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Are stable atropisomers possible for meta-meta' linked biphenols?

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ABSTRACT

This paper describes the synthesis, structure, conformation and configurational stability of novel 8-atom meta,meta'-linked biaryls, as models for controlling the ratio of atropisomers through remote central chirality. The synthesis of model compounds is described where the configuration of the linker is provided by reduced C4 and C6 sugars. Their properties have been examined by X-ray, NMR and ECD. Taken together, they provide information on the conformation of the linking chain in each case and indicate a barrier to atropisomerisation in the region of 55 KJ mol⁻¹. For the diastereomeric C6 compounds, the preferred atropisomer is defined by the configuration of the backbone secondary methyl groups. Computational analysis confirms the direction of axial chirality from ECD spectra and offers a model for the distinction between the (*R,R,R,R*) and (*S,R,R,S*) C6-isomers.

Dedicated to the memory of Jonathan Williams; a pioneer in innovative synthesis for catalysis through his mechanistic insights.

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Introduction

Stable biaryl atropisomers have played an important role in catalysis. Racemisation is avoided when *ortho*-substituents in the biphenyl are sufficiently bulky. This paper describes the synthesis, structure, conformation and configurational stability of novel 8-atom *meta,meta*'-linked biaryls, as models for an alternative approach to inhibiting atropisomerisation through the agency of remote central chirality.

The diphosphine BINAP and the bisphenol BINOL and their analogues are among the best known ligand families for asymmetric catalysis.¹ Their genesis lay in early achievements for resolution of simple biaryls and assignment of their absolute configurations.² Successful development of the catalytic asymmetric hydrogenation of prochiral alkenes, especially dehydroamino acids, by chelate biphosphine rhodium biphosphine ligands initially employed had been DIPAMP, relying on phosphorus chirality, or DIOP, based on the natural chirality of tartaric acid complexes provided an appropriate challenge.³

The ensuing rapidly emerging field of asymmetric hydrogenation led to many further ligand syntheses, and naturally this included atropisomeric biaryls. The barrier to racemisation of atropisomers may be achieved through sufficient bulk in the substituents occupying 2- and 2'-positions of both biaryl rings. Since the precursor BINOL was readily prepared and resolved,⁴ the first demonstrations of atropisomeric ligands in asymmetric hydrogenation involved respectively CH₂PPh₂ or NHPPH₂ substituents, although these were less effective catalysts than those used in the original discoveries.⁵ The synthetic development of BINAP through direct formation of the 2 and 2' C-P bonds, using PAR₂-based reagents,⁶ stimulated the continuing development of families of catalyst for diverse areas of asymmetric synthesis. Later work demonstrated that stable atropisomers could be formed from a 2,2'-dimethylbiphenyl when the other *o*-substituents were both PPh₂,⁷ and likewise the corresponding dimethylated 2,2' bisphenol was stable to racemization (Scheme 1).⁸ These developments required a biaryl with restricted rotation about the inter-aryl linkage, giving rise to the existence of stable atropisomers. In principle, a potential alternative method for restricting biaryl rotation is by remote control, through a rigid chiral entity linking two positions meta-to the inter-ring link. The shortest feasible meta-linking chain possesses six atoms, and the parent hydrocarbon C₁₈H₂₀ has been synthesised and characterised.⁹

Among the large and growing class of Diarylheptanoids natural products defined by a seven-atom *meta-meta*' linkage, several natural *o,o*'-biphenols and their ethers are found.¹⁰ Perhaps the best known is Myricanol, obtained from root bark of the Japanese Maple and also other natural sources. The X-ray structure of a derivative coupled with spectroscopic characterisation,¹¹ biosynthetic studies,¹² and later total syntheses of the racemate,^{13,14} have been described. A number of other members of this family of natural products have been isolated, and several crystal structures are accessible.^{15,16} Because the degree of rigidity of the linking chain is of specific interest for this work, the geometry of diarylheptanoids was analysed in more detail, using the CCDC database as source. The *meta*-bridging link leads to a defined inter-ring conformation, with both biaryl stereoisomers represented. The range of dihedral angles in Scheme 2c is quite narrow. Angle strain is indicated by evident bending of the biaryl, and by sp³ CCC angles significantly > 109°. The CCC angle at the sp² carbonyl group in a 9-keto analogue of Myricanol is 127°, and this ketone has a larger dihedral angle of 64.48°. Both enantiomers of Myricanol have been isolated from natural sources, in one case as a mixture of *aR* and *aS* diastereomers that co-crystallise in 1:1 ratio by crystal structure analysis.¹⁷ This implies that atropisomerisation may occur readily in diarylheptanoids.

In complete contrast, there are no related naturally occurring 8-atom *meta-meta*' linked biaryls. Only a few synthetic *bis*-amides with this structural feature are known, including the macrocyclic core of the family of Arylomycin

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peptide antibiotics.¹⁸ The current interest generated by modified Arylomycin analogues lies in their potential for treatment of infections by antibiotic-resistant bacteria (AMR). The SI of ref. 18b contains a further X-ray structure with a macrocyclic 8-atom meta-meta' linker. This structure demonstrates that the dipeptide component imposes a conformation on the macrocycle distinct from the observations described here.

A nine atom meta-meta' linker is present in lythranine alkaloids, where dynamic ¹H NMR has been observed through biaryl inversion.¹⁹ As an application to ligand design, a nine-atom meta-meta' linking chain successfully attenuates atropisomerisation in 2,2'-(diphenylphosphino)biphenyl so that the modified ligand is useful for Pd-complex catalysed asymmetric hydrogenation.²⁰

The lack of fuller information on 8-atom meta,meta'-bridged biaryls encouraged the systematic survey that is described here.

2. Discussion

2.1 Objectives

Given a lack of suitable precedents, objectives needed to be clearly defined. The first was a general route to meta-meta'-bridged biaryls for which the bridge possessed defined stereochemistry. For the simplest case, bridging the meta- and meta' positions of a suitably substituted 2,2'-biphenol with the terminal oxygens of the C4 sugar Threitol (1,2,3,4-tetrahydroxybutane) would offer a practical and flexible approach. The internal oxygen at C₂ and C₃ would be protected as a dioxolane in **9a**. (*L*)-Ethyl tartrate as precursor gives easy access to the desired (*S,S*)-intermediate.²¹ The C6 reduced sugar Mannitol is the building block for both **9a** and **9b** with four contiguous stereogenic centres,²² permitting a common retrosynthetic pathway, indicated in Scheme 3. Intermediate **9b** maintains the (*R,R,R,R*)-configuration of Mannitol whilst **9c** possesses the (*S,R,R,S*)-configuration of Iditol. With the desired products in hand, the influence of remote central chirality on conformation and preferred axial configuration of the biaryl could be defined, barriers to atropisomerisation estimated, and modelling of the interconversion step conducted. Insights into the further design of atropisomerically pure meta-meta'-bridged biphenols would be encouraging. Notably, 2,2'-binaphthols had been prepared with a high level of stereocontrol through the agency of an enantiomerically pure dioxolane in an 8-atom linking group.^{23,24}

2.2 Details of the synthetic route

All the syntheses of **1-7** outlined in Schemes 4 and 5 were carried out in a related manner. The first step initially involved base-promoted coupling of a *m*-(bromomethyl)aryl bromide **8** with the C4 precursor **9a**; this bromide was employed successfully in the synthesis of **1**, using nickel-promoted Ullmann coupling on the intermediate **10**. The procedure failed, however, when the desired targets carried 2-methoxy- or 2-hydroxy-substituents, whereas the use of stoichiometric Ni(PPh₃)₄ as the coupling reagent proved effective for the remaining targets and the more reactive aryl iodide **11a**.²⁵ This modification proved successful for compounds **2**, **4** and **6**, together with **9a**, **9b** or **9c** respectively in the second step. For the biphenols **3**, **5** and **7**, SEM protection of the hydroxyl groups was necessary for satisfactory completion of the first step, using the isolable reagent **11b**, followed by deprotection with fluoride ion in the final stage of synthesis from intermediate **12**.²⁶ Note that the (*S,S*) configuration of the dioxolane moiety in the C4 intermediate is opposite to both the (*R,R*)-configured C6 intermediates of synthesis from Mannitol.

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2.3 Solid- state structures

Crystals of compound **1** suitable for X-ray analysis were grown from CH₂Cl₂ /pentane. The compound crystallised in the P₂₁ space group as a quasi-racemic pair. This structural class has been extensively discussed, including examples possessing axial chirality albeit not simple biphenyls, are covered in reviews.²⁷ The structure is shown in Figure 1a. The averages of the inner and outer dihedral angles for the biaryl linkage were low but distinct, averaging -19.4° for one and +4.7° for the other. The first one possesses (*aS*;S,S) configuration and the second (*aR*;S,S) configuration. The components possess similar unsymmetrical C1 conformations of the linker. The closest intermolecular contacts within the pair are between the arene ring of one partner and the macrocyclic linker ring of the other.

Crystals of the corresponding di-OME biaryl **2** were grown from CH₂Cl₂ /heptane. The resulting X-ray structure is shown in Figure 2b. This compound crystallised as a single molecule in space group C2. Analysis of the structure reveals inner and outer dihedral angles at the inter-aryl bond averaging -81.8° with (*SS,aS*)-configuration; there is little strain-induced distortion apparent and the molecular C2 symmetry is apparent in the regular conformation of the linking chain. Disorder of the CMe₂ group was observed and is indicated by an arrow.

In neither case did the refinement proceed smoothly to convergence, perhaps because the crystals possess limited stability under X-ray irradiation. Nevertheless, several of the key features of their structure and biaryl conformations are revealed, and these are in accord with the results from CD spectra discussed in Section 2.4. It was not possible to prepare suitable crystals with either of the low melting, highly soluble di-OME biaryls **4** or **6**.

The biphenol analogues **3**, **5** and **7** were high-melting solids, but all attempts at crystal growth led to immediate or eventual formation of fine powders. A low energy conformational barrier is a recognised cause of crystal instability.²⁸ Much useful stereochemical information for all the compounds **2-7** was obtained from their NMR and ECD spectra as detailed below, however.

2.4 NMR analyses

The ¹H and ¹³C NMR spectra of compound **1** remain sharp at all temperatures whereas both these spectra from **2** show broadening at room temperature that is broadly independent of the solvent. Both sets of CH₂ groups in **2** showed temperature dependent line widths with benzylic protons being the more informative. At 213 K, two resolved AB quartets in 3:1 ratio were observed in the 4.10-4.80 ppm region. On raising the probe temperature gradually line width increased up to 298K, then sharpened again to a single AB quartet by 343K. Dynamic broadening is also observed in the second AB quartet that overlaps with the dioxolane ring protons. A related case of dynamic broadening in both the ¹H and ¹³C NMR spectra was observed for the closely related intermediate bis-SEM ether of **3**, although only one of the two isomers gave interpretable spectra at RT.

The ¹H NMR spectrum of **6** also shows dynamic broadening, and at low temperatures a minor species is resolved at ca. 10% of the total concentration. The benzylic protons resolve as two AB quartets at 242K, with the major component of the H_a signal strongly deshielded (Figure 2). The rate of equilibration was established by VT line shape analysis of the benzylic CH₂ region over the range 242K-331K in 11K intervals. The exchange rate corresponds to an activation free energy $\Delta G^\ddagger = 63 \text{ kJ.mol}^{-1}$ at 273K. This dynamic process is best explained as interconversion between the (*aS*)-isomer, as drawn in Fig 4, and the (*aR*)-isomer. Taken alone, however, this provides no insight into which one of these is favoured, nor the preferred conformation in solution. There is a striking difference between the chemical shifts of the diastereotopic H_x,H_{x'} and H_y,H_{y'} pairs of benzylic protons, but this is only observed in the major isomer.²⁹ Over the full temperature range ¹H NMR reveals only the single dynamic process shown in Figure 2, where this dynamic process interconverts (*aS*) and (*aR*) isomers. The magnetic equivalence of H_x and H_{x'} and of H_y and H_{y'} implies that the isomers either possess C2 symmetry, or achieve it for a ground state of C1 symmetry by a fast interconversion process on the NMR timescale.

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³³ Model building for all initial state geometries was based on the two crystal structures shown in Figure 1, applying the (*S,S*)-dioxolane configuration and correcting accordingly for the DFT results from ethers **4** and **6** in Figure 5.

³⁴ DFT calculations of electronic energy were carried out with the B3LYP-D3 functional and (6-31G(2d,p) basis set without solvent; TD-SCF calculations followed a similar protocol, in MeOH solvent according to the SMD model. Fuller details of the individual conformations are appended in the SI.

³⁵ Adapted from the *D. Phil* thesis of Andrew Mattison, Oxford, 2001.

2.5 Electronic Circular Dichroism.

An immediate concern was to establish the axial preferences of the 2,2'-methoxy compounds **2**, **4** and **6** in solution. Electronic Circular Dichroism (ECD) spectra may be informative in this regard, but due caution is required concerning assignment. On its own, the technique can usefully correlate similar chiroptical properties, but not be used safely for assignment of absolute configuration, albeit made more reliable when augmented by time-dependent DFT calculations.³⁰ ECD spectra for compounds possessing both axial and central chirality may be dominated by axial chirality.³¹ Ethers of 2,2'-biphenol biased from a 1:1 (*aS*):(*aR*) ratio by a stereogenic centre in the ether side chains, show excellent correlation between the computed sign of the Cotton effect and the sign observed by ECD.³² When the band in the region of 280 nm shows a positive Cotton effect this is indicative of (*aS*)-configuration.

On the basis of the spectra recorded in Figure 3, the positive long wavelength ECD trace for both bis-ether **2** and biphenol **3**, where the central chirality is (*S,S*), suggest a predominance of the (*aS*)-isomer in MeOH solution. For **4** and **5** derived from (*R,R,R,R*)-mannitol, the negative long wavelength ECD trace likewise suggests predominant (*aR*) configuration in MeOH solution. For diols **6** and **7**, with (*S,R,R,S*)-configuration in the linking chain, the positive long wavelength Cotton curve suggests (*aS*)-configuration. This unexpected difference shows that the rigidity of the dioxolane is overridden by the configuration of the adjacent CHMe positions.

The dimethyl ether in the Mannitol series **4** exhibits sharp ¹H NMR signals at both 218K and 298K, but slight broadening is observed at 258K. This is consistent with undetectably low levels of a second species in dynamic equilibrium.

