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Neutral tripodal receptors towards efficient trapping of oxalate

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Abstract. Tris(2-aminoethyl)amine (TREN) based pentafluorophenyl urea and 4-cyanophenyl thiourea receptors have shown encapsulation of oxalate ($C_2O_4^{2-}$) in semi-aqueous environment. A single crystal X-ray study shows trapping of planar conformer of $C_2O_4^{2-}$ in both the cases. Further solution state binding of $C_2O_4^{2-}$ is probed by ^{1}H-NMR titration study in semi-aqueous solvent.

Keywords. Anion receptor; urea; thiourea; oxalate recognition; single crystal x-ray diffraction; ^{1}H-NMR titration.

1. Introduction

Recognition of carboxylates is important as they play vital roles in various metabolic processes.[1] Simplest dicarboxylate oxalate ($C_2O_4^{2-}$) is a nutrient in human body.[2] However excess of oxalate causes renal failure, kidney stones, etc.[3] Besides its biological and environmental relevance, oxalate is a common analytical reagent. Dianionic form of oxalate ($C_2O_4^{2-}$) can exist as staggered or planar conformer. Rotational energy barrier between these two conformers is 2–6 kcal/mol.[4a–b] Although staggered conformer is the stable form of $C_2O_4^{2-}$, most of the structural reports show presence of planar $C_2O_4^{2-}$ conformer.[4b] Charged polyammonium receptors are familiar systems for binding of $C_2O_4^{2-}$.[5] Metal based receptors have also been explored for $C_2O_4^{2-}$ sensing in recent times.[6] Very few synthetic neutral receptors have been designed for the recognition of $C_2O_4^{2-}$.[7] Tren based tripodal urea/thiourea receptors have attracted a great deal of attention for anion recognition in recent times.[8] Although these class of receptors are explored for anion complexation in non-aqueous medium, recently binding propensity of these receptors in aqueous medium are also established.[8a,e,n,o] Interestingly most of the receptors tend to form dimeric capsular assembly upon encapsulation of anionic guests like sulphate, phosphates and carbonate.[8p,r,s] In our ongoing effort for anion recognition chemistry, we have recently reported recognition of $C_2O_4^{2-}$ by two structurally analogous tripodal urea receptors in semi-aqueous media where trapping of staggered *vs.* planar $C_2O_4^{2-}$ conformer is demonstrated by single crystal X-ray structural analysis.[8t] Herein, we show solid and solution states encapsulation studies of $C_2O_4^{2-}$ by two other tripodal anion receptors, pentafluorophenyl substituted urea (**L1**) and 4-cyanophenyl substituted thiourea (**L2**) and have compared the same with the recently published $C_2O_4^{2-}$ complexes of **L3** and **L4**.

2. Experimental

^{1}H-NMR and ^{13}C-NMR spectra of oxalate complexes of **L1** and **L2** i.e., **1** and **2** were recorded on Bruker 300 MHz FT-NMR spectrometer (model: DPX-300) in DMSO-d_6 and $CDCl_3$ respectively at 25°C. Solvents, tetrabutylammonium iodide and potassium oxalate were purchased from Spectrochem Ltd., India. Chemical shifts for ^{1}H and ^{13}C-NMR were reported in parts per million (ppm), calibrated to the residual solvent peak set, with coupling constants reported in Hertz (Hz).

2.1 *Synthesis of complex **1***

Receptor **L1** and TBAI (2 equiv.) are dissolved in DMSO/5% H_2O solvent mixture and excess of $K_2C_2O_4$, $2H_2O$ is added to it. The reaction mixture is then stirred for 1h and filtered for crystallization. Block shape crystals of complex **1** [(**L1**)$_2$· (C_2O_4)](TBA)$_2$ appear within a week in good yield (70%). ^{1}H-NMR (300 MHz, DMSO-d_6): 8.94 (NH, 3H), 7.38 (NH, 3H), 3.13–3.19 (8H, NCH_2CH$_2$CH$_2$CH$_3$), 3.06 (6H, NCH_2CH$_2$), 2.46 (6H, NCH$_2$CH_2), 1.51–1.62 (8H, NCH$_2$CH_2CH$_2$CH$_3$),

