

Crown ether analogues and their complexes. Solid-state and solution stereochemistry of dibenzo-15-crown-4 ether and its 2:2 complex with sodium iodide as studied by X-ray crystallography and NMR spectroscopic methods

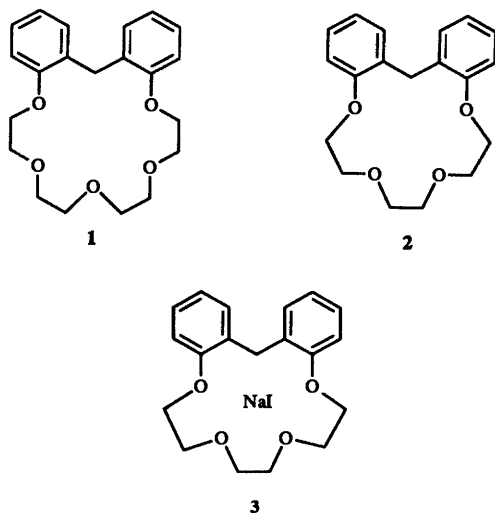
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The structures of the title systems have been determined by X-ray crystallography. The sodium iodide complex has 2:2 stoichiometry and C_i symmetry. Each sodium cation coordinates to four oxygen atoms of one macrocyclic unit and one oxygen of the other 15-membered ring of the dimer. The 400 MHz ^1H NMR spectra have been analysed and assignments made on the basis of NOESY and COSY experiments. Solution ^{13}C NMR spectra have been assigned using HETCOR methods. Solid-phase ^{13}C NMR spectra are included and the results of sodium complexation on the solid-phase ^{13}C chemical shifts are discussed. $[4\text{-}^2\text{H}_4]$ Dibenzo-15-crown-4 has been synthesized and employed as an aid in spectral assignments.

Introduction

Crown ether analogues derived from bis(2-hydroxyphenyl)methane were first reported by Vogtle *et al.*,¹ the first example being the dibenzo-18-crown-5 system shown below (1). Such



molecules may have interesting complexation features, owing to the reduced number of potential coordination sites and the steric crowding of the benzylic group. To explore such phenomena in 15-crown-5 analogues, we have prepared the novel dibenzo-15-crown-4 system 2 and have investigated the nature of its complexation with the sodium cation *via* X-ray crystallographic methods as well as solution- and solid-phase NMR spectroscopy.

The cavity of 2 appears to be too small to accommodate a sodium ion and lacks one potential coordination site, assuming a normal sodium coordination number of six, with the anion providing the sixth site. In such instances, there are several ways in which crown ether complexes can conceivably form and these are depicted in Fig. 1. The most common type of complex in this case is the 1:2 cation: crown sandwich²⁻⁴ [Fig. 1(a)]. Also, the 3:2 club sandwich [Fig. 1(b)] has been isolated⁵ in the case of Cs_2 (18-crown-6)₃. For 2:2 complexes, examples where each cation is associated with only one crown unit [Fig. 1(c)] have

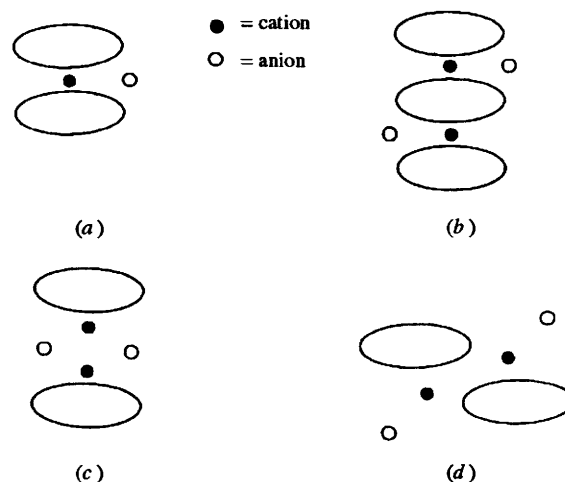


Fig. 1 Possible complexation modes in cases where the cation is too large to fit into the crown cavity: (a) sandwich type 2:1; (b) club sandwich type 3:2; (c) sandwich type 2:2 (each cation associated with only one crown); (d) sandwich type 2:2 (cations associate unequally with individual crowns)

been found.⁶ It also is conceivable that complexes could be formed where the cations associate unequally with the individual crown units [Fig. 1(d)].

