



Proton-induced supramolecular dimerization of aminomethylbenzo-15-crown-5 accompanied by a covalent dimerization of cyanoborohydride anion

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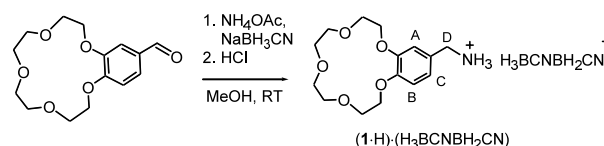
Abstract—Reductive amination of 4'-formyl[benzo-15-crown-5] with sodium cyanoborohydride in the $\text{NH}_4\text{Ac}/\text{MeOH}$ medium followed by acid addition and extraction with CHCl_3 unexpectedly lead to the isolation of the salt $(\text{B15C5-CH}_2\text{-NH}_3)^+ \cdot (\text{H}_3\text{BCNBH}_2\text{CN})^-$ with an unusual dicyanodiborohydride anion. The self-complementary 4'-ammoniomethyl[benzo-15-crown-5] cation was found to exist as a supramolecular dimer in the solid state, acetonitrile solution, and gas phase as revealed by X-ray crystallography, NMR and mass spectrometry, respectively. © 2003 Elsevier Science Ltd. All rights reserved.

Self-complementary monofunctionalized crown-ethers have proved to be useful building blocks for supramolecular architecture.^{1–5} Stoddart and co-workers successfully explored systems based on protonated secondary ammonium or 4,4'-dipyridinium functionalities threaded through large (≥ 24 -membered) crown ethers.^{2–4} Very recently, we⁵ and others⁶ reported crystalline dimers obtained from simple self-complementary aminomethylcrown ethers (benzo-18-crown-6 and crown-5, respectively). The 'non-threaded' dimer based on a well-known host–guest motif, namely benzo-18-crown-6 and R-NH_3^+ , appeared to be more stable in acetonitrile solution than more complicated interlocked systems.⁵ We now set out to explore dimerization of another simple functionalized crown ether, aminomethyl[benzo-15-crown-5]. Stability constants for the host–guest complexes of RNH_3^+ with 15C5 or B15C5 are usually ca. one magnitude smaller than those with 18C6 or B18C6.^{7,8} We report that despite this decreased stability, B15C5- RNH_3^+ motif supports self-complementary dimers in the solution, gas phase, and in the solid state. The new self-complementary dimer, $(\text{B15C5CH}_2\text{NH}_3^+)_2$, was crystallographically characterized in the form of its salt with a unique $[\text{H}_3\text{BCNBH}_2\text{CN}]^-$ counterion.

Free amine 4'-aminomethyl[benzo-15-crown-5]^{9a} (**1**) was prepared earlier⁸ from 4'-formyl-B15C5^{9b} in a five-step

synthesis with the total yield of 11.1%.^{9c} We were looking for more efficient and straightforward preparation of the target amine, as well as for crystallization of its protonated form. Synthesis of **1** via reductive amination of formyl[benzo-15-crown-5] was reported without characterization, yield or experimental details.¹⁰ In our hands, the reductive amination of 4'-formyl[benzo-15-crown-5] with sodium cyanoborohydride in a $\text{NH}_4\text{OAc}/\text{MeOH}$ medium¹¹ followed by an addition of acid and extraction with CHCl_3 unexpectedly lead to the isolation of dicyanodiborohydride salt of 4'-ammoniomethyl[benzo-15-crown-5], $[(1\cdot\text{H})]^+ \cdot [\text{H}_3\text{BCNBH}_2\text{CN}]^-$, in 14.4% yield (Scheme 1).¹² While the yield of the target product was somewhat disappointing, its crystalline nature allowed for X-ray structural analysis that revealed important insights in two areas: (1) the geometry of $(1\cdot\text{H})^+$; (2) the structure of a very unusual anion that is formed in the traditional acidic workup after reductive amination with cyanoborohydride.

The single crystal X-ray diffraction study of $[(1\cdot\text{H})] \cdot [\text{H}_3\text{BCNBH}_2\text{CN}]$ revealed the formation of a centrosymmetric (C_i) head-to-tail dimeric cation $(1\cdot\text{H})_2^{2+}$ (Fig. 1(a, c)).¹³



Scheme 1.

