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

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Abstract

Structural characterization of a hydrogen sulfate complex with a tren-based urea suggests that the anion is coordinated with six NH $\cdots$ O bonds ($d_N \cdots _O$ = 2.857 (3) to 3.092 (3) Å) and one OH $\cdots$ O bond ($d_O \cdots _O$ = 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 Quiocho, 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$_2$SO$_4$ is capable of binding a sulfate by twelve hydrogen bonds ($d_N \cdots _O$ = 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 ($d_N \cdots _O$ = 3.06–3.31 Å), two protonated amines ($d_N \cdots _O$ = 2.76 Å), and four H$_2$O molecules ($d_O \cdots _O$ = 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 $\cdots$ O hydrogen bonds ($d_N \cdots _O$ < 3.2 Å).[8b] In this communication, we report a heptacoordinated hydrogen sulfate resulting from the

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coordination of three tren-based ureas (**L**) *via* six NH ··· O bonds (d_N ··· $_O$ = 2.857(3) to 3.092(3) Å) and one OH ··· O bond (d_O ··· $_O$ = 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 CHCl₃. Crystallographic analysis[‡] of the free urea reveals that the ligand forms a pseudo-cavity 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 [**HL** · (HSO₄)] 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 (N1 ··· 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 N18 ··· O1 and N21 ··· O1 (d_N ··· $_O$ = 2.981(2) and 3.020(3) Å, respectively).

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). 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 ··· $_O$ < 3.2 Å, d_H ··· $_O$ < 2.5 Å and ∠N–H ··· O > 140°.[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 ··· $_O$ = 2.852(6) to 3.217(6) Å),[6g] Custelcean *et al.* for the 12-coordinate sulfate within metal–organic framework (d_N ··· $_O$ = 2.8516 to 3.1741 Å),[8a] and Bowman-James for the sulfate complex of tetramide (N ··· O = 3.06–3.31 A).[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-*d₆*. 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 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-*d₆* (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_d, 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).

We also performed ^{1}H NMR titrations for other oxoanions: SO_{42}^-, $H_2PO_4^-$, ClO_4^- and NO_3^- in DMSO-d_6.[16] The results show 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 $(K = 4.72)$[6h] 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 NH $\cdots$ O bonds and one OH $\cdots$ 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.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Notes and references

1. (a) Antonisse MMG, Reinhoudt DN. Chem Commun. 1998:443–448.(b) Atwood JL, Holman KT, Steed JW. Chem Commun. 1996:1401–1407.(c) Gale PA. Coord Chem Rev. 2003; 240:191–221.(d) Cormode DP, Murray SS, Cowley AR, Beer PD. Dalton Trans. 2006:5135–5140. [PubMed: 17077886]

2. Pflugrath JW, Quiocho FA. Nature. 1985; 314:257–260. [PubMed: 3885043]

3. Moyer BA, Delmau LH, Fowler CJ, Ruas A, Bostick DA, Sessler JL, Katayev E, Pantos GD, Llinares JM, Hossain MA, Kang SO, Bowman-James K. Adv Inorg Chem. 2007; 59:175–204.

4. (a) Kang SO, Hossain MA, Powell D, Bowman-James K. Chem Commun. 2005:328–330.(b) Mani G, Guchhait T, Kumar R, Kumar S. Org Lett. 2010; 12:3910–3913. [PubMed: 20704306] (c) Mendy JS, Pilate M, Horne T, Day VW, Hossain MA. Chem Commun. 2010; 46:6084–6086.(d) Saeed MA, Fronczek FR, Powell DR, Hossain MA. Tetrahedron Lett. 2010; 51:4233–4236. [PubMed: 20640221]

5. (a) Hossain MA, Llinares JM, Powell D, Bowman-James K. Inorg Chem. 2001; 40:2936–2937. [PubMed: 11399156] (b) Kang SO, Day VW, Bowman-James K. Org Lett. 2009; 11:3654–3657. [PubMed: 19640003] (c) Lakshminarayanan PS, Suresh E, Ghosh P. Inorg Chem. 2006; 45:4373–4380.

