J. Org. Chem. **1993,** *58,* 7572-7575

Notes

Why There Are No Small [*n*](9,10)Anthracenophanes

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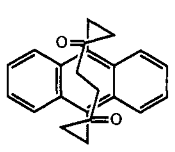
Received June 2, 1993

Para-bridged benzenes, the so-called [*n*]paracyclophanes, have a long and rich history driven by the challenges inherent in the synthesis of highly strained molecules and by the promise of improved understanding of aromaticity.[1,2] Special synthetic approaches that facilitate formation of high-strain target molecules became important with the synthesis of [7]paracyclophane[3] and also yielded the smallest easily isolable member of the series, [6]paracyclophane.[4] Success can be claimed in the preparation of [5]paracyclophane[5] too, though this compound is only stable in solution below 273 K. Transient existence for [4]paracyclophane has been demonstrated through trapping experiments and electronic spectra.[6] Numerous theoretical investigations of this series have also appeared.[7] This phase of [*n*]paracyclophane history spans 20 years and represents dramatic progress in which each new venture toward smaller bridge size was fueled by previous success.

In contrast, the dibenzologues of the [*n*]paracyclophanes, [*n*](9,10)anthracenophanes, have been much less studied. The smallest member of the family having a saturated all-carbon bridge is [10](9,10)anthracenophane, first reported in 1974.[8] No smaller hydrocarbons in this series have been reported. There are good reasons to pursue the [*n*](9,10)anthracenophanes since the inherent high reactivity of the anthracene core promises a rich chemistry for these distorted homologues of anthracene. And yet, the synthetic pursuit, only just begun, appears to have ended prematurely. In fact, some efforts in this direction have been reported:[9] Other unpublished attempts have almost certainly been made.[10] This paper provides a likely explanation for difficulties in the synthesis of small bridge [*n*](9,10)anthracenophanes and may have implications for the synthesis of other polycyclic [*n*]phanes.

3,6-Diketo[8](9,10)anthracenophane (**1**) was reported in 1974 and was described as being prone to air oxidation in solution.[11] In a later NMR study of that compound[12] we found that acid-catalyzed deuteration led to incorporation of deuterium at the benzylic positions, as well as at the positions α to the carbonyl groups, apparently due to involvement of the corresponding bridged methylenedihydroanthracene (MDA) tautomer **2**. Similarly for the dithia[*n*](9,10)anthracenophanes **3-5**, first described in 1983,[13] molecular mechanics calculations suggested that the anthracene-MDA energies are close throughout the series, and an associated NMR study provided evidence for the predominance of the MDA tautomer in base-containing DMSO-d_6 solutions.[14,15] That work suggested the importance of doing a careful computational study of the smaller [*n*](9,10)anthracenophanes and their MDA tautomers, and we now report a molecular mechanics investigation of these compounds.



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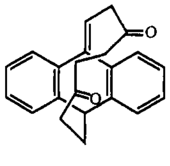

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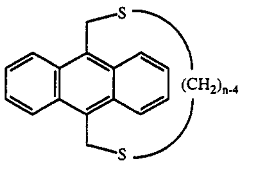
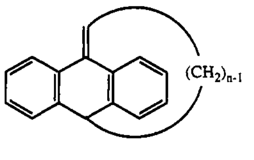


3 (n=8), 4 (n=9), 5 (n=10)



10 (n=5), 11 (n=6), 12 (n=7), 13 (n=8)

Computational Methods

Molecular mechanics calculations were performed by using the MMX force field contained in the program PCMODEL,[16] version 4. The program GMMX,[16] version 1.0, was used to conduct global searches of conformational space using primarily a statistical method in which a randomly selected subset of atoms

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(10) We have made unsuccessful attempts utilizing various approaches, but this comment refers to the probablility that others have done likewise.

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(16) PCMODEL and GMMX are available from Serena Software, P. O. Box 3076, Bloomington, IN 47402-3076.

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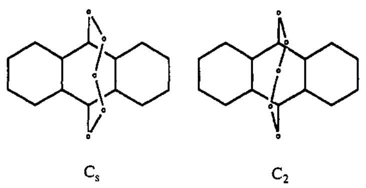


Figure 1. Stylized drawings of C_s and C_2 geometries for **6**.

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 of the lowest energy structure located were selected for final minization in PCMODEL. In some cases additional searches employing both statistical atom movement and statistical rotation of single bonds were done but these searches failed to locate any additional unique structures.

