Journal of Inclusion Phenomena **6** (1988), 237–248.

Numerical Modelling of Inclusion-Type Complexes Formed by Chiral 18-Crown-6 Ethers Bearing Sugar Moieties with Enantiomers of Phenylalanine Methyl Ester Cations

KINGA SUWIŃSKA and JANUSZ LIPKOWSKI*
Institute of Physical Chemistry, Polish Academy of Sciences, Kasprzaka 44/52, 01 224 Warsaw, Poland

(Received: 26 May 1987; in final form: 3 November 1987)

Abstract. The crystal structure of α-D-mannosido-benzo-18-crown-6·KSCN (**1**) was solved by X-ray single crystal diffractometry. $C_{28}H_{36}O_{10}$·KSCN is orthorhombic, space group $P2_12_12_1$ with $Z = 4$, $a = 8.035(4)$, $b = 9.960(2)$, $c = 38.83(2)$ Å, $M_r = 629.8$, $V = 3103.6$ Å^3, $D_x = 1.347$ g cm^{-3}, $\mu(\mathrm{Cu}K\alpha) = 2.53$ mm^{-1}, $\lambda = 1.54178$ Å, $F(000) = 1324$. Final $R = 0.043$ for 1139 unique observed reflections measured at room temperature. The potassium ion is surrounded by a nearly planar hexagon of oxygen atoms of the macrocyclic ring and lies on the plane formed by those atoms. Hexagonal pyramidal coordination is completed by the nitrogen atom of the thiocyanate anion. The SCN ion was found on the face of the macrocyclic ring opposite that for the chiral mannopyranoside moiety. The molecular structure of α-D-mannosido-18-crown-6 (**2**) and the structure of molecular complexes of **2** and α-D-glucosido-benzo-18-crown-6 (**3**) were studied by molecular mechanics methods. The results suggest enthalpy driven selectivity of complexation of the phenylalanine methyl ester (**4**) by **2** and both enthalpy and entropy effects in selective complexation of **4** by **3**.

Key words: Crystal structure, single crystal, chiral macrocycles, cyclic polyethers, mannopyranosides, complexation, host–guest interaction, molecular mechanics.

Supplementary Data relating to this article are deposited with the British Library as supplementary publication No. SUP 82061 (20 pages).

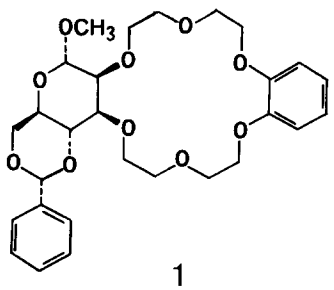
1. Introduction

Laterally substituted crown-type polyethers have proved to serve as convenient hosts for selective complexation of not only simple inorganic ions but also organic cations and, in particular, salts of the $[R\mathrm{NH}_3^+]\mathrm{A}^-$ type [1]. Selectivity of complexation of the $R\mathrm{NH}_3^+$ cations bearing chiral R moieties is an important feature of the hosts [2]. The selectivity problem has two aspects:

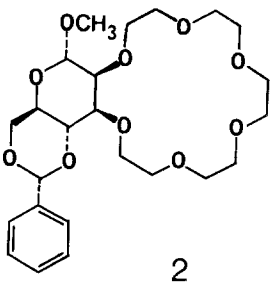
(i) selectivity on crystalline product formation, and
(ii) selectivity of complexation in solution phases.

The present study is part of a systematic approach aimed at designing complexing agents having a desired selectivity towards chiral guests of the type mentioned above. Chiral R and S cations of **4** have been chosen as a suitable guest for probing the selectivity. The hosts studied are α-D-glucosido- and α-D-mannosido-derivatives of 18-crown-6.

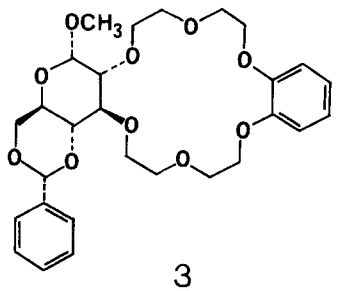
* Author for correspondence.



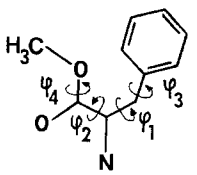
1



2



3



4

The X-ray crystal structure of **1** complexed with potassium thiocyanate is reported here; the structures of **3** complexed with KI, KSCN and (*R*)-phenylglycine methyl ester have been published elsewhere [3–5]. The problem of host–guest complexation (for **2** and **3**) is analyzed by a molecular mechanics approach.

2. Experimental

2.1. CRYSTAL STRUCTURE DETERMINATION

A single crystal of the molecular complex of **1**·KSCN of approximate dimensions $0.1 \times 0.1 \times 0.3$ mm was selected for analysis. Accurate cell dimensions were determined by the least-squares method from the setting angles of 28 reflections centered on a Siemens AED diffractometer (Cu$K\alpha$). Crystal data are given in Table 1. Intensities were collected in the ω-2θ mode with filtered Cu$K\alpha$ radiation, $\lambda = 1.54178$ Å. 3786 Reflections were recorded up to $\theta = 70°$. The intensity of a standard reflection, monitored after each group of 50 reflections, showed no observable decay during data collection. Data were corrected for Lorentz and polarization effects, but not for absorption or extinction.

