9,10-Bis(spirocyclopropyl)-9,10-dihydroanthracenes: Sterically Induced Deep Conformational Energy Wells

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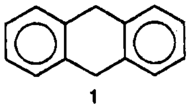
It is now generally agreed that 9,10-dihydroanthracenes (DHA's) exhibit a shallow potential well for distortions from planarity.[1−3] Substituent-dependent steric effects lead to boat, planar, and even chairlike central ring geometries. The potential energy surface has been well characterized computationally, and a much richer array of conformational interconversion pathways than suggested by mechanical models appears to be present.[4] Unfortunately, the flatness of this potential surface has prevented the unambiguous experimental demonstration of interconversion pathways. Given the level of interest and controversy that has characterized this area, it is remarkable that not one example of an experimental study that rigorously defines the conformational interconversion pathway and its associated barrier for a 9,10-DHA has been reported. We now describe the first example of a 9,10-DHA (**3**) with a pronounced barrier for conformational interconversion.



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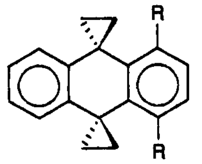

2: R = H

3: R = CH_3

In the solid state, 9,10-dihydroanthracene (**1**) is nonplanar with a boat-shaped central ring and an angle (α) of 145° between the planes containing the two aromatic rings.[5] Derivatives of **1** exhibit solid state geometries that range from planar (α = 180°) to highly folded (α = 129°).[1,27] In general, 9-substituted and *cis*-9,10-disubstituted compounds have boat-shaped central rings whereas 9,9-disubstituted, *trans*-9,10-disubstituted, and 9,9,10,10-tetrasubstituted ones are planar. In solution, **1** and its derivatives have often been assumed to have boat conformations though low-temperature ^1H and ^{13}C NMR studies[6] do not distinguish facile boat-to-boat inversion from a planar conformation. Recent molecular mechanics (MM2) and semiempirical molecular orbital calculations (AM1) suggest a very low boat-to-boat inversion barrier (0.3 and 0.5 kcal mol^{-1}, respectively) and a planar transition state for the inversion process for **1**.[7] The barrier predicted from *ab initio* calculations[8] is 1.9 kcal mol^{-1}, and this agrees with a recent UV analysis of jet-cooled samples of **1**.[9]

The spirocyclopropyl group, placed in the 9 and/or 10 position(s) of 9,10-DHA's, has the potential to create unique steric barriers for conformational interchange.[10] This is clearly demonstrated by molecular mechanics (MMX) calculations[11] for bis(spirocyclopropyl)-9,10-dihydroanthracene (**2**),[12] which exhibits both planar (ΔH_f 97.3 kcal mol^{-1}) and highly-folded boat (ΔH_f 91.3 kcal mol^{-1}) minima. Semiempirical (AM1)[13] and *ab initio* (6-31G**//3-21G(*))[14] molecular orbital calculations also support the existence of both planar and boat conformational energy minima but with much smaller differences in the energies of the two conformers, 0.6 kcal mol^{-1} (planar **2** favored) and 3.1 kcal mol^{-1} (boat **2** favored), respectively.[15] The introduction of methyl groups at positions 1 and 4 (to give analogue **3**) affords a molecule with only a highly folded boat molecular mechanics minimum.

A modified Simmons−Smith cyclopropanation[16] of the known precursor, 9-spirocyclopropyl-10-methylenedihydroanthracene (**4**),[17] afforded **2** in 37% yield.[18] The room temperature ^1H NMR spectrum of **2** is consistent with either a planar

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(3) The closely related 9-methylene-9,10-dihydroanthracenes (MDAs) are less well studied and present a very different picture. These compounds exhibit preferred geometries with a boat-shaped central ring and, in some cases, an easily measured conformational interconversion barrier.[2] In fact, as early as 1969 an example of a substituted MDA in which the two conformational isomers were isolated had been reported, and consequently there has been no controversy regarding the geometries of MDAs. This contrast to the behavior observed for 9,10-DHAs is the result of the steric interference of hydrogens or groups on the exocyclic double bond with hydrogens or groups in the peri position: (a) Curtin, D. Y.; Holubec, Z. M. *J. Org. Chem.* **1969**, 34, 3093−3096. (b) Leung, P.-T.; Curtin, D. Y. *J. Am. Chem. Soc.* **1975**, 97, 6790−6799, (c) 6799−6803.

(4) Lipkowitz, K. B. In ref 2, Chapter 7.

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(9) Shin, Y.-D.; Saigusa, H.; Zgierski, M. Z.; Zerbetto, F.; Lim, E. C. *J. Chem. Phys.* **1991**, *94*, 3511.

