Supporting information

Direct Screening of Glycan Patterns from Human Sera: A Selective Glycoprotein Microarray Strategy

Hsiu-Chung Tu,[a] Yen-Pin Lee, [a] Xuan-Yu Liu,[a] Chuan-Fa Chang,[b] Po-Chiao Lin[a] *

pclin@mail.nsysu.edu.tw

a- Department of Chemistry, National Sun Yat-sen University, Kaohsiung, Taiwan

b- Department of Medical Laboratory Science and Biotechnology, College of Medicine, National Cheng Kung University, Tainan, Taiwan

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I. Experimental Section

1. General methods and materials

^{1}H spectra were acquired at 300,400 and 500MHz. ^{13}C NMR spectra were acquired at 75, 100 and 125MHz. Respectively (unless other indicated) relate to $CDCl_3$ (calibrated at 7.26 ppm in 1H NMR and at 77.23 ppm in ^{13}C NMR) and d4-Methanol (calibrated at 3.31 ppm in 1H NMR and at 49.15 ppm in ^{13}C NMR). Fetuin (from fetal calf serum), RNase B (from bovine pancreas), HRP (Peroxidase from horseradish), Asialofetuin (type I from fetal calf-serum), Transferrin (apo – Transferrin Human), Ovalbumin and IgG all are purchased from Sigma-Aldrich. The FITC-WGA, FITC-AAL, FITC-PNA, FITC-SBA, FITC-MAL, FITC-UEA, FITC-SNA, FITC-Con A all purchased from Vector Laboratories. The epoxy slide was purchased from Arrayit (Sunneyvale, CA, USA).Water was obtained from a Milli-QR Ultrapure Water Purification System (Millipore, Billerica, MA).

2. Preparation of MFCO modified Slides.

The epoxy slides (Arrayit, USA, SuperEpoxy substrate slide (protein)) were rinsed twice with DMF (10 mL) and immersed in DMF (60 mL) with **MFCO-amine (1 mM)**. After incubating for 12 h, washing by DMF (10 mL) and DCM (10 mL) 3 times (10 mL). The, the slides were rinsed with ddH_2O and dried by nitrogen. To block the excess epoxy groups, **Compound 43** (60 mL, 0.1 M in DMF) was added to the slides. The slide was allowed to react at room temperature for 3 hour. Subsequently, washed three times with DMF (10 mL) and DCM (10mL). Individually, dried under a stream of nitrogen again.

3. Preparation of BA-m-tosyl-N_3-2 @slide

The MFCO functionalized slide was rinsed twice with sodium phosphate buffer (25 mM, pH 7.4) and immersed in the same buffer (45 mL) containing BA-m-tosyl-N_3-2 (1 mM). The slide was allowed to react at room temperature for 12 h. The slide was washed with DMF (10mL) and DCM (10mL) for 3 times and ddH_2O for twice times to obtain BA-m-tosyl-N_3-2@ slide. The obtained slide was further blocked by treating with azido choline (1mM) and allowed to react at 25 °C for 6h.

4. BA-tosyl-Functionalized Slide-Directed Immobilization of Glycoproteins.

Glycoproteins were dissolved in phosphate buffer (10mM phosphate buffer, 25mM NaCl 5mM $CaCl_2$ 0.5mM, pH 7.4) containing 20% dimethyl sulfoxide (DMSO) in specific concentrations of purpose.0.1mM. AD1500 arrayer (Biodot) was used to print glycoproteins of interest onto the functionalized slide with a spot volume of 50 nL under 85% relative humidity. The protein sample was allowed to incubate on the slide at 25°C for 12 h. the unreacted glycoproteins were then removed by washing with phosphate buffer (10mM phosphate buffer, 25mM NaCl 5mM, pH 7.4). The Slide was then incubated with deblocking (10mM phosphate buffer at pH 7.4, 25mM NaCl 5mM $CaCl_2$ 0.5mM) containing 10% glycerol for 30 min and subsequently decanted the solution. The above procedure should be repeated twice. The slide was further treated with 10 mM imidazole solution (20 mM Tris buffer, 500 mM NaCl, 10 mM imidazole pH 7.5) for 30 min to block unreacted BA-tosyl groups. Afterward, the slide was washed by washing buffer (10mM phosphate buffer at pH 6, 25mM NaCl, 5 mM $CaCl_2$) two times followed by rinsing with dd H_2O and then dried under a stream of nitrogen.

5. Glycoprotein−Lectin Interaction with the Microarray.

Fluorescein-labeled lectins (Con A-FITC and WGA-FITC, AAL-FITC, PNA-FITC, SNA-FITC, MAL-FITC, SBA-FITC, UEA,FITC) 10 μM in PBS containing 5 mM $CaCl_2$ and 5 mM $MnCl_2$ with BSA (16mg/mL) to block the surface and were incubated with the glycoprotein microarray at 25°C for 1 h. Then, the slide was washed with washing buffer (10mM PBS buffer 25mM NaCl 5mM $CaCl_2$)containing 10% glycerol 3 times and further wash by washing buffer(10mM PBS buffer 25mM NaCl 5mM $CaCl_2$) containing Tween 20 (0.05 % v/v) three times. Afterward, ddH_2O was used to rinse the slide and dried under a stream of nitrogen.

6. Protein Microarray Analysis.

To quantitatively evaluate the protein−glycoprotein interactions, the lectin−glycoprotein microarrays were analyzed by measuring the fluorescence intensities. The fluorescence signals were directly acquired by a fluorescence scanner (GE Amersham Molecular Dynamic Typhoon 9410 Molecular Imager). For each sample in lectin-binding screening, the most heterogeneous data point was removed. The fluorescence scan mode was set at 488nm as excitation wavelength with different orientation and resolution and further analyzed by ImageQuant software.

7. CuAAC directed preparation of BA-tosyl –N_3-slids.

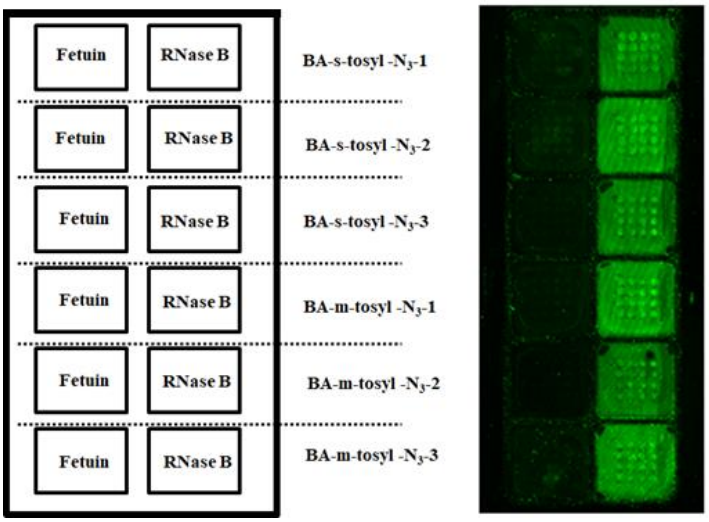


Figure S1. A series of BA –tosyl-N_3 functionlized surface for fetuin (10^{-3}M) and RNase B (10^{-3}M) immobilization and further stained with FITC-WGA and FITC-Con A.

8. Limited of Detection (LOD) of glycoproteins

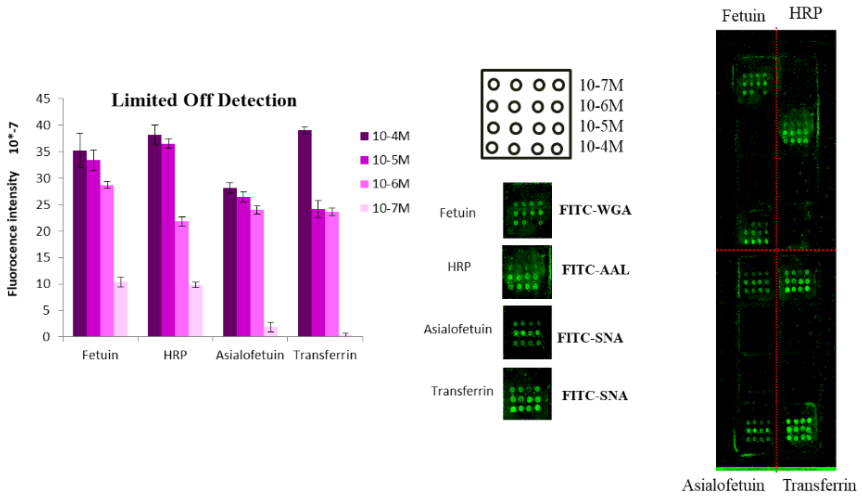


Figure S2. Limited Of Detection (LOD) of glycoproteins fetuin, HRP, Asialofetuin and transferrin. Fetuin, HRP, Asialofetuin and Transferrin at different concentration (10^{-4} M, 10^{-5} M, 10^{-6} M, 10^{-7} M) were spotted on the BA-m-tosyl-N_3 **2**@ slide and then quantitatively analyzed by incubating with corresponding lectins WGA, AAL, and SNA.

9. Epoxy slide for non-specific immobilization of seven glycoproteins spiked in E.*coli.* lysate.

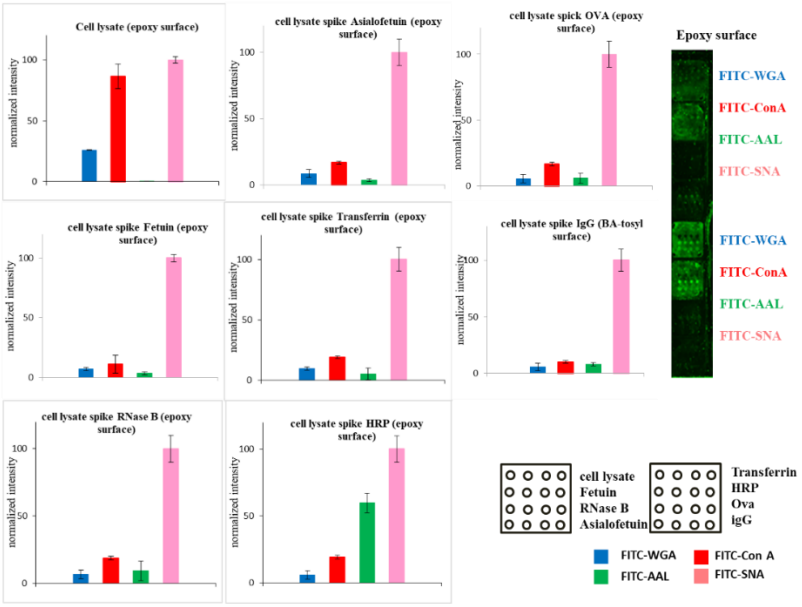


Figure S3. Seven glycoproteins including Fetuin, RNase B, Asialofetuin, Transferrin, HRP, OVA and IgG (10^{-4}M spiked in *E.coli.* lysate were spotted on epoxy slides and then quantitatively analyzed by incubating with corresponding lectins.

10. Condition optimization of FBS direct immobilization

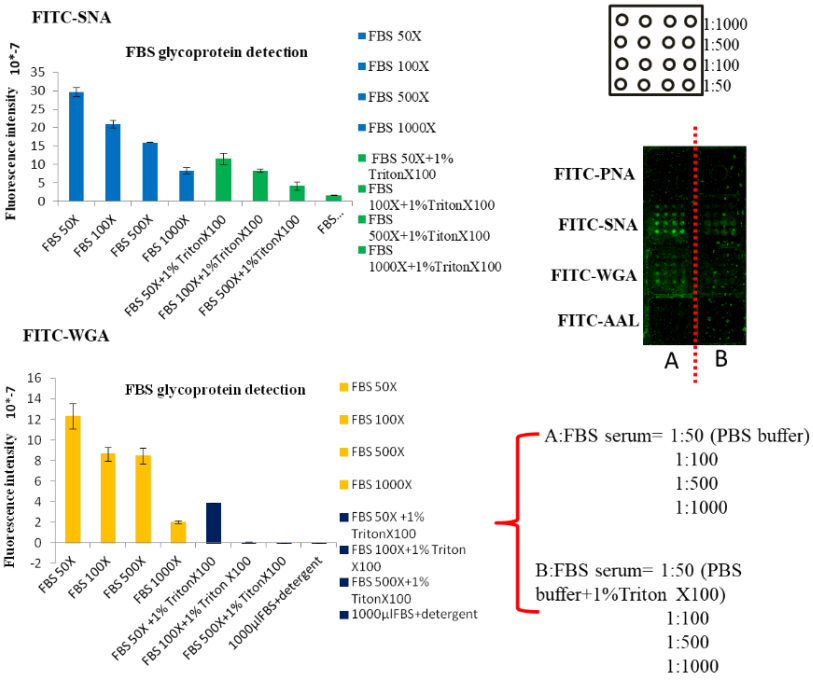


Figure S4. Condition optimization of FBS dilution for direct immobilization on BA-m-tosyl-N_3 **2**@ slide

11. Epoxy slide for non-specific immobilization of glycoproteins from FBS

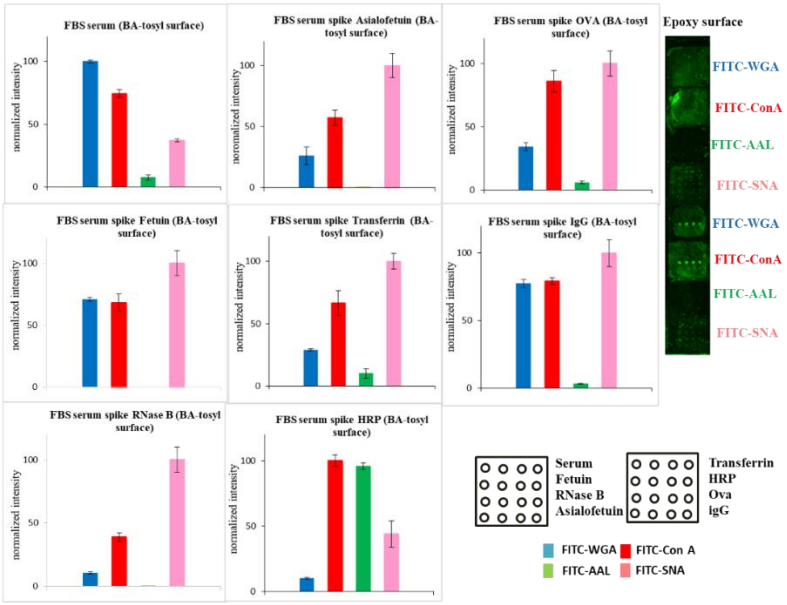


Figure S5. Seven glycoprotein including Fetuin, RNase B, Asialofetuin, Transferrin, HRP, OVA and IgG (10^{-4}M) spiked in FBS were spotted on epoxy slide and further stained with fluorescein-labeled WGA, Con A, AAL and SNA.

12. Preparation of serum samples and fabrication of serum glycoprotein microarray

Serum Samples

This study was approved by National Cheng Kung University Hospital Institutional Review Board. The serum samples of lung cancer and pancreatic cancer patients (N=8 for each cancer) were obtained from the tissue bank of National Cheng Kung University Hospital. The need for participant consent was waived by the ethics committee for serum sample form tissue bank. The venous blood from cancer-free healthy volunteers (N=8) were collected by BD Vacutainer^{TM} without anticoagulant. All the participants in this study are adult. The information on the approved participant consent form was introduced verbally to every participant by medical technologist before blood drawing. The participants also signed on the approved participant consent form. The whole blood was allowed for clot formation at room temperature within 30 minutes. The whole blood was centrifuged at 3000 rpm

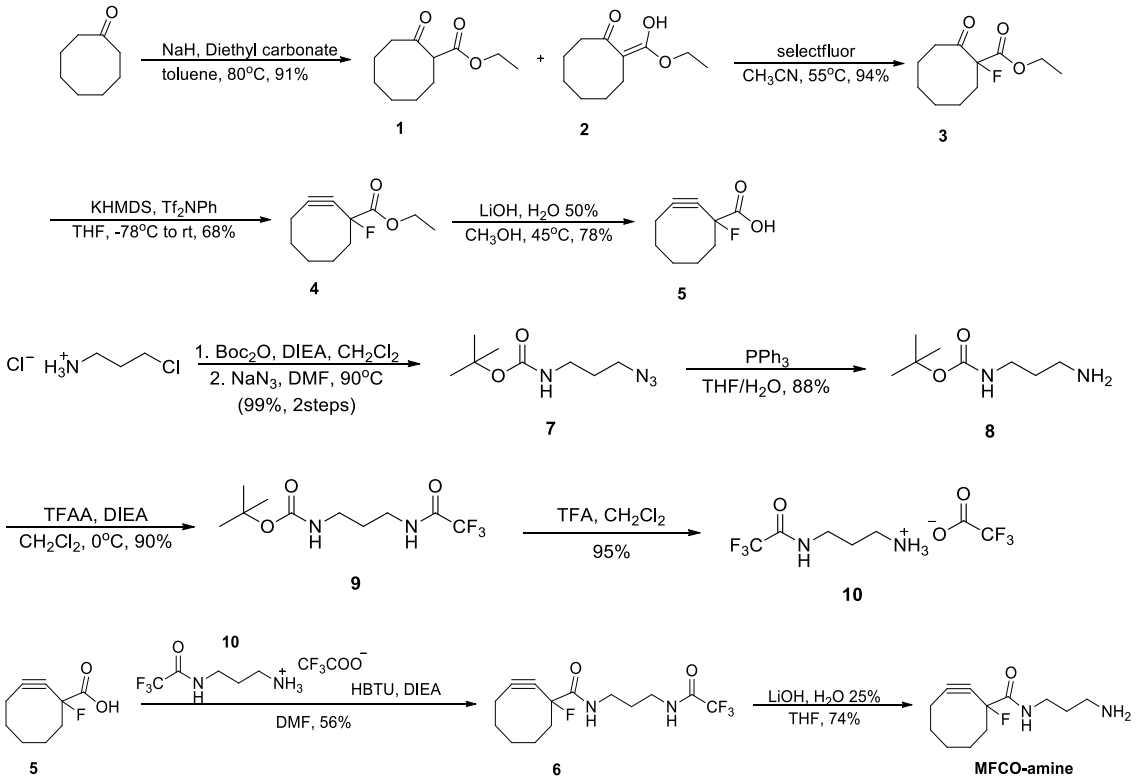
(KUBOTA/KN70) at room temperature for 10 minutes and the upper serum layer was acquired. All serum samples were stored at -80 ^{o}C.

Preparation of serum-glycoprotein microarray

According to the optimal dilution condition, three groups of human serum including healthy human sera (H-1, H-2, H-3,H-4, H-5, H-6, H-7, H-8), pancreatic cancer sera (P-1, P-2, P-3,P-4, P-5, P-6, P-7, P-8) and lung cancer sera (L-1, L-2, L-3,L-4, L-5, L-6, L-7, L-8) were diluted in phosphate buffer at pH7.4 with 20%DMSO. The optimal dilution is 2 μL serum to 100 μL phosphate buffer (10mM phosphate buffer 25mM NaCl 5mM $CaCl_2$). Then, all these diluted sera samples were spotted on microarray directly and incubated for 12 h. The washing, lectin incubation and analysis procedures were exactly the same to above mention.

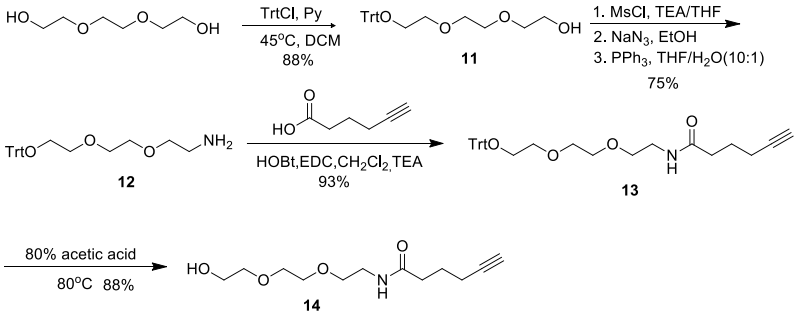
13. Synthesis pathways

a. Synthesis of MFCO-amine

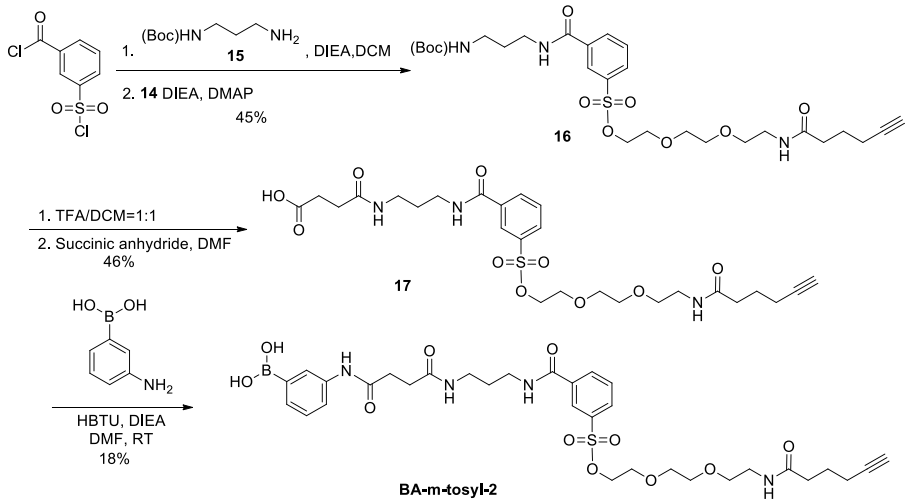


Scheme S1. Synthetic pathway of **MFCO-amine**

b. Synthesis of the BA-m-tosyl-2

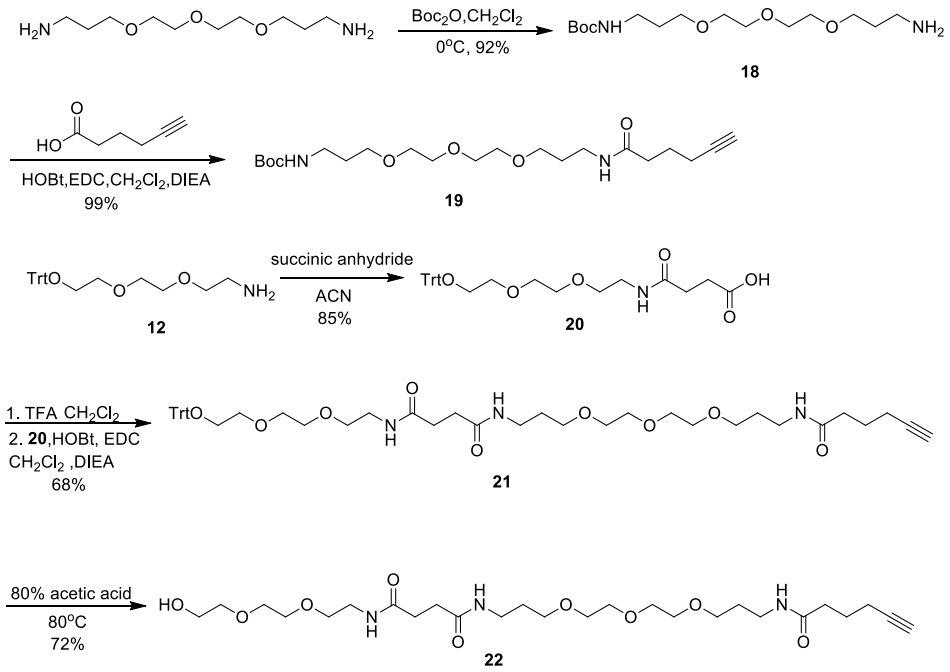


Scheme S2. Synthetic pathway of the space **14**

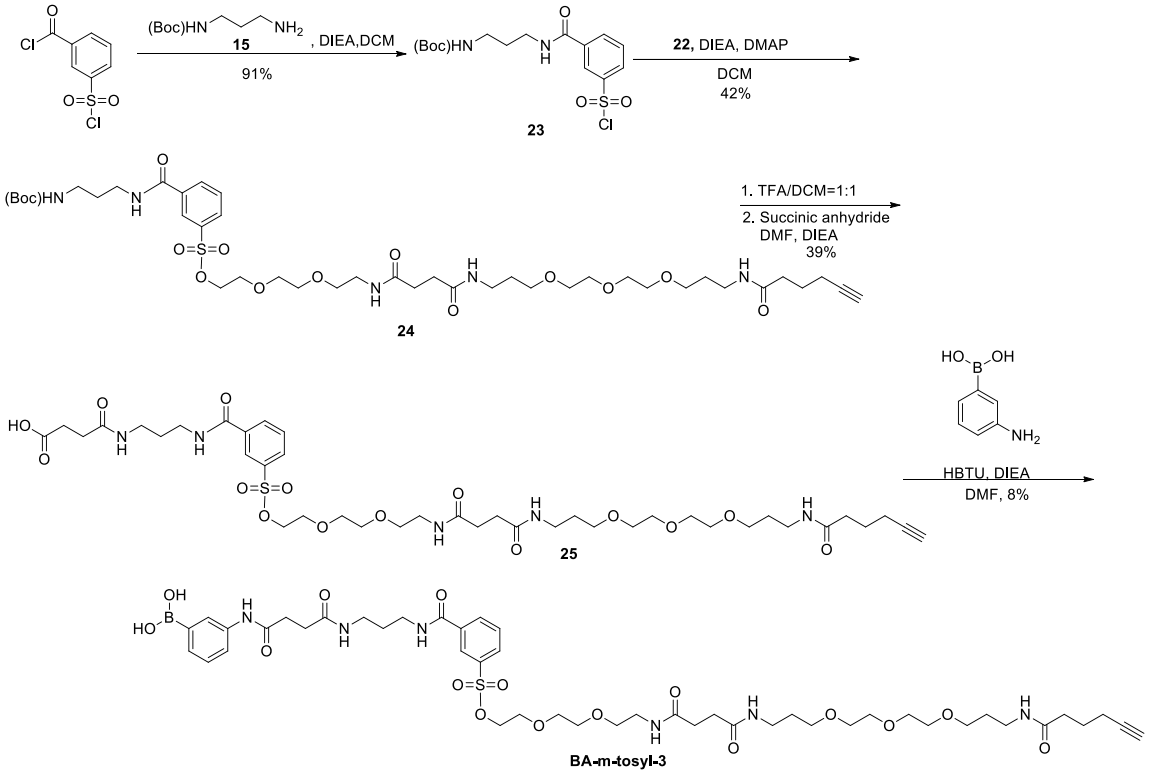


Scheme S3. Synthetic pathway of the **BA-m-tosyl-2**

c. Synthesis of the BA-m-tosyl-3

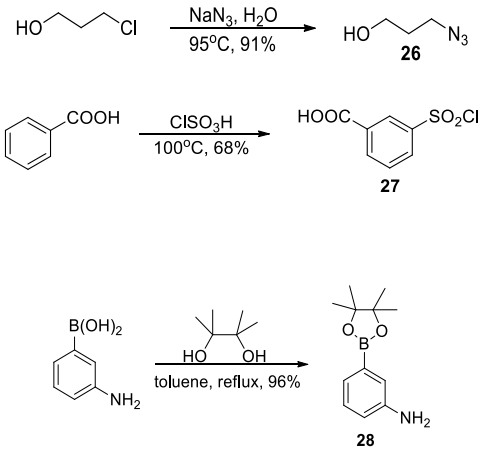


Scheme S4. Synthetic pathway of the space **22**

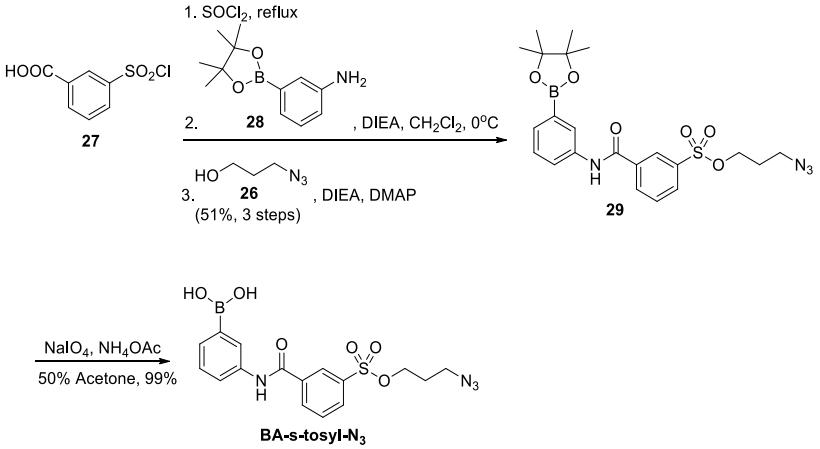


Scheme S5. Synthetic pathway of the **BA-m-tosyl-3**

d. Synthesis of the BA-s-tosyl-N_3-1

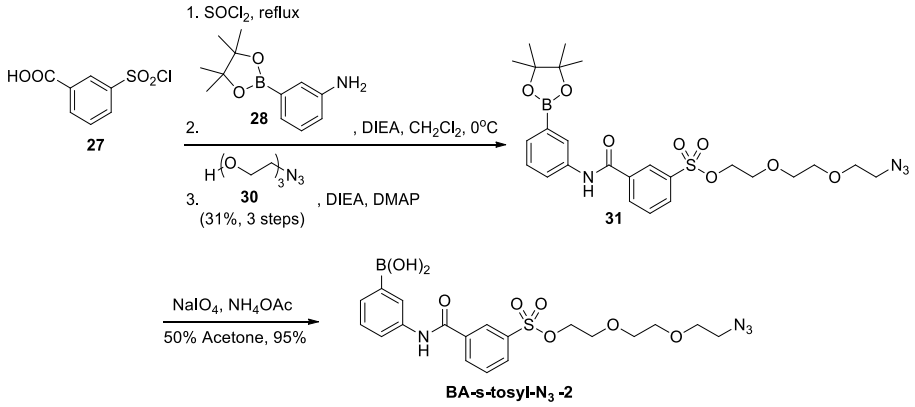


Scheme S6. Starting material preparation of the **BA-s-tosyl-N_3-1**



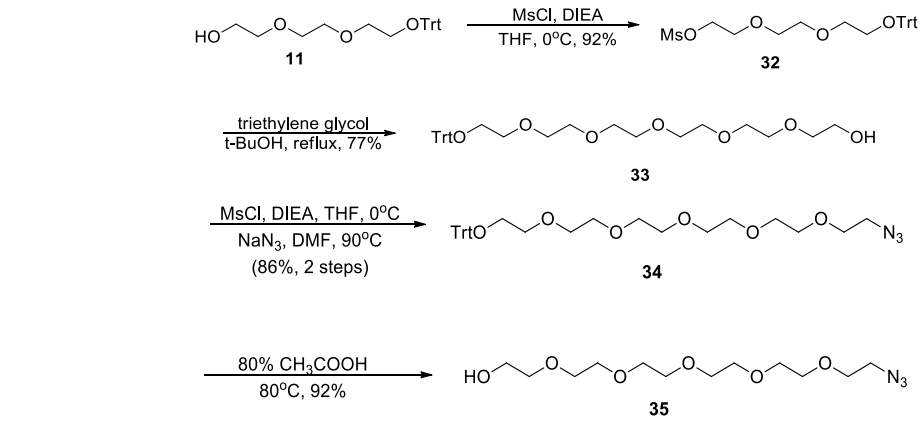
Scheme S7. Synthetic pathway of the **BA-s-tosyl-N_3-1**

e. Synthesis of the BA-s-tosyl-N_3-2

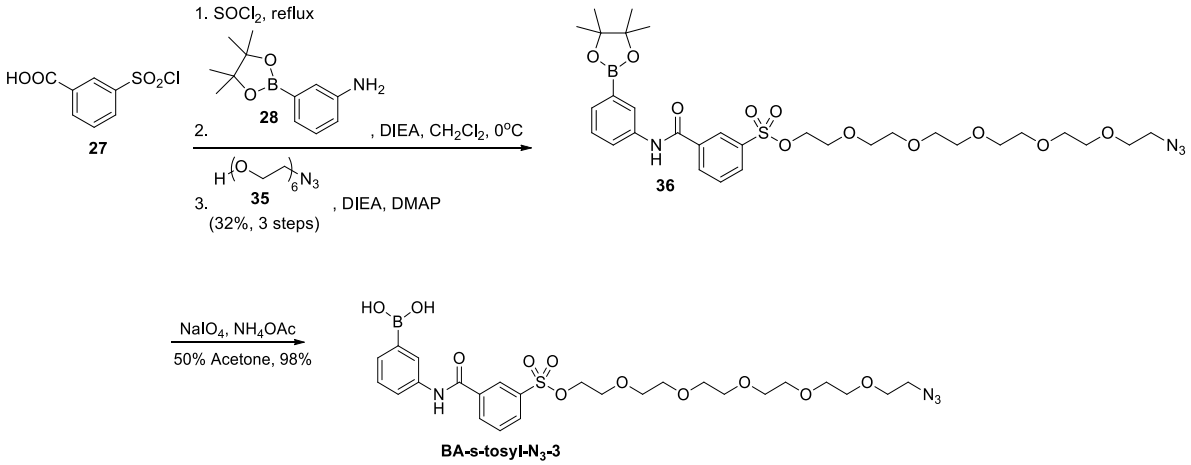


Scheme S8. Synthetic pathway of the **BA-s-tosyl-N_3-2**

f. Synthesis of the BA-s-tosyl-N_3-3

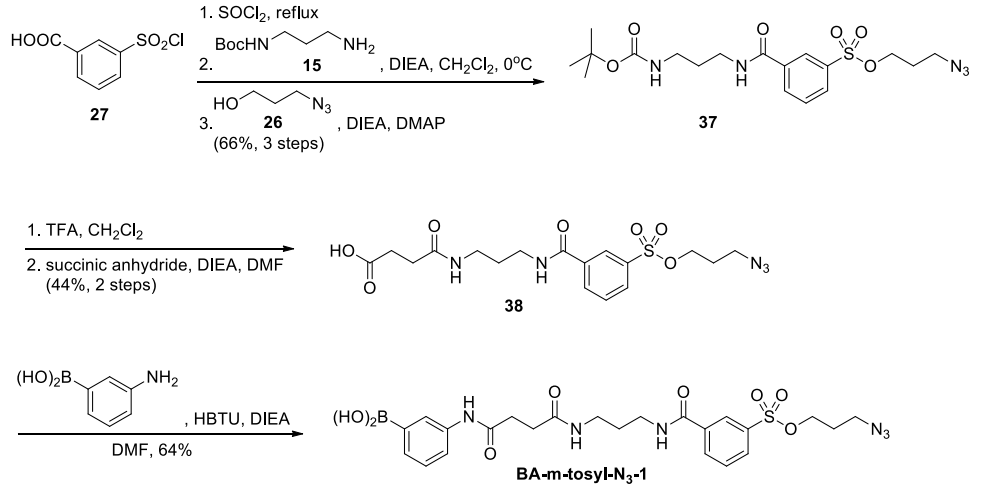


Scheme S9. Synthetic pathway of the space **Compound 35**



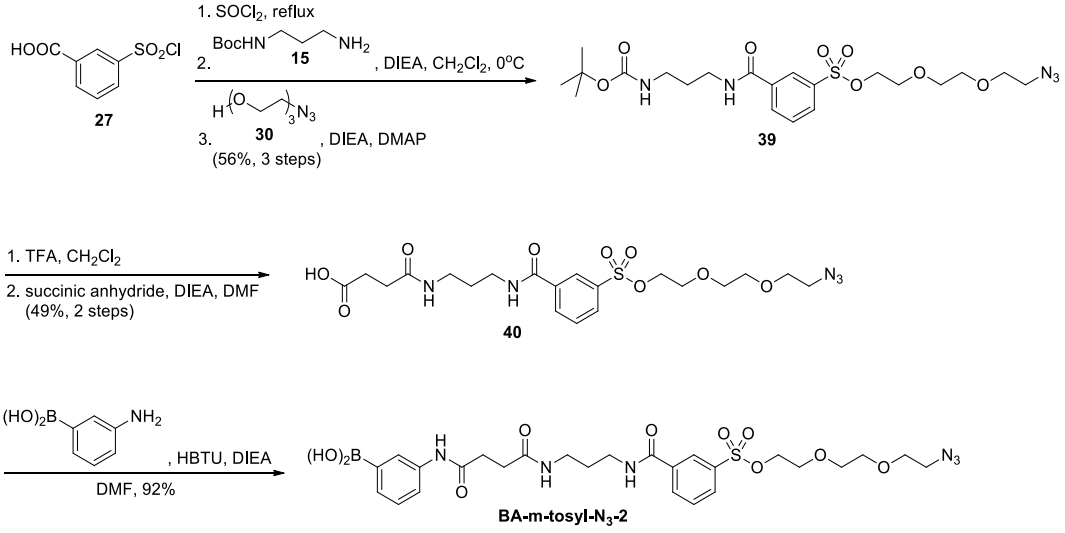
Scheme S10. Synthetic pathway of the **BA-s-tosyl-N_3-3**

g. Synthesis of the BA-m-tosyl-N_3-1



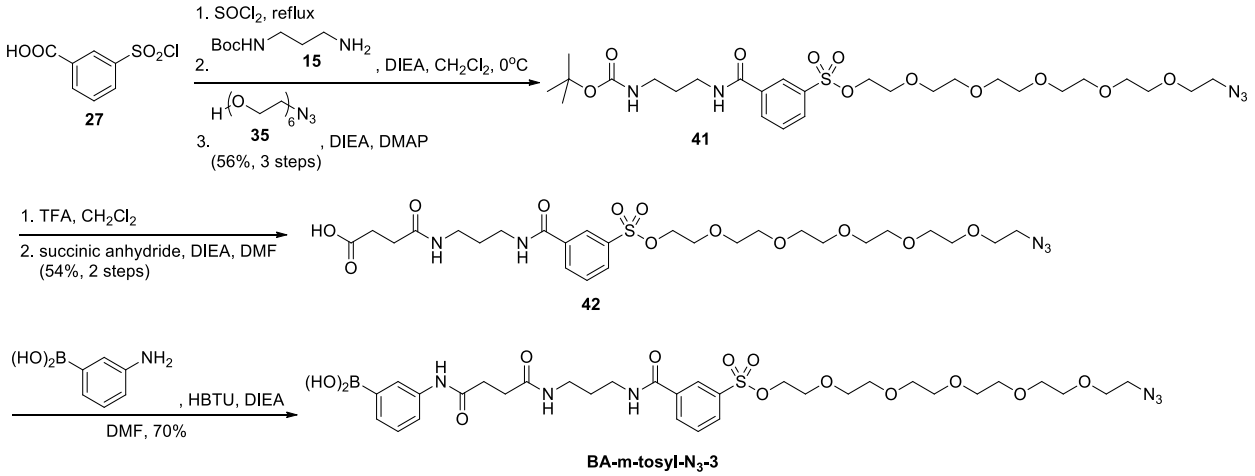
Scheme S11. Synthetic pathway of the **BA-m-tosyl-N_3-1**

h. Synthesis of the BA-m-tosyl-N_3-2



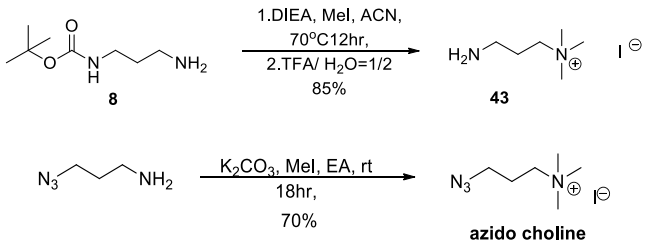
Scheme S12. Synthetic pathway of the **BA-m-tosyl-N_3-2**

i. Synthesis of the BA-m-tosyl-N_3-3



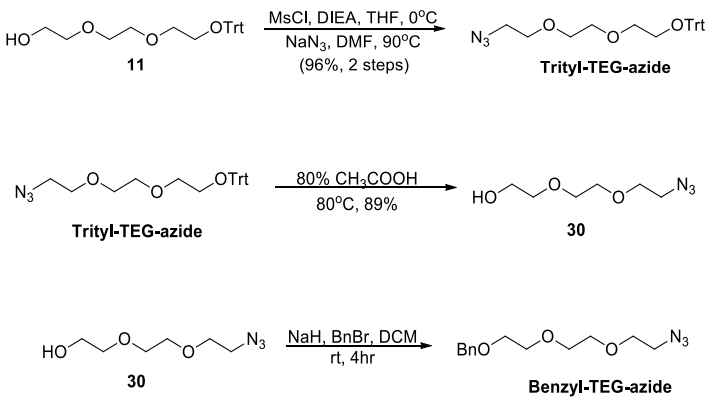
Scheme S13. Synthetic pathway of the **BA-m-tosyl-N_3-3**

j. Synthesis of Compound 43 and Azido choline



Scheme S14. Synthetic pathways of Compound 43and azido choline

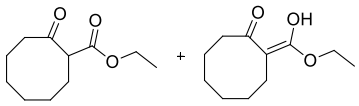
k. Synthesis of Trityl-TEG-azide and Benzyl-TEG-azide



Scheme S15. Synthetic pathway of Trityl-TEG-azide and Benzyl-TEG-azide

14. Experimental procedure and characterization of Compounds

Compound 1,2

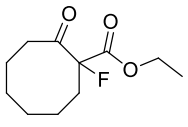


1 2

In an atmospheres of nitrogen, sodium hydride (60% dispersion；1.5 g, 37.5 mmol) was placed in anhydrous toluene (40ml) and to the stirred suspension was added diethyl carbonate (7.27 ml, 60 mmol). The mixture was heated to 80 ^{o}C stirred for 15 min. Then, cycloocanone (1.9 g, 15mmol) in toluene (10ml) was added to the reaction mixture. After 3 h, the reaction mixture was added with acetic acid (5 mL) to quench the reaction. The mixture was extracted with EA/H_2O = 3/1 for two times. The combined organic layers were dried over by $MgSO_4$, concentrated and purified by column chromatography to obtain the product **1 and 2** (2.73g, 13.79 mmol, 91%, colorless oil).

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.14 (q, *J* = 7.0 Hz, 2H), 3.56 (dd, *J* = 10.6, 4.7 Hz, 1H), 2.68-2.56 (m, 1H), 2.52-2.44 (m, 1H), 2.16-2.06 (m, 2H), 1.92-1.84 (m, 2H), 1.78-1.67 (m, 2H), 1.54-1.35 (m, 4H), 1.23 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.38, 170.30, 61.30, 57.28, 41.84, 29.11, 27.16, 25.71, 25.47, 24.74, 14.22; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.58 (s, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 2.43-2.21 (m, 4H), 1.78-1.67 (m, 2H), 1.54-1.35 (m, 6H), 1.30 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.18, 173.11, 99.39, 60.30, 32.47, 30.08, 28.89, 26.75, 26.23, 24.04, 14.48; HRMS (EI) calcd for $C_{11}H_{18}O_3$ $[M]^+$, 198.1256; found, 198.1254.

Compound 3



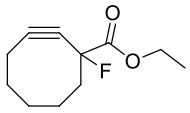
3

To stir solution of mixture **1&2** (2.68 g, 13.54mmol) in dried acetonitrile (ACN) (45 ml) were added Selecfluor (5.7 g, 16.25mmol) at room temperature. After heated in oil bath 55^{o}C for 14h, the reaction was checked by TLC and added H_2O (10 mL) to quench the reaction. The reaction mixture was extracted by EA/H_2O = 3/1 for two times. The combined organic layers were dried over by $MgSO_4$ and concentrated and

purified by flash column chromatography to obtain the desired product compound **3** (2.7 g, 12.75 mmol, 94%, colorless oil).

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.24 (q, *J* = 7.2 Hz, 2H), 2.72 (td, *J* = 12.6, 3.4 Hz, 1H), 2.68-2.50 (m, 2H), 2.28-2.20 (m, 1H), 2.04-1.94 (m, 1H), 1.91-1.83(m, 1H), 1.78-1.67 (m, 2H), 1.66-1.57 (m, 1H), 1.53-1.43 (m, 2H), 1.43-1.34 (m, 1H), 1.29 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.00 (d, J^2_{C-F} = 17 Hz,), 167.25 (d, J^2_{C-F} = 20 Hz,), 99.31 (d, J_{C-F} = 160 Hz,), 62.72, 39.06, 33.59 (d, J^2_{C-F} = 18 Hz,), 27.73 (d, J^4_{C-F} = 1 Hz,), 26.69, 24.58, 21.53 (d, J^3_{C-F} = 2 Hz,), 14.15; HRMS (EI) calcd for $C_{11}H_{18}O_3F$ $[M + H]^+$, 217.1240; found, 217.1235.

Compound 4

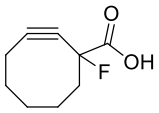


4

A solution of KHMDS (0.7 M in toluene, 17.91mL,13.125 mmol) was added to stir solution of **3** (1.2 g, 5.57 mmol) in THF (15 mL) The reaction mixture was reacted at -78^{o}C under nitrogen atmosphere. After react for 30min, the reaction mixture was added Tf_2NPh (2.2 g, 6.1 mmol) with THF (3 mL) to add slowly via syringe. After stirred for 1h, warmed to room temperature for 3h. The reaction was checked by TLC and added ammonia chloride (10 mL) to quench the reaction. The mixture was extracted by EA/H_2O = 3/1 for two times. The combined organic layers were dried over by $MgSO_4$ and concentrated and purified by flash column chromatography to obtain the desired product compound **4** (747 mg, 3.77 mmol, 68%, pale yellow oil).

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.28 (q, *J* = 7.1 Hz, 2H), 2.46-2.18 (m, 4H), 2.11-1.81 (m, 4H), 1.79-1.65 (m, 1H), 1.52-1.40(m, 1H), 1.33 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.48 (d, J^2_{C-F} = 28.5 Hz,), 108.47 (d, J^3_{C-F} = 9.8 Hz,), 91.99 (d, J_{C-F} = 185.3 Hz,), 87.21 (d, J^2_{C-F} = 32.3 Hz,), 62.50, 46.38 (d, J^2_{C-F} = 24.8 Hz,), 33.99, 29.25, 25.65, 20.71, 14.21; HRMS (EI) calcd for $C_{11}H_{16}O_2F$ $[M + H]^+$, 199.1134; found, 199.1136.

Compound 5

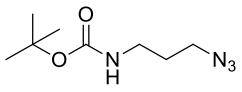


5

Compound **4** (765 mg, 3.86 mmol) and LiOH (330 mg, 7.72 mmol) were combined in 12 mL of 50% aqueous MeOH. This mixture was heated in 50 ^{o}C oil bath for 30 min and checked the reaction by TLC. After the reaction completed, cooled the solution to 0 ^{o}C and used HCl aqueous pH =2 to quench the reaction. The mixture was extracted by EA/H_2O = 1/2 for two times. The combined organic layers were dried over $MgSO_4$ and concentrated and purified by flash column chromatography to obtain the desired product compound **5** (509 mg, 2.99 mmol, 78%, pale yellow liquid).

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.49 (br, 1H, (COOH)), 2.51-2.24 (m, 4H), 2.14-1.83 (m, 4H), 1.82-1.66 (m, 1H), 1.58-1.39(m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.39 (d, $J^2_{C\text{-}F}$ = 30.0 Hz,), 109.47 (d, $J^3_{C\text{-}F}$ = 9.8 Hz,), 91.71 (d, $J_{C\text{-}F}$ = 186.0 Hz,), 86.43 (d, $J^2_{C\text{-}F}$ = 31.5 Hz,), 46.45 (d, $J^2_{C\text{-}F}$ = 24.8 Hz,), 33.98, 29.22, 25.67, 20.71; HRMS (EI) calcd for $C_9H_{10}O_2F$ $[M - H]^+$, 169.0665; found, 169.0661.

Compound 7

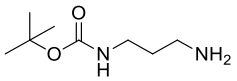


7

To a stirred solution of 3-chloropropylamine hydrochlordie (1.3 g, 10 mmole) in CH_2Cl_2 (15 mL) was added with diisopropylethylamine (DIEA) (1.92 mL, 11 mmole), and Di-*tert*-butyl dicarbonate (2.2g, 10 mmole). After reacting for 2 h at room temperature, CH_2Cl_2 was removed by reduced pressure and the mixture was extracted with 0.5M HCl /CH_2Cl_2 = 1/3 for two times. Then, the combined organic layers were dried over magnesium sulfate ($MgSO_4$). Using DIEA as solution and added sodium azide (1.9 mg, 30 mmol) in 90 ^{o}C oil bath to react for 12 h. After reaction complete, removed by reduced pressure and the crude mixture was extracted by CH_2Cl_2/H_2O = 3/1 for three times. Then, the combined organic layers were dried over $MgSO_4$, and concentrated under reduced pressure to obtain the desired product compound **7** (1.9 g, 9.86 mmol, 99%, pale yellow liquid).

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.65 (br, 1H, (NH)), 3.35 (t, *J* = 6.6 Hz, 2H), 3.20 (q, *J* = 6.5 Hz, 2H), 1.77 (quin, *J* = 6.6 Hz, 2H), 1.44 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.15, 79.66, 49.36, 38.29, 29.52, 28.59; HRMS (EI) calcd for $C_8H_{17}O_2N_4$ $[M + H]^+$, 201.1352; found, 201.1349.

Compound 8

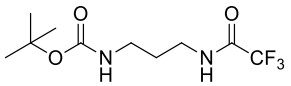


8

To a stirred solution of compound **7** (1.9 g, 9.7 mmol) in THF (18 mL) with H_2O (1.8 mL) was added triphenylphosphine (3 g, 11.64 mmole) along with ddH_2O (3.6 mL). After reacting for 12 h at room temperature, solvents were removed under reduced pressure and the crude mixture was directly purified by flash column chromatography to obtain the desired product compound **8** (2.35 g, 13.49 mmole, 95%) as a yellow oil.

^{1}H NMR (300 MHz, MeOD) δ 3.10 (t, *J* = 6.7 Hz, 2H), 2.66 (t, *J* = 7.0 Hz, 2H), 1.61 (quin, *J* = 6.8 Hz, 2H), 1.43 (s, 9H); ^{13}C NMR (75 MHz, MeOD) δ 158.76, 80.00, 39.84, 38.73, 34.24, 28.94; HRMS (EI) calcd for $C_8H_{18}O_2N_2$ $[M + H]^+$, 174.1368; found, 174.1368.

Compound 9



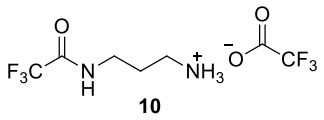
9

To a stirred solution of **8** (1.4 g, 8.24 mmol) and DIEA (4.3 mL, 24.7 mmol) in CH_2Cl_2 (33 mL) was added trifloroacetic anhydride (1.4 mL, 9.89 mmol) in CH_2Cl_2 (8 mL). Afterward,the reaction was cooled to 0^{o}C and allowed to react for further 10 min. The mixture was extracted by H_2O /CH_2Cl_2 = 1/3 for two times and 0.5M HCl /CH_2Cl_2 = 1/3 for two times. Then, the combined organic layers were dried over$MgSO_4$.Concentrated and purified by column chromatography to obtain the product **9** (2 g, 7.43 mmol, 90%, pale yellow solid).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (br, 1H, (NH)), 4.75 (br, 1H, (NH)), 3.40 (q, *J* = 6.2 Hz, 2H), 3.22 (q, *J* = 6.4 Hz, 2H), 1.68 (quin, *J* = 6.2 Hz, 2H), 1.45 (s, 9H); ^{13}C NMR

(75 MHz, $CDCl_3$) δ 157.79 (q, $J^2_{C\text{-}F}$ = 36.8 Hz), 157.24, 116.09 (q, $J_{C\text{-}F}$ = 285.8 Hz,), 79.73, 37.05, 36.58, 29.40, 28.30; HRMS (ESI-TOF) calcd for $C_{10}H_{17}O_3N_2F_3Na$ [M + Na]$^+$, 293.1089; found, 293.1088.

Compound 10

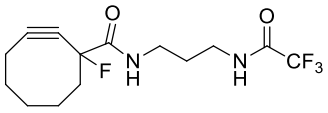


10

To a stirred solution of **9** (1.9 g, 7.32 mmol) in CH_2Cl_2 (10 mL) was added with trifloroacetic acid (5 mL). After reacting 30 min, checked by TLC to indicate the reaction complete. CH_2Cl_2 and trifluoroacetic acid were removed by reduced pressure, to obtain the desired product compound **10** (1.97 g, 6.96 mmol, 95%, pale yellow solid).

^{1}H NMR (300 MHz, MeOD) δ 3.39 (t, *J* = 6.8 Hz, 2H), 2.95 (t, *J* = 7.6 Hz, 2H), 1.91 (quin, *J* = 6.8 Hz, 2H); ^{13}C NMR (75 MHz, MeOD) δ 163.27 (q, $J^2_{C\text{-}F}$ = 33.8 Hz,), 159.64 (q, $J^2_{C\text{-}F}$ = 36.8 Hz,), 117.58 (q, $J_{C\text{-}F}$ = 285 Hz,), 38.49, 37.84, 28.23; HRMS (ESI-TOF) calcd for $C_5H_{10}ON_2F_3$ [M + H]$^+$, 171.0745; found, 171.0749.

Compound 6



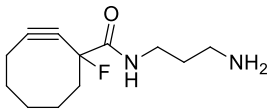
6

To a stirred solution of **5** (1 g, 6.02 mmol) in DMF (33 mL) was added **10** (1.7 g, 6.02 mmol) and HBTU (3.4 g, 9.03 mmol) to react in ice bath for 20 min. Then, added DIEA (3.14 mL, 18.05 mmol) at room temperature react for 12 min. The reaction was checked by TLC and removed solvent under reduced pressure. The mixture was extracted by 0.5M HCl /CH_2Cl_2 = 1/3 one times and combined organic solution. Dried over $MgSO_4$ and concentrated in vacuum to obtain the product. Purified by column chromatography to obtain the product **6** (1 g, 3.39 mmol, 56%, pale yellow solid).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (br, 1H, (NH)), 6.70 (br, 1H, (NH)), 3.48-3.28 (m, 4H), 2.52-2.21 (m, 4H), 2.15-1.82 (m, 4H), 1.81-1.65 (m, 3H), 1.51-1.39(m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.97 (d, $J^2_{C\text{-}F}$ = 24.8 Hz,), 157.83 (q, $J^2_{C\text{-}F}$ = 36.8 Hz,),

115.99 (q, $J_{C\text{-}F}$ = 285.8 Hz,), 109.88 (d, $J^3_{C\text{-}F}$ = 10.5 Hz), 94.36 (d, $J_{C\text{-}F}$ = 185.3 Hz), 86.91 (d, $J^2_{C\text{-}F}$ = 31.5 Hz), 46.50 (d, $J^2_{C\text{-}F}$ = 24.8 Hz), 36.42, 36.14, 33.83, 28.88, 28.71, 25.57, 20.49; HRMS (ESI-TOF) calcd for $C_{14}H_{18}O_2N_2F_4Na$ $[M + Na]^+$, 345.1202; found, 345.1199.

Compound MFCO-amine

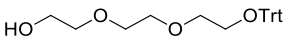


MFCO-amine

Compound **6** (322 mg,1 mmol) and 25% LiOH (128 mg, 3 mmol) in THF (20 mL) were reacted at room temperature. After reacting for 30 min, the reaction was quenched by 0.5 M NaOH and extracted by ddH2O / EA =1/3 three times. The combined organic layers were dried over $MgSO_4$ and concentrated and purified by flash column chromatography to obtain the desired product **MFCO-amine** (168 mg, 0.74mmol, 74%, pale yellow solid).

^{1}H NMR (300 MHz, MeOD) δ 3.31 (t, J = 6.5 Hz, 2H), 2.73 (t, J = 7.0 Hz, 2H), 2.44-2.21 (m, 4H), 2.14-1.80 (m, 4H), 1.74 (quin, J = 6.7 Hz, 2H), 1.68-1.59 (m, 1H), 1.51-1.37(m, 1H); ^{13}C NMR (75 MHz, MeOD) δ 171.50 (d, $J^2_{C\text{-}F}$ = 25.5 Hz), 110.32 (d, $J^3_{C\text{-}F}$ = 10.5 Hz), 95.26 (d, $J_{C\text{-}F}$ = 185.3 Hz,), 88.39 (d, $J^2_{C\text{-}F}$ = 31.5 Hz,), 47.78 (d, $J^2_{C\text{-}F}$ = 24.8 Hz), 38.99, 37.64, 35.09, 30.92, 30.23, 26.88, 21.17; HRMS (ESI-TOF) calcd for $C_{12}H_{20}ON_2F$ $[M + H]^+$, 227.1560; found, 227.1566.

Compound 11



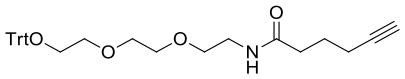
11

Pyridine (0.6 mL, 7.5 mmol) and triphenylmethyl chloride (1.4 g, 5 mmol) were added to triethylene glycol (6.7 mL, 50 mmol) in CH_2Cl_2 (100 mL). The reaction mixture was reacted at 45 ℃ for 12 h under nitrogen atmosphere. After the reaction completed, the reaction mixture was extracted by H_2O/CH_2Cl_2 = 1/2 for three times. The combined organic layers were dried over $MgSO_4$ and concentrated and purified by flash column chromatography to obtain the desired product compound **11** (1.7 g,

4.44 mmol, 89 %, pale yellow oil).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.1 Hz, 6H), 7.35-7.27 (m, 6H), 7.25-7.18 (m, 3H), 3.76-3.60 (m, 10H), 3.26 (t, *J* = 5.2 Hz, 2H), 2.32 (br, 1H, (OH)); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.26, 128.90, 127.96, 127.15, 86.82, 72.72, 71.02, 70.90, 70.73, 63.49, 62.01; HRMS (ESI-TOF) calcd for $C_{25}H_{28}O_4Na$ $[M + Na]^+$, 415.1885; found, 415.1885.

Compound 13



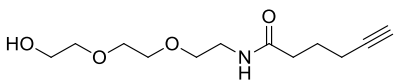
13

To a stirred solution of compound **12** (4.17 g, 10.66 mmole) in CH_2Cl_2 (53 mL) was added Hex-5-ynoic acid (1.18 mL, 10.66 mmol), HOBt (2.88 g, 21.31

11mmole) and EDC (3.3 g, 21.31 mmole) in the presence of triethyl amine (4.46 mL, 31.98mmole). After reacting for 12 h at room tempter, the reaction mixture was quenched by ddH_2O (3 mL), the crude mixture was extraction by CH_2Cl_2/H_2O = 3/1 twice. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil mixtures were purified by flash column chromatography to obtain the desired product compound **13** (4.83 g, 9.95 mmol, 93 %, as a pale oil).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49-7.45 (m, 6H), 7.32-7.20 (m, 9H), 3.74-3.62 (m, 6H), 3.58 (t, *J*=5.1 Hz, 2H), 3.46 (q, *J*=5.1 Hz, 2H), 3.26 (t, *J*=5.1 Hz, 2H), 2.18-2.10 (m, 4H), 1.91 (t, *J*=3 Hz, 1H), 1.76 (quin, *J*=7.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.40, 144.27, 128.90, 127.99, 127.21, 86.82, 83.79, 70.91, 70.64, 70.65, 70.14, 69.20, 63.53, 39.40, 35.12, 24.33, 18.03 ; HRMS (ESI): calcd for $C_{31}H_{35}NO_4Na$ $[M+Na]^+$: 508.2464, found: 508.2477.

Compound 14



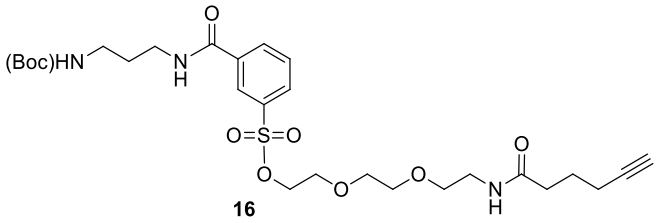
14

Compound **13** (1.4 g, 2.88 mmol) was dissolved in 80% acetic acid solution (5.76 mL), followed by heated 80^{o}C in oil bath for 3 h, The reaction was checked by TLC and concentrated in vacuum. The crude mixture was purified by column

chromatography to obtain the product compound **14** (614 g, 2.52 mmol, 88 %, pale oil).

^{1}H NMR (300 MHz, MeOD): δ 3.71-3.61 (m, 6H), 3.60-3.52 (m, 4H), 3.36 (t, *J*=5.4 Hz), 2.32 (t, *J*=7.2 Hz, 2H), 2.28-2.17 (m, 3H), 1.80 (quin, *J*=7.2 Hz, 2H); ^{13}C NMR (75 MHz, MeOD): δ 175.57, 84.35, 73.82, 71.58, 71.40, 70.68, 70.36, 62.30, 40.43, 35.91, 26.06, 18.76 ; HRMS (APCI): calcd for $C_{12}H_{21}NO_4Na$ $[M+Na]^+$: 266.1368, found: 266.1369.

Compound 16

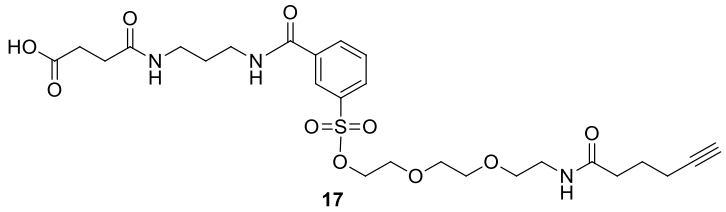


16

To a stirred solution of compound **15** (300 mg, 1.72 mmol) in CH_2Cl_2 (7 mL) was added with DIEA (450 μL, 2.58 mmol) and 4 Å molecular sieve (600 mg). 3-(chlorosulfonyl)benzoyl chloride (289 μL,1.89 mmol) in a solution of CH_2Cl_2 (8mL) was drop-wisely added to the reaction mixture by syringe. After reacting for 30 min, the ice bath was removed, and subsequently added **14** (837 mg, 3.44 mmol) DMAP (105 mg, 0.86 mmol) and DIEA (300μL, 1.72mmol) react for 12 h in room temperature. The reaction was checked by TLC until the starting material was completely converted to product which was observed in 12 h. After removing molecular sieves by celite filtration and removed CH_2Cl_2 under reduced pressure, the crude mixture was purified by flash column chromatography to obtain the desired product compound **16** (450 g, 0.77 mmol, 45%, pale oil).

^{1}H NMR (300 MHz, MeOD): δ 8.38 (s, 1H), 8.17 (d, *J*=7.8 Hz, 1H), 8.08 (d, *J*=7.8 Hz, 1H), 7.75 (t, *J*=7.8 Hz, 1H), 4.24 (t, *J*=4.2 Hz, 2H), 3.68 (t, *J*=4.2 Hz, 2H), 3.53-3.42 (m, 8H), 3.34-3.31 (m, 2H), 3.14 (t, *J*=6.9 Hz), 2.31 (t, *J*=6.9 Hz, 2H), 2.22-2.18 (m, 3H), 1.81-1.74 (m, 4H), 1.44 (s, 9H); ^{13}C NMR (75 MHz, MeOD): δ 175.61, 168.05, 158.80, 138.31, 137.27, 133.73, 131.78, 131.12, 127.97, 84.37, 80.23, 71.70, 71.63, 71.33, 70.70, 70.36, 69.88, 40.46, 38.97, 38.72, 35.95, 30.85, 28.92, 26.07, 18.76; HRMS (ESI): calcd for $C_{27}H_{42}NO_9S$ $[M+Na]^+$: 584.2642, found: 584.2637.

Compound 17

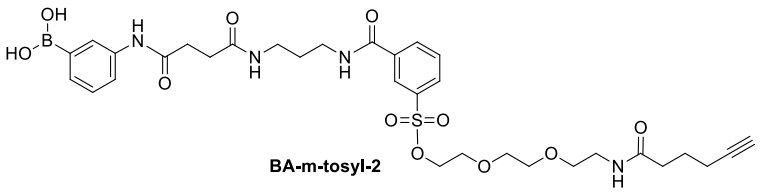


17

To a stirred solution of compound **16** (432m g, 0.74 mmole) in CH_2Cl_2 (10 mL) wasadded to trifluoroacetic acid (10 mL). After reacting 30 min, CH_2Cl_2 and trifluoroacetic acid were removed by reduced pressure. Directly, added DMF (14.8mL), succinic anhydride (96.8 mg, 0.74 mmol) and DIEA (129 mL, 0.74 mmol) to react for 12 h at room temperature. The solvent was removed under reduced pressure and the mixtures were purified by column chromatography to obtain the product compound 1**7** (198 g, 0.34 mmol, 46 %, as pale oil).

^{1}H NMR (300 MHz, MeOD): δ 8.38 (s, 1H), 8.19 (d, *J*=7.8 Hz, 1H), 8.09 (d, *J*=7.8 Hz, 1H), 7.75 (t, *J*=7.8 Hz, 1H), 4.25 (t, *J*=3.6 Hz, 2H), 3.69 (t, *J*=3.6 Hz, 2H), 3.58-3.40 (m, 8H), 3.38-3.22 (m, 4H), 2.60 (t, *J*=5.7 Hz, 2H), 2.50 (t, *J*=5.7 Hz, 2H), 2.31 (t, *J*=7.5 Hz, 2H), 2.26-2.15 (m, 3H), 1.86-1.74 (m, 4H); ^{13}C NMR (75 MHz, MeOD): δ 175.66, 175.08, 168.03, 138.27, 137.20, 133.72, 131.79, 131.15, 128.01, 84.37, 71.67, 71.31, 70.68, 70.37, 69.87, 40.46, 38.67, 38.00, 35.96, 31.98, 30.82, 30.25, 26.06, 18.75; HRMS (ESI): calcd for $C_{26}H_{37}N_3O_{10}S$ $[M+Na]^+$: 606.2097, found: 606.2114.

Compound BA-m-tosyl-2



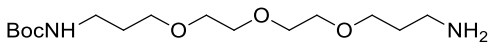
BA-m-tosyl-2

To a stirred solution of compound **17**(240 mg, 0.34 mmol) in DMF (6.8 mL) was added to 3-aminophenylboronic acid (42 mg, 0.306 mmol), HBTU (194 mg,0.51 mmol) in the presence of DIEA (118μL, 0.68mmol). After reacting for 6 h at room tempter, the reaction mixture was quenched with H_2O (3 mL) and the crude mixture was extraction by CH_2Cl_2/H_2O = 10/3 two times. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil mixtures were purified by flash column chromatography to obtain the desired product

BA-m-tosyl-2 (52 g, 0.07 mmol, 20 %, as pale yellow liquid).

^{1}H NMR (500 MHz, MeOD): δ 8.37 (s, 1H), 8.16 (d, *J*=8 Hz, 1H), 8.06 (d, *J*=8 Hz, 1H), 7.80 (m, 2H), 7.58 (d, *J*=8 Hz, 1H), 7.45-7.26 (t, 2H), 4.21 (t, *J*=4.5 Hz, 2H), 3.65 (t, J=4.5 Hz, 2H), 3.53-3.43 (m, 8H), 3.33-3.27 (m, 4H), 2.71 (t, *J*=7 Hz, 2H), 2.57 (t, *J*=7 Hz, 2H), 2.30 (t, *J*=7.5 Hz, 2H), 2.24 (t, *J*=2.5 Hz, 1H,), 2.19 (td, J_1=7 Hz, J_2=2.5 Hz, 2H), 1.84-1.75 (m, 4H); ^{13}C NMR (125 MHz, MeOD): δ 175.63, 175.12, 173.15 , 167.99, 138.23, 137.21, 133.73, 131.77, 131.11, 130.07, 129.81, 129.26, 129.26, 128.03, 84.35, 74.00, 71.68, 71.61, 71.32, 70.69, 70.38, 69.87, 64.56, 40.46, 38.61, 37.96, 35.95, 33.08, 32.14, 30.17, 26.89, 18.75; HRMS (ESI): calcd for $C_{32}H_{43}N_4O_{11}SNaB$ $[M+Na]^+$: 725.2640, found: 725.2645.

