The Effect of 10-Spirocyclopropyl and 10-Spirooxiranyl Groups on 9-Anthracenone Geometry

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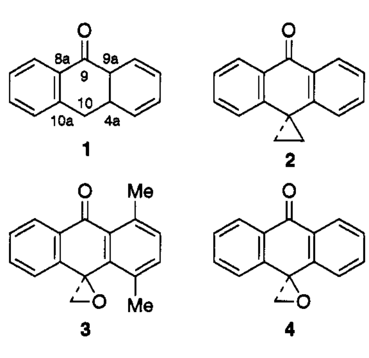
Received August 2, 1994

A number of groups have examined the geometries of 9-anthracenones (9-anthrones) using spectroscopic and computational approaches as well as X-ray crystallographic analysis. In one of the most thorough studies to date, Sygula and Rabideau *et. al.*[1] have demonstrated that 9-anthracenone (**1**), the parent member of this series, favors a planar conformation and that monosubstitution at the 10 position leads to a distortion toward more boatlike geometries (i.e., having a central ring that is more folded about the 9,10 axis) with the substituent in the pseudoaxial position and that this distortion generally increases with the steric bulk of the substituent atom or group. This is in stark contrast to the situation for the related 9,10-dihydroanthracenes which favors a folded geometry that is fairly insensitive to the size of a single pseudoaxial substituent in the 9 or 10 position.[2] For both families, the parent member has a shallow potential energy well in the vicinity of the favored conformation.

Recently, we have described unique steric effects of spirocyclopropyl groups on 9,10-dihydroanthracene conformation,[3] and the Sygula/Rabideau study prompts us to present some related findings in the 9-anthracenones. Therefore, we now report the molecular and crystal structure of 10-spirocyclopropyl-9-anthracenone (spiro[anthracene-9(10*H*),1′-cyclopropan]-10-one, **2**) and an oxirane analogue (1,4-dimethylspiro[anthracene-9(10*H*),2′-oxiran]-10-one, **3**) along with a limited computational study of these compounds and a second oxirane analogue (**4**).



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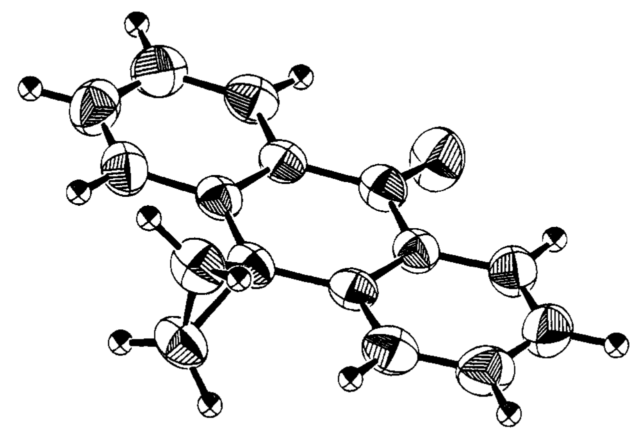

Figure 1. ORTEP drawing of the crystal structure of **2**. The thermal ellipsoids are plotted at the 50% probability level.

The preparation of spirocyclopropylanthrone **2** has been described previously.[4] Its X-ray crystal structure (Figure 1) demonstrates that molecules of **2** exhibit a planar geometry (i.e. the atoms of the 9,10-dihydroanthracene skeleton lie essentially in one plane) in the solid state.[5] This is the best geometry for conjugative interaction between the carbonyl group and the aromatic rings and it also provides a reasonable distance (*ca.* 2.25 Å) between the cyclopropyl ring hydrogens and the *peri* hydrogens of the outer six-member rings. The cyclopropyl–phenyl conjugative interaction is also maximized in this geometry, and the well-known cyclopropyl bond length asymmetry induced by this effect[6] is apparent in that the distal C–C cyclopropane bond is *ca.* 0.06 Å shorter than the vicinal bonds (Table 1). In fact, **2** was assumed to have the planar geometry in an earlier study involving NMR long-range anisotropic shielding effects of cyclopropane rings.[7] Nonetheless, a boat geometry (folded central six-member ring) has the potential of further reducing the *peri* steric interaction and, though some conjugation is sacrificed and the carbonyl carbon may have less favorable bond angles, the C10 bond angles may approach a value closer to the optimum.

