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# Synthesis of 1,2-Bridged Calix[4]arene-biscrowns in the 1,2-Alternate Conformation

Arturo Arduini<sup>a</sup>, Laura Domiano<sup>a</sup>, Andrea Pochini<sup>a</sup>\*, Andrea Secchi<sup>a</sup>, Rocco Ungaro<sup>a</sup>, Franco Ugozzoli<sup>b</sup>, Oliver Struck<sup>c</sup>, Willem Verboom<sup>c</sup>, David N. Reinhoudt<sup>c</sup>\*

<sup>a</sup>Dipartimento di Chimica Organica e Industriale dell'Università, Viale delle Scienze 43100 Parma Italy.

<sup>b</sup>Dipartimento di Chimica Generale ed Inorganica, Chimica Analitica, Chimica Fisica and Centro di Studio per la Strutturistica Diffrattometrica del C.N.R., Viale delle Scienze, 43100, Parma, Italy.

<sup>c</sup> Laboratory of Supramolecular Chemistry and Technology, University of Twente, P. O. Box 217, 7500 AE Enschede, The Netherlands

Abstract: New methods to obtain 1,2-bridged calix[4]arene-biscrowns in the 1,2-alternate conformation are described. The stereochemistry of the proximal double functionalization reaction is mainly governed by the solvent, the length of the polyether units and the base used to deprotonate the calix[4]arene. © 1997 Elsevier Science Ltd. All rights reserved.

The possibility to synthesize cyclophanes having different orientations of the binding sites in general and of the aromatic nuclei in particular, is important for the preparation of efficient and selective hosts for ions and neutral molecules. In this perspective versatile building blocks for the synthesis of specific receptors are the four stereoisomers of calix[4]arenes (*Cone, Partial Cone, 1,2-Alternate, 1,3-Alternate*).<sup>1</sup>

However, in spite of the extensive synthetic efforts carried out by us and others to obtain stereocontrolled functionalization of calix[4]arenes, only few and indirect methodologies have been reported so far for the synthesis of calix[4]arenes in the 1,2-*alternate* conformation.<sup>2</sup> Only very recently, Pappalardo *et al.* have reported the synthesis of 1,2-bridged calix[4]crown derivatives in the 1,2-*alternate* conformation starting from bis-1,2-picoline precursors.<sup>3</sup>

As part of a general project aimed at enhancing the selectivity and efficiency of calixarene hosts in molecular recognition processes, we tackled the synthesis of calix[4]arene-biscrown-5 (3) in the *cone* conformation.



After a first multistep approach,<sup>4</sup> the development of more direct procedures for the selective 1,2-functionalization of calix[4]arenes at the lower rim allowed us to design a two-step synthesis of this new class of functionalized calix[4]arenes.<sup>5</sup>

More recently we developed a direct one-step synthetic procedure to block the residual flexibility of the calix[4]arene *cone* conformation by introducing two short diethylene glycol units connecting two adjacent (proximal) phenolic oxygens to give the *cone* 1,2-bridged calix[4]arene-biscrown-3 (4) in very high yield.<sup>6</sup>

Starting from these results, the synthesis of 1,2-*alternate* conformers of calix[4]arene-biscrowns was attempted with the aim of creating, in the same host, two identical cavities in which the "hard" character of the binding sites of the crown and the "soft" of the two aromatic nuclei could co-operate, introducing new control elements in determining the selectivity and efficiency in cation recognition.

In this paper we report the synthetic results obtained in a study performed to synthesize calix[4]arenebiscrowns in the 1,2-alternate conformation.

### **RESULTS AND DISCUSSION**

Initially, we evaluated whether the direct, one-step double 1,2-bridging reaction could be useful to directly obtain also biscrowns blocked in the 1,2-*alternate* conformation. A first approach to the problem was based on a careful examination of the reaction mixture obtained in the preparation of the *cone* conformer of p-*tert*-butylcalix[4]arene-biscrown-3 (4)<sup>6</sup> which resulted in the isolation of 1,2-*alternate* isomer (5) in 6% yield. Then a systematic study on the reaction parameters that could play a role in determining the stereochemical outcome of the reaction was undertaken. In particular the effect of the ditosylate chain lenght, the solvent polarity, and the cation of the base used to deprotonate the four phenolic oxygens of the starting calix[4]arene was evaluated.

