

Supporting Information

Tris(2-aminoethyl)amine Based Tripodal Urea Receptors for Oxalate: Capsulation of Staggered vs. Planar Conformers

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Purnandhu Bose, Ranjan Dutta and Pradyut Ghosh*

Indian Association for the Cultivation of Science, 2A&2B Raja S. C. Mullick Road, Kolkata 700 032,

India. Fax: (+91) 33-2473-2805

E-mail: icpg@iacs.res.in

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Experimental Section

Reagents and general methods

Compounds **L1** was prepared as previously described literature procedure.¹ Tris-(2-aminoethyl)-amine (TREN), 3-cyanophenyl isocyanate, 3-fluorophenyl isocyanate, tetrabutylammonium iodide (TBAI) were purchased from Sigma-Aldrich and were used as received. Dichloromethane (DCM) was freshly distilled with calcium hydride. Potassium oxalate dihydrate ($K_2C_2O_4 \cdot 2H_2O$), Sodium acetate (NaOAc), Sodium benzoate (NaOBz) and Sodium terephthalate [$Na_2(C_8H_4O_4)$] were purchased from Merck, India and used as received. All solvents were procured from Merck, India. HRMS was recorded on a QtofMicro YA263 mass spectrometer. 1H -NMR and ^{13}C -NMR spectra were recorded on 500/300 MHz and 125/75 MHz Bruker DPX-500 MHz NMR and Bruker Avance 300 Spectrometer. Elemental analyses for the synthesized receptor **L2** was carried out with Perkin-Elmer 2500 series II elemental analyzer.

Single-crystal X-ray studies

Crystals suitable for single crystal X-ray diffraction studies were selected from the mother liquor and immersed in paratone oil and then mounted on the tip of a glass fibre and cemented using epoxy resin. Intensity data for the crystals of capsular aggregates **C1** and **C2** were collected using MoK_{α} ($\lambda = 0.7107 \text{ \AA}$) radiation on a Bruker SMART APEX II diffractometer equipped with CCD area detector at 100 K. The data integration and reduction were processed with SAINT² software provided with the software package of SMART APEX II. An empirical absorption correction was applied to the collected reflections with SADABS.³ The structures were solved by direct methods using SHELXTL⁴ and were refined on F^2 by the full-matrix least-squares technique using the SHELXL-97⁵ program package. Graphics were generated using PLATON⁶ and MERCURY 2.4.⁷ The non-hydrogen atoms were refined anisotropically till the convergence. In the case of crystals of **C1** and **C2**, all the hydrogen atoms were located from the difference Fourier map and refined isotropically.

¹H-NMR titration studies

All ¹H-NMR titration experiments for **L1** and **L2** were conducted on a Bruker 500 MHz spectrometer at 298 K respectively. Potassium oxalate dihydrate (K₂C₂O₄·2H₂O) was used to prepare the stock solution of anion in DMSO-*d*₆: D₂O (1:1.1) solvent system. Lower solubility of potassium oxalate in DMSO-*d*₆ or even in (1:1) DMSO-*d*₆ prevent us to maintain a similar solvent system throughout the titration. Host solution was prepared in DMSO-*d*₆: D₂O (9:1) solvent mixture. In a typical titration experiment, an aliquot of 8 μL of C₂O₄²⁻ (~40 mM) is titrated into a solution of respective host (~5 mM). Each titration experiment is repeated keeping the experimental conditions intact. To evaluate the association constants and mode of binding in case of oxalate (C₂O₄²⁻) anion with **L1** and **L2**, ¹H-NMR titrations were performed at 298 K. Aliquots of standard solution of C₂O₄²⁻ was added to the solution of **L1** and **L2** in DMSO-*d*₆. The association constants, log K were calculated by fitting the change in the –CH proton chemical shift with a 1:1 association model with non-linear least square analysis. Job's plot revealed a best fit for 1:1 host to guest binding mode. WINEQNMR 2.0⁸ was used for the evaluation of binding constants. The equation $\Delta\delta = \frac{\{([A]_0 + [L]_0 + 1/K) \pm (([A]_0 + [L]_0 + 1/K)^2 - 4[L]_0[A]_0)^{1/2}\} \Delta\delta_{\max}}{2[L]_0}$ was used for calculating association constants.

Synthesis of L1 and L2

The tripodal receptors **L1** was synthesized following literature procedure and characterization data were matched with the literature data.¹ The synthesis of new receptor **L2** was described below. 2.28 mL (20 mmol) of 3-fluorophenyl isocyanate was dissolved in 25 mL of dry dichloromethane (DCM) at room temperature in a 100 mL 2-neck round bottomed flask equipped with a dropping funnel. Then TREN (1.0 mL, 6.5 mmol) was dissolved in 25 mL of dry DCM and was added drop-wise using a dropping funnel with constant stirring. The resulting solution was stirred for another 1 h at room temperature under nitrogen atmosphere. It was then allowed to stir overnight at ambient condition. The

white precipitate formed was filtered off and washed with DCM and diethyl ether. The collected precipitate was dried in air. Yield of **L2** is 98%. ^1H NMR (500 MHz, DMSO- d_6): δ 2.593 (t, 6H, $J = 6.5$ Hz, NCH_2), 3.180 (d, 6H, $J = 5.5$ Hz, NCH_2CH_2), 6.217 (t, 3H, $J = 5.5$ Hz, NH_b), 6.672 (t, 3H, $J = 7.5$ Hz, Ar-H), 7.000 (d, 3H, $J = 9.0$ Hz, Ar-H), 7.181-7.228 (m, 3H, Ar-H), 7.428 (d, 3H, $J = 11.5$ Hz, 5 Ar-H), 8.755 (s, 3H, NH_a); ^{13}C NMR (125 MHz, DMSO- d_6): δ 38.14 (NCH_2), 54.40 (NCH_2CH_2), 104.97 (d, Ar-C, $J = 43.7$ Hz), 107.89 (d, Ar-C, $J = 35.0$ Hz), 113.99 (Ar-C), 130.68 (Ar-C), 142.99 (d, Ar-C, $J = 18.7$ Hz), 155.70 (C=O), 161.45 (Ar-C); HRMS (+ESI) calcd for $[\text{C}_{27}\text{H}_{30}\text{F}_3\text{N}_7\text{O}_3]$: [**L2** + H^+] calcd 558.2362, found 558.3456; Elemental analysis calcd: C 58.16, H 5.42, N 17.58; found: C 58.08, H 5.31, N 17.49.

10 Synthesis of **C1**

60 mg (0.10 mmol) of **L1** was dissolved in DMSO/ H_2O (20:1 v/v) and then 74 mg (~2 equiv.) of $n\text{-Bu}_4\text{N}^+\text{T}$ and excess $\text{K}_2\text{C}_2\text{O}_4 \cdot 2\text{H}_2\text{O}$ was added to the above solution. Then the mixture was stirred at room temperature for 10 minutes and then heated to 60°C . The mixture was then filtered and allowed to evaporate for crystallization. After 3-4 days, colorless block like crystals of capsular aggregate
15 [**(L1)** $_2(\text{C}_2\text{O}_4^{2-})(n\text{-Bu}_4\text{N}^+)_2$] (**C1**) suitable for single crystal X-ray diffraction analysis were obtained in 80% yield. ^1H NMR (300 MHz, DMSO- d_6): δ 0.931 (t, 12H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$, $J = 7.35$ Hz), 1.245-1.366 (m, 8H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 1.512-1.614 (m, 8H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 2.494 (NCH_2CH_2 , overlaps with solvent peak), 3.129-3.183 (m, 14H, NCH_2CH_2 and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 7.194-7.306 (m, 9H, NH_b and Ar-H), 7.648 (d, 3H, $J = 8.1$ Hz), 7.937 (s, 3H), 9.709 (s, 3H, NH_a); ^{13}C NMR (75
20 MHz, DMSO- d_6): δ 14.06 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 19.81 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 23.67 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$) 37.86 (NCH_2), 54.43 (NCH_2CH_2), 58.17 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 111.69 (CN), 119.55 (Ar-C), 120.57 (Ar-C), 122.59 (Ar-C), 124.45 (Ar-C), 129.94 (Ar-C), 142.25 (Ar-C), 155.72 (C=O), 173.58 (oxalate C=O), Elemental analysis calcd: C 65.25, H 7.69, N 17.81; found: C 65.19, H 7.64, N 17.67.

Synthesis of C2

56 mg (0.10 mmol) of **L2** was dissolved in DMSO/H₂O (20:1 v/v) and then 77 mg (~2 equiv.) of *n*-Bu₄N⁺Γ and excess K₂C₂O₄·2H₂O was added to the above solution. Then the mixture was stirred at room temperature for 10 minutes and then heated to 60°C. The mixture was then filtered and allowed to evaporate for crystallization. After one week, colorless block like crystals of capsular aggregate [(**L2**)₂(C₂O₄²⁻)(*n*-Bu₄N⁺)₂] (**C2**) suitable for single crystal X-ray diffraction analysis were obtained in 75% yield. ¹H NMR (500 MHz, DMSO-*d*₆): δ 0.914 (t, 12H, NCH₂CH₂CH₂CH₃, *J* = 7.25 Hz), 1.270-1.314 (m, 8H, NCH₂CH₂CH₂CH₃), 1.547 (8H, NCH₂CH₂CH₂CH₃), 2.464 (6H, NCH₂CH₂), 3.084-3.156 (m, 14H, NCH₂CH₂ and NCH₂CH₂CH₂CH₃), 6.554 (t, 3H, *J* = 8.0 Hz, Ar-H), 6.982-7.026 (m, 10 3H, Ar-H), 7.109 (d, 3H, Ar-H), 7.245 (s, 3H, NH_b), 7.483 (s, 3H, *J* = 12.5 Hz, Ar-H), 9.561 (s, 3H, NH_a); ¹³C NMR (75 MHz, DMSO-*d*₆): δ 14.07 (NCH₂CH₂CH₂CH₃), 19.80 (NCH₂CH₂CH₂CH₃), 23.67 (NCH₂CH₂CH₂CH₃), 38.11 (NCH₂), 55.01 (NCH₂CH₂), 58.16 (NCH₂CH₂CH₂CH₃), 104.92 (d, Ar-C, *J* = 26.4 Hz), 107.33 (d, Ar-C, *J* = 20.7 Hz), 114.12 (Ar-C), 130.11 (d, Ar-C, *J* = 9.9 Hz), 143.54 (d, Ar-C, *J* = 11.6 Hz), 155.99 (C=O), 161.32 (Ar-C), 173.53 (oxalate C=O), Elemental analysis calcd: C 62.61, H 7.88, N 13.28; found: C 62.57, H 7.84, N 13.27.

