

Seven-coordinate anion complex with a tren-based urea: Binding discrepancy of hydrogen sulfate in solid and solution states†

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Structural characterization of a hydrogen sulfate complex with a tren-based urea suggests that the anion is coordinated with six NH⋯O bonds ($d_{\text{N}\cdots\text{O}} = 2.857(3)$ to $3.092(3)$ Å) and one OH⋯O bond ($d_{\text{O}\cdots\text{O}} = 2.57(2)$ Å) from three receptors; however, in solution the anion is bound within the pseudocavity of one receptor.

Sulfate plays an important role in many biochemical processes.¹ The sulfate-binding protein (SBP) was structurally identified in 1985 by Pflugrath and Quioco, in which the amino acid residues are involved in hydrogen bonding interactions to form a seven-coordinate anion complex.² In this structure, the sulfate is present in a cleft between the two lobes of SBP and bound by seven hydrogen bonds: five from peptide NH groups (Ala173, Asp11, Gly131, Gly132, Ser45), one from a tryptophan side chain NH group (Trp192), and one from a serine OH group (Ser130). Sulfate is also of significant environmental interest.³ Therefore, an increasing attention has recently been devoted to sulfate binding with synthetic receptors which include polyamines,⁴ polyamides,⁵ ureas,⁶ indoles,⁷ self-assembled metal–organic hosts,⁸ and triazolium hosts.⁹ The oxygen atoms in oxoanions are generally coordinated with two hydrogen bonds, thus sulfate with four oxygens is often found to be octacoordinated with synthetic receptors.^{5a,10} Custelcean *et al.* have shown that a tren-based urea linked with Ag_2SO_4 is capable of binding a sulfate by twelve hydrogen bonds ($d_{\text{N}\cdots\text{O}} = 2.8516$ to 3.1741 Å),^{8a} which is consistent with Hay's prediction that each oxygen could be involved in a maximum of three hydrogen bonds.¹¹ Bowman-James *et al.* have reported a ten-coordinate sulfate complex stabilized in a tetramide-based host with four amides ($d_{\text{N}\cdots\text{O}} = 3.06$ – 3.31 Å), two protonated amines ($d_{\text{N}\cdots\text{O}} = 2.76$ Å), and four H_2O molecules

($d_{\text{O}\cdots\text{O}} = 2.71$ and 2.79 Å).¹² Wu *et al.* have characterized a multiple coordinate sulfate complex with a tris(3-pyridyl)urea showing eleven NH⋯O hydrogen bonds ($d_{\text{N}\cdots\text{O}} < 3.2$ Å).^{8b} In this communication, we report a heptacoordinated hydrogen sulfate resulting from the coordination of three tren-based ureas (**L**) via six NH⋯O bonds ($d_{\text{N}\cdots\text{O}} = 2.857(3)$ to $3.092(3)$ Å) and one OH⋯O bond ($d_{\text{O}\cdots\text{O}} = 2.57(2)$ Å), and its solution binding studies.

The tripodal urea **L** was synthesized from the reaction of tren and *p*-cyanophenyl isocyanate in CHCl_3 . Crystallographic analysis‡ of the free urea reveals that the ligand forms a pseudocavity consisting of three arms (Fig. 1). One oxygen is involved in intermolecular hydrogen bonding interactions with two NH's of another arm. The bisulfate salt was obtained from the reaction of **L** with H_2SO_4 in ethanol at room temperature. The salt crystallizes as $[\text{HL}\cdot(\text{HSO}_4)]$ where the tertiary amine is protonated. The proton on the tertiary nitrogen is pointed inside the tripodal cavity formed by the three arms, and is hydrogen-bonded with one carbonyl oxygen of a urea group ($\text{N1}\cdots\text{O34} = 2.783(2)$ Å). The molecule contains a singly-charged hydrogen sulfate to balance the charge of the cationic host. However, the anion is not encapsulated; it is held outside the cavity via two H-bonds of $\text{N18}\cdots\text{O1}$ and $\text{N21}\cdots\text{O1}$ ($d_{\text{N}\cdots\text{O}} = 2.981(2)$ and $3.020(3)$ Å, respectively).

