Supporting Information

A fluorous-tagged 'safety catch' linker for the synthesis of heterocyclic small molecules

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General Experimental

All non-aqueous reactions were performed under an atmosphere of nitrogen. Water-sensitive reactions were performed in oven-dried glassware, cooled under nitrogen before use, or flame-dried, and cooled, under vacuum if stated. Solvents were removed under reduced pressure using either a Büchi rotary evaporator and a Vacuubrand PC2001 Vario diaphragm pump, or a Genevac HT-4 evaporation system. Solvents were distilled before use when necessary and possible according to scale. Tetrahydrofuran was freshly distilled from sodium, using benzophenone as a self-indicator. Dichloromethane was freshly distilled from calcium hydride. Triethylamine was purified by refluxing with potassium hydroxide and potassium carbonate, followed by distillation under nitrogen, and was stored over potassium hydroxide. Ether refers to diethyl ether and petrol refers to petroleum spirit (b.p. 40-60 °C). Commercially available starting materials were obtained from Sigma–Aldrich or Alfa Aesar.

Flash column chromatography was carried out using silica (35-70 μm particles), with crude reaction mixtures loaded in dichloromethane or the initial solvent system, or pre-absorbed. Flash column chromatography was carried out using either hand pumps or compressed air, by a variation of the procedure described by Still, Kahn and Mitra.[1] Thin layer chromatography was carried out on commercially available pre-coated glass or aluminium plates (Merck silica 2 8 8 0 Kieselgel 60F254). Analytical HPLC was performed using either a Thermo Hypersil–Keystone achiral column (250 × 4.6 mm 8 l Hyperprep HSC18), an XTerra® analytical HPLC column, a Jupiter® analytical coloumn or an Ultron chiral column (150 × 4.6 mm ES-OVM) with a Dionex P580 pump and a PDA-100 UV detector at wavelengths between 200 and 250 nm. The purity of fluorous-tagged products which were purified by Fluorous-Solid Phase Extraction (F-SPE) alone was determined using the Jupiter® column eluting with either 75→95% MeCN–water. Fluorous-Solid Phase Extraction (F-SPE) was carried out using pre-packed Fluoro*Flash*® cartridges purchased from Fluorous Technologies Inc. Cartridges were washed extensively with *N*,*N*-dimethylformamide, and were pre-conditioned with 8:2 methanol–water. Crude reaction mixtures were loaded onto cartridges using either *N*,*N*,-dimethylformamide or dichloromethane and eluted using 8:2 methanol–

water (a fluorophobic eluent) followed by methanol (a fluorophilic solvent) using compressed air in a manner similar to that described by Curran.[2,3]

Proton and carbon NMR spectra were recorded on a Bruker Avance 500, Avance DPX300 or DRX500 spectrophotometer with an internal deuterium lock. Carbon NMR spectra were recorded with composite pulse decoupling using the waltz 16 pulse sequence. DEPT, COSY, HMQC, HMBC, TOCSY or NOESY pulse sequences were used to aid the assignment of spectra. Chemical shifts are quoted in parts per million downfield of tetramethylsilane, and coupling constants (*J*) are given in Hz. NMR spectra were recorded at 300 K unless otherwise stated.

Infra-red spectra were recorded using a Perkin–Elmer Spectrum One FT-IR spectrophotometer. Spectra of solids and foams were recorded using solid state golden gate probes whilst spectra of oils were performed neat on sodium chloride discs. Melting points were recorded on a Reichert hot stage microscope and are uncorrected. Nominal mass spectrometry was routinely performed on a Waters-Micromass ZMD spectrometer using electrospray (+) ionization. Nominal and accurate mass spectrometry using electrospray ionisation was carried out by staff in the School of Chemistry using either a Micromass LCT-KA111 or Bruker MicroTOF mass spectrometer. Field Desorption ionisation mass spectra were acquired on a Waters-Micromass GCT premier spectrometer equipped with a Linden LIFDI probe. Optical activity measurements were recorded at room temperature unless otherwise stated; units for $[\alpha]_D$ are 10^{-1} deg cm^2 g^{-1} and are omitted.

General Procedures

A. Silaketal formation using di*iso*propylsilyl ethers

N-Bromosuccinimide (3 eq.) was added to a stirred solution of the silyl ether (3.5 eq.) in dichloromethane (0.2 M) at 0 °C. The reaction mixture was allowed to warm to room temperature, stirred for 15 mins and cooled to 0 °C. The alcohol (1 eq.) and the *N*,*N*-dimethylaminopyridine (0.5 eq.) were added as a solution in triethylamine (15 eq.), rinsing the vessel containing the alcohol with dichloromethane (reaction volume) and adding this wash to the reaction mixture. The suspension was allowed to warm to room temperature and was stirred until completion was indicated by TLC.

B. Fukuyama–Mitsunobu

Diethyl azodicarboxylate or di-*tert*butyl azodicarboxylate (4 eq.) was added dropwise/portionwise to a stirred solution of the alcohol (1 eq.), the amine (4 eq) and triphenylphosphine (4 eq.) in tetrahydrofuran (0.05 M-0.2 M) at 0 °C. The solution was allowed to warm to room temperature and stirred until completion was indicated by TLC. The reaction mixture was then concentrated under reduced pressure to give the crude product.

C. Olefin metathesis using Grubbs' catalysts

The olefin metathesis catalyst **G I or HG II** (5 mol%) was added portionwise to a stirred solution of the substrate (1 eq.) in refluxing dichloromethane (1-4 mM) and the reaction mixture was stirred at reflux until completion was indicated by TLC with additional catalyst added, if necessary, periodically. The reaction mixture was then cooled to room temperature and tris(hydroxymethyl)phosphine (86 eq. relative to the catalyst) and triethylamine (*ca.* 10 eq.) added, stirred for a minimum of 1 hour, and silica (5 × amount of phosphine) added and the reaction mixture stirred for a minimum of 1 hour. The reaction mixture was filtered through a pad of Celite, washing with ethyl acetate, and the solvent removed under reduced pressure to give the crude product.

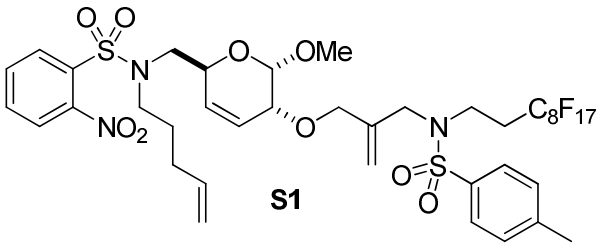
D. Cleavage from the fluorous-tagged linker

Trifluoroacetic acid was added to a solution of the substrate in dichloromethane (0.2-0.4 mM in 3% TFA/DCM) and the reaction mixture was stirred at room temperature for 16 hours. The solution was concentrated under reduced pressure to give the crude product.

Unsuccessful metathesis substrates

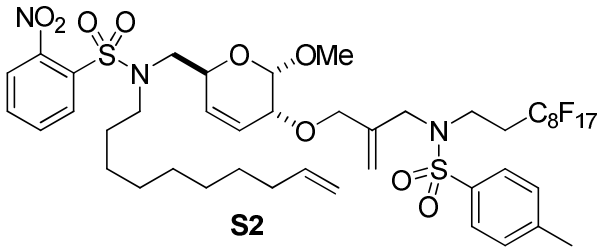
The following metathesis substrates were prepared as part of the investigation. However, metathesis did not lead to clean release of products from the fluorous-tagged linker.

***N*-{[(2*S*,5*R*,6*S*)-5-{2-[(*N*-{3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptafluorodecyl}-4-methylsulfonamido)methyl]allyloxy}-6-methoxy-5,6-dihydro-2*H*-pyran-2-yl]methyl}-2-nitro-*N*-(pent-4'-enyl)benzenesulfonamide S1**



Following general procedure **B**, diethyl azodicarboxylate (88 μL, 0.48 mmol), sulfonamide **20** (117 mg, 0.48 mmol) and alcohol **1** (100 mg, 0.12 mmol) gave a crude product after 3 hours. Purification by Fluorous Solid Phase Extraction; 5 g cartridge, loading with <1 mL DMF, eluting with 80:20 MeOH–H_2O followed by MeOH gave the fluorous fraction, *sulfonamide* **S1** (125 mg, 96%, 80% purity by HPLC) as a colourless oil, R_f 0.35 (60:40 petrol–EtOAc); δ_H (500 MHz, $CDCl_3$) 8.05 (1H, dd, *J* 7.4 and 1.7, nosyl 3-H), 7.72-7.62 (5H, m, Ar), 7.34 (2H, d, *J* 8.1, tosyl 3-H and 5-H), 5.81-5.67 (3H, m, 3-H, 4-H and 4'-H), 5.30 (1H, br. s, $NCH_2C{=}CH_A$), 5.14 (1H, br. s, $NCH_2C{=}CH_B$), 4.98 (1H, dd, *J* 17.1 and 1.5, 5'-H_A), 4.95 (1H, dd, *J* 10.3 and 1.5, 5'-H_B), 4.80 (1H, d, *J* 3.9, 6-H), 4.32-4.27 (1H, m, 2-H), 4.04-4.00 (3H, m, 5-H and 5-$COCH_2$), 3.83-3.75 (2H, m, NCH_2CCH_2), 3.56 (1H, dd, *J* 15.0 and 3.2, 2-CCH_A), 3.50 (1H, dd, *J* 15.0 and 3.6, 2-CCH_B), 3.43-3.32 (7H, m, OMe, $CF_2CH_2CH_2$ and 1'-H), 2.44 (3H, s, tosyl Me), 2.43-2.31 (2H, m, CF_2CH_2), 2.04-1.99 (2H, m, 3'-H) and 1.68 (2H, quint. *J* 7.5, 2'-H); δ_C (75 MHz, $CDCl_3$) 148.4 (nosyl 2-C), 144.4 (tosyl 4-C), 140.9 (NCH_2CCH_2), 136.1 (tosyl 1-C), 134.3 (3'-C), 134.2 (nosyl 4-C), 133.9 (nosyl 1-C), 132.0, 131.5 (nosyl 3-C and 6-C), 130.3 (tosyl 3-C and 5-C), 127.64, 127.61 (4-C and tosyl 2-C and 6-C), 125.9 (3-C), 124.5 (nosyl 5-C), 117.5 ($NCH_2C{=}CH_2$), 115.7 (5'-C), 97.1 (6-C), 72.1, (5-C), 69.7 (5-$COCH_2$), 68.2 (2-C), 56.2 (OMe), 52.1 (NCH_2CCH_2), 50.7 (1'-C), 48.6 (2-CCH_2), 40.8 ($CF_2CH_2CH_2$), 31.0 (t, $^2J_{C-F}$ 21.8, CF_2CH_2), 28.5 (3′-C), 27.2 (2′-C) and 21.9 (tosyl Me); ν_{max}/cm^{-1} (film) 2917, 2849, 1736, 1577, 1542 and 1464; *m/z* (ESI^+) 1104.2 ($[M+Na]^+$ 100%); found MNa^+ 1104.1839, $C_{39}H_{40}F_{17}N_3O_9S_2$ requires *MNa* 1104.1832.

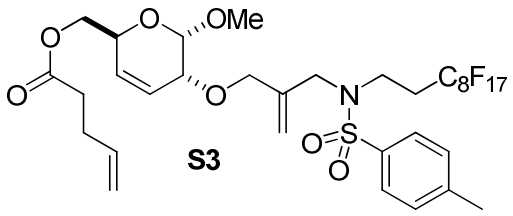
***N*-(Dec-9-enyl)-*N*-[{(2'*S*,5'*R*,6'*S*)-5'-[2-{[*N*-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)-4-methylphenylsulfonamido]methyl}allyloxy]-6'-methoxy-5',6'-dihydro-2*H*-pyran-2'-yl}methyl]-2-nitrobenzenesulfonamide S2**



S2

Following general procedure **B**, diethyl azodicarboxylate (72 μL, 0.39 mmol), sulfonamide **18** (100 mg, 0.10 mmol) and dec-9-en-1ol (73 μL, 0.39 mmol) gave the crude product after 3 hours. Purification by Fluorous Solid Phase Extraction; 2 g cartridge, loading with <200 μL dichloromethane, eluting with 80:20 MeOH–H_2O followed by MeOH gave the fluorous fraction, the *sulfonamide* **S2** (113 mg, 99%, 83% purity by HPLC) as a colourless foam, R_f 0.90 (50:50 petrol–EtOAc); δ_H (500 MHz, $CDCl_3$) 8.07-8.03 (1H, m, nosyl 3-H), 7.72-7.61 (5H, m, Ar), 7.34 (2H, ddt, *J* 8.0, tosyl 3-H and 5-H), 5.80 (1H, ddt, *J* 17.0, 10.2 and 6.9, 9-H), 5.76-5.71 (2H, m, 3'-H and 4'-H), 5.30 (1H, br. s, 5'-$COCH_2$=CH_A), 5.14 (1H, br. s, 5'-$COCH_2$=CH_B), 4.98 (1H, app. dq, *J* 17.0 and 1.4, 10-H_A), 4.92 (1H, app. dq, *J* 10.2 and 1.4, 10-H_B), 4.79 (1H, br. d, *J* 3.6, 6'-H), 4.32-4.27 (1H, m, 2'-H), 4.04-4.00 (3H, m, 5'-H and 5'-$COCH_2$), 3.81 (1H, d, *J* 15.0, NC$H_A$$CCH_2$), 3.78 (1H, d, *J* 15.0, NC$H_B$$CCH_2$), 3.55 (1H, dd, *J* 15.3 and 3.1, 2'-CCH_A), 3.51-3.44 (2H, m, 1-H), 3.43-3.35 (5H, m, $CF_2CH_2CH_2$ and OMe), 3.34 (1H, dd, *J* 15.3 and 7.5, 2'-CCH_B), 2.44 (3H, s, tosyl Me), 2.43-2.30 (2H, m, CF_2CH_2), 2.02 (2H, app. q, *J* 6.9, 8-H), 1.58-1.51 (2H, m, 2-H), 1.38-1.30 (2H, m, 7-H), 1.30-1.16 (8H, m, 3-H, 4-H, 5-H and 6-H); δ_C (75 MHz, $CDCl_3$) 148.4 (nosyl 2-C), 144.4 (tosyl 4-C), 140.9 (5'-$COCH_2C$), 139.5 (9-C), 136.1 (tosyl 1-C), 134.4 (nosyl 1-C), 133.8 (nosyl 6-C), 131.9 (nosyl 3-C), 131.4 (nosyl 4-C), 130.4 (tosyl 3-C and 5-C), 127.62 (3'-C), 127.57 (tosyl 2-C and 6-C), 125.8 (4'-C), 124.5 (nosyl 5-C), 117.5 (5'-$COCH_2C$=CH_2), 114.5 (10-C), 97.1 (6'-C), 72.1 (5'-C), 69.7 (5'-$COCH_2$), 68.1 (2'-C), 56.2 (OMe), 52.1 (NCH_2CCH_2), 50.5 (2'-CCH_2), 48.9 (1-C), 40.8 ($CF_2CH_2CH_2$), 34.1 (8-C), 31.0 (CF_2CH_2), 29.7, 29.5, 29.3, 29.2, 28.0 and 26.9 (2-C, 3-C, 4-C, 5-C, 6-C and 7-C) and 21.8 (tosyl Me); ν_{max}/cm^{-1} (film) 3077, 2929, 2857, 2254, 1732, 1597, 1545, 1455 and 1440; *m/z* (ESI^+) 1169.3 ($[M + NH_4]^+$ 100%), 1174.3 ($[M + Na]^+$ 95%); found MNa^+ 1174.2564, $C_{44}H_{50}F_{17}N_3O_9S_2$ requires *MNa* 1174.2609.

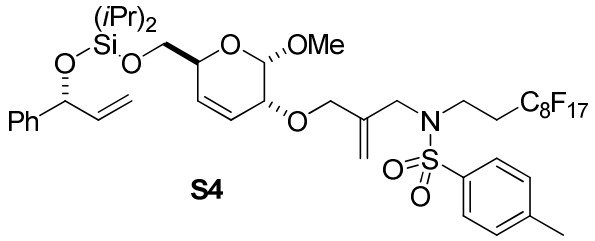
[(2*S*,5*R*,6*S*)-5-{2-[{*N*-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)-4-methylphenylsulfonamido}methyl]allyloxy}-6-methoxy-5,6-dihydro-2*H*-pyran-2-yl]methyl pent-4'-enoate S3



S3

Alcohol **1** (100 mg, 0.12 mmol) was added to a stirred solution of pent-4-enoic acid (24 mg, 0.24 mmol), ethyl-3-(3-dimethylaminopropyl)-carbodiimide (46 mg, 0.24 mmol) and 4-dimethylaminopyridine (2 mg, 0.012 mmol) in dichloromethane (1 mL). The reaction mixture was stirred for 18 hours and subsequently concentrated *in vacuo*, to give a crude product that was purified by Fluorous Solid Phase Extraction; 2 g cartridge loading with <400 μL DMF, eluting with 80:20 MeOH–H_2O followed by MeOH to give the fluorous fraction, *sulfonamide* **S3** (98 mg, 89%, >95% purity by 500 MHz ^{1}H NMR) as a colourless oil, R_f 0.24 (10:4 petrol–EtOAc); δ_H (500 MHz, $CDCl_3$) 7.70 (2H, d, *J* 8.1, tosyl 2-H and 6-H), 7.33 (2H, d, *J* 8.1, tosyl 3-H and 5-H), 5.84 (1H, ddt, 4'-H), 5.85-5.79 (1H, m, 3-H), 5.73 (1H, dt, *J* 10.7 and 1.7, 4-H), 5.31 (1H, br. s, $NCH_2C{=}CH_A$), 5.14 (br. s, $NCH_2C{=}CH_B$), 5.07 (1H, app. dq, *J* 17.1 and 1.7, 5'-H_A), 5.01 (1H, app. dq, *J* 10.3 and 1.7, 5'-H_B), 5.00-4.98 (1H, m, 6-H), 4.38-4.31 (1H, m, 2-H), 4.18 (2H, dd, *J* 5.6 and 4.7, 2-CCH_2), 4.10-4.07 (1H, m, 5-H), 4.05 (2H, s, 5-$COCH_2$), 3.84 (1H, d, *J* 15.0, NCH_ACCH_2), 3.77 (1H, d, *J* 15.0, NCH_BCCH_2), 3.51 (3H, s, OMe), 3.40-3.36 (2H, m, $CF_2CH_2CH_2$), 2.48-2.44 (2H, m, 2'-H), 2.44 (3H, s, 4'''-CCH_3), 2.43-2.36 (4H, m, CF_2CH_2 and 3'-H); δ_C (75 MHz, $CDCl_3$) 173.3 (1'-C), 144.4 (tosyl 4-C), 140.9 (NCH_2CCH_2), 136.9 (4'-C), 136.1 (tosyl 1-C), 130.3 (tosyl 3-C and 5-C), 127.6 (tosyl 2-C and 6-C), 126.8 (4-C), 126.2 (3-C), 117.5 ($NCH_2C{=}CH_2$), 116.0 (5''''-C), 97.2 (6-C), 72.1 (5-C), 69.7 (5-$COCH_2$), 67.5 (2-C), 65.8 (2-CCH_2), 56.3 (OMe), 52.0 (NCH_2CCH_2), 40.8 ($CF_2CH_2CH_2$), 33.8 (2'-C), 31.0 (t, $^2J_{C-F}$ 21.8, CF_2CH_2), 29.2 (3'-C), 21.9 (tosyl Me); ν_{max}/cm^{-1} (film); 3081, 2925, 2859, 1739, 1642, 598 and 1452; *m/z* (ESI$^+$) 929.2 ([M + NH_4]$^+$ 100%); found MNa^+ 934.1686, $C_{33}H_{34}F_{17}N_3O_7S$ requires *MNa* 934.1677.

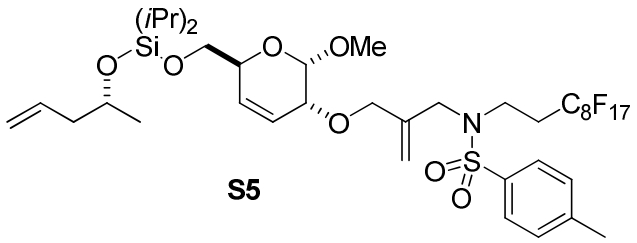
***N*-(2-{[(2*S*,3*R*,6*S*)-6-[(diisopropyl((*R*)-1'phenylallyloxy)silyloxy)methyl]-2-methoxy-3,6-dihydro-2*H*-pyran-3-yloxy]methyl}allyl)-*N*-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)-4-methylbenzenesulfonamide S4**



S4

Following general procedure **A**, (*R*)-diisopropyl(1-phenylallyloxy)silane (105 mg, 0.42 mmol) and alcohol **1** (100 mg, 0.12 mol) were stirred for 16 hours after which time methanol (2 mL) was added and the solution was concentrated under reduced pressure. The residue was then suspended in pentane (5 mL), filtered and concentrated under reduced pressure to give a crude product which was purified by Fluorous Solid Phase Extraction; 2 g cartridge, loading with <400 μL DMF, eluting with 80:20 MeOH–H_2O followed by MeOH to give the fluorous fraction, *silaketal* **S4** (102 mg, 79%, >95% purity by ^{1}H NMR spectroscopy) as a colourless oil, R_f 0.63 (80:20 petrol–EtOAc); δ_H (500 MHz, $CDCl_3$) 7.70 (2H, d, *J* 8.1, tosyl 2-H and 6-H), 7.37-7.30 (6H, m, tosyl 3-H and 5-H and phenyl 2-H, 3-H, 5-H and 6-H), 7.23 (1H, app tt, *J* 7.3 and 1.5, phenyl 4-H), 5.96 (1H, ddd, *J* 17.1, 10.3 and 5.6, 2'-H), 5.73 (1H, app d, *J* 10.7, 4-H), 5.69 (1H, app d, *J* 10.7, 5-H), 5.36 (1H, d, *J* 5.6, 1'-H), 5.31 (1H, br s, $NCH_2C=CH_A$), 5.30 (1H, app dt, *J* 17.1 and 1.3, 3'-H_A), 5.13 (1H, br s, $NCH_2C=CH_B$), 5.06 (1H, app dt, *J* 10.3 and 1.3, 3'-H_B), 4.93-4.91 (1H, m, 2-H), 4.10-4.04 (1H, m, 6-H), 4.02 (2H, s, 3-$COCH_2$), 3.82 (1H, d, *J* 15.0, NCH_ACCH_2), 3.78 (1H, d, *J* 15.0, NCH_BCCH_2), 3.72 (1H, dd, *J* 10.3 and 6.0, 6-CCH_A), 3.54 (1H, dd, *J* 10.3 and 6.0, 6-CCH_B), 3.50-3.48 (1H, m, 3-H), 3.48 (3H, s, OMe), 3.40-4.35 (2H, m, $CF_2CH_2CH_2$), 2.44 (3H, s, tosyl Me), 2.42-2.33 (2H, m, CF_2CH_2) and 1.09-0.96 (14H, m, *i*Pr); δ_C (75 MHz, $CDCl_3$) 144.2 (tosyl 4-C), 141.7 (phenyl 2-C and 6-C), 140.8 (NCH_2CCH_2), 136.0 (tosyl 1-C), 130.2 (tosyl 3-C and 5-C), 128.5, 128.4 (4-C and Ph), 127.51, 127.49 (tosyl 2-C and 6-C and 2'-C), 126.3 (5-C), 124.4 (Ph), 117.1 ($NCH_2C=CH_2$), 113.5 (3'-C), 96.9 (2-C), 75.7 (1'-C), 72.2 (6-C), 69.7 (3-C), 69.5 (3-$COCH_2$), 65.4 (6-CCH_2), 55.9 (OMe), 51.9 (NCH_2CCH_2), 40.7 ($CF_2CH_2CH_2$), 30.9 (t, $^2J_{C–F}$ 21.2, CF_2CH_2), 21.8 (tosyl Me), 17.5 (iPr CMe_2) and 12.6 (*i*Pr CMe_2); ν_{max}/cm^{-1} (film); 2958, 2869, 1599, 1494, 1463 and 1455; *m/z* (ESI$^+$) 1098.3 ([M + Na]$^+$ 100%); found MNa^+ 1098.2728, $C_{43}H_{50}F_{17}NO_7SSi$ requires *MNa* 1098.2698.

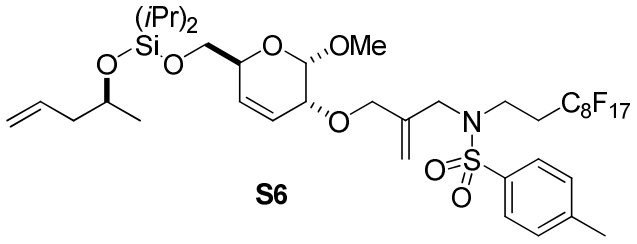
_N_-(2-{[(2_S_,3_R_,6_S_)-6-[(diisopropyl((_S_)-pent-4'-en-2'-yloxy)silyloxy)methyl]-2-methoxy-3,6-dihydro-2_H_-pyran-3-yloxy]methyl}allyl)-_N_-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)-4-methylbenzenesulfonamide S5



S5

Following general procedure **A**, (*R*)-diisopropyl(pent-4-en-2-yloxy)silane (84 mg, 0.42 mmol) and alcohol **1** (100 mg, 0.12 mol) were stirred for 16 hours after which time methanol (2 mL) was then added and the solution was concentrated under reduced pressure. The residue was then suspended in pentane (5 mL), filtered and concentrated *in vacuo*, to give a crude product which was purified by Fluorous Solid Phase Extraction; 2 g cartridge, loading with <400 μL DMF, eluting with 80:20 MeOH–H_2O followed by MeOH to give the fluorous fraction, *sila-ketal* **S5** (118 mg, 95% , 73% purity by HPLC) as a colourless oil, R_f 0.60 (80:20 petrol–EtOAc); δ_H (500 MHz, $CDCl_3$) 7.70 (2H, d, *J* 8.1, tosyl 2-H and 6-H), 7.33 (2H, d, *J* 8.1, tosyl 3-H and 5-H), 5.90 (1H, app d, *J* 10.3, 4-H), 5.83 (1H, ddt, *J* 17.1, 10.3 and 7.2, 4'-H) 5.73 (1H, app d, *J* 10.3, 5-H), 5.30 (1H, br s, $NCH_2C{=}CH_A$), 5.13 (1H, br s, $NCH_2C{=}CH_B$), 5.08-5.01 (2H, m, 5'-H), 4.95 (1H, br d, *J* 3.9, 2-H), 4.22-4.17 (1H, m, 6-H), 4.10-4.04 (2H, m, 3-H and 2'-H), 4.03 (2H, br s, 3-CCH_2O), 3.84 (1H, dd, *J* 10.3 and 6.0, 6-CCH_A), 3.82 (1H, d, *J* 15.0, NCH_ACCH_2), 3.78 (1H, d, *J* 15.0, NCH_BCCH_2), 3.72 (1H, dd, *J* 10.3 and 6.0, 6-CCH_B), 3.50 (3H, s, OMe), 3.40-4.36 (2H, m, $CF_2CH_2CH_2$), 2.44 (3H, s, tosyl Me), 2.43-2.33 (2H, m, CF_2CH_2), 2.32-2.26 (1H, m, 3'-H_A), 2.24-2.17 (1H, m, 3'-H_B), 1.18 (3H, d, *J* 6.0, 1'-H) and 1.06-0.98 (14H, m, *i*Pr); δ_C (75 MHz, $CDCl_3$) 144.3 (tosyl 4-C), 141.0 (NCH_2CCH_2), 136.2 (tosyl 1-C), 135.6 (4'-C), 130.3 (tosyl 3-C and 5-C), 128.7 (4-C), 127.6 (tosyl 2-C and 6-C), 124.6 (5-C), 118.0 (3'-C), 117.2 ($NCH_2C{=}CH_2$), 97.2 (2-C), 72.4 (6-C), 69.8 (3-C), 69.6 (3-$COCH_2$), 68.6 (2'-C), 65.6 (6-CCH_2), 56.0 (OMe), 52.0 (NCH_2CCH_2), 44.6 (3'-C), 40.8 ($CF_2CH_2CH_2$), 31.1 (t, $^2J_{C–F}$ 21.8, CF_2CH_2), 23.5 (1'-C), 21.9 (tosyl Me), 17.6 (*i*Pr CMe_2) and 12.7 (*i*Pr CMe_2); ν_{max}/cm^{-1} (film); 2926, 2929, 2868, 1598 and 1463; *m/z* (ESI^+) 1045.3 ($[M + NH_4]^+$ 100%); found MNH_4^+ 1045.3140, $C_{39}H_{54}F_{17}N_2O_7SSi$ requires *MNH*$_4$ 1045.3150.

_N_-(2-{[(2_S_,3_R_,6_S_)-6-[(Diisopropyl((_S_)-pent-4'-en-2'-yloxy)silyloxy)methyl]-2-methoxy-3,6-dihydro-2_H_-pyran-3-yloxy]methyl}allyl)-_N_-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10heptadecafluorodecyl)-4-methylbenzenesulfonamide S6

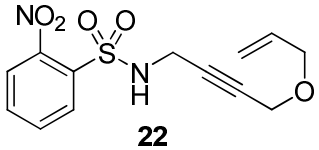


S6

Following general procedure **A**, (*S*)-diisopropyl(pent-4-en-2-yloxy)silane (84 mg, 0.42 mmol) and alcohol **1** (100 mg, 0.12 mol) were stirred for 16 hours after which time methanol (2 mL) was added and the solution was concentrated under reduced pressure. The residue was then suspended in pentane (5 mL), filtered and concentrated under reduced pressuro, to give a crude product which was purified by Fluorous Solid Phase Extraction; 2 g cartridge loading with <400 μL DMF, eluting with 8:2 MeOH–H_2O followed by MeOH to give the fluorous fraction, *sila-ketal* **S6** (105 mg, 85%, 75% purity by HPLC) as a colourless oil, R_f 0.57 (80:20 petrol–EtOAc); δ_H (500 MHz, $CDCl_3$) 7.70 (2H, d, *J* 8.1, tosyl 2-H and 6-H), 7.32 (2H, d, *J* 8.1, tosyl 3-H and 5-H), 5.90 (1H, app d, *J* 10.3, 4-H), 5.82 (1H, ddt, *J* 17.1, 10.3 and 7.2, 4'-H) 5.73 (1H, app d, *J* 10.3, 5-H), 5.30 (1H, br s, $NCH_2C=CH_A$), 5.12 (1H, br s, $NCH_2C=CH_B$), 5.07-5.05 (1H, m, 5'-H_A), 5.04-5.01 (1H, m, 5'-H_B), 4.95 (1H, br d, *J* 3.9, 2-H), 4.21-4.16 (1H, m, 6-H), 4.09-4.03 (2H, m, 3-H and 2'-H), 4.02 (2H, br s, 3-$COCH_2$), 3.84 (1H, dd, *J* 10.3 and 6.0, 6-CCH_A), 3.82 (1H, d, *J* 15.0, NCH_ACCH_2), 3.78 (1H, d, *J* 15.0, NCH_BCCH_2), 3.72 (1H, dd, *J* 10.3 and 6.0, 6-CCH_B), 3.49 (3H, s, OMe), 3.40-4.35 (2H, m, $CF_2CH_2CH_2$), 2.42 (3H, s, tosyl Me), 2.42-2.35 (2H, m, CF_2CH_2), 2.32-2.25 (1H, m, 3'-H_A), 2.23-2.17 (1H, m, 3'-H_B), 1.18 (3H, d, *J* 6.0, 1'-H) and 1.06-0.98 (14H, m, *i*Pr); δ_C (75 MHz, $CDCl_3$) 144.3 (tosyl 4-C), 141.1 (NCH_2CCH_2), 136.2 (tosyl 1-C), 135.6 (4'-C), 130.3 (tosyl 3-C and 5-C), 128.7 (4-C), 127.6 (tosyl 2-C and 6-C), 124.8 (5-C), 117.17, 117.14 (4'-C and $NCH_2C=CH_2$), 97.2 (2-C), 72.4 (6-C), 69.8 (3-C), 69.6 (3-$COCH_2$), 68.6 (2'-C), 65.6 (6-CCH_2), 56.2 (OMe), 52.0 (NCH_2CCH_2), 44.6 (3'-C), 40.8 ($CF_2CH_2CH_2$), 31.1 (t, $^2J_{C-F}$ 21.0, CF_2CH_2), 23.5 (1'-C), 21.8 (tosyl Me), 17.7 (*i*Pr CMe_2) and 12.7 (*i*Pr CMe_2); ν_{max}/cm^{-1} (film); 3077, 3045, 2928, 2868, 1598, 1494 and 1463; *m/z* (ESI^+) 1050.3 ($[M + Na]^+$ 100%); found MNa^+ 1050.2721, $C_{39}H_{50}F_{17}NO_7SSi$ requires *MNa* 1050.2698.

Synthesis of building blocks

***N*-(4-Allyloxy-but-2-ynyl)-2-nitro benzenesulfonamide 22**

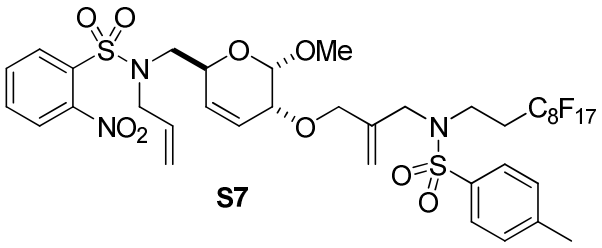


22

Following general procedure **B**, di-*t*-butyl azodicarboxylate (43.1 g, 0.19 mol), 4-(allyloxy)but-2-yn-1-ol (9.0 g, 93.8 mmol) and nosyl-Boc amine (56.6 g, 0.19 mol) gave the crude product after 2 hours. Purification by flash chromatography, eluting with 80:20 petrol–EtOAc, to give the Boc protected *sulfonamide*, along with the starting amine which co-eluted with the desired product as a 1:1 adduct. The sulfonamide mixture was then dissolved in 95:5 dichloromethane–trifluoroacetic acid (100 mL) and allowed to stir at room temperature for 24 h, after which time triethylamine (5 mL) was added dropwise at 0 °C. Brine (50 mL) was added and the aqueous layer extracted with ethyl acetate (2 × 50 mL). The organic extracts were subsequently combined, dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by flash chromatography, eluting with 80:20 petrol–EtOAc to give the *sulfonamide* **22** (18.5 g, 64% over 2 steps) as colourless needles, m.p. 45 ºC; R_f 0.74 (1:1 petrol–EtOAc); (Found: C, 50.35; H, 4.55; N, 9.25; S, 10.05; $C_{13}H_{14}N_2O_5S$ requires C, 50.31; H, 4.55; N, 9.03; S, 10.33); δ_H (500 MHz, $CDCl_3$) 8.27-8.23 (1 H, m, nosyl 3-H), 7.98-7.93 (1 H, m, nosyl 6-H), 7.84-7.76 (2 H, m, nosyl 4-H and 5-H), 5.84 (1 H, ddt, *J* 17.1, 10.5 and 5.6, allyl 2-H), 5.70 (1 H, t, *J* 5.7, N*H*), 5.22 (1 H, app. dq, *J* 17.1 and 1.7, allyl 3-H_A), 5.19 (1 H, app. dq, *J* 10.5 and 1.7, allyl 3-H_B), 4.06 (2 H, dt, *J* 6.4 and 1.9, 1-H), 3.88-3.85 (4 H, m, 4-H and allyl 1-H); δ_C (75 MHz, $CDCl_3$) 148.6 (nosyl 2-C), 134.5 (allyl 2-C), 134.1 (nosyl 4-C), 133.3 (nosyl 6-C), 133.2 (nosyl 1-C), 131.9 (nosyl 3-C), 125.9 (nosyl 5-C), 118.4 (allyl 3-C), 81.7 (3-C), 80.3 (2-C), 71.0 (allyl 1-C), 57.3 (4-C), and 34.1 (1-C); ν_{max}/cm^{-1} 3342, 3097, 3022, 2980 and 2858; *m/z* (ESI^+) 333.1 ($[M + Na]^+$ 100%); found MNa^+ 333.0516, $C_{13}H_{14}N_2NaO_5S$ requires *MNa* 333.0521.

Preparation of metathesis substrates, metathesis reactions and release of the products (see Table)

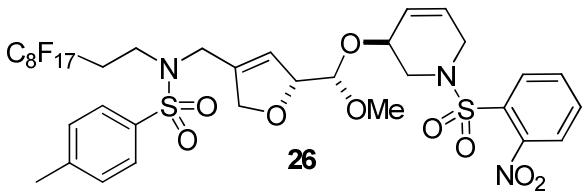
***N*-Allyl-*N*-{[(2*S*,5*R*,6*S*)-5-{[*N*'-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)-4-methylphenylsulfonamido]allyloxy}-6-methoxy-5,6-dihydro-2*H*-pyran-2-yl]methyl}-2-nitrobenzenesulfonamide S7**



S7

Following general procedure **B**, di-*tert*butyl azodicarboxylate (111 mg, 0.48 mmol), *N*-allyl-2-nitrobenzenesulfonamide **19** (117 mg, 0.48 mmol) and alcohol **1** (100 mg, 0.12 mmol) gave the crude product after 3 hours. Purification by Fluorous Solid Phase Extraction; 2 g cartridge, loading with <400 μL DMF, eluting with 80:20 MeOH–H_2O followed by MeOH, gave the fluorous fraction, *sulfonamide* **S7** (115 mg, 91%, 94% purity by HPLC) as a colourless oil, R_f 0.32 (60:40 petrol–EtOAc); δ_H (500 MHz, $CDCl_3$) 8.10-8.05 (1H, m, nosyl 3-H), 7.72-7.63 (5H, m, Ar), 7.34 (2H, d, *J* 8.1, tosyl 3-H and 5-H), 5.67-5.67 (2H, m, 3-H and 4-H), 5.67 (1H, ddt, *J* 17.1, 10.3 and 6.4, allyl 2-H), 5.29 (1H, s, 3-$COCH_2C$=CH_A), 5.20 (1H, app. dq, *J* 17.1 and 1.3, allyl 3-H_A), 5.18 (1H, app. dq, *J* 10.3 and 1.3, allyl 3-H_B), 5.12 (1H, s, 3-$COCH_2C$=CH_B), 4.77 (1H, br. d, *J* 3.9, 6-H), 4.32-4.28 (1H, m, 2-H), 4.16 (1H, dd, *J* 16.2 and 6.4, allyl 1-H_A), 4.06 (1H, dd, *J* 16.2 and 6.4, allyl 1-H_B), 4.02 (2H, br. s, 5-$COCH_2$), 4.01-3.97 (1H, m, 5-H), 3.79 (2H, br. s, NCH_2CCH_2), 3.54 (1H, dd, *J* 15.0 and 3.9, 2-CCH_A), 3.42 (1H, dd, *J* 15.0 and 8.1, 2-CCH_B), 3.39 (3H, s, OMe), 3.39-3.34 (2H, m, $CF_2CH_2CH_2$), 2.44 (3H, s, tosyl Me) and 2.44-2.30 (2H, m, CF_2CH_2); δ_C (75 MHz, $CDCl_3$) 148.3 (nosyl 2-C), 144.5 (tosyl 4-C), 140.9 (3-$COCH_2C$), 136.0 (tosyl 1-C), 134.5 (nosyl 1-C), 133.9 (nosyl 3-C), 132.8 (allyl 2-C), 132.0, 131.7 (nosyl 4-C and 6-C), 130.4 (tosyl 3-C and 5-C), 127.59, 127.56 (4-C and tosyl 2-C and 6-C), 125.8 (3-C), 124.5 (nosyl 5-C), 119.8 (allyl 3-C), 117.6 (3-$COCH_2C$=CH_2), 97.0 (6-C), 72.1 (5-C), 69.7 (5-$COCH_2$), 68.1 (2-C), 56.2 (OMe), 52.1 (NCH_2CCH_2), 51.5 (allyl 1-C), 50.2 (2-CCH_2), 40.9 ($CF_2CH_2CH_2$), 31.0 (CF_2CH_2), 21.9 (tosyl Me); ν_{max}/cm^{-1} (film); 3088, 2928, 2255, 1597, 1545 and 1494; *m/z* (ESI^+) 1076.2 ($[M + Na]^+$ 100%); found MNa^+ 1076.1514, $C_{37}H_{36}F_{17}N_3O_9S_2$ requires *MNa* 1076.1519.

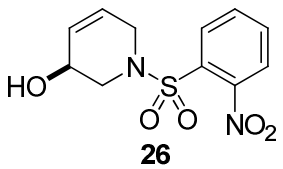
***N*-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluorodecyl)-*N*'-{[(*R*)-5-{(*S*)-methoxy[(*S*)-1'-(2-nitrophenylsulfonyl)-1',2',3',6'-tetrahydropyridin-3'-yloxy]methyl}-2,5-dihydrofuran-3-yl]methyl}-4-methylbenzenesulfonamide 26** (R = R'^F)



26

Following general procedure **C**, **HG II** (3 × 6 mg, 3 × 5 mol%) and sulfonamide **S7** (200 mg, 0.19 mmol) gave the crude product after 5 days. Purification by Fluorous Solid Phase Extraction; 2 g cartridge loading with <400 μL DMF, eluting with 80:20 MeOH–H_2O followed by MeOH to give the fluorous fraction, *sulfonamide* **26** (R = R'^{F}) (175 mg, 90%, 94% purity by HPLC) as a colourless oil, R_f 0.31 (80:20 petrol–EtOAc); δ_H (500 MHz, $CDCl_3$) 8.03 (1H, dd, *J* 7.3 and 2.1, nosyl 3-H), 7.73-7.67 (4H, m, tosyl 2-H and 6-H and nosyl 4-H and 5-H), 7.63 (1H, dd, *J* 7.3 and 2.1, nosyl 6-H), 7.34 (2H, d, *J* 8.1, tosyl 3-H and 5-H), 5.91 (1H, app. dq, *J* 10.3 and 2.1, 4'-H), 5.84-5.79 (1H, m, 5'-H), 5.71 (1H, br. s, 4-H), 4.73-4.69 (1H, m, 5-H), 4.54-4.48 (1H, m, 2-H_A), 4.44-4.39 (1H, m, 2-H_A), 4.36 (1H, d, *J* 5.1, C*H*OMe), 4.32-4.27 (1H, m, 3'-H), 3.93 (2H, br. s, 3-CC*H*$_2$), 3.90-3.88 (1H, m, 6'-H_A), 3.86 (1H, dd, *J* 12.8 and 5.1, 2'-H_A), 3.78-3.75 (1H, m, 6'-H_B), 3.43-3.37 (5H, m, OMe and $CF_2CH_2CH_2$), 3.15 (1H, dd, *J* 12.8 and 7.0, 2'-H_B) and 2.48-2.40 (5H, m, tosyl Me and CF_2CH_2); δ_C (75 MHz, $CDCl_3$) 148.3 (nosyl 2-C), 144.2 (tosyl 4-C), 137.94, 137.91 (3-C and nosyl 1-C), 135.6 (tosyl 1-C), 133.7 (nosyl 3-C), 132.0, 131.7, (nosyl 4-C and 6-C), 130.9 (tosyl 3-C and 5-C), 127.7 (4'-C), 127.2 (tosyl 2-C and 6-C), 125.44, 125.38 (5'-C and 4-C), 124.2 (nosyl 5-C), 105.1 (5-C*C*HOMe), 87.1 (5-C), 75.7 (2-C), 69.1 (3'-C), 56.1 (OMe), 46.9 (2'-C), 45.9 (3-C*C*H$_2$), 44.4 (6'-C), 40.3 ($CF_2CH_2CH_2$), 30.8 (CF_2CH_2), 21.6 (tosyl Me); ν_{max}/cm^{-1} (film) 3093, 3049, 2956, 2924, 2854, 1741, 1711, 1661, 1597 and 1547; *m/z* (ES$^+$) 1048.1 ([M + Na]$^+$ 100%); found MNa$^+$ 1048.1247, $C_{35}H_{32}F_{17}N_3O_9S_2$ requires *MNa* 1048.1201.

(*S*)-1-(2-nitrophenylsulfonyl)-1,2,3,6-tetrahydropyridin-3-ol 26 (R = H)

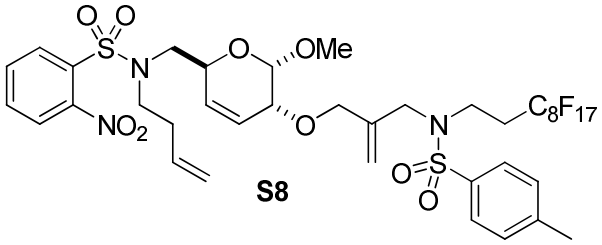


26

Following general procedure **D**, sulfonamide **26** (R = R'^{F}) (40 mg, 0.039 mmol) and 3% trifluoroacetic acid gave the crude product after 16 hours. Purification by Fluorous Solid Phase Extraction; 2 g cartridge, loading with <400 μL DMF, with 80:20 MeOH–H_2O, gave the organic fraction. Further purification by flash chromatography, eluting with 50:50 petrol–EtOAc, gave the *alcohol* **26** (R = H) (7 mg, 70%) as a colourless oil, R_f 0.12 (80:20 petrol–EtOAc); $[\alpha]_D^{20}$ +73.6 (*c*

1.00 in chloroform); δ_H (500 MHz, $CDCl_3$) 8.07 (1H, dd, *J* 7.3 and 1.7, nosyl 3-H), 7.76-7.69 (2H, m, nosyl 4-H and 6-H), 7.65 (1H, dd, *J* 7.4 and 1.7, nosyl 5-H), 5.99-5.94 (1H, m, 4-H), 5.90 (1H, dt, *J* 10.3 and 3.0, 5-H), 4.26-4.20 (1H, m, 3-H), 4.05-3.97 (1H, m, 6-H_A), 3.78-3.72 (1H, m, 6-H_B), 3.53 (1H, dd, *J* 12.8 and 3.9, 2-H_A), 3.44 (1H, m, 12.8 and 3.9, 2-H_B) and 2.00 (1H, br.d, *J* 9.0, OH); δ_C (75 MHz, $CDCl_3$) 148.7 (nosyl 2-C), 134.3 (nosyl 4-C), 132.1 (nosyl 6-C), 132.0 (nosyl 1-C), 131.6 (nosyl 3-C), 128.5 (4-C), 126.6 (5-C), 124.6 (nosyl 5-C), 63.6 (3-C), 50.1 (2-C), 44.9 (6-C); ν_{max}/cm^{-1} (film) 3518 (br), 3399 (br), 3095, 3023, 2962, 2924, 2854, 1590, 1544 and 1450; *m/z* (ESI^+) 307.0 ($[M + Na]^+$ 100%); found MNa^+ 307.0359, $C_{11}H_{12}N_2O_5S$ requires *MNa* 307.0359.

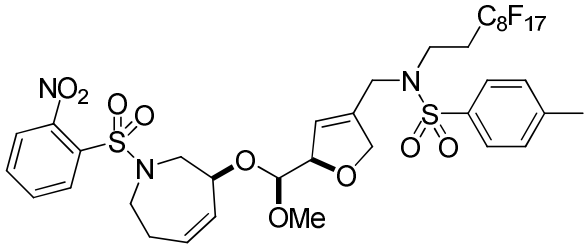
_N_-(But-3-enyl)-_N_-{[(2'_S_,5'_R_,6'_S_)-5'-{2-[(_N_-{3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl}-4-methylphenylsulfonamido)methyl]allyloxy}-6'-methoxy-5',6'-dihydro-2_H_-pyran-2'-yl]methyl}-2-nitrobenzenesulfonamide S8



Following general procedure **B**, diethyl azodicarboxylate (88 μL, 0.48 mmol), sulfonamide **20** (124 mg, 0.48 mmol) and alcohol **1** (100 mg, 0.12 mmol) gave the crude product after 3 hours. Purification by Fluorous Solid Phase Extraction; 5 g cartridge, loading with <1 mL DMF, eluting with 80:20 MeOH–H_2O followed by MeOH , gave the fluorous fraction, the *sulfonamide* **S8** (127 mg, 99%, 92% purity by HPLC) as a colourless oil, R_f 0.32 (60:40 petrol–EtOAc); δ_H (500 MHz, $CDCl_3$) 8.07-8.04 (1H, m, nosyl 3-H), 7.73-7.62 (5H, m, Ar), 7.34 (2H, d, *J* 8.1, tosyl 3-H and 5-H), 5.78-5.70 (2H, m, 3'-H and 4'-H), 5.66 (1H, ddt, *J* 17.1, 10.3 and 6.8, 3-H), 5.30 (1H, br. s, $NCH_2C{=}CH_A$), 5.14 (1H, br. s, $NCH_2C{=}CH_B$), 5.04 (1H, app. dq, *J* 17.1 and 1.5, 4-H_A), 4.99 (1H, app. dq, *J* 10.3 and 1.5, 4-H_B), 4.81 (1H, d, *J* 3.9, 6'-H), 4.32-4.28 (1H, m, 2'-H), 4.05-4.00 (3H, m, 5'-H and 5-$COCH_2$), 3.83-3.75 (2H, m, NCH_2CCH_2), 3.62-3.55 (2H, m, 1-H), 3.48 (6H, m, OMe, $CF_2CH_2CH_2$ and 2'-CCH_2), 2.44 (3H, s, tosyl Me), 2.44-2.30 (4H, m, CF_2CH_2 and 2-H); δ_C (75 MHz, $CDCl_3$) 148.1 (nosyl 2-C), 144.1 (tosyl 4-C), 140.6 (NCH_2CCH_2), 135.8 (tosyl 1-C), 134.3 (3-C), 134.0 (nosyl 4-C), 133.5 (nosyl 1-C), 131.6, 131.1 (nosyl 3-C and 6-C), 130.0 (tosyl 3-C and 5-C), 127.24, 127.22 (4'-C and tosyl 2-C and 6-C), 125.6 (3'-C), 124.2 (nosyl 5-C), 117.6 (4-C), 117.2 ($NCH_2C{=}CH_2$), 96.7 (6'-C), 71.8 (5'-C), 69.4 (5-$COCH_2$), 68.0 (2'-C), 55.9 (OMe), 51.8 (NCH_2CCH_2), 50.5 (1-C), 48.1 (2'-CCH_2), 40.5 ($CF_2CH_2CH_2$), 32.3 (2-C), 30.7 (t, $^2J_{C-F}$ 21.8,

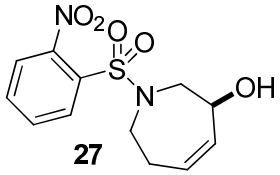
CF_2CH_2) and 21.5 (tosyl Me); ν_{max}/cm^{-1} (film) 2916, 2849, 1736, 1576, 1541 and 1471; *m/z* (ESI^+) 1090.2 ($[M + Na]^+$ 100%); found MNa^+ 1090.1706, $C_{38}H_{38}F_{17}N_3O_9S_2$ requires *MNa* 1090.1670.

_N_-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptafluorodecyl)-_N_-{[(_R_)-5-{(_S_)-methoxy[(_S_,_Z_)-1'-{2-nitrophenylsulfonyl}-2',3',6',7'-tetrahydro-1_H_-azepin-3'-yloxy]methyl}-2,5-dihydrofuran-3-yl]methyl}-4-methylbenzenesulfonamide 27 (R = R'^F)



Following general procedure **C**, sulfonamide (96 mg, 0.10mmol) and **HG II** (3 × 3 mg, 3 × 5 mol%) gave the crude product after 9 days. Purification by Fluorous Solid Phase Extraction; 2 g cartridge, loading with <400 μL DMF, eluting with 80:20 MeOH–H_2O followed by MeOH, gave the crude sulfonamide **27** (R = R'^F) (74 mg, 80%, 69% purity by HPLC) as a colourless oil. Further purification by flash chromatography gave the *sulfonamide* **27** (R = R'^F) (50 mg, 55%) as a colourless oil, R_f 0.33 (80:20 petrol–EtOAc); $[\alpha]_D^{20}$ +17.6 (*c* 1.00 in chloroform); δ_H (500 MHz, $CDCl_3$) 8.02-7.99 (1H, m, nosyl 3-H), 7.73-7.63 (5H, m, Ar), 7.34 (2H, d, *J* 8.1, tosyl 3-H and 5-H), 5.94-5.91 (1H, m, 4'-H), 5.85-5.79 (1H, m, 5'-H), 5.72 (1H, br. s, 4-H), 4.74-4.69 (1H, m, 5-H), 4.54 (1H, ddd, *J* 12.5, 5.8 and 1.8, 2-H_A), 4.46-4.40 (2H, m, 2-H_B and 3'-H), 4.37 (1H, d, *J* 5.4, C*H*OMe), 4.03-3.89 (3H, m, 3-CCH_2N and 2'-H_A), 3.83-3.76 (1H, m, 7'-H_A), 3.45-3.38 (5H, m, OMe and $CF_2CH_2CH_2$), 3.02-2.94 (2H, m, 2'-H_B and 7'-H_B), 2.50-2.39 (6H, m, tosyl Me, CF_2CH_2 and 6'-H_A) and 2.38-2.30 (1H, m, 6'-H_B); δ_C (75 MHz, $CDCl_3$) 148.0 (tosyl 4-C), 144.2 (tosyl 4-C), 137.9 (3-C), 135.8 (tosyl 1-C), 135.2 (nosyl 4-C), 133.6 (nosyl 6-C), 133.1 (nosyl 1-C), 131.7, (nosyl 3-C), 130.8 (tosyl 3-C and 5-C), 128.1 (4'-C), 127.2 (tosyl 2-C and 6-C), 125.6 (5'-C and 4-C), 124.3 (nosyl 5-C), 105.7 (5-C*C*HOMe), 87.2 (5-C), 77.5 (3'-C), 75.7 (2-C), 56.3 (OMe), 51.7 (2'-C), 48.5 (7'-C), 45.9 (3-CCH_2N), 40.3 ($CF_2CH_2CH_2$), 30.9 (t, $^2J_{C-F}$ 21.0, CF_2CH_2), 30.3 (6'-C), 21.7 (tosyl Me); ν_{max}/cm^{-1} (film) 2848, 2925, 2854, 1714, 1597, 1545 and 1453; *m/z* (ESI^+) 1062.1 (M +Na^+ 100%); found MNa^+ 1062.1386, $C_{36}H_{34}F_{17}N_3O_9S_2$ requires *MNa* 1062.1357.

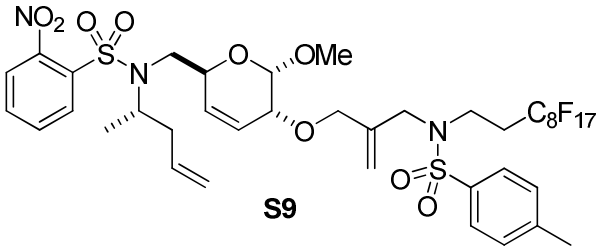
(_S_)-1-(2-Nitrophenylsulfonyl)-2,3,6,7-tetrahydro-1_H_-azepin-3-ol 27 (R = H)



27

Following general procedure **D**, sulfonamide **27** (R = R'^{F}) (46 mg, 0.045 mmol) and 3% trifluoroacetic acid in DCM gave the crude product after 16 hours. Purification by Fluorous Solid Phase Extraction; 2 g cartridge, loading with <400 μL DMF, with 80:20 MeOH–H_2O, to give the organic fraction. Further purification by flash chromatography, eluting with 60:40 petrol–EtOAc, gave the *alcohol* **27** (R = H) (10 mg, 77%) as a colourless oil, R_f 0.15 (50:50 petrol–EtOAc); $[\alpha]_D^{20}$ +42.8 (*c* 1.00 in chloroform); δ_H (500 MHz, $CDCl_3$) 8.06-8.02 (1H, m, 3'-H), 7.71-7.68 (3H, m, Ar), 7.65-7.62 (1H, m, Ar), 5.91-5.86 (1H, m, 4-H), 5.81 (1H, dtd, *J* 11.3, 5.0 and 1.5, 5-H), 4.61-4.55 (1H, m, 3-H), 3.97 (2H, t, *J* 4.3, 7-H), 3.67-3.61 (1H, m, 2-H_A), 3.53-3.46 (1H, m, 2-H_B), 2.15-2.05 (2H, m, 6-H); δ_C (75 MHz, $CDCl_3$) 144.9 (tosyl 4-C), 133.7 (nosyl 4-C), 133.6 (nosyl 1-C), 131.7, (nosyl 3-C), 131.1 (nosyl 6-C), 127.3 (4-C), 124.3 (nosyl 5-C), 119.9 (5-C), 68.8 (3-C), 45.8, 44.6 (2-C and 7-C) and 35.4 (6-C); ν_{max}/cm^{-1} (film) 3399, 3023, 2962, 2854, 1597, 1545 and 1453; *m/z* (ESI$^+$) 321.0 (M +Na$^+$ 100%); found MNa$^+$ 321.0517, $C_{12}H_{14}N_2O_5S_1$ requires *MNa* 321.0516.

_N_-[{(2_S_,5_R_,6_S_)-5-[2-{[_N_-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)-4-methylphenylsulfonamido]methyl}allyloxy]-6-methoxy-5,6-dihydro-2_H_-pyran-2-yl}methyl]-2-nitro-_N_-{(_R_)-pent-4'-en-2'-yl}benzenesulfonamide S9

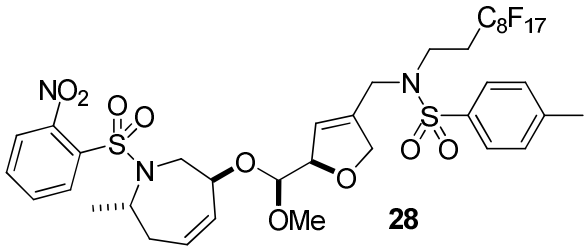


S9

Following general procedure **B**, diethyl azodicarboxylate (72 μL, 0.39 mmol), sulfonamide **18** (100 mg, 0.10 mmol) and alcohol **21** (107 μL, 0.98 mmol) gave the crude product after 3 hours. Purification by Fluorous Solid Phase Extraction; 2 g cartridge, loading with <200 μL dichloromethane, eluting with 80:20 MeOH–H_2O followed by MeOH, gave the fluorous fraction which contained approximately 70% of the starting amine. The fluorous mixture was further purified by flash chromatography, eluting with 80:20 petrol–EtOAc, to give the *sulfonamide* **S9** (28 mg, 26%) as a colourless foam, R_f 0.86 (50:50 petrol–EtOAc); δ_H (500 MHz, $CDCl_3$) 8.09-8.05 (1H, m, nosyl 3-H), 7.72-7.65 (4H, m, Ar), 7.63-7.60 (1H, m, nosyl 5-H), 7.34 (2H, d, *J* 7.9, tosyl 3-H and 5-H), 5.85-5.81 (1H, m, 3-H), 5.77-5.67 (2H, m, 4-H and 4'-H), 5.30 (1H, br. s, 5-$COCH_2C{=}CH_A$), 5.14 (1H, br.s, 5-$COCH_2C{=}CH_B$), 5.05 (1H, app. dq, *J* 17.1 and 1.4, 5'-H_A), 5.00 (1H, app. dq, *J* 10.0 and 1.4, 5'-H_B), 4.86 (1H, d, *J* 3.8, 6-H), 4.39-4.34 (1H, m, 2-H), 4.06-4.01 (3H, m, 5-H and 5-$COCH_2$), 4.01-3.94 (1H, m, 2'-H), 3.82 (1H, d, *J* 15.0, NCH_ACCH_2), 3.77 (1H, d, *J* 15.0, NCH_BCCH_2), 3.47 (1H, dd, *J* 15.6 and 3.8, 2-CCH_A), 3.41 (3H, s, OMe), 3.40-3.35 (2H,

m, $CF_2CH_2CH_2$), 3.33 (1H, dd, *J* 15.6 and 8.0, 2-CCH_B), 2.53-2.46 (1H, m, 3'-H_A), 2.44 (3H, s, tosyl Me), 2.42-2.31 (2H, m, CF_2CH_2), 2.30-2.21 (1H, m, 3'-H_B), 1.15 (3H, d, *J* 7.1, 1'-H); δ_C (75 MHz, $CDCl_3$) 148.6 (nosyl 2-C), 144.4 (tosyl 4-C), 140.9 (5-COCH_2C), 136.2 (tosyl 1-C), 135.2 (4'-C), 134.4 (nosyl 4-C), 133.7 (nosyl 1-C), 131.8, 131.7 (nosyl 3-C and nosyl 6-C), 130.3 (tosyl 3-C and 5-C), 128.0 (3-C), 127.6 (tosyl 2-C and 6-C), 125.4 (4-C), 124.5 (nosyl 5-C), 117.9 (5'-C), 117.5 (5-COCH$_2$C=CH_2), 97.2 (6-C), 72.2 (5-C), 69.7 (5-COCH_2), 68.9 (2-C), 56.2 (OMe), 55.3 (2'-C), 52.1 (NCH_2CCH_2), 48.1 (2-CCH_2), 40.9 ($CF_2CH_2CH_2$), 40.7 (3'-C), 31.1 (CF_2CH_2), 21.9 (tosyl Me), 18.9 (1′-C); ν_{max}/cm^{-1} (film) 2916, 2849, 1734, 1574, 1540 and 1470; *m/z* (ESI^+) 1104.2 ($[M + Na]^+$ 100%), 1099.2 ($[M + NH_4]^+$ 90%); found MNa^+ 1104.1791, $C_{39}H_{40}F_{17}N_3O_9S_2$ requires *MNa* 1104.1827.