*For correspondence

1.25–1.37 (8H, $NCH_2CH_2CH_2CH_3$), 0.91–0.96 (12H, $NCH_2CH_2CH_2CH_3$). ^{13}C (75 MHz, DMSO-d_6) 172.38, 155.19, 144.99, 141.73, 139.80, 138.99, 136.51, 135.69, 115.72, 58.05, 54.73, 38.49, 29.47, 23.59, 19.75, 14.01

2.2 *Synthesis of complex 2*

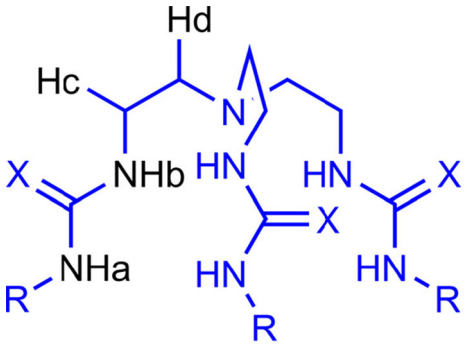
Complex **2** $[(\mathbf{L2})_2 \cdot (C_2O_4)](TBA)_2$ is synthesized similarly like complex **1**. Yield: 50%. ^{1}H-NMR (300 MHz, $CDCl_3$): 10.24 (NHa, 3H), 8.71 (NHb, 3H), 7.55–7.58 (6H, Ar-CH), 7.17–7.20 (6H, Ar-CH), 3.66 (6H, NCH_2CH_2), 3.04–3.09 (8H, $NCH_2CH_2CH_2CH_3$), 2.73 (6H, NCH_2CH_2), 1.53–1.63 (8H, $NCH_2CH_2CH_2CH_3$), 1.24–1.45 (8H, $NCH_2CH_2CH_2CH_3$), 0.97–1.01 (12H, $NCH_2CH_2CH_2CH_3$). ^{13}C-NMR (75 MHz, $CDCl_3$) 180.96, 171.91, 144.52, 132.01, 122.46, 119.38, 105.40, 135.69, 115.72, 59.03, 53.94, 42.75, 23.89, 19.78, 13.66

2.3 *X-ray crystallography*

The crystallographic data and data collection details for complexes **1** (CCDC: **914150**) and **2** (CCDC: **914148**) are given below. A crystal of suitable size is selected from the mother liquor and immersed in paratone oil, then mounted on the tip of a glass fibre and cemented using epoxy resin. Intensity data for the crystals are collected using Mo Kα (l=0.7107 Å) radiation on a Bruker SMART APEX diffractometer equipped with CCD area detector at 120 K. The data integration and reduction are processed with SAINT[9a] software. An empirical absorption correction is applied to the collected reflections with SADABS.[9b] The structures are solved by direct methods using SHELXTL[10] and refined by F^2 by the full-matrix least-squares technique using the SHELXL-97[11] program package. Graphics are generated using PLATON,[12] MERCURY 2.2[13] and ORTEP3v2. The non-hydrogen atoms are treated anisotropically. Wherever possible, the hydrogen atoms are located on a difference Fourier map and refined. In other cases, the hydrogen atoms are geometrically fixed. Crystallographic parameters for complexes **1** and **2** are tabulated in supporting information (table S1).

3. Results and Discussion

Syntheses of the receptors **L1**-**L4** (scheme 1) are reported previously.[8d,q,t] Complexes **1** and **2** are synthesized in good yield by the reaction of receptor, TBAI and excess $K_2C_2O_4$ in DMSO/5% H_2O solvent mixture. Syntheses of complexes **3** and **4** are reported previously by our group.[8t] The detailed solid and solution states binding properties of **L1** and **L2** towards $C_2O_4^{2-}$ are discussed in the next section.



