[2$_n$]Para[4$_{4-n}$]paracyclophanes; Synthesis, Structure, and Cyclic Voltammetry

By **Bengt Thulin**, Department of Organic Chemistry, Chalmers University of Technology and University of Göteborg, S–412 96 Göteborg, Sweden

Three new unsaturated [2$_n$]para[4$_{4-n}$]paracyclophanes (n = 1, 2, or 3) have been prepared by a new multiple Wittig reaction. The structures and electron delocalisation of the neutral compounds and the anions are discussed. The latter were obtained by cyclic voltammetry at a mercury drop. Unsaturated cyclophanes with electron conjugation along the perimeter form stable dianions if the number of π-electrons is $4n + 2$ in the dianions.

WE have previously reported that a convenient way to prepare [2$_4$]cyclophanes and related compounds is by a one-step Wittig reaction at low temperatures using DMF as solvent.[1] A number of these cyclophanes have been reduced at a mercury cathode in dry DMF,[2] and those having a conjugated periphery of $4n$ π-electrons undergo a reversible two-electron reduction and form rather stable dianions in contrast to most other aromatic hydrocarbons. Normally, reduction of planar aromatic or unsaturated hydrocarbons gives the radical anion which at 300—500 mV lower potential[3] may undergo a second one-electron reduction to give the dianion. An interesting explanation for the unusual two-electron reductions of the cyclophanes could be found by considering the size of the conjugated π-system involved. If the neutral cyclophanes contain $4n$ π-electrons then the dianions must have $4n + 2$ π-electrons, and could thus gain some extra resonance stabilization. What happens when similar cyclophanes with $4n + 2$ π-electrons in the neutral molecule are reduced under the same conditions? In order to obtain an answer such cyclophanes have now been prepared and reduced electrochemically. A series of unsaturated [2$_n$]para[4$_{4-n}$]paracyclophanes with n = 1, 2, or 3 have now been synthesized by multiple Wittig reactions. These compounds are not accessible by the previously described method, but by careful control of the reaction conditions and stepwise addition of the proper reactants and base, it has been possible to carry out a one-pot synthesis without isolation of the intermediates, albeit in low total yield.

RESULTS

Cyclophanes (1) and (5) with four ethylene and four butadiene bridges, respectively, have been prepared previously by a Wittig reaction between the bisphosphonium salt of 1,4-bis(bromomethyl)benzene and an equimolar amount of benzene-1,4-dicarbaldehyde or benzene-1,4-dipropenal, respectively.[4,5]

Compound (3), which is symmetrical with two ethylene and two butadiene bridges, can be prepared similarly (in 1% yield) by mixing equimolar amounts of styrene-α,4-dicarbaldehyde and the bisphosphonium salt of 1,4-bis(bromomethyl)benzene. A stepwise procedure starting with 2 mol of the dialdehyde and 1 mol of the bisphosphonium salt gives a slightly better yield of 2%. Two isomers are possible, (3a) and (3b).

The structure of (3) is confirmed by the 270-MHz n.m.r.

spectrum, which shows two sharp singlets for the two different benzene rings 2 and 4, and an AA'XX' pattern for rings 1 and 3. Consequently, isomer (3a) must be preferred since isomer (3b) would have shown two different

(1)   (5)
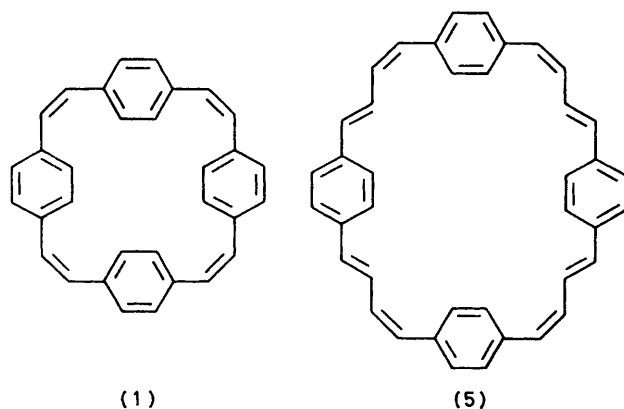
AA'XX' patterns in the aromatic region. The protons in the ethylene bridges appear as an AB quartet (J_{AB} 12 Hz) and those in the butadiene bridges as a rather complex pattern. The mass spectrum shows the molecular ion as the parent peak and little fragmentation.