Compound 18

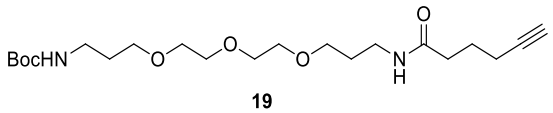


18

3,3' ((oxybis(ethane 2,1 diyl))bis(oxy))bis (propan 1 amine) (6.965mL, 31.77mmol) in CH_2Cl_2 (300 mL) was added with DIEA (2.77 Ml, 15.89 mmol) and Di-tert-butyl dicarbonate (2.6g, 11.91mmol). After reacting for 12 h at room temperature, the reaction mixture was quenched with methanol (10mL). The crude mixture was purified by column chromatography to obtain the product compound **18** (3.12g, 9.74mmol, 92%, pale oil).

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.68-3.50 (m, 12H), 3.22 (q, *J*=6Hz, 2H), 2.80 (t, *J*=6.6Hz, 2H), 1.80-1.68 (m, 4H), 1.43 (s, 9H); ^{13}C NMR (75 MHz, CDCl3): δ 156.45 , 79.23, 70.76, 70.60, 70.34, 70.30, 69.94, 69.58, 39.91, 38.62 , 31.69, 29.91, 28.67; HRMS (ESI): calcd for $C_{15}H_{33}N_2O_5$：321.2389, found: 321.2383

Compound 19



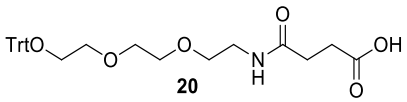
19

Compound **18** (3.12 g, 9.74 mmol) in CH_2Cl_2 (48.7 mL) was added HOBt (2.63g, 19.48 mmol), EDC (3.02 g, 19.48 mmol) and Hex-5-ynoic acid (1.09 mL, 9.74 mmol) in the presence of triethyl amine (5.1 mL, 29.23 mmol) by an additional funnel at 0

°C. After reacting for 12 h at room temperature, the reaction mixture was quenched with H_2O (3 mL), the crude mixture was extraction by CH_2Cl_2/H2O = 10/1 twice. The combined organic layers were dried over $MgSO_4$, and concentrated under reduced pressure to obtain the desired product compound **19** (3.99 g, 9.63 mmol, 99 % as a pale oil).

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.59-3.41 (m, 12H, (H6-H11)), 3.27 (q, *J*=6 Hz, 2H, (H13)), 3.11 (q, *J*=6 Hz, 2H, (H4)), 2.25-2.12 (m, 4H, (H15, H17)), 1.90 (t, *J*=2.7 Hz, 1H, (H19)), 1.82-1.62 (m, 6H, (H5, H12, H16)), 1.35 (s, 9H, (H1)) ; ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.20 (C14), 156.08 (C3), 83.69 (C18), 78.87 (C2), 70.53 (C19), 70.22 (C6-C11), 70.16 (C6-C11), 70.04 (C6-C11), 69.51 (C6-C11), 69.11 (C6-C11), 38.49 (C4), 37.85 (C13), 35.12 (C15), 29.72 (C12), 29.02 (C5), 28.47 (C1), 24.32 (C16), 17.94 (C17); HRMS (ESI): calcd for $C_{21}H_{38}N_2O_6Na$ $[M+Na]^+$: 437.2628, found: 437.2624.

Compound 20

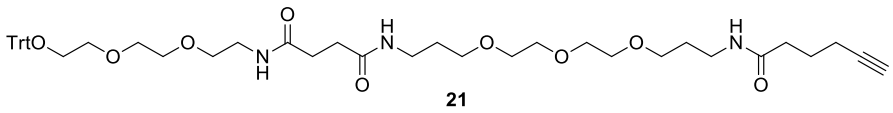


20

To a stirred solution Compound **12** (1.51 g, 3.87 mmol) in ACN (10.32 mL) was added succinic anhydride (387 mg, 3.87 mmol) by an additional funnel at 0°C for 30min. The reaction was checked by TLC to indicate the reaction complete.
The solvent was removed under reduce pressure. The crude mixture was extracted by H_2O/ CH_2Cl_2 = 1/2 for three times. The combined organic layers were dried over $MgSO_4$ and concentrated and purified by flash column chromatography to obtain the desired product compound **20** (1.61 g, 3.27 mmol, 85%, pale yellow oil).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45 (d, *J*=7.5 Hz, 6H), 7.34-7.17 (m, 9H), 3.70-3.60 (m, 6H), 3.55 (t, *J*=5.4 Hz, 2H), 3.35 (t, *J*=5.4 Hz, 2H), 3.22 (t, *J*=4.8 Hz, 2H), 2.53 (t, *J*=6.9 Hz, 2H), 2.40 (t, *J*=6.9 Hz, 2H); ^{13}C NMR (75 MHz, MeOD): δ 176.31, 174.68, 145.61, 130.01, 128.92, 128.23, 88.07, 71.91, 71.51, 70.76, 64.62, 40.61, 31.67, 30.47; HRMS (ESI): calcd for $C_{45}H_{61}N_3O_9Na$ $[M+Na]^+$: 514.2206, found: 514.2202

Compound 21

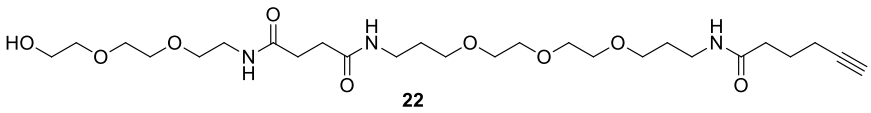


21

To a stirred solution of compound **19** (1.57 g, 3.67 mmol) in CH_2Cl_2 (18 mL) was added with HOBt (991 g, 7.34 mmol), EDC (1.14 g, 7.34 mmol) and **20** (1.8 mL, 3.67 mmol). The reaction mixture was reacted at room temperature for 30 min. After, adding DIEA (1.96 mL, 11.01 mmol) to react for 12 h at room temperature. The reaction mixture was quenched with H_2O (3 mL), the crude mixture was extracted by CH_2Cl_2/H_2O = 3/1 twice, the combined organic layers were dried over $MgSO_4$, and concentrated under reduced pressure. The resulting oil was purified by flash column chromatography to obtain the desired product compound **21**(1.96 g, 2.49 mmol, 68 %, as a pale oil).

^{1}H NMR (300 MHz, MeOD): δ 7.44 (d, *J*=7.2 Hz, 6H), 7.34-7.20 (m, 9H), 3.70-3.54 (m, 16H), 3.51 (td, J_1=6 Hz, J_2=2.4 Hz, 4H), 3.35 (t, *J*=4.8 Hz, 2H), 3.29-3.20 (m, 6H), 2.43 (s, 4H), 2.33-2.25 (m, 3H), 2.20 (td, J_1=6.9 Hz, J_2=2.4 Hz, 2H), 1.83-1.70 (m, 6H); ^{13}C NMR (75 MHz, MeOD): δ 175.61, 174.90, 174.75, 145.47, 129.92, 128.96, 128.30, 88.07, 84.50, 71.76, 71.47, 71.39, 71.20, 70.65, 70.56, 70.55, 70.00, 69.96, 64.54, 40.52, 37.88, 36.00, 32.50, 30.34, 25.96, 18.70 ; HRMS (ESI): calcd for $C_{45}H_{61}N_3O_9Na$ $[M+Na]^+$: 810.4306, found: 810.4304.

Compound 22



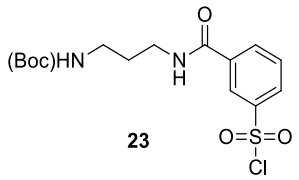
22

Compound **21** (1.96 g, 2.49 mmol) was dissolved in 80% acetic acid solution (20 mL), followed by heated to 80^{o}C and reacted for 3 h, The reaction was checked by TLC and concentrated under reduced pressure. The crude mixture was purified by column chromatography to obtain the product compound **22** (979 g, 1.79 mmol, 88 %, white solid).

^{1}H NMR (300 MHz, MeOD): δ 3.70-3.50 (m, 22H), 3.36 (t, *J*=5.4 Hz, 2H), 3.25 (t, *J*=6.9 Hz, 4H), 2.48 (s, 4H), 2.35-2.26 (m, 3H), 2.21 (td, J_1=6.9 Hz, J_2=2.4 Hz, 2H), 1.85-1.70 (m, 6H); ^{13}C NMR (75 MHz, MeOD): δ 175.45, 174.81, 174.63, 84.34, 73.81, 71.66, 71.56, 71.41, 71.36, 70.70, 70.44, 70.04, 62.30, 40.50, 38.09, 37.97,

36.02, 32.50, 32.42, 30.54, 26.07, 18.78;HRMS (ESI): calcd for $C_{26}H_{47}N_3O_9Na$ $[M+Na]^+$: 568.3210, found: 568.3216.

Compound 23

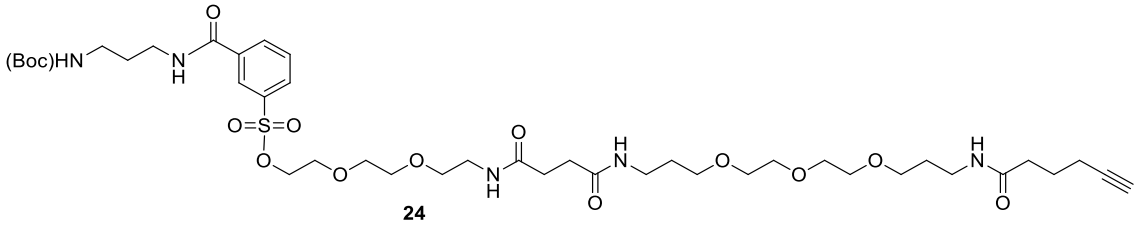


23

To a stirred solution of compound **15** (600 mg, 3.45 mmol) in CH_2Cl_2 (25 mL) was added with DIEA (601μL, 3.45 mmol) and 4 Å molecular sieve (1200 mg). 3-(chlorosulfonyl)benzoyl chloride (578 μL, 3.79 mmol) in a solution of CH_2Cl_2 (8mL) was drop-wisely added to the reaction mixture by syringe. After reacting for 30 min, the ice bath was removed to room temperature for 3 h. The reaction was checked by TLC and concentrated under reduced pressure. The crude mixture was purified by column chromatography to obtain the product **23** (1180 mg, 3.14 mmol, 91%, pale white liquid).

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.55 (s, 1H,), 8.24 (d, *J*=7.8 Hz, 1H), 8.10 (d, *J*=7.8 Hz, 1H), 7.68 (t, *J*= 7.8 Hz, 1H), 3.51 (q, *J*=6 Hz, 2H), 3.24 (q, *J*=6 Hz, 2H), 1.72 (t, *J*=5.4 Hz, 2H), 1.42 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.84, 157.50, 144.80, 136.62, 133.92, 130.21, 129.31, 125.97, 80.10, 37.23, 36.50, 29.95, 28.51 HRMS (ESI): calcd for $C_{15}H_{22}O_5N_2SCl$ $[M+H]^+$: 377.0938, found: 377.0934.

Compound 24



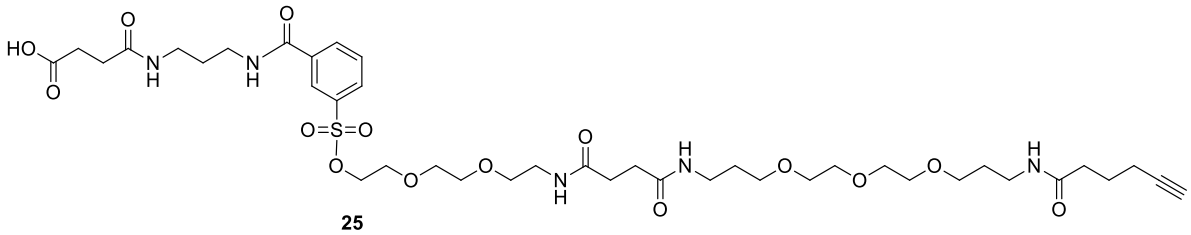
24

To a stirred solution of compound **23** (1.19 g, 3.17 mmol) in CH_2Cl_2 (10 mL) was added DIEA (1.10 mL, 6.34 mmol), DMAP (193 mg, 1.585 mmol) and **22** (864 mg, 1.585 mmol) to react for 12 h at room temperature. The reaction was checked by TLC until the starting material was completely converted to product which was observed in

12 h. After removing molecular sieves by filtration and removed CH_2Cl_2 under reduced pressure, the crude mixture was purified by flash column chromatography to obtain the desired product compound **24** (589 mg, 0.66 mmol, 42%, pale yellow liquid).

^{1}H NMR (300 MHz, MeOD): δ 8.37 (s, 1H), 8.17 (d, *J*=7.8 Hz, 1H), 8.08 (d, *J*=7.8 Hz, 1H), 7.74 (t, *J*=7.8 Hz, 1H), 4.23 (t, *J*=4.2 Hz, 2H), 3.70-3.41 (m, 24H), 3.24 (t, *J*=6.6 Hz, 4H), 3.13 (t, *J*=6.6 Hz, 2H), 2.46 (s, 4H), 2.31-2.18 (m, 5H), 1.83-1.68 (m, 8H), 1.43 (s, 9H) ; ^{13}C NMR (75 MHz, MeOD): δ 175.37, 174.79, 174.63, 167.98, 158.73, 138.28, 137.26, 133.76, 131.78, 131.15, 127.96, 84.36, 80.20, 71.67, 71.36, 70.72, 70.45, 70.05, 69.88, 40.54, 39.00, 38.74, 37.98, 36.03, 32.50, 30.84, 30.54, 28.94, 26.07, 18.79; HRMS (ESI): calcd for $C_{41}H_{68}N_5O_{14}S$ $[M+H]^+$: 886.4483, found: 886.4476.

Compound 25



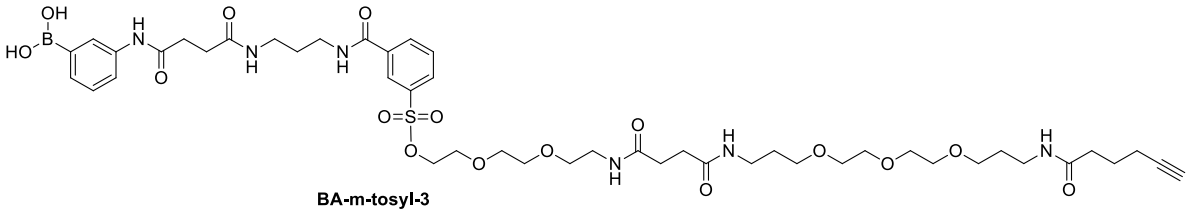
25

To a stirred solution of compound **24** (410 mg, 0.46 mmol) in CH_2Cl_2 (20 mL) was added with trifluoroacetic acid (10 mL) to react for 1 h. The reaction was checked by TLC to indicate the reaction completed. CH_2Cl_2 and trifluoroacetic acid were removed by reduced pressure. The crude mixture was extracted by Hexane/H_2O = 1/10 for two times. The combined water phase layers were collected and concentrated under reduced pressure to obtain the desired product compound. Directly, added DMF (5.73 mL), succinic anhydride (173 mg, 1.72 mmol) and DIEA (221.8 mL, 1.72 mmol) to react for 12h at room temperature. Until checked by TLC and concentrated the reaction in vacuum. The crude mixture was purified by column chromatography to obtain the product compound **25** (216 g, 0.24 mmol, 53 %, pale yellow liquid).

^{1}H NMR (300 MHz, MeOD): δ 8.38 (s, 1H), 8.19 (d, *J*=7.8 Hz, 1H), 8.08 (d, *J*=7.8 Hz, 1H), 7.75 (t, *J*=7.8 Hz, 1H), 4.24 (t, *J*=3.9 Hz, 2H), 3.72-3.41 (m, 22H), 3.38-3.20(m, 8H), 2.68-2.55 (m, 4H), 2.48 (s, 4H), 2.34-2.17 (m, 5H), 1.86-1.69 (m, 8H); ^{13}C NMR (75 MHz, MeOD): δ 175.39, 174.97, 174.86, 174.68, 174.48, 167.92,

138.22, 137.20, 133.72, 131.77, 131.16, 127.98, 84.35, 71.62, 71.32, 70.67, 70.44, 70.02, 69.84, 43.90, 40.5, 38.66, 37.98, 36.01, 32.49, 32.43, 32.07, 30.81, 30.50, 30.25, 26.05, 18.76; HRMS (ESI): calcd for $C_{40}H_{63}N_5O_{15}NaS$ $[M+Na]^+$: 908.3938, found: 908.3964.

Compound BA-m-tosyl-3

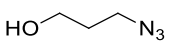


BA-m-tosyl-3

To a stirred solution of compound **25** (216 mg, 0.24 mmol) in DMF (8.8 mL) was added 3-aminophenylboronic acid (32 mg, 0.232 mmol) and HBTU (139 mg, 0.37 mmol) in the presence of DIEA (129 μl, 0.37mmol). After reacting for 6 h at room temperature, the reaction mixture was quenched with H_2O (3 mL), the crude mixture was extraction by CH_2Cl_2/H_2O = 10/3 twice. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil mixture was purified by flash column chromatography to obtain the desired product **BA-m-tosyl-3** (40 g, 0.04 mmol, 16 %, pale yellow liquid).

^{1}H NMR (500 MHz, MeOD): 8.38 (s, 1H), 8.17 (d, *J*=8 Hz, 1H), 8.06 (d, *J*=8 Hz, 1H), 7.99-7.80 (m, 1H), 7.72 (t, *J*=8 Hz, 1H), 7.58 (d, *J*=7.5 Hz, 1H), 7.46-7.23 (m, 2H), 4.21 (t, *J*=4.5 Hz, 2H), 3.68-3.44 (m, 26H), 3.27-3.22 (m, 4H), 2.71 (t, *J*=7 Hz, 2H), 2.58 (t, *J*=7 Hz, 2H), 2.47 (t, *J*=4.5 Hz, 4H), 2.32-2.27 (m, 2H), 2.26 (t, J=2.5 Hz), 2.21 (td, J_1=7 Hz, J_2=2.5 Hz, 2H), 1.86-1.71 (m, 8H); ^{13}C NMR (125 MHz, MeOD): δ 175.43, 175.10, 174.82, 174.67, 3, 125.91, 84.32, 74.00, 71.66, 71.66, 71.37, 71.34, 70.71, 70.43, 70.05, 70.01, 69.86, 64.56, 40.54, 38.64, 38.00, 37.96, 36.03, 33.10, 32.49, 32.42, 32. 16, 30.53, 30.18, 26.09, 18.78; HRMS (ESI): calcd for $C_{46}H_{69}N_6O_{16}NaSB$ $[M+Na]^+$: 1027.4482, found: 1027.4493.

Compound 26

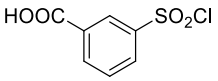


26

To stirred solution of 3-cloropropanol (1.6 g, 20 mmol) in ddH_2O (20 mL) was added sodium azide (3.9 g, 60 mmol) to react for 12 h at 95 ^oC. The reaction was checked by TLC and the mixture was extracted by H_2O/ CH_2Cl_2 = 1/3 for two times. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil mixture was purified by flash column chromatography to obtain the desired product **26** (1.8 g, 18.25 mmol, 91%, colorless liquid).

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.82-3.71 (m, 2H), 3.46 (t, *J* = 6.5 Hz, 2H), 1.84 (quin, *J* = 6.3 Hz, 2H), 1.46 (br, 1H, (OH)); ^{13}C NMR (75 MHz, $CDCl_3$) δ 60.18, 48.74, 31.68; HRMS (EI) calcd for $C_3H_8ON_3$ $[M + H]^+$, 102.0667; found, 102.0665.

Compound 27

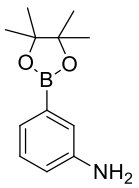


27

To a stirred solution of benzoic acid (1221 mg, 10 mmol) in chlorosulfonic acid (5 mL). The reaction mixture was heated to 100^{o}C and reacted for 12 h. Then, the solvent was removed under reduced pressure. The resulting oil mixture was purified by flash column chromatography to obtain the desired product **27** (1505 mg, 6.82 mmol, 68 %, white solid).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.48 (d, *J* = 7.7 Hz, 1H), 8.30 (d, *J* = 8.2 Hz, 1H), 7.80 (t, *J* = 7.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.17, 145.27, 136.62, 131.84, 131.36, 130.50, 128.99; HRMS (EI) calcd for $C_7H_5O_4Cl$ $[M]^+$, 219.9597; found, 219.9591.

Compound 28



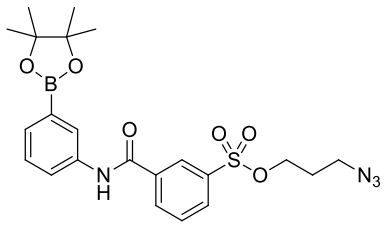
28

To a stirred solution of 3-amino boronic acid (3 g, 20 mmol) in toluene (50 mL) was added pinacol (2.8 mg, 24 mmol) and allowed to reflux in Dean-stark condition for 3 h. The solvent was removed under reduced pressure and purified by column

chromatography to obtain the product **28** (4.2 g, 19.18 mmol, 96 %, pale yellow solid).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24-7.16 (m, 2H), 7.14 (d, *J* = 2.1 Hz, 1H), 6.79 (d, *J* = 7.4 Hz, 1H), 1.34 (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.96, 128.92, 125.14, 121.31, 118.20, 83.88, 25.04; HRMS (ESI-TOF) calcd for $C_{12}H_{19}O_2BN$ $[M + H]^+$, 220.1509; found, 220.1507.

Compound 29

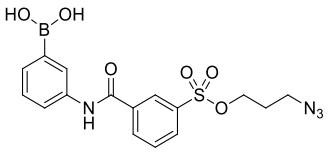


29

To a stirred solution of compound **27** (331 mg, 1.5 mmol) was added thionyl chloride (5 mL). After reacting for 12 h, the solvent was removed under reduced pressure. The resulting mixture was dissolved in CH_2Cl_2 (10 mL) with DIEA (0.52 mL, 3 mmol) and 4 Å molecular sieve (662 mg) in flask A. **28 (**263 mg, 1.2 mmol) was dissolved in CH_2Cl_2 (5 mL) (Flask B) in ice bathe and slowly added to the flask A. After 15 min, the reaction was added DIEA (0.52 mL, 3 mmol), DMAP (92 mg, 0.75 mmol) and **26** (182 mg, 1.8 mmol) to react for 3 h at room temperature. After the reaction completed, the mixture was extracted by 0.5 M HCl /CH_2Cl_2 = 1/3 for two times. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure for further purification by column chromatography to obtain the product **29** (297 mg, 0.61 mmol, 51 %, pale yellow liquid).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (s, 1H), 8.20 (d, *J* = 7.9 Hz, 1H), 8.11-8.04 (m, 2H, NH), 8.00 (d, *J* = 8.3 Hz, 1H), 7.83 (d, *J* = 1.5 Hz, 1H), 7.71 (t, *J* = 7.9 Hz, 1H), 7.62 (d, *J* = 7.2 Hz, 1H), 7.41 (t, *J* = 7.7 Hz, 1H), 4.19 (t, *J* = 5.9 Hz, 2H), 3.40 (t, *J* = 6.4 Hz, 2H), 1.93 (quin, *J* = 6.1 Hz, 2H), 1.34 (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.96, 137.14, 136.51, 136.41, 133.09, 131.45, 130.63, 130.09, 128.72, 126.89, 126.45, 123.85, 84.12, 67.94, 49.29, 28.47, 24.97; HRMS (ESI-TOF) calcd for $C_{22}H_{27}O_6BN_4NaS$ $[M + Na]^+$, 509.1642; found, 509.1641.

Compound BA-s-tosyl-N_3-1

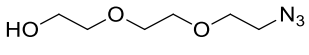


BA-s-tosyl-N_3-1

To a stirred solution of **29** (107 mg, 0.22 mmol) in 50% acetone solution (4.4 mL) was added sodium periodate (106 mg, 0.5 mmol) and ammonium acetate (38 mg, 0.5 mmol) to react at room temperature for 12 h. to the reaction mixture was extracted by brine / EA = 1/3 for two times. The combined organic layers were dried over $MgSO_4$ and concentrated and purified by flash column chromatography to obtain the desired product compound **BA-s-tosyl-N_3-1** (88 mg, 0.22 mmol, 99 %, white solid).

^{1}H NMR (300 MHz, MeOD) δ 8.49 (s, 1H), 8.30 (d, *J* = 7.7 Hz, 1H), 8.12 (d, *J* = 7.9 Hz, 1H), 8.03-7.88 (m, 1H), 7.80 (t, J = 7.9 Hz, 1H), 7.82-7.74 (m, 1H), 7.62-7.31 (m, 2H), 4.20 (t, *J* = 5.9 Hz, 2H), 3.39 (t, *J* = 6.5 Hz, 2H), 1.90 (quin, *J* = 6.2 Hz, 2H); ^{13}C NMR (75 MHz, MeOD) δ 166.63, 138.80, 137.97, 137.85, 134.17, 131.83, 131.63, 131.21, 129.24, 128.30, 124.73, 69.58, 48.52, 29.52; HRMS (ESI-TOF) calcd for $C_{16}H_{17}O_6BN_4NaS$ $[M + Na]^+$, 427.0860; found, 427.0852.

Compound 30

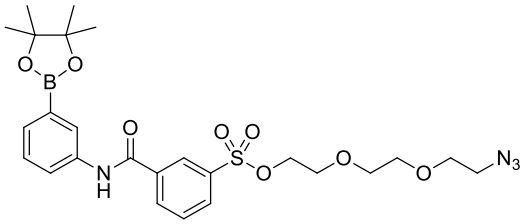


30

To a stirred solution of Trityl-TEG-N_3 in 80% acetic acid solution (5.39 mL) was heated for 1h at 80^{o}C oil bath. The solvent was removed under reduced pressure and the reaction mixture was purified by flash column chromatography to obtain the desired product compound **30** (201 g, 1.15 mmol, 89 %, colorless liquid).

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.74 (t, *J* = 4.1 Hz, 2H), 3.71-3.66 (m, 6H), 3.65-3.59 (m, 2H), 3.40 (t, *J* = 5.1 Hz, 2H), 2.24 (br, 1H, (OH)); ^{13}C NMR (75 MHz, $CDCl_3$) δ 72.72, 70.88, 70.60, 70.25, 61.99, 50.89; HRMS (APCI) calcd for $C_6H_{14}O_3N_3$ $[M + H]^+$, 176.1035; found,176.1029.

Compound 31

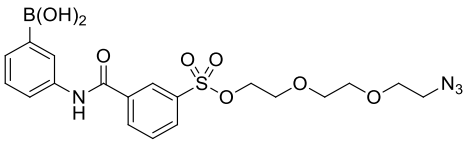


31

To a stirred solution of compound **27** (331 mg, 1.5 mmol) was added thionyl chloride (5 mL). After reacting for 12 h, the solvent was removed under reduced pressure. The resulting mixture was dissolved in CH_2Cl_2 (10 mL) with DIEA (0.52 mL, 3 mmol) and 4 Å molecular sieve (662 mg) in flask A. **28 (**263 mg, 1.2 mmol) was dissolved in CH_2Cl_2 (5 mL) (flask B) in ice bathe and slowly added to the flask A. After 15 min, the reaction was added DIEA (0.39 mL, 2.25 mmol), DMAP (73 mg, 0.60 mmol) and **30** (210 mg, 1.20 mmol) to react for 6 h at room temperature. After the reaction completed, the mixture was extracted by 0.5 M HCl /CH_2Cl_2 = 1/3 for two times. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure for further purification by column chromatography to obtain the product **31** (208 mg, 0.37 mmol, 31 %, pale yellow liquid).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.39 (s, 1H), 8.21 (d, *J* = 7.9 Hz, 1H), 8.13-8.08 (m, 1H), 8.05 (br, 1H, (NH)), 8.01 (d, *J* = 8.5 Hz, 1H), 7.83 (d, *J* = 1.5 Hz, 1H), 7.70 (t, *J* = 7.8 Hz, 1H), 7.62 (d, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 4.27 (t, *J* = 4.4 Hz, 2H), 3.74 (t, *J* = 4.7 Hz, 2H), 3.62 (t, *J* = 4.8 Hz, 2H), 3.59 (s, 4H), 3.35 (t, *J* = 5.1 Hz, 2H), 1.35 (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.89, 137.25, 136.84, 136.46, 133.13, 131.45, 130.86, 130.03, 128.82, 126.78, 126.30, 123.72, 84.18, 70.83, 70.67, 70.07, 68.83, 50.80, 25.06; HRMS (ESI-TOF) calcd for $C_{25}H_{34}O_8BN_4S$ $[M + H]^+$, 561.2146; found, 561.2186.

Compound BA-s-tosyl-N_3-2



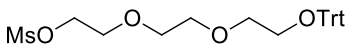
BA-s-tosyl-N_3-2

To a stirred solution of **31** (126 mg, 0.23 mmol) in 50% acetone solution (4.5 mL) was added sodium periodate (108 mg, 0.51 mmol) and ammonium acetate (39 mg,

0.51 mmol) to react at room temperature for 12 h. To the reaction mixture was extracted by brine / EA = 1/3 for two times. The combined organic layers were dried over $MgSO_4$ and concentrated and purified by flash column chromatography to obtain the desired product compound **BA-s-tosyl-N_3-2** (102 mg, 0.21 mmol, 95 %, pale yellow oil).

^{1}H NMR (300 MHz, MeOD) δ 8.49 (s, 1H), 8.29 (d, *J* = 7.7 Hz, 1H), 8.12 (d, *J* = 7.9 Hz, 1H), 8.03-7.89 (m, 1H), 7.84-7.73 (m, 2H), 7.62-7.32 (m, 2H), 4.26 (t, *J* = 4.1 Hz, 2H), 3.70 (t, *J* = 4.4 Hz, 2H), 3.60 (t, *J* = 4.8 Hz, 2H), 3.55 (s, 4H), 3.34-3.28 (m, 2H,); ^{13}C NMR (75 MHz, MeOD) δ 166.49, 138.73, 138.02, 137.67, 134.05, 131.84, 131.49, 131.07, 129.20, 128.20, 127.90, 124.44, 71.61, 71.40, 71.08, 69.75, 51.72; HRMS (ESI-TOF) calcd for $C_{19}H_{23}O_8BN_4NaS$ $[M + Na]^+$, 501.1227; found, 501.1236.

Compound 32

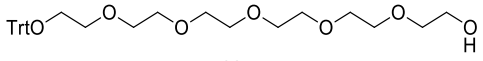


32

To a stirred solution of **11** (1.5 g, 3.97 mmol) was added DIEA (2.08 mL, 11.92 mmol) and methanesulfonyl chloride (0.46 g, 5.96 mmol) in THF (17 mL). The reaction was stirred in 0^{o}C for 1h. Checked by TLC to indicate the reaction completed and removed THF under reduced pressure. The mixture was concentrated and purified by flash column chromatography to obtain the desired product compound **32** (1.7 g, 3.64 mmol, 92 %, pale white solid).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49-7.42 (m, 6H), 7.34-7.27 (m, 6H), 7.25-7.18 (m, 3H), 4.40-4.33 (m, 2H), 3.82-3.75 (m, 2H), 3.71-3.63 (m, 6H), 3.24 (t, *J* = 5.2 Hz, 2H), 2.96 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.27, 128.92, 128.00, 127.21, 86.82, 70.95, 69.44, 69.63, 63.53, 37.85; HRMS (ESI-TOF) calcd for $C_{26}H_{30}O_6NaS$ $[M + Na]^+$, 493.1661; found, 493.1648.

Compound 33

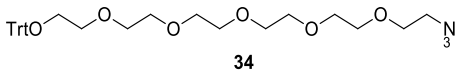


33

To a stirred solution of triethylene glycol (1.54 g, 11.46 mmol) and potassium ter-Butyl alcohol (803 g, 7.16 mmol) in oil bath to reflux. After that 30 min, added **32** (1.35 g, 2.86 mmol) to react for 30 min. Checked by TLC to indicate the reaction complete and extracted by brine / EA = 1/3 for two times. The combined organic solution was dried over by $MgSO_4$. Concentrated in vacuum and purified by column chromatography to obtain the product **33** (1.1 g, 2.19 mmol, 77 %, pale yellow liquid).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49-7.42 (m, 6H), 7.33-7.26 (m, 6H), 7.25-7.18 (m, 3H), 3.73-3.62 (m, 20H), 3.61-3.56 (m, 2H), 3.23 (t, *J* = 5.3 Hz, 2H), 2.80 (br, 1H, (OH)); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.37, 128.95, 127.96, 127.13, 86.76, 72.80, 70.90, 70.81, 70.51, 63.56, 61.95; HRMS (ESI-TOF) calcd for $C_{31}H_{40}O_7Na$ [M + Na]$^+$, 547.2672; found, 547.2675.

Compound 34

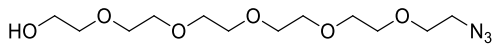


34

To a stirred solution of **33** (2.4 g, 4.53 mmol) in THF (15 mL) was added DIEA (2.37 mL, 13.60 mmol) and methanesulfonyl chloride (0.53 g, 6.80 mmol) to dissolve in solution of THF (4.53 mL). The reaction was reacted at 0^{o}C for 1h. Checked by TLC to indicate the reaction complete. Removed THF under reduced pressure and added DMF (9.07 mL) as a solvent with sodium azide (884 mg, 13.60 mmol) to react for 12 h at 90 ^{o}C. Extracted by H_2O /CH_2Cl_2 = 1/3 for two times and combined organic solution was dried over by $MgSO_4$. Concentrated in vacuum and purified by column chromatography to obtain the product **34** (2.1 g, 3.88 mmol, 86 %, pale yellow liquid).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.4 Hz, 6H), 7.34-7.26 (m, 6H), 7.25-7.18 (m, 3H), 3.71-3.61 (m, 20H), 3.36 (t, *J* = 5.1 Hz, 2H), 3.23 (t, *J* = 5.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.34, 128.93, 127.95, 127.12, 86.75, 70.99, 70.88, 70.82, 70.21, 63.54, 50.88; HRMS (ESI-TOF) calcd for $C_{31}H_{39}O_6N_3Na$ [M + Na]$^+$, 572.2737; found, 572.2736.

Compound 35

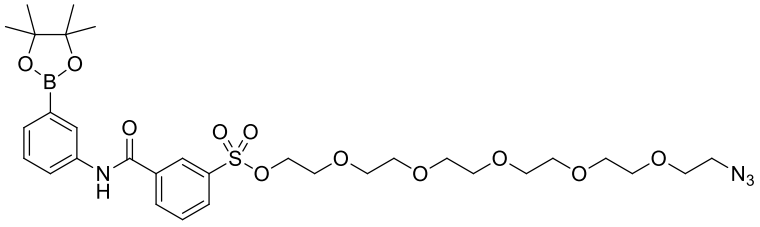


35

To a stirred solution of **34** (222 mg, 0.4 mmol) in 80% acetic acid solution (2.2 mL). The reaction was heated at 80 ^{o}C for 1 h. Checked by TLC to indicate the reaction complete. Removed solution under reduced pressure and concentrated in vacuum. Purified by column chromatography to obtain the product **35** (114 g, 0.37 mmol, 92 %, pale yellow liquid).

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.77-3.64 (m, 20H), 3.63-3.57 (m, 2H), 3.39 (t, *J* = 5.1 Hz, 2H), 2.82 (br, 1H, (OH)); ^{13}C NMR (75 MHz, $CDCl_3$) δ 72.86, 70.86, 70.78, 70.52, 70.24, 61.96, 50.93; HRMS (ESI-TOF) calcd for $C_{12}H_{25}O_6N_3Na$ $[M + Na]^+$, 330.1641; found, 330.1642.

Compound 36



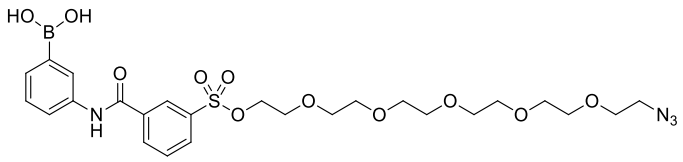
36

To a stirred solution of compound **27** (331 mg, 1.5 mmol) was added thionyl chloride (5 mL). After reacting for 12 h, the solvent was removed under reduced pressure. The resulting mixture was dissolved in CH_2Cl_2 (10 mL) with DIEA (0.52 mL, 3 mmol) and 4 Å molecular sieve (662 mg) in flask A. **28 (**263 mg, 1.2 mmol) was dissolved in CH_2Cl_2 (5 mL) (flask B) in ice bathe and slowly added to the flask A. After 15 min, the reaction was added DIEA (0.39 mL, 2.25 mmol), DMAP (73 mg, 0.60 mmol) and **35** (369 mg, 1.2 mmol) to react for 6 h at room temperature. After the reaction completed, the mixture was extracted by 0.5 M HCl /CH_2Cl_2 = 1/3 for two times. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure for further purification by column chromatography to obtain the product **36** (266 mg, 0.38 mmol, 32 %, pale yellow liquid).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.65 (br, 1H, (NH)), 8.54 (s, 1H), 8.30 (d, *J* = 7.7 Hz, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 7.96 (s, 1H), 7.70 (t, *J* = 7.8 Hz, 1H), 7.60 (d, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.7 Hz, 1H), 4.27 (t, *J* = 4.5 Hz, 2H), 3.73-3.47 (m, 20H), 3.29 (t, *J* = 5.2 Hz, 2H), 1.35 (s, 12H); ^{13}C NMR (75 MHz,

$CDCl_3$) δ 163.87, 137.59, 136.84, 136.54, 133.47, 131.25, 131.00, 129.84, 128.72, 127.06, 126.50, 123.83, 84.12, 70.74, 70.69, 70.53, 70.16, 70.09, 68.63, 50.79, 25.11; HRMS (ESI-TOF) calcd for $C_{31}H_{45}O_{11}BN_4NaS$ $[M + Na]^+$, 715.2796; found, 715.2793.

Compound BA-s-tosyl-N_3-3

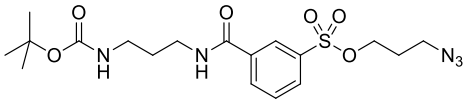


BA-s-tosyl-N_3-3

To a stirred solution of **36** (149 mg, 0.22 mmol) in 50% acetone solution (4.3 mL) was added sodium periodate (104 mg, 0.48 mmol) and ammonium acetate (37 mg, 0.48 mmol) to react at room temperature for 12 h. To the reaction mixture was extracted by brine / EA = 1/3 for two times. The combined organic layers were dried over $MgSO_4$ and concentrated and purified by flash column chromatography to obtain the desired product compound **BA-s-tosyl-N_3-3** (129 mg, 0.21 mmol, 98 %, pale yellow oil).

^{1}H NMR (300 MHz, MeOD) δ 8.50 (s, 1H), 8.33-8.26 (m, 1H), 8.16-8.09 (m, 1H,), 8.04-7.91 (m, 1H), 7.84-7.73 (m, 2H), 7.62-7.32 (m, 2H), 4.29-4.22 (m, 2H), 3.68 (t, *J* = 4.5 Hz, 2H), 3.65-3.58 (m, 10H), 3.58-3.54 (m, 4H), 3.54-3.51 (m, 4H), 3.36-3.31 (m, 2H); ^{13}C NMR (75 MHz, MeOD) δ 166.47, 138.85, 138.12, 137.76, 134.17, 131.94, 131.51, 131.13, 129.23, 128.25, 127.97, 124.54, 71.70, 71.56, 71.09, 69.73, 51.80; HRMS (ESI-TOF) calcd for $C_{25}H_{35}O_{11}BN_4NaS$ $[M + Na]^+$, 633.2014; found, 633.2021.

Compound 37



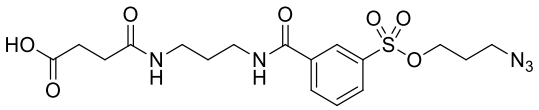
37

To a stirred solution of compound **27** (552 mg, 2.5 mmol) was added thionyl chloride (8 mL). After reacting for 12 h, the solvent was removed under reduced pressure. The resulting mixture was dissolved in CH_2Cl_2 (18 mL) with DIEA (0.87 mL, 5 mmol) and 4 Å molecular sieve (1104 mg) in flask A. **15 (**349 mg, 2 mmol) was dissolved

in CH_2Cl_2 (7 mL) (flask B) in ice bathe and slowly added to the flask A. After 15 min, the reaction was added DIEA (0.87 mL, 5 mmol), DMAP (122 mg, 1 mmol) and **26** (526 mg, 3 mmol) to react for 4 h at room temperature. After the reaction completed, the mixture was extracted by 0.5 M HCl /CH_2Cl_2 = 1/3 for two times. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure for further purification by column chromatography to obtain the product **37** (586 mg, 1.33 mmol, 66 %, pale yellow liquid).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.43 (s, 1H), 8.19 (d, *J* = 7.8 Hz, 1H), 8.07-7.99 (m, 1H), 7.75 (br, 1H, (NH)), 7.67 (t, *J* = 7.8 Hz, 1H), 4.85 (br, 1H, (NH)), 4.18 (t, *J* = 5.9 Hz, 2H), 3.53 (q, *J* = 6.1 Hz, 2H), 3.39 (t, *J* = 6.5 Hz, 2H), 3.27 (q, *J* = 6.4 Hz, 2H), 1.91 (quin, *J* = 6.3 Hz, 2H), 1.73 (quin, *J* = 6.2 Hz, 2H), 1.46 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.34, 157.01, 136.10, 135.95, 132.47, 130.07, 129.67, 126.55, 79.39, 67.72, 47.10, 37.07, 36.45, 29.71, 28.27; HRMS (ESI-TOF) calcd for $C_{18}H_{27}O_6N_5NaS$ $[M + Na]^+$, 464.1580; found, 464.1581.

Compound 38



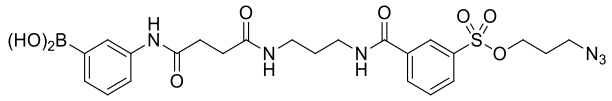
38

To a stirred solution of **37** (535 mg, 1.21 mmol) in CH_2Cl_2 (20 mL) was added with trifluoroacetic acid (3 mL) for 1 h. CH_2Cl_2 and trifluoroacetic acid were removed by reduced pressure. After that, added DMF (24.24 mL), succinic anhydride (134 mg, 1.33 mmol) and DIEA (1.06 mL, 6.06 mmol) to react for 1h at room temperature. Checked by TLC to indicate the reaction complete. Extracted by1M HCl / EA = 1/3 for two times and extracted again by 1M NaOH/EA = 1/1 to make product dissolve in water. The solution was adjusted to pH 1 with HCl. Then the mixture was extracted with 1M HCl/ EA =1/1. Combined organic solution and dried over by $MgSO_4$. Concentrated in vacuum and purified by column chromatography to obtain the product. **38** (237 mg, 0.54 mmol, 44 %, pale yellow liquid).

^{1}H NMR (300 MHz, MeOD) δ 8.38 (s, 1H), 8.19 (d, *J* = 7.7 Hz, 1H), 8.09 (d, *J* = 7.9 Hz, 1H), 7.76 (t, *J* = 7.9Hz, 1H), 4.18 (t, *J* = 5.9 Hz, 2H), 3.45 (t, *J* = 6.7 Hz, 2H), 3.38 (t, *J* = 6.5 Hz, 2H), 3.31-3.24 (m, 2H), 2.61 (t, *J* = 6.8 Hz, 2H), 2.48 (t, *J* = 6.5 Hz, 2H), 1.89 (quin, *J* = 6.2 Hz, 2H), 1.81 (quin, *J* = 6.8 Hz, 2H); ^{13}C NMR (75 MHz,

MeOD) δ 176.38, 174.85, 167.86, 137.84, 137.16, 133.77, 131.66, 131.18 , 127.89, 69.57 , 48.47, 38.59, 37.92, 31.70, 30.40, 30.13, 29.46 ; HRMS (ESI-TOF) calcd for $C_{17}H_{22}O_7N_5S$ $[M - H]^+$, 440.1240; found, 440.1249.

Compound BA-m-tosyl-N_3-1

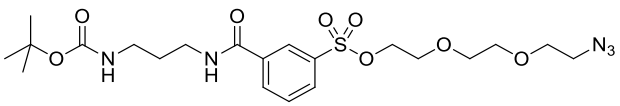


BA-m-tosyl-N_3-1

To a stirred solution of compound **38** (121 mg, 0.27 mmol) in DMF (5.48 mL) was added 3-aminophenylboronic acid (47 mg, 0.30 mmol) and HBTU (156 mg, 0.41 mmol) in the presence of DIEA (100 μl, 0.55mmol). After reacting for 1 h at room temperature, the reaction mixture was quenched with H_2O (3 mL), the crude mixture was extraction by CH_2Cl_2/H_2O = 10/3 twice. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil mixture was purified by flash column chromatography to obtain the desired product **BA-m-tosyl-N_3-1** (98mg, 0.18 mmol, 64 %, pale yellow liquid).

^{1}H NMR (300 MHz, MeOD) δ 8.40-8.35 (m, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 8.09-8.02 (m, 1H), 7.83-7.72 (m, 1H), 7.71 (t, *J* = 7.9 Hz, 1H), 7.63-7.52 (m, 1H), 7.50-7.18 (m, 2H), 4.14 (t, *J* = 5.9 Hz, 2H), 3.45 (t, *J* = 6.7 Hz, 2H), 3.38-3.32 (m, 2H), 3.30-3.25 (m, 2H), 2.71 (t, *J* = 6.7 Hz, 2H), 2.58 (t, *J* = 6.5 Hz, 2H), 1.91-1.76 (m, 4H); ^{13}C NMR (75 MHz, MeOD) δ 175.05, 173.14, 167.86, 138.97, 137.7, 137.05, 133.73, 131.59, 131.14, 130.56, 129.07, 127.86, 126.74, 123.2, 69.54, 48.41, 38.57, 37.92, 33.06, 32.13, 30.02, 29.38; HRMS (ESI-TOF) calcd for $C_{23}H_{29}O_8BN_6NaS$ $[M + Na]^+$, 583.1758; found, 583.1754.

Compound 39



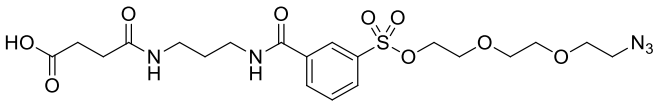
39

To a stirred solution of compound **27** (552 mg, 2.5 mmol) was added thionyl chloride (8 mL). After reacting for 12 h, the solvent was removed under reduced pressure. The resulting mixture was dissolved in CH_2Cl_2 (7 mL) with DIEA (0.87 mL, 5 mmol) and

4 Å molecular sieve (1104 mg) in flask A. **15 (**349 mg, 2 mmol) was dissolved in CH_2Cl_2 (7 mL) (flask B) in ice bathe and slowly added to the flask A. After 15 min, the reaction was added DIEA (0.87 mL, 5 mmol), DMAP (122 mg, 1 mmol) and **30** (526 mg, 3 mmol) to react for 4 h at room temperature. After the reaction completed, the mixture was extracted by 0.5 M HCl /CH_2Cl_2 = 1/3 for two times. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure for further purification by column chromatography to obtain the product **39** (586 mg, 1.33 mmol, 56 %, pale yellow liquid).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.42 (s, 1H), 8.16 (d, *J* = 7.9 Hz, 1H), 8.08-8.01 (m, 1H), 7.64 (t, *J* = 7.8 Hz, 1H), 7.58 (br, 1H, (NH)), 4.83 (br, 1H, (NH)), 4.25 (t, *J* = 4.6 Hz, 2H), 3.72 (t, *J* = 4.9 Hz, 2H), 3.64 (t, *J* = 4.8 Hz, 2H), 3.59 (s, 1H), 3.53 (q, *J* = 6.1 Hz, 2H), 3.36 (t, *J* = 5.1 Hz, 2H), 3.26 (q, *J* = 6.4 Hz, 2H), 1.74 (quin, *J* = 6.3 Hz, 2H), 1.46 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.48, 157.14, 136.55, 136.00, 132.51, 130.32, 129.68, 126.67, 79.67, 70.73, 70.56, 70.04, 69.94, 68.71, 50.68, 37.18, 36.50, 29.93, 28.43; HRMS (ESI-TOF) calcd for $C_{21}H_{33}O_8N_5NaS$ $[M + Na]^+$, 538.1948; found, 538.1958.

Compound 40

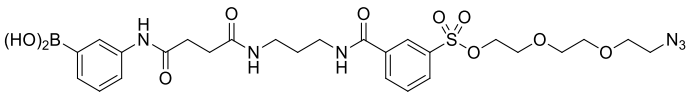


40

To a stirred solution of **39** (577 mg, 1.12 mmol) in CH_2Cl_2 (10 mL) was added with trifluoroacetic acid (5 mL) for 1 h. CH_2Cl_2 and trifluoroacetic acid were removed by reduced pressure. After that, added DMF (22.40 mL), succinic anhydride (123 mg, 1.23 mmol) and DIEA (0.98 mL, 5.60 mmol) to react for 1h at room temperature. Checked by TLC to indicate the reaction complete. Extracted by 1M HCl / EA = 1/3 for two times and extracted again by 1M NaOH/EA = 1/1 to make product dissolve in water. The solution was adjusted to pH 1 with HCl. Then the mixture was extracted with 1M HCl/ EA =1/1. Combined organic solution and dried over by $MgSO_4$. Concentrated in vacuum and purified by column chromatography to obtain the product. **40** (284 mg, 0.55 mmol, 49 %, pale yellow liquid).

^{1}H NMR (300 MHz, MeOD) δ 8.40-8.36 (m, 1H), 8.18 (dt, *J* = 8.1, 1.3 Hz, 1H), 8.08 (dt, *J* = 8.5, 1.1 Hz, 1H), 7.75 (t, *J* = 7.8 Hz, 1H,), 4.26-4.21 (m, 2H), 3.68 (t, *J* = 4.4 Hz, 2H), 3.61 (t, *J* = 4.7 Hz, 2H), 3.55 (s, 4H), 3.45 (t, *J* = 6.7 Hz, 2H), 3.36-3.32 (m, 2H), 3.30-3.24 (m, 2H), 2.61 (t, *J* = 6.2 Hz, 2H), 2.48 (t, *J* = 6.2 Hz, 2H), 1.81 (quin, *J* = 6.8 Hz, 2H); ^{13}C NMR (75 MHz, MeOD) δ 176.46, 174.96, 168.04, 138.35, 137.23, 133.70, 131.82, 131.12, 128.01, 71.79, 71.69, 71.61, 71.30, 69.92, 51.90, 38.64, 37.98, 31.79, 30.47, 30.27; HRMS (ESI-TOF) calcd for $C_{20}H_{29}O_9N_5NaS$ $[M + Na]^+$, 538.1584; found, 538.1588.

Compound BA-m-tosyl-N_3-2

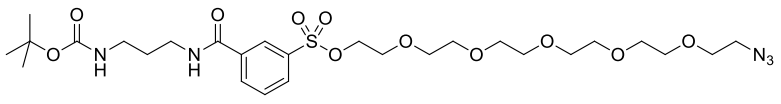


BA-m-tosyl-N_3-2

To a stirred solution of compound **40** (258 mg, 0.50 mmol) in DMF (10 mL) was added 3-aminophenylboronic acid (85 mg, 0.55 mmol) and HBTU (285 mg, 0.75 mmol) in the presence of DIEA (170 μl, 0.11mmol). After reacting for 2 h at room temperature, the reaction mixture was quenched with H_2O (3 mL), the crude mixture was extraction by CH_2Cl_2/H_2O = 10/3 twice. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil mixture was purified by flash column chromatography to obtain the desired product. **BA-m-tosyl-N_3-2** (291 mg, 0.46 mmol, 92 %, pale yellow liquid).

^{1}H NMR (300 MHz, MeOD) δ 8.37 (s, 1H), 8.15 (d, *J* = 7.7 Hz, 1H), 8.15 (d, *J* = 7.9 Hz, 1H), 7.76 (s, 1H), 7.70 (t, *J* = 7.8 Hz, 1H), 7.58 (d, *J* = 7.6 Hz, 1H), 7.46-7.31 (m, 1H), 7.25 (t, *J* = 7.7 Hz, 2H), 4.23-4.17 (m, 2H), 3.65 (t, *J* = 4.5 Hz, 2H), 3.59 (t, *J* = 4.7 Hz, 2H), 3.52 (s, 4H), 3.44 (t, *J* = 6.9 Hz, 2H), 3.38-3.32 (m, 2H), 3.30-3.25 (m, 2H), 2.71 (t, *J* = 6.8 Hz, 2H), 2.58 (t, *J* = 6.4 Hz, 2H), 1.81 (quin, *J* = 6.6 Hz, 2H); ^{13}C NMR (75 MHz, MeOD) δ 175.07, 173.10, 167.78, 138.86, 137.81, 136.85, 133.56, 131.59, 131.01, 130.61, 129.06, 127.80, 126.66, 123.26, 71.55, 71.44, 71.26, 70.94, 69.59, 51.62, 38.50, 37.93, 32.96, 31.99, 29.94 ; HRMS (ESI-TOF) calcd for $C_{26}H_{35}O_{10}BN_6NaS$ $[M + Na]^+$, 657.2126; found, 657.2125.

Compound 41

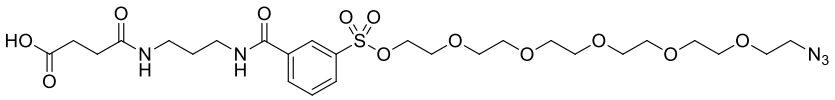


41

To a stirred solution of compound **27** (331 mg, 1.5 mmol) was added thionyl chloride (5 mL). After reacting for 12 h, the solvent was removed under reduced pressure. The resulting mixture was dissolved in CH_2Cl_2 (18 mL) with DIEA (0.52 mL, 3 mmol) and 4 Å molecular sieve (662 mg) in flask A. **15 (**209 mg, 1.2 mmol) was dissolved in CH_2Cl_2 (5 mL) (flask B) in ice bathe and slowly added to the flask A. After 15 min, the reaction was added DIEA (0.52 mL, 3 mmol), DMAP (73 mg, 0.6 mmol) and **35** (533 mg, 1.8 mmol) to react for 4 h at room temperature. After the reaction completed, the mixture was extracted by 0.5 M HCl /CH_2Cl_2 = 1/3 for two times. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure for further purification by column chromatography to obtain the product. **41** (438 mg, 0.68 mmol, 56 %, pale yellow liquid).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.43 (s, 1H), 8.19 (d, *J* = 7.8 Hz, 1H), 8.04 (d, *J* = 7.9 Hz, 1H), 7.76 (br, 1H), 7.64 (t, *J* = 7.8 Hz, 1H), 4.96 (br, 1H, (NH)), 4.23 (t, *J* = 4.6 Hz, 2H), 3.69 (t, *J* = 4.7 Hz, 2H), 3.66-3.57 (m, 20H), 3.37 (t, *J* = 5.1 Hz, 2H), 3.24 (q, *J* = 6.2 Hz, 2H), 1.79-1.69 (m, 2H), 1.45 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.48, 157.04, 136.53, 135.96, 132.69, 130.37, 129.63, 126.60, 79.58, 70.64, 70.55, 70.42, 70.00, 69.90, 68.59, 50.70, 37.22, 36.55, 29.93 , 28.45; HRMS (ESI-TOF) calcd for $C_{27}H_{45}O_{11}N_5NaS$ $[M + Na]^+$, 670.2734; found, 670.2743.

Compound 42

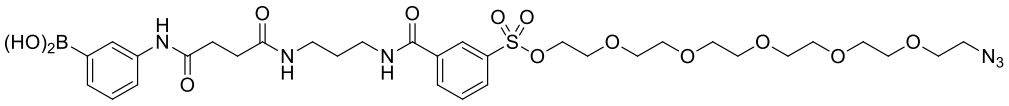


42

To a stirred solution of **41** (345 mg, 0.53 mmol) in CH_2Cl_2 (6 mL) was added with trifluoroacetic acid (5 mL) for 1 h. CH_2Cl_2 and trifluoroacetic acid were removed by reduced pressure. After that, added DMF (10 mL), succinic anhydride (59 mg, 0.57 mmol) and DIEA (0.46 mL, 2.67 mmol) to react for 1h at room temperature. Checked by TLC to indicate the reaction complete. Extracted organic layer by1M HCl / EA = 1/3 for two times and 1M NaOH/EA = 1/1 to make product dissolve in water. The solution was adjusted to pH 1 with HCl. Then the mixture was extracted with 1M HCl/ EA =1/1. Combined organic solution and dried over by $MgSO_4$. Concentrated in vacuum and purified by column chromatography to obtain the product. **42** (186 mg, 0.29 mmol, 54 %, pale yellow liquid).

^{1}H NMR (300 MHz, MeOD) δ 8.38 (s, 1H), 8.19 (d, *J* = 7.9 Hz, 1H), 8.08 (d, *J* = 8.1 Hz, 1H), 7.75 (t, *J*= 7.8 Hz, 1H), 4.27-4.20 (m, 2H), 3.67 (t, *J* = 4.9 Hz, 2H), 3.65-3.56 (m, 14H), 3.54 (s, 4H), 3.49-3.41 (m, 2H), 3.36 (t, *J* = 4.9 Hz, 2H), 3.31-3.24 (m, 2H), 2.61 (t, *J* = 6.2 Hz, 2H), 2.49 (t, *J* = 6.2 Hz, 2H), 1.81 (quin, *J* = 6.8 Hz, 2H); ^{13}C NMR (75 MHz, MeOD) δ 176.34, 174.89, 167.96 , 138.27, 137.17, 133.74, 131.84 , 131.15, 127.99, 71.72, 71.65, 71.21, 69.83, 51.90, 38.65, 37.99, 31.75, 30.41, 30.27; HRMS (ESI-TOF) calcd for $C_{26}H_{41}O_{12}N_5NaS$ $[M + Na]^+$, 670.2370; found, 670.2363.

Compound BA-m-tosyl-N_3-3

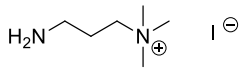


BA-m-tosyl-N_3-3

To a stirred solution of compound **42** (182 mg, 0.28 mmol) in DMF (5.62 mL) was added 3-aminophenylboronic acid (48 mg, 0.31 mmol) and HBTU (160 mg, 0.42 mmol) in the presence of DIEA (100 μl, 0.56mmol). After reacting for 2 h at room temperature, the reaction mixture was quenched with H_2O (3 mL), the crude mixture was extracted by CH_2Cl_2/H_2O = 10/3 twice. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The resulting oil mixture was purified by flash column chromatography to obtain the desired product **BA-m-tosyl-N_3-3** (151 mg, 0.20 mmol, 70 %, pale yellow liquid).

^{1}H NMR (300 MHz, MeOD) δ 8.38 (s, 1H), 8.16 (d, *J* = 7.8 Hz, 1H, 8.09-8.02 (m, 1H), 7.83-7.71 (m, 1H), 7.71 (t, *J* = 7.7 Hz, 1H), 7.57 (d, *J* = 6.3 Hz, 1H), 7.49-7.21 (m, 2H), 4.21 (t, *J* = 4.3 Hz, 2H), 3.67-3.56 (m, 16H), 3.52 (s, 4H), 3.45 (t, *J* = 6.8 Hz, 2H), 3.38-3.33 (m, 2H), 3.31-3.26 (m, 2H), 2.71 (t, *J* = 6.7 Hz, 2H), 2.58 (t, *J* = 6.6 Hz, 2H), 1.82 (quin, *J* = 6.6 Hz, 2H); ^{13}C NMR (75 MHz, MeOD) δ 174.99, 173.04, 167.81, 139.00, 137.95, 137.00, 133.69, 131.70, 131.13, 130.63, 129.03, 127.90, 126.81 , 123.40, 71.64, 71.44, 70.98, 69.66, 51.76, 38.60, 37.95, 33.06, 32.12, 30.09; HRMS (ESI-TOF) calcd for $C_{32}H_{47}O_{13}BN_6NaS$ $[M + Na]^+$, 789.2913; found, 789.2906.

Compound 43

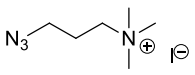


43

To a stirred solution of compound **8** (400 mg, 2.3 mmol) in ACN (11.5mL) was added DIEA (297mg, 2.3 mmol) and iodomethane (1304 mg, 9.19 mmol). The reaction mixture was heated at 70 ℃ for 16 h under nitrogen atmosphere. ACN was removed under reduced pressure. The crude mixture was extracted by H_2O/CH_2Cl_2 = 1/2 for three times. The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. After that, the crude mixture was directly added trifluoroacetic acid (9.7mL) and H_2O (0.3mL) to react for 4h. Concentrated in vacuum and purified by column chromatography to obtain the product. **43** (290 mg, 1.19 mmol, 52%, pale yellow oil).

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.53-3.44(m, 2H), 3.19 (s, 9H), 3.06(t, *J* = 7.5 Hz 2H), 2.25-2.12 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 64.5, 54.0, 37.7, 22.6; HRMS (ESI) calcd for $C_6H_{17}IN_2$ $[M + I]^-$, 370.9481; found, 370.9473.

Compound azido choline

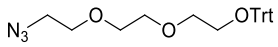


azido choline

A 100 mL round bottom flask was charged with 3-azidopropan-1-amine (200 mg, 0.74 mmol) and ethyl acetate (25mL). Followed by addition of K_2CO_3 (149mg, 2.3 mmol) and iodomethane (652 mg, 9.19 mmol). The mixture were stirred vigorously for 18 h. The mixture was filtered by vacuum using a course sintered funnel and washed with ethyl acetate (20mL) for two times. The solid was dissolved in ethanol and gravity filtered to separate excess K_2CO_3. The solvent was evaporated and solid was again dissolved in ethanol. Filtered ethanol and removed by rotary evaporation to give analytically pure **azido choline** (189 mg, 0.56 mmol, 70%, white fluffy powders).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.85-3.73 (m, 4H), 3.49 (s, 9H), 2.45-2.38 (m, 2H);
^{13}C NMR (75 MHz, $CDCl_3$) δ 65.19, 54.22, 48.72, 23.53; HR-ESI calcd for $C_6H_{15}N_4$ $[M - I]^+$, 143.1297; found, 143.1302

Compound Trityl-TEG-azide

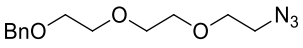


Trityl-TEG-azide

To a stirred solution of **11** (1.6 g, 3.97mmol) was added DIEA (2.08 mL, 11.92 mmol) and methanesulfonyl chloride (0.46 g, 5.96 mmol) in THF (17 mL). The reaction was stirred in 0^{o}C for 1h. Checked by TLC to indicate the reaction complete. Removed THF under reduced pressure. The mixture was added DMF (7.94 mL) and sodium azide (775 mg, 11.92 mmol) to react for 12 h at 90 ^{o}C oil bath. After, checked by TLC and the mixture was extracted with H_2O /CH_2Cl_2 = 1/3 for two times. Combined organic layer and dried over by $MgSO_4$. To concentrate in vacuum and purified by column chromatography to obtain the product **Trityl-TEG-azide** (1.6 g, 3.83 mmol, 96 %, pale yellow liquid).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51-7.42 (m, 6H), 7.34-7.26 (m, 6H), 7.25-7.18 (m, 3H), 3.74-3.65 (m, 8H), 3.38 (t, *J* = 5.1 Hz, 2H), 3.25 (t, *J* = 5.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.27, 128.86, 127.90, 127.08, 86.71, 71.02, 70.93, 70.22, 63.50, 50.86; HRMS (ESI-TOF) calcd for $C_{25}H_{27}O_3N_3Na$ $[M + Na]^+$, 440.1950; found, 440.1942.

Compound Benzyl-TEG-N_3



Benzyl-TEG-N_3

To a stirred solution of **31** (150 mg, 0.85 mmol) in CH_2Cl_2 (6 mL) was added NaH (2.08 mL, 11.92 mmol) to react 5 min. Then, added benzyl bromide (163 mg, 0.97 mmol) to react for 4 h. Checked by TLC to indicate the reaction complete. The mixture was extracted with H_2O /CH_2Cl_2 = 1/3 for two times. Combined organic layer and dried over by $MgSO_4$. To concentrate in vacuum and purified by column chromatography to obtain the product **Benzyl-TEG-N_3** (190 mg, 0.71 mmol, 83 %, white gel).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.27 (m, 5H), 4.57 (s, 2H), 3.71-3.62 (m, 12H), 3.38 (t, *J* = 4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.74, 128.51, 127.89, 127.76, 73.39,71.52, 70.857, 70.19, 69.59, 50.83, 42.88; HRMS ESI calcd for $C_{13}H_{19}N_3O_3Na$ $[M + Na]^+$, 288.1324; found, 288.1328

III. ^{1}H & ^{13}C NMR Spectra

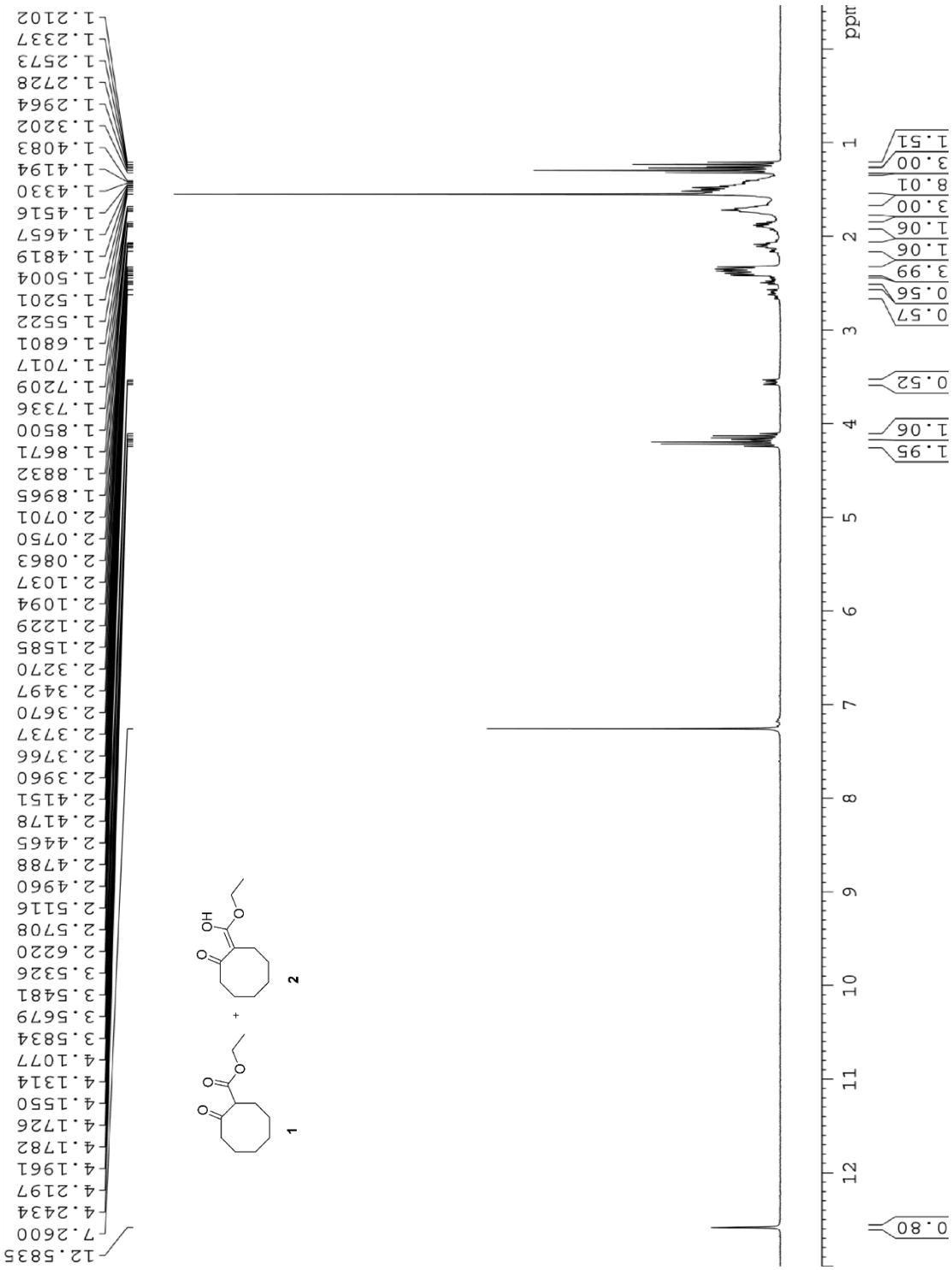


Figure S6. ^{1}H NMR spectrum of Compound **1,2** in $CDCl_3$.

