Tormented aromatic compounds

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Abstract — The chemistry of compounds containing aromatic rings which have been twisted, prodded, or bent is described.

INTRODUCTION

For several years we have pursued the synthesis, and structural and spectroscopic characterization, of highly strained organic molecules in which a variety of relatively unreactive functional groups are forced to be very close together. Our working hypothesis has been that the enforced proximity of these functional groups, often much closer than the sum of their van der Waals radii, should enhance their mutual reactivity, and that by balancing intramolecular strain with functional group reactivity, we might discover molecules with unusual bonding arrangements and unusual spectroscopic and physical properties. The extremely close contact of a hydrogen atom or other functional group with the π-system of an aromatic ring is an important feature of many of the compounds discussed in the present paper, and a variety of chemical consequences, arising from purely steric interactions or from more subtle electronic perturbations, have been observed in these systems.
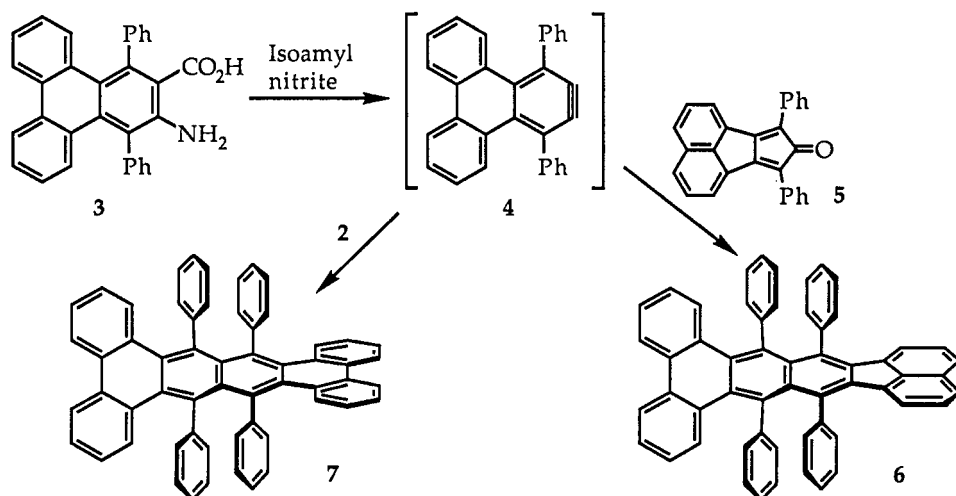
TWISTED POLYCYLIC AROMATIC HYDROCARBONS

The very first tormented aromatic compound which we investigated was 9,18-diphenyl-tetrabenz[*a,c,h,j*]anthracene (1). It is obvious that this molecule cannot be planar, for the steric requirements of a phenyl group and two hydrogen atoms are far greater than the space between the benzo groups, and when molecular mechanics calculations (MMPI) were used to evaluate possible conformations of 1, four potential energy minima were found, all corresponding to nonplanar geometries. A conformation of D_2 symmetry, with an end-to-end twist of more than 60°, was calculated to be most stable. In principle, 1 might be formed by the addition of 9,10-phenanthryne to phencyclone (2) followed by the loss of carbon monoxide. However, our initial attempts to generate 9,10-phenanthryne under mild conditions in the presence of 2 gave none of the desired product. We soon resorted to drastic measures, and ultimately heated a mixture of 2 and 9-bromophenan-threne to 340 °C for four hours in the absence of solvent. Fractionation of the resulting complex, black, solid mixture gave compound 1 in 4% yield as bright yellow crystals (ref.
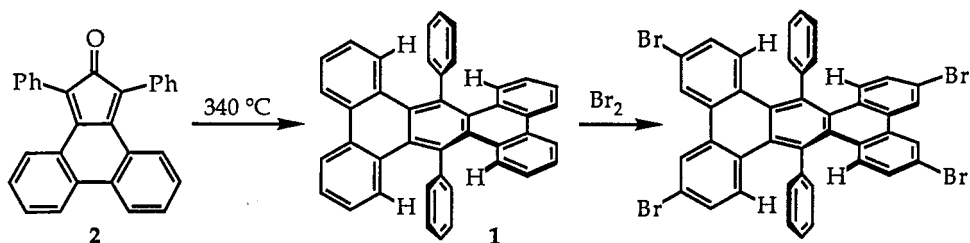
1). This result was pseudoserendipitous, for we subsequently found that the 9-bromo-phenanthrene was not required, and that compound 1 is formed upon pyrolysis of pure solid 2! Labeling studies indicated that both phenyl groups were derived from the same molecule of 2 (ref. 2), and we propose that pyrolysis of 2 gives 9,10-phenanthryne which in turn reacts with as yet undecomposed 2 to give the desired hydrocarbon. However, all attempts to trap 9,10-phenanthryne in the pyrolysis mixture have failed.