Cyclophanes (2) and (4) are less symmetrical than (3) and not accessible by the previously described methods. However, they can be prepared by a stepwise Wittig reaction at −40 °C in dry DMF as solvent and with lithium ethoxide

(3a)   (3b)
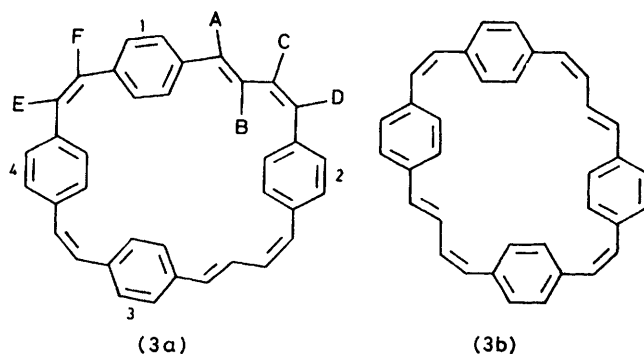
as base. Compound (2), which contains three cis-ethylene bridges and one cis,trans-butadiene bridge, is then synthesized from two different dialdehydes, viz. benzene-1,4-dicarbaldehyde and styrene-α,4-dicarbaldehyde, and 2 equiv.
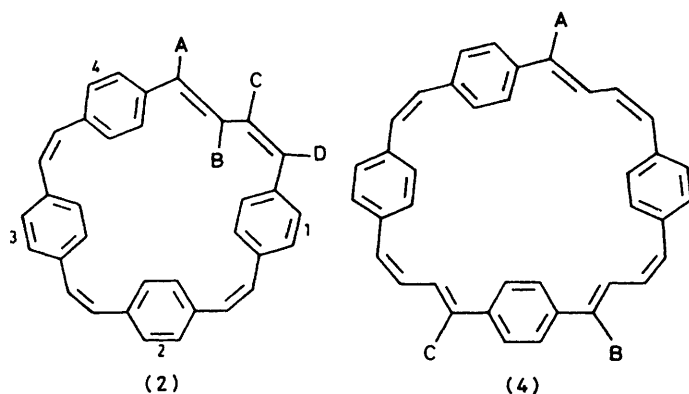
of the bistriphenylphosphonium salt from 1,4-bis(bromo-methyl)benzene.

