[2₆]Paracyclophanes — Large Ring Compounds with Extended π-Systems

ILONA RASTON and OLOF WENNERSTRÖM*

Department of Organic Chemistry, Chalmers University of Technology and University of Göteborg, S-412 96 Göteborg, Sweden

Two [2₆]paracyclophanes with unsaturated bridges, containing perimeters with 36 π-electrons, have been prepared by fourfold Wittig reactions. Attempts to prepare cyclophanes with even larger π-systems are reported. The reversible two-electron reduction of the [2₆]paracyclophanes to the corresponding dianions is compared to that of [2₄]paracyclophanetetraene and correlated with the energies of the lowest unoccupied molecular orbitals (LUMOs) in the cyclophanes which have been calculated by simple Hückel theory.

Large carbocyclic compounds with conjugated π-systems around the ring have been extensively studied. The synthetic problems encountered in attempted preparation of such compounds are manifold, however, and have prevented more complete investigations of the many aspects of this type of compound which are of such interest for the development of theoretical models applicable to conjugated π-systems. Another major problem encountered in the annulenes is their flexibility, which increases with ring size, and the large number of rapidly interconverting isomers and conformers.[1] A relatively rigid and planar molecule is essential for π-electron delocalization which is a phenomenon of major interest in the annulenes.[1] These problems can be overcome by, for example, the preparation of rigid annulenes, as accomplished by the groups of Boekelheide[2] and Vogel.[3a]

The introduction of benzene rings into the annulenes changes their properties. This prevents bond-isomerization and endows a more rigid structure on the π-systems but, unfortunately, also

diminishes the properties connected with π-electron delocalization over the molecule in the ground state.[3b] Large ring compounds consisting of aromatics linked by vinylene bridges behave essentially as normal open chain compounds.[4] We have recently found that certain cyclophanes can be reduced to dianions in a reversible two-electron process.[5] One very interesting condition for this is that the cyclophanes must contain a perimeter of 4n π-electrons in the neutral molecule. The rapid rotation of the benzene rings on the NMR time scale in the cyclophanes becomes hindered in the dianions, resulting in nonequivalence of inner and outer protons. A large difference in chemical shift for these two types of proton is observed, due to strong diamagnetic ring currents in the dianions.[6] It thus seems as if large paracyclophanes with unsaturated bridges, and their dianions, might be interesting model compounds for theoretical investigations of the conditions and effects of conjugation in large cyclic π-systems. In this paper, the synthesis and reduction of two cyclophanes of this type are described.

RESULTS AND DISCUSSION

Synthesis. Fourfold Wittig reactions between aromatic dialdehydes and bisphosphonium salts from bis(halomethyl)arenes have proved to be a facile method of preparing large cyclophanes with vinylene linkages between the aromatics.[4] Although the yields may be low, which is certainly expected for reactions in which four *cis* double bonds are formed in a one-pot reaction sequence, the simplicity of the approach outweighs the low yields and makes large cyclophanes readily available.

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*To whom correspondence should be addressed.
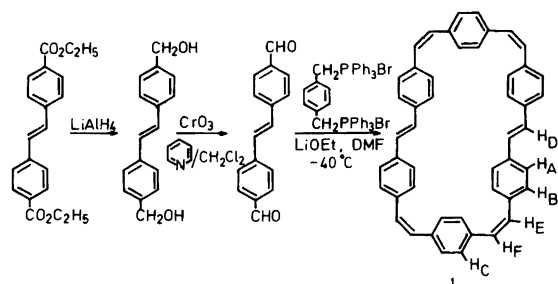
Scheme 1.

trans-Stilbene-4-4'-dicarbaldehyde reacts with the bisphosphonium salt from 1,4-bis(bromomethyl)benzene and base at $-30\,°C$ in DMF to give *cis,cis,trans,cis,cis,trans*-[2₆]paracyclophane-hexaene, *1*, in 5 % yield (Scheme 1). The structure of the cyclophane follows from its mass and ¹H NMR spectrum. The latter shows the simple pattern expected for the cyclophane assuming rapid rotation of the benzene rings and the *trans*-double bond bridge, *i.e.* a singlet and an AA'XX'-pattern for the aromatic protons and a singlet and an AB-pattern for the olefinic *trans* and *cis* protons, respectively. The temperature-dependence of the NMR spectrum of *1* was checked. No significant broadening of the signals was observed down to 200 K in CD_2Cl_2, implying rapid rotation of the benzene rings and the *trans*-vinylene groups on the NMR time scale.

