***Supplementary Information***

# IrAAC-based construction of dual sequence-defined polytriazoles

Xiaojun Wang, [a] Xueyan Zhang,[a] Yong Wang, [b] Shengtao Ding*[a]

[a]*State Key Laboratory of Organic-Inorganic Composites, College of Chemical Engineering, Beijing University of Chemical Technology, Beijing 100029, China.*
[b] *BGI-Shenzhen, Beishan Industrial Zone, Shenzhen 518083, China.*

## Table of Contents

# I. General information

All air or moisture sensitive reactions were conducted in oven-dried glassware under nitrogen atmosphere using dry solvents. Flash column chromatography was performed over silica gel (200-300 mesh) purchased from Qingdao Puke Co., China. Alkyne and common organic chemicals were purchased from commercial suppliers, such as Sigma-Aldrich® and J&K® Scientific Ltd., and used as received. Iridium complexes were purchased from Strem® Chemicals, Inc.

**NMR.** $^{1}H$ and $^{13}C$ spectrum were collected on a Bruker AV 400 MHz NMR spectrometer using residue solvent peaks as an internal standard ($^{1}H$ NMR: $CDCl_3$ at 7.26 ppm, $^{13}C$ NMR: $CDCl_3$ at 77.0 ppm).

**MS.** ESI-MS was measured using Agilent 6540 UHD Accurate-Mass Q-TOF LC/MS. MALDI-TOF-MS was measured on a AB Sciex 5800 MALDI–TOF/TOF mass spectrometer using α-cyano-4-hydroxycinnamic acid (CHCA) or 2,5-dihydroxybenzoic acid (DHB) as the matrix.

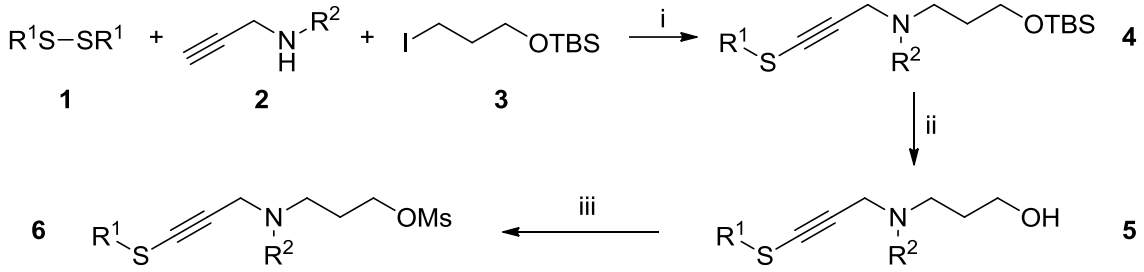
**MS/MS.** MS/MS spectra were acquired using collision-induced dissociation fragmentation. The MALDI-TOF-MS/MS experiments were conducted on a AB Sciex 5800 MALDI–TOF/TOF Mass Spectrometer. The sample was dissolved in MeOH containing 10 mM $NH_4OAc$. The ESI-MS/MS experiments were conducted using Agilent 6540 UHD Accurate-Mass Q-TOF LC/MS. The sample was dissolved in MeOH.

**SEC.** Sequence-defined oligomer samples (5 mg) were dissolved in THF (1 mL) and filtered prior to injection. SEC analyses were performed on a Waters 1525 Gel chromatography with three mixed-bed GPC columns in series (three Waters Styragel HT3 THF (7.8*300mm Column)), and THF mobile phase run at 35 ℃ for 40 min. The differential refractive index of each compound was monitored using a WAT038040 (2414) detector.

**Thermogravimetric analysis (TGA)**. TGA were performed on a thermogravimetric analyzer (Mettler TGA/DSC3+) at a heating rate of 10 ºC/min from 30 ºC to 800 ºC under the nitrogen atmosphere.

**Theoretical monoisotopic mass**. All of the theoretical *m*/*z* values are monoisotopic mass values calculated by using ChemBioOffice 2010.

## II. Preparation of 1-thioalkyne substrates



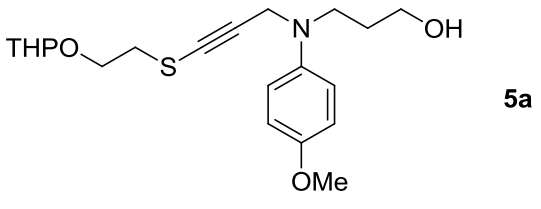

**Scheme S1**. Synthesis of 1-thioalkynes.

**General procedures**.

**i.** At -78 $^{o}$C, to solution of prop-2-yn-1-amine **2** (1.0 eq.) in THF (0.25 M) under $N_2$ atmosphere was slowly added *n*-BuLi (2.0 eq.). The reaction mixture was stirred at the same temperature for 1 h before disulfide **1** (1.0 eq.) and iodides **3** (1.0 eq.) were added. Then the reaction mixture was allowed to warm to room temperature and stirred for 2 h before a saturated aqueous $NH_4Cl$ solution was added. The aqueous phase was separated and extracted with ethyl acetate for three times. The combined organic phase was washed with brine, dried over $Na_2SO_4$, and evaporated under vacuum to give the crude product of thioalkyne **4**.

**ii.** The TBS-protected product was dissolved in THF (0.5 M), TBAF·$3H_2O$ (1.0 eq.) was added at 0 $^{o}$C and stirred another 20 minutes. TLC indicated completion of reaction. Upon completion, EA was added and the mixture was washed by water and brine. The organic layer was dried over $MgSO_4$, evaporated under vacuum to give the crude product, which was then purified by silica gel flash column chromatography to give the pure desired product **5**.

**iii.** Product **5** was dissolved in DCM (0.5 M) with subsequent addition of $Et_3N$ (2.0 eq.) and 4-dimethylaminopyridine (DMAP, 1 mol %). Then the solution of methanesulfonyl chloride (TsCl, 1.5 eq.) in DCM (1.0 M) was slowly added into the previous mixture. The reaction mixture was stirred at room temperature until the reaction completed (confirmed by TLC), and then washed with brine (three times), dried over $Na_2SO_4$, filtered, and evaporated under vacuum to give the residue of thioalkyne involving OMs group, which was then purified by silica gel flash column chromatography to give the pure desired product **6**.



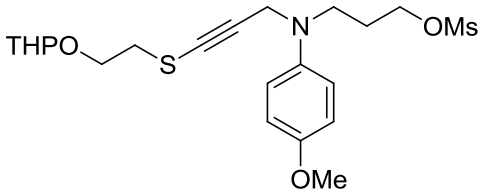

**5a**

**3-((4-methoxyphenyl)(3-((2-((tetrahydro-2*H*-pyran-2-yl)oxy)ethyl)thio)prop-2-yn-1-yl)amino)propan-1-ol (5a)**

Rf = 0.2 (PE/EA = 2:1).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.91 (d, *J* = 9.0 Hz, 2 H), 6.83 (d, *J* = 9.0 Hz, 2 H), 4.60 (t, *J* = 3.4 Hz, 1 H), 4.01 (s, 2 H), 3.95 – 3.82 (m, 2 H), 3.75 (s, 2 H), 3.72 (t, *J* = 5.8 Hz, 2 H), 3.68 – 3.62 (m, 1 H), 3.52 – 3.45 (m, 1 H), 3.36 (t, *J* = 6.6 Hz, 2 H), 2.84 (td, *J* = 6.6, 3.5 Hz, 2 H), 1.83 – 1.66 (m, 4 H), 1.61 – 1.48 (m, 4 H).

**$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 153.88, 142.80, 119.02, 114.45, 98.85, 89.79, 73.81, 65.49, 62.10, 61.76, 55.53, 49.98, 43.96, 35.02, 30.40, 29.60, 25.32, 19.17.



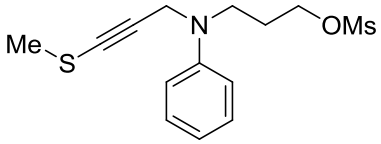

**6a**

**3-((4-methoxyphenyl)(3-((2-((tetrahydro-2*H*-pyran-2-yl)oxy)ethyl)thio)prop-2-yn-1-yl)amino)propyl methanesulfonate (6a)**

Rf = 0.3 (PE/EA = 2:1).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.88 (d, *J* = 9.2 Hz, 2 H), 6.83 (d, *J* = 9.2 Hz, 2 H), 4.59 (t, *J* = 3.7 Hz, 1 H), 4.31 (t, *J* = 6.0 Hz, 2 H), 4.00 (s, 2 H), 3.95 – 3.82 (m, 2 H), 3.76 (s, 3 H), 3.67 – 3.61(m, 1 H), 3.52 – 3.46 (m, 1 H), 3.36 (t, *J* = 6.7 Hz, 2 H), 2.99 (s, 3 H), 2.86 (td, *J* = 6.6, 2.8 Hz, 2 H), 1.99 (dt, *J* = 13.0, 6.4 Hz, 2 H), 1.85 – 1.67 (m, 2 H), 1.62 – 1.48 (m, 4 H).

**$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 153.73, 142.49, 118.53, 114.60, 98.95, 89.85, 67.98, 65.54, 62.21, 55.60, 47.77, 43.92, 37.26, 35.18, 30.50, 27.23, 25.39, 19.33.



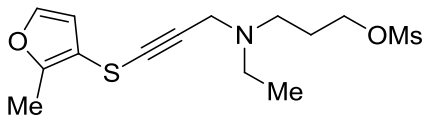

**6c**

**3-((3-(methylthio) prop-2-yn-1-yl)(phenyl)amino)propyl methanesulfonate (6c)**

Rf = 0.5 (PE/EA = 2:1).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.29 (t, *J* = 7.2 Hz, 2 H), 6.89 – 6.80 (m, 3 H), 4.35 (t, *J* = 6.0 Hz, 2 H), 4.14 (s, 2 H), 3.54 (t, *J* = 6.8 Hz, 2 H), 3.01 (s, 3 H), 2.37 (s, 3 H), 2.15 – 2.09 (m, 3 H).

**$^{13}$C NMR** (100 MHz, CDCl3) δ 147.63, 129.06, 118.07, 114.03, 88.75, 75.33, 67.78, 47.07, 41.82, 36.99, 27.05, 18.86.



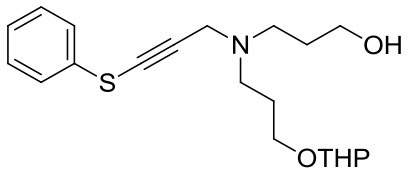

**6d**

**3-(ethyl (3-((2-methylfuran-3-yl) thio) prop-2-yn-1-yl) amino) propyl methanesulfonate (6d)**

Rf = 0.2 (PE/EA = 2:1).

**$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 1.4 Hz, 1 H), 6.42 (d, *J* = 1.1 Hz, 1 H), 4.32 – 4.23 (m, 2 H), 3.45 (s, 2 H), 2.99 (s, 3 H), 2.57 (td, *J* = 6.8, 3.1 Hz, 2 H), 2.54 – 2.46 (m, 2 H), 2.33 (s, 3 H), 1.86 (td, *J* = 6.6, 4.3 Hz, 2 H), 1.02 (t, *J* = 7.1 Hz, 3 H).

**$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 141.57, 141.00, 113.48, 68.40, 61.44, 49.02, 47.57, 42.55, 39.57, 37.23, 27.04, 12.64, 11.87, 8.19.




**5b**

**3-((3-(phenylthio)prop-2-yn-1-yl)(3-((tetrahydro-2*H*-pyran-2-yl)oxy)propyl) amino)propan-1-ol (5b)**

Rf = 0.3 (DCM/MeOH = 20:1).

**$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.40 (d, *J* = 7.7 Hz, 2 H), 7.32 (t, *J* = 7.9 Hz, 2 H), 7.21 (t, *J* = 7.3 Hz, 1 H), 4.56 (t, *J* = 4.2 Hz, 1 H), 4.40 (s, 1H), 3.86 – 3.76 (m, 4 H), 3.72 (s, 2 H), 3.50 – 3.42 (m, 2 H), 2.79 (t, *J* = 5.8 Hz, 2 H), 2.71 – 2.61 (m, 2 H), 1.84 – 1.77 (m, 3 H), 1.74 – 1.67 (m, 3 H), 1.57 – 1.48 (m, 4 H).

**$^{13}$C NMR** (100 MHz, $CDCl_3$) δ 128.96, 126.19, 125.80, 98.68, 93.64, 73.19, 70.90, 65.19, 63.38, 62.14, 53.25, 53.06, 50.78, 50.56, 42.87, 41.28, 30.47, 28.10, 28.00, 27.49, 25.23, 19.42.

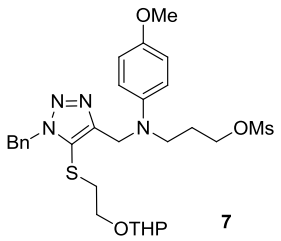
## III. Synthesis and characterization of sequence-defined oligotriazoles

**General procedure for the two steps of ISG strategy and deprotection of THP group**.

**iv.** ***IrAAC.*** In a glove box, to an oven-dried vial was added the building unit involving azide group (1.0 eq.), thioalkyne monomer (1.05-1.5 eq.), $[Ir(COD)Cl]_2$ (4-6 mol %) and DCE (0.5 M). The vial was capped and removed from the glove box. The reaction mixture was stirred at room temperature for 2-6 h until the reaction completed (confirmed by TLC), and then concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to give the desired product.

**v.** ***Azidation.*** The building unit involving OMs group (1.0 eq.) and $NaN_3$ (1.5 eq.) were added to DMF. The reaction mixture was then heated to 80 $^oC$ for 2-5 h until the reaction completed, which was confirmed by TLC. The solution was then cooled to room temperature, diluted with ethyl acetate, washed with brine (three times), dried over $Na_2SO_4$, filtered, and evaporated under vacuum. The crude product was purified by column chromatography on silica gel to afford the related pure building unit involving azide group.

**vi.** ***Deprotection.*** The THP-protected **18** was dissolved in MeOH (0.5 M), and HCl (3.0 eq.) was slowly added at $0^oC$ and stirred another 20 minutes. TLC indicated completion of reaction. Upon completion, $NaHCO_3$ was added and the product was extracted by ethyl ether. The organic layer was dried over $MgSO_4$, filtered, and evaporated under vacuum to give the residue, which was then purified by silica gel flash column chromatography.

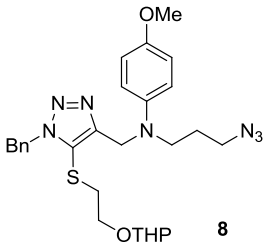



**7**

**7** was prepared as brown oil from benzyl azide (2.4 mmol, 0.32 g, 1.2 eq.) and **6a** (2.0 mmol, 0.92 g, 1.0 eq.) in 85% yield (1.00 g).

Rf = 0.3 (DCM/MeOH = 20:1).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 3 H), 7.22 (d, *J* = 7.8 Hz, 2 H), 6.91 (d, *J* = 9.0 Hz, 2 H), 6.78 (d, *J* = 9.1 Hz, 2 H), 5.62 (s, 2 H), 4.41 (d, *J* = 11.7 Hz, 3 H), 4.24 (t, *J* = 6.1 Hz, 2 H), 3.73 (s, 3 H), 3.77 – 3.70 (m, 1 H), 3.64 – 3.57 (m, 1 H), 3.43 (t, *J* = 7.2 Hz, 3 H), 3.29 (dt, *J* = 10.7, 6.1 Hz, 1 H), 2.94 (s, 3 H), 2.52 (dt, *J* = 6.3, 1.6 Hz, 2 H), 2.00 – 1.94 (m, 2 H), 1.73 – 1.45 (m, 6 H).

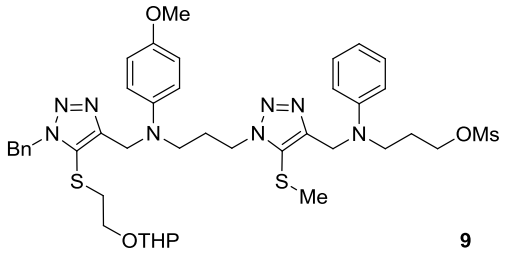



**8**

**8** was prepared as yellow oil from **7** (1.70 mmol, 1.00 g, 1.0 eq.) in 91% yield (0.83g).

Rf = 0.4 (DCM/MeOH = 20:1).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.19 (m, 5 H), 6.91 (d, *J* = 9.0 Hz, 2 H), 6.78 (d, *J* = 9.0 Hz, 2 H), 5.62 (s, 2 H), 4.43 (s, 2 H), 4.39 (t, *J* = 3.5 Hz, 1 H), 3.73 (s, 1 H), 3.77 – 3.71 (m, 1 H), 3.65 – 3.59 (m, 1 H), 3.45 – 3.37 (m, 3 H), 3.31 – 3.26 (m, 3 H), 2.54 (dt, *J* = 6.2, 2.0 Hz, 2 H), 1.85 – 1.78 (m, 2 H), 1.77 – 1.68 (m, 1 H), 1.65 – 1.40 (m, 5 H).

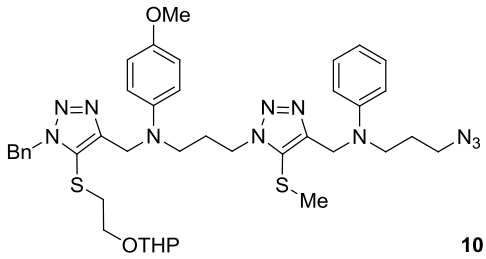



**9**

**9** was prepared as yellow oil from **8** (1.5 mmol, 0.80 g, 1.0 eq.) and **6c** (1.8 mmol, 0.56 g, 1.2 eq.) in 77% yield (0.98 g).

Rf = 0.2 (DCM/MeOH = 20:1).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.28 (m, 3 H), 7.26 – 7.19 (m, 4 H), 6.95 – 6.88 (m, 4 H), 6.78 – 6.72 (m, 4 H), 5.64 (s, 2 H), 4.58 (s, 2 H), 4.45 (s, 2 H), 4.43 – 4.35 (m, 3 H), 4.30 (t, *J* = 6.0 Hz, 2 H), 3.75 (s, 3 H), 3.78 – 3.73 (m, 1 H), 3.66 – 3.60 (m, 3 H), 3.46 – 3.39 (m, 3 H), 3.33 – 3.27 (m, 5 H), 2.99 (s, 3 H), 2.54 (dt, *J* = 6.2, 1.9 Hz, 2 H), 2.18 (t, *J* = 7.0 Hz, 2 H), 2.12 (q, *J* = 6.6 Hz, 2 H), 2.07 (s, 3 H), 1.78 – 1.47 (m, 6 H).

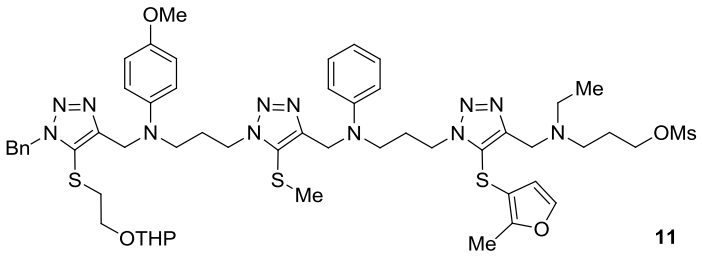



**10**

**10** was prepared as yellow oil from **9** (1.10 mmol, 0.95 g, 1.0 eq.) in 84% yield (0.75g)

Rf = 0.3 (DCM/MeOH = 20:1).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.26 (m, 3 H), 7.25 – 7.16 (m, 4 H), 6.98 – 6.83 (m, 4 H), 6.79 – 6.65 (m, 3 H), 5.62 (s, 2 H), 4.56 (s, 2 H), 4.43 (s, 2 H), 4.40 – 4.30 (m, 3 H), 3.72 (s, 3 H), δ 3.76 – 3.70 (m, 1 H), 3.65 – 3.53 (m, 3 H), 3.48 – 3.31 (m, 5 H), 3.30– 3.24 (m, 1 H), 2.52 (t, *J* = 5.0 Hz, 2 H), 2.15 (t, *J* = 7.2 Hz, 2 H), 2.04 (s, 3 H), 1.98 – 1.86 (m, 2 H), 1.76 – 1.45 (m, 6 H).

