Stereoisomeric *p*-Quinodimethanes

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The *p*-quinodimethanes have served well in a number of specialized synthetic applications, most notably for the synthesis of [2.2]cyclophanes.[1] The characteristic reactions that occur spontaneously in these compounds, cyclodimerization, cross-coupling between different quinodimethanes, polymerization, and *in situ* Diels-Alder chemistry, account for almost all of the synthetic uses. Although structural studies are complicated by the high reactivity of *p*-quinodimethanes, several reports of the spectroscopic characteristics of these compounds at low temperatures, including electronic, vibrational[2], nuclear magnetic resonance[3] and photoelectron[4] spectroscopy, have appeared. Theoretical approaches have also amplified understanding of the chemistry and structure of these labile molecules.[5] Nonetheless, significant questions regarding the solid state and solution structure remain, and these require studies on compounds that can be isolated.

A small number of isolable 9,10-anthraquinodimethanes[6−8] have been described briefly in the literature. Our own first effort in this area included the first X-ray crystal structure of an isolable all-carbon quinodimethane, namely **1**.[9,10] There have been no reports of stereoisomerism in isolable quinodimethanes though compounds capable of stereoisomerism (geometric isomers) such as E,E-1,4-dimethyl-9,10-(bis)ethylidene-9,10-dihydroanthracene ((*E,E*)-**2**), among the simplest of anthraquinodimethanes capable of having geometric isomers, have been reported.[7] We are interested in whether the more

Table 1. Calculated Energies of the Diastereomeric quinodimethanes

isomer	MM3: strain energy (kcal/mol)	AM1: ΔH_f (kcal/mol)	3-21G/6-31G relative energy (kcal/mol)
E,E	77.75	59.84	0.00
E,Z	78.04	61.00	0.35
Z,Z	78.78	62.18	0.62

sterically-hindered stereoisomers, in the case of **2**, (*E,Z*)-**2** and (*Z,Z*)-**2**, can be prepared and are isolable. In addition, we intend to explore the synthetic utility of the stereoisomerism and also synthetic applications of *p*-quinodimethanes that go beyond those requiring use of *in situ* generation.[11] We now describe the stereoisomers of **2**.

1   **E,E-2**
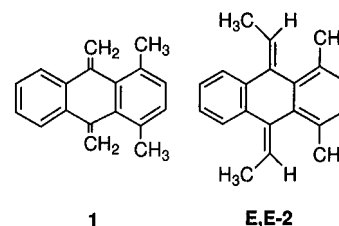
Results and Discussion

The structures of the three stereoisomers of **2** were calculated using molecular mechanics (MM3), semi-empirical MO (AM1), and *ab initio* MO (RHF/3-21G/6-31G) techniques. The expected order in the relative energies (Table 1) was found (*E,E* < *E,Z* < *Z,Z*) but surprisingly the range in strain energy was only *ca.* 1 kcal mol^{-1} and, at the AM1 level, *ca.* 1.2 kcal mol^{-1} separated the heats of formation of (*E,E*)-**2** from (*E,Z*)-**2**, and (*E,Z*)-**2** from (*Z,Z*)-**2**. The three isomers have total energies that lie within a range of 0.62 kcal mol^{-1} at the 3-21G/6-31G level. These relatively small differences in energy demonstrate that the methyl−methyl steric interactions in (*E,Z*)-**2** and in (*Z,Z*)-**2** make only a small contribution to the thermodynamic stability of these compounds. If the relative energies are accurate to within *ca.* 1 kcal mol^{-1}, one might reasonably expect a mixture of stereoisomers in the synthesis of **2** under conditions that equilibrate the isomeric products.

(1) See: (a) Vögtle, F. *Cyclophane Chemistry, Synthesis, Structure and Reactions*; John Wiley and Sons, Ltd.: Chichester, 1993. (b) Dieterich, F. *Cyclophanes*; Royal Society of Chemistry: Cambridge, 1991. (c) Keehn, P. M.; Rosenfeld, S. M., Eds.; *Cyclophanes*; Academic Press: New York, 1983.

