Supporting information for:

Convenient Synthesis of Multivalent Zinc(II)-Dipicolylamine Complexes for Molecular Recognition

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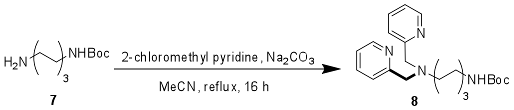
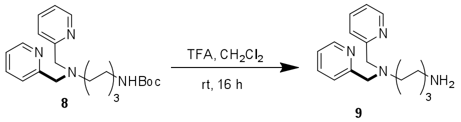
1. Materials

Reagents and starting materials were purchased from commercial suppliers and used without further purification.

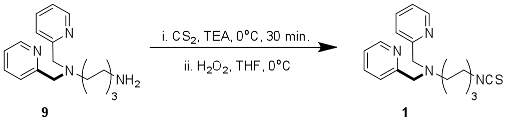
2. Synthesis



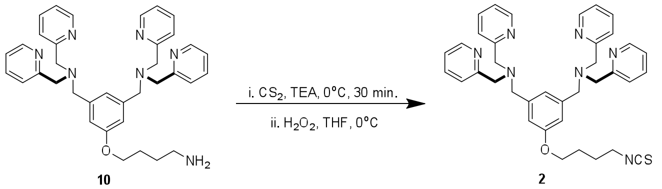
Compound 8: *N*-*t*-butoxycarbonyl-6-aminohexylamine (**7**)[S1] (0.80 g, 3.70 mmol) in CH_3CN (20 mL) was added dropwise to a solution of 2-chloromethyl pyridine (1.22 g, 7.41 mmol) and Na_2CO_3 (7.84 g, 74.10 mmol) in CH_3CN (50 mL) under stirring. Then the reaction mixture was refluxed under argon overnight. After cooling to room temperature, the solid was filtered and the residue was evaporated to remove solvents. This crude material was purified using column chromatography to provide the target product **8** as yellow oil (80%). ^1H NMR ($CDCl_3$, 300MHz): δ 8.44 (m, 2H), 7.58 (m, 2H), 7.46 (d, *J* = 7.80 Hz, 2H), 7.07 (m, 2H), 4.63 (br, 1H), 3.73 (s, 4H), 2.99 (m, 2H), 2.46 (t, *J* = 7.35 Hz, 2H), 1.37 (m, 17H). HRMS (ESI): m/z: calculated for $C_{23}H_{34}N_4O_2Na$ $[M+Na]^+$ 421.2579, found 421.2574.



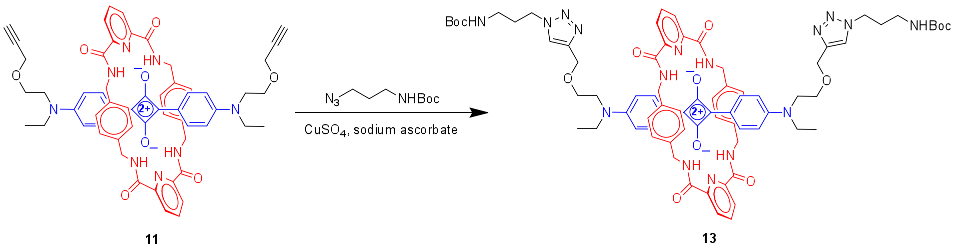
Compound 9: Compound **8** (1.20 g, 3.02 mmol) was dissolved in CH_2Cl_2 (50 mL), followed by addition of TFA (2.2 mL, 30.15 mmol) at 0 °C. The reaction mixture was allowed to stir at room temperature overnight. After removing solvent, the crude product was washed with ether to provide **9** as a sticky brown oil quantitatively. ^1H NMR (CD_3OD, 300 MHz): δ 8.68 (m, 2H), 7.97 (m, 2H), 7.54 (m, 4H), 4.58 (s, 4H), 3.24 (m, 2H), 2.90 (t, *J* = 7.50 Hz, 2H), 1.83 (m, 2H), 1.65 (m, 2H), 1.40 (m, 4H). HRMS (ESI): m/z: calculated for $C_{18}H_{27}N_4$ $[M+H]^+$ 299.2236, found 299.2230.



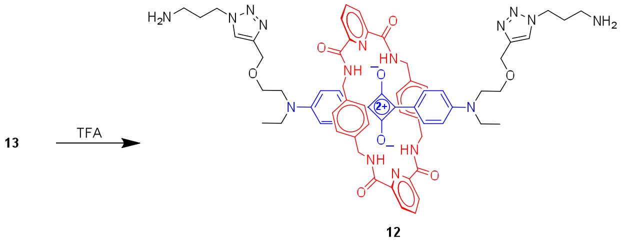
Compound 1: To a stirred solution of **9** (480 mg, 1.61 mmol) and TEA (0.45 mL, 3.22 mmol) in THF (40 mL) was added carbon disulfide (0.65 mL, 10.73 mmol) at 0 °C. Stirring was continued for 0.5 h followed by dropwise addition of hydrogen peroxide (30%, 0.99 mL, 10.73 mmol) with the reaction temperature maintained at 0 °C. The reaction mixture was evaporated under reduced pressure and the residue purified by chromatography on a silica gel column to afford **1** as a pale yellow oil (39.6%). ^1H NMR ($CDCl_3$, 500 MHz) δ 8.50 (m, 2H), 7.64 (m, 2H), 7.51 (d, *J* = 8.00 Hz, 2H), 7.13 (m, 2H), 3.78 (s, 4H), 3.44 (t, *J* = 6.50 Hz, 2H), 2.52 (t, *J* = 7.25 Hz, 2H), 1.61 (m, 2H), 1.52 (m, 4H), 1.29 (m, 4H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 159.6, 148.5, 136.1, 122.5, 121.6, 60.11, 53.8, 44.6, 29.47, 26.5, 26.1, 26.0. HRMS (ESI): m/z: calculated for $C_{19}H_{24}N_4SNa$ $[M+Na]^+$ 363.1619, found 363.1614.