***N*-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluorodecyl)-*N*-[{(*R*)-5-[(*S*)-methoxy{(3'*S*,7'*R*, *Z*)-7'-methyl-1-(2-nitrophenylsulfonyl)-2',3',6',7'-tetrahydro-1*H*-azepin-3'-yloxy}methyl]-2,5-dihydrofuran-3-yl}methyl]-4-methylbenzenesulfonamide 28** (R = R'^{F})

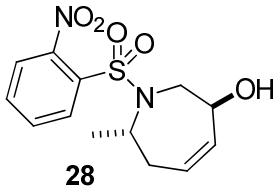


28

Following general procedure **C**, **HG II** (2 × 3 mg, 2 × 5 mol%) and sulfonamide **S9** (45 mg, 0.042 mmol) gave the crude product after 6 days. Purification by Fluorous Solid Phase Extraction; 2 g cartridge, loading with <400 μL DMF, eluting with 80:20 MeOH–H_2O followed by MeOH to give the crude sulfonamide **28** (R = R'^{F}) (43 mg, 98%, 85% purity by HPLC) as a colourless oil. Further purification by flash chromatography, eluting with 70:30 petrol–EtOAc, gave the *sulfonamide* **28** (R = R'^{F}) (31 mg, 71%) as a colourless oil, R_f 0.87 (50:50 petrol–EtOAc); δ_H (500 MHz, $CDCl_3$) 8.13-8.09 (1H, m, nosyl 3-H), 7.69 (2H, d, *J* 8.1, tosyl 2-H and 6-H), 7.68-7.64 (2H, m, nosyl 4-H and 6-H), 7.62-7.59 (1H, m, nosyl 5-H), 7.34 (2H, d, *J* 8.1, tosyl 3-H and 5-H), 5.77-5.65 (3H, m, 4-H, 4'-H and 5'-H), 4.77-4.72 (1H, m, 5-H), 4.52 (1H, ddd, *J* 12.7, 5.7 and 1.8, 2-H_A), 4.41 (1H, app. dt, *J* 12.7 and 1.8, 2-H_B), 4.37 (1H, d, *J* 4.7, C*H*OMe), 4.32-4.26 (1H, m, 3'-H), 4.16-4.08 (1H, m, 7'-H), 3.92 (2H, s, 3-CCH_2N), 3.75 (1H, dd, *J* 15.0 and 6.2, 2'-H_A), 3.67 (1H, dd, *J* 15.0 and 3.0, 2'-H_B), 3.43-3.36 (5H, m, OMe and $CF_2CH_2CH_2$), 2.62 (1H, dt, *J* 15.0 and 4.1, 6'-H_A), 2.51-2.37 (5H, m, tosyl Me and CF_2CH_2), 2.15 (1H, dt, *J* 15.0 and 6.8, 6'-HB); δ_C (75 MHz, $CDCl_3$) 148.1 (nosyl 2-C), 144.1 (tosyl 4-C), 137.6 (3-C), 135.7 (tosyl 1-C), 134.0 (nosyl 4-C), 133.2 (4-C), 132.1 (nosyl 1-C), 131.5, 131.4 (nosyl 3-C and nosyl 6-C), 130.0 (tosyl 3-C and 5-C), 127.4 (4'-C), 127.2 (tosyl

2-C and 6-C), 125.7 (5'-C), 124.0 (nosyl 5-C), 104.9 (*C*HOMe), 87.3 (5-C), 75.7 (2-C), 74.8 (3'-C), 56.3 (OMe), 52.8 (7'-C), 46.9 (2'-C), 46.0 (3-C*C*H_2N), 40.3 ($CF_2CH_2CH_2$), 33.2 (6'-C), 30.9 (CF_2CH_2), 21.5 (tosyl Me) and 19.4 (7'-C*C*H_3); ν_{max}/cm^{-1} (film) 3095, 3031, 2924, 2853, 1598, 1545 and 1455; *m/z* (ESI^+) 1076.1 ($[M + Na]^+$ 100%); found MNa^+ 1076.1472, $C_{37}H_{36}F_{17}N_3O_9S_2$ requires *MNa* 1076.1514.

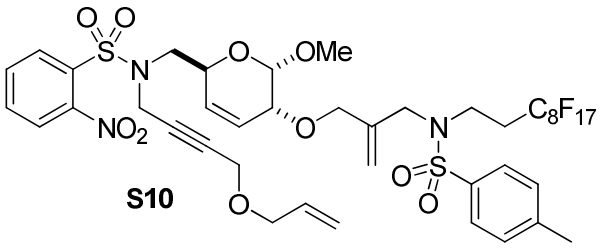
(*S*)-[(*R*)-7-methyl]-1-(2-Nitrophenylsulfonyl)-2,3,6,7-tetrahydro-1*H*-azepin-3-ol 28 (R = H)



28

Following general procedure **D**, sulfonamide **28** (R = R'^{F}) (30 mg, 0.028 mmol) and 3% trifluoroacetic acid gave the crude product after 16 hours. Purification by Fluorous Solid Phase Extraction; 2 g cartridge, loading with <400 μL DMF, with 80:20 MeOH–H_2O, gave the organic fraction. Further purification by flash chromatography, eluting with 60:40 petrol–EtOAc, gave the *alcohol* **28** (R = H) (6 mg, 62%) as a colourless oil, R_f 0.17 (50:50 petrol–EtOAc); $[\alpha]_D^{20}$ +128.8 (*c* 0.50 in chloroform); δ_H (500 MHz, $CDCl_3$) 8.15-8.12 (1H, m, nosyl 3-H), 7.77-7.66 (3H, m, Ar), 5.86-5.81 (1H, m, 4-H), 5.80-5.74 (1H, m, 5-H), 4.48-4.43 (1H, m, 3-H), 4.38-4.30 (1H, m, 7-H), 3.88-3.82 (1H, m, 2-H_A), 3.65 (1H, dd, *J* 15.9 and 3.3, 2-H_B), 2.73 (1H, d, *J* 8.0, OH), 2.61-2.54 (1H, m, 6-H_A), 2.26-2.18 (1H, m, 6-H_B) and 1.14 (3H, d, *J* 6.6, 7-C*C*H_3); δ_C (75 MHz, $CDCl_3$) 148.3 (nosyl 2-C), 134.0 (nosyl 1-C), 133.8 (4-C), 133.5 (nosyl 4-C), 131.6 (nosyl 6-C), 131.1 (nosyl 3-C), 126.5 (5-C), 124.2 (nosyl 5-C), 69.8 (3-C), 53.0 (7-C), 48.2 (2-C), 34.1 (6-C) and 18.3 (7-C*C*H_3); ν_{max}/cm^{-1} (film) 3523, 3096, 3026, 2977, 2934 and 1543; *m/z* (ESI^+) 335.1 ($[M + Na]^+$ 100%); found MNa^+ 335.0666, $C_{13}H_{16}N_2O_5S$ requires *MNa* 335.0672.

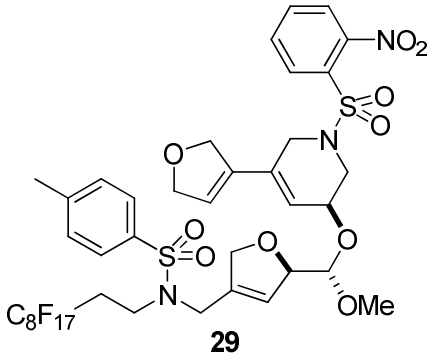
***N*-[4-(allyloxy)but-2-ynyl]-*N*-{[(2'*S*,5'*R*,6'*S*)-5'-{2-[(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)-4-methylphenylsulfonamido]methyl}allyloxy)-6'-methoxy-5',6'-dihydro-2*H*-pyran-2'-yl]methyl}-2-nitrobenzenesulfonamide S10**



S10

Following general procedure **B**, diethyl azodicarboxylate (133 μL, 0.72 mmol), sulfonamide **22** (226 mg, 0.72 mmol) and alcohol **1** (150 mg, 0.18 mmol) gave the crude product after 3 hours. The crude product was purified by Fluorous Solid Phase Extraction; 2 g cartridge, loading with <400 μL, eluting with 80:20 MeOH–H_2O followed by MeOH to give the fluorous fraction, which was purified further by flash chromatography, eluting with 80:20 petrol–EtOAc, to give the *sulfonamide* **S10** (198 mg, 96%, 64% purity by HPLC) as a colourless oil, R_f 0.35 (60:40 petrol–EtOAc); $[\alpha]_D^{20}$ −15.2 (*c* 1.00 in chloroform); δ_H (500 MHz, $CDCl_3$) 8.12-8.07 (1H, m, nosyl 3-H), 7.73-7.63 (5H, m, Ar), 7.60-7.43 (1H, m, nosyl 5-H), 7.35 (2H, d, *J* 8.2, tosyl 3-H and 5-H), 5.84 (1H, ddt, *J* 17.2, 10.2 and 1.5, *4-C* allyl 2-H), 5.80-5.72 (2H, m, 3'-H and 4'-H), 5.31 (1H, br. s, $NCH_2C{=}CH_A$), 5.25 (1H, app. dq, *J* 17.2 and 1.5, *4-C* allyl 3-H_A), 5.21 (1H, app. dq, *J* 10.2 and 1.5, *4-C* allyl 3-H_B), 5.14 (1H, br. s, $NCH_2C{=}CH_B$), 4.85 (1H, br. d, *J* 3.8, 6'-H), 4.44-4.34 (3H, m, 4-H and 2'-H), 4.05-3.99 (5H, m, 1-H, 5'-$COCH_2$ and 5'-H), 3.91 (2H, dt, *J* 5.6 and 1.5, *4-C* allyl 1-H), 3.80 (2H, br. s, NCH_2CCH_2), 3.66 (1H, dd, *J* 15.1 and 3.3, 2'-CCH_A), 3.54 (1H, dd, *J* 15.1 and 7.4, 2'-CCH_B), 3.44 (3H, s, OMe), 3.42-3.34 (2H, m, $CF_2CH_2CH_2$), 2.45 (3H, s, tosyl Me) and 2.43-4.28 (2H, m, CF_2CH_2); δ_C (75 MHz, $CDCl_3$) 148.6 (nosyl 2-C), 144.4 (tosyl 4-C), 140.9 (NCH_2CCH_2), 136.2 (tosyl 1-C), 134.2 (nosyl 1-C), 134.1 (*4-C* allyl-2-C), 133.6 (nosyl 3-C), 132.0, 131.7 (nosyl 4-C and 6-C), 130.4 (tosyl 3-C and 5-C), 127.6 (tosyl 2-C and 6-C), 127.4 and 126.1 (3'-C and 4'-C), 124.5 (nosyl 5-C), 118.3 (*4-C* allyl 3-C), 117.6 ($NCH_2C{=}CH_2$), 97.1 (6'-C), 82.1 and 80.1 (2-C and 3-C), 72.1 (5'-C), 70.9 (*4-C* allyl 1-C), 69.8 (5-$COCH_2$), 68.8 (2'-C), 57.5 (4-C), 56.2 (OMe), 52.1 (NCH_2CCH_2), 50.4 (2'-CCH_2), 40.8 ($CF_2CH_2CH_2$), 39.2 (1-C), 31.0 (t, $^2J_{C-F}$ 21.0, CF_2CH_2), 21.9 (tosyl Me); ν_{max}/cm^{-1} (film); 2927, 2857, 1728, 1597, 1545 and 1439; *m/z* (ES^+) 1144.2 ($[M + Na]^+$ 100%); found MNa^+ 1144.1776, $C_{41}H_{40}F_{17}N_3O_{10}S_2$ requires *MNa* 1144.1781.

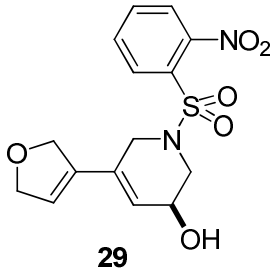
***N*-{[(*R*)-5-{(*S*)-[(*S*)-5'-(2'',5''-dihydrofuran-3''-yl)-1'-(2-nitrophenylsulfonyl)-1',2',3',6'-tetrahydropyridin-3'-yloxy](methoxy)methyl}-2,5-dihydrofuran-3-yl]methyl}-*N*-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)-4-methylbenzenesulfonamide 29** (R = R'^{F})



29

Following general procedure **C**, **HG II** (11 mg, 5 mol%) and sulfonamide **S10** (360 mg, 0.32 mmol) gave the crude product after 3 days. Purification by Fluorous Solid Phase Extraction; loading with <400 μL DMF, eluting with 80:20 MeOH–H_2O followed by MeOH, gave the fluorous fraction. Further purification by flash chromatography, eluting with 60:40 petrol–EtOAc, gave the *sulfonamide* **29** (R = R'^{F}) (179 mg, 51%) as a colourless oil, R_f 0.29 (80:20 petrol–EtOAc); $[\alpha]_D^{20}$ +6.4 (*c* 1.00 in chloroform); δ_H (500 MHz, $CDCl_3$) 8.07-8.03 (1H, m, nosyl 3-H), 7.74-7.68 (4H, m, Ar), 7.66-7.62 (1H, m, nosyl 5-H), 7.35 (2H, d, *J* 8.1, tosyl 3-H and 5-H), 5.90 (1H, s, 4''-H), 5.71 (1H, br. s, 4-H), 5.61-5.59 (1H, m, 4'-H), 4.75 (4H, s, 2''-H and 5''-H), 4.72-4.68 (1H, m, 5-H), 4.52 (1H, ddd, *J* 12.8, 5.6 and 1.7, 2-H_A), 4.46-4.43 (1H, m, 2-H_B), 4.43-4.37 (1H, m, 3'-H), 4.35 (1H, d, *J* 5.6, C*H*OMe), 4.14-4.12 (1H, m, 6'-H_A), 3.96-3.91 (3H, m, 3-CCH_2N and 6'-H_B), 3.89 (1H, dd, *J* 12.8 and 5.6, 2'-H_A), 3.42-3.38 (5H, m, OMe and $CF_2CH_2CH_2$), 3.13 (1H, dd, *J* 12.8 and 7.7, 2'-H_B) and 2.50-2.37 (5H, m, tosyl Me and CF_2CH_2); δ_C (75 MHz, $CDCl_3$) 148.8 (nosyl 2-C), 144.6 (tosyl 4-C), 138.5 (3-C), 136.4 (3''-C), 136.1 (tosyl 1-C), 134.2 (nosyl 1-C), 132.3, 132.1 (nosyl 3-C and 4-C), 131.3 (tosyl 3-C and 5-C), 130.4 (nosyl 6-C), 129.7 (5'-C), 127.6 (tosyl 2-C and 6-C), 125.7 (4-C), 125.3 (4'-C), 124.6 (nosyl 5-C), 123.2 (4''-C), 105.6 (*C*HOMe), 87.34 (5-C), 77.6 (2''-C or 5''-C), 76.1 (2-C), 75.0 (2''-C or 5''-C), 69.6 (3'-C), 56.6 (OMe), 47.3 (2'-C), 46.3 (3-CCH_2N), 45.1 (6'-C), 40.7 ($CF_2CH_2CH_2$), 31.2 (t, $^2J_{C-F}$ 21.5, CF_2CH_2) and 21.9 (tosyl Me); ν_{max}/cm^{-1} (film) 2918, 2850, 1751, 1597, 1546 and 1455; *m/z* (ESI$^+$) 1116.1 (M +Na^+ 100%); found MNa^+ 1116.1465, $C_{39}H_{36}F_{17}N_3O_{10}S_2$ requires *MNa* 1116.1468.

(*S*)-5-(2',5'-dihydrofuran-3'-yl)-1-(2-nitrophenylsulfonyl)-1,2,3,6-tetrahydropyridin-3-ol 29 (R = H)

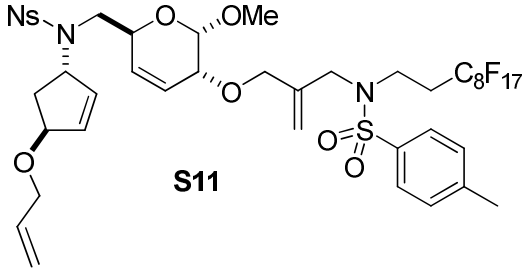


29

Following general procedure **D**, sulfonamide **29** (R = R'^{F}) (19 mg, 0.012 mmol) and 3% trifluoroacetic acid gave the crude product after 16 hours. Purification by Fluorous Solid Phase Extraction; 2 g cartridge, loading with <400 μL DMF, with 80:20 MeOH–H_2O, gave the organic fraction. Further purification by flash chromatography, eluting with 70:30 petrol–EtOAc, gave the *alcohol* **29** (R = H) (4 mg, 67%) as a colourless oil, R_f 0.47 (EtOAc); $[\alpha]_D^{20}$ +30.0 (*c* 1.00 in chloroform); δ_H (500 MHz, $CDCl_3$) 8.10-8.07 (1H, m, nosyl 3-H), 7.77-7.70 (2H, m, nosyl 4-H and 6-H), 7.67-7.64 (1H, m, nosyl 5-H), 5.97 (1H, br. s, 4'-H), 5.66-5.63 (1H, m, 4-H), 4.82-4.72 (4H,

m, 2'-H and 5'-H), 4.34-4.30 (1H, m, 3-H), 4.22 (1H, br. d, *J* 16.4, 6-H_A), 3.93 (1H, br. d, *J* 16.4, 6-H_B), 3.51 (1H, dd, *J* 13.1 and 4.4, 2-H_A), 3.45 (1H, dd, *J* 13.1 and 3.9, 2-H_B) and 2.03 (1H, br. s, OH); δ_C (75 MHz, $CDCl_3$) 148.2 (nosyl 2-C), 135.9 (3'-C), 133.9 (nosyl 1-C), 131.7, 131.4 (nosyl 3-C and 4-C), 131.1 (nosyl 6-C), 129.8 (5-C), 124.9 (4-C), 124.2 (nosyl 5-C), 123.3 (4'-C), 76.5 (2'-C or 5'-C), 74.5 (2'-C or 5'-C), 63.2 (3-C), 49.5 (2-C) and 44.7 (6-C); ν_{max}/cm^{-1} (film) 3344 (br), 2928, 2918, 2849, 1746, 1567 and 1541; *m/z* (ESI^+) 370.1 ($[M + NH_4]^+$ 100%), 375.1.2 ($[M + Na]^+$ 68%); found MNa^+ 375.0626, $C_{15}H_{16}N_2O_6S$ requires *MNa* 375.0621.

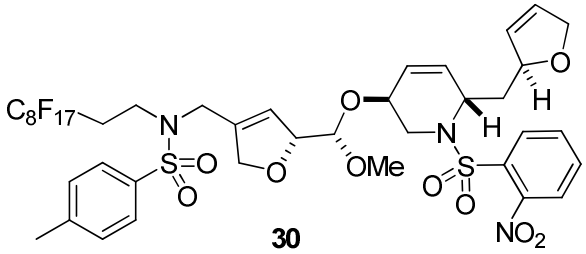
_N_-[(1*S*,4*S*)-4-(Alloxy)cyclopent-2-enyl]-_N_-[{(2'*S*,5'*R*,6'*S*)-5'-[2-{[_N_-(3,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)-4-methylphenylsulfonamido]methyl}allyloxy]-6'-methoxy-5',6',-dihydro-2*H*-pyran-2'-yl}methyl]-2-nitrobenzenesulfonamide S11



Following general procedure **B**, diethyl azodicarboxylate (72 μL, 0.39 mmol), sulfonamide **18** (100 mg, 0.10 mmol) and alcohol **23** (55 mg, 0.39 mmol) gave the crude product after 3 hours. Purification by Fluorous Solid Phase Extraction; 2 g cartridge, loading with <200 μL dichloromethane, eluting with 80:20 MeOH–H_2O followed by MeOH , gave the fluorous fraction, the *sulfonamide* **S11** (110 mg, 98%, 83% purity by HPLC) as a colourless foam, R_f 0.83 (40:60 petrol–EtOAc); δ_H (500 MHz, $CDCl_3$) 8.11-8.08 (1H, m, nosyl 3-H), 7.74-7.63 (5H, m, Ar), 7.34 (2H, d, *J* 8.1, tosyl 3-H and 5-H), 6.11-6.08 (1H, m, 3-H), 5.89 (1H, ddd, *J* 17.1, 10.8 and 5.6, allyl 2-H), 5.80-5.77 (1H, m, 2-H), 5.74 (2H, s, 3'-H and 4'-H), 5.30 (1H, s, $NCH_2C=CH_A$), 5.27 (1H, app. dq, *J* 17.2 and 1.4, allyl 3-H_A), 5.22-5.15 (2H, m, allyl 3-H_B and 1-H), 5.14 (1H, s, $NCH_2C=CH_B$), 4.82 (1H, d, *J* 3.8, 6'-H), 4.70-4.66 (1H, m, 4-H), 4.32-4.28 (1H, m, 2'-H), 4.05-3.92 (5H, m, allyl 1-H, 5'-$COCH_2$ and 5'-H), 3.82 (1H, d, *J* 15.0, NCH_ACCH_2), 3.78 (1H, d, *J* 15.0, NCH_BCCH_2), 3.39 (3H, s, OMe), 3.39-3.35 (2H, m, $CF_2CH_2CH_2$), 3.27 (1H, dd, *J* 15.4 and 3.7, 2'-CCH_A), 3.17 (1H, dd, *J* 15.4 and 8.6, 2'-CCH_B), 2.44 (3H, s, tosyl Me), 2.43-2.32 (2H, m, CF_2CH_2), 2.31-2.24 (1H, m, 5-H_A) and 2.15 (1H, ddd, *J* 14.8, 8.3 and 2.9, 5-H_B); δ_C (75 MHz, $CDCl_3$) 148.6 (nosyl 2-C), 144.4 (tosyl 4-C), 141.0 (5'-$COCH_2C$), 136.9 (2-C or 3-C), 136.1 (tosyl 1-C), 135.2 (allyl 2-C), 134.5 (2-C or 3-C), 134.2 (nosyl 1-C), 134.0 (nosyl 4-C), 132.0 (nosyl 3-C), 131.8 (nosyl 6-C), 130.3 (tosyl 3-C and 5-C), 127.64 (3'-C), 127.57 (tosyl 2-C and 6-C), 125.6 (4'-C), 124.6 (nosyl 5-C), 117.49 (5'-$COCH_2C=CH_2$ or allyl 3-C), 117.46 (5'-$COCH_2C=CH_2$ or allyl 3-C),

97.1 (6'-C), 83.0 (4-C), 72.2 (5'-C), 70.6 (allyl 1-C), 69.7 (5'-CO*C*H_2), 68.6 (2'-C), 64.9 (1-C); 56.1 (OMe), 52.1 (N*C*H_2CH_2), 48.9 (2'-C*C*H_2), 40.8 (CF_2CH_2*C*H_2), 36.2 (5-C), 31.0 (CF_2*C*H_2) and 21.8 (tosyl Me); ν_{max}/cm^{-1} 3080, 2986, 2929, 2862, 2252, 1746, 1597 and 1545; *m/z* (ESI^+) 1158.2 ($[M + Na]^+$ 100%); found MNa^+ 1158.1947, $C_{42}H_{42}F_{17}N_3O_{10}S_2$ requires *MNa* 1158.1932.

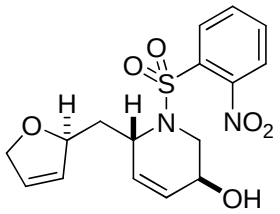
_N_-[{(*R*)-5-[(*S*)-{(3'*S*,6'*S*)-6'-[{(*S*)-2'',5''-dihydrofuran-2''-yl}methyl]-1'-(2-nitrophenylsulfonyl)-1',2',3',6'-tetrahydropyridin-3'-yloxy}(methoxy)methyl]-2,5-dihydrofuran-3-yl}methyl]-*N*-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptafluorodecyl)-4-methylbenzenesulfonamide 30 (R = R'^{F})



30

Following general procedure **C**, **HG II** (6 × 3 mg, 6 × 5 mol%) and sulfonamide **S11** (110 mg, 0.097 mmol) gave the crude product after 7 days. Purification by Fluorous Solid Phase Extraction; 2 g cartridge loading with <200 μL dichloromethane, eluting with 80:20 MeOH–H_2O followed by MeOH , gave the fluorous fraction (93 mg, 87%, 69% purity by HPLC). Further purification by flash chromatography, eluting with 70:30 petrol–EtOAc, gave the *sulfonamide* **30** (R = R'^{F}) (93 mg, 87%) as a colourless oil, R_f 0.75 (50:50 petrol–EtOAc); δ_H (500 MHz, $CDCl_3$) 8.08 (1H, dd, *J* 7.5 and 1.8, nosyl 3-H), 7.72-7.57 (5H, m, Ar), 7.35 (2H, dd, *J* 8.1, tosyl 3-H and 5-H), 5.87-5.83 (2H, m, 3''-H and 4''-H), 5.79-5.75 (1H, m, 4'-H), 5.74-5.69 (2H, m, 5'-H and 4-H), 4.77-4.71 (1H, m, 2''-H), 4.69-4.65 (1H, m, 5-H), 4.62-4.55 (2H, m, 6'-H and 5''-H_A), 4.51-4.45 (2H, m, 5''-H_B and 2-H_A), 4.42-4.37 (1H, m, 2-H_B), 4.29 (1H, dd, *J* 5.6, 5-CC*H*OMe), 4.16 (1H, dd, *J* 13.8 and 6.2, 2'-H_A), 4.13-4.08 (1H, m, 3'-H), 3.94 (2H, s, 3-CCH_2N), 3.48-3.35 (2H, m, and CF_2C*H*$_2$), 3.34 (3H, s, OMe), 3.02 (1H, dd, *J* 13.8 and 9.6, 2'-H_B), 2.51-2.37 (5H, m, CF_2CH_2C*H*$_2$ and tosyl Me), 1.85 (1H, ddd, *J* 14.2, 7.9 and 3.4, 6'-CC*H*$_A$), 1.75-1.66 (1H, m, 6'-CC*H*$_B$); δ_C (75 MHz, $CDCl_3$) 148.3 (nosyl 2-C), 144.6 (tosyl 4-C), 138.3 (3-C), 136.1 (tosyl 1-C), 134.2 (nosyl 1-C), 133.9 (nosyl 4-C), 132.0 (nosyl 3-C), 131.6 (nosyl 6-C), 130.8 (3''-C or 4''-C), 130.4 (tosyl 3-C and 5-C); 129.7 (4'-C or 5'-C), 128.4 (4'-C or 5'-C); 127.55 (tosyl 2-C and 6-C), 127.4 (3''-C or 4''-C), 125.9 (4-C), 124.3 (nosyl 5-C), 106.0 (5-C*C*HOMe), 87.4 (5-C), 83.1 (2''-C), 76.0 (2-C), 75.2 (5''-C), 69.0 (3'-C), 56.3 (OMe), 52.7 (6'-C), 46.1 (3-C*C*H_2N), 43.4 (2'-C), 40.6 (CF_2*C*H_2), 40.4 (6'-C*C*H_2), 31.2 (CF_2*C*H_2) and 21.9 (tosyl Me); ν_{max}/cm^{-1} 3093, 2986, 2929, 2854, 2254, 1597 and 1546; *m/z* (ESI^+) 1130.2 ($[M + Na]^+$ 100%); found MNa^+ 1130.1605, $C_{40}H_{38}F_{17}N_3O_{10}S_2$ requires *MNa* 1130.1619.

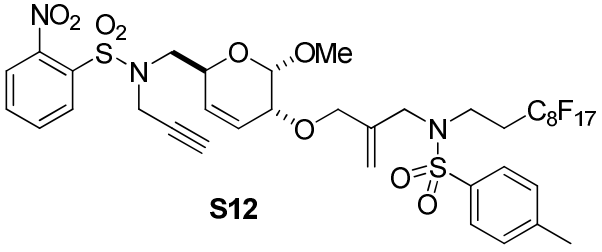
(3*S*)-6*S*-[{(2'*S*)-2',5'-dihydrofuran-2'-yl}methyl]-1-(2-nitrophenylsulfonyl)-1,2,3,6-tetrahydropyridin-3-ol 30 (R = H)



30

Following general procedure **D**, sulfonamide **30** (R = R'^{F}) (47 mg, 0.042 mmol) and 3% trifluoroacetic acid gave the crude product after 16 hours. Purification by Fluorous Solid Phase Extraction; 2 g cartridge loading with <400 μL DMF, with 80:20 MeOH–H_2O, gave the organic fraction. Further purification by flash chromatography, eluting with 70:30 petrol–EtOAc, gave the *alcohol* **30** (R = H) (6 mg, 37%) as a colourless oil, R_f 0.75 (EtOAc); $[\alpha]_D^{20}$ −126.8 (*c* 1.00 in chloroform); δ_H (500 MHz, $CDCl_3$) 8.11-8.06 (1H, m, nosyl 3-H), 7.71-7.64 (2H, m, nosyl 4-H and 6-H), 7.62-7.59 (1H, m, nosyl 5-H), 5.90-5.84 (2H, m, 4-H and 3'-H), 5.76-5.70 (2H, m, 5-H and 4'-H), 4.80-4.73 (1H, m, 2'-H), 4.63-4.54 (2H, m, 6-H and 5'-H_A), 4.51-4.45 (1H, m, 5'-H_B), 4.22-4.14 (1H, m, 3-H), 4.10 (1H, dd, *J* 13.8 and 6.2, 2-H_A), 2.99 (1H, dd, *J* 13.8 and 9.8, 2-H_B), 1.87 (1H, ddd, *J* 14.2, 7.6 and 3.4, 6-CC*H*$_A$), 1.78-1.69 (2H, m, 6-CC*H*$_B$ and OH); δ_C (75 MHz, $CDCl_3$) 147.8 (nosyl 2-C), 133.8 (nosyl 1-C), 133.5 (nosyl 4-C), 131.6 (nosyl 6-C), 131.2 (nosyl 3-C), 130.3 (4-C or 3'-C), 129.4 (5-C or 4'-C), 129.3 (5-C or 4'-C), 127.0 (4-C or 3'-C), 124.1 (nosyl 5-C), 82.8 (2'-C), 74.8 (5'-C), 62.8 (3-C), 52.3 (6-C), 45.0 (2-C), 40.2 (6-C*C*H$_2$); ν_{max}/cm^{-1} (film) 3390 (br), 3399 (br), 2921, 2853, 1590, 1544, 1454 and 1439; *m/z* (ESI$^+$) 389.1 ([M + Na]$^+$ 100%); found MNa$^+$ 389.0768, $C_{16}H_{18}N_2O_6S$ requires *MNa* 389.0778.

***N*-{[(2*S*,5*R*,6*S*)-5-{2-[(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)-4-methylphenylsulfonamido]methyl}allyloxy)-6-methoxy-5,6-dihydro-2*H*-pyran-2-yl]methyl}-2-nitro-*N*-(prop-2'-ynyl)benzenesulfonamide S12**

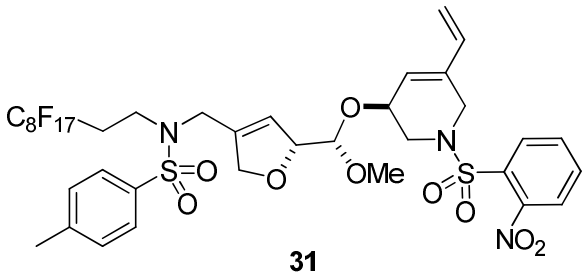


S12

Following general procedure **B**, diethyl azodicarboxylate (72 μL, 0.39 mmol), sulfonamide **18** (100 mg, 0.10 mmol) and propargyl alcohol **24** (23 μL, 0.39 mmol) gave the crude product after 3 hours.

Purification by Fluorous Solid Phase Extraction; 2 g cartridge, loading with <200 μL dichloromethane, eluting with 80:20 MeOH–H_2O followed by MeOH , gave the fluorous fraction, *sulfonamide* **S12** (102 mg, 98%, 87% purity by HPLC) as a colourless foam, R_f 0.83 (40:60 petrol–EtOAc); δ_H (500 MHz, $CDCl_3$) 8.08 (1H, d, *J* 7.5, nosyl 3-H), 7.75-7.62 (5H, m, Ar), 7.34 (2H, d, *J* 7.8, tosyl 3-H and 5-H), 5.77 (1H, d, *J* 10.8, 3-H), 5.74 (1H, d, *J* 10.8, 4-H), 5.30 (1H, s, 5-$COCH_2C=CH_A$), 5.14 (1H, s, 5-$COCH_2C=CH_B$), 4.85 (1H, d, *J* 3.3, 6-H), 4.46-4.30 (3H, m, 1'-H and 2-H); 4.03-4.01 (3H, m, 5-$COCH_2$ and 5-H), 3.82 (1H, d, *J* 15.2, NCH_ACCH_2), 3.78 (1H, d, *J* 15.2, NCH_BCCH_2), 3.67 (1H, dd, *J* 15.1 and 2.1, 2-CCH_A), 3.55 (1H, dd, *J* 15.1 and 7.7, 2-CCH_B), 3.43 (3H, s, OMe), 3.41-3.34 (2H, m, $CF_2CH_2CH_2$), 2.44 (3H, s, tosyl Me), 2.44-2.32 (2H, m, CF_2CH_2), 2.16 (1H, t, *J* 2.4, 3'-H); δ_H (75 MHz, $CDCl_3$) 148.6 (nosyl 2-C), 144.4 (tosyl 4-C), 140.9 (5-$COCH_2C$), 136.1 (tosyl 1-C), 134.2 (nosyl 1-C), 133.5 (nosyl 6-C), 132.0 (nosyl 3-C), 131.6 (nosyl 4-C), 130.3 (tosyl 3-C and 5-C), 127.6 (tosyl 2-C and 6-C), 127.4 (3-C), 126.1 (4-C), 124.5 (nosyl 5-C), 117.5 (5-$COCH_2C=CH_2$), 97.1 (6-C), 77.6 (3'-C), 74.2 (2'-C), 72.1 (5-C), 69.7 (5-$COCH_2$), 68.8 (2-C), 56.2 (OMe), 52.1 (NCH_2CCH_2), 50.3 (2-CCH_2), 40.8 (CF_2CH_2), 38.9 (1'-C), 31.0 ($CF_2CH_2CH_2$), 21.8 (tosyl Me); ν_{max}/cm^{-1} 3289, 2989, 2928, 2869, 1737, 1597 and 1546; *m/z* (ES^+) 1074.1 ($[M + Na]^+$ 100%) and 1069.2 ($[M + NH_4]^+$ 40%); found MNa^+ 1074.1316, $C_{37}H_{34}F_{17}N_3O_9S_2$ requires *MNa* 1074.1357.

_N_-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)-_N_-[{(_R_)-5-[(_S_)-methoxy{(_S_)-1'-(nitrophenylsulfonyl)-5'-vinyl-1',2',3',6'-tetrahydropyridin-3'-yloxy}methyl]-2,5-dihydrofuran-3-yl}methyl]-4-methylbenzenesulfonamide 31 (R = R'^{F})

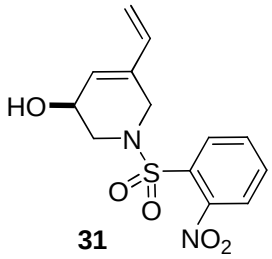


31

Sulfonamide **S12** (110 mg, 0.10 mmol) was dissolved in dichloromethane (60 mL) and the solution was de-gassed. Ethylene was bubbled through the solution for 10 minutes and the solution was heated at reflux under an atmosphere of ethylene. Following general procedure **C** under an atmosphere of ethylene, **HG II** (3 mg, 5 mol%) gave the crude product after 4 days. Purification by Fluorous Solid Phase Extraction; 2 g cartridge, loading with <200 μL DCM, eluting with 80:20 MeOH–H_2O followed by MeOH, gave the fluorous fraction (83%, 65% purity by HPLC), which was further purified by flash chromatography, eluting with 75:25 petrol–EtOAc, to give the *sulfonamide* **31** (R = R'^{F}) (58 mg, 53%) as a colourless oil, R_f 0.73 (50:50 petrol–EtOAc),

$[\alpha]_D^{20}$ +29.2 (*c* 2.00 in chloroform); δ_H (500 MHz, $CDCl_3$) 8.06-8.02 (1H, m, nosyl 3-H), 7.74-7.77 (4H, m, Ar), 7.65-7.62 (1H, m, nosyl 5-H), 7.35 (2H, d, *J* 8.0, tosyl 3-H and 5-H), 6.29 (1H, dd, *J* 17.8 and 11.1, 5'-CC*H*), 5.86 (1H, br. s, 4'-H), 5.71 (1H, br. s, 4-H), 5.20 (1H, d, *J* 17.8, 5'-CCHCH_A), 5.14 (1H, d, *J* 11.1, 5'-CCHCH_B), 4.73-4.69 (1H, m, 5-H), 4.54-4.49 (1H, m, 2-H_A), 4.45-4.40 (1H, m, 2-H_B), 4.40-4.35 (2H, m, 5-CC*H*OMe and 3'-H), 4.09 (1H, d, *J* 16.5, 6'-H_A), 3.93 (2H, s, 3-CCH_2N), 3.90-3.83 (2H, m, 6'-H_B and 2'-H_A), 3.44-3.38 (5H, m, OMe and $CF_2CH_2CH_2$), 3.13 (1H, dd, *J* 12.7 and 7.4, 2-H_B) and 2.50-2.38 (5H, m, tosyl Me and CF_2CH_2); δ_C (75 MHz, $CDCl_3$) 148.8 (nosyl 2-C), 144.6 (tosyl 4-C), 138.4 (3-C), 136.1 (tosyl 1-C), 135.7 (4'-C), 135.0 (5'-C), 134.2 (nosyl 1-C), 132.3 (nosyl 4-C), 132.1 (nosyl 3-C), 131.2 (nosyl 6-C), 130.4 (tosyl 3-C and 5-C), 128.0 (5'-C*C*H), 127.6 (tosyl 2-C and 6-C), 125.8 (4-C), 124.6 (nosyl 5-C), 114.7 (5'-CCH*C*H_2), 105.7 (5-C*C*HOMe), 87.4 (5-C), 76.1 (2-C), 69.9 (3'-C), 56.6 (OMe), 47.5 (6'-C), 46.3 (3-C*C*H_2N), 44.3 (2'-C), 40.6 (CF_2*C*H_2), 31.2 (CF_2CH_2*C*H_2) and 21.9 (tosyl Me); ν_{max}/cm^{-1} 3094, 2917, 2854, 2255, 1598 and 1546; *m/z* (ES^+) 1074.1 ($[M + Na]^+$ 100%); found MNa^+ 1074.1334, $C_{37}H_{34}F_{17}N_3O_9S_2$ requires *MNa* 1074.1357

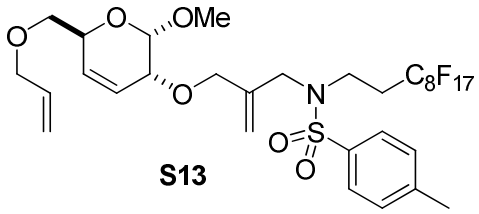
(*S*)-1-(2-nitrophenylsulfonyl)-5-vinyl-1,2,3,6-tetrahydropyridin-3-ol 31 (R = H)



31

Following general procedure **D**, the sulfonamide **31** (R = R'^{F}) (30 mg, 29 μmol) and 3% trifluoroacetic acid gave the crude product after 16 hours. Purification by Fluorous Solid Phase Extraction; 2 g cartridge loading with <400 μL DMF, with 80:20 MeOH–H_2O, gave the organic fraction. Further purification by flash chromatography, eluting with 50:50 petrol–EtOAc, gave the *alcohol* **31** (R = H) (2 mg, 23%) as a colourless oil, R_f 0.78 (petrol–EtOAc); $[\alpha]_D^{20}$ +8.0 (*c* 0.25 in chloroform); δ_H (500 MHz, $CDCl_3$) 8.09-8.06 (1H, m, nosyl 3-H), 7.76-7.70 (2H, m, nosyl 4-H and nosyl 6-H), 7.66-7.63 (1H, m, nosyl 5-H), 6.31 (1H, dd, *J* 17.9 and 11.0, vinyl 1-H), 5.92-5.89 (1H, m, 4-H), 5.27 (1H, d, *J* 17.9, vinyl 2-H_A), 5.19 (1H, d, *J* 11.0, vinyl 2-H_B), 4.33-4.27 (1H, m, 3-H), 4.18 (1H, d, *J* 16.7, 6-H_A), 3.85 (1H, d, *J* 16.7, 6-H_B), 3.53 (1H, dd, *J* 13.0 and 4.1, 2-H_A), 3.42 (1H, dd, *J* 13.0 and 3.6, 2-H_B), 1.97 (1H, br. d, *J* 8.4, OH); δ_C (75 MHz, $CDCl_3$) 148.4 (nosyl 2-C), 135.34 (vinyl 1-C), 135.25 (nosyl 1-C), 134.0 (nosyl 6-C), 131.7 (nosyl 3-C), 131.6 (5-C), 131.2 (nosyl 4-C), 127.6 (4-C), 124.3 (nosyl 5-C), 115.0 (vinyl 2-C), 63.6 (3-C), 49.9 (2-C), 44.0 (6-C); ν_{max}/cm^{-1} (film) 3380 (br), 3095 (br), 3095, 2918, 2850, 1543, 1453 and 1439; *m/z* (ESI^+) 333.1 ($[M + Na]^+$ 100%); found MNa^+ 333.0501, $C_{13}H_{14}N_2O_5S$ requires *MNa* 333.0516.

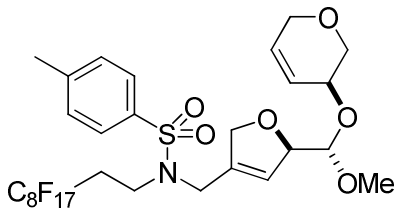
***N*-(2-{[(2*S*,3*R*,6*S*)-6-(Alloxymethyl)-2-methoxy-3,6-dihydro-2*H*-pyran-3-yloxy]methyl}allyl)-*N*-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)-4-methylbenzenesulfonamide S13**



S13

Sodium hydride (9.6 mg, 0.24 mmol) was added portionwise to a stirred solution of alcohol **1** (100 mg, 0.12 mmol) in tetrahydrofuran (2 mL) at 0 °C. After 30 minutes, allyl bromide (21 μL, 0.24 mmol) was added and the reaction mixture was allowed to warm to room temperature and stirred for 16 hours. Methanol (2 mL) was subsequently added and the solvents were removed under reduced pressure. Purification by Fluorous Solid Phase Extraction; 2 g cartridge, loading with <400 μL DMF, eluting with 80:20 MeOH–H_2O followed by MeOH, gave the fluorous fraction, the *sulfonamide* **S13** (75 mg, 72%, 93% purity by HPLC) as a colourless oil, R_f 0.80 (70:30 petrol–EtOAc); δ_H (500 MHz, $CDCl_3$) 7.70 (2H, d, *J* 8.1, tosyl 2-H and 6-H), 7.33 (2H, d, *J* 8.1, tosyl 3-H and 5-H), 5.92 (1H, ddt, *J* 17.1, 10.3 and 5.6, allyl 2-H), 5.79 (1H, app. d, *J* 10.7, 5-H), 5.75 (1H, app. d, *J* 10.7, 4-H), 5.30 (1H, br. s, $NCH_2C{=}CH_A$), 5.28 (1H, app. dq, *J* 17.1 and 1.7, allyl 3-H_A), 5.20 (1H, app. dq, *J* 10.3 and 1.7, allyl 3-H_B), 5.13 (1H, br. s, $NCH_2C{=}CH_B$), 5.00 (1H, br. d, *J* 3.9, 2-H), 4.35-4.30 (1H, m, 6-H), 4.10-4.07 (1H, m, 3-H), 4.07-4.04 (2H, m, allyl 1-H), 4.03 (2H, br. s, 3-$COCH_2$), 3.84 (1H, app. d, *J* 15.0, NCH_ACCH_2), 3.77 (1H, app. d, *J* 15.0, NCH_BCCH_2), 3.52 (3H, s, OMe), 3.51-3.49 (2H, m, 6'-CCH_2) and 3.41-3.35 (2H, m, $CF_2CH_2CH_2$) and 2.44-2.32 (5H, m, tosyl Me and CF_2CH_2); δ_C (75 MHz, $CDCl_3$) 144.3 (tosyl 4-C), 141.0 (NCH_2CCH_2), 136.2 (tosyl 1-C), 134.9 (allyl 2-C), 130.3 (tosyl 3-C and 5-C), 128.0 (5-C), 127.6 (tosyl 2-C and 6-C), 125.2 (4-C), 117.7 and 117.3 (allyl 3-C and $NCH_2C{=}CH_2$), 97.3 (2-C), 72.9 (allyl 1-C), 72.5 (3-C), 72.2 (6-CCH_2), 69.7 (3-$COCH_2$), 68.4 (6-C), 56.2 (OMe), 52.0 (NCH_2CCH_2), 40.8 ($CF_2CH_2CH_2$), 31.1 (t, $^2J_{C-F}$ 21.8, CF_2CH_2), 21.9 (tosyl Me); ν_{max}/cm^{-1} (film); 2981, 2926, 2861, 1598 and 1494; *m/z* (ESI^+) 887.2 ($[M + NH_4]^+$ 100%); found MNa^+ 892.1559, $C_{31}H_{32}F_{17}NO_6S$ requires *MNa* 892.1577.

***N*-{[(*R*)-5-{(*S*)-[(*S*)-3',6'-dihydro-2*H*-pyran-3'-yloxy](methoxy)methyl}-2,5-dihydrofuran-3-yl]methyl}-*N*-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptafluorodecyl)-4-methylbenzenesulfonamide 32** (R = R'^F)

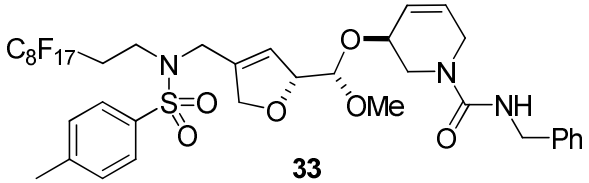


32

Following general procedure **C**, **HG II** (2 × 2 mg, 2 × 5 mol%) and sulfonamide (45 mg, 0.05 mmol) gave the crude product after 2 days. Purification by Fluorous Solid Phase Extraction; loading with <400 μL DMF, eluting with 80:20 MeOH–H_2O followed by MeOH, gave the fluorous fraction. Further purification by flash chromatography, eluting with 80:20 petrol–EtOAc, gave the *sulfonamide* **32** (R = R'^{F}) (22 mg, 51%) as a colourless oil, R_f 0.45 (80:20 petrol–EtOAc); $[\alpha]_D^{20}$ +12.4 (*c* 1.00 in chloroform); δ_H (500 MHz, $CDCl_3$) 7.69 (2H, d, *J* 8.2, tosyl 2-H and 6-H), 7.34 (2H, d, *J* 8.2, tosyl 3-H and 5-H), 5.95-5.92 (2H, m, 4'-H and 5'-H), 5.77-5.73 (1H, m, 4-H), 4.81-4.74 (1H, m, 5-H), 4.51 (1H, ddq, *J* 12.8, 5.6 and 1.8, 2-H_A), 4.47-4.39 (1H, m, 2-H_B), 4.36 (1H, d, *J* 5.1, C*H*OMe), 4.15-4.06 (3H, m, 3'-H and 6'-H), 3.95-3.90 (2H, m, 3-CCH_2), 3.84 (1H, dd, *J* 11.5 and 3.9, 2'-H_A), 3.75 (1H, dd, *J* 11.5 and 4.6, 2'-H_B), 3.43-3.38 (5H, m, OMe and $CF_2CH_2CH_2$) and 2.46-2.45 (5H, m, tosyl Me and CF_2CH_2); δ_C (75 MHz, $CDCl_3$) 144.5 (tosyl 4-C), 138.1 (3-C), 136.1 (tosyl 1-C), 130.4 (tosyl 3-C and 5-C), 130.3 (5'-C), 127.5 (tosyl 2-C and 6-C), 126.1 (4-C), 125.7 (4'-C), 105.2 (*C*HOMe), 87.4 (5-C), 76.1 (2-C), 68.6 (3'-C), 68.5 (2'-C), 65.5 (6'-C), 56.3 (OMe), 46.3 (3-C*C*H_2N), 40.6 ($CF_2CH_2CH_2$), 31.3 (CF_2CH_2, t, $^2J_{C-F}$ 21.4) and 21.9 (tosyl Me); ν_{max}/cm^{-1} (film) 3093, 2956, 2924, 1741, 1644 and 1597 *m/z* (ESI$^+$) 864.1 (M + Na$^+$ 100%); found MNa$^+$ 864.1262, $C_{29}H_{28}F_{17}NO_6S$ requires *MNa* 864.1258.

Further functionalisation of metathesis products

(*S*)-*N*-Benzyl-5-[(*S*)-[(*R*)-4'-{[*N*-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)-4-methylsulfonamido]methyl}-2',5'-dihydrofuran-2'-yl](methoxy)methoxy]-5,6-dihydropyridine-1(2*H*)-carboximide 33 (R = R'^{F})

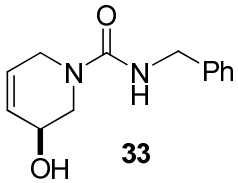


33

Thiophenol (5.3 μL, 0.048 mmol) was added dropwise to a solution of sulfonamide **26** (25 mg, 0.024 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (7.3 μL, 0.048 mmol) in acetonitrile (1.0 mL) and stirred at room temperature for 1 hour. Benzyl isocyanate (32 mg, 0.24 mmol) was added and

the reaction mixture was stirred for a further 2 hours. The solution was concentrated under nitrogen and purified by Fluorous Solid Phase Extraction; 2 g cartridge loading with <400 μL DMF, eluting with 80:20 MeOH–H_2O followed by MeOH to give the fluorous fraction, the *urea* **33** (R = R'^{F}) (20 mg, 87%, >90% purity by ^{1}H NMR spectroscopy) as a colourless oil, R_f 0.31 (8:2 petrol–EtOAc); δ_H (500 MHz, $CDCl_3$) 7.65-7.61 (1H, m, Ph), 7.60 (2H, d, *J* 8.1, tosyl 2-H and 6-H), 7.27 (2H, d, *J* 8.1, tosyl 3-H and 5-H), 7.26-7.14 (4H, m, Ph), 5.94-5.85 (2H, m, 3-H and 4-H), 5.84-5.80 (1H, m, NH), 5.57 (1H, br. s, 3'-H), 4.54-4.49 (1H, m, 2'-H), 4.37 (1H, dd, *J* 14.6 and 5.6, NCH_APh), 4.32-4.21 (3H, m, 5'-H_A, 2-H_A and NCH_BPh), 4.12 (1H, d, *J* 6.5, C*H*OMe), 3.98-3.94 (1H, m, 5-H), 3.91-3.86 (1H, m, 5'-H_B), 3.79 (1H, d, *J* 15.5, 4'-CCH_A), 3.72 (1H, d, *J* 15.5, 4'-CCH_B), 3.67 (1H, dd, *J* 14.3 and 2.8, 6-H_A), 3.53 (1H, dd, *J* 18.3 and 1.6, 2-H_B), 3.37-3.26 (6H, m, OMe, 6-H_B and $CF_2CH_2CH_2$), 2.37 (3H, s, tosyl Me), 2.36-2.25 (2H, m, CF_2CH_2); δ_C (75 MHz, $CDCl_3$) 158.2 (C=O), 144.2 (tosyl 4-C), 139.8 (phenyl 1-C), 137.4 (4'-C), 135.6 (tosyl 1-C), 130.3 (3-C), 130.0 (tosyl 3-C and 5-C), 128.5 (Ph), 127.9 (Ph), 127.2 (Ph), 127.1 (tosyl 2-C and 6-C), 125.5 (3'-C), 124.8 (4-C), 106.9 (*C*HOMe), 87.3 (2'-C), 75.1 (5'-C), 72.2 (5-C), 54.7 (OMe), 47.2 (6-C), 45.9 (4'-C*C*H_2N), 45.1 (N*C*H_2Ph), 43.5 (2-C), 40.3 ($CF_2CH_2CH_2$), 30.8 (CF_2CH_2), 21.6 (tosyl Me); ν_{max}/cm^{-1} (film) 2948, 2925, 2854, 1634 and 1538.

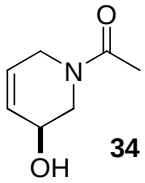
(*S*)-*N*-Benzyl-5-hydroxy-5,6-dihydropyridine-1(2*H*)-carboximide 33 (R = H)



33

Following general procedure **D**, sulfonamide **33** (R = R'^{F}) (13 mg, 0.012 mmol) and 3% trifluoroacetic acid gave a crude product after 16 hours. Purification by Fluorous Solid Phase Extraction; 2 g cartridge, loading with <400 μL DMF, with 80:20 MeOH–H_2O, gave the organic fraction. Further purification by flash chromatography, eluting with 99:1 DCM–MeOH, gave the *alcohol* **33** (R = H) (3.4 mg, 82%) as a colourless oil, R_f 0.27 (EtOAc); $[\alpha]_D^{20}$ +36.0 (*c* 1.00 in chloroform); δ_H (500 MHz, $CDCl_3$) 7.35-7.25 (5H, m, Ph), 5.99-5.94 (1H, m, 4-H), 5.86 (1H, dt, *J* 10.0 and 3.0, 3-H), 4.93 (1H, br. s, N*H*), 4.48-4.39 (2H, m, NHCH_2Ph), 4.23-4.19 (1H, m, 5-H), 4.11 (1H, app. d, *J* 17.3, 2-H_A), 3.71 (1H, app. d, *J* 17.3, 2-H_B), 3.62 (1H, dd, *J* 13.5 and 3.2, 6-H_A), 3.47 (1H, dd, *J* 13.5 and 2.6, 6-H_B); δ_C (75 MHz, $CDCl_3$) 198.2 (C=O), 128.7 (Ph), 128.1 (phenyl 1-C), 127.83 (4-C), 127.79 (Ph), 127.76 (3-C), 127.4 (phenyl 4-C), 63.7 (5-C), 48.2 (6-C), 45.1 (NH*C*H_2Ph) and 43.8 (2-C); ν_{max}/cm^{-1} (film) 3344 (br),3061, 3035, 2923, 2852, 1682, 1680, 1646 and 1537; *m/z* (ESI$^+$) 255.1 ([M + Na]$^+$ 100%); found MNa^+ 255.1096, $C_{13}H_{16}N_2O_2$ requires *MNa* 255.1104.

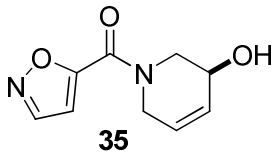
(*S*)-5-Hydroxy-5,6-dihydropyridine-1(2*H*)-acetate 34 (R = H)



34

Following general procedure D, thiophenol (14 μL, 0.13 mmol), sulfonamide **26** (65 mg, 63.4 μmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (19 μL, 0.13 mmol) were stirred for 20 minutes. Pyridine (47 μL, 0.76 mmol) and acetic anhydride (48 μL, 0.63 mmol) were added and the reaction mixture was stirred for a further 16 hours. The solution was concentrated under nitrogen and purified by Fluorous Solid Phase Extraction; 2 g cartridge loading with <400 μL DMF, eluting with 8:2 MeOH–H_2O followed by MeOH to give the fluorous fraction, the crude sulfonamide **34** (R = R'^{F}) (53 mg). Without further purification, **34** (R = R'^{F}) was dissolved in 3% trifluoroacetic acid according to general procedure D and stirred for 16 hours to give a crude product which was purified by Fluorous Solid Phase Extraction; 2 g cartridge, loading with <400 μL DMF, with 80:20 MeOH–H_2O to give the organic fraction. Further purification by flash chromatography, eluting with 30:70 petrol–EtOAc, gave the *alcohol* **34** (R = H) (6 mg, 67% over 2 steps; 70:30 mixture of rotamers) as a colourless oil, R_f 0.17 (EtOAc); $[\alpha]_D^{20}$ +82.8 (*c* 1.00 in chloroform); δ_H (500 MHz, $CDCl_3$) 6.01-5.89 (3H, m, 3-H^{maj}, 4-H^{maj} and 4-H^{min}), 5.84-5.80 (1H, m, 3-H^{min}), 4.46 (1H, br. d, *J* 18.9, 2-H_A^{maj}), 4.29-4.24 (1H, m, 5-H^{min}), 4.22-4.18 (1H, m, 5-H^{maj}), 3.99 (1H, br.d, *J* 17.2, 2-H_A^{min}), 3.92-3.87 (1H, m, 2-H_B^{min}), 3.77 (1H, dd, *J* 13.1 and 3.9, 6-H_A^{min}), 3.73-3.66 (3H, m, 6-H_B^{min}, 2-H_B^{maj} and 6-H_A^{maj}), 3.48 (1H, dd, *J* 13.6 and 3.2, 6-H_B^{maj}), 2.18 (3H, s, CH_3^{maj}), 2.12 (3H, s, CH_3^{min}); δ_C (75 MHz, $CDCl_3$) 170.7 (C=O^{maj} and C=O^{min}), 130.0 (4-C^{min}), 129.0 (4-C^{maj}), 127.6 (3-C^{maj}), 126.1 (3-C^{min}), 64.3 (5-C^{maj}), 64.0 (5-C^{min}), 51.0 (6-C^{maj} and 6-C^{min}), 45.8 (2-C^{min}), 42.0 (2-C^{maj}); 22.1 (*C*H_3^{min}), 21.7 (*C*H_3^{maj}); ν_{max}/cm^{-1} (film) 3373 (br.), 2922, 2853, 1710, 1623 and 1446; *m/z* (TOF MS EI^+) 123.1 ([M – H_2O] 100%); found [M – H_2O] 123.0679, C_7H_9NO requires [*M– H_2O*] 123.0684.

