Biscyclophanes. Part 2:[1] Regioselectivity in the Acid-catalysed Cycloalkylation of Benzylbenzylic Alcohol (BBA)

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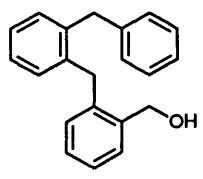
o-Benzylbenzylic alcohols (*o*-BBAs), in which the terminal benzyl alcohol is substituted by repeating benzyl chains all in the *ortho* sense, have been found to have conspicuous regioselectivity in acid-catalysed cycloalkylation, giving rise to various cyclophanes as intramolecular Friedel–Crafts alkylation products. The structure of the cyclisation products was largely dependent upon the size of the benzylic alcohols. Acidic treatment of 2-nuclear *o*-BBA **6** gave a [1.1]orthocyclophane **7** with a 6-membered ring, whereas 3-nuclear *o*-BBA **1** afforded [1.1.1]orthocyclophane **2** with a 9-membered ring in preference to a 6-membered-ring product. Higher homologues, such as 4- and 5-nuclear *o*-BBAs, gave rise to $[1._4](1,2)(1,2)(1,2)(1,3)$cyclophanes **14** and **25** with a 13-membered ring unit, respectively. Cyclophanes with a larger-than-13-membered ring have never been isolated as cycloalkylation products of *o*-BBA. Generalisations have been made about the priority of formation of cycles in the cycloalkylation of *o*-BBA in acid, to give a cycloalkylation rule, which involves the priority order of 13-membered ring > 9-membered ring > 6-membered ring. The regioselectivity was consistent with the acid-catalysed cycloalkylation of α,ω-benzylbenzylic diols, which yielded common-nuclear biscyclophanes. The sizes and structures of the biscyclophane products are also dependent upon the sizes and structures of the terminal benzylic diols.

Recently[1] we reported a preliminary study on the acid-catalysed Friedel–Crafts reaction of lower homologues of terminal *o*-benzylbenzylic alcohols (*o*-BBAs) consisting of a repeating benzyl chain, which gave intramolecular alkylation products. In this article, the term *o*-BBA refers to a terminal benzyl alcohol in which some benzene rings are bound with benzylic methylenes all in the *ortho* sense. It was shown in the foregoing work[1] that upon treatment with conc. H_2SO_4, 3-nuclear *o*-BBA **1** consisting of three benzene nuclei gave rise to a cyclisation product [1.1.1]orthocyclophane **2** with a rigid 9-membered ring conformation.

This reaction feature must account for the correct structure of a common-nuclear bisorthocyclophane **5** which was obtained by treatment of either the α,ω-benzylbenzylic diol 1,3-bis-{2-(hydroxymethyl)benzyl]benzyl}benzene **3** or the 1,4-isomer **4** with conc. H_2SO_4. In the preceding paper,[1] we used the class name 'common-nuclear biscyclophane' for the new family of cyclophanes, such as compound **5**, which has two cyclophane rings connected by a common benzene ring.

It was of interest to investigate the acid-catalysed cyclisation using various homologues of terminal *o*-BBA. The present paper describes a general regioselectivity in the acid-catalysed Friedel–Crafts reaction of terminal benzylbenzylic alcohols and diterminal benzylbenzylic diols, which brings about intramolecular cyclisation, providing new cyclophanes and common-nuclear biscyclophanes.



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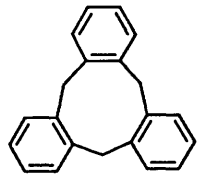

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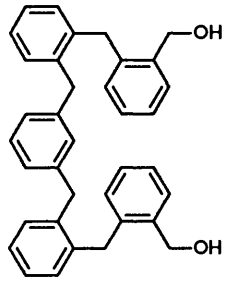

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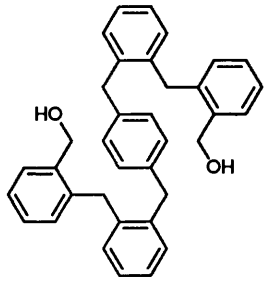

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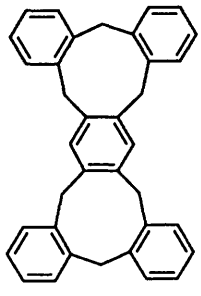

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Results and Discussion

In the preceding work[1] we obtained cycloalkylation products bearing the [1.1.1]orthocyclophane moiety of a 9-membered ring conformation by acidic treatment of benzylbenzylic alcohols, such as **1**, **3** and **4** that contain *o*-BBA unit(s) of three benzene nuclei connected in the *ortho* sense. In the present work, the acid-catalysed cycloalkylation behaviour has been fully investigated by using BBAs of various sizes, which afforded higher members of cyclophane and common-nuclear biscyclophane families.

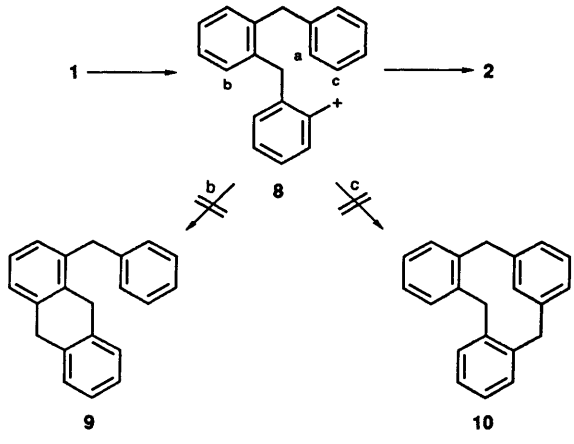
We found that there was obvious regioselectivity in acid-catalysed cycloalkylation of *o*-BBAs, and that the ring size of the cyclisation product was dependent upon the size and structure of the benzylic alcohols used. In the first place, acid-catalysed

cycloalkylation of the lowest member of *o*-BBA was examined. Upon treatment with anhydrous phosphoric acid (H_3PO_4/P_2O_5), *o*-BBA **6** gave rise to a [1.1]orthocyclophane, 9,10-dihydroanthracene **7**. However, the formation of hydrocarbon **7** from the cyclisation of the alcohol **6** in H_2SO_4 was much less effective than in H_3PO_4, and the cyclisation product was contaminated with side-products.

6 **7**

Reagents: H_3PO_4, P_2O_5

Whatever the difference between the effects of H_2SO_4 and H_3PO_4, there is a clear possibility of the formation of [1.1]orthocyclophane in the acid-catalysed cycloalkylation of *o*-BBA. In spite of this, treatment of the *o*-BBA **1** with H_2SO_4 afforded [1.1.1]orthocyclophane **2** with a 9-membered ring as the unique product.[1] However, in the acid-catalysed cycloalkylation of the alcohol **1** there is the possibility of cyclisation so as to generate plausible cycles **2**, **9** and **10**, which might be produced respectively by attacking the envisioned reaction sites, the a-, b- and c-position of the intermediate benzylic cation **8**. However, regioisomers **9** and **10** were not found.



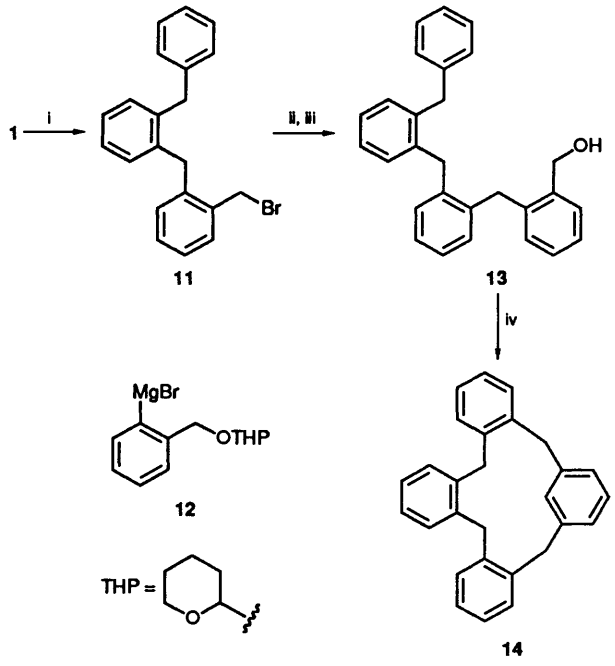
9 **10**

In view of the results obtained in the acid-catalysed cycloalkylation of the *o*-BBAs **1** and **6**, it is clear that there is regioselectivity in the cyclisation of *o*-BBA, which involves the [1.1.1]orthocyclophane ring being formed in preference to the [1.1]orthocyclophane ring; that is, Rule 1 applies.

Rule 1.

Formation Preference;
[1.1.1]Orthocyclophane cycle > [1.1]Orthocyclophane cycle

Further experiments were carried out in order to elucidate the cyclisation behaviour of higher homologues of *o*-BBA, bearing more than three benzene nuclei. For this purpose, an *o*-BBA **13** composed of four benzene nuclei was synthesised (Scheme 1). The terminal benzylic alcohol **1**[1] was treated in dichloromethane (CH_2Cl_2) with dry HBr gas, to give the corresponding benzylic bromide **11**. Subsequent reaction of the bromide **11**, in the presence of CuI, with the Grignard reagent **12** prepared from 2-bromobenzyl THP ether, followed by removal of THP protecting group in the resultant coupling product, afforded 4-nuclear *o*-BBA **13**. Treatment of a solution of the alcohol **13** in AcOH with conc. H_2SO_4 brought about cycloalkylation, providing a new [1.$_n$]cyclophane **14**, with a 13-membered ring, as the main product.



Scheme 1 *Reagents:* i, HBr gas, CH_2Cl_2; ii, Grignard **12**, CuI, THF; iii, TsOH, MeOH; iv, H_2SO_4, AcOH

