65. Crystal Structures of Chiral Ionophores: Bis(9,9′-spirobifluorene)-26-crown-4 and -32-crown-6

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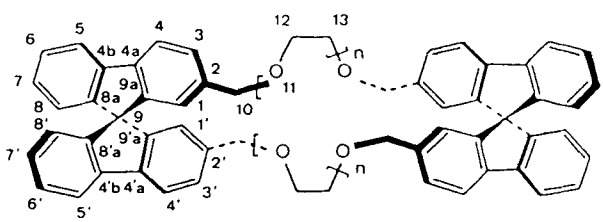
The X-ray crystal structures of bis(9,9′-spirobifluorene)-26-crown-4·benzene solvate (monoclinic, a = 15.47 Å, b = 11.265 Å, c = 15.220 Å, β = 91.54°, space group $C2$) and bis(9,9′-spirobifluorene)-32-crown-6·dichloromethane solvate (tetragonal, a = 20.958 Å, c = 11.779 Å, space group $P4_12_12$) are described. Both compounds act as enantioselective ionophores for α-aminoalcohols.

Introduction. – Chiral ionophores are potentially able to act as enantioselective hosts for certain biologically active guest molecules. Best known are compounds using α,α′-binaphthyl (*Cram et. al* [1]) or 9,9′-spirobifluorene (*Prelog* [2]) as chiral parts. Poly(9,9′-spirobifluorene) crown ethers were first obtained as by-products of the synthesis of mono(9,9′-spirobifluorene) crown ethers from 2,2′-bis(bromomethyl)-9,9′-spirobifluorene and ethylene- or diethylene-glycol alcoholates [3]. The bis(9,9′-spirobifluorene) crown ethers **1** and **2** showed high enantioselectivity for salts of α-aminoalcohols like ephedrin [4] and their synthesis was, therefore, improved [5].



1 n = 1 **2** n = 2

Attempts to crystallize these crown ethers with guest molecules have not been successful so far. Compounds **1** and **2** have a tendency to strongly bind solvent molecules. Compound **1** crystallizes with 2 molecules of benzene and compound **2** with CH_2Cl_2. Both crystal structures were established, and they will serve as starting models for molecular modelling studies to find possible conformations of host-guest complexes.

Discussion. – Both the bis(9,9′-spirobifluorene)-26-crown-4 and the bis(9,9′-spirobifluorene)-32-crown-6 molecules have twofold crystallographic symmetry. In the monoclinic structure of the smaller 26-crown-4 compound, the twofold axis is at (0, y, ½), in the tetragonal 32-crown-6 compound it is a diagonal relating (x, y, z) and $(y, x, 1\text{-}z)$. In *Fig. 1* and *2*, the two structures are depicted along their twofold rotation axes. The planar

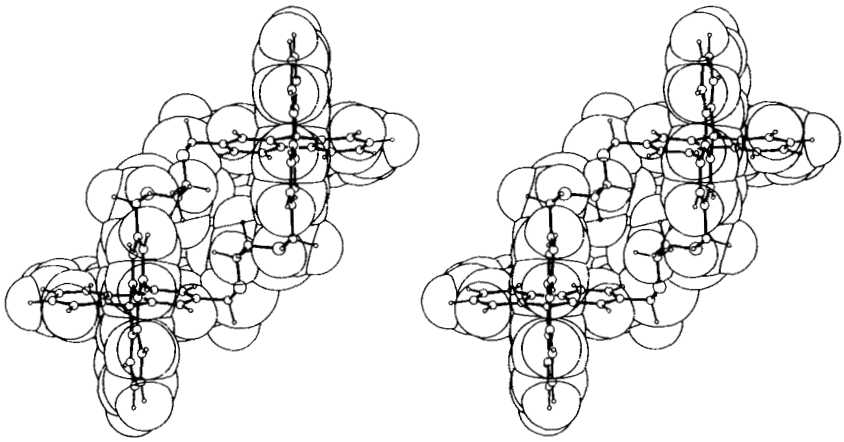


Fig. 1. *Stereoview of the structure of bis(9,9′-spirobifluorene)-26-crown-4* (**1**) *along the crystallographic twofold rotation axis*

