JOURNAL OF PHYSICAL ORGANIC CHEMISTRY
J. Phys. Org. Chem. 2001; **14:** 43–51

NMR spectroscopic and molecular modelling studies of the solution structure and complexational behaviour of some bis(benzo crown ether)s

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Received 16 May 2000; revised 5 September 2000; accepted 20 September 2000

ABSTRACT: Structural information about the bis(benzo crown ether)s **I–VI** and their complexes with alkali metal cations was deduced from the ^{13}C NMR chemical shifts, the salt-induced ^{1}H and ^{13}C chemical shifts and the vicinal $^{1}H,^{1}H$ coupling constants. Especially the isomerism with respect to the amide O═C—NH bonds and imine fragments were assigned by various useful NMR parameters ($\delta_{C=O}$, $^{1}J_{N,H}$, $^{1}J_{C,H}$) and proved to be *E*,*E*-*anti*,*anti*. Furthermore, stereochemical information about preferred conformations about flexible bonds was obtained from 2D ROESY NMR experiments. The complex formation (2:1 complexes and 'sandwich-like' 1:1 complexes, respectively) were determined also by ^{23}Na NMR spectroscopy. The conformational study of the crown ethers was accompanied and corroborated by molecular dynamics and quantum chemical calculations. Copyright © 2000 John Wiley & Sons, Ltd.

KEYWORDS: NMR spectroscopy; configuration; conformation; bis(benzo crown ether)s; alkali metal complexes

INTRODUCTION

Bis(benzo crown ether)s have been widely studied owing to their ability to form complexes selectively with alkali metal cations.[1 2] These compounds consist of two crown ether units in the same molecule; therefore the usual 2:1 but also 'sandwich-like' 1:1 complexation is possible.

It was the objective of this work to assign the isomerism of the bis(benzo crown ether)s **I–VI** along the linking chain (amide O═C—NH bond and imine fragment) of a series of heteroarylene-bridged carbonyl-hydrazone bis(benzo-15-crown-5 ether)s (cf. Scheme 1) by NMR spectroscopy and accompanying molecular modelling. Furthermore, aim to determine the solution conformation of the bis(benzo crown ether)s **I–VI** and the variation of the conformation during complexation of alkali metal cations by means of NMR spectroscopy.

RESULTS AND DISCUSSION

Stereochemistry of bis(benzo crown ether)s

The ring inversion of the macrocyclic polyether rings in the bis(benzo crown ether)s **I–VI** is fast on the NMR time-scale at ambient temperature; accordingly, averaged signals for an unknown number of conformers were obtained in each case. Moreover, only one set of ^{1}H and ^{13}C signals was detected for these compounds without any line broadening. From single resonances of especially H-12 and NH protons up to −50 °C and the configurational behaviour of similar bis(benzo crown ether)s[3] on the existence of only one configuration of the amide bonds was concluded (cf. Scheme 2; *E*,*Z* with respect to the amide bond O═C—NH). The same information came from only one signal for the carbonyl resonances C-10 in the ^{13}C NMR spectrum.

^{1}H NMR spectra. The ^{1}H NMR spectra exhibit five characteristic absorption ranges: the NH protons at δ = 11.81–12.21 ppm (H-11), the OCH_2 crown ether protons (H-19–H-22 at δ = 3.76–4.20 ppm), the H-12 methine protons at δ = 8.21–8.42 ppm, the H-5 methylene protons (3.78–5.08 ppm) and the aromatic protons (H-1–H-4, H-6–H-9 at δ = 7.36–8.45 ppm). Proton chemical shifts and relevant coupling constants are given in Tables 1 and 2. The aromatic protons H-14, H-15 and H-16 can be readily differentiated by the vicinal and long-range H,H coupling; H-16 was found at higher field due to the *ortho*-OR substituent.

The multiplets of the crown ether protons H-19–H-22 can be readily differentiated, owing to the aromatic ring current effect[4] they are low field shifted the nearer they are positioned to the benzo ring (δ: H-19 > H-20 > H-21, H-22).

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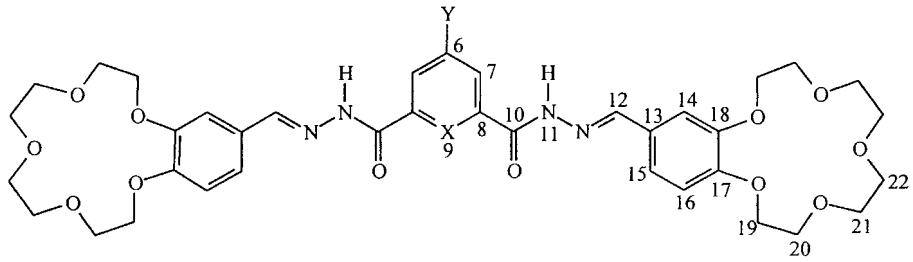
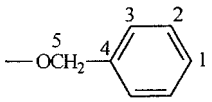
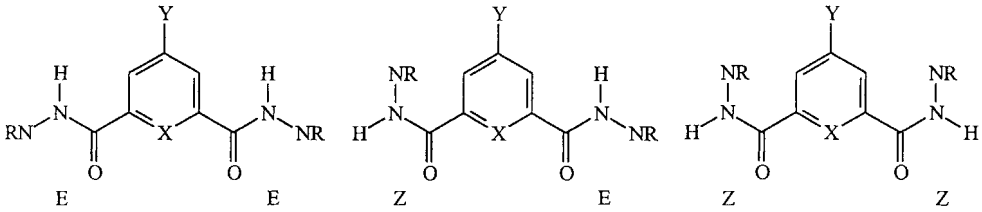