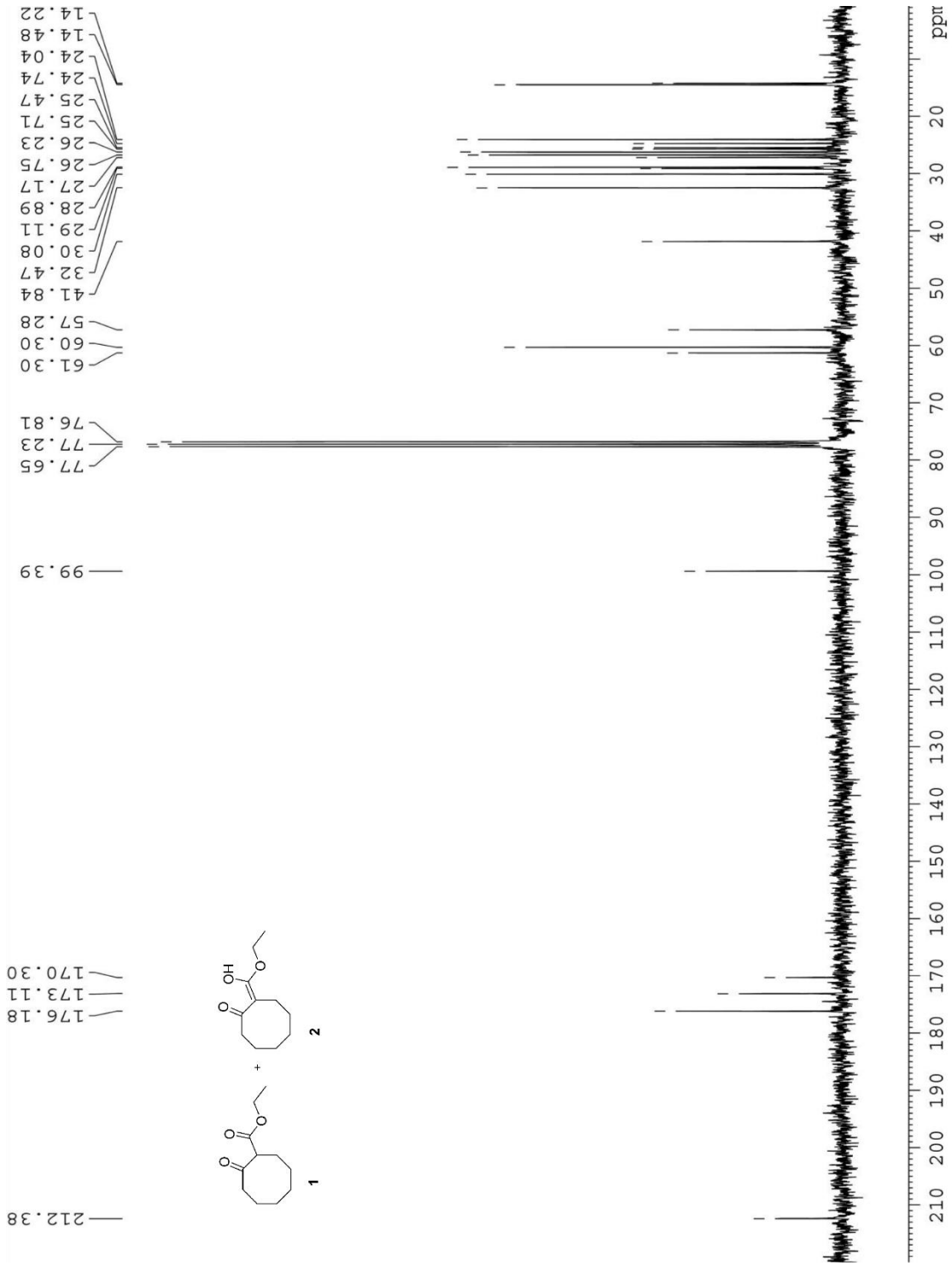


Figure S7. ^{13}C NMR spectrum of Compound **1,2** in $CDCl_3$.

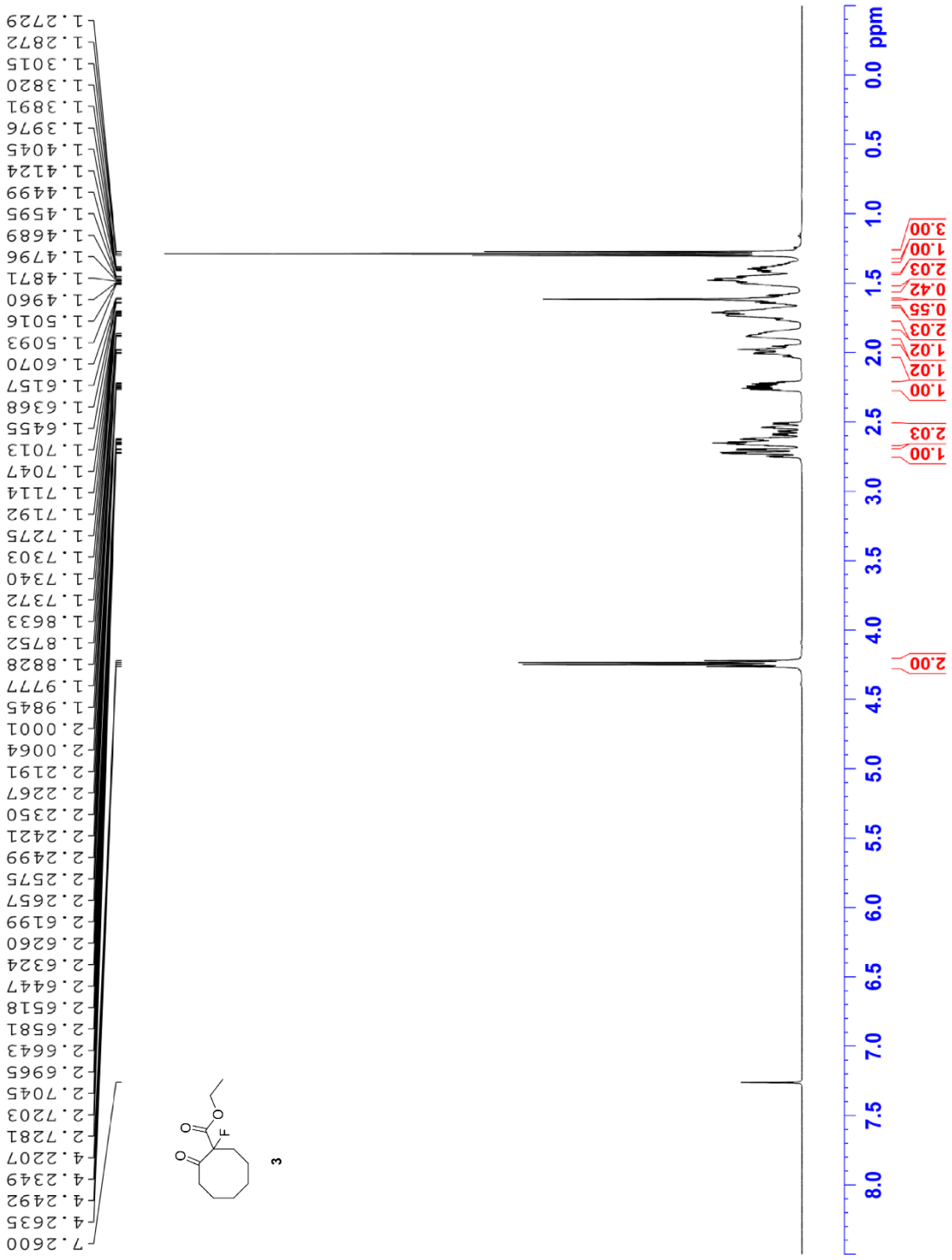


Figure S8. ^{1}H NMR spectrum of Compound **3** in $CDCl_3$.

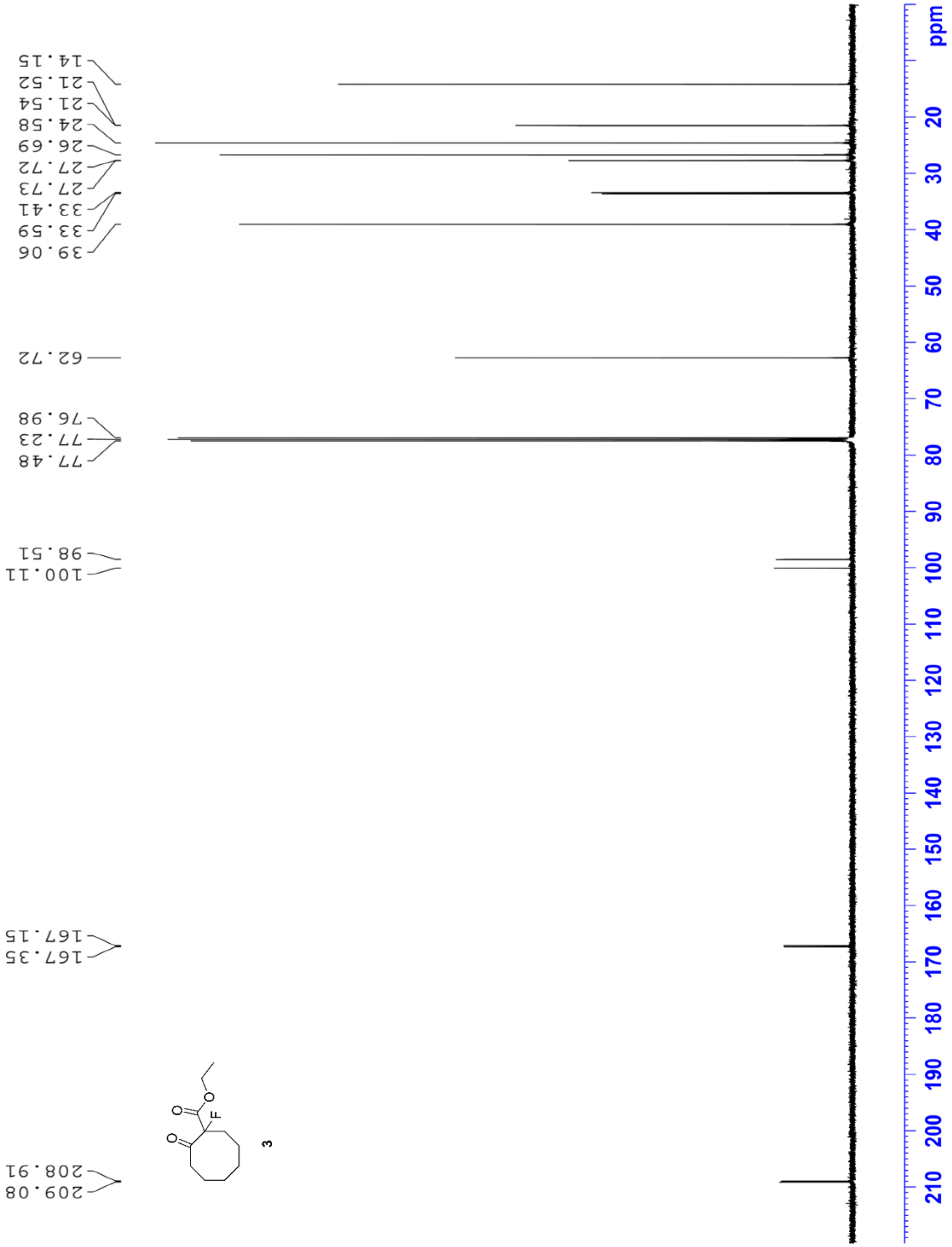


Figure S9. ^{13}C NMR spectrum of Compound **3** in $CDCl_3$

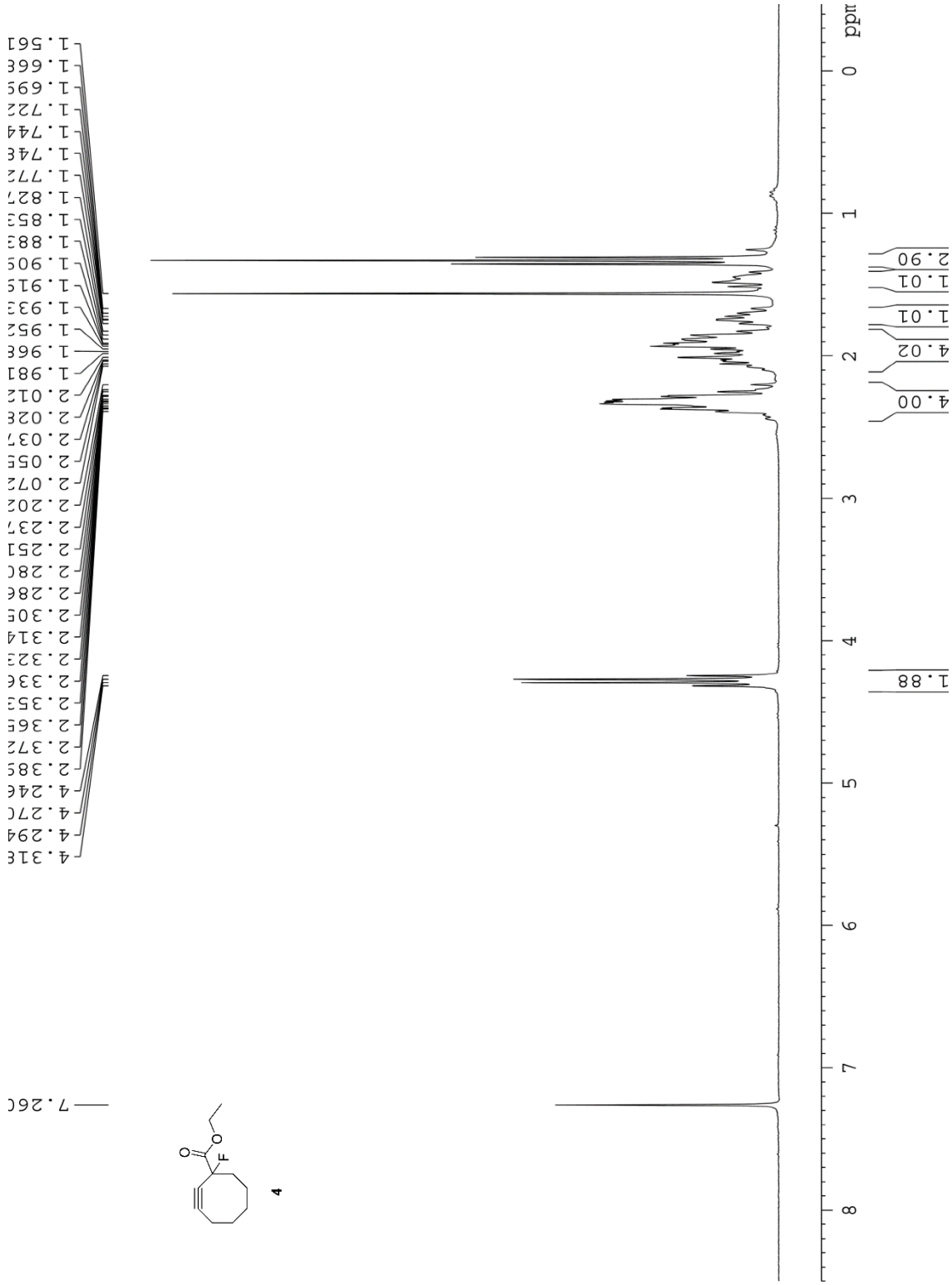


Figure S10. ^{1}H NMR spectrum of Compound **4** in $CDCl_3$

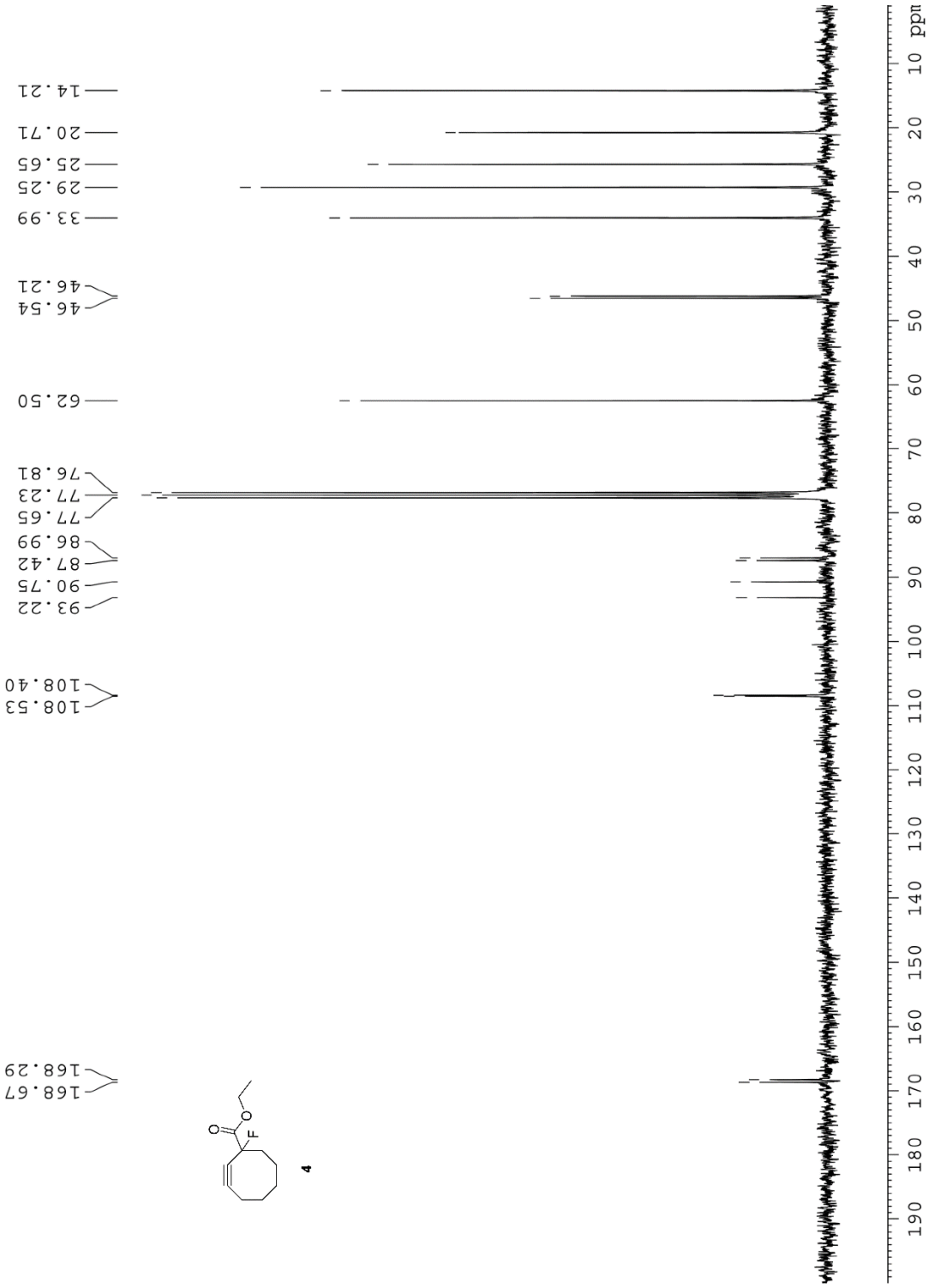


Figure S11. ^{13}C NMR spectrum of Compound **4** in $CDCl_3$

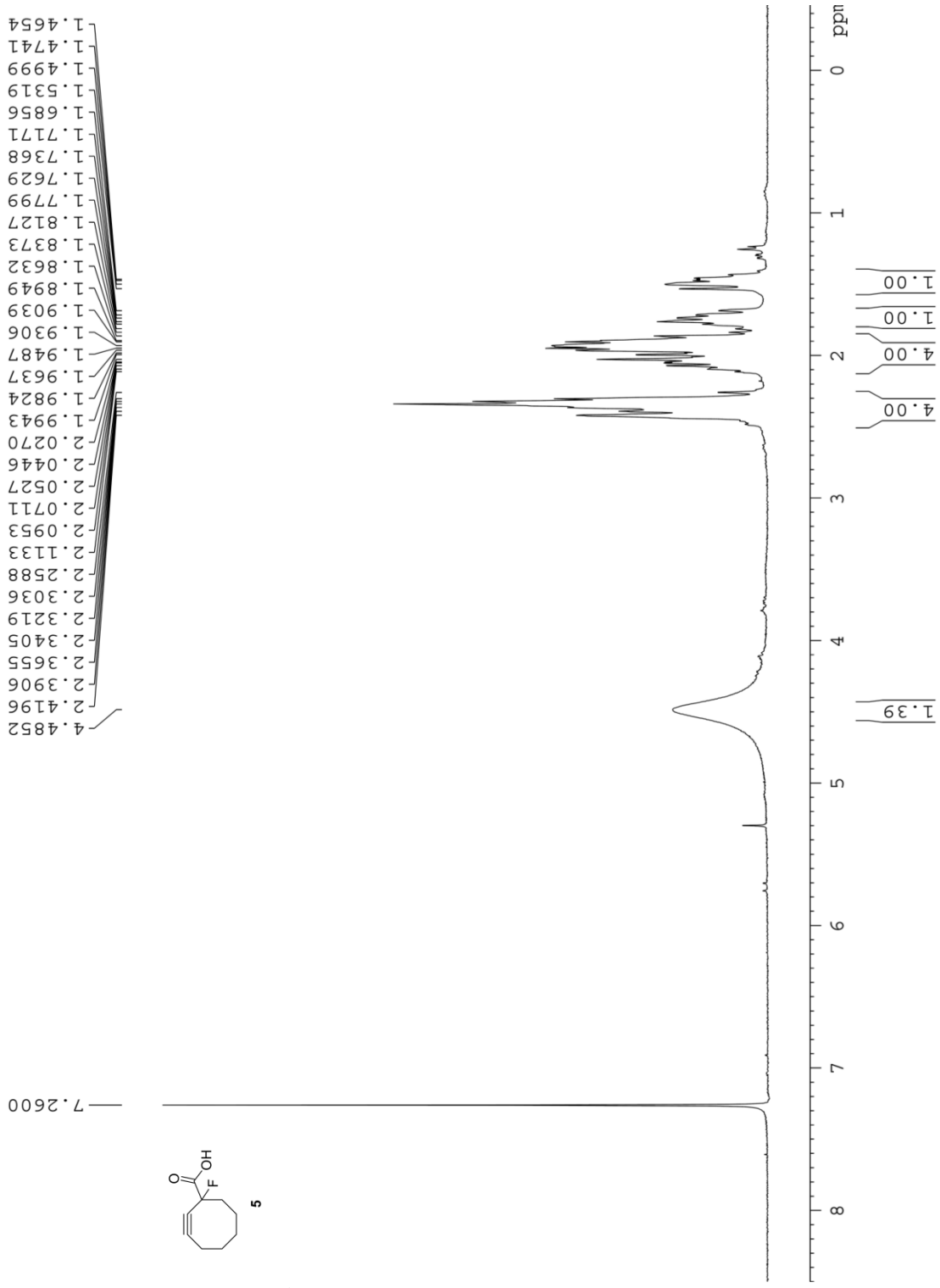


Figure S12. ^{1}H NMR spectrum of Compound **5** in $CDCl_3$

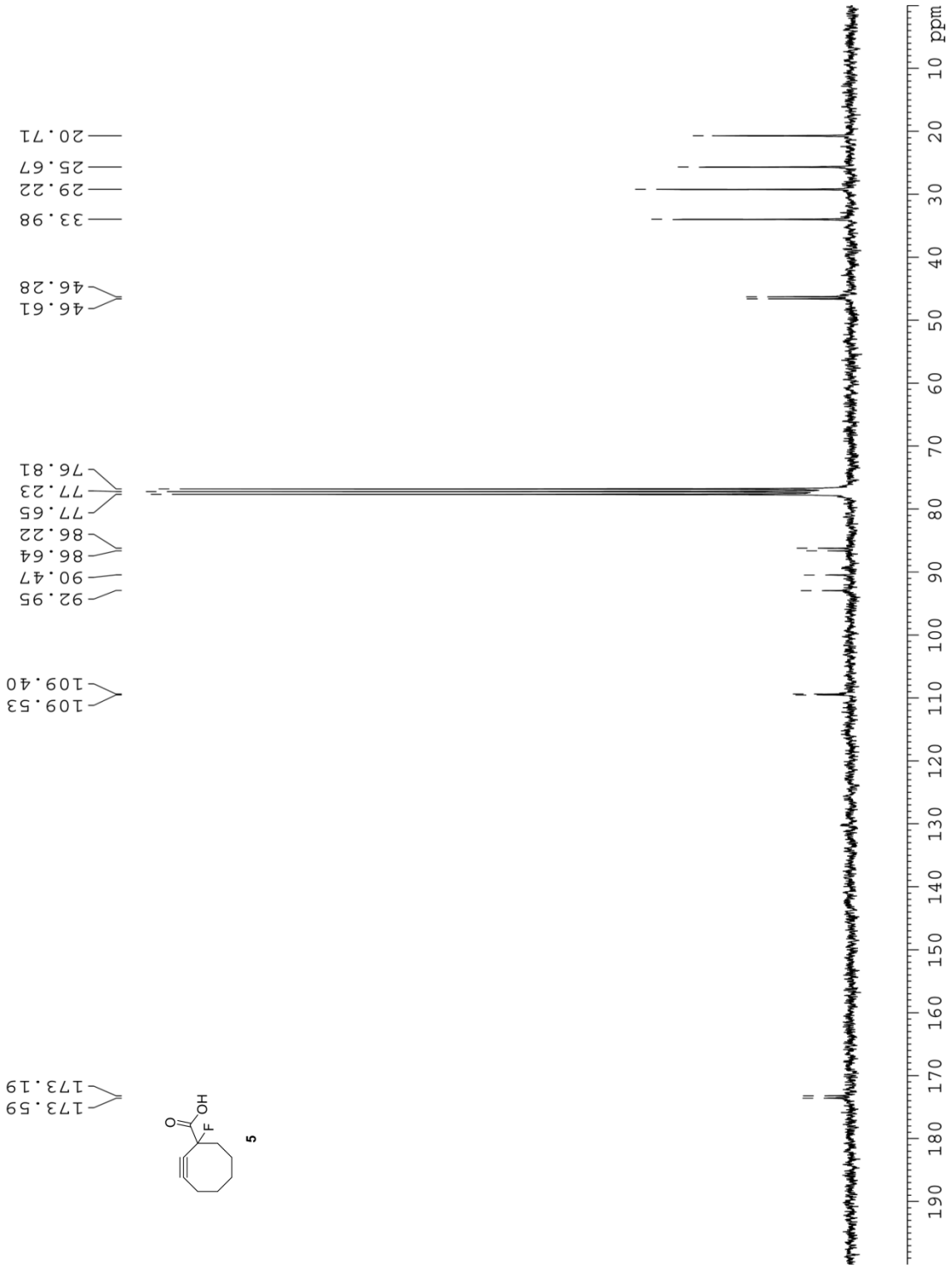


Figure S13. ^{13}C NMR spectrum of Compound **5** in $CDCl_3$

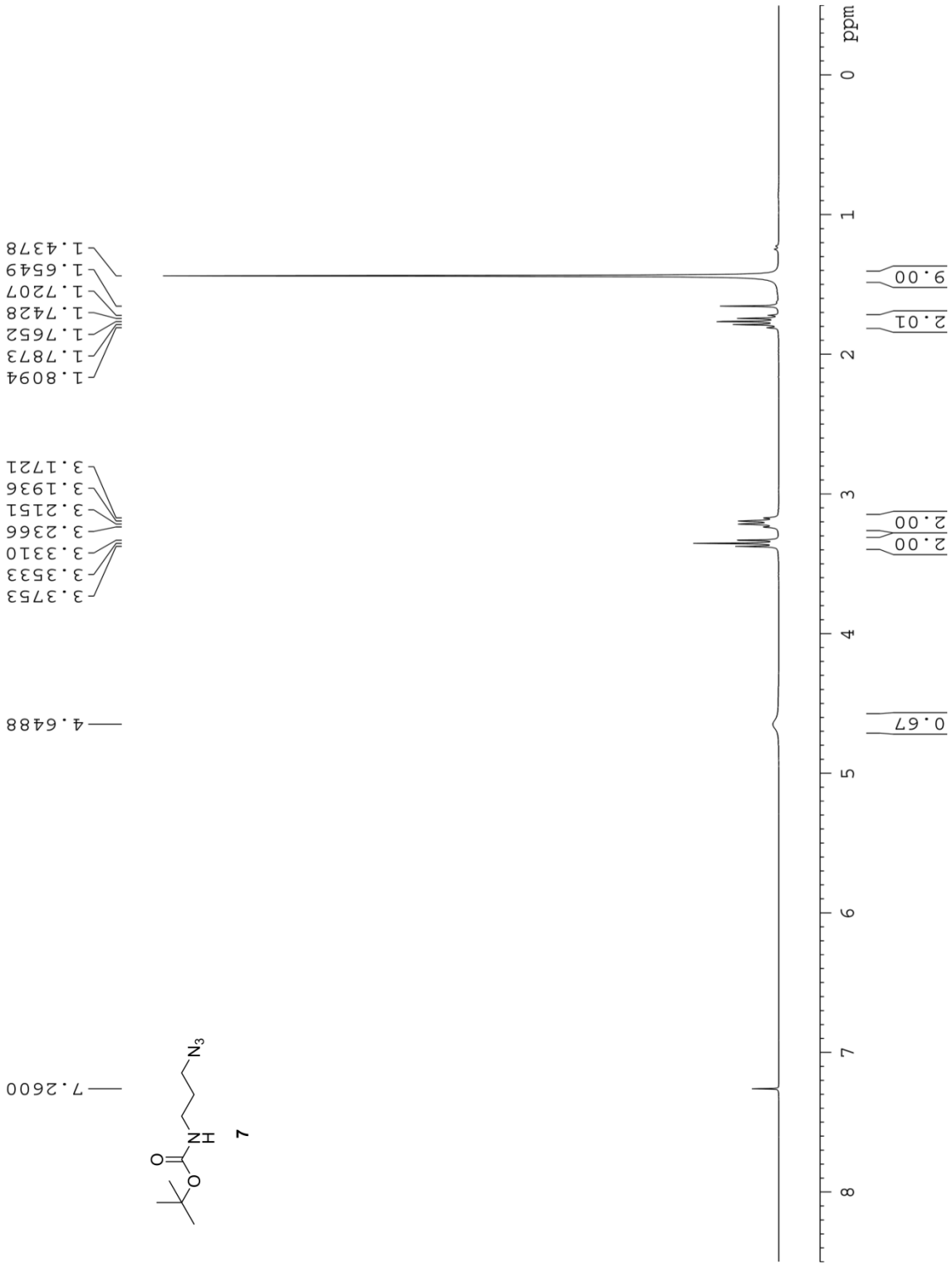


Figure S14. ^{1}H NMR spectrum of Compound **7** in $CDCl_3$

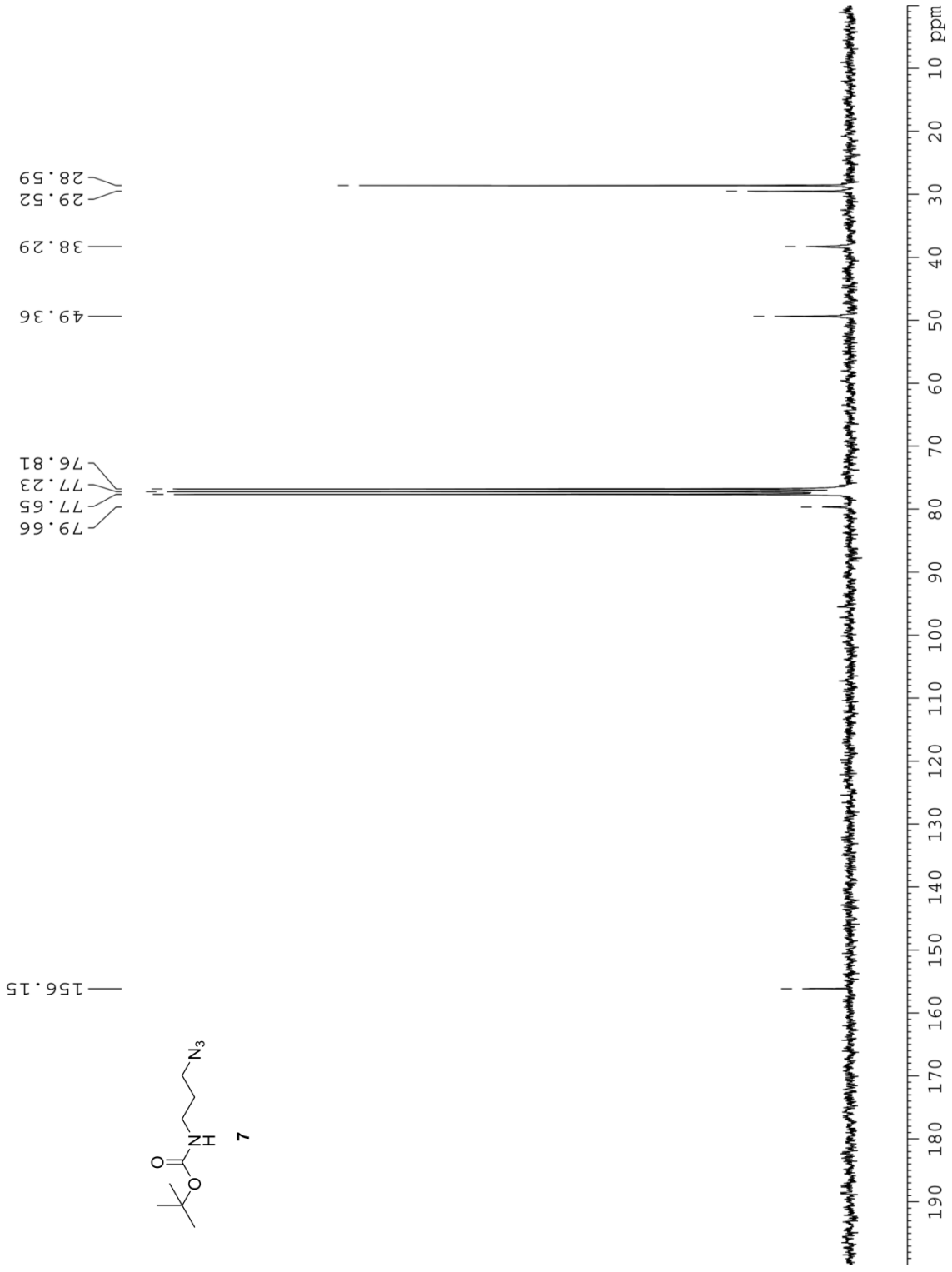


Figure S15. ^{13}C NMR spectrum of Compound **7** in $CDCl_3$.

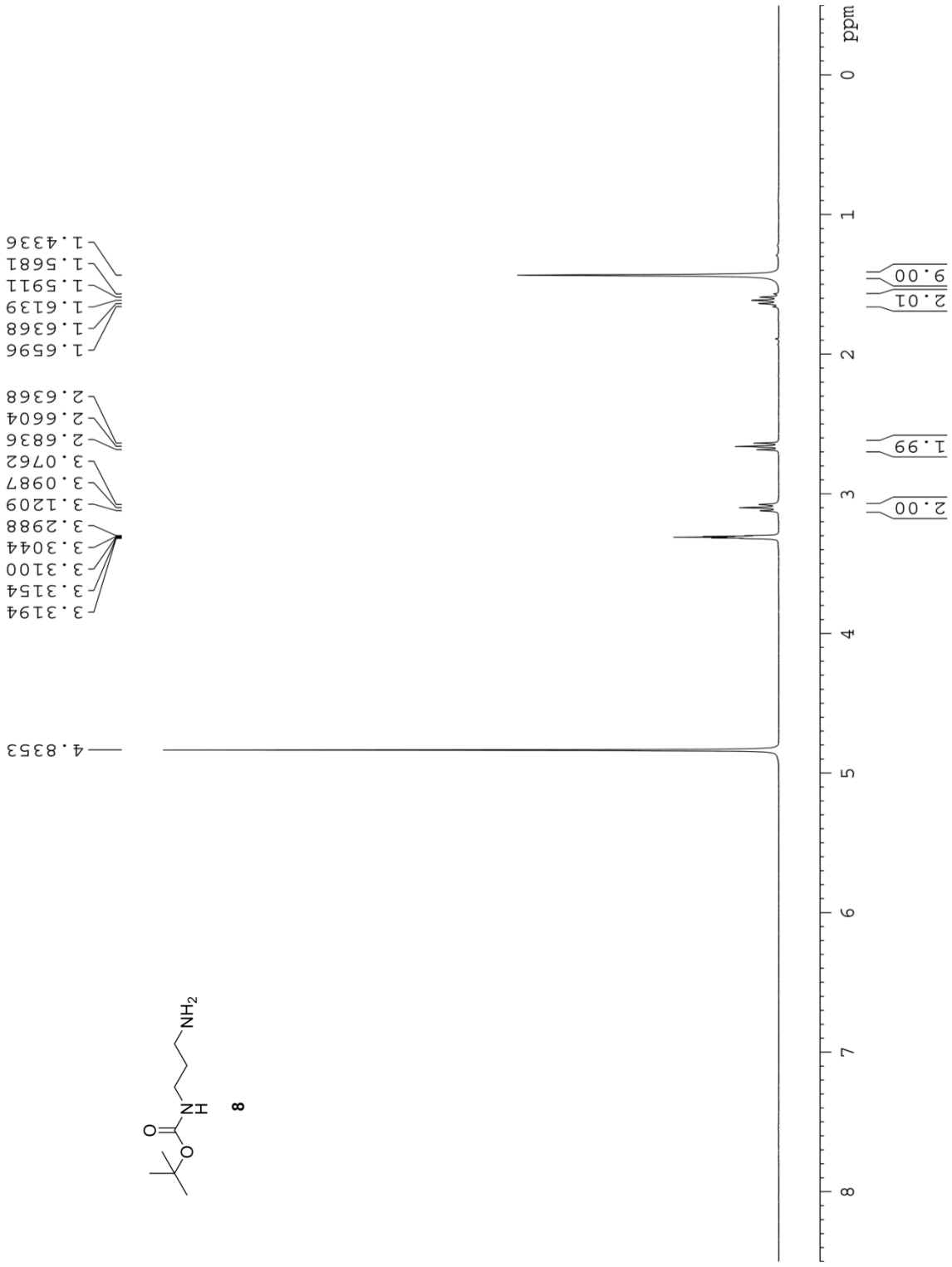


Figure S16. ^{1}H NMR spectrum of Compound **8** in MeOD

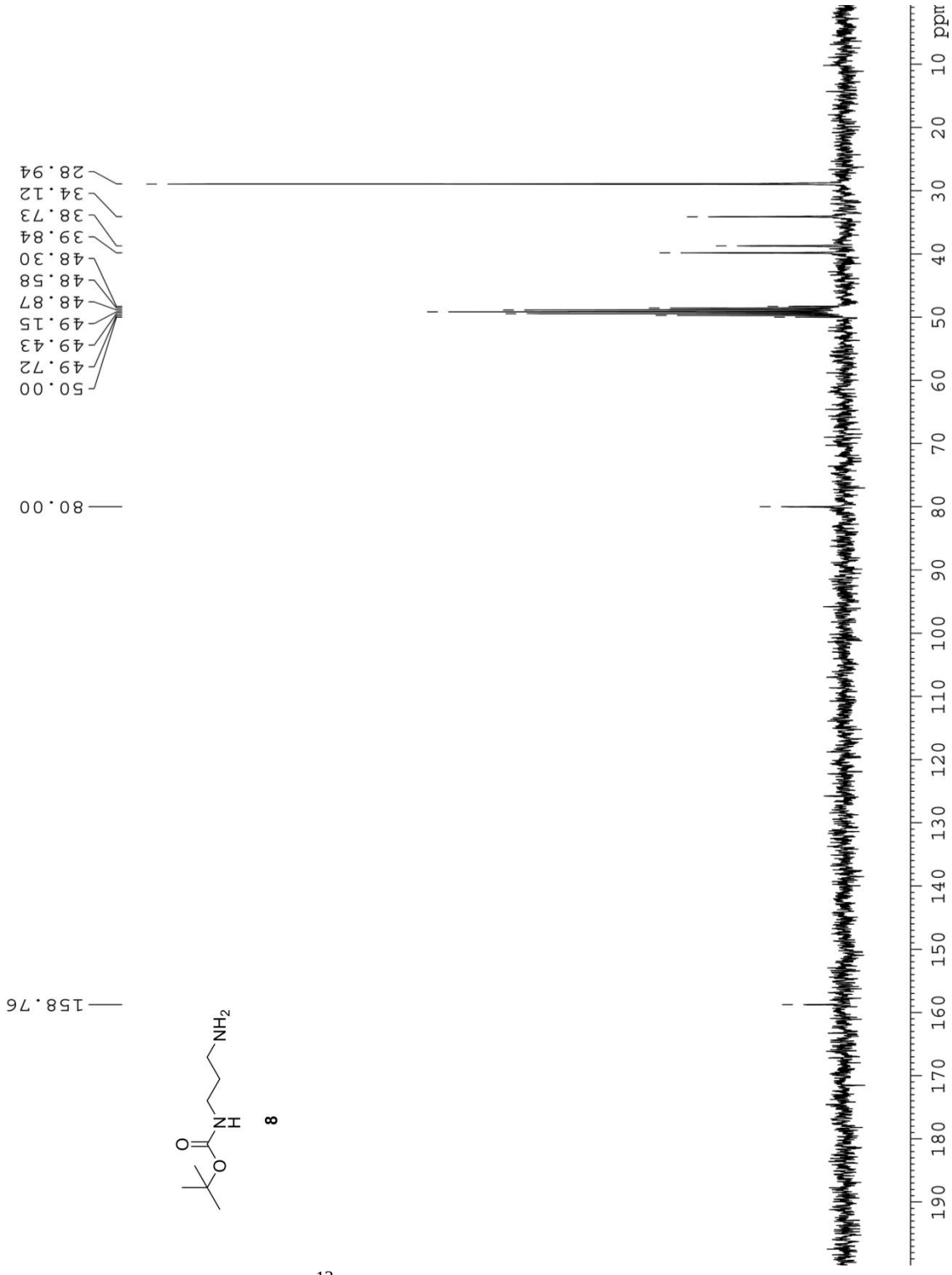


Figure S17. ^{13}C NMR spectrum of Compound **8** in MeOD

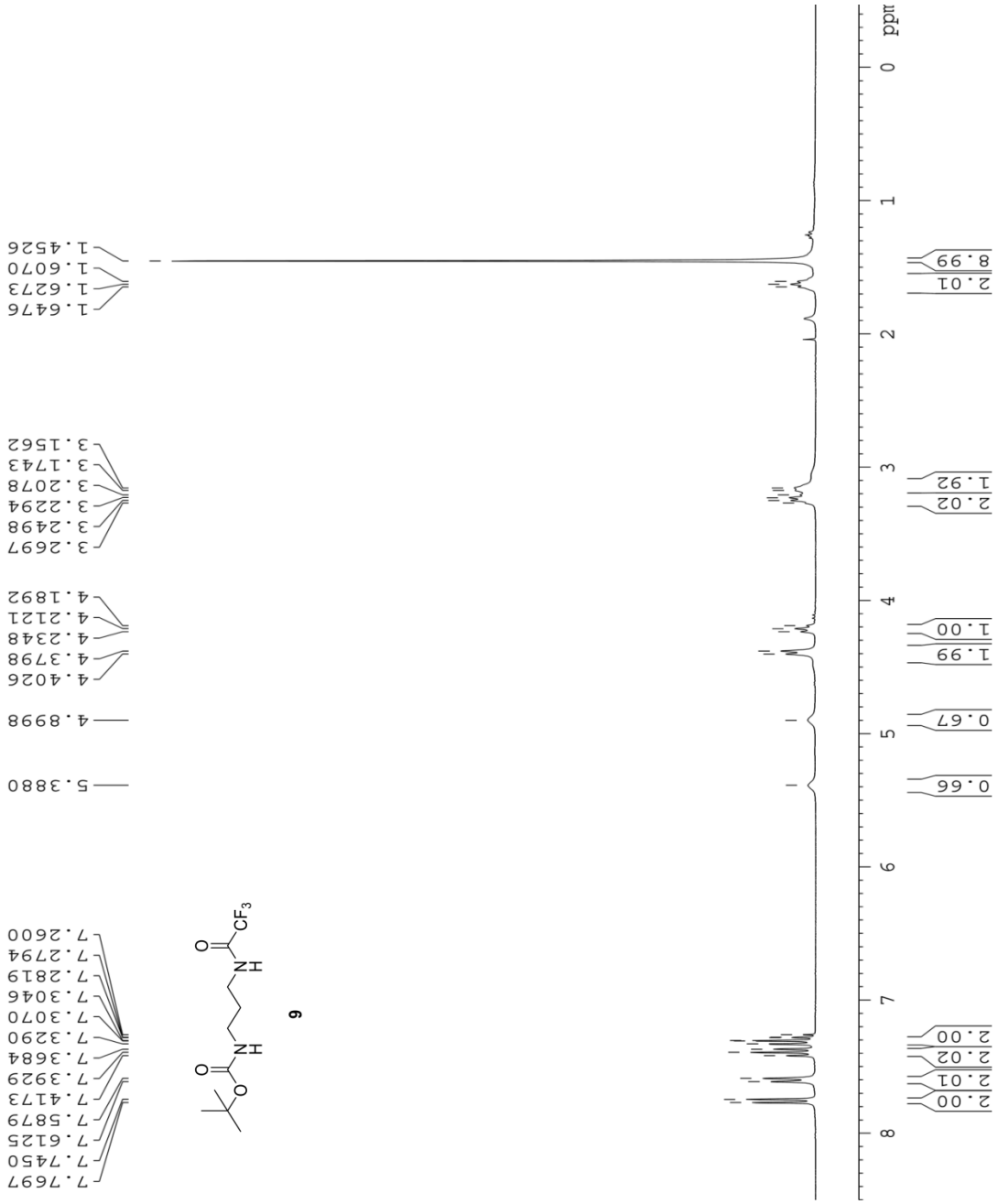


Figure S18. ^{1}H NMR spectrum of Compound **9** in $CDCl_3$.

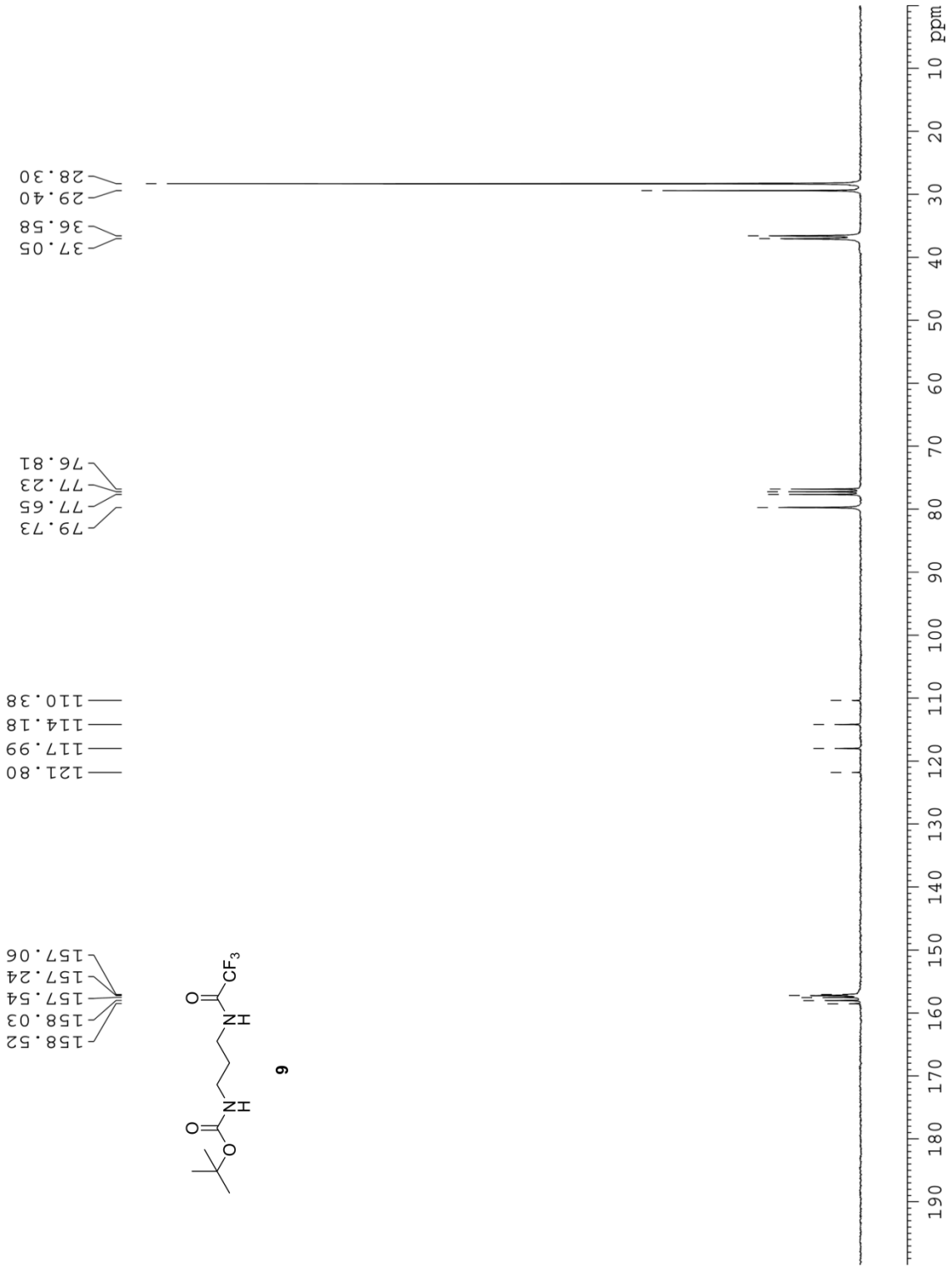


Figure S19. ^{13}C NMR spectrum of Compound **9** in $CDCl_3$

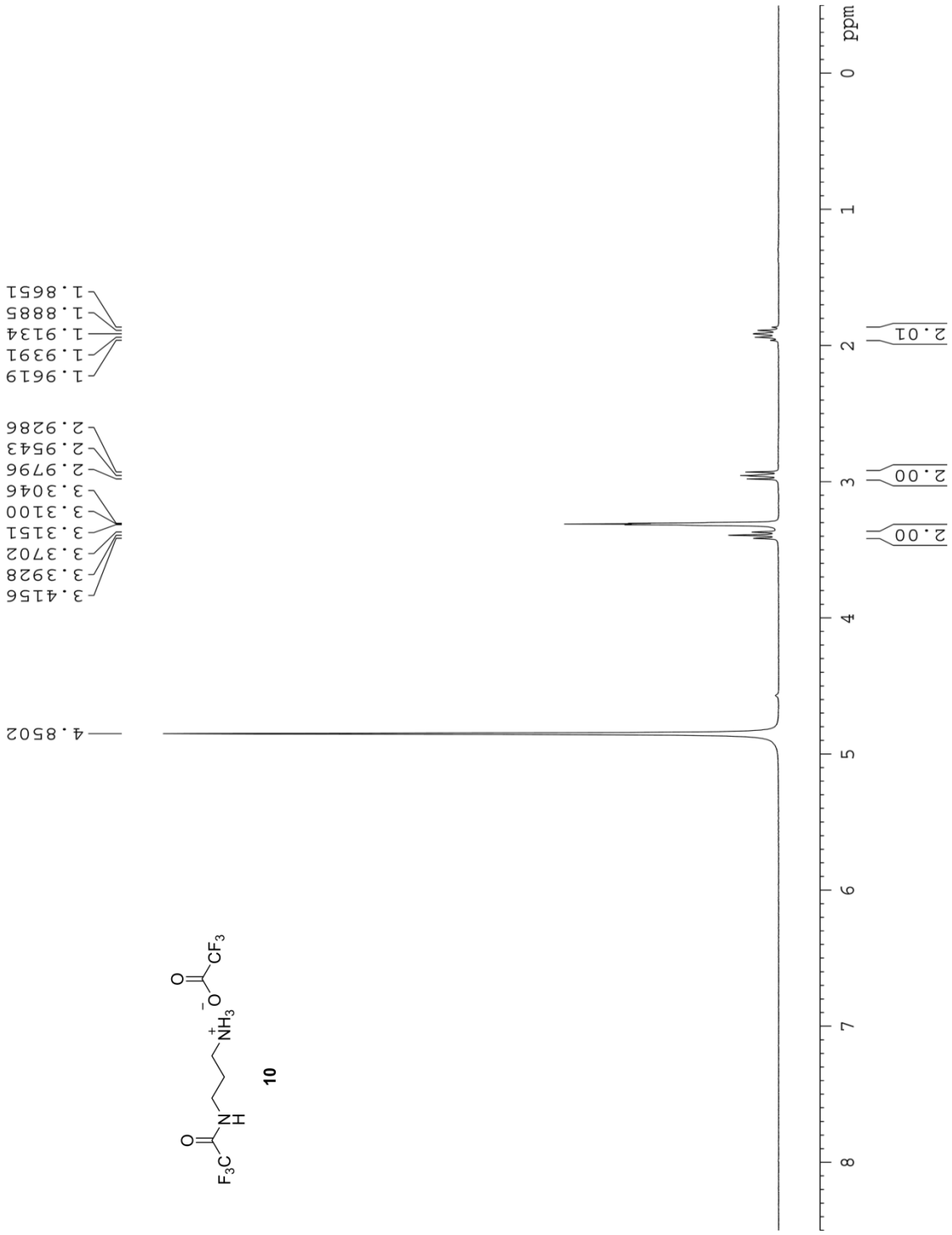


Figure S20. ^{1}H NMR spectrum of Compound **10** in MeOD.

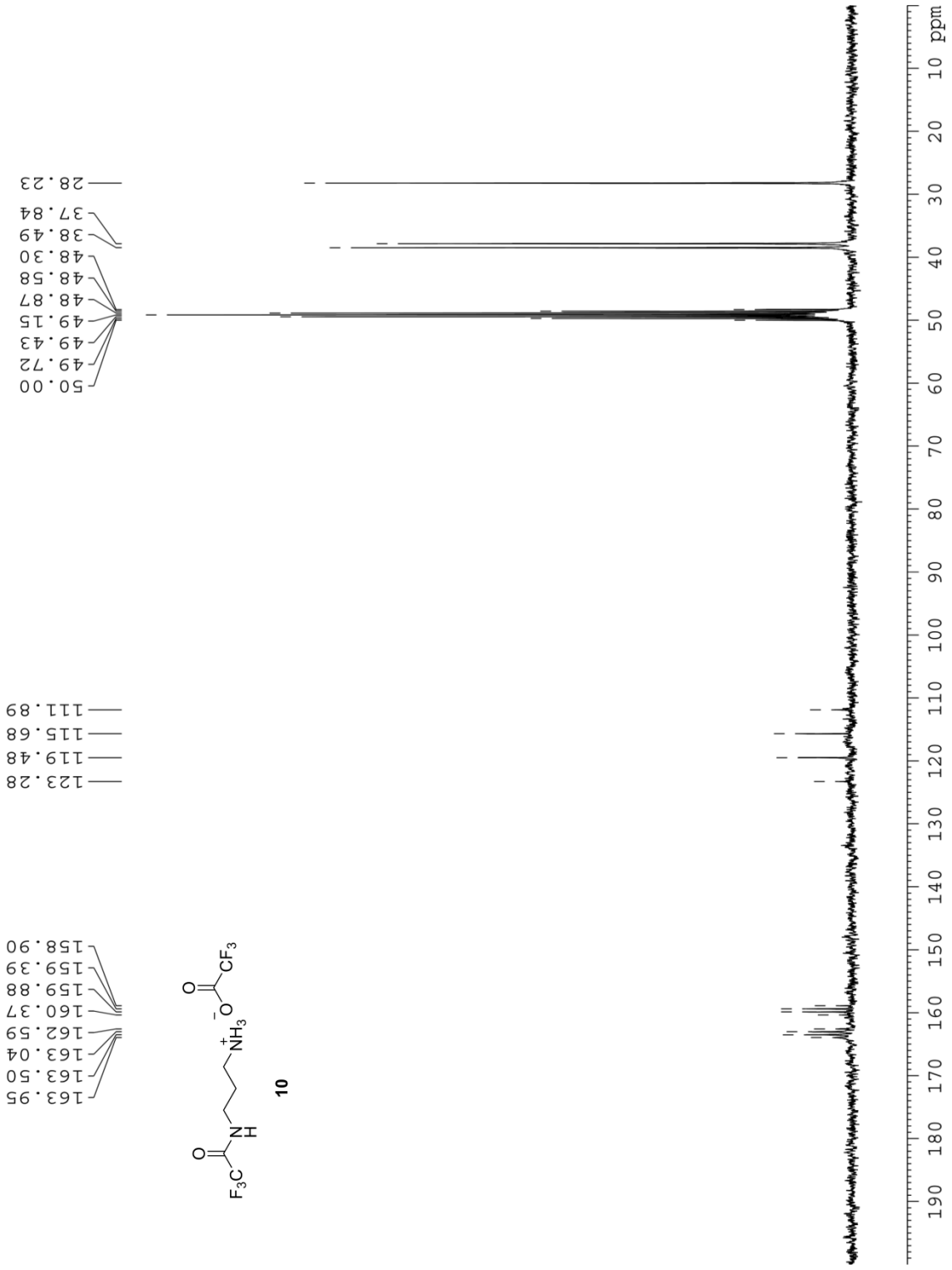


Figure S21. ^{13}C NMR spectrum of Compound **10** in MeOD.

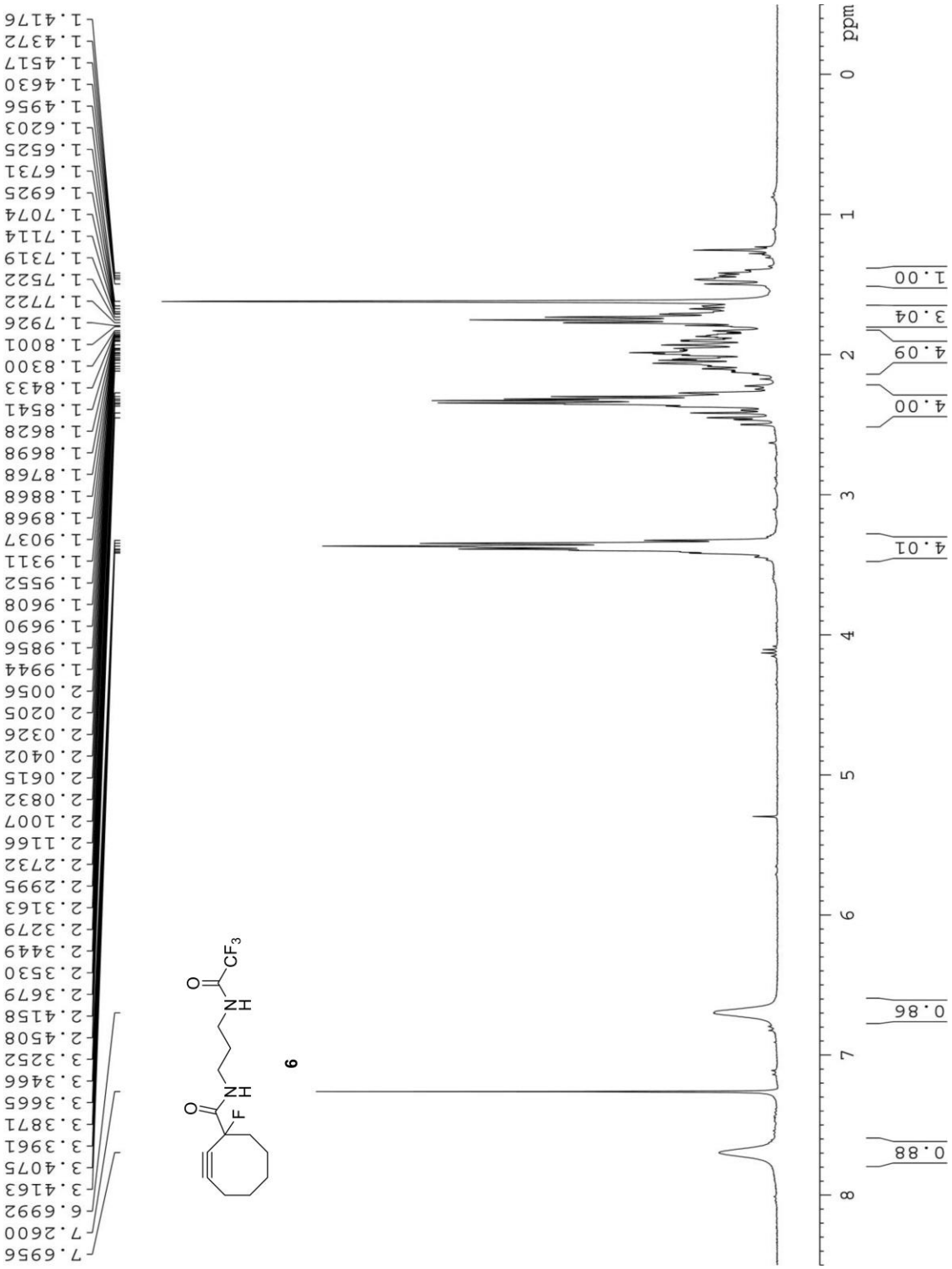


Figure S22. ^{1}H NMR spectrum of Compound **6** in $CDCl_3$.

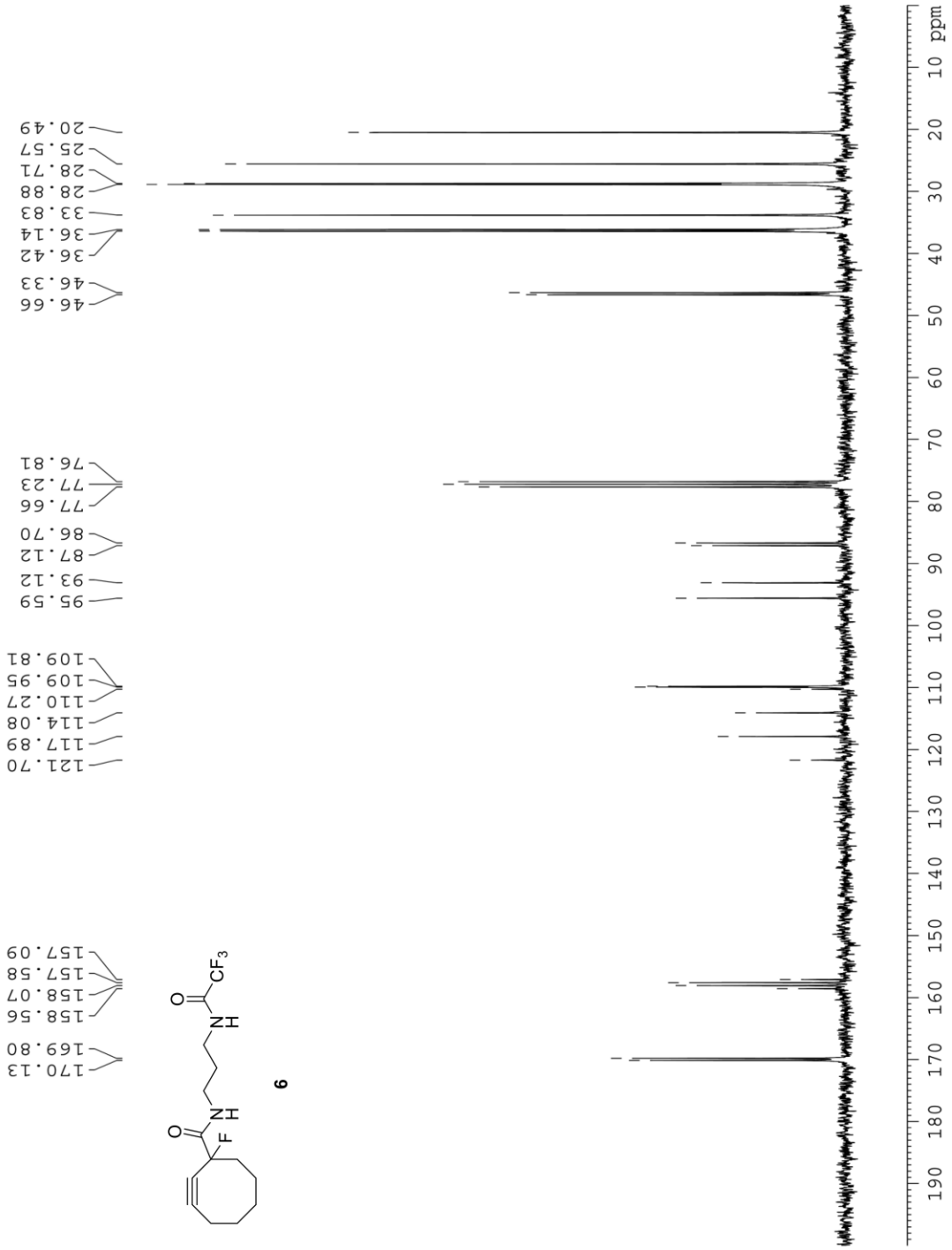


Figure S23. ^{13}C NMR spectrum of Compound **6** in $CDCl_3$

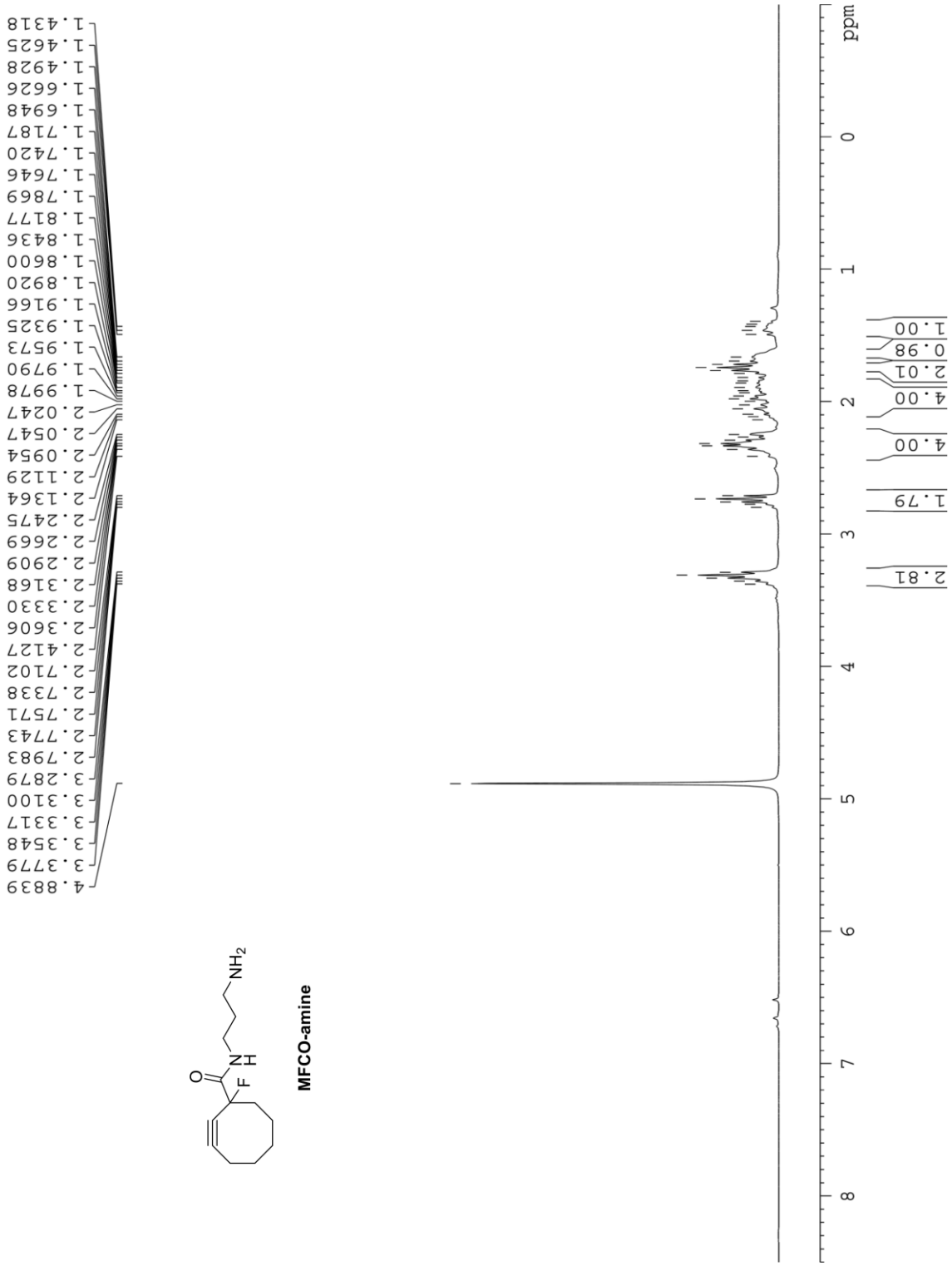


Figure S24. ^{1}H NMR spectrum of Compound **MFCO-amine** in D_2O.