2.6 DFT and TD-DFT calculations.

In order to make the results of ECD measurements secure, a set of DFT and TD-DFT calculations were carried out to complement experiment. For each of the three ethers, there are four basic geometries, representing the minimum energy states of the C1 and C2 conformations for both (*aR*) and (*aS*) isomers.³³ These are single point calculations and limited by the fact that the C1 species in particular are conformationally labile, less so the C2 species. Gratifyingly, the computed sign of the Cotton curve in the long wavelength region accords with the ECD experiments and gives greater confidence to the assignments (Figure 4). For (*S,S*)-**2** all fall within a 1.1 kcal.mol⁻¹ range with the C1 conformer of the (*S,S,aS*)-isomer most stable, and the C2 isomer of the (*S,S,aR*) isomer the least stable. The results accord with the observed 3:1 ratio between (*aS*) and (*aR*) observed by NMR, indicated to be in favour of the (*aS*) isomer by ECD, and consistent with the X-ray structure of **2**. Wider differences were found between the computed minimum energies for the four conformers of both (*R,R,R,R*)-**4** and (*S,R,R,S*)-**6**. For **4**, both (*aR*) isomers are lower in energy than either (*aS*)-isomer, with (*aS*)-C2 forbiddingly high. For **6**, the trend is similar but surprisingly in reverse - (*aS*)-C2 is favoured, but of similar energy to the (*aR*)-C2 isomer whilst the (*aR*)-C2 isomer is strongly disfavoured. Hence the configuration of the CHMe centres, not the dioxolane, is the main factor controlling the relative stability of isomers. The key dihedral angles arising from DFT calculations for the most stable forms of **4** and **6** are shown in Figure 4. For structure **4**, the two C-methyl groups occupy one *exo*- and one *endo*-position in the macrocyclic ring, whilst for structure **6** these methyl groups are both *exo*-. Inspection of the least favoured (*aR*)-C2 form of **6** makes this clear; in this isomer the methyl groups occupy *endo*-positions such that there are close H-H interactions with the biaryl moiety, and the relatively rigid C2 structure is destabilised by short (ca. 2 Å) H---H interactions. Likewise, for **4**, where the unfavourable C2-(*aS*)-isomer has similar close contacts above and below the mean plane. All the macrocyclic rings are strained, and analysis the different C2 structures reveal the origins of the differences in energy.

3 Conclusions

The synthesis of compounds **1-7** together with the studies described here provide a template towards attaining the original goal. As synthesized, these structures are not rigid enough to produce stable atropisomers. That especially applies to the diols, that would have far greater potential for catalysis than the ethers. All interconvert rapidly on the NMR timescale between (*aR*) and (*aS*)-forms at all temperatures, but the close comparison of their behaviour in ECD analysis suggest that they are subject to the same conformational constraints. Given the ready availability of reduced sugars as the source of chirality, design of a variant that replaced the CHMe group with a bulkier CHR group would have favourable consequences. For **4**, the observed energy difference between the (*aR*) and (*aS*) isomers could be raised to the point where it was the exclusive contributor to any catalytic process, enhancing selectivity. For **6**, replacing the CHMe with a more sterically demanding group could make the C2-conformer with methyl groups *endo*- to the macrocyclic ring the only accessible conformer.

Additional Information: The SI of this paper contains crystal structure data associated with Figure 2, and the structures and coordinates for the calculations summarized in Figure 4 together with models of the C2 structures (GV6; embedded in .pptx format). Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC 2033961-2033962. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

4. Experimental³⁵

4.1 General

Reactions involving air-sensitive reagents were performed under a dry Ar atmosphere using standard vacuum line techniques with syringe or cannula transfers, using deoxygenated solvents. Chiral gas-liquid chromatographic analyses were performed on a Thermoquest Trace GC with 25m β -CYDEX capillary column; chiral HPLC were recorded using Jasco PU-980 equipment and UV detector, a 250mm Diacel OD column.

¹H NMR spectra were normally recorded on Brüker DPX or AMX machines. Abbreviations used in the description of spectra are: br = broad, m = multiplet, s = singlet, d = doublet, t = triplet, q = quartet, qu = quintet, dd = doublet of doublets, dt = doublet of triplets, td = triplet of doublets, J = coupling constant.

Exact masses were measured by ES-MS on a Waters 2790-Micromass LCT or V.G. Autospec spectrometer.

ECD spectra were recorded on a Jasco J720 spectrometer.

All DFT calculations were carried out on the Oxford University ARC facility using Gaussian16 together with Gaussview6.

Extreme caution was exercised when handling benzyl halides, with all operations being performed while wearing gloves and working in a fume hood. Where possible they were used without further purification.

4.2 Synthesis of 1; Threitol series

(*S,S*)-**9a** (162mg, 1 mmol) in THF (2 ml) was cautiously added to pentane washed NaH (from 60% dispersion in mineral oil, 125mg, 3.1mmol) in THF (6 ml) at 0° C, and stirred at room temperature for 2h. 3-bromobenzyl bromide **8**, dissolved in THF (2ml), was added and the solution further stirred for 14h at room temperature then at 60° C for 6h. Water (5ml) was added and THF removed *in vacuo*. Further H₂O (10ml) was added before extraction with ether (3 x 20ml). The combined organics were washed with brine (20ml), dried over MgSO₄, filtered and the solvent removed *in vacuo*. Flash chromatography (pentane/ethyl acetate, 10:1) gave the product **10** as a clear oil (516mg, 100%) ¹H NMR (500 MHz, CDCl₃) δ 7.50 (s, 2H, 2-ArH), 7.42 (d, 2H, J = 7.7 Hz, 4-ArH), 7.24 (d, 2H, J = 7.6 Hz, 6-ArH), 7.21 (dd, 2H, J = 7.6 Hz, J' = 7.6 Hz, 5-ArH), 4.56 (s, 4H, CH₂ benzyl), 4.05 (m, 2H, CH), 3.63 (m, 4H, CHCH₂), 1.45 (s, 6H, C(CH₃)₂). ¹³C NMR (125.8 MHz, CDCl₃) δ 140.3 (Ar), 130.6 (ArH), 130.4 (ArH), 129.9 (ArH), 125.9 (ArH), 122.4 (Ar), 109.7 ((CH₃)₂C), 77.3 (CH₂), 72.6 (CH₂), 70.8 (CH), 26.9 (Me). IR (Thin film) 3060 (w, Ar-H), 2985 (s), 2964 (s), 1570 (s), 1474 (s), 1428 (s), 1369 (s), 1211(s), 1087 (s), 848 (m), 778 (s), 691 (m), 671 (m). MS m/z (CI+) 501.1 (MH⁺, 100%), 518.1 (MNH₄⁺, 25%). HRMS C₂₁H₂₅O₄Br calc. 501.010, found 501.009; $[\alpha]_D^{25} = -7.5$, c = 0.1g/100ml, CHCl₃.

Synthesis of (10S,14S)-12,12-dimethyl-8,11,13,16-tetraoxatetracyclo[16.3.1.1^{2,6}.0^{10,14}]tricosal[1(22),2,4,6(23),18,20]hexaene 1

Using Caubere's procedure, intramolecular Ullmann coupling of **10** was carried out on a 1 mmol scale. Removal of solvent *in vacuo* gave a pale yellow solid, that was recrystallised from CH₂Cl₂/ pentane to give **1** as a white crystalline solid (205 mg, 60%). m.p. 169° C. ¹H NMR (500 MHz, CDCl₃) δ 7.83 (s, 2H, J = 7.6 Hz, H-22 & 23), 7.59 (d, 2H, J = 7.6 Hz, H-3 & 21 or H-5 & 19), 7.41 (dd, 2H, J = 7.6 Hz, J' = 7.6 Hz, H-4 & 20), 7.07 (d, 2H, J = 7.6 Hz, H-3 & 21 or H-5 & 19), 4.89 (d, 2H, J = 15.6 Hz, 1 x H-7 & 17), 4.78 (d, 2H, J = 15.6 Hz, 1 x H-7 & 17), 4.46 (m, 2H, H-14 & 15), 3.89 (d, 2H, J = 10.7 Hz, 1 x H-9 & 15), 3.75 (dd, 2H, J = 10.7 Hz, J' = 4.8 Hz, 1 x H-9 & 15). ¹³C NMR (125.8 MHz, CDCl₃) δ 140.2 (Ar), 138.5 (Ar), 129.1 (ArH), 125.9 (ArH), 124.1 (ArH), 123.2 (ArH), 109.5 ((CH₃)₂C), 76.8 (CH), 70.3 (CH₂), 68.6 (CH₂), 26.7 (Me). IR (KBr disk) 2986 (m), 2870 (s), 1076 (s), 1027 (s), 769 (s) cm⁻¹. MS m/z (APCI+) 341.2 (MH⁺, 5%), 359.1 (MNH₄⁺, 15%), 375.0 (MCl⁺, 5%). HRMS C₂₁H₂₅O₄ (calc. 341.175, found 341.175). $[\alpha]_D = -29.2$ (MeOH, c = 0.20 g./100 ml). UV (MeOH) λ_{max} 210 nm ($\epsilon = 42000$ M⁻¹cm⁻¹), 260 nm ($\epsilon = 19000$ M⁻¹cm⁻¹). ECD (MeOH) 215 ($\Delta\epsilon = -20$ M⁻¹cm⁻¹), 230 ($\Delta\epsilon = +12$ M⁻¹cm⁻¹), 290 ($\Delta\epsilon = +1$ M⁻¹cm⁻¹) nm.

4.2 Synthesis of 2

In situ preparation of 3-iodo-4-methoxybenzyl bromide 11a

Dibenzoyl peroxide (40mg) in CCl₄ (10ml) was dried over anhydrous MgSO₄ and added to 2-iodo-4-methylanisole (992 mg, 4mmol). *N*-Bromosuccinamide (718 mg, 4 mmol) was added to the solution and the suspension stirred vigorously at reflux whilst being irradiated with a 60 W tungsten filament lamp for 2h. After filtration, the majority of the solvent was removed *in vacuo* to give a deep red solution. *NB Removing all solvent led to decomposition.* ¹H NMR analysis showed c. 70% conversion. The product was dissolved in CH₂Cl₂, washed with thiosulfate, dried over anhydrous MgSO₄ and the CH₂Cl₂ removed by *in vacuo* azeotropic distillation with THF to give a solution of product **11a**. ¹H NMR (200 MHz, CDCl₃) δ 7.83 (d, 1H, J = 2 Hz, 2-ArH), 7.36 (dd, 1H, J = 9 Hz, J' = 2 Hz, 6-ArH), 6.79 (d, 1H, J = 9 Hz, 5-ArH), 4.46 (s, 2H, CH₂), 3.90 (s, 3H, OMe). ¹³C NMR (50.3MHz, CDCl₃) δ 158.1 (Ar), 140.0 (ArH), 131.9 (Ar), 130.4 (ArH), 110.8 (ArH), 85.9 (Ar), 56.4 (OMe), 23.3 (CH₂). MS m/z (CI) 326/328 (MH⁺).

Synthesis of 2,3-O-isopropylidene-1,4-bis-O-(4-methoxy-3-iodophenylmethyl)-D-threitol **12**

Compound (*S,S*)-**9a** was added at 0°C in THF (1ml) to pentane-washed NaH (from 94 mg, 60% in mineral oil, 1.56 mmol). The reaction mixture was stirred for 1h then raised to RT and stirred for a further 1h. A solution of **11a** (2 mmol) in THF (c. 1.5ml) was added and the mixture stirred at room temperature for 2h then at 60°C for 18h. Water (10 ml) was added before extraction with ether (3 x 20 ml). The combined organics were washed with brine (20 ml), dried over anhydrous MgSO₄, filtered and the solvent removed *in vacuo*. Silica gel chromatography gave product **12** (yellow oil) (184mg, 43%). ¹H NMR (400 MHz, CDCl₃): δ 7.75 (d, 2H, J= 2.0 Hz, 2-ArH), 7.25 (dd, 2H, J= 8.4 Hz, J'= 2.0 Hz, 6-ArH), 6.77 (d, 2H, J= 8.4 Hz, 5-ArH), 4.47, (s, 4H, CH₂ benzyl), 4.01 (m, 2H, CH), 3.87 (s, 6H, OMe), 3.58 (m, 4H, CHCH₂), 1.43 (s, 6H, CMe₂). ¹³C NMR (100.6, CDCl₃) δ 157.6 (Ar), 138.9 (ArH), 132.1 (Ar), 129.1 (ArH), 110.6 (ArH), 109.7 ((CH₃)₂C), 85.8 (Ar), 77.4 (CH), 72.2 (CH₂), 70.6 (CH₂), 56.4 (OCH₃), 27.0 (Me). IR (thin film) 2985 (s), 2937 (s), 1721 (w), 1600 (s), 1494 (s), 1462 (s), 1441 (s), 1370 (s), 1257 (s, br), 1092 (s, br), 892 (m), 848 (m), 812 (s), 756 (m), 664 (s) cm⁻¹. MS *m/z* (CI+) 672.0 (MNH₄⁺, 0.25%).

Synthesis of (1*S*, 14*S*)-12,12-dimethyl-3,21-dimethoxy-8,11,13,16-tetraoxatetracyclo[16.3.1.1^{2,6}.0^{10,14}]tricoso [1(22),2,4,6(23),18,20]hexaene **2**

A solution of compound **12** (65mg, 0.1 mmol) and (PPh₃)₄Ni (166mg, 0.15 mmol) in DMF (15 ml) under Ar was stirred at 0°C for 15 min and 25°C for 1h., then for 48h at 50°C. After aqueous workup, drying and silica chromatography this gave **2** a white solid (22mg, 55%), m.p. 194°C. ¹H NMR (500 MHz, CDCl₃, 298K) δ 7.25 (s, br, 2H, H-22 & 23), 7.09 (d, br, 2H, J= 8.2, H-4 & 20), 6.92 (d, br, 2H, J= 8.3, H-5 & 19), 4.9-4.5 (m, vbr, 4H, 2 x H-7 & 17), 4.25 (m, vbr, 2H, H-10 & 14), 3.92 (m, 2H, 1 x H-9 & 15), 3.87 (s, 6H, OMe), 3.74 (m, br, 2H, 1 x H-9 & 15), 1.47 (s, 6H, Me) ppm. ¹³C NMR (100.6, CD₂Cl₂, 203K) δ (Major conformer) 155.3 (Ar), 131.6 (ArH), 130.5 (Ar), 128.1 (Ar), 126.2 (ArH), 110.2 (ArH), 108.6 ((CH₂)₂C), 76.3 (CH), 69.6 (CH₂), 68.7 (CH₂), 55.6 (OMe), 26.1 (Me) ppm; (NB Minor conformer not assigned). MS *m/z* (APCI+) 401.2 (MH⁺, 60%), 423.1 (MNa⁺, 20%). C₂₃H₂₈O₆ requires C= 68.98%, H= 7.05%. Found C 68.63%, H 6.53%. [α]_D²⁰ = +15.7 (DCM, c= 0.02g/100ml). UV (MeOH) λ_{max} 220 (ε 24000 M⁻¹cm⁻¹), 290 (ε 5000 M⁻¹cm⁻¹) nm. CD (MeOH) 215 (Δε= -25 M⁻¹cm⁻¹), 230 (Δε= +20 M⁻¹cm⁻¹), 290 (Δε= +2 M⁻¹cm⁻¹) nm.