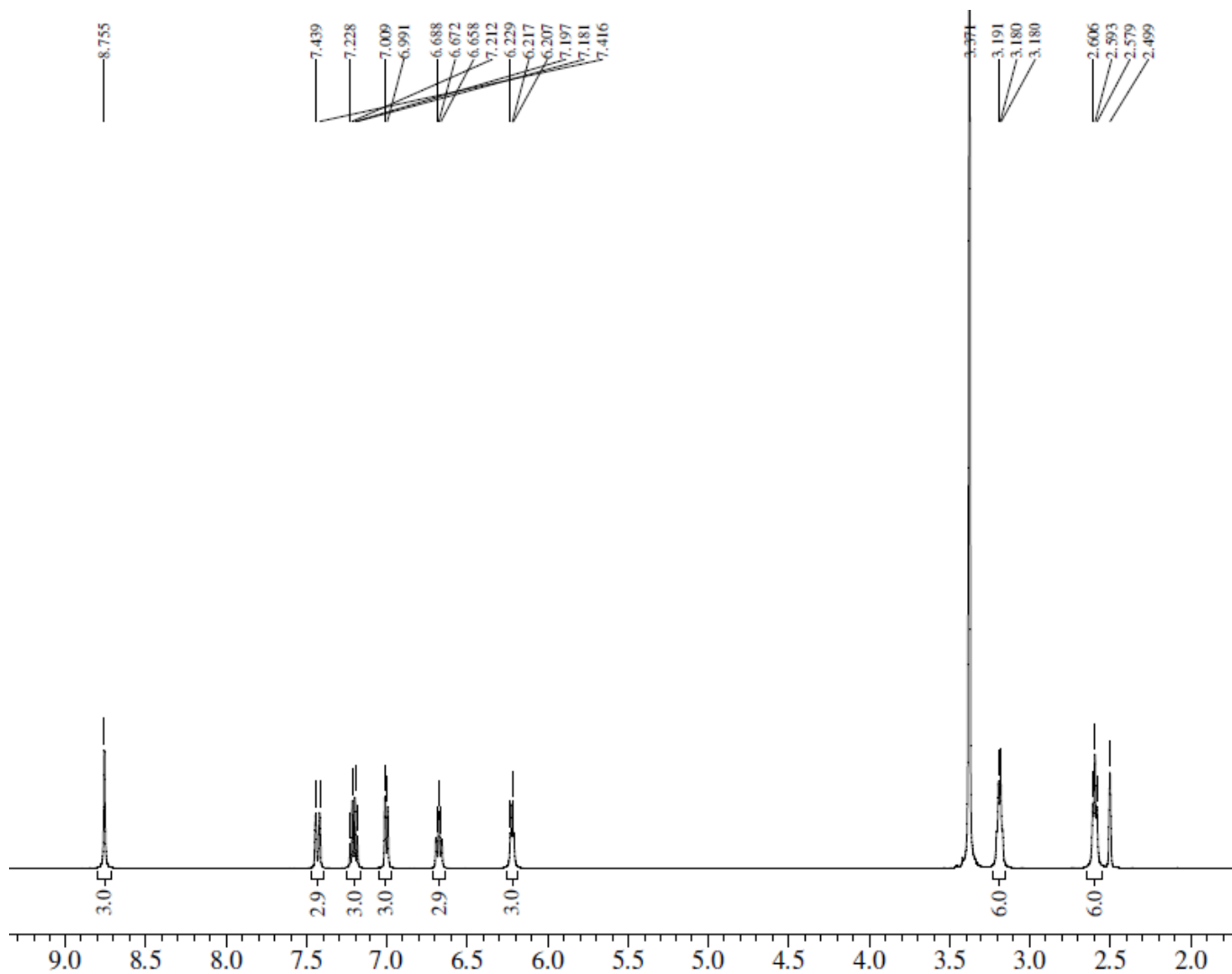


Figure 1S. ¹H-NMR spectra of L2 in DMSO-*d*₆ at 298K.

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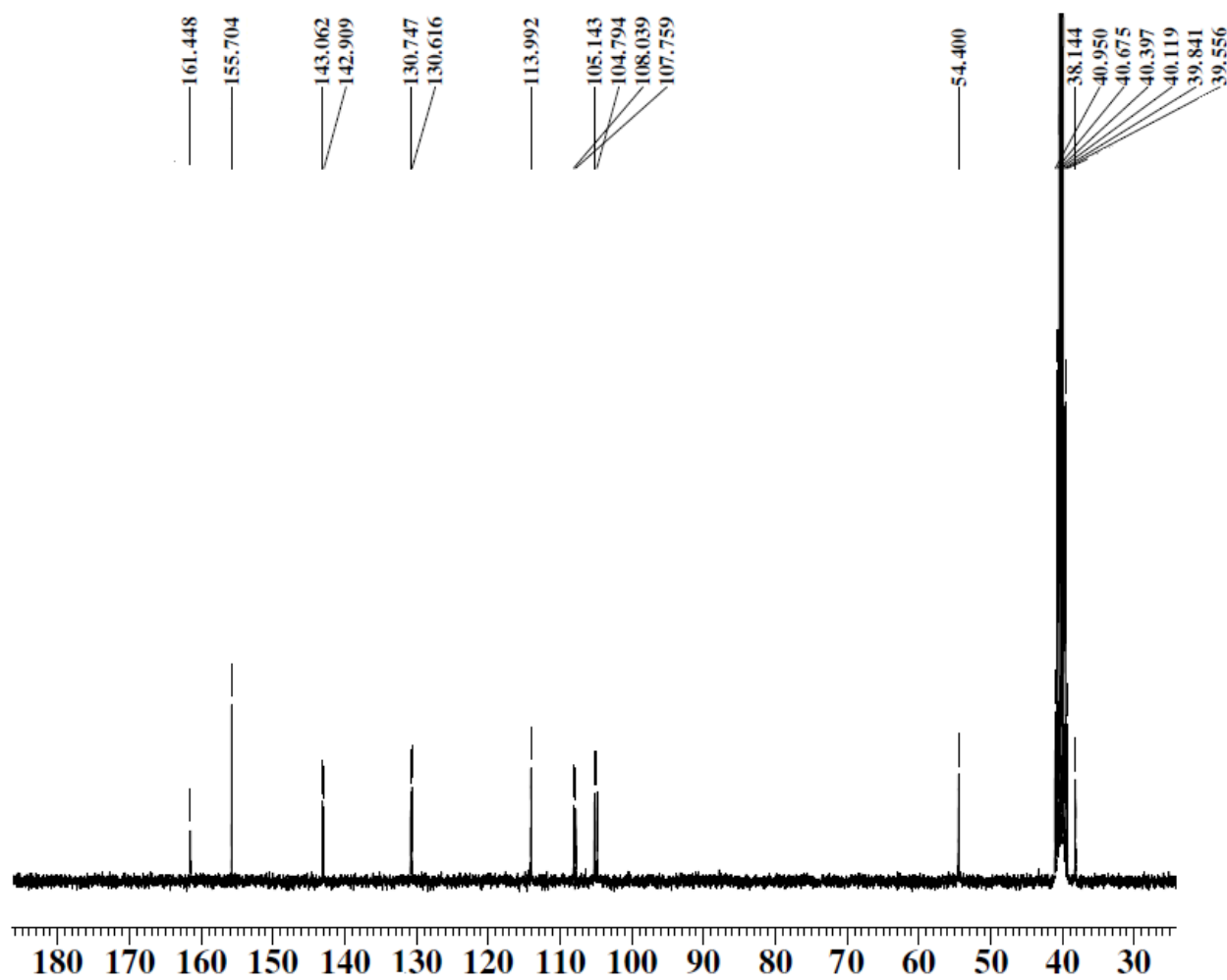


Figure 2S. ^{13}C -NMR spectra of L2 in $\text{DMSO-}d_6$ at 298K.

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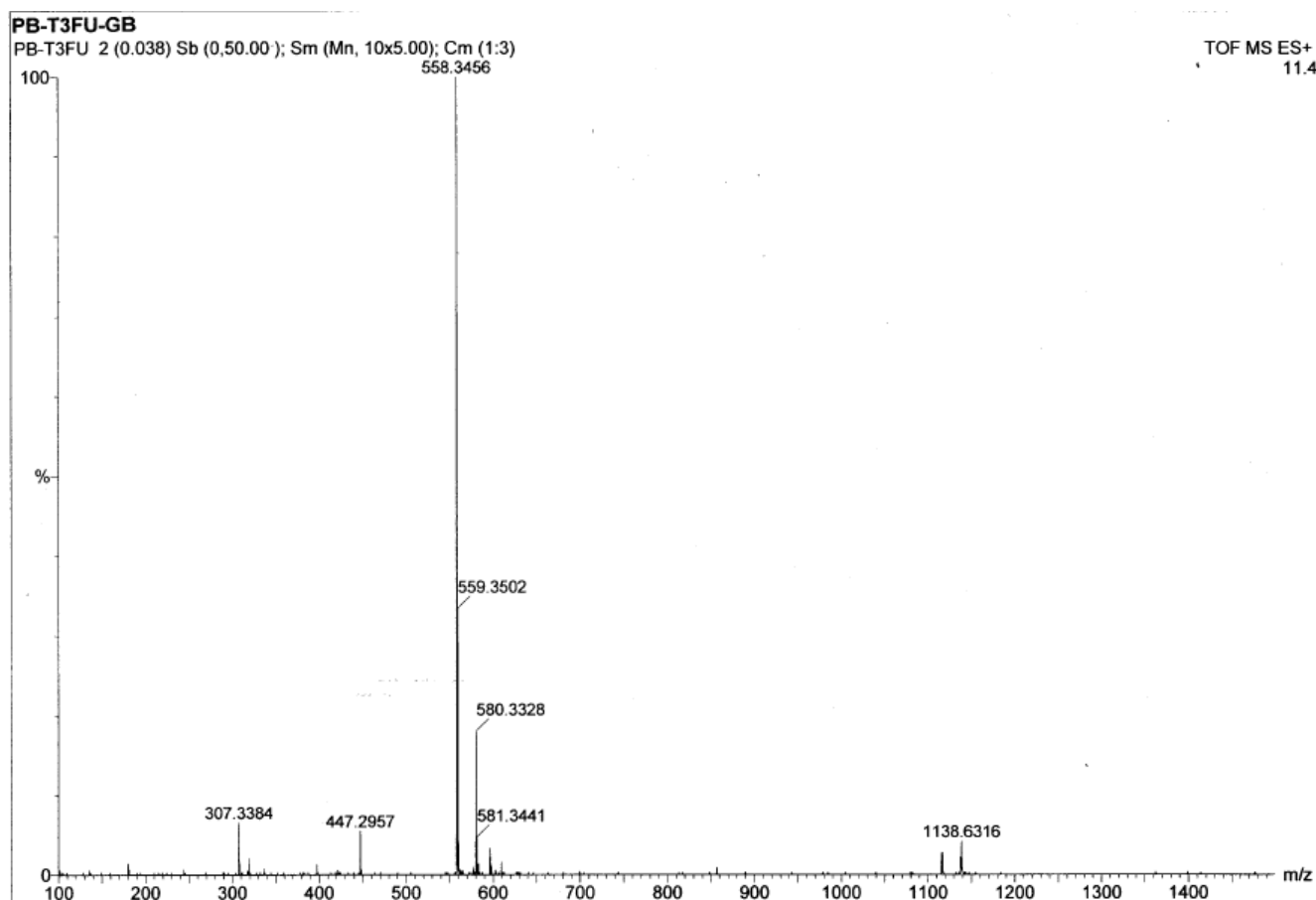


Figure 3S. (+ve) HRMS spectra of **L2**.