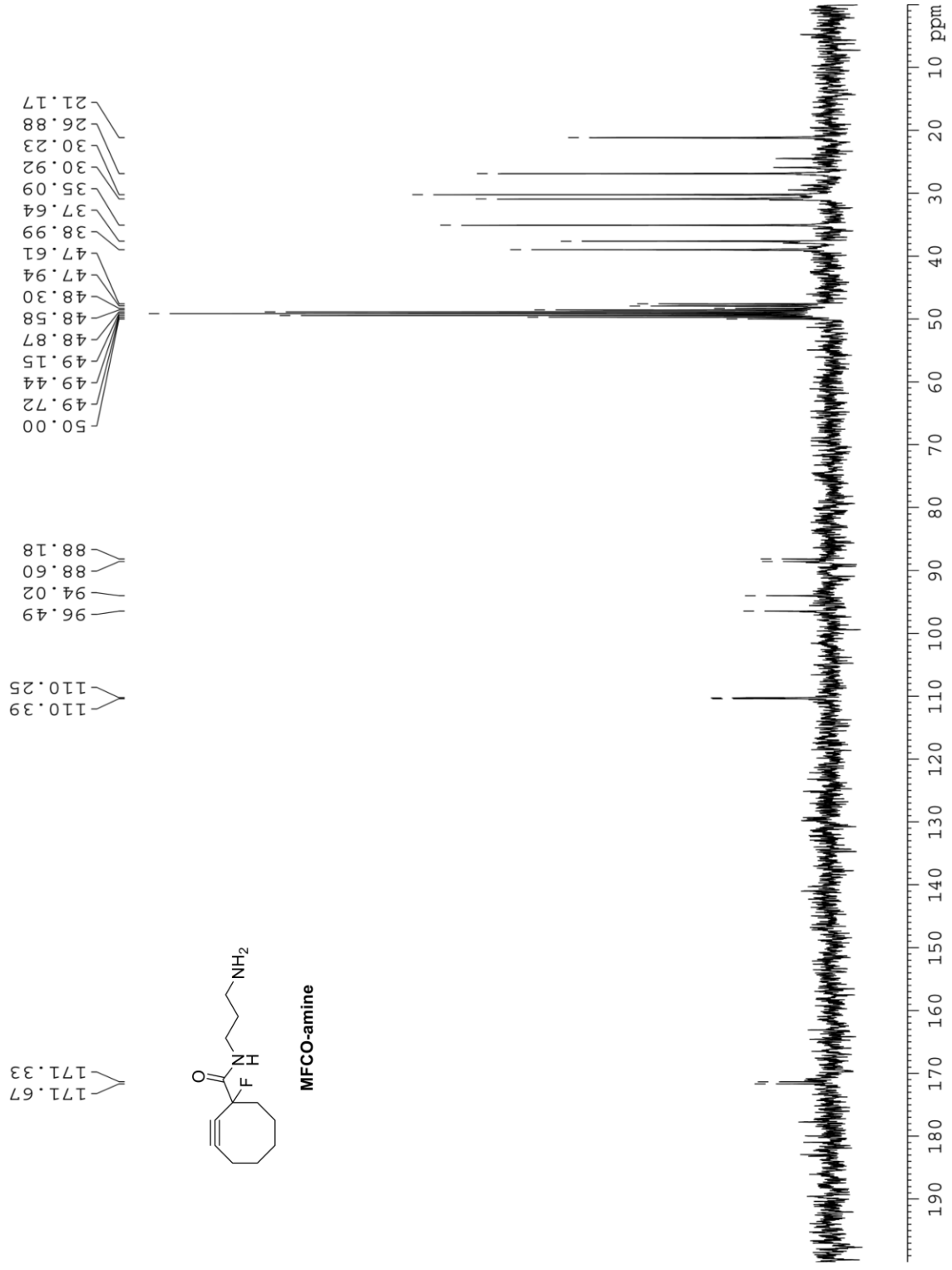


Figure S25. ^{13}C NMR spectrum of Compound **MFCO-amine** in D_2O.

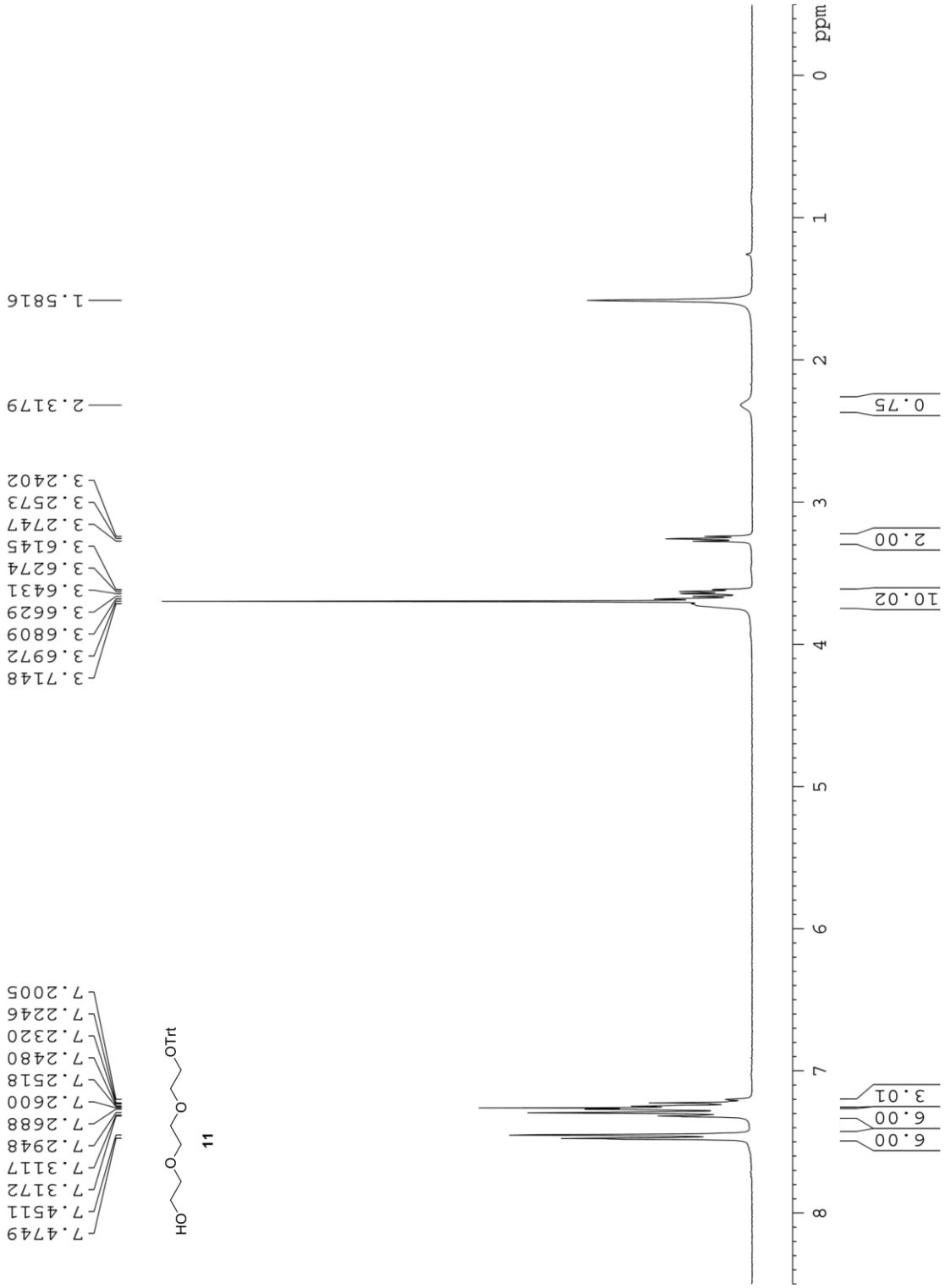


Figure S26. ^{1}H NMR spectrum of Compound **11** in $CDCl_3$.

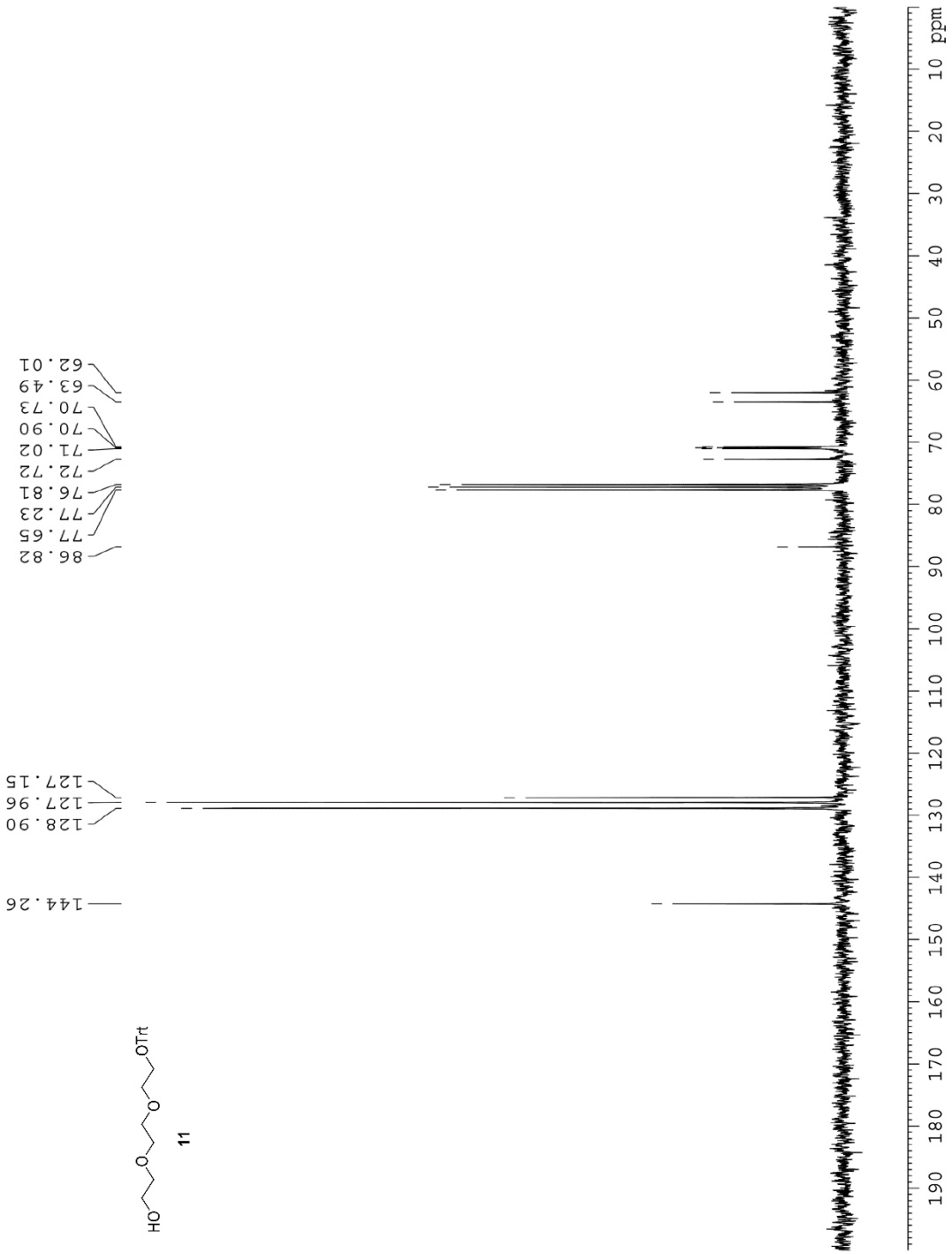


Figure S27. ^{13}C NMR spectrum of Compound **11** in $CDCl_3$.

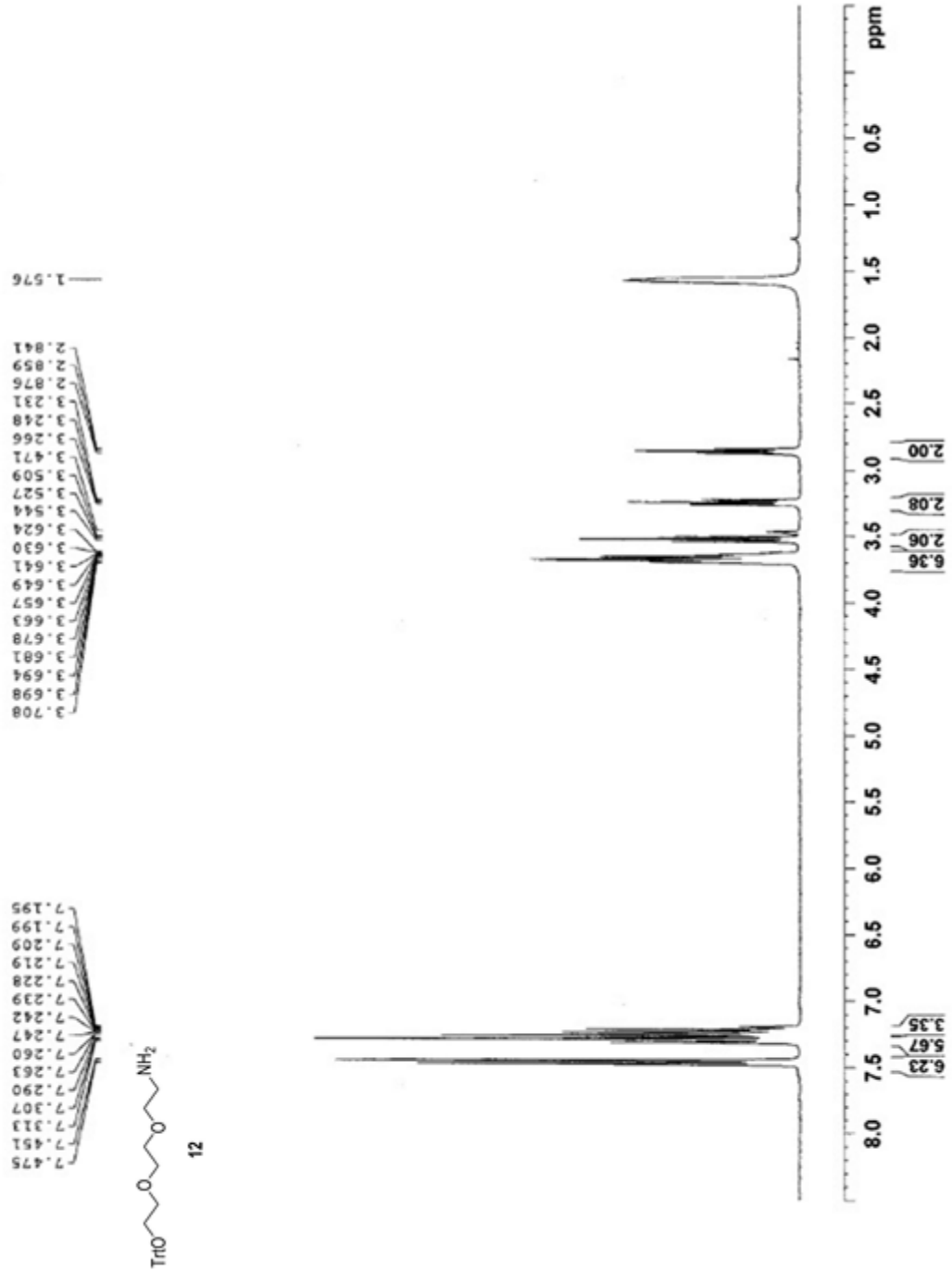


Figure S28. ^{1}H NMR spectrum of Compound **12** in $CDCl_3$.

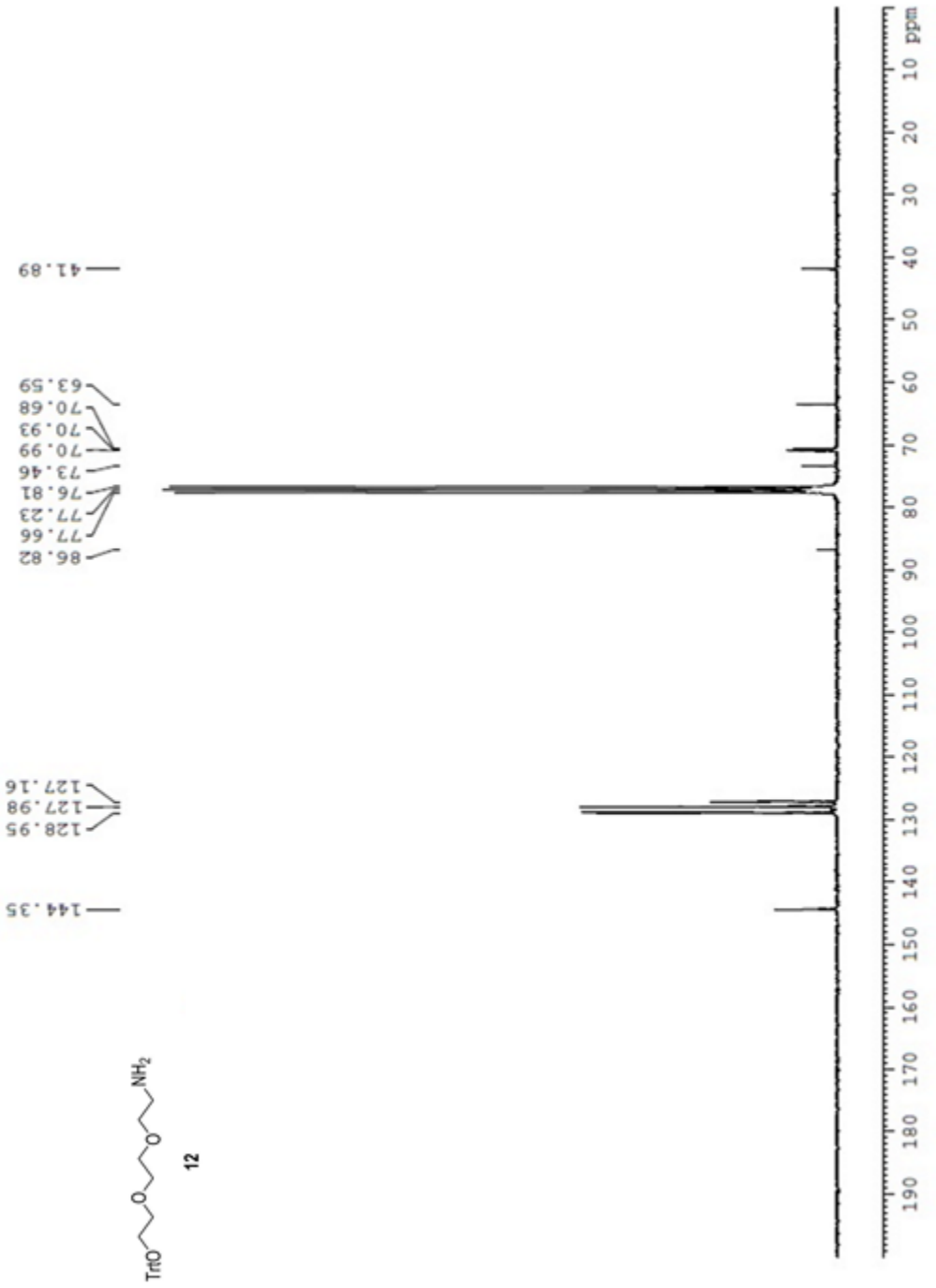


Figure S29. ^{13}C NMR spectrum of Compound **12** in $CDCl_3$.

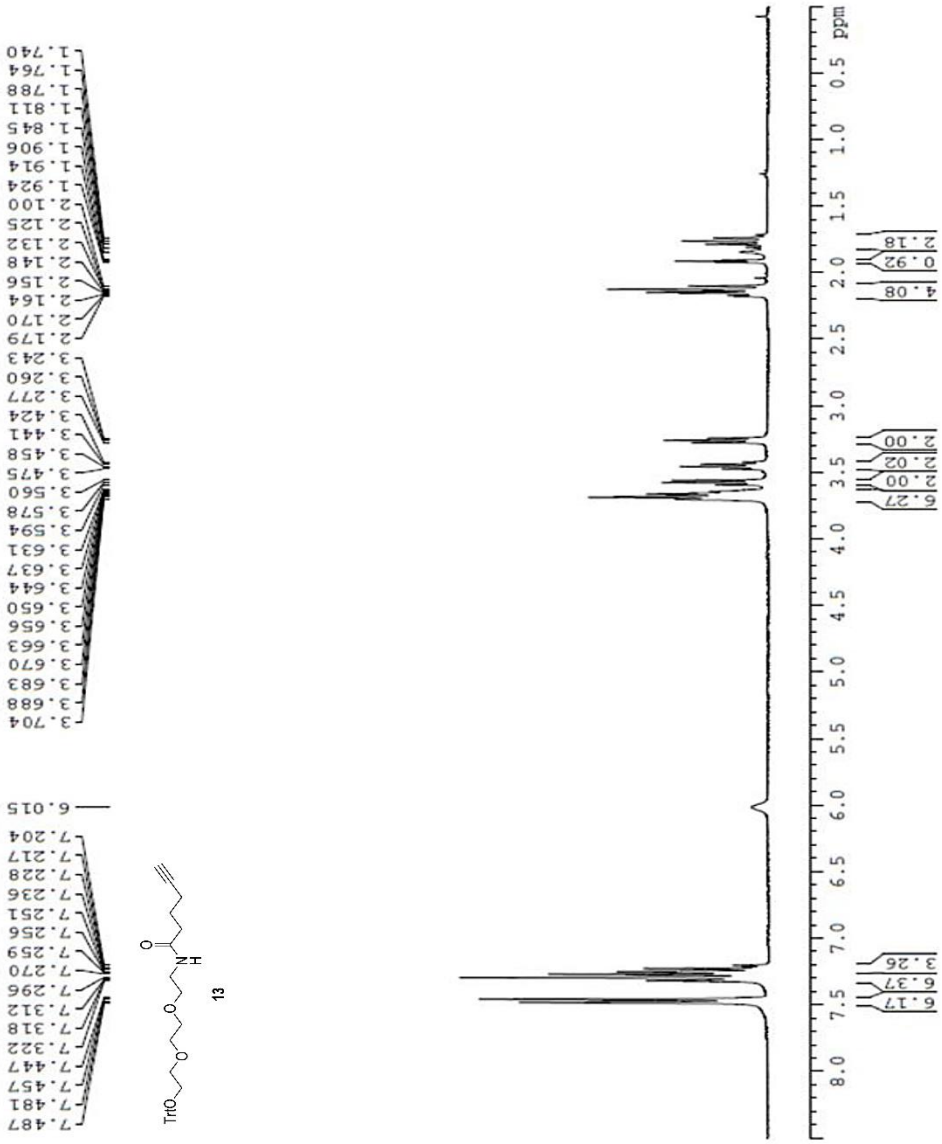


Figure S30. ^{1}H NMR spectrum of Compound **13** in $CDCl_3$

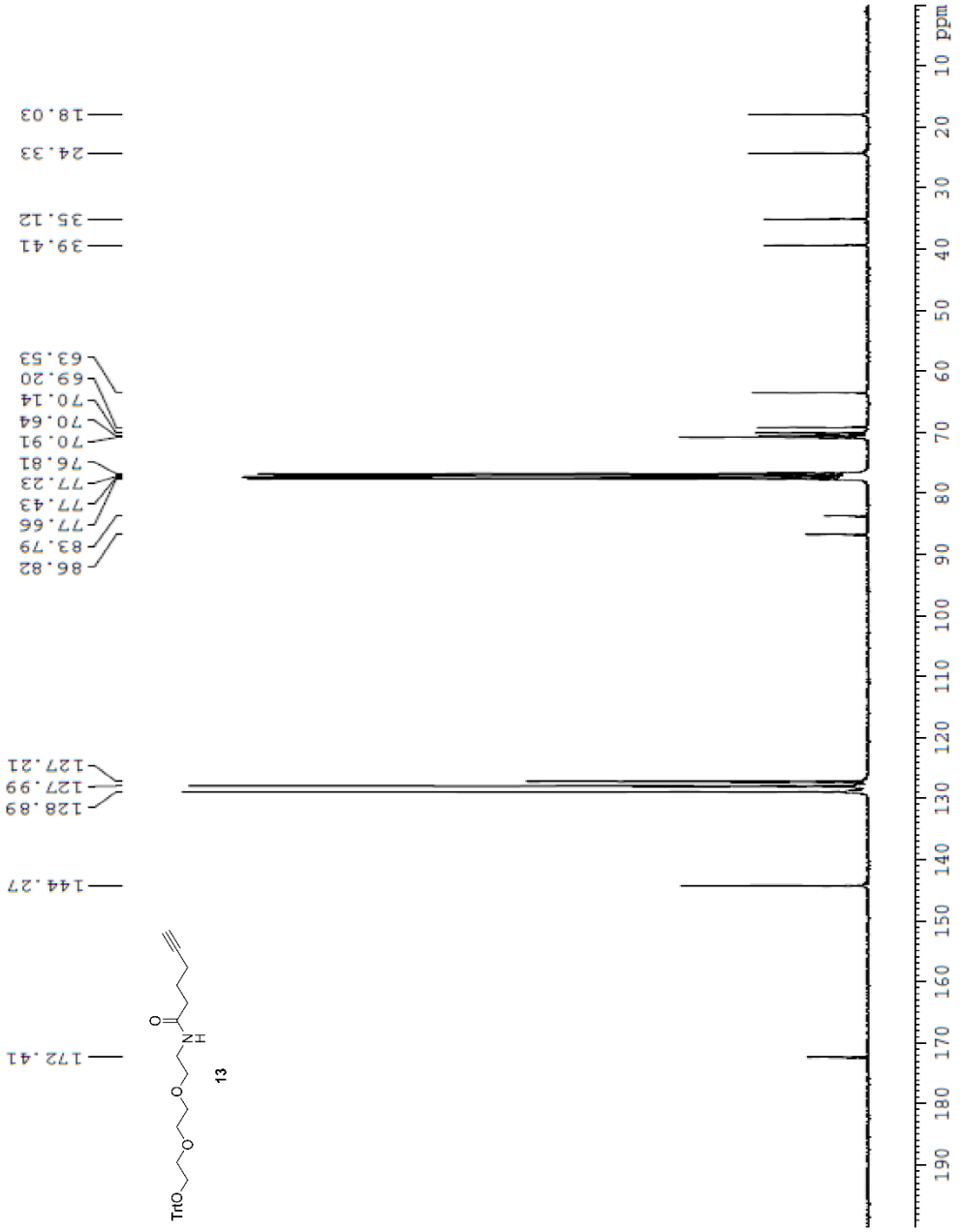


Figure S31. ^{13}C NMR spectrum of Compound **13** in $CDCl_3$

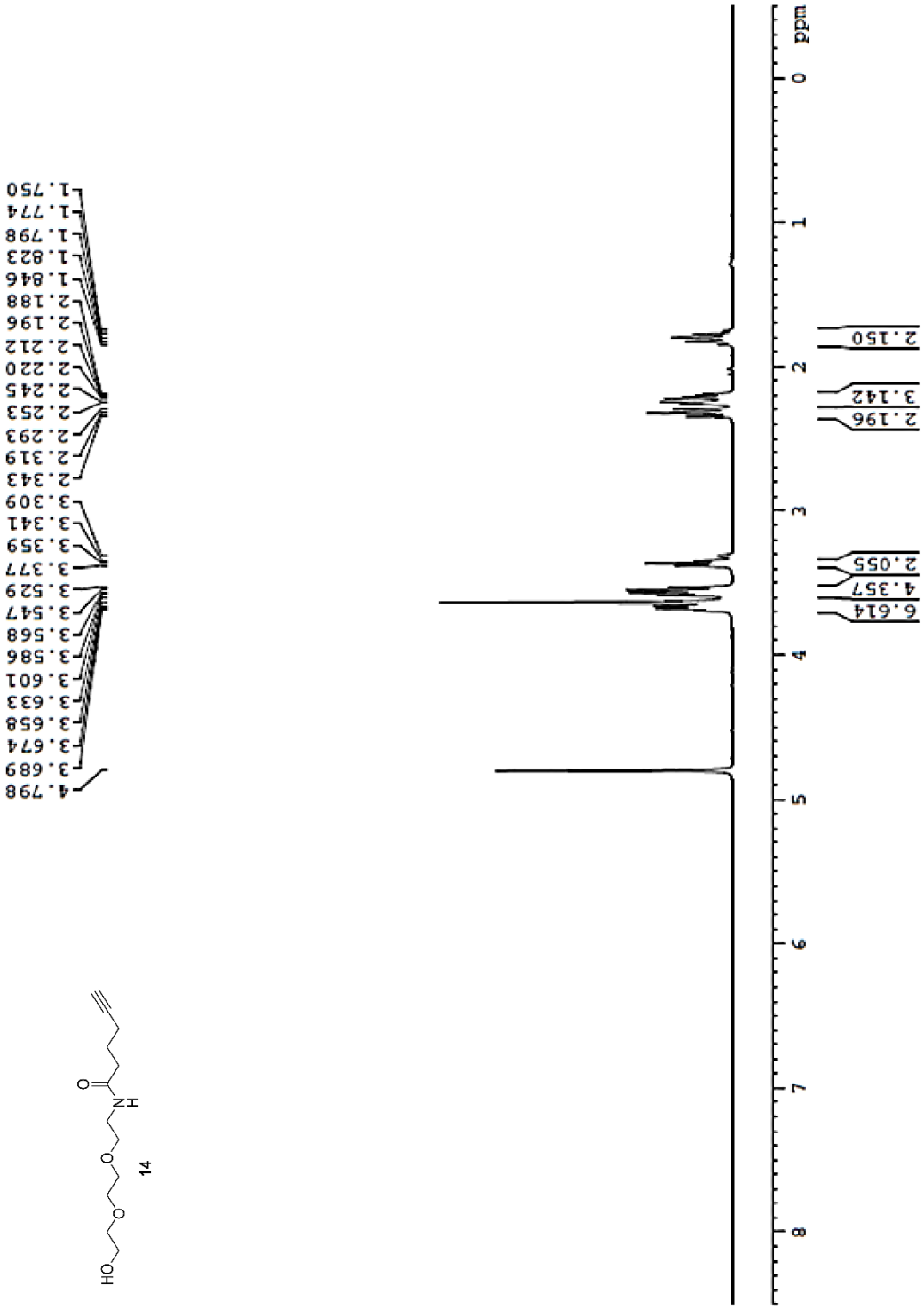


Figure S32. ^{1}H NMR spectrum of Compound **14** in MeOD.

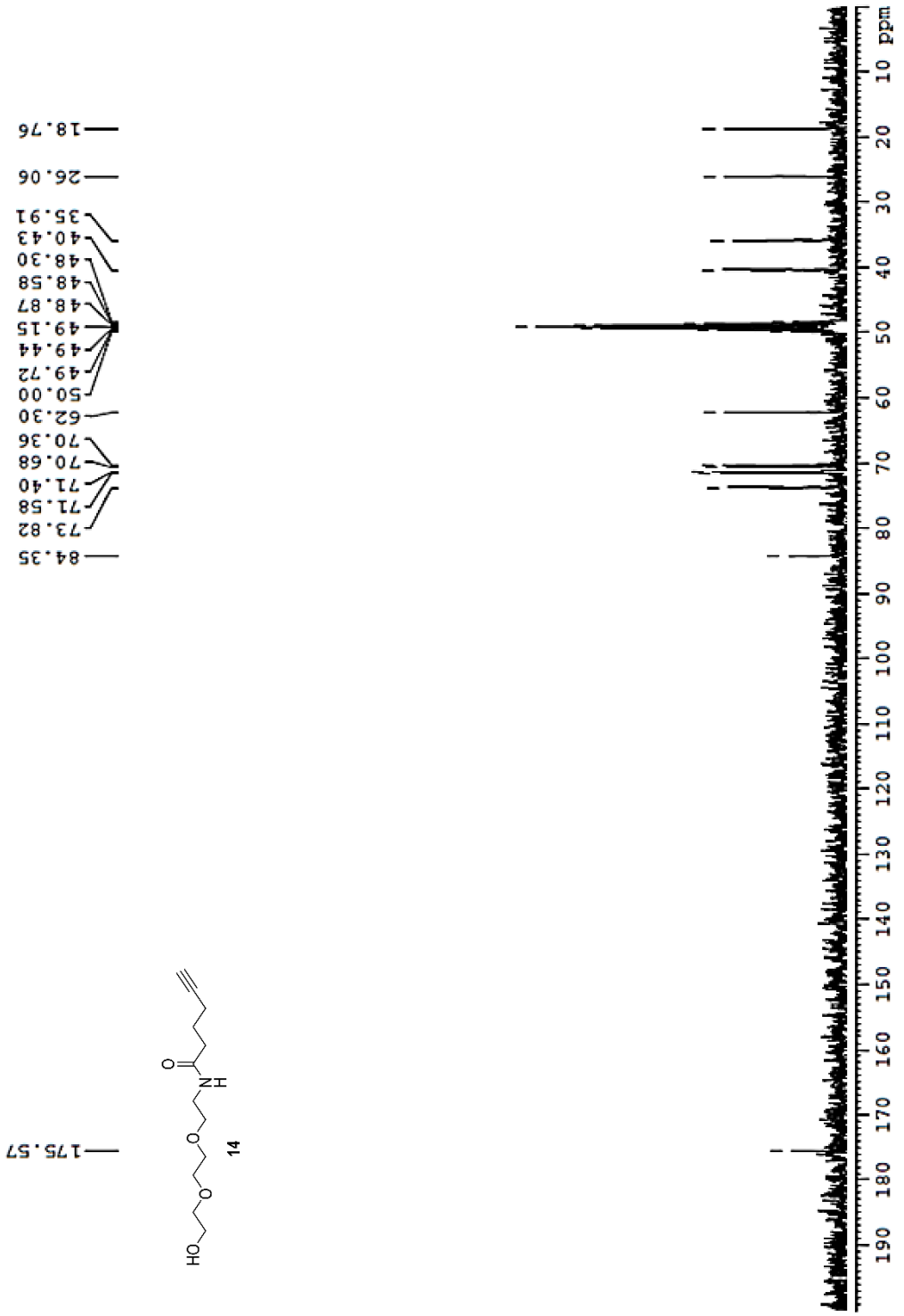


Figure S33. ^{13}C NMR spectrum of Compound **14** in MeOD.

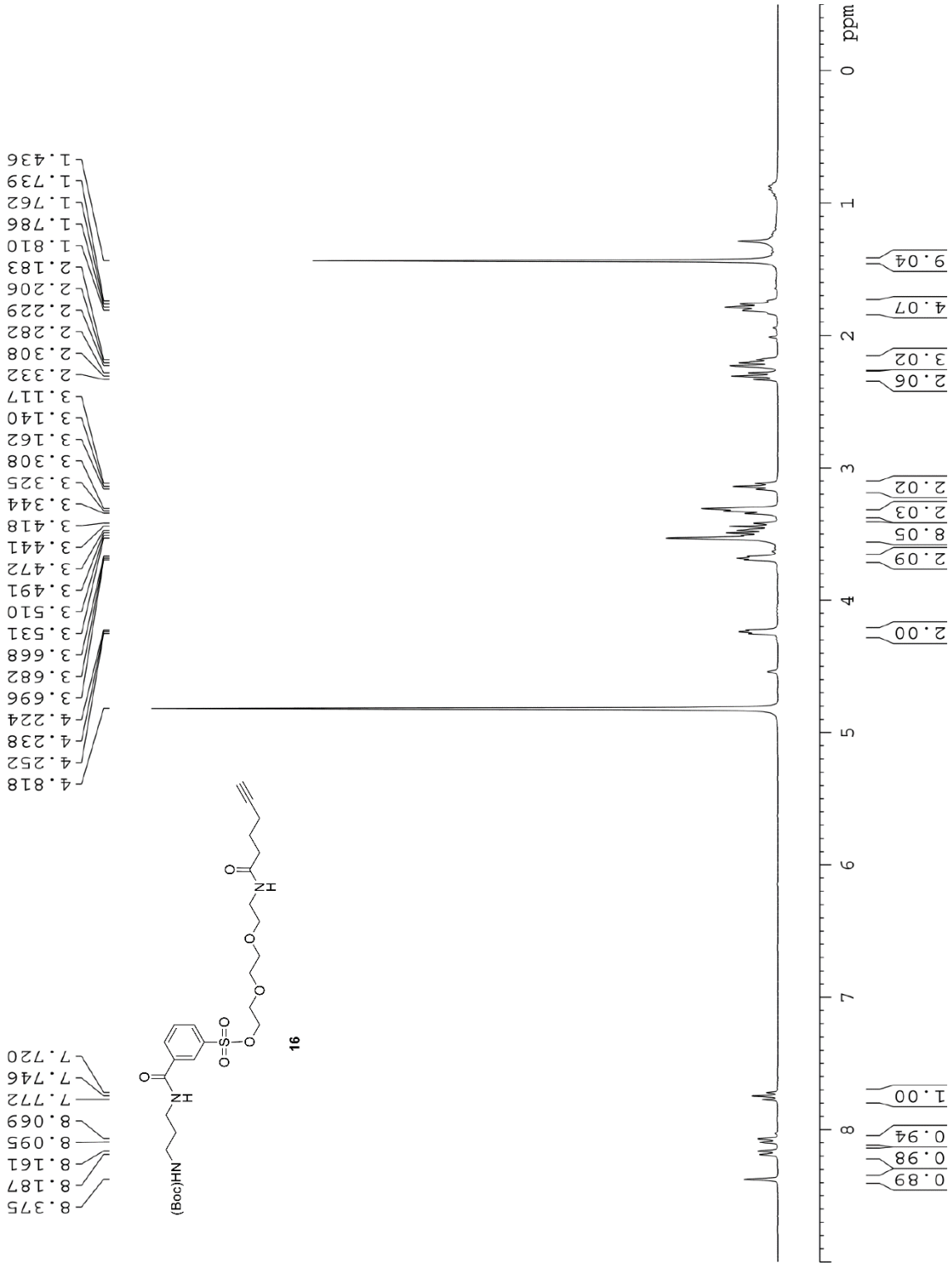


Figure S34. ^{1}H NMR spectrum of Compound **16** in MeOD.

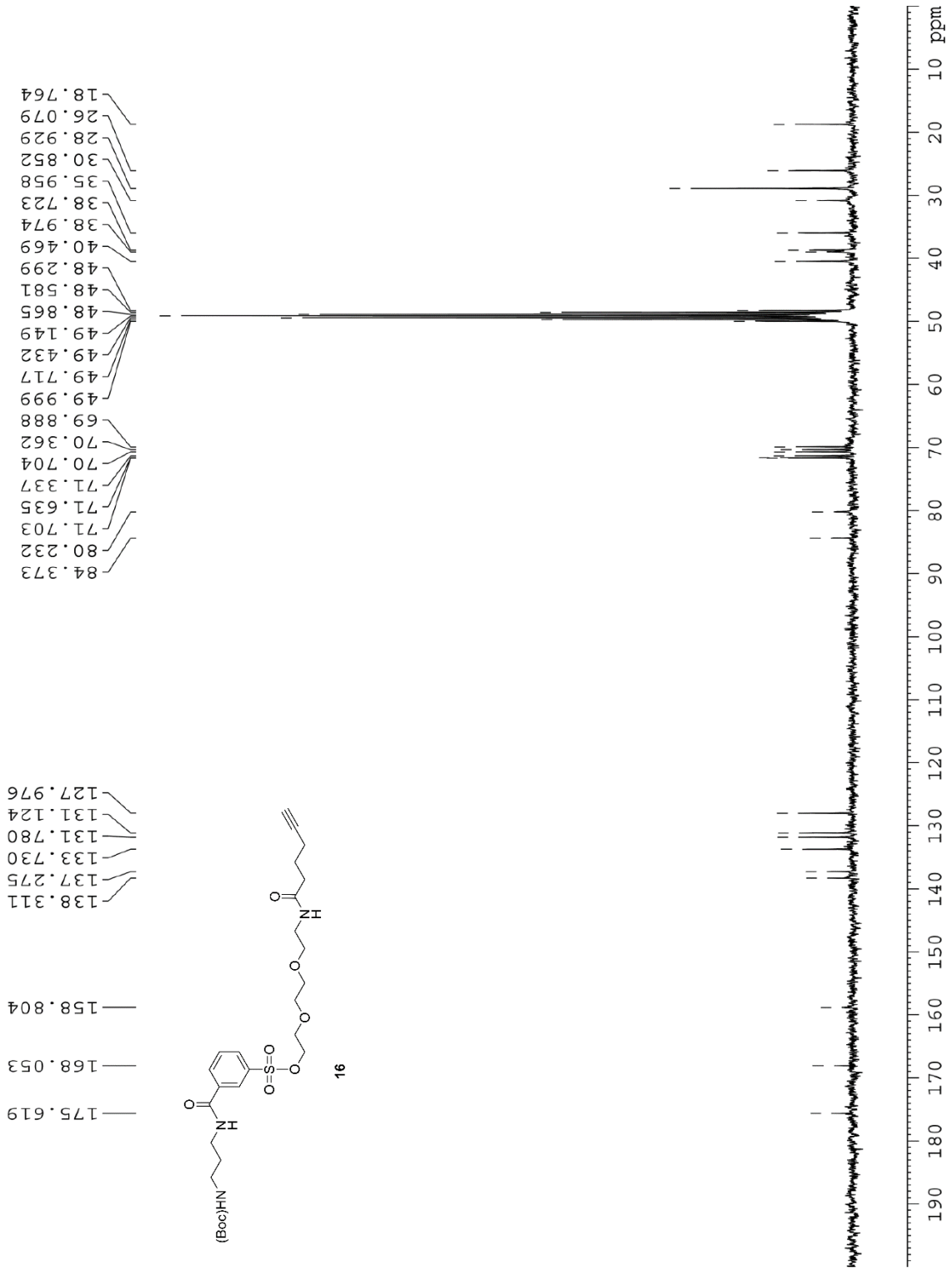


Figure S35. ^{13}C NMR spectrum of Compound **16** in MeOD.

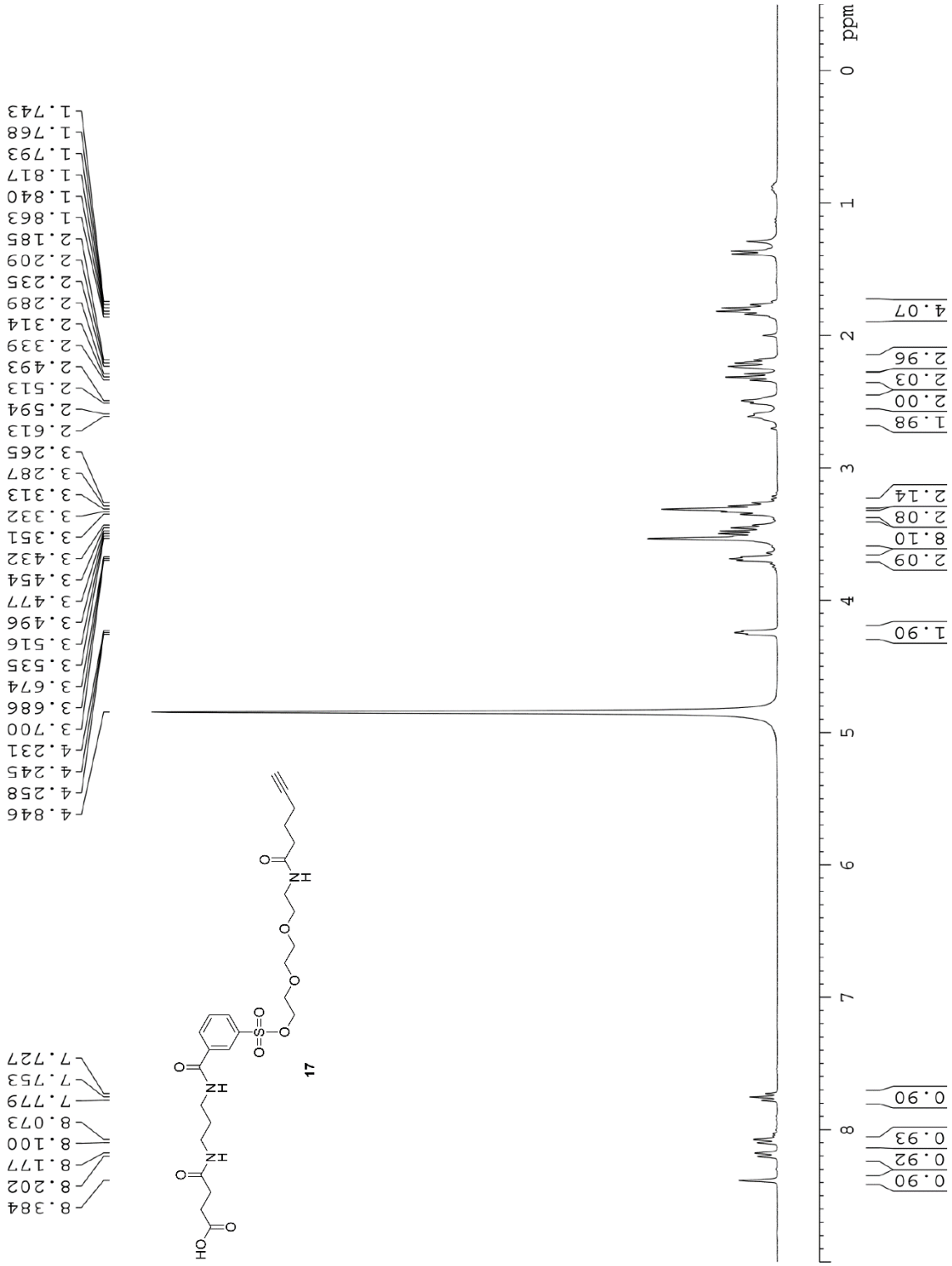


Figure S36. ^{1}H NMR spectrum of Compound **17** in MeOD.

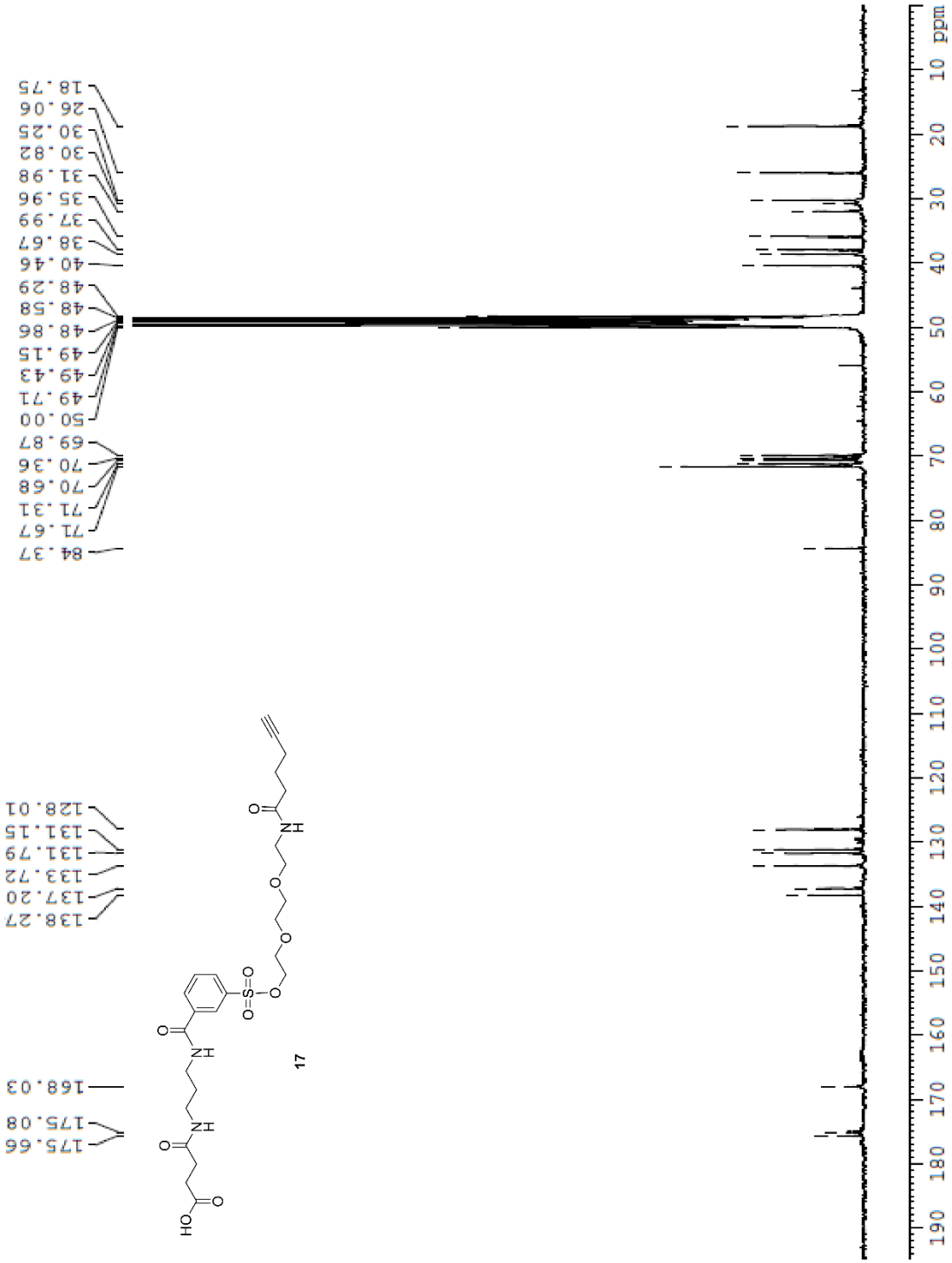


Figure S37. ^{13}C NMR spectrum of Compound **17** in MeOD.

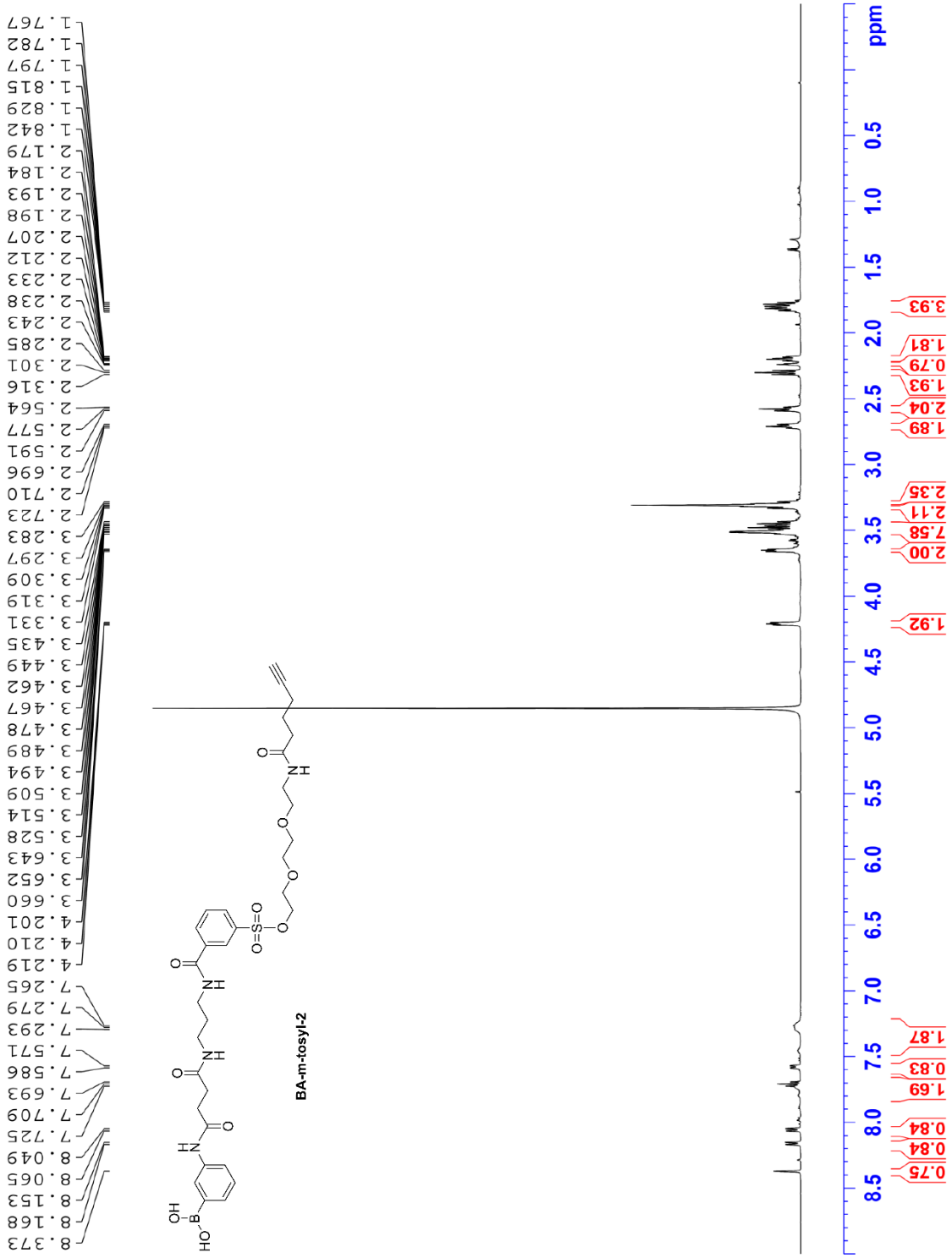


Figure S38. ^{1}H NMR spectrum of Compound **BA-m-tosyl-2** in MeOD.

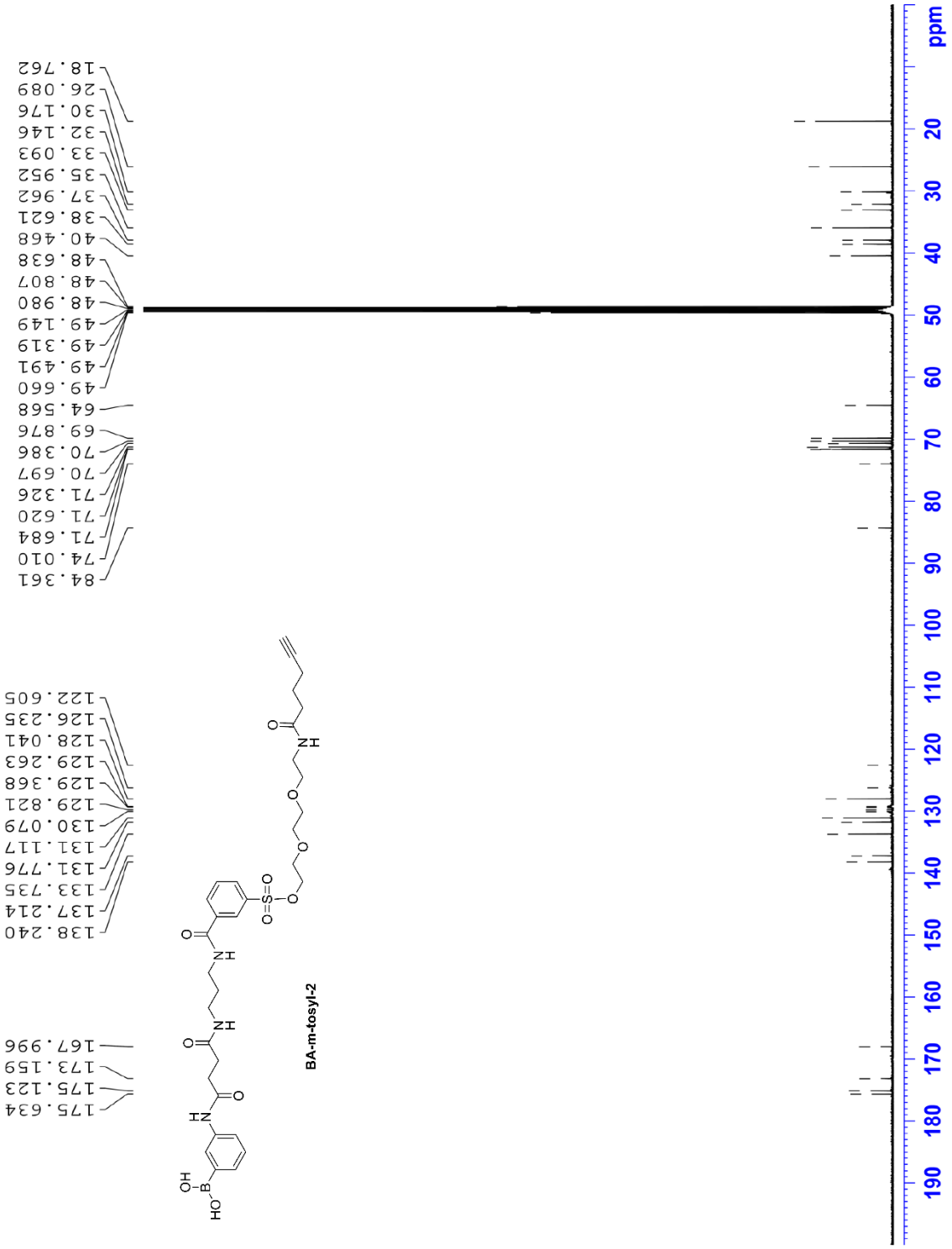


Figure S39. ^{13}C NMR spectrum of Compound **BA-m-tosyl-2** in MeOD.

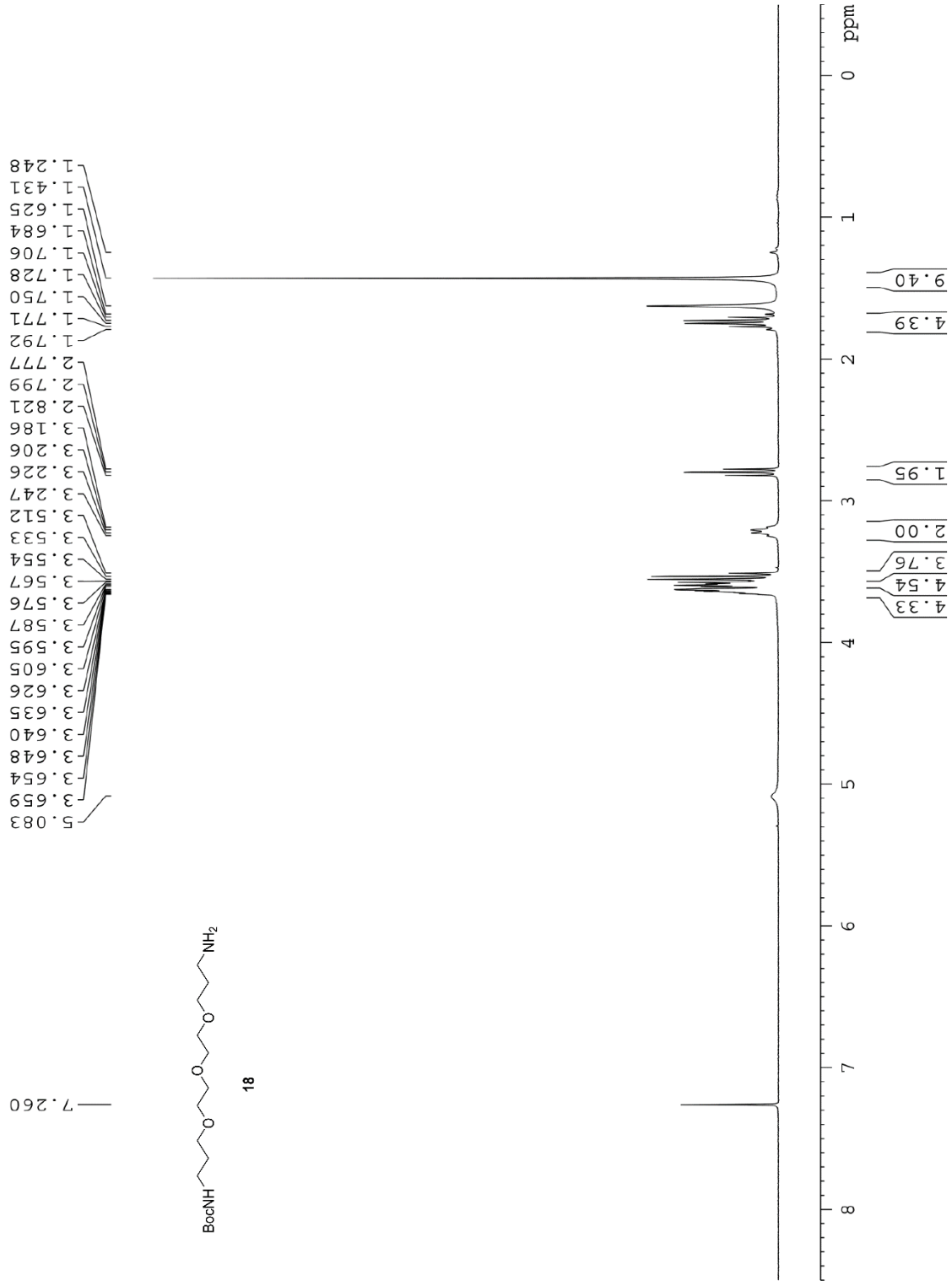


Figure S40. ^{1}H NMR spectrum of Compound **18** in $CDCl_3$.

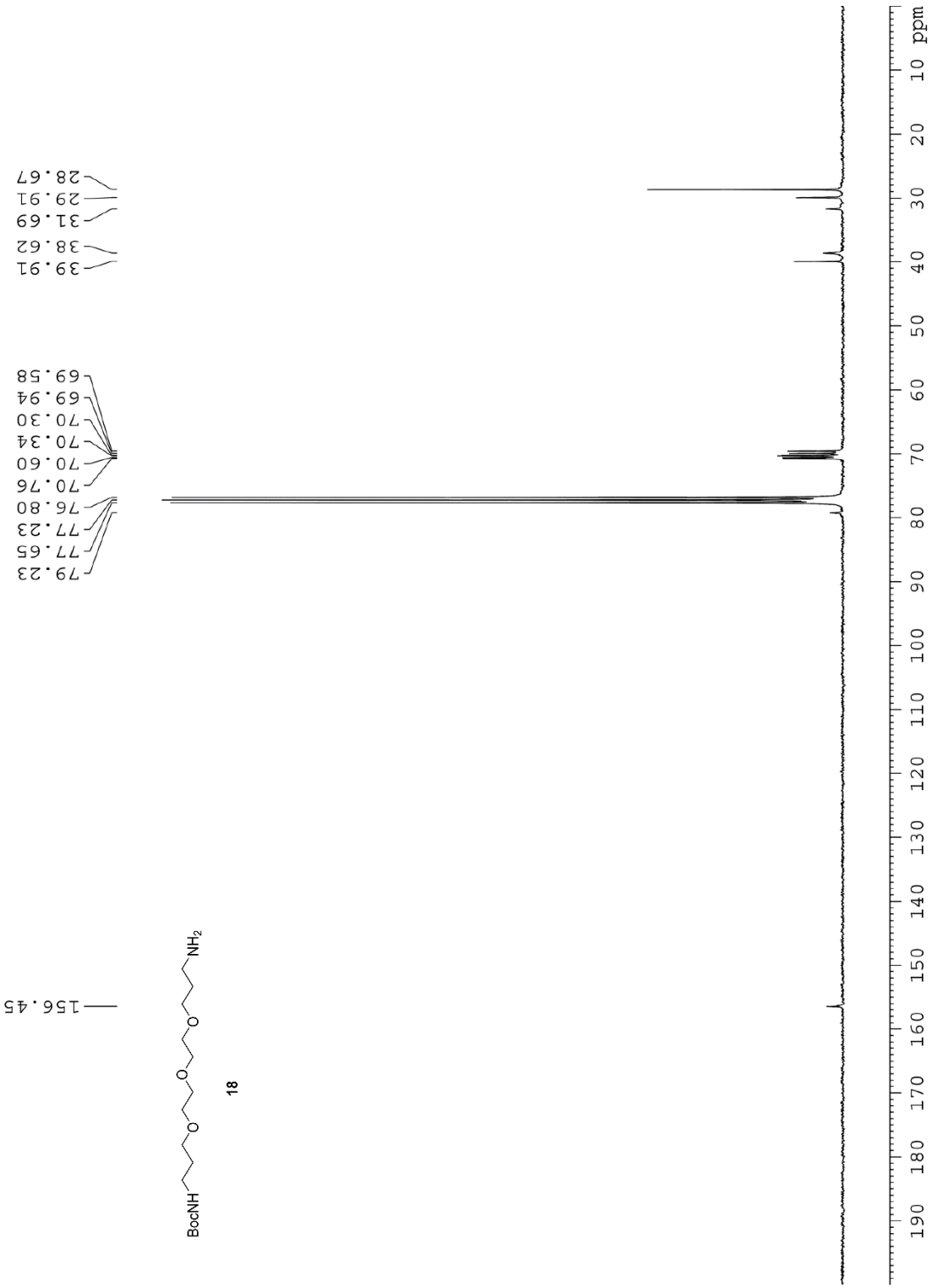


Figure S41. ^{13}C NMR spectrum of Compound **18** in $CDCl_3$.