Using diethylene glycol ditosylate we verified that neither the use of the less polar toluene as the reaction solvent, nor the use of other bases (*e.g.* <sup>1</sup>BuOK, <sup>1</sup>BuORb or <sup>1</sup>BuOCs) led to higher percentages of **5**. Also the attempts to prepare the monocrown-3 derivative of **1** by decreasing the ratio among calixarene and diethylene glycol ditosylate to 1:1 failed, giving only the biscrown-3 derivatives. This behaviour demonstrates that with the short diethylene glycol chain, the second bridging process is faster than the first.



A sufficient quantity for complete characterization of 5 could be easily isolated by flash chromatography of the mixture obtained by the direct synthesis of 1,2-bridged calix[4]arene-biscrown-3 in the *cone* conformation already reported due to the large difference in polarity of the two conformers.

The <sup>1</sup>H NMR spectrum of this conformer shows specific features due to the presence of a singlet at 3.87 ppm and two doublets at 4.54 and 3.19 ppm for the methylene protons of the calixarene. In the mean time the four hydrogens of the diethylene glycol units facing the two opposite aromatic walls resonate as a multiplet at 2.27 ppm while in the *cone* conformer they resonate at 3.90 ppm.

The reaction of 1 and triethylene glycol ditosylate was completely different. Reaction of 1 with 5 eq. of NaH in DMF and 2.2 eq. of triethylene glycol ditosylate afforded *cone* biscrown-4 (6)<sup>6</sup> in 45% yield. However, using 'BuOK as the base and toluene as the solvent the 1,2-*alternate* conformer 7 was obtained in 40% yield. Using NaH and decreasing the molar ratio between p-*tert*-butylcalix[4]arene (1) and ditosylate to 1 : 0.5 the bridging process led to 75% yield (with respect to the ditosylate) of the 1,2-bridged crown-4 derivative (8).

This remarkable stereochemical control in the double 1,2-bridging process of p-*tert*-butylcalix[4]arene can be tentatively attributed to the different size and "hard-soft" character of the counter cation of the base used to deprotonate the starting calix[4]arene and on the ability of the solvent to tighten the ion pairs formed. In fact, the small and "hard" sodium ion in DMF probably better co-ordinates to the "hard" oxygens of the already present crown, hence directing the second reaction to the *cone* isomer. On the contrary, as verified also by our previous studies,<sup>7</sup> using the larger and "softer" potassium ion in toluene the co-ordination of the cation by two "soft" aromatic walls and the reacting ditosylate is preferred, hence giving rise to the 1,2-*alternate* conformation.



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This hypothesis is supported by the results obtained in the double 1,2-bridging of 1 with tetraethylene glycol ditosylate. In fact using <sup>t</sup>BuORb in toluene, a different, but not selective, stereochemical pathway was observed.



In this case, the first crown is probably large enough to accomodate the larger rubidium ion. Even in toluene the stereochemical outcome is not as strict as in the case of crown-4 and all the three biscrown-5 stereoisomers could be isolated (35% of *cone* conformer  $3^5$ , 10% of 1,2-*alternate* conformer 9, and 15% of the 1,3-alternate conformer  $10^7$ ).

In order to achieve a better stereochemical control, a two-step reaction, using  $2^5$  as an intermediate, was studied. Treating monocrown-5 (2) with <sup>t</sup>BuOCs in toluene and then adding one equivalent of tetraethylene glycol ditosylate the 1,2-alternate biscrown-5 (9) was obtained in 38% yield.

A final observation, contrary to what was observed by Pappalardo *et al.*<sup>3</sup> is that the absence of the *tert*butyl groups at the upper rim of the starting calix[4]arene results in a complete lack of stereocontrol in the synthesis of biscrown-4 derivatives. Starting from calix[4]arene 11 or 1,2-bridged calix[4]arene-crown-4 (12)<sup>8</sup> (NaH in DMF or 'BuOK or 'BuOCs in toluene) only 1,2-bridged calix[4]arene-biscrown-4 (13) in the *cone* conformation could be isolated.



