Biscyclophanes. Part 1: Synthesis of a Common-nuclear Bis[1.1.1]orthocyclophane, First Member of a New Family of Cyclophanes

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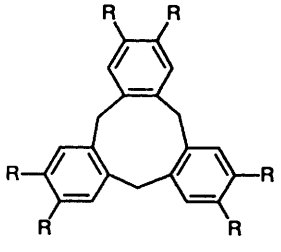
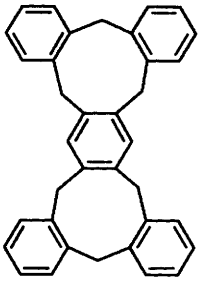
Synthesis of new orthocyclophane hosts has been investigated by the acid-catalysed intramolecular Friedel–Crafts cycloalkylation of terminal benzylbenzylic alcohols that bear repeating benzyl chains. Treatment of 2-(2-benzylbenzyl)benzyl alcohol **6** with concentrated sulfuric acid in acetic acid medium gave rise to a cyclisation product, [1.1.1]orthocyclophane **2**. Similar cyclisation behaviour was observed under the same reaction conditions by the use of diterminal benzylbenzylic diols, which provided a common-nuclear bisorthocyclophane. Treatment of a solution of either the α,ω-benzylic diols 1,3-bis-{2-[2-(hydroxymethyl)benzyl]benzyl}benzene **16** in acetic acid or the 1,4-isomer **20** in acetic acid–dimethyl sulfoxide with concentrated sulfuric acid provided heptacyclo-[19.15.0.0^{3,19}.0^{5,10}.0^{12,17}.0^{23,28}.0^{30,35}]hexatriaconta-1(21),2,5(10),6,8,12(17),13,15,19,23(28),24,26,-30(35),31,33-pentadecaene **3** which is the first member of a family of novel biscyclophanes.

There has been tremendous interest in the synthesis[1] and inclusion behaviour[2] of cyclophanes. In spite of extensive studies on cyclophanes, only a few of the [1$_n$]orthocyclophanes, such as [1$_3$]- and [1$_4$]-orthocyclophanes have, until recently, been reported.[3] The present paper reports the reaction behaviour of benzylbenzylic alcohols in acid, which provide new orthocyclophanes as cyclisation products. It was known prior to this work that terminal benzylbenzylic alcohols, which contain a repeating benzyl chain, are subject to intramolecular, rather than intermolecular, Friedel–Crafts alkylation, even in the presence of benzene, to give cyclic compounds. Therefore, we carried out a new synthesis of [1.1.1]orthocyclophane **2**, which involves the treatment of a solution of the benzylbenzylic alcohol **6** in acetic acid with conc. sulfuric acid, to give an intramolecular Friedel–Crafts alkylation product. Herein, we also describe the preparation of a new family of cyclophanes which are composed of two cyclophane rings connected by a common benzene ring. In this paper, such a cyclophane is referred to as a 'common-nuclear biscyclophane'. A common-nuclear bis[1.1.1]orthocyclophane **3** of rigid crown conformation was obtained by treatment of α,ω-benzylbenzylic diols, **16** or **20**, with sulfuric acid, to give an intramolecular bis-cyclisation product.



1 R = OMe
2 R = H



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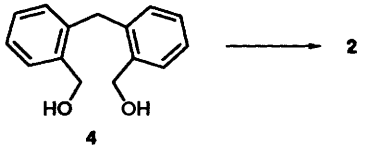
Results and Discussion

Cyclisation behaviour of benzylbenzylic alcohols containing a repeating benzyl chain has been investigated: Acid-catalysed Friedel–Crafts reaction of terminal benzylbenzylic alcohols of smaller size gave a cyclophane, and that of α,ω-benzylbenzylic diols of larger size gave a common-nuclear biscyclophane as intramolecular cycloalkylation product. Whereas cyclotriveratrylene (CTV)[3a] **1** was prepared by the acid-catalysed condensation of veratrole and formaldehyde, the parent hydrocarbon [1.1.1]orthocyclophane **2** was synthesized[3b,c] in 74.5% yield by treatment of 2,2′-bis(hydroxymethyl)diphenylmethane **4** with conc. sulfuric acid in benzene solution [equation (1)].



