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SYNTHESIS OF AN OCTAMETHYL-18-CROWN-6 DERIVATIVE AND THE X-RAY CRYSTAL STRUCTURE OF ITS 2:1 COMPLEX WITH BORANE–AMMONIA

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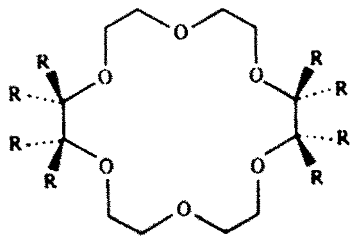
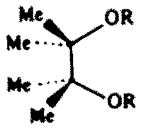
Abstract The synthesis of 2,2,3,3,11,11,12,12-octamethyl-1,4,7,10,13,16-hexaoxacyclooctadecane (2) from pinacol (3) by a sequence of reactions (3 → 4 → 5 → 6 + 5 → 2) involving alkylation (3 → 4), ozonolysis and reduction (4 → 5), tosylation (5 → 6), and cyclisation (5 + 6 → 2) is reported. With borane–ammonia, the octamethyl-18-crown-6 derivative 2 forms a crystalline 2:1 complex, $(BH_3NH_3)_2 \cdot 2$. X-Ray crystallography reveals the two guest BH_3NH_3 molecules are hydrogen bonded in a centrosymmetric manner to the opposite faces of the host 2, which adopts an all-*gauche* $(ag^+a\ ag^-a)_3$ conformation.

Recently, we reported[1] that 18-crown-6 (1) forms a crystalline 1:1 complex with the reducing agent, BH_3NH_3. As a consequence of the formal positive charge, which resides on the N atom of BH_3NH_3, we concluded that the host–guest complexing arrangement with *two neutral* BH_3NH_3 guest molecules binding to opposite faces of the 18-crown-6 host 1 might be rendered unstable because of cationic repulsion. We have since discovered that this is not necessarily the case when the 18-crown-6 constitution 1 carries substituents.

Here, we report the four-step synthesis of an octamethyl-18-crown-6 derivative 2 from pinacol (3). X-Ray crystallography reveals that in the readily formed 2:1 crystalline complex $(BH_3NH_3)_2 \cdot 2$, the two guests do in fact bind to opposite faces of the host. This observation has had[2] important consequences in the design and preparation of chiral reagent complexes for use in enantioselective reductions of prochiral ketones.



1 R = H
2 R = Me



3 R = H
4 R = $CH_2CH=CH_2$
5 R = CH_2CH_2OH
6 R = CH_2CH_2OTs

RESULTS AND DISCUSSION

The bis-2-hydroxyethyl ether 5 of pinacol (3), and the derived bistosylate 6, were easily prepared in good overall yields *via* the diallyl ether 4: (i) Treatment of 3 in dimethoxyethane with allyl bromide in the presence of sodium hydride afforded 4 in 78% yield. (ii) Ozonolysis of 4 in methanol followed by a reductive work-up with sodium borohydride yielded *ca* 80% of the diol 5. (iii) The diol 5 was readily converted (73%) into its bistosylate 6. Initially, this bistosylate 6 was prepared by us in connection with the synthesis of some di-(1,2,3)benzamacrobicyclic polyethers.[3] Subsequently, it came to our attention that 5 and 6 have also been prepared by Ando *et al.*[4] by a similar route. However, their procedure for making the diallyl ether 5 from pinacol (3) gives a much lower yield (39%) than ours and involves the use of liquid ammonia, potassium, and dry benzene. Reaction of equimolar amounts of 5 and 6 in tetrahydrofuran with sodium hydride as base gave the octamethyl-18-crown-6 derivative 2 as a crystalline compound in 22% yield without having to resort to chromatography. Irrespective of whether 2 was treated with 1 or 2 equivalents of BH_3NH_3 in methanolic solution, the crystalline 2:1 complex, $(BH_3NH_3)_2 \cdot 2$, was obtained. A single crystal suitable for X-ray structural analysis was isolated after slow cooling of a methanolic solution.

