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Synthesis of New Ortho-, Meta- and Para[2_4]cyclophanes *via* Wittig Reactions and Hydrogenations

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[2_4]Metaparametaparacyclophanetetraene and isomers of [2_4]metacyclophanetetraene and [2_4]orthoparaorthoparacyclophanetetraene, as well as their derivatives with saturated bridges, have been prepared by Wittig reactions at low temperatures followed by catalytic hydrogenations. An attempted synthesis of [2_4]orthometaorthometacyclophanetetraene is also reported.

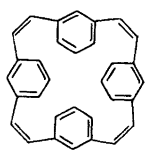
A general discussion of the use of the Wittig reaction for the synthesis of [2_4]cyclophanetetraenes and some related compounds is also presented together with some mechanistic considerations.

Cyclophanes, which is the common name for ring compounds built from aromatic rings bridged by shorter or longer chains,[1] have been extensively studied during the last twenty years. Several reviews have appeared,[2–4] mostly dealing with small cyclophanes. A number of methods for their synthesis have been reported, but there are few general methods for the preparation of larger cyclophanes. The treatment of bis(halomethyl)benzenes with sodium gives mixtures of cyclophanes of different ring sizes.[5–7] A few attempts to use the Wittig reaction for the synthesis of larger cyclophanes have also been reported.[8–12]

We have recently developed a convenient method for the preparation of [2_4]cyclophanetetraenes and some related compounds by Wittig reactions at low temperatures.[13–14] In this paper we report the synthesis of some new ortho-, meta- and para[2_4]cyclophanetetraenes and [2_4]cyclophanes by this method.

RESULTS AND DISCUSSION

[2_4]*Metacyclophanes.* Benzene-1,3-dicarbaldehyde and the bisphosphonium salt from 1,3-bis(chloromethyl)benzene react fast at −40 °C on addition of base in dimethylformamide (DMF). A mixture of all-*cis*, *1*, and *cis,cis,cis,-trans*, *2*, [2_4]metacyclophanetetraene in a 40/60 ratio was isolated from the reaction mixture. The mixture was quantitatively hydrogenated to [2_4]metacyclophane, *3*.[7] The mixture of isomers of [2_4]metacyclophanetetraene was difficult to separate. However, a small sample of pure all-*cis* isomer, *1*, was obtained by preparative TLC.



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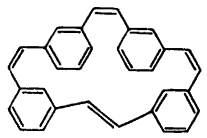

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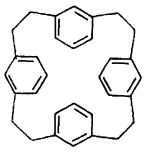

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The structure of the all-*cis* isomer of [2_4]metacyclophanetetraene, *1*, follows from the simple NMR spectrum. The olefinic protons give a sharp singlet, and the aromatic protons give an A_2BX pattern which is simplified on irradiation at ν_X. On standing in solution in daylight or better on irradiation in a photoreactor, the all-*cis* isomer rearranges to the *cis,cis,cis,trans*

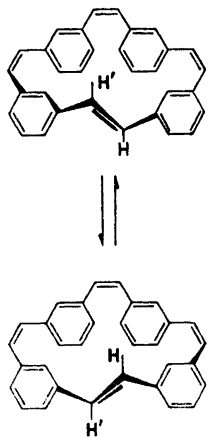


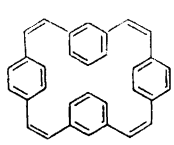
Fig. 1. Equilibration of the olefinic *trans* protons in *cis,cis,cis,trans*-[2$_4$]metacyclophanetetraene.

isomer. The structure of the latter follows from the chemical transformations and spectral data. The NMR spectrum was obtained by subtraction of the spectrum of the all-*cis* isomer from the spectrum of the mixture. The assignment of the aromatic region was simplified by decoupling experiments. The olefinic protons appear as two sharp singlets and a pair of doublets (J 12.5 Hz) in the spectrum. The simple olefinic region was rationalized to be due to a fast equilibrium of the olefinic *trans* protons by rotation around the adjacent single bonds. Such a process should create an apparent plane of symmetry perpendicular to the *trans* and opposite *cis* double bonds and simplify the NMR spectrum as observed (Fig 1). However, a preferred conformation in which the *trans* bond is perpendicular to the adjacent benzene rings (C_2 symmetry), should also give the observed spectrum.