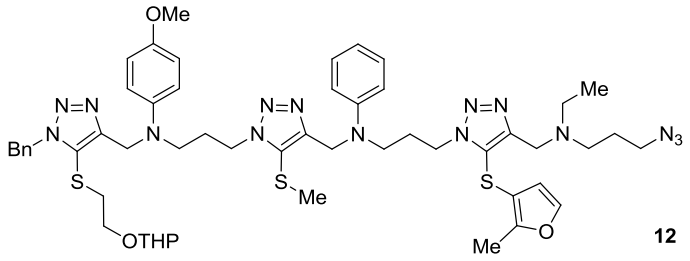



**11**

**11** was prepared as yellow oil from **10** (0.9 mmol, 0.73 g, 1.0 eq.) and **6d** (1.08 mmol, 0.36 g, 1.2 eq.) in 50% yield (0.50 g).

Rf = 0.4 (DCM/MeOH = 15:1).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 3 H), 7.25 – 7.15 (m, 5 H), 6.92 – 6.81 (m, 4 H), 6.79 – 6.65 (m, 3 H), 6.19 (d, *J* = 7.4 Hz, 1 H), 5.62 (s, 2 H), 4.85 – 4.73 (m, 1 H), 4.52 (d, *J* = 6.5 Hz, 2 H), 4.42 (s, 2 H), 4.40 – 4.26 (m, 6 H), 3.72 (s, 3 H), δ 3.76 – 3.71 (m, 1 H), 3.65 – 3.33 (m, 7 H), 3.31 – 3.24 (m, 1 H), 2.97 (s, 2 H), 2.78 (s, 1 H), 2.75 – 2.58 (m, 3 H), 2.51 (dt, *J* = 6.1, 2.5 Hz, 2 H), 2.35 (s, 3 H), 2.25 – 2.10 (m, 4 H), 2.02 (s, 3 H), 1.70 – 1.44 (m, 6 H), 1.34 – 1.21 (m, 3 H), 1.19 – 1.08 (m, 2 H).

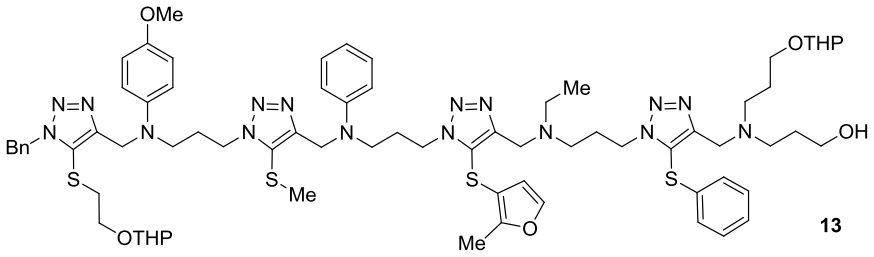



**12**

**13** was prepared as colorless oil from **12** (0.40 mmol, 0.45 g, 1.0 eq.) in 71% yield (0.30g)

Rf = 0.4 (DCM/MeOH = 20:1).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.24 – 7.18 (m, 3 H), 7.15 – 7.13 (m, 2 H), 7.12 – 7.06 (m, 3 H), 6.85 – 6.72 (m, 4 H), 6.71 – 6.59 (m, 3 H), 6.06 (d, *J* = 2.0 Hz, 1 H), 5.54 (s, 2 H), 4.47 (s, 2 H), 4.35 (s, 2 H), 4.32 – 4.24 (m, 5 H), 3.71 (s, 2 H), 3.65 (s, 3 H), 3.68 – 3.63 (m, 1 H), 3.56 – 3.50 (m, 1 H), 3.46 (t, *J* = 6.8 Hz, 2 H), 3.39 – 3.29 (m, 3 H), 3.28 – 3.16 (m, 3 H), 2.53 (s, 3 H), 2.44 (dt, *J* = 6.2, 2.2 Hz, 2 H), 2.27 (s, 3 H), δ 2.17 – 2.03 (m, 4 H), 1.94 (s, 3 H), 1.80 – 1.70 (m, 2 H), 1.67 – 1.38 (m, 6 H), 1.03 (t, *J* = 6.2 Hz, 3 H).

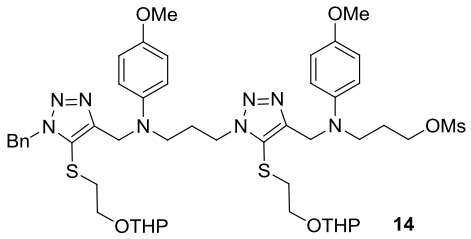



**13** was prepared as yellow oil from **12** (0.25 mmol, 0.26 g, 1.0 eq.) and **5b** (0.30 mmol, 0.13 g, 1.2 eq.) in 45% yield (0.16 g).

Rf = 0.3 (DCM/MeOH = 15:1).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.42 – 7.26 (m, 3 H), 7.26 – 7.19 (m, 5 H), 7.19 – 7.12 (m, 4 H), 7.01 – 6.92 (m, 2 H), 6.89 – 6.84 (m, 2 H), 6.84 – 6.78 (m, 2 H), 6.76 – 6.72 (m, 2 H), 6.71 – 6.66 (m, 1 H), 6.10 (d, *J* = 2.0 Hz, 1 H), 5.61 (s, 2 H), 4.57 – 4.50 (m, 3 H), 4.41 (s, 2 H), 4.38 – 4.32 (m, 7 H), 3.90 – 3.76 (m, 4 H), 3.76 – 3.68 (m, 9 H), 3.62 – 3.57 (m, 1 H), 3.52 (t, *J* = 7.2 Hz, 1 H), 3.49 – 3.40 (m, 3 H), 3.40 – 3.34 (m, 3 H), 3.29 – 3.24 (m, 1 H), 2.76 – 2.73 (m, 2 H), 2.70 – 2.60 (m, 2 H), 2.53 – 2.45 (m, 6 H), 2.30 (s, 3 H), 2.21 – 2.09 (m, 4 H), 2.00 (s, 3 H), 1.90 – 1.77 (m, 4 H), 2.00 – 1.77 (m, 4 H), 1.55 – 1.45 (m, 8 H), 1.02 (t, *J* = 7.1 Hz, 3 H).

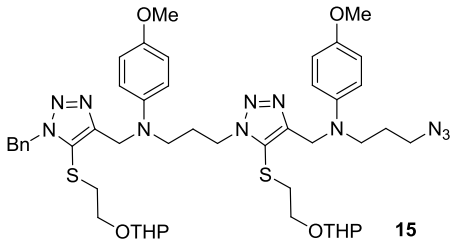
**ESI-MS** *m/z* calcd. for $C_{73}H_{99}N_{16}O_7S_4$ $(M+H)^+$ 1439.6765, found 1439.6768.




**14** was prepared as yellow oil from **8** (2.00 mmol, 0.54 g, 1.0 eq.) and **5b** (2.40 mmol, 1.10 g, 1.2 eq.) in 82 % yield (1.63 g).

Rf = 0.4 (DCM/MeOH = 20:1).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.26 – 7.19 (m, 3 H), 7.16 – 7.12 (m, 2 H), 6.87 – 6.78 (m, 4 H), 6.73 – 6.66 (m, 4 H), 5.54 (s, 2 H), 4.38 – 4.29 (m, 8 H), 4.17 (t, *J* = 6.1 Hz, 2 H), 3.71 – 3.65 (m, 2 H), 3.64 (s, 6 H), 3.63 – 3.59 (m, 1 H), 3.56 – 3.50 (m, 1 H), 3.39 – 3.29 (m, 7 H), 3.23 – 3.17 (m, 1 H), 2.87 (s, 3 H), 2.65 (td, *J* = 6.5, 0.7 Hz, 2 H), 2.43 (td, *J* = 6.2, 2.3 Hz, 2 H), 2.07 (t, *J* = 6.9 Hz, 2 H), 1.91 (t, *J* = 6.4 Hz, 2 H), 1.71 – 1.62 (m, 2 H), 1.56 – 1.50 (m, 2 H), 1.47 – 1.36 (m, 8 H).

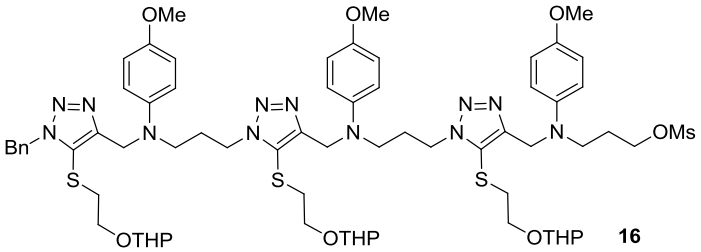



**15**

**15** was prepared as colorless oil from **14** (1.60 mmol, 1.63 g, 1.0 eq.) in 92% yield (1.4 g).

Rf = 0.4 (DCM/MeOH = 30:1).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.28 (m, 3 H), 7.27 – 7.20 (m, 2 H), 7.00 – 6.84 (m, 2 H), 6.84 – 6.74 (m, 4 H), 5.64 (s, 2 H), 4.45 (s, 4 H), 4.44 – 4.37 (m, 4 H), 3.80 – 3.68 (m, 9 H), 3.65 – 3.59 (m, 1 H), 3.49 – 3.25 (m, 10 H), 2.81– 2.68 (m, 2 H), 2.52 (dt, *J* = 6.2, 2.0 Hz, 2 H), 2.24 – 2.12 (m, 2 H), 2.00 – 1.91 (m, 2 H), 1.78 – 1.70 (m, 2 H), 1.67 – 1.45 (m, 10 H).

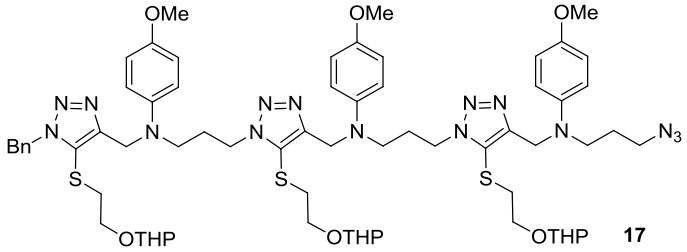



**16**

**16** was prepared as yellow oil from **15** (1.40 mmol, 1.32 g, 1.0 eq.) and **5b** (1.68 mmol, 0.78 g, 1.2 eq.) in 83 % yield (1.62 g).

Rf = 0.3 (DCM/MeOH = 20:1).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.32 – 7.26 (m, 3 H), 7.23 – 7.18 (m, 2 H), 6.96 – 6.84 (m, 6 H), 6.80 – 6.72 (m, 5 H), 5.61 (s, 2 H), 4.47 – 4.35 (m, 13 H), 4.24 (t, *J* = 6.1 Hz, 2 H), 3.76 – 3.72 (m, 3 H), 3.71 (s, 3H), 3.71 (s, 3 H), 3.69 (s, 3 H), 3.69 – 3.55 (m, 3 H), 3.44 – 3.11 (m, 11 H), 3.29 – 3.23 (m, 1 H), 2.94 (s, 3 H), 2.77 – 2.65 (m, 4 H), 2.49 (dt, *J* = 6.6, 2.1 Hz, 2 H), 2.15 (q, *J* = 7.5 Hz, 4 H), 1.98 (t, *J* = 6.4 Hz, 2 H), 1.74 – 1.43 (m, 18 H).

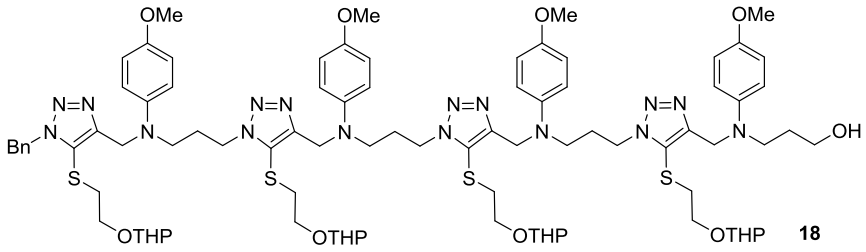



**17**

**17** was prepared as colorless oil from **16** (1.16 mmol, 1.60 g, 1.0 eq.) in 92% yield (1.44 g).

Rf = 0.3 (DCM/MeOH = 30:1).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 3 H), 7.26 – 7.20 (m, 2 H), 6.98 – 6.86 (m, 6 H), 6.83 – 6.74 (m, 6 H), 5.63 (s, 2 H), 4.49 – 4.37 (m, 13 H), 3.79 – 3.76 (m, 2 H), 3.74 (s, 3 H), 3.73 (s, 3 H), 3.72 (s, 3H), 3.70 – 3.58 (m, 2 H), 3.47 – 3.37 (m, 10 H), 3.37 – 3.25 (m, 4 H), 2.80 – 2.67 (m, 4 H), 2.52 (dt, *J* = 6.2, 2.2 Hz, 2 H), 2.17 (q, *J* = 7.1 Hz, 4 H), 1.84 (t, *J* = 7.2 Hz, 2 H), 1.79 – 1.40 (m, 19 H).



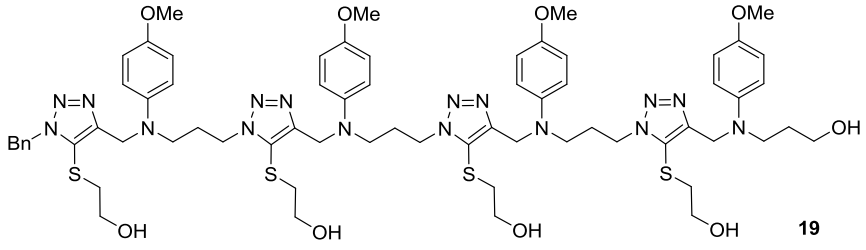
**18**

**18** was prepared as yellow oil from **17** (0.9 mmol, 1.21 g, 1.0 eq.) and **5b** (1.08 mmol, 0.41 g, 1.2 eq.) in 70% yield (1.08 g).

Rf = 0.2 (DCM/MeOH = 20:1).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.31 – 7.26 (m, 2 H), 7.25 (s, 1 H), 7.22– 7.17 (m, 5 H), 6.93 (d, *J* = 9.0 Hz, 2 H), 6.88 – 6.82 (m, 6 H), 6.77 (d, *J* = 9.0 Hz, 2 H), 6.79 – 6.70 (m, 6 H), 5.60 (s, 2 H), 4.44 – 4.35 (m, 18 H), 3.77 – 3.73 (m, 5 H), 3.71 (s, 3 H), 3.70 (s, 3 H), 3.69 (s, 3 H), 3.68 (s, 3 H), 3.67 – 3.55 (m, 5 H), 3.45 – 3.33 (m, 15 H), 3.32 – 3.23 (m, 2 H), 2.76 – 2.64 (m, 6 H), 2.49 (dt, *J* = 6.2, 2.3 Hz, 2 H), 2.14 (q, *J* = 7.2 Hz, 6 H), 1.77 (q, *J* = 6.1 Hz, 2 H), 1.74 – 1.64 (m, 4 H), 1.61 – 1.40 (m, 20 H).

**MALDI-TOF-MS** *m/z* calcd. for $C_{87}H_{121}N_{16}O_{13}S_4$ $(M+H)^+$ 1725.8, found 1725.5.



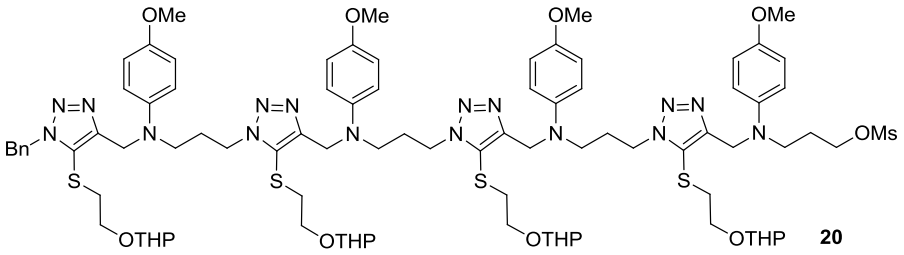
**19**

**19** was prepared as white solid from **18** (0.3 mmol, 0.52 g, 1.0 eq.) in 79% yield (0.33 g).

Rf = 0.2 (DCM/MeOH = 15:1).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 3 H), 7.22 – 7.16 (m, 2 H), 7.09 – 6.88 (m, 8 H), 6.84 – 6.75 (m, 8 H), 5.59 (s, 2 H), 4.42 – 4.29 (m, 14 H), 3.72 (s, 12 H), 3.60 (t, *J* = 5.7 Hz, 2 H), 3.53 (t, *J* = 5.8 Hz, 6 H), 3.39 (t, *J* = 5.7 Hz, 2 H), δ 3.33 – 3.21 (m, 8 H), 2.73 (t, *J* = 5.2 Hz, 6 H), 2.47 (t, *J* = 5.6 Hz, 2 H), 2.12 (t, *J* = 7.2 Hz, 6 H), 1.71 (t, *J* = 6.2 Hz, 2 H).

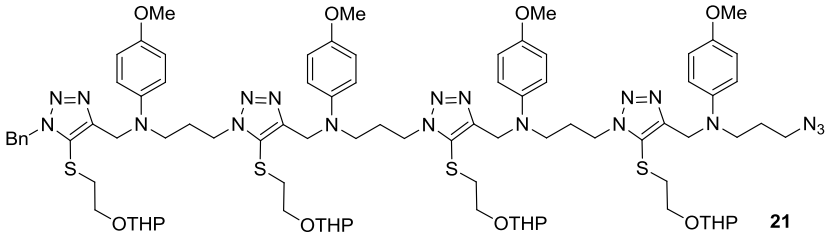
**ESI-MS** *m/z* calcd. for $C_{67}H_{89}N_{16}O_9S_4$ $(M+H)^+$ 1389.5881, found 1389.5930.




**20** was prepared as yellow oil from **18** (0.25 mmol, 0.44 g, 1.0 eq.), MsCl (0.32 mmol, 0.37 g, 1.25 eq.) and $Et_3N$ (0.38 mmol, 0.38 g, 1.5 eq.) in 99% yield (0.46 g).

Rf = 0.2 (DCM/MeOH = 30:1).

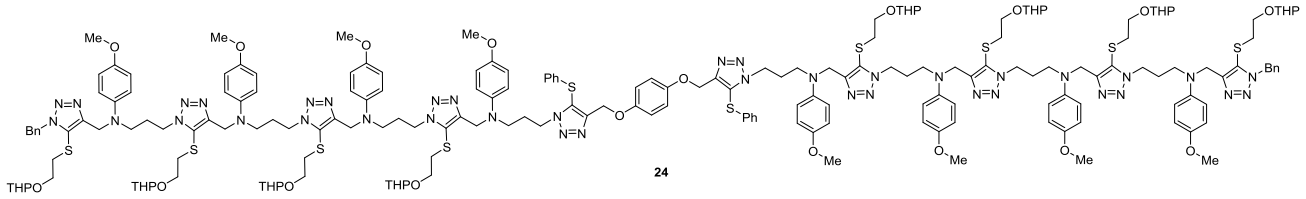
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.31 – 7.26 (m, 3 H), 7.23 – 7.17 (m, 2 H), 6.95 – 6.82 (m, 8 H), 6.79 – 6.71 (m, 8 H), 5.60 (s, 2 H), 4.46 – 4.34 (m, 18 H), 4.23 (t, *J* = 6.1 Hz, 2 H), 3.74 – 3.61 (m, 19 H), 3.61 – 3.54 (m, 1 H), 3.45 – 3.31 (m, 15 H), 3.30 – 3.22 (m, 1 H), 2.94 (s, 3H), 2.76 – 2.63 (m, 6 H), 2.49 (dt, *J* = 6.2, 2.3 Hz, 2 H), 2.15 (t, *J* = 7.6 Hz, 6 H), 1.97 (t, *J* = 6.4 Hz, 2 H), 1.75 – 1.65 (m, 4 H), 1.61 – 1.40 (m, 20 H).




**21** was prepared as colorless and oil from **20** (0.2 mmol, 0.36 g, 1.0 eq.) in 96% yield (0.33 g).

Rf = 0.3 (DCM/MeOH = 30:1).