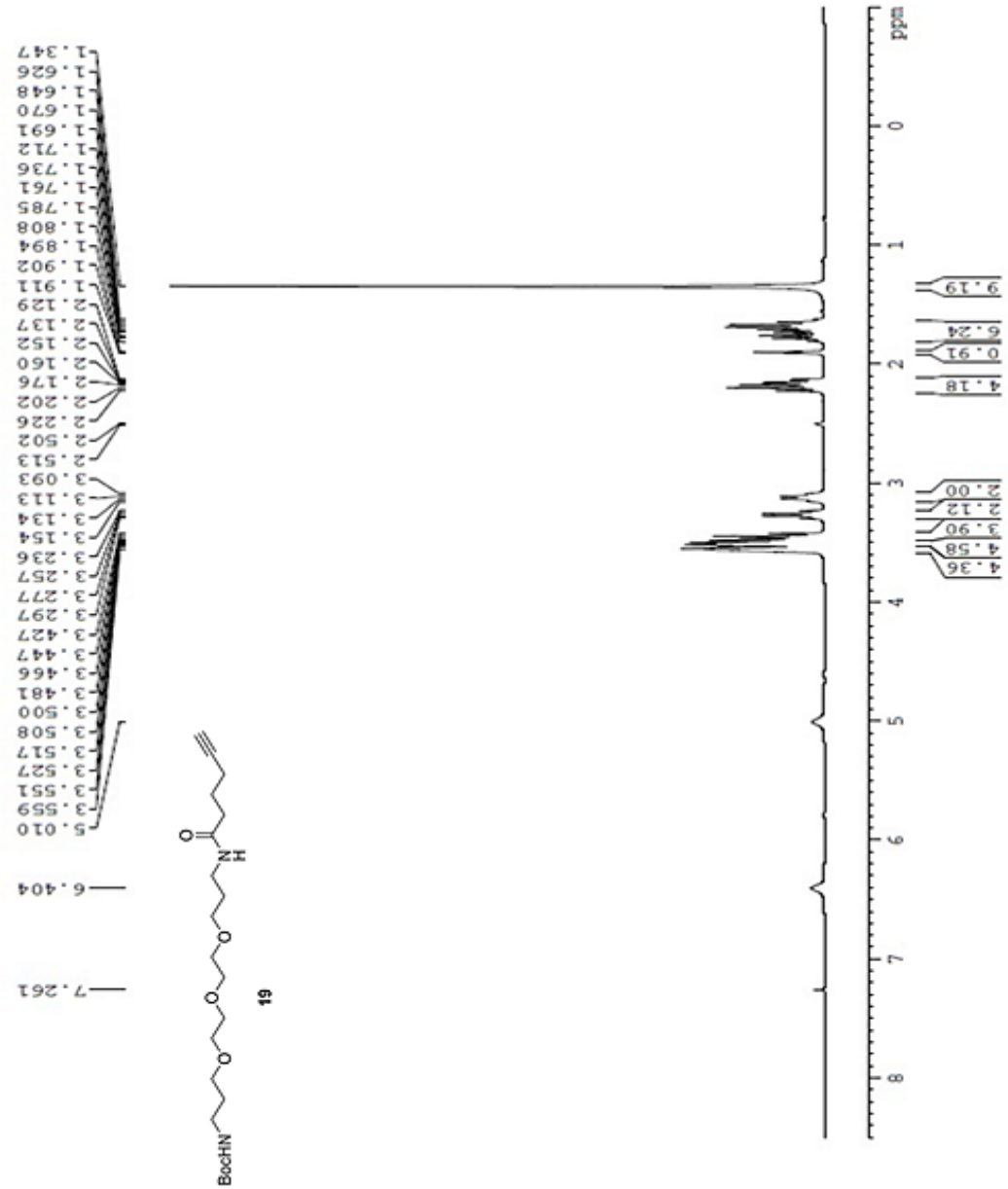


Figure S42. ^{1}H NMR spectrum of Compound **19** in $CDCl_3$.

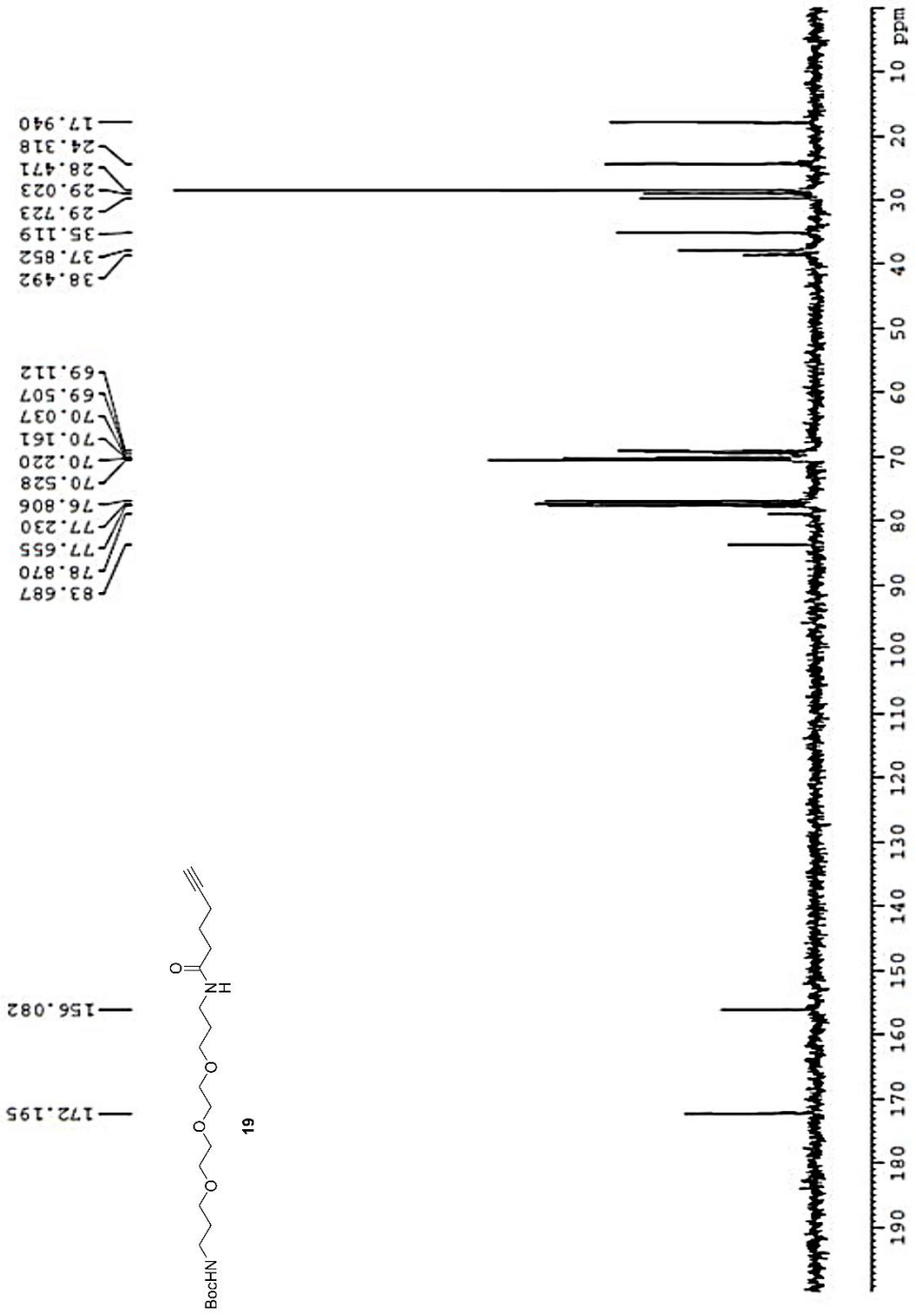


Figure S43. ^{13}C NMR spectrum of Compound **19** in $CDCl_3$.

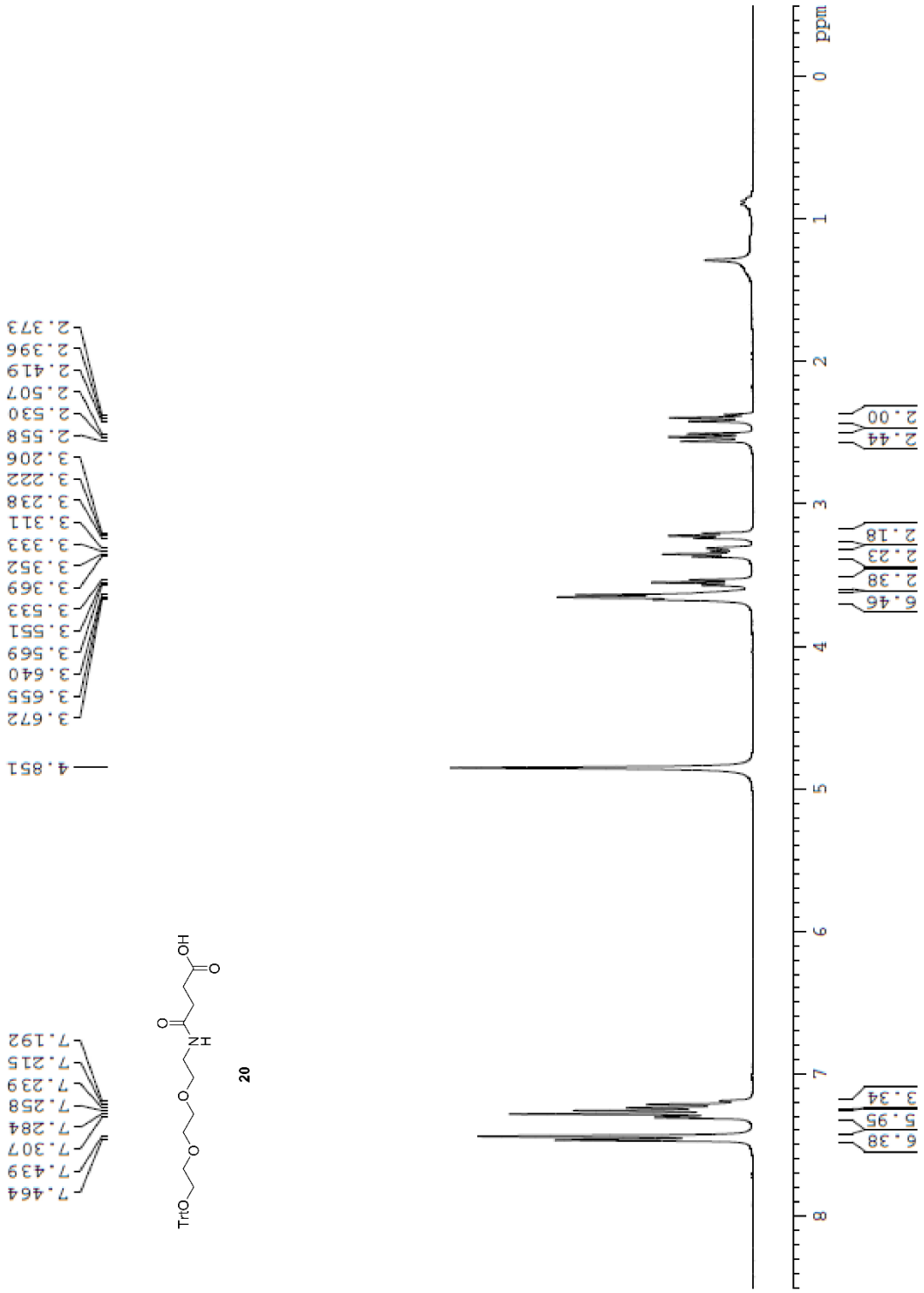


Figure S44. ^{1}H NMR spectrum of Compound **20** in MeOD.

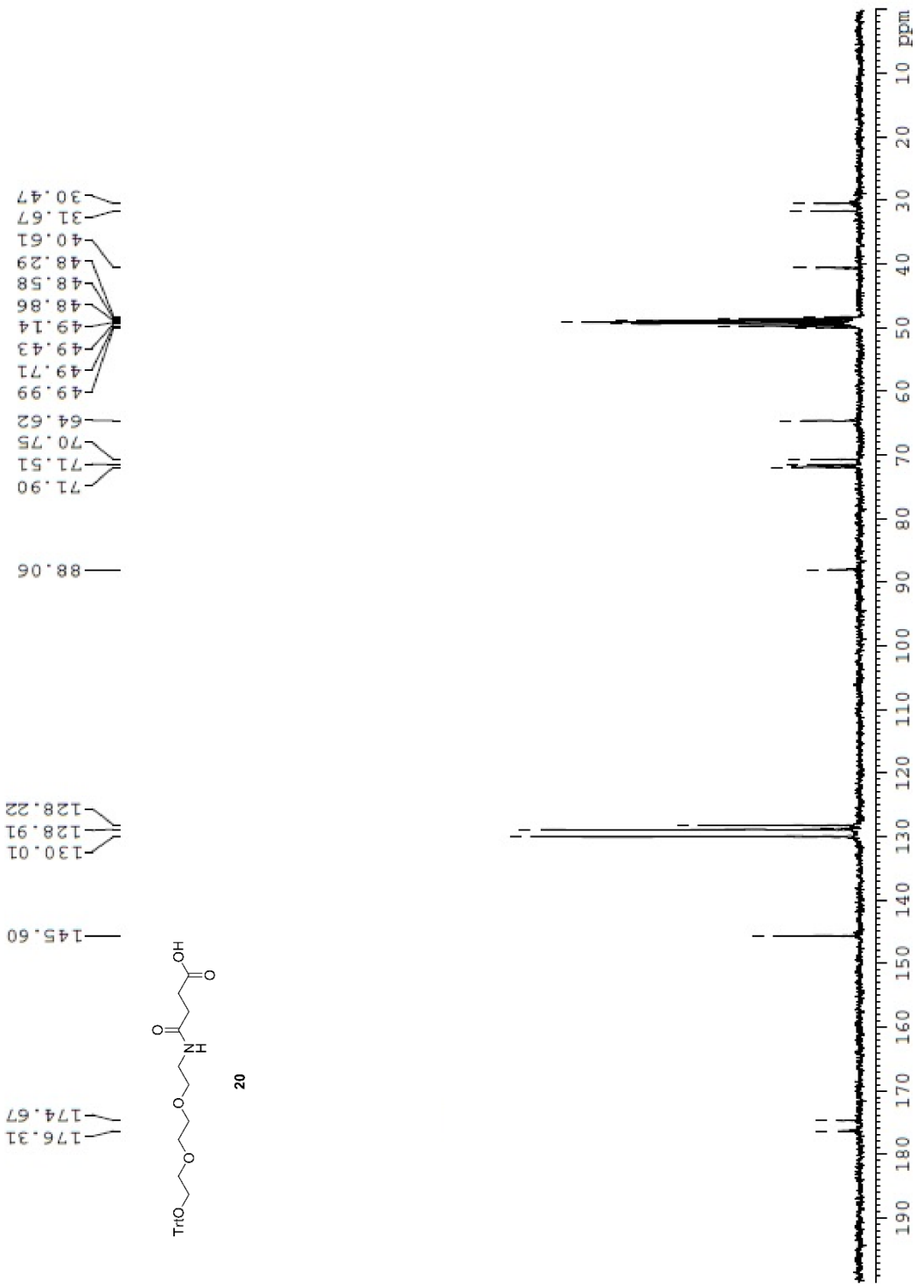


Figure S45. ^{13}C NMR spectrum of Compound **20** in MeOD.

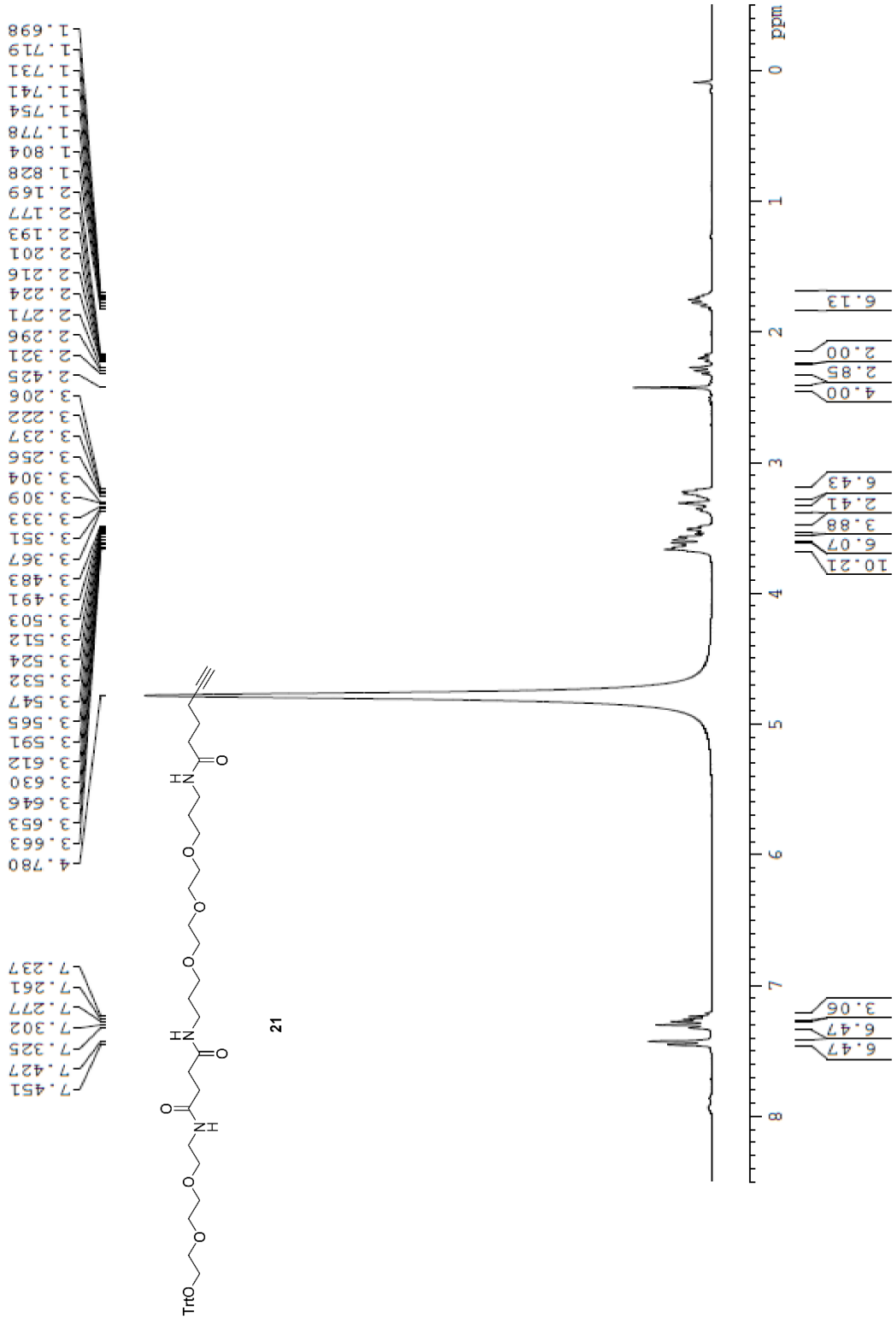


Figure S46. ^{1}H NMR spectrum of Compound **21** in MeOD.

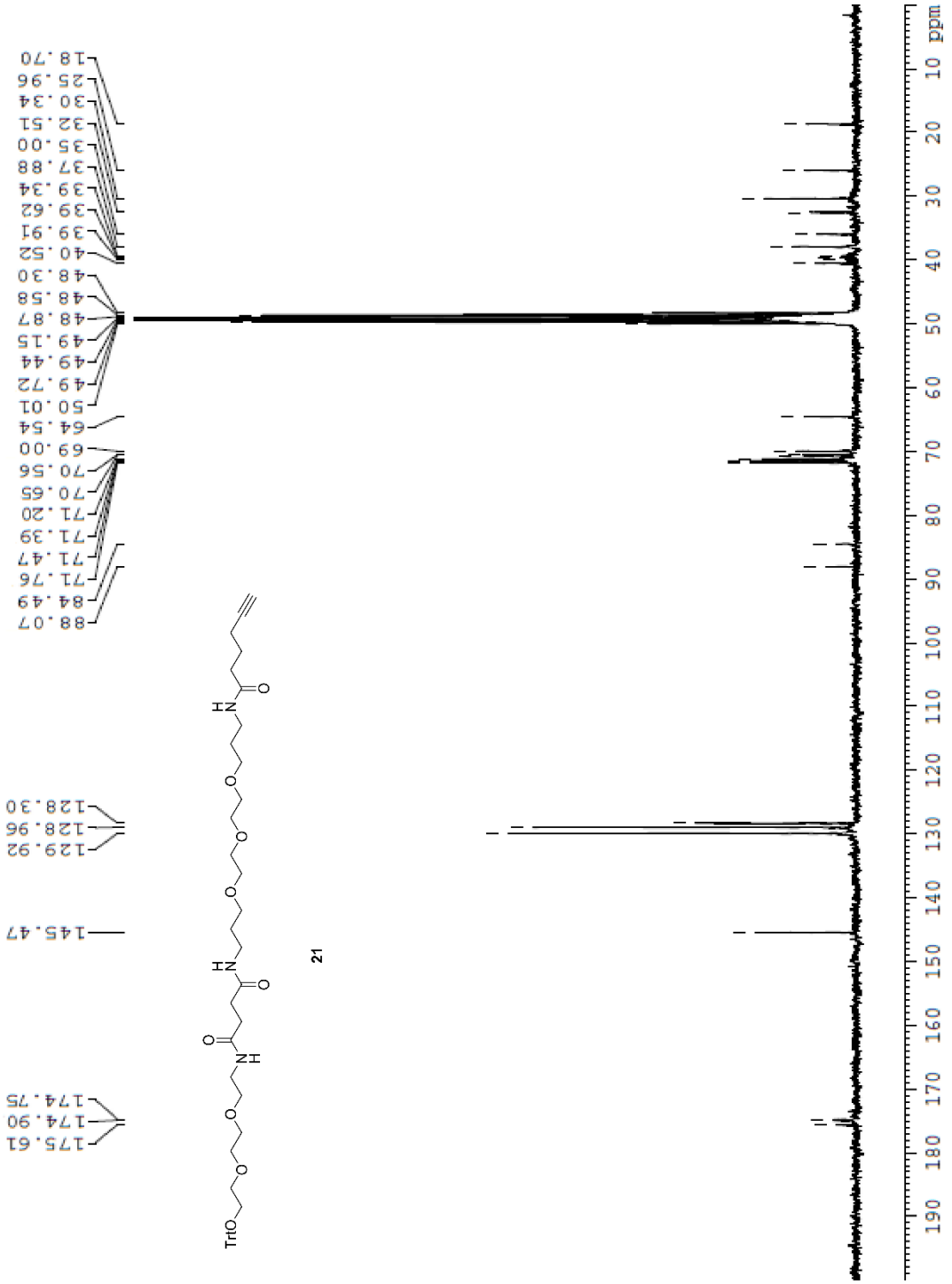


Figure S47. ^{13}C NMR spectrum of Compound **21** in MeOD.

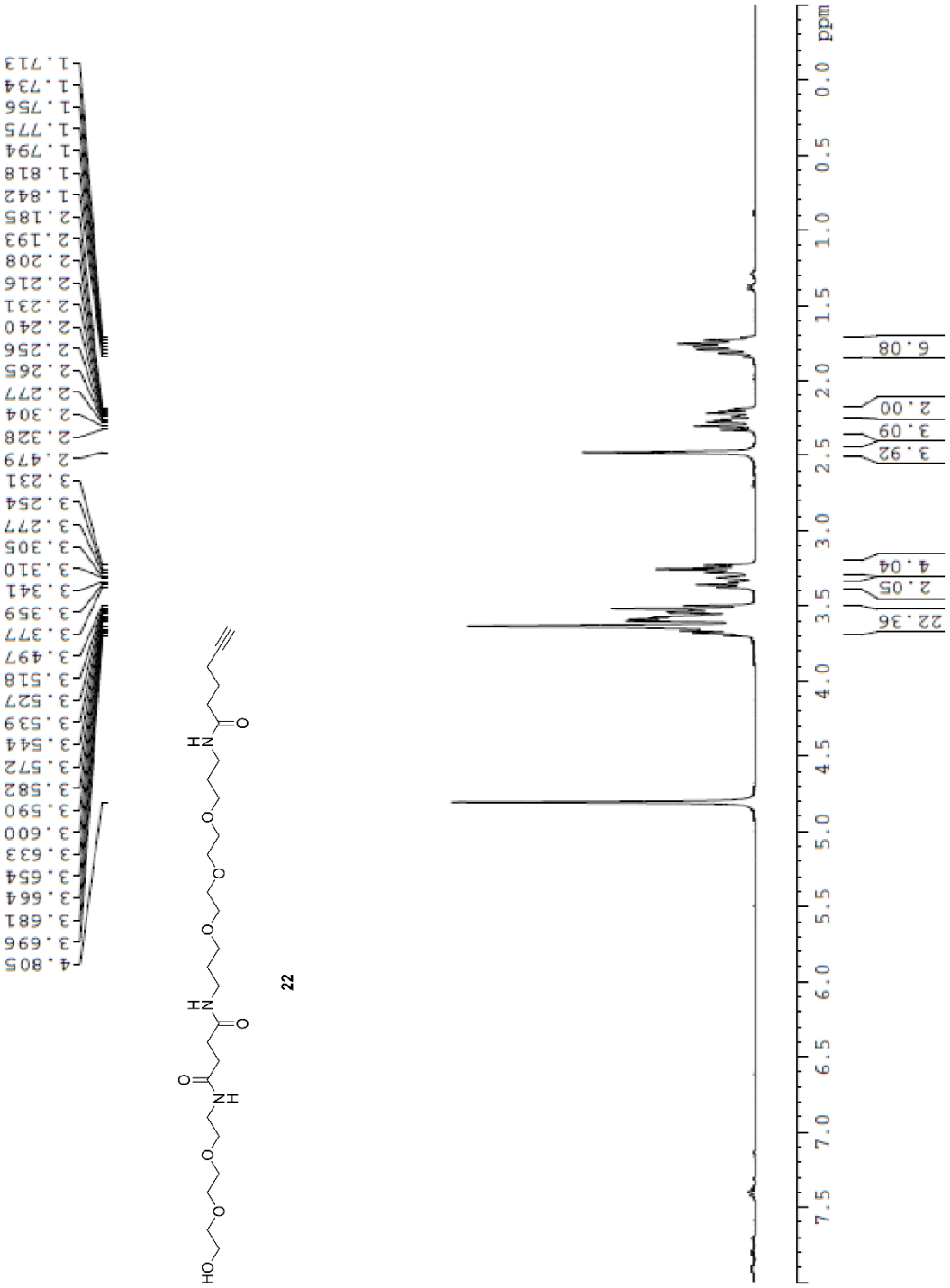


Figure S48. ^{1}H NMR spectrum of Compound **22** in MeOD.

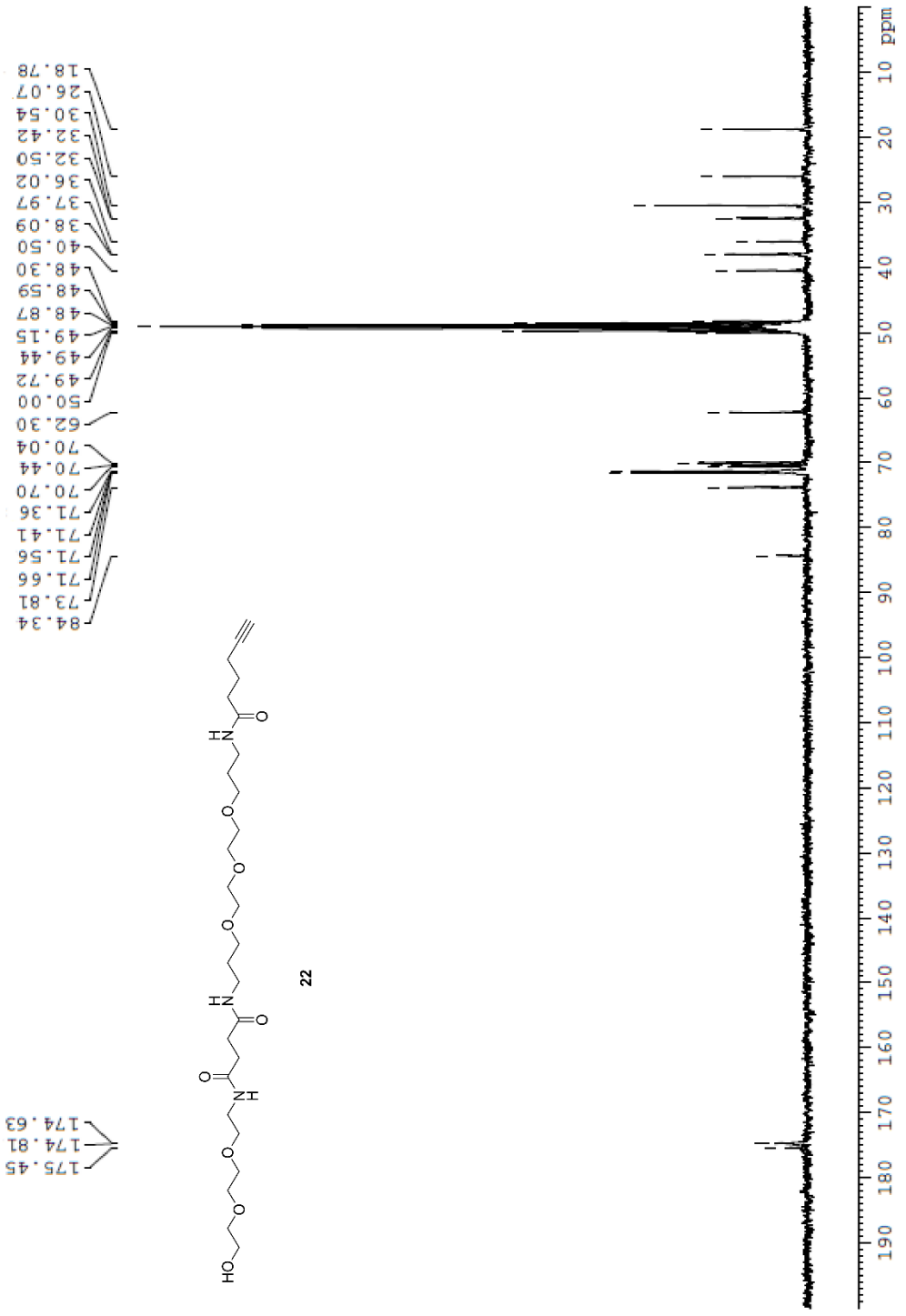


Figure S49. ^{13}C NMR spectrum of Compound **22** in MeOD.

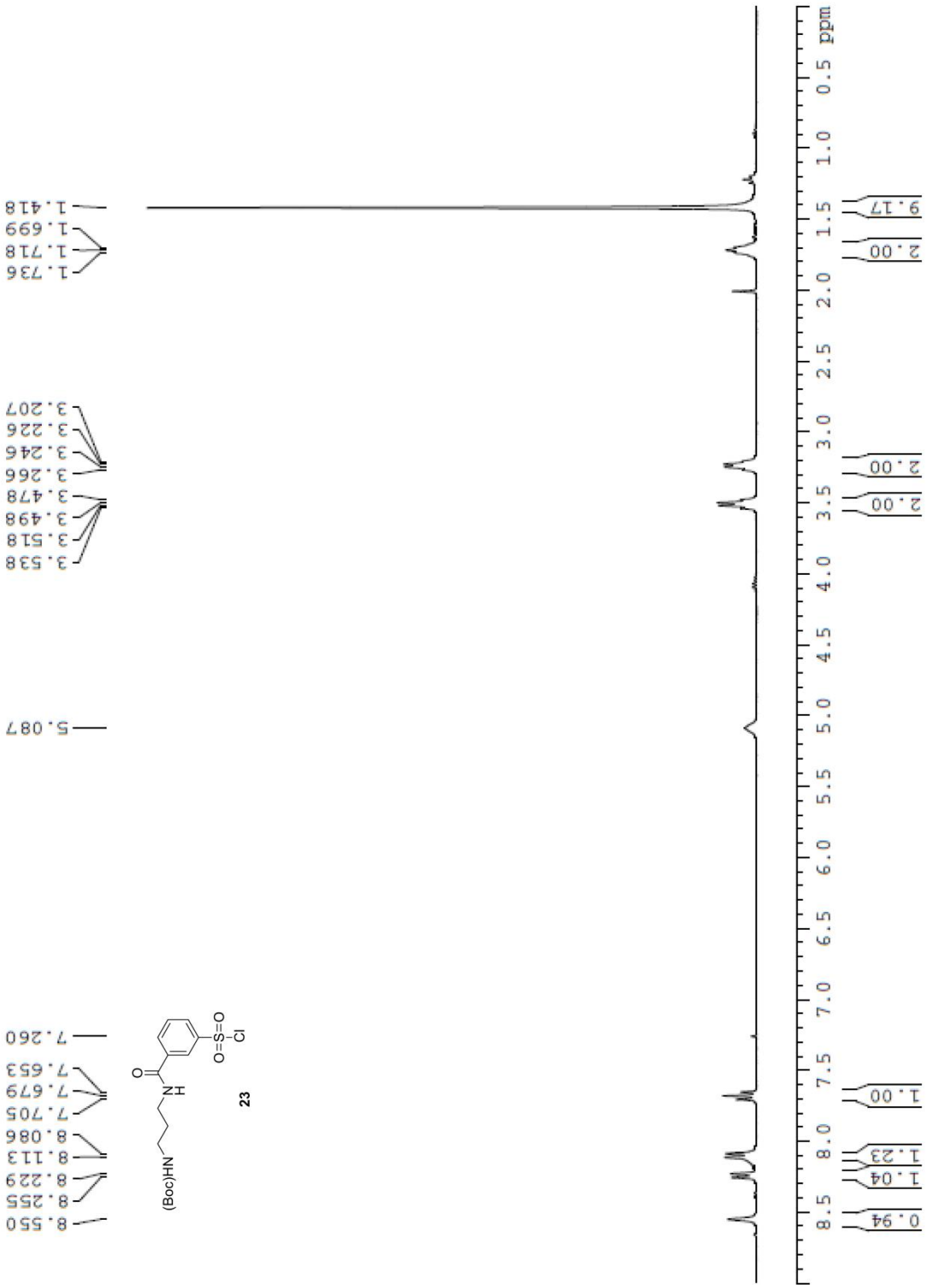


Figure S50. ^{1}H NMR spectrum of Compound **23** in $CDCl_3$.

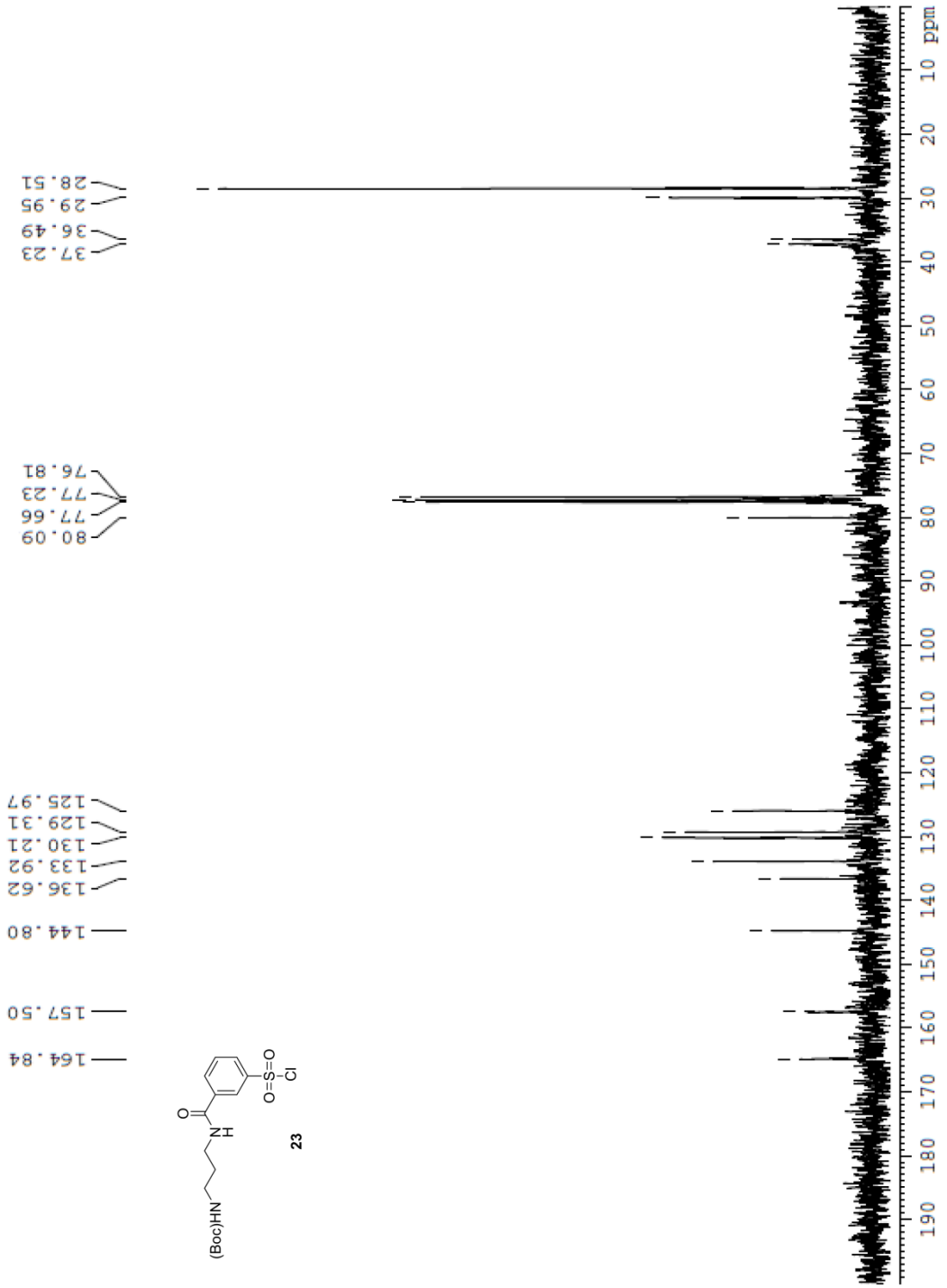


Figure S51. ^{13}C NMR spectrum of Compound **23** in $CDCl_3$.

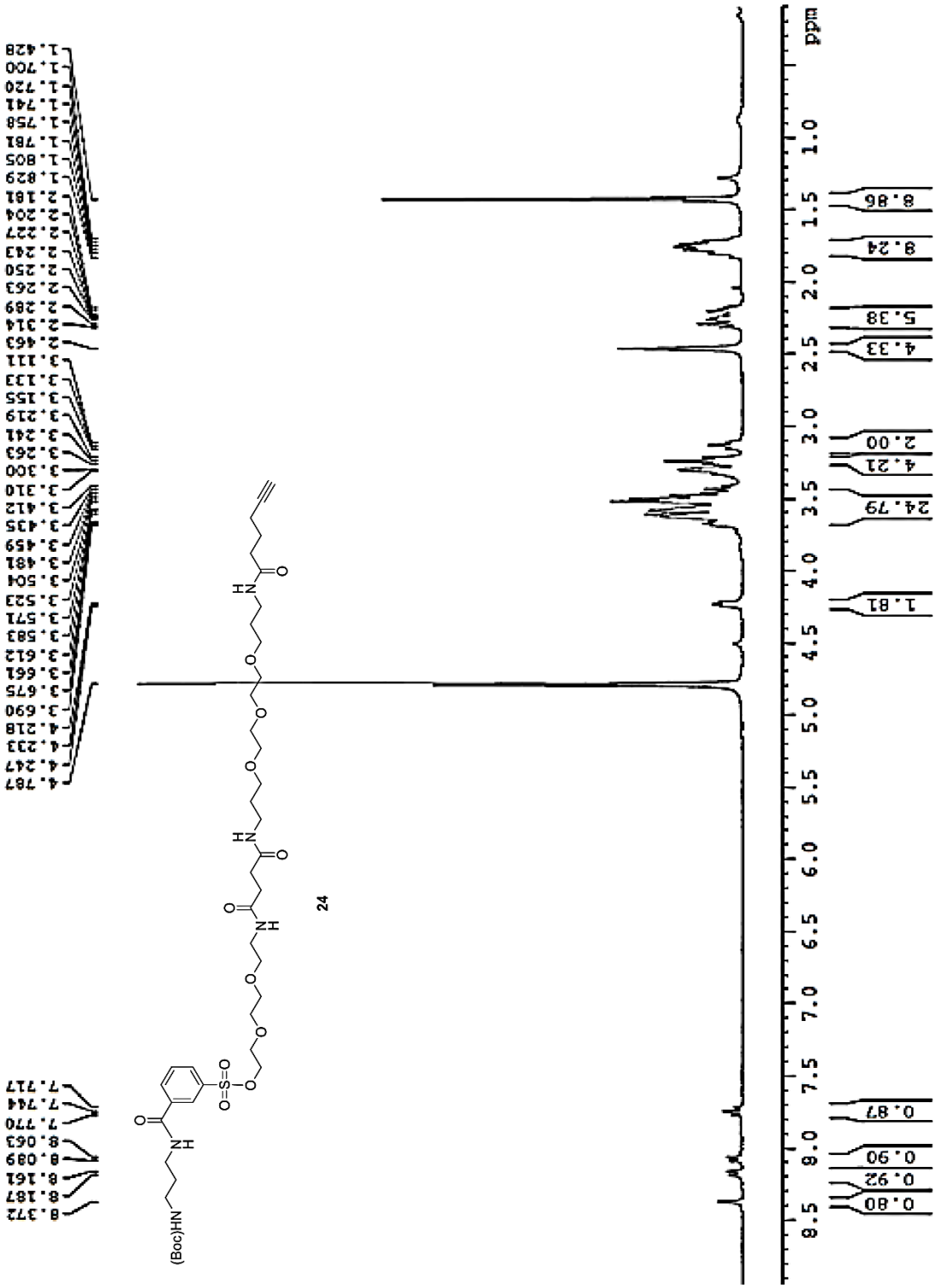


Figure S52. ^{1}H NMR spectrum of Compound **24** in MeOD.

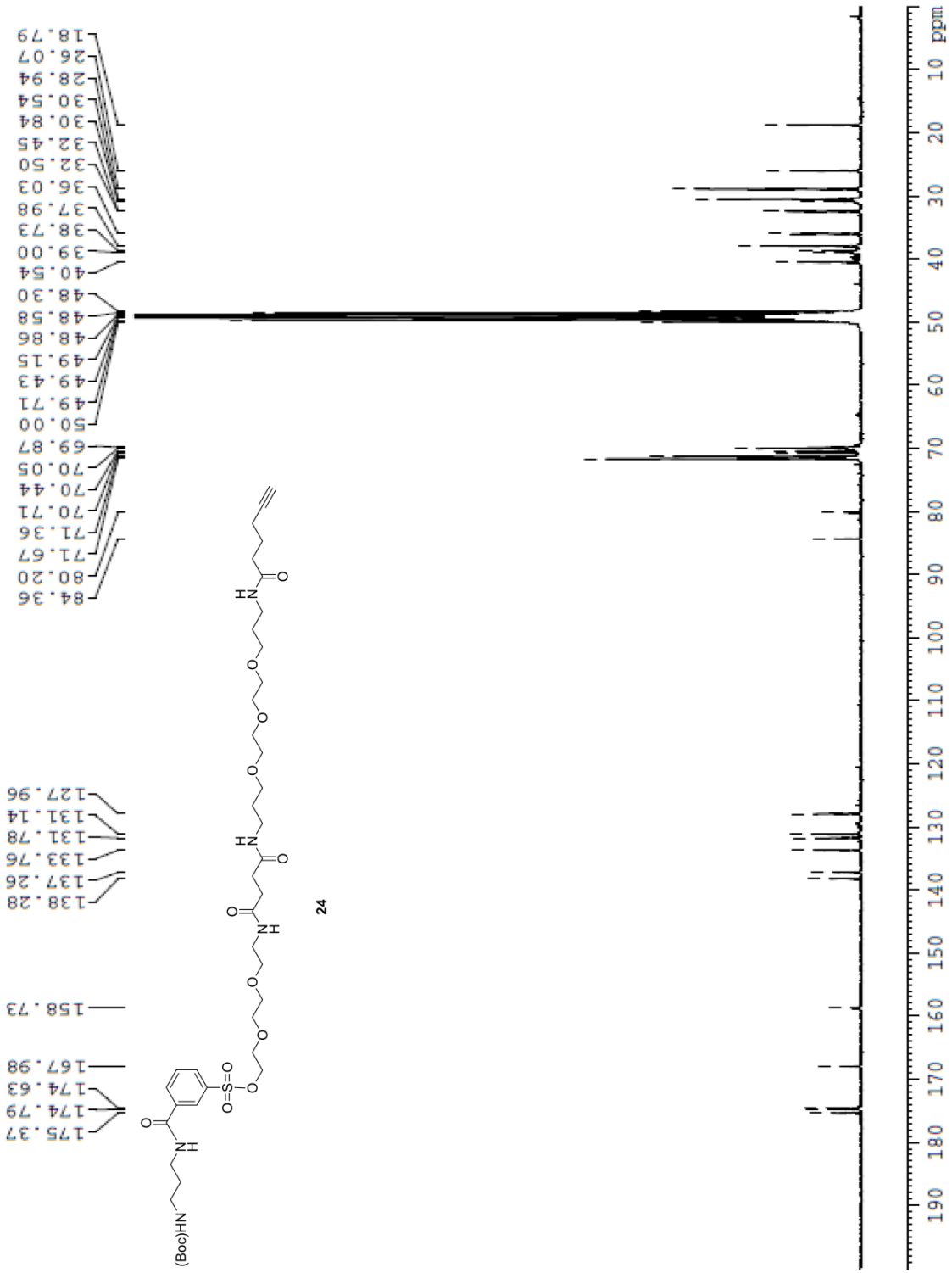


Figure S53. ^{13}C NMR spectrum of Compound **24** in MeOD.

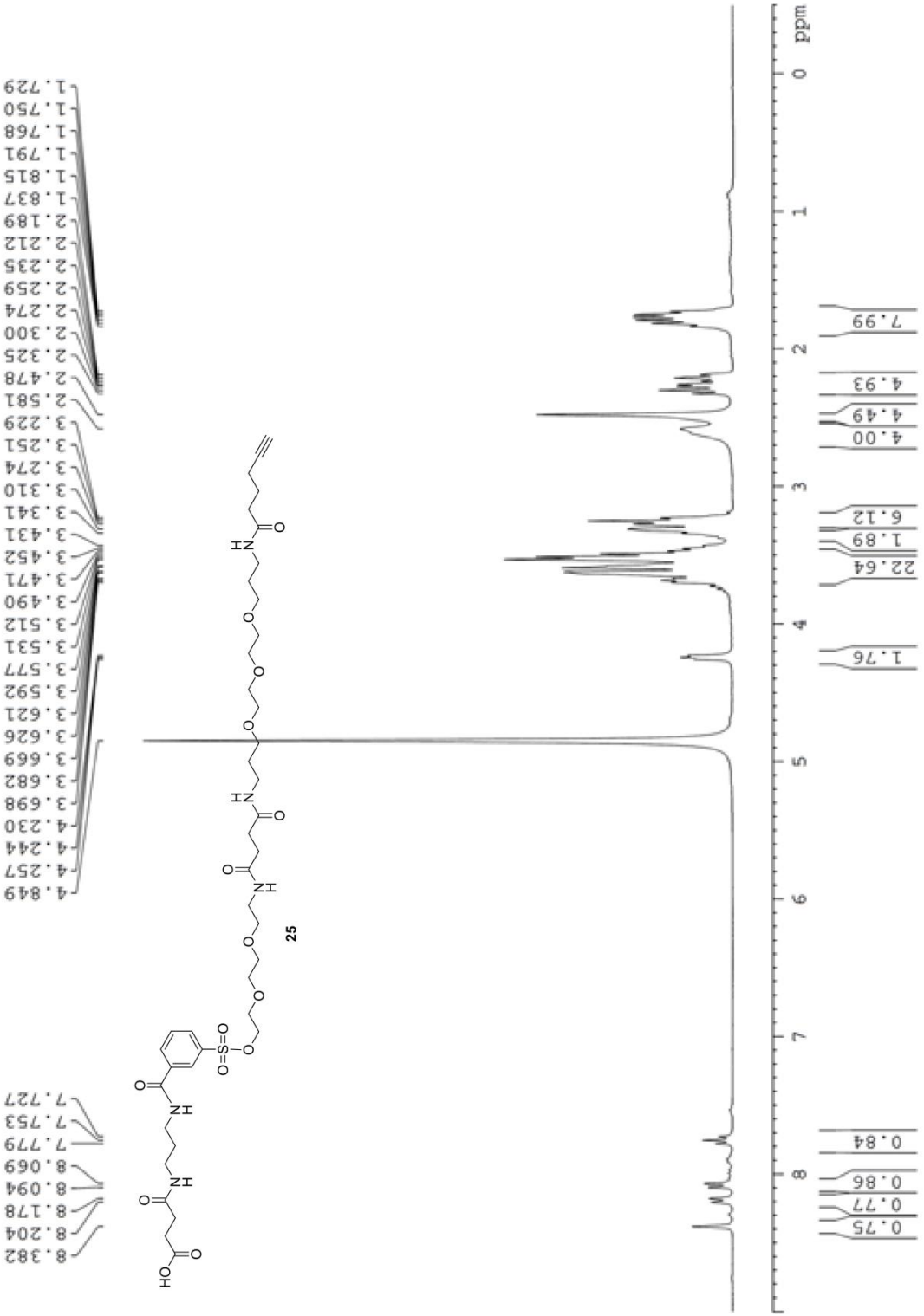


Figure S54. ^{1}H NMR spectrum of Compound **25** in MeOD.

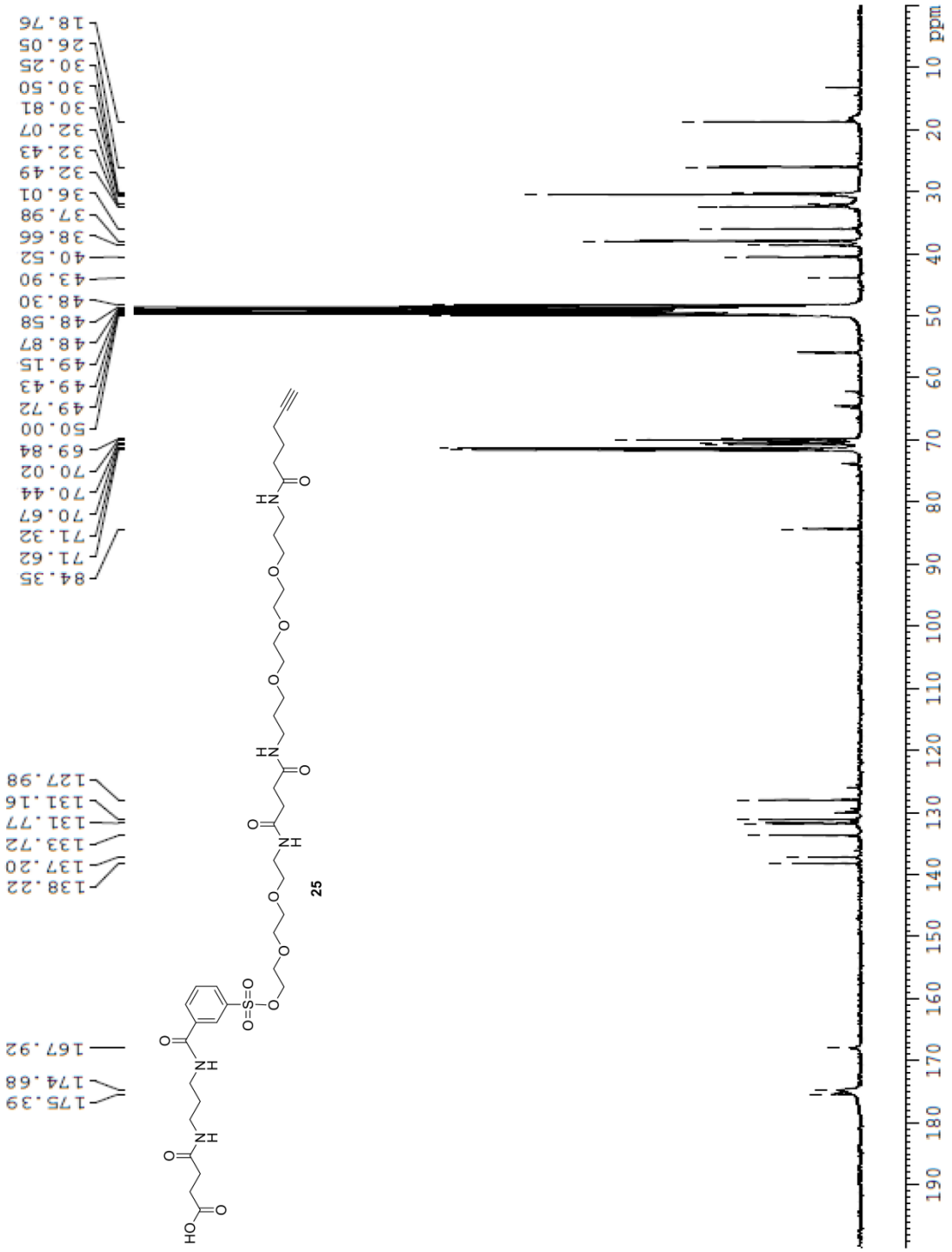


Figure S55. ^{13}C NMR spectrum of Compound **25** in MeOD.

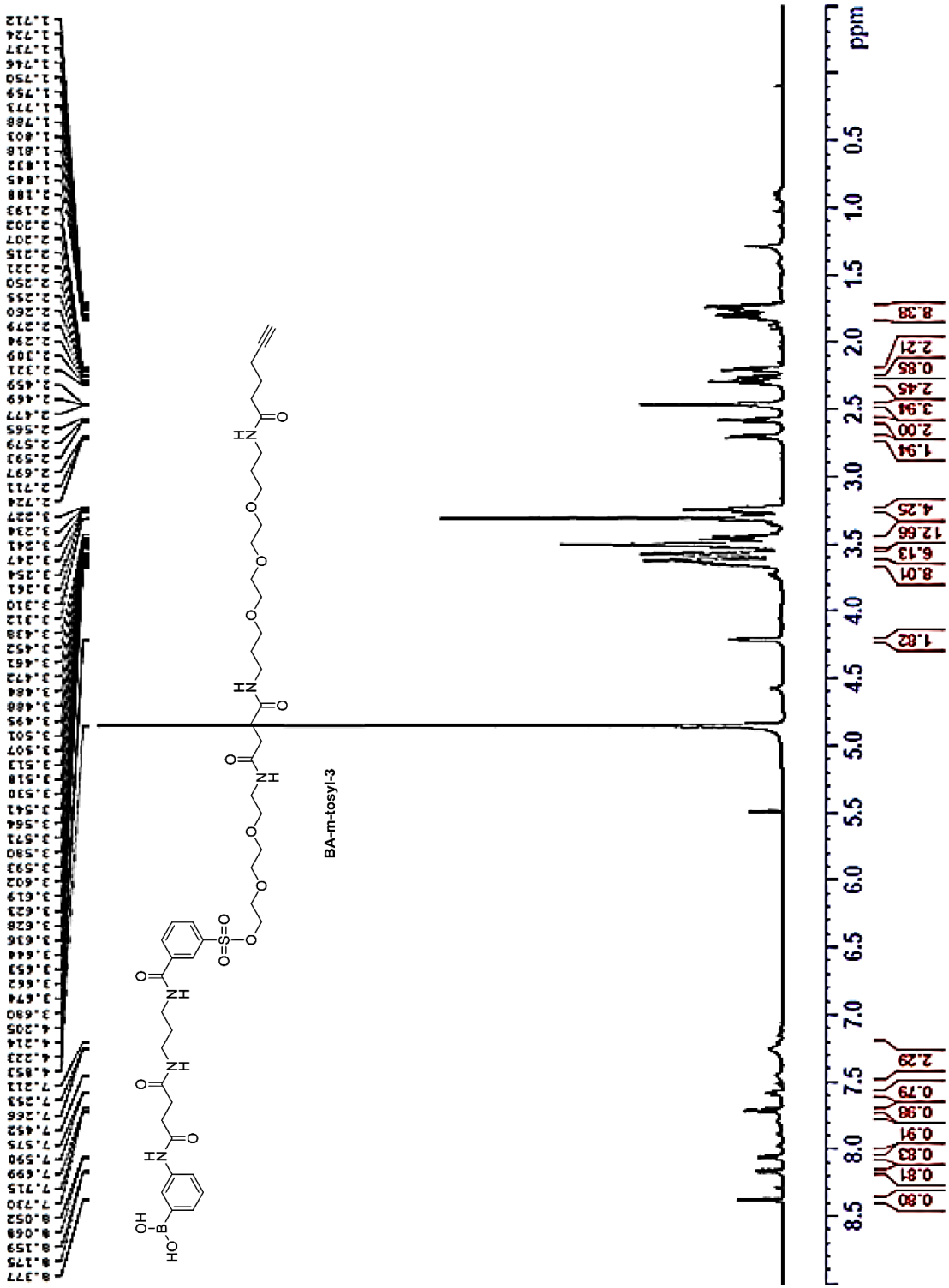


Figure S56. ^{1}H NMR spectrum of Compound **BA-m-tosyl-3** in MeOD.

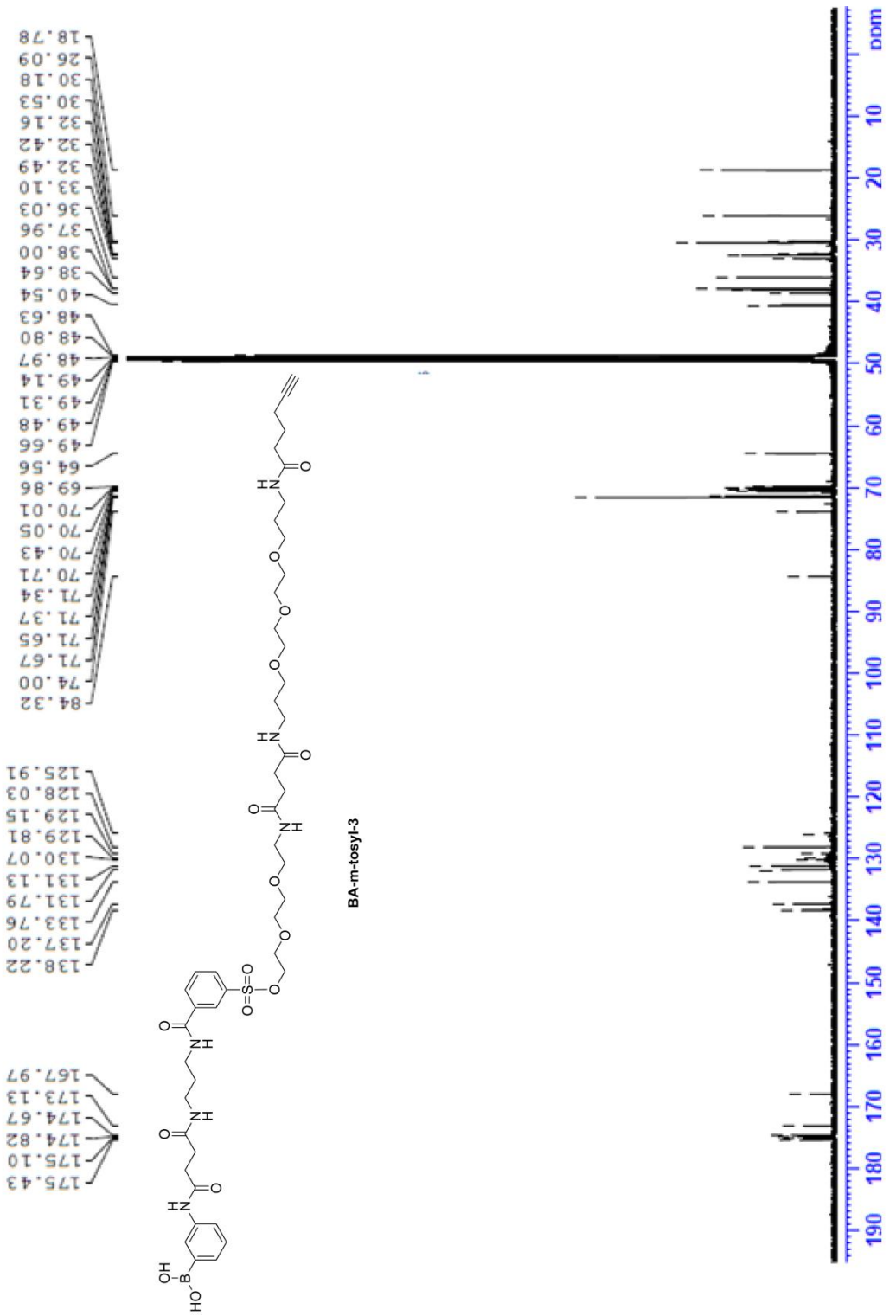


Figure S57. ^{13}C NMR spectrum of Compound **BA-m-tosyl-3** in MeOD.

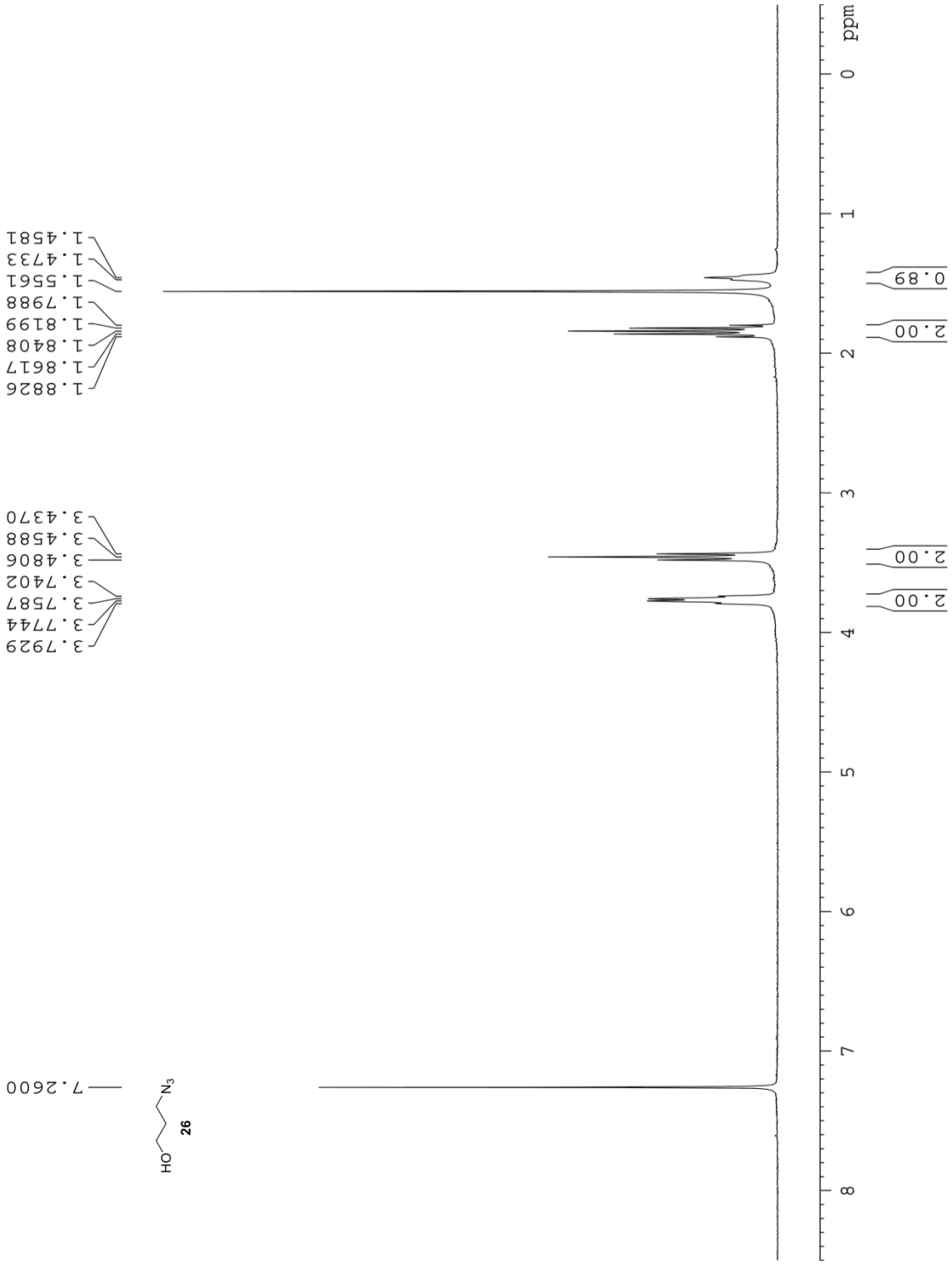


Figure S58. ^{1}H NMR spectrum of Compound **26** in $CDCl_3$.

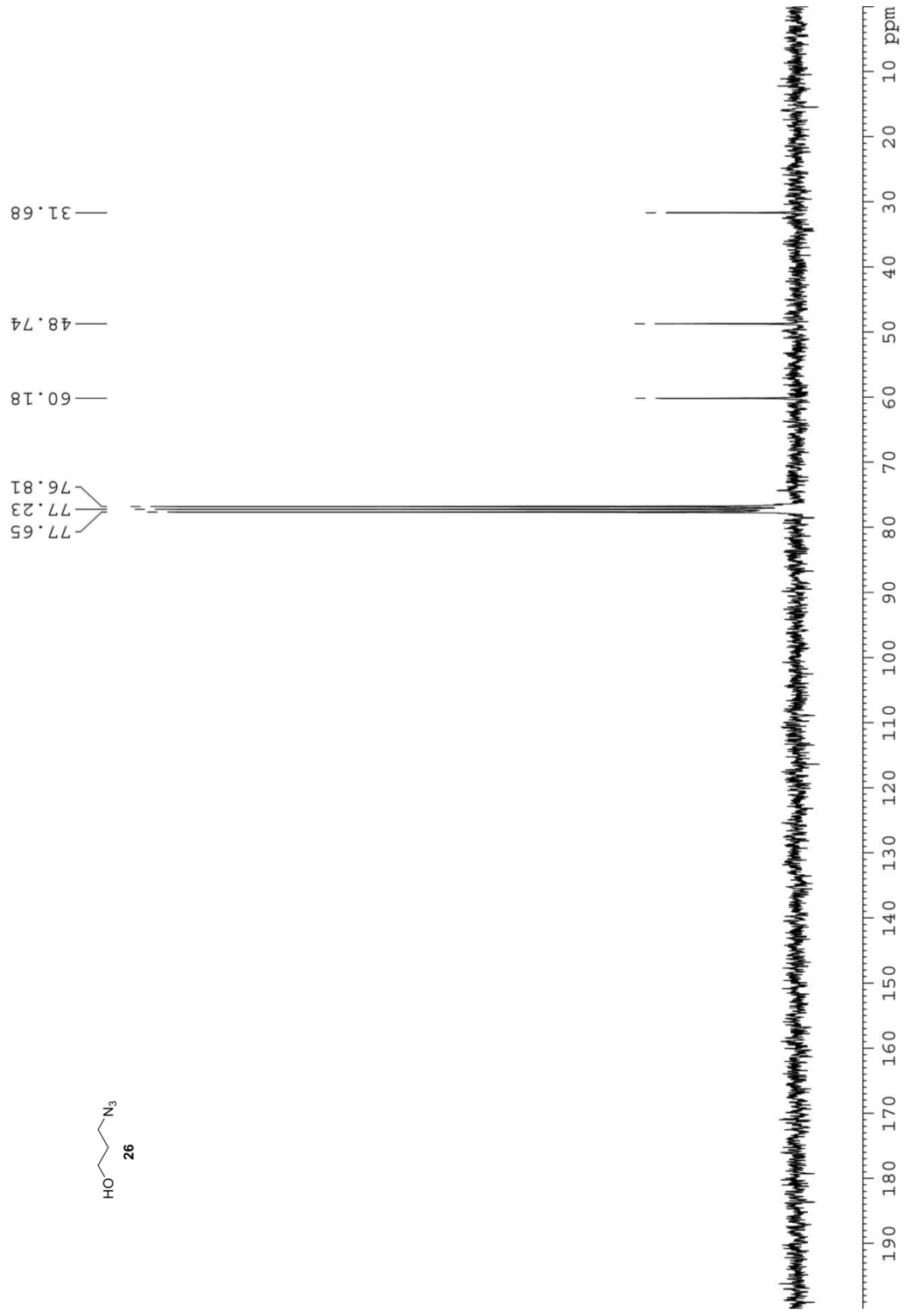


Figure S59. ^{13}C NMR spectrum of Compound **26** in $CDCl_3$.