The structure was solved by tangent-formula refinement [6] applied to 400 reflections. Ten of 42 non-hydrogen atoms in the asymmetric unit were found in the best *E*-map; the remaining 32 atoms were found after two successive electron density calculations in their correct positions ($R = 0.22$) [7]. Subsequent refinement was based on 829 observations above threshold, $F_0 \geqslant 2\sigma(F_0)$. The full-matrix least-squares refinement of the heavy-atom model with only K^+ anisotropic led to $R = 0.14$. Anisotropic refinement of this model was unsuccessful because of an insufficient number of observations. A new larger crystal with approximate dimensions $0.2 \times 0.2 \times 0.3$ mm was selected for the second data collection.

Table I. Crystal data

Molecular formula: $C_{28}H_{36}O_{10}$·KSCN
$M_r = 629.76$
orthorhombic, space group $P2_12_12_1$
a = 8.035(4) Å
b = 9.960(2) Å
c = 38.83(2) Å
$V = 3103.6$ Å^3
$Z = 4$
$F(000) = 1324$
$D_x = 1.347$ g cm^{-3}
μ(Cu$K\alpha$) = 2.53 mm^{-1}
$\lambda = 1.54178$ Å

Conditions of the experiment were the same; only the θ_{max} for $l > 3$ was reduced to 60°. 2749 Reflections were recorded; 1139 observed ($F_0 \geqslant 2\sigma F_0$) unique reflections were used to refine the already existing structure model anisotropically. All the H atoms could be located by the three-dimensional Fourier difference synthesis very near to their expected positions; they were introduced into the structure model at their calculated positions with $U_{iso} = 0.05$. No attempt was made to refine either the hydrogen atom positions or the thermal parameters. The conventional refinement converged to $R = 0.046$.

The results obtained at this stage were unsatisfactory in several respects: the bond lengths O(35)—C(36) and C(36)—C(37) appeared to be unreasonably short (1.31 and 1.40 Å, respectively), the thermal parameters of those three atoms were nearly twice as large as those of the neighbouring nonhydrogen atoms, and the electron density difference synthesis revealed a peak (0.3 e Å^{-3}) located in the vicinity of the atom O(35). These problems suggested that the structure is partially disordered.

A disordered model of the structure was constructed by means of the force-field method [8] assuming that the group O(35)—CH_2(37) is disordered over two different sites. The 'ideal' geometry for the two possible conformations was found. The conformation of the major component was calculated using, as starting coordinates, the positions of O(35) and C(36) already refined; the minor component was based on the positions of C(36) and the 0.3 e Å^{-3} difference density peak; the initial site occupancy factors were chosen as 0.8 and 0.2. At convergence, the site occupancy factors associated with the O(35)—CH_2(36) group in the two conformations were 0.76 and 0.24. The final R index was 0.043 for 1139 observations, $R_w = (\Sigma\, w(F)^2/\Sigma\, w(F_0)^2)^{1/2} = 0.048$ where $w = 1/(\sigma^2(F) + 0.044(F)^2)$. In the final difference map, calculated after the last cycle of refinement, the maximum and minimum peaks were 0.18 and −0.23 e Å^{-3}, respectively. Table II lists the final coordinates of nonhydrogen atoms. Atomic scattering factors were taken from [9]. No attempt was made to establish the absolute configuration of the complex. The absolute configuration of the sugar moiety found in the structure analysis was the same as the configuration of the starting material used for the synthesis of the title compound.

2.2. CONFORMATIONAL ANALYSIS

There were two separate parts in the conformational analysis procedure:

(i) construction of **2** and **4**, and
(ii) potential energy map calculations in complexes formed by **2** and **3** with **4**.

Table II. Atomic fractional coordinates for non-hydrogen atoms ($\times 10^4$) and isotropic thermal parameters ($\times 10^4$ Å^2).