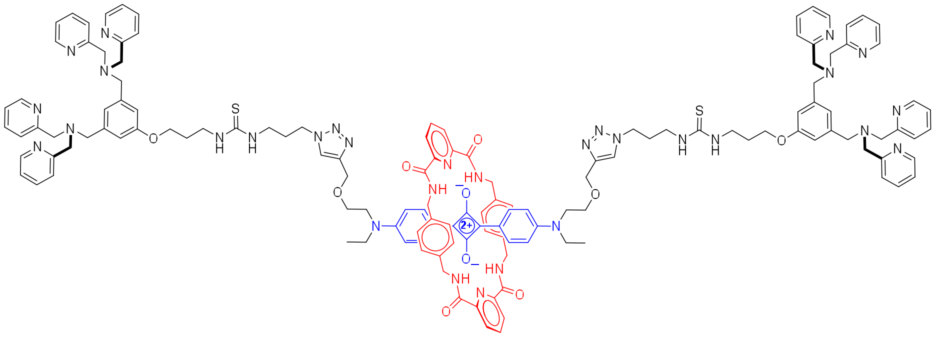
Compound 2: To a stirred solution of **10** [S2] (520 mg, 0.885 mmol) and TEA (123 µL, 0.885 mmol) in THF (20 mL) was added carbon disulfide (214 µL, 3.539 mmol) at 0 °C. Stirring was continued for 0.5 h followed by dropwise addition of hydrogen peroxide (30%, 109 µL, 3.539 mmol) while the reaction temperature was maintained at 0 °C. The reaction mixture was evaporated under reduced pressure, and the residue was subjected to column chromatography to afford **2** as a pale yellow oil (54%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.49 (m, 4H), 7.59 (m, 8H), 7.12 (m, 4H), 7.06 (s, 1H), 6.83 (s, 2H), 3.98 (t, *J* = 4.80 Hz, 2H), 3.79 (s, 8H), 3.64 (s, 4H), 3.58 (t, *J* = 5.10 Hz, 2H), 1.89 (m, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 159.6, 158.8, 148.9, 140.6, 136.4, 122.7, 121.9, 121.6, 113.4, 66.6, 60.0, 58.5, 44.8, 26.9, 26.3. HRMS (FAB): m/z: calculated for $C_{37}H_{40}N_7OS$ $[M+H]^+$ 630.3015, found 630.3001. IR (KBr) ν (cm^{-1}) 2109.



Compound 13: Bis-alkyne **11** (21.4 mg, 0.021 mmol)[S3] and *N*-*tert*-butoxycarbonyl-3-azidopropylamine (16.8 mg, 0.084 mmol) were dissolved in a mixture of chloroform and water (8 mL, 1:1 v/v), followed by addition of $CuSO_4.5H_2O$ (2.6 mg, 0.011 mmol) and sodium ascorbate (8.3 mg, 0.042 mmol) in one portion. The reaction mixture was stirred at room temperature overnight, and the organic layer was separated. After washing with EDTA solution, the solvent was removed and the residue purified by column chromatography to provide **13** as a blue solid (90%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 10.02 (t, *J* = 5.55 Hz, 4H), 8.49 (d, *J* = 8.10 Hz, 4H), 8.13 (t, *J* = 7.80 Hz, 2H), 8.06 (d, *J* = 8.70 Hz, 4H), 7.69 (s, 2H), 6.59 (s, 8H), 6.17 (d, *J* = 8.70 Hz, 4H), 4.99 (t, *J* = 5.85 Hz, 2H), 4.61 (s, 4H), 4.52 (d, *J* = 5.10 Hz, 8H), 4.44 (t, *J* = 6.75 Hz, 4H), 3.67 (t, *J* = 5.10 Hz, 4H), 3.53 (t, *J* = 5.10 Hz, 4H), 3.43 (m, 4H), 3.13 (m, 4H), 2.09 (m, 4H), 1.42 (s, 18H), 1.13 (t, *J* = 7.05 Hz, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 185.1, 184.2, 166.9, 163.5, 153.5, 149.5, 144.3, 138.8, 136.5, 133.5, 128.9, 125.2, 123.1, 118.9, 111.5, 67.7, 64.5, 50.1, 47.5, 46.1, 43.3, 37.2, 30.8, 29.6, 28.3, 12.1. MS (MALDI): m/z: 1415.9 $[M-2H]^+$.

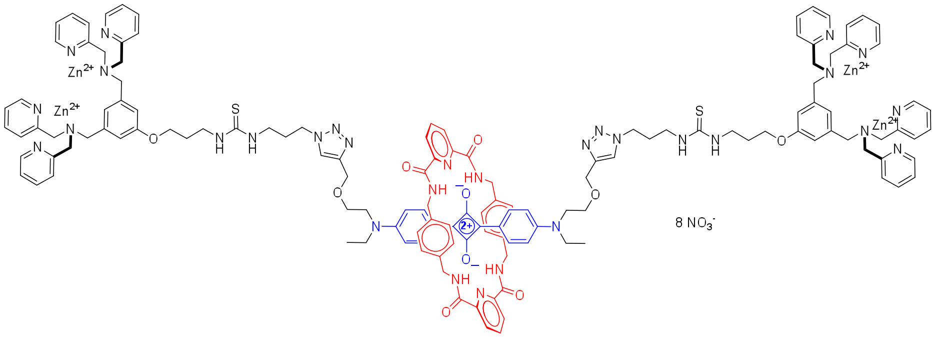


Compound 12: Squaraine rotaxane **13** (26.8 mg, 0.019 mmol) was dissolved in dichloromethane (1.0 mL), followed by slow addition of TFA (56 µL, 0.754 mmol) at 0 °C. After stirring at room temperature overnight, the solvent was removed and the sticky solid was washed with chloroform several times to afford **12** as a blue solid in quantitative yield. ^{1}H NMR (CD_3OD, 300 MHz) δ 10.16 (t, *J* = 5.85 Hz, 4H), 8.48 (d, *J* = 7.50 Hz, 4H), 8.32 (t, *J* = 7.80 Hz, 2H), 8.03 (d, *J* = 9.30 Hz, 4H), 7.99 (s, 2H), 6.57 (s, 8H), 6.29 (d, *J* = 9.00 Hz, 4H), 4.60 (s, 4H), 4.53 (m, 12H), 3.64 (m, 8H), 3.48 (m, 4H), 2.99 (t, *J* = 7.80 Hz, 4H), 2.26 (m, 4H), 1.13 (t, *J* = 7.20 Hz, 6H). ^{13}C NMR (CD_3OD, 75 MHz) δ 187.0, 183.5, 165.2, 155.4, 150.5, 146.0, 140.9, 137.9, 134.6, 129.9, 126.6, 125.3, 119.9, 113.0, 69.1, 65.0, 51.3, 47.2, 44.2, 38.1, 36.3, 29.1, 12.4. MS (MALDI): m/z: 1219.8 $[M]^+$.



