Supporting Information

Iterative click reactions using trivalent platforms for sequential molecular assembly

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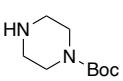
Contents

General Information

All reactions were performed with dry glassware under atmosphere of argon, unless otherwise noted. Analytical thin-layer chromatography (TLC) was performed on precoated (0.25 mm) silica-gel plates (Merck Chemicals, Silica Gel 60 F_{254}, Cat. No. 1.05715). Column chromatography was conducted using silica-gel (Kanto Chemical Co., Inc., Silica Gel 60, spherical, particle size 40–50 μm, Cat. No. 37562-85). Melting points (Mp) were measured on an OptiMelt MPA100 (Stanford Research Systems), and are uncorrected. ^{1}H NMR spectra were obtained with a Bruker AVANCE 400 spectrometer at 400 MHz. ^{13}C NMR spectra were obtained with a Bruker AVANCE 400 spectrometer at 101 MHz. ^{19}F NMR spectra were obtained with a Bruker AVANCE 400 spectrometer at 376 MHz. All NMR measurements were carried out at 25 ºC. $CDCl_3$ (Kanto Chemical Co. Inc., Cat. No. 07663-23) was used as a solvent for obtaining NMR spectra. Chemical shifts (δ) are given in parts per million (ppm) downfield from tetramethylsilane (δ 0.00 for ^{1}H NMR) or the solvent peak (δ 77.2 for ^{13}C NMR in $CDCl_3$) as an internal reference with coupling constants (*J*) in hertz (Hz). The abbreviations s, d, t, q, m, and br signify singlet, doublet, triplet, quartet, multiplet, and broad, respectively. The abbreviations s, d, q, and m signify singlet, doublet, quartet, and multiplet respectively. IR spectra were measured on a Shimadzu IRSpirit spectrometer with the absorption band given in cm^{-1}. High-performance liquid chromatography (HPLC) was performed on a Shimadzu Prominence HPLC system (CBM-20A lite, LC-20AD × 2, DGU-20A3R, SUS316L, and CTO-20A) equipped with a Shimadzu SPD-20A UV/Vis detector. High-resolution mass spectra (HRMS) were measured on a JEOL JMS-T100CS "AccuTOF CS" mass spectrometer under positive electrospray ionization (ESI^{+}) conditions or JMS-700 (JEOL, Tokyo, Japan) mass spectrometer under electron impact ionization (EI) conditions.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. 2-Iodo-3-(propargyloxy)phenyl triflate (**3d**),[S1] 4-(propargyloxy)benzaldehyde (**3e**),[S2] 4-(propargyloxy)benzaldehyde (**3e**),[S2] (propargylaminocarbonyl)ferrocene (**3f**),[S3] 5-((3a*S*,4*S*,6a*R*)-2-oxohexahydro-1*H*-thieno[3,4-*d*]imidazol-4-yl)-*N*-(prop-2-yn-1-yl)pentanamide (**3i**),[S4] 5-(dimethylamino)-*N*-(2-mercaptoethyl)naphthalene-1-sulfonamide (**4d**),[S5] (1α,8α,9α)-bicyclo[6.1.0]non-4-yn-9-ylmethanol (**11**),[S6] 4-(tert-butyldimethylsilyloxy)phenyl acetylene (**12a**),[S7] 4-hydroxy-*N*-(2-(2-(prop-2-yn-1-yloxy)ethoxy)ethyl)benzamide (**12b**),[S8] and tris[(1-benzyl-*1H*-1,2,3-triazol-4-yl)methyl]amine (TBTA)[S9] were prepared according to the reported methods.

Structures of Modules 2–4 and 7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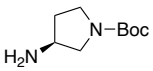
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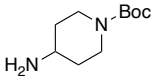
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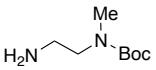
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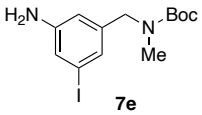
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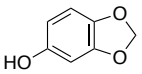
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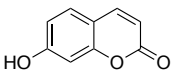
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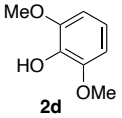
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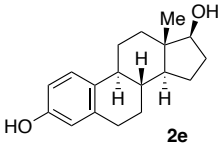
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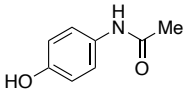
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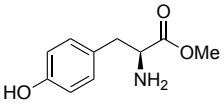
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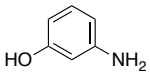
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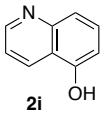
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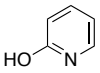
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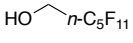
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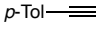
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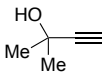
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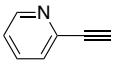
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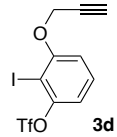
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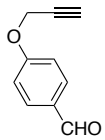
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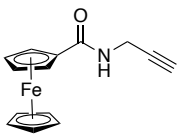
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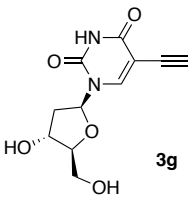
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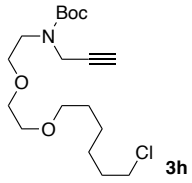
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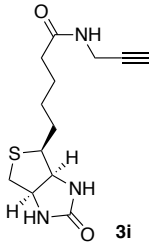
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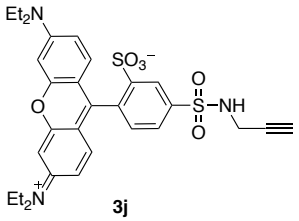
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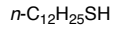
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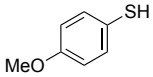
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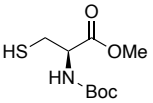
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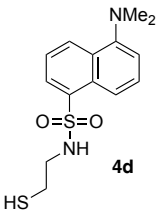
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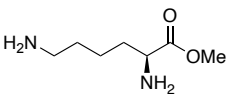
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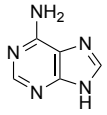
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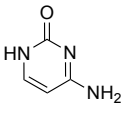
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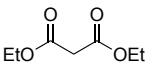
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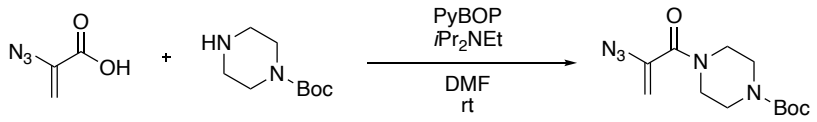
Experimental Procedures

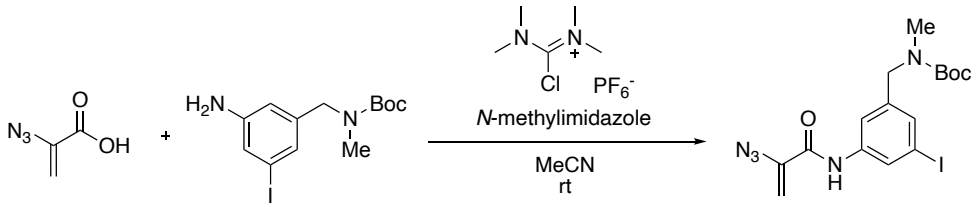
Synthesis of tert-butyl 4-(2-azidoacryloyl)piperazine-1-carboxylate



To a solution of 2-azidoacrylic acid (33.9 mg, 0.300 mmol) and *tert*-butyl piperazine-1-carboxylate (83.8 mg, 0.450 mmol) dissolved in DMF (1.5 mL) was added *i*-Pr_2NEt (93.1 mg, 0.720 mmol) and (benzotriazol-1-yloxy)(trispyrrolidino)phosphonium hexafluorophosphate (PyBOP) (18.7 mg, 0.360 mmol) at 0 ºC. After warming to room temperature, the mixture was stirred for 14 h at the same temperature. Then, to the mixture was added saturated aqueous sodium bicarbonate (10 mL). The mixture was extracted with EtOAc (15 mL × 3). The combined organic extract was washed with brine (10 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (silica-gel 10 g, *n*-hexane/EtOAc = 2/1) to give *tert*-butyl 4-(2-azidoacryloyl)piperazine-1-carboxylate (54.1 mg, 0.192 mmol, 64%) as a colorless solid.

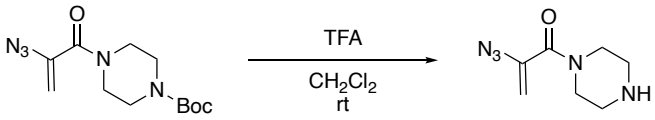
According to the procedure for preparing *tert*-butyl 4-(2-azidoacryloyl)piperazine-1-carboxylate, *tert*-butyl (*S*)-3-aminopyrrolidine-1-carboxylate, *tert*-butyl 4-(2-azidoacrylamido)piperidine-1-carboxylate, and *tert*-butyl (2-(2-azidoacrylamido)ethyl)(methyl)carbamate were prepared from 2-azidoacrylic acid and the corresponding amines.

Synthesis of tert-butyl (3-(2-azidoacrylamido)-5-iodobenzyl)(methyl)carbamate



To a solution of 2-azidoacrylic acid (11.3 mg, 0.100 mmol) and *tert*-butyl (3-amino-5-iodobenzyl)(methyl)carbamate (60.0 mg, 0.130 mmol) dissolved in MeCN (600 μL) were added *N*-methylimidazole (28.7 mg, 0.350 mmol) and chloro-*N,N,N′,N*′-tetramethylformamidinium hexafluorophosphate (33.7 mg, 0.120 mmol) at 0 ºC. After warming to room temperature, the mixture was stirred for 14 h at the same temperature. Then, to the mixture was added saturated aqueous sodium bicarbonate (2 mL). The mixture was extracted with EtOAc (5 mL × 3). The combined organic extract was washed with brine (2 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (silica-gel 3 g, *n*-hexane/EtOAc = 1/1) to give *tert*-butyl (3-(2-azidoacrylamido)-5-iodobenzyl)(methyl)carbamate (28.3 mg, 62.0 μmol, 62%) as a pale yellow oil.

Synthesis of 2-azido-1-(piperazin-1-yl)prop-2-en-1-one

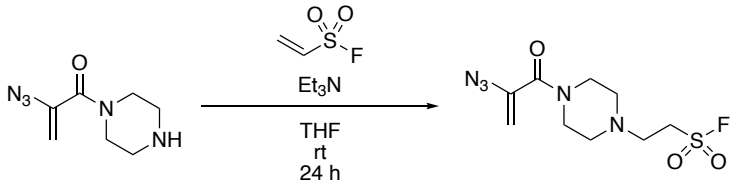


To a solution of *tert*-butyl 4-(2-azidoacryloyl)piperazine-1-carboxylate (0.281 g, 1.00 mmol) in CH_2Cl_2 (10 mL) was slowly added trifluoroacetic acid (2.0 mL, 26.1 mmol) at 0 °C. After stirring for 2.5 h at room temperature, to the mixture was added saturated 1 M aqueous NaOH (40 mL). The mixture was extracted with CH_2Cl_2 (100 mL × 3). The combined organic extract was washed with brine (20 mL), and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure to give 2-azido-1-(piperazin-1-yl)prop-2-en-1-one (0.161 g, 0.887 mmol, 89%) as a colorless oil.

According to the procedure for preparing 2-azido-1-(piperazin-1-yl)prop-2-en-1-one, (*S*)-2-azido-*N*-(pyrrolidin-3-yl)acrylamide, 2-azido-*N*-(piperidin-4-yl)acrylamide, 2-azido-*N*-(2-

(methylamino)ethyl)acrylamide, and 2-azido-*N*-(3-iodo-5-((methylamino)methyl)phenyl)acrylamide were prepared from the corresponding 2-azidoacrylamides.

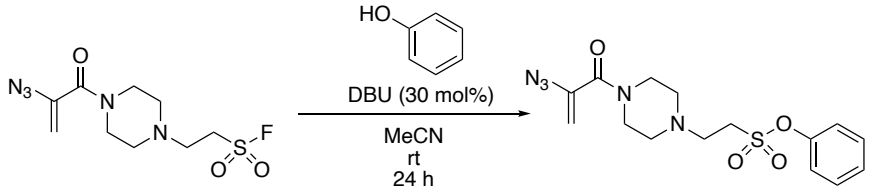
*Synthesis of 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonyl fluoride (**1a**)*



To a solution of 2-azido-1-(piperazin-1-yl)prop-2-en-1-one (1.34 g, 7.40 mmol) in THF (32.0 mL) was added ethenesulfonyl fluoride (0.736 mL, 8.9 mmol) and triethylamine (1.23 mL, 8.88 mmol) at room temperature. After stirring for 24 h at the same temperature, the mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (silica-gel 80 g, CH_2Cl_2/MeOH = 30/1) to give 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonyl fluoride (**1a**) (1.73 g, 5.94 mmol, 80%) as a colorless solid.

According to the procedure for preparing2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonyl fluoride (**1a**), (*S*)-2-(3-(2-azidoacrylamido)pyrrolidin-1-yl)ethane-1-sulfonyl fluoride (**1b**), 2-(4-(2-azidoacrylamido)piperidin-1-yl)ethane-1-sulfonyl fluoride (**1c**), 2-((2-(2-azidoacrylamido)ethyl)(methyl)amino)ethane-1-sulfonyl fluoride (**1d**), and 2-((3-(2-azidoacrylamido)-5-iodobenzyl)(methyl)amino)ethane-1-sulfonyl fluoride (**1e**) were prepared from the corresponding 2-azidoacrylamides.

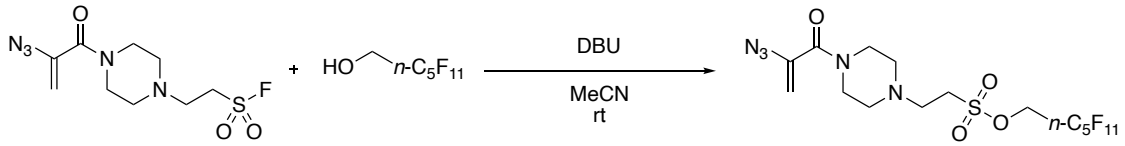
*A typical procedure for the SuFEx reaction of **1a** with alcohols*



To a solution of 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonyl fluoride (**1a**) (14.6 mg, 50 μmol) in acetonitrile (500 μL) was added phenol (5.6 mg, 60 μmol) and DBU (2.3 μL, 15 μmol) at room temperature. After stirring for 24 h at the same temperature, to the mixture was added water (10 mL). The mixture was extracted with CH_2Cl_2 (10 mL × 3). The combined organic extract was washed with aq. sat. K_2CO_3 (10 mL) and brine (20 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (CH_2Cl_2/MeOH = 30/1) to give phenyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9a**) (16.8 mg, 46.0 μmol, quant.) as a pale yellow oil.

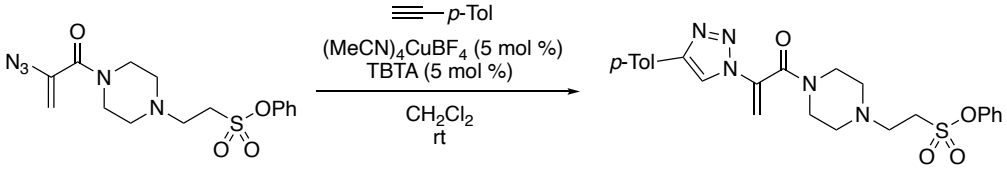
According to the procedure for preparing phenyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9a**), benzo[*d*][1,3]dioxol-5-yl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9b**), 2-oxo-2*H*-chromen-7-yl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9c**), 2,6-dimethoxyphenyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9d**), (8*R*,9*S*,13*S*,14*S*)-17-hydroxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9e**), 4-acetamidophenyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9f**), methyl (*S*)-2-amino-3-(4-(((2-(4-(2-azidoacryloyl)piperazin-1-yl)ethyl)sulfonyl)oxy)phenyl)propanoate (**9g**), 3-aminophenyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9h**) quinolin-5-yl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9i**), and pyridin-2-yl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9j**) were prepared from **1a** and the corresponding alcohols.

*Synthesis of 2,2,3,3,4,4,5,5,6,6,6-undecafluorohexyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9k**)*



To a solution of 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonyl fluoride (**1a**) (14.6 mg, 50 μmol) in acetonitrile (500 μL) was added 2,2,3,3,4,4,5,5,6,6,6-undecafluorohexan-1-ol (18.0 mg, 60 μmol) and DBU (9.1 μL, 60 μmol) at room temperature. After stirring for 24 h at the same temperature, the mixture was concentrated under reduced pressure. The residue was purified by preparative TLC (CH_2Cl_2/MeOH = 10/1) to give 2,2,3,3,4,4,5,5,6,6,6-undecafluorohexyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9k**) (26.8 mg, 47.0 μmol, 94%) as a pale yellow solid.

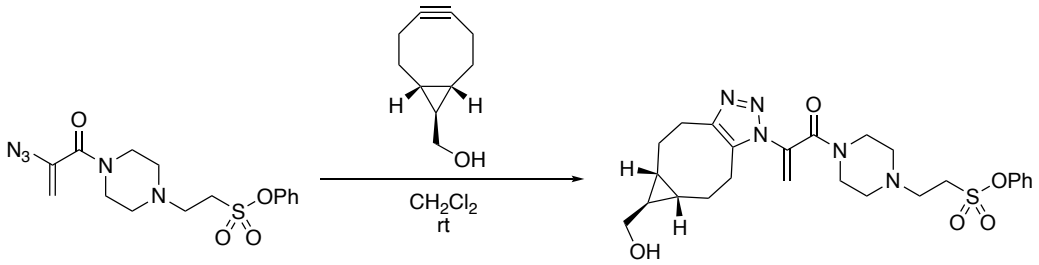
*A typical procedure for the CuAAC reaction of **9a** with alkynes*



To a solution of phenyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9a**) (36.5 mg, 0.100 mmol) in CH_2Cl_2 (6.0 mL) were added *p*-ethynyltoluene (17.0 μL, 0.150 mmol), $(MeCN)_4CuBF_4$ (1.6 mg, 5.0 μmol), and tris(benzyltriazolylmethyl)amine (TBTA) (2.6 mg, 5.0 μmol) at room temperature. After stirring for 24 h at the same temperature, to the mixture was added water (10 mL). The mixture was extracted with CH_2Cl_2 (20 mL × 2). The combined organic extract was washed with brine (10 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (CH_2Cl_2/MeOH = 15/1) to give phenyl 2-(4-(2-(4-(4-tolyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10a**) (39.2 mg, 0.100 mmol, quant.) as a colorless oil.

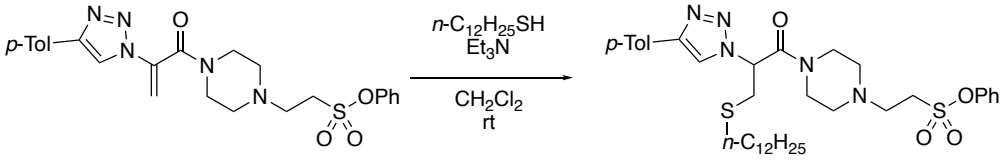
According to the procedure for preparing phenyl 2-(4-(2-(4-(4-tolyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10a**), triazoles **10b**–**10j** were prepared from **9a** and the corresponding alkynes.

*Synthesis of phenyl 2-(4-(2-((5aR,6R,6aS)-6-(hydroxymethyl)-5,5a,6,6a,7,8-hexahydrocyclopropa[5,6]cycloocta[1,2-d][1,2,3]triazol-1(4H)-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10k**)*



To a solution of phenyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9a**) (18.2 mg, 50.0 μmol) in CH_2Cl_2 (1.0 mL) was added ((1*R*,8*S*,9*r*)-bicyclo[6.1.0]non-4-yn-9-yl)methanol (**11**) (12.3 mg, 60.0 μmol) at room temperature. After stirring for 24 h at the same temperature, the mixture was concentrated under reduced pressure. The residue was purified by preparative TLC (*n*-hexane/EtOAc = 1/1) to give phenyl 2-(4-(2-((5a*R*,6*R*,6a*S*)-6-(hydroxymethyl)-5,5a,6,6a,7,8-hexahydrocyclopropa[5,6]cycloocta[1,2-*d*][1,2,3]triazol-1(4*H*)-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10k**) (25.2 mg, 42.0 μmol, 84%) as a colorless solid.

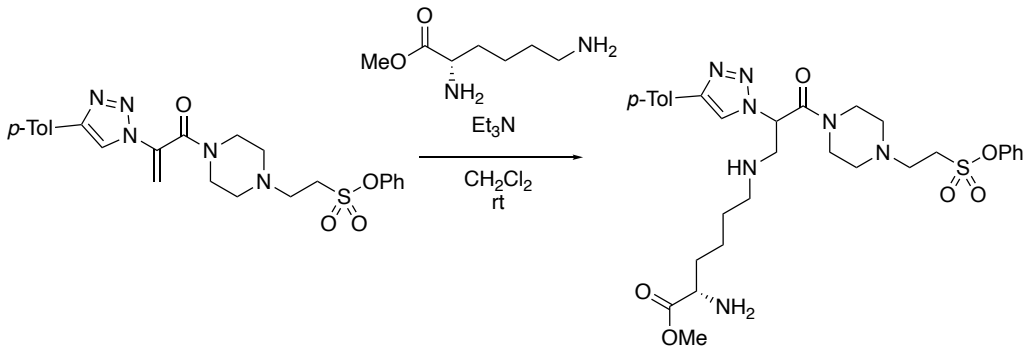
*A typical procedure for the Michael addition of thiols to **10a***



In a 0.3 mL screw-top V-vial® with a solid-top cap (Sigma-Aldrich, Cat. No. Z115118), to a solution of phenyl 2-(4-(2-(4-(4-tolyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10a**) (24.1 mg, 50.0 μmol) in CH_2Cl_2 (0.20 mL) were added triethylamine (8.4 μL, 60 μmol) and dodecanethiol (14.3 μL, 60.0 μmol) at 0 °C. After stirring for 24 h at room temperature, the mixture was concentrated under reduced pressure. The resulting residue was purified by preparative TLC (CH_2Cl_2/MeOH = 20/1) to give phenyl 2-(4-(3-(dodecylthio)-2-(4-(4-tolyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**5a**) (29.9 mg, 43.8 μmol, 88%) as a colorless oil.

According to the procedure for preparing triazole **5a**, triazoles **5b**–**5d** were prepared from **10a** and the corresponding thiols.

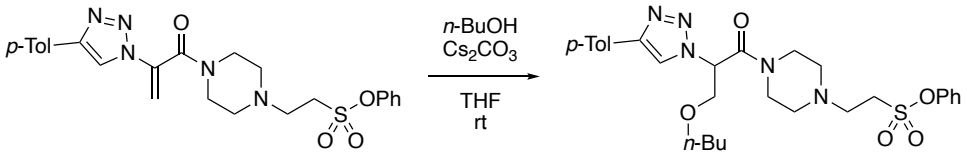
*A typical procedure for the Michael addition of amines to **10a***



In a 0.3 mL screw-top V-vial® with a solid-top cap (Sigma-Aldrich, Cat. No. Z115118), to a solution of phenyl 2-(4-(2-(4-(4-tolyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10a**) (24.1 mg, 50.0 μmol) in CH_2Cl_2 (0.20 mL) were added triethylamine (8.4 μL, 60 μmol) and methyl L-lysinate (18.5 mg, 60.0 μmol) at 0 °C. After stirring for 24 h at room temperature, the mixture was concentrated under reduced pressure. The resulting residue was purified by preparative TLC (CH_2Cl_2/MeOH = 20/1) to give methyl N^6-(3-oxo-3-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propyl)-L-lysinate (**5e**) (39.5 mg, 50 μmol, 83%) as a colorless oil.

According to the procedure for preparing triazole **5e**, triazoles **5f** and **5g** were prepared from methyl *L*-lysinate, 9*H*-purin-6-amine and 6-aminopyrazin-2(1*H*)-one, respectively, with **10a**.

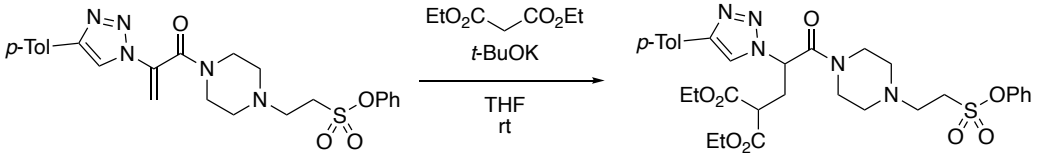
*Synthesis of phenyl 2-(4-(3-butoxy-2-(4-(p-tolyl)-1H-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**5h**)*



In a 0.3 mL screw-top V-vial® with a solid-top cap (Sigma-Aldrich, Cat. No. Z115118), to a solution of phenyl 2-(4-(2-(4-(4-tolyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10a**) (19.5 mg, 50.0 μmol) in THF (0.20 mL) were added butanol (18.3 μL, 0.200 mmol) and cesium carbonate (39.1 mg, 0.120 mmol) at room temperature. After stirring for 24 h at the same temperature, the mixture was concentrated under reduced

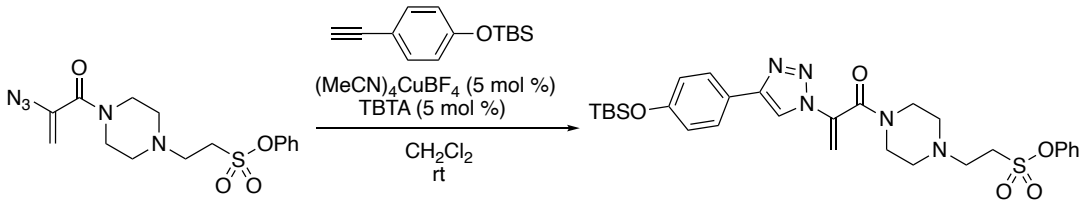
pressure. The residue was purified by preparative TLC (*n*-hexane/EtOAc = 1/1) to give phenyl 2-(4-(3-butoxy-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**5h**) (19.0 mg, 41.0 μmol, 82%) as a colorless oil.

*Synthesis of diethyl 2-(3-oxo-3-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)-2-(4-(p-tolyl)-1H-1,2,3-triazol-1-yl)propyl)malonate (**5i**)*



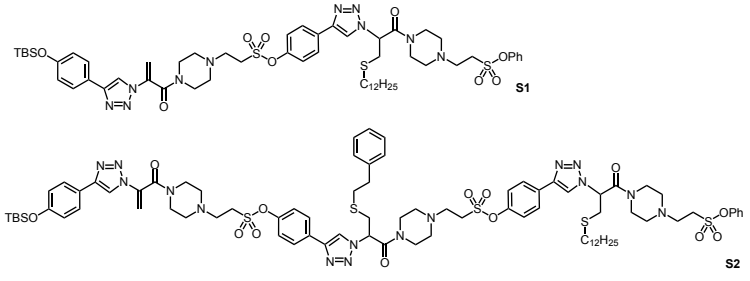
In a 0.3 mL screw-top V-vial® with a solid-top cap (Sigma-Aldrich, Cat. No. Z115118), to a mixture of phenyl 2-(4-(2-(4-(4-tolyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10a**) (19.5 mg, 50.0 μmol) and diethyl malonate (11.4 μL, 75.0 μmol) was added sodium *tert*-butoxide (5.6 mg, 50 μmol) dissolved in THF (0.20 mL) at room temperature. After stirring for 24 h at the same temperature, to the mixture was added saturated aqueous ammonium chloride (5 mL). The mixture was extracted with EtOAc (20 mL × 2). The combined organic extract was washed with brine (5 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (*n*-hexane/EtOAc = 1/1) to give diethyl 2-(3-oxo-3-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propyl)malonate (**5i**) (32.0 mg, 50.0 μmol, quant.) as a colorless solid.

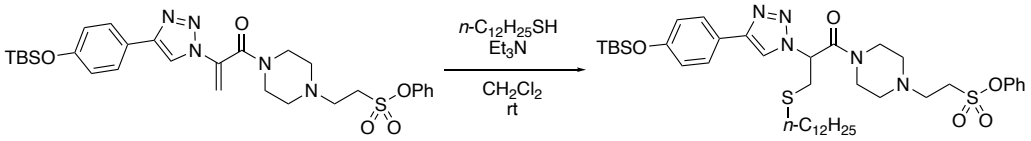
*Typical procedures for the iterative click reactions from **9a***



To a solution of phenyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9a**) (18.2 mg, 50.0 μmol) in CH_2Cl_2 (1.0 mL) were added *tert*-butyl(4-ethynylphenoxy)dimethylsilane (**12a**) (13.9 mg, 60.0 μmol), $(MeCN)_4CuBF_4$ (1.6 mg, 2.5 μmol), and TBTA (2.6 mg, 2.5 μmol) at room temperature. After stirring for 24 h at the same temperature, to the mixture was added water (10 mL). The mixture was extracted with CH_2Cl_2 (20 mL × 2). The combined organic extract was washed with brine (10 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (CH_2Cl_2/MeOH = 15/1) to give phenyl 2-(4-(2-(4-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**13a**) (24.5 mg, 41.0 μmol, 82%) as a colorless oil.

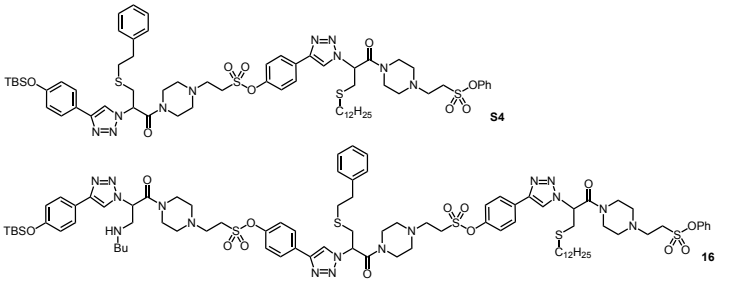
According to the procedure for preparing **13a** from **12a** with **9a**, triazoles **13b** and **13c** were prepared from the corresponding alkynes **12b** and **12c**, respectively. Also, triazoles **S1** and **S2** were prepared from the corresponding azides under the same conditions. The isolated yield of **S2** was calculated from the actual weight obtained as a diastereomeric mixture after the purification.

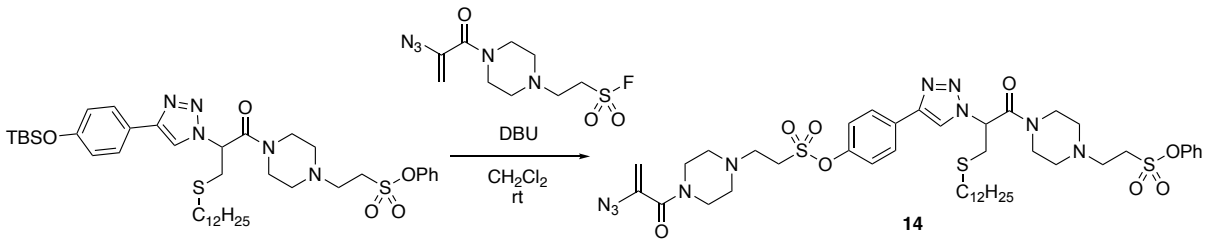




In a 0.3 mL screw-top V-vial® with a solid-top cap (Sigma-Aldrich, Cat. No. Z115118), to a solution of phenyl 2-(4-(2-(4-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**13a**) (17.9 mg, 30.0 μmol) in CH_2Cl_2 (0.20 mL) were added triethylamine (6.0 μL, 36 μmol) and dodecanethiol (10.3 μL, 36.0 μmol) at 0 °C. After stirring for 24 h at room temperature, the mixture was concentrated under reduced pressure. The resulting residue was purified by preparative TLC (CH_2Cl_2/MeOH = 20/1) to give phenyl 2-(4-(2-(4-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-1*H*-1,2,3-triazol-1-yl)-3-(dodecylthio)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**S3**) (23.9 mg, 30.0 μmol, quant.) as a colorless oil.

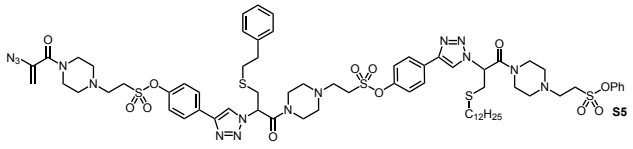
According to the procedure for preparing triazole **14** from **9a**, bis(trizole) **S2** and tris(triazole) **16** were prepared from triazole **14** and bis(trizole) **S2**, respectively, with 2-phenylethanethiol, buthylamine, and 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonyl fluoride (**1a**). Also, triazoles **S4** and **16** were prepared from the corresponding acrylamides under the same conditions. The isolated yields of **S4** and **16** were calculated from the actual weights obtained as diastereomeric mixtures after the purification.



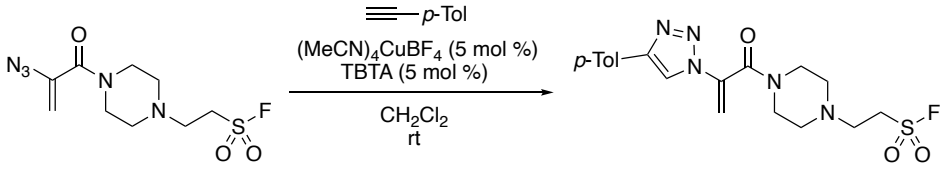


To a solution of phenyl 2-(4-(2-(4-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-1*H*-1,2,3-triazol-1-yl)-3-(dodecylthio)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**S1**) (85.2 mg, 0.106 mmol) in CH_2Cl_2 (800 μL) was added 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonyl fluoride (**1a**) (37.2 mg, 0.127 mmol) and DBU (19.3 μL, 0.127 mmol) at room temperature. After stirring for 24 h at the same temperature, the mixture was concentrated under reduced pressure. The residue was purified by preparative TLC (CH_2Cl_2/MeOH = 30/1) to give 4-(1-(3-(dodecylthio)-1-oxo-1-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)propan-2-yl)-1*H*-1,2,3-triazol-4-yl)phenyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**14**) (119 mg, 99.6 μmol, 97%) as a pale yellow solid.

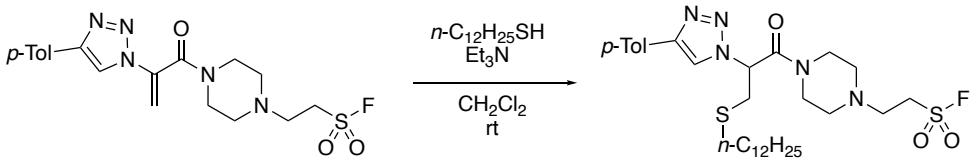
According to the procedure for preparing triazole **14** from **9a**, bis(trizole) **S2** and tris(triazole) **16** were prepared from triazole **14** and bis(trizole) **S2**, respectively, with 2-phenylethanethiol, buthylamine, and 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonyl fluoride (**1a**). Also, triazole **S5** was prepared from silyl ether **S4** under the same conditions. The isolated yield of **S5** was calculated from the actual weight obtained as a diastereomeric mixture after the purification.



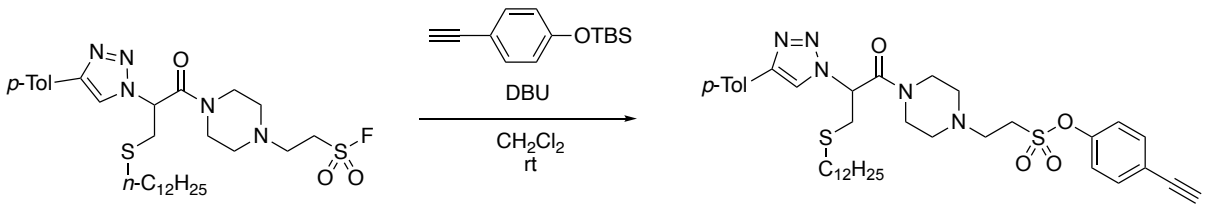
*Synthesis of 4-(1-(3-(4-(2-(fluorosulfonyl)ethyl)piperazin-1-yl)-3-oxoprop-1-en-2-yl)-1H-1,2,3-triazol-4-yl)phenyl 2-(4-(3-(dodecylthio)-2-(4-(p-tolyl)-1H-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**15**)*



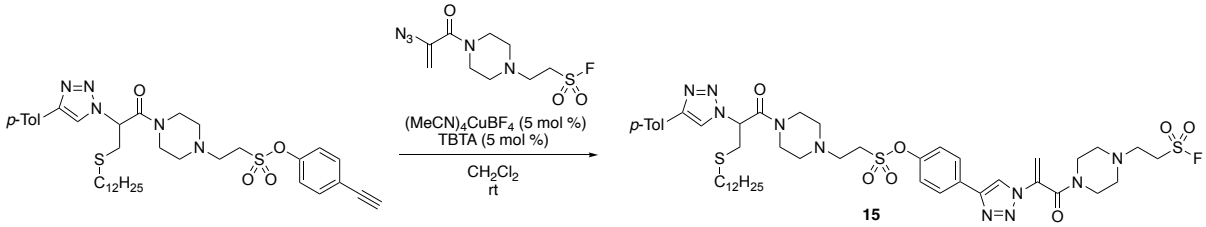
To a solution of 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonyl fluoride (**1a**) (21.8 mg, 75.0 μmol) in CH_2Cl_2 (6.0 mL) were added *p*-ethynyltoluene (11.4 μL, 90.0 μmol), $(MeCN)_4CuBF_4$ (1.2 mg, 3.8 μmol), and TBTA (2.0 mg, 3.8 μmol) at room temperature. After stirring for 24 h at the same temperature, to the mixture was added water (10 mL). The mixture was extracted with CH_2Cl_2 (20 mL × 2). The combined organic extract was washed with H_2O (10 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (CH_2Cl_2/MeOH = 15/1) to give 2-(4-(2-(4-(4-tolyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonyl fluoride (**S6**) (23.7 mg, 75.0 μmol, quant.) as a colorless solid.



In a 0.3 mL screw-top V-vial® with a solid-top cap (Sigma-Aldrich, Cat. No. Z115118), to a solution of 2-(4-(2-(4-(4-tolyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonyl fluoride (**S6**) (18.3 mg, 30.0 μmol) in CH_2Cl_2 (0.20 mL) were added triethylamine (6.0 μL, 36 μmol) and dodecanethiol (10.3 μL, 36.0 μmol) at 0 °C. After stirring for 24 h at room temperature, the mixture was concentrated under reduced pressure. The resulting residue was purified by preparative TLC (CH_2Cl_2/MeOH = 20/1) to give 2-(4-(3-(dodecylthio)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonyl fluoride (**S7**) (23.9 mg, 30.0 μmol, quant.) as a colorless oil.



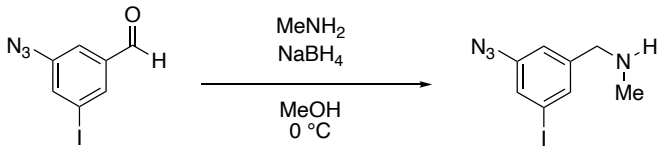
To a solution of 2-(4-(3-(dodecylthio)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonyl fluoride (**S7**) (60.2 mg, 0.100 mmol) in CH_2Cl_2 (600 μL) was added *tert*-butyl(4-ethynylphenoxy)dimethylsilane (**12a**) (27.8 mg, 0.120 mmol) and DBU (18.3 μL, 0.120 mmol) at room temperature. After stirring for 24 h at the same temperature, the mixture was concentrated under reduced pressure. The residue was purified by preparative TLC (CH_2Cl_2/MeOH = 30/1) to give 4-ethynylphenyl 2-(4-(3-(dodecylthio)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**S8**) (61.4 mg, 88.0 μmol, 88%) as a pale yellow solid.



To a solution of 4-ethynylphenyl 2-(4-(3-(dodecylthio)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**S8**) (21.8 mg, 75.0 μmol) in CH_2Cl_2 (6.0 mL) were added *p*-

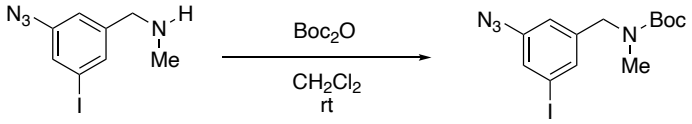
ethynyltoluene (11.4 μL, 90.0 μmol), $(MeCN)_4CuBF_4$ (1.2 mg, 3.8 μmol), and TBTA (2.0 mg, 3.8 μmol) at room temperature. After stirring for 24 h at the same temperature, to the mixture was added water (10 mL). The mixture was extracted with CH_2Cl_2 (20 mL × 2). The combined organic extract was washed with H_2O (10 mL) and dried with Na_2SO_4. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (CH_2Cl_2/MeOH = 15/1) to give bis(triazole) **15** (74.9 mg, 75.0 μmol, quant.) as a colorless solid.

Synthesis of 1-(3-azido-5-iodophenyl)-N-methylmethanamine



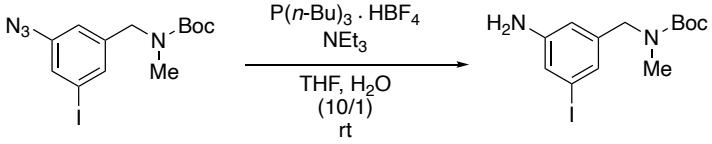
To a solution of 3-azido-5-iodobenzaldehyde (208 mg, 0.762 mmol) in MeOH (2.4 mL) was added methylamine (88.0 μL, 0.762 mmol) at room temperature. After stirring for 20 min at the same temperature, to the mixture was added sodium borohydride (14.4 mg, 0.381 mmol) at 0 ºC. After stirring for 1 h at the same temperature, the mixture was concentrated under reduced pressure. The resulting residue was purified by preparative TLC (*n*-hexane/EtOAc = 1/1) to give 1-(3-azido-5-iodophenyl)-*N*-methylmethanamine (210 mg, 0.730 mmol, quant.) as a colorless oil.

Synthesis of tert-butyl (3-azido-5-iodobenzyl)(methyl)carbamate



To a solution of 1-(3-azido-5-iodophenyl)-*N*-methylmethanamine (220 mg, 0.763 mmol) in CH_2Cl_2 (1.0 mL) was added di-*tert*-butyl dicarbonate (212 μL, 0.916 mmol) at 0 ºC. After warming to room temperature, the mixture was stirred for 12 h at the same temperature. Then, the mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (silica-gel 11 g, *n*-hexane/EtOAc = 4/1) to give *tert*-butyl (3-azido-5-iodobenzyl)(methyl)carbamate (214 mg, 0.572 mmol, 75%) as a colorless oil.

Synthesis of tert-butyl (3-amino-5-iodobenzyl)(methyl)carbamate

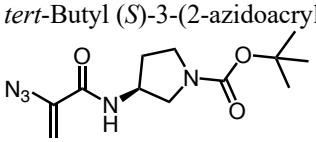


To a solution of *tert*-butyl (3-azido-5-iodobenzyl)(methyl)carbamate (214 mg, 0.573 mmol) and triethylamine (16.3 μL, 0.116 mmol) dissolved in THF (2.3 mL) and H_2O (230 μL) was added tributylphosphine tetrafluoroborate (166 mg, 0.573 mmol) at room temperature. After stirring for 12 h at the same temperature, the mixture was concentrated under reduced pressure. The residue was purified by preparative TLC (*n*-hexane/EtOAc = 1/1) to give 4-(ethoxycarbonyl)aniline (118 mg, 0.324 mmol, 57%) as a colorless oil.

Characterization Data of New Compounds

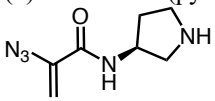
2-(4-(2-(4-(4-Tolyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonyl fluoride (**S6**) was identical in spectra data with that reported in the literature.[S10]

tert-Butyl (*S*)-3-(2-azidoacrylamido)pyrrolidine-1-carboxylate



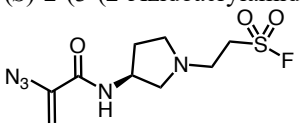
Pale yellow oil; TLC R_f 0.33 (*n*-hexane/EtOAc = 1/1); ^{1}H and ^{13}C NMR analysis show the presence of rotational isomers. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.47 (s, 9H), 1.82–1.94 (m, 1H), 2.13–2.24 (m, 1H), 3.15–3.30 (m, 1H), 3.38–3.51 (m, 2H), 3.62–3.68 (m, 1H), 4.44–4.52 (m, 1H), 5.21 (d, 1H, J = 2.0 Hz), 6.19 (d, 1H, J = 2.0 Hz), 6.40–6.53 (br, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 28.5, 30.8, 43.7, 49.7, 51.5, 79.7, 106.9, 138.2, 154.5, 160.4; IR (NaCl, cm^{-1}) 1131, 1166, 1410, 1416, 1525, 1682, 1698, 2119; HRMS (ESI$^+$) *m/z* 304.1384 ([M + Na]$^+$ $C_{12}H_{19}N_5NaO_3^+$ requires 304.1386).

(*S*)-2-Azido-*N*-(pyrrolidin-3-yl)acrylamide



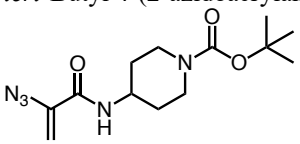
Pale yellow oil; TLC R_f 0.28 (CH_2Cl_2/MeOH = 10/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.61–1.71 (m, 1H), 2.14–2.23 (m, 1H), 2.75–2.83 (m, 1H), 2.92–2.99 (m, 1H), 3.04–3.12 (m, 1H), 3.13–3.20 (m, 1H), 5.19 (d, 1H, J = 2.0 Hz), 6.18 (d, 1H, J = 2.0 Hz), 6.54 (br s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 33.1, 45.7, 50.6, 53.6, 106.5, 138.5, 160.2; IR (NaCl, cm^{-1}) 1521, 1539, 1652, 2117; HRMS (ESI$^+$) *m/z* 204.0862 ([M + Na]$^+$ $C_7H_{11}N_5NaO^+$ requires 204.0861).

(*S*)-2-(3-(2-Azidoacrylamido)pyrrolidin-1-yl)ethane-1-sulfonyl fluoride (**1b**)



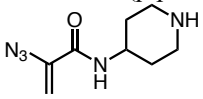
Pale yellow oil; TLC R_f 0.42 (CH_2Cl_2/MeOH = 15/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.69–1.76 (m, 1H), 2.28–2.40 (m, 2H), 2.56–2.61 (m, 1H), 2.77–2.81 (m, 1H), 3.03–3.10 (m, 2H), 3.10–3.18 (m, 1H), 3.58–3.63 (m, 2H), 4.48–4.55 (m, 1H), 5.20 (d, 1H, J = 2.0 Hz), 6.15 (d, 1H, J = 2.0 Hz); ^{13}C{^{1}H} NMR ($CDCl_3$,126 MHz): δ 32.2, 48.2, 49.0, 50.3 (d, J = 14.9 Hz), 52.0, 59.5, 106.6, 138.5, 160.1; ^{19}F{^{1}H} NMR ($CDCl_3$, 376 MHz): δ 58.8 (1F, s); IR (NaCl, cm^{-1}) 1199, 1403, 1519, 1612, 1666, 2122; HRMS (ESI$^+$) *m/z* 314.0700 ([M + Na]$^+$ $C_9H_{14}FN_5NaO_3S^+$ requires 314.0699).

tert-Butyl 4-(2-azidoacrylamido)piperidine-1-carboxylate



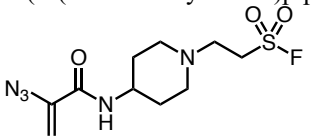
Pale yellow oil; TLC R_f 0.42 (*n*-hexane/EtOAc = 1/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.30–1.42 (m, 2H),1.47 (s, 9H), 1.90–1.94 (m, 2H), 2.83–2.94 (m, 2H), 3.90–4.15 (m, 3H), 5.20 (d, 1H, J = 2.0 Hz), 6.18 (d, 1H, J = 2.0 Hz), 6.26–6.34 (br, 1H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 28.4, 31.8, 42.7 (br), 47.0, 79.8, 106.7, 138.4, 154.7, 159.8; IR (NaCl, cm^{-1}) 1141, 1170, 1239, 1366, 1428, 1525, 1614, 1678, 1682, 2121; HRMS (ESI$^+$) *m/z* 318.1543 ([M + Na]$^+$ $C_{13}H_{21}N_5NaO_3^+$ requires 318.1542).