Tolan-4,4'-dicarbaldehyde reacts under similar conditions with the bisphosphonium salt from 1,4-bis(bromomethyl)benzene to give all-*cis*-[2₆]para-cyclophanetetraenediyne, *2*, in 12 % yield (Scheme 2). The mass spectrum shows the molecular ion and the doubly charged molecular ion. The high symmetry of the cyclophane is revealed by its ¹H NMR spectrum which consists of a singlet and an
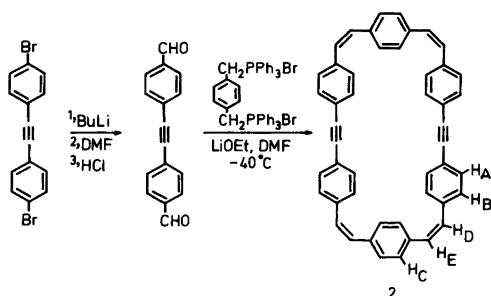
AA'XX'-pattern for the aromatic protons and an AB-pattern for the olefinic protons.

In an attempt to prepare an even larger cyclophane with eight benzene rings, four *cis* double bonds, and four triple bonds, we reacted tolan-4,4'-dicarbaldehyde with the bistriphenylphosphonium salt from 4,4'-bis(bromomethyl)tolan (Scheme 3) under the standard conditions.[4] The dialdehyde and the bisphosphonium salt were prepared by standard procedures from bibenzyl, which was treated with bromine to give $\alpha,\alpha',4,4'$-tetrabromobibenzyl. The product was refluxed with base to give 4,4'-dibromotolane, which, upon treatment with butyllithium and dimethylformamide followed by hydrolysis, gave tolan-4,4'-dicarbaldehyde. A portion of the dialdehyde was reduced with sodiumborohydride to the dialcohol which, upon reaction with hydrobromic acid, gave 4,4'-bis(bromomethyl)-
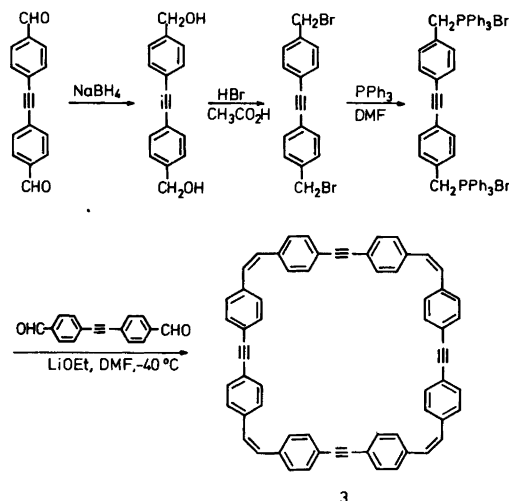
Scheme 2.

Scheme 3.

tolan. The bisphosphonium salt was generated in DMF by addition of triphenylphosphine (see also Scheme 3). The Wittig reaction between the dialdehyde and the bisphosphonium salt in the presence of base gave only trace amounts of products isolated after careful chromatography of the ethereal extract of the reaction product. The mass spectra of two of the products showed the molecular ion at m/e 808 consistent with a [2₈]paracyclophane-tetraenetetrayne. The ¹H NMR spectra revealed the products to be the all-*cis* isomer and the *cis,trans,cis,trans*-isomer. The latter was not present in the reaction mixture but formed slowly from the all-*cis* isomer, probably by a light-induced *cis-trans* isomerization. The all-*cis* isomer shows an unusually simple ¹H NMR spectrum consisting of an AA'XX'-pattern for the aromatic protons and a singlet for the olefinic protons. The *cis,trans,cis,trans*-isomer shows two AA'XX'-patterns for the aromatic protons and two singlets for the olefinic protons, consistent with the assumption of rapid rotation of the benzene rings as well as the *trans*-double bonds. In one of the Wittig reactions, a product with a mass spectrum similar to those above but with a molecular ion of m/e 606 was observed and isolated. The ¹H NMR spectrum was very simple, consisting of just one AA'XX'-pattern in the aromatic region and a singlet in the olefinic region. The compound is most likely the [2₆]paracyclo-phanetrienetriyne. Its formation can be rationalized either by assuming impurities of a mono-phosphonium salt monoaldehyde in the Wittig reaction, originating from incomplete reduction of the dialdehyde to the dialcohol, or by assuming air oxidation of a small proportion of the intermediate ylid groups to aldehyde groups, which ultimately could lead to cyclophanes with three double bonds instead of the even number expected.