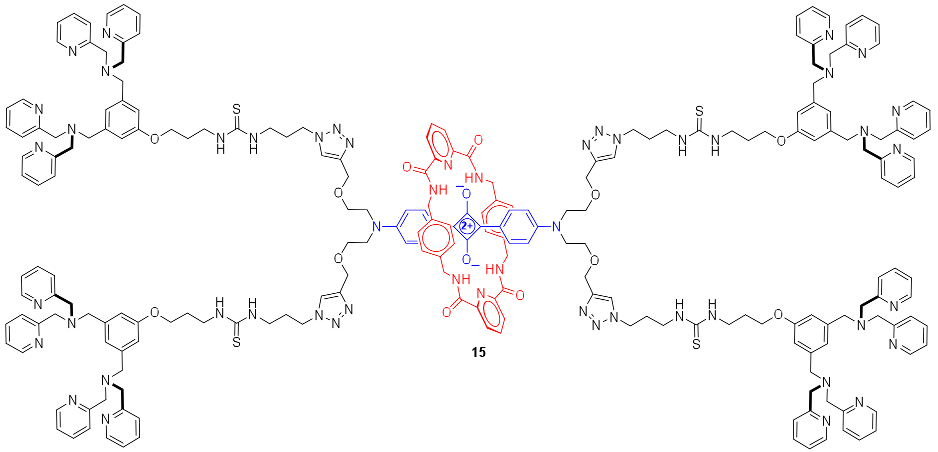
14

Compound 14: Squaraine rotaxane dye **12** (18.9 mg, 0.016 mmol) was dissolved in anhydrous DMF (1.5 mL), followed by addition of triethylamine (43 µL, 0.310 mmol). Then **2** (19.0 mg, 0.062 mmol) in anhydrous DMF (0.5 mL) was added with stirring. The reaction mixture was allowed to stir at room temperature in darkness under Ar overnight, and then the solvent was removed under vacuum. Purification by column chromatography and size-exclusion chromatography (bio-beads) gave **14** as a blue solid (40%). ^{1}H NMR (CDCl$_3$, 300 MHz) δ 10.06 (t, *J* = 5.55 Hz, 4H), 8.47 (m, 10H), 8.12 (t, *J* = 7.95 Hz, 2H), 8.03 (d, *J* = 9.30 Hz, 4H), 7.59 (m, 18H), 7.11 (t, *J* = 5.40 Hz, 8H), 7.03 (s, 2H), 6.81 (s, 4H), 6.58 (s, 8H), 6.18 (d, *J* = 4.65 Hz, 4H), 4.59 (s, 4H), 4.52 (d, *J* = 5.10 Hz, 8H), 4.39 (t, *J* = 6.60 Hz, 4H), 3.96 (t, *J* = 5.25 Hz , 4H), 3.78 (s, 16H), 3.63 (m, 28H), 2.17 (t, *J* = 6.30 Hz, 4H), 1.81 (m, 8H), 1.13 (t, *J* = 6.90 Hz, 6H). MS (MALDI): m/z: 2478.8 [M]$^+$.



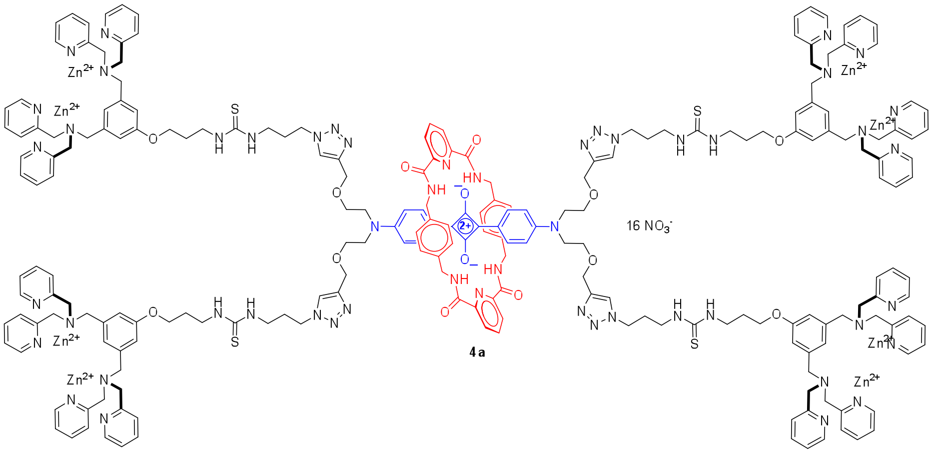
3

Compound 3: Compound **14** (4.46 mg, 1.80 µmol) and Zn(NO$_3$)$_2$.6H$_2$O (2.30 mg, 7.38 µmol) were dissolved in a mixture of methanol (2.0 mL) and water (0.2 mL). The mixture was stirred at room temperature for half an hour, then evaporated under vacuum to provide the zinc complex, **3**, which was dissolved in deionized water (1.23 mL) to provide a stock solution.