Semiempirical molecular orbital calculations were performed with the program HyperChem[17] using the AM1 method and complete (RHF) geometry optimization. The Polak-Ribiere conjugate-gradient algorithm was employed, and all calculations converged successfully and had final gradients less than 0.1. Input structures for these calculations were generated by molecular mechanics procedures using the MM+ force field in HyperChem. All calculations described in this paper were performed on a Silicon Graphics Iris Indigo workstation.

Angles ϕ and α (defined in Figure 3) were calculated as previously described.[14] As noted in that work, the description of ø is somewhat problematic since the four central atoms of the anthracene ring do not necessarily lie in the same plane. They are in the same plane for calculated structure **6** and are very nearly so for **8** and **9**. The deviation from planarity (defined further in reference 14 as angle β) is 3.7° for **7**. Angles ϕ and α reported in Table II are averages of the two analogous angles in each structure: Since no symmetry constraints were applied in the molecular mechanics calculations, these angles may differ though generally only slight differences were found (0–1.4° for ϕ, 0–1.5° for α).

Results and Discussion

We have calculated global minimum energy structures for [*n*](9,10)anthracenophanes **6–9** and the corresponding bridged MDA tautomers **10–13** using molecular mechanics procedures. Minimum energy structures were located by using the global search program GMMX,[16] employing primarily a statistical search on coordinates. Structures located in this fashion were then subjected to molecular mechanics minimization using the MMX force field.

The [*n*](9,10)Anthracenophanes. Not surprisingly, these structures bear great resemblence to the molecular mechanics structures of the corresponding [*n*]paracyclophanes reported by Allinger et al. some 20 years ago.[18] As pointed out by those authors, members of the series with an odd number of bridge methylene groups are able to have geometries with either C_s or C_2 symmetry (Figure 1). For C_2 symmetry, the central methylene group may have its hydrogens pointing into the aryl ring or away from it. For compounds with an even number of bridge methylenes, reasonable staggering of hydrogens in the bridge demands geometries with C_2 symmetry. Like Allinger, we have found that the preferred geometry for bridge lengths of 5 (compound **6**) and 7 (compound **8**) is C_s and for 6 (compound **7**) is C_2 (Figure 2). For a bridge length of 8 (compound **9**), however, the lowest energy structure that we found is neither C_s nor C_2. That structure has the benzylic methylene groups canted in the same direction (like C_s structures) but has the remaining methylene groups arranged (hydrogens staggered) so as to preclude C_s symmetry. A structure having C_2 symmetry has a heat of formation 1 kcal above this global minimum (Table I).

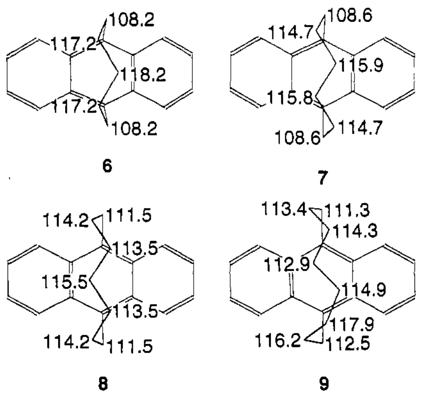
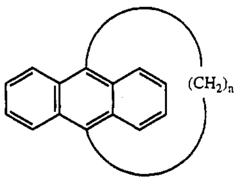


Figure 2. Minimum energy geometries and selected bond angles for anthracenophanes **6–9**.



6 (n=5), 7 (n=6), 8 (n=7), 9 (n=8)

The lowest energy structures for **6–9** are compared in Table II to the corresponding [*n*]paracyclophane structures calculated by Allinger[18] and Carballeira et al.[19] using a force field due to Boyd[20] and Tsuzuki and Tanabe[21] using MM2[22] with newly-refined parameters established through *ab initio* molecular orbital calculations. Our deformation angle ϕ (defined in Figure 3) is larger by 5.5–7.6° than the angle reported by Allinger for the corresponding [*n*]paracyclophanes. Except in the case of **6** our angle is larger in similar or greater measure than those [*n*]paracyclophane angles described by Carballeria et al.[19] and by Tsuzuki and Tanabe.[21] It is interesting to note that in the most recent molecular mechanics study of [*n*]paracyclophanes[21] ϕ is consistently lower than experimental values from X-ray diffraction studies of derivatives of these compounds though it falls within 1° for [8]paracyclophane. Our angle α, in contrast, is consistently smaller than the corresponding angle calculated by Allinger for [*n*]paracyclophanes and generally smaller than the values reported by others. There is also less distortion in our own bridge carbon bond angles compared to Allinger.