The reaction sequence is shown in the Scheme. The first step is the formation of the slightly coloured mono-ylide
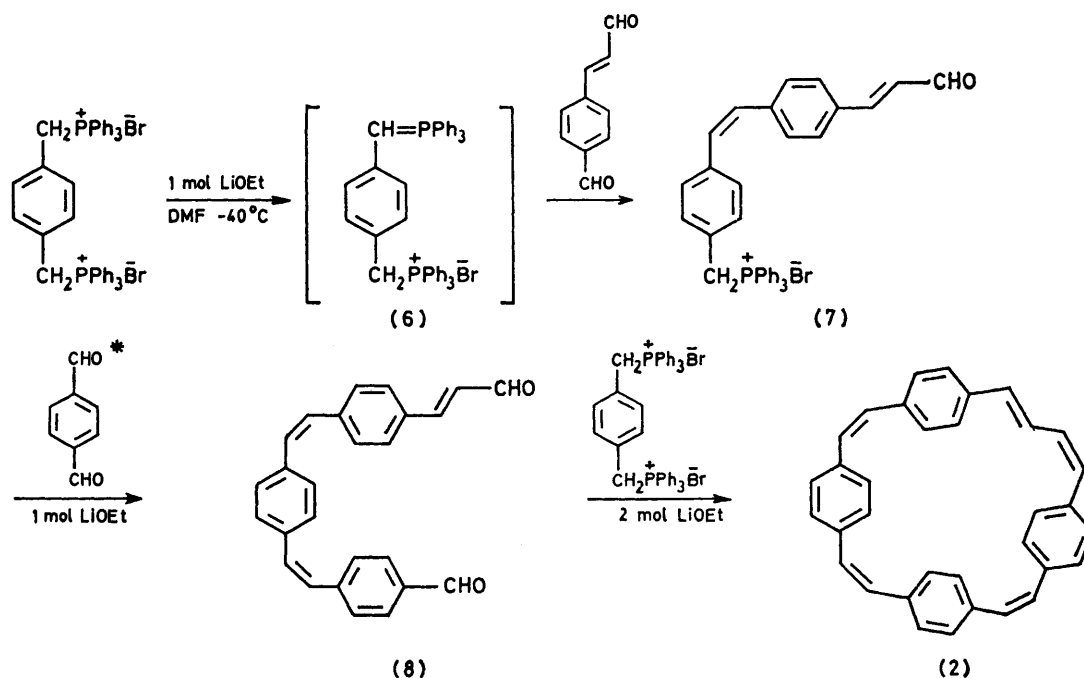

(2)   (4)

(6), by addition of one mol of base to a suspension of one mol of bisphosphonium salt in dry DMF at —40 °C. The mono-ylide then formed is reacted with 1 mol of styrene-α,4-dicarbaldehyde to give intermediate (7). The second

second step, *i.e.* the rate of the proton exchange, is slower at low temperature. Furthermore the reaction between (6) and styrene-α,4-dicarbaldehyde is much faster than the competing side-reactions mainly due to the high reactivity of the arylaldehyde group.

Cyclophane (2), or [2₃]para[4]paracyclophanepentaene is formed in 1% yield together with trace amounts of (1) and (3), which makes the isolation procedure difficult. After the usual work-up, (2) can be purified by column chromatography on silica gel using di-isopropyl ether–light petroleum as eluant Because of the low symmetry of the molecule the ¹H n.m.r. spectrum becomes very complex. It shows three different AA′XX′ patterns and a singlet for the aromatic protons, and a complex pattern for the olefinic protons, of which H_A and H_B in the butadiene bridge could be assigned. In contrast to the n.m.r. spectrum the mass spectrum is beautifully simple and shows the molecular ion as the parent peak, doubly charged ions, and almost no fragmentation. The cyclophane formed upon hydrogenation of (2) confirms the proposed structure. Its ¹H n.m.r. spectrum shows two AA′XX′ patterns, a singlet for the ethane bridges, and two complex signals from the butane part.

Cyclophane (4), [2]para[4₃]paracyclophaneheptaene, is prepared by exactly the same method as for (2), benzene-


SCHEME   * Addition of benzene-1,4-dipropenal gives (4)

mol of dialdehyde is then added, followed by a second mol of base. The unsymmetrical dialdehyde (8), thus formed is finally ring-closed to (2) by adding the remaining mol of the bisphosphonium salt and 2 mol of base. However, small amounts of (1) and (3) are also formed and this shows the equilibrium in the second step in the reaction sequence, *i.e.* proton exchange between (7) and (6), which allows the more stabilized ylide of (7) to be formed. This can react further with the styrene-α,4-dicarbaldehyde to form a symmetrical dialdehyde instead of (8). The outcome of the

1,4-dipropenal being added in the third step (Scheme). Cyclophane (4) is thus formed in 0.8% yield, together with trace amounts of (3) and (5), and can be purified in the same way as (2). The compounds are eluted in the order (3), (4), and (5). The ¹H n.m.r. spectrum of (4) is too complex to allow a concrete assignment, but the mass spectrum shows the molecular ion as the parent peak, doubly charged ions, and almost no fragmentation. Hydrogenation of (4) gives the saturated cyclophane with one ethane and three butane bridges.