6. (a) Wu B, Yang X-J, Janiak C, Gerhard Lassahn P. Chem Commun. 2003:902–903.(b) Wu B, Huang X, Xia Y, Yang X-J, Janiak C. CrystEngComm. 2007; 9:676–685.(c) Jose DA, Kumar DK, Ganguly B, Das A. Inorg Chem. 2007; 46:5817–5819. [PubMed: 17589988] (d) Zhuge F, Wu B, Liang J, Yang J, Liu Y, Jia C, Janiak C, Tang N, Yang X. Inorg Chem. 2009; 48:10249–10256. [PubMed: 19788259] (e) Custelcean R, Sellin V, Moyer BA. Chem Commun. 2007:1541–1543.(f) Custelcean R, Bosano J, Bonnesen PV, Kertesz V, Hay BP. Angew Chem, Int Ed. 2009; 48:4025–4029.(g) Ravikumar I, Ghosh P. Chem Commun. 2010; 46:1082–1084.(h) Ravikumar I, Lakshminarayanan PS, Arunachalam M, Suresh E, Ghosh P. Dalton Trans. 2009:4160–4168. [PubMed: 19452065]

7. (a) Kim J, Juwarker H, Liu X, Lah MS, Jeong KS. Chem Commun. 2010; 46:764–766.(b) Gale PA, Hiscock JR, Jie CZ, Hursthouse MB, Light ME. Chem Sci. 2010; 1:215–220.

8. (a) Custelcean R, Moyer BA, Hay BP. Chem Commun. 2005:5971–5973.(b) Wu B, Liang J, Yang J, Jia C, Yang X-J, Zhang H, Tangb N, Janiak C. Chem Commun. 2008:1762–1764.

9. Schulze B, Friebe C, Hager MD, Günther W, Köhn U, Jahn BO, Görls H, Schubert US. Org Lett. 2010; 12:2710–2713. [PubMed: 20481556]

10. Bowman-James K. Acc Chem Res. 2005; 38:671–678. [PubMed: 16104690]

11. Hay BP, Firman TK, Moyer BA. J Am Chem Soc. 2005; 127:1810–1811. [PubMed: 15701016]

12. Kang SO, Day VW, Bowman-James K. Org Lett. 2009; 11:3654–3657. [PubMed: 19640003]

13. Pirard B, Baudoux G, Durant F. Acta Crystallogr, Sect B: Struct Sci. 1995; B51:103–107.

14. Schneider HJ, Kramer R, Simova S, Schneider U. J Am Chem Soc. 1988; 110:6442–6448.

15. Werner F, Schneider HJ. Helv Chim Acta. 2000; 83:465–478.

16. Titrations with Na_2SO_4 were hampered due to the solubility problem in DMSO-d_6. We, therefore, used $ZnSO_4$ which was previously used by other groups in DMSO-d_6.[8b]

17. Hofmeister F. Naunyn-Schmiedebergs Arch Pharmacol. 1888; 24:247–260.

18. (a) Cotton, FA.; Wilkinson, G. Advanced Inorganic Chemistry. 5. Wiley; New York: 1988. p. 10-22.(b) Duan L, Fischer A, Xu Y, Sun L. J Am Chem Soc. 2009; 131:10397–10399. [PubMed: 19601625]