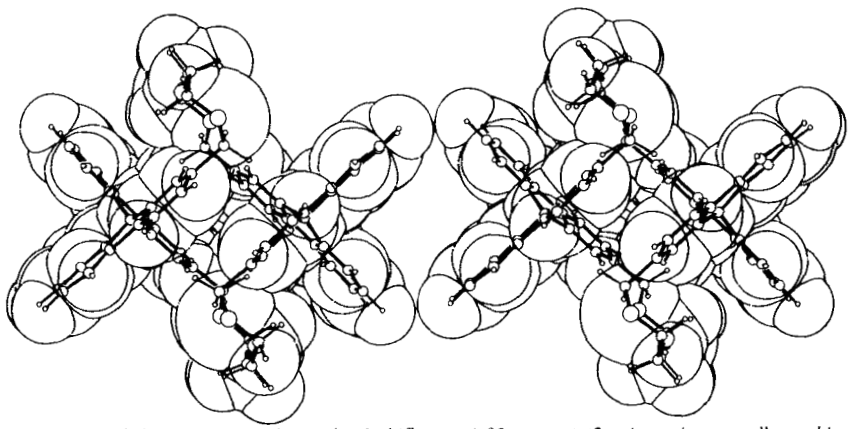


Fig. 2. *Stereoview of the structure of bis(9,9′-spirobifluorene)-32-crown-6* (**2**) *along the crystallographic twofold rotation axis*

parts of the 9,9′-spirobifluorene moieties are perpendicular. The bis(9,9′-spirobifluorene)-26-crown-4 molecule adopts a conformation with $g^-ag^+ag^-$ torsion angles around the ether linkages. The CH_2–CH_2 bridge is pointing to the inside of the molecule. This leads to a compact conformation with distances of 4.19 Å between opposite C-atoms and 11.11 Å between the spiro-atoms. By moving the CH_2–CH_2 bridge outside, a cavity is created, ready to receive a guest molecule. The conformation of bis(9,9′-spirobifluorene)-32-crown-6 is radically different, the spiro-atoms are only 6.65 Å apart. The crown ether chains bridging the spirobifluorene parts are on the outside of the molecule, and there is no preformed cavity. To dock a guest molecule, a substantial rearrangement has to occur involving all parts of the molecule. This effect is not uncommon in crown ethers. 18-crown-6 for instance also adopts a compact conformation in the uncomplexed state, and changes its conformation drastically to adopt metal ions of various sizes or different guest molecules [6].

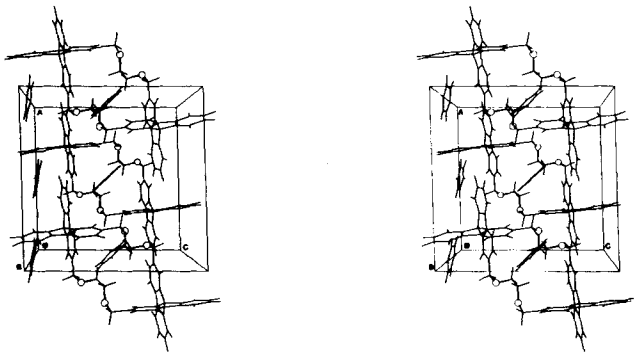


Fig. 3. *Packing of bis(9,9'-spirobifluorene)-26-crown-4* (**1**) *and benzene solvent molecules in the unit cell*

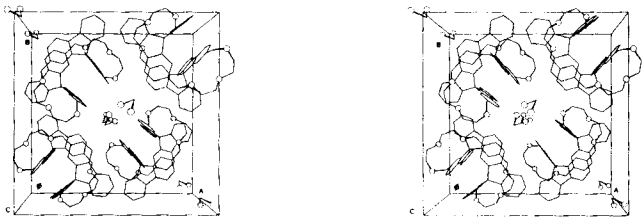


Fig. 4. *Packing of bis(9,9'-spirobifluorene)-32-crown-6* (**2**) *and CH_2Cl_2 solvent molecules in the unit cell*

The packing of ionophore molecules and solvent in the crystal is shown in *Figs. 3* and *4*. There are no unusual features in this, in both cases the respective solvent molecules fill holes in the crystal structures.

