

Encapsulated sulfates: insight to binding propensities†

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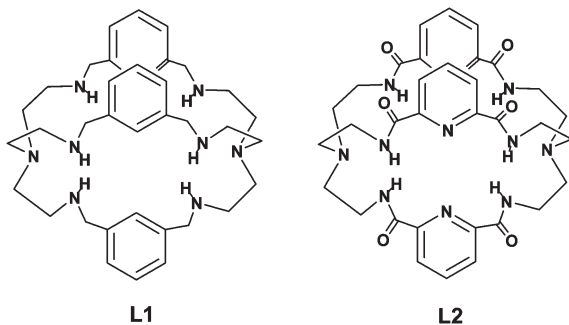
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Two crystal structures of sulfate inclusion complexes in an aza- and amido-cryptand represent the first examples of encapsulated sulfate in synthetic cryptand receptors and indicate penta- and octa-coordination, respectively.

Selective recognition of sulfate is readily accomplished in biology by a sulfate binding protein.¹ This highly selective receptor encapsulates the tetrahedral dianion in a net of seven hydrogen bonds. Sulfate is also a prevalent anion in the environment, and much recent attention has focused on its role as a contaminant in nuclear waste. In this regard, the deleterious effect of sulfate has been recognized as a major impediment to clean-up efforts, a result of its sparing solubility in the borosilicate glass used for vitrification.² While it would be highly cost-effective to remove sulfate prior to vitrification, reports of 'synthetic' receptors with high affinity and selectivity are relatively scarce,^{3–7} and only limited crystallographic^{4,6,7} and modeling data⁸ exist. In fact, in a class of ligands that figures prominently in the field of anion coordination, bicyclic cryptands, there have been no crystallographic reports of encapsulated sulfate, and only a few examples of other tetrahedral anions.⁹ Herein we report two crystal structures of encapsulated sulfate, one in the non-preorganized polyammonium cryptand **L1**, and the other in the preorganized amide-based cryptand, **L2**. The two structures provide a significant insight into the influence of host preorganization and topological complementarity in design strategies. An increased understanding of the binding propensities of sulfate based on structural data can ultimately aid in addressing the problem of sulfate in the environment.



L1¹⁰ and **L2**¹¹ were prepared as previously reported. The sulfate salt of **L1** precipitated after adding H₂SO₄ to **L1** in CH₃OH. Crystals suitable for X-ray analysis were grown from a CH₃OH–H₂O mixture.‡ Crystals of the sulfate complex of **L2** were grown

by slow evaporation of an CH₃CN solution of **L2** in the presence of excess [(*n*-Bu)₄N][HSO₄].‡

Although both **L1** and **L2** crystallize with one encapsulated SO₄^{2–}, the observed coordination numbers and geometries are different. **L1** crystallized as the octaprotonated aza-cryptand with one SO₄^{2–} inside the cavity (Fig. 1). Two additional SO₄^{2–} and two HSO₄[–] ions lie outside the cavity in addition to several H₂O and CH₃OH molecules of crystallization. Despite the high degree of hydrogen bond availability on **L1**, the internally held SO₄^{2–} is bound to only five ammonium hydrogens (Fig. 1A), which includes only the two bridgehead amines and the secondary ammonium hydrogens on the 'east' side of the cryptand. The secondary ammonium hydrogens on the 'west' side of **L1** are pointed outward, with hydrogen bond interactions with the external sulfates and solvent molecules. On the other hand, H₂L2(SO₄) is neutral, with the complementary dipositive charge being provided by the protonated bridgehead amines (Fig. 2). In contrast to **L1**, **L2** efficiently utilizes all eight available hydrogens to 'coordinate' to the SO₄^{2–} (Fig. 2A), with

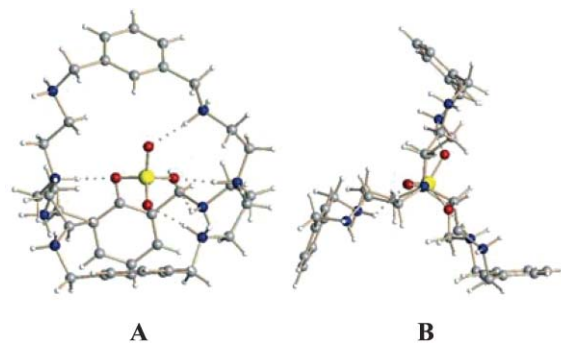


Fig. 1 Perspective views of [H₈L1(SO₄)]⁶⁺: (A) side view, (B) end-on view. Only the receptor and internal sulfate are shown for clarity.