(2) (a) Pearson, J. M.; Six, H. A.; Williams, D. J.; Levy, M. *J. Am. Chem. Soc.* **1971**, *93*, 5034. (b) Pebalk, A. V.; Barashkov, N. N.; Kozlov, Yu. A.; Kardash, I. Ye; Provednikov, A. N. *Polym. Sci. USSR* **1981**, *23*, 2933.
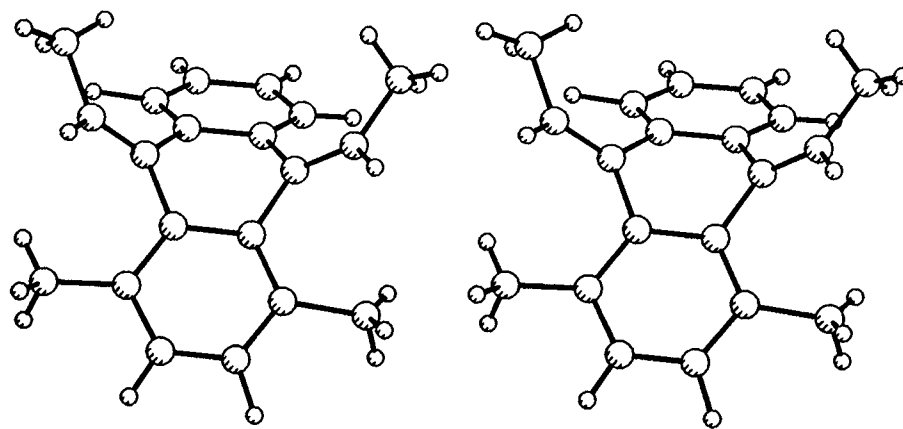
(3) Williams, D. J.; Pearson, J. M.; Levy, M. *J. Am. Chem. Soc.* **1970**, *92*, 1436.

(4) Allan, M.; Heilbronner, E.; Kaupp, G. *Helv. Chim. Acta* **1976**, *59*, 1949.

(5) (a) Coulson, C. A.; Craig, D. P.; Maccoll, A.; Pullman, A. *Disc Far. Soc.* **1947**, *2*, 36. (b) Gleicher, G.J.; Newkirk, D. D.; Arnold, J. C. *J. Am. Chem. Soc.* **1973**, *95*, 2526. (c) Dewar, M. J. S. *J. Am. Chem. Soc.* **1982**, *104*, 1447.

(6) Dickerman, S. C.; Berg, J. H.; Haase, J. R.; Varma, R. *J. Am. Chem. Soc.* **1967**, *89*, 5457.

(7) Bowden, B. F.; Cameron, D. W. *Tetrahedron Lett.* **1977**, 383.

(8) In stark contrast to the limited activity in the general area of isolable *p*-quinodimethane hydrocarbon chemistry, there is a significant and current (though narrowly-focussed) literature on *p*-quinodimethanes with strong electron-withdrawing (principally cyano) groups on the vinyl carbons. The potential application of the donor-acceptor properties of these compounds to the creation of new magnetic materials drives interest in this chemistry. Nonetheless, even here for the anthraquinodimethanes, there is less than full understanding of structure and conformational behavior. (a) Torres, E.; Panetta, C. A.; Metzger, R. M. *J. Org. Chem.* **1987**, 52, 2944. (b) Torres, E.; Panetta, C. A.; Heimer, N. E.; Clark, B. J.; Hussey, C. L. *J. Org. Chem.* **1991** 56, 3737. (c) Marshallsay, G. J.; Bryce, M. R. *J. Org. Chem.* **1994**, 59, 6847. (d) Martin, N.; Segura, L.; Seoane, C.; de la Cruz, P.; Langa, F.; Ortí, E.; Viruela, P. M.; Viruela, R. *J. Org. Chem.* **1995**, 60, 4077. (e) Martin, N.; Segura, L.; Seoane, C.; Ortí, E.; Viruela, P. M.; Viruela, R.; Albert, A.; Cano, F. H.; Vidal-Gancedo, J.; Rovira, C.; Veciana, J. *J. Org. Chem.* **1996**, 61, 3041. (f) Ortí, E.; Viruela R.; Viruela, P. M. *J. Phys. Chem.* **1996**, 100, 6138.

(9) For a detailed description of the preparation of **1** by the method of Bowden and Cameron[7] see, Rosenfeld, S.; VanDyke, S. *J. Chem. Educ.* **1991**, 68, 691.

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

(11) Rosenfeld, S.; White Tingle, C. *J. Am. Chem. Soc.* **1994**, *116*, 12049-12050.

Figure 1. Stereo PLUTO drawing of the crystal structure of (*E*,*E*)-**2**.