Experimental. – The reflection intensities for both compounds were measured with a four-circle diffractometer (ENRAF-NONIUS CAD 4) using graphite-monochromatized Mo$K\alpha$ radiation. For crystal data of **1** and **2** see *Table 1*.

Table 1. *Crystal Data of the Compounds* **1** *and* **2**

Compound	(**1**)·2 C_6H_6 $C_{58}O_4H_{44}\cdot 2\,C_6H_6$	(**2**)·CH_2Cl_2 $C_{62}O_6H_{52}\cdot CH_2Cl_2$
Mol. weight	805 + 156.2 = 961.2	893.1 + 85.0 = 978.1
Space group	Monoclinic $C2$ (C_2^3)	Tetragonal $P4_12_12$ (D_4^4)
a [Å]	15.47(1)	20.958(7)
b [Å]	11.265(9)	20.958(7)
c [Å]	15.220(4)	11.779(9)
β [°]	91.54(5)	
V [Å^3]	2651.4	5173.8
Z	2	4
d_x [g/cm^3]	1.20	1.26
Range	0···25°	0···26°
Reflections		
Measured	2474	2932
Used	1159 > $2\sigma(I)$	1532 > $2\sigma(I)$
Final R	0.067	0.077

Table 2. *Atomic Coordinates and Isotropic (U_{iso} [Å^2]) or Equivalent Temperature Factors for C(10)–C(15) (U_{eq} [Å^2])[a]) with Estimated Standard Deviations in Parentheses for Bis(9,9'-spirobifluorene)-26-crown-4* (**1**)

	x	*y*	*z*	U_{iso} or U_{eq}
C(1)	–0.0632(6)	0.6932(–)	0.7672(6)	0.039(3)
C(2)	–0.0127(7)	0.5946(15)	0.7468(7)	0.046(3)
C(3)	–0.0537(7)	0.4858(15)	0.7318(7)	0.053(3)
C(4)	–0.1419(7)	0.4716(16)	0.7374(7)	0.055(3)
C(4a)	–0.1912(6)	0.5711(14)	0.7566(6)	0.032(3)
C(4b)	–0.2833(6)	0.5872(15)	0.7645(6)	0.034(3)
C(5)	–0.3524(7)	0.5064(15)	0.7591(7)	0.054(4)
C(6)	–0.4349(8)	0.5466(16)	0.7742(8)	0.055(4)
C(7)	–0.4503(8)	0.6620(15)	0.7952(8)	0.056(4)
C(8)	–0.3833(7)	0.7463(15)	0.8003(7)	0.048(3)
C(8a)	–0.3009(6)	0.7060(14)	0.7853(6)	0.037(3)
C(9)	–0.2165(6)	0.7792(14)	0.7853(6)	0.036(3)
C(9a)	–0.1501(7)	0.6814(15)	0.7702(7)	0.036(3)
C(1')	–0.2253(6)	0.8574(14)	0.6245(7)	0.038(3)
C(2')	–0.2180(7)	0.9553(15)	0.5695(7)	0.042(3)
C(3')	–0.1998(7)	1.0658(16)	0.6044(7)	0.045(3)
C(4')	–0.1907(7)	1.0819(16)	0.6931(7)	0.047(3)
C(4'a)	–0.1979(7)	0.9863(14)	0.7499(7)	0.037(3)
C(4'b)	–0.1887(7)	0.9715(15)	0.8459(7)	0.041(3)
C(5')	–0.1682(8)	1.0574(17)	0.9103(8)	0.063(4)
C(6')	–0.1608(8)	1.0184(16)	0.9969(9)	0.065(4)
C(7')	–0.1741(8)	0.9003(16)	1.0193(9)	0.065(4)
C(8')	–0.1949(7)	0.8130(16)	0.9533(7)	0.048(3)
C(8'a)	–0.1987(6)	0.8534(14)	0.8686(7)	0.035(3)
C(9'a)	–0.2156(7)	0.8733(15)	0.7132(7)	0.038(3)
C(10)	0.0840(7)	0.6083(15)	0.7436(9)	0.046
O(11)	0.1095(5)	0.7133(13)	0.6961(5)	0.049
C(12)	0.0896(8)	0.7046(16)	0.6059(7)	0.052
C(13)	0.1126(7)	0.8195(15)	0.5622(8)	0.051
O(14)	0.2041(5)	0.8333(13)	0.5639(5)	0.049
C(15)	0.2332(8)	0.9422(16)	0.5302(7)	0.054
C(1solv)	0.0	0.3910(26)	0.5	0.096(8)
C(2solv)	0.0526(9)	0.3269(18)	0.5580(9)	0.072(4)
C(3solv)	0.0537(10)	0.2088(19)	0.5602(10)	0.078(4)
C(4solv)	0.0	0.1493(23)	0.5	0.086(7)
C(5solv)	0.0	0.5694(32)	0.0	0.132(10)
C(6solv)	0.0759(13)	0.5037(20)	0.0131(11)	0.108(6)
C(7solv)	0.0723(13)	0.3817(20)	0.0147(12)	0.114(6)
C(8solv)	0.0	0.3193(28)	0.0	0.105(8)