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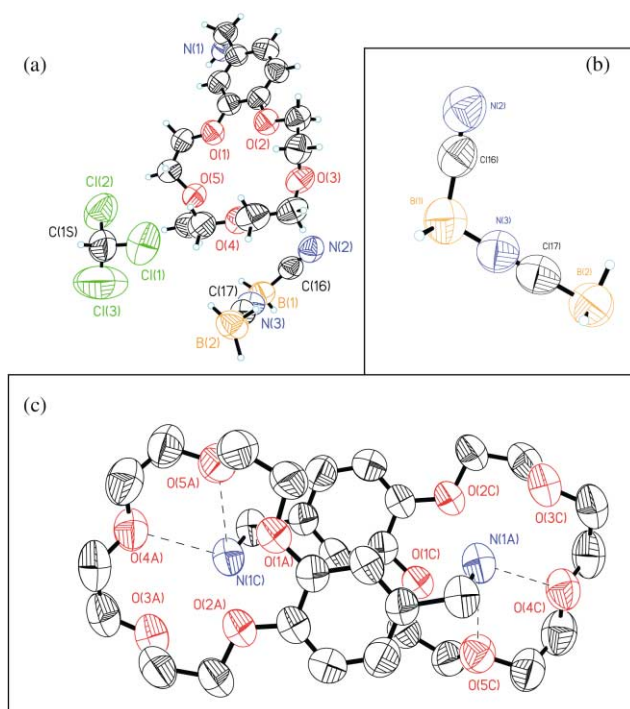


Figure 1. Crystal structure of (a) $(1\cdot H)\cdot(H_3BCNBH_2CN)\cdot CHCl_3$; (b) $[H_3BCNBH_2CN]$: B(2)–C(17) 1.559, C(17)–N(3) 1.158, B(1)–C(16) 1.586, C(16)–N(2) 1.111 Å; N(3)–C(17)–B(2) 178.9, C(17)–N(3)–B(1) 178.9, N(3)–B(1)–C(16) 109.8°; (c) $[(1\cdot H)_2]^{2+}$: N(1A)–O(1C) 3.046, N(1A)–O(2C) 3.144, N(1A)–O(3C) 3.074, N(1A)–O(4C) 2.864, N(1A)–O(5C) 2.887 Å.

The ammonium group of each dimer's component is coordinated by the oxygens of the complementary B15C5 residue. The $N^+\cdots O$ bond lengths range from 2.864 [O4] to 3.144 [O2] with an average $N^+\cdots O$ separation of 3.00 Å. The shortest $N^+\cdots O$ contacts (2.864 Å [O4] and 2.887 Å [O5]) involve the crown oxygen atoms participating in a single hydrogen bond each. The less basic aryl ether oxygens O1, O2 together with O3 exhibited longer $N^+\cdots O$ distances (3.046, 3.144 and 3.074 Å, correspondingly) indicative of a trifurcated hydrogen bond. The oxygen atoms in the macrocyclic ring are approximately coplanar, with the mean deviation from the O_5 plane of 0.198 Å (maximum deviations are for O4, O3, and O5: –0.15, +0.248, and 0.247 Å, respectively). The N atom of the ammonium group is displaced by 1.889 Å from the mean plane of the five macrocyclic oxygen atoms. This distance is among the shortest ammonium–crown ether separations reported in the literature for the RNH_3^+ –15C5 ring systems, which usually are in the range of 1.82–2.34 Å.^{14–20} Such a short distance might be explained by the ‘chelate effect’ of two simultaneous crown–ammonim interactions.

Interestingly, the effect of π – π stacking between the aromatic rings of benzo-15-crown-5 derivative $(1\cdot H)^+$ ₂ appears to be minimal compared to a pronounced effect in an analogous dimer based on B18C6– NH_3^+ recognition motif.⁵ The interplanar separation of two

parallel benzene rings (3.68 Å) is larger than that for a compound containing benzo-18-crown-6 (3.40 Å). Also, the two rings are shifted with respect to each other, resulting in a significantly larger centroid–centroid separation (4.53 Å) compared to 3.87 Å for the B18C6 dimeric analog.⁵ Metric parameters of a recently characterized $(15C5-CH_2NH_3)_2^{2+}$ dimer⁶ are very similar to those reported here for $(1\cdot H)_2^{2+}$. Since the former compound does not have aromatic rings, the geometry of both dimers is defined primarily by the RNH_3^+ –15C5 interactions rather than by additional π – π stacking. In both structurally characterized self-complementary dimers based on 15C5– RNH_3^+ recognition site, each ammonium group is coordinated by one crown ether ring.⁶ Consequently, the ‘chelate effect’ in the dimerization successfully competes with a well-known preference of B15C5 to form sandwich 2:1 complexes with ammonium cations.^{14–20}

