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Conformational subtlety in large polyphenylene molecules

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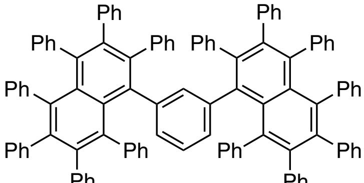
Abstract—1,3-Bis(nonaphenyl-3-biphenylyl)benzene (**3**), a large polyphenylene molecule ($C_{138}H_{94}$), was prepared by the Diels–Alder addition of 2 equiv. of 1-(pentaphenylphenyl)-2-phenylacetylene to 1,3-bis(3-oxo-2,4,5-triphenylcyclopenta-1,4-dienyl)benzene, and its X-ray structure was determined. The experimental structures of decaphenylbiphenyl (**4**) and **3** were compared with calculated structures of these molecules obtained by using methods ranging from molecular mechanics to hybrid density functional theory. Surprisingly, none of the computational methods examined correctly predicted the experimentally observed conformations of both **3** and **4**. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

Recent years have seen tremendous growth in the synthesis of polyphenylene nanostructures, in terms of both the number and the size of molecules prepared.[1] Hundreds of new, very large hydrocarbons have been reported, but their structural characterization has rarely been complete. Indeed, a search of the Cambridge Structural Database[2] (CSD, V5.19, April 2000) found only seven X-ray crystal structures of carbon or hydrocarbon molecules containing more than 100 carbon atoms.[3–8] Of these, two are derivatives of fullerenes, and of the remaining hydrocarbons, only 1,3-bis(heptaphenyl-1-naphthyl)benzene[7] (**1**, $C_{110}H_{74}$) and 1,3,5-tris(pentaphenylphenyl)benzene[7] (**2**, $C_{114}H_{78}$), from our laboratory, can be considered to be polyphenylene nanostructures.

In the absence of rigorous experimental data, modern computational methods have been employed to generate three-dimensional structures of polyphenylene nanostructures. However, the great size of these molecules has two serious consequences: (1) every molecule has a large number of conformational degrees of freedom and, frequently, a large number of accessible conformations differing only slightly in energy, and (2) only relatively low-level computational methods can be employed for the full geometry optimization of any given conformation.

In the present paper, we report the synthesis and X-ray crystal structure of a new polyphenylene nanostructure, compound **3** ($C_{138}H_{94}$), and we compare the X-ray structures of two large polyphenylene molecules—**3** and decaphenylbiphenyl[9]



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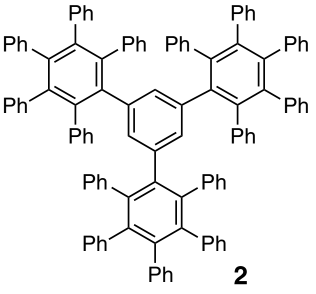

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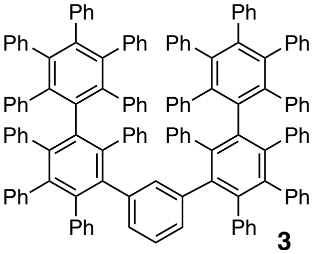

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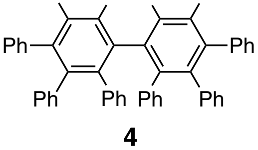

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Keywords: polyphenylene; polycycles; hydrocarbons; ab initio calculations; conformational analysis.

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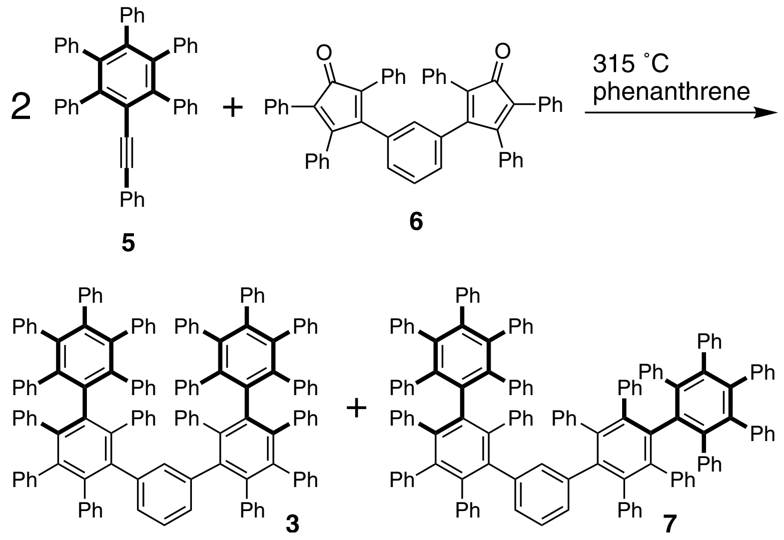


Scheme 1.