(10) NMR shielding effects of the cyclopropyl group on adjacent peri protons in spirocyclopropyl DHAs have been examined as a conformational probe: Ryder, M. T.; Rosenfeld, S. M. *Org. Magn. Reson.* **1983**, *21*(1), 24−27.

(11) Molecular mechanics calculations were performed using the MMX force field in the computer program PCMODEL, version 4.5 (Serena Software, Bloomington, IN): Gajewski, J. J.; Gilbert, K. E.; McKelvey, J. In *Advances in Molecular Modeling*; Liotta, D., Ed.; JAI Press Inc.: London, 1993; Vol. 2, pp 65−92.

(12) The IUPAC name for **2** is dispiro[cyclopropane-1,9′(10′*H*)-anthracene-10′,1″-cyclopropane].

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(15) Both semiempirical (AM1 with complete RHF geometry optimization) and *ab initio* (Hartree−Fock 6-31G**//3-21G(*)) molecular orbital calculations were performed with the program Spartan, version 3.1 (Wavefunction, Inc.), on a Silicon Graphics Iris Indigo2 XZ workstation. The AM1 heats of formation were 107.08 kcal mol^{-1} (planar **2**) and 107.69 kcal mol^{-1} (boat **2**). Total energies from single-point 6-31G** calculations on structures from full geometry optimization with no symmetry restrictions at the HF/3-21G(*) level were −690.918 907 5 (planar **2**) and -690.923 897 9 au (boat **2**).

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(17) Bailin, S. J.; Grande, K. D.; Kunin, A.; Thanabalasundrum, S.; Rosenfeld, S. M. *Synth. Commun.* **1981**, *11*(2), 141−145.

(18) Mp: 193−194.5 °C; ^1H NMR (100 MHz, $CDCl_3$): δ 1.46 (s, 8H), 6.88−7.23 (m, 8H). High-resolution mass spectrum calcd for $C_{18}H_{16}$: 232.1252. Found 232.1245.

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conformation or rapidly interconverting boat conformations. At −80 °C the 400 MHz ^{1}NMR spectrum (toluene-d_8) is essentially unchanged and no peak broadening is observed. Interestingly, though, there is an upfield shift of ca. 0.2 PPM in the peri proton signal, which may be due to enhanced shielding of that proton by the cyclopropyl ring, an effect that would be maximized in the planar conformation.[10] X-ray crystallographic analysis[19] showed that **2** has a planar geometry ($\alpha = 179°$) for the 9,10-DHA core in the solid state.

The dimethyl analogue **3** was prepared in 60% yield[20] by double cyclopropanation of 1,4-dimethyl-9,10-anthraquinodimethane (**5**).[21,22] The room temperature 100 MHz ^{1}H NMR spectrum of **3** is striking in that two broad resonances at δ 1.1 and 2.0 for the cyclopropyl protons are present. At 400 MHz, each of these is split into two separate but still broad peaks, providing clear evidence that **3** has a preferred boat conformation with a conformational interconversion barrier that is accessible on the NMR time scale. Variable temperature ^{13}C NMR spectra of **3** (100 MHz, toluene-d_8) show separate resonances for the pseudoaxial (δ 10.71) and pseudoequatorial (δ 17.84) cyclopropyl carbons, narrow singlets at −80 °C, that progressively broaden and coalesce at higher temperatures (T_c 60 °C). The rate of conformational interconversion at 60 °C, calculated by the method of Gutowsky and Holm,[23] is 1543 s^{-1}, corresponding to a free energy of activation of 14.7 kcal mol^{-1} using the approach of Calder and Garratt.[24]

In light of these results, it is not surprising that the X-ray crystallographic analysis of **3**[25] shows that this molecule exists in the most "superfolded" boat geometry ($\alpha = 127°$)[26] so far reported[27] for a 9,10-DHA. Even in this geometry, a significant distortion of the cyclopropyl groups in which the bond angles around the quaternary cyclopropyl carbons are ca. 4° larger on the cyclopropyl faces nearest the aryl methyl groups is present as is a corresponding bend of the methyl groups that shows up as a ca. 7° difference in the bond angles about the peri carbons.

It is well-known that aromatic substituents induce bond-length asymmetry in cyclopropanes and that the largest effects occur in the so-called bisected conformation.[28] Consequently, the crystal structures of **2** and **3** provide a definitive example of this effect. For **2**, the distal C−C cyclopropane bond (1.478 Å) is ca. 0.05 Å shorter than the vicinal bonds (1.533 Å). The AM1 calculations reproduce this effect well, giving the values 1.493 Å (distal) and 1.524 Å (vicinal). In **3**, a similar contraction of the distal bond (ca. 1.49, 1.48 Å; for the two crystallographically independent molecules in the unit cell) occurs, but here the pseudoequatorial vicinal bond (1.51, 1.51 Å) is also shortened compared to the pseudoaxial vicinal bond (1.53, 1.53 Å) which is of the same length as the vicinal bonds of **2**.