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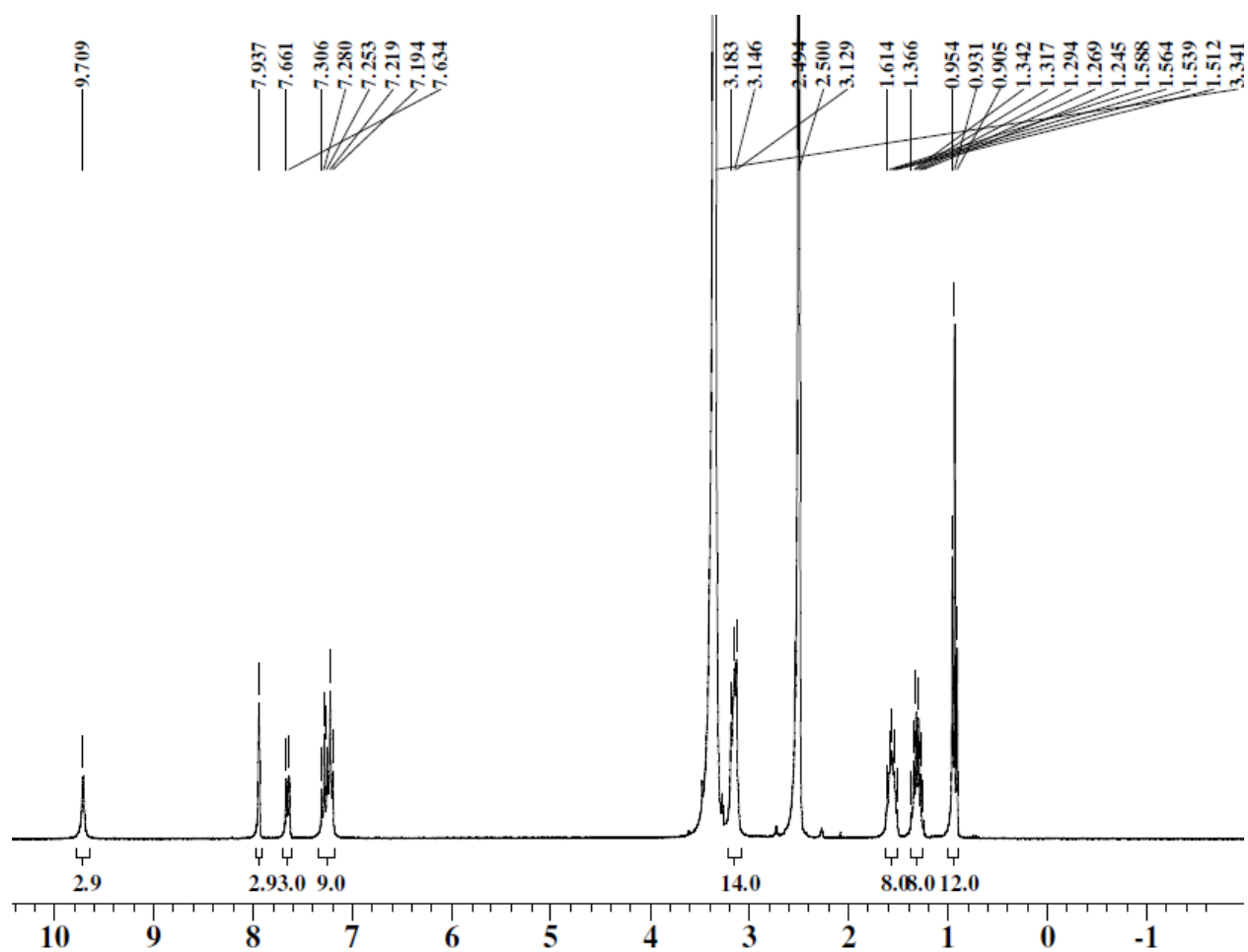


Figure 4S. $^1\text{H-NMR}$ spectra of C1 in $\text{DMSO-}d_6$ at 298K.

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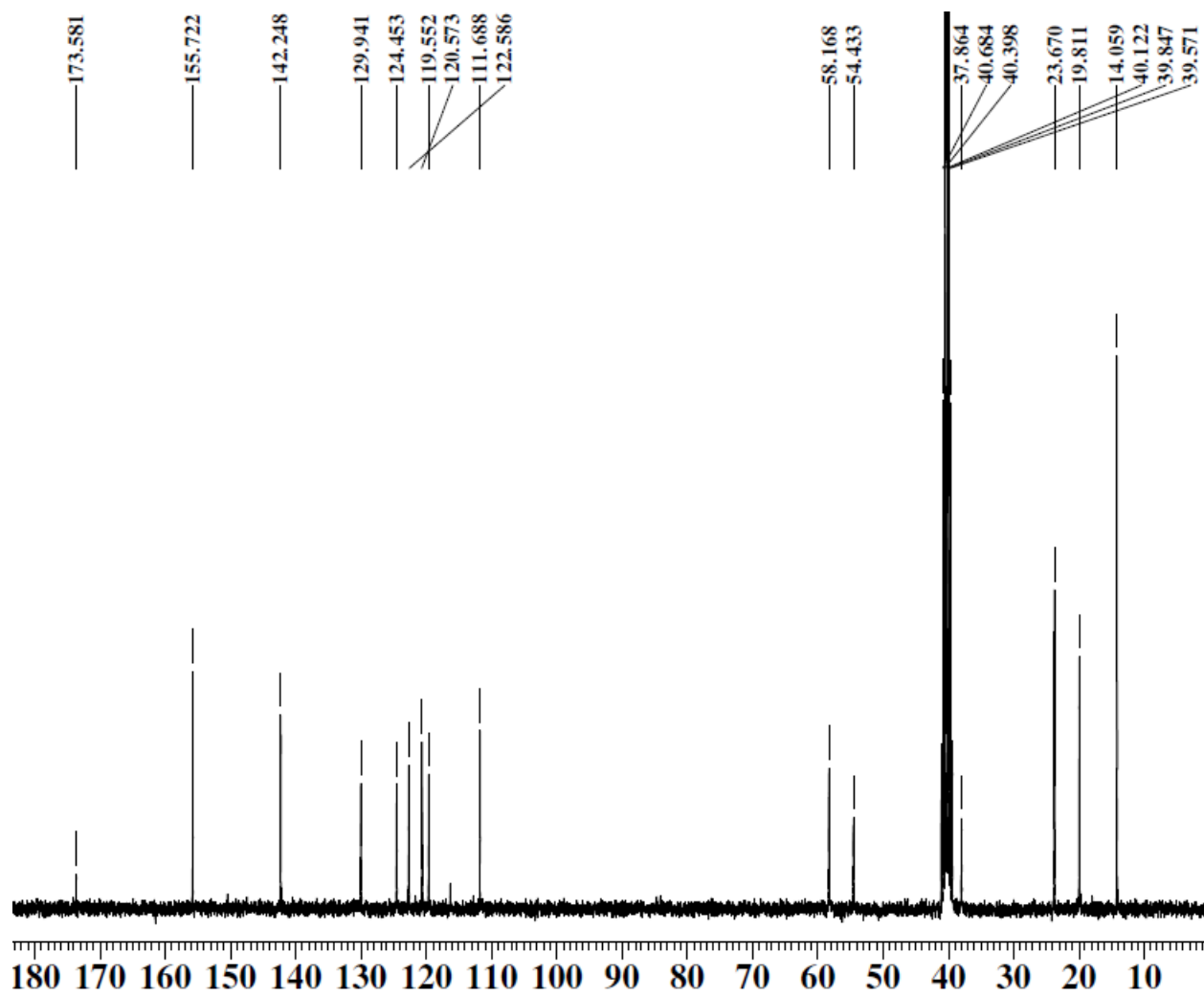


Figure 5S. ^{13}C -NMR spectra of **C1** in $\text{DMSO-}d_6$ at 298K.