Tables 1 and 2 record the bond lengths and bond angles respectively for $(BH_3NH_3)_2 \cdot 2$. Torsional angles for the C—C and C—O bonds in macrocyclic ring are shown in Fig. 1. There is a crystallographic centre of symmetry at the centre of the macrocycle, which, despite the presence of the Me groups on C(8) and C(9),

Table 1. Bond lengths (Å)

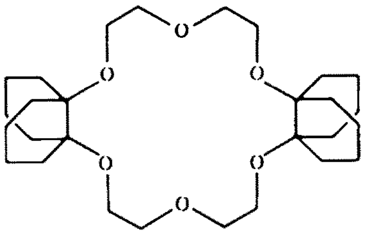
O(1)–C(2)	1.423(3)	O(1)–C(9′)	1.447(2)
C(2)–C(3)	1.485(3)	C(3)–O(4)	1.418(2)
O(4)–C(5)	1.410(2)	C(5)–C(6)	1.480(3)
C(6)–O(7)	1.417(3)	O(7)–C(8)	1.443(2)
C(8)–C(9)	1.547(3)	C(8)–C(10)	1.518(3)
C(8)–C(11)	1.526(3)	C(9)–C(12)	1.521(3)
C(9)–C(13)	1.522(3)		
N–B	1.595(3)		

Table 2. Bond angles (deg.)

C(2)—O(1)—C(9′)	117.2(1)	O(1)—C(2)—C(3)	109.0(2)
C(2)—C(3)—O(4)	110.1(2)	C(3)—O(4)—C(5)	111.5(1)
O(4)—C(5)—C(6)	110.7(2)	C(5)—C(6)—O(7)	109.6(2)
C(6)—O(7)—C(8)	116.5(1)	O(7)—C(8)—C(9)	104.1(1)
O(7)—C(8)—C(10)	109.1(2)	C(9)—C(8)—C(10)	111.8(2)
O(7)—C(8)—C(11)	110.5(2)	C(9)—C(8)—C(11)	111.6(2)
C(10)—C(8)—C(11)	109.7(2)	C(8)—C(9)—C(12)	112.3(2)
C(8)—C(9)—C(13)	111.0(2)	C(12)—C(9)—C(13)	109.6(2)
C(8)—C(9)—O(1′)	104.3(1)	C(12)—C(9)—O(1′)	109.8(2)
C(13)—C(9)—O(1′)	109.7(2)		

adopts a conformation (ignoring the Me substituents) that approximates to D_{3d} symmetry for the polyether ring. Two of the Me groups on C(8) and C(9) are oriented pseudo-*trans*-diaxial (antiperiplanar) and the other two are oriented pseudo-diequatorial (synclinal). Whilst necessarily (symmetry constraint) adopting a parallel alignment, the B—N bonds (1.595(3) Å) in the guest molecules are not normal to the mean plane of the six O atoms in the host. They are inclined at 7° from the normal to this plane with the N atoms displaced by 1.64(1) Å from the plane. The through-the-ring N···N′ distance of 3.30(1) Å is short compared with the distances of 3.48(1) and 3.37(1) Å observed[5] for $[trans\text{-}PtCl_2(PMe_3)NH_3]_2 \cdot 1$ and $[Cu(NH_3)_4H_2O \cdot 1]_n^{2+}[PF_6]_{2n}$, respectively. The tilted approach of the guest molecule is associated with the formation of two normal [N—H···O] H-bonds and one long [N—H···O] interaction to each face of the macrocycle (see caption to Fig. 1). In their H-bonding interactions, each NH_3 group assumes the characteristic perching orientation[6] with respect to the nearer triangle of O atoms on the appropriate face of the macrocycle. The BH_3 and NH_3 groups adopt a conventional near-staggered conformation with a H_a—N—B—H_b torsional angle of 52°. The B···C(Me) distances are 3.98 and 4.15 Å to C(12) and C(10′), respectively.

Substitution of the 18-crown-6 constitution is known[7] to influence the stoichiometry of crystalline complexes with alkali metal salts: thus, the didecalino-18-crown-6 7 invariably forms 1:1 complexes: no 2:1 (cation:ligand) complexes of the sandwich type have so far been characterised. The isolation of a 2:1 (guest:host) crystalline complex between BH_3NH_3 and 2 suggests that substitution of the 18-crown-6 constitution may encourage the emergence of this stoichiometry for face-to-face complexes where cationic repulsion between two bound guests is not a serious consideration. The occurrence of other examples[2,8,9] of 2:1 crystalline complexes between BH_3NH_3 and 18-crown-6 derivatives in our laboratories recently support this hypothesis.



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EXPERIMENTAL

TLC was carried out on glass plates coated with silica gel (Merck GF 254). All m.ps and b.ps are uncorrected. ^1H-NMR Spectra (internal TMS) were recorded on a Perkin Elmer R34 at 220 MHz in $CDCl_3$.