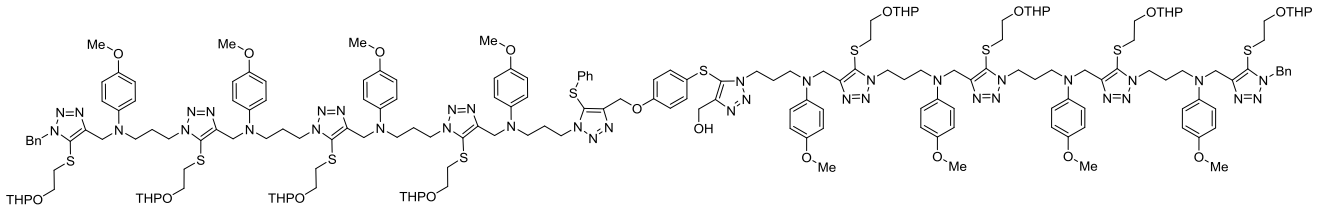
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.10 – 8.06 (m, 2 H), 7.39 (t, *J* = 8.0 Hz, 2 H), 7.34 – 7.18 (m, 15 H), 7.16 – 7.10 (m, 4 H), 6.90 (t, *J* = 8.0 Hz, 2 H), 5.66 (s, 2 H), 4.97 (s, 2 H), 4.48 (s, 2 H), 4.42 (t, *J* = 8.0 Hz, 2 H), 4.34 (t, *J* = 8.0 Hz, 2 H), 4.27 – 4.25 (m, 4 H), 4.18 (t, *J* = 8.0 Hz, 2 H), 3.89 (t, *J* = 8.0 Hz, 2 H), 3.46 (t, *J* = 8.0 Hz, 2 H), 3.11 (t, *J* = 8.0 Hz, 2 H), 3.04 – 3.02 (m, 4 H), 2.96 – 2.80 (m, 6 H), 2.67 – 2.58 (m, 4 H), 1.94 – 1.82 (m, 1 H), 1.66 – 1.64 (m, 2 H), 1.44 – 1.25 (m, 2 H), 1.04 – 0.98 (m, 4 H), 0.92 (t, *J* = 8.0 Hz, 3 H), 0.38 (s, 9 H).




**24** was prepared as yellow oil from **21** (0.06 mmol, 0.10 g, 2.2 eq.) and **22** (0.03 mmol, 12 mg, 1 eq.) in 43% yield (0.05 g).

Rf = 0.2 (DCM/MeOH = 10:1).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.26 (m, 6 H), 7.23 – 7.14 (m, 10 H), 7.04 – 7.00 (m, 4 H), 6.88 – 6.79 (m, 20 H), 6.76 – 6.70 (m, 16 H), 5.61 (s, 4 H), 5.07 (s, 4 H), 4.43 – 4.37 (m, 30 H), 4.35 – 4.29 (m, 8 H), 3.76 – 3.72 (m, 6 H), 3.71 (s, 6 H), 3.70 (s, 6 H), 3.69 (s, 12 H), 3.68 – 3.63 (m, 6 H), 3.62 – 3.56 (m, 2 H), 3.44 – 3.31 (m, 30 H), 3.28 – 3.23 (m, 2 H), 2.68 (t, *J* = 6.3 Hz, 12 H), 2.49 (dt, *J* = 6.1, 2.3 Hz, 4 H), 2.15 (t, *J* = 6.8 Hz, 12 H), 2.04 (t, *J* = 7.2 Hz, 4 H), 1.80 – 1.65 (m, 10 H), 1.62 – 1.54 (m, *J* = 11.8, 2.3 Hz, 10 H), 1.52 – 1.39 (m, 32 H).



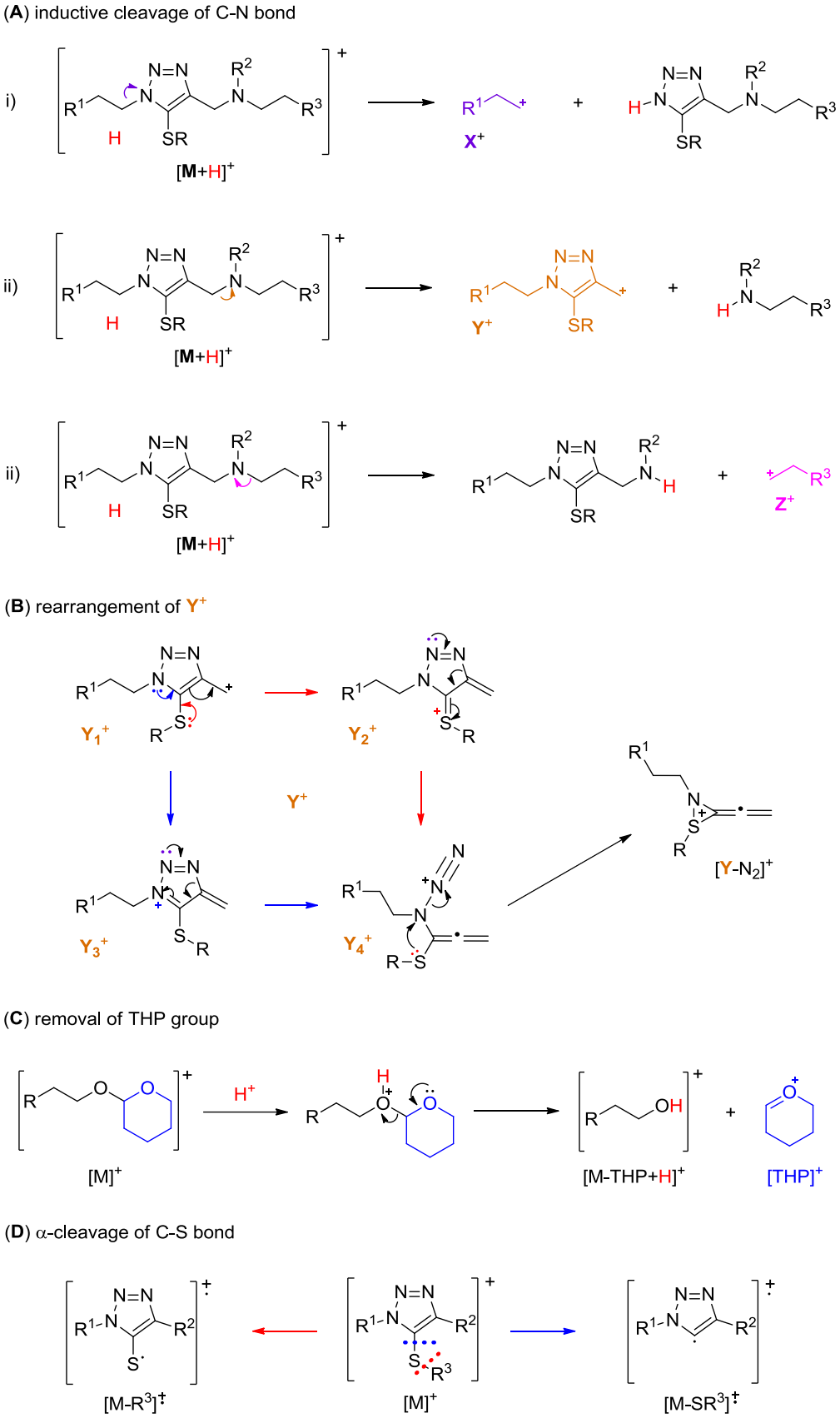
**25**

**25** was prepared as yellow oil from **21** (0.11 mmol, 0.19 g, 2.2 eq.) and **23** (0.05 mmol, 16 mg, 1 eq.) in 70% yield (0.13 g).

Rf = 0.2 (DCM/MeOH = 10:1).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.26 (m, 8 H), 7.23 – 7.14 (m, 7 H), 7.08 – 6.98 (m, 4 H), 6.89 – 6.79 (m, 16 H), 6.78 – 6.70 (m, 16 H), 5.61 (s, 4 H), 5.07 (s, 2 H), 4.74 (d, *J* = 5.1 Hz, 2 H), 4.43 – 4.36 (m, 30 H), 4.35 – 4.27 (m, 6 H), 3.76 – 3.62 (m, 38 H), 3.62 – 3.56 (m, 2 H), 3.47 – 3.22 (m, 32 H), 2.68 (t, *J* = 5.8 Hz, 12 H), 2.49 (td, *J* = 6.1, 2.3 Hz, 4 H), 2.15 (p, *J* = 6.8 Hz, 12 H), 2.05 (q, *J* = 7.1 Hz, 4 H), 1.84 – 1.34 (m, 52 H).

# IV. Tandem mass spectrometry analysis of tetramers 13 and 19




**Scheme S2**. Possible mechanisms for fragmentation patterns.

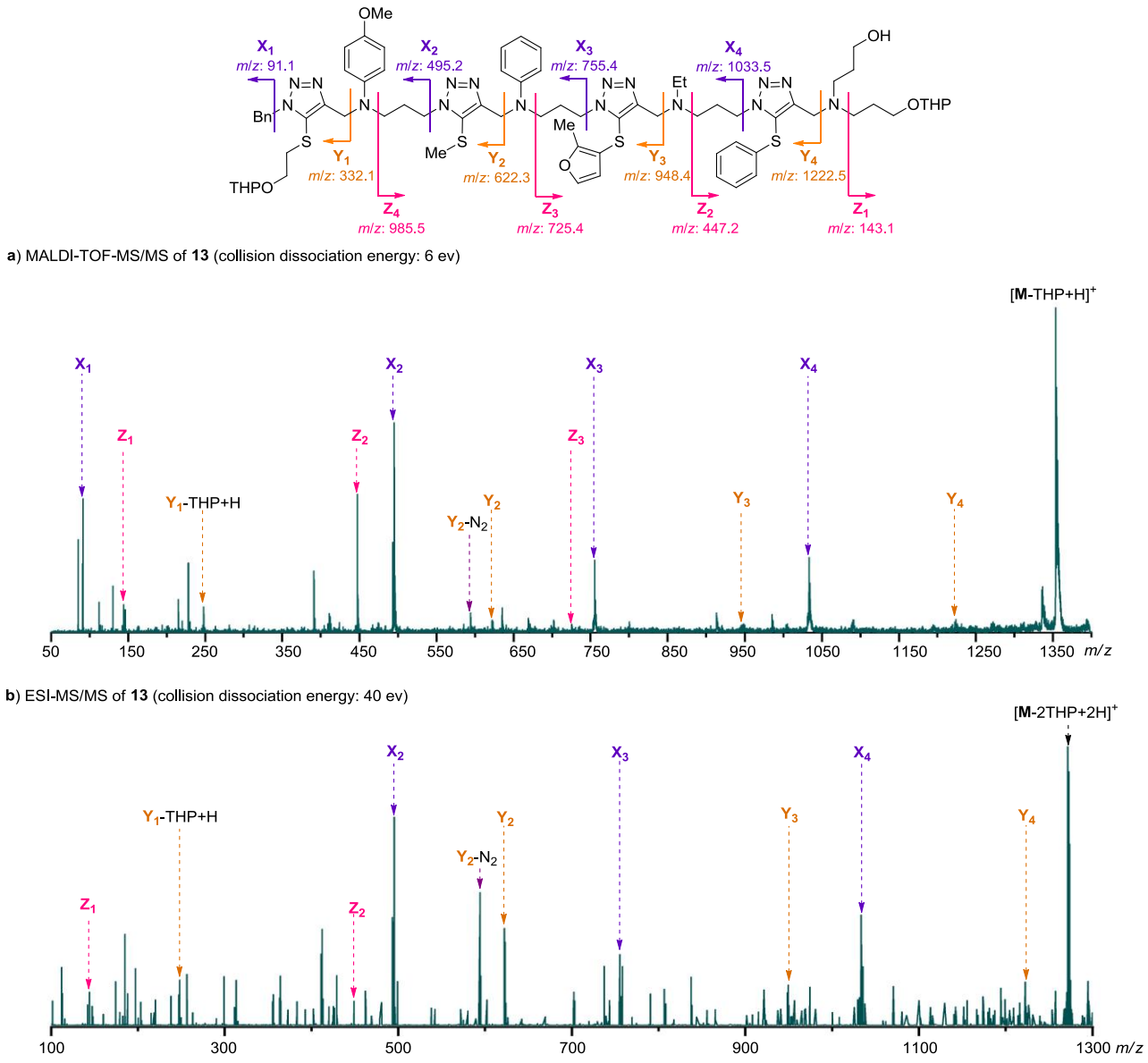



**Figure S1**. Comparison of MALDI-TOF-MS/MS spectra (**a,** collision dissociation energy: 6 eV) and ESI-MS/MS spectra (**b**, collision dissociation energy: 40 eV) of $[M_{\mathbf{13}}+H]^+$.

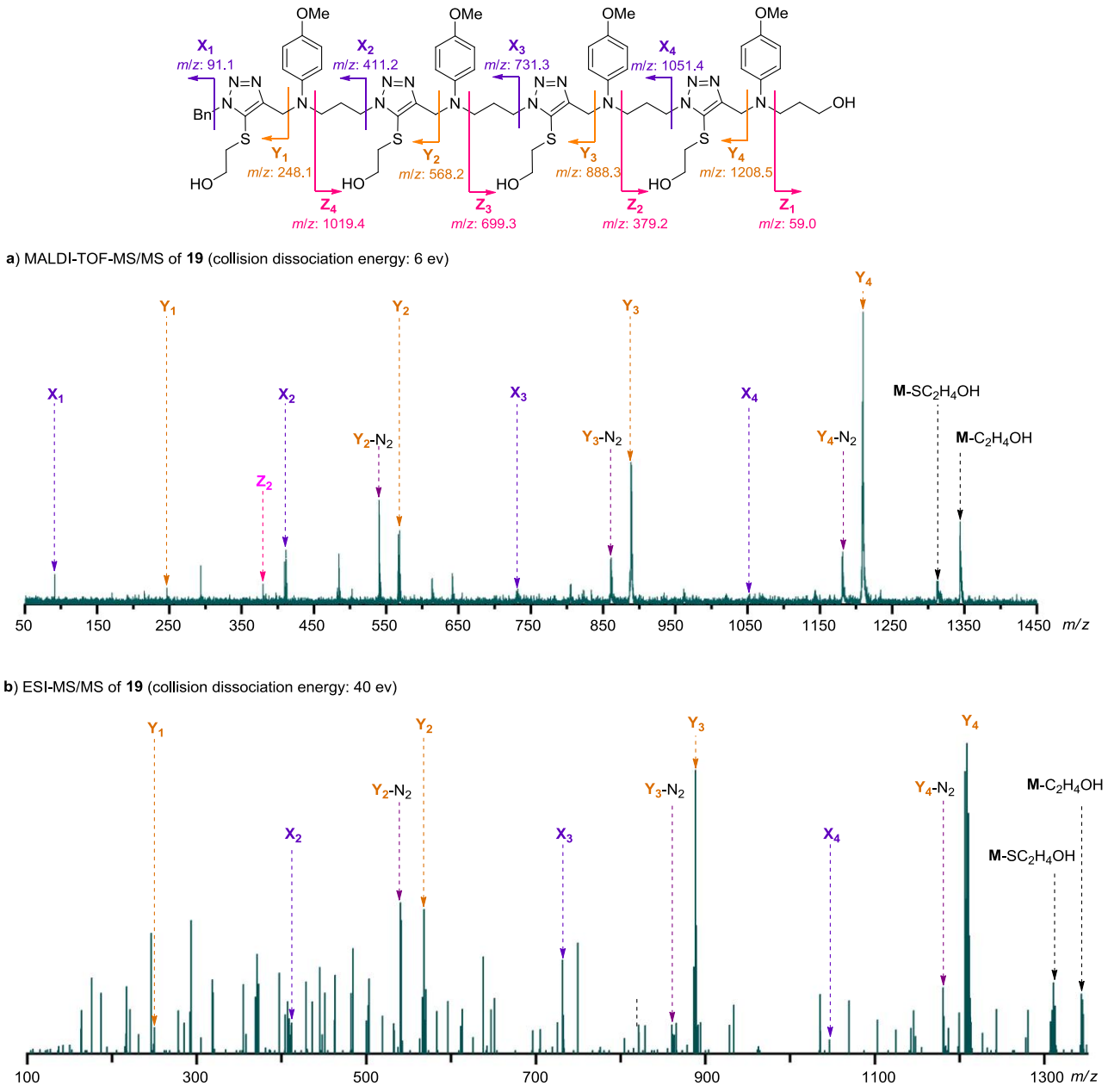



**Figure S2**. Comparison of MALDI-TOF-MS/MS spectra (**a,** collision dissociation energy: 6 eV) and ESI-MS/MS spectra (**b**, collision dissociation energy: 40 eV) of $[M_{\mathbf{19}}+H]^+$.