The X-ray crystal structure of 1 is remarkable (ref. 1). The anthracene nucleus is twisted by 65.7° overall, and the center ring by 23.6°, both data in good agreement with molecular mechanics calculations. The twisting deformation results from nonbonded repulsions between the benzo hydrogens and the *ipso* carbons of the phenyl substituents; these C—H contacts range from 2.33 to 2.43 Å in the X-ray structure. Despite the extreme deformation of the anthracene nucleus, however, compound 1 is extremely stable; for example, the solid may be heated to 400 °C in air without melting or decomposition. Interestingly, treatment of 1 with bromine in methylene chloride at room temperature gives only 3,6,12,15-tetrabromo-1; this is surprising, for an alternative reaction, oxidation to (planar) hexabenzocoronene, would relieve the steric strain.


Encouraged by the stability of compound 1, we have attempted to prepare and characterize crystallographically polycyclic aromatic hydrocarbons with even greater twists. The most successful approach thus far has made use of the heavily substituted aryne 4 (ref. 3). The anthranilic acid derivative 3 was prepared from phencyclone (2) in three steps, and 3 serves as a convenient precursor of 4 via diazotization with isoamyl nitrite at 80 °C.

When this reaction was carried out in the presence of excess acecyclone (5), the polycycle 6 was formed in 10% yield, and the X-ray structure of this compound showed it to be twisted, as expected, by 62.6°. However, the reaction of 4 with phencyclone was of greater interest. The desired product, 9,10,19,20-tetraphenyltetrabenzo[a,c,j,l]naphthacene (7), was predicted to have an end-to-end twist of 94° by molecular mechanics calculations [MM2(85)]. This material, however, was formed in only 1% yield, and, in contrast to all other twisted polycyclic aromatic compounds which we have prepared (approximately 20 different structures), it is unstable, slowly decomposing at room temperature. Compound 7 has been characterized by its NMR, UV, and mass spectra, but we have so far been unable to obtain single crystals of 7 for X-ray analysis.

In-CYCLOPHANES

The polycyclic aromatic compounds described above are twisted due to nonbonded interactions between the phenyl substituents and the hydrogens of the neighboring benzo groups, which may be as close as 2.3 Å. But how short can a nonbonded contact between a methine hydrogen and an aromatic ring be in a stable molecule? When we first considered this problem, the closest crystallographically documented approach of a

hydrogen to an aromatic ring was 2.16 Å in [2,2]metaparacyclophane-1,9-diene (ref. 4), but even in this highly strained molecule, the hydrogen has some freedom to bend away from the ring. We wished to prepare a compound in which an aliphatic hydrogen would be forced directly into the center of an aromatic ring, and we had the good fortune to discover that the structure of the known (ref. 5) macrocycle 2,8,17-trithia[4^{5,12}][9]metacyclophane (8) had been misassigned as the "out" isomer; the hydrogen is actually on the inside as shown (ref. 6). An X-ray analysis showed that the methine was pointed directly at the aromatic ring with the hydrogen only 2.21 Å from the ring center. Molecular mechanics calculations [MM2(85)] suggested that such "in" geometries would be strongly preferred for the even smaller cyclophanes 9, 10, and 11; only in 12 are the two isomers of comparable steric energy.

| | 8 | 9 | 10 | 11 | 12 |
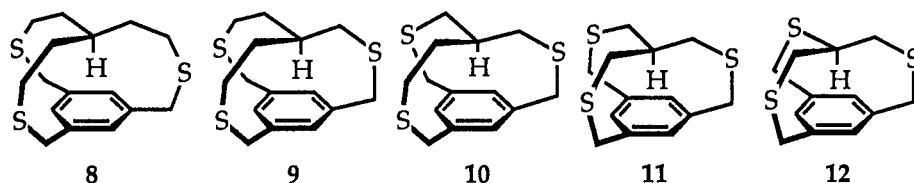
Steric Energies
[MM2(85); kcal/mol]

	8	9	10	11	12
in-isomer	19.8	24.6	28.6	37.4	58.2
out-isomer	27.0	35.2	40.0	48.2	58.8