4.3 Synthesis of 3

[2-(2-iodo-4-methylphenoxy)methoxy]ethyl]trimethylsilane **11b**

2-Iodo-4-methylphenol (3.9g, 16.7mmol) was dissolved in DCM (40ml) under an Ar atmosphere. Diisopropylethylamine (6.21g, 8.4ml, 48mmol) was added. The solution was cooled to 0°C and 2-(trimethylsilyl)ethoxymethyl chloride (4.2g, 4.5ml, 25mmol) added.. After 18 h. at RT, workup (MgSO₄), drying, removal of solvent *in vacuo* and silica chromatography gave the reactant SEM ether as a yellow oil, (4.5g, 74%). ¹H NMR (400 MHz, CDCl₃) δ, 1H, 1.9 Hz, 3-ArH), 7.09 (dd, 1H, J= 8.4 Hz, J'= 1.9 Hz, 5-ArH), 6.99 (d, 1H, J= 8.4 Hz, 6-ArH), 5.26 (s, 2H, OCH₂O), 3.82 (m, 2H, OCH₂CH₂), 2.27 (s, 3H, ArMe), 0.98 (m, 2H, CH₂Si), 0.03 (s, 9H, SiMe₃). ¹³C NMR (100.6, CDCl₃) δ 154.1(Ar-O), 139.7 (ArH), 133.1 (Ar), 129.9 (ArH), 114.9 (ArH) 93.5 (OCH₂O), 87.2 (Ar-I), 66.5 (OCH₂CH₂), 20.0 (ArCH₃), 18.0 (CH₂Si), 1.4 ((SiCH₃)₃). IR (thin film) 3029 (w), 2953 (s), 2822 (s), 2897 (s), 1489 (s), 1235 (s), 1095 (s), 1038 (s), 993 (s), 860 (s), 836 (s), 758 (m), 729 (m), 694 (m), 665 (m) cm⁻¹. MS *m/z* (APCI+) 382 (MNH₄⁺, 50%). HRMS C₁₃H₂₅NO₂SiI (calc. 382.0699, found 382.0695). This product (3.64g, 10 mmol) was reacted at reflux in CCl₄ (40 ml) with dibenzoyl peroxide (100 mg) in dry and *N*-bromo-succinimide (1.78g, 10mmol) under Ar for 4 h. Silica chromatography gave **11b** as a clear oil (2.13g, 48%). ¹H NMR (400 MHz, CDCl₃) δ, 1H, J= 2.2 Hz, 3-ArH), 7.32 (dd, 1H, J= 8.5 Hz, J'= 2.2 Hz, 5-ArH), 7.05 (d, 1H, J= 8.5 Hz, 6-ArH), 5.29 (s, 2H, OCH₂O), 4.42 (s, 2H, CH₂Br), 3.79 (m, 2H, OCH₂CH₂), 0.96 (m, 2H, CH₂Si), 0.02 (s, 9H, SiMe₃). ¹³C NMR (100.6 MHz, CDCl₃) δ 139.9 (ArH), 132.8 (Ar), 130.3 (ArH), 114.7 (ArH), 93.3 (OCH₂O), 87.0 (Ar), 66.8 (OCH₂CH₂), 32.1 (CH₂Br), 18.0 (CH₂Si), 1.4 (Si(CH₃)₃). IR (Thin film) 2953 (s), 2925 (m), 2905 (m), 1597 (m), 1489 (s), 1242 (s), 1220 (s), 1155 (m), 1097 (s), 1037 (s), 984 (s), 916 (m), 859 (s), 836 (s), 758 (w), 694 (w) cm⁻¹. MS *m/z* (CI+) 460/462 (MNH₄⁺, 10%).

1,4-bis-O-[3-iodo-4-[[2-(trimethylsilyl)ethoxymethoxy] phenylmethyl]-2,3-O-isopropylidene-(*S,S*)-threitol **13**

Diol **9a** (113 mg, 0.7 mmol) in THF (4ml) was stirred with twofold excess NaH for 1 h. at RT, and **11b** (745mg, 1.68mmol) in THF (6ml). A further twofold excess of NaH was added. After 18h at RT, MeOH was added. Volatiles were removed in *vacuo* and the residue added to H₂O (20ml) and ether (20ml). Workup, drying and silica chromatography gave SEM ether **13** as a clear oil (454 mg, 76%). ¹H NMR (400 MHz, CDCl₃) δ 7.76 (d, 2H, J= 2.0 Hz, 2-ArH), 7.23 (dd, 2H, J= 8.4 Hz, J'= 2.0 Hz, 6-ArH), 7.04 (d, 2H, J= 8.4 Hz, 5-ArH), 5.28 (s, 4H, OCH₂O), 4.48 (s, 4H, CH₂ benzyl), 4.01 (m, 2H, CH), 3.79 (m, 4H, OCH₂CH₂), 3.58 (m, 4H, CHCH₂), 1.43 (s, 6H, CH₃ dioxolane), 0.95 (m, 4H, CH₂Si), 0.00 (s, 18H, Si(CH₃)₃). ¹³C NMR (100.6, CDCl₃) δ 155.7 (Ar), 138.8 (ArH), 133.2 (Ar), 129.0 (ArH), 114.6 (ArH), 109.7 (CMe₂), 93.3 (OCH₂O), 87.1 (Ar), 77.4 (CH), 72.2 (benzyl), 70.6 (CHCH₂), 66.6 (OCH₂CH₂), 27.0 (Me of dioxolane), 18.0 (CH₂Si), -1.4 (SiMe₃). IR (Thin film) 2953 (s), 2934 (s), 1738 (m), 1600 (s), 1489 (s), 1237 (s), 1094 (s), 1038 (s), 988 (s), 917 (m), 835 (s), 757 (m), 694 (m), 664 (m) cm⁻¹. MS *m/z* (APCI+) 904 (MNH₄⁺, 5%)

(10*S*,14*S*)-12,12-dimethyl-3,21-dihydroxy-8,11,13,16-tetraoxatetracyclo[16.3.1.1^{2,6}.0^{10,14}]tricosal[1(22),2,4,6(23),18,20]hexaene

Ni(PPh₃)₄ (1.04g, 0.94mmol) and SEM ether **13** (454mg, 0.51mmol) in dry DMF (50ml) were shielded from light and stirred for 20 min at 0°C, 40 min at RT and 18 h at 50°C. Workup, drying and chromatography (4:1 pentane / ethyl acetate) to give coupled SEM ether **14** as a yellow oil, with single spot TLC (183 mg, 57%). m.p. 223–225°C. ¹H NMR (250 MHz, CDCl₃, 233K) δ (mixture of isomers) 7.4–7.0 (m, 6H, H-4,5,19,20,22 & 23), 5.27 (m, 4H, OCH₂O), 4.89 (d, 1.6H, J= 14.8 Hz, 1 x H-7 & 17 - major isomer), 4.66 (d, 1.6H, J= 14.9 Hz, 1 x H-7 & 17 - major isomer), 4.53 (d, 0.4H, J= 13.9 Hz, 1 x H-7 & 17 - minor isomer), 4.4–4.2 (m, 2.4H, 1 x H-7 & 17 - minor isomer and H-10 & 14), 4.0–3.5 (m, 8H, OCH₂CH₂ and 2 x H-9 & 15), 1.51 (s, 6H, Me-12), 0.94 (m, 4H, CH₂Si), -0.02 (s, 18H, SiMe₃) ppm. ¹³C NMR (62.9MHz, CDCl₃, 233K) δ major isomer 154.7 (Ar), 132.8 (ArH), 132.3 (Ar), 129.9 (ArH), 127.2 (Ar), 116.0 (Ar), 110.9 (CMe₂), 109.9 (ArH), 94.4 (OCH₂O), 77.0 (C-10 & 14), 70.8 (CH₂CH₂Si or C-7 & 17), 69.3 (CH₂CH₂Si or C-7 & 17), 66.6 (C-9 & 15), 27.2 (CMe₂), 18.5 (CH₂Si), -0.7 (SiMe₃) ppm. IR (Thin film) 2952 (s), 2925 (s), 2896 (s), 2870 (s), 1610 (w), 1580 (w), 1503 (s), 1404 (w), 1380 (m), 1249 (s), 1222 (m), 1169 (m), 1085 (s), 1003 (s), 938 (m), 919 (m), 859 (s), 836 (s), 759 (w), 694, 665 (m) cm⁻¹. MS *m/z* (CI⁺) 932.0 (MNH₄⁺, 20%), 550.4 ([M-CH₂CH₂SiMe₃]NH₄⁺, 20%). Deprotection of **13** (183mg, 0.29mmol) follows the procedure described for the final step to **2** and gave **3**; white solid (41mg, 38%). ¹H NMR (500 MHz, CD₂Cl₂, 298K) δ 7.43 (d, 2H, J= 2.2 Hz, H-22 & 23), 7.77 (dd, 2H, J= 8.2 Hz, J'= 2.2 Hz, H-5 & 19), 6.95 (d, 2H, J= 8.2 Hz, H-4 & 20), 6.93 (s, br, 2H, OH), 4.79 (d, 2H, J= 14.9 Hz, 1 x H-7 & 17), 4.67 (d, 2H, J= 14.9 Hz, 1 x H-7 & 17), 4.33 (m, 2H, H-10 & 14), 3.94 (m, 2H, 1 x H-9 & 15), 3.79 (m, 2H, 1 x H-9 & 15), 1.46 (s, 6H, Me). ¹³C NMR (100.6 MHz, d₆-acetone, 298K) δ 152.7 (Ar), 131.9 (Ar), 131.3 (ArH), 126.8 (Ar), 126.7 (ArH), 117.0 (ArH), 111.4 (CMe₂) 78.0 (C-10 & 14), 70.8 (C-9 & 15), 70.2 (C-7 & 17), 26.7 (Me); IR (KBr disk) 3300 (s, br), 2965 (m), (m) 2920 (s), 2857 (s), 1590 (w), 1640 (w), 1500 (s), 1450 (s), 1420 (s), 1372(s), 1237 (s), 1164 (s), 1068 (s), 1020 (m), 818 cm⁻¹. MS *m/z* (APCI⁻) 371.4 (M⁻, 100%). HRMS C₂₁H₂₃O₆ calc. 371.1495 found 371.1485. UV (MeOH) λ_{max} 221 nm (ε = 26000 M⁻¹cm⁻¹), 298 nm (ε = 9000 M⁻¹cm⁻¹). CD (MeOH) 220 (Δε = -18.2 M⁻¹cm⁻¹), 236 (Δε = +3.3 M⁻¹cm⁻¹), 294 (Δε = +2.4 M⁻¹cm⁻¹) nm.

4.4 Methyl ether series; synthesis of **4** and **6**

The precursor diols **9b** and **9c** were prepared according to the literature.²² The sequence for preparation of compounds **4** and **5** followed that for **2**, using stoichiometric (PPh₃)₄Ni in the coupling step with **11a**.

(*R,R,R,R*)-1,6-dideoxy-2,5-bis-*O*-(4-methoxy-3-iodophenyl methyl)-3,4-*O*-isopropylidene-mannitol **15**

Similarly to that described for SEM ether **13**. Flash chromatography was carried out twice: firstly elution with 4:1 pentane / EtOAc then elution with neat EtOAc to give product **15** as a yellow oil (108 mg, 66%); ¹H NMR (400 MHz, CDCl₃) δ 7.73 (d, 2H, J= 2.0 Hz, 2-ArH), 7.20 (dd, 2H, J= 8.3 Hz, J'= 2.0 Hz, 6-ArH), 6.71 (d, 1H, J= 8.4 Hz, 5-ArH), 4.49 (2H, d, J= 11.6 Hz, CHH benzyl), 4.34 (2H, d, J= 11.6 Hz, CHH benzyl), 3.87 (m, 2H, CHCHMe), 3.84 (s, 6H, OMe), 3.62 (m, 2H, CHMe), 1.40 (s, 6H, CMe₂), 1.24 (d, 6H, J= 6.2 Hz, CHCH₃). ¹³C NMR (100.6, CDCl₃) δ 157.5 (Ar), 138.9 (ArH), 132.7 (Ar), 129.1 (ArH), 110.6 (ArH), 109.7 (CMe₂), 85.7 (Ar), 81.5 (CH), 76.1 (OMe), 69.5 (CH₂), 56.4 (CH), 27.3 (CMe₂), 15.2 (CHMe₂). IR (Thin Film) 2928 (s), 1600 (m), 1492 (s), 1458 (m), 1378 (m), 1255 (s), 1080 (m, br), 1048 (m), 875 (w), 808 (m), 663 (m) cm⁻¹. MS *m/z* (APCI⁺) 700.1 (MNH₄⁺, 0.25%). HRMS was not obtainable for the parent ion.

(*R,R,R,R*)-9,12,12,15-tetramethyl-3,21-dimethoxy-8,11,13,16-tetraoxatetracyclo[16.3.1.1^{2,6}.0^{10,14}]tricosal[1(22),2,4,6(23),18,20]hexaene **4**.

From **15**, similarly to the final stage in synthesis of **2**; compound **4** was obtained as a white solid (15mg, 53%) m.p. 59–60°C. ¹H NMR (500 MHz, d₈-toluene, 258K) δ 7.53 (d, 2H, J= 1.8 Hz, H-22 & H-23), 6.81 (dd, 2H, J= 8.5 Hz, J'= 1.8 Hz, H-5 & 19), 6.62 (d, 2H, J= 8.6 Hz, H-4 & 20), 4.82 (d, 2H, J= 14.8 Hz, 1 x H-7 & 17), 4.17 (d, 2H, 14.7 Hz, 1 x H-7 & 17), 4.06 (m, 2H, H-10 & 14), 3.64 (m, 2H, H-9 & 15), 3.48 (s, 6H, OMe), 1.34 (s, 6H, 2 x Me-12), 1.13 (d, 6H, d= 5.7 Hz, Me-9 & 15). ¹³C NMR, (100.6, CD₂Cl₂, 203K) δ 154.9 (Ar), 132.3 (ArH), 129.9 (Ar), 128.0 (Ar), 125.2 (ArH), 110.1 (ArH), 109.9 (CMe₂), 82.7 (OMe), 75.5 (CH), 66.8 (CH₂), 55.6 (CH), 27.0 (CMe₂), 13.4 (Me). IR (KBr disk) 2990 (m), 2927 (s), 2915 (m), 1505 (s), 1460 (m), 1450 (m), 1410 (m), 1380 (m), 1370 (m), 1276 (s), 1250 (s), 1170 (m), 1074 (s), 1027 (s), 804 (w) cm⁻¹. MS *m/z* (APCI⁺) 429.2 (MH⁺, 10%), 451.3 (MNa⁺, 10%). HRMS C₂₅H₃₃O₆ (calc. 429.228, found 429.228). CD (MeOH) 215 (Δε = +55 M⁻¹cm⁻¹), 230 (Δε = -45 M⁻¹cm⁻¹), 290 (Δε = -5 M⁻¹cm⁻¹) nm.