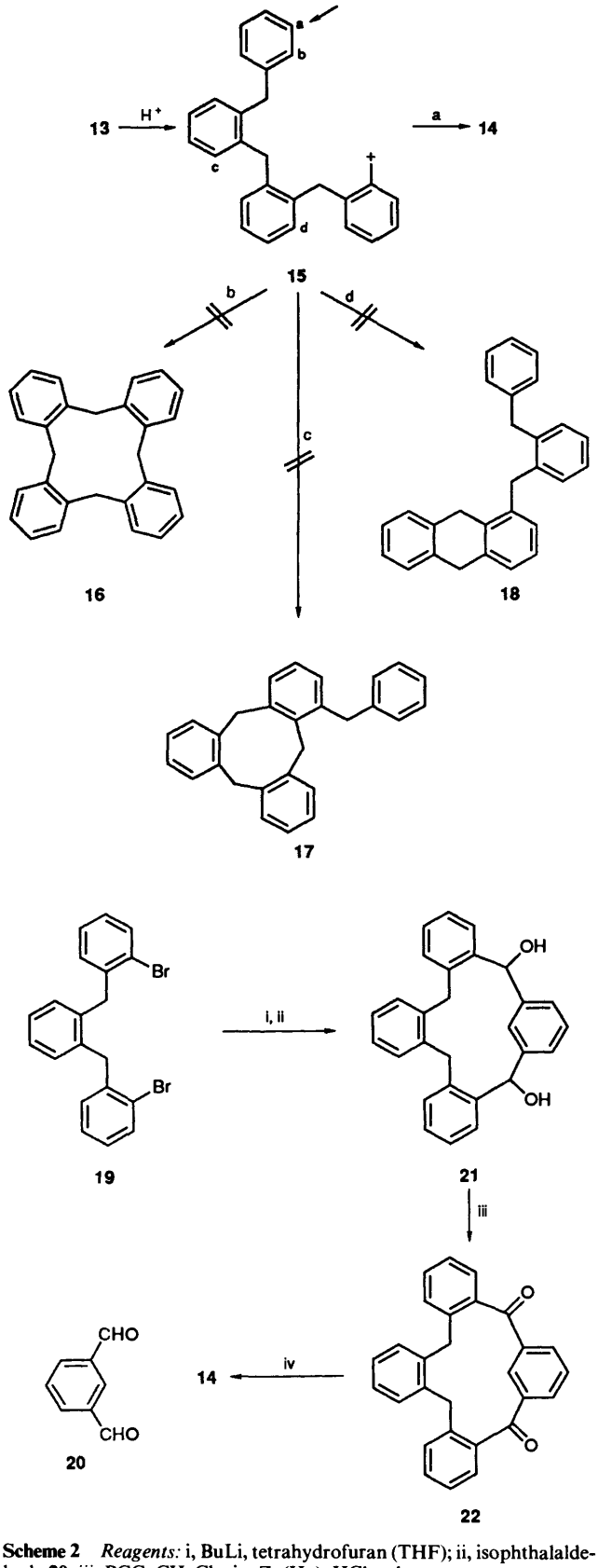
This reaction is surprising, and the result can account for a feature of the acid-catalysed cycloalkylation of *o*-BBA, namely a pronounced selectivity that depends upon the size of the benzylic alcohol. There are, in fact, other possible modes of cyclisation which would give cycles **16**, **17** and **18** by attacking, respectively, the b-, c- and d-position of the intermediate benzylic cation **15**. In contrast to our expectation of obtaining [1.$_4$]orthocyclophane **16**,*[2] the actual product was [1.1.1.1]-(1,2)(1,2)(1,2)(1,3)cyclophane **14**, ruling out the other regioisomers **16**, **17**, and **18**.

The new cyclophane **14** was characterised by means of ^1H NMR, ^{13}C NMR and MS spectra. The aromatic proton resonances of the cyclophane **14** were in four groups, three for the protons outside and the other for the proton inside the ring. In view of Sato's report,[3] a signal upfield at δ 6.19 is a characteristic peak for an inner aromatic proton, whereas multiplets downfield at δ 7.31–6.58 account for outer aromatic protons. The benzylic proton resonance appeared as two singlets at δ 4.02 and 3.64, showing the existence of two kinds of benzylic protons in different environments. The absence of AB quartets for the benzylic proton absorption reveals the flexible conformation of the 13-membered cycle. The ^{13}C NMR spectrum gave two resonances for benzylic carbons and 13 for aromatic carbons. The high-resolution mass spectrum gave exact mass M^+ 360.1890 ($C_{28}H_{24}$ requires M 360.1878).

The structure of cyclophane **14** could also be verified by comparison with an authentic sample synthesised *via* another pathway (Scheme 2). Treatment of an aromatic dibromide **19**[4] with 2 moles of butyllithium (BuLi) to give the corresponding dilithio reagent, followed by reaction with isophthalaldehyde **20**, gave cyclic diol **21**. Oxidation of the diol **21** with pyridinium chlorochromate (PCC) to the corresponding cyclic diketone **22**, followed by Clemmensen reduction, furnished a cyclic product which was identical in all respects (IR, NMR, MS) with the cyclophane **14**.

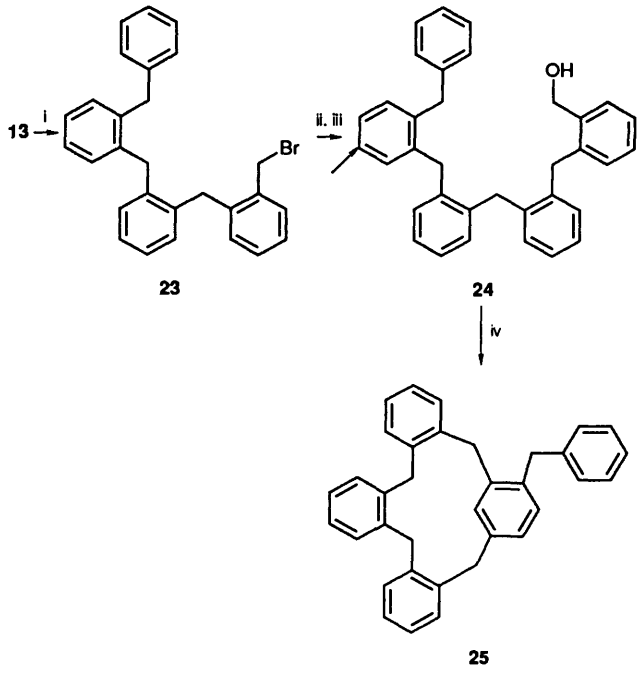
The features of the cycloalkylation have also been probed as to a higher homologue of *o*-BBA composed of five benzene

* [1.$_4$]Orthocyclophane **16** and [1.$_5$]orthocyclophane **27** could be prepared by other synthetic procedures (ref. 2).



Scheme 2 *Reagents:* i, BuLi, tetrahydrofuran (THF); ii, isophthalaldehyde **20**; iii, PCC, CH_2Cl_2; iv, Zn(Hg), HCl, toluene

nuclei. For this purpose, the chain of the *o*-BBA **13** was lengthened to increase the number of benzene rings by one, as illustrated in Scheme 3. Treatment of the alcohol **13** in CH_2Cl_2 with HBr gas gave the corresponding benzylic bromide **23**. Coupling of the bromide **23** in THF with the Grignard **12** in the



Scheme 3 *Reagents:* i, HBr gas, CH_2Cl_2; ii, Grignard **12**, CuI, THF; iii, TsOH, MeOH; iv, H_2SO_4, AcOH

presence of CuI, followed by removal of THP protecting group of the resultant product, afforded the 5-nuclear *o*-BBA **24**. Treatment of a solution of the alcohol **24** in AcOH with conc. H_2SO_4 furnished again a 13-membered cycle **25**, never generating a cycle larger than the 13-membered ring. The structure of product **25** can be verified by NMR and MS spectra: The ^1H NMR spectrum displays a multiplet at δ 7.29–6.61 for the outer aromatic protons resonance and a characteristic singlet at δ 6.15 for the inner aromatic proton, which are consistent with those observed in the 13-membered cycle **14**. The striking evidence was the ^{13}C NMR spectrum, which revealed 28 resonances for aromatic carbons and five for benzylic carbons. The EIMS gave peaks of *m/z* 450 (M^+) and 359 ($M^+ - PhCH_2$), and HRMS gave the exact mass M^+, 450.2383 ($C_{35}H_{30}$ requires M, 450.2348).

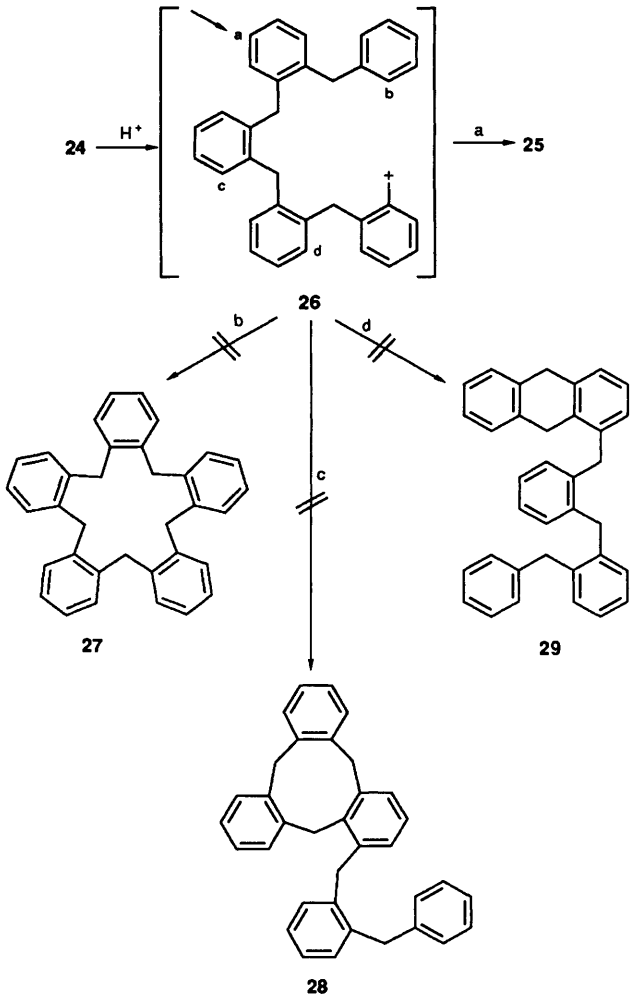
The cyclisation of the *o*-BBA **24** to the cycle **25** must proceed by attack at the a-position of the intermediate benzylic cation **26**. However, there are the other plausible reaction sites b, c and d as well in the cation **26**, from which the other cyclisation products **27**, **28** and **29** may be obtained, respectively. However, compound **25** was the unique product, ruling out the generation of compound **27**[2] that was, in fact, one of the goals of our research. From this result we can deduce that the regioselectivity in the cycloalkylation of *o*-BBAs is largely dependent upon the size of the *o*-BBA.

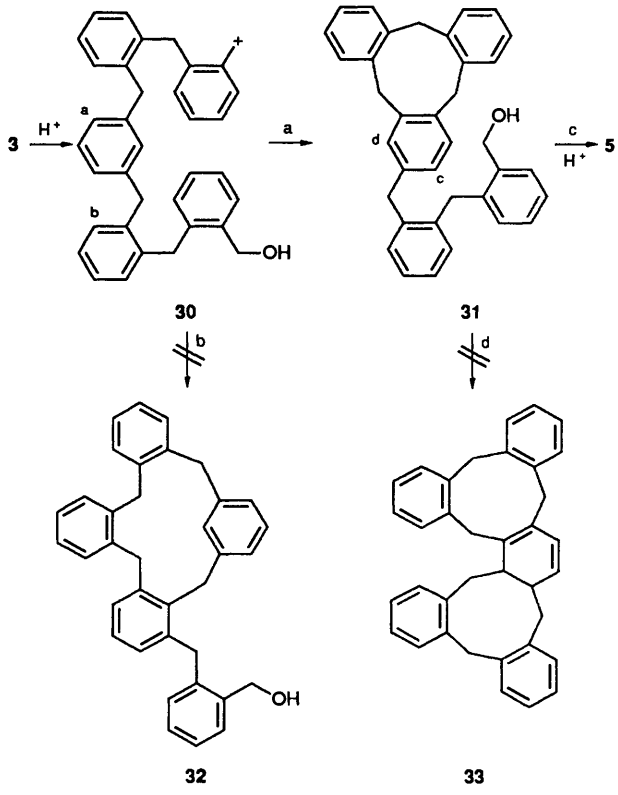
In the light of the cycloalkylation of *o*-BBAs **1**, **6**, **13** and **24**, it was seen that the 13-membered cycle of the [1.4](1,2)(1,2)(1,2)-(1,3)cyclophane unit, such as compound **14**, is formed in preference to the other cycles; the next in ease of formation is the 9-membered cycle of the [1.1.1]orthocyclophane unit, and the generation of the 6-membered ring of the [1.1]orthocyclophane unit is most difficult. The formation of any other, larger cycle was excluded. Herein, the selectivity rule (Rule 2) could be summarised as follows.

Rule 2.