Electrochemistry and Hückel calculations. As mentioned above, several cyclophanes formally with a perimeter of 4n π-electrons undergo a completely reversible two-electron reduction to their dianions at a mercury electrode in DMF.[5] The reduction potential has been found to be proportional to the energy of the LUMO orbital obtained from simple Hückel calculations, even for cyclophanes that are far from planar as neutral species.[7] Within the Hückel approximation, cyclophanes 1 and 2 are similar. The energy of their LUMO orbitals is the same as that of [2₄]paracyclophanetetraene, 6, (0.254 β). In fact, the HOMO and LUMO orbitals in these three cyclophanes can be regarded as arising

from the degenerate nonbonding orbitals in the (4n) annulenes which have been split by the bridging benzene rings, to give a bonding and an anti-bonding orbital in the cyclophanes. The magnitude of the splitting does not depend on the size of the cyclophane, but only on the relative proportion of double bonds and benzene rings, in the series of unsaturated [2ₙ]paracyclophanes (n is even).

Cyclic voltammetry of 1 and 2 at a mercury drop in dry DMF containing tetraethylammonium perchlorate as supporting electrolyte and with [2₄]paracyclophanetetraene as a standard gave similar results. Both cyclophanes are reduced at −1.70 V *vs.* SCE, which is exactly the same reduction potential as that of [2₄]paracyclophanetetraene.[5] However, the latter undergoes a completely reversible two-electron reduction whereas the cyclophanes 1 and 2 undergo the same type of two-electron process, but less reversibly. Apparently, the dianions from 1 and 2 are more prone to abstract protons from the residual water in the solvent or from the solvent itself.

The dianion of [2₄]paracyclophanetetraene is planar enough to sustain a diamagnetic ring current when subjected to a strong magnetic field.[6] By analogy, the cyclophanes 1 and 2 should behave similarly. According to Haddon,[8] ring current should increase with the size of a cyclic conjugated π-system, whereas the resonance energy should decrease with ring size. Thus the dianions of cyclophanes 1 and 2, if conformationally rigid, could well display large diamagnetic ring current effects. It is interesting to note the differences in the UV spectra of the cyclophanes 1, 2 and 4 (Table 1). The photoexcitation process is too fast to allow for conformational changes whereas the electrochemical reduction allows for relaxation to the equilibrium geometries of the cyclophanes and their dianions. The simple Hückel calculations used here should, of course, better represent the latter situation. It seems reasonable to conclude that considerable geometrical changes occur in the cyclophanes on reduction to the dianions.

Most recent theories of electronic effects in large conjugated systems, and particularly in the annulenes, result in similar predictions of the resonance stabilization in charged and neutral systems with the same number of π-electrons.[8,9a] The total effect is small in annulenes with more than 18−22 π-electrons, and should be much smaller in cyclophanes with conjugated perimeters. In a recent paper, however, Bates *et al.*[9b] give consider-

Table 1. Comparison of calculated LUMO energies, reduction potentials (*vs. SCE*) and absorption maxima for cyclophanes 6, 2 and 1.

Cyclophane	Calculated energy of LUMO (β)	ΔE_{red} (V) to the dianions	λ_{max} (nm)	ε
6	−0.254	−1.70	304	57 500
2	−0.254	−1.70	324	86 000
1	−0.254	−1.70	344	116 000

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5   6
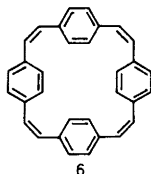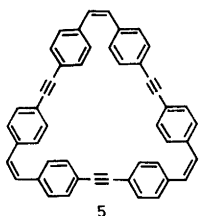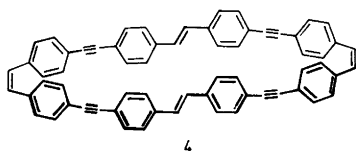
ably larger values for the resonance energy in annulene-dianions. The effect of Hückel's rule should be negligible for π-systems of the size and type discussed here. Nevertheless, an alternating behaviour has been observed for the reduction potential of a series of closely related cyclophanes with increasing number of π-electrons around the perimeter.[4] Further, the reversible transfer of two electrons to the cyclophanes with 4n-π-electron perimeters is difficult to rationalize without assuming some extra stabilization of the dianions, relative to the radical anions, to compensate for the inter-electronic repulsion. For many aromatic hydrocarbons this repulsion results in a separation of the potentials for the reduction to the radical anions and the dianions of *ca.* 500 mV.[9c]

The Hückel calculations have shown the importance of the HOMO and LUMO orbitals for comparison with experimental reuction potentials. It might be adequate to restrict the discussion of these large conjugated systems to include only the frontier orbitals rather than all the orbitals and the total π-electron energy, as is usually done when discussing resonance effects.