Results and discussion

The structure and numbering scheme for dibenzo-15-crown-4, 2, is depicted. Fig. 2 shows the ORTEP plot for 3, while the ORTEP of the NaI complex, 3, is presented in Fig. 3. Solid-phase ^{13}C spectra of 2 and 3 are depicted in Figs. 4 and 5, respectively. Table 1 contains the crystallographic data for 2 and 3; atomic parameters, bond lengths, bond angles, torsion angles and anisotropic temperature factors have been deposited at the Cambridge Crystallographic Data Centre.† In Table 2 are collected the ^1H NMR data while ^{13}C NMR chemical shifts are in Table 3.

† For details of the CCDC deposition scheme, see 'Instructions for Authors (1995)', *J. Chem. Soc., Perkin Trans. 2*, 1995, issue 1.

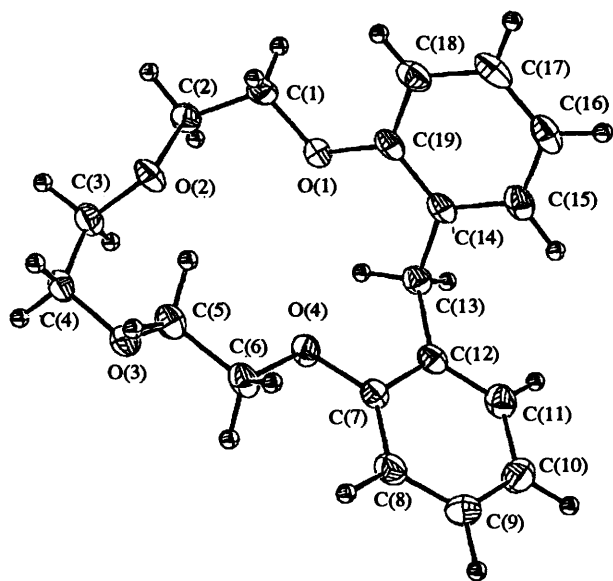


Fig. 2 ORTEP plot of dibenzo-15-crown-4 ether **2**

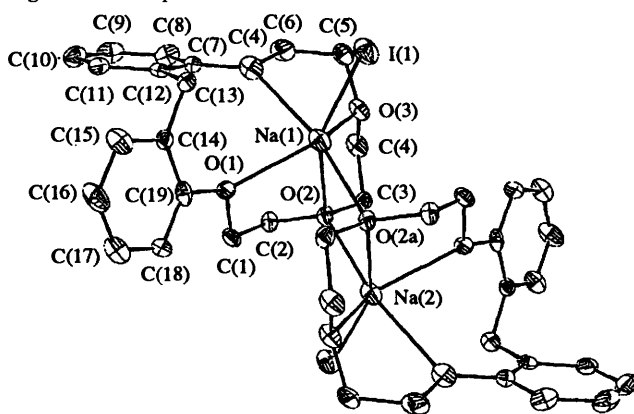


Fig. 3 ORTEP plot of 2:2 dibenzo-15-crown-4 dimeric complex **3** with NaI

(i) X-Ray crystal structures

The ORTEP plot of **2** (Fig. 2) shows that the molecule adopts an asymmetric conformation in the crystal. The O–C–O torsion angles are $61.6(1)^\circ$, $72.6(1)^\circ$ and $79.1(1)^\circ$, for the O2–C3–C4–O3, O1–C1–C2–O2 and O3–C5–C6–O4 units, respectively. Hence the latter two units show substantial deviations from the expected *gauche* conformations of such units in normal crown ethers.^{7,8} Conversely, the C–O–C–C units of crown ethers normally exhibit *transoid* geometry.^{7,8} Results for **2** are consistent with this preference, with the notable exception of C5–O3–C4–C3 where the torsion angle is $92.4(1)^\circ$. The C3–O2–C2–C1 unit has a slightly contracted torsion angle [$-165.7(1)^\circ$], while the other three such units deviate by less than 10° from the ideal *trans* geometry.

