Supplementary Information

Dichlorotriazine-based multivalent probe for selective affinity labeling of carbohydrate binding proteins

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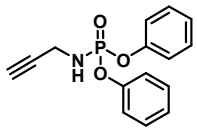
1. General experimental methods

NMR experiments were performed at 293 K on JEOL ECX 300 and JEOL ECX 400 and processed with Delta software. The spectra are referenced internally according to residual solvent signals of $CDCl_3$ (^{1}H NMR; δ=7.26 ppm and ^{13}C NMR; δ=77.0 ppm), D_2O (^{1}H NMR; δ=4.79 ppm and ^{13}C NMR; δ=0.0 ppm), and pyridine-d_5 (^{1}H NMR; δ=7.19 ppm and ^{13}C NMR; δ=123.5 ppm). Positive ion ESI-TOF MS data were obtained by JEOL AccuTOF mass spectrometer. MALDI-TOF-mass spectra were acquired by UltrafleXtreme (Bruker Daltonics) and autoflex speed TOF/TOF (Bruker Daltonics). Unless noted otherwise, all chemical reagents were purchased from Wako Chemicals, TCI, Sigma-Aldrich. Column chromatography was performed using Silica gel 60 (spherical, particle size 40-100 μm; Kanto). Gold-nanoparticles (AuNPs) were characterized by agarose gel electrophoresis experiments performed on ATTO Submerge-Mini WSE-1710, UV-visible spectrometry recorded on a NanoDrop ND-1000 spectrophotometer (Thermo Fisher Scientific), dynamic Light Scattering (DLS) using Zeta-nanosizer (Nano S, Malvern, UK). The SDS-PAGE and agarose gels were scanned with Canon CanoScan LiDE 210.

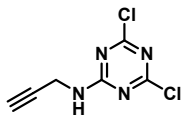
2. Synthesis of lipoic acid derivatives (7-18)

Compound **7**



To a solution of diphenyl chlorophosphite (210 μL, 1.00 mmol, 1.1 equiv.) in anhydrous CH_2Cl_2 (1.8 mL) was added triethylamine (TEA) (140 μL, 1.00 mmol, 1.1 equiv.) and propargylamine (58 μL, 0.91 mmol, 1.0 equiv.) at 0 °C. The reaction mixture was stirred at room temperature for 22 hours. The reaction was quenched by addition of deionized H_2O (dI H_2O; 5 mL). The organic layer was separated, and the aqueous layer was washed twice with CH_2Cl_2. The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified using silica gel flash column chromatography (hexane/ethyl acetate (EtOAc) = 1/0 to 1/1) to give compound **7** as white solid (234 mg, 0.81 mmol, 90%). ^{1}H NMR (300 MHz, $CDCl_3$): δ7.36-7.17 (m, 10H), 3.87 (m, 2H), 3.59 (dd, *J*=6.5 Hz, 1H), 2.24 (t, *J*=2.8 Hz, 1H) ; ^{13}C NMR (75 MHz, $CDCl_3$): δ150.7 (×2), 129.8 (×4), 125.2 (×2), 120.4 (×4), 80.3, 72.2, 31.4; HRMS (ESI-TOF) calcd for $C_{15}H_{14}N_1Na_1O_3P_1$ $[M+Na]^+$: 310.0609; Found 310.0615.

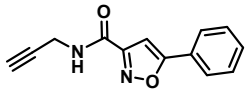
Compound **8**



To a solution of cyanuric chloride (185 mg, 1.00 mmol, 1.0 equiv.) in anhydrous tetrahydrofuran (THF)-CH_2Cl_2 (1:4 v/v, 3.3 mL), propargylamine (64 μL, 1.0 mmol, 1.0 equiv.) and *N, N*-diisopropylethylamine (DIPEA) (284 μL, 1.67 mmol, 1.67 equiv.) in anhydrous THF-CH_2Cl_2 (2:1 v/v, 2.7 mL) was added dropwise at 0 °C. The reaction was stirred at 0 °C for 90 min, then at room temperature for another 2 hours. The solvent was concentrated *in vacuo*. The crude product was purified by silica gel flash column chromatography using CH_2Cl_2 to obtain compound **8** (138 mg, 0.68 mmol, 68%) as white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ6.85 (s, 1H), 4.30 (dd, *J*=2.4, 3.4 Hz, 2H), 2.30 (t,

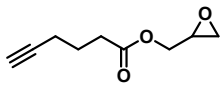
J=2.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ171.3, 170.2, 165.6, 77.8, 72.9, 31.4; HRMS (ESI-TOF) calcd for $C_6H_5Cl_2N_4$ $[M+H]^{+\cdot}$ 202.9891; Found 202.9904.

Compound **9**

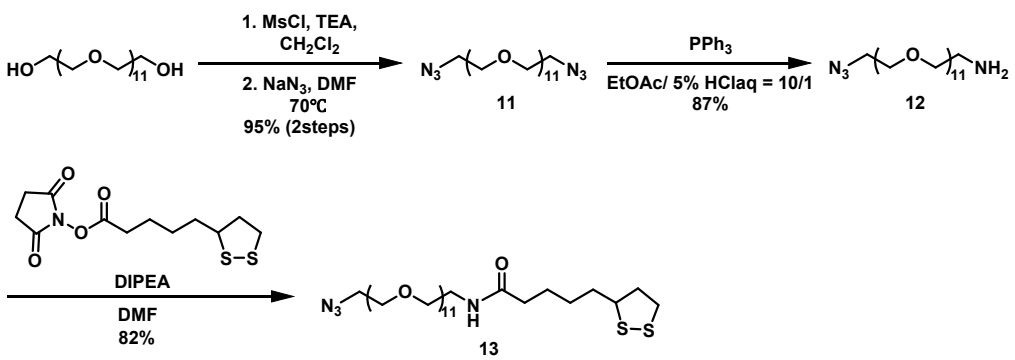


To a solution of 5-phenylisoxazole-3-carboxylic acid (50.0 mg, 0.264 mmol, 1.0 equiv.), 1-hydroxybenzotriazole (HOBt) (40.4 mg, 0.264 mmol, 1.0 equiv.) and 1-(3-dimethyl aminopropyl)-3-ethyl carbodiimide hydrochloride (EDC·HCl) (55.6 mg, 0.291 mmol, 1.1 equiv.) in anhydrous acetonitrile (MeCN) (1.32 mL) was added propargylamine (20 μL, 0.31 mmol, 1.2 equiv.) at room temperature. The reaction was stirred at room temperature for 20 hours and was concentrated *in vacuo*. The residue was diluted with 26 mL CH_2Cl_2 and was treated with 10% $NaHCO_3$aq. The organic layer was separated, washed with brine, which was then dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by recrystallization (hexane/ EtOAc) to give compound **9** (18.4 mg, 0.080 mmol, 31%) as white solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ7.79 (s, 2H), 7.47 (s, 3H), 7.18 (s, 1H), 6.98 (s, 1H), 4.27 (s, 2H), 2.29 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ171.8, 158.7 (×2), 130.9 (×2), 129.2, 126.7, 126.0 (×2), 99.2, 78.7, 72.3, 29.3; HRMS (ESI-TOF) calcd for $C_{13}H_{10}N_2Na_1O_2$ $[M+Na]^+$: 249.0640; Found 249.0649.

Compound **10**



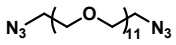
Hexynoic acid (176 μL, 1.60 mmol, 1.2 equiv.) and DMAP (16.4 mg, 0.134 mmol, 0.10 equiv.) were dissolved in heptane (13.4 mL) at 0 ℃. After stirring for 10 minutes, glycidol (98 μL, 1.3 mmol, 1.0 equiv.) and *N*,*N*-dicyclohexylcarbodiimide (DCC; 304 mg, 1.47 mmol, 1.0 equiv.) were added at room temperature, which was stirred at room temperature for 4 hours. The reaction mixture was filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (hexane/ EtOAc = 100/0 to 80/20) to give compound **10** (120 mg, 0.708 mmol, 55%) as clear liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ4.41-3.97 (m, 1H), 3.90-3.86 (m, 1H), 3.19-3.13 (m, 1H), 2.81 (t, *J*=4.3 Hz, 1H), 2.62-2.61 (m, 1H), 2.49-2.46 (m, 2H), 2.31-2.22 (m, 2H), 1.96-1.95 (m, 1H), 1.86-1.79 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ172.9, 83.2, 69.3, 65.0, 49.4, 44.7, 32.7, 23.6, 17.9; ESI-TOF MS calcd for $C_9H_{13}O$ $[M+H]^+$: 169.08; Found 169.38.



Scheme S1. Synthesis of azide-PEG11-lipoate **13**.

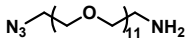
Compounds **11**-**13** were synthesized according to the published procedures. [1,2]

Compound **11**



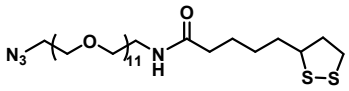
To a solution of dodeca ethylene glycol (200 mg, 0.366 mmol, 1.0 equiv.) and TEA (306 μL, 2.20 mmol, 6.0 equiv.) in anhydrous CH_2Cl_2 (4.0 mL) methanesulfonyl chloride (MsCl, 114 μL, 1.46 mmol, 4.0 equiv.) in anhydrous CH_2Cl_2 (4.0 mL) was added dropwise. After stirring at 0 ℃ for 2 hours, the reaction mixture was diluted 10-fold with CH_2Cl_2 and washed with 1 M HClaq three times and once with brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was dissolved in anhydrous DMF (0.78 mL), to which sodium azide (101 mg, 1.56 mmol, 4.0 equiv.) was added. The mixture was stirred at 70 ℃ for 3 hours. The reaction mixture was diluted 50-fold with diethyl ether (Et_2O), filtered, and concentrated *in vacuo* to give compound **11** (210 mg, 0.35 mmol, 95%) as a yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ3.68-3.63 (m, 44H), 3.37 (t, *J*=4.3 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ70.7 (×20), 70.1 (×2), 50.8 (×2) ; HRMS (ESI-TOF) calcd for $C_{24}H_{48}N_6Na_1O_{11}$ $[M+Na]^+$: 619.3279; Found 619.3250.

Compound **12**



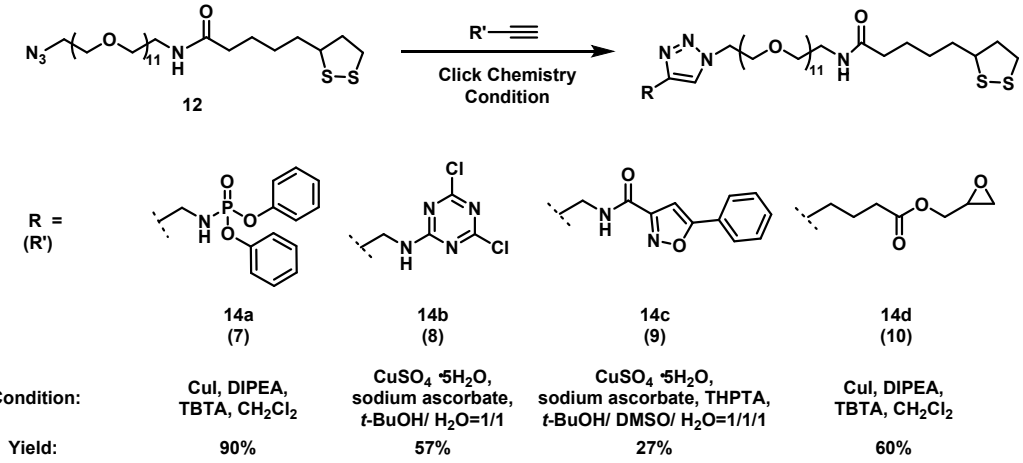
To a solution of compound **11** (237 mg, 0.399 mmol, 1.0 equiv.) in EtOAc (2.0 mL) and 5% HClaq (final 0.5%, 398 μL) was added triphenylphosphine (PPh_3) (115 mg, 0.438 mmol, 1.1 equiv.) in EtOAc (2.0 mL) dropwise at 0 ℃. The reaction was stirred at room temperature for 22 hours. The reaction mixture was diluted 20-fold with dI H_2O and washed with EtOAc three times. To the aqueous layer, 2 N NaOHaq and brine were added and washed with CH_2Cl_2 five times. The organic layer was concentrated *in vacuo* to give compound **12** (198 mg, 0.347 mmol, 87%) as a yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ3.66-3.61 (m, 44H), 3.49 (t, *J*=4.8 Hz, 2H), 3.36 (t, *J*=5.0 Hz, 2H), 2.84 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ73.2, 70.6 (×18), 70.3 (×2), 70.1, 50.8, 41.8; HRMS (ESI-TOF) calcd for $C_{24}H_{51}N_4O_{11}$ $[M+H]^+$: 571.3559; Found 571.3554.

Compound **13**



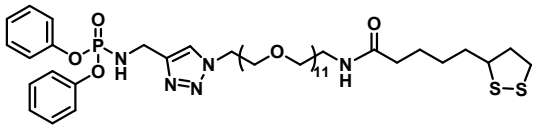
To a solution of α-lipoic acid (296 mg, 1.43 mmol, 1.0 equiv.) and *N*-hydroxysuccinimide (NHS; 182 mg, 1.58 mmol, 1.1 equiv.) in anhydrous CH_2Cl_2 was added EDC·HCl (302 mg, 1.58 mmol, 1.1 equiv.) at 0 ℃. The reaction was stirred at 0 ℃ for 10 min then, at room temperature for 1 hour. The reaction mixture was diluted 10-fold with CH_2Cl_2 and washed with dIH_2O four times, 10% NH_4Claq three times, and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by silica gel flash column chromatography using $CHCl_3$ to provide lipoyl NHS ester (331 mg, 1.09 mmol, 76%) as a yellow solid. Compound **12** (145 mg, 0.26 mmol, 1.0 equiv.) was dissolved in anhydrous DMF (425 μL), was added with lipoyl NHS ester (109 mg, 0.36 mmol, 1.4 equiv.) and DIPEA (178 μL, 1.02 mmol, 4.0 equiv.) The reaction was stirred at room

temperature for 22 hours. It was then diluted 20-fold with CH_2Cl_2 and washed with 5% $NaHCO_3$aq three times, 1% NH_4Claq three times, and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by silica gel flash column chromatography ($CHCl_3$/ MeOH/ AcOH = 100/0/0 to 97/3/0.1) to provide compound **13** (159 mg, 0.21 mmol, 82%) as yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ6.37 (s, 1H), 3.64-3.62 (m, 42H), 3.53 (m, 2H), 3.40 (m, 4H), 3.13 (m, 2H), 2.44 (m, 1H), 2.18 (t, *J*=7.4 Hz, 2H), 1.89 (m, 1H), 1.66 (m, 5H), 1.46 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ172.9, 70.6 (×18), 70.3, 70.1, 70.0 (×2), 56.5, 50.8, 40.3, 39.2, 38.6, 36.4, 34.8, 29.3, 25.5; HRMS (ESI-TOF) calcd for $C_{32}H_{62}N_4Na_1O_{12}S_2$ $[M+Na]^+$: 781.3703; Found 781.3672.



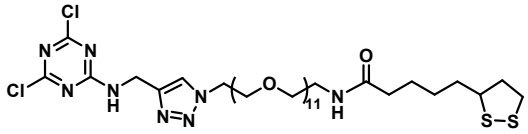
Scheme S2. Click chemistry-mediated coupling of electrophilic groups to azide-PEG11 lipoate (**14a-14d)**.

Compound **14a**



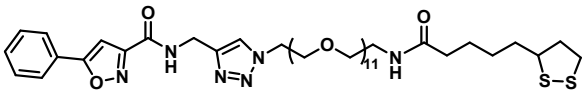
To a solution of compound **13** (32.2 mg, 0.0424 mmol, 1.0 equiv.) and compound **7** (16.5 mg, 0.0574 mmol, 1.2 equiv.) in anhydrous CH_2Cl_2 (478 µL) was added DIPEA (0.83 µL, 4.8 µmol, 0.10 equiv.), tris [(1-benzyl-1*H*-1, 2, 3-triazol-4-yl) methyl] amine (TBTA; 0.3 mg, 0.57 µmol, 0.012 equiv.), and CuI (0.1 mg, 0.57 µmol, 0.012 equiv.) and was stirred at room temperature for 16 hours. The Quadra Pure-IDA® resin was added to the reaction mixture which was stirred at room temperature for another 2 hours. The mixture was filtered and concentrated *in vacuo*. The crude product was purified by silica gel flash column chromatography (CH_2Cl_2/MeOH= 100/0 to 94/6) to give compound **14a** (40.2 mg, 0.038 mmol, 90%) as yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ7.54 (s, 1H), 7.33-7.12 (m, 11H), 6.22 (s, 1H), 4.41 (m, 2H), 3.98 (quin, *J*=6.6 Hz, 1H), 3.80 (t, *J*=5.0 Hz, 2H), 3.63-3.53 (m, 44H), 3.42 (q, *J*=4.9 Hz, 2H), 3.12 (m, 2H), 2.44 (m, 1H), 2.17 (t, *J*=7.4 Hz, 2H), 1.89 (m, 1H), 1.65 (m, 5H), 1.44 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ172.9, 150.8 (×2), 146.0, 129.8 (×4), 125.1 (×2), 123.0, 120.5 (×4), 70.6 (×18), 70.3, 70.0, 69.4 (×2), 56.5, 50.3, 40.3, 39.2, 38.6, 37.5, 36.4, 34.8, 29.0, 25.5; HRMS (ESI-TOF) calcd for $C_{47}H_{76}N_5Na_1O_{15}P_1S_2$ $[M+Na]^+$: 1068.4415; Found 1068.4412.