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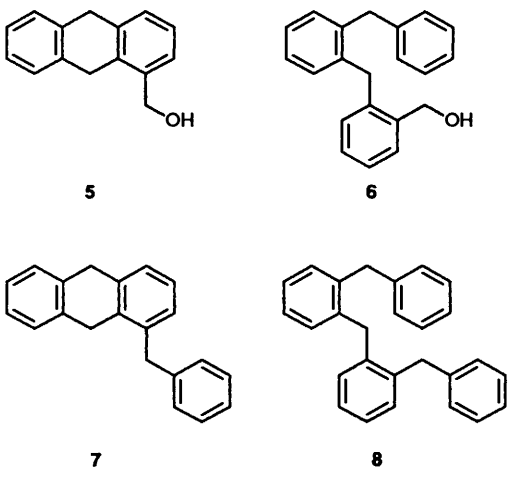
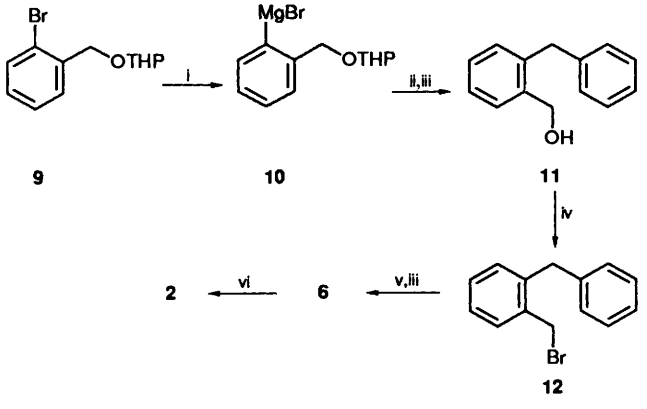
Reagents: C_6H_6, H_2SO_4 (74.5% yield)

The reaction is thought to proceed through the intermediates formed by primary Friedel–Crafts alkylation, followed by the secondary alkylation of the intermediate. The plausible intermediates are species **5** and **6**, which are formed, respectively, by intramolecular Friedel–Crafts alkylation of diol **4** and intermolecular alkylation of diol **4** with benzene. Of the two intermediates, compound **6** is likely to be the principal one, since it is a monosubstituted product with respect to the alkylated benzene ring, whereas the anthracene **5** is a 1,2,3-trisubstituted product that is sterically difficult to produce. Hence, the reaction does not give compound **7**, which is a secondary alkylation product of compound **5**. The benzylic alcohol **6** is probably the only intermediate that will undergo a second alkylation, to give a cyclic product **2** and an acyclic product **8**. Actually, the main product of the reaction was the cyclophane **2**. This is interpreted to mean that the reaction was run preferentially *via* intramolecular condensation, rather than intermolecular condensation with benzene, of the benzylic alcohol **6**, to provide compound **2** as the main product (74.5%). Thus, the conversion of **4** ⟶ **2** in acid is thought to proceed *via* the intermediate **6**, which then gives the nine-membered ring of product **2** as the most stable one of the possible intramolecular cycloalkylation products.

This assumption was verified by the series of experiments shown in Scheme 1. 2-Benzylbenzyl alcohol **11** was prepared in excellent yield (92%) by the reaction of a Grignard reagent **10**, prepared from 2-bromobenzyl tetrahydropyran-2-yl (THP) ether **9**, with benzyl bromide in the presence of copper(I) iodide, followed by removal of the THP group in the resultant condensation product. The benzylic alcohol **11** was then

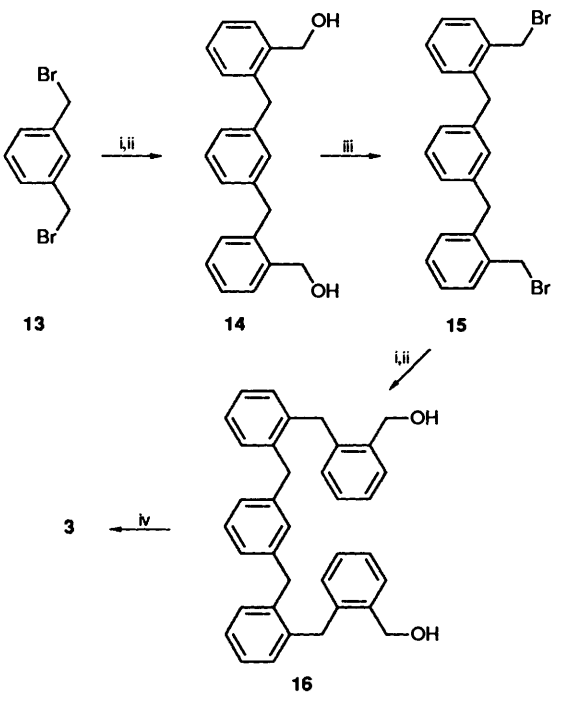


converted, by treatment in dichloromethane with HBr gas, into the corresponding bromide **12** in reasonable yield (90%). The benzylbenzylic alcohol **6** was obtained in good yield (89%) by reaction of bromide **12** with the Grignard reagent **10**, followed by removal of the THP group in the resultant coupling product. Treatment of a solution of compound **6** in acetic acid with conc. sulfuric acid gave tetracycle **2** as crystals in 92% yield.



