HO-CH₃-(CH₂)₄-CHO + Ph₂P=C≡C=0 → Δ

HO-(CH₂)₄-CHO + THPO-(CH₂)₄-CH₀ → 10

cis-stilbene-1,2-diol: m.p. 91°C/0.01 torr; 57564-56-4:
2,2'-bis(bromomethyl)-9,9'-spirobifluorene and bis(9,9'-spirobifluorene)-[32]crown-6


Chiral Poly(9,9'-spirobifluorene) Crown Ethers

By Max Dobler, Miljenko Dumić, Martin Egli, and Vladimir Prelog

The first two members of the poly(9,9'-spirobifluorene) crown ether series, bis(9,9'-spirobifluorene)-[26]crown-4 and bis(9,9'-spirobifluorene)-[32]crown-6 5, were initially obtained as side products in the preparation of the corresponding mono(9,9'-spirobifluorene) crown ethers from 2,2'-bis(bromomethyl)-9,9'-spirobifluorene 1 and the alkoxydes of ethylene glycol and diethylene glycol, respectively. Direct synthesis via condensation of 1 with alkoxydes of the two dihydroxy ethers 2 and 3 in the presence of potassium tert-butoxide affords the cyclic products only in moderate, nonreproducible yields.

In the meantime, it has been found that the two bis(9,9'-spirobifluorene) crown ethers 4 and 5 exhibit, as ionophores, high enantioselectivity for salts of biologically active α-amino alcohols (e.g., ephedrine), thus enhancing their interest. We have attempted to improve the second procedure of preparation of the compounds 4 and 5 by modifying the reaction conditions. It was finally possible to obtain 4 and 5 reproducibly in 40–50% yield by reaction of 1 with the dihydroxy ethers 2 and 3, which may be prepared quantitatively, under the conditions of phase-transfer catalysis.[12]

Upon investigation of the crude products by thin layer chromatography, the two bis(9,9'-spirobifluorene) crown ethers 4 and 5 were found to be accompanied by several closely related compounds, which could be separated by chromatography on silica gel. These compounds were identified as poly(9,9'-spirobifluorene) crown ethers 4 and 5.

It is therefore advantageous that their sense of chirality, or absolute configuration, is known.

Characteristic of the poly(9,9'-spirobifluorene) crown ethers is the strong binding of solvent and crystallization
with solvent molecules. Thus, 4 crystallizes with two molecules of benzene (mp = 122–124°C) and 5 with one molecule of dichloromethane (mp = 153–156°C). The results of the X-ray analyses are presented in Figures 1 and 2.

The 26-membered compound 4 has a structure similar to those of other crown ethers having the same ring size. The shape and size of its chiral cavity account for its complexing abilities and the observed enantioselectivity. The structure of the 32-membered compound 5 differs: the 9,9'-spirobifluorene moieties are closer to each other (separation of the two spiro atoms in 4, 11.09 Å; in 5, 6.65 Å) and the two oxygen-containing chains lie to the side so that no cavity for a guest molecule is present. The host molecule must first adapt itself to the guest by a significant conformational change. Such an “induced fit” has often been observed for natural as well as for synthetic ionophores.

### Experimental Procedure

Poly(9,9'-spirofluorene) crown ethers 4, 6, 8, and 9: (S)-(−)-2,2'-bis(bromomethyl)-9,9'-spirobifluorene 1 (502 mg) in 5 mL of toluene was added over 2 h with vigorous stirring to a solution of KOtBu (447 mg) and CsI (259 mg) in 25 mL of ethylene glycol at 70°C. The reaction mixture was then heated for an additional 13 h. After dilution with water and acidification, it was extracted with 500 mL of benzene. The washed benzene extracts, containing the dihydroxy ether 2 in practically quantitative yield, were concentrated to 200 mL, treated with an additional 478 mg of 1 as well as with tetrahydroxy ether 2 in practically quantitative yield, were concentrated to 200 mL, treated with an additional 478 mg of 1 as well as with tetra- butylammonium hydrogen sulfate (97 mg), acetonitrile (100 mL), and 200 mL of 50% sodium hydroxide solution, and vigorously stirred for 20 h at room temperature. The reaction mixture was diluted with water and acidified. The benzene layer was separated, washed, dried with MgSO₄, and evaporated. The residue (840 mg) afforded 4·2C₆H₆ (323 mg) after recrystallization from benzene. By flash chromatography of the mother liquor on silica gel 60 (Merck) with benzene/ethyl acetate (9:1) and recrystallization, an additional 70 mg of 4·2C₆H₆ was obtained from the first fractions. The later fractions were rechromatographed and gave 6 (82.5 mg), 8 (14.1 mg), and 9 (1.0 mg). The final fractions contained the dihydroxy ethers with five (74.5 mg; 