L1, R = -C_6F_5, X = O
L2, R = -*p*CNC_6H_4, X = S
L3, R = -*m*CNC_6H_4, X = O
L4, R = -*m*FC_6H_4, X = O

Scheme 1. Chemical structures of the receptors **L1-L4**

3.1 *Structural description of complex 1*

Crystals of complex **1** are obtained by the reaction of **L1** and TBAI (~2 equiv.) with excess of $K_2C_2O_4$ in DMSO/5% water solvent mixture. Complex **1** crystallizes in triclinic crystal system with P-1 space group. Asymmetric unit of complex **1** contains two **L1** units, one $C_2O_4^{2-}$, two TBA countercations and two DMSO as solvent of crystallization. Two units of **L1** form a dimeric capsular assembly that completely encapsulates one $C_2O_4^{2-}$ in its cavity (figure 1). Binding of $C_2O_4^{2-}$ in complex **1** is assisted by twelve N-H$\cdots$O interactions between four oxygen atoms of $C_2O_4^{2-}$ and twelve –NH groups of two **L1**. Four oxygen atoms of the encapsulated $C_2O_4^{2-}$ namely O9, O10, O11 and O12 are involved in three N-H$\cdots$O interactions each. The N$\cdots$O bond distances in **1** vary from 2.84 to 3.04 Å, whereas the N-H$\cdots$O angles range from 153 to 169° (table S2). The capsular dimension of **1** from apical N$\cdots$N distance is measured as 10.75 Å. The encapsulated $C_2O_4^{2-}$ in complex **1** is found to be a planar conformer of $C_2O_4^{2-}$. The torsion angle of planar $C_2O_4^{2-}$ conformer is measured to be 3.06°. The bond length around the central C-C bond of $C_2O_4^{2-}$ is found to be 1.56 Å, which suggests single bond character of the C-C bond (table 1). Interestingly $C_2O_4^{2-}$ encapsulation in complex **1** is also facilitated by orthogonal C-F$\cdots$C=O interaction[14] (figure 2). Each C=O group of the $C_2O_4^{2-}$ are in close contact with the C-F group of $-C_6F_5$ ring. The F$\cdots$C bond distance of two

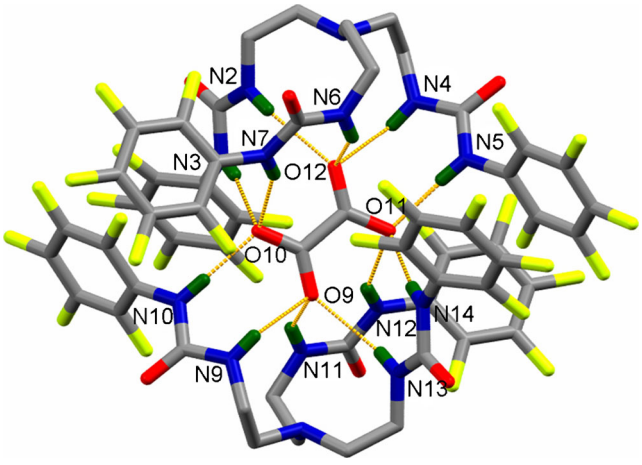


Figure 1. Crystal structure of complex **1** showing complete encapsulation of $C_2O_4^{2-}$ inside the dimeric capsular assembly of **L1**. Non-acidic hydrogens, tetrabutylammonium countercations and solvents are omitted for clarity.

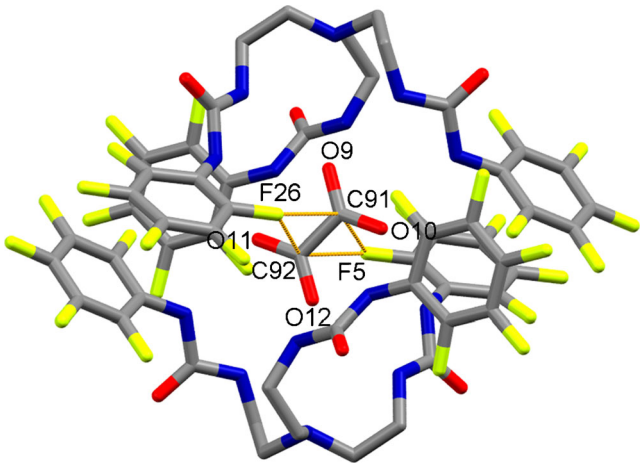


Figure 2. View of orthogonal C-F···C=O interactions in complex **1**.

orthogonal C-F···C=O interactions are measured as 2.96 Å for C9-F5···C91-O10 and 2.98 Å for C50-F26···C92-O11. The F···C=O angles associated with the two C-F···C=O contacts are 92.36° (F5···C91-O10) and 90.84° (F26···C92-O11).

