Stereochemical and Skeletal Diversity Arising from Amino Propargylic Alcohols

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I. Materials and Methods:

Experimental. Dry solvents were dispensed from a solvent purification system that passes solvents through packed columns (THF and CH_2Cl_2: dry neutral alumina; toluene: dry neutral alumina and Q5 reactant). Unless otherwise stated, all reagents were obtained from commercial sources and used without further purification. Infrared spectra were recorded on a Nicolet IR100 FTIR from Thermo Scientific. ^{1}H NMR spectra were recorded on Varian Unity/Inova I500 and I600 (500MHz and 600MHz) spectrometer. ^{1}H data are reported as follows: chemical shift in parts per million relative to residual protonated solvent ($CHCl_3$: d 7.26, C_6H_6: d 7.15, DMSO-d_6: d 2.54), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broadened), coupling constant (Hz), and integration. ^{13}C magnetic resonance spectra were recorded on Varian Unity/Inova I500 and (126MHz) spectrometer. ^{13}C chemical shifts are reported in parts per million relative to solvent ($CHCl_3$: d 77.0). All ^{13}C spectra were determined with broadband decoupling. Microwave heating was performed using Explorer®-48 positions, CEM. High-resolution mass spectra were obtained through the Harvard University mass spectrometry facility. All reactions were magnetically stirred and monitored by thin-layer chromatography (TLC) using E. Merck silica gel 60 F254 precoated plates (0.25 mm). Flash chromatography was performed either on EM Science silica gel 60 (230–400 mesh) or using a CombiFlash companion system (Teledyne ISCO, Inc.) with pre-packed FLASH silica gel columns (Biotage, Inc.). Optical

rotations were obtained using digital polarimeter Autopol IV (Rudolph research Analytical) with a 1 mL cell and a 1 dm path length. SFC/MS chromatography was performed with a Berger analytic SFC (Waters ZQ Mass Spectrometer) using CO_2 and MeOH or MeOH/*i*-PrOH as the mobile phase and using a Chiralcel® OD-H column or a Chiralpak® AD-H column purchased from Chiral Technology Inc. (column length: 4.6x250mm, pore size: 5um).

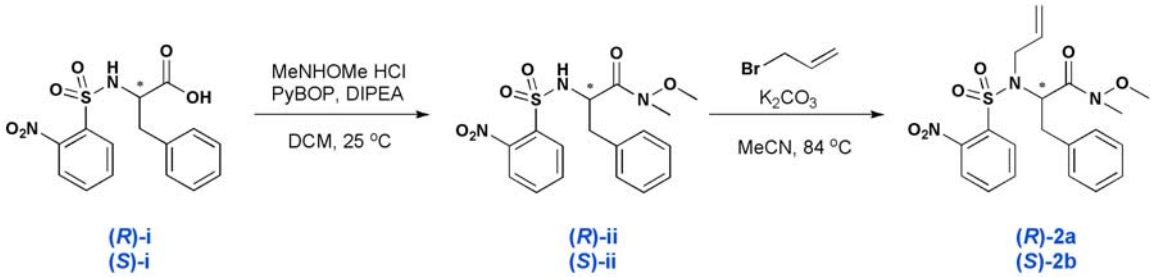
Computational. We used Pipeline Pilot (Accelrys, Inc.; San Diego, CA, USA) to generate SMILES[1] representations of all four possible stereoisomers (**a**-**d**) for each of the compounds studied (**1**-**14**). 3D models were built for each stereoisomer structure and then expanded to a set of conformers by a conformational sampling run, both performed in Molecular Operating Environment (MOE 2007.09; Chemical Computing Group; Montreal, QC, Canada) using default sampling and energy-minimization parameters and keeping only conformers with free energies within 2 kcal of the global minimum of the search. Resulting conformers were again filtered after being manually inspected for spatial defects, and unfavorable interactions.

For each compound we kept unique conformers of diastereomeric pairs (**a** and **b**) of low free energy. Because enantiomeric compounds have identical PMI ratios, we considered conformers of both **a** and **d** as "**a**", **b** and **c** as "**b**" for PMI analysis. In order to retain the geometry of common fragments present in **1-14** throughout the 3D-models, we used the lowest energy conformer of **1** as a seed structure for new models of diastereomeric pairs of **5**, **6**, **8**, **10**, and **11**. By dialing in actual dihedral angles of **1** and performing local minimization on ring-forming atoms of the new product structures, we built 3D structures, for all **a**, that are of comparable geometry for the common molecular fragment in these compounds. We then performed an all-atom local minimization with default minimization parameters in MOE where heavy atoms were constrained to their current positions using a quadratic force constant to keep the resulting minimum close to the original coordinates. New structures of **6** and **11** were then used as seed structures for compound sets **7** and **9**, and **12**, **13**, **14**, respectively.

In our implementation of Sauer and Schwartz[2] PMI ratio method, we calculated ratios of the smallest and medium eigenvalues of the diagonalized mass tensor to the largest (i.e., $X = \mathbf{I}_{small}/\mathbf{I}_{large}$, $Y = \mathbf{I}_{medium}/\mathbf{I}_{large}$). The Y coordinate of these ratios was then scaled by $\sqrt{3}$ to produce an equilateral PMI space, to allow meaningful Euclidean distances between compounds to be computed in the resulting PMI space.

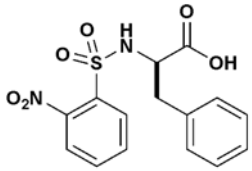
II. Experimental procedures

Scheme 1s. Synthetic route to derivatives (*R*)-**2a** and (*S*)-**2b**.[a]



[a] Compounds **(*R*)-i** and **(*S*)-i** were prepared from D- and L-phenylalanine respectively by the known procedure.[3] Compound **(*S*)-i** is a known compound.[4]

(*R*)-2-(2-nitrophenylsulfonamido)-3-phenylpropanoic acid *(R)*-i

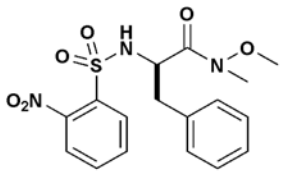


Yield 86% (white solid); IR (neat, cm^{-1}) ν = 3321, 3095, 3030, 1727, 1539, 1355, 1168, 1103; $[\alpha]_D^{20}$ = + 81.8 $cm^3\ g^{-1}\ dm^{-1}$ (c = 0.49 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, CDCl3) δ = 7.93 (d, *J*= 8.0, 1H), 7.83 (d, *J*= 8.0, 1H), 7.68 (t, *J*=7.5, 1H), 7.64 (t, *J*=7.5, 1H), 7.22 – 7.18 (m, 3H), 7.13 – 7.11 (m, 2H), 5.94 (d, *J*=8.5, 1H), 4.48 (ddd, *J*=5.0, 7.5, 13.5, 1H), 3.21 (dd, *J*=5.0, 14.0, 1H), 3.05 (dd, *J*=7.5, 14.0, 1H); ^{13}C NMR (126 MHz, CDCl3) δ = 175.4, 147.2, 134.4, 133.9, 133.6, 133.0, 130.2, 129.2, 128.7, 127.5, 125.6, 57.4, 38.6. HRMS (EI) calcd. for $[C_{15}H_{14}N_2O_6S]$ $(M+H)^+$ 351.0645, found 351.0642.

General procedure for amidation

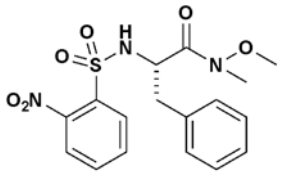
To a solution of (*R*)- or (*S*)-2-(2-nitrophenylsulfonamido)-3-phenylpropanoic acid (1 equiv.), **(*R*)-i** or **(*S*)-i** respectively, *N*,*N*-diisopropylethylamine (1 equiv.) in dry dichloromethane (0.2M) at 0 ºC, benzotriazol-1-yloxy tripyrrolidinophosphonium hexafluorophospate (pyBOP, 1.1 equiv.), *N*,*O*-dimethylhydroxylamine hydrochloride (2 equiv.) and *N*,*N*-diisopropylethylamine (2 equiv.) were added. The resulting solution was stirred for 30 min at 0 ºC and then it was allowed to warm to room temperature and stirred under nitrogen for 4h. The mixture was diluted with dichloromethane, quenched with 3N aqueous HCl and the aqueous layer was extracted with dichloromethane. The combined organic phases were washed with saturated aqueous $NaHCO_3$, brine, dried over sodium sulfate, filtered and evaporated under reduced pressure. The resulting residue was purified by silica gel chromatography (Hex/EtOAc 1:1).

(*R*)-*N*-methoxy-*N*-methyl-2-(2-nitrophenylsulfonamido)-3-phenylpropanamide (*R*)-ii



Yield 83% (pale yellow solid); IR (neat, cm^{-1}) ν = 3300, 3095, 3028, 2939, 1662, 1541, 1441, 1412, 1385, 1349, 1168, 1079; $[\alpha]_D^{20}$ = + 12.1 $cm^3\ g^{-1}\ dm^{-1}$ (c = 0.43 g cm^3, $CHCl_3$);^{1}H NMR (500 MHz, CDCl3) δ = 7.87 (d, *J*=8.0, 1H), 7.84 (d, *J*=8.0, 1H), 7.65 (t, *J*=7.5, 1H), 7.59 (t, *J*=7.5, 1H), 7.21 – 7.12 (m, 5H), 6.23 (d, *J*=9.0, 1H), 4.88 – 4.83 (m, 1H), 3.55 (s, 3H), 3.06 (dd, *J*=6.0, 13.5, 1H), 2.96 (s, 3H), 2.91 (dd, *J*=7.0, 13.5, 1H); ^{13}C NMR (126 MHz, CDCl3) δ = 170.60, 147.53, 135.66, 134.55, 133.20, 132.52, 129.98, 129.44, 128.44, 127.12, 125.47, 61.49, 55.36, 39.42, 31.99; HRMS (EI) calcd. for $[C_{17}H_{19}N_3O_6S]$ $(M+H)^+$ 394.1067, found 394.1069.

(*S*)-*N*-methoxy-*N*-methyl-2-(2-nitrophenylsulfonamido)-3-phenylpropanamide (*S*)-ii

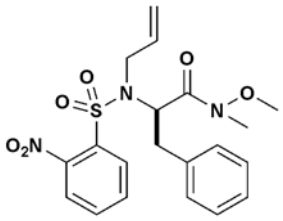


Yield 83% (pale yellow solid); IR (neat, cm^{-1}) ν = 3300, 3095, 3028, 2938, 1662, 1541, 1441, 1412, 1385, 1350, 1168, 1079; $[\alpha]_D^{20}$ = – 12.7 $cm^3\ g^{-1}\ dm^{-1}$ (c = 0.33 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, CDCl3) δ = 7.87 (d, *J*=8.0, 1H), 7.83 (d, *J*=8.0, 1H), 7.65 (t, *J*=7.5, 1H), 7.59 (t, *J*=7.5, 1H), 7.19 – 7.12 (m, 5H), 6.25 (m, 1H), 4.85 – 4.84 (m, 1H), 3.55 (s, 3H), 3.06 (dd, *J*=6.0, 13.5, 1H), 2.96 (s, 3H), 2.90 (dd, *J*=7.0, 13.5, 1H); ^{13}C NMR (126 MHz, CDCl3) δ = 170.5, 147.4, 135.6, 134.5, 133.2, 132.5, 129.9, 129.3, 128.4, 127.0, 125.4, 61.4, 55.3, 39.3, 31.9; HRMS (EI) calcd. for $[C_{17}H_{19}N_3O_6S]$ $(M+H)^+$ 394.1067, found 394.1064.

General procedure for *N*-Allylation

In a 250 mL pear flask, (*R*)- or (*S*)-*N*-methoxy-*N*-methyl-2-(2-nitrophenylsulfonamido)-3-phenylpropanamide (1 equiv.), **(*R*)-ii** or **(*S*)-ii** respectively, was dissolved in acetonitrile (0.2M) to give a pale yellow solution. Potassium carbonate (1.2 equiv.) and 3-bromoprop-1-ene (1.2 equiv.) were added and the resulting suspension was heated to 84°C and stirred under nitrogen for 3h. The solvent was evaporated under reduced pressure and the residue taken up with water and dichloromethane. The two phases were separated and the aqueous layer was extracted with dichloromethane. The combined organic phases were dried over sodium sulfate, filtered and evaporated under reduced pressure. The resulting residue was purified by silica gel chromatography (Hex/EtOAc 3:2).

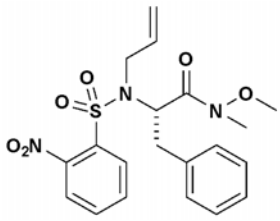
(*R*)-2-(*N*-allyl-2-nitrophenylsulfonamido)-*N*-methoxy-*N*-methyl-3-phenylpropanamide (2a)



Yield 97% (yellow oil); IR (neat, cm^{-1}) ν = 3088, 3028, 2940, 1665, 1544, 1440, 1372, 1165; $[\alpha]_D^{20}$ = + 50.6 $cm^3\ g^{-1}\ dm^{-1}$ (c = 0.65 g cm^3,

$CHCl_3$); SFC: Chiralcel® OD-H column; 5% MeOH, 95% $sfCO_2$, $t_R^{(major)}$ = 12 min, area = 100% (> 99% ee) (racemic compound t_R = 12.18 min, 13.46 min); ^{1}H NMR (500 MHz, CDCl3) δ = 7.92 (d, *J*=8.0, 1H), 7.68 – 7.64 (m, 1H), 7.61 – 7.57 (m, 2H), 7.27 – 7.18 (m, 5H), 5.89 – 5.81 (m, 1H), 5.30 – 5.23 (m, 2H), 5.08 (d, *J*=10.0, 1H), 4.45 (dd, *J*=6.5, 16.5, 1H), 4.30 (dd, *J*=6.0, 16.5, 1H), 3.34 (m, 4H), 3.05 – 2.93 (m, 4H); ^{13}C NMR (126 MHz, CDCl3) δ = 170.0, 148.2, 136.3, 135.3, 133.9, 133.3, 131.4, 130.9, 129.4, 128.4, 126.8, 124.0, 117.6, 61.2, 56.5, 48.2, 36.9, 31.7; HRMS (EI) calcd. for $[C_{20}H_{23}N_3O_6S]$ $(M+H)^+$ 434.1380, found 434.1388.

(*S*)-2-(*N*-allyl-2-nitrophenylsulfonamido)-*N*-methoxy-*N*-methyl-3-phenylpropanamide (2b)

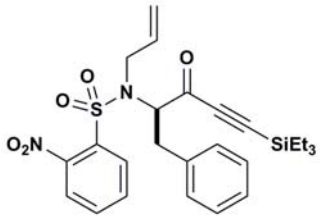


Yield 98% (yellow oil); IR (neat, cm^{-1}) ν = 3088, 3028, 2940, 1665, 1544, 1440, 1372, 1165, 1127, 1062; $[\alpha]_D^{20}$ = – 47.3 cm^3 g^{-1} dm^{-1} (c = 0.52 g cm^3, $CHCl_3$); SFC: Chiralcel® OD-H column; 5% MeOH, 95% $sfCO_2$, $t_R^{(major)}$ = 13.33 min, area = 100% (>99% ee) (racemic compound t_R = 12.18 min, 13.46 min); ^{1}H NMR (500 MHz, CDCl3) δ = 7.91 (d, *J*=8.0, 1H), 7.65 – 7.56 (m, 3H), 7.27 – 7.18 (m, 5H), 5.83 (ddd, *J*=6.0, 11.0, 16.5, 1H), 5.29 – 5.22 (m, 2H), 5.07 (d, *J*=10, 1H), 4.43 (dd, *J*=5.5, 16.5, 1H), 4.29 (dd, *J*=5.5, 16.5, 1H), 3.40 – 3.24 (m, 4H), 3.01 – 2.93 (m, 4H); ^{13}C NMR (126 MHz, CDCl3) δ = 170.0, 148.2, 136.4, 135.3, 134.0, 133.3, 131.4, 130.9, 129.5, 128.4, 126.9, 124.0, 117.6, 61.2, 56.6, 48.2, 36.9, 31.7; HRMS (EI) calcd. for $[C_{20}H_{23}N_3O_6S]$ $(M+H)^+$ 434.1380, found 434.1386.

General procedure for the preparation of *α,β*-acetylenic ketones 3a-b

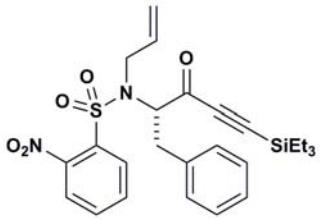
In a flame-dried flask, triethyl(ethynyl)silane (2.8 equiv.) was dissolved in dry THF (0.5M), the resulting colorless solution was cooled to – 78 °C and *n*-butyllithium (2.5 M in hexanes, 2.6 equiv.) was added dropwise. (*NOTE:* recently opened *n*-butyllithium is recommended). The reaction mixture was stirred under nitrogen for 1h, allowing the temperature to rise up to – 50 °C. Then, the reaction was cooled to – 78 °C and a solution of Weinreb amide derivative **2a** or **2b** (1 equiv.) in dry THF (0.5M) was added. The reaction mixture was stirred under nitrogen for 75 min allowing the temperature to rise up to – 45 °C. The reaction mixture was quenched with saturated aqueous NH_4Cl. The aqueous layer was extracted with diethyl ether and the combined organic phases were washed with brine, dried over sodium sulfate, filtered and evaporated under reduced pressure. The resulting residue was purified by silica gel chromatography (Hex/EtOAc 4:1).

(*R*)-*N*-allyl-2-nitro-*N*-(3-oxo-1-phenyl-5-(triethylsilyl)pent-4-yn-2-yl)benzenesulfonamide (3a)



Yield 72% (yellow oil); IR (neat, cm^{-1}) ν = 3089, 3029, 2957, 2913, 2876, 2147, 1681, 1545, 1371, 1167, 1008; $[\alpha]_D^{20}$ = – 47.1 cm^3 g^{-1} dm^{-1} (c = 0.41 g cm^3, $CHCl_3$); SFC: Chiralpak® AD-H (2 columns); 10% MeOH/*i*-PrOH (4:1), 95% $sfCO_2$, $t_R^{(major)}$ = 4.32 min, area = 98.38 % (97% ee) (racemic compound t_R = 3.81 min, 4.31 min); ^{1}H NMR (500 MHz, CDCl3) δ = 7.79 – 7.77 (m, 1H), 7.65 – 7.62 (m, 1H), 7.57 – 7.52 (m, 2H), 7.29 – 7.24 (m, 4H), 7.23 – 7.21 (m, 1H), 5.80 (ddd, *J*=6.0, 11.0, 16.5, 1H), 5.20 (d, *J*=16.5, 1H), 5.11 (d, *J*=10.0, 1H), 5.09 – 5.07 (m, 1H), 4.10 (dd, *J*=6.5, 16.5, 1H), 3.95 (dd, *J*=6.5, 16.5, 1H), 3.60 (dd, *J*=6.0, 14.5, 1H), 3.02 (dd, *J*=8.5, 14.5, 1H), 1.00 (t, *J*=8.0, 9H), 0.67 (q, *J*=8.0, 6H); ^{13}C NMR (126 MHz, CDCl3) δ = 183.9, 136.3, 134.5, 133.6, 133.3, 131.5, 131.1, 129.2, 128.6, 126.9, 124.0, 118.8, 101.7, 101.7, 68.6, 49.4, 34.8, 7.2, 3.6; HRMS (EI) calcd. for $[C_{26}H_{32}N_2O_5SSi]$ $(M+H)^+$ 513.1874, found 513.1869.

(*S*)-*N*-allyl-2-nitro-*N*-(3-oxo-1-phenyl-5-(triethylsilyl)pent-4-yn-2-yl)benzenesulfonamide (3b)



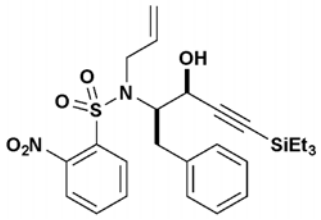
Yield 79% (yellow oil); IR (neat, cm^{-1}) ν = 3089, 3029, 2957, 2913, 2876, 2148, 1681, 1545, 1371, 1167, 1008; $[\alpha]_D^{20}$ = + 42.5 cm^3 g^{-1} dm^{-1} (c = 0.53 g cm^3, $CHCl_3$); SFC: Chiralpak® AD-H (2 columns); 10% MeOH/*i*-PrOH (4:1), 95% $sfCO_2$, $t_R^{(major)}$ = 3.85 min, area = 98 % (96% ee) (racemic compound t_R = 3.81 min, 4.31 min); ^{1}H NMR (500 MHz, CDCl3) δ = 7.79 – 7.77 (m, 1H), 7.65 – 7.62 (m, 1H), 7.57 – 7.52 (m, 2H), 7.27 – 7.24 (m, 4H), 7.23 – 7.21 (m, 1H), 5.81 (ddd, *J*=6.0, 11.0, 16.5, 1H), 5.21 (d, *J*=16.5, 1H), 5.11 (d, *J*=10.5, 1H), 5.09 – 5.07 (m, 1H), 4.10 (dd, *J*=6.5, 16.5, 1H), 3.95 (dd, *J*=6.5, 16.5, 1H), 3.60 (dd, *J*=6.0, 14.5, 1H), 3.02 (dd, *J*=8.0, 14.5, 1H), 1.00 (t, *J*=8.0, 9H), 0.67 (q, *J*=8.0, 6H); ^{13}C NMR (126 MHz, CDCl3) δ = 183.9, 136.3, 134.5, 133.5, 133.3, 131.5, 131.1, 129.2, 128.5, 126.9, 124.0, 118.7, 101.7, 101.6, 68.7, 49.4, 34.8, 7.2, 3.6; HRMS (EI) calcd. for $[C_{26}H_{32}N_2O_5SSi]$ $(M+Na)^+$ 535.1693, found 535.1696.

General procedure for diastereoselective reduction of α,β-acetylenic ketones 3a-b

In a flame-dried flask, (*R*)- or (*S*)-1-methyl-3,3-diphenylhexahydropyrrolo[1,2-c][1,3,2] oxazaborolidine (1.0 M in toluene, 1.1 equiv.) and borane tetrahydrofuran complex solution (1.0

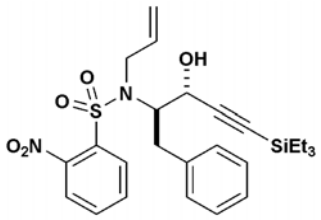
M in THF, 1.1 equiv.) were dissolved in dry THF at 0°C and the resulting colorless solution was stirred for 30 min under nitrogen. The mixture was cooled to – 78 °C and the appropriate enantiomer of the substrate (1 equiv.), dissolved in dry THF (0.1M), was slowly added by syringe pump (1.6 mL/h). The temperature was maintained between – 70 °C and – 50 °C. The reaction mixture was cautiously quenched by addition of MeOH at 0 °C. After 30 min of stirring at room temperature, the mixture was concentrated under reduced pressure. The residue was purified by silica gel chromatography (Hex/EtOAc 4:1).

_N_-allyl-_N_-((2_R_,3_S_)-3-hydroxy-1-phenyl-5-(triethylsilyl)pent-4-yn-2-yl)-2-nitrobenzene sulfonamide (4a)



Yield 80% (inseparable mixture of diastereomers, *anti*/*syn* = 9:91) (yellow oil); IR (neat, cm^{-1}) ν = 3523, 3087, 3028, 2955, 2912, 2875, 2169, 1544, 1372, 1350, 1163, 1005; $[\alpha]_D^{20}$ = + 3.3 cm^3 g^{-1} dm^{-1} (c = 0.12 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, CDCl3) δ = 7.92 (d, *J*=8, 1H), 7.65 – 7.62 (m, 1H), 7.58 – 7.53 (m, 2H), 7.21 – 7.19 (m, 4H), 7.18 – 7.16 (m, 1H), 5.95 (ddd, *J*=6.0, 11.0, 16.5, 1H), 5.32 – 5.28 (m, 2H), 5.14 (d, *J*=10.0, 1H), 4.56 (dd, *J*=7.0, 16.5, 1H), 4.46 – 4.45 (m, 1H), 4.30 – 4.25 (m, 2H), 4.27 – 4.24 (m, 1H), 3.20 (dd, *J*=8.5, 14.5, 1H), 3.12 (dd, *J*=6.5, 14.5, 1H), 2.42 (d, *J*=7.0, 1H), 1.03 (t, *J*=8.0, 9H), 0.65 (q, *J*=8.0, 6H); ^{13}C NMR (126 MHz, CDCl3) δ = 137.0, 135.8, 133.5, 133.4, 131.7, 131.6, 129.1, 128.5, 128.4, 126.8, 124.1, 117.8, 104.3, 91.3, 63.6, 63.1, 47.5, 36.0, 7.4, 4.1; HRMS (EI) calcd. for $[C_{26}H_{34}N_2O_5SSi]$ $(M+H)^+$ 515.2030, found 515.2030.

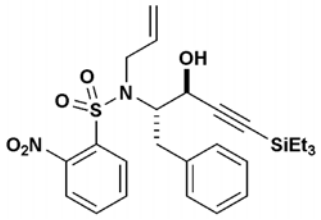
_N_-allyl-_N_-((2_R_,3_R_)-3-hydroxy-1-phenyl-5-(triethylsilyl)pent-4-yn-2-yl)-2-nitrobenzene sulfonamide (4b)



Yield 99% (inseparable mixture of diastereomers, *anti*/*syn* = 90:10) (yellow oil); IR (neat, cm^{-1}) ν = 3525, 3087, 3028, 2955, 2912, 2875, 2171, 1545, 1371, 1352, 1162, 1006; $[\alpha]_D^{20}$ = – 75.8 cm^3 g^{-1} dm^{-1} (c = 0.12 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, CDCl3) δ = 7.58 (d, *J*=8.0, 1H), 7.56 – 7.53 (m, 1H), 7.46 (d, *J*=8.0, 1H), 7.42 – 7.38 (m, 1H), 7.13 – 7.06 (m, 5H), 6.01 (ddd, *J*=6.0, 10.0, 16.5, 1H), 5.31 (d, *J*=17.5, 1H), 5.18 (d, *J*=10.0, 1H), 4.45 (m, 1H), 4.30 – 4.25 (m, 2H), 4.04 (dd, *J*=7.5, 16.5, 1H), 3.29 (dd, *J*=10.0, 15.0, 1H), 2.88 (dd, *J*=10.0, 15.0, 1H), 2.73 (br, 1H), 1.01 (t, *J*=8.0, 9H), 0.64 (q, *J*=8.0, 6H); ^{13}C NMR (126 MHz, CDCl3) δ = 147.8, 137.0, 135.7, 133.5, 133.1, 131.5, 131.0, 129.1, 128.4, 126.6, 124.0,

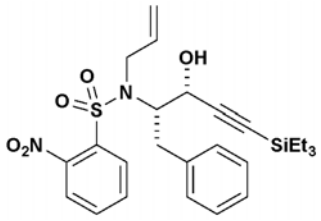
118.1, 105.3, 90.0, 65.3, 64.0, 47.7, 34.8, 7.4, 4.1; HRMS (EI) calcd. for [$C_{26}H_{34}N_2O_5SSi$] $(M+H)^+$ 515.2030, found 515.2032.

_N_-allyl-_N_-((2_S_,3_S_)-3-hydroxy-1-phenyl-5-(triethylsilyl)pent-4-yn-2-yl)-2-nitrobenzene sulfonamide (4c)



Yield 87% (inseparable mixture of diastereomers, *anti*/*syn* = 90:10) (yellow oil); IR (neat, cm^{-1}) ν = 3523, 3087, 3028, 2955, 2924, 2875, 2172, 1544, 1372, 1162, 1006; $[\alpha]_D^{20}$ = + 68.3 cm^3 g^{-1} dm^{-1} (c = 0.36 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, CDCl3) δ = 7.58 – 7.53 (m, 2H), 7.47 (d, *J*=8.0, 1H), 7.41 – 7.38 (m, 1H), 7.14 – 7.06 (m, 5H), 6.05 – 5.97 (m, 1H), 5.33 – 5.28 (m, 1H), 5.18 (d, *J*=10.0, 1H), 4.48 – 4.45 (m, 1H), 4.29 – 4.25 (m, 2H), 4.05 (dd, *J*=7.5, 16.5, 1H), 3.29 (dd, *J*=5.0, 15.0, 1H), 2.88 (dd, *J*=10.0, 15.0, 1H), 2.73 (d, *J*=8.0, 1H), 1.01 (t, *J*=8.0, 9H), 0.64 (q, *J*=8.0, 6H); ^{13}C NMR (126 MHz, CDCl3) δ = 147.7, 137.0, 135.7, 133.5, 133.1, 131.5, 130.9, 129.1, 128.4, 126.6, 124.0, 118.1, 105.3, 90.0, 65.3, 63.9, 47.7, 34.8, 7.4, 4.1; HRMS (EI) calcd. for [$C_{26}H_{34}N_2O_5SSi$] $(M+H)^+$ 515.2030, found 515.2031.

_N_-allyl-_N_-((2_S_,3_R_)-3-hydroxy-1-phenyl-5-(triethylsilyl)pent-4-yn-2-yl)-2-nitrobenzene sulfonamide (4d)

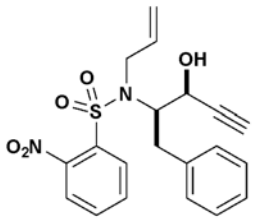


Yield 80% (inseparable mixture of diastereomers, *anti*/*syn* = 9:91) (yellow oil); IR (neat, cm^{-1}) ν = 3527, 2955, 2911, 2875, 2161, 1544, 1371, 1350, 1163, 1005; $[\alpha]_D^{20}$ = – 4.0 cm^3 g^{-1} dm^{-1} (c = 0.65 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, CDCl3) δ = 7.92 (d, *J*=8.0, 1H), 7.65 – 7.62 (m, 1H), 7.57 – 7.53 (m, 2H), 7.21 – 7.19 (m, 4H), 7.18 – 7.16 (m, 1H), 5.96 (ddd, *J*=6.0, 11.0, 16.5, 1H), 5.33 – 5.27 (m, 1H), 5.15 (d, *J*=10.0, 1H), 4.57 (dd, *J*=7.0, 16.5, 1H), 4.46 – 4.44 (m, 1H), 4.30 – 4.25 (m, 3H), 3.19 (dd, *J*=8.5, 14.5, 1H), 3.12 (dd, *J*=6.5, 14.5, 1H), 2.42 (d, *J*=6.5, 1H), 1.04 (t, *J*=8.0, 9H), 0.65 (q, *J*=8.0, 6H); ^{13}C NMR (126 MHz, CDCl3) δ = 148.1, 137.3, 136.1, 133.8, 133.7, 132.0, 131.8, 129., 128.8, 127.0, 124.4, 118.1, 104.6, 91.5, 63.9, 63.3, 47.7, 36.2, 7.7, 4.4; HRMS (EI) calcd. for [$C_{26}H_{34}N_2O_5SSi$] $(M+H)^+$ 515.2030, found 515.2020.

General procedure for triethylsilyl group (TES) cleavage

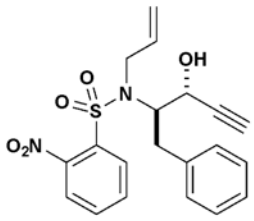
In a flask, the TES-protected propargylic alcohol was dissolved in wet THF (0.1M) and a 1:1 molar ratio tetrabutylammonium fluoride (TBAF)/acetic acid solution (1.6 equiv.) was added at 0 °C. The reaction mixture was stirred under nitrogen for 5h. The mixture was diluted with EtOAc and quenched with saturated aqueous NH_4Cl. The two phases were separated and the aqueous layer was extracted with EtOAc. The combined organic phases were washed with brine, dried over sodium sulfate, filtered and evaporated under reduced pressure. The resulting residue was purified by silica gel chromatography (Hex/EtOAc 3:2).

_N_-allyl-_N_-((2_R_,3_S_)-3-hydroxy-1-phenylpent-4-yn-2-yl)-2-nitrobenzenesulfonamide (1a)



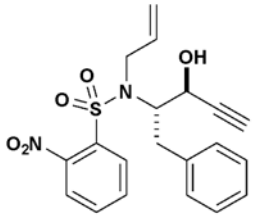
Yield 90% (pale yellow oil); IR (neat, cm^{-1}) ν = 3519, 3288, 3088, 3028, 2931, 2161, 1543, 1372, 1346, 1162, 1062; $[\alpha]_D^{20}$ = + 15.5 $cm^3\ g^{-1}\ dm^{-1}$ (c = 0.52 g cm^3, $CHCl_3$); ^1H NMR (500 MHz, CDCl3) δ = 7.86 (d, *J*=8.0, 1H), 7.63 (t, *J*=7.5, 1H), 7.56 – 7.52 (m, 2H), 7.21 – 7.14 (m, 5H), 5.95 (ddd, *J*=6.0, 11.0, 16.5, 1H), 5.31 (d, *J*=16.5, 1H), 5.16 (d, *J*=10.0, 1H), 4.52 – 4.50 (m, 1H), 4.46 (dd, *J*=6.5, 16.5, 1H), 4.33 – 4.28 (m, 1H), 4.24 (dd, *J*=6.0, 16.5, 1H), 3.20 (dd, *J*=8.0, 14.0, 1H), 3.10 (dd, *J*=7.0, 14.0, 1H), 2.65 (d, *J*=2.5, 1H), 2.51 (d, *J*=7.0, 1H); ^{13}C NMR (126 MHz, CDCl3) δ = 147.7, 136.9, 135.7, 133.5, 133.4, 131.6, 129.1, 128.5, 128.4, 126.8, 124.1, 118.1, 81.7, 76.4, 63.4, 63.2, 47.5, 35.4; HRMS (EI) calcd. for $[C_{20}H_{20}N_2O_5S]$ $(M+H)^+$ 401.1165, found 401.1158.

_N_-allyl-_N_-((2_R_,3_R_)-3-hydroxy-1-phenylpent-4-yn-2-yl)-2-nitrobenzenesulfonamide (1b)



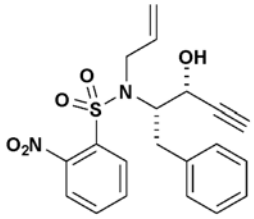
Yield 96% (white crystals). The purified compound was crystallized from $CHCl_3$/Hexanes. IR (neat, cm^{-1}) ν = 3523, 3289, 3088, 3028, 2930, 2118, 1543, 1372, 1347, 1162, 1063; $[\alpha]_D^{20}$ = – 51.5 $cm^3\ g^{-1}\ dm^{-1}$ (c = 0.40 g cm^3, $CHCl_3$); ^1H NMR (500 MHz, CDCl3) δ = 7.65 (d, *J*=8.0, 1H), 7.57 (t, *J*=7.5, 1H), 7.49 – 7.42 (m, 2H), 7.17 – 7.07 (m, 5H), 6.07 – 5.98 (m, 1H), 5.33 (d, *J*=17.5, 1H), 5.20 (d, *J*=10.0, 1H), 4.45 – 4.43 (m, 1H), 4.34 – 4.27 (m, 2H), 4.08 (dd, *J*=8.0, 16.5, 1H), 3.25 (dd, *J*=7.5, 14.0, 1H), 2.90 (dd, *J*=10.0, 15.0, 1H), 2.83 (br, 1H), 2.53 (d, *J*=2.5, 1H); ^{13}C NMR (126 MHz, CDCl3) δ = 147.7, 136.8, 135.7, 133.4, 133.2, 131.5, 131.1, 129.1, 128.4, 126.7, 124.0, 118.2, 82.6, 75.3, 64.8, 63.2, 48.0, 34.9; HRMS (EI) calcd. for $[C_{20}H_{20}N_2O_5S]$ $(M+H)^+$ 401.1165, found 401.1164.

_N_-allyl-_N_-((2_S_,3_S_)-3-hydroxy-1-phenylpent-4-yn-2-yl)-2-nitrobenzenesulfonamide (1c)



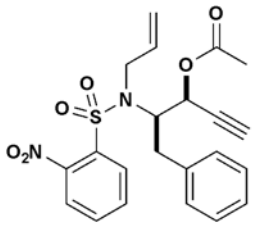
Yield 89% (white crystals). The purified compound was crystallized from $CHCl_3$/Hexanes. IR (neat, cm^{-1}) ν = 3523, 3289, 3089, 3028, 2930, 2118, 1543, 1372, 1347, 1162, 1063; $[\alpha]_D^{20}$ = + 52.5 cm^3 g^{-1} dm^{-1} (c = 0.52 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, CDCl3) δ = 7.64 (d, *J*=8.0, 1H), 7.56 (t, *J*=7.5, 1H), 7.48 – 7.42 (m, 2H), 7.15 – 7.08 (m, 5H), 6.06 – 5.98 (m, 1H), 5.32 (d, *J*=17.5, 1H), 5.20 (d, *J*=10.0, 1H), 4.45 – 4.43 (m, 1H), 4.33 – 4.29 (m, 2H), 4.08 (dd, *J*=8.0, 16.5, 1H), 3.26 (dd, *J*=5.0, 14.0, 1H), 2.90 (dd, *J*=10.0, 15.0, 1H), 2.90 – 2.87 (m, 1H), 2.53 (d, *J*=2.5, 1H); ^{13}C NMR (126 MHz, CDCl3) δ = 147.7, 136.8, 135.7, 133.4, 133.2, 131.5, 131.1, 129.1, 128.4, 126.7, 124.0, 118.2, 82.5, 75.3, 64.8, 63.1, 47.9, 34.9; HRMS (EI) calcd. for $[C_{20}H_{20}N_2O_5S]$ $(M+H)^+$ 401.1165, found 401.1160.

_N_-allyl-_N_-((2_S_,3_R_)-3-hydroxy-1-phenylpent-4-yn-2-yl)-2-nitrobenzenesulfonamide (1d)



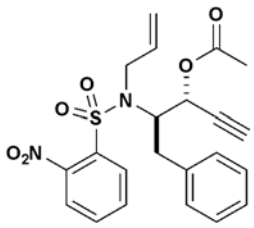
Yield 92% (pale yellow oil); IR (neat, cm^{-1}) ν = 3524, 3288, 3088, 3028, 2917, 2117, 1543, 1372, 1347, 1162, 1062; $[\alpha]_D^{20}$ = – 15.2 cm^3 g^{-1} dm^{-1} (c = 0.47 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, CDCl3) δ = 7.87 (d, *J*=8, 1H), 7.63 (t, *J*=7.5, 1H), 7.56 – 7.52 (m, 2H), 7.21 – 7.15 (m, 5H), 5.95 (ddd, *J*=6, 11, 16.5, 1H), 5.32 (d, *J*=17, 1H), 5.16 (d, *J*=10, 1H), 4.51 (m, 1H), 4.46 (dd, *J*=6.5, 16.5, 1H), 4.32 – 4.29 (m, 1H), 4.24 (dd, *J*=7, 16.5, 1H), 3.20 (dd, *J*=8, 14, 1H), 3.11 (dd, *J*=6.5, 14, 1H), 2.66 (d, *J*=2.5, 1H), 2.47 (br, 1H); ^{13}C NMR (126 MHz, CDCl3) δ = 147.8, 137.0, 135.7, 133.5, 133.4, 131.7, 131.6, 129.1, 128.5, 126.8, 124.1, 118.1, 81.7, 76.4, 63.4, 63.2, 47.5, 35.5; HRMS (EI) calcd. for $[C_{20}H_{20}N_2O_5S]$ $(M+H)^+$ 401.1165, found 401.1164.

(3_S_,4_R_)-4-(_N_-allyl-2-nitrophenylsulfonamido)-5-phenylpent-1-yn-3-yl acetate (6a)[5]



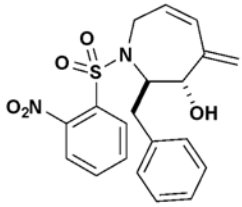
Yield 90% (whote powder); IR (neat, cm^{-1}) ν = 3282, 3090, 3029, 2918, 2124, 1745, 1534, 1371, 1353, 1226, 1164, 1031; $[\alpha]_D^{20}$ = + 55.4 cm^3 g^{-1} dm^{-1} (c = 0.50 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, CDCl3) δ = 7.84 (d, *J*=8.0, 1H), 7.65 – 7.62 (m, 1H), 7.59 – 7.53 (m, 2H), 7.28 – 7.18 (m, 5H), 5.78 –5.71 (m, 1H), 5.45 (dd, *J*=2.5, 10.0, 1H), 5.22 (d, *J*=17.0, 1H), 5.06 (dd, *J*=10.0, 1H), 4.59 (td, *J*=5.0, 8.0, 1H), 4.43 (dd, *J*=5.5, 17.5, 1H), 4.25 (dd, *J*=6.5, 17.0, 1H), 3.15 (d, *J*=7.5, 2H), 2.62 (d, *J*=2.5, 1H), 1.97 (s, 3H); ^{13}C NMR (126 MHz, CDCl3) δ = 169.1, 147.8, 136.3, 135.0, 134.1, 133.3, 131.7, 131.5, 129.1, 128.6, 127.0, 124.1, 117.6, 78.5, 76.8, 63.8, 60.4, 47.3, 36.1, 20.7; HRMS (EI) calcd. for $[C_{22}H_{22}N_2O_6S]$ $(M+H)^+$ 443.1271, found 443.1263.

(3_R_,4_R_)-4-(_N_-allyl-2-nitrophenylsulfonamido)-5-phenylpent-1-yn-3-yl acetate (6b)[5]



Yield 90% (white solid); IR (neat, cm^{-1}) ν = 3287, 3089, 3029, 2917, 2126, 1747, 1544, 1372, 1353, 1225, 1164, 1023; $[\alpha]_D^{20}$ = + 4.5 cm^3 g^{-1} dm^{-1} (c = 0.24 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, CDCl3) δ = 7.58 (t, *J*=7.5, 1H), 7.49 (d, *J*=8.0, 1H), 7.40 – 7.34 (m, 2H), 7.30 – 7.24 (m, 5H), 5.79 (ddd, *J*=6.0, 10.0, 16.5, 1H), 5.38 (dd, *J*=2.0, 7.0, 1H), 5.29 (d, *J*=17.5, 1H), 5.15 (d, *J*=10.0, 1H), 4.72 (dd, *J*=1.5, 6.5, 1H), 4.08 – 4.06 (m, 2H), 3.29 (dd, *J*=6.5, 14.0, 1H), 3.04 (dd, *J*=8.5, 14.0, 1H), 2.43 (d, *J*=2.5, 1H), 2.09 (s, 3H); ^{13}C NMR (126 MHz, CDCl3) δ = 169.2, 148.4, 136.8, 134.7, 133.4, 133.2, 131.3, 130.9, 129.3, 128.7, 127.0, 123.6, 118.5, 78.7, 76.1, 63.7, 62.1, 47.5, 35.5, 20.7; HRMS (EI) calcd. for $[C_{22}H_{22}N_2O_6S]$ $(M+H)^+$ 443.1271, found 443.1267.