4,7-*Dioxa*-5,5,6,6-*tetramethyldeca*-1,9-*diene*[4] (4)

A soln of 3 (30 g, 254 mmol) in dry dimethoxyethane (DME) (200 ml) was added dropwise with stirring to a suspension of NaH (26.8 g, 558 mmol, 50% dispersion in oil) in dry DME (250 ml) under N_2. The soln was stirred at 55° for 1.5 hr and then allowed to cool to room temp. Allyl bromide (76.9 g, 635 mmol) was added and the suspension heated under reflux for 20 hr. Further NaH (6.2 g, 129 mmol, 50% dispersion in oil) and allyl bromide (15.4 g, 127 mmol) were added. The reaction was heated under reflux for 16 hr, cooled to room temp, and filtered (Hyflo Supercell). The filtrate was concentrated *in vacuo* to afford a pale oil, which was distilled to give 4 (39.3 g, 78%), b.p. 106–112°/45 mm, lit.[4] b.p. 76–81°/19 Torr. (Found: C, 72.3; H,

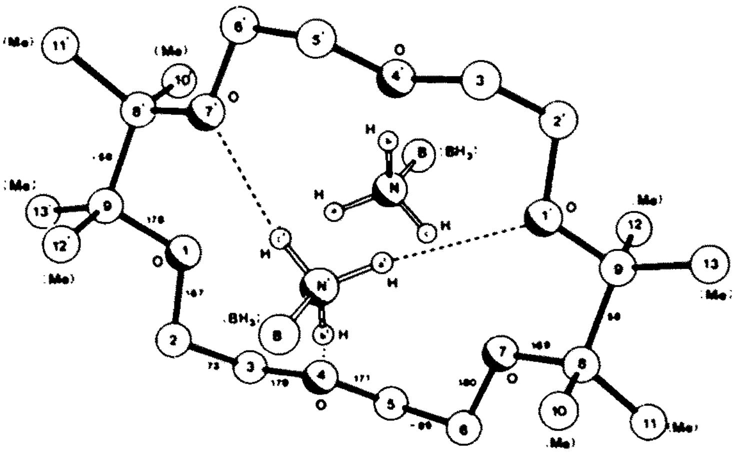

Fig. 1. Crystal structure of $(BH_3NH_3)_2 \cdot 2$. The torsional angles (°) around the macrocyclic ring are indicated beside the relevant C—C and C—O bonds. Hydrogen bonding distances R[N···O] (Å), R[H···O] (Å), angles (θ_N and θ_H°) between COC planes and (*a*) NO vectors and (*b*) HO vectors, N—H···O angles (°) at H atoms: [N···O(1)] 3.38, [H_a···O] 2.46, (*a*) 4.3, (*b*) 0, H_a 160; [N···O(7)] 3.16, [H_c···O] 2.21, (*a*) 4.2, (*b*) 4.3, H_c, 169; [N···O(4′)] 3.04, [H_b···O] 2.14, (*a*) 14.5, (*b*) 7.1, H_b 155. Non-bonded [N···O] (Å) distances, angles (θ_N°) between COC planes and NO vectors: [N···O(4)] 3.17, 78; [N···O(1′)] 3.26, 64; [N···O(7′)] 3.50, 65.

10.9%. $C_{12}H_{22}O_2$ requires: C, 72.7; H, 11.1%), δ 1.18 (12H, s, 4 × Me), 3.97 (4H, d × t, J = 4, 2 Hz, 2 × $OC\underline{H}_2CH{=}CH_2$), 5.05 (2H, bd, J_{cis} = 10 Hz, 2 × $OCH_2CH{=}CH\underline{H}$ (*cis*)), 5.25 (2H, bd, J_{trans} = 18 Hz, 2 × $OCH_2CH{=}CH\underline{H}$ ((trans)), and 5.82 6.00 (2H, m, J = 18, 10, 4, 4Hz, 2 × $OCH_2C\underline{H}{=}CH_2$).

3,6-*Dioxa*-4,4,5,5-*tetramethyloctane*-1,8-*diol*[4] (5)

The ether **4** (13.0 g, 65 mmol) was dissolved in dry MeOH (400 ml). O_3 was passed through the soln at −50° until reaction was complete (KI test). A soln of $NaBH_4$ (4.96 g, 130 mmol) in H_2O MeOH (3 : 1 v/v, 60 ml) was added dropwise while the temp was maintained below −20°. The soln was allowed to warm up to −5°, before the pH was adjusted to *ca* 7.5 with conc HCl and the soln concentrated *in vacuo*. The residue was dissolved in EtOAc (200 ml), which was washed with sat NaCl aq soln, separated, dried ($MgSO_4$), and concentrated *in vacuo* to give crude **5** as a brown solid (10.8 g, 80%). This product (*ca* 95% pure by TLC) was used in the next step without further purification. A small sample was crystallised from Et_2O light petroleum (b.p. 60–80°) to afford crystals of pure **5**, m.p. 46 47°. (Found: C, 58.3; H, 10.6%. $C_{10}H_{22}O_4$ requires: C, 58.3; H, 10.7%), δ 1.17 (12H, s, 4 × Me), 2.60 (2H, bs, 2 × OH), 3.52 (4H, t, J = 5 Hz, 2 × OCH_2CH_2OH) and 3.64 (4H, bm, 2 × $OCH_2C\underline{H}_2OH$).