For the complex of **2** with NaI, *i.e.* **3**, the observed structure (Fig. 3) is a 2:2 dimer of the type shown schematically in Fig. 1(d). This dimer has C_2 symmetry with each sodium ion complexed to four oxygens of one crown unit and one oxygen of the neighbouring macrocyclic system. Coordination with an iodide ion completes the sixth site for each cation and from an examination of the bond angles the geometry about the sodium cation is best described as distorted octahedral.

In the individual crown units of **3** (Fig. 4), the four oxygen atoms form an approximately tetragonal plane with Na–O bond distances ranging from 2.352(5) to 2.779(5) Å. It is of interest to note that the bond distance to O2a of the neighbouring crown unit is 2.575(5) Å, *i.e.*, considerably shorter than the Na–O4 distance of 2.779(5) Å. The diameter of the

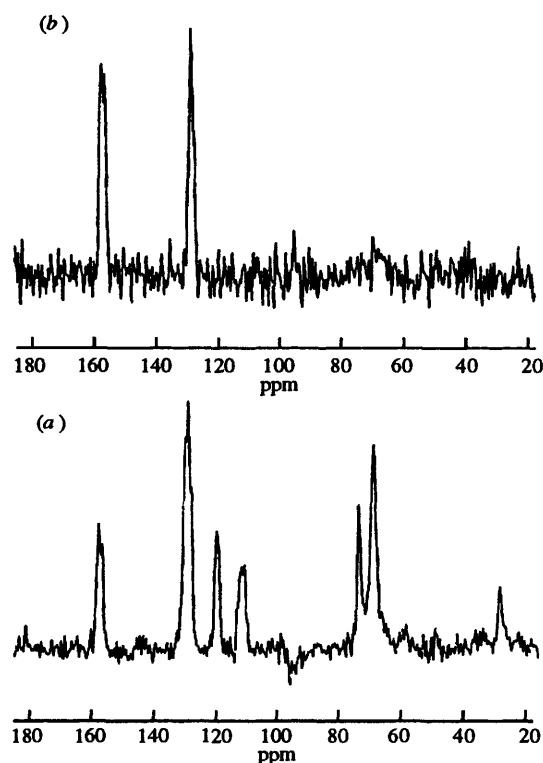


Fig. 4 Normal (a) and dipolar dephased (b) 45.3 MHz ^{13}C CPMAS spectrum of **2**

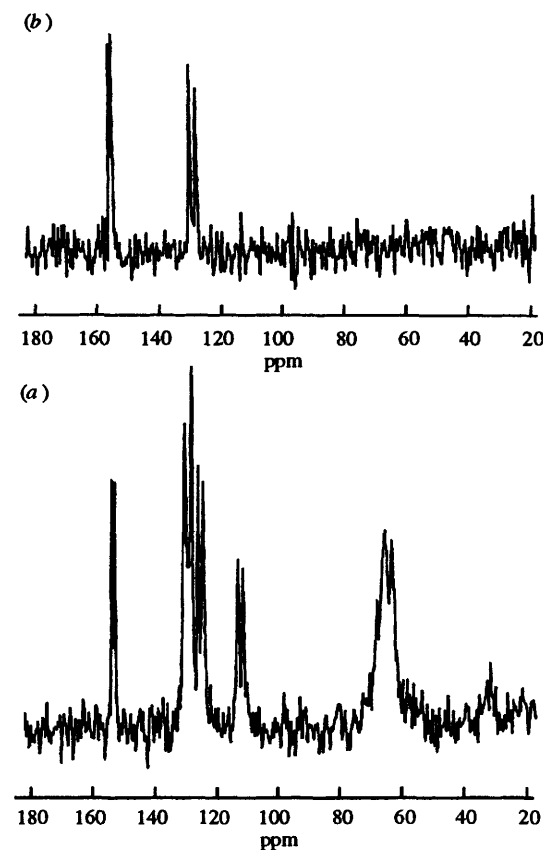


Fig. 5 Normal (a) and dipolar dephased (b) 45.3 MHz ^{13}C CPMAS spectrum of **3**

binding cavity can be found by determining the average diagonal distance between oxygen atoms (4.079 Å) and subtracting twice the van der Waals radius of oxygen (*i.e.* 2×1.4 Å). This results in an effective cavity diameter of

ca. 1.3 Å, which is clearly too small to accommodate the Na cation which has a diameter of 1.9–2.4 Å.⁹