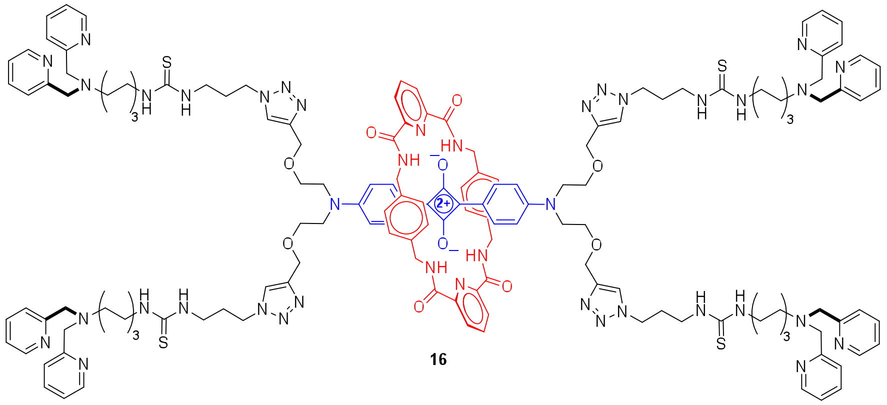
15

Compound 15: Compund **4c** [S4] (32.0 mg, 0.021 mmol) was dissolved in anhydrous DMF (1 mL), followed by addition of triethylamine (146 µL, 1.046 mmol). Then **2** (105.5 mg, 0.168 mmol) in anhydrous DMF (0.8 mL) was added into the solution upon agitation. The reaction mixture was allowed to stir at room temperature in darkness under Ar overnight, and then the solvents were removed under vacuum. After purification by column chromatography and size-exclusion chromatography (bio-beads), **15** was obtained as a blue solid (40%). ^{1}H NMR (CDCl$_3$, 300 MHz) δ 10.03 (t, *J* = 5.70 Hz, 4H), 8.45 (m, 20H), 8.12 (t, *J* = 7.80 Hz, 2H), 8.04 (d, *J* = 8.70 Hz, 4H), 7.72 (s, 4H), 7.58 (m, 32H), 7.10 (t, *J* = 6.00 Hz, 16H), 7.02 (s, 4H), 6.78 (s, 8H), 6.56 (s, 8H), 6.21 (d, *J* = 9.00 Hz, 4H), 4.53 (m, 16H), 4.40 (t, *J* = 6.15 Hz, 8H), 3.92 (t, *J* = 5.40 Hz, 8H), 3.78 (s, 32H), 3.62 (m, 48H), 2.17 (m, 8H), 1.78 (m, 16H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 185.0, 184.6, 163.6, 159.5, 158.9, 154.0, 149.3, 148.9, 144.4, 140.3, 139.0, 136.5, 133.4, 128.8, 125.2, 123.2, 122.8, 122.0, 121.6, 119.2, 113.6, 112.0, 67.6, 67.3, 64.4, 60.0, 58.5, 51.5, 47.7, 44.0, 43.4, 41.2, 29.8, 29.6, 26.6, 25.9. MS (ESI): m/z: 1350.1 $[M+3H]^{3+}$.



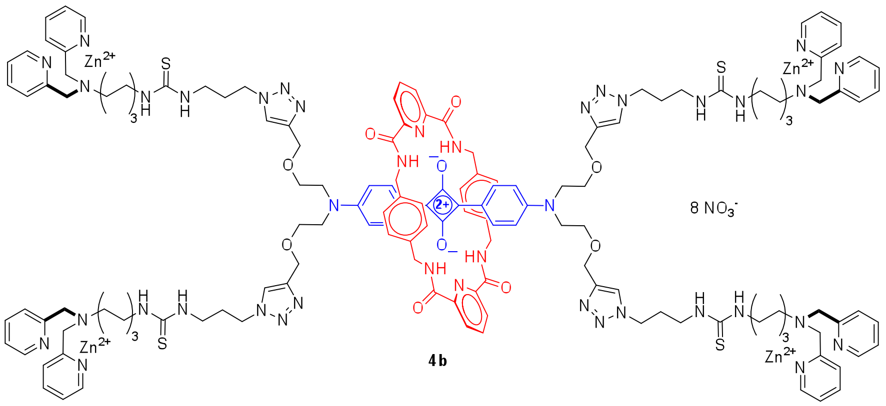
4a

Compound 4a: Compound **15** (4.98 mg, 1.23 μmol) and $Zn(NO_3)_2.6H_2O$ (3.11 mg, 10.46 μmol) were dissolved in a mixture of methanol (3.5 mL) and water (0.4 mL). The mixture was stirred at room temperature for half an hour, then evaporated under vacuum to provide the zinc complex, **4a**, which was dissolved in deionized water (1.23 mL) to give a stock solution.



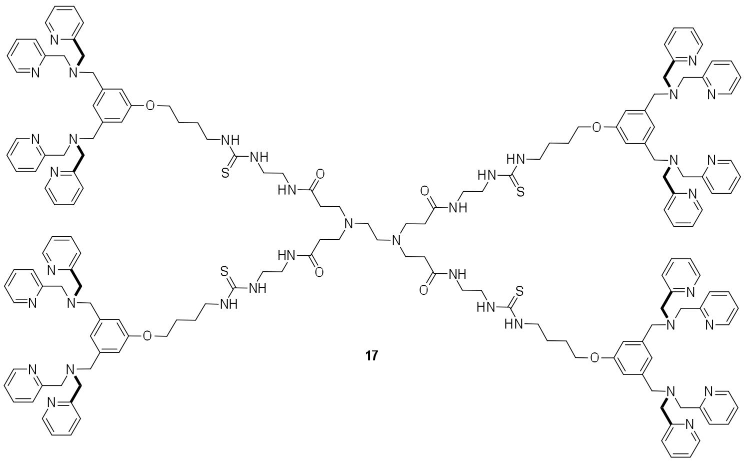
16

Compound 16: Compound **4c** (36 mg, 0.024 mmol) was dissolved in anhydrous DMF (3.0 mL), followed by the addition of TEA (0.21 μL, 1.509 mmol). Then **1** (86.9 mg, 0.255 mmol) was added into the solution upon agitation. The reaction mixture was allowed to stir at room temperature in darkness under Ar overnight, and then DMF was removed under vacuum. After purification by column chromatography and size-exclusion chromatography (bio-beads), **16** was obtained as a blue solid (36.7%). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 10.04 (t, *J* = 5.75 Hz, 4H), 8.46 (m, 12H), 8.14 (t, *J* = 8.00 Hz, 2H), 8.04 (d, *J* = 9.00 Hz, 4H), 7.70 (s, 4H), 7.64 (m, 8H), 7.46 (d, *J* = 8.00 Hz, 8H), 7.13 (m, 8H), 6.55 (s, 8H), 6.21 (d, *J* = 9.50 Hz, 4H), 4.54 (s, 8H), 4.50 (d, *J* = 5.00 Hz, 8H), 4.42 (t, *J* = 6.75 Hz, 8H), 3.92 (t, *J* = 5.55 Hz, 8H), 3.75 (s, 16H), 3.60 (m, 32H), 2.47 (t, *J* = 7.25 Hz, 8H), 2.20 (m, 8H), 1.49 (m, 16H), 1.23 (m, 16H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 185.1, 184.6, 163.6, 159.6, 154.0, 149.3, 148.8, 144.4, 139.0, 136.6, 136.4, 133.4, 128.9, 125.3, 123.2, 123.1, 122.0, 119.2, 112.0, 67.6, 64.4, 60.4, 54.1, 51.5, 47.7, 44.0, 43.4, 41.2, 29.9, 29.6, 28.7, 26.6, 26.4. HRMS (ESI): m/z: calculated for $C_{154}H_{191}N_{40}O_{10}S_4$ $[M+H]^+$ 2888.4550, found 2888.4670.