(**4**, $C_{72}H_{50}$)—with the results of calculations ranging from molecular mechanics to hybrid density functional theory. Surprisingly, none of the computational methods examined are able to predict correctly the experimentally observed conformations of both **3** and **4**.

2. Results

2.1. Synthesis and X-ray structure of compound 3

Compound **3** was prepared by the Diels–Alder reaction of two known compounds: 1-(pentaphenylphenyl)-2-phenylacetylene[10] (**5**) and the biscyclopentadienone **6**.[7] When **5** and **6** were heated in a sealed tube to 315°C (with phenanthrene as solvent), a mixture of double Diels–Alder adducts was obtained. An analysis of the high-field aromatic resonances in the ^1H NMR spectrum of this mixture suggested that the two principal constituents were present in a 3:2 ratio. The minor component is now known to be the *meta*,*meta*,*meta*-isomer **3**, and the major component is suspected to be the *meta*,*meta*,*para*-isomer **7**. The ^1H NMR spectrum of **3**, which possesses C_2 symmetry, shows one high field doublet at δ 5.43, while the less symmetric, putative **7** shows two such doublets (δ 5.32 and 5.55). Unfortunately, spectroscopic methods are not adequate to distinguish the C_2-symmetric *meta*,*meta*,*meta*-isomer **3** from a possible C_2-symmetric *para*,*meta*,*para*-isomer (which is, in fact, what we had expected to be the major product of this reaction). It is for such reasons that we believe that X-ray crystallography is essential for the proper characterization of complex polyphenylene molecules. The growth of single crystals large enough for X-ray diffraction studies usually requires pure samples, but the chromatographic separation of the various components of the mixture was extremely difficult. However, we were fortunate enough to obtain crystals of pure compound **3** (but not **7**) by direct crystallization of a partially purified sample (Scheme 1).

Single crystals of compound **3** were first obtained from xylenes. The crystals proved to be monoclinic, space group *C*2/*c*, *Z*=4; thus each molecule of **3** lies on a special position and possesses crystallographic C_2 symmetry, a fact which greatly simplified the solution and refinement of the structure. Several solvent molecules are also present in the unit cell, but they are highly disordered; based primarily on NMR data, the crystal formula is $C_{138}H_{94}\cdot 2C_8H_{10}$ [(compound **3**)(xylenes)$_2$]. It was necessary to employ the SQUEEZE/BYPASS procedure[11] to account for the disordered solvent electron density. This is a very effective method for dealing with disordered solvent which we have used successfully in the refinement of several polyphenyl aromatic crystal structures,[7,9,12,13] and, using the SQUEEZE-processed data set, the structure refined to a satisfactory $R(F)$=0.079. Compound **3** is larger than all but two of the hydrocarbon structures in the CSD.[8]

The molecular structure of compound **3** is illustrated in Fig. 1. The overall structure is relatively globular, with maximum dimensions of approximately 23 Å×19 Å×14 Å. The molecule curls upon itself to form a narrow cleft, but this cleft is too small to accommodate any guest solvent molecules. If one assumes that the crystal conformation is the principal conformation present in solution, then the high-field doublet in the ^1H NMR spectrum of **3** probably belongs to the symmetry-equivalent C36 and C36A protons, which lie 2.88 Å from the faces of the C6A and C6 phenyl groups, respectively. Further discussion of the conformation of compound **3** is presented in the context of the computational work.