It seems as if further studies of these large cyclophanes and their dianions could give valuable

experimental results to test present theories of π-electron delocalization, ring current effects, and resonance stabilization in large conjugated π-systems.

EXPERIMENTAL

cis,cis,trans,cis,cis,trans-[2₆]*Paracyclophanehexaene. trans*-Stilbene-4,4′-dicarboxylic acid diethylester[10] was reduced with lithiumaluminum hydride in refluxing diethylether to give 4,4′-bis(hydroxymethyl)-*trans*-stilbene (75 %, m.p. 268 − 270 °C).[11] MS (50 eV): *m/e* 240 (M⁺, 100 %), 238 (26), 179 (42, 178 (42), 113 (14), 103 (14), and 91 (12). Abs. mass 240.1154; calc. for $C_{16}H_{16}O_2$ 240.1150. NMR (270 MHz, pyridine-d_5): δ 7.62 (m) 8H, 7.31 (s) 2H, 4.95 (s) 4H.

The diol was oxidized by a solution of chromium trioxide in pyridine − dichloromethane to *trans*-stilbene-4,4′-dicarbaldehyde (82%, m.p. 165 °C[12]). MS (50 eV): *m/e* 236 (M⁺, 100 %), 235 (37), 179 (50), 178 (60), 176 (12), 152 (10), 89 (11). Abs. mass 236.078; calc. for $C_{16}H_{12}O_2$ 236.084. NMR (270 MHz CDCl₃): δ 9.99 (s) 2 H, 7.86 (m) 4 H, 7.68 (m) 4 H, 7.27 (s) 2 H. The dialdehyde (13 mmol) was reacted with the bistriphenylphosphonium salt from 1,4-bis(bromomethyl)benzene (13 mmol) and lithium ethoxide in dry DMF at −30 °C under the standard conditions.[4] The product mixture in DMF was diluted with water and extracted with diethylether and dichloromethane. The combined organic phases were washed with water, dried (MgSO₄) and the solvents evaporated. The residue was stirred with ethanol to remove triphenylphosphine oxide and recrystallized from chloroform − methanol to give cis,cis,trans,cis,cis,trans-[2₆]-paracyclophanehexa-ene (122 mg, 5 %, m.p. 278 − 280 °C). IR (KBr): 3000 (m), 1598 (m), 1505 (s), 1420 (s), 960 (s), 940 (s), 890 (s) and 830 (vs) cm⁻¹. UV (ethanol): λ_{max} 344 nm ε 116 000 and 244 nm 52 000. NMR (270 MHz, CDCl₃): d 7.34 and 7.27 (16 H, AA′BB′-pattern, J8 Hz, H_A and H_B), 7.20 (8 H, s, H_C), 7.03 (4 H, s, H_D), 6.58 and 6.54 (8 H, AB-pattern, J 12 Hz, H_E and H_F). MS (50eV): *m/e* 612 (M⁺, 100 %), 306

$(M^{2+}, 14)$. Abs. mass 612.289; calc. for $C_{48}H_{36}$ 612.282.

[2₆]*Paracyclophanetetraenediyne.* 4,4'-Dibromo-tolan[13] was treated with butyl-lithium in diethyl-ether, followed by dry DMF, and, finally, dilute hydrochloric acid to give tolan-4,4'-dicarbaldehyde (58 %, m.p. 213–214 °C).[14] MS (50 eV): m/e 234 $(M^+, 100 \%)$, 233 (63), 176 (38), 151 (14). Abs. mass 234.063; calc. for $C_{16}H_{10}O_2$ 234.068. NMR (270 MHz, CDCl₃): δ 10.03 (s) 2 H, 7.87 (m) 4 H, 7.67 (m) 4 H.