3.2 *Structural description of complex 2*

Complex **2** is synthesized similarly like **1**, by reacting **L2**, TBAI and excess $K_2C_2O_4$ in DMSO/5% H_2O solvent mixture. Unit of cell of complex **2** contains two **L2** units, one $C_2O_4^{2-}$ and two TBA countercations. Dimeric assembly of **L2** encapsulates one $C_2O_4^{2-}$ in complex **2** like complex **1** (figure 3). Each oxygen atom of the encapsulated $C_2O_4^{2-}$ involves in three N-H···O interactions with the –NH group of **L2**, resulting total twelve N-H···O contacts. The N···O bond distances in **2** range from 2.95 to 3.14 Å, whereas the N-H···O angles vary from 150 to 178° (table S3). The capsular dimension of **2** is smaller (10.08 Å) than that of **1**. The encapsulated $C_2O_4^{2-}$ in complex **2** is also planar $C_2O_4^{2-}$ conformer like **1**. The torsion angle and central C-C bond distance of the planar $C_2O_4^{2-}$ conformer are measured as 0.02° and 1.49 Å respectively (table 1).

3.3 *Comparative structural description of complex 1-4*

All the receptors form dimeric capsular assembly upon encapsulation of $C_2O_4^{2-}$ irrespective of ligand functionality. However the dimeric capsules differ in terms of conformation of encapsulated $C_2O_4^{2-}$ and capsular dimension. Structural analysis of $C_2O_4^{2-}$ complexes of **L1**, **L2** and **L4** reveal planar conformation of the encapsulated $C_2O_4^{2-}$. Planar nature of $C_2O_4^{2-}$ is evident from the dihedral angles of O-C-C-O bond of $C_2O_4^{2-}$, which are measured as 3.06, 0.02 and 0.12° for complexes **1**, **2** and **4** respectively (figure 5). Only in case of complex **3**, staggered $C_2O_4^{2-}$ conformer is obtained with torsion angle 68.8°.[8t] Capsular dimension of dimeric capsules vary substantially from moving planar to staggered $C_2O_4^{2-}$ conformer. Capsular dimension based on apical N···N distance is found to be highest for complex **4** having planar $C_2O_4^{2-}$ conformer, whereas staggered $C_2O_4^{2-}$ encapsulating capsule shows smallest capsular size of 9.82 Å[8t] (figures 4 and 5). Staggered *vs.* planar conformer encapsulation is observed in single crystal X-ray studies. Thus, this is purely a solid state property of the complexes. Attached moiety in the urea/thiourea receptor influences the electronic as well as steric properties of the receptors. This could affect the guest

Table 1. O-C-C-O torsion angle, C-C bond distance of $C_2O_4^{2-}$ and capsular dimension of complexes **1–4**.

Compound	Torsion angle (°)	C-C distance (Å)	Capsular dimension (Å)
Complex **1**	3.06	1.56	10.75
Complex **2**	0.02	1.49	10.08
Complex **3**[8t]	68.81	1.50	9.82
Complex **4**[8t]	0.12	1.58	10.82
$K_2C_2O_4$,$2H_2O$	0.00	1.59	–

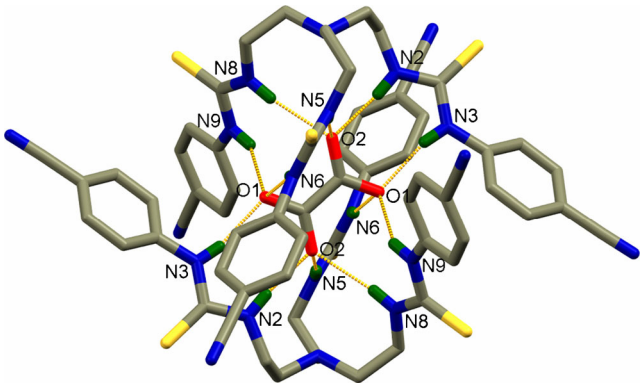


Figure 3. Crystal structure of complex **2** showing complete encapsulation of $C_2O_4^{2-}$ *via* twelve N-H···O interactions. Non-acidic hydrogens and tetrabutylammonium countercations are omitted for clarity.

binding pattern in dimeric capsules in solid state which is reflected in this particular case. Capsular sizes of the oxalate capsules depend on the substituent nature of the receptor. For example, complex **3** shows similar capsular size as that of SO_4^{2-} complex of **L3**.[8b] Similarly, $HAsO_4^{2-}$ complex of **L1** shows capsular sizes similar to complex **1**.[8n]