(*S,R,R,S*)-1,6-dideoxy-2,5-bis-*O*-(4-methoxy-3-iodophenylmethyl)-3,4-*O*-isopropylideneiditol **17**

A similar procedure to the synthesis of **12**, from **9c** and **11a**, gave product **17** as a yellow oil (60 mg, 36%). ¹H NMR (500 MHz, CDCl₃) δ 7.74 (d, 2H, J= 2.0 Hz, 2-ArH), 7.24 (dd, 2H, J= 8.4 Hz, J'= 2.1 Hz, 6-ArH), 6.76 (d, 2H, J= 8.415-ArH), 4.54 (d, 2H, J= 11.8 Hz, CHH benzyl), 4.36 (d, 2H, J= 11.8 Hz, CHH benzyl), 4.00(m, 2H, CH), 3.86 (s, 6H, OMe), 3.54 (m, 2H, CH), 1.42 (s, 6H, CMe₂), 1.21 (d, 6H, J= 6.4 Hz, CHCH₃). ¹³C NMR (125.8 MHz, CDCl₃) δ 157.5 (Ar), 138.9 (ArH), 132.8 (Ar), 129.1 (ArH), 110.6 (ArH), 109.0 (CMe₂), 85.7 (Ar), 79.3 (CH), 73.6 (OMe), 69.7 (CH₂), 56.4 (CH), 27.2 (CMe₂), 15.8 (CHMe₂). IR (Thin Film) 2983 (s), 2934 (s), 1600 (m), 1493 (s), 1254 (s), 1086 (s, br), 1049 (s), 1019 (s), 878, (w), 809 (m) cm⁻¹. MS *m/z* (APCI⁺) 699.9 (MNH₄⁺, 1%). HRMS was not obtainable for the parent ion

(*S,R,R,S*)-9,12,12,15-tetramethyl-3,21-dimethoxy-8,11,13,16-tetraoxatetracyclo[16.3.1.1^{2,6}.0^{10,14}]tricoso[1(22),2,4,6(23),18,20]hexaene **6**.

From **17**, similarly to the synthesis of **2**; white solid recrystallised from pentane, (0.016 g., 58%, m.p. 60-63°C). ¹H NMR (400 MHz, CDCl₃) δ 7.38 (s, 2H, H-22 & 23), 7.13 (d, 2H, J = 8.3 Hz, H-5 & 19), 6.93 (d, 2H, J = 8.3 Hz, H-4 & 21), 4.93 (d, br, 2H, J = 14.3, 1 x H-7 & 17), 4.47 (d, br, 2H, J = 14.3 Hz, 1 x H-7 & 17), 3.94 (s, 6H, OMe), 3.79 (m, 2H, H-9,10,14 & 15), 1.53 (s, 6H, CH₃-12), 1.29 (d, 6H, J = 6.4 Hz, Me-9 & 15). ¹³C NMR (100.6, CDCl₃) δ 156.6 (Ar), 135.4 (ArH), 129.8 (Ar), 129.6 (Ar), 126.7 (ArH), 114.1 (ArH), 111.5 ((CH₃)₂C), 80.4 (CH), 73.4 (CH₂ benzyl), 68.7 (OMe), 56.5 (CHMe), 28.3 ((CH₃)₂C), 15.5 (CHCH₃). IR (KBr disk) 3000 (m), 2933 (s), 2895 (m), 2880 (m), 1610 (w), 1580 (w), 1506 (s), 1455 (m), 1414 (m) 1378 (m), 1268 (s), 1245 (s), 1163 (m), 1076 (s), 1031 (s), 992 (w), 957 (w), 914 (w), 866 (w), 805 (m), 756 (m) cm⁻¹. MS *m/z* (APCI⁺) 429.3 (MH⁺, 10%). HRMS C₂₅H₃₃O₆ (calc. 429.228, found 429.228). CD (MeOH) 215 (Δε = -30 M⁻¹cm⁻¹), 230 (Δε = +30 M⁻¹cm⁻¹), 290 (Δε = +3 M⁻¹cm⁻¹) nm.

4.5 Synthesis of meta-bridged bis-biphenols **5** and **7**

(*R,R,R,R*)-1,6-dideoxy-2,5-bis-*O*-[3-iodo-4-[[2-(trimethylsilyl)ethoxy]methoxy]phenylmethyl]-3,4-*O*-isopropylidene mannitol **16**

Synthesis from **9b** and **11b**, similarly to the synthesis of compound **3**; workup, drying and chromatography (8:1 pentane / ethyl acetate) gave the product **16** as a clear oil (570mg, 62%). ¹H NMR (400 MHz, CDCl₃) δ 7.75 (d, 2H, J = 1.9 Hz, 2-ArH), 7.20 (dd, 2H, J = 8.4 Hz, J' = 1.9 Hz, 6-ArH), 7.01 (d, 2H, J = 8.4 Hz, 5-ArH), 5.26 (s, 4H, OCH₂O), 4.50 (d, 2H, J = 11.6 Hz, CHH benzyl), 4.44 (d, 2H, J = 11.6 Hz, CHH benzyl), 3.89 (m, 2H CHCHMe), 3.87 (m, 4H, CH₂CH₂), 3.63 (m, 2H, CHCHMe), 1.40 (s, 6H, CMe₂), 1.24 (d, 6H, J = 6.2 Hz). ¹³C NMR (100.6 MHz, CDCl₃) δ 155.6 (Ar), 138.8 (ArH), 133.7 (Ar), 129.0 (ArH), 114.5 (ArH), 109.7 (Ar), 93.3 (OCH₂O), 87.0 (CMe₂), 81.4 (CH), 76.1 (CH), 69.6 (CH₂), 66.6 (CH₂), 27.2 (CMe₂), 17.9 (CH₂Si), 15.2 (CHMe), -1.4 (SiMe₃). IR (Thin film) 2953 (s), 2905 (s), 1505 (m), 1498 (s), 1380 (m), 1249 (s), 1096 (s), 1040 (m), 970 (m), 870 (m), 836 (m) cm⁻¹. MS *m/z* (APCI⁺) 932 (MNH₄⁺, 20%).

(*R,R,R,R*)-9,12,12,15-tetramethyl-3,21-bis-[2-(trimethylsilyl)ethoxy]methoxy-8,11,13,16-tetraoxatetracyclo[16.3.1.1^{2,6}.0^{10,14}]tricoso[1(22), 2,4,6(23),18,20]hexaene **5**

Synthesis from **16** similarly to the procedure for **3**; giving the SEM-protected intermediate as an oily solid, (280mg, 68%). ¹H NMR (500 MHz, CDCl₃, 233K - only major diastereoisomer assignable) δ 7.40 (s, 2H, H-22 & 23), 7.25 (d, 2H, J = 8.4 Hz, H-5 & 19), 7.08 (d, 2H, J = 8.4 Hz, H-4 & 20), 5.26 (d, 2H, J = 7.3 Hz, OCHHO), 5.22 (d, 2H, J = 7.3 Hz, OCHHO), 4.97 (d, 2H, J = 15.0 Hz, 1 x H-7 & 17), 4.50 (d, 2H, J = 15.0 Hz, 1 x H-7 & 17), 4.20 (m, 2H, H-10 & 14), 3.85 (m, 2H, H-9 & 15), 3.72 (m, 2H, OCHHCH₂), 3.62 (m, 2H, OCHHCH₂), 1.44 (s, 6H, 2 x Me-12), 1.28 (d, 6H, J = 5.6 Hz, Me-9 & 15), 1.0-0.8 (m, 6H, CH₂Si), -0.04 (s, 18H, SiMe₃). ¹³C NMR (125.8 MHz, CDCl₃, 233K - only major diastereoisomer assignable) δ 154.0 (Ar), 133.3 (Ar), 132.3 (ArH), 130.2 (Ar), 125.9 (ArH), 116.1 (ArH), 111.0 (C-12), 94.5 (OCH₂O), 83.6 (C-10 & 14), 76.7 (C-9 & 15), 67.8 (C-7 & 17), 66.5 (OCH₂CH₂), 28.0 (2 x Me-12), 18.5 (CH₂Si), 14.6 (Me-9 & 15), -0.8 (SiMe₃). IR (Thin film) 2962 (s), 2915 (s), 1610 (w), 1587 (w), 1584 (s), 1455 (m), 1404 (m), 1381 (m), 1260 (s), 1089 (s, br), 1010 (s), 918 (m), 884 (s), 735 (m), 694 (m). MS *m/z* (CI⁺) 679.3 (MNH₄⁺, 2%), 562.1 ([M-OCH₂CH₂SiMe₃]NH₄⁺, 1%), 545.1 ([M-OCH₂CH₂SiMe₃]H⁺, 3%). After deprotection with TBAF similarly to the preparation of **3**, workup and silica chromatography gave product **6** as a white solid (57 mg, 34%). m.p. 110-111°C. ¹H NMR (400 MHz, d₆-acetone, 298K) δ 7.63 (d, 2H, J = 2.2 Hz, H-22 & 23), 7.07 (dd, 2H, J = 8.5 Hz, J' = 2.2 Hz, H-5 & 19), 6.93 (d, 2H, J = 8.5 Hz, H-4 & 20), 4.86 (d, 2H, J = 14.5 Hz, 1 x H-7 & 17), 4.57 (d, 2H, J = 14.5 Hz, 1 x H-7 & 17), 4.22 (m, 2H, H-10 & 14), 3.95 (m, 2H, H-9 & 15), 3.2-2.8 (s, br, 2H, OH), 1.45 (s, 6H, Me-9 & 15), 1.31 (d, 6H, J = 5.9 Hz, 2 x Me-12). ¹³C NMR (100.6 MHz, d₆-acetone) δ 153.3 (Ar), 133.2 (ArH), 132.5 (Ar), 127.5 (Ar), 126.7 (ArH), 117.6 (ArH), 111.3 (C-12), 84.8 (C-10 & 14), 78.0 (C-9 & 15), 68.2 (C-7 & 17), 28.1 (2 x Me-12), 14.8 (Me-9 & 15). IR (KBr disk) 3300 (s, br), 2989 (s), 2932 (s), 1630 (w), 1586 (w), 1503 (m), 1453 (m), 1420 (s), 1372 (s), 1250 (s), 1211 (s), 1161 (s), 1073 (s), 1023 (s), 862 (w), 813 (m), 737 (m), 666 (m) cm⁻¹. MS *m/z* (APCI⁻) 399.40 (M⁻, 100%). HRMS C₂₃H₂₇O₆ calc. 399.1808 found 399.1794. UV (MeOH) λ_{max} 210 (ε = 30000 M⁻¹cm⁻¹), 300 (ε = 7000 M⁻¹cm⁻¹) nm. CD (MeOH) 219 (Δε = +25.9 M⁻¹cm⁻¹), 236 (Δε = -5.7 M⁻¹cm⁻¹), 293 (Δε = -5.0 M⁻¹cm⁻¹) nm.

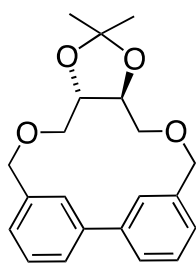
(*S,R,R,S*)-1,6-dideoxy-2,5-bis-*O*-[3-iodo-4-[[2-(trimethylsilyl)ethoxy]methoxy]phenylmethyl]-3,4-*O*-isopropylideneiditol **18**

From **9c** and **11b**, as for **16**; giving a clear oil **18** (523mg, 81%). ¹H NMR (400 MHz, CDCl₃) δ 7.76 (d, 2H, J = 2.0 Hz, 2-ArH) 7.23 (dd, 2H, J = 8.4 Hz, J' = 2.0 Hz, 6-ArH), 7.04 (d, 2H, J = 8.4 Hz, 5-ArH), 5.28 (s, 4H, OCH₂O), 4.56 (d, 2H, J = 11.9 Hz, CHH benzyl), 4.37 (d, 2H, J = 11.9 Hz, CHH benzyl), 4.00 (m, 2H, CHCHMe), 3.78 (m, 4H, OCH₂CH₂), 3.54 (m, 2H, CHMe), 1.43 (s, 6H, CMe₂), 1.21 (d, 6H, CHCH₃), 0.96 (m, 4H, CH₂Si), 0.00 (SiMe₃). ¹³C NMR (100.6, CDCl₃) δ 155.5 (Ar), 138.7 (ArH), 133.8 (Ar), 128.9 (ArH), 114.6 (ArH), 109.5 (CMe₂), 93.3 (OCH₂O), 87.0 (Ar), 79.3 (CH), 73.6 (CH), 69.7 (CH₂), 66.6 (CH₂), 27.1 (CMe₂), 18.0 (CH₂Si), 15.8 (CHMe), 1.4 (SiMe₃). IR (Thin film) 2953 (s), 2897 (s), 1613 (m), 1587 (w), 1512 (s), 1379 (m), 1249 (s), 1224 (s), 1172 (m), 1152 (m), 1088 (s), 1005 (s), 918 (m), 859 (s), 835 (s), 756 (w), 694 (w) cm⁻¹. MS *m/z* (APCI⁺) 932 (MNH₄⁺, 20%).

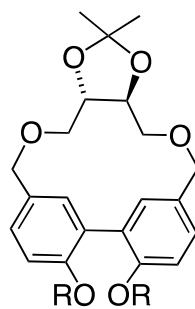
(*9S,10R,14R,15S*)-9,12,12,15-tetramethyl-3,21-dihydroxy-8,11,13,16-tetraoxatetracyclo[16.3.1.1^{2,6}.0^{10,14}]tricoso[1(22), 2,4,6(23),18,20]hexaene **7**.

Synthesis of intermediate SEM ether **18** (as for **16**): (187mg, 48%). ¹H NMR (500 MHz, CDCl₃, 233K) δ 7.29 (d, 2H, J = 1.7Hz, H-22 & 23), 7.20 (d, 2H, J = 8.3, H-4 & 21), 7.09 (dd, 2H, J = 8.3 Hz, J' = 1.7Hz, H-5 & 19), 5.29 (d, 2H, J = 7.4 Hz, OCHHO), 5.25 (d, 2H, J = 7.4 Hz, OCHHO), 4.90 (d, 2H, J = 14.7 Hz, 1 x H-7 & 17), 4.49 (s, 2H, H-10 & 14), 4.46 (d, 2H, J = 14.7 Hz, 1 x H-7 & 17), 3.77 (m, 4H, OCH₂CH₂), 3.66 (m, 2H, H-9 & 15), 1.50 (s, 6H, Me-12), 1.26, (d, 6H, J = 6.5 Hz Me-9 & 15), 0.93 (m, 4H, CH₂Si), -0.03 (s, 18H, SiMe₃). ¹³C NMR (125.8 MHz, CDCl₃, 233K),

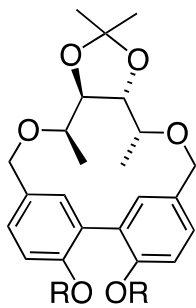
δ 155.7 (Ar), 135.1 (ArH), 131.7 (Ar), 129.1 (Ar) 127.0 (ArH) 115.3 (ArH), 111.3 (C-12), 94.0 (OCH₂O), 80.3 (C-10 & 14), 72.7 (C-9 & 15), 68.6 (C-7 & 17), 66.6 (OCH₂CH₂), 28.4 (Me-12), 18.5 (CH₂Si), 15.7 (Me-9 & 15), -0.8 (SiMe₃). IR (Thin film) 2953 (s), 2930 (s), 2905 (s), 1611 (m), 1511 (s), 1378 (s), 1249 (s), 1225 (s), 1152 (m), 1088 (s), 1005 (s), 918 (m), 859 (s), 835 (s), 694 (m) cm⁻¹. Deprotection as for **3**; chromatography of the crude product (1:1 pentane / ethyl acetate) gave compound **7** as a white solid (40mg, 37%). m.p. 183°C. ¹H NMR (400 MHz, CDCl₃, 298K) δ 7.56 (d, 2H, J= 2.0 Hz, H-22 & 23), 7.27 (s, 2H, OH), 7.00 (dd, 2H, J= 8.2 Hz, J'= 2.0 Hz, H-5 & 19), 6.88 (d, 2H, J= 8.2 Hz, H-4 & 20), 4.92 (2H, d, J= 14.9 Hz, 1 x H-7 & 17), 4.46 (m, 2H, H-10 & 14), 4.45 (d, 2H, J= 14.9 Hz, 1 x H-7 & 17), 3.78 (m, 2H, H-9 & 15), 1.51 (s, 6H, Me-12), 1.30 (d, 6H, J= 6.4 Hz, Me-9 & 15). ¹³C NMR (100.6, d₆-acetone, 298K) δ 153.6 (Ar), 134.1 (ArH), 132.4 (Ar), 127.5 (Ar), 127.3 (ArH), 117.3 (ArH), 111.5 (CMe₂), 81.0 (C-10 & 14), 75.5 (C-9 & 15), 69.2 (C-7 & 17), 28.6 (Me-12), 15.8 (Me-9 & 15). IR (KBr disk) 322 (s, br), 3040.