Compound **14b**



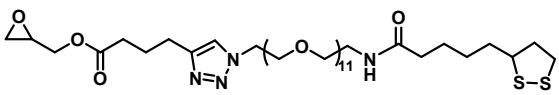
Compound **13** (57.8 mg, 0.0762 mmol, 1.0 equiv.) and compound **8** (18.6 mg, 0.0916 mmol, 1.2 equiv.) were dissolved in *t*BuOH-MQ H_2O (1:1 v/v, 2.3 mL) and 1 M $CuSO_4$aq (15 μL, 15 μmol, 0.20 equiv.), and 1 M sodium ascorbate aq (15 mg, 15 μmol, 0.20 equiv.) were added at room temperature. The reaction mixture was stirred at 50 ℃ for 24 hours then concentrated *in vacuo*. The residue was dissolved in EtOAc (7.6 mL) and washed with H_2O. The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was purified by silica gel flash column chromatography (CH_2Cl_2/MeOH= 100/0 to 94/6) to give compound **14b** (41.6 mg, 0.043 mmol, 57%) as yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ7.83 (s, 1H), 6.27 (s, 1H), 4.74 (d, *J*=5.9 Hz, 2H), 4.51 (s, 1H), 3.83 (s, 2H), 3.61-3.52 (m, 44H), 3.42 (s, 2H), 3.12 (m, 2H), 2.43 (m, 1H), 2.16 (t, *J*=7.4 Hz, 2H), 1.88 (m, 1H), 1.64 (m, 5H), 1.44 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ172.9, 170.8, 170.0, 165.7, 143.1, 123.8, 70.6 (×18), 70.3, 70.0, 69.4 (×2), 56.5, 50.5, 40.3, 39.2, 38.6, 37.1, 36.4, 34.8, 29.0, 25.5; HRMS (ESI-TOF) calcd for $C_{38}H_{66}Cl_2N_8Na_1O_{12}S_2$ $[M+Na]^+$: 983.3545; Found 983.3516.

Compound **14c**



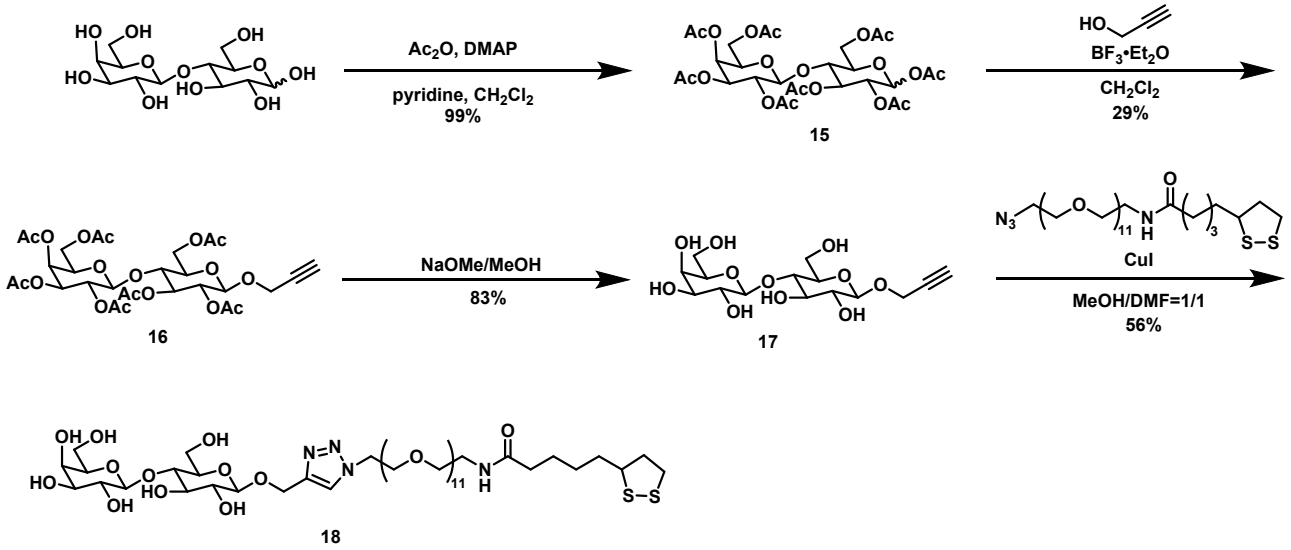
Compound **13** (36.1 mg, 0.0476 mmol, 1.0 equiv.), compound **9** (10.8 mg, 0.0478 mmol, 1.0 equiv.), and tris (3-hydroxypropyltriazolylmethyl) amine (THPTA; 51.6 mg, 0.119 mmol, 2.5 equiv.) was dissolved in *t*BuOH/ DMSO/ dI H_2O =1/ 1/ 1 (950 μL) and $CuSO_4{\cdot}5H_2O$ (29.7 mg, 0.119 mmol, 2.5 equiv.) and sodium ascorbate (46.6 mg, 0.238 mmol, 5.0 equiv.) were added with. The reaction was stirred at 50 ℃ for 9 hours and after that at room temperature for 14 hours. The Quadra Pure-IDA® resin was added to the reaction mixture to quench, which was stirred at room temperature for another 2 hours. The reaction mixture was filtered and concentrated *in vacuo*. The crude product was purified by silica gel flash column chromatography ($CHCl_3$/ MeOH = 100/0 to 90/10) to give compound **14c** (12.4 mg, 0.013 mmol, 27%) as yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ7.80 (t, *J*=4.1 Hz, 2H), 7.47 (m, 4H), 6.96 (s, 1H), 6.24 (s, 1H), 4.74 (d, *J*=5.9 Hz, 1H), 4.53 (t, *J*=5.0 Hz, 2H), 3.87 (t, *J*=5.0 Hz, 2H), 3.65-3.53 (m, 44H), 3.44 (q, *J*=4.9 Hz, 2H), 3.13 (m, 2H), 2.45 (m, 1H), 2.18 (t, *J*=7.4 Hz, 2H), 1.90 (m, 1H), 1.66 (m, 5H), 1.45 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ172.9, 171.7, 159.0 (×2), 143.9, 130.9(×3), 129.3, 126.0 (×2), 123.7, 99.2, 70.6 (×18), 70.3, 70.0, 69.5 (×2), 56.5, 50.4, 40.3, 39.2, 38.6, 36.4, 35.1, 34.8, 29.1, 25.5; HRMS (ESI-TOF) calcd for $C_{45}H_{72}N_6Na_1O_{14}S_2$ $[M+Na]^+$: 1007.4442; Found 1007.4446.

Compound **14d**



Compound **13** (35.1 mg, 0.0462 mmol, 1.0 equiv.) and compound **10** (8.7 mg, 0.052 mmol, 1.2 equiv.) were dissolved in anhydrous CH_2Cl_2 (472 μL) was added DIPEA (0.82 μL, 4.7 μmol, 0.10 equiv.), TBTA (0.3 mg, 0.57

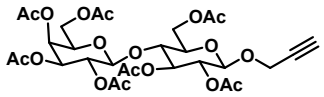
μmol, 0.012 equiv.), and CuI (0.1 mg, 0.57 μmol, 0.012 equiv.) at room temperature. The reaction was stirred at room temperature for 15 hours. The Quadra Pure-IDA® resin was added to the reaction mixture to quench, which was stirred at room temperature for another 2 hours. The reaction mixture was filtered and concentrated *in vacuo*. The crude product was purified by silica gel flash column chromatography (CH_2Cl_2/ MeOH= 100/0 to 94/6) to give compound **14d** (25.5 mg, 0.027 mmol, 60%) as yellow liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ7.49 (s, 1H), 6.24 (s, 1H), 4.50 (t, *J*=5.0 Hz, 2H), 4.41 (dd, *J*=2.8, 9.6 Hz, 1H), 3.90 (t, *J*=6.2 Hz, 1H), 3.84 (t, *J*=5.2 Hz, 2H), 3.64-3.52 (m, 44H), 3.44 (t, *J*=5.0 Hz, 2H), 3.15 (m, 3H), 2.84 (t, *J*=4.5 Hz, 1H), 2.75 (t, *J*=7.6 Hz, 2H), 2.64 (m, 1H), 2.42 (m, 1H), 2.18 (t, *J*=6.0 Hz, 2H), 2.01 (m, 3H), 1.66 (m, 5H), 1.45 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$):δ173.1, 172.9, 147.0, 122.3, 70.6 (×18), 70.3, 70.0, 69.7 (×2), 65.0, 56.5, 50.2, 49.5, 44.8, 40.3, 39.2, 38.6, 36.4, 34.8, 33.4, 29.1, 25.5, 25.0, 24.7; HRMS (ESI-TOF) calcd for $C_{41}H_{74}N_4Na_1O_{15}S_2$ $[M+H]^+$: 949.4490; Found 949.4479.



Scheme S3. Synthesis of lactose lipoate (**15-18)**.

Compound **15** was synthesized according to the published procedure.[3]

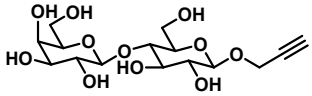
Compound **16**



Compound **16** was synthesized according to the published procedure.[4] To a solution of compound **15** (613 mg, 0.903 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (4.5 mL) propargyl alcohol (105 μL, 1.81 mmol, 2.0 equiv.) and BF_3-Et_2O (223 μL, 1.81 mmol, 2.0 equiv.) was added dropwise and the reaction mixture was stirred at room temperature for 2 hours. An additional batch of BF_3-Et_2O (223 μL, 1.81 mmol, 2.0 equiv.) was added and stirred at room temperature for 22 hours. Potassium carbonate (1.0 g) was added, and stirring was continued for a further 1.5 hours. The reaction mixture was then washed with H_2O (50 mL×2), and the aqueous layer was extracted with CH_2Cl_2 (10 mL×2). The combined organic layer was washed with brine, then dried over Na_2SO_4, and concentrated *in vacuo*. The crude product was purified by silica gel flash column chromatography (EtOAc/hexane =60:40 to 0:100) to give compound **16** (174 mg, 0.258 mmol, 29%) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$): *δ*5.32 (d, *J* = 3.5 Hz, 1H),

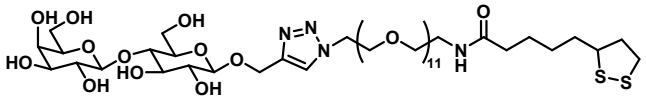
5.21 (t, J = 9.3 Hz, 1H), 5.09 (dd, J = 7.8, 9.9 Hz, 1H), 4.92 (m, 2H), 4.72 (d, J = 7.9 Hz, 1H), 4.47 (m, 2H), 4.31 (d, J = 2.1 Hz, 2H), 4.08 (m, 3H), 3.85 (m, 1H), 3.78 (m, 1H), 3.61 (m, 1H), 2.45 (s, 1H), 2.13-1.94 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$): δ170.3-169.7 (O$\underline{C}$HCH$_3$), 101.0, 97.8, 78.0, 76.0, 75.5, 72.6, 72.6, 71.2, 70.9, 70.6, 69.0, 66.5, 61.7, 60.7, 55.8, 20.8-20.5 (OCO$\underline{C}$H$_3$); HRMS (ESI-TOF) calcd for $C_{29}H_{38}O_{18}Na$ $[M+Na]^+$: 697.1956; Found 697.1948.

Compound **17**



Compound **16** (177 mg, 0.262 mmol, 1.0 equiv.) dissolved in MeOH (4.6 mL) was added sodium methoxide (5.0 M in MeOH, 0.18 mL, 0.92 mmol, 3.5 equiv.) dropwise. The reaction mixture was stirred at room temperature for 30 minutes. Amberlite IR-120 (PLUS) ion-exchange resin was added and the reaction mixture was stirred for 30 minutes. The resin was then removed by filtration and the resulting solution was concentrated *in vacuo* to give compound **17** (83.0 mg, 0.218 mmol, 83%). ^{1}H NMR (300 MHz, D_2O): δ4.63 (d, J = 7.9 Hz, 1H), 4.44 (m, 2H), 3.92 (m, 2H), 3.70 (m, 9H), 3.50 (m, 1H), 3.31 (m, 1H), 2.87 (t, J = 2.4 Hz, 1H); ^{13}C NMR (75 MHz, D_2O): δ102.9, 100.3, 78.7, 78.2, 76.3, 75.3, 74.8, 74.3, 72.6, 72.5, 70.9, 68.5, 61.0, 59.9, 56.6; HRMS (ESI-TOF) calcd for $C_{15}H_{24}O_{11}Na$ $[M+Na]^+$: 403.1216; Found 403.1200.

Compound **18**



Compound **17** (19 mg, 0.051 pmol, 1.0 equiv.) and compound **13** (58 mg, 0.076 pmol, 1.5 equiv.) were dissolved in DMF/MeOH (1:1, 1.0 mL). The mixture was flushed with argon. Then, CuI (5 mg, 0.025 pmol, 0.50 equiv.) was added and the mixture was stirred at room temperature for 24 hours. The Quadra Pure-IDA® resin was added to the reaction mixture, which was further stirred for 2 hours. The reaction mixture was filtered and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography ($CHCl_3$ after that CH_2Cl_2/MeOH/H_2O = 60/10/1 to 65/25/4) to give compound **18** (32 mg, 0.028 mmol, 56%). ^{1}H NMR (300 MHz, pyridine-d_5): δ 8.57 (s, 1H), 8.16 (s, 1H), 5.30 (d, J = 12.0 Hz, 1H), 5.02 (m, 4H), 4.49 (m, 8H), 4.27 (m, 1H), 4.13 (m, 3H), 3.80 (m, 3H), 3.65-3.56 (m, 42H), 3.50 (m, 3H), 3.00 (m, 2H), 2.33 (t, J = 7.2 Hz, 2H), 2.20 (m, 1H), 1.71 (m, 3H), 1.44 (m, 4H); ^{13}C NMR (75 MHz, pyridine-d_5): δ 179.2, 145.0, 124.8, 105.8, 103.6, 82.0, 77.2, 76.6, 76.5, 75.1, 74.6, 72.4, 70.8 (×18), 70.5 (×2), 70.0, 69.5 (×2), 63,0, 61.9, 56.8, 50.2 (×2), 40.4, 39.7, 38.6, 36.2, 34.9, 29.2, 25.9; ESI-TOFMS calcd for $C_{47}H_{86}N_4O_{23}S_2Na$ $[M+Na]^+$: 1161.5022; Found 1161.5096.

3. Synthesis and characterization of affinity labeling probes 1-6.

3-1. Synthesis of citrate-coated AuNPs

Citrate-coated AuNPs were synthesized according to the published procedure.[3,5] Briefly, 1 mM aqueous solution of

hydrogen tetrachliroaurate (III) trihydrate ($HAuCl_4 \cdot H_2O$) was heated to boil vigorously and stirred using a magnetic stirrer hot plate (MR 3004 safety S, Heidolph). Then, 2 mL of a 38.8 mM aqueous solution of trisodium citrate dihydrate heated to 80 ℃ was added, and the mixture was stirred at 100 ℃ for 10 minutes. The color of the solution changed from colorless to deep red. The diameter of citrate-coated AuNPs was calculated from the maximum absorption wavelength of the UV/Vis spectra according to the reported protocol.[6] The diameter was calculated to be 13 nm. UV/Vis spectrometric analysis is described in 3-3.

3-2. Functionalization of gold-nanoparticle probes 1-6

Functionalization of AuNPs was conducted according to the previously reported procedure.[3,7] Bis (*p*-sulfonatophenyl) phenylphosphine dihydrate dipotassium salt (BSPP; 2 mg) was added to the solution of AuNPs (13 nm, 10 nM, 4 mL) in a 15 mL tube and was mixed at 50 ℃ for 1 hour on an orbital shaker. The BSSP-coated AuNP was collected by centrifugation at 18,000 × g at 4 ℃ for 1 hour and the removal of the supernatant. The BSPP-coated AuNPs were washed with MilliQ H_2O and centrifuged three times and diluted in 2 mL MeOH. Each of the stock solution of lipoic acid derivatives (**14a-14d**, *p*-sulfonyl fluoride-PEG11-lipoate) was first mixed with lactose-PEG11-lipoate (**18**) in MeOH (10 mM, 10 μL) at a 1:2 v/v ratio and added to a solution of the BSPP-coated AuNPs in a 1.5 mL tube. The resultant mixture was stirred at 25 ℃ for 17 hours on an orbital shaker. The functionalized AuNPs were washed with MeOH and MilliQ H_2O and centrifuged three times. The concentrations of the functionalized AuNPs were determined by the UV-VIS spectrometric analysis according to the reported method.[6]

3-3. UV/Vis spectrometric analysis

The 1 μL stock solution of citrate-coated AuNPs, BSPP-coated AuNP, and probes **1-6** in MilliQ H_2O was recorded on a NanoDrop ND-1000 spectrophotometer. The concentration of each solution is as the following: 15 nM citrate-coated AuNPs, 10 nM BSPP-coated AuNPs, and 10 nM probes **1-6**.

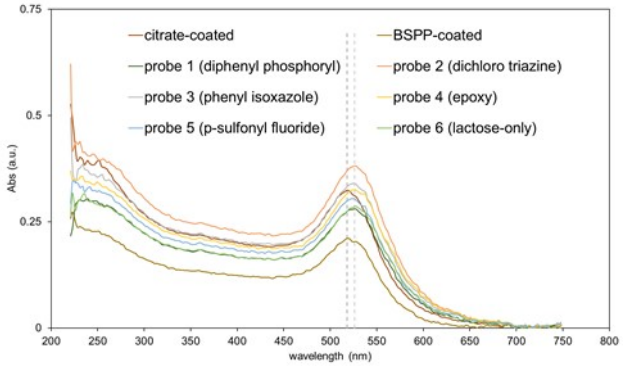


Figure S1. UV/Vis spectra of citrate-coated AuNPs (15 fmol), BSPP-coated AuNPs, and probes **1-6** (10 fmol).

3-4. MALDI-TOF-MS analysis

A matrix solution (10 mg/mL of 2, 5-dihydroxybenzoic acid, DHA, in MeCN/ H_2O=1/ 1) and the stock solution for probes **1-6** were spotted onto the sample plate. All the MALDI-TOF MS spectra were acquired over the mass range m/z = 520-2490 in the linear mode on Autoflex Speed TOF/TOF (Bruker Daltonics).

Table S1. MALDI-TOF mass peaks corresponding to ligands **14a−14d** and **18** derived from probes **1-6**.

Probe	Compound	Chemical formula	Calcd.	Obs.
1	**18**	$C_{47}H_{86}N_4O_{23}S_2Na$	1161.51	1161.66
	13a	$C_{47}H_{76}N_5O_{15}PS_2Na$	1068.45	1068.62
2	**18**	$C_{47}H_{86}N_4O_{23}S_2Na$	1161.51	1161.65
	13b	$C_{38}H_{66}Cl_2N_8O_{12}S_2Na$	985.36	985.12
3	**18**	$C_{47}H_{86}N_4O_{23}S_2Na$	1161.51	1161.54
	13c	$C_{45}H_{73}N_6O_{14}S_2$	985.45	985.35

Probe	Compound	Chemical formula	Calcd.	Obs.
4	**18**	$C_{47}H_{86}N_4O_{23}S_2Na$	1161.51	1161.91
	13d	$C_{41}H_{74}N_4O_{15}S_2Na$	949.46	949.72
5	**18**	$C_{47}H_{86}N_4O_{23}S_2Na$	1161.51	1161.65
	p-sulfonyl fluoride-PEG(11)-lipoate	$C_{42}H_{70}FN_5O_{15}S_3$	999.40	-
6	**18**	$C_{47}H_{86}N_4O_{23}S_2Na$	1161.51	1161.62

3-5. Agarose gel electrophoresis analysis

An aqueous stock solution of probes **1-6** (10 μL, 0.1 pmol) was each suspended in 50% glycerol in MilliQ H_2O (10 μL), which were electrophoresed in 0.5% agarose gel for 30 minutes at 100 V in 0.5×TBE buffer (44.5 mM Tris, 44.5 mM boric acid, 1 mM EDTA). The resultant gels were visualized by scanning with CanoScan Lide 210.