(2*R*,3*S*,*Z*)-2-benzyl-4-methylene-1-(2-nitrophenylsulfonyl)-2,3,4,7-tetrahydro-1*H*-azepin-3-ol (5a)



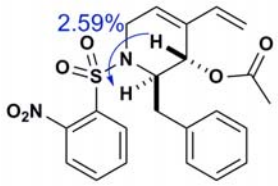
In a 15 mL flask, **1a** (0.0947 g, 0.236 mmol) was dissolved in dry toluene (0.05M) to give a colorless solution. Hoveyda-Grubbs 2nd generation catalyst (7.41 mg, 0.012 mmol) was added and the reaction mixture was stirred at room temperature under ethylene atmosphere (balloon) for 30 min. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography (Hex/EtAOc 1:1) to give **5a** in 50% yield as a pale yellow oil (0.048 mg, 0.120 mmol; *endo*/*exo* = 10: 1.5, inseparable on silica). Spectroscopic data for the major regioisomer: IR (neat, cm^{-1}) ν = 3530, 3090, 3028, 2924, 2855, 1543, 1372, 1340, 1162, 1126; ^{1}H NMR (500 MHz, CDCl3) δ = 7.81 (d, *J*=8.0, 1H), 7.70 (t, *J*=7.5, 1H), 7.52 – 7.49 (m, 2H), 7.19 – 7.14 (m, 5H), 6.06 (d, *J*=11.5, 1H), 5.68 –5.64 (m, 1H), 5.35 (s, 1H), 5.04 (s, 1H), 4.42 (dd, *J*=6.0, 19.0, 1H), 4.34 – 4.30 (m, 1H), 4.27 – 4.24 (m, 1H), 3.72 – 3.68 (m, 1H), 3.04 – 3.01 (m, 2H), 2.33 (d, *J*=2.5, 1H); ^{13}C NMR (126 MHz, CDCl3) δ = 145.5, 136.7, 133.3, 133.2, 131.3, 130.3, 129.6, 129.1, 128.4, 127.3, 126.8, 123.8, 118.8, 74.0, 63.1, 43.9, 37.1; HRMS (EI) calcd. for $[C_{20}H_{20}N_2O_5S]$ $(M+Na)^+$ 423.0985, found 423.0981.

General procedure for enyne metathesis reaction of 6a-b

In a 50 mL flask, the appropriate enyne substrate **6a** or **6b** (1 equiv.) was dissolved in dry dichloromethane (0.05M) to give a colorless solution. Hoveyda-Grubbs 2nd generation catalyst (20 mol%) was added and the reaction mixture was stirred under ethylene atmosphere (balloon) at 45 °C for 7h (*syn*-diastereomer) and for 10h (*anti*-diastereomer). The solvent was removed under

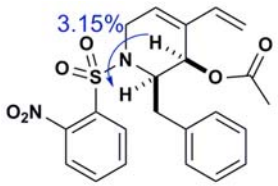
reduced pressure. The residue was purified by silica gel chromatography (Hex/EtAOc 7:3). The two diastereoisomeric products **7a** and **7b** are inseparable on silica.

(2*R*,3*S*)-2-benzyl-1-(2-nitrophenylsulfonyl)-4-vinyl-1,2,3,6-tetrahydropyridin-3-yl-acetate (7a)



Yield 68% (white powder); IR (neat, cm^{-1}) ν = 3091, 3028, 2956, 2853, 1735, 1543, 1371, 1234, 1165; $[\alpha]_D^{20}$ = – 22.5 cm^3 g^{-1} dm^{-1} (c = 0.20 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, CDCl3) δ = 7.65 (d, *J*=8.0, 1H), 7.58 – 7.56 (m, 2H), 7.47 – 7.43 (m, 1H), 7.12 – 7.07 (m, 5H), 6.35 (dd, *J*=10.5, 17.5, 1H), 6.09 – 6.08 (m, 1H), 5.42 (s, 1H), 5.11 (m, 2H), 4.60 (dd, *J*=4, 20.0, 1H), 4.52 (td, *J*=1.5, 8.0, 1H), 4.08 (d, *J*=20, 1H), 2.81 – 2.72 (m, 2H), 1.93 (s, 3H); ^{13}C NMR (126 MHz, CDCl3) δ = 170.9, 147.5, 136.6, 135.5, 134.3, 132.9, 131.9, 131.0 130.7, 129.1, 128.4, 128.1, 127.0, 124.1, 113.6, 65.1, 57.7, 41.7, 35.7, 20.9; HRMS (EI) calcd. for $[C_{22}H_{22}N_2O_6S]$ $(M+Na)^+$ 435.1090, found 465.1086. The relative configuration was confirmed by NOE experiment.

(2*R*,3*R*)-2-benzyl-1-(2-nitrophenylsulfonyl)-4-vinyl-1,2,3,6-tetrahydropyridin-3-yl-acetate (7b)



Yield 49% (pale yellow powder); IR (neat, cm^{-1}) ν = 3092, 3028, 2978, 2936, 1740, 1542, 1370, 1231, 1163; $[\alpha]_D^{20}$ = – 44.4 cm^3 g^{-1} dm^{-1} (c = 0.18 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, CDCl3) δ = 7.86 (d, *J*=8.0, 1H), 7.58 – 7.50 (m, 3H), 7.04 – 7.06 (m, 5H), 6.20 (dd, *J*=11.0, 17.5, 1H), 6.02 – 6.01 (m, 1H), 5.76 – 5.75 (br, 1H), 5.23 (d, *J*=17.5, 1H), 5.09 (d, *J*=11.5, 1H), 4.66 (m, 1H), 4.48 – 4.44 (m, 1H), 4.06 – 4.03 (m, 1H), 2.89 (dd, *J*=5.0, 14.5, 1H), 2.73 (dd, *J*=5.0, 9.5, 1H), 1.92 (s, 3H); ^{13}C NMR (126 MHz, CDCl3) δ =170.1, 147.0, 137.4, 133.7, 133.3, 133.2, 132.0, 131.1, 128.9, 128.1, 128.1, 126.4, 124.6, 123.8, 115.2, 68.6, 54.7, 41.1, 32.4, 20.5; HRMS (EI) calcd. for $[C_{22}H_{22}N_2O_6S]$ $(M+Na)^+$ 465.1090, found 465.1083. The relative configuration was confirmed by NOE experiment.

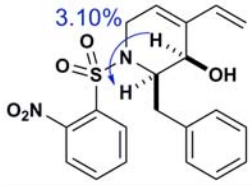
General procedure for the cycloisomerization reaction of enynes 1a-b

In a 10 mL microwave vial, the appropriate diastereomer **1a** or **1b** (1 equiv.) was dissolved in 1,2-dichloroethane (0.05M) to give a pale yellow solution. Indium(III) chloride (15 mol%) was added and the reaction was irradiated at 90 °C for 20 minutes. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography (Hex/EtAOc 7:3).

(2*R*,3*S*)-2-benzyl-1-(2-nitrophenylsulfonyl)-4-vinyl-1,2,3,6-tetrahydropyridin-3-ol (8a)

Yield 70% (colorless oil); IR (neat, cm^{-1}) ν = 3537, 3091, 3027, 2922, 2851, 1542, 1371, 1162, 1022; $[\alpha]_D^{20}$ = + 53.7 cm^3 g^{-1} dm^{-1} (c = 0.09 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, Benzene) δ = 7.76 (d, *J*=8.0, 1H), 6.98 – 6.94 (m, 4H), 6.93 – 6.90 (m, 1H), 6.64 – 6.61 (m, 1H), 6.57– 6.53 (m, 1H), 6.47 – 6.43 (m, 1H), 6.06 (dd, *J*=11.0, 17.5, 1H), 5.25 (d, *J*=17.5, 1H), 5.16 – 5.15 (m, 1H), 4.92 (d, *J*=12.5, 1H), 4.31 (dd, *J*=5.0, 20.0, 1H), 4.26 – 4.24 (m, 1H), 4.16 (d, *J*=8.0, 1H), 3.59 (d, *J*=20.0, 1H), 2.81 (dd, *J*=5.5, 13.0, 1H), 2.33 (dd, *J*=10.0, 13.0, 1H), 1.99 (br, 1H); ^{13}C NMR (126 MHz, CDCl3) δ = 147.5, 137.0, 135.8, 134.8, 133.6, 133.1, 131.9, 131.4, 129.1, 128.6, 126.8, 125.3, 124.3, 114.0, 63.4, 60.9, 41.6, 36.1; HRMS (EI) calcd. for $[C_{20}H_{20}N_2O_5S]$ $(M+H)^+$ 401.1165, found 401.1158. The relative configuration was determined by NOE experiment.

(2*R*,3*R*)-2-benzyl-1-(2-nitrophenylsulfonyl)-4-vinyl-1,2,3,6-tetrahydropyridin-3-ol (8b)



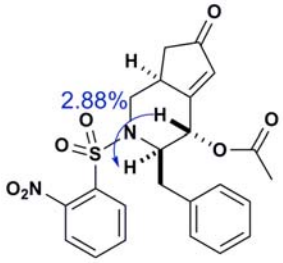
Yield 69% (white powder); IR (neat, cm^{-1}) ν = 3535, 3090, 3027, 2892, 1541, 1367, 1338, 1160, 1090; $[\alpha]_D^{20}$ = – 109.0 cm^3 g^{-1} dm^{-1} (c = 0.11 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, CDCl3) δ = 7.67 (dd, *J*=8.0, 1H), 7.53 – 7.52 (m, 2H), 7.44 – 7.41 (m, 1H), 7.06 – 7.05 (m, 2H), 6.97 – 6.92 (m, 3H), 6.34 (dd, *J*=11.5, 17.5, 1H), 5.89 (m, 1H), 5.50 (d, *J*=18.0, 1H), 5.20 (d, *J*=12.5, 1H), 4.81 (m, 1H), 4.40 – 4.36 (m, 1H), 4.32 (m, 1H), 4.14 – 4.10 (m, 1H), 3.18 (dd, *J*=5.0, 14.0, 1H), 2.61 (dd, *J*=10.0, 14.0, 1H), 2.10 (br, 1H); ^{13}C NMR (126 MHz, CDCl3) δ = 146.9, 137.9, 136.4, 134.6, 133.8, 132.9, 131.9, 130.7, 129.0, 128.0, 126.3, 124.4, 123.4, 115.8, 66.6, 59.3, 42.2, 30.8; HRMS (EI) calcd. for $[C_{20}H_{20}N_2O_5S]$ $(M+H)^+$ 401.1165, found 401.1172. The relative configuration was determined by NOE experiment.

General procedure for the Pauson-Khand reaction

In a flame-dried flask, the appropriate diastereomer **6a** or **6b** (1 equiv.) was dissolved in dry THF (0.05M) to give a colorless solution. Cobalt octacarbonyl (1.05 equiv) was added and the resulting orange reaction mixture was stirred for 1h under nitrogen. The solution was then cooled to 0 °C and 4-methylmorpholine 4-oxide (2 equiv) was added. The reaction was stirred for 3h at room temperature and then 2 more equiv of 4-methylmorpholine 4-oxide were added and the reaction mixture was stirred for further 3h under nitrogen. The mixture was passed through a short silica plug and eluted with EtOAc (15 mL) and DCM/EtOH 4:1 (15 mL). The filtrate was

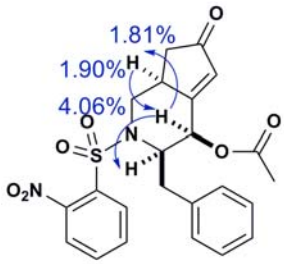
concentrated under reduced pressure and the residue purified by flash chromatography (Hex/EtOAc 1:1).

(3*R*,4*S*,7a*S*)-3-benzyl-2-(2-nitrophenylsulfonyl)-6-oxo-2,3,4,6,7,7a-hexahydro-1*H*-cyclopenta [c]pyridin-4-yl acetate (9a)



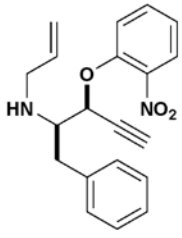
Yield 70% (white powder); IR (neat, cm^{-1}) ν = 3093, 3028, 2919, 2850, 1741, 1716, 1636, 1543, 1371, 1233, 1164, 1127, 1062; $[\alpha]_D^{20}$ = – 125.0 cm^3 g^{-1} dm^{-1} (c = 0.12 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, CDCl3) δ = 7.67 (d, *J*=8.0, 1H), 7.63 – 7.62 (m, 2H), 7.53 – 7.49 (m, 1H), 7.20 – 7.12 (m, 5H), 6.25 (d, *J*=1.5, 1H), 5.46 (d, *J*=2.0, 1H), 4.71 (t, *J*=8.0, 1H), 4.32 (dd, *J*=6.5, 13.5, 1H), 3.50 – 3.45 (m, 1H), 3.02 – 2.97 (m, 1H), 2.82 (dd, *J*=7.5, 13.5, 1H), 2.73 (dd, *J*=8.5, 13.5, 1H), 2.65 (dd, *J*=7.0, 19.0, 1H), 2.10 (dd, *J*=2.5, 19.0, 1H), 1.96 (s, 3H); ^{13}C NMR (126 MHz, CDCl3) δ = 206.2, 170.6, 169.9, 147.5, 135.6, 133.8, 133.3, 132.5, 132.0, 130.9, 129.0, 128.8, 127.3, 124.3, 68.2, 59.1, 47.6, 38.3, 37.2, 34.6, 20.8; HRMS (EI) calcd. for $[C_{23}H_{22}N_2O_7S]$ $(M+H)^+$ 471.1220, found 471.1228. The relative configuration was determined by NOE experiment.

(3*R*,4*R*,7a*S*)-3-benzyl-2-(2-nitrophenylsulfonyl)-6-oxo-2,3,4,6,7,7a-hexahydro-1*H*-cyclopenta [c]pyridin-4-yl acetate (9b)



Yield 55% (white powder); IR (neat, cm^{-1}) ν = 3093, 3028, 2917, 2849, 1747, 1711, 1632, 1541, 1367, 1227, 1161, 1058; $[\alpha]_D^{20}$ = – 142.3 cm^3 g^{-1} dm^{-1} (c = 0.25 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, CDCl3) δ = 7.77 (d, *J*=8.0, 1H), 7.61 – 7.56 (m, 2H), 7.51 – 7.47 (m, 1H), 6.97 – 6.93 (m, 5H), 6.19 (s, 1H), 5.85 (d, *J*=6.0, 1H), 4.74 – 4.69 (m, 1H), 4.43 (dd, *J*=6.0, 13.5, 1H), 3.27 – 3.22 (m, 1H), 3.07 (dd, *J*=11.5, 14.0, 1H), 2.90 (dd, *J*=5.0, 15.0, 1H), 2.68 – 2.58 (m, 2H), 2.21 (dd, *J*=2.5, 19.0, 1H), 2.04 (s, 3H); ^{13}C NMR (126 MHz, CDCl3) δ = 205.0, 173.8, 169.2, 147.0, 136.3, 133.5, 133.0, 132.1, 131.1, 128.8, 128.7, 128.2, 126.6, 124.8, 72.0, 58.6, 46.5, 41.4, 38.3, 31.8, 20.4; HRMS (EI) calcd. for $[C_{23}H_{22}N_2O_7S]$ $(M+H)^+$ 471.1220, found 471.1227. The relative configuration was determined by NOE experiment.

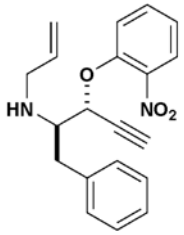
(2*R*,3*S*)-*N*-allyl-3-(2-nitrophenoxy)-1-phenylpent-4-yn-2-amine (10a)



In 10 mL-flask, **1a** (0.0083 g, 0.021 mmol) was dissolved in THF (0.207 mL, 0.1M). The resulting solution was cooled to 0 °C and TBAF (0.065 mL, 0.065

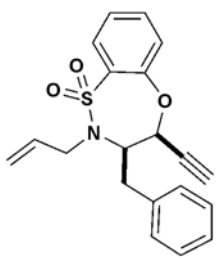
mmol) was added. The reaction mixture was stirred under nitrogen for 30 min, then it was quenched with saturated aqueous NH_4Cl, the solvent removed under reduced pressure and the residue was loaded on TLC plate. The plate was developed using Hex/EtOAc 7:3. Yield 50% (yellow oil); IR (neat, cm^{-1}) ν = 3287, 3062, 3027, 2923, 2858, 2116, 1605, 1524, 1484, 1349, 1277, 1248; $[\alpha]_D^{20}$ = – 4.5 cm^3 g^{-1} dm^{-1} (c = 0.2 g cm^3, $CHCl_3$); ^{1}H NMR (600 Hz, CDCl3) δ = 7.87 (d, *J*=7.0, 1H), 7.51 (t, *J*=7.0, 1H), 7.32 – 7.21 (m, 6H), 7.07 (t, *J*=7.0, 1H), 5.80 (ddd, *J*=5.0, 9.5, 14.0, 1H), 5.14 (d, *J*=15.0, 1H), 5.07 (d, *J*=8.5, 1H), 4.83 (m, 1H), 3.38 – 3.36 (m, 2H), 3.36 –3.34 (m, 1H), 3.06 (dd, *J*=5.0, 12.0, 1H), 3.00 (dd, *J*=5.0, 12.0, 1H), 2.67 (d, *J*=2.5, 1H), 1.67 (br, 1H); ^{13}C NMR (126 MHz, CDCl3) δ = 150.7, 140.2, 138.3, 137.6, 133.9, 129.4, 129.3, 128.5, 126.5, 125.7, 121.3, 116.2, 78.6, 78.0, 71.6, 61.6, 50.3, 37.2; HRMS (EI) calcd. for $[C_{20}H_{20}N_2O_3S]$ $(M+H)^+$ 337.1546, found 337.1546.

(2*R*,3*R*)-*N*-allyl-3-(2-nitrophenoxy)-1-phenylpent-4-yn-2-amine (10b)



In 50 mL-flask, **1b** (0.123 g, 0.307 mmol) was dissolved in THF (6.14 mL, 0.1M) and DBU (0.139 mL, 0.921 mmol) was added. The reaction mixture was heated to 64 °C and stirred under nitrogen for 4h. Then the reaction was quenched with water, EtOAc was added and the two phases were separated. The aqueous layer was extracted with EtOAc and the combined organic phases were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (Hex/EtOAc 7:3). Yield 70% (yellow oil); IR (neat, cm^{-1}) ν = 3287, 3062, 3027, 2918, 2116, 1605, 1525, 1483, 1350, 1277, 1248; $[\alpha]_D^{20}$ = + 10.8 cm^3 g^{-1} dm^{-1} (c = 0.16 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, CDCl3) δ = 7.91 (d, *J*=8.0, 1H), 7.53 (t, *J*=7.0, 1H), 7.30 – 7.21 (m, 6H), 7.09 (t, *J*=8.0, 1H), 5.78 (ddd, *J*=5.0, 9.5, 14.0, 1H), 5.13 (d, J=17.0, 1H), 5.05 (d, *J*=10.0, 1H), 4.82 (m, 1H), 3.35 – 3.34 (m, 2H), 3.32 – 3.28 (m, 1H), 3.19 (dd, *J*=6.0, 14.0, 1H), 2.89 (dd, *J*=7.5, 14.0, 1H), 2.61 (d, *J*=2.0, 1H), 1.63 (br, 1H); ^{13}C NMR (126 MHz, CDCl3) δ = 150.7, 140.1, 138.4, 136.7, 134.0, 129.4, 128.5, 126.4, 125.8, 121.2, 116.2, 116.1, 79.2, 70.9, 61.5, 50.4, 36.8; HRMS (EI) calcd. for $[C_{20}H_{20}N_2O_3S]$ $(M+H)^+$ 337.1546, found 337.1556.

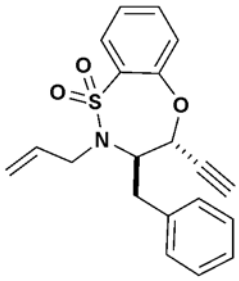
(3*R*,4*S*)-3-benzyl-4-ethynyl-2-prop-2-en-1-yl-3,4-dihydro-2*H*-5,1,2-benzoxathiazepine 1,1-dioxide (11a)



In a 100 mL flame-dried flask, propargylic alcohol **1a** (0.450 g, 1.124 mmol) was dissolved in dry THF (11.24 mL). The resulting colorless solution was

cooled −10 ºC and sodium hydride (0.081 g, 3.37 mmol) was added. The reaction was stirred under nitrogen for 5h, maintaining the temperature between −10 ºC and 0 ºC. Then, the reaction mixture was quenched with saturated aqueous NH_4Cl at 0 ºC. Diethyl ether and water were added and the two phases were separated. The aqueous layer was extracted with diethyl ether and the combined organic phases were dried over Na_2SO_4, filtered and evaporated under reduced pressure. The resulting residue was purified by silica gel chromatography (Hex/EtOAc 7:3). Yield 75% (white solid). The purified compound was crystallized from $CHCl_3$/Hexanes. IR (neat, cm^{-1}) ν = 3275, 3065, 3028, 2929, 2119, 1589, 1467, 1447, 1345, 1171, 1073, 1007; $[\alpha]_D^{20}$ = – 27.1 $cm^3\ g^{-1}\ dm^{-1}$ (c = 0.63 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, DMSO, T = 65 °C) δ = 7.75 (d, *J*=8.0, 1H), 7.66 (t, *J*=8.0, 1H), 7.39 (t, *J*=8.0, 1H), 7.36 – 7.35 (m, 4H), 7.29 – 7.26 (m, 2H), 5.46 (ddd, *J*=6.0, 11.0, 16.5, 1H), 5.07 – 5.03 (m, 2H), 4.95 (d, *J*=10.5, 1H), 4.46 (br, 1H), 3.99 (dd, *J*= 5.0, 16.5, 1H), 3.82 (d, *J*=2.5, 1H), 3.48 (dd, *J*=5.0, 17.0, 1H), 3.36 – 3.31 (m, 1H), 3.16 (dd, *J*=6.0, 14.5, 1H); ^{13}C NMR (126 MHz, CDCl3, T = 55 °C) δ = 152.6, 136.7, 135.7, 135.5, 133.8, 129.3, 128.8, 128.7, 127.1, 125.7, 124.8, 116.9, 80.7, 77.1, 70.5, 63.2, 48.9, 35.8; HRMS (EI) calcd. for $[C_{20}H_{19}NO_3S]$ $(M+H)^+$ 354.1158, found 354.1161.

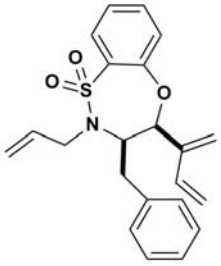
(3*R*,4*R*)-3-benzyl-4-ethynyl-2-prop-2-en-1-yl-3,4-dihydro-2*H*-5,1,2-benzoxathiazepine 1,1-dioxide (11b)



In a 50 mL flame-dried flask, propargylic alcohol **1b** (0.106 g, 0.264 mmol) was dissolved in dry THF (5.28 mL). The resulting colorless solution was cooled 0 ºC and sodium hydride (0.019 g, 0.792 mmol) was added. The reaction was stirred under nitrogen for 5h, allowing the temperature to rise to room temperature. Then, the reaction mixture was quenched with saturated aqueous NH_4Cl at 0 ºC. Diethyl ether and water were added and the two phases were separated. The aqueous layer was extracted with diethyl ether and the combined organic phases were dried over Na_2SO_4, filtered and evaporated under reduced pressure. The resulting residue was purified by silica gel chromatography (Hex/EtOAc 4:1). Yield 35% (white solid); IR (neat, cm^{-1}) ν = 3278, 3066, 3028, 2923, 2850, 2127, 1593, 1470, 1443, 1340, 1155, 1075; $[\alpha]_D^{20}$ = – 8.8 $cm^3\ g^{-1}\ dm^{-1}$ (c = 0.11 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, CDCl3, T = 55 °C) δ = 7.82 (d, *J*=7.5, 1H), 7.44 (t, *J*=8.0, 1H), 7.34 – 7.32 (m, 4H), 7.28 – 7.25 (m, 1H), 7.20 (t, *J*=7.5, 1H), 7.15 (d, *J*=7.5, 1H), 5.59 (d, *J*=10, 1H), 5.02 – 4.96 (m, 1H), 4.90 (d, *J*=17.0, 1H), 4.83 (d, *J*=10.0 1H), 3.76 (t, *J*=10.0, 1H), 3.53 (m, 2H), 3.32 – 3.27 (m, 1H), 3.17 (dd, *J*=3.5, 14.0, 1H), 2.77 (d, *J*=2.0, 1H); ^{13}C NMR (126 MHz, CDCl3, T = 55 °C) δ =

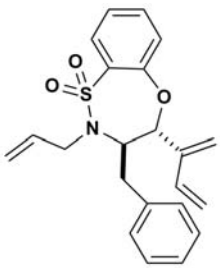
154.0, 137.7,133.4, 132.3, 130.2, 128.4, 128.3, 126.6, 124.1, 121.9, 119.1, 79.2, 77.1, 75.7, 67.5, 55.3, 37.2; HRMS (EI) calcd. for [$C_{20}H_{19}NO_3S$] $(M+Na)^+$ 376.0977, found 376.0974.

(3*R*,4*S*)-3-benzyl-4-(1-methylideneprop-2-en-1-yl)-2-prop-2-en-1-yl-3,4-dihydro-2*H*-5,1,2-benzoxathiazepine (12a)



In 25 mL flame-dried pear flask, **11a** (0.100 g, 0.283 mmol) was dissolved in dry benzene (5.66 mL) to give a colorless solution. Hoveyda-Grubbs 2nd generation catalyst (8.86 mg, 0.014 mmol) was added and the resulting green solution was stirred under ethylene atmosphere (balloon) for 45 min at room temperature. The reaction mixture was concentrated to about 2 mL, $Pb(OAc)_4$ (8.7 mg, 5 equiv to the amount of Grubbs catalyst) was added and the resulting mixture was stirred under nitrogen for 18h at room temperature. The solvent was evaporated under reduced pressure and the residue was purified by silica gel chromatography (Hex/EtOAc 9:1). Yield 56% (white powder); IR (neat, cm^{-1}) ν = 3086, 3064, 3027, 2926, 2855, 1589, 1468, 1447, 1350, 1263, 1229, 1169, 1072, 1012; $[\alpha]_D^{20}$ = + 91.3 $cm^3\ g^{-1}\ dm^{-1}$ (c = 0.15 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, Benzene) δ = 7.85 (d, *J*=8.0, 1H), 7.47 – 7.46 (m, 2H), 7.14 – 7.10 (m, 2H), 7.03 (t, *J*=7.0, 1H), 6.85 – 6.79 (m, 2H), 6.66 (t, *J*=7.0, 1H), 6.07 (dd, *J*=11.0, 18.0, 1H), 5.74 (s, 1H), 5.22 (s, 1H), 4.99 (ddd, *J*=4.0, 11.0, 17.5, 1H), 4.80 – 4.77 (m, 2H), 4.57 (d, *J*=10.0, 1H), 4.50 (d, *J*=17.0, 1H), 4.46 (m, 1H), 4.15 – 4.10 (m, 1H), 3.87 (dd, *J*=5.0, 15.0, 1H), 3.61 – 3.57 (m, 1H), 2.89 (dd, *J*=3.0, 14.0, 1H), 2.77 (dd, *J*=8.0, 15.0, 1H); ^{13}C NMR (126 MHz, CDCl3) δ = 156.5, 142.5, 138.7, 136.1, 135.8, 134.2, 133.2, 130.0, 128.2, 128.0, 126.0, 124.7, 123.3, 118.7, 118.1, 114.4, 81.0, 64.5, 53.7, 32.6; HRMS (EI) calcd. for [$C_{22}H_{23}NO_3S$] $(M+H)^+$ 382.1471, found 382.1475.

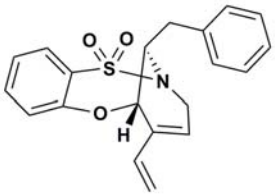
(3*R*,4*R*)-3-benzyl-4-(1-methylideneprop-2-en-1-yl)-2-prop-2-en-1-yl-3,4-dihydro-2*H*-5,1,2-benzoxathiazepine (12b)



12b was obtained from **11b** (0.0115 g, 0.033 mmol) according to the procedure described for the diastereomer **12a**. 10 mol% of Hoveyda-Grubbs 2nd generation catalyst were used in this case and the reaction mixture was stirred for 6h. The residue was loaded on TLC plate. The plate was developed using Hex/EtOAc 9:1. Yield 39% (white powder); IR (neat, cm^{-1}) ν = 3086, 3065, 3028, 2933, 2866, 1594, 1470, 1443, 1339, 1265, 1227, 1154, 1075; $[\alpha]_D^{20}$ = + 23.3 $cm^3\ g^{-1}\ dm^{-1}$ (c = 0.24 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, Benzene)

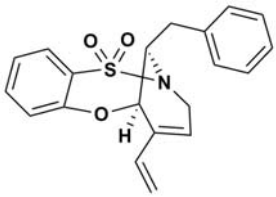
δ = 7.90 (d, J=8.0, 1H), 7.29 – 7.28 (m, 2H), 7.09 – 7.06 (m, 2H), 7.02 – 6.89 (m, 1H), 6.79 – 6.73 (m, 2H), 6.57 (t, *J*=8.0, 1H), 6.26 (dd, *J*=12.5, 18.0, 1H), 5.76 – 5.74 (m, 1H), 5.45 (d, *J*=18.0, 1H), 5.01 (s, 1H), 4.97 – 4.95 (m, 1H), 4.95 (buried s, 1H), 4.90 – 4.87 (m, 1H), 4.58 – 4.53 (m, 2H), 3.82 (m, 1H), 3.55 – 3.45 (m, 2H), 3.43 – 3.38 (m, 1H), 2.57 (dd, *J*=3.0, 13.0, 1H); ^{13}C NMR (126 MHz, CDCl3) δ = 155.04, 143.50, 138.03, 134.75, 133.25, 132.55, 130.15, 128.35, 128.26, 126.42, 123.42, 121.58, 119.07, 119.00, 116.86, 86.74, 65.77, 55.49, 36.93; HRMS (EI) calcd. for $[C_{22}H_{23}NO_3S]$ $(M+H)^+$ 382.1471, found 382.1474.

(10*R*,14*S*)-14-benzyl-11-ethenyl-9-oxa-2-thia-1-azatricyclo[8.3.1.0^{3,8}]tetradeca-3,5,7,11-tetraene 2,2-dioxide (13a)



In 25 mL flame-dried pear flask, **11a** (0.055 g, 0.156 mmol) was dissolved dry DCM (7.78 mL) to give a colorless solution. Grubbs catalyst 1st generation (3.84 mg, 4.67 μmol) was added and the resulting pink solution was stirred under nitrogen for 2h at room temperature. The reaction mixture was concentrated to about 2 mL, $Pb(OAc)_4$ (9 mg, 5 equiv to the amount of Grubbs catalyst) was added and the resulting mixture was stirred under nitrogen for 18h at room temperature. The solvent was evaporated under reduced pressure and the residue was purified by silica gel chromatography (Hex/EtOAc 1:1). The purified compound was crystallized from $CHCl_3$/Hexanes. Yield 95 % (white solid); IR (neat, cm^{-1}) ν = 3063, 3027, 2924, 2852, 1589, 1466, 1444, 1344, 1167, 1072; $[\alpha]_D^{20}$ = – 77.7 cm^3 g^{-1} dm^{-1} (c = 0.09 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, CDCl3) δ = 7.80 (d, *J*=8.0, 1H), 7.38 – 7.33 (m, 3H), 7.29 – 7.24 (m, 3H), 7.16 (t, *J*=7.0, 1H), 6.92 (d, *J*=8.0, 1H), 6.08 (dd, *J*=11.0, 17.5, 1H), 5.70 – 5.69 (m, 1H), 5.54 (d, *J*=17.5, 1H), 5.19 (d, *J*=11.0, 1H), 4.97 – 4.93 (m, 2H), 4.15 (dd, *J*=4.0, 21.0, 1H), 3.93 (d, *J*=21.0, 1H), 2.99 (dd, *J*=7.0, 14.0, 1H), 2.78 (dd, *J*=9.5, 14.0, 1H); ^{13}C NMR (126 MHz, CDCl3) δ =151.3, 136.4, 134.1, 133.7, 130.2, 129.01, 128.9, 128.8, 128.2, 127.0, 125.0, 124.0, 114.6, 70.2, 58.4, 41.8, 35.8; HRMS (EI) calcd. for $[C_{20}H_{19}NO_3S]$ $(M+H)^+$ 354.1158, found 354.1162.

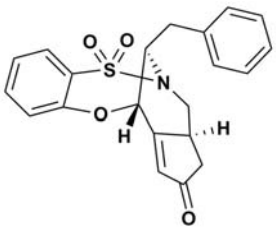
(10*R*,14*R*)-14-benzyl-11-ethenyl-9-oxa-2-thia-1-azatricyclo[8.3.1.0^{3,8}]tetradeca-3,5,7,11-tetraene 2,2-dioxide (13b)



13b was obtained from **11b** (0.0115 g, 0.033 mmol) according to the enyne metathesis procedure described for the compound **12b**. Yield 19% (white solid); IR (neat, cm^{-1}) ν = 3063, 3027, 2930, 1589, 1468, 1443, 1350, 1333, 1167, 1068; $[\alpha]_D^{20}$ = + 81.6 cm^3 g^{-1} dm^{-1} (c = 0.12 g

cm^3, $CHCl_3$); ^{1}H NMR (600 MHz, CDCl3) δ = 7.82 (d, *J*=8.0, 1H), 7.42 – 7.41 (m, 2H), 7.38 – 7.36 (m, 2H), 7.29 – 7.27 (m, 2H), 7.17 (t, *J*=7.5, 1H), 7.03 (d, *J*=8.0, 1H), 5.90 (dd, *J*=11.0, 17.5, 1H), 5.62 (m, 1H), 5.51 (d, *J*=17.5, 1H), 5.10 (d, *J*=11.0, 1H), 4.94 (s, 1H), 4.40 (dd, *J*=3.5, 17.0, 1H), 4.00 (d, *J*=17.0, 1H), 3.72 (dd, *J*=7.5, 11.5, 1H), 3.58 (dd, *J*=5.0, 10.0, 1H), 3.52 (dd, *J*=4.0, 11.5, 1H); ^{13}C NMR (126 MHz, CDCl3) δ = 150.7, 139.0, 135.8, 135.0, 133.4, 133.0, 129.7, 129.2, 128.7, 128.0, 126.7, 125.3, 123.9, 114.7, 68.7, 63.6, 50.0, 37.1; HRMS (EI) calcd. for [$C_{20}H_{19}NO_3S$] $(M+H)^+$ 354.1158, found 354.1158.

Compound (14a)



14a was obtained from **11a** (0.158 g, 0.447 mmol) according to the reported general procedure for the Pauson-Khand reaction. In the work-up phase, the filtrate was washed with 5% $CuSO_4$ aqueous solution. The aqueous phase was extracted with EtOAc. The combined organic layers were washed once with brine, dried over Na_2SO_4 and evaporated under reduced pressure. The residue was purified by silica gel chromatography (Hex/EtOAc 1:1). The purified compound was crystallized from $CHCl_3$/Hexanes. Yield 26% (pale yellow solid); IR (neat, cm^{-1}) ν = 3064, 3029, 2924, 2854, 1716, 1621, 1589, 1466, 1341, 1261, 1207, 1166, 1000; $[\alpha]_D^{20}$ = – 130.0 cm^3 g^{-1} dm^{-1} (c = 0.04 g cm^3, $CHCl_3$); ^{1}H NMR (500 MHz, Benzene) δ = 7.89 (d, *J*=8.0, 1H), 7.09 – 7.03 (m, 3H), 6.88 – 6.87 (m, 2H), 6.77 (t, *J*=8.0, 1H), 6.69 (d, *J*=8.0, 1H), 6.59 (t, *J*=8.0, 1H), 5.69 (d, *J*=2.0, 1H), 5.21 (t, *J*=8.5, 1H), 4.62 (d, *J*=2.0, 1H), 3.78 (dd, *J*=8.0, 15.0, 1H), 2.38 (dd, *J*=7.5, 14.0, 1H), 2.30 (dd, *J*=11.5, 15.0, 1H), 2.07 (dd, *J*=10.0, 15.0, 1H), 2.03 – 2.01 (m, 1H), 1.39 (dd, *J*=6.5, 18.5, 1H), 1.01 (dd, *J*=3.0, 18.5, 1H); ^{13}C NMR (126 MHz, CDCl3) δ = 205.1, 169.5, 152.5, 136.7, 135.5, 134.9, 129.2, 129.1, 128.8, 127.4, 124.9, 124.8, 73.9, 60.8, 46.5, 40.1, 35.2, 35.1; HRMS (EI) calcd. for [$C_{21}H_{19}NO_4S$] $(M+H)^+$ 382.1107, found 382.1110.

References

(1) Weininger, D. A. *J. Chem. Inf. Comput. Sci.* **1988**, *28*, 31-36.

(2) Sauer, W. H.; Schwarz, M. K. *J. Chem. Inf. Comput. Sci.* **2003**, *43*, 987-1003.

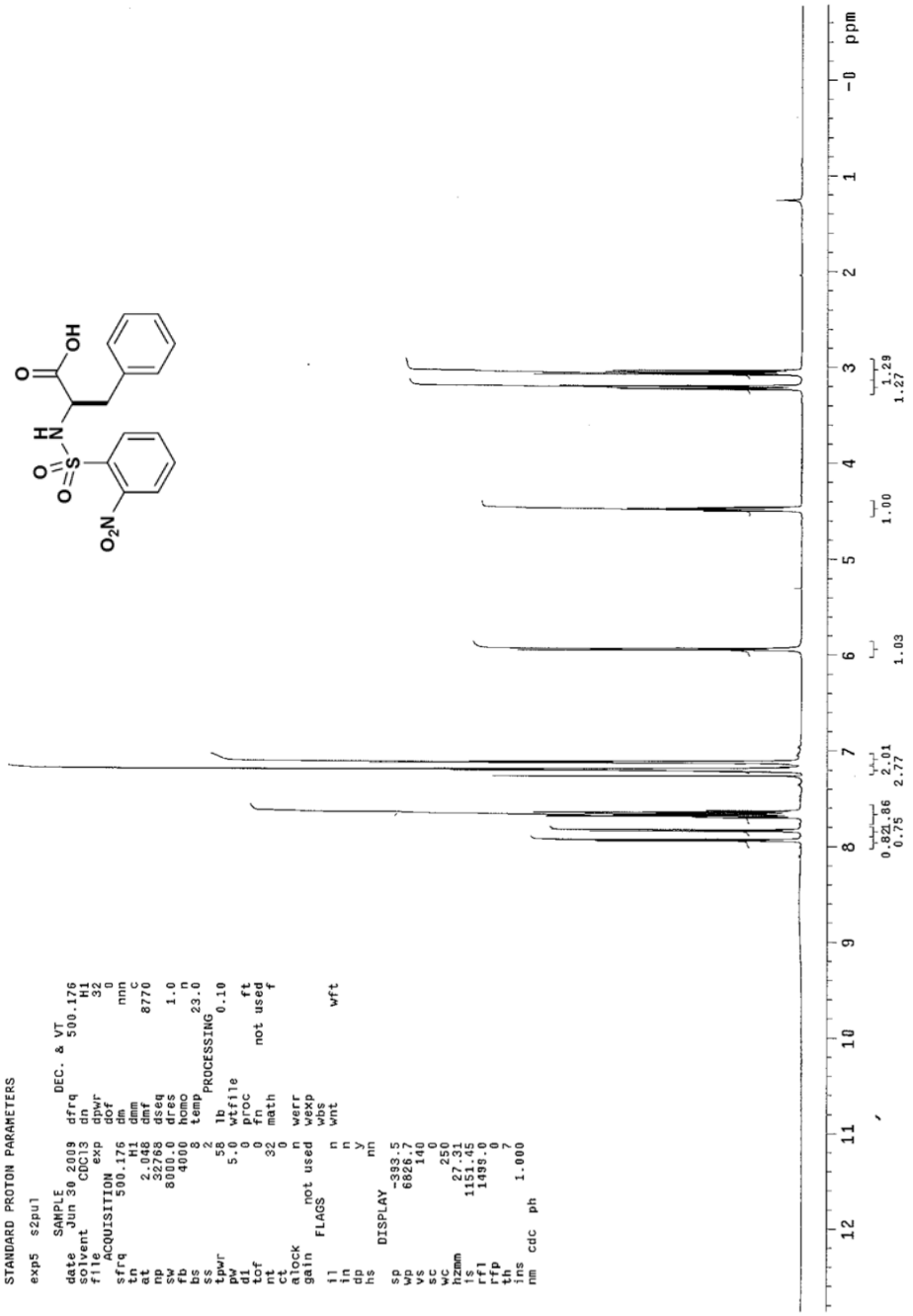
(3) Fukuyama, T.; Jow, C-K.; Cheung, M. *Tetrahedron Lett.* **1995**, *36*, 6373-6374.

(4) Miller, S. C.; Scanlan, T. S. *J. Am. Chem. Soc.* **1998**, *120*, 2690-2691.