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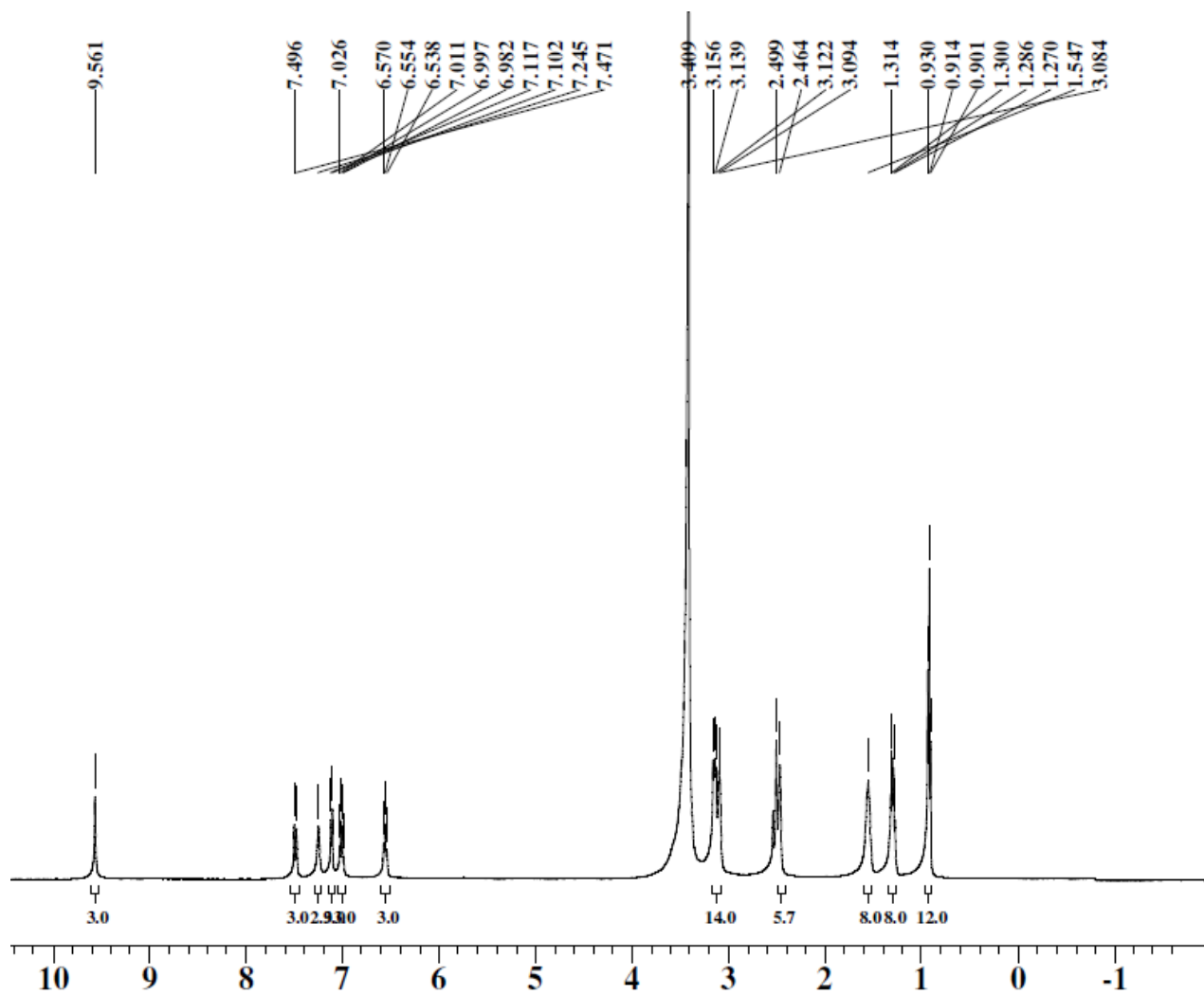


Figure 6S. ¹H-NMR spectra of C2 in DMSO-*d*₆ at 298K.

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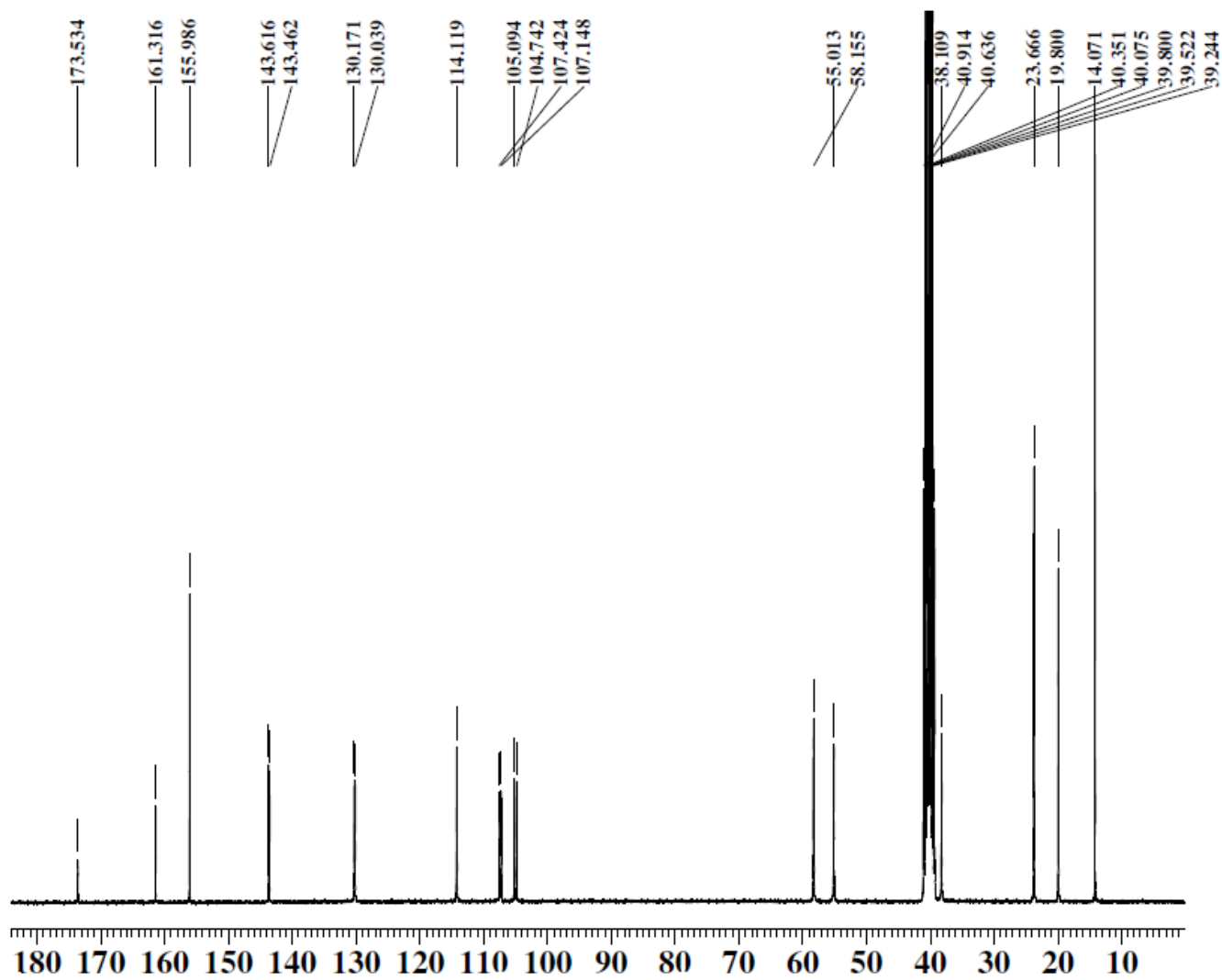
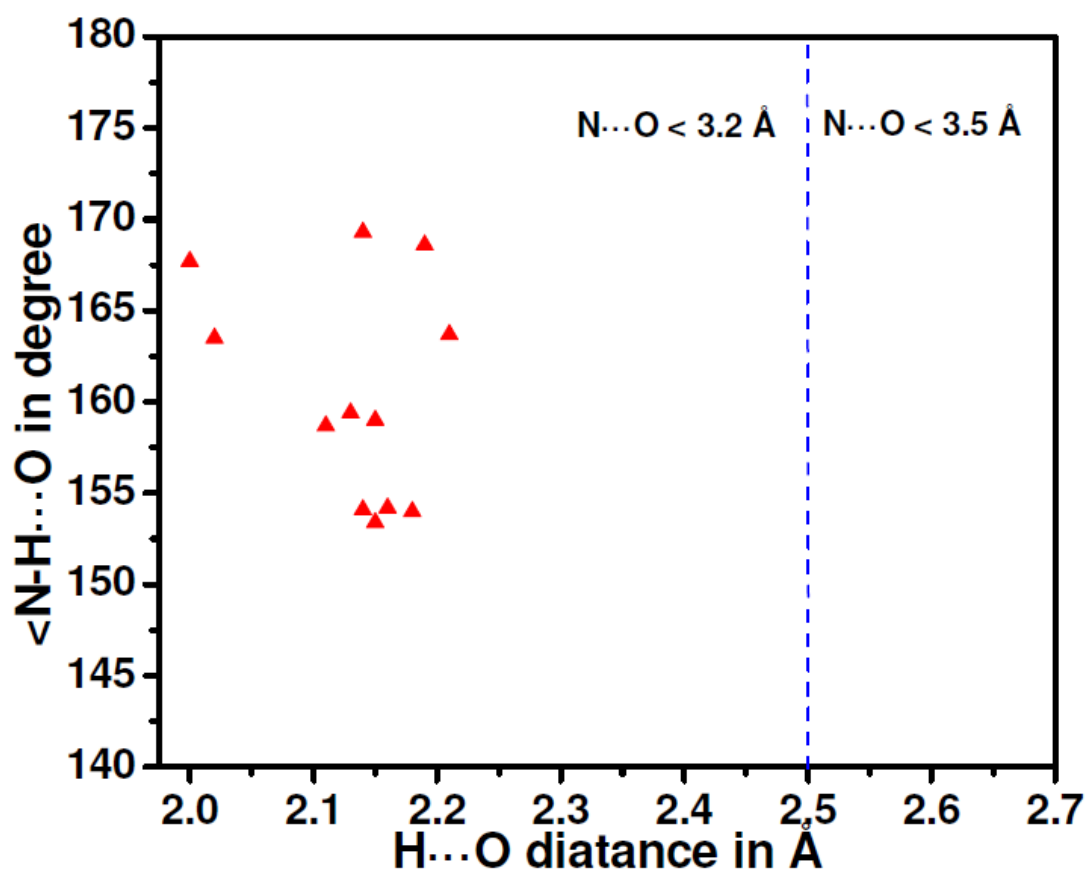