Scheme 1 *Reagents and conditions:* i, Mg, THF, reflux; ii, $PhCH_2Br$, CuI, THF; iii, TsOH, MeOH, reflux; iv, HBr gas, CH_2Cl_2; v, Grignard **10**, CuI, THF; vi, conc. H_2SO_4, AcOH

The intramolecular Friedel–Crafts cyclisation behaviour of the benzylbenzylic alcohol **6** led us to synthesize a common-nuclear biscyclophane from α,ω-benzylbenzylic diols that have two alcoholic moieties, one on each side of the repeating benzyl chain. A novel biscyclophane **3** has been synthesized *via* acid-catalysed Friedel–Crafts reaction of a benzylbenzylic diol **16** that was prepared by a synthetic procedure as shown in Scheme 2. 1,3-Bis-[2-(hydroxymethyl)benzyl]benzene **14** was prepared by the reaction of 1,3-bis(bromomethyl)benzene **13** and the Grignard **10** in the presence of copper(I) iodide, followed by removal of the THP group in the resultant Grignard coupling product, to give a crystalline solid in 72% overall yield. The diol **14** was converted into the corresponding dibromide **15** by treatment with HBr gas in dichloromethane, to give a crystalline product in 82% yield. The dibromide **15** was in turn treated in THF with the Grignard **10** in the presence of copper(I) iodide, followed by removal of the THP group in the resultant coupling product, to give the solid α,ω-benzylbenzylic diol **16** in 62% yield. The diol **16** could not be dissolved in hot, stirred AcOH. However, agitation in a sonicator did give a clear solution. Treatment of a solution of diol **16** in acetic acid with conc. sulfuric acid furnished a novel, common-nuclear bisorthocyclophane **3** as a crystalline solid, m.p. > 300 °C, in 32% yield.

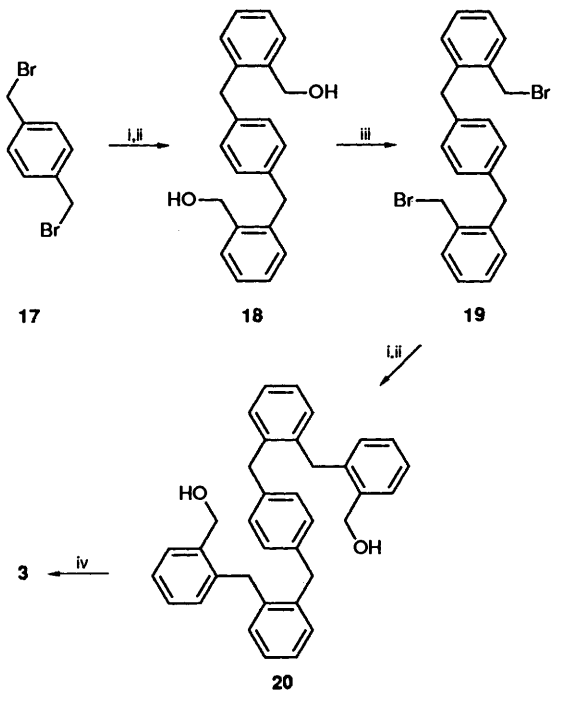


Scheme 2 *Reagents and conditions:* i, Grignard **10**, CuI, THF; ii, TsOH, MeOH, reflux; iii, HBr gas, CH_2Cl_2; iv, H_2SO_4, AcOH

The biscyclophane **3** could also be prepared by the acid-catalysed Friedel–Crafts reaction of the benzylbenzylic diol **20** that was prepared starting from 1,4-bis(bromomethyl)benzene **17** as shown in Scheme 3. A benzylic diol **18** was prepared in 84% yield by the reaction of Grignard **10** with the benzylic dibromide **17**, followed by removal of the THP group in the resulting coupling product. The diol **18** was converted by treatment with HBr gas into the corresponding dibromide **19** in 61% yield. The reaction of dibromide **19** with the Grignard **10** in the presence of copper(I) iodide, followed by removal of the THP group in the resultant coupling product, furnished the α,ω-benzylbenzylic diol **20** in 76% yield. The diol **20**, different from the *meta* isomer **16**, did not dissolve in acetic acid even when heated and agitated in a sonicator, but it dissolved easily in dimethyl sulfoxide (DMSO). Treatment of a solution of diol **20** in AcOH–DMSO (3:1 v/v) with conc. sulfuric acid resulted in the intramolecular Friedel–Crafts bisalkylation which provided the biscyclophane **3** in 36% yield.

The structure of the biscyclophane **3** was verified by spectral data. The ^1H NMR spectrum shows two AB quartets[3b] for methylene protons, at δ 4.83 (2 H, axial) and δ 3.66 (2 H, equatorial), and at δ 4.79 (4 H, axial) and δ 3.69 (4 H, equatorial), which reveal the existence of two kinds of methylenes, *i.e.* 4 inner methylenes and 2 outer methylenes. These proton resonances also show the rigid, nine-membered ring conformation of compound **3**, since the AB quartets appear at just the equivalent frequencies as those of the nine-membered ring of [1.1.1]orthocyclophane **2** that has an AB quartet[3b,c] at δ 4.90 (3 H, axial) and 3.74 (3 H, equatorial). The ^{13}C NMR spectrum discloses the expected 8 signals for aromatic carbons and two for benzylic carbons. The high-resolution mass spectrum gives *m/z* 462.2324 (M^+) for $C_{36}H_{30}$ (calc. M, 462.2348).