Single crystals of compound **3** were also obtained from pyridine. These crystals were smaller, but a weak X-ray data set was collected. This pyridine solvate proved to be essentially isomorphous with the xylene solvate; the unit cell parameters were very similar, and the structure was solved and refined in the space group *C*2/*c* with *Z*=4. The polyphenylene hydrocarbons in the two different solvates adopt very similar conformations, and the principal difference between the two crystal forms lies in the number and orientation of the included solvent molecules. The pyridine solvate appears to have the formula $C_{138}H_{94}\cdot 3C_5H_5N$ [(compound **3**)(pyridine)$_3$], and the pyridines are more nearly ordered (although it is not possible to distinguish

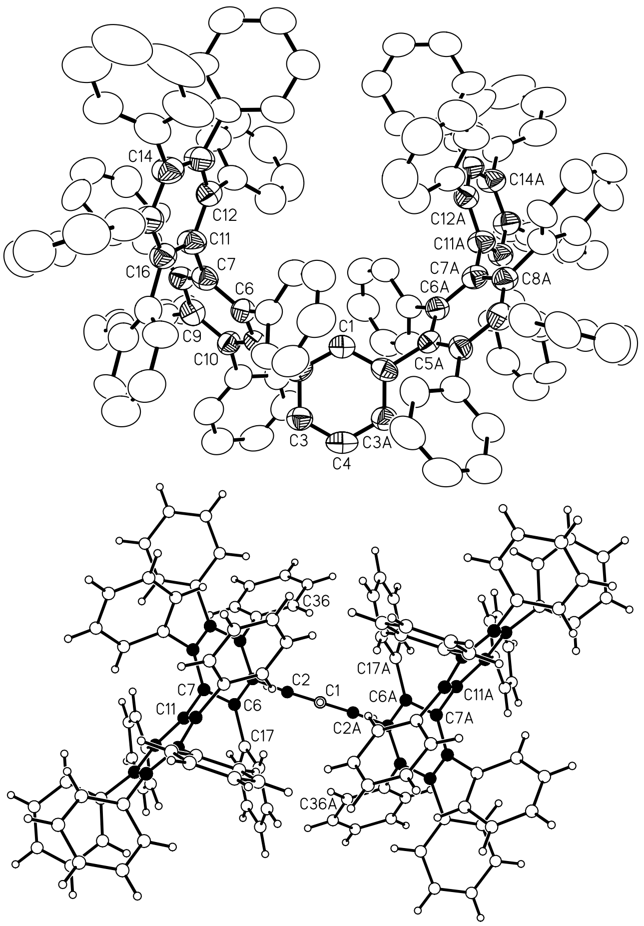


Figure 1. Molecular structure of compound **3**. In the top view, thermal ellipsoids have been drawn at the 50% probability level, and hydrogens have been omitted for clarity.

the carbon and nitrogen atoms in these rings). The solvent molecules are found in sinusoidal channels, and there are no unusually close contacts between molecules of **3** and the included solvent. Indeed, the structure seems to be governed by favorable contacts between molecules of **3**, and the solvent merely fills the remaining space.

2.2. Computational studies of compounds 3 and 4

Compound **3** is composed exclusively of benzene rings, perhaps the most common of all organic substructures; therefore, one might expect that any modern computational method would suffice to predict the ground state conformation of **3**. However, this is most certainly *not* the case! In order to understand the conformational options open to a molecule as complex as **3**, one must first consider the simpler molecule **4** (decaphenylbiphenyl), which is essentially half of **3**.

X-ray analysis of decaphenylbiphenyl has shown it to adopt an unusual C_1-symmetric structure in which one of the biphenyl rings is distorted into a boat conformation.[9] Several other extremely crowded biphenyls, most notably dekakis(dichloromethyl)biphenyl,[14] exist in similar C_1 conformations, so this structure is not likely to be the result of crystal packing forces. Our original report of the structure of **4** included only semiempirical molecular orbital calculations for comparison because of **4**'s large size and our limited computational resources,[9] but we have now been able to reexamine the conformational preferences of **4** with a wide variety of computational methods, and the results are summarized in Table 1.

Full geometry optimizations were performed for structures possessing C_1, C_2, and D_2 symmetry using molecular mechanics (Sybyl,[15] MMFF[16]), semiempirical MO methods (AM1,[17] PM3[18]), low-level ab initio Hartree–Fock theory (HF/STO-3G, HF/3-21G[19]), and hybrid density functional theory [B3LYP/6-31G(d)[20–22]]. Typical C_1, C_2, and D_2 structures of **4** are illustrated in Fig. 2. All of the methods examined find two conformational minima for **4**. One of these is the intuitively attractive D_2 conformation, and the other is the experimentally observed C_1 conformation. (In two cases the second minimum actually possesses C_2 symmetry, but for most methods the C_2 structure is calculated to be a transition state.) However, there is no agreement among these methods as to which is the more stable conformation! PM3 and HF/STO-3G find the C_1 conformation to be of lowest energy; MMFF and AM1 find the C_2 conformation to be the ground state (in these two cases a C_1 starting point yields the C_2 structure upon optimization), and Sybyl, HF/STO-3G, and B3LYP/6-31G(d) prefer the D_2 conformation. The results could not be more disparate, and it is especially disturbing that there was no convergence of results as more sophisticated computational methods were employed.