Several interesting changes in the conformation of the 15-membered rings occur upon complexation. First of all, there are contractions in all the O–C–O angles with changes of ca. 4°, 11° and 21° for the O1–C1–C2–O2, O2–C3–C4–O3 and O3–C5–C6–O4 networks, respectively. Recently¹⁰ a comparison

of experimental and theoretical changes in the geometries of O–C–O units in crown ethers upon alkali-metal cation complexation has been published. Given complete conformational freedom, there is a tendency for a planar five-membered chelate to form. Hence it is expected that the O–C–O torsion angles will contract somewhat upon formation of **3**. This also has some influence on the observed ¹³C chemical shift changes in solid **2** vs. **3** (*vide infra*).

For the C–C–O–C units of **3**, there are three in which the geometries change markedly upon complexation. The C2–O2–C3–C4 torsion angle in **3** is 74.2(5)°, a contraction of 100.3° from that observed in **2**. Also for the C4–O3–C5–C6 network there has been a contraction of 103.8° upon complexation with the Na cation to give an angle of –71.3(5)° in **3**. By contrast, the C5–O3–C4–C3 angle has expanded by 75.7° to a value of 168.1(7)° in **3**.

Table 1 Crystallographic data for **2** and **3**

	2	3
Formula	C ₁₉ H ₂₂ O ₄	C ₁₉ H ₂₂ INaO ₄
Crystal system	Triclinic	Monoclinic
Space group	P $\bar{1}$	P2/c
a/Å	9.4072(18)	10.003(4)
b/Å	11.677(4)	16.639(4)
c/Å	8.3147(24)	12.059(4)
α/deg	106.58(3)	90.0
β/deg	105.800(19)	108.02(3)
γ/deg	100.516(21)	90.0
Z (molecules/cell)	2	4
D _c /g cm ⁻³	1.292	1.616
F(000)	336.14	925.62
μ/mm ⁻¹	0.08	1.70
Crystal dimensions (mm)	0.2 × 0.2 × 0.2	0.2 × 0.2 × 0.2
V/Å ³	808.0(4)	1908.7(10)
Radiation (λ/Å)	Mo-Kα (0.709 30)	Mo-Kα (0.709 30)
Octants measured	h (–11 to +10) k (0 to +13) l (–9 to +9)	h (–11 to +11) k (0 to +19) l (0 to +14)
Max. 2θ	49.9	49.9
T/°C	–100	–110
No. reflections meas'd.	2995	3556
No. unique reflections	2813	3356
No. obs'd. reflections	2419	2733
max shift/δ ratio	0.083	0.073
No. of atoms	45	47
No. of variables	296	227
R _f (significant refl.)	0.047	0.045
R _f (all refl.)	0.055	0.070
R _w (significant refl.)	0.065	0.070
R _w (all refl.)	0.065	0.070
Goodness of fit	2.01	1.82

Table 3 ¹³C NMR chemical shifts (δ_c from TMS ± 0.1)

	2 (sol'n.) ^a	1 (solid)	3 (sol'n.) ^b	3 (solid)
C1	68.1	68.5	69.1	64.1
C2	69.6	68.5	69.9	66.5
C3	70.1	72.5	70.4	66.5
C4	70.1	72.5	70.4	66.5
C5	69.6	68.5	69.9	66.5
C6	68.1	68.5	69.1	64.1
C7	156.6	157.5	157.6	155.4
C8	111.9	111.7	113.1	112.5
C9	126.9	128.2	127.9	(130.0) ^b
C10	120.5	118.8	121.1	125.5
C11	130.4	128.2	130.9	(131.5) ^b
C12	130.1	128.2	130.7	127.2
C13	28.9	27.5	29.4	30.2
C14	130.1	128.2	130.7	129.3
C15	130.4	128.2	130.9	(131.5) ^b
C16	120.5	118.8	121.1	125.5
C17	126.9	128.2	127.9	(130.3) ^b
C18	111.9	110.2	113.1	114.1
C19	156.6	157.3	157.6	154.4

^a 0.1 mol dm⁻³ in CDCl₃. ^b 0.1 mol dm⁻³ in (CD₃)₂CO. ^b Possible interchange of assignments.