[2$_4$]*Metaparametaparacyclophanetetraenes.* Benzene-1,3-dicarbaldehyde and the bisphosphonium salt from 1,4-bis(bromomethyl)-benzene react under the standard conditions to give all-*cis* [2$_4$]metaparametaparacyclophanetetraene, *4*. The product was quantitatively hydrogenated to [2$_4$]metaparametaparacyclophane, *5*. The compounds were identified by their simple mass and NMR spectra. The NMR spectrum of *4* showed a pair of doublets (J 12 Hz) for the olefinic protons, a sharp singlet for the protons in the parasubstituted rings, and a broad triplet, a broad singlet, and a doublet of doublets for the protons in the metasubstituted rings. Cyclophane *5* showed a marked upfield shift for the isolated protons in the metasubstituted rings, δ 5.88. The equivalent protons in [2$_2$]metacyclophane appear at δ 4.25 due to the shielding by the aromatic rings.[7] The same assumption should lead to a favoured conformation of [2$_4$]metaparametaparacyclophane, *5*, in which the isolated protons in the metasubstituted rings are sandwiched between the parasubstituted rings. In such a conformation all hydrogens in the bridges are staggered.

The reaction of benzene-1,4-dicarbaldehyde and the bisphosphonium salt from 1,3-bis(chloromethyl)benzene gives all-*cis*-[2$_4$]metaparametaparacyclophanetetraene, *4*, as above but also a small amount of an isomer, possibly *cis,cis,cis,trans*-[2$_4$]metaparametaparacyclophanetetraene. The latter shows a rather complex NMR spectrum as expected for an asymmetric [2$_4$]cyclophanetetraene. Although the aromatic region of the spectrum was too complex to be easily interpreted, an analysis of the olefinic region showed two AB-systems (J 12.5 and 16 Hz), a singlet, and one half of an AB-system (J 12.5 Hz). The other half could be hidden behind the singlet and a line from another doublet.

[2$_4$]*Orthoparaorthoparacyclophanes.* The Wittig reaction between benzene-1,2-dicarbaldehyde and the bisphosphonium salt from 1,4-bis(bromomethyl)benzene gave two isomers of [2$_4$]orthoparaorthoparacyclophanetetraene and one isomer of [2$_6$](orthopara)$_3$cyclophanehexa-



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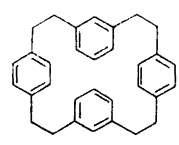

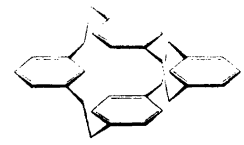

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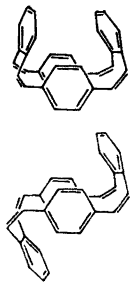

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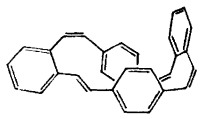

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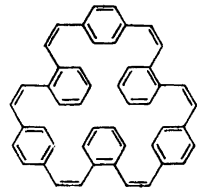

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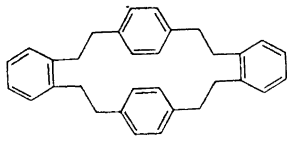

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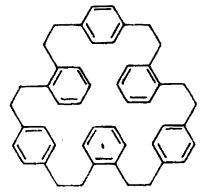

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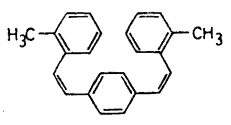
ene. On separation by column chromatography, the reaction mixture gave first the *cis,cis,cis,-trans* isomer *7*, containing a small amount of the all-*cis* isomer *6*, followed by the all-*cis* isomer of the [2$_6$]cyclophanehexanene, *8*. The isomers *6* and *7* of [2$_4$]orthoparaorthoparacyclophanetetraene were separated by gradient sublimation.

The structures of the orthoparacyclophanes follow from their mass and NMR spectra. The NMR spectrum of all-*cis*-[2$_4$]orthoparaorthoparacyclophanetetraene, *6*, is fairly simple. The olefinic protons appear as a pair of doublets (J 12.5 Hz) and the aromatic protons as a sharp singlet and two symmetrical multiplets (an AA'BB'-system) for the parasubstituted and the orthosubstituted rings, respectively.

All-*cis*-[2$_4$]orthoparaorthoparacyclophanetetraene, *6*, could exist in two conformations with a barrier of interconversion. The structure of the isolated product has not been assigned, however.

The *cis,cis,cis,trans* isomer *7*, shows a more complex spectrum from which the olefinic region can be interpreted. At maximum sixteen lines from four AB-systems can be expected. Thirteen of these lines are present in the spectrum. Two are broadened, and their areas correspond to two lines each. The missing line can be calculated to coincide exactly with another line. Three of the coupling constants correspond to normal *cis*-couplings in olefins and the fourth to a normal *trans*-coupling. Hydrogenation of the mixture of [2$_4$]orthoparaorthoparacyclophanetetraenes gives the saturated cyclophane *9*. The NMR spectrum of the product shows two singlets for the aromatic protons and two triplets for the aliphatic protons in the bridges, an AA'BB'-system. All-*cis*-[2$_6$](orthopara)$_3$-cyclophanehexaene, *8*, also gives a simple NMR spectrum, similar to that of the smaller all-*cis*-orthoparacyclophane *6*. Hydrogenation gives [2$_6$](orthopara)$_3$cyclophane, *10*.