The Relative Energies of the Tautomers. Global minimum energy geometries were located for the methylenedihydroanthracene (MDA) tautomers (**10–13**) of **6–9** (Table I) employing the previously described procedures. A comparison of the energies of corresponding tautomers is striking. For each pair, the MDA tautomer has lower

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[17] HyperChem is a product of Autodesk, Inc. The author gratefully acknowledges the gift of this software through the Autodesk grants program.

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Table I. Minimum Energy Geometries for 6–9 and 10–13

compd	symmetry	steric energy (kcal/mol)	heat of formation (kcal/mol)
6	C_s	75.6	87.9
7	C_2	65.8	69.8
8	C_s	58.3	54.6
9a		53.5	42.9
9b	C_2	55.0	43.9
10		54.8	67.0
11		47.6	53.9
12		48.4	48.6
13		46.5	40.3

Table II. Comparison of Calculated Molecular Parameters of the [*n*](9,10)Anthracenophanes and the Corresponding [*n*]Paracyclophanes

compd		ϕ,[d] deg	α,[d] deg
6		33.9	20.6
[5]paracyclophane	(a)[a]	26.5	28.6
	(b)[b]	35.9	17.0
7		28.1	13.2
[6]paracyclophane	(a)	22.4	18.1
	(b)	22.8	16.3
	(c)[c]	15.7	22.5
8		23.8	7.2
[7]paracyclophane	(a)	18.2	10.2
	(b)	15.0	12.4
	(c)	12.4	13.2
9a		21.0	4.7
9b		19.2	2.6
[8]paracyclophane	(a)	12.5	5.1
	(b)	9.0	8.1
	(c)	8.1	7.4

[a] Allinger.[18] [b] Carballeira et al.[19] [c] Tsuzuki and Tanabe.[21] [d] Angles ϕ and α are defined in Figure 3.

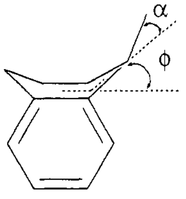

Figure 3. Definition of the angles ϕ and α.

heat of formation: At a bridge length (n) of 8 the difference is only 2.6 kcal/mol but it grows to 6 kcal/mol at $n = 7$, 15.9 kcal/mol at $n = 6$, and 20.9 kcal/mol at $n = 5$!

The Bridged Methylenedihydroanthracenes. The MDA in nonbridged systems is typically the less stable partner of the tautomeric pair,[23] though a number of exceptions, in which steric crowding at the 9,10 and peri positions reverses this situation, have been reported.[24] Interestingly, the simplest member of the series, 9-methylene-9,10-dihydroanthracene, has been prepared:[25] Semiempirical molecular orbital calculations suggest that this compound is ca. 40 kJ/mol less stable than its anthracene counterpart.[23]

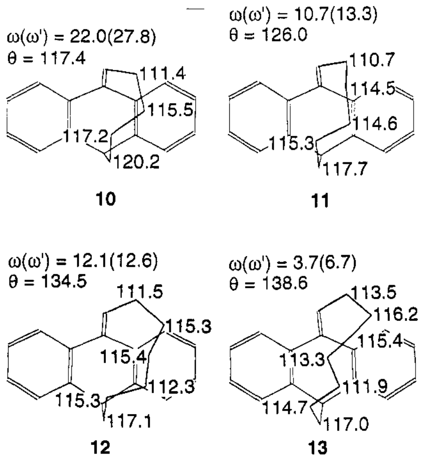

Figure 4. Molecular mechanics geometries and selected angles for **10–13**. Angle ω is the C–C–C–C dihedral of the exocyclic double bond and ω' is the corresponding C–C–C–H angle. Angle θ is the C–C–C–C–C dihedral angle defined by the two exocyclic double bond carbons and two ring fusion carbons in the dihydroanthracene ring.

No bridged MDAs have so far been isolated. Nonetheless, this family of compounds is of some significance in its own right. It is expected, for example, based on examination of mechanical models, that the exocyclic double bond will have an increasingly twisted geometry[26] as bridge length is reduced introducing the possibility of increased diradical character in the ground state. Also, since each bridged MDA exists as an enantiomeric pair, interconvertible through rotation about the exocyclic double bond, members of the series with shorter bridges will be closer to the transition state for enantiomer interconversion.

The lowest energy molecular mechanics structures for **10–13** appear in Figure 4. All structures exhibit the expected boatlike central 6-membered ring with increasing puckering as the bridge becomes shorter, a feature evident in the changes in dihedral angle θ which shrinks with increased puckering. The twist of the exocyclic double bond (angles ω and ω') is very slight at a total bridge length of 8 (MDA **13**) but substantially larger for a bridge length of 5 (MDA **10**), at which point the exocyclic carbon is also somewhat pyramidal.