Table 2 ¹H NMR chemical shifts and coupling constant data

	δ _H (± 0.001)		² J (± 0.1 Hz)	³ J (± 0.1 Hz)	⁴ J (± 0.1 Hz)
	2 ^a	3 ^b			
H1	4.114	4.121	–10.8	6.9, 2.3	
H1'			–10.8	6.9, 2.3	
H2	3.816	3.785	–10.8	6.9, 2.3	
H2'			–10.8	6.9, 2.3	
H3	3.711	3.660			
H4	3.711	3.660			
H5	3.816	3.785	–10.8	6.9, 2.3	
H5'			–10.8	6.9, 2.3	
H6	4.114	4.121	–10.8	6.9, 2.3	
H6'			–10.8	6.9, 2.3	
H8	6.822	6.931		6.9	1.5
H9	7.148	7.154		6.9	2.3
				7.6	
H10	6.863	6.847		7.6	1.5
				7.2	
H11	7.065	7.036		7.2	2.3
H13	4.103	4.068			
H15	7.065	7.036		7.2	2.3
H16	6.863	6.847		7.2	1.5
				7.6	
H17	7.148	7.154		7.6	2.3
				6.9	
H18	6.822	6.931		6.9	1.5

^a CDCl₃ as the solvent. ^b (CD₃)₂CO as the solvent.

A further change in geometry upon complexation occurs in the relative orientation of the aromatic rings in **2** and **3**. In **1** the C7–C12–C13–C14 angle is 84.1(1)°, while in **3** this angle expands to 121.0(7)°. Concomitantly, the C1–C12–C13–C14 angle contracts from –94.6(2)° in **2** to –59.3(5)° in **3**.

There are also some significant changes in bond angles upon complexation, the most notable being in the region of the 15-membered ring most remote from the aromatic rings. For example the O2–C3–C4 and O3–C5–C6 angles expand by 6.0° and 3.5°, respectively upon complexation, while coordination with the sodium cation results in a contraction of the O3–C4–C3 angles of 4.1°.

(ii) Solution NMR assignments

The starting point for the assignment of the ¹H spectrum of **2** is the assignment of the aromatic protons H8 and H18 *ortho* to oxygen as the most shielded aromatics, resonating at 6.822 ppm. A NOESY correlation is found between this resonance and the most deshielded aliphatic multiplet centred at 4.114 ppm, thus establishing the identity of the protons H1,1' and H6,6'. From subsequent COSY experiments, the origin of all proton resonances could be established. The protons on C1 and C6 interact with those on C2 and C5, respectively, to produce AA'XX' type spectra which were analysed iteratively to give the coupling constants shown in Table 2.

With the ¹H assignments in hand, the resonances for all protonated carbons could be assigned *via* ¹J ¹H¹³C HETCOR spectra. The only carbons not assigned *via* this method are the quaternary carbons and the benzylic carbon, which were readily assigned using 2-methylanisole as a model.¹¹

It is interesting to note for **2** that the most deshielded aliphatic protons (on C1,6), resonating at 4.114 ppm, are bonded to the most shielded carbon (at 68.1 ppm). Aromatic carbons C8 and C18 show high field ¹³C absorption at 111.9 ppm consistent with their disposition *ortho* to an oxygen atom.¹² The quaternary aromatic carbons C7 and C19 are the most deshielded (at 156.6 ppm) consistent with their direct connection to oxygen. Results for **3** are comparable, although the solvent is (CD₃)₂CO while **2** was examined in CDCl₃.

(iii) Solid-phase ¹³C NMR spectra

In the solid phase, ¹³C spectral multiplicity will reflect the asymmetric unit in the crystal if no unusual crystal packing effects or non-equivalent molecules in the unit cell are present.¹³ For both **2** and **3**, these complicating effects are not present in the crystal structures and hence one expects to observe 19 ¹³C resonances for each material in the absence of peak overlap. From spectra depicted in Figs. 4 and 5 it is clear that extensive peak overlap is present, but the spectra are consistent with a lack of conformational averaging in these solids.