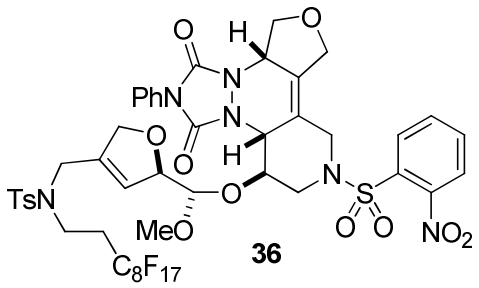
(*S*)-[5-Hydroxy-5,6-dihydropyridin-1(2*H*)-yl](isoxazol-5'-yl)methanone 35



35

Following general procedure D, thiophenol (12 μL, 0.11 mmol), sulfonamide **26** (28 mg, 27.3 μmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (79 μL, 0.11 mmol) were stirred for 20 minutes. DMAP (13 mg, 0.13 mmol) and isoxazolyl-5-carbonyl chloride (11 μL, 0.11 mmol) were sequentially added and the reaction mixture was stirred for a further 16 hours. The reaction mixture was concentrated under reduced pressure and purified by Fluorous Solid Phase Extraction (2 g cartridge, loading with <400 μL DMF), eluting with 80:20 methanol–water, followed by methanol, to give the fluorous fraction. The crude sulfonamide was subsequently dissolved in a solution of 3% trifluoroacetic acid in dichloromethane and stirred for 16 hours. The crude product was concentrated under reduced pressure and purified by Fluorous Solid Phase Extraction (2 g cartridge, loading with <400 μL DMF), eluting with 80:20 methanol–water, to give the organic fraction. Further purification by flash chromatography, eluting with 30:70 petrol–EtOAc, gave the *alcohol* **35** (3 mg, 57% over 2 steps; 65:35 mixture of rotamers) as a colourless oil, R_f 0.0.38 (EtOAc); $[\alpha]_D^{20}$ +108.8 (*c* 0.25 in chloroform); δ_H (500 MHz, $CDCl_3$) 8.33 (2H, d, *J* 1.8, 3'-$H^{maj\ \&\ min}$ or 4'-$H^{maj\ \&\ min}$), 6.87-6.83 (2H, m, 3'-$H^{maj\ \&\ min}$ or 4'-$H^{maj\ \&\ min}$), 6.03-5.94 (3H, m, 3-H^{maj}, 4-H^{maj} and 3-H^{min} or 4-H^{min}), 5.86-5.81 (1H, m, 3-H^{min} or 4-H^{min}), 4.47 (1H, br. d, *J* 18.2, 2-$H_A{}^{maj}$), 4.42-4.31 (3H, m, 5-H^{maj}, 5-H^{min} and 2-$H_A{}^{min}$), 4.20 (1H, br. d, *J* 18.2, 2-$H_B{}^{min}$), 4.03-3.97 (1H, m, 2-$H_B{}^{maj}$), 3.93-3.87 (3H, m, 6-$H_A{}^{maj}$, 6-H^{min}), 3.75 (1H, dd, *J* 13.8 and 3.4, 6-$H_B{}^{maj}$), 2.02 (1H, br.s, OH^{min}), 1.88 (1H, br. s, OH^{maj}); δ_C (75 MHz, $CDCl_3$) 163.2 (5'-C^{maj} and 5'-C^{min}), 158.1 (C=O^{maj}), 157.7 (C=O^{min}), 150.3 (3'-C^{min} or 4'-C^{min}), 150.1 (3'-C^{maj} or 4'-C^{maj}), 129.0 (3-C^{min} or 4-C^{min}), 127.9 (3-C^{maj} or 4-C^{maj}), 127.3 (3-C^{maj} or 4-C^{maj}), 126.1 (3-C^{min} or 4-C^{min}), 108.3 (3'-C^{min} or 4'-C^{min}), 107.7 (3'-C^{maj} or 4'-C^{maj}), 63.7 (5-C^{maj}), 63.5 (5-C^{min}), 50.4 (6-C^{maj}), 46.8 (6-C^{min}), 45.8 (2-C^{min}) and 42.7 (2-C^{maj}); ν_{max} /cm^{-1} (film) 3400 (br), 3042, 2962, 2920, 2850, 1633, 1580, 1482 and 1428; *m/z* (ESI^+) 195.1 ($[M + H]^+$ 100%), 217.1 ($[M + Na]^+$ 72%); found MH^+ 195.0759, $C_9H_{11}N_2O_3$ requires *MH* 195.0764.

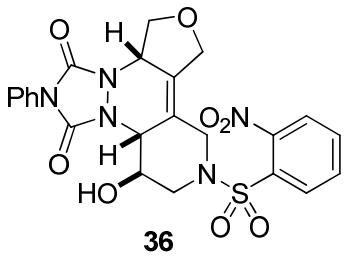
_N_-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluorodecyl)-_N_-[{(_R_)-5-[(_S_)-methoxy{(3'a_S_,8'a_R_,9'_R_)-11'-(2-nitrophenylsulfonyl)-5',7'-dioxo-6'-phenyl-3',3'a,5',6',7',8'a,9',10',11',12'-decahydro-1_H_-furo[3',4'-e]pyrido[4',3'-c][1',2',4']triazolo[1',2'-a]pyridazin-9'-yloxy}methyl]-2,5-dihydrofuran-3-yl}methyl]-4-methylbenzenesulfonamide 36 (R = R'^F)



36

4-Phenyl-[1,2,4]-triazole-3,5-dione (51 mg, 0.29 mmol) was added to a solution of sulfonamide **29** (80 mg, 73.1μmol) in dichloromethane (1 mL) and stirred for 20 minutes. The reaction mixture was concentrated under reduced pressure to give a crude product which was purified by Fluorous Solid Phase Extraction; 2 g cartridge, loading with <200 μL DCM, with 80:20 MeOH–H_2O followed by MeOH to give the fluorous fraction, the *fused tetracycle* **36** (R = R'^{F}) (80 mg, 86%, 87% purity by HPLC) as a white foam, R_f 0.67 (EtOAc); δ_H (500 MHz, $CDCl_3$) 8.10 (1H, dd, *J* 7.5 and 1.8, nosyl 3-H), 7.81-7.68 (3H, m, nosyl 4-H, 5-H and 6-H), 7.64 (2H, d, *J* 7.9, tosyl 2-H and 6-H), 7.50-7.42 (5H, m, Ph), 7.34 (2H, d, *J* 7.9, tosyl 3-H and 5-H), 5.69 (1H, s, 4-H), 4.78-4.74 (1H, m, 5-H), 4.64 (1H, app. t, *J* 7.9, 3'-H), 4.59-4.53 (2H, m, 1'-H_A and 8'a-H), 4.46 (1H, d, *J* 13.7, 1'-H_B), 4.42 (1H, d, *J* 3.6, C*H*OMe), 4.40-4.37 (2H, m, 2-H), 4.29 (1H, dd, *J* 13.8 and 1.7, 12'-H_A), 4.24-4.18 (1H, m, 3'a-H_A), 4.04 (1H, dd, *J* 13.0 and 4.6, 10'-H_A), 3.85 (1H, app. td, *J* 10.3 and 4.6, 9'-H), 3.78-3.72 (2H, m, 3'-H_B and 3-CC*H*$_A$), 3.48 (3H, s, OMe), 3.43 (1H, d, *J* 13.8, 12'-H_B), 3.38-3.20 (3H, m, 3-CC*H*$_B$ and $CF_2CH_2CH_2$), 3.01 (1H, dd, *J* 13.0 and 10.3, 10'-H_B), 2.46 (3H, s, tosyl Me), 2.42-2.17 (2H, m, CF_2CH_2); δ_C (75 MHz, $CDCl_3$) 156.7 (5'-C or 7'-C), 151.0 (5'-C or 7'-C), 148.4 (nosyl 2-C), 144.5 (tosyl 4-C), 137.8 (3-C), 136.2 (tosyl 1-C), 135.4 (12'b-C), 134.8 (nosyl 4-C), 132.5 (nosyl 6-C), 131.9 (nosyl 1-C), 131.6 (nosyl 3-C), 131.3 (phenyl 1-C), 130.3 (tosyl 3-C and 5-C), 129.4 (phenyl 2-C and 6-C or phenyl 3-C and 5-C), 128.6 (phenyl 4-C), 127.5 (tosyl 2-C and 6-C), 126.1 (phenyl 2-C and 6-C or phenyl 3-C and 5-C), 126.0 (4-C), 125.0 (nosyl 5-C), 120.1 (12'a-C), 105.4 (*C*HOMe), 87.6 (5-C), 76.2 (2-C), 75.4 (9'-C), 71.0 (3'-C), 66.9 (1'-C), 59.5 (OMe), 59.3 (3'a-C), 57.5 (8'a-C), 48.6 (10'-C), 47.1 (12'-C), 45.8 (3-C*C*H$_2$), 40.3 ($CF_2CH_2CH_2$), 31.1 (CF_2CH_2), 21.9 (tosyl Me); ν_{max} /cm^{-1} (film) 3071, 2926, 2866, 2254, 1780, 1723, 1599, 1544, 1503 and 1426; *m/z* (ESI$^+$) 1291.2 ([M + Na]$^+$ 100%); found MNa$^+$ 1291.1834, $C_{47}H_{41}F_{17}N_6O_{12}S_2$ requires *MNa* 1291.1845.

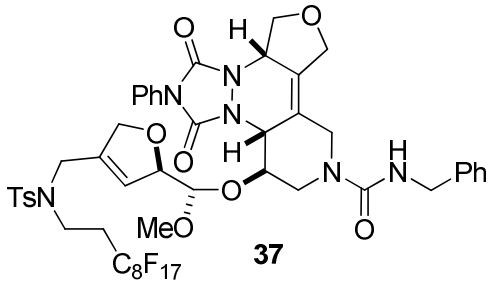
(3a*S*,8a*R*,9*R*)-9-Hydroxy-11-(2-nitrophenylsulfonyl)-6-phenyl-3,3a,9,10,11,12-hexahydro-1*H*-furo[3,4-e]pyrido[4,3-c][1,2,4]triazolo[1,2-a]pyridazine-5,7(6*H*,8a*H*)-dione 36 (R = H)



36

Following general procedure D, sulfonamide **35** (R = R'^{F}) (55 mg, 43.4 μmol) gave the crude product after 16 hours, which was purified by Fluorous Solid Phase Extraction; 2 g cartridge, loading with <200 μL dichloromethane, eluting with 80:20 MeOH–H_2O, to give the organic fraction (15 mg, 65%, 83% purity by HPLC). Further purification by flash chromatography, eluting with 99:1 DCM–MeOH, gave the *sulfonamide* **36** (R = H) (13 mg, 59%) as a colourless foam, R_f 0.57 (EtOAc), $[\alpha]_D^{20}$ +130.2 (*c* 1.00 in chloroform); δ_H (500 MHz, $CDCl_3$) 8.09 (1H, dd, *J* 7.5 and 1.7, nosyl 3-H), 7.79-7.68 (3H, m, nosyl 4-H, 5-H and 6-H), 7.54-7.34 (5H, m, Ph), 4.77-4.64 (3H, m, 1-H_A, 3-H_A and 8a-H), 4.55 (1H, d, *J* 13.8, 1-H_B), 4.39 (1H, dd, *J* 14.3 and 2.0, 12-H_A), 4.26-4.19 (1H, m, 3a-H), 4.08-4.01 (1H, m, 9-H), 3.93 (1H, ddd, *J* 13.3, 5.1 and 2.0, 10-H_A), 3.76 (1H, dd, *J* 9.8 and 8.8, 3-H_B), 3.49 (1H, br. d, *J* 14.3, 12-H_B), 3.01-2.91 (2H, m, 10-H_B and OH); δ_C (75 MHz, $CDCl_3$) 155.1 (2 × C=O), 148.4 (nosyl 2-C), 134.73 (12b-C), 134.65 (nosyl 4-C), 132.5 (nosyl 6-C), 132.2 (nosyl 1-C), 131.7 (nosyl 3-C), 130.9 (phenyl 1-C), 129.7 (phenyl 2-C and 6-C or phenyl 3-C and 5-C), 129.1 (phenyl 4-C), 125.8 (phenyl 2-C and 6-C or phenyl 3-C and 5-C), 124.9 (nosyl 5-C), 118.5 (12a-C), 72.8 (9-C), 71.3 (3-C), 67.3 (1-C), 59.8 (8a-C), 57.8 (3a-C), 50.4 (10-C), 46.9 (12-C); ν_{max} /cm^{-1} 3418 (br), 3095, 3003, 2924, 2869, 1760, 1713, 1599, 1544, 1503 and 1428; *m/z* (ESI$^+$) 550.1 ([M + Na]$^+$ 100%); found MNa^+ 550.0998, $C_{23}H_{21}N_5O_8S$ requires *MNa* 550.1003.

(3a*S*,8a*R*,9*R*)-*N*-Benzyl-9-[(*S*)-{(*R*)-4'-[{*N*-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)-4-methylsulfonamido}methyl]-2',5'-dihydrofuran-2'-yl}(methoxy)methoxy]-5,7-dioxo-6-phenyl-3,3a,6,7,8a,9,10,12-octahydro-1*H*-furo[3,4-e]pyrido[4,3-c][1,2,4]triazolo[1,2-a]pyridazine-11(5*H*)-carboxamide 37 (R = R'^{F})

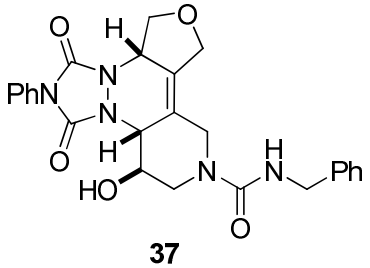


37

Thiophenol (6 μL, 50.4 μmol) was added dropwise to a solution of sulfonamide **35** (R = R'^{F}) (32 mg, 25 μmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (8 μL, 50.4 μmol) in acetonitrile (1.0 mL)

and stirred at room temperature for 1 hour. Benzyl isocyanate (17 mg, 0.13 mmol) was added and the reaction mixture was stirred for a further 16 hours. Purification by Fluorous Solid Phase Extraction; 2 g cartridge, loading with <200 μL dichloromethane, eluting with 80:20 MeOH–H_2O followed by MeOH, gave the fluorous fraction, the *carboximide* **37** (R = R'^{F}) (24 mg, 79%, >95% purity by ^{1}H NMR spectroscopy) as a colourless foam, R_f 0.64 (EtOAc); δ_H (500 MHz, $CDCl_3$) 7.63 (2H, d, *J* 8.2, tosyl 2-C and 6-C), 7.49-7.42 (4H, m, Ph), 7.37-7.27 (8H, m, Ar), 5.68 (1H, s, 3'-H), 5.15 (1H, t, *J* 5.4, NH), 4.76-4.72 (1H, m, 2'-H), 4.71 (1H, d, *J* 14.1, 1-H_A), 4.66-4.61 (2H, m, 3-H_A and 8a-H), 4.55 (1H, d, *J* 14.2, 12-H_A), 4.53-4.47 (1H, m, 1-H_B), 4.47 (1H, dd, *J* 14.7 and 5.4, NC*H*$_A$Ph), 4.39 (1H, dd, *J* 14.7 and 5.4, NC*H*$_B$Ph), 4.36-4.31 (1H, m, 5'-H_A), 4.31 (1H, d, *J* 4.2, C*H*OMe), 4.29-4.24 (1H, m, 5'-H_B), 4.23-4.17 (1H, m, 3a-H), 3.87 (1H, dd, *J* 14.4 and 4.3, 10-H_A), 3.76 (1H, d, *J* 15.5, 4'-CC*H*$_A$), 3.74-3.65 (2H, m, 9-H and 3-H_B), 3.49 (1H, d, *J* 14.2, 12-H_B), 3.41 (1H, d, *J* 15.5, 4'-CC*H*$_B$), 3.37 (3H, s, OMe), 3.33-3.20 (2H, m, $CF_2CH_2CH_2$), 3.18 (1H, dd, *J* 14.4 and 5.3, 10-H_B), 2.45 (3H, s, tosyl Me), 2.40-2.18 (2H, m, CF_2CH_2); δ_C (75 MHz, $CDCl_3$) 157.5 (5-C or 7-C), 156.9 (5-C or 7-C), 150.7 (11-N*C*=O), 144.5 (tosyl 4-C), 139.4 (NCH_2-phenyl 1-C), 137.8 (4'-C), 136.2 (tosyl 1-C), 133.4 (12b-C), 131.9 (6-N-phenyl 1-C), 130.3 (tosyl 3-C and 5-C), 129.4 (phenyl 2-C and 6-C or phenyl 3-C and 5-C), 129.1 (phenyl 2-C and 6-C or phenyl 3-C and 5-C), 128.6 (phenyl 4-C), 128.2 (phenyl 2-C and 6-C or phenyl 3-C and 5-C), 128.0 (phenyl 4-C), 127.5 (tosyl 2-C and 6-C), 125.93 (phenyl 2-C and 6-C or phenyl 3-C and 5-C), 125.87 (3'-C), 121.8 (12a-C), 105.5 (*C*HOMe), 87.8 (2'-C), 76.3 (9-C), 76.1 (5'-C), 71.1 (3-C), 67.4 (1-C), 59.2 (3a-C), 58.5 (OMe), 57.5 (8a-C), 48.4 (10-C), 45.93 (N*C*H$_2$Ph or 12-C), 45.91 (N*C*H$_2$Ph or 12-C), 45.7 (4'-C*C*H$_2$), 40.5 ($CF_2CH_2CH_2$), 31.1 (CF_2CH_2) and 21.9 (tosyl Me); ν_{max} /cm^{-1} 2958, 2923, 2853, 1779, 1722, 1639, 1599, 1532, 1503, 1455 and 1423; *m/z* (ESI$^+$) 1239.3 ([M + Na]$^+$ 100%); found MNa$^+$ 1239.2535, $C_{49}H_{45}F_{17}N_6O_9S$ requires *MNa* 1239.2589.

(3a*S*,8a*R*,9*R*)-*N*-Benzyl-9-hydroxy-5,7-dioxo-6-phenyl-3,3a,6,7,8a,9,10,12-octahydro-1*H*-furo[3,4-e]pyrido[4,3-c][1,2,4]triazolo[1,2-a]pyridazine-11(5*H*)-carboxamide 37 (R = H)



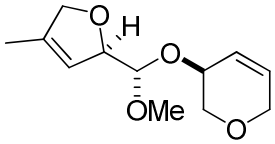
37

Following general procedure D, sulfonamide **36** (R = R'^{F}) (55 mg, 43.4 μmol) gave the crude product after 16 hours. Purification by Fluorous Solid Phase Extraction; 2 g cartridge, loading with <200 μL dichloromethane, eluting with 80:20 MeOH–H_2O, gave the organic fraction (8 mg, 90%, 86% purity by HPLC). Further purification by flash chromatography, eluting with 99:1 DCM–

MeOH, gave the *sulfonamide* **37** (R = H) (6 mg, 67%) as a colourless foam, R_f 0.41 (95:5 DCM–MeOH), $[\alpha]_D^{20}$ –85.2 (*c* 1.00 in chloroform); δ_H (500 MHz, $CDCl_3$) 7.53-7.39 (5H, m, Ph), 7.37-7.26 (5H, m, Ph), 5.08 (1H, t, *J* 5.7, N*H*), 4.77-4.65 (4H, m, 1-H_A, 3-H_A, 8a-H and O*H*), 4.59 (1H, d, *J* 15.5, 12-H_A), 4.55 (1H, d, *J* 13.9, 1-H_B), 4.44 (1H, dd, *J* 14.5 and 5.7, NC*H*$_A$Ph), 4.39 (1H, dd, *J* 14.5 and 5.7, NC*H*$_B$Ph), 4.25-4.19 (1H, m, 3a-H), 3.99-3.93 (1H, m, 9-H), 3.71-3.61 (3H, m, 10-H_A, 12-H_B and 3-H_B), 3.25 (1H, dd, *J* 14.5 and 8.0, 10-H_B); δ_C (75 MHz, $CDCl_3$) 157.1 (11-N*C*=O), 154.4 (5-C or 7-C), 152.7 (5-C or 7-C), 138.8 (phenyl 1-C), 132.5 (12a-C or 12b-C), 130.5 (phenyl 1-C), 129.3 (phenyl 2-C and 6-C or phenyl 3-C and 5-C), 128.7 (phenyl 2-C and 6-C or phenyl 3-C and 5-C), 127.8, 127.7, (phenyl 4-C and phenyl 2-C and 6-C or phenyl 3-C and 5-C), 127.5 (phenyl 4-C), 125.3 (phenyl 2-C and 6-C or phenyl 3-C and 5-C), 119.5 (12a-C or 12b-C), 73.8 (9-C), 71.3 (3-C), 67.7 (1-C), 60.3 (3a-C), 57.3 (8a-C), 50.4 (10-C), 45.58 (12-C or N*C*H_2Ph) and 45.55 (12-C or N*C*H_2Ph); ν_{max} /cm^{-1} 3383 (br), 3065, 3031, 2926, 2869, 1776, 1714, 1666, 1630, 1539, 1504 and 1427; *m/z* (ESI^+) 498.2 ($[M + Na]^+$ 100%); found MNa^+ 498.1764, $C_{25}H_{25}N_5O_5S$ requires *MNa* 498.1748.

Validation and synthesis of the fluorous-tagged linkers

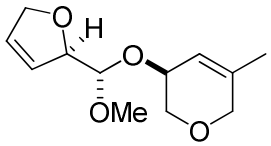
3-[Methoxy-(4′-methyl-2′,5′-dihydro-furan-2-′yl)-methoxy]-3,6-dihydro-2*H*-pyran 10



10

G2 (10 mg, 6 μmol, 0.03 eq.) was added to a stirred solution of the triene **8** (50 mg, 0.197 mmol) in dichloromethane (25 mL) at 45 °C and stirred for 1.5 h before additional catalyst (10 mg, 6 μmol, 0.03 eq.) was added and stirred for a further 2.5 h at 45 °C. The solvent was removed under reduced pressure and residue purified using flash chromatography, eluting with 90:10 petrol–EtOAc containing 1% triethylamine, to give the *bicycle* **10** (41 mg, 92%) as a colourless oil, R_f 0.20 (80:20 petrol–EtOAc); $[\alpha]_D$ +150.4 (*c* 1.00 in methanol); 1190, 1138 and 1082; δ_H (500 MHz, $CDCl_3$) 5.97 (1H, ddd, *J* 10.4, 9.3 and 2.5, 5-H), 5.92 (1H, br d, *J* 10.4, 4-H), 5.45 (1H, br s, 3'-H), 4.76-4.74 (1H, m, 2'-H), 4.52 (1H, dd, *J* 12.3 and 9.3, 6-H_a), 4.46 (1H, br d, *J* 12.4, 6-H_b), 4.34 (1H, d, *J* 5.8, MeOC*H*), 4.18 (1H, br s, 3-H), 4.15 (1H, d, *J* 16.8, 5'-H_a), 4.05 (1H, d, *J* 16.8, 5'-H_b), 3.88 (1H, dd, *J* 11.4 and 4.1, 2-H_a), 3.75 (1H, dd, *J* 11.4 and 5.2, 2-H_b), 3.44 (3H, s, OMe) and 1.77 (3H, s, Me); δ_C (125 MHz, $CDCl_3$) 138.5 (4'-C), 129.6 (4-C), 125.8 (5-C), 119.9 (3'-C), 105.3 (MeO*C*), 87.3 (2'-C), 78.3 (6-C), 68.4 (2-C), 67.8 (3-C), 65.2 (5'-C), 55.5 (OMe) and 12.4 (4′-C*C*H_3); ν_{max}/cm^{-1} 3039, 2838 and 1447; *m/z* (ES+) 244 (100%, MNH_4^+). (Found: MNa^+ 249.1098, $C_{12}H_{18}O_4Na$ requires *MNa*, 249.1103).

3-[(2',5'-Dihydrofuran-2'-yl)-methoxymethoxy]-5-methyl-3,6-dihydro-2*H*-pyran 11

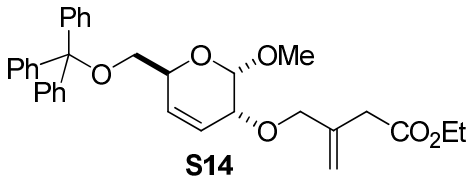


11

G2 (10 mg, 6 μmol, 0.03 eq.) was added to a stirred solution of the triene **9** (50 mg, 0.197 mmol) in dichloromethane (25 mL) at 45 °C and stirred for 1.5 h before additional catalyst (10 mg, 6 μmol, 0.03 eq.) was added and stirred for a further 2.5 h at 45 °C. The solvent was removed under reduced pressure and residue purified using flash chromatography, eluting with 90:10 petrol–EtOAc containing 1% triethylamine, to give the *bicycle* **11** (39 mg, 88%) as a colourless oil, R_f 0.25 (70:30 petrol–EtOAc); $[\alpha]_D$ +165.6 (*c* 1.00 in chloroform); δ_H (500 MHz, $CDCl_3$) 5.93 (1H, dd, *J* 6.2 and 1.6, 3'-H), 5.78 (1H, ddd, *J* 6.2, 4.0 and 1.7, 4'-H), 5.63 (1H, d, *J* 1.6, 4-H), 4.73 (1H,

dd, *J* 5.6 and 1.6, 2'-H), 4.60 (1H, dd, *J* 14.8 and 9.2, 5'-H_a), 4.57 (1H, dd, *J* 14.8 and 4.6, 5'-H_b), 4.30 (1H, d, *J* 5.6, MeOC*H*), 4.05-4.04 (1H, m, 3-H), 3.95 (1H, br d, *J* 16.1, 2-H_a), 3.84 (1H, br d, *J* 16.1, 2-H_b), 3.71 (1H, d, *J* 14.2, 6-H_a), 3.70 (1H, d, *J* 14.2, 6-H_b), 3.38 (3H, s, OMe) and 1.59 (3H, s, Me); δ_C (125 MHz, $CDCl_3$) 136.7 (5-C), 128.6 (3'-C), 126.1 (4'-C), 120.0 (4-C), 104.9 (MeO*C*), 86.9 (2'-C), 75.7 (5'-C), 68.5 (2-C), 68.4 (3-C), 68.2 (6-C), 55.7 (OMe) and 18.6 (5-C*C*H_3); ν_{max}/cm^{-1} 2955, 2855, 1446 and 1350 *m/z* (ES+) 249 (100%, MNa^+). (Found: MNH_4^+ 244.1543, $C_{12}H_{18}O_4$ requires *MNH4*, 244.1541).

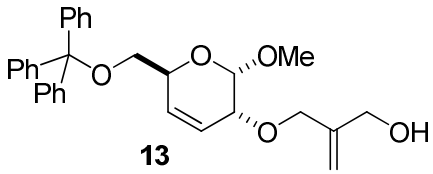
Methyl 2-(ethyl 2′-(*O*-methyl)-acrylate)-3,4-deoxy-6-*O*-triphenylmethyl-α-D-gluco-hex-3-enopyranoside S14



S14

Sodium hydride (425 mg, of a 60% dispersion in mineral oil, 10.62 mmol, 1.5 eq.) was added to a stirred solution of the alcohol **12** (2.85 g, 7.08 mmol) in *N*,*N*-dimethyl formamide (100 mL) at 0 °C. Once effervescence had ceased, ethyl α-(bromomethyl)-acrylate (1.95 mL, 14.16 mmol, 2.0 eq.) was added dropwise, the reaction mixture was allowed to warm at room temperature and stirred for 13 h. The reaction mixture was cooled to 0 °C, quenched with saturated aqueous ammonium chloride solution (50 mL), diluted with ether (500 mL), washed with brine (2 × 100 mL), dried ($MgSO_4$), solvent removed under reduced pressure and the crude product was purified by flash chromatography (gradient elution: 10:0→39:1→19:1 petrol–EtOAc) to give the *acrylate* **S14** (3.29 g, 90%) as a colourless oil, R_f 0.15 (9:1 petrol–EtOAc); $[\alpha]_D$ −22.0 (*c* 2.00 in chloroform); δ_H (500 MHz, $CDCl_3$) 7.45 (6H, d, *J* 7.8, Ph), 7.27 (6H, app t, *J* 7.8 and 7.5, Ph), 7.20 (3H, d, *J* 7.5, Ph), 6.31 (1H, d, *J* 1.0, 3′-H_a), 5.94 (1H, d, *J* 1.0, 3′-H_b), 5.83 (1H, app d, *J* 10.6, 3-H), 5.78 (1H, app d, *J* 10.6, 4-H), 5.00 (1H, d, *J* 3.9, 1-H), 4.32 (2H, br s, 1′-H), 4.26-4.25 (1H, m, 5-H), 4.19 (2H, q, *J* 7.1, Et), 4.16-4.15 (1H, m, 2-H), 3.50 (3H, s, OMe), 3.24 (1H, dd, *J* 9.4 and 5.9, 6-H_a), 3.16 (1H, dd, *J* 9.4 and 5.4, 6-H_b) and 1.27 (3H, t, *J* 7.2, Et); δ_C (125 MHz, $CDCl_3$) 166.2 (CO), 144.5 (Ph), 137.8 (2′-C) 129.2 (Ph), 128.9 (4-C), 128.3 (Ph), 127.5 (Ph), 126.3 (3′-C), 124.9 (3-C), 97.4 (1-C), 87.1 (Ph_3C), 72.7 (1′-C), 68.6 (5-C), 67.6 (2-C), 66.4 (6-C), 61.1 (Et), 56.3 (OMe) and 14.7 (Et); ν_{max}/cm^{-1} 3086, 3058, 3020, 2984, 2929, 2869, 1724, 1715, 1639 and 1597; *m/z* (ES+) 243.2 (100%, Ph_3C^+) and 537.4 (50%, MNa^+). (Found: MNa^+ 537.2259, $C_{32}H_{34}O_6$ requires *MNa*, 537.2253).

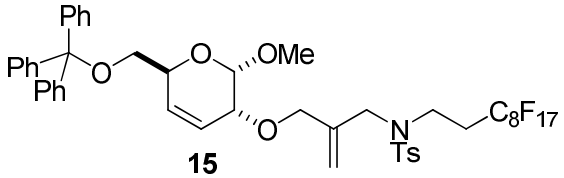
Methyl 2-*O*-(2′-oxymethyl)-allyl-3,4-deoxy-6-*O*-triphenylmethyl-α-D-gluco-hex-3-enopyranoside 13



13

Di*iso*butylaluminium hydride (0.67 mL, 1.00 mmol, 1.5 M solution in toluene) was added dropwise to a stirred solution of the acrylate **S14** (130 mg, 0.25 mmol) in tetrahydrofuran (10 mL) at −78 °C. The solution was stirred at this temperature for 1.5 hours, after which time the reaction mixture was quenched with 1 M aqueous sodium hydroxide solution (2 mL), allowed to warm to room temperature and filtered through celite, washing with EtOAc (20 mL). The filtrate was diluted with brine (100 mL), extracted with EtOAc (5 × 10 mL), dried ($MgSO_4$) and the solvent removed under reduced pressure to give a crude product which was purified by flash chromatography, eluting with 90:10→80:20 petrol–EtOAc, to give the *alcohol* **13** (103 mg, 86%) as a colourless foam, R_f 0.40 (1:1 petrol–EtOAc); $[\alpha]_D$ −24.0 (*c* 1.00 in chloroform); δ_H (500 MHz, $CDCl_3$) 7.46 (6H, d, *J* 7.6, Ph), 7.29 (6H, dd, *J* 7.6 and 7.3, Ph), 7.22 (3H, d, *J* 7.6, Ph), 5.84 (1H, d, *J* 10.6, 3-H), 5.74 (1H, dd, *J* 10.6 and 0.9, 4-H), 5.14 (1H, app s, 3′-H_a), 5.11 (1H, app s, 3′-H_b), 5.00 (1H, d, *J* 3.8, 1-H), 4.23-4.25 (1H, m, 5-H), 4.23 (1H, d, *J* 13.3, 1′-H_a), 4.18 (2H, s, 2′-CCH_2), 4.15 (1H, d, *J* 13.3, 1′-H_b), 4.10-4.08 (1H, m, 2-H), 3.50 (3H, s, OMe), 3.23 (1H, dd, *J* 9.4 and 5.9, 6-H_a), 3.15 (1H, dd, *J* 9.4 and 5.3, 6-H_b) and 1.43 (1H, br s, OH); δc (125 MHz, $CDCl_3$) 145.7 (2′-C), 144.4 (Ph), 129.1 (Ph), 128.9 (4-C), 128.3 (Ph), 127.5 (Ph), 124.9 (3-C), 113.9 (3′-C), 97.1 (1-C), 87.1 (Ph_3C), 71.8 (5-C), 71.2 (1′-C), 68.6 (2-C), 66.3 (6-C), 64.9 (2′-CCH_2) and 56.2 (OMe); ν_{max}/cm^{-1} 3466, 3086, 3058, 3033, 2925, 2870, 1656, 1597, 1491, 1448, 1397; *m/z* (ES+) 242.9 (100%, Ph_3C^+) and 490.1 (25%, MNH_4^+). (Found: MNa^+ 495.2167, $C_{30}H_{32}O_5Na$ requires *MNa*, 495.2147).

(2″*S*,3″*R*,6″*S*)-*N*-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-decyl)-*N*-[2′-(2″-methoxy-6″-trityloxymethyl-3″,6″-dihydro-2″*H*-pyran-3″-yloxymethyl)-allyl]-4‴-methyl-benzenesulfonamide 15

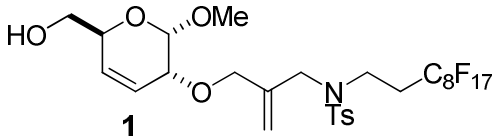


15

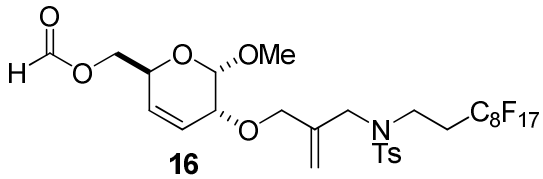
By general procedure **B**, the alcohol **13** (335 mg, 0.71 mmol), triphenylphosphine (2 eq.), DEAD (2 eq.) and the sulfonamide **14** (2 eq.) gave a crude product after 3 h. The crude product was purified by flash chromatography, eluting with 90:10→85:15→80:20 petrol–EtOAc), to give the *tertiary*

sulfonamide **15** (528 mg, 70%) as a colourless foam, R_f 0.15 (9:1 petrol–EtOAc); δ_H (500 MHz, $CDCl_3$) 7.76 (2H, d, *J* 8.2, 2′′′-H), 7.52 (6H, d, *J* 7.5, *ortho* trityl), 7.39-7.34 (8H, m, *meta* trityl and 3′′′-H), 7.30 (3H, t, *J* 7.3, *para* trityl), 5.90 (1H, br d, *J* 4′′-H), 5.79 (1H, br d, *J* 5′′-H), 5.37 (1H, s, 3′-H_a), 5.19 (1H, s, 3′-H_b), 5.03 (1H, d, *J* 3.4, 2′′-H), 4.30 (1H, br s, 6′′-H), 4.12 (1H, br s, 3′′-H), 4.09 (2H, s, 2′-CCH_2O), 3.91 (1H, d, *J* 15.0, 1′-H_a), 3.84 (1H, d, *J* 15.0, 1′-H_b), 3.56 (3H, s, OMe), 3.48-3.43 (2H, m, 1-H), 3.30 (dd, *J* 9.3 and 6.0, 6′′-CCH_a), 3.21 (1H, dd, *J* 9.3 and 5.4, 6′′-CCH_b) and 2.48-2.38 (5H, m, 2-H and 4′′′-CCH_3); δ_C (150 MHz, $CDCl_3$) 144.0 (*ipso* trityl), 143.9 (4′′′-C), 140.6 (2′-C), 135.8 (1′′′-C), 129.9 (3′′′-C), 128.7 (*ortho* trityl), 128.5 (4′′-C), 127.8 (*meta* trityl), 127.2 (2′′′-C), 127.0 (*para* trityl), 124.2 (5′′-C), 116.9 (3′-C), 96.8 (2′′-C), 86.6 (O*C*$(Ph)_3$), 71.9 (3′′-C), 69.3 (2′-C*C*H_2O), 68.2 (6′′-C), 65.9 (6′′-C*C*H_2O), 55.7 (OMe), 51.6 (1′-C), 40.4 (1-C), 21.5 (t, $^2J_{C–F}$ 21.7, 2-C) and 21.5 (4′′′-C*C*H_3); ν_{max}/cm^{-1} 3087, 3054, 3027, 2927, 2868, 1657, 1598, 1489, 1448 and 1399 (Found: MNa^+ 1094.2360, $C_{47}H_{42}F_{17}NO_6S$ requires *MNa* 1094.2354).

(2′′*S*,3′′*R*,6′′*S*)-*N*-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-decyl)-*N*-[2′-(2′′-methoxy-6′′-oxymethyl-3′′,6′′-dihydro-2′′*H*-pyran-3′′-yloxymethyl)-allyl]-4′′′-methyl-benzenesulfonamide 1



1



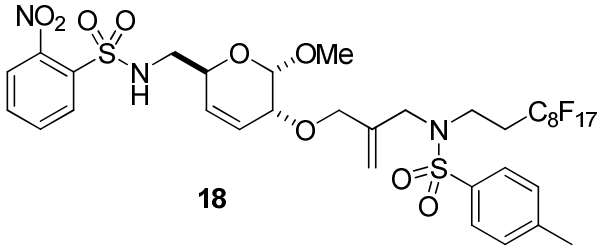
16

The protected alcohol **15** (525 mg, 0.49 mmol) and triethylsilane (114 μL, 0.98 mmol, 2 eq.) were dissolved in a 10:10:1 mixture of formic acid–THF–water and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was diluted with toluene (100 mL) and concentrated under educed pressure to give a crude product which was purified by flash chromatography, eluting with 80:20→60:40→50:50 petrol–EtOAc, to give *alcohol* **1** (105 mg, 26%) as colourless needles, m.p. 85.9-88.4 °C (from EtOAc); R_f 0.28 (1:1 petrol–EtOAc); $[\alpha]_D$ +0.8 (*c* 1.00 in chloroform); δ_H (500 MHz, $CDCl_3$) 7.72 (2H, d, *J* 8.3, 2′′′-H), 7.76 (2H, d, *J* 8.3, 3′′′-H), 5.83 (1H, dd, *J* 10.6 and 1.9, 5′′-H), 5.76 (1H, dd, *J* 10.6 and 1.8, 4′′-H), 5.34 (1H, s, 3′-H_a), 5.17 (1H, s, 3′-H_b), 5.04 (1H, d, *J* 3.9, 2′′-H), 4.29-4.26 (1H, m, 6′′-H), 4.13-4.11 (1H, m, 3′′-H), 4.08 (2H, s, 2′-CCH_2O), 3.84 (1H, d, *J* 15.1, 1′-H_a), 3.81 (1H, d, *J* 15.1, 1′-H_b), 3.76 (1H, dd, *J* 11.4 and 1.8, 6′′-CCH_a), 3.64 (1H, dd, *J* 11.4 and 6.1, 6′′-CCH_b), 3.54 (3H, s, OMe), 3.42-3.39 (2H, m, 1-H), 2.47 (3H, s, 4′′′-CCH_3), 2.43-2.36 (2H, m, 2-H) and 1.92 (1H, br s, OH); δ_C (75 MHz, $CDCl_3$) 144.4 (4′′′-C), 140.9 (2′-C), 136.0 (1′′′-C), 130.4 (3′′′-C), 127.6 (2′′′-C), 127.3 (4′′-C), 126.1 (3′′-C), 117.5 (3′-C), 97.3 (2′′-C), 72.3 (3′′-C), 69.8 (5′′-C), 69.7 (2′-C*C*H_2O), 65.3 (6′′-C*C*H_2O), 56.2

(OMe), 52.1 (1′-C), 40.9 (1-C), 31.1 (t, $^{t}J_{C–F}$ 21.4, 2-C) and 21.9 (4‴-C*C*H$_3$); ν_{max}/cm^{-1} 3522, 3016, 2961, 2928, 2901, 2863 and 1464; *m/z* (ES+) 852 (100%, MNa$^+$). (Found: MNa$^+$ 852.1289, $C_{28}H_{28}F_{17}NO_6S$ requires *MNa*, 852.1258).

Also obtained was *(2″S,3′R,6″S)-N-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-decyl)-N-[2′-(2″-methoxy-6″-formoxymethyl-3″,6″-dihydro-2″H-pyran-3″-yloxymethyl)-allyl]-4‴-methyl-benzenesulfonamide* **16** (231 mg, 55%) as colourless needles, m.p. 77.6-78.2 °C (from $CHCl_3$); R_f 0.86 (1:1 petrol–EtOAc); $[\alpha]_D$ –10.8 (*c* 1.00 in chloroform); δ_H (500 MHz, $CDCl_3$) 8.12 (1H, s, CHO), 7.71 (2H, d, *J* 8.3, 2‴-H), 7.35 (2H, d, *J* 8.3, 3‴-H), 5.85 (1H, dd, *J* 10.6 and 1.2, 5″-H), 5.76 (1H, dd, *J* 10.6 and 1.8, 4″-H), 5.33 (1H, s, 3′-H$_a$), 5.16 (1H, s, 3′-H$_b$), 5.02 (1H, d, *J* 3.9, 2″-H), 4.42-4.41 (1H, m, 6″-H), 4.28 (1H, dd, *J* 11.5 and 4.0, 6″-CCH$_a$), 4.25 (1H, dd, *J* 11.5 and 6.0, 6″-CCH$_b$), 4.13-4.11 (1H, m, 3″-H), 4.07 (1H, d, *J* 12.3, 2′-CCH$_a$), 4.06 (1H, d, *J* 12.3, 2′-CCH$_b$), 3.85 (1H, d, *J* 15.0, 1′-H$_a$), 3.79 (1H, d, *J* 15.0, 1′-H$_b$), 3.54 (3H, s, OMe), 3.41-3.38 (2H, m, 1-H), 2.46 (3H, s, 4‴-CCH$_3$) and 2.43-2.36 (2H, m, 2-H); δ_C (75 MHz, $CDCl_3$) 161.1 (CHO), 144.4 (4‴-C), 140.8 (2′-C), 136.0 (1‴-C), 130.3 (3‴-C), 127.6 (2‴-C), 126.7 (5″-C), 126.3 (4″-C), 117.6 (3′-C), 97.3 (2″-C), 72.0 (3″-C), 69.7 (2′-C*C*H$_2$), 67.2 (6″-C), 65.3 (6″-C*C*H$_2$), 56.4 (OMe), 52.1 (1′-C), 40.9 (1-C), 31.0 (t, $^{2}J_{C–F}$ 21.3, 2-C) and 21.9 (4‴-C*C*H$_3$); ν_{max}/cm^{-1} 3043, 2928, 2857, 1726, 1657, 1598, 1494 and 1399; *m/z* (ES+) 880 (100%, MNa$^+$). (Found: MNa$^+$ 880.1202, $C_{29}H_{28}F_{17}NO_7S$ requires *MNa*, 880.1207).

_N_-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluorodecyl)-_N_-[2-{[(2_S_,3_R_,6_S_)-2-methoxy-6-{(2-nitrophenylsulfonamido)methyl}-3,6-dihydro-2_H_-pyran-3-yloxy]methyl}allyl]-4-methylbenzenesulfonamide 18



18

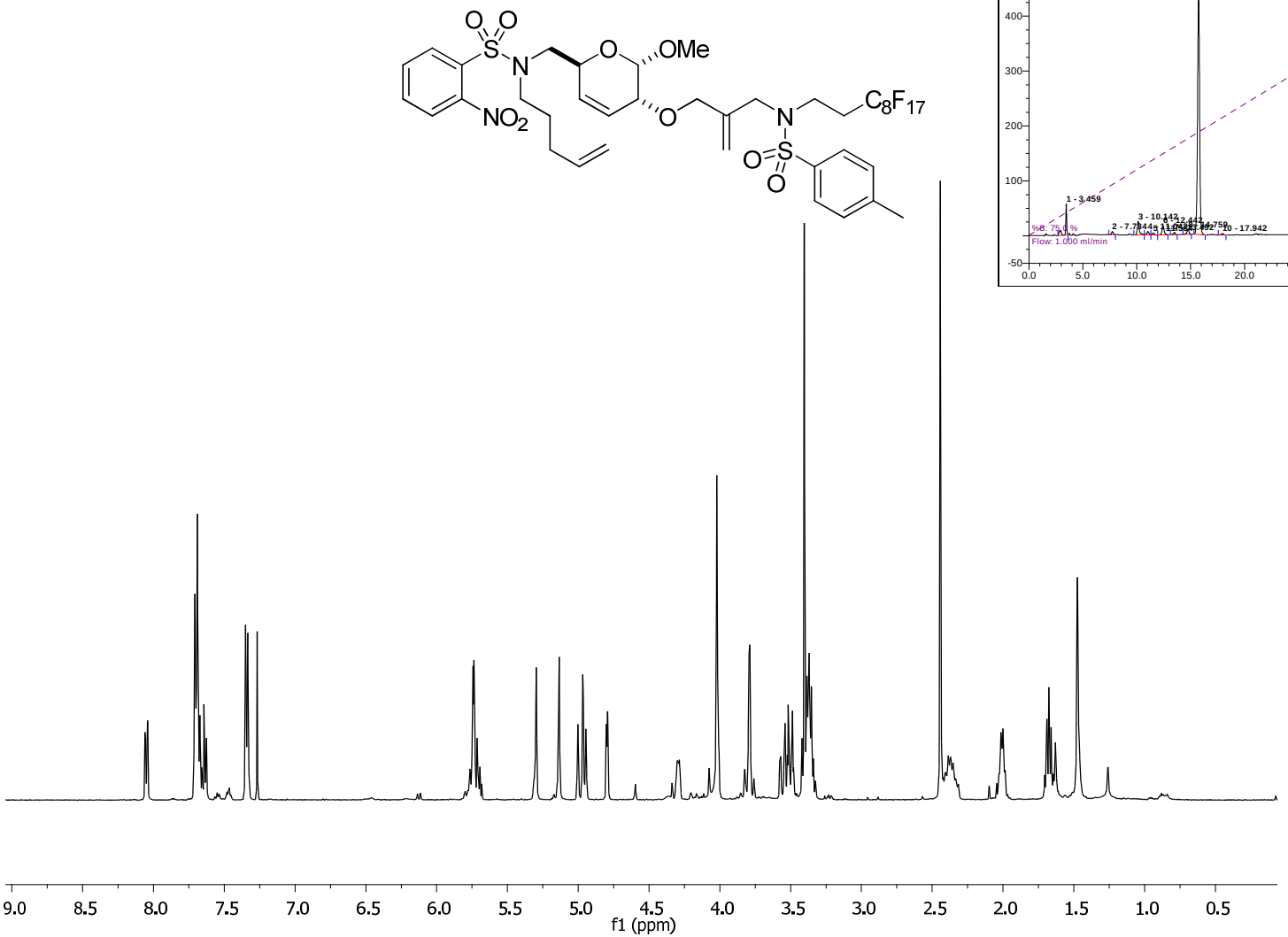
Following general procedure **B**, diethyl azodicarboxylate (441 μL, 2.41 mmol), nosyl-Boc-amine (728 mg, 2.41 mmol) and alcohol **1** (500 mg, 0.60 mmol) gave the crude product after 3 hours. The crude product was purified by Fluorous Solid Phase Extraction; 10 g cartridge, loading with <1.00 mL dichloromethane, eluting with 80:20 MeOH–H_2O followed by MeOH to give the fluorous fraction, the Boc-protected sulfonamide **17**. Sulfonamide **17** (1.20 g, 1.08 mmol) was subsequently dissolved in dimethyl sulfoxide (40 mL) and heated at reflux for 20 minutes. The dimethyl

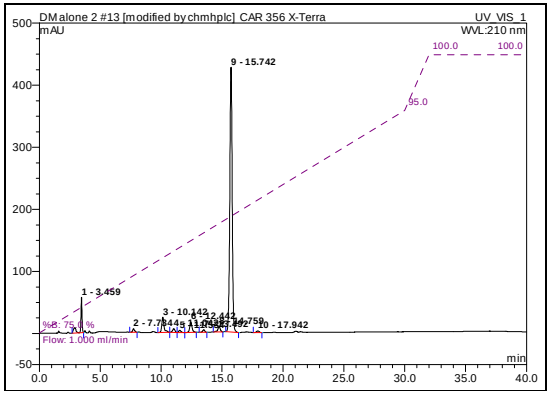
sulfoxide was removed under reduced pressure to give a crude product which was purified by flash chromatography, eluting with 50:50 petrol–EtOAc, to give *sulfonamide* **18** (1.01 g, 88% over 2 steps) as a colourless foam, R_f 0.43 (50:50 petrol–EtOAc); $[\alpha]_D^{20}$ +40.4 (*c* 1.00 in chloroform); δ_H (500 MHz, $CDCl_3$) 8.14 (1H, dd, *J* 7.5 and 3.4, nosyl 3-H), 7.90 (1H, dd, *J* 7.5 and 3.4, nosyl 6-H), 7.79-7.72 (2H, m, nosyl 4-H and 5-H), 7.69 (2H, d, *J* 8.1, tosyl 2-H and 6-H), 7.34 (2H, d, *J* 8.1, tosyl 3-H and 5-H), 5.72-5.67 (2H, m, 5-H and NH), 5.57 (1H, app. d, *J* 10.3, 4-H), 5.28 (1H, s, $NCH_2C{=}CH_AH_B$), 5.12 (1H, s, $NCH_2C{=}CH_AH_B$), 4.80 (1H, d, *J* 3.7, 2-H), 4.23-4.18 (1H, m, 6-H), 3.97 (2H, s, 3-$COCH_2$), 3.91-3.88 (1H, m, 3-H), 3.81 (1H, d, *J* 15.0, NCH_ACCH_2), 3.74 (1H, d, *J* 15.0, NCH_BCCH_2), 3.45 (1H, ddd, *J* 13.3, 6.5 and 3.4, 6-CCH_A), 3.19 (1H, ddd, *J* 13.3, 8.8 and 5.7, 6-CCH_B), 3.38 (3H, s, OMe), 3.38-3.33 (2H, m, $CF_2CH_2CH_2$), 2.44 (3H, s, tosyl Me), 2.42-2.29 (2H, m, CF_2CH_2); δ_H (75 MHz; $CDCl_3$) 148.0 (nosyl 2-C), 144.1 (tosyl 4-C), 140.4 (3-$COCH_2CCH_2$), 135.8 (tosyl 1-C), 134.3 (nosyl 1-C), 133.6 (nosyl 6-C), 132.8 (nosyl 3-C), 131.0 (nosyl 4-C), 130.0 (tosyl 3-C and 5-C), 127.2 (tosyl 2-C and 6-C), 126.7 (5-C), 126.4 (4-C), 125.5 (nosyl 5-C), 117.3 (3-$COCH_2C{=}CH_2$), 96.8 (2-C), 71.8 (3-C), 69.4 (3-$COCH_2$), 67.1 (6-C), 55.9 (OMe), 51.7 (NCH_2CCH_2), 47.3 (6-CCH_2), 40.4 ($CF_2CH_2CH_2$), 30.6 (CF_2CH_2), 21.5 (tosyl Me); ν_{max}/cm^{-1} 3354, 3095, 2990, 2934, 2869, 1597, 1538 and 1443; *m/z* (ES^+) 1036.1 ($[M + Na]^+$ 100%); found MNa^+ 1036.1189, $C_{34}H_{32}F_{17}N_3O_9S_2$ requires *MNa* 1036.1201.

References

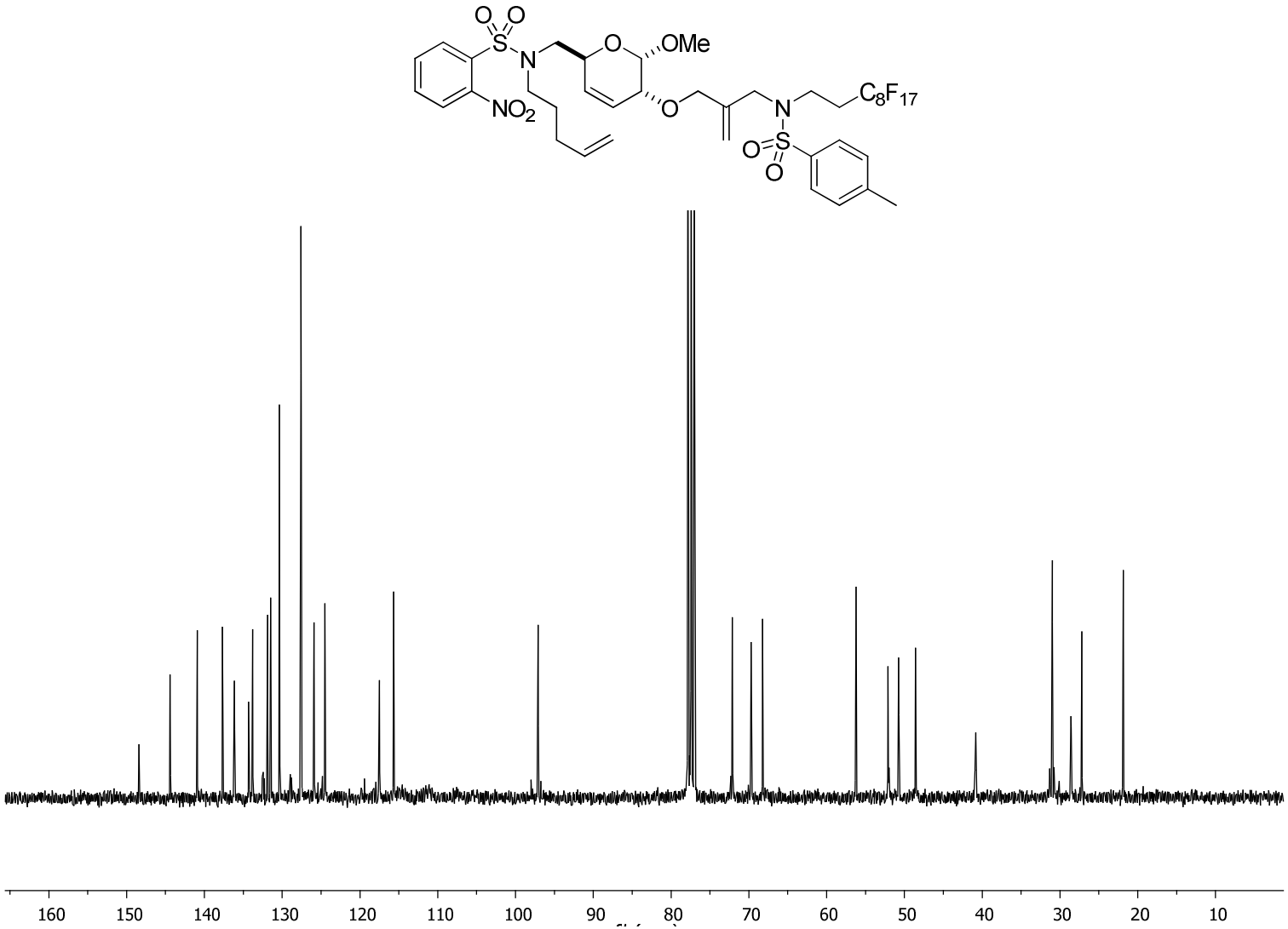
1. W. C. Still, M. Kahn, and A. Mitra, *J. Org. Chem.*, 1978. **43**, 2923.
2. Z. Luo, Q. Zhang, Y. Oderaotoshi, and D. P. Curran, *Science*, 2001. **291**, 1766.
3. D. P. Curran and Z. Luo, *J. Am. Chem. Soc.*, 1999. **121**, 9069.