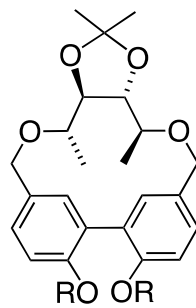
1



2 R = OMe
3 R = H

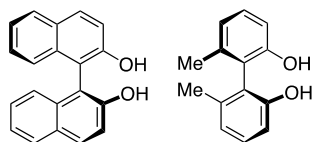


4 R = Me
5 R = H



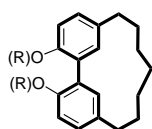
6 R = OMe
7 R = H

Target meta-meta linked biphenols

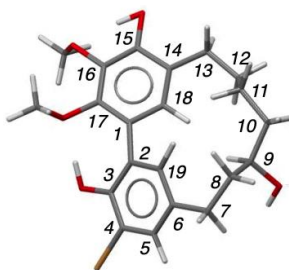


Scheme 1. Tetrasubstituted biphenols are stable to atropisomerisation.

(a)



(b)



(c)

**Stereochemical information from
8 structures in the CCDC database**

The conformation of the bridge is uniform and rigid;

Dihedrals 7,8 9,10, and 13,12,11,10: $167.75 \pm 1.57^\circ$

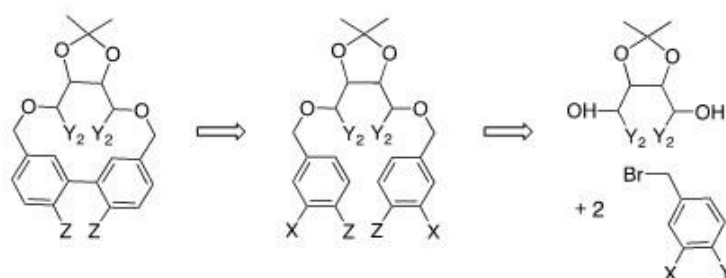
Dihedral 17,1,2,3: $44.1 \pm 2.8^\circ$

Dihedral 18,1,2,19: $32.0 \pm 1.6^\circ$

5 structures (*S*, *aS*), 1 (*R*, *aR*) configuration;

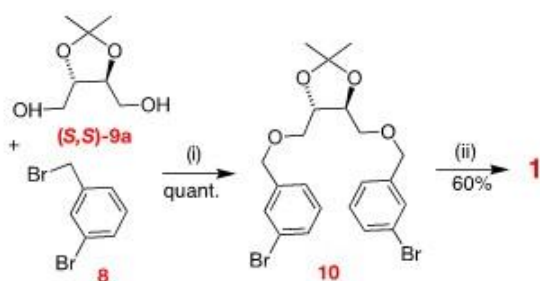
1 is (*S*,*aR*)

Scheme 2. a) The structural basis of tricyclic diarylheptanoid natural products; b) the X-ray structure of (*aR*,*3S*,*5S*) Alnusdiol from the heartwood of *Betula maximowicz*, showing the 6,14 linking chain conformation; c) analysis of the conformational data derived from CCDC-deposited structures that shows little variation in geometry across the series, independent of the axial configuration.



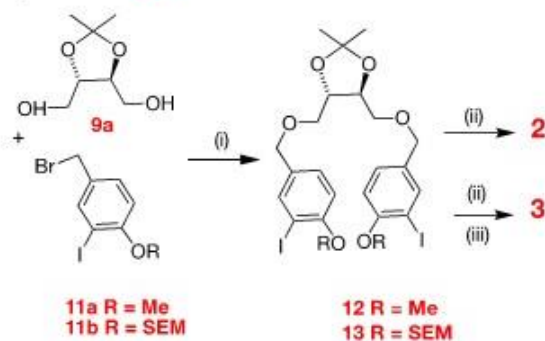
Scheme 3. Retrosynthesis of *meta-meta'*-bridged biaryls and the products derived.
 X = Br, I; Y₂ = H,H, (*R,R*) H,Me or (*S,S*) H,Me; Z = H, OMe or OH

Synthesis of 1



(i) NaH, THF; RT then 60°C; (ii) NaH, bipyridine, anhyd Ni(OAc)₂, KI, t-AmOH, 60°C.

Synthesis of 2, 3

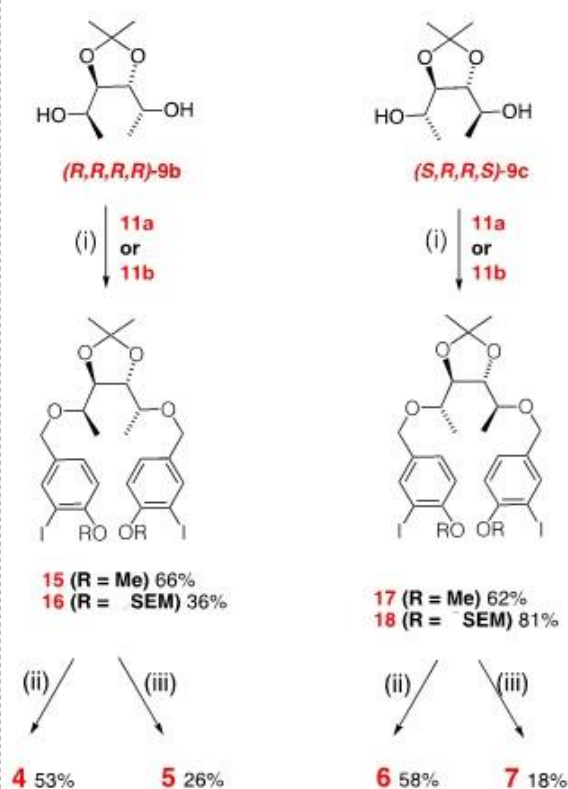


For **2**: (i) NaH, THF; 2 h, RT; 18 h, 60°C; (ii) Ni(PPh)₄, DMF, 48 h, 50°C. (**11a** was used w/o isolation, see **4.2**). 24% overall

For **3**: (i) xs. NaH, THF, 19 h., RT to; (ii) Ni(PPh)₄, DMF, 1 h RT; 18 h, 50°C, to SEM ether **14**; (iii) 4 A MS, TBAF, 18 h. RT then 2 h 50°C. 17% overall.

Scheme 4. Synthesis of products in the Threitol series.

Synthesis of (*R,R,R,R*)-4 & 5, (*S,R,R,S*)-6 & 7



For **4, 6**: (i),(ii) As **2**, with minor alterations see Section **4.4**

For **5, 7**: (i), As **3**, with minor alterations see Section **4.5**. **11b** (caution!) and the SEM ethers of **5** and **7** were also characterised.

Scheme 5. Synthesis of products in the Mannitol and Iditol series.

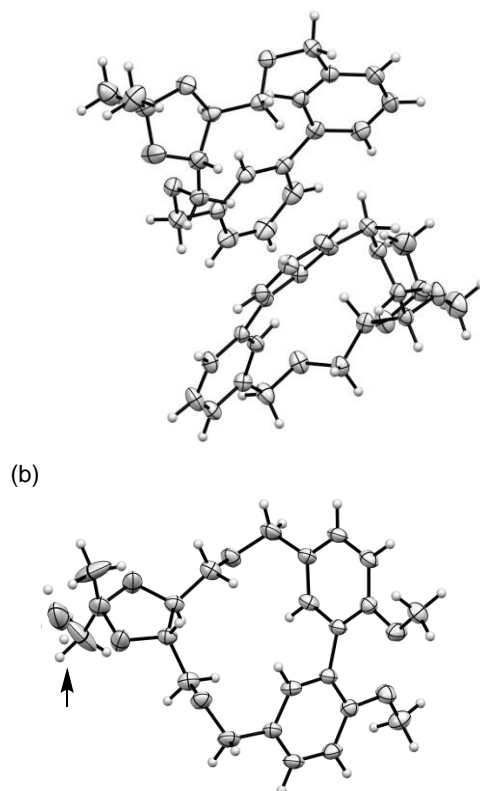


Figure 1. X-ray derived structures of **1** (a) and **2** (b) contrasting the geometry about the inter-aryl bond. For quasi-racemate **1**: monoclinic, $P2_1$, $Z = 4$, $R_{\text{obs}} = 0.0450$, $\omega R_{\text{obs}} = 0.0825$. For **(S,R,S)**-**2**: monoclinic, C_2 , $Z = 2$, $R_{\text{obs}} = 0.0394$, $\omega R_{\text{obs}} = 0.064$; see SI for collection & refinement details.

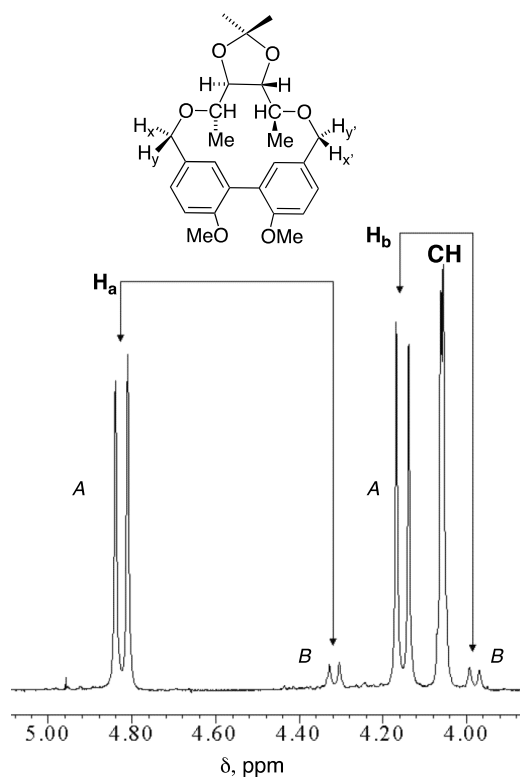


Figure 2. Low temperature (242K) ^1H NMR spectrum of compound **(S,R,R,S)**-**6** in toluene- d_8 for the benzylic region, showing **(aR)**, **(aS)** (not assigned at this stage) isomers in 10:1 ratio; and the spin correlations of the $A = B$ exchange pathways between individual protons of each AB pair, H_a or H_b . **CH** refers to the dioxolane tertiary protons.

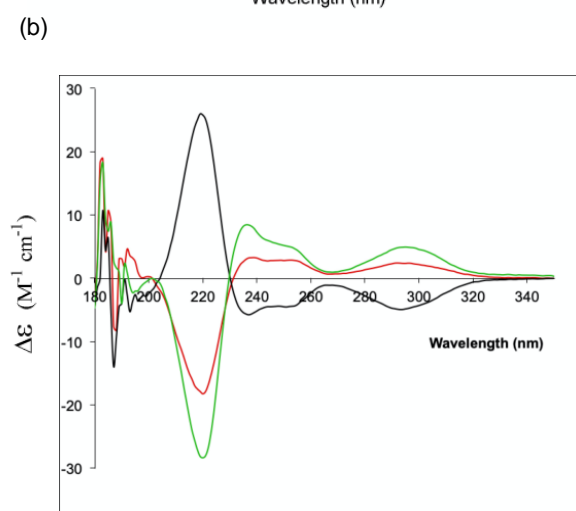
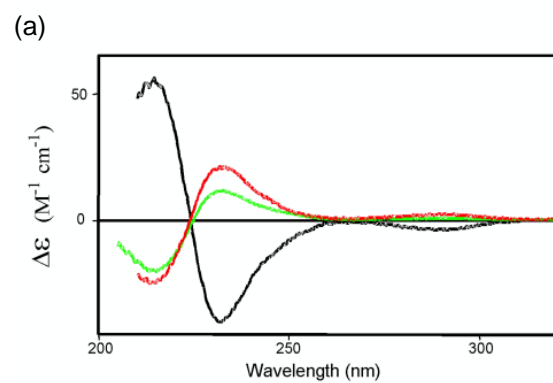
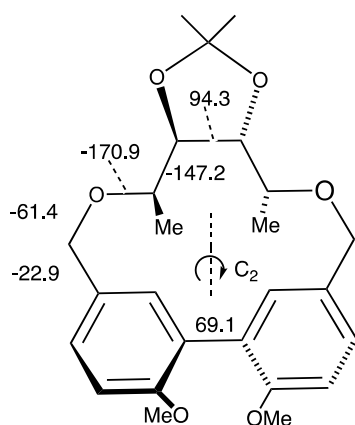


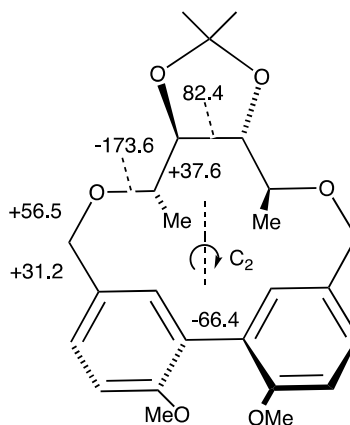
Figure 3. ECD spectra recorded in MeOH for samples of *bis*-ethers **2**, **4** and **6**; at 0.01mg/ml; Figure 2b, CD spectra of biphenols **3**, **5** and **7** (0.1 mg/ml in MeOH), showing the same trends as methyl ethers with the same configuration in the 280 -300 nM region; Green trace **2** & **3**, Black trace **4** & **6**, Red trace **5** & **7**.

