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The Preparation and Absolute Configurations of Enantiomerically Pure C_4-Symmetric Tetraalkoxyresorcin[4]arenes Obtained from Camphorsulfonate Derivatives

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The preparation of a series of diastereoisomeric tetracamphorsulfonates derived from racemic tetramethoxyresorcin[4]arenes was achieved by reactions with an excess of (*S*)-(+)-10-camphorsulfonyl chloride in pyridine followed by isolation using flash chromatography. Tetradeprotonation of a number of tetramethoxyresorcin[4]arenes using *n*-butyllithium in tetrahydrofuran, followed by reactions using (*S*)-(+)-10-camphorsulfonyl chloride, gave the same tetracamphorsulfonates. Mono-, di- and tricamphorsulfonates were also prepared following selective deprotonation. In the reactions with tetraisopropyloxy- and tetracyclopentyloxyresorcin[4]arenes, only the mono- and dicamphorsulfonates were formed. X-ray crystallographic analysis established the absolute configurations of three diastereoisomerically pure tetracamphorsulfonates, including a diastereoisomer prepared from 6,12,18,24-tetramethoxy-2,8,14,20-tetrakis(2-methylpropyl)resorcin[4]arene. An additional pair of diastereoisomers was also prepared using (*R*)-(–)-10-camphorsulfonyl chloride and 6,12,18,24-tetramethoxy-2,8,14,20-tetrakis(2-methylpropyl)resorcin[4]arene, for one of which the structure was confirmed by an additional X-ray structure determination. Hydrolytic removal of the camphorsulfonyl residue(s) from the various diastereoisomers gave enantiomers of known absolute configurations. In some cases, the chiral nonracemic tetraalkoxyresorcin[4]arenes were converted into known tetrabenzoxazine derivatives by using *N*,*N*-bis(methoxymethyl)[(*S*)-(–)-(α-methylbenzyl)]amine in thermal or microwave-assisted reactions.

The chemistry of calixarenes is widely studied and has provided a diverse range of molecular assemblies that have been used for a variety of purposes; the topic continues to generate considerable interest.[1] The acid-catalysed interaction of aldehydes with resorcinol provides a high-yield route to a range of cyclic tetramers that has made the study of resorcin[4]arenes, for example **1**, particularly attractive.[2] The dissymmetry generated by the unsymmetrical substitution of calixarenes is recognized as being related to the nonplanar structures of the parent compounds,[3a] although a number of chiral calixarene conformers are racemized thermally by processes involving "through-the-annulus rotation".[3b] The first example of the optical resolution of a chiral calixarene used chiral liquid chromatography.[3c] Although considerable effort has been devoted to the synthesis of inherently chiral calixarenes, in the vast majority of published examples the products have been obtained as racemates, which have defied resolution except by using chiral HPLC techniques.[4] This has inevitably meant that only very small amounts of optically pure material has been available for use in other studies. A solution to this problem was provided by studies carried out by us[5a,5b] and others,[5c] with the use of chiral nonracemic (α-methylbenzyl)amines, and resulted in the highly diastereoselective formation of tetrabenzoxazines derived from a number of resorcin[4]arenes, for example the compounds **2**. The methylation of the residual phenolic hydroxy groups present in the single diastereoisomers was achieved in high yields on multigram scales in order to preclude diastereoisomerization as well as the loss of axial chirality after ring opening of the 1,3-oxazine ring and removal of the chiral auxiliary.[6a] The representation of the compounds **2** in Figure 1 is drawn by using the convention that the polar groups are viewed from above and the pendant groups (R) are in pseudoaxial orientations: the stereogenic centres at the inter-ring

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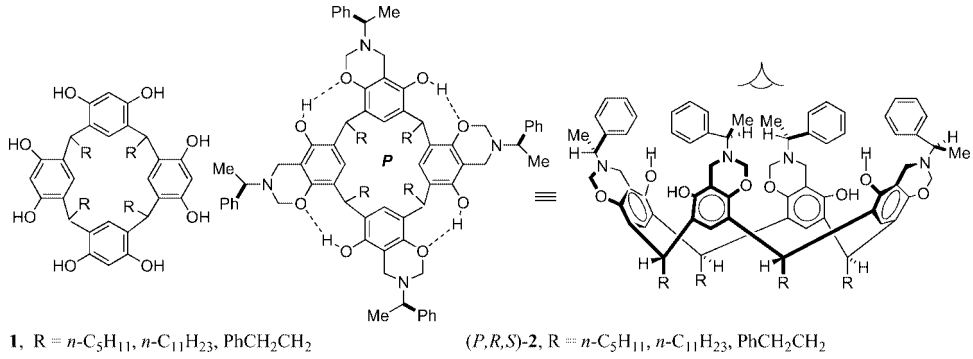
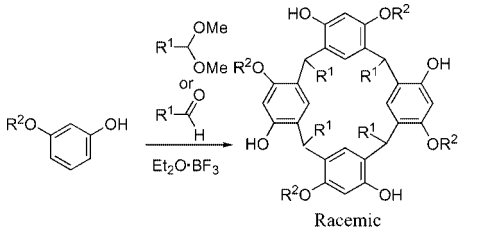


Figure 1. Representation of resorcin[4]arenes, including axial stereochemistry.

positions are therefore of *S*-chirality, the axis of chirality being *P* (= axial-*R*).[6b] Additional examples, including those where chiral nonracemic resorcin[4]arenes have been prepared in excess of 10 g, have also been reported.[6b]

The boron trifluoride catalysed reaction of, for example, octanal with 3-methoxyphenol, that resulted in the formation of a racemic tetramethoxyresorcin[4]arene, provided a route to a range of tetramethoxyresorcin[4]arene derivatives.[7] We extended the method to the preparation of additional tetraalkoxyresorcin[4]arene derivatives:[8] the racemic tetraalkoxyresorcin[4]arenes **4a**–**f** were prepared, in each case in good to excellent yields, as shown in Scheme 1, by the interaction of boron trifluoride (200 mol-%) with, for example, 1,1-dimethoxyalkanes or aldehydes and the 3-alkoxyphenol derivatives **3a**–**c**.



3a, R^2 = Me
3b, R^2 = *i*Pr
3c, R^2 = *c*-C_5H_9

4a, R^1 = *n*-C_3H_7, R^2 = Me
4b, R^1 = *n*-C_5H_{11}, R^2 = Me
4c, R^1 = *n*-C_7H_{15}, R^2 = Me
4d, R^1 = *n*-$C_{11}H_{23}$, R^2 = Me
4e, R^1 = *n*-C_5H_{11}, R^2 = *i*Pr
4f, R^1 = *n*-C_5H_{11}, R^2 = *c*-C_5H_9

Scheme 1. Formation of racemic tetraalkoxyresorcinarenes.

The preparation of the racemic tetramethoxyresorcin[4]-arene related to **4a**–**f**, accomplished by the treatment of 3-methylbutanal with 3-methoxyphenol, conversion into a pair of monocamphorsulfonates followed by separation and isolation on a small scale by chiral HPLC in 13% and 16% yields, has been reported previously.[4k,4l] However, the absolute configurations of the enantiomers that were obtained after hydrolysis were not established. In our related work, we initially studied reactions of the resorcinarenes **4a**–**f**. The conversion into diastereoisomeric camphorsulfonates could be achieved, in principle, either by a reaction of the racemic tetramethoxyresorcin[4]arenes with (*S*)-(+)-10-camphorsulfonyl chloride in pyridine or by using our low-temperature deprotonation protocol,[6] in which hydroxyresorcin[4]arenes are treated with *n*-butyllithium at –78 °C in THF followed by reaction with the electrophile, in this case (*S*)-(+)-10-camphorsulfonyl chloride. It is clear that the establishment of the absolute configurations of the (*S*)-(+)-10-camphorsulfonates followed by hydrolysis would allow for the determination of the absolute configurations of the enantiomers of the tetraalkoxyresorcin[4]arenes. The absolute configurations of the enantiomeric tetraalkoxyresorcin[4]arenes could also be established by reference to the known absolute configurations of chiral nonracemic tetrabenzoxazines such as the compounds **5** and **6**, whose structures were known from X-ray crystallographic data.[6b] When the study, conducted at Loughborough and Curtin, including the determination of the absolute configurations of a number of camphorsulfonates derived from racemic tetraalkoxyresorcin[4]arenes and their hydrolysis products, was almost ready for publication, the absolute configurations of the tetramethoxyresorcinarenes **7** derived from 3-methylbutanal and 3-methoxyphenol were published.[9] The Loughborough and Curtin groups were surprised that the results of their study were not in agreement with the published results, and the Loughborough group therefore repeated their experiments. The Loughborough group also prepared and used the racemic mixture of resorcin[4]arenes **7** in order to prepare tetracamphorsulfonates also with the use of (*S*)-(+)-10-camphorsulfonyl chloride. A very recent publication[10] also used the absolute configurations that were reported earlier.[9] The Bielefeld group repeated the experiments with an enantiomerically pure sample of compound **7**,[11] that involved the formation of a crystalline amide: those results confirmed the initial results of the Loughborough and Curtin groups. We now report a full account of all of our studies (Figure 2).

We were able to prepare tetracamphorsulfonate derivatives **8a**–**d** and **8a′**–**d′** shown in Scheme 2, in high yields, from the tetraalkoxyresorcin[4]arenes **4a**–**d** by heating them under reflux in pyridine with an excess of freshly prepared (*S*)-(+)-10-camphorsulfonyl chloride. Lower yields were obtained when using commercial (*S*)-(+)-10-camphorsulfonyl chloride. Separation of the 1:1 mixtures of diastereoisomers was achieved by chromatography on silica gel. However, we

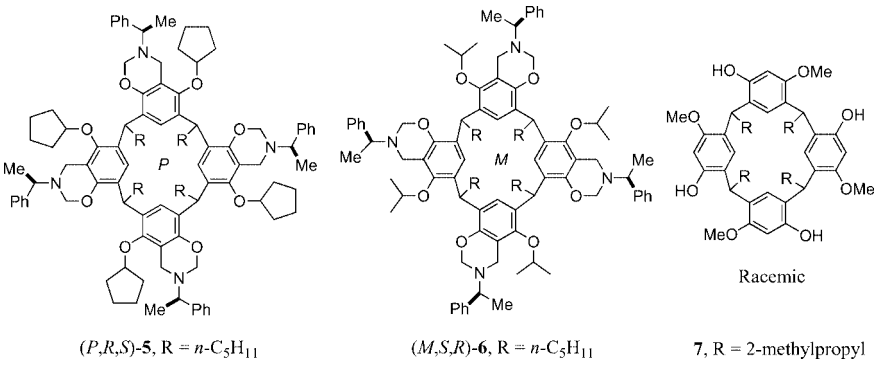
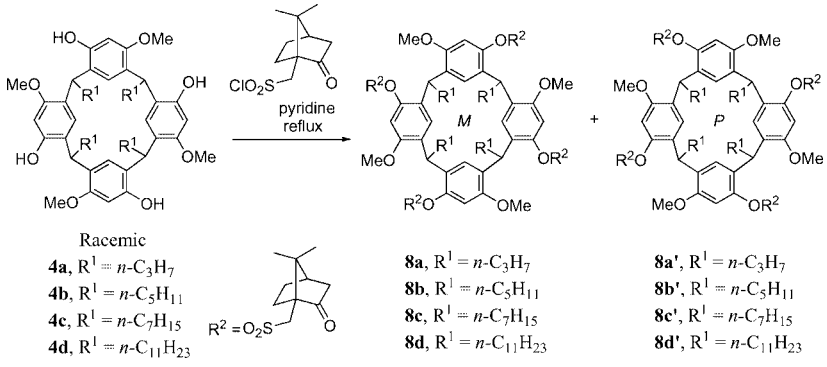


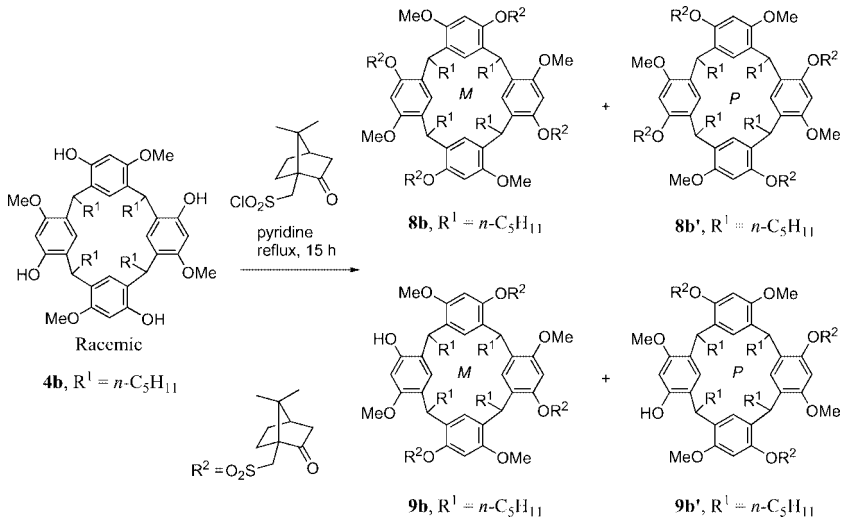
Figure 2. Absolute configurations of chiral nonracemic tetrabenzoxazines and a racemic resorcinarene.

were only able to obtain a good recovery of the faster eluting diastereoisomer in some cases, possibly due to instability during the isolation process in one isomer in each case. For example, when using the resorcinarene **4a**, although NMR spectra of the crude reaction mixtures indicated, as expected, that the diastereoisomers of the 4,10,16,22-tetracamphorsulfonyloxy-6,12,18,24-tetramethoxy-2,8,14,20-tetra-*n*-propylresorcin[4]arenes were formed as a 1:1 mixture, they were isolated in 46% and 23% yields. In one reaction with resorcinarene **4b**, we isolated a pair of diastereoisomeric tricamphorsulfonates in addition to the expected tetracamphorsulfonates. Thus, when we heated a solution of the resorcinarene **4b** under reflux for 15 h in pyridine together with 12 equiv. (*S*)-(+)-10-camphorsulfonyl chloride, we obtained a mixture of two tricamphorsulfonates **9b** and **9b′** in 22% yield together with the two tetracamphorsulfonates **8b** and **8b′** in 28% yield. The tricamphorsulfonates were formed in a 1:4 ratio while the tetracamphorsulfonates were formed in a 4:1 ratio as shown in Scheme 3. This suggests that there is increasing difficulty in the sequential addition of camphorsulfonyl residues to the hydroxy groups, which results from steric problems that particularly affect the slower eluting diastereoisomer of the tricamphorsulfonate. That effect provides an explanation of the apparent diastereoselectivity in the latter reaction. Crystals of the first eluting diastereoisomers **8a** and **8b** that were suitable for X-ray crystallographic analysis were obtained, and the crystal structures are shown in Figure 3 and Figure 4. Because of the potential confusion that has arisen in defining the absolute configuration of some C_4 symmetric resorcin[4]arenes, we introduced the convention of using the prefix (*P*)- or (*M*)- when defining the priority of substituents around an axis of chirality,[6b] by reference to the Cahn, Ingold and Prelog convention,[12a] and subsequent discussions concerning axial chirality,[12b,c,d] together with the discussion of a new kind of stereoisomerism, cycloenantiomerism and cyclodiastereomerism by Prelog and his co-workers, which can be considered when the two directions in a cyclic structure can be distinguished.[13] The crystal structures established that the two diastereoisomers were (*M*,*S*,*R*)-4,10,16,22-tetracamphorsulfonyloxy-6,12,18,24-tetramethoxy-2,8,14,20-tetra-*n*-propylresorcin[4]arene (**8a**) and (*M*,*S*,*R*)-4,10,16,22-tetracamphorsulfonyloxy-6,12,18,24-tetramethoxy-2,8,14,20-tetra-*n*-pentylresorcin[4]-arene (**8b**) (see Figures 3 and 4).

The influence of steric problems became even more evident when we studied the reactions of (*S*)-(+)-10-camphorsulfonyl chloride with the tetraalkoxyresorcin[4]arenes **4e** and **4f** with bulkier head groups. In a reaction in which 8 equiv. freshly prepared (*S*)-(+)-10-camphorsulfonyl chloride, the tetraisopropyloxyresorcin[4]arene **4e** and DMAP were heated under reflux in pyridine, we were only able to obtain a mixture of diastereoisomeric monocamphorsulfonates in a combined yield of 56%. The products **10e** and **10e′**, shown in Scheme 4, were separated by flash chromatography on silica gel after the prior separation from unchanged tetraisopropyloxyresorcin[4]arene **4e**. In similar reactions, in which we omitted the DMAP and used the resorcinarenes **4e** or **4f** in pyridine, we obtained mixtures of two dicamphorsulfonates in a combined yield of 64% when



Scheme 2. The formation of tetracamphorsulfonates from racemic resorcinarenes.



Scheme 3. The formation of tri- and tetracamphorsulfonates from the racemic resorcinarene **4b**.

