



## Synthesis of a Molecular Mill Designed from a Calix[4]-bis-crown

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Received 24 June 1998; accepted 26 September 1998

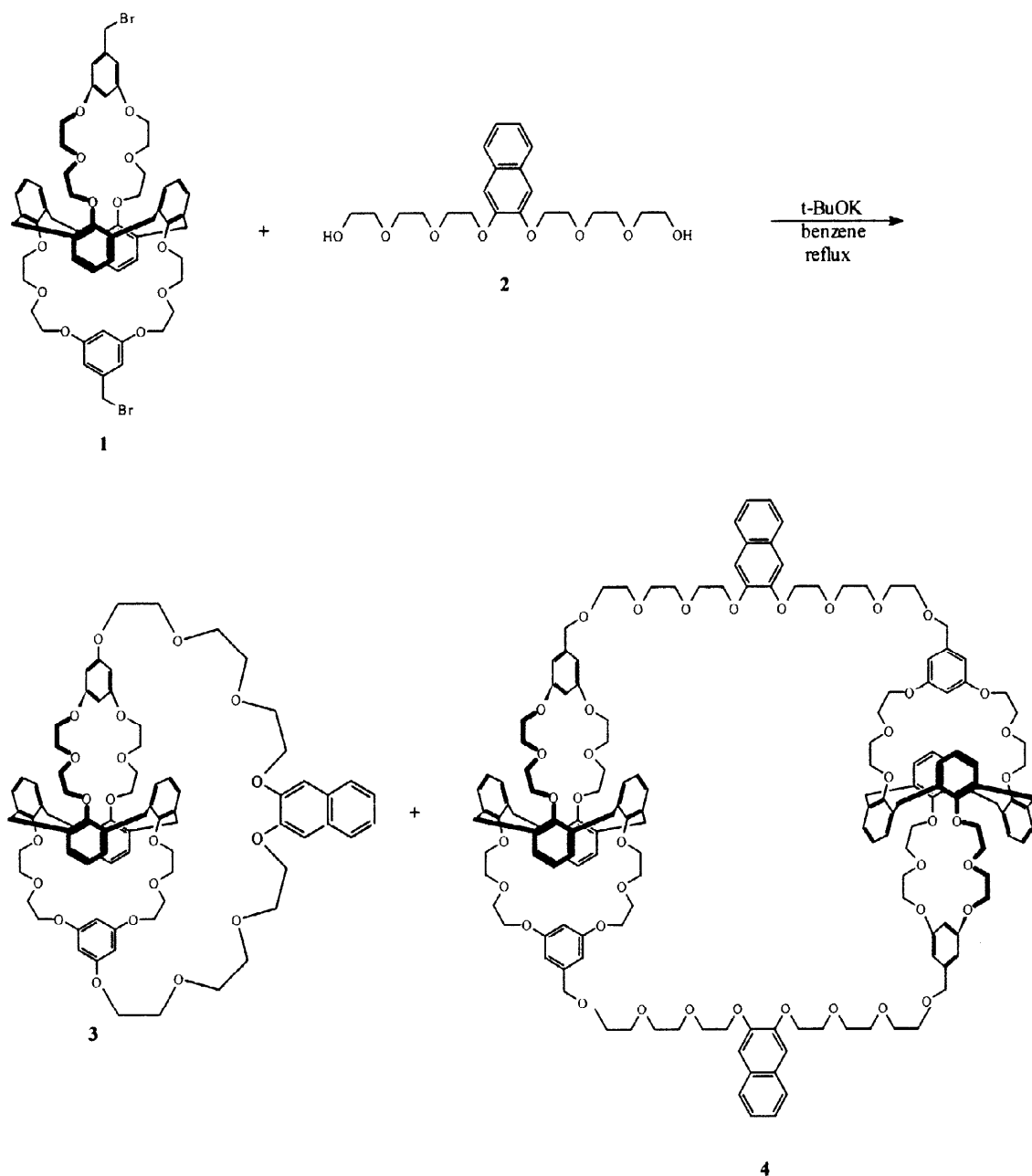
**Abstract:** The synthesis of molecular mill **4** has been achieved by condensing the dibromomethyl derivative of a calix[4]-bis-crown **1** with naphtho polyether diol **2** in high dilution conditions. © 1998 Published by Elsevier Science Ltd. All rights reserved.

One of the consequences of the research dealing with molecular architectures is the development of synthetic strategies for constructing artificial systems with a precise disposition of atoms and functional groups to obtain a desired behaviour.<sup>1</sup> Structure-directed synthesis<sup>2</sup> and molecular engineering<sup>3</sup> are approaches to the development of general capabilities for producing new organic material manufactured at the molecular level. In this context molecular machines are in vogue but there is no clear definition of what they are or what they are directed to.<sup>4</sup> They behave as machines with reference to classical mechanics as for transmissions of motions, forces and energy in molecular structures.<sup>5–7</sup> Thus, it has been described molecular propellers,<sup>8</sup> bevel gears,<sup>9–13</sup> a molecular brake<sup>14</sup> and a molecular ratchet.<sup>15</sup> Macrocyclic structures have also provided molecular turnstiles<sup>16</sup> and molecular pendula based on calixarenes.<sup>17,18</sup>

In the present Note we describe the construction of a *molecular mill* depicted as molecule **4**. With reference to our previous work,<sup>19</sup> two calix[4]-bis-crown-6 moieties acting as *rotors* were linked at tops and bottoms by polyether loops to maintain the whole structure.