Atom	x/a	y/b	z/c	U_{eq}
K	6303(3)	4652(2)	9357(5)	623
N	3284(9)	5190(9)	9414(2)	1024
C	2114(11)	5067(8)	9216(2)	608
S	661(4)	4827(3)	8966(1)	977
C(1)	10218(9)	798(2)	8143(2)	557
C(2)	11932(10)	560(9)	8096(2)	749
C(3)	12571(11)	−740(9)	8096(2)	793
C(4)	11427(12)	−1759(9)	8132(2)	832
C(5)	9751(11)	−1528(10)	8171(2)	813
C(6)	9136(10)	−201(8)	8174(2)	641
C(7)	9670(9)	2289(8)	8148(2)	476
O(8)	9745(6)	2767(5)	7807(1)	570
C(9)	9259(10)	4133(9)	7799(2)	685
C(10)	7487(9)	4280(8)	7940(2)	623
C(11)	7491(9)	3693(7)	8304(2)	415
O(12)	7994(6)	2322(5)	8279(1)	518
O(13)	6993(7)	5654(6)	7952(1)	634
C(14)	5412(9)	5832(9)	8094(2)	628
C(15)	5294(9)	5262(8)	8465(2)	562
C(16)	5788(9)	3794(8)	8456(2)	541
O(17)	4166(7)	5176(8)	7909(2)	863
C(18)	3927(12)	5740(12)	7581(2)	1182
O(19)	6428(6)	5922(5)	8695(1)	511
C(20)	5992(11)	7266(8)	8785(2)	643
C(21)	7314(11)	7799(8)	9013(2)	677
O(22)	7076(6)	7355(5)	9352(1)	616
C(23)	8506(9)	7618(8)	9560(2)	612
C(24)	8162(10)	7374(8)	9928(2)	638
O(25)	7874(8)	5913(5)	9965(1)	595
C(26)	7375(8)	5504(9)	10284(2)	489
C(27)	7428(9)	6311(9)	10570(2)	598
C(28)	6877(10)	5873(9)	10888(2)	706
C(29)	6169(10)	4601(10)	10910(2)	723
C(30)	6108(9)	3765(9)	10626(2)	615
C(31)	6710(8)	4216(8)	10317(2)	466
O(32)	6773(6)	3442(8)	10023(2)	628
C(33)	6108(10)	2083(8)	10041(2)	715
C(34)	6514(10)	1349(8)	9724(2)	674
O(35[a])	5581(8)	2047(7)	9454(2)	621
C(36[a])	5713(11)	1312(10)	9138(3)	615
C(37)	5017(11)	2012(8)	8859(2)	798
O(38)	5816(6)	3269(5)	8802(1)	595
O(35[b])	6528(15)	1803(14)	9394(6)	672
C(36[b])	5090(17)	1627(16)	9214(8)	650

[a] s.o.f. = 0.76 [b] s.o.f. = 0.24

Construction of **2** was performed by means of the MMI program [8] using as the starting structure the crown part of the known structure of **3** [4]. A similar procedure was used in order to find the geometry of the *R* enantiomer of **4** starting with the N—C bond length of 1.415 Å. First the allowed conformations of the free (*R*)-guest molecule **4** were studied using the nonbonded energy function proposed by Giglio [10].

$$U(r) = A \exp(-Br)/r^D - Cr^6.$$

Minimum energy conformations were found when $\varphi_1 \approx -45$, 90 or 180° and when $\varphi_2 \approx 10$ and 170°. For the *S* enantiomer of **4** these angles have the opposite signs.

Two molecular complexes between macrocyclic host molecules **2** (with the geometry calculated above) and **3** (geometry taken from [4]) and guest molecule **4** were examined in order to calculate the host–guest potential energy interaction. In both cases the N—C bond of **4** was perpendicular to the r.m.s. plane of the six oxygen atoms of the macrocyclic ring and the N atom of the $-NH_3^+$ group was at a distance of 1.15 Å from that plane (according to [11]). The potential energy maps were calculated for all the six combinations of angles φ_1 and φ_2 in the function of φ_3, φ_4 and φ_5, where φ_5 is the rotation of the guest cation aroung the N—C bond. The energy minima found were refined in 6-dimensional space to obtain the φ coordinates for each miminum. The same procedure was performed for the complexes of both host molecules **2** and **3** in the complexes with both R and S enantiomers of **4**.

3. Results and Discussion

3.1. CRYSTAL STRUCTURE OF α-D-MANNOSIDO-BENZO-18-CROWN-6(1)·KSCN

The geometry of the macrocyclic complex is displayed in Figure 2 [12]. Bond distances and angles are given in Figure 1 and Table III. The torsion angles in the macrocyclic 18-membered ring are listed in Table IV. The bond distances and angles found in this structure are in agreement with those reported for the complexes of **3** [3–5]. Also the torsion angles are, to some extent, similar to those structures. The energetically preferred conformations about

Table III. Distances (Å) and angles (°) involving the potassium and thiocyanate ions and the disordered part of the macrocyclic ring. E.s.d.s are in parentheses.

C—S	1.537(9)
N—C	1.212(12)
K···N	2.801(8)
S—C—N	176.7(8)
K···N—C	134.5(6)
C(34)—O(35[a])	1.358(23)
O(35[a])—C(36[a])	1.360(25)
C(36[a])—C(37)	1.435(31)
C(33)—C(34)—O(35)	128.8(9)
C(34)—O(35[a])—C(36[a])	115.7(1.6)
O(35[a])—C(36[a])—C(37)	119.5(1.6)
C(36[a])—C(37)—O(38)	111.5(9)