2-Azido-*N*-(piperidin-4-yl)acrylamide



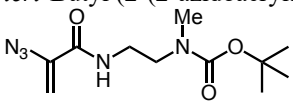
Pale yellow oil; TLC R_f 0.21 (CH_2Cl_2/MeOH = 15/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.31–1.41 (m, 2H), 1.91–2.02 (m, 2H), 2.65–2.76 (m, 2H), 3.05–3.14 (m, 2H), 3.84–3.96 (m, 1H), 5.19 (d, 1H, J = 2.0 Hz), 6.18 (d, 1H, J = 2.0 Hz), 6.21–6.39 (br, 1H); ^{13}C NMR ($CDCl_3$,126 MHz): δ 33.3, 45.4, 47.2, 106.6, 138.6, 159.7; IR (NaCl, cm^{-1}) 1521, 1538, 1614, 1652, 1668, 2116; HRMS (ESI$^+$) *m/z* 196.1201 ([M + H]$^+$ $C_8H_{14}N_5O^+$ requires 196.1198).

2-(4-(2-Azidoacrylamido)piperidin-1-yl)ethane-1-sulfonyl fluoride (**1c**)



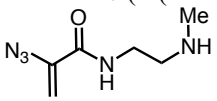
Pale yellow oil; TLC R_f 0.42 (CH_2Cl_2/MeOH = 15/1); ^1H and ^{13}C NMR analysis show the presence of rotational isomers. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.47–1.58 (m, 2H), 1.93–2.06 (m, 2H), 2.23–2.32 (m, 2H), 2.84–2.92 (m, 2H), 2.94–3.00 (m, 2H), 3.53–3.60 (m, 2H), 3.80–3.89 (m, 1H), 5.21 (d, 1H, J = 2.0 Hz), 6.19 (d, 1H, J = 2.0 Hz), 6.23–6.33 (br, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 126 MHz): δ 31.8, 46.5, 49.2 (d, J = 14.4 Hz), 51.3, 51.9, 106.7, 138.4, 159.9; $^{19}F\{^1H\}$ NMR ($CDCl_3$, 376 MHz): δ 58.2 (1F, s); IR (NaCl, cm^{-1}) 1196, 1395, 1521, 1539, 1652, 2123; HRMS (ESI^+) *m/z* 328.0858 ($[M + Na]^+$ $C_{10}H_{16}FN_5NaO_3S_1^+$ requires 328.0856).

tert-Butyl (2-(2-azidoacrylamido)ethyl)(methyl)carbamate



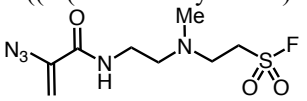
Pale yellow oil; TLC R_f 0.42 (*n*-hexane/EtOAc = 1/1); ^1H and ^{13}C NMR analysis show the presence of rotational isomers. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.48 (s, 9H), 2.85–2.93 (br, 3H), 3.39–3.48 (br, 4H), 5.12–5.21 (br, 1H), 6.05–6.22 (br, 1H), 6.64 and 7.20 (two br s signals, total 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 28.3, 34.7, 39.0, 46.9, 80.1, 106.1, 138.7, 157.1, 161.3; IR (NaCl, cm^{-1}) 1157, 1244, 1393, 1525, 1682, 1698, 2119; HRMS (ESI^+) *m/z* 292.1386 ($[M + Na]^+$ $C_{11}H_{19}N_5NaO_3^+$ requires 292.1386).

2-Azido-*N*-(2-(methylamino)ethyl)acrylamide



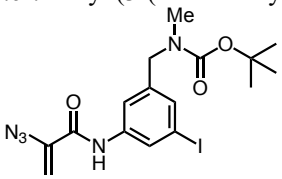
Pale yellow solid; TLC R_f 0.21 (CH_2Cl_2/MeOH = 15/1); ^1H NMR ($CDCl_3$, 400 MHz): δ 2.45 (s, 3H), 2.77 (t, 2H, J = 5.8 Hz), 3.41 (dt, 2H, J = 5.8, 5.8 Hz), 5.19 (d, 1H, J = 2.0 Hz), 6.17 (d, 1H, J = 2.0 Hz), 6.82–6.94 (br, 1H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 36.1, 38.9, 50.3, 106.4, 138.7, 160.8; IR (NaCl, cm^{-1}) 1256, 1539, 1609, 1652, 2117, 3309; HRMS (ESI^+) *m/z* 192.0864 ($[M + Na]^+$ $C_6H_{11}N_5NaO^+$ requires 192.0861).

2-((2-(2-Azidoacrylamido)ethyl)(methyl)amino)ethane-1-sulfonyl fluoride (**1d**)



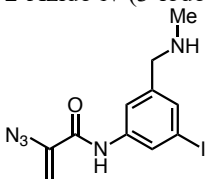
Pale yellow solid; TLC R_f 0.42 (CH_2Cl_2/MeOH = 15/1); ^1H NMR ($CDCl_3$, 400 MHz): δ 2.35 (s, 3H), 2.63 (t, 2H, J = 5.8 Hz), 3.04 (td, 2H, J = 6.5, 2.0 Hz), 3.44 (dt, 2H, J = 5.8, 5.8 Hz), 3.59 (td, 2H, J = 6.5, 2.7 Hz), 5.19 (d, 1H, J = 2.0 Hz), 6.12 (d, 1H, J = 2.0 Hz), 6.85–6.95 (br, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$,126 MHz): δ 36.7, 41.1, 49.3 (d, J = 13.6 Hz), 51.1, 55.8, 106.4, 138.7, 160.9; $^{19}F\{^1H\}$ NMR ($CDCl_3$, 376 MHz): δ 58.8 (1F, s); IR (NaCl, cm^{-1}) 1199, 1397, 1521, 1539, 1669, 2123; HRMS (ESI^+) *m/z* 302.0707 ($[M + Na]^+$ $C_8H_{14}FN_5NaO_3S^+$ requires 302.0699).

tert-Butyl (3-(2-azidoacrylamido)-5-iodobenzyl)(methyl)carbamate



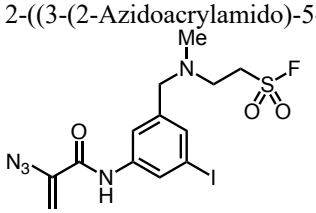
Pale yellow oil; TLC R_f 0.42 (*n*-hexane/EtOAc = 1/1); ^1H and ^{13}C NMR analysis show the presence of rotational isomers. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.48–1.52 (br, 9H), 2.80–2.91 (br, 3H), 4.32–4.43 (br, 2H), 5.33 (d, 1H, J = 2.3 Hz), 6.32 (d, 1H, J = 2.3 Hz), 7.35–7.47 (br, 2H), 7.89–8.06 (br, 1H), 8.07–8.13 (br, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 28.4, 34.2, 51.3, 52.0, 80.2, 94.4, 107.9, 118.0, 127.5, 132.6, 138.1, 141.3, 155.6, 158.3; HRMS (ESI^+) *m/z* 480.0509 ($[M + Na]^+$ $C_{16}H_{20}IN_5NaO_3^+$ requires 480.0509).

2-Azido-*N*-(3-iodo-5-((methylamino)methyl)phenyl)acrylamide



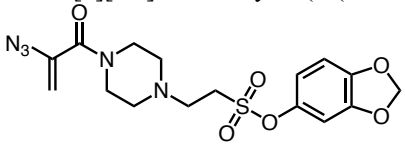
Pale yellow oil; TLC R_f 0.48 (CH_2Cl_2/MeOH = 15/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.45 (s, 3H), 3.71 (s, 2H), 5.32 (d, 1H, *J* = 2.0 Hz), 6.31 (d, 1H, *J* = 2.0 Hz), 7.49 (dd, 1H, *J* = 1.7, 1.7 Hz), 7.52 (dd, 1H, *J* = 1.7, 1.7 Hz), 7.95 (dd, 1H, *J* = 1.7, 1.7 Hz), 8.10 (br s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 36.0, 55.1, 94.3, 107.8, 119.0, 127.3, 133.6, 138.0, 138.2, 143.3, 158.3; IR (NaCl, cm^{-1}) 931, 1446, 1531, 1578, 1599, 1694, 2130; HRMS (ESI$^+$) *m/z* 358.0164 ([M + H]$^+$ $C_{11}H_{13}IN_5O^+$ requires 358.0165).

2-((3-(2-Azidoacrylamido)-5-iodobenzyl)(methyl)amino)ethane-1-sulfonyl fluoride (**1e**)



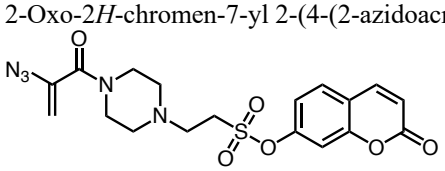
Pale yellow oil; TLC R_f 0.44 (*n*-hexane/EtOAc = 2/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.30 (s, 3H), 3.04 (td, 2H, *J* = 7.1, 1.0 Hz), 3.54 (s, 2H), 3.59 (td, 2H, *J* = 7.1, 3.4 Hz), 5.33 (d, 1H, *J* = 2.4 Hz), 6.32 (d, 1H, *J* = 2.4 Hz), 7.46–7.48 (m, 1H), 7.53–7.56 (m, 1H), 7.96–7.98 (dd, 1H, *J* = 1.7, 1.7 Hz), 8.09 (br s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 41.7, 49.1 (d, *J* = 14.0 Hz), 50.7, 61,0, 94.3, 107.9, 119.4, 127.8, 134.0, 138.1, 138.2, 141.1, 158.3; ^{19}F NMR ($CDCl_3$, 376 MHz): δ 58.2 (1F, s); IR (NaCl, cm^{-1}) 895, 1203, 1266, 1420, 1529, 1578, 1697, 2130, 3054; HRMS (ESI$^+$) *m/z* 489.9823 ([M + Na]$^+$ $C_{13}H_{15}FIN_5NaO_3S^+$ requires 489.9822).

Benzo[*d*][1,3]dioxol-5-yl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9b**)



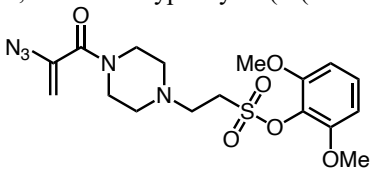
Colorless solid; TLC R_f 0.68 (CH_2Cl_2/MeOH = 15/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.55–2.63 (m, 4H), 3.02 (t, 2H, *J* = 7.4 Hz), 3.45 (t, 2H, *J* = 7.4 Hz), 3.61–3.72 (br, 4H), 5.06 (d, 1H, *J* = 2.1 Hz), 5.11 (d, 1H, *J* = 2.1 Hz), 6.04 (s, 2H), 6.74 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.78–6.83 (m, 2H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 42.0 (br), 47.1 (br), 47.7, 51.5, 52.4 (br), 53.0 (br), 102.2, 104.0, 104.2, 108.2, 114.9, 139.5, 142.9, 146.8, 148.4, 163.3; IR (NaCl, cm^{-1}) 858, 1035, 1160, 1367, 1482, 1644, 2109, 2908; HRMS (ESI$^+$) *m/z* 432.0953 ([M + Na]$^+$ $C_{16}H_{19}N_5NaO_6S^+$ requires 432.0954).

2-Oxo-2*H*-chromen-7-yl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9c**)



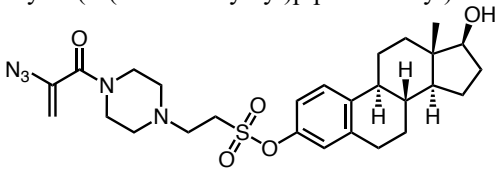
Colorless solid; TLC R_f 0.45 (CH_2Cl_2/MeOH = 15/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.55–2.63 (m, 4H), 3.06 (t, 2H, *J* = 7.2 Hz), 3.54 (t, 2H, *J* = 7.2 Hz), 3.62–3.72 (br, 4H), 5.07 (d, 1H, *J* = 2.1 Hz), 5.12 (d, 1H, *J* = 2.1 Hz), 6.47 (d, 1H, *J* = 9.6 Hz), 7.24–7.31 (m, 2H), 7.57 (d, 1H, *J* = 8.5 Hz), 7.73 (d, 1H, *J* = 9.6 Hz); ^{13}C NMR ($CDCl_3$,101 MHz): δ 41.9 (br), 47.0 (br), 48.8, 51.5, 52.4 (br), 53.2 (br), 104.0, 110.8, 117.0, 117.9, 118.6, 129.2, 139.5, 142.5, 150.7, 154.7, 159.8, 163.3; IR (NaCl, cm^{-1}) 852, 985, 1111, 1170, 1229, 1259, 1367, 1611, 1639, 1732, 2106; HRMS (ESI$^+$) *m/z* 456.0952 ([M + Na]$^+$ $C_{18}H_{19}N_5NaO_6S^+$ requires 456.0954).

2,6-Dimethoxyphenyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9d**)



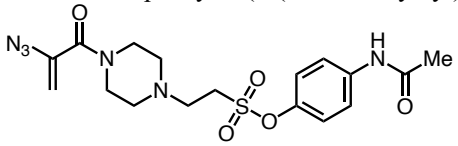
Pale yellow oil; TLC R_f 0.68 (CH_2Cl_2/MeOH = 15/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.55–2.63 (m, 4H), 3.08–3.14 (m, 2H), 3.61–3.71 (m, 6H), 3.90 (s, 6H), 5.06 (d, 1H, J = 2.1 Hz), 5.11 (d, 1H, J = 2.1 Hz), 6.64 (d, 2H, J = 8.5 Hz), 7.20 (dd, 1H, J = 8.5 Hz); ^{13}C NMR ($CDCl_3$,101 MHz): δ 42.0 (br), 47.2 (br), 50.3, 51.8, 52.2 (br), 53.1 (br), 56.3, 103.9, 105.0, 127.5, 128.1, 139.6, 153.3, 163.3; IR (NaCl, cm^{-1}) 868, 1111, 1153, 1263, 1306, 1366, 1483, 1614, 1644, 2107; HRMS (ESI$^+$) *m/z* 448.1265 ([M + Na]$^+$ $C_{17}H_{23}N_5NaO_6S^+$requires 448.1267).

(8*R*,9*S*,13*S*,14*S*)-17-Hydroxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9e**)



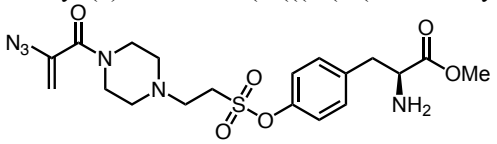
Colorless solid; TLC R_f 0.38 (*n*-hexane/EtOAc = 1/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.80 (s, 3H), 1.19–1.62 (m, 6H), 1.68–1.77 (m, 2H), 1.87–1.99 (m, 2H), 2.10–2.36 (m, 3H), 2.52–2.58 (m, 4H), 2.86–2.93 (m, 2H), 3.04 (t, 2H, J = 7.4 Hz), 3.45 (t, 2H, J = 7.4 Hz), 3.60–3.71 (br, 4H), 3.75 (t, 1H, J = 8.56 Hz), 5.06 (d, 1H, J = 2.0 Hz), 5.11 (d, 1H, J = 2.0 Hz), 6.98–7.06 (m, 2H), 7.31–7.35 (m, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 11.1, 23.1, 26.1, 26.9, 30.0, 30.6, 36.6, 38.4, 41.9 (br), 43.2, 44.1, 47.1 (br), 47.8, 50.0, 51.6, 52.3 (br), 53.1 (br), 81.8, 104.0, 118.8, 121.9, 127.0, 139.1, 139.5, 139.8, 146.7, 163.3; IR (NaCl, cm^{-1}) 920, 1130, 1169, 1244, 1367, 1445, 1490, 1614, 1639, 2107, 2927; HRMS (ESI$^+$) *m/z* 566.2413 ([M + Na]$^+$ $C_{27}H_{37}N_5NaO_5S^+$ requires 566.2413).

4-Acetamidophenyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9f**)



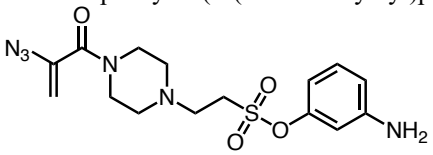
Colorless solid; TLC R_f 0.48 (CH_2Cl_2/MeOH = 15/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.19 (s, 3H), 2.55–2.63 (m, 4H), 3.02 (t, 2H, J = 7.3 Hz), 3.45 (t, 2H, J = 7.3 Hz), 3.60–3.71 (m, 4H), 5.06 (d, 1H, J = 2.2 Hz), 5.11 (d, 1H, J = 2.2 Hz), 7.22 (d, 2H, J = 9.0 Hz), 7.58 (d, 2H, J = 9.0 Hz), 7.78 (br s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 24.5, 41.9 (br), 47.1 (br), 47.8, 51.5, 52.3 (br), 53.1 (br), 104.0, 121.2, 122.6, 137.3, 139.5, 144.7, 163.3, 168.7; IR (NaCl, cm^{-1}) 868, 1150, 1366, 1503, 1614, 1634, 1644, 2107, 2931, 3315; HRMS (ESI$^+$) *m/z* 445.1274 ([M + Na]$^+$ $C_{17}H_{22}N_6NaO_5S^+$ requires 445.1270).

Methyl (*S*)-2-amino-3-(4-(((2-(4-(2-azidoacryloyl)piperazin-1-yl)ethyl)sulfonyl)oxy)phenyl)propanoate (**9g**)



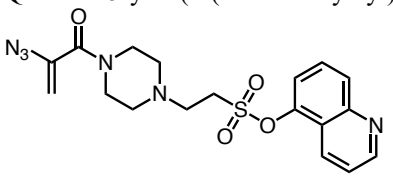
Pale yellow oil; TLC R_f 0.26 (CH_2Cl_2/MeOH = 15/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.55–2.63 (m, 4H), 2.86–2.92 (m, 1H), 3.03 (t, 2H, J = 7.4 Hz), 3.07–3.14 (m, 1H), 3.46 (t, 2H, J = 7.4 Hz), 3.60–3.70 (br, 4H), 3.72–3.78 (m, 4H), 5.06 (d, 1H, J = 2.1 Hz), 5.11 (d, 1H, J = 2.1 Hz), 7.20–7.30 (m, 4H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 40.3, 41.9 (br), 47.0 (br), 48.0, 51.6, 52.2, 52.3 (br), 53.1 (br), 55.7, 104.0, 122.1, 130.9, 136.9, 139.5, 147.8, 163.3, 175.2; IR (NaCl, cm^{-1}) 868, 1147, 1366, 1644, 1732, 2107, 2904; HRMS (ESI$^+$) *m/z* 467.1714 ([M + Na]$^+$ $C_{19}H_{26}N_6NaO_6S^+$ requires 467.1713).

3-Aminophenyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9h**)



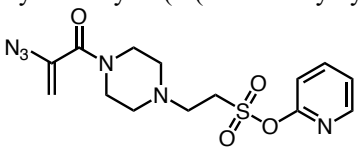
Pale yellow oil; TLC R_f 0.30 (CH_2Cl_2/MeOH = 15/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.55–2.63 (m, 4H), 3.02 (t, 2H, J = 7.4 Hz), 3.44 (t, 2H, J = 7.4 Hz), 3.59–3.73 (br, 4H), 3.84–3.92 (br, 2H), 5.06 (d, 1H, J = 2.1 Hz), 5.11 (d, 1H, J = 2.1 Hz), 6.61–6.65 (m, 3H), 7.14–7.20 (m, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 41.9 (br), 47.1 (br), 47.8, 51.5, 52.3 (br), 53.1 (br), 104.0, 108.3, 111.1, 113.9, 130.5, 139.5, 148.2, 150.1, 163.3; IR (NaCl, cm^{-1}) 811, 1121, 1171, 1360, 1615, 1634, 2106; HRMS (ESI$^+$) *m/z* 403.1164 ([M + Na]$^+$ $C_{15}H_{20}N_6NaO_4S^+$ requires 403.1164).

Quinolin-5-yl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9i**)



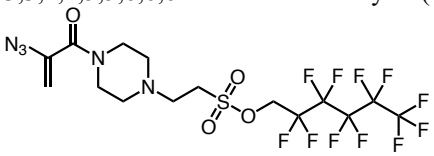
Pale yellow oil; TLC R_f 0.28 (CH_2Cl_2/MeOH = 15/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.55–2.63 (m, 4H), 3.08–3.13 (m, 2H), 3.60–3.71 (m, 6H), 5.06 (d, 1H, J = 2.1 Hz), 5.11 (d, 1H, J = 2.1 Hz), 7.51–7.59 (m, 2H), 7.75 (t, 1H, J = 8.2 Hz), 8.13 (d, 1H, J = 8.6 Hz), 8.49–8.53 (m, 1H), 8.99–9.02 (m, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 41.9 (br), 47.0 (br), 48.9, 51.6, 52.4 (br), 53.1 (br), 104.0, 118.9, 122.0, 123.0, 128.7, 129.1, 130.5, 139.5, 144.1, 149.0, 151.4, 163.3; IR (NaCl, cm^{-1}) 897, 1003, 1171, 1362, 1615, 1644, 2107; HRMS (ESI$^+$) *m/z* 417.1338 ([M + H]$^+$ $C_{18}H_{21}N_6O_4S^+$ requires 417.1340).

Pyridin-2-yl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9j**)



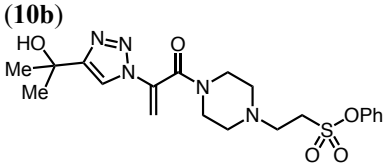
Colorless solid; TLC R_f 0.37 (CH_2Cl_2/MeOH = 15/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.55–2.63 (m, 4H), 3.08–3.13 (m, 2H), 3.58–3.70 (br, 4H), 3.88–3.93 (m, 2H), 5.05 (d, 1H, J = 2.1 Hz), 5.10 (d, 1H, J = 2.1 Hz), 7.14–7.18 (m, 1H), 7.29–7.33 (m, 1H), 7.83–7.89 (m, 1H), 8.35–8.37 (m, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 41.9 (br), 47.1 (br), 50.8, 51.6, 52.2 (br), 53.0 (br), 103.9, 115.9, 122.9, 139.6, 140.6, 148.1, 157.5, 163.3; IR (NaCl, cm^{-1}) 869, 1211, 1372, 1435, 1651, 2104; HRMS (ESI$^+$) *m/z* 389.1010 ([M + Na]$^+$ $C_{14}H_{18}N_6NaO_4S^+$ requires 410.2016).

3,3,4,4,5,5,6,6,6-Undecafluorohexyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9k**)



Pale yellow solid; TLC R_f 0.28 (CH_2Cl_2/MeOH = 10/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.53–2.57 (m, 4H), 2.96 (t, 2H, J = 7.1), 3.46 (t, 2H, J = 7.1), 3.60–3.71 (br, 4H), 4.67–4.71 (m, 2H), 5.07 (d, 1H, J = 2.1 Hz), 5.11 (d, 1H, J = 2.1 Hz); ^{13}C NMR ($CDCl_3$,101 MHz): δ 41.8 (br), 47.0 (br), 49.2, 51.5, 52.3 (br), 53.1 (br), 63.1 (t, J = 27.0 Hz), 104.0, 108.5–118.6 (m), 139.5, 163.3; IR (NaCl, cm^{-1}) 804, 1035, 1171, 1254, 1367, 1446, 1466, 1634, 2109; HRMS (ESI$^+$) *m/z* 594.0643 ([M + Na]$^+$ $C_{15}H_{16}F_{11}N_5NaO_4S^+$ requires 594.0645).

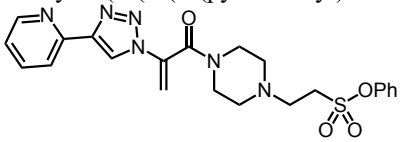
Phenyl 2-(4-(2-(4-(2-hydroxypropan-2-yl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10b**)



Colorless solid; TLC R_f 0.48 (CH_2Cl_2/MeOH = 10/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.66 (s, 6H), 2.45–2.64 (br, 4H), 3.03 (t, 2H, J = 7.3 Hz), 3.46 (t, 2H, J = 7.3 Hz), 3.51–3.82 (m, 4H), 5.36 (d, 1H, J = 1.8 Hz), 5.94 (d, 1H, J = 1.8 Hz), 7.27–7.46 (m, 5H), 7.78 (s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 30.4, 42.0 (br), 47.1 (br), 47.9, 51.5, 52.1 (br), 52.8 (br), 68.6, 108.2, 118.0, 122.0, 127.5, 130.1, 136.6, 149.0, 156.1, 162.6; IR (NaCl, cm^{-1}) 867, 1000,

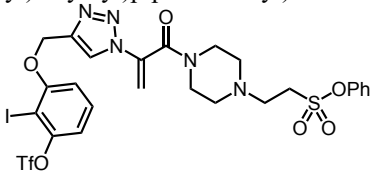
1030, 1144, 1169, 1266, 1369, 1443, 1468, 1488, 1641, 1651; HRMS (ESI^+) *m/z* 472.1633 ($[M + Na]^+$ $C_{20}H_{27}N_5NaO_5S^+$ requires 472.1631).

Phenyl 2-(4-(2-(4-(pyridin-2-yl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10c**)



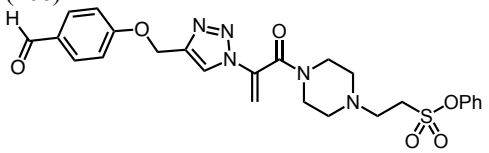
Pale yellow oil; TLC R_f 0.46 (CH_2Cl_2/MeOH = 15/1); ^1H NMR ($CDCl_3$, 400 MHz): δ 2.48–2.67 (br, 4H), 3.04 (t, 2H, *J* = 7.4 Hz), 3.45 (t, 2H, *J* = 7.4 Hz), 3.50–3.58 (br, 2H), 3.77–3.84 (br, 2H), 5.45 (d, 1H, *J* = 2.1 Hz), 6.05 (d, 1H, *J* = 2.1 Hz), 7.26–7.31 (m, 3H), 7.32–7.38 (m, 1H), 7.41–7.46 (m, 2H), 7.83 (ddd, 1H, *J* = 7.8, 7.7, 1.7 Hz), 8.22 (d, 1H, *J* = 7.9 Hz), 8.46 (s, 1H), 8.62 (d, 1H, *J* = 4.4 Hz); ^{13}C NMR ($CDCl_3$,101 MHz): δ 42.0 (br), 47.0 (br), 48.0, 51.5, 52.1 (br), 52.8 (br), 108.5, 120.3, 120.6, 122.0 (two signals overlapped), 123.4, 127.4, 130.1, 136.8, 137.1, 148.7, 149.0, 149.6, 162.3; IR (NaCl, cm^{-1}) 865, 1023, 1144, 1367, 1470, 1602, 1651; HRMS (ESI^+) *m/z* 491.1478 ($[M + Na]^+$ $C_{22}H_{24}N_6NaO_4S^+$ requires 491.1477).

Phenyl 2-(4-(2-(4-((2-iodo-3-(((trifluoromethyl)sulfonyl)oxy)phenoxy)methyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10d**)



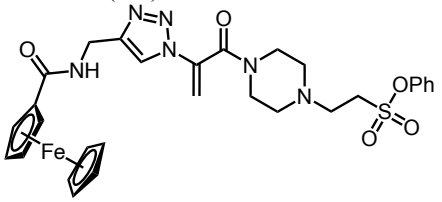
Colorless solid; TLC R_f 0.60 (CH_2Cl_2/MeOH = 15/1); ^1H NMR ($CDCl_3$, 400 MHz): δ 2.45–2.65 (br, 4H), 3.03 (t, 2H, *J* = 7.3 Hz), 3.46 (t, 2H *J* = 7.3 Hz), 3.50–3.60 (br, 2H), 3.73–3.83 (br, 2H), 5.37 (s, 2H), 5.46 (d, 1H, *J* = 2.1 Hz), 6.04 (d, 1H, *J* = 2.1 Hz), 6.99–7.08 (m, 2H), 7.27–7.31 (m, 2H), 7.32–7.38 (m, 1H), 7.39–7.48 (m, 3H), 8.07 (s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 42.1 (br), 47.1 (br), 48.0, 51.5, 52.2 (br), 52.9 (br), 63.7, 83.5, 109.3, 111.9, 115.0, 121.9, 122.0, 127.5, 130.1, 130.6, 136.4, 143.8, 149.0, 151.3, 158.9, 162.4; ^{19}F NMR ($CDCl_3$, 376 MHz): δ –73.2 (1F, s); IR (NaCl, cm^{-1}) 865, 1037, 1141, 1219, 1267, 1367, 1423, 1455, 1488, 1588, 1651; HRMS (ESI^+) *m/z* 794.0038 ($[M + Na]^+$ $C_{25}H_{25}F_3IN_5NaO_8S_2^+$ requires 794.0039).

Phenyl 2-(4-(2-(4-((4-formylphenoxy)methyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10e**)



Colorless oil; TLC R_f 0.49 (CH_2Cl_2/MeOH = 15/1); ^1H NMR ($CDCl_3$, 400 MHz): δ 2.45–2.66 (br, 4H), 3.02 (t, 2H, *J* = 7.4 Hz), 3.45 (t, 2H J = 7.4 Hz), 3.51–3.61 (br, 2H), 3.71–3.82 (br, 2H), 5.34 (s, 2H), 5.44 (d, 1H, *J* = 2.1 Hz), 6.05 (d, 1H, *J* = 2.1 Hz), 7.12–7.17 (m, 2H), 7.28–7.32 (m, 2H), 7.33–7.38 (m, 1H), 7.42–7.47 (m, 2H), 7.86–7.83 (m, 2H), 8.00 (s, 1H), 9.92 (s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 42.0 (br), 47.2 (br), 48.0, 51.5, 52.1 (br), 52.9 (br), 61.9, 109.4, 115.1, 121.9, 122.0, 127.5, 130.1, 130.5 132.1, 136.2, 143.7, 149.0, 162.4, 162.9, 190.8; IR (NaCl, cm^{-1}) 865, 1003, 1144, 1163, 1247, 1367, 1488, 1599, 1651, 1694; HRMS (ESI^+) *m/z* 548.1577 ($[M + Na]^+$ $C_{25}H_{27}N_5NaO_6S^+$requires 548.1580).

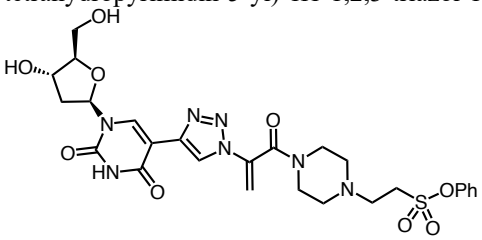
Phenyl 2-(4-(2-(4-((ferrocennylcarbonylamino)methyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10f**)



Pale yellow solid; TLC R_f 0.22 (CH_2Cl_2/MeOH = 15/1); ^1H NMR ($CDCl_3$, 400 MHz): δ 2.42–2.63 (br, 4H), 3.00 (t, 2H *J* = 7.4 Hz), 3.42 (t, 2H, *J* = 7.4 Hz), 3.46–3.53 (br, 2H), 3.72–3.80 (br, 2H), 4.16 (s, 5H), 4.36 (dd, 2H, *J* = 1.9, 1.9 Hz), 4.66 (d, 2H, *J* = 6.0 Hz), 4.70 (dd, 2H, *J* = 1.9, 1.9 Hz), 5.38 (d, 1H, *J* = 2.1 Hz), 5.96 (d, 1H, *J* = 2.1 Hz), 6.58 (dd, 1H, *J* = 5.9, 5.9 Hz), 7.26–7.30 (m, 2H), 7.32–7.38 (m, 1H), 7.41–7.46 (m, 2H), 7.95 (s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 34.8, 42.0 (br), 47.0 (br), 47.9, 51.4, 52.0 (br), 52.7 (br), 68.2, 69.8, 70.7, 75.2,

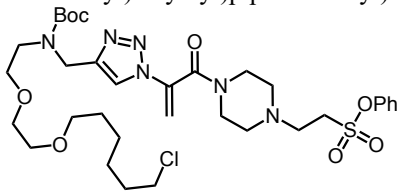
108.3, 121.0, 122.0, 127.4, 130.1, 136.6, 145.6, 149.0, 162.4, 170.7; IR (NaCl, cm^{-1}) 865, 1001, 1144, 1286, 1367, 1435, 1445, 1538, 1651; HRMS (ESI^+) *m/z* 655.1405 ($[M + Na]^+$ $C_{29}H_{32}FeN_6NaO_5S_1^+$requires 655.1402).

Phenyl 2-(4-(2-(4-(1-((2*R*,4*S*,5*R*)-4-hydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10g**)



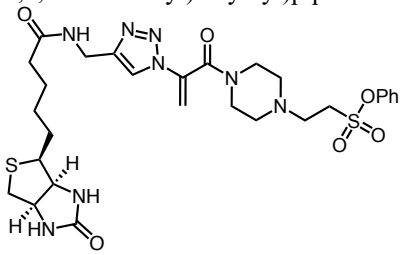
Colorless solid; TLC R_f 0.22 (CH_2Cl_2/MeOH = 10/1); ^1H NMR (CD_3OD, 400 MHz): δ 2.28–2.41 (m, 2H), 2.50–2.70 (m, 4H), 3.03 (t, 2H, *J* = 7.2 Hz), 3.53–3.68 (m, 4H), 3.72–3.89 (m, 4H), 3.97–4.13 (m, 1H), 4.46–4.49 (m, 1H), 5.52 (d, 1H, *J* = 2.5 Hz), 6.08 (d, 1H, *J* = 2.5 Hz), 6.37 (t, 1H, *J* = 6.7 Hz), 7.31–7.50 (m, 5H), 8.63 (s, 1H), 8.78 (s, 1H); ^{13}C NMR (CD_3OD,101 MHz): δ 43.0, 44.5, 50.9, 54.0, 54.4, 55.0, 64.3, 73.8, 88.5, 90.6, 107.5, 110.3, 122.7, 124.7, 129.8, 132.5, 139.5, 140.2, 142.9, 152.2, 152.9, 164.5, 165.8; IR (NaCl, cm^{-1}) 1144, 1622, 1712; HRMS (ESI^+) *m/z* 640.1803 ($[M + Na]^+$ $C_{26}H_{31}N_7NaO_9S^+$requires 640.1802).

Phenyl 2-(4-(2-(4-(((*tert*-butoxycarbonyl)(2-(2-((6-chlorohexyl)oxy)ethoxy)ethyl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10h**)



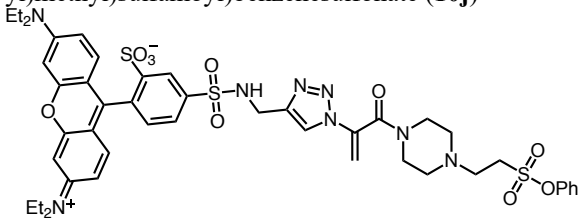
Colorless solid; TLC R_f 0.48 (CH_2Cl_2/MeOH = 15/1); ^1H and ^{13}C NMR analysis show the presence of rotational isomers. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.35–1.52 (m, 13H), 1.58–1.67 (m, 2H), 1.72–1.82 (m, 2H), 2.46–2.65 (m, 4H), 3.03 (t, 2H, *J* = 7.3 Hz), 3.41–3.83 (m, 18H), 4.58–4.63 (br, 2H), 5.33–5.39 (br, 1H), 5.89–5.98 (br, 1H), 7.26–7.48 (m, 5H), 7.78–7.87 (br, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 25.4, 26.7, 28.5, 29.5, 32.6, 41.9, 42.9, 45.1, 47.0, 48.0, 51.5, 52.1, 52.8, 69.7, 70.1, 70.2, 70.4, 71.3, 80.2, 107.8 (br), 121.1 (br), 122.0, 127.4, 130.1, 136.9 (br), 145.9 (br), 146.4, 149.0, 155.6 (br), 162.5 : IR (NaCl, cm^{-1}) 865, 1037, 1144, 1169, 1267, 1366, 1412, 1455, 1651, 1694, 2864, 2936; HRMS (ESI^+) *m/z* 727.3250 ($[M + H]^+$ $C_{33}H_{52}ClN_6O_8S^+$ requires 727.3250).

Phenyl 2-(4-(2-(4-((5-((3a*R*,4*R*,6a*S*)-2-oxohexahydro-1*H*-thieno[3,4-*d*]imidazol-4-yl)pentanamido)methyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10i**)



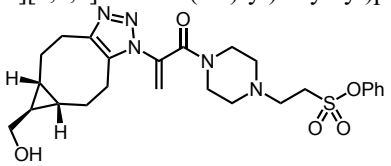
Colorless solid; TLC R_f 0.20 (CH_2Cl_2/MeOH = 10/1); ^1H NMR (CD_3OD, 400 MHz): δ 1.39–1.44 (m, 2H), 1.57–1.75 (m, 4H), 2.27 (t, 2H, *J* = 7.4 Hz), 2.51–2.68 (m, 4H), 2.71 (d, 1H, *J* = 12.7 Hz), 2.92–2.96 (m, 1H), 3.02 (t, 2H, *J* = 7.2 Hz), 3.17–3.23 (m, 1H), 3.52–3.57 (br, 2H), 3.64 (t, 2H, *J* = 7.2 Hz), 3.72–3.80 (br, 2H), 4.28–4.32 (m, 1H), 4.47–4.53 (m, 3H), 5.50 (d, 1H, *J* = 2.5 Hz), 6.04 (d, 1H, *J* = 2.5 Hz), 7.33–7.39 (m, 3H), 7.45–7.51 (m, 2H), 8.23 (s, 1H); ^{13}C NMR (CD_3OD,101 MHz): δ 25.3, 28.0, 28.3, 28.4, 34.0, 35.1, 39.7, 41.7, 51.2, 51.6, 52.2, 53.4, 55.6, 60.2, 61.9, 107.7, 121.0, 121.9, 127.0, 129.7, 136.7, 149.4, 162.9, 164.7, 174.7; HRMS (ESI^+) *m/z* 669.2243 ($[M + Na]^+$ $C_{28}H_{38}N_8NaO_6S_2^+$requires 669.2253).

2-(6-(Diethylamino)-3-(diethyliminio)-3*H*-xanthen-9-yl)-5-(*N*-((1-(3-oxo-3-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)prop-1-en-2-yl)-1*H*-1,2,3-triazol-4-yl)methyl)sulfamoyl)benzenesulfonate (**10j**)



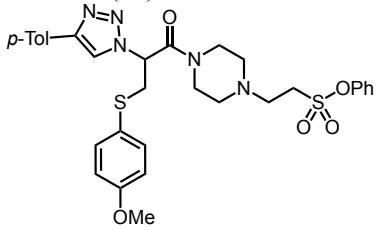
red solid; TLC R_f 0.48 (CH_2Cl_2/MeOH = 10/1); ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.21 (t, 12H, J = 7.0 Hz), 2.36–2.44 (br, 2H), 2.48–2.54 (m, 2H), 2.86–2.91 (m, 2H), 3.52–3.77 (m, 12H), 4.25 (d, 2H, J = 6.0 Hz), 5.44 (d, 2H, J = 2.4 Hz), 6.06 (d, 2H, J = 2.4 Hz), 6.92–7.09 (m, 5H), 7.33–7.41 (m, 3H), 7.42–7.53 (m, 3H), 7.89–8.00 (m, 1H), 8.47–8.49(m, 2H), 8.59 (t, 2H, J = 6.0 Hz); ^{13}C NMR (DMSO-$d_6$101 MHz): δ 12.9, 38.4, 41.8 (br), 45.7, 46.9 (br), 47.8, 51.4, 51.9 (br), 52.4 (br), 95.8, 108.5, 113.9, 114.1, 122.1, 122.7, 126.3, 127.2, 127.8, 130.6, 131.1, 133.2, 133.6, 136.5, 141.8, 144.5, 148.4, 149.3, 155.5, 157.6, 157.9, 162.2; HRMS (ESI$^+$) *m/z* 961.3042 ([M + H]$^+$ $C_{45}H_{53}N_8O_{10}S_3^+$ requires 961.3041).

Phenyl 2-(4-(2-((5a*R*,6*R*,6a*S*)-6-(hydroxymethyl)-5,5a,6,6a,7,8-hexahydrocyclopropa[5,6]cycloocta[1,2-*d*][1,2,3]triazol-1(4H)-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10k**)



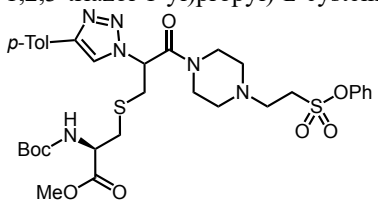
Colorless solid; TLC R_f 0.38 (CH_2Cl_2/MeOH = 15/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.71–0.91 (m, 3H), 1.32–1.42 (m, 2H), 2.37–2.58 (m, 6H), 2.61–2.71 (m, 1H), 2.83–2.97 (m, 4H), 3.08–3.18 (m, 1H), 3.41–3.58 (m, 6H), 3.61–3.79 (br, 2H), 5.81 (d, 1H, J = 1.2 Hz), 5.84 (d, 1H, J = 1.2 Hz), 7.23–7.58 (m, 5H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 22.1, 22.3, 22.9, 25.6, 26.9, 27.5, 27.9, 42.2 (br), 46.5 (br), 47.9, 51.5, 52.2 (br), 52.8 (br), 66.3, 119.1, 122.0, 127.5, 130.1, 135.0, 137.3, 145.5, 149.0, 163.5; IR (NaCl, cm^{-1}) 865, 1027, 1144, 1367, 1442, 1634, 2926, 3401; HRMS (ESI$^+$) *m/z* 538.2100 ([M + Na]$^+$ $C_{25}H_{33}N_5NaO_5S^+$ requires 538.2100).

Phenyl 2-(4-(3-((4-methoxyphenyl)thio)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**5b**)



Colorless solid; TLC R_f 0.48 (CH_2Cl_2/MeOH = 20/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.10–2.18 (m, 1H), 2.31–2.37 (m, 1H), 2.40 (s, 3H), 2.49– 2.60 (m, 2H), 2.92–2.97 (m, 2H), 3.37–3.44 (m, 3H), 3.45–3.54 (m, 2H), 3.55–3.63 (m, 2H), 3.74 (s, 3H), 3.76–3.83 (m, 1H), 5.77 (dd, 1H, J = 7.3, 7.3 Hz), 6.82–6.87 (m, 2H), 7.23–7.29 (m, 4H), 7.31–7.46 (m, 5H), 7.69 (d, 2H J = 8.1 Hz), 7.90 (s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 21.4, 39.0, 42.4, 45.7, 47.9, 51.4, 52.2, 52.8, 55.3, 58.3, 115.0, 117.9, 122.0, 123.5, 125.6, 127.3, 127.5, 129.5, 130.1, 134.7, 138.2, 148.3, 149.0, 159.8, 165.1; IR (NaCl, cm^{-1}) 865, 1144, 1246, 1367, 1493, 1651, 1656, 2835, 2927, 2939; HRMS (ESI$^+$) *m/z* 622.2151 ([M + H]$^+$ $C_{31}H_{36}N_5O_5S_2^+$ requires 622.2152).

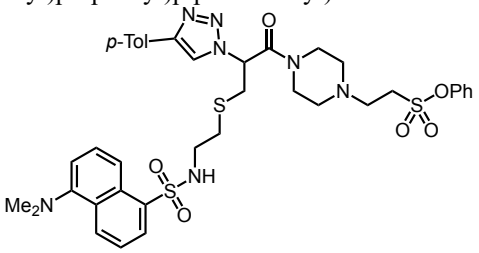
Methyl *N*-(*tert*-butoxycarbonyl)-*S*-(3-oxo-3-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propyl)-L-cysteinate (**5c**)



Colorless oil; TLC R_f 0.32 (CH_2Cl_2/MeOH = 15/1); ^{1}H and ^{13}C NMR analysis show the presence of diastereomers and rotational isomers. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.45 (s, 9H), 2.12–2.22 (m, 1H), 2.33–2.43 (m, 4H), 2.54–

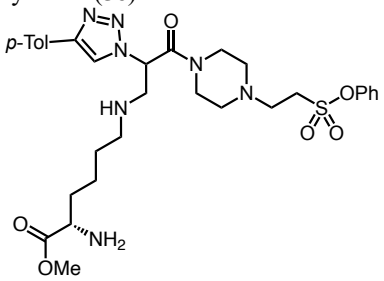
2.64 (m, 2H), 2.90–3.18 (m, 4H), 3.38–3.47 (m, 3H), 3,49–3.85 (m, 7H), 4.51–4.60 (m, 1H), 5.32–5.43 (m, 1H), 5.86–5.97 (m, 1H), 7.24–7.45 (m, 7H), 7.71–7.79 (m, 2H), 7.96 (s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 21.3, 28.29, 28.32, 35.3, 35.5, 42.6, 45.9, 47.9, 51.4, 52.2, 52.8, 52.9, 53.3, 58.7 (br), 80.4, 117.6, 122.0, 125.6, 127.3, 127.4, 129.6, 130.1, 138.4, 148.5, 149.0, 164.9 (br), 171.2; IR (NaCl, cm^{-1}) 865, 1040, 1144, 1167, 1193, 1241, 1264, 1366, 1455, 1651, 1665, 2926; HRMS (ESI^+) *m/z* 739.2556 ($[M + Na]^+$ $C_{33}H_{44}N_6NaO_8S_2^+$ requires 739.2560).

Phenyl 2-(4-(3-((2-((5-(dimethylamino)naphthalene)-1-sulfonamido)ethyl)thio)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**5d**)



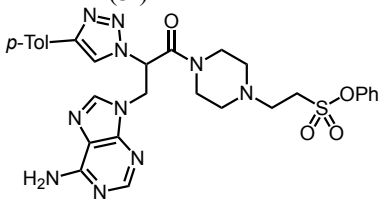
Pale yellow oil; TLC R_f 0.42 (CH_2Cl_2/MeOH = 15/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.19–2.25 (m, 1H), 2.37–2.44 (m, 4H), 2.52–2.63 (m, 3H), 2.71–2.80 (m, 1H), 2.88 (s, 6H), 2.92–3.05 (m, 4H), 3.12–3.26 (m, 2H), 3.40 (t, 2H *J* = 7.4 Hz), 3.56–3.77 (m, 4H), 5.93–6.04 (m, 2H), 7.20 (d, 1H, *J* = 7.5 Hz), 7.26 (d, 1H, *J* = 7.5 Hz), 7.26–7.34 (m, 1H), 7.38–7.43 (m, 2H), 7.38–7.45 (m, 2H), 7.74 (d, 2H *J* = 8.1 Hz), 7.95 (s, 1H), 8.24–8.28 (m, 2H), 8.35 (d, 2H *J* = 8.5 Hz), 8.55 (d, 2H *J* = 8.5 Hz); ^{13}C NMR ($CDCl_3$,101 MHz): δ 21.3, 33.6, 34.9, 42.6, 42.8, 45.4, 45.9, 47.9, 51.4, 52.3, 52.7, 58.8, 115.3, 117.8, 118.7, 122.0, 123.2, 125.6, 127.2, 127.4, 128.7, 129.5, 129.56, 129.61, 129.9, 130.1, 130.7, 134.5, 138.4, 148.5, 149.0, 152.0, 165.0; IR (NaCl, cm^{-1}) 867, 1144, 1163, 1266, 1369, 1654; HRMS (ESI^+) *m/z* 814.2493 ($[M + Na]^+$ $C_{38}H_{45}N_7NaO_6S_3^+$ requires 814.2491).

Methyl *N*-(3-oxo-3-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propyl)-L-lysinate (**5e**)



Pale yellow oil; TLC R_f 0.48 (CH_2Cl_2/MeOH = 10/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.35–1.56 (m, 5H), 1.68–1.77 (m, 1H), 2.12–2.18 (m, 1H), 2.32–2.42 (m, 4H), 2.53–2.72 (m, 4H), 2.91–2.98 (m, 2H), 3.13–3.20 (m, 1H), 3.36–3.85 (m, 11H), 5.85 (dd, 1H, *J* = 6.8, 6.8 Hz), 7.23–7.28 (m, 4H), 7.31–7.36 (m, 1H), 7.39–7.45 (m, 2H), 7.74 (d, 2H, *J* = 8.1 Hz), 8.01 (s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 21.3, 23.2, 29.7, 34.6, 42.3, 45.7, 47.9, 49.4, 51.4, 51.7, 52.0, 52.3, 52.8, 54.3, 59.1, 118.2, 122.0, 125.6, 127.40, 127.42, 129.6, 130.1, 138.3, 148.3, 149.0, 165.4, 176.5; IR (NaCl, cm^{-1}) 865, 1144, 1367, 1456, 1488, 1651, 1732, 2930; HRMS (ESI^+) *m/z* 642.3067 ([M + H]$^+$ $C_{31}H_{44}N_7O_6S^+$ requires 642.3068).