The reaction between benzene-1,4-dicarbaldehyde and the bisphosphonium salt from 1,2-bis(chloromethyl)benzene gave a small amount of all-*cis*[2$_6$](orthopara)$_3$cyclophanehexaene, *8*, and a mixture of isomers of 1,4-bis(2-methylstyryl)benzenes. The purified *cis,cis* isomer, *11*, of the latter slowly rearranged to the *trans,trans* isomer, *12*, a highly fluorescent compound.



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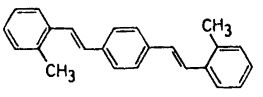

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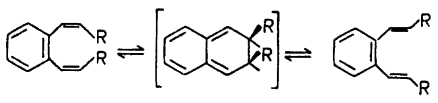
Reduction of one phosphonium group in a bisphosphonium salt in a Wittig reaction has been observed before.[10] It could be caused by impurities of moisture but also by intermolecular side reactions as it is observed only in reactions with the bisphosphonium salt from 1,2-bis(chloromethyl)benzene.

cis-trans Isomerisations around double bonds are usually slow in the absence of light. However, 1,2-divinylbenzenes can undergo *cis-trans* isomerisations at both double bonds simultaneously *via* a dihydronaphthalene intermediate, formed by a disrotatory electrocyclic ring-closure (Scheme 1). The activation energy for this process should be lowered in certain ring compounds such as these orthoparacyclophantetraenes. The process has not yet been observed experimentally, however.



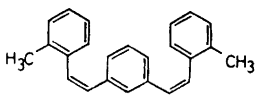
Scheme 1.

Attempted synthesis of [2$_4$]*orthometaorthometacyclophane.* The Wittig reaction between benzene-1,2-dicarbaldehyde and the bisphosphonium salt from 1,4-bis(bromomethyl)benzene gave a complex mixture of products. The usual separation gave no cyclophane which could be identified. Hydrogenation of the first eluted compound(s), which gave a reproducible but complicated NMR spectrum, did not give any simple [2$_4$]cyclophane.

Nor did the Wittig reaction between benzene-1,3-dicarbaldehyde and the bisphosphonium salt from 1,2-bis(chloromethyl)benzene give any cyclophane which could be identified. However, products from reduction of one of the phosphonium groups, 1,3-bis-(2-methylstyryl)benzenes, were observed, in analogy with the corresponding reaction with benzene-1,4-dicarbaldehyde. *cis,cis*-1,3-Bis(2-methylstyryl)-benzene, *13*, and the *cis,trans* isomer, *14*, were obtained according to their NMR spectra. Hydrogenation gave the same product, 1,3-bis-[2-(2-tolyl)ethyl]benzene, *15*.

The use of the Wittig reaction for the synthesis of [2$_4$]*cyclophanetetraenes.* Cyclophanes have been prepared by a number of methods including the Wittig reaction.[2–14] Small cyclophanes with considerable strain energy usually require other methods of preparation, whereas large and less strained cyclophanes have successfully been prepared by double and in a few cases multiple Wittig reactions.[10–14] The main problem with the Wittig reaction is the control of the *cis/trans* ratio. A high ratio is desirable in most cases but difficult to achieve experimentally by a general method. The *cis/trans* ratio of the double bonds in Wittig reactions is reported to depend on a variety of factors including the solvent, the ions present, the stability of the ylid and the reactivity of the aldehyde.[15] Unstabilized ylids or phosphoranes usually give a high *cis/trans* ratio in Wittig reactions. This has been explained as being due to a kinetically controlled formation of the betaine which upon elimination of phosphine oxide gives *cis* double bonds.[15] Our reactions are restricted to aromatic phosphoranes which are relatively stable and thus not expected to give *cis* double bonds selectively. We have found that in multiple Wittig reactions between aromatic aldehydes and phosphoranes a polar solvent like DMF favours the formation of *cis* double bonds and that a low temperature is essential. A slow addition of base also improves the yields of the cyclophanes. Dilution techniques are not necessary.