## V. NMR Spectra

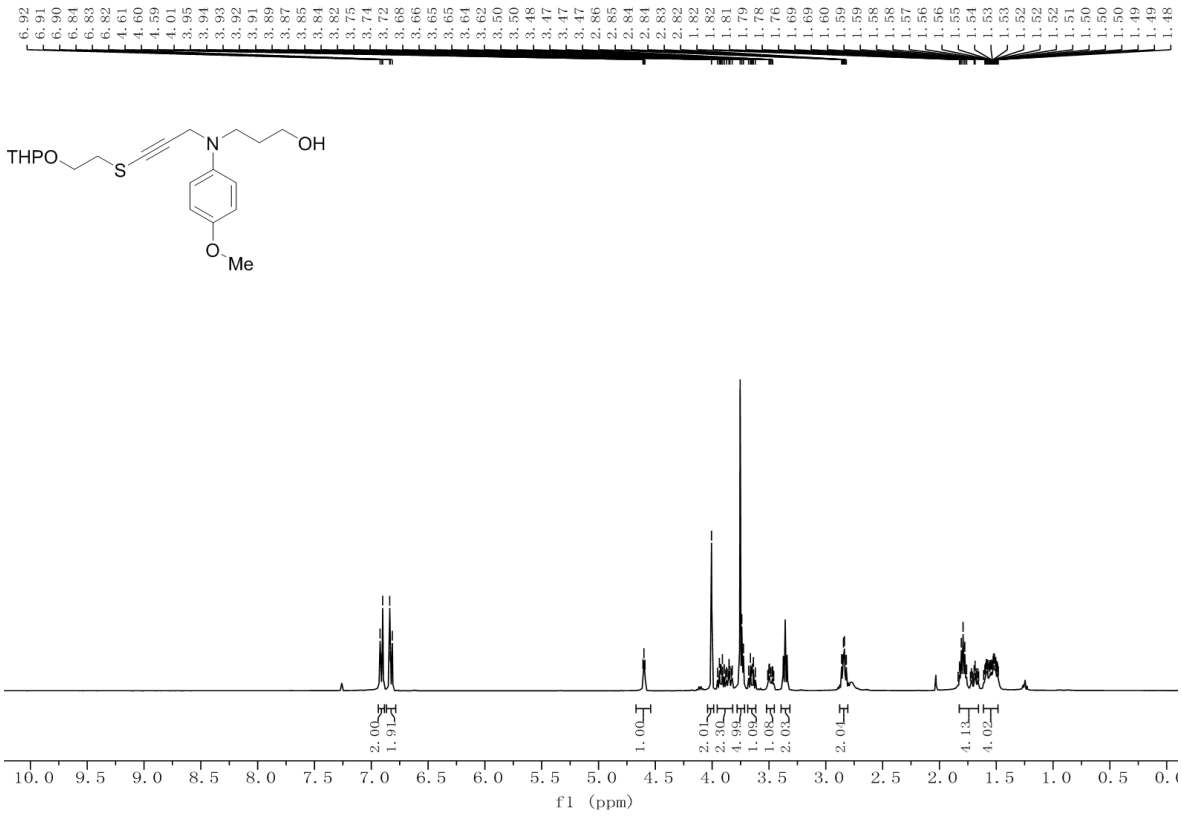



**Figure S3**. $^{1}$H NMR spectra of **5a**.

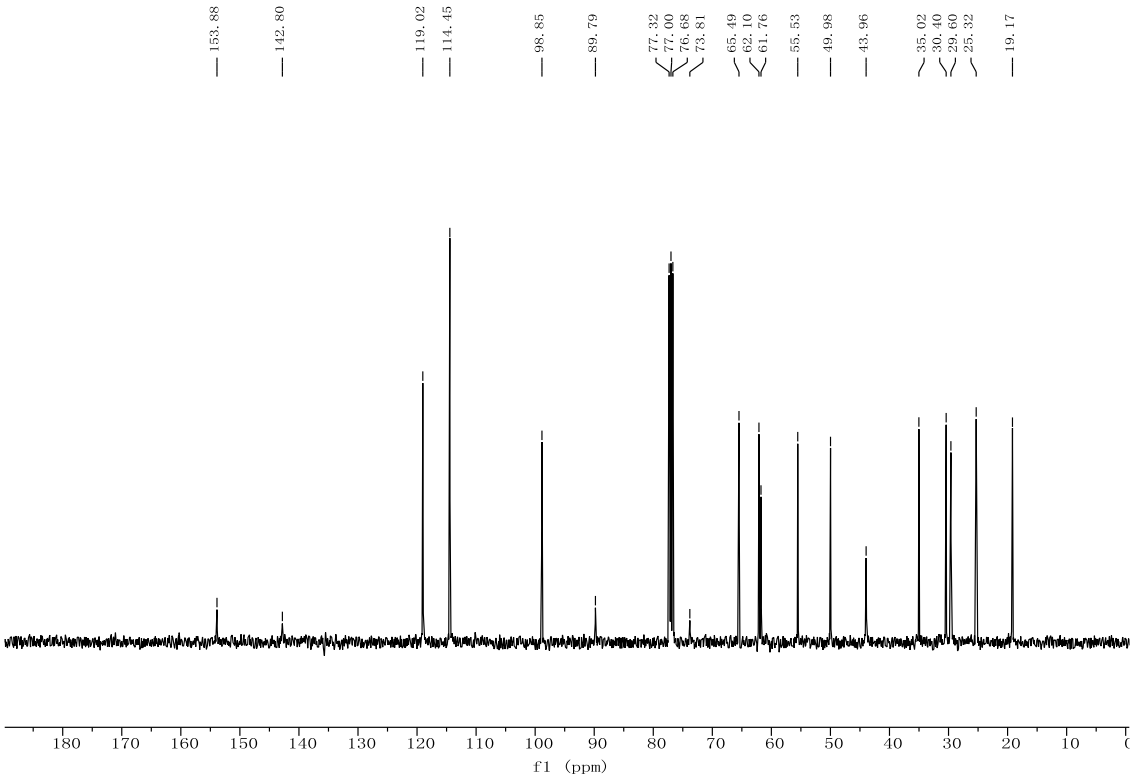



**Figure S4**. $^{13}$C NMR spectra of **5a**.

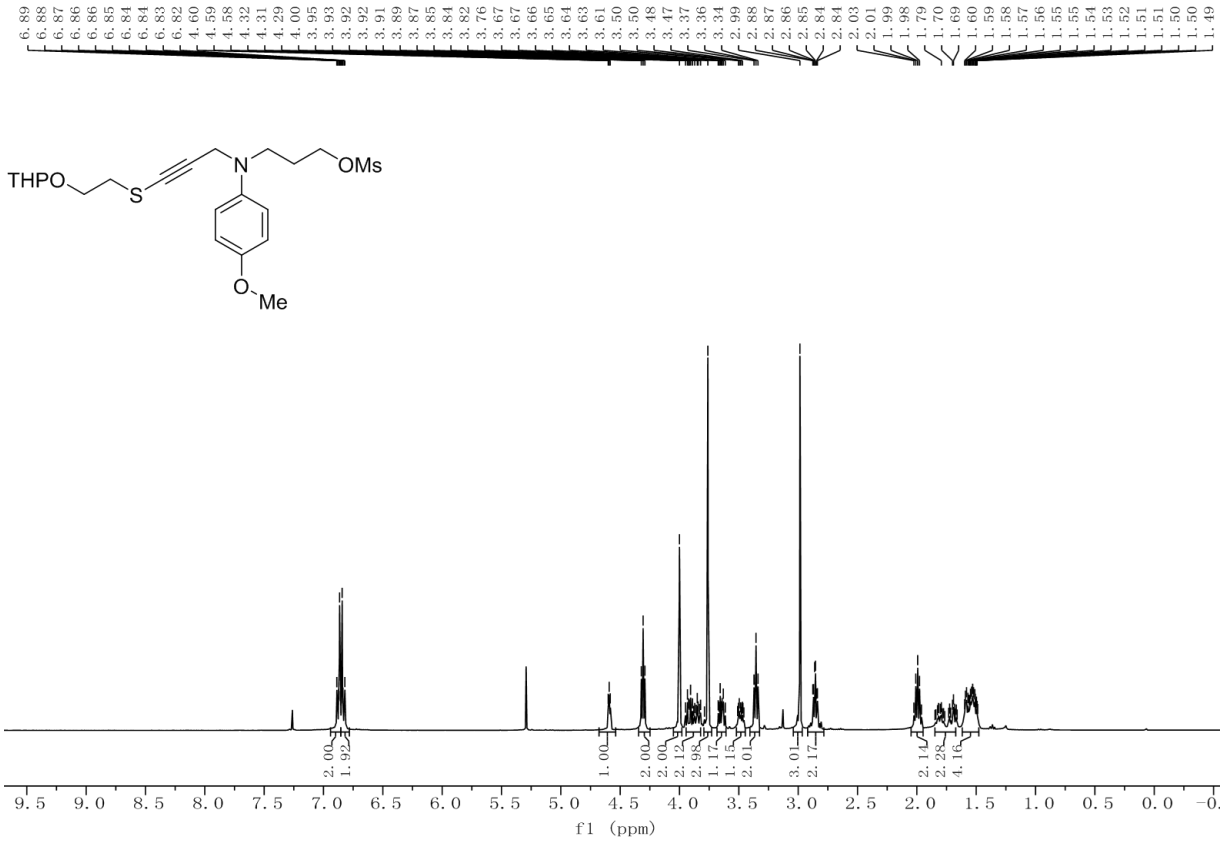



**Figure S5**. $^{1}$H NMR spectra of **6a**.

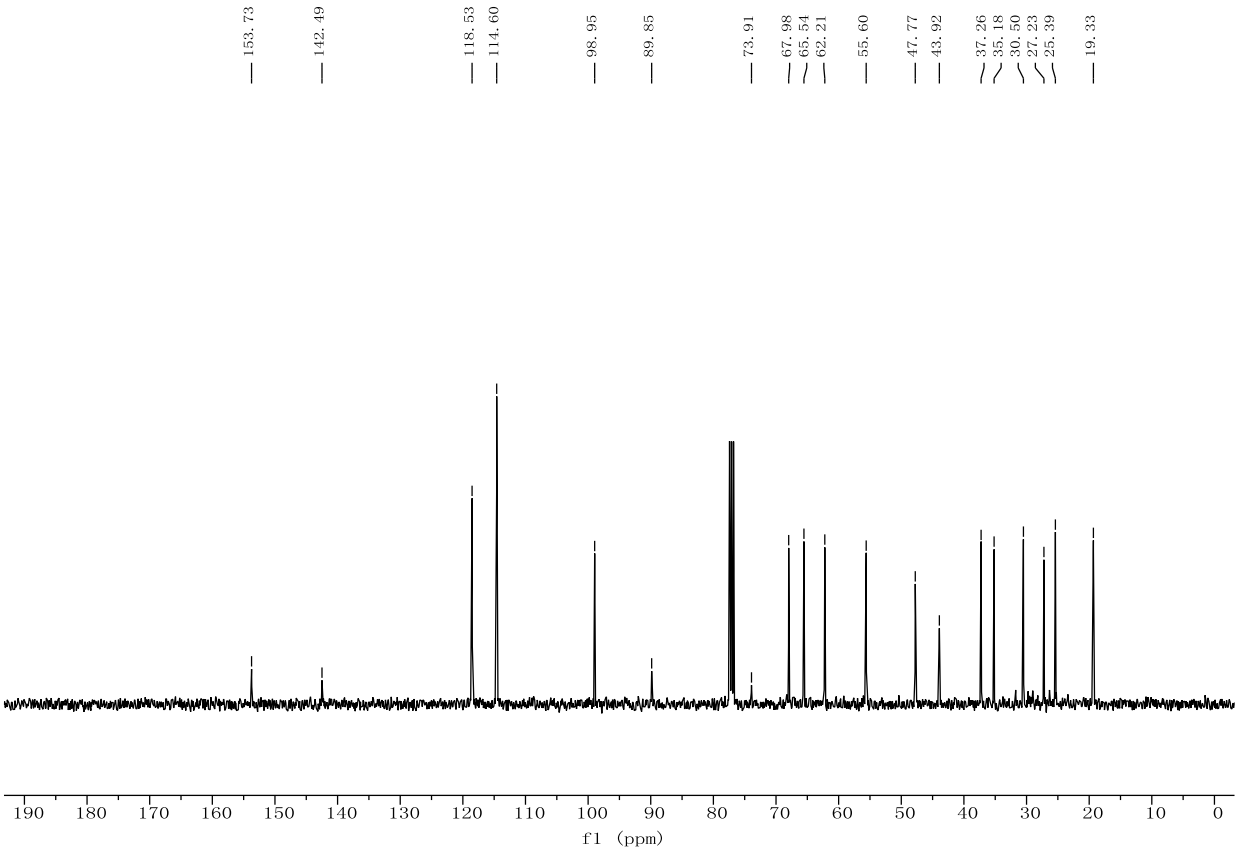



**Figure S6**. $^{13}$C NMR spectra of **6a**.

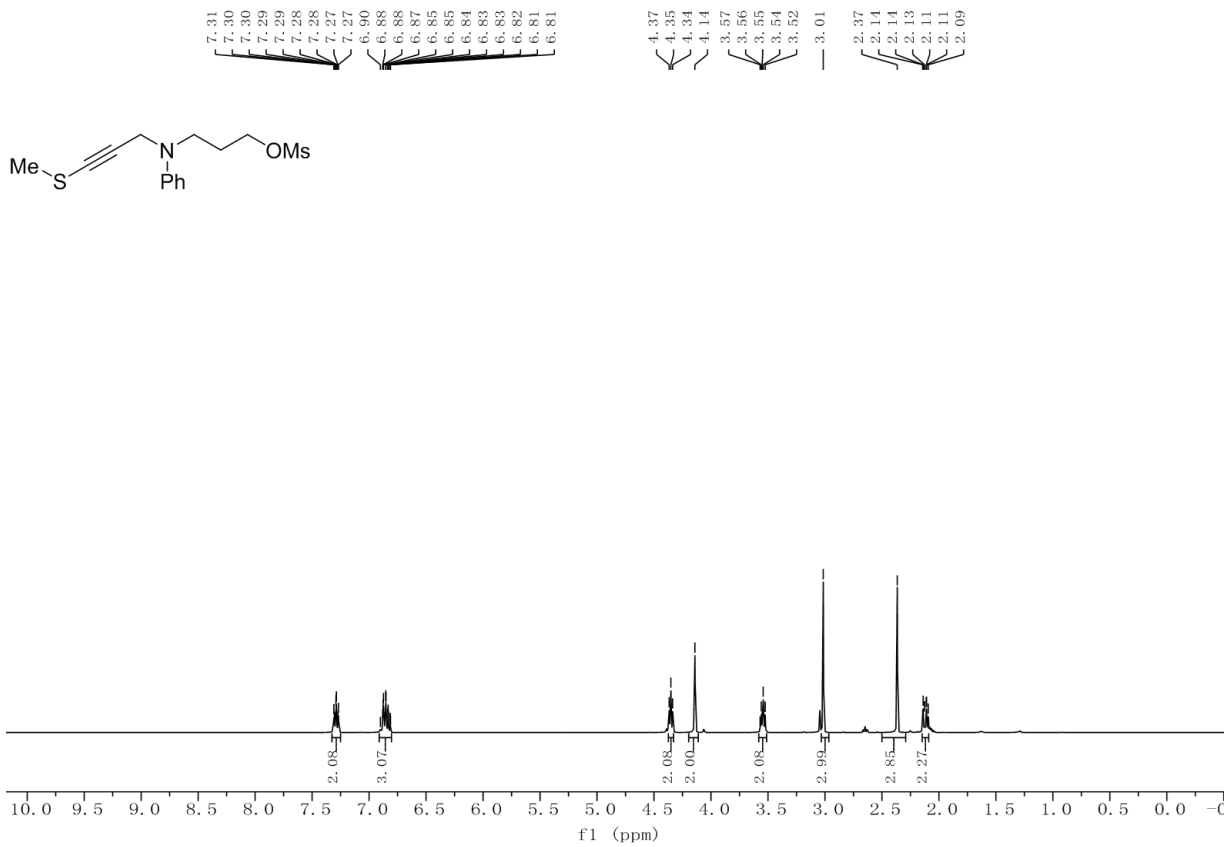



**Figure S7**. $^{1}$H NMR spectra of **6c**.

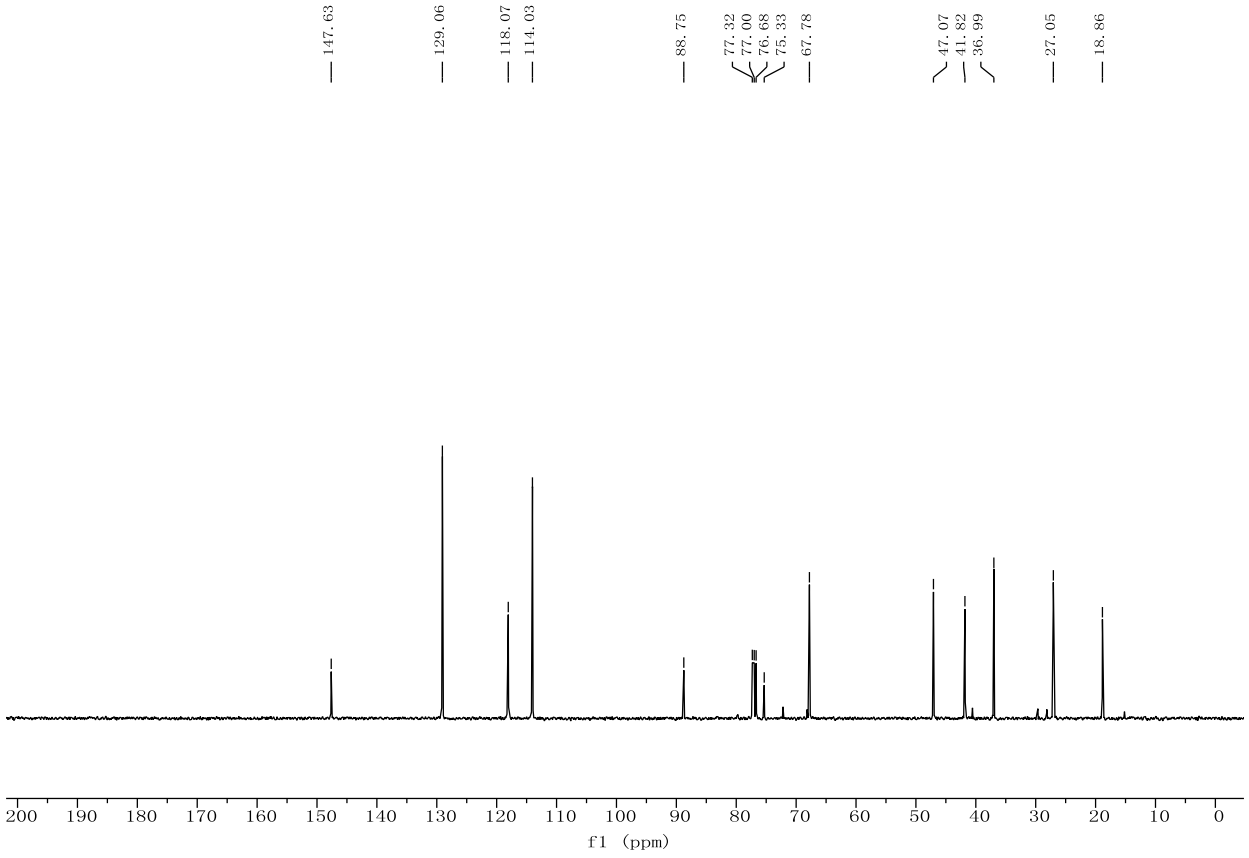



**Figure S8**. $^{13}$C NMR spectra of **6c**.

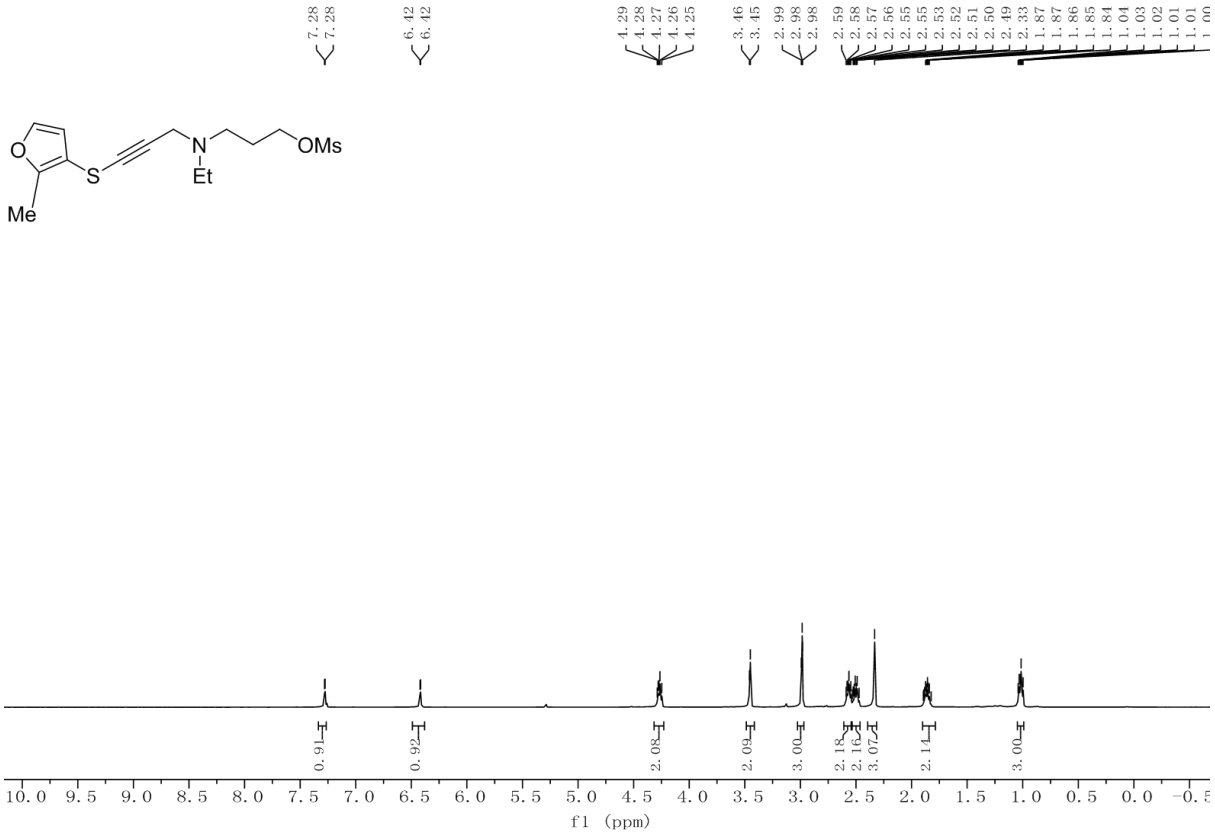