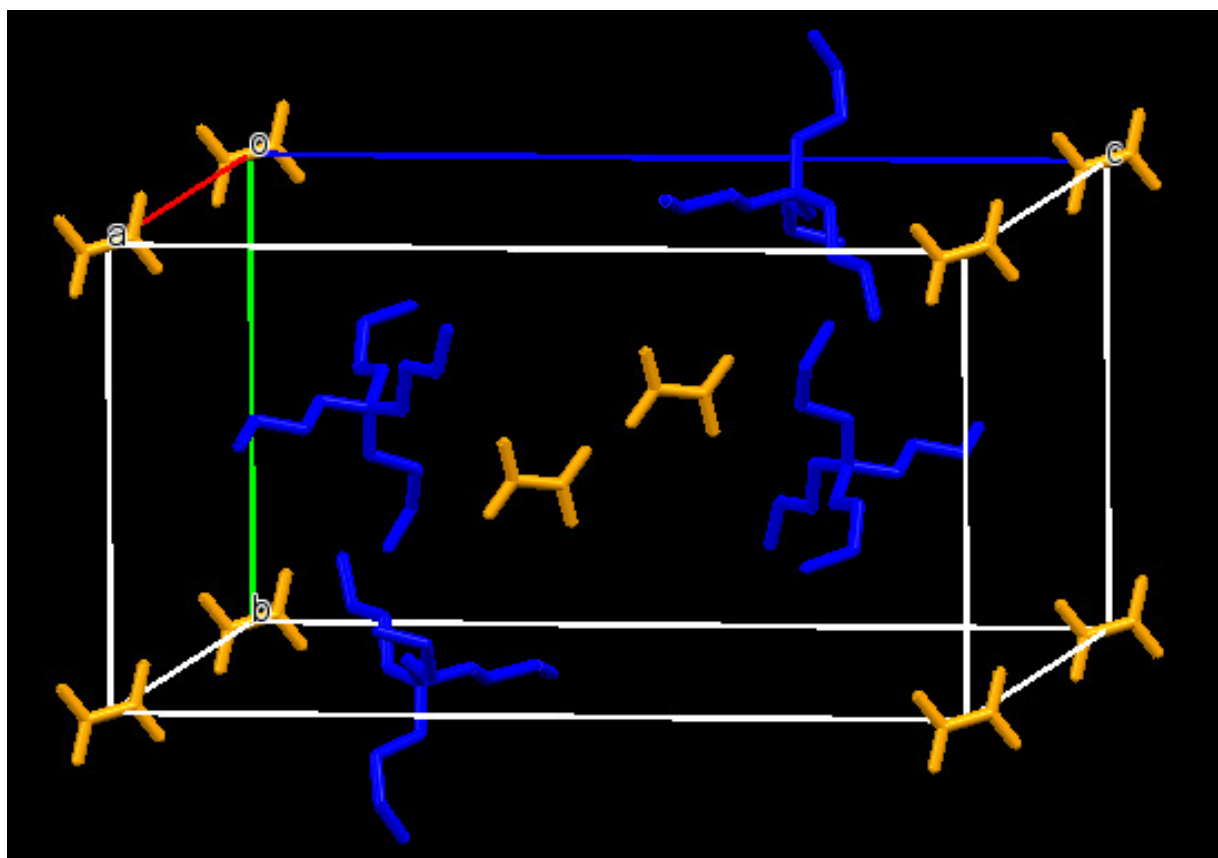
Figure 7S. ^{13}C -NMR spectra of **C2** in $\text{DMSO-}d_6$ at 298K.



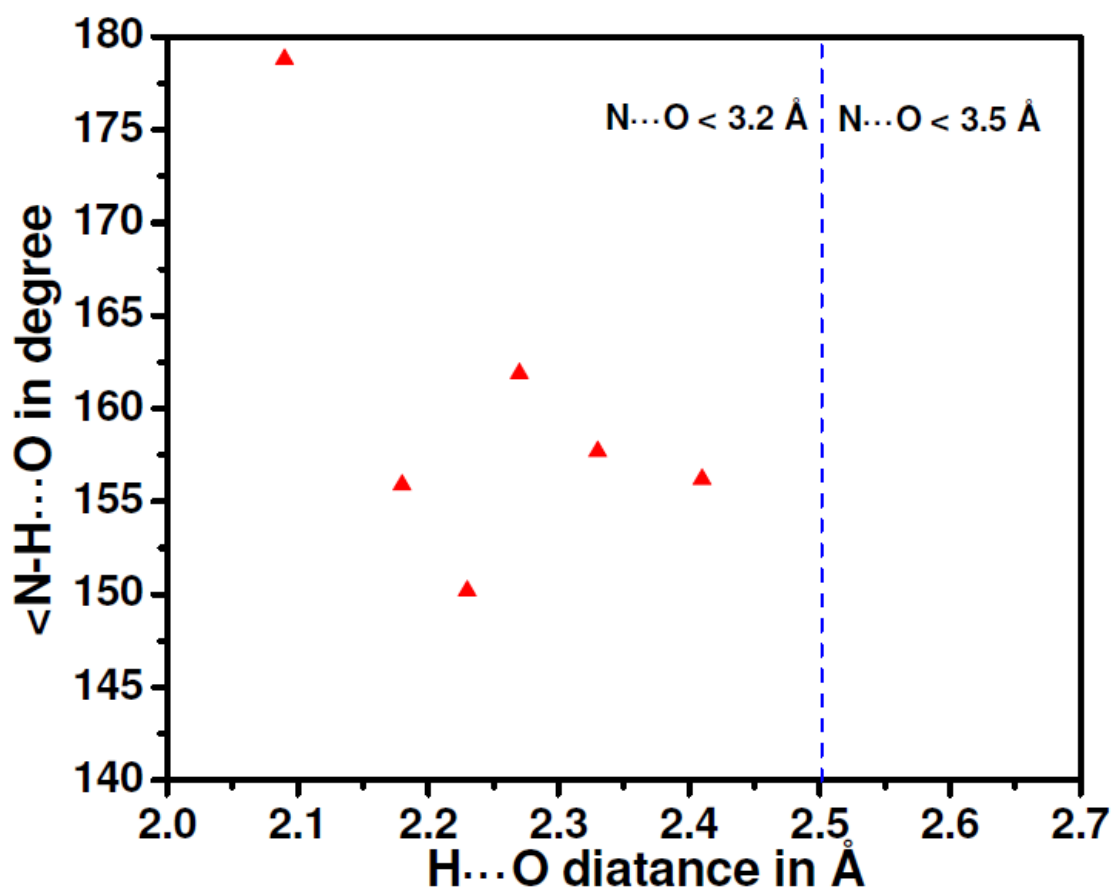
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Figure 8S. The scatter plot of N-H...O vs. H...O distances of the hydrogen bonds in **C1**.

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10 **Figure 9S.** Crystal packing of oxalate and tetrabutylammonium counter cations in the unit cell of **C2**.



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Figure 10S. The scatter plot of N–H...O vs. H...O distances of the hydrogen bonds in C2.

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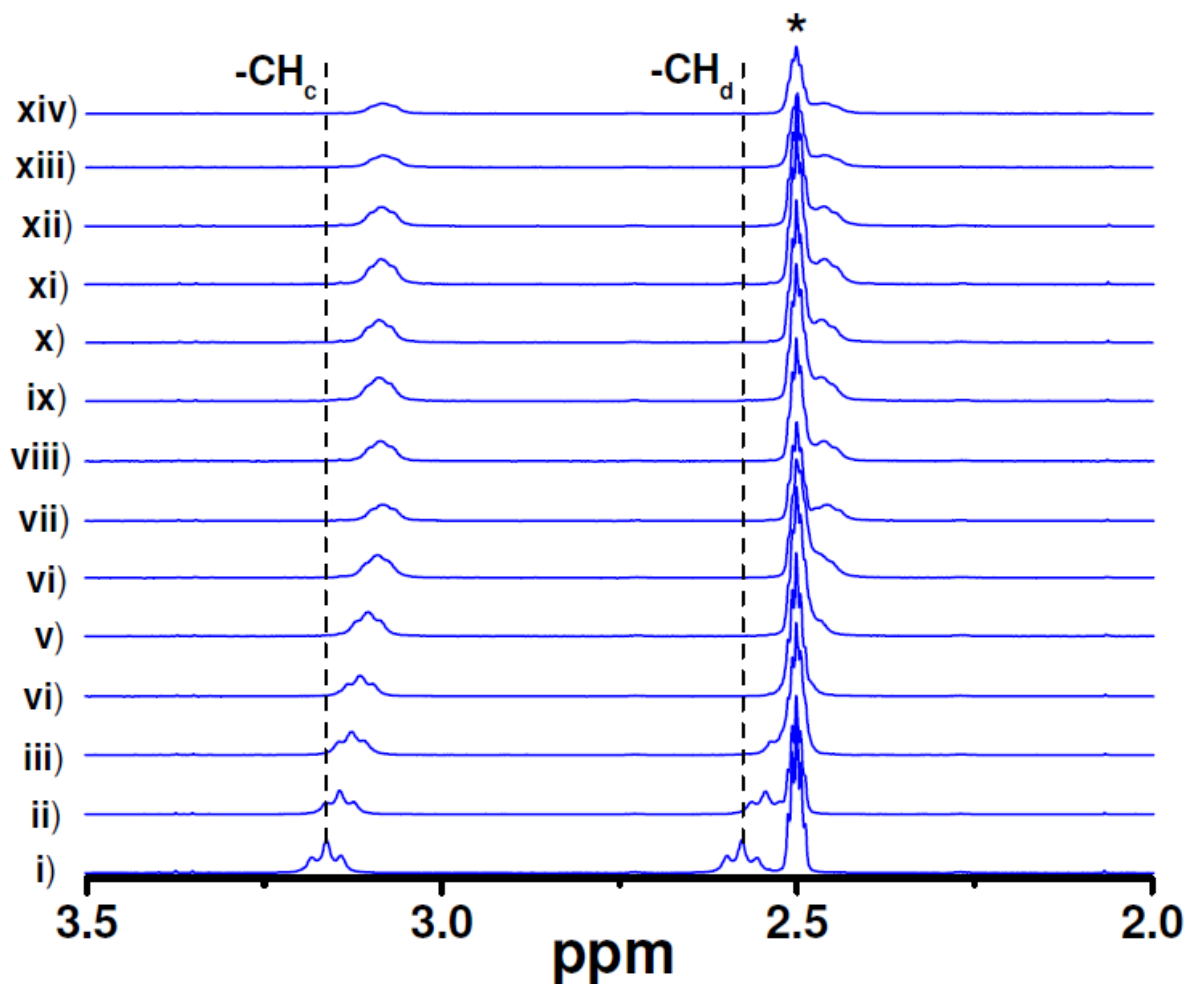


Figure 11S. a) Partial $^1\text{H-NMR}$ (300 MHz) spectral changes of **L1** in $\text{D}_2\text{O}:\text{DMSO-}d_6$ (1:9, v/v) with added standard $\text{K}_2\text{C}_2\text{O}_4$ solution in $\text{D}_2\text{O}:\text{DMSO-}d_6$ (1.1:1, v/v) (298 K) ($[\text{L1}]_0 = 4.94$ mM). Ratio of concentration $[\text{C}_2\text{O}_4^{2-}]/[\text{L1}]$: (i) 0, (ii) 0.129, (iii) 0.258, (iv) 0.387, (v) 0.517, (vi) 0.646, (vii) 0.775, (viii) 0.904, (ix) 1.033, (x) 1.162, (xi) 1.421, (xii) 1.938, (xiii) 2.584 and (xiv) 2.971 ($[\text{L1}]$ is varied from 4.94 to 3.61 mM by the addition of aliquots of 39.91 mM $\text{K}_2\text{C}_2\text{O}_4$) (* indicates the $\text{DMSO-}d_6$ solvent peak).

