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A novel calix[4]arene-based neutral semicarbazone receptor for anion recognition

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Abstract—A series of novel calix[4]arene-based neutral semicarbazone and thiosemicarbazone receptors have been synthesized and characterized. The molecular receptor **4a** recognizes HSO_4^- in preference to other anions (Cl^-, Br^-, I^-, ClO_4^-, $H_2PO_4^-$ and PF_6^-) through a 1:1 binding-stoichiometry.

Anion recognition is extremely important for resolving biological, chemical and environmental issues.[1,2] Though a large volume of research data is available on recognition of cations, very few molecular receptors have been examined for anions.[3] Different strategies adopted for anion recognition essentially consist of either acquiring the positively charged molecular hosts, which interact with anions through electrostatic interactions[4,5] or by utilizing the neutral molecular hosts, which recognize anions through donor–acceptor attributes, hydrophobic effects and hydrogen bonds.[6] The directional nature of hydrogen bonds has recently been explored for better selectivity in recognition processes.[6] It was envisaged that the phenolic oligomers represented by calix[*n*]arenes could in principle provide excellent platforms for construction of attractive recognition sites for host–guest interactions[7] and it should be possible to design molecular receptors for anion recognition by employing activated amides, urea and thiourea functionalities.[8,9] To the best of our knowledge, the utilization of calixarenes bearing semicarbazone and thiosemicarbazone subunits at their lower rim have not been examined for anion recognition despite the availability of facile synthetic protocols. We report herein, the synthesis, characterization and anion binding properties of a novel calix[4]arene receptors bearing two semicarbazone and thiosemicarbazone moieties at the distal 1,3-positions. These receptors were found to demonstrate significant binding ability for tetrahedral HSO_4^- ions in preference to other anions including Cl^-, Br^-, I^-, ClO_4^-, $H_2PO_4^-$ and PF_6^-.

The required starting material, calix[4]arene **1** was obtained by using a literature procedure.[10a] Dibromoalkylation of **1** was achieved by refluxing with 1,3-dibromopropane in the presence of K_2CO_3 in CH_3CN for 48–96 h to give **2** in 87% yield.[10b] Compounds **3a** and **3b** were obtained in 86% and 83% yields, respectively, when bis(bromopropyl)-calix[4]arene **2** was refluxed with *p*-hydroxybenzaldehyde or *p*-hydroxyacetophenone in the presence of K_2CO_3 in anhydrous acetonitrile under a nitrogen atmosphere.[11] Treatment of **3a** and **3b** with semicarbazide or thiosemicarbazide reagents[12] gave **4a**–**d**[13] in good yields as illustrated in Scheme 1.

Compounds **4a**–**d** were characterized by analysis of their ^{1}H NMR, ^{13}C NMR, FAB-MS and FT-IR spectra. For example, the ^{1}H NMR spectrum of **4a** showed a typical AB pattern represented by two pairs of doublets at δ 3.29 and δ 4.14 for the axial and equatorial protons, respectively, which indicated that **4a** existed in a symmetrical cone conformation. This was further confirmed by the observation of a distinct signal at δ 31.2 for the methylene carbon in the ^{13}C NMR spectrum.[13] The azo-methine proton (HC=N) appeared as a non-exchangeable singlet at δ 7.59 while the $-NH_2$, –OH and –NH protons appeared at δ 5.77, 8.12 and 10.09, respectively. These signals disappeared on deuteration with D_2O. Individual assignment of the –OH, –NH and $-NH_2$ protons were further confirmed by

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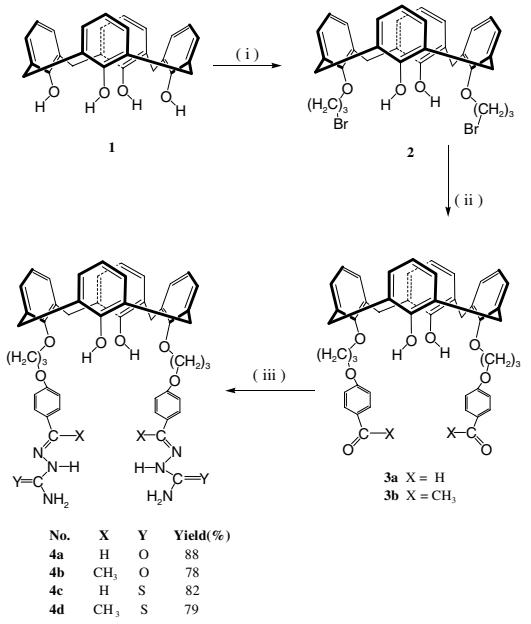