500 MHz ^{1}H NMR of S1

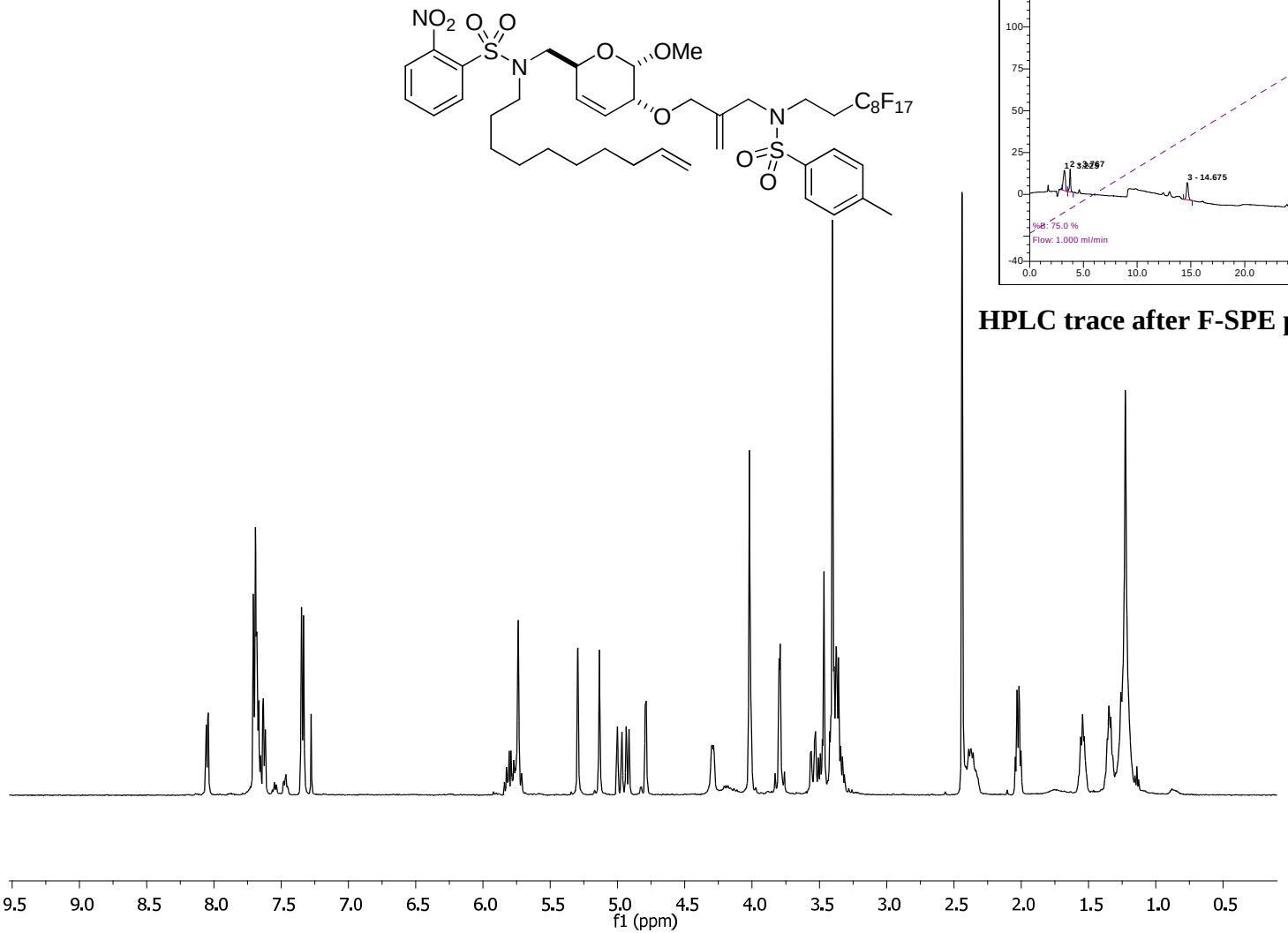


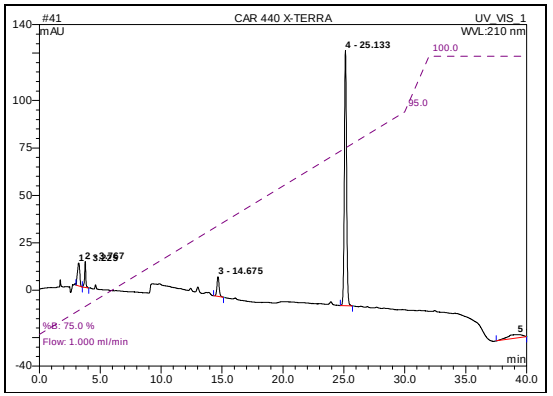


75 MHz ^{13}C NMR of S1



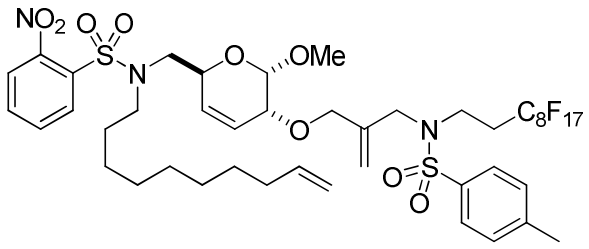
500 MHz ^{1}H NMR of S2 (F-SPE purified only)

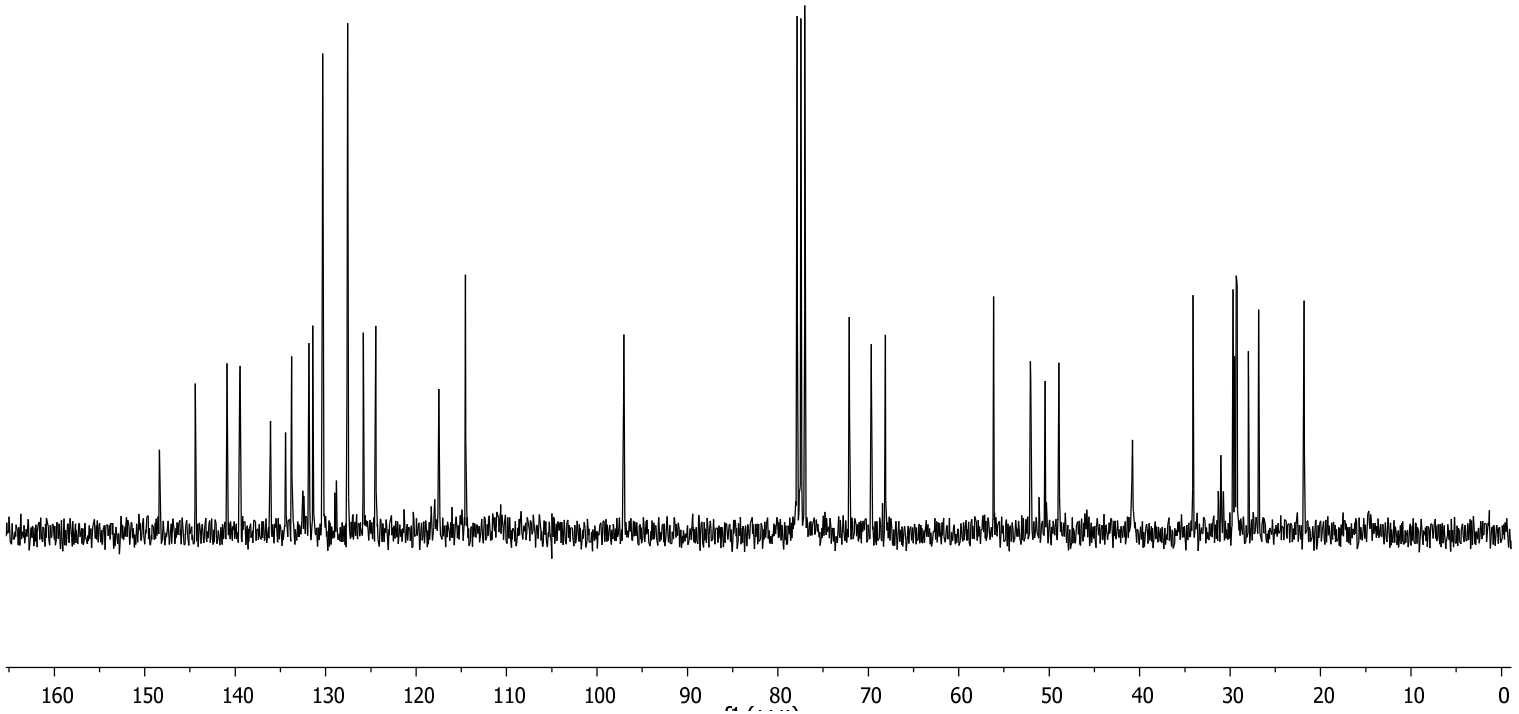




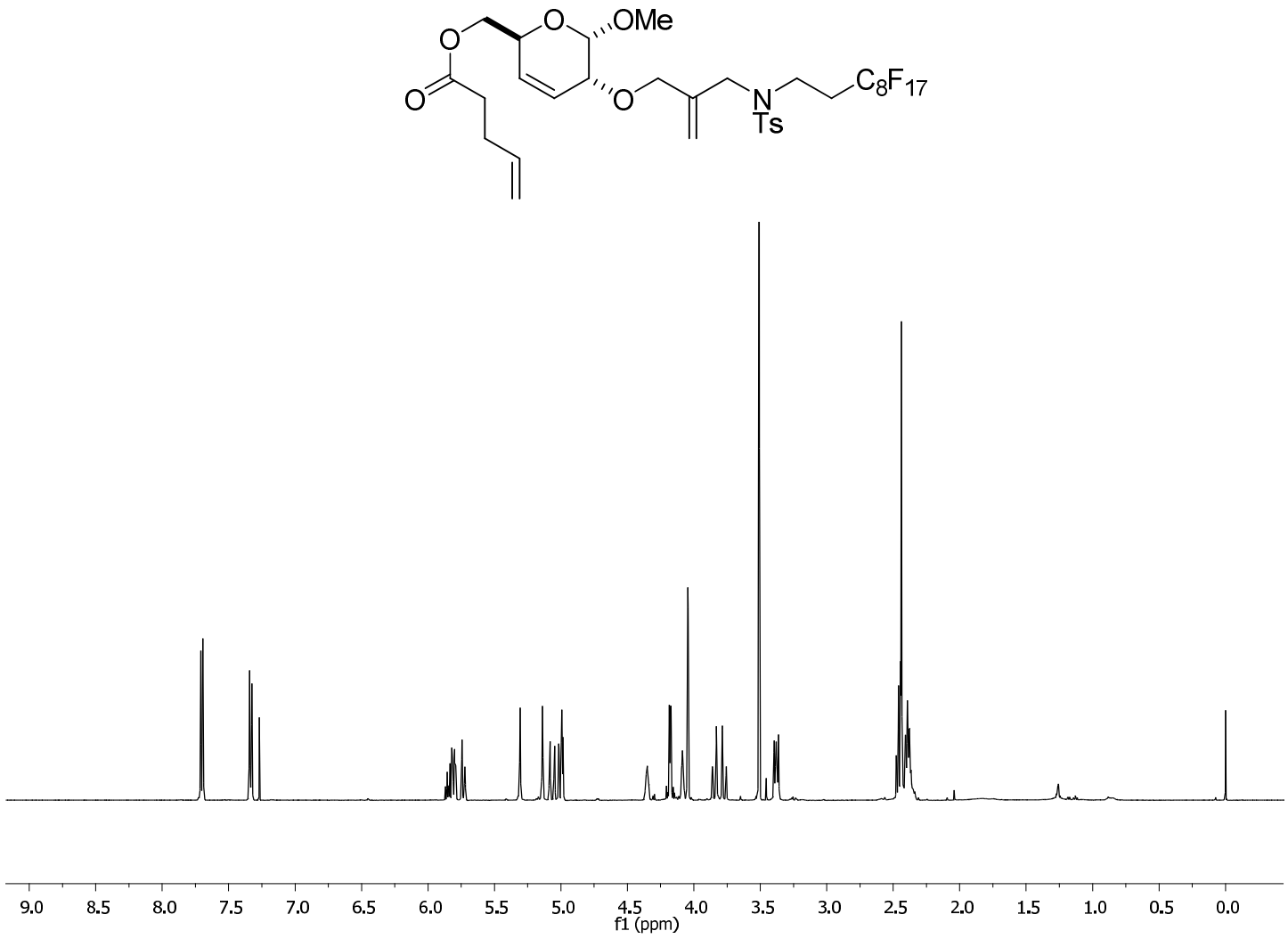
HPLC trace after F-SPE purification only

75 MHz ^{13}C NMR of S2

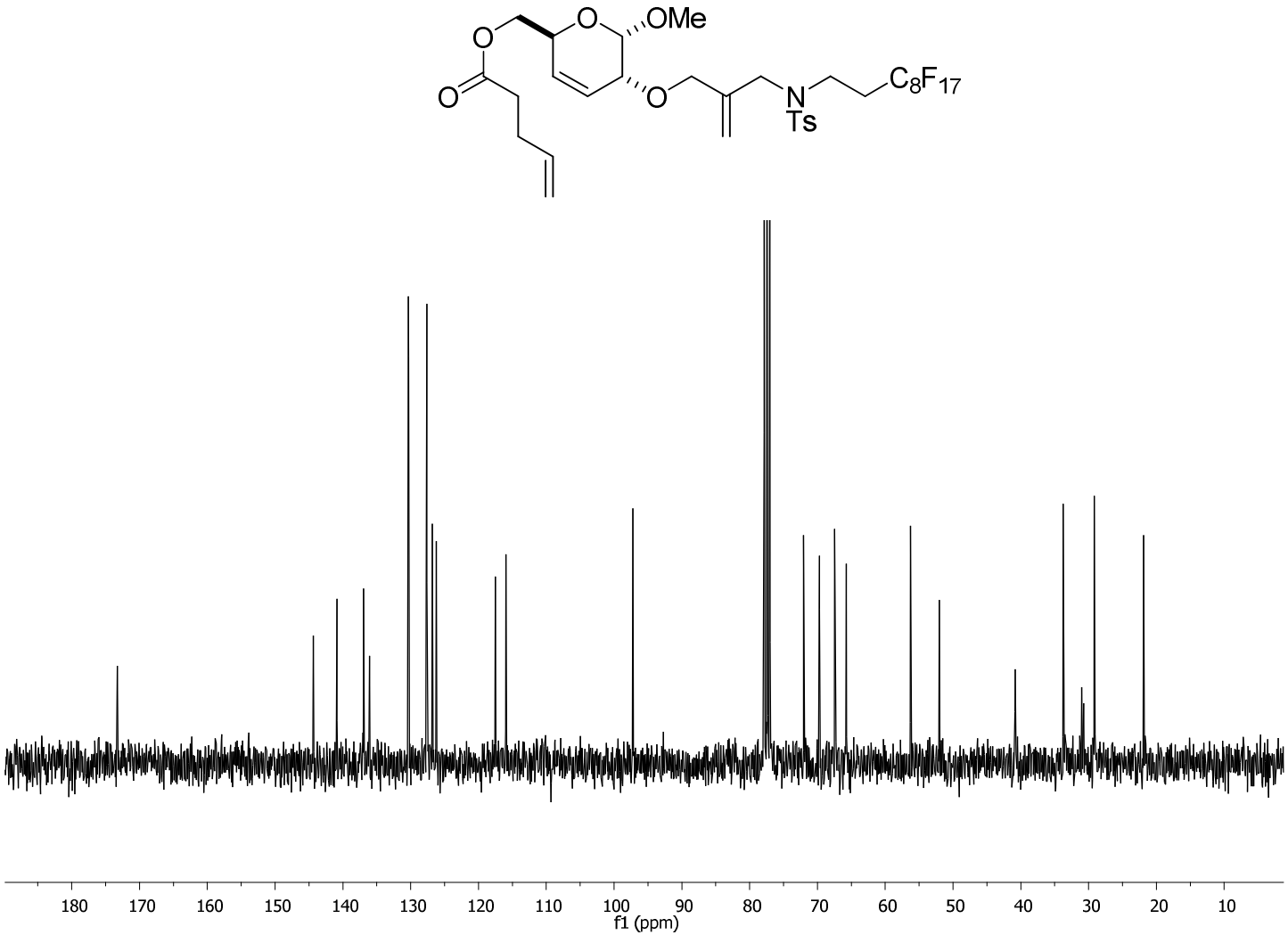




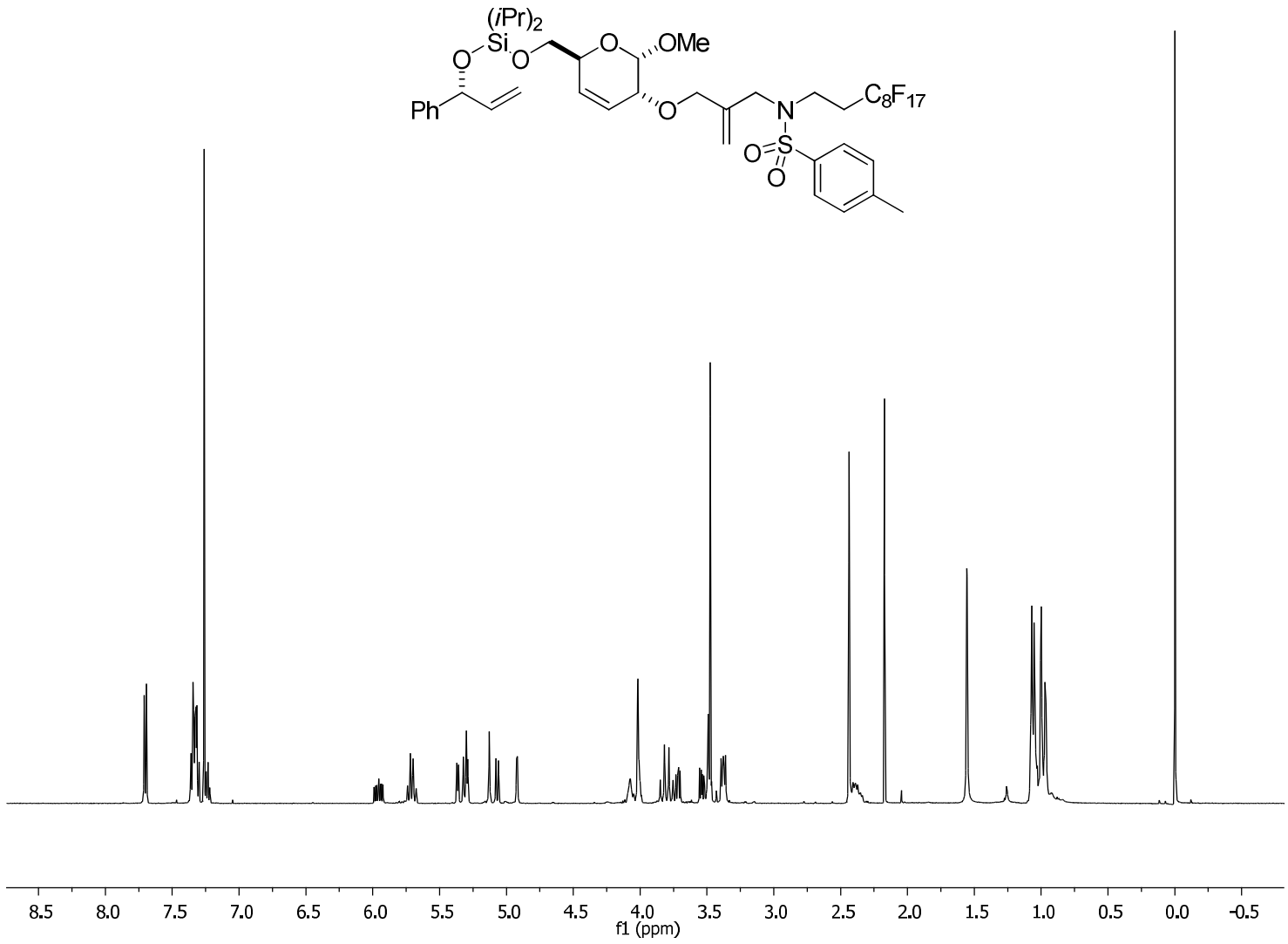
500 MHz ^{1}H NMR of S3 (F-SPE purified only)



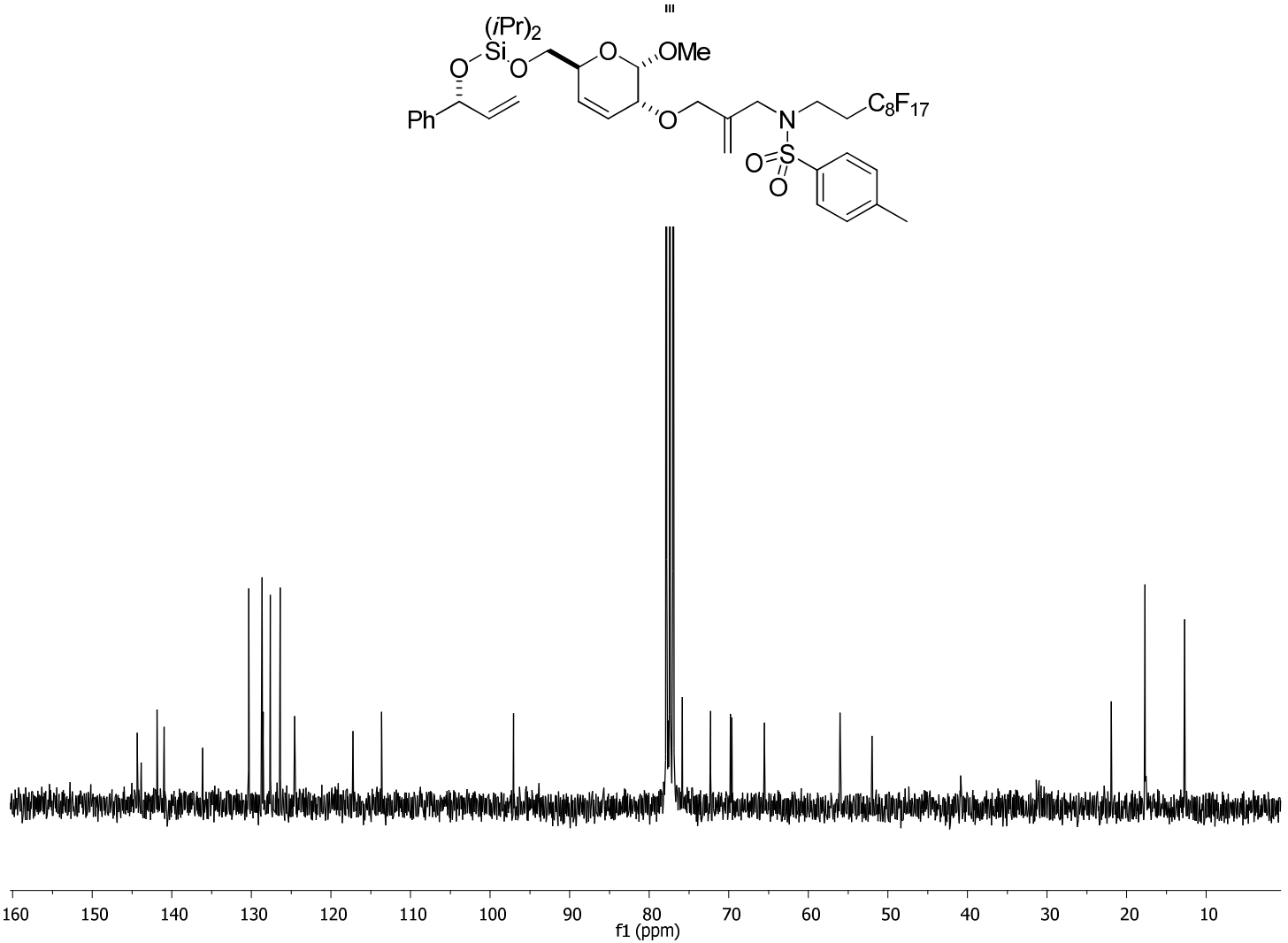
75 MHz ^{13}C NMR of S3



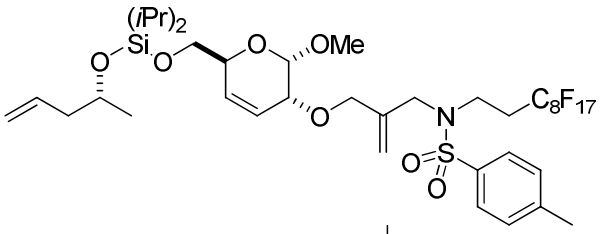
500 MHz ^{1}H NMR of S4 (F-SPE purified only)

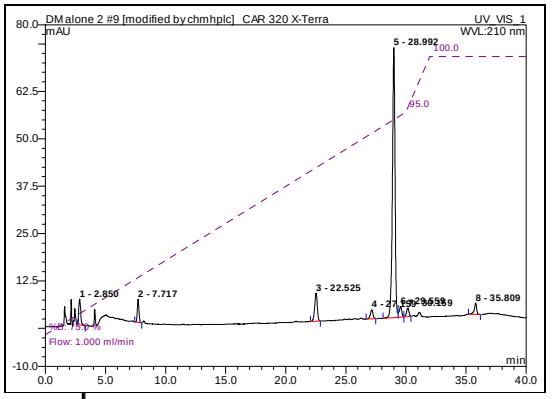


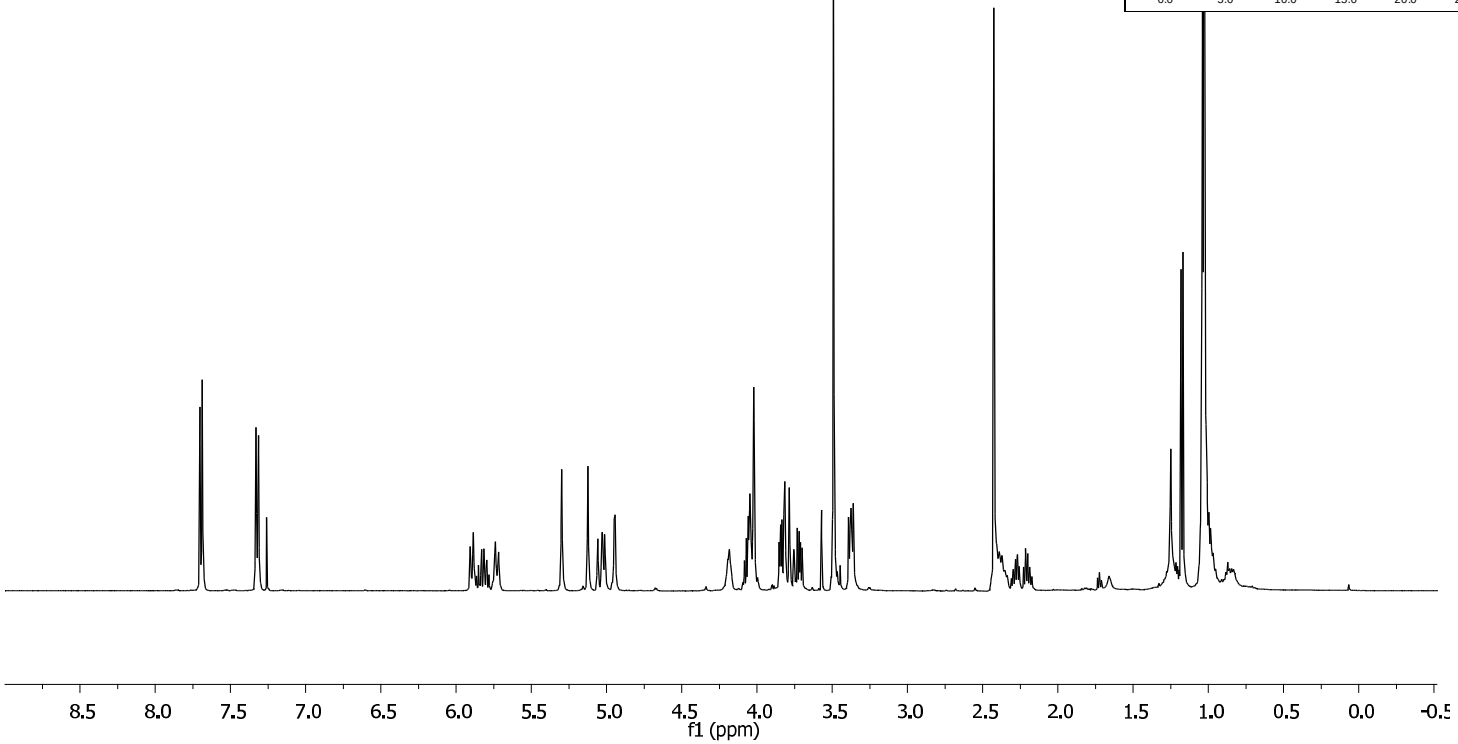
75 MHz ^{13}C NMR of S4



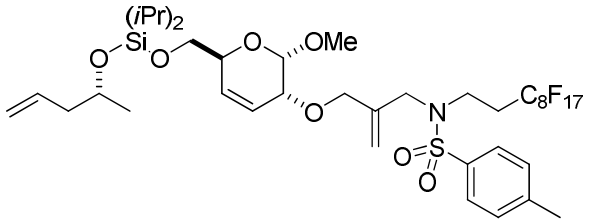
500 MHz ^{1}H NMR of S5 (F-SPE purified only)

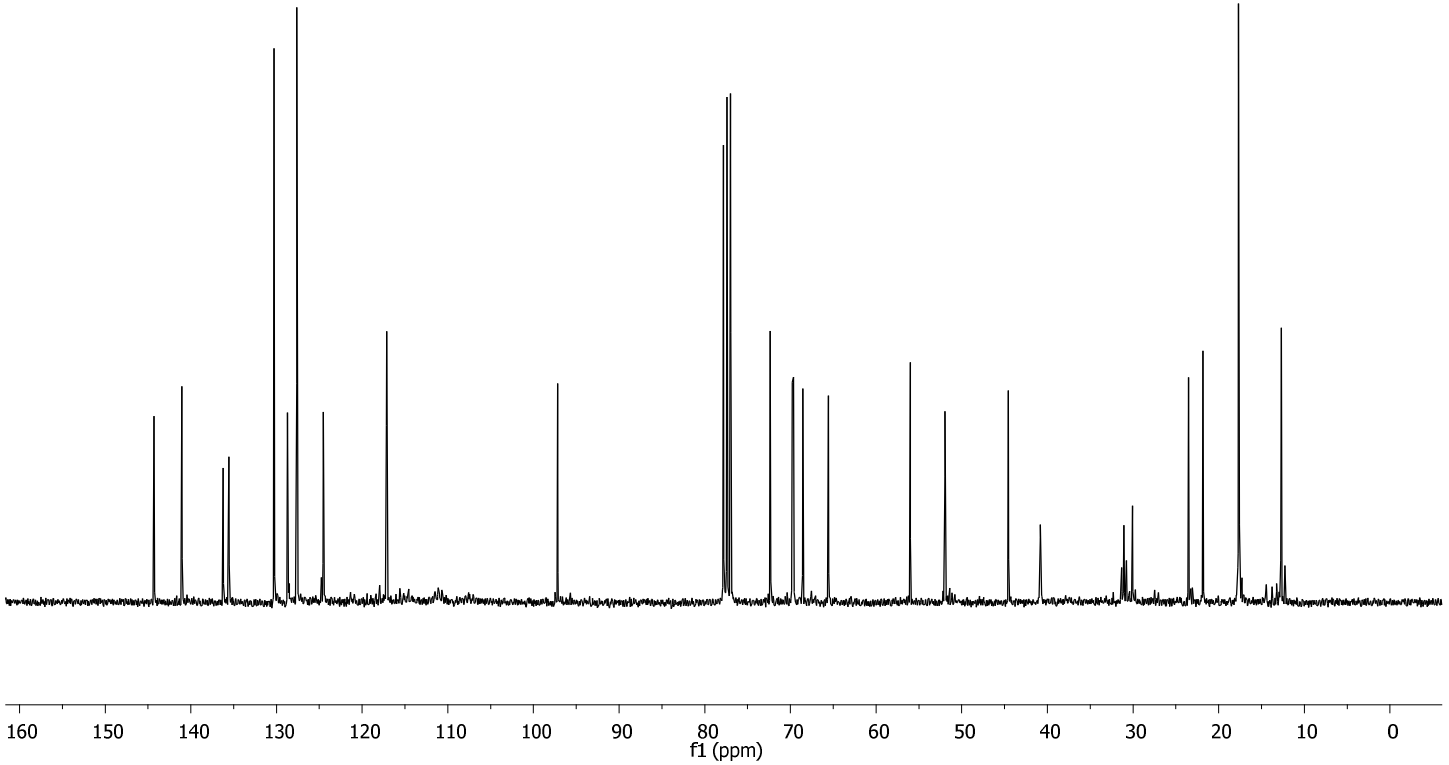




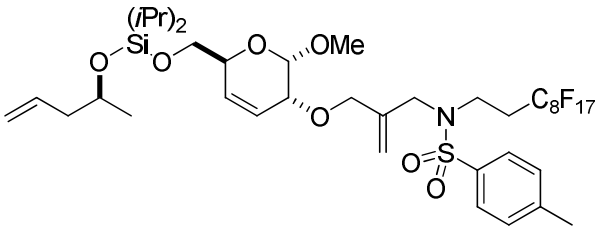


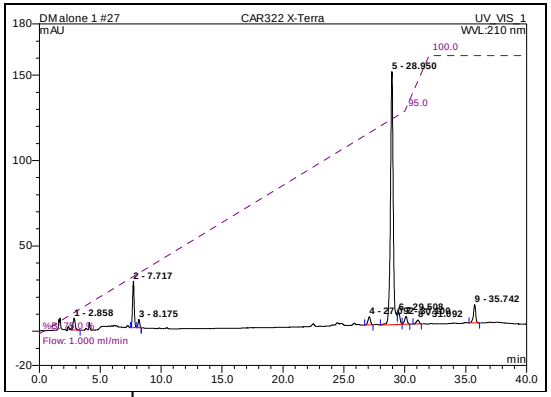
75 MHz ^{13}C NMR of S5

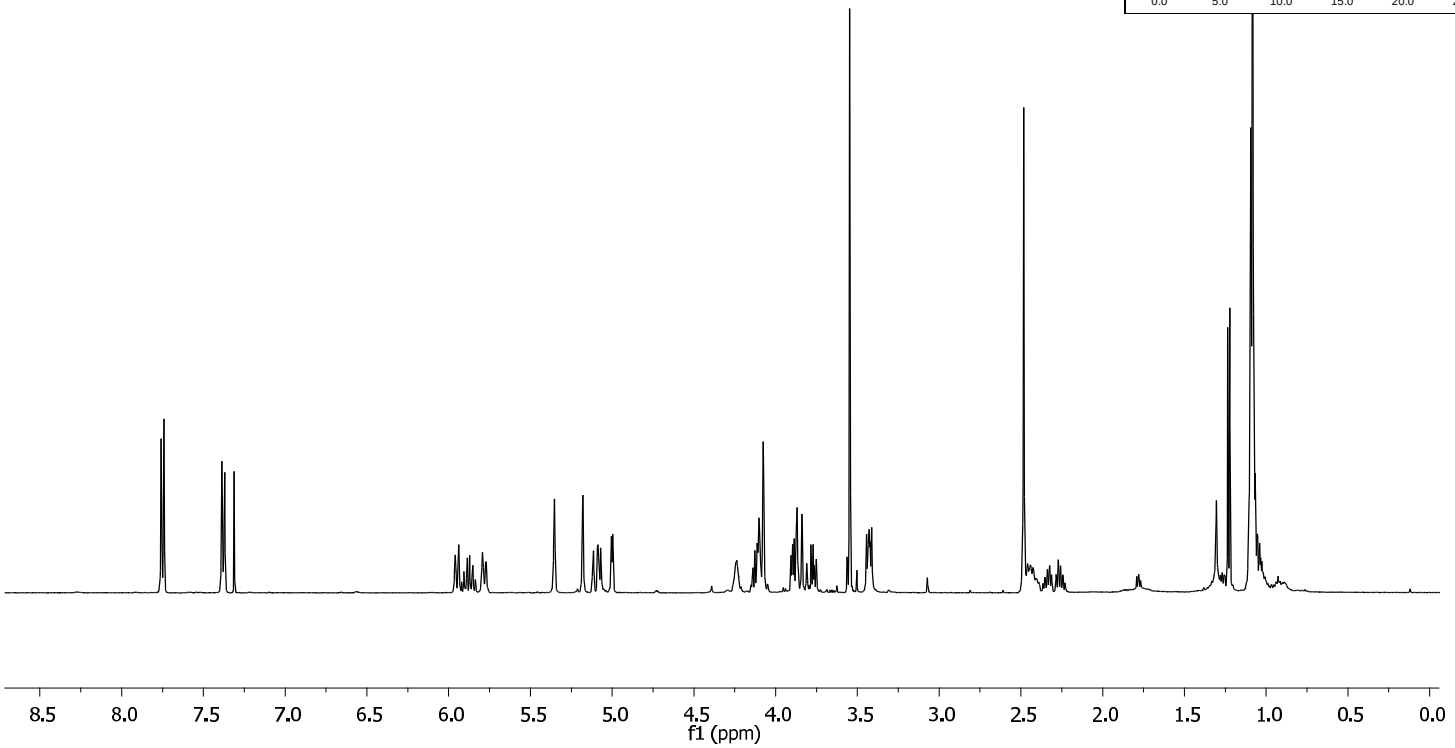




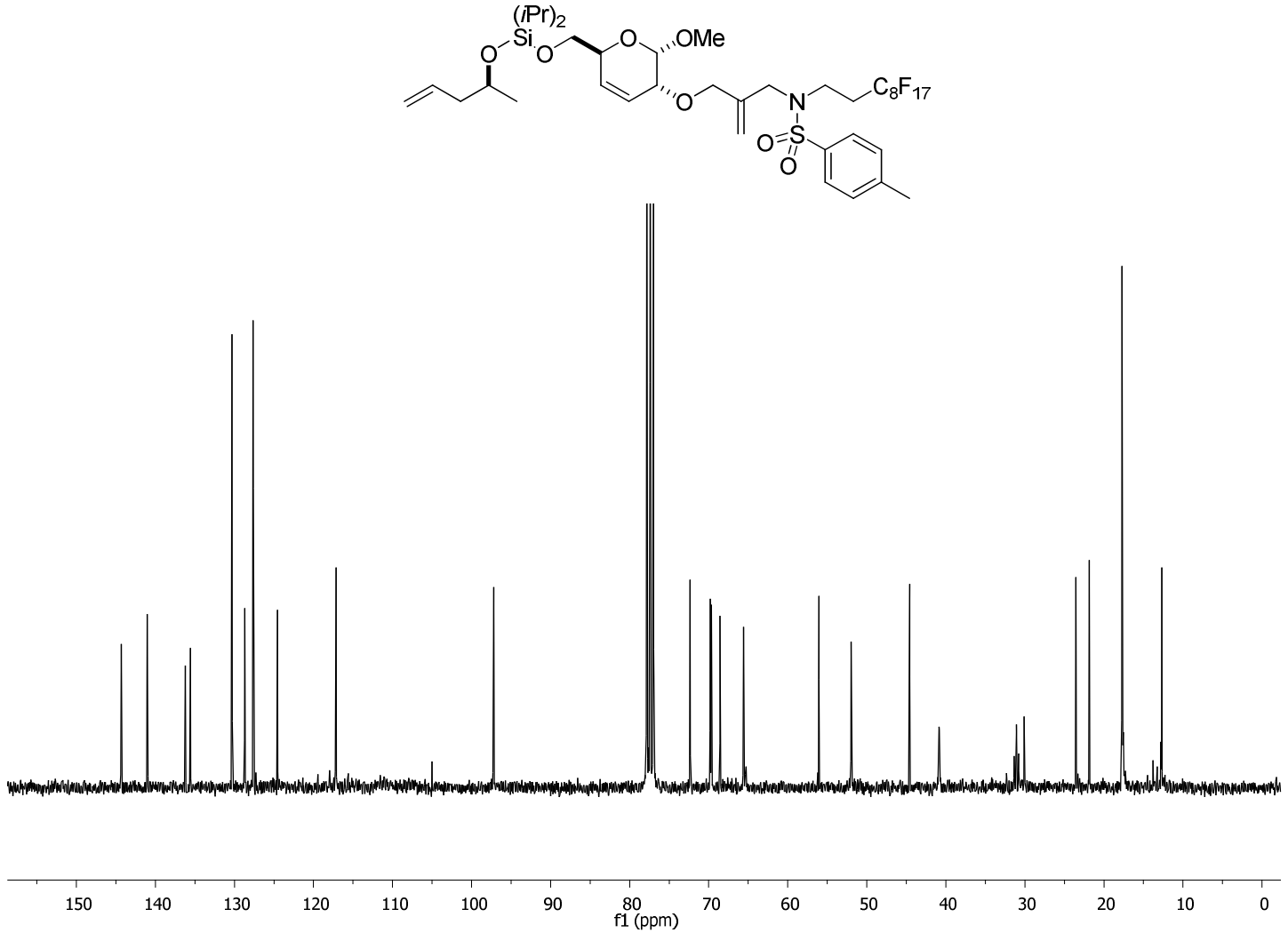
500 MHz ^{1}H NMR of S6 (F-SPE purified only)



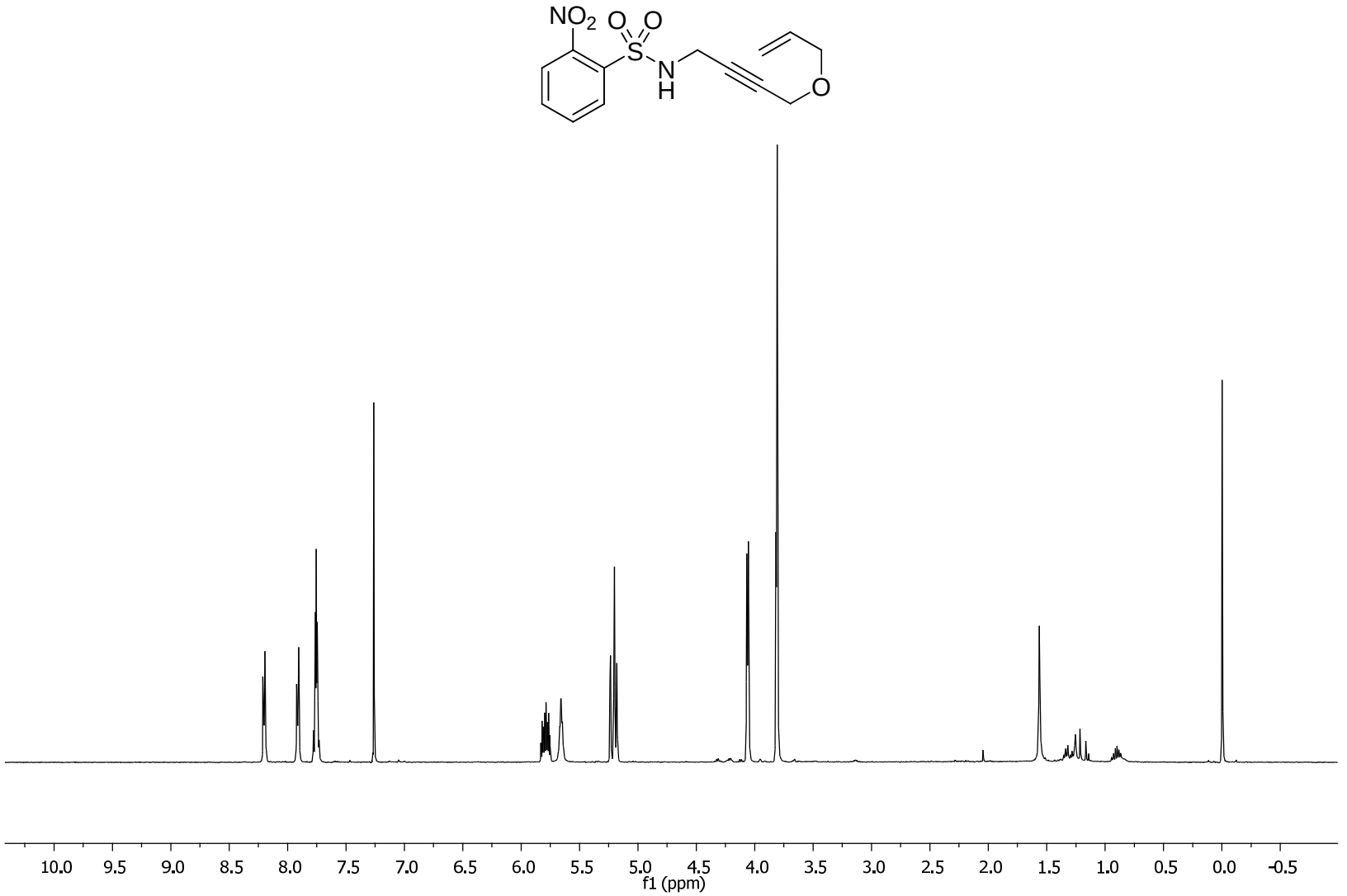




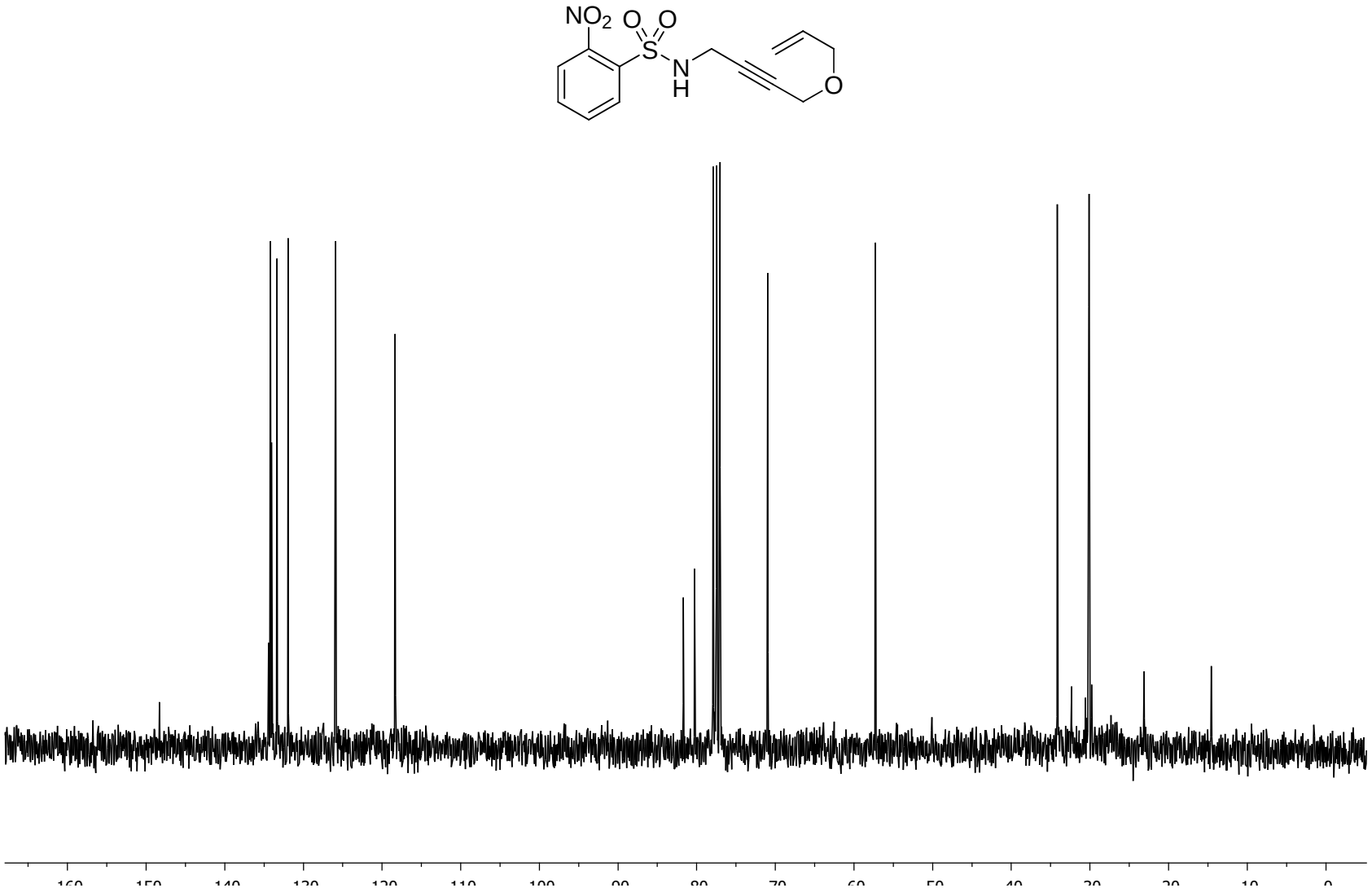
75 MHz ^{13}C NMR of S6



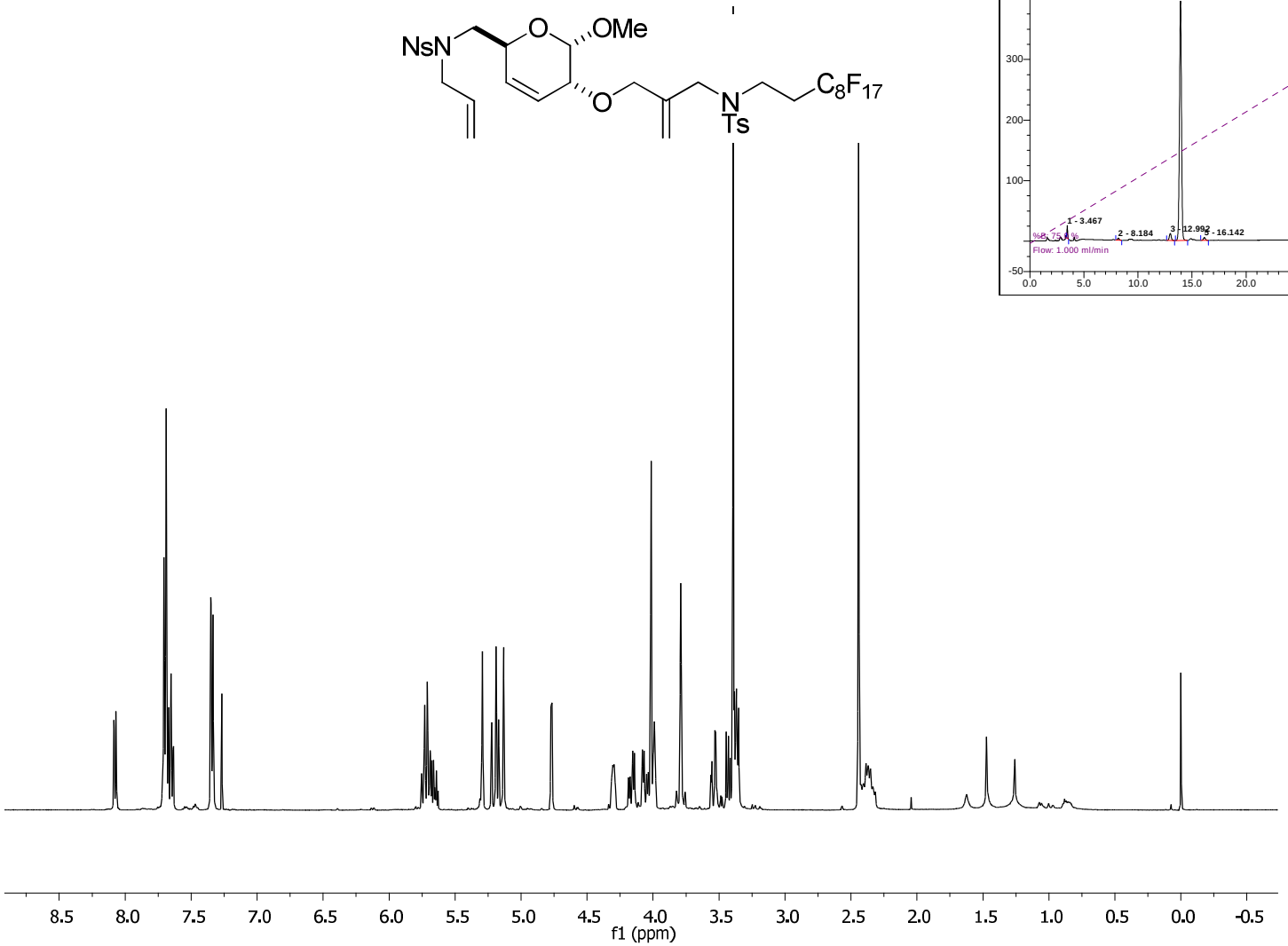
500 MHz ^{1}H NMR of 22

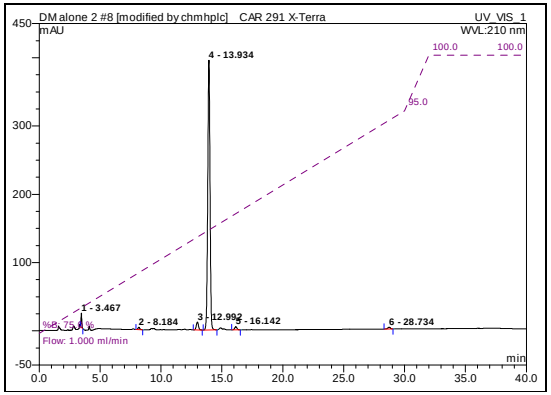


75 MHz ^{13}C NMR of 22

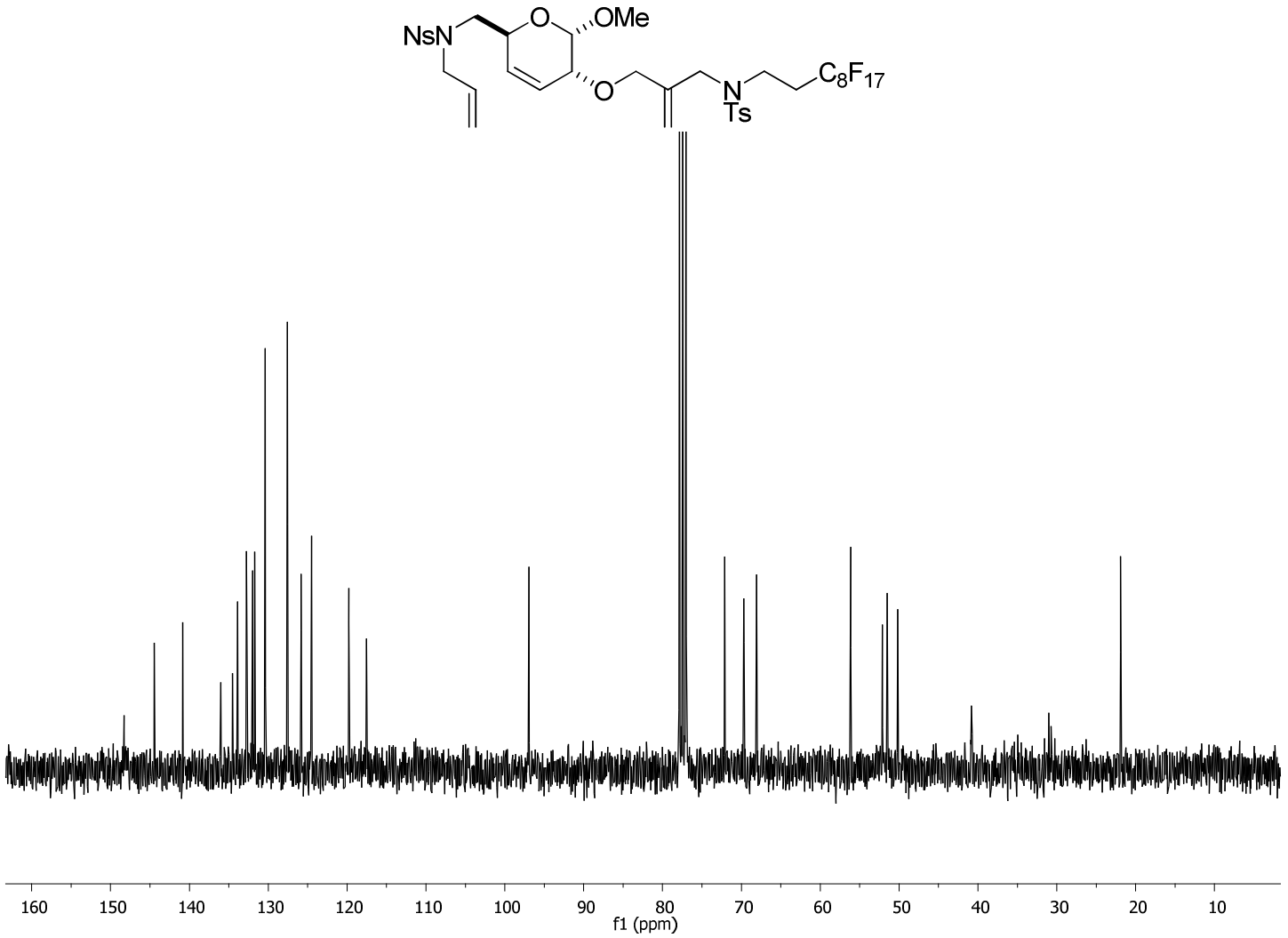


500 MHz ^{1}H NMR of S7 (F-SPE purified only)

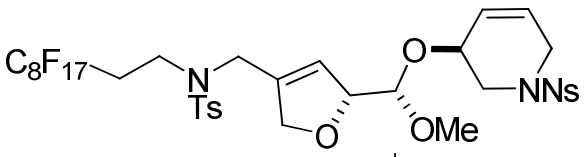


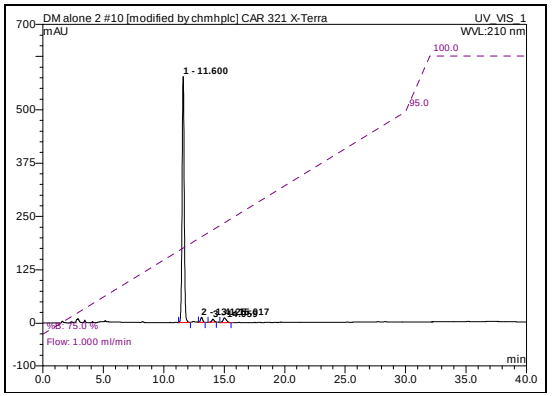


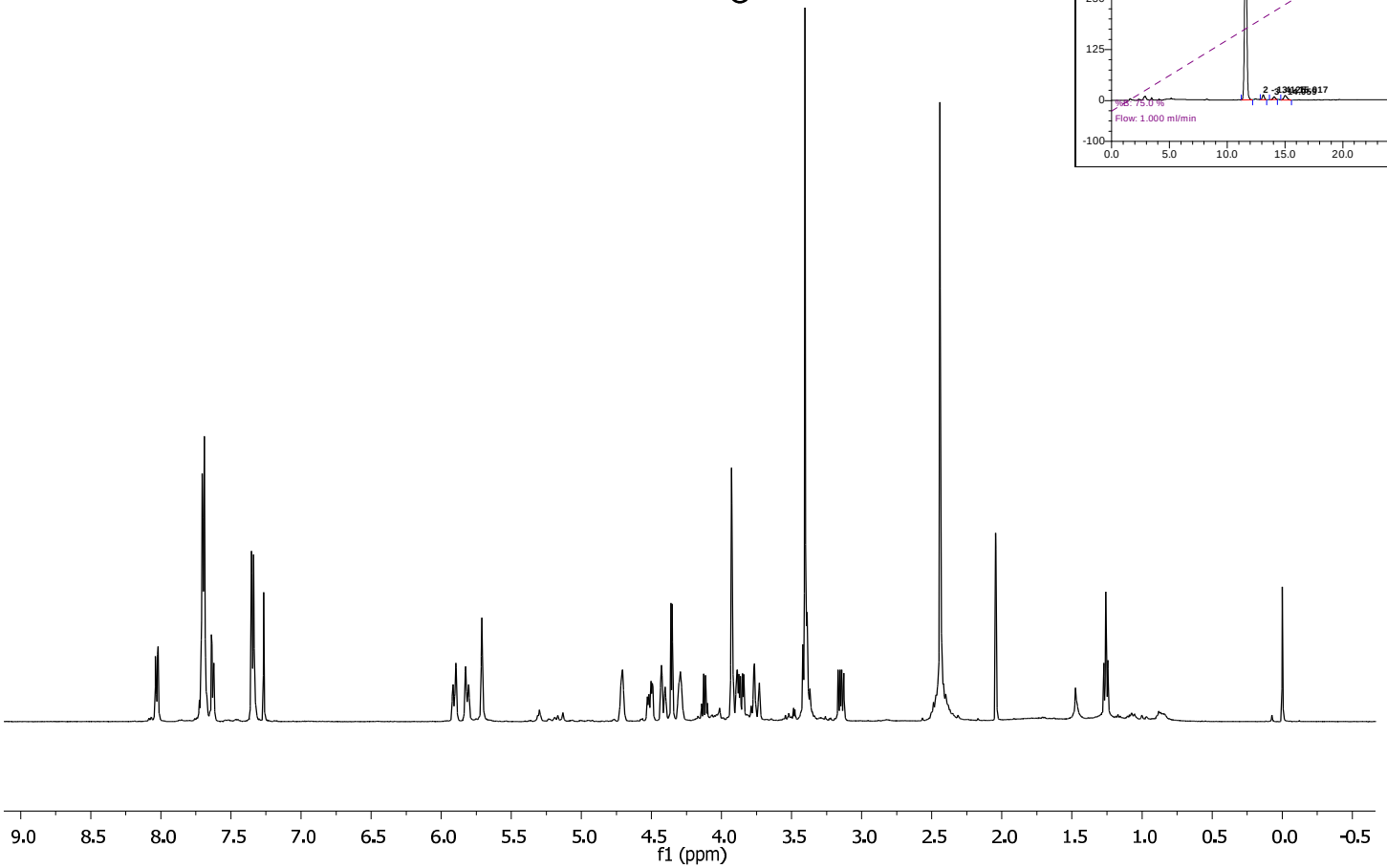
75 MHz ^{13}C NMR of S7



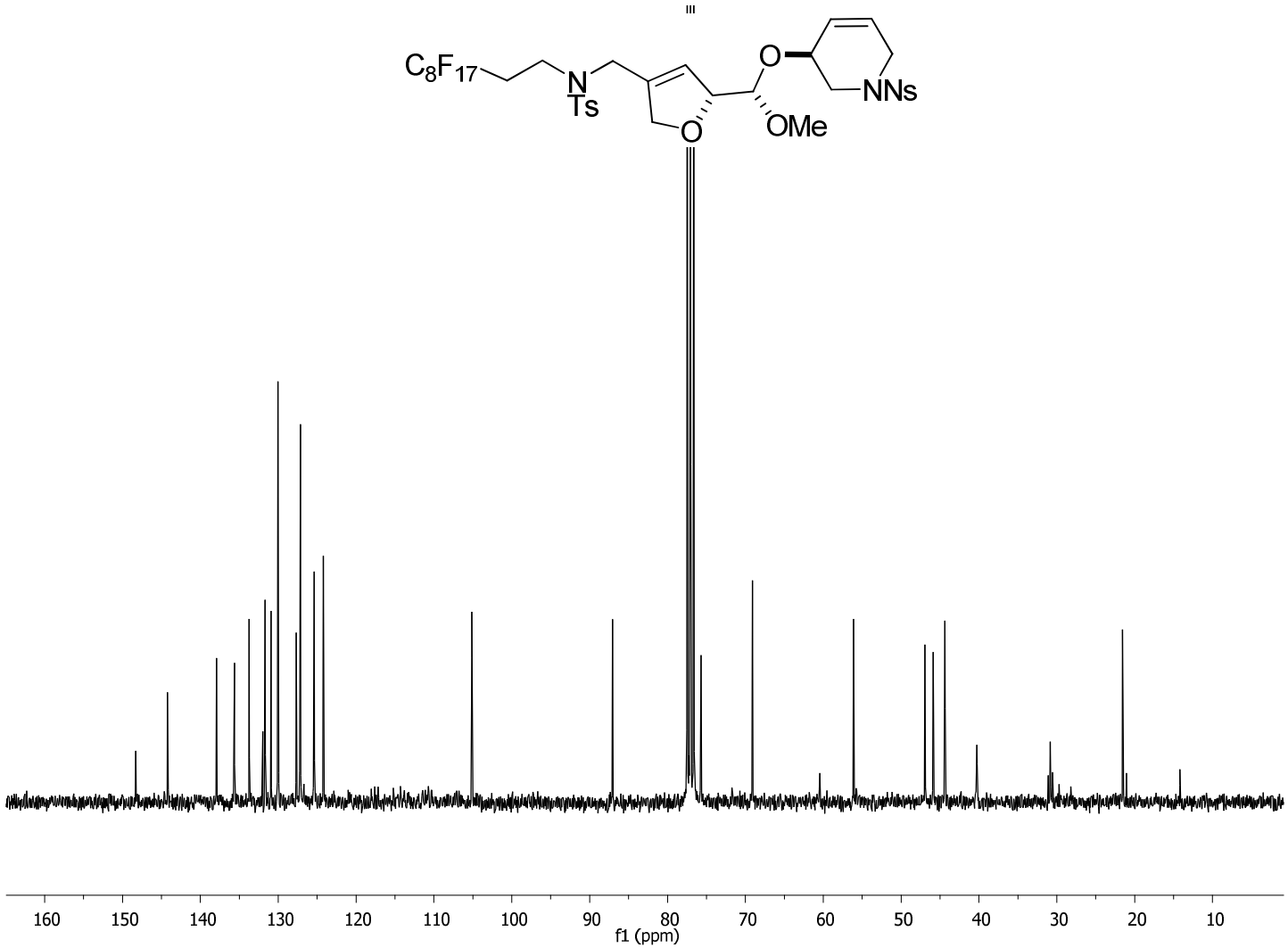
^{1}H NMR of 26 (R = R'^{F}) **(F-SPE purified only)**