1,8 - *Bis* - O - *toluene* - p - *sulphonyl* - 3,6 - *dioxa* - 4,4,5,5 - *tetramethyloctane* - 1,8 - *diol*[4] (6)

The diol **5** (11.6 g, 56 mmol) was reacted with *p*-toluenesulphonyl chloride (32 g, 169 mmol) in dry C_5H_5N (100 ml) at −25° for 16 hr. A conventional work-up procedure afforded 27.2 g of **6** as a crude white soild. Crystallisation from EtOAc-light petroleum (b.p. 60 80°) gave pure **6**, m.p. 123 124°, lit.[4] m.p. 123° (from EtOH). (Found: C, 55.9; H, 6.6; S, 12.4%. $C_{24}H_{34}O_8S_2$ requires: C, 56.0; H, 6.6; S, 12.5%), δ 1.05 (12H, s, 4 × Me), 2.46 (6H, s, 2 × $ArCH_3$), 3.58 (4H, t, J = 4 Hz, 2 × OCH_2CH_2OTs), 4.09 (4H, t, J = 4 Hz, 2 × $OCH_2C\underline{H}_2OTs$), and 7.35 and 7.80 (2 × 4H, 2 × d, J = 7 Hz, aromatic protons).

2,2,3,3,11,11,12,12 - *Octamethyl* - 1,4,7,10,13,16 - *hexaoxacyclooctadecane* (2)

The diol **5** (2.5 g, 12.1 mmol), dissolved in dry THF (50 ml), was added dropwise with stirring to a suspension of NaH (1.46 g, 30.4 mmol, 50% dispersion in oil) in dry THF (100 ml) under N_2. The soln was heated under reflux for 1 hr and then allowed to cool to 40°. The bistosylate **6** (6.9 g, 13.4 mmol), dissolved in dry THF (100 ml) was added dropwise with stirring during 2 hr. The mixture was heated under reflux for 28 hr and then allowed to cool to room temp. The minimum quantity of H_2O was added to destroy excess of NaH and the suspension was filtered (Hyflo Supercell). The filtrate was concentrated *in vacuo* to give a crude product (5.0 g). Trituration under light petroleum afforded a solid which was filtered off. Further trituration of this solid with Et_2O gave a ppt which was removed by filtration. The filtrate was concentrated *in vacuo* to give a solid which was crystallised from light petroleum (b.p. 60–80°) to afford colourless crystals of **2** (1.23 g, 22%), m.p. 129–133°. (Found: *M* + 1 (mass spec.), 377; C, 63.7; H, 10.9%. $C_{20}H_{40}O_6$ requires: *M*, 376; C, 63.8; H, 10.7%), δ 1.17 (24H, s, 8 × Me), 3.55 (8H, t, J = 5 Hz, 2 × CH_2OCH_2), and 3.69 (8H, t, J = 5 Hz, 4 × $C\underline{H}_2OCMe_2$).

Isolation of $(BH_3NH_3)_2 \cdot 2$

A soln of **2** (18.1 mg, 0.05 mmol) in MeOH (1.5 ml) was added to BH_3NH_3 (3.0 mg, 0.1 mmol) and the suspension was heated until refluxing began. When the resulting clear soln was allowed to cool to room temp, it afforded colourless crystals of $(BH_3NH_3)_2 \cdot 2$ (14.1 mg, 67%), m.p. 152–153° (dec). (Found: C, 54.9; H, 12.1; N, 6.2%. $C_{20}H_{52}B_2N_2O_6$ requires: C, 54.8; H, 11.9; N, 6.2%.)

Single crystals of $(BH_3NH_3)_2 \cdot 2$, suitable for examination by X-ray crystallography, were obtained by very slow cooling of a MeOH soln.