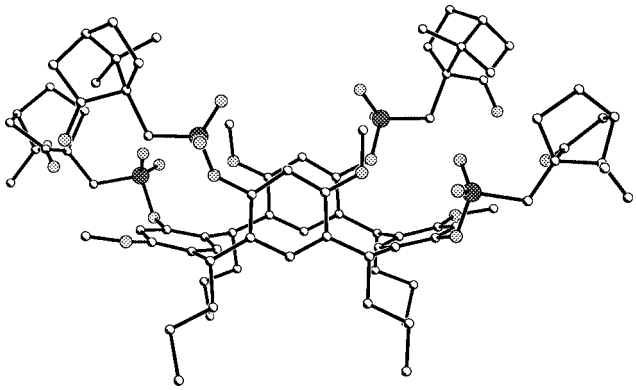


Figure 3. X-ray structure of the tetracamphorsulfonate (*M*,*S*,*R*)-**8a**; the hydrogen atoms are omitted for clarity.

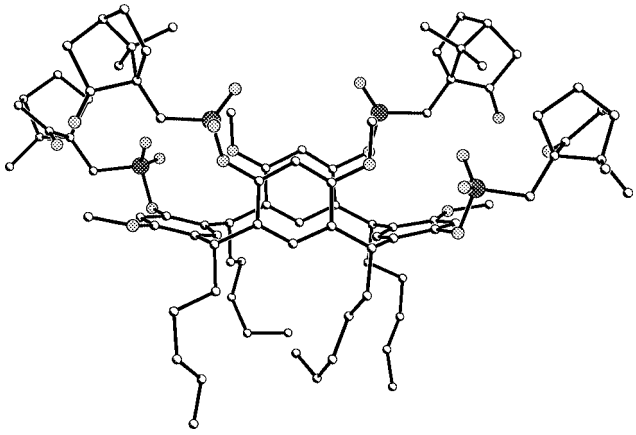
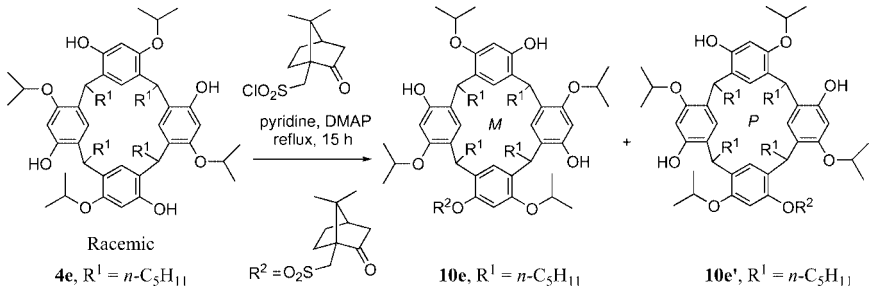


Figure 4. X-ray structure of the tetracamphorsulfonate (*M*,*S*,*R*)-**8b**; the hydrogen atoms are omitted for clarity.

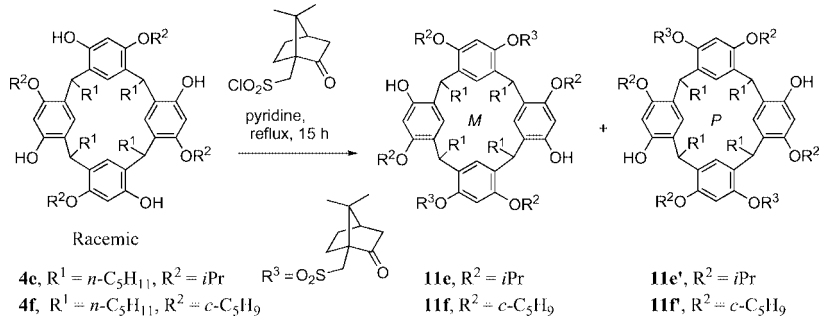
using **4e** and in 46% yield when using **4f**. Although we do not have a crystal structure of any of the diastereoisomers of those dicamphorsulfonates, the steric problems noted above suggest that it is most likely that they are the distally substituted compounds **11e** and **11f**, and **11e′** and **11f′** shown in Scheme 5. We will return to this question below, in connection with reactions of anions generated by using an excess of *n*-butyllithium in tetrahydrofuran.

We next turned our attention to deprotonation of the racemic tetraalkoxyresorcin[4]arenes using our previously disclosed deprotonation protocol,[6a] in which *n*-butyllithium in hexanes is added to a solution of an appropriate resorcin[4]arene derivative in anhydrous tetrahydrofuran at –78 °C. As well as allowing for the possibility of preparing mono- and dicamphorsulfonates, we hoped to access some of the tetracamphorsulfonates in improved yields. In a reaction of the racemic tetramethoxyresorcin[4]arene **4b**, the addition of 1.2 equiv. *n*-butyllithium at –78 °C was followed, after 2 h, by the addition of a THF solution of freshly prepared (*S*)-(+)-10-camphorsulfonyl chloride (1.3 equiv.). After allowing the reaction mixture to warm to room temperature over 12 h, normal workup was followed by initial chromatographic separation of the reaction mixture on silica gel to give unchanged tetramethoxyresorcin[4]arene **4b** together with mixtures of diastereoisomeric mono- and dicamphorsulfonates. Repeated chromatography of the mono- and dicamphorsulfonate mixtures allowed the isolation of a pair of monocamphorsulfonates each in 25% yield, together with a pair of dicamphorsulfonates each in 9% yield. In a reaction in which the amounts of *n*-butyllithium and (*S*)-(+)-10-camphorsulfonyl chloride were increased to 2.2 and 2.3 equiv., respectively, we obtained the mono- and dicamphorsulfonates each in 33% yield, as shown in Scheme 6. Finally, the diastereoisomeric tetracamphorsulfonates were obtained in combined yields of 60% and 74% when reactions of the tetra-anion with freshly prepared (*S*)-(+)-10-camphorsulfonyl chloride were carried out as shown in Scheme 7, in the first case initially at –78 °C and in the latter case initially at 0 °C.

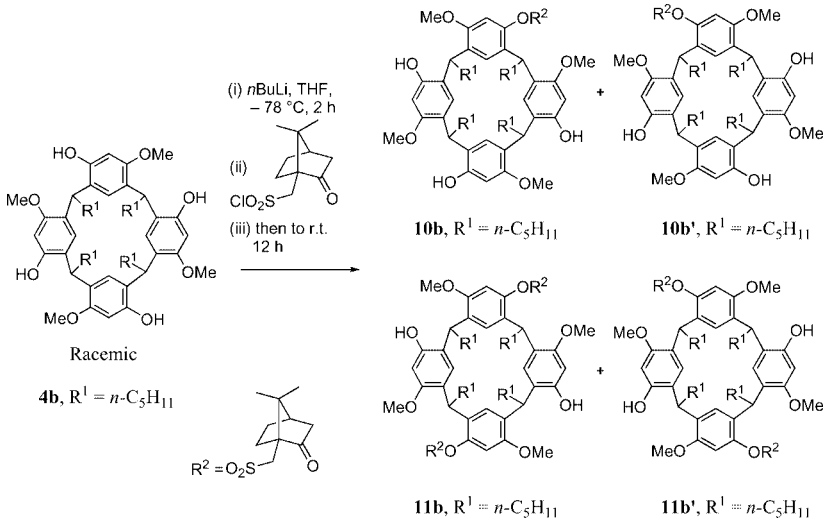
Reactions of (*S*)-(+)-10-camphorsulfonyl chloride with anions derived from the racemic tetraisopropyloxy- and tetracyclopentyloxyresorcin[4]arenes **4e** and **4f** provided an



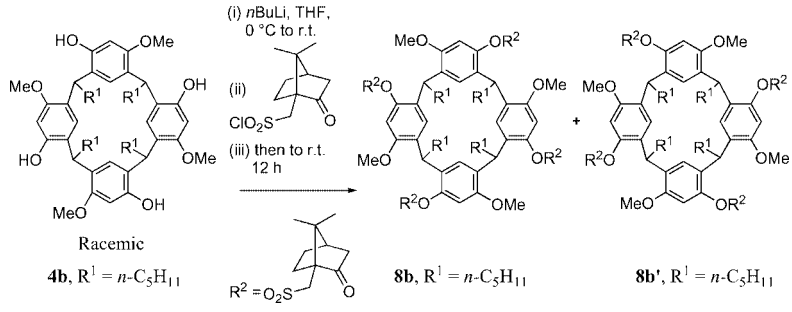
Scheme 4. The formation of monocamphorsulfonates from the racemic resorcinarene **4e**.



Scheme 5. The formation of dicamphorsulfonates from the racemic resorcinarenes **4e** and **4f**.

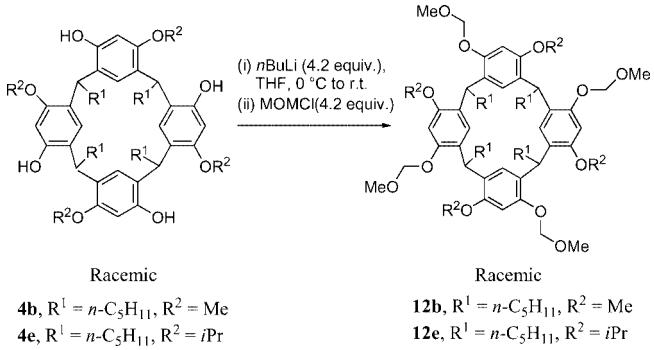


Scheme 6. The formation of mono- and dicamphorsulfonates from the anions of the racemic resorcinarene **4b**.



Scheme 7. The formation of tetracamphorsulfonates from a tetra-anion.

interesting confirmation of the steric problems associated with the introduction of more than two camphorsulfonyl residues on the tetraalkoxyresorcin[4]arene scaffold. That we were able to prepare a tetra-anion from the tetraisopropyloxyresorcin[4]arene **4e** was shown by the reaction with methoxymethyl chloride, which gave the racemate of the MOM ethers **12e** in 46% yield, as shown in Scheme 8. This result may be compared to the analogous reaction with the tetramethoxyresorcin[4]arene **4b**, from which the MOM ethers **12b** were obtained in 90% yield.



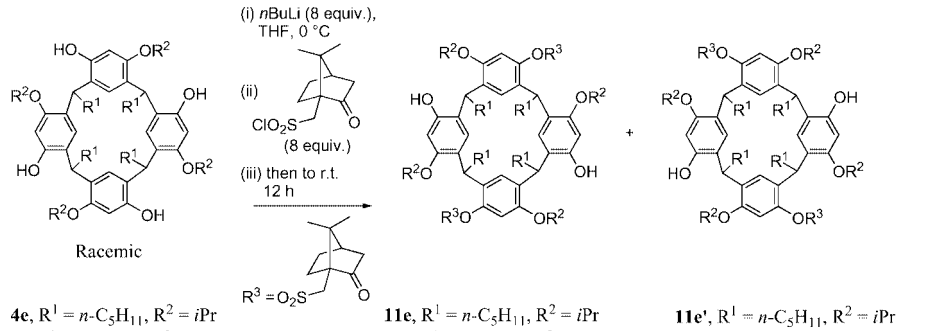
4b, $R^1 = n\text{-}C_5H_{11}$, R^2 = Me
4e, $R^1 = n\text{-}C_5H_{11}$, $R^2 = i$Pr
12b, $R^1 = n\text{-}C_5H_{11}$, R^2 = Me
12e, $R^1 = n\text{-}C_5H_{11}$, $R^2 = i$Pr

Scheme 8. The formation of tetrakis(methoxymethyl) ethers from tetra-anions.

Our initial reactions with anions derived from the racemic tetraisopropyloxy- and tetracyclopentyloxyresorcin[4]-arenes **4e** and **4f** were carried out by using 2.1 equiv. *n*-butyllithium and 2.1 equiv. (*S*)-(+)-10-camphorsulfonyl chloride. In the reactions with racemic **4e**, we obtained the monocamphorsulfonates **10e** and **10e′** in a combined yield of 48% together with a mixture of dicamphorsulfonates in 18% yield. Similarly, a reaction with the racemic **4f** gave the monocamphorsulfonates **10f** and **10f′** in 46% yield together with the dicamphorsulfonates **11f** and **11f′** in 22% yield. In view of the fact that we had found the more highly substituted derivatives easier to separate, we decided to attempt to prepare tetracamphorsulfonates from the resorcinarenes **4e** and **4f**. A reaction of the racemic tetraisopropyloxyresorcin[4]arene **4e** with *n*-butyllithium (8 equiv.) at 0 °C followed by the addition of an excess of (*S*)-(+)-10-camphorsulfonyl chloride gave, however, a mixture of the diastereoisomeric dicamphorsulfonates **11e** and **11e′** in a combined yield of 82%, as shown in Scheme 9. No trace of a tri- or tetracamphorsulfonate was detected. A similar reaction with the racemic compound **4f** gave a mixture of the diastereoisomeric dicamphorsulfonates **11f** and **11f′** in a combined yield of 56%, also shown in Scheme 9. We ascribe the failure to form tetracamphorsulfonates in these latter reactions to steric hindrance to the sulfonylation reaction that we noted to a lesser extent in the reaction with methoxymethyl chloride, illustrated in Scheme 8.

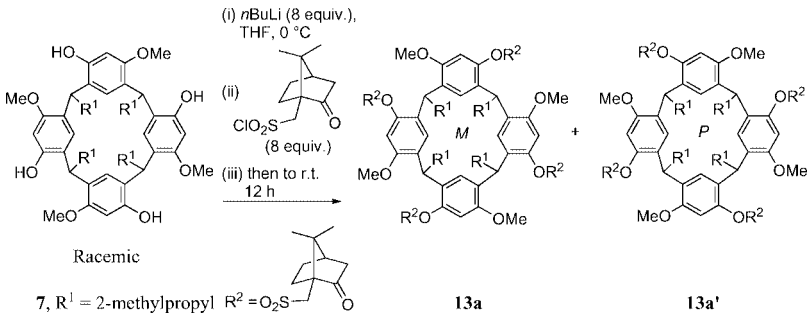
Finally, we prepared the tetracamphorsulfonates **13a** and **13a′** by using (*S*)-(+)-10-camphorsulfonyl chloride (Scheme 10) and **13b** and **13b′** by using freshly prepared (*R*)-(–)-10-camphorsulfonyl chloride (Scheme 11) from the racemic resorcin[4]arene **7** by the tetra-anion route. The structures of the tetracamphorsulfonates **13a** and **13b** were confirmed by the X-ray crystal structures shown in Figure 5 and Figure 6.[14]

The structures of the various camphorsulfonates were established by using a variety of analytical techniques in addition to X-ray crystallography.[14] The number of camphorsulfonyl residues present in each of the products followed from high resolution (MALDI-TOF) mass spectrometric data in which the observed ion clusters in the molecular ion region matched the calculated intensities. ^{1}H and ^{13}C NMR spectroscopic data of the mono-, tri- and tetracamphorsulfonates were unexceptional. The identification of the diastereoisomeric tetracamphorsulfonates was facilitated by inspection of the ^{1}H NMR spectra. The difference in the chemical shifts of the two aromatic methine hydrogen atoms was ca. 0.08 ppm in the case of the first eluting diastereoisomer and ca. 0.17 ppm in the case of the second eluting diastereoisomer, as illustrated for the compounds **8b** and **8b′** in Figure 7 and Figure 8, respectively. In the case of the dicamphorsulfonates, two possible mixtures could have been formed. However, at present it has not been possible to obtain crystals that are suitable for X-ray analysis from any of the dicamphorsulfonates reported in this paper. Also, it was not possible to distinguish between the two possible regioisomers on the basis of NMR measurements carried out at different temperatures. The steric problems that we observed in the reactions of the racemic tetraisopropyloxy- and tetracyclopentyloxyresorcin[4]arenes **4e** and **4f** strongly support our suggestion that the tetraalkoxyresorcinarenes are distally disubstituted in the dicamphorsulfonates.

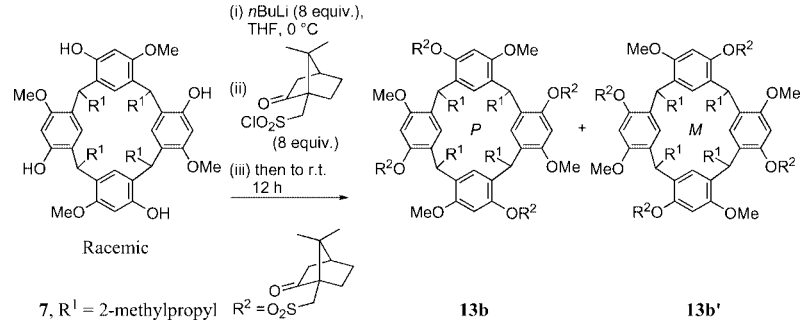


4e, $R^1 = n\text{-}C_5H_{11}$, $R^2 = i$Pr
4f, $R^1 = n\text{-}C_5H_{11}$, $R^2 = c\text{-}C_5H_9$
11e, $R^1 = n\text{-}C_5H_{11}$, $R^2 = i$Pr
11f, $R^1 = n\text{-}C_5H_{11}$, $R^2 = c\text{-}C_5H_9$
11e', $R^1 = n\text{-}C_5H_{11}$, $R^2 = i$Pr
11f', $R^1 = n\text{-}C_5H_{11}$, $R^2 = c\text{-}C_5H_9$

Scheme 9. The formation of dicamphorsulfonates from tetra-anions.