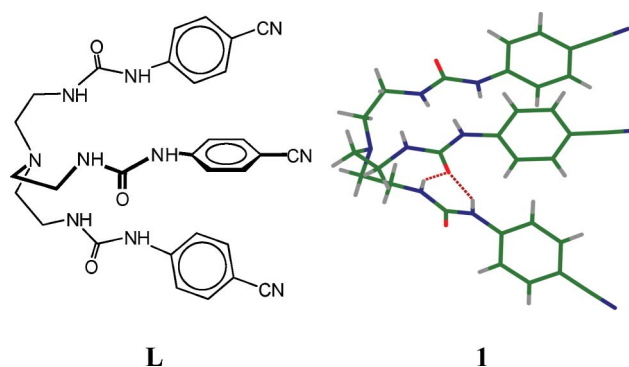


Fig. 1 Tren-based urea (**L**) and its X-ray structure (**I**).

Examining the coordination environment of hydrogen sulfate suggests that it is coordinated with multiple hydrogen bonds comprised of several NH⋯O bonds and one OH⋯O bond in the lattice framework formed by three tren ureas (Fig. 2).

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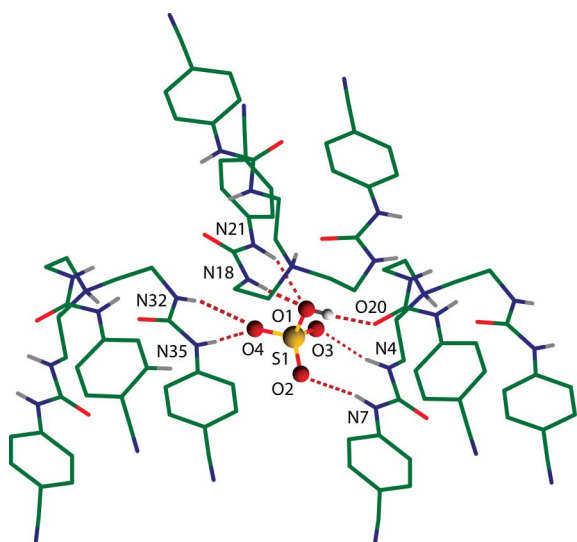


Fig. 2 X-ray structure of the hydrogen sulfate complex with **L** showing seven hydrogen bonds (six NH...O and one OH...O bonds).

The coordination environment of the anion is shown in Fig. 2, and the hydrogen bonding parameters are listed in Table 1. The nature of the hydrogen-bonding interactions involved in the complex can be evaluated from a correlation of H...O distance and N-H...O angle in the strong hydrogen-bonding interactions region of $d_{N\cdots O} < 3.2$ Å, $d_{H\cdots O} < 2.5$ Å and $\angle N-H\cdots O > 140^\circ$.^{8b,13} It is clear that all six NH...O hydrogen bonds fall within the hydrogen bonding range (see Fig. S6 in ESI). This interpretation is further supported by the work from Ghosh *et al.* for the 14-coordinate sulfate complex of a pentafluorophenyl-substituted tripodal urea receptor ($d_{N\cdots O} = 2.852(6)$ to $3.217(6)$ Å),⁶⁸ Custelcean *et al.* for the 12-coordinate sulfate within metal-organic framework ($d_{N\cdots O} = 2.8516$ to 3.1741 Å),^{8a} and Bowman-James for the sulfate complex of tetramide (N...O = 3.06 – 3.31 Å).¹² We, therefore, conclude that hydrogen sulfate is coordinated by a total of seven hydrogen bonds comprised of six NH...O bonds and one OH...O bond (Fig. 3). While each of the three tren ureas contributes two hydrogen-bond donors *via* NH groups from a single arm, one tren unit acts as a hydrogen-bond acceptor through its carbonyl oxygen.

In order to evaluate the binding affinity of **L** for anions, ¹H NMR titration studies were performed in DMSO-*d*₆. The addition of *n*-Bu₄NHSO₄ to **L** resulted in a significant downfield shift of both NH signals ($\Delta\delta_{\max} = 0.87$ and 0.60 ppm), suggesting an interaction of NH groups with the anion. The change in the

Table 1 H-bonding parameters (Å, °) for the bisulfate complex of **L**

D—H...O	H...O	D...O	$\angle DHO$
O1—H1A...O20 ^a	1.79(3)	2.573(2)	178(3)
N4—H4...O3 ^b	2.15(3)	2.979(3)	169(2)
N7—H7...O2 ^b	2.12(3)	2.936(3)	171(2)
N18—H18...O1	2.23(2)	2.981(2)	159(2)
N21—H21...O1	2.20(2)	3.020(3)	153(2)
N32—H32...O4 ^a	2.40(2)	3.092(3)	142(2)
N35—H35...O4 ^a	2.06(3)	2.857(3)	170(2)

^a $\frac{1}{2}-x, -\frac{1}{2}+y, \frac{1}{2}-z$, ^b $\frac{1}{2}-x, \frac{1}{2}+y, \frac{1}{2}-z$.