The biscyclophane **3** is insoluble in ordinary solvents such as diethyl ether, hexane, benzene and alcohols, but is slightly soluble in dichloromethane and chloroform. During the purification, compound **3** appeared to show strong binding properties toward dichloromethane and diethyl ether. Purification of crude product **3** by chromatography on silica gel with



Scheme 3 *Reagents and conditions:* i, Grignard **10**, CuI, THF; ii, TsOH, MeOH, reflux; iii, HBr gas, CH_2Cl_2; iv, H_2SO_4, AcOH–DMSO

dichloromethane as eluent gave a pale yellow solid. The yellow impurity could be removed completely not by chromatography, but washing of the crystals several times with diethyl ether gave a colourless, crystalline product. The proton NMR spectrum showed strong proton signals for dichloromethane and diethyl ether even after the crystals had been well dried in air and degassed *in vacuo*. The solvent molecule was lost only by heating of the crystals for several hours under reduced pressure, thereby regenerating pure compound **3**. After repeated recrystallisation, however, the solvent could easily be removed by simple air-drying, confirming that the affinity between compound **3** and solvent observed above was but a simple adsorption of solvent molecules.

In conclusion, we have known in this investigation that the acid-catalysed intramolecular Friedel–Crafts reaction of α,ω-benzylbenzylic diols of the types **16** and **20** was prone to (1,2)(4,5)-biscyclisation to form a biscyclophane with two 9-membered rings. Thus, treatment of either diol **16** or **20** with conc. sulfuric acid afforded (1,2)(4,5)-bis[1.1.1]orthocyclophane **3**. However, the corresponding (1,2)(3,4)-biscyclisation product was not formed probably because of the structural disadvantage (steric hindrance) involved in forming a 1,2,3,4-tetrasubstituted compound. It was also noticed that [1.1.1]orthocyclophane **2** and bis[1.1.1]orthocyclophane **3** do not show complexation properties toward solvent molecules, which is different from the situation with cyclotriveratrylene (CTV) **1** that shows binding forces toward solvent molecules, such as dichloromethane and chloroform, because of the presence of methoxy functions.

Experimental

All anhydrous reactions were conducted with the usual precautions for rigorous exclusion of air and moisture. THF was purified by being refluxed for 4–5 h with sodium benzophenone ketyl under nitrogen, followed by distillation prior to use. Flash chromatography was carried out on silica gel 60 (E. M. Merck, particle size 0.040–0.063 mm, 230–400 mesh ASTM). ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AC-80 and/or a Varian VXR-200s NMR spectrometer to an internal standard of tetramethylsilane. All chemical shifts (δ) are reported in parts per million, and J-values are in Hz. IR spectra were obtained on a Perkin-Elmer Model 782 spectrometer. Microanalyses were performed on a YANACO MT-2 CHN CORDER or Carloerba EA 1108. Mass spectra were recorded on a VG-7025 normal geometry or Shimadzu-LKB 9000 GC/MS system. All m.p.s were uncorrected. When necessary, chemicals were purified according to the reported procedure.[4] Light petroleum refers to the fraction boiling in the range 35–60 °C.

2-Bromobenzyl Tetrahydropyranyl Ether **9**.—This compound was prepared by the usual protecting method.[5] To a mixture of 2-bromobenzyl alcohol (10.0 g, 53.5 mmol) and a catalytic amount of toluene-*p*-sulfonic acid (*p*-TsOH, 1.0 g) in dichloromethane (100 cm^3) was added dropwise a solution of 3,4-dihydro-2*H*-pyran (5.10 g, 60.6 mmol) in dichloromethane (50 cm^3) and the mixture was stirred at room temperature for 12 h. Work-up and chromatography (silica gel; dichloromethane) gave the title compound **9** (14.0 g, 97%) as an oil; ν_{max}/cm^{-1} 3070, 2950, 1595, 1570, 1035, 1025 and 750; δ_H(80 MHz; $CDCl_3$) 7.58–7.00 (4 H, m, ArH), 4.93–4.47 (3 H, m, OCHO in THP ring and $ArCH_2O$), 4.07–3.42 (2 H, m, OCH_2 in THP ring) and 1.68–1.52 (6 H, m, 3 × CH_2 in THP ring).