Initially, non-protonated carbons can be identified by the appearance in the dipolar dephased experiment, while the resonances for protonated sites normally are not observed under such conditions. The two resonances at lowest field are resolved in spectra of both **2** and **3** and must arise from the C7, 19 sites which are not equivalent in the crystal structures. The dipolar dephased spectrum of the 3,4-[²H₄] derivative of **2** shows a resonance at 72.5 ppm, thereby establishing the most deshielded aliphatic resonance as arising from C3 and C4.

There are substantial upfield shifts (2–6 ppm) in the resonances for the oxygenated carbons C1 to C6 in the complex **3** as opposed to the free crown **2**. The X-ray crystal structure of **3** shows contractions in each of the three O–C–C–O angles ranging from 4 to 21° (*vide supra*). Earlier *ab initio* ¹³C chemical shifts from these laboratories¹⁴ for ethylene glycol, indicate that increased shielding at carbon is present as the O–C–C–O torsion angle contracts below 90°. Hence we attribute at least part

of the increased shielding at C1 to C6 of **3** to this factor. Further shielding may be expected from an induced dipole effect. Coordination of the ethereal oxygens with the sodium cation will render the oxygens more positive. Accordingly this may result in an induced increase in electron density at the carbon atoms bonded directly to oxygen, thereby shielding them.

Regarding solid-phase aromatic carbon resonances, the largest shift differences upon complexation occur at the C10 and C16 sites, which are *para* to O1 and O4, respectively. The complexation effects here are deshielding and amount to 6.7 ppm. Our interpretation of the deshielding is that it must be electronic, with the following rationale. Coordination of O1 and O4 to the sodium cation will clearly render the oxygen lone pairs of electrons less available for conjugative release into the aromatic rings. This will decrease the electron density at both the *ortho* and *para* sites and thus deshielding is anticipated at these sites in **3** relative to **2**. In accord with this is the observation of concomitant deshielding at the C8 and C18 positions **3** relative to **2**. Of course at the *ortho* sites, there is the possibility of steric factors influencing the ¹³C shielding, hence one cannot make an unambiguous interpretation regarding the origin of the *ortho* effects in these materials.

In conclusion, it is clear that interesting and novel stereochemical features result when 'structurally perturbed' crown ether analogues such as **2** form complexes. Also, the complementarity of X-ray crystallographic methods and solid-state and solution NMR for probing these features has again been demonstrated.

Experimental

(i) Materials

Compound **2** was prepared by first dissolving bis(2-hydroxyphenyl)methane (Aldrich, 2.00 g, 10 mmol) in 300 cm³ of anhydrous acetonitrile and adding LiH (160 mg, 20 mmol). The mixture was stirred for 15 min and then triethyleneglycol ditosylate¹⁵ (4.6 g, 10 mmol), dissolved in 150 cm³ of acetonitrile, was added dropwise. The mixture was refluxed for 3 days under nitrogen. After cooling, the white precipitate was removed by filtration and washed with dichloromethane. The filtrate was concentrated *via* rotary evaporation and purified by column chromatography on silica gel using 1:1 ethyl acetate–light petroleum as the eluent. Solid fractions were combined and recrystallized from ether to give **2**, mp 86–88 °C, in 60% yield.

For the preparation of [3,4-²H₄]-**2**, [²H₄]ethylene glycol (MSD Isotopes, 98 atom%) was used as the starting material. Subsequent conversion into diethyl([²H₄]ethane-1,2-diyldioxy)diacetate **4** was carried out *via* the following method. A dry 200 cm³ two-necked flask was charged with dichloromethane (spectrograde, 100 cm³), [²H₄]ethylene glycol (3.0 g, 0.045 mol) and ethyl diazoacetate (10.36 g, 0.09 mol). The mixture was cooled with stirring in an ice bath for 15 min. A catalytic amount (150 mg) of BF₃–diethyl ether was added over 2 min, and the reaction mixture was stirred until the evolution of nitrogen gas ceased (3 h). Following solvent removal by rotary evaporation, the crude product was purified *via* flash column chromatography on silica gel (grade 60, 230–400 mesh) using 1:1 hexane–diethylether as the eluent. The product was a yellow oil. δ_c(CDCl₃) 170.0, 69.9 (CD₂), 68.0, 60.2, 13.7.