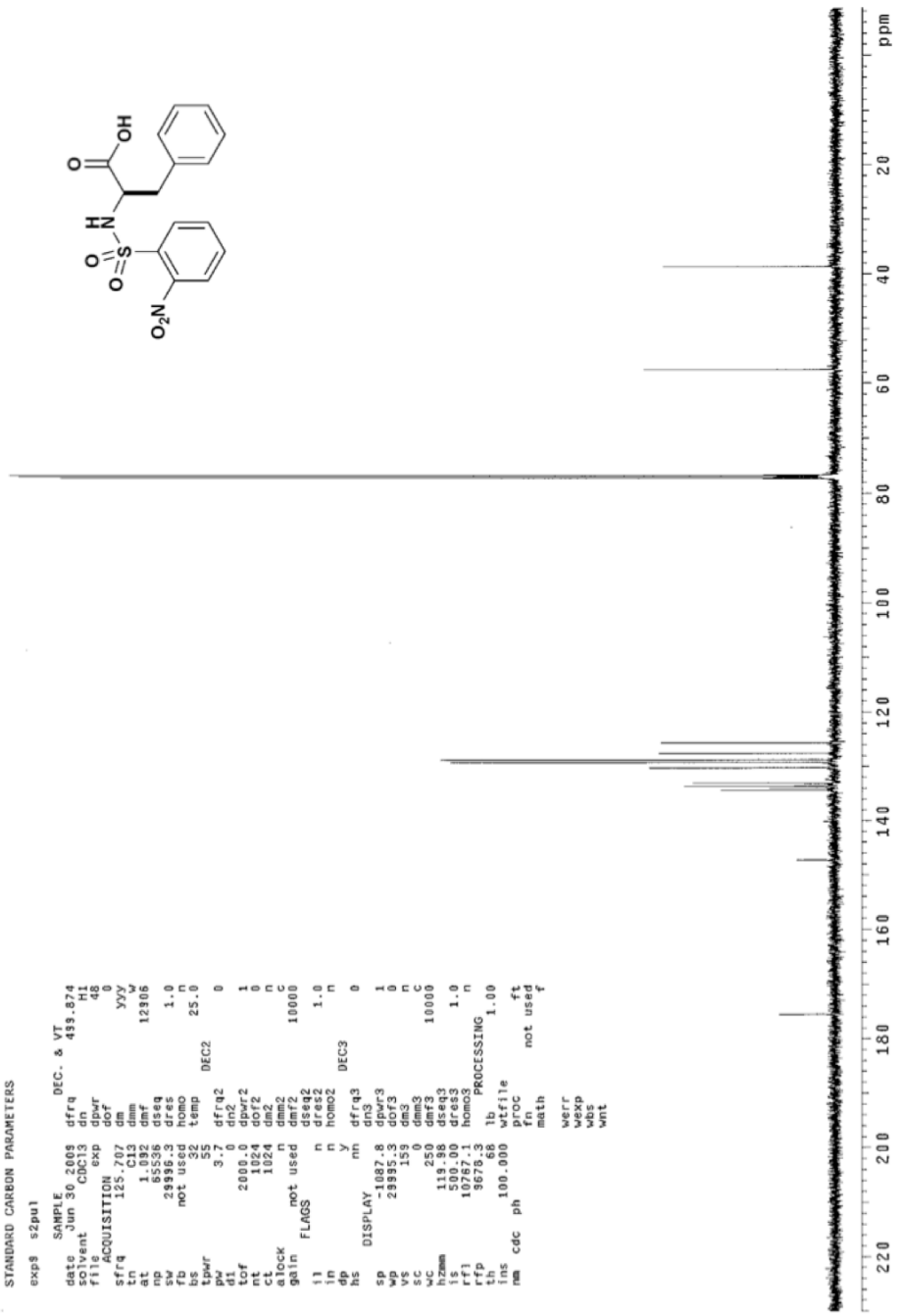
(5) For the acetylation of the amino propagylic alcohols **1a** and **1b** see: Hofle, G.; Steglich, W.; Vorbruggen, H. *Angew. Chemie* **1978**, *90*, 602-615; *Angew. Chemie Int. Ed.* **1978**, *17*, 569-583;

III. ^{1}H and ^{13}C NMR spectra

Spectral data for (*R*)-2-(2-nitrophenylsulfonamido)-3-phenylpropanoic acid *(R)*-i

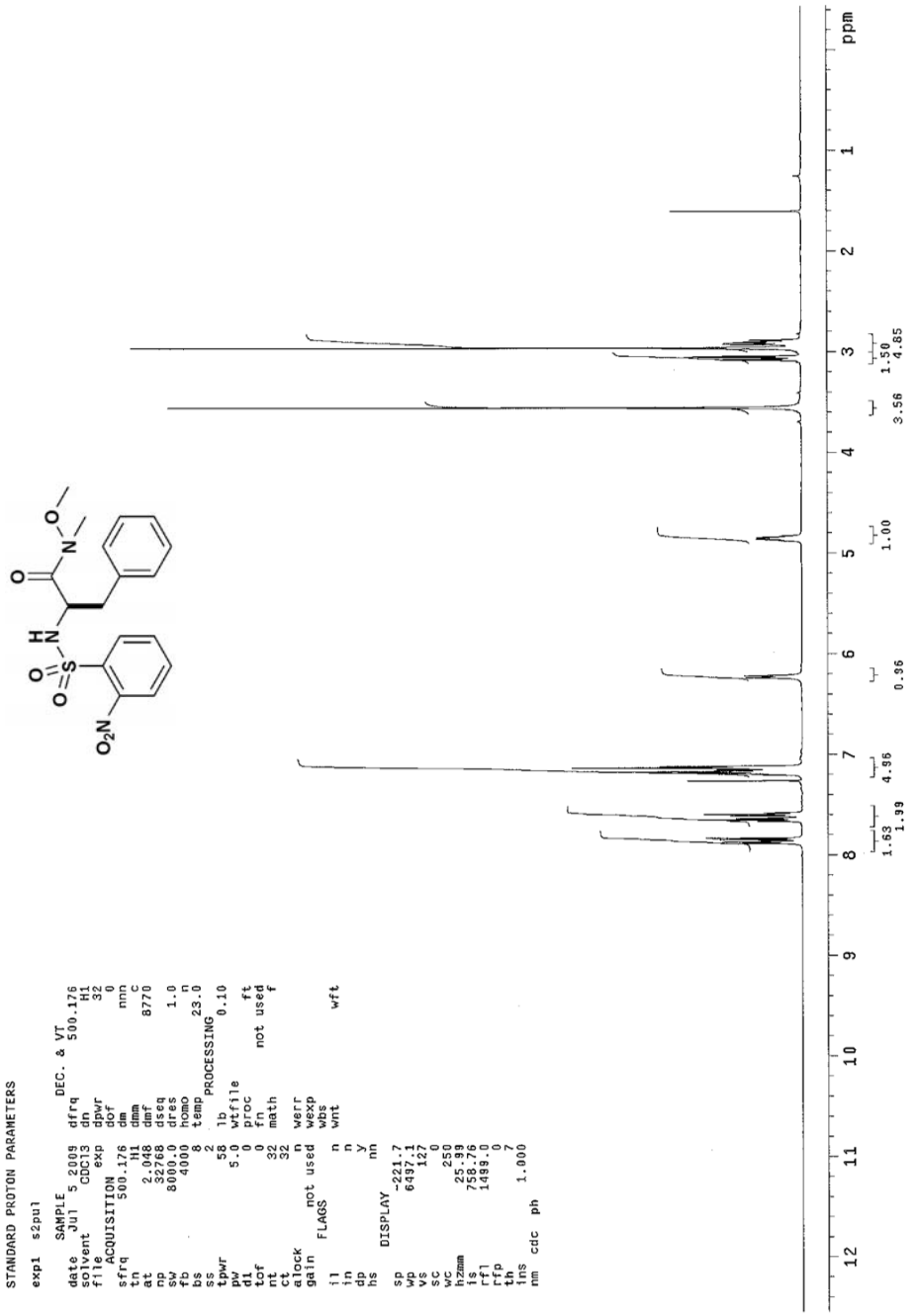


^{1}H NMR (500 MHz, $CDCl_3$) of compound **(*R*)-i**

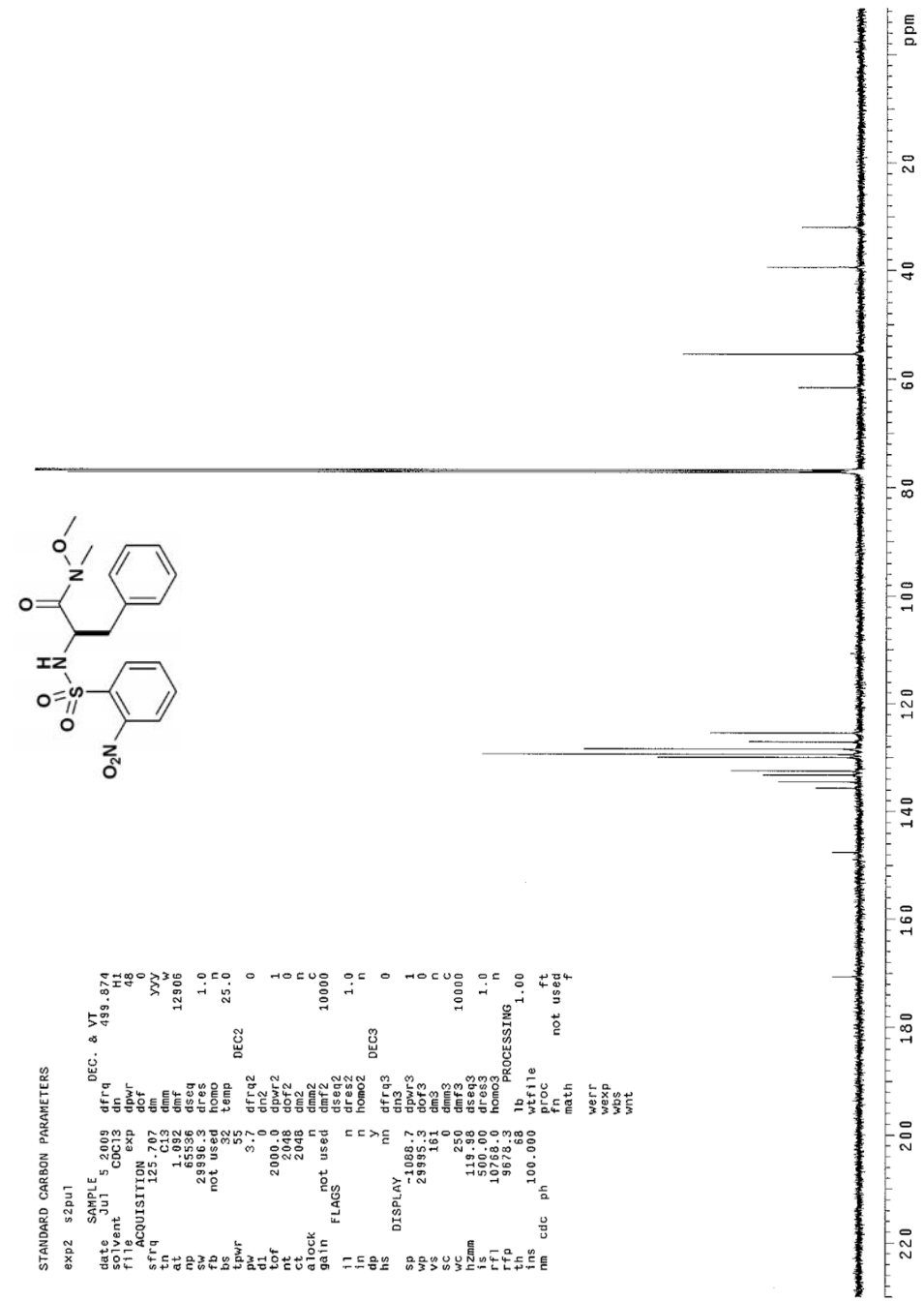


^{13}C NMR (500 MHz, $CDCl_3$) of compound **(*R*)-i**

Spectral data for (*R*)-*N*-methoxy-*N*-methyl-2-(2-nitrophenylsulfonamido)-3-phenylpropanamide (*R*)-ii

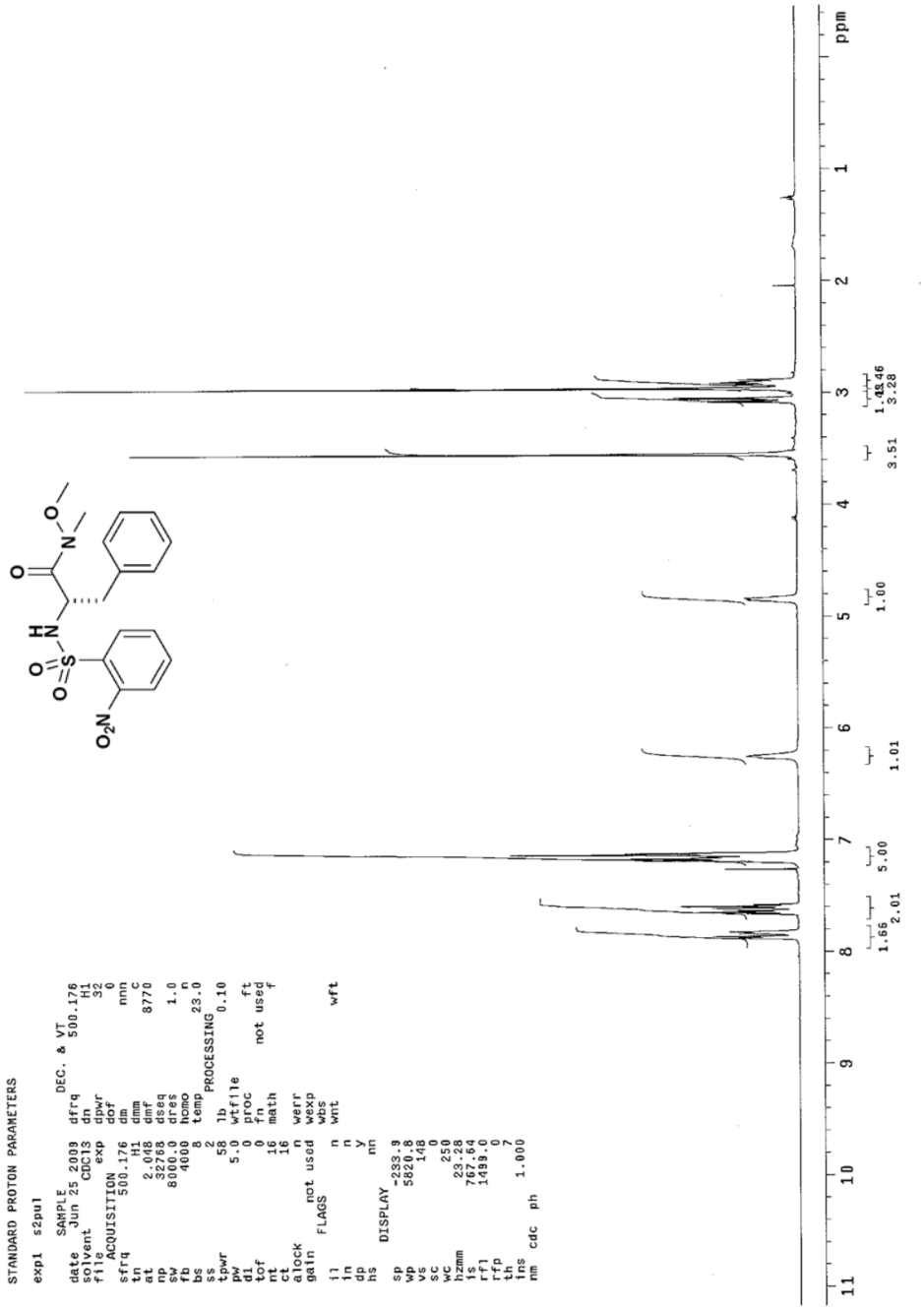


^{1}H NMR (500 MHz, $CDCl_3$) of compound **(*R*)-ii**

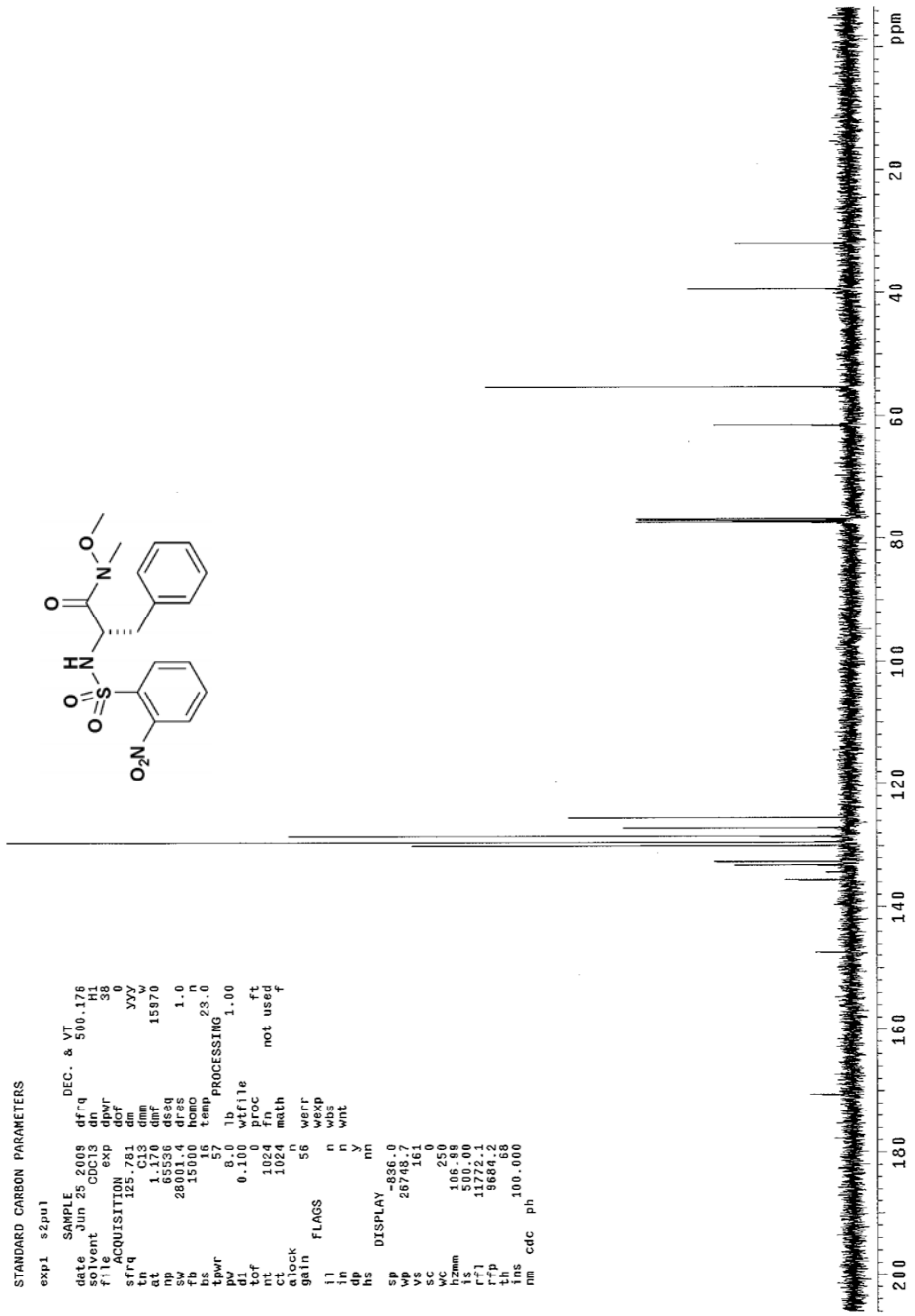


^{13}C NMR (126 MHz, $CDCl_3$) of compound **(*R*)-ii**

Spectral data for *S*)-*N*-methoxy-*N*-methyl-2-(2-nitrophenylsulfonamido)-3-phenylpropanamide (*S*)-ii

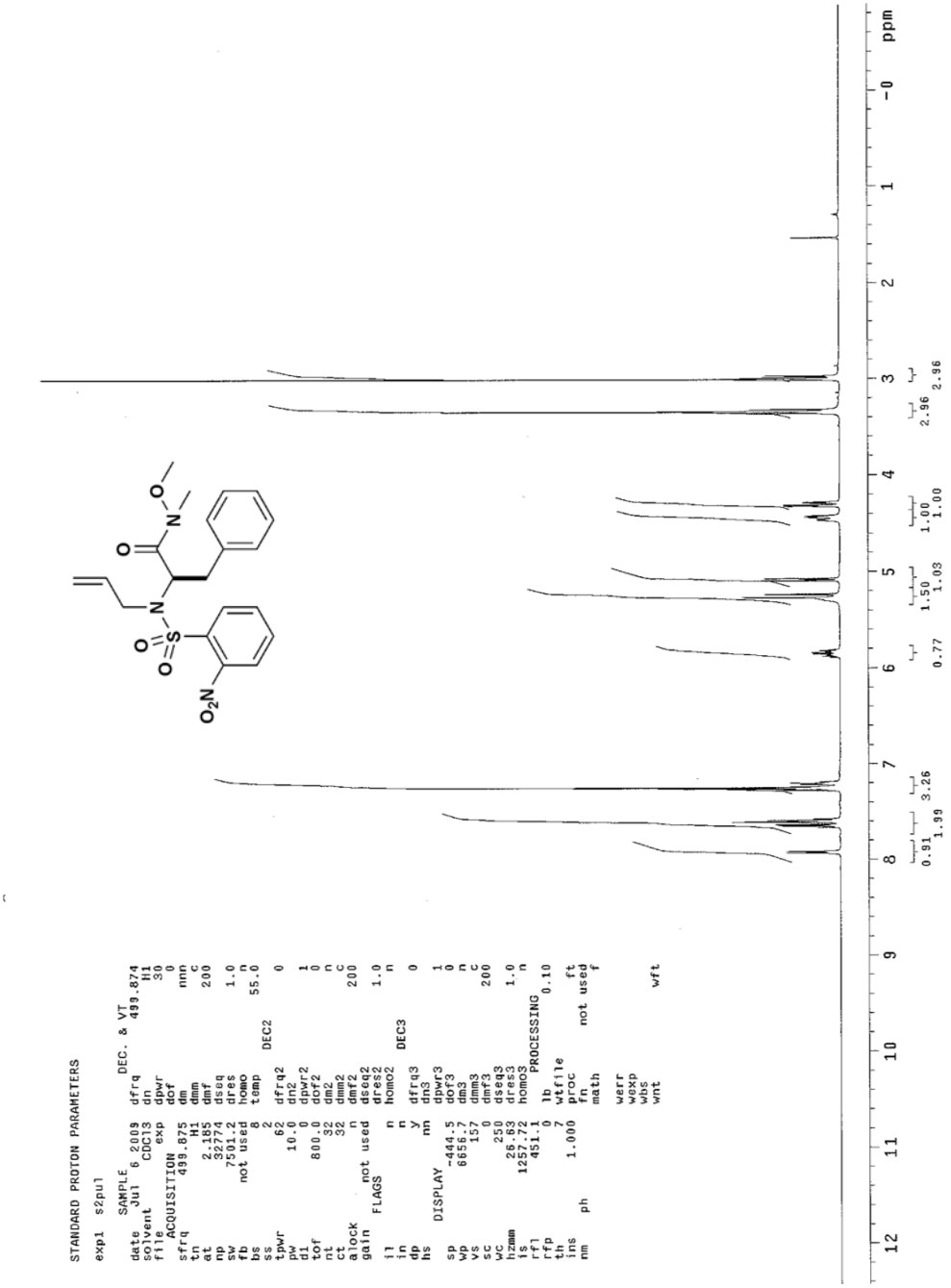


^{1}H NMR (500 MHz, $CDCl_3$) of compound **(*S*)-ii**

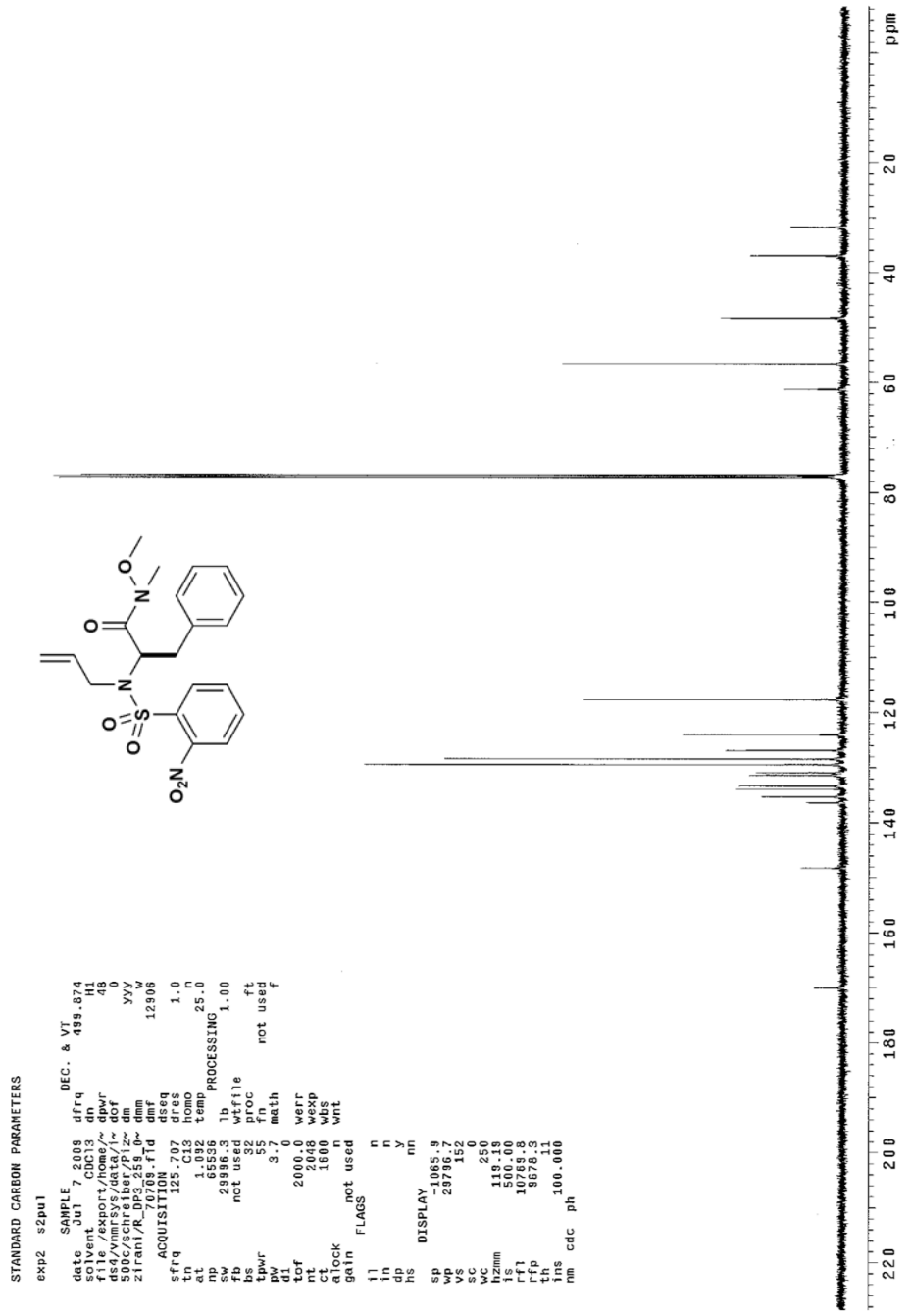


^{13}C NMR (126 MHz, $CDCl_3$) of compound **(*S*)-ii**

Spectral data for(*R*)-2-(*N*-allyl-2-nitrophenylsulfonamido)-*N*-methoxy-*N*-methyl-3-phenylpropanamide (2a)

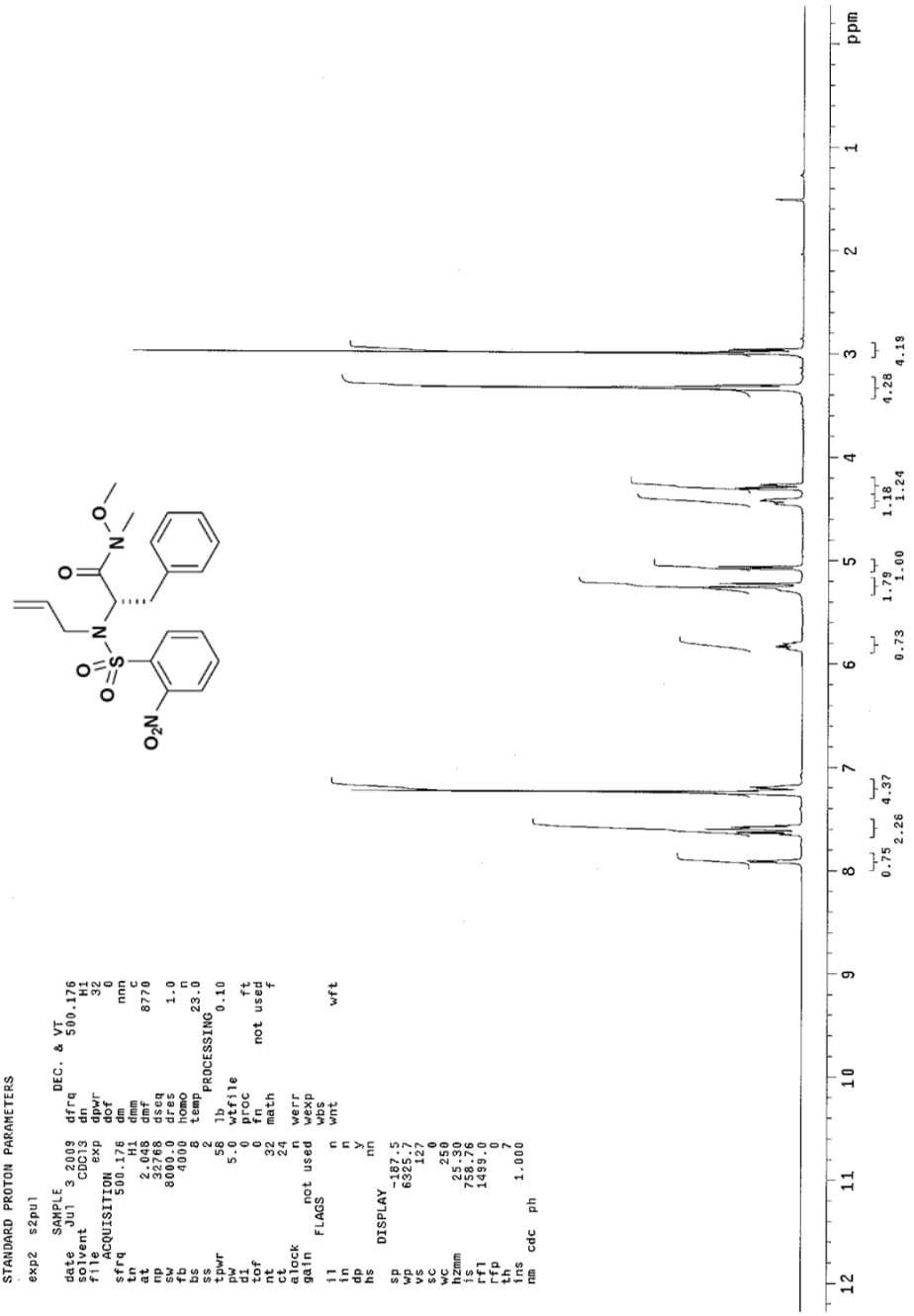


^{1}H NMR (500 MHz, $CDCl_3$) of compound **2a**

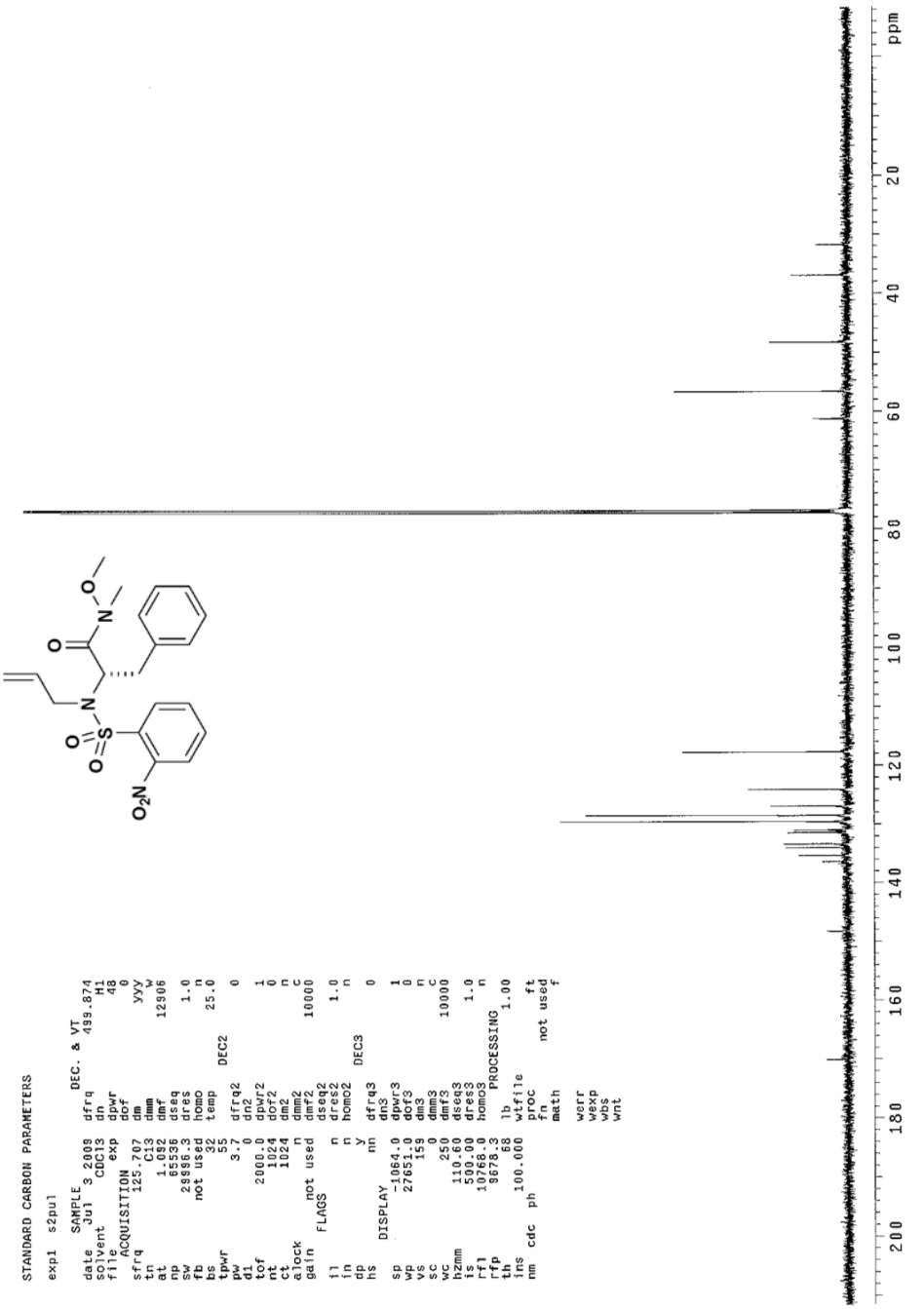


^{13}C NMR (126 MHz, $CDCl_3$) of compound **2a**

Spectral data for (*S*)-2-(*N*-allyl-2-nitrophenylsulfonamido)-*N*-methoxy-*N*-methyl-3-phenylpropanamide (2b)

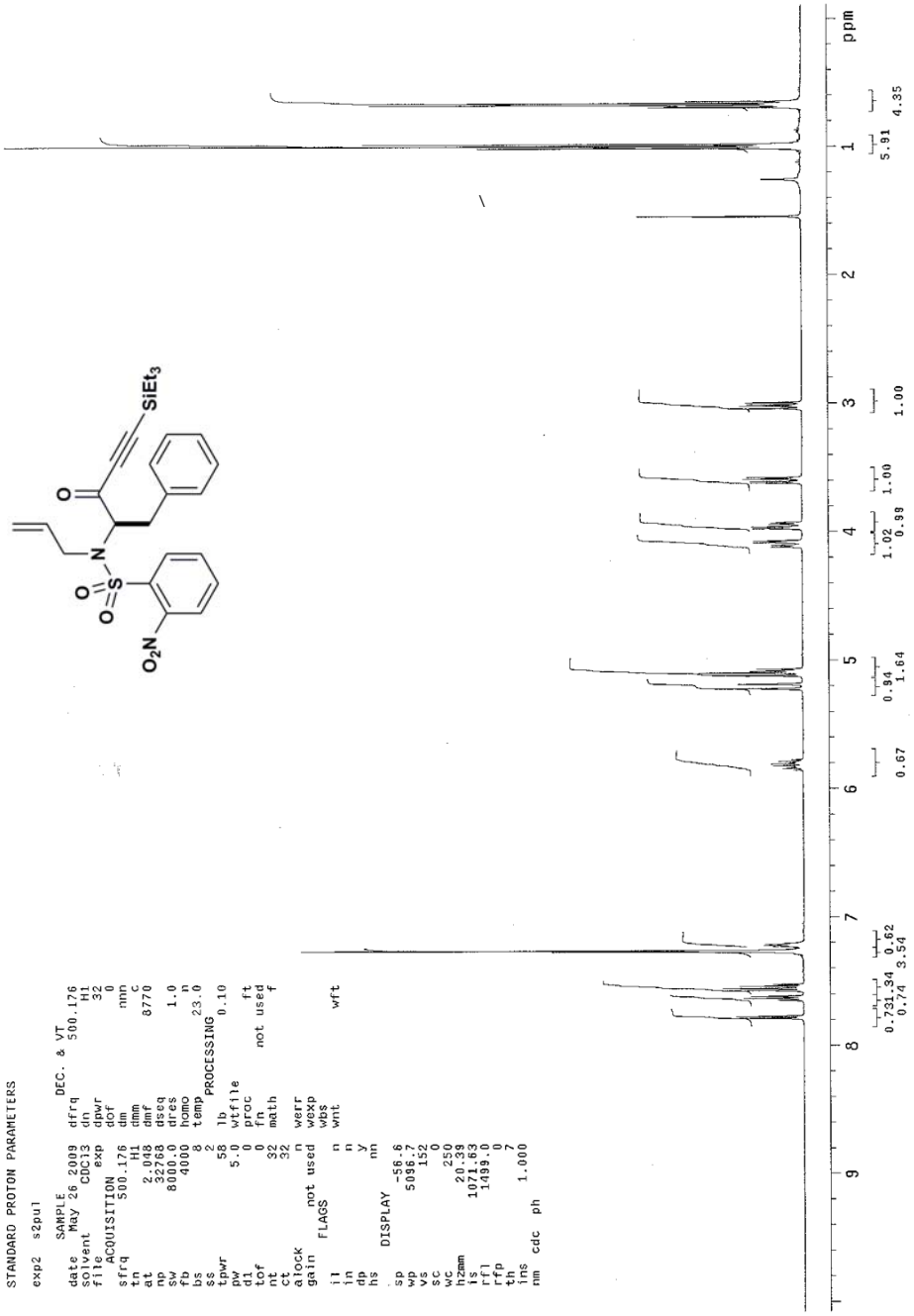


^{1}H NMR (500 MHz, $CDCl_3$) of compound **2b**

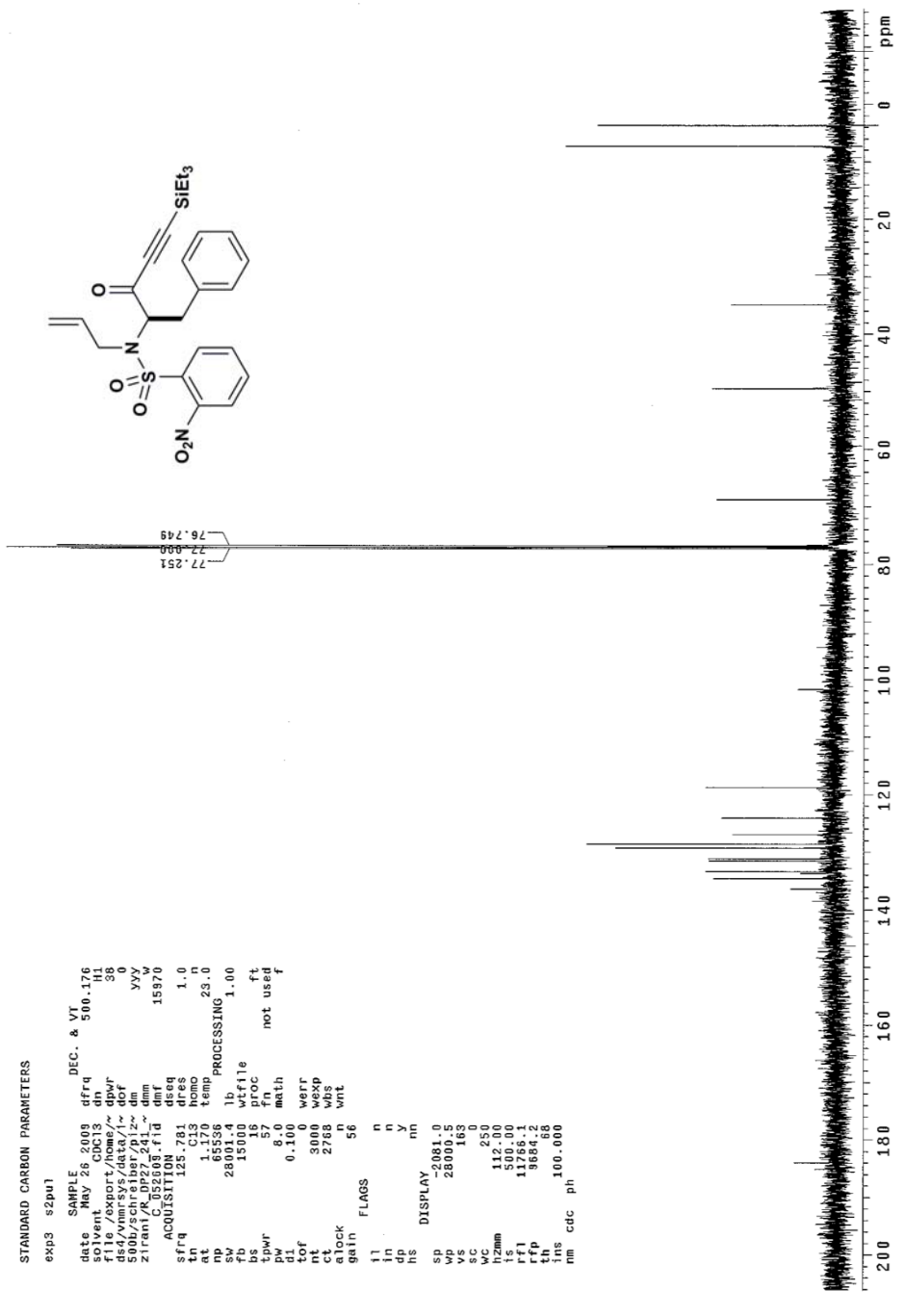


^{13}C NMR (126 MHz, $CDCl_3$) of compound **2b**

Spectral data for (*R*)-*N*-allyl-2-nitro-*N*-(3-oxo-1-phenyl-5-(triethylsilyl)pent-4-yn-2-yl)benzenesulfonamide (3a)