3.4 *Solution state $C_2O_4^{2-}$ binding study*

Solution state binding study of **L1** and **L2** with $C_2O_4^{2-}$ is carried out by ^{1}H-NMR titration. A solution of **L1** in DMSO-d_6/D_2O (9:1, v/v) is titrated against a solution of $K_2C_2O_4$ in D_2O/DMSO-d_6 (1.1:1, v/v) solvent mixture. Gradual upfield shift of CHc/d proton is observed upon

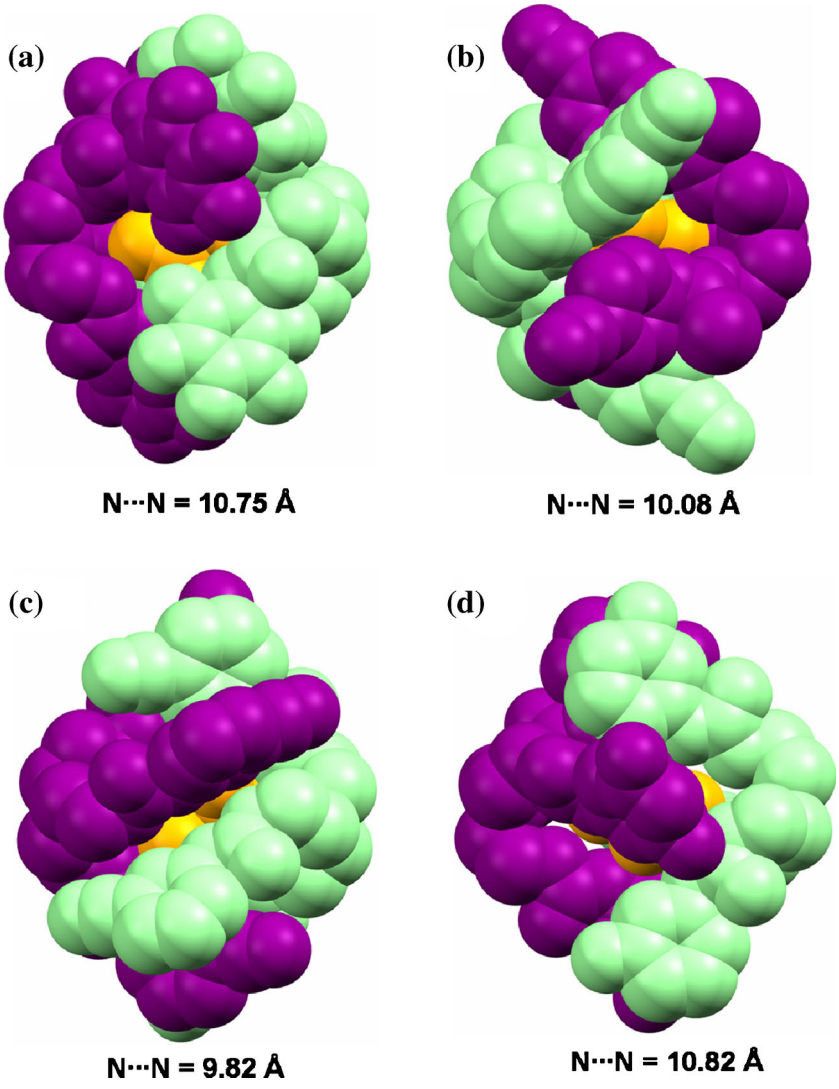


Figure 4. Comparative structural view of (**a**) complex **1**; (**b**) complex **2**; (**c**) complex **3** and; (**d**) complex **4** with the capsular dimensions.

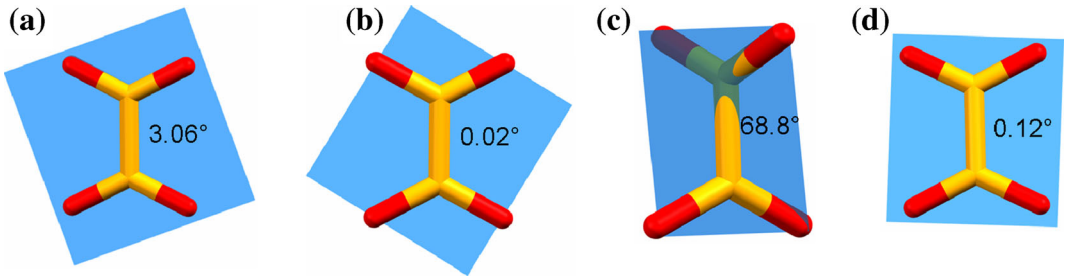


Figure 5. Close-up view of $C_2O_4^{2-}$ conformer in (**a**) complex **1**; (**b**) complex **2**; (**c**) complex **3** and; (**d**) complex **4** with their respective torsion angle.