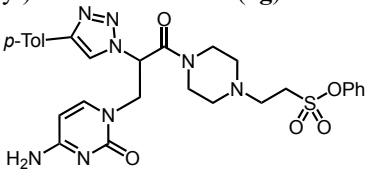
Phenyl 2-(4-(3-(6-amino-9*H*-purin-9-yl)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**5f**)



Colorless solid; TLC R_f 0.32 (CH_2Cl_2/MeOH = 15/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.08–2.15 (m, 1H), 2.20–2.28 (m, 1H), 2.37–2.45 (m, 5H), 2.87–2.94 (m, 2H), 3.34–3.39 (m, 2H), 3,48–3.64 (m, 3H), 3.65–3.74 (m, 1H), 4.81 (dd, 1H *J* = 6.9, 6.9 Hz), 5.00 (dd, 1H, *J* = 7.7, 7.7 Hz), 5.78–5.84 (br, 2H), 6.39–6.45 (m, 1H), 7.23–7.28 (m, 4H), 7.30–7.36 (m, 1H), 7.38–7.45 (m, 2H), 7.57 (s, 1H), 7.72 (d, 2H *J* = 8.1 Hz), 8.05 (s, 1H), 8.39 (s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 21.4, 42.5, 45.7, 45.9, 47.7, 51.3, 52.1, 52.4, 57.5, 117.7, 119.5, 122.0, 125.7,

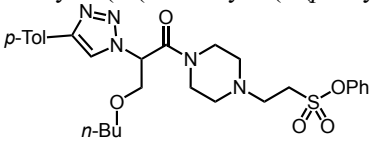
126.9, 127.5, 130.0, 130.1, 138.7, 140.7, 148.9, 149.0, 150.1, 153.4, 155.5, 163.6; IR (NaCl, cm^{-1}) 865, 1144, 1366, 1470, 1595, 1651, 1656; 6; HRMS (ESI^+) *m/z* 639.2221 ($[M + Na]^+$ $C_{29}H_{32}N_{10}NaO_4S^+$ requires 639.2226).

Phenyl 2-(4-(3-(6-amino-2-oxopyrazin-1(2*H*)-yl)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**5g**)



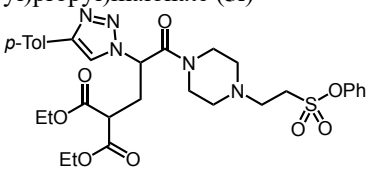
Colorless solid; TLC R_f 0.31 (CH_2Cl_2/MeOH = 15/1); ^1H NMR ($CDCl_3$, 400 MHz): δ 2.25–2.52 (m, 7H), 2.94 (t, 2H, *J* = 7.0 Hz), 3.41 (t, 2H, *J* = 7.3 Hz), 3.53–3.79 (m, 4H), 4.14–4.23 (m, 1H), 4.54 (dd, 1H, *J* = 13.7, 5.5 Hz), 5.57 (d, 1H, *J* = 7.2 Hz), 6.31 (dd, 1H, *J* = 8.4, 5.5 Hz), 6.99 (d, 1H *J* = 7.3 Hz), 7.21–7.34 (m, 5H), 7.38–7.43 (m, 2H), 7.71 (d, 2H, *J* = 8.1 Hz), 8.17 (s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 21.3, 42.4, 45.6, 47.8, 51.3, 52.2, 52.5, 52.8, 57.3, 94.7, 119.1, 122.0, 125.6, 127.1, 127.4, 129.6, 130.0, 138.4, 146.0, 148.3, 148.9, 156.6, 164.0, 166.3; IR (NaCl, cm^{-1}) 865, 1144, 1279, 1367, 1488, 1651, 1666; HRMS (ESI^+) *m/z* 615.2115 ($[M + Na]^+$ $C_{28}H_{32}N_8NaO_5S^+$ requires 615.2114).

Phenyl 2-(4-(3-butoxy-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**5h**)



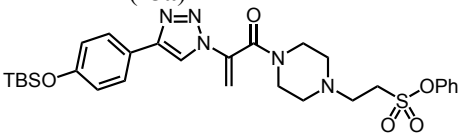
Colorless solid; TLC R_f 0.43 (CH_2Cl_2/MeOH = 15/1); ^1H NMR ($CDCl_3$, 400 MHz): δ 0.89 (t, 3H, *J* = 7.4 Hz), 1.25–1.34 (m, 2H), 1.47–1.55 (m, 2H), 2.29–2.36 (m, 1H), 2.37–2.46 (m, 4H), 2.53–2.61 (m, 2H), 2.95–3.11 (m, 2H), 3.40–3.54 (m, 4H), 3.57–3.80 (m, 4H), 3.94 (dd, 1H, *J* = 9.7, 6.9 Hz), 4.08 (dd, 1H, *J* = 9.7, 6.9 Hz), 5.95 (dd, 1H, *J* = 6.9, 6.9 Hz), 7.23–7.30 (m, 4H), 7.32–7.37 (m, 1H), 7.41–7.46 (m, 2H), 7.73–7.76 (m, 2H), 8.09 (s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 13.9, 19.2, 21.3, 31.4, 42.3, 45.9, 47.9, 51.4, 52.3, 52.8, 58.5, 70.7, 71.7, 118.7, 122.0, 125.6, 127.5, 127.6, 130.0, 130.1, 138.2, 148.1, 149.0, 165.0; IR (NaCl, cm^{-1}) 867, 1127, 1144, 1169, 1266, 1370, 1488, 1655; HRMS (ESI^+) *m/z* 578.2411 ($[M + Na]^+$ $C_{28}H_{37}N_5NaO_5S^+$ requires 578.2413).

Diethyl 2-(3-oxo-3-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propyl)malonate (**5i**)



Colorless solid; TLC R_f 0.61 (CH_2Cl_2/MeOH = 15/1); ^1H NMR ($CDCl_3$, 400 MHz): δ 1.25 (t, 3H, *J* = 7.1 Hz), 1.30 (t, 3H, *J* = 7.1 Hz), 2.34–2.48 (m, 5H), 2.52–2.65 (m, 3H), 2.68–2.78 (m, 1H), 2.99 (t, 2H, *J* = 7.3 Hz), 3.09 (dd, 1H, *J* = 9.7, 5.0 Hz), 3.39–3.47 (m, 2H), 3.58–3.67 (m, 1H), 3.68–3.76 (m, 3H), 4.12–4.29 (m, 4H), 5.95 (dd, 1H, *J* = 10.3, 5.5 Hz), 7.24–7.30 (m, 4H), 7.33–7.37 (m, 1H), 7.41–7.46 (m, 2H), 7.73–7.76 (m, 2H), 8.12 (s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 13.99, 14.01, 21.3, 32.1, 42.4, 45.7, 47.6, 47.9, 51.4, 52.3, 52.8, 57.3, 62.09, 62.15, 118.3, 122.0, 125.6, 127.4, 129.6, 130.1 (two signals overlapped), 138.3, 148.6, 149.0, 165.5, 168.3, 168.4; IR (NaCl, cm^{-1}) 867, 1146, 1266, 1658, 1730, 1744, 2986, 3055; HRMS (ESI^+) *m/z* 664.2418 ($[M + Na]^+$ $C_{31}H_{39}N_5NaO_8S^+$requires 664.2417).

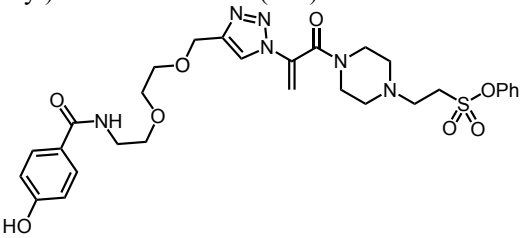
Phenyl 2-(4-(2-(4-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**13a**)



Colorless oil; TLC R_f 0.52 (CH_2Cl_2/MeOH = 15/1); ^1H NMR ($CDCl_3$, 400 MHz): δ 0.23 (s, 6H), 1.01 (s, 9H), 2.44–2.64 (br, 4H), 3.01 (t, 2H, *J* = 7.3 Hz), 3.44 (t, 2H, *J* = 7.3 Hz), 3.48–3.55 (br, 2H), 3.74–3.82 (br, 2H), 5.38 (d, 1H, *J* = 2.0 Hz), 5.99 (d, 1H, *J* = 2.0 Hz), 6.91 (d, 2H, *J* = 8.6 Hz), 7.25–7.44 (m, 5H), 7.73 (d, 2H, *J* = 8.6 Hz), 8.02 (s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ –4.4, 18.3, 25.7, 41.9 (br), 47.0 (br), 47.9, 51.5, 52.1 (br), 52.8 (br), 108.1, 117.1, 120.6, 122.0, 123.0, 127.2, 127.5, 130.1, 136.7, 148.1, 149.0, 156.2, 162.6; IR (NaCl, cm^{-1})

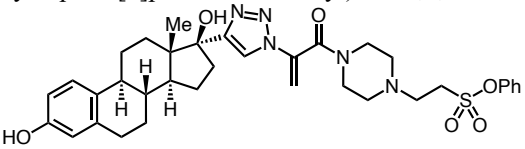
864, 911, 1023, 1146, 1269, 1367, 1495, 1562, 1651, 2858, 2931; HRMS (ESI$^+$) *m/z* 620.2337 ([M + Na]$^+$ $C_{29}H_{39}N_5NaO_5SSi^+$ requires 620.2339).

Phenyl 2-(4-(2-(4-((2-(2-(4-hydroxybenzamido)ethoxy)ethoxy)methyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**13b**)



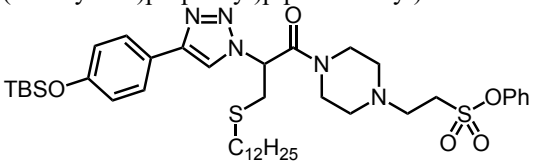
Colorless oil; TLC R_f 0.36 (CH_2Cl_2/MeOH = 10/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.49–2.63 (m, 4H), 3.02 (t, 2H, *J* = 7.3 Hz), 3.46 (t, 2H, *J* = 7.3 Hz), 3.50–3.56 (m, 2H), 3.60–3.82 (m, 10H), 4.70 (s, 2H), 5.33 (d, 1H, *J* = 2.4 Hz), 5.78 (d, 1H, *J* = 2.4 Hz), 6.69 (d, 2H, *J* = 8.5 Hz), 6.84–6.89 (m, 1H), 7.26–7.31 (m, 2H), 7.32–7.36 (m, 1H), 7.40–7.46 (m, 2H), 7.54–7.58 (m, 2H), 7.84 (s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 39.5, 42.1 (br), 47.2 (br), 47.9, 51.4, 52.0 (br), 52.7 (br), 64.4, 69.5, 70.1, 70.2, 107.8, 115.3, 120.9, 122.0, 125.5, 127.5 (two signals overlapped), 128.9, 130.1, 136.3, 149.0, 160.0, 162.7, 167.5; IR (NaCl, cm^{-1}) 867, 1104, 1144, 1171, 1233, 1267, 1367, 1445, 1488, 1505, 1632; HRMS (ESI$^+$) *m/z* 651.2216 ([M + Na]$^+$ $C_{29}H_{36}N_6NaO_8S^+$ requires 651.2213).

Phenyl 2-(4-(2-(4-((8*S*,9*R*,13*R*,14*R*,17*S*)-3,17-dihydroxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-17-yl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**13c**)



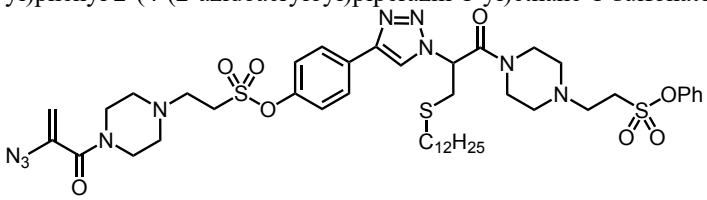
Colorless solid; TLC R_f 0.42 (CH_2Cl_2/MeOH = 10/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.63 (ddd, 1H, *J* = 12.7, 12.7, 4.0 Hz), 1.02 (s, 3H), 1.21–1.56 (m, 4H), 1.68–1.85 (m, 3H), 1.87–2.09 (m, 3H), 2.23–2.41 (m, 2H), 2.56 (m, 4H), 2.86–2.93 (m, 2H), 3.02 (t, 2H, *J* = 7.4 Hz), 3.45 (t, 2H, *J* = 7.4 Hz), 3.60–3.71 (br, 4H), 5.37 (d, 1H, *J* = 2.2 Hz), 5.93 (d, 1H, *J* = 2.2 Hz), 6.32 (br s, 1H), 6.48 (d, 1H, *J* = 2.5 Hz), 6.55 (dd, 1H, *J* = 8.4, 2.5 Hz), 6.96 (d, 1H, *J* = 8.4 Hz), 7.23–7.31 (m, 2H), 7.31–7.37 (m, 1H), 7.41–7.46 (m, 2H), 7,80 (s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 14.2, 23.5, 26.1, 27.3, 29.6, 32.9, 38.1, 39.3, 42.1 (br), 43.0, 47.2 (br), 47.4, 48.0, 48.4, 51.5, 52.1 (br), 52.8 (br), 82.6, 107.9, 112.7, 115.2, 119.9, 122.0, 126.3, 127.5, 130.1, 132.1, 136.6, 138.0, 149.0, 153.8, 154.3, 162.8; IR (NaCl, cm^{-1}) 867, 1023, 1144, 1231, 1286, 1360, 1446, 1455, 1634, 2931; HRMS (ESI$^+$) *m/z* 684.2835 ([M + Na]$^+$ $C_{35}H_{43}N_5NaO_6S^+$ requires 684.2832).

Phenyl 2-(4-(2-(4-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-1*H*-1,2,3-triazol-1-yl)-3-(dodecylthio)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**S3**)



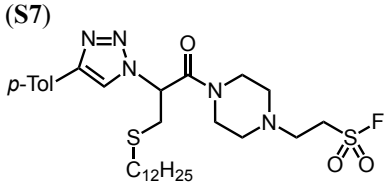
Colorless solid; TLC R_f 0.54 (CH_2Cl_2/MeOH = 15/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.23 (s, 6H), 0.91 (t, 3H, *J* = 6.9 Hz), 1.01 (s, 9H), 1.24–1.38 (m, 18H), 1.52–1.61 (m, 2H), 2.20–2.28 (m, 1H), 2.37–2.44 (m, 1H), 2.47–2.65 (m, 4H), 2.92–3.01 (m, 2H), 3.06 (dd, 1H, *J* = 13.6, 6.2 Hz), 3.37–3.44 (m, 3H), 3.55–3.84 (m, 4H), 5.86 (dd, 1H, *J* = 8.6, 6.2 Hz), 6.87–6.93 (AA'BB', 2H), 7.26–7.46 (m, 5H), 7.69–7.75 (AA'BB', 2H), 7.96 (s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ –4.4, 14.2, 18.3, 22.7, 25.7, 28.8, 29.2, 29.4, 29.5, 29.60 (two signals overlapped), 29.65, 29.67, 31.9, 33.0, 34.7, 42.5, 45.9, 48.0, 51.4, 52.3, 52.9, 58.8, 117.4, 120.6, 122.0, 123.5, 127.0, 127.4, 130.1, 148.3, 149.0, 156.0, 165.3; IR (NaCl, cm^{-1}) 864, 912, 1146, 1264, 1367, 1469, 1493, 1651, 2856, 2927, 2953; HRMS (ESI$^+$) *m/z* 822.4091 ([M + Na]$^+$ $C_{41}H_{65}N_5NaO_5S_2Si^+$ requires 822.4094).

4-(1-(3-(Dodecylthio)-1-oxo-1-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)propan-2-yl)-1*H*-1,2,3-triazol-4-yl)phenyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**14**)



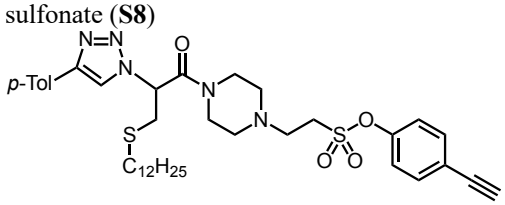
Pale yellow oil; TLC R_f 0.48 (CH_2Cl_2/MeOH = 10/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.88 (t, 3H, J = 6.8 Hz), 1.22–1.37 (m, 18H), 1.52–1.60 (m, 2H), 2.26–2.34 (m, 1H), 2.37–2.44 (m, 1H), 2.47–2.65 (m, 8H), 2.93–3.11 (m, 5H), 3.33–3.48 (m, 5H), 3.56–3.79 (m, 8H), 5.04 (d, 1H, J = 2.1 Hz), 5.09 (d, 1H, J = 2.1 Hz), 5.89 (dd, 1H, J = 8.4, 6.4 Hz), 7.23–7.29 (m, 2H), 7.31–7.44 (m, 3H), 7.46–7.54 (m, 2H), 7.68–7.72 (m, 2H), 8.12 (s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 14.2, 22.7, 28.8, 29.2, 29.4, 29.5, 29.57, 29.59, 29.63, 29.64, 31.9, 33.0, 34.8, 41.9 (br), 42.5, 46.0, 47.1 (br), 48.0, 51.4, 51.5, 52.2, 52.3 (br), 52.7 (br), 52.8, 53.5, 58.7, 104.0, 118.8, 122.0, 122.5, 127.3, 127.4, 129.7, 130.1, 139.5, 146.8, 148.7, 148.9, 163.3, 165.2; IR (NaCl, cm^{-1}) 867, 1041, 1148, 1370, 1465, 1498, 1651, 2854, 2926, 3289; HRMS (ESI$^+$) *m/z* 979.3964 ([M + Na]$^+$ $C_{44}H_{64}N_{10}NaO_8S_3^+$ requires 979.3968); ; HPLC analysis: R*t* = 35.2 min [column: Shiseido CAPCELL PAK MG II (4.6 mm i.d. × 250 mm); mobile phase: MeOH:H_2O = 40:60 (0─5 min), linear gradient from 40:60 to 99:1 (5─30 min), 99:1 (30─50 min); flow rate: 1.00 mL/min; detection: UV at 254 nm].

2-(4-(3-(Dodecylthio)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonyl fluoride (**S7**)



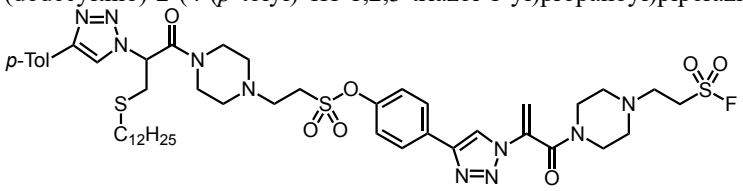
Colorless oil; TLC R_f 0.48 (CH_2Cl_2/MeOH = 20/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.90 (t, 3H, J = 6.9 Hz), 1.21–1.39 (m, 18H), 1.52–1.62 (m, 2H), 2.19–2.26 (m, 1H), 2.38–2.44 (m, 4H), 2.47–2.58 (m, 2H), 2.59–2.68 (m, 2H), 2.93 (t, 2H, J = 6.8 Hz), 3.07 (dd, 1H, J = 13.6, 6.0 Hz), 3.43 (dd, 1H, J = 13.6, 8.7 Hz), 3.52–5.60 (m, 3H), 3.65–3.73 (m, 1H), 3.75–3.91 (m, 2H), 5.87 (dd, 1H, J = 8.7, 6.0 Hz), 7.26 (d, 2H, J = 7.9 Hz), 7.74 (d, 2H, J = 8.1 Hz), 8.02 (s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 14.2, 21.3, 22.7, 28.8, 29.2, 29.4, 29.5, 29.6, 29.66, 29.67, 31.9, 33.0, 34.6, 42.5, 45.9, 48.8 (d, J = 17.9 Hz), 51.0, 52.1, 52.6, 58.8, 117.8, 125.6, 127.3, 129.6, 121.6, 138.3, 148.4, 165.3; ^{19}F NMR ($CDCl_3$, 376 MHz): δ 59.0 (1F, s); IR (NaCl, cm^{-1}) 1199, 1409, 1463, 1651, 1656, 2853, 2924; HRMS (ESI$^+$) *m/z* 610.3254 ([M + H]$^+$ $C_{30}H_{49}FN_5O_3S_2^+$ requires 610.3255).

4-Ethynylphenyl 2-(4-(3-(dodecylthio)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**S8**)



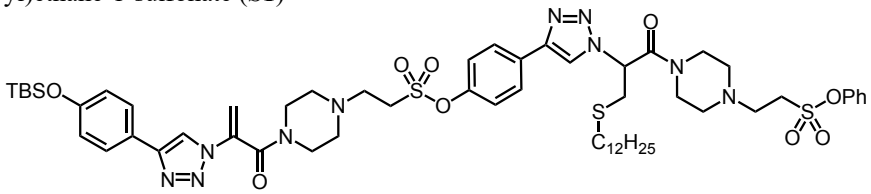
Pale yellow oil; TLC R_f 0.67 (CH_2Cl_2/MeOH = 20/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.89 (t, 3H, J = 6.8 Hz), 1.21–1.38 (m, 18H), 1.52–1.60 (m, 2H), 2.18–2.25 (m, 1H), 2.34–2.42 (m, 4H), 2.45–2.65 (m, 4H), 2.93–2.97 (m, 2H), 3.07 (dd, 1H, J = 13.5, 6.2 Hz), 3.14 (s, 1H), 3.52–3.44 (m, 4H), 3.63–3.84 (m, 3H), 5.87 (dd, 1H, J = 8.6, 6.2 Hz), 7.20–7.27 (m, 4H), 7.53 (d, 2H, J = 8.6 Hz), 7.74 (d, 2H, J = 8.1 Hz), 8.03 (s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 14.2, 21.3, 22.7, 28.8, 29.2, 29.4, 29.5, 29.60, 29.65 (two signals overlapped), 29.67, 31.9, 33.0, 34.7, 42.5, 45.9, 48.2, 51.4, 52.2, 52.8, 58.9, 78.6, 82.1, 117.8, 121.6, 122.1, 125.6, 127.4, 129.6, 133.9, 138.3, 148.4, 148.8, 165.3; HRMS (ESI$^+$) *m/z* 708.3610 ([M + H]$^+$ $C_{38}H_{54}N_5O_4S_2^+$ requires 708.3612).

4-(1-(3-(4-(2-(Fluorosulfonyl)ethyl)piperazin-1-yl)-3-oxoprop-1-en-2-yl)-1*H*-1,2,3-triazol-4-yl)phenyl 2-(4-(3-(dodecylthio)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**15**)



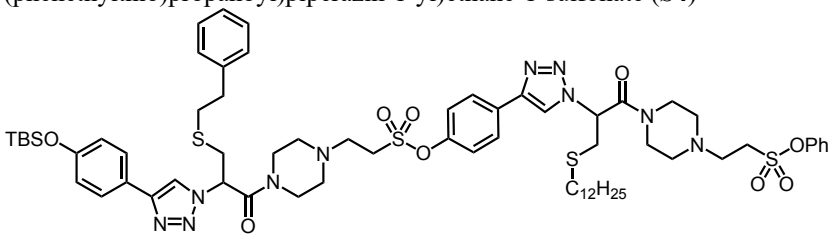
Colorless oil; TLC R_f 0.56 (CH_2Cl_2/MeOH = 20/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.89 (t, 3H, *J* = 6.8 Hz), 1.20–1.38 (m, 18H), 1.51–1.60 (m, 2H), 2.19–2.26 (m, 1H), 2.35–2.43 (m, 4H), 2.47–2.65 (m, 8H), 2.92–3.02 (m, 4H), 3.07 (dd, 1H, *J* = 11.9, 6.2 Hz), 3.37–3.47 (m, 3H), 3.54–3.84 (m, 10H), 5.43 (d, 1H, *J* = 2.0 Hz), 5.86 (dd, 1H, *J* = 8.4, 6.2 Hz), 6.06 (d, 1H, *J* = 2.0 Hz), 7.25 (d, 2H, *J* = 8.0 Hz), 7.34 (d, 2H, *J* = 8.7 Hz), 7.73 (d, 2H *J* = 8.0 Hz), 7.90 (d, 2H, *J* = 8.7 Hz), 8.02 (s, 1H), 8.14 (s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 14.2, 21.3, 22.7, 28.8, 29.2, 29.4, 29.5, 29.60, 29.65, 29.66, 31.9, 33.0, 34.7, 42.0, 42.5, 45.9, 47.2, 48.2, 48.9 (d, *J* = 10.2 Hz), 51.0, 51.4, 52.0, 52.3, 52.7, 52.8, 58.9, 108.9, 117.9, 118.5, 122.6, 125.6, 127.4, 127.5, 129.1, 129.6, 136.3, 138.3, 146.7, 148.4, 148.8, 162.5, 165.2; ^{19}F NMR ($CDCl_3$, 376 MHz): δ 59.2 (1F, s); HRMS (ESI$^+$) *m/z* 999.4416 ([M + H]$^+$ $C_{47}H_{68}FN_{10}O_7S_3^+$ requires 999.4413); HPLC analysis: R*t* = 35.3 min [column: Shiseido CAPCELL PAK MG II (4.6 mm i.d. × 250 mm); mobile phase: MeOH:H_2O = 40:60 (0─5 min), linear gradient from 40:60 to 99:1 (5─30 min), 99:1 (30─50 min); flow rate: 1.00 mL/min; detection: UV at 254 nm].

4-(1-(3-(Dodecylthio)-1-oxo-1-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)propan-2-yl)-*1H*-1,2,3-triazol-4-yl)phenyl 2-(4-(2-(4-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**S1**)



Pale yellow oil; TLC R_f 0.43 (CH_2Cl_2/MeOH = 15/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.23 (s, 6H), 0.89 (t, 3H, *J* = 6.8 Hz), 1.00 (s, 9H), 1.20–1.37 (m, 18H), 1.51–1.61 (m, 2H), 2.26–2.33 (m, 1H), 2.37–2.44 (m, 1H), 2.47–2.65 (m, 8H), 2.94–3.11 (m, 5H), 3.34–3.49 (m, 5H), 3.51–3.82 (m, 8H), 5.39 (d, 1H, *J* = 1.9 Hz), 5.86–5.92 (m, 1H), 6.00 (d, 1H, *J* = 1.9 Hz), 6.92 (d, 2H, *J* = 8.5 Hz), 7.24–7.29 (m, 2H), 7.30–7.37 (m, 3H), 7.38–7.44 (m, 2H), 7.73 (d, 2H, *J* = 8.5 Hz), 7.89 (d, 2H, *J* = 8.6 Hz), 8.00 (s, 1H), 8.11 (s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ –4.4, 14.2, 18.3, 22.7, 25.7, 28.8, 29.2, 29.4, 29.57, 29.60, 29.65, 31.9, 33.0, 34.8, 42.5, 46.0, 47.9, 48.1, 51.4, 51.5, 52.2, 52.8, 58.7, 108.2, 117.1, 118.7, 120.6, 122.0, 122.5, 130.0, 130.1, 136.7, 146.9, 148.1, 148.7, 149.0, 156.2, 162.6, 165.2; HRMS (ESI$^+$) *m/z* 1211.5250 ([M + Na]$^+$ $C_{58}H_{84}N_{10}NaO_9S_3Si^+$ requires 1211.5252); HPLC analysis: R*t* = 38.1 min [column: Shiseido CAPCELL PAK MG II (4.6 mm i.d. × 250 mm); mobile phase: MeOH:H_2O = 40:60 (0─5 min), linear gradient from 40:60 to 99:1 (5─30 min), 99:1 (30─50 min); flow rate: 1.00 mL/min; detection: UV at 254 nm].

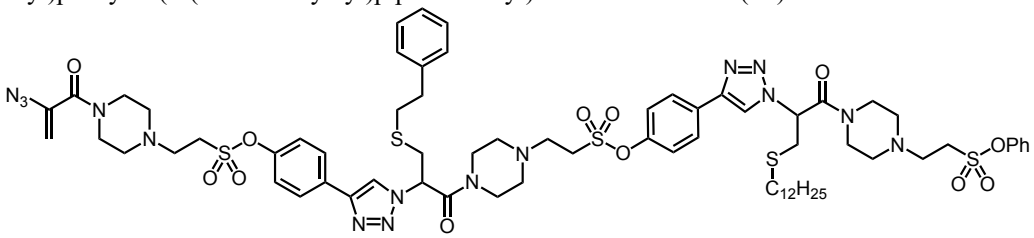
4-(1-(3-(Dodecylthio)-1-oxo-1-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)propan-2-yl)-1*H*-1,2,3-triazol-4-yl)phenyl 2-(4-(2-(4-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-1*H*-1,2,3-triazol-1-yl)-3-(phenethylthio)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**S4**)



Pale yellow oil; TLC R_f 0.48 (CH_2Cl_2/MeOH = 20/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.23 (s, 6H), 0.89 (t, 3H, *J* = 6.9 Hz), 1.01 (s, 9H), 1.24–1.38 (m, 19H), 1.52–1.61 (m, 2H), 2.18–2.24 (m, 1H), 2.26–2.34 (m, 1H), 2.35–2.45 (m, 2H), 2.49–2.66 (m, 6H), 2.74–2.82 (m, 2H), 2.84–2.90 (m, 2H), 2.91–3.00 (m, 4H), 3.01–3.12 (m, 2H), 3.34–3.44 (m, 5H), 3.53–3.81 (m, 8H), 5.78–5.83 (m, 1H), 5.87–5.93 (m, 1H), 6.90–6.96 (m, 2H), 7.16–7.34 (m, 8H), 7.39–7.44 (m, 4H), 7.71–7.74 (m, 2H), 7.88–7.93 (m, 2H), 7.95 (s, 1H), 8.12 (s, 1H); ^{13}C NMR analysis shows the presence of diastereomers. ^{13}C NMR ($CDCl_3$,101 MHz): δ –4.4, 14.2, 18.3, 22.7, 25.7, 28.8, 29.2, 29.4, 29.5, 29.61, 29.65, 31.9, 33.0, 34.4, 34.7, 34.8, 36.1, 42.5, 45.9, 46.0, 47.9, 48.1, 51.27, 51.36, 51.40, 52.2, 52.8, 58.7, 58.9, 117.4, 118.8, 120.6, 122.0, 126.6, 127.0, 127.5, 128.56, 128.58, 129.7, 130.1, 139.8, 146.8, 148.3,

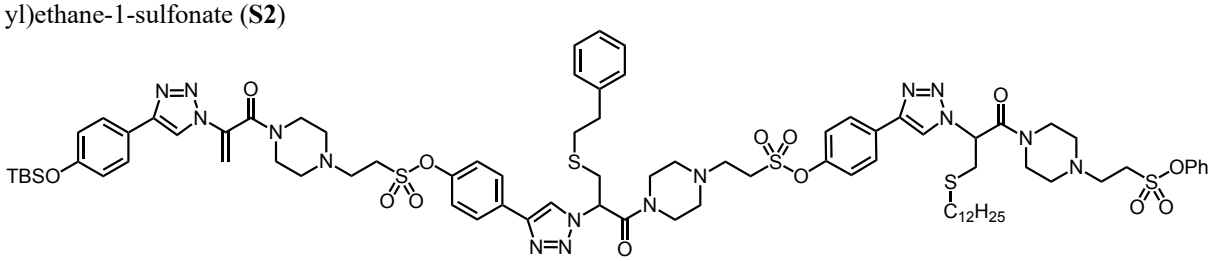
148.7, 149.0, 156.0, 165.15, 165.21; HRMS (ESI$^+$) *m/z* 1349.5756 ([M + Na]$^+$ $C_{66}H_{94}N_{10}NaO_9S_4Si^+$ requires 1349.5755); HPLC analysis: R*t* = 38.1 min [column: Shiseido CAPCELL PAK MG II (4.6 mm i.d. × 250 mm); mobile phase: MeOH:H_2O = 40:60 (0─5 min), linear gradient from 40:60 to 99:1 (5─30 min), 99:1 (30─50 min); flow rate: 1.00 mL/min; detection: UV at 254 nm].

4-(1-(1-(4-(2-((4-(1-(3-(Dodecylthio)-1-oxo-1-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)propan-2-yl)-1*H*-1,2,3-triazol-4-yl)phenoxy)sulfonyl)ethyl)piperazin-1-yl)-1-oxo-3-(phenethylthio)propan-2-yl)-1*H*-1,2,3-triazol-4-yl)phenyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**S5**)



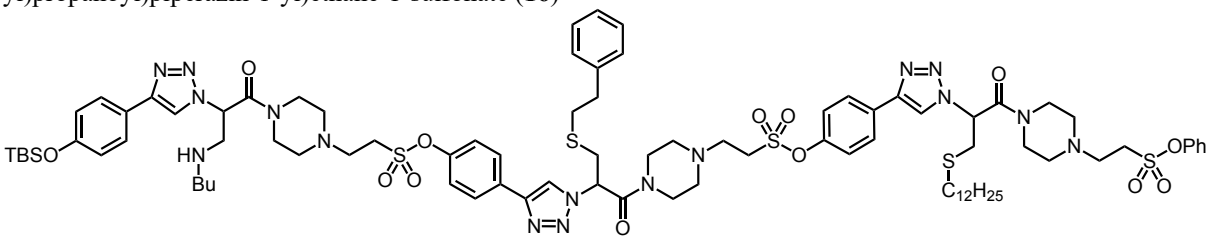
Pale yellow oil; TLC R_f 0.32 (CH_2Cl_2/MeOH = 15/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.89 (t, 3H, *J* = 6.9 Hz), 1.22–1.38 (m, 18H), 1.52–1.61 (m, 2H), 2.23–2.33 (m, 2H), 2.36–2.45 (m, 2H), 2.50–2.65 (m, 9H), 2.77–2.83 (m, 2H), 2.86–2.91 (m, 2H), 2.93–3.00 (m, 4H), 3.01–3.11 (m, 5H), 3.34–3.51 (m, 8H), 3.56–3.81 (m, 12H), 5.05 (d, 1H, *J* = 2.1 Hz), 5.10 (d, 1H, *J* = 2.1 Hz), 5.83–5.92 (m, 2H), 7.16–7.45 (m, 14H), 7.86–7.92 (m, 4H), 8.09 (s, 1H), 8.12 (s, 1H); ^{13}C NMR analysis shows the presence of diastereomers. ^{13}C NMR ($CDCl_3$,101 MHz): δ 14.2, 22.7, 28.8, 29.2, 29.4, 29.57, 29.60, 29.65, 29.66, 31.6, 31.9, 33.0, 34.4, 34.8, 34.9, 36.1, 42.5, 46.0, 42.5, 46.0, 47.9, 48.1, 51.36, 51.40, 51.5, 52.2, 52.8, 52.9, 58.69, 58.74, 104.0, 118.8, 122.0, 122.5, 122.6, 126.7, 127.3, 127.5, 128.55, 128.61, 129.67, 129.70, 130.1, 139.4, 139.7, 146.8, 146.9, 148.6, 148.7, 148.9, 163.3, 165.1, 165.2 ; HRMS (ESI$^+$) *m/z* 742.7937 ([M + 2H]$^{2+}$ $C_{69}H_{95}N_{15}O_{12}S_5^{2+}$ requires 742.7939); HPLC analysis: R*t* = 38.1 min [column: Shiseido CAPCELL PAK MG II (4.6 mm i.d. × 250 mm); mobile phase: MeOH:H_2O = 40:60 (0─5 min), linear gradient from 40:60 to 99:1 (5─30 min), 99:1 (30─50 min); flow rate: 1.00 mL/min; detection: UV at 254 nm].

4-(1-(1-(4-(2-((4-(1-(3-(Dodecylthio)-1-oxo-1-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)propan-2-yl)-1*H*-1,2,3-triazol-4-yl)phenoxy)sulfonyl)ethyl)piperazin-1-yl)-1-oxo-3-(phenethylthio)propan-2-yl)-1H-1,2,3-triazol-4-yl)phenyl 2-(4-(2-(4-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**S2**)



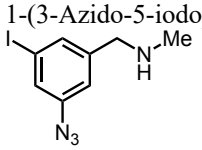
Pale yellow oil; TLC R_f 0.38 (CH_2Cl_2/MeOH = 15/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.23 (s, 6H), 0.89 (t, 3H, *J* = 6.8 Hz), 1.01 (s, 9H), 1.22–1.38 (m, 18H), 1.52–1.61 (m, 2H), 2.23–2.33 (m, 2H), 2.36–2.46 (m, 2H), 2.48–2.65 (m, 9H), 2.77–2.83 (m, 2H), 2.84–2.91 (m, 2H), 2.93–3.11 (m, 9H), 3.33–3.50 (m, 8H), 3.51–3.84 (m, 12H), 5.39 (d, 1H, *J* = 2.0 Hz), 5.82–5.93 (m, 2H), 6.00 (d, 1H, *J* = 2.0 Hz), 6.90–6.94 (m, 2H), 7.17–7.45 (m, 14H), 7.70–7.74 (m, 2H), 7.89 (d, 4H, *J* = 8.4 Hz), 7.97 (s, 1H), 8.09 (s, 1H), 8.12 (s, 1H); ^{13}C NMR analysis shows the presence of diastereomers. ^{13}C NMR ($CDCl_3$,101 MHz): δ –4.4, 14.2, 18.3, 22.7, 25.7, 28.8, 29.2, 29.4, 29.57, 29.60, 29.65, 29.66, 30.5, 31.9, 33.0, 34.4, 34.8, 34.9, 36.1, 42.0, 42.5, 46.0, 47.0, 46.0, 47.0, 47.95, 48.10, 48.13, 51.36, 51.40, 51.44, 51.47, 52.2, 52.8, 52.9, 58.70, 58.76 108.2, 117.1, 118.8, 120.6, 122.0, 122.54, 122.56, 123.0, 126.6, 127.2, 127.3, 127.5, 128.55, 128.61, 129.65, 129.70, 130.1, 136.7, 139.7, 146.8, 146.9, 148.1, 148.6, 148.7, 149.0, 156.2, 162.6, 165.1, 165.2; HRMS (ESI$^+$) *m/z* 858.8580 ([M + 2H]$^{2+}$ $C_{83}H_{115}N_{15}O_{13}S_5Si^{2+}$ requires 858.8580); HPLC analysis: R*t* = 38.1 min [column: Shiseido CAPCELL PAK MG II (4.6 mm i.d. × 250 mm); mobile phase: MeOH:H_2O = 40:60 (0─5 min), linear gradient from 40:60 to 99:1 (5─30 min), 99:1 (30─50 min); flow rate: 1.00 mL/min; detection: UV at 254 nm].

4-(1-(1-(4-(2-((4-(1-(3-(Dodecylthio)-1-oxo-1-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)propan-2-yl)-1*H*-1,2,3-triazol-4-yl)phenoxy)sulfonyl)ethyl)piperazin-1-yl)-1-oxo-3-(phenethylthio)propan-2-yl)-1*H*-1,2,3-triazol-4-yl)phenyl 2-(4-(3-(butylamino)-2-(4-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**16**)



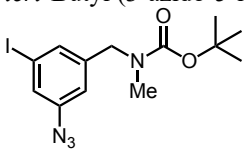
Colorless solid; TLC R_f 0.48 (CH_2Cl_2/MeOH = 10/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.23 (s, 6H), 0.86–0.93 (m, 6H), 1.00 (s, 9H), 1.22–1.38 (m, 20H), 1.39–1.46 (m, 2H), 1.52–1.61 (m, 2H), 2.17–2.33 (m, 3H), 2.36–2.46 (m, 3H), 2.50–2.70 (m, 10H), 2.77–2.83 (m, 2H), 2.84–2.91 (m, 2H), 2.93–3.01 (m, 6H), 3.03–3.11 (m, 2H), 3.13–3.21 (m, 1H), 3.34–3.46 (m, 8H), 3.50–3.84 (m, 14H), 5.82–5.93 (m, 3H), 6.89–6.93 (m, 2H), 7.17–7.45 (m, 14H), 7.70–7.74 (m, 2H), 7.87–7.92 (m, 4H), 7.97 (s, 1H), 8.08 (s, 1H), 8.11 (s, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ –4.4, 14.0, 14.2, 18.3, 20.3, 22.7, 25.7, 28.8, 29.2, 29.4, 29.53, 29.57, 29.60, 29.65, 31.9, 32.1, 33.0, 34.4, 34.8, 34.9, 36.1, 42.3, 42.5, 45.7, 46.01, 46.04, 47.9, 48.1, 51.31, 51.32, 51.36, 51.39, 51.4, 51.7, 52.2, 52.8, 52.9, 58.69, 58.74, 117.8, 118.7, 120.6, 122.0, 122.6, 123.6, 126.7, 127.0, 127.3, 127.5, 128.55, 128.61, 129.63, 129.69, 130.1, 139.7, 146.85, 146.89, 148.1, 148.7, 148.9, 156.0, 165.1, 165.2, 165.5; IR (NaCl, cm^{-1}) 867, 911, 1148, 1170, 1197, 1254, 1367, 1489, 1651, 1656, 2854, 2927; HRMS (ESI$^+$) *m/z* 895.4026 ([M + 2H]$^{2+}$ $C_{87}H_{126}N_{16}O_{13}S_5Si^{2+}$ requires 895.4029); HPLC analysis: R*t* = 38.1 min [column: Shiseido CAPCELL PAK MG II (4.6 mm i.d. × 250 mm); mobile phase: MeOH:H_2O = 40:60 (0─5 min), linear gradient from 40:60 to 99:1 (5─30 min), 99:1 (30─50 min); flow rate: 1.00 mL/min; detection: UV at 254 nm].

1-(3-Azido-5-iodophenyl)-*N*-methylmethanamine



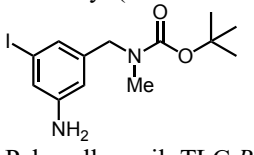
Pale yellow oil; TLC R_f 0.20 (*n*-hexane/EtOAc = 1/1); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.45 (s, 3H), 3.69 (s, 2H), 6.96–6.98 (m, 1H), 7.26 (dd, 1H, *J* = 1.8 Hz), 7.46 (dd, 1H, *J* = 1.8 Hz); ^{13}C NMR ($CDCl_3$,101 MHz): δ 36.0, 55.0, 94.7, 118.1, 126.5, 133.6, 141.3, 144.1; IR (NaCl, cm^{-1}) 844, 1290, 1435, 1440, 1566, 1591, 2113, 2790, 2843; HRMS (ESI$^+$) *m/z* 288.9951 ([M + H]$^+$ $C_8H_{10}IN_4^+$ requires 288.9950).

tert-Butyl (3-azido-5-iodobenzyl)(methyl)carbamate



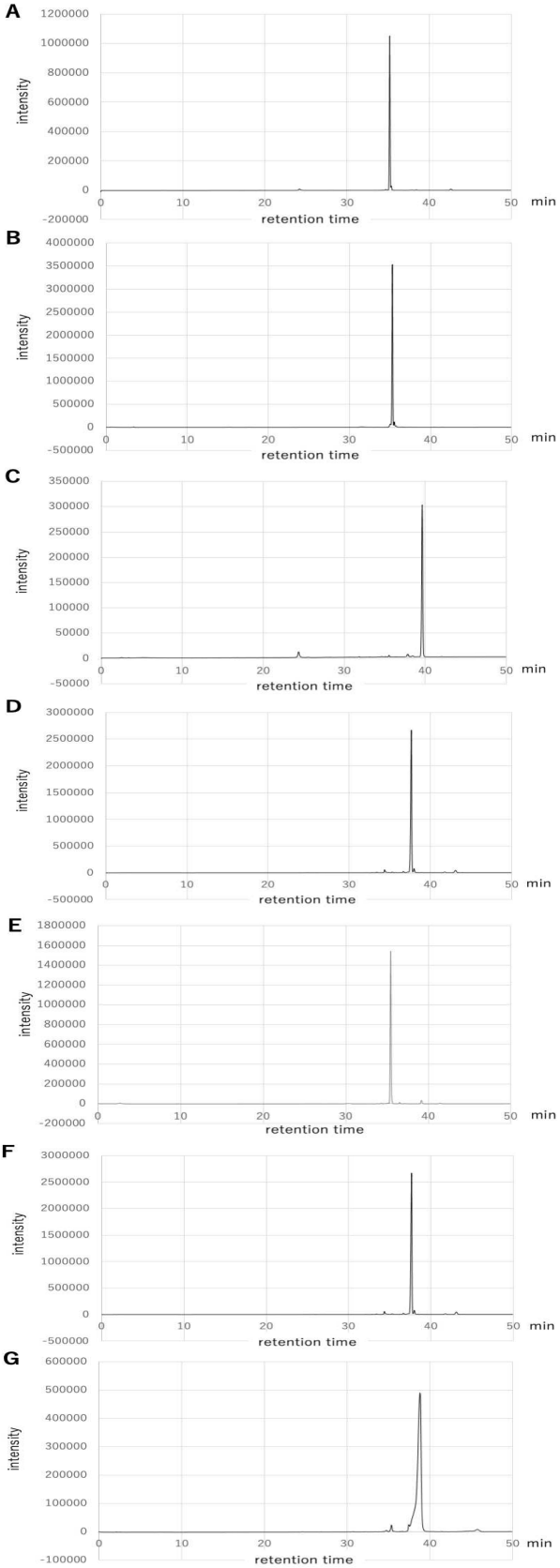
Pale yellow oil; TLC R_f 0.70 (*n*-hexane/EtOAc = 6/1); ^{1}H and ^{13}C NMR analysis show the presence of rotational isomers. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.43–1.58 (br, 9H), 2.79–2.92 (br, 3H), 4.30–4.42 (br, 2H), 6.82–6.90 (br, 1H), 7.27–7.31 (br, 1H), 7.35–7.39 (br, 1H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 28.4, 34.3, 51.1 (br), 51.8 (br), 80.3 (br), 94.7, 117.3 (br), 126.7, 132.8 (br), 141.6, 155.4 (br), 156.1 (br); IR (NaCl, cm^{-1}) 878, 1147, 1173, 1290, 1366, 1392, 1445, 1480, 1568, 1595, 1694, 2114, 2930, 2976; HRMS (ESI$^+$) *m/z* 411.0291 ([M + Na]$^+$ $C_{13}H_{17}IN_4NaO_2^+$ requires 411.0294).

tert-Butyl (3-amino-5-iodobenzyl)(methyl)carbamate



Pale yellow oil; TLC R_f 0.70 (*n*-hexane/EtOAc = 1/1); ^{1}H and ^{13}C NMR analysis show the presence of rotational isomers. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.42–1.58 (br, 9H), 2.77–2.89 (br, 3H), 3.65–3.79 (br, 2H), 4.23–4.32 (br, 2H), 6.40–6.55 (br, 1H), 6.90–7.00 (br, 2H); ^{13}C NMR ($CDCl_3$,101 MHz): δ 28.5, 34.1, 51.9 (br), 51.9 (br), 80.0 (br), 95.1, 112.9 (br), 113.6 (br), 122.5 (br), 126.2 (br), 126.6 (br), 141.2 (br), 147.9, 155.7 (br); IR (NaCl, cm^{-1}) 877, 1147, 1246, 1393, 1448, 1462, 1566, 1682, 2976, 3358; HRMS (ESI$^+$) *m/z* 385.03863 ([M + Na]$^+$ $C_{13}H_{19}IN_2NaO_2^+$ requires 385.03889).