Nr.	X	Y	Z
I	-CH=	H	
II	-N=	H	
III	-CH=	OCH_3	
IV	-CH=		H
V	-CH=		Cl
VI	-CH=		NO_2

Scheme 1



Scheme 2

Table 1. ^{1}H chemical shifts $\delta(^1H)$ (ppm), of the bis(benzo crown ether)s **I–VI** in $CDCl_3$–CD_3OD (80:20)

Compound	H-1	H-2	H-3	H-5	H-6	H-7	H-9	H-11	H-12	H-14	H-15	H-16	H-19	H-20	H-21,22
I	–	–	–	–	7.49	7.99	8.27	11.85	8.21	7.55	7.11	6.84	4.18	3.92	3.75
II	–	–	–	–	8.12	8.45	–	12.21	8.42	7.66	7.21	6.87	4.20	3.94	3.78
III	–	–	–	3.78	–	7.48	7.81	11.87	8.21	7.51	7.11	6.86	4.19	3.91	3.77
IV	7.39	7.39	7.39	4.96	–	7.55	7.79	11.87	8.21	7.48	7.09	6.83	4.16	3.90	3.77
V	–	7.36	7.36	4.93	–	7.53	7.81	11.81	8.21	7.48	7.08	6.83	4.15	3.91	3.76
VI	–	8.24	7.60	5.08	–	7.56	7.86	11.85	8.22	7.47	7.08	6.82	4.16	3.90	3.76

Table 2. Homonuclear coupling constants of the aromatic protons *J* (Hz), of the bis(benzo crown ether)s **I–VI**

Compound	$^3J_{ortho}$ (H-2, H-3)	$^3J_{ortho}$ (H-6, H-7)	$^3J_{ortho}$ (H-15, H-16)	$^4J_{meta}$ (H-7, H-9)	$^4J_{meta}$ (H-14, H-15)
I	–	7.75	8.25	1.25	1.45
II	–	7.80	8.30	–	1.40
III	–	–	8.30	1.30	1.80
IV	(n.o.)	–	8.30	1.40	1.70
V	(n.o.)	–	8.30	1.40	1.70
VI	8.70	–	8.35	1.30	1.60

^{13}C NMR spectra. The assignment of the corresponding ^{13}C NMR spectra was established from the unequivocally assigned ^{1}H NMR spectra by means of both HMQC and HMBC 2D NMR experiments (Table 3). Stereochemically relevant information is available from the chemical shifts of C-14 and C-16 in the γ fragments C-14—C-18—O—C-19′ and C-16—C-17—O—C-19. High-field shifts of the terminal carbons are significant for in-plane

Table 3. ^{13}C chemical shifts $\delta(^{13}C)$ (ppm), of the bis(benzo crown ether)s **I–VI** in $CDCl_3$–CD_3OD (80:20)

Compound	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10
I	–	–	–	–	–	129.3	131.5	133.6	126.1	165.0
II	–	–	–	–	–	139.3	126.1	150.9	–	160.9
III	–	–	–	–	–	160.1	117.0	134.9	117.9	164.8
IV	128.3	127.7	128.7	136.3	70.4	159.2	117.9	134.8	117.9	164.9
V	134.6	128.5	128.6	133.7	70.1	158.7	117.5	134.6	117.5	164.3
VI	147.4	123.5	127.4	143.5	70.0	158.3	117.4	134.7	117.4	164.1

	C-12	C-13	C-14	C-15	C-16	C-17	C-18	C-19	C-20	C-21	C-22
I	150.0	127.4	110.7	123.6	112.9	151.6	149.6	68.9	69.6	70.5	71.2
II	148.7	127.4	111.3	123.4	112.9	151.7	149.5	68.9	69.6	70.5	71.1
III	149.8	127.3	110.4	123.5	112.7	151.5	149.5	68.8	69.6	70.4	71.1
IV	149.5	127.3	110.0	123.6	112.71	151.5	149.6	68.7	69.5	70.4	71.1
V	149.3	126.9	110.2	123.1	12.5	151.2	149.2	68.5	69.2	70.1	70.8
VI	149.5	126.9	110.2	123.0	112.5	151.3	149.2	68.5	69.1	70.7	70.7

Table 4. ^{15}N chemical shifts $\delta(^{15}N)$ (ppm), and coupling constants, J (Hz), of the bis(benzo crown ether)s **I–VI** in $CDCl_3$–CD_3OD (80:20)