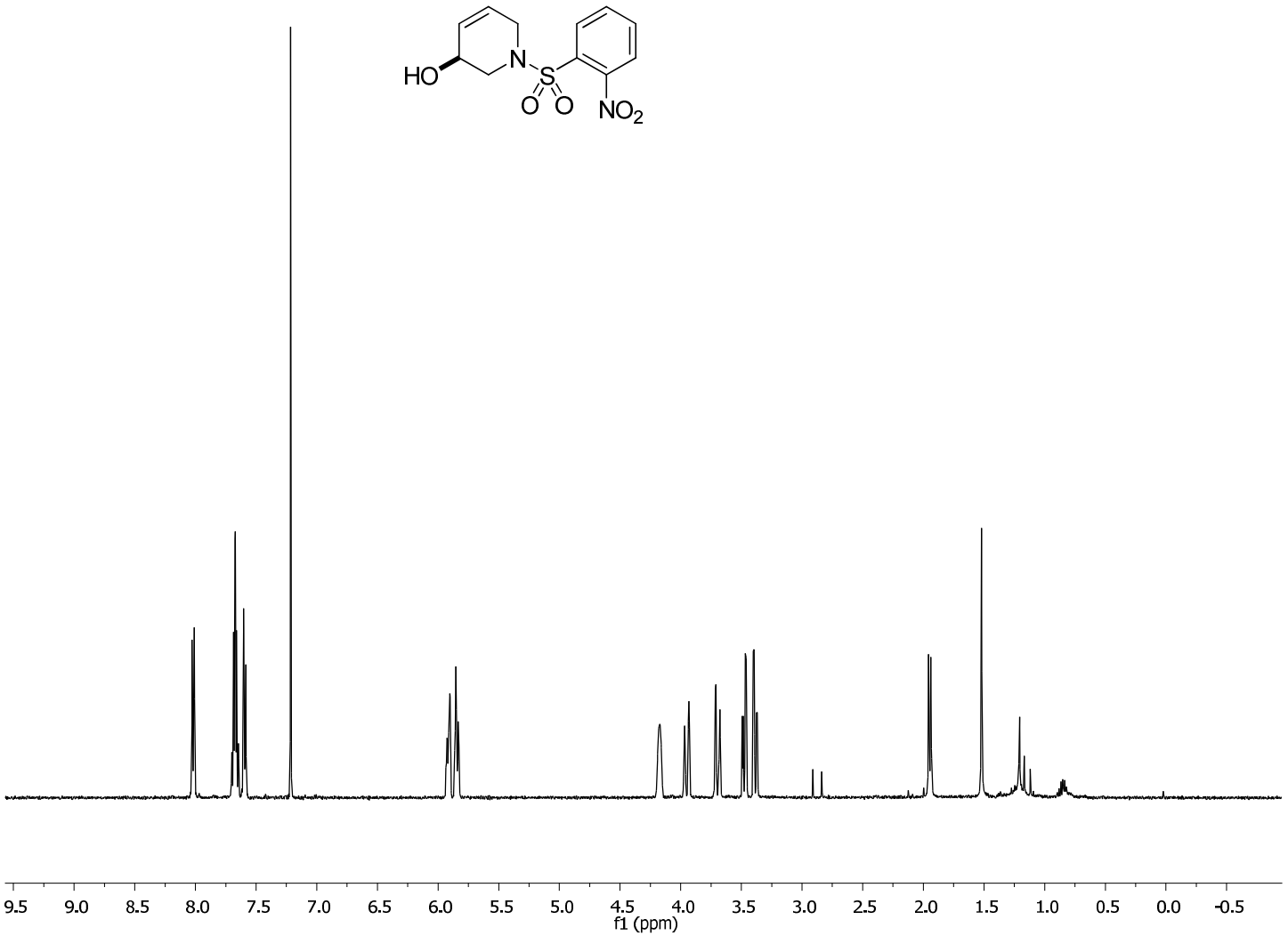




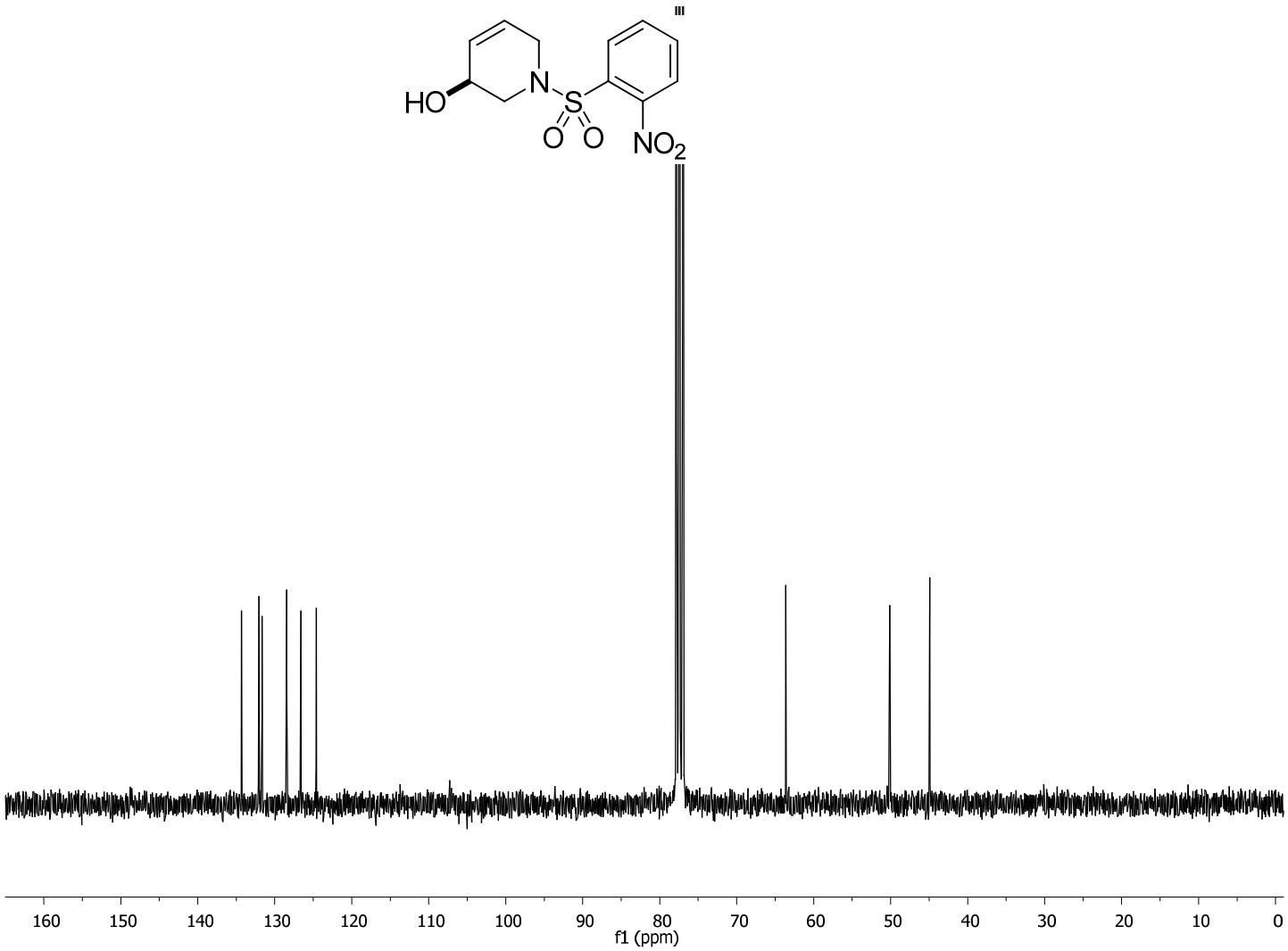
75 MHz ^{13}C NMR of 26 (R = R'^{F})



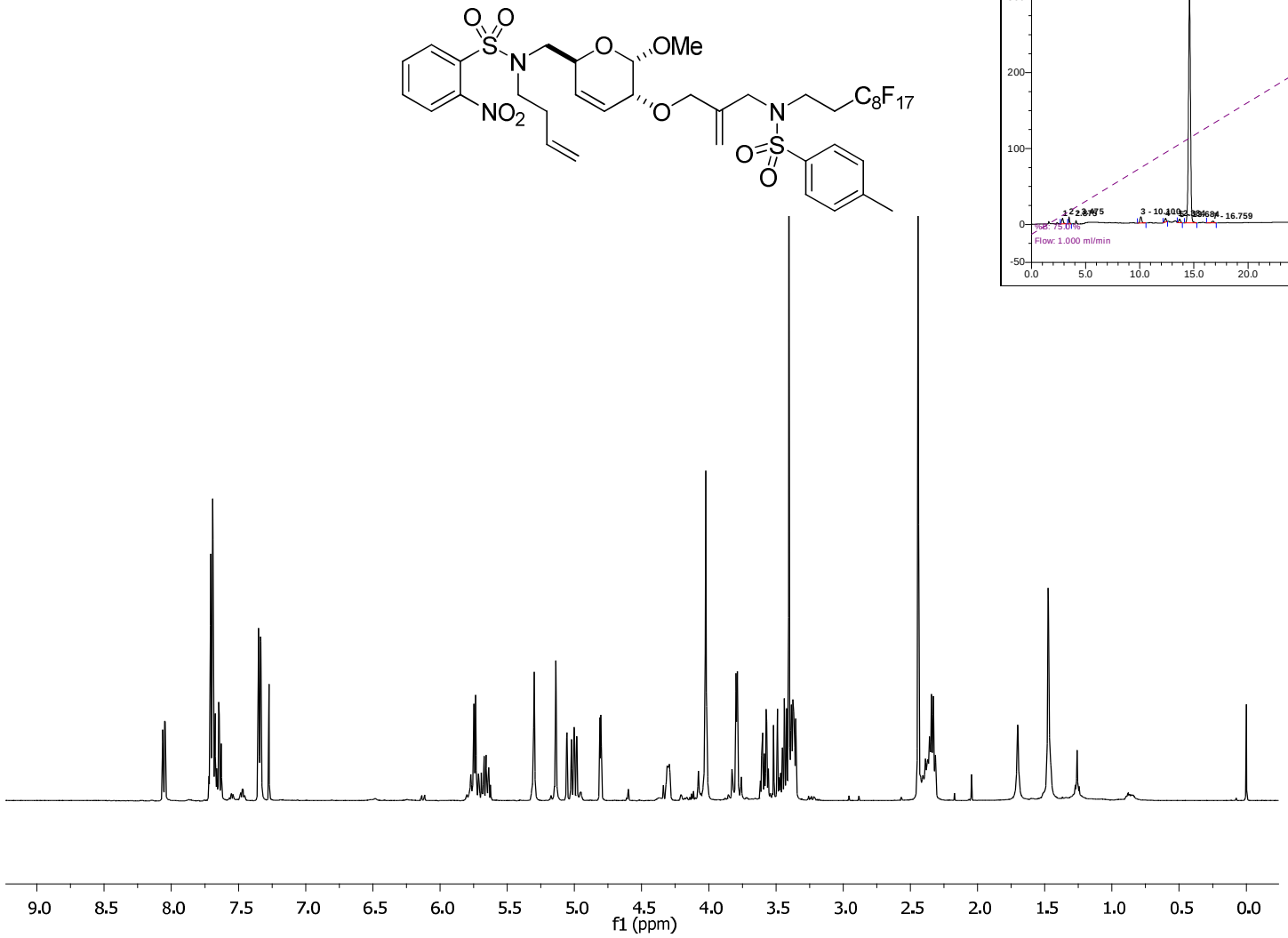
500 MHz ^{1}H NMR of 26 (R = H)

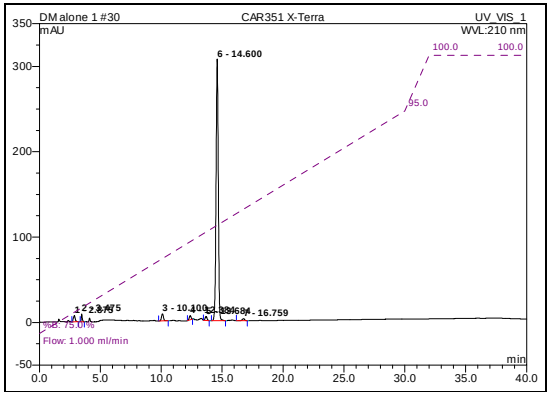


75 MHz ^{13}C NMR of 26 (R = H)

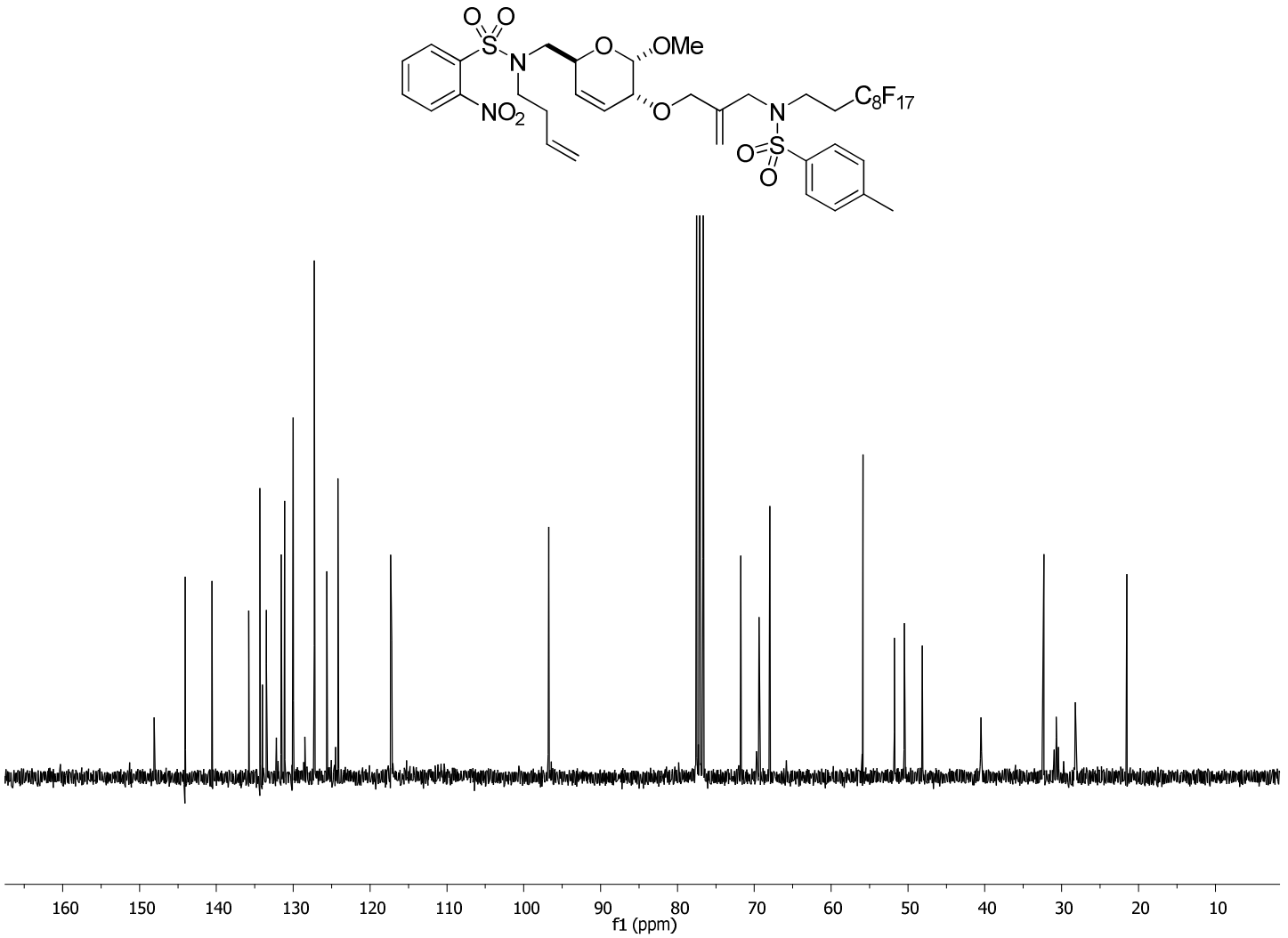


500 MHz ^{1}H NMR of S8 (F-SPE purified only)

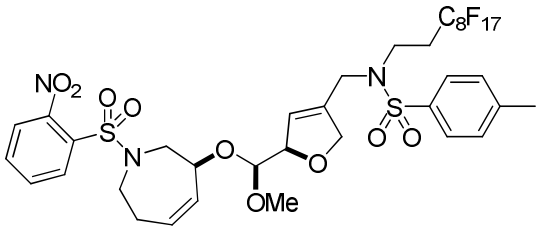


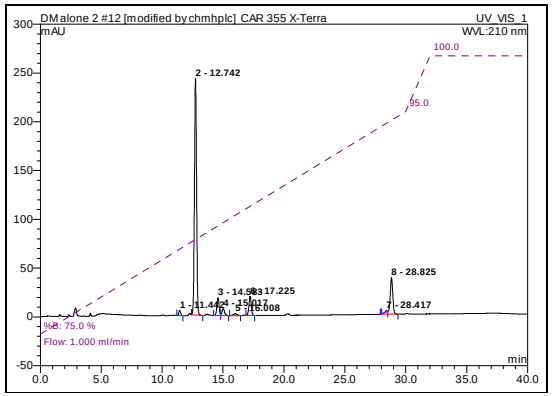


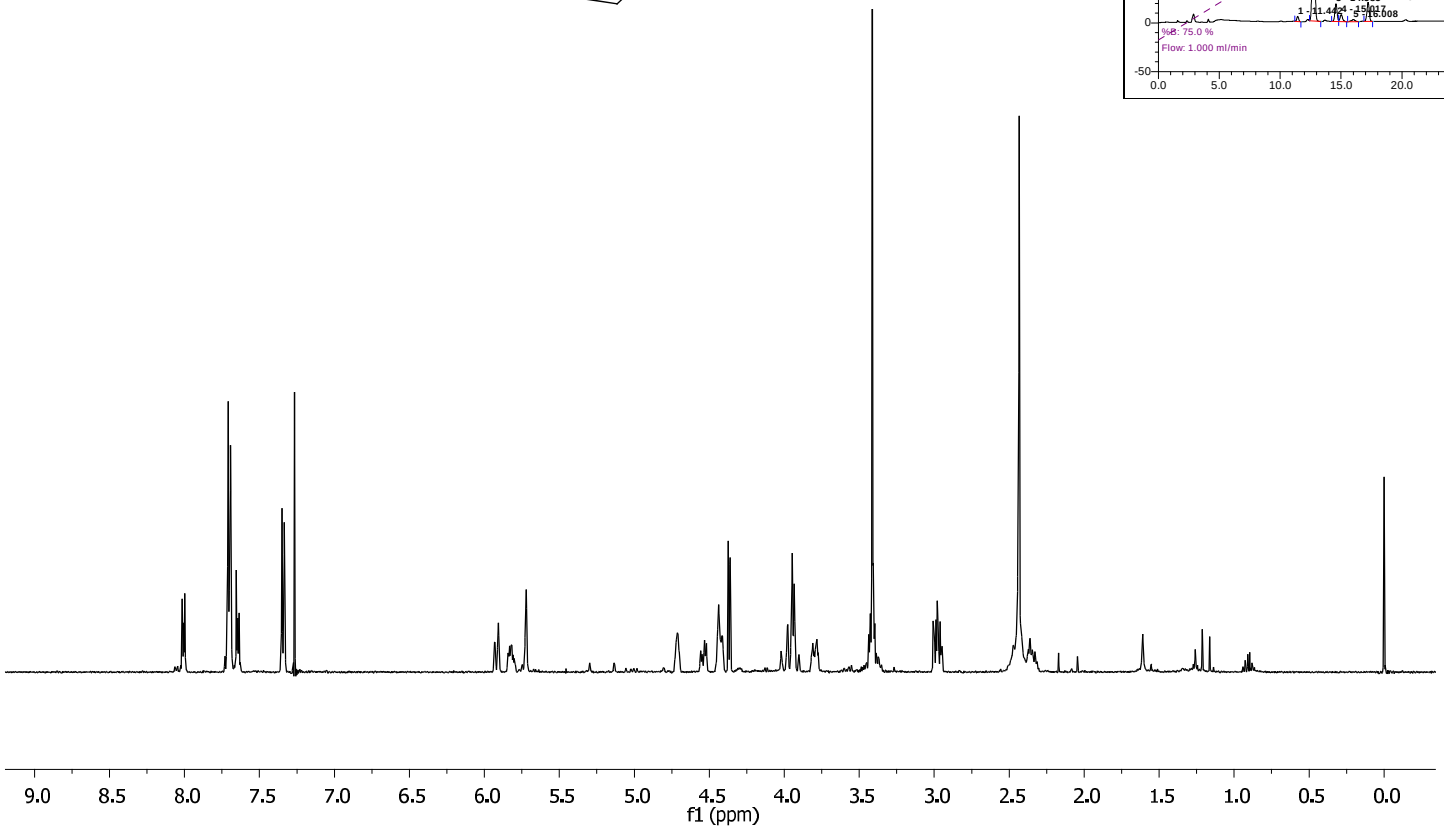
75 MHz ^{13}C NMR of S8



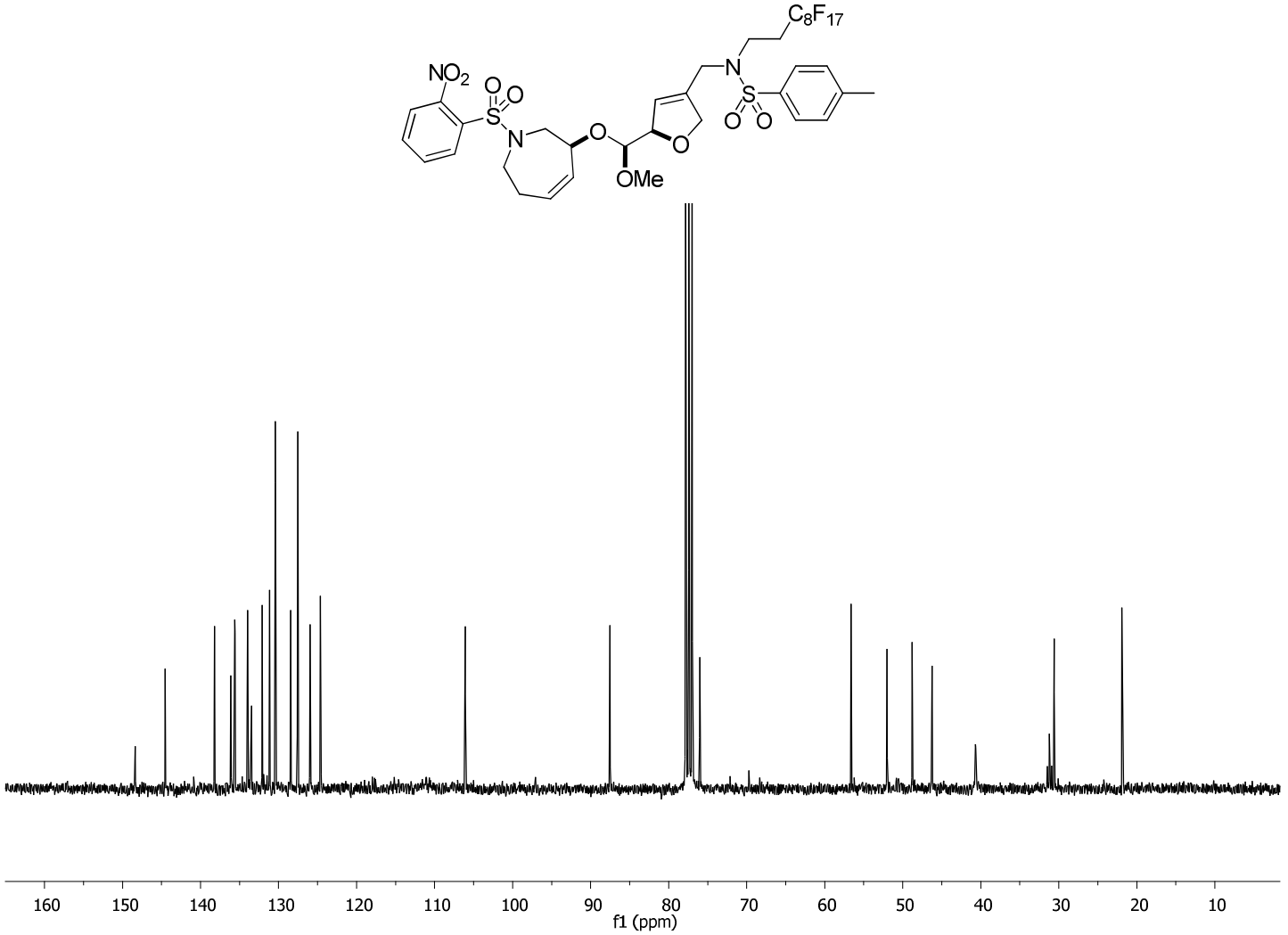
^{1}H NMR of 27 (R = R'^{F}) **(F-SPE purified only)**



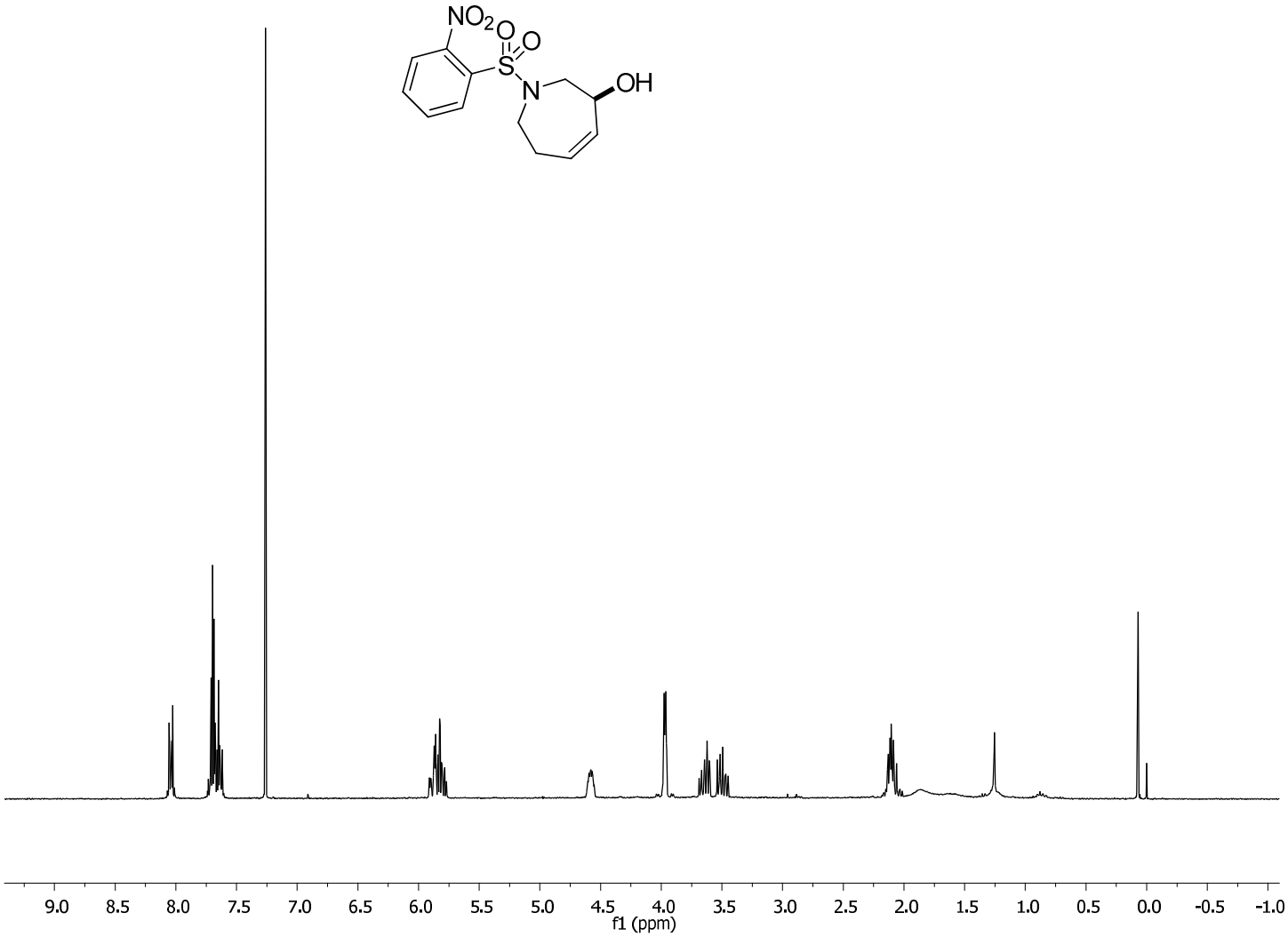




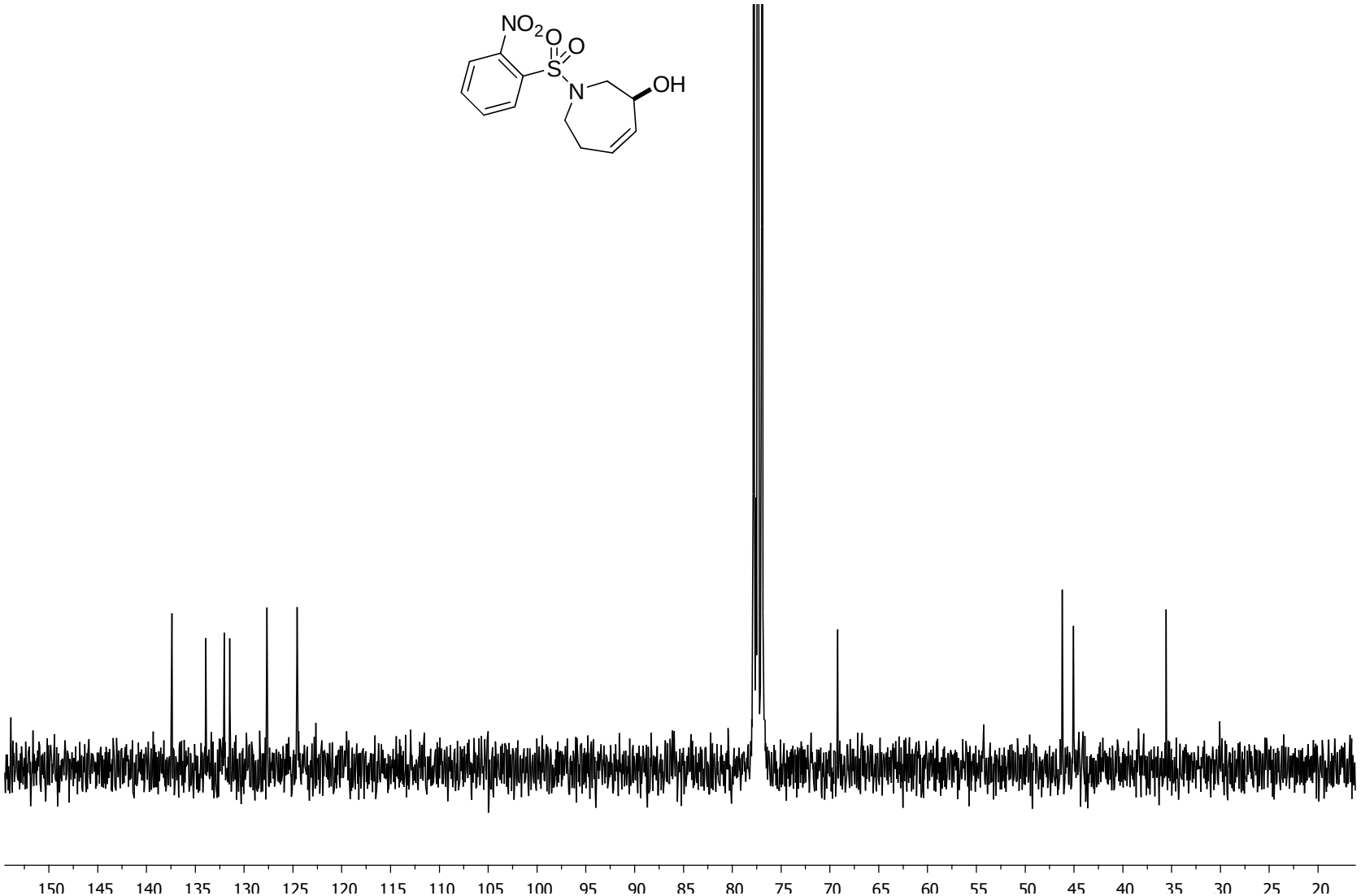
75 MHz ^{13}C NMR of 27 (R = R'^{F})



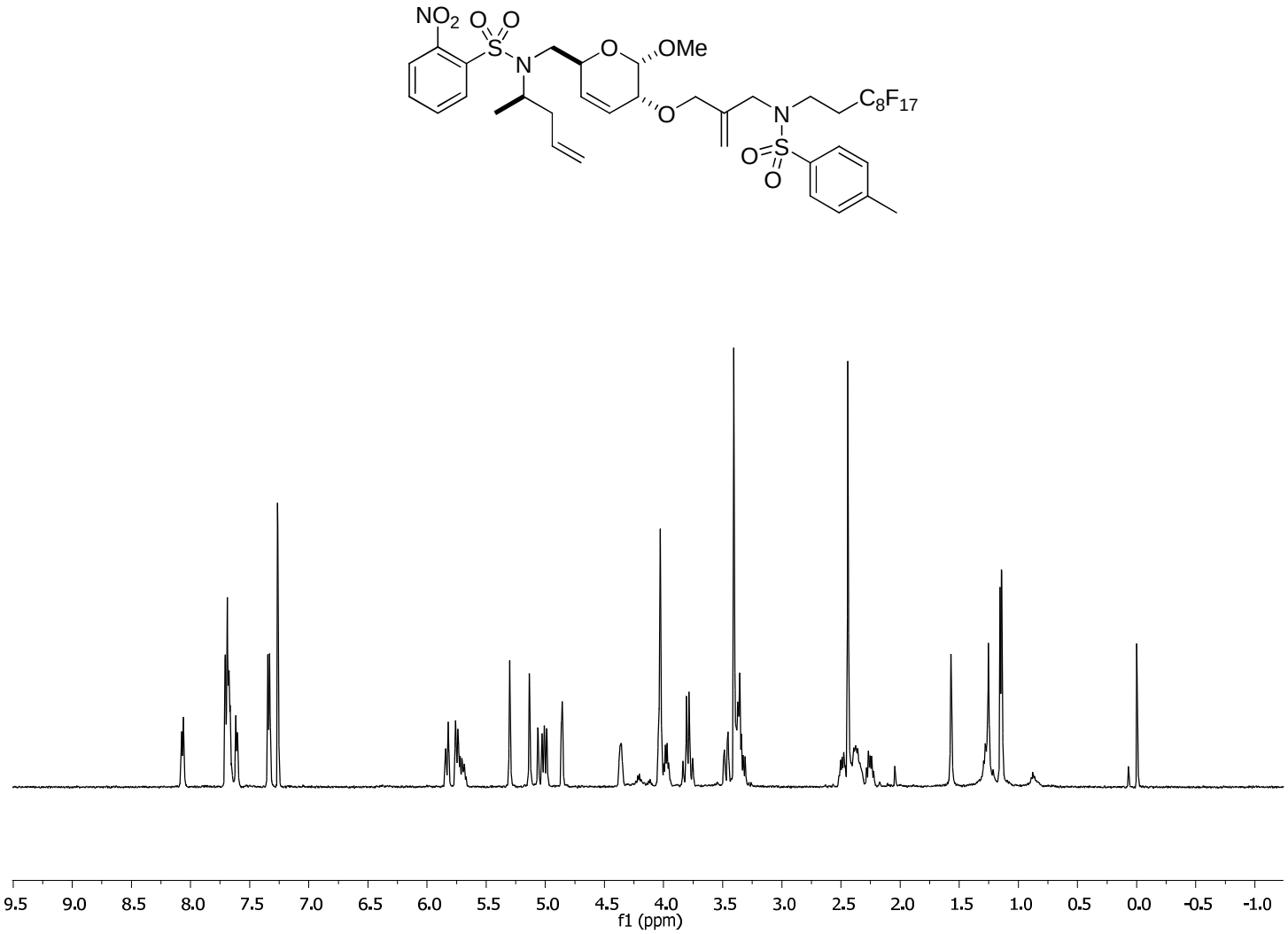
500 MHz ^{1}H NMR of 27 (R = H)



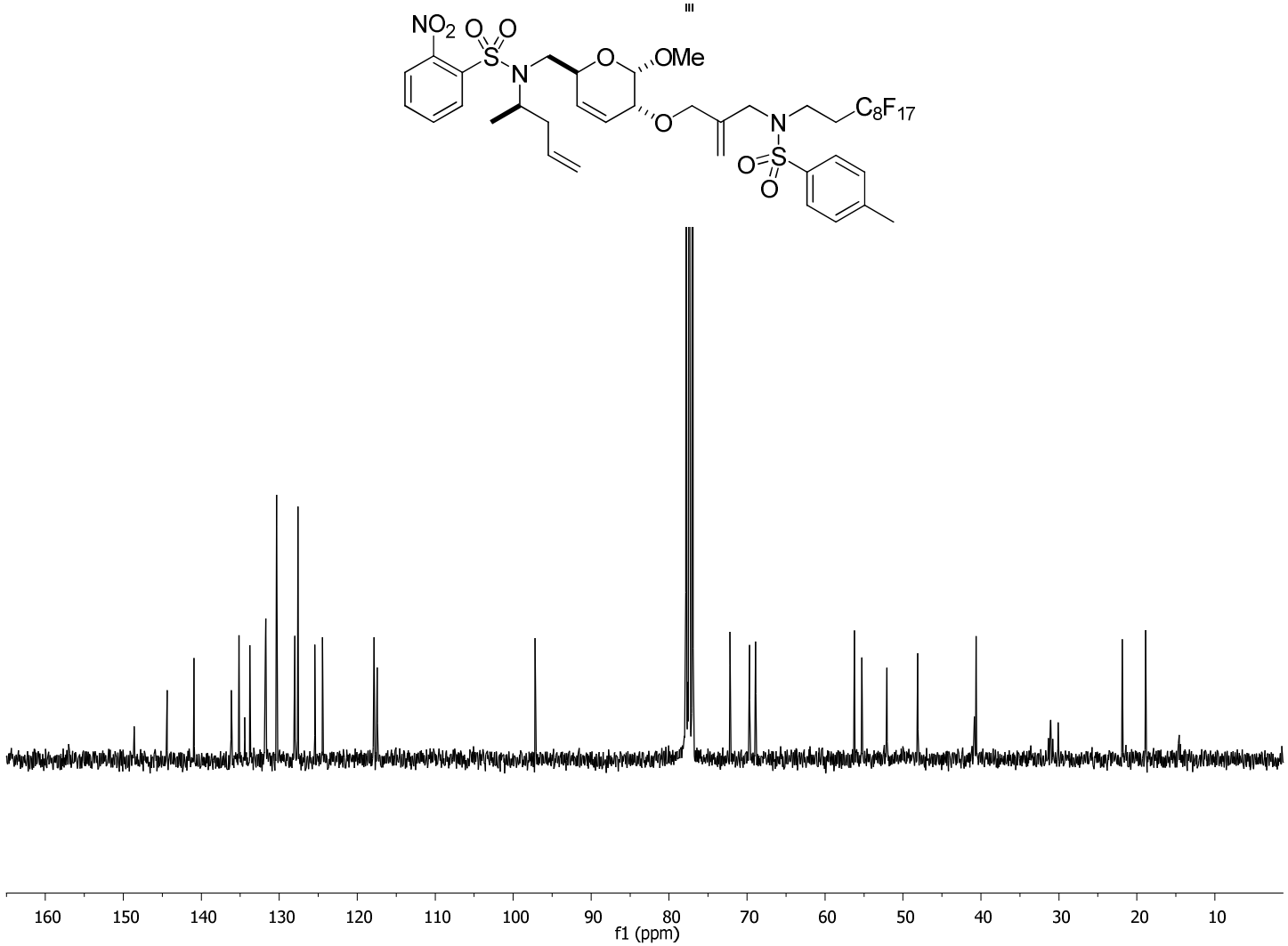
75 MHz ^{13}C NMR of 27 (R = H)



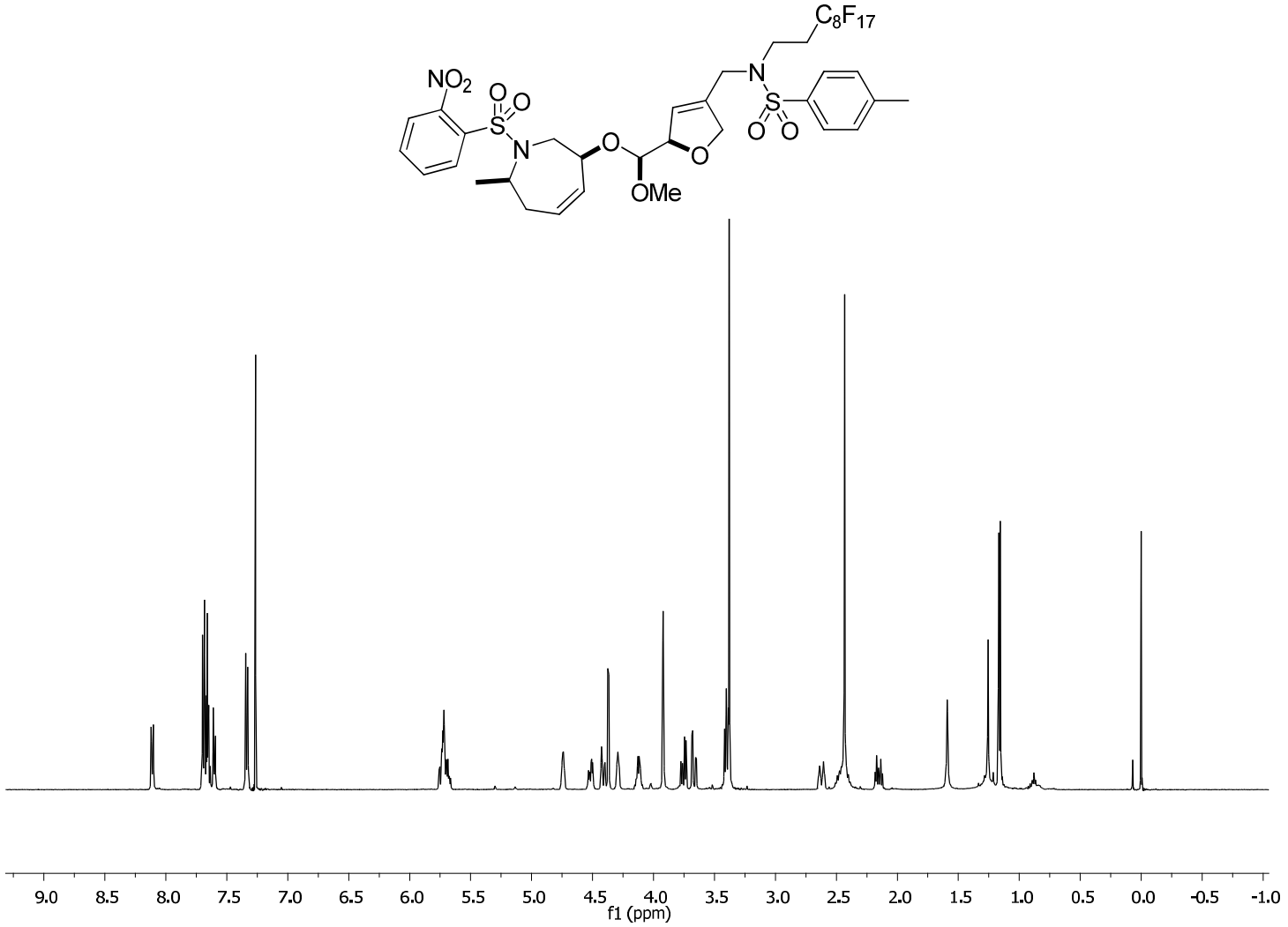
500 MHz ^{1}H NMR of S9



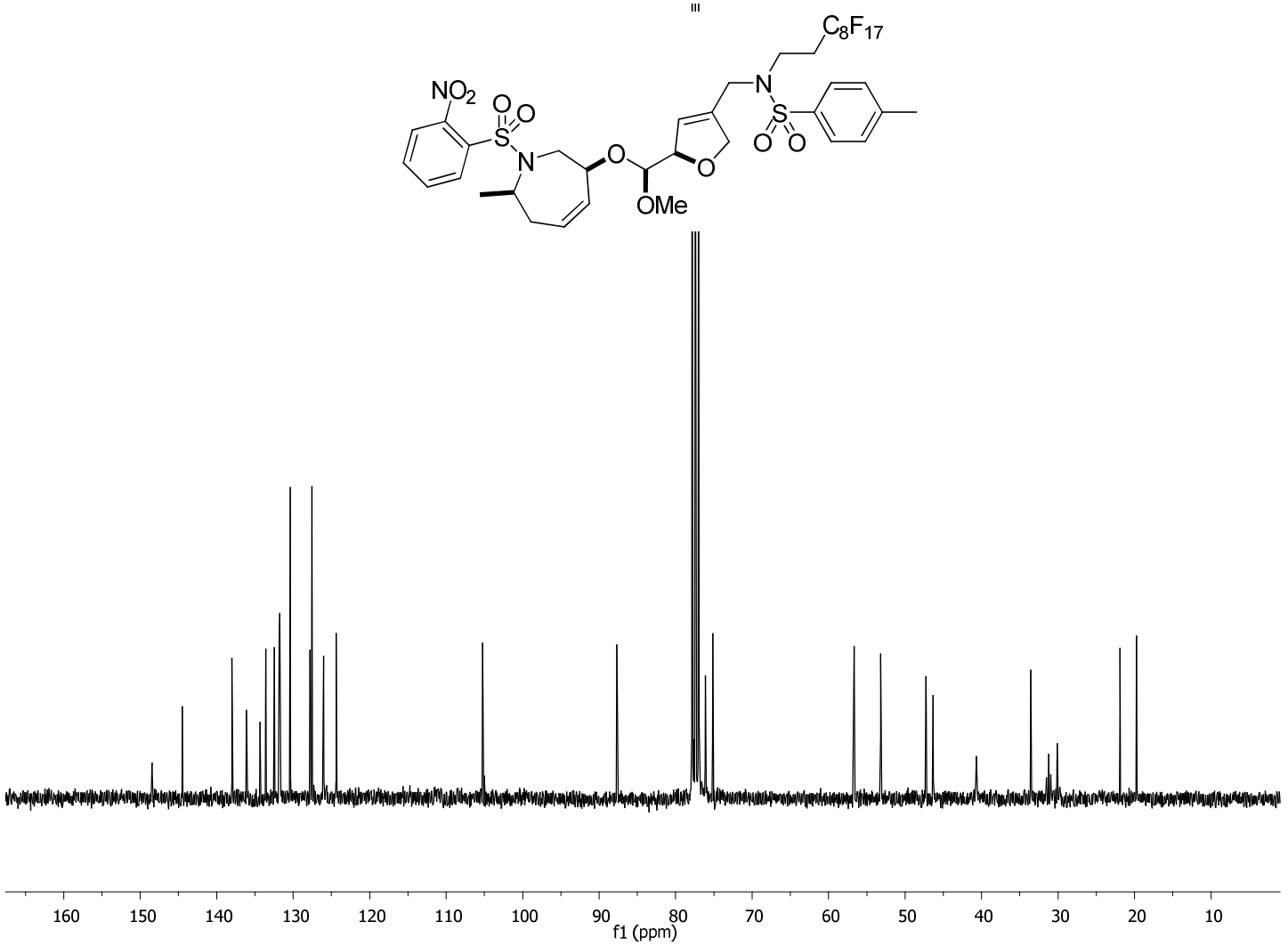
75 MHz ^{13}C NMR of S9



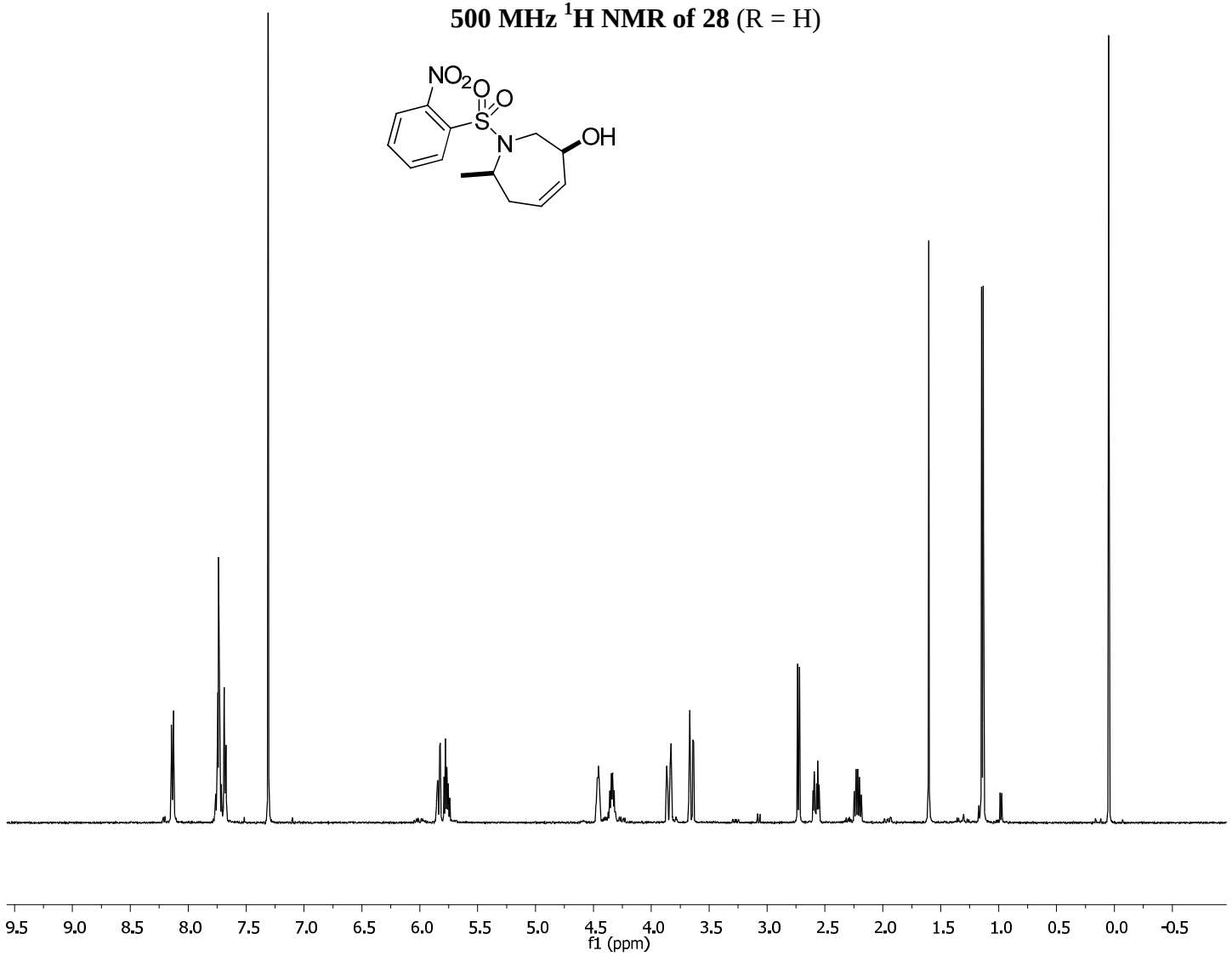
500 MHz ^{1}H NMR of 28 (R = R'^{F})



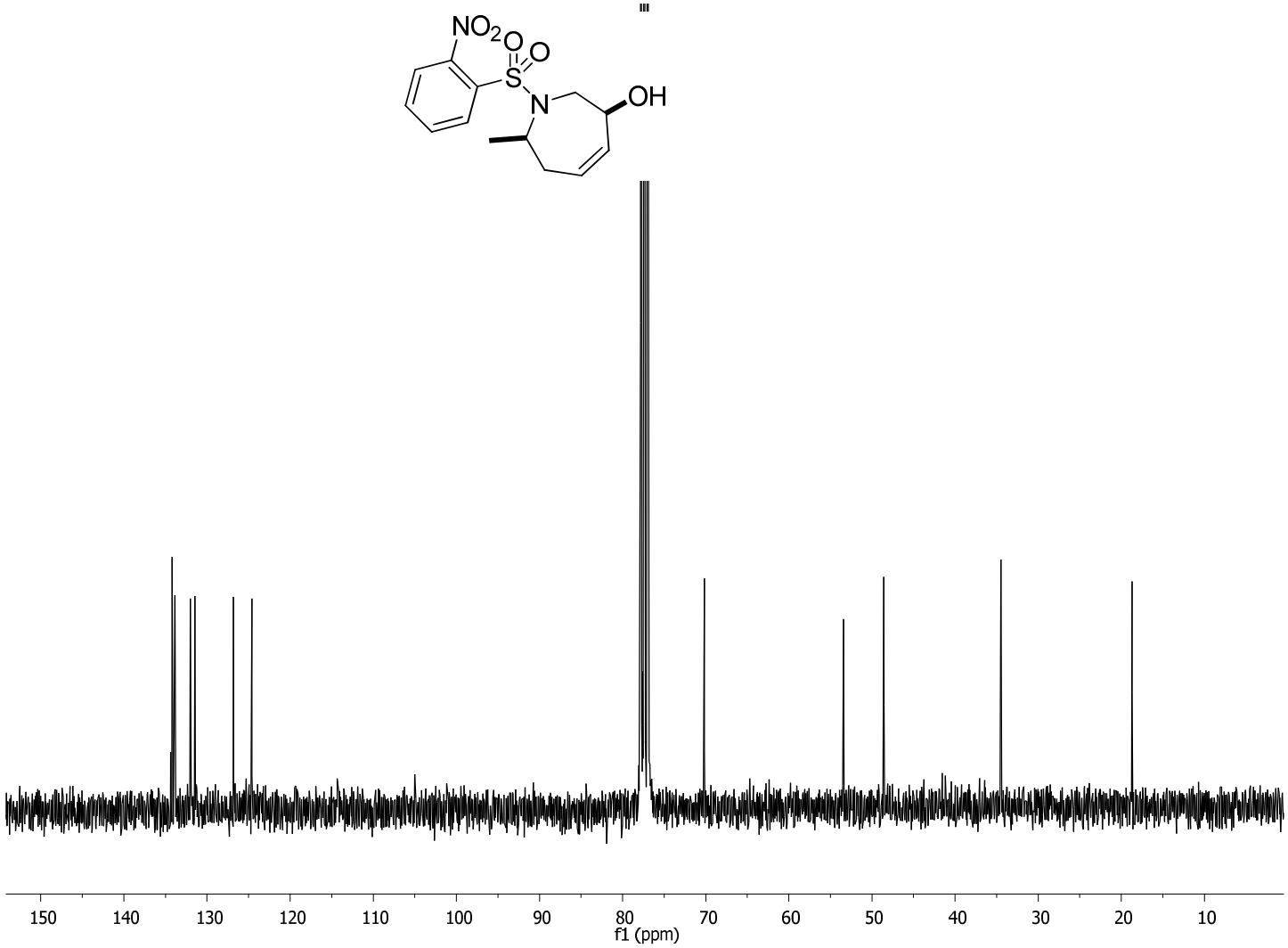
75 MHz ^{13}C NMR of 28 (R = R'^{F})



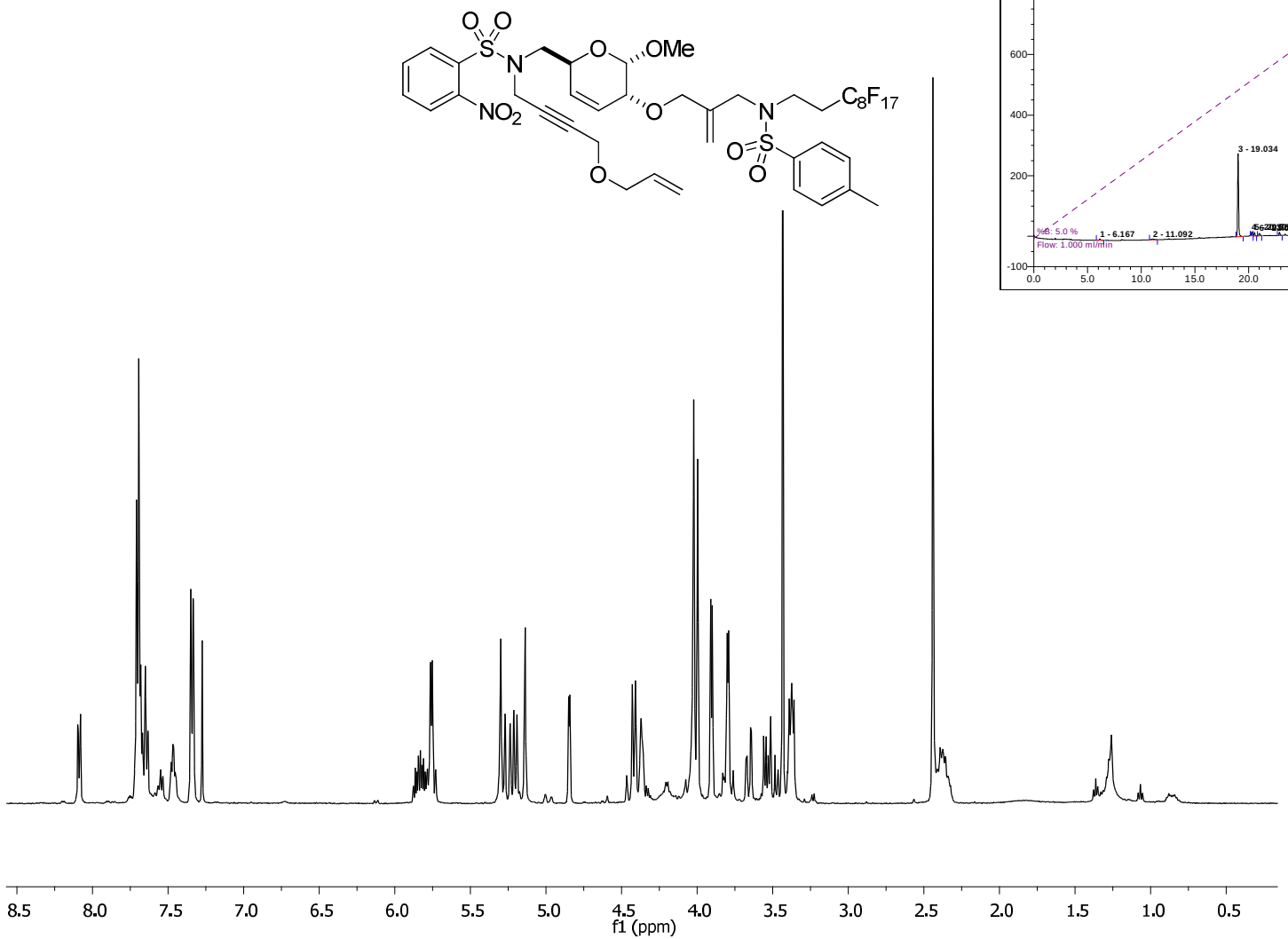
500 MHz ^{1}H NMR of 28 (R = H)