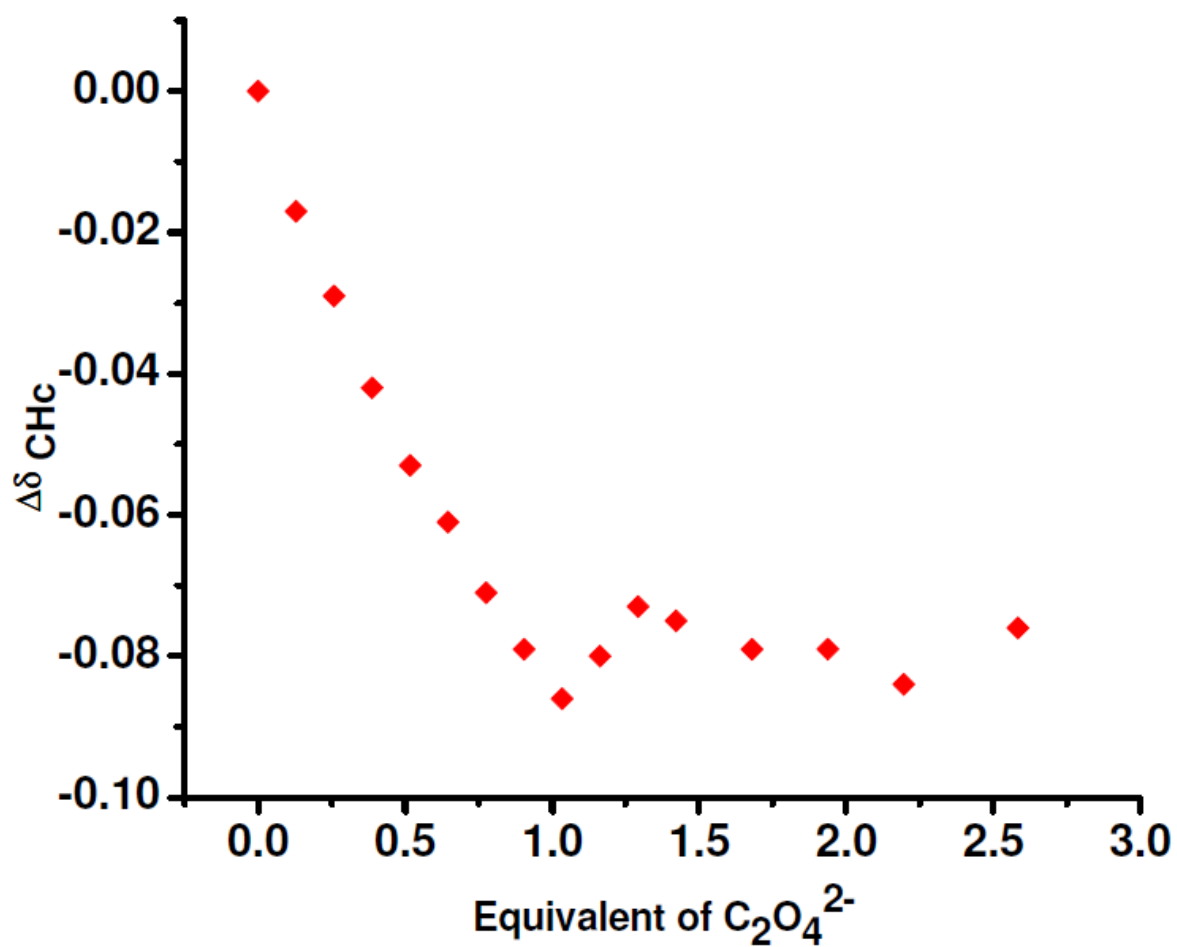


Figure 12S. Plot shows the change in chemical shift of the $-CH_c$ of **L1** with increasing amounts of standard $K_2C_2O_4$ solution at 298K.

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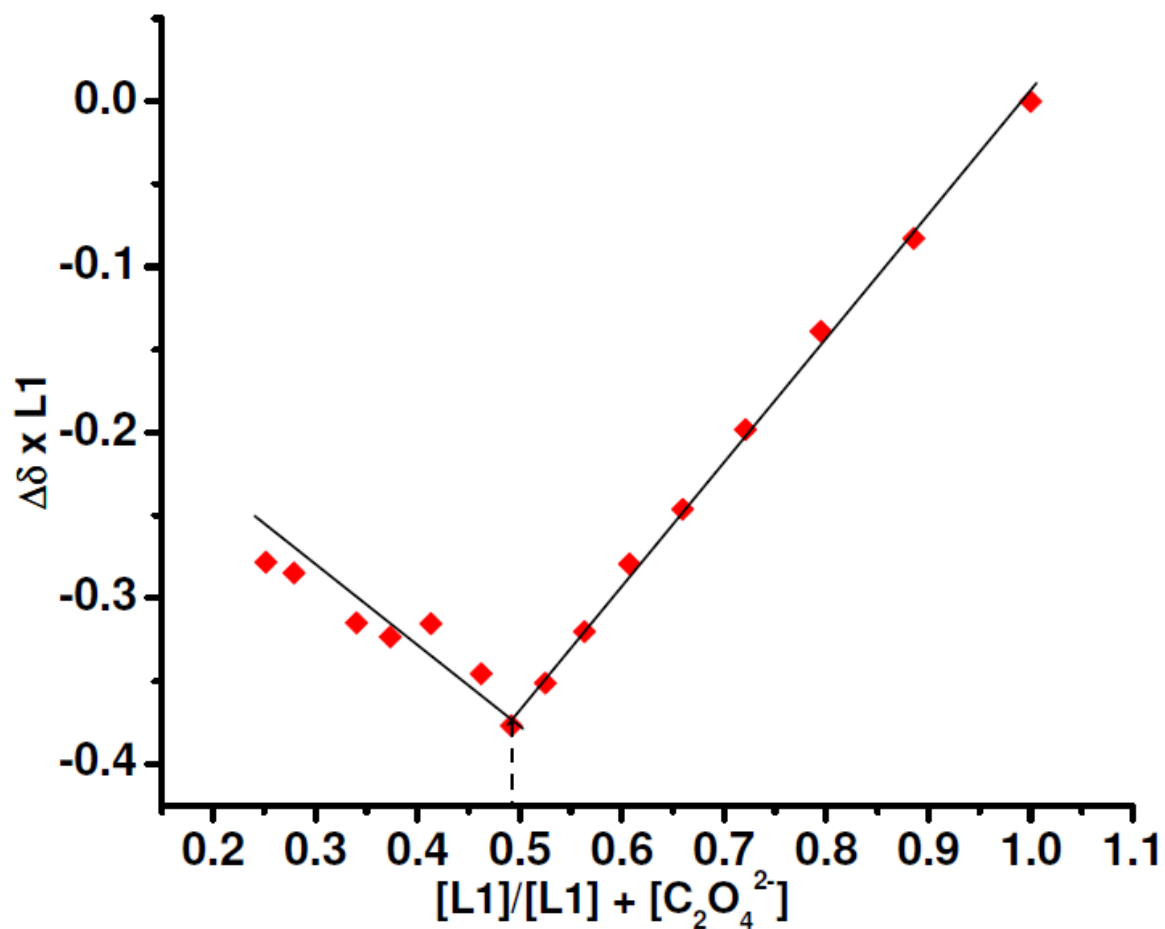
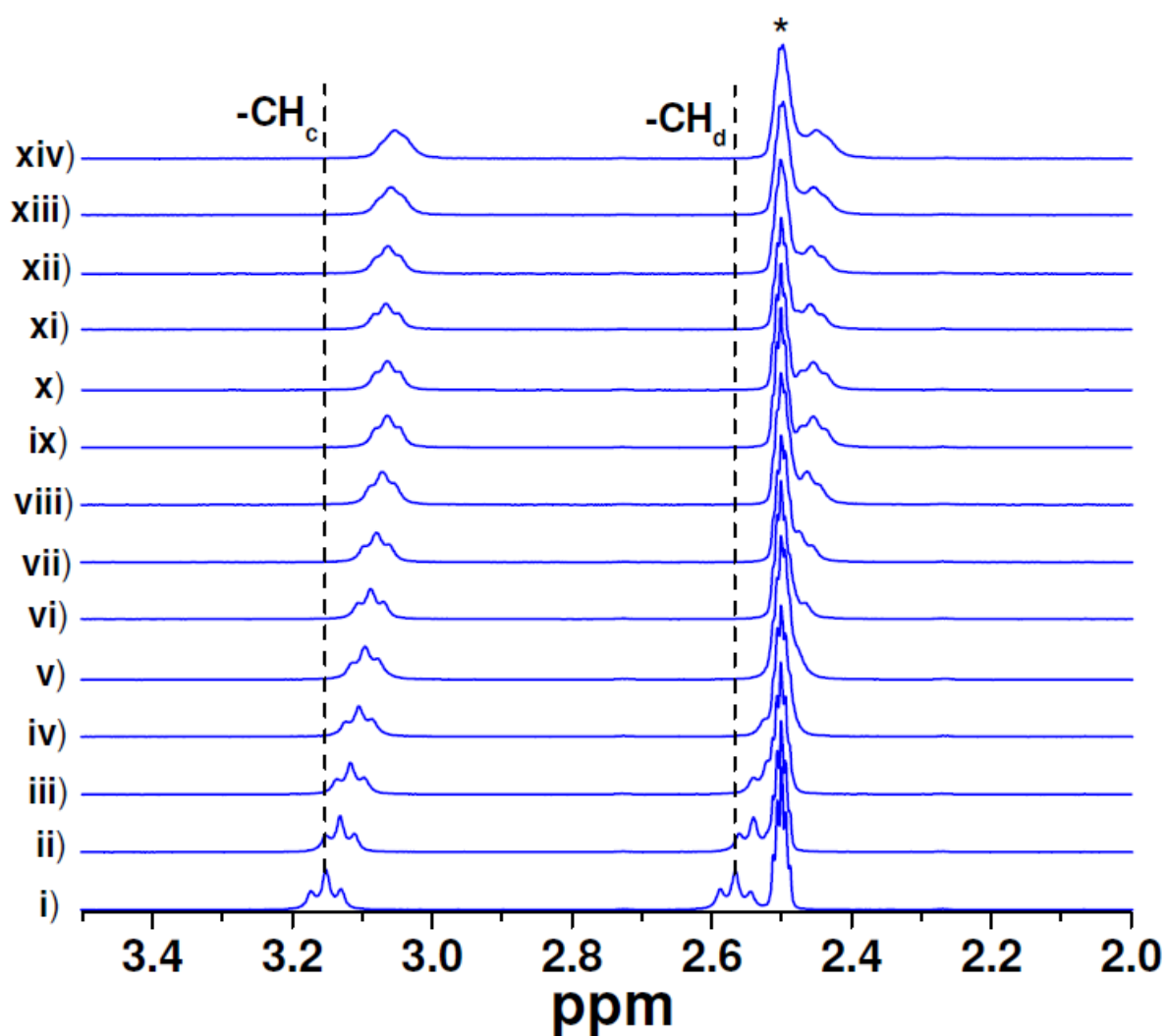


Figure 13S. Job's Plot of L1 with $K_2C_2O_4$ in DMSO- d_6 / D_2O (1:1.1)(v/v) at 298K.