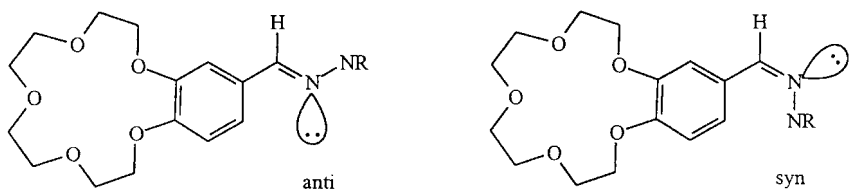
Compound	δ(—CH=*N*—NH—)	^2J(H-12,N)	δ(—CH=N—*N*H—)	^1J(H-11,N)	^1J(C-12,H-12)
I	304.40	6.20	153.40	95.1	160.18
II	300.20	6.20	149.51	99.4	158.58
III	–	–	–	–	161.63
IV	304.25	6.86	153.40	94.4	162.60
V	304.15	8.30	153.28	95.9	160.33
VI	304.40	6.43	153.53	94.4	163.16

interactions. Owing to the high-field position of both α-OCH_2 and of C-14/C-16, respectively, the more or less in-plane position of these fragments in the bis(benzo crown ether)s **I–VI** can be concluded.[5] The same information is obtained from ROEs H-14/α-CH_2 and H-16/α-CH_2 (cf. Table 5). For assigning the stereochemistry of the studied bis(benzo crown ether)s **I–VI** from both the ^1H and ^{13}C NMR spectra a number of useful NMR parameters were employed.

Isomerism of the amide bonds. In order to prove the *E–Z* isomerism of the two amide bonds (cf. Scheme 2), the position of the signals of both the C=O carbon and the NH proton in the NMR spectra were considered. The carbonyl resonances were found between 160.9 and 165.0 ppm, and therefore it was concluded that the *E,E* isomer is present (for the corresponding *Z,Z* isomer δ(C=O) = 169.9–177.0 ppm is expected).[6]

The ^{15}N chemical shifts[7] and the $^1J_{N,H}$ coupling constants[8] have also been successfully employed to estimate the configuration at amide bonds (Table 4). The corresponding parameters were determined by $^{15}N,^1H$ HMQC experiments. The ^{15}N chemical shifts were found between −149.5 and −153.5 ppm and −300.2 and −304.4 ppm. The corresponding $^1J_{N,H}$ coupling constants (94.4–99.4 Hz) are characteristic for the *E,E* isomer;[8] in the *Z,Z* isomer they proved to be much smaller (90 Hz).[8]

Syn–anti isomerism of the imine fragments (Scheme 3). ROEs between the NH protons and the imine proton H-12 were found in **I–VI** and proved unequivocally the *anti* position of the NH proton and the imine nitrogen lone pair. Also the direct coupling $^1J_{C\text{-}12,H\text{-}12}$ can be employed to assign the *syn–anti* isomerism; the experimentally obtained values $^1J_{C\text{-}12,H\text{-}12}$ = 158.6–163.2 Hz proved characteristic for the *anti* arrangement.[9] In case of



Scheme 3

Table 5. Relative intensity of the ROE cross peaks as obtained from ROESY 2D NMR spectra of the bis(benzo crown ether)s **I–VI**

ROE	**I**	**II**	**III**	**IV**	**V**	**VI**
H-11 ↔ H-12	ROE[a]	ROE	ROE	ROE	ROE	ROE
H-11 ↔ H-7	50%	ROE	45%	51%	53%	52%
H-11 ↔ H-9	50%	–	55%	49%	47%	48%
H-12 ↔ H-14	51%	51%	44%	51%	51%	46%
H-12 ↔ H-15	49%	49%	56%	49%	49%	54%
H-12 ↔ H-16	ROE	ROE	ROE	ROE	ROE	ROE
H-6 ↔ H-7	ROE	ROE	–	–	–	–
H-14 ↔ H-19	ROE	ROE	ROE	ROE	ROE	ROE
H-15 ↔ H-19′	ROE	ROE	ROE	ROE	ROE	ROE
H-16 ↔ H-19	ROE	ROE	ROE	ROE	ROE	ROE
H-19 ↔ H-20	ROE	ROE	ROE	ROE	ROE	ROE
H-5 ↔ H-7	–	–	ROE	ROE	ROE	ROE
H-2 ↔ H-3	–	–	–	ROE	ROE	ROE

[a] ROE = cross peak obtained in the 2D ROESY experiment still significant; ROE(H-7 ↔ H-11) + ROE(H-9 ↔ H-11) = 100%, and ROE(H-12 ↔ H-14) + ROE(H-12 ↔ H-15) = 100%, respectively.

the *syn* position values $^{1}J_{\text{C-12,H-12}} > 185$ Hz would be expected.[9]

Rotation about the C-8—C-10 and C-12—aryl bonds. In order to study quantitatively the conformational equilibrium of the rotations about the C-8—C-10 and the C-12—aryl bonds, ROESY 2D NMR spectra were recorded and the ROE cross peaks obtained were integrated. The ROE values are given in Table 5. From these results, and with the understanding that the rotation about the C-8—C-10 and the C-12—aryl bonds is fast on the NMR time-scale,[10] the two in-plane conformations were found with similar populations (cf. ROEs H-7/H-11 and H-9/H-11; ROEs H-12/H-14 and H-12/H-15).