Table 2. ¹H NMR (400 MHz, CDCl₃) Peak Assignments
(PPM) for the Stereoisomers of 2

proton(s)	(*E*,*E*)-**2**	(*E*,*Z*)-**2**	(*Z*,*Z*)-**2**
peri methyl	2.47 (s)	2.29 (s), 2.49 (s)	2.32 (s)
allylic methyl	2.04 (d)	1.77 (d), 2.01 (d)	1.79 (d)
vinyl	5.97 (q)	5.92 (q), 6.01 (q)	5.91 (q)
2,3-aryl	6.99 (s)	7.05 (AB q)	7.15 (s)
5,8-aryl	7.46 (m)	–	–
6,7-aryl	7.24 (m)	–	–

In accord with these computational results, samples of **2** prepared by the previously reported dehydration of the corresponding diol in acidic methanol *but not subjected to purification* have ¹H NMR spectra that show all peaks corresponding to (*E*,*E*)-**2** but also smaller peaks that might reasonably be assigned to (*E*,*Z*)-**2**. A number of much less intense peaks are present as well. In reverse-phase HPLC of these samples two fully resolved peaks, the smaller one later shown to have a still smaller shoulder upon rechromatography, were observed and a small, pure sample of (*E*,*E*)-**2** was isolated in this fashion. A sample of *ca.* 8 mg of the minor component(s) of the mixture was also isolated. This latter sample consisted of (*E*,*Z*)-**2**[12] with a smaller amount of (*Z*,*Z*)-**2** as demonstrated by ¹H NMR spectroscopy: peak assignments for all three isomers (Table 2) were confirmed by homonuclear spin decoupling and 1D NOE difference experiments which included experiments on mixtures enriched in the minor isomers through photolysis.[13] The *peri* methyl, allylic methyl, and vinyl hydrogen resonances in

the *Z*,*Z*-isomer are all shifted upfield in comparison with the corresponding peaks for the *E*,*E*-isomer and this pattern is repeated for the *Z* double bond of the *E*,*Z*-isomer. The 2,3-aryl protons exhibit a trend in the opposite direction. By careful integration of peaks in a sample of the equilibrium mixture containing all three isomers, the percent composition was established to be *ca.* 78% *E*,*E*, 21% *E*,*Z*, and 1% *Z*,*Z*. This corresponds to a difference in free energy of 2.6 kcal mol⁻¹ for *E*,*E* and *Z*,*Z* isomers and only 0.78 kcal mol⁻¹ for *E*,*E* and *E*,*Z* isomers.

It is now established that isolable 9,10-anthraquinodimethanes have geometries in the solid state and in solution in which the central six-member ring is in a boat conformation.[14] The only quantitative measure, however, of the extent of folding of these molecules comes from the X-ray crystal structure of **1** in which the angle between the least squares planes of the outer six-member rings is 37.39°. Despite this significant degree of folding, there remains a steric interaction between the vinyl hydrogens and *peri* methyl groups sufficient to cause a 4-5° expansion of several bond angles around the 1,4 and 9,10 carbons. For **2**, we were successful in obtaining suitable crystals for X-ray structure determination[15] of the *E*,*E*-isomer only, but the resulting structure (Figure 1) provides some interesting contrasts with the structure of **1** and also supplies a calibration on the quality of the calculated structural features of (*E*,*Z*)-**2** and (*Z*,*Z*)-**2**. The angle between the least squares planes of the outer six-member rings in the crystal structure of (*E*,*E*)-**2** is 45.08° and this increased folding compared to **1** is apparently due to the addition of a new *peri* interaction involving the allylic methyl groups: The most expanded bond angles about the 9,10 carbons (124.1(6)°, 125.5(6)°) face the 5,8 *peri* hydrogens and the bond angles at C13 and C15 are significantly enlarged as well. Some distortion of the exocyclic double bonds is also evident in the deviation from 0° and 180° of the dihedral angles that include the double bond carbons (-1(1)°, -175.1(6)°, -3(1)°, 170.6(6)°). The average length of the exocyclic double bonds is 1.337(9) Å, reflecting the lack of significant conjugation with the aryl rings.

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(12) (*E*,**Z**)-**2** is a pair of conformational enantiomers. However, although the ¹H NMR spectrum (CDCl₃) of a sample of **2** photolytically enriched in the minor isomers and with the chiral solvating agent (CSA) (*S*)-(+)-2,2,2-trifluoro-1-(9-anthryl)ethanol added shows resolution of many of the peaks of (*E*,*Z*)-**2** into pairs of identical peaks, some peaks of (*E*,*E*)-**2** and (*Z*,*Z*)-**2** are also resolved into pairs. There is some ambiguity, therefore, in whether we are observing the individual conformational enantiomers of (*E*,*Z*)-**2**, a result that would indicate that they interconvert only slowly on the NMR time scale at ambient temperature. In this regard, it is interesting that the analogous conformational interconversion has been examined in anthraquinone diimines by NMR: Boone, H. W.; Bruck, M. A.; Bates, R. B.; Padius, A. B.; Hall, Jr., H. K. *J. Org. Chem.* **1995**, *60*, 5279.