2-Benzylbenzyl Alcohol **11**.—Grignard reagent **10** was prepared by slow, dropwise addition of a solution of the THP ether **9** (10.0 g, 36.9 mmol) in THF (50 cm^3) to magnesium turnings (2.0 g, 82 mmol) immersed in stirred THF (20 cm^3), followed by reflux of the mixture for 3 h under nitrogen. To a stirred, cooled (0 °C) solution of benzyl bromide (4.50 g, 26.3 mmol) and a catalytic amount of copper(I) iodide (0.5 g) in THF (20 cm^3) was added dropwise under nitrogen the Grignard reagent **10** prepared above. The mixture was allowed to warm to room temperature and was stirred for 15 h. To this reaction mixture was added aq. ammonium chloride, the solvent was removed under reduced pressure, the aqueous layer was extracted with dichloromethane, and the extract was washed with water and dried over anhydrous magnesium sulfate. After evaporation of the solvent, the crude product was chromatographed once on silica gel with dichloromethane as eluent to give a condensation product (~7.0 g, 94%), a THP ether, which was deprotected without further purification.

A solution of this crude product and *p*-TsOH (0.5 g) in methanol (60 cm^3) was refluxed for 6 h, then cooled, aq. sodium hydrogen carbonate (10 cm^3) was added, and the solvent was evaporated off. The aqueous layer was extracted with dichloromethane, and the extract was dried (anhyd. $MgSO_4$), and evaporated under reduced pressure. The crude product was purified by chromatography (silica gel; dichloromethane) and recrystallised from light petroleum to give the title compound **11** (4.79 g, 92%), m.p. 40–41 °C (lit.,[6] b.p. 114 °C/0.1 mmHg); ν_{max}/cm^{-1} 3600–3200 (OH), 1600, 1450, 1000, 750, 732 and 700; δ_H(80 MHz; $CDCl_3$) 7.45–7.01 (9 H, m, ArH), 4.41 (2 H, d, J 6, $ArCH_2O$), 4.07 (2 H, s, $ArCH_2Ar$) and 1.55 (1 H, t, J 6, OH). The spectral data of compound **11** thus prepared agreed well in all respects with those in the literature,[6] although no m.p. had been previously reported. In the previous paper,[6] compound **11** was prepared *via* a different route from the present procedure and was reported as an oil, with a boiling point. However, we obtained it crystalline after repeated purification.

2-Benzylbenzyl Bromide **12**.—Into a solution of the benzylic alcohol **11** (3.21 g, 16.2 mmol) in dichloromethane (70 cm^3) was passed dry hydrogen bromide (HBr) gas at room temperature until the solution was saturated, whereupon the cloudy solution

turned to orange. After repeated saturation the flask was stoppered, and the mixture was stirred for more than 5 h, until TLC (silica gel; dichloromethane) showed only one spot (R_f ~1.0). The solution was washed successively with water, aq. $NaHCO_3$, and water, dried (anhyd. $MgSO_4$), and evaporated. The crude product was chromatographed (silica gel; dichloromethane) and recrystallised from hexane to give the benzylic bromide **12** (3.81 g, 90%) as needles, m.p. 42.5–43.5 °C (lit.,[6b,c] 43.5–44.2 °C); ν_{max}/cm^{-1} 3050, 3020, 1600, 1450, 1430, 1060 and 760; δ_H(80 MHz; $CDCl_3$) 7.31–7.19 (9 H, m, ArH), 4.45 (2 H, s, $ArCH_2Br$) and 4.15 (2 H, s, $ArCH_2Ar$). The spectral data of compound **12** thus prepared were consistent with those in the literature.[6b,c]

2-(2-*Benzylbenzyl*)*benzyl Alcohol* **6**.—To a cooled (0 °C) solution of the bromide **12** (2.30 g, 8.81 mmol) in THF (20 cm^3) containing CuI (0.3 g) was added by cannulation under nitrogen the Grignard reagent **10** prepared from the THP ether **9** (3.20 g, 11.8 mmol) in THF, and the mixture was stirred overnight at room temperature. The reaction mixture was then quenched with aq. NH_4Cl and the solvent was removed by evaporation under reduced pressure. The aqueous layer was extracted with dichloromethane, washed successively with aq. $NaHCO_3$ and water, dried (anhyd. $MgSO_4$), and evaporated under reduced pressure. The crude product was chromatographed (silica gel; dichloromethane) to give the viscous, oily coupling product (3.1 g, 95%), a THP ether, which was deprotected without further purification.

Deprotection was carried out by refluxing of a solution of the crude product in methanol containing *p*-TsOH (0.5 g) for 5 h, followed by work-up and chromatographic separation as described in the preparation of compound **11**, to give the *title compound* **6** (2.27 g, 89%) as a crystalline solid, m.p. 91–92 °C (Found: C, 86.9; H, 7.1. $C_{21}H_{20}O$ requires C, 87.46; H, 6.99%); ν_{max}(KBr)/cm^{-1} 3600–3200 (OH), 1600, 1450, 1000, 755 and 745; δ_H(80 MHz; $CDCl_3$) 7.45–6.85 (13 H, m, ArH), 4.46 (2 H, d, *J* 6, $ArCH_2O$), 3.99 (4 H, s, $ArCH_2Ar$) and 1.32 (1 H, t, *J* 6, OH); *m/z* 270 ($M^+ - H_2O$), 255, 192, 179, 165, 152, 119 and 91.