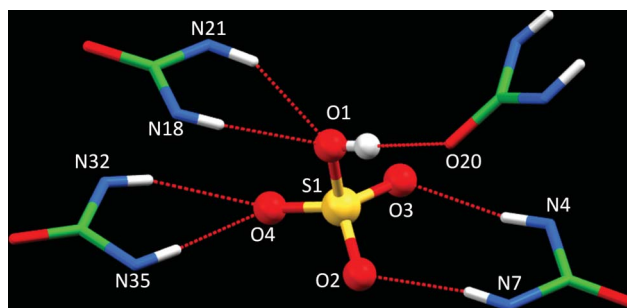


Fig. 3 The coordination environment of bisulfate showing seven hydrogen bonds from three ureas.

chemical shift of NH resonances of NMR spectra, as recorded with an increasing amount of anion solution at room temperature, gave the best fit for a 1 : 1 binding model, yielding a binding constant of $\log K = 3.0$ (Fig. 4).¹⁴ The observed binding constant is much higher than that observed for singly-charged bisulfate in an amide-based cryptand ($\log K = 1.83(3)$).^{4a} The solution binding mode was further confirmed by 2D NOESY NMR experiments of both free ligand and hydrogen sulfate complex in DMSO-*d*₆ (Fig. 5) As shown in Fig. 5A, the free ligand shows two strong NOESY contacts between H_b...H_c and H_a...H_b, an observation which is also supported by single crystal structure of **L** showing distances of H_b...H_c = 2.30 and H_a...H_b = 2.08 Å. Upon the addition of bisulfate, H_c proton on aromatic ring shifts more downfield as compared to H_a, leading the reversal of the relative position of these two protons (see Fig S9a in ESI). The NOESY between H_a and H_b is absent in the complex, while the contact between H_b and H_c becomes significantly weaker; indicating a conformational change of the ligand due to encapsulation of a bisulfate anion (Fig. 6). Similar changes were reported by Schneider *et al.* in the optimized structure of chloride complex of a tren-based urea ligand.¹⁵ The 1 : 1 binding stoichiometry in DMSO-*d*₆ was further verified by the Job's plot showing a maximum at the 0.5 mole fraction of **L** (see ESI).

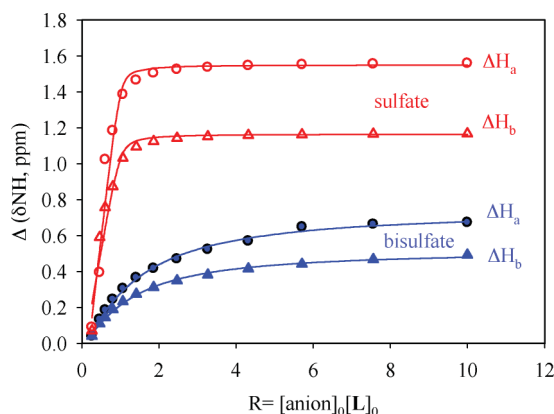


Fig. 4 ¹H NMR titration curves of **L** (2 mM) with *n*-Bu₄NHSO₄ (●, ▲) and ZnSO₄ (○, △) in DMSO-*d*₆. Net changes in the chemical shifts of NH are shown against the increasing amount of anion (20 mM). H1 = CH₂NHCO and H2 = CONHAr.

We also performed ¹H NMR titrations for other oxoanions: SO₄²⁻, H₂PO₄⁻, ClO₄⁻ and NO₃⁻ in DMSO-*d*₆.¹⁶ The results show

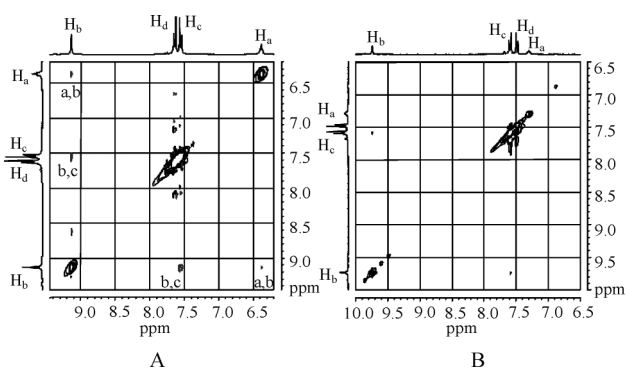


Fig. 5 2D NOESY NMR experiments of **L** in absence (A) and presence (B) of hydrogen sulfate (5 equiv.) in DMSO-*d*₆.