Table 1. Calculated energies of conformations of compounds **3** and **4** (n.d., not determined)

Cmpd./conf.	Computational method						
	Sybyl	MMFF	AM1	PM3	HF/STO-3G	HF/3-21G	B3LYP/6-31G(d)
4/C_1	0.00[a]	0.00[a]	353.45[b] (0.00[a])	331.61[b] (0.00[a])	−2722.139547 (0.00[a])	−2740.295913[c] (0.00[a])	−2773.780742[c] (0.00[a])
4/C_2	0.59	0.00	353.45 (0.00)	331.64 (0.03)	−2722.139050 (0.31)	−2740.295857 (0.04)	−2773.779979 (0.48)
4/D_2	−5.63	1.01	355.50 (2.05)	333.09 (1.48)	−2722.145985 (−4.04)	−2740.293814 (1.32)	−2773.783590 (−1.79)
3/C_2-*closed-d*	0.00	0.00	692.94 (0.00)	640.32 (0.00)	−5216.394838 (0.00)	−5251.166530 (0.00)	n.d.
3/C_2-*closed-b*1	16.68	4.52	690.13 (−2.81)	642.49 (2.17)	−5216.379885 (9.38)	−5251.167885 (−0.85)	n.d.
3/C_2-*closed-b*2	9.90	−1.64	689.32 (−3.62)	638.56 (−1.76)	−5216.380611 (8.93)	−5251.171681 (−3.23)	n.d.
3/C_2-*open-d*	8.32	7.26	695.28 (2.34)	645.83 (5.51)	−5216.388050 (4.26)	n.d.	n.d.
3/C_2-*open-b*1	17.44	8.74	693.48 (0.54)	646.09 (5.77)	−5216.373112 (13.63)	n.d.	n.d.
3/C_2-*open-b*2	16.02	1.60	690.13 (−2.81)	640.04 (−0.28)	−5216.380601 (8.93)	−5251.170261 (−2.34)	n.d.

[a] Relative energy (referenced to the X-ray conformations) in kcal/mol.

[b] Enthalpy of formation in kcal/mol.

[c] Energy in a.u. (1 a.u.=627.503 kcal/mol).

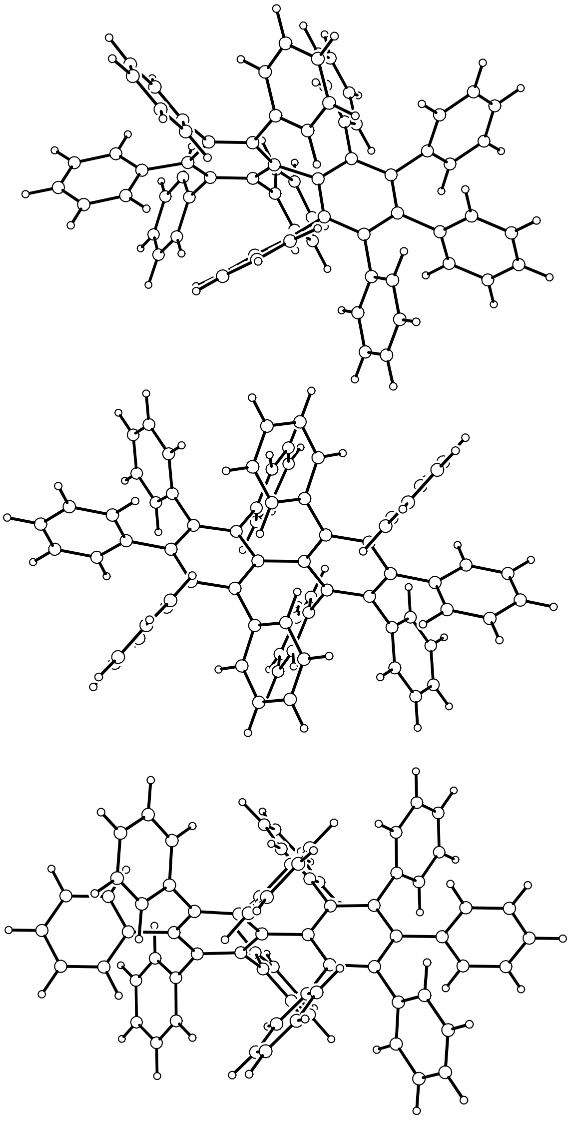


Figure 2. Typical structures of the C_1- (top), C_2- (middle), and D_2-symmetric (bottom) conformations of compound **4**. The C_1 structure is the X-ray structure, the C_2 and D_2 structures were generated by using the MMFF force field.