**Figure S9**. $^{1}$H NMR spectra of **6d**.

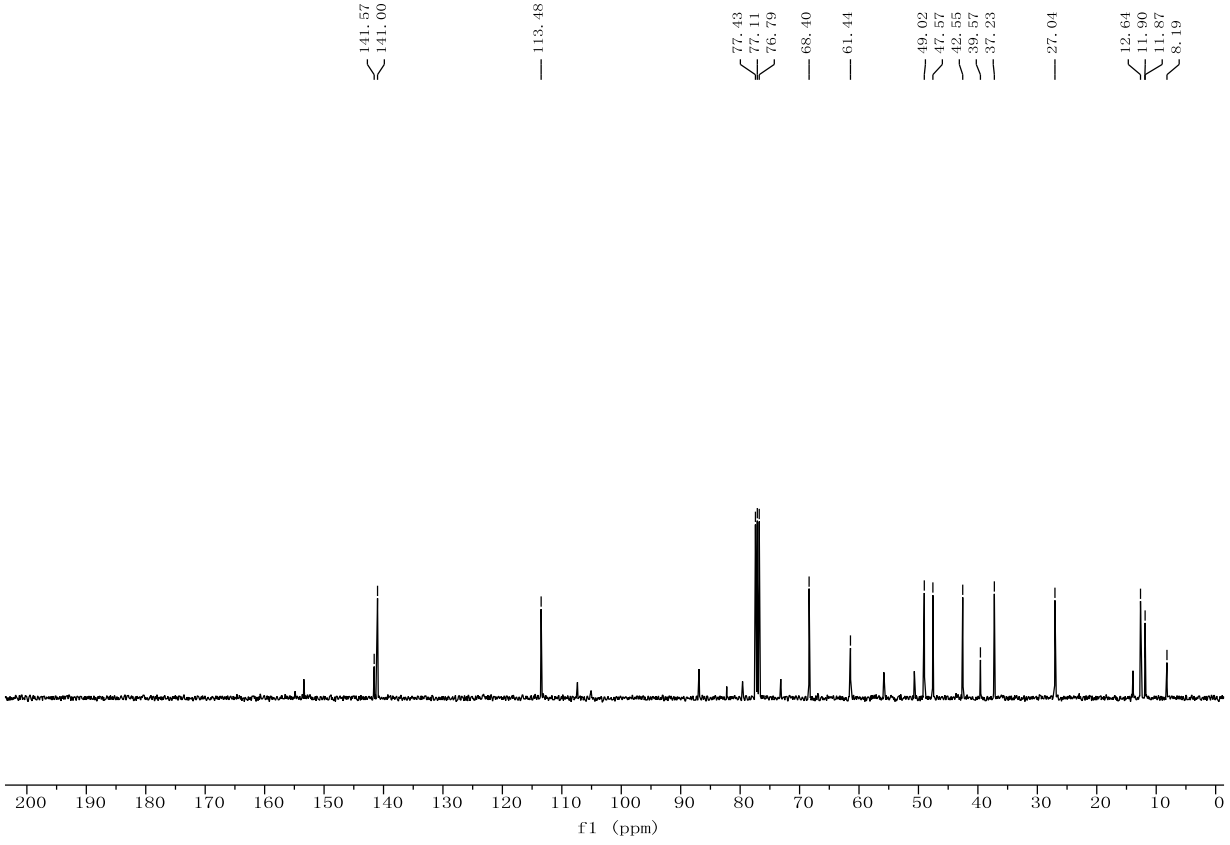



**Figure S10**. $^{13}$C NMR spectra of **6d**.

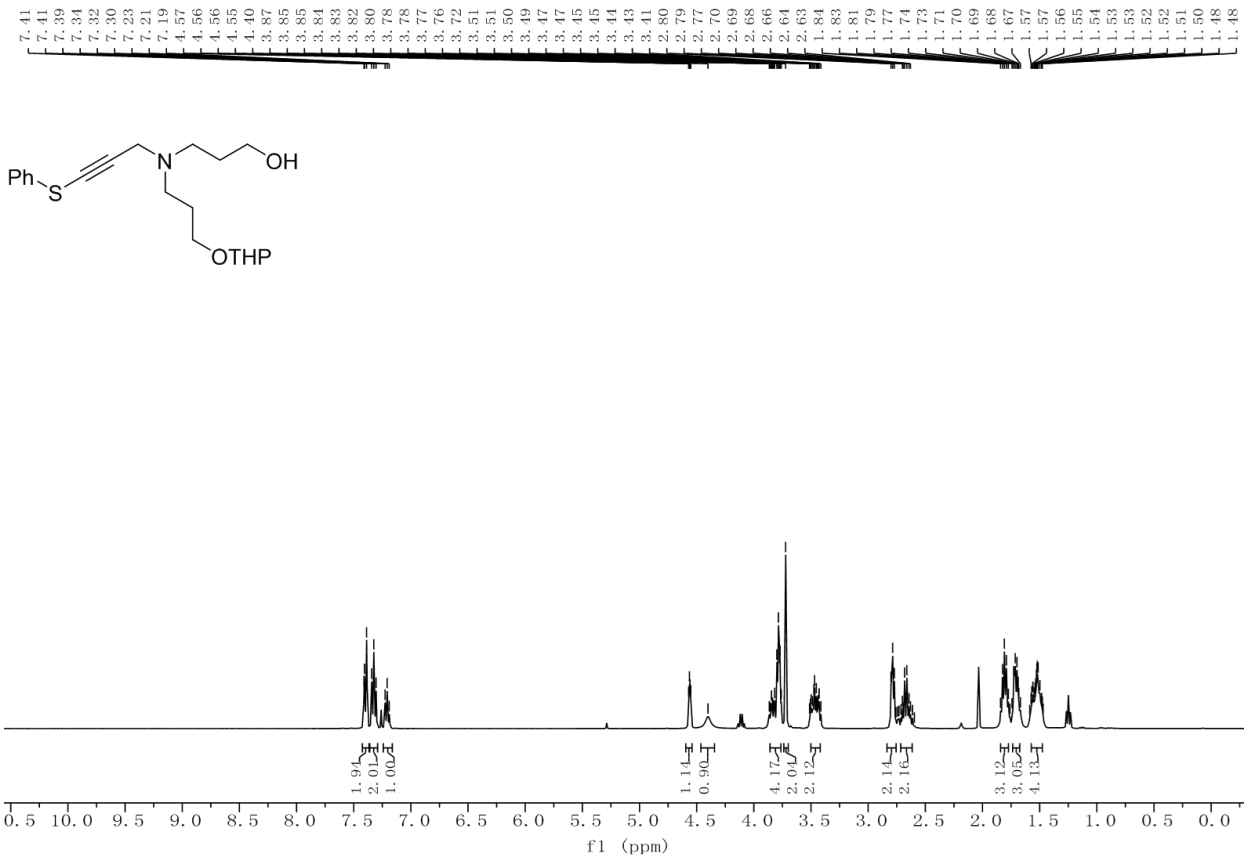



**Figure S11**. $^{1}$H NMR spectra of **5b**.

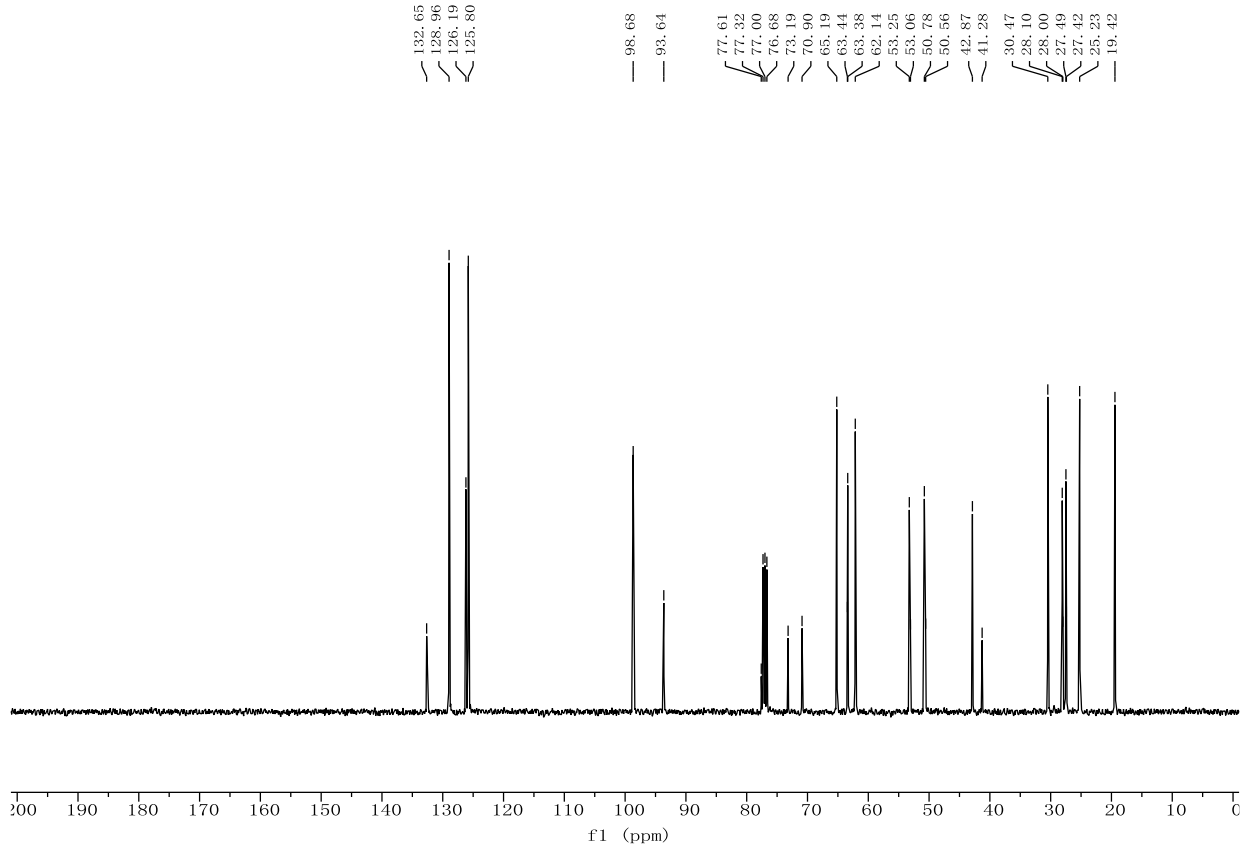



**Figure S12**. $^{13}$C NMR spectra of **5b**.

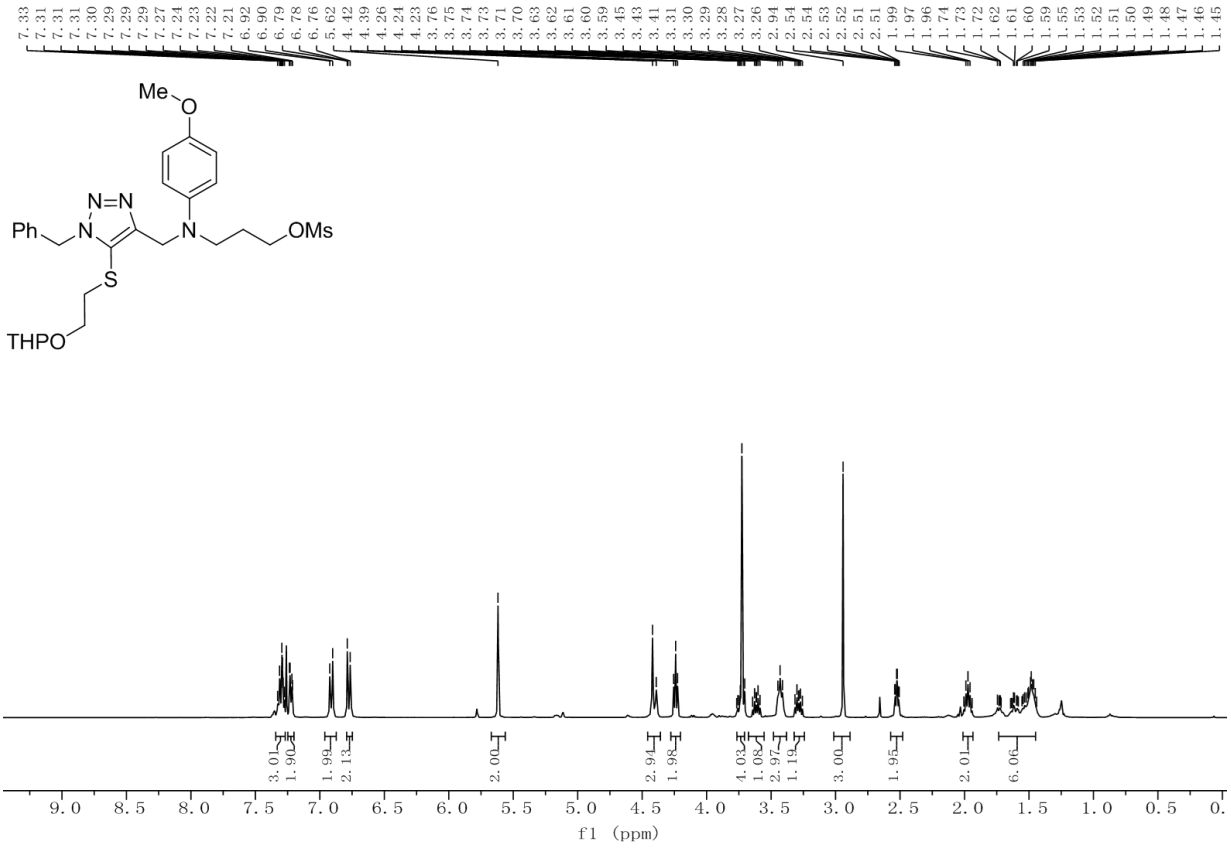



**Figure S13**. $^{1}$H NMR spectra of **7**.

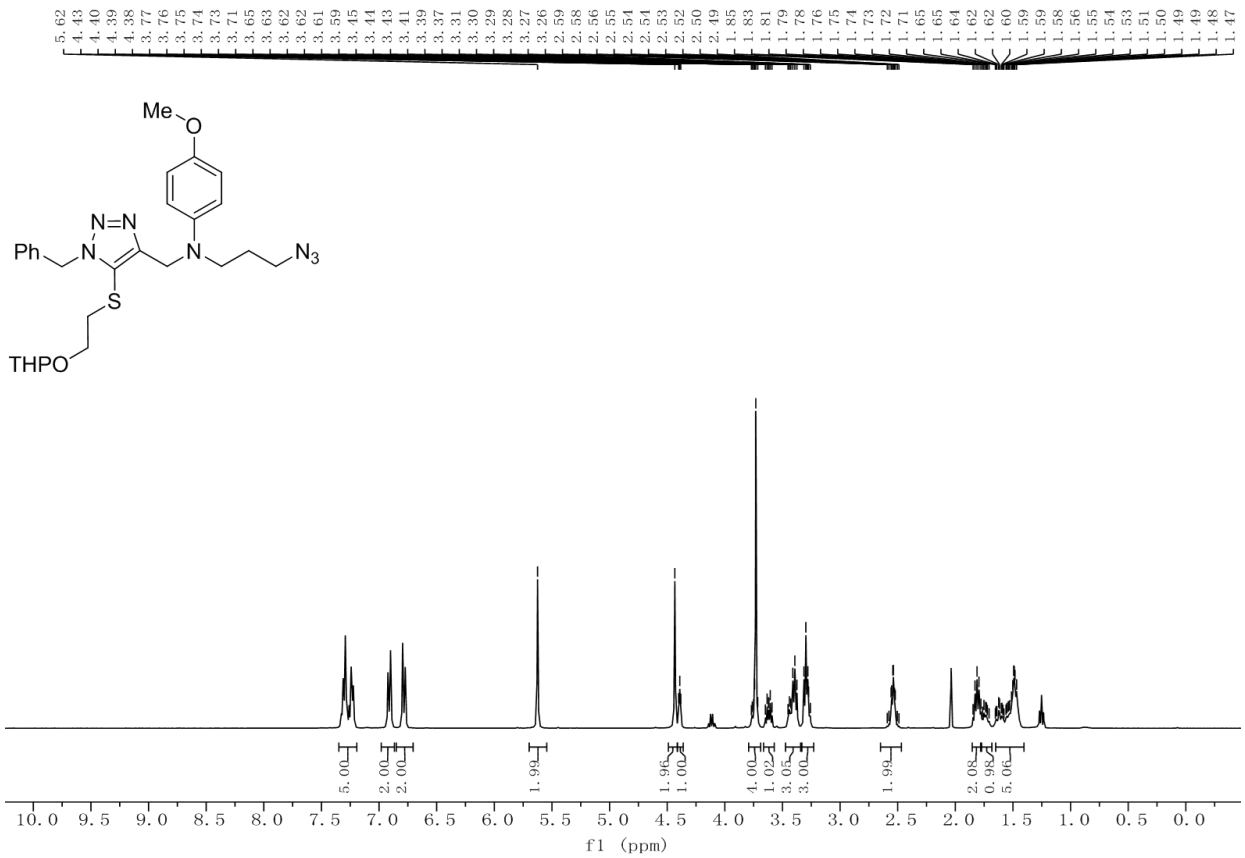



**Figure S14**. $^{1}$H NMR spectra of **8**.

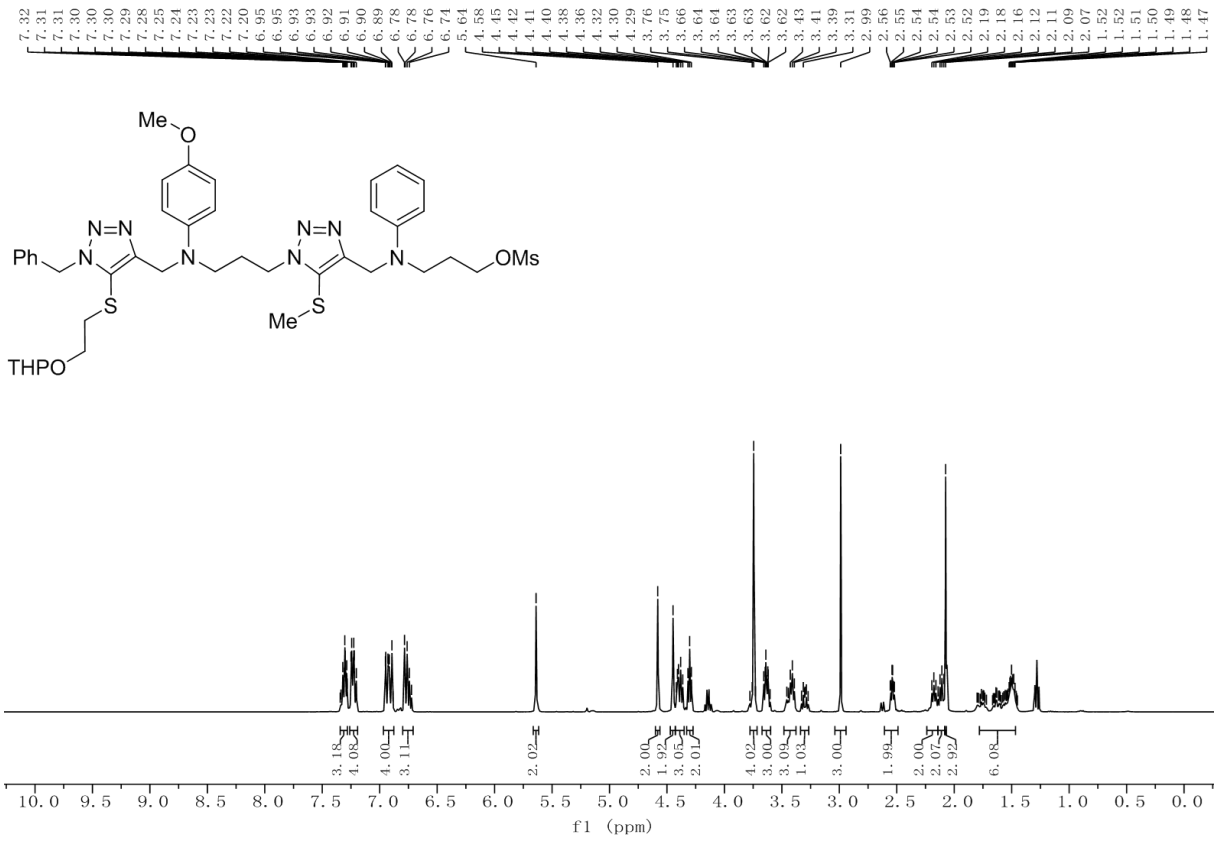