X-Ray structural analysis of $(BH_3NH_3)_2 \cdot 2$

Crystal data. $C_{20}H_{52}B_2N_2O_6$, $M = 438.26$, crystal dimensions 0.55 × 0.40 × 0.08 mm, monoclinic, $a = 8.253(2)$, $b = 12.721(4)$, c 12.973(5) Å, $\beta = 91.53(3)°$, $U = 1361.6$ Å^3 (by least squares refinement on diffractometer angles for 18 automatically centred reflections, $\lambda = 1.5418$ Å), space group $P2_1/n$, $Z = 2$, $D_c = 1.07$ g cm^{-3}, μCu-$K_\alpha = 5.71$ cm^{-1}.

Measurements. Data were collected with graphite monochromatized Cu-K_α radiation using the ω-scan measuring routine. 1329 Independent reflections were measured ($\theta \leq 50°$) of which 1302 had $|F_0| > 3\sigma(|F_0|)$ and were classed as observed. The net count of two reflections, the $\bar{2}\,\bar{1}\,\bar{2}$ and 2 1 0, measured as references every 50 reflections did not alter significantly during data collection (*ca* 18 hr) indicating that no deterioration of the crystal had occurred. The data were brought to a uniform arbitrary scale by these reflections and Lorentz and polarisation corrections were applied. No absorption corrections were applied.

Structure analysis. The structure was solved by direct methods. An *E*-map computed for phase solution with highest "figure of merit" gave the positions of all the non-H atoms. These atoms were refined anisotropically. The carbon H atoms, with the exception of those associated with the Me groups, which were refined as rigid bodies, were placed at calculated positions (C—H = 0.96 Å), assigned isotropic thermal parameters, $U(H) = 1.2U_{eq}(C)$, and allowed to ride on their parent C atoms. The H atoms of the NH_3 and BH_3 groups were clearly resolved in a ΔF map where they appeared as the six strongest residual peaks. These groups were refined as rigid bodies. Refinement was by block-cascade full matrix least squares. A weighting scheme $w^{-1} = \sigma^2(F_0) + 0.0005(F_0{}^2)$ with $\sigma(F_0)$ derived from counting statistics gave satisfactory agreement analyses. The final values of *R* and R_w were 0.042 and 0.050, respectively. The maximum residual electron density[*] in the final ΔF map was 0.15 eÅ^{-3}.

Computations were carried out on an Eclipse S140 using the SHELXTL program system.[10]

Final atomic coordinates,[†] including those of the hydrogen atoms, and thermal parameters have been deposited with the Editors as supplementay data.[‡]

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REFERENCES

[1] H. M. Colquhoun, G. Jones, J. M. Maud, J. F. Stoddart and D. J. Williams, *J. Chem. Soc. Dalton Trans.* 63 (1984).

[2] B. L. Allwood, H. Shahriari-Zavareh, J. F. Stoddart and D. J. Williams, *J. Chem. Soc. Chem. Commun.* 1461 (1984).

[3] D. R. Alston, A. M. Z. Slawin, J. F. Stoddart and D. J. Williams, *Angew. Chem. Int. Ed. Engl.* **23**, 821 (1984).

[4] N. Ando, S. Ohi, Y. Yamamoto, J. Oda and Y. Inouye, *Bull. Inst. Chem. Res., Kyoto Univ.* **58**, 293 (1980).

[5] H. M. Colquhoun, D. F. Lewis, J. F. Stoddart and D. J. Williams, *J. Chem. Soc. Dalton Trans.* 607 (1983).

[6] D. J. Cram and K. N. Trueblood, *Top. Curr. Chem.* **98**, 43 (1981).

[7] K. Kobiro, Y. Tanaka, K. Okubo, Y. Hiramatsu, K. Kakiuchi, Y. Tobe and Y. Odaira, *Chem. Lett.* 1507 (1983); K. Kobiro, K. Kakiuchi, Y. Tobe and Y. Odaira, *Chem. Lett.* 487 (1984).

[8] B. L. Allwood, S. F. Fuller, P. C. K. Y. Ning, A. M. Z. Slawin,

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[*] Calculated from observed data.

[†] The atomic coordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full citation for this communication.

[‡] Supplementary data and structural factors are available. See Notice to Authors, *Tetrahedron* **40** (2), ii (1984).

J. F. Stoddart and D. J. Williams, *J. Chem. Soc. Chem. Commun.* 1356 (1984).

[9] H. Shahriari-Zavareh, J. F. Stoddart, M. K. Williams, B. L. Allwood and D. J. Williams, *J. Incl. Phenom.* submitted.

[10] G. M. Sheldrick, SHELXTL, *An Integrated System for Solving, Refining, and Displaying Crystal Structures from Diffraction Data*, University of Göttingen, Federal Republic of Germany (1978). Revised version (1983).