19. Kang SO, Powell D, Bowman-James K. J Am Chem Soc. 2005; 127:13478–13479. [PubMed: 16190694]
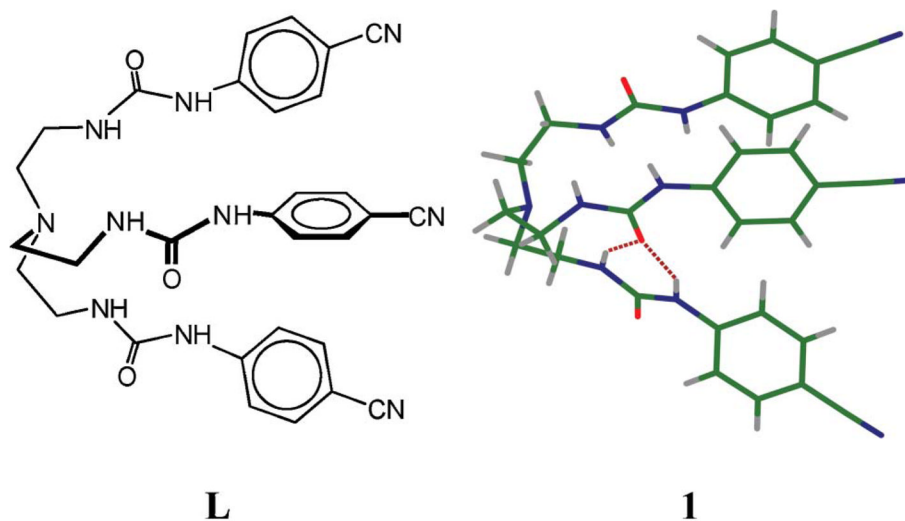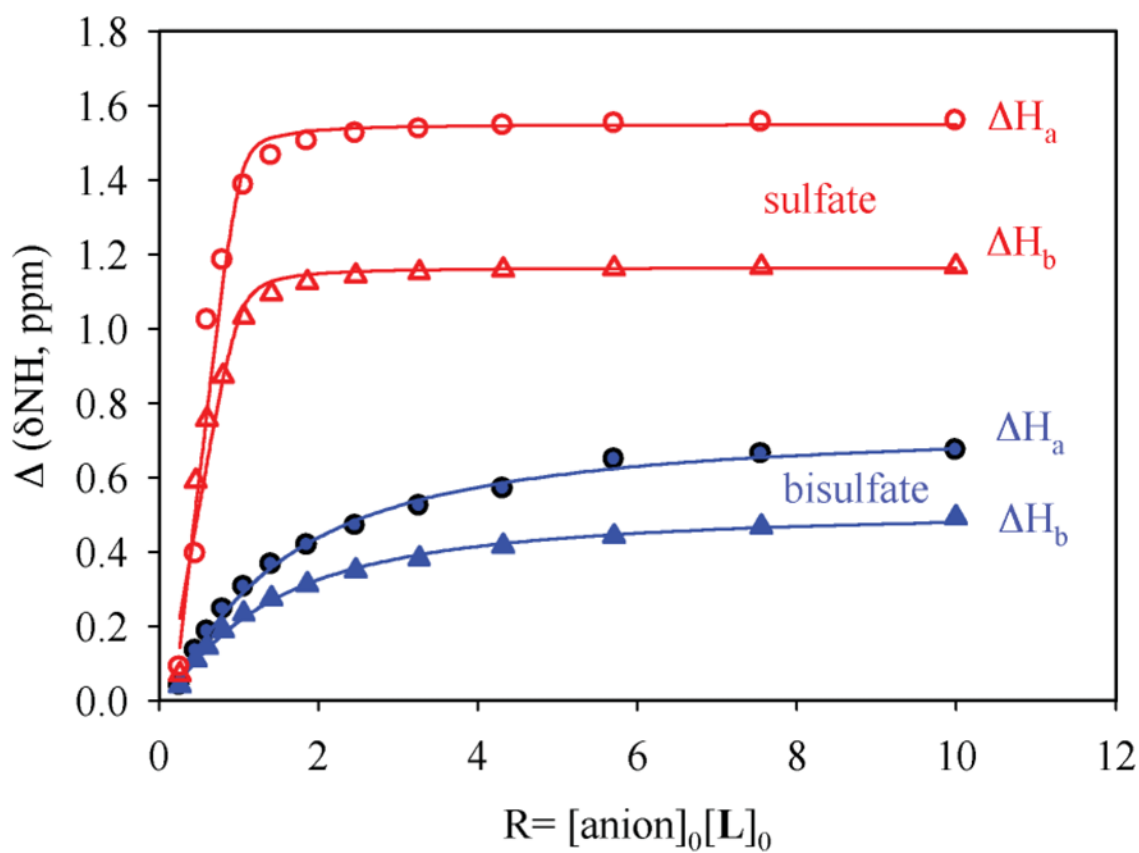
Fig. 1.
Tren-based urea (**L**) and its X-ray structure (**1**).
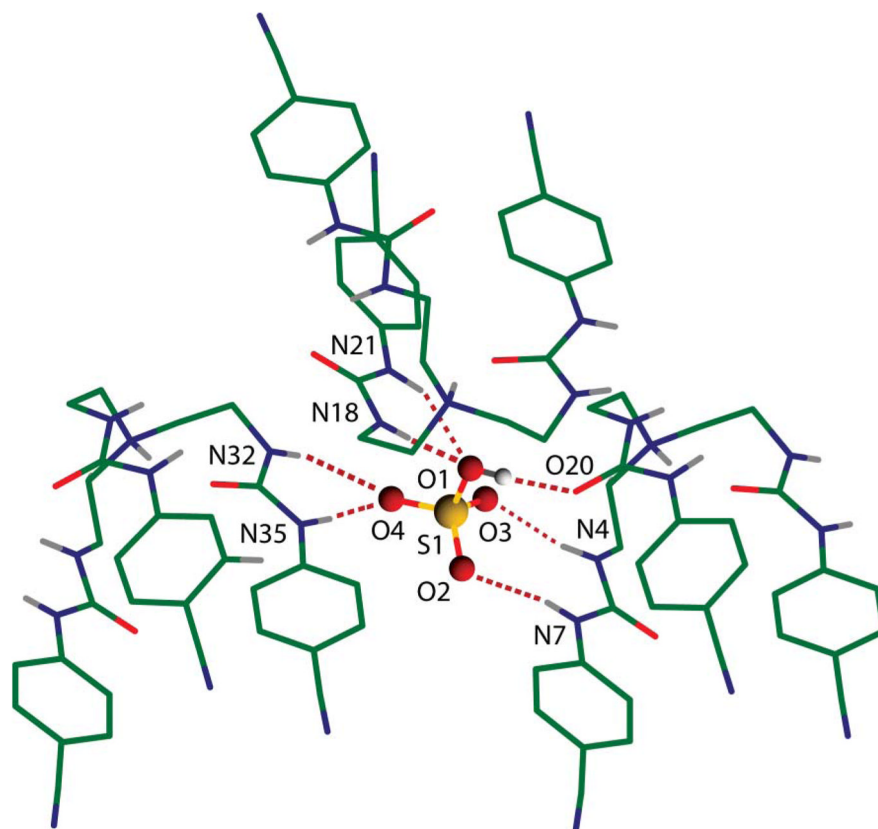
Fig. 2.