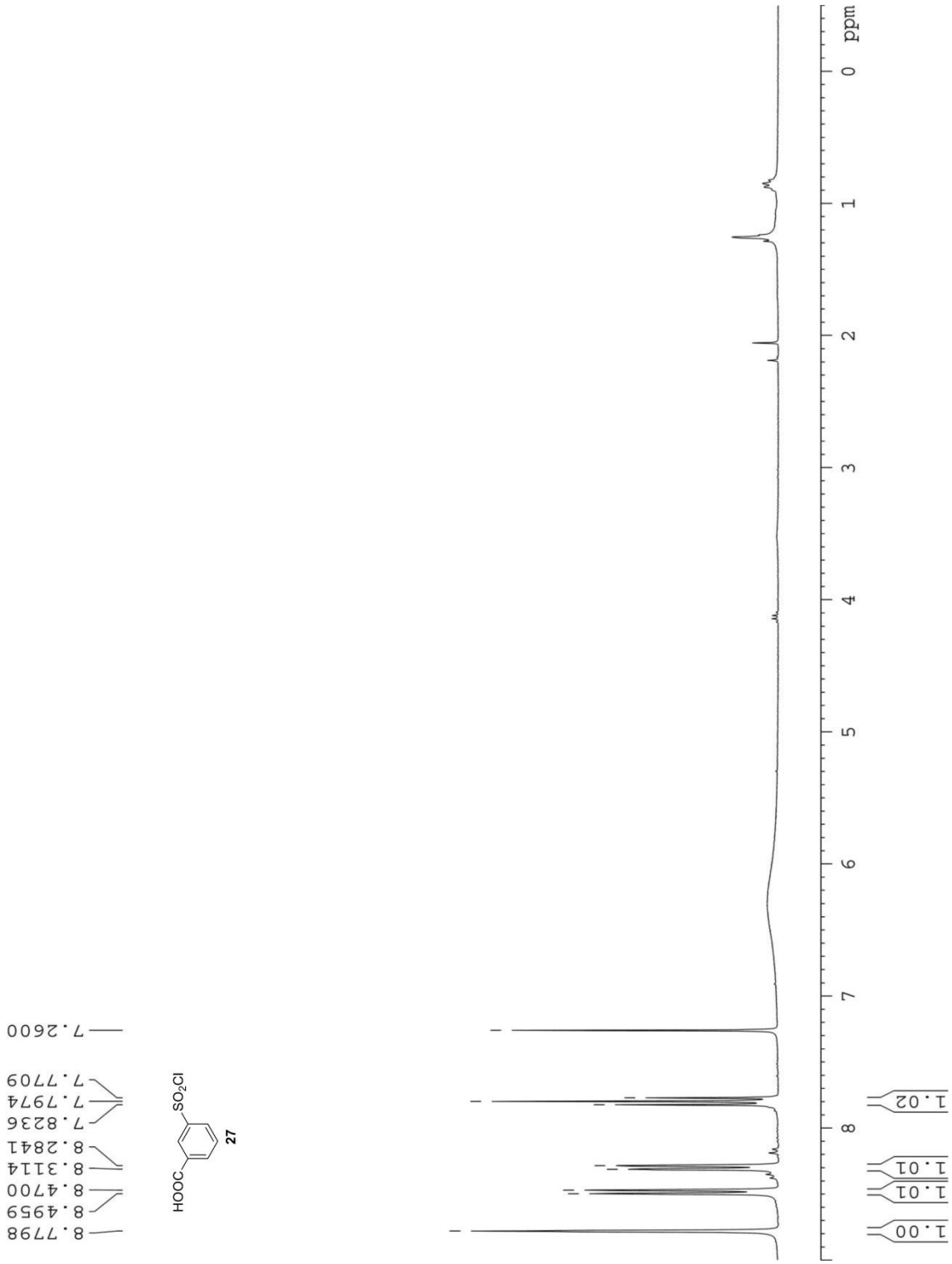


Figure S60. ^{1}H NMR spectrum of Compound **27** in $CDCl_3$.

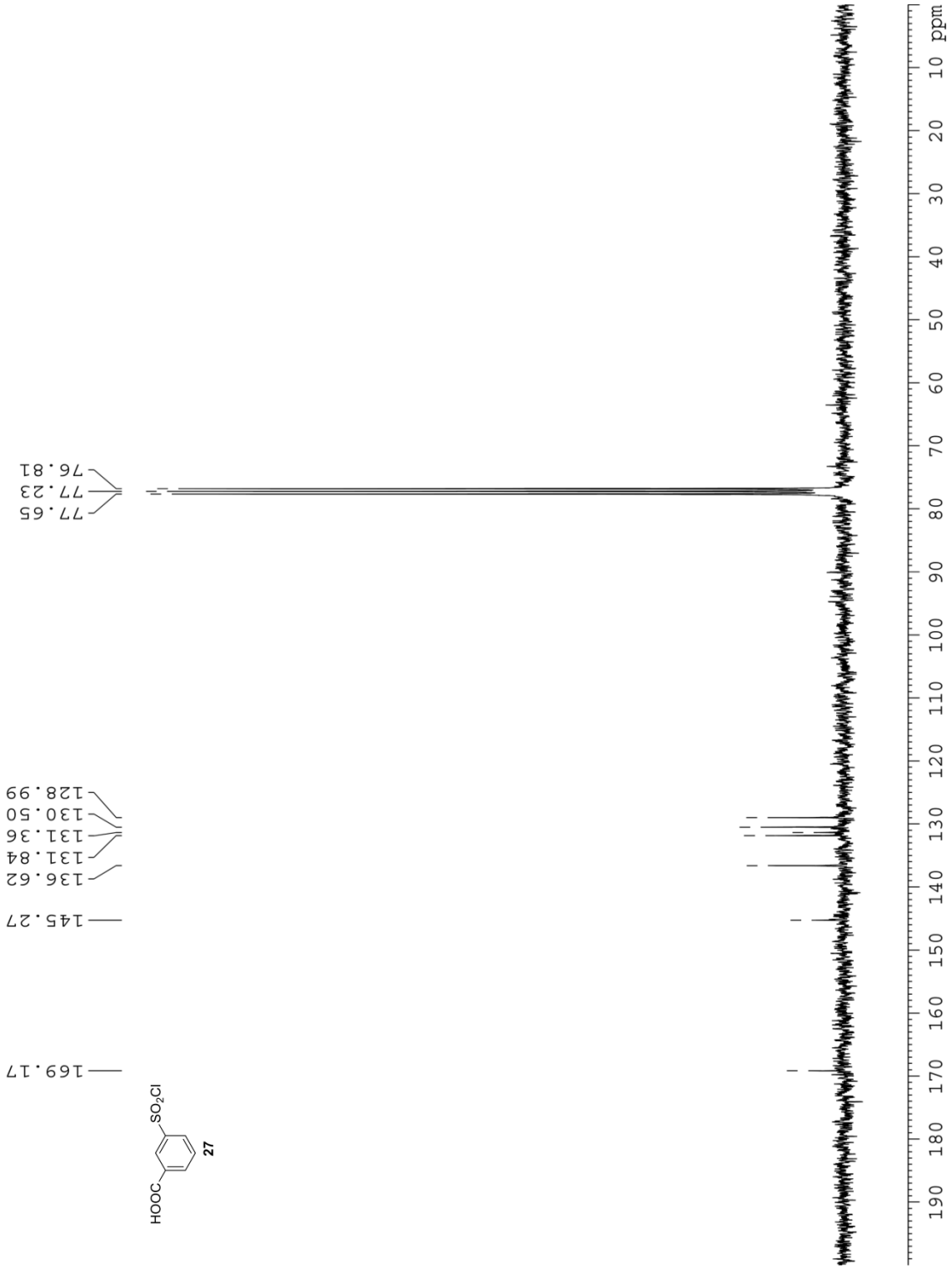


Figure S61. ^{13}C NMR spectrum of Compound **27** in $CDCl_3$.

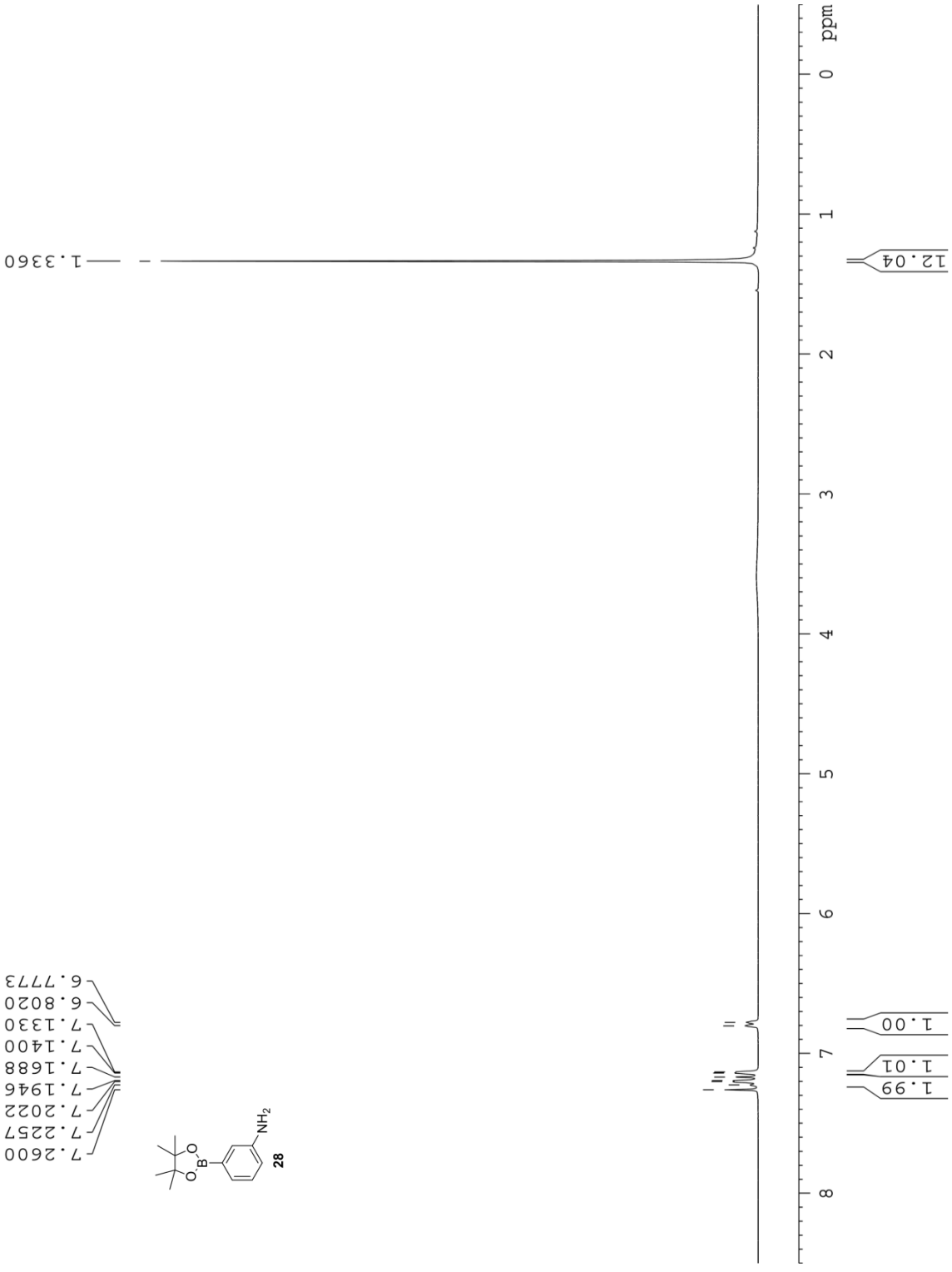


Figure S62. ^{1}H NMR spectrum of Compound **28** in $CDCl_3$.

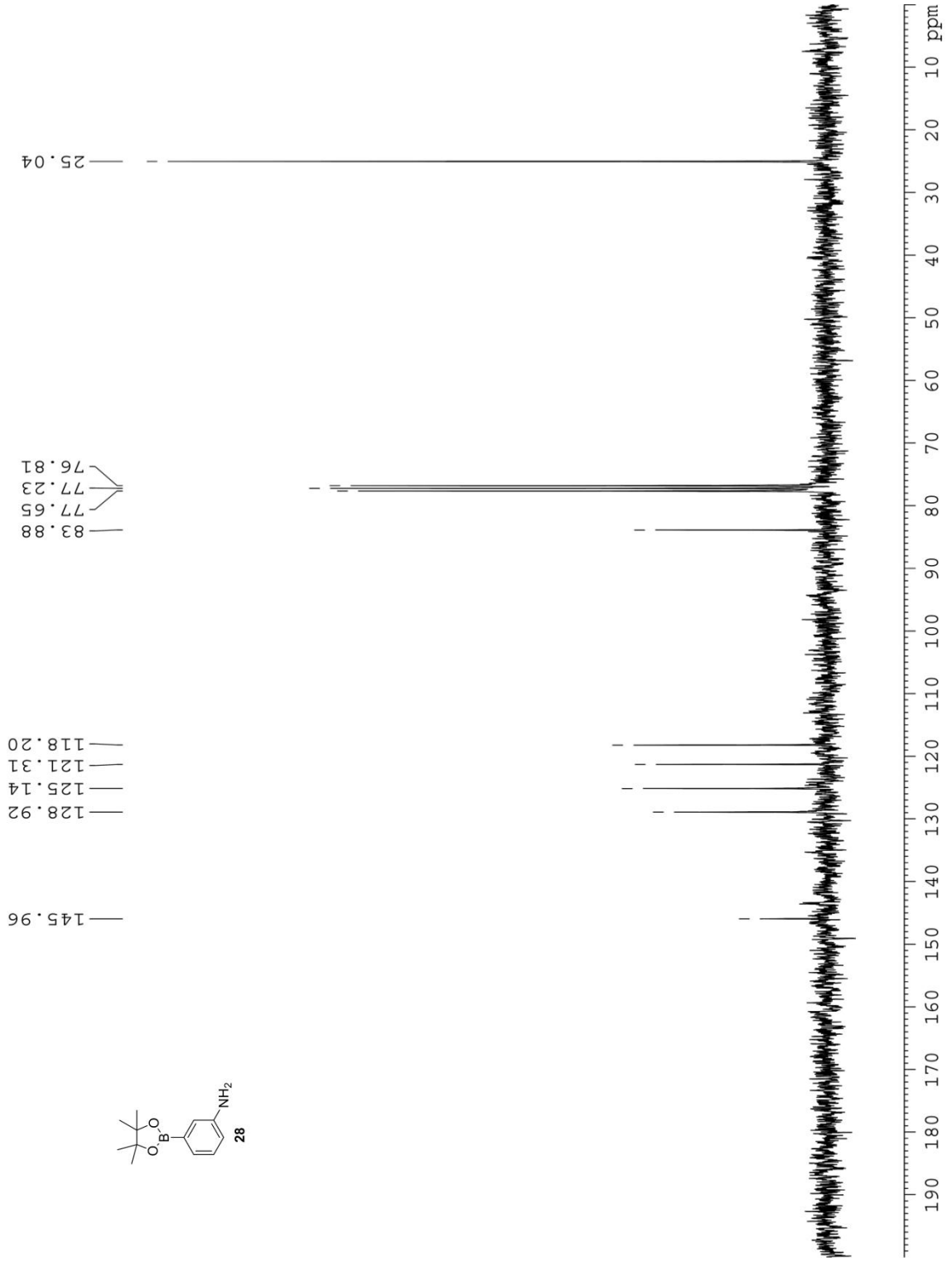


Figure S63. ^{13}C NMR spectrum of Compound **28** in $CDCl_3$.

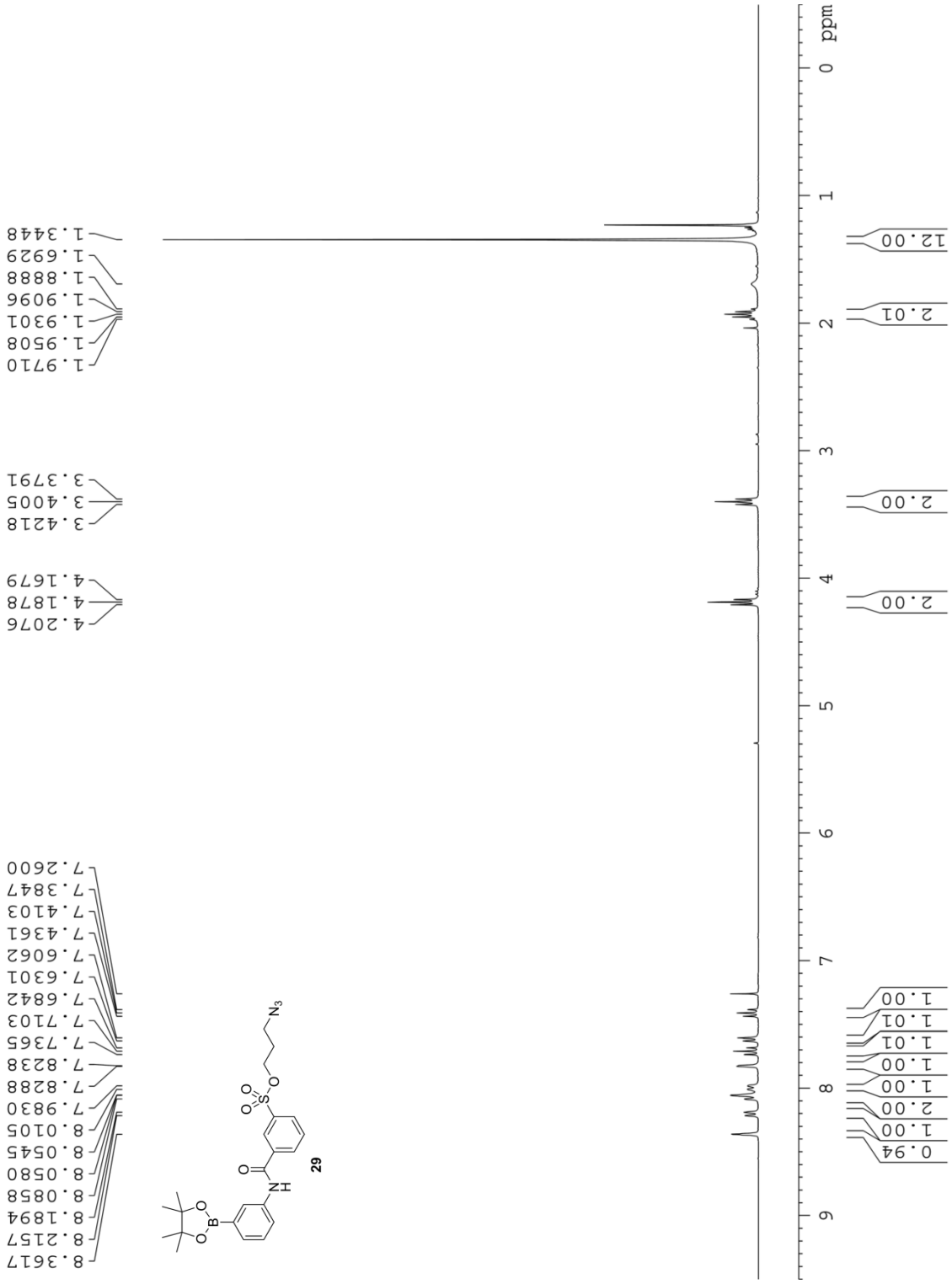


Figure S64. ^{1}H NMR spectrum of Compound **29** in $CDCl_3$.

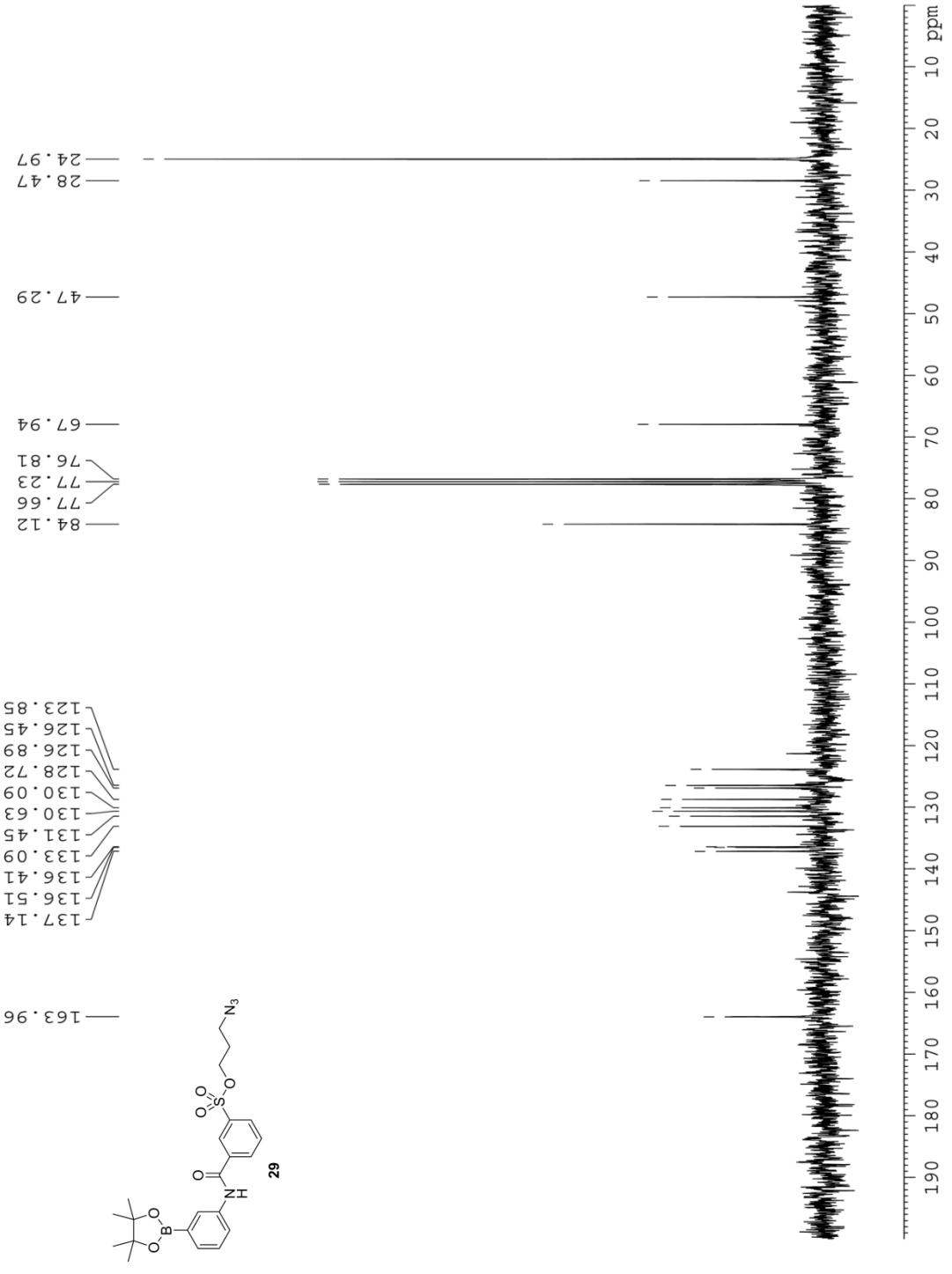


Figure S65. ^{13}C NMR spectrum of Compound **29** in $CDCl_3$.

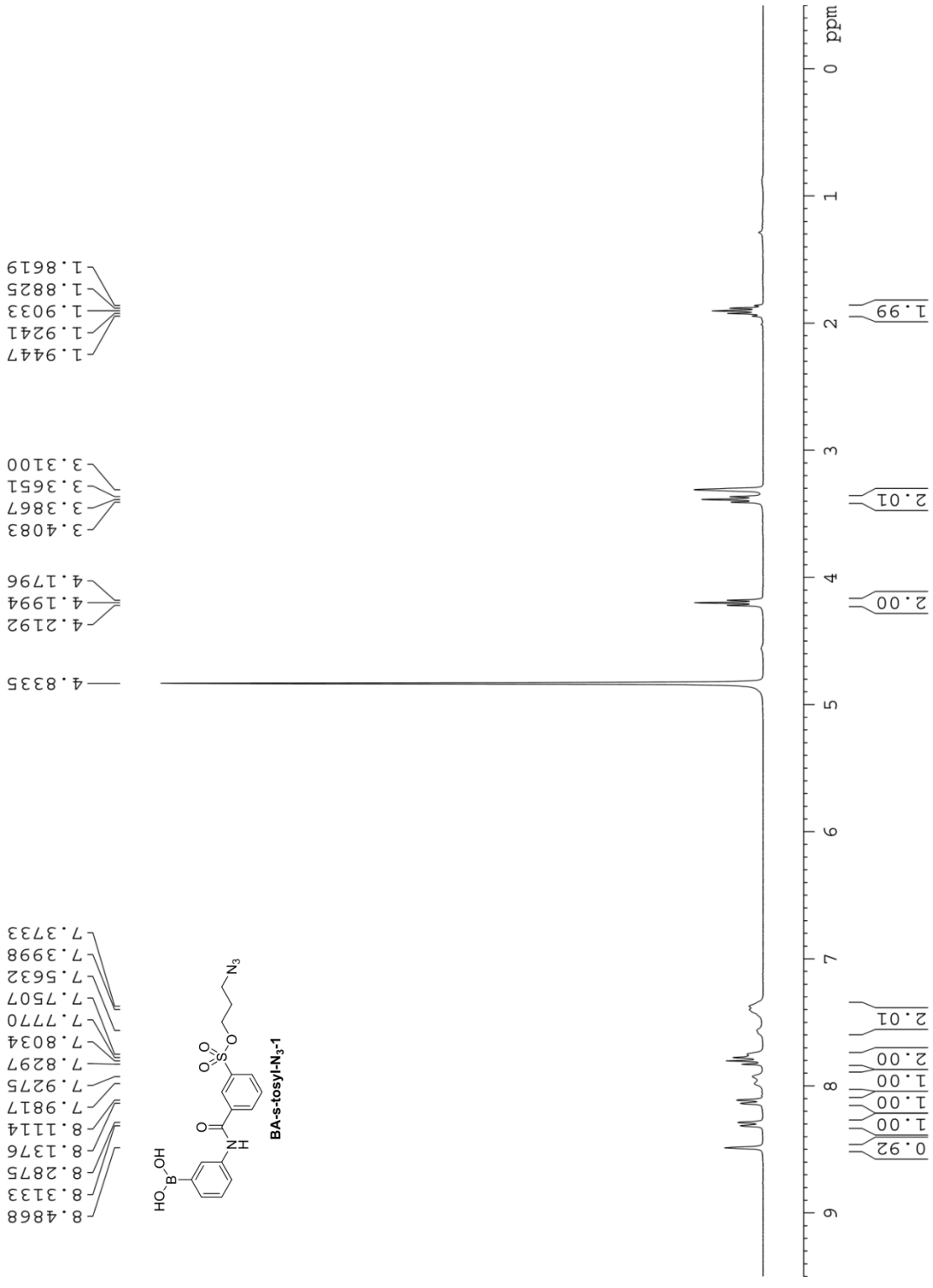


Figure S66. ^{1}H NMR spectrum of Compound **BA-s-tosyl-N_3-1** in MeOD.

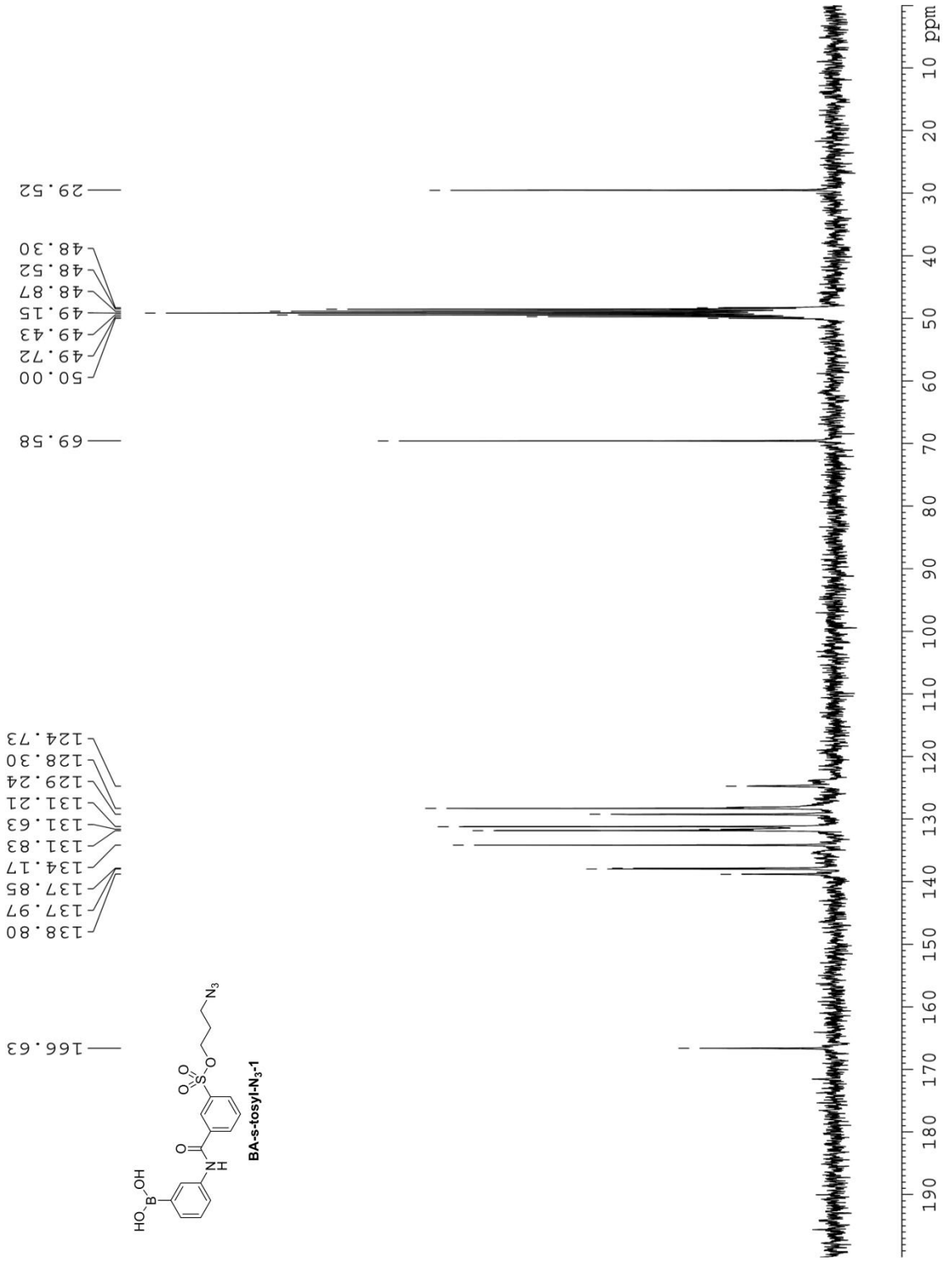


Figure S67. ^{13}C NMR spectrum of Compound **BA-s-tosyl-N_3-1** in MeOD.

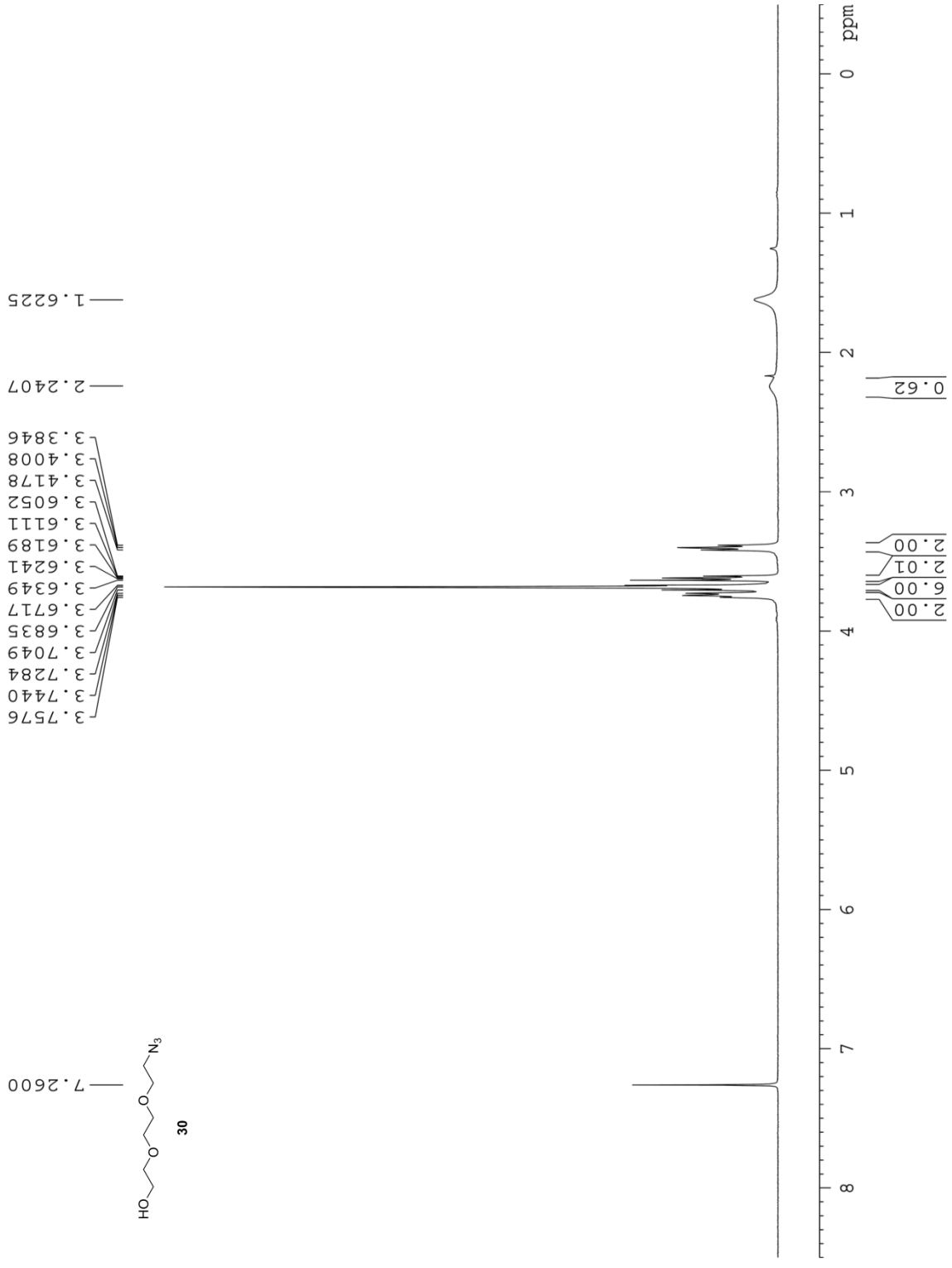


Figure S68. ^{1}H NMR spectrum of Compound **30** in $CDCl_3$.

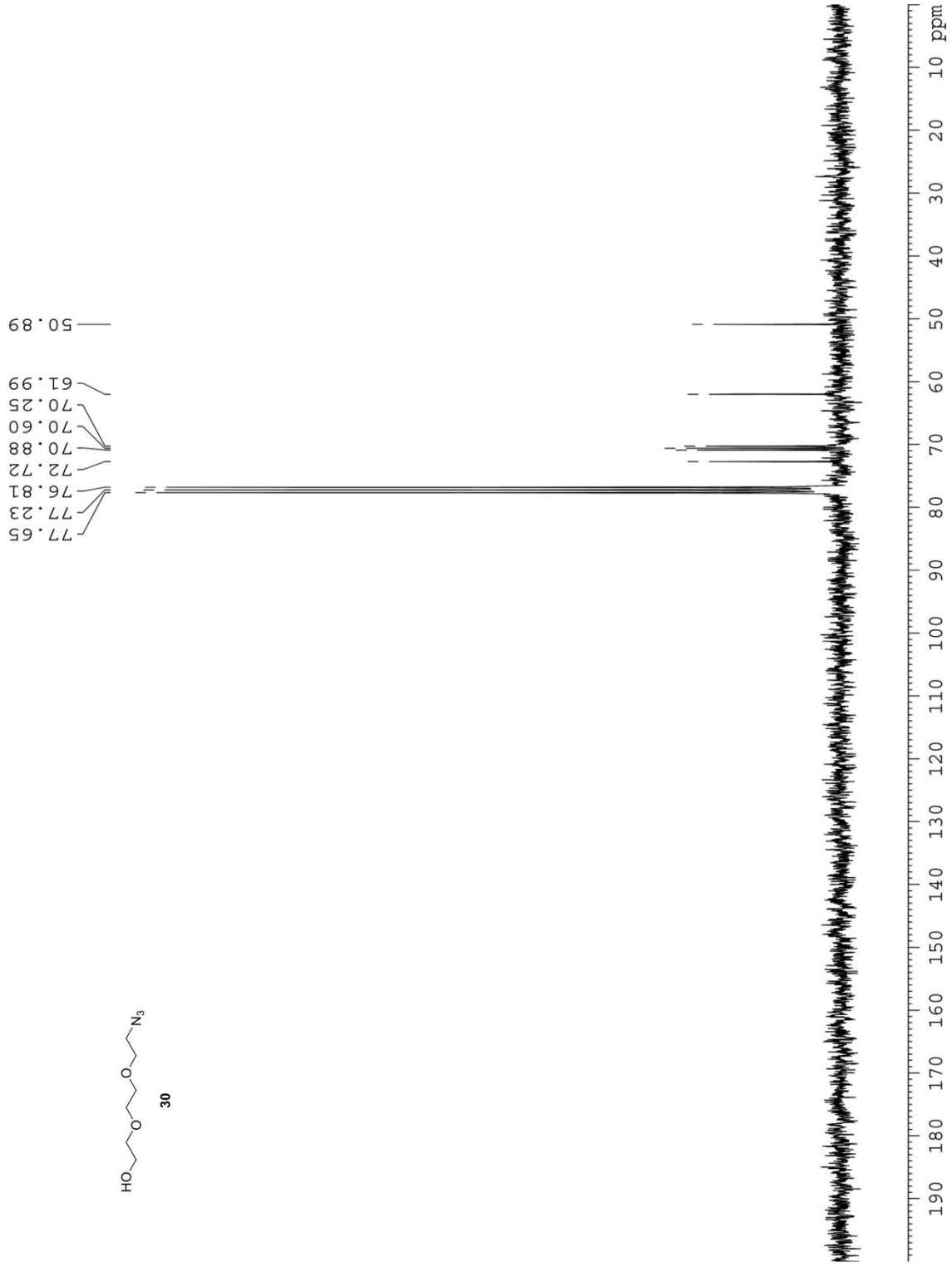


Figure S69. ^{13}C NMR spectrum of Compound **30** in $CDCl_3$.

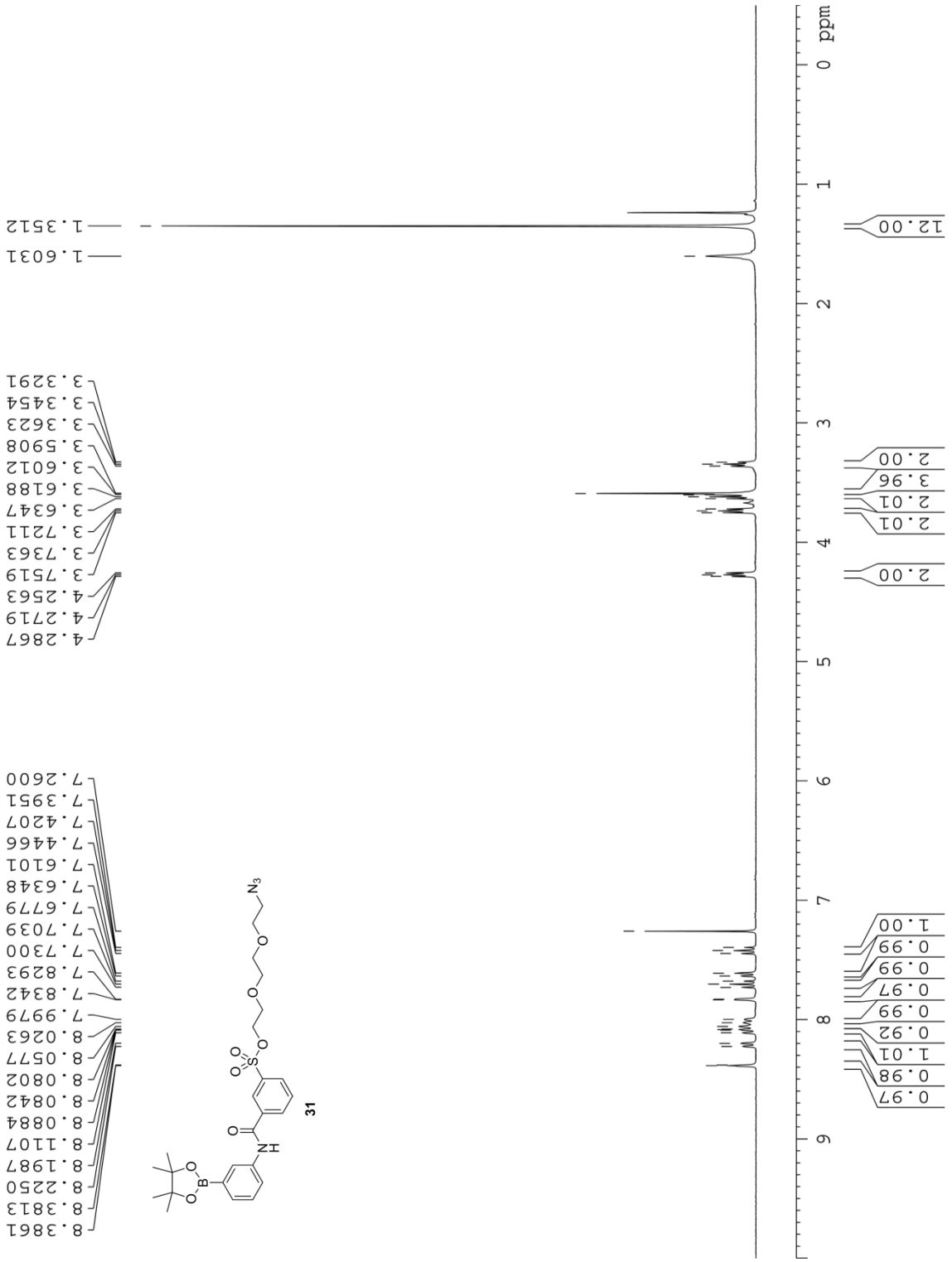


Figure S70. ^{1}H NMR spectrum of Compound **31** in $CDCl_3$.

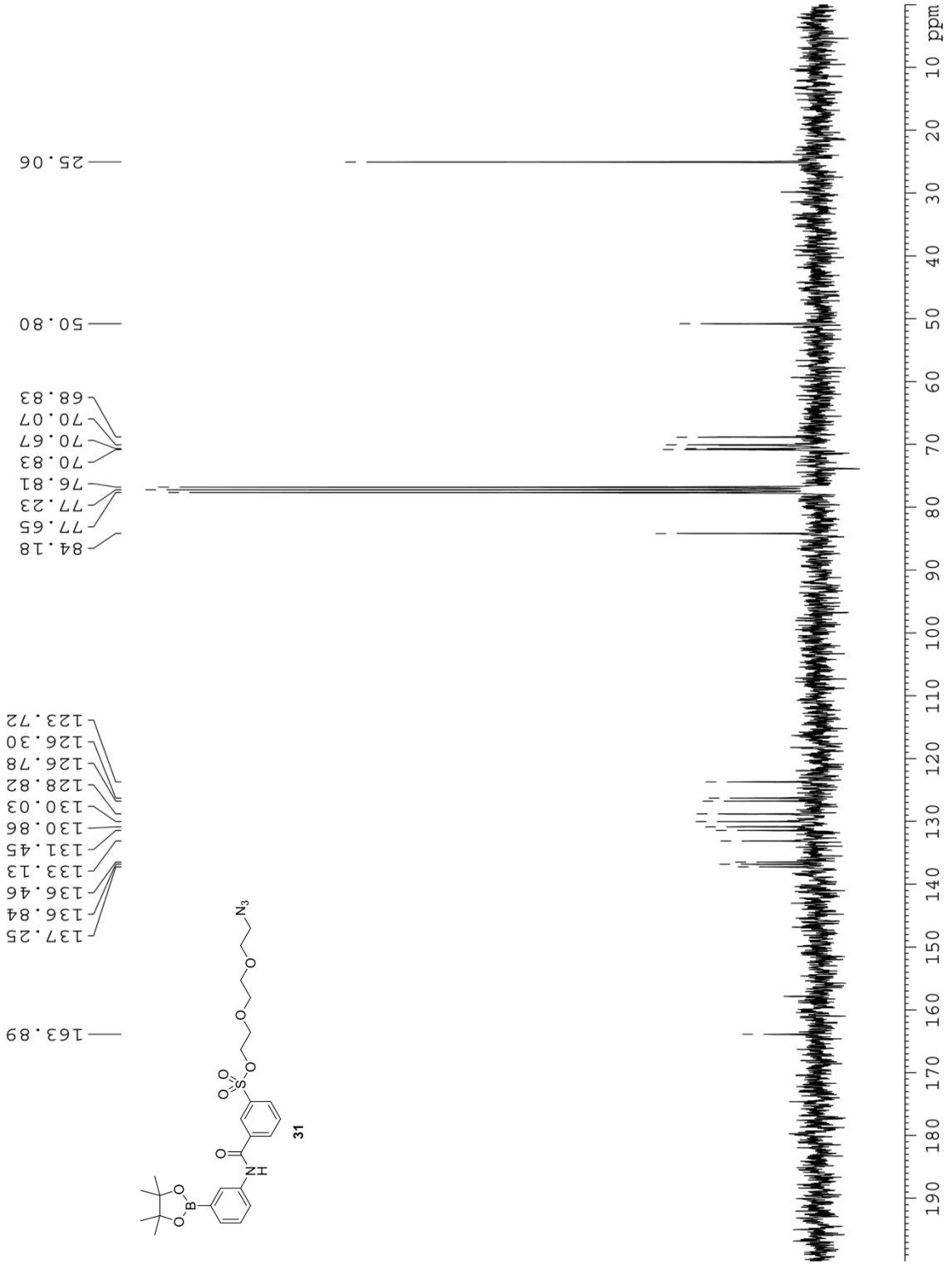


Figure S71. ^{13}C NMR spectrum of Compound **31** in $CDCl_3$.

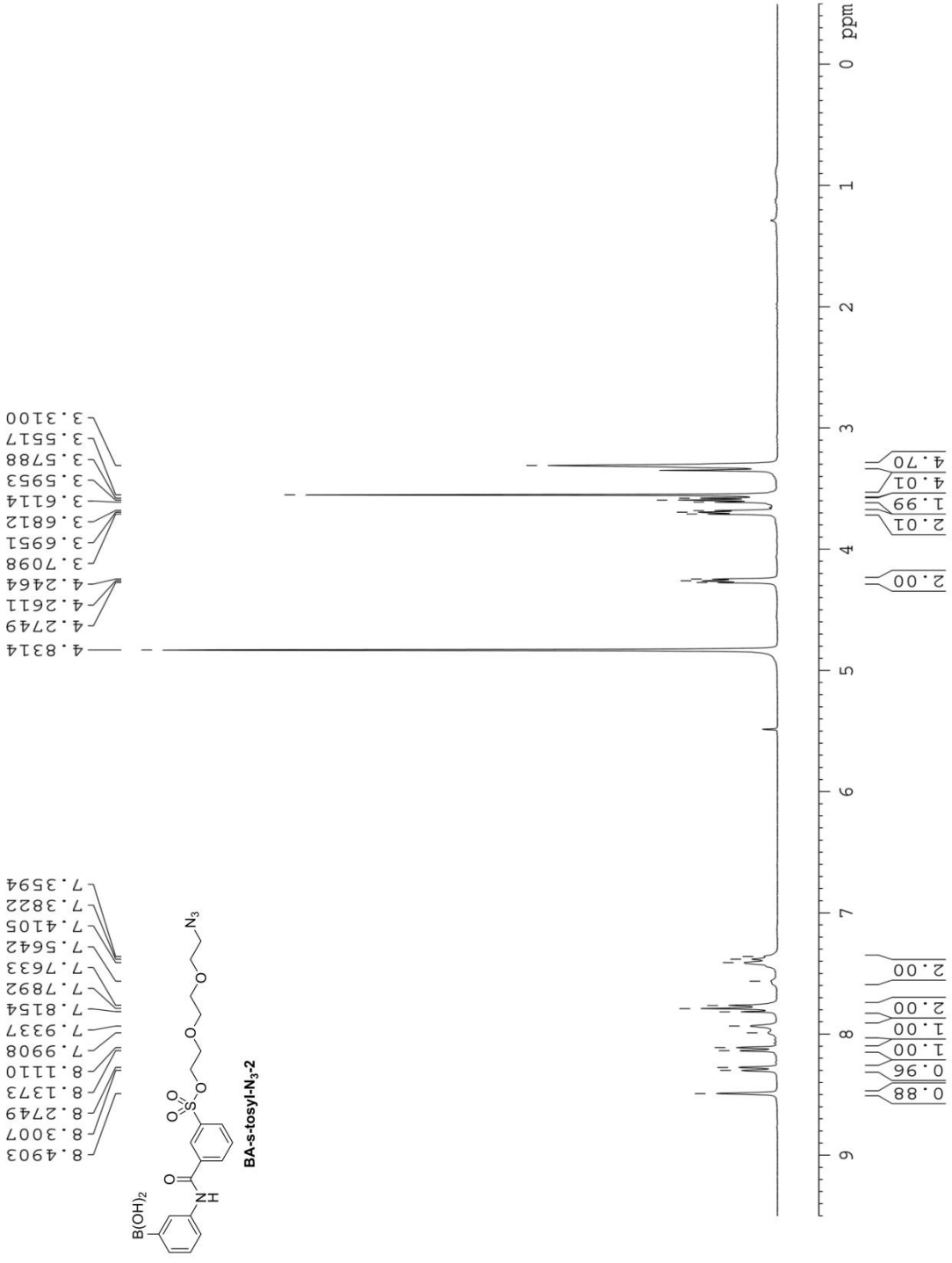


Figure S72. ^{1}H NMR spectrum of Compound **BA-s-tosyl-N_3-2** in MeOD.

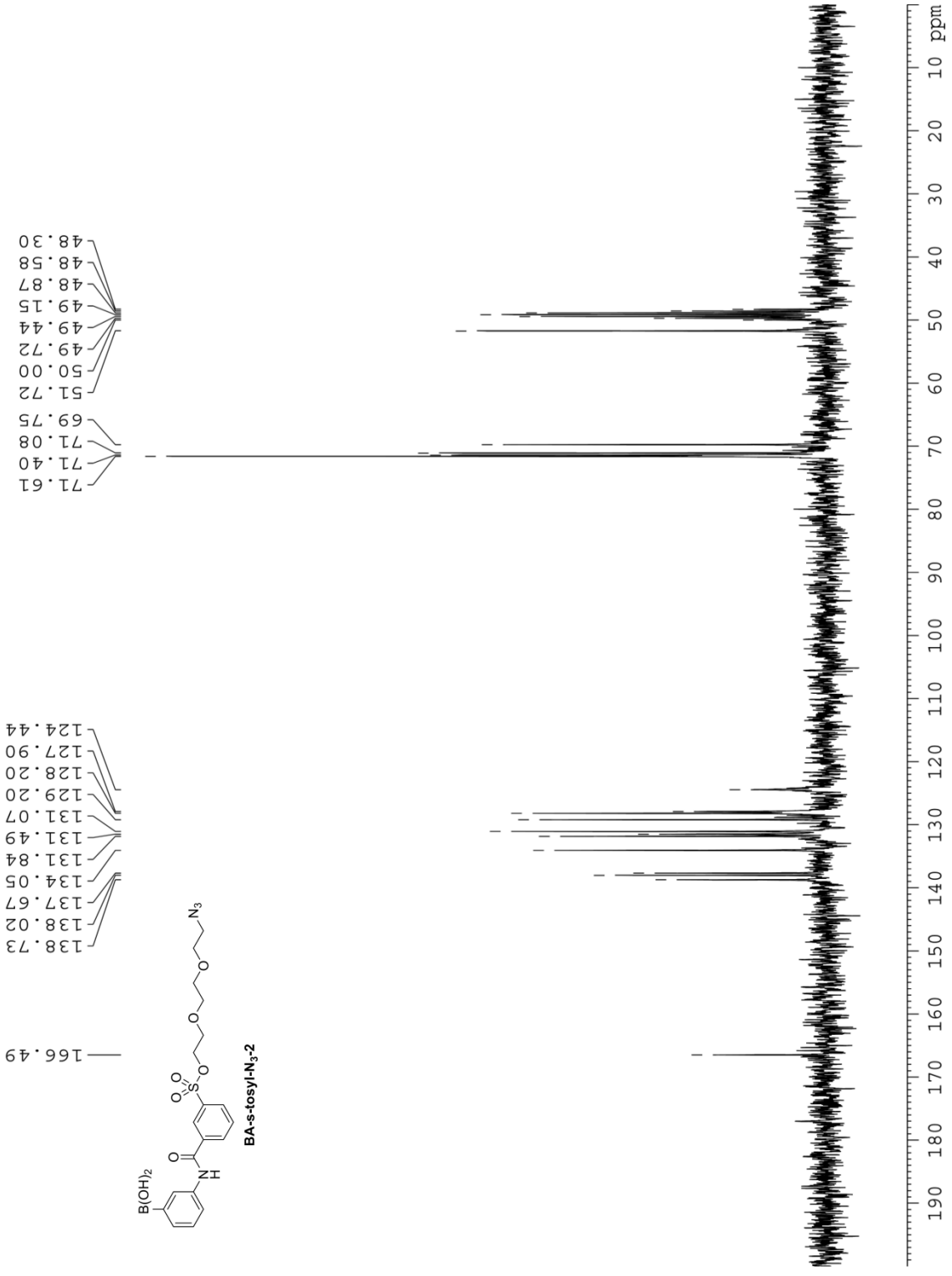


Figure S73. ^{13}C NMR spectrum of Compound **BA-s-tosyl-N_3-2** in $CDCl_3$.

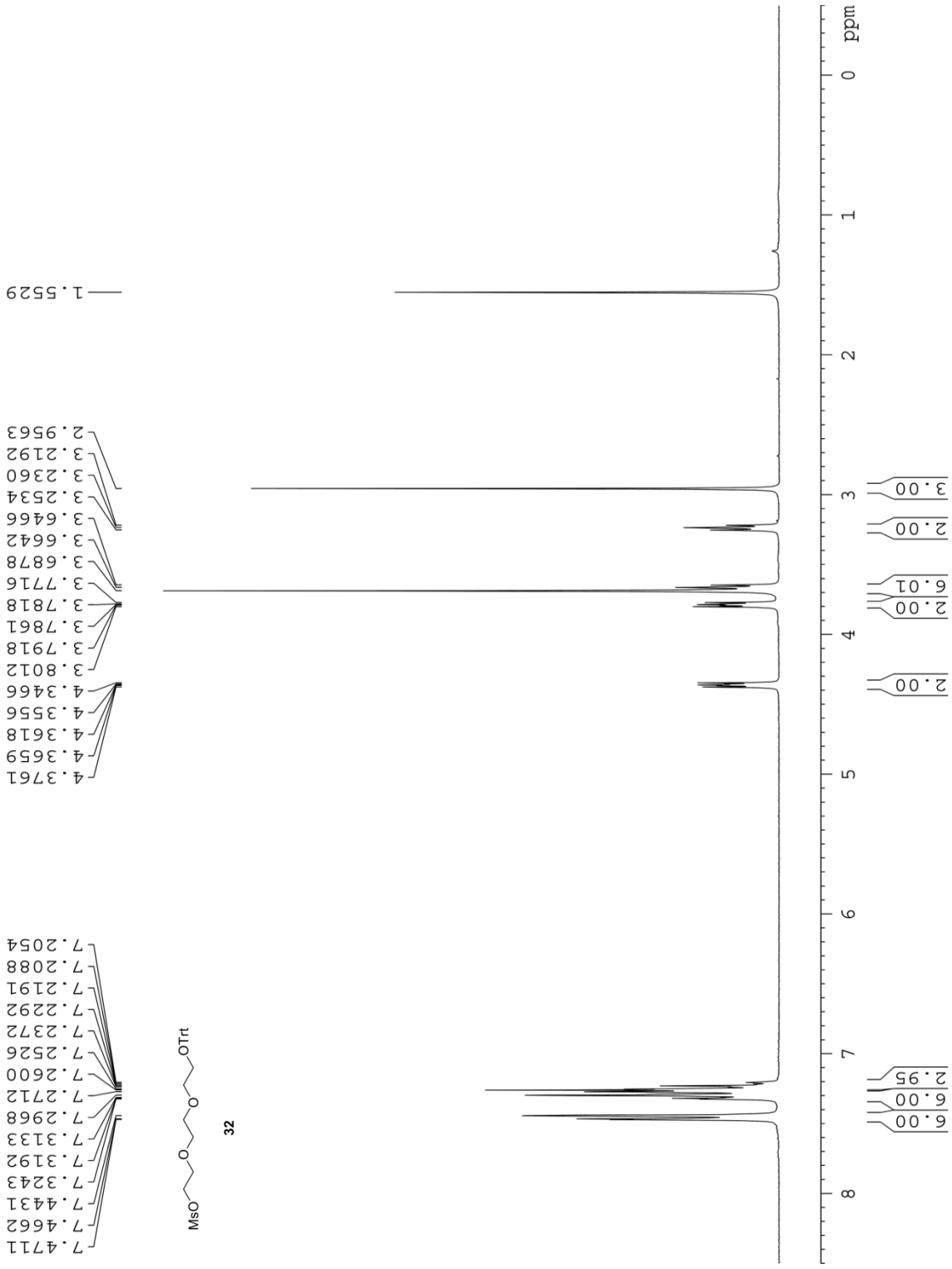


Figure S74. ^{1}H NMR spectrum of Compound **32** in $CDCl_3$.

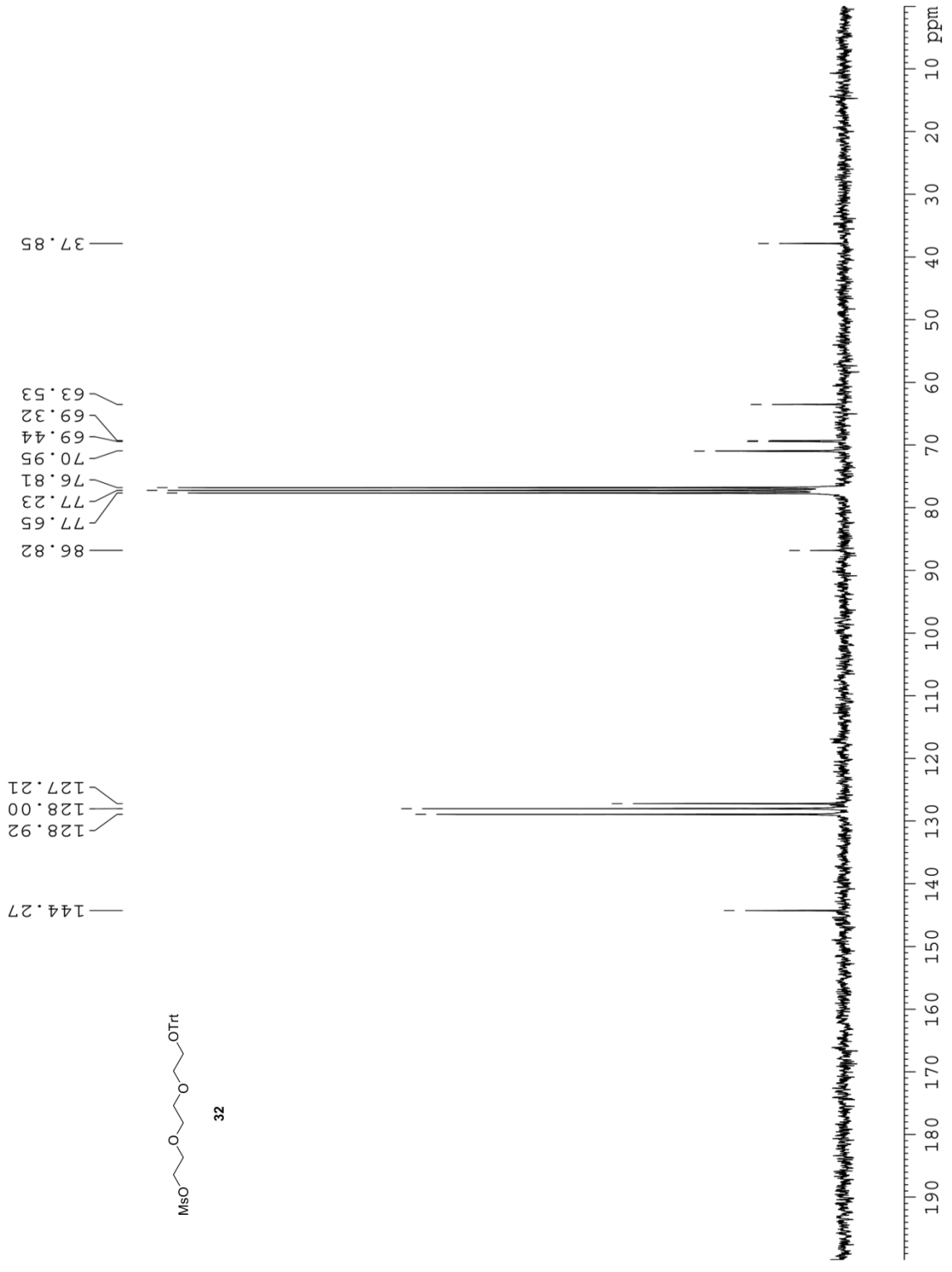


Figure S75. ^{13}C NMR spectrum of Compound **32** in $CDCl_3$.

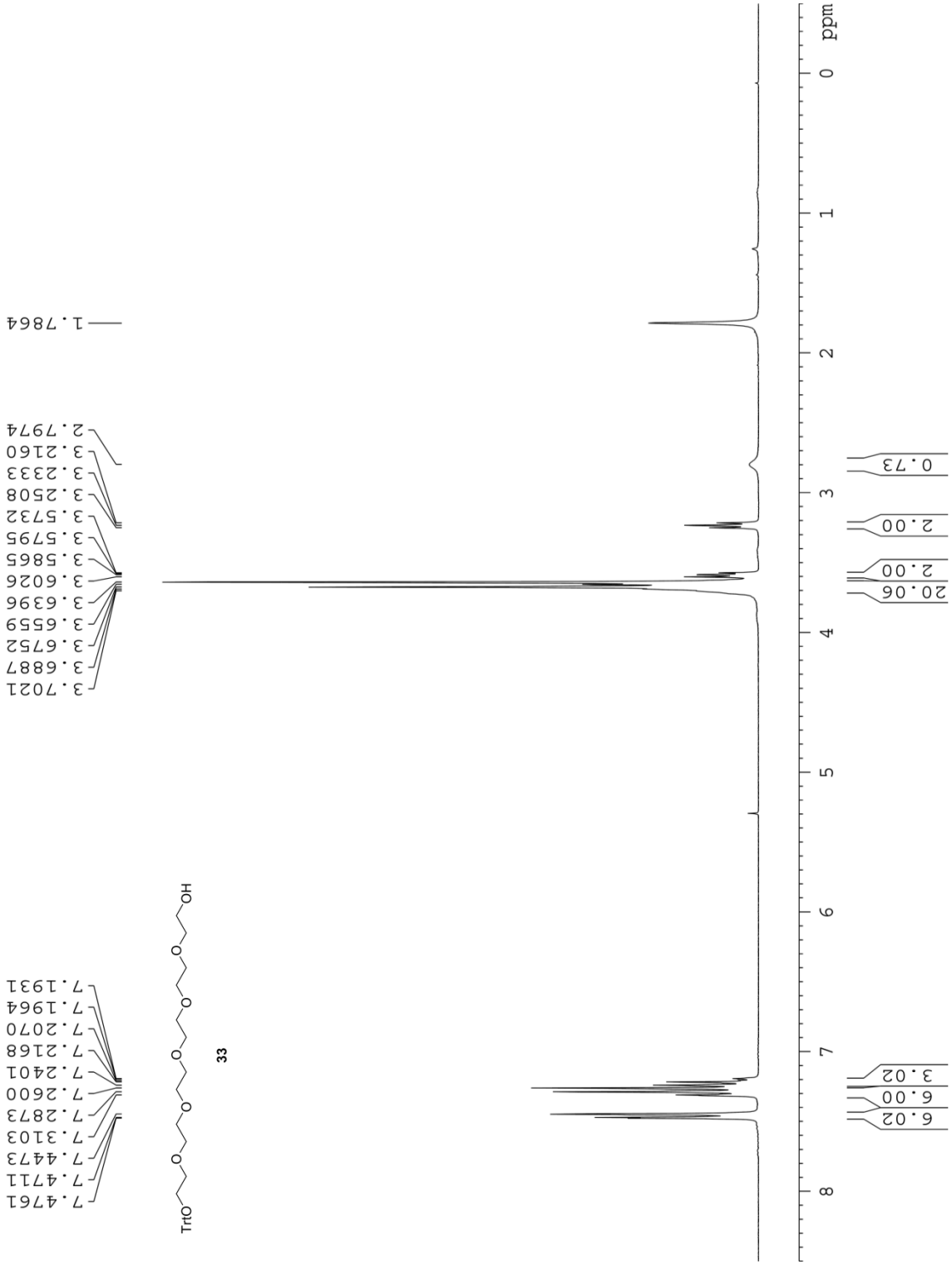


Figure S76. ^{1}H NMR spectrum of Compound **33** in $CDCl_3$.