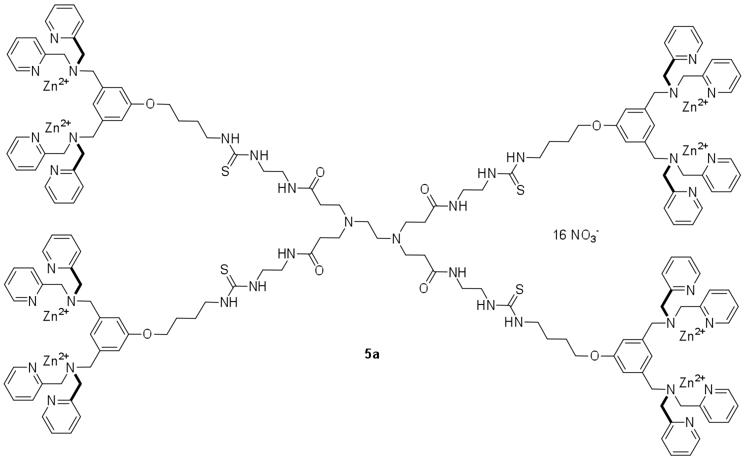
4b

Compound 4b: Compound **16** (1.82 mg, 0.63 µmol) and $Zn(NO_3)_2.6H_2O$ (0.78 mg, 2.58 µmol) were dissolved in a mixture of methanol (1.0 mL) and water (0.2 mL). The mixture was stirred at room temperature for half an hour, then evaporated under vacuum to provide the zinc complex, **4b**, which was dissolved in deionized water (0.63 mL) to provide a stock solution.



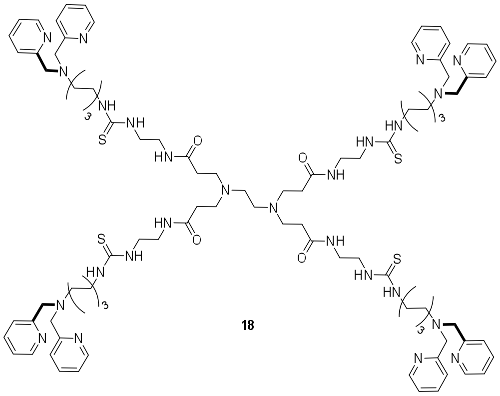
17

Compound 17: Commercial PAMAM-G0 (39 mg in 20% methanol, 0.015 mmol) was evaporated to remove methanol, then treated with **2** (76.2 mg, 0.121 mmol) in DMF (1.8 mL), followed by addition of triethylamine (33 µL). The reaction mixture was allowed to stir at room temperature overnight under argon, then DMF was removed under vacuum. The residual sticky oil was purified using column chromatography to provide **17** as a brown gel (77.9%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.46 (m, 16H), 7.56 (m, 32H), 7.09 (m, 16H), 7.02 (s, 4H), 6.78 (s, 8H), 3.91 (t, *J* = 4.95 Hz, 8H), 3.76 (s, 32H), 3.60 (m, 24H), 3.36 (m, 16H), 2.50 (m, 20H), 1.77 (m, 16H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.8, 159.7, 159.1, 149.0, 140.5, 136.6, 122.9, 122.1, 121.6, 113.6, 67.4, 60.1, 58.6, 51.1, 50.3, 44.1, 39.5, 34.1, 26.7, 26.0. IR (KBr) ν (cm^{-1}) 3280, 2930, 1150. Mass spectral analysis did not observe a parent ion, in agreement with literature studies demonstrating extensive fragmentation due to retero-Michael mechanisms. [S5]



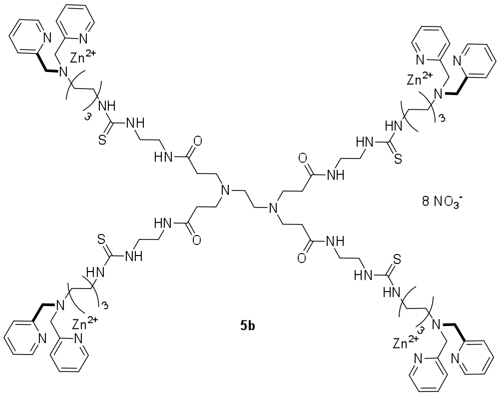
5a

Compound 5a: Compound **17** (6.40 mg, 2.11 μmol) and $Zn(NO_3)_2.6H_2O$ (5.27 mg, 17.71 μmol) were dissolved in a mixture of methanol (5.0 mL) and water (0.5 mL). The mixture was stirred at room temperature for half an hour, then evaporated under vacuum to provide the zinc complex, **5a**, which was dissolved in deionized water (2.11 mL) to provide a stock solution.