Conformational variations during the complexation of alkali metal ions to I–VI

After assigning the *E,E-anti,anti* isomerism of the amide bonds and the imine fragments of **I–VI**, in continuation of previous studies,[5] the complexation of these bis(benzo crown ether)s with alkali metal cations was studied. High-field shifts of the ^{1}H resonances (especially of the aromatic protons) during complexation were interpreted as the formation of 'sandwich-like' complexes; from low-field shifts, conventional complexation of the cations within the cavity of the two crown ether moieties was concluded and in the latter case chemical shifts of nuclei in the linking chain remained constant.[8]

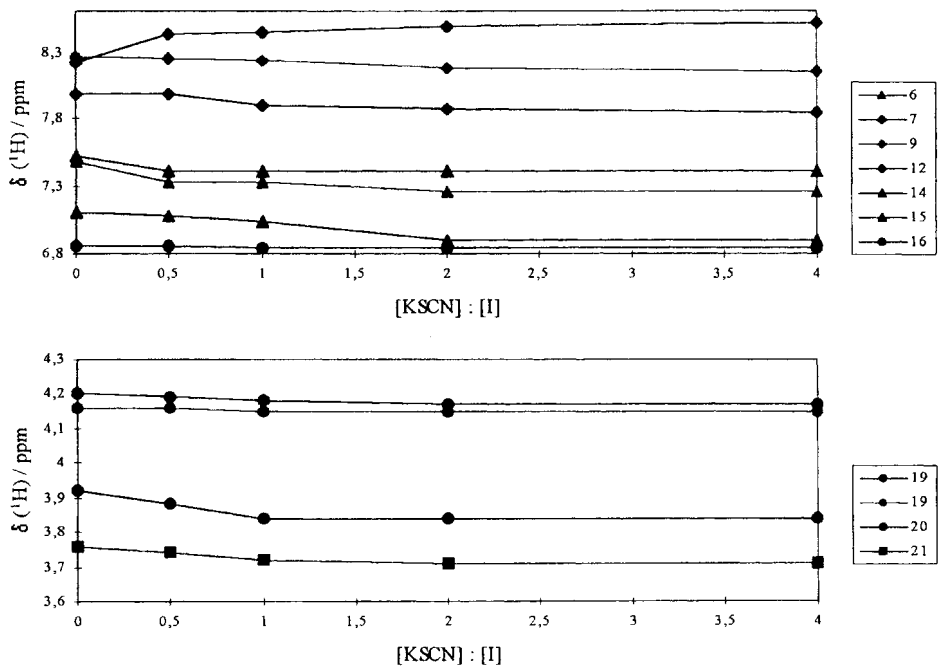


Figure 1. ^{1}H chemical shifts of **I** at different [KSCN]/[**I**] molar ratios

Table 6. ^{1}H chemical shift variations, $\Delta\delta(^1H)$ (ppm), of the bis(benzo crown ether)s in $CDCl_3$–CD_3OD (80:20) during the complexation with Na^+ and K^+ cations

	I:Na^+		**II**:Na^+		**II**:Na^+		**IV**:Na^+		**V**:Na^+		**I**:K^+	
No.	1:1	1:2	1:1	1:2	1:1	1:2	1:1	1:2	1:1	1:2	1:1	1:2
1	–	–	–	–	–	–	0.02[a]	0.05[a]	–	–	–	–
2	–	–	–	–	–	–	0.02[a]	0.05[a]	0.04[a]	0.08[a]	–	–
3	–	–	–	–	–	–	0.02[a]	0.05[a]	0.00[a]	0.02[a]	–	–
5	–	–	–	–	0.11	0.15[a]	0.21	0.26	0.20	0.27	–	–
6	0.02	0.10	0.01	0.05	–	–	–	–	–	–	−0.16	−0.23
7	0.01	0.11	−0.01	0.04	0.03	0.15	0.05	0.16[a]	0.03	0.14	−0.08	−0.11
9	0.21	0.32	–	–	0.25	0.37	0.30	0.41	0.26	0.39	−0.03	−0.09
12	0.44	0.66	0.33	0.44	0.47	0.69	0.51	0.71	0.48	0.69	0.23	0.27
14	0.00	0.15	0.12	0.31	0.05	0.22	0.06	0.23	0.04	0.21	−0.20	−0.10
15	0.10	0.20	0.36	0.59	0.12	0.22	0.13	0.23[a]	0.12	0.22	−0.07	−0.21
16	0.04	0.14	0.00	0.15	0.03	0.13	0.04	0.14	0.03	0.14	−0.05	−0.01
19	0.02	0.11	0.05	0.11	0.02	0.11	0.04	0.13	0.04	0.13	−0.09	−0.03
20	0.01	0.01	−0.01	0.04	0.00	0.02[a]	0.01	0.04	0.00	0.04	−0.09	−0.08
21, 22	0.02	0.04	0.01	0.01	0.01	0.03	0.00	0.02	0.01	0.02	−0.04	−0.05

[a] Signal broading and overcrowding.

^{1}H NMR spectroscopy. The changes in the proton chemical shifts of bis(benzo crown ether) **I** subject to the molar ratio [KSCN]/[**I**] are depicted in Fig. 1 (see also Table 6). The high-field shift of especially the aromatic protons with growing complexation was interpreted as the formation of 'sandwich-like' complexes; therefore, the conformation of the linking chain has to be changed. These shielding variations are mainly caused by the anisotropy effects of the two benzo crown ether units.

In contrast, the Na^+ cation, when added to $CDCl_3$–CD_3OD solutions of the bis(benzo crown ether)s, shift the resonances of almost all the protons to lower field (Table 6). Therefore, conventional fixation of the cations within the cavity of the two crown ether units was concluded.