**Chemical Synthesis.** The synthesis of **4** was conducted as outlined in the Scheme I. An excess of naphtho polyether diol **2**,<sup>19</sup> added into two portions, was reacted with dibromomethyl derivative **1**<sup>19</sup> in high dilution conditions in the presence of t-BuOK as base in refluxing benzene for 180 h. After work up, chromatography of the crude residue on silica, with a 8:2 dichloromethane:acetone mixture as eluent, yielded the 2+2 condensation product **4** and the already known 1+1 bridged **3**<sup>19</sup> as a by-product.<sup>20</sup> The respective yields were 5% and 20% in agreement with a less hindered 2+2 condensation leading to a higher yield of **4**. Analytical data were in agreement with the proposed structures.<sup>20</sup> The main difference in the <sup>1</sup>H-NMR spectra was observed for the triplet shifts at 6.05 ppm and 6.43 ppm (*J* = 7.5 Hz) corresponding to the *para*-ArH of the calix unit for **3** and **4**, respectively. The upfield shift observed for the 1+1 condensation product can be attributed to a shielding of the polyether chain nearby these protons.

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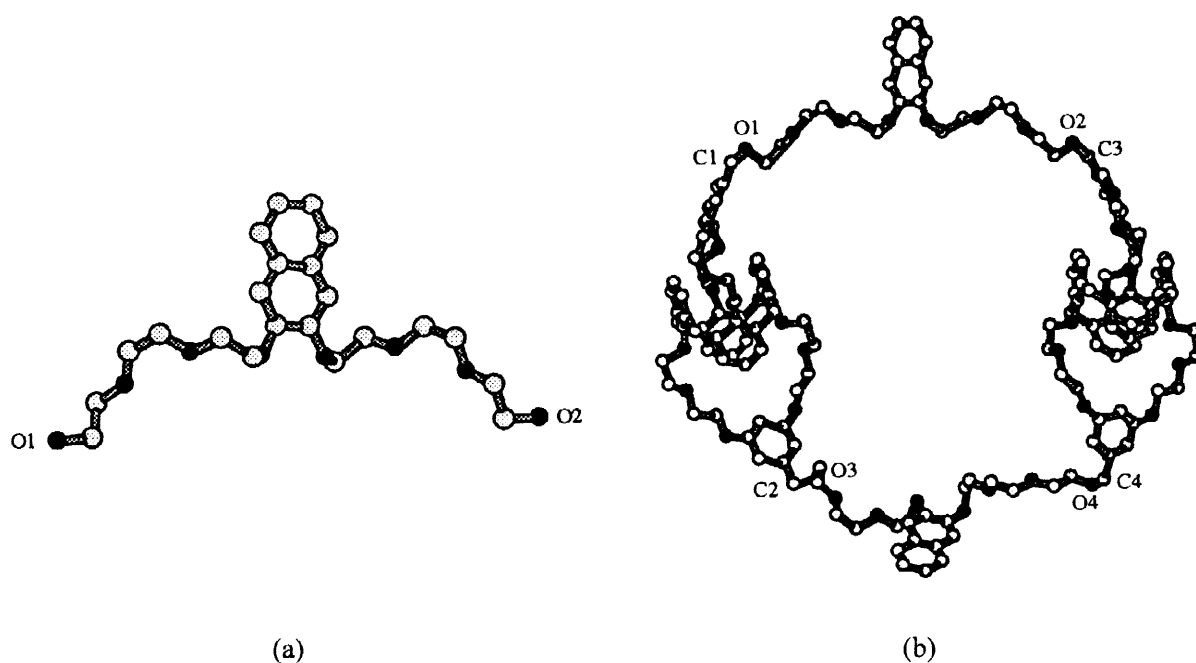


**Scheme 1.** Synthesis of 3 and 4.

**Molecular Modelling Study of Mill 4.** In order to investigate the potential structure of the mill 4 from a topological and energetical points of view, we underwent a molecular modelling study with the help of the SYBYL v6.1 program from Tripos inc. In a first step, we built up a geometrical model of the calix[4]-bis-crown-6, which is optimized with the MAXIMIN2 energy minimizer running with the Tripos force field. In a second step, we performed a systematic search of different naphthyl-polyglycols, in order to determine the lower-energy conformers where the terminal intermolecular O1-O2 distances must ranged from 18.0 to 21.0

Å. The geometry of the conformer corresponding to the greatest distance O1-O2 (19.37 Å) is selected and optimized (Figure 1a). Finally, a basic model of the mill 4 is set-up by interconnecting two calix[4]-bis-crown-6 models with two naphthyl-polyglycol structures and the geometry of the resulting model is optimized with SYBYL.