Tetracyclo[15.4.0.0^{3,8}.0^{10,15}]*henicosa*-1(17),3(8),4,6,10(15),-11,13,18,20-*nonaene* **2**.—In a 200 cm^3 round-bottomed flask equipped with a dropping funnel was placed a mixture of acetic acid (20 cm^3) and conc. sulfuric acid (20 cm^3). To this stirred mixture was added very slowly a solution of the benzylic alcohol **6** (0.60 g, 2.1 mmol) in AcOH (30 cm^3) over a period of 8–10 h at room temperature. After additional stirring of the mixture for 6 h, it was poured carefully into ice–water (100 cm^3) and extracted with dichloromethane, and the extract was washed successively with aq. $NaHCO_3$ and water, dried (anhyd. $MgSO_4$), and evaporated under reduced pressure. The crude product was chromatographed (silica gel; dichloromethane) to give the title compound **2** (0.52 g, 92%), m.p. 277–278 °C (lit.,[3b,c] 274–276 °C) as a crystalline solid (Found: C, 93.1; H, 6.5. Calc. for $C_{21}H_{18}$: C, 93.29; H, 6.71%); ν_{max}/cm^{-1} 3044, 2910, 1490, 1472, 1440, 745 and 712; δ_H(80 MHz; $CDCl_3$) 7.43–7.01 (12 H, m, ArH), 4.91 (3 H, d, *J*, 13, ArCH*H*Ar, quasi-axial) and 3.74 (3 H, d, *J* 13 Hz, ArC*H*HAr, quasi-equatorial); δ_C(50.29 MHz; $CDCl_3$) 139.47, 130.05, 126.94 (Ar) and 37.16 ($ArCH_2Ar$); *m/z* 270 (M^+), 255, 192, 179 and 91.

1,3-*Bis*-[2-(*hydroxymethyl*)*benzyl*]*benzene* **14**.—1,3-Bis(bromomethyl)benzene **13** (10.0 g, 37.9 mmol) was dissolved in THF (50 cm^3), followed by the addition of CuI (0.5 g), and the solution was cooled to 0 °C. To this solution was added dropwise under nitrogen the Grignard reagent **10** prepared by the usual procedure from the THP ether **9** (27.5 g, 101 mmol) in THF, and the temperature of the mixture was gradually raised to ambient. After the mixture had been stirred overnight, aq. NH_4Cl (10 cm^3) was added and the solvent was evaporated under reduced pressure, the residue was extracted with dichloromethane, and the extract was washed with water. The extract was dried over anhyd. $MgSO_4$, and the solvent was removed under reduced pressure to give the oily condensation product, a di-THP ether. This crude product was deprotected directly without purification, by the usual method using *p*-TsOH and methanol. The crude deprotection product was purified by chromatography (silica gel; dichloromethane) to provide the crystalline *title compound* **14** (8.70 g, 72%), m.p. 99–100 °C (Found: C, 82.95; H, 7.0. $C_{22}H_{22}O_2$ requires C, 82.99; H, 6.96%); ν_{max}/cm^{-1} 3600–3200 (OH), 1600, 1440, 1010, 770 and 742; δ_H(80 MHz; $CDCl_3$) 7.33–6.91 (12 H, m, ArH), 4.57 (4 H, d, *J* 5, $ArCH_2O$), 4.01 (4 H, s, $ArCH_2Ar$) and 1.57 (2 H, t, *J* 5, OH); *m/z* 300 ($M^+ - H_2O$), 282 ($M^+ - 2H_2O$), 267 and 178.

1,3-*Bis*-[2-(*bromomethyl*)*benzyl*]*benzene* **15**.—To a solution of the benzylic diol **14** (4.00 g, 12.6 mmol) in dichloromethane (150 cm^3) was passed dry HBr gas by bubbling it through the solution at room temperature, until the cloudy solution turned to orange. After the equivalent experimental procedure as in the conversion of alcohol **11** into bromide **12**, the crude product was purified by chromatography on silica gel [mixed solvent of dichloromethane–hexane (1:2 v/v) as eluent] to furnish the crystalline *title compound* **15** (4.60 g, 82%), m.p. 74–75 °C (Found: C, 59.4; H, 4.5. $C_{22}H_{20}Br_2$ requires C, 59.49; H, 4.54%); ν_{max}/cm^{-1} 3020, 2910, 1600, 1450, 770 and 758; δ_H(80 MHz; $CDCl_3$) 7.32–6.91 (12 H, m, ArH), 4.41 (4 H, s, $ArCH_2Br$) and 4.09 (4 H, s, $ArCH_2Ar$); *m/z* 446:444:442 (M^+; 1:2:1), 283, 179 and 105.