[a] s.o.f. = 0.24

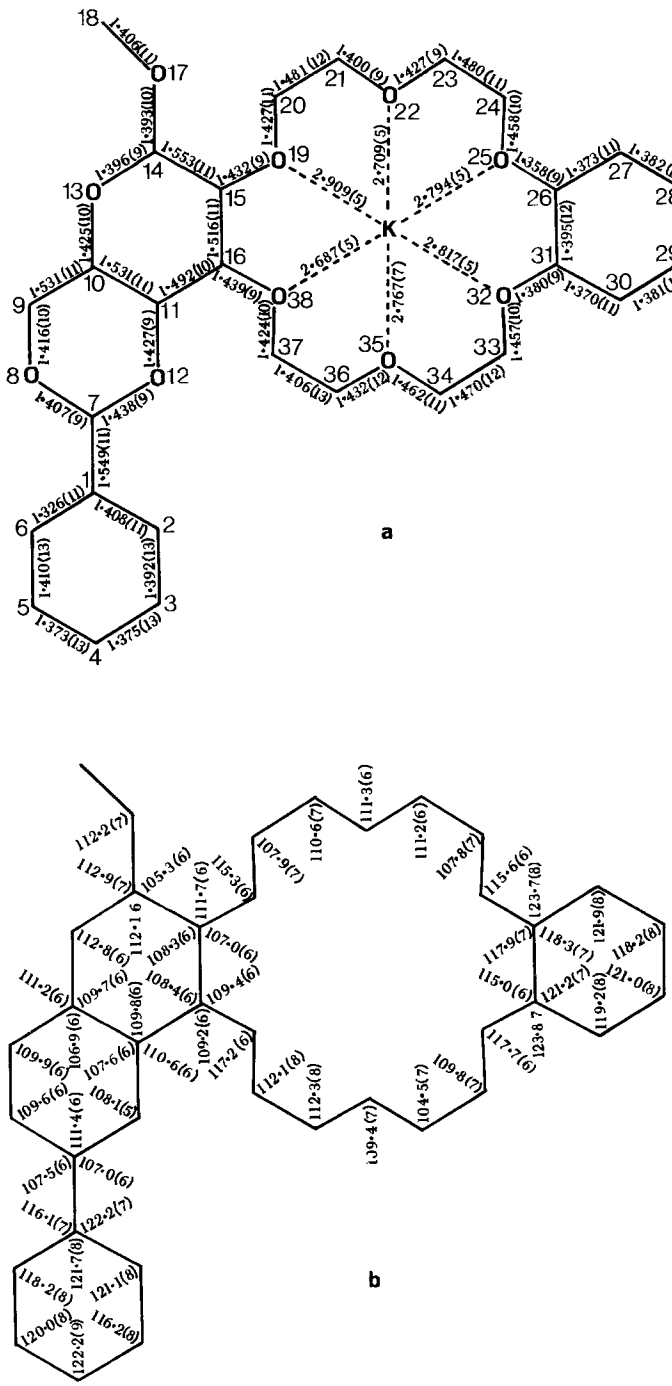


Fig. 1. (a) The numbering of the atoms and distances (Å) and (b) bond angles in the macrocyclic ligand (e.s.d.s are in parentheses. Dashed lines are $K^+ \cdots O$ distances).

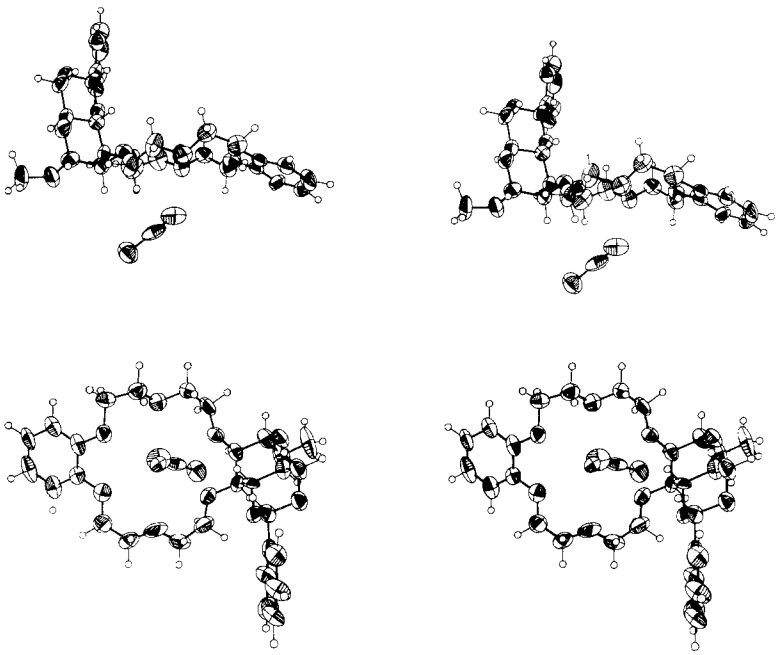


Fig. 2. *Top*: stereoview along the direction parallel to the mean plane of the six oxygens. The ellipsoids are drawn at the 50% probability level [12]. *Bottom*: molecular stereoview in the direction perpendicular to the mean plane of the six O atoms.