[a]) $U_{eq} = {}^{i}/_{3} \sum_{ij} a^*_i \cdot a^*_j \cdot \mathbf{a}_i \cdot \mathbf{a}_j \cdot U_{ij}$.

Structure Analysis and Refinement. Compound **1**. The structure was solved using a preliminary version of SHELX84 [7] and refined by least squares analysis. Using isotropic temperature factors an *R* value of 0.090 was obtained. In view of the small number of reflections (1159 with $I > 2\sigma(I)$) only the atoms C(10) to C(15) in the crown ether chain were refined anisotropically. H-Atoms were introduced at calculated positions. The final *R* value (unit weights) was 0.067. The atomic coordinates are given in *Table 2* and details of the molecular topography in *Table 4*.

Compound **2**. The structure was solved by direct methods using MULTAN80 [8]. A fragment of 13 atoms was extended to the complete molecule by a series of weighted *Fourier* syntheses. Refinement was by least squares analysis using anisotropic temperature factors. H-Atoms were introduced at calculated positions and not refined.

The final R factor (unit weights) was 0.077. The atomic coordinates are given in *Table 3* and details of the molecular topography in *Table 4*.

Table 3. *Atomic Coordinates and Equivalent Temperature Factors* (U_{eq} [Å^2])[a]) *with Estimated Standard Deviations in Parentheses for Bis(9,9'-spirobifluorene)-32-crown-6* (**2**)

	x	y	z	U_{eq}
C(1)	0.2496(5)	0.2655(5)	0.6782(9)	0.043
C(2)	0.2665(6)	0.3289(5)	0.6570(11)	0.055
C(3)	0.3302(6)	0.3459(6)	0.6559(12)	0.073
C(4)	0.3784(7)	0.3008(6)	0.6707(12)	0.072
C(4a)	0.3615(6)	0.2382(5)	0.6882(10)	0.050
C(4b)	0.4018(5)	0.1795(5)	0.7020(8)	0.045
C(5)	0.4679(5)	0.1705(6)	0.7000(9)	0.054
C(6)	0.4914(6)	0.1105(6)	0.7086(10)	0.066
C(7)	0.4505(6)	0.0588(6)	0.7168(9)	0.057
C(8)	0.3840(5)	0.0666(5)	0.7179(9)	0.047
C(8a)	0.3616(4)	0.1278(5)	0.7113(8)	0.036
C(9)	0.2913(5)	0.1491(5)	0.7181(8)	0.044
C(9a)	0.2973(5)	0.2218(5)	0.6954(7)	0.034
C(1')	0.2464(5)	0.1050(5)	0.5283(8)	0.041
C(2')	0.2002(6)	0.0659(5)	0.4802(8)	0.051
C(3')	0.1531(4)	0.0350(5)	0.5446(10)	0.044
C(4')	0.1547(5)	0.0422(5)	0.6613(9)	0.045
C(4'a)	0.1998(5)	0.0789(4)	0.7108(8)	0.037
C(4'b)	0.2131(5)	0.0946(4)	0.8328(7)	0.041
C(5')	0.1820(5)	0.0725(5)	0.9298(8)	0.049
C(6')	0.2061(5)	0.0925(5)	1.0314(10)	0.057
C(7')	0.2582(6)	0.1347(6)	1.0411(10)	0.060
C(8')	0.2871(5)	0.1561(5)	0.9416(9)	0.056
C(8'a)	0.2650(4)	0.1345(4)	0.8363(8)	0.040
C(9'a)	0.2457(5)	0.1118(5)	0.6442(9)	0.042
C(10)	0.2154(5)	0.3781(5)	0.6308(9)	0.059
O(11)	0.1606(4)	0.3653(3)	0.6952(7)	0.065
C(12)	0.1123(5)	0.4114(5)	0.6720(11)	0.074
C(13)	0.0531(5)	0.3901(5)	0.7302(11)	0.073
O(14)	0.0284(4)	0.3370(4)	0.6722(7)	0.076
C(15)	–0.0259(6)	0.3078(6)	0.7268(12)	0.079
C(16)	–0.0419(5)	0.2485(6)	0.6627(11)	0.077
O(17)	–0.0038(4)	0.1948(4)	0.6890(6)	0.069
C(18)	0.0606(5)	0.1979(5)	0.6526(8)	0.051
C(solv)	0.4409(15)	0.4409(15)	0.0	0.101
Cl(solv)	0.4601(5)	0.4935(5)	0.1132(9)	0.156