Conformer	Isomer	Free Energy, kcal.mol ⁻¹	Relative energy ^{1,2}	ECD result
(aR)-4	(<i>R,R,R,R</i>) C2	-1422.98737	0	+ (aR) 272.4 nm
(aS)-4	(<i>R,R,R,R</i>) C2	-1422.97873	+5.42, (1.45)	- (aS) 277.3 nm
(aR)-4	(<i>R,R,R,R</i>) C1	-1422.98559	+1.91, (1.11)	+ (aR) 282.4 nm
(aS)-4	(<i>R,R,R,R</i>) C1	-1422.98751	-0.09, (3.68)	- (aS) 278.4 nm
(aR)-6	(<i>S,R,R,S</i>) C2	-1422.97631	+5.34, (6.32)	+ (aR) 279.9 nm
(aS)-6	(<i>S,R,R,S</i>) C2	-1422.98482	0	- (aS) 276.2 nm
(aR)-6	(<i>S,R,R,S</i>) C1	-1422.98460	+0.14, (2.04)	+ (aR) 277.0 nm
(aS)-6	(<i>S,R,R,S</i>) C1	-1422.98179	+1.90, (4.68)	- (aS) 273.2 nm

¹Free Energies relative to the most stable C2 conformer (highlighted) of **4** or **6** at 298K; ²Relative electronic energies (no solvent) bracketed



a) DFT-derived torsion angles for (*R,R,R,R*)-**4**



b) DFT-derived torsion angles for (*S,R,R,S*)-**6**

Figure 4. Results from calculations on the four conformational isomers of both compounds **4** and **6** showing the accord between observed ECD results and TD SCF predictions, and the dihedral angle map for their more stable C2 conformers.

Supplementary information

General

DFT calculations were carried out on Arcus-B (the Oxford University supercomputer) using the Gaussian16 and Gaussview6 programs.¹ For standard minimizations, we utilized the B3LYP functional with dispersion corrections applied as recommended by Grimme, and the 6-31g(2d,p) basis set for all atoms.² TD-DFT calculations for assessment of ECD-derived configurations were conducted through TD-SCRF procedures available in GV6/Gaussian16; c.f. relevant literature.³

¹ Gaussian 09, Revision D.01: M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford, CT, USA, 2009.

² (a) S. Grimme, A. Hansen, J. G. Brandenburg and C. Bannwarth, *Chem. Rev.*, (2016), *116*, 5105-5154; (b) M. Steinmetz and S. Grimme, *ChemistryOpen*, 2013, *2*, 115- 124.

³ Y.Ding, X-C La, D. Ferreira, *J. Nat. Prod.* (2009) *72* 327–33.

Structure solution for compound 1 (CCDC 2033961)

1. X-ray structure analyses

Crystals of 1 suitable for X-ray analysis were grown from a CH₂Cl₂/pentane mixture

Empirical Formula.	C ₂₁ H ₂₄ O ₄
Formula weight	340.40
Temperature	180(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic; Space group: P2 (1)
Unit cell dimensions	a = 9.9774 (6), b = 13.4793, c = 13.0420 (8) α = 90 deg., β = 90.8340 (10) deg., γ = 90 deg.
Z	4
Density (calculated)	1.289 Mgm ⁻¹
Absorption Coefficient	0.088 mm ⁻³
F(000)	728
Crystal character	Colourless blocks:: 0.36 x 0.30 x 0.30 mm
Maximum θ.	28.58 deg.
Index ranges	-12 ≤ h ≤ 12, -15 ≤ k ≤ 18, -17 ≤ l ≤ 13
Reflections measured	10650; Unique reflections 7241 [R(int) = 0.0281]
Structure solution	Direct Methods; light atoms found by Fourier methods
Structure refinement	Full matrix least-squares on F ²
Data / restraints / parameters	1807 / 1 / 142
Goodness-of-fit on F ²	0.926
R* indices	R ₁ = 0.0450, wR ₂ = 0.0928
Largest diff. peak and hole	0.169 and -0.182 e.Å ³

Structure solution for compound 2 (CCDC 2033962)

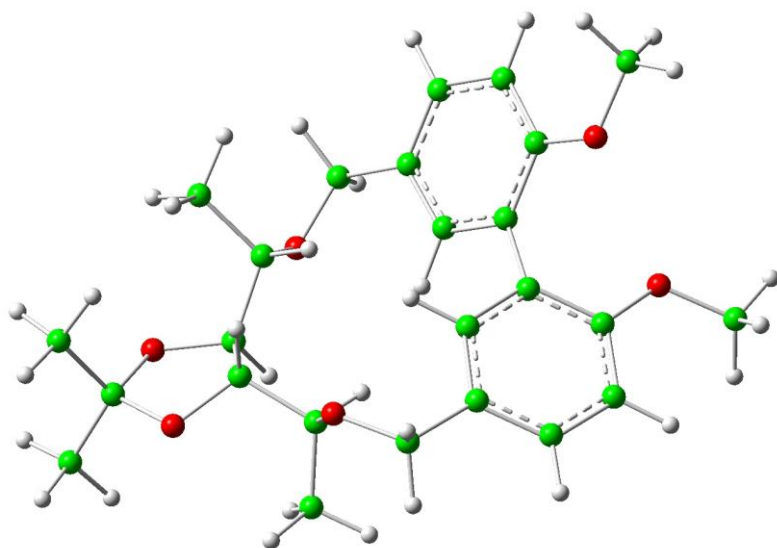
Empirical formula	C ₂₃ H ₂₈ O ₆
Formula weight	400.45
Temperature	210(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic; Space group C2
Unit cell dimensions	a = 15.6032 (6), b = 13.3312 (7), c = 5.0891 (2) $\alpha = 90$ deg., $\beta = 105.786$ (2) deg., $\gamma = 90$ deg.
Z	2
Density (calculated)	1.306 Mgm ⁻³
Absorption Coefficient	0.094 mm ⁻¹
F(000)	428
Crystal character	Colourless blocks; 0.40 x 0.15 x 0.15 mm
Maximum θ	28.53 deg.
Index ranges	-20 ≤ h ≤ 19, -17 ≤ k ≤ 9, -6 ≤ l ≤ 6
Reflections measured	3134
Unique reflections	1807 [R(int) = 0.0242]
Structure solution	Direct Methods; light atoms found by Fourier methods
Structure refinement	Full matrix least-squares on F ²
Data / restraints / parameters	7241 / 1 / 456
Goodness-of-fit on F ²	1.483
R* indices	R ₁ = 0.0394, wR ₂ = 0.0641
Largest diff. peak and hole	0.160 and -0.204 e.Å ³

2. DFT calculations for key structures

SSSSaSC2

-
- Zero-point correction= 0.533967 (Hartree/Particle)
- Thermal correction to Energy= 0.563438
- Thermal correction to Enthalpy= 0.564382
- Thermal correction to Gibbs Free Energy= 0.475036
- Sum of electronic and zero-point Energies= -1422.928440
- Sum of electronic and thermal Energies= -1422.898970
- Sum of electronic and thermal Enthalpies= -1422.898025
- Sum of electronic and thermal Free Energies= -1422.987372
- SSSSaSC2
- 0 1
- C 4.96514900 -0.00307600 0.10519200
- O 4.11494000 1.09920900 0.40375300
- C 2.76951400 0.63484600 0.41223900
- H 2.49695100 0.28216300 1.41525800
- C 1.79373900 1.74736200 0.01586500
- H 0.94072800 1.26009500 -0.46845100
- O 1.35292900 2.34209100 1.24647300
- C 0.28235500 3.28020900 1.16126800
- H 0.57005300 4.15747400 0.56785300
- H 0.14526400 3.62436200 2.19286500
- C -1.00582400 2.69920100 0.61766900
- C -1.99055700 3.50293900 0.04589200
- H -1.84995000 4.57901600 -0.00538900
- C -3.16251700 2.94803500 -0.47162400
- H -3.90876700 3.59969600 -0.90706600
- C -3.34202200 1.56107700 -0.47830100
- O -4.40911500 0.93080700 -1.04280700
- C -5.43638900 1.73489500 -1.61392300
- H -6.18780800 1.03695300 -1.98631200
- H -5.05490000 2.33698300 -2.44622300
- H -5.88979800 2.39229700 -0.86372600
- C -2.35170200 0.73108400 0.07461300
- C -1.22858700 1.32517600 0.64950300
- H -0.48699700 0.67865700 1.10196000
- C 5.46353900 -0.66144300 1.38589300
- H 4.62559600 -0.91168300 2.04054900
- H 6.13402600 0.01817900 1.92006600
- H 6.01037600 -1.57866600 1.14992800
- O 4.15735300 -0.93214600 -0.63683300
- C 2.78699400 -0.54078100 -0.57720700
- H 2.47878800 -0.19906100 -1.57266700
- C 1.84855500 -1.68920200 -0.17350400
- H 1.00539900 -1.23741400 0.36127100
- O 1.36663300 -2.25029300 -1.40588300
- C 0.31447200 -3.20793800 -1.30985000

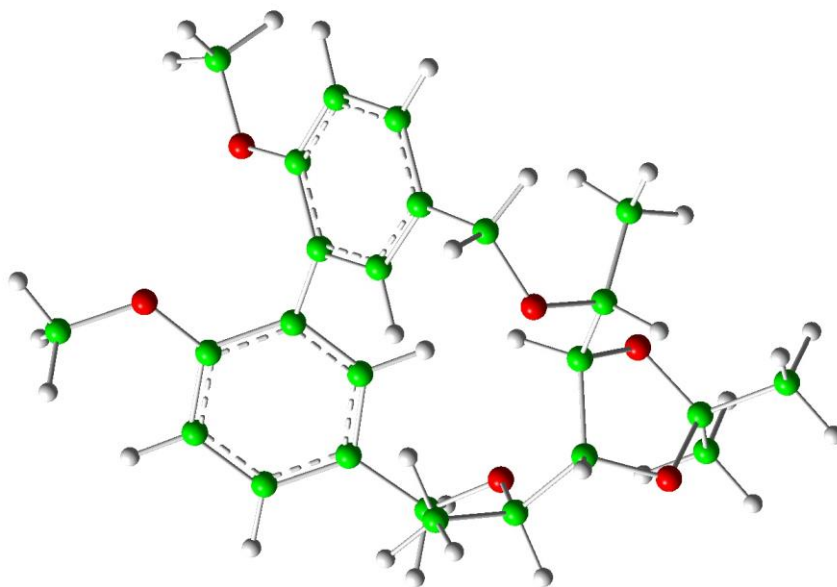
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- H 0.13446800 -3.51192300 -2.34752600
- C -0.95591200 -2.67007700 -0.68607600
- C -1.88857800 -3.50847400 -0.07829500
- H -1.71667000 -4.58085900 -0.05076700
- C -3.04764000 -2.99351600 0.50565300
- H -3.75287300 -3.67127000 0.96878400
- C -3.26621100 -1.61273800 0.53815400
- O -4.32217700 -1.02005700 1.16099000
- C -5.29313100 -1.85970100 1.77773800
- H -6.04492600 -1.18797500 2.19490700
- H -4.85031600 -2.45570200 2.58365600
- H -5.76516800 -2.52527900 1.04650800
- C -2.32902000 -0.74791000 -0.05279500
- C -1.21642900 -1.30212100 -0.68522800
- H -0.51390100 -0.62918800 -1.16140200
- C 6.09178600 0.49112100 -0.78295000
- H 6.74999800 -0.33947500 -1.05226800
- H 6.68288900 1.24720200 -0.25873800
- H 5.67801000 0.92938000 -1.69484500
- C 2.38564100 2.76244000 -0.95134900
- H 3.16691300 3.35412100 -0.46809800
- H 2.82376800 2.24734400 -1.81142900
- H 1.60990900 3.43428800 -1.32753200
- C 2.49340100 -2.72895800 0.72882300
- H 3.30597400 -3.24647700 0.21335200
- H 2.89966600 -2.24758300 1.62215000
- H 1.75438500 -3.46285700 1.06063400



SSSSaRC2

- Zero-point correction= 0.534117 (Hartree/Particle)
- Thermal correction to Energy= 0.563450
- Thermal correction to Enthalpy= 0.564394
- Thermal correction to Gibbs Free Energy= 0.476104
- Sum of electronic and zero-point Energies= -1422.920722
- Sum of electronic and thermal Energies= -1422.891388
- Sum of electronic and thermal Enthalpies= -1422.890444
- Sum of electronic and thermal Free Energies= -1422.978734
-
- SSSSaRC2
-
- 0 1
- C -4.26826800 -0.25051800 -0.93877600
- C -5.40549800 0.76192100 -0.98345700
- H -5.26234500 1.53228200 -0.22222300
- H -5.44938500 1.23637400 -1.96794500
- H -6.36019500 0.26047400 -0.79838900
- O -4.21289600 -0.81094300 0.37655500
- C -2.90267800 -0.65079200 0.92985900
- H -3.03195400 -0.35036900 1.97327400
- C -2.12566500 -1.98220800 0.92907400
- O -1.63655000 -2.20665600 -0.40138400
- C -0.66411800 -3.23212400 -0.60145300
- H -0.84934100 -4.09078300 0.05580900
- H -0.82071400 -3.57481000 -1.63101700
- C 0.74776700 -2.70810800 -0.41640200
- C 1.84260000 -3.50579500 -0.09139400
- H 1.73229100 -4.58349800 -0.00960600
- C 3.09246800 -2.93155100 0.16051100
- H 3.92385700 -3.57510100 0.41729600
- C 3.25464300 -1.54061100 0.15268600
- O 4.40977000 -0.90507800 0.49565100
- C 5.53215400 -1.70237100 0.85887200
- H 6.33483800 -0.99949700 1.08724800
- H 5.31836700 -2.31161900 1.74431300
- H 5.84240500 -2.35254800 0.03326000
- C 2.15872600 -0.71971700 -0.16710600
- C 0.95502300 -1.33739700 -0.49954300
- H 0.12134900 -0.70959100 -0.77060200
- C -4.42489100 -1.34759300 -1.98119900
- O -3.00614000 0.38508100 -1.14561900
- C -2.30974800 0.49787900 0.09475900
- H -1.25493700 0.34948000 -0.11539200
- C -2.46754400 1.90005500 0.72651300
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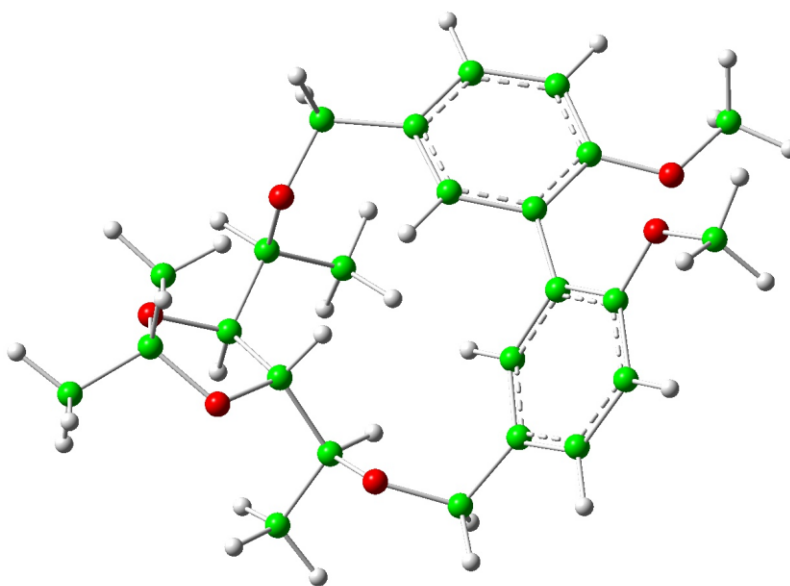
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- H 1.25778200 4.53825800 0.36049700
- C 2.57452200 3.07082700 -0.48868000
- H 3.16108400 3.81785800 -1.00746800
- C 2.86990700 1.71140000 -0.64055300
- O 3.85560000 1.22956300 -1.44637800
- C 4.67400200 2.16642300 -2.13942300
- H 5.39546800 1.57182300 -2.70191100
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- H -3.60333100 -2.05989600 -1.88871200
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- C -1.07354100 -1.99732500 2.03429600
- H -0.50541500 -2.92944400 2.03861400
- H -0.37057500 -1.16803300 1.95509100
- H -1.58783100 -1.91879700 2.99736000