The situation is similar for **3**. A survey of the conformation space of **3** with molecular mechanics shows numerous low-energy minima. However, since the compound crystallizes with C_2 symmetry, we focused on the C_2-symmetric conformations, of which six were located. These fall into two classes, *closed* conformations, as in the X-ray structure, in which the molecule curls upon itself, and *open* conformations in which the polyphenylbiphenyl 'wings' are spread apart. Within these classes, there are structures where the polyphenylbiphenyl wings adopt D_2-like conformations (e.g. C_2-*closed-d*), and others where one of the benzene rings in each wing adopts a boat conformation as in the X-ray structure of **4** (e.g. C_2-*open-b*2). The X-ray structure of **3** exhibits the C_2-*closed-d* conformation, and the C_2-*closed-b*2 and C_2-*open-b*2 conformations are illustrated for comparison in Fig. 3.

Full geometry optimizations were conducted for each of the C_2 conformations of **3** at a variety of levels up to HF/3-21G;

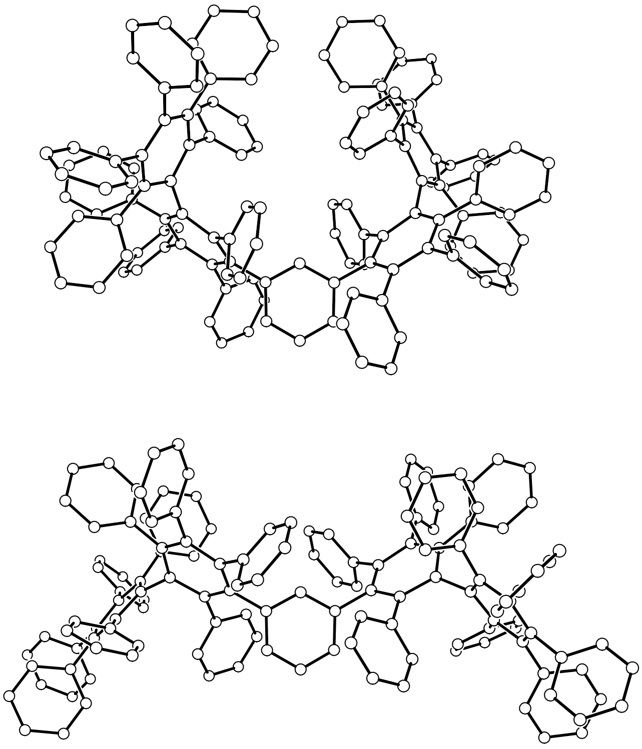


Figure 3. Examples of *closed* and *open* conformations of compound **3**. The C_2-*closed-b*2 (top) and C_2-*open-b*2 (bottom) conformations generated by using the MMFF force field are illustrated.