Regioselectivity in Cycloalkylation of o-*BBA*;
13-Membered ring > 9-Membered ring > 6-Membered ring

It was now of interest to investigate the acid-catalysed



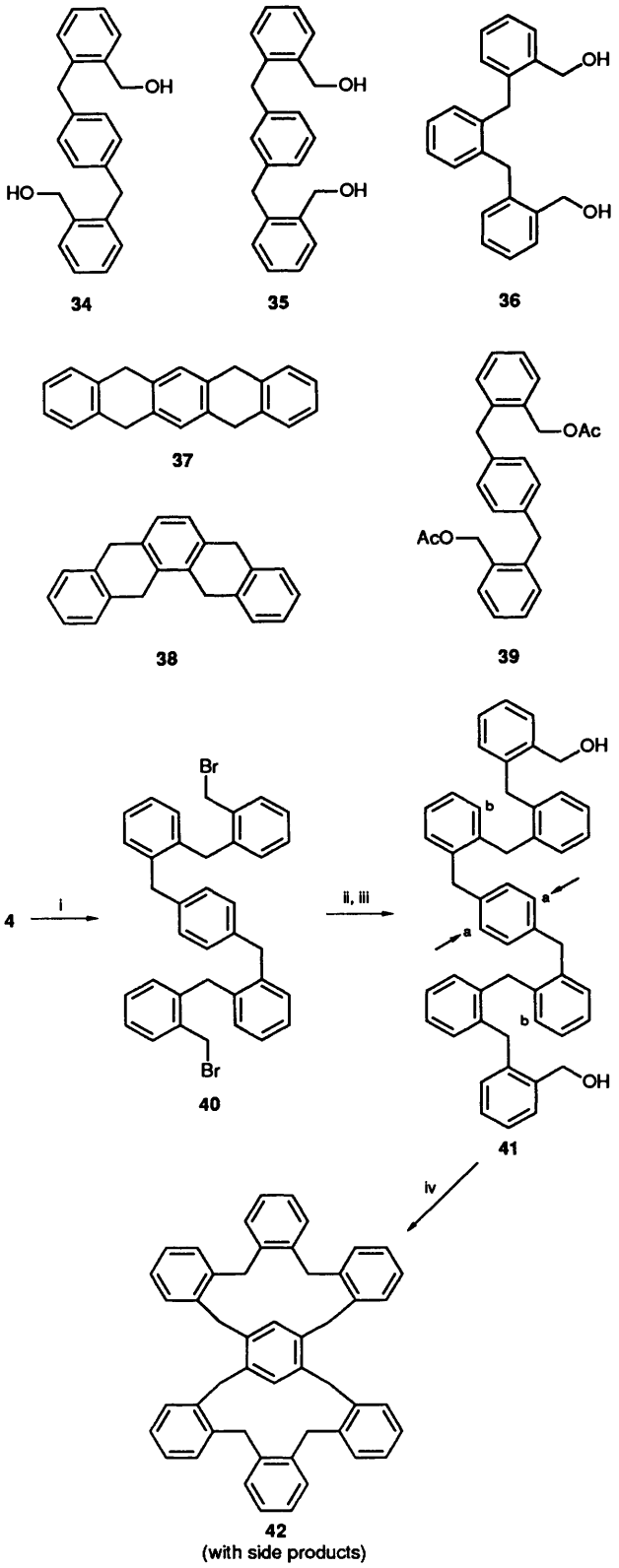


cycloalkylation as to diterminal benzylbenzylic diols. It was known that the cycloalkylation features of *o*-BBA are always consistent with those of α,ω-benzylbenzylic diols that are composed of *o*-BBA moieties, giving rise to common-nuclear biscyclophanes. In our previous work [1] this regioselectivity was partly confirmed by treating the α,ω-benzylbenzylic diols **3** and **4** with conc. H_2SO_4, to give the biscyclophane **5**. Since both of the diols **3** and **4** bear, respectively, two 3-nuclear *o*-BBA units in the molecule, the formation of bisorthocyclophane **5** can now be expected in view of the regioselectivity rule. In the acid-catalysed biscyclisation of alcohol **3**, the first cyclisation must proceed *via* the intermediate benzylic cation **30**, giving rise to monocyclisation intermediates **31** and **32** by attacking, respectively, the a- and b-position of cation **30**. The final product **5** will then be produced by a second cyclisation of the monobenzylic alcohols **31** and **32**. Of these, the formation of the alcohol **31** will be preferred, for the alcohol **32** is structurally unfavourable because of steric hindrance due to the generation of a 1,2,3-trisubstituted benzene nucleus. Thus, the actual biscyclisation product **5** must be obtained *via* the cyclisation of the mono-ol **31** in which the c-position is the preferred reaction site. The formation of the [1.1.1](1,2)(3,4)bisorthocyclophane **33** could also be expected from the cyclisation of the mono-ol **31**, by attack at the d-positon, but this must be very difficult, for the biscyclophane **33** has a 1,2,3,4-tetrasubstituted benzene ring that is structurally unfavourable to produce. By the same token, this could also be why the biscyclophane **33** was not formed by treatment of benzylic diol **4** with conc. H_2SO_4.

Further investigation was carried out by using the other homologues of α,ω-benzylbenzylic diol, lower and higher than compound **3**. In the first place, biscycloaddition of the lower homologues of benzylbenzylic diols 1,4-bis-[2-(hydroxymethyl)-benzyl]benzene **34**,[1] the 1,3-isomer **35**,[1] and the 1,2-isomer **36**[5] was examined for this purpose. In spite of many attempts at cyclisation by treatment with a variant of acids, the benzylic diols **34** and **35** did not yield any biscyclisation product; neither 5,8,13,14-tetrahydropentaphene **38**, which was not expected anyway because of the presence of the sterically hindered 1,2,3,4-tetrasubstituted benzene ring, nor 5,7,12,14-tetrahydropentacene **37** thought to be a plausible product, was formed. When the solid (or a solution in CH_2Cl_2) of diol **34** or **35** was treated with anhydrous phosphoric acid (H_3PO_4/P_2O_5), a polymeric product was formed, which could not be extracted with organic solvents because of its insolubility. On the other hand, when a solution of the diol **34** in AcOH was treated with H_2SO_4, diacetate **39** was the sole product, which was in contrast to the reaction of diols **3** and **4** which gave the biscyclophane **5** under the same reaction conditions. Despite many attempts, treatment of diols **35** and **36** with various acids did not give either the biscyclisation products **37** and **38**, or the corresponding diacetate. The difficulty in formation of the 6-membered cycle, compared with the 9-membered cycle, in the acid-catalysed cyclisation of benzylic alcohols was revealed again by these experiments.

A higher α,ω-benzylbenzylic diol, 1,4-bis-{2-[2-(2-hydroxymethylbenzyl)benzyl]benzyl}benzene **41** [1] was prepared for further investigation (Scheme 4). The benzylic diol **4** was converted into the corresponding dibromide **40** by treatment in CH_2Cl_2 with dry HBr gas. Subsequent reaction of the bromide **40** with the Grignard **12** in the presence of CuI, followed by removal of the THP protecting group in the resultant coupling product, afforded the benzylic diol **41**. Treatment of a solution of the diol **41** in AcOH with conc. H_2SO_4 resulted in a new biscyclophane **42** that is composed of two 13-membered ring units with a common benzene nucleus.

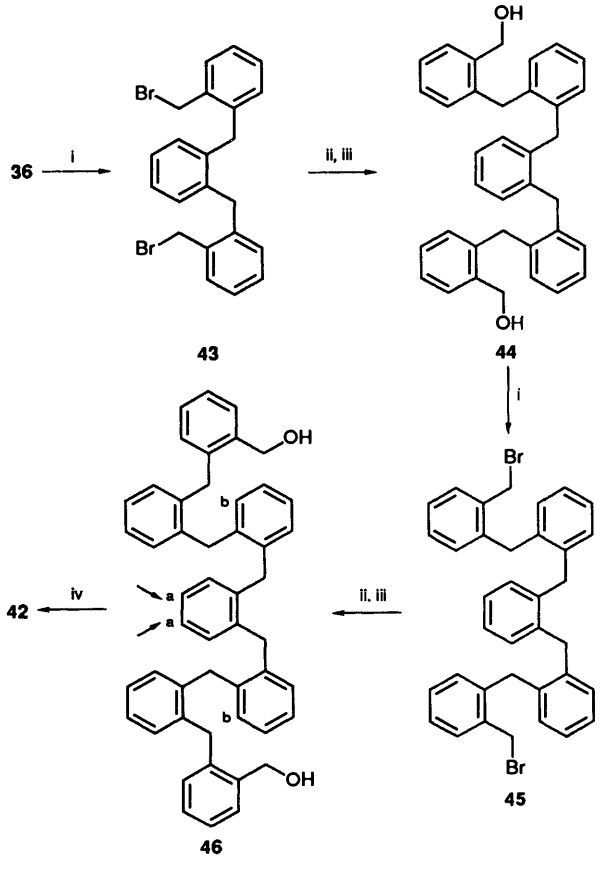
The biscyclophane **42**, as in the case of the monocyclophane **14**, also displayed an aromatic proton resonance divided into four groups. Of these a singlet upfield at δ 6.10 reveals the protons inside and a multiplet (three groups) downfield at δ



Scheme 4 *Reagents:* i, HBr gas, CH_2Cl_2; ii, Grignard **12**, CuI, THF; iii, TsOH, MeOH; iv, H_2SO_4, AcOH

7.27–6.63 the protons outside the ring. The benzylic protons gave rise to two singlets at δ 3.94 and 3.71 but no AB multiplicity, showing the flexibility of the biscyclophane **42**. The hydrocarbon **42** was so insoluble in organic solvents that it could not be purified by recrystallisation, but only by chromatography. The exact mass M^+ 642.3294 recorded by high-resolution mass spectrometry was well in agreement with the calculated one (M 642.3287 for $C_{50}H_{42}$). This was a stimulating result, confirming again the regioselectivity in the cycloalkylation, since the diol **41** possesses two 4-nuclear *o*-BBA moieties, and this set-up is responsible for the generation of a biscyclisation product bearing two 13-membered rings.

For further investigation, 1,2-bis-{2-[2-(2-hydroxymethylbenzyl)benzyl]benzyl}benzene **46**, a regioisomer of the diol **41**, was also prepared (Scheme 5). Treatment of the benzylic



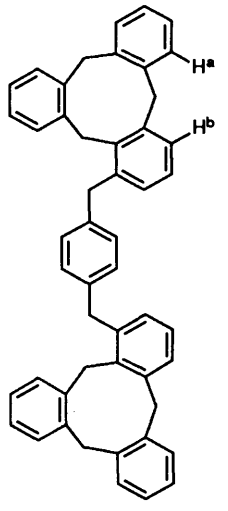
Scheme 5 *Reagents:* i, HBr gas, CH_2Cl_2; ii, Grignard **12**, CuI, THF; iii, TsOH, MeOH; iv, H_2SO_4, AcOH

diol **36** with HBr gas in CH_2Cl_2 gave the corresponding dibromide **43**.[5] Coupling of the dibromide **43** with the Grignard **12** in the presence of CuI, followed by removal of the THP protecting group in the resultant product, provided α,ω-benzylbenzylic diol **44**, which was then converted into the corresponding dibromide **45** by treatment with HBr gas. Subsequent reaction of the dibromide **45** with the Grignard **12** in the presence of CuI, followed by removal of the THP protecting group in the coupling product, furnished the diterminal benzylic diol **46**. Treatment of a solution of the diol **46** in AcOH with conc. H_2SO_4 gave rise to a cyclisation product identical in all respects (NMR, IR, MS) with the biscyclophane **42** as prepared from the diol **41**.