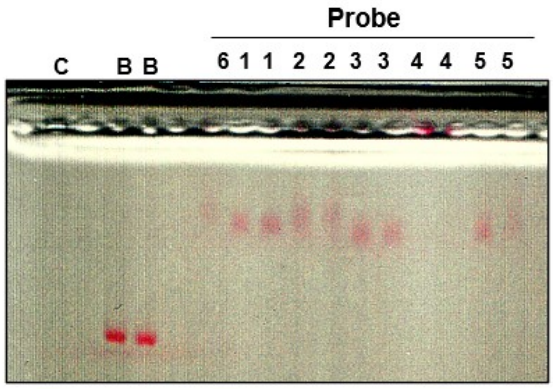


Figure S2. Agarose gel of citrate-coated AuNPs (C), BSPP-coated AuNPs (B), and probes **1-6** (0.1 pmol).

3-6. Dynamic Light Scattering (DLS) analysis

DLS measurements were performed at 25 °C in triplicate using a plastic cuvette using a Zeta-nanosizer (Nano S, Malvern, UK). The hydrodynamic radius (R_h) was calculated using the Stokes-Einstein equation from size-number plots.

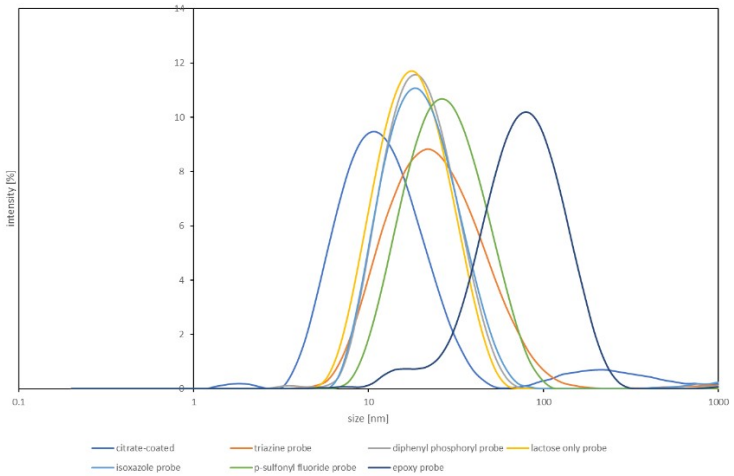


Figure S3. A representative DLS data showing the hydrodynamic radius distribution of citrate coated AuNP (1.4

pmol), and probes **1-6** (1.0 pmol). The concentration of each solution is 14 nM citrate-coated AuNPs, and 10 nM probes **1-6**.

Table S2. Hydrodynamic diameter of probes **1-6**.

	Hydrodynamic diameter [nm]
Citrate coated AuNPs	21±0.21
Probe **1**	38±1.5
Probe **2**	44±5.1
Probe **3**	38±0.40
Probe **4**	164±13
Probe **5**	50±2.3
Probe **6**	54±2.6

4. Binding affinity analysis of probe 6

PNA (1 μg) was incubated with varied amounts of probe **6** (36, 18, 6.0, 1.8, 0.60, 0.18, 0.060, 0 pmol) in 60 μL of HEPES reaction buffer (10 mM HEPES, pH 7.4, 150 mM NaCl, 1 mM $MnCl_2$, 1 mM $CaCl_2$) in PCR tubes on a rotary mixer at 4 ℃ for 2 hours. The mixtures were centrifuged at 18,000 × g for 30 minutes. The supernatant was removed and the precipitated probes were washed with PBS (NaH_2PO_4 2.9 mM, Na_2HPO_4 9.0 mM, NaCl 136.9 mM, pH 7.4) (200 μL) followed by centrifugation at 18,000 × g for 30 minutes. The washing step was repeated two times to isolate the probe-protein complex in the pellet. The pellet was suspended in 6×Laemmli sample buffer (187 mM Tris-HCl, 3.8% SDS, 2.0 M glycerol, 0.28 mM bromophenol blue, pH 6.8) containing 0.6 M DTT (final 0.1 M) and incubated 10 minutes at 95 ℃ three times. The sample was resolved by SDS-PAGE using 10% gel. The resultant gel was stained by coomassie brilliant blue (CBB) stain. The K_d values were obtained by the non-linear curve fitting analysis of the plots of the intensity of the protein bands using Graphpad Prism 5 (Graphpad Software, Inc.). The dissociation constant for PNA was calculated based on an assumption that lactose probe binds PNA monomer at a 1:1 ratio.[3]

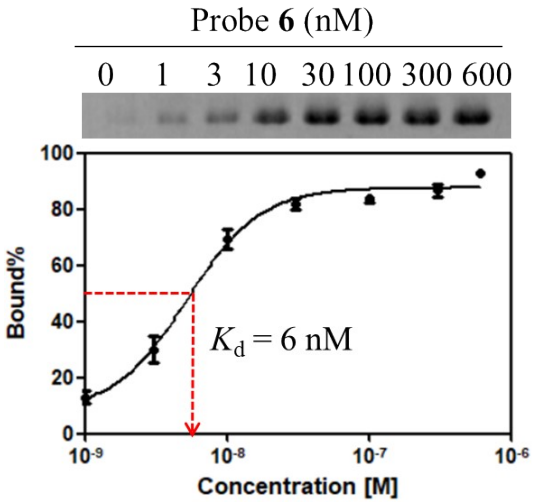


Figure S4. A plot showing the dose-dependent binding of probe **6** to PNA (0.1 pmol) by an affinity pull-down assay gel-based imaging. Each data point represents the average of triplicate data. Top panel shows a representative gel-imaging data of the probe-bound protein bands by SDS-PAGE and CBB staining.

5. Affinity labeling experiments

PNA (0.4 μg) was incubated with probes **1**-**5** (2 pmol, 50 nM) in 40 μL HEPES reaction buffer on a rotary mixer at 4 ℃ for 2 hours. For probe **3**, the reaction mixture was irradiated at 254 nm at a distance of 1 cm on ice for 30 minutes using a UV lamp (AS ONE, Handy UV Lamp SLUV-4 254/ 365 nm). For affinity labeling reactions with PNA in the presence of BSA, PNA (0.4 μg) and BSA (2.0 μg) were incubated with probes **1**-**5** (2 pmol, 50 nM) in 40 μL HEPES reaction buffer on a rotary mixer at 4 ℃ for 2 hours. The mixture was diluted with 200 μL PEG dilution buffer (6.5% PEG8000 in PBS). Then, the solution was centrifuged at 18,000 × g at 4 ℃ for 10 minutes and the supernatant was removed. The pellet was suspended and incubated in lactose-containing wash buffer (0.5 M lactose/ 1% *n*-octyl-*β*-D-glucoside (OG) / 6.5% PEG8000 in PBS) on a rotary mixer at 25 ℃ for 30 minutes. The mixture was then centrifuged at 20,000 × g for 20 minutes and the supernatant was removed. The washing step was repeated two times. The resultant pellet was further washed with PBS and the mixture was centrifuged at 20,000 ×g for 20 minutes then the supernatant was removed. This washing step was repeated once more. The pellet was suspended in 6×Laemmli sample buffer containing 0.6 M DTT and incubated for 10 minutes at 95 ℃ three times. The sample was resolved by SDS-PAGE using 10% gel. The resultant gel was stained by CBB. The labeling yields were calculated based on the relative band intensity of the probe-labeled protein bands to that of the input PNA used in a given reaction.

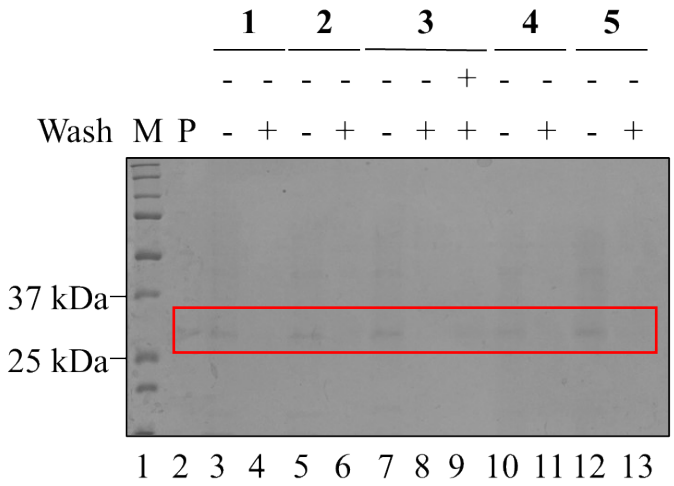


Figure S5. Affinity labeling of probes **1-5** (50 nM) and PNA (0.4 μg, 100 nM) M: molecular marker, P: PNA input (lane 2). UV (254 nm): irradiation with UV light, Wash: washing was performed in the post labeling step. The cropped section indicated with a red rectangles is shown in Fig.2(a) in the main text.

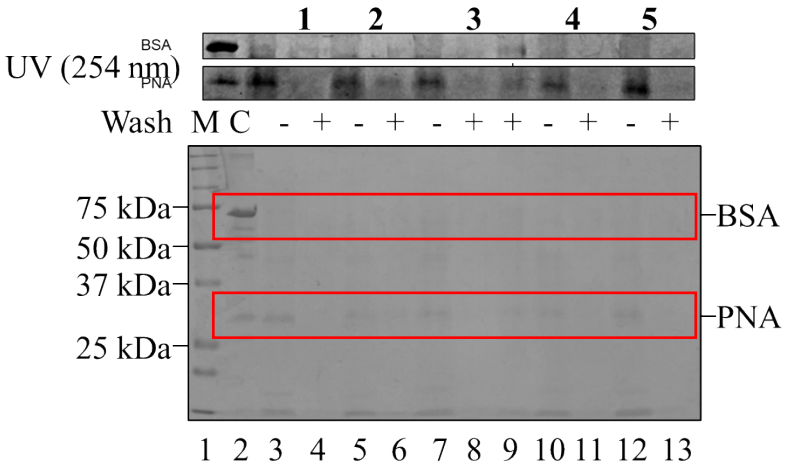


Figure S6. Affinity labeling for PNA (0.4 μg, 100 nM) by probes **1-5** (50 nM) in the presence of BSA (2.0 μg, 1.5 μM). M: molecular marker, C: protein used for a given reaction. UV: irradiation with UV light, Wash: washing was performed in the post labeling step. The cropped section indicated with a red rectangles is shown in Fig.2(b) in the main text.

6. Determination of the probe-labeled sites on PNA

6-1. Enrichment of probe 2-labeled PNA

PNA (10 μg, 91 pmol, 1.0 equiv.) was incubated with probe **2** (100 pmol, 100 nM, 1.1 equiv.) in 1 mL of HEPES reaction buffer on a rotary mixer at 4 ℃ for 22 hours. The mixture was diluted with PEG dilution buffer. Then, the solution was centrifuged at 18,000 × g at 4 ℃ for 1 hour and the supernatant was removed. The pellet was suspended in lactose wash buffer and the mixed solution was agitated on a rotary mixer at 25 ℃ for 30 minutes. The mixture was then centrifuged at 18,000 × g for 1 hour and the supernatant was removed. The washing step was repeated two times. The resultant pellet was further washed with PBS and the mixture was centrifuged at 18,000 × g for 1 hour.

The supernatant was removed. This washing step was repeated one more time. The pellet was suspended in 6×Laemmli sample buffer containing 0.6 M DTT (final 0.1 M) and incubated for 30 minutes at 75 ℃. The sample was resolved by SDS-PAGE using 10% gel. The resultant gel was stained by CBB and the protein band was cut out and diced into 1 mm pieces, which were transferred into a microcentrifuge tube.

6-2. In-gel tryptic digestion

The gel pieces were incubated in MeCN/25 mM NH_4HCO_3 = 3/1 for 5 minutes, then remove the supernatant. The same procedure was performed using MeCN and 25 mM NH_4HCO_3, respectively. The destaining step was repeated twice, then the same procedure was performed using MeCN/25 mM NH_4HCO_3 (3/1) and MeCN. After dehydration, the gel pieces were added 10 mM DTT in 25 mM NH_4HCO_3 solution, and the tubes were incubated at 55-60 ℃ for 1 hour. After removal of the supernatant, the gel pieces were added 55 mM iodoacetamide in 25 mM NH_4HCO_3 solution and incubated at room temperature for 45 minutes in the dark. After the carbamide methylation, the gel pieces were washed with 25 mM NH_4HCO_3 and MeCN/25 mM NH_4HCO_3 (3/1) and dehydrated by the addition of MeCN. The dehydrated gels were added to trypsin solution (0.1 μg/μL) and incubated at 37 ℃ overnight. The resulting solution was collected by MeCN.

6-3-1. LC-MS/MS analysis of the labeled peptide fragment

LC-MS/MS analysis was performed following the procedure as reported previously.[3] The trypsin-digested peptide samples were analyzed using a mass spectrometer (LTQ Orbitrap velos, Thermo Scientific) coupled with nano-LC (EASY-nLC II, Thermo Scientific). The peptides were desalted and concentrated on the trap column (Capillary Ex-Nano Mono cap C18 Trap Column, 0.075 mm i.d. × 50 mm, GL sciences), and were then separated on an analytical column (Capillary Ex-Nano Mono cap C18 Nano-flow, 0.075 mm i.d. × 150 mm, GL sciences). For liquid chromatography, the following gradient was used (A, 0.1% formic acid/H_2O; B, 70% MeCN, 0.1% formic acid in H_2O): 0 min 0% B; 0–2 min 0-29% B; 2–42 min 29-85% B; 42–47 min 85-100% B, 47– 52 min 100% B, 300 nL/min. A top ten data-dependent acquisition MS method was used.

6-3-2. MALDI-MS/MS analysis of the labeled peptide fragment

1 μL of the obtained tryptic peptides and an equal volume of the DHB matrix solution (10 mg/mL DHB in H_2O: MeCN, 1:1 v/v containing 0.3% trifluoroacetic acid) were mixed in a 1.5-mL microcentrifuge tube. Then, 2 μL of the mixture was spotted on MTP 384 target plate (Bruker) and left to dry at room temperature. MALDI-TOF MS was performed using an UltrafleXtreme MALDI-TOF/TOF mass spectrometer (Bruker). The mass spectra were acquired over the m/z range of 1000-5000 in Reflectron Positive ion modes (RP mode). Tandem mass spectrometry (MS/MS) analysis was performed using LIFT mode. The data obtained was processed using BioTools (version 3.2, Bruker) and searched using Mascot search algorithm(version 2.4) against a modified human protein database (Swiss-Prot human protein database).

6-4. Data analysis

The mass spectrometric data obtained were processed using PEAKS studio Xpro software (Bioinformatics Solutions

Inc.). Precursor and fragment mass tolerance were set to 5 ppm and 0.5 Da respectively. To compare amino acid residues modified by dichlorotriazine probes, peptide identifications were accomplished with variable modification of the following structures (Fig. S8) on the amino acid residues.

Since valine has no nucleophilic side chain residue and Val62 and Val202 were the N-terminal residue of the labeled peptide fragment, we speculated that Ser64 and Lys203, respectively, may have initially reacted with the dichlorotriazine moiety of the probe and later migrated to the N-terminal amino groups of Val62 and Val202 during the process of MS sample preparation and analysis. Both Ser64 and Lys203 were also observed as labeled sites in a separate set of peptide fragments (see Table S3).

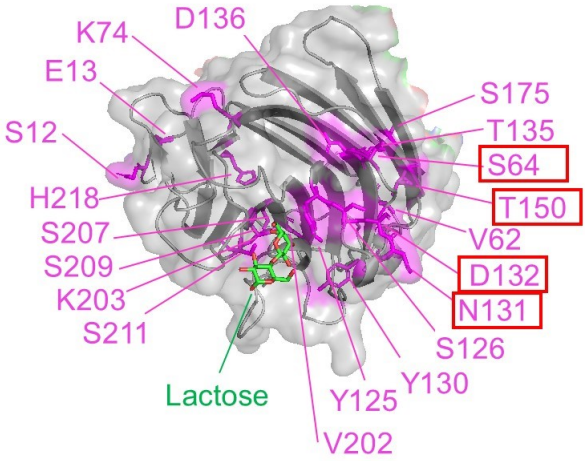


Figure S7. The labeled amino acid residues inferred from the four trials of MS analysis were mapped onto the X-ray structure of a lactose-PNA complex (PDB: 2PEL). All the labeled amino acid residues detected through four replicate experiments are shown in magenta with those that were detected more than twice were highlighted with red rectangles. The lactose molecule bound in the ligand binding pocket is shown with a green stick model.