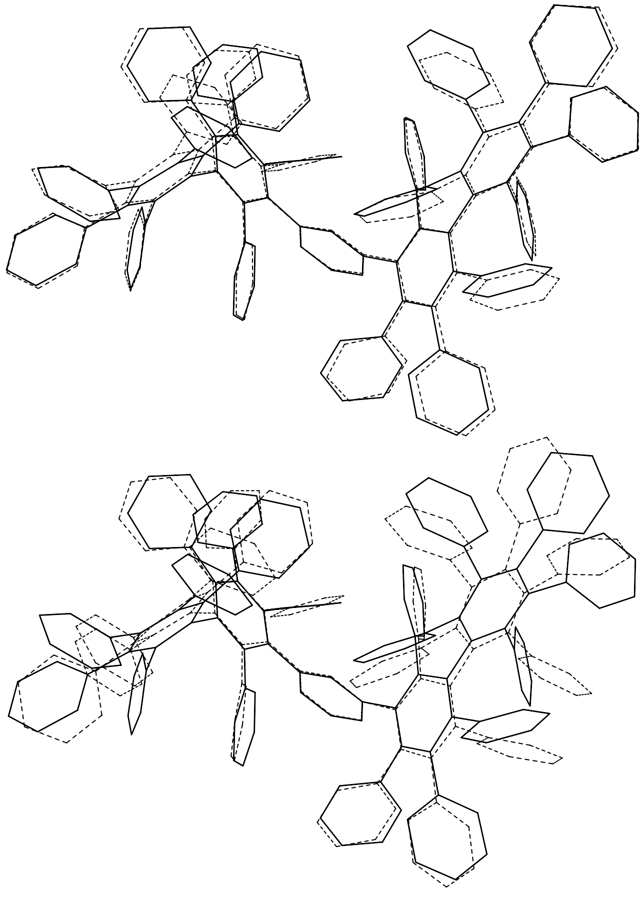


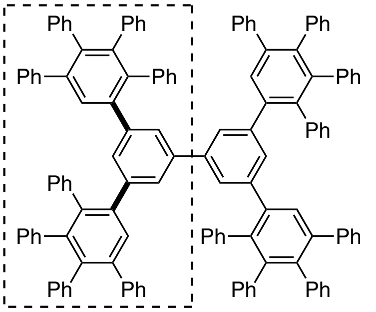
Figure 4. Least-squares fits of the X-ray structure of compound **3** (solid line) with the C_2-*closed-d* conformation (top, dotted line) and the C_2-*closed-b*2 conformation (bottom, dotted line) generated by HF/3-21G calculations.

unfortunately, **3** is too large to permit a B3LYP/6-31G(d) optimization in a reasonable amount of time. These results are also summarized in Table 1. The experimentally observed C_2-*closed-d* conformation was found to be of lowest energy by the Sybyl and HF/STO-3G calculations, but, interestingly, the remaining four methods found the C_2-*closed-b*2 conformation to be the ground state. As shown in Fig. 3, the *open* and *closed* conformations are quite distinct, but differences between two *closed* conformations are more subtle. The most easily seen difference between the C_2-*closed-d* and C_2-*closed-b*2 conformations is the orientation of the peripheral phenyl groups. This is obvious in Fig. 4, which shows least-squares fits (calculated by using the OFIT function in SHELXTL[23]) of the X-ray structure of **3** and the HF/3-21G-calculated C_2-*closed-d* and C_2-*closed-b*2 conformations (rms deviations 0.357 and 0.883 Å, respectively). The C_2-*closed-d* conformation is clearly a much better fit to the experimental structure, and the small differences between the X-ray and calculated structures might easily be due to packing forces.

The question remains: are crystal packing forces sufficient to cause **3** to adopt a higher energy conformation (C_2-*closed-d*) in the solid than that calculated for the gas phase (C_2-*closed-b*2)? This is always a possibility, but the C_2-*closed-d* conformation is observed in not one, but *two* crystal structures, and, as mentioned previously, these two X-ray structures are very similar; when compared by OFIT, they show an rms deviation of only 0.125 Å. Therefore, in the absence of other data, the C_2-*closed-d* conformation must be presumed to be the true ground state conformation of **3**.

3. Discussion

Recent papers[24–28] from the Müllen laboratory illustrate a commonly used strategy for calculating the structures of very large molecules. They have performed molecular mechanics calculations on a variety of dendrimeric polyphenylene structures, the *smallest* of which is compound **8** ($C_{132}H_{92}$). For this and larger molecules, they employed the MM2(85) force field[29] and their search strategy was as follows.[25] First, the geometry of half the molecule (enclosed by dotted lines) was optimized by minimizing the energy of a large number of conformations generated by rotations about the emboldened bonds. Then, two copies of the lowest energy conformation were joined to give the complete molecule, and this was optimized by minimizing the energy of conformations generated by rotation about the central bond. Similar methods were used to simulate the structures of compounds with as many as 400 carbon atoms.