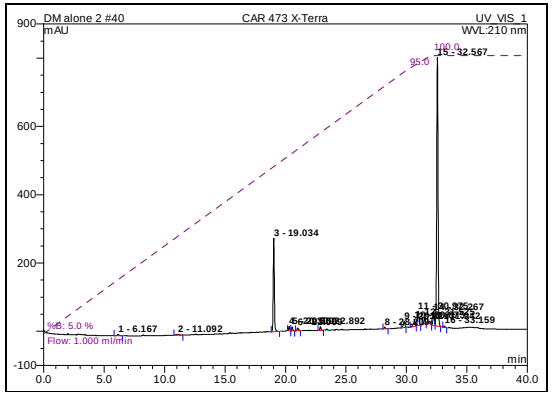


75 MHz ^{13}C NMR of 28 (R = H)

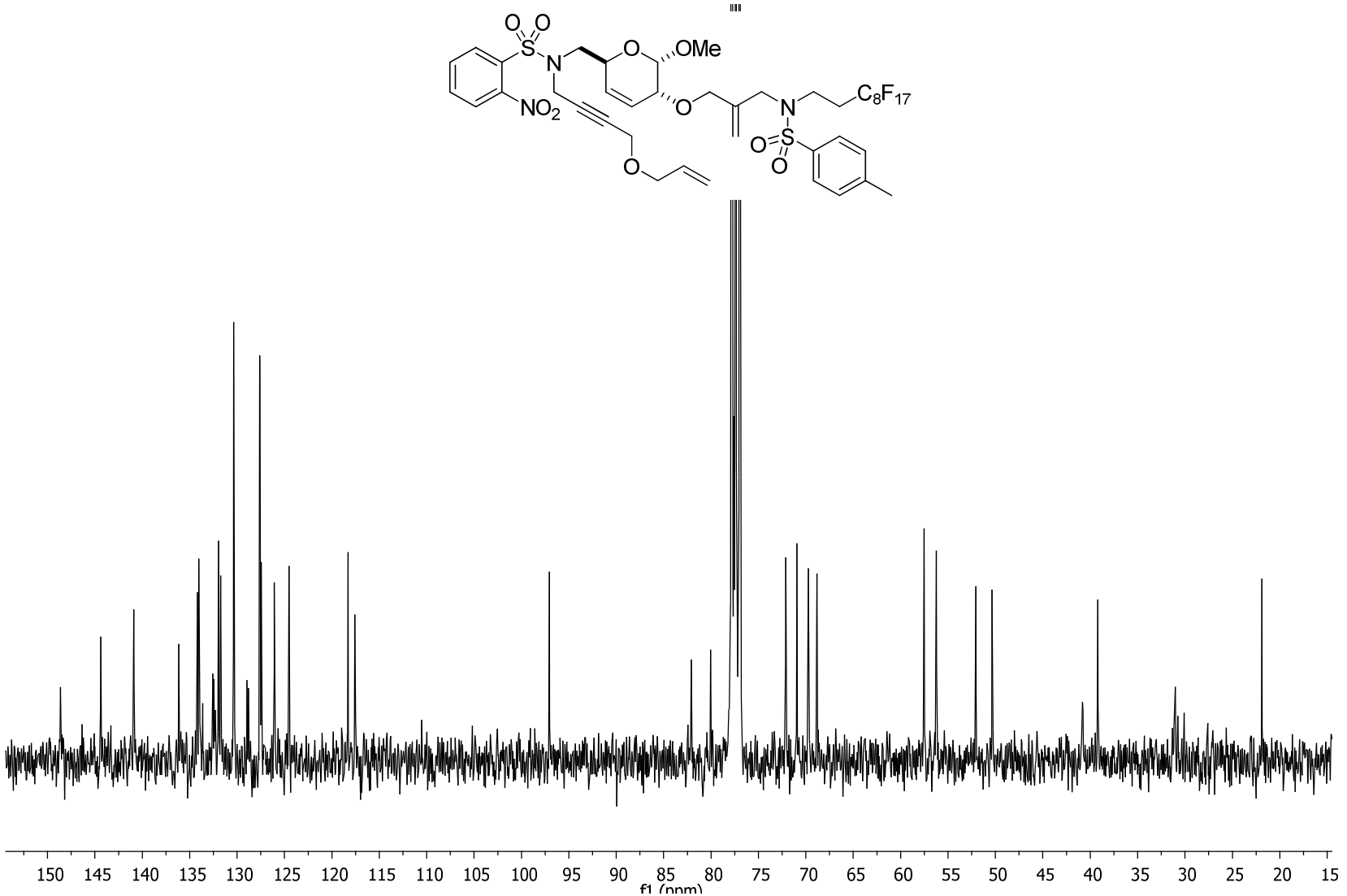


500 MHz ^{1}H NMR of S10 (F-SPE purified only)

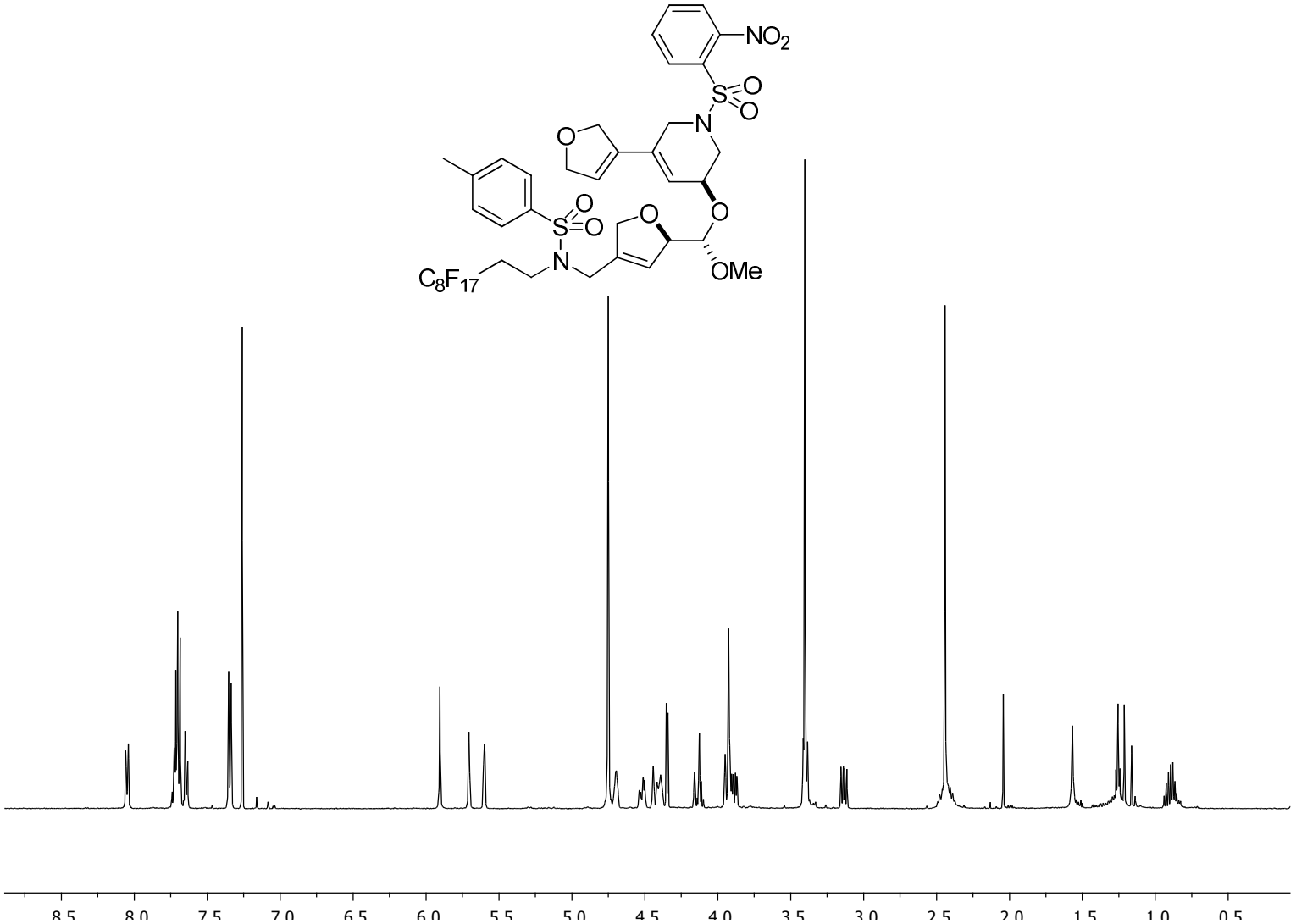




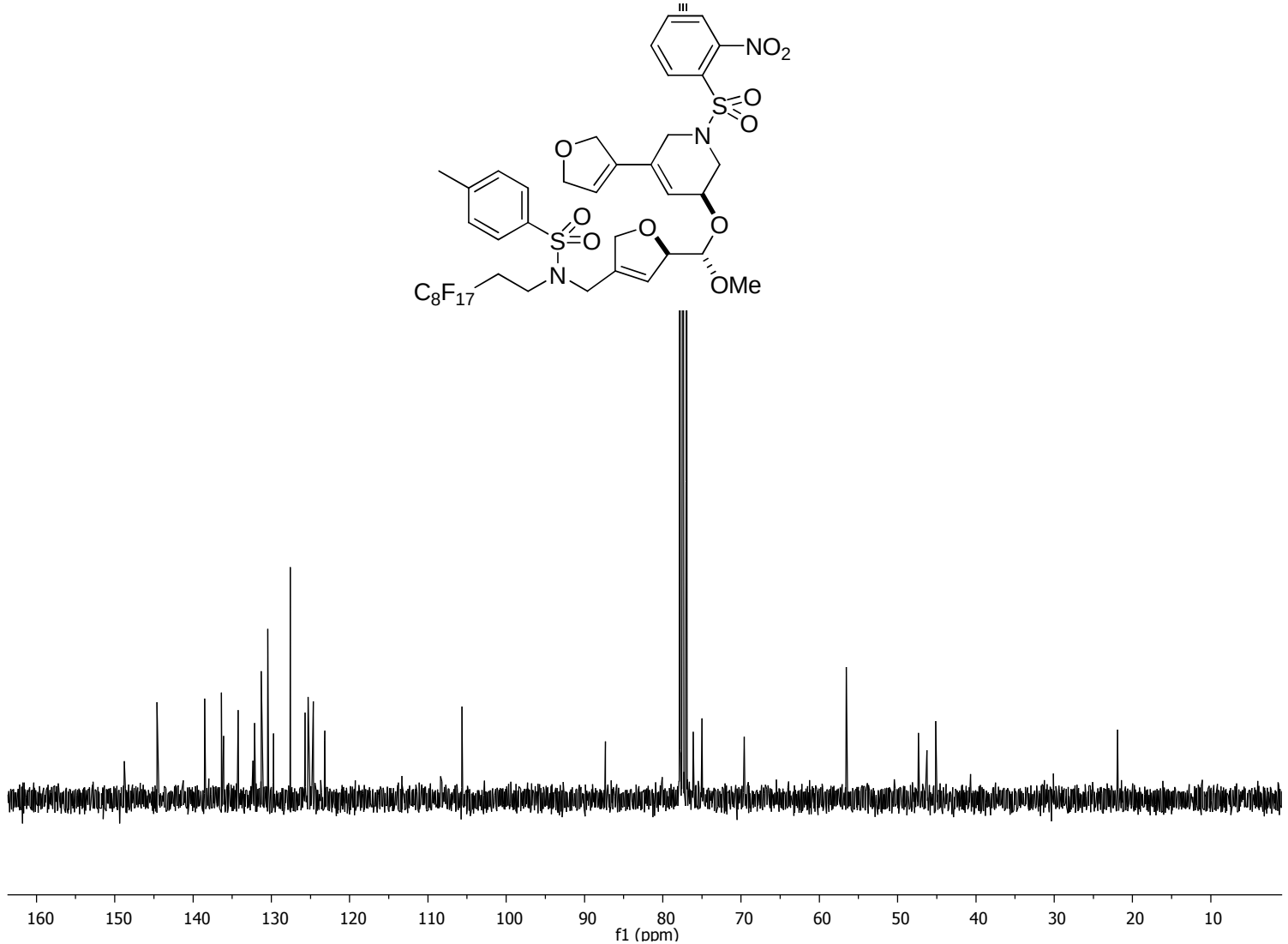
75 MHz ^{13}C NMR of S10



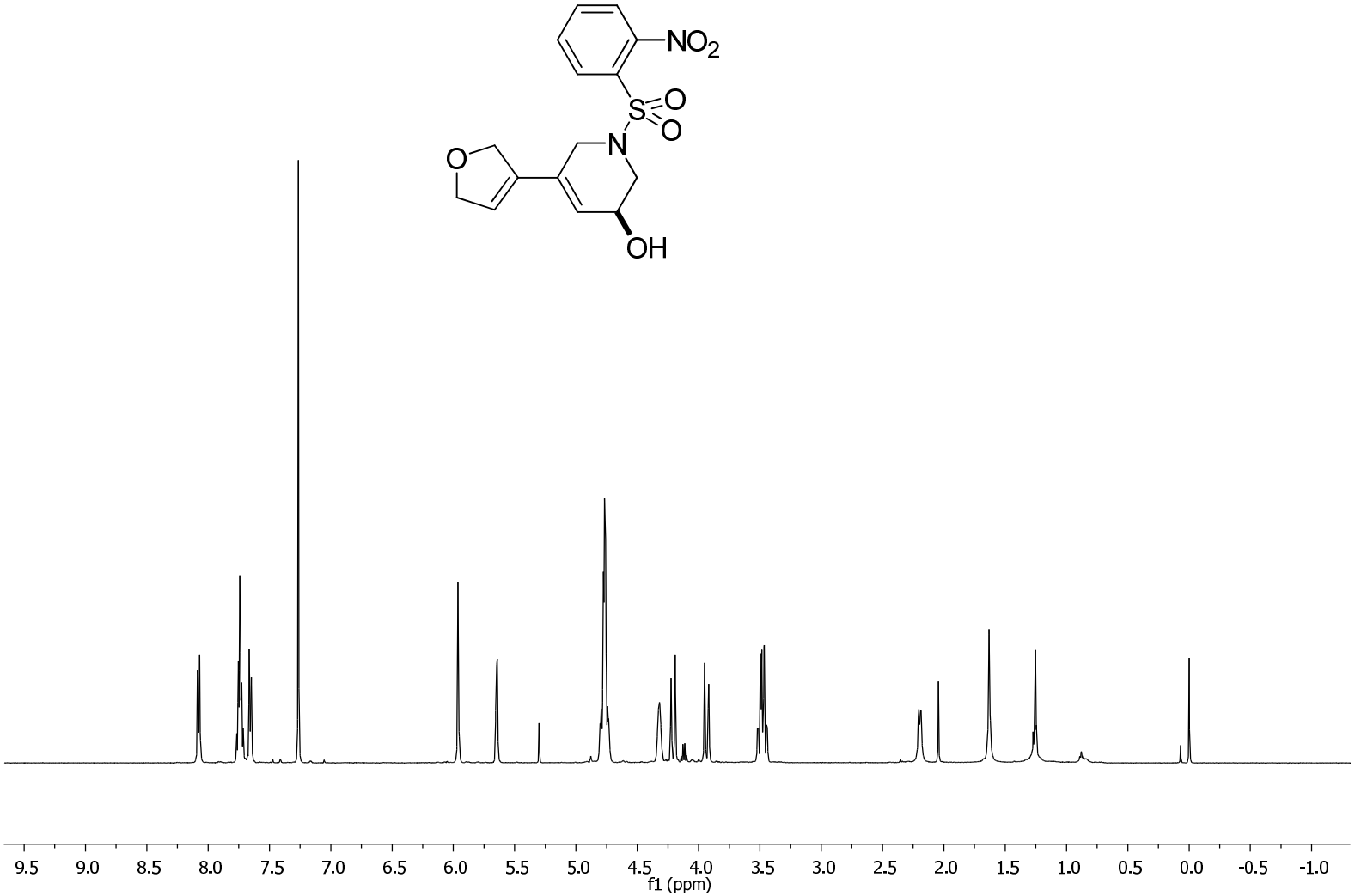
500 MHz ^{1}H NMR of 29 (R = R'^{F})



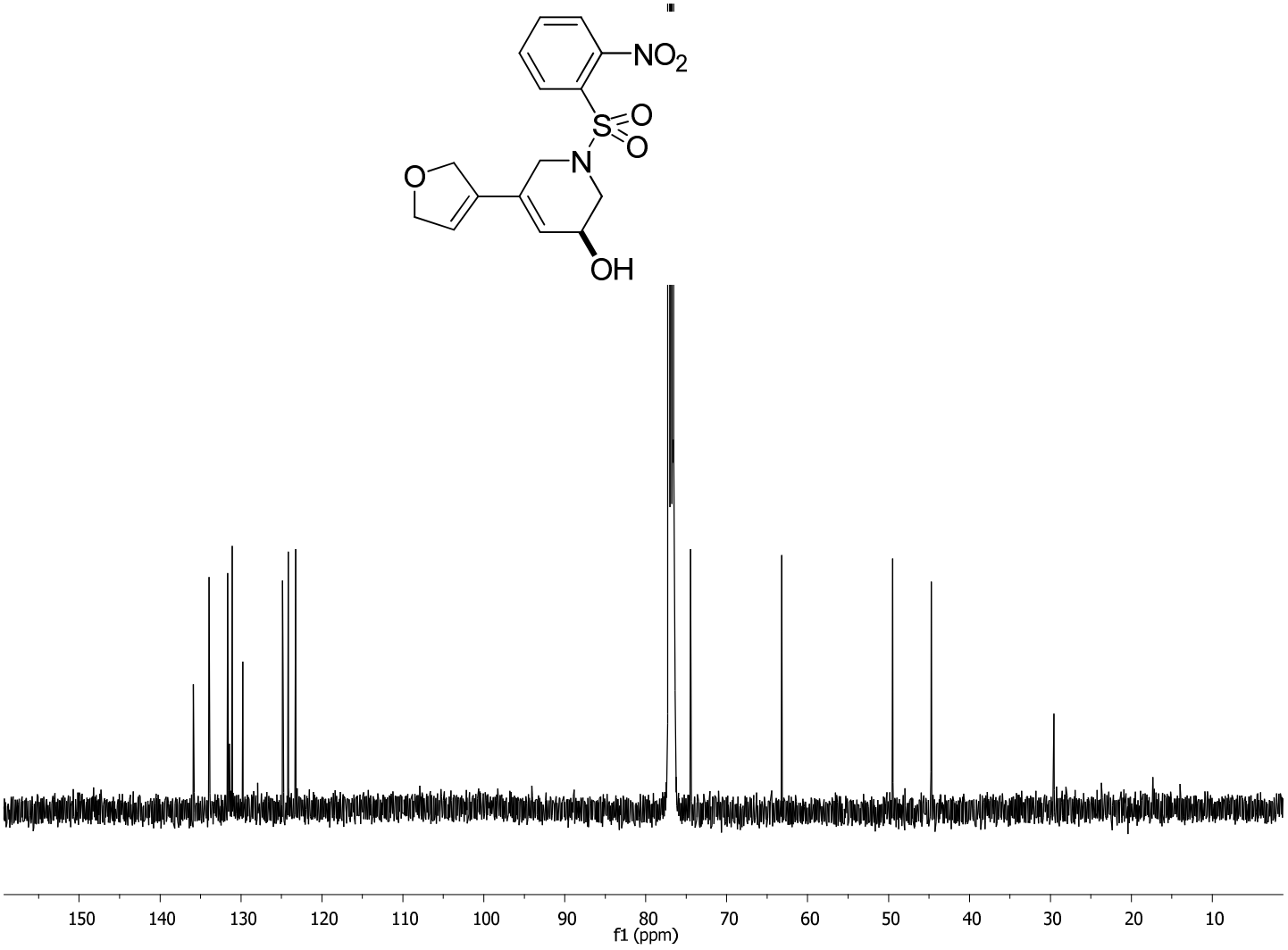
75 MHz ^{13}C NMR of 29 (R = R'^{F})



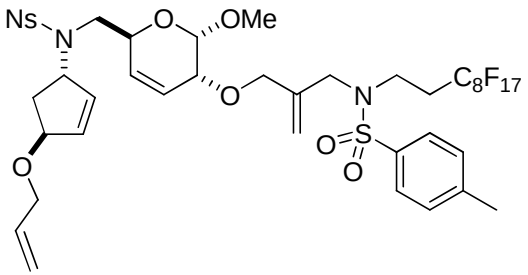
500 MHz ^{1}H NMR of 29 (R = H)

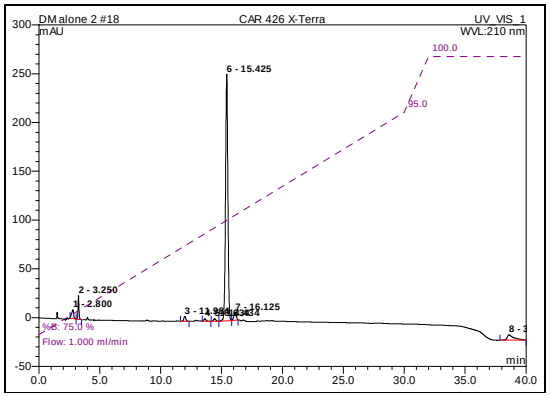


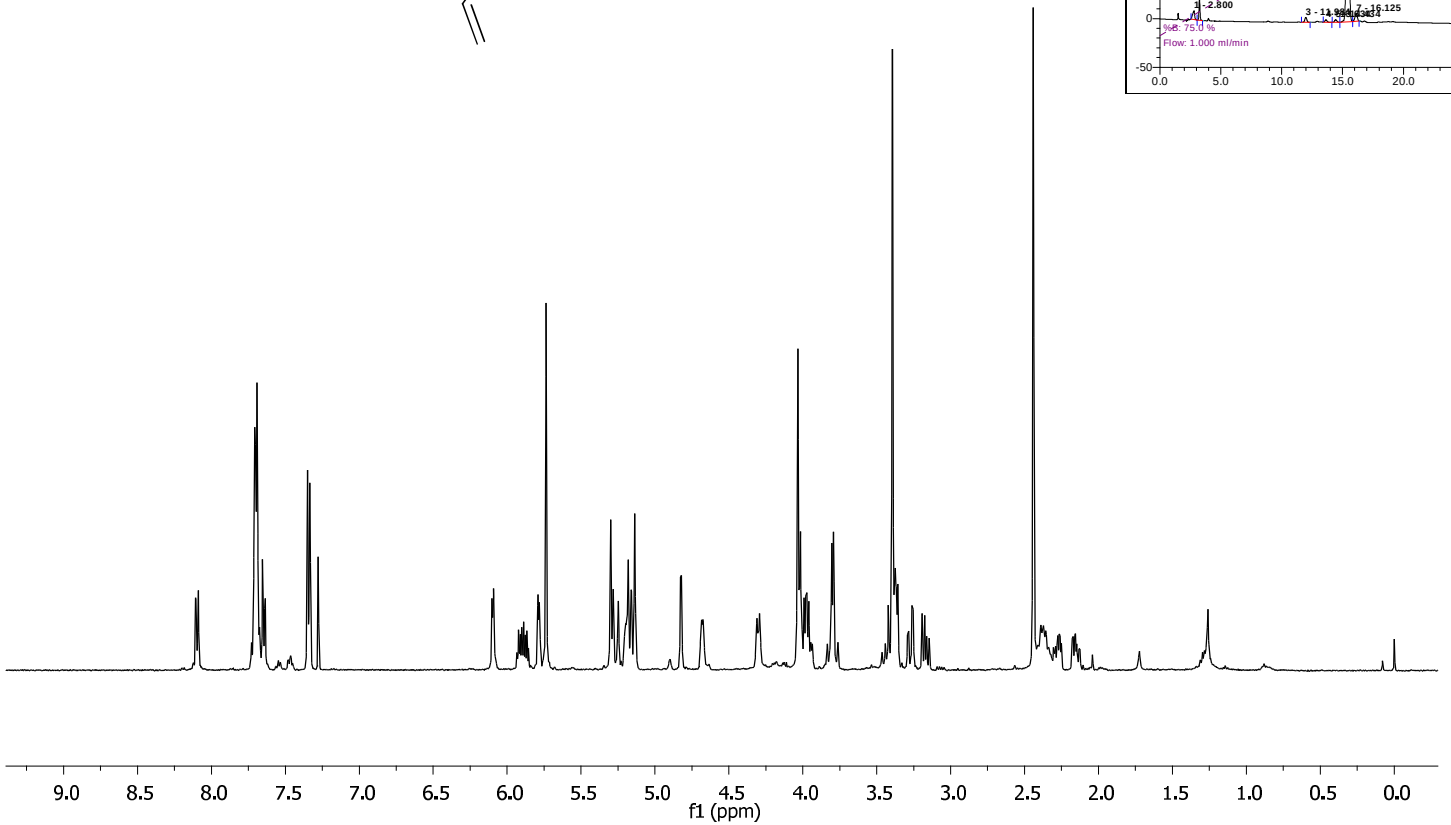
75 MHz ^{13}C NMR of 29 (R = H)



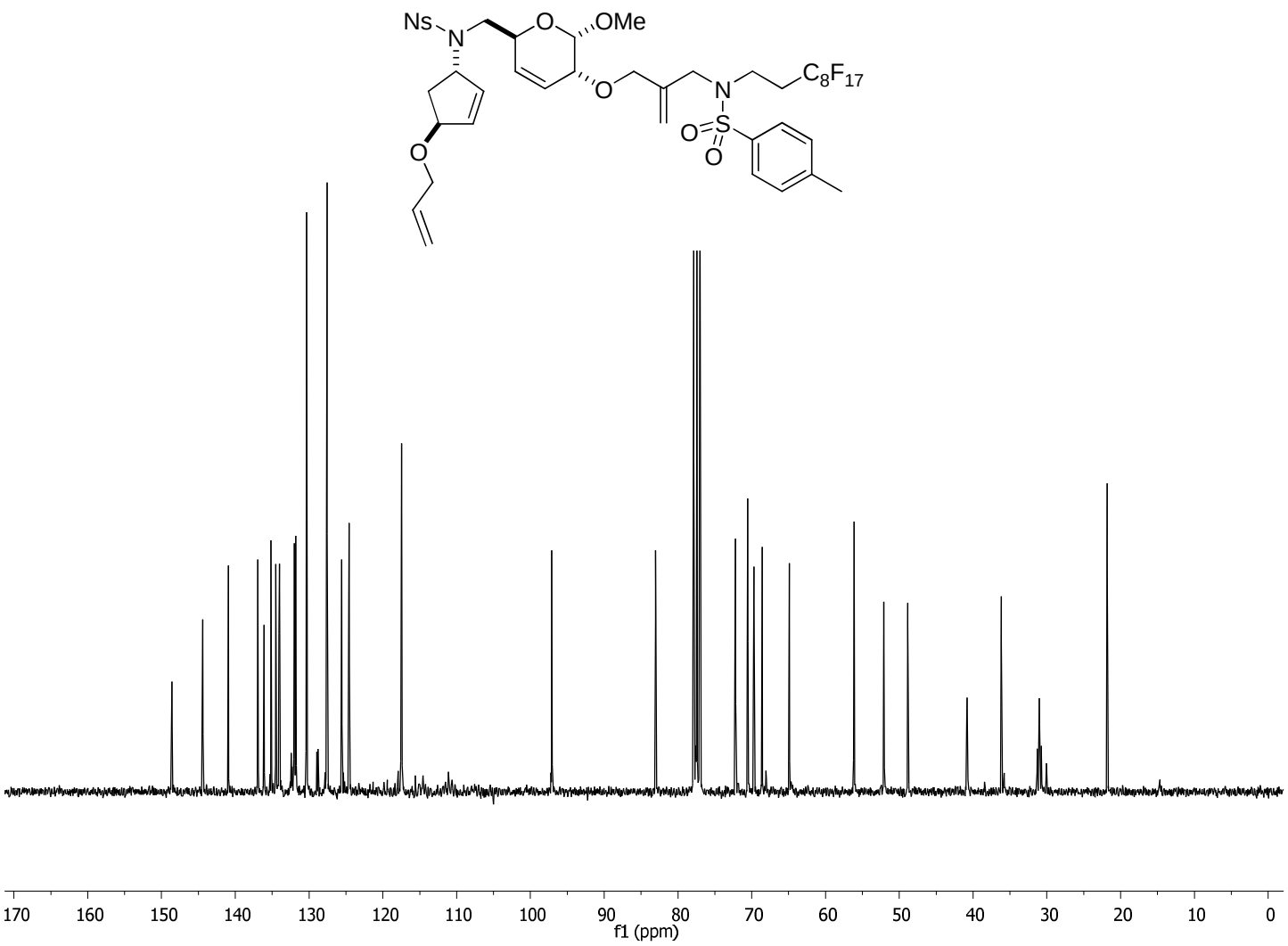
500 MHz ^{1}H NMR of S11 (F-SPE purified only)



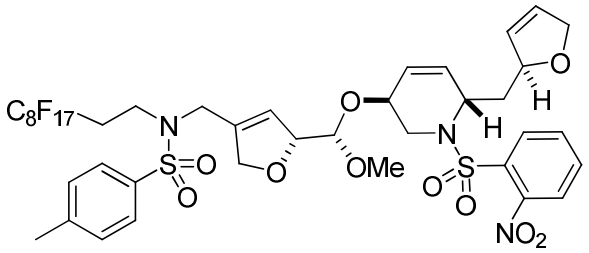


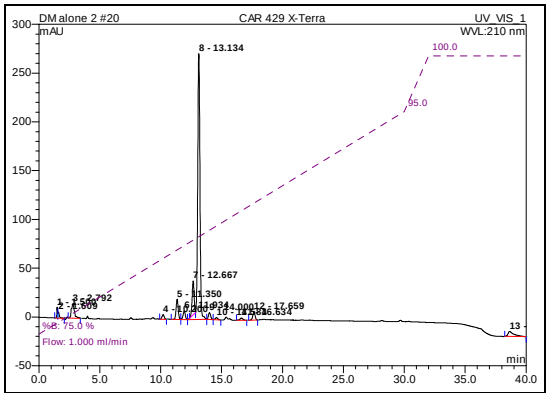


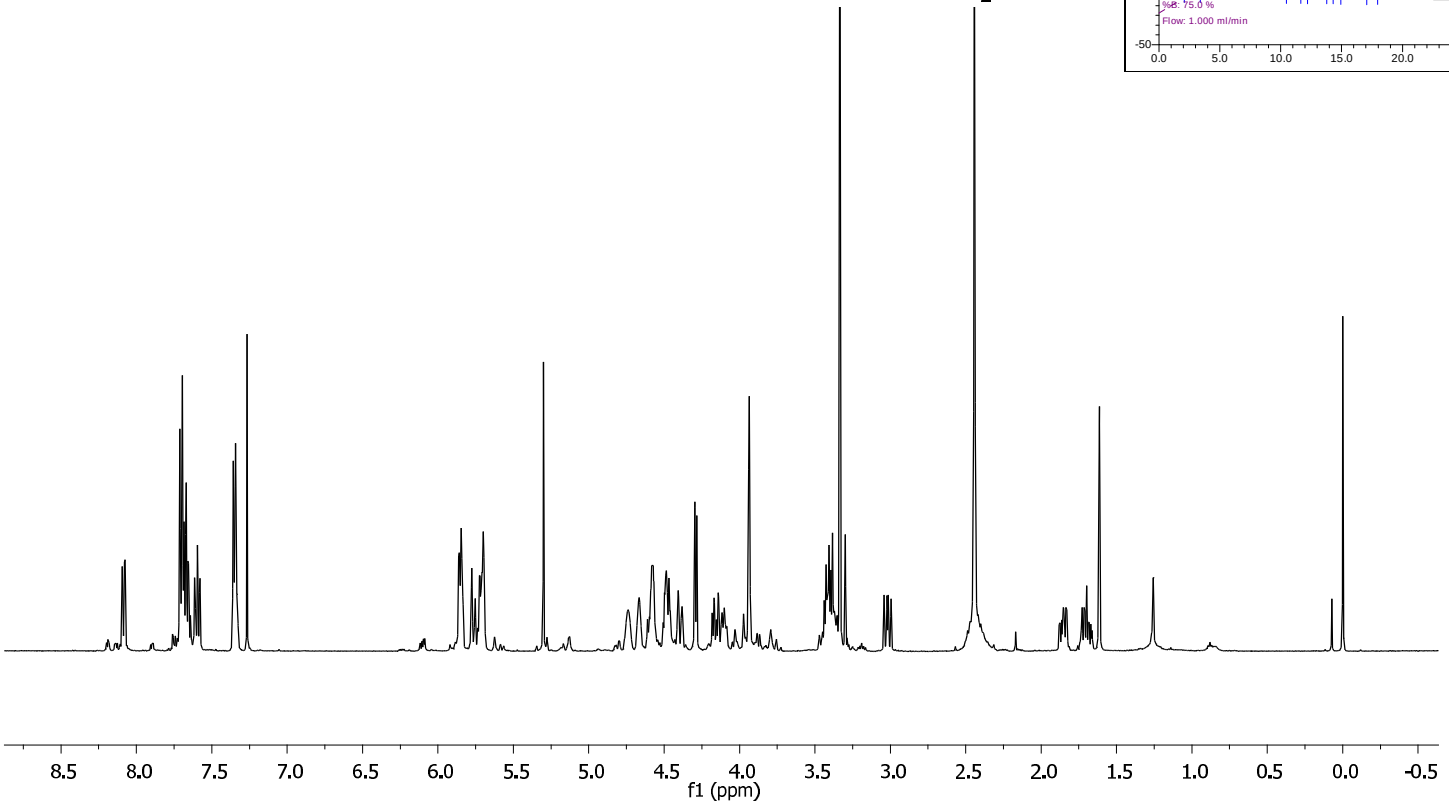
75 MHz ^{13}C NMR of S11



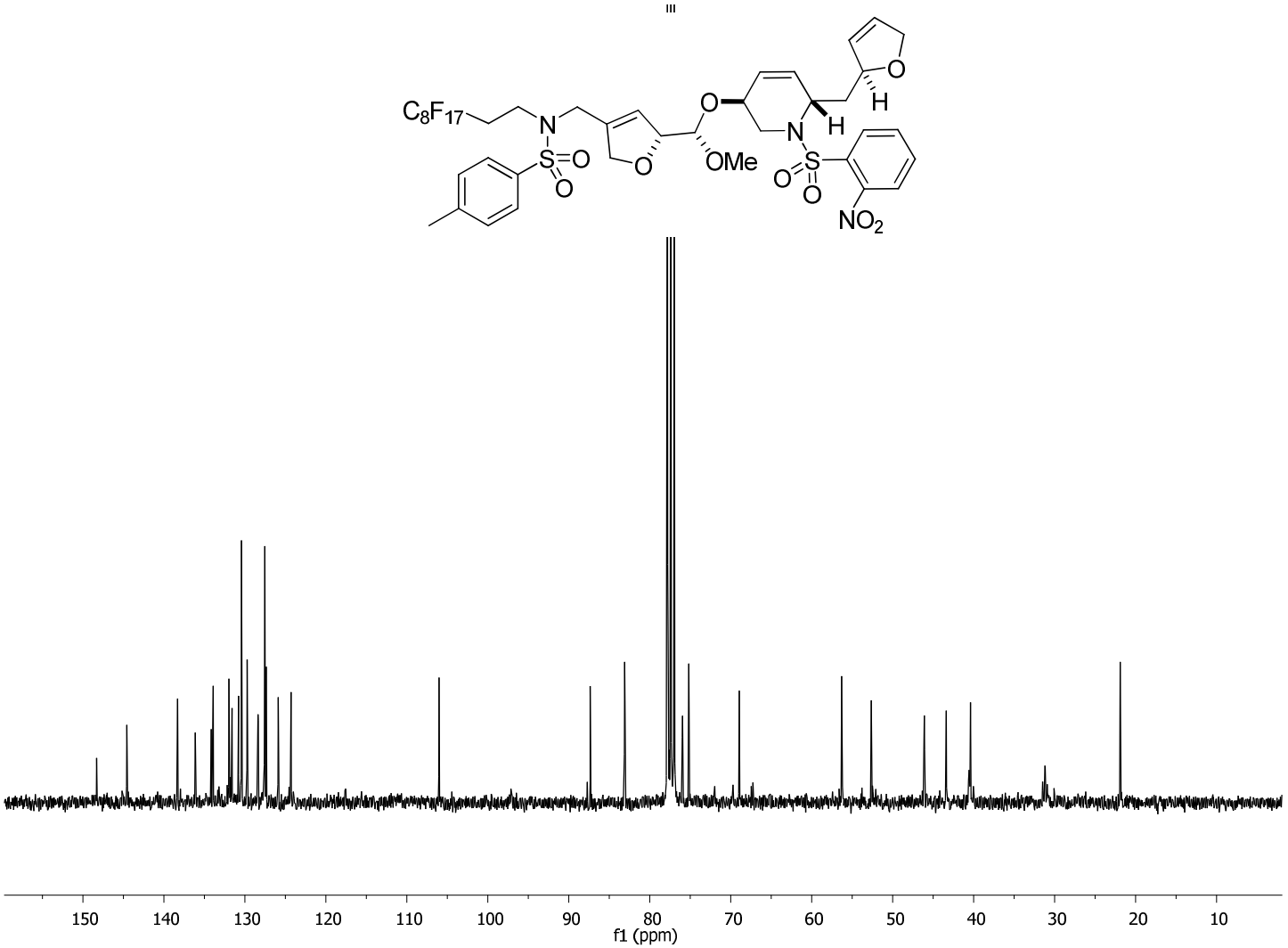
^{1}H NMR of 30 (R = R'^{F}) **(F-SPE purified only)**



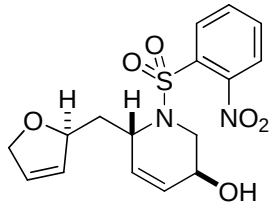


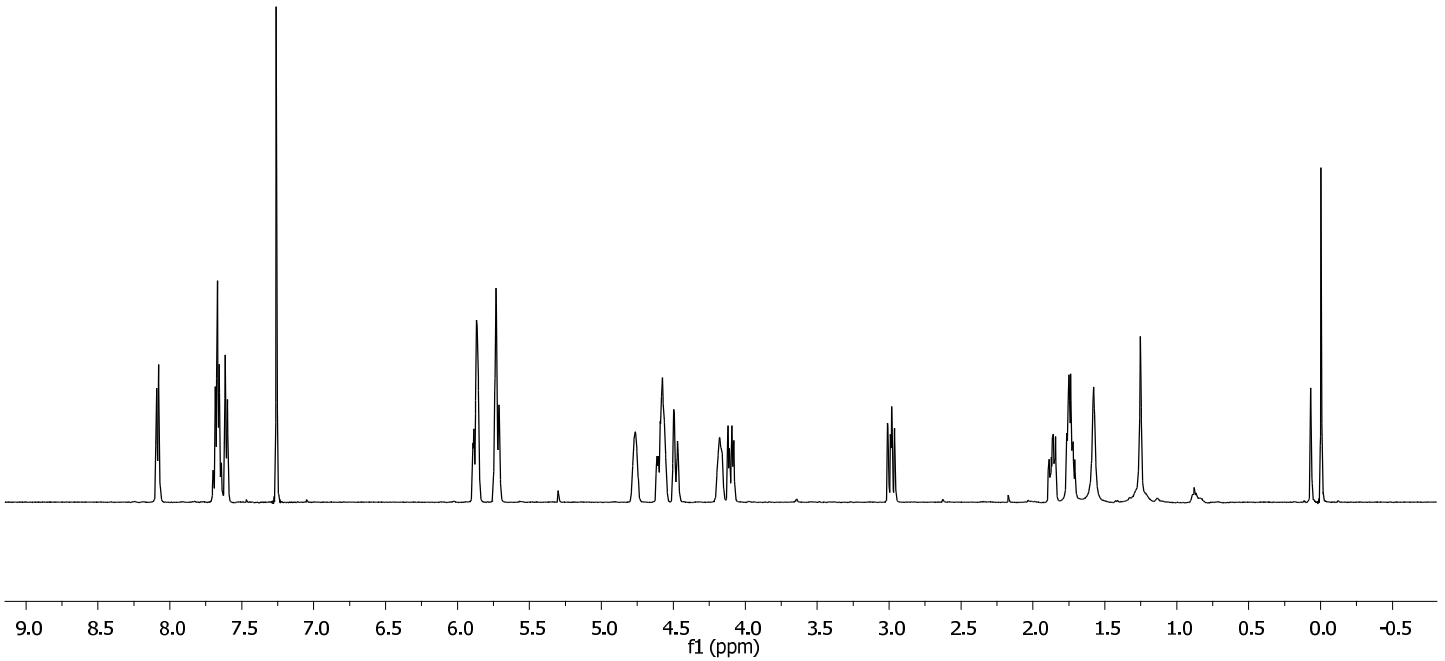


75 MHz ^{13}C NMR of 30 (R = R'^{F})

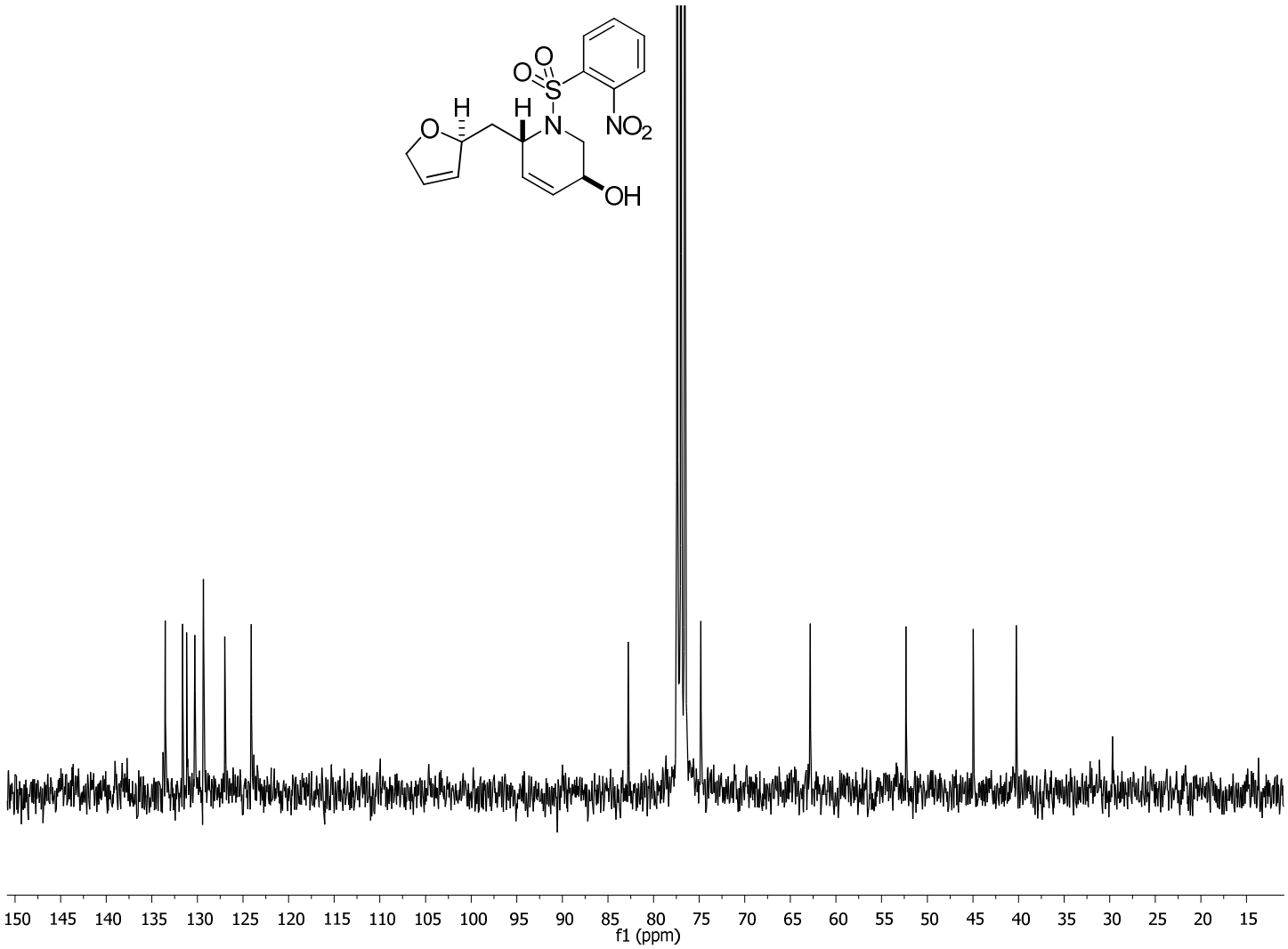


500 MHz ^{1}H NMR of 30 (R = H)

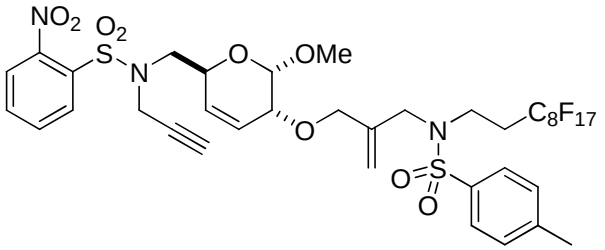


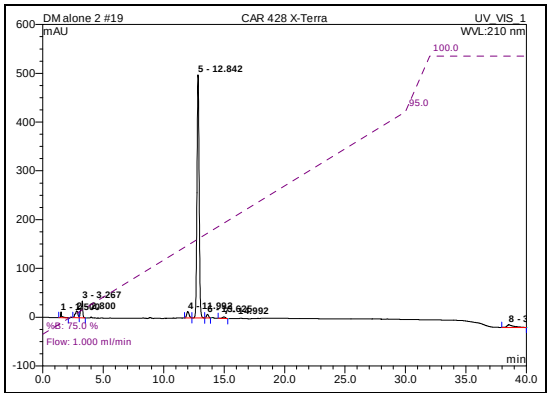


75 MHz ^{13}C NMR of 30 (R = H)

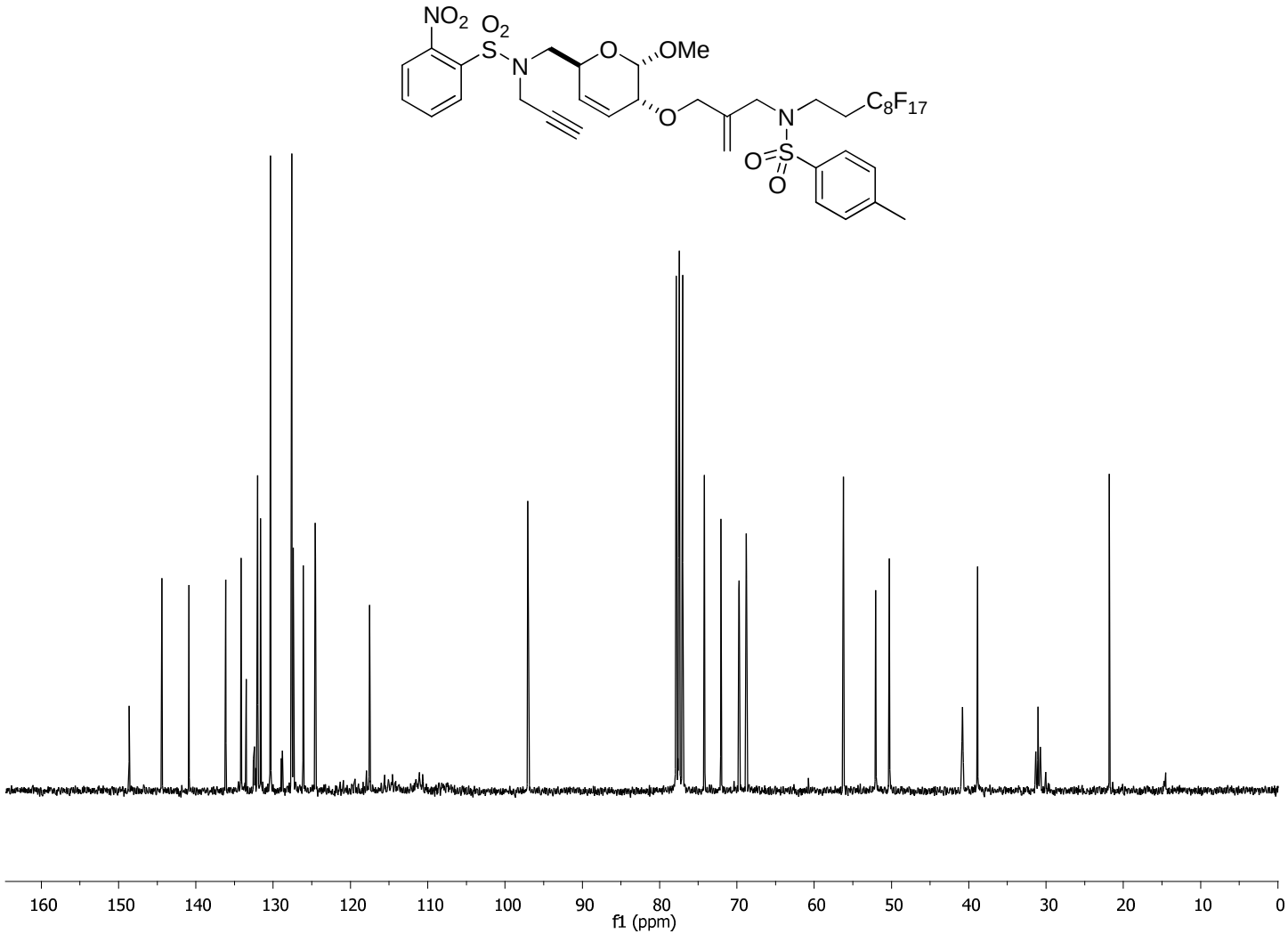


500 MHz ^{1}H NMR of S12 (F-SPE purified only)

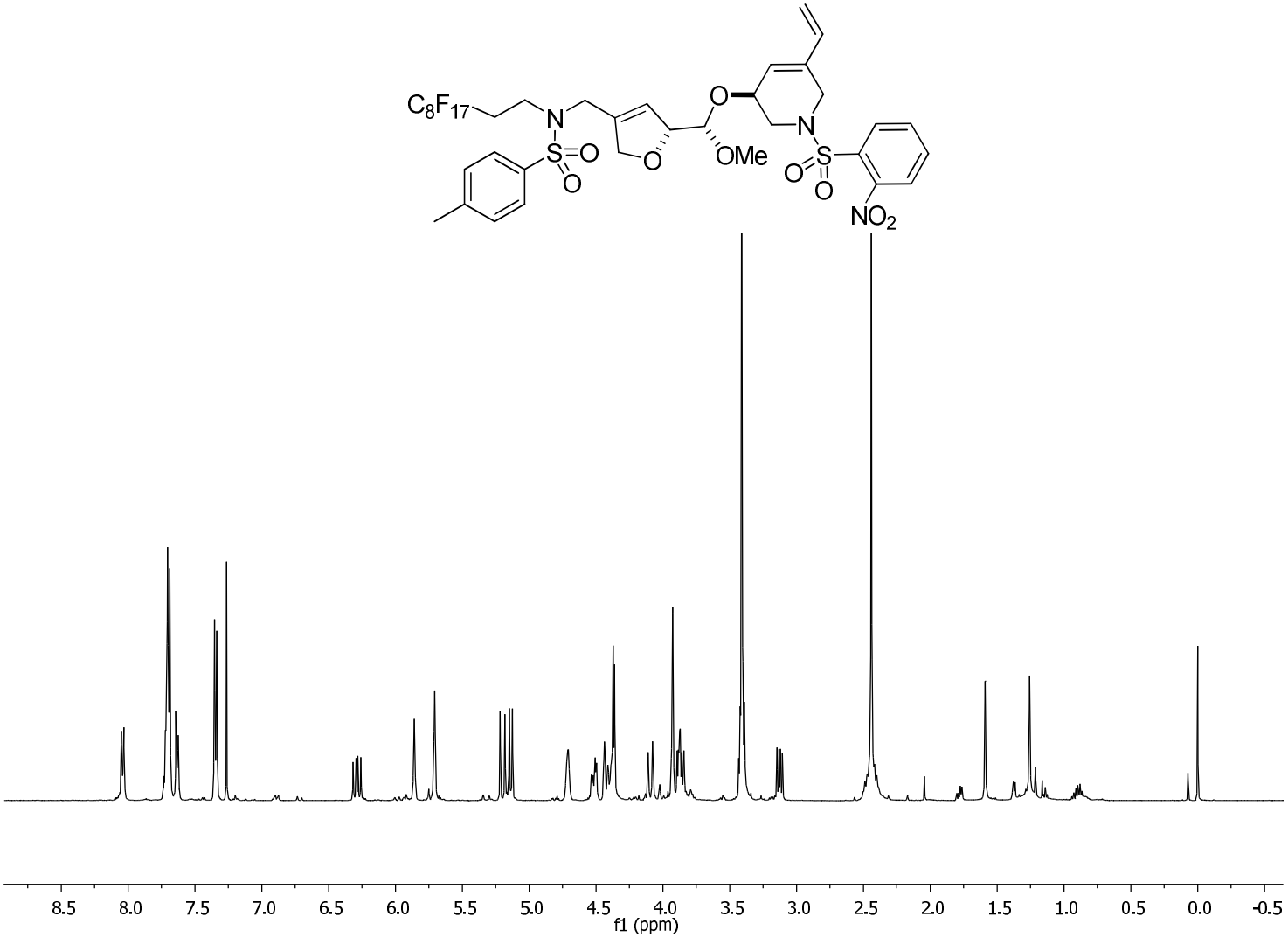




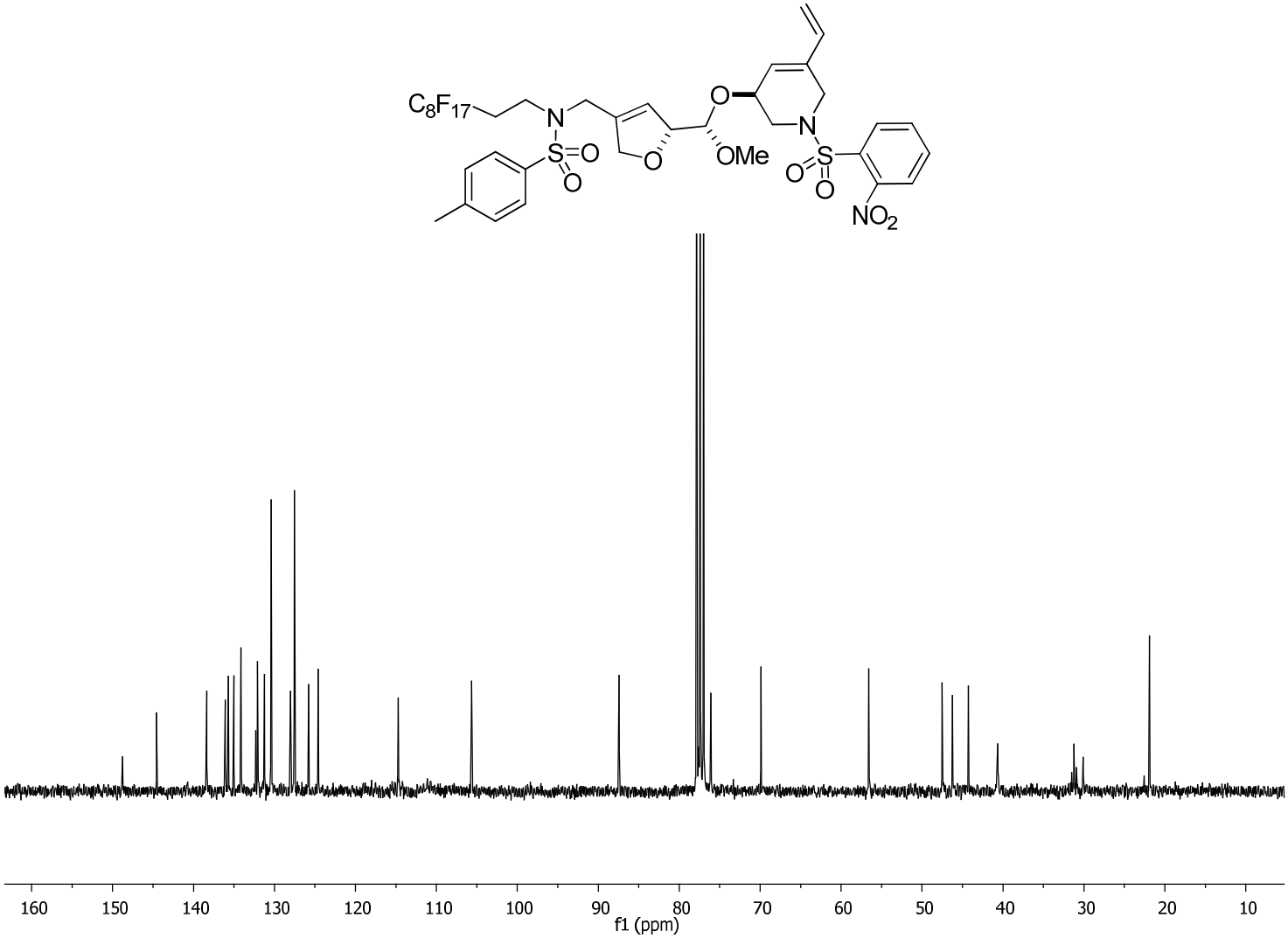
75 MHz ^{13}C NMR of S12



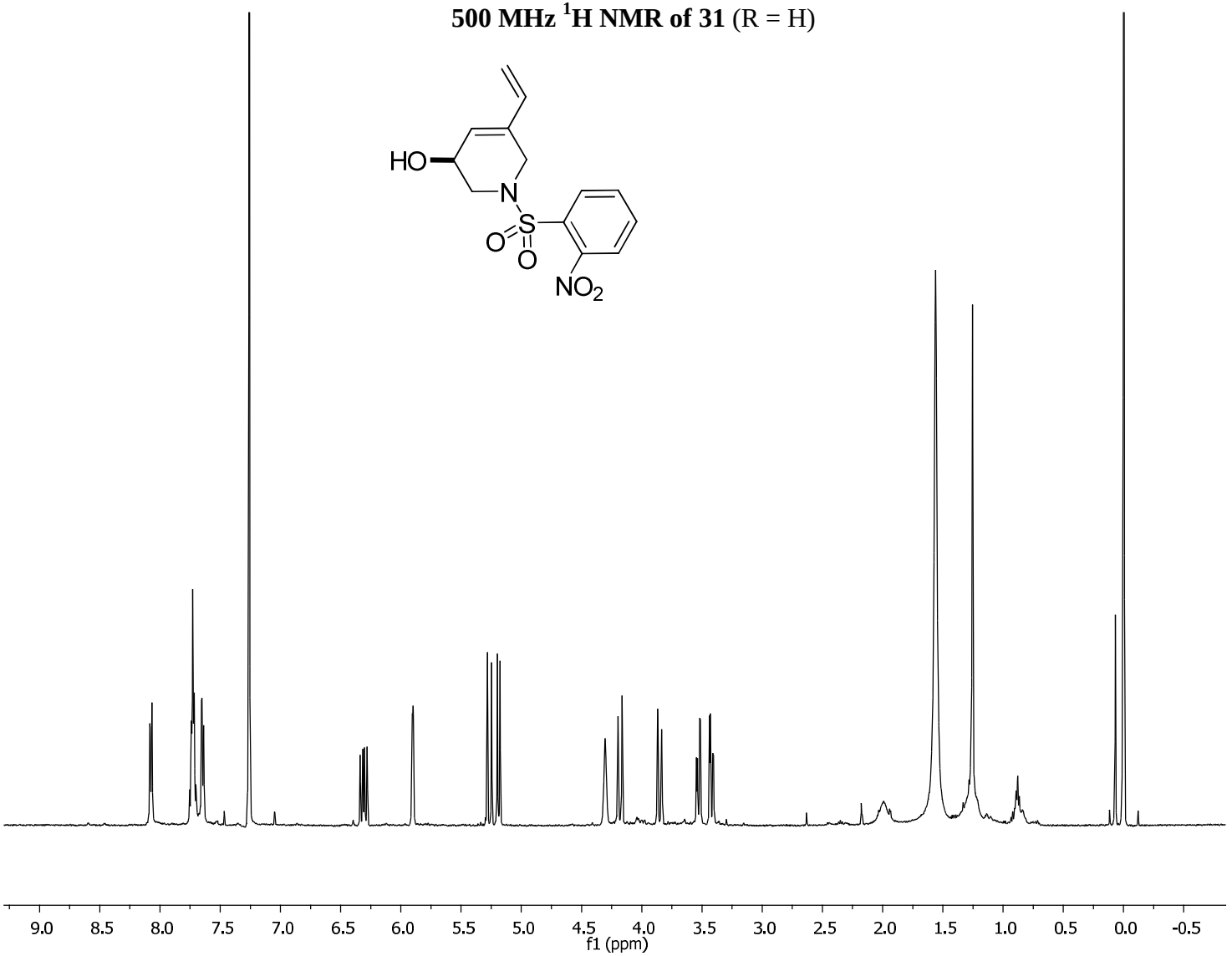
500 MHz ^{1}H NMR of 31 (R = R'^{F})