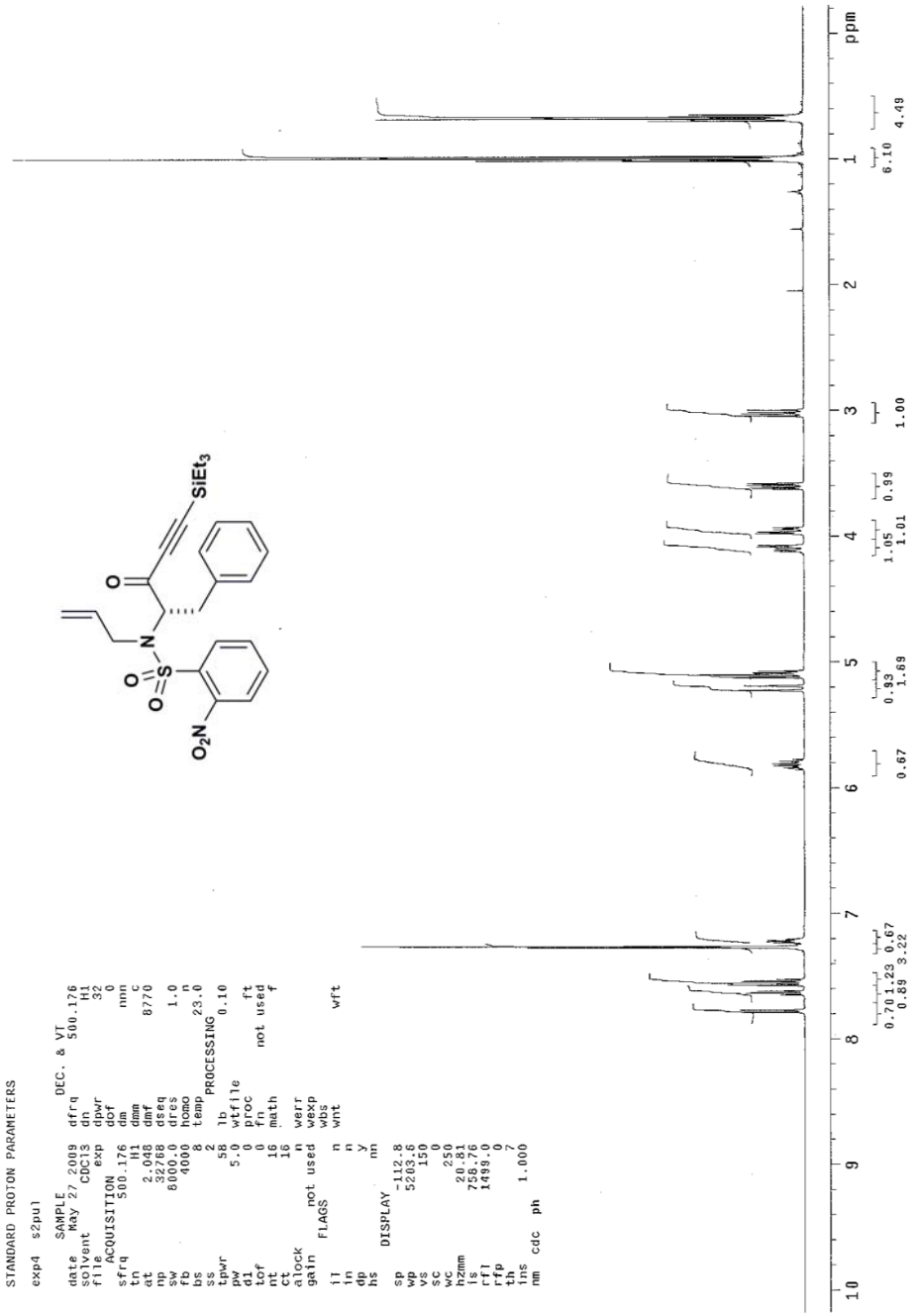


^{1}H NMR (500 MHz, $CDCl_3$) of compound **3a**

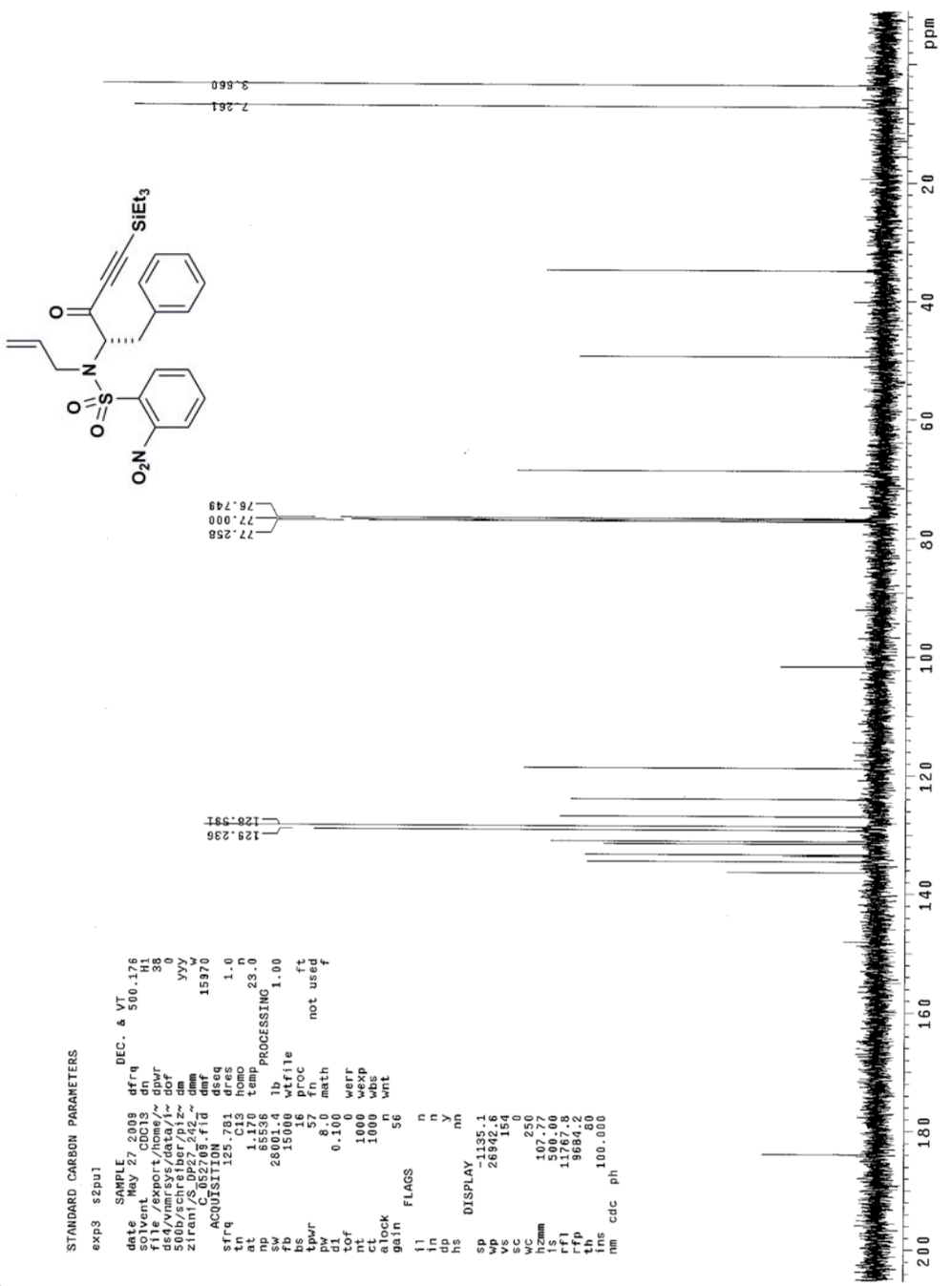


^{13}C NMR (126 MHz, $CDCl_3$) of compound **3a**

Spectral data for (*S*)-*N*-allyl-2-nitro-*N*-(3-oxo-1-phenyl-5-(triethylsilyl)pent-4-yn-2-yl)benzenesulfonamide (3b)

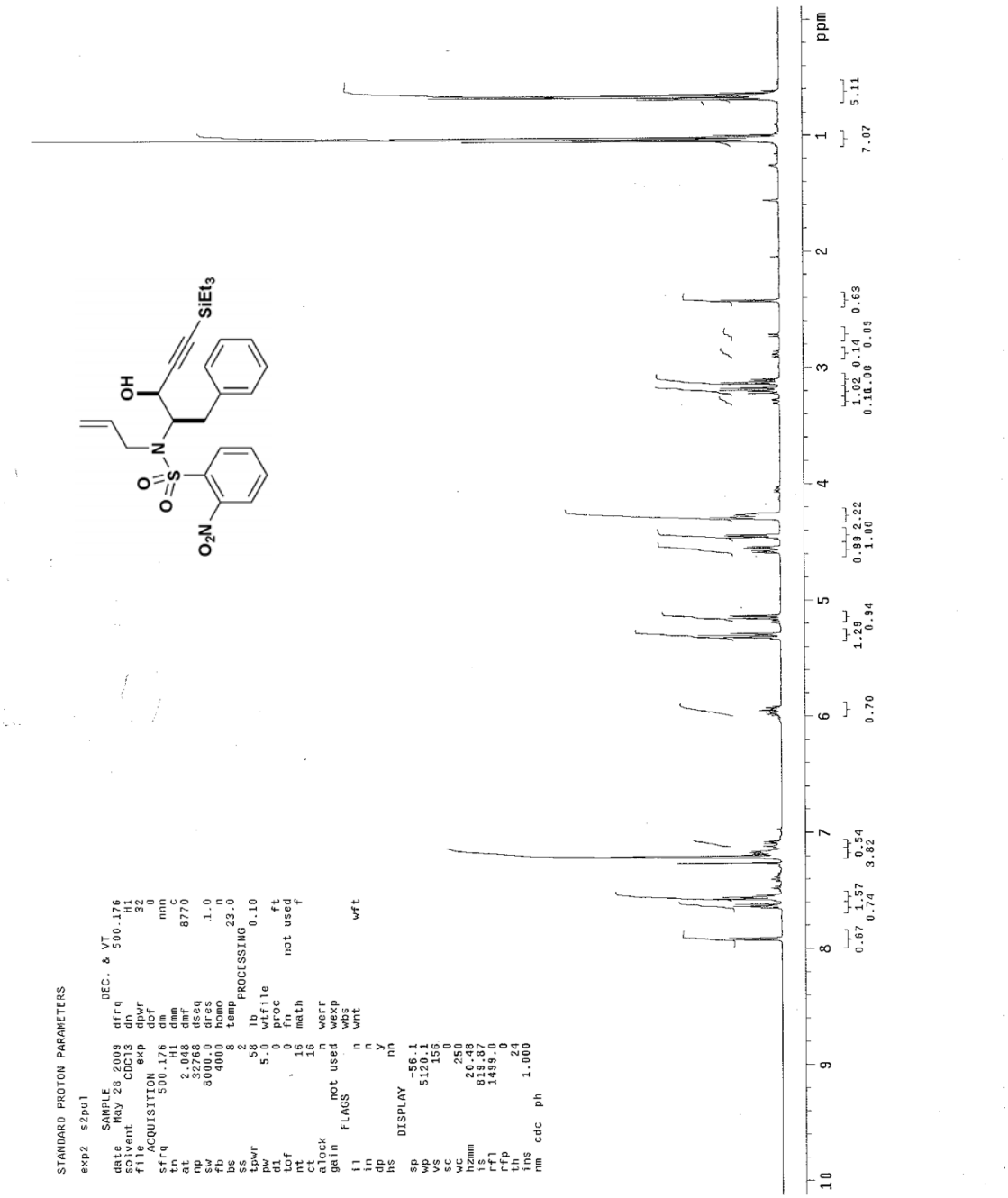


^{1}H NMR (500 MHz, $CDCl_3$) of compound **3b**

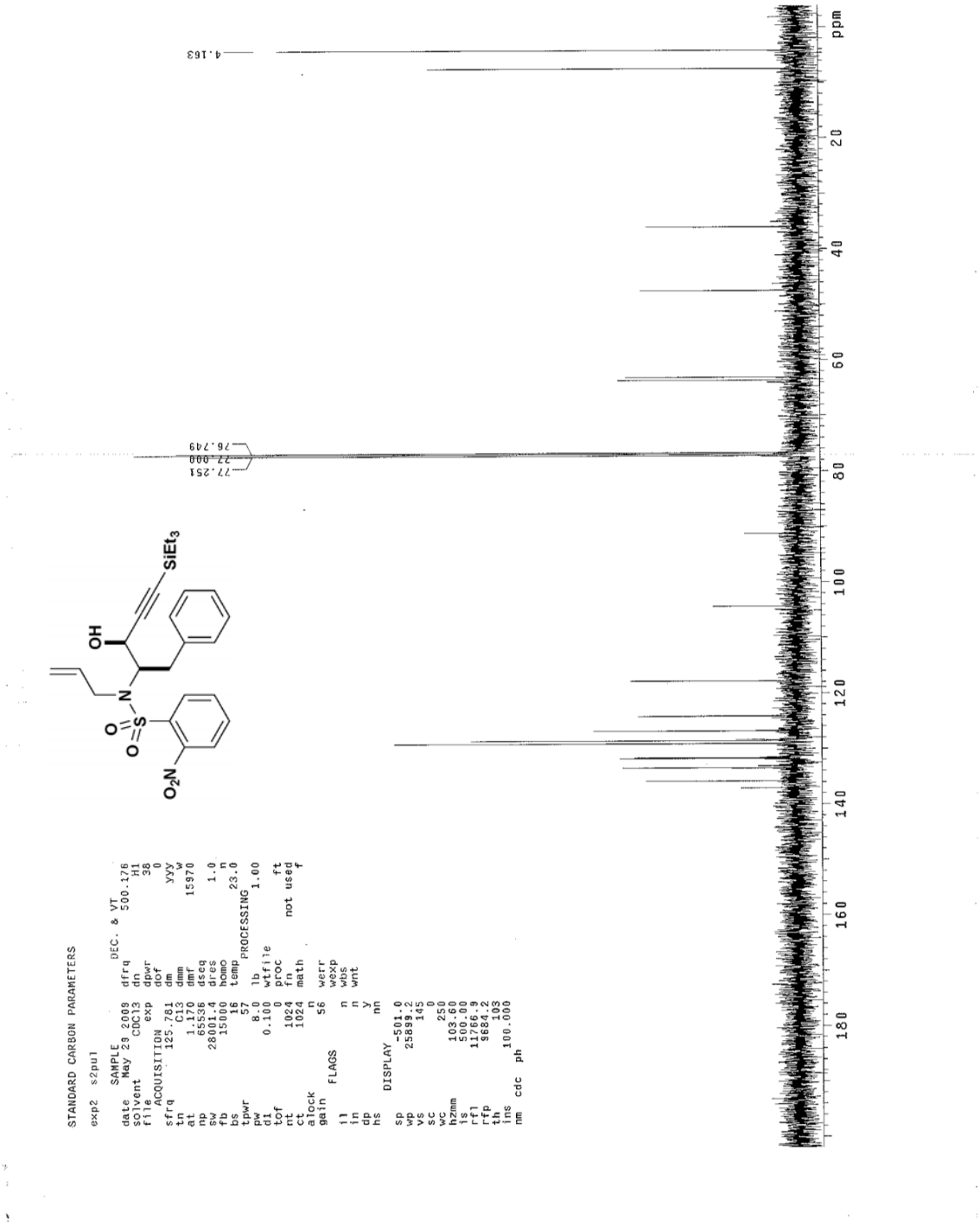


^{13}C NMR (126 MHz, $CDCl_3$) of compound **3b**

Spectral data for *N*-allyl-*N*-((2*R*,3*S*)-3-hydroxy-1-phenyl-5-(triethylsilyl)pent-4-yn-2-yl)-2-nitrobenzene sulfonamide (4a)

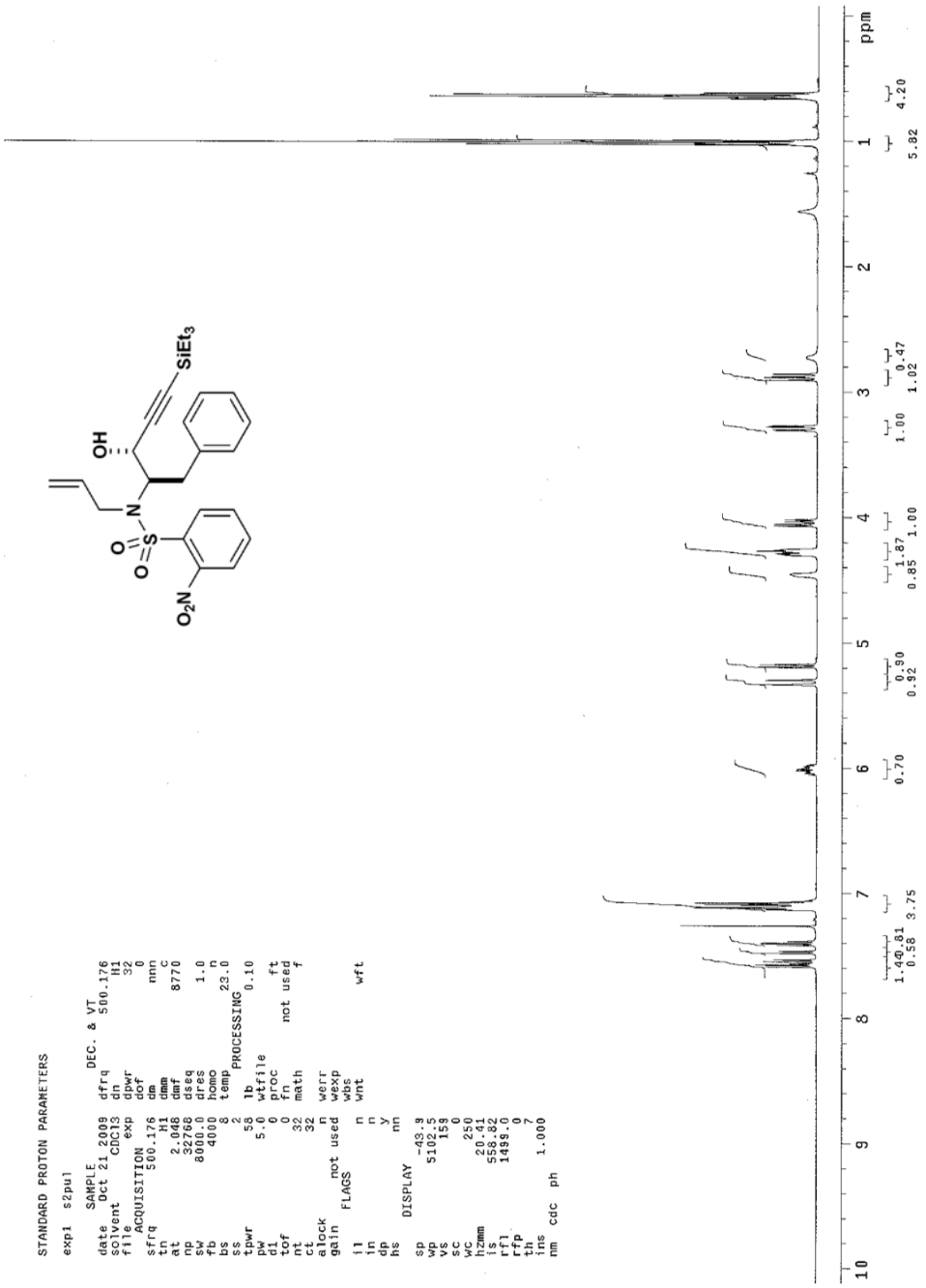


^{1}H NMR (500 MHz, $CDCl_3$) of compound **4a**

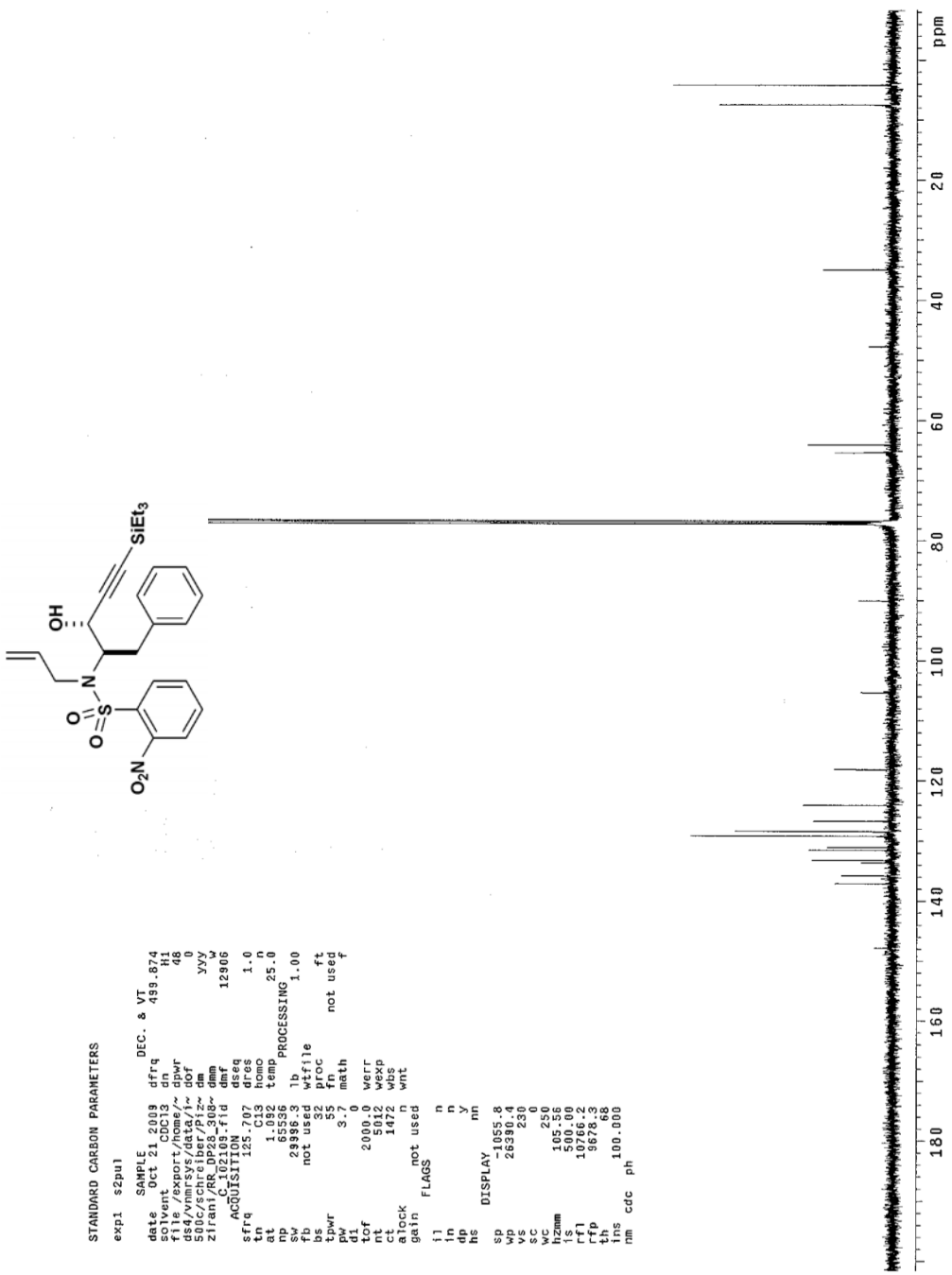


^{13}C NMR (126 MHz, $CDCl_3$) of compound **4a**

Spectral data for *N*-allyl-*N*-((2*R*,3*R*)-3-hydroxy-1-phenyl-5-(triethylsilyl)pent-4-yn-2-yl)-2-nitrobenzene sulfonamide (4b)

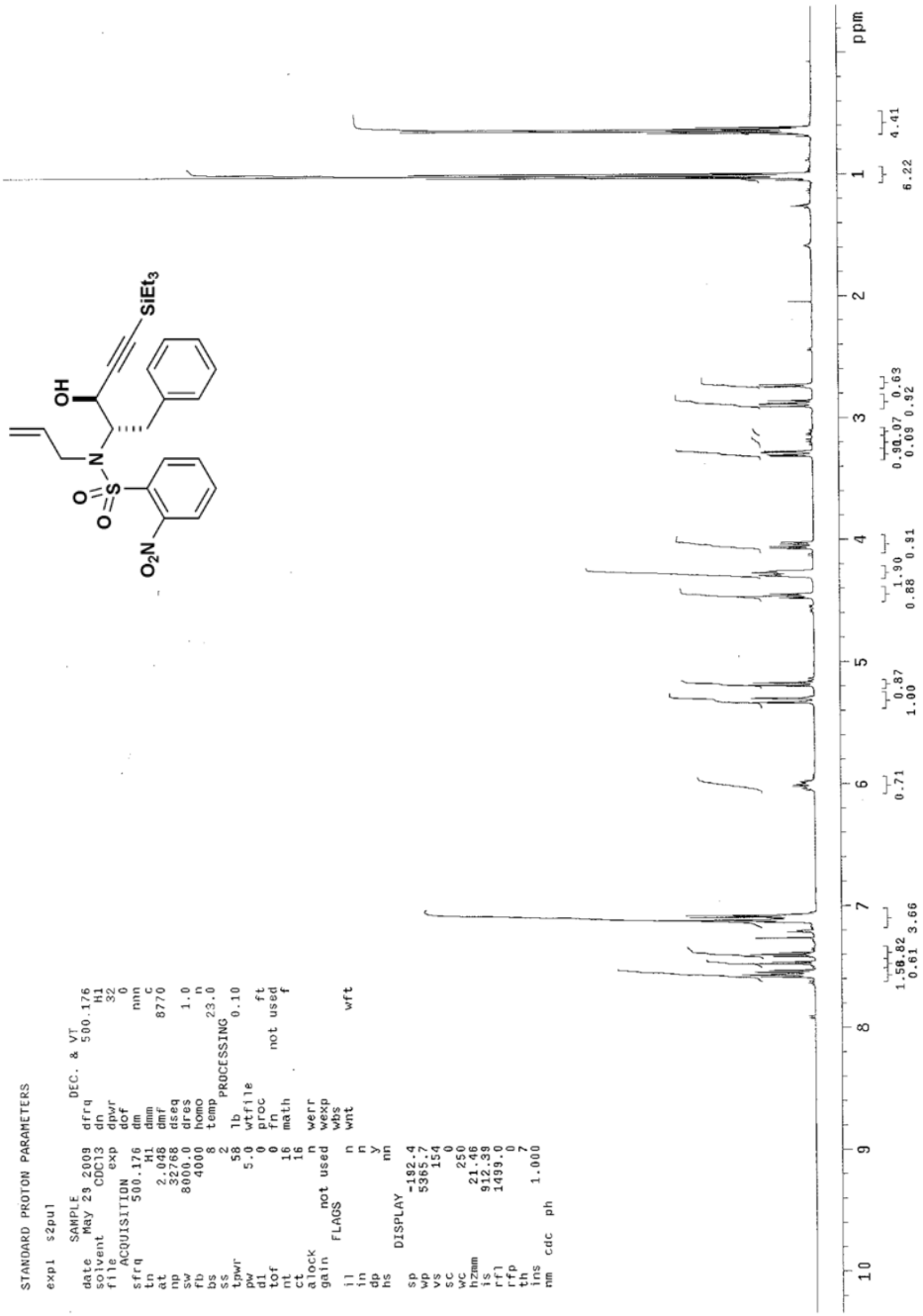


^{1}H NMR (500 MHz, $CDCl_3$) of compound **4b**

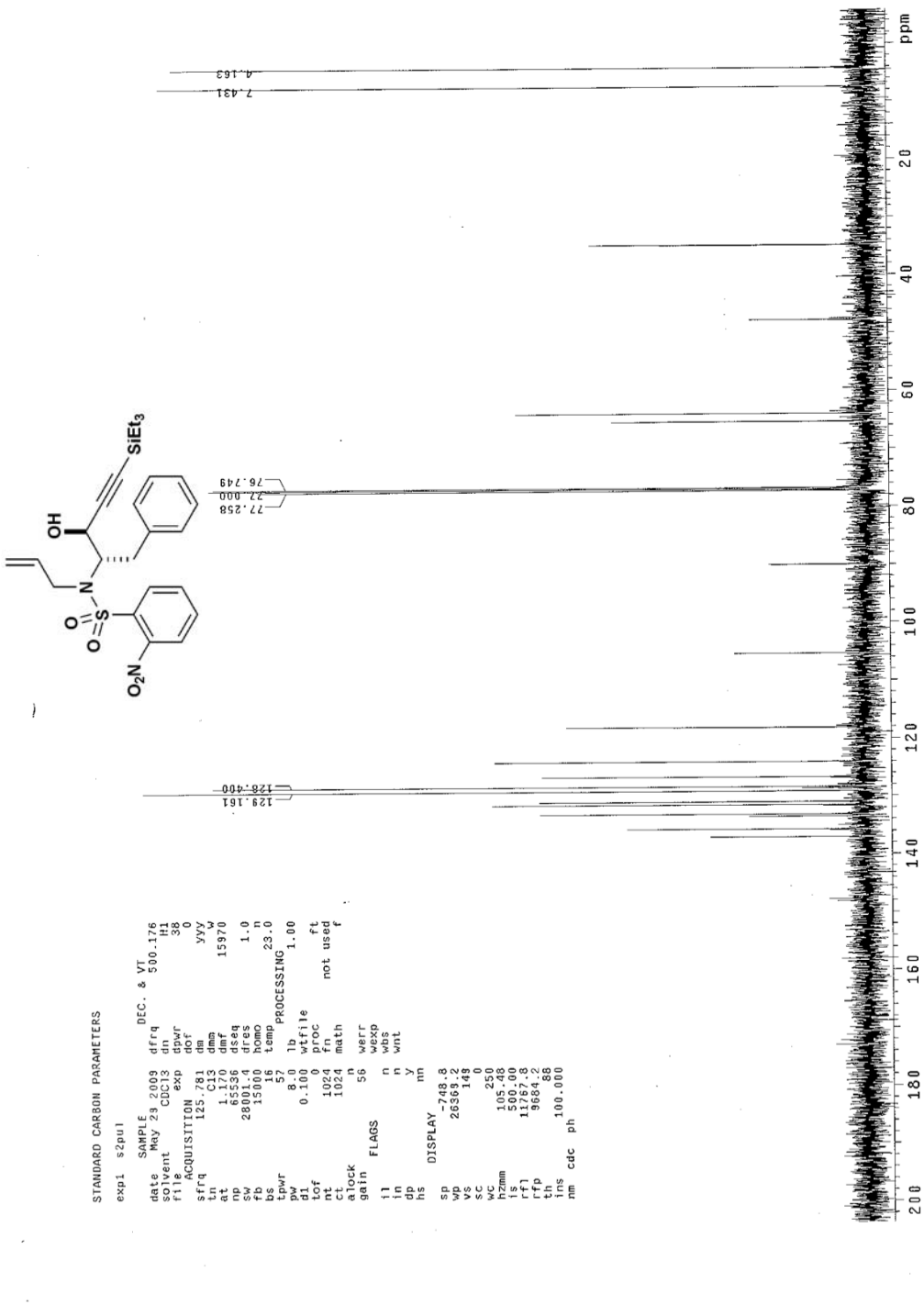


^{13}C NMR (126 MHz, $CDCl_3$) of compound **4b**

Spectral data for *N*-allyl-*N*-((2*S*,3*S*)-3-hydroxy-1-phenyl-5-(triethylsilyl)pent-4-yn-2-yl)-2-nitrobenzene sulfonamide (4c)

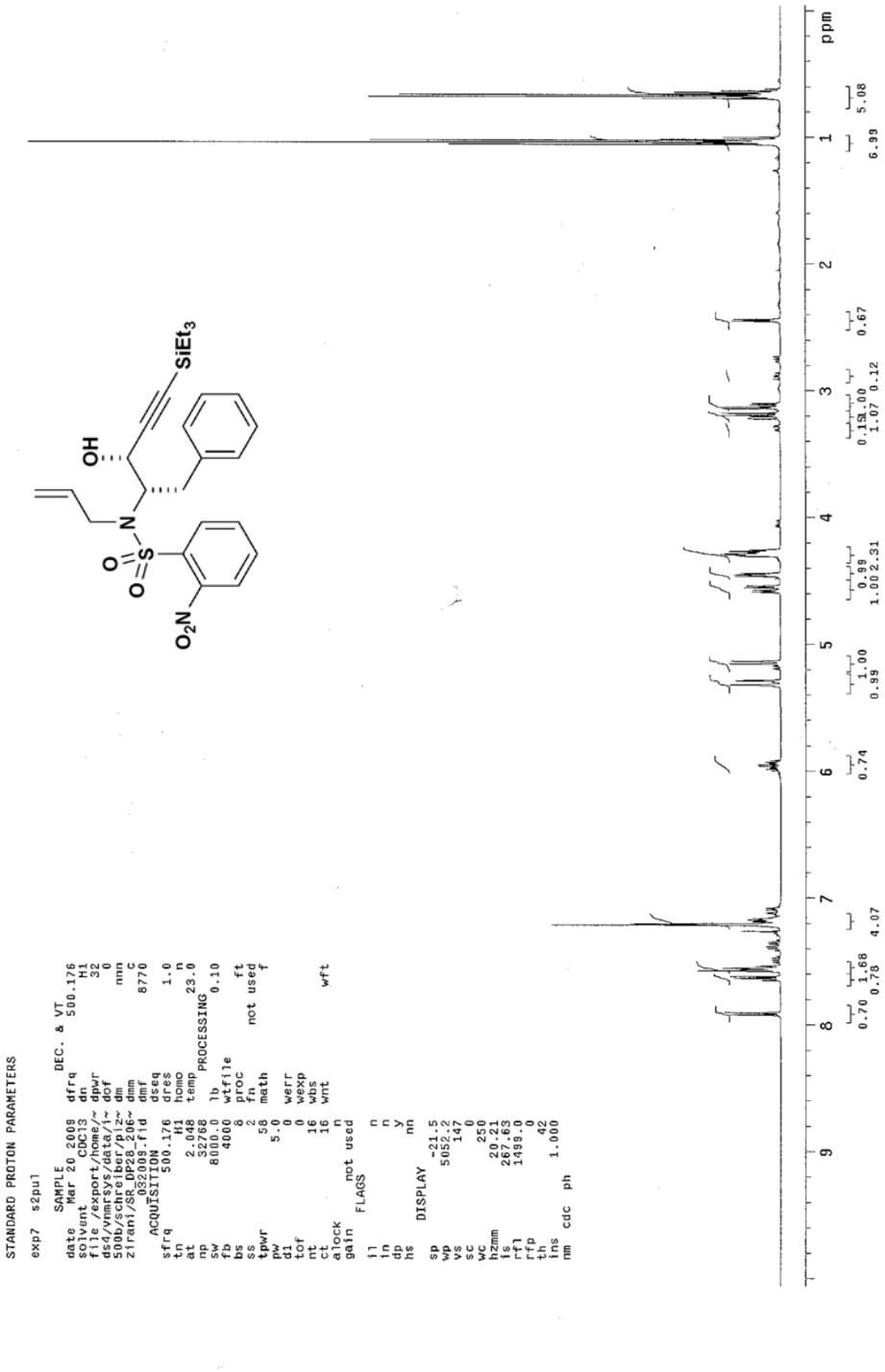


^{1}H NMR (500 MHz, $CDCl_3$) of compound **4c**

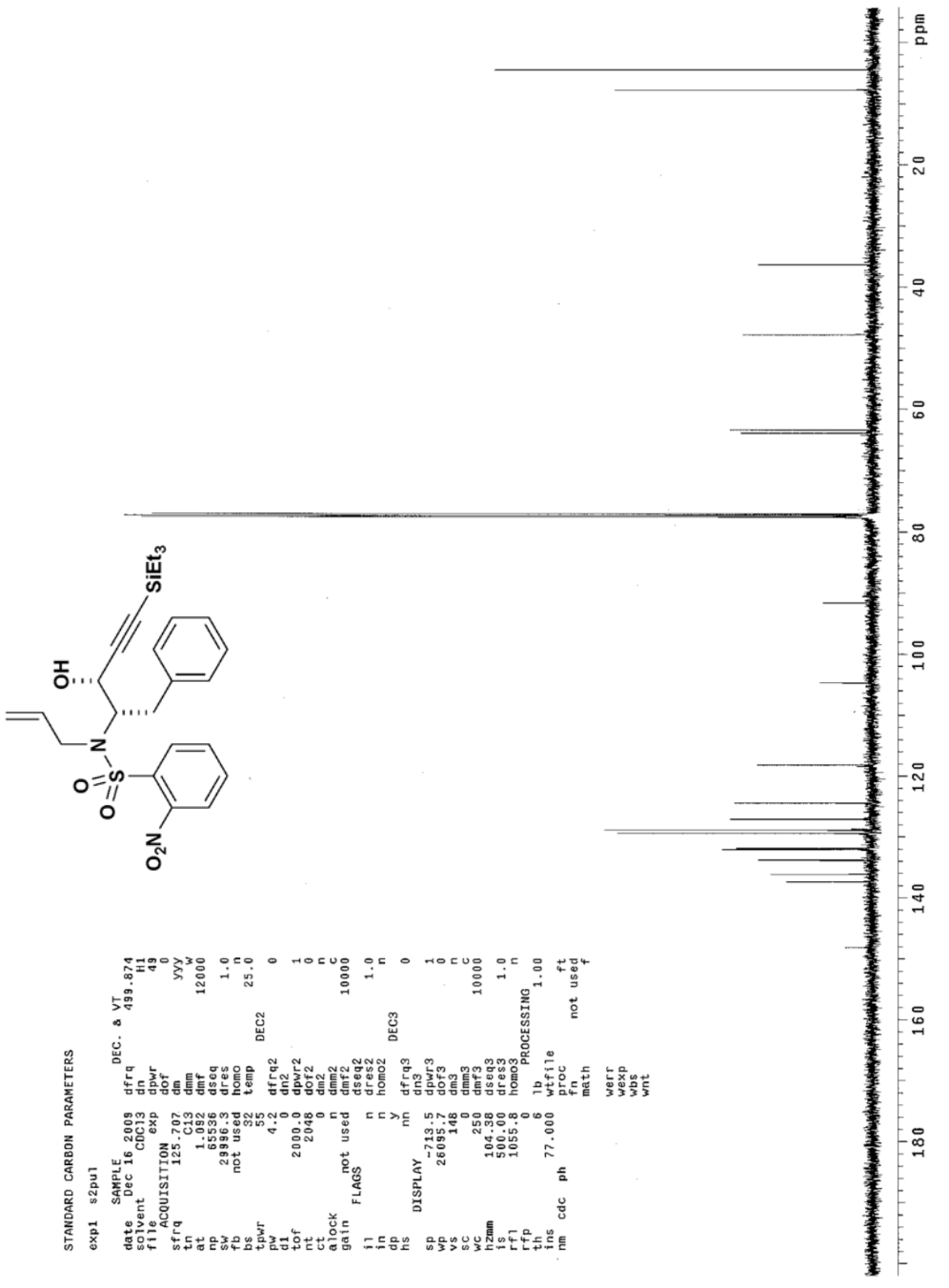


^{13}C NMR (126 MHz, $CDCl_3$) of compound **4c**

Spectral data for *N*-allyl-*N*-((2*S*,3*R*)-3-hydroxy-1-phenyl-5-(triethylsilyl)pent-4-yn-2-yl)-2-nitrobenzene sulfonamide (4d)