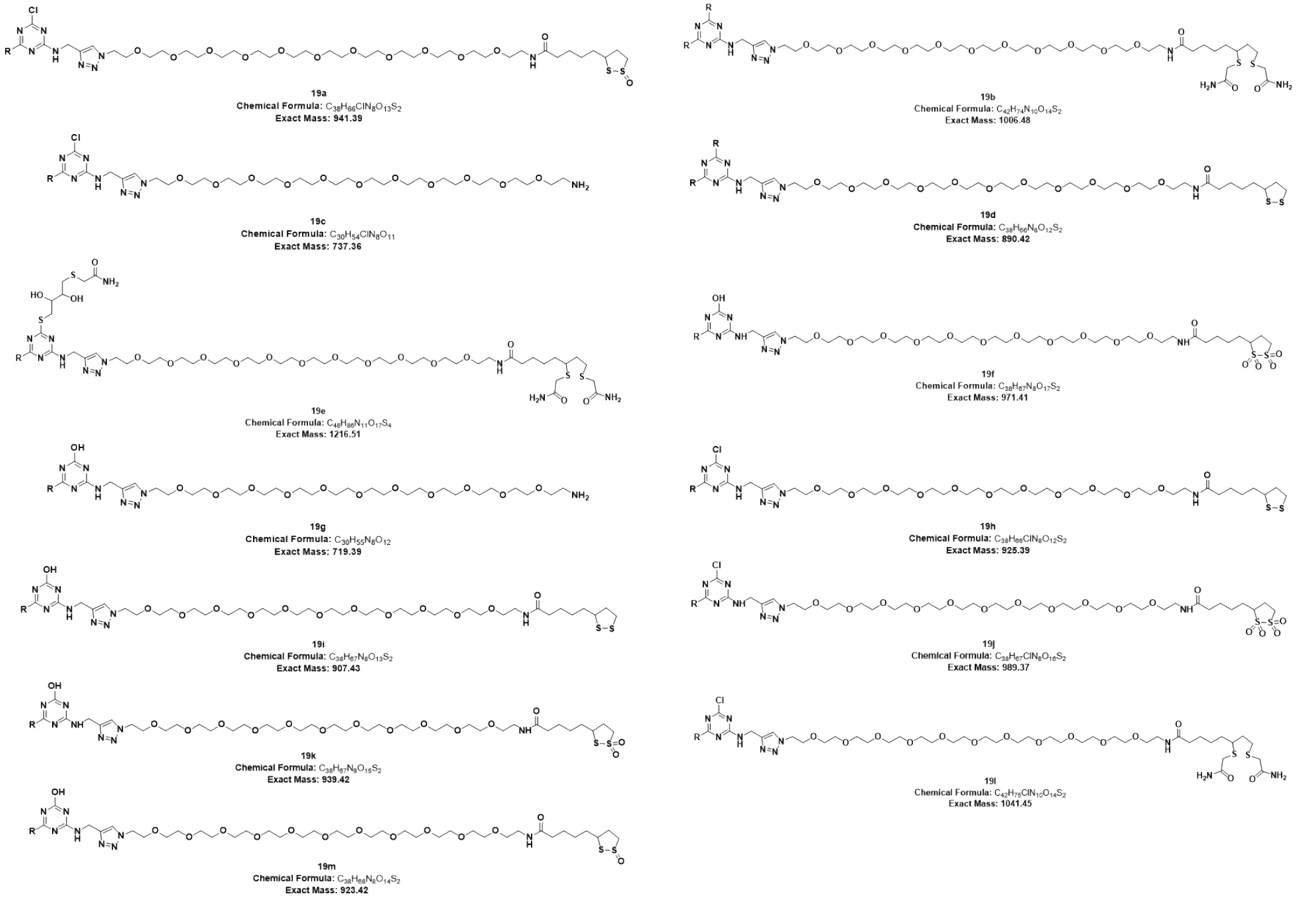


Figure S8. Expected structures and the corresponding mass values detected by MALDI-MS and LC-MS/MS for the labels derived from the protein reactive dichlorotriazine moiety **19a-19m**.

(a)

1-50 AETVSFNFNSFSEGNPAINFQGDVTVLSNGNIQLTNLNKVNSVGRVLYAM
51-100 PVRIWSSATGNVASFLTSFSFEMKDIKDYDPADGIIFFIAPEDTQIPAGS
101-150 IGGGTLGVSDTKGAGHFVGVEFDTYSNSEYNDPPTDHVGIDVNSVDSVKT
151-200 VPWNSVSGAVVKVTVIYDSSTKTLSVAVTNDNGDITTIAQVVDLKAKLPE
201-236 RVKFGFSASGSLGGRQIHLIRSWSFTSTLITTTRRS

(b)

1-50 AETVSFNFNSFSEGNPAINFQGDVTVLSNGNIQLTNLNKVNSVGRVLYAM
51-100 PVRIWSSATGNVASFLTSFSFEMKDIKDYDPADGIIFFIAPEDTQIPAGS
101-150 IGGGTLGVSDTKGAGHFVGVEFDTYSNSEYNDPPTDHVGIDVNSVDSVKT
151-200 VPWNSVSGAVVKVTVIYDSSTKTLSVAVTNDNGDITTIAQVVDLKAKLPE
201-236 RVKFGFSASGSLGGRQIHLIRSWSFTSTLITTTRRS

(c)

1-50 AETVSFNFNSFSEGNPAINFQGDVTVLSNGNIQLTNLNKVNSVGRVLYAM
51-100 PVRIWSSATGNVASFLTSFSFEMKDIKDYDPADGIIFFIAPEDTQIPAGS
101-150 IGGGTLGVSDTKGAGHFVGVEFDTYSNSEYNDPPTDHVGIDVNSVDSVKT
151-200 VPWNSVSGAVVKVTVIYDSSTKTLSVAVTNDNGDITTIAQVVDLKAKLPE
201-236 RVKFGFSASGSLGGRQIHLIRSWSFTSTLITTTRRS

(d)

Figure S9. The labeled residues of PNA (P02872) that were observed twice are highlighted in red and once are in fuchsia pink. Lactose binding residues are highlighted in gray. (a) First trial, (b) second trial, (c) third trial, (d) fourth trial.

Table S3. Peptide ID list of MALDI-MS and LC-MS/MS analysis of PNA reacted with probe **3a**. (a) First trial, (b) second trial, (c) third trial, (d) fourth trial.

(a) Entry 1: MALDI-MS

Entry	Peptide	Mass	m/z	Intensity
1	T(+941.39)VPWNSVSGAVVK	2283.10	2284.234	-

(b) Entry 2-4: LC-MS, Entry 5: MALDI-MS

Entry	Peptide	Mass	m/z	Intensity
2	GAGHFVGVEFDTYSNSEYND(+924.39)(+888.41)	4019.702	804.949	1.99E+06
3	V(+718.39)AS(+79.97)FLTSFSFEMK	2291.08	1146.5494	4.02E+03
4	VK(+988.36)FGFSASGSLGGR	2357.08	1179.5498	7.69E+05
5	T(+941.39)VPWNSVSGAVVK	2283.10	2284.3137	-

(c) Entry 6-12: LC-MS, Entry 13: MALDI-MS

Entry	Peptide	Mass	m/z	Intensity
6	G(+42.01)(+1006.44)IIFFIAPEDTQIPAGSIGGGTLGVSDTK	3908.932	1303.9792	4.43E+06
7	YDSSTKTLS(+736.35)VAVTNDNGDITTIAQVVDLK	3803.908	1268.9841	2.54E+06
8	S(+79.97)E(+1217.47)GNPAINFQGDVTVLSNGNIQLTNLNK	4253.924	1064.495	-
9	IWSSATGNVASFLTSFSFEMK(+1004.47)DIKDYDPADGIIFFIAPEDTQIPAGSIGGGTLGVSDTK	7188.486	1438.7056	2.03E+06
10	A(+888.41)S(+79.97)FLTSFSFEMK	2362.034	788.3466	2.76E+06
11	V(+1040.44)KFGFSASGSLGGR	2409.159	804.0601	1.51E+06
12	GAGHFVGVEFDTY(+1004.47)S(+736.35)(+736.35)	3961.829	991.4645	4.30E+04
13	QIH(+939.42)LIR	1716.89	1717.8272	-

(d) Entry 14-17: LC-MS

Entry	Peptide	Mass	m/z	Intensity
14	GAGHFVGVEFDTYSNSEYN(+718.39)D(+1040.44)	3965.738	1322.9236	1.34E+06
15	N(+1022.48)DPPTD(+972.37)HVGIDVNSVDSVK	4001.802	1334.938	1.97E+05
16	YND(+924.39)PPT(+906.42)DHVGIDVNSVDSVK	4000.822	1334.6018	3.20E+05
17	VNSVGRVLYAMPV(+1006.44)R(+970.40)	3536.694	885.188	2.65E+05

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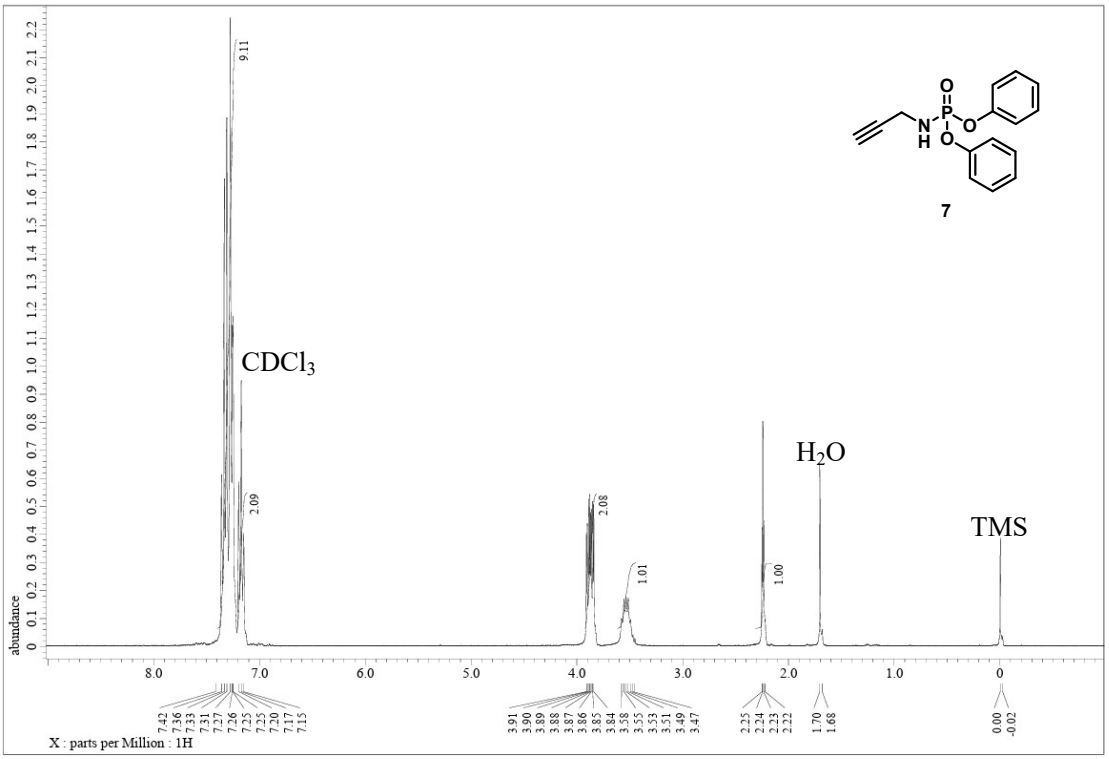
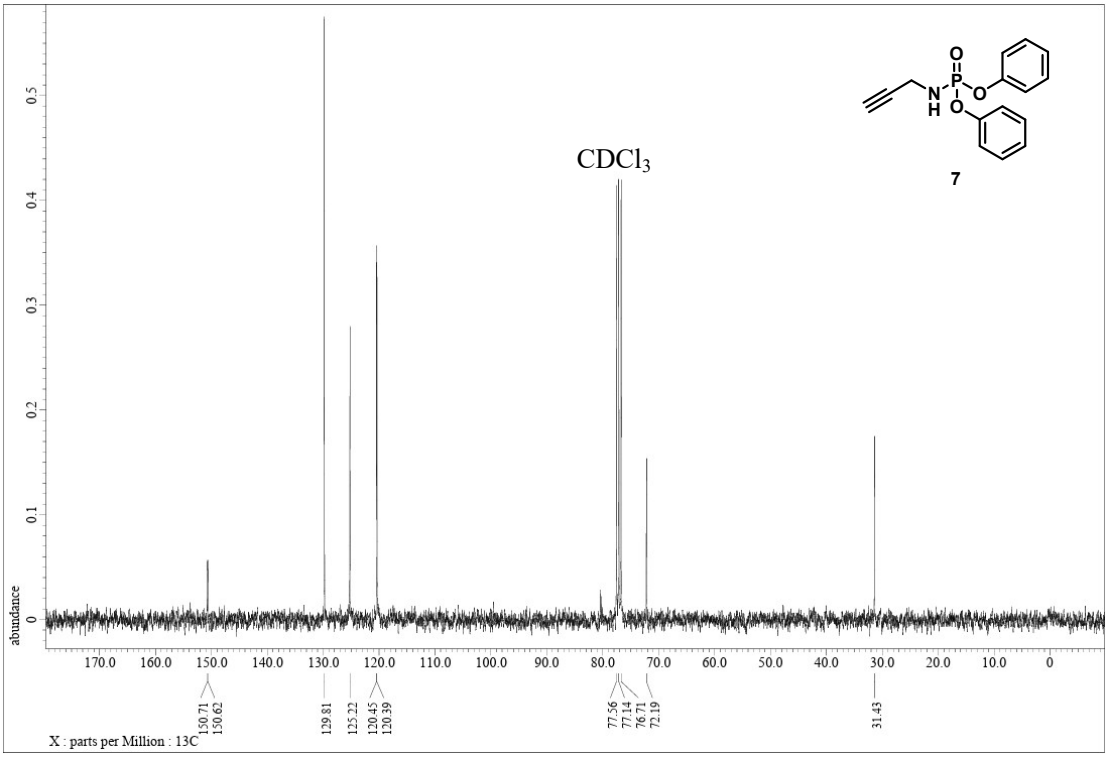
NMR spectra

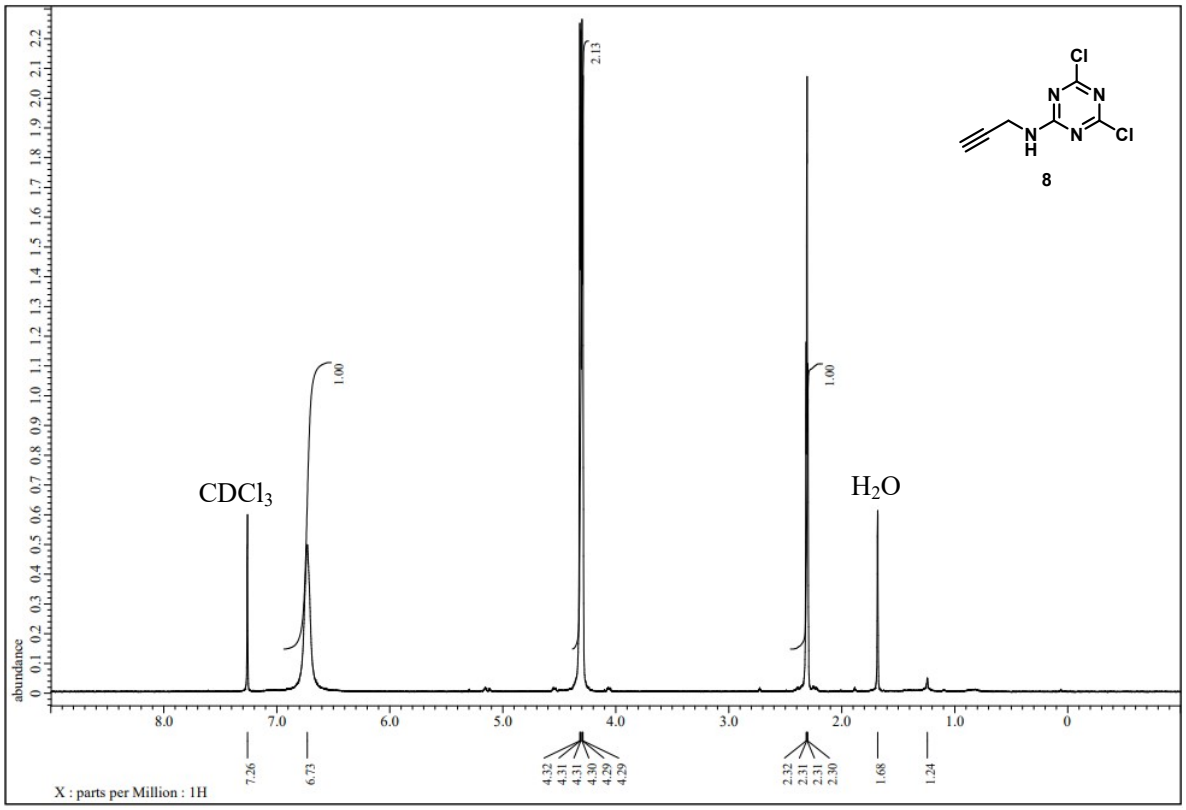
^{1}H NMR spectra of compound **7** ($CDCl_3$, 300 MHz).



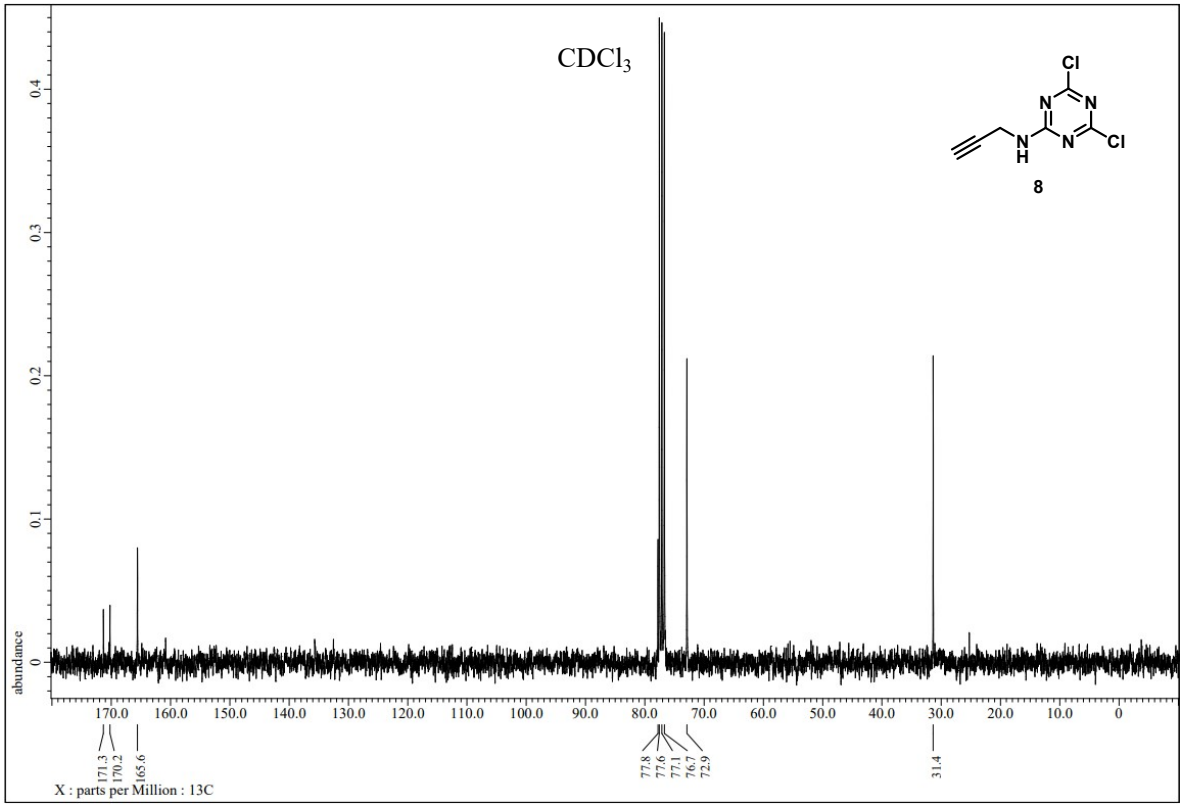
^{13}C NMR spectra of compound **7** ($CDCl_3$, 75 MHz).