This is an expected result, because the diol **46** also contains two 4-nuclear *o*-BBA units in the molecule where the central benzene ring is a common nucleus, and this system can form a biscyclophane bearing two 13-membered ring units. This reaction feature reveals again the cycloalkylation rule of the *o*-BBAs, which involves the formation of a 13-membered cycle predominantly over 9-membered and 6-membered cycles.

The fact that both of the diols **41** and **46** generated the identical product, cyclophane **42**, as an acid-catalysed cyclisation product must mean that both of the reactions must proceed by attack, respectively, at the a-position in the diols **41**

and **46** to give a 13-membered ring. However, cyclisation of the diol **46** was found to be more effective to give a comparatively clean product (16%), whereas that of the diol **41** gave the product (10%) contaminated by a lot of impurities which were responsible for the lower yield. This can presumably be accounted for by assuming that the conversion of the diol **46** into the biscyclophane **42** is a kinetically favoured reaction compared with that of the diol **41** to the biscyclophane **42**, because two a-sites of the diol **46** are sterically less hindered than those of the diol **41** that already have substituents, benzylic groups, *ortho* to the a-positions. In the cyclisation of the diols **41** and **46**, however, there are other possibilities of formation of biscyclophanes containing 9-membered rings, such as those shown in structures **47** and **48**, by attack at the b-position of the diols **41** and **46**, respectively. However, such cyclisation products were not produced, probably because of the steric disadvantage due to the formation of a 1,2,3-trisubstituted benzene ring. It is known that in the 9-membered ring of [1.3]orthocyclophane, the aromatic hydrogen atoms (*e.g.* H^a and H^b in structures **47** and **48**) on two adjacent rings are almost within contact distance (2.5 ± 0.1 Å between their centres) and thus there is not much room at these positions for a substituent.[6]



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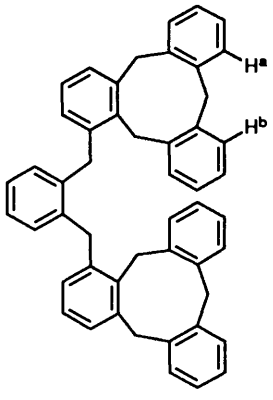

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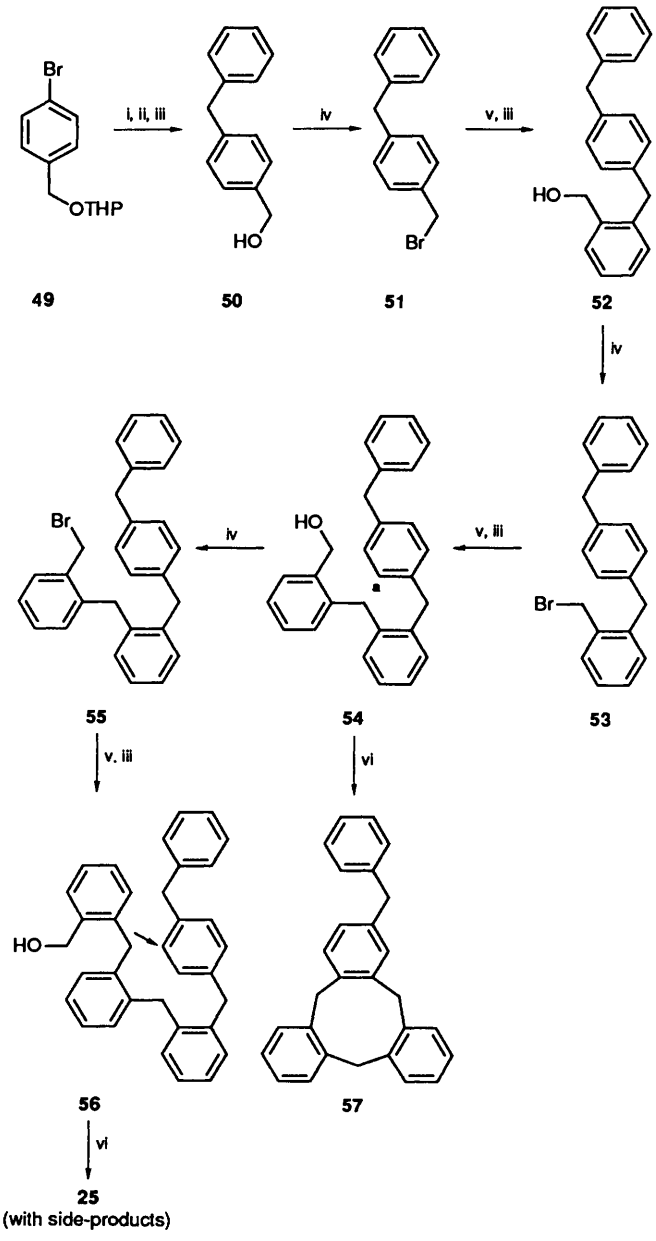
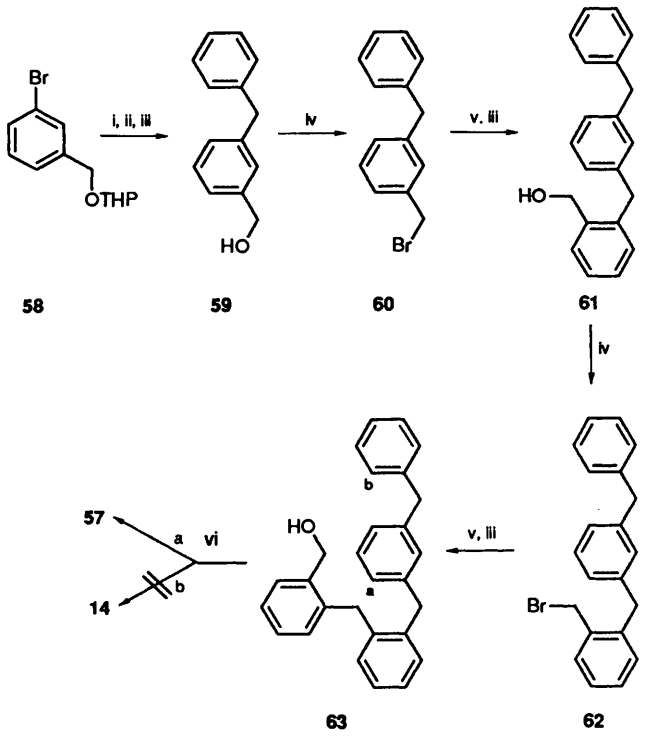


Scheme 6 *Reagents:* i, Mg, THF; ii, $PhCH_2Br$, CuI; iii, TsOH, MeOH; iv, HBr gas, CH_2Cl_2; v, Grignard **12**, CuI; vi, H_2SO_4, AcOH

The less effective cyclisation of the diol **41** to the biscyclophane **42** was similar to the acid-catalysed cyclisation behaviour of a benzylic alcohol **56** which was prepared as shown in Scheme 6. Treatment of a solution of the diol **56** in AcOH with H_2SO_4 gave rise to a mixture of the 13-membered cycle **25** and some side-products, but no 9-membered cycle. This result may be because formation of the 13-membered cycle is hindered by a substituent group located *ortho* to the reaction site, thereby giving rise to the side-products. This presents a striking contrast to the cyclisation of the diol **24** in acid to give the 13-membered cycle **25** in reasonable yield, since there is no steric hindrance at the reaction site (a-positon) in the intermediate cation **26**. On the other hand, however, treatment of mono-ol **54** with H_2SO_4 gave rise to 9-membered cycle **57** in moderate yield, despite the steric hindrance due to the presence of a substituent group *ortho* to the reaction site (a-position) in the molecule **54**.

The acid-catalysed cycloalkylation of *o*-BBAs in general gave rise to a 13-membered cycle in preference to a 9-membered one, but it was noted that this occurred when the formation of the 9-membered cycle was seriously restricted by the formation of a 1,2,3-trisubstituted benzene ring. For example, as mentioned above, treatment of the *o*-BBA **13** with H_2SO_4 gave exclusively the 13-membered cycle **14**, and none of the 9-membered cycle **17** that bears a 1,2,3-trisubstituted benzene ring. Thus, presumably the reactions were kinetically controlled. However, it is necessary to probe the preference of formation between the 9- and 13-membered cycles by using reactions in which formation of a 1,2,3-trisubstituted benzene ring is not involved.

In order to interpret the kinetics of the acid-catalysed cycloalkylation of BBAs, we probed the cyclisation behaviour of a benzylic alcohol, **63**, which was prepared as illustrated in Scheme 7. The benzylic alcohol **63** has two plausible reaction sites (a- and b-position), which must be responsible for the formation of the 9-membered cycle **57** and the 13-membered cycle **14**, respectively. As a matter of fact, however, treatment of a solution of the benzylic alcohol **63** in AcOH with H_2SO_4 provided exclusively the 9-membered cycle **57**, and none of the 13-membered cycle **14**. This is contradictory to the cyclisation feature of *o*-BBAs observed thus far, where the formation of 13-membered cycle **14** was preferred. The cyclisation of the benzylic alcohol **63** to the 9-membered cycle **57** shows the preference of formation of a 9-membered cycle over that of a 13-membered



Scheme 7 *Reagents:* i, Mg, THF; ii, $PhCH_2Br$, CuI; iii, TsOH, MeOH; iv, HBr gas, CH_2Cl_2; v, Grignard **12**, CuI; vi, H_2SO_4, AcOH

cycle, since the two reaction sites (a- and b-position) in the alcohol **63** are equally hindered by one substituent, respectively, present in the *ortho* position. This may be interpreted to mean that the intermediate benzylic cation attacked preferentially the nearer reaction site, the a-position, to give the 9-membered ring **57**.

In conclusion, acid-catalysed alkylation was investigated by the use of various terminal benzylbenzylic alcohols and diterminal benzylic diols, to give some new cyclophanes and a new common-nuclear biscyclophane. It was noted that there exists a pronounced regioselectivity in the cycloalkylation of *o*-BBAs in acid medium, which involves the priority in the order of 13-membered ring > 9-membered ring > 6-membered ring. Cycles larger than 13-membered was not generated, and steric effects are responsible for the regioselectivity. It was also noticed that although the 13-membered cycle was the preferred product in the cyclisation of *o*-BBAs, the formation of 9-membered cycles can be preferred in the cyclisation of other BBAs, where a 1,2,3-trisubstituted benzene ring is not formed in the 9-membered cyclic product.

Experimental

All m.p.s were measured on an Electrothermal digital melting point apparatus and were uncorrected. Flash chromatography was carried out using 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 Carloerba EA 1108. Mass spectra were recorded on a VG-7025 with normal geometry. Chemicals were purified by use of the reported procedure,[7] when necessary.

General Procedure A.—Conversion of a benzylic alcohol into the corresponding benzylic bromide. Into a solution of a benzylic alcohol (10.0 mmol) in CH_2Cl_2 (80 cm^3) was passed dry HBr gas at room temperature until the mixture was saturated, whereupon the cloudy solution turned to orange. After repeated saturation, the reaction flask was stoppered, and the mixture was stirred for 4–5 h, until the reaction mixture showed only one spot (R_f ~ 1.0) on TLC (SiO_2; CH_2Cl_2). The solution was washed successively with water, aq. $NaHCO_3$, and again with water, dried (anhyd. $MgSO_4$), and evaporated under reduced pressure. The crude product was chromatographed on silica gel, to give the corresponding benzylic bromide.