HPLC Charts of Triazoles. [(A) 14 (B) 15 (C) S1 (D) S4 (E) S5 (F) S2 (G) 16]



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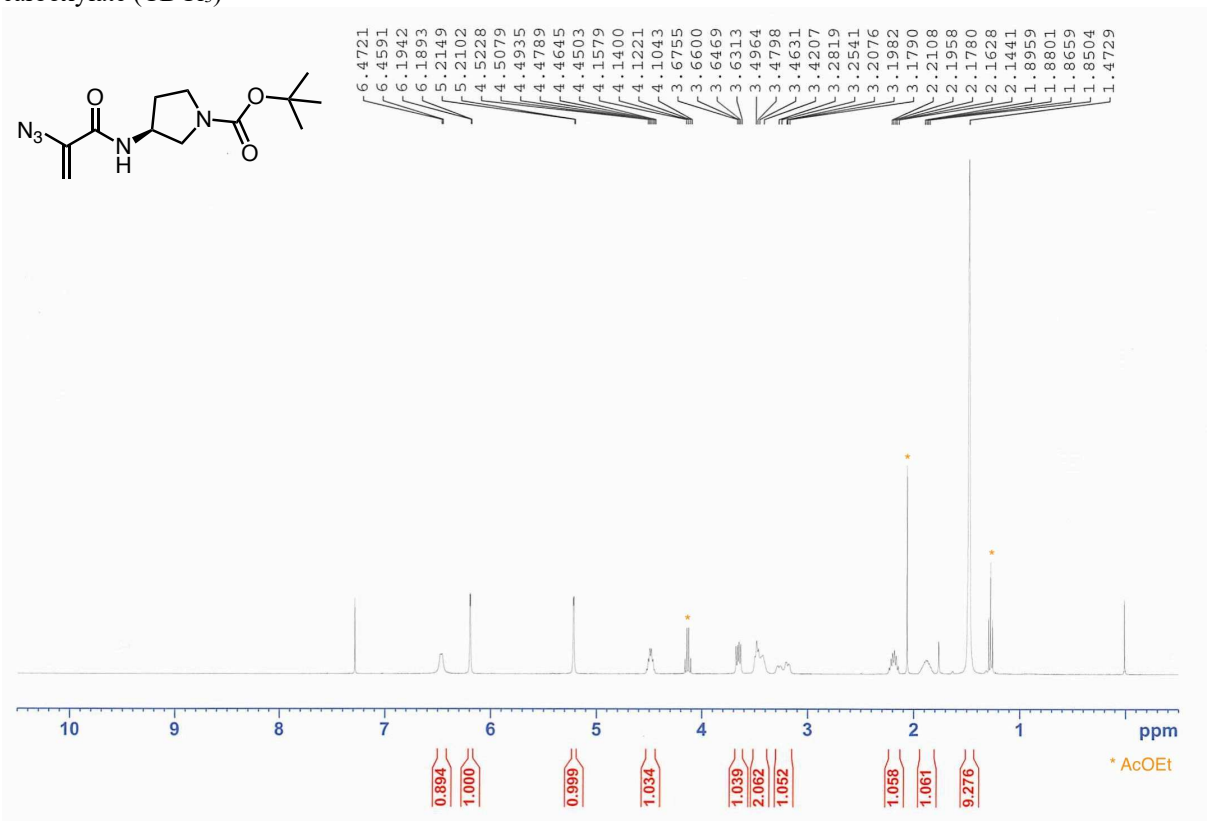
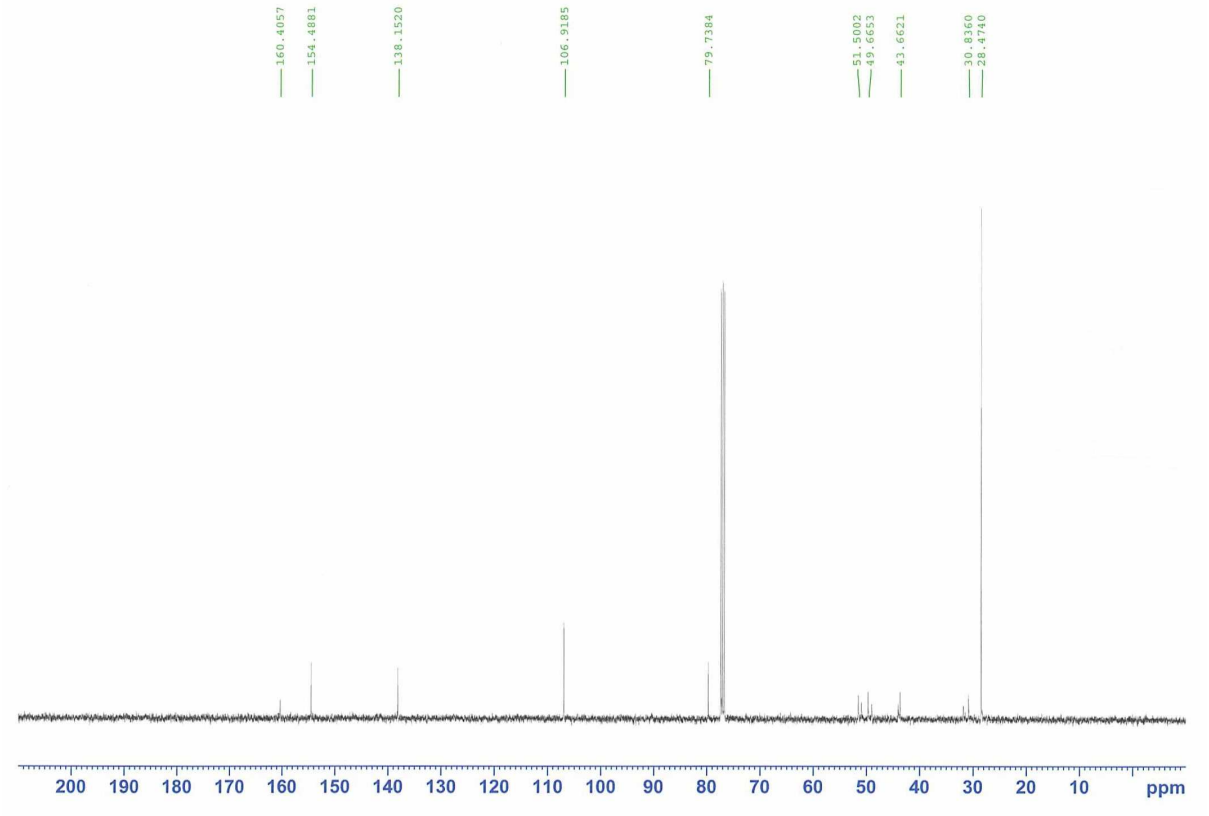
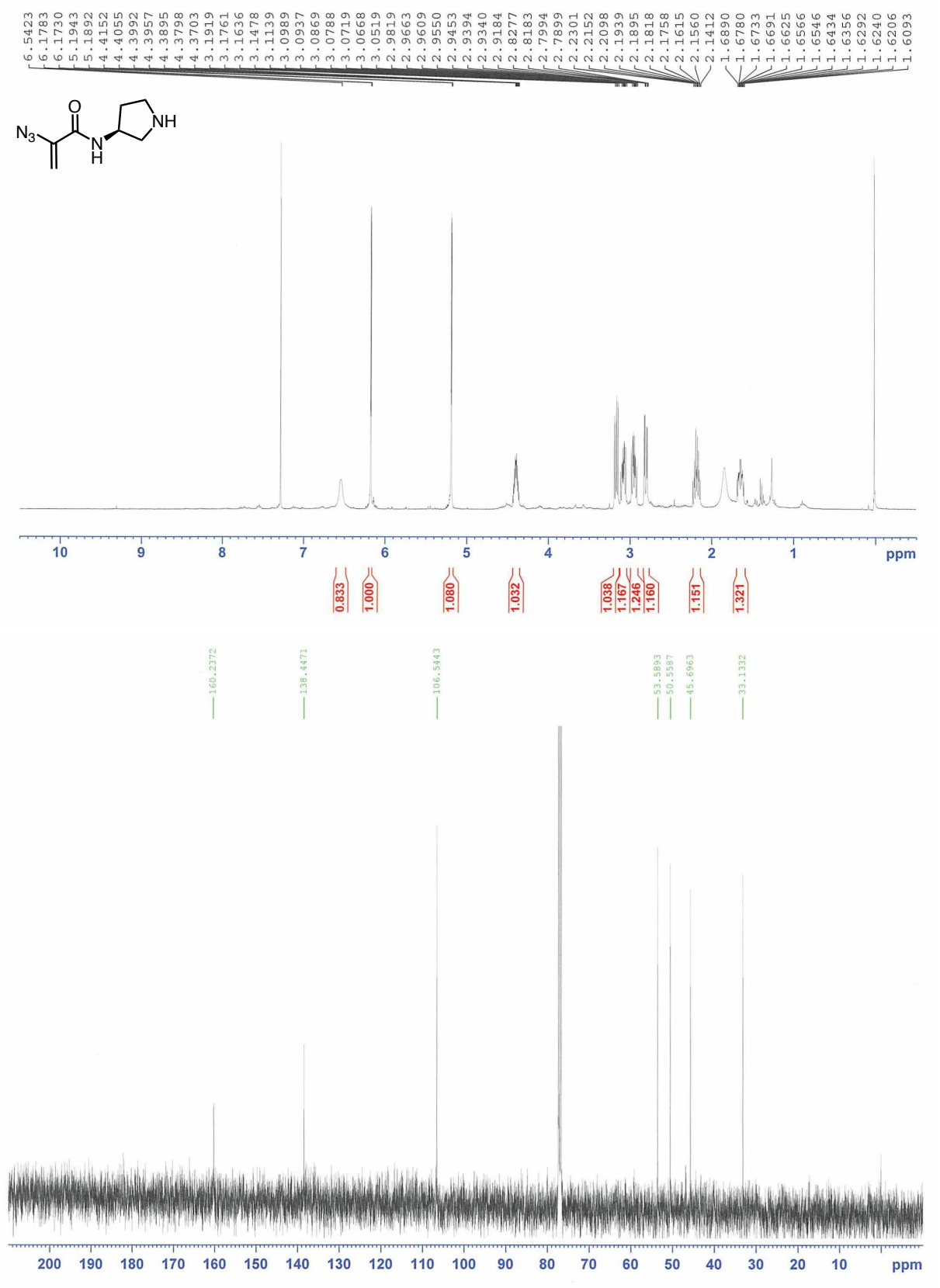
^{1}H and ^{13}C NMR Spectra of Compounds

^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of *tert*-butyl (*S*)-3-(2-azidoacrylamido)pyrrolidine-1-carboxylate ($CDCl_3$)

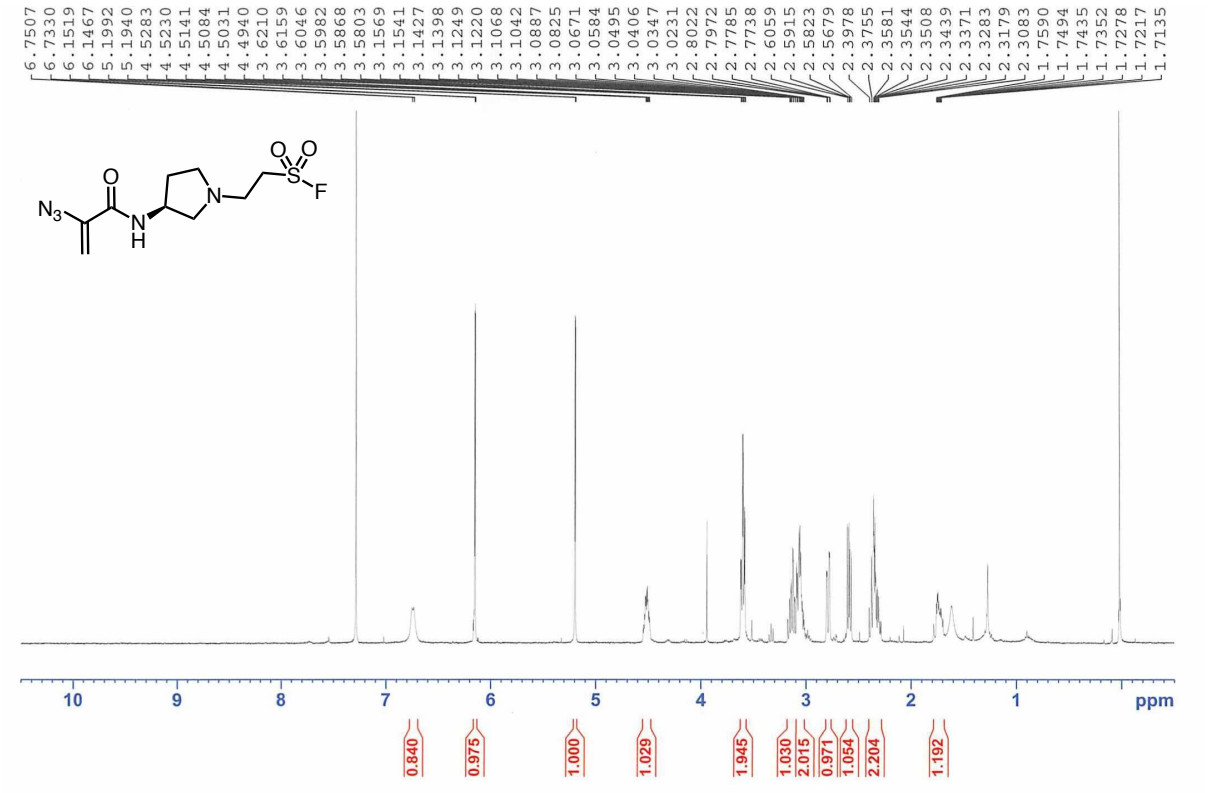


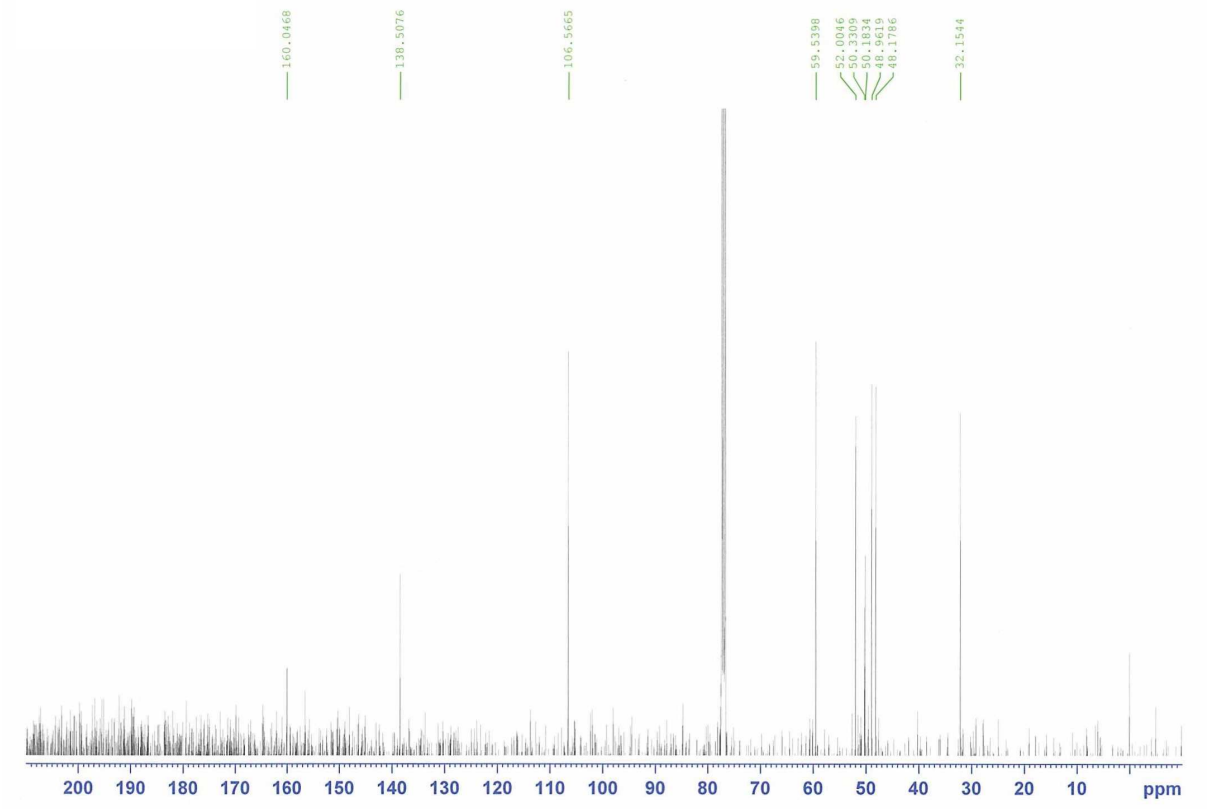


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of (*S*)-2-azido-*N*-(pyrrolidin-3-yl)acrylamide ($CDCl_3$)

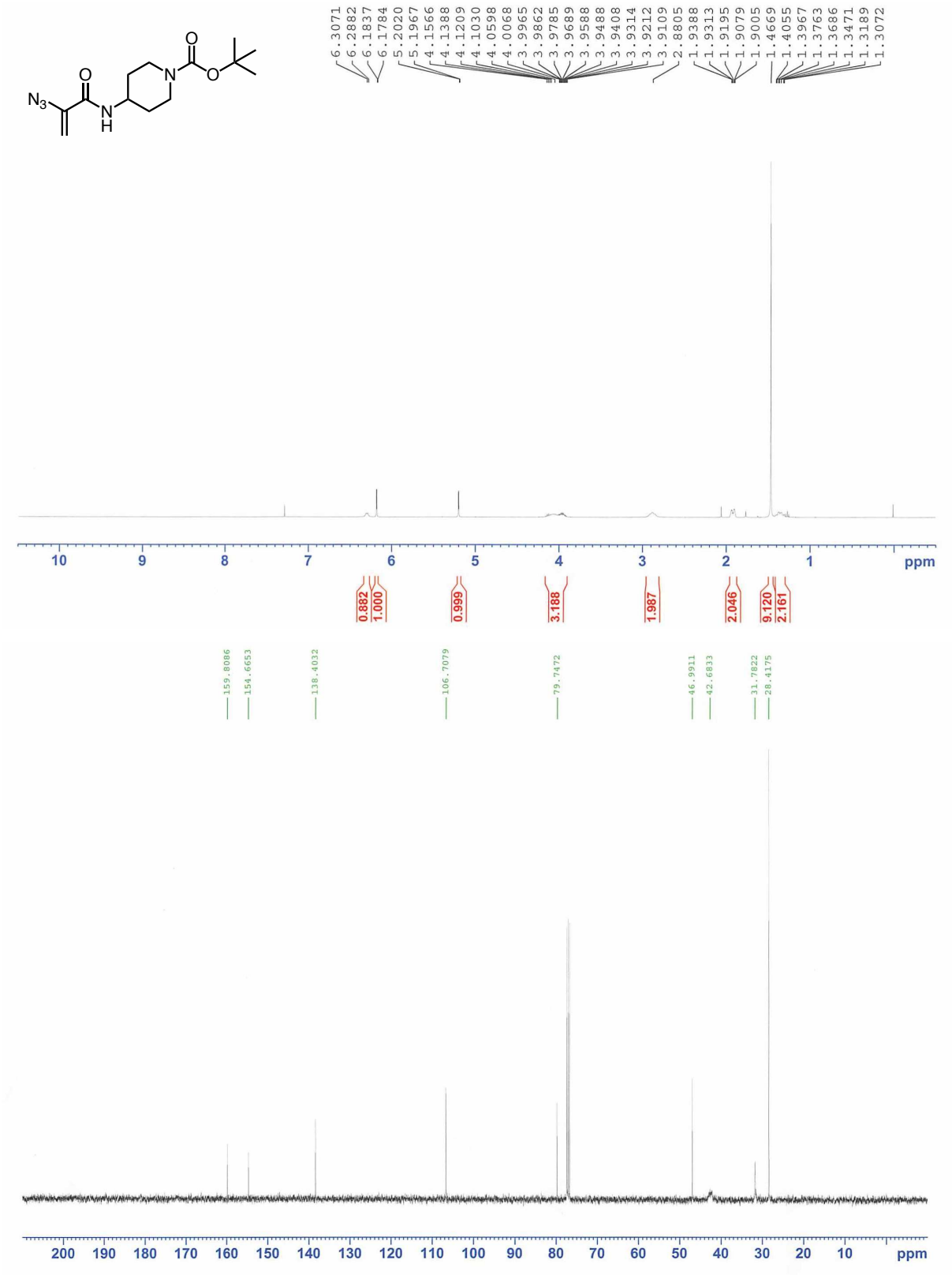


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of (*S*)-2-(3-(2-azidoacrylamido)pyrrolidin-1-yl)ethane-1-sulfonyl fluoride (**1b**) ($CDCl_3$)

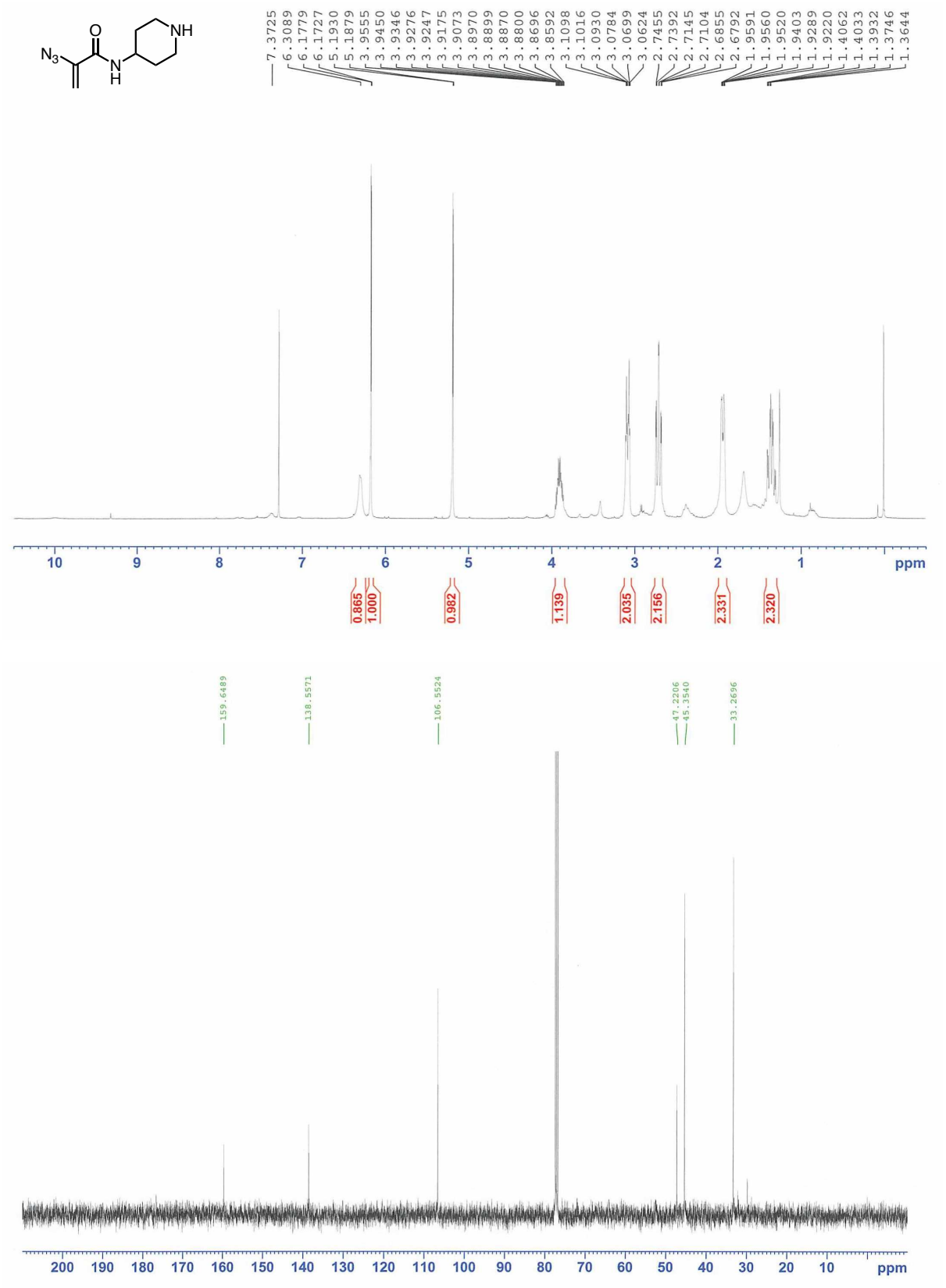




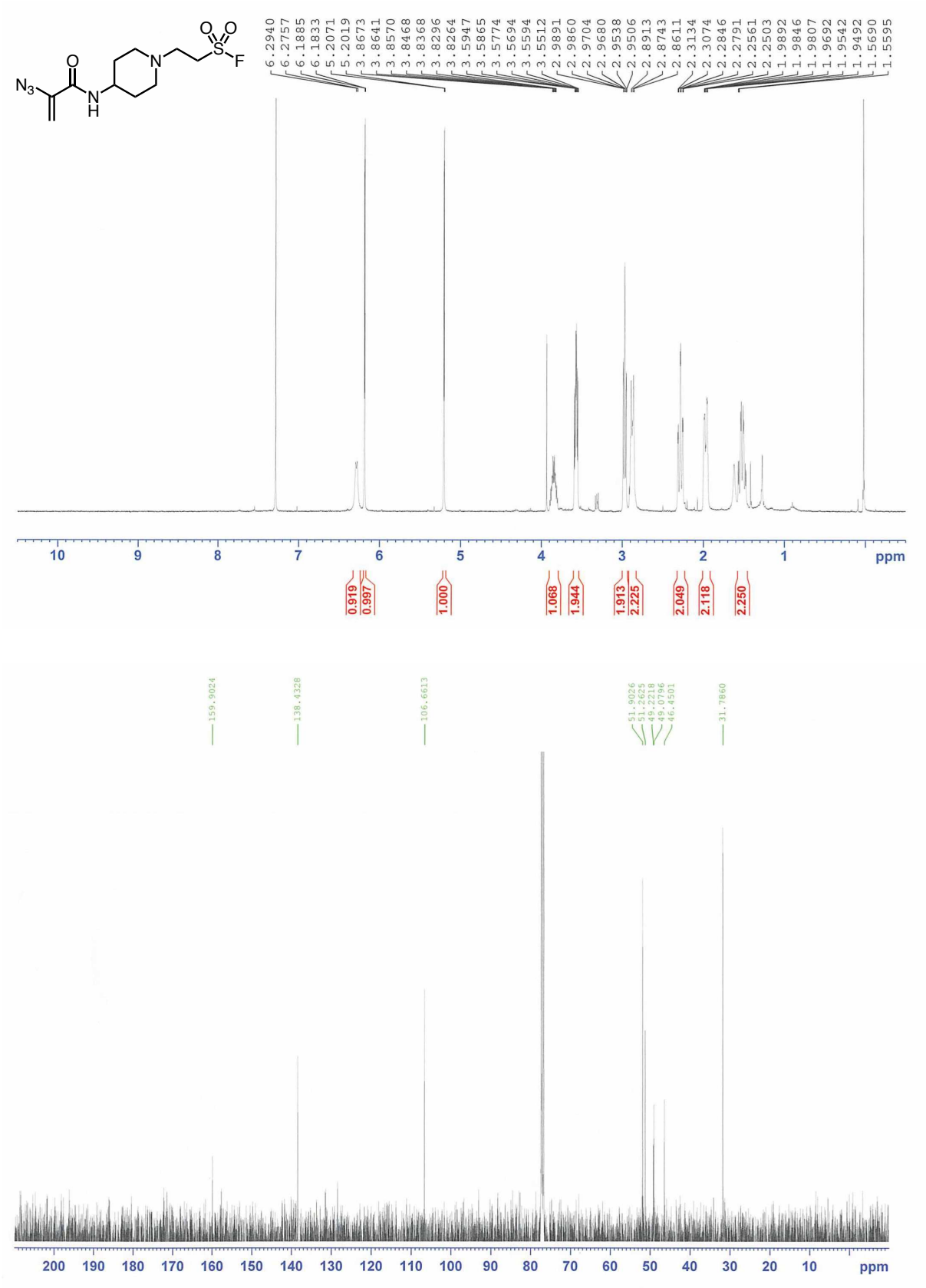
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of *tert*-butyl 4-(2-azidoacrylamido)piperidine-1-carboxylate ($CDCl_3$)



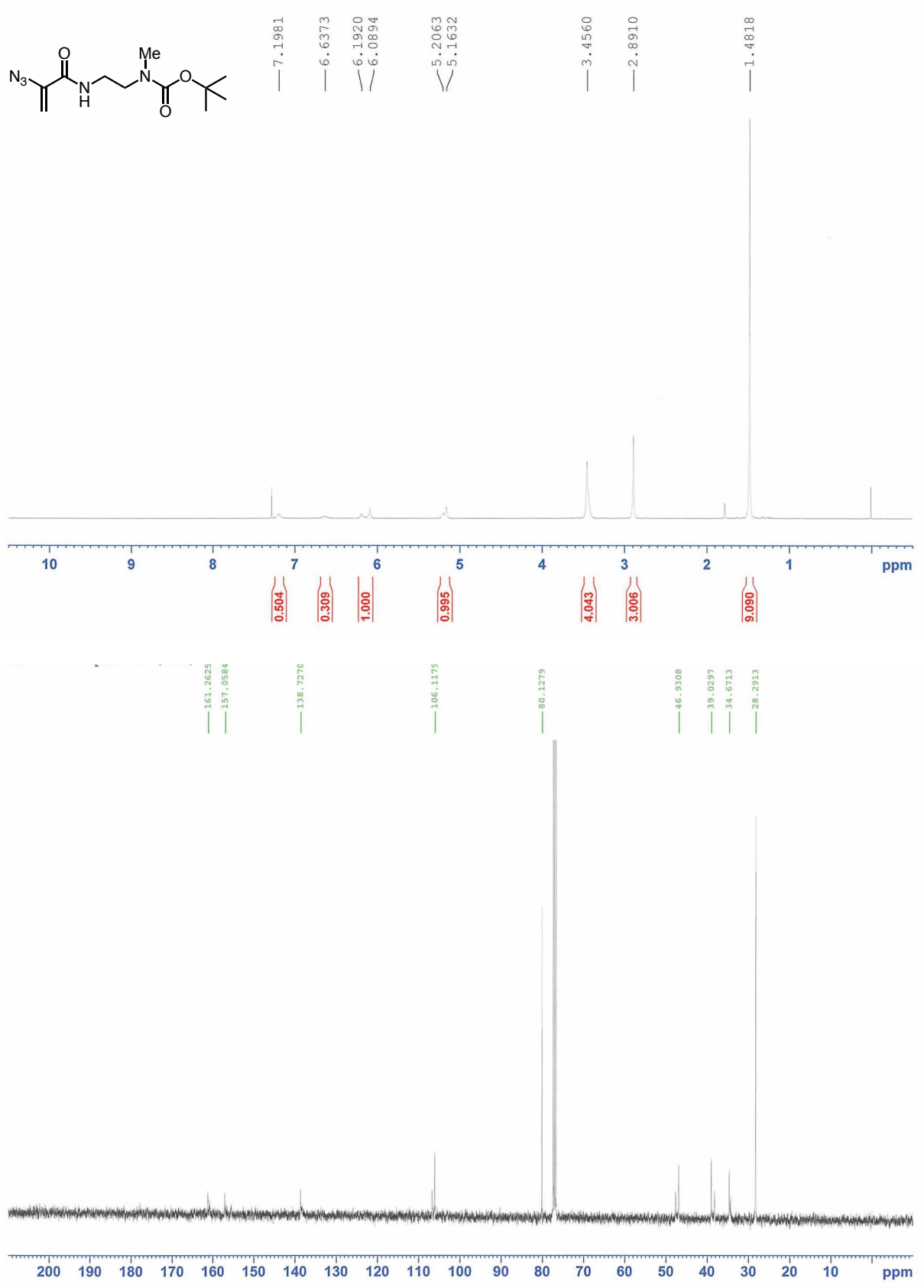
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 2-azido-*N*-(piperidin-4-yl)acrylamide ($CDCl_3$)



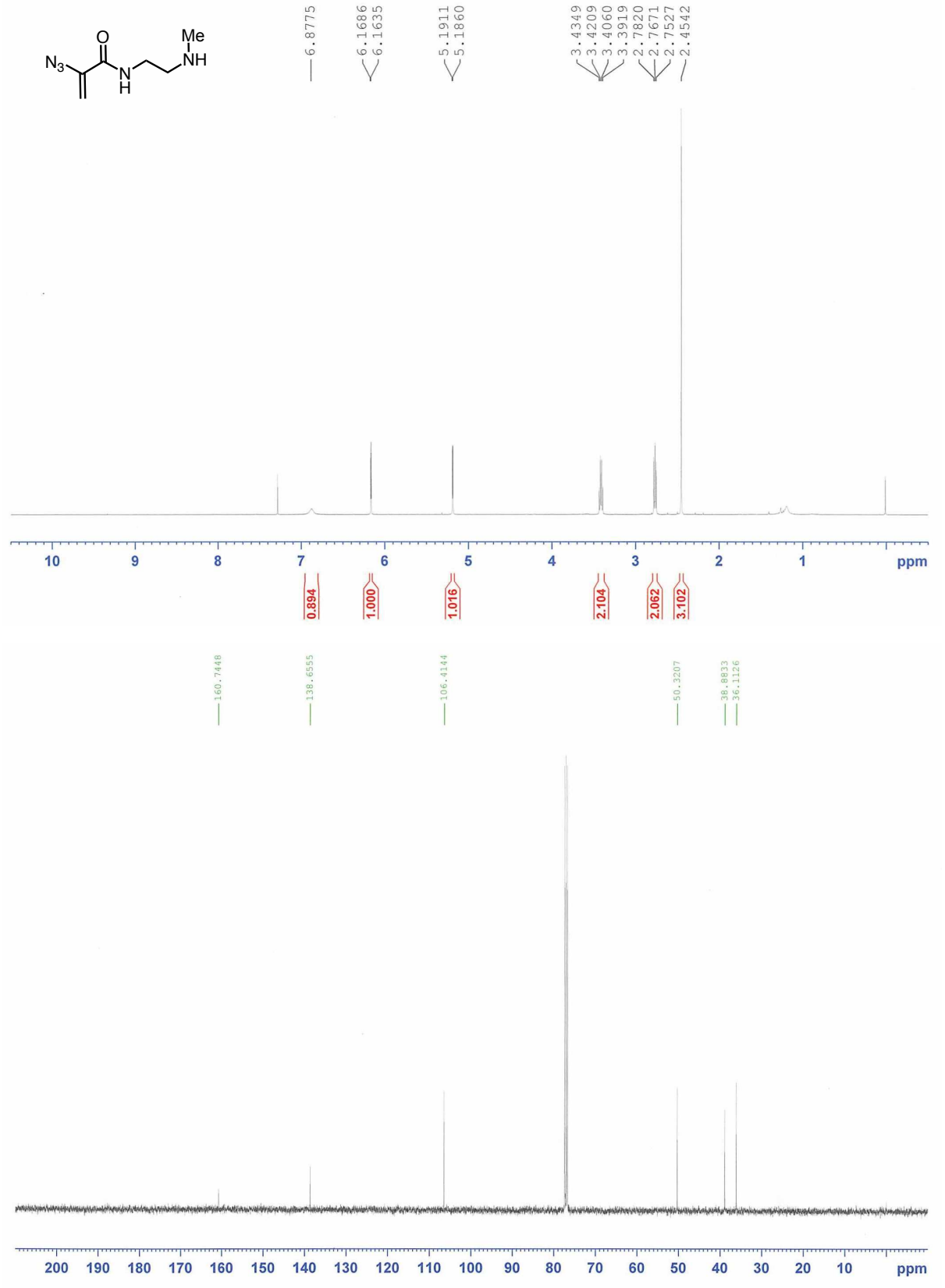
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 2-(4-(2-azidoacrylamido)piperidin-1-yl)ethane-1-sulfonyl fluoride (**1c**) ($CDCl_3$)



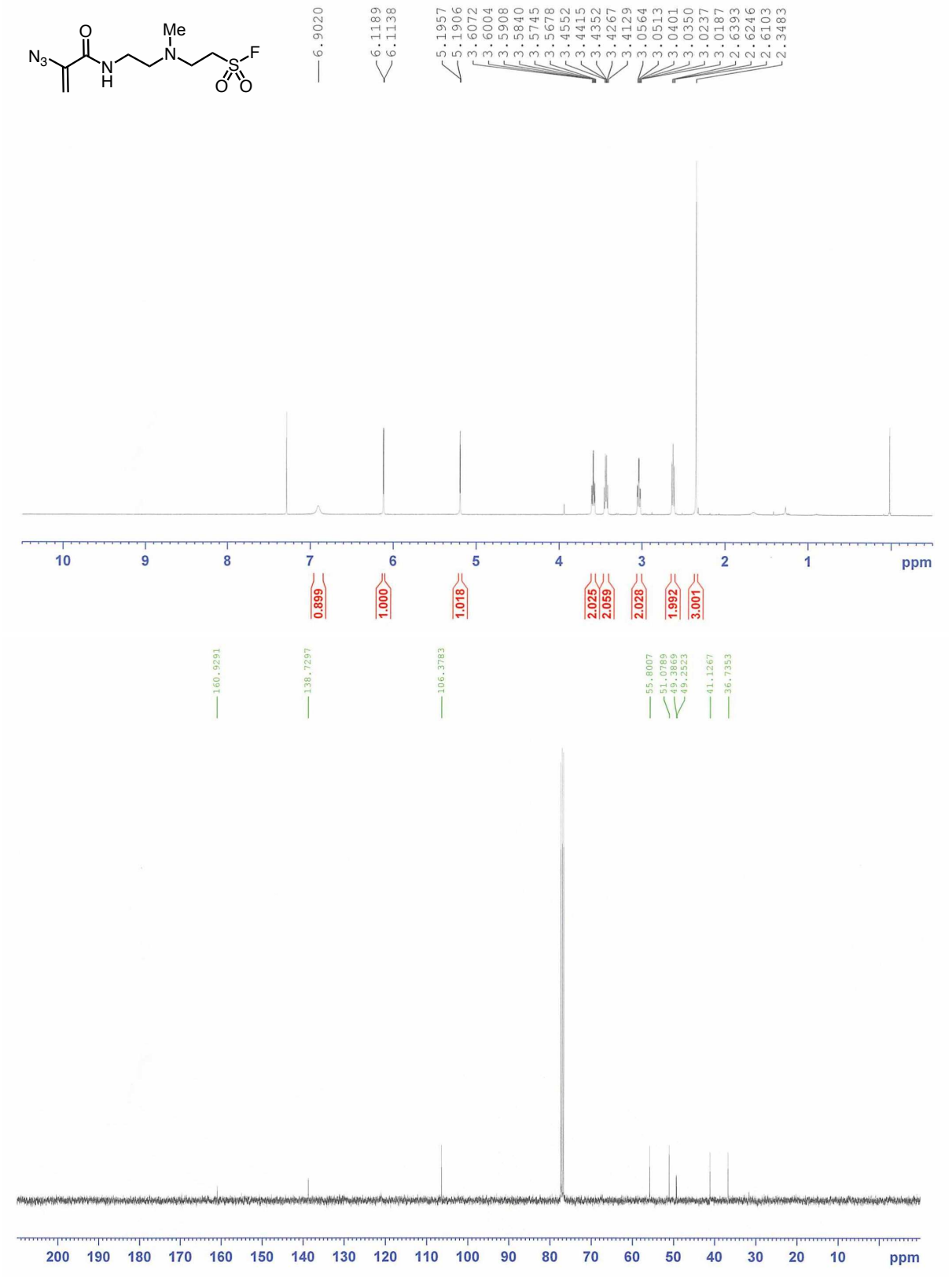
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of *tert*-butyl (2-(2-azidoacrylamido)ethyl)(methyl)carbamate ($CDCl_3$)



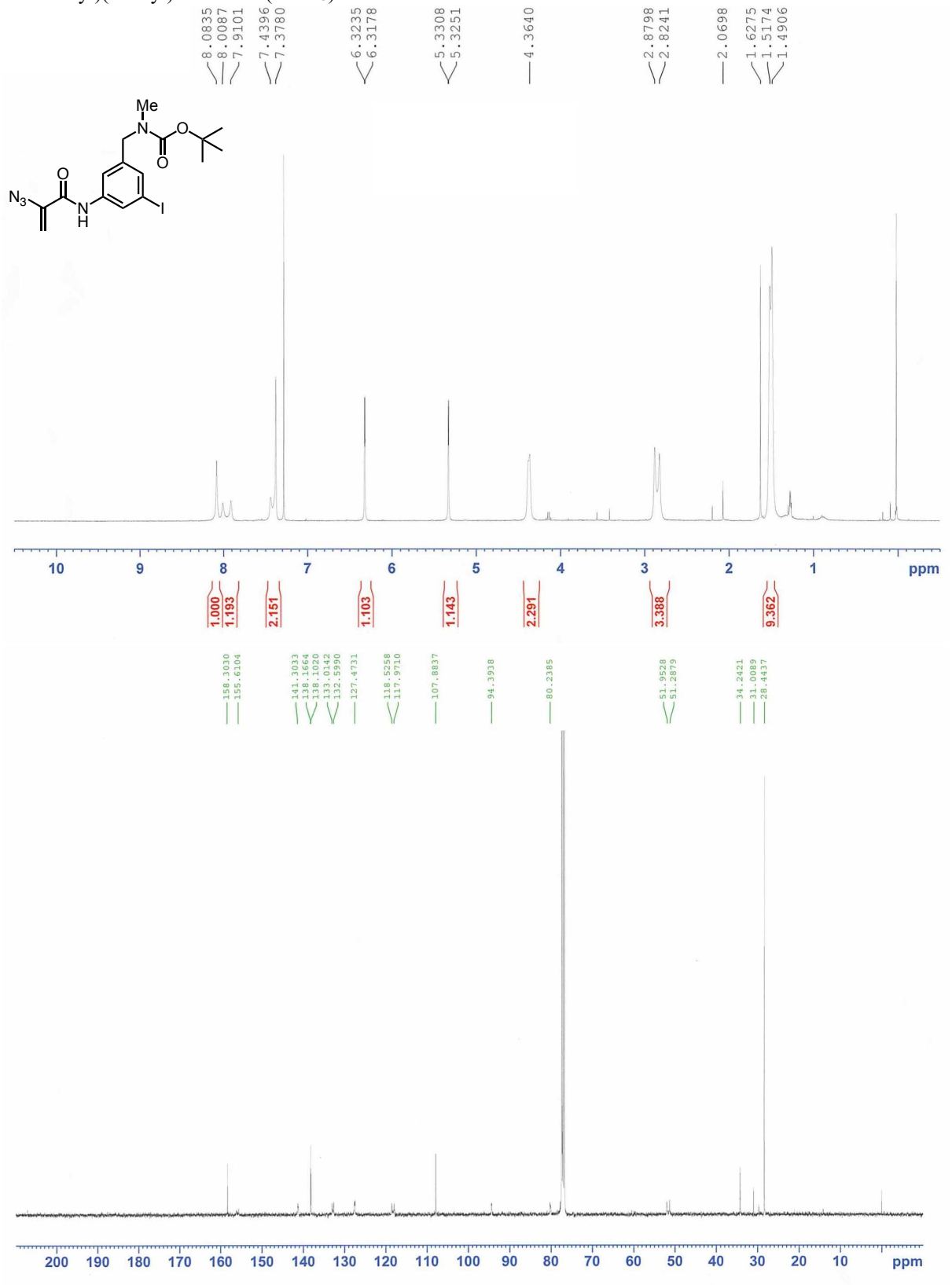
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 2-azido-*N*-(2-(methylamino)ethyl)acrylamide ($CDCl_3$)



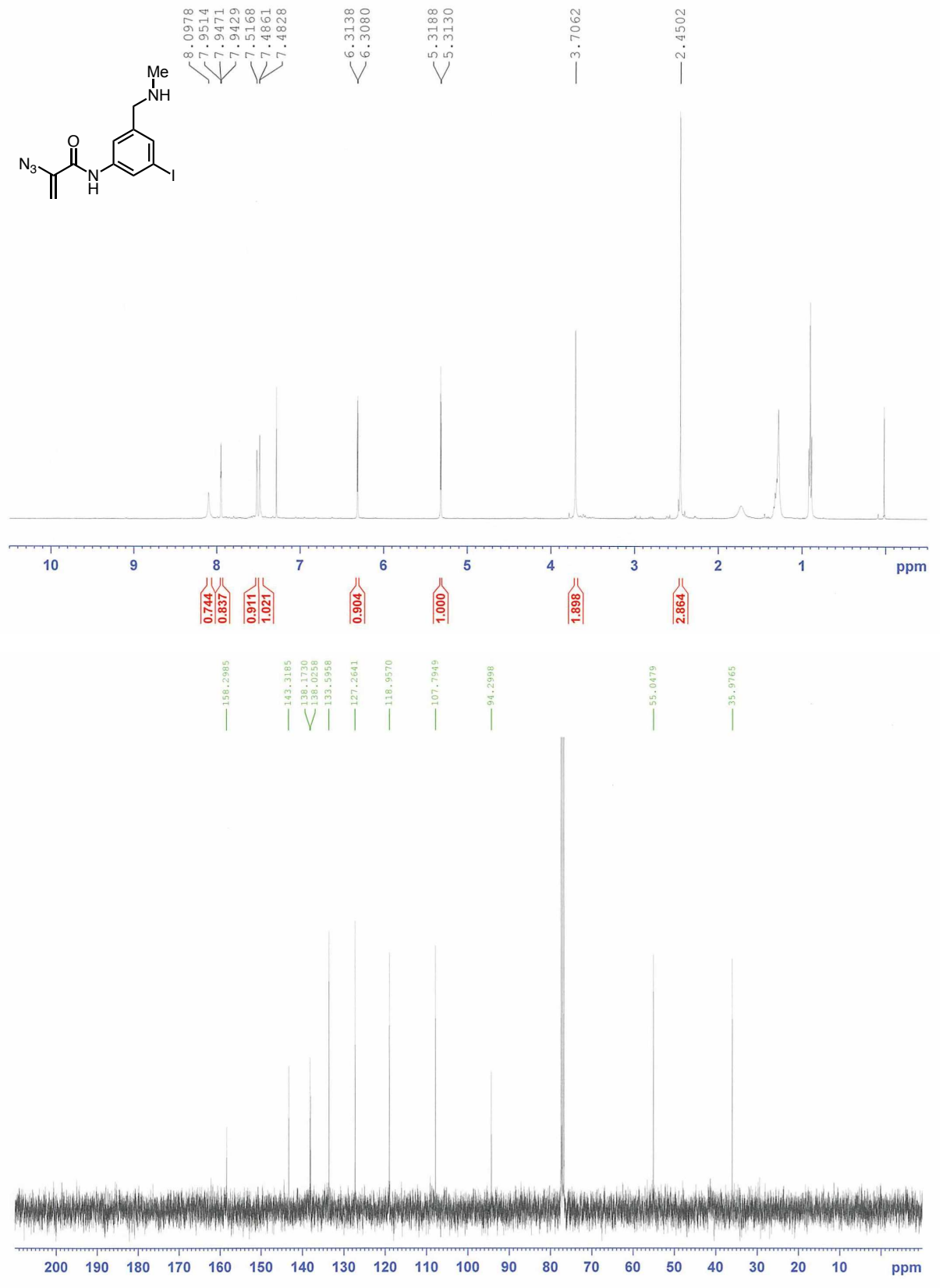
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 2-((2-(2-azidoacrylamido)ethyl)(methyl)amino)ethane-1-sulfonyl fluoride (**1d**) ($CDCl_3$)



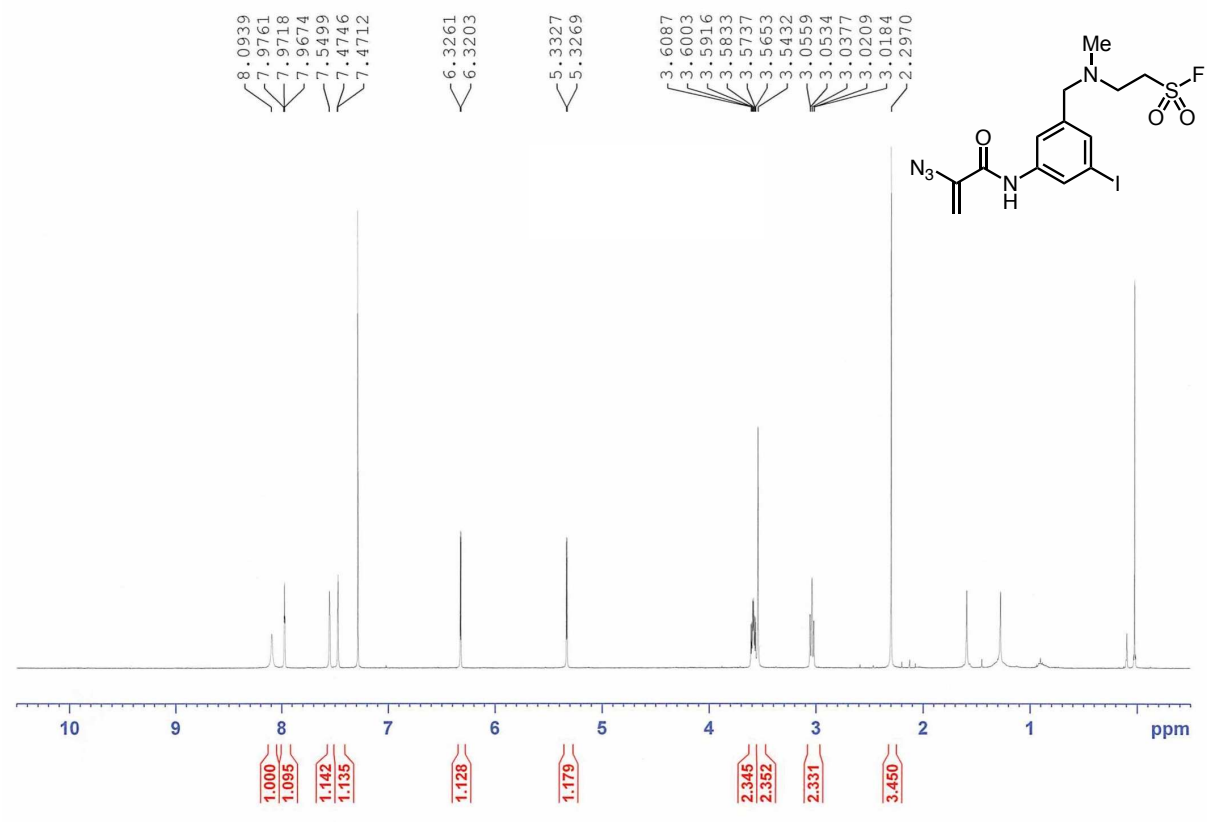
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of *tert*-butyl (3-(2-azidoacrylamido)-5-iodobenzyl)(methyl)carbamate ($CDCl_3$)