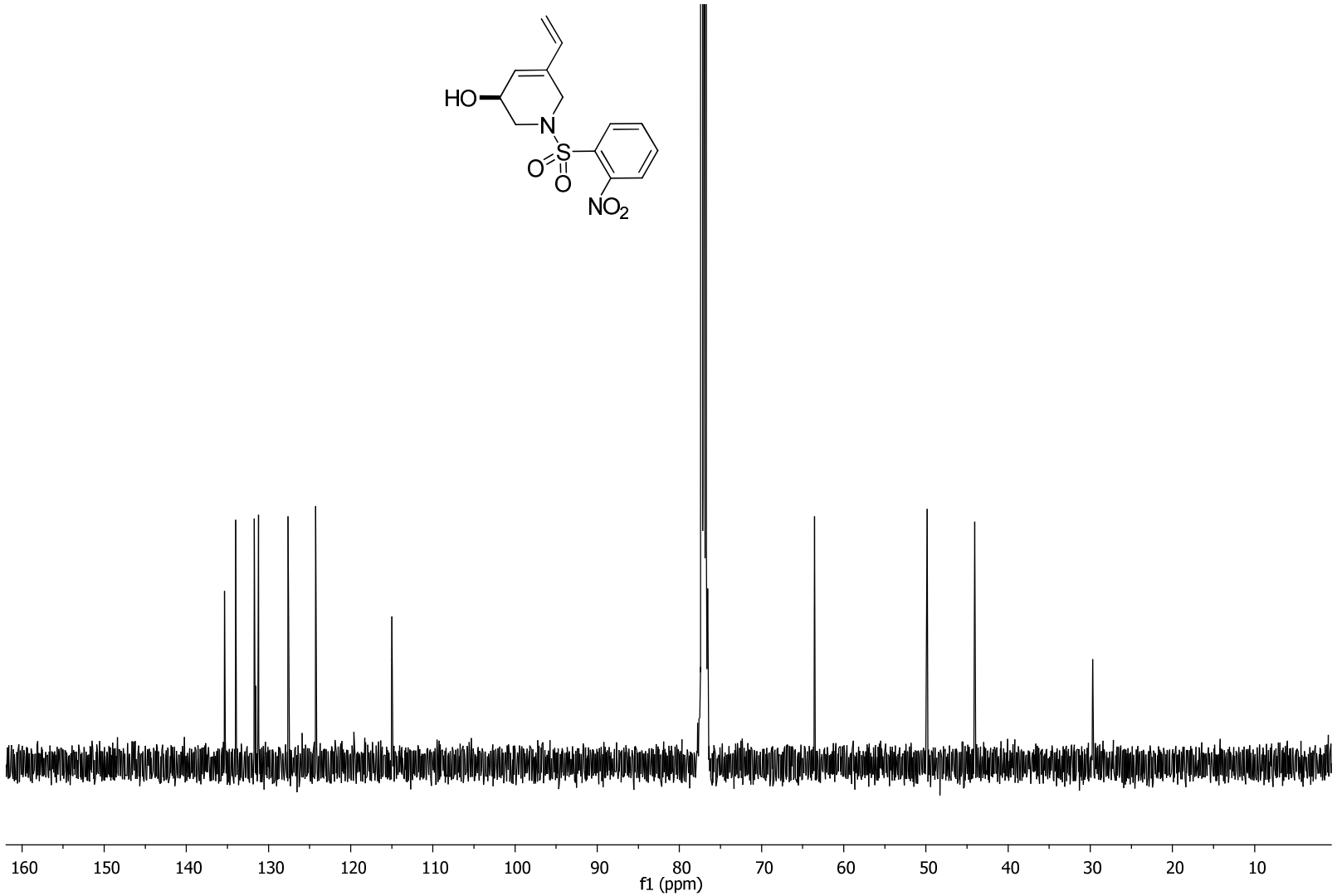
75 MHz ^{1}H NMR of 31 (R = R'^{F})



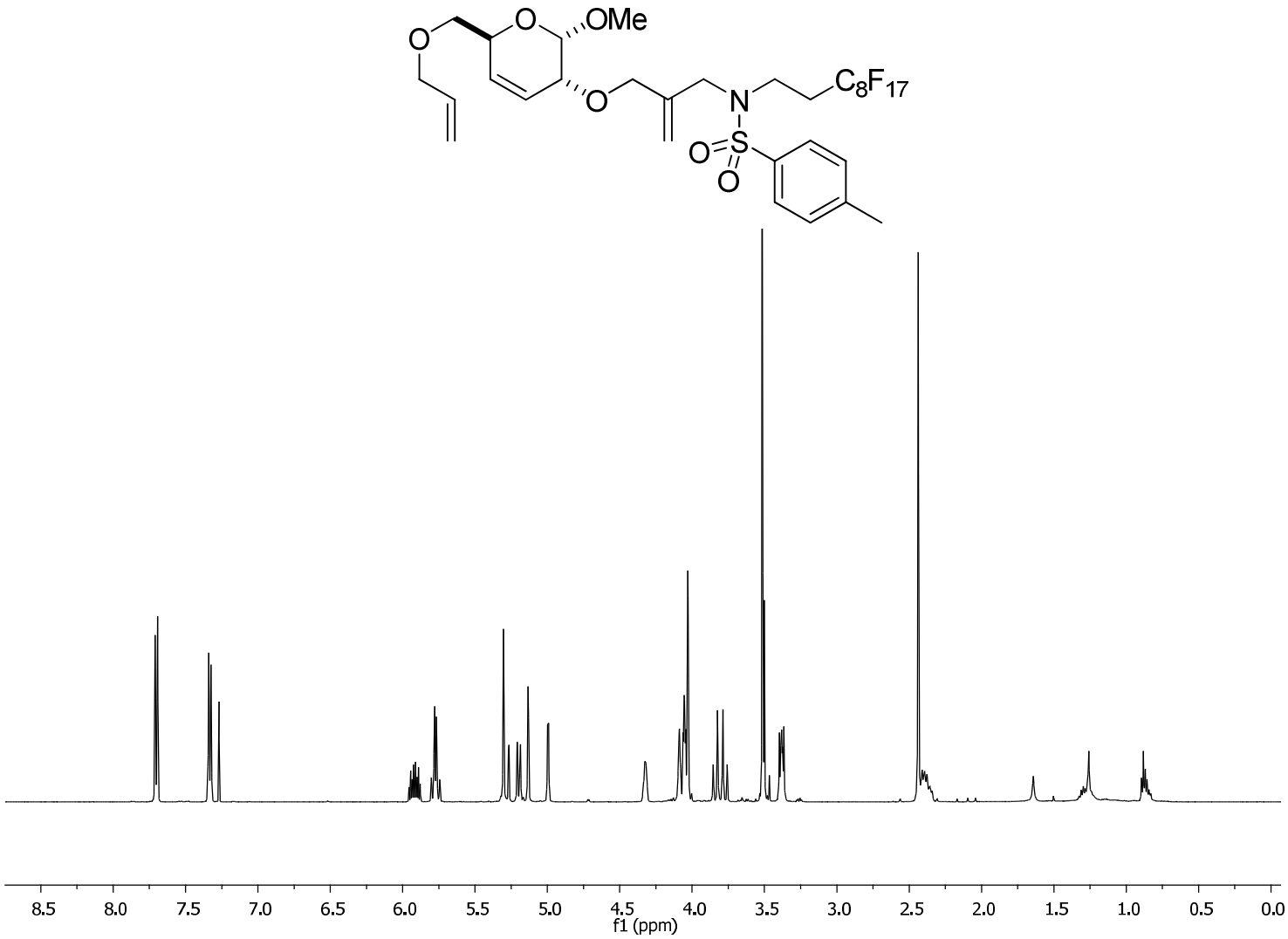
500 MHz ^{1}H NMR of 31 (R = H)



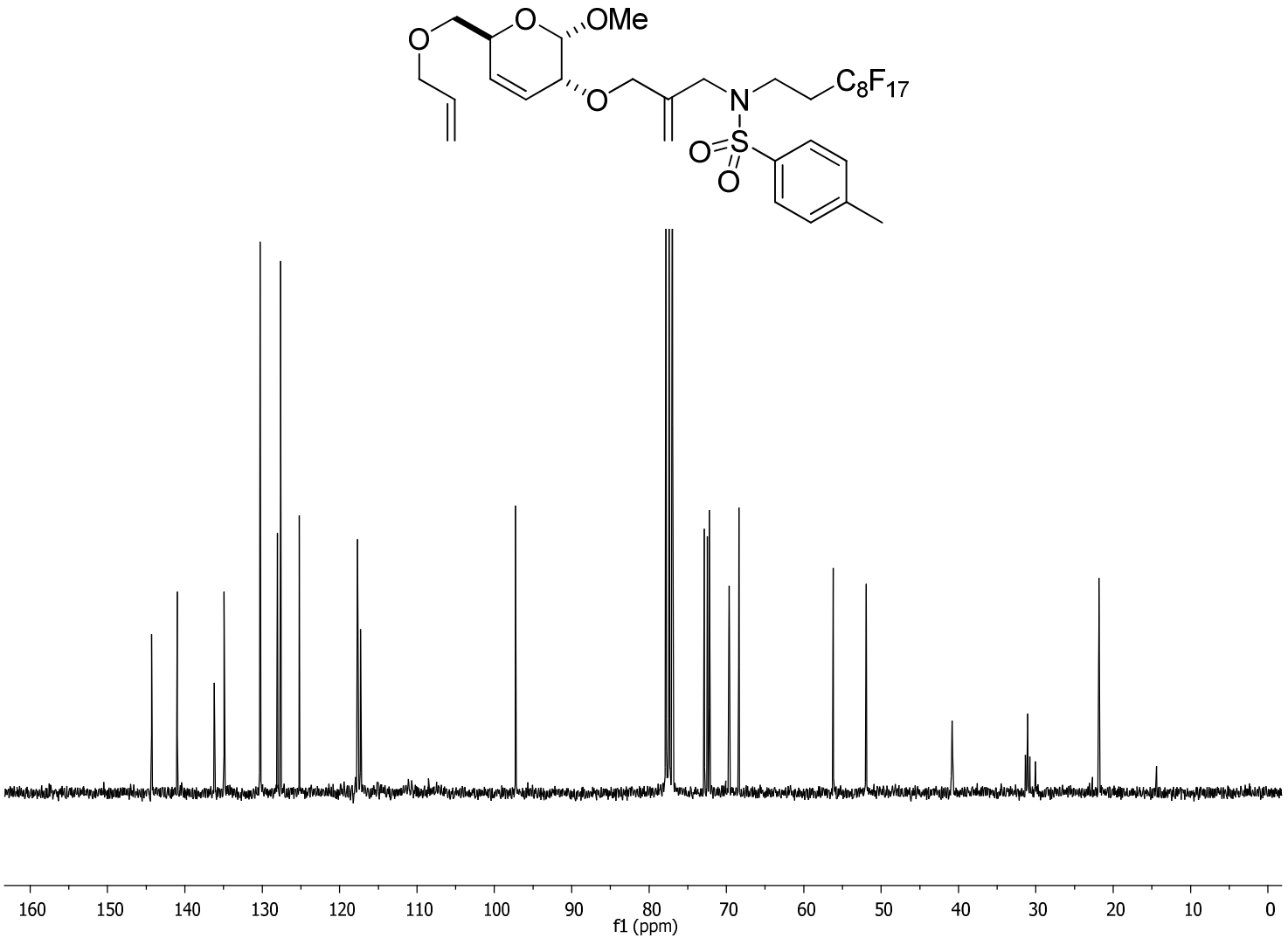
75 MHz ^{13}C NMR of 31 (R = H)



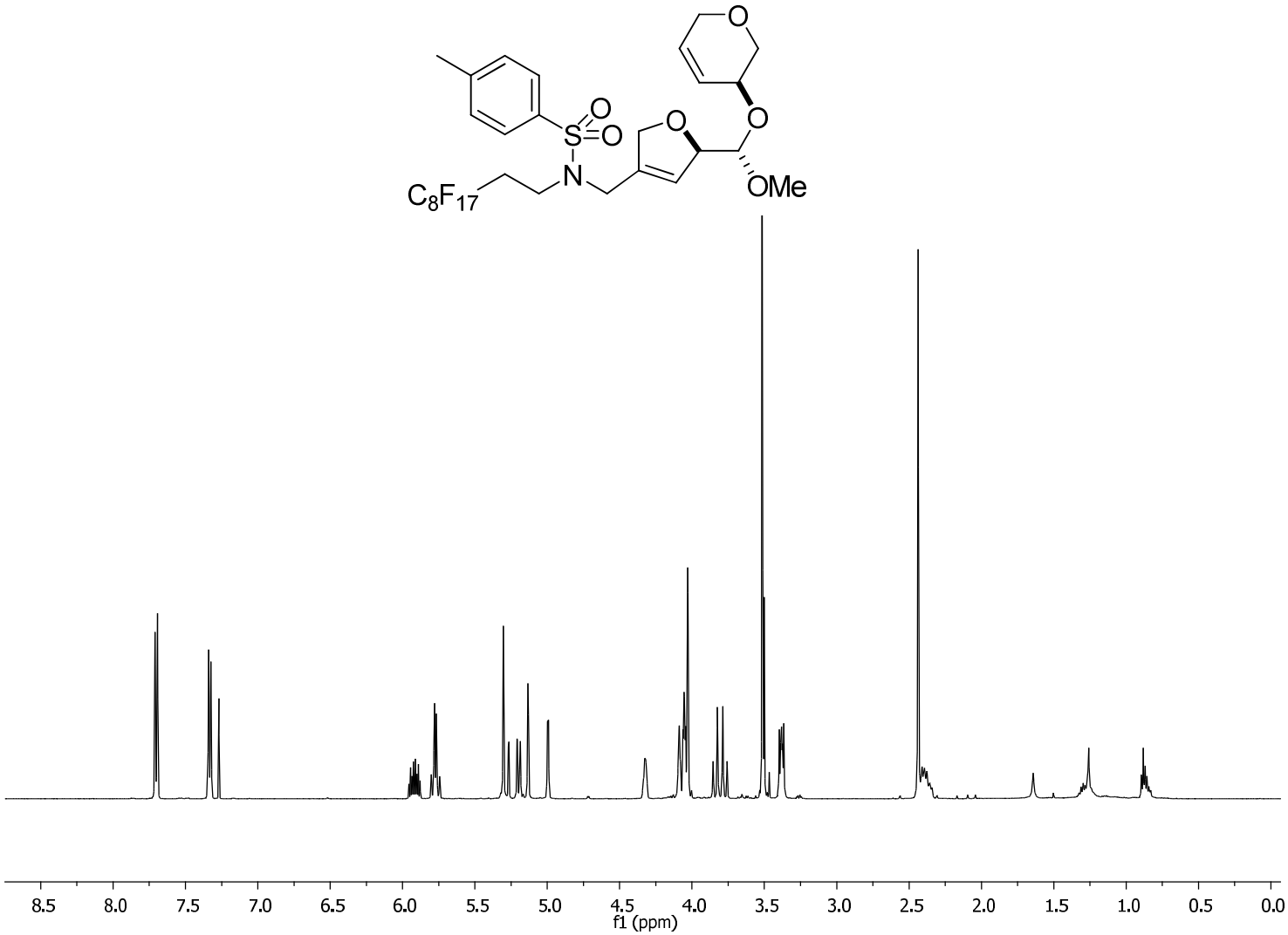
500 MHz ^{1}H NMR of S13



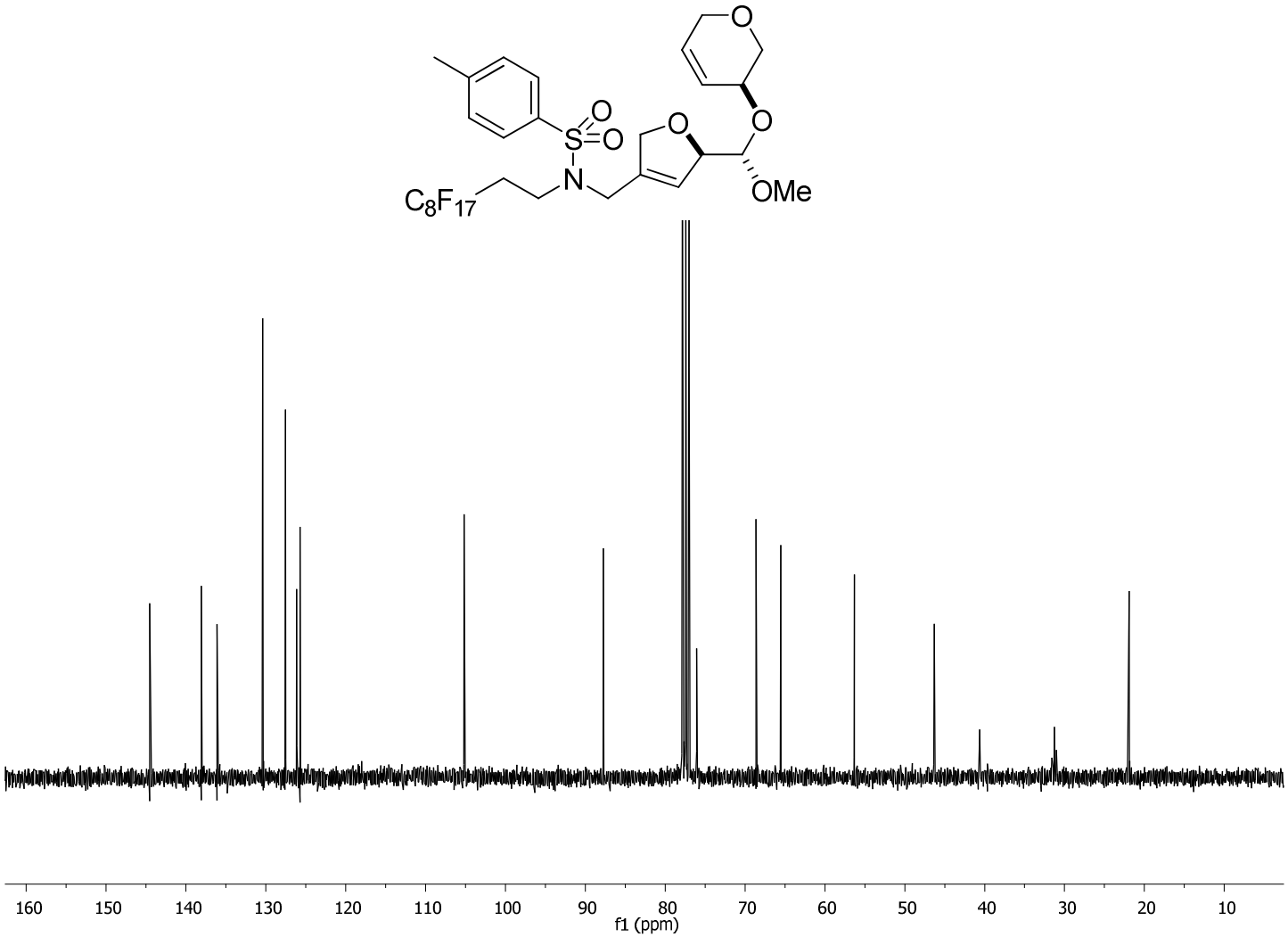
75 MHz ^{1}H NMR of S13



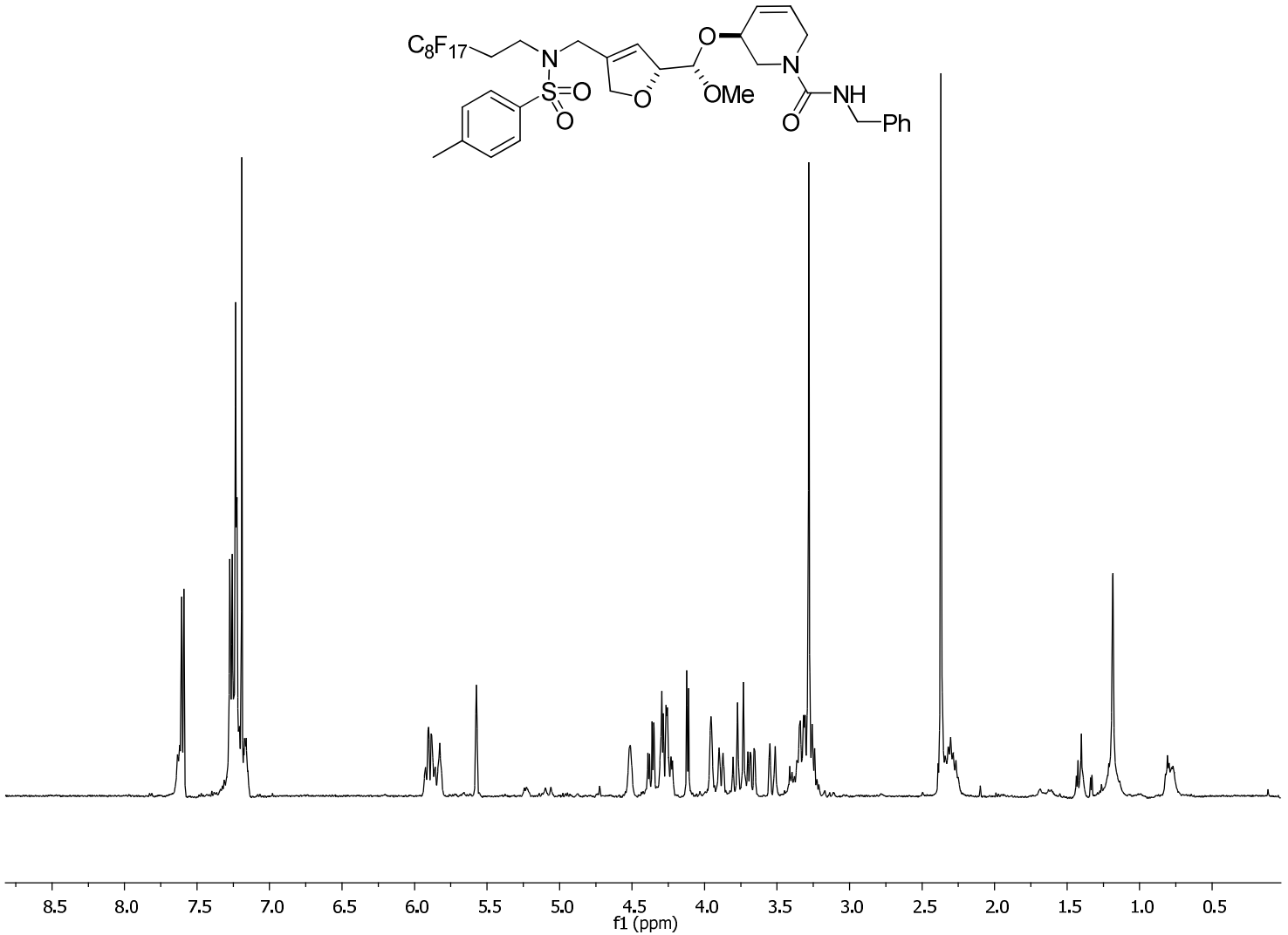
500 MHz ^{1}H NMR of 32 (R = R'^{F})



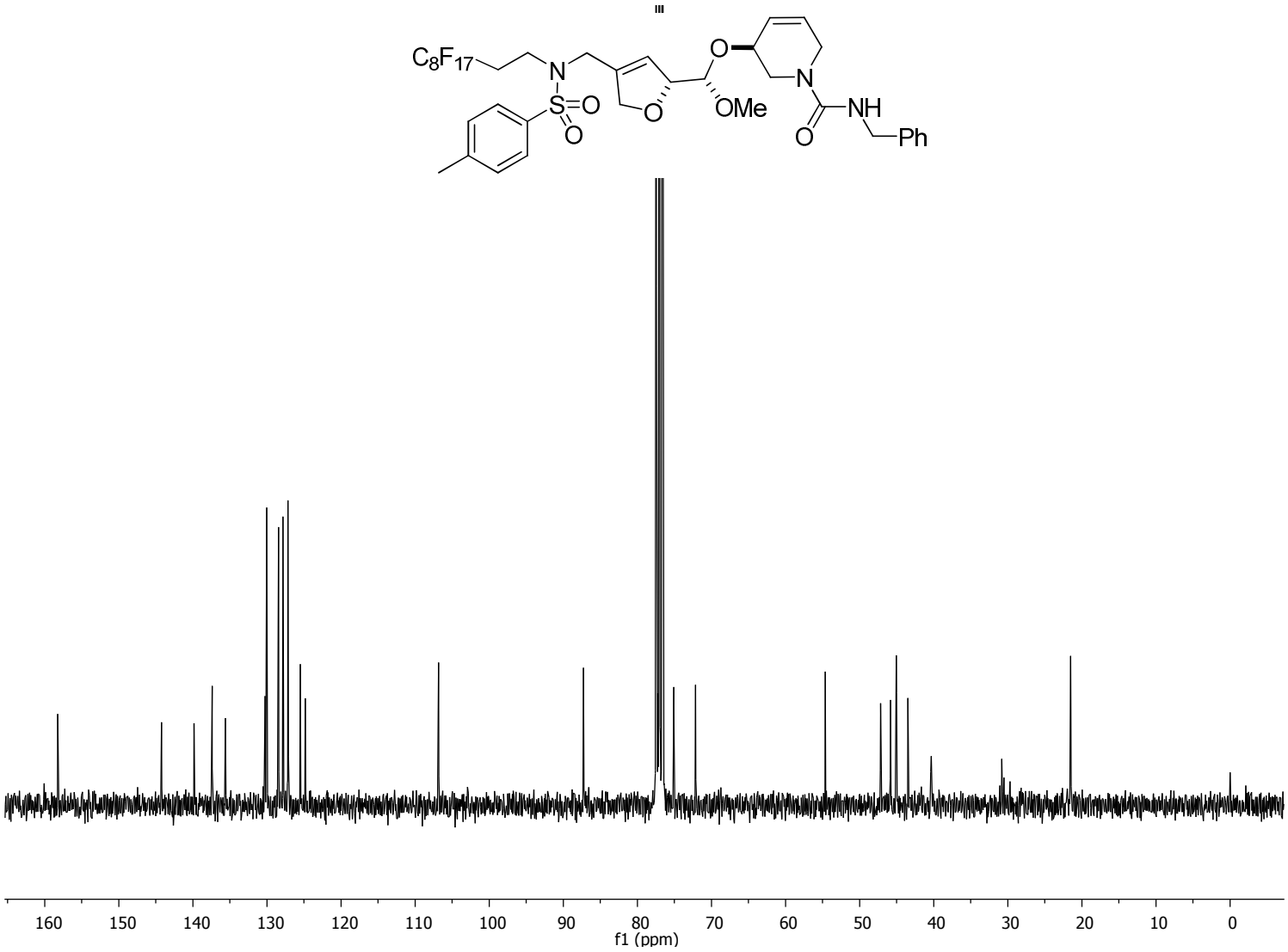
75 MHz ^{13}C NMR of 32 (R = R'^{F})



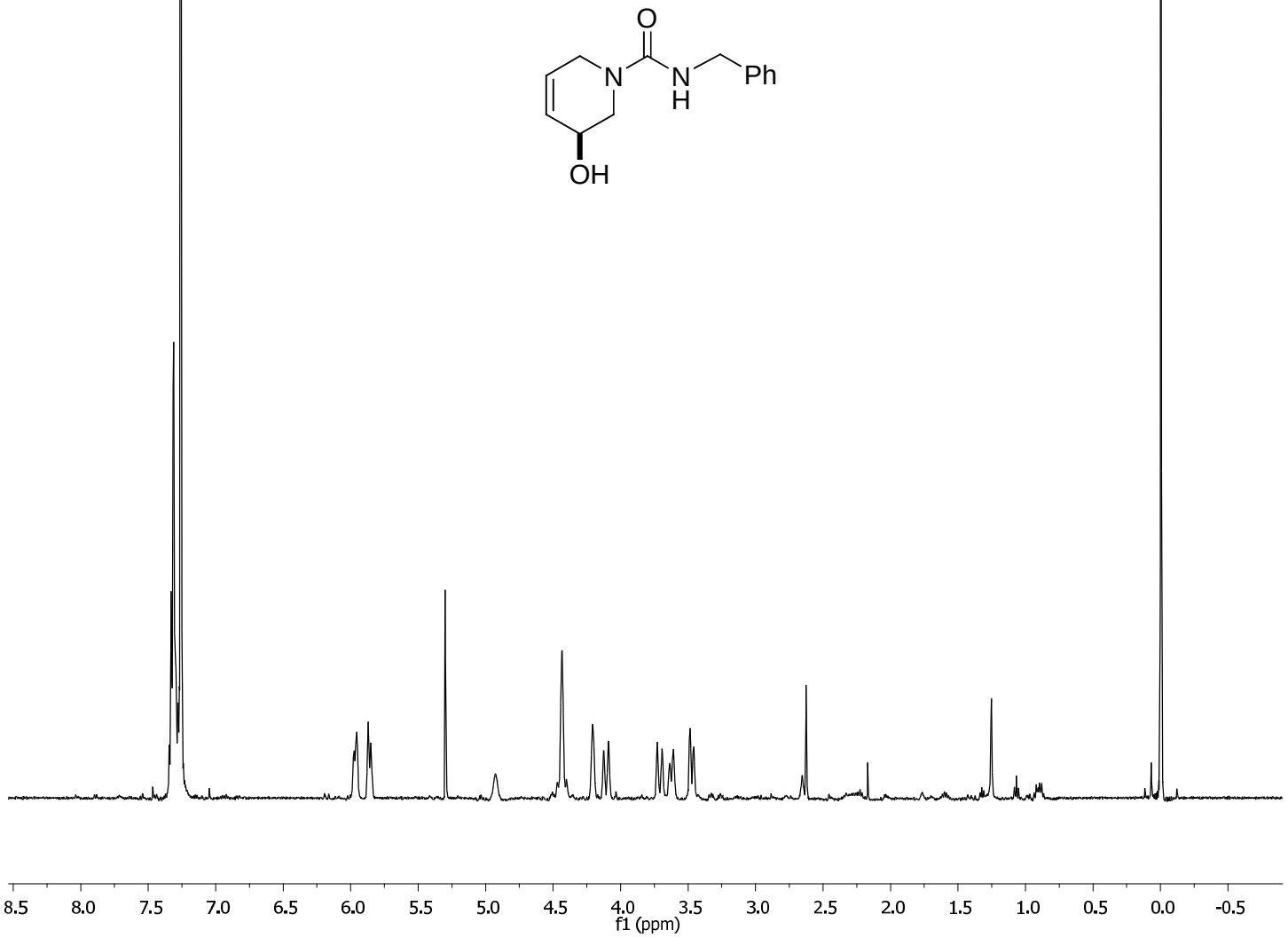
^{1}H NMR of 33 (R = R'^{F}) **(F-SPE purified only)**



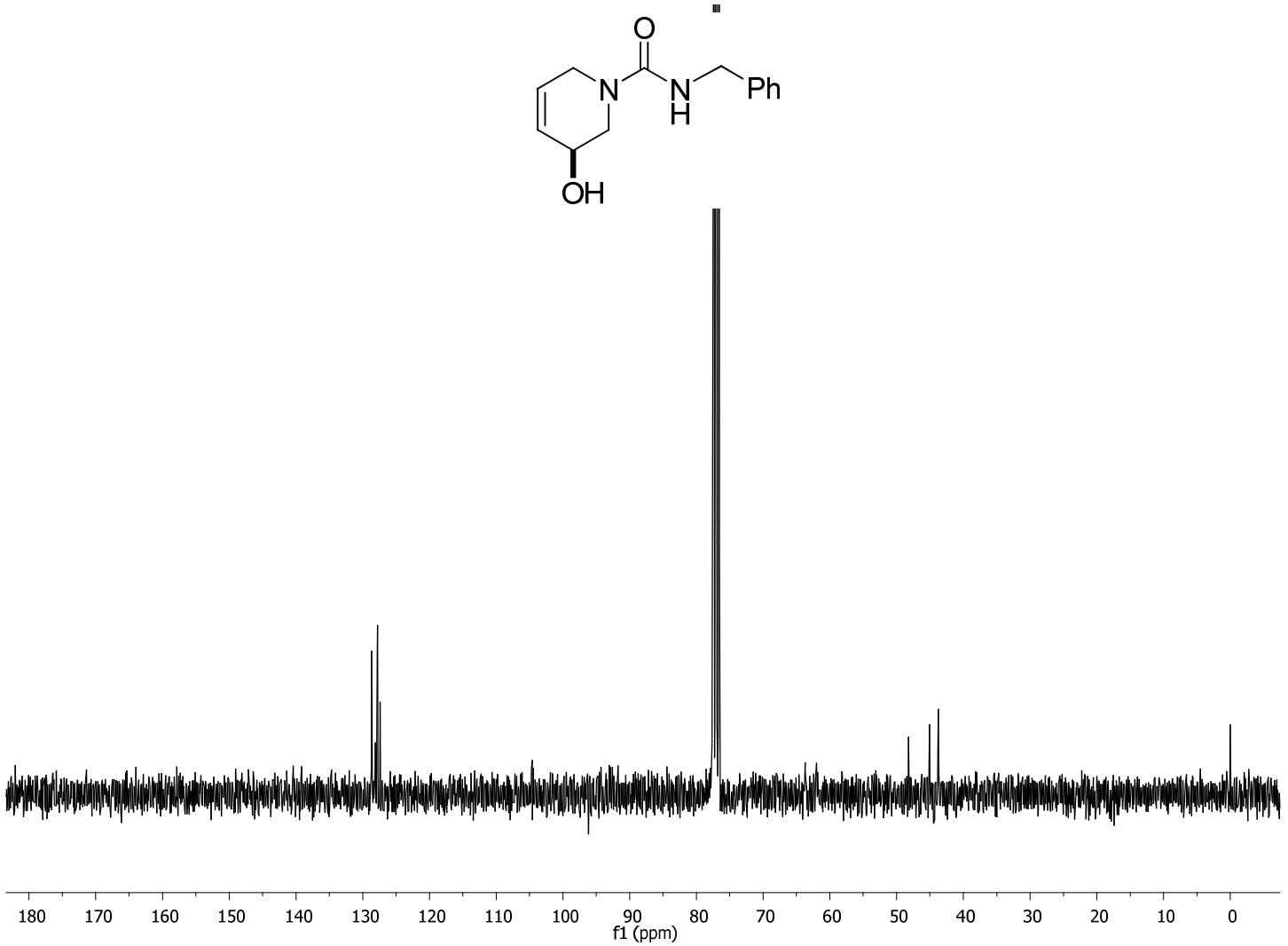
75 MHz ^{13}C NMR of 33 (R = R'^{F})



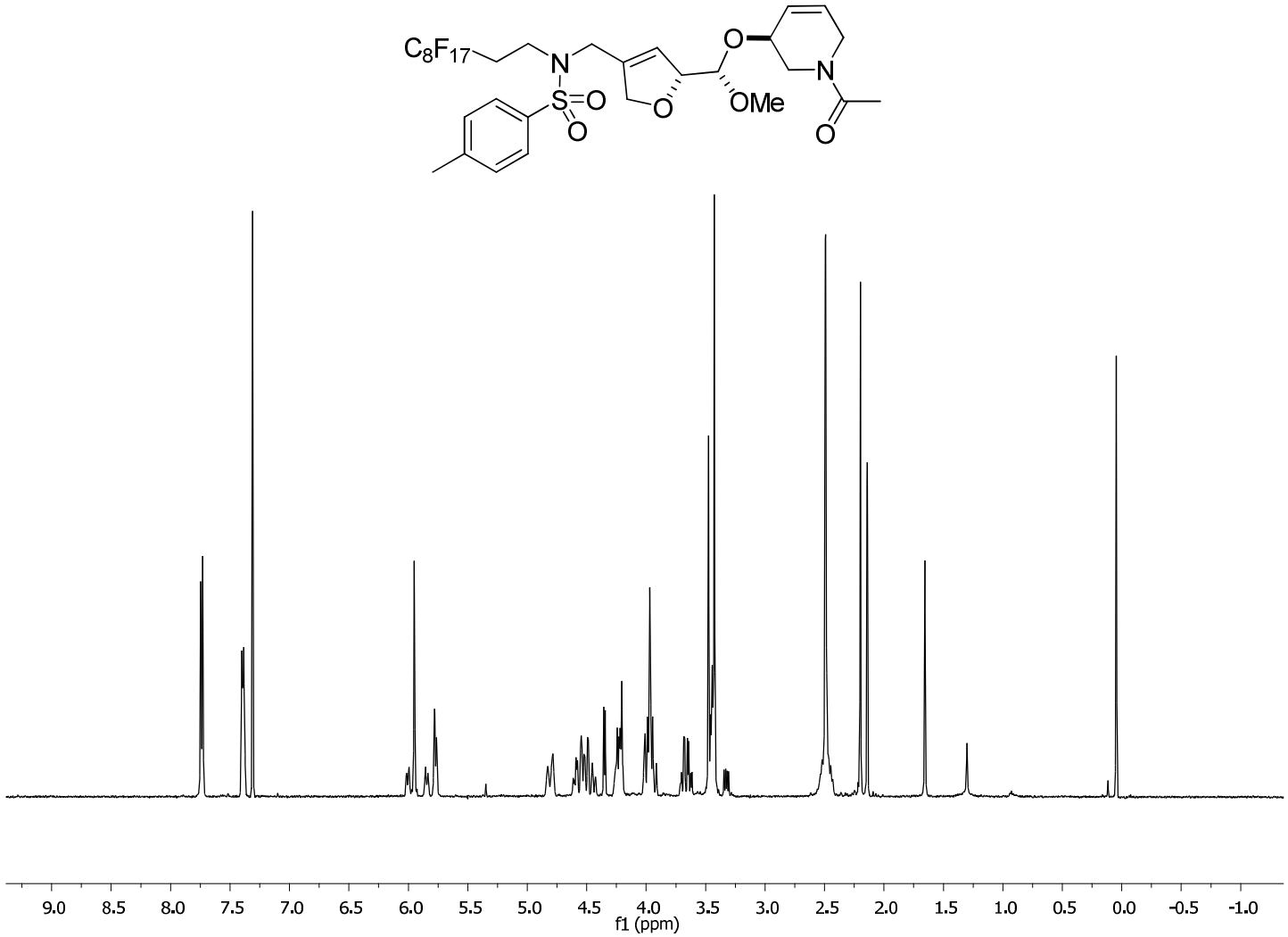
500 MHz ^{1}H NMR of 33 (R = H)



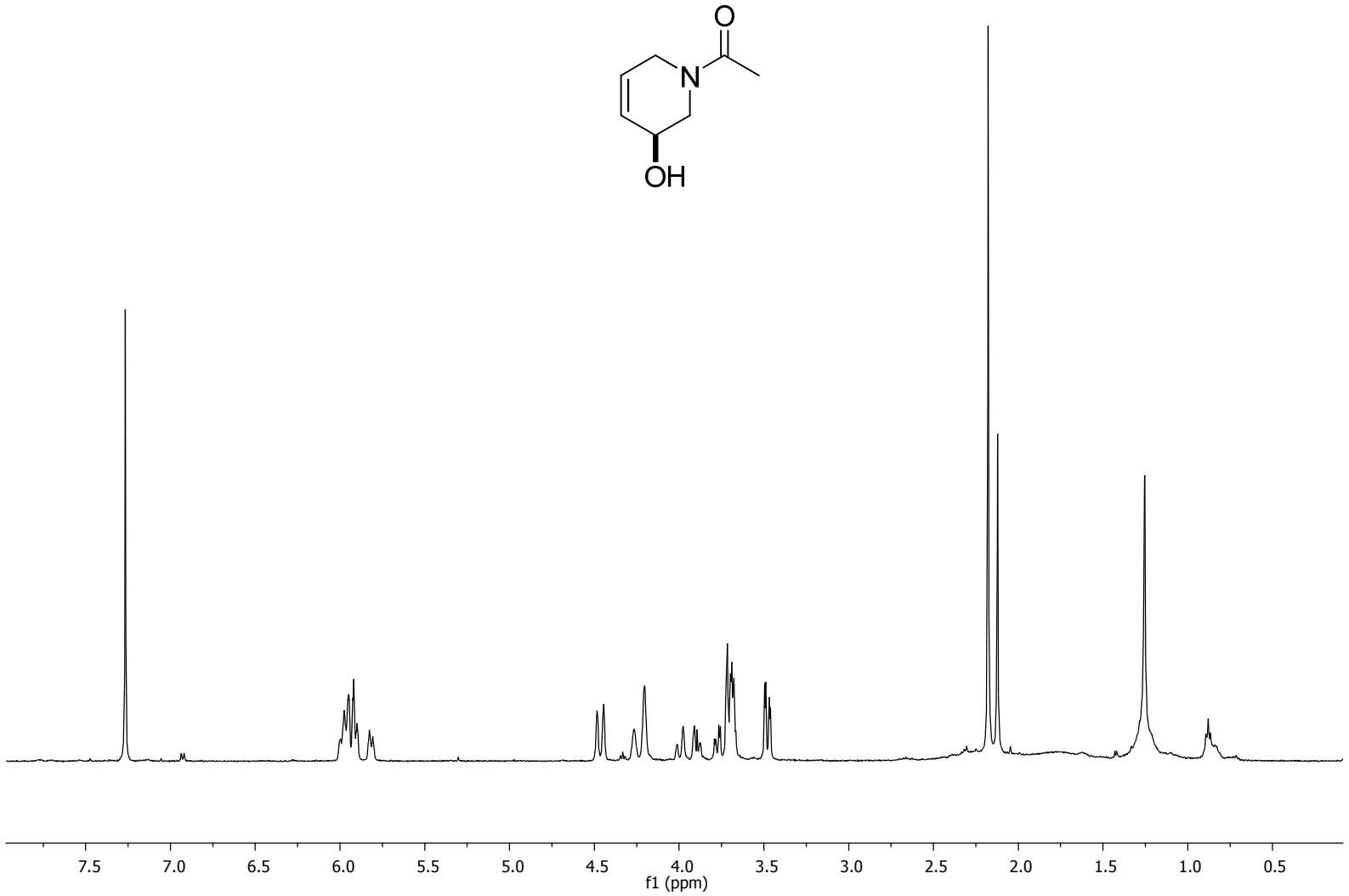
75 MHz ^{13}C NMR of 33 (R = H)



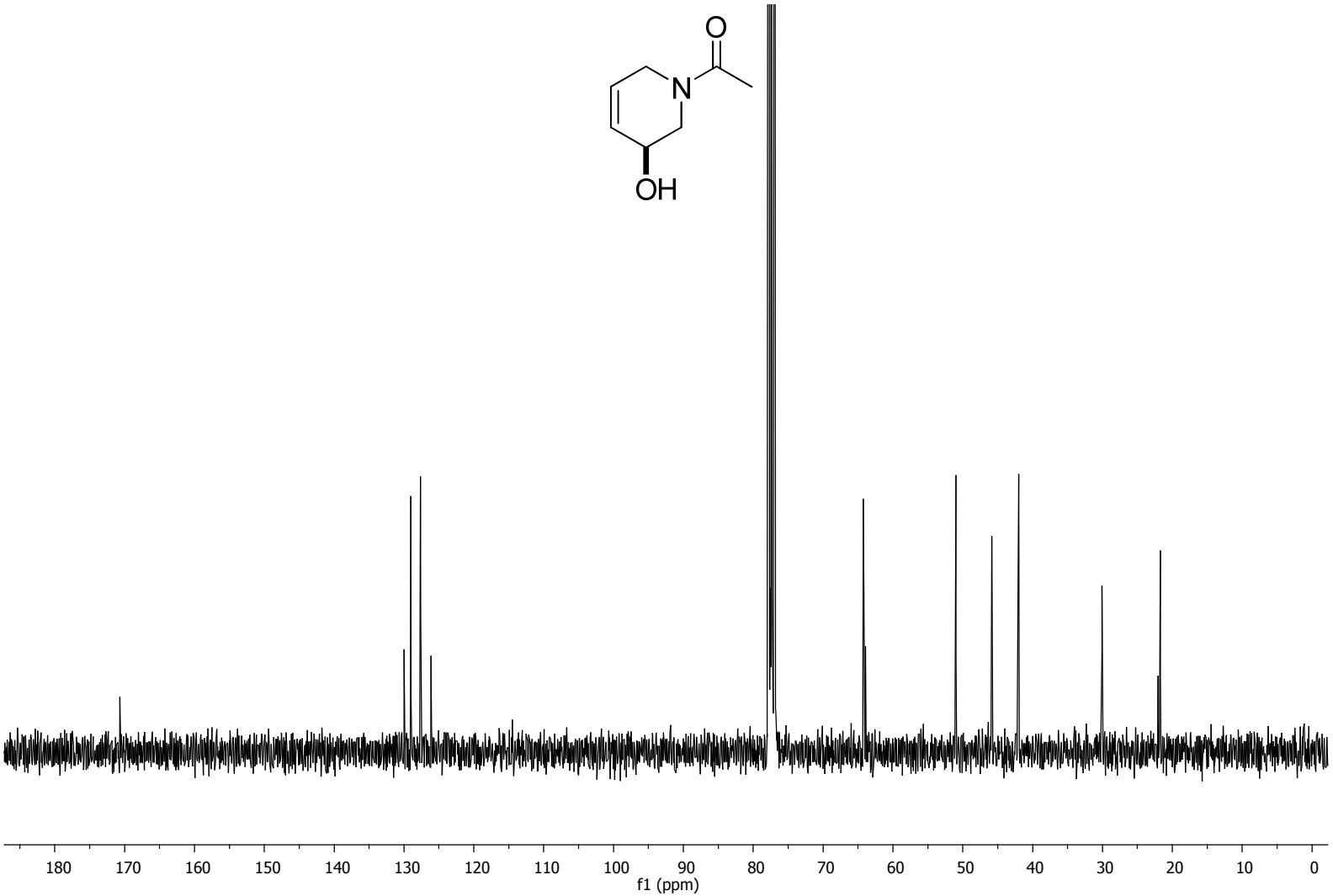
^{1}H NMR of 34 (R = R'^{F}) **(F-SPE purified only)**



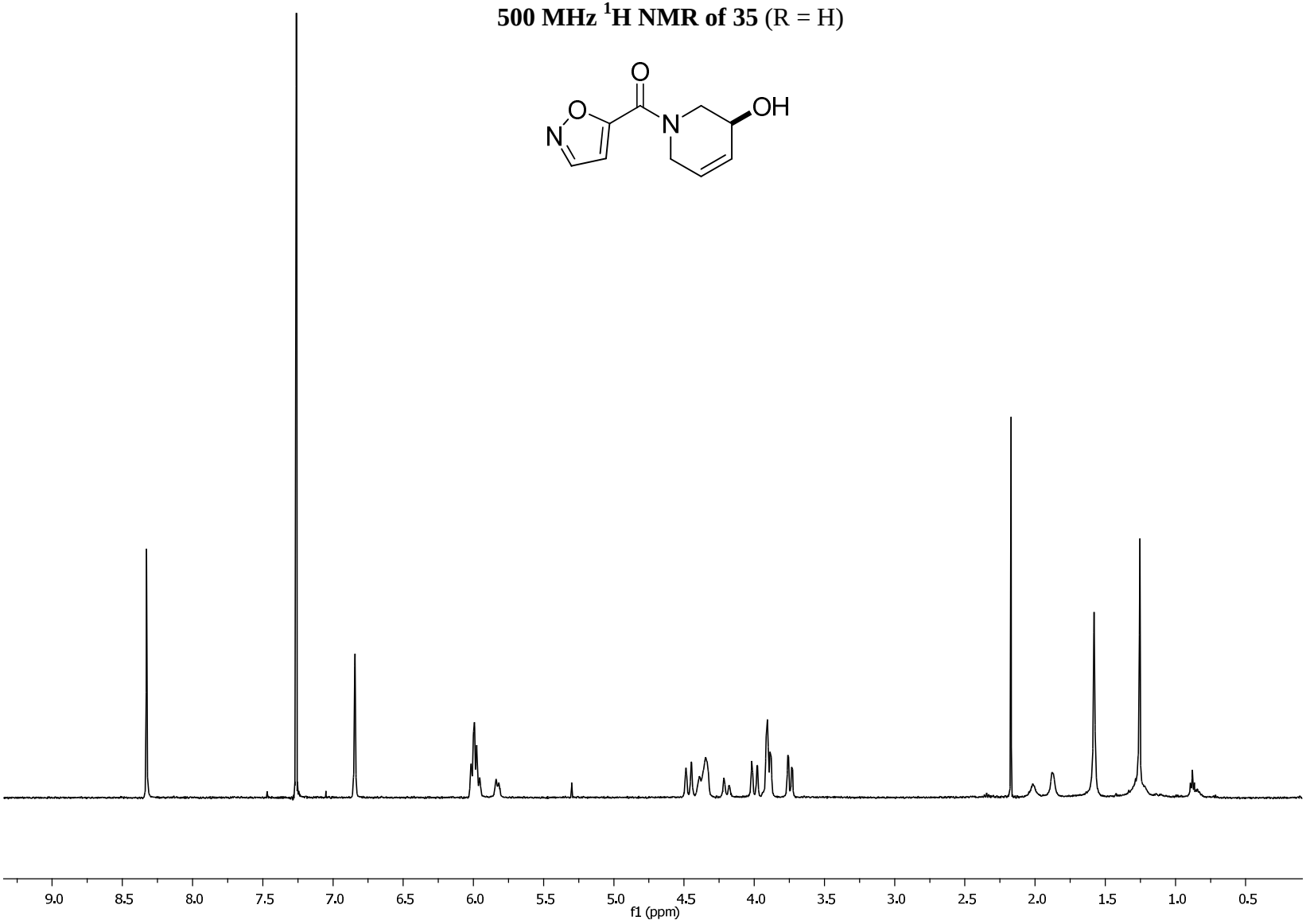
500 MHz ^{1}H NMR of 34 (R = H)



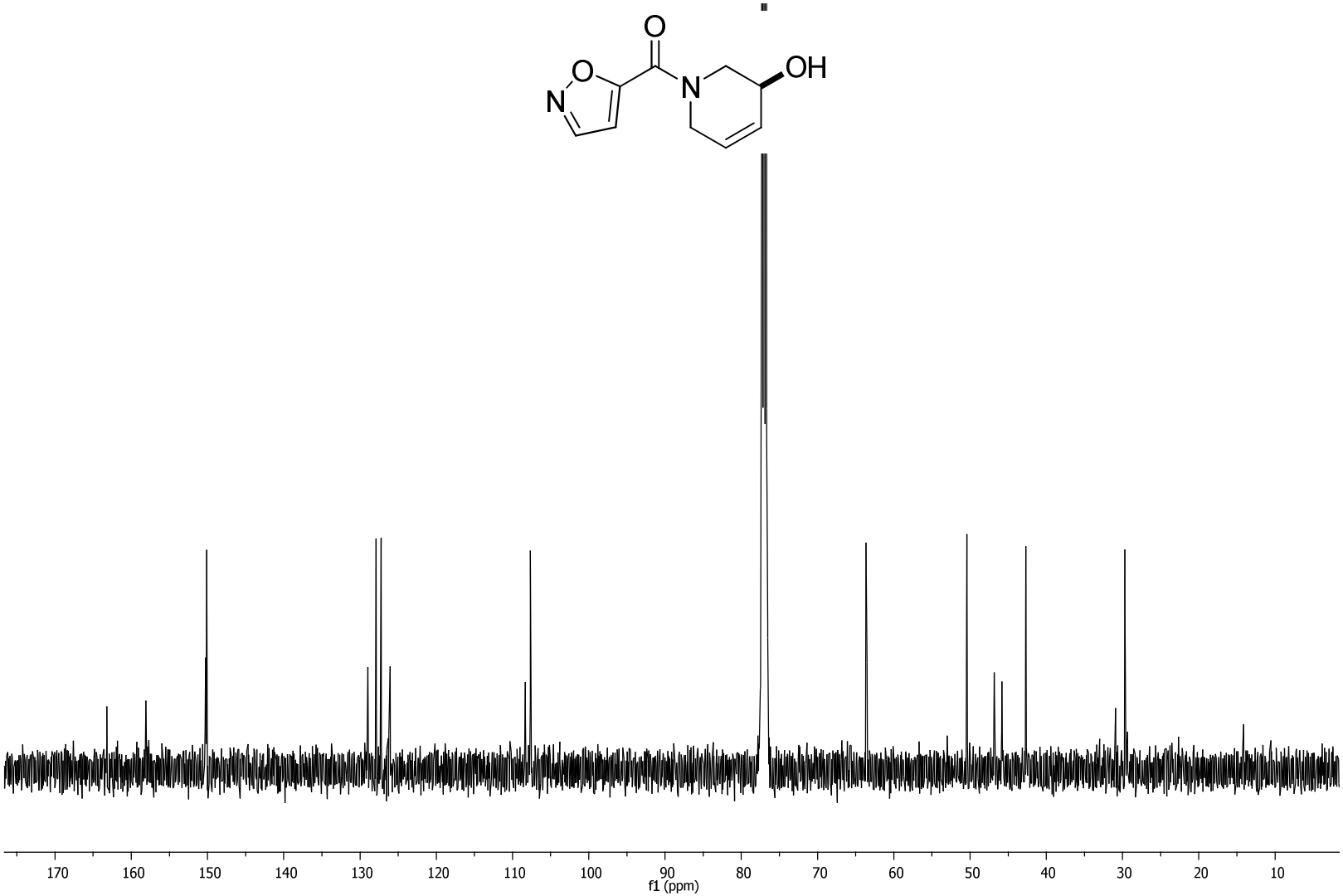
75 MHz ^{13}C NMR of 34 (R = H)



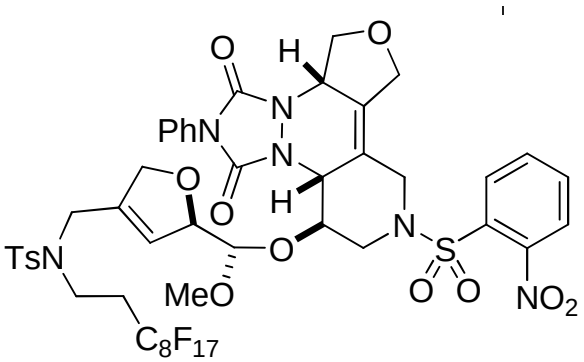
500 MHz ^{1}H NMR of 35 (R = H)

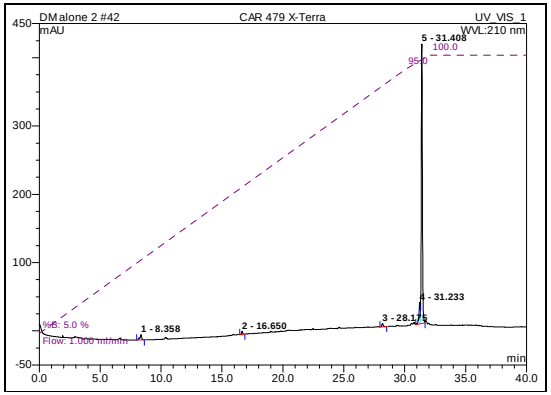


75 MHz ^{13}C NMR of 35 (R = H)



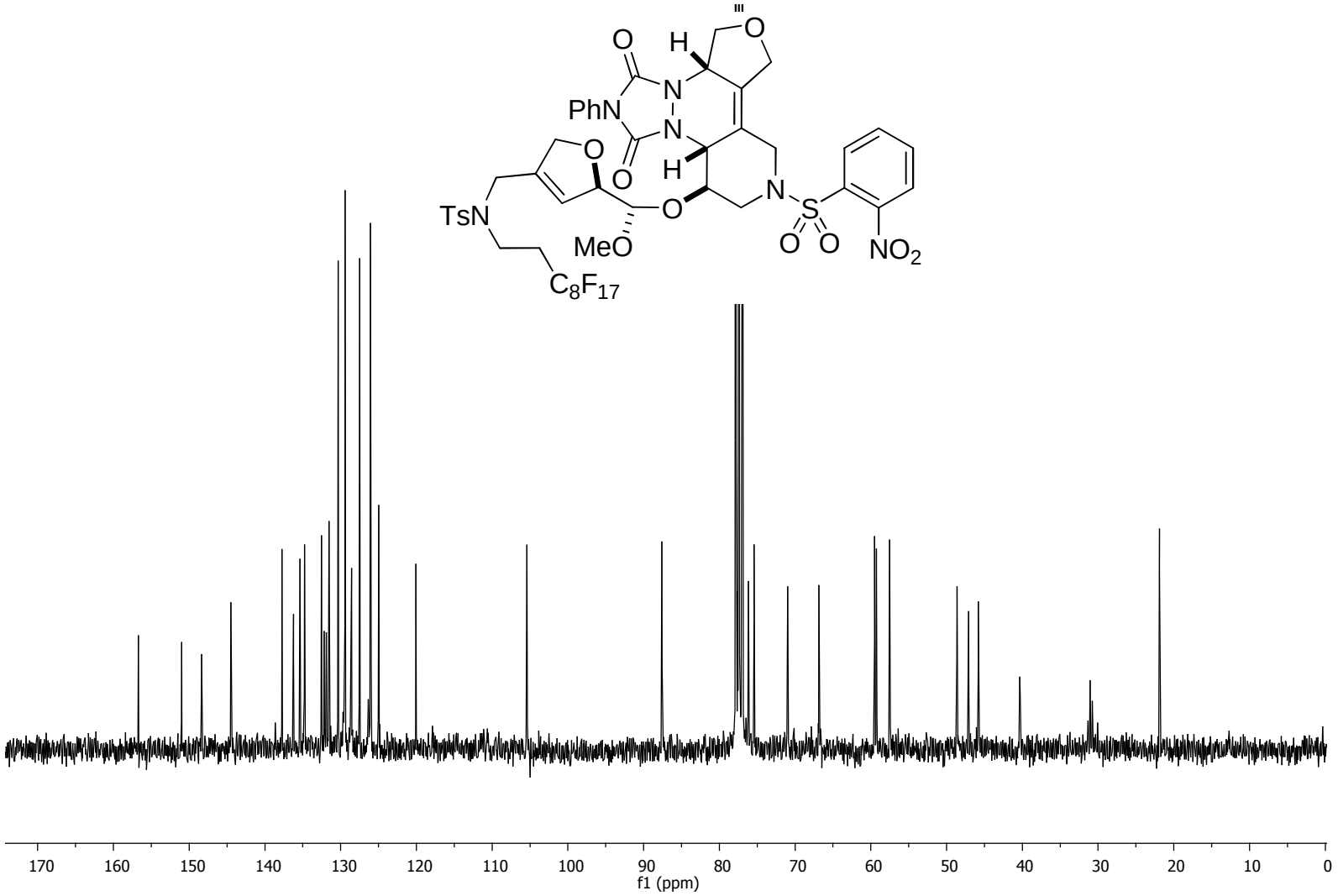
^{1}H NMR of 36 (R = R'^{F}) **(F-SPE purified only)**



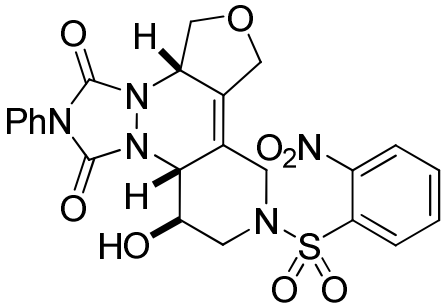


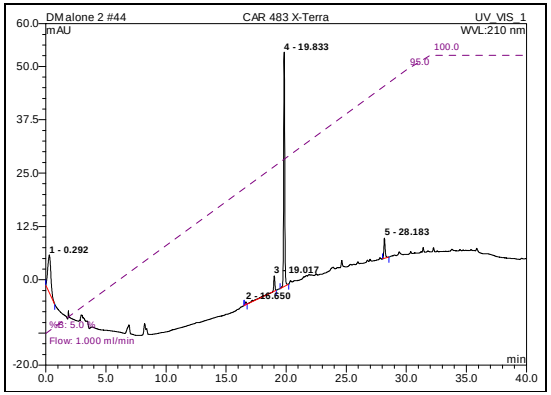
HPLC trace after F-SPE purification only