The <sup>1</sup>H NMR spectra of the 1,2-*alternate* biscrowns 5, 7, and 9 are strongly dependent on the length of the crown ether and show the bridge protons adjacent to the phenolic oxygens at 2.27, 2.85 and 2.96 ppm for biscrown-3 (5), -4 (7), and -5 (9), respectively, while the aromatic protons experience two doublets at 7.38 and 6.94 for 5, 7.30 and 7.04 for 7, and 7.24 and 7.05 ppm for 9.<sup>3</sup>

The X-ray crystal structure of the 1,2-alternate conformer of 1,2-bridged p-tert-butycalix[4]arenebiscrown-3 (5) is reported in Figure 1. The conformational parameters  $\varphi$  and  $\kappa$  and the dihedral angles summarized in Table 1, give a complete and unequivocal description of the molecular conformation whose Symbolic Representation is  $C_1$  +-,++,-+,-.<sup>9</sup>

In the observed conformation the molecule possesses two intramolecular cavities, quite similar each other in shape and dimensions, circumscribed by the oxygen atoms O(1A), O(1D) and  $O(1^*)$  and the aromatic surfaces of the phenolic rings B and C on the top side, and on the bottom by the O(1B), O(1C) and  $(O1^*)$  and the aromatic clouds of the phenolic rings A and D.

The crystallographic study shows that the reciprocal orientation of the "hard" and "soft" moieties are not optimal for cooperation in the complexation processes because the axis of the "hemicup" formed by the two aromatic nuclei B and C points away from the barycentre of the three oxygen atoms O(1A), O(1D),  $O(1^*)$ of the crown moiety in the top of the molecule, and the same geometry is observed in the bottom part of the molecule.



Fig. 1. Perspective view of 5. The hydrogen atoms have been omitted for clarity.

Moreover, also the two dihedral angles between phenolic rings: B-C 107.2(2)° and A-D 109.8(2)°, strongly differ from the value of 90° requested for ideal ' $\eta^{6}$  like" cation<sup>---</sup> $\pi$  interactions.

An estimation of the unfavourable preorganization can be obtained from the distances calculated between the barycentre of the "hard" and "soft" binding sites and the binding sites themselves which are spread over values which range from 2.88-4.0 Å for the oxygen atoms whereas the distances involving the carbon atoms of the aromatic rings varies from 2.3 to 3.5 Å.

	φ	ĸ	
D-A	78.5(6)	-83.3(6)	
A-B	139.8(5)	142.2(6)	
B-C	-78.1(6)	80.7(6)	
C-D	-139.5(5)	-127.5(5)	
A-R	120.8(1)		
B-R	243.5(1)		
C-R	241.0(1)		
D-R	115.6(1)		

**Table 1.** Conformational parameters  $\varphi$  and  $\kappa$  (°)<sup>9</sup> and dihedral angles (°) between least-squares planes through phenolic rings and molecular reference plane R.<sup>10</sup>

## CONCLUSIONS

In this paper we have further confirmed that the stereochemical outcome of tetra-functionalization of calix[4]arene at the lower rim is strongly dependent on the reaction conditions. In particular using a low polarity solvent and "soft" cations it is possible, probably due to a template effect, to direct the synthesis of 1,2-bridged calix[4]arene-biscrowns-4 and -5 towards the 1,2-alternate conformer.

#### **EXPERIMENTAL SECTION**

Melting points were recorded on an Electrothermal apparatus and are uncorrected. Mass spectra were recorded on a Finningan Mat SSQ710 spectrometer in the CI mode (CH<sub>4</sub>). <sup>1</sup>H NMR spectra were recorded on Bruker instruments operating at 300 and 400 MHz, while <sup>13</sup>C NMR spectra at 75 MHz using TMS as internal standard. Preparative column chromatography was performed on silica gel (Merck, particle size 0.040-0.063 nm, 230-240 mesh). Analytical TLC was performed on precoated silica gel plates (Merck, 60 F<sub>254</sub>). Elemental analyses were performed at the Dipartimento Chimico Farmaceutico of the University of Parma.