Scheme 1. Reagents and conditions: (i) Br–$(CH_2)_3$–Br, K_2CO_3, CH_3CN, reflux; (ii) *p*-hydroxybenzaldehyde or *p*-hydroxyacetophenone, K_2CO_3, CH_3CN, reflux; (iii) NH_2–NH–C(Y)–NH_2, methanol, 50 °C, reflux.

comparison with those of their precursor compounds, NOESY experiments and quantitative integrals. The FT-IR spectrum exhibited a sharp peak at 1605 cm^{-1} for the >C=N– absorptions.

The synthesized compounds **4a–d** were examined for their interaction with various anions (Cl^-, Br^-, I^-, ClO_4^-, HSO_4^-, $H_2PO_4^-$ and PF_6^-) in the form of their tetrabutylammonium salts. The recognition characteristics of **4a** were investigated in detail by ^1H NMR experiments in deuterated chloroform, which revealed a significant downfield shift for the NH and CH proton resonances on addition of tetrabutylammonium hydrogen sulfate while no change in the chemical shifts occurred when Cl^-, Br^-, I^-, ClO_4^-, $H_2PO_4^-$ and PF_6^- were added under the same experimental conditions (Table 1). Similar downfield shifts for the NH and CH proton resonances were also observed for receptor **4c** on addition of tetrabutylammonium hydrogen sulfate in d_6-acetone (**4c** had poor solubility in $CDCl_3$).

The ^1H NMR titration experiments conducted in $CDCl_3$[14] indicated that the NH signal at δ 10.09 and

Table 1. Chemical shift values ($\Delta\delta$, ppm) of the NH, CH and OH proton resonances of **4a** upon addition of 100 equiv of anions (as tetrabutylammonium salts) in $CDCl_3$ (300 MHz and 298 K)

Anion	NH	CH	OH
Cl	ns[a]	ns	ns
Br	ns	ns	ns
I	ns	ns	ns
ClO_4	ns	ns	ns
HSO_4	0.47	0.21	ns
H_2PO_4	ns	ns	ns
PF_6	ns	ns	ns

[a] ns indicates no change in chemical shift.

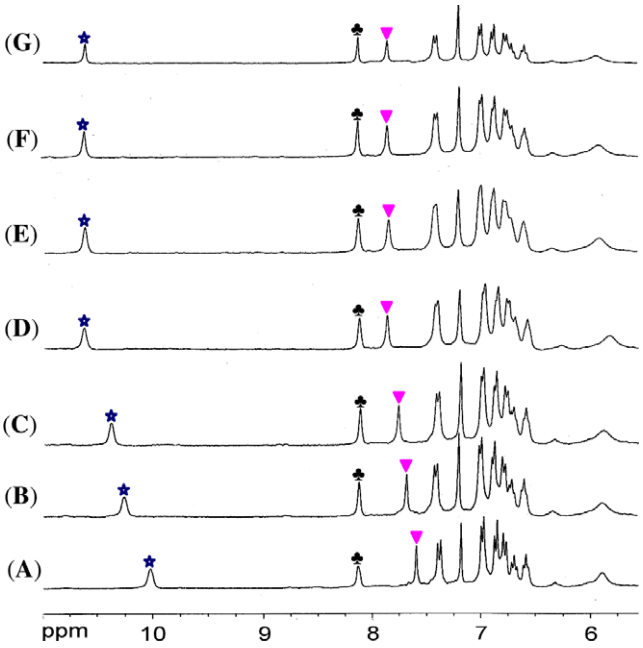


Figure 1. Partial ^1H NMR (300 MHz and 298 K) spectra of host **4a** (10 mM) upon addition of various aliquots of TBA·HSO_4 (40 mM) in $CDCl_3$. (A) Host **4a**; (B) **4a** + 0.5 equiv of HSO_4^- (C) **4a** + 0.75 equiv of HSO_4^- (D) **4a** + 1.0 equiv of HSO_4^- (E) **4a** + 1.5 equiv of HSO_4^- (F) **4a** + 2.0 equiv of HSO_4^- (G) **4a** + 2.5 equiv of HSO_4^- (☆ = NH, ▼ = CH, ♣ = OH).