75 MHz ^{13}C NMR of 36 (R = R'^{F})



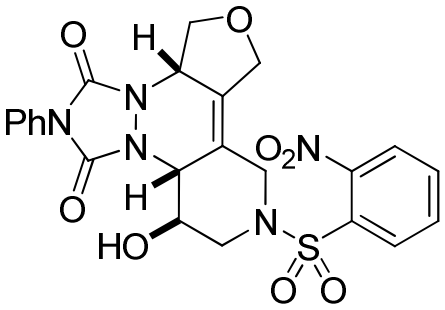
^{1}H NMR of 36 (R = H) after F-SPE only



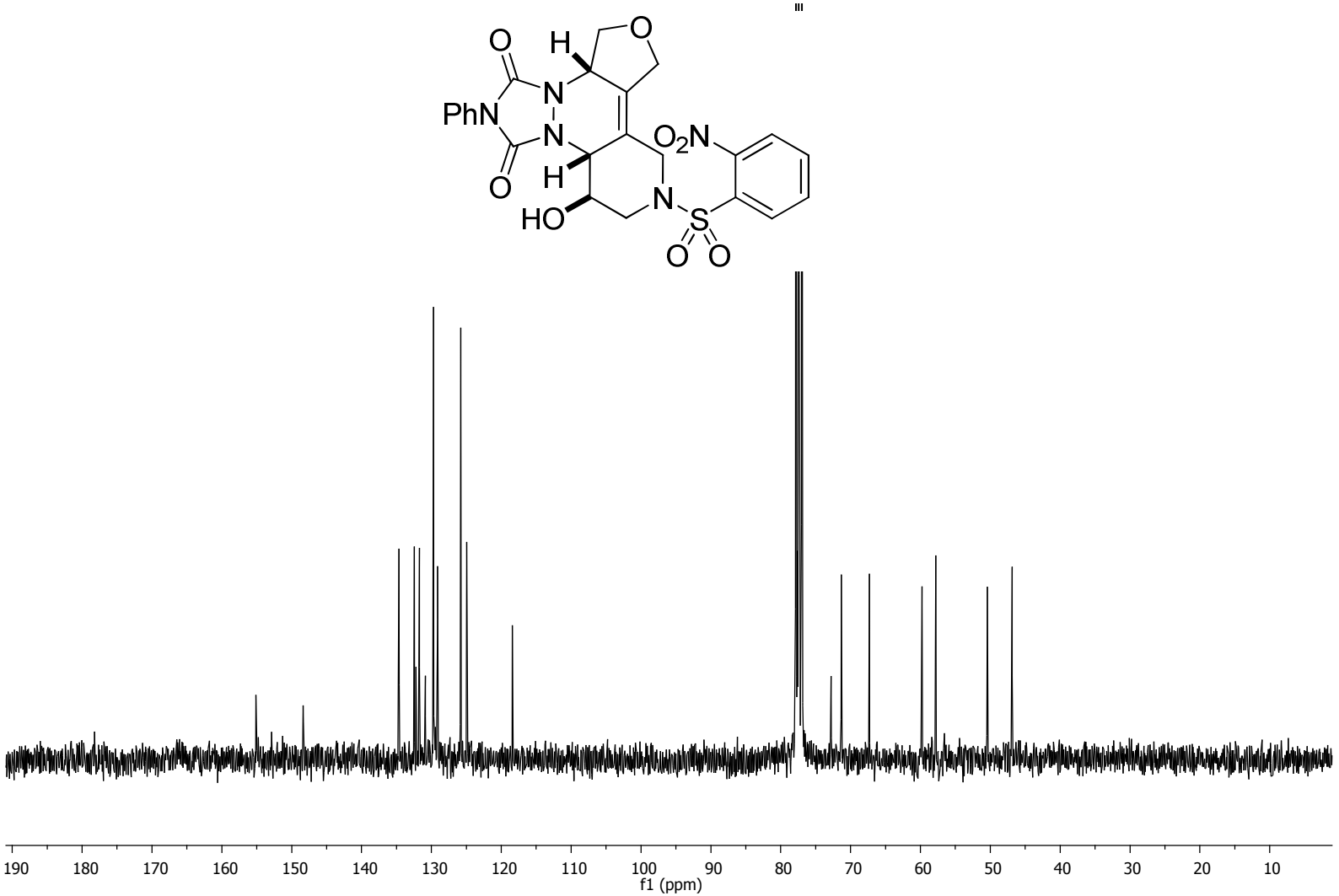


HPLC trace after F-SPE purification only

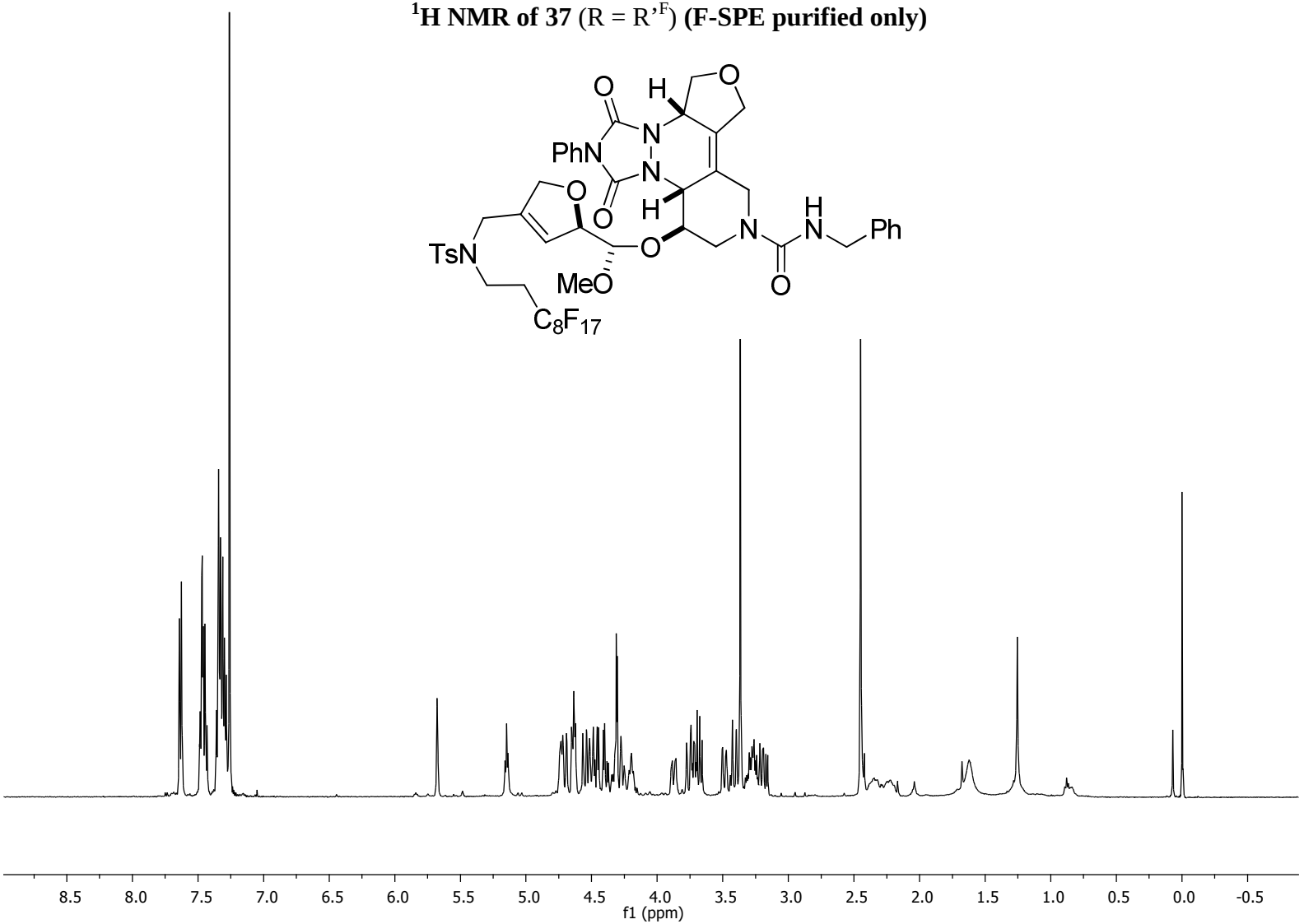
500 MHz ^{1}H NMR of 36 (R = H)



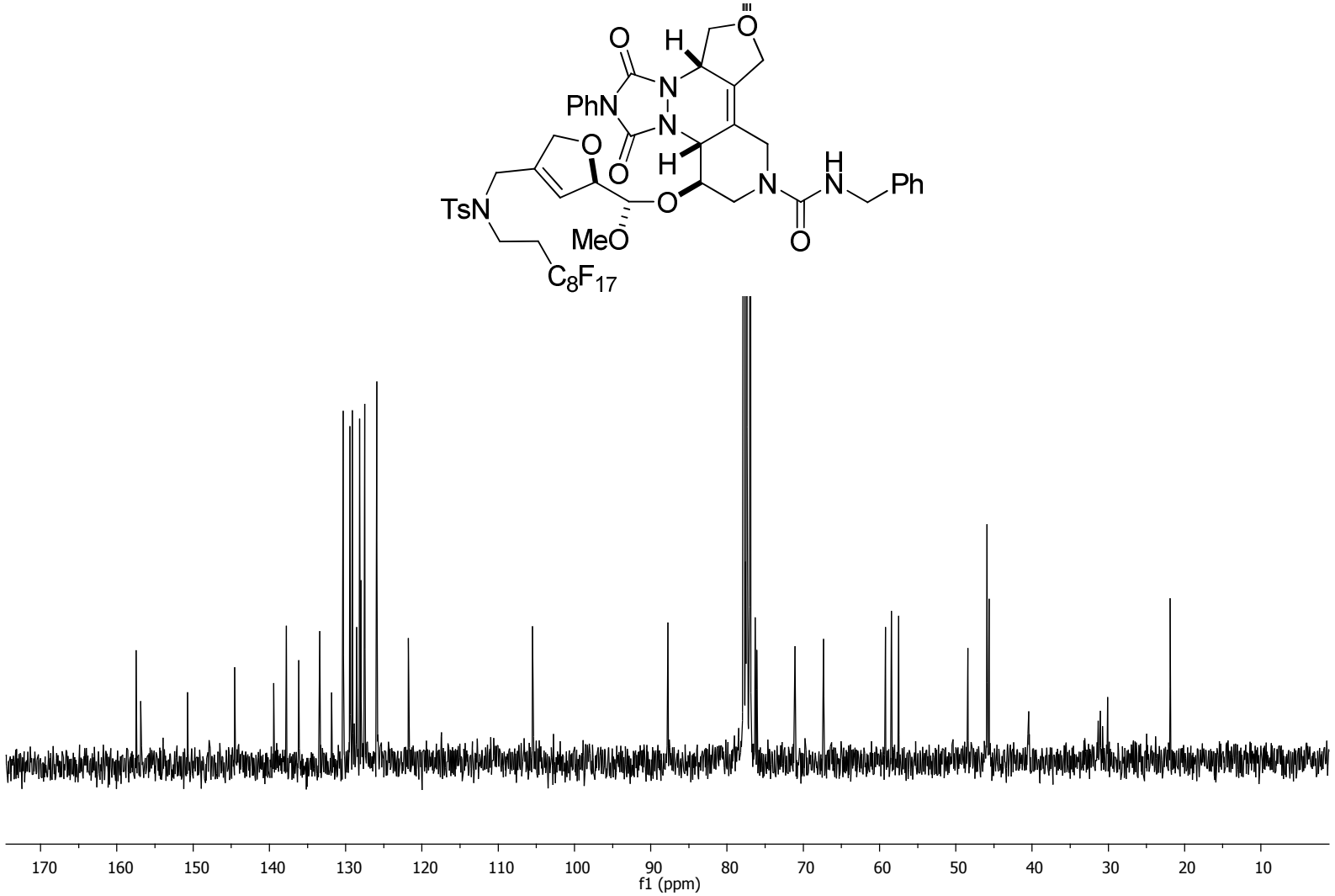
75 MHz ^{13}C NMR of 36 (R = H)



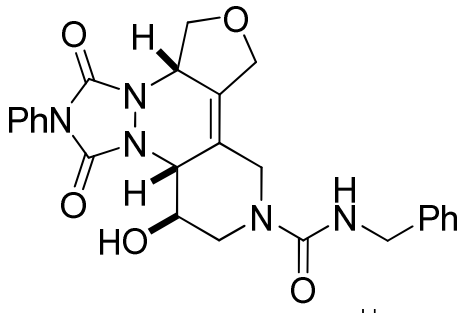
^{1}H NMR of 37 (R = R'^{F}) **(F-SPE purified only)**

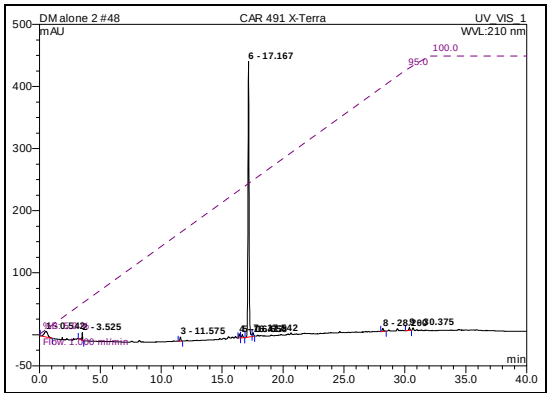


75 MHz ^{13}C NMR of 37 (R = R'^{F})

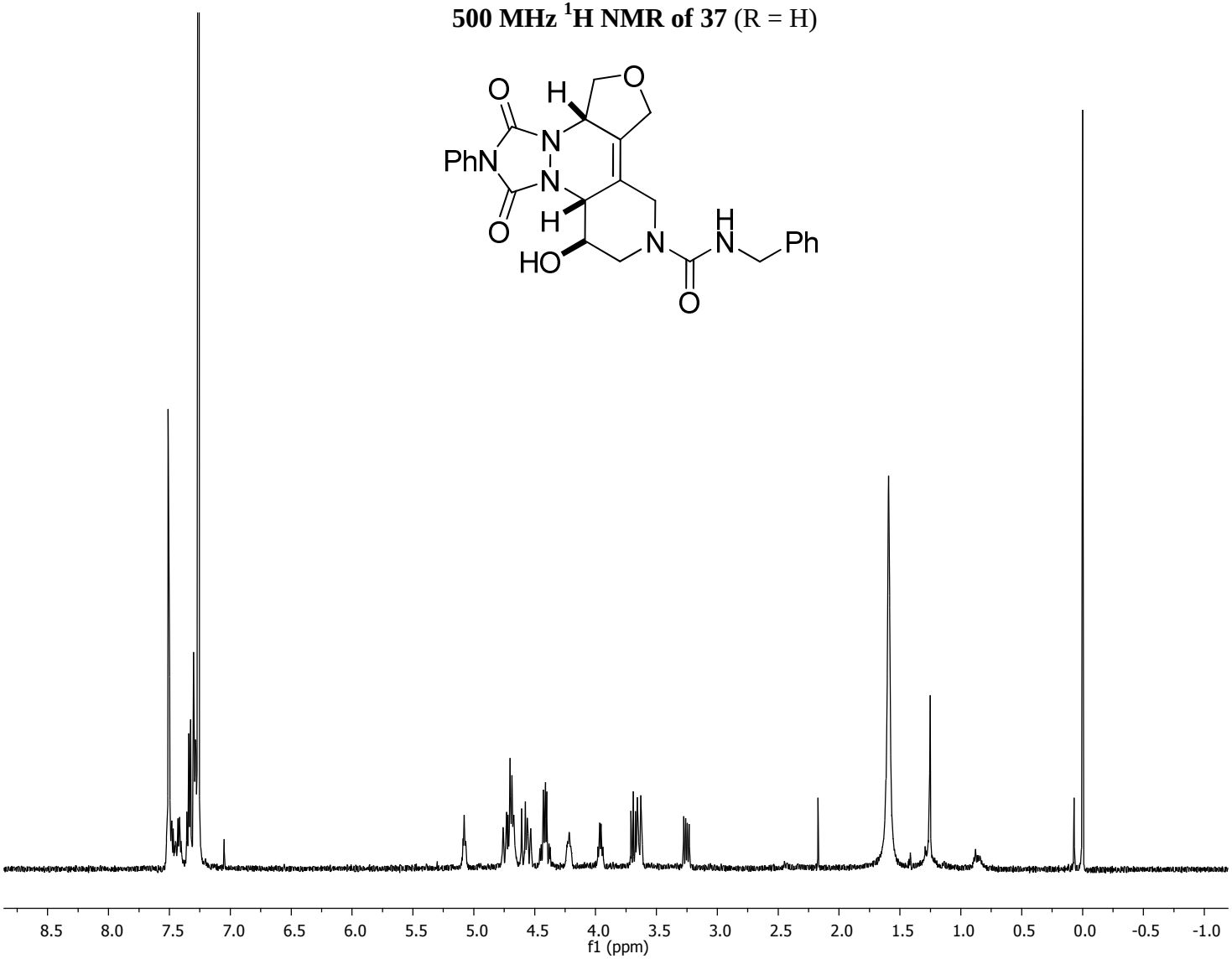


^{1}H NMR of 37 (R = H) **(after F-SPE only)**

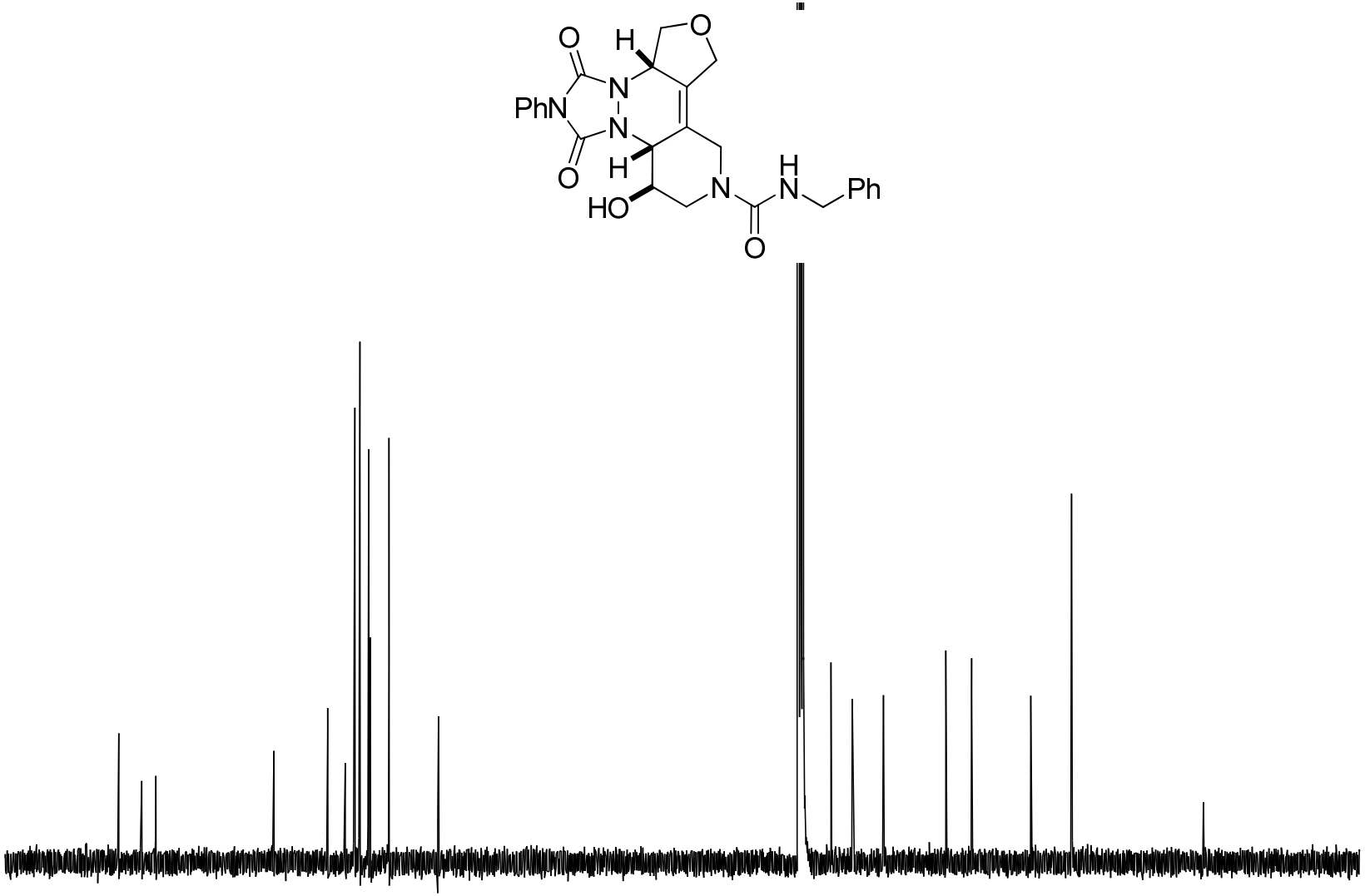




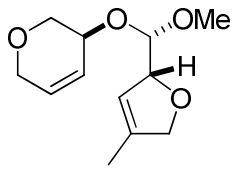
500 MHz ^{1}H NMR of 37 (R = H)



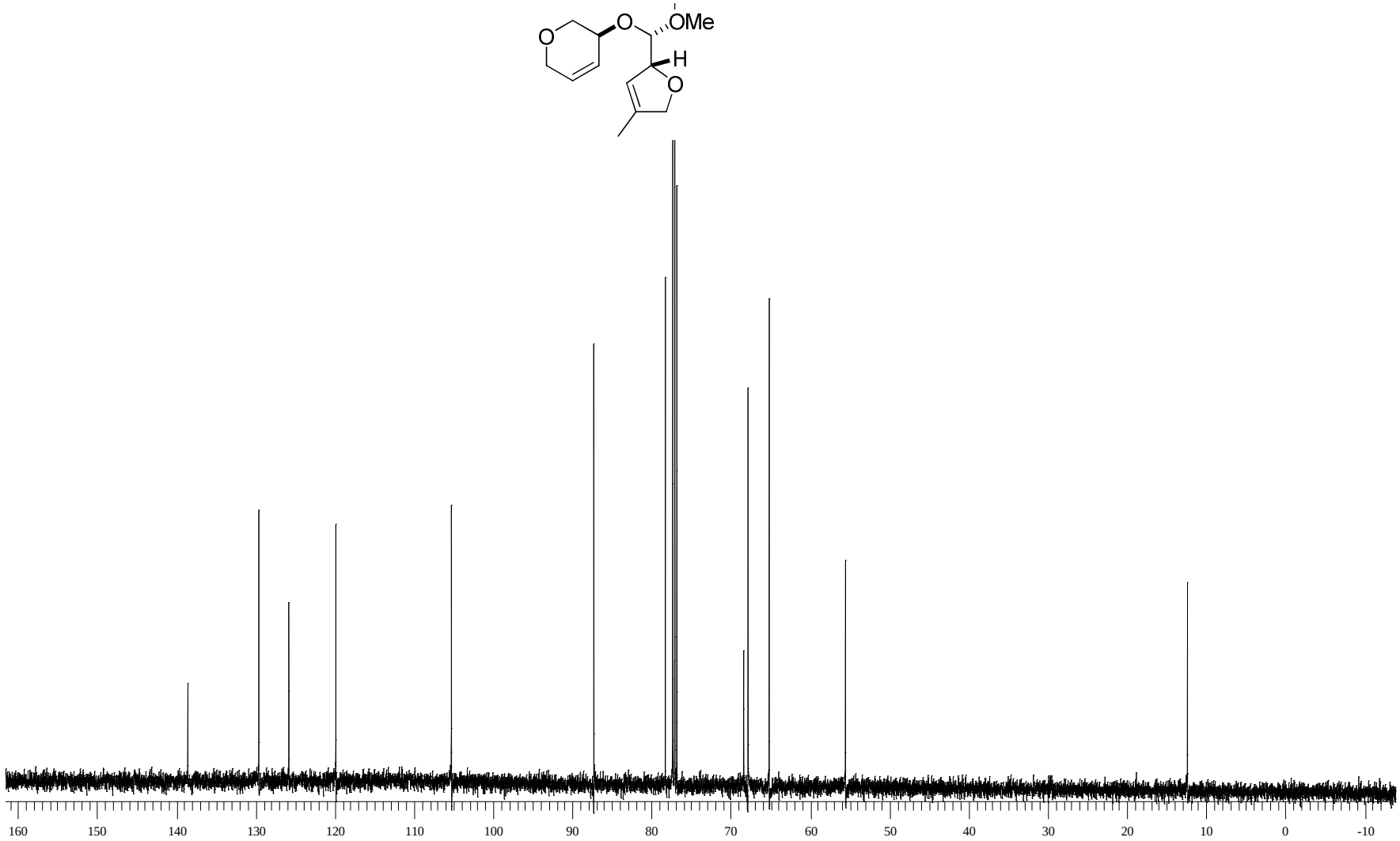
75 MHz ^{13}C NMR of 37 (R = H)



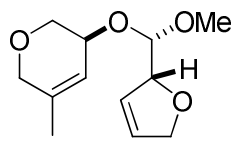
500 MHz ^{1}H NMR of 10



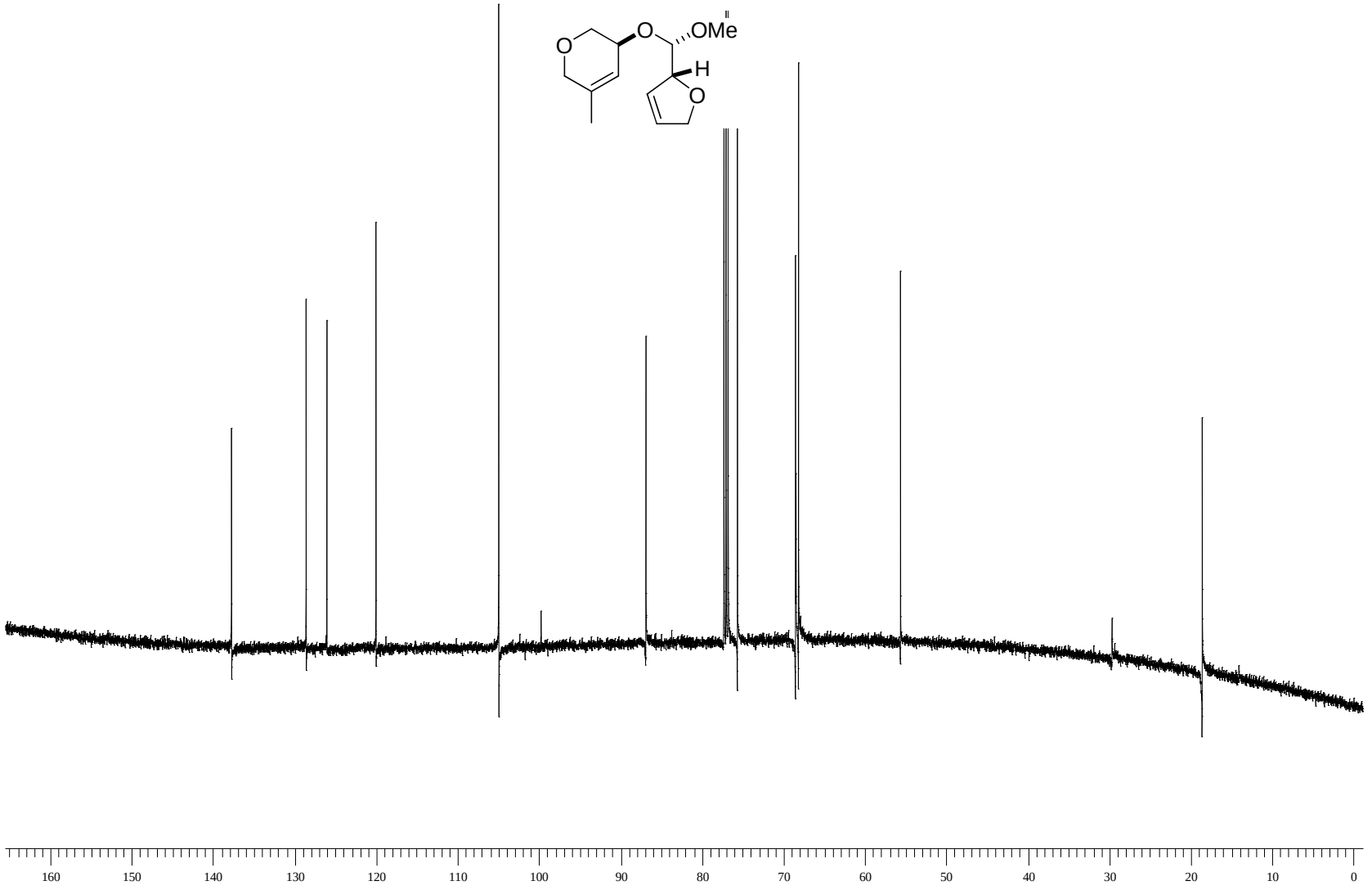
75 MHz ^{13}C NMR of 10



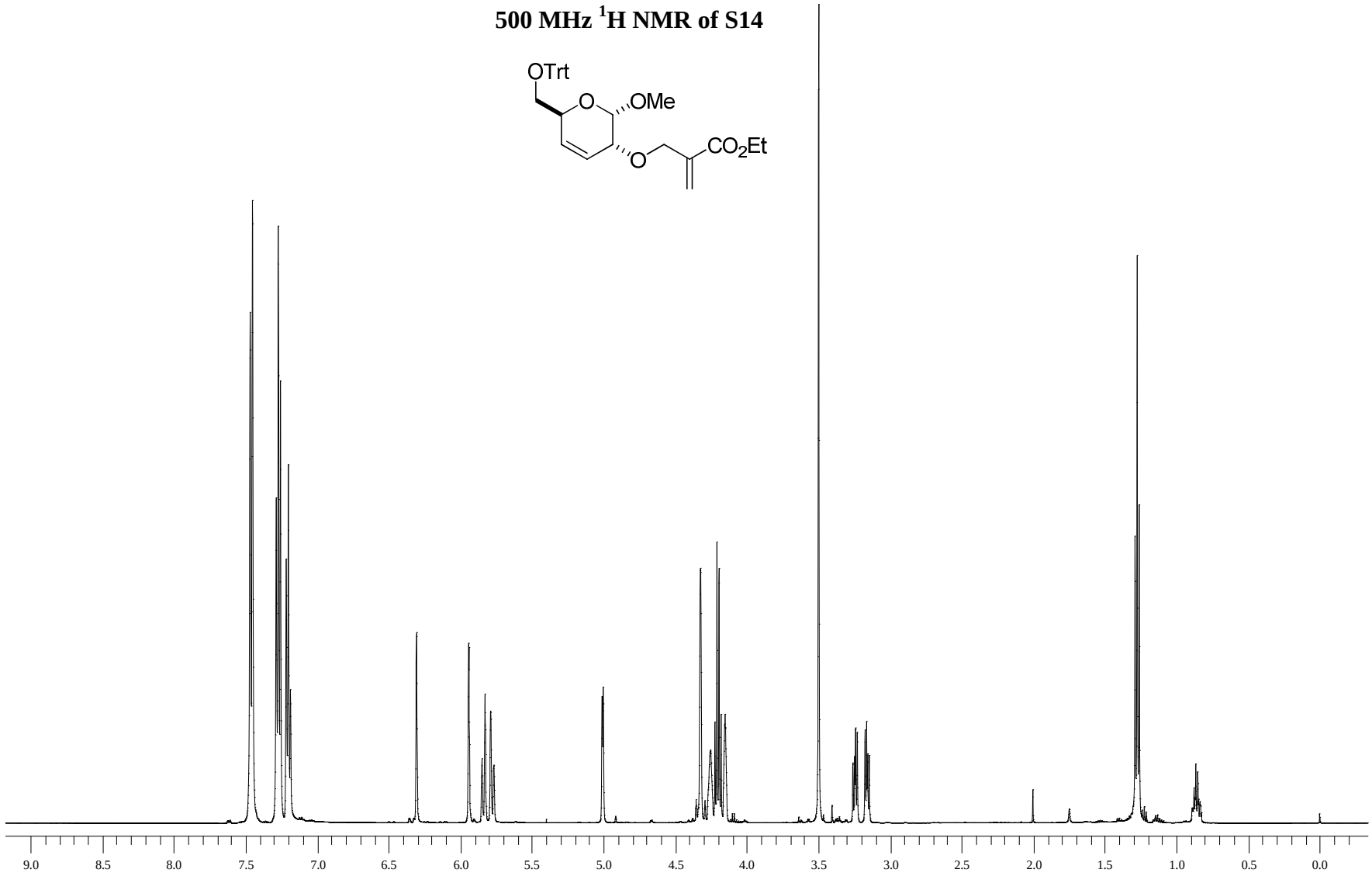
500 MHz ^{1}H NMR of 11



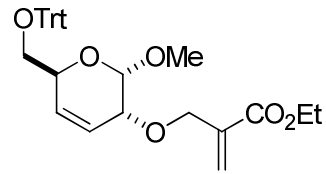
75 MHz ^{13}C NMR of 11



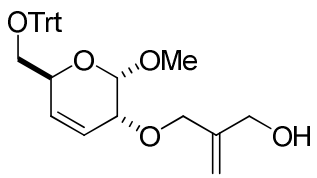
500 MHz ^{1}H NMR of S14



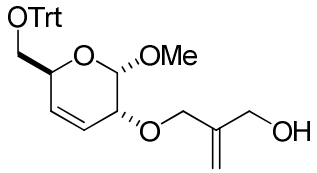
75 MHz ^{13}C NMR of S14



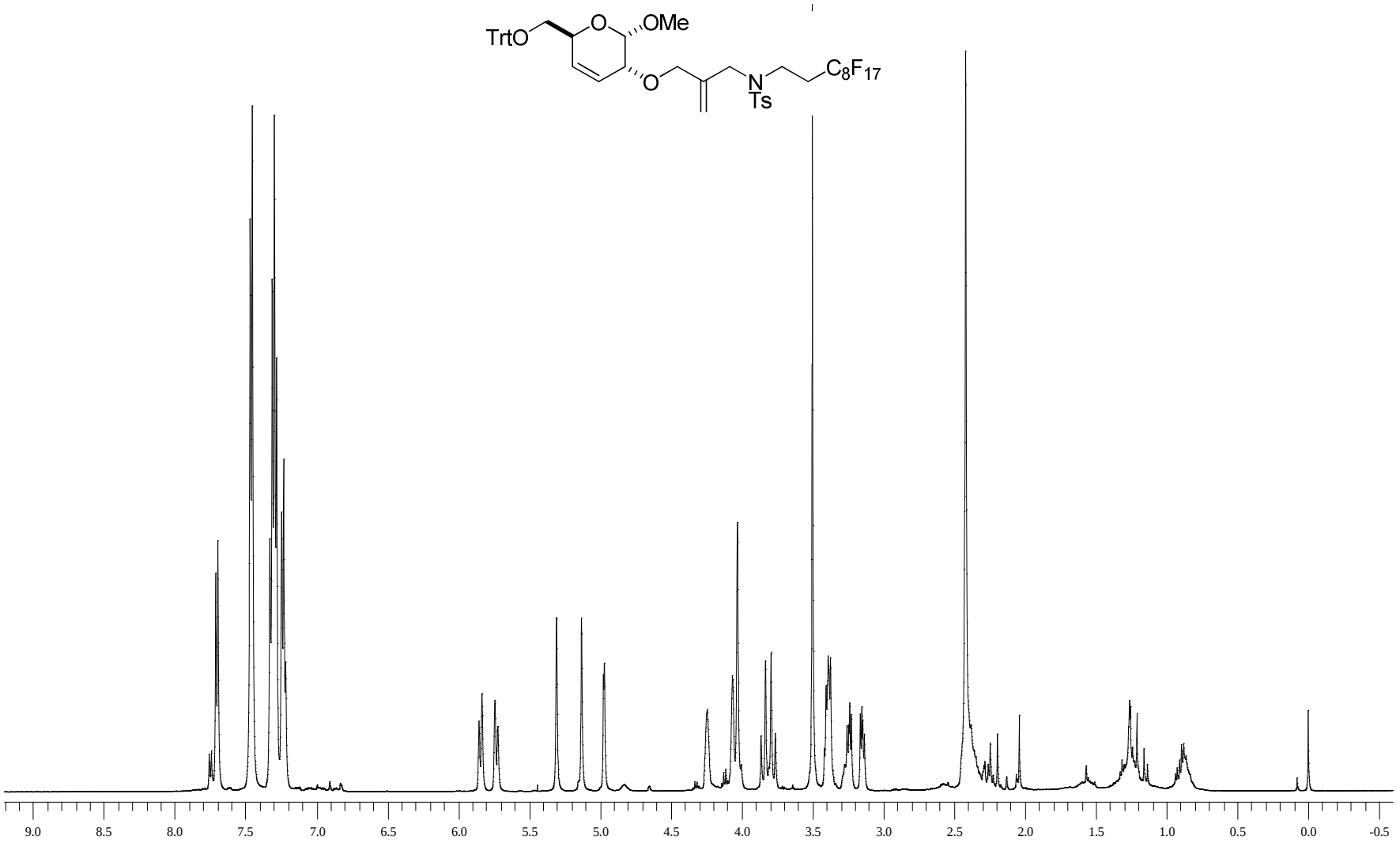
500 MHz ^{1}H NMR of 13



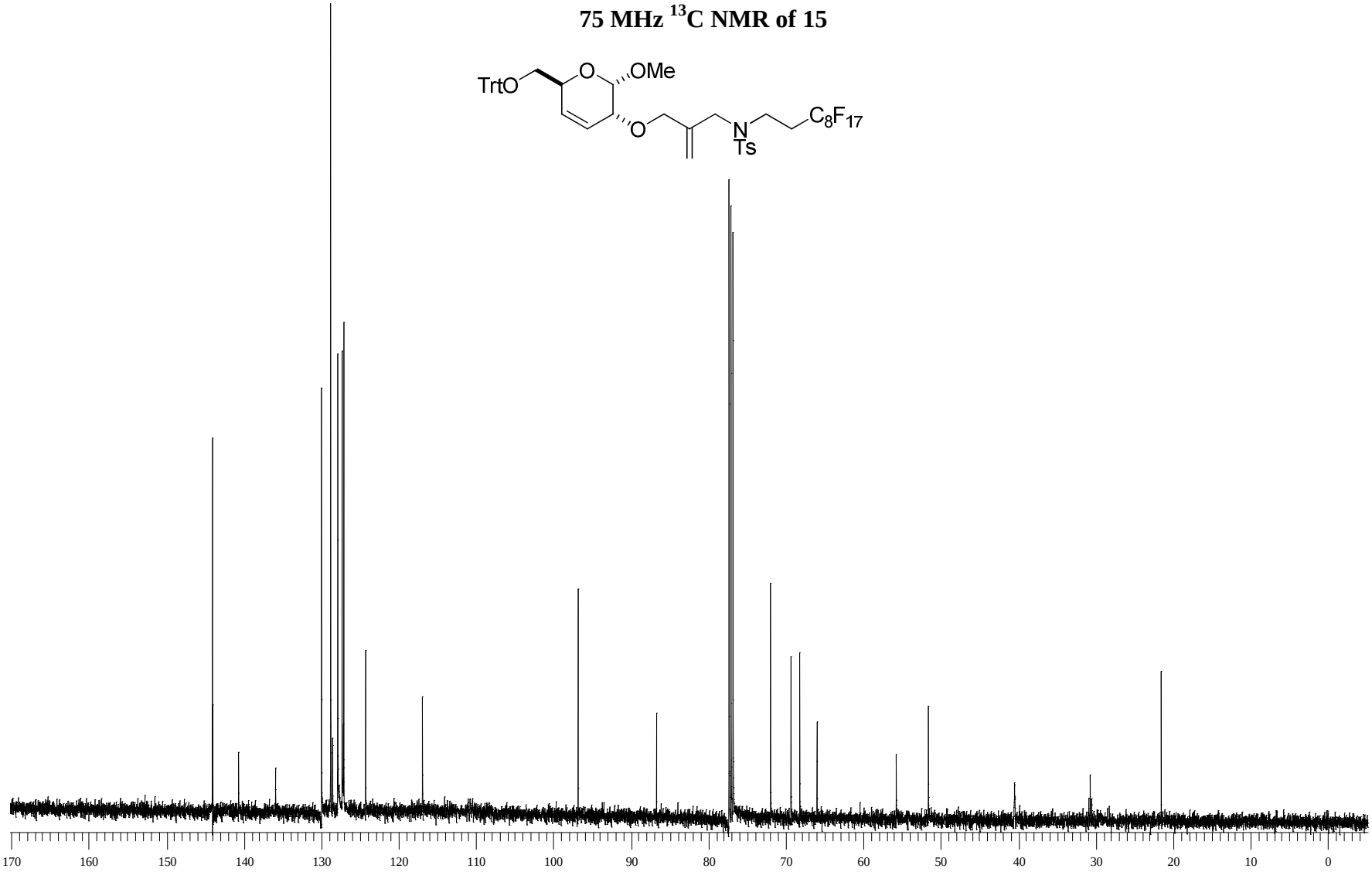
75 MHz ^{13}C NMR of 13



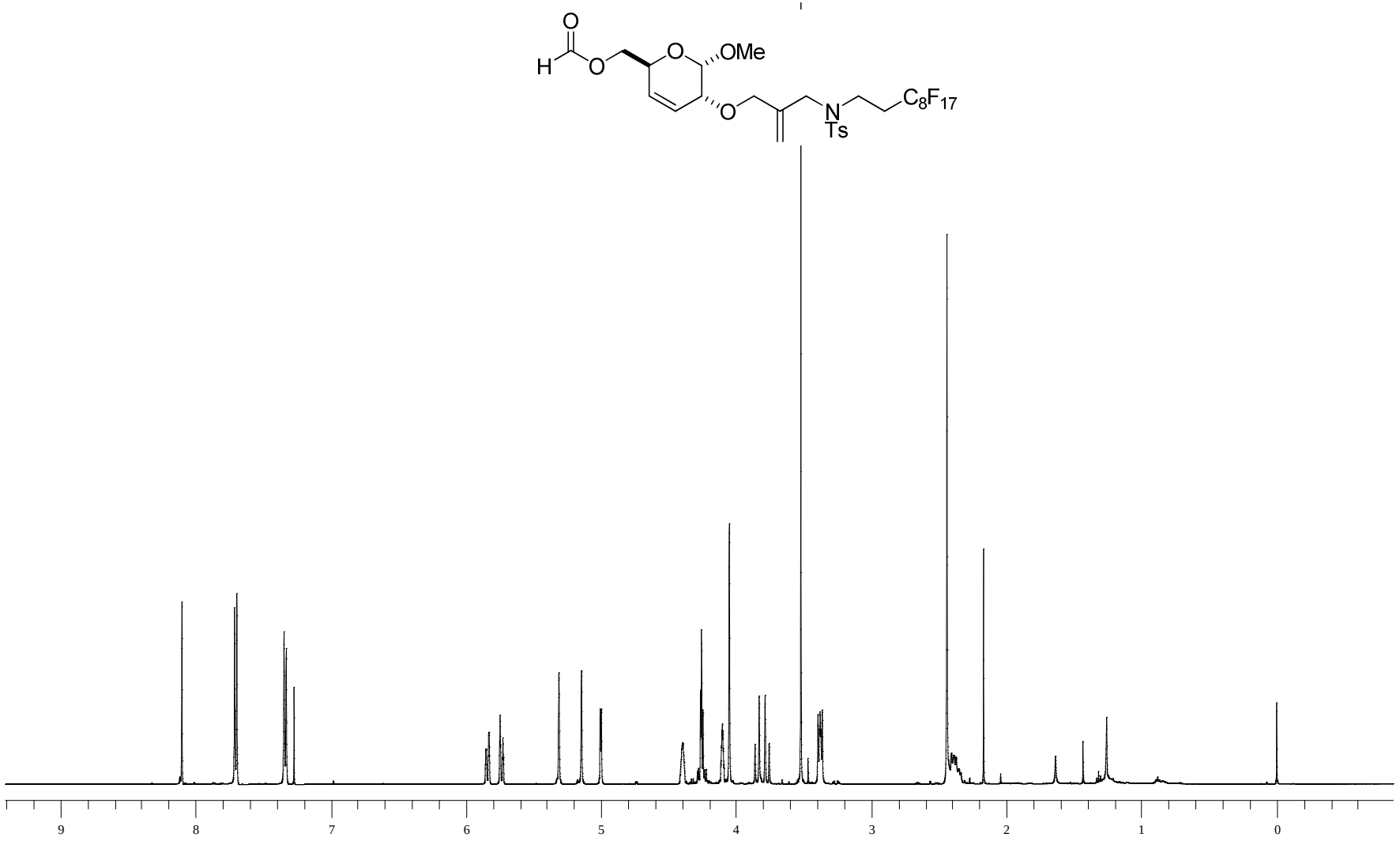
500 MHz ^{1}H NMR of 15



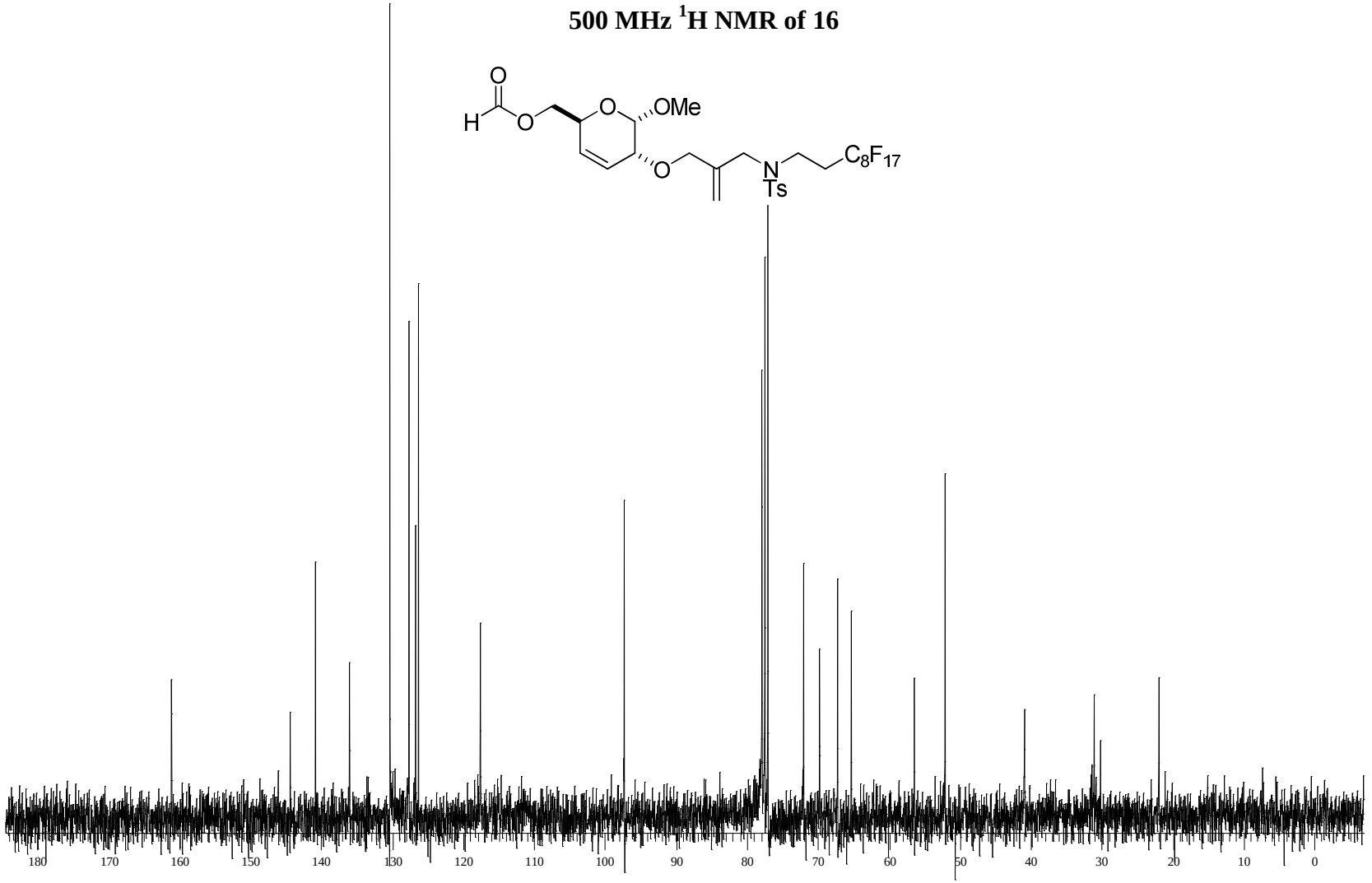
75 MHz ^{13}C NMR of 15



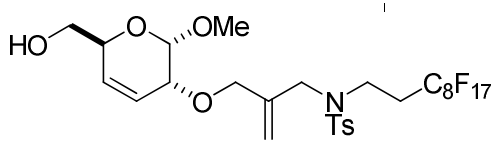
500 MHz ^{1}H NMR of 16

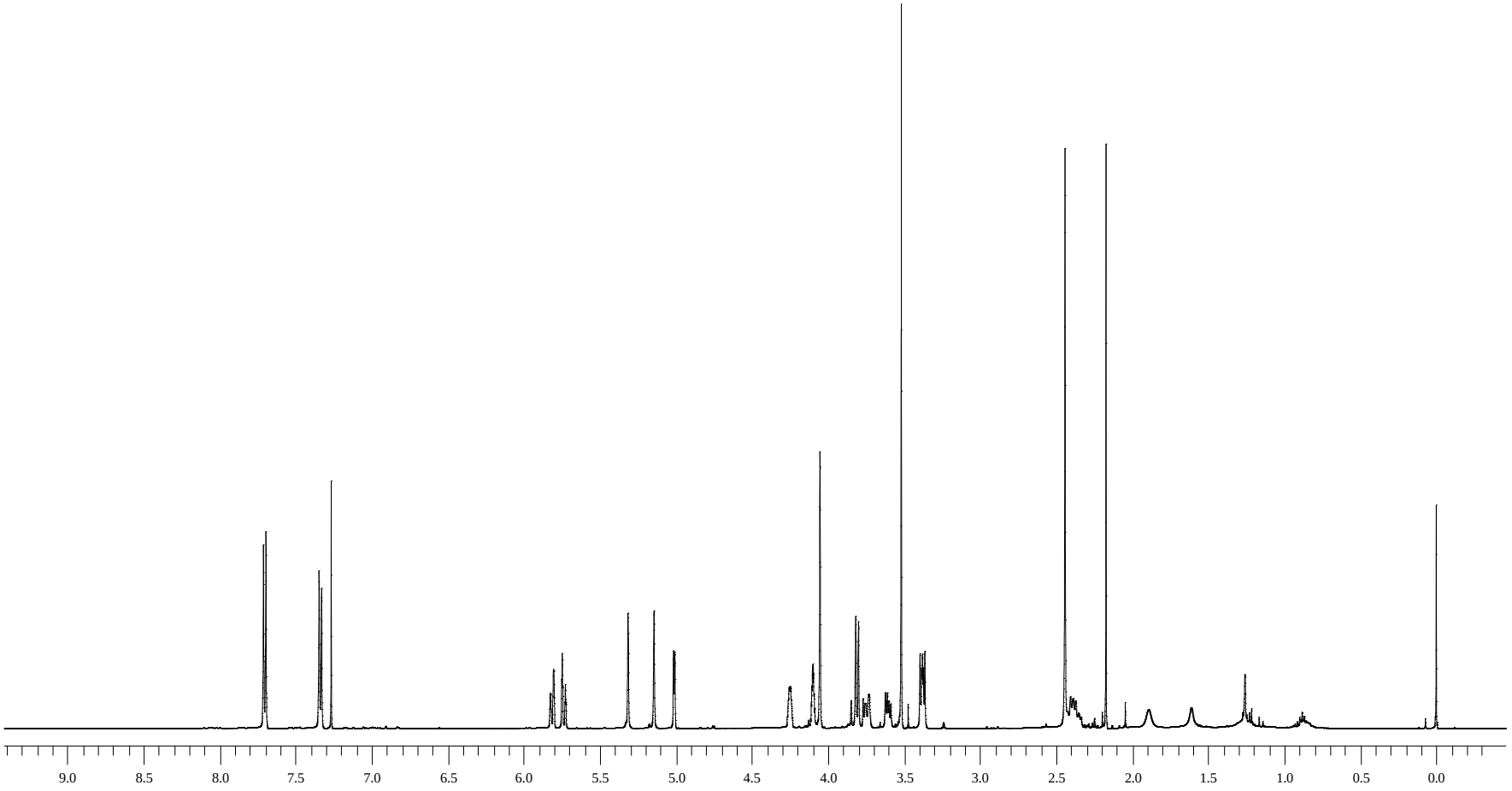


500 MHz ^{1}H NMR of 16

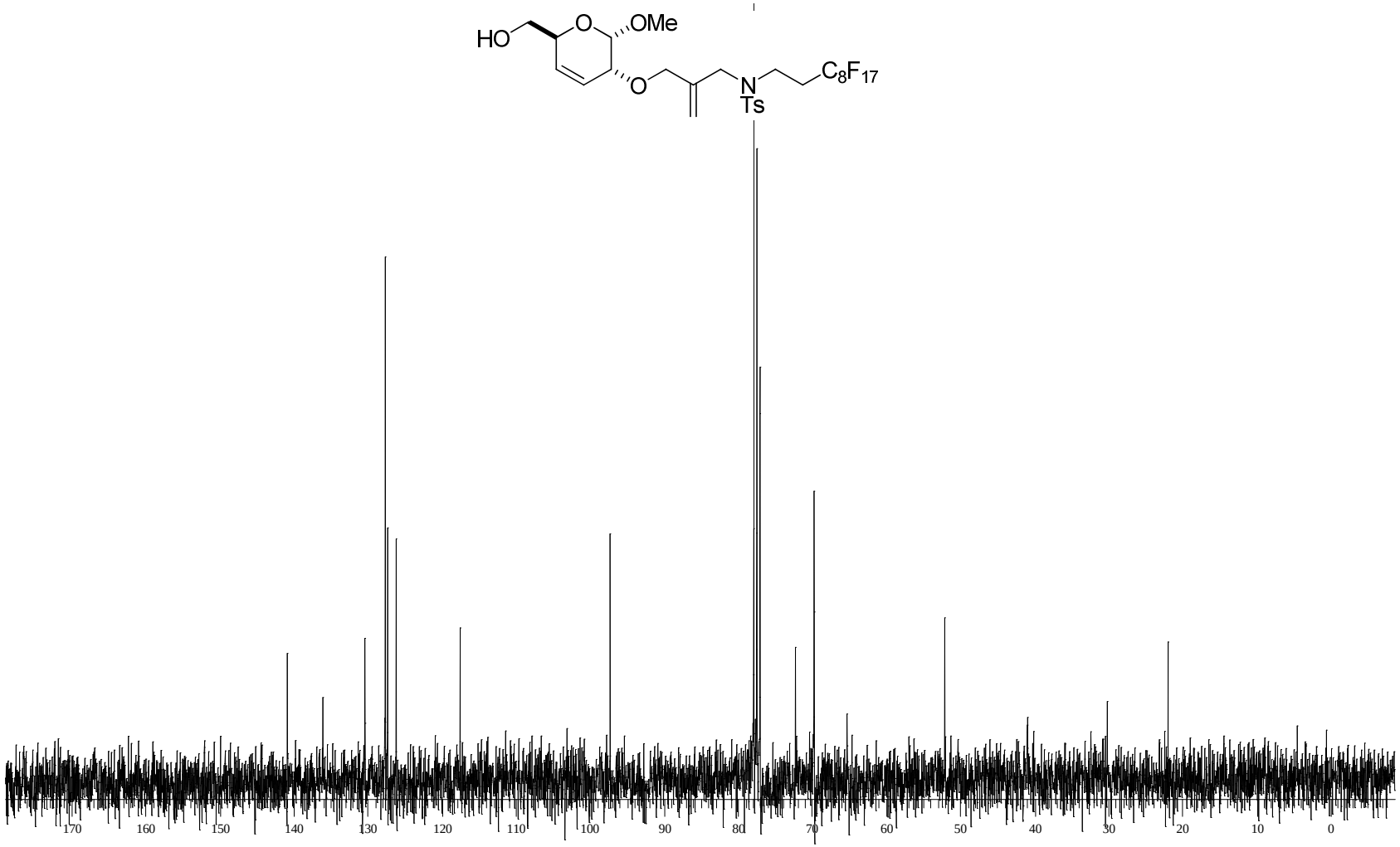


500 MHz ^{1}H NMR of 1

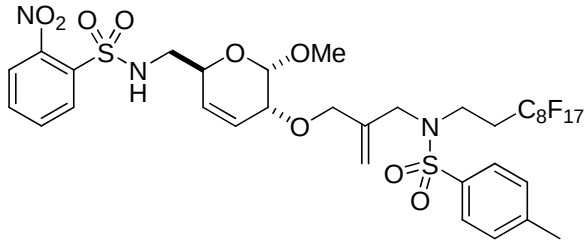


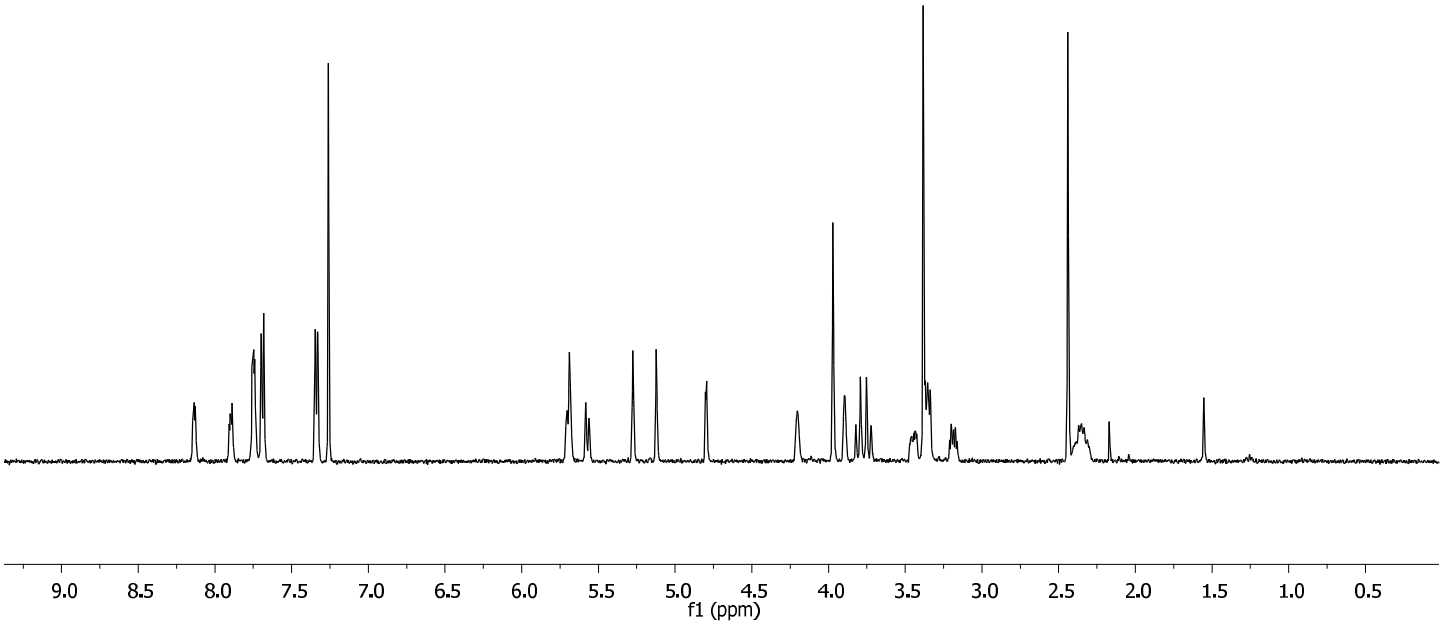


500 MHz ^{1}H NMR of 1



500 MHz ^{1}H NMR of 18





75 MHz ^{13}C NMR of 18