Scheme 10. The formation of tetracamphorsulfonates from the racemic resorcinarene **7** by using (*S*)-(+)-10-camphorsulfonyl chloride.



Scheme 11. The formation of tetracamphorsulfonates from the racemic resorcinarene **7** by using (*R*)-(–)-10-camphorsulfonyl chloride.

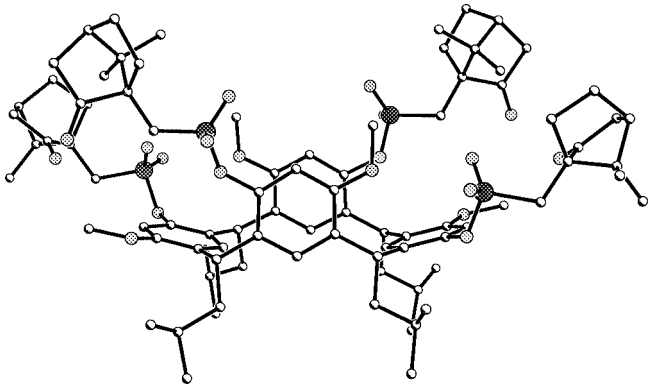


Figure 5. X-ray structure of the tetracamphorsulfonate (*M*,*S*,*R*)-**13a**; the hydrogen atoms are omitted for clarity.

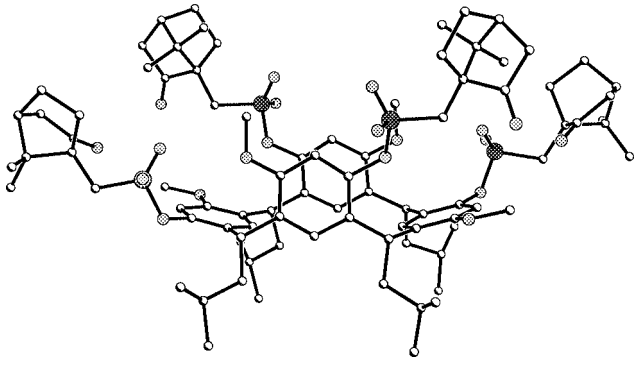


Figure 6. X-ray structure of the tetracamphorsulfonate (*P*,*R*,*S*)-**13b**; the hydrogen atoms are omitted for clarity.

We turned our attention next to the hydrolysis of the pure diastereoisomeric camphorsulfonates in order to obtain enantiomerically pure tetraalkoxyresorcin[4]arenes. Hydrolysis of the camphorsulfonates was achieved by heating aqueous alcoholic sodium hydroxide solutions under reflux. The results, illustrated for the first eluting diastereoisomer derived from (*S*)-(+)-10-camphorsulfonyl chloride, are shown for the hydrolyses of the tetracamphorsulfonates in Scheme 12 and for those of the dicamphorsulfonates in Scheme 13. The most important conclusion that emerged from those reactions is that, as expected, the hydrolyses of each of the first eluting diastereoisomers derived from reactions with (*S*)-(+)-10-camphorsulfonyl chloride gave enantiomerically pure tetraalkoxyresorcin[4]arenes that each had specific rotations with the same sign: in the case of the first eluting diastereoisomers a (+)-specific rotation. The hydrolysis of the second eluting diastereoisomer in each case gave the (–) enantiomer; for example, **13a′** gave (*M*,*R*)-(–)-**7**. In the case of the hydrolysis of the diastereoisomers **13b** and **13b′** that were obtained by using (*R*)-(–)-10-camphorsulfonyl chloride, hydrolysis of the first eluting diastereoisomer gave, as anticipated, the enantiomer (*M*,*R*)-(–)-**7**, shown in Scheme 14, and the second eluting diastereoisomer gave the enantiomer (*P*,*S*)-(+)-**7**.

As an additional confirmation of the absolute configurations of some of the chiral nonracemic tetraalkoxyresorcinarenes, we had the possibility of comparing NMR spectroscopic data for some tetrabenzoxazine derivatives which we had obtained from reactions of tetraalkoxyresorcinarenes with chiral nonracemic *N*,*N*-bis(methoxymethyl)(α-methylbenzyl)amine derivatives.[6b] Compound **14** was pre-

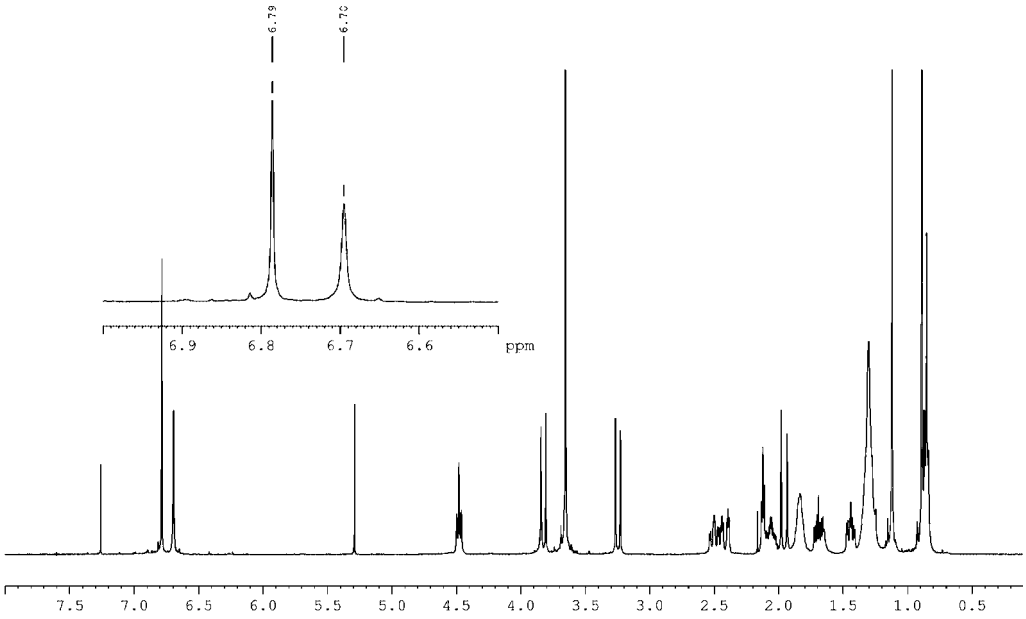


Figure 7. The ^{1}H NMR spectrum of tetracamphorsulfonate (*M*,*S*,*R*)-**8b**.

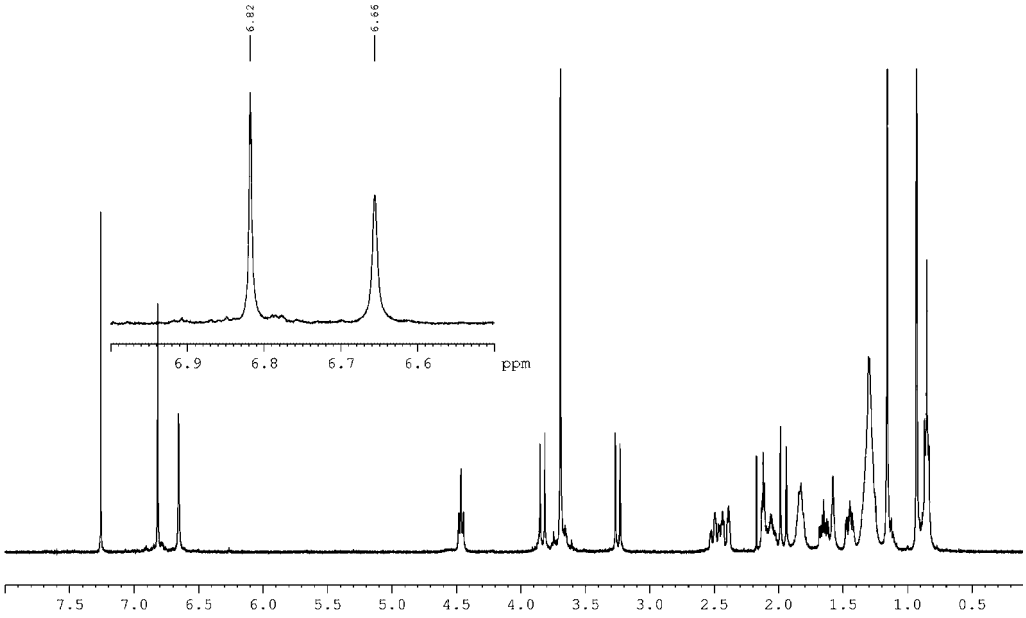
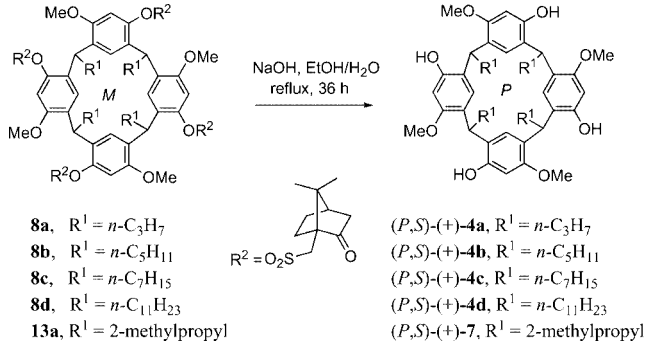
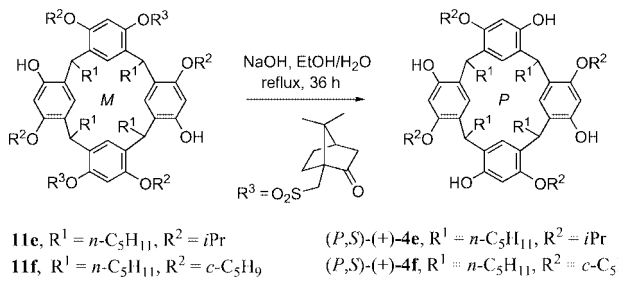


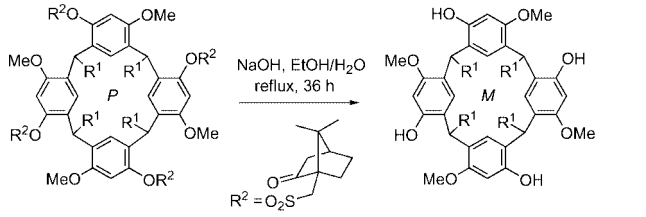
Figure 8. The ^{1}H NMR spectrum of tetracamphorsulfonate (*P*,*S*,*S*)-**8b**′.



Scheme 12. Hydrolyses of the first eluting tetracamphorsulfonates derived from (*S*)-(+)-10-camphorsulfonyl chloride.



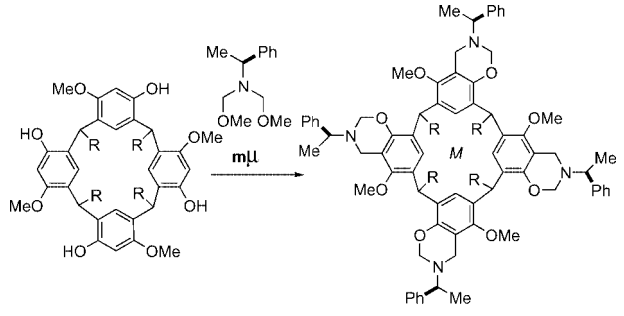
Scheme 13. Hydrolyses of the first eluting dicamphorsulfonates derived from (*S*)-(+)-10-camphorsulfonyl chloride.



13b, R^1 = 2-methylpropyl (*M*,*R*)-(–)-**7**, R^1 = 2-methylpropyl

Scheme 14. Hydrolysis of the first eluting tetracamphorsulfonate derived from (*R*)-(–)-10-camphorsulfonyl chloride.

pared in 46% yield from (*P*,*S*)-(+)-**4b** by using *N*,*N*-bis(methoxymethyl)[(*S*)-(–)-(α-methylbenzyl)]amine; its absolute configuration was known from an earlier study.[6a] The structures of the diastereoisomers (*P*,*R*,*S*)-**5** and (*M*,*S*,*R*)-**6** were known from the results of X-ray structure determinations.[6b] We prepared compound (*P*,*R*,*S*)-**5** and compound (*M*,*R*,*R*)-**6′**, the diastereoisomer of compound (*M*,*S*,*R*)-**6**, from (*M*,*R*)-(–)-**4f** in 58% yield and (*P*,*S*)-(+)-**4e** in 53% yield by using *N*,*N*-bis(methoxymethyl)[(*R*)-(+)-(α-methylbenzyl)]amine. These experiments also confirmed the assignments of the absolute configurations of enantiomerically pure tetraalkoxyresorcin[4]arenes. In the case of the racemic tetramethoxyresorcin[4]arene **7**, we reported earlier the synthesis of the diastereoisomeric tetrabenzoxazines by using the microwave-enhanced method: separation of the diastereoisomers gave compounds whose NMR spectra could be compared with compounds that had been obtained previously.[6b] We prepared the diastereoisomer **15a** from the chiral nonracemic tetramethoxyresorcin[4]arene (*P*,*S*)-(+)-**7** by the microwave-enhanced method shown in Scheme 15. Spectroscopic data confirmed the anticipated structure as **15a** and as a result provided additional confirmation of the structures of the enantiomeric tetramethoxyresorcin[4]arenes (*P*,*S*)-(+)-**7** and (*M*,*R*)-(–)-**7**.



(*P*,*S*)-(+)-**7**, R = 2-methylpropyl (*M*,*S*,*R*)-**15a**

Scheme 15. The synthesis of the tetrabenzoxazine (*M*,*S*,*R*)-**15a** from the resorcinarene (*P*,*S*)-(+)-**7**.

Conclusions

In this study we have shown that it is possible to prepare and isolate diastereoisomeric mono-, di-, tri- and tetracamphorsulfonates from a range of tetraalkoxyresorcin[4]arenes. The absolute configurations of the diastereoisomers were established by a combination of X-ray crystallographic and NMR spectroscopic studies. Hydrolysis of the single diastereoisomeric camphorsulfonates gave a series of tetraalkoxyresorcin[4]arenes in which the (+) enantiomers were shown to be of (*P*,*S*)- chirality and the (–) enantiomers were of (*M*,*R*)- chirality. Further confirmation of the absolute stereochemistry of the tetramethoxyresorcin[4]arene (*P*,*S*)-(+)-**7** was provided by its conversion into the tetrabenzoxazine derivative **15a**. These results correct the assignment of the absolute stereochemistry of the tetramethoxyresorcin-[4]arene (+)-**7** and also of (–)-**7**. Furthermore, the absolute stereochemistries of diastereoisomeric tetrakis(2-methylbutyloxy) ethers derived from the compounds (*P*,*S*)-(+)-**7** and (*M*,*R*)-(–)-**7** and a pair of diastereoisomeric tetrakis(2-methylbutyloxy)resorcin[4]arenes that were reported in the earlier study.[9]

Experimental Section

General Experimental Detail: All infrared spectra were obtained with a Perkin–Elmer Paragon 1000 FT-IR and a Bruker Vector 22 FTIR spectrometer; thin film spectra were acquired by using sodium chloride plates. All ^{1}H and ^{13}C NMR spectra were measured at 400.13 and 100.62 MHz with a Bruker DPX 400/Avance 400 MHz spectrometer in deuteriochloroform solution, unless otherwise stated, by using TMS (tetramethylsilane) as the internal reference. Electron-impact (EI) and fast atom bombardment (FAB) mass spectra were recorded with a Jeol-SX102 instrument. Electrospray (ES) and MALDI-TOF spectra were recorded by the EPSRC national mass spectrometry service at the University of Wales, Swansea. Analysis by GCMS was carried out with a Fisons GC 8000 series (AS 800) instrument, by using a 15 m × 0.25 mm DB-5 column and a low-resolution electron-impact mass spectrometer. Melting points were recorded with an Electrothermal-IA 9100 melting point instrument and are uncorrected. Optical rotation values were measured with an Optical Activity-polAAar 2001 instrument and a Perkin–Elmer 141 polarimeter operating at λ = 589 nm, which corresponds to the sodium D line, at the temperatures indicated. Microanalyses were performed with a Perkin–Elmer Elemental Analyser 2400 CHN. Silica gel was used as the adsorbent in all chromatographic manipulations. Reactions were monitored by thin layer chromatography (TLC) on aluminium-backed plates coated with Merck Kieselgel 60 F254 silica gel. TLC plates were visualized by UV radiation at a wavelength of 254 nm or stained by exposure to an ethanol solution of phosphomolybdic acid (acidified with concentrated sulfuric acid) followed by charring where appropriate. Reactions requiring anhydrous conditions were carried out by using flame-dried glassware under a nitrogen atmosphere unless otherwise stated. Reaction solvents were used as obtained commercially unless otherwise stated. Light petroleum (b.p. 40–60 °C) was distilled from calcium chloride prior to use. Ethyl acetate was distilled from calcium sulfate or chloride. Dichloromethane was distilled from calcium hydride. Tetrahydrofuran was distilled under a nitrogen atmosphere from the sodium/benzophenone ketyl radical. Microwave reactions were carried out in a CEM Discover focused microwave set at a maximum of 300 W.