The association process of the self-complementary molecule was also studied in solution. The 1H NMR (300 MHz) spectrum of the solution of $[(1\cdot H)\cdot(H_3BCNBH_2CN)]$ (10^{-3} M) in DMSO- d_6 showed relatively sharp signals with chemical shifts typical for monomeric $(1\cdot H)^+$ (Fig. 2(a)). Apparently, such polar solvent as DMSO prevent the self-aggregation of $(1\cdot H)^+$. In contrast, the 1H NMR spectrum in less polar CD_3CN showed sharply resolved upfield shifted aromatic signals, which can be attributed to an association process. The most pronounced upfield shift was observed for the *meta*-coupled doublet ($J=1.9$ Hz) of the aromatic proton A, 6.6 ppm compared to 7.1 ppm in DMSO solution (Fig. 2(e)). The position of doublet A might be affected by the ‘ring current effect’ which occurs in the cyclic head-to-tail dimer (Fig. 1(c)), wherein proton A is situated within a shielding zone.²¹

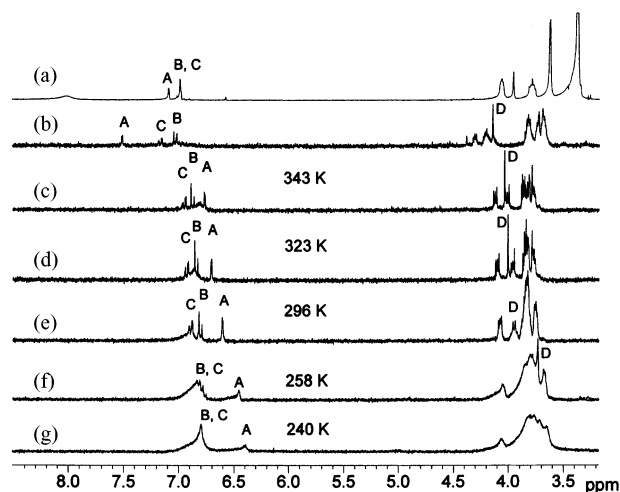


Figure 2. 1H NMR spectra of $(1\cdot H)(H_3BCNBH_2CN)$: (a) 10^{-2} M solution in DMSO- d_6 at 296 K; (b) 10^{-3} M solution in acetonitrile- d_3 with excess KI added at 296 K; (c)–(g) 10^{-3} M solution in acetonitrile- d_3 at different temperatures. Signals are labeled according to Scheme 1.

The temperature-dependent ^1H NMR spectra of the acetonitrile solution of $[(1\cdot\text{H})]\cdot[\text{H}_3\text{BCNBH}_2\text{CN}]$ (Fig. 2(c–g)) indicate that the yield of the dimer increases with decreasing temperature as expected for an association process. The *meta*-coupled proton A and benzylic protons are the most sensitive toward dimerization and showed pronounced upfield shifts ($\Delta\delta=0.38$ and 0.32 ppm, respectively) from 343 to 240 K. It was shown for other self-complementary crown-ethers that they can form three cyclic stereoisomeric dimers.⁴ ‘Threaded’ dimers and the ‘non-threaded’ dimer of $\text{B18C6-CH}_2\text{NH}_3^+$ showed slow exchange between the supramolecular stereoisomers in solution on the NMR time scale.^{4,5} In the case of $(1\cdot\text{H})_2^{2+}$ here, decreasing the temperature caused broadening of the signals, but no separation of the signals of different species occurred even at 240 K indicating a fast exchange between the stereoisomers of $(1\cdot\text{H})_2^{2+}$ and a monomer $(1\cdot\text{H})^+$.

Increasing the temperature to 343 K caused a downfield shift of proton signals, especially A. However, even at 343 K, the positions of the signals are still upfield shifted (6.78, 6.85, 6.92 ppm for A, B and C, respectively) compared to the spectrum of monomeric $(1\cdot\text{H})^+$ in DMSO at rt (Fig. 2(a)), where no association occurs. This indicates, that even at 343 K the dimerization is substantial in acetonitrile.

The dimer can be completely destroyed by the addition of KI to the acetonitrile solution (Fig. 2(b)). Judging from the position of the signals of the aromatic protons (similar to the monomer in DMSO- d_6), no interaction between catechol rings of the two B15C5 residues occurs in the K^+ complex of **1**.