**Figure S15**. $^{1}$H NMR spectra of **9**.

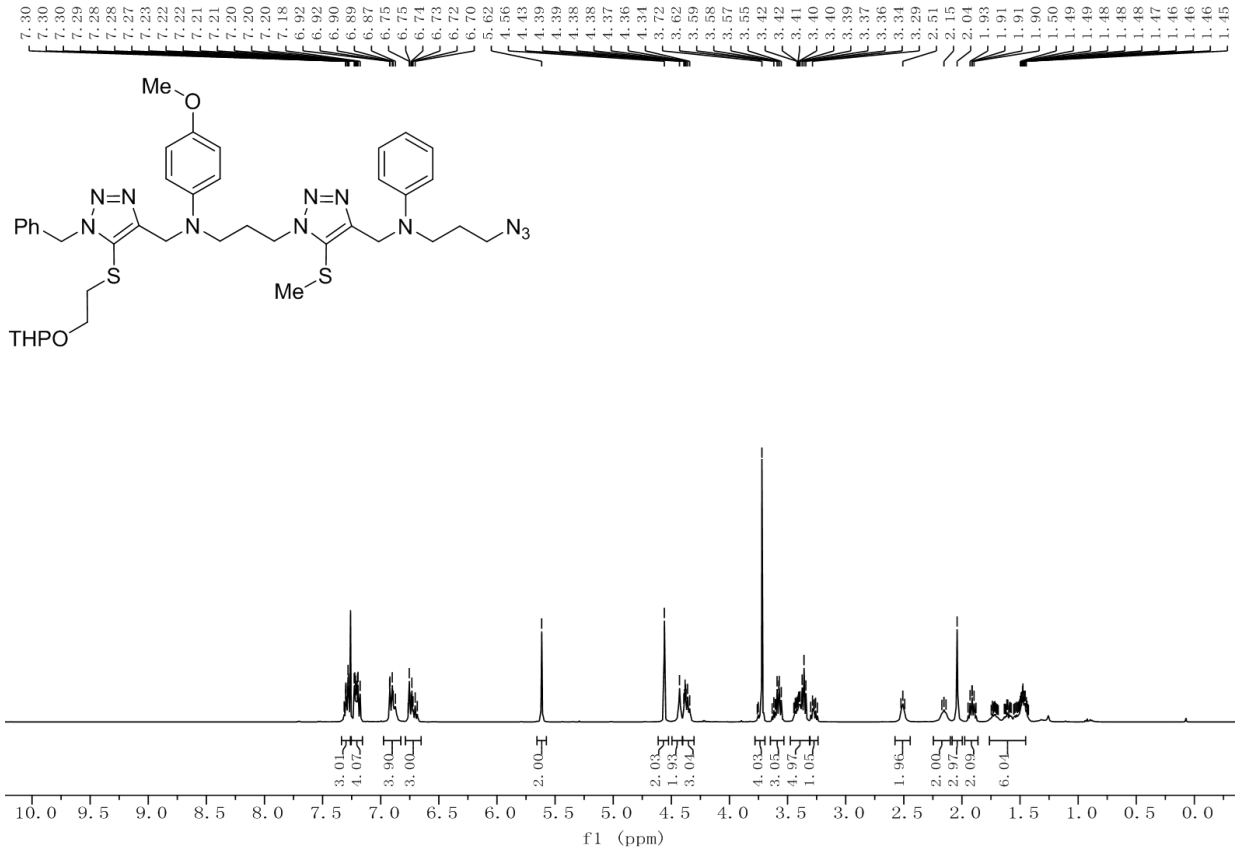



**Figure S16**. $^{1}$H NMR spectra of **10**.

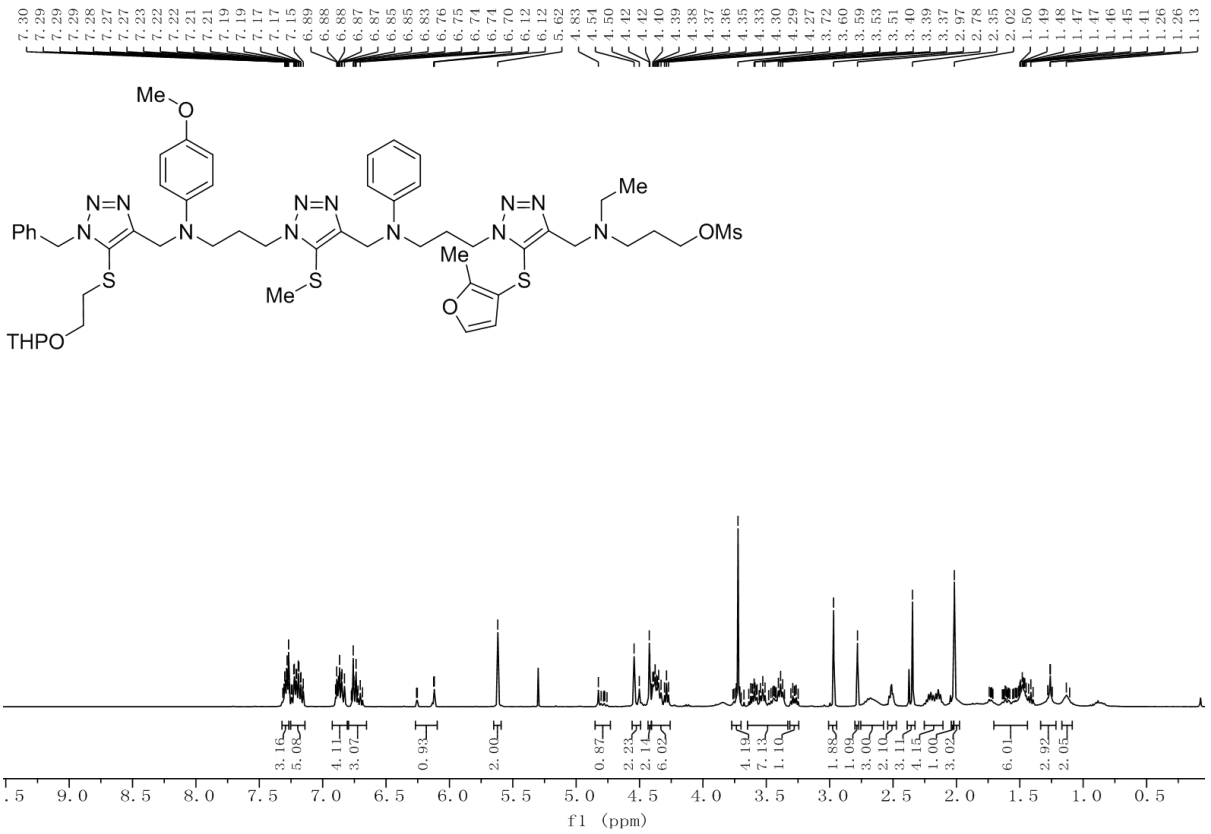



**Figure S17**. $^{1}$H NMR spectra of **11**.

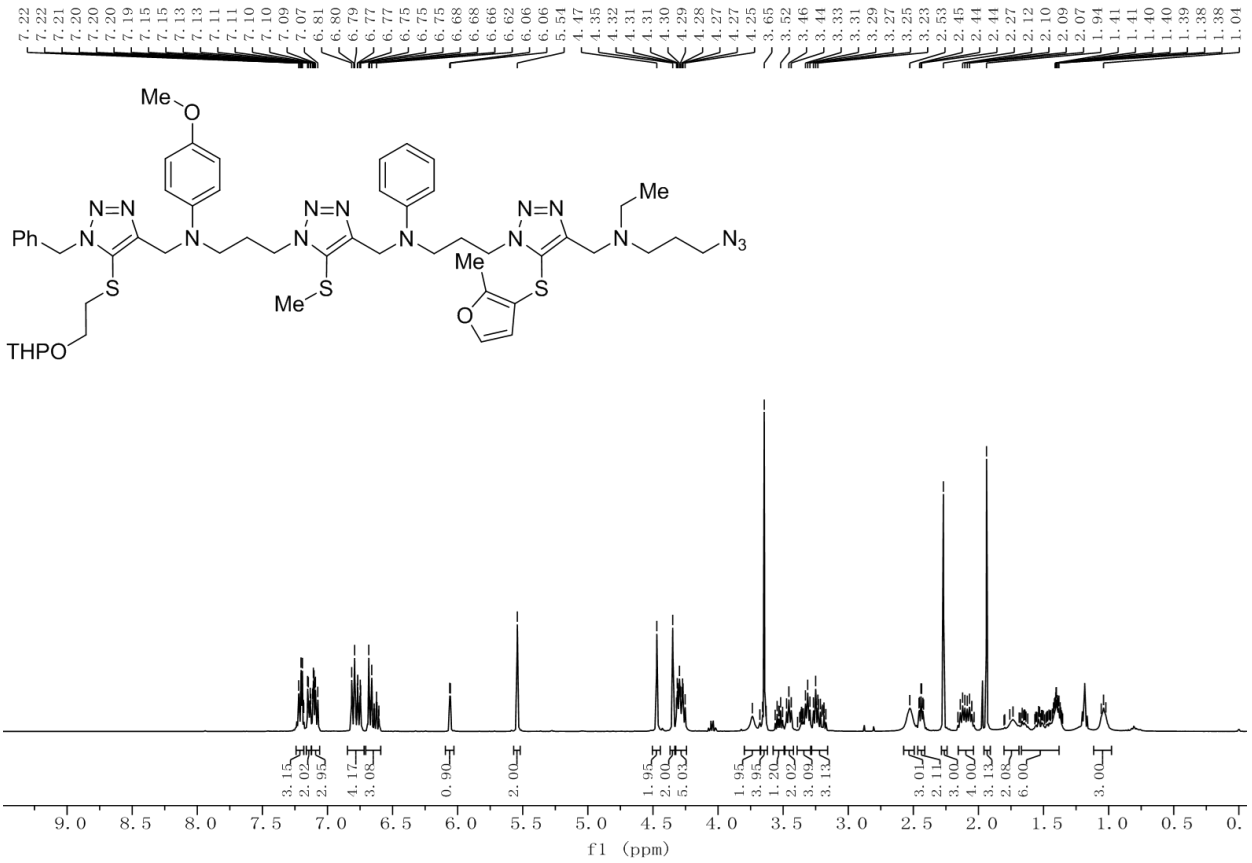



**Figure S18**. $^{1}$H NMR spectra of **12**.

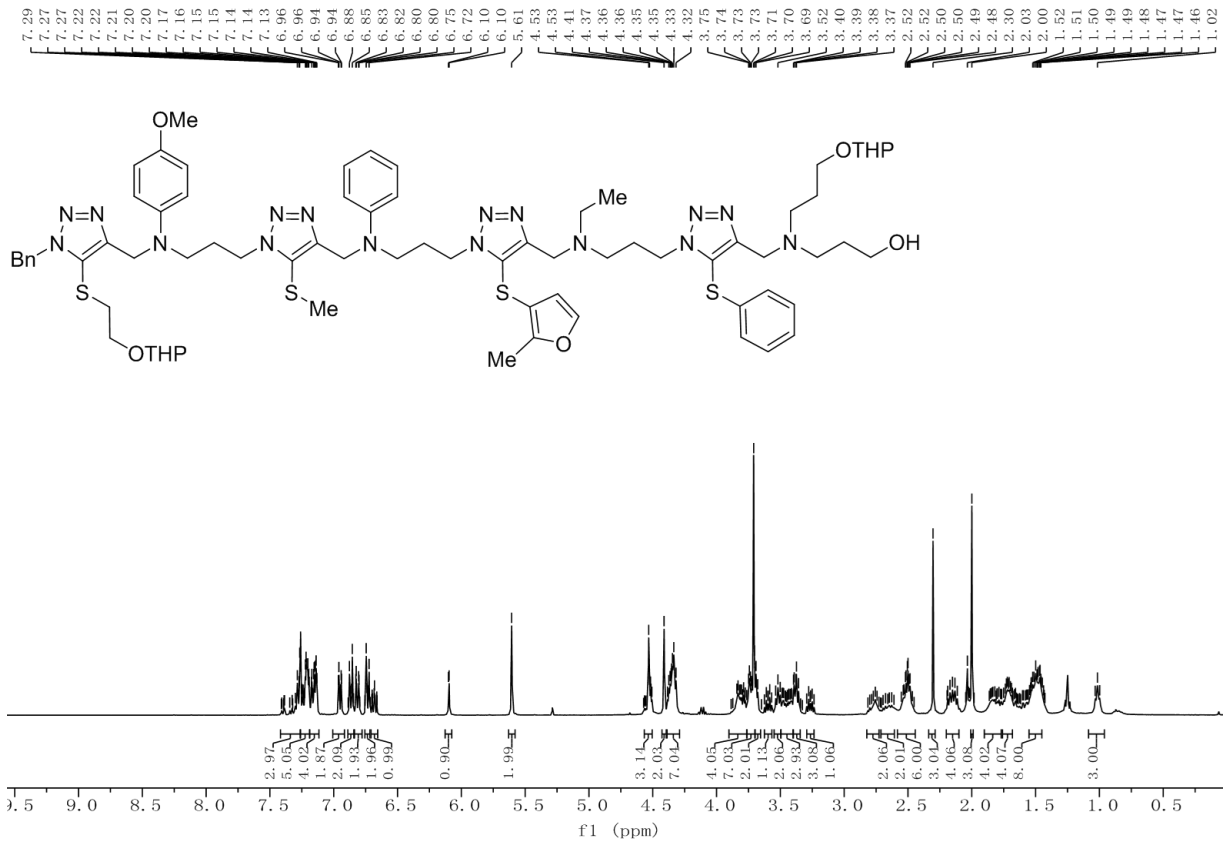



**Figure S19**. $^{1}$H NMR spectra of **13**.

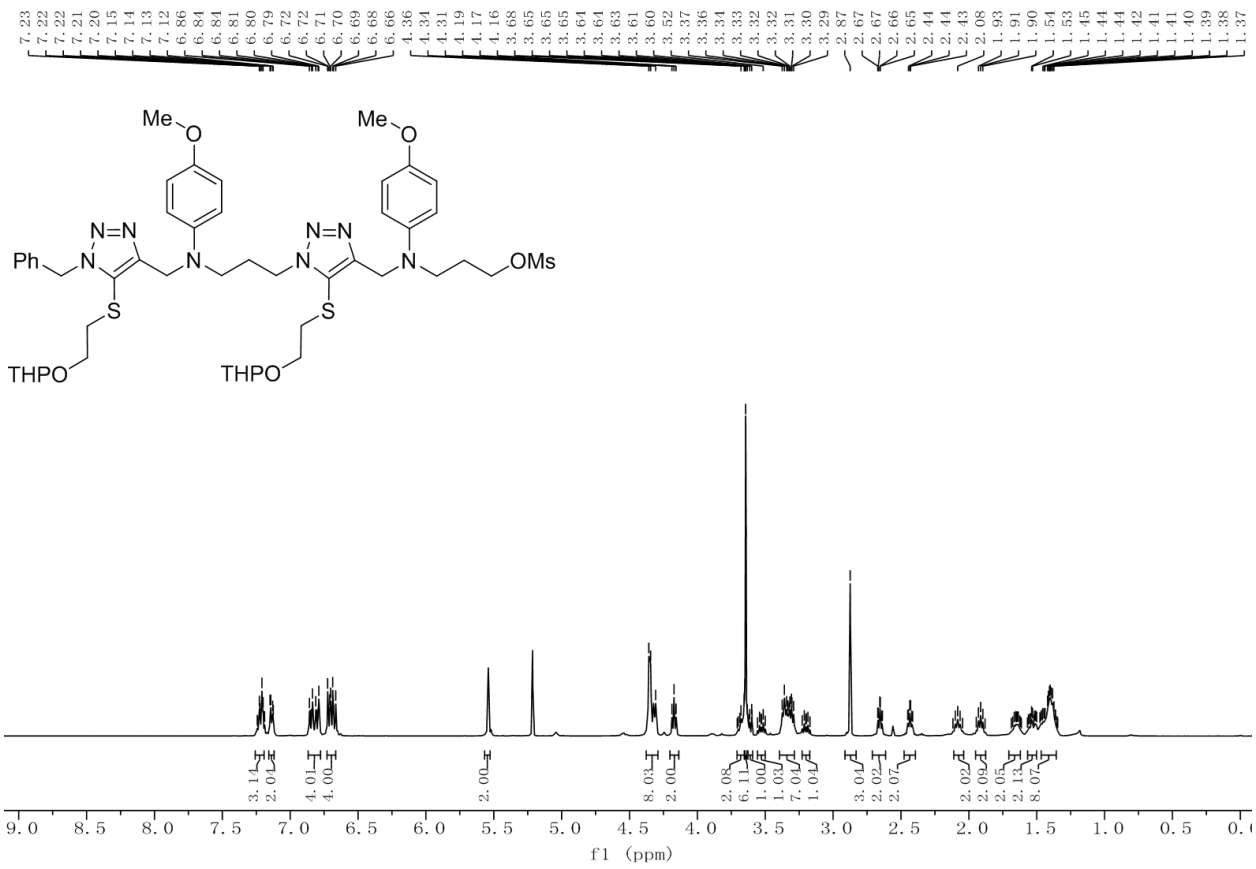



**Figure S20**. $^{1}$H NMR spectra of **14**.

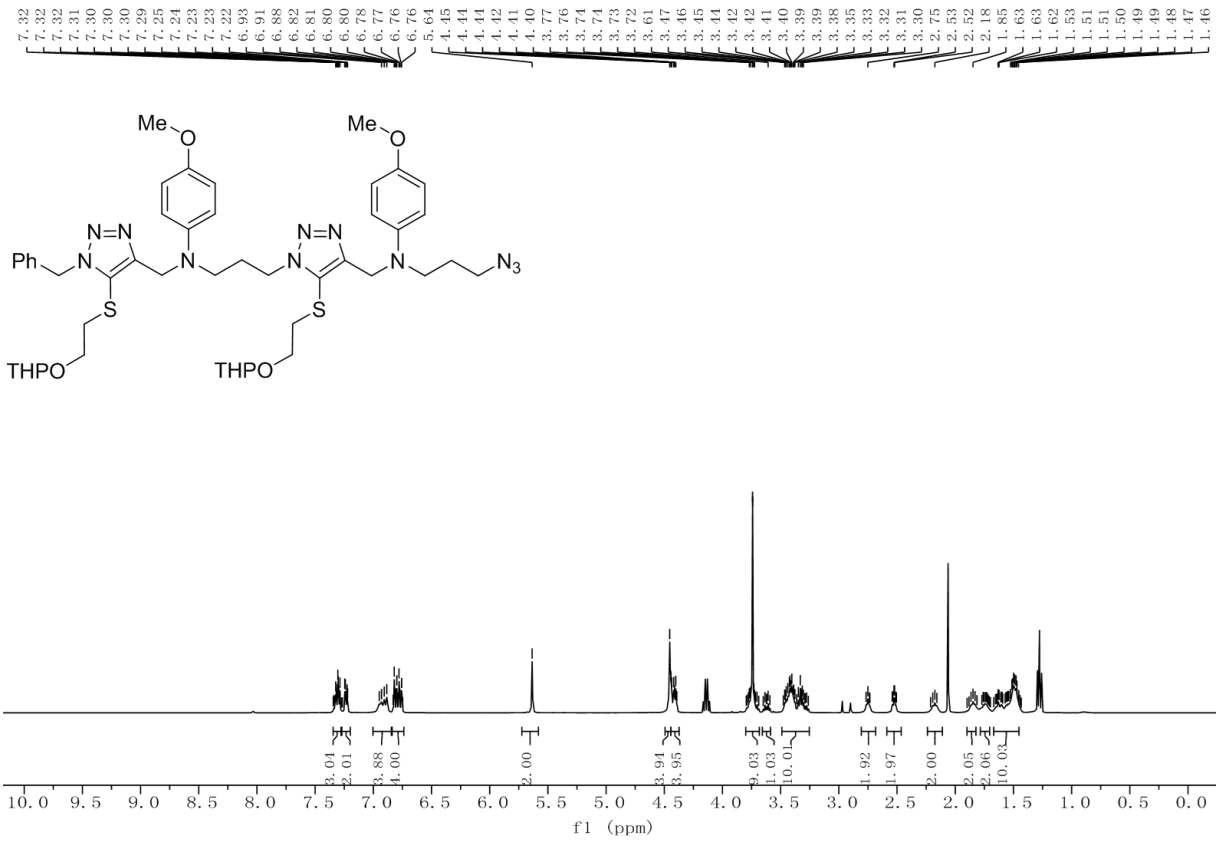