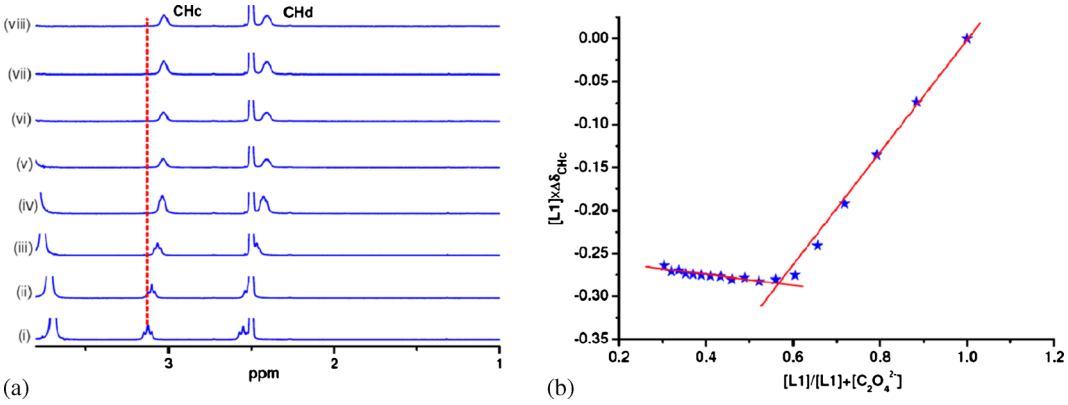


Figure 6. (**a**) Partial ^{1}H-NMR (300 MHz) spectral changes of **L1** in DMSO-d_6/D_2O (9:1)(v/v) with added standard $K_2C_2O_4$ solution in DMSO-d_6/D_2O (1:1.1) (298 K) ([**L1**]$_0$ = 3.41 mM). Ratio of concentration [$C_2O_4^{2-}$]/[**L1**]: (i) 0, (ii) 0.13, (iii) 0.39, (iv) 0.65, (v) 0.92, (vi) 1.17, (vii) 1.44, (viii) 1.70; (**b**) Job's plot for **L1** with $K_2C_2O_4$ in DMSO-d_6/D_2O (1:1.1) ([**L1**] is varied from 3.41 to 2.67 mM by the addition of aliquots of 27.92 mM $K_2C_2O_4$).

