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## Unusual complexes of trapped methanol with azacryptandst

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### Abstract

Structural analysis of sulfate complexes of two different azacryptands crystallized under identical conditions in the presence of methanol and water reveals that one methanol is selectively trapped in each cavity, assisted by the specific arrangements of three external sulfates close to one tren unit.

Methanol is ubiquitous in nature and is known to bind to an active site of corrinoid protein through the interaction between methanolic hydroxyl group and zinc ion.<sup>1</sup> It is extensively used as a solvent in laboratory and industry and also as a supplement to gasoline.<sup>2</sup> Due to its poor ability to interact with a synthetic receptor, very little is known about methanol binding.<sup>3</sup>



Although azacryptands have been shown to coordinate with cations and anions,<sup>4</sup> their binding to neutral species remains relatively unexplored. Protonated azacryptands have the potential to coordinate with H-bond acceptor atoms in neutral molecules. However, such complexation can be hampered due to the presence of counter anions that preferentially bind to the host macrocycles.<sup>5</sup> If a counterion is chosen that shows only weak interaction with the macrocycle, then such a cryptand can also act as a host to a neutral molecule. This approach has been applied successfully to bind water in a *p*-xylyl-based cryptand using iodide,<sup>6</sup> perchlorate,<sup>7</sup> picrate,<sup>8</sup> or phosphate<sup>10</sup> as a counter anion. In this communication, we report two novel and remarkable crystal structures of trapped methanol within bicyclic cryptands **L1** and **L2**, each grown from its sulfate salt in water–methanol mixtures under similar conditions. The specific H-bonding interactions of one tren unit with three sulfates located at the outside lead to the complete inclusion of one methanol molecule in the cavity.

The ligands **L1** and **L2** were synthesized following the literature procedure.<sup>10</sup> The sulfate complexes were obtained by titrating the ligands with sulfuric acid in water. Crystals suitable for X-ray analysis were grown by vapor diffusion of methanol to the salts dissolved

†Electronic supplementary information (ESI) available: Two crystallographic data in CIF format, and the synthetic procedure, crystallographic details and Cartesian coordinates of DFT calculations in pdf format. CCDC reference numbers 755129 and 755130. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c0ce00162g

in a mixture of water and methanol. Although the ligands consist of two different linking spacers, both of them were found to be hexaprotonated, each with several water molecules and one methanol. However, the methanol is trapped within the bicyclic cavity in both the cryptands (Fig. 1). ‡

The ligand **L1** containing three thiophene spacers crystallizes with sulfate anions in the triclinic space group  $P\bar{1}$ . The general shape of this complex is more elongated than similar complexes with different counterions as shown by the distances between the bridgehead nitrogens (9.457 Å this study, 6.096 Å for the chloride complex 10b and 5.528 Å for the nitrate 11 complex). Despite the presence of several H-bond donors, the cavity does not contain any sulfate or water. However, the single methanol present in the complex is coordinated inside the macrocyclic cavity by two strong hydrogen bonds ( $N17\cdots O1S = 2.947(5)$  and  $N36\cdots O1S = 2.832(5)$  Å) with secondary amines of the right side tren unit as shown in Fig. 1A. The other tren unit is involved in coordinating three external sulfate groups (one  $HSO_4^-$  and two  $SO_4^{2-}$ ), each being cleft between the arms through two  $NH\cdots O$  bonds with protonated secondary amines (Fig. 2A). Thus all six protons on the secondary nitrogens of one tren unit are involved in hydrogen bonding with three external anions.

The ligand **L2** with *p-xylyl* spacers is slightly larger than **L1** and its sulfate salt crystallizes in the monoclinic space group  $P2_1/c$ , with six protonated amines. The complex contains one crystalline methanol which is again trapped in the void of the ellipsoid cavity, with one strong  $N\cdots O$  bond ( $N13\cdots O1S = 2.884(18)$  Å) *via* the methanolic oxygen with a protonated amine of one tren unit (Fig. 1B). The trapped molecule lies almost linearly along the pseudo-threefold axis passing through the apical nitrogen atoms, N1 and N16. The distance between the apical atoms is 9.786 Å. The other tren is coordinated to three sulfates in a manner similar to that observed in the structure of the **L1** complex as shown in Fig. 2B.

In order to determine the binding energies and stability of **L1** and **L2** complexes with methanol, we have performed quantum-chemical investigation with the Gaussian 03 program package<sup>12</sup> using density functional theory at the M052x/6-31+G(d) level of theory.<sup>13</sup> Geometries of water and methanol molecules were fully optimized. Initial geometries of ligands **L1** and **L2** and their complexes with methanol were derived from the crystallographic coordinates with corrected lengths of bonds that involve hydrogen atoms. Single-point energies were calculated for those structures. The binding energy was computed as  $\Delta E = E(\text{cryptand-methanol}) - E(\text{cryptand}) - E(\text{methanol})$ . The basis set superposition error was corrected through counterpoise approach.<sup>14</sup> The results are  $-0.59$  kcal mol<sup>-1</sup> for **L1**-methanol complex and  $-5.90$  kcal mol<sup>-1</sup> for **L2**-methanol complex. Therefore in both cases formation of the complex is accompanied by release of the energy and stabilization of the system. Stability of the methanol complexes with the cryptands was further compared to the stability of their water complexes. This was done by optimizing the position of the encapsulated small molecule inside the cryptand, whose geometry was frozen. The binding energies for all four complexes are shown in Table 1.