General Procedure B.—Coupling of aryl Grignard reagent **12** *with a benzylic bromide.* A Grignard reagent **12** was prepared by slow addition of a solution of 2-bromobenzyl tetrahydropyran-2-yl (THP) ether (10.0 mmol) in THF (50 cm^3) to magnesium turnings (20 mmol) immersed in stirred THF (20 cm^3), followed by refluxing for 3 h under nitrogen. To a cooled (0 °C), stirred solution of a benzylic bromide (8.0 mmol) in THF (50 cm^3) containing CuI (0.5 g) was added dropwise the Grignard reagent **12** prepared above; the mixture was allowed to warm to room temperature, and was then stirred for 12 h. To this reaction mixture was added aq. NH_4Cl, the solvent was removed under reduced pressure, the aqueous layer was extracted with CH_2Cl_2, and the extract was washed with water, dried (anhyd. $MgSO_4$), and condensed. The THP protecting group in the crude coupling product was removed, without further purification.

A solution of this crude product and *p*-TsOH (0.5 g) in MeOH (50 cm^3) was refluxed for 5–6 h, and then cooled to room temperature. To this reaction mixture was added aq. $NaHCO_3$ (10 cm^3) and the solvent was removed under reduced pressure. The reaction mixture was extracted several times with CH_2Cl_2, and the combined organic layer was washed with water, dried ($MgSO_4$), and concentrated. The crude product was purified by chromatography (SiO_2; CH_2Cl_2) to give a terminal benzylic alcohol in which the number of benzene rings was increased by one compared with the starting material. When the product was a diol (usually insoluble), the reaction mixture was directly filtered off, without extraction, and the solid product was washed several times successively with water and diethyl ether to remove water- and ether-soluble impurities, and this gave the pure product.

General Procedure C.—Acid-catalysed cyclisation of BBA. In a 250-cm^3 round-bottomed flask equipped with a dropping funnel were placed AcOH (40 cm^3) and conc. H_2SO_4 (40 cm^3). To this stirred mixture was added slowly a solution of benzylbenzylic alcohol (1.00 g) in AcOH (50 cm^3) over a period of 8–10 h at room temperature. After being stirred for an additional 6 h, the mixture was poured into ice–water (150 cm^3) and extracted with CH_2Cl_2. The extract was washed successively with aq. $NaHCO_3$ and water, dried (anhyd. $MgSO_4$), and evaporated at reduced pressure. The crude product was purified by chromatography on silica gel.

2-(2-*Benzylbenzyl*)*benzyl Bromide* **11**.—This compound was synthesised by use of General Procedure A, which involves treatment of the benzylic alcohol **1** (3.28 g, 11.4 mmol) with dry HBr gas in CH_2Cl_2 (80 cm^3), followed by work-up, and chromatographic purification (SiO_2; CH_2Cl_2) of the crude product, to give the *title compound* **11** (3.88 g, 97%) as a crystalline solid, m.p. 49.0–50.0 °C (Found: C, 71.75; H, 5.5. $C_{21}H_{19}Br$ requires C, 71.80; H, 5.45%); ν_{max}(KBr)/cm^{-1} 3050, 3010, 2930, 2850, 1600, 1580, 1490, 1450, 1430, 810, 780, 750, 700 and 560; δ_H(80 MHz; $CDCl_3$) 7.28–6.88 (13 H, m, ArH), 4.35 (2 H, s, $ArCH_2Br$), 4.06 (2 H, s, $ArCH_2Ar$) and 4.00 (2 H, s, $ArCH_2Ar$); *m/z* 352 and 350 (M^+, 1 : 1), 179 and 91.

2-[2-(2-*Benzylbenzyl*)*benzyl*]*benzyl Alcohol* **13**.—This compound was prepared by following General Procedure B, which involves preparation of Grignard reagent **12** from 2-bromobenzyl THP ether (3.17 g, 11.7 mmol), followed by reaction with the benzylic bromide **11** (2.75 g, 7.83 mmol), removal of the protecting group from the resultant coupling product, work-up, and purification of the crude product by chromatography (SiO_2; CH_2Cl_2), to give the crystalline *title compound* **13** (2.61 g, 88%), m.p. 97.2–98.4 °C (Found: C, 88.8; H, 7.0. $C_{28}H_{26}O$ requires C, 88.85; H, 6.92%); ν_{max}(KBr)/cm^{-1} 3500, 3060, 3020, 2950, 2900, 1600, 1490, 1450, 1040, 780, 750, 700 and 620; δ_H(200 MHz; $CDCl_3$) 7.38–6.83 (17 H, m, ArH), 4.41 (2 H, s, ArCH_2O), 3.89 (2 H, s, ArCH_2Ar), 3.85 (2 H, s, ArCH_2Ar), 3.80 (2 H, s, ArCH_2Ar) and 1.34 (1 H, br s, OH); *m*/*z* 360 (M$^+$ − H_2O), 282, 269, 192, 179, 165, 91 and 77.

Pentacyclo[22.3.1.0^{3,8}.0^{10,15}.0^{17,22}]*octacosa*-1(27),3(8),4,6,10(15),11,13,17(22),18,20,24(28),25-*dodecaene* **14**.—This compound was prepared by means of General Procedure C, which involves treatment of the benzylic alcohol **13** (1.00 g, 2.64 mmol) with an acid mixture of AcOH/H_2SO_4 (40 cm^3 : 40 cm^3), work-up, and purification of the crude product by chromatography on silica gel [mixed solvent of CH_2Cl_2–n-C_6H_{14} (1 : 5, v/v) as eluant], to give the powdery *title compound* **14** (0.48 g, 50%), m.p. 160 °C (decomp.) (Found: C, 93.25; H, 6.7%; M$^+$, 360.1890. $C_{28}H_{24}$ requires C, 93.29; H, 6.71%; M, 360.1878); ν_{max}(KBr)/cm^{-1} 3060, 3010, 2930, 2850, 1600, 1480, 1450, 780, 760, 620 and 610; δ_H(200 MHz; $CDCl_3$) 7.31–6.58 (15 H, m, outer ArH), 6.19 (1 H, s, inner ArH), 4.02 (4 H, s, ArCH_2Ar) and 3.64 (4 H, s, ArCH_2Ar); δ_C(50.29 MHz; $CDCl_3$) 139.901, 139.768, 138.409, 137.572, 133.252, 130.801, 129.200, 128.690, 127.295, 126.798, 126.725, 126.434, 126.142 (Ar), and 39.818 and 36.226 (ArCH_2Ar); *m*/*z* 360 (M$^+$), 282, 269, 255 and 179.

Pentacyclo[22.3.1.0^{3,8}.0^{10,15}.0^{17,22}]*octacosa*-1(27),3(8),4,6,10(15),11,13,17(22),18,20,24(28),25-*dodecaen*-2,23-*dione* **22**.—In a 100 cm^3 three-necked round-bottomed flask was placed, under nitrogen, a solution of the dibromide **19**[4] (0.83 g, 2.0 mmol) in dry THF (50 cm^3) and the mixture was cooled to −78 °C. To this solution was added carefully BuLi (1.9 cm^3; 2.5 mol dm^{-3} in hexane) through a syringe, and the mixture was stirred for 30 min, to give a pale yellow solution. To this stirred dilithio reagent at −78 °C was added dropwise a solution of isophthalaldehyde **20** (0.27 g, 2.0 mmol) in THF (50 cm^3) and the mixture was stirred for 1 h then allowed to warm to room temperature, water was added, and the solvent was removed under reduced pressure. The residual mixture was extracted with CH_2Cl_2, and the organic layer was washed successively with aq. $NaHCO_3$ and water, dried ($MgSO_4$), and evaporated under reduced pressure. The crude condensation product, a cyclic diol, being difficult to purify, was oxidized directly without purification.

To a solution of the crude product in CH_2Cl_2 (50 cm^3) were added Celite (2 g) and PCC (1.5 g), and the mixture was stirred for 6 h at room temperature before being filtered by suction. The precipitate was washed several times with a mixed solvent of Et_2O–CH_2Cl_2, the filtrate was treated with active charcoal, and the solution was evaporated under reduced pressure. The crude product was purified by chromatography on silica gel with n-C_6H_{14}–CH_2Cl_2 (1 : 1, v/v) as eluant, and then recrystallised from n-C_6H_{14}/CH_2Cl_2, to give the *crystalline dione* **22** in 20–30% yield based on the dibromide **17**: m.p. 242.5–243.5 °C (Found: C, 86.5; H, 5.25. $C_{28}H_{20}O_2$ requires C, 86.57; H, 5.19%); ν_{max}(KBr)/cm^{-1} 3050, 3020, 2950, 2850, 1660, 1600, 1480, 1440, 1300, 935, 790, 740, 725, 650 and 640; δ_H(200 MHz; $CDCl_3$) 8.49–7.09 (15 H, m, outer ArH), 6.76–6.69 (1 H, m, inner ArH), and 3.74 (4 H, AB quartet, *J* 3, 1.6, ArCH_2Ar); δ_C(50.29 MHz; $CDCl_3$) 197.194 (C=O), 138.587, 137.372, 136.534, 136.134, 133.579, 132.203, 129.976, 129.801, 127.493, 126.991, 126.299 (Ar) and 36.180 (ArCH_2Ar); *m*/*z* 388 (M$^+$), 370, 194 and 165.

Clemmensen Reduction of the Cyclic Diketone **22**.—A mixture of zinc (9 g) and $HgCl_2$ (0.9 g) was treated with a solution of conc. HCl (3 cm^3) in water (10 cm^3) for 60 min. To the resulting amalgamated zinc was added a solution of the cyclic diketone **22** (78 mg, 0.20 mmol) in toluene (10 cm^3), followed by additional conc. HCl (20 cm^3) that was diluted with water (10 cm^3). The mixture was refluxed for 1–2 days, during which time additional HCl was added in small potions, 3 cm^3 every 4 h. The reaction mixture, after being cooled, was filtered, and the organic layer was washed with water, dried ($MgSO_4$), and evaporated. The crude product was chromatographed on silica gel [mixed solvent of CH_2Cl_2–n-C_6H_{14} (1 : 5, v/v) as eluant] to give a powdery compound that was identical in all respects (TLC, IR, NMR, MS) with the 13-membered cyclophane **14**.

2-[2-(2-*Benzylbenzyl*)*benzyl*]*benzyl Bromide* **23**.—This compound was prepared by use of General Procedure A, which involves treatment of the benzylic alcohol **13** (2.63 g, 6.95 mmol) with HBr gas in CH_2Cl_2, work-up, chromatography (SiO; CH_2Cl_2), and recrystallisation from CH_2Cl_2, to give the crystalline *title compound* **23** (3.05 g, 99%), m.p. 121–123 °C (Found: C, 75.9; H, 5.9. $C_{28}H_{25}Br$ requires C, 76.19; H, 5.71%); ν_{max}(KBr)/cm^{-1} 3060, 2940, 1600, 1490, 1450, 780, 750, 730, 720, 700 and 605; δ_H(80 MHz; $CDCl_3$) 7.30–6.88 (17 H, m, ArH), 4.33 (2 H, s, ArCH_2Br), 3.96 (2 H, s, ArCH_2Ar) and 3.91 (4 H, s, 2 × ArCH_2Ar); *m*/*z* 442 and 440 (M$^+$, 1 : 1), 269, 193 and 179.