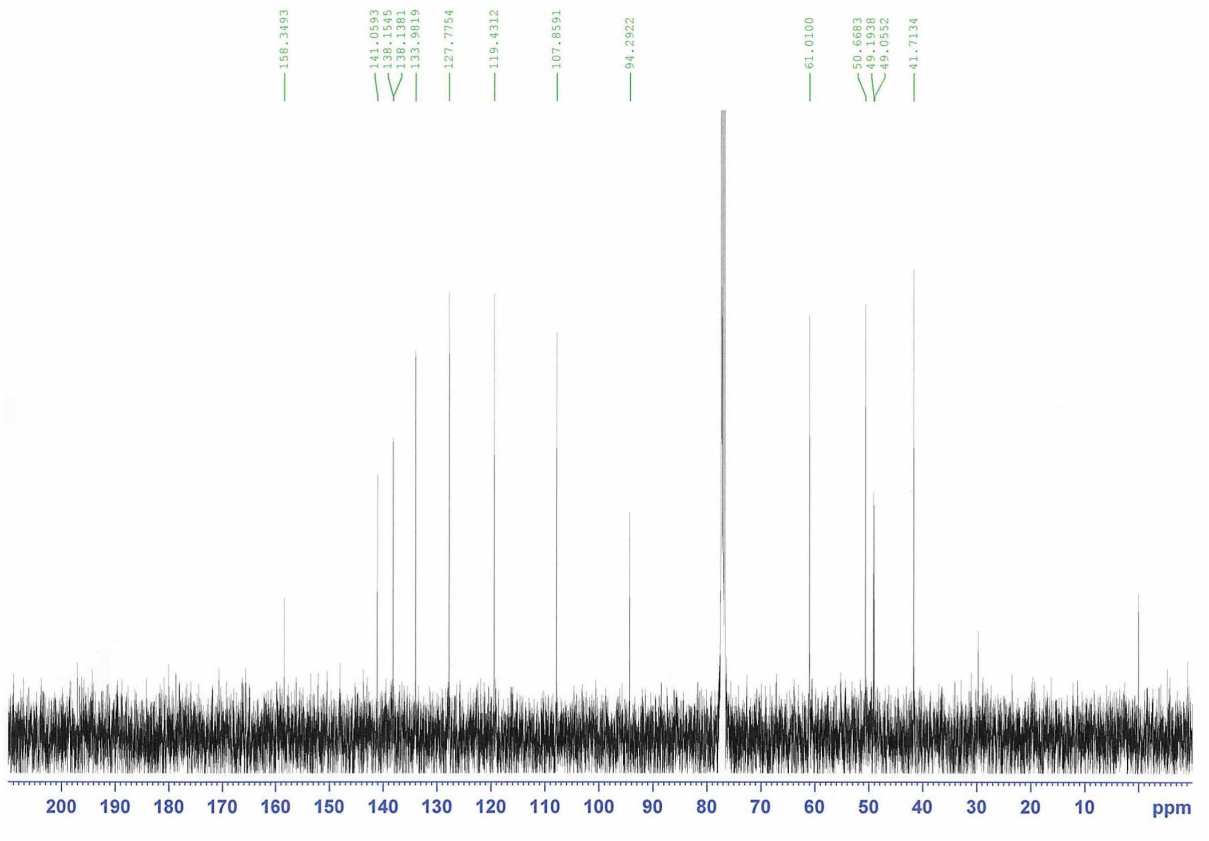


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 2-azido-*N*-(3-iodo-5-((methylamino)methyl)phenyl)acrylamide ($CDCl_3$)

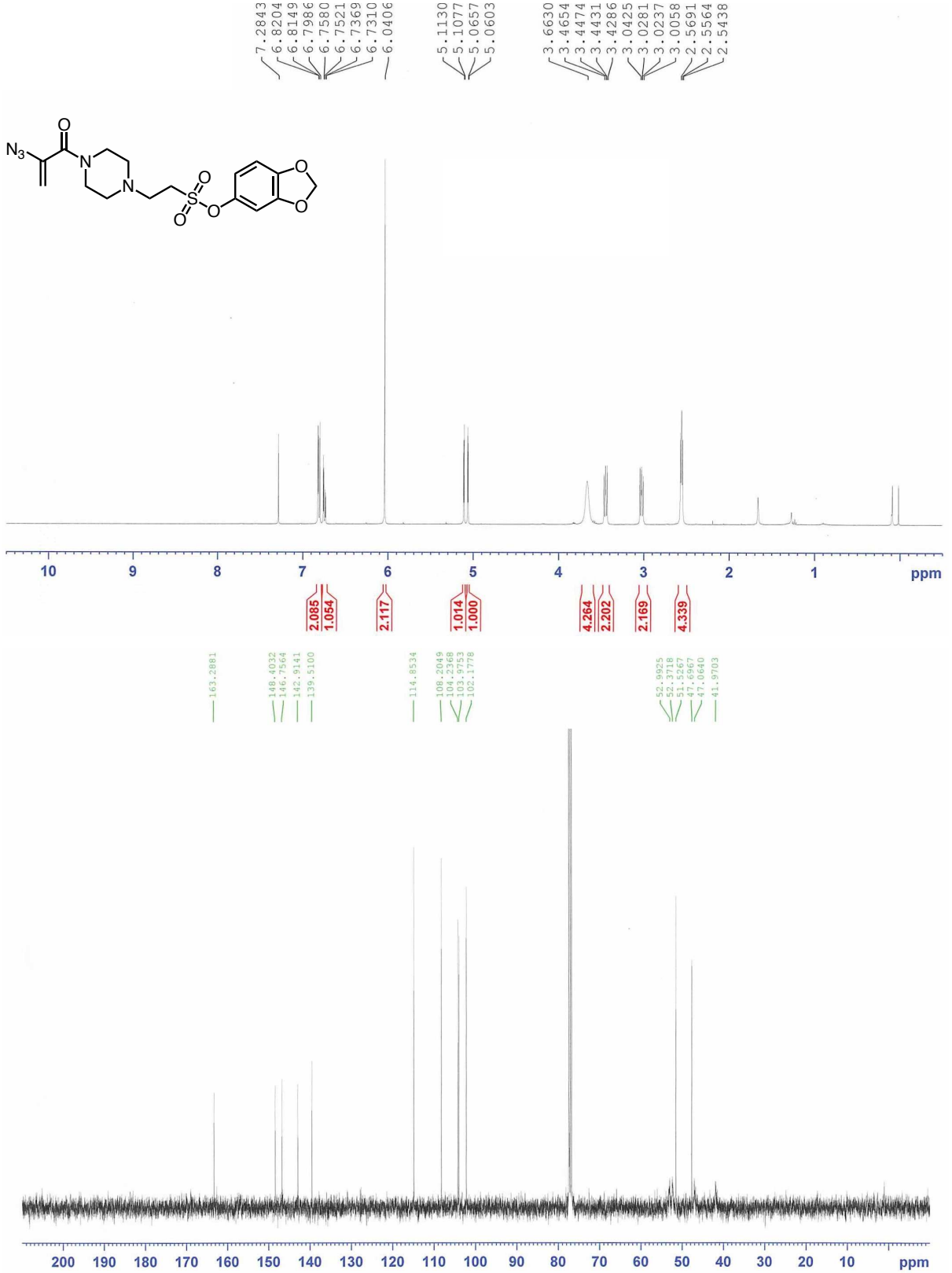


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 2-((3-(2-azidoacrylamido)-5-iodobenzyl)(methyl)amino)ethane-1-sulfonyl fluoride (**1e**) ($CDCl_3$)

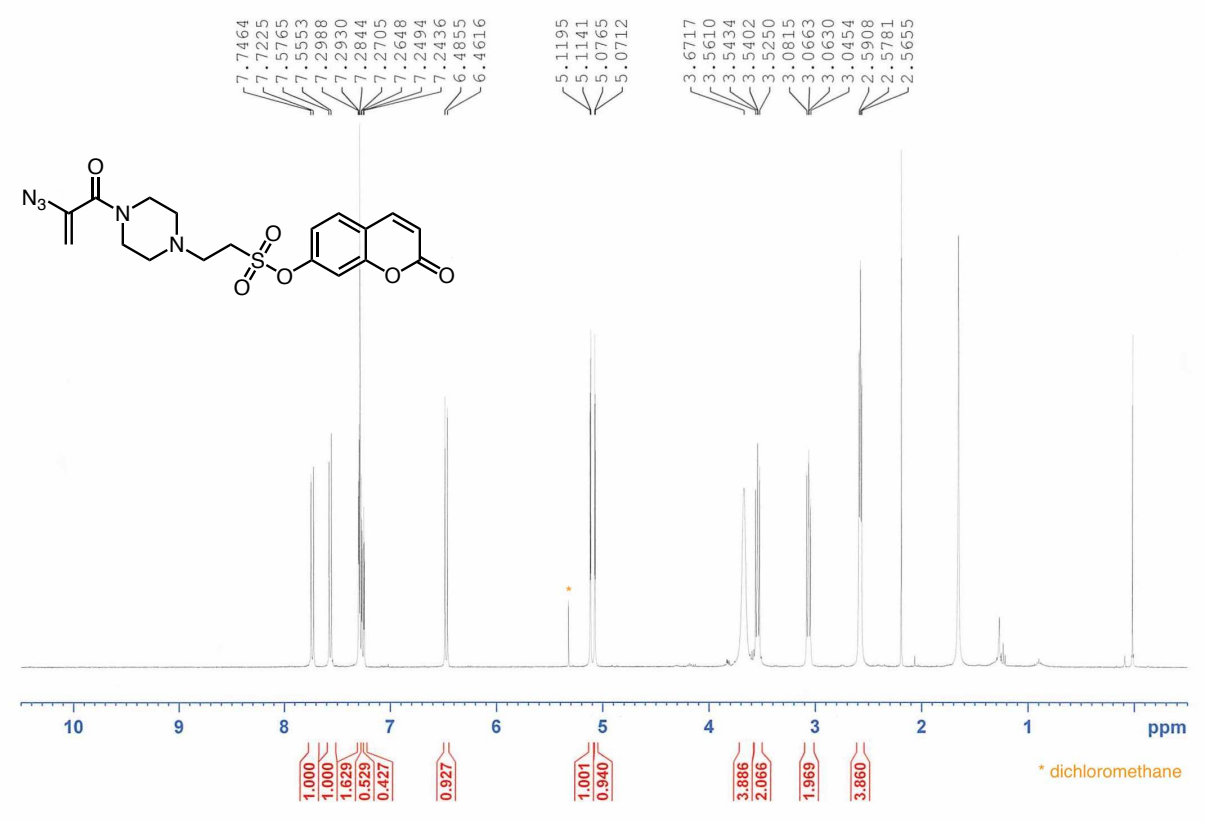


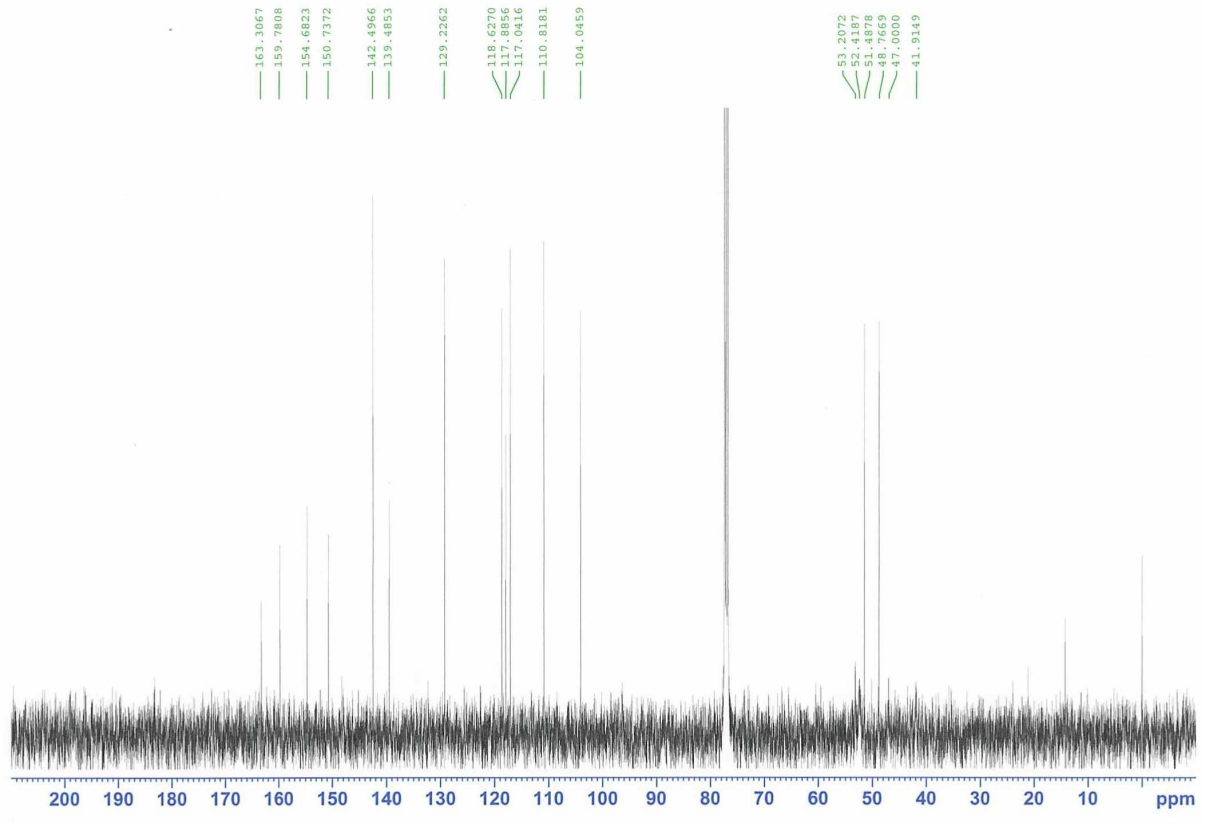


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of benzo[*d*][1,3]dioxol-5-yl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9b**) ($CDCl_3$)

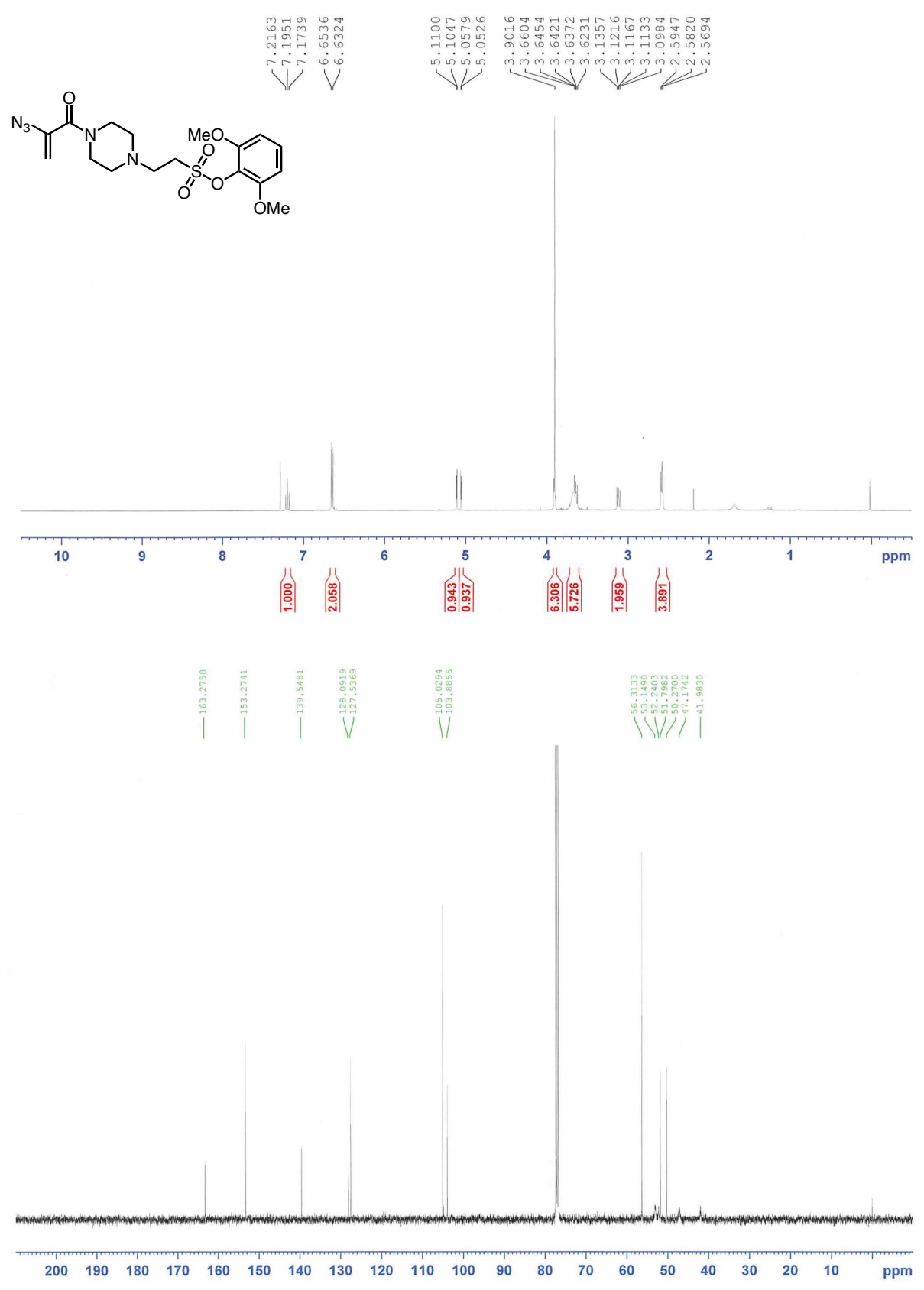


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 2-oxo-2*H*-chromen-7-yl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9c**) ($CDCl_3$)

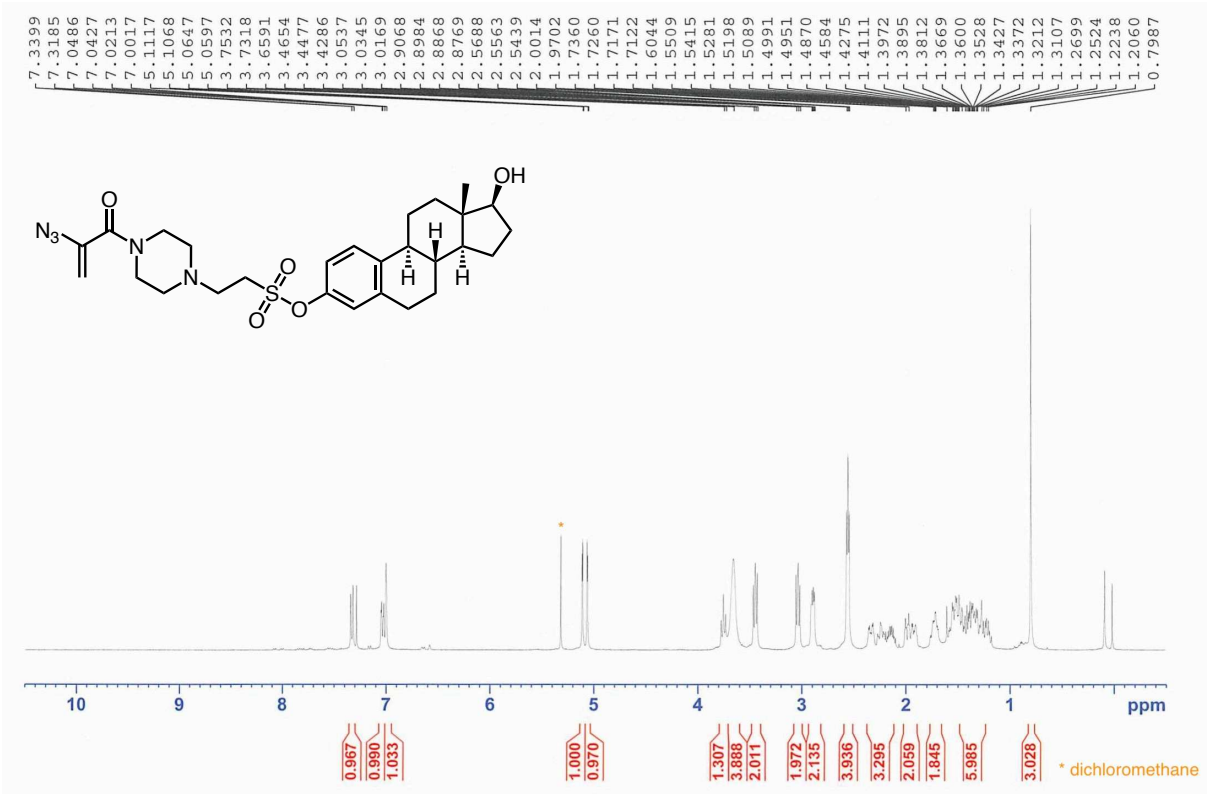


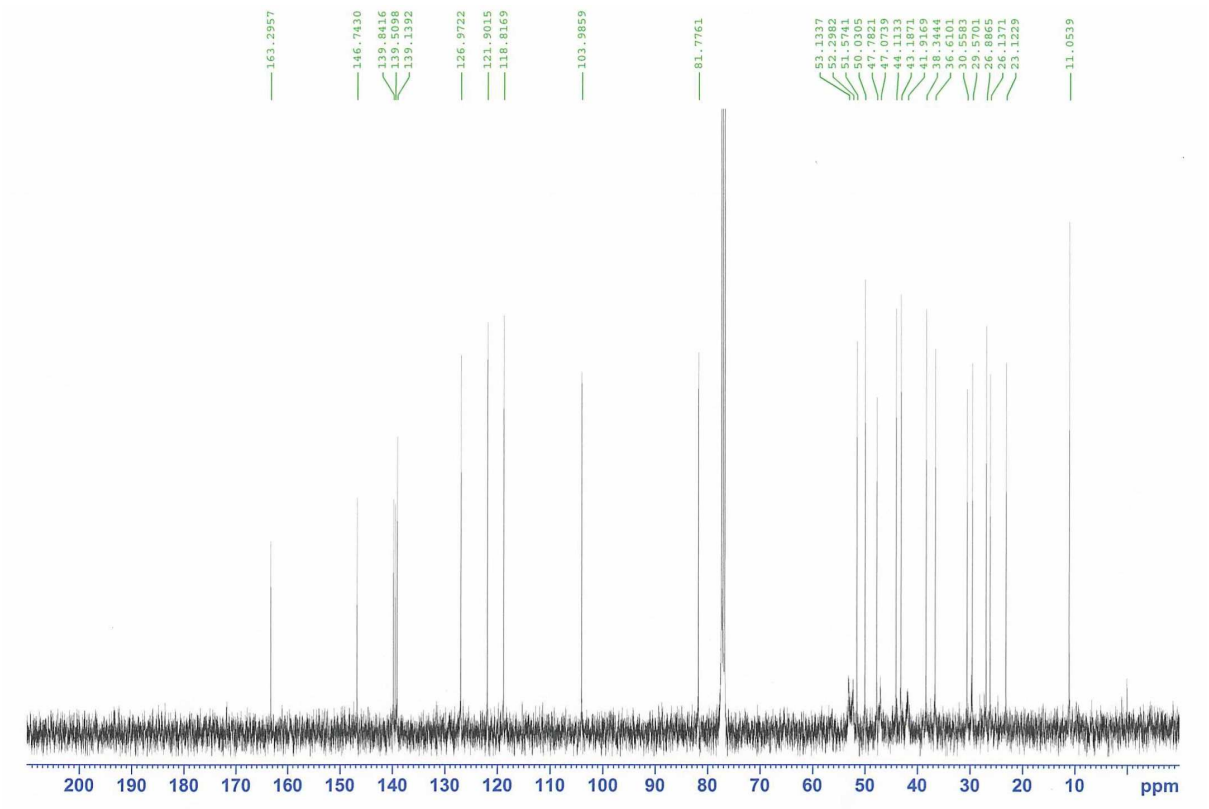


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 2,6-dimethoxyphenyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9d**) ($CDCl_3$)

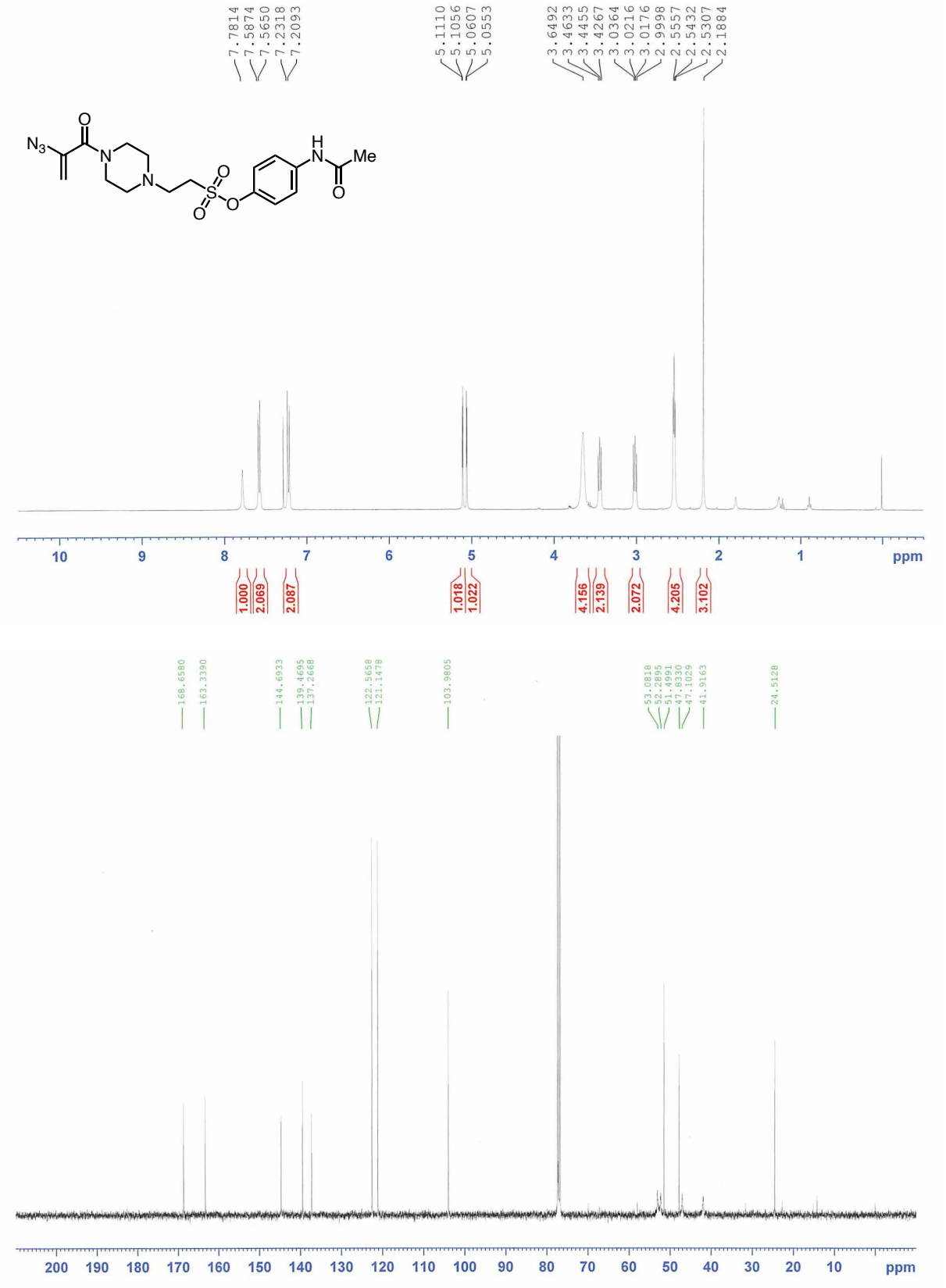


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of (8*R*,9*S*,13*S*,14*S*)-17-hydroxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9e**) ($CDCl_3$)

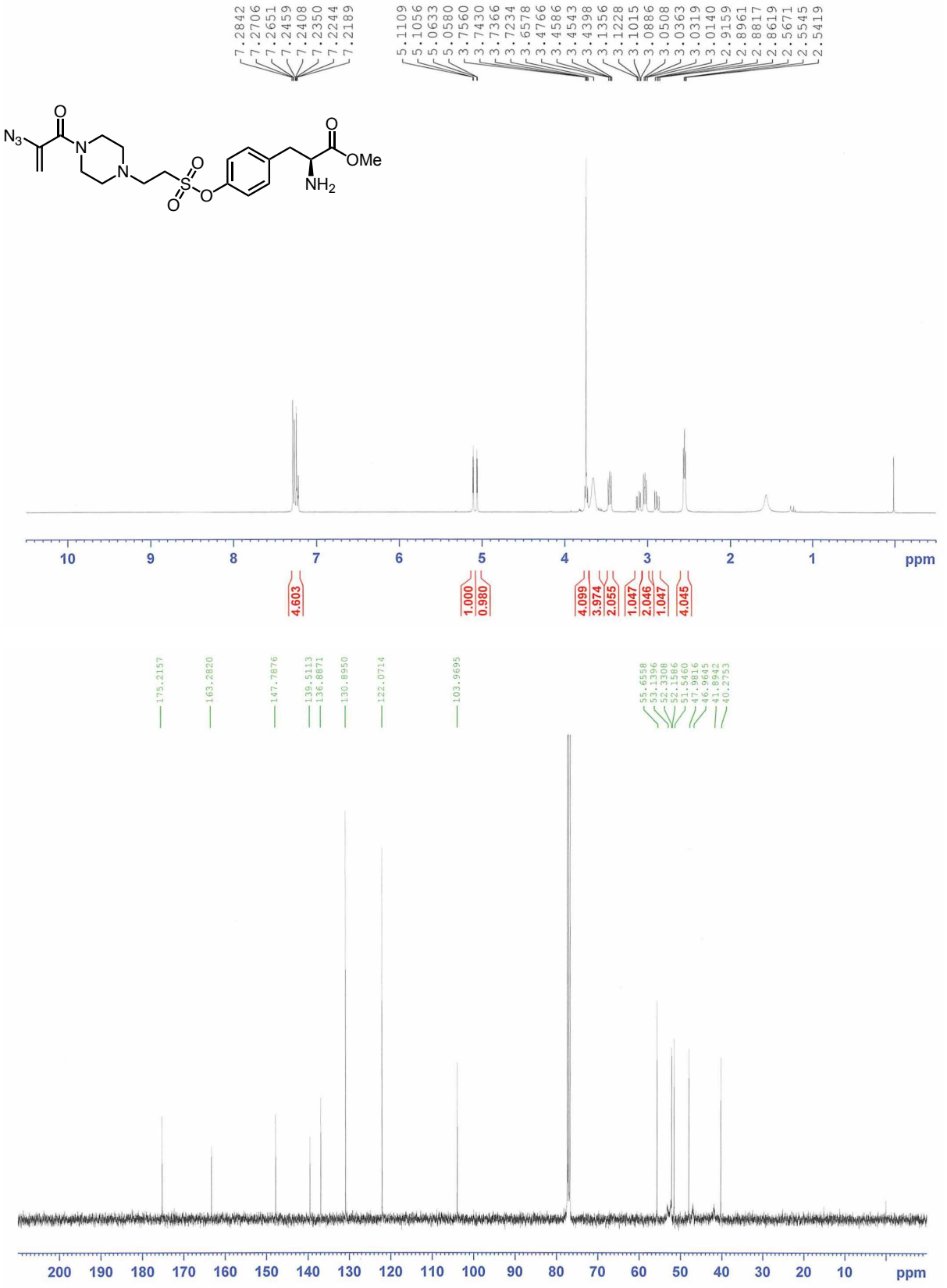




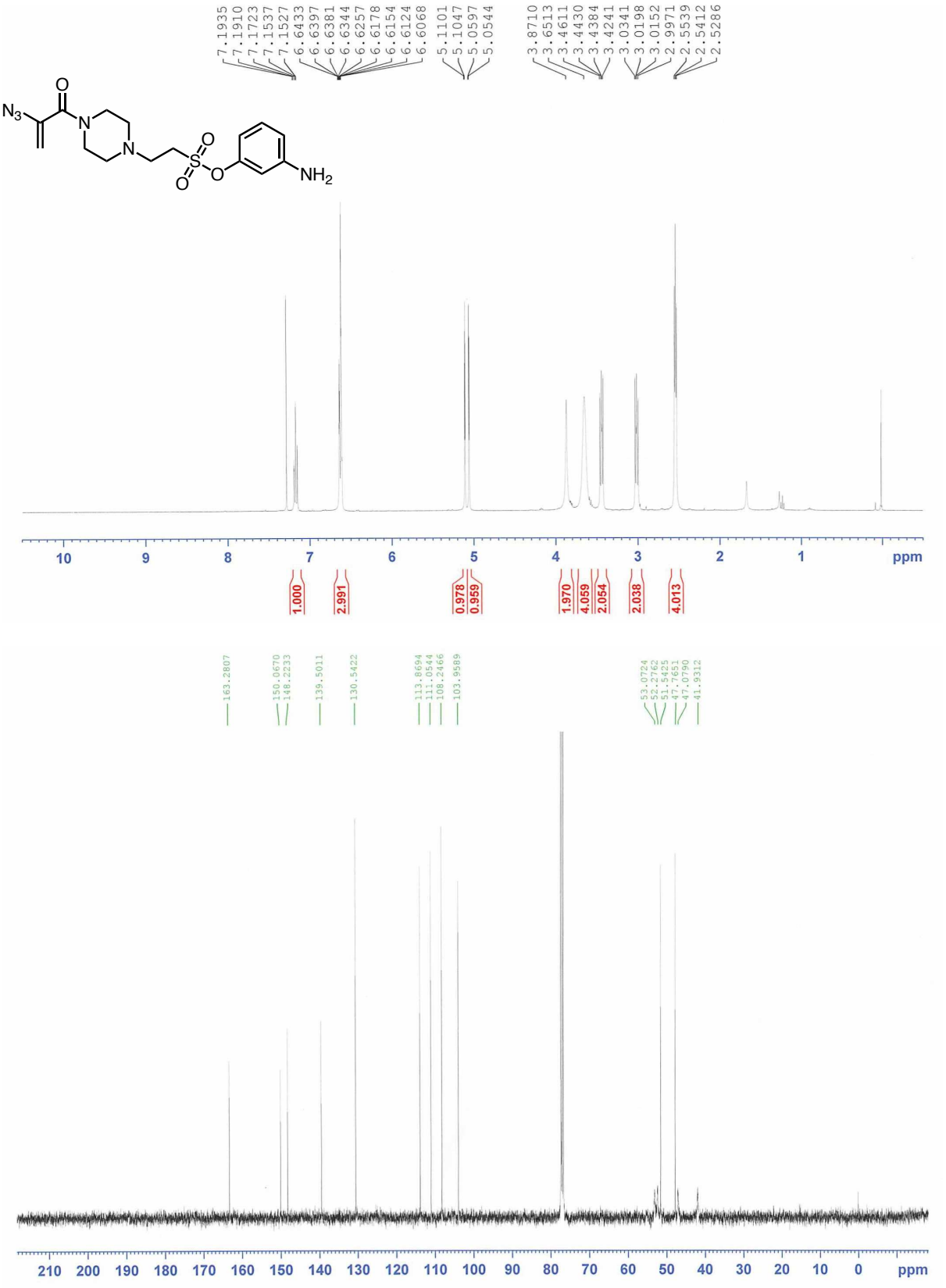
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4-acetamidophenyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9f**) ($CDCl_3$)



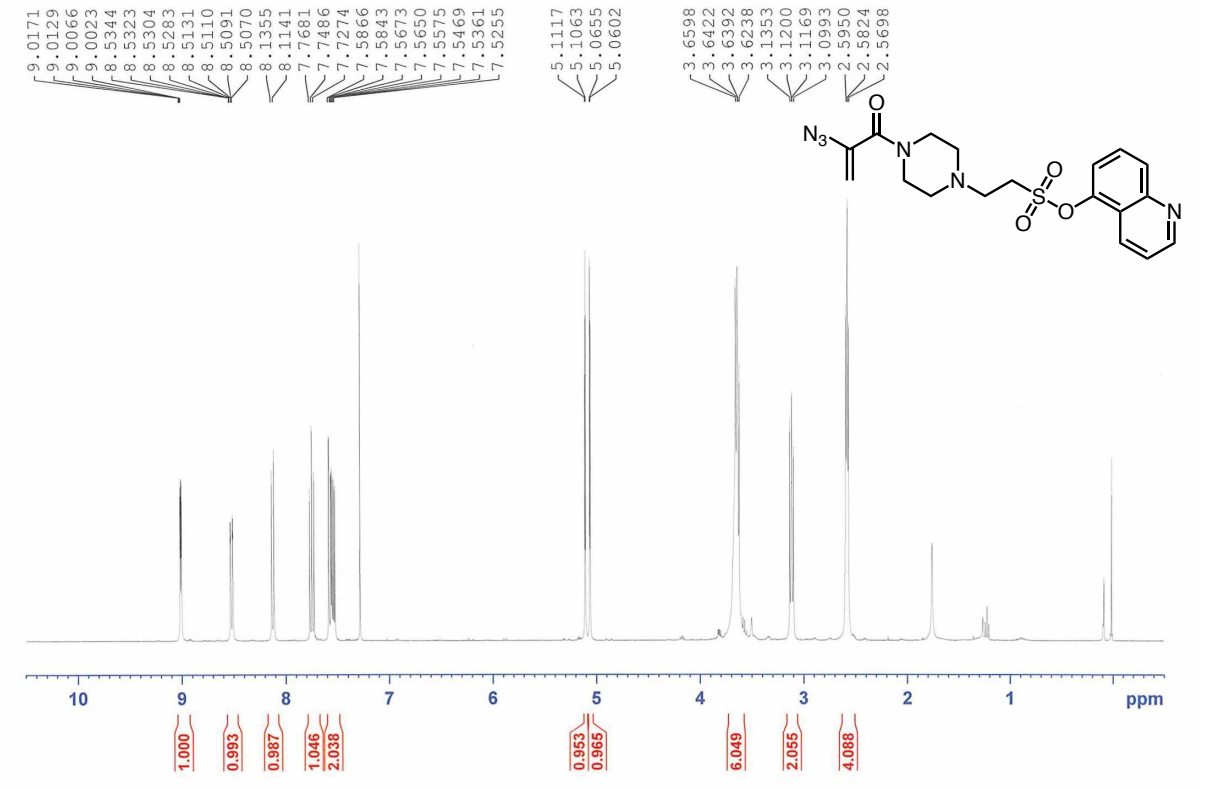
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of methyl (*S*)-2-amino-3-(4-(((2-(4-(2-azidoacryloyl)piperazin-1-yl)ethyl)sulfonyl)oxy)phenyl)propanoate (**9g**) ($CDCl_3$)

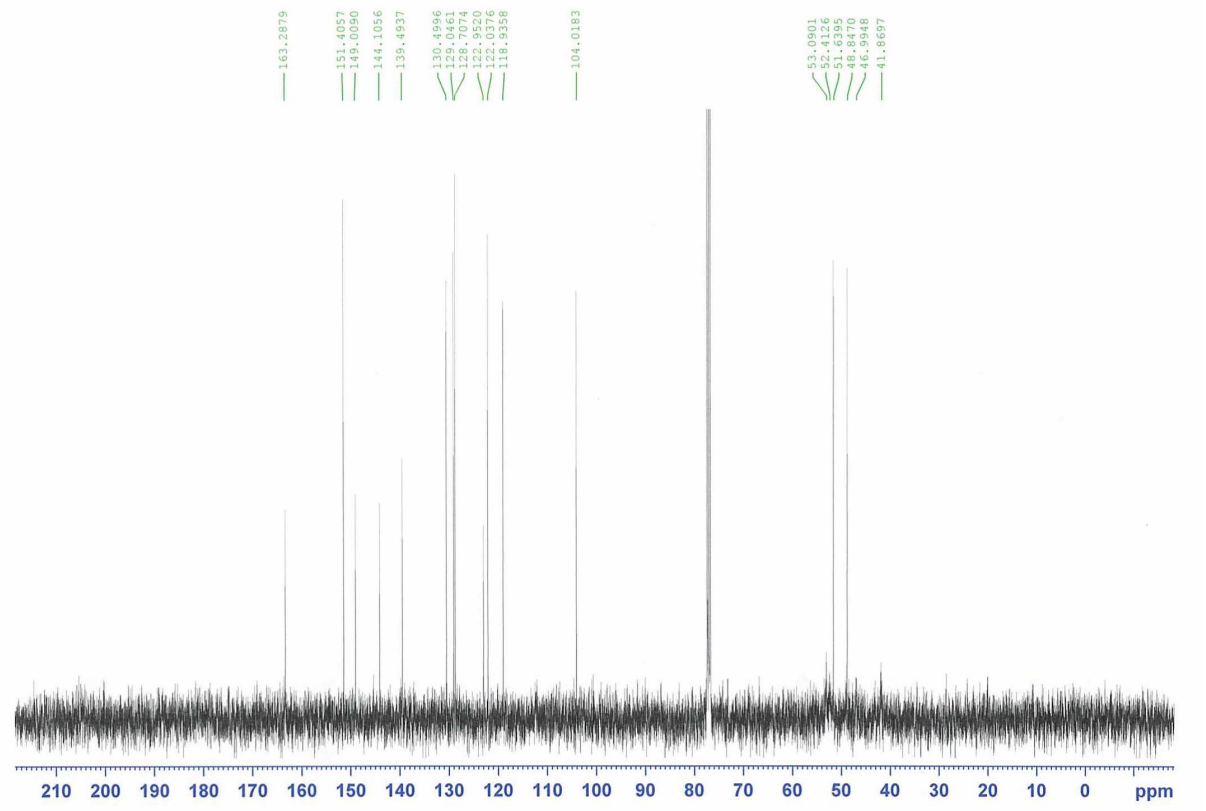


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 3-aminophenyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9h**) ($CDCl_3$)

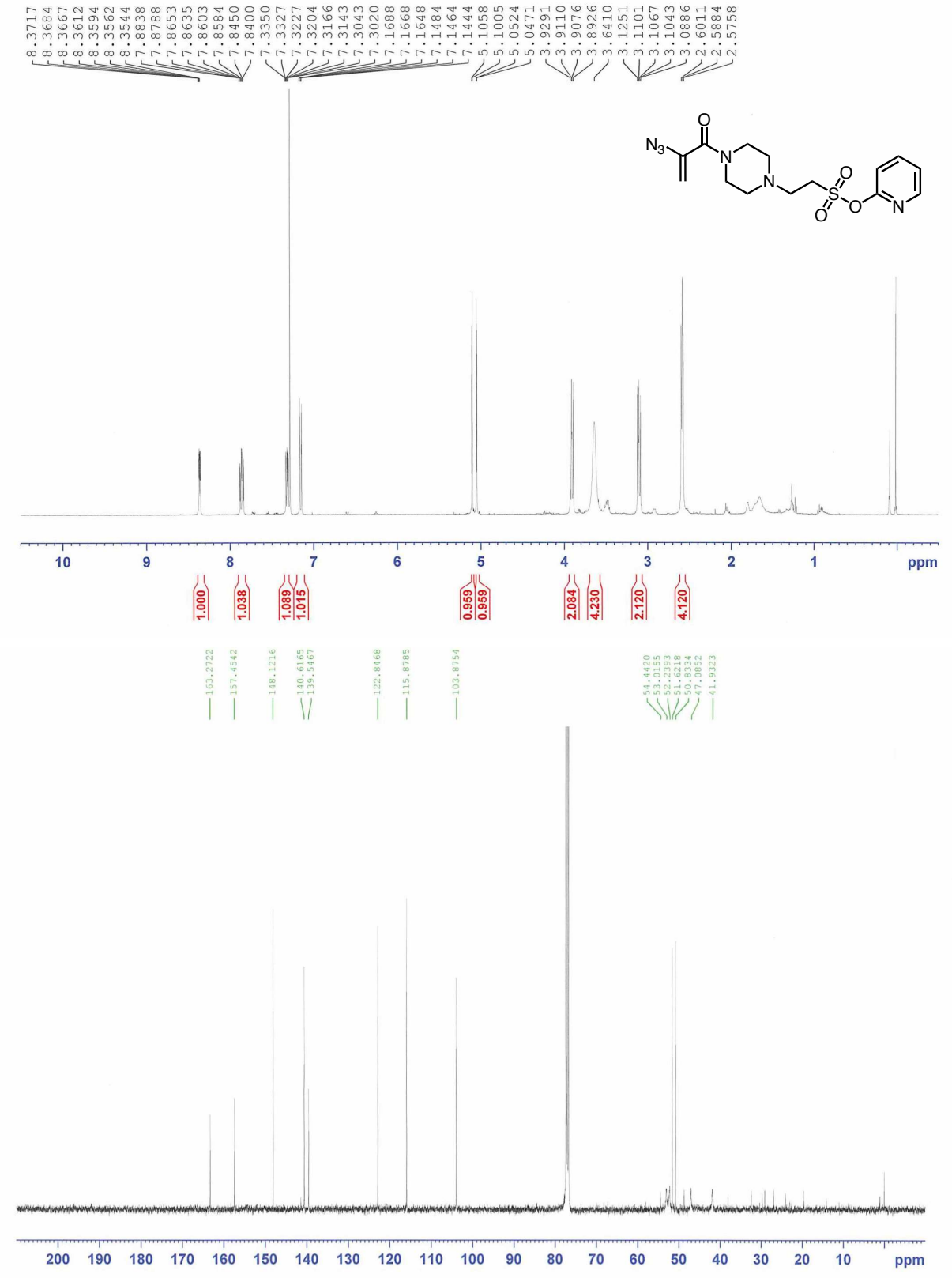


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of quinolin-5-yl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9i**) ($CDCl_3$)