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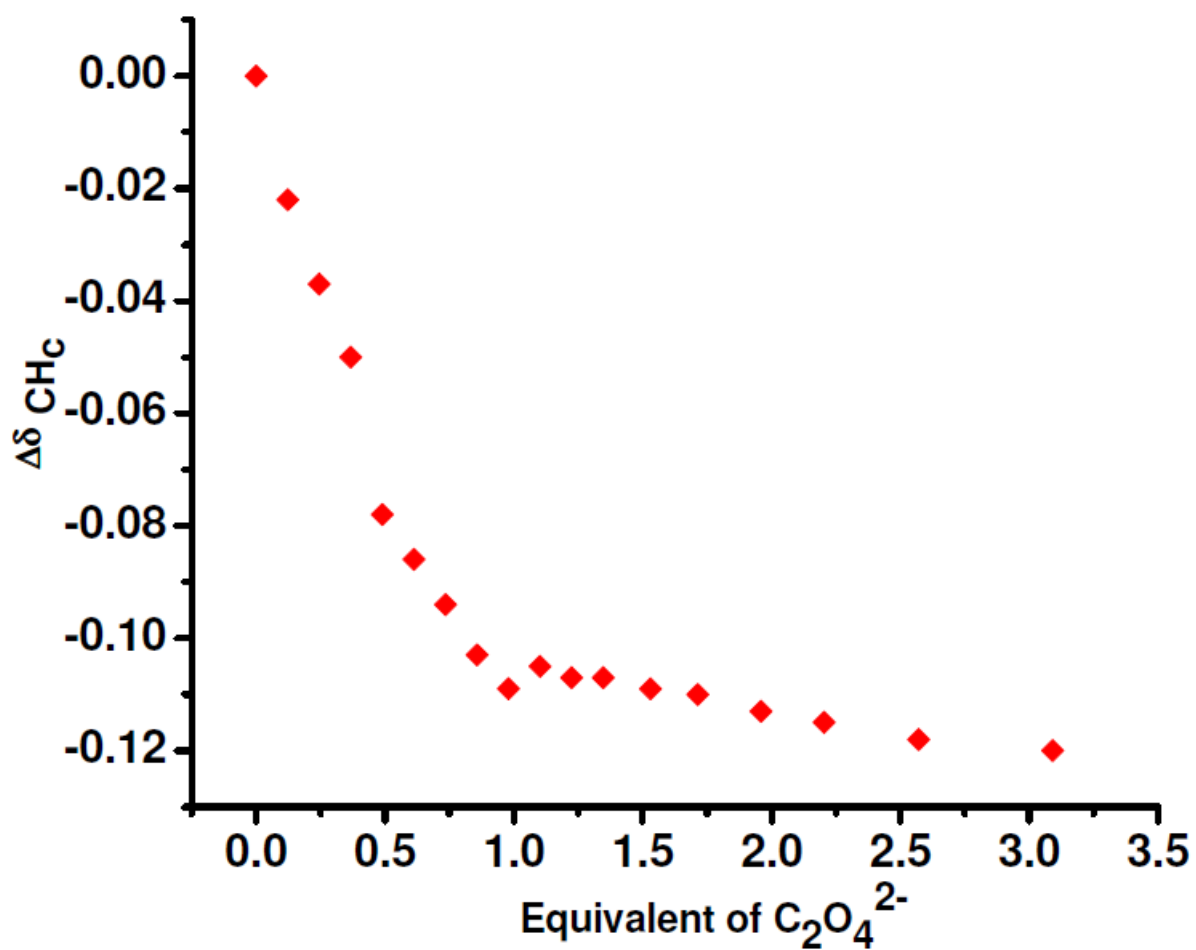


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Figure 14S. (a) Partial ¹H-NMR (300 MHz) spectral changes of **L2** in DMSO-*d*₆ with added standard K₂C₂O₄ solution in DMSO-*d*₆/D₂O (1:1.1) (298 K) ([**L2**]₀ = 4.77 mM). Ratio of concentration [C₂O₄²⁻]/[**L2**]: (i) 0, (ii) 0.122, (iii) 0.245, (iv) 0.367, (v) 0.490, (vi) 0.612, (vii) 0.734, (viii) 0.857, (ix) 0.979, (x) 1.012, (xi) 1.350, (xii) 1.714, (xiii) 2.203 and (xiv) 3.091 ([**L1**] is varied from 4.77 to 3.39 mM by the addition of aliquots of 36.49 mM K₂C₂O₄) (* indicates the DMSO-*d*₆ solvent peak).

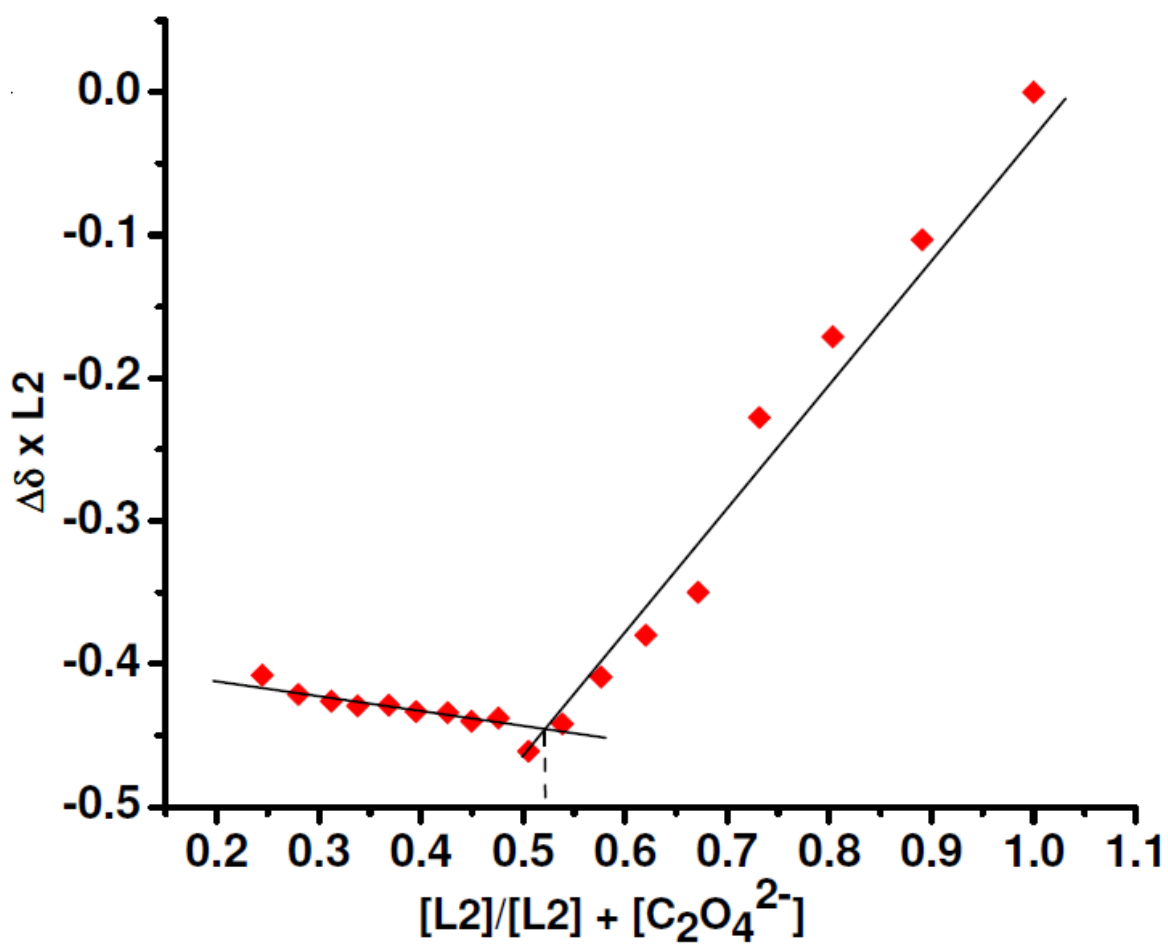
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10 **Figure 15S.** Plot shows the change in chemical shift of the $-CH_c$ of L2 with increasing amounts of standard $K_2C_2O_4$ solution at 298K.