DISCUSSION

In the series of $[2_n]$para$[4_{4-n}]$paracyclophanes ($n = 0$, 1, 2, 3, or 4) described here, the number of conjugated π-electrons around the periphery ranges from 24 to 32. This is obtained by introducing different numbers of butadiene bridges between the *para*-substituted benzene rings. The members of the series are thus formally

S - trans   **S - cis**
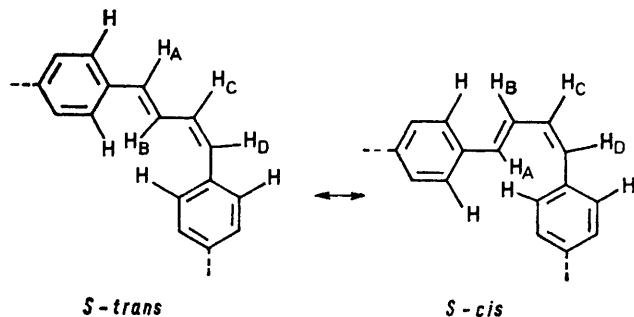
either $4n$ π-electron systems [rings (1), (3), and (5)] or $4n + 2$ π-electron systems [rings (2) and (4)].

The structure of (1) has been determined by X-ray crystallography which shows that the molecule is relatively planar, with the benzene rings tilted *ca.* 35° from the average molecular plane.[6] Inspection of molecular

(Table) in compounds (3) and (5), in which there is a 1 p.p.m. difference in chemical shift between the inner protons H_B compared to compounds (2) and (4). The compounds (3) and (5) may thus be regarded as paratropic.

When cyclophanes (1)—(5) are electrochemically reduced at a mercury cathode in dry DMF, two different modes of behaviour are observed (Table). Compounds (1), (3), and (5) are reversibly reduced.[2] The separation of the cathodic and anodic peaks in their cyclic voltammograms is typical of a reversible two-electron process.[8,9] The dianions thus formed are rather stable, and the anodic peak is not much affected by addition of water to the DMF solution. The reduction potential becomes more anodic as the planarity of the molecules increases, and the most planar cyclophane, (5), is reversibly reduced at −1.53 V, which is 170 mV more anodic than for (1), and compound (3) is reduced at a potential halfway between these values. Under the same conditions used for the reduction of (1), (3), and (5), compounds (2) and (4) behave differently. Their cyclic voltammograms show two cathodic peaks with 330 and 250 mV separation, respectively, and a slightly reversible anodic peak. The anodic peak disappears on addition of water to the DMF solution, suggesting a fast protonation of the reduced species. From these results, it is obvious

The longest-wavelength u.v. absorption maximum, chemical shifts (δ) for protons H_B and H_C (270 MHz, CDCl$_3$) in the butadiene bridges, and the reduction potentials (V *vs.* s.c.e. in DMF) from cyclic voltammetry of compounds (1)—(5)

Compound	λ_{max}./nm	(log ε)	δ H_B	H_C	Reduction potential	Type of process	Type of ring system
(1) [4]	303	(4.76)			−1.70	Rev. 2 e	paratropic
(2)	315	(4.87)	6.90	*ca.* 6.55	−1.87, −2.20	Irrev.	diatropic
(3)	330	(4.70)	7.95	6.36	−1.60	Rev 2 e	paratropic
(4)	345	(4.72)	6.64—6.48		−1.67, −1.92	Irrev.	diatropic
(5) [5]	345, 360	(4.87)	7.89	6.35	−1.53	Rev .2 e	paratropic

models (CPK) shows the successive replacement of the ethylene bridges by butadiene units facilitates attainment of planarity. This is also apparent from a comparison of the u.v. spectra of cyclophanes (1)—(5) (Table), which show progressive bathochromic shifts. Of the two possible orientations of the butadiene bridges, the *S-trans* conformation is considered for cyclophane (5).[5] This gives the most planar and least strained structure and accounts for the large coupling constant between H_B and H_C (J_{BC} 12 Hz). A similar large coupling constant is also observed in cyclophanes (2) and (3) (J_{BC} 11 Hz), suggesting the same *S-trans* orientation of the bridges. An *S-cis* configuration would lead to more strained and less planar structures, and also to greater steric interactions between bridge and ring protons as shown.