Table IV. Torsion angles (°) in the macrocyclic 18-membered ring. E.s.d.s are in parentheses

C(16)—C(15)—O(19)—C(20)	−169.6(8)
C(15)—O(19)—C(20)—C(21)	−178.4(8)
O(19)—C(20)—C(21)—O(22)	−80.9(6)
C(20)—C(21)—O(22)—C(23)	167.8(8)
C(21)—O(22)—C(23)—C(24)	171.1(8)
O(22)—C(23)—C(24)—O(25)	65.6(6)
C(23)—C(24)—O(25)—C(26)	−174.9(8)
C(24)—O(25)—C(26)—C(31)	166.2(9)
O(25)—C(26)—C(31)—O(32)	6.7(6)
C(26)—C(31)—O(32)—C(33)	179.6(9)
C(31)—O(32)—C(33)—C(34)	−171.2(8)
O(32)—C(33)—C(34)—O(35[a])	−65.7(6)
C(33)—C(34)—O(35[a])—C(36[a])	−172.7(9)
C(34)—O(35[a])—C(36[a])—C(37)	−172.7(1.0)
O(35[a])—(36[a])—C(37)—O(38)	60.3(7)
C(36[a])—(37)—O(38)—C(16)	152.9(9)
C(37)—O(38)—C(16)—C(15)	133.2(8)
O(38)—C(16)—C(15)—O(19)	54.9(5)
O(32)—C(33)—C(34)—O(35[b])	−38.7(1.1)
C(33)—C(34)—O(35[b])—C(36[b])	−92.8(1.7)
C(34)—O(35[b])—C(36[b])—C(37)	−176.8(2.3)
O(35[b])—(36[b])—C(37)—O(38)	−42.4(1.6)
C(36[b])—C(37)—O(38)—C(16)	−178.1(1.2)

[a] s.o.f. = 0.76. [b] s.o.f. = 0.24.

Table V. Equation of the least-squares plane through the six oxygen atoms and their deviations (Å). $X = a$, $Y = a \times (a \times b)$, $Z = a \times b$. E.s.d.s are in parentheses.

Plane A:

$$0.9554X - 0.2310Y - 0.1839Z = -2.7018$$

$$\sum \Delta^2 = 0.1978 \text{ Å}^2, \langle \Delta^2 \rangle^{1/2} = 0.1816 \text{ Å},$$

Plane B:

$$0.9652X - 0.1832Y - 0.1866Z = -2.4640$$

$$\sum \Delta^2 = 0.2727 \text{ Å}^2, \langle \Delta^2 \rangle^{1/2} = 0.2132 \text{ Å},$$

	Plane A	Plane B
O(19)	0.059(5)	0.061(5)
O(22)	−0.243(5)	−0.175(5)
O(25)	0.243(5)	0.241(5)
O(32)	−0.054(5)	−0.182(5)
O(35[a])	−0.241(6)	
O(35[b])		0.384(13)
O(38)	0.126(5)	−0.005(5)

[a] s.o.f. = 0.76. [b] s.o.f. = 0.24.

the C—C and C—O bonds in crown ethers are *gauche* (*g*) and *anti* (*a*), respectively. The sequence of dihedral angles along the macrocyclic ring is $aag^-aag^+aa0aag^-aag^+aag^+$ if the major component of the disordered fragment is considered. For the minor component the rather unusual conformation ag^-g^-a of the C(32)—CH_2(33)—CH_2(34)—O(35**)—CH_2(36**) fragment is observed. Consequently, the $K^+ \cdots O(35)$ intramolecular distance for the minor component is elongated by 0.076 Å when compared with the major component.

The potassium ion is coordinated to the six O atoms of the macrocyclic ring. The $K^+ \cdots O$ distances are within the range of 2.687(5)–2.909(5) Å (average 2.790(5) Å). The least-squares plane through the six oxygen atoms and their deviations from that plane are presented in Table V. The K^+ cation lies on this plane. Additional coordination to the nitrogen atom of the thiocyanate anion is observed ($K^+ \cdots N$ distance equal to 2.801(8) Å). The resulting coordination polyhedron is a distorted hexagonal pyramid. This additional coordination was not observed for related compounds [3, 4].

The equation for the least-squares plane of the eighteen atoms forming the macrocyclic ring (the disordered part of the macrocycle considered in the calculations was the major one) is:

$$0.9550X - 0.2331Y - 0.1836Z = -2.7253$$

$$X = a, \; Y = a \times (a \times b), \qquad Z = a \times b; \qquad \sum \Delta^2 = 2.520 \text{ Å}^2; \qquad \langle \Delta^2 \rangle^{1/2} = 0.355 \text{ Å};$$

the thiocyanate ion forming with the plane an angle of 54.3(2)°.

The chiral substituent is located on the opposite side of the macrocycle from the SCN-ion. The least-squares plane defined by the atoms C(7) to C(16) is inclined to the macrocyclic ring with an angle equal to 66.4(1)° (an angle of 30° was found in the structure

containing D-glucose as the chiral substituent [3–5]. The present molecule is expected to be a more selective recognition agent for organic cations considering steric interactions between the macrocyclic ligand and the guest species.

The intermolecular contacts between symmetry related molecules of **1**·KSCN in the crystal are consistent with van der Waals packing. The shortest contacts are: $K^+ \cdots S^i$ 3.542 Å, $S \cdots H(11)^i$ 2.74 Å, $C(30) \cdots C(36^{**})^{ii}$ 3.278 Å, $O(32) \cdots H(33b)^{ii}$ 2.45 Å, $N \cdots H(33a)^{iii}$ 2.54 Å, $C(30) \cdots H(36c)^{ii}$ 2.61 Å and $H(21a) \cdots H(36a)^{iv}$ 2.28 Å, [symmetry related positions: (i) $1+x, y, z$; (ii) $1/2+x, 1/2-y, 2-z$; (iii) $-1/2+x, 1/2-y, 2-z$; (iv) $x, 1+y, z$].