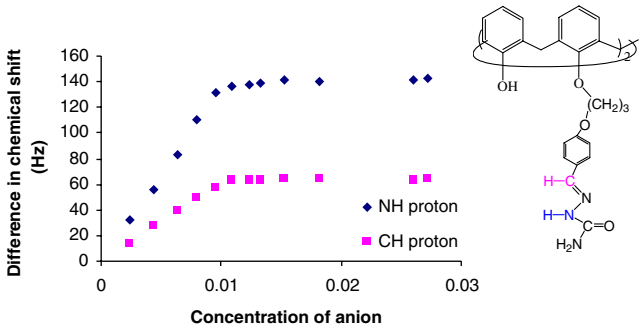


Figure 2. ^1H NMR titration curve of **4a** with TBA·HSO_4 ($CDCl_3$, 300 MHz and 298 K).

the CH signal at δ 7.59 for receptor **4a** were markedly affected by addition of tetrabutylammonium hydrogen sulfate while no effect on the chemical shift was observed for the phenolic OH signal at δ 8.12. Figure 1 illustrates that maximum downfield shifts were observed for the NH and CH protons of **4a** upon addition of 1.0 equiv of TBA·HSO_4. Various aliquots of a 40 mM solution of tetrabutylammonium hydrogen sulfate were added to a 10 mM solution of **4a** and the chemical shifts of the NH proton were recorded at each concentration until the saturation point was observed (Fig. 2). Analysis of saturation data with a nonlinear regression curve-fitting programme WinEQNMR,[15] revealed a 1:1 complex formation with a binding constant of 4.5×10^3 M^{-1}. A Job plot experiment further confirmed the 1:1 binding-stoichiometry with maximum complexation at 0.5 mol fraction of anion as shown in Figure 3.

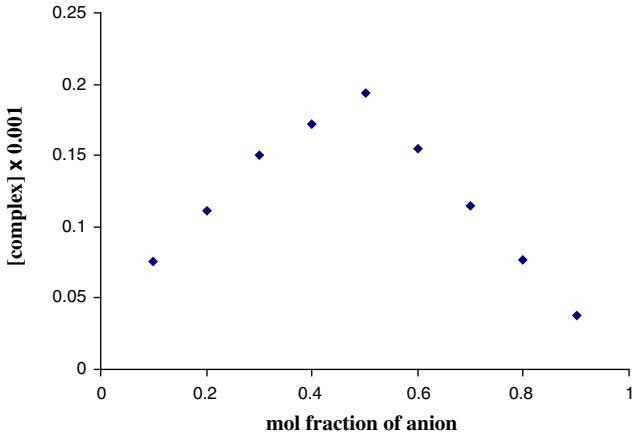
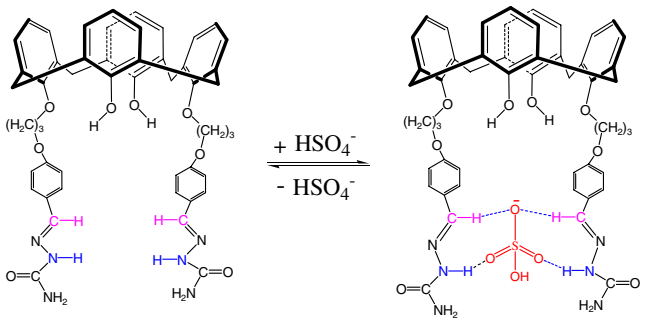


Figure 3. Job plot of the titration of 0.01 M TBA·HSO_4 with 10^{-2} M receptor **4a** in $CDCl_3$.