There is no simple way to determine the *cis/trans* ratio in the Wittig reactions carried out by the method described here. The ratio can also vary considerably between similar



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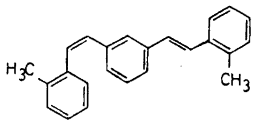

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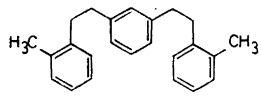

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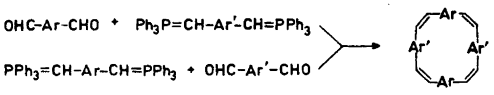
reactions as discussed below. However, some indications of the *cis/trans* ratio can be obtained from the total yield of the fourfold Wittig reaction which at best is 15 %. This corresponds to an average of 62 % yield in each step and thus to a minimum *cis/trans* ratio of 1.64. The actual ratio should be considerably higher. In two cases *cis-trans* isomers of the [2$_4$]cyclophanetetraenes have been isolated from the Wittig reactions. Neglecting other factors than statistical ones, one arrives at a *cis/trans* ratio of 2.67 in the reaction that gives [2$_4$]metacyclophanetetraenes. In the Wittig reaction that gives [2$_4$]orthoparaorthoparacyclophanetetraenes and [2$_6$](orthopara)$_3$-hexaene other factors than statistical ones apparently dominate.

In order to analyse the influence of the stability and reactivity of the dialdehyde and the diphosphorane on the yield of the [2$_4$]cyclophanetetraene in the Wittig reaction, we have carried out some double experiments (Scheme 2). A dialdehyde from one arene, Ar, was reacted with a diphosphorane from another arene, Ar′, and then the dialdehyde from the latter arene, Ar′, was reacted with a diphosphorane of the first arene, Ar. Both reactions should give the same product.



Scheme 2.

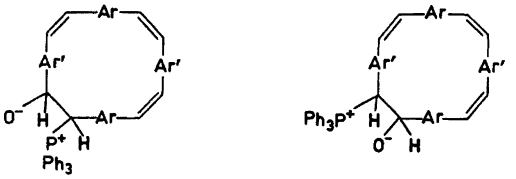


Fig. 2. Two slightly different ring precursors of a [2$_4$]cyclophanetetraene.

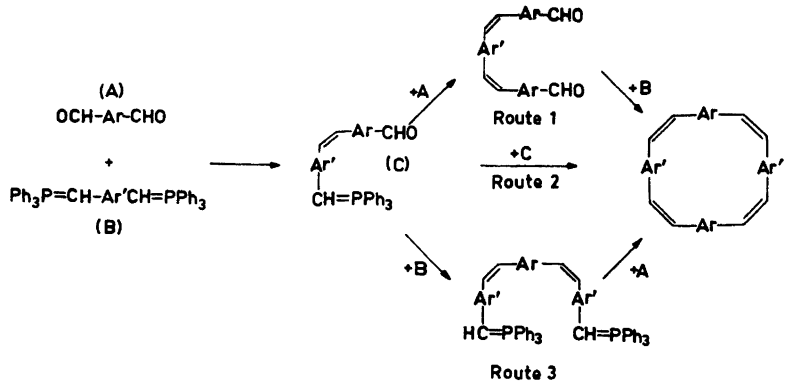
In these reactions strain effects and other stereochemical factors are almost but not quite the same. The experimental results show a variation in product patterns and yields (Table 1). This is probably due to small changes in the *cis/trans* ratio caused by the different stability and reactivity of the aldehydes and the phosphoranes but could also depend on the steric conditions when the last double bond is formed (Fig. 2).

A [2$_4$]cyclophanetetraene can be formed from two equivalents of an aromatic dialdehyde and an aromatic diphosphorane by three different routes (Scheme 3). Of the nine possible Wittig reactions in Scheme 3, the three that lead to the final product are the same. The other six are all slightly different, occurring between aldehydes and phosphoranes of different reactivity and stability. If the two aldehyde groups or the two phosphorane groups are strongly conjugated as, *e.g.*, in the *ortho* or *para* positions in benzene or in the 2,5-positions in thiophene or

Table 1. Yields of [2$_4$]cyclophanetetraenes from Wittig reactions between two equivalents of aromatic dialdehydes and diphosphoranes.

Dialdehyde	Diphosphorane from bisphosphonium salt from	Cyclophane	Yields[a] %
1,4-Benzene	1,3-bis(chloromethyl)benzene	*4*	1.8
		isomer	0.5
1,3-Benzene	1,4-bis(bromomethyl)benzene	*4*	7
1,4-Benzene	1,2-bis(chloromethyl)benzene	*8*	<1
1,2-Benzene	1,4-bis(bromomethyl)benzene	*6*	<1
		7	5
		8	4
1,4-Benzene	2,5-bis(chloromethyl)thiophene	Ref. 14	4
2,5-Thiophene	1,4-bis(bromomethyl)benzene	Ref. 14	8
1,4-Benzene	2,5-dibromo-1,4-bis(bromomethyl)benzene	Ref. 14	10
2,5-Dibromo-1,4-benzene	1,4-bis(bromomethyl)-benzene	Ref. 14	9

[a] By weight after column chromatography.