General Procedure 1: The corresponding resorcinarene was dissolved in dry pyridine (10 mL) under a nitrogen atmosphere and (*S*)-(+)-camphorsulfonyl chloride added in several portions at room temperature. The mixture was then heated under reflux overnight. The bulk of the pyridine was removed at reduced pressure and the

residue stirred with dilute hydrochloric acid (30 mL) for 30 min. The mixture was then extracted with diethyl ether (2 × 30 mL), and the combined organic phases were washed with dilute hydrochloric acid (2 × 30 mL), water (1 × 30 mL), brine (1 × 30 mL) and dried with anhydrous magnesium sulfate (or anhydrous sodium sulfate). The ether was removed under reduced pressure to give a mixture of the desired compounds.

General Procedure 2: The corresponding resorcinarene was dissolved in tetrahydrofuran (50 mL) and the solution was cooled down to –78 °C (or 0 °C). *n*-Butyllithium (2.5 M in hexanes) was slowly added to the solution and the reaction mixture was stirred for 30 min at –78 °C (or 0 °C). A solution of a camphorsulfonyl chloride in tetrahydrofuran (10 mL) was then slowly added with a cannula to the reaction mixture. The mixture was warmed to room temperature and was stirred for 12 h. A solution of hydrochloric acid (3.5 M) was then added to bring the pH below 7, and the phases were separated. The aqueous phase was then extracted with diethyl ether (3 × 25 mL). The combined organic phases were washed with brine, dried with anhydrous magnesium sulfate (or anhydrous sodium sulfate) and concentrated under reduced pressure to give a mixture of the desired compounds.

General Procedure 3: The corresponding resorcinarene was dissolved in methanol or ethanol (10 mL). Water (1 mL) and sodium hydroxide were added, and the mixture was heated under reflux overnight. The solvent was removed under reduced pressure. Water (approx. 10 mL) was then added to the residue. The pH of the mixture was then adjusted to pH 2 with hydrochloric acid (conc.) and the acidified mixture extracted with dichloromethane (2 × 10 mL). The combined organic phases were dried with anhydrous magnesium sulfate (or sodium sulfate), and the solvent was removed under reduced pressure.

Compounds (*M*,*S*,*R*)-8a and (*P*,*S*,*S*)-8a′: General procedure 1 with 6,12,18,24-tetramethoxy-2,8,14,20-tetrapropylresorcin[4]arene (**4a**)[6b] (2.00 g, 2.8 mmol) and (*S*)-(+)-camphorsulfonyl chloride (5.63 g, 22.5 mmol) gave a diastereoisomeric mixture which was placed on a column of silica gel and eluted with CH_2Cl_2/EtOAc (93:7). The resulting glassy solids were crystallized from methanol to give:

Compound (*M*,*S*,*R*)-8a: As colourless crystals (2.02 g, 46%). M.p. 189–191 °C (Softens 165 °C). $[\alpha]_D^{25}$ +61.3 (*c* = 6.2). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 2958, 2873, 1748, 1498, 1357 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.90 (s, 12 H), 0.95 (t, *J* = 7.4 Hz, 12 H), 1.14 (s, 12 H), 1.30–1.50 (m, 12 H), 1.65–1.75 (m, 4 H), 1.79–1.90 (m, 8 H), 1.97 (d, *J* = 18.8 Hz, 4 H), 2.01–2.16 (m, 8 H), 2.38–2.57 (m, 8 H), 3.26 and 3.84 (AB, *J* = 14.8 Hz, 8 H), 3.67 (s, 12 H), 4.52 (t, *J* = 7.4 Hz, 4 H), 6.73 (s, 4 H), 6.80 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.9, 20.4, 20.6, 21.7, 25.8, 27.6, 36.4, 37.7, 43.2, 43.6, 48.5, 49.1, 56.6, 58.8, 105.4, 126.9, 129.0, 131.7, 146.4, 156.1, 214.7 ppm.

Compound (*P*,*S*,*S*)-8a′: As a glassy solid (1.02 g, 23%). $[\alpha]_D^{25}$ +2.6 (*c* = 4.2). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 2957, 2872, 1749, 1498, 1357 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.92–0.96 (m, 24 H), 1.17 (s, 12 H), 1.30–1.51 (m, 12 H), 1.61–1.71 (m, 4 H), 1.79–1.88 (m, 8 H), 1.97 (d, *J* = 18.4 Hz, 4 H), 2.00–2.16 (m, 8 H), 2.37–2.56 (m, 8 H), 3.26 and 3.85 (AB, *J* = 15.0 Hz, 8 H), 3.70 (s, 12 H), 4.50 (t, *J* = 7.3 Hz, 4 H), 6.68 (s, 4 H), 6.83 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.9, 20.4, 20.7, 21.7, 25.8, 27.6, 36.6, 37.5, 43.1, 43.7, 48.5, 49.3, 56.6, 58.8, 105.5, 126.9, 128.8, 131.5, 146.5, 156.1, 214.6 ppm. MS: *m*/*z* = 1568.6 $[M]^+$.

Compounds (*M*,*S*,*R*)-8b and (*P*,*S*,*S*)-8b′ and Compounds 9b and 9b′: General procedure 1 with 6,12,18,24-tetramethoxy-22,8,14,20-tetrapentylresorcin[4]arene (**4b**) (0.20 g, 0.24 mmol) and (*S*)-(+)-camphorsulfonyl chloride (0.72 g, 2.88 mmol) gave a diastereoisomeric mixture, which was placed on a column of silica gel and eluted with CH_2Cl_2/Et_2O (96:4) to give:

Compound (*M*,*S*,*R*)-8b: As a colourless foam (0.095 g, 23%). $[\alpha]_D^{25}$ +41.8 (*c* = 1.1, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 2955, 2929, 2858, 1747, 1497, 1455, 1356, 1193, 1129, 1068, 1053, 831 and 810 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.85 (t, *J* = 7.0 Hz, 12 H), 0.89 (s, 12 H), 1.12 (s, 12 H), 1.24–1.35 (m, 24 H), 1.44 (ddd, *J* = 12.7, 9.3, 3.8 Hz, 4 H), 1.68 (ddd, *J* = 14.0, 9.3, 4.3 Hz, 4 H), 1.79–1.86 (m, 8 H), 1.99 (d, *J* = 18.4 Hz, 4 H), 2.03–2.13 (m, 8 H), 2.41 (dt, *J* = 9.3, 3.8 Hz, 4 H), 2.51 (ddd, *J* = 14.0, 11.9, 4.3 Hz, 4 H), 3.24 and 3.82 (AB, *J* = 15.0 Hz, 8 H), 3.65 (s, 12 H), 4.48 (t, *J* = 7.3 Hz, 4 H), 6.69 (s, 4 H), 6.78 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 19.7, 19.9, 22.6, 25.1, 26.9, 27.7, 32.1, 34.7, 36.0, 42.5, 42.9, 47.9, 48.5, 55.9, 58.1, 104.7, 126.2, 128.3, 131.1, 145.7, 155.4, 214.0 ppm. MS (FAB): calcd. for $[C_{92}H_{128}O_{20}S_4 + H]^+$ 1681.7960; found 1681.7935.

Compound (*P*,*S*,*S*)-8b′: As a colourless foam (0.023 g, 5.5%). $[\alpha]_D^{25}$ +12.3 (*c* = 1.2, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 2954, 2928, 2856, 1747, 1613, 1582, 1496, 1356, 1277, 1193, 1179, 1067, 1053, 832 and 810 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.85 (t, *J* = 7.0 Hz, 12 H), 0.93 (s, 12 H), 1.16 (s, 12 H), 1.25–1.36 (m, 24 H), 1.38–1.49 (m, 4 H), 1.65 (ddd, *J* = 14.0, 9.2, 4.4 Hz, 4 H), 1.79–1.85 (m, 8 H), 1.97 (d, *J* = 18.4 Hz, 4 H), 2.01–2.17 (m, 8 H), 2.41 (dt, *J* = 9.3, 3.6 Hz, 4 H), 2.46 (ddd, *J* = 14.0, 12.0, 3.8 Hz, 4 H), 3.25 and 3.85 (AB, *J* = 14.8 Hz, 8 H), 3.70 (s, 12 H), 4.47 (t, *J* = 7.2 Hz, 4 H), 6.66 (s, 4 H), 6.82 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 19.7, 20.0, 22.6, 25.1, 26.9, 27.7, 32.0, 34.6, 36.2, 42.4, 43.0, 47.8, 48.6, 55.9, 58.1, 104.8, 126.2, 128.2, 130.9, 145.8, 155.5, 213.8 ppm. MS (MALDI-TOF): *m*/*z* = 1704.8 $[M + Na]^+$; the isotopic distribution of the observed data matched the theoretical $[M + Na]^+$ isotopic distribution.

Compound 9b: As a colourless foam (0.017 g, 4.8%). $[\alpha]_D^{25}$ +34.4 (*c* = 1.0, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3478, 2956, 2927, 2855, 1746, 1495, 1356, 1262, 1193, 1179, 1068, 1053, 1022, 809 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.84 (m, 12 H), 0.89 (s, 3 H), 0.91 (s, 3 H), 1.15 (s, 3 H), 1.16 (s, 3 H), 1.18 (s, 3 H), 1.23 (s, 3 H), 1.38–1.27 (m, 24 H), 1.46 (m, 1 H), 1.78–1.60 (m, 3 H), 2.00–1.82 (m, 11 H), 2.18–2.02 (m, 6 H), 2.61–2.39 (m, 6 H), 3.22 and 3.87 (AB, *J* = 14.8 Hz, 2 H), 3.25 and 3.89 (AB, *J* = 14.8 Hz, 2 H), 3.32 and 3.77 (AB, *J* = 14.8 Hz, 2 H), 3.60 (s, 3 H), 3.66 (s, 3 H), 3.74 (s, 3 H), 3.86 (s, 3 H), 4.24 (t, *J* = 7.1 Hz, 1 H), 4.57 (m, 3 H), 6.27 (s, 1 H), 6.75 (s, 1 H), 6.78 (s, 1 H), 6.85 (s, 1 H), 6.89 (s, 1 H), 6.90 (s, 1 H), 6.92 (s, 1 H), 7.06 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 19.8, 19.9, 20.0, 22.4, 22.5, 22.6, 22.7, 25.1, 25.2, 26.8, 27.4, 27.5, 27.6, 27.7, 29.7, 31.9, 32.0, 32.1, 34.3, 34.7, 35.1, 35.2, 35.3, 35.5, 35.8, 42.5, 42.8, 42.9, 47.8, 47.9, 48.1, 48.2, 48.3, 55.7, 55.8, 55.9, 56.1, 58.1, 58.2, 99.8, 104.3, 104.4, 104.8, 120.9, 123.9, 125.1, 125.7, 126.1, 126.8, 127.9, 129.7, 129.9, 130.5, 131.1, 131.5, 145.6, 145.8, 146.0, 152.6, 154.1, 155.1, 155.5, 156.4, 214.1 ppm. MS (MALDI-TOF): *m*/*z* = 1490.7 $[M + Na]^+$; the isotopic distribution of the observed data matched the theoretical $[M + Na]^+$ isotopic distribution.

Compound 9b′: As a colourless foam (0.065 g, 18%). $[\alpha]_D^{25}$ –46.7 (*c* = 1.2, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3482, 2954, 2928, 2857, 1748, 1496, 1356, 1278, 1194, 1179, 1067, 1053, 832, 811 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.85 (m, 12 H), 0.86 (s, 3 H), 0.91 (s, 3 H), 0.92 (s, 3 H), 1.14 (s, 3 H), 1.17 (s, 3 H), 1.18 (s, 3 H), 1.36–1.25 (m, 24 H), 1.45 (m, 3 H), 1.61 (m, 1 H), 1.73 (m, 2 H), 2.00–1.86 (m, 11 H), 2.14–2.04 (m, 6 H), 2.58–2.38 (m, 6 H), 3.21 and 3.78 (AB, *J* = 14.9 Hz, 2 H), 3.29 and 3.89 (AB, *J* = 14.9 Hz, 2 H), 3.29 and 3.93 (AB, *J* = 14.9 Hz, 2 H), 3.61 (s, 3 H), 3.65 (s, 3 H), 3.79

(s, 3 H), 3.86 (s, 3 H), 4.24 (t, J = 7.2 Hz, 1 H), 4.52 (m, 2 H), 4.59 (t, J = 7.1 Hz, 1 H), 6.26 (s, 1 H), 6.67 (s, 1 H), 6.79 (s, 1 H), 6.80 (s, 1 H), 6.91 (s, 1 H), 6.93 (s, 1 H), 6.94 (s, 1 H), 7.07 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 19.7, 19.9, 20.1, 22.5, 22.6, 22.7, 25.1, 25.2, 25.3, 26.8, 26.9, 27.4, 27.5, 27.6, 27.7, 31.9, 32.0, 32.1, 34.5, 34.9, 35.2, 35.4, 35.6, 42.4, 42.5, 42.9, 43.0, 47.8, 47.9, 48.3, 48.4, 48.5, 55.6, 55.8, 55.9, 56.1, 58.1, 99.7, 104.3, 104.4, 105.0, 120.5, 123.5, 125.0, 125.7, 126.0, 126.8, 127.6, 129.6, 129.8, 130.1, 131.1, 131.6, 145.6, 145.7, 146.0, 152.7, 154.2, 154.9, 155.6, 156.4, 214.1 ppm. MS (MALDI-TOF): m/z = 1490.7 $[M + Na]^+$; the isotopic distribution of the observed data matched the theoretical $[M + Na]^+$ isotopic distribution.

General procedure 2 with 6,12,18,24-tetramethoxy-2,8,14,20-tetrapentylresorcin[4]arene (**4b**) (1.0 g, 1.2 mmol), *n*-butyllithium (2.5 M in hexanes, 4.9 mL, 9.7 mmol) and (*S*)-(+)-camphorsulfonyl chloride (3.0 g, 12.1 mmol) at 0 °C gave a diastereoisomeric mixture which was placed on a column of silica gel and eluted with CH_2Cl_2/Et_2O (96:4) to give compound (*M*,*S*,*R*)-**8b** (0.683 g, 33%) and compound (*P*,*S*,*S*)-**8b′** (0.675 g, 33%).

Compounds (*M*,*S*,*R*)-8c and (*P*,*S*,*S*)-8c′: General procedure 1 with 2,8,14,20-tetraheptyl-6,12,18,24-tetramethoxyresorcin[4]arene (**4c**) (0.50 g, 0.53 mmol) and (*S*)-(+)-camphorsulfonyl chloride (1.07 g, 4.3 mmol) gave a diastereoisomeric mixture which was placed on a column of silica gel and eluted with CH_2Cl_2/EtOAc (95:5) to give:

Compound (*M*,*S*,*R*)-8c: As a colourless solid (0.38 g, 39%). $[\alpha]_D^{25}$ +46.7 (c = 4.1). IR (DCM): $\tilde{\nu}_{max}$ = 2928, 2856, 1749, 1498, 1358 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, J = 6.8 Hz, 12 H), 0.90 (s, 12 H), 1.13 (s, 12 H), 1.18–1.39 (m, 40 H), 1.41–1.48 (m, 4 H), 1.66–1.75 (m, 4 H), 1.79–1.89 (m, 8 H), 1.97 (d, J = 18.4 Hz, 4 H), 2.02–2.16 (m, 8 H), 2.38–2.57 (m, 8 H), 3.26 and 3.84 (AB, J = 14.8 Hz, 8 H), 3.67 (s, 12 H), 4.49 (t, J = 7.2 Hz, 4 H), 6.71 (s, 4 H), 6.80 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.8, 20.4, 20.6, 23.4, 25.8, 27.6, 28.7, 30.0, 30.6, 32.7, 35.5, 36.8, 43.2, 43.6, 48.5, 49.1, 56.6, 58.8, 105.4, 126.9, 129.0, 131.8, 146.4, 156.1, 214.7 ppm. MS: m/z = 1793.9 $[M]^+$.