The enhanced selectivity of calix[4]arene semicarbazone receptor **4a** towards HSO_4^- ions could be attributed to the influence of hydrogen bonding. Preliminary observations of the chemical shift for the NH and CH proton resonances upon addition of HSO_4^- to a $CDCl_3$ solution of **4a** indicated that both the NH and CH protons participate in the formation of co-operative hydrogen bonds with the anionic oxygens while the phenolic protons of the calix[4]arene skeleton do not. Hence the chemical shift of the OH signal remained unaffected during the titration (Fig. 1).

In the cases of **4b** and **4d** (X = CH_3, Y = O, S), no significant shift in the NH proton resonance was observed thereby indicating that the azo-methine proton (HC=N) is important for the specificity and anion binding. This is probably due to appropriate distances between the NH and CH protons, which provide a proper binding site in **4a** for entrapment of HSO_4^- ions such that the three oxygen atoms of the tetrahedral HSO_4^- ion form hydrogen bonds with the NH and CH protons of the semicarbazone subunit. A possible model for the **4a**–HSO_4^- complex is shown in Scheme 2, which is being explored further.

In conclusion, we have synthesized a series of novel calix[4]arene-based neutral semicarbazone and thiosemicarbazone receptors **4a**–**d**, which selectively recognize



Scheme 2. Possible binding model of **4a** with HSO_4^-.

HSO_4^- in preference to Cl^-, Br^-, I^-, ClO_4^-, $H_2PO_4^-$ and PF_6^- ions. The enhanced selectivity of **4a** for HSO_4^- could be due to strong hydrogen bond interactions between the receptor NH and CH protons through 1:1 binding-stoichiometry. Further investigations to understand the exact nature of the binding of HSO_4^- with **4a** are in progress.

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References and notes

1. (a) Krik, K. L. *Biochemistry of Halogens and Inorganic Halides*; Plenum Press: New York, 1991; p 591; (b) de Silva Frausto, J. J. R.; Williams, R. J. P. *Struct. Bond. (Berlin)* **1976**, *29*, 67.
2. (a) Beer, P. D.; Hopkins, P. K.; McKinney, J. D. *Chem. Commun.* **1999**, 1253–1254; (b) *Ullman's Encyclopedia of Industrial Chemistry*, 6th ed.; Wiley-VCH: New York, Germany, 1998.
3. (a) Schmidtchen, F. P.; Berger, M. *Chem. Rev.* **1997**, *97*, 1609–1646; (b) Beer, P. D.; Gale, P. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 486–516; (c) Snowden, T. S.; Anslyn, V. *Curr. Opin. Chem. Biol.* **1999**, *3*, 740–746.
4. Llinares, J. M.; Powell, D.; Bowman-James, K. *Coord. Chem. Rev.* **2003**, *240*, 57–75.
5. Best, M. D.; Tobey, S. L.; Anslyn, E. V. *Coord. Chem. Rev.* **2003**, *240*, 3–15.
6. (a) Antonisse, M. M. G.; Reinhoudt, D. N. *Chem. Commun.* **1998**, 443–448; (b) Sessler, J. L.; Camiolo, S.; Gale, P. A. *Coord. Chem. Rev.* **2003**, *240*, 17–55; (c) Boiocchi, M.; Del Boca, L.; Gomez, D. E.; Fabbrizzi, L.; Licchelli, M.; Monzani, E. *J. Am. Chem. Soc.* **2004**, *126*, 16507–16514; (d) Gunnlaugsson, T.; Kruger, P. E.; Jensen, P.; Tierney, J.; Ali, H. D. P.; Hussey, G. M. *J. Org. Chem.* **2005**, *70*, 10875–10878.
7. (a) Gutsche, C. D. In *Calixarenes: Monographs in Supramolecular Chemistry*; Stoddart, J. F., Ed.; The Royal Society of Chemistry: Cambridge, UK, 1989; (b) Gutsche, C. D. In *Calixarenes Revisited: Monographs in Supramolecular Chemistry*; Stoddart, J. F., Ed.; The Royal Society of Chemistry: Cambridge, UK, 1998; (c) Chawla, H. M.; Pant, N.; Srivastava, B.; Upreti, S. *Org. Lett.* **2006**, *8*, 2237–2240; (d) Chawla, H. M.; Singh, S. P.; Sahu, S. N.; Upreti, S. *Tetrahedron* **2006**, *62*, 7854–7865; (e) Chakrabarti, A.; Chawla, H. M.; Francis, T.; Pant, N.; Upreti, S. *Tetrahedron* **2006**, *62*, 1150–1157; (f) Chawla, H. M.; Singh, S. P.; Upreti, S. *Tetrahedron* **2006**, *62*, 2901–2911; (g) Chawla, H. M.; Pant, N.; Srivastava, B. *Tetrahedron Lett.* **2005**, *46*, 7259–7262; (h) Chawla, H. M.; Srinivas, K. *J. Chem. Soc., Chem. Commun.* **1994**, 2593–2594; (i) Chawla, H. M.; Srinivas, K. *J. Org. Chem.* **1996**, *61*, 8464–8467.
8. (a) Bondy, C. R.; Loeb, S. J. *Coord. Chem. Rev.* **2003**, *240*, 77–99; (b) Tumcharern, G.; Tuntulani, T.; Coles, S. G.; Hursthouse, M. B.; Kilburn, J. D. *Org. Lett.* **2003**, *5*, 4971–4974; (c) Morzherin, Y.; Rudkevich, D. M.; Verboom, W.; Reinhoudt, D. N. *J. Org. Chem.* **1993**, *58*,