The *in*-cyclophanes 9-11 were prepared with surprising ease in one-step condensations of 1,3,5-tris(mercaptomethyl)benzene with the appropriate tribromoalkanes (ref. 7). The X-ray structures of compounds 10 and 11 showed that their *in*-methine hydrogens were only 1.81 and 1.69 Å, respectively, from the mean planes of the aromatic rings. The latter is nearly 0.47 Å closer than ever observed previously, and a high degree of steric compression of the methine group in 11 is indicated by its IR C-H stretching band at 3260 cm^{-1}. Compound 11 provides an interesting point of comparison for various commonly employed types of molecular mechanics calculations and semiempirical and *ab initio* molecular orbital calculations. The critical methine-arene distances obtained by a variety of these methods are tabulated below.
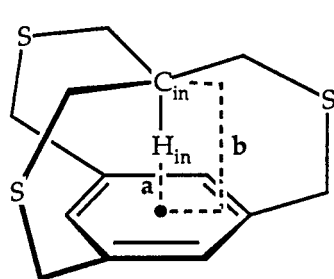
Method	a (Å)	b (Å)
X-ray	1.69	2.78
MMPI	1.937	3.005
MM2(85)	1.815	2.894
MNDO	1.911	3.011
AM1	1.799	2.910
PM3	1.823	2.930
STO-3G	1.728	2.786
3-21G*	1.739	2.785
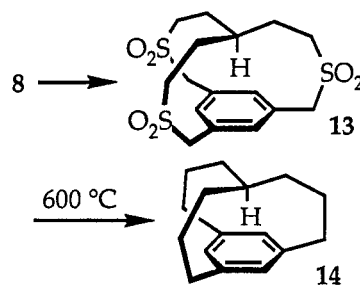
We were unable to synthesize compound 12 by a direct condensation reaction; therefore, we explored various ring contraction methods for the preparation of smaller *in*-cyclophanes than 11. Peracid oxidation of compound 8 gave the trisulfone 13, and pyrolysis of this material under vacuum gave the hydrocarbon 14 in 11% isolated yield, as well as products which had undergone only one or two extrusions of sulfur dioxide (ref. 8). Compound 14 exhibits a proton NMR *in*-hydrogen resonance at δ -4.03, and its IR spectrum features a C-H stretching band at 3325 cm^{-1}, suggesting that 14 is even more congested than 11. No X-ray structure has been obtained of this waxy solid material, but *ab initio* calculations at the 3-21G level indicate that the *in*-hydrogen is only 1.658 Å from the center of the aromatic ring. Further ring contraction experiments have been unsuccessful. When compounds 9 and 10 were subjected to oxidation and pyrolysis, no *in*-cyclophane products were obtained, and the very strained compound 11 was destroyed by peracid oxidation. Compound 14 remains the most congested *in*-cyclophane to be prepared to date.

In-HETEROPHANES

In the cyclophanes described above, the *in*-methine hydrogens and aromatic carbons were forced to reside at interatomic distances much less than the sum of their van der Waals radii, but there was no evidence of electronic interactions between these functional groups. (The exotic NMR and infrared bands result from aromatic ring current effects and steric compression, respectively.) How might heteroatoms behave if brought into similar proximity to aromatic rings? There are many heterophanes which contain first-row elements (ref. 9), but we speculated that second-row elements, with their greater polarizability and potentially accessible *d*-orbitals, if substituted for the apical methine groups of our *in*-cyclophanes, might give rise to the most interesting electronic and structural effects. The syntheses of silicon- and phophorus-containing *in*-heterophanes (ref. 10) are illustrated below. The X-ray crystal structure of **17** shows the silicon atom to be 3.34 Å from the centroid of the basal aromatic ring (with a hydrogen-arene distance of approximately 1.9 Å), while the X-ray structure of **18** reveals the phosphorus-arene distance to be only 2.90 Å.