Compound (*P*,*S*,*S*)-8c′: As a colourless solid (0.16 g, 17%). $[\alpha]_D^{25}$ +5.6 (c = 5.7). IR (DCM): $\tilde{\nu}_{max}$ = 2928, 2856, 1749, 1498, 1358 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, J = 6.7 Hz, 12 H), 0.94 (s, 12 H), 1.167 (s, 12 H), 1.17–1.38 (m, 40 H), 1.40–1.56 (m, 4 H), 1.60–1.70 (m, 4 H), 1.77–1.88 (m, 8 H), 1.97 (d, J = 18.4 Hz, 4 H), 2.01–2.15 (m, 8 H), 2.36–2.55 (m, 8 H), 3.25 and 3.84 (AB, J = 15.0 Hz, 8 H), 3.70 (s, 12 H), 4.47 (t, J = 7.3 Hz, 4 H), 6.66 (s, 4 H), 6.83 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.8, 20.4, 20.7, 23.4, 25.8, 27.6, 28.7, 30.0, 30.5, 32.7, 35.3, 36.9, 43.1, 43.6, 48.5, 49.3, 56.5, 58.8, 105.5, 126.9, 128.8, 131.6, 146.4, 156.1, 214.6 ppm. MS: m/z = 1793.9 $[M]^+$.

Compounds (*M*,*S*,*R*)-8d and (*P*,*S*,*S*)-8d′: General procedure 1 with 6,12,18,24-tetramethoxy-2,8,14,20-tetraundecylresorcin[4]arene (**4d**) (0.50 g, 0.43 mmol) and (*S*)-(+)-camphorsulfonyl chloride (0.86 g, 3.4 mmol) gave a diastereoisomeric mixture which was placed on a column of silica gel and eluted with CH_2Cl_2/EtOAc (93:7) to give:

Compound (*M*,*S*,*R*)-8d: As a glassy solid (0.33 g, 38%). $[\alpha]_D^{25}$ +51.4 (c = 3.6). IR (DCM): $\tilde{\nu}_{max}$ = 2925, 2854, 1749, 1498, 1358 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.83–0.92 (m, 24 H), 1.15 (m, 12 H), 1.17–1.37 (m, 72 H), 1.40–1.50 (m, 4 H), 1.65–1.75 (m, 4 H), 1.78–1.90 (m, 8 H), 1.97 (d, J = 18.5 Hz, 4 H), 2.01–2.16 (m, 8 H), 2.37–2.56 (m, 8 H), 3.25 and 3.83 (AB, J = 15.0 Hz, 8 H), 3.66 (s, 12 H), 4.48 (t, J = 7.2 Hz, 4 H), 6.70 (s, 4 H), 6.79 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.8, 20.4, 20.6, 23.4, 25.8, 27.6, 28.7, 30.1, 30.4, 30.5, 30.6, 30.7, 32.6, 35.5, 36.8, 43.2, 43.6, 48.5, 49.1, 56.6, 58.8, 105.4, 126.9, 129.0, 131.8, 146.4, 156.1, 214.6 ppm. MS: m/z = 2018.0 $[M]^+$.

Compound (*P*,*S*,*S*)-8d′: As a glassy solid (0.17 g, 20%). $[\alpha]_D^{25}$ +0.14 (c = 7.02). IR (DCM): $\tilde{\nu}_{max}$ = 2928, 2856, 1749, 1498, 1358 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, J = 6.5 Hz, 12 H), 0.94 (s, 12 H), 1.167 (s, 12 H), 1.17–1.37 (m, 72 H), 1.38–1.50 (m, 4 H), 1.60–1.71 (m, 4 H), 1.76–1.87 (m, 8 H), 1.97 (d, J = 18.5 Hz, 4 H), 2.00–2.15 (m, 8 H), 2.35–2.54 (m, 8 H), 3.25 and 3.84 (AB, J = 15.0 Hz, 8 H), 3.70 (s, 12 H), 4.47 (t, J = 7.2 Hz, 4 H), 6.65 (s, 4 H), 6.82 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.8, 20.4, 20.7, 23.4, 25.8, 27.6, 28.8, 30.1, 30.4, 30.5, 30.57, 30.64, 32.6, 35.3, 36.9, 43.1, 43.6, 48.5, 49.3, 56.5, 58.8, 105.5, 126.9, 128.8, 131.6, 146.4, 156.1, 214.6 ppm. MS: m/z = 2018.3 $[M]^+$.

Compounds 10e and 10e′ and Compounds 11e and 11e′: General procedure 2 with 6,12,18,24-tetraisopropopyloxy-2,8,14,20-tetrapentylresorcin[4]arene (**4e**) (1.0 g, 1.07 mmol), *n*-butyllithium (2.5 M in hexanes, 0.86 mL, 2.14 mmol) and (*S*)-(+)-camphorsulfonyl chloride (0.540 g, 2.14 mmol) at –78 °C gave a diastereoisomeric mixture which was placed on a column of silica gel and eluted with CH_2Cl_2/EtOAc (99:1) to give:

Compound 10e: As a yellow foam (0.310 g, 25%). $[\alpha]_D^{25}$ +60.0 (c = 2.0, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3395, 2955, 2928, 2858, 1747, 1493, 1373, 1111, 846 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.84–0.91 (m, 15 H), 1.15 (s, 3 H), 1.19–1.38 (m, 31 H), 1.39–1.43 (m, 18 H), 1.67–1.75 (m, 1 H), 1.95 (d, J = 18.5 Hz, 1 H), 2.07–2.23 (m, 10 H), 2.40–2.47 (m, 1 H), 2.56–2.64 (m, 1 H), 3.25 and 3.80 (AB, J = 14.9 Hz, 2 H), 4.22–4.32 (m, 3 H), 4.38 (septet, J = 6.1 Hz, 1 H), 4.54–4.60 (m, 2 H), 4.68–4.72 (m, 2 H), 6.26 (s, 1 H), 6.32 (s, 1 H), 6.40 (s, 1 H), 6.87 (s, 1 H), 7.14 (s, 1 H), 7.21 (s, 1 H), 7.24 (s, 1 H), 7.25 (s, 1 H), 7.31 (s, 1 H), 7.32 (s, 1 H), 7.55 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 14.2, 19.7, 20.0, 21.6, 21.8, 21.8, 21.9, 22.0, 22.03, 22.2, 22.6, 22.7, 22.74, 22.8, 25.2, 26.9, 27.5, 27.7, 27.8, 31.8, 32.0, 32.1, 33.4, 33.5, 34.7, 42.5, 42.9, 47.9, 58.2, 70.0, 71.4, 71.7, 72.1, 101.6, 101.8, 102.7, 107.2, 122.6, 122.6, 123.2, 123.4, 123.9, 124.1, 125.1, 125.6, 126.1, 128.1, 132.2, 132.4, 145.0, 150.8, 151.4, 152.2, 152.4, 153.3, 214.02 ppm. MS (MALDI-TOF): m/z = 1173.7 $[M + Na]^+$; the isotopic distribution of the observed data matched the theoretical $[M + Na]^+$ isotopic distribution.

Compound 10e′: As a yellow foam (0.30 g, 24%). $[\alpha]_D^{25}$ –31.3 (c = 1.5, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3385, 2954, 2927, 2857, 2360, 1747, 1493, 1373, 1111, 845 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.84–0.91 (m, 15 H), 1.14 (s, 3 H), 1.19–1.43 (m, 49 H), 1.70–1.79 (m, 1 H), 1.97 (d, J = 18.5 Hz, 1 H), 2.07–2.22 (m, 10 H), 2.37–2.43 (m, 1 H), 2.49–2.60 (m, 1 H), 3.23 and 3.88 (AB, J = 14.5 Hz, 2 H), 4.24–4.33 (m, 3 H), 4.38 (septet, J = 6.3 Hz, 1 H), 4.50–4.60 (m, 2 H), 4.64–4.72 (m, 2 H), 6.26 (s, 1 H), 6.32 (s, 1 H), 6.40 (s, 1 H), 6.90 (s, 1 H), 7.12 (s, 1 H), 7.21 (s, 1 H), 7.23 (s, 1 H), 7.24 (s, 1 H), 7.27 (s, 1 H), 7.33 (s, 1 H), 7.57 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 14.2, 19.7, 19.9, 21.6, 21.7, 21.8, 21.9, 22.0, 22.1, 22.2, 22.6, 22.68, 22.74, 22.8, 25.1, 26.9, 27.6, 27.75, 27.8, 31.8, 32.0, 32.1, 33.4, 33.5, 34.7, 42.5, 42.9, 46.7, 47.9, 58.0, 70.1, 71.4, 71.7, 71.9, 101.6, 101.7, 102.7, 107.3, 122.5, 122.6, 123.1, 123.4, 124.1, 125.4, 125.7, 126.1, 127.2, 132.0, 132.1, 145.1, 150.8, 151.4, 152.2, 152.4, 153.3, 153.4, 154.6, 213.8 ppm. MS (FAB): m/z = 1168.8 $[M + NH_4]^+$; the isotopic distribution of the observed data matched the theoretical $[M + NH_4]^+$ isotopic distribution.

Compound 11e: As a colourless foam (0.120 g, 8%), $[\alpha]_D^{25}$ +27.8 (c = 1.2, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3500, 2954, 2928, 2857, 1748, 1494, 1372, 1189, 1114, 1053, 850 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.81–0.92 (m, 24 H), 1.01 (s, 3 H), 1.17 (s, 3 H), 1.23–1.44 (m, 46 H), 1.59–1.67 (m, 2 H), 1.70–2.14 (m, 12 H), 2.38–2.44 (m, 3 H), 2.49–2.60 (m, 1 H), 3.29 and 3.65 (AB, J = 15.2 Hz, 2 H), 3.34 and 3.84 (AB, J = 15.2 Hz, 2 H), 4.20–4.32 (m, 3 H), 4.51–4.61 (m, 4 H), 4.75 (t, J = 7.6 Hz, 1 H), 6.22 (s, 1 H), 6.42 (s, 1 H),

6.52 (s, 1 H), 6.54 (s, 1 H), 6.80 (s, 1 H), 6.86 (s, 1 H), 6.89 (s, 1 H), 6.92 (s, 1 H), 7.08 (s, 1 H), 7.33 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 14.1, 19.66, 19.74, 19.8, 20.0, 21.5, 21.7, 21.8, 21.86, 21.87, 21.9, 22.18, 22.2, 22.57, 22.60, 22.61, 22.8, 25.1, 25.2, 26.8, 26.9, 27.5, 27.6, 29.7, 31.9, 32.0, 32.2, 34.3, 34.5, 34.54, 34.8, 35.7, 36.2, 42.4, 42.5, 43.0, 47.6, 47.8, 48.1, 58.1, 58.2, 69.9, 70.9, 71.5, 71.6, 101.9, 102.0, 107.2, 107.6, 114.5, 122.5, 123.5, 123.97, 124.0, 124.1, 128.1, 125.8, 125.9, 126.5, 128.6, 130.9, 132.0, 133.0, 145.2, 146.1, 152.0, 152.2, 152.3, 152.8, 152.9, 154.7, 214.0 ppm. MS (MALDI-TOF): *m*/*z* = 1387.8 [M + Na]$^+$; the isotopic distribution of the observed data matched the theoretical [M + Na]$^+$ isotopic distribution.

Compound 11e′: As a colourless foam (0.120 g, 8%). $[\alpha]_D^{25}$ +11.2 (*c* = 1.3, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3500, 2954, 2927, 2857, 1748, 1495, 1373, 1190, 1114, 1053, 850 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.81–0.92 (m, 24 H), 1.06 (s, 3 H), 1.24 (s, 3 H), 1.23–1.44 (m, 46 H), 1.50–1.59 (m, 1 H), 1.67–1.75 (m, 1 H), 1.77–2.14 (m, 12 H), 2.34–2.43 (m, 3 H), 2.52–2.64 (m, 1 H), 3.12 and 3.68 (AB, *J* = 14.7 Hz, 2 H), 3.25 and 3.93 (AB, *J* = 14.7 Hz, 2 H), 4.23–4.32 (m, 3 H), 4.51–4.59 (m, 4 H), 4.74 (t, *J* = 7.6 Hz, 1 H), 6.23 (s, 1 H), 6.42 (s, 1 H), 6.49 (s, 1 H), 6.50 (s, 1 H), 6.81 (s, 1 H), 6.90 (s, 1 H), 6.91 (s, 1 H), 6.93 (s, 1 H), 7.06 (s, 1 H), 7.32 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.09, 14.1, 14.13, 19.7, 19.8, 19.9, 20.0, 21.4, 21.7, 21.76, 21.8, 21.85, 21.9, 22.1, 22.2, 22.58, 22.59, 22.62, 22.8, 25.2, 25.6, 26.8, 26.9, 27.4, 27.5, 28.0, 31.9, 31.94, 32.0, 32.2, 33.4, 34.3, 34.5, 35.7, 36.3, 42.4, 42.5, 43.0, 43.2, 47.7, 47.76, 47.82, 48.3, 58.09, 58.11, 70.1, 70.9, 71.0, 71.4, 101.7, 102.0, 106.8, 107.1, 114.5, 122.3, 123.9, 123.95, 124.0, 125.7, 125.9, 126.4, 128.4, 130.5, 131.9, 132.6, 145.0, 146.2, 152.1, 152.2, 152.3, 152.8, 152.9, 154.7, 213.6, 213.9 ppm. MS (MALDI-TOF): *m*/*z* = 1387.8 [M + Na]$^+$; the isotopic distribution of the observed data matched the theoretical [M + Na]$^+$ isotopic distribution.

Compounds 11e and 11e′: General procedure 1 with 6,12,18,24-tetraisopropopyloxy-2,8,14,20-tetrapentylresorcin[4]arene (**4e**) (0.10 g, 0.11 mmol) and (*S*)-(+)-camphorsulfonyl chloride (0.43 g, 1.90 mmol) gave a diastereoisomeric mixture which was placed on a column of silica gel and eluted with CH_2Cl_2/EtOAc (96:4) to give compound **11e** (0.049 g, 34%) and compound **11e′** (0.044 g, 30%).

General procedure 2 with 6,12,18,24-tetraisopropopyloxy-2,8,14,20-tetrapentylresorcin[4]arene (**4e**) (0.20 g, 0.21 mmol), *n*-butyllithium (2.5 M in hexanes, 0.68 mL, 1.71 mmol) and (*S*)-(+)-camphorsulfonyl chloride (0.54 g, 2.14 mmol) at 0 °C gave a diastereoisomeric mixture which was placed on a column of silica gel and eluted with CH_2Cl_2/EtOAc (98:2) to give compound **11e** (0.13 g, 41%) and compound **11e′** (0.13 g, 41%).

Compounds 10f and 10f′ and Compounds 11f and 11f′: General procedure 2 with 6,12,18,24-tetracyclopentyloxy-2,8,14,20-tetrapentylresorcin[4]arene (**4f**) (1.0 g, 0.96 mmol), *n*-butyllithium (2.5 M in hexanes, 0.76 mL, 1.92 mmol) and (*S*)-(+)-camphorsulfonyl chloride (0.48 g, 1.92 mmol) at –78 °C gave a diastereoisomeric mixture which was placed on a column of silica gel and eluted with CH_2Cl_2 to give:

Compound 10f: As a yellow foam (0.28 g, 23%). $[\alpha]_D^{25}$ +26.7 (*c* = 0.9, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3393, 2954, 2927, 1747, 1618, 1493, 1172 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.83–0.89 (m, 12 H), 0.90 (s, 3 H), 1.15 (s, 3 H), 1.16–1.36 (m, 24 H), 1.39–1.56 (m, 2 H), 1.59–1.71 (m, 9 H), 1.77–2.00 (m, 25 H), 2.08–2.19 (m, 9 H), 2.38–2.44 (m, 1 H), 2.54–2.61 (m, 1 H), 3.21 and 3.80 (AB, *J* = 14.8 Hz, 2 H), 4.19–4.28 (m, 3 H), 4.54–4.63 (m, 2 H), 4.72–4.75 (m, 1 H), 4.84 (quintet, *J* = 4.0 Hz, 1 H), 4.93 (quintet, *J* = 2.8 Hz, 1 H), 6.22 (s, 1 H), 6.31 (s, 1 H), 6.41 (s, 1 H), 6.87 (s, 1 H), 7.06 (s, 1 H), 7.08 (s, 1 H), 7.12 (s, 1 H), 7.17 (s, 1 H), 7.22 (s, 1 H), 7.32 (s, 1 H), 7.42 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 14.2, 19.7, 20.0, 22.6, 22.66, 22.7, 22.8, 23.7, 23.8, 23.83, 24.0, 24.1, 24.12, 24.4, 24.5, 25.3, 27.4, 27.7, 27.8, 29.7, 31.6, 31.8, 31.9, 32.0, 32.3, 32.4, 32.5, 32.7, 32.8, 32.9, 32.9, 33.0, 33.2, 33.24, 33.3, 33.5, 33.7, 34.6, 34.8, 35.8, 42.5, 42.9, 47.5, 47.8, 58.2, 79.0, 80.8, 80.9, 81.2, 101.2, 101.6, 102.4, 106.7, 121.8, 122.1, 122.9, 123.2, 123.3, 124.8, 125.1, 125.4, 125.8, 127.4, 132.0, 132.1, 144.9, 151.1, 151.6, 151.9, 152.9, 153.1, 153.2, 154.9, 214.0 ppm. MS (MALDI-TOF): *m*/*z* = 1277.8 [M + Na]$^+$; the isotopic distribution of the observed data matched the theoretical [M + Na]$^+$ isotopic distribution.