7602–7605; (d) Beer, P. D.; Gale, P. A.; Hesek, D. *Tetrahedron Lett.* **1995**, *36*, 767–770; (e) Cameron, B. R.; Loeb, S. J. *Chem. Commun.* **1997**, 573–574; (f) Wu, J. L.; He, Y. B.; Zeng, Z. Y.; Wei, L. H.; Meng, L. Z.; Yang, T. X. *Tetrahedron* **2004**, *60*, 4309–4314.

9. (a) Wu, F. Y.; Li, Z.; Wen, Z. C.; Zhou, N.; Zhao, Y. F.; Jiang, Y. B. *Org. Lett.* **2002**, *4*, 3203–3205; (b) Cho, E. J.; Moon, J. W.; Ko, S. W.; Lee, J. Y.; Kim, S. K.; Yoon, J.; Nam, K. C. *J. Am. Chem. Soc.* **2003**, *125*, 12376–12377; (c) Kim, K. S.; Yoon, J. *Chem. Commun.* **2002**, 770–771; (d) Dudic, M.; Lhotak, P.; Stibor, I.; Lang, K.; Proskova, P. *Org. Lett.* **2003**, *5*, 149–152.
10. (a) Iqbal, M.; Mangiafico, T.; Gutsche, C. D. *Tetrahedron* **1987**, *43*, 4917–4930; (b) Li, Z. T.; Ji, G. H.; Zhao, C. X.; Yuan, S. D.; Ding, H.; Huang, C.; Du, A. L.; Wei, M. *J. Org. Chem.* **1999**, *64*, 3572–3584.
11. *General procedure for the synthesis of compounds* **3a**,**b**: A mixture of **2** (1.17 mmol), potassium carbonate (7.19 mmol) and *p*-hydroxybenzaldehyde (or *p*-hydroxyacetophenone) (4.5 mmol) was stirred under reflux in 20 mL of anhydrous acetonitrile for 48 h. The reaction mixture was cooled to room temperature and then carefully neutralized with dilute hydrochloric acid and extracted with chloroform. The organic layer was washed with water, dried over Na_2SO_4 and evaporated to dryness. The white solid residue was purified by column chromatography on silica gel using hexane/ethyl acetate (gradient from 9.5:0.5 to 8:2) as eluent. Selected analytical data for compounds **3a**,**b** are given below: Compound **3a**: yield (86%); mp >240 °C. IR (KBr): 3360 (OH); 1689 (C=O). Anal. Calcd for $C_{48}H_{44}O_8$: C, 76.99; H, 5.92. Found: C, 76.69; H, 5.76. FAB-MS *m*/*z* Calcd: 748. Found 748 (M^+). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.36 (q, 4H, $J = 5.9$ Hz, –CH_2–CH_2–CH_2–), δ 3.36 (d, 4H, $J = 12.9$ Hz, Ar–CH_2–Ar), δ 4.12 (t, 4H, $J = 5.5$ Hz, –OCH_2), δ 4.20 (d, 4H, $J = 12.9$ Hz, Ar–CH_2–Ar), δ 4.48 (t, 4H, $J = 6.2$ Hz, –CH_2O), δ 6.64 (t, 2H, $J = 7.3$ Hz, Ar-*H*), δ 6.72 (t, 2H, $J = 7.6$ Hz, Ar-*H*), δ 6.90 (d, 4H, $J = 7.4$ Hz, Ar-$H_{benzaldehyde}$), δ 7.03 (d, 4H, $J = 7.2$ Hz, Ar-*H*), δ 7.06 (d, 4H, $J = 7.1$ Hz, Ar-*H*), δ 7.79 (d, 4H, $J = 7.4$ Hz, Ar-$H_{benzaldehyde}$), δ 8.01 (s, 2H, D_2O exchange –O*H*), δ 9.83 (s, 2H, C*H*O). ^{13}C NMR ($CDCl_3$): δ 29.7, 31.3, 64.8, 72.5, 114.8, 119.7, 125.7, 127.8, 128.6, 129.6, 131.9, 133.1, 151.2, 152.9, 191.8.
Compound **3b**: yield (83%); mp >245 °C. IR (KBr): 3336 (OH); 1675 (C=O). Anal. Calcd for $C_{50}H_{48}O_8$: C, 77.30; H, 6.23. Found: C, 77.18; H, 5.86. FAB-MS *m*/*z* Calcd: 776. Found 777 ($M+H^+$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.28–2.32 (m, 4H, –CH_2–CH_2–CH_2–), δ 2.41 (s, 6H, –COCH_3), δ 3.28 (d, 4H, $J = 12.9$ Hz, Ar–CH_2–Ar), δ 4.04 (t, 4H, $J = 5.1$ Hz, –OCH_2), δ 4.14 (d, 4H, $J = 12.9$ Hz, Ar–CH_2–Ar), δ 4.38 (t, 4H, $J = 6.2$ Hz, –CH_2O), δ 6.55 (t, 2H, $J = 7.4$ Hz, Ar-*H*), δ 6.63 (t, 2H, $J = 7.6$ Hz, Ar-*H*), δ 6.81 (d, 4H, $J = 7.4$ Hz, Ar-*H*), δ 6.89 (d, 4H, $J = 8.4$ Hz, Ar-$H_{acetophenone}$), δ 6.95 (d, 4H, $J = 7.5$ Hz, Ar-*H*), δ 7.80 (d, 4H, $J = 8.4$ Hz, Ar-$H_{acetophenone}$), δ 7.96 (s, 2H, D_2O exchange –O*H*). ^{13}C NMR ($CDCl_3$): δ 26.2, 29.7, 31.2, 64.7, 72.6, 114.1, 115, 119.2, 125.6, 127.8, 128.4, 129.0, 130.3, 130.5, 133.1, 151.2, 153.0, 162.7, 196.8.
12. Zengin, G.; Huffman, J. W. *Turk. J. Chem.* **2006**, *30*, 139–144.
13. *General procedure for the synthesis of compounds* **4a**–**d**: A solution of **3a**–**b** (1.3 mmol) in 20 mL of methanol was treated with 17.0 mL of semicarbazide/thiosemicarbazide solution.[12] The mixture was refluxed on a water bath (50 °C) until crystallization began. Further crystallization was allowed to continue at room temperature and the product obtained was filtered and dried under vacuum to give calix[4]arene-bis(semicarbazone) derivatives **4a**–**d** as white solids. Selected analytical data for compounds **4a**–**d** are given below: Compound **4a**: yield (88%); mp = 267 ± 5 °C. IR (KBr): 3336 (OH); 1689 (C=O); 1605 (C=N). Anal. Calcd for $C_{50}H_{50}N_6O_8$: C, 69.59; H, 5.84; N, 9.74. Found: C, 69.30; H, 5.92; N, 9.59. FAB-MS *m*/*z* Calcd: 862. Found 863 ($M+H^+$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.30–2.34 (m, 