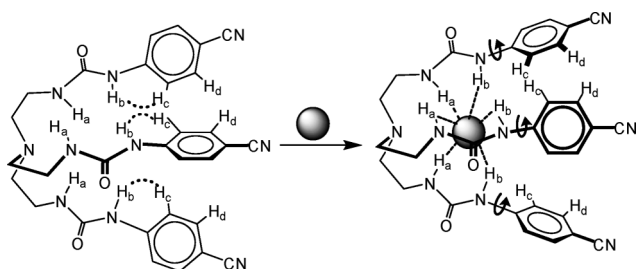


Fig. 6 Proposed binding mode of **L** for hydrogen sulfate in solution.

that the host forms a strong 1 : 1 complex with SO_4^{2-} giving the binding constant of $\log K = 4.7$ which is comparable to that observed for a pentafluorophenyl-substituted tripodal urea ($K = 4.72$)^{6b} or nitrophenyl-substituted tripodal urea ($\log K = 4.97$).^{6c} Clearly, an additional charge on SO_4^{2-} compared to HSO_4^- plays a role for stronger electrostatic interactions, resulting in a stronger binding of SO_4^{2-} . The ligand also binds H_2PO_4^- strongly with the binding constant of $\log K = 4.2$. On the other hand, the addition of ClO_4^- and NO_3^- did not result in any appreciable change in the NMR resonances (see ESI). Therefore, the binding largely depends on the relative basicity of the anions included in this study and is in accordance with the Hofmeister series.¹⁷

In summary, we have presented a seven coordinate complex of hydrogen sulfate formed by three tren-based receptors in solid state. The anion is coordinated with six $\text{NH} \cdots \text{O}$ bonds and one $\text{OH} \cdots \text{O}$ hydrogen bond. In contrast, the ligand was found to encapsulate a single anion within its cavity in solution, suggesting an obvious discrepancy of binding mode from that observed in solid state. While many examples exist for seven-coordinate complexes with metal ions,¹⁸ to the best of our knowledge, there is just one structure of seven-coordinate anion complex reported by Bowman-James and coworkers, where one sulfate is encapsulated by an amide-based cryptand with four hydrogen-bonds to the cryptand and three additional hydrogen-bonds to the crystalline water molecules.¹⁹ The seven coordinate complex in our case has been resulted from the packing influence of the crystal, which represents a rare example of a heptacoordinated anion with a synthetic receptor.

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Notes and references

‡ Crystal data for **L**: $\text{C}_{30}\text{H}_{30}\text{N}_{10}\text{O}_3$, $M = 578.64$, triclinic, $a = 8.7312(11)$ Å, $b = 12.8400(17)$ Å, $c = 13.6820(18)$ Å, $\alpha = 91.989(3)^\circ$, $\beta = 107.888(2)^\circ$, $\gamma = 100.753(2)^\circ$, $V = 1427.1(3)$ Å³, $T = 100(2)$ K, space group $P\bar{1}$, $Z = 2$, 16034 reflections measured, 7004 independent reflections ($R_{\text{int}} = 0.0320$). The final R_1 values were 0.0495 ($I > 2\sigma(I)$). The final $wR(F^2)$ values were 0.1166 ($I > 2\sigma(I)$). CCDC 814969. Crystal data for $\text{HL}^+ \cdot \text{HSO}_4^-$: $\text{C}_{30}\text{H}_{31}\text{N}_{10}\text{O}_3 \cdot \text{HO}_4\text{S}$, $M = 676.72$, monoclinic, $a = 12.696(2)$ Å, $b = 12.411(2)$ Å, $c = 20.491(4)$ Å, $\beta = 103.912(9)^\circ$, $V = 3134.1(9)$ Å³, $T = 100(2)$ K, space group $P2_1/n$, $Z = 4$, 29878 reflections measured, 7849 independent reflections ($R_{\text{int}} = 0.0716$). The final R_1 value was 0.0587 ($I > 2\sigma(I)$). The final $wR(F^2)$ value was 0.1188 ($I > 2\sigma(I)$). CCDC 795639.

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