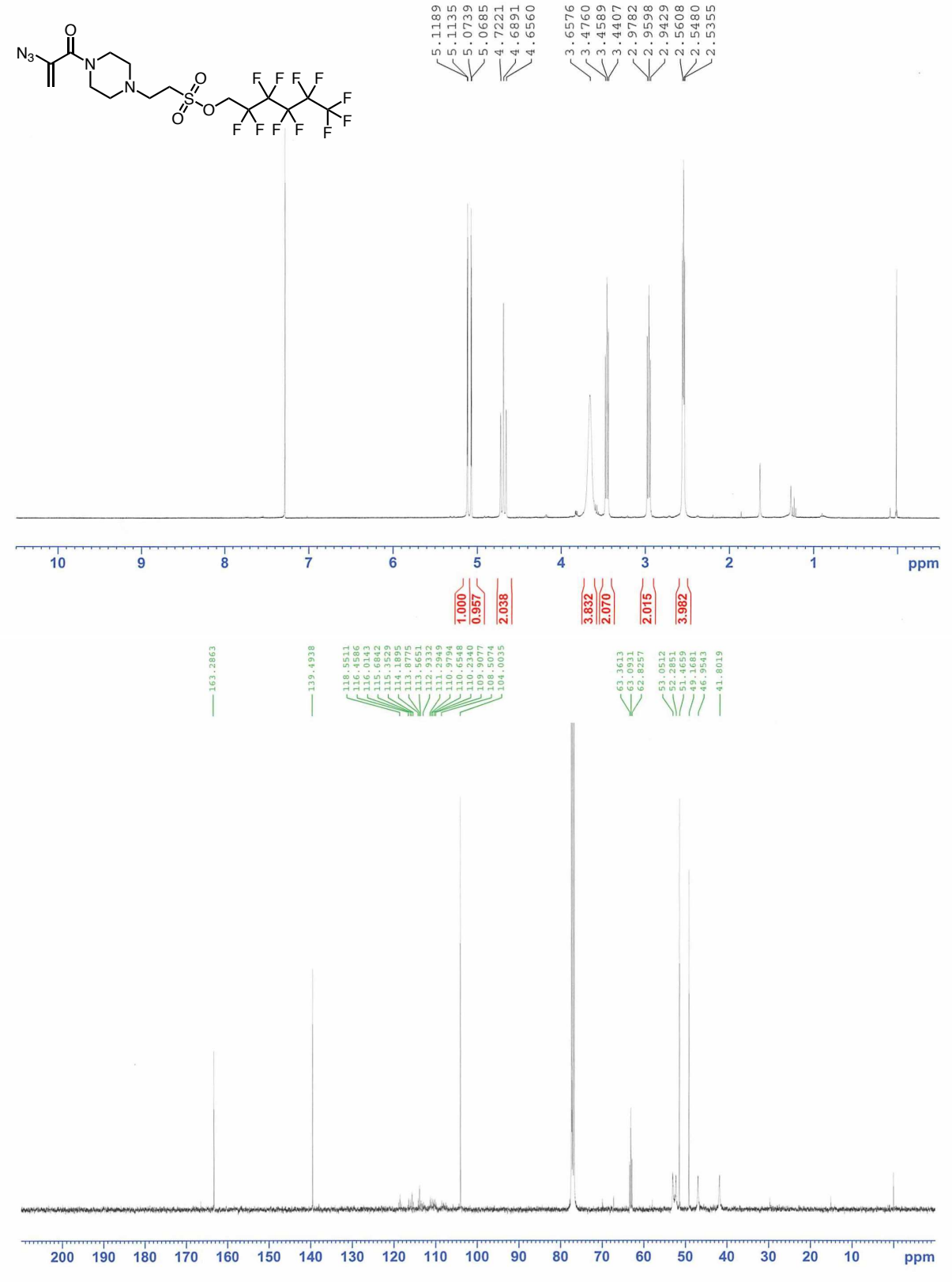




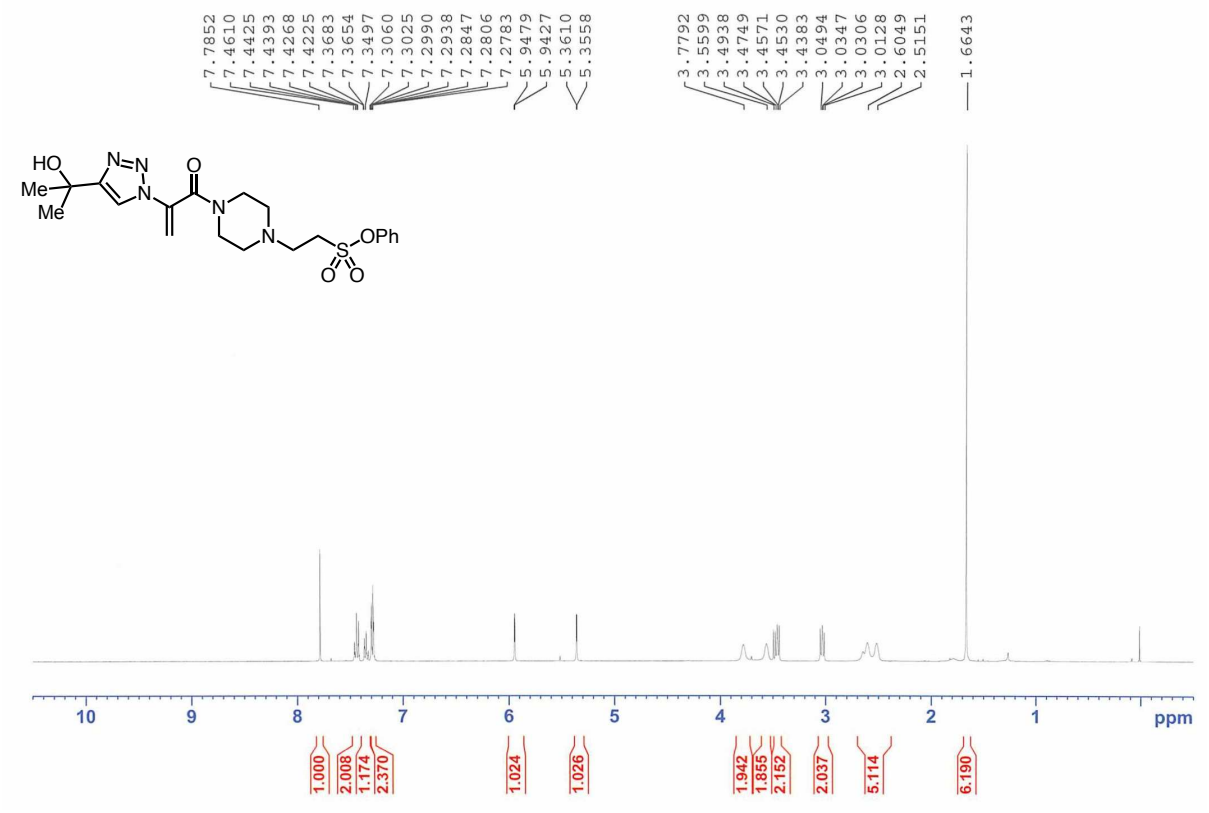
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of pyridin-2-yl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9j**) ($CDCl_3$)

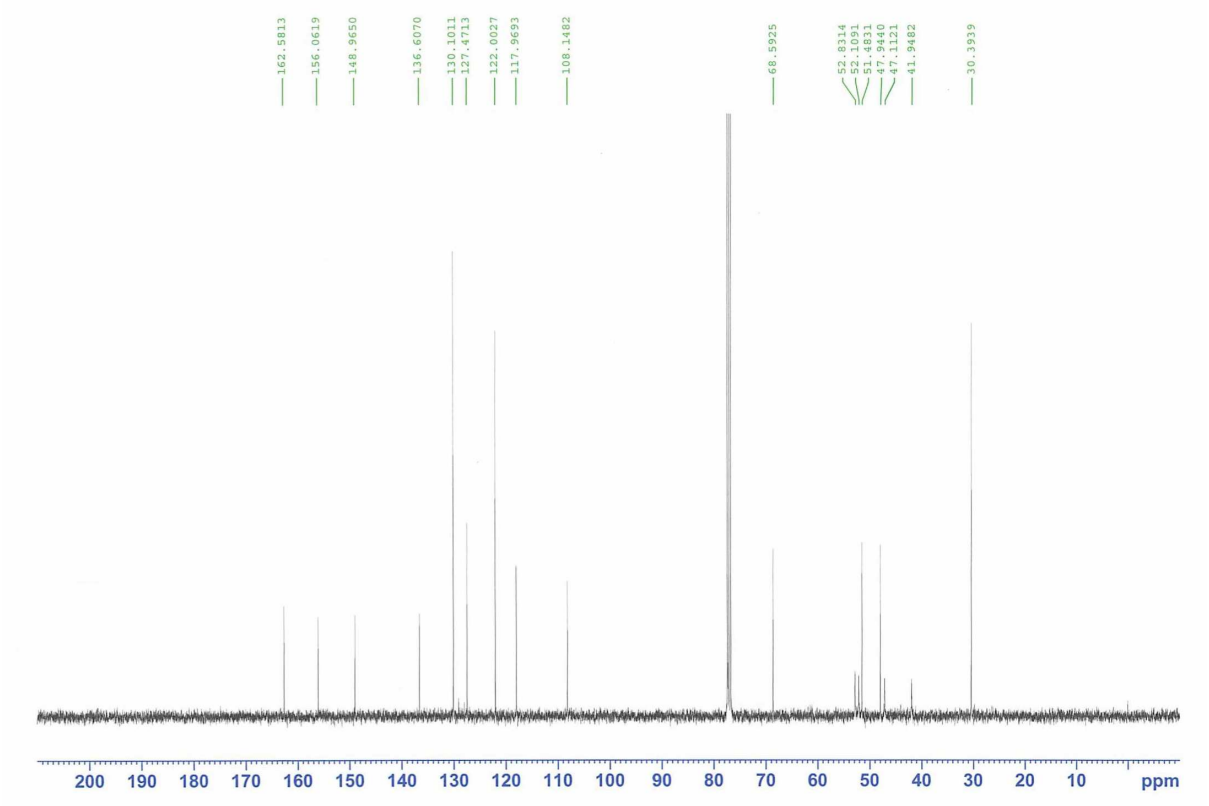


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 3,3,4,4,5,5,6,6,6-undecafluorohexyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**9k**) ($CDCl_3$)

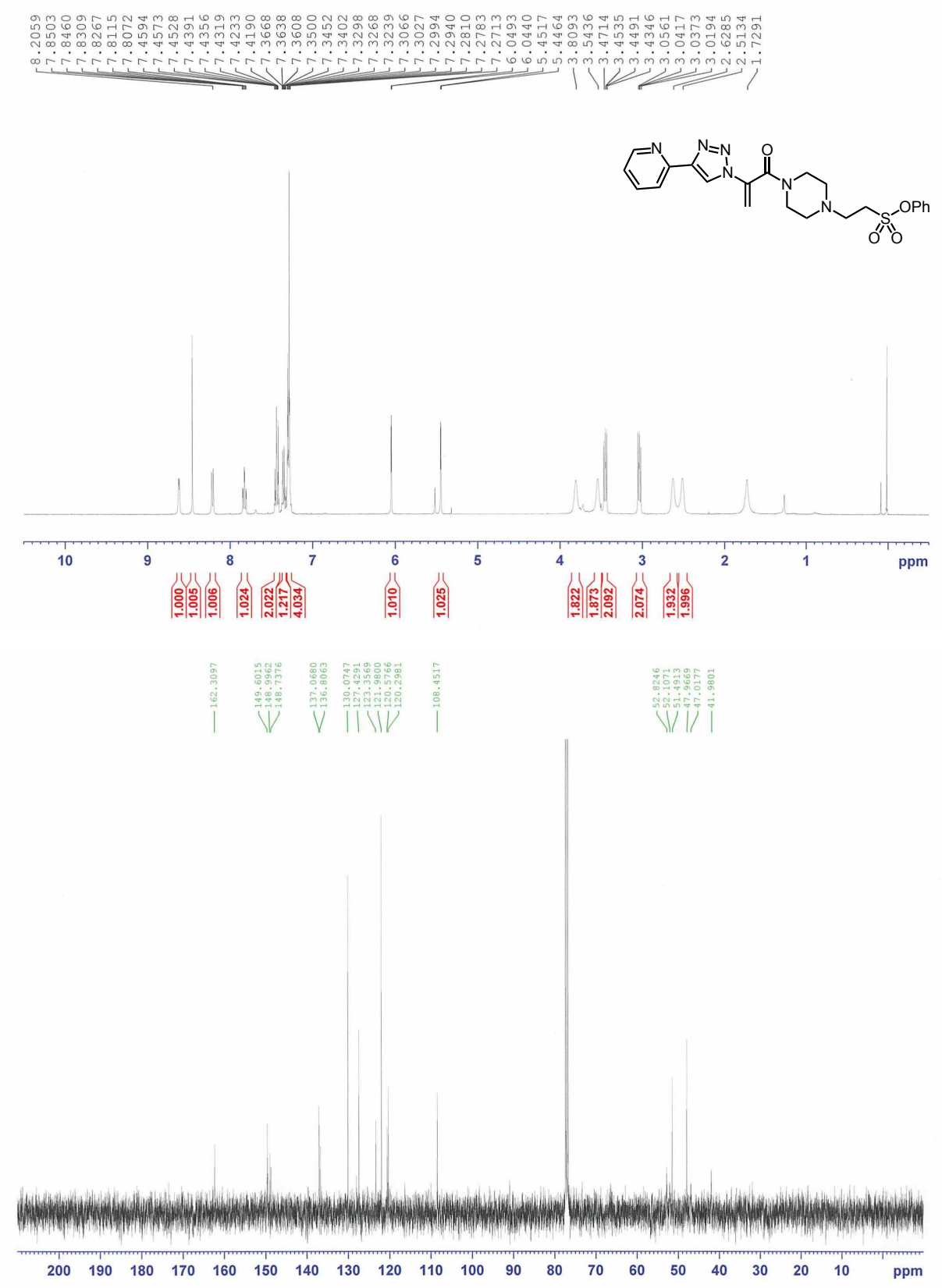


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of phenyl 2-(4-(2-(4-(2-hydroxypropan-2-yl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10b**) ($CDCl_3$)

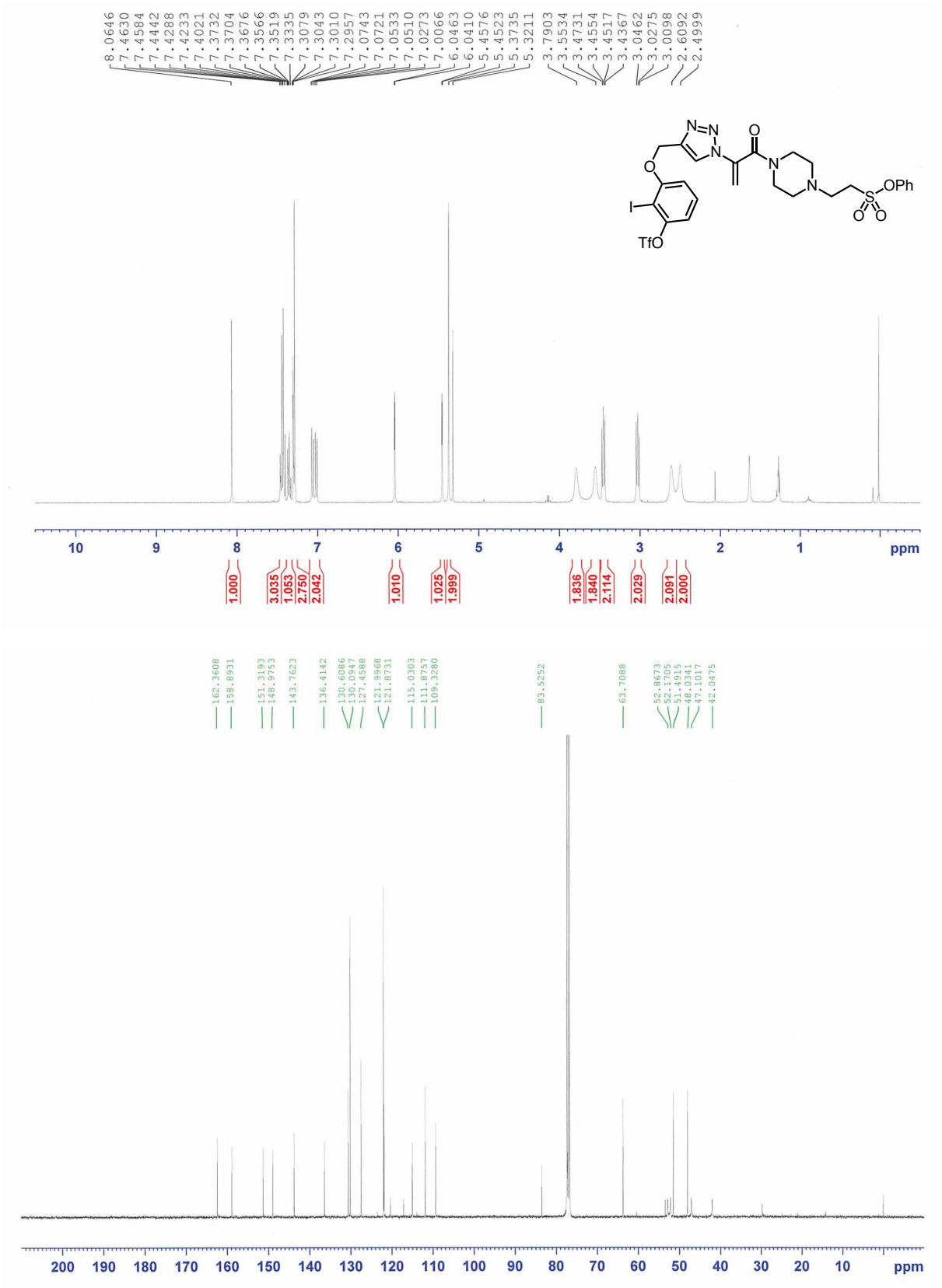




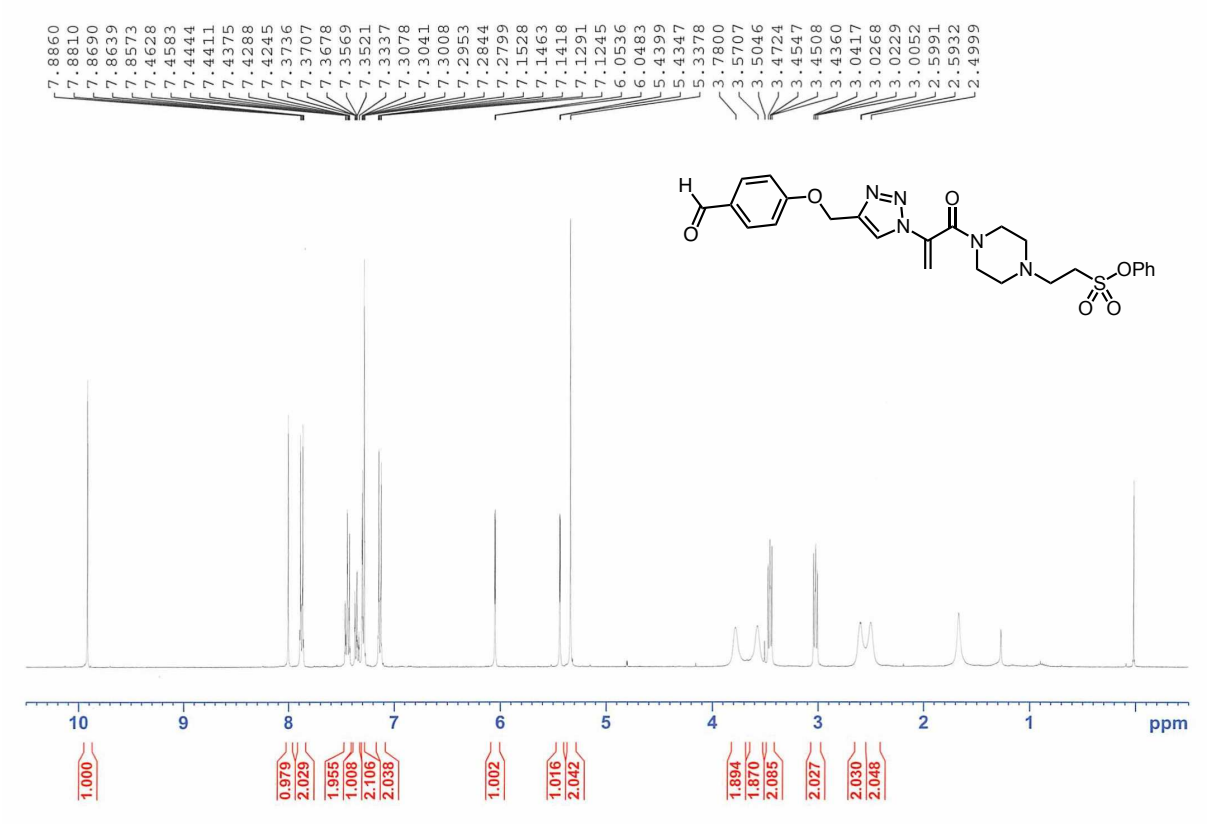
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of phenyl 2-(4-(2-(4-(pyridin-2-yl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10c**) ($CDCl_3$)

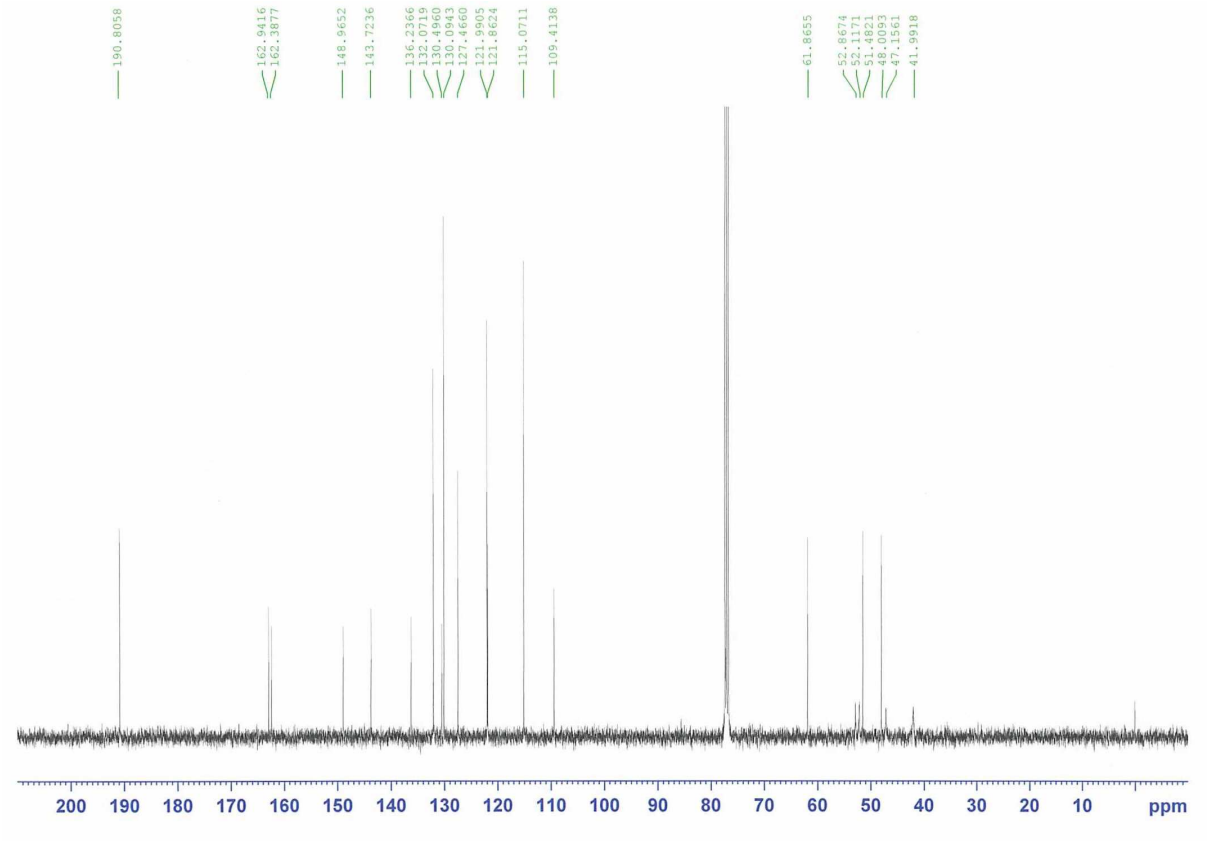


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of phenyl 2-(4-(2-(4-((2-iodo-3-(((trifluoromethyl)sulfonyl)oxy)phenoxy)methyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10d**) ($CDCl_3$)

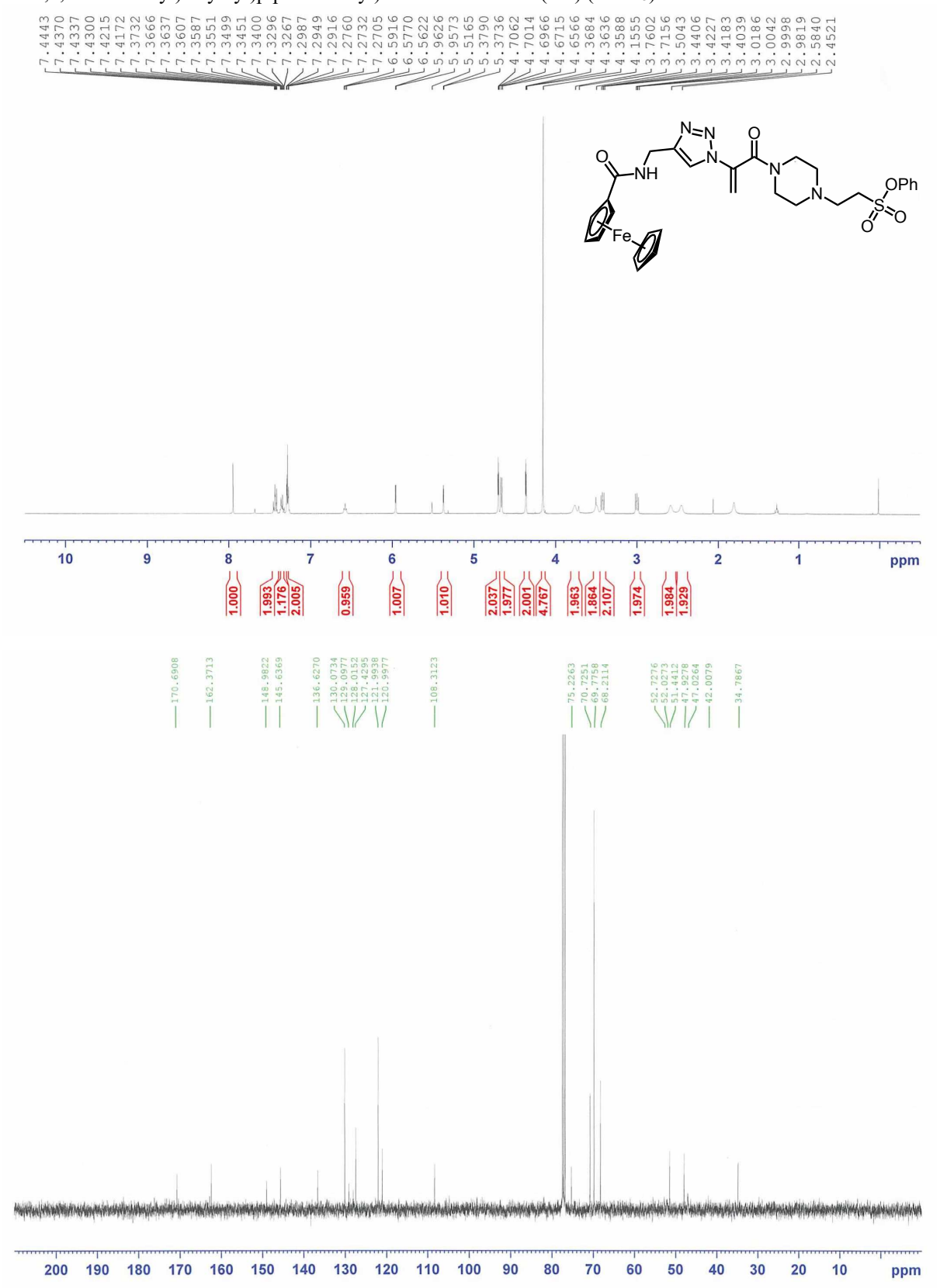


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of phenyl 2-(4-(2-(4-((4-formylphenoxy)methyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10e**) ($CDCl_3$)

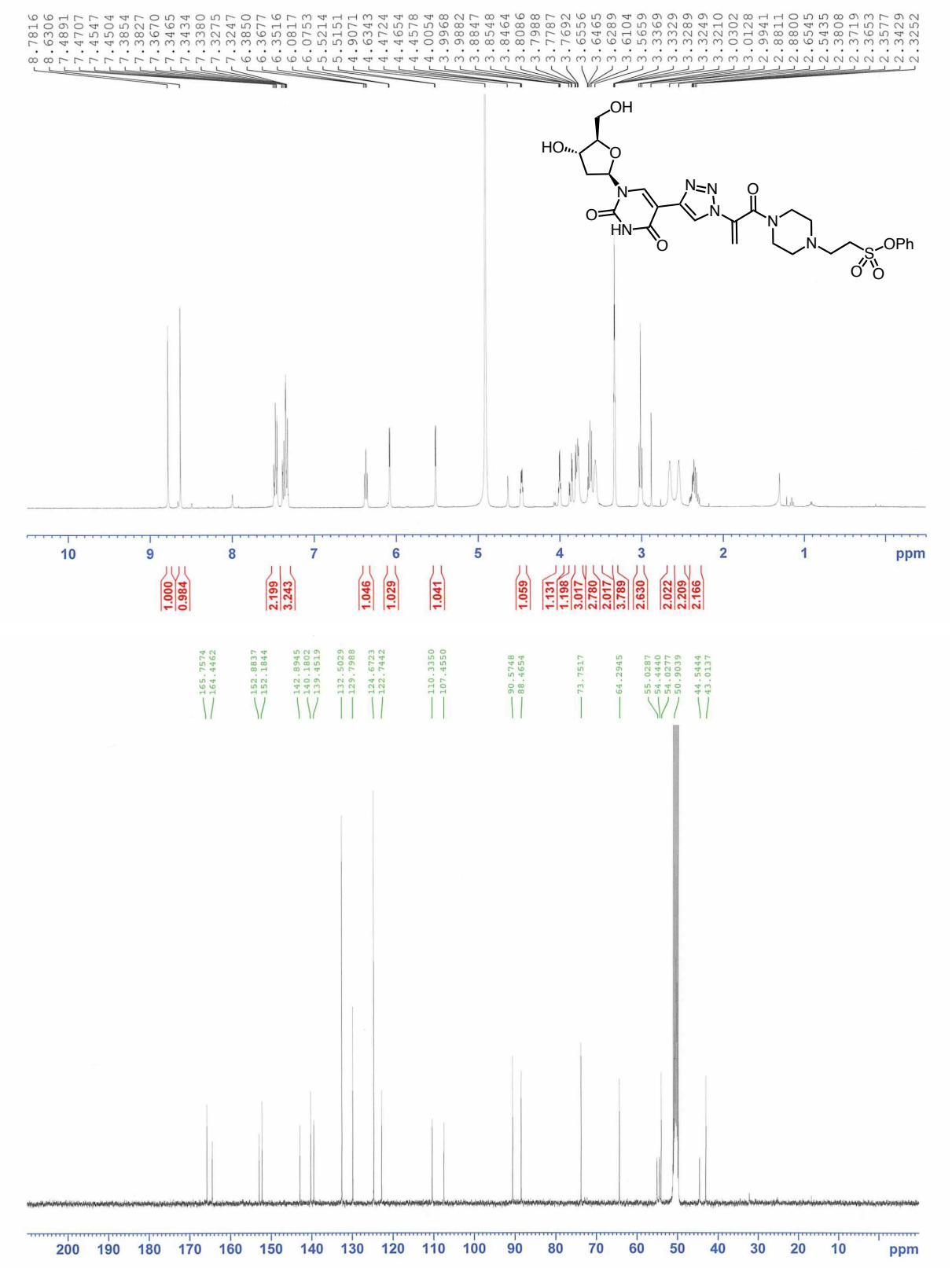




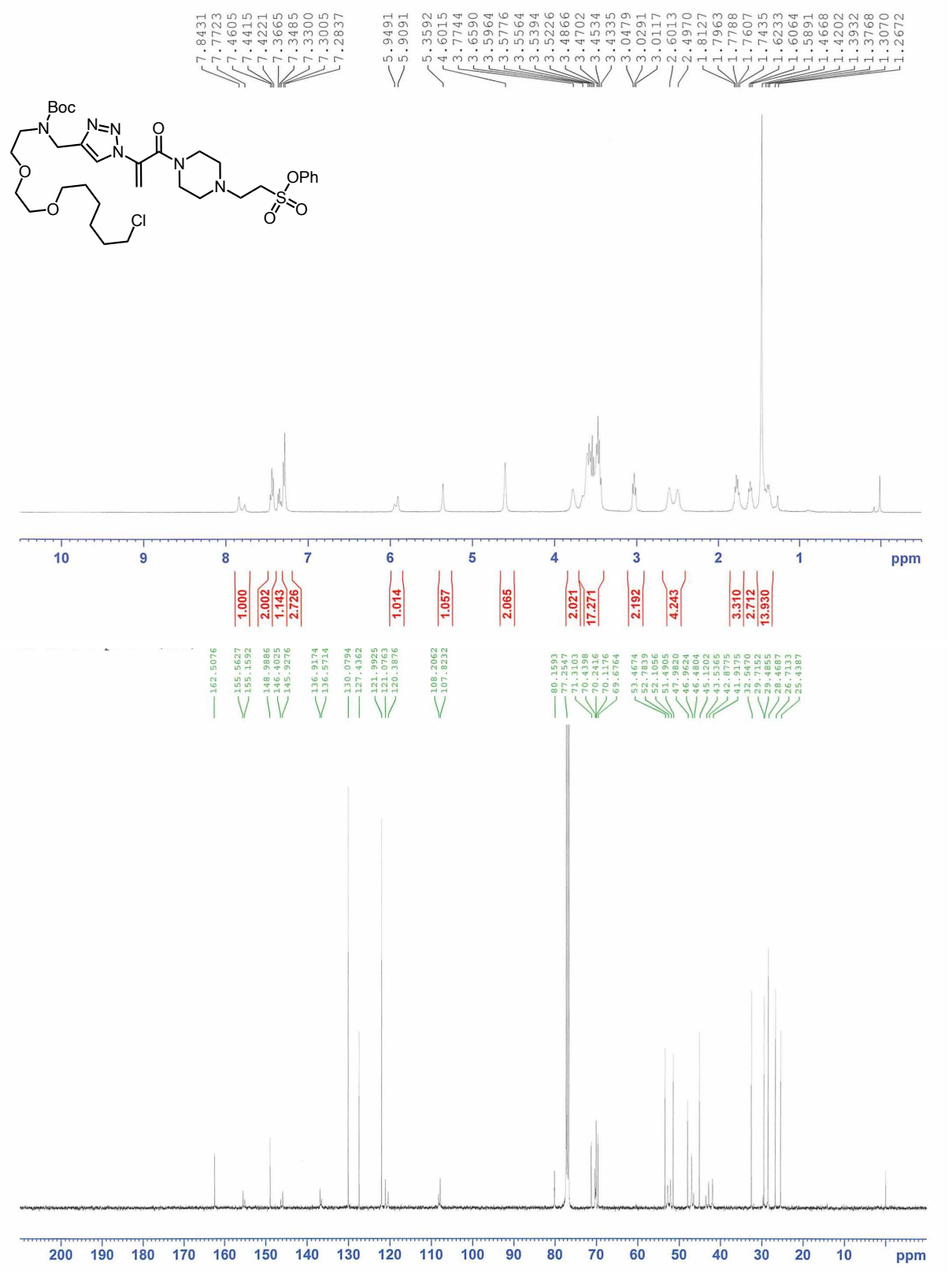
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of phenyl 2-(4-(2-(4-((ferrocennylcarbonylamino)methyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10f**) ($CDCl_3$)



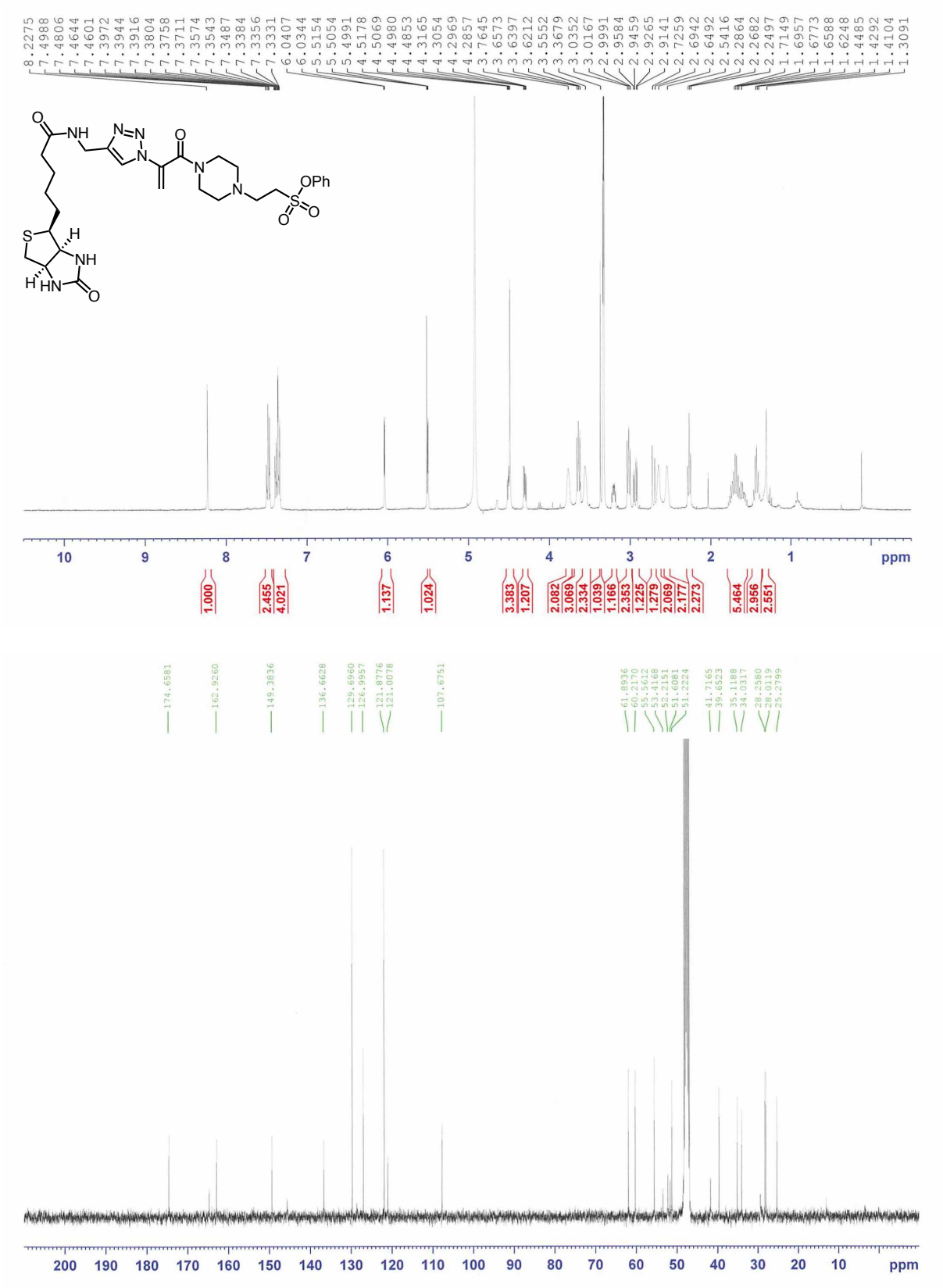
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of phenyl 2-(4-(2-(4-(1-((2*R*,4*S*,5*R*)-4-hydroxy-5-(hydroxymethyl)tetrahydrofuran-2-yl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10g**) (CD_3OD)



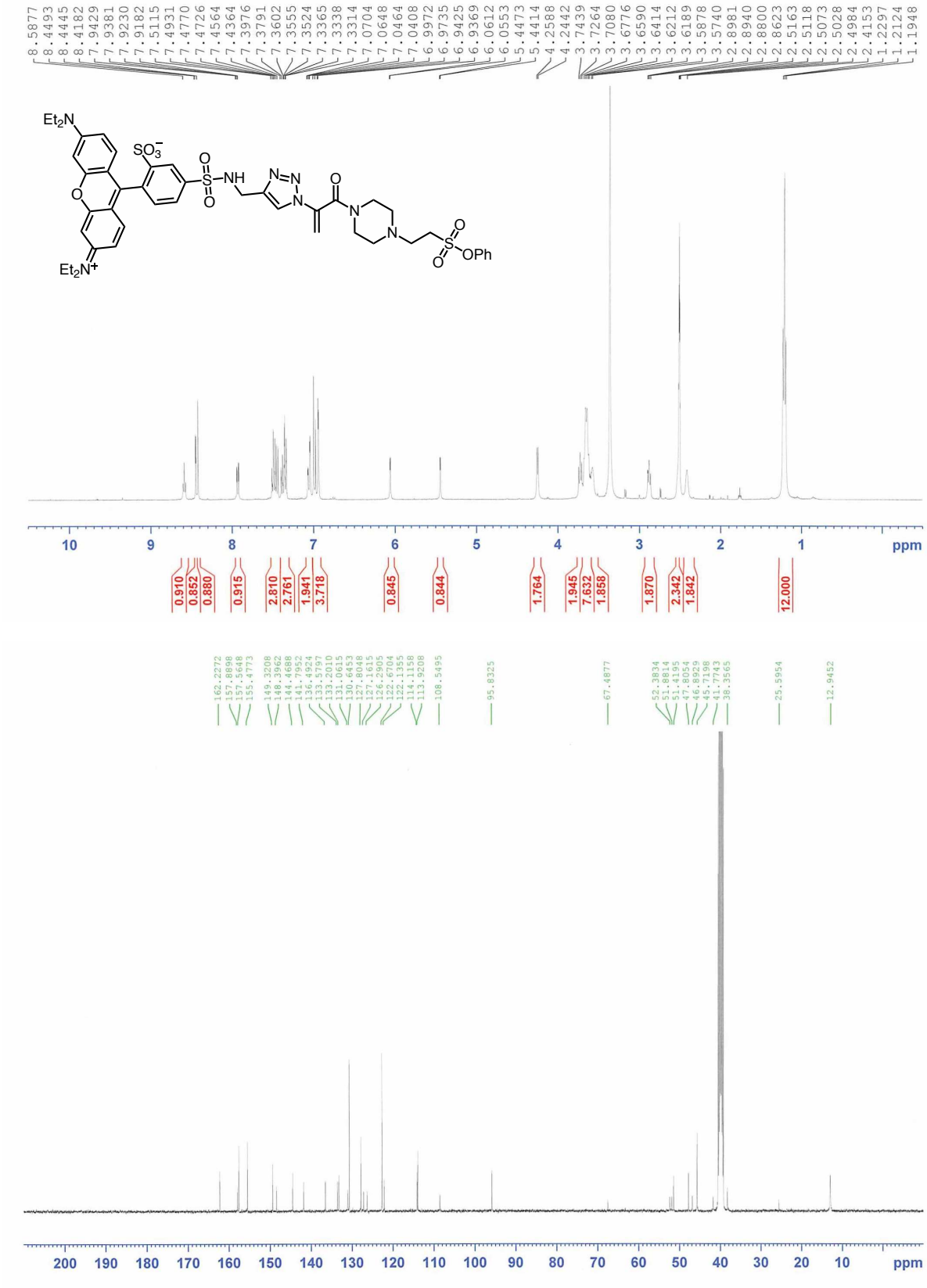
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of phenyl 2-(4-(2-(4-(((*tert*-butoxycarbonyl)(2-(2-((6-chlorohexyl)oxy)ethoxy)ethyl)amino)methyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10h**) ($CDCl_3$)



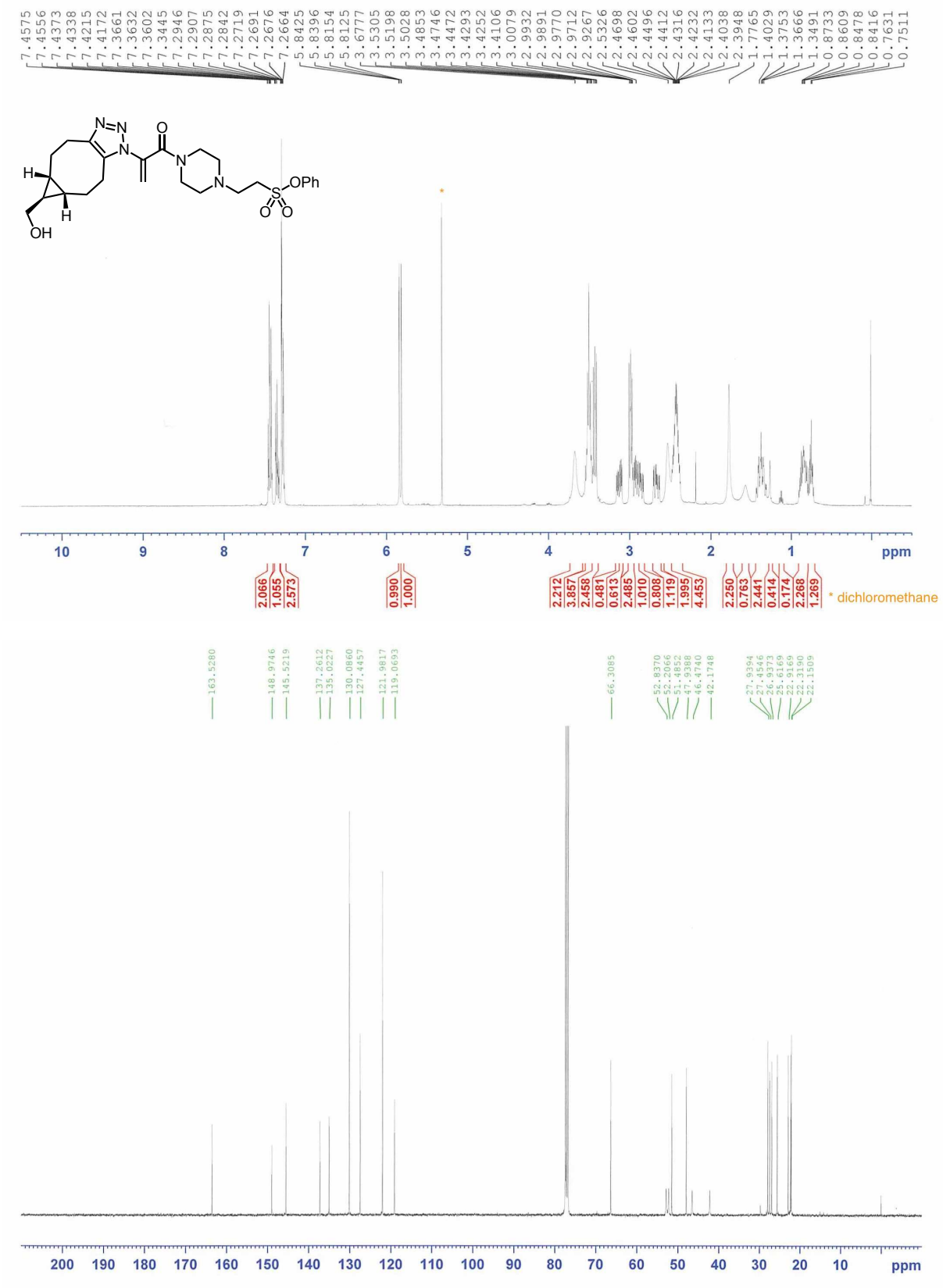
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of phenyl 2-(4-(2-(4-((5-((3a*R*,4*R*,6a*S*)-2-oxohexahydro-1*H*-thieno[3,4-*d*]imidazol-4-yl)pentanamido)methyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10i**) (CD_3OD)



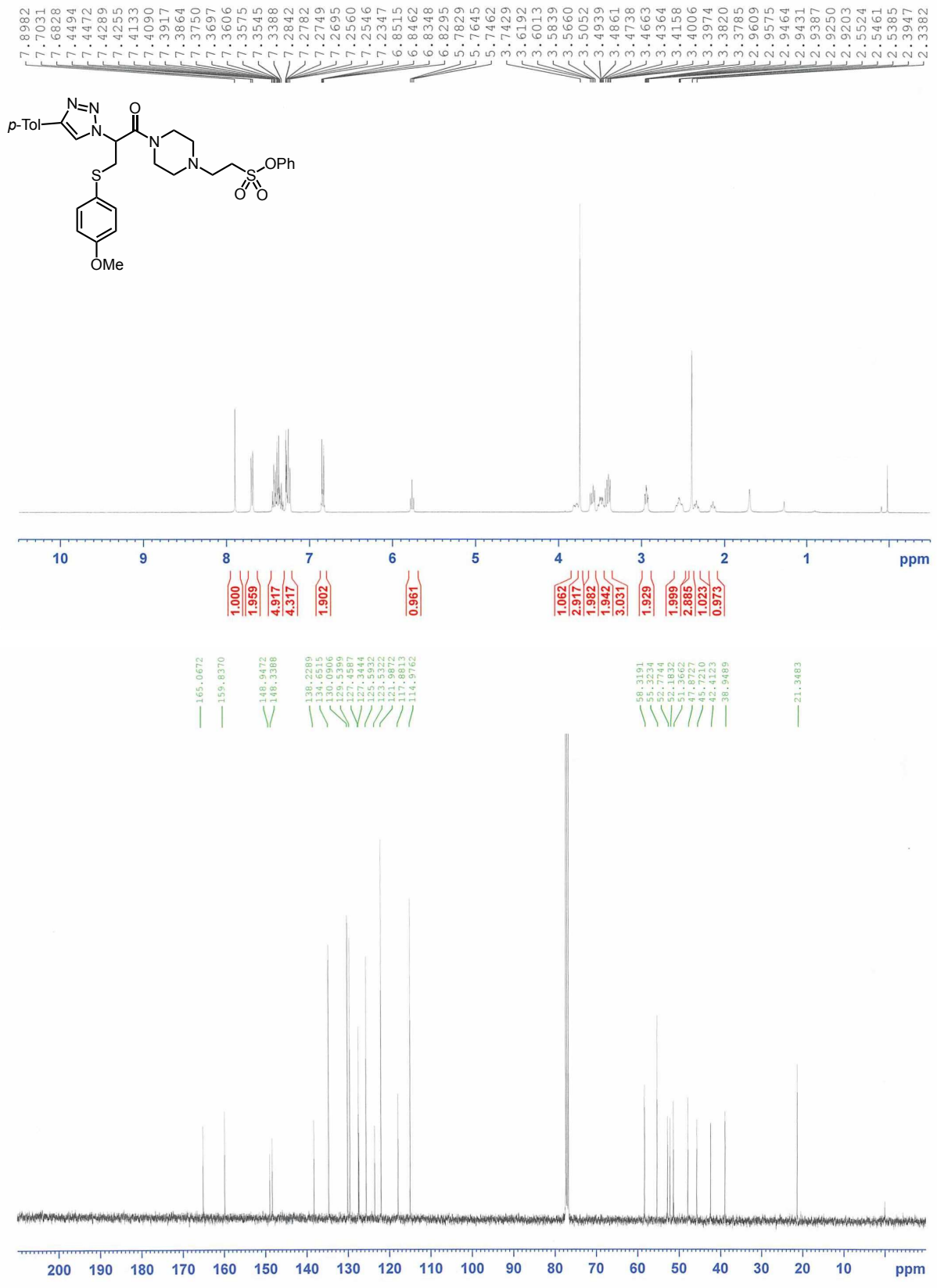
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 2-(6-(diethylamino)-3-(diethyliminio)-3*H*-xanthen-9-yl)-5-(*N*-((1-(3-oxo-3-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)prop-1-en-2-yl)-1*H*-1,2,3-triazol-4-yl)methyl)sulfamoyl)benzenesulfonate (**10j**) (DMSO-d_6)