4H, –CH_2–CH_2–CH_2–), δ 3.29 (d, 4H, $J = 12.8$ Hz, Ar–CH_2–Ar), δ 3.92 (t, 4H, $J = 5.4$ Hz, –OCH_2), δ 4.14 (d, 4H, $J = 12.8$ Hz, Ar–CH_2–Ar), δ 4.23 (t, 4H, $J = 5.6$ Hz, –CH_2O), δ 5.77 (br s, 4H, D_2O exchange –NH_2), δ 6.56 (t, 2H, $J = 7.2$ Hz, Ar-*H*), δ 6.66 (t, 2H, $J = 7.3$ Hz, Ar-*H*), δ 6.74 (d, 4H, $J = 8.3$ Hz, Ar-$H_{benzaldehyde}$), δ 6.84 (d, 4H, $J = 7.4$ Hz, Ar-*H*), δ 6.96 (d, 4H, $J = 7.3$ Hz, Ar-*H*), δ 7.37 (d, 4H, $J = 8.3$ Hz, Ar-$H_{benzaldehyde}$), δ 7.59 (s, 2H, –C*H*N), δ 8.12 (s, 2H, D_2O exchange –O*H*), δ 10.09 (s, 2H, D_2O exchange –N*H*). ^{13}C NMR ($CDCl_3$): δ 29.7, 31.2, 64.8, 72.5, 114.7, 119.2, 125.7, 128.7, 128.5, 129, 131.9, 133.1, 151.2, 152.9, 163.7, 190.7.
Compound **4b**: yield (78%); mp = 263 ± 4 °C. IR (KBr): 3408 (OH); 1702 (C=O); 1602 (C=N). Anal. Calcd for $C_{52}H_{54}N_6O_8$: C, 70.09; H, 6.11; N, 9.43. Found: C, 69.98; H, 6.01; N, 9.59. FAB-MS *m*/*z* Calcd: 890. Found 891 ($M+H^+$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.02 (s, 6H, –CCH_3), δ 2.32–2.36 (m, 4H,–CH_2–CH_2–CH_2–), δ 3.30 (d, 4H, *J*= 12.1 Hz, Ar–CH_2–Ar), δ 3.92 (br s, 4H, –OCH_2), δ 4.18 (d, 4H, $J = 12.1$ Hz, Ar–CH_2–Ar), δ 4.29 (br s, 4H, –CH_2O), δ 6.32 (br s, 4H, D_2O exchange –NH_2), δ 6.84–6.89 (m, 12H, Ar-*H*), δ 6.97 (d, 4H, $J = 8.3$ Hz, Ar-$H_{acetophenone}$), δ 7.47 (d, 4H, $J = 8.3$ Hz, Ar-$H_{acetophenone}$), δ 8.27 (s, 2H, D_2O exchange –O*H*), δ 8.45 (s, 2H, D_2O exchange –N*H*). ^{13}C NMR ($CDCl_3$): δ 26.4, 29.7, 31.2, 64.8, 72.5, 114.7, 119.2, 125.7, 128.7, 128.5, 129.0, 131.9, 133.1, 151.2, 152.9, 163.7, 195.7.
Compound **4c**: yield (82%); mp = 261 ± 5 °C. IR (KBr): 3304 (OH); 1089 (C=S); 1604 (C=N). Anal. Calcd for $C_{50}H_{50}N_6O_6S_2$: C, 67.09; H, 5.63; N, 9.39. Found: C, 67.18; H, 5.82; N, 9.14. FAB-MS *m*/*z* Calcd: 894. Found 895 ($M+H^+$). ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ 2.45 (q, 4H, $J = 5.6$ Hz, –CH_2–CH_2–CH_2–), δ 3.44 (d, 4H, $J = 12.8$ Hz, Ar–CH_2–Ar), δ 4.23 (t, 4H, $J = 4.2$ Hz, –OCH_2), δ 4.30 (d, 4H, $J = 12.8$ Hz, Ar–CH_2–Ar), δ 4.56 (t, 4H, $J = 4.1$ Hz, –CH_2O), δ 6.58 (t, 2H, $J = 7.3$ Hz, Ar-*H*), δ 6.69 (t, 2H, $J = 7.4$ Hz, Ar-*H*), δ 7.00 (d, 4H, $J = 7.5$ Hz, Ar-*H*), δ 7.07 (d, 4H, $J = 8.3$ Hz, Ar-$H_{benzaldehyde}$), δ 7.12 (d, 4H, $J = 7.4$ Hz, Ar-*H*), δ 7.40 (br s, 4H, D_2O exchange –NH_2), δ 7.73 (d, 4H, $J = 8.3$ Hz, Ar-$H_{benzaldehyde}$), δ 8.09 (s, 2H, –C*H*N), δ 8.38 (s, 2H, D_2O exchange –O*H*), δ 10.34 (s, 2H, D_2O exchange –N*H*). ^{13}C NMR ($(CD_3)_2CO$): δ 29.7, 30.9, 64.7, 72.9, 114.9, 119.2, 125.3, 127.9, 128.6, 129.0, 129.2, 142.6, 146.2, 150.2, 205.4.
Compound **4d**: yield (79%); mp = 266 ± 5 °C. IR (KBr): 3336 (OH); 1091 (C=S); 1587 (C=N). Anal. Calcd for $C_{52}H_{54}N_6O_6S_2$: C, 67.65; H, 5.90; N, 9.10. Found: C, 67.48; H, 5.85; N, 9.31. FAB-MS *m*/*z* Calcd: 922. Found 923 ($M+H^+$). ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ 2.21 (s, 6H, –CCH_3), δ 2.42–2.46 (m, 4H, $J = 5.4$ Hz, –CH_2–CH_2–CH_2–), δ 3.42 (d, 4H, $J = 12.7$ Hz, Ar–CH_2–Ar), δ 4.21 (t, 4H, $J = 4.0$ Hz, –OCH_2), δ 4.33 (d, 4H, $J = 12.7$ Hz, Ar–CH_2–Ar), δ 4.58 (t, 4H, $J = 4.2$ Hz, –CH_2O), δ 6.56 (t, 2H, $J = 7.4$ Hz, Ar–*H*), δ 6.63 (t, 2H, $J = 7.5$ Hz, Ar-*H*), δ 7.12 (d, 4H, $J = 7.5$ Hz, Ar-*H*), δ 7.17 (d, 4H, $J = 8.3$ Hz, Ar-$H_{acetophenone}$), δ 7.22 (d, 4H, $J = 7.4$ Hz, Ar-*H*), δ 7.42 (br s, 4H, D_2O exchange –NH_2), δ 7.78 (d, 4H, $J = 8.3$ Hz, Ar-$H_{acetophenone}$), δ 8.36 (s, 2H, D_2O exchange –O*H*), δ 10.32 (s, 2H, D_2O exchange –N*H*). ^{13}C NMR ($(CD_3)_2CO$): δ 27.2, 29.4, 30.4, 65.7, 73.6, 114.4, 117.6, 125.7, 126.9, 128.7, 129.3, 129.8, 145.2, 149.2, 200.4.

14. ^{1}H NMR titration: A 10 mM solution of the host **4a** was prepared in $CDCl_3$. To 0.5 mL of **4a** solution, 0–5 equiv of tetrabutylammonium hydrogen sulfate (40 mM) were added to an NMR tube and the spectra were recorded. The chemical shifts of the NH and CH protons were followed and plotted against the equivalents of $TBA{\cdot}HSO_4$ added. Job plot: Stock solutions of the host **4a** (10 mM) and tetrabutylammonium hydrogen sulfate (10 mM) were prepared in $CDCl_3$. A total volume of 500 μL of **4a** and $TBA{\cdot}HSO_4$ were added to nine NMR tubes in the following volume ratios: 50:450, 100:400, 150:350, 200:300, 250:250, 200:300, 150:350, 100:400, 50:450.
15. Hynes, M. *J. Chem. Soc., Dalton Trans.* **1993**, 311–312.