^{13}C NMR spectroscopy. The ^{13}C chemical shifts should be even more useful for deducing conformational

Table 7. ^{13}C chemical shift variations $\Delta\delta(^{13}C)$ (ppm) of the bis(benzo crown ether)s **I–VI** in $CDCl_3$–CD_3OD (80:20) during complexation with Na^+ cations

No.	**I** (1:1)	**I** (1:2)	**II** (1:1)	**II** (1:2)	**III** (1:1)	**III** (1:2)	**IV** (1:1)	**IV** (1:2)	**V** (1:1)	**V** (1:2)	**VI** (1:1)	**VI** (1:2)
1	–	–	–	–	–	–	−0.09	−0.09	0.17	0.25	0.00	0.00
2	–	–	–	–	–	–	0.02	0.03	−0.03	−0.01	−0.10	−0.05
3	–	–	–	–	–	–	−0.04	−0.04	0.04	0.10	0.01	0.10
4	–	–	–	–	–	–	0.14	0.13	−0.13	−0.12	0.30	0.22
5	–	–	–	–	–	–	0.17	0.13	−0.62	−1.42	0.11	0.18
6	0.12	0.27	−0.08	0.02		0.30	−0.04	0.06	−0.04	0.05	−0.14	0.08
7	0.55	0.89	0.07	0.16	0.47	0.81	0.41	0.75	1.08	1.53	0.59	0.91
8	−0.38	−0.57	−0.27	−0.67	−0.35	−0.49	−0.34	−0.53	−0.24	−0.46	−0.51	−0.59
9	0.38	0.32	–	–	0.56	0.61	0.53	0.56	0.90	0.76	0.54	0.54
10	−0.22	−0.27	0.04	0.14	−0.30	−0.33	−0.29	−0.36	−0.21	−0.21	−0.33	−0.30
12	−0.35	−0.70	−0.01	−0.03	−0.26	−0.60	−0.23	−0.38	−0.44	−0.51	−0.52	−0.80
13	0.82	1.46	0.78	1.53	0.73	1.43	0.62	1.25	0.47	1.24	1.02	1.65
14	0.49	0.58	1.00	1.99	0.61	0.69	0.58	0.67	0.52	0.70	0.47	0.51
15	0.36	0.61	0.47	0.13	0.32	0.63	0.25	0.25	0.06	0.52	0.41	0.71
16	0.13	0.25	0.14	0.50	0.09	0.21	0.08	0.15	0.07	0.16	0.08	0.18
17	−1.32	−2.42	−1.52	−2.82	−1.19	−2.38	−1.11	−2.38	−0.89	−2.02	−1.66	−2.68
18	−1.13	−2.05	−1.30	−2.35	−1.04	−1.99	−0.98	−1.87	−0.72	−1.71	−1.37	−2.20
19	−0.78	−1.33	−0.53	−0.95	−0.62	−1.24	−0.56	−1.17	−0.45	−1.14	−0.94	−1.47
19	−0.67	−1.27	−0.84	−1.46	−0.69	−1.27	−0.63	−1.20	0.13	0.19	−0.84	−1.39
20	−0.85	−1.47	−0.74	−1.32	−0.65	−1.26	−0.61	−1.20	−0.46	−1.19	−0.89	−1.39
20	−0.76	−1.36	−0.82	−1.41	−0.71	−1.34	−0.72	−1.35	−0.42	−1.05	−0.95	−1.49
21	−1.05	−1.72	−1.25	−2.10	−1.16	−2.03	−0.84	−1.55	−0.34	−1.04	−1.19	−1.73
22	−1.16	−2.07					−1.01	−1.89	−0.75	−1.74	−1.40	−2.16
22	−1.25	−2.08	−1.01	−1.68	−1.66	−1.80	−0.96	−1.79	−0.69	−1.63	−1.31	−2.07