Mass spectroscopy confirmed the existence of dimers (rather than higher oligomers) in the gas phase. Electrospray mass spectra taken in positive mode revealed three intense signals at 595 (70%), 376 (30%) and 281 (100%) corresponding to $[(1)(1\cdot\text{H})]^+$, $[(1\cdot\text{H})\cdot\text{BH}_2(\text{CN})\text{--}\text{BH}_2(\text{CN})]^+$ and $[1\text{--}\text{NH}_3]^+$, respectively. No higher order oligomers were found in negative mode spectra: 833 $[(1)_2\{\text{BH}_2(\text{CN})\text{BH}_2(\text{CN})\}]^-$ (100%) and 456 $[1\cdot\{\text{BH}_2(\text{CN})\text{BH}_2(\text{CN})\}_2]^-$ (70%).

The single crystal X-ray study of $[(1\cdot\text{H})]\cdot[\text{H}_3\text{BCN--BH}_2\text{CN}]$ revealed the formation of an unusual $[\text{H}_3\text{BCNBH}_2\text{CN}]^-$ anion (Fig. 1(c)). This anion was synthesized earlier, but was not characterized structurally.^{22–25} Our crystallographic data confirmed the connectivity of the dicyanodiborohydride anion previously ascribed by other means. We found that two fragments of the anion, $\text{H}_3\text{B}(2)\text{--C}(17)\text{--N}(3)$ and $\text{H}_2\text{B}(1)\text{--C}(16)\text{--N}(2)$, are practically linear (179 and 178°, correspondingly) with a tetrahedral angle (109°) between them (Fig. 1(b)). The C–N distance in a bridging nitrile group (1.158 Å) is slightly longer than that in the terminal one (1.111 Å). Bond lengths in the dimerized anion are similar to those in the parent $[\text{H}_3\text{BCN}]^-$ anion being in the range of 1.56–1.58 Å for the B–C distance and 1.11–1.15 Å for the C≡N bond.^{26–28} Some elongation of the bridging C–N bond is in good agreement with the parameters of a related molecule

$[\text{Pt}(\text{dppm})(\text{CNBH}_2\text{CN})_2]$,²⁹ wherein the average bridging C≡N bond length is 1.17 Å. The closest related structurally characterized compound containing the $\text{BH}_2\text{CNBH}_2\text{CN}$ fragment is cyclohexa(cyanoborane), $(\text{BH}_2\text{CN})_6$, which has bond lengths of 1.56 Å for B–C, 1.56 and 1.14 Å for B–N, and a C–B–N angle of 107.0°.³⁰

The dicyanodiborohydride anion is known to form upon the reaction of H_3BCN^- and acid:²³



It is reasonable to assume that this reaction is responsible for the formation of dicyanodiborohydride from unconsumed NaBH_3CN during the acidic workup of the reaction mixture obtained after reductive amination, when an excess of NaBH_3CN was used. This large anion was co-extracted into organic phase as an ion pair with a bulky cation of the dimeric amino-crown.

In addition to crystallographic characterization, the dicyanodiborohydride anion was clearly identified in the bulk material isolated from the reductive amination of formyl-B15C5.¹² The ^{11}B NMR (CD_3CN , 96.259 MHz) spectrum of $[(1\cdot\text{H})]\cdot[\text{H}_3\text{BCNBH}_2\text{CN}]$ consists of two multiplets: a triplet at -28.2 ppm ($J_{\text{B--H}}=103$ Hz) and quartet at -43.5 ppm ($J_{\text{B--H}}=92$ Hz) (Fig. 3), which are in agreement with the literature.²² The ^1H NMR (CD_3CN , 300 MHz) spectrum of the compound showed two signals belonging to the BH_3 and BH_2 groups which appear as two quartets with very large coupling constants. The quartet at ~ 0.5 ppm ($J_{\text{H--B}}=92$ Hz) can be assigned to the terminal BH_3 group. A more broad resonance of the bridging BH_2 group (δ : ~ 2.1 ppm, $J_{\text{H--B}}=103$ Hz) partially overlapped with the signal of acetonitrile. The anion has two characteristic bands in the IR spectrum corresponding to the different types of the CN groups.^{22,23} The medium intensity band at 2208 cm^{-1} belongs to the terminal CN, and the strong band at 2256 cm^{-1} corresponds to the bridging cyanide. Two strong bands at 2409 and 2366 cm^{-1} are assigned to B–H stretching vibrations²² (Fig. 4).