2-{2-[2-(2-*Benzylbenzyl*)*benzyl*]*benzyl*}*benzyl Alcohol* **24**.—This alcohol was prepared by following General Procedure B, which involves reaction of the bromide **23** (2.50 g, 5.67 mmol) in THF (50 cm^3) containing CuI (0.5 g) with the Grignard reeagent **12** (6.5 mmol), removal of the THP protecting group in the coupling product by refluxing in MeOH (60 cm^3) with *p*-TsOH (0.5 g), usual work-up, and purification of the crude product by chromatography (SiO_2; CH_2Cl_2), to give the *title compound* **24** (2.51 g, 95%) as a crystalline solid, m.p. 87.3–88.6 °C (Found: C, 89.55; H, 6.95. $C_{35}H_{32}O$ requires C, 89.70; H, 6.88%); ν_{max}(KBr)/cm^{-1} 3500–3100 (OH), 3060, 2900, 1600, 1490, 1450, 1050, 1030, 740 and 700; δ_H(200 MHz; $CDCl_3$) 7.33–6.88 (21 H, m, ArH), 4.38 (2 H, s, ArCH_2O), 3.83 (2 H, s, ArCH_2Ar), 3.78 (4 H, s, 2 × ArCH_2Ar) and 3.72 (2 H, s, ArCH_2Ar); *m*/*z* 450 (M$^+$ − H_2O), 359, 345, 282, 269, 255, 192, 179 and 91.

25-*Benzylpentacyclo*[22.3.1.0^{3,8}.0^{10,15}.0^{17,22}]*octacosa*-1(27),3(8),4,6,10(15),11,13,17(22),18,20,24(28),25-*dodecaene* **25**.—This compound was obtained by following General Procedure C, which involves treatment of the alcohol **24** (1.20 g, 2.56 mmol) with an acidic mixture of H_2SO_4–AcOH (40 cm^3 : 40 cm^3), work-up, and purification of the crude product by chromatography on silica gel [mixed solvent of CH_2Cl_2–n-C_6H_{14} (1 : 5, v/v) as eluant], to give the crystalline *title compound* **25** (0.71 g, 62%), m.p. 170–171 °C (Found: C, 93.3; H, 6.7%; M$^+$, 450.2383. $C_{35}H_{30}$ requires C, 93.29; H, 6.71%; M, 450.2348); ν_{max}(KBr)/cm^{-1} 3060, 3020, 2900, 1600, 1490, 1450, 800, 770 and 700; δ_H(200 MHz; $CDCl_3$) 7.29–6.61 (19 H, m, outer ArH), 6.15 (1 H, t, inner ArH), 4.01 (4 H, s, 2 × ArCH_2Ar), 3.85 (2 H, s, ArCH_2Ar), 3.66 (2 H, s, ArCH_2Ar) and 3.54 (2 H, s, ArCH_2Ar); δ_C(50.29 MHz; $CDCl_3$) 140.251, 139.342, 138.965, 138.079, 137.958, 137.485, 137.340, 136.976, 136.599, 136.017, 132.693, 132.632, 132.571, 130.679, 130.509, 130.060, 129.162, 129.101, 128.677, 128.398, 127.791, 126.481, 126.396, 126.262, 126.165, 126.117, 126.092 and 125.983 (Ar) and 39.343, 38.615, 37.802, 35.982 and 35.897 (ArCH_2Ar); *m*/*z* 450 (M$^+$), 359, 281, 267, 255, 179 and 91.

1,2-*Bis*-[2-(*hydroxymethyl*)*benzyl*]*benzene* **36**.—This benzylic diol was prepared by means of General Procedure B, which involves preparation of the Grignard reagent **12** by using 2-bromobenzyl THP ether (11.0 g, 40.6 mmol), followed by reaction in THF (30 cm^3) with 1,2-bis(bromomethyl)benzene (4.0 g, 15.2 mmol) in the presence of CuI (0.5 g), removal of the THP protecting group in the coupling product by reflux in methanol (70 cm^3) with TsOH (1.5 g), work-up, and purification of the crude product by chromatography (SiO_2; CH_2Cl_2), to give the *title compound* **36** (3.63 g, 75%) as a crystalline solid, m.p. 118.5–119.5 °C (Found: C, 82.95; H, 7.0. $C_{22}H_{22}O_2$ requires C, 82.99; H, 6.96%); ν_{max}(KBr)/cm^{-1} 3500–3100br(OH), 3070, 3030, 2900, 2850, 1600, 1490, 1450, 1100 and 1050; δ_H(80 MHz; $CDCl_3$) 7.38–6.91 (12 H, m, ArH), 4.51 (4 H, s, ArCH_2O), 4.02 (4 H, s, 2 × ArCH_2Ar) and 1.86 (2 H, s, 2 × OH); *m/z* 300 ($M^+ - H_2O$), 282 ($M^+ - 2H_2O$), 267 and 179.

1,4-*Bis*-[2-(*acetoxymethyl*)*benzyl*]*benzene* **39**.—A solution of the diol **34** (0.318 g, 1.00 mmol) in AcOH (20 cm^3) was added dropwise to a mixture of conc. H_2SO_4/AcOH (40 cm^3/40 cm^3) for a period of 5–6 h, and was stirred for an additional 5 h. The reaction mixture was poured into ice–water and extracted with CH_2Cl_2, and the organic layer was washed successively with aq. $NaHCO_3$ and water, dried ($MgSO_4$), and concentrated. The crude product was chromatographed (SiO_2; CH_2Cl_2) to give the *diacetate* **39** as needles (0.25 g, 62%), m.p. 106.5–107.5 °C (Found: C, 77.55; H, 6.6. $C_{26}H_{26}O_4$ requires C, 77.59; H, 6.51%); ν_{max}(KBr)/cm^{-1} 3020, 2970, 2900, 1725, 1600, 1485, 1375, 1250, 1025 and 755; δ_H(200 MHz; $CDCl_3$) 7.38–7.13 (8 H, m, ArH), 7.01 (4 H, s, ArH), 5.07 (4 H, s, ArCH_2O), 4.01 (4 H, s, ArCH_2Ar) and 1.96 (6 H, s, MeC=O); δ_C(50.29 MHz; $CDCl_3$) 170.661 (C=O), 139.419, 137.927, 133.875, 130.550, 129.810, 128.670, 128.633, and 126.583 (Ar), 64.305 (ArCH_2O), 37.953 (ArCH_2Ar) and 20.773 (*Me*C=O); *m/z* 282 ($M^+ - 2$ AcOH) and 179.

1,4-*Bis*-{2-[2-(*bromomethyl*)*benzyl*]*benzyl*}*benzene* **40**.—This compound was prepared by following General Procedure A, which involves treatment of the benzylic diol **4** (2.01 g, 4.03 mmol) with dry HBr gas in CH_2Cl_2 (150 cm^3), usual work-up, purification of the crude product by chromatography (SiO_2; CH_2Cl_2), and recrystallisation from CH_2Cl_2–n-C_6H_{14} (1:5, v/v), to give the *title compound* **40** (1.96 g, 78%) as a crystalline solid, m.p. 171–172 °C (Found: C, 69.2; H, 5.4. $C_{36}H_{32}Br_2$ requires C, 69.24; H, 5.17%); ν_{max}(KBr)/cm^{-1} 3060, 2900, 1590, 1450, 850, 765, 720, 605 and 510; δ_H(80 MHz; $CDCl_3$) 7.34–6.82 (20 H, m, ArH), 4.36 (4 H, s, ArCH_2Br), 4.06 (4 H, s, ArCH_2Ar) and 3.96 (4 H, s, ArCH_2Ar); *m/z* 626, 624 and 622 (M^+, 1:2:1), 546 and 544 ($M^+ - HBr$, 1:1), 466 ($M^+ - 2HBr$), 283, 269, 193 and 179.

1,4-*Bis*-{2-[2-(2-(*hydroxymethyl*)*benzyl*)*benzyl*]*benzyl*}-*benzene* **41**.—This diol was prepared by following General Procedure B, which involves reaction of the Grignard **12** (5.0 mmol) with the dibromide **40** (1.01 g, 1.62 mmol) in THF (70 cm^3) in the presence of CuI (0.5 g), and removal of the THP protecting group in the coupling product by reflux with *p*-TsOH (1 g) in methanol (60 cm^3). After work-up, the crude product was filtered off and washed successively with distilled water and diethyl ether to remove the water- and ether-soluble impurities, to give the *title compound* **41** (0.59 g, 54%) as a crystalline solid, m.p. 146–147 °C (Found: C, 88.4; H, 6.9. $C_{50}H_{46}O_2$ requires C, 88.46; H, 6.83%); ν_{max}(Kbr)/cm^{-1} 3530, 3450, 3050, 2890, 1595, 1510, 1485, 1450, 1050, 1010, 755 and 745; δ_H(200 MHz; $CDCl_3$) 7.33–6.86 (28 H, m, ArH), 4.37 (4 H, d, *J* 6, ArCH_2O), 3.83 (4 H, s, ArCH_2Ar), 3.80 (4 H, s, ArCH_2Ar), 3.79 (4 H, s, ArCH_2Ar) and 1.41 (2 H, t, *J* 6, OH); δ_C(50.29 MHz; $CDCl_3$) 139.104, 138.702, 138.606, 138.473, 138.364, 137.927, 130.429, 129.834, 129.762, 129.677, 128.706, 128.099, 127.893, 126.643, 126.571, 126.522 and 126.486 (Ar), 63.068 (ArCH_2O), and 38.766, 36.144 and 35.259 (ArCH_2Ar); *m/z* 642 ($M^+ - 2H_2O$), 462 and 179.

Nonacyclo[24.22.1.$1^{2.25}$.$0^{4.9}$.$0^{11.16}$.$0^{18.23}$.$0^{28.33}$.$0^{35.40}$.$0^{42.47}$] *pentaconta*-1(49),2(50),4(9),5,7,11(16),12,14,18(23),19,21,25,28(33),29,31,35(40),36,38,42(47),43,45-*henicosaene* **42**.—This compound was prepared by use of General Procedure C, which involves slow addition of a solution of the diol **41** (0.34 g, 0.50 mmol) in AcOH (60 cm^3) to a stirred mixture of H_2SO_4–AcOH (40 cm^3/40 cm^3), and the mixture was stirred for 10 h at room temperature. After work-up, the crude product was chromatographed (SiO_2; CH_2Cl_2) to give a solid product, which was washed thoroughly with diethyl ether to remove the ether-soluble impurities, to give the *title compound* **42** (0.032 g, 10%) as a crystalline solid, m.p. > 300 °C (decomp.) (Found: C, 93.4; H, 6.6%; M^+, 642.3294. $C_{50}H_{42}$ requires C, 93.42; H, 6.58%; M, 642.3287); ν_{max}(KBr)/cm^{-1} 3060, 2880, 1485, 1450, 795, 745 and 635; δ_H(200 MHz; $CDCl_3$) 7.27–6.63 (24 H, m, outer ArH), 6.10 (2 H, br s, inner ArH), 3.94 (8 H, s, ArCH_2Ar) and 3.71 (8 H, s, ArCH_2Ar); *m/z* 642 (M^+), 357, 282 and 179. The compound **42** was so insoluble that a ^{13}C NMR spectrum could not be obtained.