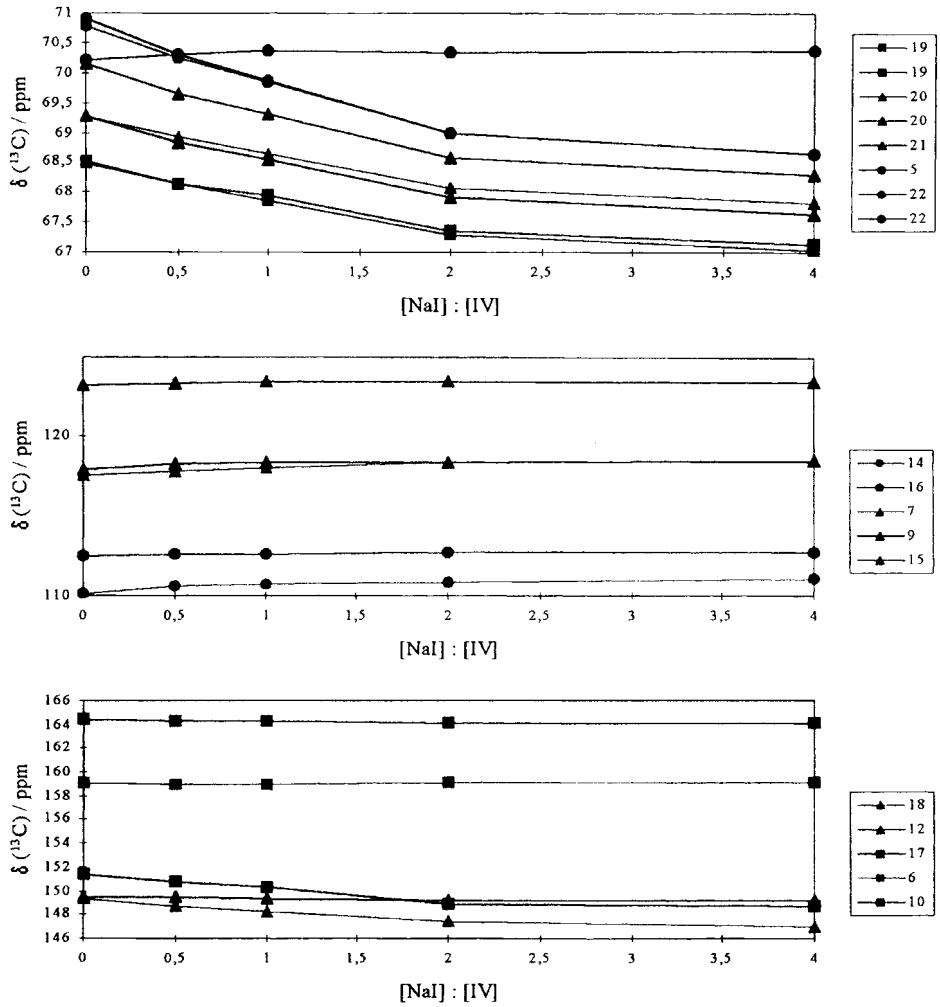


Figure 2. ^{13}C chemical shifts of *IV* at different [NaI/[**IV**] molar ratios

variations during alkali metal complexation owing to their more characteristic dependence on the stereochemistry. The ^{13}C chemical shifts for the free crown ethers and their complexes with NaI were recorded in $CDCl_3$/CD_3OD (80:20). The ^{13}C chemical shifts $\Delta\delta$ at [NaI]/[crown ether] molar ratios of 1:1 and 2:1 are collected in Table 7. Typical δ vs [NaI]/[crown ether] molar ratio curves are depicted in Fig. 2. From the shape of the δ–concentration curves it can be concluded that the complexation proceeds gradually. First, 1:1 complexes will be formed (only small low-field shifts) and later 1:2 (stronger low-field shifts) host–guest complexes. The changes in the carbon resonances C-1–C-12 of the linking chain are very small, and therefore it can concluded that the linking chain was not changed during the complexation with Na^+ ions.

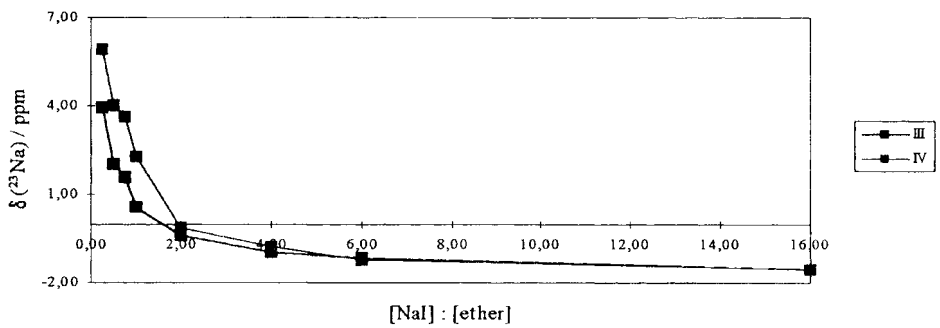


Figure 3. ^{23}Na chemical shifts in the corresponding complexes of **III** and **IV** at different [NaI]/[bis(benzo crown ether] molar ratios

Table 8. Isomerism of the amide O=C—NH bond and the imine fragment in the lowest energy conformations of the bis(benzo crown ether)s **I–VI** as calculated

Compound	Amide bond		Imine fragment	
I	*Z*	*Z*	*anti*	*anti*
II	*E*	*E*	*anti*	*anti*
III	*E*	*Z*	*syn*	*anti*
IV	*E*	*E*	*anti*	*anti*
V	*E*	*Z*	*syn*	*syn*
VI	*E*	*Z*	*syn*	*syn*

^{23}Na NMR spectroscopy. The complexation of the Na^+ ions by the structurally related bis(benzo crown ether)s was further investigated by means of ^{23}Na NMR spectroscopy. In order to study the growing complex formation, the coronands were added to NaI solutions, and the dependence of the ^{23}Na chemical shifts on the [NaI]/[coronand] molar ratio was investigated (Fig. 3). The exchange between the free and the complexed sodium ions is fast on the NMR time-scale and averaged shifts were therefore obtained.