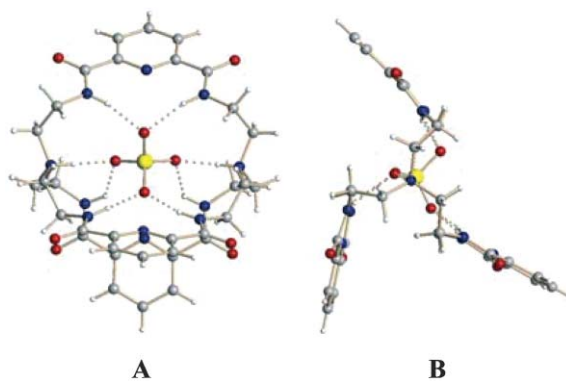


Fig. 2 Perspective views of H₂L2(SO₄): (A) side view, (B) end-on view.

† Electronic supplementary information (ESI) available: ¹H NMR information, titration spectra of **L2**, and additional ORTEP drawings and hydrogen bond data for **L1** and **L2**. See <http://www.rsc.org/suppdata/cc/b4/b411904e/>

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each SO_4^{2-} oxygen held by two relatively strong ($<3 \text{ \AA}$) hydrogen bonds. As can be seen from the end-on views, both sulfates are approximately centered along the bridgehead axis (Figs. 1B and 2B).

Comparison of the structural differences between the two cryptands provides information on the binding propensities of tetrahedral ions. In **L1** the five-coordinate geometry reflects inefficient usage of the total hydrogen bonding capacity for the internal sulfate. The scattered orientation of the three NH_2^+ groups on the 'western' side of the receptor might in part be mandated by the presence of the external sulfates and solvent molecules vying for hydrogen bonds. Considering the location of the five amines hydrogen bonded with the encapsulated SO_4^{2-} , the resulting five-coordinate geometry is somewhat like a distorted trigonal bipyramid (Fig. 3A).

In **L2**, sulfate binding is maximized by the utilization of all eight NHs. The inward orientation of the amide hydrogens is undoubtedly aided by the preorganizing influence of the pyridine spacer, *i.e.*, the hydrogen attracting ability of the pyridine nitrogen lone pairs. We have consistently noted increased anion affinities with receptors containing pyridine as opposed to *m*-xylyl spacers, that could be related to this preorganization effect.¹² The geometry of the $\text{H}_2\text{L2}(\text{SO}_4)$ complex, again based on the NH positions, resembles a bicapped trigonal prism (Fig. 3B). **L2** represents the second eight-coordinate structure that we have obtained for SO_4^{2-} , the first being a sandwich complex of SO_4^{2-} between two tetraamide macrocycles.⁶ Hay and coworkers have reported that even higher coordination numbers should be attainable for sulfate, based on modeling studies.⁸

A direct comparison of the affinities of **L1** and **L2** for sulfate considering solely hydrogen bonding contributions is not straightforward, since in both cases electrostatic and solvent influences will also affect binding. Affinities for **L1** determined by potentiometric methods in water vary with pH, and high binding was observed for both $\text{H}_6\text{L1}^{6+}$ and $\text{H}_7\text{L1}^{7+}$ ($\log K = 4.43(1)$ and $4.97(5)$, respectively).¹³ Clearly the binding of **L1** with sulfate is significantly enhanced by electrostatic interactions with the multiply-charged host. Because of sparing water solubility, the affinity of **L2** for sulfate was determined using NMR techniques in CDCl_3 , CD_3CN and $\text{DMSO-}d_6$ ¹¹ (Fig. 4). Results indicated strong binding in the former two solvents, $\log K = 4.96(5)$ and $4.74(3)$, respectively. Weaker binding was observed in DMSO ($\log K = 1.83(3)$), a reflection of the strong solvating tendencies associated with this polar solvent.

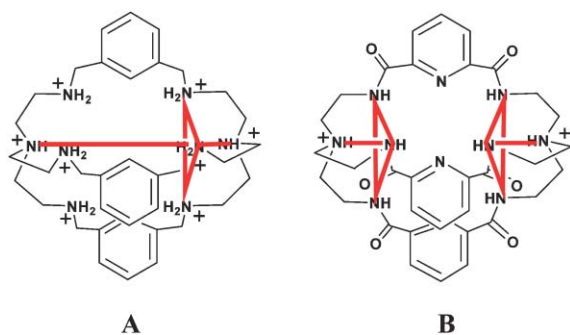


Fig. 3 Coordination geometries for (A) $[\text{H}_8\text{L1}(\text{SO}_4)]^{6+}$ and (B) $\text{H}_2\text{L2}(\text{SO}_4)$.