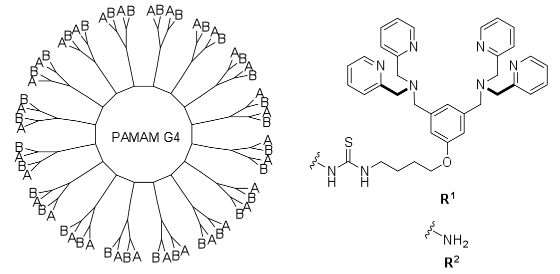
18

Compound 18: Commercial **PAMAM-G0** (100 mg in 20% methanol, 0.039 mmol) in a vial was evaporated to remove methanol. Then **1** (105 mg, 0.310 mmol) in anhydrous DMF (1.8 mL) was added into the vial, and followed by addition of TEA (86 μL). The reaction mixture was allowed to stir at room temperature overnight under argon and then DMF was removed under vacuum. The residual sticky oil was subjected to column chromatography to provide **18** as brown gel (75%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.49 (m, 8H), 7.66 (m, 8H), 7.52 (m, 8H), 7.14 (m, 8H), 3.78 (s, 16H), 3.59 (m, 24H), 2.51 (m, 28H), 1.52 (m, 16H), 1.25 (m, 16H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 182.5, 174.5, 160.1, 149.1, 136.8, 123.2, 122.2, 67.9, 60.6, 54.6, 50.3, 46.4, 39.4, 33.9, 29.5, 29.1, 27.3, 27.1, 25.4. HRMS (ESI): m/z: calculated for $C_{98}H_{149}N_{26}NaO_2S_5$ $[M+Na+H]^{+2}$ 952.5424, found 952.5450. IR (KBr) ν (cm^{-1}) 3260, 2930, 1049. Mass spectral analysis did not observe a parent ion, in agreement with literature studies demonstrating extensive fragmentation due to retero-Michael mechanisms.[S5]



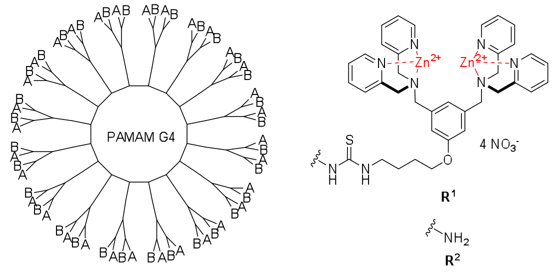
5b

Compound 5b: Compound **18** (2.10 mg, 0.11 μmol) and $Zn(NO_3)_2.6H_2O$ (1.80 mg, 6.06 μmol) were dissolved in a mixture of methanol (1.0 mL) and water (0.2 mL). The mixture was stirred at room temperature for half an hour, then evaporated under vacuum to give the zinc complex, which was dissolved in deionized water (1.12 mL) to provide a stock solution.



19, A = R^1, B = R^2

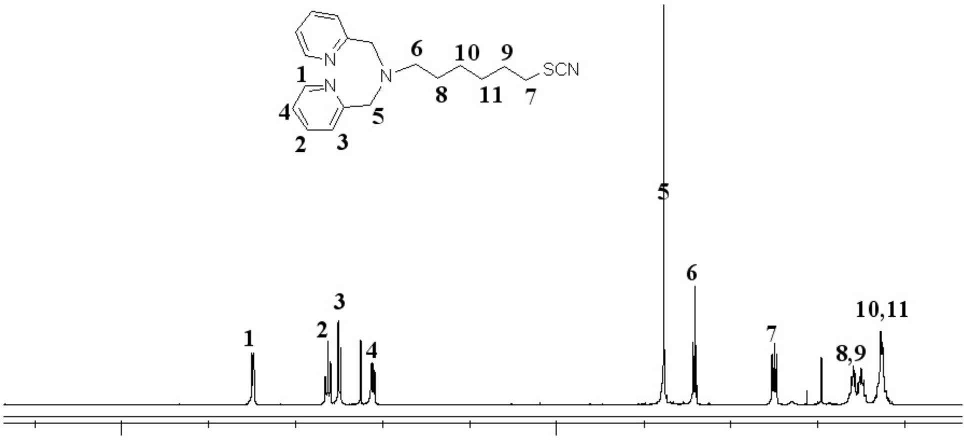
Compound 19: Commercial PAMAM G4 (96.4 mg in 10% methanol, 0.7 μmol) was evaporated in a vial to remove methanol, then treated with **2** (40.8 mg, 0.0648 mmol) in DMF (1.0 mL), followed by triethylamine (19 μL). The reaction mixture was allowed to stir at room temperature under argon for one week and then all solvents were removed under vacuum. After purification by column chromatography and size-exclusion-chromatography (bio-beads), **19** was obtained as a brown solid. The ^{1}H NMR spectrum indicated around 52% of the amine units on PAMAM G4 are functionalized with **2**. ^{1}H NMR (CDCl$_3$, 300 MHz) δ 8.44 (m, 4H), 7.55 (m, 8H), 7.08 (m, 8H), 6.77 (br, 1H), 6.58 (m, 2H), 4.18-1.68 (m, 45 H). ^{13}C NMR (CDCl$_3$, 75 MHz) δ 173.2, 159.5, 159.0, 148.8, 145.2, 140.3, 136.6, 127.9, 127.6, 125.6, 125.4, 122.8, 122.0, 121.3, 113.5, 67.3, 64.4, 59.9, 58.5, 52.0, 50.1, 44.2, 40.3, 34.4, 31.9, 29.6, 29.4, 29.3, 29.2, 29.1, 28.6, 26.7, 25.9, 25.1, 25.0. IR (KBr) ν (cm^{-1}) 3420, 3290, 2920, 1149. Mass spectral analysis did not observe a parent ion, in agreement with literature studies demonstrating extensive fragmentation due to retero-Michael mechanisms. [S5]