Accordingly, semiempirical molecular orbital calculations using the AM1 method and full geometry optimization were performed to establish whether a minimum energy boat geometry exists and if so how its energy compares to that of the planar conformation. Using planar and folded starting geometries for these calculations, we did in fact locate two potential energy minima. Interestingly, the planar geometry, favored in the crystal, has a ΔH_f (48.66 kcal mol^{-1}) that is only 1.65 kcal mol^{-1} lower than that for the boat geometry. The AM1 calculations for planar **2** reproduce the observed cyclopropyl bond length asymmetry well (Table 1). The boat is a highly-folded structure as is evident in the large values for the central ring dihedral angles α1 and α2 (Table 2). The significantly larger value for dihedral α1 (*ca.* 11 °C)

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(5) The authors have deposited atomic coordinates for structures **2** and **3** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.
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Table 1. Measured and Calculated (AM1) Lengths (Å) of Vicinal and Distal Bonds in the Three-Membered Rings of 2–4

	X-ray		AM1	
	vic	dist	vic	dist
2 (planar)	1.536(2), 1.537(2)	1.478(3)	1.526, 1.526	1.493
2 (boat)			1.525(ax), 1.515(eq)	1.492
3x	1.482(9), 1.430(6)	1.419(8)	1.502(ax), 1.443(eq)	1.432
3y			1.456(ax), 1.493(eq)	1.427
4x			1.503(ax), 1.449(eq)	1.430
4y			1.454(ax), 1.496(eq)	1.428

Table 2. Calculated (AM1) Dihedral Angles[a] for the Central Six-Membered Ring of the Boat Conformations of 2–4

angle	2	3x[b]	3y	4x[c]	4y[c]
α1 (deg)	36.73	36.37	43.07	22.07	32.34
α2 (deg)	25.98	29.09	31.49	15.10	25.00

[a] Angle α1 is the average of the absolute values of torsional angle C10a–C10–C4a–C9a and its symmetry related partner. Angle α2 is the average of the absolute values of torsional angle C8a–C9–C9a–C4a and its symmetry-related partner. [b] The angles analogous to α1 and α2 in the X-ray structure of **3** have the values 26.1(7)° and 26.5(7)°, respectively. Here, however, each pair of angles is not a symmetry-related pair. Therefore the individual values are of interest and these are α1, −27.6(7) and 24.8(7); α2, −28.2(7) and 24.8(7). [c] The angles analogous to α1 and α2 in the molecular mechanics (MMX) structures of **4x** and **4y** are 27.8° (**4x**, angle α1), 18.8° (**4x**, angle α2), 36.4° (**4y**, angle α1), and 24.0 (**4y**, angle α2).

demonstrates that the spirocyclopropyl bearing end of the central six-member ring is more bent than the carbonyl end of that ring. Since we expect the bending to be primarily driven by *peri* steric interactions at the spirocyclopropyl end, this is not surprising. Moreover, Sygula and Rabideau found this to be a consistent pattern in molecular mechanics (MM2) geometries of ten monosubstituted 9-anthracenones and in the X-ray crystal structures of bromo-, isopropyl-, and tert-butyl-substituted members of the series. In methyl- and phenyl-substituted compound crystal structures, however, those workers found that the central ring bend was more nearly similar at the two ends of the ring and attributed this difference to crystal packing forces.

Nearly all 9-anthracenones for which crystal structures have been reported exhibit either boat[8] or planar[9] geometries. However, Rauwald, Lohse, and Bats[10] have established that 10-(β-D-glucopyranosyl)-1,8-dihydroxy-3-(hydroxymethyl)-9(10*H*)-anthracenone (aloin), the pharmaceutically-significant major component of a number of species of aloe, has an envelope conformation with C10 raised from the plane of the five remaining carbons of the central ring. Also, Skrzat and Roszak[11] have reported a shallow chairlike geometry for 10-(4-acetoxyphenyl)-10-hydroxy-9(10*H*)-anthracenone. To probe the existence of additional conformational energy minima for **2**, we carried out a series of molecular mechanics (MMX) calculations using global search techniques. No chairlike or envelope geometries were located using this approach and the lowest energy geometry was a highly-folded boat (dihedrals: α1 = 36.5°, α2 = 32.8°). A nearly planar (very shallow boat with dihedrals α1 = 2–3° and α2 = 3.1–5.9°) local minimum was located at *ca.* 2.2 kcal mol^{-1} higher in energy. However, since the electronic effects due to the cyclopropyl–phenyl interaction are not represented in the molecular mechanics force field, the accuracy of these calculations is expected to be lower than that of the molecular orbital approach described earlier and this is evidenced by the incorrect prediction of a boat geometry for the global minimum using this method.