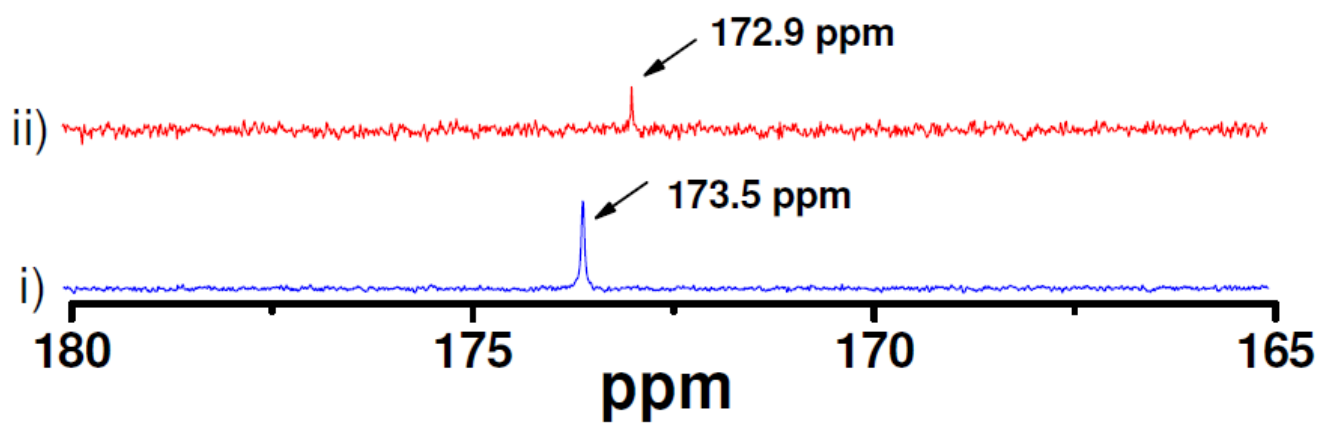
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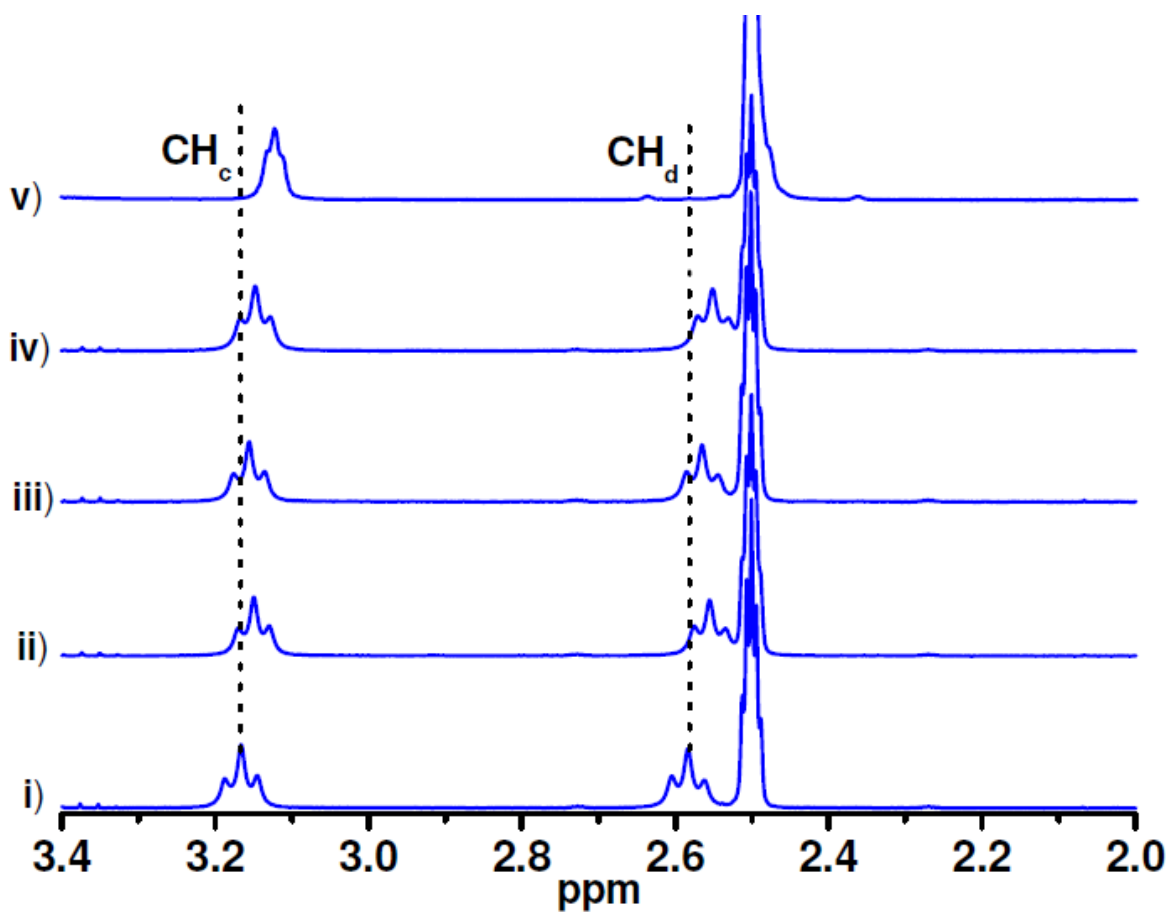
Figure 16S. Job's Plot of **L2** with $K_2C_2O_4$ in $DMSO-d_6/D_2O$ (1:1.1)(v/v) at 298K.

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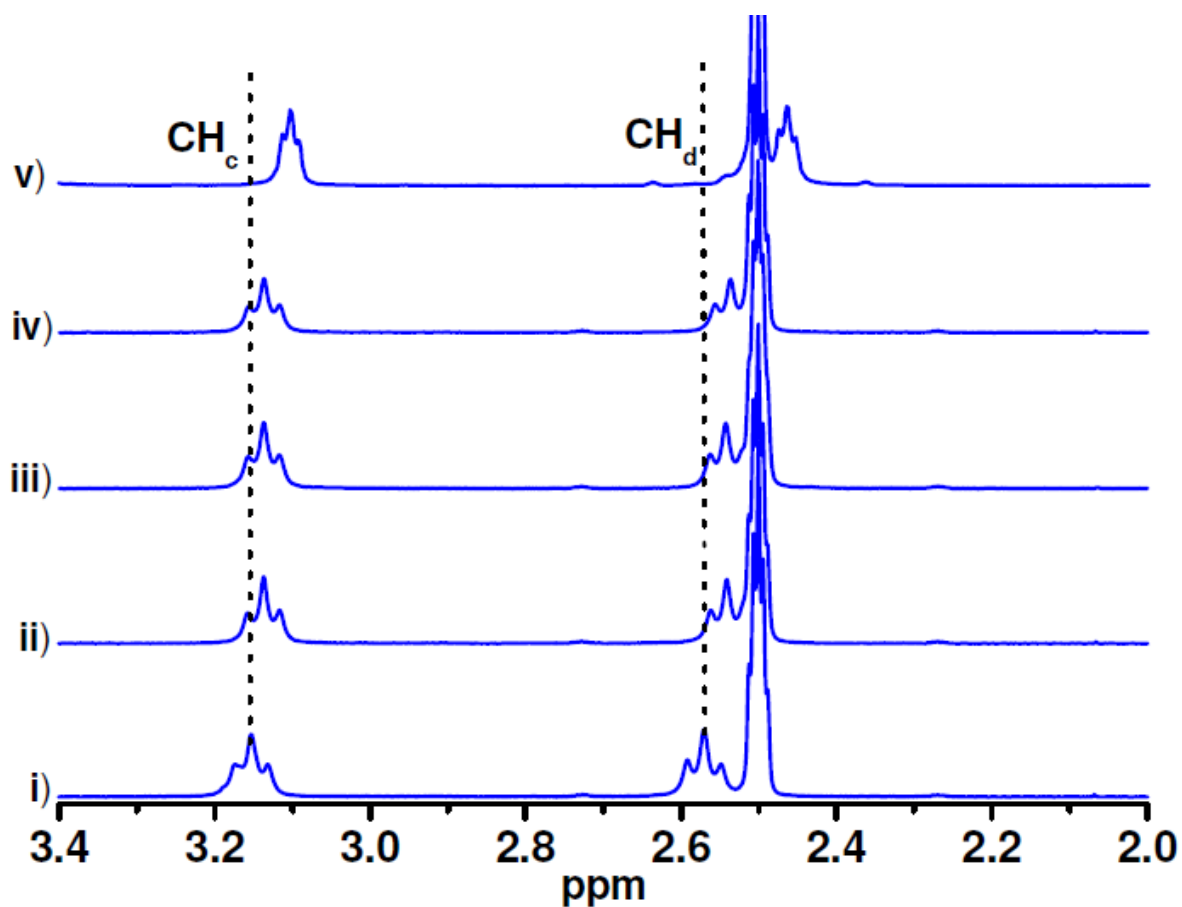
10 **Figure 17S.** Different peak positions of oxalate carbon observed in partial ^{13}C NMR spectra of (i) **C1** and (ii) **C2** respectively.

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Figure 18S. a) Partial ¹H-NMR (300 MHz) spectral changes of **L1** i) in D₂O:DMSO-*d*₆ (1:9, v/v) with added standard 2 equivalents of ii) NaOAc; iii) NaOBz; iv) Na₂(terephthalate) and v) K₂C₂O₄ solution in D₂O: DMSO-*d*₆ 10 (1.1:1, v/v) (298 K).



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Figure 19S. a) Partial $^1\text{H-NMR}$ (300 MHz) spectral changes of **L2** i) in $\text{D}_2\text{O}:\text{DMSO-}d_6$ (1:9,v/v) with added standard 2 equivalents of ii) NaOAc; iii) NaOBz; iv) $\text{Na}_2(\text{terephthalate})$ and v) $\text{K}_2\text{C}_2\text{O}_4$ solution in $\text{D}_2\text{O}:\text{DMSO-}d_6$ (1.1:1, v/v) (298 K).

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Table 1S. Crystallographic parameters of **C1** and **C2**.

Parameters	C1	C2
CCDC Number	914147	914149
Molecular formula	C ₉₄ H ₁₃₂ N ₂₂ O ₁₀	C ₄₄ H ₆₅ F ₄ N ₈ O ₅
Formula weight	1730.22	862.04
Crystal system	Triclinic	Monoclinic
Space group	P-1	P2(1)/c
a (Å)	12.541(3)	13.761(5)
b (Å)	13.299(3)	14.036(5)
c (Å)	33.259(9)	25.220(9)
α (°)	91.050(7)	90.00
β (°)	93.994(7)	103.680(10)
γ (°)	117.167(7)	90.00
V (Å ³)	4915(2)	4733(3)
Z	2	4
d _{calc} (g/cm ³)	1.169	1.210
Crystal size (mm ³)	0.60 x 0.30 x 0.26	0.40 x 0.30 x 0.20
F(000)	1860	1844
μ Mo Kα (mm ⁻¹)	0.078	0.091
T(K)	100(2)	100(2)
θ range (deg)	1.72-25.00	1.52-25.00
Reflections collected	53158	32998
Independent reflections	16958	8333
Parameters	1143	554
R ₁ ;wR ₂	0.0965; 0.2751	0.0783; 0.2411
GOF (F ²)	1.149	1.063

Table 2S. Interatomic distances, and angles for the H-bonding Interactions of the encapsulated $C_2O_4^{2-}$ in **C1**.

D-H...A	d (H...A), Å	d (D...A), Å	< D-H-A °
N2-H2...O9 ^a	2.210	3.045(6)	163.7
N3-H3...O10 ^a	2.000	2.843(5)	167.7
N5-H5...O9 ^a	2.140	2.942(5)	154.1
N6-H6...O9 ^a	2.150	2.945(4)	153.4
N8-H8...O10 ^a	2.140	2.988(5)	169.3
N9-H9...O8 ^a	2.130	2.953(5)	159.4
N12-H12...O7 ^a	2.190	3.033(6)	168.6
N13-H13...O8 ^a	2.020	2.855(6)	163.5
N15-H15...O7 ^a	2.160	2.958(6)	154.2
N16-H16...O7 ^a	2.180	2.973(5)	154.0
N18-H18...O8 ^a	2.150	2.969(5)	159.0
N19-H19...O10 ^a	2.110	2.930(4)	158.7

^a x, y, z

Table 3S. Interatomic distances, and angles for the H-bonding Interactions of the encapsulated $C_2O_4^{2-}$ in **C2**.

D-H...A	d (H...A), Å	d (D...A), Å	< D-H-A °
N2-H2...O4 ^a	2.230	3.006(3)	150.2
N3-H3...O5 ^a	2.180	2.983(3)	155.9
N4-H4...O4 ^a	2.270	3.095(4)	161.9
N5-H5...O4 ^a	2.410	3.216(4)	156.2
N6-H6...O4 ^a	2.090	2.954(4)	178.8
N7-H7...O5 ^a	2.330	3.142(4)	157.7

^a x, y, z

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