(13) To create samples of **2** enriched in the minor stereoisomers, we photolyzed acetone solutions of the equilibrium mixture of **2** with the unfiltered beam of a mercury arc lamp. At the photostationary state these enriched samples were *ca.* one-half (*E*,*Z*)-**2** and one-third (*Z*,*Z*)-**2** (NMR). Although side-products were formed in some photolyses, there was little loss of **2** in general during photolysis. Attempts to manipulate the ratio of isomers further through triplet-sensitized cis-trans isomerization were unsuccessful: Irradiation at 365 nm in the presence of benzanthrone (*E*_T 46 kcal mol⁻¹) produced no change in the equilibrium ratios of isomers and other sensitizers of higher triplet energy (benzil, nitrobenzene, phenanthrene, 9,10-anthraquinone) produced large amounts of side-products.

(14) The only solution-phase experimental evidence for the boat geometry in hydrocarbon systems is a single dipole moment measurement.[6]

(15) The authors have deposited atomic coordinates for **2** 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, UK.

Table 3. Comparison of Bond Angles (deg) from Semiempirical MO and *ab Initio* MO Calculated Structures for All Three Isomers and Bond Angles from the X-ray Crystal Structure of (*E,E*)-2.
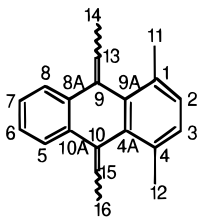
	C14C13C9	C13C9C8A	C13C9C9A	C16C15C10	C15C10C10A	C15C10C4A	C11C1C9A	C11C1C2	C12C4C4A	C12C4C3
(*E,E*)-**2** X-ray[a]	127.1(6)	125.5(6)	120.8(6)	129.1(7)	124.1(6)	122.8(6)	122.9(6)	118.4(6)	123.3(6)	119.3(5)
(*E,E*)-**2** AM1	126.0	124.3	122.3	126.0	124.3	122.3	122.8	118.1	122.8	118.1
(*E,E*)-**2** ab initio	127.0	125.1	122.7	127.0	125.0	122.7	123.3	118.6	123.3	118.6
(*E,Z*)-**2** AM1	126.0	124.2	122.5	126.6	120.5	126.5	122.8	118.1	123.0	117.9
(*E,Z*)-**2** *ab initio*	127.1	125.0	122.7	126.9	121.4	126.5	123.3	118.6	123.5	118.4
(*Z,Z*)-**2** AM1	126.5	120.5	126.6	126.5	120.4	126.6	123.1	117.8	123.1	117.8
(*Z,Z*)-**2** ab initio	126.8	121.3	126.5	126.8	121.3	126.5	123.5	118.4	123.5	118.4

[a] Estimated standard deviations in the least significant figure are given in parentheses.

Although the *ab initio* calculated structure for (*E,E*)-**2** is slightly more folded than the X-ray structure and the semiempirical calculated structure is slightly less folded than the X-ray structure, both have bond lengths and bond angles that are close to the X-ray values. The RMS deviations from the X-ray values of the C-C bond lengths are 0.014 Å (3-21G), 0.018 Å (AM1), and 0.062 Å (MM3). Bond angle distortions in (*E,E*)-**2** are reproduced well in both AM1 and 3-21G calculated structures (Table 3) with the average deviations from the X-ray values being 1° (AM1) and 0.7° (3-21G). Presumably then the calculated angles in (*E,Z*)-**2** and (*Z,Z*)-**2** are sufficiently accurate to reflect trends caused by the double bond isomerism, the most significant being the expansion of bond angles in carbons of *Z* double bonds (e.g. C13-C9-C9A in (*Z,Z*)-**2**) due to the allylic methyl/*peri* methyl interaction.