15 X = Si-H
16 X = P

17 X = Si-H
18 X = P
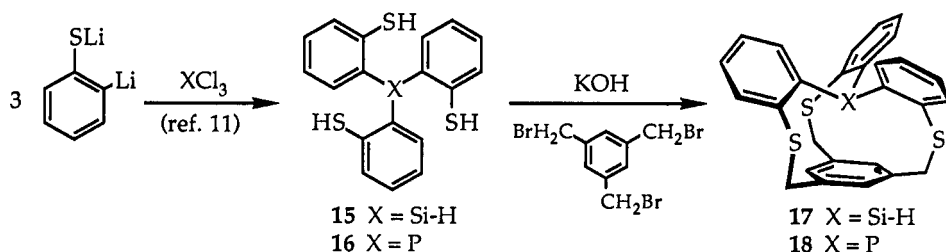
The spectroscopic properties of the silaphane **17** are analogous to those of the apical methine *in*-cyclophanes; the unusually high-field Si-H proton NMR resonance (δ 1.04) and the high frequency Si-H stretching band in the IR (2457 cm^{-1}) are most notable. On the other hand, the spectral properties of the phosphaphane **18** are remarkable (ref 10). The proton-decoupled ^{13}C NMR spectrum of **18** shows spin-spin coupling between the phosphorus and *all* of the aromatic carbons. In particular, the basal methine carbon resonance is a doublet with J_{PC} = 7.5 Hz — greater than the coupling to most of the aryl carbons of the triarylphosphine part of the molecule (J_{PC} = 40, 22, 4.5, 2, 1.5, and 1 Hz). The apparent "through-space" coupling is unlikely to result from normal through-bond interactions (6 bonds) for the reason that no coupling is observed between the phosphorus and the bridging methylene carbons. The ^{31}P NMR spectrum of compound **18** shows a single resonance at δ 5.0, quite a bit downfield from the δ -26.7 resonance of the starting tris(2-mercaptophenyl)phosphine (**16**). This shift, which is further downfield than any of the resonances in a ^{31}P NMR study of 30 triaryl phosphines (ref. 12), is in the opposite direction from that which would result from simple ring current effects, and it suggests a more phosphonium-like character for the phosphorus of **18**. In addition to its unusual spectroscopic characteristics, the phosphorus of **18** is remarkably unreactive. It is not protonated by anhydrous HBr in chloroform, and heating **18** for 24 hours in refluxing 2:1 acetic acid and 30% hydrogen peroxide yields only the corresponding trisulfone; the phosphorus is not attacked! The unusual ^{13}C and ^{31}P NMR properties of **18** show that there is an electronic interaction between the phosphine and the basal ring, but these data do not tell us if there is an attraction between them (i.e. a bond). Furthermore, the low reactivity and inward pyramidalization of the phosphine may be attributed to steric encumbrance and bond angle constraints. Notably, the crystallographically observed phosphorus-to-ring distance is 0.2 Å less than the *ca.* 3.1 Å gap calculated for **18** by both MMPI (which treats the interaction as purely repulsive) and MNDO, but inasmuch as it is much longer than the corresponding distance in typical η^6-arene metal complexes, any attractive force between the phosphine and basal arene in **3**, if one exists at all, must be relatively weak.

BENT DITHIATETRAZOCINES

The 1,5,2,4,6,8-dithiatetrazocines were first reported from the Woodward group in 1981 (ref. 13) and exhibit a remarkable structural dichotomy. In most derivatives the hetero-cycle is planar and easily understood as a 10 π-electron aromatic system (19). However, where both (ref. 13) or one (ref. 14) of the R groups is a dimethylamino group, the hetero-cycle is sharply folded (20) with a dihedral angle of *ca.* 100°. In the bent forms, the S-S distance is only 2.4-2.5 Å; thus we have been attracted to the bent dithiatetrazocines by our interest in transannular interactions. One question comes immediately to mind: do the bent dithiatetrazocines retain any aromatic character, and, in particular, a ring current?
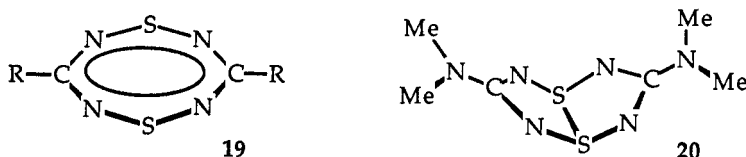
In order to address this issue, we prepared a cyclophane containing the dithiatetrazocine ring system. N,N'-Dimethyl-1,8-octanediamine was converted to the bisguanidine 21, and this material was treated with sulfur dichloride and DBU under conditions of modest dilution (40 mM). Most of the product was polymeric, but the cyclophane 22 was isolated in 1.1% yield by column chromatography (ref. 15). An X-ray structure of this material shows the geometry of the dithiatetrazocine ring to be almost identical to that observed in 20. The compound adopts a *cis* confromation as shown, and the octamethylene chain passes over one edge of the dithiatetrazocine. However, the chemical shifts of the proton NMR resonances of the six internal methylene groups of the bridging chain fall in the range of δ 0.9-1.6, and provide little evidence of a ring current in these molecules.
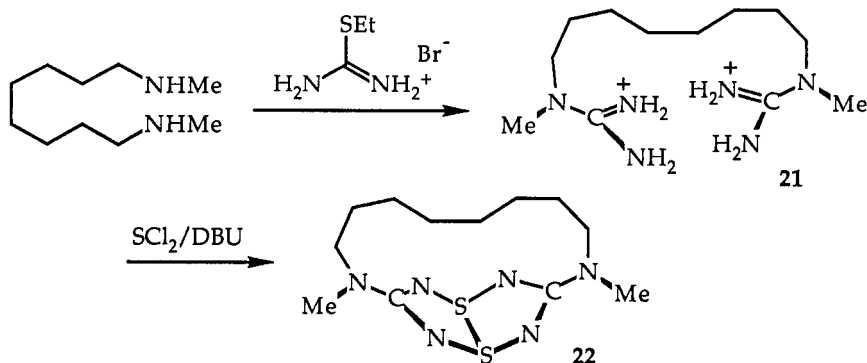
Acknowledgment

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