The results clearly show that the formation of methanol complex is more favorable than that of water complex with ligand **L1**, supporting the trapping of methanol in the presence of water as observed in the crystallographic structure. The bond distances,  $N36\cdots O1S$  (2.832(5) Å) in **L1** and  $N13\cdots O1S$  (2.884(18) Å) in **L2** are very close to the corresponding calculated values, 2.885 and 3.134 Å, respectively, which are also in agreement with the reported values (3.056(6) and 3.099(6) Å) observed in the azametallacrown encapsulating two methanol molecule.<sup>3d</sup> The difference in binding energies of **L2** complexes is insignificantly small, therefore in this case we assume that preferable encapsulation of methanol is due to steric and electronic factors.

In conclusion, we have structurally characterized two azacryptands that are capable of binding a single methanol selectively from sulfate and water species. There are striking similarities between the two complexes with respect to the encapsulated methanol and three cleft-bound sulfate groups. Jiang and coworkers characterized a sulfate complex of **L2** grown in an aqueous solution that contained several water molecules in the cavity.<sup>9</sup> Bowman-James and coworkers isolated crystals of a sulfate complex with a *m*-xylyl analogue in which the cavity contained a sulfate group.<sup>15</sup> The arrangement of three external sulfates coordinating to one tren unit appears to open the other tren unit making it capable of receiving polar neutral species from the solution. This study outlines a simple strategy for binding neutral molecules that can be extended to other systems.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

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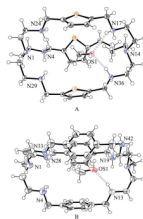
## Notes and references

‡ Crystal data:  $2[\text{H}_6\text{L1}(\text{CH}_3\text{OH})]\cdot 3\text{SO}_4\cdot 6\text{HSO}_4\cdot 11\text{H}_2\text{O}$ ,  $M = 2378.83$ , triclinic,  $a = 11.8698(14)$  Å,  $b = 14.1475(18)$  Å,  $c = 16.133(2)$  Å,  $\alpha = 97.812(7)^\circ$ ,  $\beta = 96.193(7)^\circ$ ,  $\gamma = 101.013(8)^\circ$ ,  $V = 2609.5(6)$  Å<sup>3</sup>,  $T = 100(2)$  K, space group  $P-1$ ,  $Z = 1$ ,  $\mu(\text{CuK}\alpha) = 3.751$  mm<sup>-1</sup>, 35 685 reflections measured, 9417 independent reflections ( $R_{\text{int}} = 0.0794$ ). The final  $R_1$  value was 0.0573 ( $I > 2\sigma(I)$ ).

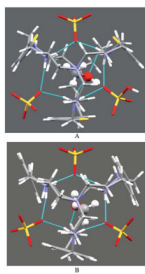
For  $\text{H}_6\text{L2}(\text{CH}_3\text{OH})\cdot 3\text{SO}_4\cdot 12\text{H}_2\text{O}$ ,  $M = 1141.33$ , monoclinic,  $a = 15.303(2)$  Å,  $b = 16.583(2)$  Å,  $c = 23.124(3)$  Å,  $\alpha = 90.00^\circ$ ,  $\beta = 104.234(8)^\circ$ ,  $\gamma = 90.00^\circ$ ,  $V = 5688.0(13)$  Å<sup>3</sup>,  $T = 100(2)$  K, space group  $P2_1/c$ ,  $Z = 4$ ,  $\mu(\text{CuK}\alpha) = 1.918$  mm<sup>-1</sup>, 11 543 reflections measured, 1749 independent reflections ( $R_{\text{int}} = 0.0719$ ). The final  $R_1$  value was 0.0777 ( $I > 2\sigma(I)$ ).

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**Fig. 1.** ORTEP views of [H<sub>6</sub>L1(CH<sub>3</sub>OH)]<sup>6+</sup> (A) and [H<sub>6</sub>L2(CH<sub>3</sub>OH)]<sup>6+</sup> (B) motifs showing encapsulated methanol inside the cavity. Thermal ellipsoids are drawn at the 40% probability level.



**Fig. 2.** Crystal views of  $[\text{H}_6\text{L1}(\text{CH}_3\text{OH})(2\text{SO}_4)(\text{HSO}_4)]^+$  (A) and  $[\text{H}_6\text{L2}(\text{CH}_3\text{OH})(3\text{SO}_4)]$  (B) motifs showing encapsulated methanol (ball and stick) and three cleft bound sulfates.

**Table 1**Binding energies ( $\text{kcal mol}^{-1}$ ) of the optimized complexes

L1		L2	
H <sub>2</sub> O	CH <sub>3</sub> OH	H <sub>2</sub> O	CH <sub>3</sub> OH
-0.61	-9.94	-13.24	-12.78