[a]) $U_{eq} = \frac{1}{3} \sum_{ij} a^*_i \cdot a^*_j \cdot \mathbf{a}_i \cdot \mathbf{a}_j \cdot U_{ij}$.

Table 4. *Molecular Topography for Bis(9,9'-spirobifluorene)-26-crown-4* (**1**) *and -32-crown-6* (**2**). Estimated standard deviations are: for **1**, bond lengths, 0.013···0.017 Å; bond angles, 0.9···1.3°, for **2**, bond lengths, 0.013···0.018 Å; bond angles, 0.8···1.2°.

a) *9,9'-Spirobifluorene*	**1**	**2**
Benzene rings		
Mean bond distance (24 bonds)	1.389 ± 0.019 Å	1.385 ± 0.017 Å
Range	1.353···1.436 Å	1.351···1.420 Å
Mean bond angles (24 angles)	120.0 ± 2.0°	120.0 ± 2.0°
Range	115.8···123.6°	116.3···123.4°
Five-membered rings		
Single bonds (6 bonds)	1.509 ± 0.040 Å	1.522 ± 0.022 Å
Range	1.445···1.544 Å	1.500···1.552 Å
Bond angles (8 angles, without spiro-atom)	109.6 ± 1.0°	109.6 ± 1.8°
Range	107.6···110.8°	107.3···112.4°
Bond angles at spiro-atom	100.8°, 102.2°	101.1°, 101.4°

b) *26- and 32-Membered rings*

		1			**2**		
i	j	*d*(i–j) [Å]	Angle at i [°]	Torsion angle [°]	*d*(i–j) [Å]	Angle at i [°]	Torsion angle [°]
C(9)	C(9a)	1.528	111.9	61.9	1.552	117.4	45.5
C(9a)	C(1)	1.353	127.4	–175.8	1.371	128.5	–178.8
C(1)	C(2)	1.398	119.4	180.0	1.398	118.5	176.5
C(2)	C(10)	1.506	119.2	–45.5	1.518	120.2	36.2
C(10)	O(11)	1.447	112.6	–68.6	1.402	109.7	179.6
O(11)	C(12)	1.402	112.1	176.4	1.426	110.4	172.3
C(12)	C(13)	1.502	109.0	68.6	1.486	107.5	–72.0
C(13)	O(14)	1.424	109.5	–175.7	1.405	108.7	174.3
O(14)	C(15)	1.408	114.6	–68.9	1.443	114.2	–173.8
C(15)	C(16)				1.492	107.7	80.7
C(16)	O(17)				1.414	115.2	–69.6
O(17)	C(18)				1.418	115.8	–64.2
C(15, 18)	C(2')	1.536	113.7	–35.6	1.569	111.7	131.5
C(2')	C(1')	1.391	120.4	–176.8	1.389	118.0	176.7
C(1')	C(9'a)	1.366	118.8	–176.8	1.373	128.3	177.6
C(9'a)	C(9)	1.526	128.1	55.2	1.511	117.4	59.3

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