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If such calculations are used to generate plausible structures of polyphenylene nanostructures, then the approach is fully satisfactory. However, if the intent is to predict accurately the lowest-energy conformation of a particular molecule, then this approach entails considerable risk. First of all, conformational searches in which the starting structures are generated by varying a only a few torsion angles may overlook potentially important conformations which require significant bond angle or bond length distortions.[30] Second, where the energies of the relevant conformations differ only in the sum of many small steric penalties or subtle variations in inter-ring conjugation, a very accurate assessment of these effects may be required, and empirical force fields are probably inadequate. With regard to the first point, by using sufficiently powerful computers, enough time, and a bit of chemical intuition, there is little doubt that all of the chemically significant, low-energy conformations can be located. The second point—evaluation of the relative energies of the various conformations—is the most serious problem for computational studies of polyphenylene nanostructures.

Compounds **3** and **4**, in which polyphenylbiphenyls are the key structural units, present such a computational challenge. The appropriate potential minima can be located easily enough, but the relative energies of even extremely different conformations (such as the *closed* and *open* structures in Fig. 3) can be very close. It is clear from the data in Table 1 that the Sybyl, HF/STO-3G, and B3LYP/6-31G(d) methods favor D_2-like structures for these polyphenylbiphenyls, and the MMFF, AM1, PM3, and HF/3-21G methods favor boat-containing conformations to varying degrees. Since the experimental structure of **3** is in the former category and that of **4** in the latter, we have the rather unexpected result that *none* of the seven computational methods examined correctly predicts the ground state conformations of *both* **3** and **4**.

The energy differences between the conformations are not terribly large for such big molecules, but they are significant. For compound **4**, the D_2 conformation is variously estimated to be from 5.6 kcal/mol more stable to 2.0 kcal/mol less stable than the C_1 structure (see Table 1). For compound **3**, the range of relative energies is twice as large: the C_2-*closed-d* conformation is estimated to be from 9.9 kcal/mol more stable to 3.6 kcal/mol less stable than the C_2-*closed-b*2 conformation. Even if the comparisons are limited to ab initio methods, the ranges are almost as large. In such circumstances, we cannot say that any of these computational methods is fully satisfactory for dealing with polyphenylene nanostructures.

Our conclusion, then, is that more *experimental* structures of polyphenylene molecules are necessary! Our own experience has indicated that pure samples of large polyphenyl aromatic compounds are relatively easy to crystallize, and the slow crystallization of mixtures sometimes deposits X-ray quality crystals as well.[7,9,12,13] With modern CCD-based diffractometers, acceptable X-ray data sets are usually easy to obtain. The solution and refinement of these structures can be challenging, mainly because of the propensity of these compounds to include disordered solvent in the crystals, but recent improvements in structure solution and refinement algorithms have eased this burden considerably. There is no longer any good reason for the paucity of rigorous structural data for polyphenylene nanostructures, and we encourage other research groups to characterize their wonderful molecules by X-ray crystallography.

4. Experimental

4.1. General

The synthesis[36] and X-ray structure[9] of decaphenylbiphenyl (**4**) have been reported previously.

4.1.1. 1,3-Bis(nonaphenyl-3-biphenylyl)benzene (3). 1-(Pentaphenylphenyl)-2-phenylacetylene[10] (**5**, 161.5 mg, 289 μmol), 1,3-bis(3-oxo-2,4,5-triphenylcyclopenta-1,4-dienyl)benzene[7] (**6**, 82.4 mg, 119 μmol), and phenanthrene (250 mg) were mixed together in a screw-capped tube and then heated at 315°C for 2 h. The resulting brown solid was subjected to silica gel column chromatography (99:1 hexanes–acetone) to give 65.4 mg of a mixture of single and double Diels–Alder adducts (FAB MS *m/z* 1752 and 1222). This mixture was further purified by preparative silica gel TLC (1:1 hexanes–benzene) to yield a mixture of the two bis(nonaphenylbiphenylyl)benzene isomers **3** and **7** (12.6 mg, 7.2 μmol, 6% yield). These compounds were not separable by chromatography, but slow crystallization of this mixture from xylenes gave single crystals of compound **3**, which were individually separated from the remaining material under a microscope. **3**: mp 246–249°C; ^1H NMR ($CDCl_3$) δ 5.43 (d, $J=8$ Hz, 2H), 5.62 (br, 2H), 5.9–6.1 (m, 8H), 6.3–7.2 (m, ~80H), 7.49 (br, 2H), 7.67 (br d, $J=8$ Hz, 2H); FAB MS, *m/z* 1752 (M+H [$^{13}C_1$], 100).