Scheme 3.

furan, one would expect a considerable change in reaction rate between the first and the second Wittig reaction of these derivatives. The second route in Scheme 3 should then be favoured. In Wittig reactions with strongly conjugated dialdehydes, a significant decrease in the rate of consumption of the intermediate phosphorane or ylid is observed after addition of half the required amount of base.

A comparison with other syntheses of [2_4] *cyclophanes by Wittig reactions.* Although the examples of bis-Wittig reactions or twofold Wittig reactions for the synthesis of cyclophanes or other ring compounds are numerous,[12] fourfold Wittig reactions have only been reported in a few cases.[13] Elix and Sargent have studied the reaction between furan-2,5-dicarbaldehyde and the bisphosphonium salt from 1,2-bis(chloromethyl)-benzene and reported the isolation of four isomers of [2](2,5)furano[2]-ortho[2](2,5)furano[2]orthocyclophanetetraene. The reaction conditions were similar to those reported here, except for the temperature which was kept at 90 °C during the fast reaction.[10] However, the NMR data reported by Elix and Sargent are not consistent with ours. They have found unusually small *cis* couplings in the olefinic bridges (2 – 4 Hz) and variable *trans* couplings (6 – 16 Hz). We have observed, in more than twenty different [2_4]cyclophanetetraenes and [2_6]cyclophanehexaenes, coupling constants of 12 – 13 Hz which we have assigned to normal *cis* couplings and in a few cases coupling constants of 16 Hz assigned to *trans* couplings.[13–14] One of the isomers of the [2_4]furanoorthocyclophanetetraene prepared by Elix and Sargent, showed a simple NMR spectrum with a pair of doublets (*J* 12 Hz) in the olefinic region. This isomer should be the all-*cis* isomer and not the all-*trans* isomer as suggested by the authors.

In an earlier paper Elix reported two isomers of [2_4](2,5)-furanophanetetraene, the all-*trans* and the *trans,trans,trans,cis* isomer, from a fourfold Wittig reaction.[9] Such cyclophanes should be highly strained as is apparent on inspection of models of the compounds. An alternative structure for one of the isomers, the *cis,trans,cis,trans*-[2_4](2,5)-furanophanetetraene, which is considered in the paper, seems more reasonable. In our hands, similar Wittig reactions gave the all-*cis* isomers of [2_4](2,5)-thiophenophanetetraene and [2_4](2,5)furano-thiophenophanetetraene as the only isolated products.[16]

The large number of isomers of cyclophanes of different ring sizes and stability which are the possible products from the type of Wittig reactions described here makes isolation, purification and characterisation difficult in many cases. The elemental analysis does not give information about ring size or *cis-trans* isomerism. Mass spectral data can be misleading since the smaller rings are rather volatile and stable in the spectrometer. However, NMR data combined with MS data should reveal the structure of the cyclophane in most cases although the olefinic and aromatic regions of the NMR spectra may be complex.

Conclusions. The Wittig reaction has many advantages over other methods for the preparation of large cyclophanes. The reaction conditions are mild enough to permit variation of

the arene as well as the substituents. Unsaturated bridges are introduced directly, which may be desirable for further reactions, *e.g.* photochemical ring closures.[17–19] The double bonds can easily be hydrogenated over palladium if desired. The experimental procedure is simple; high dilution techniques, which often are necessary in the synthesis of ring compounds, are not essential. Starting materials are often easily available, and the reaction can be used to produce gram quantities of [2$_4$]cyclophanes in spite of the low over-all yields.

EXPERIMENTAL

Melting points were determined on a Reichert hot stage apparatus. UV spectra were recorded with a Beckman DK-2A, MS with an AEI MS 902, IR spectra with a Beckman IR 9 and NMR spectra with a Bruker WH 270.

Phosphonium salts. The bistriphenylphosphonium salts from 1,4-bis(bromomethyl)benzene, 1,3-bis(chloromethyl)benzene and 1,2-bis(chloromethyl)benzene were all prepared by the standard procedure[20] from commercial bis(halomethyl)benzenes and triphenylphosphine in dry dimethylformamide (DMF). The salts were carefully dried at 110°C in vacuum before use.

Aldehydes. Commercial 1,4-, 1,3- and 1,2-benzene dicarbaldehydes were recrystallised before use.

Wittig reaction, general procedure.[14] The Wittig reactions were run in a three-necked flask equipped with a mechanical stirrer and a dropping funnel. The aldehyde and the phosphonium salt (10 mmol of each) were dissolved or suspended in dry DMF (250 ml). The flask was flushed with nitrogen, and a slow stream of nitrogen was maintained during the reaction which was run in a cooling bath at −35 or −40 °C. A freshly prepared solution of lithium ethoxide in ethanol was added dropwise to the reaction mixture at such a rate as to allow the coloured ylid to be consumed between successive additions. The reaction time varied from a few hours to a few days. When no colour change was observed on addition of base, the reaction mixture was warmed to room temperature and diluted with water (*ca.* 250 ml). The mixture was extracted with diethyl ether three times, and the ether extract was washed with water several times, dried over sodium sulfate and the solvent distilled. The residue was chromatographed on silica gel with tetrachloromethane as eluent. The cyclophanes were usually recrystallised from mixtures of tetrachloromethane and methanol.

