-methoxy-, 2-*tert*-butoxy-, and 3-methoxycarbonyl), adopts a significantly boatlike conformation, with prow and stern angles of approximately 30° and 12° at carbons 1 and 4. Such a molecule is even more interesting than the boat distortion in *cyclo*-anthracene, since the distortion in *cyclo*-anthracene is forced upon the molecule by the ring fusion geometry, while the distortion in the molecule reported by Regitz and co-workers is purely steric in origin.

Conclusions

The simplest cyclic polyacene, *cyclo*-anthracene, is a stable minimum on the MNDO potential energy surface.

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[8] Maas, G.; Fink, J.; Wingert, H.; Blatter, K.; Regitz, M. *Chem. Ber.* 1987, *120*, 819.

J. Org. Chem. 1992, 57, 1033–1035

The optimized molecule is symmetrical about a plane bisecting the top and bottom portions of the molecule and contains two opposed cyclopropano groups connected by a strong double bond. One of the hexagonal rings in the molecule is best described as a cyclohexatriene moiety frozen in one of the Kékulé structures of benzene. This cyclohexatriene moiety contains abnormally long bonds which are calculated to exhibit multiple-bond character.

Acknowledgment. We thank the Northern Arizona University Computer Services for their generous donation of computer time and resources and the Office of Grant and Contract Services and the Organized Research Committee of Northern Arizona University for their support. We gratefully acknowledge the Department of Computer Science and Engineering of the College of Engineering and Technology, Lanny J. Mullens, Chair, for allowing our use of the Apollo/Hewlett-Packard 4600 computers. This is also a contribution from the Apollo/Hewlett-Packard Undergraduate Computer Project in Computer-Aided Molecular Design and Computational Chemistry, Earle B. Hoyt, Jr., director.

Supplementary Material Available: Tables of final atomic coordinates, molecular orbital energies, and calculated vibrational frequencies for *cyclo*-anthracene (5 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Elucidation of the Relative and Absolute Stereochemistry of Lobatriene, a Marine Diterpene, by a Modified Mosher Method

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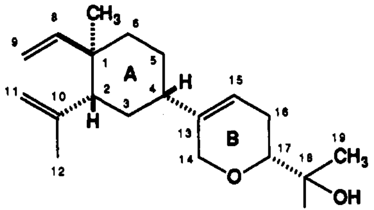
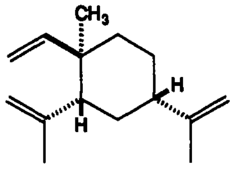
We have recently demonstrated the versatility of a modified Mosher method to elucidate the absolute configuration of organic compounds possessing a secondary alcohol moiety.[1] This method has been further extended to the absolute configurations of primary amines such as amino acids.[2] This method seems to be superior to other chemical methods in that it utilizes the chemical shift differences of many protons, and it as well has a self-examining function.[1] Although application of the method is limited to the compounds possessing a hydroxyl (or an amino) group, it should be employed for non-hydroxyl compounds that have the functional group that can be converted to a secondary alcohol. In this report we describe another application of the method used to determine the stereochemistry of a marine diterpene.

In the course of our searches for pharmaceutically active components from the Okinawan soft coral of the genus *Sinularia flexibilis*,[3] we isolated lobatriene (1) as a moderately cytotoxic substance together with (+)-β-elemene (2). Lobatriene has been obtained from the Great Barrier Reef soft coral of the *Lobophytum* species, and its structure has been deduced by comparison of its NMR properties with those of its analogues and 2.[4]

We at first confirmed the validity of the proposed relative stereochemistry of the substituents on ring A by extensive analysis of the NMR (500 MHz) data including COSY, H–C COSY, and NOESY spectra. We next turned our attention on the stereochemistry of the dimethylhydroxymethyl group at C-17 of ring B relative to the asymmetric centers of ring A. The dimethylhydroxymethyl group was deduced to exist in an equatorial position because H-17 (δ 3.25) appears as a doublet of doublets (J = 4 and 11 Hz). If ring B has a particular conformation with respect to ring A, NMR spectroscopy should be advantageous to deduce the stereochemical relationship between the substituents on rings A and B.[5] The NOEs (see **1a**) observed in the phase-sensitive NOESY spectrum are, however, quite confusing: Several unusual NOE cross peaks (e.g. $H_5 \rightleftarrows H_{15}$ and also $H_5 \rightleftarrows H_{14}$) appear from the protons on ring A to those on ring B. This anomaly must be owing to the rapid (on an NMR time scale) rotation of the rings around single bond C_4–C_{13}. The rotation seemed not to retard even at −40 °C, because most of the NOEs shown in **1a** were still observed at this temperature. Epoxidation of the double bond $C_{13}{=}C_{15}$ (to afford diepoxide **3**), which was done to increase the sterical bulkiness around C_{13}–C_{15}, was ineffective in slowing down the rotation. We therefore performed some chemical reactions to determine separately the absolute configurations of the substituents of rings A and B.



1; lobatriene



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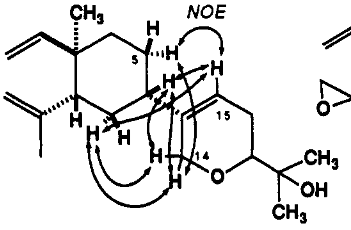
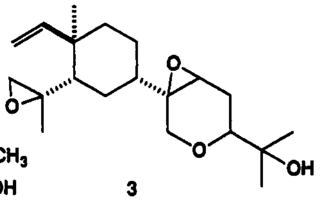


1 a



3

Lobatriene (1) was treated with lithium in liquid ammonia,[6] which resulted in the unusual product 4. On the contrary, reduction of 1 with lithium in ethylamine[7] gave diol 5, in which the vinyl and isopropenyl groups on ring A were also saturated. The CD spectrum of 5 measured in the presence of a lanthanide shift reagent[8] exhibited the first negative Cotton effect [λ 307 ($\Delta\epsilon$ −9), 294 (0), 283 ($\Delta\epsilon$ +8) nm] to indicate the R configuration at C-17. This finding was verifed by the modified Mosher's method: The (R)- and (S)-MTPA (methoxy(trifluoromethyl)phenylacetic acid) esters of the diol (5; 1 mg in each reaction) were

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