Sodium cyanoborohydride is a well-known mild and selective reducing agent for a variety of organic transformations, including reductive amination of aldehydes and ketones. It is considered to be acid-stable under conditions of Borch reduction and subsequent work up.^{11,31,32} Our results show that under usual con-

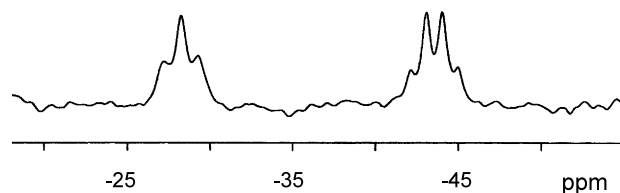


Figure 3. ^{11}B NMR spectrum (96.259 MHz) of $(1\cdot\text{H})(\text{H}_3\text{BCNBH}_2\text{CN})$ (with $\text{BF}_3\cdot\text{Et}_2\text{O}$ as an external reference standard).

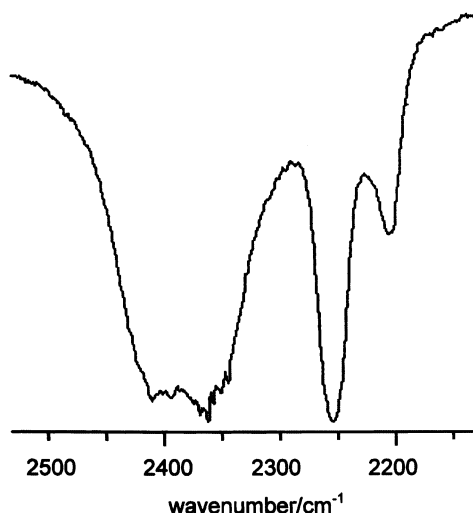


Figure 4. Partial IR spectrum of (1·H)(H₃BCNBH₂CN) in a KBr pellet.

ditions with a large (usually 10–20-fold) excess of NaBH₃CN^{11,33,34} and acidic work-up an unusual anion, [H₃BCNBH₂CN][−], may be formed, and co-extracted into the non-polar organic phase with a bulky cation (in our case, a supramolecular dimer of (1·H)⁺). The formation of such an anion might affect the yield of the target amines and should be considered when developing protocols for the isolation of amines after reductive amination with sodium cyanoborohydride.

Acknowledgements

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- (a) 1(1,2)-(4'-Aminomethylbenzena)-2,5,11,14-pentaoxacyclotetradecaphane; (b) 1(1,2)-(4'-formylbenzena)-2,5,11,14-pentaoxacyclotetradecaphane; (c) benzo-[15-crown-5] was formylated with POCl₃ and *N*-methylformanilide with work up previously used for B18C6 analog,⁸ that allowed to improve the yield of the target from 26 to 40%.
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- (a) 1(1,2)-(4'-Ammoniomethylbenzena)-2,5,11,14-pentaoxacyclotetradecaphane; (b) 4'-formyl[benzo-15-crown-5] (30 mg, 0.10 mmol) was dissolved in dry MeOH (7 ml) and NH₄OAc (2.34 g, 35 mmol) was added. The mixture was stirred for 30 min at rt and NaBH₃CN (130 mg, 2 mmol) was added portionwise during 1 h. After stirring for 30 h, additional amount of NaBH₃CN was added (0.05 g, 0.8 mmol) and the mixture was stirred for additional 1 h. The solution was made acidic by the addition of aqueous HCl (reaction of universal paper pH<2), stirred for 20 min and then the solvent was removed under vacuum. The residue was redissolved in 4 ml of H₂O and extracted with CHCl₃ (4 ml×4). The volume of the combined chloroform extracts was reduced to 2 ml. Precipitation occurred after 2 days, giving 5.5 mg (14.4%) of crystals suitable for X-ray crystallography. Subsequent chloroform extraction from basic aqua solution gave the mixture of monoalkylated and dialkylated amines.
- Crystal data*: C₁₈H₃₀B₂Cl₃N₃O₅, *M*=496.42, triclinic, space group *P* $\bar{1}$, *a*=10.0597(11), *b*=11.7649(14), *c*=12.5398(15) Å, α =98.497(2), β =106.385(3), γ =109.668(3)°, *V*=1291.5(3) Å³, *Z*=2, *T*=293(2) K, 8296 reflections collected, 5438 independent (*R*(int)=0.0277), 301 parameters, final *R* indices [*I*>2σ(*I*)] *R*₁ and *wR*₂ are 0.1152 and 0.3251, respectively. Hydrogen atoms (except for those bonded to boron atoms) were calculated by geometrical methods and refined as a riding model. Hydrogen atoms of the BH₃(CN)BH₂CN anion were refined independently.
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