Compounds  $1^{11}$ ,  $2^5$ ,  $11^{11}$  and  $12^8$  were synthesized according to literature procedures. Commercial toluene was stored over LiAlH<sub>4</sub> prior to use; DMF was freshly distilled under reduced pressure and stored over molecular sieves  $3^{\text{Å}}$ ; THF was freshly distilled from sodium benzophenone and stored over molecular sieves  $4^{\text{Å}}$ . NaH (50% in oil) was washed twice with dry toluene, dried and stored under nitrogen. All other reagents and solvents were of reagent grade quality, obtained from commercial suppliers, and used without further purification. All reactions were carried out in a dry nitrogen atmosphere.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-27,28-biscrown-3-calix[4]arene 1,2-alternate conformer (5): To a suspension of 1 (3.00 g, 4.63 mmol) in DMF (250 mL) was added NaH (0.56 g, 23.33 mmol). After the reaction mixture was stirred for 1 h, the temperature was increased to 50 °C and diethylene glycol ditosylate (4.80 g, 11.58 mmol) dissolved in DMF (50 mL) was added. When the ditosylate had disappeared (verified by TLC, *ca.* 4h) the excess of NaH was eliminated by addition of a minimal quantity of methanol (Caution!). Subsequently the mixture was extracted with ethyl acetate (2 X 100 mL). The combined organic layers were evaporated to give a residue which was purified by column chromatography (hexane/ethyl acetate = 4/1) and gave 0.218 g (6% yield) of the 1,2-alternate isomer 5, (R<sub>f</sub> = 0.7) as a white solid: m.p.> 300 °C; MS *m*/z = 789 (MH<sup>+</sup>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.38 and 6.94 (2d, 8H, J = 2.4 Hz, ArH), 4.54 (d, 2H, J = 11.9 Hz, ArCH<sub>2</sub>Ar axial), 3.87 (s, 4H, ArCH<sub>2</sub>Ar), 3.57 (t, 8H, J = 7.3 Hz, ArOCH<sub>2</sub>-CH<sub>2</sub>O), 3.44 (t, 4H, ArOCH<sub>2</sub>-CH<sub>2</sub>O), 3.19 (d, 2H, ArCH<sub>2</sub>Ar equatorial), 2.27 (m, 4H, ArOCH<sub>2</sub>-CH<sub>2</sub>O), 1.32 (s, 36H, C(CH<sub>3</sub>)<sub>3</sub>). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 152.8, 145.0, 135.1, 132.8, 125.1, 123.9 (ArC), 74.8, 72.4 (OCH<sub>2</sub>-CH<sub>2</sub>O), 39.1, 29.2 (ArCH<sub>2</sub>Ar), 34.1, 31.7 (C(CH<sub>3</sub>)<sub>3</sub>). From the column also 2.19 g (60% yield) of the *cone* conformer **4** (Rf = 0.4) could be collected.<sup>6</sup>