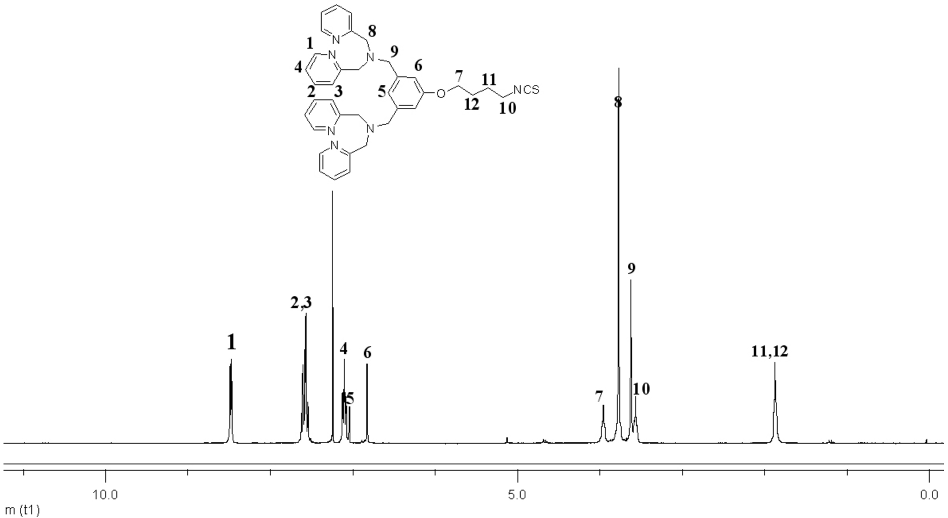
6, A = R^{1}, B = R^{2}

Compound 6: Compound **19** (5.60 mg, 0.10 μmol) and Zn(NO$_3$)$_2$.6H$_2$O (4.05 mg, 13.61 μmol) were dissolved in a mixture of methanol (2.0 mL) and water (0.2 mL). The mixture was stirred at room temperature for half an hour, then evaporated under vacuum to provide the zinc complex, **6**, which was dissolved in deionized water (1.02 mL) to give a stock solution.

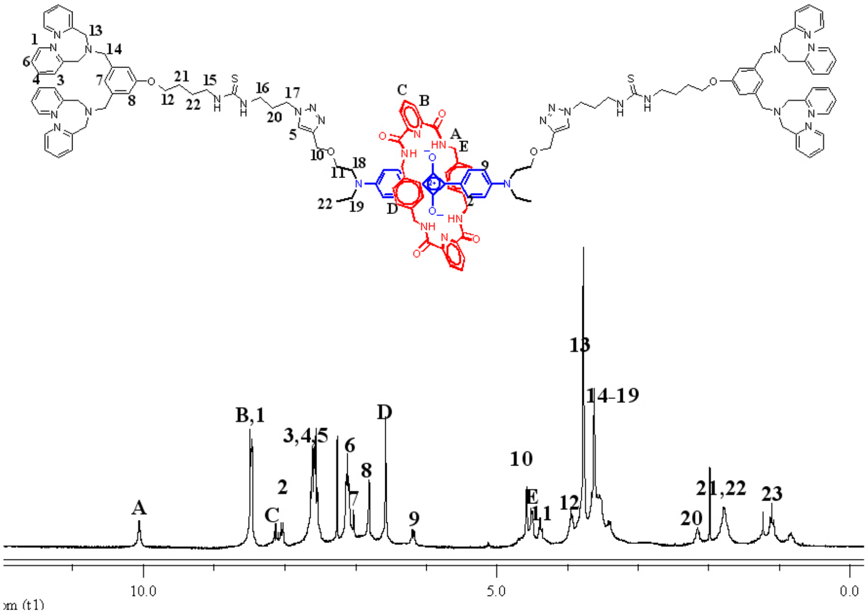
3. ^{1}H NMR spectra



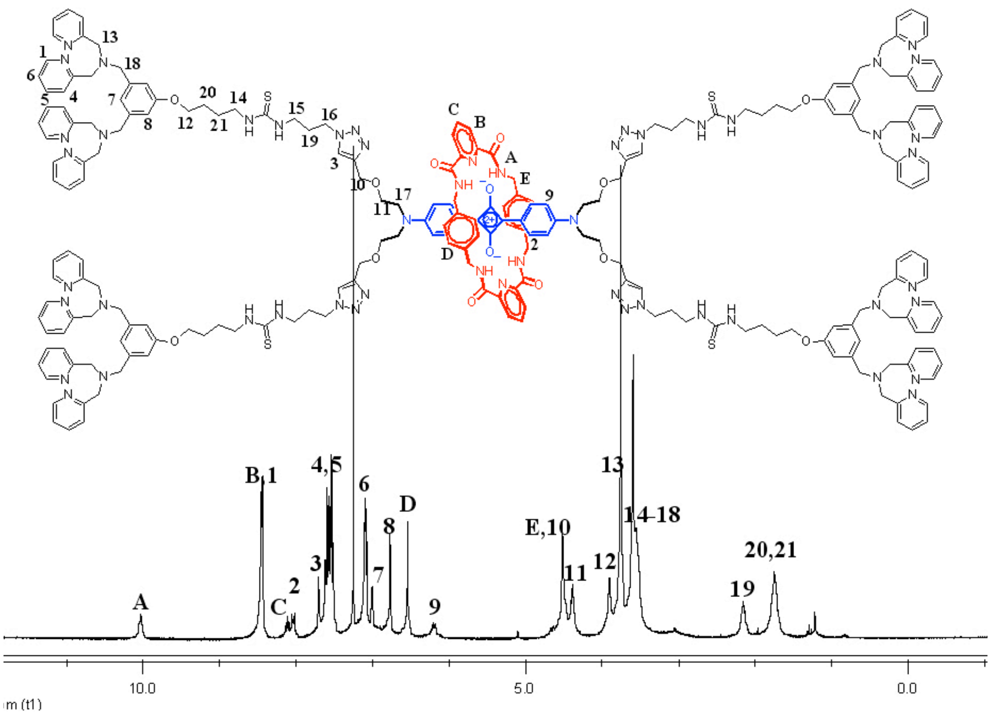
^{1}H NMR of **1** (500 MHz, CDCl$_3$)