The chemical shift variations of the sodium ion represent changes in the Na^+ solvation shell because, during complexation, the solvent molecules are replaced by the macrocyclic ligands.[11] This is demonstrated by growing low-field shifts with increasing Na^+ complexation of the bis(benzo crown ether)s **III** and **IV** in Fig. 3

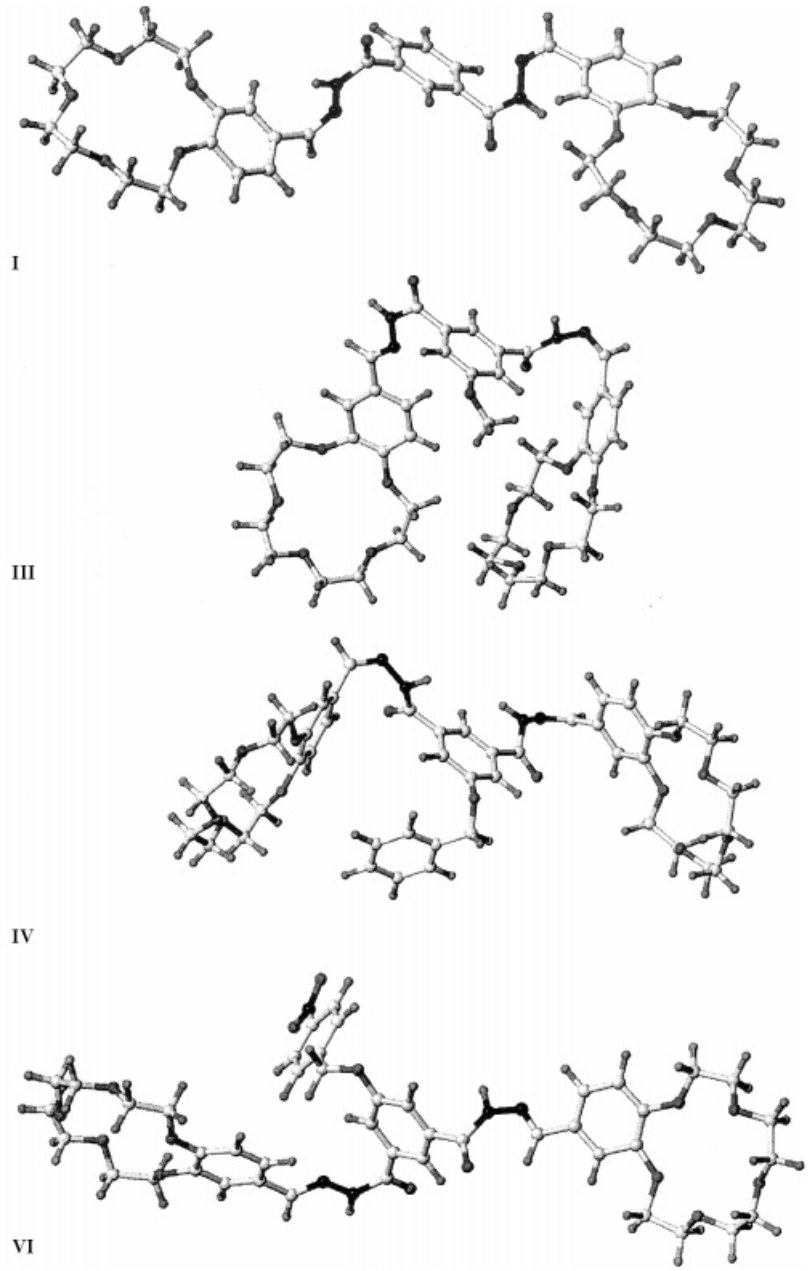


Figure 4. The lowest energy conformations of **I**, **III**, **IV** and **VI**

Table 9. Infrared frequences ν (cm^{-1}) of the bis(benzo crown ether)s **I–VI** in KBr

	I	II	III	IV	V	VI
ν(NH)	3200	3200	3200	3190	3200	3200
$\nu(CH_2)$	2865; 2915	2855; 2915	2855; 2910	2855; 2910	2860; 2915	2860; 2915
ν(amide I)	1645	1660	1640	1635	1650	1650
ν(C—O—C) aliph.	1125	1125	1125	1120	1125	1125
ν(C—O—C) arom.	1260	1260	1260	1260	1260	1260

with respect to the Na^+ resonance of the free, solvated sodium ion. The δ vs [salt]/[coronand] molar ratio curves show a single sharp bend when the molar ratio is approximately 1:2. Accordingly, the formation of 1:2 host–guest complexes was corroborated.

Molecular modelling studies

In order to find the preferred conformers of lowest energy for the bis(benzo crown ether)s **I–VI**, molecular dynamic (MD) simulations at 500 K were carried out, and also Grid search calculations were performed. As a result, different ground-state conformers (MD, 500 conformers; Grid search, **I–III** 1024 conformers and **IV–VI** *ca* 20 000 conformers) were obtained. After the MD simulation and Grid search, all of these structures were used as the starting geometry for a subsequent TRIPOS energy minimization. After this procedure, the most stable 60 conformers thus obtained were further optimized by PM3 energy minimization. These calculations were done with molecular mechanical correction of the O=C—NH bonds (keyword: mmok).

The preferred isomerism found in the experimental NMR study, i.e. the *E,E* isomer with respect to the amide O=C—NH bonds and the *anti* position with respect to the imine fragment, were found generally along the lowest energy conformations of the calculated structures (see Table 8), but not with generally the lowest energy. The corresponding structure with *E,E* configuration in **I** is at least 5.5 kcal mol^{-1} less stable than the lowest energy conformation, in **III** 1.1 kcal mol^{-1}, in **V** 3.6 kcal mol^{-1} and in **VI** 6.7 kcal mol^{-1}. The difference in energy between the lowest energy conformation and the corresponding structure in the *anti,anti* configuration were found to be at least 2 kcal mol^{-1} in **II** and 3.6 kcal mol^{-1} in **V**.