In summary, the three stereoisomers of quinodimethane **2** have calculated energies (AM1) that lie with a 2.4 kcal mol^{-1} range, and all three are present in the equilibrium mixture, a fact which demonstrates that the range of free energies for these isomers is only 2.6 kcal mol^{-1}. The X-ray crystal structure of (*E,E*)-**2** shows that this isomer exists in a boat conformation analogous to the reported solid state structure of the simpler quinodimethane **1** though somewhat more folded due to additional *peri* interactions. Finally, both semiempirical (AM1) and *ab initio* (3-21G) calculated structures of (*E,E*)-**2** reproduce the features of the X-ray structure reasonably well.

Experimental Section

General Procedures. All solvents and reagents were obtained from Fisher Scientific or Aldrich Chemical Company and were used as acquired except as noted below. The 1,4-dimethyl-9,10-bis(ethylidene)-9,10-dihydroanthracene (**2**) was prepared by dehydration of 1,4-dimethyl-9,10-diethyl-9,10-dihydroxy-9,10-dihydroanthracene in acidic methanol as previously described.[7] Details of the preparation of both compounds are given in the Supporting Information. NMR spectra were run at 400 MHz (^{1}H) or 100 MHz (^{13}C) in CDCl$_3$ (TMS reference) on a JEOL Eclipse 400 NMR spectrometer. RP HPLC was done on a Rainin Instrument Company Inc. high performance liquid

chromatograph fitted with a Rainin semi-preparative column module (80-299-C5) with a C18 stationary phase (10 mm, 1 diam X 25 cm length) using a 75:25 mixture of HPLC grade acetonitrile (J. T. Baker) and distilled water as the mobile phase. Preparative scale photolysis of **2** was carried out by irradiation of a degassed 7.5 mM acetone (Fisher Spectrograde) solution, cooled in an ice bath and kept under nitrogen, with the unfiltered beam of a Hanovia 450 watt medium-pressure mercury arc lamp.

Calculations. Minimum energy molecular mechanics (MM3) structures were calculated from atomic coordinates entered graphically and were reminimized using a semiempirical MO model (AM1). AM1 geometries were verified to be true energy minima by vibrational frequency analysis. The AM1 structures were used as starting structures for the *ab initio* calculations which were done at the restricted Hartree-Fock level using the 3-21G basis set followed by a single-point calculation at the 6-31G level. The total energies (Hartrees) were as follows: (*E,E*)-**2** (−768.999434), (*E,Z*)-**2** (−768.998871), (*Z,Z*)-**2** (−768.998442). All calculations were performed by using the program Spartan, version 4 (Wavefunction, Inc.).

X-ray Structure Determination. A clear chunk crystal of **2** was grown by vapor diffusion (hexane/methanol). Data collection was done at ambient temperature on a Rigaku AFC6S diffractometer with graphite-monochromated molybdenum K$_\alpha$ radiation (λ = 0.71069 Å). The structure was solved by direct methods.[16,17] Neutral atom scattering factors were taken from Cromer and Waber.[18] Crystal data for **2**: Thirteen reflections were used for the unit cell determination, corresponding to a monoclinic cell in the space group P2$_1$ (no. 4) with the following lattice parameters: *a* = 8.887(3) Å, *b* = 8.78(2) Å, *c* = 9.957(3) Å, α = 94.29(1)°, β = 101.65(3)°, *V* = 761.9(2) Å^3. For *Z* = 2 and formula weight 260.38, the calculated density was 1.136 g

(16) Some hydrogens were refined isotropically and some were left in calculated positions unrefined. (a) Gilmore, C. J. MITHRIL, an integrated direct methods computer program. *J. Appl. Crystallogr.* **1984**, *17*, 42. (b) Beurskens, P.T. DIRDIF: Direct Methods for Difference Structures-An Automatic Procedure for Phase Extension and Refinement of Difference Structure Factors; Technical Report 1984/1, Crystallography Laboratory, Toernooiveld, 6525 Ed Nijmegen, The Netherlands.

(17) All calculations were performed by using the TEXSAN, TEXRAY Structure Analysis Package, version 2.1, of Molecular Structure Corporation, The Woodlands, TX.

(18) Cromer, D. T.; Waber, J. T. *International Tables for X-ray Crystallography*, Vol. IV; The Kynoch Press: Birmingham, England, 1974; Tables 2.3.1 and 2.2A.

cm^{-3}. Of the 1985 reflections collected 1871 were unique. $R = 0.044$ ($R_w = 0.035$).

Supporting Information Available: Details of the preparation of **2**, calculated bond lengths for the stereoisomers of **2**, ORTEP drawing and bond lengths from the X-ray crystal structure of (*E,E*)-**2** (4 pages). This material is contained in 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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