3.2. NUMERICAL MODELLING OF THE HOST–GUEST COMPLEX STRUCTURES

The results of the empirical force field calculations of the host–guest complexes are summarized in Table VI and illustrated in Figures 3 and 4. A common feature of the results

Table VI. Torsion angles for the energetically preferred conformations and orientations of the guest cation **4** in the complexes with the ligands **2** and **3**

Host	Guest	No.	φ_1	φ_2	φ_3	φ_4	φ_5	E(kJ/mol)[a]
		I	−48	−160	40	127	130	31.0
		II	−51	−176	51	−127	120	9.2
2	*R*	III	−52	180	54	−33	138	18.9
		IV	−51	−170	49	52	132	0.0
		V	−47	5	66	−46	136	4.6
		I	49	175	125	−48	68	10.5
		II	48	168	122	42	66	15.1
		III	49	−170	123	115	72	0.0
2	*S*	IV	43	−159	138	−38	144	11.7
		V	49	−7	119	−29	69	20.5
		VI	47	5	118	50	69	5.0
		VII	46	34	139	−30	146	12.1
		VIII	47	27	136	39	148	5.9
		I	−48	−170	56	−52	−136	55.3
		II	−38	154	46	−102	66	0.0
		III	−42	178	48	51	38	14.7
3	*R*	IV	−47	−171	50	52	74	2.5
		V	−44	−3	60	−49	71	4.2
		VI	−43	5	64	−48	−137	61.6
		VII	−47	−158	54	56	−135	54.0
		I	47	171	129	−53	83	0.0
		II	48	178	126	52	82	0.8
		III	51	180	135	−48	−11	13.0
3	*S*	IV	56	−171	135	30	−19	31.4
		V	52	−168	134	126	−12	23.9
		VI	48	4	122	48	−11	10.9
		VII	46	−2	118	48	84	2.9

[a] in relation to the lowest energy minimum.