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-27,28-biscrown-4-calix[4]arene 1,2-alternate conformer (7): A two-necked 250 mL round bottom flask equipped with a Dean-Stark trap was loaded with 1 (1.00 g, 1.54 mmol), toluene (200 mL) and 'BuOM (7.70 mmol, M = K or Cs) and the mixture was refluxed for 3 h. The temperature was then decreased to 80 °C and triethylene glycol ditosylate (1.77 g, 3.85 mmol) dissolved in toluene (20 mL) was added. When the ditosylate had disappeared (verified by TLC, *ca.* 48 h) the reaction mixture was cooled to room temperature and poured in cold aqueous HCl (10% w/v, 100 mL). The organic phase was then separated, washed with water (2 X 100 mL) and evaporated to dryness to give a residue which was purified by column chromatography (hexane/ethyl acetate = 2/3) to afford 0.54 g of 7 (40% yield) as a white solid: m.p.>300 ° C (dec.); MS *m*/z = 877 (MH<sup>+</sup>); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.30 and 7.04 (2d, 8H, J = 2.3 Hz, Ar<u>H</u>), 4.40 (d, 2H, J = 12.3 Hz, ArC<u>H</u><sub>2</sub>Ar axial), 3.88 (s, 4H, ArC<u>H</u><sub>2</sub>Ar), 3.7-3.3 (m, 20H, OC<u>H</u><sub>2</sub>-C<u>H</u><sub>2</sub>O), 3.18 (d, 2H, ArC<u>H</u><sub>2</sub>Ar equatorial), 2.85 (dt, 4H, J = 4.9 and 10.2 Hz, ArOC<u>H</u><sub>2</sub>-CH<sub>2</sub>O), 1.38 (s, 36H, C(C<u>H</u><sub>3</sub>)<sub>3</sub>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 153.3, 144.5, 134.3, 132.2, 125.7, 125.0 (Ar<u>C</u>), 69.9, 69.4, 67.9 (OCH<sub>2</sub>-CH<sub>2</sub>O), 3.8.9 and 28.5 (Ar<u>C</u>H<sub>2</sub>Ar), 34.0 (<u>C</u>(CH<sub>3</sub>)<sub>3</sub>), 31.7 (C(<u>C</u>H<sub>3</sub>)<sub>3</sub>). Anal. Calcd. for C<sub>56</sub>H<sub>76</sub>O<sub>8</sub>: C, 76.67; H, 8.73. Found C, 76.21; H, 8.05.

**5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-dihydroxy-27,28-crown-4-calix[4]arene** (8): To a suspension of 1 (1.00 g, 1.54 mmol) in DMF (100 mL) was added NaH (0.19 g, 7.70 mmol) and the reaction mixture was stirred at room temperature for 1 h. Then triethylene glycol ditosylate (0.35 g, 0.77 mmol) dissolved in DMF (10 mL) was added and the mixture stirred at 50 °C. When the starting ditosylate had disappeared methanol (10 mL) was added dropwise (Caution!) to remove the excess of NaH. The resulting solution was evaporated to dryness and the residue taken up with aqueous HCl (10% w/v, 100 mL) and extracted with ethyl acetate (100 mL). The turbid organic layer was separated, the unreacted 1 (0.15 g) filtered

off and the filtrate evaporated to give a residue which was purified by column chromatography (hexane/ethyl acetate = 65/35) to give 0.437 g (75% yield) of 7 as a white solid: m.p. = 110-112 °C; MS m/z = 762 (M<sup>+</sup>); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 8.80 (s, 2H, OH), 7.08 and 6.95 (2d, 4H, J = 1.9 Hz, ArH), 7.02 and 6.99 (2d, 4H, J = 1.7 Hz, ArH), 4.68 (d, 1H, J = 12.3 Hz, ArCH<sub>2</sub>Ar axial), 4.30 (d, 3H, J = 12.6 Hz, ArCH<sub>2</sub>Ar axial), 4.2-3.6 (m, 12H, CH<sub>2</sub>-CH<sub>2</sub>), 3.4-3.3 (m, 4H, ArCH<sub>2</sub>Ar equatorial), 1.22 and 1.15 (2s, 36H, C(CH<sub>3</sub>)<sub>3</sub>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 151.3, 149.1, 146.7, 142.5, 134.1, 132.8, 128.7, 128.2, 126.0, 125.9, 125.5, 125.2 (ArC), 75.3, 71.3, 69.8 (CH<sub>2</sub>-CH<sub>2</sub>), 33.8, 34.0, 32.8, 32.7, 31.5, 31.2, 30.1 (ArCH<sub>2</sub>Ar and C(CH<sub>3</sub>)<sub>3</sub>). Anal. Calcd. for C<sub>50</sub>H<sub>66</sub>O<sub>6</sub>: C, 78.70; H, 8.72. Found: C, 77.93; H, 9.03 (consistent with C<sub>50</sub>H<sub>66</sub>O<sub>6</sub>: 1/2 H<sub>2</sub>O).