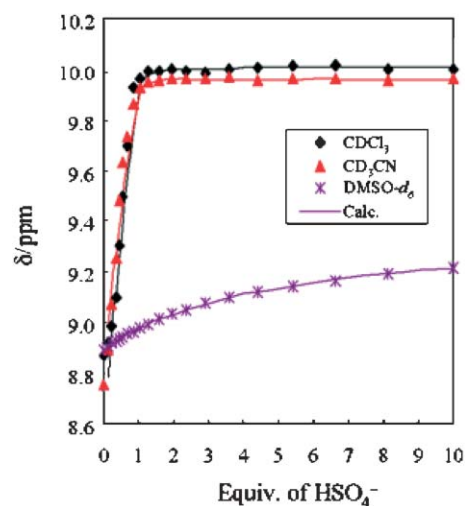


Fig. 4 Chemical shift of the amide protons of **L2** (2 mM) with increasing $[\text{HSO}_4^-]$ in CDCl_3 , CD_3CN and $\text{DMSO-}d_6$.

In summary, in nature high affinity and selectivity for sulfate are achieved by the strategic placement of hydrogen bonds to interact with the anionic substrate, but in the world of synthetic receptors, structural data is especially limited for the environmentally important sulfate anion. The two sulfate complexes reported herein represent the first structural examples of encapsulated sulfate in synthetic cryptand receptors. Penta- and octa-coordination are observed for **L1** and **L2** *via* NH hydrogen bonds from the ligand to SO_4^{2-} oxygen atoms, giving rise to pseudo-trigonal bipyramidal and bicapped trigonal prismatic geometries, respectively. The more efficient use of coordination sites in **L2** may be facilitated by a preorganization effect involving the lone electron pairs on the pyridine nitrogens. As a result of protonation of its bridgehead amines, $\text{H}_2\text{L2}^{2+}$ also possesses a dipositive charge to complement the dinegative SO_4^{2-} , resulting in a neutral complex after encapsulation. Together these two structures provide welcome crystallographic data for sulfate binding with synthetic receptors, and will ultimately aid in the design of more selective receptors for the elusive dianion as well as for other tetrahedral anionic species.

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Notes and references

‡ *Crystal data:* for $[\text{H}_8\text{L1}(\text{SO}_4)][\text{SO}_4]_2 \cdot 5.25\text{H}_2\text{O} \cdot 2\text{CH}_3\text{OH}$: $\text{C}_{38}\text{H}_{82.5}\text{N}_8\text{O}_{27.25}\text{S}_5$, $M = 1247.92$, crystal size $0.37 \times 0.30 \times 0.13 \text{ mm}^3$, triclinic, $P\bar{1}$, $a = 13.4300(8)$, $b = 13.5957(9)$, $c = 16.3025(10) \text{ \AA}$, $\alpha = 108.026(2)$, $\beta = 98.526(2)$, $\gamma = 95.226(2)^\circ$, $V = 2769.4(3) \text{ \AA}^3$, $Z = 2$, $d_{\text{calc}} = 1.496 \text{ g cm}^{-3}$, $T = 100(2) \text{ K}$, $F(000) = 1329$, $\mu(\text{Mo-K}\alpha) = 0.303 \text{ mm}^{-1}$, 10295 independent reflections (17543 measured), $wR2 = 0.1106$, $R1 = 0.0392$, and GOF on $F^2 = 1.032$; CCDC 244228. For

[H₂L2(SO₄)]·2(H₂O)·CH₃CN: C₃₅H₄₈N₁₂O₁₂S: *M* = 860.91, crystal size 0.15 × 0.15 × 0.14 mm³, monoclinic, *P*2₁/*n*, *a* = 12.402(2), *b* = 14.566(3), *c* = 22.629(5) Å, α = 90°, β = 97.793(4)°, γ = 90°, *V* = 4050.1(14) Å³, *Z* = 4, *d*_{calc} = 1.412 g cm⁻³, *T* = 100(2) K, *F*(000) = 1816, μ(Mo-Kα) = 0.157 mm⁻¹, 31526 independent reflections (31526 measured), *wR*₂ = 0.1790, *R*₁ = 0.0637, and GOF on *F*² = 0.899; CCDC 244229. See <http://www.rsc.org/suppdata/cc/b4/b411904e/> for crystallographic data in .cif or other electronic format.

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