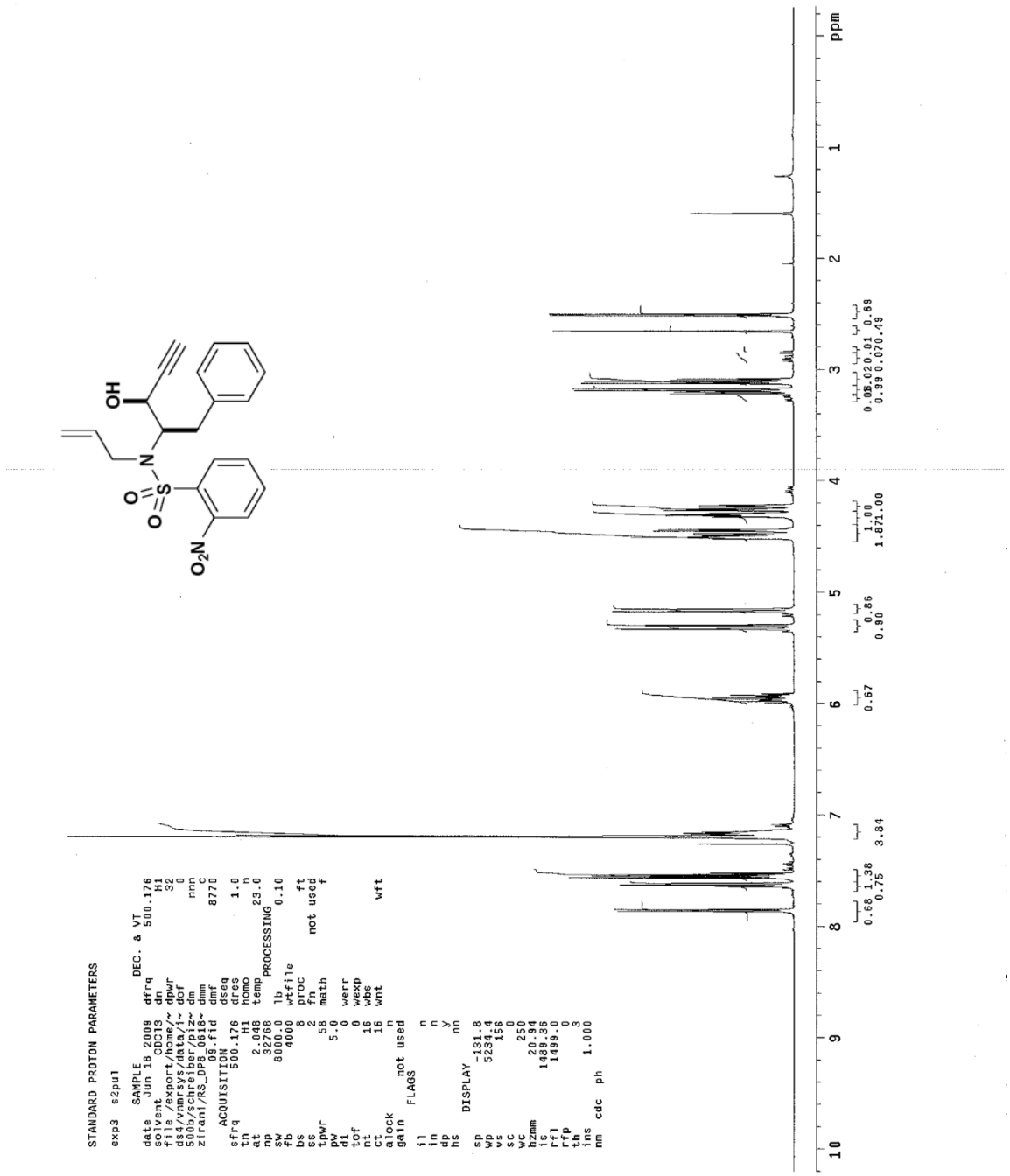


^{1}H NMR (500 MHz, $CDCl_3$) of compound **4d**

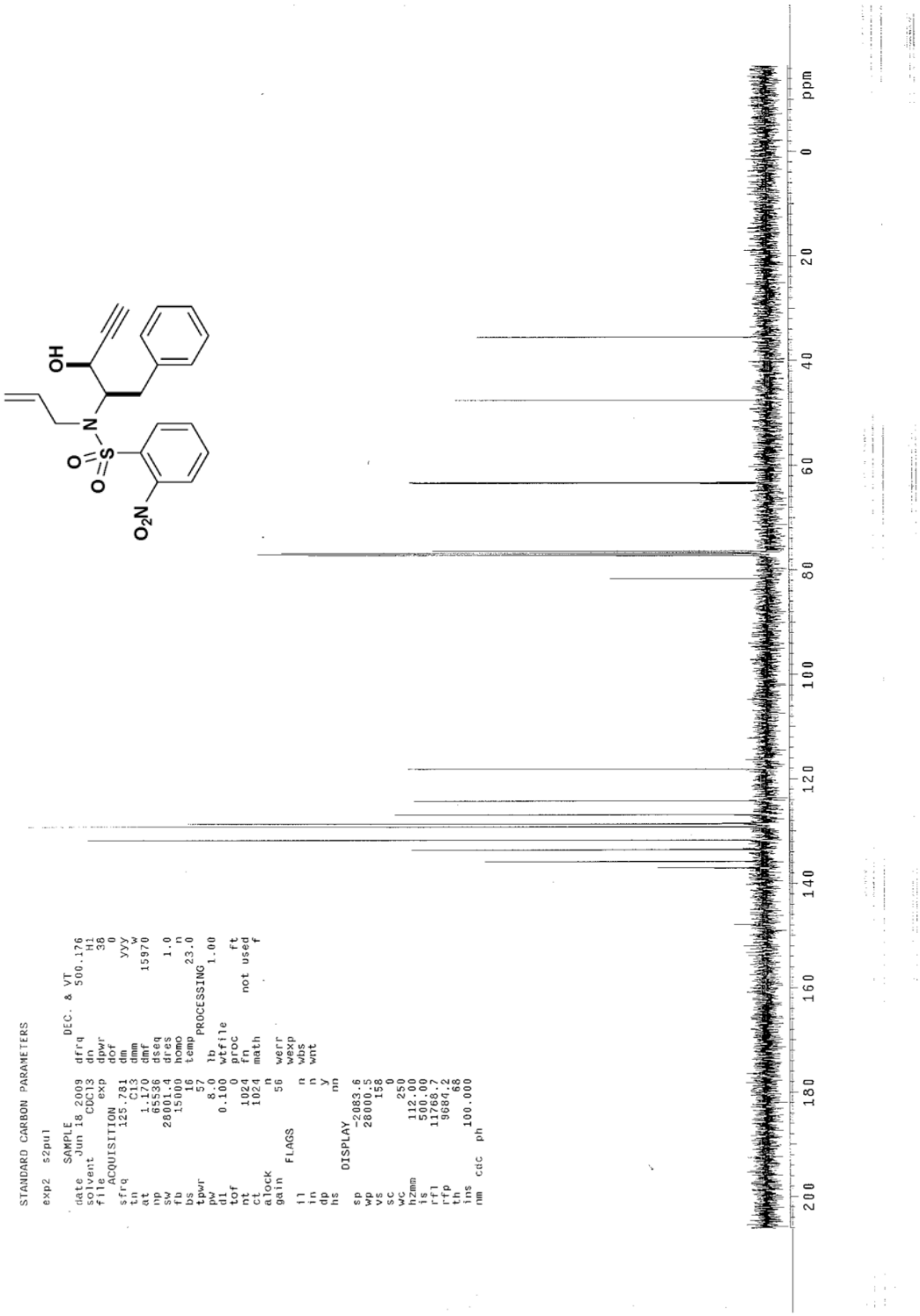


^{13}C NMR (126 MHz, $CDCl_3$) of compound **4d**

Spectral data for *N*-allyl-*N*-((2*R*,3*S*)-3-hydroxy-1-phenylpent-4-yn-2-yl)-2-nitrobenzenesulfonamide (1a)

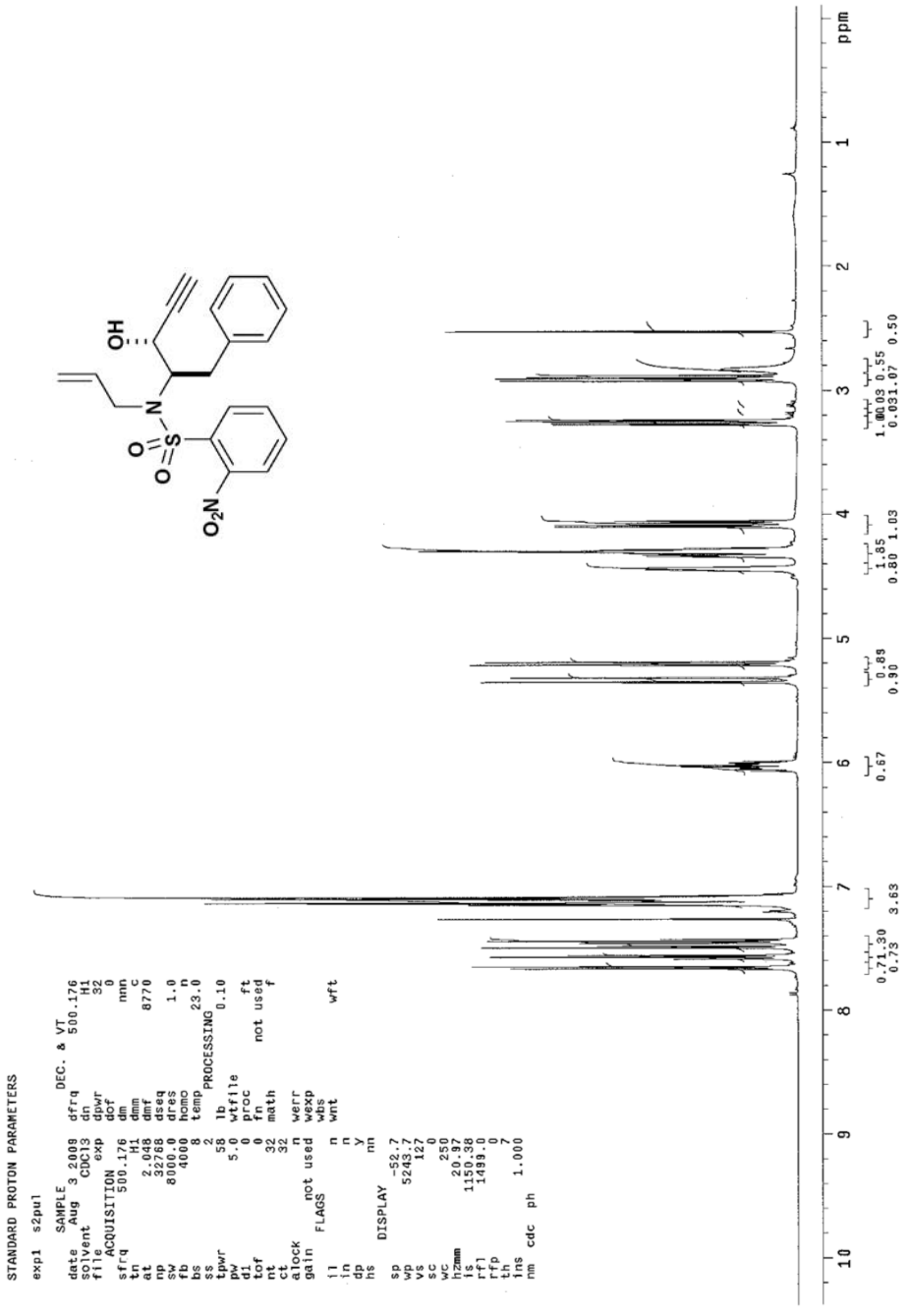


^{1}H NMR (500 MHz, $CDCl_3$) of compound **1a**

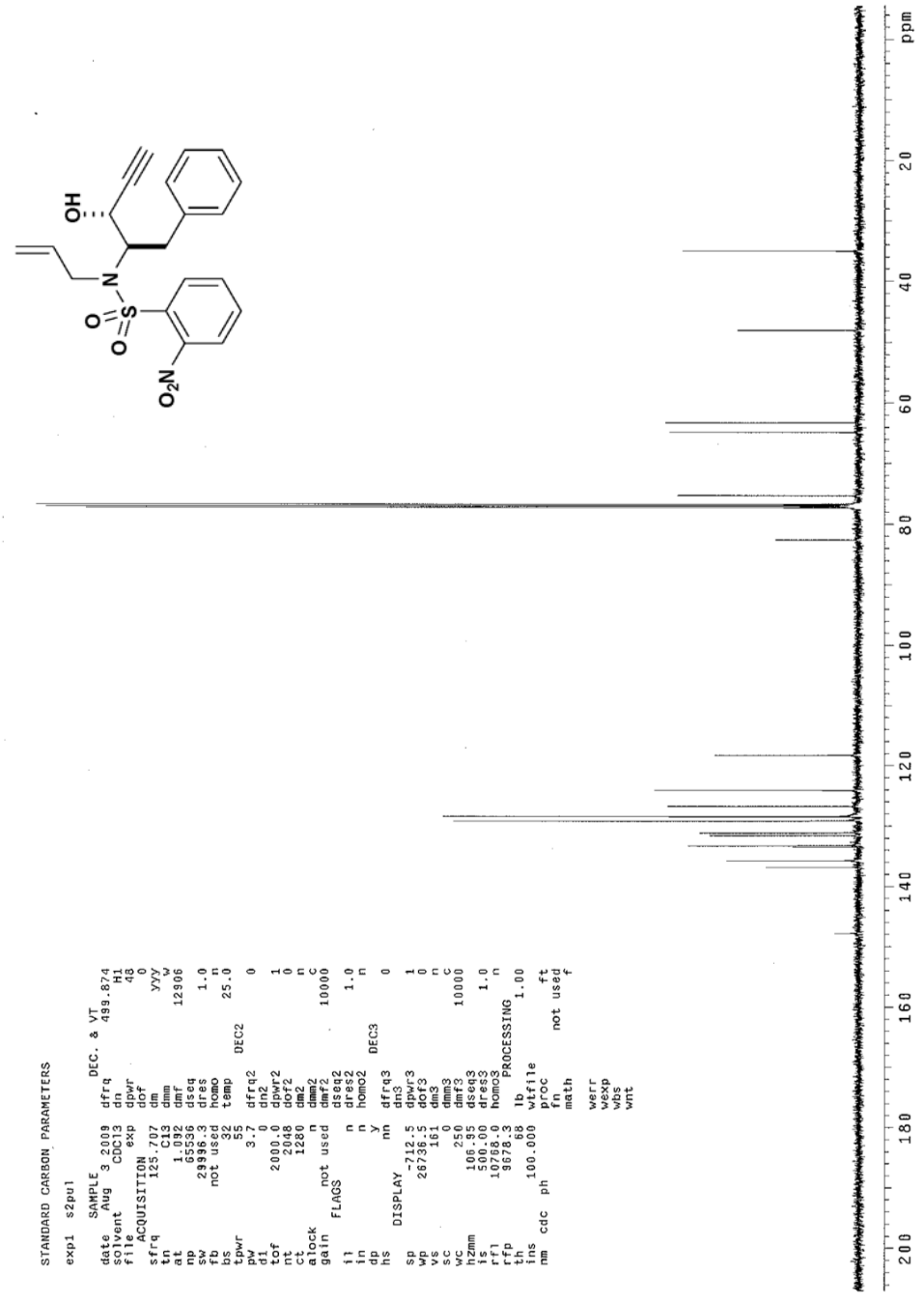


^{13}C NMR (126 MHz, $CDCl_3$) of compound **1a**

Sectral data for *N*-allyl-*N*-((2*R*,3*R*)-3-hydroxy-1-phenylpent-4-yn-2-yl)-2-nitrobenzenesulfonamide (1b)

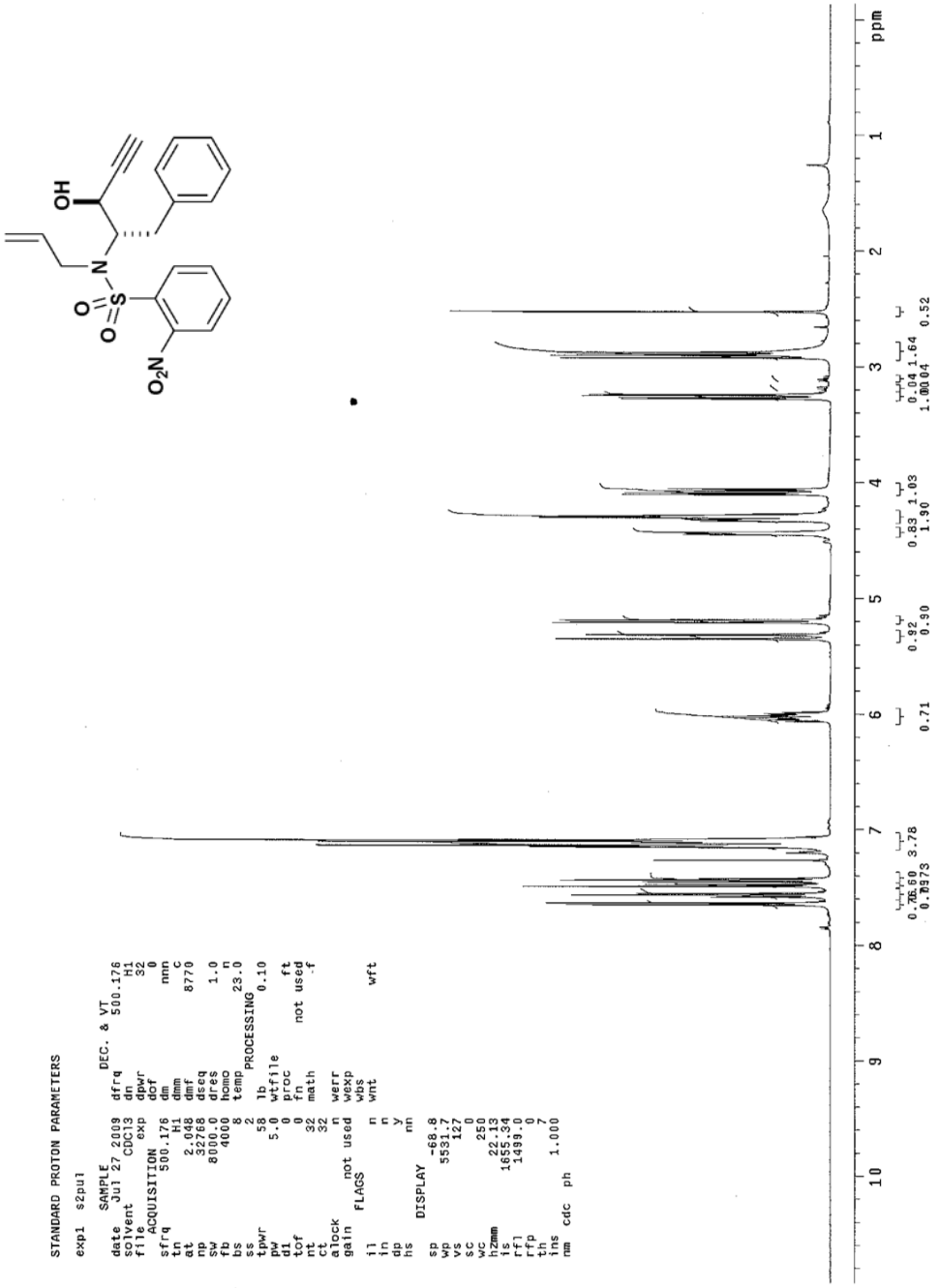


^{1}H NMR (500 MHz, $CDCl_3$) of compound **1b**

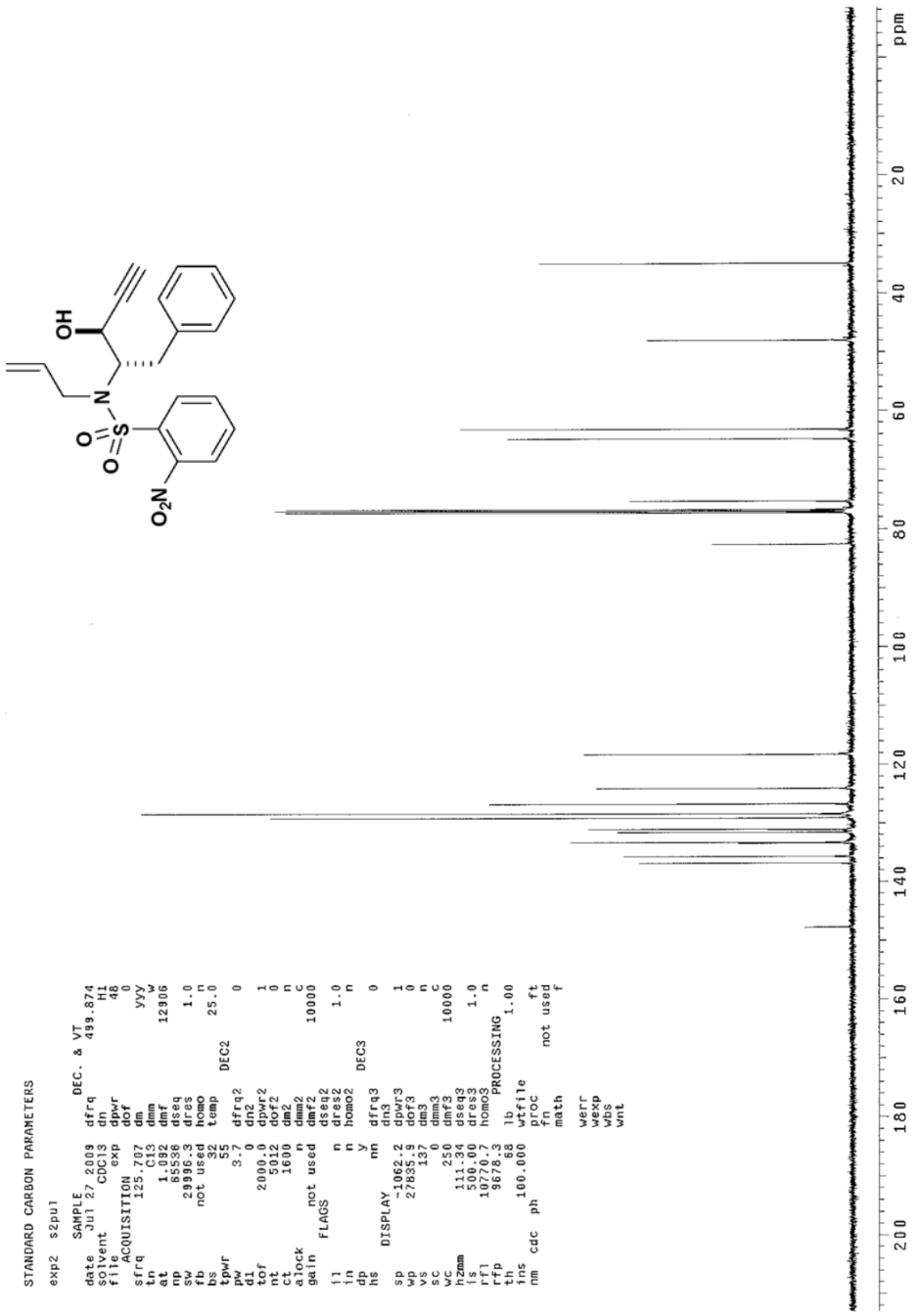


^{13}C NMR (126 MHz, $CDCl_3$) of compound **1b**

Spectral data for *N*-allyl-*N*-((2*S*,3*S*)-3-hydroxy-1-phenylpent-4-yn-2-yl)-2-nitrobenzenesulfonamide (1c)

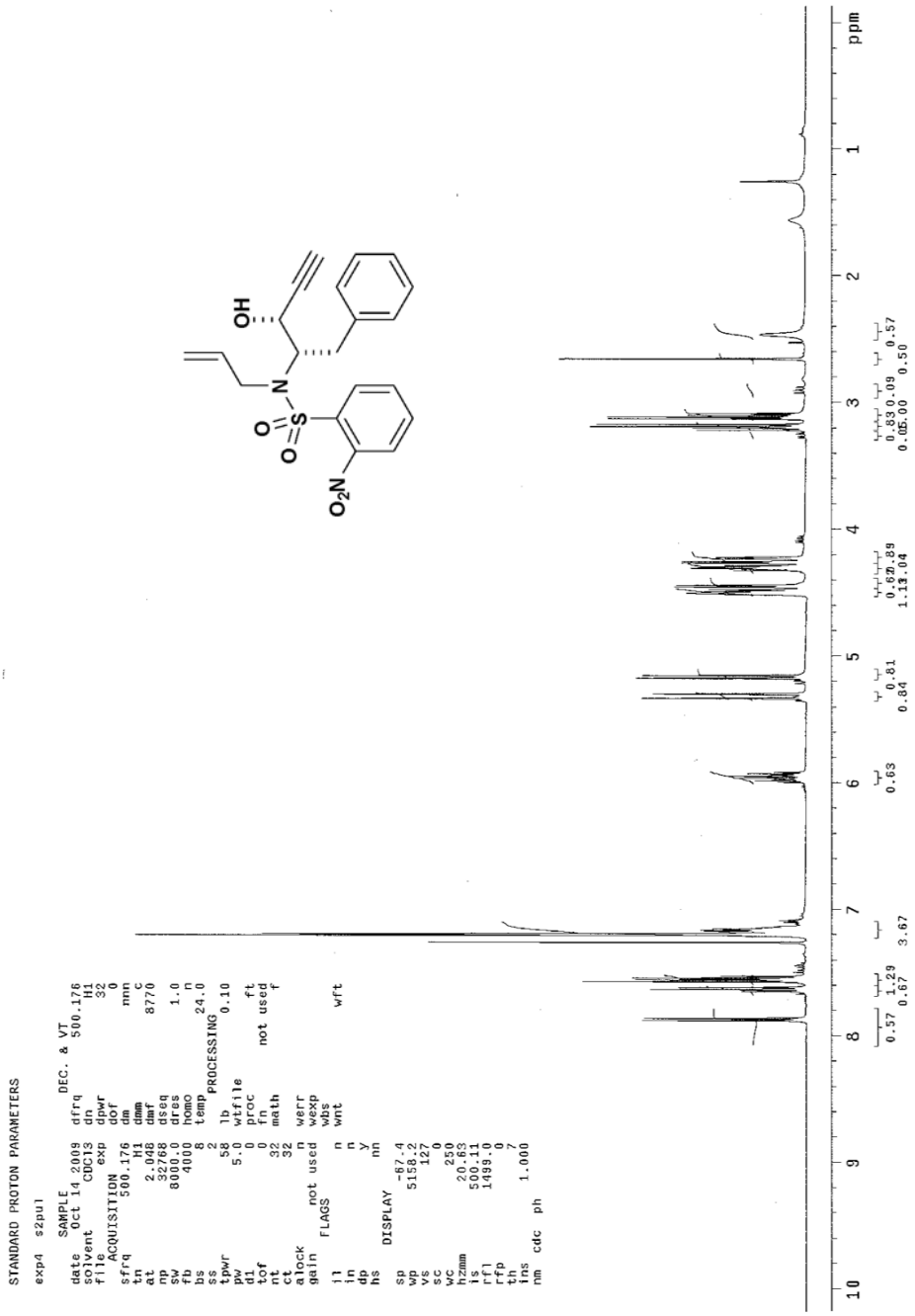


^{1}H NMR (500 MHz, $CDCl_3$) of compound **1c**

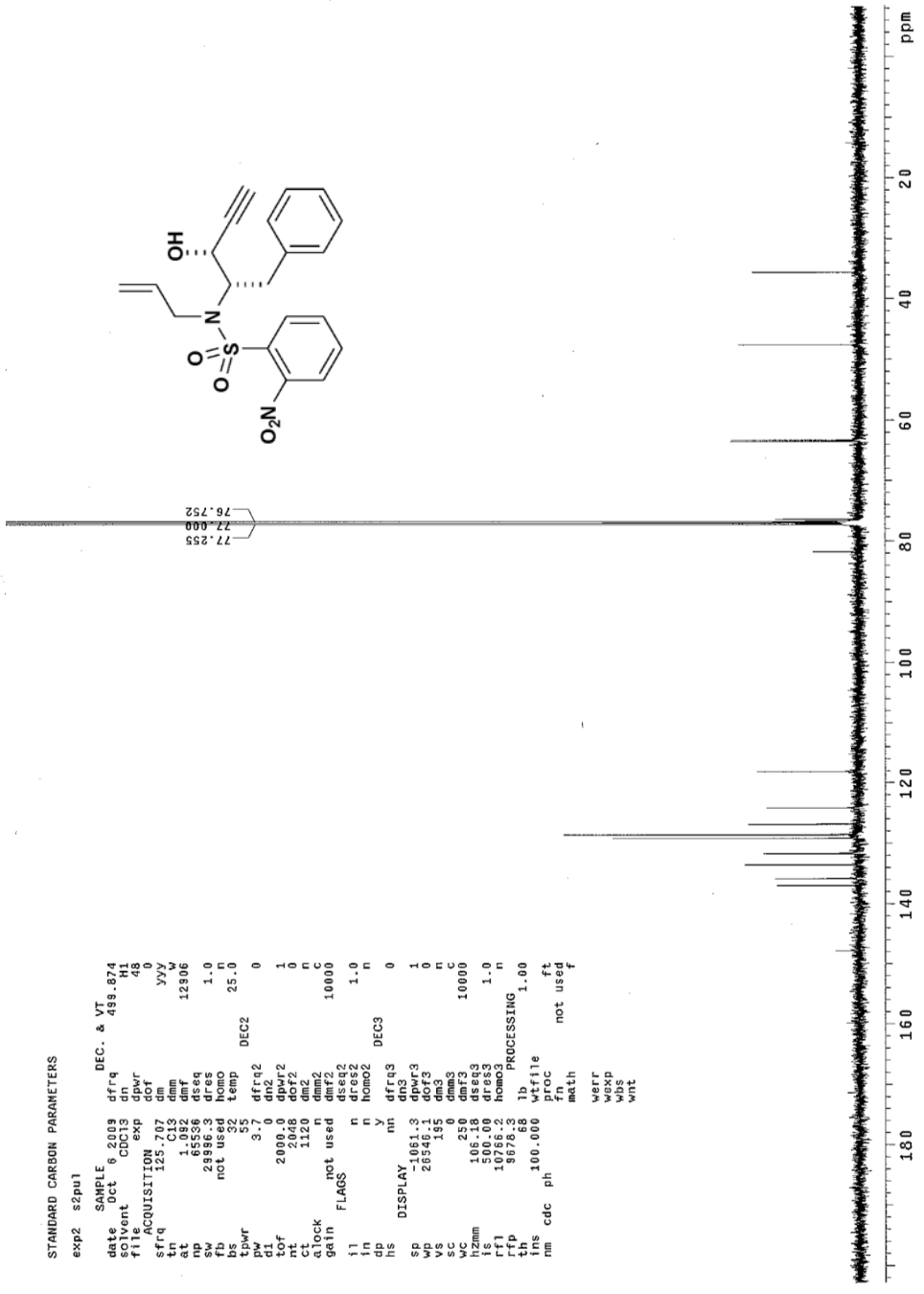


^{13}C NMR (126 MHz, $CDCl_3$) of compound **1c**

Spectral data for *N*-allyl-*N*-((2*S*,3*R*)-3-hydroxy-1-phenylpent-4-yn-2-yl)-2-nitrobenzenesulfonamide (1d)

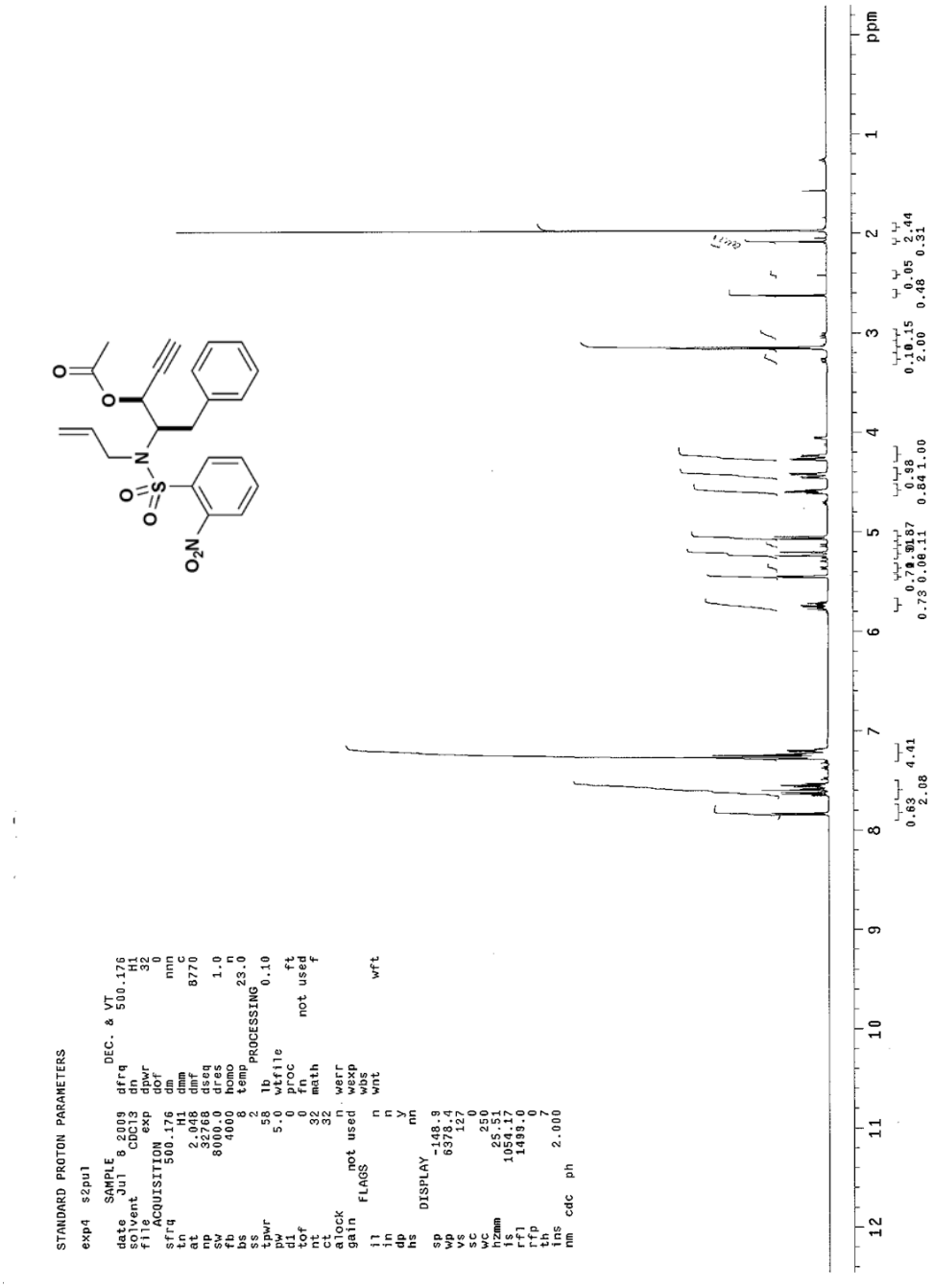


^{1}H NMR (500 MHz, $CDCl_3$) of compound **1d**

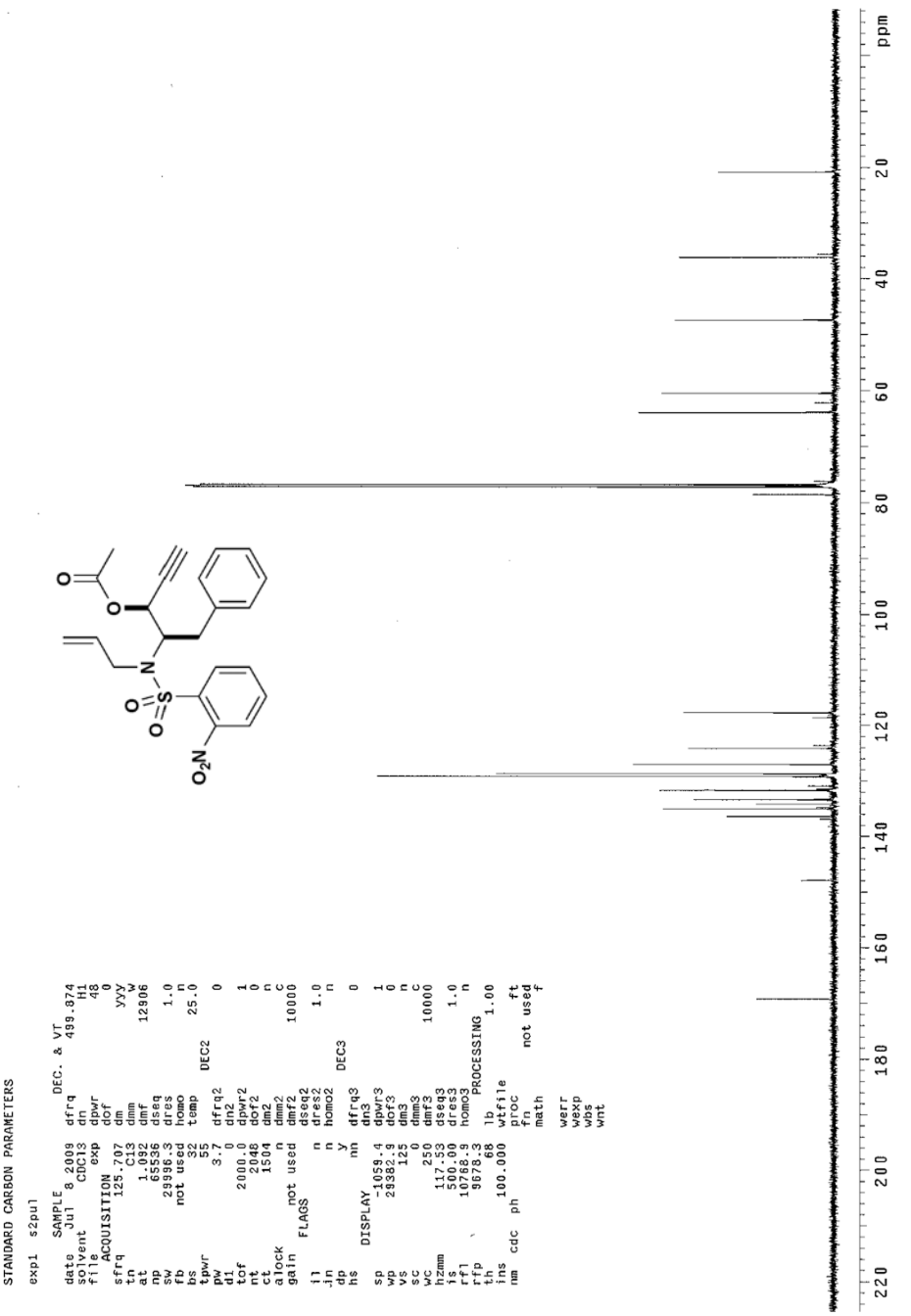


^{13}C NMR (126 MHz, $CDCl_3$) of compound **1d**

Spectral data for (3*S*,4*R*)-4-(*N*-allyl-2-nitrophenylsulfonamido)-5-phenylpent-1-yn-3-yl acetate (6a)

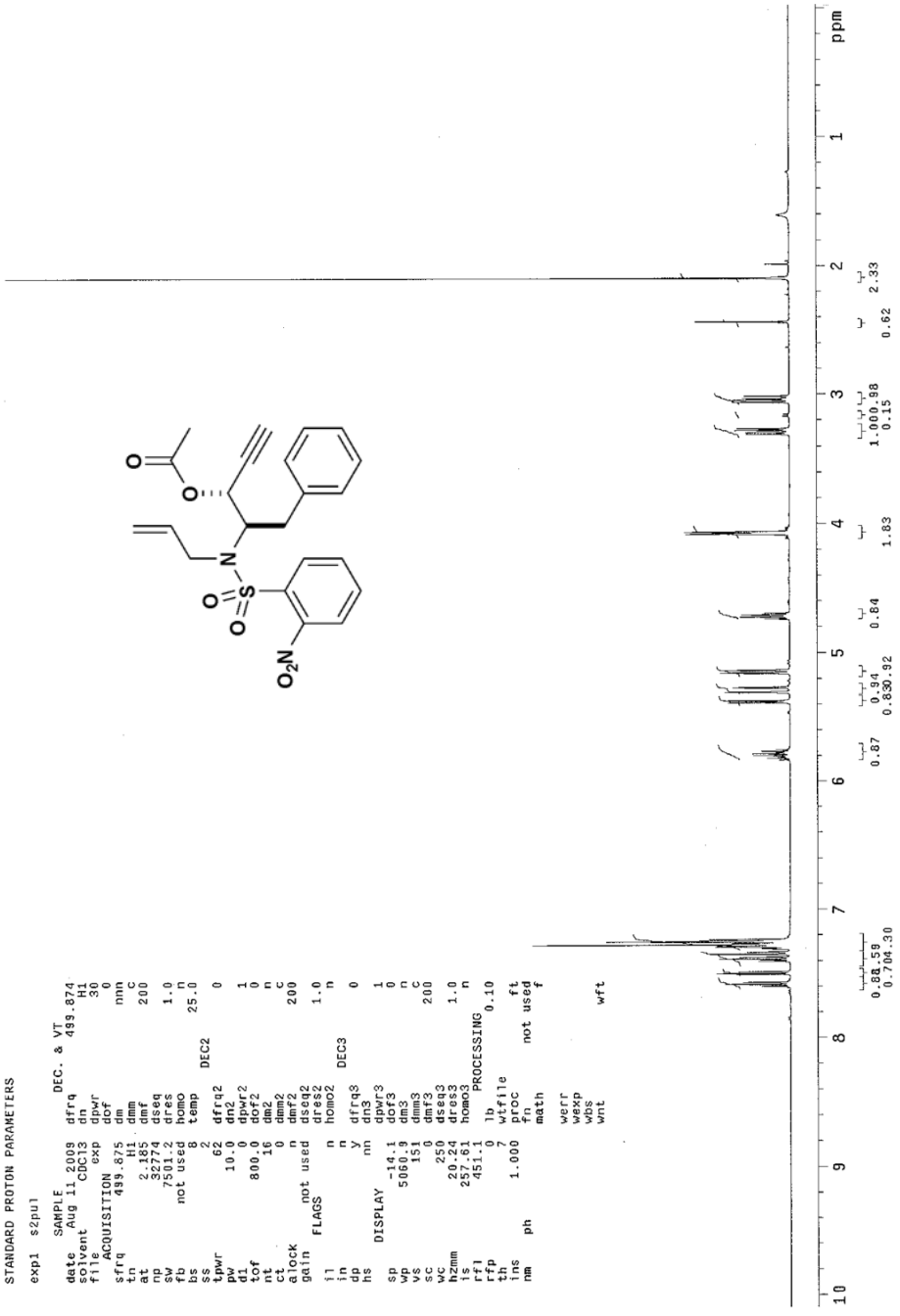


^{1}H NMR (500 MHz, $CDCl_3$) of compound **6a**

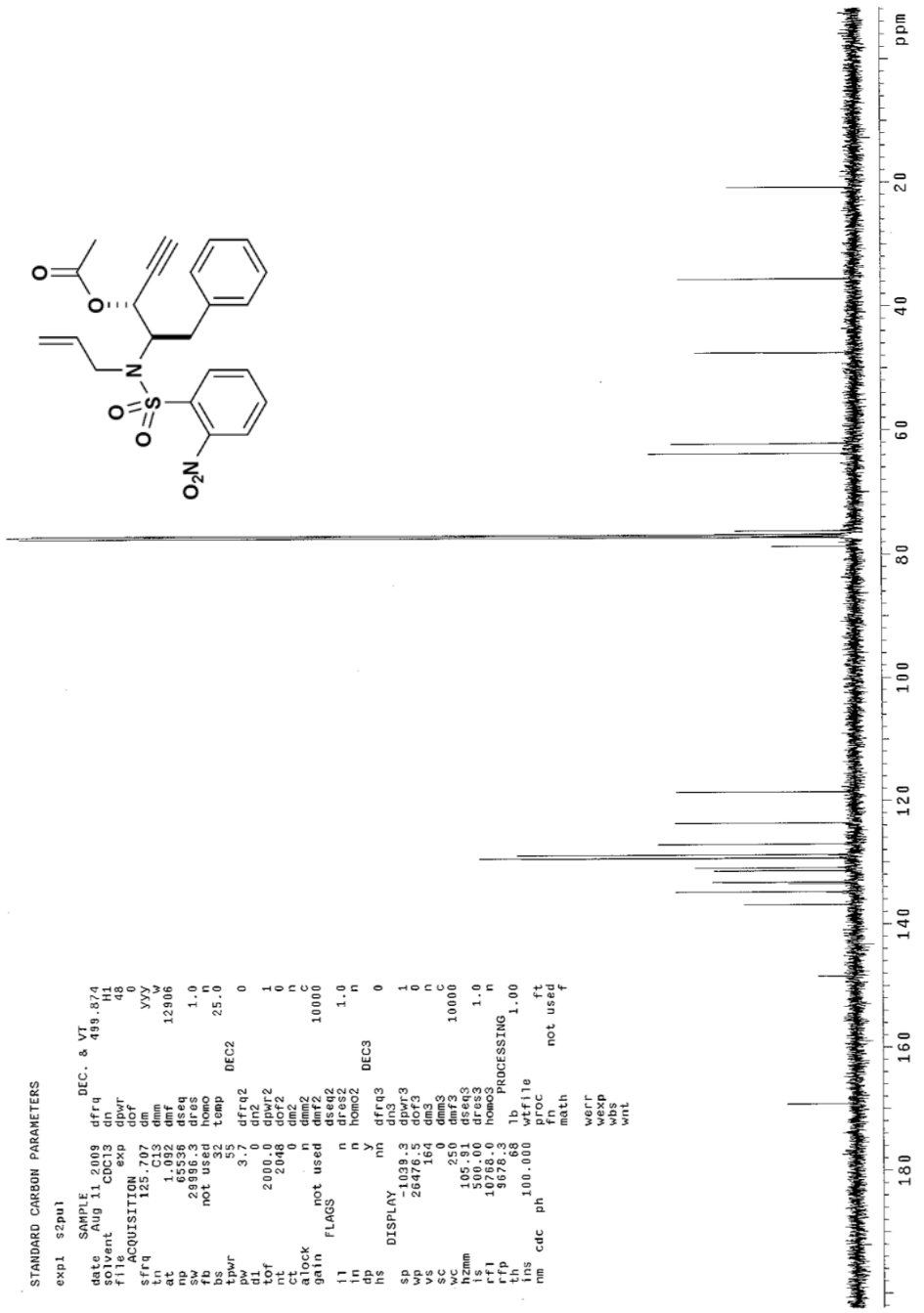


^{13}C NMR (126 MHz, $CDCl_3$) of compound **6a**

Spectral data for (3*R*,4*R*)-4-(*N*-allyl-2-nitrophenylsulfonamido)-5-phenylpent-1-yn-3-yl acetate (6b)