The oxirane analogue of **2** (**4**) has been described previously[12] and presents an interesting contrast. We were unfortunately unable to obtain a crystal structure of **4** but AM1 calculations offer some insight. Two different boat conformations for **4** are possible, and we were able to locate potential energy minima for both. The conformation with the oxirane methylene group in the pseudoaxial position (**4x**) is favored energetically by 4.25 kcal mol^{-1} (23.67 vs 27.92 kcal mol^{-1}) over the one with the pseudoequatorial methylene (**4y**). The central ring dihedral angles (Table 2) demonstrate that **4x** is substantially less folded than **4y**, and this is certainly a result of the lesser steric demand of the oxygen nonbonded electron pairs compared to that of the methylene hydrogens. For both geometries, the carbonyl end of the central six-member ring is less bent. Not unexpectedly, **4y** has dihedral angles that are very similar to the analogous angles in the AM1 structure for the boat form of **2** since the steric requirements of the methylene groups of the three-membered rings in both compounds are the principal determinant of the extent of folding. Despite repeated attempts, we were unable to locate a planar minimum energy geometry for **4** and we conclude that the planar geometry in this compound does not represent a minimum on the potential energy surface.[13] We were likewise unsuccessful in locating a planar energy minimum using molecular mechanics coupled with global search techniques. In fact, this latter approach yielded only the two boat structures described above (**4x**, ΔH_f = 19.25 kcal mol^{-1}; **4y**, ΔH_f = 24.20 kcal mol^{-1}).

The 1,4-dimethyl analogue of **4** (**3**) was easily available from 1,4-dimethyl-9,10-anthraquinone by a previously described method and we were able to obtain an X-ray crystal structure for a racemic sample of this compound (Figure 2). The observed geometry has the oxirane methylene group in the pseudoaxial position and both ends of the central six-member ring are bent to a similar degree. As in the case of **4**, we were unable to locate a planar AM1 minimum energy geometry but did find geometries corresponding to **4x** and **4y** (**3x** and **3y**). The geometry with the oxirane methylene pseudoaxial (**3x**) has a calculated ΔH_f of 13.70 kcal mol^{-1}, nearly 5 kcal mol^{-1} lower in energy than the other boat conformer (18.57 kcal mol^{-1}). The added methyl groups in **3** *vs* **4** have little effect on the energy *difference* between the x and y conformers though they dramatically alter the extent of folding (Table 2): **3y** is the most folded structure of all that we have calculated. It should be noted,

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(13) The reaction of **4** with dimethylsulfonium methylide is stereospecific, affording only the corresponding *trans* bisepoxide.[12b] A qualitative assessment of conformational preference, based on NMR shielding effects of the oxirane group, suggested that **4** exists as a mixture of roughly equal amounts of **4x** and **4y** in solution and that the stereospecificity does not arise out of a preference for one of these conformations.[12a] It appears now that **4x** is probably strongly favored and therefore the stereospecificity in the reaction with dimethylsulfonium methylide must result from a preference for attack at one face of the carbonyl group of **4x**.

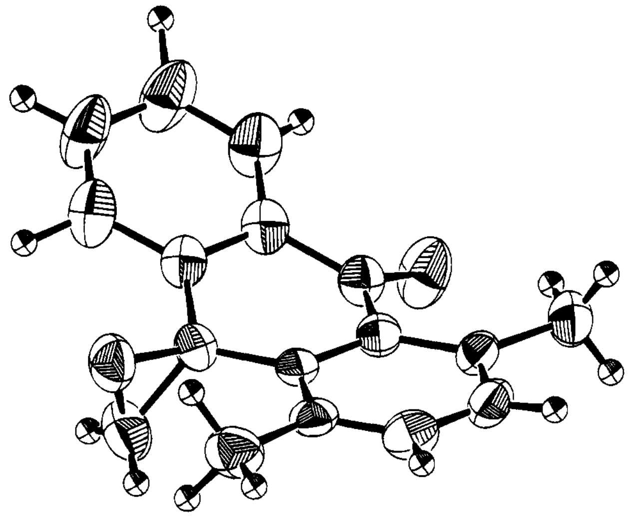

Figure 2. ORTEP drawing of the crystal structure of **3**. The thermal ellipsoids are plotted at the 50% probability level.

however, that the agreement between the crystal structure of **3** and the calculated geometry **3x** is poor in that the spirooxirane-substituted end of the central six-membered ring is significantly more bent in the calculated structure. A somewhat greater flattening of the crystal structure geometry compared to an MM2 calculated structure of 10-methyl-9-anthracenone has been attributed to the effects of crystal packing forces[1] and that is the likely explanation here as well.