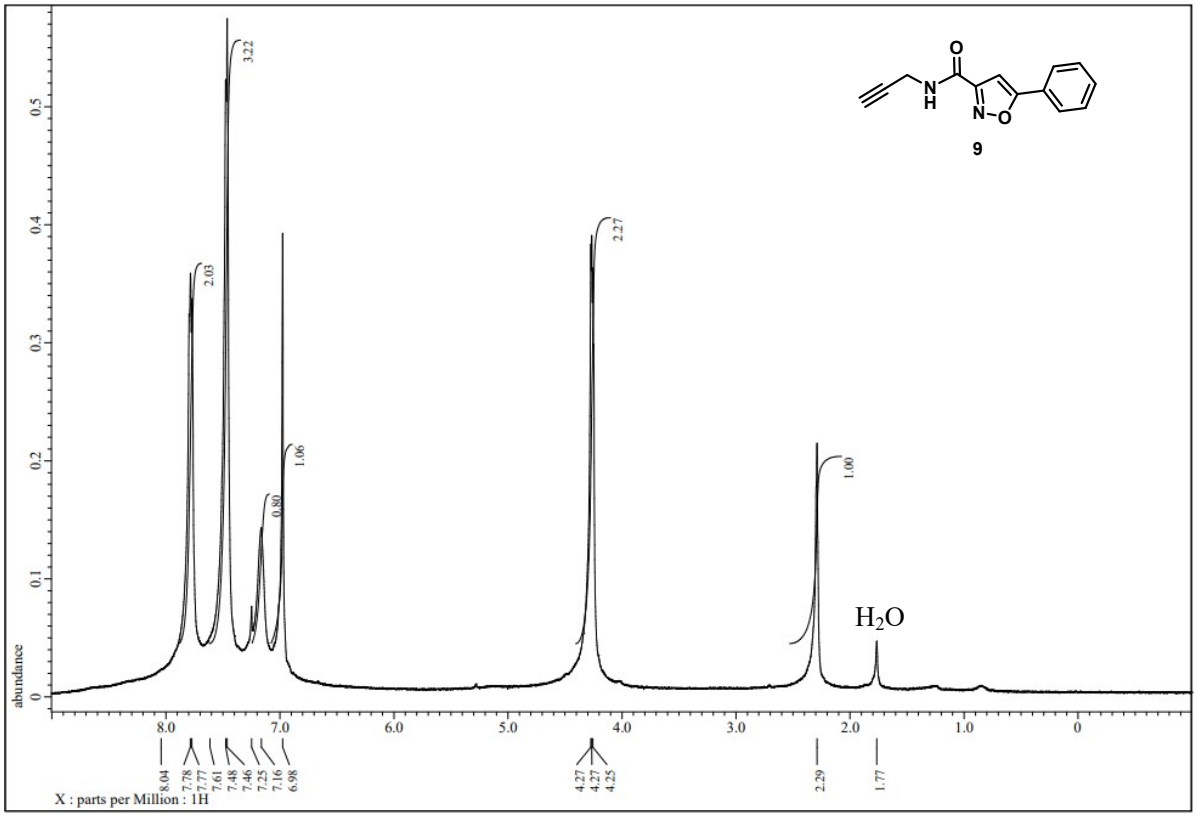
^{1}H NMR spectra of compound **8** ($CDCl_3$, 300 MHz).



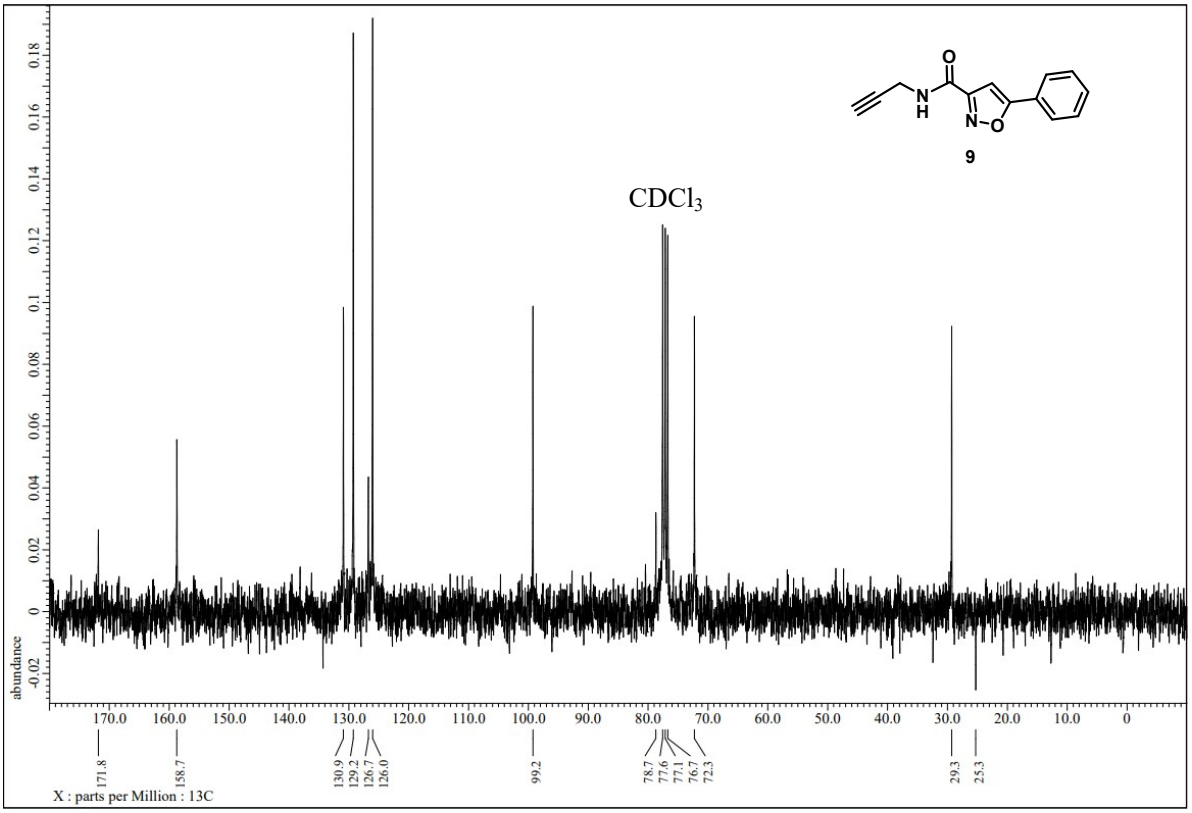
^{13}C NMR spectra of compound **8** ($CDCl_3$, 75 MHz).



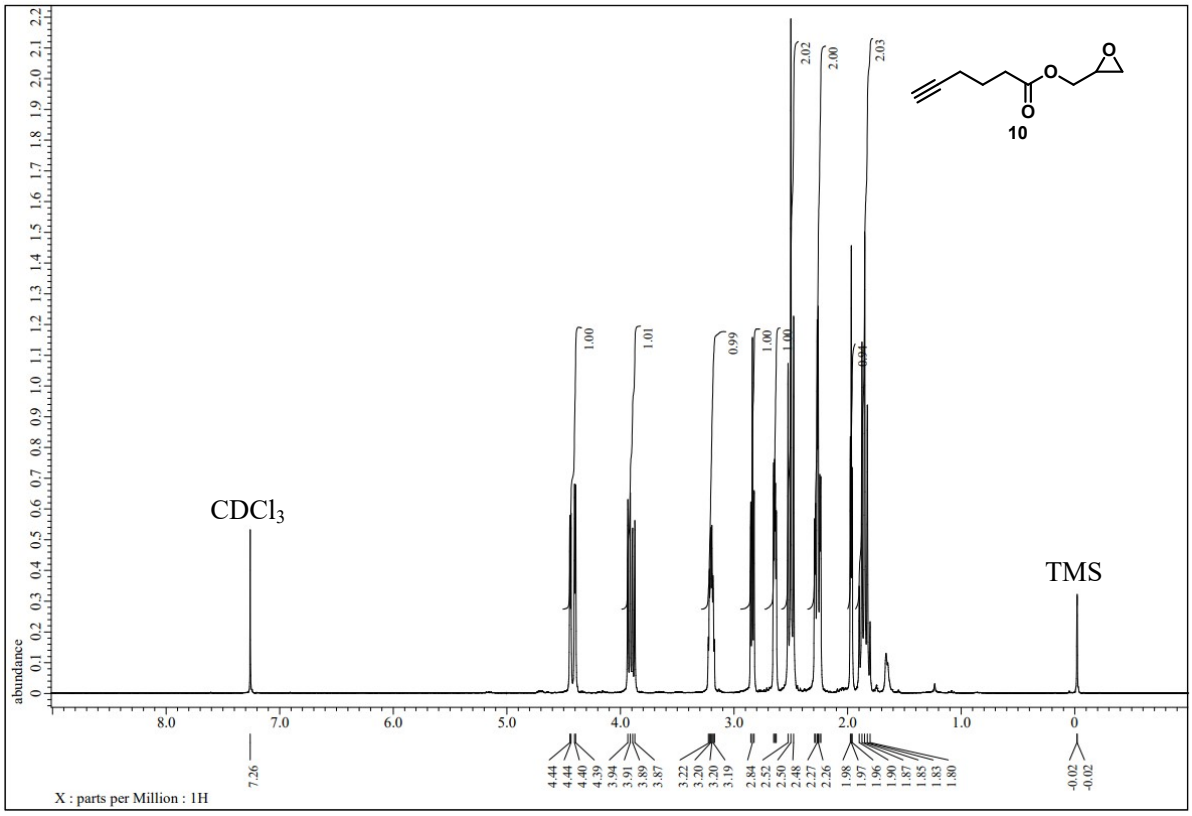
^{1}H NMR spectra of compound **9** ($CDCl_3$, 300 MHz).



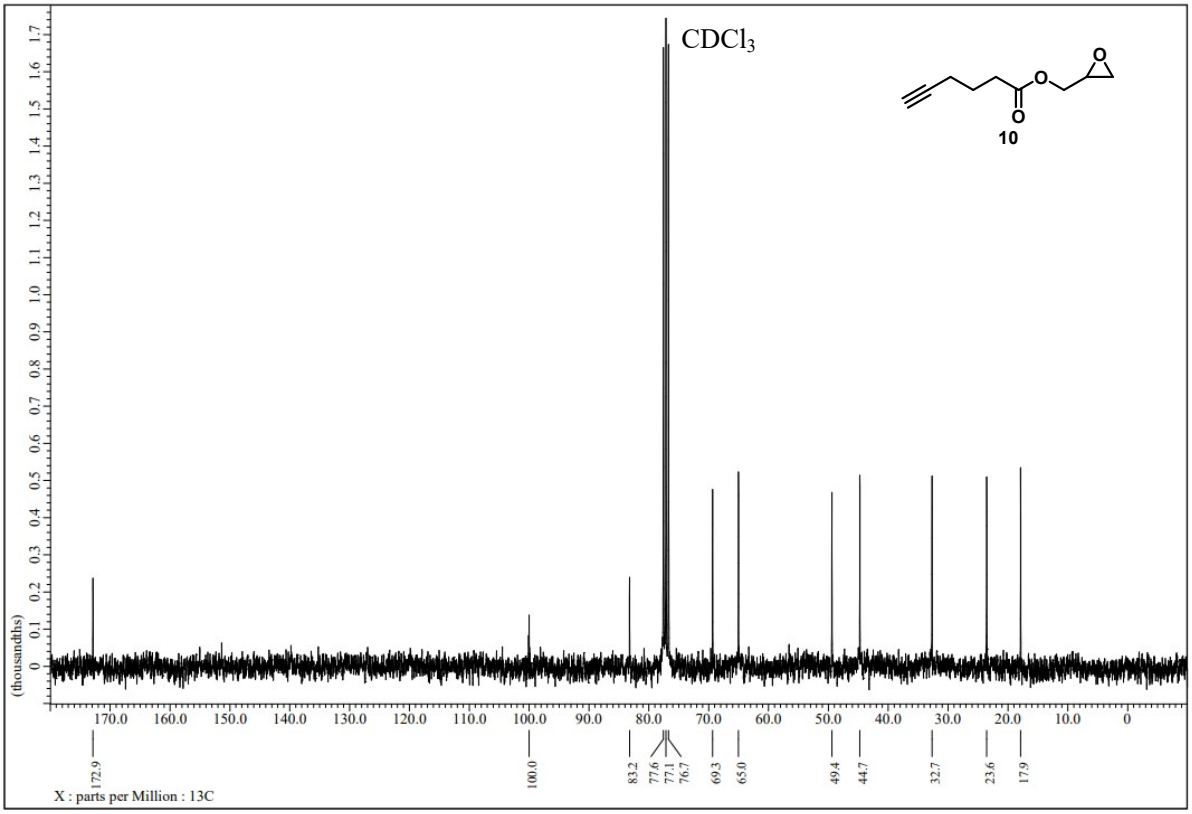
^{13}C NMR spectra of compound **9** ($CDCl_3$, 75 MHz).



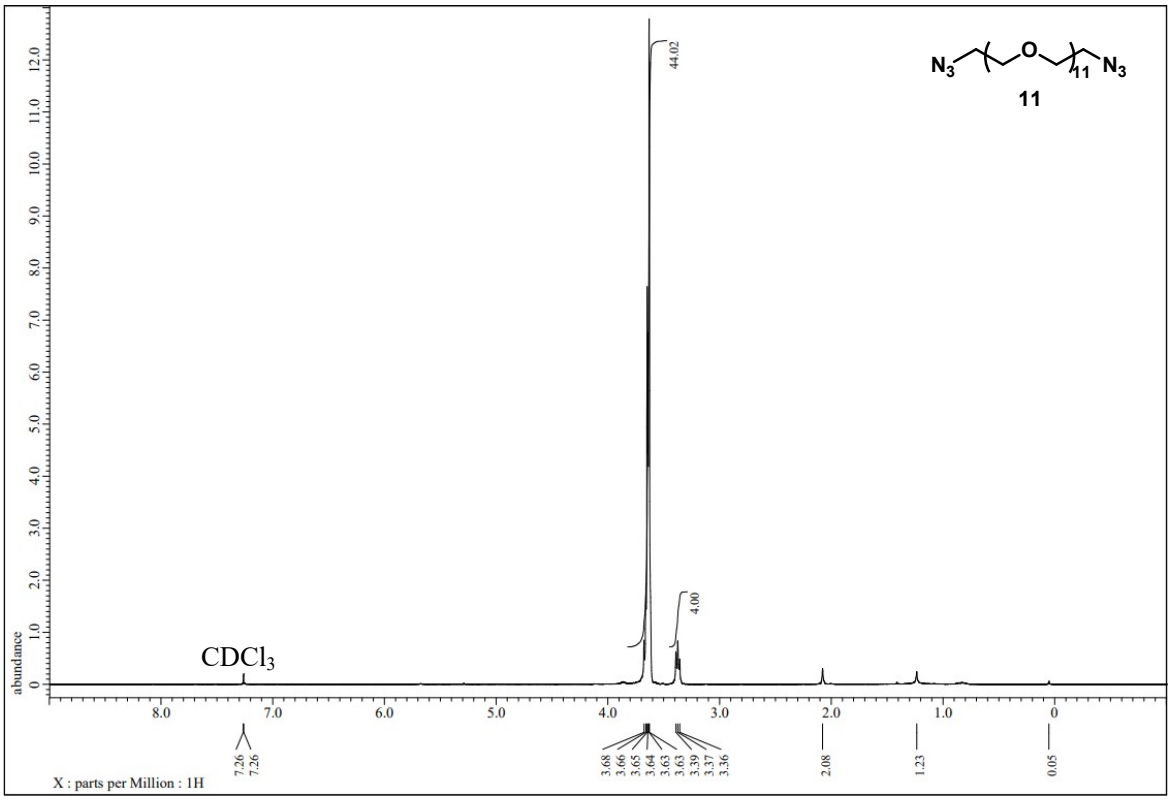
^{1}H NMR spectra of compound **10** ($CDCl_3$, 300 MHz).



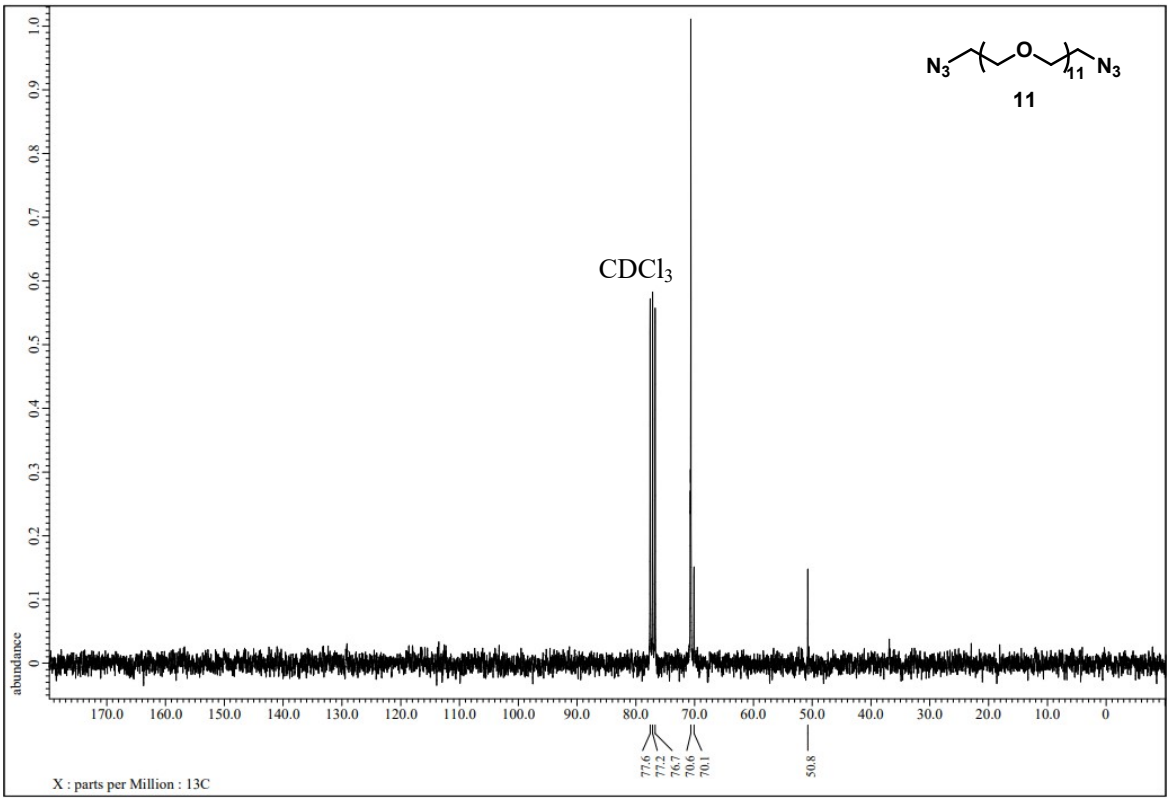
^{13}C NMR spectra of compound **10** ($CDCl_3$, 75 MHz).