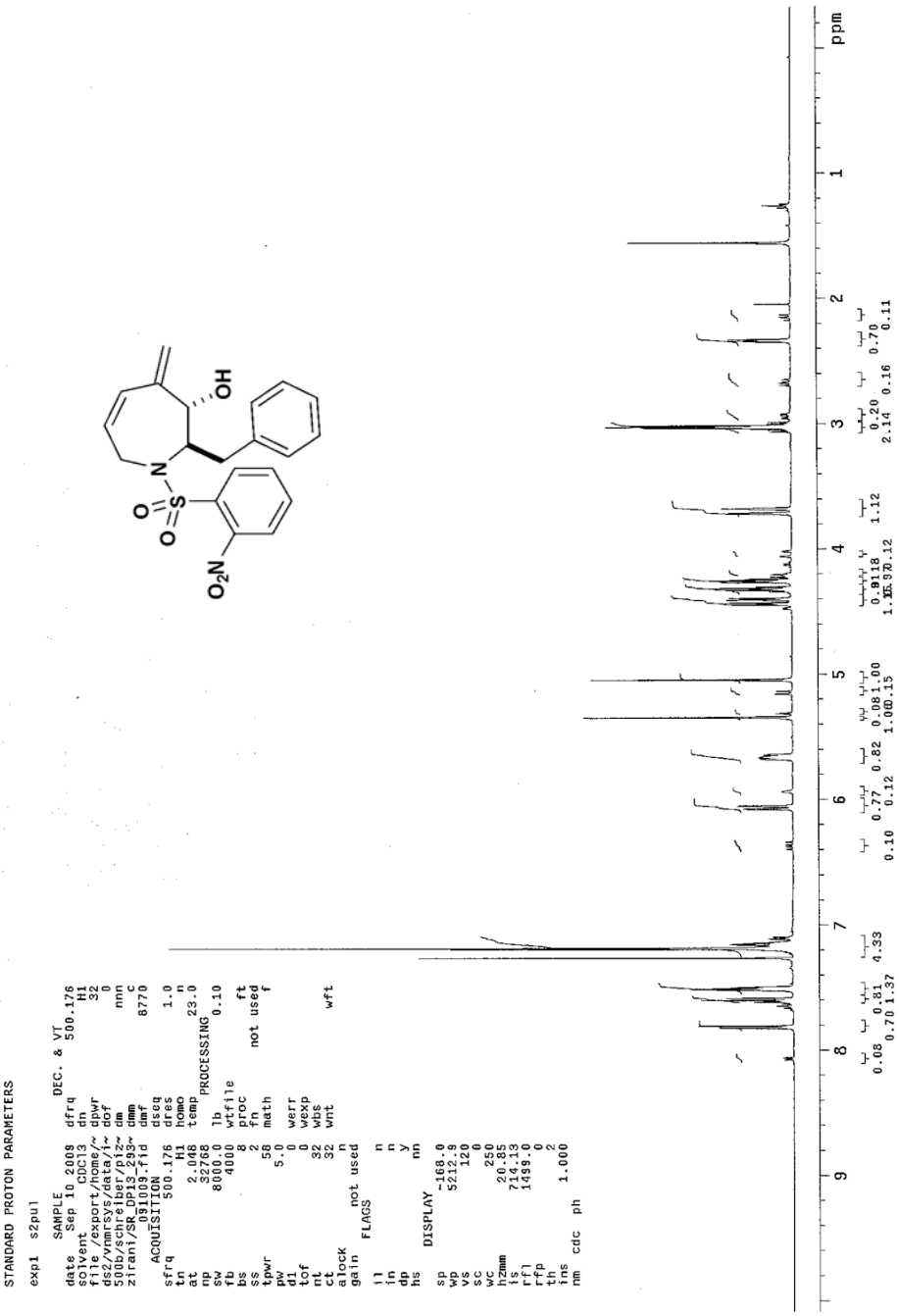


^{1}H NMR (500 MHz, $CDCl_3$) of compound **6b**

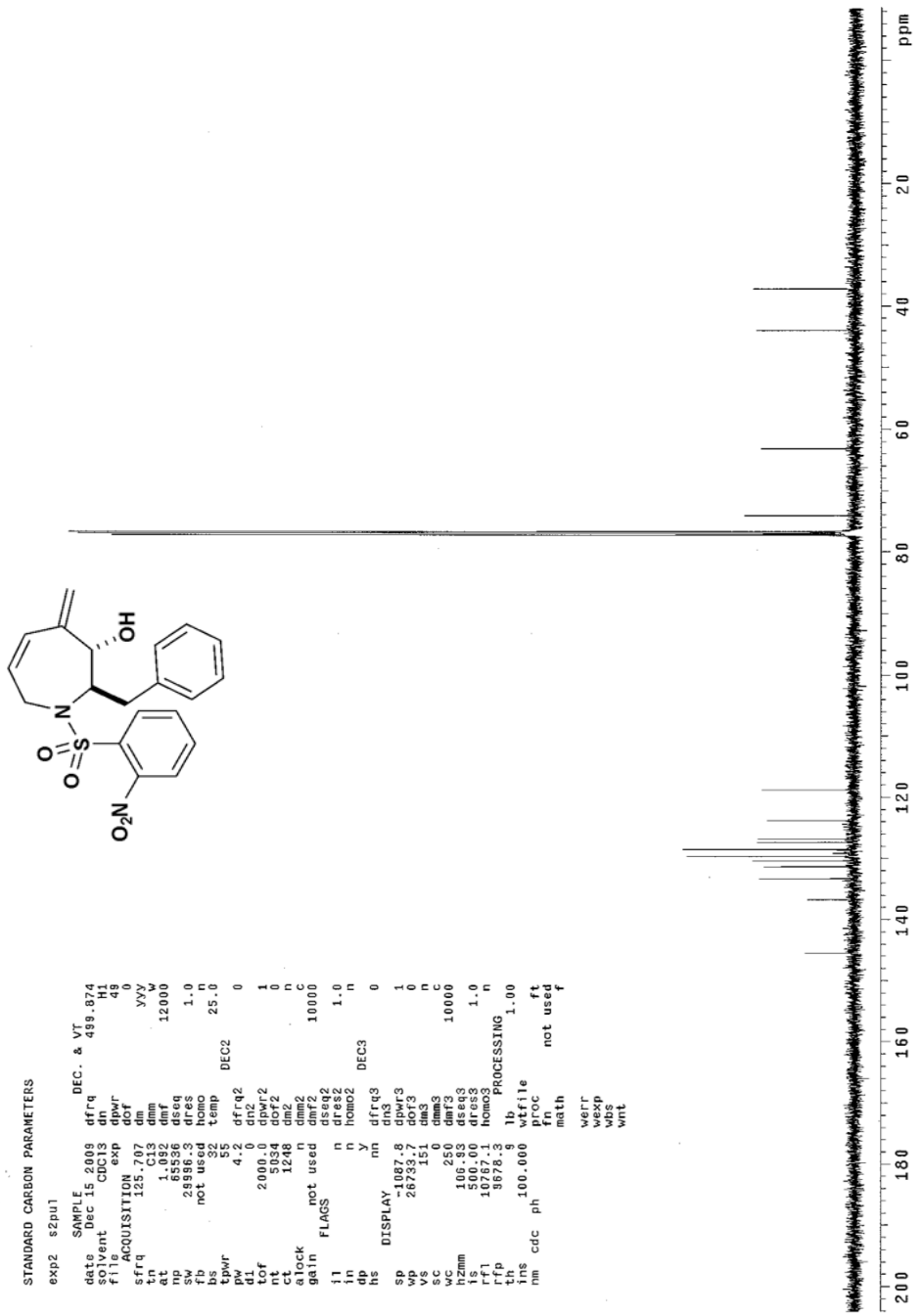


^{13}C NMR (126 MHz, $CDCl_3$) of compound **6b**

Spectral data for (2*R*,3*S*,*Z*)-2-benzyl-4-methylene-1-(2-nitrophenylsulfonyl)-2,3,4,7-tetrahydro-1*H*-azepin-3-ol (5a)

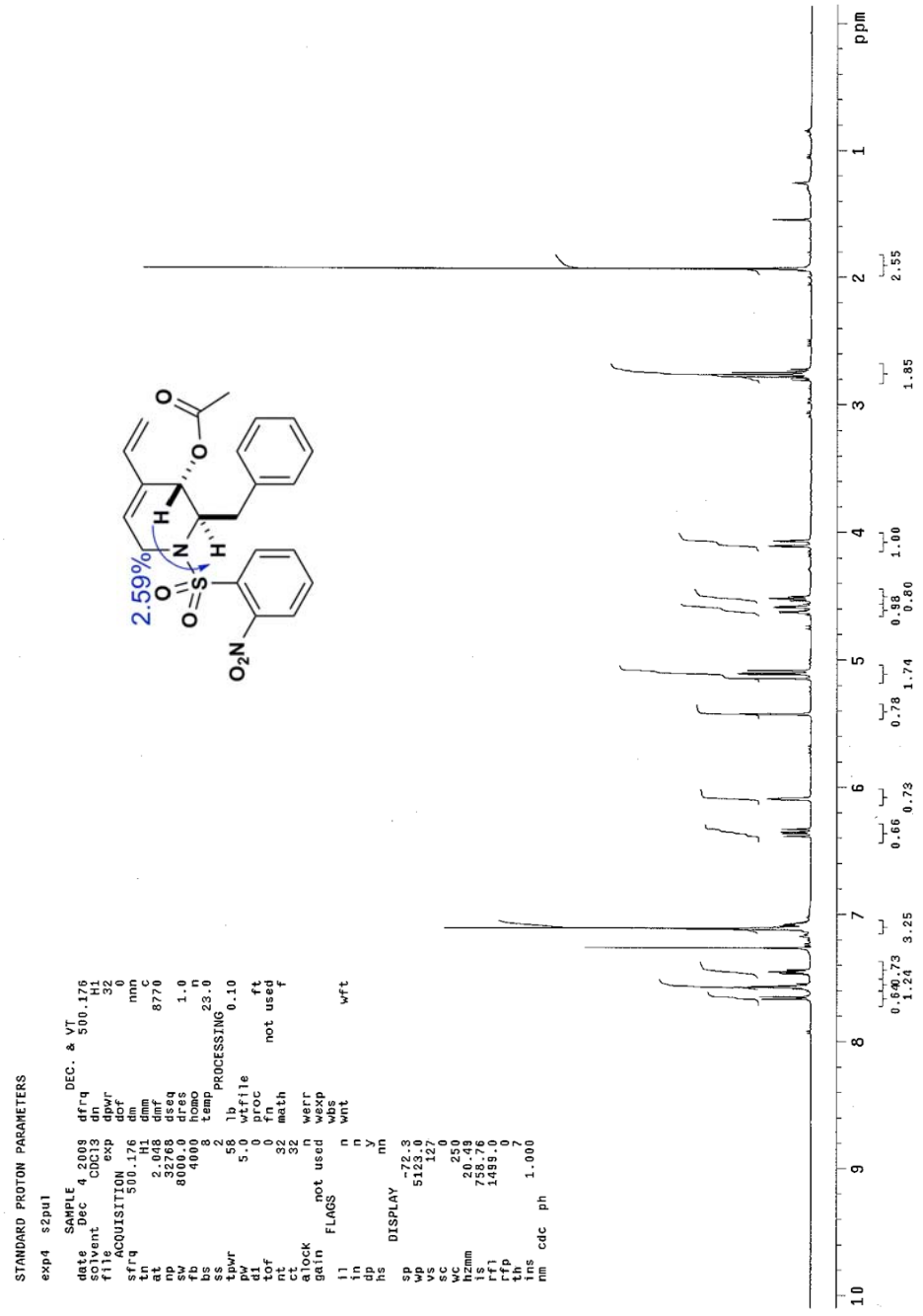


^{1}H NMR (500 MHz, $CDCl_3$) of compound **5a**

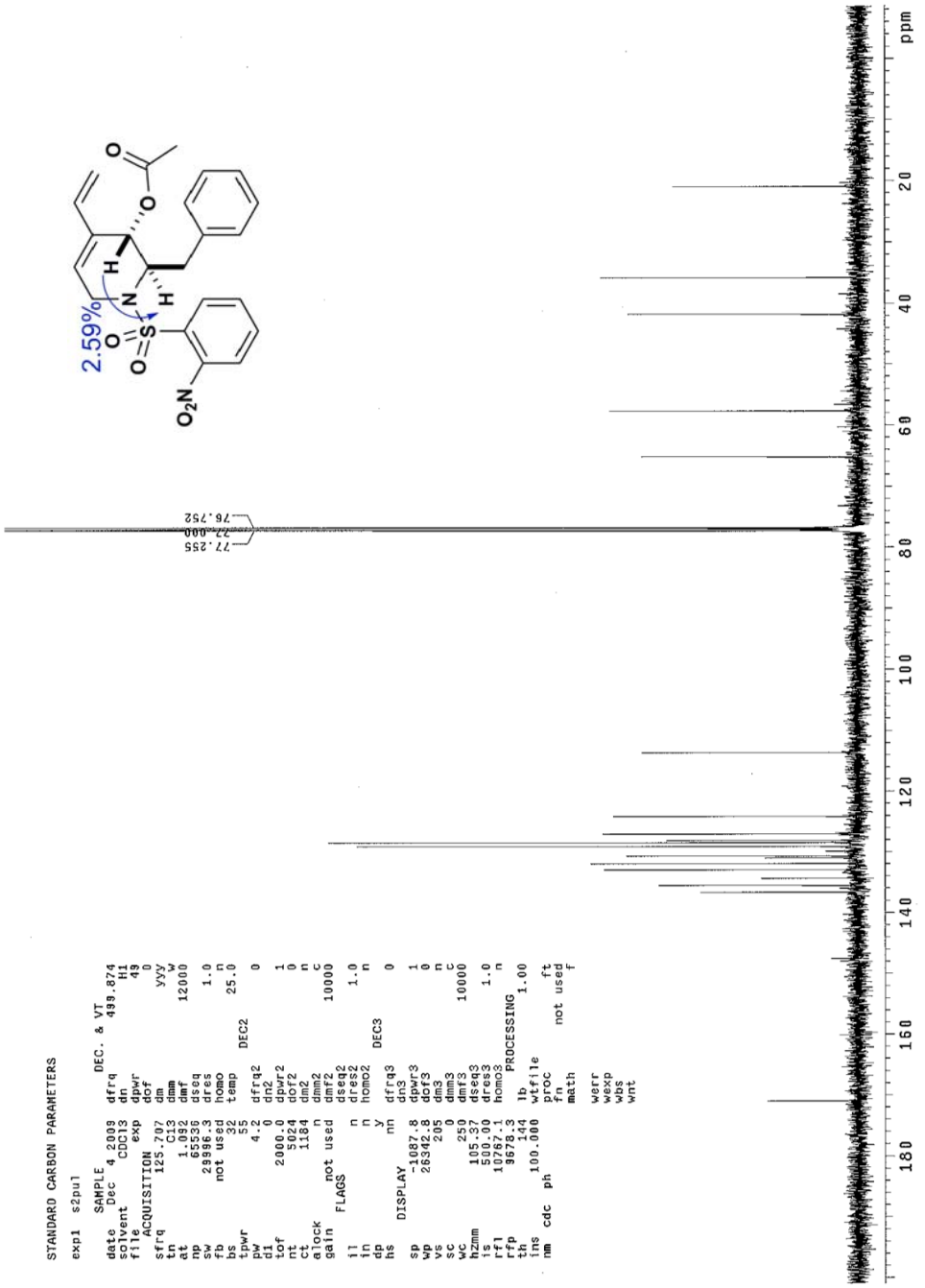


^{13}C NMR (126 MHz, $CDCl_3$) of compound **5a**

Spectral data for (2*R*,3*S*)-2-benzyl-1-(2-nitrophenylsulfonyl)-4-vinyl-1,2,3,6-tetrahydropyridin-3-yl-acetate (7a)

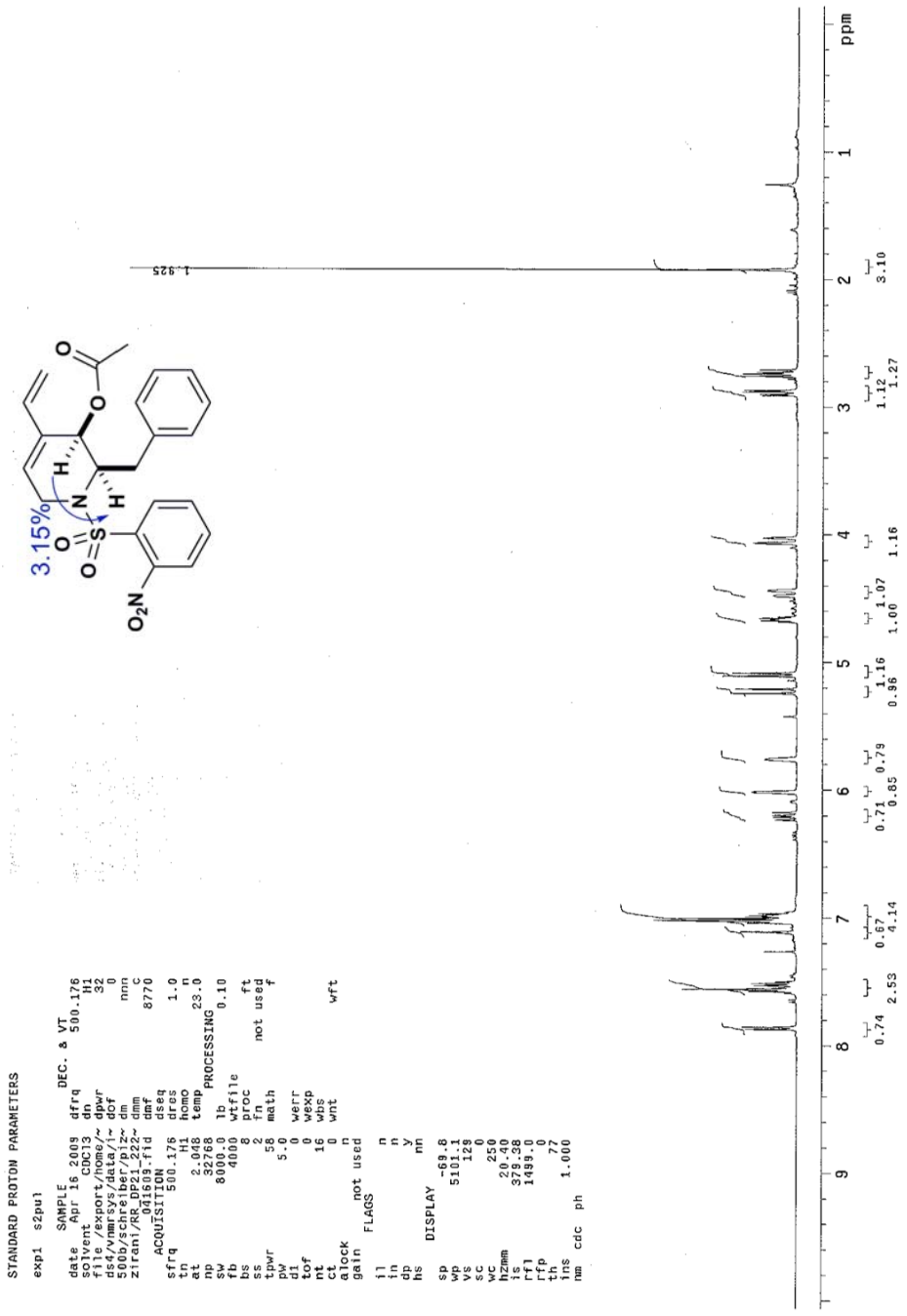


^{1}H NMR (500 MHz, $CDCl_3$) of compound **7a**

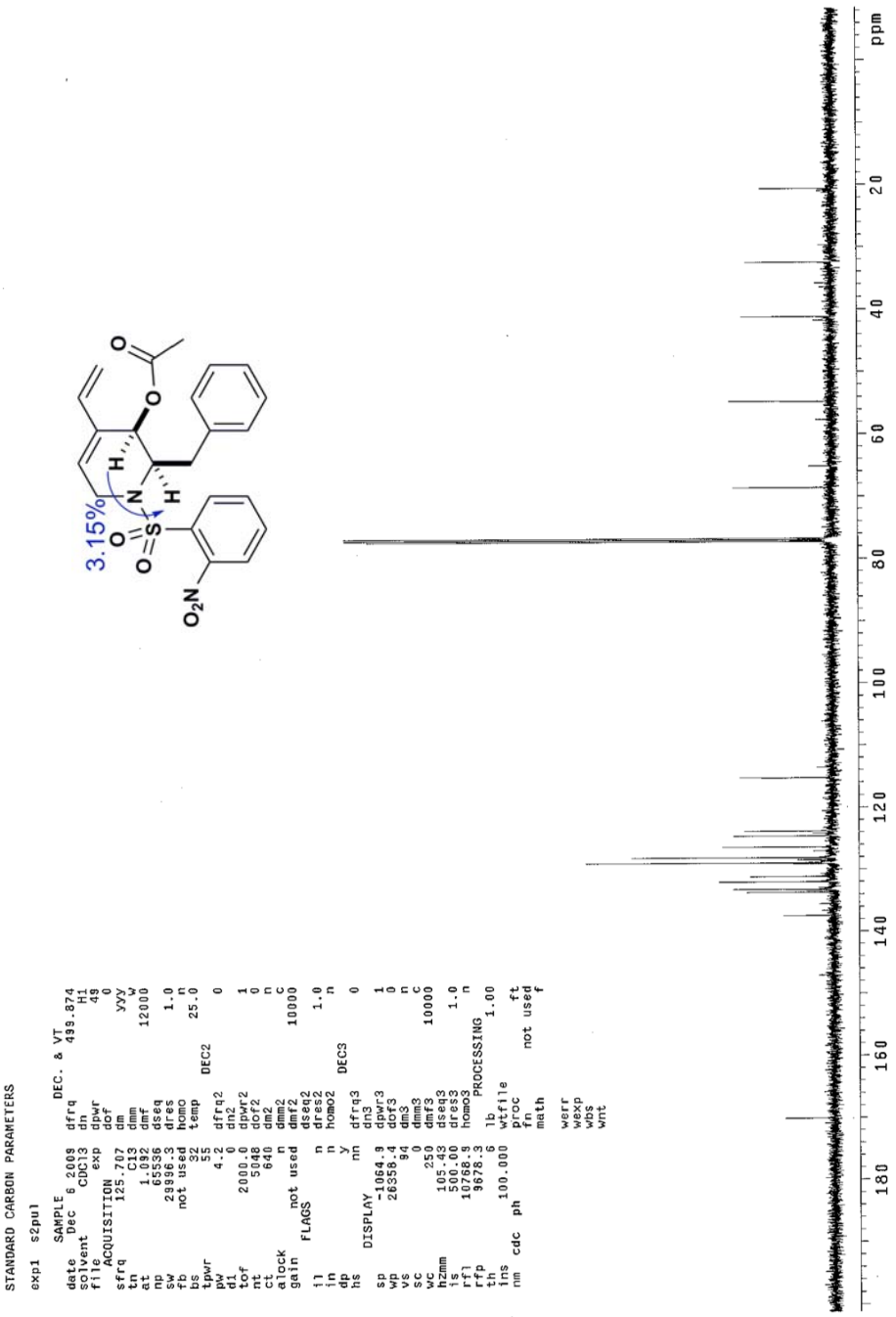


^{13}C NMR (126 MHz, $CDCl_3$) of compound **7a**

Spectral data for (2*R*,3*R*)-2-benzyl-1-(2-nitrophenylsulfonyl)-4-vinyl-1,2,3,6-tetrahydropyridin-3-yl-acetate (7b)

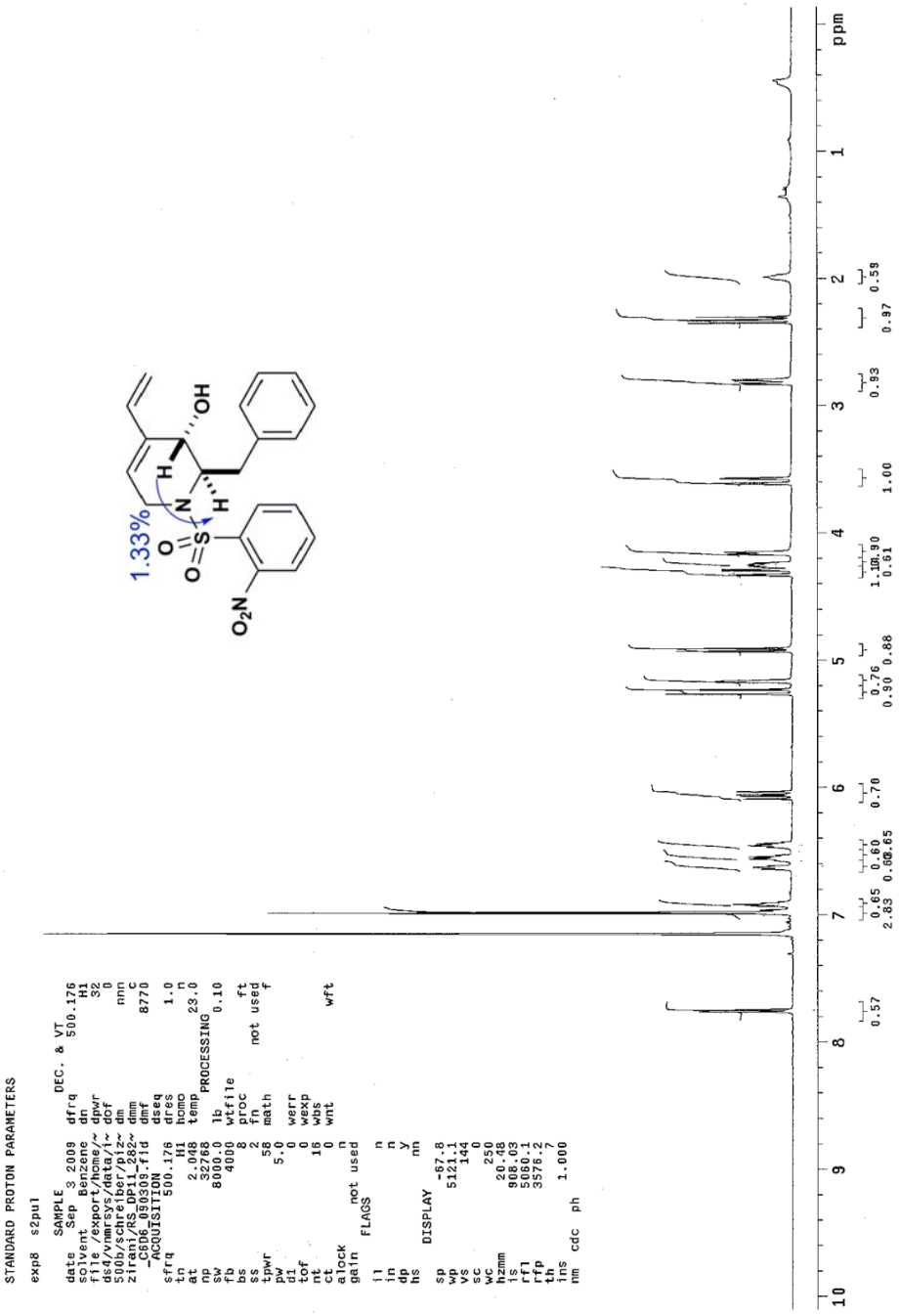


^{1}H NMR (500 MHz, $CDCl_3$) of compound **7b**

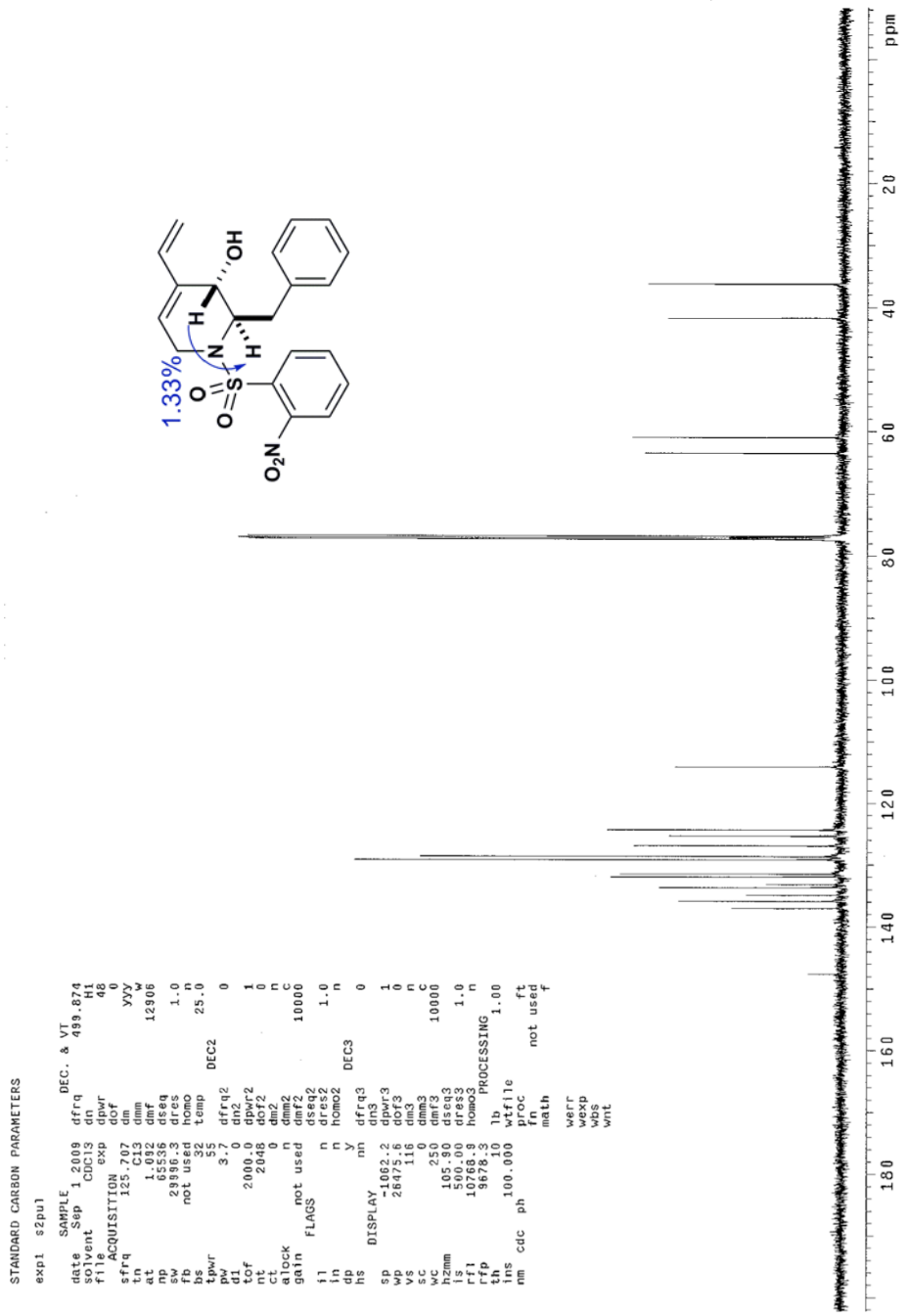


^{13}C NMR (126 MHz, $CDCl_3$) of compound **7b**

Spectral data for (2*R*,3*S*)-2-benzyl-1-(2-nitrophenylsulfonyl)-4-vinyl-1,2,3,6-tetrahydropyridin-3-ol (8a)

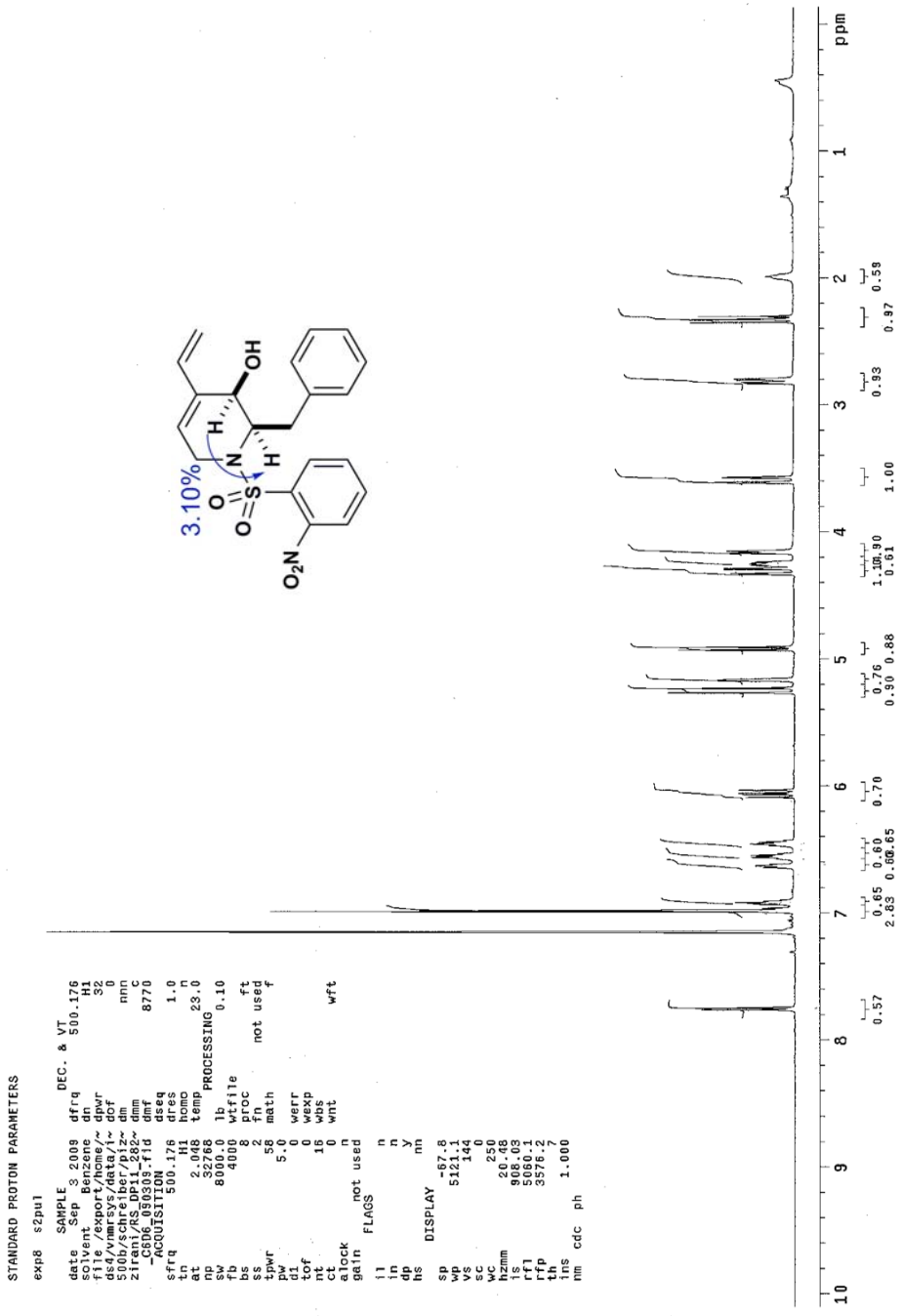


^{1}H NMR (500 MHz, Benzene) of compound **8a**

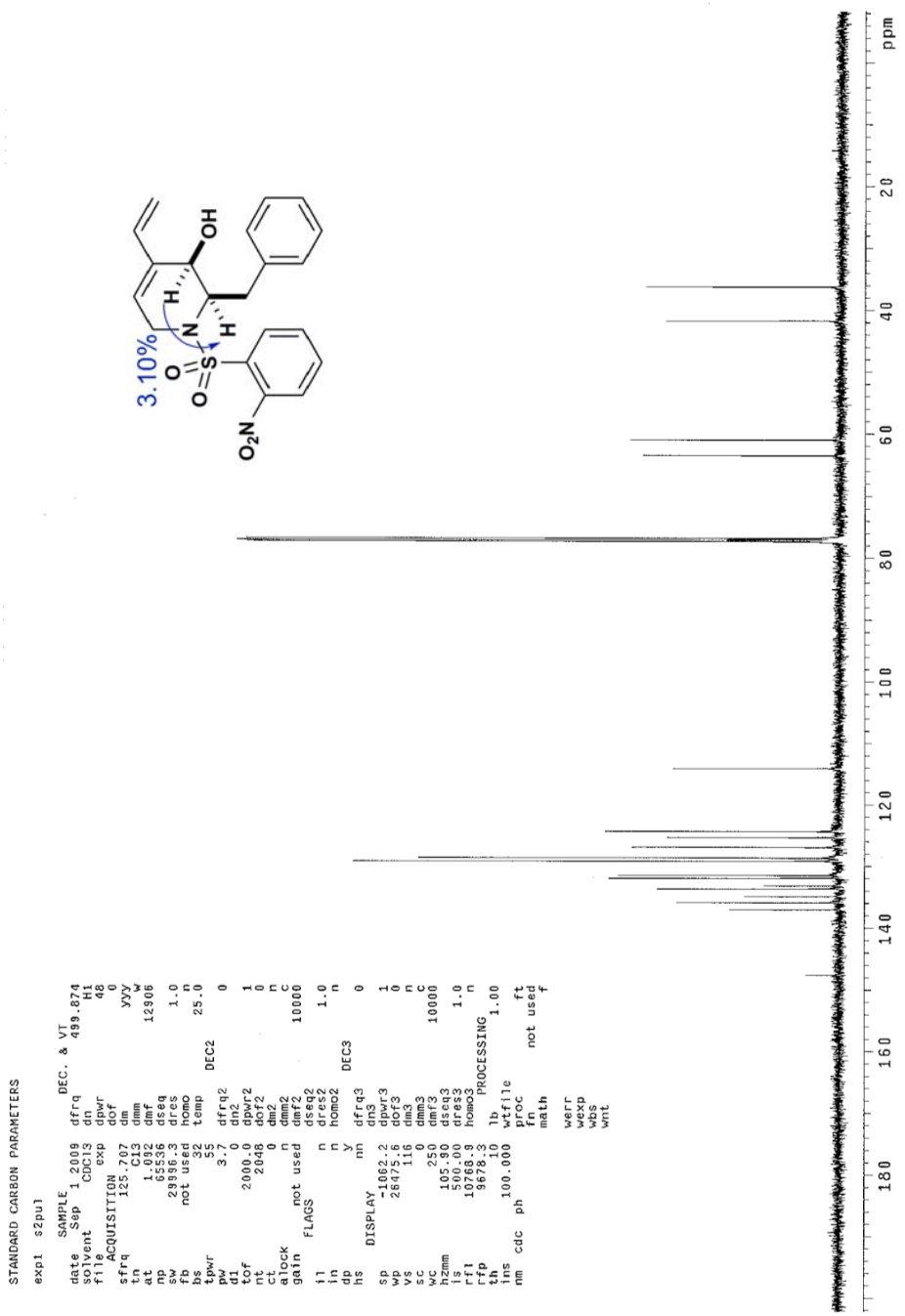


^{13}C NMR (126 MHz, $CDCl_3$) of compound **8a**

Spectral data for (2*R*,3*R*)-2-benzyl-1-(2-nitrophenylsulfonyl)-4-vinyl-1,2,3,6-tetrahydropyridin-3-ol (8b)