In the calculated model of the mill 4 (Figure 1b), the distances O1-O2 and O3-O4 in the glycolic chains were measured respectively as 19.49 Å and 19.68 Å and the distances C1-C2 and C3-C4 in the calix[4] parts about 20.61 Å. The centers of the two calixarene globes were located 24.81 Å from each others, indicating that no interfering steric hindrance takes place between the calixarenes moieties. This result was in agreement with a free rotation of the calix rotors around Ar-CH<sub>2</sub>-O- as deduced from the presence of a well-resolved singlet at 4.53 ppm for these protons.<sup>20</sup>



**Figure 1.** Optimized structures of: (a) naphthyl polyglycols model, (b) molecular mill 4

Systems similar to **3** and **4** in which the calix globes are replaced by triptycene units have been reported.<sup>21,22</sup> Triptycenocrown ethers<sup>21</sup> were described to perform *rope-skipping* in which the triptycene rotation was slowed-down by coordination of thallium by the crown ether loop.<sup>22</sup> Bis-triptycenecrown ethers in which two triptycene gears are connected by two polyoxyethylene links at their axles showed correlated rotation.<sup>22</sup> In this regard, further studies of synthetic, structural and physical-chemical properties are in progress to develop other molecular devices designed by using known technomimetics as starting point.

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20. **Preparation of 3 and 4:** 0.600 g (1.41 mmol) of naphtho polyether diol **2**, 1.532 g (13.36 mmol) of t-BuOK were mechanically stirred at room temperature in 5000 mL of benzene for 1 h 30 mn. Then, 1.507 g (1.35 mmol) of dibromomethyl derivative **1**, dissolved in 1000 mL of benzene was added. After 160 h reflux, it was added 2.912 g (6.81 mmol) of **2**. The reacting mixture was refluxed for additional 20 h. After cooling to room temperature the solvents were removed under reduced pressure. The crude product was washed with CH<sub>2</sub>Cl<sub>2</sub>, filtered, and the organic layer was evaporated to dryness. The residue was chromatographed on silica column with a 8:2 dichloromethane:acetone mixture as eluent to yield first 0.108 g of product **3** followed by 0.198 g of product **4**.  
**Analytical data of 3.** White solid. Mp 90-91 °C. Mp lit. 89-91 °C.<sup>24</sup> 200 MHz <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$  in ppm 7.63 (dd, 2H, *J* = 3.5 Hz, ArH-naphtho); 7.32 (dd, 2H, *J* = 3.5 Hz, ArH-naphtho); 7.13 (s, 2H, ArH-naphtho); 6.94 (d, 8H, *J* = 7.5 Hz, meta-ArH-calix); 6.67 (s, 6H, ArH-benzo); 6.05 (t, 4H, *J* = 7.5 Hz, para-ArH-calix); 4.54 (s, 4H, ArCH<sub>2</sub>O); 4.31 (m, 8H, ArCH<sub>2</sub>CH<sub>2</sub>); 4.18 (t, 4H, *J* = 6.0 Hz, ArOCH<sub>2</sub>CH<sub>2</sub>); 3.97 (m, 8H, ArOCH<sub>2</sub>CH<sub>2</sub>O); 3.81-3.75 (m, 20H, CH<sub>2</sub>CH<sub>2</sub>O); 3.57 (s, 8H, ArCH<sub>2</sub>Ar); 3.81-3.75 (m, 16H, CH<sub>2</sub>CH<sub>2</sub>O); Yield 5%.  
**Analytical data of 4.** White solid. Mp 121-122 °C. 200 MHz <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$  in ppm 7.65 (dd, 4H, *J* = 3.5 Hz, ArH-naphtho); 7.31 (dd, 4H, *J* = 3.5 Hz, ArH-naphtho); 7.15 (s, 4H, ArH-naphtho); 7.05 (d, 16, *J* = 7.5 Hz, meta-ArH-calix); 6.66 (s, 4H, ArH-benzo); 6.61 (s, 8H, ArH-benzo); 6.43 (t, 8H, *J* = 7.5 Hz, para-ArH-calix); 4.53 (s, 8H, ArCH<sub>2</sub>O); 4.28 (m, 24H, ArOCH<sub>2</sub>CH<sub>2</sub>); 3.99-3.89 (m, 40H, CH<sub>2</sub>CH<sub>2</sub>O); 3.80-3.78 (m, 24H, CH<sub>2</sub>CH<sub>2</sub>O); 3.73-3.64 (m, 20H, CH<sub>2</sub>CH<sub>2</sub>O); 3.45 (s, 16H, ArCH<sub>2</sub>Ar); Yield 20%. Mass spectrum (FAB+, NAB): *m/z* 2746.9 (M+, calc. 2745.3). *Anal. Found* C, 70.10; H, 6.72 *Calc. for* C<sub>160</sub>H<sub>184</sub>O<sub>40</sub> C, 69.95; H, 6.75.
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