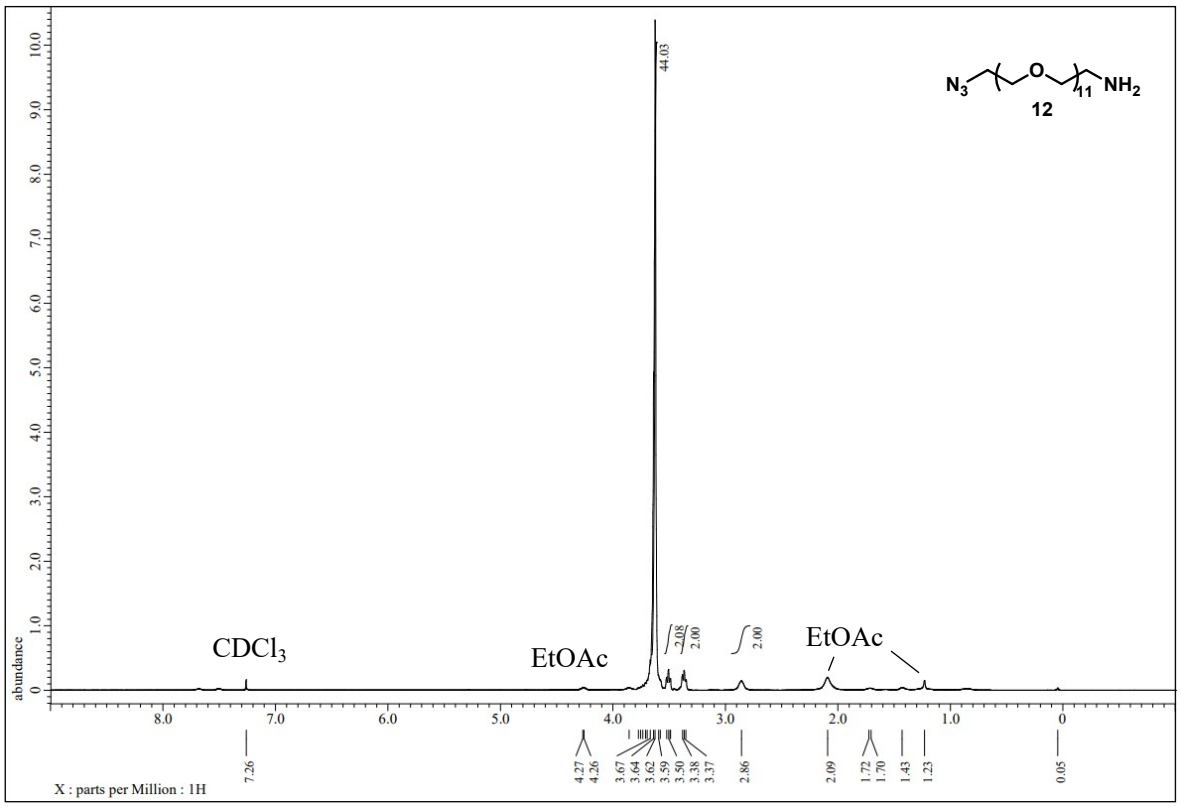
^{1}H NMR spectra of compound **11** ($CDCl_3$, 300 MHz).



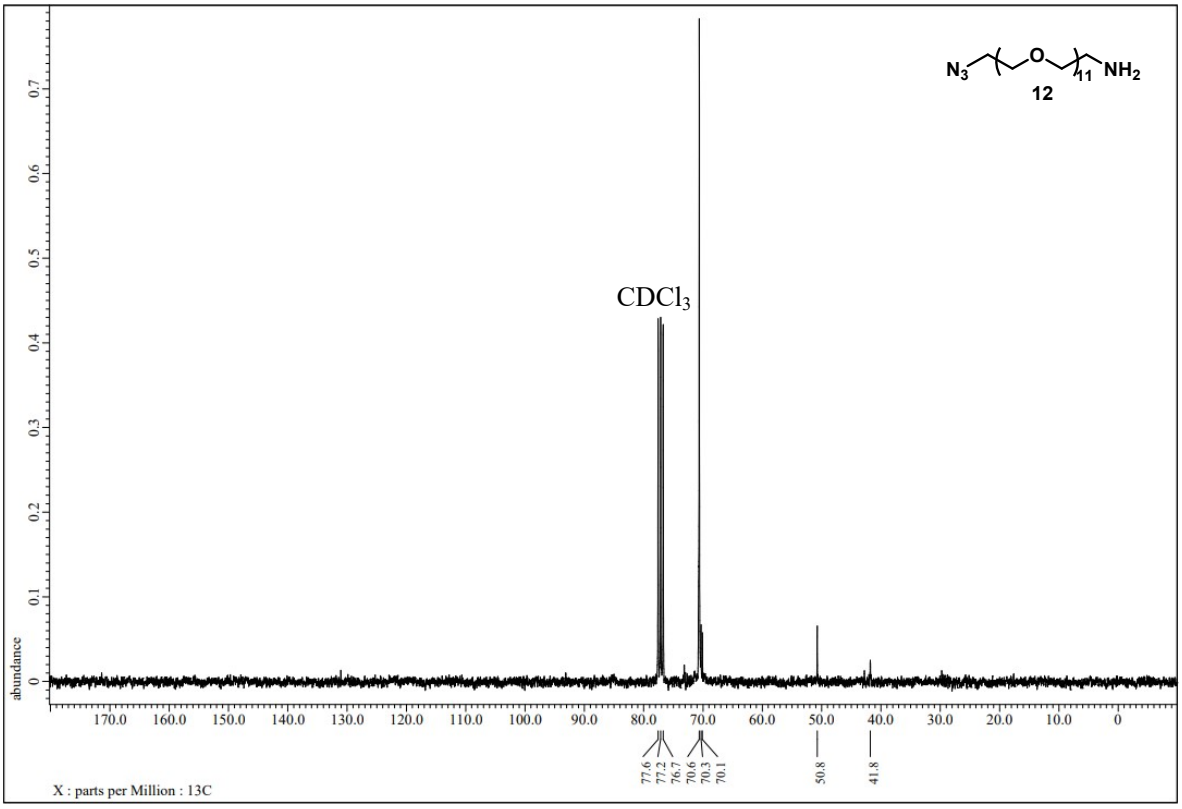
^{13}C NMR spectra of compound **11** ($CDCl_3$, 75 MHz).



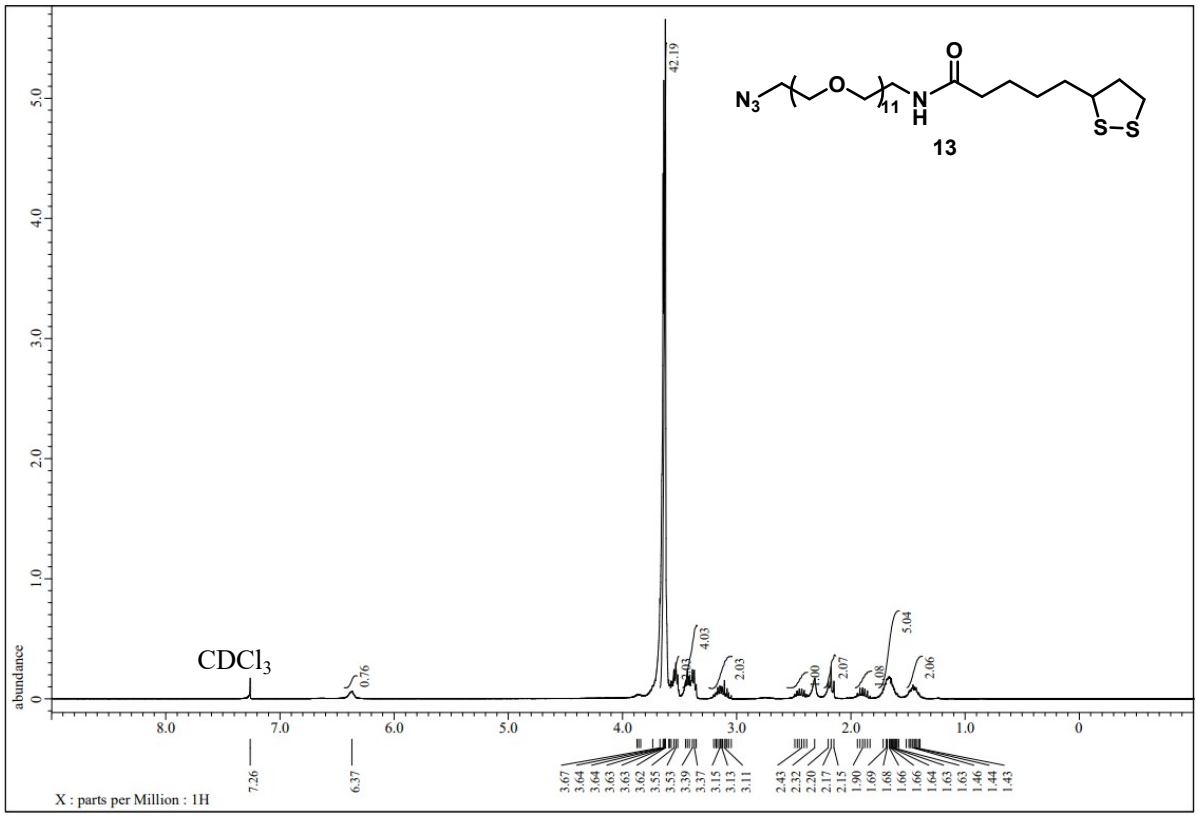
^{1}H NMR spectra of compound **12** ($CDCl_3$, 300 MHz).



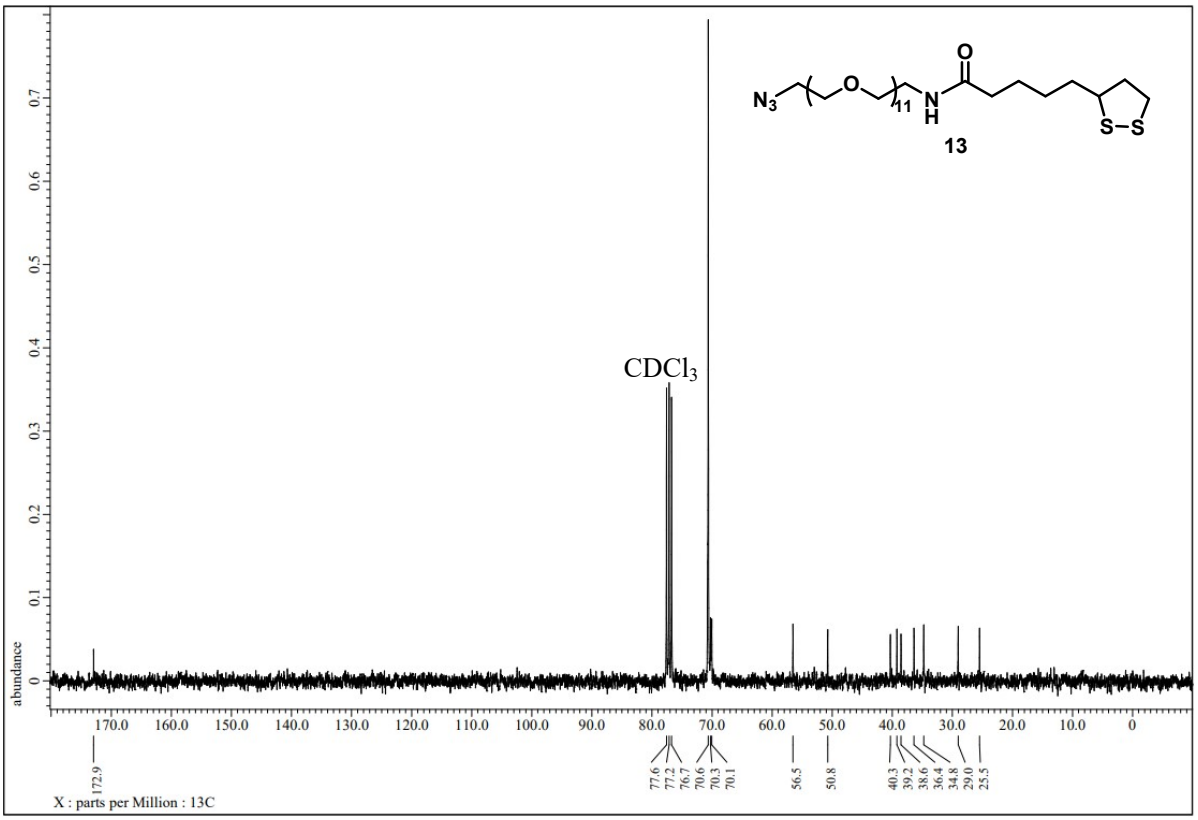
^{13}C NMR spectra of compound **12** ($CDCl_3$, 75 MHz).



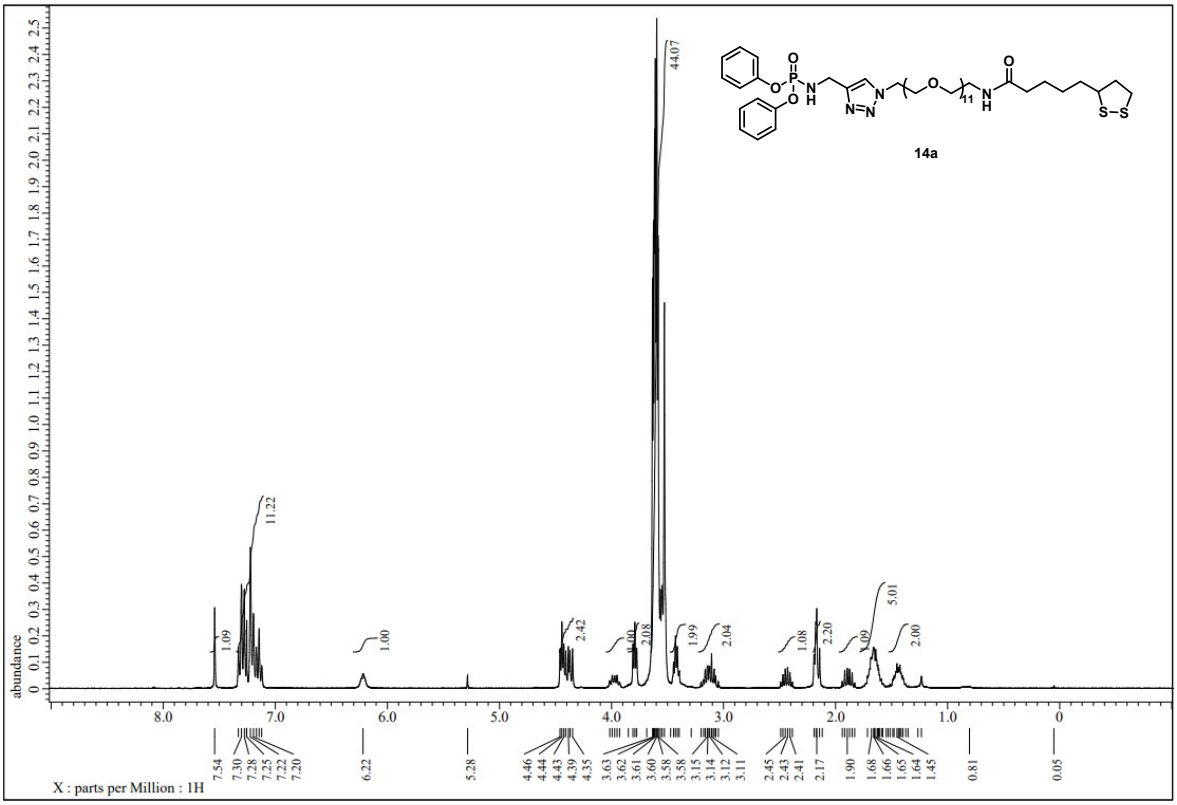
^{1}H NMR spectra of compound **13** ($CDCl_3$, 300 MHz).