### Table 1: Poly(9,9'-spirofluorene) crown ethers [4]

<table>
<thead>
<tr>
<th>Ring members</th>
<th>Empirical formula</th>
<th>M₀ calcd</th>
<th>M⁺ found (MS)</th>
<th>Yield</th>
<th>Rₓ</th>
<th>[α]₁₀⁰ [a]</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 Bis</td>
<td>C₉₀H₄₀O₁₂</td>
<td>805.0 + 2C₂H₆, 961.2</td>
<td>M⁺ 884 [b]</td>
<td>42</td>
<td>0.48 [c]</td>
<td>+ 13 8</td>
</tr>
<tr>
<td>6 Tetra</td>
<td>C₁₉₈H₉₆O₁₂</td>
<td>1610.9</td>
<td>[M + Na]⁺ 1631 [d]</td>
<td>10.5</td>
<td>0.37 [e]</td>
<td>− 12</td>
</tr>
<tr>
<td>8 Hexa</td>
<td>C₁₉₈H₉₆O₁₂</td>
<td>2415.0</td>
<td>[M + K]⁺ 2451 [d]</td>
<td>2</td>
<td>0.28 [f]</td>
<td>− 41</td>
</tr>
<tr>
<td>9 Octa</td>
<td>C₃₂₂H₁₅₆O₂₆</td>
<td>3229.0</td>
<td>[M + Na]⁺ 3243.4 [c]</td>
<td>0.1</td>
<td>0.20 [c]</td>
<td>− 29</td>
</tr>
<tr>
<td>5 Bis</td>
<td>C₉₀H₄₀O₁₂</td>
<td>893.1 + CH₂Cl₂, 978.0</td>
<td>M⁺ 892 [b]</td>
<td>45</td>
<td>0.56 [f]</td>
<td>− 11</td>
</tr>
<tr>
<td>7 Tetra</td>
<td>C₁₉₆H₉₆O₁₂</td>
<td>1786.2</td>
<td>[M + K]⁺ 1823 [d]</td>
<td>7</td>
<td>0.37 [f]</td>
<td>− 13</td>
</tr>
</tbody>
</table>

[a] CHCl₃, c = 1. [b] Recorded on a Hitachi-Perkin Elmer RMU-6E; direct injection, El, 70 eV. [c] Benzene/ethyl acetate (9:5). [d] Recorded on a KRATOS MS 50; FAB, matrix 3-nitrobenzyl alcohol + KI, Xe 6 kV. [e] Recorded by Dr. F. Raschdorf, Ciba-Geigy, Basel, on a VG Micromass ZAB with high-field magnet; FAB, matrix 3-nitrobenzyl alcohol, Xe 7 kV. [f] Recorded by Dr. F. Raschdorf, Ciba-Geigy, Basel, on a VG Micromass ZAB with high-field magnet; FAB, matrix 3-nitrobenzyl alcohol, Xe 7 kV.
First Sixfold Bridge-Formation in One Step**

By Wolfram Kissener and Fritz Vögtle*

While threefold,[10] fourfold,[9] and fivefold[8] bridging between two benzene rings in one step have all been successfully demonstrated in the past 15 years in the synthesis of the phanes 1-3, the realization of a sixfold bridging, e.g. to give the ten-membered “superphane hexasulfide” 4, in one step has not proven possible, despite numerous efforts.[11-13]

We assume that all previous attempts at achieving this aim have remained unsuccessful, not because of the number of bridges involved, but primarily because of the steric strain. Working on this basis we have now found that even six bridges can indeed be coupled intermolecularly if sterically less demanding starting materials are allowed to react with each other using the cesium effect[13] and dilution principle. An example is the reaction of hexakis[3-(bromomethyl)phenyl]benzene 5[14] with the corresponding hexa-thiol 6[15] to give 7.

Using a general procedure previously optimized by us in earlier work,[12,13] this reaction resulted in precipitation of the 22-membered polycyclic hexasulfide 7 as pale yellow crystals (m.p. >320°C) in ca. 0.1% yield. The mass spec-

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[4] We thank Prof. J. Selbl for the mass spectra.
[5] 6-8 had not been obtained in crystalline form up to now. Complexing ability: V. Prelog et al., unpublished.

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Fig. 1. Crystal structure of 4-2Cl2H along the crystallographic two-fold axis.
The benzene molecule drawn in the center lies 5.7 Å below the crown ether ring. Important bond distances, bond angles, and torsion angles: spirobi-

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Fig. 2. Crystal structure of 5-CH2Cl2 along the crystallographic two-fold axis. Important bond distances, bond angles, and torsion angles: spirobi-

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