Compound 10f′: As a yellow foam (0.27 g, 22%). $[\alpha]_D^{25}$ +4.6 (*c* = 1.3, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3393, 2953, 2928, 1747, 1583, 1493, 1169 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.83–0.92 (m, 15 H), 1.15 (s, 3 H), 1.16–1.36 (m, 24 H), 1.39–1.56 (m, 2 H), 1.59–2.00 (m, 34 H), 2.09–2.21 (m, 9 H), 2.39–2.43 (m, 1 H), 2.48–2.59 (m, 1 H), 3.21 and 3.86 (AB, *J* = 14.5 Hz, 2 H), 4.19–4.30 (m, 3 H), 4.54–4.62 (m, 2 H), 4.71–4.74 (m, 1 H), 4.82 (quintet, *J* = 4.1 Hz, 1 H), 4.93 (m, 1 H), 6.22 (s, 1 H), 6.31 (s, 1 H), 6.42 (s, 1 H), 6.89 (s, 1 H), 7.06 (s, 1 H), 7.07 (s, 1 H), 7.09 (s, 1 H), 7.16 (s, 1 H), 7.22 (s, 1 H), 7.33 (s, 1 H), 7.44 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 14.2, 19.7, 20.0, 22.6, 22.66, 22.74, 22.8, 23.7, 23.8, 23.9, 24.0, 24.1, 24.2, 24.4, 24.5, 25.1, 26.9, 27.4, 27.6, 27.8, 31.6, 31.8, 31.9, 32.0, 32.3, 32.4, 32.5, 32.7, 32.8, 32.9, 33.0, 33.1, 33.2, 33.5, 33.7, 34.6, 35.0, 36.0, 42.5, 42.9, 47.9, 48.0, 58.0, 79.1, 80.8, 80.9, 81.1, 101.3, 101.6, 102.5, 106.7, 121.8, 122.1, 122.9, 123.2, 123.4, 124.9, 125.0, 125.4, 125.8, 127.4, 131.8, 132.0, 144.5, 151.0, 151.5, 151.9, 152.9, 153.2, 153.3, 155.0, 213.8 ppm. MS (MALDI-TOF): *m*/*z* = 1277.8 [M + Na]$^+$; the isotopic distribution of the observed data matched the theoretical [M + Na]$^+$ isotopic distribution.

Compound 11f: As a colourless foam (0.15 g, 10%), $[\alpha]_D^{25}$ +25.7 (*c* = 1.3, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3501, 2954, 2928 2869, 2358, 1748, 1493, 1454, 1357, 1171 and 832 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.77 (s, 3 H), 0.82–0.89 (m, 12 H), 0.92 (s, 3 H), 0.97 (s, 3 H), 1.18 (s, 3 H), 1.20–1.36 (m, 24 H), 1.37–1.56 (m, 2 H), 1.59–2.19 (m, 48 H), 2.33–2.45 (m, 3 H), 2.55–2.63 (m, 1 H), 3.14 and 3.61 (AB, *J* = 14.9 Hz, 2 H), 3.29 and 3.82 (AB, *J* = 14.9 Hz, 2 H), 4.17–4.25 (m, 2 H), 4.47–4.54 (m, 2 H), 4.70–4.84 (m, 4 H), 6.19 (s, 1 H), 6.33 (s, 1 H), 6.34 (s, 1 H), 6.41 (s, 1 H), 6.74 (s, 1 H), 6.88 (s, 3 H), 7.05 (s, 1 H) and 7.30 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 14.14, 19.6, 19.7, 19.8, 20.0, 22.58, 22.6, 22.7, 23.9, 24.0, 24.10, 24.14, 24.2, 24.3, 25.2, 25.3, 26.8, 26.9, 27.4, 27.6, 27.9, 31.88, 31.9, 32.0, 32.1, 32.3, 32.5, 32.6, 32.7, 32.8, 32.92, 33.1, 33.4, 34.3, 34.5, 35.8, 36.5, 42.4, 42.5, 43.0, 47.4, 47.77, 47.8, 48.1, 58.1, 58.2, 78.9, 80.1, 80.8, 101.0, 101.6, 106.5, 106.8, 121.6, 123.2, 123.7, 124.0, 125.5, 125.8, 125.9, 126.4, 128.2, 130.3, 131.4, 132.5, 145.2, 146.1, 152.0, 152.3, 152.57, 152.6, 153.0, 154.9, 213.9, 217.1 ppm. MS (MALDI-TOF): *m*/*z* = 1491.8 [M + Na]$^+$; the isotopic distribution of the observed data matched the theoretical [M + Na]$^+$ isotopic distribution.

Compound 11f′: As a colourless foam (0.15 g, 10%), $[\alpha]_D^{25}$ +5.8 (*c* = 1.2, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3500, 2954, 2928, 2868, 1749, 1494, 1455, 1356, 1172, 1051 and 833 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (s, 3 H), 0.90–0.96 (m, 12 H), 0.97 (s, 3 H), 1.11 (s, 3 H), 1.23 (s, 3 H), 1.25–1.37 (m, 24 H), 1.39–1.56 (m, 2 H), 1.59–2.17 (m, 47 H), 2.20 (t, *J* = 4.3 Hz, 1 H), 2.38–2.51 (m, 3 H), 2.61–2.67 (m, 1 H), 3.14 and 3.61 (AB, *J* = 14.9 Hz, 2 H), 3.29 and 3.82 (AB, *J* = 14.9 Hz, 2 H), 4.17–4.25 (m, 2 H), 4.47–4.54 (m, 2 H), 4.70–4.84 (m, 4 H), 6.19 (s, 1 H), 6.33 (s, 1 H), 6.34 (m, 1 H), 6.41 (s, 1 H), 6.74 (s, 1 H), 6.88 (s, 3 H), 7.05 (s, 1 H), 7.30 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 14.14, 19.6, 19.7,

19.8, 20.0, 22.58, 22.6, 22.7, 23.9, 24.0, 24.1, 24.14, 24.2, 24.3, 25.2, 25.3, 26.8, 26.9, 27.4, 27.6, 27.9, 31.88, 31.9, 32.0, 32.1, 32.3, 32.5, 32.6, 32.7, 32.8, 32.9, 33.1, 33.4, 34.3, 34.5, 35.8, 36.5, 42.4, 42.5, 43.0, 47.4, 47.7, 47.8, 48.1, 58.1, 58.2, 78.9, 80.1, 80.8, 101.0, 101.6, 106.6, 106.8, 121.6, 123.2, 123.7, 124.0, 125.5, 125.8, 125.9, 126.4, 128.2, 130.3, 131.4, 132.5, 145.2, 146.1, 152.0, 152.3, 152.57, 152.6, 153.0, 154.9, 213.9, 217.1 ppm. MS (MALDI-TOF): *m*/*z* = 1491.8 $[M + Na]^+$; the isotopic distribution of the observed data matched the theoretical $[M + Na]^+$ isotopic distribution.

Compounds 11f and 11f′: General procedure 1 with 6,12,18,24-tetracyclopentyloxy-4,10,16,22-tetrahydroxy-2,8,14,20-tetrapentylresorcin[4]arene (**4f**) (0.50 g, 0.48 mmol) and (*S*)-(+)-camphorsulfonyl chloride (1.44 g, 5.77 mmol) gave a diastereoisomeric mixture which was placed on a column of silica gel and eluted with CH_2Cl_2/EtOAc (98:2) to give compound **11f** (0.16 g, 23%) and compound **11f′** (0.16 g, 23%).

General procedure 2 with 6,12,18,24-tetracyclopentyloxy-4,10,16,22-tetrahydroxy-2,8,14,20-tetrapentylresorcin[4]arene (**4f**) (0.20 g, 0.19 mmol), *n*-butyllithium (2.5 M in hexanes, 0.62 mL, 1.54 mmol) and (*S*)-(+)-camphorsulfonyl chloride (0.48 g, 1.92 mmol) at 0 °C to give the diastereoisomeric mixture which was placed on a column of silica gel and eluted with CH_2Cl_2/EtOAc (99:1) to give compound **11f** (0.08 g, 28%) and compound **11f′** (0.08 g, 28%).

Compounds 10b and 10b′ and Compounds 11b and 11b′: General procedure 2 with 4,10,16,22-tetrahydroxy-6,12,18,24-tetramethoxy-2,8,14,20-tetrapentylresorcin[4]arene (**4b**) (0.20 g, 0.24 mmol), *n*-butyllithium (2.5 M in hexanes, 0.12 mL, 0.29 mmol) and (*S*)-(+)-camphorsulfonyl chloride (0.80 g, 0.31 mmol) at –78 °C gave a diastereoisomeric mixture which was placed on a column of silica gel and eluted with CH_2Cl_2/EtOAc (98:2) to give:

Compound 10b: As a yellow foam (0.06 g, 25%). $[\alpha]_D^{25}$ +48.8 (*c* = 1.7, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3402, 2923, 2856, 1732, 1614, 1494, 1455, 1372, 1291, 1238, 1193, 1169, 902, 835, 810 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.79 (t, *J* = 7.2 Hz, 12 H), 0.84 (s, 3 H), 1.07 (s, 3 H), 1.12–1.35 (m, 24 H), 1.62 (m, 1 H), 1.98–2.10 (m, 11 H), 2.35 (td, *J* = 14.4, 4.2 Hz, 1 H), 2.46 (m, 1 H), 3.23 and 3.76 (AB, *J* = 15.0 Hz, 2 H), 3.65 (s, 3 H), 3.75 (s, 6 H), 3.76 (s, 3 H), 3.84 (s, 3 H), 4.24 (m, 3 H), 4.64 (t, *J* = 7.1 Hz, 1 H), 6.23 (s, 1 H), 6.27 (s, 1 H), 6.28 (s, 1 H), 7.05 (s, 1 H), 7.06 (s, 1 H), 7.11 (s, 1 H), 7.12 (s, 1 H), 7.13 (s, 1 H), 7.18 (s, 1 H), 7.20 (s, 1 H), 7.25 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 19.7, 19.9, 22.6, 22.7, 25.5, 26.8, 27.5, 27.6, 27.7, 31.8, 31.9, 32.0, 32.1, 33.1, 33.3, 33.5, 34.2, 34.3, 35.7, 42.5, 43.0, 47.7, 47.8, 55.7, 55.8, 56.3, 58.2, 99.8, 99.9, 104.6, 122.7, 123.6, 123.7, 123.9, 124.2, 124.5, 124.7, 124.9, 126.1, 131.3, 131.8, 145.4, 152.5, 153.0, 153.1, 153.2, 153.7, 154.1, 156.1, 214.1 ppm. MS (MALDI-TOF): *m*/*z* = 1061.7 $[M + Na]^+$; the isotopic distribution of the observed data matched the theoretical $[M + Na]^+$ isotopic distribution.

Compound 10b′: As a yellow foam (0.06 g, 25%). $[\alpha]_D^{25}$ –27.6 (*c* = 1.8, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3405, 2928, 2856, 1745, 1614, 1586, 1494, 1445, 1353, 1291, 1194, 903, 835, 809 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.70–0.84 (m, 18 H), 1.18–1.28 (m, 24 H), 1.66 (m, 1 H), 1.89 (m, 1 H), 1.97–2.08 (m, 11 H), 2.30 (td, *J* = 14.0, 4.0 Hz, 1 H), 2.48 (m, 1 H), 3.19 and 3.84 (AB, *J* = 14.7 Hz, 2 H), 3.66 (s, 3 H), 3.74 (s, 3 H), 3.75 (s, 3 H), 3.85 (s, 3 H), 4.19 (m, 3 H), 4.61 (t, *J* = 7.2 Hz, 1 H), 6.23 (s, 1 H), 6.27 (s, 1 H), 6.28 (s, 1 H), 6.85 (s, 1 H), 7.12 (s, 2 H), 7.13 (s, 1 H), 7.18 (s, 1 H), 7.20 (s, 1 H), 7.24 (s, 1 H), 7.27 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 19.7, 19.9, 22.6, 22.7, 25.1, 26.9, 27.5, 27.7, 31.8, 31.9, 32.0, 33.1, 33.3, 33.4, 34.0, 34.4, 35.8, 37.6, 42.6, 42.9, 47.7, 47.8, 55.6, 55.8, 56.3, 58.0, 99.7, 99.9, 100.3, 104.4, 108.6, 122.7, 122.8, 123.6, 124.0, 124.1, 124.6, 124.7, 124.9, 126.2, 131.1, 131.6, 145.1, 152.5, 153.0, 153.1, 153.2, 153.6, 154.1, 156.1, 214.0 ppm. MS (FAB): *m*/*z* = 1061.7 $[M + Na]^+$; the isotopic distribution of the observed data matched the theoretical $[M + Na]^+$ isotopic distribution.

Compound 11b: As a yellow foam (0.027 g, 9%). $[\alpha]_D^{25}$ –6.3 (*c* = 1.0, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3468, 2928, 2856, 1746, 1615, 1585, 1495, 1463, 1356, 1290, 1193, 1067, 1053, 905, 831, 736 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.79 (m, 12 H), 0.85 (s, 3 H), 0.91 (s, 3 H), 1.09 (s, 3 H), 1.16 (s, 3 H), 1.18–1.38 (m, 24 H), 1.44 (m, 1 H), 1.62–1.74 (m, 2 H), 1.80–1.98 (m, 3 H), 2.04–2.16 (m, 5 H), 2.38–2.61 (m, 3 H), 3.22 and 3.79 (AB, *J* = 15.0 Hz, 2 H), 3.32 and 3.86 (AB, *J* = 15.0 Hz, 2 H), 3.60 (s, 3 H), 3.82 (s, 6 H), 3.83 (s, 3 H), 4.23 (m, 2 H), 4.55 (t, *J* = 6.7 Hz, 1 H), 4.75 (t, *J* = 7.7 Hz, 1 H), 6.23 (s, 1 H), 6.41 (s, 1 H), 6.86 (s, 1 H), 6.89 (s, 2 H), 6.99 (s, 1 H), 7.11 (s, 1 H), 7.36 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 19.8, 20.0, 20.1, 22.7, 25.4, 27.0, 27.5, 27.6, 27.7, 32.0, 32.1, 33.1, 34.0, 34.3, 34.5, 36.1, 36.3, 42.6, 43.0, 47.7, 47.9, 48.2, 55.6, 56.0, 56.2, 58.2, 99.5, 100.1, 104.3, 104.9, 121.9, 123.5, 123.8, 125.2, 125.4, 126.2, 129.3, 130.3, 131.2, 131.6, 145.7, 146.0, 152.5, 153.0, 153.8, 153.9, 154.9, 156.5, 214.2 ppm. MS (MALDI-TOF): *m*/*z* = 1275.6 $[M + Na]^+$; the isotopic distribution of the observed data matched the theoretical $[M + Na]^+$ isotopic distribution.

Compound 11b′: As a yellow foam (0.027 g, 9%). $[\alpha]_D^{25}$ –10.4 (*c* = 1.3, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3482, 2927, 2856, 1748, 1497, 1466, 1356, 1291, 1194, 1067, 905, 832 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.79 (m, 6 H), 0.80 (m, 6 H), 0.82 (m, 3 H), 0.84 (s, 3 H), 1.06 (s, 3 H), 1.10 (s, 3 H), 1.12–1.30 (m, 24 H), 1.39 (m, 1 H), 1.50–1.60 (m, 2 H), 1.69 (m, 1 H), 1.87 (m, 3 H), 2.15 (m, 3 H), 2.37 (m, 3 H), 2.53 (m, 1 H), 3.15 and 3.73 (AB, *J* = 14.9 Hz, 2 H), 3.22 and 3.88 (AB, *J* = 14.9 Hz, 2 H), 3.57 (s, 3 H), 3.78 (s, 6 H), 3.79 (s, 3 H), 4.17 (m, 2 H), 4.49 (t, *J* = 7.0 Hz, 1 H), 4.67 (t, *J* = 7.8 Hz, 1 H), 6.18 (s, 1 H), 6.35 (s, 1 H), 6.60 (s, 1 H), 6.61 (s, 1 H), 6.82 (s, 1 H), 6.84 (s, 1 H), 6.85 (s, 1 H), 6.95 (s, 1 H), 7.04 (s, 1 H), 7.29 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 19.7, 19.9, 20.0, 22.5, 22.6, 22.7, 25.4, 25.5, 26.8, 26.9, 27.4, 27.5, 27.6, 27.7, 31.9, 32.0, 32.1, 33.1, 33.9, 34.2, 34.4, 36.0, 36.2, 42.4, 42.5, 42.9, 43.1, 47.8, 47.9, 48.0, 48.2, 55.5, 56.0, 56.1, 56.2, 58.2, 99.4, 100.0, 104.3, 104.7, 122.0, 123.3, 123.4, 123.7, 125.1, 125.2, 125.4, 126.0, 129.0, 130.1, 131.0, 131.4, 145.5, 145.9, 152.5, 152.9, 153.8, 153.9, 154.9, 156.4, 214.1 ppm. MS (MALDI-TOF): *m*/*z* = 1252.7 $[M]^+$; the isotopic distribution of the observed data matched the theoretical $[M]^+$ isotopic distribution.