X-ray structure of the hydrogen sulfate complex with **L** showing seven hydrogen bonds (six NH ⋯ O and one OH ⋯ O bonds).
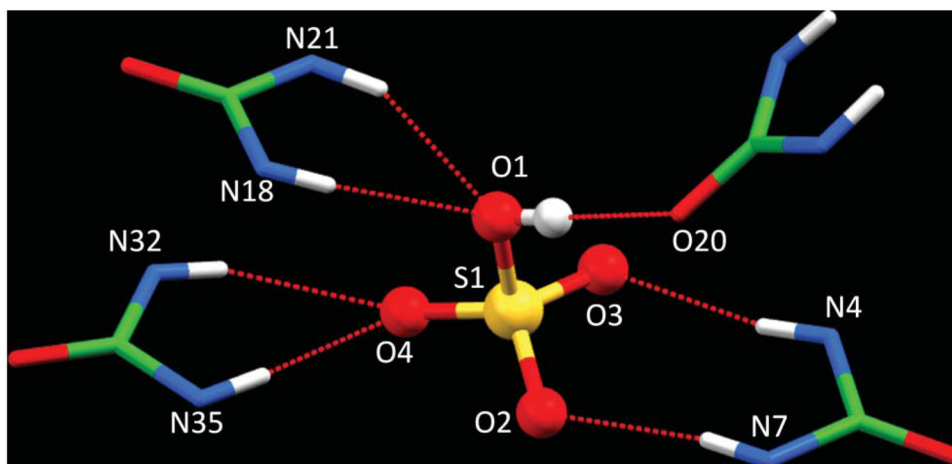
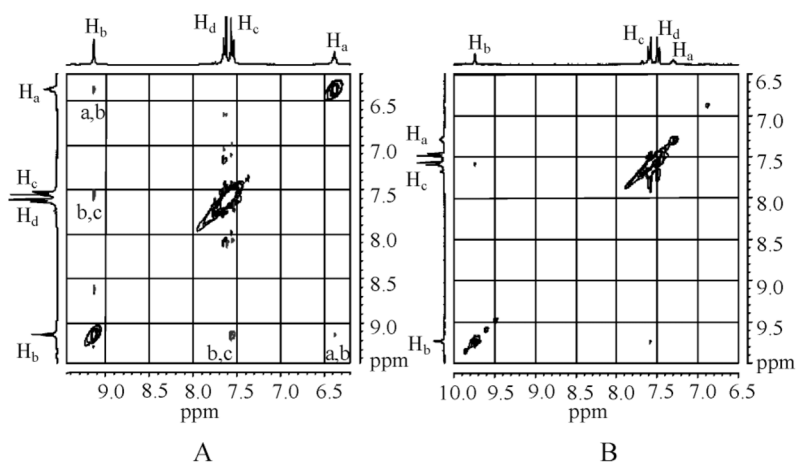**Fig. 3.**
The coordination environment of bisulfate showing seven hydrogen bonds from three ureas.