**Figure S21**. $^{1}$H NMR spectra of **15**.

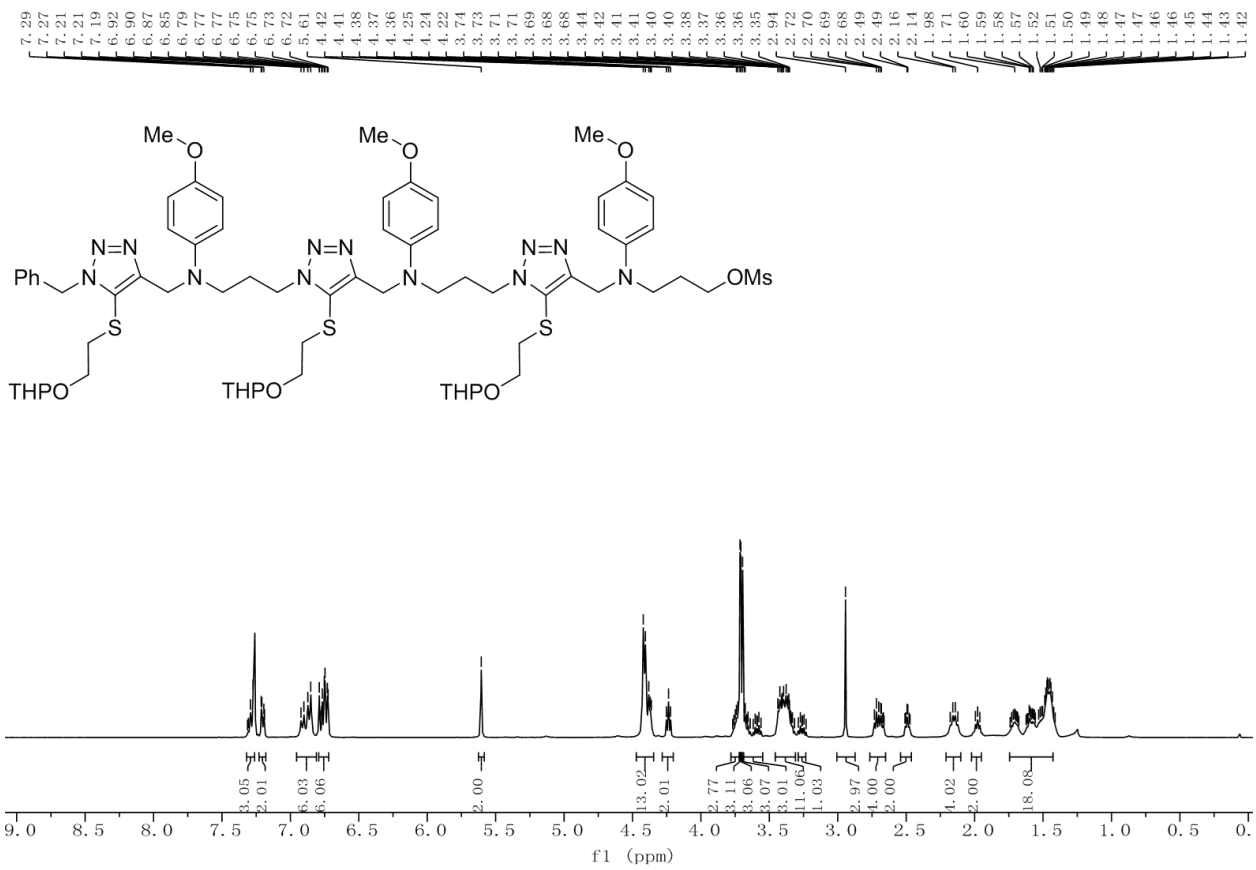



**Figure S22**. $^{1}$H NMR spectra of **16**.

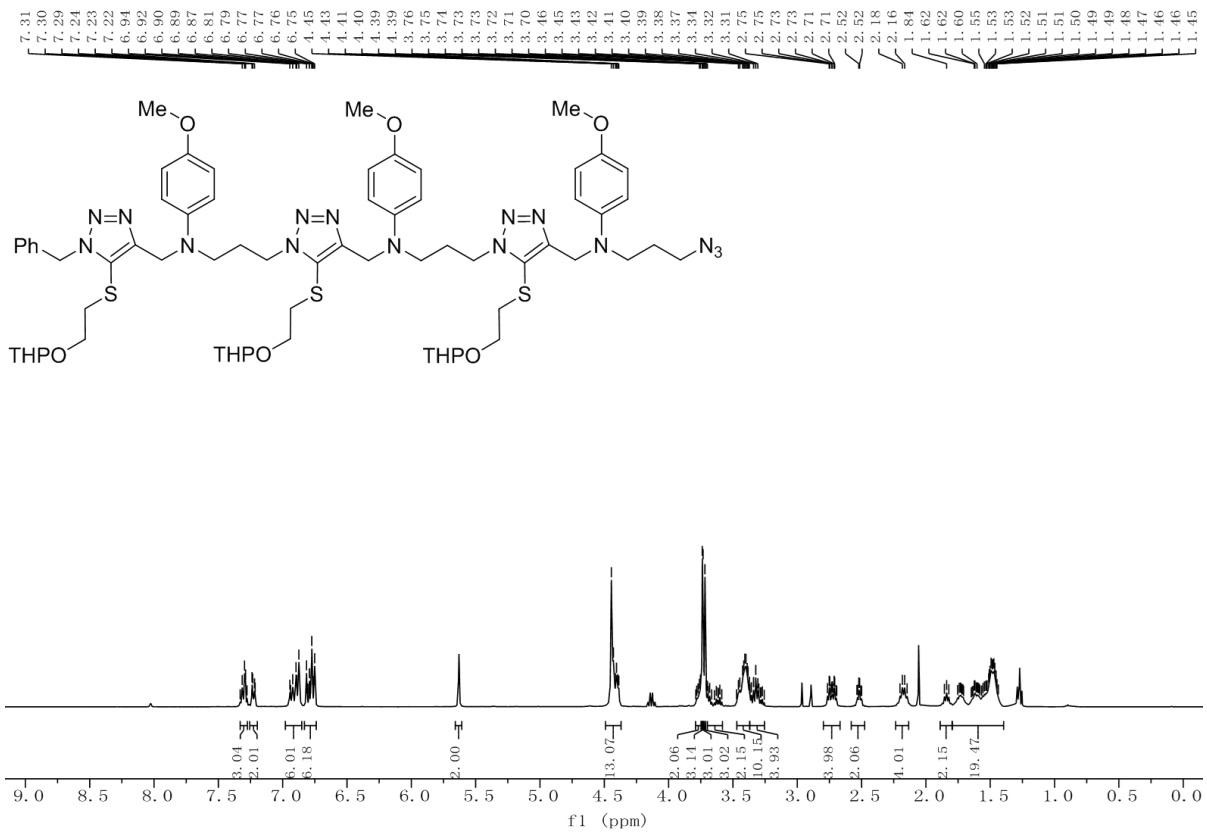



**Figure S23**. $^{1}$H NMR spectra of **17**.

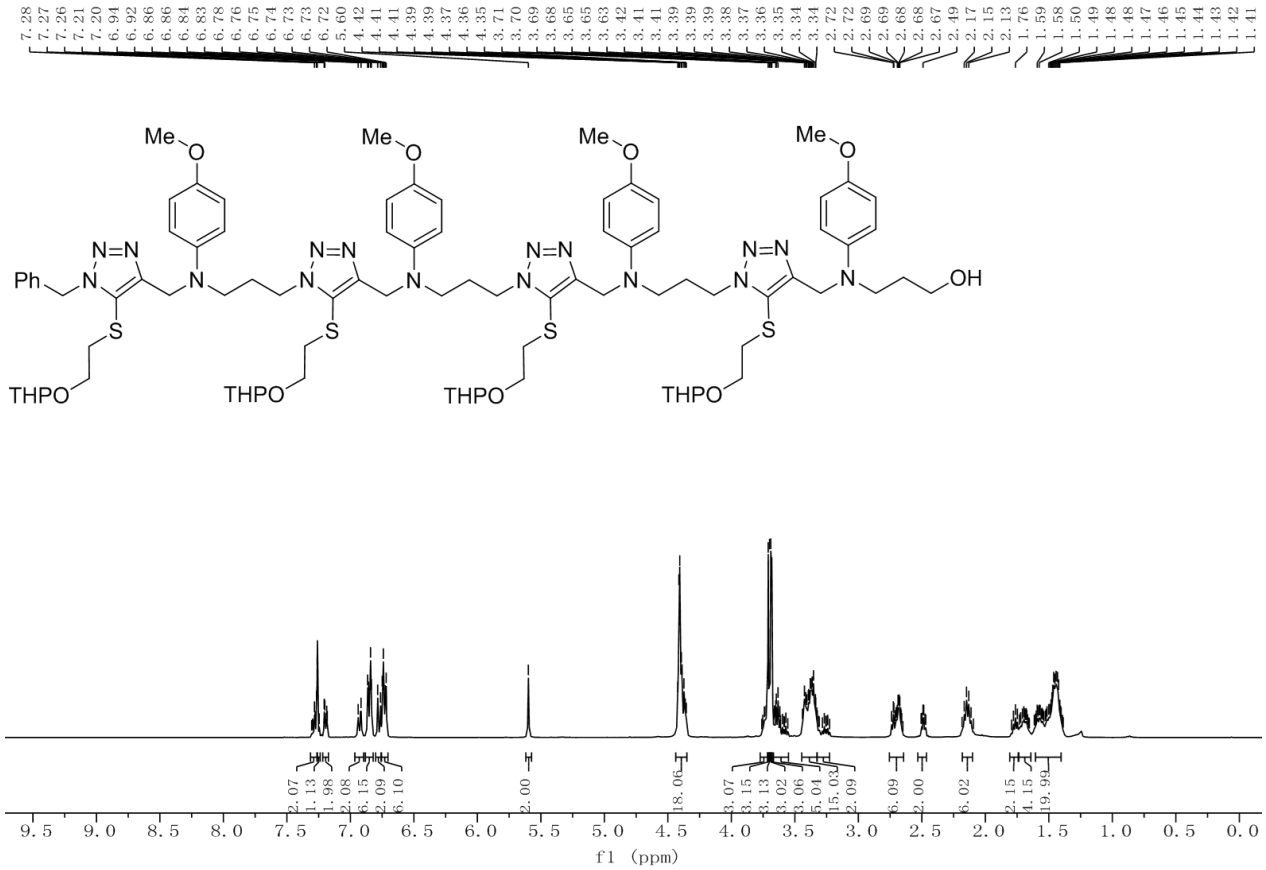



**Figure S24**. $^{1}$H NMR spectra of **18**.

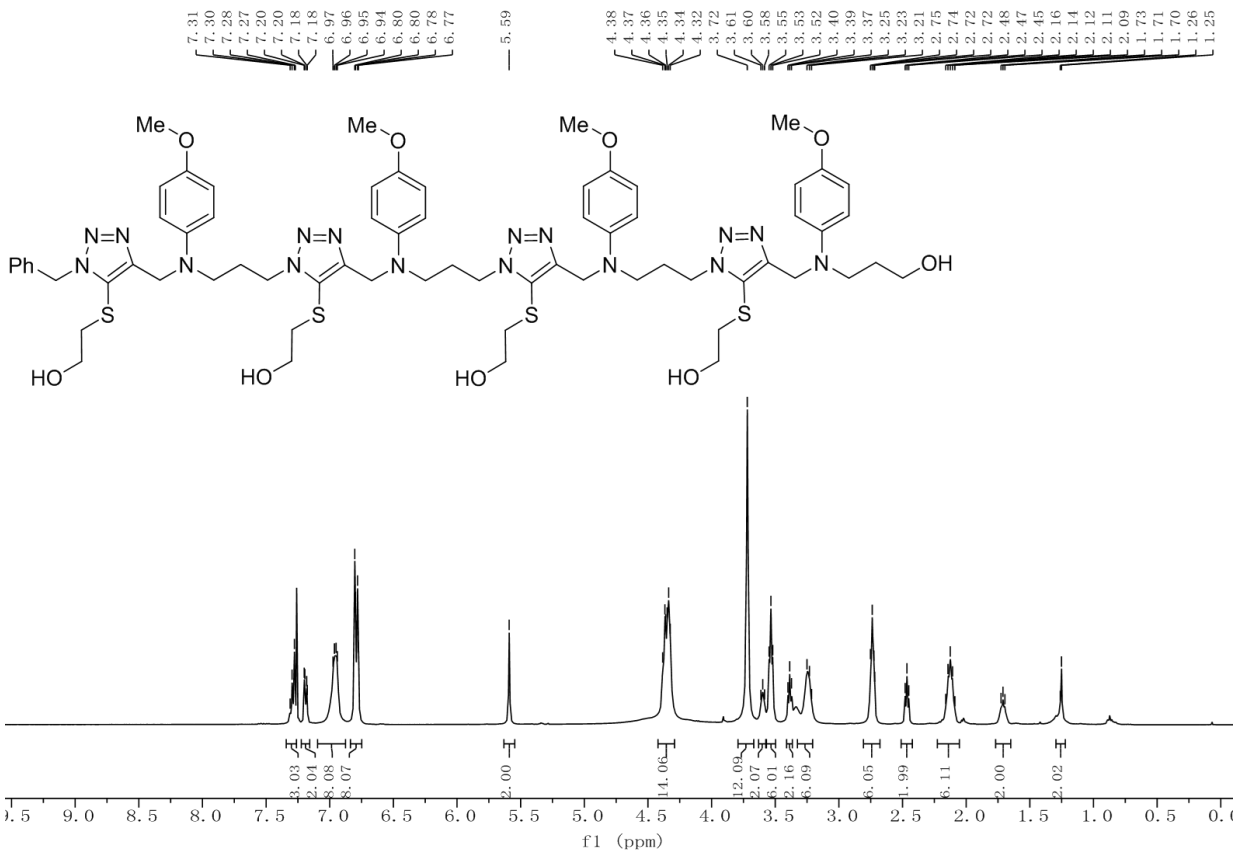



**Figure S25**. $^{1}$H NMR spectra of **19**.

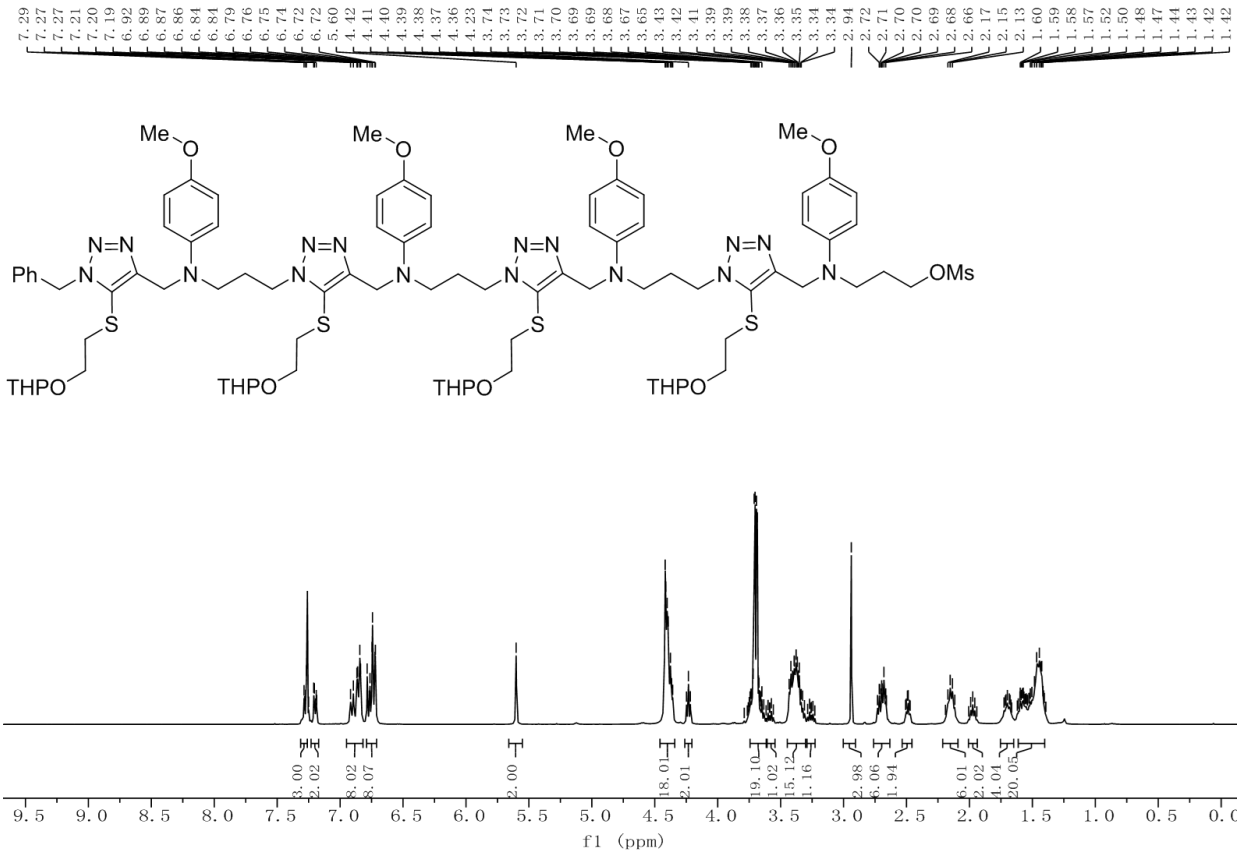



**Figure S26**. $^{1}$H NMR spectra of **20**.

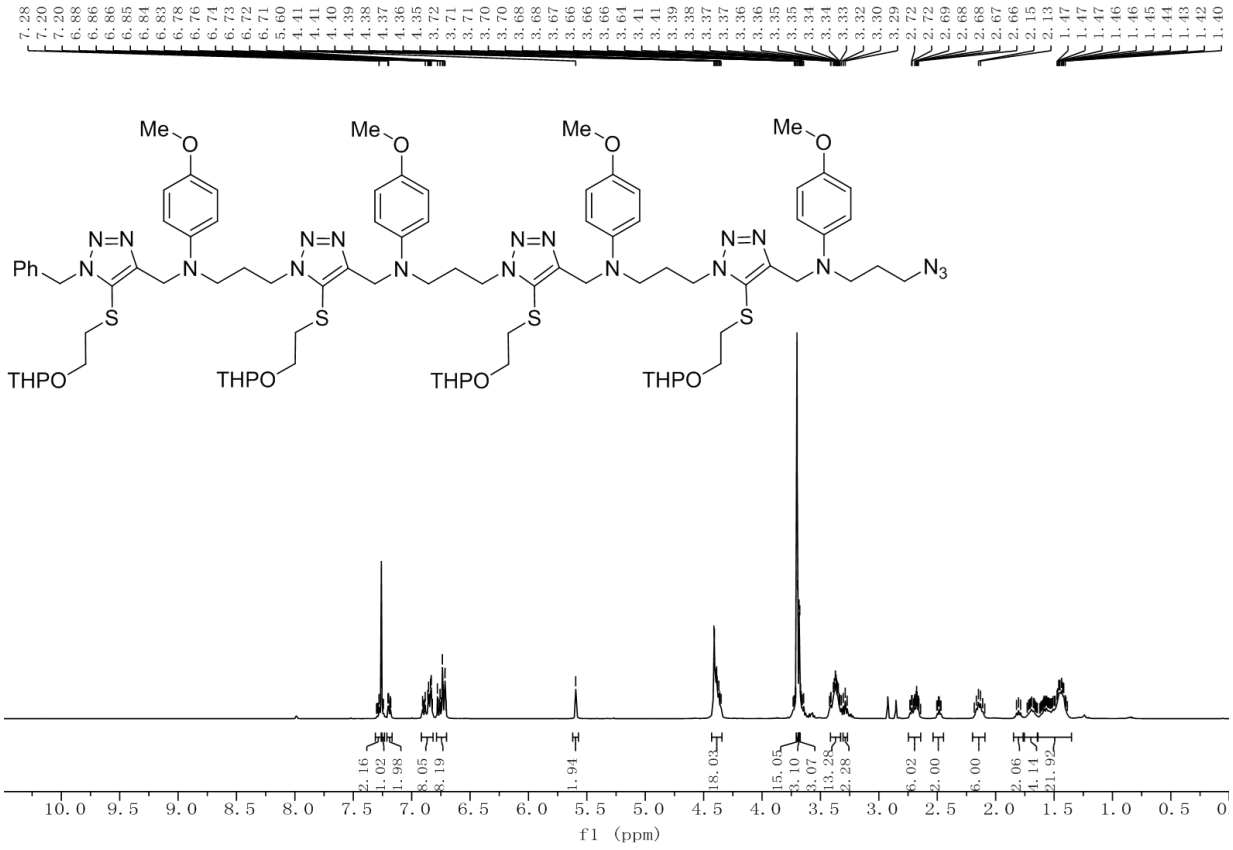