Compound 12b: 4,10,16,22-Tetrahydroxy-6,12,18,24-tetramethoxy-2,8,14,20-tetrapentylresorcin[4]arene (**4b**) (0.50 g, 0.6 mmol) was dissolved in tetrahydrofuran (20 mL) under nitrogen and the solution was cooled down to –78 °C. *n*-Butyllithium (2.5 M in hexanes, 2.0 mL, 4.9 mmol) was slowly added to the solution, and the reaction mixture was stirred for 30 min at –78 °C. Methoxymethyl chloride (370 μL, 4.9 mmol) was then added to the reaction mixture. The mixture was warmed to room temperature and was stirred for 12 h. Brine (20 mL) was then added and the phases were separated. The aqueous phase was then extracted with diethyl ether (3 × 10 mL). The combined organic phases were washed with brine, dried with anhydrous sodium sulfate and concentrated under reduced pressure. The residue was placed on a column of silica gel and eluted with EtOAc/hexane (15:85) to give compound **12b** as a colourless foam (0.55 g, 90%). IR (DCM): $\tilde{\nu}_{max}$ = 2924, 1610, 1582, 1495, 1279, 1147, 731 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 7.0 Hz, 12 H), 1.22–1.39 (m, 24 H), 1.80–1.87 (m, 8 H), 3.34 (s, 12 H), 3.64 (s, 12 H), 4.50 (t, *J* = 7.6 Hz, 4 H), 4.74 and 4.86

(AB, J = 6.4 Hz, 8 H), 6.51 (s, 4 H), 6.66 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 22.7, 27.8, 32.2, 34.9, 35.5, 55.9, 55.7, 95.6, 99.9, 126.0, 126.9, 127.4, 153.5, 155.5 ppm. MS (FAB): calcd. for $[C_{60}H_{88}O_{12}]^+$ 1000.6276; found 1000.6293.

Compound 12e: 4,10,16,22-Tetrahydroxy-6,12,18,24-tetraisopropyloxy-2,8,14,20-tetrapentylresorcin[4]arene (**4e**) (0.35 g, 0.4 mmol) was dissolved in tetrahydrofuran (10 mL) under nitrogen, and the solution was cooled down to 0 °C. *n*-Butyllithium (2.5 M in hexanes, 0.9 mL, 2.2 mmol) was slowly added to the solution, and the reaction mixture was stirred for 30 min at 0 °C. Methoxymethyl chloride (170 μL, 2.2 mmol) was then added to the reaction mixture. The mixture was warmed to room temperature and was stirred for 12 h. Brine (20 mL) was then added, and the phases were separated. The aqueous phase was then extracted with diethyl ether (3 × 10 mL). The combined organic phases were washed with brine, dried with anhydrous sodium sulfate and concentrated under reduced pressure. The residue was placed on a column of silica gel and eluted with EtOAc/hexane (20:80) to give compound **12e** as a colourless foam (0.191 g, 46%). IR (DCM): $\tilde{\nu}_{max}$ = 2953, 2928, 2857, 1609, 1581, 1496, 1284, 1149, 1117, 1058, 1101 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.84 (t, J = 6.9 Hz, 12 H), 0.94–1.03 (m, 8 H), 1.19–1.41 (m, 40 H), 1.74–1.85 (m, 8 H), 3.38 (s, 12 H), 4.34 (septet, J = 5.3 Hz, 4 H), 4.50 (t, J = 7.5 Hz, 4 H), 4.86 (m, 8 H), 6.49 (s, 4 H), 6.66 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 21.8, 22.3, 22.7, 27.8, 32.1, 35.0, 35.4, 55.7, 69.8, 95.2, 101.6, 126.4, 128.2, 153.4, 153.5 ppm. MS (FAB): calcd. for $[C_{68}H_{104}O_{12} + H]^+$ 1113.7608; found 1113.7624.

Compounds (*M*,*S*,*R*)-13a and (*P*,*S*,*S*)-13a′: General procedure 2 with 6,12,18,24-tetramethoxy-2,8,14,20-tetrakis(2-methylpropyl) resorcin[4]arene (**7**) (1.0 g, 1.3 mmol), *n*-butyllithium (2.5 M in hexanes, 4.2 mL, 10.4 mmol) and (*S*)-(+)-camphorsulfonyl chloride (2.6 g, 10.4 mmol) at 0 °C gave a diastereoisomeric mixture which was placed on a column of silica gel and eluted with CH_2Cl_2/EtOAc (97:3) to give:

Compound (*M*,*S*,*R*)-13a: As colourless crystals (0.54 g, 26%). M.p.>248 °C (decomp.). $[\alpha]_D^{25}$ +43.3 (c = 0.49, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 2954, 1748, 1611, 1496, 1366, 1178, 1073, 1005, 924, 835 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (s, 12 H), 0.94 (d, J = 6.0 Hz, 12 H), 0.96 (d, J = 6.0 Hz, 12 H), 1.12 (s, 12 H), 1.40–1.50 (ddd, J = 4.0, 8.0, 13.5 Hz, 4 H), 1.57–1.64 (m, 4 H), 1.66–1.71 (m, 12 H), 1.96 (d, J = 18.6 Hz, 4 H), 2.01–2.10 (m, 4 H), 2.13 (t, J = 4.1 Hz, 4 H), 2.36–2.53 (m, 8 H), 3.26 and 3.84 (AB, J = 15.2 Hz, 8 H), 3.67 (s, 12 H), 4.63 (t, J = 6.8 Hz, 4 H), 6.65 (s, 4 H), 6.82 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.7, 19.9, 22.8, 22.9, 25.1, 25.8, 26.9, 33.9, 42.5, 42.9, 43.9, 47.9, 48.5, 55.9, 58.1, 104.9, 126.4, 128.3, 131.0, 145.7, 155.4, 214.0 ppm. MS (FAB): calcd. for $[C_{88}H_{120}O_{20}S_4 + H]^+$ 1625.7334; found 1625.7352.

Compound (*P*,*S*,*S*)-13a′: As a colourless foam (0.51 g, 24%). $[\alpha]_D^{25}$ +10.0 (c = 1.2, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 2953, 1747, 1496, 1362, 1179, 1067, 924, 834 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (t, J = 5.0 Hz, 24 H), 0.95 (s, 12 H), 1.16 (s, 12 H), 1.42–1.48 (ddd, J = 3.4, 9.2, 12.4 Hz, 4 H), 1.56–1.66 (m, 8 H), 1.71 (t, J = 7.0 Hz, 8 H), 1.96 (d, J = 18.4 Hz, 4 H), 2.02–2.09 (m, 4 H), 2.12 (t, J = 4.4 Hz, 4 H), 2.37–2.52 (m, 8 H), 3.25 and 3.84 (AB, J = 15.0 Hz, 8 H), 3.71 (s, 12 H), 4.61 (t, J = 7.4 Hz, 4 H), 6.59 (s, 4 H), 6.85 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.7, 20.0, 22.76, 22.77, 25.1, 25.8, 26.9, 34.2, 42.4, 43.0, 43.5, 47.8, 48.6, 55.9, 58.1, 104.9, 126.3, 128.1, 130.7, 145.9, 155.5, 213.8 ppm. MS (FAB): calcd. for $[C_{88}H_{120}O_{20}S_4]^+$ 1624.7256; found 1624.7234.

Compounds (*P*,*R*,*S*)-13b and (*M*,*R*,*R*)-13b′: General procedure 2 with 6,12,18,24-tetramethoxy-2,8,14,20-tetrakis(2-methylpropyl)-resorcin[4]arene (**7**) (1.0 g, 1.3 mmol), *n*-butyllithium (2.5 M in hexanes, 4.2 mL, 10.4 mmol) and (*R*)-(–)-camphorsulfonyl chloride (2.6 g, 10.4 mmol) at 0 °C gave a diastereoisomeric mixture which was placed on a column of silica gel and eluted with CH_2Cl_2/EtOAc (97:3) to give:

Compound (*P*,*R*,*S*)-13b: As colourless crystals (0.76 g, 36%). $[\alpha]_D^{25}$ –49.6 (c = 1.1, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 2955, 1747, 1612, 1496, 1366, 1180, 1067, 1005, 917, 835 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (s, 12 H), 0.94 (d, J = 6.0 Hz, 12 H), 0.96 (d, J = 6.0 Hz, 12 H), 1.12 (s, 12 H), 1.40–1.50 (ddd, J = 4.0, 8.0, 13.5 Hz, 4 H), 1.57–1.64 (m, 4 H), 1.66–1.71 (m, 12 H), 1.96 (d, J = 18.4 Hz, 4 H), 2.01–2.10 (m, 4 H), 2.13 (t, J = 4.1 Hz, 4 H), 2.36–2.53 (m, 8 H), 3.26 and 3.83 (AB, J = 14.8 Hz, 8 H), 3.66 (s, 12 H), 4.63 (t, J = 7.4 Hz, 4 H), 6.64 (s, 4 H), 6.82 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.7, 19.9, 22.8, 22.9, 25.1, 25.8, 26.9, 33.9, 42.5, 42.9, 43.9, 47.9, 48.5, 55.9, 58.1, 104.9, 126.4, 128.3, 131.0, 145.7, 155.4, 214.0 ppm. MS (FAB): calcd. for $[C_{88}H_{120}O_{20}S_4]^+$ 1624.7256; found 1624.7395.

Compound (*M*,*R*,*R*)-13b′: As a colourless foam (0.74 g, 35%). $[\alpha]_D^{25}$ –12.8 (c = 1.6, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 2955, 1747, 1497, 1367, 1179, 918, 836 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (s, J = 5.0 Hz, 12 H), 0.94 (d, J = 6.4 Hz, 24 H), 1.15 (s, 12 H), 1.42–1.48 (ddd, J = 3.4, 9.2, 12.4 Hz, 4 H), 1.56–1.66 (m, 8 H), 1.71 (t, J = 7.0 Hz, 8 H), 1.96 (d, J = 18.4 Hz, 4 H), 2.02–2.09 (m, 4 H), 2.12 (t, J = 4.4 Hz, 4 H), 2.37–2.52 (m, 8 H), 3.25 and 3.84 (AB, J = 15.2 Hz, 8 H), 3.70 (s, 12 H), 4.60 (t, J = 7.2 Hz, 4 H), 6.59 (s, 4 H), 6.85 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.7, 20.0, 22.76, 22.77, 25.1, 25.8, 26.9, 34.2, 42.4, 43.0, 43.5, 47.8, 48.6, 55.9, 58.1, 104.9, 126.3, 128.1, 130.7, 145.9, 155.5, 213.8 ppm. MS (FAB): calcd. for $[C_{88}H_{120}O_{20}S_4]^+$ 1624.7256; found 1624.7480.

4,10,16,22-Tetrahydroxy-6,12,18,24-tetramethoxy-2,8,14,20-tetrapropylresorcin[4]arene [(*P*,*S*)-(+)-4a]: General procedure 3 with (*M*,*S*,*R*)-**8a** (0.52 g, 0.33 mmol) and sodium hydroxide (1.32 g, 33.1 mmol). The residue was crystallized from methanol to yield compound (*P*,*S*)-(+)-**4a** as pale orange plates (0.21 g, 89%). M.p. 212–213 °C. $[\alpha]_D^{25}$ +88.5 (c = 2.6). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.99 (t, J = 7.4 Hz, 12 H), 1.32 (hex, J = 7.4 Hz, 8 H), 2.20 (q, J = 7.4 Hz, 8 H), 3.84 (s, 12 H), 4.31 (t, J = 8.0 Hz, 4 H), 6.35 (s, 4 H), 7.24 (s, 4 H), 7.51 (s, 4 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.7, 21.7, 33.4, 36.7, 56.6, 100.7, 124.5, 125.3, 125.4, 153.7, 154.4 ppm. $C_{44}H_{56}O_8$ (712.91) calcd. C 74.1, H 7.9; found C 73.8, H 7.8.

4,10,16,22-Tetrahydroxy-6,12,18,24-tetramethoxy-2,8,14,20-tetrapropylresorcin[4]arene [(*M*,*R*)-(–)-4a]: General procedure 3 with (*P*,*S*,*S*)-**8a′** (0.16 g, 0.10 mmol) and sodium hydroxide (0.41 g, 10.2 mmol). The residue was crystallized from methanol to yield compound (*M*,*R*)-(–)-**4a** as pale orange plates (0.057 g, 78%), M.p. 212–213 °C. $[\alpha]_D^{25}$ –89.2 (c = 1.2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.99 (t, J = 7.4 Hz, 12 H), 1.32 (hex, J = 7.2 Hz, 8 H), 2.20 (q, J = 7.2 Hz, 8 H), 3.84 (s, 12 H), 4.31 (t, J = 8.0 Hz, 4 H), 6.35 (s, 4 H), 7.24 (s, 4 H), 7.50 (s, 4 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.7, 21.7, 33.4, 36.7, 56.6, 100.7, 124.5, 125.3, 125.4, 153.7, 154.4 ppm. $C_{44}H_{56}O_8 \cdot CH_3OH$ (744.95) calcd. C 72.6, H 8.1; found C 72.7, H 8.0.

4,10,16,22-Tetrahydroxy-6,12,18,24-tetramethoxy-2,8,14,20-tetrapentylresorcin[4]arene [(*P*,*S*)-(+)-4b]: General procedure 3 with **11b** (0.1 g, 0.08 mmol) and sodium hydroxide (0.6 g, 15.0 mmol). The residue was placed on a column of silica gel and eluted with CH_2Cl_2/EtOAc (98:2) to yield compound (*P*,*S*)-(+)-**4b** as a colourless foam (0.05 g, 70%). $[\alpha]_D^{25}$ +52.5 (c = 1.1, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3403, 2927, 2856, 1619, 1588, 1495, 1464, 1335, 1293, 1239,

1196, 1166, 1089, 1018, 901, 836 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.89 (t, J = 7.0 Hz, 12 H), 1.25–1.38 (m, 24 H), 2.15–2.20 (m, 8 H), 3.83 (s, 12 H), 4.26 (t, J = 7.6 Hz, 4 H), 6.34 (s, 4 H), 7.21 (s, 4 H), 7.52 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.1, 21.7, 26.8, 30.9, 32.1, 32.9, 54.8, 98.9, 122.6, 123.6, 123.7, 151.9, 152.6 ppm. MS (FAB): calcd. for $[C_{52}H_{72}O_8 + H]^+$ 825.5319; found 825.5306.

General procedure 3 with (*M*,*S*,*R*)-**8b** (0.4 g, 0.23 mmol) and sodium hydroxide (3.0 g, 75 mmol). The residue was placed on a column of silica gel and eluted with CH_2Cl_2/EtOAc (98:2) to yield compound (*P*,*S*)-(+)-**4b** as a colourless foam (0.126 g, 65%).

4,10,16,22-Tetrahydroxy-6,12,18,24-tetramethoxy-2,8,14,20-tetrapentylresorcin[4]arene [(*M*,*R*)-(–)-4b]: General procedure 3 with **11b′** (0.1 g, 0.08 mmol) and sodium hydroxide (0.6 g, 15.0 mmol). The residue was placed on a column of silica gel and eluted with CH_2Cl_2/EtOAc (98:2) to yield compound (*M*,*R*)-(–)-**4b** as a colourless foam (0.05 g, 70%). $[\alpha]_D^{25}$ –51.6 (c = 1.1, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3403, 2927, 2856, 1619, 1588, 1495, 1464, 1335, 1293, 1239, 1196, 1166, 1089, 1018, 901, 836 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.89 (t, J = 7.0 Hz, 12 H), 1.25–1.38 (m, 24 H), 2.15–2.20 (m, 8 H), 3.83 (s, 12 H), 4.26 (t, J = 7.6 Hz, 4 H), 6.34 (s, 4 H), 7.21 (s, 4 H), 7.52 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.1, 21.7, 26.8, 30.9, 32.1, 32.9, 54.8, 98.9, 122.6, 123.6, 123.7, 151.9, 152.6 ppm. MS (FAB): calcd. for $[C_{52}H_{72}O_8 + NH_4]^+$ 842.5565; found 842.5558.

General procedure 3 with (*P*,*S*,*S*)-**8b′** (0.34 g, 0.20 mmol) and sodium hydroxide (2.5 g, 62.5 mmol). The residue was placed on a column of silica gel and eluted with CH_2Cl_2/EtOAc (98:2) to yield compound (*M*,*R*)-(–)-**4b** as a colourless foam (0.105 g, 64%).