1,2-*Bis*-[2-(*bromomethyl*)*benzyl*]*benzene* **43**.—This benzylic dibromide was prepared by means of General Procedure A, which involves treatment of the benzylic diol **36** (2.01 g, 6.31 mmol) in CH_2Cl_2 (150 cm^3) with HBr gas, work-up, and purification of the crude product by chromatography on silica gel [mixed solvent of CH_2Cl_2–n-C_6H_{14} (1:2, v/v) as eluant], to give the crystalline *title compound* **43** (2.31 g, 82%) as a powdery solid, m.p. 119–120 °C (Found: C, 59.45; H, 4.6. $C_{22}H_{20}Br_2$ requires C, 59.49; H, 4.54%); ν_{max}(KBr)/cm^{-1} 3050, 2920, 1600, 1450, 720 and 600; δ_H(80 MHz; $CDCl_3$) 7.34–6.87 (12 H, m, ArH), 4.39 (4 H, s, ArCH_2Br) and 4.10 (4 H, s, ArCH_2Ar); *m/z* 446, 444 and 442 (M^+, 1:2:1), 283, 179 and 105.

1,2-*Bis*-{2-[2-(*hydroxymethyl*)*benzyl*]*benzyl*}*benzene* **44**.—This diol was prepared according to General Procedure B, which involves reaction of the Grignard reagent **12** (20 mmol) with the dibromide **43** (4.00 g, 9.00 mmol) in THF (50 cm^3) in the presence of CuI (0.4 g), removal of the THP protecting group in the coupling product, and work-up, to give a crystalline solid which was insoluble in organic solvents. The crude product was thoroughly washed successively with distilled water and diethyl ether, to give the powdery *title compound* **44** (3.20 g, 71%) as a powdery solid, m.p. 174–175 °C (Found: C, 86.7; H, 7.0. $C_{36}H_{34}O_2$ requires C, 86.71; H, 6.87%); ν_{max}(KBr)/cm^{-1} 3500–3100br(OH), 3010, 2900, 1600, 1450, 1050, 1000 and 740; δ_H[80 MHz; $CDCl_3$ + $(CD_3)_2SO$ (3:1)] 7.48–6.72 (20 H, m, ArH), 4.50 (4 H, s, ArCH_2O), 3.98 (4 H, s, ArCH_2Ar), 3.90 (4 H, s, ArCH_2Ar) and 1.64 (2 H, s, OH); *m/z* 480 ($M^+ - H_2O$), 462 ($M^+ - 2H_2O$), 267, 192 and 179.

1,2-*Bis*-{2-[2-(*bromomethyl*)*benzyl*]*benzyl*}*benzene* **45**.—This dibromide was prepared by following General Procedure A, which involves treatment of the benzylic diol **44** (3.40 g, 6.82 mmol) with HBr gas in CH_2Cl_2 (150 cm^3), usual work-up, chromatography (SiO_2; CH_2Cl_2), and recrystallisation from CH_2Cl_2–n-C_6H_{14} (1:2, v/v), to give *title compound* **45** (3.80 g, 89%) as a powdery solid, m.p. 121–122 °C (Found: C, 69.2; H, 5.25. $C_{36}H_{32}Br_2$ requires C, 69.24; H, 5.17%); ν_{max}(KBr)/cm^{-1} 3050, 2900, 1600, 1490, 1450 and 745; δ_H(80 MHz; $CDCl_3$) 7.32–6.67 (20 H, m, ArH), 4.30 (4 H, s, ArCH_2Br), 3.94 (4 H, s, ArCH_2Ar) and 3.83 (4 H, s, ArCH_2Ar); δ_C(20.15 MHz; $CDCl_3$) 138.971, 138.333, 138.215, 137.669, 135.647, 130.363, 130.004, 129.613, 129.459, 128.885, 126.711 and 126.546 (Ar), and 36.163, 35.286 and 31.610 (ArCH_2); *m/z* 626, 624 and 622 (M^+, 1:2:1), 544 and 542 ($M^+ - HBr$, 1:1), 464 ($M^+ - 2HBr$), 283 and 269.

1,2-Bis-{2-[2-(2-(hydroxymethyl)benzyl)benzyl]benzyl}-benzene **46**.—This benzylic diol was prepared by use of General Procedure B, which involves reaction of the Grignard reagent **12** (7.50 mmol) with the dibromide **45** (2.00 g, 3.20 mmol) in THF (70 cm^3) in the presence of CuI (0.5 g), removal of the THP protecting group in the coupling product, and work-up, to give a solid product that was insoluble in organic solvents. The crude product was washed successively with distilled water and diethyl ether to remove the water- and ether-soluble impurities, to give the crystalline *title compound* **46** (1.40 g, 64%) as a powdery solid, m.p. 77–78 °C (Found: C, 88.4; H, 7.0. $C_{50}H_{46}O_2$ requires C, 88.46; H, 6.83%); ν_{max}(KBr)/cm^{-1} 3500–3100 (OH), 3050, 2900, 1600, 1450, 1210, 1040, 1010 and 750; δ_H(200 MHz; $CDCl_3$) 7.35–6.81 (28 H, m, ArH), 4.32 (4 H, d, *J* 5, ArCH_2O), 3.74 (4 H, s, ArCH_2Ar), 3.70 (4 H, s, ArCH_2Ar), 3.69 (4 H, s, ArCH_2Ar) and 1.43 (2 H, t, *J* 5, OH); δ_C(50.29 MHz; $CDCl_3$) 138.733, 138.661, 138.515, 138.369, 138.248, 137.860, 129.852, 129.622, 129.561, 129.428, 129.367, 128.081, 127.826, 126.516 (Ar) and 62.964 (ArCH_2O), 36.308, 36.151 and 35.229 (ArCH_2Ar); *m/z* 642 ($M^+ - 2H_2O$), 552, 462, 267 and 179.

Cyclisation of the Diol **46** *to the Biscyclophane* **42**.—Compound **42** could also be obtained from the diol **46** according to General Procedure C, which involves slow addition of a solution of the diol **46** (0.80 g, 1.2 mmol) in AcOH (60 cm^3) to a mixture of H_2SO_4–AcOH (40 cm^3:40 cm^3), followed by stirring of the mixture for 10 h at room temperature. After usual work-up, the crude product was chromatographed (SiO_2; CH_2Cl_2) to give a solid product, which was then washed thoroughly with diethyl ether to remove the ether-soluble impurities, to give a crystalline compound (0.12 g, 16%), which was identical in all respects (IR, NMR, MS) with the biscyclophane **42** that was obtained from the diol **41**.

4-Benzylbenzyl Alcohol **50**.—This alcohol was prepared according to General Procedure B, which involves the preparation of an excess of the Grignard reagent from 4-bromobenzyl tetrahydropyran-2-yl ether **49** (11.5 g, 42.4 mmol) in THF, followed by reaction with benzyl bromide (6.60 g, 38.6 mmol) in the presence of CuI, removal of the THP protecting group of the coupling product, work-up, and chromatography (SiO_2; CH_2Cl_2), to give the *title compound* **50** (7.20 g, 94%) as a powdery solid, m.p. 41–42 °C (Found: C, 84.8; H, 7.2. $C_{14}H_{14}O$ requires C, 84.81; H, 7.12%); ν_{max}(KBr)/cm^{-1} 3340, 3035, 2920, 1495, 1040 and 735; δ_H(80 MHz; $CDCl_3$) 7.40–7.00 (9 H, m, ArH), 4.65 (2 H, d, *J* 5.5, ArCH_2O), 3.98 (2 H, s, ArCH_2Ar) and 1.58 (1 H, t, *J* 5.5, OH); *m/z* 198 (M^+), 167, 107, 91 and 79.

4-Benzylbenzyl Bromide **51**.—This compound was prepared by following General Procedure A, which involves treatment of the alcohol **50** (5.15 g, 26.0 mmol) with dry HBr gas in CH_2Cl_2, work-up, and purification by chromatography (SiO_2; CH_2Cl_2), to give the *title compound* **51** (5.47 g, 81%) as a crystalline solid which melts easily at room temperature (Found: C, 64.4; H, 5.1. $C_{14}H_{13}Br$ requires C, 64.39; H, 5.02%); ν_{max}(NaCl window)/cm^{-1} 2975, 2860, 1120, 730 and 700; δ_H(80 MHz; $CDCl_3$) 7.40–7.00 (9 H, m, ArH), 4.43 (2 H, s, ArCH_2Br) and 3.94 (2 H, s, ArCH_2Ar); *m/z* 262 and 260 (M^+, 1:1), 181 and 165.

2-(4-Benzylbenzyl)benzyl AlcohoK **52**.—This compound was prepared according to General Procedure B, which involves the reaction of an excess of Grignard reagent **12** with the bromide **51** (4.70 g, 18.0 mmol) in the presence of a catalytic amount of CuI, removal of the THP protecting group in the coupling product, work-up, and chromatographic purification (SiO_2; CH_2Cl_2), to give the *title compound* **52** (4.79 g, 92%) as a powdery solid, m.p. 48–49 °C (Found: C, 87.4; H, 7.1. $C_{21}H_{20}O$ requires C, 87.46; H, 6.99%); ν_{max}(KBr)/cm^{-1} 3380, 3030, 2930, 1495, 1455, 1025 and 740; δ_H(80 MHz; $CDCl_3$) 7.50–6.90 (13 H, m, ArH), 4.60 (2 H, d, *J* 5.6, ArCH_2O), 4.02 (2 H, s, ArCH_2Ar), 3.92 (2 H, s, ArCH_2Ar) and 1.50 (1 H, t, *J* 5.6, OH); *m/z* 270 ($M^+ - H_2O$), 179 and 165.

2-(4-Benzylbenzyl)benzyl Bromide **53**.—This bromide was prepared by use of General Procedure B, which involves treatment of the alcohol **52** (5.82 g, 20.2 mmol) with dry HBr gas in CH_2Cl_2, work-up, and purification by chromatography (SiO_2; CH_2Cl_2) to give the *title compound* **53** (6.85 g, 97%) as a powdery solid, m.p. 63–64 °C (Found: C, 71.8; H, 5.5. $C_{21}H_{19}Br$ requires C, 71.80; H, 5.45%); ν_{max}(KBr)/cm^{-1} 3060, 3020, 2900, 1600, 1510, 1450, 1430, 1020, 775, 760, 715 and 700; δ_H(80 MHz; $CDCl_3$) 7.50–6.91 (13 H, m, ArH), 4.44 (2 H, s, ArCH_2Br), 4.11 (2 H, s, ArCH_2Ar) and 3.94 (2 H, s, ArCH_2Ar); *m/z* 352 and 350 (M^+, 1:1), 179 and 91.

2-[2-(4-Benzylbenzyl)benzyl]benzyl Alcohol **54**.—This compound was prepared by following General Procedure B, which involves reaction of an excess of the Grignard reagent **12** with the bromide **53** (6.58 g, 18.7 mmol) in the presence of CuI, removal of the THP protecting group in the coupling product, work-up, and purification of the crude product by chromatography (SiO_2; CH_2Cl_2), to give the *title compound* **54** (6.34 g, 89%) as a powdery solid, m.p. 72–73 °C (Found: C, 88.8; H, 7.1. $C_{28}H_{26}O$ requires C, 88.85; H, 6.92%); ν_{max}(KBr)/cm^{-1} 3370, 1450, 1105 and 730; δ_H(80 MHz; $CDCl_3$) 7.50–6.70 (17 H, m, ArH), 4.42 (2 H, d, *J* 5.64, ArCH_2O), 3.97 (2 H, s, ArCH_2Ar), 3.94 (4 H, s, ArCH_2Ar) and 1.27 (1 H, t, *J* 5.64, OH); δ_C(50.29 MHz; $CDCl_3$) 141.055, 138.823, 138.750, 138.605, 138.435, 137.852, 137.804, 130.366, 129.845, 129.372, 128.801, 128.704, 128.267, 127.879, 127.709, 126.557, 126.435, 126.338 and 125.865 (Ar), 62.872 (ArCH_2OH), and 41.360, 38.727 and 35.148 (ArCH_2Ar); *m/z* 360 ($M^+ - H_2O$), 269, 192, 179 and 91.