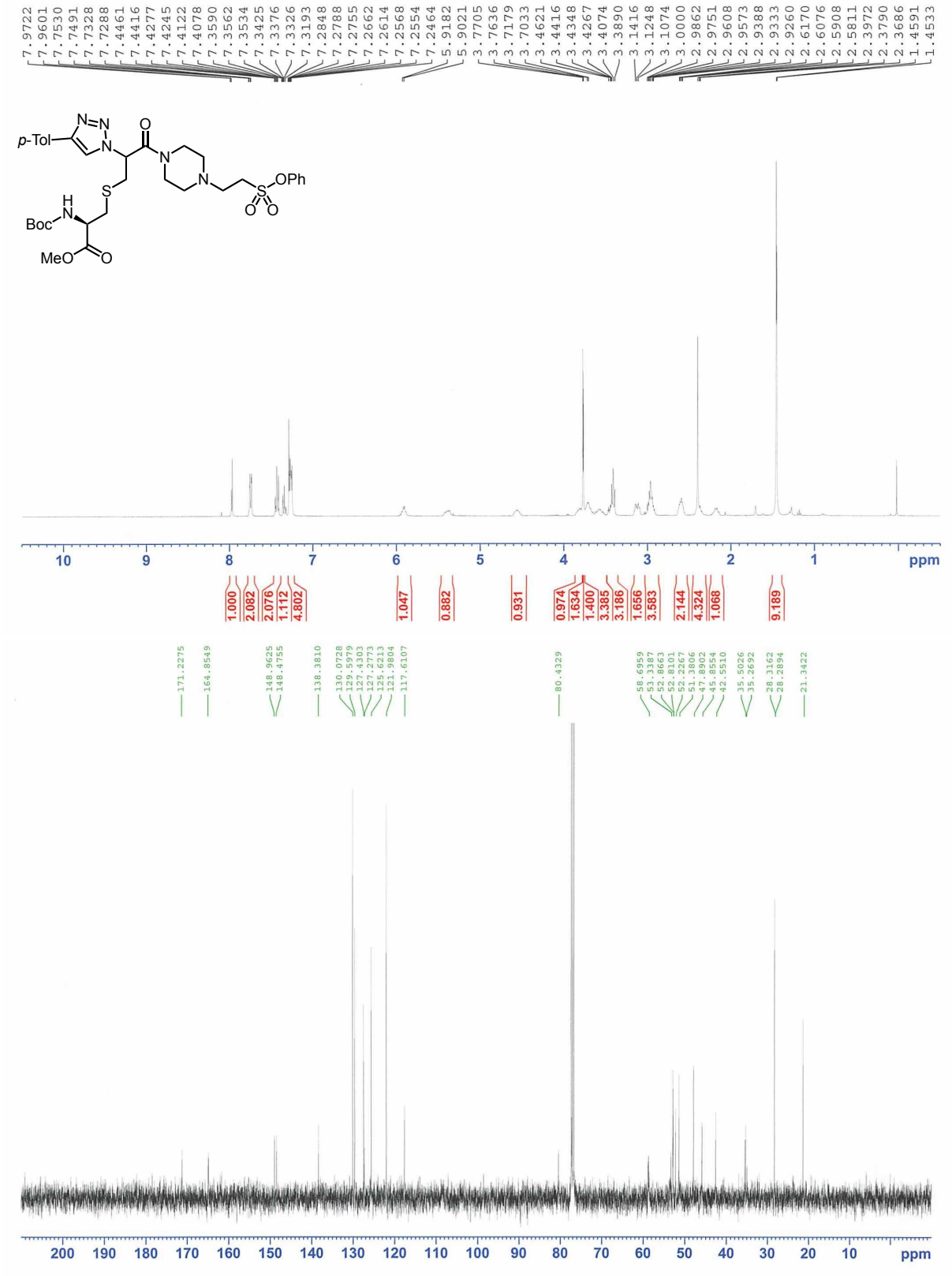
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of phenyl 2-(4-(2-((5a*R*,6*R*,6a*S*)-6-(hydroxymethyl)-5,5a,6,6a,7,8-hexahydrocyclopropa[5,6]cycloocta[1,2-*d*][1,2,3]triazol-1(4H)-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**10k**) ($CDCl_3$)



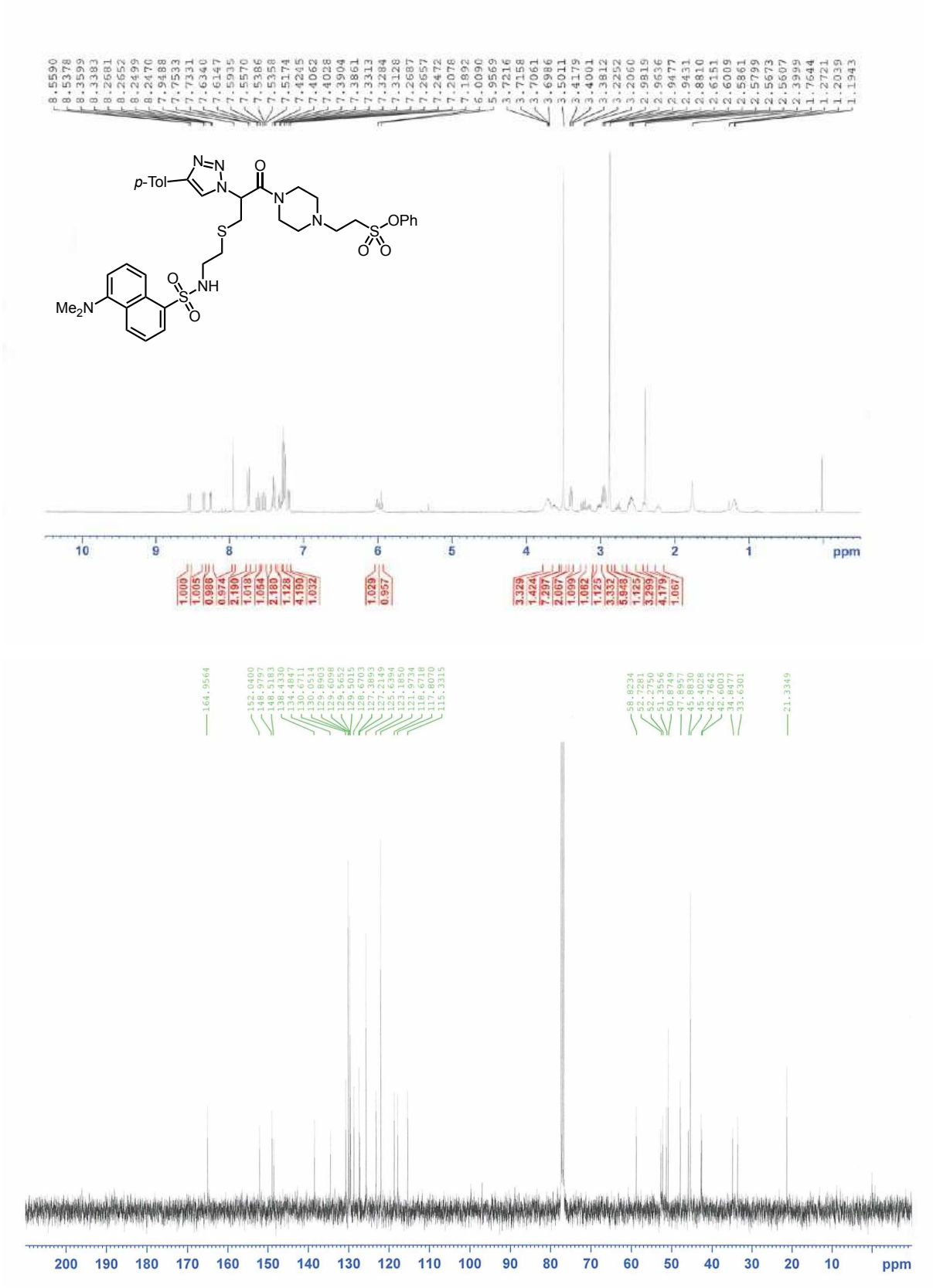
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of phenyl 2-(4-(3-((4-methoxyphenyl)thio)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**5b**) ($CDCl_3$)



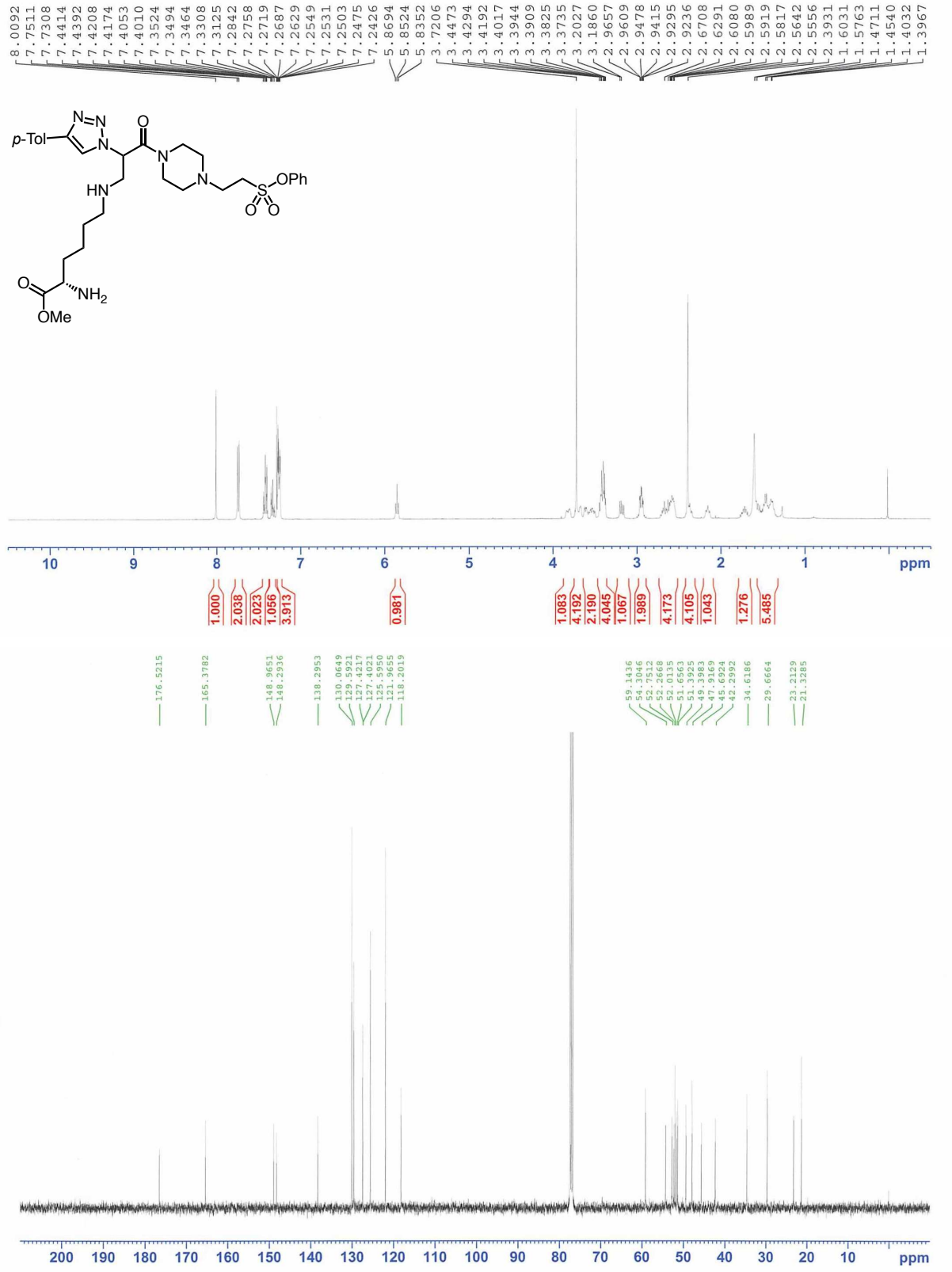
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of methyl *N*-(*tert*-butoxycarbonyl)-*S*-(3-oxo-3-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propyl)-L-cysteinate (**5c**) ($CDCl_3$)



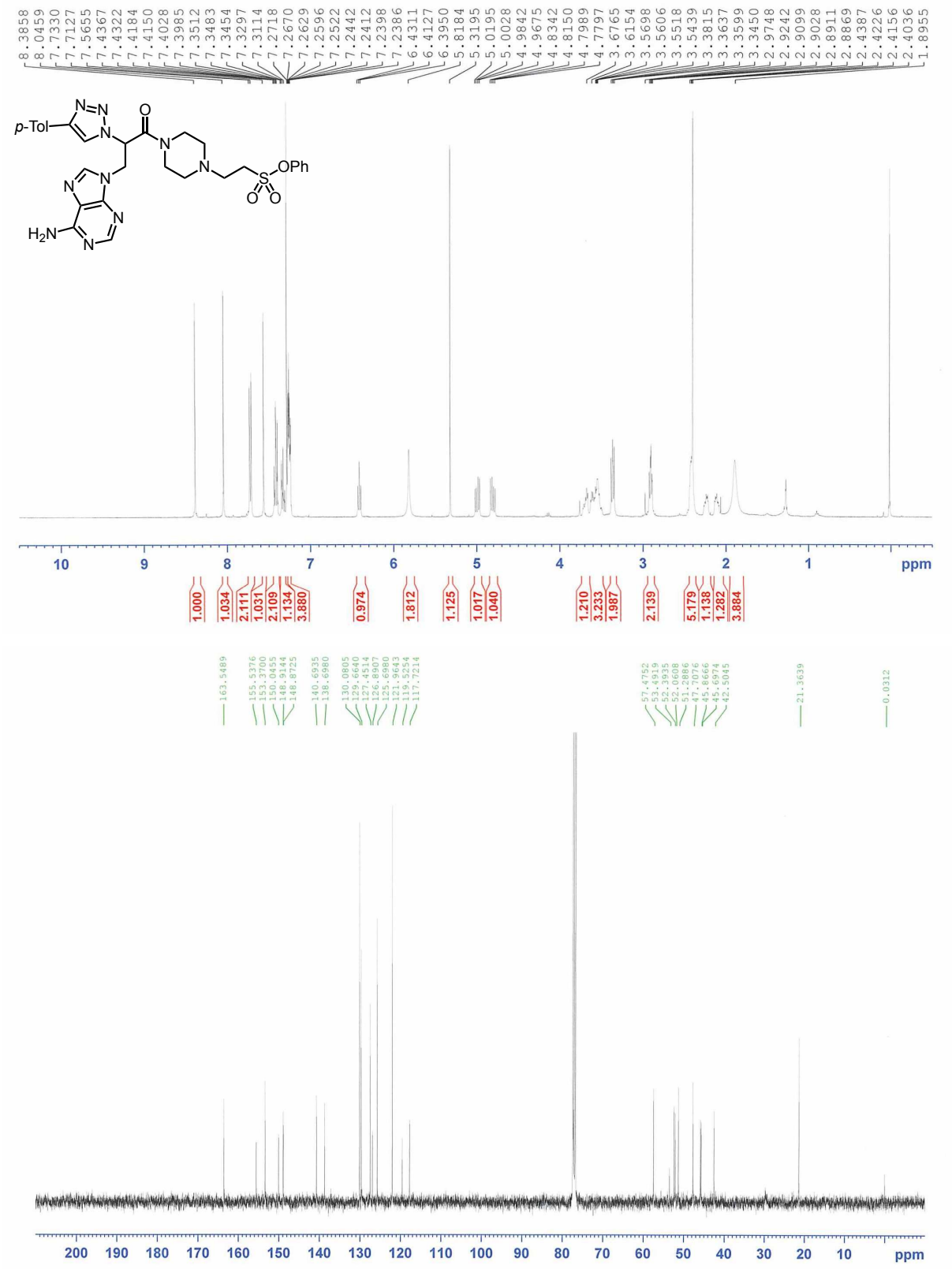
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of phenyl 2-(4-(3-((2-((5-(dimethylamino)naphthalene)-1-sulfonamido)ethyl)thio)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**5d**) ($CDCl_3$)



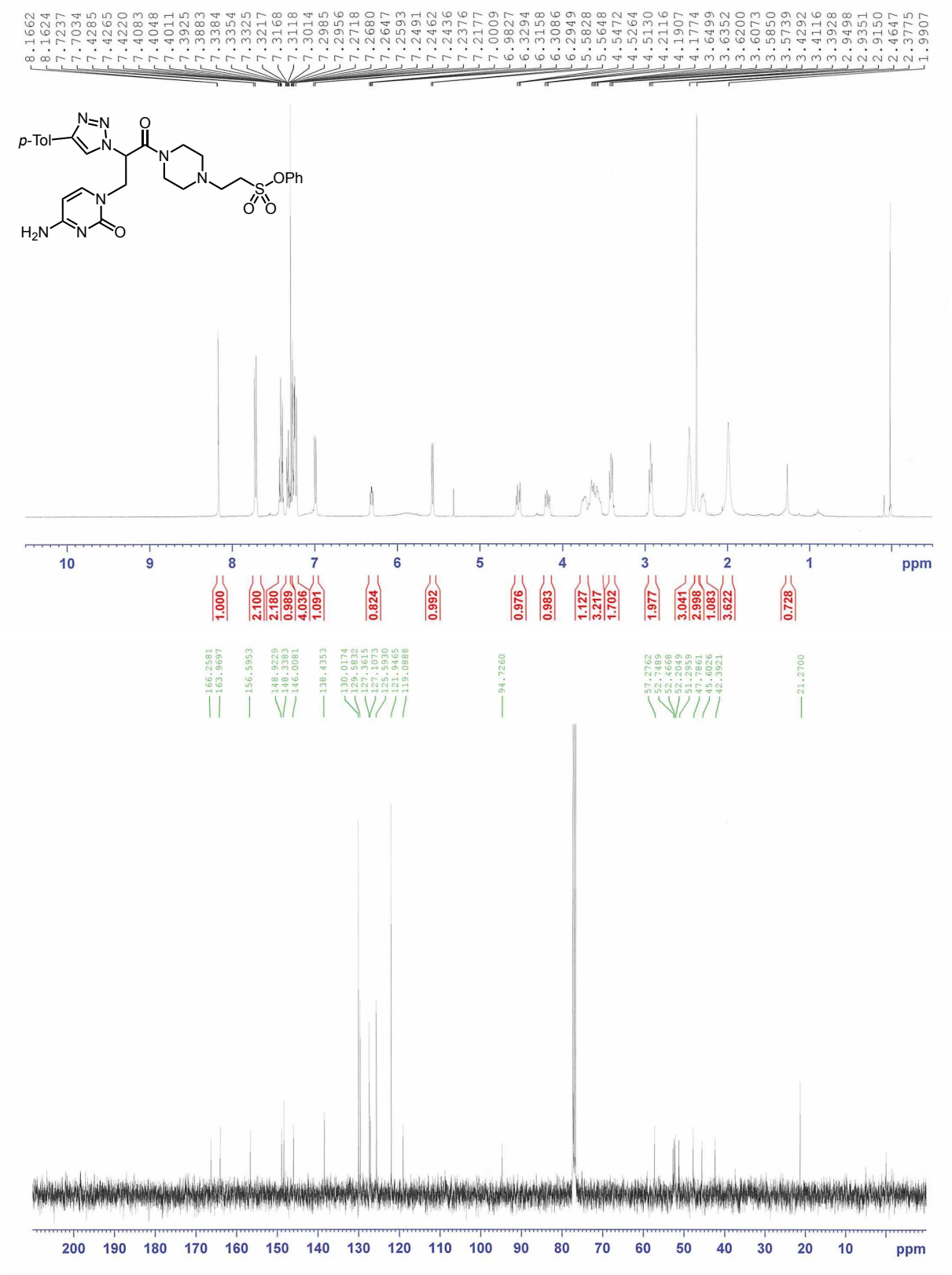
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of methyl *N*-(3-oxo-3-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propyl)-L-lysinate (**5e**) ($CDCl_3$)



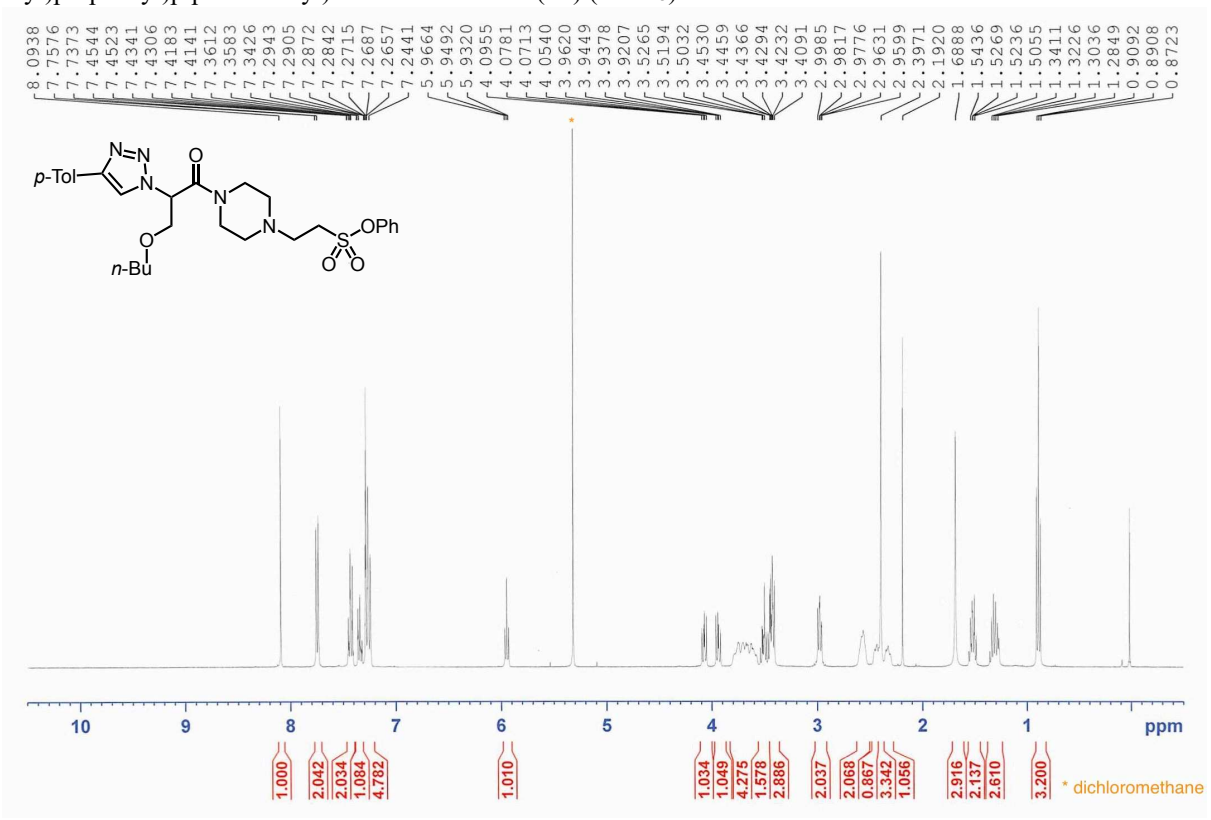
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of phenyl 2-(4-(3-(6-amino-9*H*-purin-9-yl)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**5f**) ($CDCl_3$)

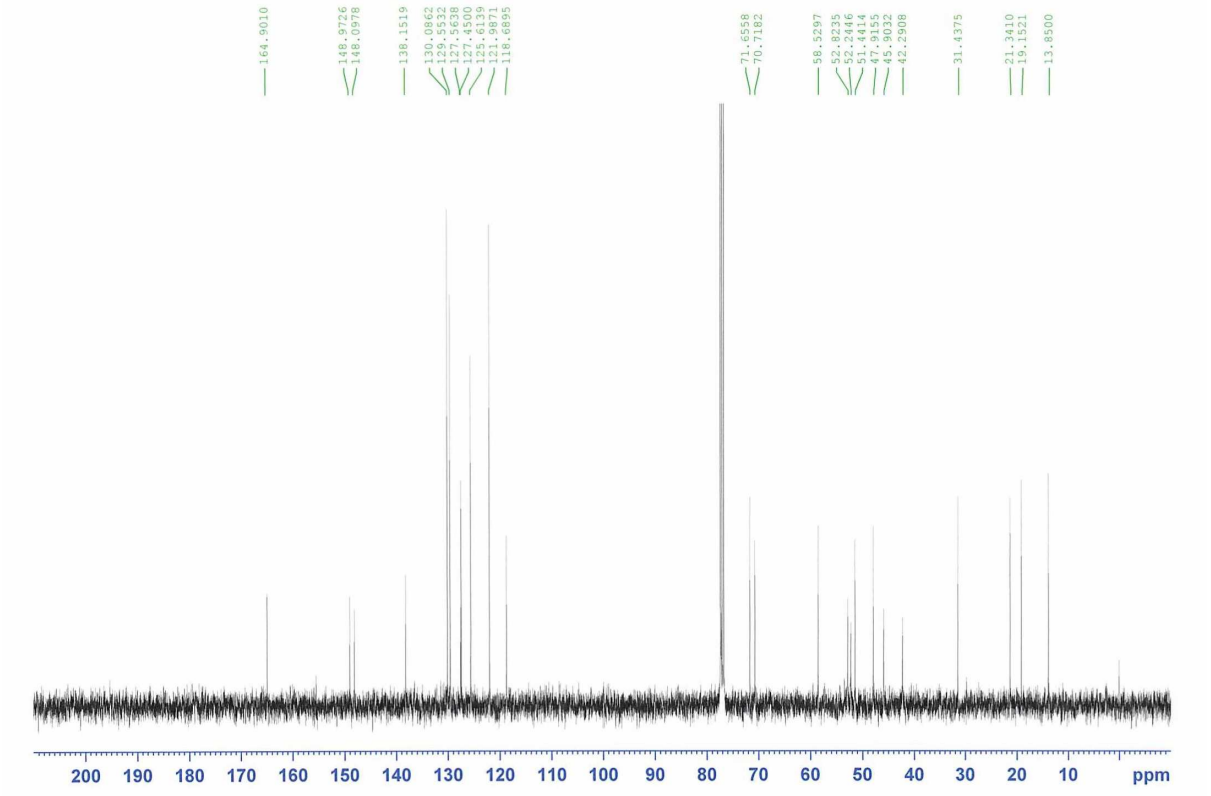


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of phenyl 2-(4-(3-(6-amino-2-oxopyrazin-1(2*H*)-yl)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**5g**) ($CDCl_3$)

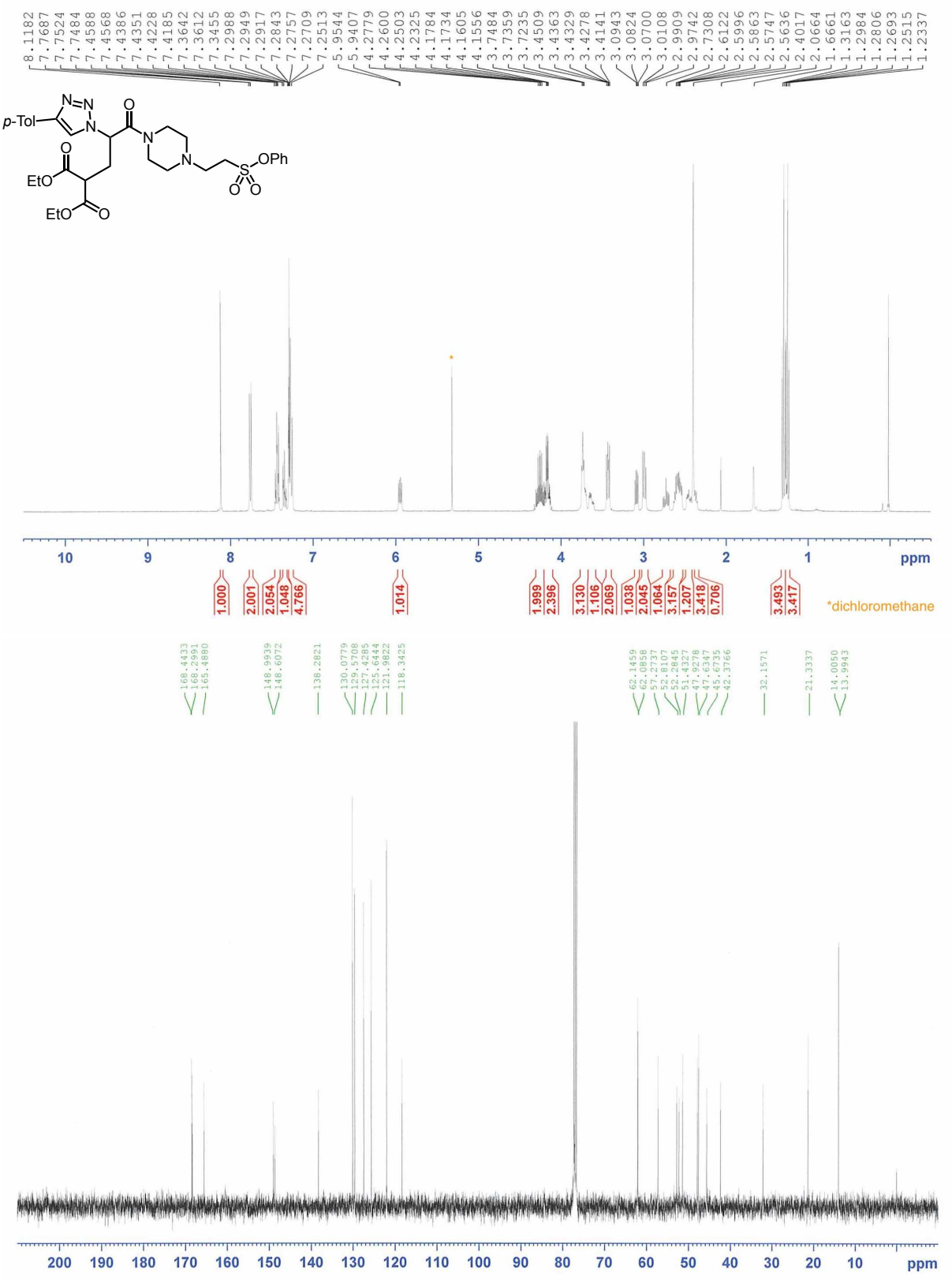


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of phenyl 2-(4-(3-butoxy-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**5h**) ($CDCl_3$)

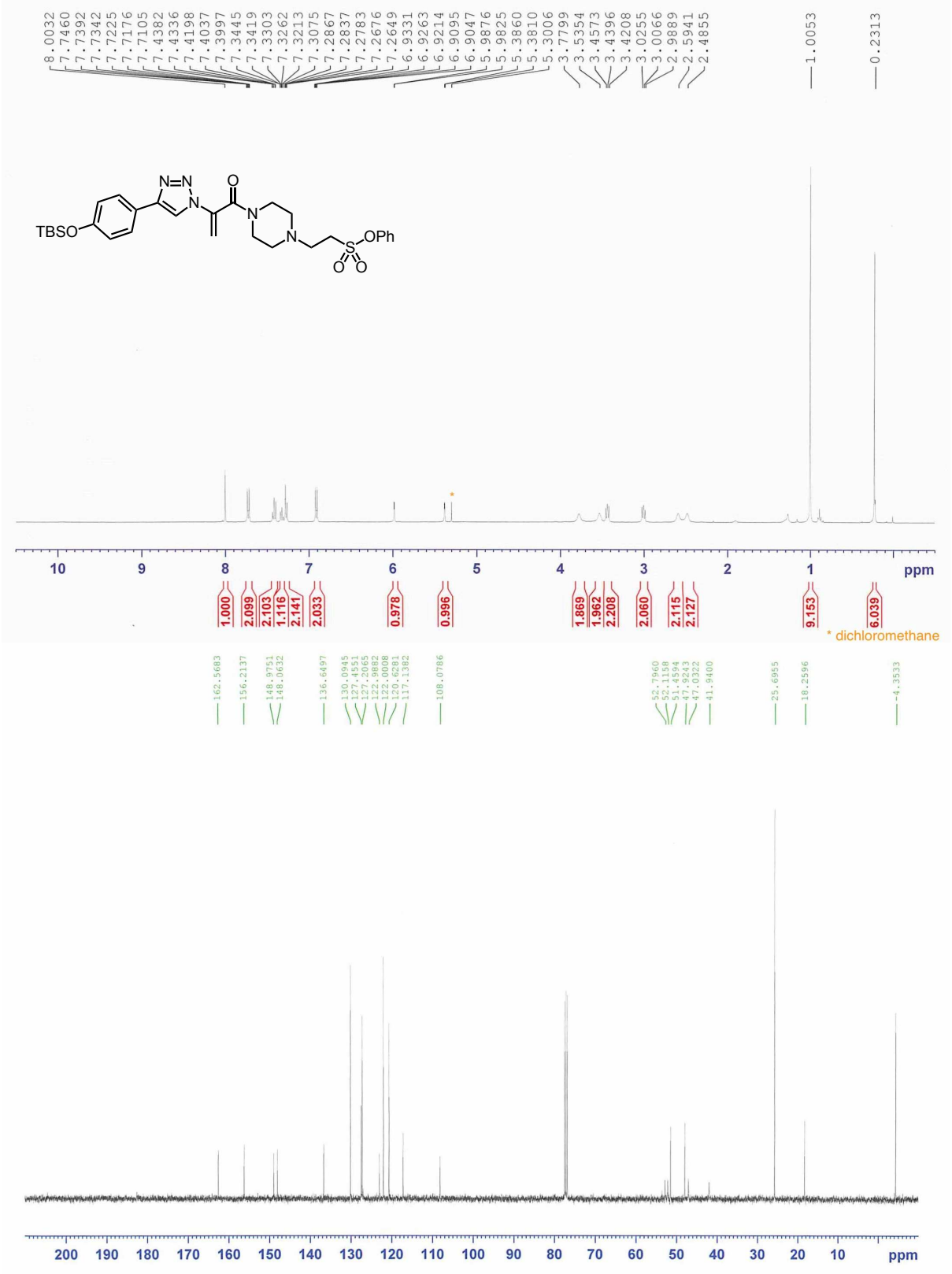




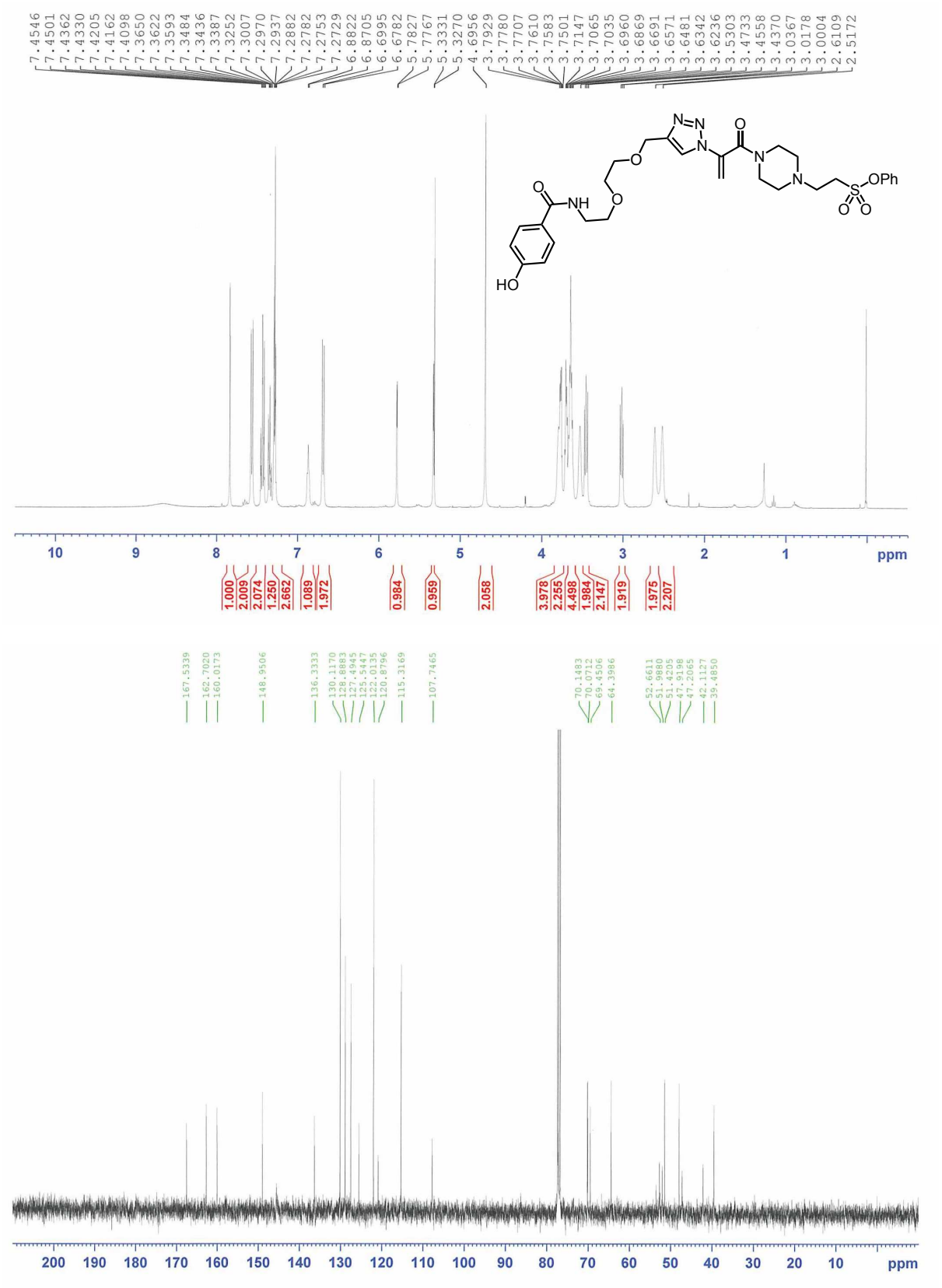
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of diethyl 2-(3-oxo-3-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propyl)malonate (**5i**) ($CDCl_3$)



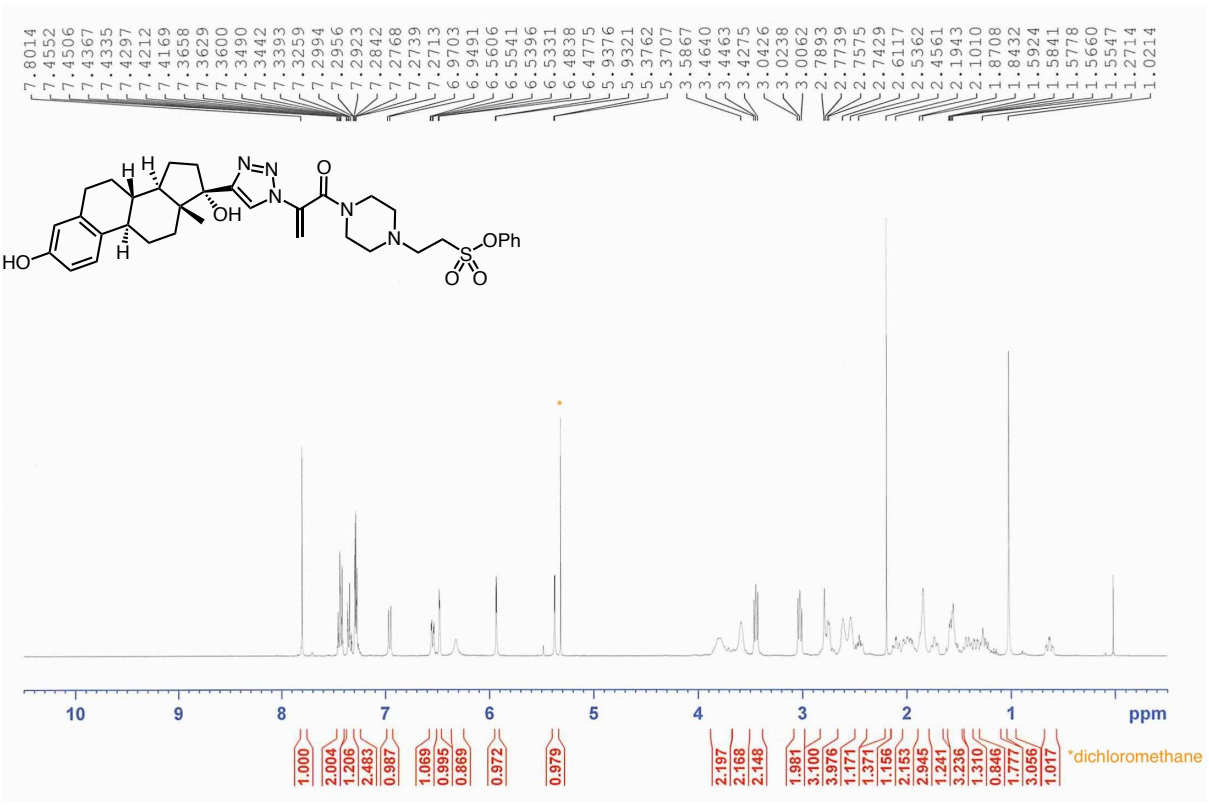
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of phenyl 2-(4-(2-(4-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**13a**) ($CDCl_3$)

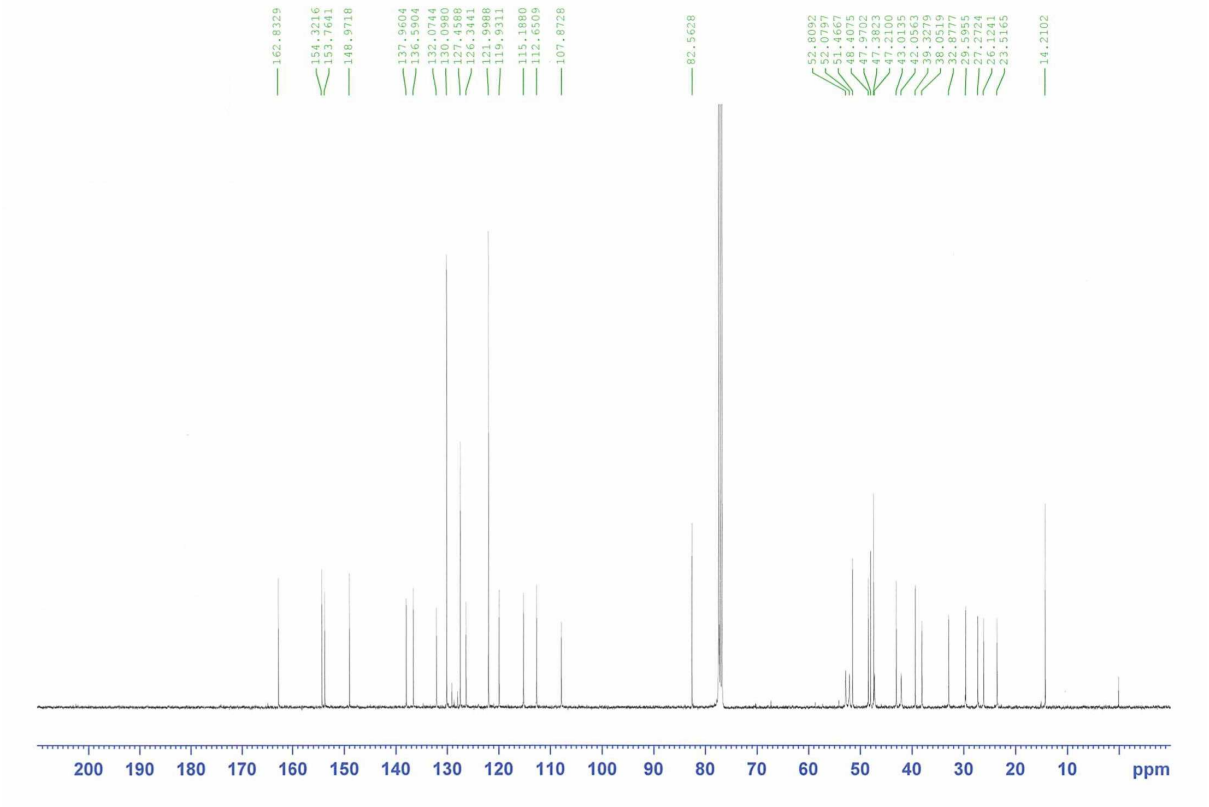


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of phenyl 2-(4-(2-(4-((2-(2-(4-hydroxybenzamido)ethoxy)ethoxy)methyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**13b**) ($CDCl_3$)

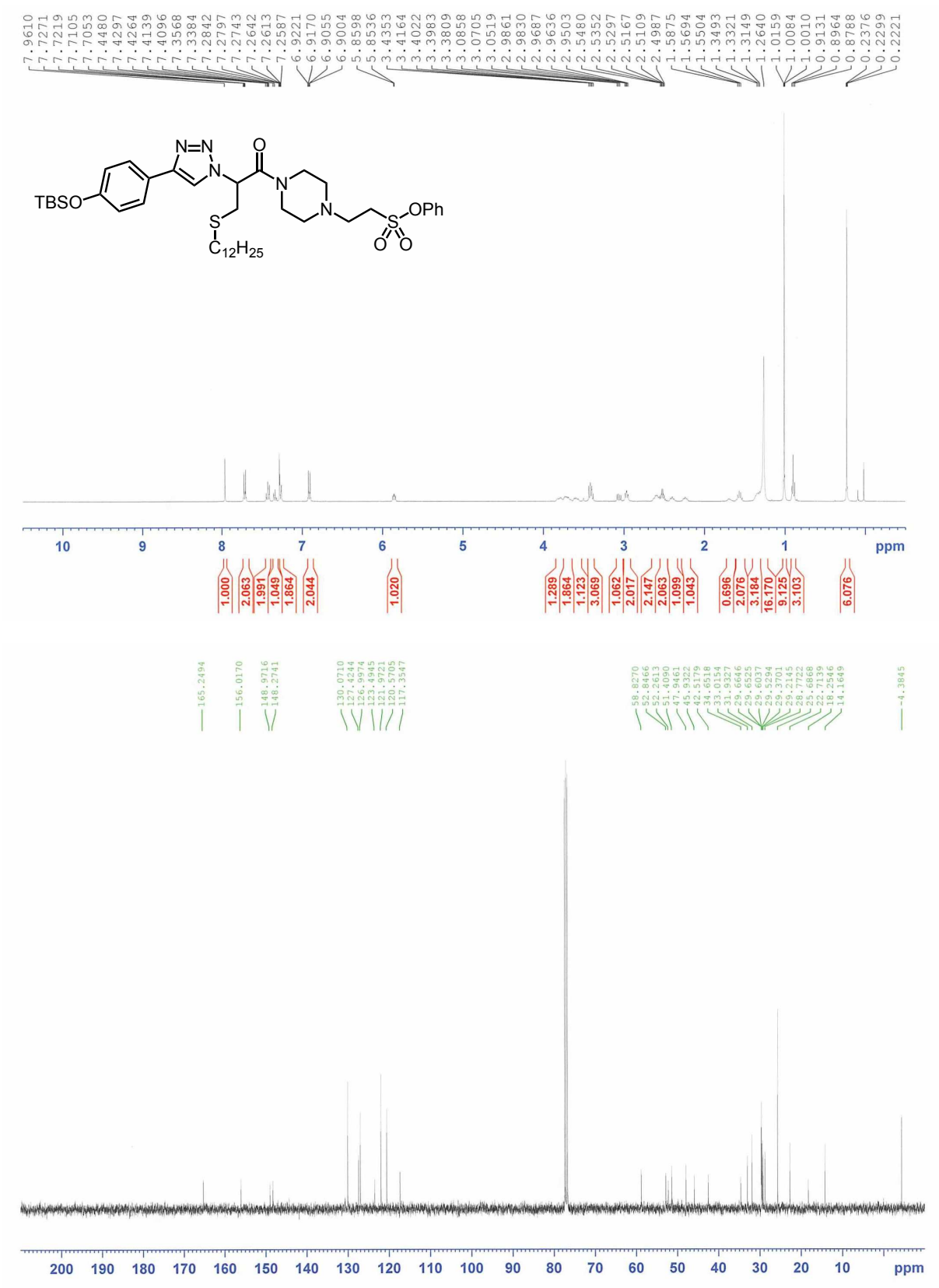


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of phenyl 2-(4-(2-(4-((8*S*,9*R*,13*R*,14*R*,17*S*)-3,17-dihydroxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-17-yl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**13c**) ($CDCl_3$)