2,8,14,20-Tetraheptyl-4,10,16,22-tetrahydroxy-6,12,18,24-tetramethoxyresorcin[4]arene [(*P*,*S*)-(+)-4c]: General procedure 3 with (*M*,*S*,*R*)-**8c** (0.37 g, 0.2 mmol) and sodium hydroxide (1.6 g, 40 mmol). The residue was crystallized from methanol to yield compound (*P*,*S*)-(+)-**4c** as colourless plates (0.16 g, 84%). M.p. 141.7–142.5 °C. $[\alpha]_D^{25}$ +65.4 (c = 1.3). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.90 (m, 12 H), 1.20–1.42 (m, 40 H), 2.10–2.28 (m, 8 H), 3.84 (s, 12 H), 4.27 (t, J = 8.0 Hz, 4 H), 6.35 (s, 4 H), 7.23 (s, 4 H), 7.52, (s, 4 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.8, 23.3, 28.8, 30.0, 30.3, 32.6, 33.8, 34.7, 56.6, 100.7, 124.4, 125.3, 125.4, 153.7, 154.3 ppm. $C_{60}H_{88}O_8$ (937.34) calcd. C 76.9, H 9.5; found: C 76.9, H 9.6.

2,8,14,20-Tetraheptyl-4,10,16,22-tetrahydroxy-6,12,18,24-tetramethoxyresorcin[4]arene [(*M*,*R*)-(–)-4c]: General procedure 3 with (*P*,*S*,*S*)-**8c′** (0.32 g, 0.18 mmol) and sodium hydroxide (0.71 g, 17.8 mmol). The residue was crystallized from methanol to yield compound (*M*,*R*)-(–)-**4c** as colourless plates (0.12 g, 70%). M.p. 140.6–141.8 °C. $[\alpha]_D^{25}$ –66.1 (c = 1.9). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.90 (m, 12 H), 1.17–1.46 (m, 40 H), 2.10–2.28 (m, 8 H), 3.84 (s, 12 H), 4.27 (t, J = 7.8 Hz, 4 H), 6.35 (s, 4 H), 7.22 (s, 4 H), 7.54 (s, 4 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.8, 23.3, 28.8, 30.0, 30.4, 32.6, 33.8, 34.7, 56.6, 100.7, 124.4, 125.3, 125.4, 153.7, 154.3 ppm. MS (FAB): calcd. for $[C_{60}H_{88}O_8]^+$ 936.6479; found 936.6469.

4,10,16,22-Tetrahydroxy-6,12,18,24-tetramethoxy-2,8,14,20-tetraundecylresorcin[4]arene [(*P*,*S*)-(+)-4d]: General procedure 3 with (*M*,*S*,*R*)-**8d** (0.11 g, 0.05 mmol) and sodium hydroxide (0.22 g, 5.5 mmol). The residue was crystallized from methanol to yield compound (*P*,*S*)-(+)-**4d** as tan microcrystals (0.05 g, 79%). M.p. 148.5–149.5 °C. $[\alpha]_D^{25}$ +51.0 (c = 1.3). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.89 (m, 12 H), 1.12–1.48 (m, 72 H), 2.07–2.29 (m, 8 H), 3.84 (s, 12 H), 4.27 (t, J = 7.4 Hz, 4 H), 6.35 (s, 4 H), 7.22 (s, 4 H), 7.53 (s, 4 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.8, 23.4, 28.8, 30.1, 30.42, 30.44, 30.5, 32.6, 33.8, 34.7, 56.6, 100.7, 124.4, 125.3, 125.4, 153.6, 154.3 ppm. $C_{76}H_{120}O_8 \cdot CH_3CH_2OH$ (1207.83) calcd. C 77.6, H 10.5; found: C 77.9, H 10.7.

4,10,16,22-Tetrahydroxy-6,12,18,24-tetramethoxy-2,8,14,20-tetraundecylresorcin[4]arene [(*M*,*R*)-(–)-4d]: General procedure 3 with (*P*,*S*,*S*)-**8d′** (0.064 g, 0.03 mmol) and sodium hydroxide (0.15 g, 3.8 mmol). The residue was crystallized from methanol to yield compound (*M*,*R*)-(–)-**4d** as pale orange waxy microcrystals (0.022 g, 60%), M.p. 146.5–147.5 °C (softens 141–143). $[\alpha]_D^{25}$ –46.9 (c = 1.0). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.90 (m, 12 H), 1.22–1.42 (m, 72 H), 2.16–2.23 (m, 8 H), 3.84 (s, 12 H), 4.28 (t, J = 7.8 Hz, 4 H), 6.35 (s, 4 H), 7.22 (s, 4 H), 7.52 (s, 4 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.8, 23.4, 28.8, 30.1, 30.41, 30.44, 30.5, 32.6, 33.7, 34.7, 56.5, 100.7, 124.4, 125.3, 125.4, 153.6, 154.3 ppm.

4,10,16,22-Tetrahydroxy-6,12,18,24-tetraisopropoxy-2,8,14,20-tetrapentylresorcin[4]arene [(*P*,*S*)-(+)-4e]: General procedure 3 with **10e** (0.09 g, 0.08 mmol) and sodium hydroxide (0.2 g, 5.0 mmol). The residue was placed on a column of silica gel and eluted with CH_2Cl_2/EtOAc (99:1) to yield compound (*P*,*S*)-(+)-**4e** as a colourless foam (0.065 g, 89%). $[\alpha]_D^{25}$ +36.8 (c = 1.3, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3372, 2928, 2858, 1618, 1584, 1492, 1111, 939, 849, 735 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, J = 7.0 Hz, 12 H), 1.19–1.38 (m, 48 H), 2.10–2.29 (m, 8 H), 4.28 (t, J = 7.9 Hz, 4 H), 4.55 (septet, J = 6.1 Hz, 4 H), 6.35 (s, 4 H), 7.23 (s, 4 H), 7.72 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 21.8, 21.9, 22.7, 27.8, 33.4, 34.0, 37.6, 71.7, 102.5, 123.7, 125.4, 125.6, 151.7, 152.8 ppm. MS (FAB): calcd. for $[C_{60}H_{88}O_8 + H]^+$ 937.6557; found 937.6571.

General procedure 3 with **11e** (0.11 g, 0.08 mmol) and sodium hydroxide (0.44 g, 11.0 mmol). The residue was placed on a column of silica gel and eluted with CH_2Cl_2/EtOAc (99:1) to yield compound (*P*,*S*)-(+)-**4e** as a colourless foam (0.06 g, 82%)

4,10,16,22-Tetrahydroxy-6,12,18,24-tetraisopropoxy-2,8,14,20-tetrapentylresorcin[4]arene [(*M*,*R*)-(–)-4e]: General procedure 3 with **10e′** (0.09 g, 0.08 mmol) and sodium hydroxide (0.2 g, 5.0 mmol). The residue was placed on a column of silica gel and eluted with CH_2Cl_2/EtOAc (99:1) to yield compound (*M*,*R*)-(–)-**4e** as a colourless foam (0.06 g, 82%). $[\alpha]_D^{25}$ –36.5 (c = 1.2, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3372, 2928, 2858, 1618, 1584, 1492, 1111, 939, 849, 735 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, J = 7.0 Hz, 12 H), 1.19–1.38 (m, 48 H), 2.10–2.29 (m, 8 H), 4.28 (t, J = 7.9 Hz, 4 H), 4.55 (septet, J = 6.1 Hz, 4 H), 6.35 (s, 4 H), 7.23 (s, 4 H), 7.72 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 21.8, 21.9, 22.7, 27.8, 33.4, 34.0, 37.6, 71.7, 102.5, 123.7, 125.4, 125.6, 151.7, 152.8 ppm. MS (FAB): calcd. for $[C_{60}H_{88}O_8]^+$ 936.6474; found 936.6474.

General procedure 3 with **11e′** (0.175 g, 0.13 mmol) and sodium hydroxide (0.90 g, 22.5 mmol). The residue was placed on a column of silica gel and eluted with CH_2Cl_2/EtOAc (99:1) to yield compound (*M*,*R*)-(–)-**4e** as a colourless foam (0.10 g, 83%).

6,12,18,24-Tetracyclopentyloxy-4,10,16,22-tetrahydroxy-2,8,14,20-tetrapentylresorcin[4]arene [(*P*,*S*)-(+)-4f]: General procedure 3 with **11f** (0.10 g, 0.07 mmol) and sodium hydroxide (0.44 g, 11.0 mmol). The residue was placed on a column of silica gel and eluted with CH_2Cl_2 to yield compound (*P*,*S*)-(+)-**4f** as a colourless foam (0.051 g, 72%). $[\alpha]_D^{25}$ +12.0 (c = 1.0, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3370, 2927, 2857, 1619, 1585, 1493, 1166, 973 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, J = 7.0 Hz, 12 H), 1.20–1.37 (m, 24 H), 1.60–1.75 (m, 8 H), 1.83–1.97 (m, 24 H), 2.03 (m, 4 H), 2.13 (m, 4 H), 4.24 (t, J = 7.8 Hz, 4 H), 4.78 (m, 4 H), 6.36 (s, 4 H),

7.23 (s, 4 H), 7.62 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 22.7, 23.7, 24.0, 27.7, 31.9, 32.4, 32.9, 33.2, 34.0, 81.1, 102.5, 123.6, 125.1, 125.3, 152.0, 152.7 ppm. MS (FAB): calcd. for $[C_{68}H_{96}O_8 + H]^+$ 1041.7183; found 1041.7179.

General procedure 3 with **10f** (0.10 g, 0.08 mmol) and sodium hydroxide (0.22 g, 5.5 mmol). The residue was placed on a column of silica gel and eluted with CH_2Cl_2 to yield compound (*P*,*S*)-(+)-**4f** as a colourless foam (0.062 g, 75%).

6,12,18,24-Tetracyclopentyloxy-4,10,16,22-tetrahydroxy-2,8,14,20-tetrapentylresorcin[4]arene [(*M*,*R*)-(–)-4f]: General procedure 3 with **11f′** (0.11 g, 0.07 mmol) and sodium hydroxide (0.44 g, 11.0 mmol). The residue was placed on a column of silica gel and eluted with CH_2Cl_2 to yield compound (*M*,*R*)-(–)-**4f** as a colourless foam (0.06 g, 76%). $[\alpha]_D^{25}$ –12.3 (*c* = 1.1, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3370, 2927, 2857, 1619, 1585, 1493, 1166, 973 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 7.0 Hz, 12 H), 1.20–1.37 (m, 24 H), 1.60–1.75 (m, 8 H), 1.83–1.97 (m, 24 H), 2.03 (m, 4 H), 2.13 (m, 4 H), 4.24 (t, *J* = 7.8 Hz, 4 H), 4.78 (m, 4 H), 6.36 (s, 4 H), 7.23 (s, 4 H), 7.62 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 22.7, 23.7, 24.0, 27.7, 31.9, 32.4, 32.9, 33.2, 34.0, 81.1, 102.5, 123.6, 125.1, 125.3, 152.0, 152.7 ppm. MS (FAB): calcd. for $[C_{68}H_{96}O_8 + H]^+$ 1041.7183; found 1041.7176.

General procedure 3 with **10f′** (0.11 g, 0.09 mmol) and sodium hydroxide (0.22 g, 5.5 mmol). The residue was placed on a column of silica gel and eluted with CH_2Cl_2 to yield compound (*M*,*R*)-(–)-**4f** as a colourless foam (0.071 g, 78%)

4,10,16,22-Tetrahydroxy-6,12,18,24-tetramethoxy-2,8,14,20-tetrakis(2-methylpropyl)resorcin[4]arene [(*P*,*S*)-(+)-7]: General procedure 3 with **13a** (0.24 g, 0.15 mmol) and sodium hydroxide (2.0 g, 50.0 mmol). The residue was placed on a column of silica gel and eluted with Petroleum Ether/EtOAc (8:2) to yield compound (*P*,*S*)-(+)-**7** as a colourless foam (0.09 g, 80%). $[\alpha]_D^{25}$ +65.3 (*c* = 1.1, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3397, 2952, 2866, 1618, 1588, 1496, 1089, 908 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 (d, *J* = 6.8 Hz, 12 H), 0.94 (d, *J* = 6.8 Hz, 12 H), 1.44 (septet, *J* = 6.8 Hz, 4 H), 2.07 (t, *J* = 7.2 Hz, 8 H), 3.83 (s, 12 H), 4.41 (t, *J* = 7.8 Hz, 4 H), 6.35 (s, 4 H), 7.21 (s, 4 H), 7.54 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.7, 22.8, 26.0, 30.6, 42.9, 55.9, 100.0, 124.0, 124.5, 124.6, 152.9, 153.6 ppm.

4,10,16,22-Tetrahydroxy-6,12,18,24-tetramethoxy-2,8,14,20-tetrakis(2-methylpropyl)resorcin[4]arene [(*M*,*R*)-(–)-7]: General procedure 3 with **13a′** (0.2 g, 0.12 mmol) with sodium hydroxide (2.0 g, 50.0 mmol). The residue was placed on a column of silica gel and eluted with Petroleum Ether/EtOAc (8:2) to yield (*M*,*R*)-(–)-**7** as a colourless foam (0.07 g, 74%). $[\alpha]_D^{25}$ –65.5 (*c* = 1.0, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3397, 2952, 2866, 1618, 1588, 1496, 1089, 908 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 (d, *J* = 6.8 Hz, 12 H), 0.94 (d, *J* = 6.8 Hz, 12 H), 1.44 (septet, *J* = 6.8 Hz, 4 H), 2.07 (t, *J* = 7.2 Hz, 8 H), 3.83 (s, 12 H), 4.41 (t, *J* = 7.8 Hz, 4 H), 6.35 (s, 4 H), 7.21 (s, 4 H), 7.54 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.7, 22.8, 26.0, 30.6, 42.9, 55.9, 100.0, 124.0, 124.5, 124.6, 152.9, 153.6 ppm.

General procedure 3 with **13b** (0.22 g, 0.14 mmol) with sodium hydroxide (2.0 g, 50.0 mmol). The residue was placed on a column of silica gel and eluted with Petroleum Ether/EtOAc (8:2) to yield (*M*,*R*)-(–)-**7** as a colourless foam (0.08 g, 78%). $[\alpha]_D^{25}$ –65.6 (*c* = 6.2, $CHCl_3$). IR (DCM): $\tilde{\nu}_{max}$ = 3397, 2952, 2866, 1618, 1588, 1496, 1089, 908 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 (d, *J* = 6.8 Hz, 12 H), 0.94 (d, *J* = 6.8 Hz, 12 H), 1.44 (septet, *J* = 6.8 Hz, 4 H), 2.07 (t, *J* = 7.2 Hz, 8 H), 3.83 (s, 12 H), 4.41 (t, *J* = 7.8 Hz, 4 H), 6.35 (s, 4 H), 7.21 (s, 4 H), 7.54 (s, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.7, 22.8, 26.0, 30.6, 42.9, 55.9, 100.0, 124.0, 124.5, 124.6, 152.9, 153.6 ppm.

Tetrabenzoxazine (*M*,*S*,*R*)-15a:[6b] Tetramethoxyresorcinarene (*P*,*S*)-(+)-**7** (0.10 g, 0.16 mmol) was suspended in *N*,*N*-bis(methoxymethyl)[(*S*)-(–)-(α-methylbenzyl)]amine (0.33 g, 1.56 mmol) in a CEM microwave tube. The suspension was heated under microwave irradiation at 140 °C for 2 × 10 min (without cooling). The orange oil obtained was placed on a column of silica gel and eluted with light petroleum/ethyl acetate (6:4) to yield tetrabenzoxazine (*M*,*S*,*R*)-**15a** as a colourless foam (0.15 g, 71%). $[\alpha]_D^{25}$ –124.7 (*c* = 1.0, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}_{max}$ = 2951, 2864, 2359, 1589, 1469, 1365, 1235, 1095, 942, 753 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (d, *J* = 10.0 Hz, 12 H), 0.96 (d, *J* = 10.0 Hz, 12 H), 1.39 (d, *J* = 6.5 Hz, 12 H), 1.52–1.61 (m, 4 H), 1.65–1.72 (m, 4 H), 1.76–1.83 (m, 4 H), 3.26 (s, 12 H), 3.80 (q, *J* = 6.5 Hz, 4 H), 3.86 (d, *J* = 17.0 Hz, 4 H), 4.17 (d, *J* = 16.9 Hz, 4 H), 4.55–4.62 (m, 12 H), 6.70 (s, 4 H), 7.17–7.35 (m, 20 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3, 22.8, 22.9, 25.9, 33.1, 44.6, 44.9, 57.2, 60.1, 79.6, 112.3, 124.7, 127.3, 127.6, 128.4, 128.7, 144.0, 150.0, 153.6 ppm. MS (FAB): calcd. for $[C_{88}H_{108}O_8N_4]^+$ 1348.8167; found 1348.8189.

Supporting information (see also the footnote on the first page of this article): Synthesis and spectroscopic data for the tetrabenzoxazines (*P*,*R*,*S*)-**5**, (*M*,*R*,*R*)-**6′** and (*M*,*S*,*R*)-**14**.

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[14] CCDC-609240 and CCDC-614078–614080 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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