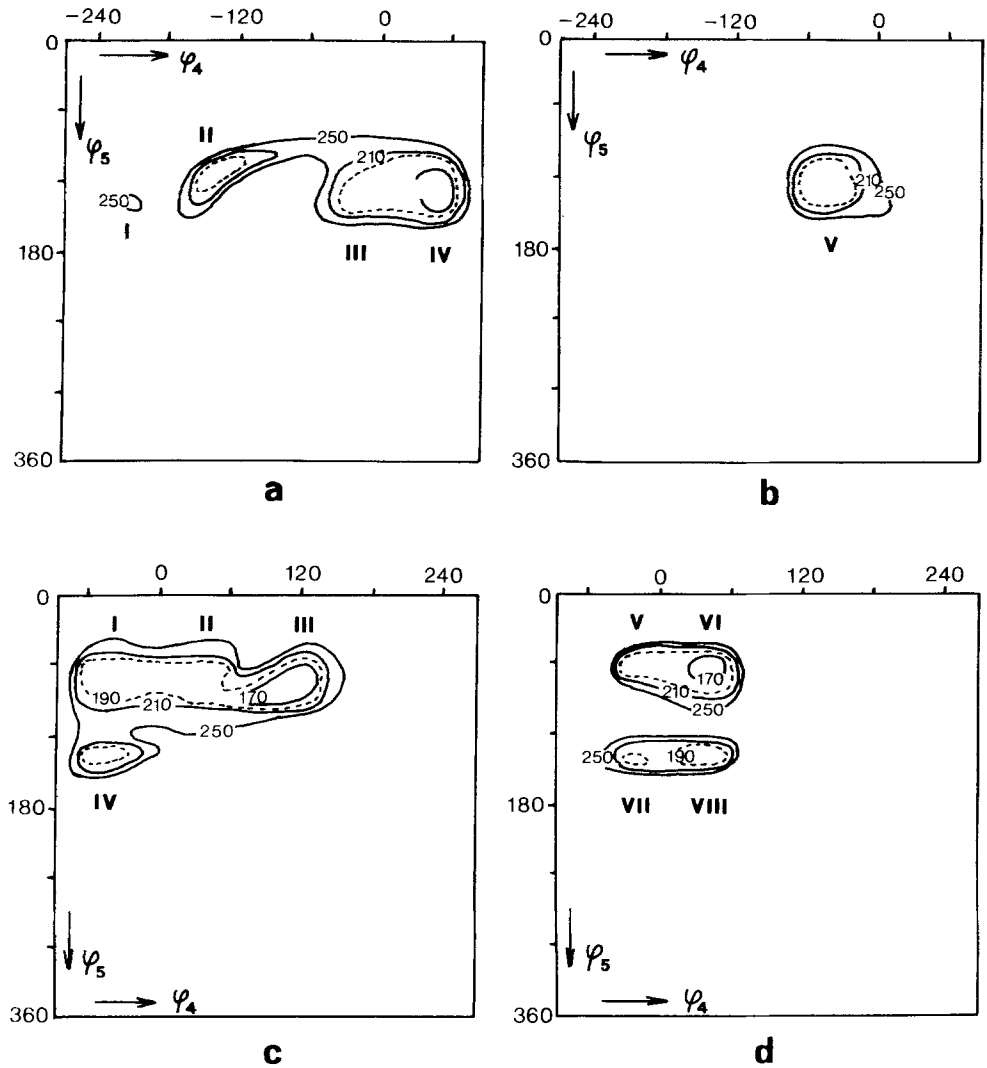


Fig. 3. Maps of potential energy calculated for the complex of the host **2** with the guest **4**. (a) complex with the *R* enantiomer of **4**: cross sections at $\varphi_1 = -50$, $\varphi_2 = 190$, $\varphi_3 = 47°$; (b) complex with the *R* enantiomer of **4**: cross sections at $\varphi_1 = -47$, $\varphi_2 = 5$, $\varphi_3 = 66°$; (c) complex with the *S* enantiomer of **4**: cross sections at $\varphi_1 = 46$, $\varphi_2 = -172$, $\varphi_3 = 130°$; (d) complex with the *S* enantiomer of **4**: cross sections at $\varphi_1 = 47$, $\varphi_2 = 10$, $\varphi_3 = 128°$.

obtained for both hosts is that there are several energy minima found in each case. In particular:

A. α-D-*Mannosido*-18-*crown*-6 (**2**)

The *R* enantiomer of the guest cation may assume just one orientation with respect to the host (at $\varphi_5 = 130°$). At that minimum the guest cation may adopt different internal conformations (denoted in Table VI and Figure 3 by φ_1, through φ_4). The *S* enantiomer of the guest may adopt two orientations ($\varphi_5 = 68$ and 146°, respectively) and at each of the two orientations different conformations of the guest are possible.