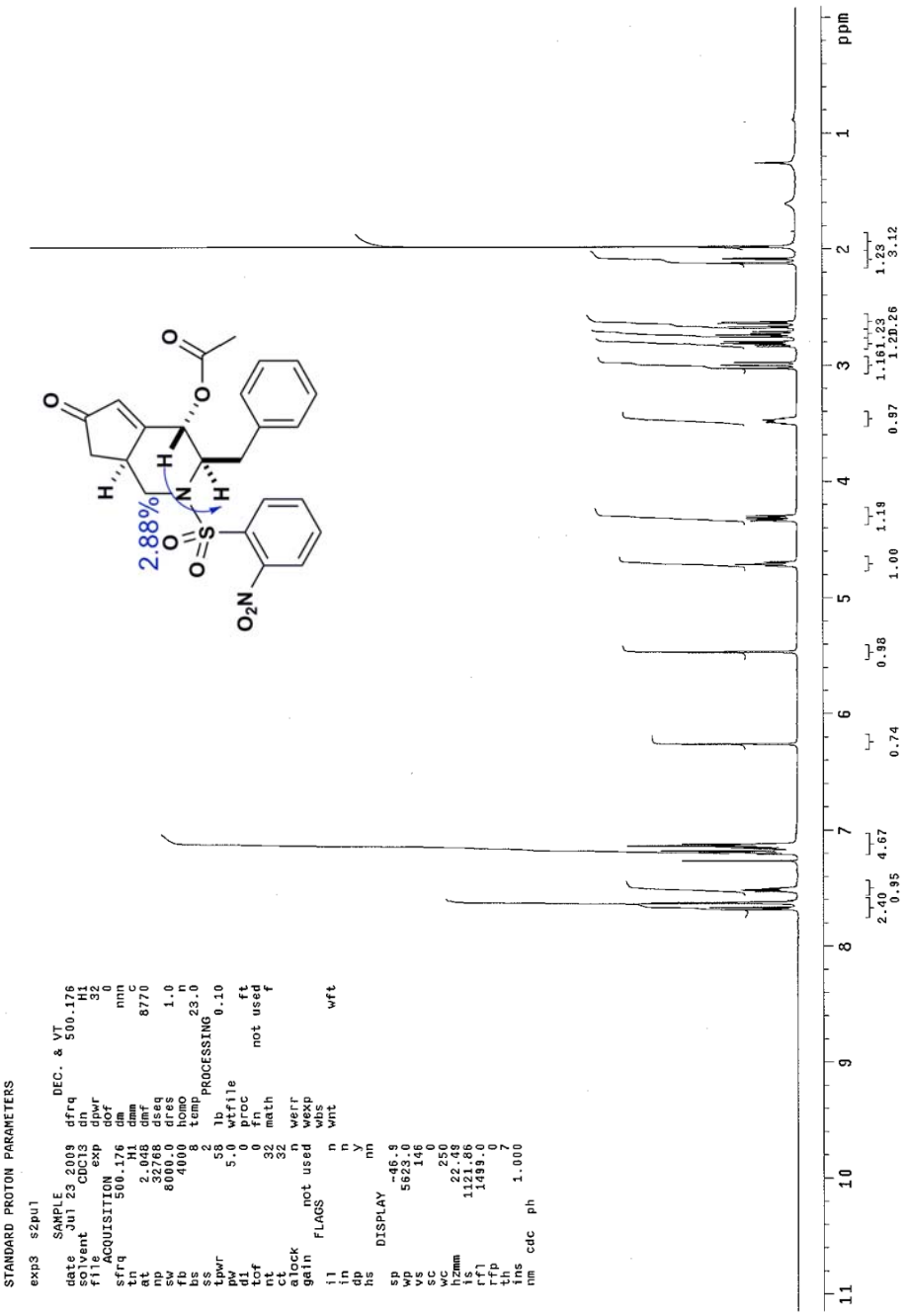


^{1}H NMR (500 MHz, Benzene) of compound **8b**

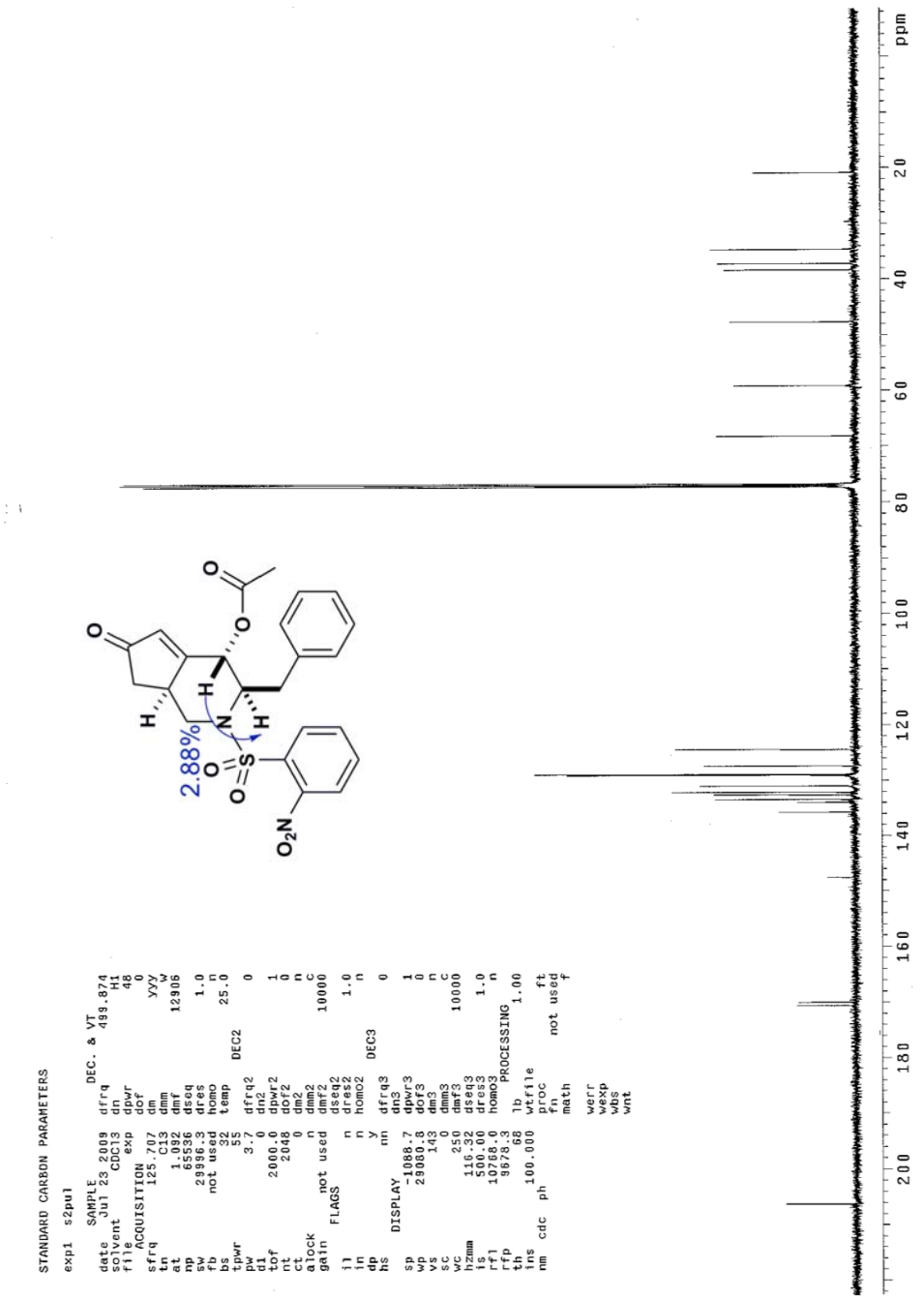


^{13}C NMR (126 MHz, $CDCl_3$) of compound **8b**

Spectral data for (3*R*,4*S*,7a*S*)-3-benzyl-2-(2-nitrophenylsulfonyl)-6-oxo-2,3,4,6,7,7a-hexahydro-1*H*-cyclopenta [c]pyridin-4-yl acetate (9a)

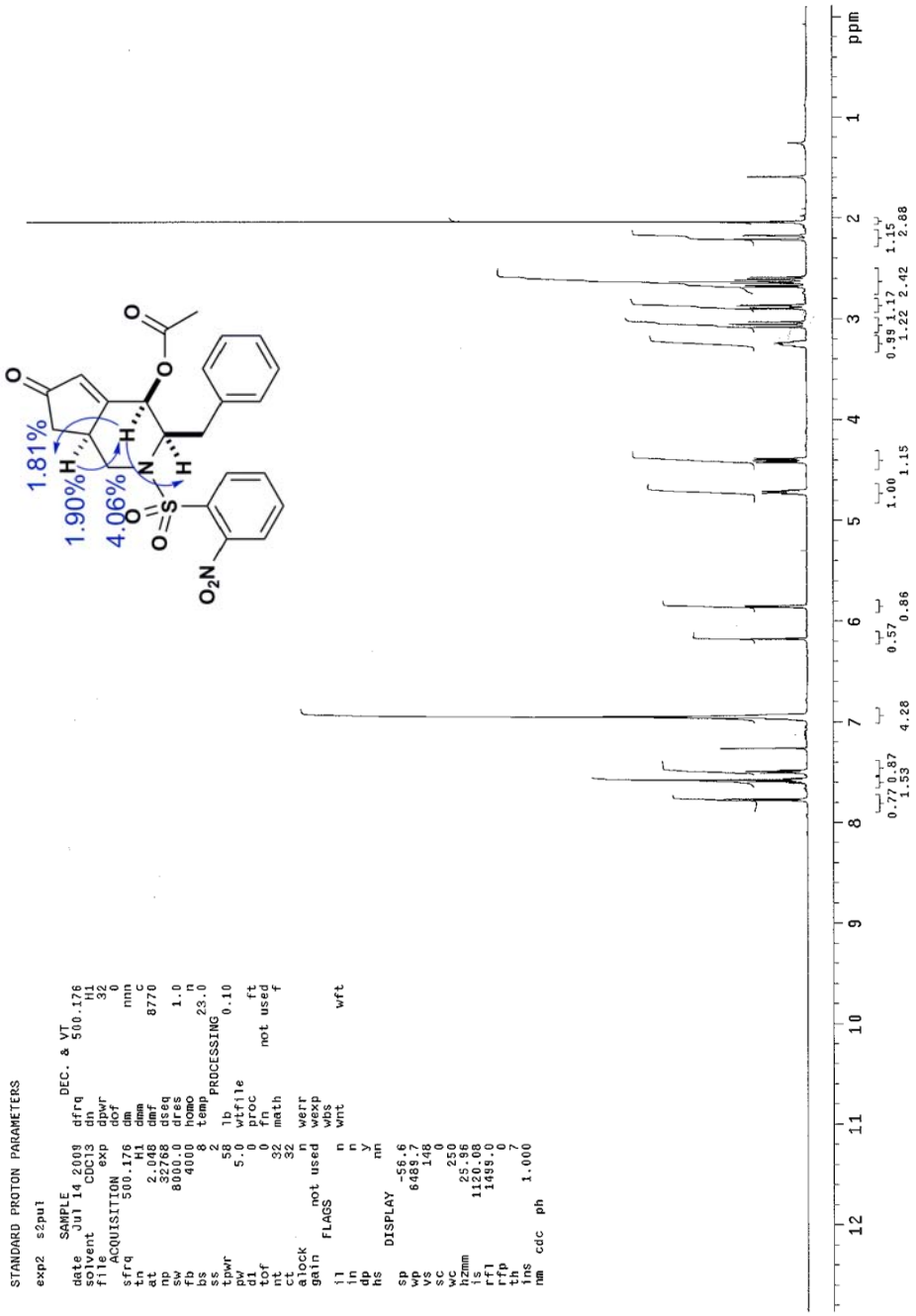


^{1}H NMR (500 MHz, $CDCl_3$) of compound **9a**

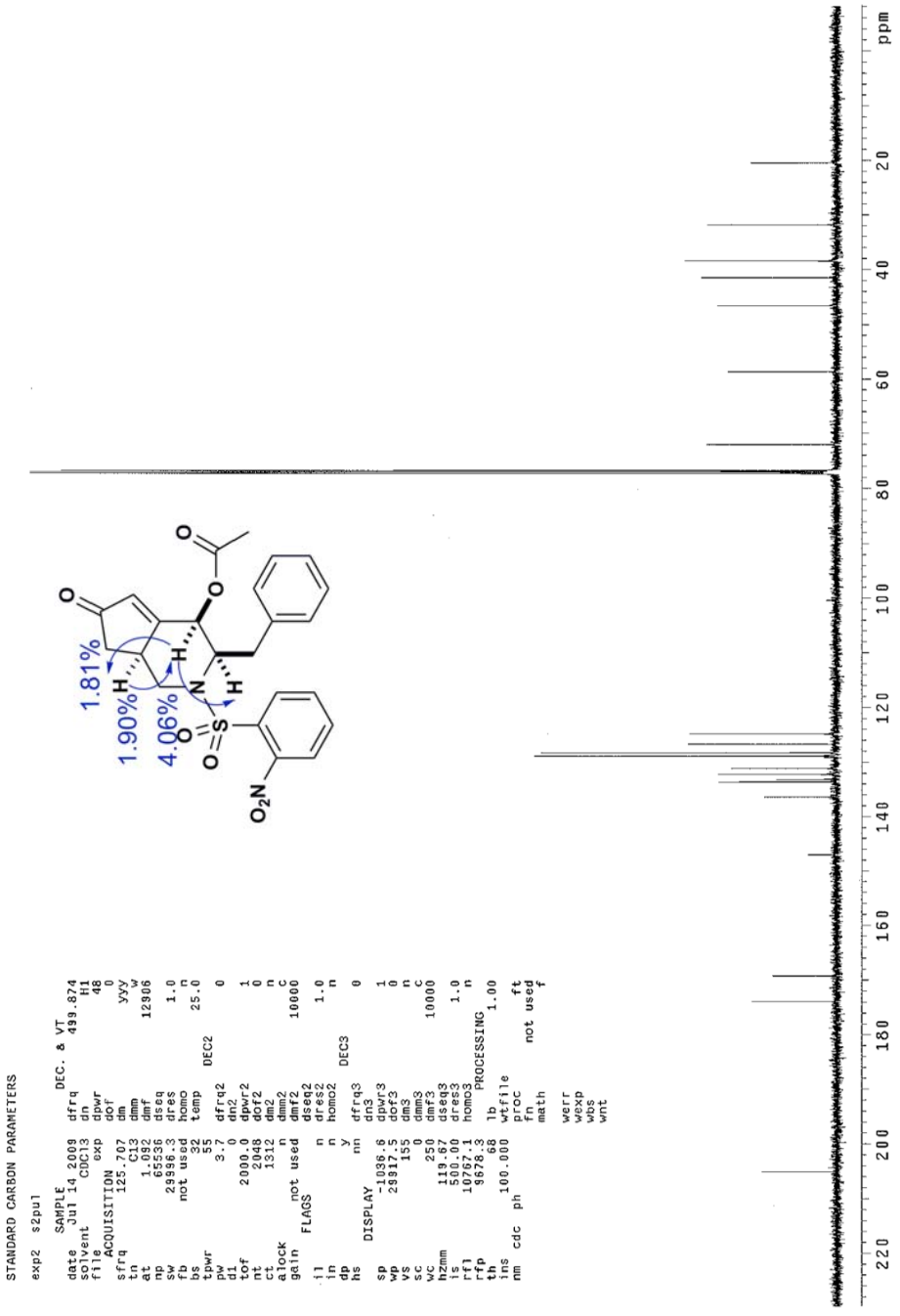


^{13}C NMR (126 MHz, $CDCl_3$) of compound **9a**

Spectral data for (3*R*,4*R*,7a*S*)-3-benzyl-2-(2-nitrophenylsulfonyl)-6-oxo-2,3,4,6,7,7a-hexahydro-1*H*-cyclopenta [c]pyridin-4-yl acetate (9b)

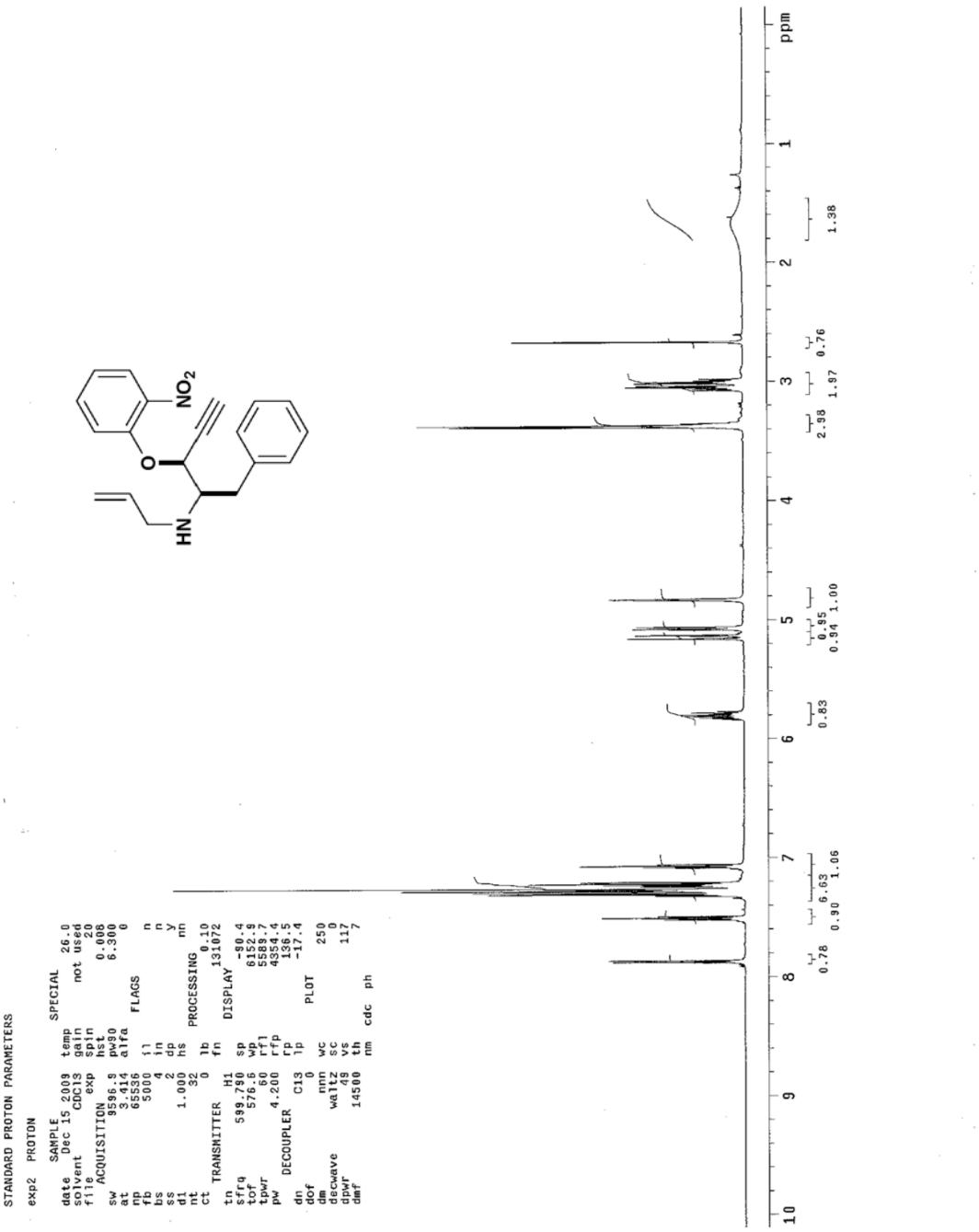


^{1}H NMR (500 MHz, $CDCl_3$) of compound **9b**

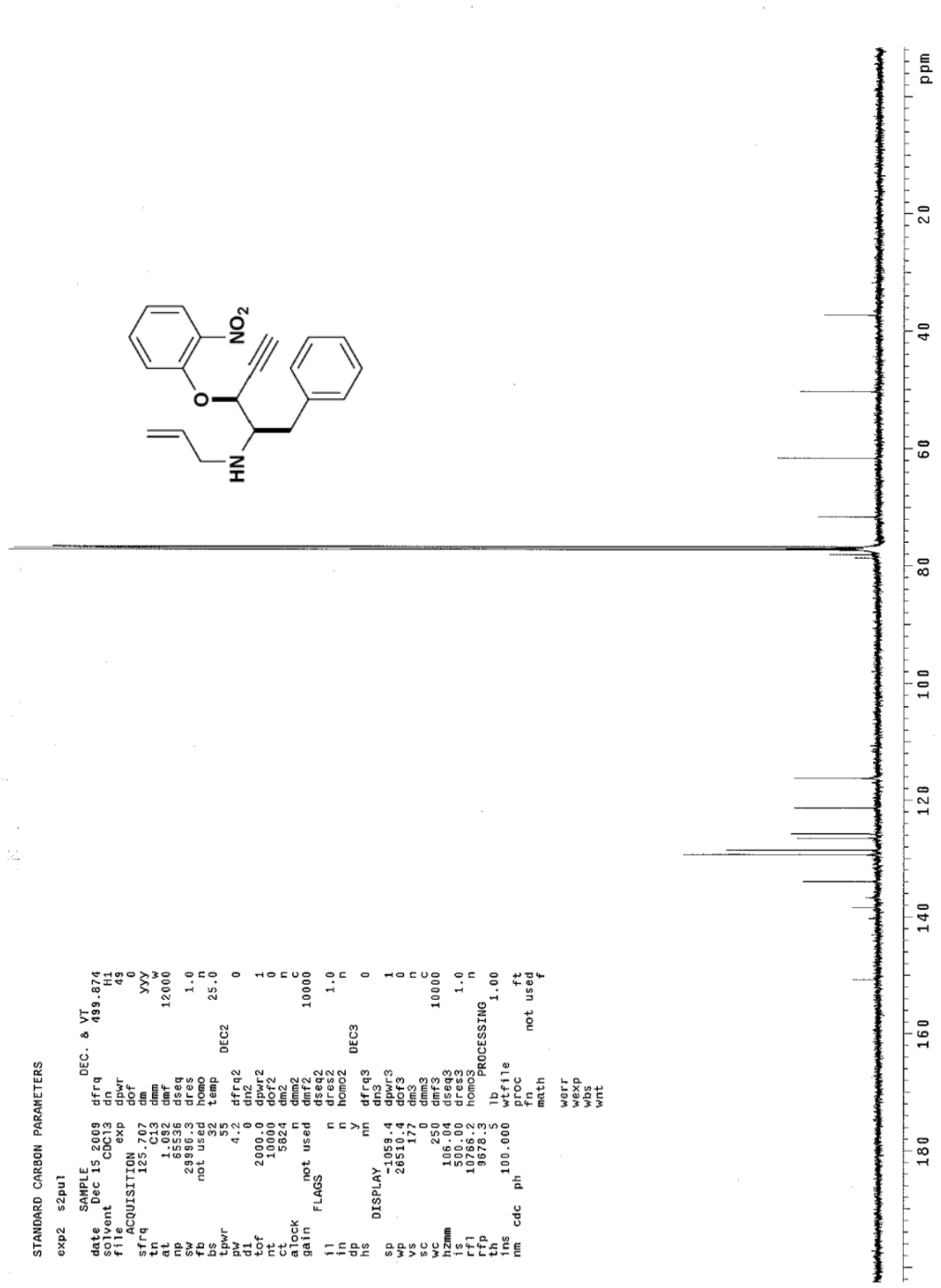


^{13}C NMR (126 MHz, $CDCl_3$) of compound **9b**

Spectral data for (2*R*,3*S*)-*N*-allyl-3-(2-nitrophenoxy)-1-phenylpent-4-yn-2-amine (10a)

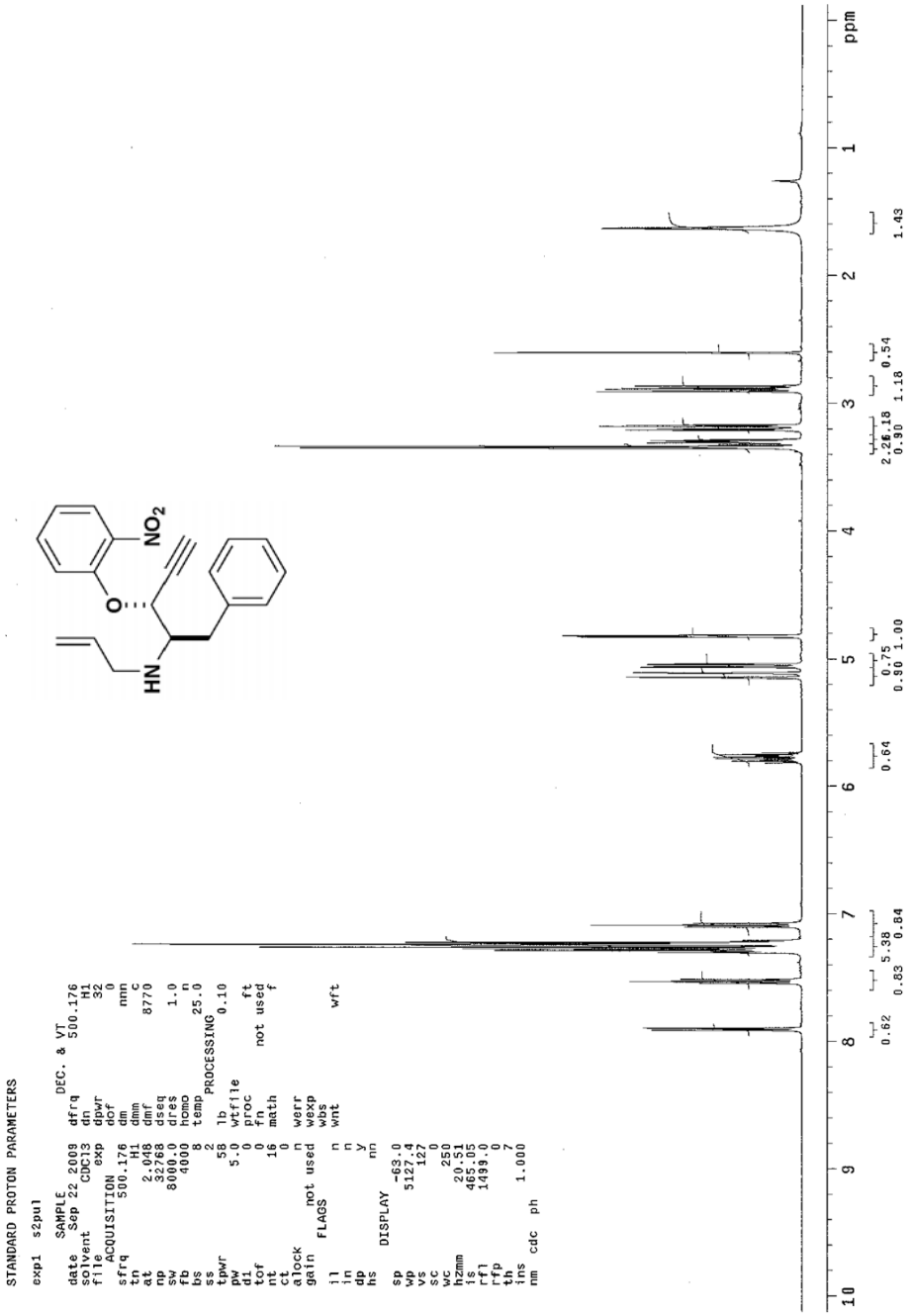


^{1}H NMR (600 MHz, $CDCl_3$) of compound **10a**

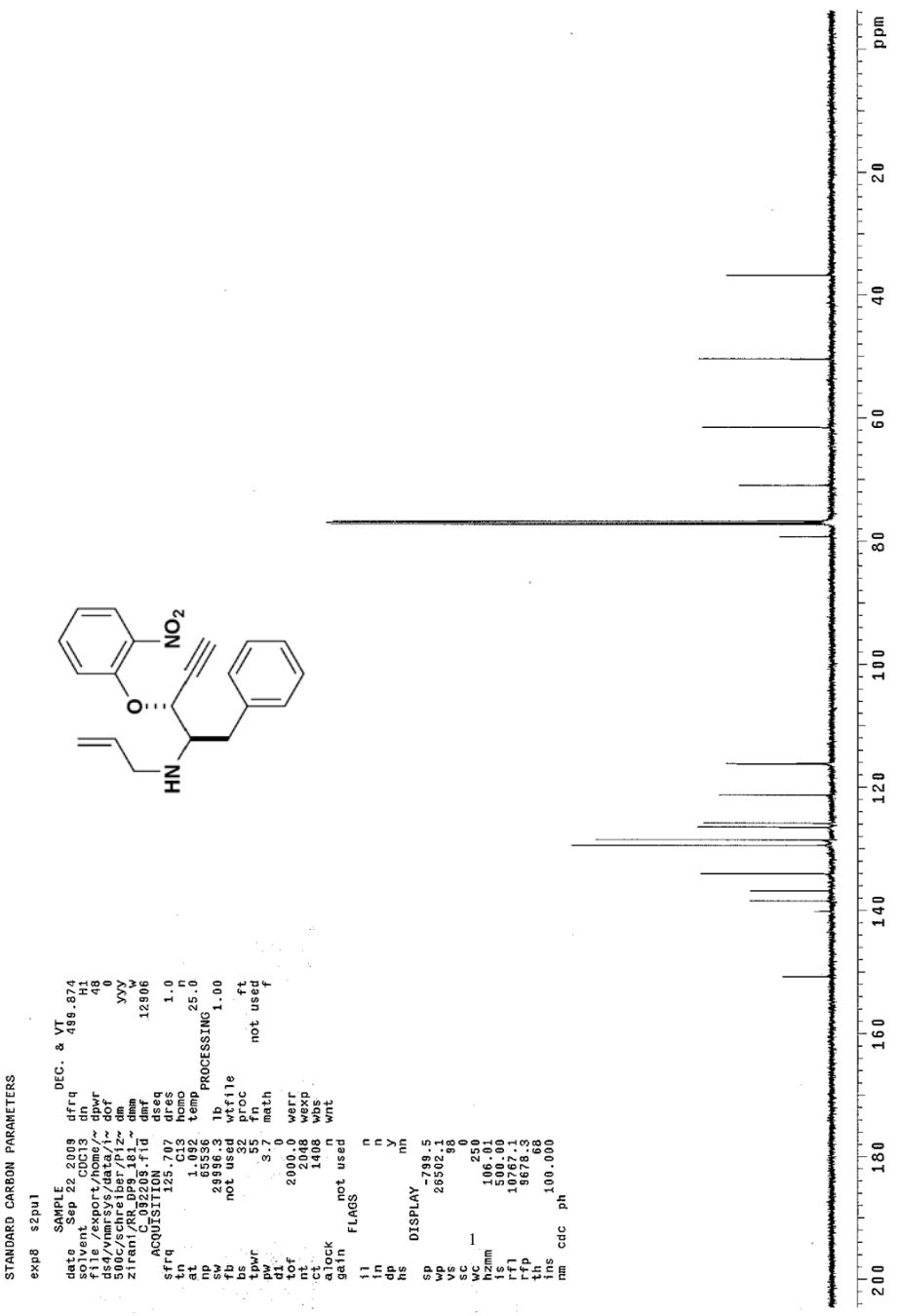


^{13}C NMR (126 MHz, $CDCl_3$) of compound **10a**

Spectral data for (2*R*,3*R*)-*N*-allyl-3-(2-nitrophenoxy)-1-phenylpent-4-yn-2-amine (10b)

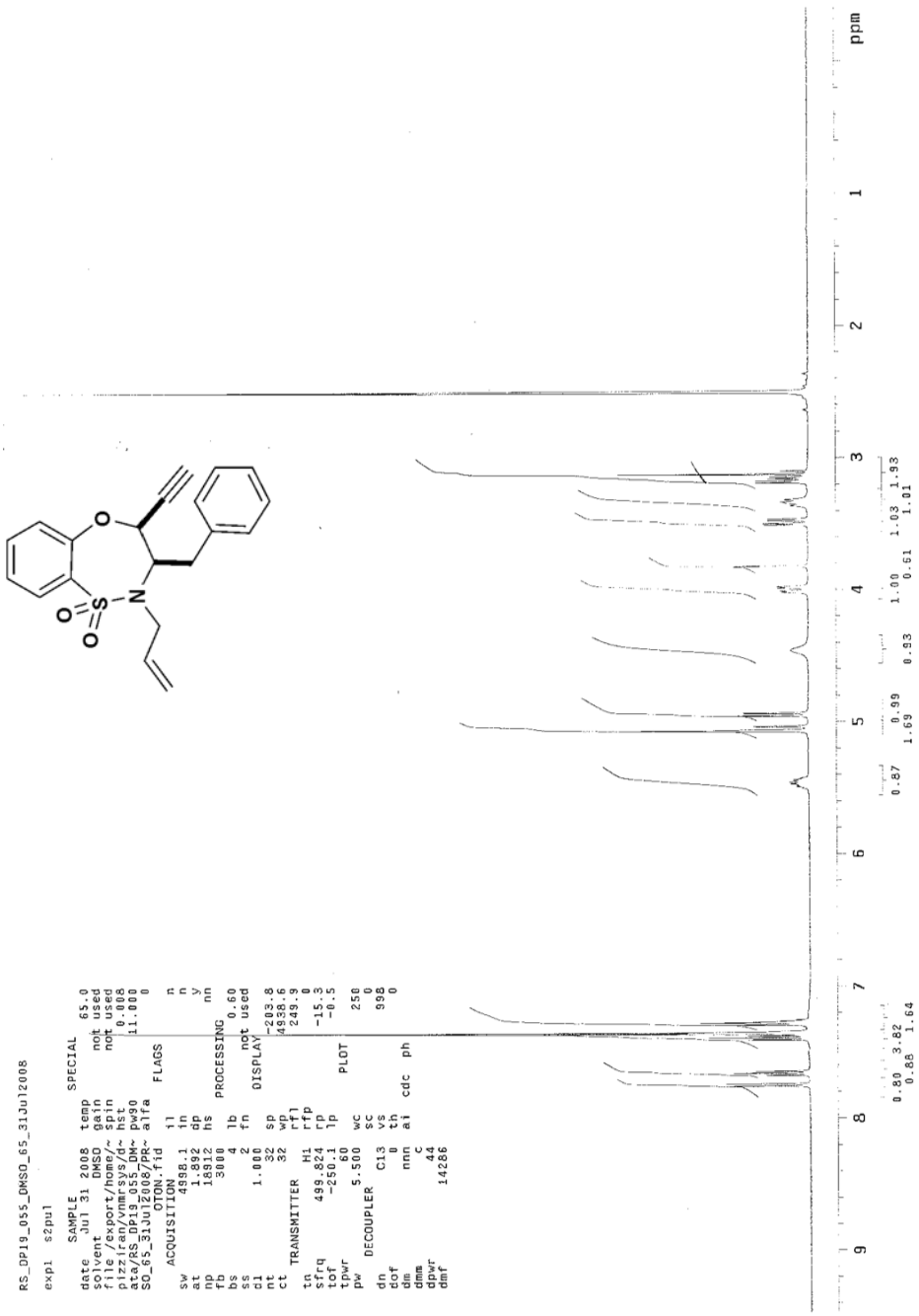


^{1}H NMR (500 MHz, $CDCl_3$) of compound **10b**

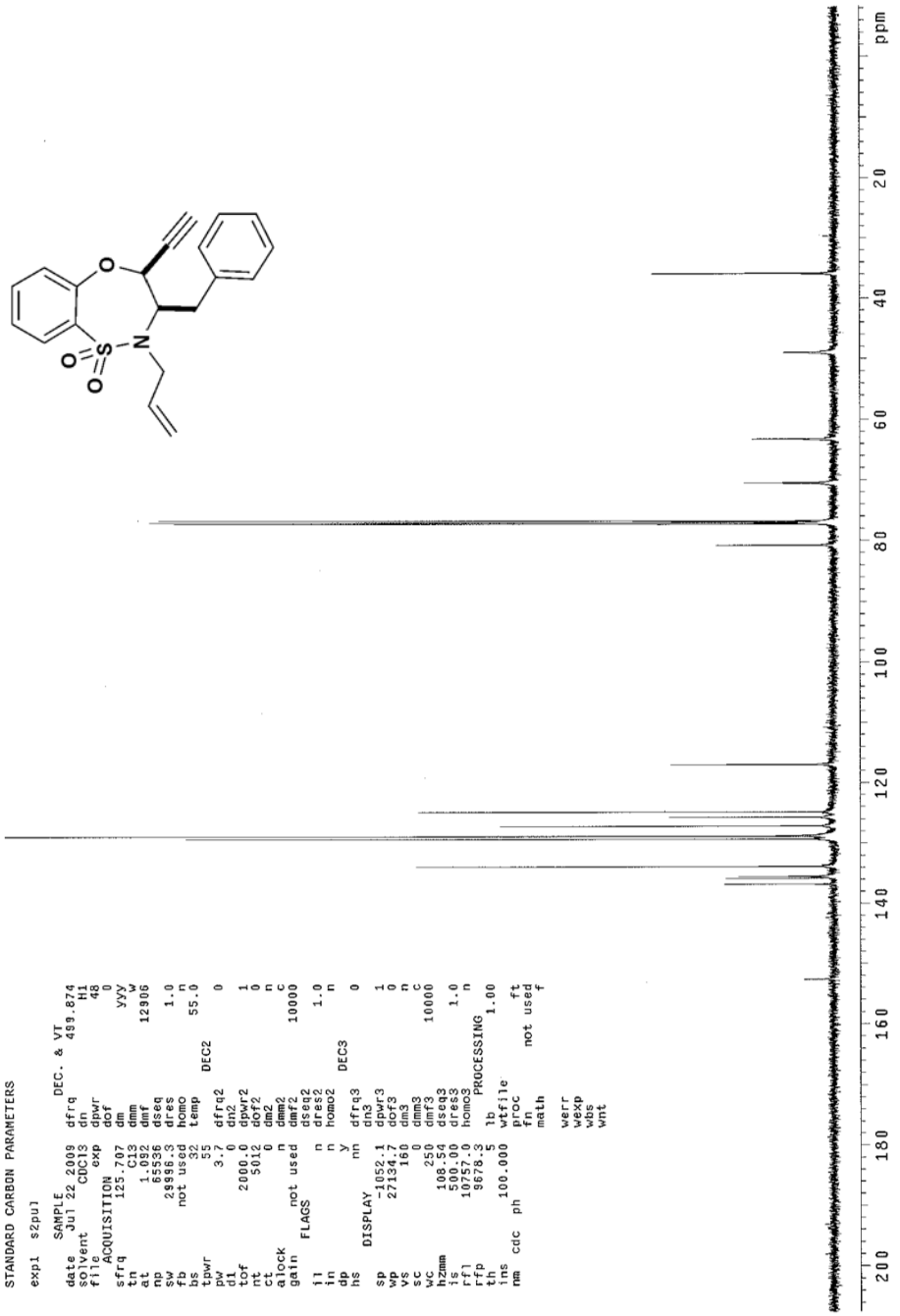


^{3}C NMR (126 MHz, $CDCl_3$) of compound **10b**

Spectral data for (3*R*,4*S*)-3-benzyl-4-ethynyl-2-prop-2-en-1-yl-3,4-dihydro-2*H*-5,1,2-benzoxathiazepine 1,1-dioxide (11a)

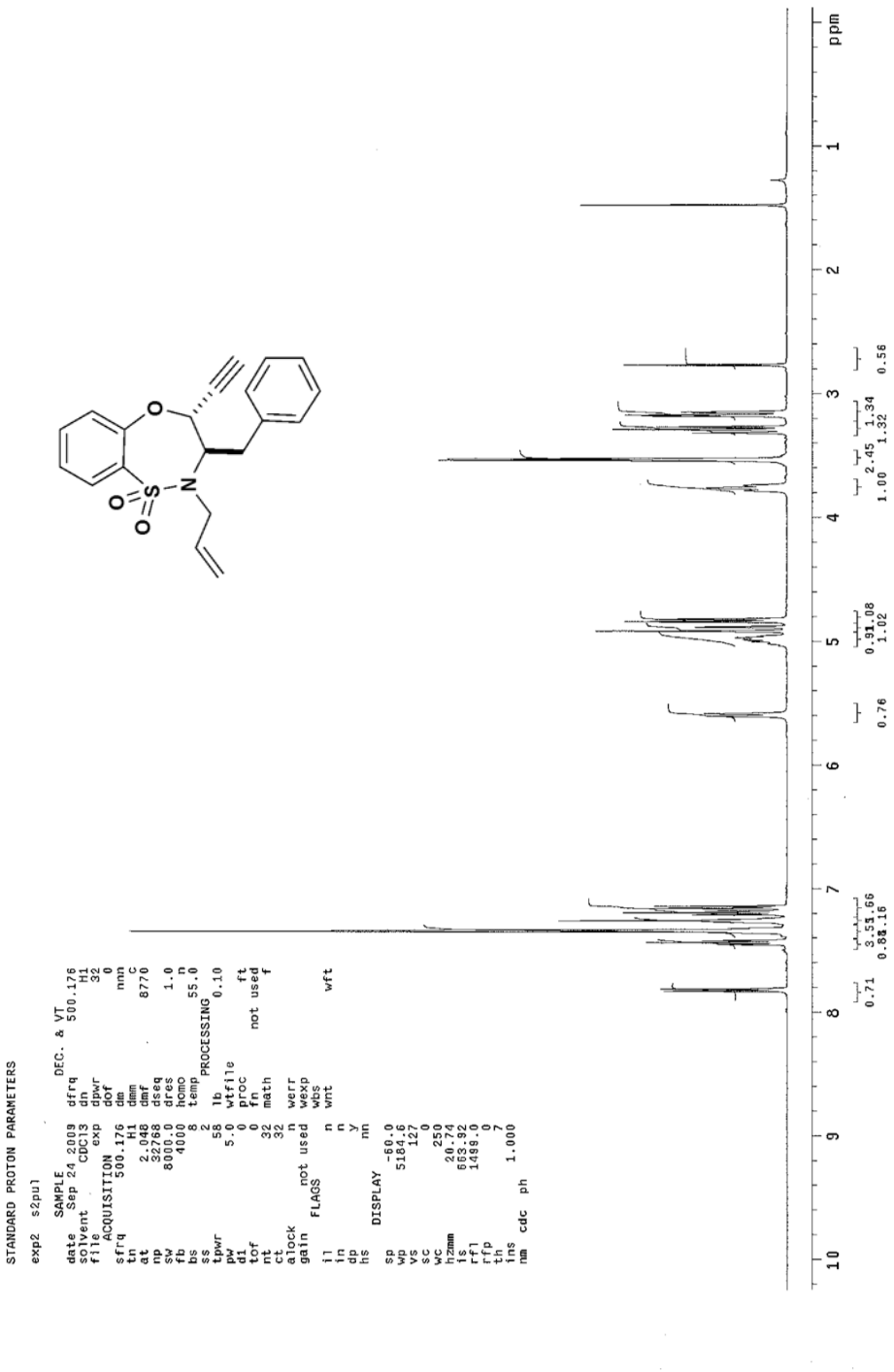


^{1}H NMR (500 MHz, DMSO, T = 65 °C) of compound **11a**

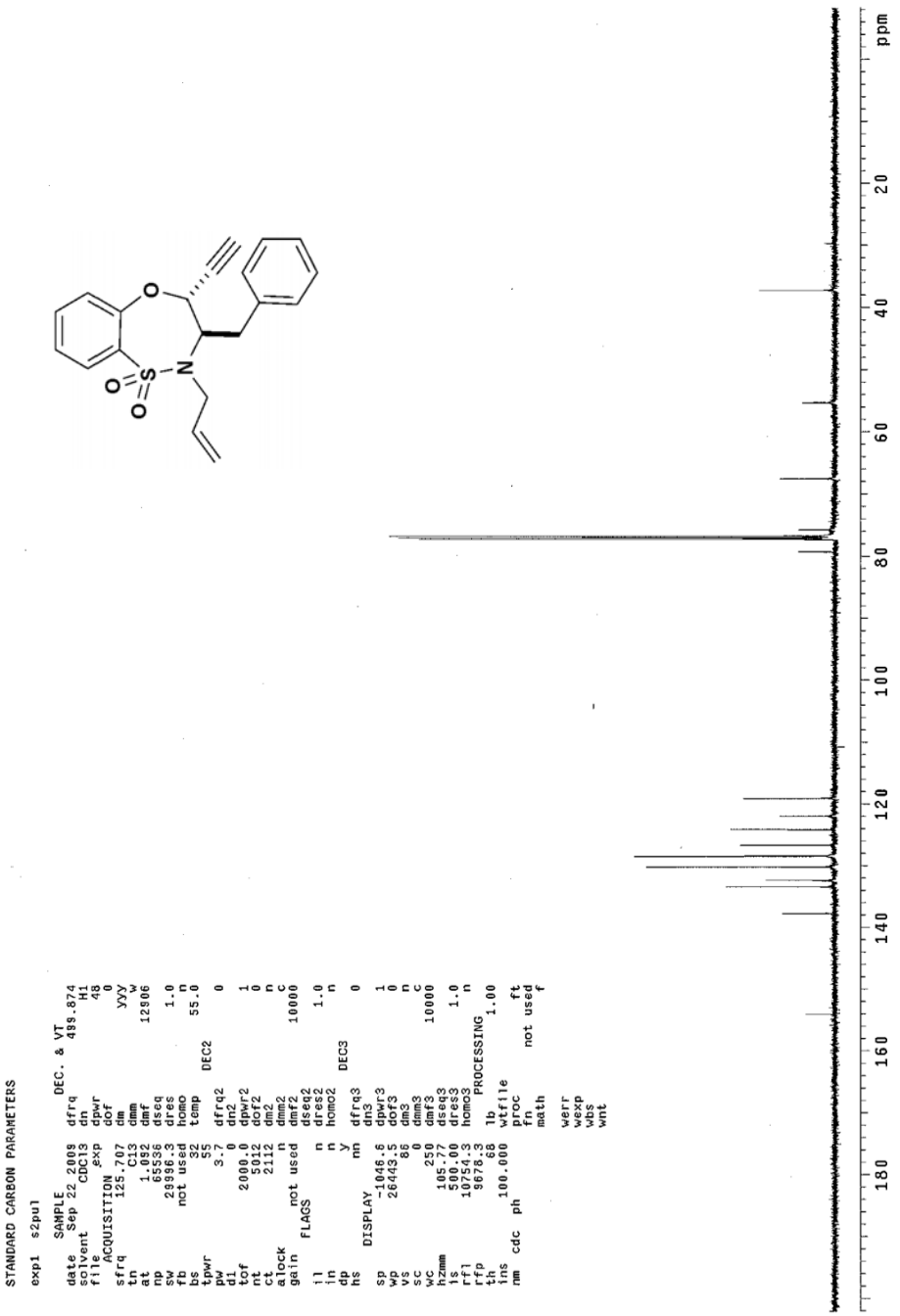


^{13}C NMR (126 MHz, $CDCl_3$, T = 55 °C) of compound **11a**

Spectral data for (3*R*,4*R*)-3-benzyl-4-ethynyl-2-prop-2-en-1-yl-3,4-dihydro-2*H*-5,1,2-benzoxathiazepine 1,1-dioxide (11b)