4.1.2. X-ray crystallographic analysis of compound 3. A colorless blade of **3** (from xylenes) was cut to 0.35 mm×0.10 mm×0.03 mm, mounted on a glass fiber with silicone grease, and transferred to a Nonius KappaCCD diffractometer, where MoKα radiation ($\lambda=0.71073$ Å) was employed for data collection at 200 K. A total of 20,200 reflections ($\theta_{max}=22.46°$) were indexed, integrated, and corrected for Lorentz and polarization effects by using the program DENZO,[37] and they were then merged to 7648 reflections ($R_{int}=0.096$) by using the program SCALEPACK.[37] Postrefinement of the unit cell parameters gave $a=32.9796(15)$ Å, $b=12.7258(4)$ Å, $c=30.8399(14)$ Å, $\alpha=90°$, $\beta=113.861(1)°$, $\gamma=90°$, and $V=11837.0(8)$ Å^3. The structure was solved by direct methods in the space group $C2/c$ (No. 15), and it was refined by full-matrix least-squares on F^2 using Siemens SHELXTL.[23] The title molecule was found on a special position possessing crystallographic C_2 symmetry (thus $Z=4$). Two additional sites of ill-defined residual electron density were attributed to disordered solvent molecules. (The crystal formulation of $C_{138}H_{94}\cdot 2C_8H_{10}$—two xylenes per molecule of **3**—is based on ^1H NMR analysis of the X-ray sample, but the solvent sites in the crystal are large enough to hold as many as three xylenes per molecule of **3**.) Refinement attempts with numerous discrete-atom disordered solvent models, however, were less than fully satisfactory. For this reason the SQUEEZE/BYPASS procedure[11] implemented in PLATON[38] was used to account for the solvent electron density. The resulting SQUEEZE-processed data set was employed in all subsequent cycles of least-squares. All nonhydrogen atoms were refined anisotropically, with hydrogens riding [C–H=0.95 Å, $U(H)=1.2U(C)$]. The refinement converged to $R(F)=0.0788$, $wR(F^2)=0.1612$, and $S=1.257$ for 2924 reflections with $I>2\sigma(I)$, and $R(F)=0.2070$, $wR(F^2)=0.1998$, and $S=0.904$ for 7648 unique reflections, 623 parameters, and 0 restraints.

Small crystals of the title compound were also obtained from pyridine solution. Diffraction data obtained from these crystals showed them to be isomorphous with those from xylenes; the unit cell parameters were $a=32.428(3)$ Å, $b=12.6583(9)$ Å, $c=31.419(3)$ Å, $\alpha=90°$, $\beta=114.68(2)°$, and $\gamma=90°$. Although the X-ray data were weak, the structure was solved and refined in the space group $C2/c$ to $R(F)=0.156$. In this refinement, all six-membered rings were treated as ideal, rigid hexagons, the carbon atoms of the title molecule were refined anisotropically, and the atoms of the solvent were refined isotropically. This crystal form appears to have the formula $C_{138}H_{94}\cdot 3C_5H_5N$.

4.2. Computational studies

Molecular mechanics calculations (Sybyl,[15] MMFF[16]) were performed by using the SPARTAN[39] program package (Version 5.0), and its built-in default thresholds for wave function and gradient convergence were employed. Semiempirical molecular orbital calculations (AM1,[17] PM3[18]) were performed by using SPARTAN (Version 5.1) for compound **3** and by using GAUSSIAN 94[40] for compound **4**. All ab initio (HF/STO-3G, HF/3-21G[19]), and hybrid density functional [B3LYP/6-31G(d)[20–22]] calculations were performed by using GAUSSIAN 98,[40] again employing the default convergence criteria. The function OFIT in Siemens SHELXTL[23] was used to determine the best fit of the experimental and calculated geometries and the deviations of the atomic positions; all carbon atoms were employed for the fitting.

Acknowledgements

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30. An excellent example (with which we are very familiar) is the case of the Rebek diacid–diamine complexes, where the mode of diamine binding was controversial. Rebek originally proposed that two hydrogen bonds were made in the complex,[31] but a molecular dynamics simulation of the pyrazine complex, which varied only a few torsional angles, indicated that only one H-bond could be made;[32] in this constrained simulation the cleft of the Rebek diacid was unable to open wide enough to accommodate both H-bonds. However, X-ray structures of the pyrazine and quinoxaline complexes showed that two H-bonds were indeed formed,[33,34] and a subsequent simulation with fewer geometric constraints confirmed this analysis.[35]
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