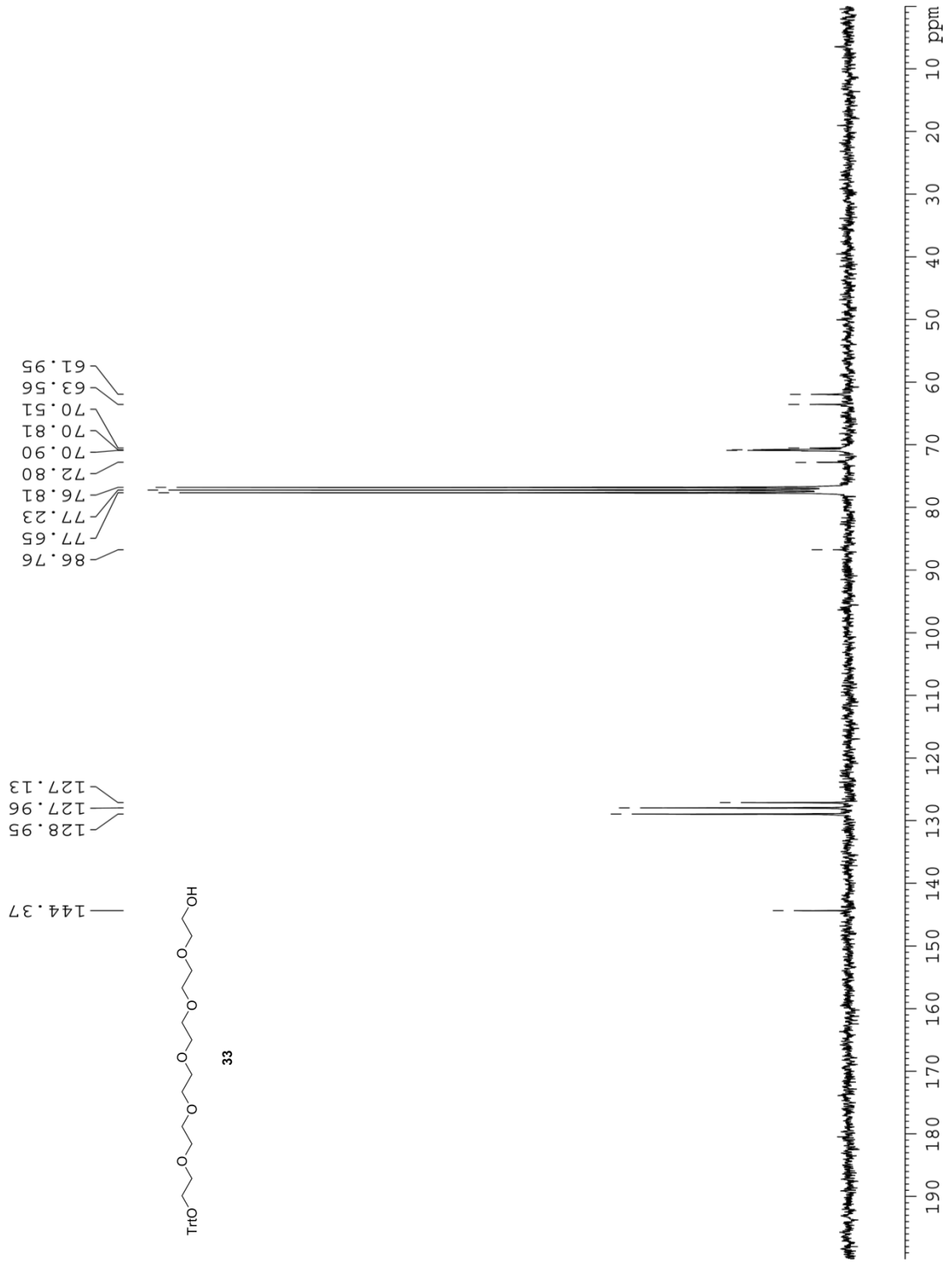


Figure S77. ^{13}C NMR spectrum of Compound **33** in $CDCl_3$.

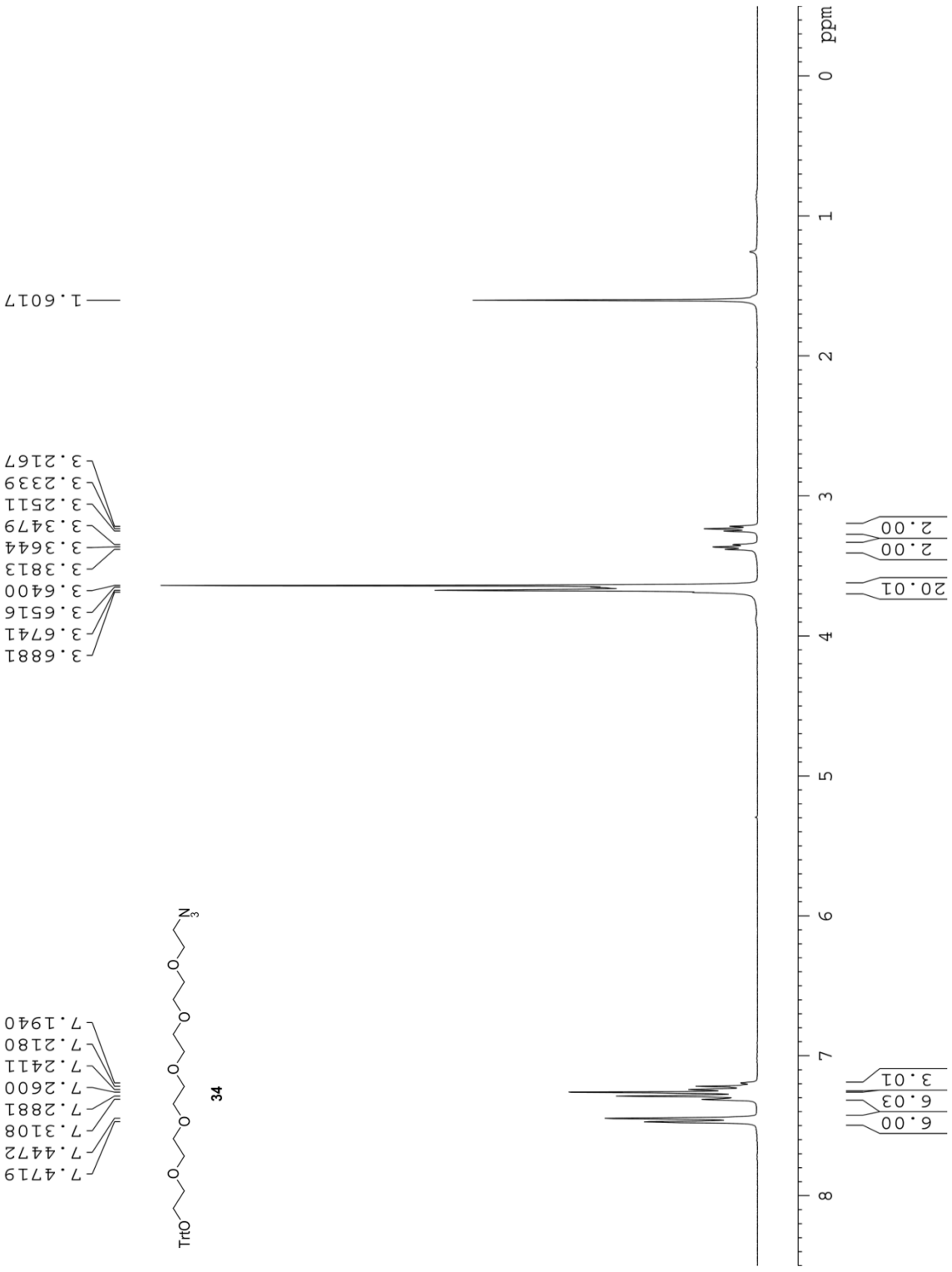


Figure S78. ^{1}H NMR spectrum of Compound **34** in $CDCl_3$.

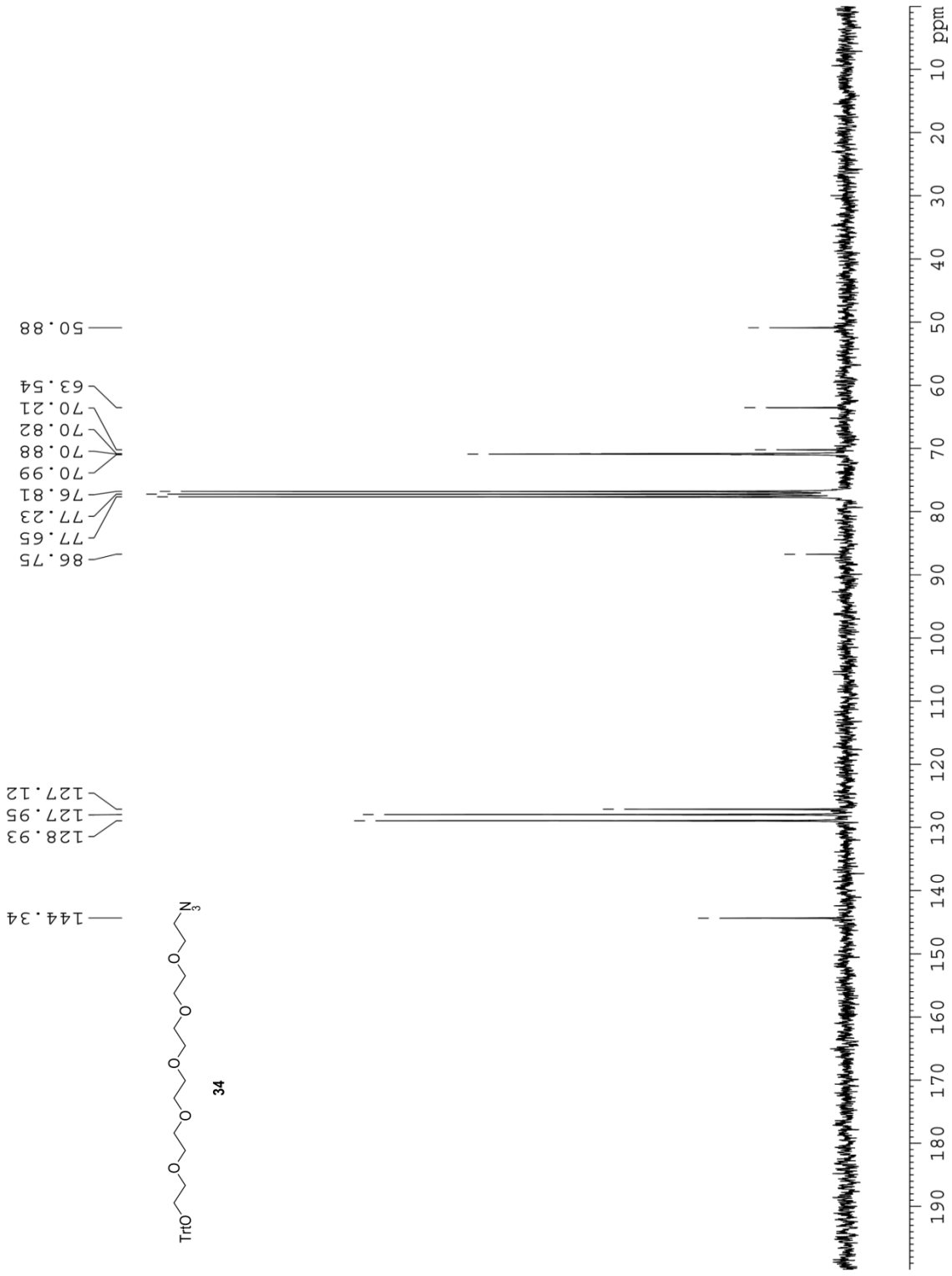


Figure S79. ^{13}C NMR spectrum of Compound **34** in $CDCl_3$.

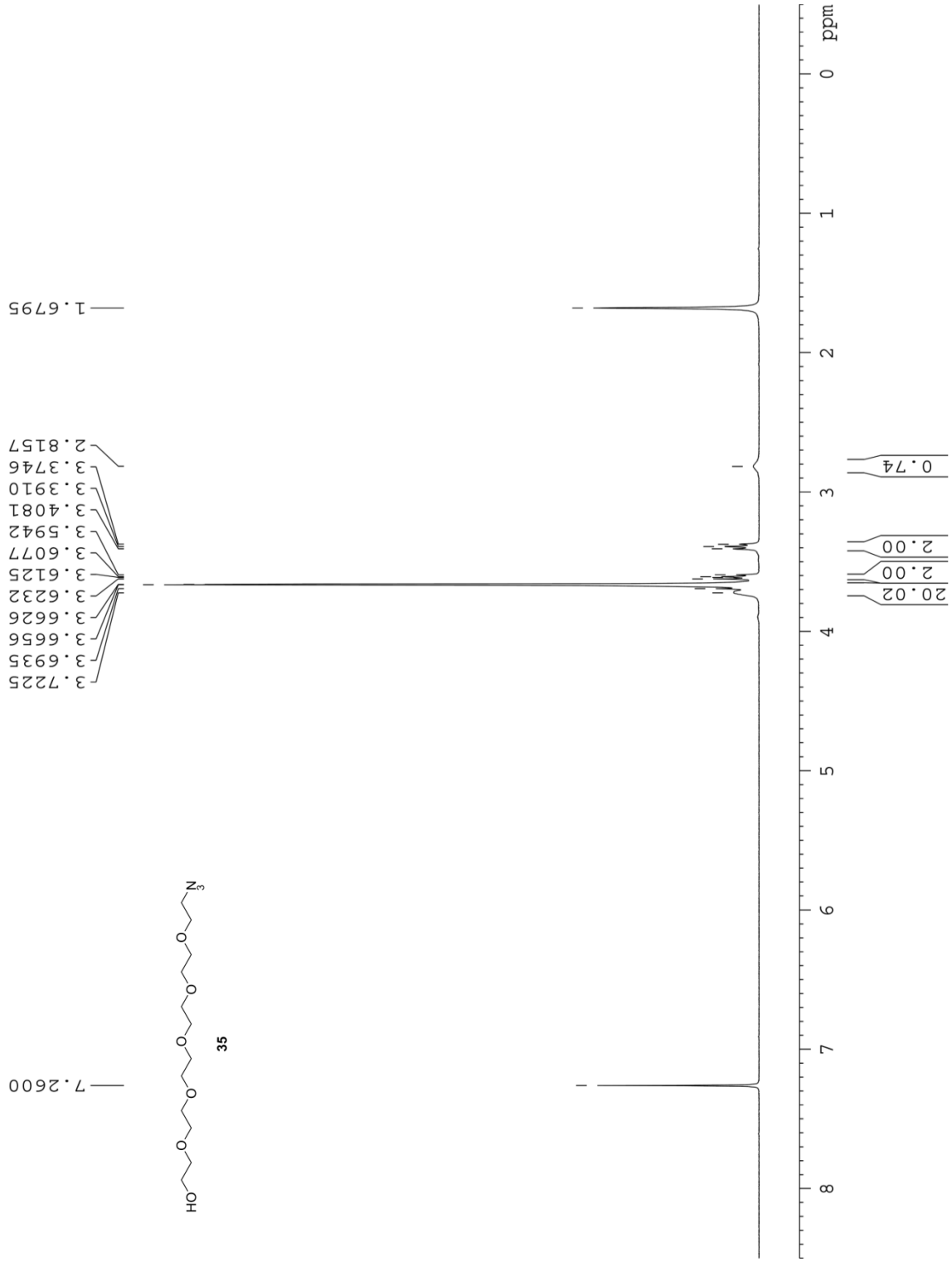


Figure S80. ^{1}H NMR spectrum of Compound **35** in $CDCl_3$.

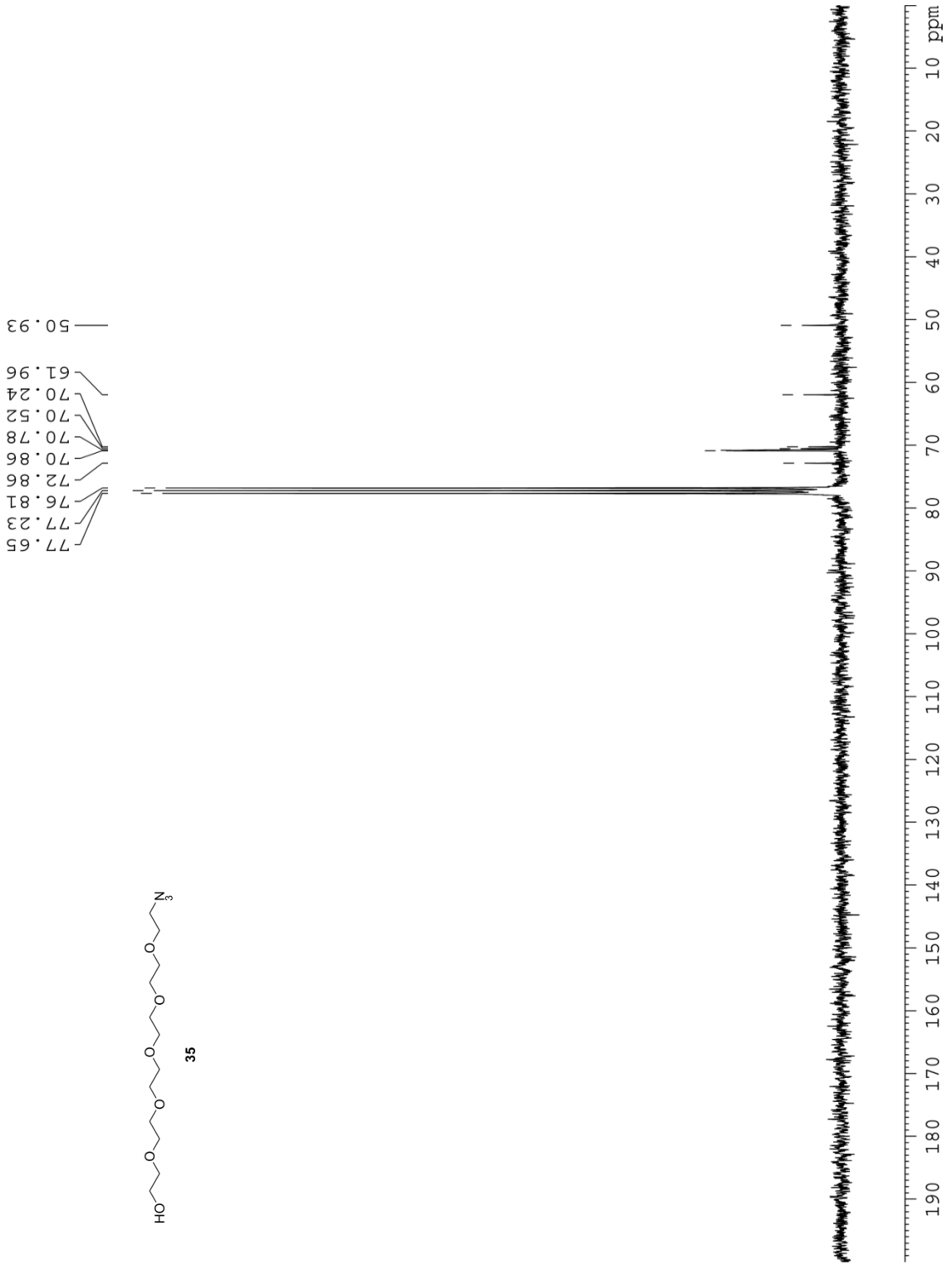


Figure S81. ^{13}C NMR spectrum of Compound **35** in $CDCl_3$.

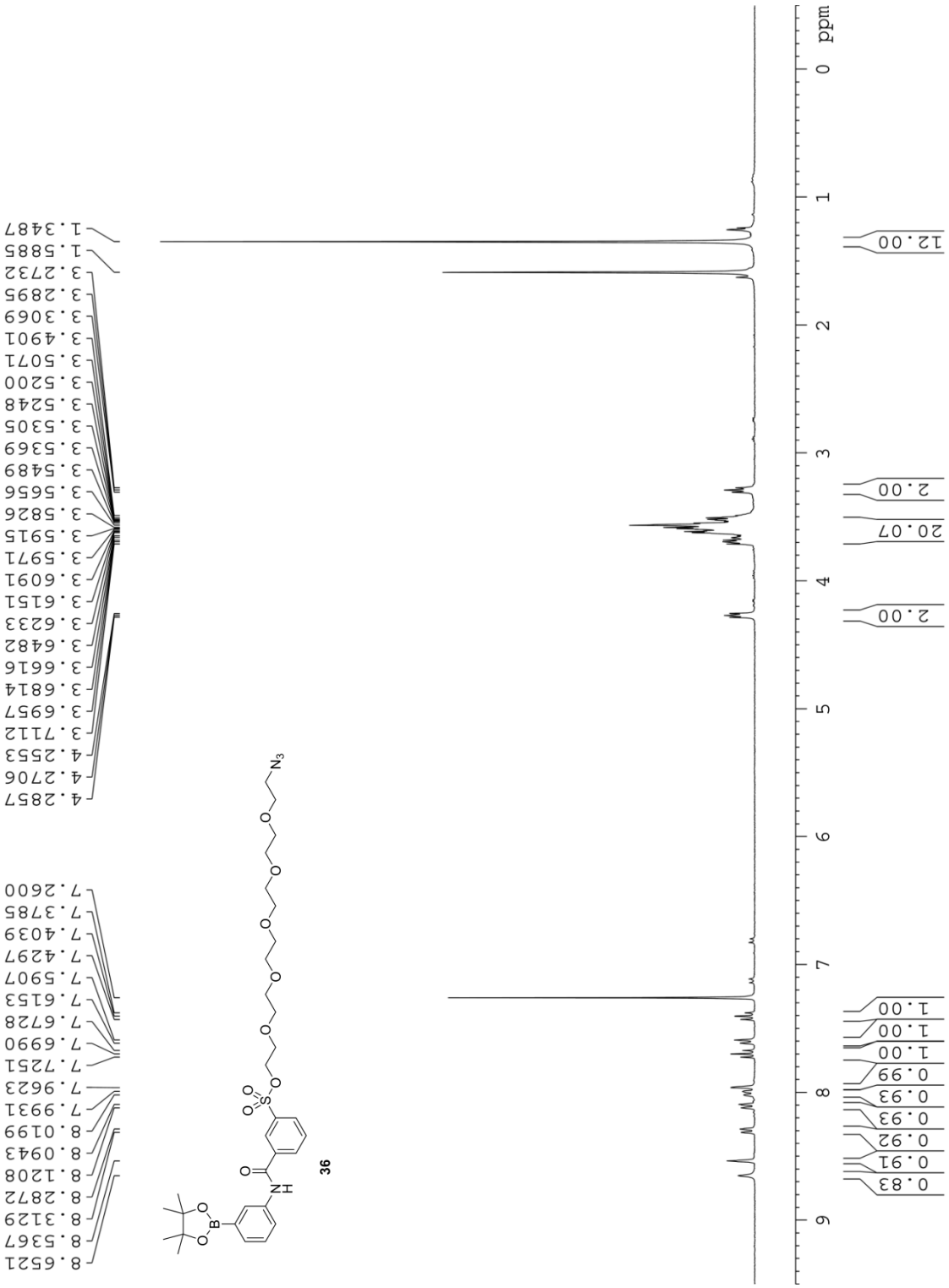


Figure S82. ^{1}H NMR spectrum of Compound **36** in $CDCl_3$.

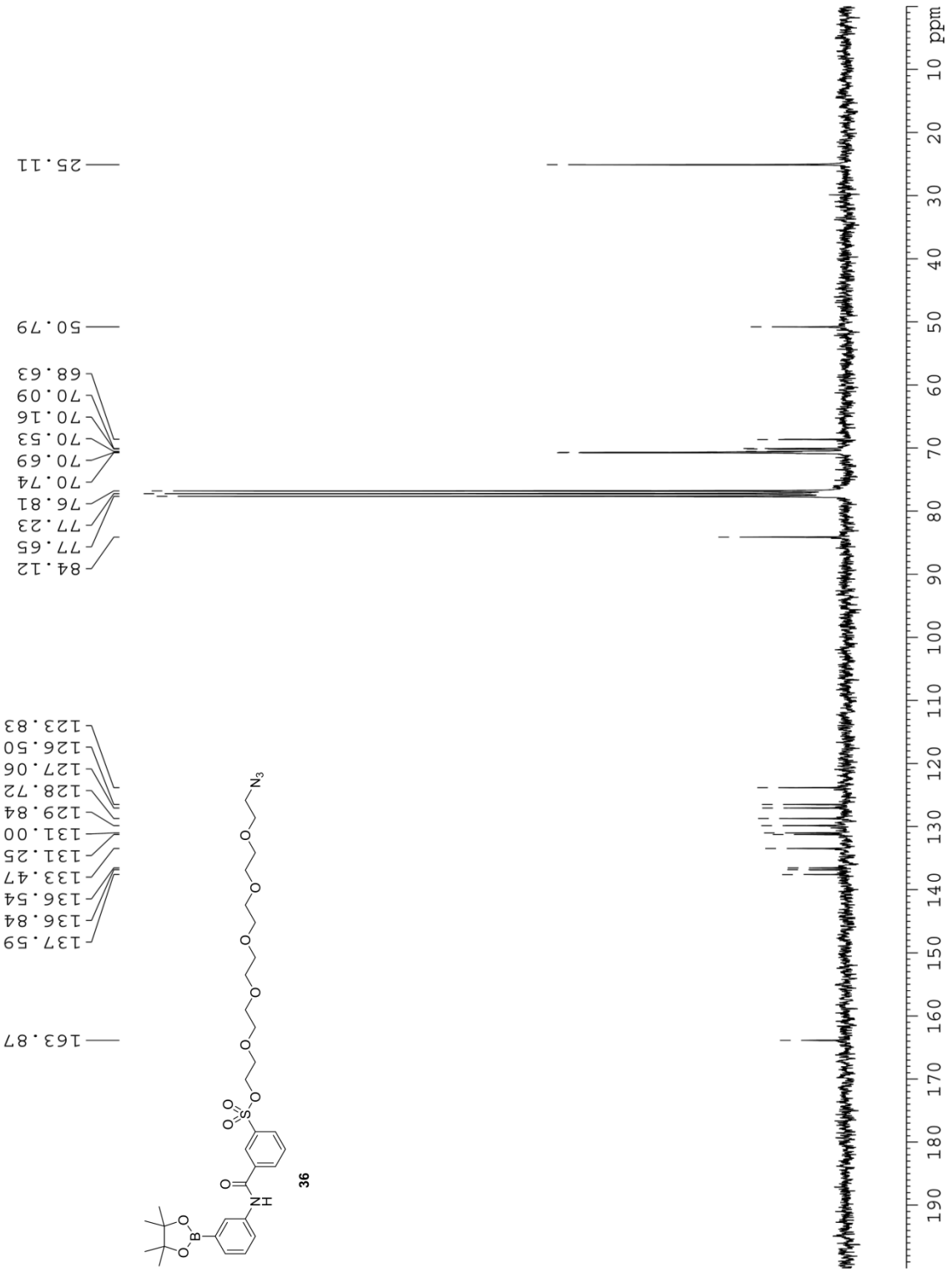


Figure S83. ^{13}C NMR spectrum of Compound **36** in $CDCl_3$.

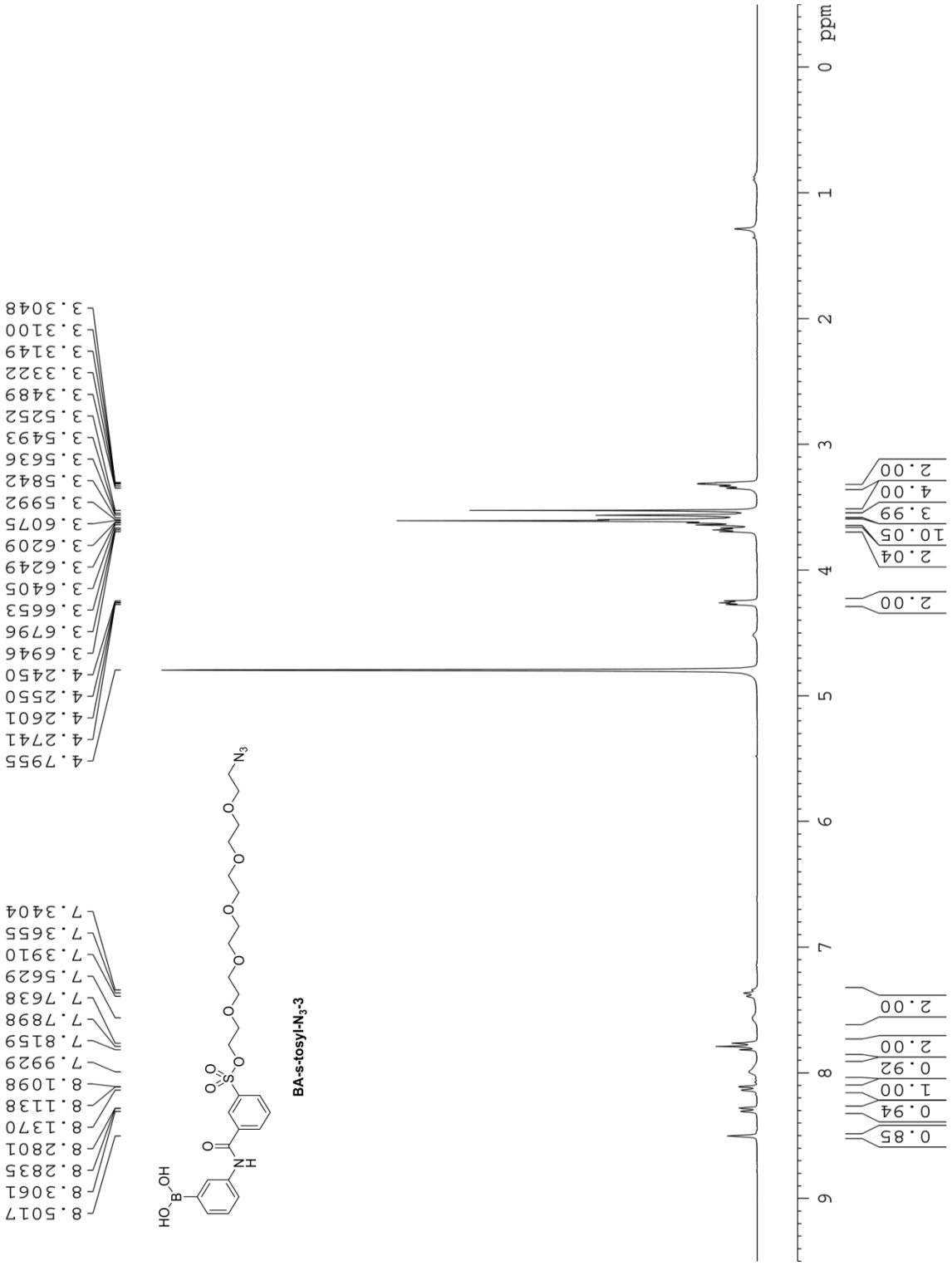


Figure S84. ^{1}H NMR spectrum of Compound **BA-s-tosyl-N_3-3** in MeOD.

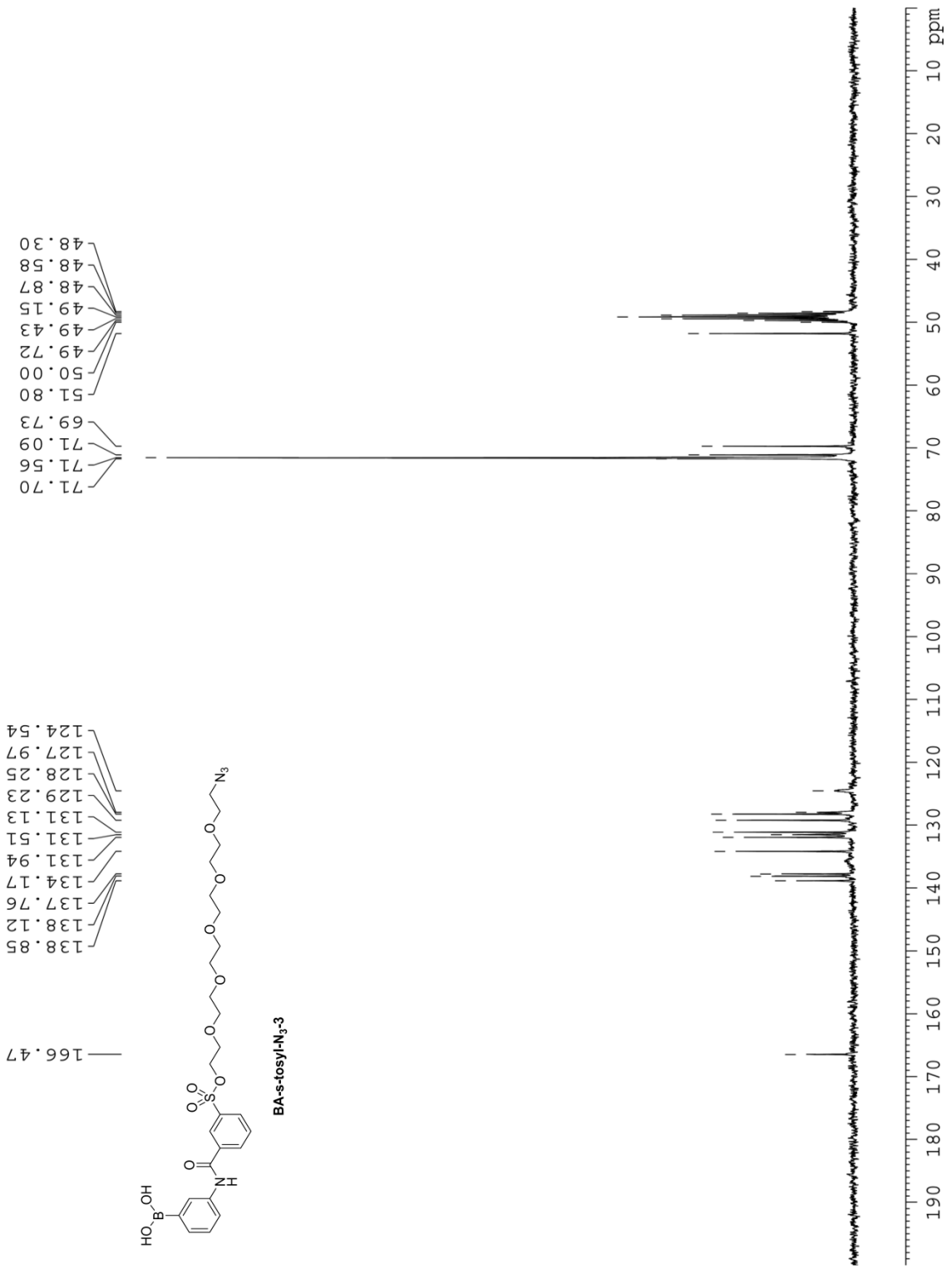


Figure S85. ^{13}C NMR spectrum of Compound **BA-s-tosyl-N_3-3** in MeOD.

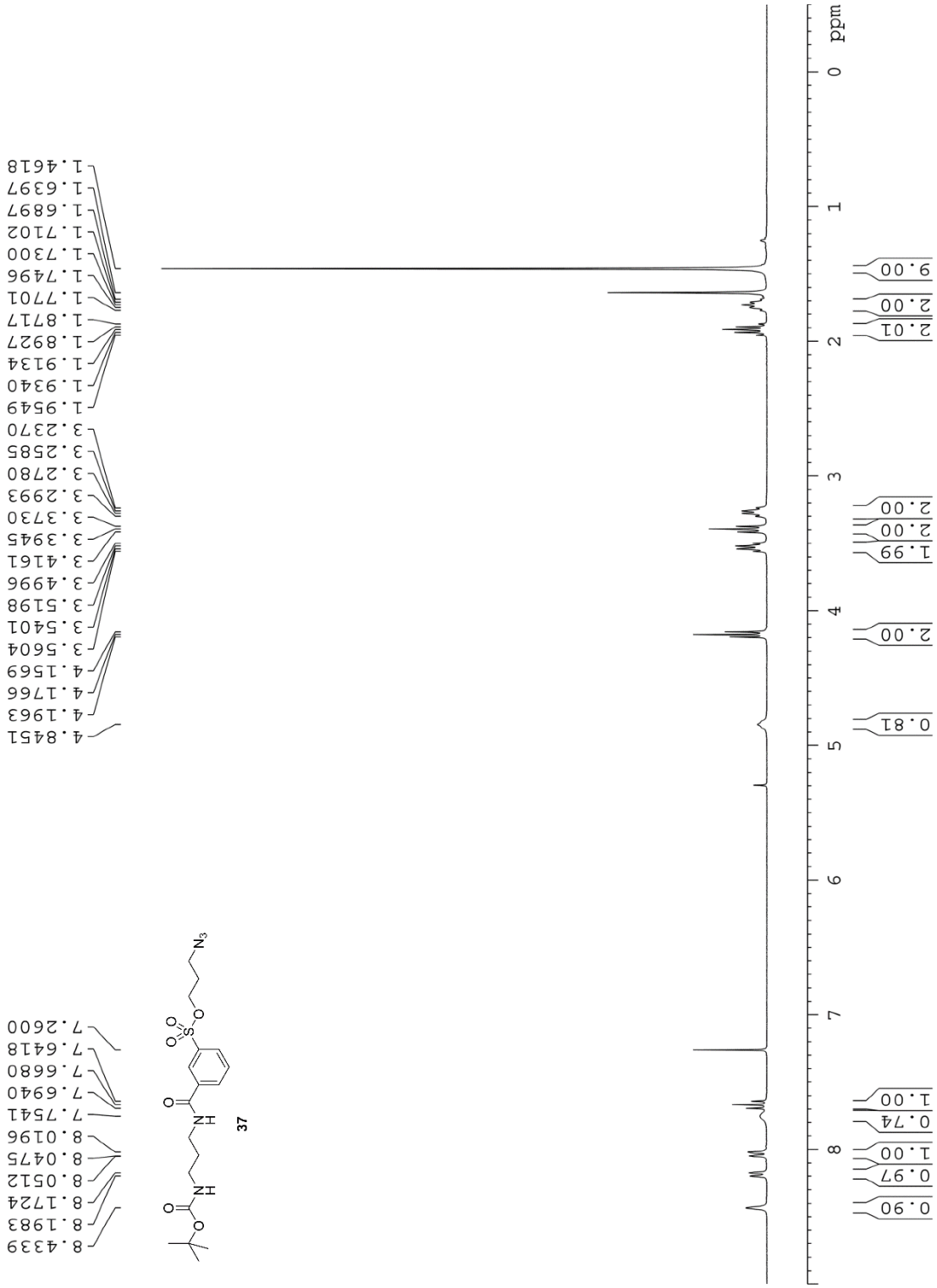


Figure S86. ^{1}H NMR spectrum of Compound **37** in $CDCl_3$.

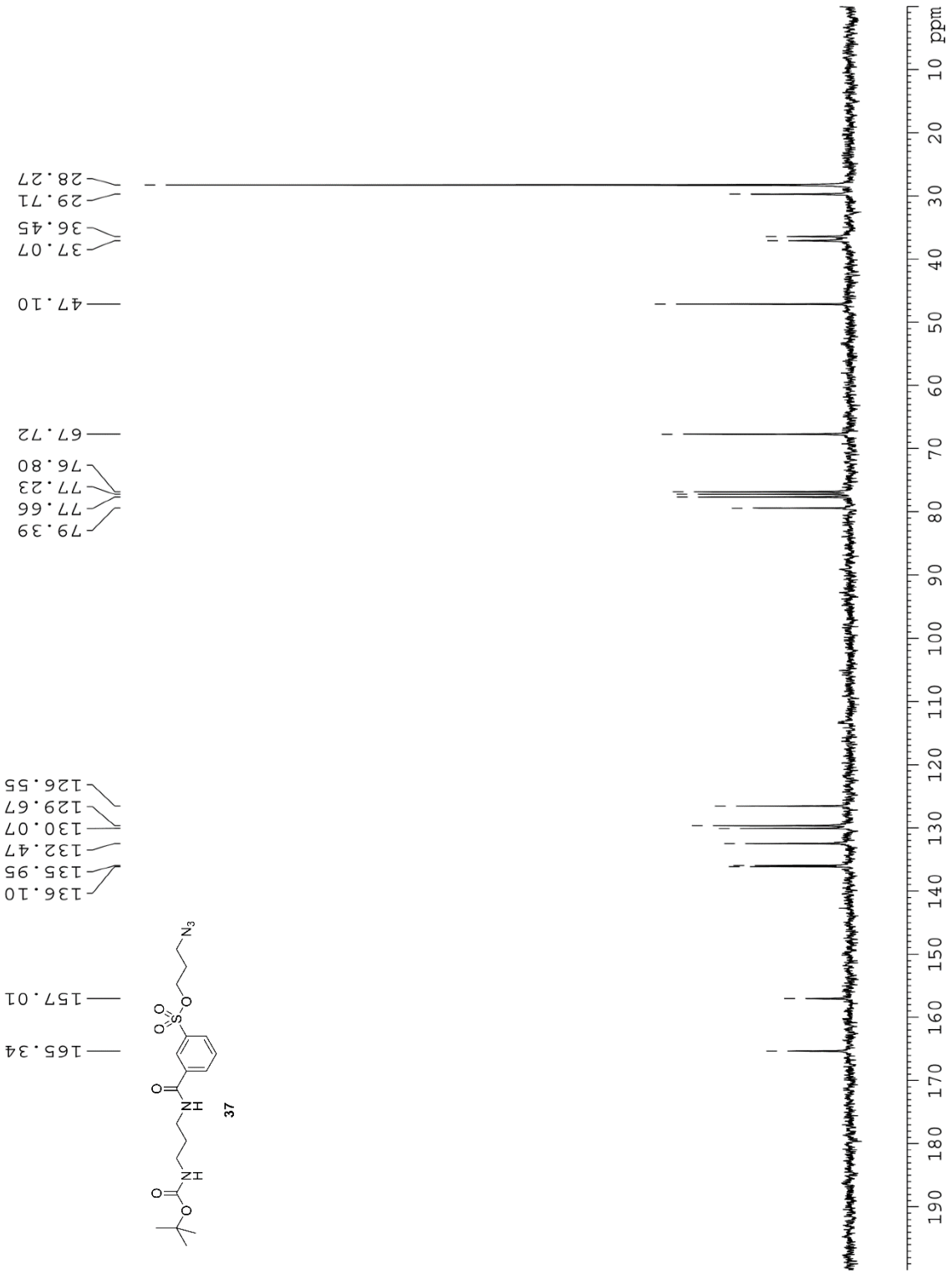


Figure S87. ^{13}C NMR spectrum of Compound **37** in $CDCl_3$.

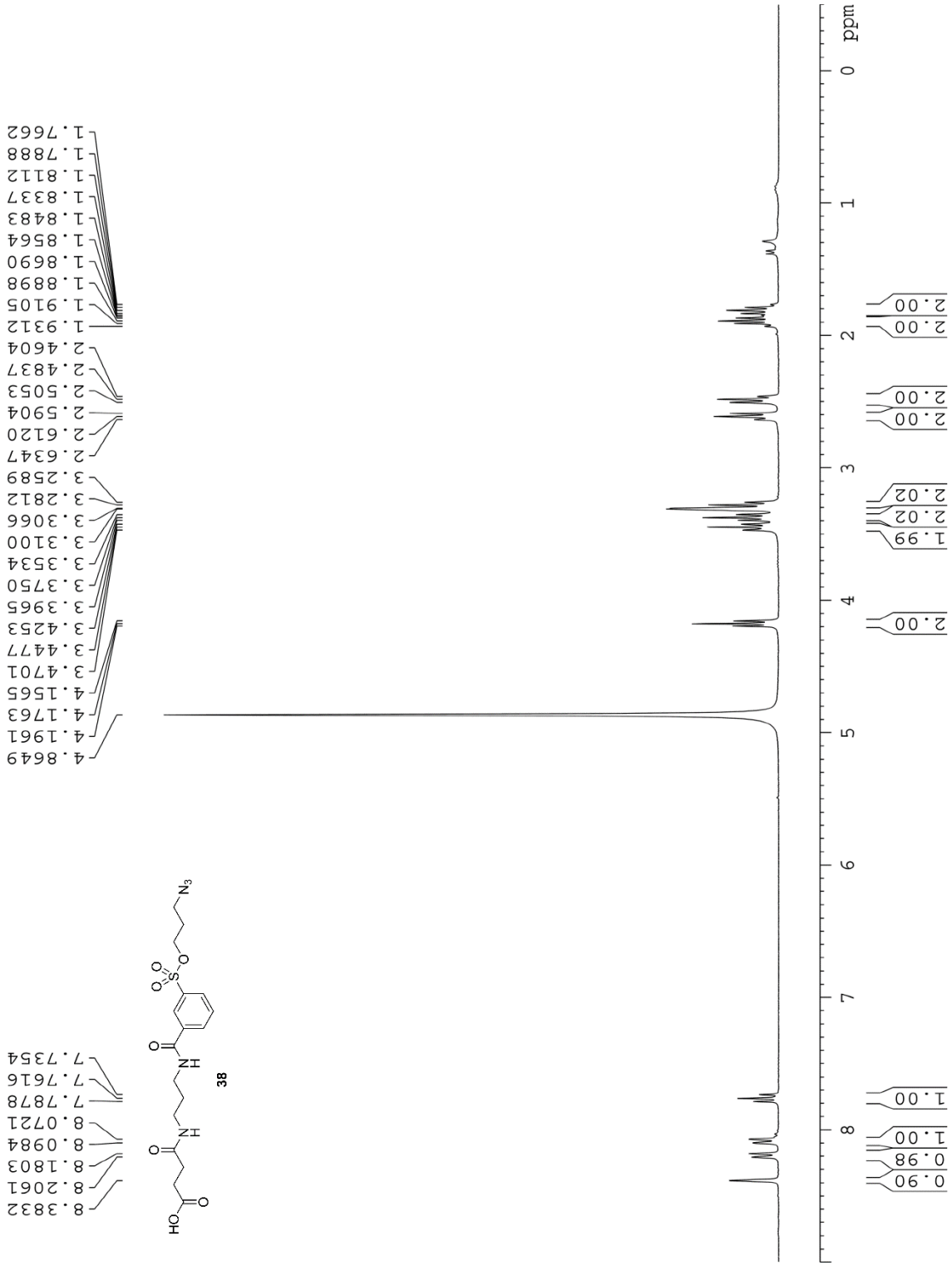


Figure S88. ^{1}H NMR spectrum of Compound **38** in MeOD.

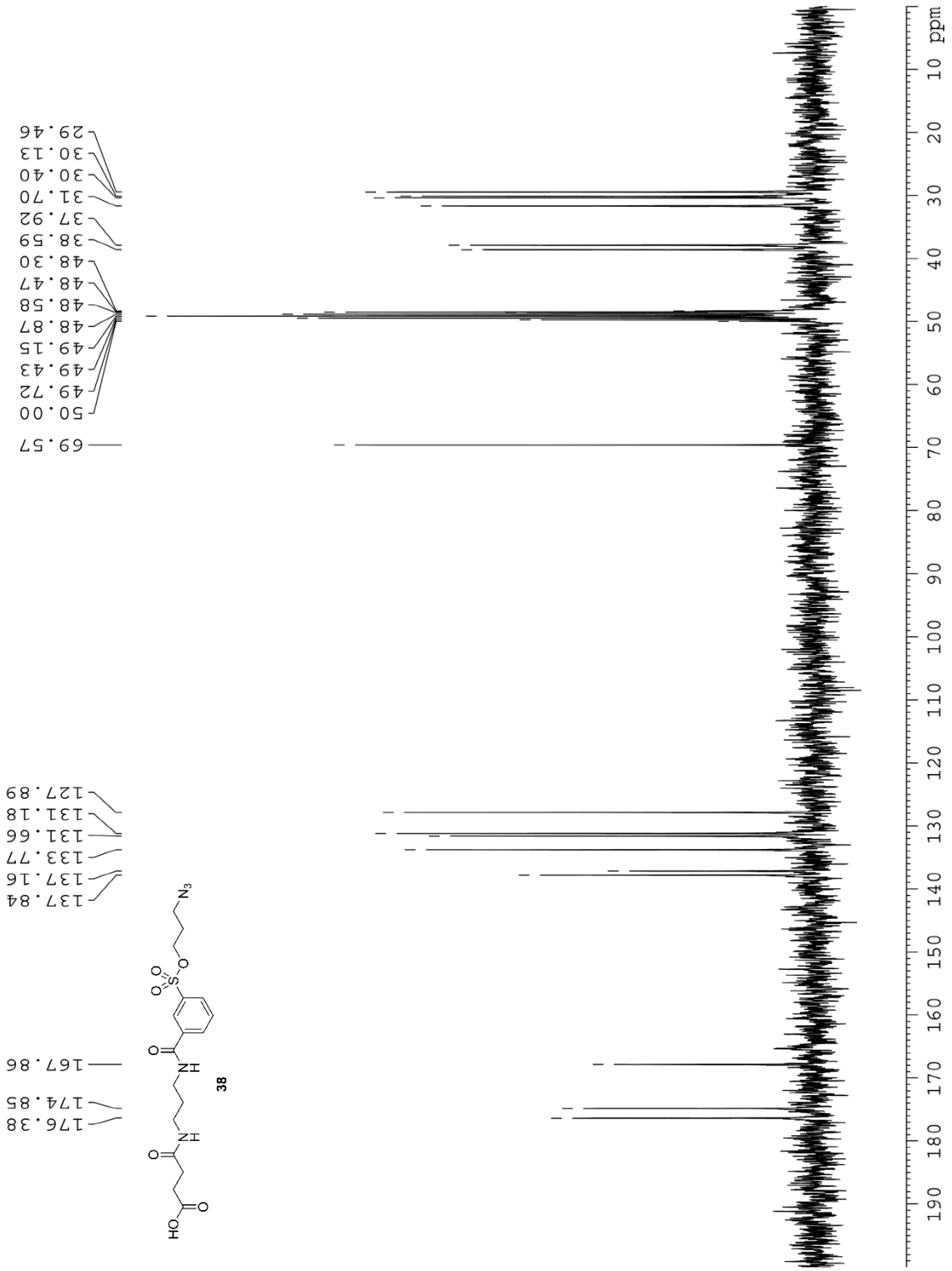


Figure S89. ^{13}C NMR spectrum of Compound **38** in MeOD.

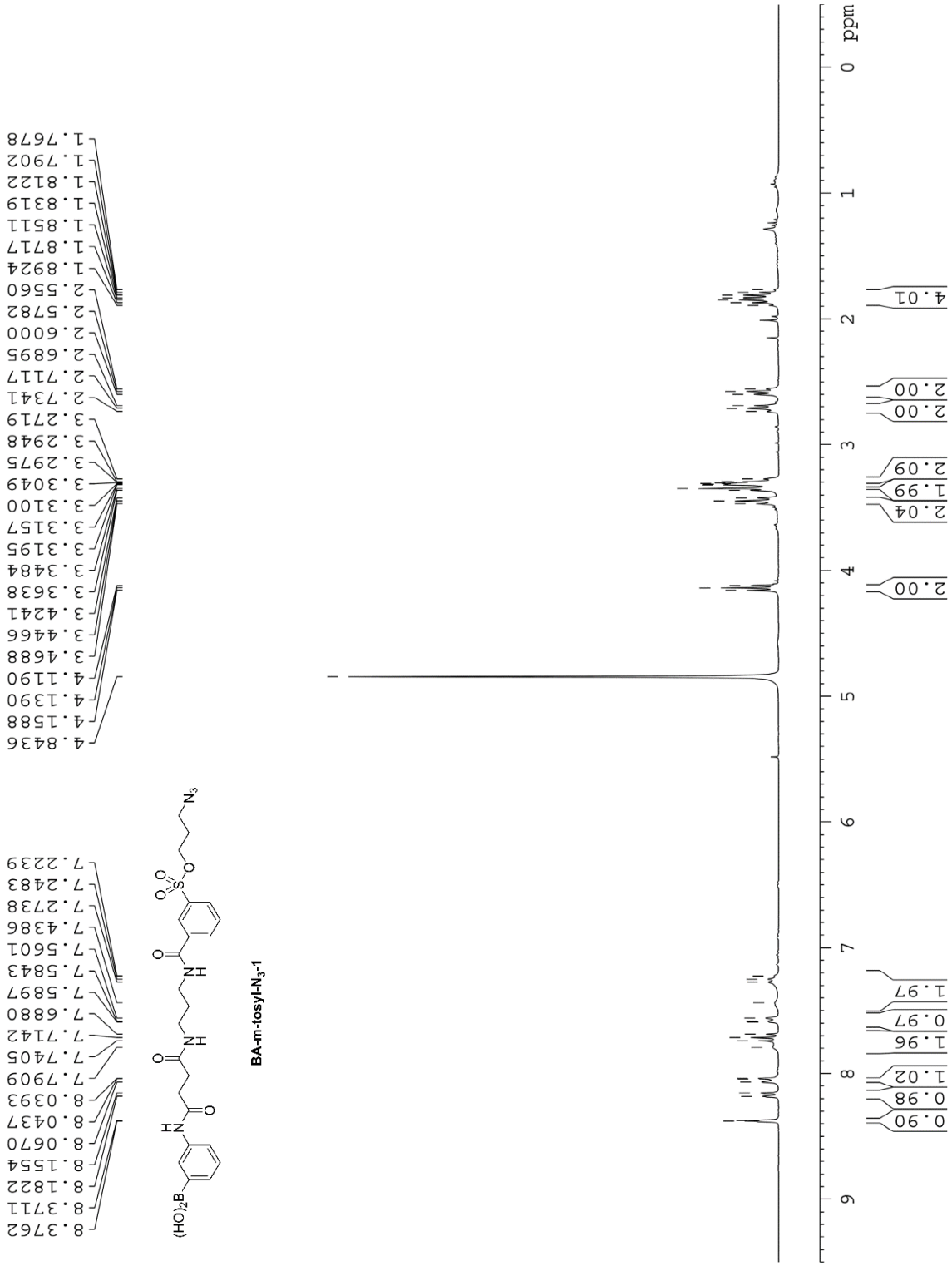


Figure S90. ^{1}H NMR spectrum of Compound **BA-m-tosyl-N_3-1** in MeOD.

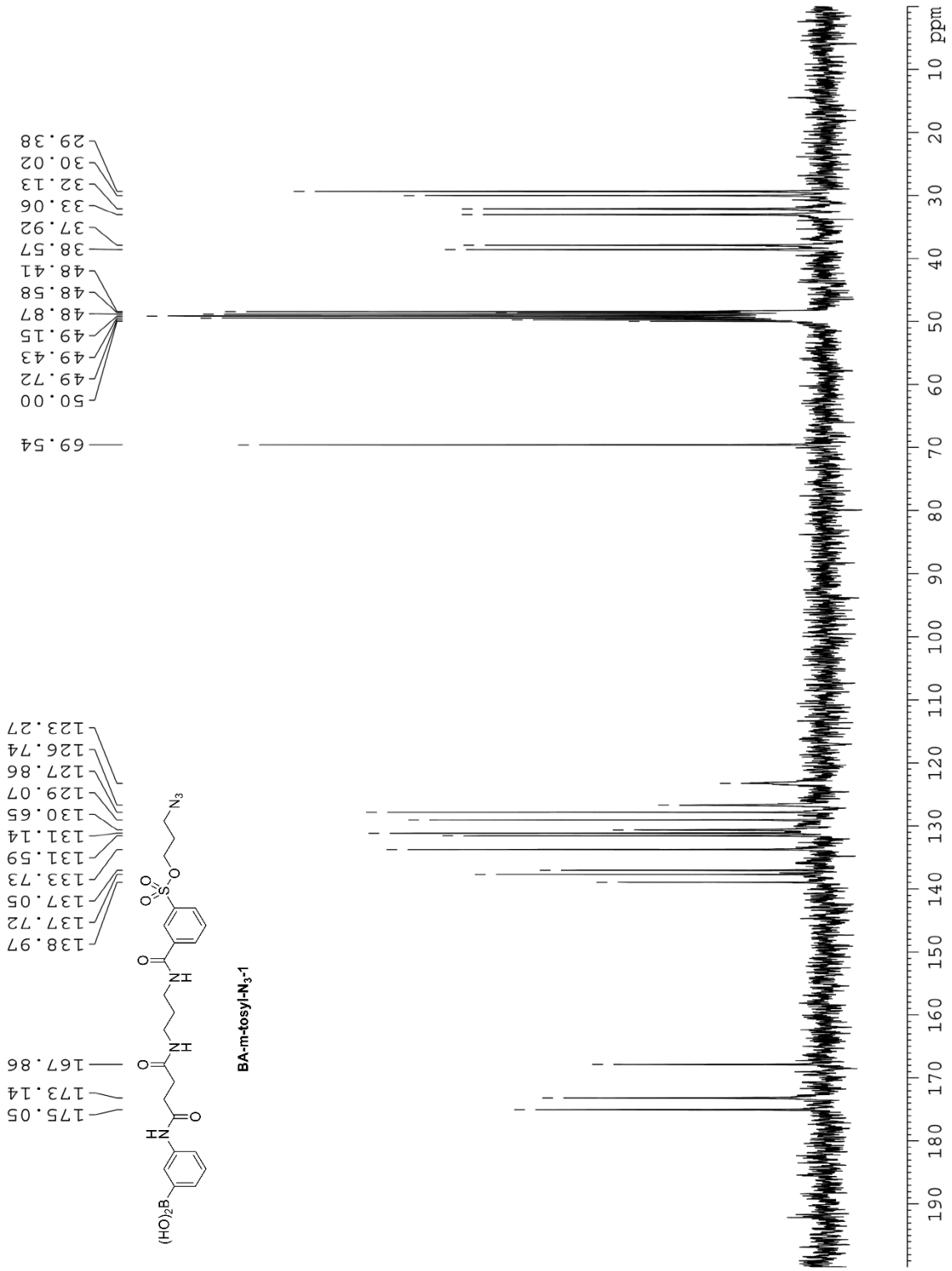


Figure S91. ^{13}C NMR spectrum of Compound **BA-m-tosyl-N_3-1** in MeOD.

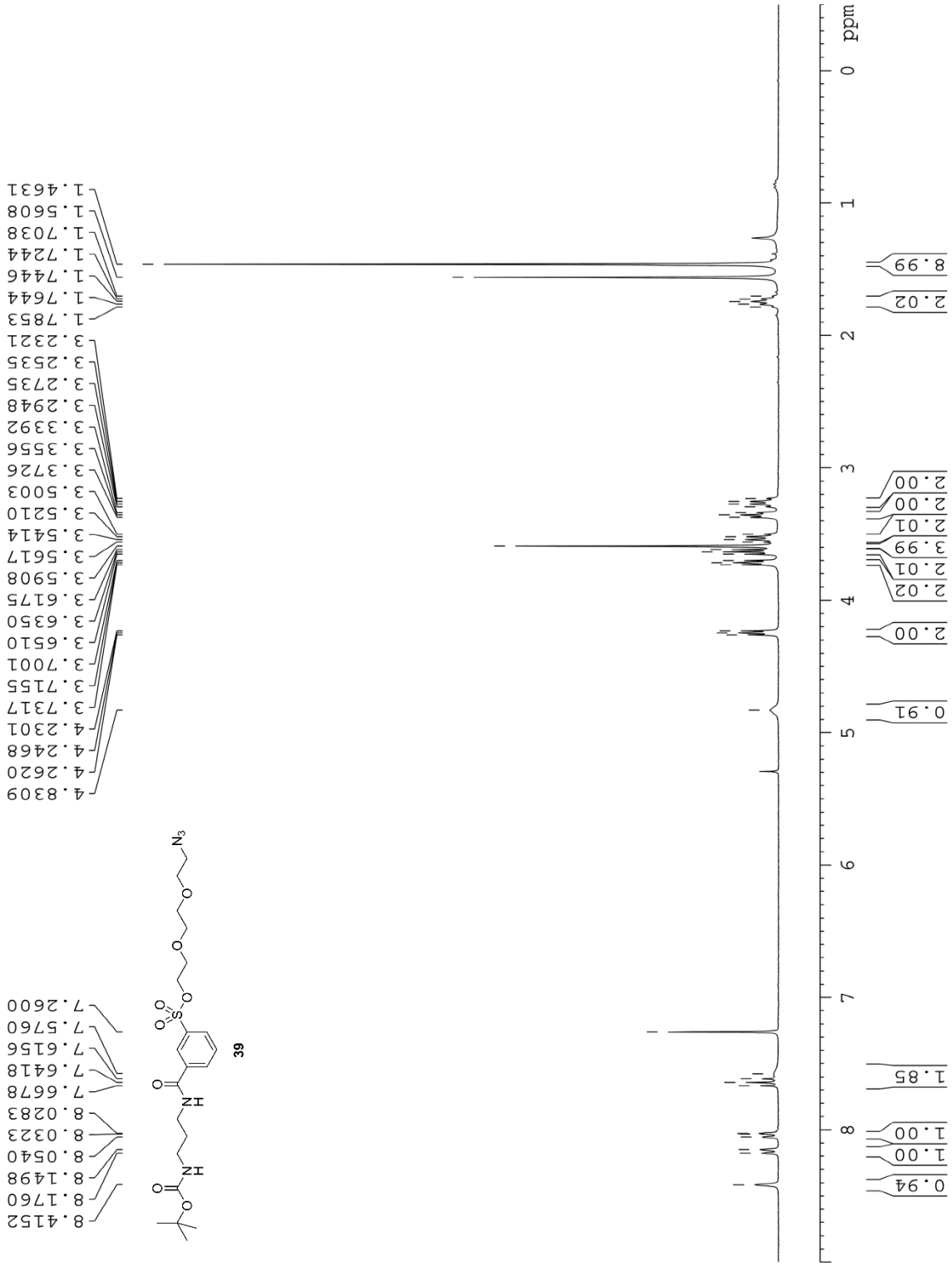


Figure S92. ^{1}H NMR spectrum of Compound **39** in $CDCl_3$.

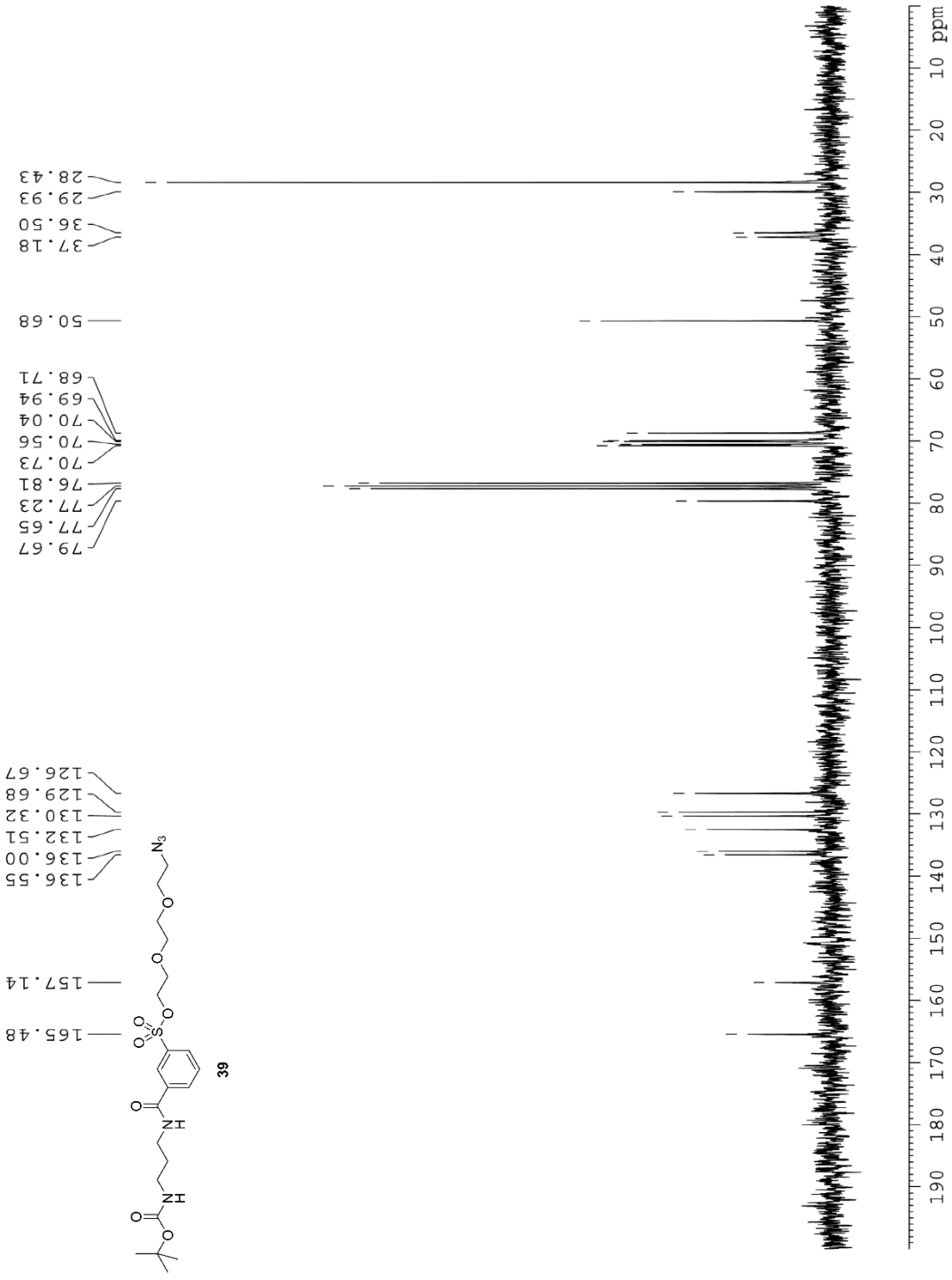


Figure S93. ^{13}C NMR spectrum of Compound **39** in $CDCl_3$.

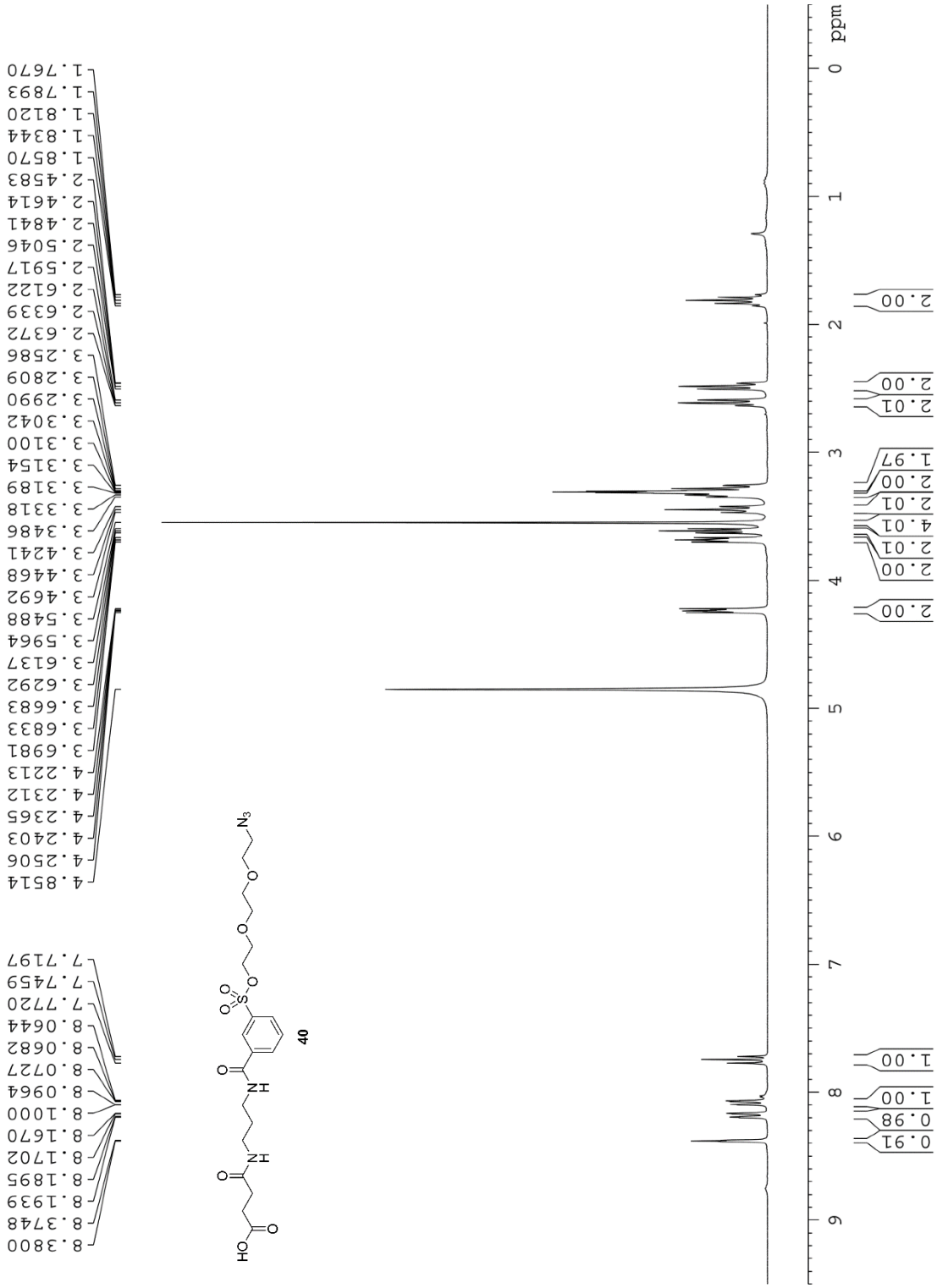


Figure S94. ^{1}H NMR spectrum of Compound **40** in MeOD.