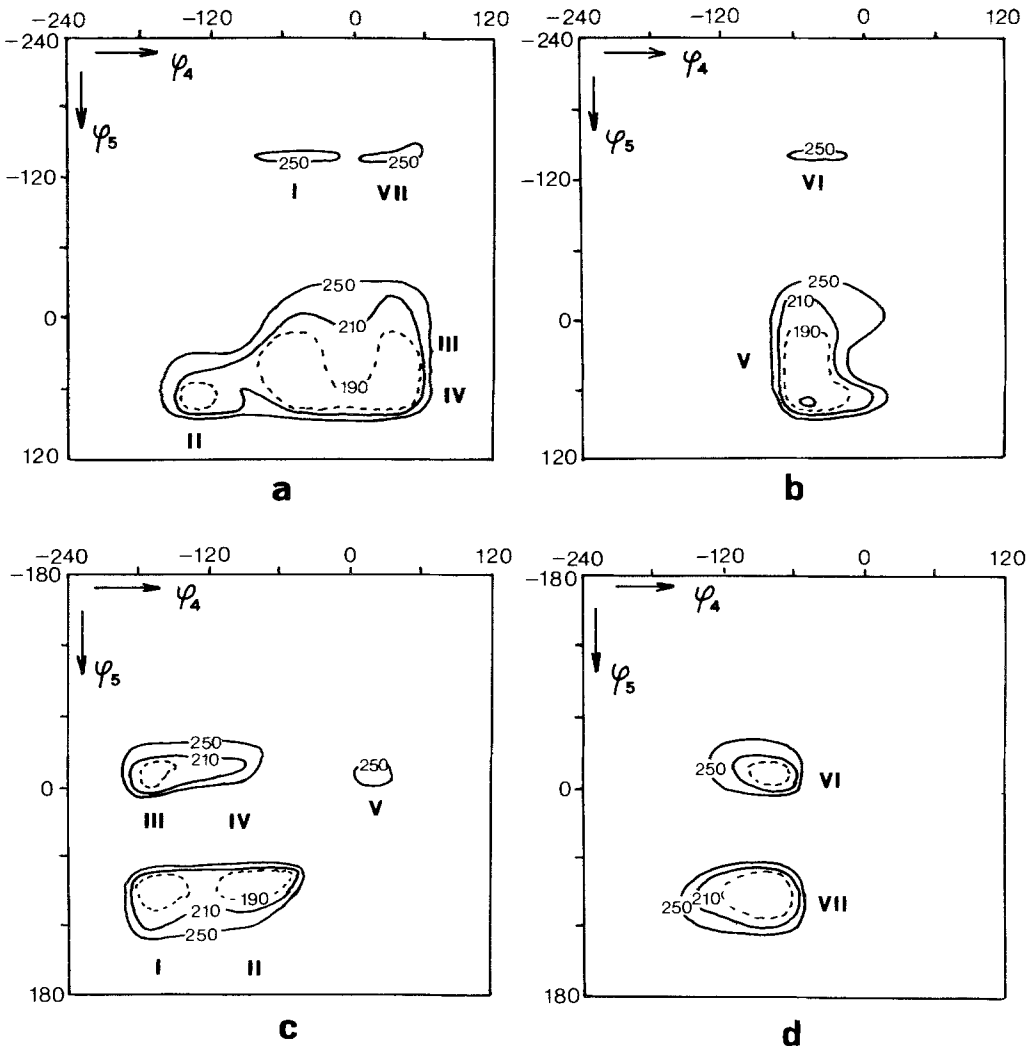


Fig. 4. Maps of potential energy calculated for the complex of the host **3** with the guest **4**. (a) complex with the *R* enantiomer of **4**: cross sections at $\varphi_1 = -45$, $\varphi_2 = 176$, $\varphi_3 = 52°$; (b) complex with the *R* enantiomer of **4**: cross sections at $\varphi_1 = -44$, $\varphi_2 = 1$, $\varphi_3 = 62°$; (c) complex with the *S* enantiomer of **4**: cross sections at $\varphi_1 = 50$, $\varphi_2 = 180$, $\varphi_3 = 130°$; (d) complex with the *S* enantiomer of **4**: cross sections at $\varphi_1 = 47$, $\varphi_2 = 1$, $\varphi = 120°$.

B. α-D-*Glucosido-benzo*-18-*crown*-6 (**3**)

There are two favourable orientations of the guest *R* cation differing by 164° when the *R* cation moiety is rotated around the $H_3N^+—R$ bond. The energy minimum found at $\varphi_5 = 60°$ is significantly deeper (*ca.* 54 kJ/mol) than the one found at $\varphi_5 = -136°$; the energy barrier between the minima being higher than 200 kJ/mol. Again, the guest moiety may adopt different conformations at each of the minima. In the case of the *S* enantiomer of the guest, the energy minima, found at −11 and 83° are shallower by at least 10 kJ/mol than those observed with the *R* form, and are separated by the energy barrier of *ca.* 200 kJ/mol.

Analysis of the energy calculations reported above suggests the possibility of selective complexation of enantiomeric guests by the substituted crown receptors. By inspection of the energy maps 3a through 3d an 'entropy driven' selectivity mechanism is suggested since the *R* enantiomer has only one good orientation in the complex while the *S* enantiomer has two good orientations of nearly equal energy and with only a moderate energy barrier between them. The *S*-selectivity is expected. The only experimental data on selectivity recently available for a similar system concerns phenylethylamine as the guest molecule, where *S*-selectivity was observed [2].

A more complex situation is found for **3**. The *R* enantiomer of the guest may assume two orientations (Figure 4) at two rather diffuse energy minima. The *S* enantiomer however, can adopt two orientations for which the energy minima are sharp. In this case the complex containing the *S* enantiomer should be 'enthalpy stabilized' while the entropy factor could be of primary importance on stabilisation of the complex with the *R* guest. Evaluation of the relative importance of these two different mechanisms for complexation is not possible from these data alone. Experimental data on a similar system with phenylethylamine as the guest however, showed *R*-selectivity [2].

In view of the rather well known difficulties in obtaining crystalline complexes of the macrocyclic crown receptors with organic guest species, the numerical modelling approach provides valuable information on selectivity mechanisms. In the case of enantio-selectivity this information may also be useful for understanding the selectivity of complexation in solution phases, provided the solvent used in the experiments is achiral.

Acknowledgements

This work was supported within the PAN-CNR scientific cooperation programme (03.10 research programme of PAN). The authors wish to thank Professor G. D. Andreetti for helpful discussions, Dr M. Pietraszkiewicz for kindly providing the crystals and Dr G. Bocelli for his kind assistance in X-ray data collection.

References

1. J. F. Stoddart: *Chem. Soc. Rev.* **8**, 85 (1979).
2. D. Gehin, P. Di Cesare, and B. Gross: *J. Org. Chem.* **51**, 1906 (1986).
3. K. Suwińska, M. Pietraszkiewicz, J. Lipkowski, J. Jurczak, G. D. Andreetti, and G. Bocelli: *J. Mol. Struct.* **75**, 221 (1981).
4. K. Suwińska and G. D. Andreetti: *J. Incl. Phenom.* **1**, 71, (1973).
5. A. Courtois, L. el Masdouri, D. Gehin, and B. Gross: *Acta Crystallogr.* **C42**, 850 (1986).
6. G. Germain, P. Main, and M. M. Woolfson: *MULTAN. A computer program for automatic determination of crystal structure.* University of York, England (1977).
7. G. M. Sheldrick: *SHELX76. Program for crystal structure determination.* University of Cambridge, England (1976).
8. N. L. Allinger: *J. Am. Chem. Soc.* **99**, 8127 (1977).
9. *International Tables for X-ray Crystallography.* Vol. IV, pp. 99–100 and 149–150. Kynoch Press. (Present distributor D. Reidel, Dordrecht.) (1974).
10. E. Giglio: *Nature* **222**, 339 (1969).
11. E. Maverick, L. Grossenbacher, and K. N. Trueblood: *Acta Crystallogr*, **B35**, 2233 (1979).
12. C. K. Johnson: *ORTEPII.* Report ORNL-5138. Oak Ridge National Laboratory, Tennessee (1976).