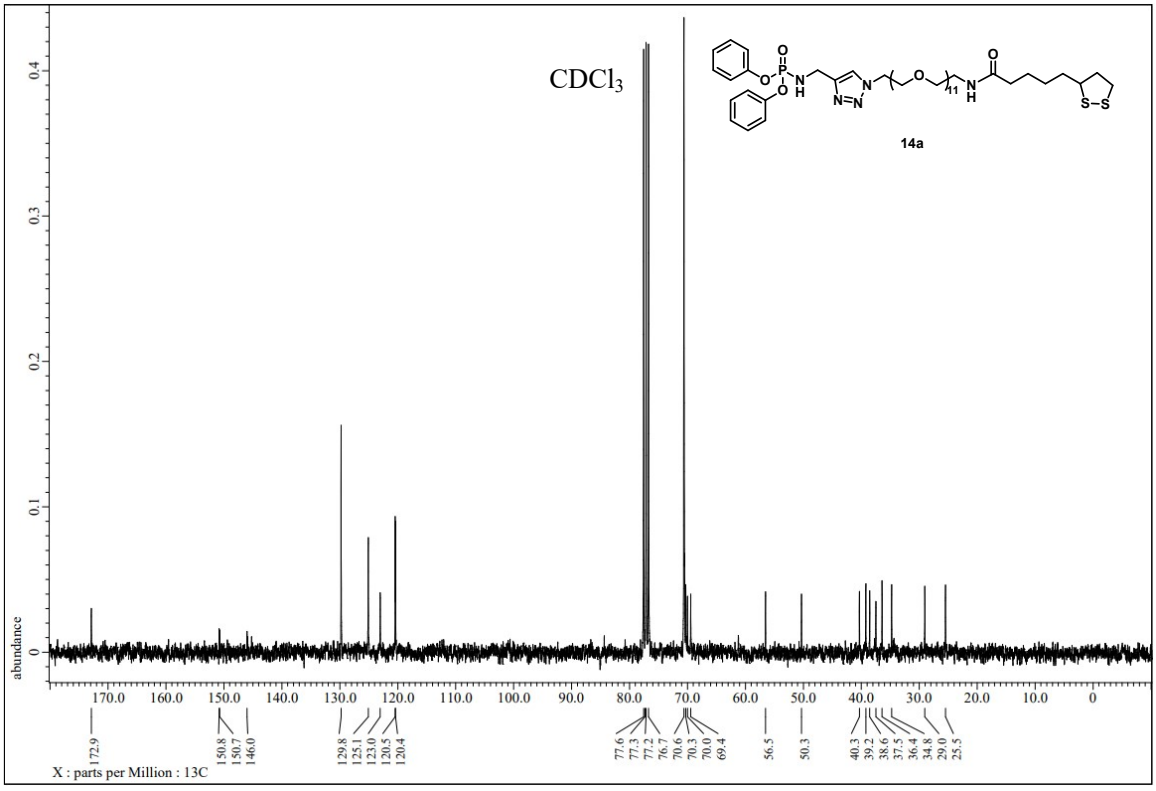
^{13}C NMR spectra of compound **13** ($CDCl_3$, 75 MHz).



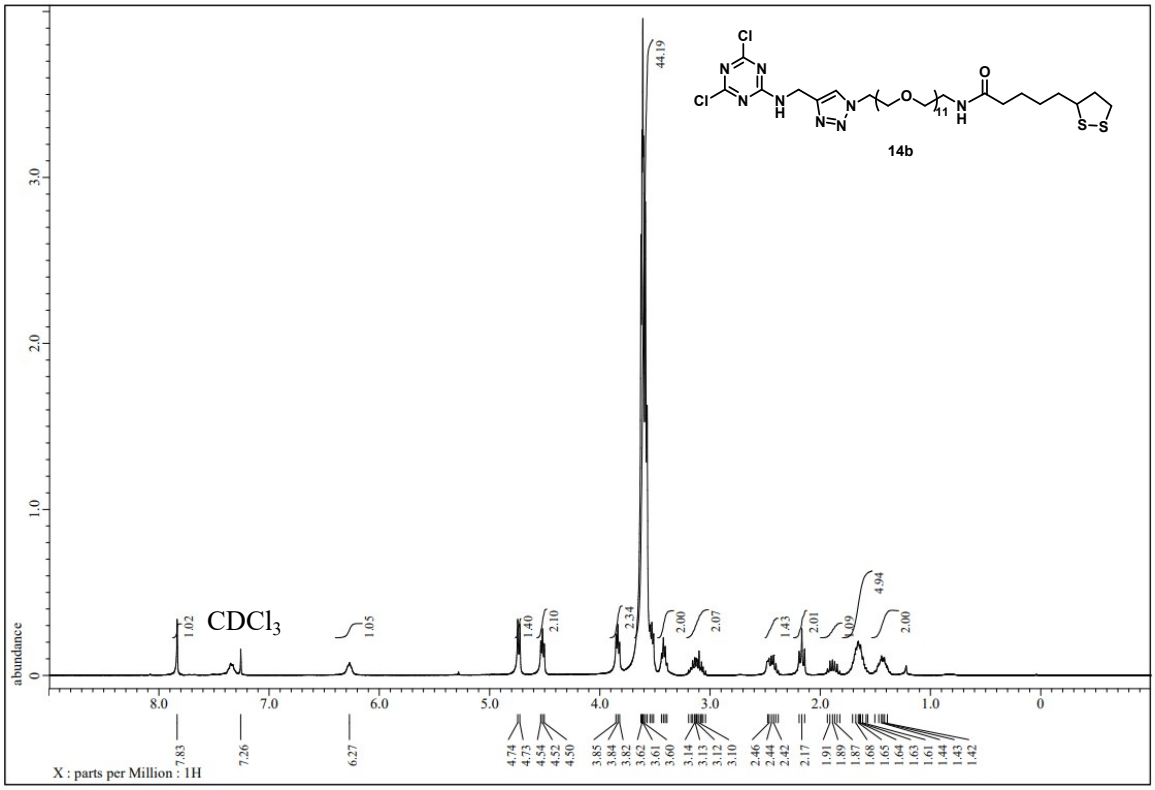
^{1}H NMR spectra of compound **14a** ($CDCl_3$, 300 MHz).



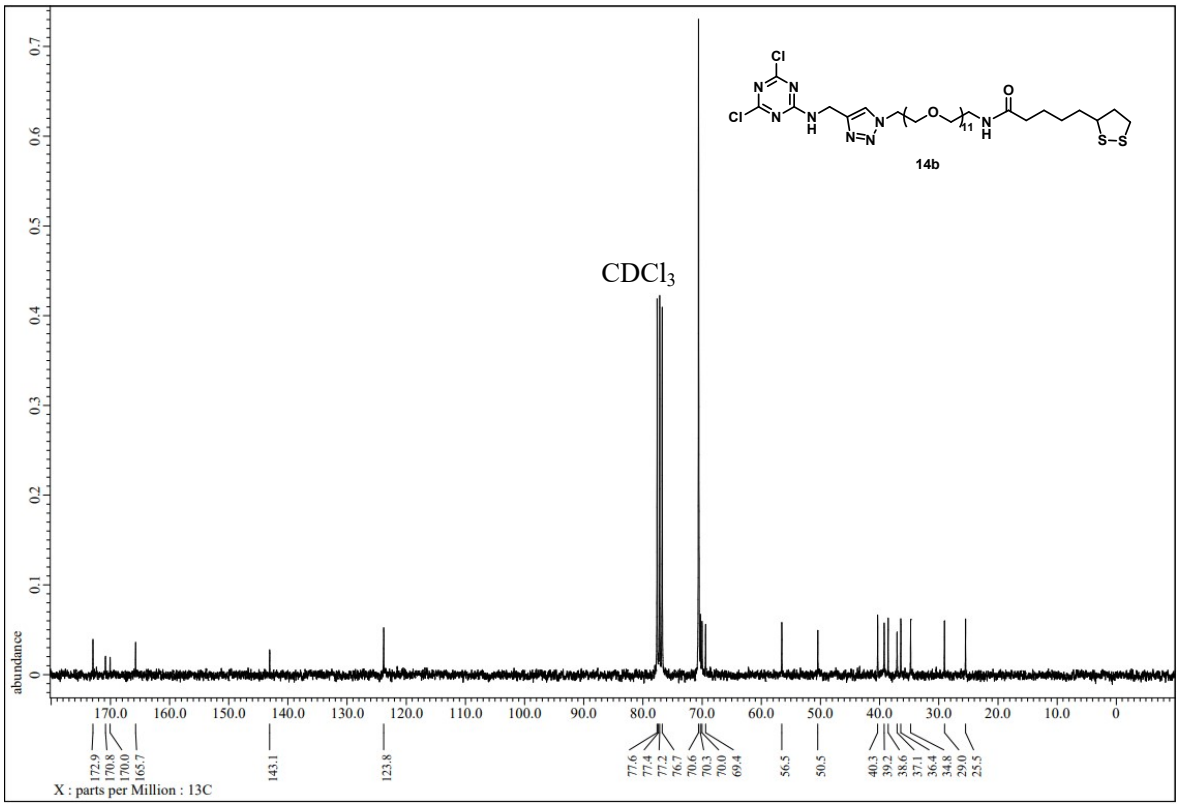
^{13}C NMR spectra of compound **14a** ($CDCl_3$, 75 MHz).



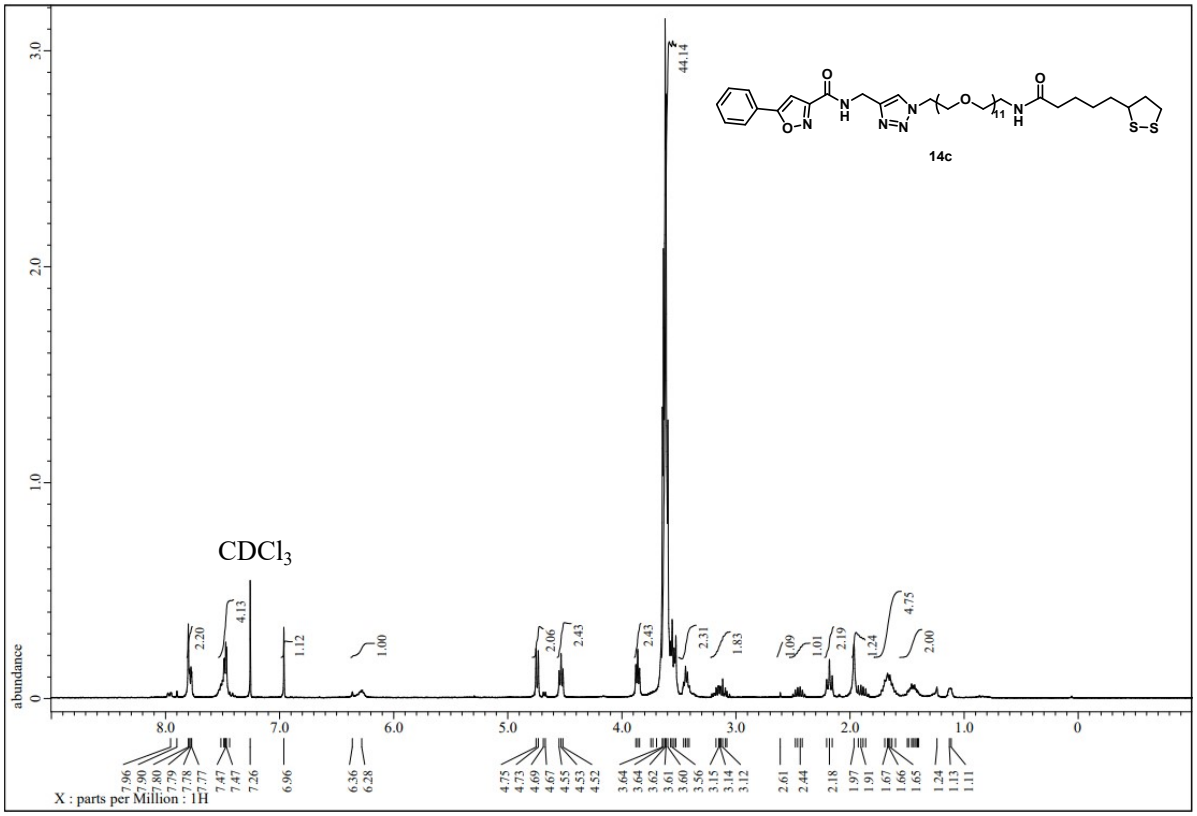
^{1}H NMR spectra of compound **14b** ($CDCl_3$, 300 MHz).



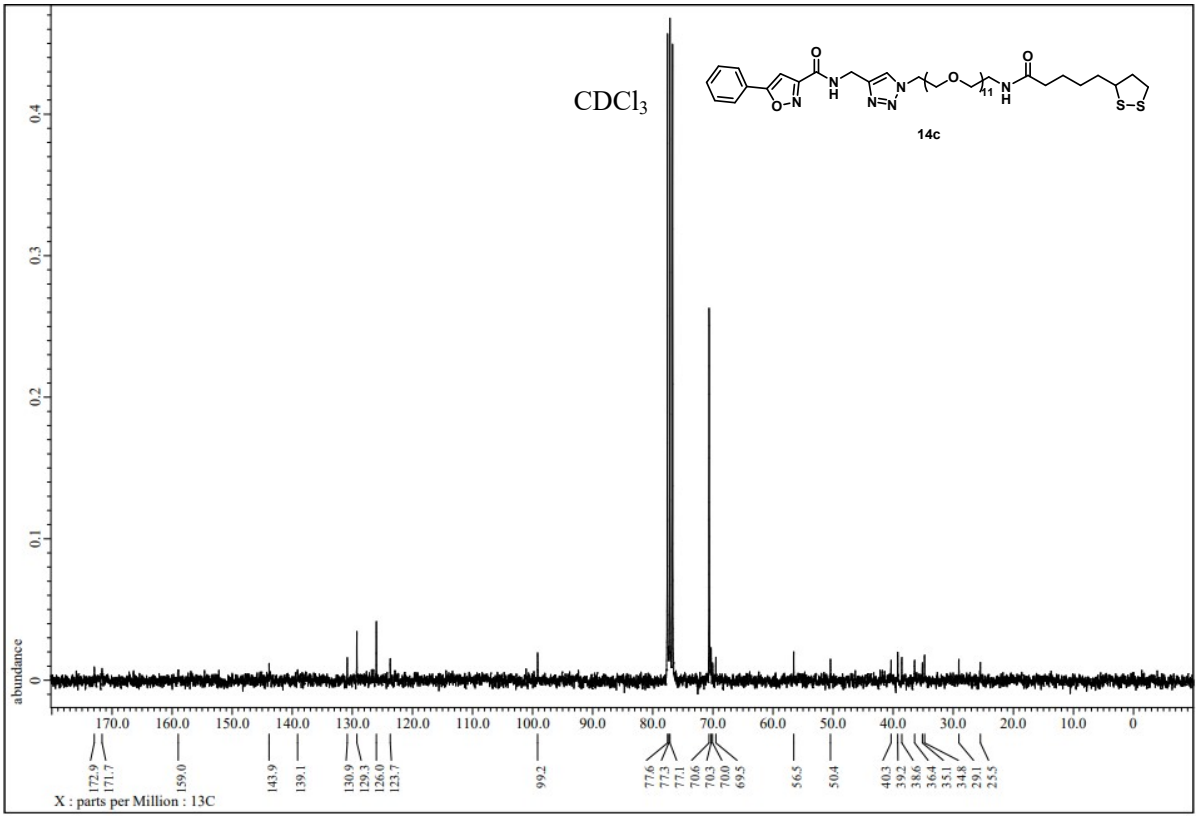
^{13}C NMR spectra of compound **14b** ($CDCl_3$, 75 MHz).



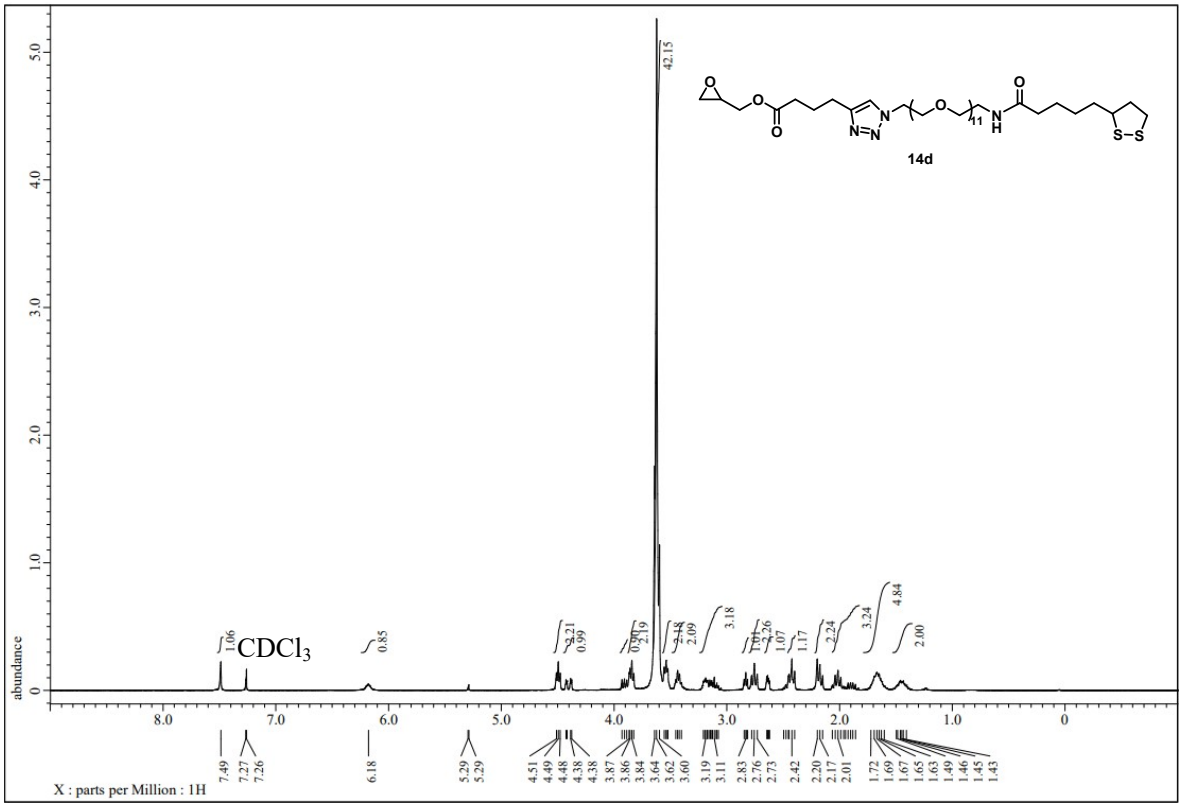
^{1}H NMR spectra of compound **14c** ($CDCl_3$, 300 MHz).