2-[2-(4-Benzylbenzyl)benzyl]benzyl Bromide **55**.—This bromide was prepared by use of General Procedure A, which involves treatment of the alcohol **54** (3.50 g, 9.26 mmol) with dry HBr gas in CH_2Cl_2, work-up, and purification of the crude product by chromatography (SiO_2; CH_2Cl_2), to give the *title compound* **55** (3.94 g, 96%) as a powdery solid, m.p. 78.5–79.0 °C (Found: C, 76.2; H, 5.75. $C_{28}H_{25}Br$ requires C, 76.19; H, 5.71%); ν_{max}(KBr)/cm^{-1} 3060, 3020, 2880, 1595, 1510, 1490, 1450, 1430, 1210, 855, 750 and 730; δ_H(80 MHz; $CDCl_3$) 7.50–6.80 (17 H, m, ArH), 4.34 (2 H, s, ArCH_2Br), 4.06 (2 H, s, ArCH_2Ar), 3.96 (2 H, s, ArCH_2Ar) and 3.93 (2 H, s, ArCH_2Ar); δ_C(50.29 MHz; $CDCl_3$) 141.128, 139.163, 138.762, 137.864, 137.828, 135.729, 130.476, 130.403, 130.184, 129.723, 128.959, 128.826, 128.741, 128.340, 126.775, 126.654, 126.605 and 125.926 (Ar) and 41.457, 38.776, 35.270 and 31.812 (ArCH_2Ar); *m/z* 442 and 440 (M^+, 1:1), 269, 179, 165 and 91.

2-{2-[2-(4-Benzylbenzyl)benzyl]benzyl}benzyl Alcohol **56**.—This compound was prepared by means of General Procedure B, which involves reaction of an excess of the Grignard reagent **12** with the bromide **55** (3.30 g, 7.48 mmol) in the presence of CuI, removal of the THP protecting group in the resultant coupling product, work-up, and purification of the crude product by chromatography (SiO_2; CH_2Cl_2), to give the *title compound* **56** (2.98 g, 85%) as an oil (Found: C, 89.65; H, 6.9. $C_{35}H_{32}O$ requires C, 89.70; H, 6.88%); ν_{max}(KBr)/cm^{-1} 3350, 3020, 2900, 1600, 1490, 1450, 1150 and 740; δ_H(80 MHz; $CDCl_3$) 7.50–6.80 (21 H, m, ArH), 4.41 (2 H, d, *J* 5.8, ArCH_2O), 3.89 (2 H, s, ArCH_2Ar), 3.87 (4 H, s, ArCH_2Ar), 3.81 (2 H, s, ArCH_2Ar) and 1.18 (1 H, t, *J* 5.8, OH); δ_C(20.15 MHz; $CDCl_3$) 141.104, 139.042, 138.741, 138.557, 138.441, 138.349, 137.911, 137.631, 130.426, 129.778, 129.582, 129.383, 128.835, 128.729, 128.366, 127.981, 127.614, 126.612, 126.495 and 125.956 (Ar), 62.970

(ArCH_2O), and 41.426, 38.780, 36.106 and 35.223 (ArCH_2Ar); *m/z* 468 (M^+), 450 ($M^+ - H_2O$), 269, 179 and 91.

5-*Benzyltetracyclo*[15.4.0.0^{3,8}.0^{10,15}]*henicosa*-1(17),3(8),4,6,10(15),11,13,18,20-*nonaene* **57**.—This cyclophane was obtained by following General Procedure C, which involves treatment of the benzylic alcohol **54** (0.600 g, 1.59 mmol) with an acidic mixture of AcOH/conc. H_2SO_4 (40 cm^3/40 cm^3), work-up, and purification of the crude product by chromatography on silica gel [CH_2Cl_2–n-C_6H_{14} (1:5, v/v) as eluant], to give the *title compound* **57** (0.315 g, 55%) as a crystalline solid, m.p. 176–177 °C (Found: C, 93.2; H, 6.8%; M^+, 360.1879. $C_{28}H_{24}$ requires C, 93.29; H, 6.71%; M, 360.1878); ν_{max}(KBr)/cm^{-1} 3020, 2920, 1495, 1475 and 725; δ_H(200 MHz; $CDCl_3$) 7.39–6.86 (16 H, m, ArH), 4.88 (1 H, d, *J* 13.4, ArCH*H*Ar, quasi-axial), 4.85 (1 H, d, *J* 13.4, ArCH*H*Ar, quasi-axial), 4.84 (1 H, d, *J* 13.4, ArCH*H*Ar, quasi-axial), 3.87 (2 H, s, ArCH_2Ar), 3.73 (1 H, d, *J* 13.4, ArC*H*HAr, quasi-equatorial), 3.71 (1 H, d, *J* 13.4, ArC*H*HAr, quasi-equatorial) and 3.68 (1 H, d, *J* 13.4, ArC*H*HAr, quasi-equatorial); δ_C(50.29 MHz; $CDCl_3$) 140.950, 139.531, 139.506, 139.446, 139.409, 137.177, 130.504, 130.115, 129.994, 128.914, 128.356, 127.507, 126.876 and 125.954 (Ar), and 41.328, 37.069 and 36.778 (ArCH_2Ar); *m/z* 360 (M^+), 269, 179 and 91.

3-*Benzylbenzyl Alcohol* **59**.—This compound was synthesised by means of General Procedure B, which involves preparation of a Grignard reagent from 3-bromobenzyl THP ether **58** (20.3 g, 75.0 mmol), followed by reaction with benzyl bromide (8.55 g, 50.0 mmol) in the presence of CuI, and removal of the THP protecting group of the resultant coupling product by reflux with TsOH (0.3 g) in MeOH (50 cm^3). After work-up, the crude product was chromatographed (SiO_2; CH_2Cl_2) to give the *title compound* **59** (9.77 g, 99%) as an oil (Found: C, 84.75; H, 7.2. $C_{14}H_{14}O$ requires C, 84.81; H, 7.12%); ν_{max}(NaCl window)/cm^{-1} 3500–3200 (OH), 3020, 2900, 1600, 1500, 1460, 1030, 735 and 705; δ_H(80 MHz; $CDCl_3$) 7.40–7.01 (9 H, m, ArH), 4.60 (2 H, br, ArCH_2O), 3.97 (2 H, s, ArCH_2Ar) and 1.63 (1 H, br, OH); *m/z* 198 (M^+), 181, 167 and 107.

3-*Benzylbenzyl Bromide* **60**.—This bromide was prepared according to General Procedure A, which involves treatment of the alcohol **59** (8.00 g, 40.4 mmol) with dry HBr gas in CH_2Cl_2, work-up, and purification by chromatography (SiO_2; CH_2Cl_2), to give the *title compound* **60** (9.30 g, 89%) as an oil (Found: C, 64.4; H, 5.1. $C_{14}H_{13}Br$ requires C, 64.39; H, 5.02%); ν_{max}(NaCl window)/cm^{-1} 3060, 3020, 2920, 1600, 1495, 1450, 1215, 730 and 705; δ_H(80 MHz; $CDCl_3$) 7.36–6.99 (9 H, m, ArH), 4.39 (2 H, s, ArCH_2Br) and 3.94 (2 H, s, ArCH_2Ar); *m/z* 262 and 260 (M^+, 1:1), 181 and 169.

2-(3-*Benzylbenzyl*)*benzyl Alcohol* **61**.—This compound was prepared according to General Procedure B, which involves reaction of an excess of the Grignard reagent **12** with the bromide **60** (5.22 g, 20.0 mmol) in the presence of CuI, and removal of the THP protecting group in the coupling product, followed by purification by chromatography (SiO_2; CH_2Cl_2), to give the *title compound* **61** (5.25 g, 91%) as an oil (Found: C, 87.4; H, 7.0. $C_{21}H_{20}O$ requires C, 87.46; H, 6.99%); ν_{max}(NaCl window)/cm^{-1} 3350, 3040, 2920, 1600, 1500, 1460, 1030, 1000, 750 and 700; δ_H(200 MHz; $CDCl_3$) 7.38–6.88 (13 H, m, ArH), 4.58 (2 H, d, *J* 5.9, ArCH_2O), 4.00 (2 H, s, ArCH_2Ar), 3.89 (2 H, s, ArCH_2Ar) and 1.38 (1 H, t, *J* 5.9, OH); *m/z* 270 ($M^+ - H_2O$) 179 and 91.

2-(3-*Benzylbenzyl*)*benzyl Bromide* **62**.—This compound was prepared by means of General Procedure A, which involves treatment of the alcohol **61** (2.88 g, 10.0 mmol) with dry HBr gas in CH_2Cl_2, followed by work-up and chromatographic purification (SiO_2; CH_2Cl_2), to give the *title compound* **62** (3.49 g, 99%) as an oil (Found: C, 71.8; H, 5.5. $C_{21}H_{19}Br$ requires C, 71.80; H, 5.45%); ν_{max}(NaCl window)/cm^{-1} 3060, 3020, 2920, 1600, 1495, 1455, 1225, 1210, 760 and 700; δ_H(80 MHz; $CDCl_3$) 7.41–6.90 (13 H, m, ArH), 4.43 (2 H, s, ArCH_2Br), 4.10 (2 H, s, ArCH_2Ar) and 3.93 (2 H, s, ArCH_2Ar); *m/z* 352 and 350 (M^+, 1:1), 260, 217 and 181.

2-[2-(3-*Benzylbenzyl*)*benzyl*]*benzyl Alcohol* **63**.—This alcohol was prepared by following General Procedure B, which involves reaction of an excess of the Grignard reagent **12** with the bromide **62** (1.75 g, 5.00 mmol) in the presence of CuI, and removal of the protecting group in the coupling product, followed by purification of the crude product by chromatography (SiO_2; CH_2Cl_2), to give the *title compound* **63** (1.60 g, 85%) as an oil (Found: C, 88.8; H, 7.0. $C_{28}H_{26}O$ requires C, 88.85; H, 6.92%); ν_{max}(NaCl window)/cm^{-1} 3400 (OH), 3040, 2925, 1600, 1495, 1460, 1050, 750 and 705; δ_H(200 MHz; $CDCl_3$) 7.39–6.83 (17 H, m, ArH), 4.39 (2 H, d, *J* 6, ArCH_2O), 3.94 (4 H, s, two ArCH_2Ar), 3.90 (2 H, s, ArCH_2Ar) and 1.35 (1 H, br, OH); *m/z* 360 ($M^+ - H_2O$), 269, 192, 179 and 91.

Cyclisation of the Benzylic Alcohol **63** *to the Cyclophane* **57**.—The compound **57** could also be obtained from the benzylic alcohol **63** according to General Procedure C, which involves slow addition of a solution of the alcohol **63** (0.600 g, 1.59 mmol) in AcOH (60 cm^3) to a mixture of H_2SO_4–AcOH (40 cm^3/40 cm^3), followed by stirring of the mixture for 10 h at room temperature. After usual work-up, the crude product was chromatographed (SiO_2; CH_2Cl_2–n-C_6H_{14}) to give a crystalline compound (0.350 g, 61%), which was identical in all respects (IR, NMR, MS) with the cyclophane **57** obtained from the alcohol **54**.

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