SSSSaRC1

- Zero-point correction= 0.533626 (Hartree/Particle)
- Thermal correction to Energy= 0.563233
- Thermal correction to Enthalpy= 0.564177
- Thermal correction to Gibbs Free Energy= 0.474554
- Sum of electronic and zero-point Energies= -1422.928445
- Sum of electronic and thermal Energies= -1422.898838
- Sum of electronic and thermal Enthalpies= -1422.897893
- Sum of electronic and thermal Free Energies= -1422.987516
- SSSSaRC1
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- 0 1
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- H 6.12562800 0.63018800 0.43419300 L
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- H 5.77896100 1.14540700 2.10407500 L
- C 0 4.26200300 -0.09960900 1.21340400 L
- C 0 3.60796000 -0.56236400 2.51111700 L
- H 0 2.56476500 -0.83161800 2.33881200 L
- H 0 3.65576100 0.23437100 3.25916500 L
- H 0 4.13205400 -1.43988500 2.90107400 L
- O 0 3.55198100 0.99291000 0.64651400 L
- C 0 2.54845800 0.46845600 -0.22319900 L
- H 0 1.63045800 0.28282500 0.34089300 L
- C 0 2.23430700 1.51689400 -1.29275700 L
- H 0 1.52753600 1.06616800 -1.99667200 L
- O 0 1.60645100 2.61479700 -0.60854300 L
- C 0 0.46784600 3.20986200 -1.24857500 L
- H 0 0.49525800 2.99569200 -2.32404500 L
- H 0 0.55759700 4.29368500 -1.12316000 L
- C 0 -0.81877000 2.72068900 -0.62568400 L
- C 0 -1.08836600 1.35351000 -0.61876700 L
- H 0 -0.41238300 0.68016800 -1.12805700 L
- C 0 -2.17631200 0.79093200 0.04552100 L
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- C 0 -2.20295200 -0.69223700 0.11414900 L
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- C 0 -0.78914400 -2.67720000 0.35858700 L
- C 0 -1.85667000 -3.46930800 -0.05720700 L
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- C 0 -3.09122000 -2.89558900 -0.37199800 L
- H 0 -3.89806900 -3.53391100 -0.70766600 L

- C 0 -3.26493900 -1.50817100 -0.31773000 L
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- H 0 0.67660800 -3.57199300 1.67070000 L
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- O 0 1.60112600 -2.22077200 0.49768700 L
- C 0 2.19633700 -2.06226500 -0.79178000 L
- H 0 2.81375000 -2.95116700 -0.99190400 L
- C 0 3.15518100 -0.86998000 -0.70710500 L
- H 0 3.61168900 -0.75581500 -1.69624700 L
- O 0 4.20067300 -1.14145000 0.23091600 L
- O 0 -4.39772700 -0.86775600 -0.71912700 H
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- C 0 -5.49322000 -1.65832200 -1.16831000 H
- H 0 -6.28522000 -0.95195500 -1.42185200 H
- H 0 -5.22684800 -2.24113400 -2.05735100 H
- H 0 -5.84644800 -2.33308900 -0.38055400 H
- C 0 -5.01925400 1.91444800 2.06119700 H
- H 0 -5.53628700 2.58293200 1.36384100 H
- H 0 -5.74420800 1.24467700 2.52619700 H
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- C 0 3.45185800 2.02740300 -2.05148300 H
- H 0 4.16455900 2.48755300 -1.36289000 H
- H 0 3.95760600 1.22044100 -2.59032400 H
- H 0 3.13895200 2.77669900 -2.78468700 H
- C 0 1.21338900 -1.89441900 -1.94709300 H
- H 0 0.56639800 -2.76812100 -2.04822200 H
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-



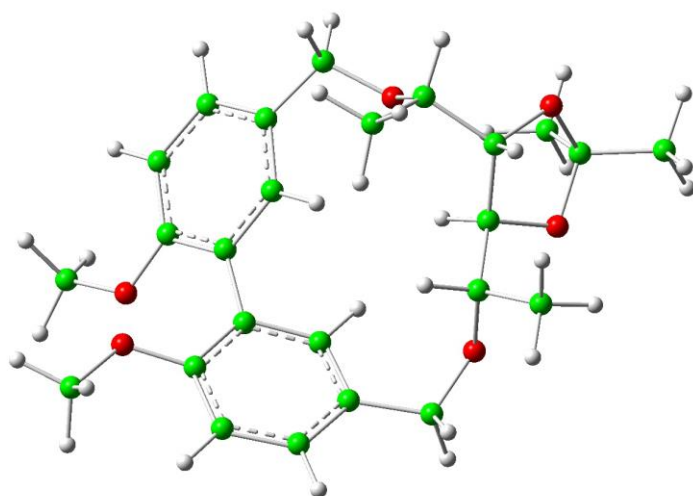
SSSSaSC1

- Zero-point correction= 0.533773 (Hartree/Particle)
- Thermal correction to Energy= 0.563350
- Thermal correction to Enthalpy= 0.564294
- Thermal correction to Gibbs Free Energy= 0.475059
- Sum of electronic and zero-point Energies= -1422.926874
- Sum of electronic and thermal Energies= -1422.897297
- Sum of electronic and thermal Enthalpies= -1422.896353
- Sum of electronic and thermal Free Energies= -1422.985588

SSSSaSC1

-
- 0 1
- C -5.83674800 -0.20223800 -1.18691200
- H -6.15946900 0.59758600 -0.51522100
- H -6.48082200 -1.07358800 -1.04150400
- H -5.93869300 0.13633100 -2.22174700
- C -4.39356400 -0.56506300 -0.89358200
- C -3.86596700 -1.68215600 -1.78852500
- H -2.83060300 -1.91845600 -1.53639000
- H -3.92215300 -1.38159100 -2.83882400
- H -4.46836500 -2.58488400 -1.65072100
- O -3.60473300 0.60924900 -1.01703900
- C -2.53356800 0.51413600 -0.07583200
- H -1.71205800 -0.05953100 -0.51055500
- C -2.02039400 1.92465500 0.21636100
- O -1.51321900 2.40430800 -1.04361800
- C -0.45532300 3.35369200 -0.96542300
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- H -0.39942400 3.79545300 -1.96712000
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- C 1.07258100 1.36921000 -0.71072700
- H 0.27802800 0.76900500 -1.13368200
- C 2.22630400 0.71862400 -0.26293700
- C 3.26256000 1.50481000 0.27549000
- C 3.10846600 2.89396700 0.35299400
- H 3.89439200 3.50752000 0.77342800
- C 1.91477200 3.49714800 -0.04338200
- H 1.79915500 4.57033600 0.08042700
- C 2.15976600 -0.76299000 -0.17511200
- C 0.98748200 -1.27070300 0.38161900
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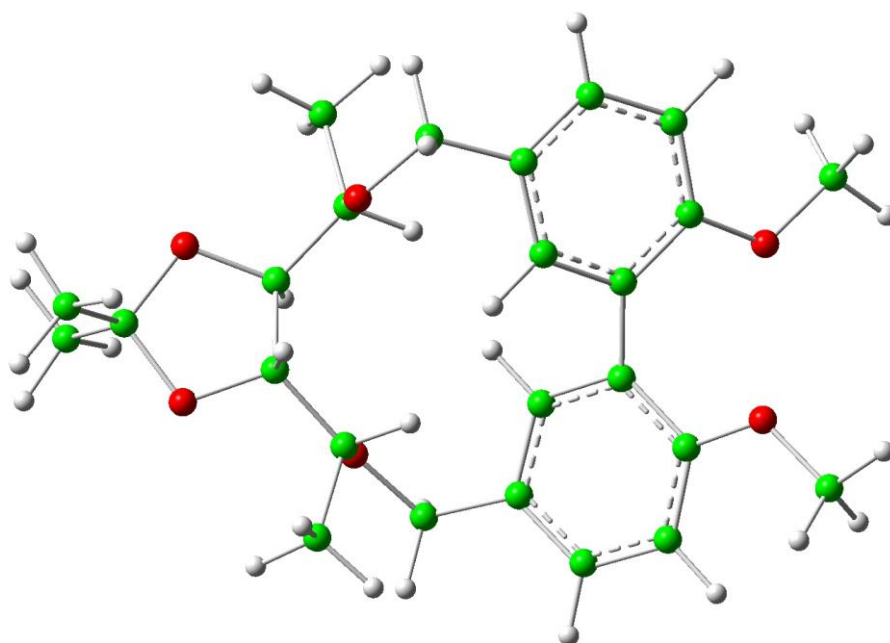
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- H 3.58911300 -3.77281400 -0.89050300
- C 3.11044600 -1.68286400 -0.65477600
- C -0.63954000 -3.04389300 1.04729800
- H -0.95573000 -3.99305000 0.59812800
- H -0.59313500 -3.20395700 2.13055600
- O -1.61559900 -2.05544900 0.72115300
- C -2.25550300 -1.32400600 1.76877300
- C -3.16292100 -0.29142000 1.08799500
- H -3.54793500 0.37451600 1.86720900
- O -4.27981900 -0.95297600 0.48210600
- O 4.20514300 -1.16275500 -1.27445400
- O 4.34650300 0.83805300 0.76057300
- C 5.20006800 -2.06314900 -1.75026200
- H 5.61969200 -2.66032500 -0.93301500
- H 4.79956100 -2.72944900 -2.52263300
- H 5.98366200 -1.43863300 -2.18216000
- C 5.40423300 1.59887900 1.33413900
- H 5.84157100 2.28795800 0.60305300
- H 5.06159300 2.16267000 2.20923400
- H 6.15792600 0.87297600 1.64322400
- H -1.19380200 1.83606000 0.93039600
- H -2.91430400 -2.00863800 2.32238100
- C -1.31806100 -0.64941400 2.76913200
- H -0.60844600 -1.35949700 3.20021800
- H -0.75384000 0.17392200 2.32604400
- H -1.91733100 -0.24339200 3.58998100
- C -3.07718300 2.88000800 0.75394000
- H -3.93720100 2.91672200 0.08068800
- H -3.41957000 2.57036000 1.74557900
- H -2.66272600 3.88755500 0.84892000



RSSRaRC2

- Zero-point correction= 0.534059 (Hartree/Particle)
- Thermal correction to Energy= 0.563529
- Thermal correction to Enthalpy= 0.564473
- Thermal correction to Gibbs Free Energy= 0.475353
- Sum of electronic and zero-point Energies= -1422.926118
- Sum of electronic and thermal Energies= -1422.896648
- Sum of electronic and thermal Enthalpies= -1422.895704
- Sum of electronic and thermal Free Energies= -1422.984824
- RSSRaRC2Z
- 0 1
- C -4.88659900 0.00000100 -0.00000300
- C -5.71939300 0.41255900 1.20270000
- H -5.06361900 0.65460600 2.04358100
- H -6.32071400 1.29426100 0.96206200
- H -6.39150300 -0.39926600 1.49460200
- O -4.02413100 -1.09197700 0.33656800
- C -2.69834400 -0.57616100 0.50556400
- H -2.58494800 -0.16744800 1.51687500
- C -1.67888900 -1.69895400 0.35861300
- O -1.53782400 -2.02038500 -1.03037400
- C -0.51298800 -2.96746200 -1.36079000
- H -0.76601900 -3.96634400 -0.98502300
- H -0.53986600 -3.01373000 -2.45497300
- C 0.85595500 -2.56168600 -0.86103500
- C 1.80272700 -3.47021700 -0.39408800
- H 1.60095800 -4.53684300 -0.43449500
- C 3.01398800 -3.02868100 0.14645400
- H 3.73003300 -3.75837400 0.50104900
- C 3.26597300 -1.66078800 0.29827300
- O 4.36422400 -1.15106200 0.91967300
- C 5.33715900 -2.06409000 1.41861200
- H 6.11994200 -1.44909800 1.86514900
- H 4.90997900 -2.72236200 2.18341000
- H 5.76529100 -2.66883600 0.61159700
- C 2.31475600 -0.72727800 -0.15105300
- C 1.16245300 -1.20758800 -0.77113700
- H 0.43877900 -0.48747000 -1.13140700
- C -5.71942200 -0.41255000 -1.20269000
- O -4.02413000 1.09197100 -0.33659400
- C -2.69833800 0.57615500 -0.50557200
- H -2.58493200 0.16744200 -1.51688100
- C -1.67888400 1.69894900 -0.35861000
- O -1.53782800 2.02038200 1.03037800
- C -0.51299100 2.96745600 1.36080200
- H -0.76602300 3.96634100 0.98504300
- H -0.53987000 3.01371300 2.45498500

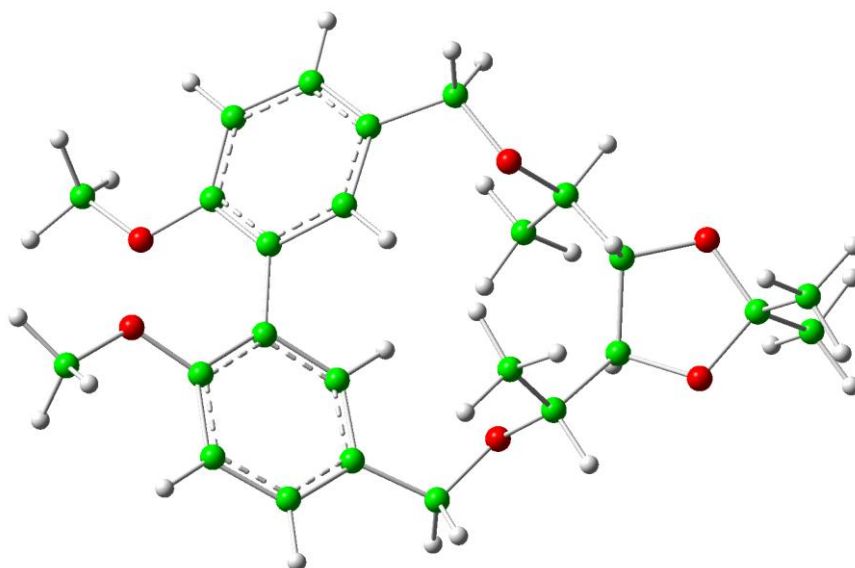
- C 0.85595100 2.56168500 0.86104500
- C 1.80271600 3.47021700 0.39408800
- H 1.60094300 4.53684200 0.43449000
- C 3.01397600 3.02868400 -0.14645900
- H 3.73001600 3.75837900 -0.50106200
- C 3.26596600 1.66079100 -0.29827300
- O 4.36421500 1.15106700 -0.91967900
- C 5.33714500 2.06409700 -1.41862400
- H 6.11992900 1.44910500 -1.86516000
- H 4.90996100 2.72236400 -2.18342300
- H 5.76527800 2.66884700 -0.61161200
- C 2.31475400 0.72728000 0.15106200
- C 1.16245400 1.20758700 0.77115100
- H 0.43878400 0.48746900 1.13142500
- H -5.06366700 -0.65460400 -2.04358200
- H -6.32074800 -1.29424500 -0.96203800
- H -6.39152800 0.39928200 -1.49457800
- H -0.73290500 1.29686600 -0.73480300
- H -0.73291200 -1.29687000 0.73481100
- C -2.05597400 2.91462500 -1.20011100
- H -2.27511800 2.60372300 -2.22630100
- H -2.93998400 3.40955600 -0.78937100
- H -1.23278800 3.63270000 -1.23898000
- C -2.05598600 -2.91462800 1.20011000
- H -2.27514000 -2.60372600 2.22629800
- H -2.93999300 -3.40956000 0.78936300
- H -1.23280100 -3.63270400 1.23898800