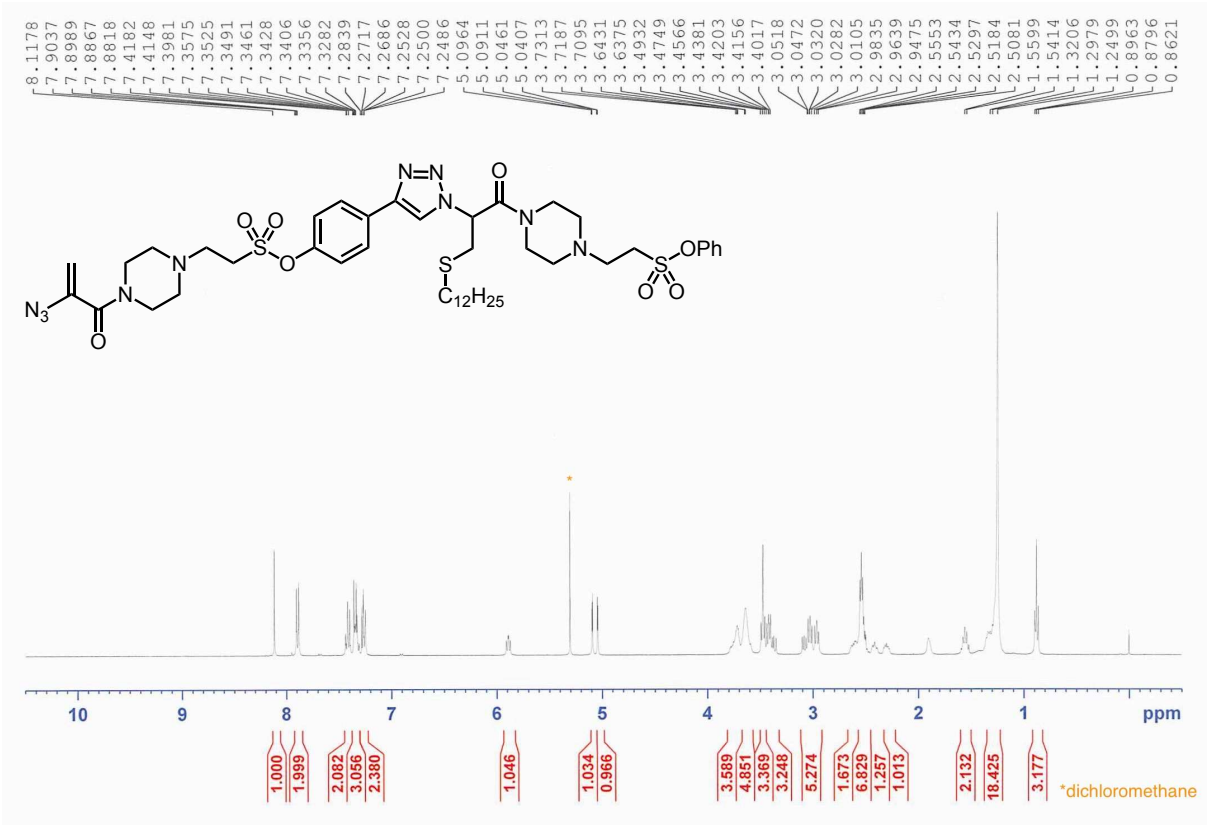


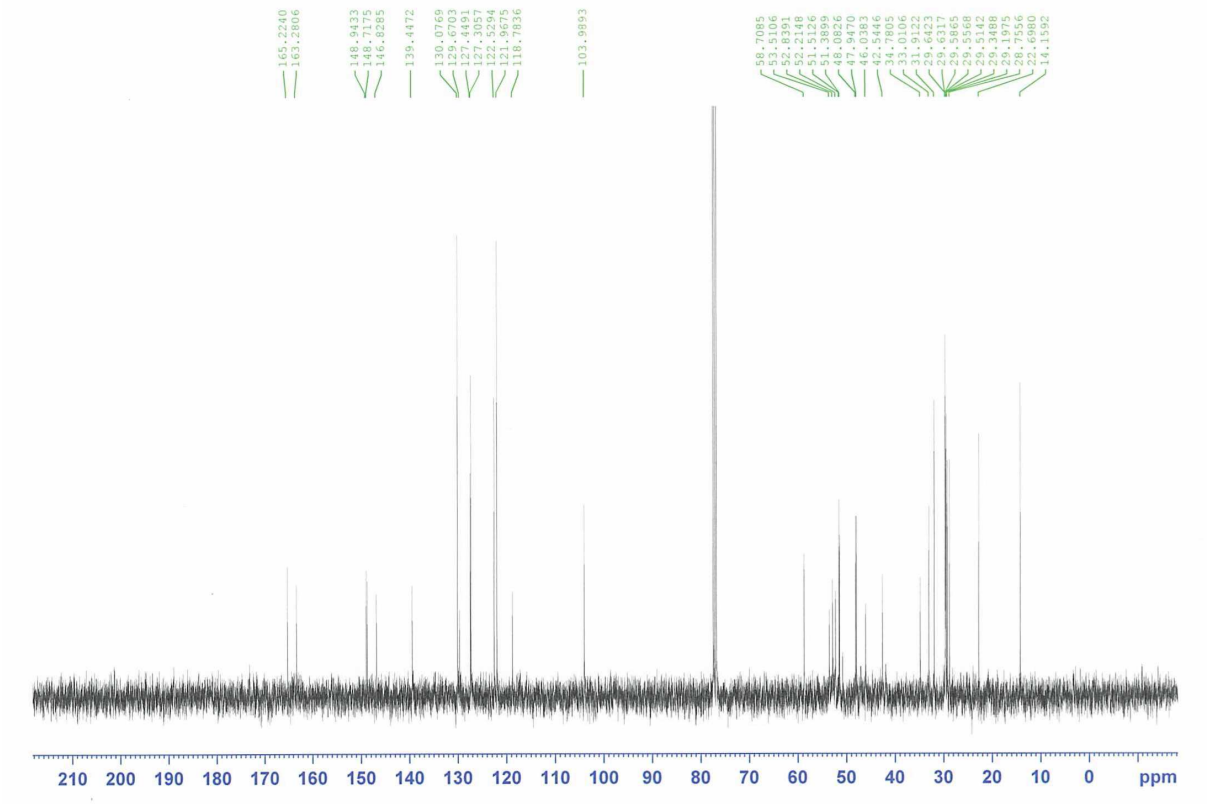


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of phenyl 2-(4-(2-(4-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-1*H*-1,2,3-triazol-1-yl)-3-(dodecylthio)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**S3**) ($CDCl_3$)

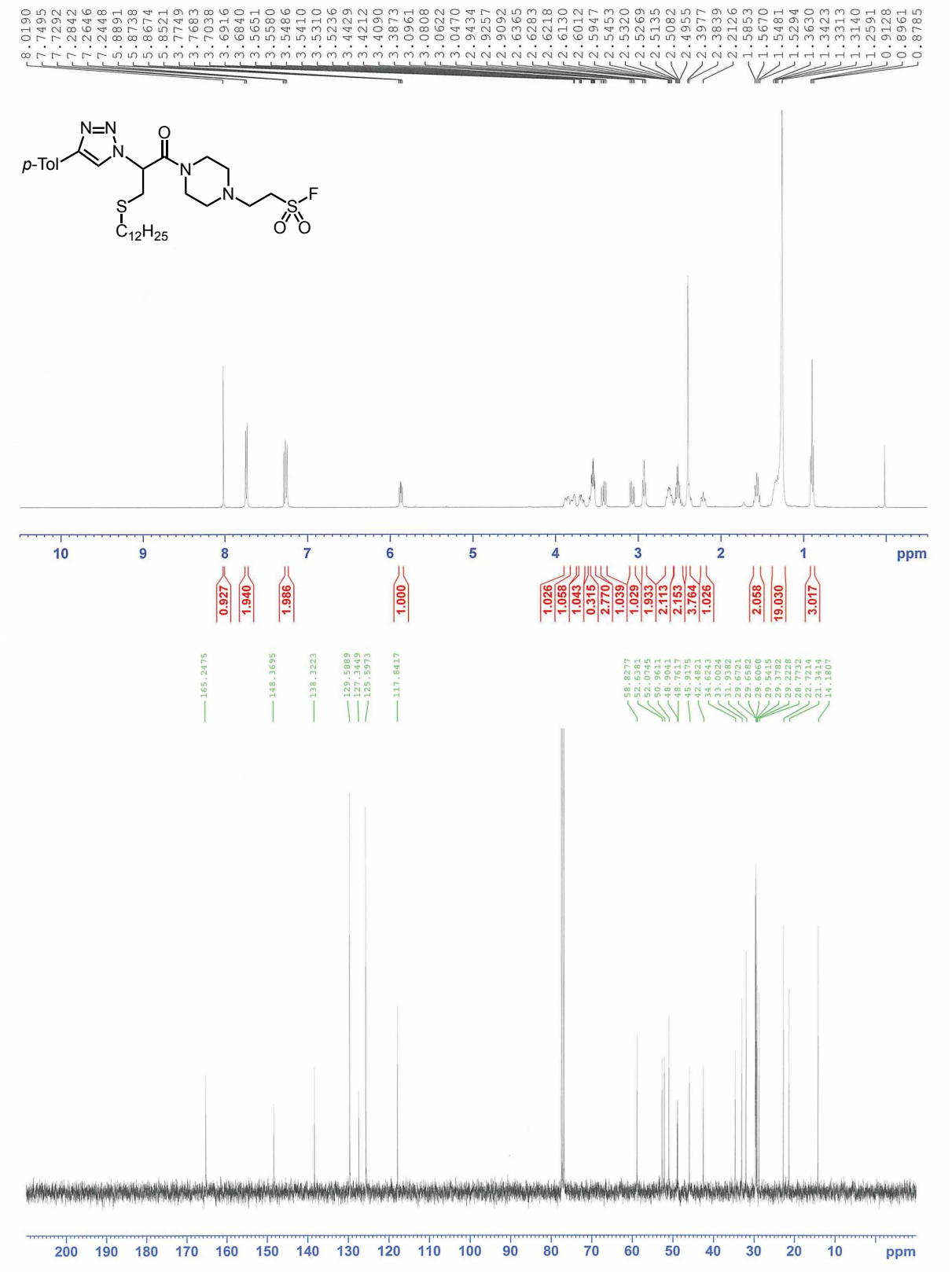


^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4-(1-(3-(dodecylthio)-1-oxo-1-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)propan-2-yl)-1*H*-1,2,3-triazol-4-yl)phenyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**14**) ($CDCl_3$)

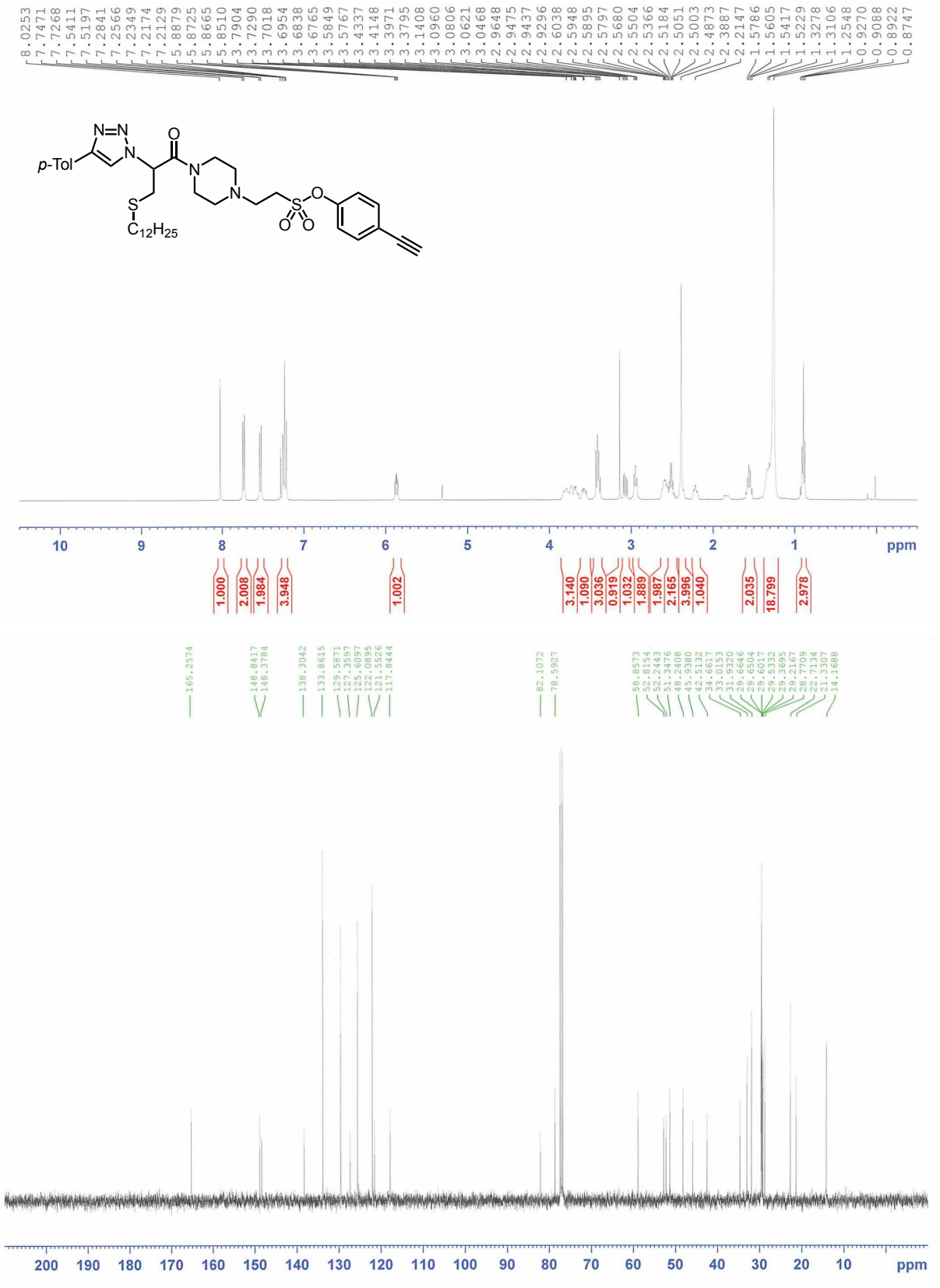




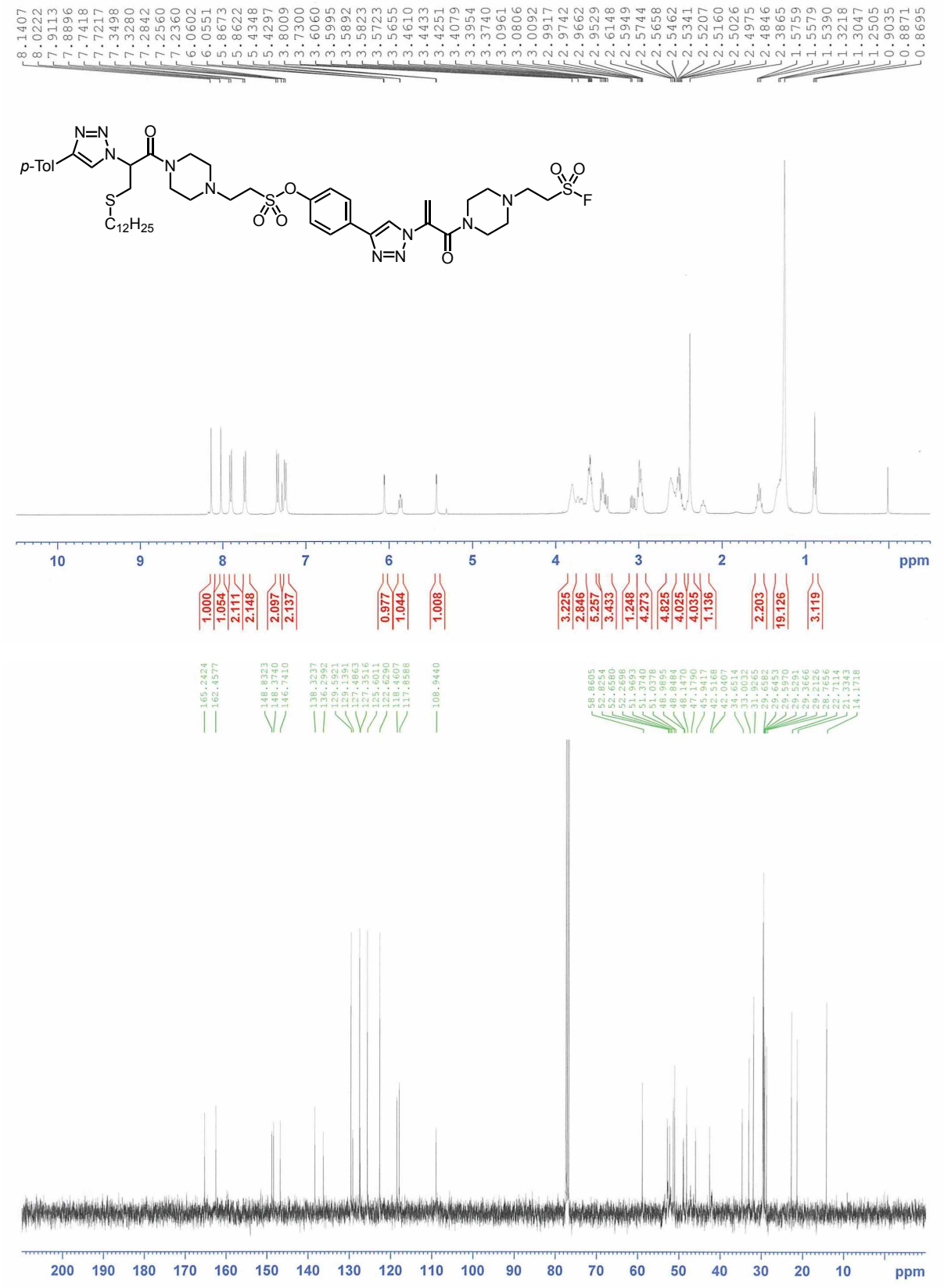
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 2-(4-(3-(dodecylthio)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonyl fluoride (**S7**) ($CDCl_3$)



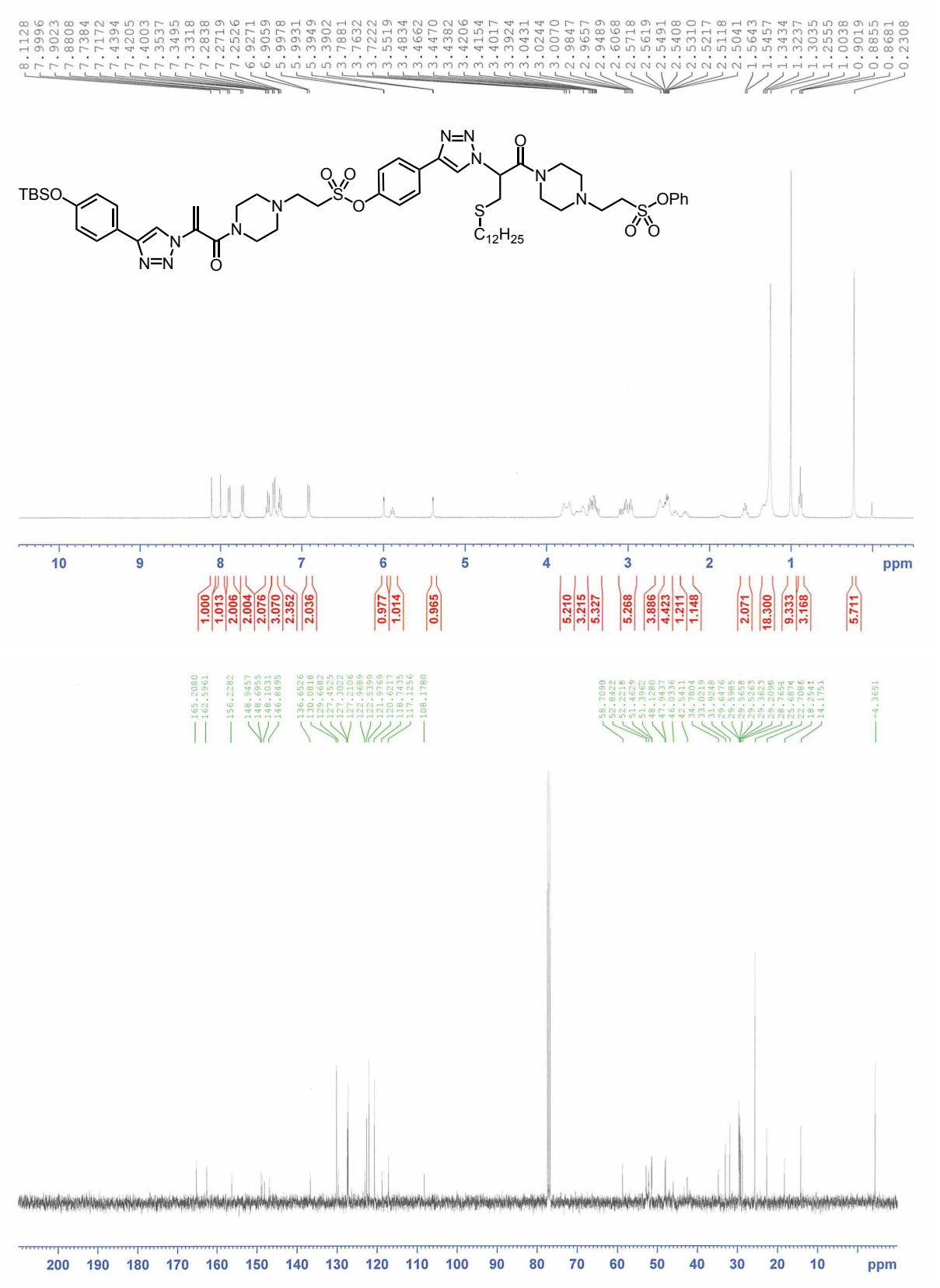
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4-ethynylphenyl 2-(4-(3-(dodecylthio)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**S8**) ($CDCl_3$)



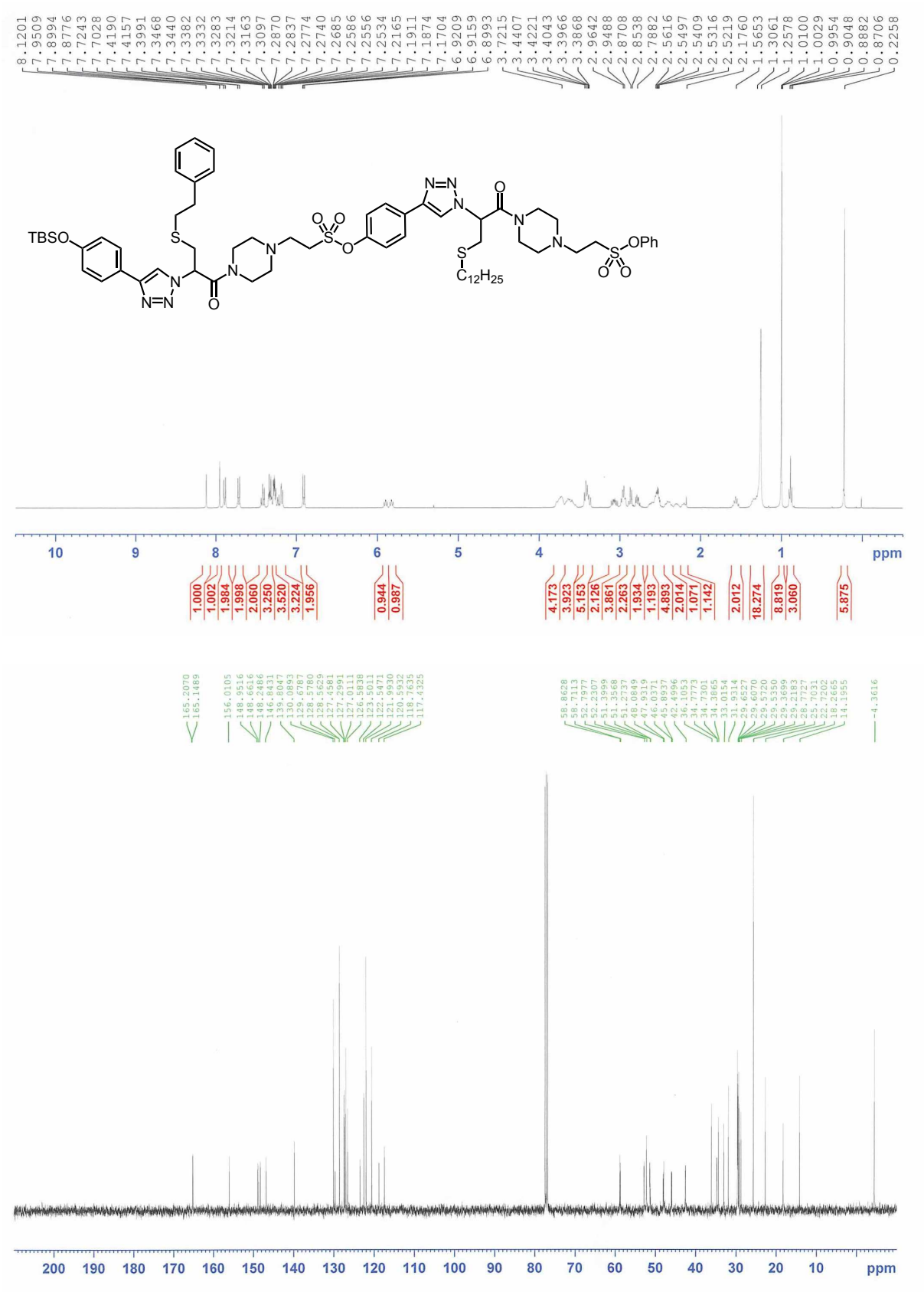
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4-(1-(3-(4-(2-(fluorosulfonyl)ethyl)piperazin-1-yl)-3-oxoprop-1-en-2-yl)-1*H*-1,2,3-triazol-4-yl)phenyl 2-(4-(3-(dodecylthio)-2-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**15**) ($CDCl_3$)



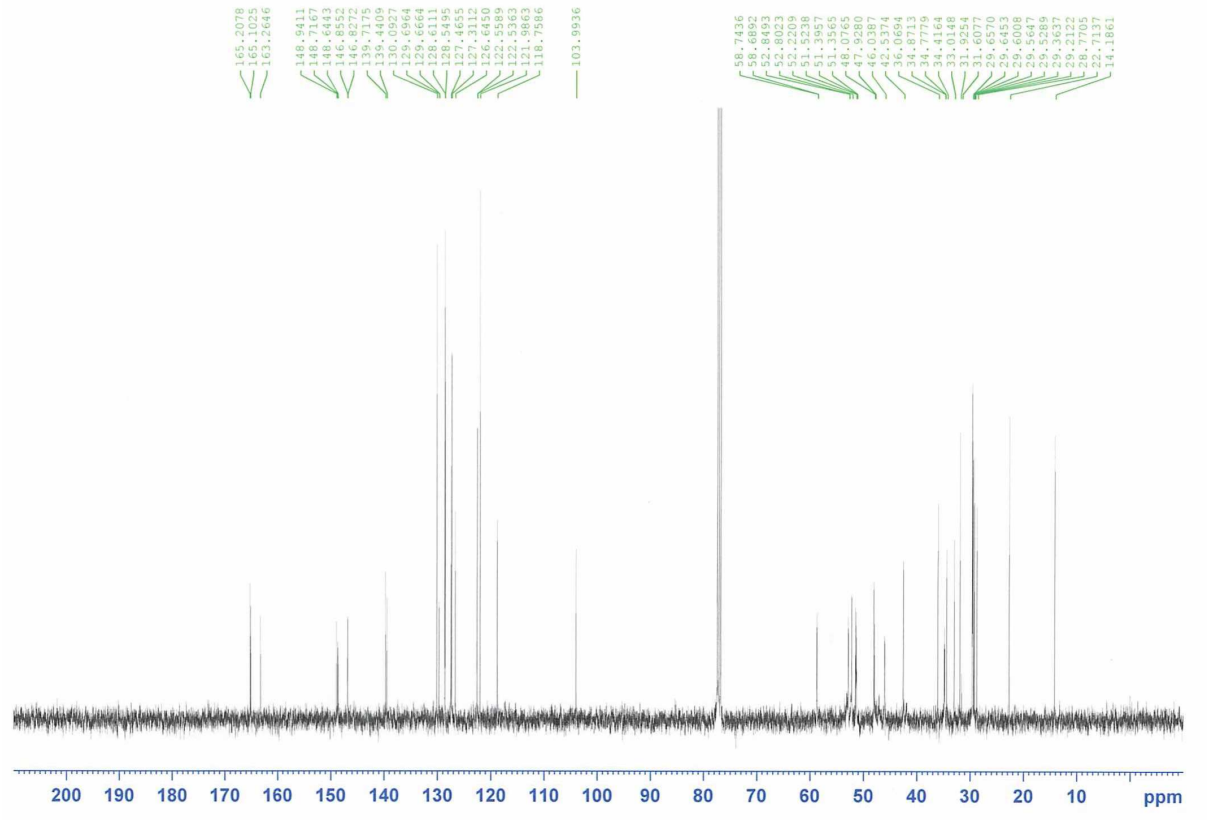
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4-(1-(3-(dodecylthio)-1-oxo-1-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)propan-2-yl)-*1H*-1,2,3-triazol-4-yl)phenyl 2-(4-(2-(4-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**S1**) ($CDCl_3$)



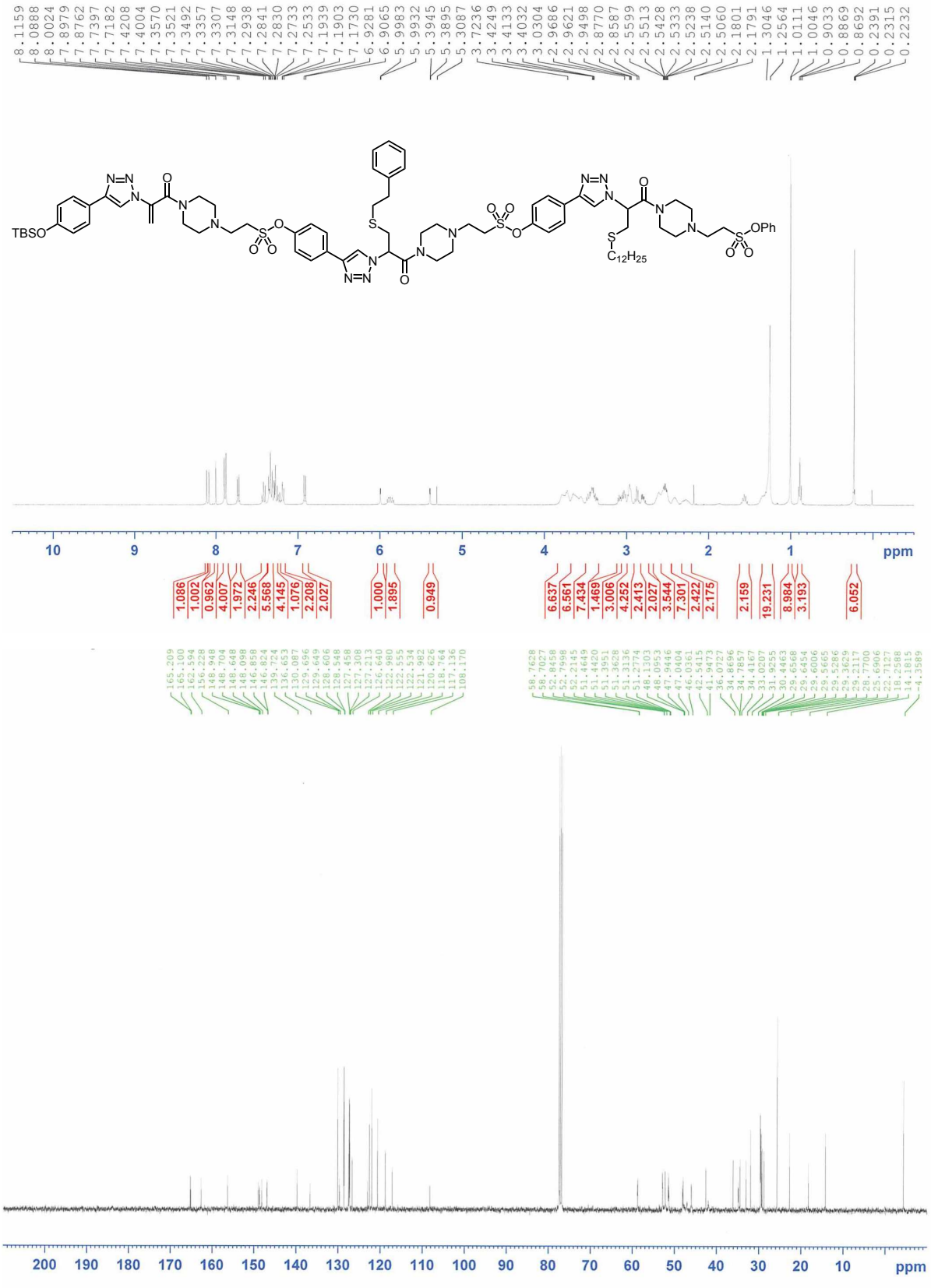
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4-(1-(3-(Dodecylthio)-1-oxo-1-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)propan-2-yl)-1*H*-1,2,3-triazol-4-yl)phenyl 2-(4-(2-(4-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-1*H*-1,2,3-triazol-1-yl)-3-(phenethylthio)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**S4**) ($CDCl_3$)



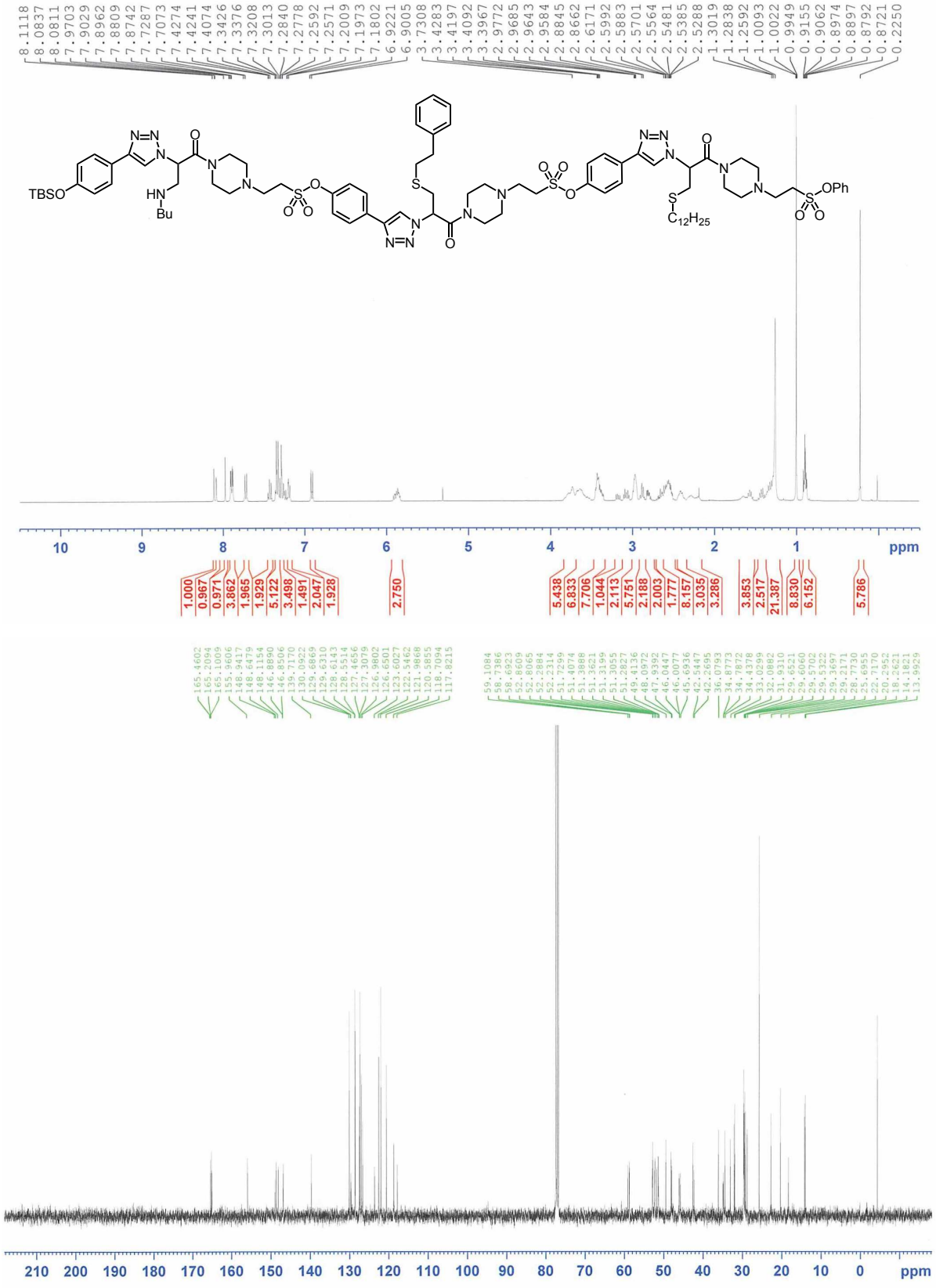
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4-(1-(1-(4-(2-((4-(1-(3-(dodecylthio)-1-oxo-1-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)propan-2-yl)-1*H*-1,2,3-triazol-4-yl)phenoxy)sulfonyl)ethyl)piperazin-1-yl)-1-oxo-3-(phenethylthio)propan-2-yl)-1*H*-1,2,3-triazol-4-yl)phenyl 2-(4-(2-azidoacryloyl)piperazin-1-yl)ethane-1-sulfonate (**S5**) ($CDCl_3$)



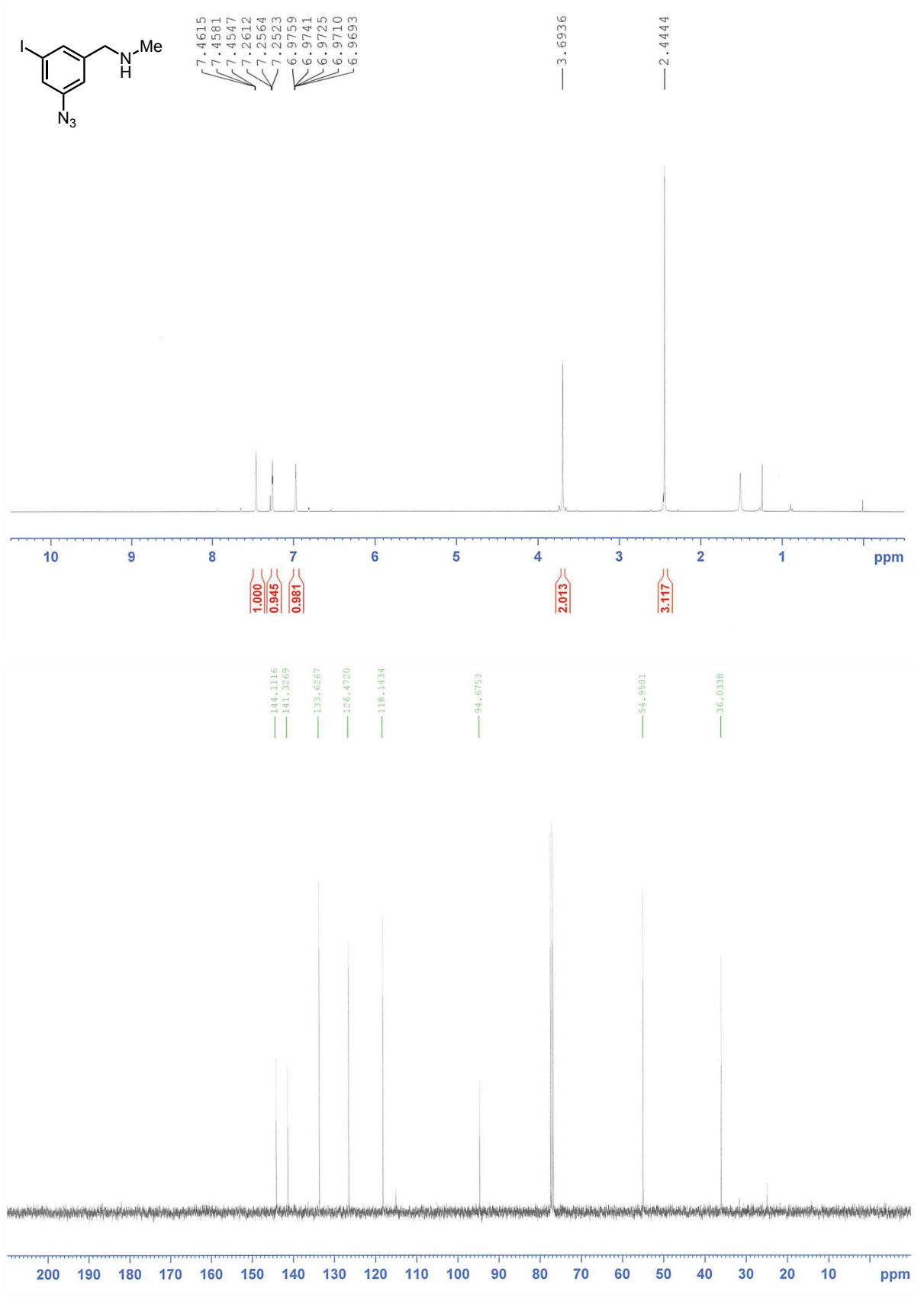
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4-(1-(1-(4-(2-((4-(1-(3-(dodecylthio)-1-oxo-1-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)propan-2-yl)-1*H*-1,2,3-triazol-4-yl)phenoxy)sulfonyl)ethyl)piperazin-1-yl)-1-oxo-3-(phenethylthio)propan-2-yl)-1H-1,2,3-triazol-4-yl)phenyl 2-(4-(2-(4-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-1*H*-1,2,3-triazol-1-yl)acryloyl)piperazin-1-yl)ethane-1-sulfonate (**S2**) ($CDCl_3$)



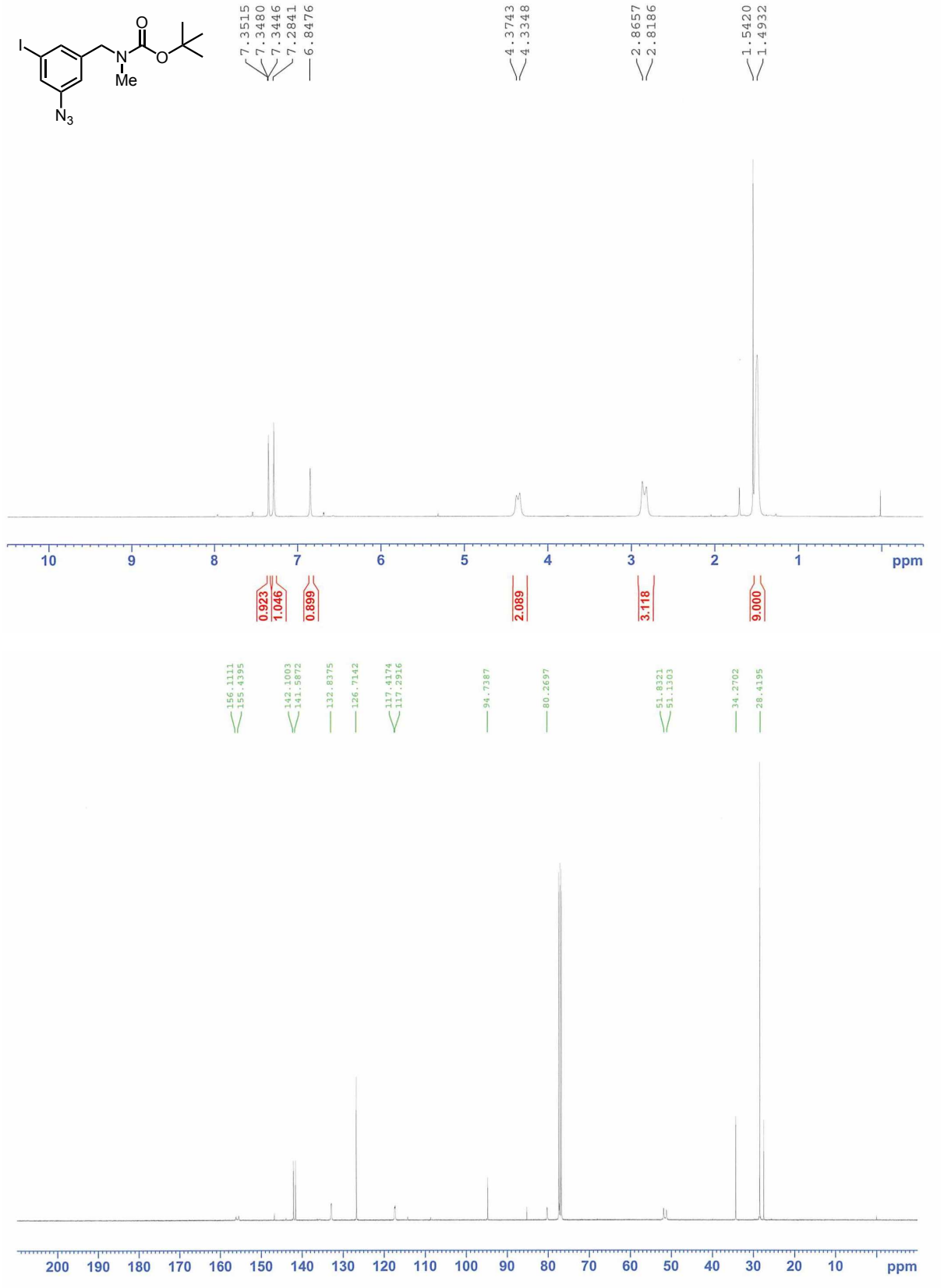
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4-(1-(1-(4-(2-((4-(1-(3-(dodecylthio)-1-oxo-1-(4-(2-(phenoxysulfonyl)ethyl)piperazin-1-yl)propan-2-yl)-1*H*-1,2,3-triazol-4-yl)phenoxy)sulfonyl)ethyl)piperazin-1-yl)-1-oxo-3-(phenethylthio)propan-2-yl)-1*H*-1,2,3-triazol-4-yl)phenyl 2-(4-(3-(butylamino)-2-(4-(4-((*tert*-butyldimethylsilyl)oxy)phenyl)-1*H*-1,2,3-triazol-1-yl)propanoyl)piperazin-1-yl)ethane-1-sulfonate (**16**) ($CDCl_3$)



^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 1-(3-azido-5-iodophenyl)-*N*-methylmethanamine ($CDCl_3$)



^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of *tert*-butyl (3-azido-5-iodobenzyl)(methyl)carbamate ($CDCl_3$)



^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of *tert*-butyl (3-amino-5-iodobenzyl)(methyl)carbamate ($CDCl_3$)