1,3-*Bis*-{2-[2-(*hydroxymethyl*)*benzyl*]*benzyl*}*benzene* **16**.—To a solution of the dibromide **15** (4.00 g, 9.00 mmol) and CuI (0.4 g) in THF (50 cm^3), cooled to 0 °C, was added slowly by cannulation under nitrogen the Grignard reagent **10** prepared from bromide **9** (6.00 g, 22.1 mmol) in the routine manner. After being stirred overnight at room temperature, the reaction mixture was quenched with aq. NH_4Cl (50 cm^3), and the solvent was removed by evaporation under reduced pressure. The aqueous layer was extracted with dichloromethane, and the extract was washed successively with aq. $NaHCO_3$ and water, and evaporated under reduced pressure to give the oily coupling product, a di-THP ether. This crude product was deprotected directly, without further purification, by being refluxed for 6 h in methanol containing a catalytic amount of *p*-TsOH. After the mixture had cooled to room temperature, aq. $NaHCO_3$ (20 cm^3) was added and the solvent was evaporated off under reduced pressure. The crude, pale yellow product was filtered off and washed successively with distilled water and diethyl ether to remove water-soluble and ether-soluble impurities, to give the powdery *title compound* **16** (2.80 g, 62%), m.p. 115–116 °C (Found: C, 86.5; H, 6.8. $C_{36}H_{34}O_2$ requires C, 86.71; H, 6.87%); ν_{max}/cm^{-1} 3600–3100 (OH), 3060, 2980, 1600, 1460, 1025 and 740; δ_H(80 MHz; $CDCl_3$ + [$^2H_6$]DMSO) 7.47–6.75 (20 H, m, ArH), 4.46 (4 H, d, *J* 5, $ArCH_2O$), 4.03 (2 H, t, *J* 5, OH), 3.93 (4 H, s, $ArCH_2ArCH_2O$) and 3.90 (4 H, s, $ArCH_2Ar$); *m/z* 480 ($M^+ - H_2O$), 462 ($M^+ - 2H_2O$), 267, 192 and 179.

Heptacyclo[19.15.0.0^{3,19}.0^{5,10}.0^{12,17}.0^{23,28}.0^{30,35}]*hexatriaconta*-1(21),2,5(10),6,8,12(17),13,15,19,23(28),24,26,30(35),31,-33-*pentadecaene* **3**.—In a 200 cm^3 round-bottomed flask equipped with a dropping funnel was placed a mixture of AcOH (20 cm^3) and conc. H_2SO_4 (20 cm^3). To this stirred mixture was slowly added dropwise a solution of the benzylic diol **16** (0.30 g, 0.60 mmol) in AcOH (30 cm^3) over a period of 30 h at room temperature. After being stirred for a further 12 h, the mixture was carefully poured into ice–water (100 cm^3) and extracted with dichloromethane, and the extract was washed successively

with aq. $NaHCO_3$ and water, dried (anhyd. $MgSO_4$), and evaporated under reduced pressure. The crude, orange solid product was chromatographed on silica gel with dichloromethane as eluent, to give a pale yellow solid. The yellow impurity could be removed only by washing the solid several times with diethyl ether, to give a white, crystalline solid. This solid appeared to be an inclusion complex between **3** and solvent, since the solvent could not be removed by simple air-drying or even by degassing under reduced pressure, but *was* removed by heating of the crystals *in vacuo*, However, when the solid was purified by repeated recrystallisation from dichloromethane–hexane, followed by washing with diethyl ether, the solvent was removed with ease, to afford *biscyclophane* **3** (0.090 g, 32%), m.p. >300 °C, as a crystalline solid (Found: C, 93.3; H, 6.3%; M^+, 462.2324. $C_{36}H_{30}$ requires C, 93.46; H, 6.54%; M, 462.2348); ν_{max}/cm^{-1} 3050, 2970, 1600, 1500, 1495, 1470, 1445, 738 and 720; δ_H(200 MHz; $CDCl_3$) 7.37–6.81 (18 H, m, ArH), 4.83 (2 H, d, *J* 14, axial ArCH*H*Ar), 4.79 (4 H, d, *J* 14, axial ArCH*H*Ar), 3.69 (4 H, d, *J* 14, equatorial ArC*H*HAr) and 3.66 (2 H, d, *J* 14, equatorial ArC*H*HAr); δ_C(50.29 MHz; $CDCl_3$) 139.382, 139.224, 137.901, 131.556, 129.942, 129.833, 126.812, 126.788 (Ar) and 36.969 and 36.920 (ArCH_2Ar); *m/z* 462 (M^+), 371, 282, 267, 191 and 179.