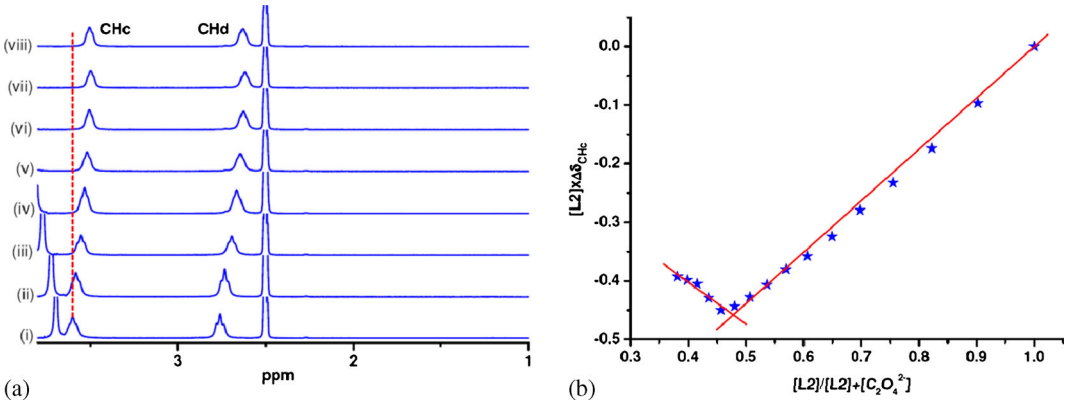


Figure 7. (**a**) Partial ^{1}H-NMR (300 MHz) spectral changes of **L2** in DMSO-d_6/D_2O (9:1)(v/v) with added standard $K_2C_2O_4$ solution in DMSO-d_6/D_2O (1:1.1) (298 K) ([**L2**]$_0$ = 5.49 mM). Ratio of concentration [$C_2O_4^{2-}$]/[**L2**]: (i) 0, (ii) 0.11, (iii) 0.32, (iv) 0.54, (v) 0.76, (vi) 0.97, (vii) 1.19, (viii) 1.41; (**b**) Job's plot for **L2** with $K_2C_2O_4$ in DMSO-d_6/D_2O (1:1.1) ([**L2**] is varied from 5.49 to 4.22 mM by the addition of aliquots of 29.67 mM $K_2C_2O_4$).

Table 2. Binding constant and free energy change of **L1**-**L4** with $C_2O_4^{2-}$.

Compound	log K	ΔG (kcal/mol)
L1	4.26	−5.85
L2	5.37	−7.37
L3	4.82[8t]	−6.62
L4	4.29[8t]	−5.89

addition of aliquots of $C_2O_4^{2-}$. On the other hand, NHa/b peaks disappear during titration. In case of **L1**, upfield shift of 0.095 ppm is observed for CHc upon addition of ∼1 equivalent of $C_2O_4^{2-}$ (figures 6a and S5). Whereas in case of **L2**, 0.097 ppm upfield shift of CHc proton is found upon addition of ∼1 equivalent of $C_2O_4^{2-}$ (figures 7a and S6). Job's plot analysis based CHc proton shift shows 1:1 binding between **L1**/**L2** with $C_2O_4^{2-}$ (figures 6b and 7b). Both the receptors **L1** and **L2** show high binding affinity (∼10^4) towards $C_2O_4^{2-}$ in DMSO-d_6/D_2O (9:1, v/v) (table 2). Similar order of binding constant values for $C_2O_4^{2-}$ are also reported previously with other tripodal urea receptors **L3** and **L4**.[8t]

4. Conclusion

Thus we have demonstrated efficient encapsulation of two conformers of $C_2O_4^{2-}$ in semi-aqueous solvent by simple tripodal urea/thiourea receptors. Further, this study generalizes the $C_2O_4^{2-}$ encapsulation by simple tripodal neutral receptors with urea/thiourea functionalities. The single crystal X-ray structural study reveals trapping of $C_2O_4^{2-}$ inside the dimeric capsular assembly of the receptors by multiple N-H···O interactions. Three of the receptors show evidence of planar $C_2O_4^{2-}$ encapsulation whereas one receptor encapsulates staggered $C_2O_4^{2-}$ conformer. Solution state ^{1}H-NMR titration studies establish 1:1 (host/guest) binding between receptor and $C_2O_4^{2-}$ in semi-aqueous solvent. All the receptors bind $C_2O_4^{2-}$ with high binding constant (∼10^4) in semi-aqueous solvent.

Supplementary Information

Spectral data (^{1}H, ^{13}C NMR) for complex **1** and **2** are provided. Crystallographic table, selected geometric parameter and hydrogen bonding table for complex **1** and **2** are also provided. Equivalent plots of ^{1}H-NMR titration data for **L1** and **L2** with $C_2O_4^{2-}$. The electronic supplementary information can be seen at www.ias.ac.in/chemsci.