Reduction of **4** to [²H₄]triethylene glycol was accomplished in 75% yield as follows. A dry 500 cm³ three-necked flask equipped with a condenser, dropping funnel and Ar inlet was cooled in an ice–salt bath. LiAlH₄ (0.91 g, 0.022 mol) was suspended in anhydrous THF (50 cm³). To this suspension was added **4** (4.92 g, 0.02 mol) dropwise with stirring. The reaction mixture was then stirred for 3 h at 5 °C and subsequently allowed to come to room temperature. After suction filtration

and washing with THF, the solvent was removed from the filtrate to give 3.8 g of crude product, which was then purified by extraction with $\text{CH}_2\text{Cl}_2\text{-H}_2\text{O}$. Removal of the water by rotary evaporation gave 2.4 g (75%) of $[\text{}^2\text{H}_4]\text{triethylene glycol}$. $\delta_{\text{c}}[(\text{CD}_3)_2\text{CO}]$ 73.0, 69.9 (CD_2) and 61.1. Conversion into the required $[\text{}^2\text{H}_4]\text{triethylene glycol ditosylate}$ was carried as described earlier.¹⁵ The NaI complex **3** was prepared by dissolving NaI (120 mg, 0.8 mmol) in the minimum amount of hot methanol. In a separate container, **3** (250 mg, 0.8 mmol) was dissolved in 10 cm^3 of hot ethyl acetate. The ethyl acetate solution was added to the methanol solution and hot methanol was added dropwise until all solids dissolved. Upon cooling, 260 mg of **3** (70% yield), mp 154–157 °C (decomp.) was obtained.

(ii) Solution NMR spectra

All spectra were recorded using a Bruker AMX-400 spectrometer equipped with a 5 mm inverse probe and an Aspect X32 computer. An Aspect 3000 processing controller was used and the standard microprograms employed are in the Bruker Software library.

For the ^1H ^{13}C HETCOR experiments, the free induction decays were typically acquired using 1024 data points for each of the 512 values of the evolution time, with a digital resolution of ca. 8 Hz in *F2* and 4 Hz in *F1*. The raw data were zero filled in *F1* prior to transformation using the qsin window function for both *F1* and *F2*. Proton relaxation delays were set at 1 s. For one-bond couplings, delays were set to emphasize couplings of 140 Hz. NOESY spectra were obtained with mixing times of 0.3 s.

(iii) Solid-phase NMR spectra

^{13}C CPMAS spectra were obtained at 45.3 MHz using a Bruker CXP-180 spectrometer with a 4.24T cryomagnet and a Doty Scientific magic angle spinning probe. Samples were contained in 7 mm diameter zirconia or silicon nitride rotors with Kel-F end caps. ^1H 90° pulse lengths were typically 4.5 μs and spinning rates were 4 to 5 kHz. Dipolar dephased spectra were obtained by interruption of the ^1H decoupling for 40 μs immediately following the cross-polarization sequence. Chemical shifts were measured relative to external hexamethylbenzene (HMB) and then corrected to the TMS (tetramethylsilane) scale (HMB methyl resonance at 16.9 ppm).

(iv) Crystallographic structures and structure solutions

A summary of the crystal data is presented in Table 1. All measurements were made on a Rigaku diffractometer with $\text{Mo-K}\alpha$ radiation. The $\theta/2\theta$ scan technique with profile analysis was employed. The space group for **2** was determined by comparing solutions in *P1* and $\overline{P1}$, while that for **3** was determined by systematic absences. Unit cell parameters were obtained by

refining the setting angles of 25 reflections with 2θ angles in the range of 40–50°. Lorentz and polarization factors were applied, but correction for absorption was applied only for **3**.

Structures were solved by direct methods plus Fourier maps and were refined by full-matrix least-squares analysis with weights based on counting statistics. All the atoms were refined anisotropically except for the hydrogens, which were refined isotropically. For **2**, the hydrogens were found by the Fourier difference map, whereas for **3**, the hydrogen positions were calculated. All calculations were performed using the NRCVAX crystallographic software package.¹⁶

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