1,4-*Bis*-[2-(*hydroxymethyl*)*benzyl*]*benzene* **18**.—A slight excess of the Grignard reagent **10** was treated under nitrogen with the dibromide **17** (5.28 g, 20.0 mmol) in the presence of CuI (0.5 g) for 12 h. After aqueous work-up, the crude product was refluxed with *p*-TsOH (0.5 g) in methanol for 4 h to remove the THP protection group in the resulting coupling product. The reaction mixture was neutralised with aq. $NaHCO_3$, solvent was evaporated off under reduced pressure, and the solid product was filtered off. The crude, pale yellow product was washed successively several times with distilled water and diethyl ether to remove water-soluble and ether-soluble impurities, to give the *title compound* **18** (5.36 g, 84%) as a powdery solid, m.p. 145–146 °C (Found: C, 82.4; H, 7.0. $C_{22}H_{22}O_2$ requires C, 82.99; H, 6.96%); ν_{max}/cm^{-1} 3600–3200 (OH), 3010, 2900, 1600, 1435, 1000, 770, 745 and 720; δ_H(80 MHz; $CDCl_3$) 7.49–7.12 (12 H, m, ArH), 4.71 (4 H, d, *J* 6, ArCH_2O), 4.13 (4 H, s, ArCH_2Ar) and 1.50 (2 H, t, *J* 6, OH); *m/z* 300 ($M^+ - H_2O$), 282 ($M^+ - 2H_2O$), 267, 179 and 91.

1,4-*Bis*-[2-(*bromomethyl*)*benzyl*]*benzene* **19**.—This compound was prepared by conversion of the alcohol **18** into the corresponding bromide, by the same procedure as that for the conversion of alcohol **11** into bromide **12**. The benzylic diol **18** (2.00 g, 6.28 mmol) was treated with HBr gas in dichloromethane for more than 5 h. Work-up, chromatography (silica gel; dichloromethane), and recrystallisation from dichloromethane gave the *title compound* **19** (1.70 g, 61%) as needles, m.p. 157 °C (Found: C, 59.3; H, 4.4. $C_{22}H_{20}Br_2$ requires C, 59.49; H, 4.54%); ν_{max}/cm^{-1} 3020, 2930, 1600, 1505, 1450, 770, 755, 705 and 615; δ_H(80 MHz; $CDCl_3$) 7.29–7.06 (12 H, m, ArH), 4.44 (4 H, s, ArCH_2Br) and 4.12 (4 H, s, ArCH_2Ar); δ_C(20.15 MHz; $CDCl_3$) 139.722, 137.961, 135.886, 130.981, 130.713, 129.065, 128.911, 127.021 (Ar) and 37.967 and 31.674 (ArCH_2Ar); *m/z* 446:444:442 (M^+; 1:2:1), 366:364 (M^+ – HBr; 1:1), 283, 179 and 105.

1,4-*Bis*-{2-[2-(*hydroxymethyl*)*benzyl*]*benzyl*}*benzene* **20**.—This compound was prepared by the same synthetic procedure as that for the conversion of bromide **15** into alcohol **16**. Grignard reagent **10**, prepared from bromide **9** (3.00 g, 11.1 mmol) in THF, was treated for 10 h under nitrogen, in the presence of CuI (0.5 g), with a solution of the dibromide **19** (2.00 g, 4.50 mmol) in THF (150 cm^3). After aqueous work-up, the biscondensation product, a di-THP ether, was deprotected without purification by being refluxed with *p*-TsOH (1 g) in methanol for 5 h. The reaction mixture was treated with aq. $NaHCO_3$, the solvent was removed, and the solid product was filtered off. The crude product was washed successively several times with water and diethyl ether, to give the *title compound* **20** (1.76 g, 76%) as a powdery solid, m.p. 168.5–169.5 °C (Found: C, 86.3; H, 6.9. $C_{36}H_{34}O_2$ requires C, 86.71; H, 6.87%); ν_{max}/cm^{-1} 3240 (OH), 3050, 2890, 1590, 1480, 1450, 1040, 1005 and 745; δ_H(80 MHz; $CDCl_3$) 7.24–6.68 (20 H, m, ArH), 4.30 (4 H, d, *J* 6, ArCH_2O), 3.77 (4 H, s, ArCH_2Ar), 3.73 (4 H, s, ArCH_2Ar) and 2.49 (2 H, br s, OH); *m/z* 480 ($M^+ - H_2O$), 462 ($M^+ - 2H_2O$), 267, 192 and 179.

Synthesis of Heptacycle **3** *from Diol* **20**.—The bisorthocyclophane **3** could also be prepared from the benzylic diol **20** by similar treatment as from the diol **16**. The benzylic diol **20** did not dissolve in AcOH, but *was* soluble in DMSO. Thus, compound **20** (0.30 g, 0.60 mmol) was dissolved in DMSO (10 cm^3) and the solution was added to AcOH (30 cm^3). After prolonged addition (30 h) of the solution of diol **20** in AcOH–DMSO to a mixture of AcOH (20 cm^3) and conc. H_2SO_4 (20 cm^3), the reaction mixture was stirred overnight. After work-up, the crude solid product was chromatographed on silica gel with dichloromethane as eluent; the product was washed several times with diethyl ether, and recrystallisation from dichloromethane–hexane gave the biscyclisation product (0.10 g, 36%), which had identical spectral data with those of compound **3** obtained from diol **16** (*vide supra*).

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