**5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,26-27,28-biscrown-5-calix[4]arene 1,2-alternate** conformer (9): A two-necked 250 mL round bottom flask equipped with a Dean-Stark trap was loaded with **2** (1.00 g, 1.24 mmol), toluene (150 mL) and <sup>1</sup>BuOCs (1.03 g, 3.72 mmol) and the mixture was refluxed for 3 h. The temperature was then decreased to 80 °C and tetraethylene glycol ditosylate (0.75 g, 1.49 mmol) dissolved in toluene (25 mL) was added. When the starting ditosylate had disappeared the reaction mixture was cooled to room temperature and poured in cold aqueous HCl (10% w/v, 100 mL). After workup as described for **7**, the organic phase was purified by column chromatography (hexane/ethyl acetate = 7/3) to give 0.42 g (35% yield) of **9** as a white solid: m.p. > 300° C; MS *m/z* = 965 (MH<sup>+</sup>); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.24 and 7.05 (2d, 8H, J = 2.4 Hz, Ar<u>H</u>), 4.31 (d, 2H, J = 12.3 Hz, ArC<u>H</u><sub>2</sub>Ar axial), 3.86 (s, 2H, ArC<u>H</u><sub>2</sub>Ar), 3.6-3.3 (m, 28H, OCH<sub>2</sub>CH<sub>2</sub>O), 3.15 (d, 2H, ArC<u>H</u><sub>2</sub>Ar equatorial), 2.96 (dt, 4H, J = 6.7 and 9.2 Hz, OC<u>H</u><sub>2</sub>-CH<sub>2</sub>O), 1.35 (s, 36H, C(C<u>H</u><sub>3</sub>)<sub>3</sub>); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 153.5, 144.3, 134.0, 131.9, 125.5, 125.3 (Ar<u>C</u>), 71.3, 70.8, 70.4, 69.3 (OCH<sub>2</sub>-CH<sub>2</sub>O), 39.1 and 29.3 (Ar<u>C</u>H<sub>2</sub>Ar), 34.2 (<u>C</u>(CH<sub>3</sub>)<sub>3</sub>), 31.6 (C(<u>C</u>H<sub>3</sub>)<sub>3</sub>). Anal. Calcd. for C<sub>60</sub>H<sub>84</sub>O<sub>10</sub>: C, 74.65; H, 8.77. Found: C, 73.17; H, 8.87 (consistent with C<sub>60</sub>H<sub>84</sub>O<sub>10</sub>H<sub>2</sub>O).

**Reaction of 1 with tetraethylene glycol ditosylate:** Following the procedure described for the preparation of 7, 1 (1.00 g, 1.54 mmol) was treated with <sup>1</sup>BuORb (1.22 g, 7.70 mmol) and reacted with tetraethylene glycol ditosylate (1.70 g, 3.39 mmol). After workup and column chromatography (hexane/ethyl acetate = 85/15), 0.52 g (35% yield) of the *cone* conformer (3)<sup>5</sup>, ( $R_f = 0.1$ ), 0.15 g (10% yield) of the 1,2-*alternate* conformer (9), ( $R_f = 0.4$ ) and 0.15 g (10% yield) of the 1,3-*alternate* conformer (10)<sup>7</sup> ( $R_f = 0.6$ ) could be obtained.