The lowest energy conformations of **I, III, IV** and **VI** obtained with the present calculation procedure are depicted in Fig. 4. The general discussion of the calculated structures obtained can be summarized as follows:

(i) The amide fragment (generally planar, however, both *E* and *Z* isomers have been found in the energetically most stable structures) is not in-plane with the adjacent aromatic moiety: for the C-7—C-8—C-10—N-11 dihedral angle *syn* but also *anti* conformations were found.
(ii) The amidine moiety was found to be planar and the dihedral angles C-10—N-11—N—C-12 proved to prefer the *anti* conformation; however, *gauche* and eclipsed conformations were also calculated.
(iii) The calculated structures show no remarkable preference for the N—C-12—C-13—C-15 fragments; the *gauche*, *anti* and also the *syn* conformations expected were found; the same is true for the relevant conformations of substituent Y in **III**–**VI**.
(iv) In addition, both stretched type (**I, II, IV, VI**) and a

Table 10. Electron ionization mass spectrometer data for the bis(benzo crown ether)s **I–VI**

m/z	I (%)	II (%)	III (%)	IV (%)	V (%)	VI (%)
M	3	0.2	0.4	0.5	–	–
588	6	10	3	6	15	26
293	8	4	10	10	10	8
M −293	22	20	6	7	3	–
178	4	7	16	3	5	7
161	100	100	100	100	99	38
146	36	40	36	40	45	31
105	22	30	20	23	24	12
45	55	92	42	54	100	100
91 (tropylium ion)	–	–	–	94	–	–
125/127	–	–	–	–	92	–
136	–	–	–	–	–	14

'sandwich-like' type (**III, V**) conformations of the bis(benzo crown ether)s studied were calculated; hence, also the complexation of cations larger than sodium seem to be already pre-organized.

EXPERIMENTAL

The bis(benzo crown ether)s **I–VI** were synthesized by condensation reactions of 4-formylbenzo-15-crown-5 ether and the corresponding dicarboxylic acid dihydrazides in benzene, continuously removing the water, and employing catalytic amounts of *p*-toluenesulfonic acid.[12,13] Structural analysis was performed by mass spectrometry (Table 9), by IR spectroscopy (Table 10) and the present NMR investigations.

N′,N‴-Bis(2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-benzopentaoxapentadecin-15-ylmethylidene)isophtalhydrazide, **I**: m.p.: 247–249 °C.

N′,N‴-Bis(2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-benzopentaoxapentadecin-15-ylmethylidene)pyridine-2,4-dicarbohydrazide, **II**: m.p.: 170–172 °C.

N′,N‴-Bis(2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-benzopentaoxapentadecin-15-ylmethylidene)-5-methoxyisophtalhydrazide, **III**: m.p.: 250–252 °C.

N′,N‴-Bis(2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-benzopentaoxapentadecin-15-ylmethylidene)-5-benzyloxyisophthalhydrazide, **IV**: m.p.: 266–268 °C.

N′,N‴-Bis(2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-benzopentaoxapentadecin-15-ylmethylidene)-5-(4-chlorobenzyloxy)isophtalhydrazide, **V**: m.p.: 242–244 °C.

N′,N‴-Bis(2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-benzopentaoxapentadecin-15-ylmethylidene)-5-(4-nitrobenzyloxy)isophthalhydrazide, **VI**: m.p.: 225–227 °C.

The ^{1}H, ^{13}C and ^{15}N NMR spectra were recorded at 300.13, 75, 47 and 30.41 MHz, respectively (Bruker ARX 300) in $CDCl_3/CD_3OD$ (4 :1) solution (5 mm probe tube, ambient temperature, deuterated solvents as internal lock). Typical conditions for ^{13}C: 30° pulses, 2 s repetition time, sufficient number of scans, 32K data points.

The ^{1}H, ^{13}C and ^{15}N NMR spectra were assigned by H,H COSY, HMQC and HMBC 2D NMR experiments using the Bruker standard software.

The molecular dynamics calculations were carried out with the TRIPOS force field[14] at 1000 K. The quantum chemical calculations were carried out with the PM3 method[15] within the SYBYL[16] (MOPAC 6.0[17]) software. The calculations were performed on Silicon Graphics IRIS-INDIGO XS24 and IBM RS6000 computers.

CONCLUSIONS

The stereochemistry of the studied bis(benzo crown ether)s **I–VI**, assigned by NMR spectroscopy, proved to be the *E*,*E* isomer with respect to the amide O═C—NH bonds ($\delta_{C=O}$, $^{1}J_{N,H}$) and the *anti* isomer (ROE, $^{1}J_{C,H}$) with respect to the imine fragment. This stereochemistry, proved unequivocally by NMR spectroscopy, could be corroborated only in some cases by the lowest energy conformations calculated by the accompanying molecular modelling.

^{1}H, ^{13}C and ^{23}Na NMR chemical shifts are impressive in indicating the variations in the conformations of the bis(benzo crown ether)s during their complexation to alkali metal cations. The bis(benzo crown ether)s studied were found to form 1:2 host–guest complexes with sodium cations and 1:1 'sandwich-like' complexes with potassium cations.

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