RSSRaSC2 (Me endo ArH---HCH₂ 2.03 Å)

- Zero-point correction= 0.533231 (Hartree/Particle)
- Thermal correction to Energy= 0.562881
- Thermal correction to Enthalpy= 0.563825
- Thermal correction to Gibbs Free Energy= 0.472204
- Sum of electronic and zero-point Energies= -1422.915283
- Sum of electronic and thermal Energies= -1422.885633
- Sum of electronic and thermal Enthalpies= -1422.884689
- Sum of electronic and thermal Free Energies= **-1422.976310**
- RSSRaSC2
- 0 1
- C 5.35443600 0.00000900 0.00005100
- O 4.49057000 -1.13281900 -0.13195900
- C 3.16220800 -0.66184300 -0.39657400
- H 3.05210700 -0.45221000 -1.46626300
- C 2.19927900 -1.81556800 -0.04693100
- H 2.81476100 -2.72544200 -0.03099400
- O 1.30013800 -1.92109500 -1.15975200
- C 0.38672500 -3.01821600 -1.13908200
- H 0.78289600 -3.84506800 -0.53652700
- H 0.32771300 -3.37549200 -2.17478100
- C -0.98534300 -2.60275500 -0.64518600
- C -1.94946500 -3.49206700 -0.17226400
- H -1.75483300 -4.56090000 -0.16318800
- C -3.17228400 -3.02199800 0.31524000
- H -3.89698300 -3.73401900 0.68831500
- C -3.43726100 -1.64771700 0.38292000
- O -4.55927400 -1.11530600 0.94288100
- C -5.54450100 -2.00857400 1.45137300
- H -6.34708000 -1.37771700 1.83671500
- H -5.14344300 -2.62416400 2.26448500
- H -5.93962600 -2.65726800 0.66161400
- C -2.47799300 -0.73716800 -0.09141600
- C -1.29813500 -1.25199300 -0.63032300
- H -0.56904000 -0.55134800 -1.00577400
- C 6.18792000 0.18757600 -1.25709100
- H 6.53369200 0.25989100 -2.13032900
- H 6.86930100 -0.65749800 -1.38932200
- H 6.77957300 1.10487700 -1.18471000
- O 4.49056500 1.13283900 0.13201300
- C 3.16219000 0.66186400 0.39656400
- H 3.05203800 0.45223100 1.46624800
- C 2.19927700 1.81559000 0.04687600
- H 2.81476500 2.72546000 0.03093400
- O 1.30011400 1.92114300 1.15967700
- C 0.38669500 3.01825700 1.13896200
- H 0.78285600 3.84508300 0.53636400

- H 0.32768800 3.37558600 2.17464300
- C -0.98537500 2.60276400 0.64509900
- C -1.94954800 3.49206200 0.17225300
- H -1.75495100 4.56090200 0.16320500
- C -3.17237600 3.02197300 -0.31520500
- H -3.89711500 3.73398400 -0.68822300
- C -3.43732100 1.64768600 -0.38290800
- O -4.55935100 1.11525900 -0.94281700
- C -5.54464100 2.00851400 -1.45121000
- H -6.34722800 1.37764600 -1.83651900
- H -5.14365900 2.62414500 -2.26432800
- H -5.93973200 2.65716800 -0.66140100
- C -2.47800200 0.73715100 0.09135200
- C -1.29812600 1.25199400 0.63020400
- H -0.56899000 0.55136000 1.00559500
- C 6.18785300 -0.18756000 1.25723700
- H 6.86922800 0.65751300 1.38950400
- H 6.77950700 -1.10486100 1.18488700
- H 5.53357800 -0.25987400 2.13044000
- C 1.51405800 -1.67747900 1.30499300
- H 0.94180100 -0.75165700 1.37866200
- H 0.84742400 -2.52158500 1.49595200
- H 2.27810500 -1.67225800 2.08942900
- C 1.51408300 1.67747600 -1.30505800
- H 0.94183500 0.75164900 -1.37872200
- H 0.84744700 2.52157400 -1.49604300
- H 2.27814400 1.67224700 -2.08948100
-



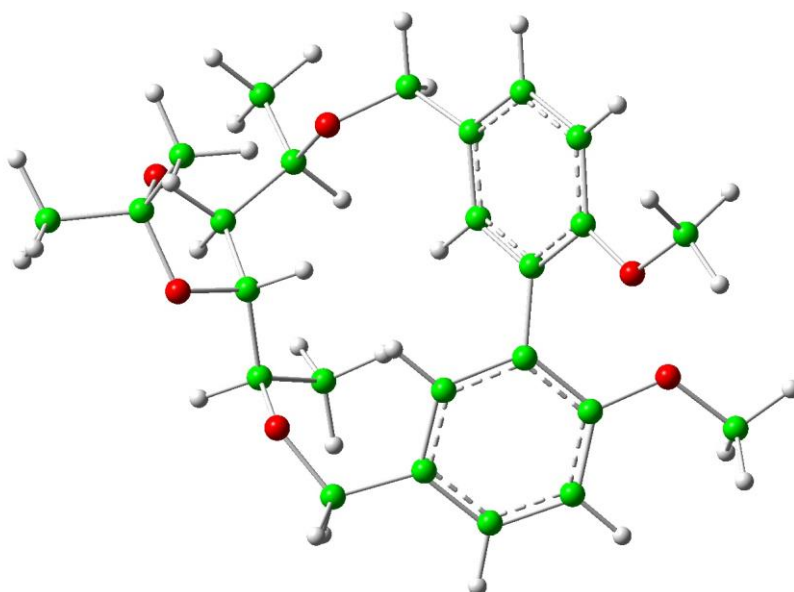
SRRSaRC1

- Zero-point correction= 0.533231 (Hartree/Particle)
- Thermal correction to Energy= 0.562881
- Thermal correction to Enthalpy= 0.563825
- Thermal correction to Gibbs Free Energy= 0.472204
- Sum of electronic and zero-point Energies= -1422.915283
- Sum of electronic and thermal Energies= -1422.885633
- Sum of electronic and thermal Enthalpies= -1422.884689
- Sum of electronic and thermal Free Energies= -1422.984600

-
- RSSRaSC1X

-
- 0 1
- C -5.46691200 0.43236000 -1.79852200
- H -5.81156000 1.29417300 -1.22111500
- H -6.21933600 -0.35906100 -1.74596600
- H -5.34554600 0.72738300 -2.84445800
- C -4.14783000 -0.06372700 -1.23711700
- C -3.59445400 -1.26671800 -1.99392200
- H -2.64869100 -1.59196000 -1.55810700
- H -3.43872100 -1.00710200 -3.04513800
- H -4.30298800 -2.09869800 -1.94102900
- O -3.22495900 1.01627800 -1.24531300
- C -2.36734100 0.87310000 -0.11093800
- H -1.50820100 0.24894100 -0.36888600
- C -1.87759900 2.26834300 0.27902100
- O -1.15223300 2.73453300 -0.88051800
- C -0.00629400 3.56455000 -0.73573600
- H -0.16357400 4.35108600 0.01225300
- H 0.09155100 4.06892200 -1.70472000
- C 1.25170000 2.77859100 -0.41784000
- C 1.24609200 1.39748000 -0.56881500
- H 0.36202400 0.92293600 -0.96833500
- C 2.29734200 0.58027000 -0.15470900
- C 3.45759400 1.19534500 0.34896400
- C 3.51390900 2.59115800 0.43735100
- H 4.39631700 3.07712100 0.83293300
- C 2.41005800 3.37009800 0.08229500
- H 2.45942300 4.44677800 0.21962300
- C 2.00289700 -0.87373500 -0.08368000
- C 0.82223400 -1.22800400 0.56598600
- H 0.25299100 -0.44248900 1.04519400
- C 0.33645900 -2.53324800 0.60689200
- C 1.09715600 -3.52664700 -0.00191100
- H 0.75301800 -4.55679400 0.00499400
- C 2.30341000 -3.21654400 -0.63813400
- H 2.86741400 -4.00771000 -1.11451200

- C 2.75384600 -1.89462200 -0.69798300
- C -0.98533200 -2.79089500 1.28785800
- H -1.31246100 -3.82158100 1.11213000
- H -0.88876900 -2.65535200 2.37125000
- O -1.99021000 -1.90225400 0.77677400
- C -2.55115600 -0.97585700 1.70982500
- C -3.24811600 0.13753700 0.91877600
- H -3.66623100 0.84414500 1.64594400
- O -4.33251500 -0.39002700 0.14715700
- O 3.87313900 -1.50015600 -1.36362200
- O 4.44702200 0.36523800 0.78277100
- C 4.66968500 -2.50108700 -1.98948400
- H 5.04464200 -3.22550500 -1.25794500
- H 4.10886400 -3.02591900 -2.77096000
- H 5.51085400 -1.97233500 -2.44032100
- C 5.62288700 0.95142600 1.33121400
- H 6.13435500 1.58185100 0.59529900
- H 5.39392100 1.54354000 2.22454000
- H 6.27047000 0.11713600 1.60539200
- H -2.76297300 2.91165400 0.38408800
- H -1.74437600 -0.50848000 2.29012600
- C -3.52575700 -1.67187300 2.65396000
- H -3.95634900 -0.95322200 3.35892900
- H -4.33631300 -2.13287300 2.08251200
- H -3.02012000 -2.45023600 3.23237500
- C -1.12127000 2.27481700 1.60210600
- H -0.29483300 1.56417600 1.62183900
- H -0.72769500 3.26863900 1.82624900
- H -1.81828700 2.01922200 2.40508900



SRRSaSC1

- Zero-point correction= 0.533781 (Hartree/Particle)
- Thermal correction to Energy= 0.563402
- Thermal correction to Enthalpy= 0.564346
- Thermal correction to Gibbs Free Energy= 0.474929
- Sum of electronic and zero-point Energies= -1422.922942
- Sum of electronic and thermal Energies= -1422.893321
- Sum of electronic and thermal Enthalpies= -1422.892376
- Sum of electronic and thermal Free Energies= -1422.981793
- RSSRaRC1
-
- 0 1
- C 0 -4.69317100 -1.01053100 2.26277100 L
- H 0 -5.39244100 -1.30201100 1.47481300 L
- H 0 -5.17556300 -0.28095100 2.91880900 L
- H 0 -4.43317900 -1.89201500 2.85517300 L
- C 0 -3.44622200 -0.40977600 1.64128400 L
- C 0 -2.41920100 0.02738900 2.68048500 L
- H 0 -1.51675100 0.40471900 2.19797800 L
- H 0 -2.15419800 -0.82089000 3.31842200 L
- H 0 -2.83417800 0.82132100 3.30815500 L
- O 0 -2.88843200 -1.36253300 0.74711100 L
- C 0 -2.30900700 -0.65828800 -0.35378300 L
- H 0 -1.25851600 -0.45349000 -0.15164200 L
- C 0 -2.44021200 -1.56727900 -1.58232400 L
- H 0 -3.49995400 -1.84939900 -1.62504900 L
- O 0 -1.77133100 -2.81834200 -1.33597600 L
- C 0 -0.46889200 -3.08825800 -1.88287400 L
- H 0 -0.38404300 -2.67075300 -2.88987600 L
- H 0 -0.43350000 -4.17789300 -1.97385500 L
- C 0 0.67989900 -2.61927600 -1.02184000 L
- C 0 1.02403000 -1.26948300 -0.98669400 L
- H 0 0.49173000 -0.56667700 -1.61416300 L
- C 0 2.00794000 -0.75434000 -0.14537400 L
- C 0 2.74046900 -1.65324800 0.65161800 L
- C 0 2.44991800 -3.02001400 0.59571400 L
- H 0 3.00191100 -3.72205100 1.20679500 L
- C 0 1.41571700 -3.48883700 -0.21814100 L
- H 0 1.18747600 -4.55075900 -0.22073100 L
- C 0 2.06599300 0.72482900 -0.03618000 L
- C 0 0.85112800 1.35396400 0.23574000 L
- H 0 0.00202500 0.73608500 0.47826200 L
- C 0 0.67839700 2.72881300 0.19173500 L
- C 0 1.79891700 3.51158000 -0.08856700 L
- H 0 1.71366300 4.59391200 -0.13257500 L
- C 0 3.04327600 2.92141000 -0.31879800 L
- H 0 3.89356600 3.55430200 -0.53747300 L
- C 0 3.18450900 1.52766000 -0.30897800 L

- C O -0.69242100 3.32098900 0.45037400 L
- H O -0.70015500 3.84593200 1.41294800 L
- H O -0.92864600 4.06692300 -0.31766900 L
- O O -1.71770300 2.33712400 0.54788400 L
- C O -2.36441200 1.96045400 -0.67265300 L
- H O -1.61268000 1.77413400 -1.45152600 L
- C O -3.13356700 0.64593500 -0.42432400 L
- H O -3.88146600 0.55867400 -1.22134600 L
- O O -3.83945600 0.69665200 0.81731200 L
- O O 4.34432500 0.87404800 -0.59796900 H
- O O 3.67373200 -1.10380700 1.47434200 H
- C O 5.50253900 1.65460300 -0.87546500 H
- H O 6.30595600 0.93964500 -1.05937900 H
- H O 5.35951100 2.27824300 -1.76518800 H
- H O 5.76830900 2.28893000 -0.02247900 H
- C O 4.42933600 -1.97630300 2.30964000 H
- H O 5.00932900 -2.69110900 1.71554500 H
- H O 5.10998500 -1.33418200 2.87060100 H
- H O 3.78163600 -2.51885600 3.00725500 H
- C O -2.08583500 -0.88871000 -2.89845900 H
- H O -1.07601900 -0.47348000 -2.91690600 H
- H O -2.18387400 -1.59802700 -3.72536300 H
- H O -2.78663700 -0.07072500 -3.08405500 H
- C O -3.32846800 3.05228300 -1.12844000 H
- H O -3.80220900 2.76840300 -2.07341400 H
- H O -4.10962500 3.19979000 -0.37563800 H
- H O -2.81449200 4.00371900 -1.28685400 H
-