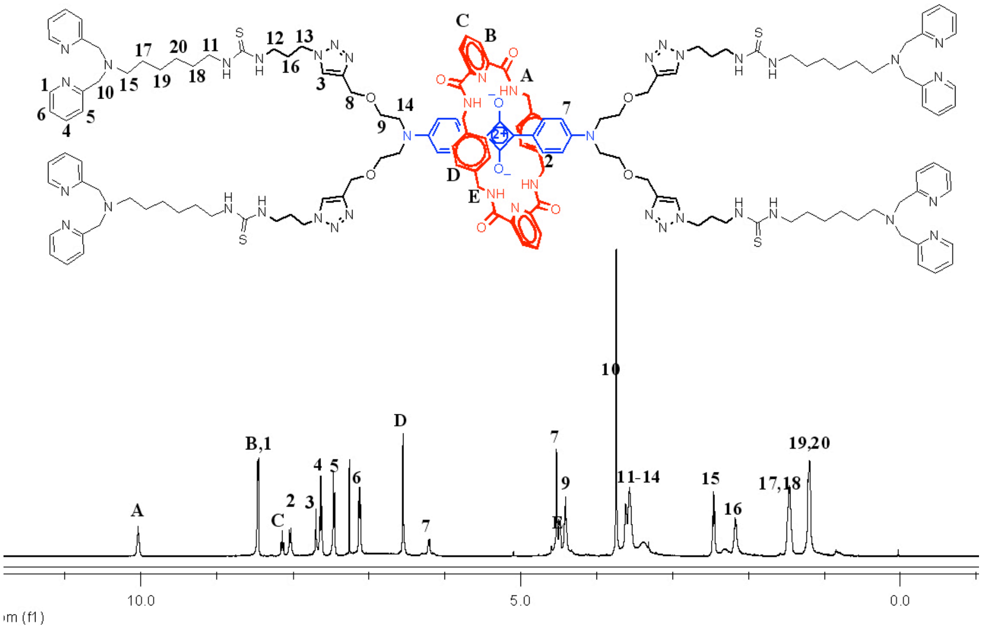
^{1}H NMR of **2** (300 MHz, CDCl$_3$)



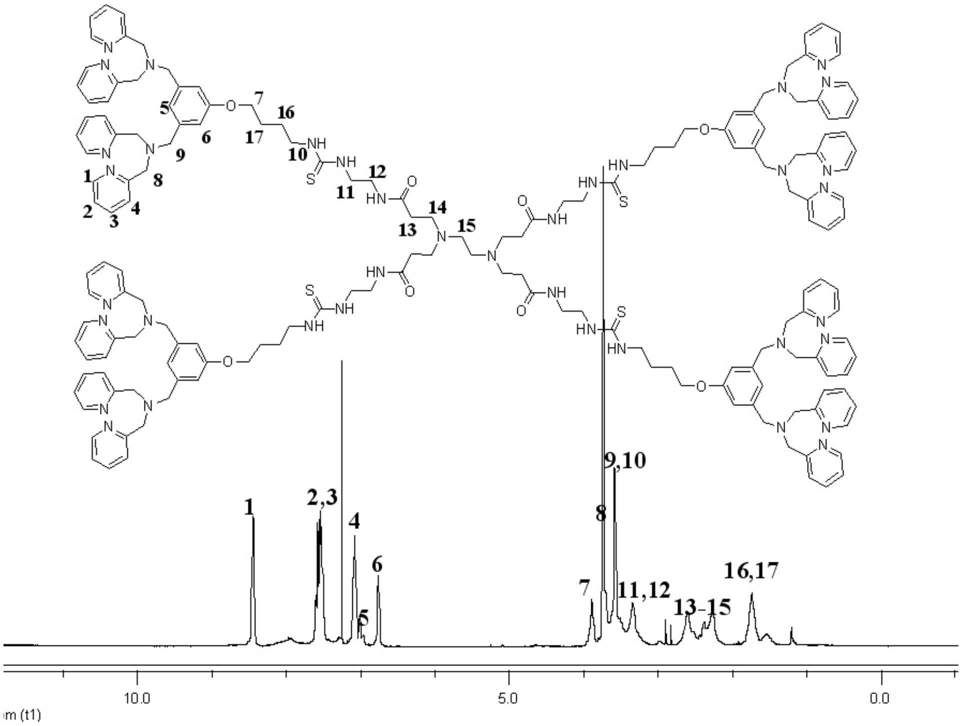
^{1}H NMR of **14** (300 MHz, CDCl$_3$)



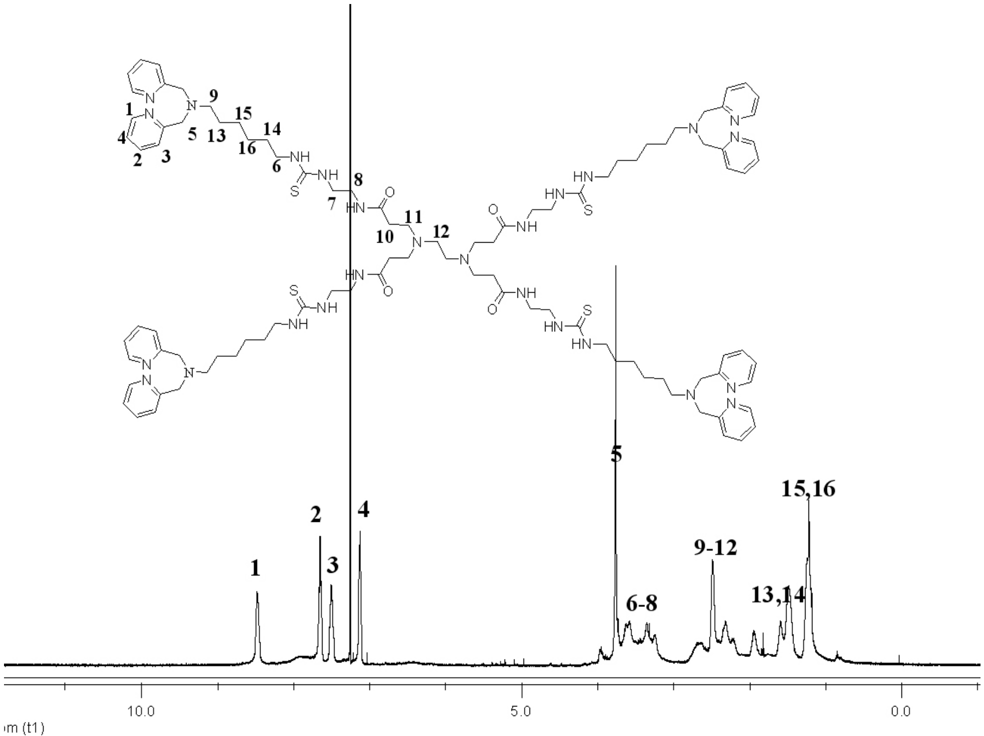
^{1}H NMR of **15** (300 MHz, CDCl$_3$)



^{1}H NMR of **16** (500 MHz, CDCl$_3$)



^{1}H NMR of **17** (300 MHz, $CDCl_3$)



^{1}H NMR of **18** (300 MHz, $CDCl_3$)

4. References

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