Fig. 4.
^{1}H NMR titration curves of **L** (2 mM) with n-Bu$_4$ NHSO$_4$ (●, ▲) and ZnSO$_4$ (○, △) in DMSO-d_6. Net changes in the chemical shifts of NH are shown against the increasing amount of anion (20 mM). H1 = CH$_2$ NHCO and H2 = CONHAr.

Fig. 5.
2D NOESY NMR experiments of **L** in absence (A) and presence (B) of hydrogen sulfate (5 equiv.) in DMSO-d_6.
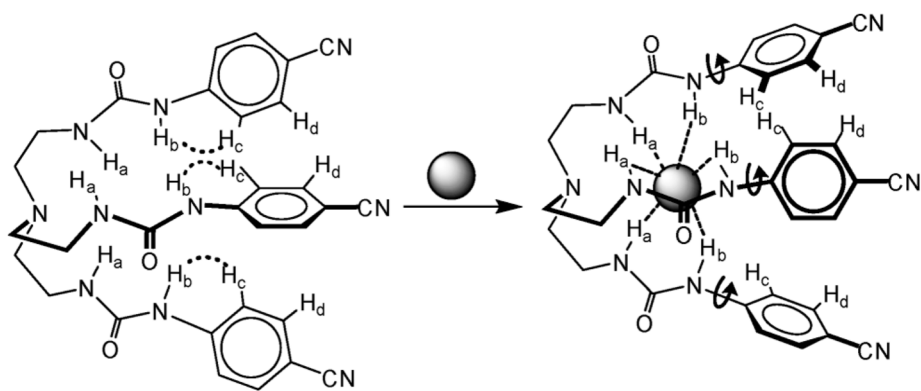
Fig. 6.
Proposed binding mode of **L** for hydrogen sulfate in solution.

Table 1

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

D—H ⋯ O	H ⋯ O	D ⋯ O	∠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} $\frac{1}{2} - x$, $\frac{1}{2}+y$, $\frac{1}{2} - z$.