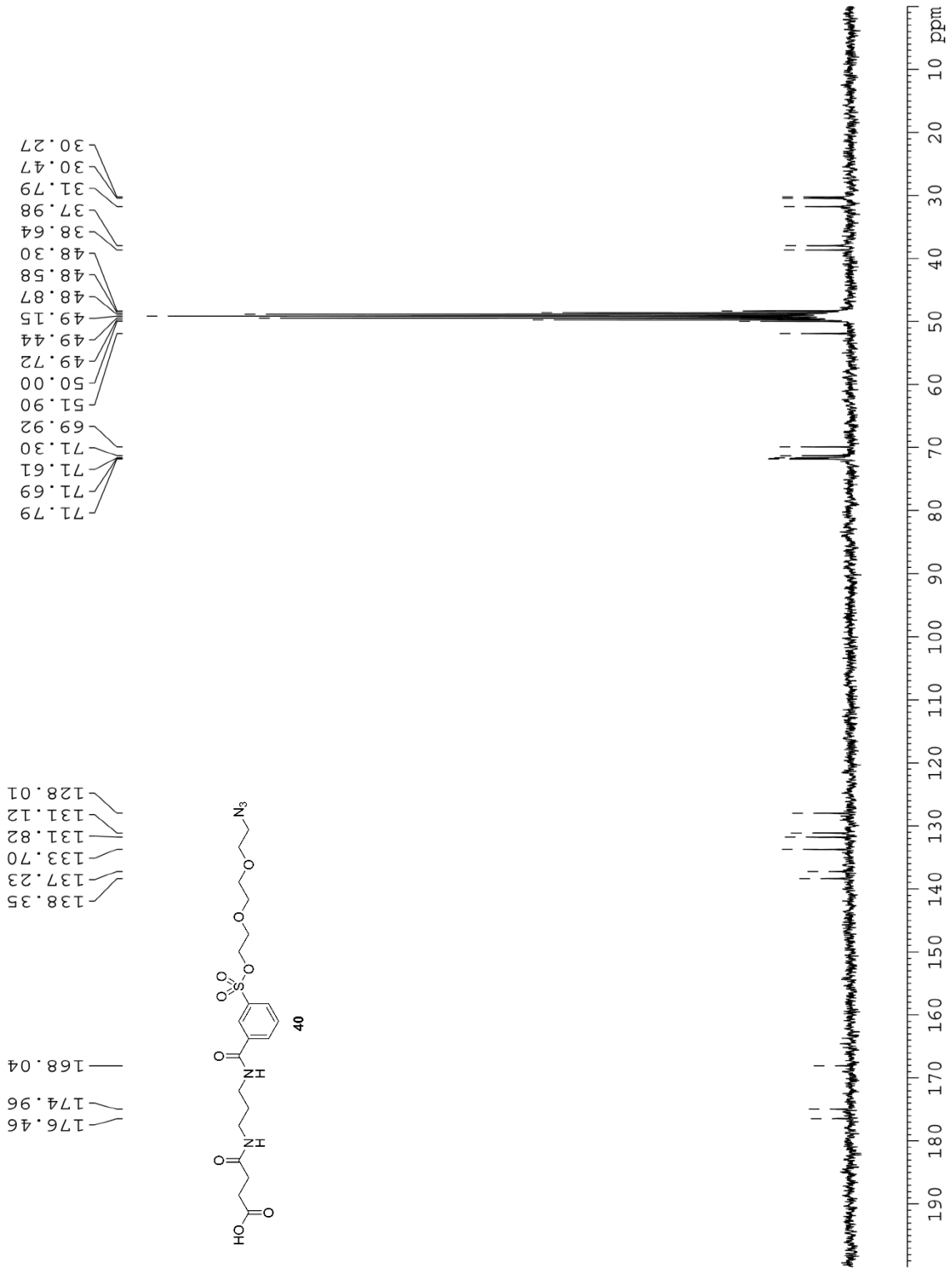


Figure S95. ^{13}C NMR spectrum of Compound **40** in MeOD.

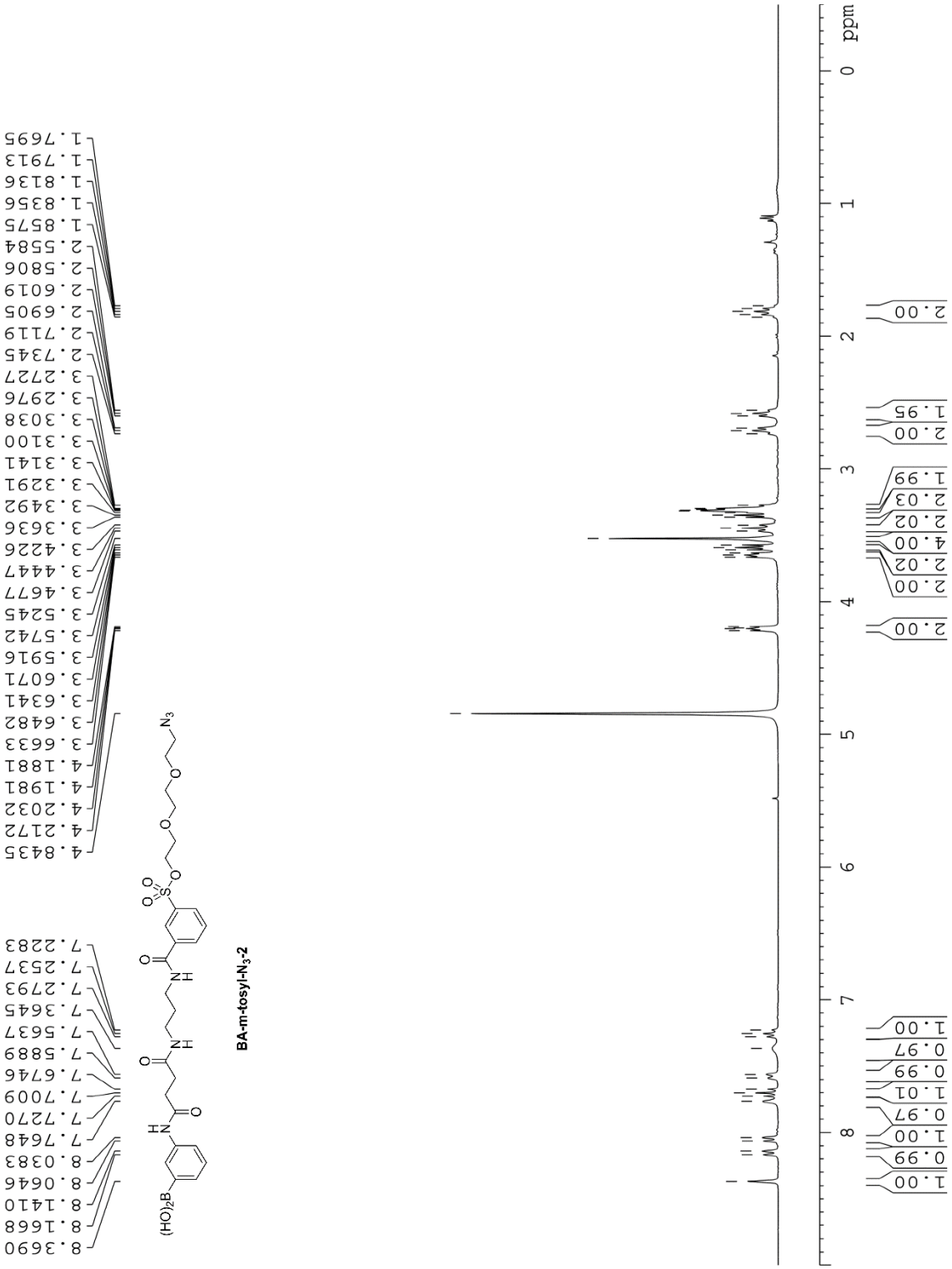


Figure S96. ^{1}H NMR spectrum of Compound **BA-m-tosyl-N_3-2** in MeOD.

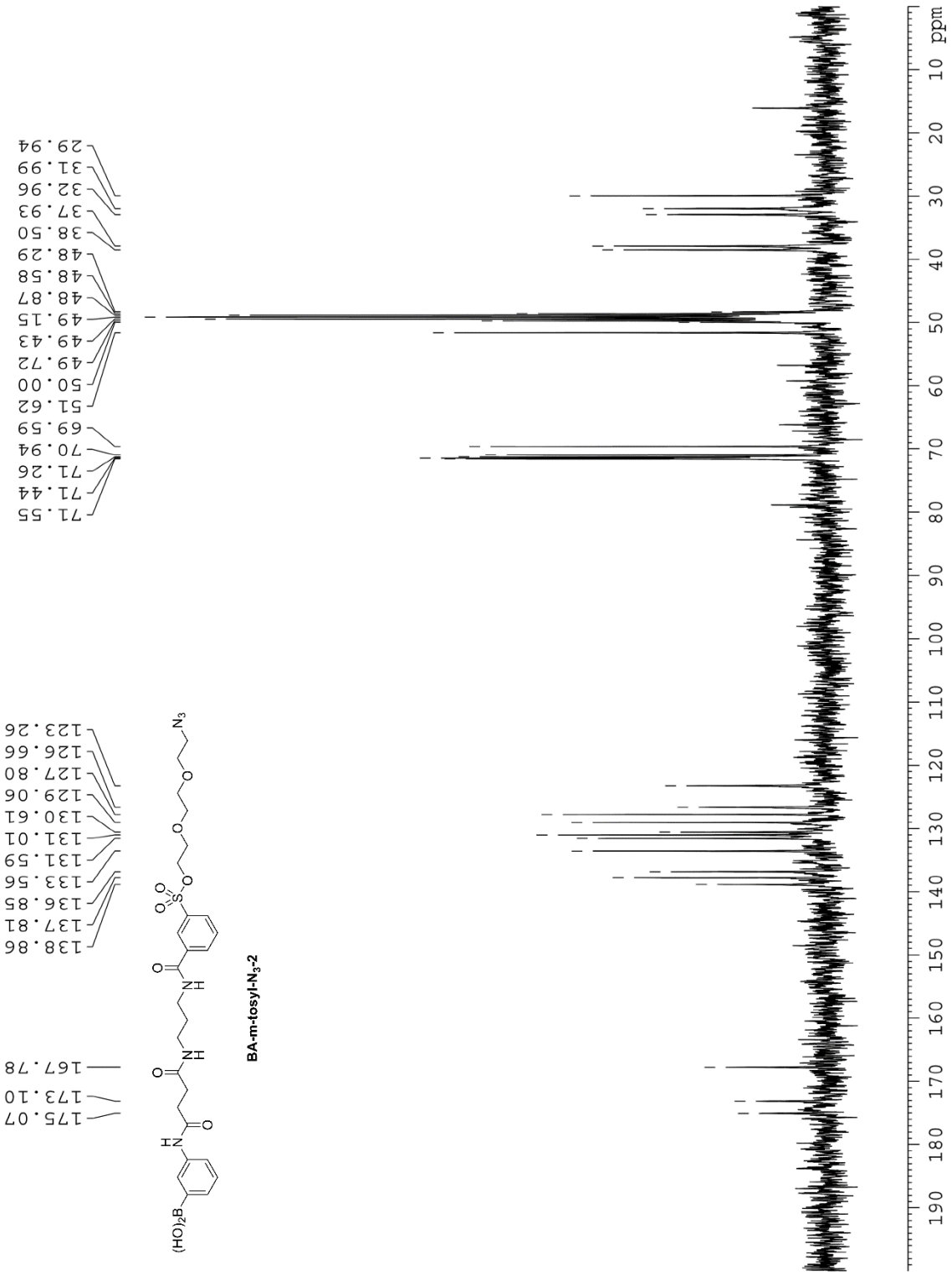


Figure S97. ^{13}C NMR spectrum of Compound **BA-m-tosyl-N_3-2** in MeOD.

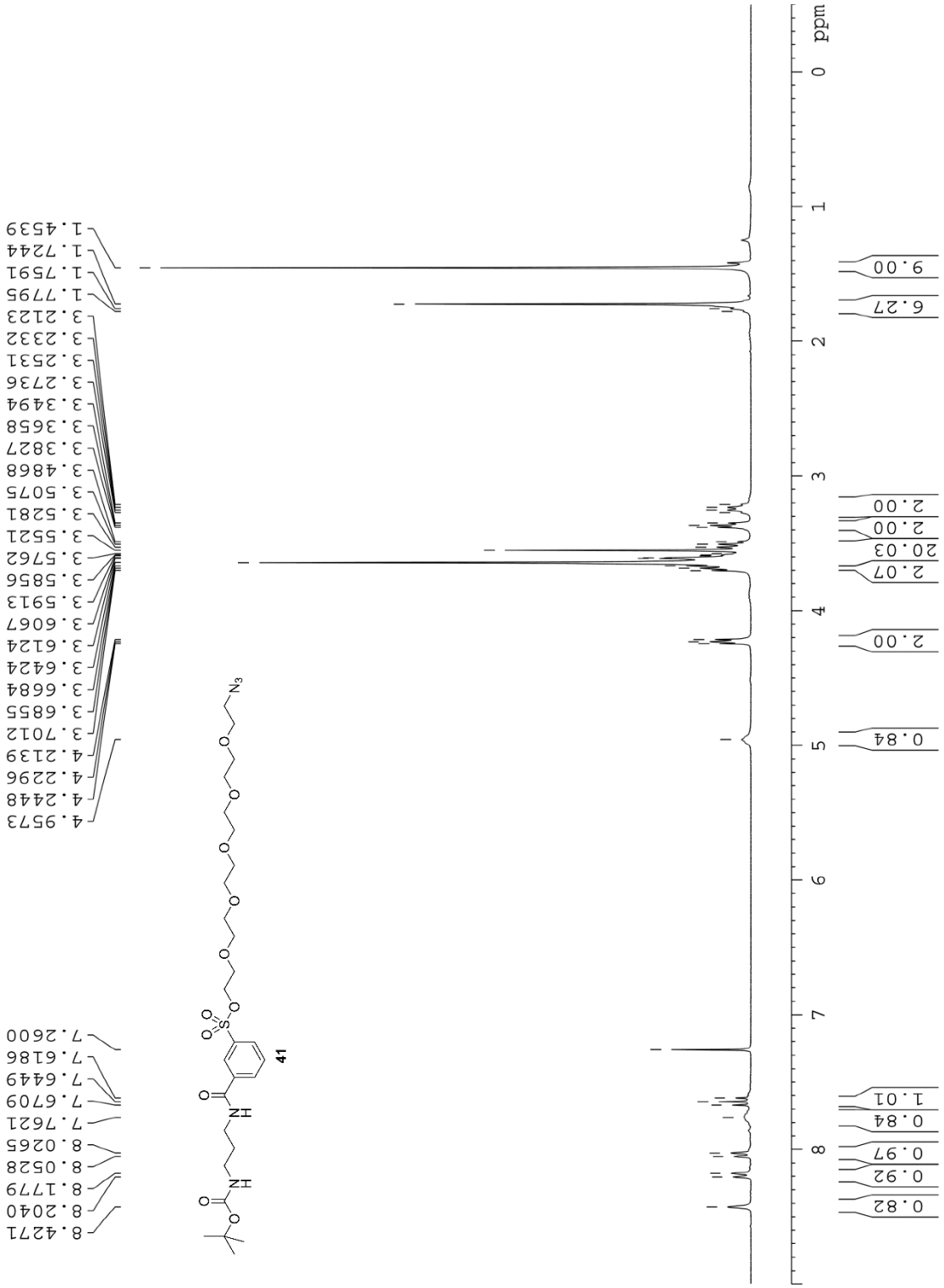


Figure S98. ^{1}H NMR spectrum of Compound **41** in $CDCl_3$.

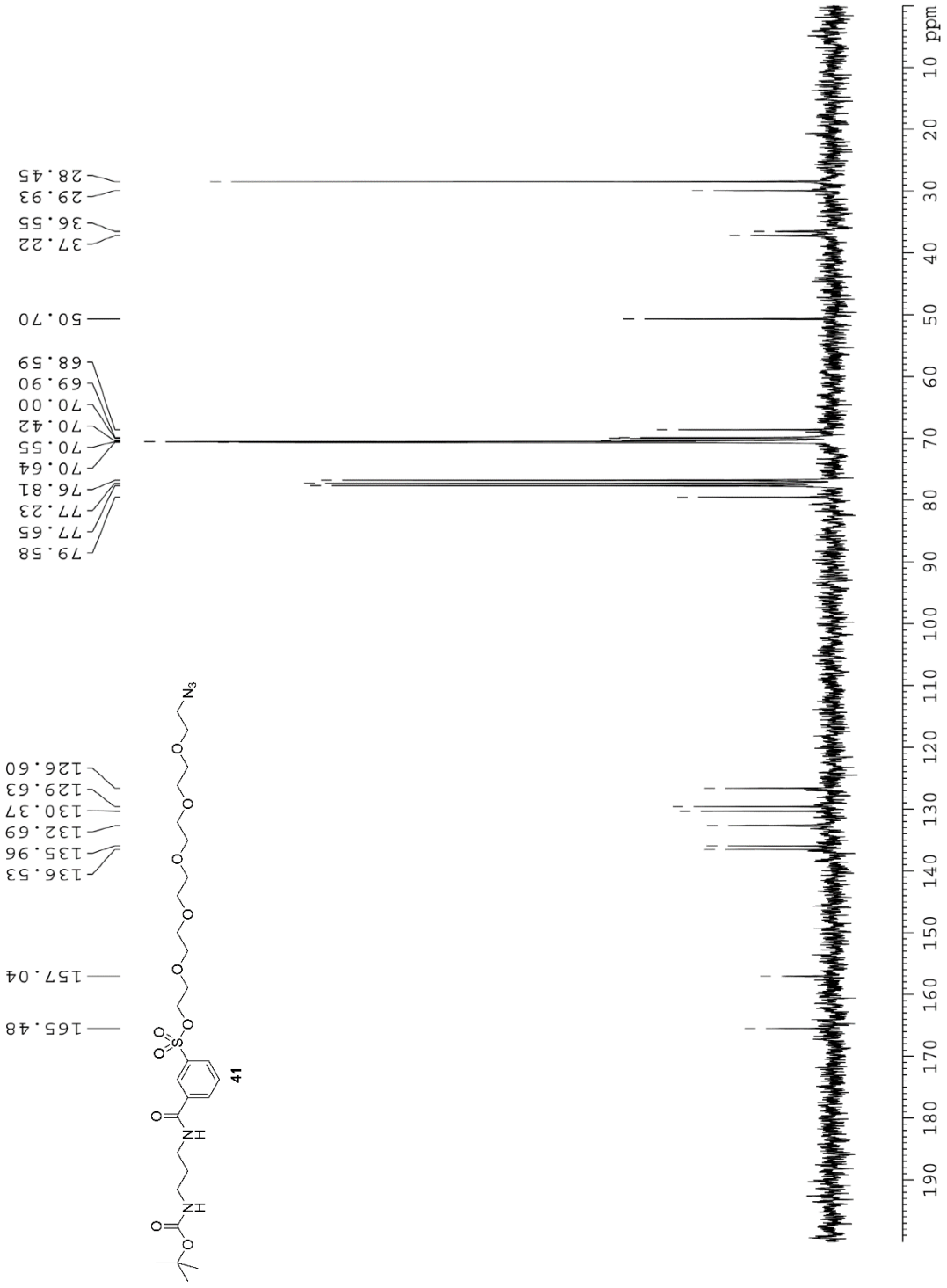


Figure S99. ^{13}C NMR spectrum of Compound **41** in $CDCl_3$.

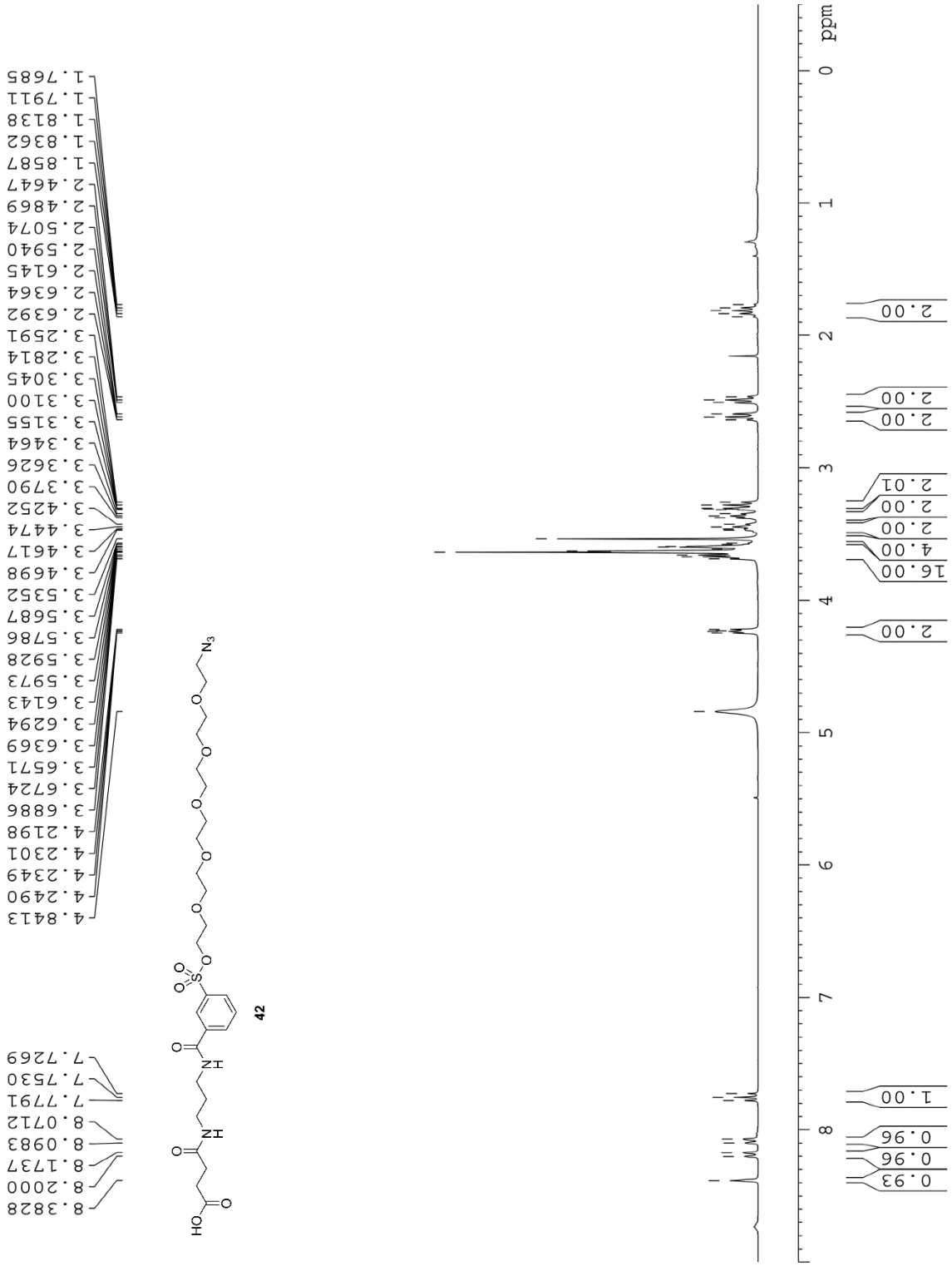


Figure S100. ^{1}H NMR spectrum of Compound **42** in MeOD.

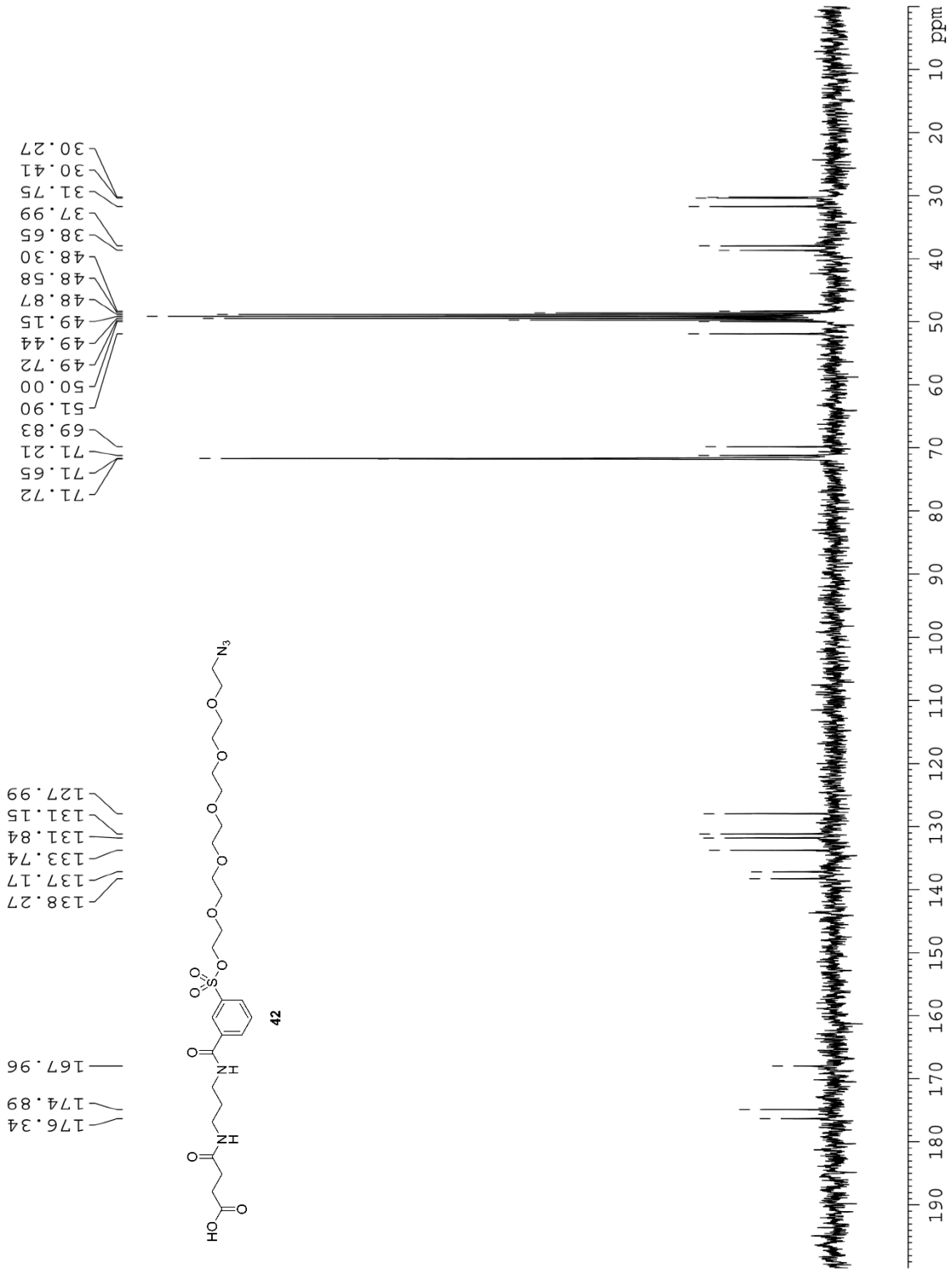


Figure S101. ^{13}C NMR spectrum of Compound **42** in MeOD.

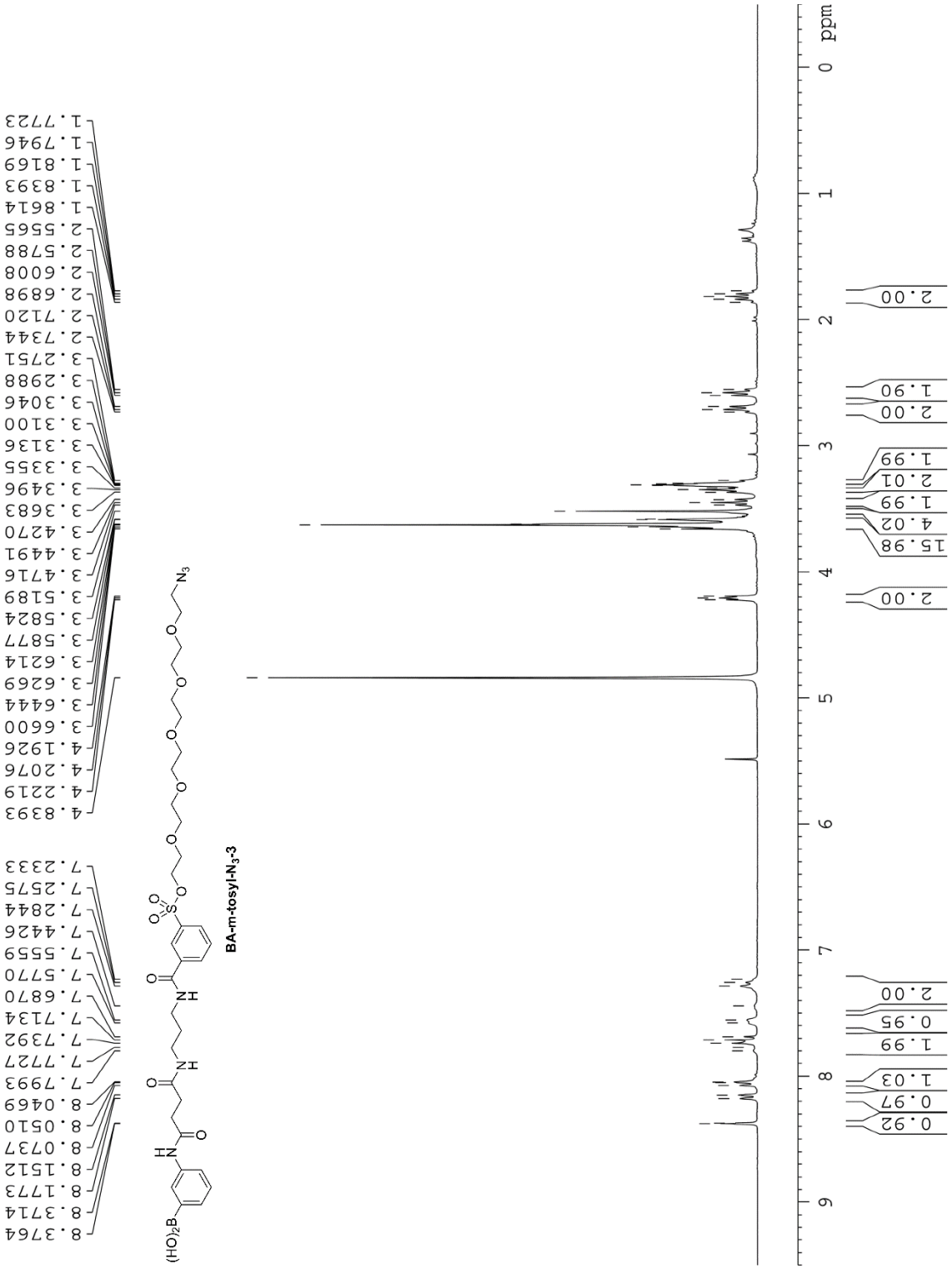


Figure S102. ^{1}H NMR spectrum of Compound **BA-m-tosyl-N_3-3** in MeOD.

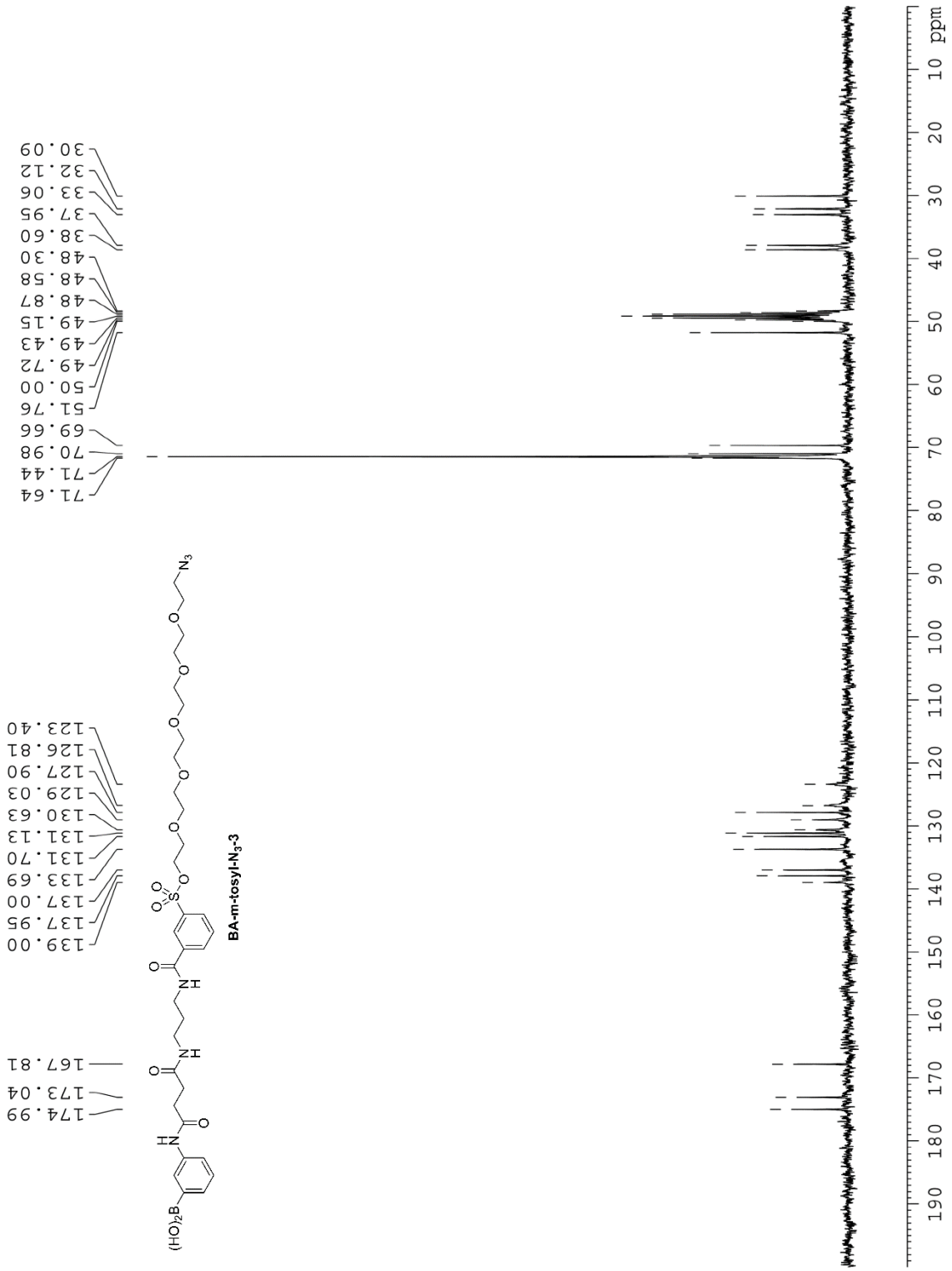


Figure S103. ^{13}C NMR spectrum of Compound **BA-m-tosyl-N_3-3** in MeOD.

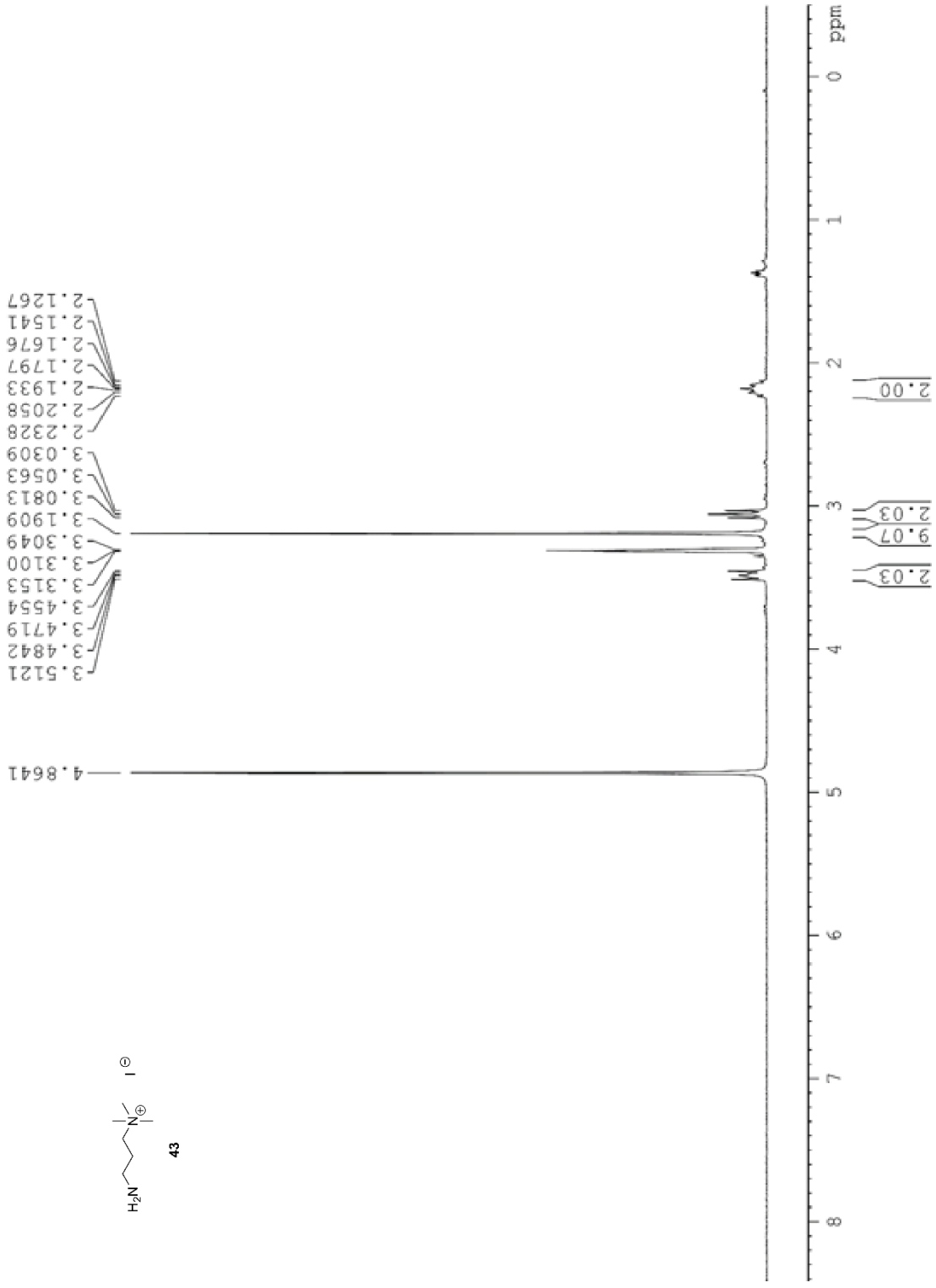


Figure S104. ^{1}H NMR spectrum of Compound **43** in MeOD.

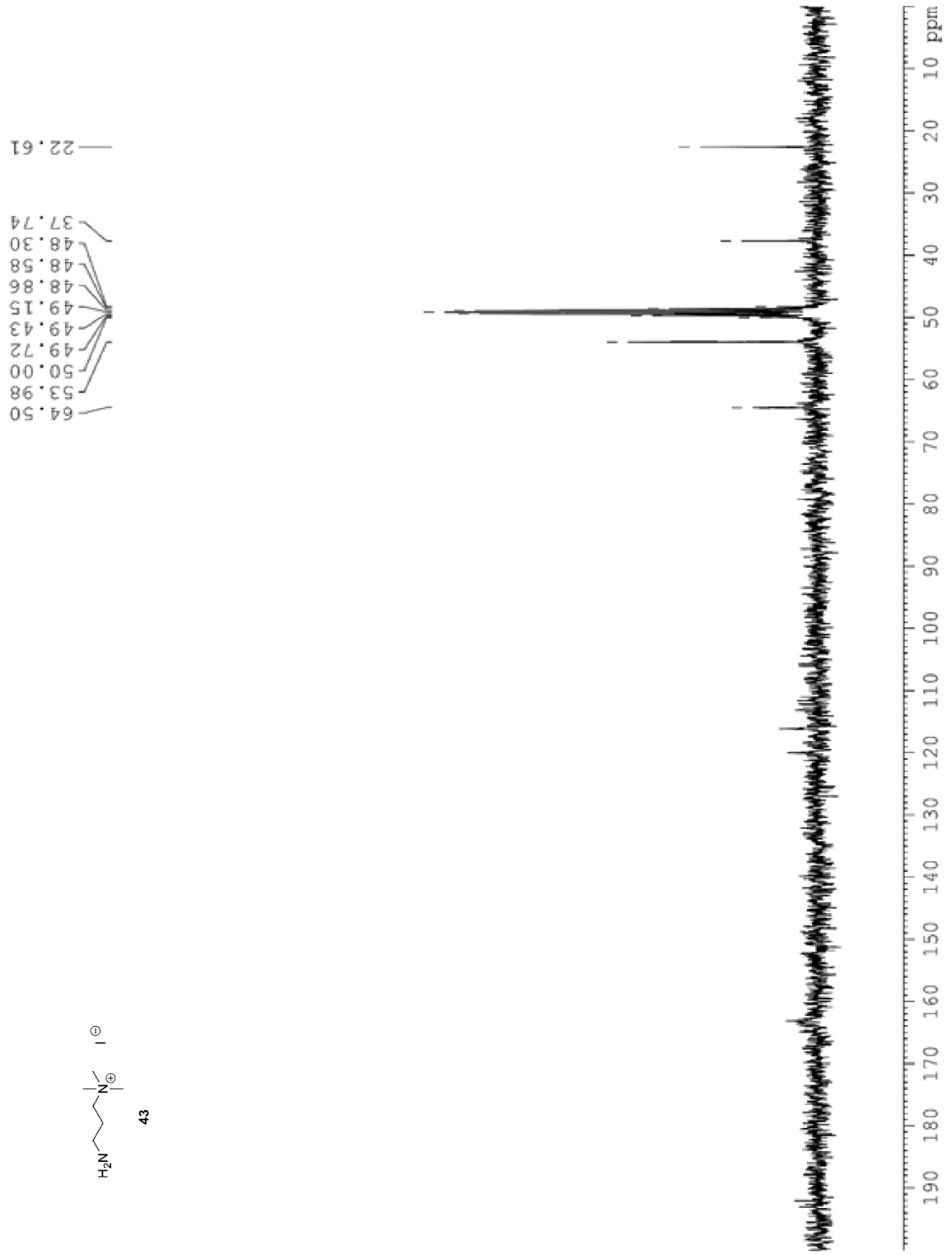


Figure S105. ^{13}C NMR spectrum of Compound **43** in MeOD.

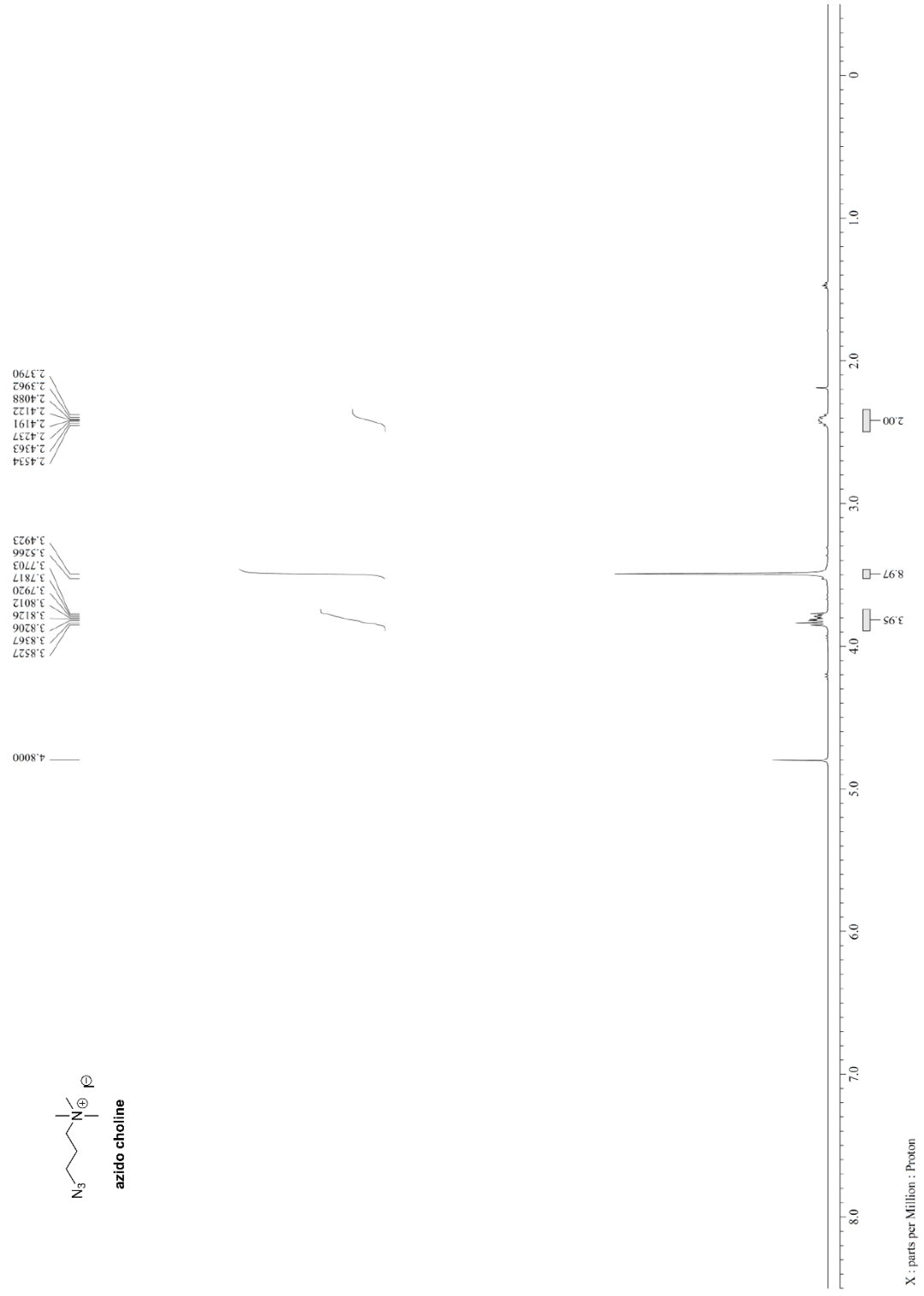


Figure S106. ^{1}H NMR spectrum of Compound **azido choline** in MeOD.

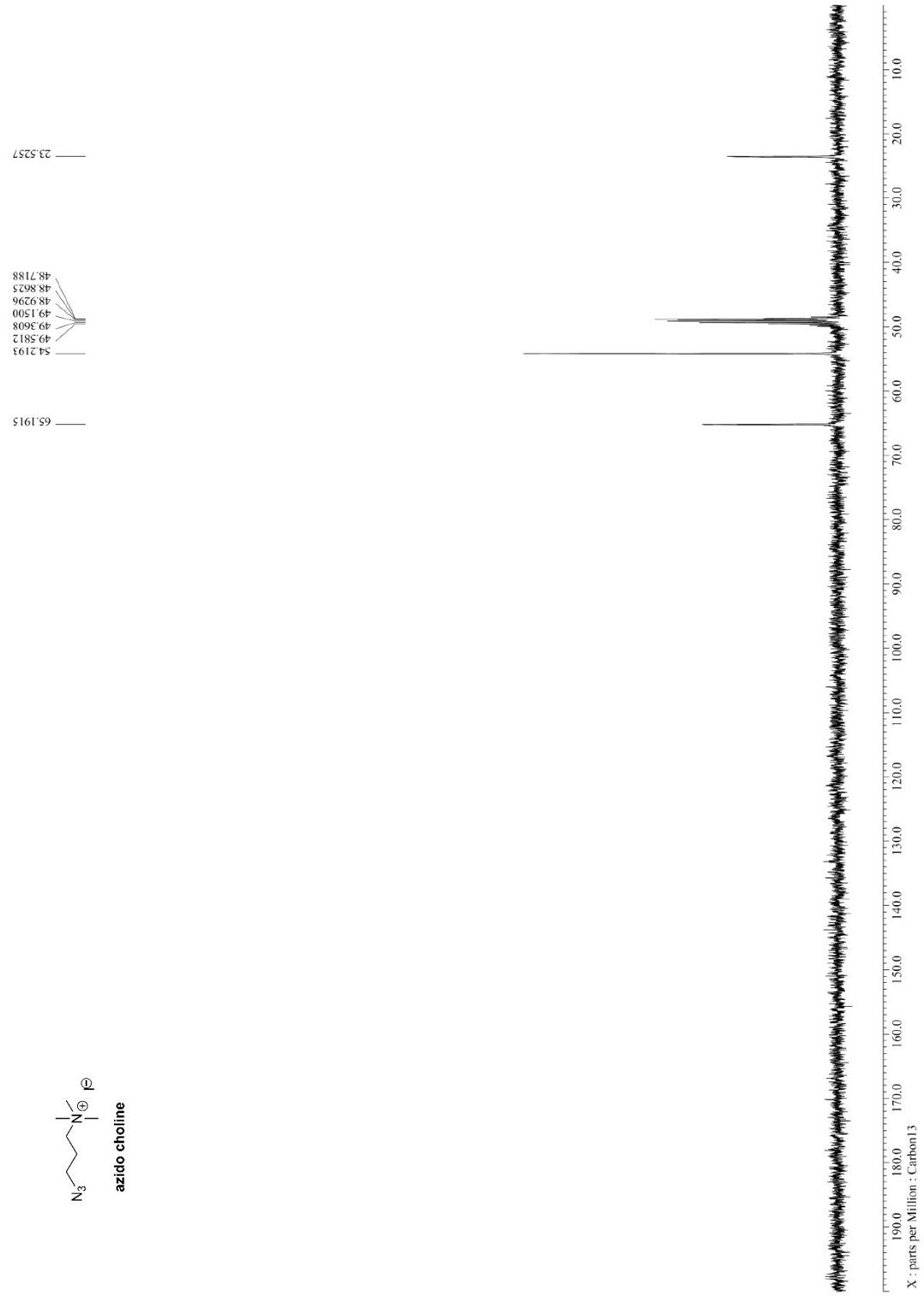


Figure S107. ^{13}C NMR spectrum of Compound **azido choline** in MeOD.

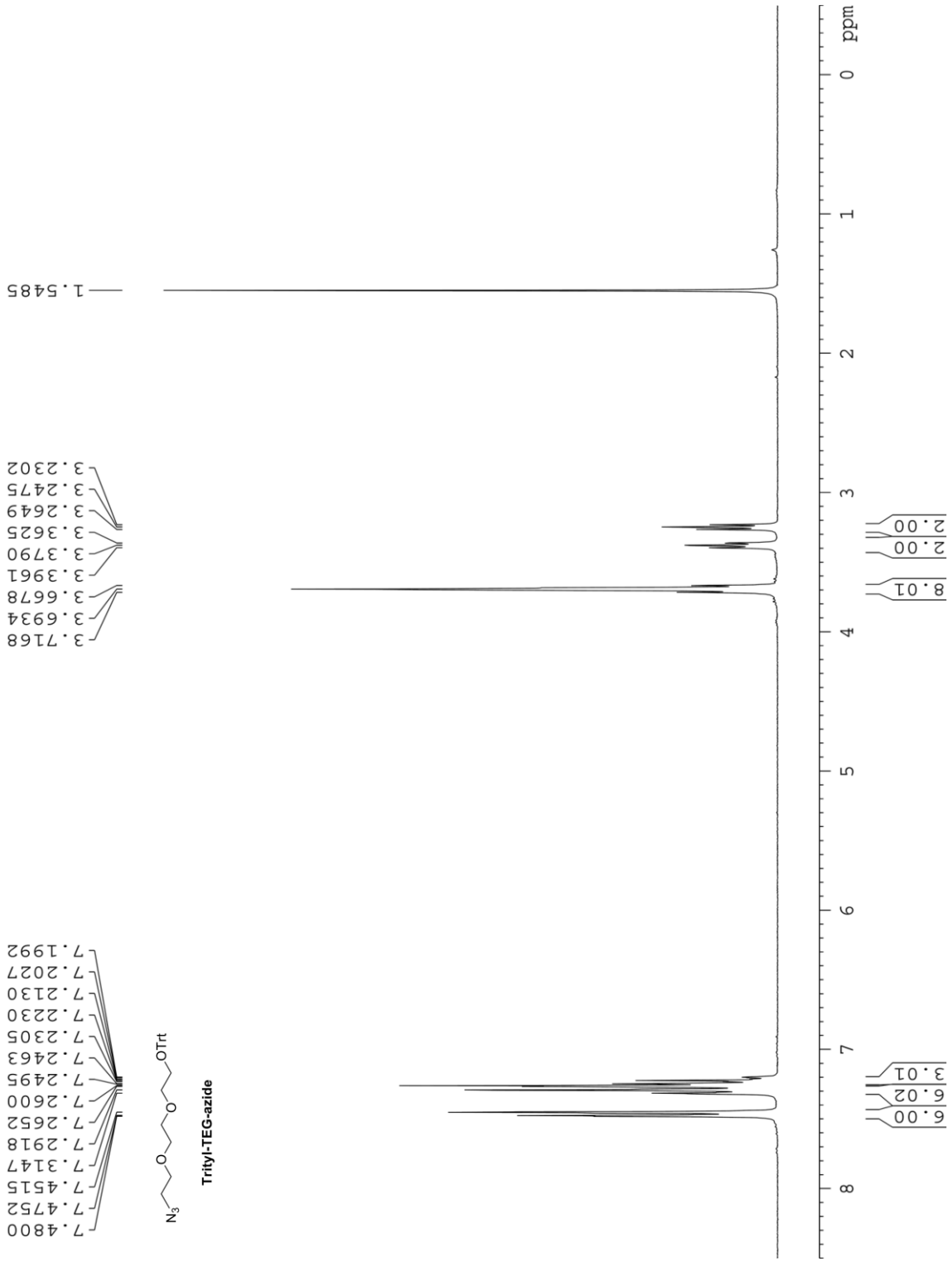


Figure S108. ^{1}H NMR spectrum of Compound **Trityl-TEG-azide** in $CDCl_3$.

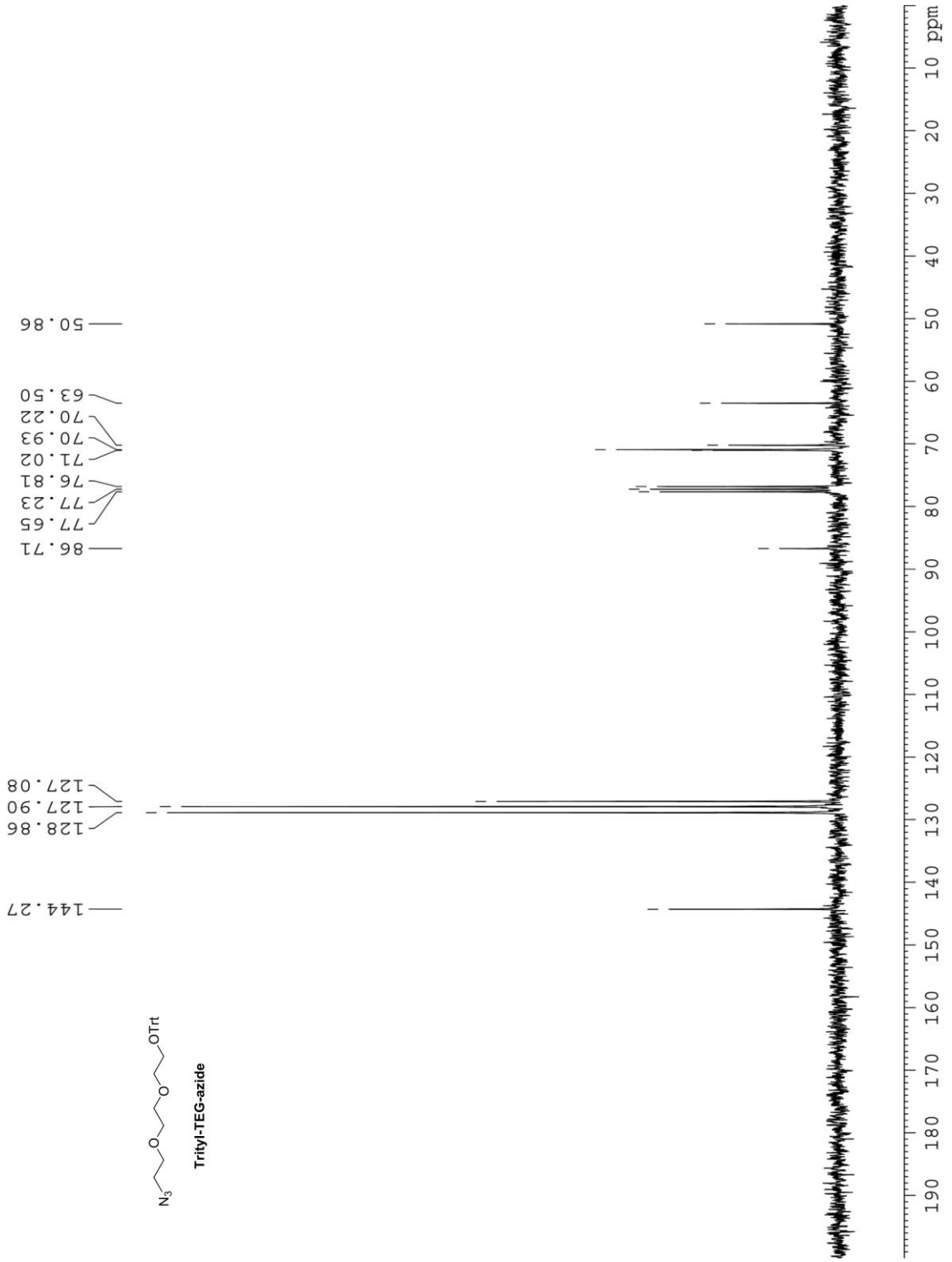


Figure S109. ^{13}C NMR spectrum of Compound **Trityl-TEG-azide** in $CDCl_3$.

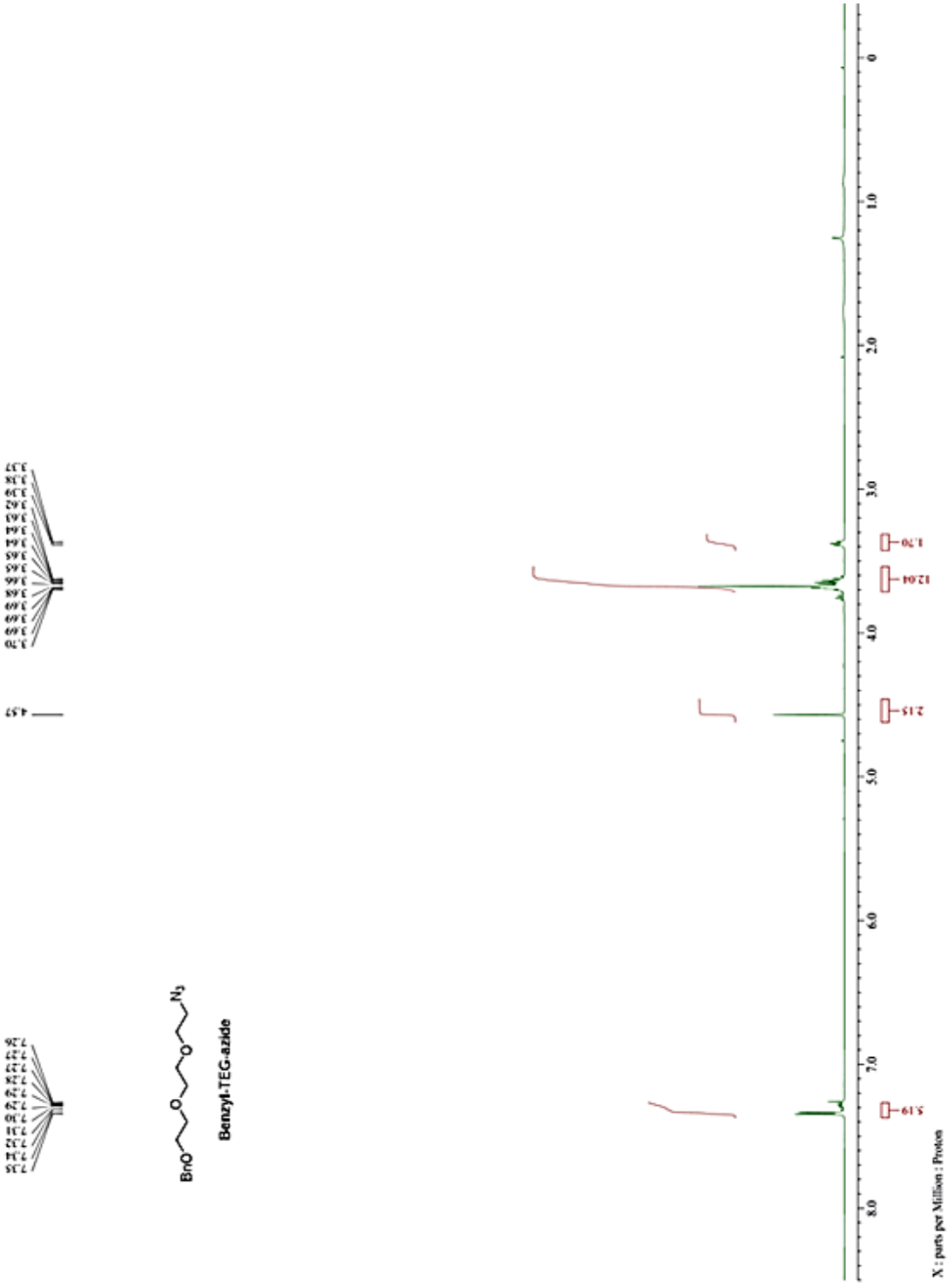


Figure S110. ^{1}H NMR spectrum of Compound **Benzyl-TEG-azide** in $CDCl_3$.

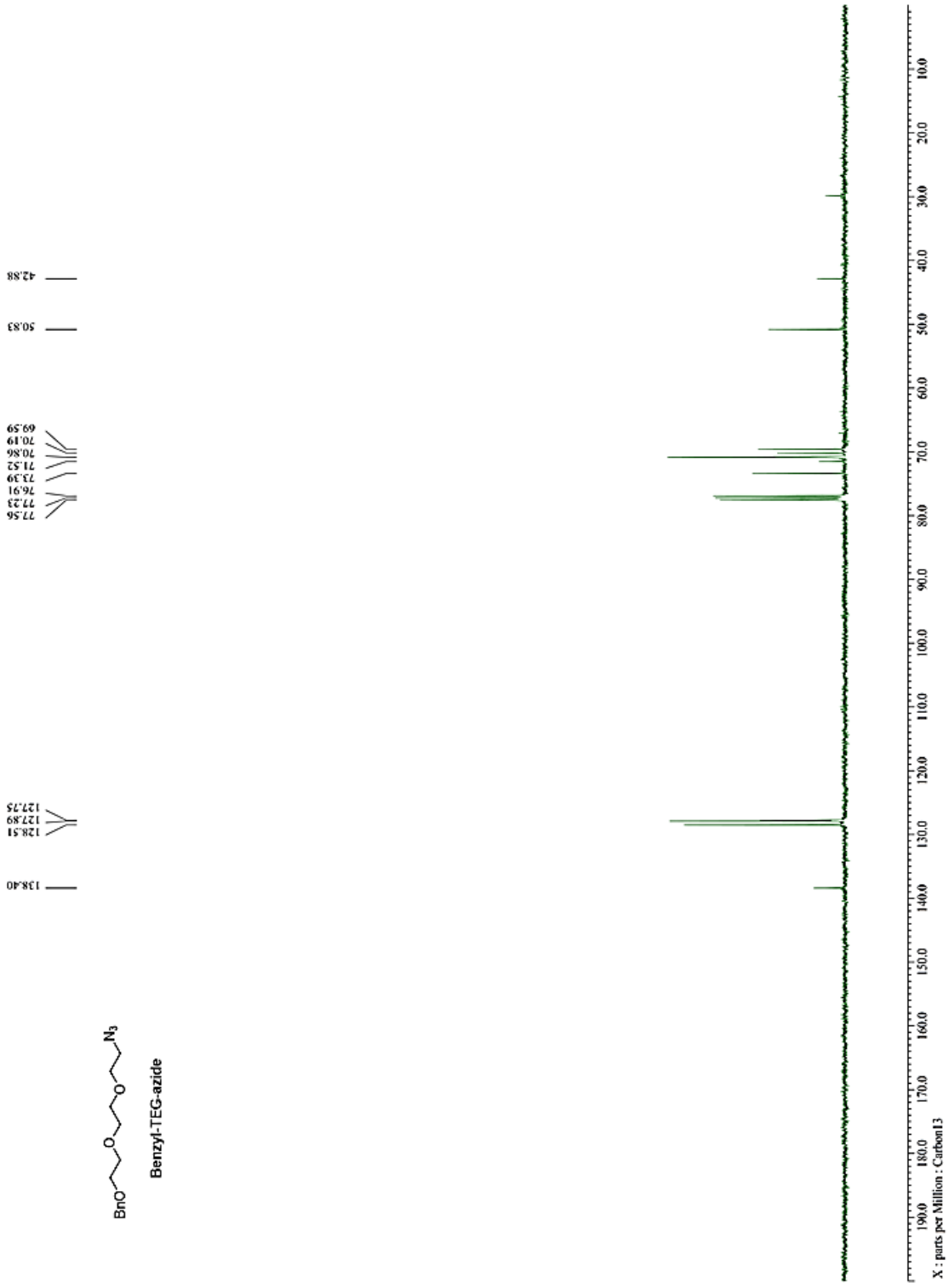


Figure S111. ^{13}C NMR spectrum of Compound **Benzyl-TEG-azide** in $CDCl_3$.