**Figure S27**. $^{1}$H NMR spectra of **21**.

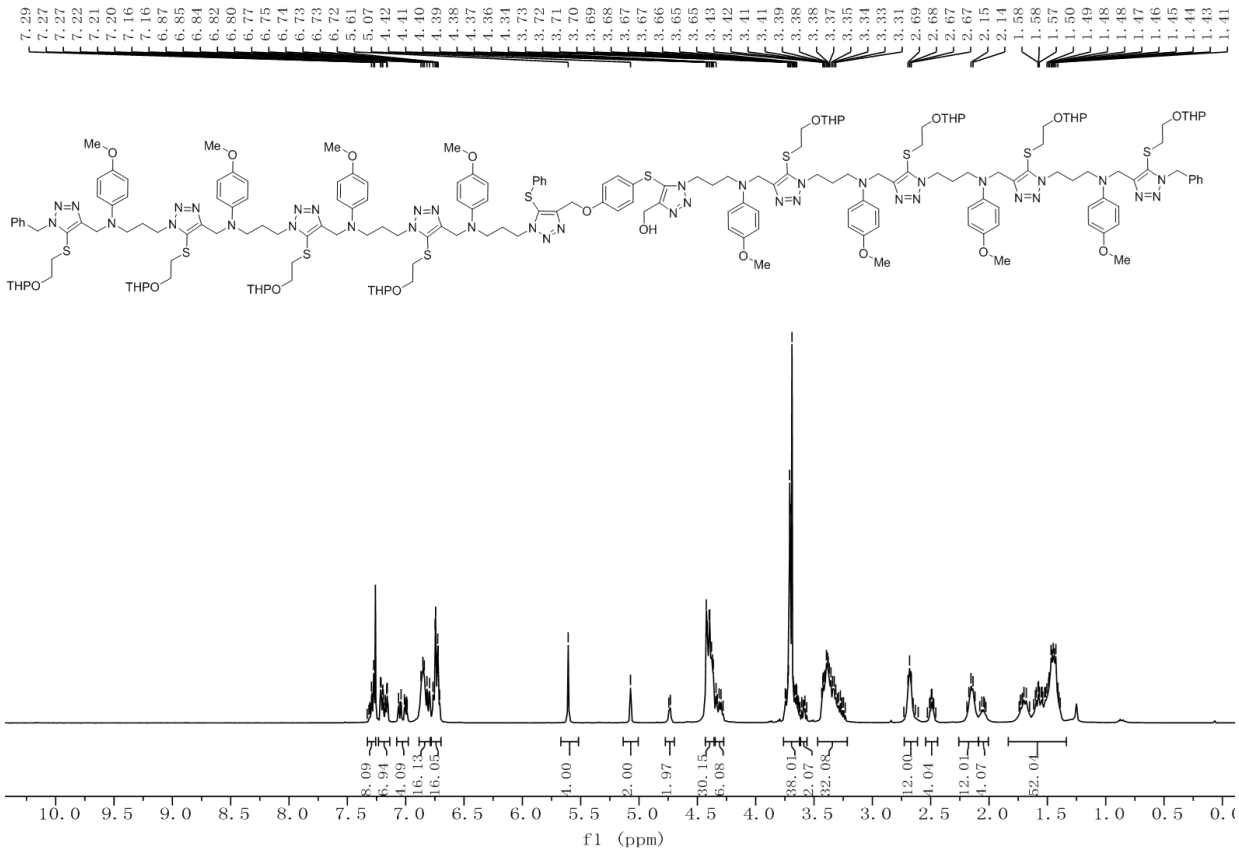



**Figure S28**. $^{1}$H NMR spectra of **24**.

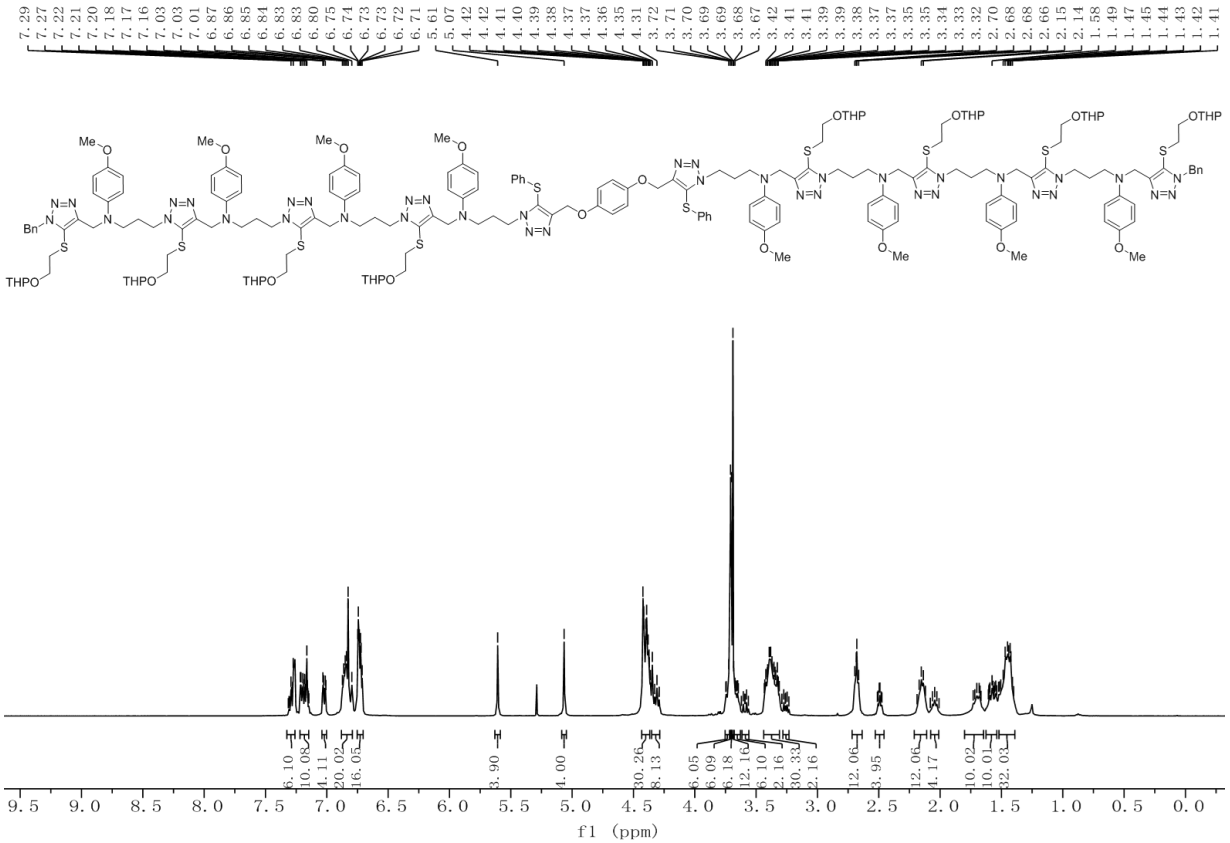



**Figure S29**. $^{1}$H NMR spectra of **25**.

## VI. MS Spectra

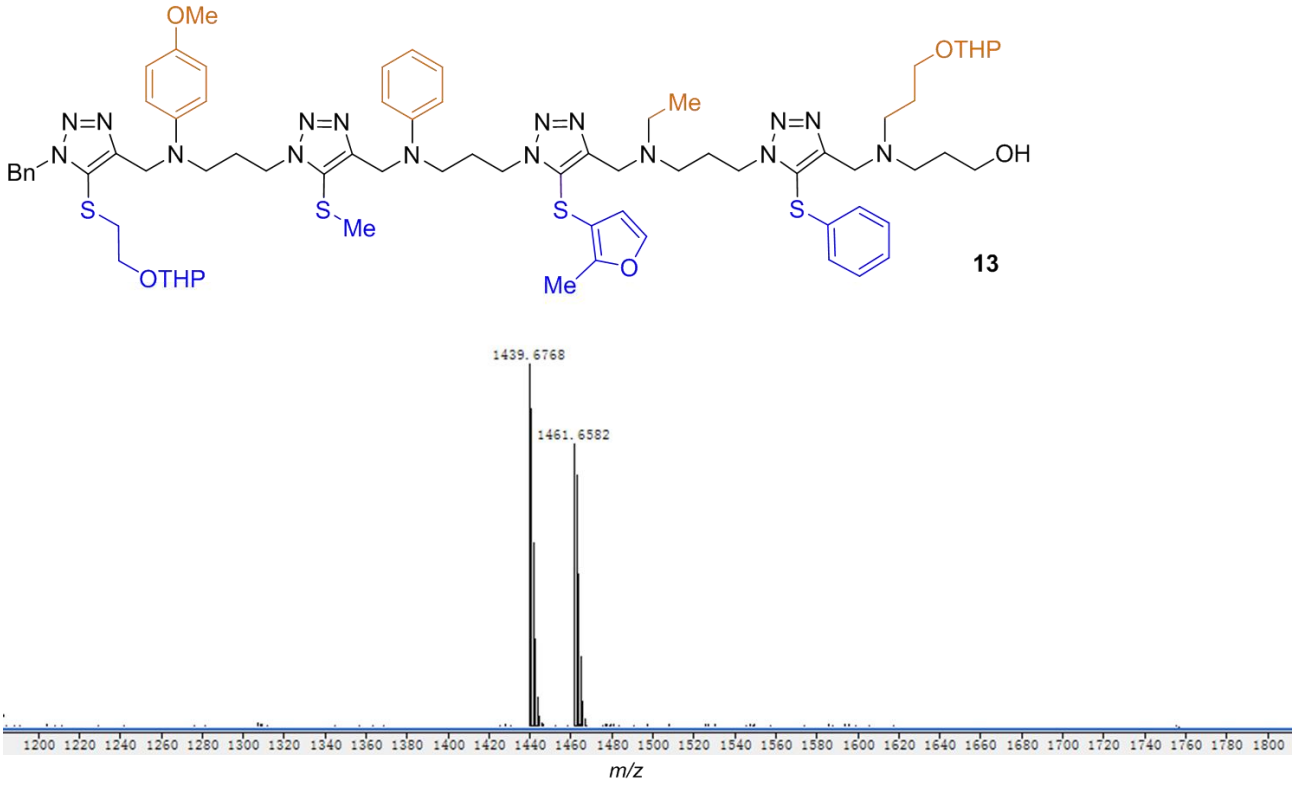



**Figure S30**. ESI-MS spectra of **13**.

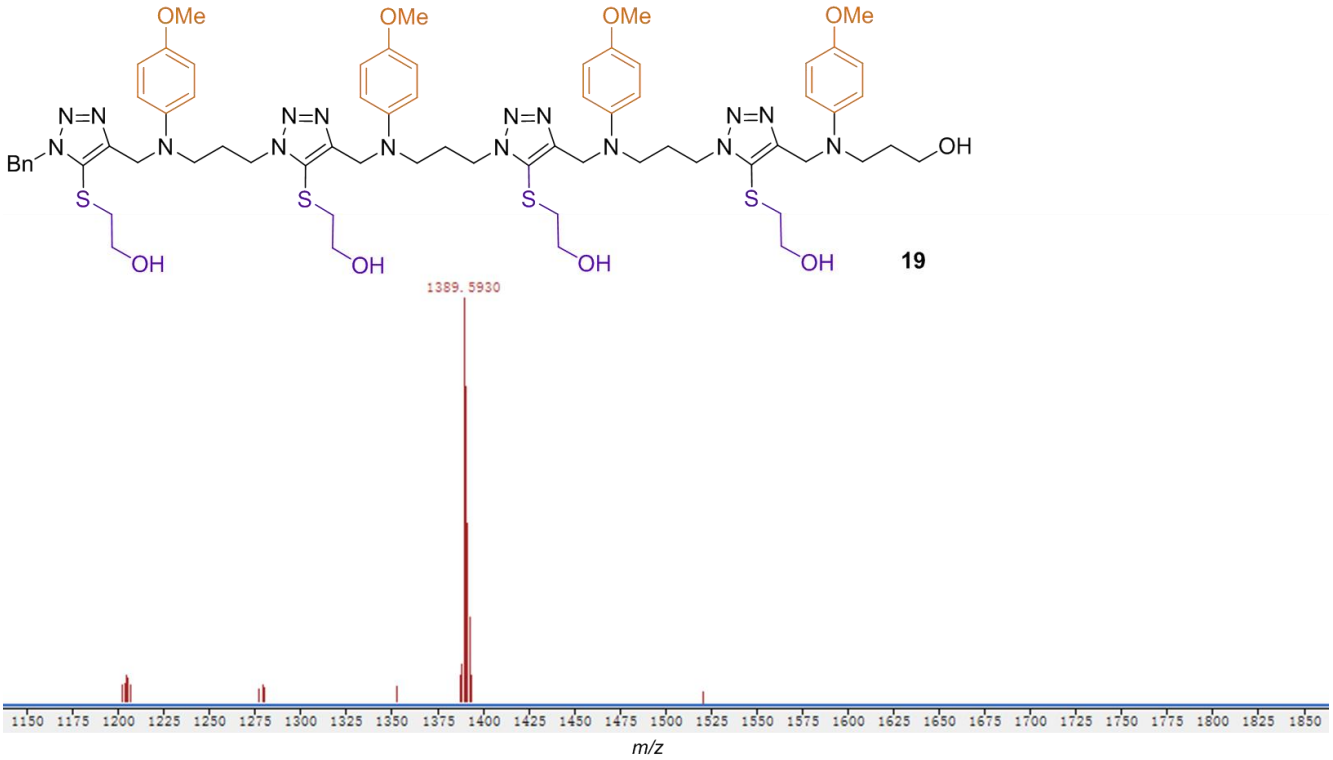



**Figure S31**. ESI-MS spectra of **19**.

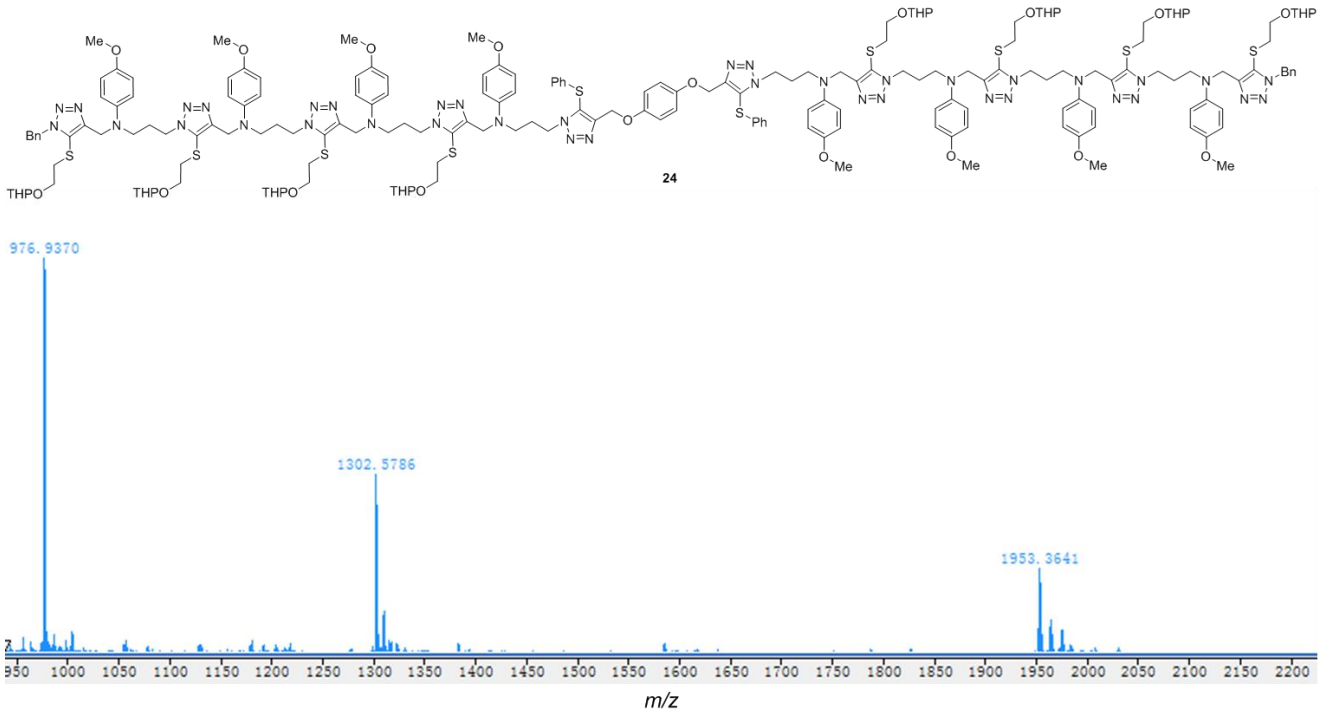



**Figure S32**. ESI-MS spectra of **24**.

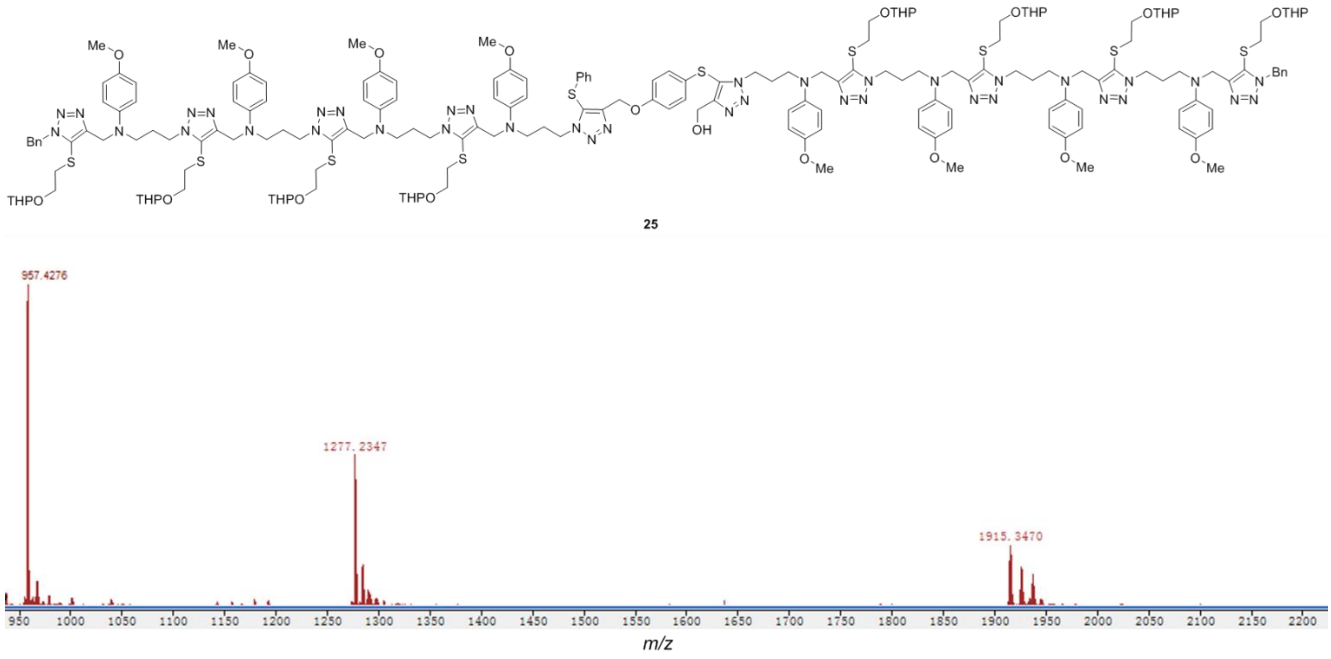



**Figure S33**. ESI-MS spectra of **25**.