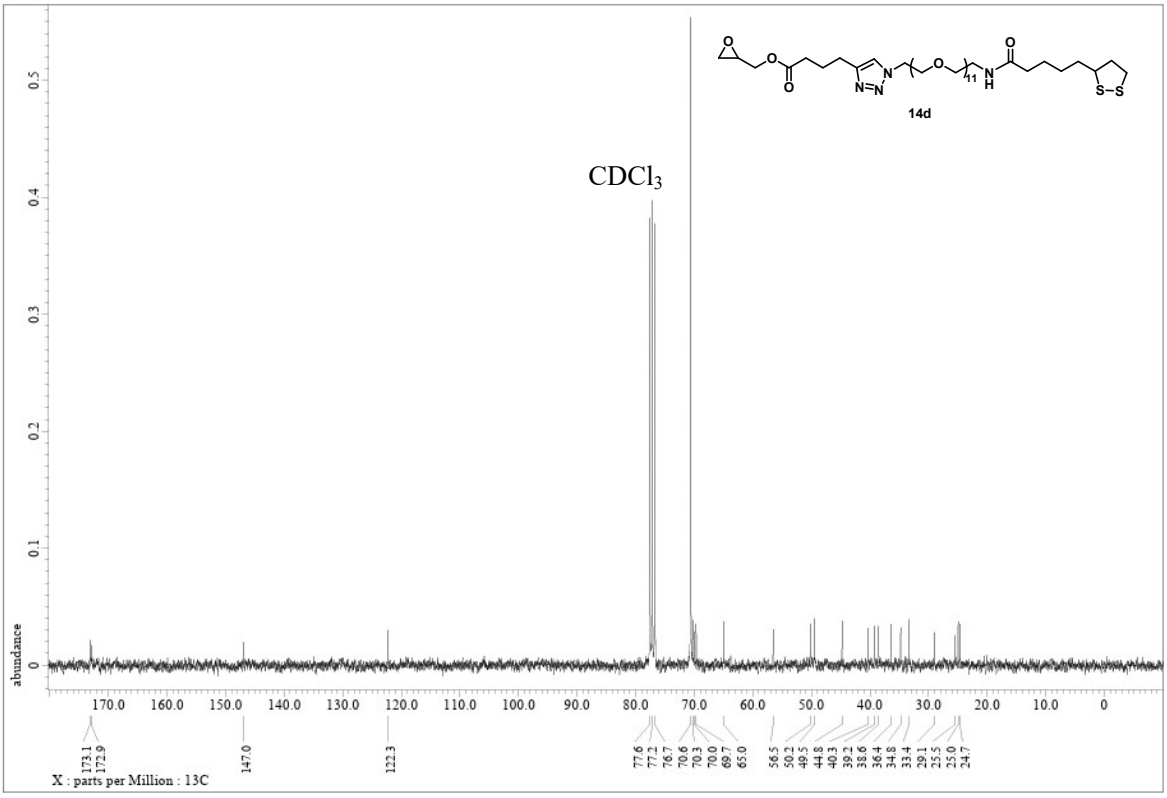
^{13}C NMR spectra of compound **14c** ($CDCl_3$, 75 MHz).



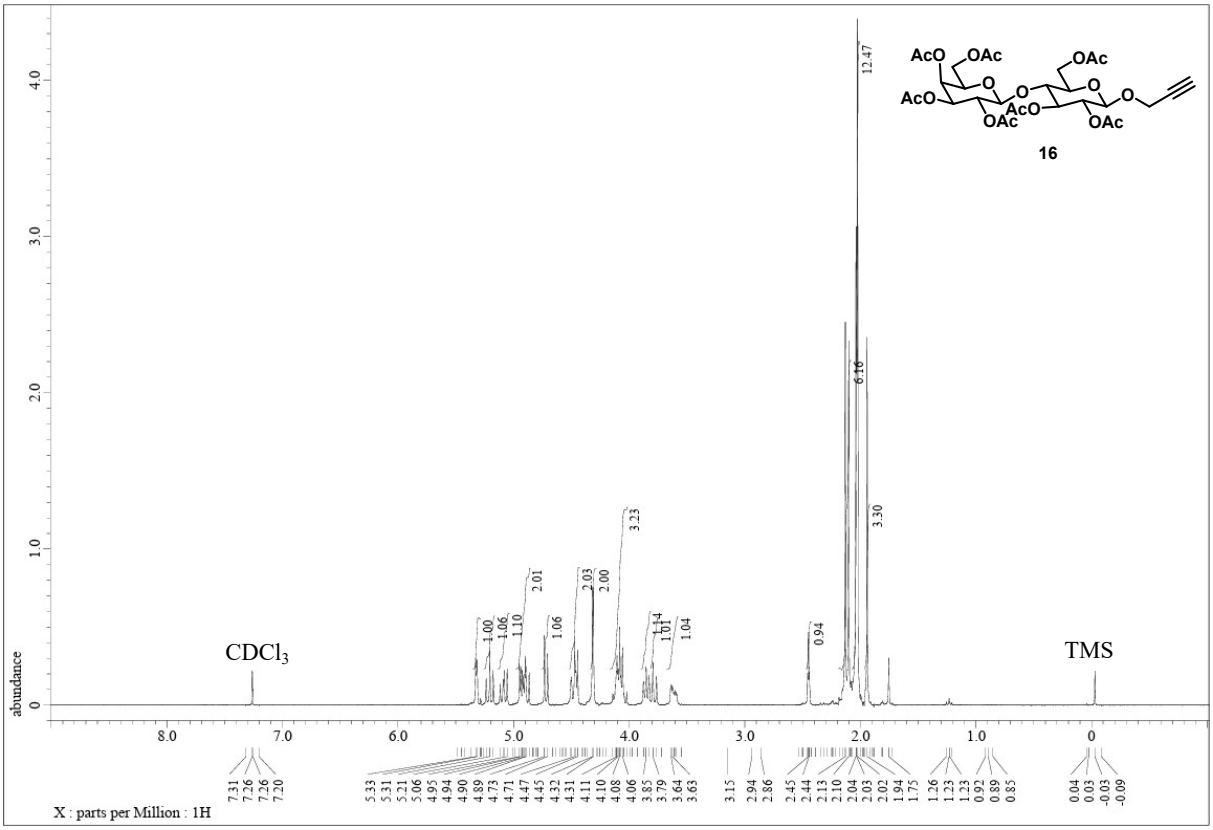
^{1}H NMR spectra of compound **14d** ($CDCl_3$, 300 MHz).



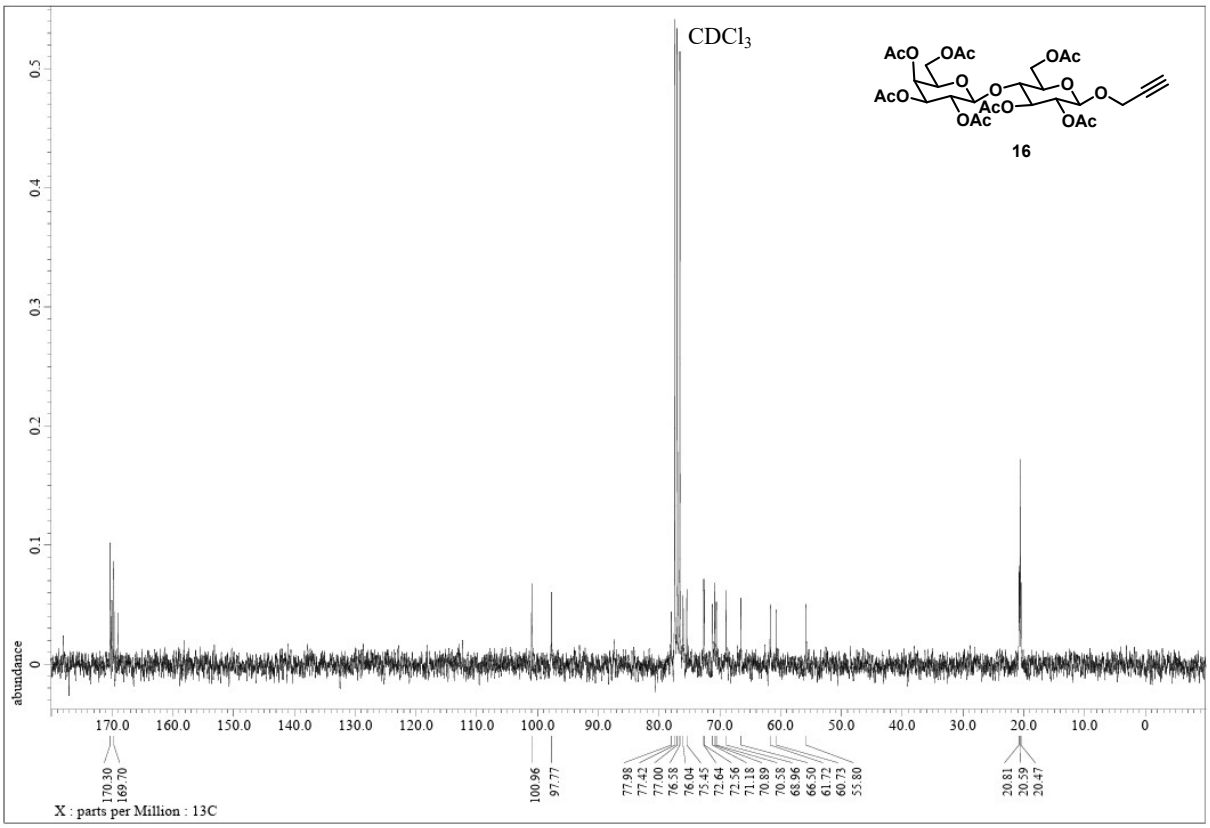
^{13}C NMR spectra of compound **14d** ($CDCl_3$, 75 MHz).



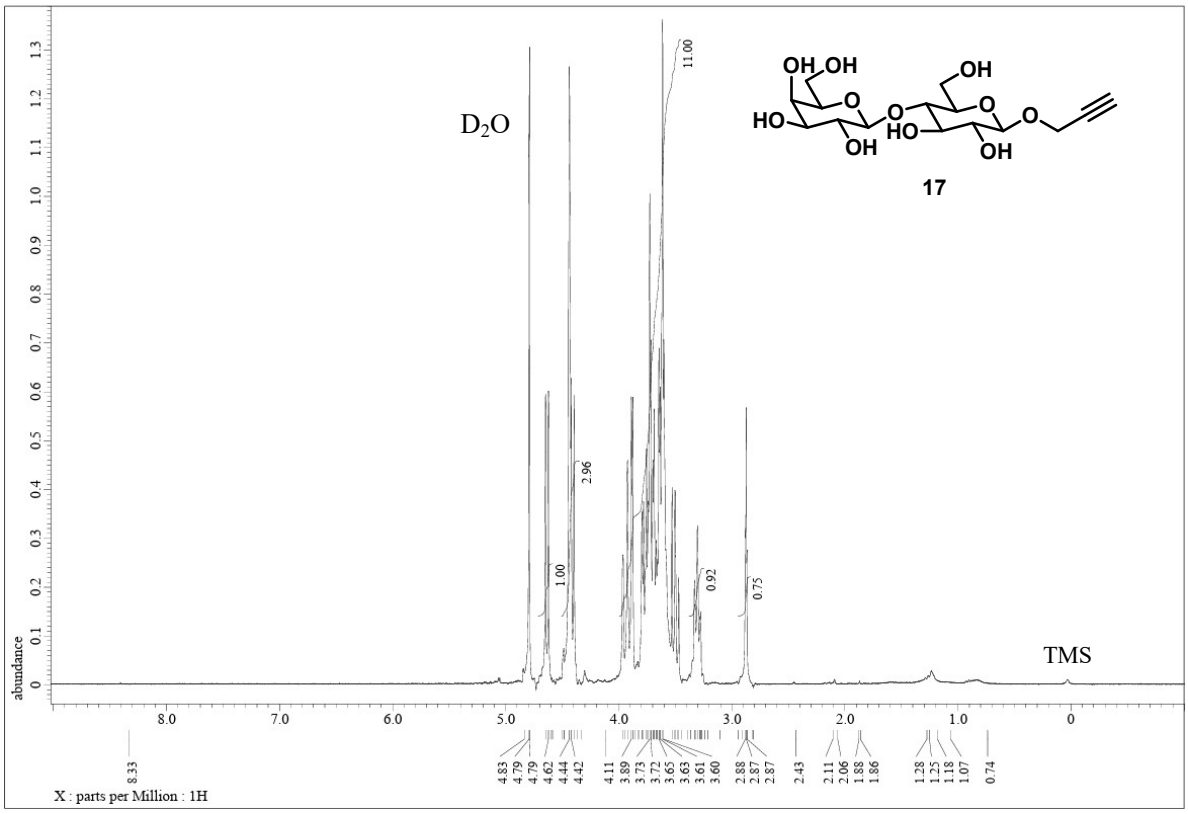
^{1}H NMR spectra of compound **16** ($CDCl_3$, 300 MHz).



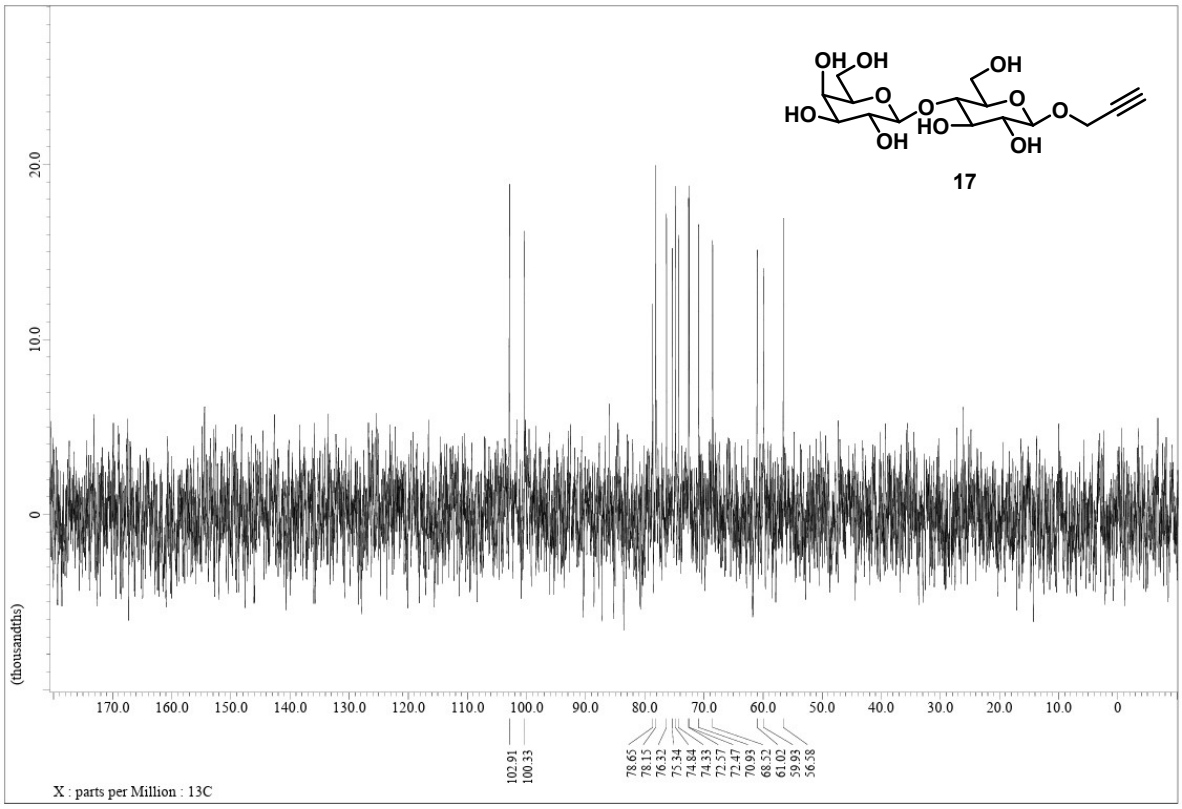
^{13}C NMR spectra of compound **16** ($CDCl_3$, 75 MHz).



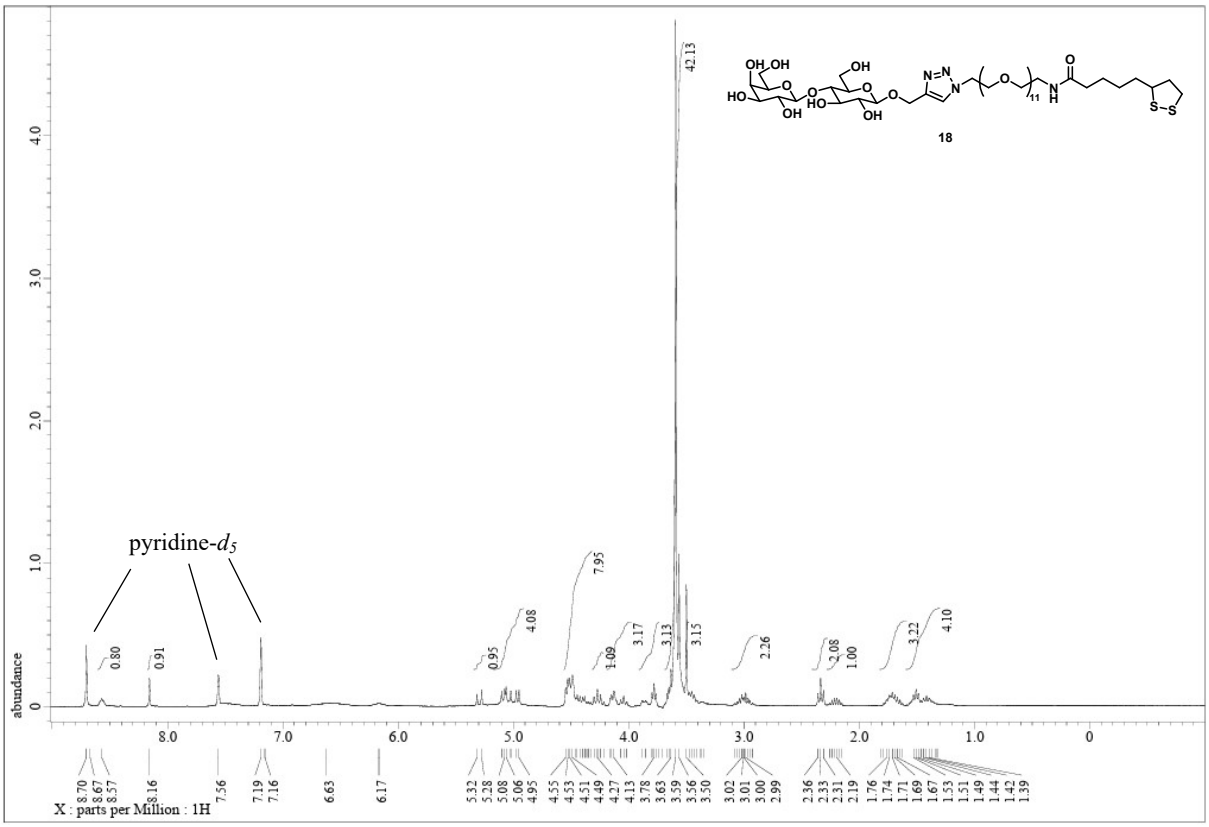
^{1}H NMR spectra of compound **17** (D_2O, 300 MHz).



^{13}C NMR spectra of compound **17** (D_2O, 75 MHz).



^{1}H NMR spectra of compound **18** (pyridine-d_5, 300 MHz).



^{13}C NMR spectra of compound **18** (pyridine-d_5, 75 MHz).