In conclusion, steric interactions between cyclopropyl hydrogens and peri methyl groups in 9,10-DHA **3** lead to a solid state structure with a superfolded boat geometry and a solution phase barrier for boat-to-boat conformational interconversion that is easily measured on the NMR time scale. For **2**, the solid state structure is planar though molecular mechanics, semiempirical MO, and *ab initio* MO calculations of structure all support the existence of both planar and boat geometries with the boat geometry favored at the most rigorous level of calculation attempted.

Acknowledgment. We are grateful to the Camille and Henry Dreyfus Foundation Scholar/Fellow Program for Undergraduate Institutions for support of this research and to the National Science Foundation Research in Undergraduate Institutions Instrumentation Program (Grant No. 8818307) for creation of The New England Molecular Structure Center at Keene State College. We also thank Professor Robert G. Linck (Smith College) for helpful discussions of the computational chemistry and Kim Nesheim for preliminary work on the project.

Supplementary Material Available: Complete synthetic procedures and spectral data for **2** and **3** and tables of crystallographic data including positional and thermal parameters, bond angles and distances, and torsional angles (30 pages); tables of observed and calculated structure factors (48 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.

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(19) Crystal data for **2**: Crystallization of **2** from acetone at 0 °C yielded clear prism crystals of X-ray quality. The compound crystallized with a mirror plane bisecting the molecule into two equivalent asymmetric units, or fragments, each consisting of a single aromatic ring with an attached cyclopropyl group. The crystallographically determined fragment and its symmetry-generated analogue become the 9,10-DHA moiety when the two are connected and expanded across the mirror plane. Data collection was done at ambient temperature on a Rigaku AFC6S diffractometer with graphite-monochromated molybdenum Kα radiation (λ = 0.710 69 Å). Twenty-five reflections were used for the unit cell determination, corresponding to an orthorhombic cell in the space group *Pbca* (No. 61) with the following lattice parameters: a = 13.517(7) Å, b = 14.949(8) Å, c = 6.080(3) Å, V = 1229(1) Å^3. For Z = 4 and formula weight 232.32, the calculated density was 1.256 g cm^{-3}. A total of 2090 reflections were collected. The structure was solved by direct methods. R = 0.041 (R_w = 0.039). All calculations were performed using the TEXSAN, TEXRAY Structure Analysis Package, version 2.1, of Molecular Structure Corporation, The Woodlands, TX.

(20) Mp: 113−114 °C. ^{1}H NMR (400 MHz, CDCl$_3$): δ 0.90 (br s, 2H), 1.04 (br s, 2H), 1.97 (br s, 2H), 2.07 (br s, 2H), 2.46 (s, 6H), 6.80 (s, 2H), 7.06−7.12 (m, 2H), 7.16−7.21 (m, 2H). High-resolution mass spectrum calcd for $C_{20}H_{20}$: 260.1565. Found: 260.1565.

(21) (a) Bowden, B. F.; Cameron, D. W. *Tetrahedron Lett.* **1977**, 383. (b) Rosenfeld, S.; VanDyke, S. *J. Chem. Educ.* **1991**, *68*, 691.

(22) Rosenfeld, S.; Jasinski, J. P. *J. Org. Chem.* **1991**, *56*(2), 878.

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(24) Calder, I. C.; Garratt, P. J. *J. Chem. Soc. (B)* **1967**, 660.

(25) Crystal data for **3**: Crystallization of **3** from pentane yielded clear prism crystals of X-ray quality. Data collection and refinement was done as it was for **2**. The unit cell was monoclinic in the space group $P2_1/c$ (No. 14) with the following lattice parameters: a = 15.296(3) Å, b = 7.483(1) Å, c = 26.836(5) Å, β = 106.42(1)°, V = 2946(2) Å^3. For Z = 8 and formula weight 260.38, the calculated density was 1.174 g cm^{-3}. Of the 5829 reflections that were collected, 5610 were unique. R = 0.061 (R_w = 0.085).

(26) There are two molecules in the asymmetric unit differing only slightly in their geometries. The angles between the least-squares planes of the aromatic rings are 127° and 131°, respectively.

(27) Most 9,10-DHAs that have been characterized crystallographically have α greater than 145°. The striking exception is *trans*-9-isopropyl-10-methyl-9,10-dihydroanthracene with α = 129°, and this geometry has been referred to as "superfolded:" Stanford, R. H. *Acta Crystallogr., Sect. B* **1973**, *29*, 2849.

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