It is obvious that these compounds (1)—(5) are rather planar, and since their π-electrons may be considered to be conjugated in a ring, they should be able to sustain a ring current, the nature of which would depend on the number of π-electrons.[7] Small effects are present

that the difference in behaviour of these rings upon reduction can be attributed to a resonance stabilization present in a system containing $4n + 2$ π-electrons; thus stabilization plays a role in such large ring systems.[10]

EXPERIMENTAL

N.m.r. spectra were obtained on a Bruker WH 270 instrument using CDCl$_3$ as solvent. I.r. spectra were obtained on a Beckman IR 9, u.v. spectra on a Beckman DK2, and mass spectra on an A.E.I. MS 902 instrument. Melting points were determined on a Reichert hot stage apparatus. The cyclic voltammograms were obtained at a hanging mercury drop electrode in dry DMF containing tetraethylammonium perchlorate (0.1M) at scan rates of 25 mV s^{-1}.[11] The reduction potentials were measured against a standard Ag–AgNO$_3$ electrode.[12] All potentials reported here are converted to the s.c.e. scale by adding 0.43 V.

Styrene-α,4-dicarbaldehyde and *benzene-1,4-dipropenal* [5] were prepared by Wittig reactions between benzene-1,4-dicarbaldehyde and the triphenylphosphonium salt from 2-(bromomethyl)-1,3-dioxolan followed by acid hydrolysis.[13] Styrene-α,4-dicarbaldehyde was formed in 30% yield, m.p.

93—95 °C; δ 10.06 (1 H, s), 9.77 (1 H, dd, J 7.5 Hz), 7.84 (4 H, AA'XX' pattern, J 8 Hz), 7.52 (1 H, d, J 16 Hz), 6.81 (1 H, dd, J 16 and 7.5 Hz).

Cyclophane (3) was prepared by a Wittig reaction starting from 2 mol of styrene-α,4-dicarbaldehyde and 1 mol of the bisphosphonium salt of 1,4-bis(bromomethyl)benzene in dry DMF at −40 °C with lithium ethoxide as base. After addition of 2 mol of base the remaining bisphosphonium salt was added followed by a further 2 mol of base to yield *compound* (3) in 2% yield, m.p. 214—215 °C; δ 7.95 (2 H, H_B, dd, J_{BC} 11 Hz), 7.83 (4 H, ring 2 or 4, s), 7.82 (8 H, rings 1 and 3, AA'XX' pattern, J_{AX} 8 Hz), 7.81 (4 H, s, ring 2 or 4), 6.65 (2 H, H_A, d, J_{AB} 16 Hz), 6.50 (2 H, H_D, d, J_{CD} 11.5 Hz), 6.42 (4 H, H_E and H_F, AB quartet, J_{EF} 12 Hz), and 6.36 (2 H, H_C, t); m/e 460 (M^+, 100%), 459 (8), 230 (M^{++}, 8), and 229 (8) (Found: M^+, 460.216 ± 0.008. $C_{36}H_{28}$ requires M, 460.219; $\lambda_{max.}$ (cyclohexane) 330 nm (ε 50 500); $\nu_{max.}$ (KBr) 3 015w, 2 800s, 1 600m, 1 440m, 1 380m, 990m, 880s, and 820s cm^{-1}.