The aldehyde (10 mmol) was reacted with the bistriphenylphosphonium salt from 1,4-bis(bromomethyl)benzene (10 mmol) and lithium ethoxide in dry DMF at -40 °C under the standard conditions.[4] The reaction mixture was diluted with water and extracted with diethyl ether.

The organic phase was dried and the solvent distilled off. Careful chromatography of the residue on a silica gel column with tetrachloromethane as eluant gave [2₆]paracyclophanetetraenediyne (363 mg, 12 %, m.p. 265–270 °C) IR (KBr): 3000 (w), 1595 (m), 1505 (m), 1410 (m), 890 (s) and 830 (vs). UV (ethanol): λ_{max} 324 nm ε 86 000 and 237 nm ε 48 600. NMR (270 MHz, CDCl₃): d 7.39 and 7.27 (16 H, AA'BB'-pattern, J 8 Hz, H_A and H_B), 7.19 (8 H, s, H_C), 6.58 and 6.53 (8 H, AB-pattern, J 12 Hz, H_D and H_E). MS (34 eV): m/e 608 $(M^+, 100\%)$, 304 $(M^{2+}, 7)$. Abs. mass 608.253; calc. for $C_{48}H_{32}$ 608.250.

[2₈]*Paracyclophanetetraenetetrayne* 3. Tolan-4,4'-dicarbaldehyde was reduced with sodium boro-hydride in ethanol to 4,4'-bis(hydroxymethyl)tolan (93 %, m.p. 214–215 °C). MS (50 eV): m/e 238 $(M^+, 100 \%)$, 237 (12), 221 (15), 191 (14), 179 (20), 178 (35). Abs. mass 238.095; calc. for $C_{16}H_{14}O_2$ 238.099. NMR (270 MHz, DMSO-d_6): δ 7.51 (m) 4 H, 7.37 (m) 4 H, 5.24 (br tr) 2 H, 4.53 (br d) 4 H.

The diol was treated with hydrobromic acid (30 %) in acetic acid to give 4,4'-bis(bromomethyl)tolan (83 %, m.p. 187–190 °C). MS (50eV): m/e 366 (5 %), 364 (10), 362 (6) M^+, 285 (61), 283 (62) $M^+ -$ Br, 205 (30), 204 $(M^+ -2$ Br, 100), 202 (26), 102 (37). NMR (270 MHz, CDCl₃): δ 7.64 (m) 4 H, 7.38 (m) 4 H, 4.50 (s) 4 H.

The bisbromomethyl compound was converted to its bistriphenylphosphonium salt by treatment with triphenylphosphine in dry DMF up to 154 °C (87 %). Tolan-4,4'-dicarbaldehyde (5 mmol) and the bisphosphonium salt (5 mmol) were suspended in dry DMF and lithium ethoxide was added dropwise at -40 °C under the standard conditions.[4] The usual work-up and separation on a silica gel column gave small amounts of an unstable product identified as the all-*cis*-isomer of [2₈]paracyclophanetetraenetetrayne. NMR (270 MHz, CDCl₃): d 7.39 and 7.24 (32 H, AA'BB'-pattern, J 8 Hz, aromatic protons), 6.60 (8 H, s, olefinic protons). MS (50 eV): m/e 808 $(M^+, 100\%)$, 404 $(M^{2+}, 30)$.

Abs. mass 808.303; calc. for $C_{64}H_{40}$ 808.313.

On standing, the cyclophane gave rise to a new compound, tentatively assigned as the *cis,trans,-cis, trans*-isomer 4 on the basis of its NMR spectrum (270 MHz, CDCl₃): δ 7.44 and 7.42 (16 H, AA'BB'-pattern, aromatic protons), 7.29 and 6.94 (16 H, AA'BB'-pattern, J 8 Hz, aromatic protons), 7.01 (4 H, s, olefinic protons), 6.81 (4 H, s, olefinic protons).

From a preliminary experiment, another cyclophane was isolated and identified as [2₆]paracyclophanetrienetriyne, 5, from its simple NMR and MS. ^{1}H NMR (270 MHz, CDCl₃): d 7.32 and 7.04 (24 H, AA'BB'-pattern, J 8 Hz, aromatic protons) and 6.70 (6 H, s, olefinic protons). MS (50 eV): m/e 606 $(M^+, 100 \%)$, 303 $(M^{2+}, 13)$. Abs. mass 606.230; calc. for $C_{48}H_{30}$ 606.235.

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