**25,26-27,28-Biscrown-4-calix[4]arene (13):** Following the procedure described for the preparation of **9**, treating **12** (1.00 g, 1.86 mmol) with 'BuOK or 'BuOCs (5.58 mmol) and using triethylene glycol ditosylate (1.02 g, 2.23 mmol), 0.48 g of **13** was obtained after workup and recrystallization from ethanol: m.p. = 234-236 °C; MS m/z = 653 (MH<sup>+</sup>); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 6.67$  (d, 8H, J = 7.3 Hz, ArH), 6.59 (t, 4H, ArH), 4.98 (d, 2H, J = 13.0 Hz, ArCH<sub>2</sub>Ar axial), 4.38-4.36 (m, 6H, ArCH<sub>2</sub>Ar and OCH<sub>2</sub>-CH<sub>2</sub>O), 4.2-4.1 and 3.9-3.6 (m, 20H, OCH<sub>2</sub>-CH<sub>2</sub>O), 3.22 and 3.12 (2d, 4H, ArCH<sub>2</sub>Ar equatorial); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 156.2$ , 135.6, 134.5, 128.3, 128.2, 122.3 (ArC), 73.3, 70.9, 70.4 (OCH<sub>2</sub>CH<sub>2</sub>O), 31.2, 29.9 (Ar<u>C</u>H<sub>2</sub>Ar). Anal. Calcd. for C<sub>40</sub>H<sub>44</sub>O<sub>8</sub>: C, 73.60; H, 6.79. Found: C, 73.16; H, 7.02.

A transparent single crystal of c.a. 0.2x0.3x0.4 mm, grown from toluene, suitable for X-ray analysis was mounted on a glass rod without protection from the air. Crystal data:  $C_{59}H_{68}O_{6}$ , molecular weight 789.106; orthorhombic a = 17.973(3), b = 19.813(3), c = 13.257(2) Å; V = 4721(1) Å<sup>3</sup>; space group  $Pna2_i$ ; Z = 4;  $D_{calcd} = 1.11 \text{ g/cm}^{-3}$ ;  $\mu_{Cu-K_{c}} = 5.544 \text{ cm}^{-1}$ . X-ray diffraction measurements were performed at room temperature on a Siemens A.E.D. diffractometer using graphite monochromatized radiation Cu-K $\alpha$  radiation  $(\lambda = 1.541788 \text{ Å})$ . The cell parameters were determined by least squares analysis of the setting angles of 29 reflections found in a random search on the reciprocal space. The intensities were calculated from a profile analysis according to the Lehmann and Larsen method.<sup>12</sup> During the systematic data collection two standard reflections, collected every 100, showed no significant fluctuations. All the +h, +k, +l reflections in the range  $6^{\circ} \le 2\theta \le 140^{\circ}$  were measured by the step scanning method with scan width from [ $\theta$ -0.65]° to [ $\theta$ +0.65+ $\Delta\lambda\lambda^{-1}$ tg $\theta$ <sup>1</sup>°. A total of 4987 were measured. The 3658 observed reflections (I $\geq$ 2 $\sigma$ I) were used in the refinement. The intensities were corrected for Lorentz and polarization but not for absorption effects. The structure was solved by Direct Methods using SIR92.<sup>10</sup> The best FOM Emap showed the coordinates of all non-hydrogen atoms. The structure was completed by Fourier  $\Delta F$  map and then refined by blocked full-matrix least-squares methods on F using SHELX76.<sup>13</sup> Parameters refined were: the overall scale factor, the atomic coordinates and anisotropic thermal parameters for all the non-hydrogen atoms with the exception of the methyl carbon atoms of the *tert*-butyl group at the phenolic units which were affected by a severe static disorder and treated with isotropic temperature factors. In particular the tert-butyl groups at the phenolic unit A were disordered over three different orientations, those at the phenolic unit B disordered over two, whereas the disorder around the tert-butyl groups at the rings C and D was not rationalizable.

All the hydrogen atoms were placed at their calculated positions with the geometrical constraint C-H 1.0 Å and refined "riding" on their corresponding carbon atoms. The atomic scattering factors of the non-hydrogen atoms were taken from Cromer and Waber,<sup>14</sup> the values of  $\Delta f$  ' and  $\Delta f$  " were those of Cromer.<sup>15</sup> The geometrical calculations were obtained by PARST.<sup>16</sup> All the calculations were carried out on the GOULD ENCORE91 of the Centro di Studio per la Strutturistica Diffrattometrica of C.N.R., Parma. List of the atomic coordinates of the non-hydrogen atoms (Table SI), list of the thermal parameters for the non-hydrogen atoms (Table SII), list of the atomic coordinates of the hydrogen atoms (Table SII) and a full list of the bond distances and angles (Table SIV) have been deposited at the Cambridge Crystallographic DataCentre.

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