Cyclophanes (2) and (4) were formed in a stepwise Wittig reaction. To a suspension of 1 mol of the bisphosphonium salt from 1,4-bis(bromomethyl)benzene in dry DMF at −40 °C was added 1 mol base (LiOEt). The solution became slightly orange. After 1 h 1 mol of α,4-styryl-dicarbaldehyde was added and the colour disappeared after 5 min, and the second mol of aldehyde was then added (benzene-1,4-dicarbaldehyde or benzene-1,4-dipropenal). Base (1 mol) was then added at such a rate that the colour of the ylide disappeared between additions. Finally 1 mol of the above phosphonium salt was added, followed by 2 mol of base. The work-up procedure was the same as described previously.[1] Column chromatography on silica gel with a mixture of di-isopropyl ether–light petroleum (b.p. 40—60 °C) (1 : 10), gave *cyclophane* (2) in 1% yield, m.p. 194—195 °C; δ 7.29 (4 H, s, ring 2 or 3), 7.28 (4 H, ring 1 or 4, AA'XX' pattern, J_{AX} 8 Hz), 7.24 (4 H, ring 1 or 4), 7.18 (4 H, ring 2 or 3, AA'XX' pattern, J_{AX} 8 Hz), 6.90 (1 H, H_B, dd, J_{BC} 11 Hz), 6.75 (1 H, H_A, d, J_{AB} 16 Hz), and 6.71—6.40 (8 H, H_C and H_D, three different AB quartets); m/e 434 (M^+, 100%), 433 (7), and 217 (M^{++},

6) (Found: M^+, 434 ± 0.008. $C_{34}H_{26}$ requires M, 434.203); $\lambda_{max.}$ (cyclohexane) 315 nm (ε 75 000); $\nu_{max.}$ (KBr) 3 000s, 1 600m, 1 480m, 1 420m, 980m, 880s, and 820s cm^{-1}.

Cyclophane (4) was formed in 0.8% yield, m.p. 206—208 °C; δ 7.82—7.12 (16 H, aromatic protons), 6.87, 6.84, and 6.83 (3 H, protons A, B, and C, J 16 Hz), and 6.64—6.48 (11 H, olefinic protons); m/e 486 (M^+, 100%), 485 (5), 484 (7), and 243 (M^{++}, 10) (Found: M^+, 486 ± 0.008. $C_{38}H_{30}$ requires M, 486.235); $\lambda_{max.}$ (cyclohexane) 345 nm (ε 52 800); $\nu_{max.}$ (KBr) 3 020w, 2 800m, 1 580m, 1 430m, 1 180(br), 1 120s, 720s, and 695s cm^{-1}.

REFERENCES

[1] B. Thulin, O. Wennerström, I. Somfai, and B. Chmielarz, *Acta Chem. Scand.*, 1977, **B31**, 135.
[2] K. Ankner, B. Lamm, B. Thulin, and O. Wennerström, *J.C.S. Perkin II*, 1980, **9**, 1301.
[3] M. E. Peover, in 'Electroanalytical Chemistry', vol. 2, ed. A. J. Bard, Dekker, New York, 1967, p. 7.
[4] B. Thulin, O. Wennerström, and H.-E. Högberg, *Acta Chem. Scand.*, 1975, **B29**, 138.
[5] D. Tanner, B. Thulin, and O. Wennerström, *Acta Chem. Scand.*, 1979, **B33**, 464.
[6] E. Ljungström, O. Lindquist, and O. Wennerström, *Acta Cryst.*, 1978, **B34**, 1899.
[7] F. Sondheimer, *Accounts Chem. Res.*, 1972, **5**, 81.
[8] D. S. Polcyn and I. Shain, *Analyt. Chem.*, 1966, **38**, 370.
[9] R. S. Nicholson, *Analyt Chem.*, 1965, **37**, 1351.
[10] M. J. S. Dewar and G. J. Gleicher, *J. Amer. Chem. Soc.*, 1965, **87**, 685.
[11] B. Lamm, and K. Ankner, *Acta Chem. Scand.*, 1978, **B32**, 31.
[12] J. N. Butler, *Adv. Electrochem. Eng.*, 1970, **7**, 77 (p. 117).
[13] T. M. Cresp, M. V. Sargent, and P. Vogel, *J.C.S. Perkin I*, 1974, 37.