An interesting feature of the geometries of the tautomeric pairs is that, though the competing forces that lead to the optimal structure differ for the two tautomers, the resultant gross geometries are somewhat similar. For example, in a comparison of the structures for **6** and **10**, the central 6-membered rings can be overlayed with only a 0.063 Å average deviation (0.068 Å root mean squared deviation) of the six carbons. Much larger deviations are present in the bridge carbons since **10** incorporates a trigonal carbon in the bridge and also has a much smaller bond angle at position 10.

Accuracy of the Energies and Geometries of the Calculated Structures. Since none of the compounds described in this paper have been prepared, no direct comparisons with experimental data are possible. However, for the [*n*](9,10)anthracenophanes, some assurance is available from the fact that the MMX force field applied here is a descendent of the earlier force field used by Allinger in the [*n*]paracyclophanes of comparable bridge length. Also, our own previous work on 2,8-dithia[9](9,10)anthracenophane demonstrated fairly good agree-

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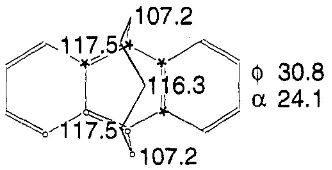
ment between geometries calculated with the MMX force field[14] and one from X-ray crystallographic examination of the same compound.[27] The molecular mechanics calculation did, however, exaggerate the bending of the anthracene ring (calcd ϕ 12.2°, expl ϕ 6.6°), and that is presumably the case in the present study. While no useful comparisons to experimental geometries are available for the bridged MDAs, Bartmess and Griffith recently demonstrated that the MMX force field provides excellent agreement with tautomerization enthalpies determined by solution calorimetry and by examination of gas-phase ion/molecule chemistry for a series of benzoannelated toluenes.[28]

Semiempirical molecular orbital calculations provide an alternative comparison for both geometries and energies. The AM1 method in particular has been used successfully in the determination of structures and energies in tautomeric systems.[29] Therefore, we applied this approach to anthracenophane **6** and MDA **10** using full geometry optimization on input structures derived through molecular mechanics calculations.

The AM1 geometry for anthracenophane **6** is quite similar to the molecular mechanics geometry but with slightly less bending of the anthracene ring and greater distortion of the benzylic bond (Figure 5). That structure has a heat of formation of 92.2 kcal/mol (compared to 87.9 kcal/mol for the corresponding molecular mechanics structure).

For MDA **10**, the AM1 geometry differs most notably from the corresponding molecular mechanics geometry around the exocyclic double bond. Dihedral ω is less than half the molecular mechanics value and less than half the value for ω' reflecting substantial distortion of the exocyclic carbon. The AM1 heat of formation for **10** is 64.4 kcal/mol compared to 67.0 kcal/mol for the corresponding molecular mechanics calculation. So the difference in energy for tautomers **6** and **10** is 27.8 kcal/mol compared to 20.9 kcal/mol from the molecular mechanics calculations.



C-C-C-C Dihedral Angles(deg)

bridge C1-C2	52.1(55.2)
bridge C2-C3	114.1(109.7)
δ	35.3(37.6)
β	53.3(51.7)

Figure 5. Geometry and selected angles for **6** from semiempirical MO calculations (AM1). The corresponding angles from molecular mechanics appear in parentheses or in Figure 2 or Table II. Angle δ is the average of the four C–C–C–C dihedral angles of the central six membered ring of the anthracene moiety analogous to the one defined by the starred carbons. Angle β is the average of the four C–C–C–C dihedral angles analogous to the one defined by the carbons marked with circles.

Prospects for the Synthesis of Small [*n*](9,10)-Anthracenophanes. Even if some caution is exercised in evaluating the relative energies of the anthracenophane–MDA tautomeric pairs, it seems that for $n = 7$ and below the MDA tautomer is likely to result from any synthetic attempt unless special precautions are taken to forestall tautomerization of the final product. Also, if the synthetic target is the bridged MDA itself, it may be important to consider the kinetic stability expected for these compounds. In this regard, the previously observed oxidations by air of **1** and **3** may not result from direct oxidation of the anthracene itself but from oxidation of small amounts of the corresponding tautomer present under equilibrium conditions. Finally, these findings have implications for other polynuclear bridged aromatic compounds both with regard to their synthesis and the potential utility of the corresponding tautomeric equilibrium in host–guest chemistry and related areas.

Acknowledgment. This work was supported by a William and Flora Hewlett Foundation Award of Research Corporation and by the Camille and Henry Dreyfus Scholar/Fellow Program for Undergraduate Institutions. The calculation of angles ϕ and α by Karen Leanza is gratefully acknowledged.

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