Hydrogenation. The [2$_4$]cyclophanetetraenes were quantitatively hydrogenated at atmospheric pressure in benzene solution after 24 h with palladium on charcoal as a catalyst.

Photoisomerisation. The cyclophanes, dissolved in $CDCl_3$ in NMR tubes, were irradiated with light of maximum intensity around 300 nm in a Rayonet reactor. The photoisomerisations were followed by NMR spectroscopy.

[2$_4$]*Metacyclophanes.* Benzene-1,3-dicarbaldehyde and the bisphosphonium salt from 1,3-bis(chloromethyl)benzene gave, after 2 h reaction and isolation, a mixture of isomers, 40 % all-*cis* and 60 % *cis,cis,cis,trans*, of [2$_4$]metacyclophanetetraene, *1* and *2*. NMR ($CDCl_3$): δ 7.86 (4 H, s), 7.13 (4 H, t), 7.07 (8 H, dd), J_{ortho} 8 Hz, J_{meta} 1.5 Hz, 6.32 (8 H, s). δ 7.48–7.02 (12 H, aromatic protons), 6.65, 6.59 and 6.53 (6 H, two pair of d, J 12.5 Hz). 6,40 (2 H, s, *trans* protons). IR (KBr): 1597 (m), 1578 (m), 1480 (m), 1430 (m), 965 (s), 920 (s), 905 (s), 820 (s), 810 (s), 783 (s) and 695 (s) cm^{-1}. UV (C_6H_{12}): 283 nm, ε = 43 000.

The mixture was hydrogenated to give [2$_4$]metacyclophane, *3* (180 mg, 9 %, m.p. 130–132 °C, lit. 132–133 °C [7]). NMR ($CDCl_3$): δ 7.05 (4 H, t), 6.81 (8 H, dd), 6.53 (4 H, s), J_{ortho} 7.5 Hz, J_{meta} 1.7 Hz, 2.78 (16 H, s).

[2$_4$]*Metaparametaparacyclophanes.* Benzene-1,3-dicarbaldehyde and the bisphosphonium salt from 1,4-bis(bromomethyl)benzene gave, after 2 h reaction and isolation, all-*cis*-[2$_4$]-metaparametaparacyclophanetetraene, *4* (143 mg, 7 %, m.p. 225 °C). NMR ($CDCl_3$): δ 7.18 (4 H, t), 7.14 (4 H, s), 6.98 (8 H, dd), J_{ortho} 8 Hz, 6.91 (8 H, s, para substituted ring), 6.63 and 6.46 (8 H, pair of d, J 12 Hz). IR (KBr): 1575 (m), 1508 (m), 1417 (m), 922 (s), 868 (s), 847 (s), 788 (s), 700 (s) cm^{-1}. UV ($_6CH_{12}$): 237 nm, ε = 44 000 and 292 nm, ε = 35 500. MS (70 eV): *m/e* 408 (M^+, 100 %), 204 (12) and 203 (14). Abs. mass: Found 408.188; calc. for $C_{32}H_{24}$ 408.188.

Hydrogenation gave [2$_4$]metaparametaparacyclophane, *5* (m.p. 198–201 °C). NMR ($CDCl_3$): δ 7.13 (4 H, t), 6.93 (8 H, dd), 5.88 (4 H, s), J_{ortho} = 7.5 Hz, J_{meta} = 1.5 Hz, 6.81 (8 H, s, para substituted ring), 2.73 (16 H, s). IR (KBr): 3025 (m), 2930 (s), 2850 (m), 1608 (m), 1515 (m), 1487 (m), 810 (m), 795 (s), 707 (s) and 540 (s) cm^{-1}. MS (70 eV): *m/e* 416 (M^+, 69 %), 311 (43), 208 (92), 206 (27), 194 (49), 119 (41), 117 (41), 105 (100), 104 (83), 103 (36) and 91 (46).

Benzene-1,4-dicarbaldehyde and the bisphosphonium salt from 1,3-bis(chloromethyl)benzene gave, in a slower reaction, all-*cis*-[2$_4$]-metaparametaparacyclophanetetraene, *4* (36 mg, 1.8 %). A later fraction from the column chromatography contained an isomer, probably *cis,cis,cis,trans*-[2$_4$]metaparametaparacyclophanetetraene, (10 mg, 0.5 %). Both isomers yielded [2$_4$]metaparametaparacyclophane, *5*, on hydrogenation.