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References

1. (a) Janausch I G, Zientz E, Tran Q H, Kröger A and Unden G 2002 *Biochim. Biophys. Acta, Bioenerg.* **39** 1553; (b) Yurgel S N and Kahn M L 2004 *FEMS Microbiol. Rev.* **28** 489
2. Libert B and Franceschi V R 1987 *J. Agric. Food Chem.* **35** 926
3. (a) Holmes R P and Kennedy M 2000 *Kidney Int.* **57** 1662; (b) Al-Wahsh I A, Harry H T, Palmer R G, Reddy M B and Massey L K 2005 *J. Agric. Food Chem.* **53** 5670
4. (a) Bean P A 2012 *J. Chem. Educ.* **89** 417; (b) Dinnebier R E, Vensky S, Panthöfer M and Jansen M 2003 *Inorg. Chem.* **42** 1499
5. (a) Nelson J, Nieuwenhuyzen M, Pál I and Town R M 2004 *Dalton Trans.* 229; (b) Mateus P, Delgado R, Brandão P and Félix V 2011 *Chem. Eur. J.* **17** 7020; (c) Mateus P, Delgado R, Brandão P and Félix V 2012 *J. Org. Chem.* **77** 4611
6. (a) Tang L, Park J, Kim H -J, Kim Y, Kim S J, Chin J and Kim K M 2008 *J. Am. Chem. Soc.* **130** 12606; (b) Hu M and Feng G 2012 *Chem. Commun.* **48** 6951; (c) Rhaman M M, Fronczek F R, Powell D R and Hossain M A 2014 *Dalton Trans.* **43** 4618
7. Jiménez M B, Alcázar V, Peláez R, Sanz F, Arriba Á L F and Caballero M C 2012 *Org. Biomol. Chem.* **10** 1181
8. (a) Raposo C, Almaraz M, Martín M, Weinrich V, Mussõns M L, Alcázar V, Caballero M C and Morán J R 1995 *Chem. Lett*. 759; (b) Custelcean R, Moyer B A and Hay B P 2005 *Chem. Commun.* 5971; (c) Lakshminarayanan P S, Suresh E and Ghosh P 2006 *Inorg.Chem.* **45** 4372; (d) Lakshminarayanan P S, Ravikumar I, Suresh E and Ghosh P 2007 *Chem. Commun.* 5214; (e) Jose A, Kumar K, Ganguly B and Das A 2007 *Inorg. Chem.* **46** 5817; (f) Custelcean R, Remy P, Bronnesen P V, Jiang D and Moyer B A 2008 *Angew. Chem., Int. Ed.* **47** 1866; (g) Ravikumar I, Lakshminarayanan P S, Arunachalam M, Suresh E and Ghosh P 2009 *Dalton Trans.* 4160; (h) Custelcean R, Bock A and Moyer B A 2010 *J. Am. Chem. Soc.* **132** 7177; (i) Busschaert N, Gale P A, Haynes C J E, Light M E, Moore S J, Tong C C, Davis J T and Harrell Jr. W A 2010 *Chem. Commun*. **46** 6252; (j) Ravikumar I and Ghosh P 2010 *Chem. Commun.* **46** 1082; (k) Dey S K and Das G 2011 *Chem. Commun.* **47** 4983; (l) Dey S K and Das G 2011 *Dalton Trans.* **40** 12048; (m) Pramanik A, Powell D R, Wong B M and Hossain M A 2012 *Inorg. Chem.* **51** 4274;

(n) Dutta R, Bose P and Ghosh P 2013 *Dalton Trans.* **42** 11371; (o) Busschaert N, Wenzel M, Light M E, Hernández P-I, Tomás R-P and Gale P A 2011 *J. Am. Chem. Soc.* **133** 14136; (p) Arunachalam M and Ghosh P 2011 *Chem. Commun.* **47** 8477; (q) Bose P, Dutta R, Santra S, Chowdhury B and Ghosh P 2012 *Eur. J. Inorg. Chem.* 5791; (r) Akhuli B, Ravikumar I and Ghosh P 2012 *Chem. Sci.* **3** 1522; (s) Custelcean R 2013 *Chem. Commun.* **49** 2173; (t) Bose P, Dutta R and Ghosh P 2013 *Org. Biomol. Chem.* **11** 4581

9. (a) SAINT and *XPREP*, 5.1 ed.; Siemens Industrial Automation Inc.: Madison, WI, 1995 Sheldrick G M; (b) *SADABS*, *Empirical absorption correction program*; University of Göttingen: Göttingen, Germany, 1997
10. Sheldrick G M 1997 *SHELXTL* Reference manual: Version 5.1; Madison, WI: Bruker AXS
11. Sheldrick G M 1997 *SHELXL-97*: Program for crystal structure refinement; University of Göttingen: Göttingen, Germany
12. Spek A L 1997 *PLATON-97*; University of Utrecht: Utrecht, The Netherlands
13. Mercury 2.2 supplied with Cambridge Structural Database, CCDC, Cambridge, UK
14. (a) Olsen J A, Banner D W, Seiler P, Sander U O, D'Arcy A, Stihle M, Müller K and Diederich, F 2003 *Angew. Chem. Int. Ed.* **42** 2507; (b) Fischer, F R, Schweizer W B and Diederich, F 2007 *Angew. Chem. Int. Ed*. **46** 8270