Conclusions

We have reported crystallographically determined structures and associated calculations for 10-spirocyclopropyl- and 10-spirooxiranylanthracenones representing the extremes of the range of previously described 9-anthracenone geometries. The spirocyclopropyl group in **2** is responsible for altering the 9-anthracenone potential energy surface so that both planar and highly-folded boat minimum energy geometries exist, a finding that parallels our previous work on 9,10-dispirocyclopropyl-9,10-dihydroanthracenes. While the planar geometry is favored for **2**, the boat conformation is less than two kcal mol^{-1} higher in energy and AM1 calculations predict that a spirocyclopropyl group is roughly equivalent to a single *tert*-butyl group in the 10-position in its ability to cause folding of the central ring of 9-anthracenones. In contrast, incorporation of the spirooxiranyl group appears to lead to boat geometries only, with the larger (methylene) group favored in the pseudoaxial position. These observations point toward the importance of steric interactions in determining the geometries of 9-anthracenones, 9,10-dihydroanthracenes, and perhaps structurally similar compounds substituted with spirocyclic three-membered rings.

Experimental Section

^1H NMR spectra were run on a Bruker WP100SY spectrometer at 100 MHz (TMS reference), and IR spectra were run on a Nicolet 20 DXC FTIR spectrometer.

1,4-Dimethylspiro[anthracene-9(10*H*),2′-oxiran]-10-one (3). Compound **3** was prepared in 84% yield from 1,4-dimethyl-9,10-anthraquinone[14] exactly as described previously for **4**: mp 85–90 °C; ^1H NMR ($CDCl_3$) δ 2.58 (s, 3H), 2.73 (s, 3H), 3.0 (d, 1H), 3.4 (d, 1H), 7.25 (m, 4H), 8.2 (m, 4H); IR (thin film, NaCl disk) 1666, 1258 cm^{-1}.

Calculations. Semiempirical molecular orbital calculations were performed with the program HyperChem, release 2. The AM1 method with complete (RHF) geometry optimization, employing the Polak–Ribiere conjugate-gradient algorithm, was used. All calculations converged successfully and had final gradients less than 0.1. Molecular mechanics calculations were performed using the MMX force field[15] in the computer program PCMODEL, version 4.5 (Serena Software, Bloomington, IN). Global searches were performed with the companion program GMMX, version 1, using a statistical search on coordinates in which a randomly selected subset of atoms is chosen for movement. Each structure alteration is followed by energy minimization and then comparison to previously located structures. Unique minimum energy structures within 3 kcal mol^{-1} of the lowest energy structure located were selected for final minimization in PCMODEL. All calculations were done on a Silicon Graphics Iris Indigo workstation.

X-ray Structure Determination. Experimental details of the X-ray crystallographic structure determination of **2** and **3** follow. Both structures were solved by direct methods.[16,17] Neutral atom scattering factors were taken from Cromer and Waber.[18]

Crystal Data for 2. Crystallization of **2** from CH_2Cl_2 at low temperature yielded clear prism crystals of X-ray quality. Data collection was done at ambient temperature on a Rigaku AFC6S diffractometer with graphite-monochromated molybdenum Kα radiation (λ = 0.71069 Å). Twenty-three reflections were used for the unit cell determination, corresponding to a monoclinic cell in the space group $P2_1/c$ (no. 14) with the following lattice parameters: a = 8.351(2) Å, b = 10.074(3) Å, c = 13.332(3) Å, β = 100.07(2)°, V = 1104.3(5) Å^3. For Z = 4 and formula weight 220.27, the calculated density was 1.325 g cm^{-3}. Theta range 5° to 55°. Of the 2204 reflections collected, 2057 were unique. The structure was solved by direct methods. R = 0.046 (R_w = 0.054).

Crystal Data for 3. Crystallization of **3** from diethyl ether yielded clear prism crystals of X-ray quality. Data collection and structure refinement were done as described above. Twenty-five reflections were used for the unit cell determination, corresponding to a monoclinic cell in the space group $P2_1/a$ (no. 14) with the following lattice parameters: a = 9.214(5) Å, b = 14.488(3) Å, c = 10.160(3) Å, β = 112.04(3)°, V = 1257.2(8) Å^3. For Z = 4 and formula weight 250.30, the calculated density was 1.322 g cm^{-3}. Theta range 5° to 50°. Of the 3183 reflections collected, 3006 were unique. R = 0.072 (R_w = 0.084). In this structure, the three hydrogens of the methyl group on C1 and the hydrogen on C6 would not refine isotropically and were therefore left in their calculated positions without further refinement.

Acknowledgment. This work was supported by a William and Flora Hewlett Foundation Award of Research Corporation and by the Camille and Henry Dreyfus Foundation Scholar/Fellow Program for Undergraduate Institutions. The New England Molecular Structure Center at Keene State College was created through a grant from the National Science Foundation Research in Undergraduate Institutions Instrumentation Program (grant no. 8818307).

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