[2$_4$]*Orthoparaorthoparacyclophanes.* Benzene-1,2-dicarbaldehyde and the bisphosphonium salt from 1,4-bis(bromomethyl)benzene gave

after a slow Wittig reaction, a mixture of *cis,cis,cis,trans*-[2$_4$]orthoparaorthoparacyclophanetetraene, *7* and minor amounts of all-*cis*-[2$_4$]orthoparaorthoparacyclophanetetraene, *6*. The isomers were separated by gradient sublimation (150 °C, 10^{-3} mmHg). Later fractions from the column chromatography yielded all-*cis*-[2$_6$](orthopara)$_3$cyclophanehexaene, *8*. The orthoparacyclophanes were identified by their mass and NMR spectra (see also Table 1).

All-*cis*-[2$_4$]orthoparaorthoparacyclophanetetraene, *6* (< 1 %, m.p. 180 – 190 °C). NMR ($CDCl_3$): δ 7.41 – 7.33 and 7.28 – 7.20 (8 H, ortho substituted ring), 6.74 (8 H, s), 6.38 and 6.19 (8 H, pair of d, J = 12.5 Hz). IR (KBr): 3015 (m), 1607 (m), 1512 (m), 1480 (m), 1420 (s), 1190 (m), 958 (s), 885 (s), 840 (s), 770 sh and 760 (s) cm^{-1}. MS (70 eV): *m/e* 408 (M$^+$, 100 %), 318 (12), 317 (44), 315 (15), 305 (17), 304 (60), 303 (10), 302 (15), 289 (10), 217 (28), 215 (18), 205 (17), 204 (79), 203 (27), 202 (33), 191 (12), 189 (17), 165 (11), 115 (11), 91 (29) and 49 (34). Abs. mass: Found 408.188; calc. for $C_{32}H_{24}$ 408.188.

cis,cis,cis,trans-[2$_4$]Orthoparaorthoparacyclophanediene, *7* (102 mg, 5 %, m.p. 215 – 217 °C). NMR ($CDCl_3$): δ 7.57 – 6.82 (16 H, aromatic protons), 6.68 – 5.65 (6 H, olefinic *cis* protons), 6.52 and 6.33 (2 H pair of d, olefinic *trans* protons, J = 16.5 Hz). IR (KBr): 3020 (m), 1510 (m), 1480 (m), 1447 (m), 1428 (m), 980 (s), 850 (s) and 770 (s) cm^{-1}. UV (C_6H_{12}): 232 nm, ε = 38 000, 250 nm (sh) and 313 nm, ε = 70 300. MS (70 eV): *m/e* 408 (M$^+$, 100 %), 317 (35), 315 (14), 305 (13), 304 (49), 217 (21), 215 (14), 205 (17), 204 (59), 203 (23), 202 (22) and 91 (15). Abs. mass: Found 408.187; calc. for $C_{32}H_{24}$ 408.188.

All-*cis*-[2$_6$](orthopara)$_3$cyclophanehexaene, *8* (77 mg, 3.8 %, m.p. 257 – 260 °C). NMR ($CDCl_3$): δ 7.05 (12 H, s), 7.20 and 6.97 (12 H, ortho substituted ring), 6.62 and 6.51 (12 H, pair of d, J 12.5 Hz), m.p. 257 – 260 °C. IR (KBr): 3015 (m), 1607 (m), 1510 (m), 1480 (m), 1420 (s), 958 (m), 885 (s), 840 (m) and 760 (s) cm^{-1}. UV (C_6H_{12}): 229 nm, ε = 47 000 and 312 nm, ε = 39 500. MS: *m/e* 612 (M$^+$, 81 %), 610 (23), 497 (37), 317 (50), 315 (27), 305 (28), 304 (26), 303 (24), 302 (24), 293 (27), 291 (23), 289 (23), 219 (23), 218 (21), 217 (86), 216 (21), 215 (45), 205 (78), 204 (78), 203 (74), 202 (53), 191 (60), 165 (22), 115 (34), 105 (21), 91 (100). Abs. mass: Found 612.280; calc. for $C_{48}H_{36}$ 612.282.

The *cis,cis,cis,trans*-isomer *7* was hydrogenated to give [2$_4$]orthoparaorthoparacyclophane, *9* (m.p. 248 – 252 °C). NMR ($CDCl_3$): δ 7.17 (8 H, ortho substituted ring), 6.83 (8 H, s), 2.66 and 2.19 (16 H pair of t, J 7.2 Hz). IR (KBr): 3020 (m), 2940 (s), 2865 (m), 1517 (s), 1493 (m), 1466 (s), 800 (s) and 750 (s) cm^{-1}. MS: *m/e* 416 (M$^+$, 23 %), 311 (30), 221 (12), 219 (17), 209 (56), 208 (40), 207 (100), 206 (11), 205 (20), 193 (37), 192 (19), 191 (14), 179 (19), 178 (24), 129 (15), 119 (68), 118 (40), 117 (70), 115 (26), 105 (80), 104 (60), 103 (14), 91 (53). Abs. mass: Found 416.249; calc. for $C_{32}H_{32}$ 416.250.