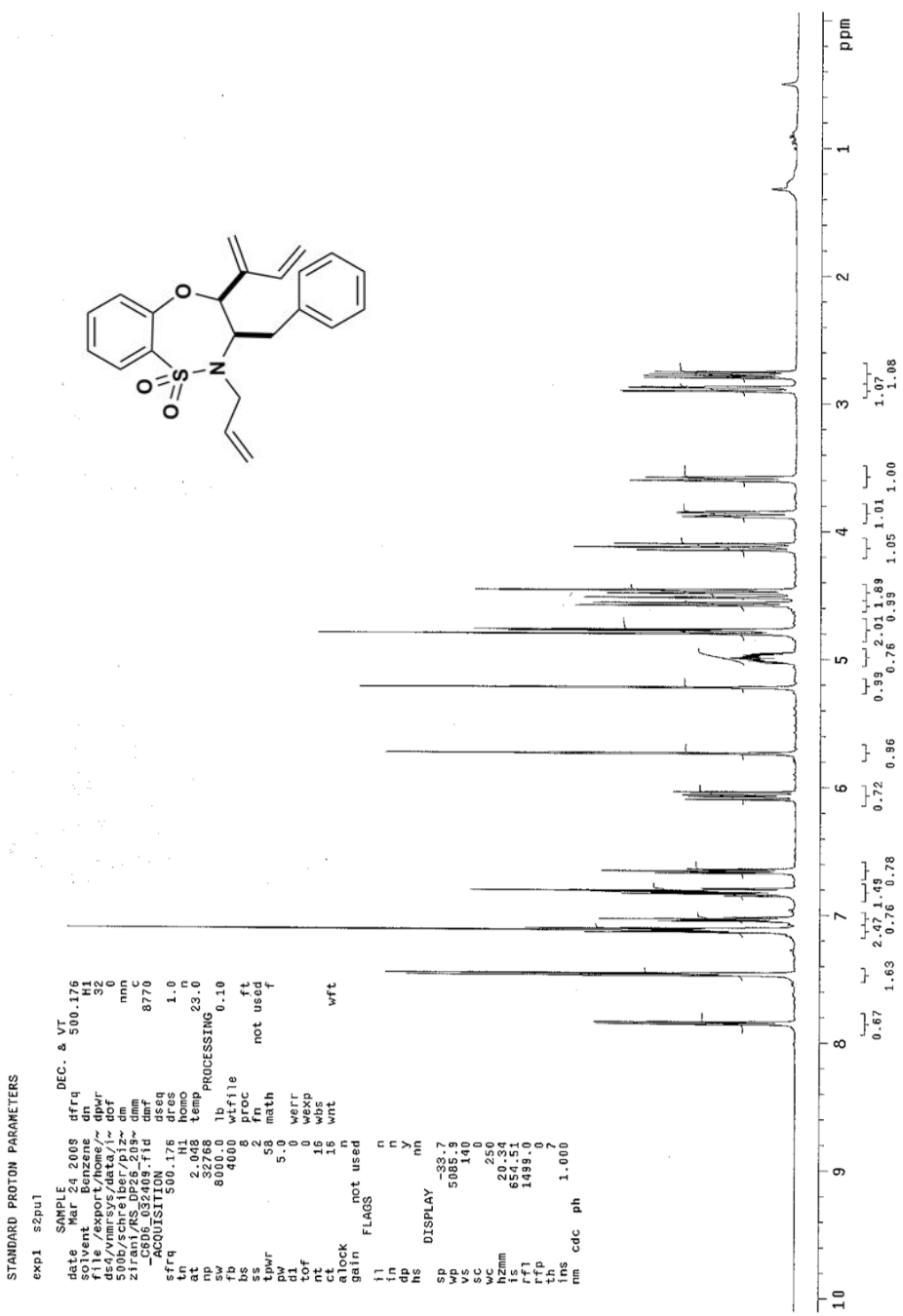


^{1}H NMR (500 MHz, CDCl3, T = 55 °C) of compound **11b**

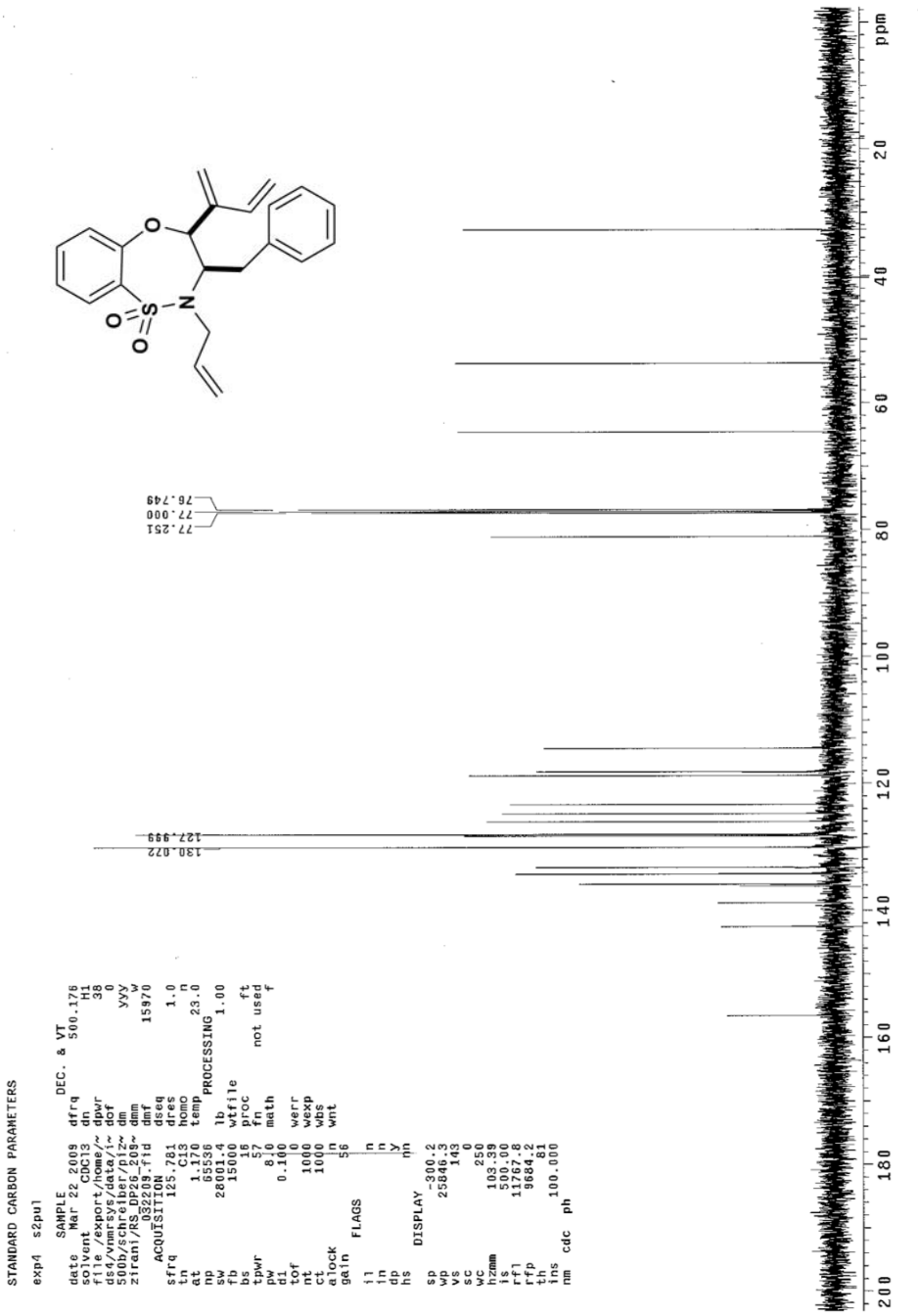


^{13}C NMR (126 MHz, $CDCl_3$, T = 55 °C) of compound **11b**

Spectral data for (3*R*,4*S*)-3-benzyl-4-(1-methylideneprop-2-en-1-yl)-2-prop-2-en-1-yl-3,4-dihydro-2*H*-5,1,2-benzoxathiazepine (12a)

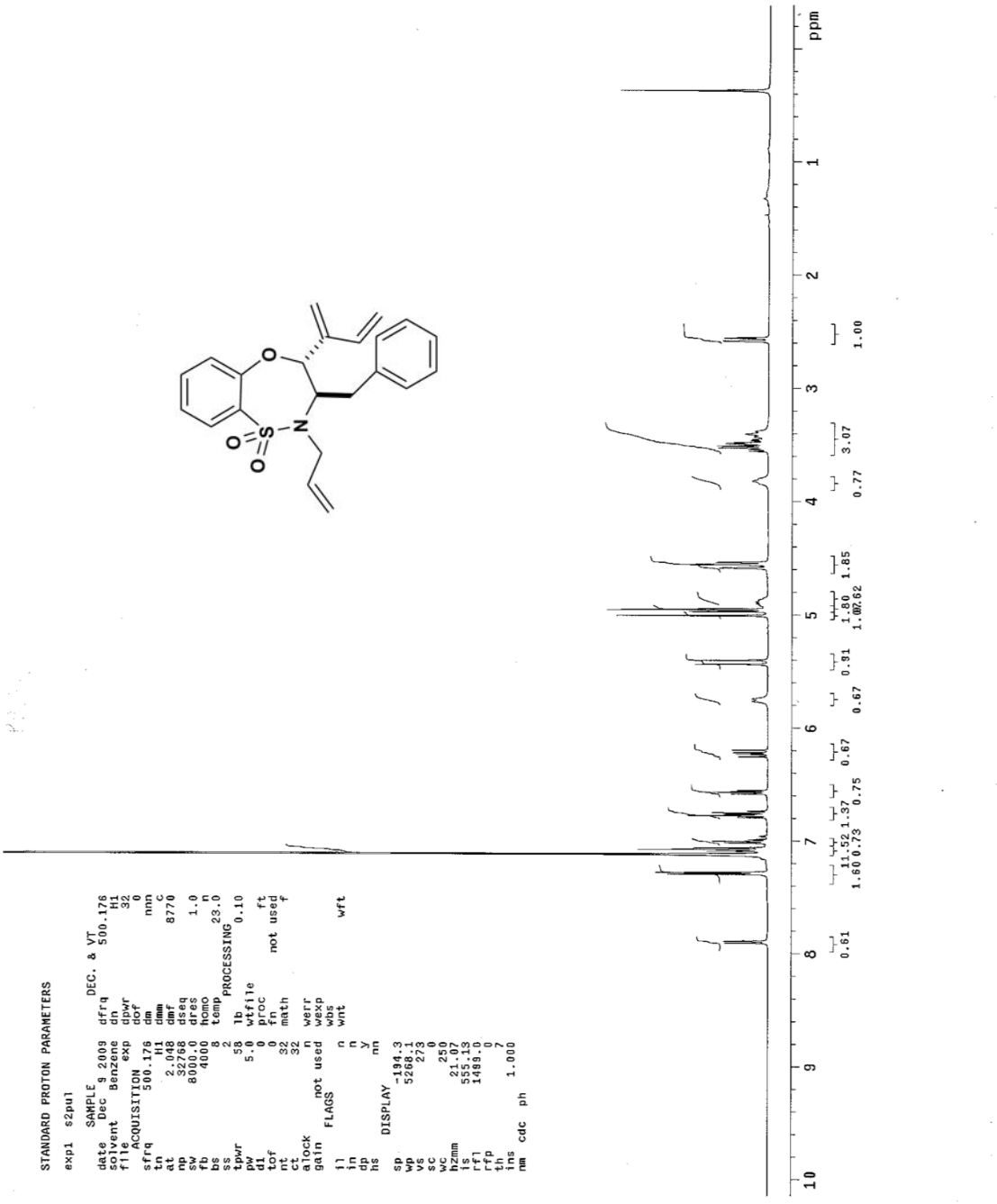


^{1}H NMR (500 MHz, Benzene) of compound **12a**

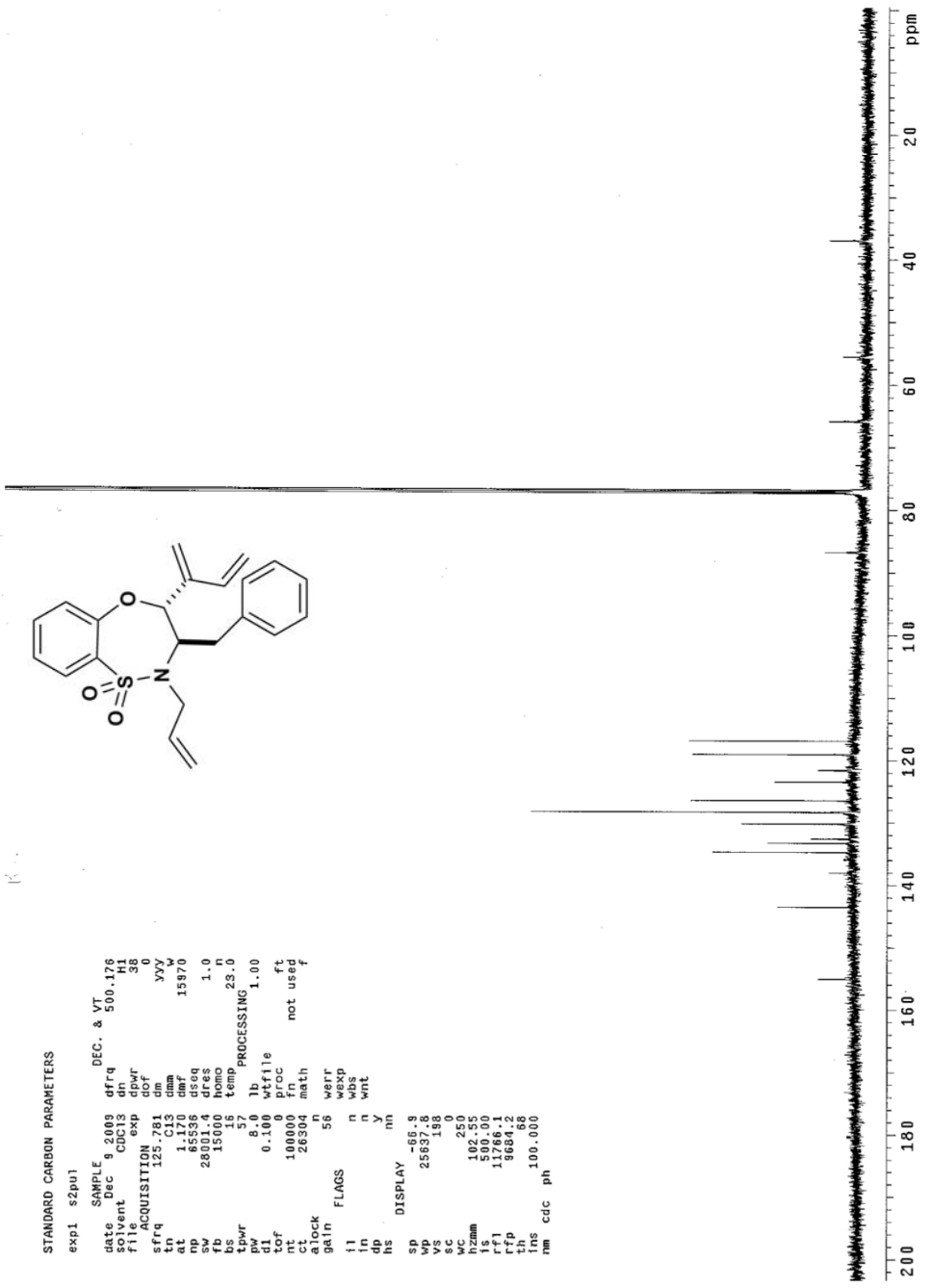


^{13}C NMR (126 MHz, $CDCl_3$) of compound **12a**

Spectral data for (3*R*,4*R*)-3-benzyl-4-(1-methylideneprop-2-en-1-yl)-2-prop-2-en-1-yl-3,4-dihydro-2*H*-5,1,2-benzoxathiazepine (12b)

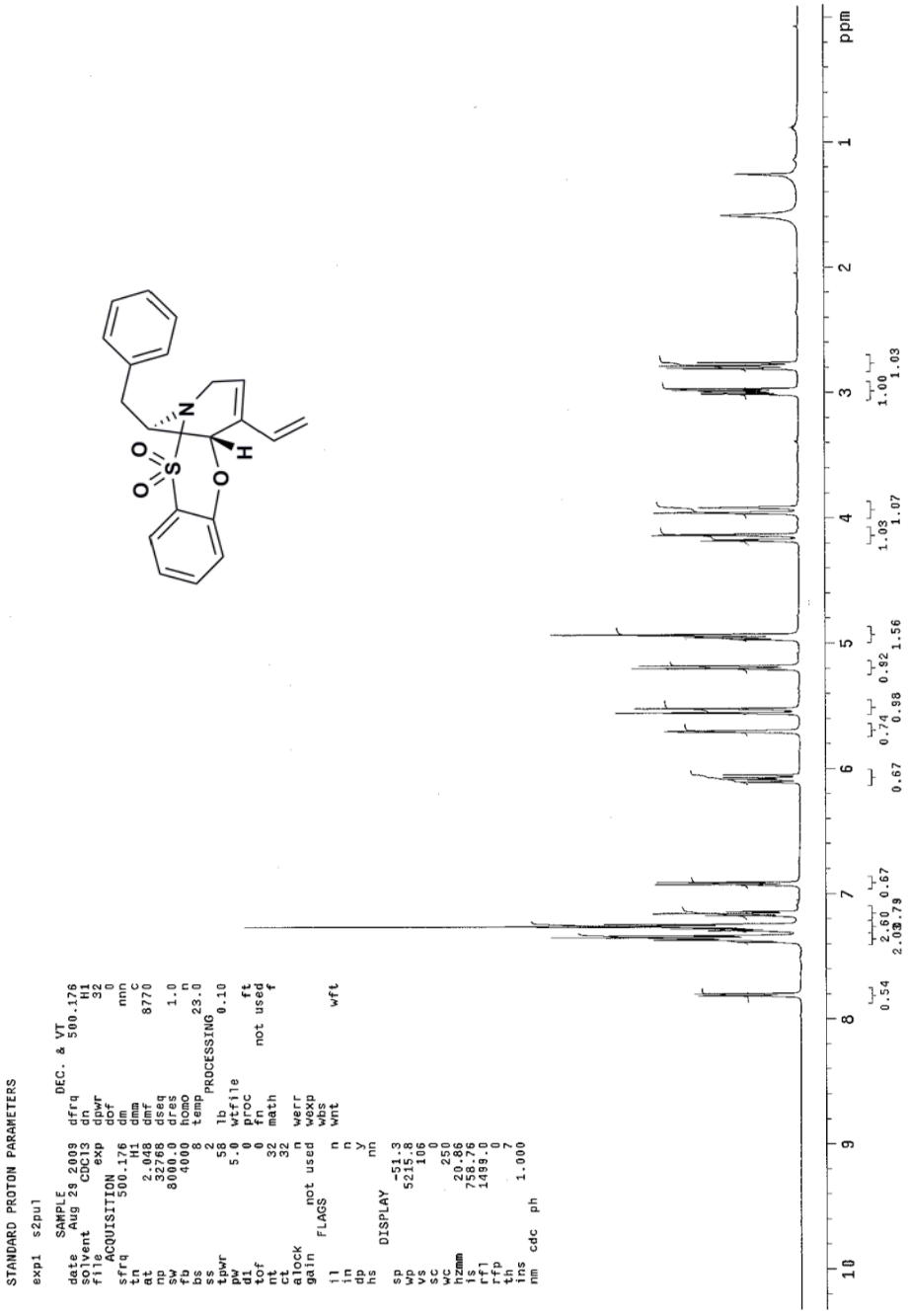


^{1}H NMR (500 MHz, Benzene) of compound **12b**

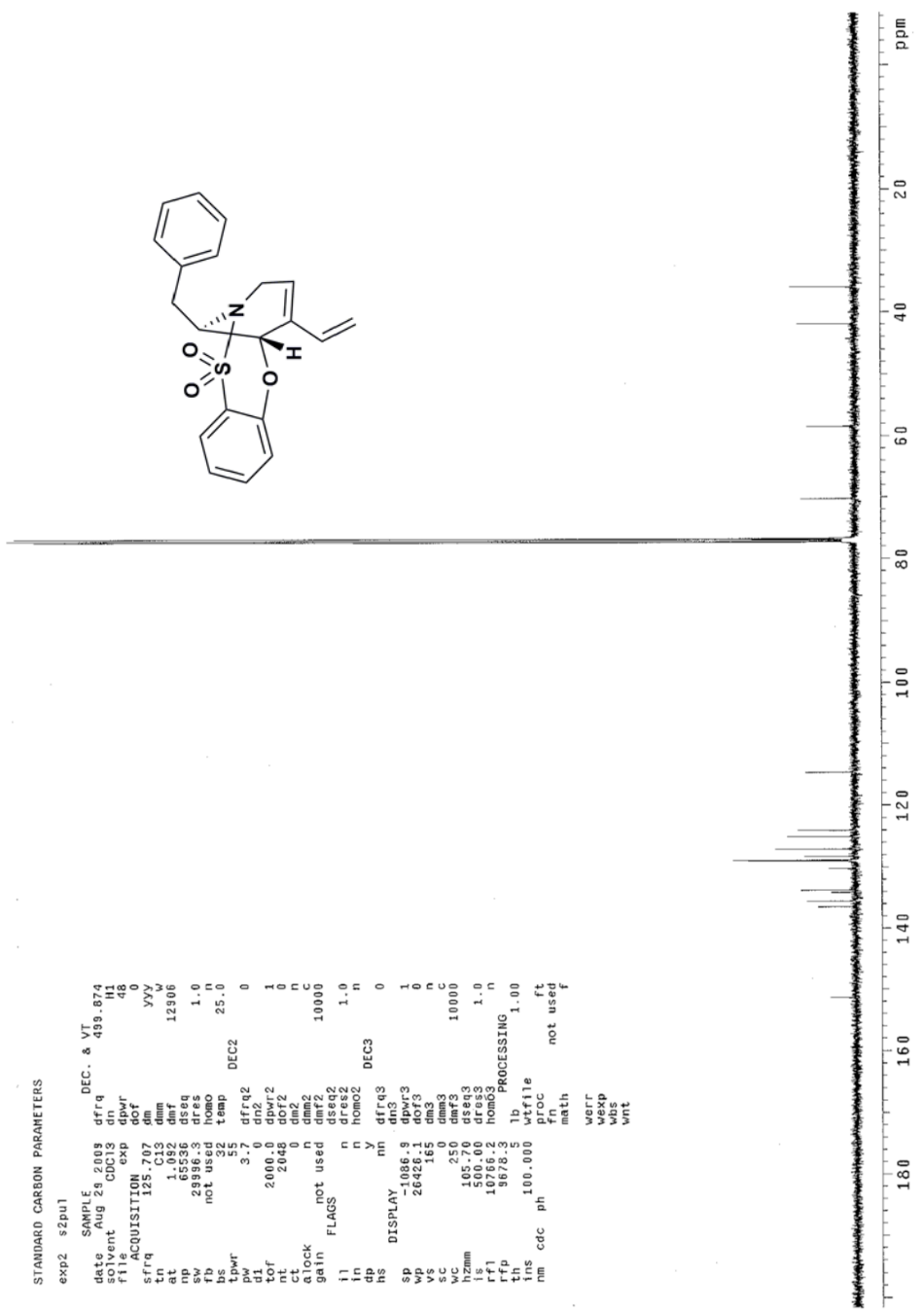


^{13}C NMR (126 MHz, $CDCl_3$) of compound **12b**

Spectral data for (10*R*,14*S*)-14-benzyl-11-ethenyl-9-oxa-2-thia-1-azatricyclo[8.3.1.0^{3,8}]tetradeca-3,5,7,11-tetraene 2,2-dioxide (13a)

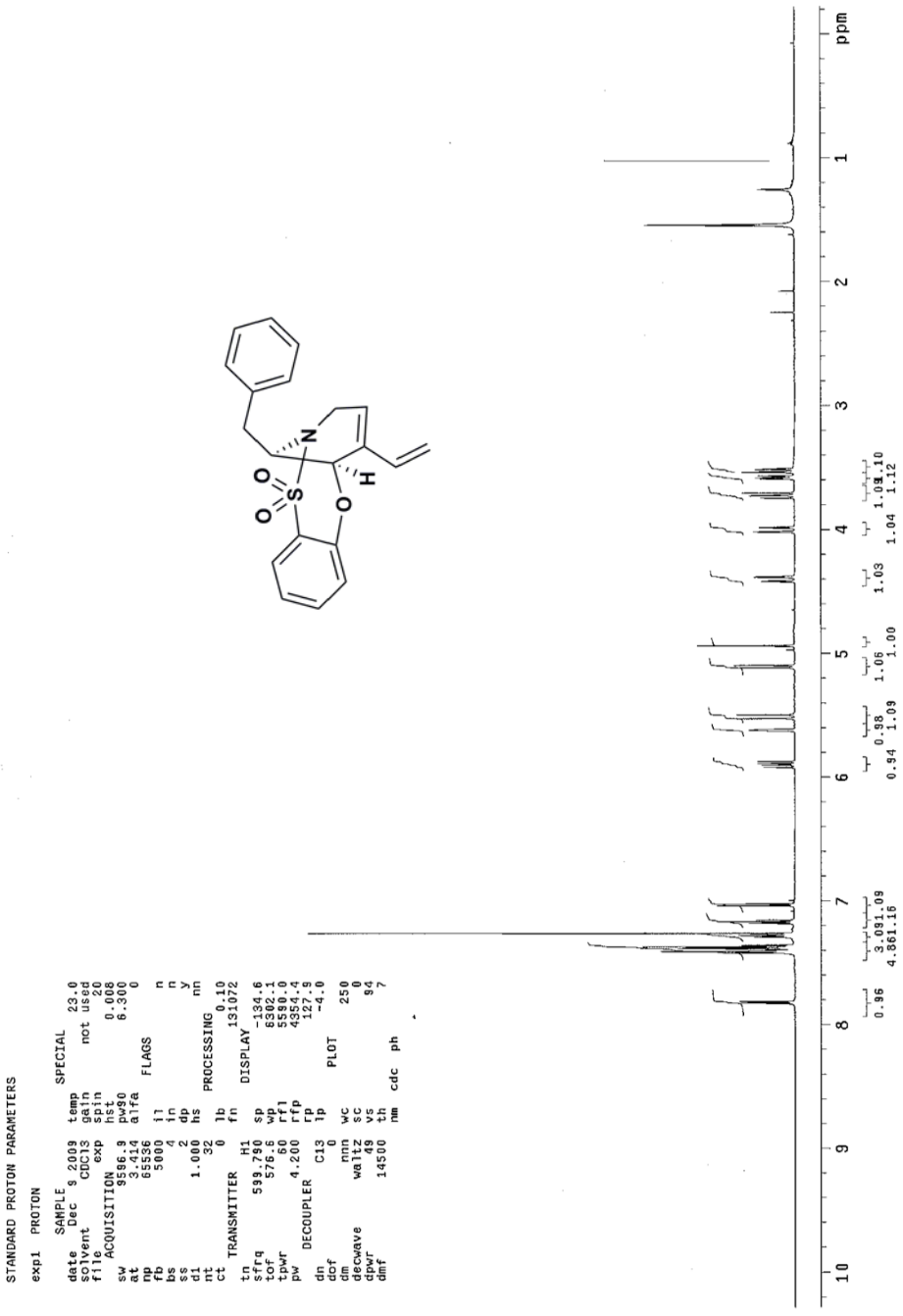


^{1}H NMR (500 MHz, CDCl3) of compound **13a**

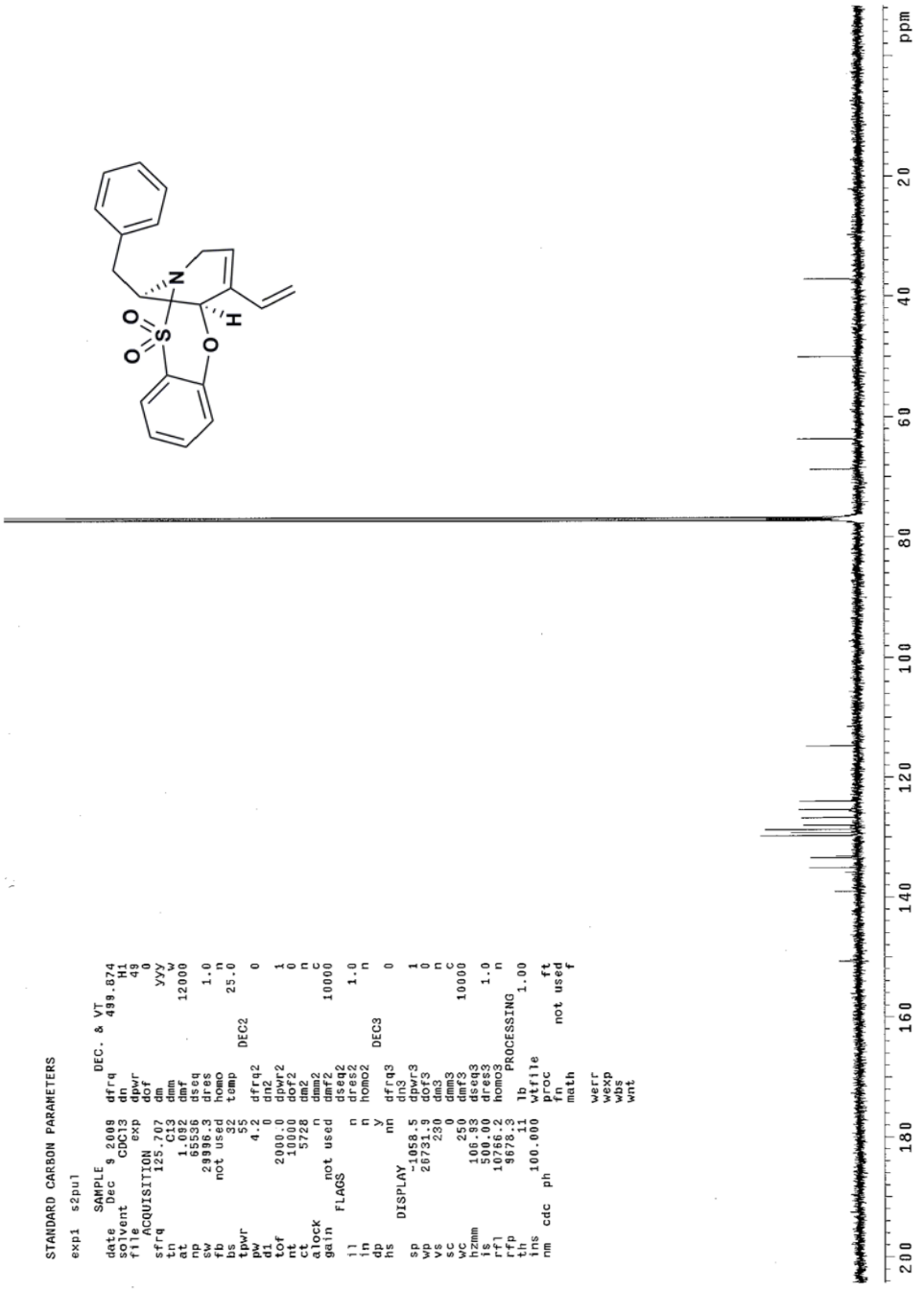


^{13}C NMR (126 MHz, $CDCl_3$) of compound **13a**

Spectral data for (10*R*,14*R*)-14-benzyl-11-ethenyl-9-oxa-2-thia-1-azatricyclo[8.3.1.0^{3,8}]tetradeca-3,5,7,11-tetraene 2,2-dioxide (13b)

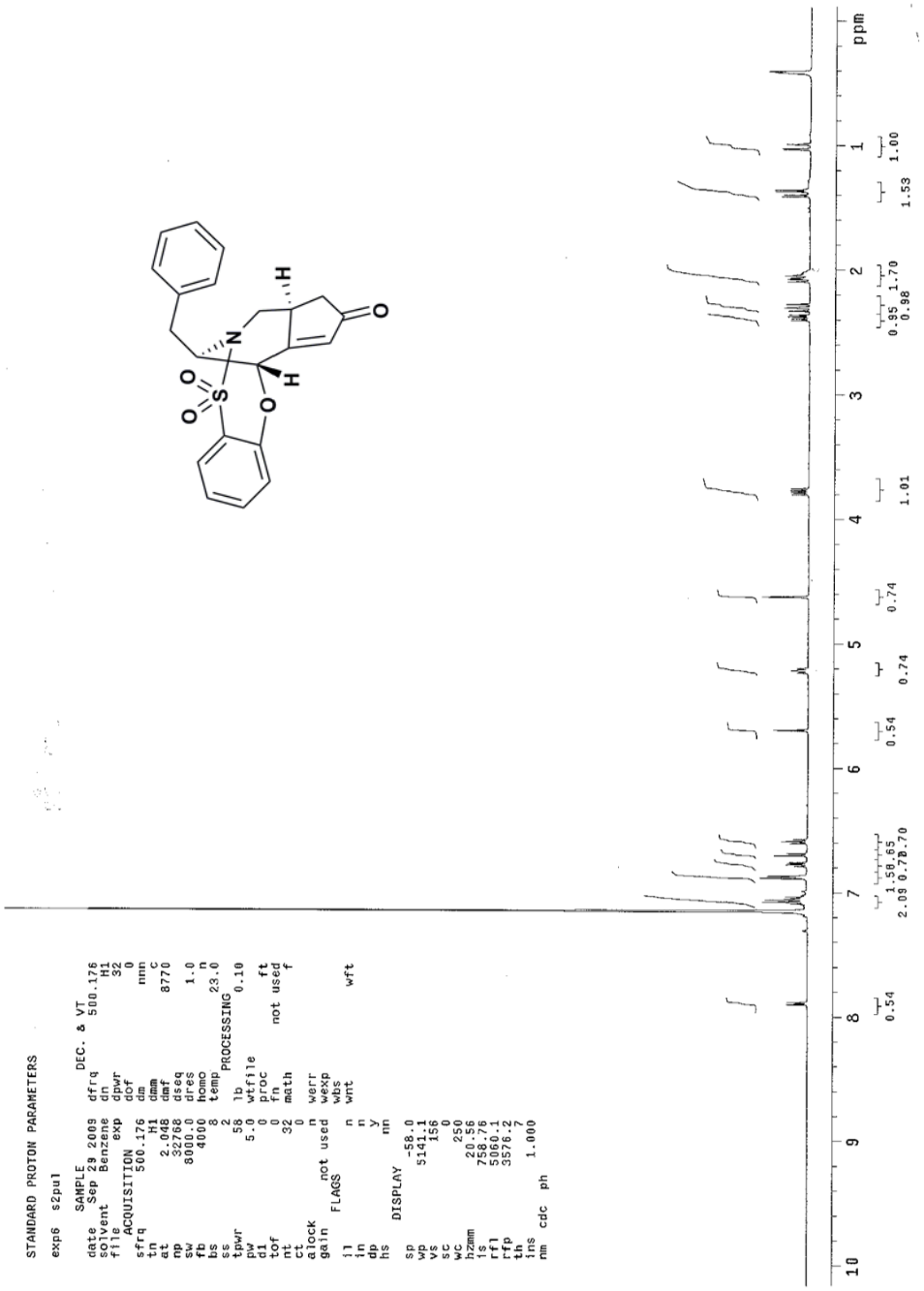


^{1}H NMR (600 MHz, CDCl3) of compound **13b**

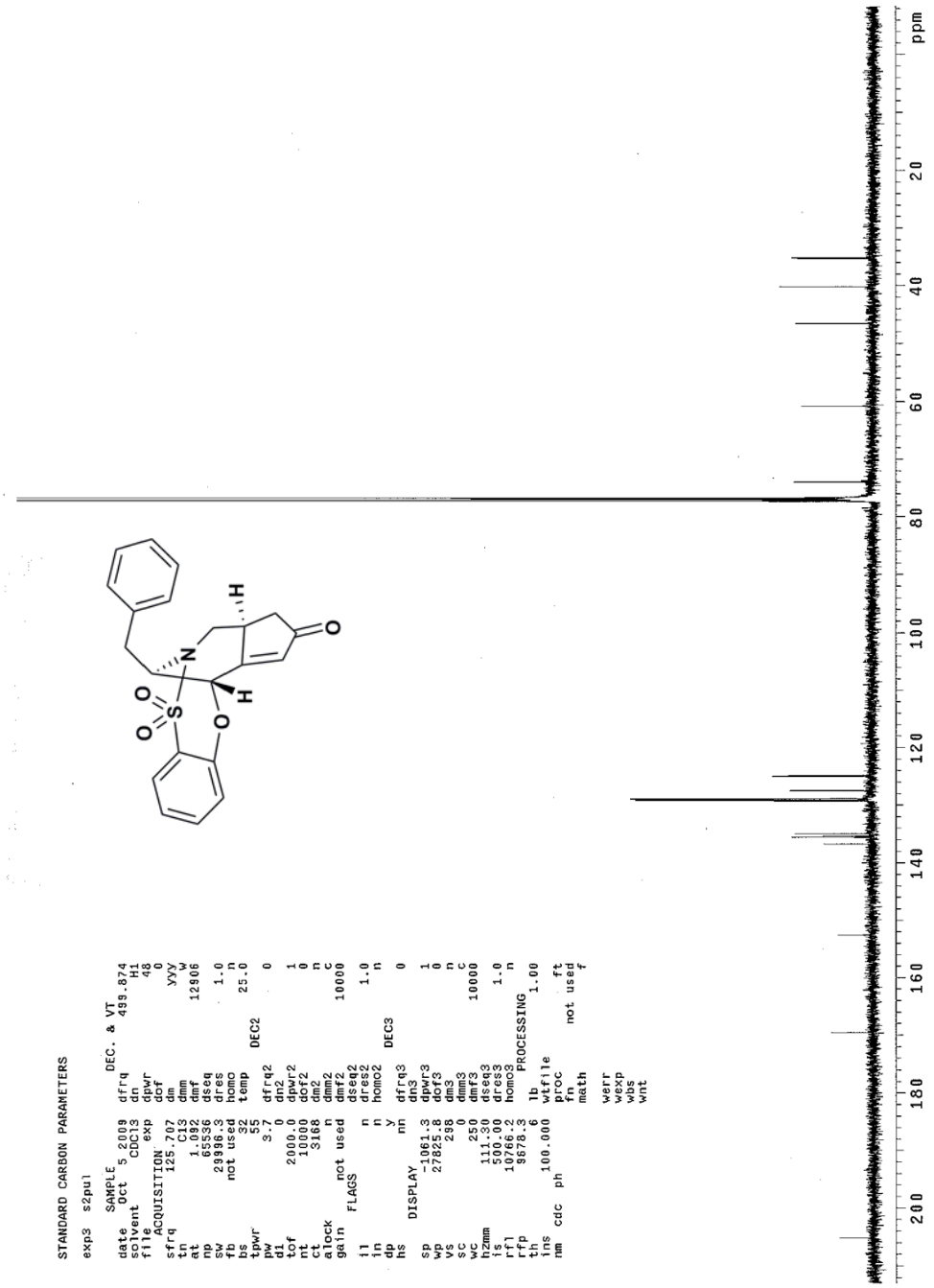


^{13}C NMR (126 MHz, $CDCl_3$) of compound **13b**

Spectral data for compound (14a)



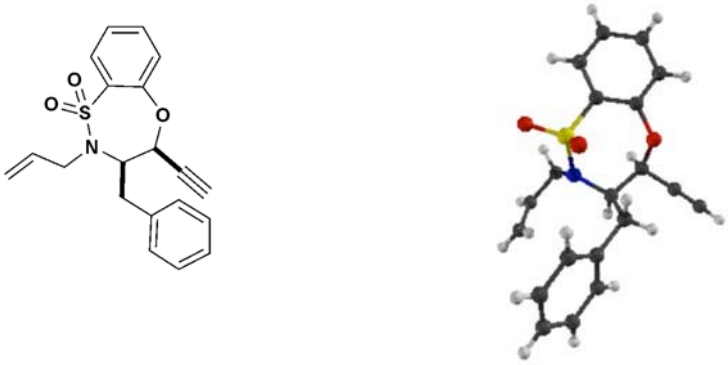
^{1}H NMR (500 MHz, Benzene) of compound **14a**



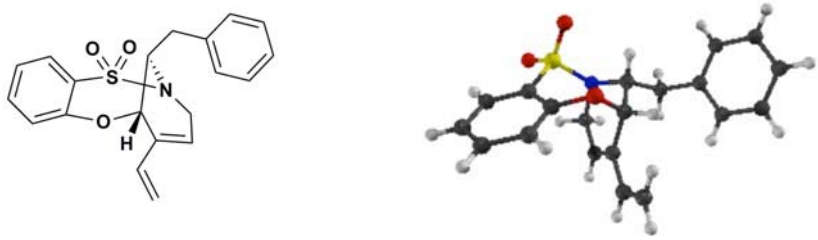
^{13}C NMR (126 MHz, $CDCl_3$) of compound **14a**

IV. X–Ray structures for compounds 11a, 13a and 14a

X–Ray structure of compound 11a (CCDC 768364)



X–Ray structure of compound 13a (CCDC 768365)



X–Ray structure of compound 14a (CCDC 768366)