The cyclophane *8* was hydrogenated to give [2$_6$](orthopara)$_3$cyclophane, *10* (m.p. 248 – 250 °C). NMR ($CDCl_3$): δ 7.30 (12 H, s, para substituted ring), 7.33 – 7.10 (12 H, ortho substituted ring), 2.94 (24 H, m). IR (KBr): 3020 (m), 2950 (s), 2930 sh, 2870 (m), 1515 (s), 1490 (m), 1465 (s), 820 (m), 800 (s) and 750 (s) cm^{-1}. MS: *m/e* 624 (M$^+$, 18 %), 311 (31), 310 (13), 223 (18), 221 (42), 219 (28), 209 (47), 208 (24), 207 (74), 206 (17), 205 (39), 193 (34), 192 (18), 191 (18), 179 (25), 178 (25), 165 (13), 131 (17), 129 (19), 119 (99), 118 (19), 117 (57), 115 (30), 105 (100), 104 (35), 91 (54), 79 (11), 78 (16), 77 (19).

Benzene-1,4-dicarbaldehyde and the bisphosphonium salt from 1,2-bis(chloromethyl)benzene gave after the standard reaction, isolation and separation a small amount of all-*cis*-[2$_6$](orthopara)$_3$cyclophanehexaene, *8* (< 1 %). A mixture of 1,4-bis(2-methylstyryl)benzenes were also formed in the Wittig reaction. *cis,cis*-1,4-Bis(2-methylstyryl)benzene, *11* [NMR ($CDCl_3$): δ 7.13 (6 H, m, orthosubstituted ring), 7.01 (2 H, m, orthosubstituted ring), 6.90 (4 H, s, parasubstituted ring), 6.59 and 6.51 (4 H, pair of d, olefinic protons, J = 12.5 Hz) and 2.22 (6 H, s, methyl groups)] slowly rearranged to the *trans,trans*-isomer *12* [NMR ($CDCl_3$): δ 7.66 (2 H, d, J 6.5 Hz, orthosubstituted ring), 7.51 (4 H, s, parasubstituted ring), 7.35 and 7.00 (4 H, pair of d, J 16 Hz, olefinic protons), 7.19 (6 H, m, orthosubstituted ring) and 2.44 (6 H, s, methyl groups)].

Attempted synthesis of [2$_4$]*orthometaorthometacyclophanes*. Benzene-1,2-dicarbaldehyde and the bisphosphonium salt from 1,3-bis(chloromethyl)benzene were reacted under the standard conditions to give a complex mixture of products. Column chromatography on silica gel gave no identified products. The first fractions containing products from the Wittig reaction gave a reproducible but complex NMR spectrum, indicating the presence of cyclophanes among the products. Hydrogenation of these fractions gave no simple product which excludes the possibility of a single cyclophane as dominant product. The total yield was low and the mixture was not further investigated.

Benzene-1,3-dicarbaldehyde and the bisphosphonium salt from 1,2-bis(chloromethyl)benzene gave no product identified as a cyclophane either. However, products from the reduction of the phosphonium groups were observed. The first eluated product showed the NMR spectrum expected for *cis,cis*-1,3-bis(2-methylstyryl)benzene, *13* [δ 7.16 – 6.85 (12 H, m, aromatic protons), 6.55 and 6.44 (4 H, pair of d, J 12 Hz, olefinic protons) and 2.18 (6 H, s, methyl protons)]. A later fraction showed an NMR spectrum ($CDCl_3$) consistent with a mixture of some *cis,cis*-isomer *13* and mainly the *trans,cis-isomer* *14* [δ 7.52 – 6.95

(m, aromatic protons), 6.99 and 6.85 (pair of d, J 16 Hz, olefinic *trans* protons), 6.69 and 6.62 (pair of d, J 12 Hz, olefinic *cis* protons), 2.33 and 2.28 (s, methyl protons)]. Both isomers gave the same product on hydrogenation, 1,3-bis[2-(2-tolyl)ethyl]benzene, *15* [NMR: δ 7.20 (1 H, t), 7.03 (2 H, d of d) and 6.94 (1 H, broad s) protons in the metasubstituted ring, 7.11 (8 H, broad s, protons in the orthosubstituted rings), 2.84 (8 H, m, methylene protons) and 2.28 (6 H, s, methyl protons)].

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