Supporting Information

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(A) Experimental section

General methods

All starting materials were taken at Enamine. Column chromatography was performed using Kieselgel Merck 60 (230-400 mesh) as the stationary phase. Reverse phase column chromatography was performed using C_{18}-modified silica gel as a stationary phase, column: SunFire Waters, 5 μm, 19 mm × 100 mm. ^{1}H-, ^{19}F-, ^{13}C-NMR spectra were recorded on at 500 or 400 MHz, 376 MHz and 125 or 101 MHz respectively. Chemical shifts are reported in ppm downfield from TMS (^{1}H, ^{13}C) or $CFCl_3$ (^{19}F) as internal standards. Mass spectra were recorded on an LC-MS instrument with chemical ionization (CI). LC-MS data were acquired on Agilent 1200 HPLC system equipped with DAD/ELSD/LCMS-6120 diodematrix and mass-selective detector, column: Poroshell 120 SBC18, 4.6 mm × 30 mm. Eluent, A, acetonitrile–water with 0.1% of FA (99: 1); B, water with 0.1% of FA.

General procedure for AQ-amide preparation

Appropriate Boc/Cbz/TFA – amino acid (3 mmol, 1 equiv), HOBT (3 mmol, 450 mg, 1 equiv) and quinolin-8-amine (3.6 mmol, 520 mg, 1.2 equiv) were dissolved in dry DCM. EDC*HCl (3 mmol, 576 mg, 1 equiv) was added to the solution and the reaction mixture was stirred for 12 h. After that, a saturated aqueous solution of $CuSO_4$ was added (to get rid of the excess of AQ), the organic layer was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. A crude residue was purified by column chromatography. (Typical eluents: DCM/EtOAc/Hex = 2/2/5, DCM/EtOAc/Hex = 1/1/4).

General procedure for CH-arylation

The corresponding Boc/Cbz/TFA – amide (0.2 mmol, 1 equiv), $(BnO)_2PO_2H$ (0.04 mmol, 11 mg, 0.2 equiv), dry AgOAc (0.4 mmol, 67 mg, 2 equiv) and ArI/HetI (0.6 mmol, 3 equiv) were mixed in toluene (0.2 mL) to obtain a 1 M solution. The reaction mixture was purged with Argon and $Pd(OAc)_2$ (0.02 mmol, 0.1 equiv) was added. The reaction vessel was placed into the oil bath, heated to 120 °C and stirred for 24 h. Then, the mixture was cooled to rt, diluted with DCM and filtered through the celite plug. The filtrate was concentrated under reduced pressure and the crude material was purified by column chromatography or preparative HPLC.

(B) Data description

(2*S*,4*S*)-benzyl 4-cyclohexyl-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Cbz – 1)

White solid, mp 97 – 98 °C, yield 80%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.53, 10.37 (rotameric singlets, 1H), 8.73 (m, 2H), 8.14 (d, *J* = 7.5 Hz, 1H), 7.60 – 7.33 (m, 6H), 7.25 – 6.78 (m, 2H), 5.44 – 5.03 (m, 3H), 4.80 – 4.54 (m, 1H), 4.02 – 3.73 (m, 1H), 3.40 – 3.00 (m, 1H), 2.45 (m, 1H), 2.17 (m, 1H), 1.97 – 1.47 (m, 6H), 1.44 – 1.05 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.4, 170.1, 155.2, 154.4, 147.9, 138.1, 136.2, 135.7, 133.7, 133.4, 128.0, 127.5, 127.4, 127.2, 126.8, 121.4, 121.0, 116.2, 115.9, 66.7, 61.9, 59.9, 52.9, 51.2, 50.8, 43.2, 42.2, 41.3, 34.8, 33.5, 31.4, 30.9, 25.8, 25.5. LC/MS: 458(M + H^+). Anal. calcd for $C_{28}H_{31}N_3O_3$: C, 73.50; H, 6.83; N, 9.18. Found: C, 73.37; H, 6.60; N, 9.45. $[\alpha]_D^{21}$ – 52° (c 1,0, CH_3OH).

(2*S*,3*S*,4*R*)-benzyl 4-cyclohexyl-3-phenyl-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Cbz – 1a)

Yellow oil, yield 80%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.38, 9.31 (rotameric singlets, 1H), 8.56-8.46 (m, 2H), 8.13-8.03 (m, 1H), 7.50-7.31 (m, 5H), 7.25-7.07 (m, 3H), 7.06-6.94 (m, 3H), 6.95-6.75 (m, 2H), 5.26-5.02 (m, 2H), 4.76-4.65 (m, 1H), 4.20-4.05 (m, 1H), 3.60-3.51 (m, 1H), 3.49-3.35 (m, 1H), 3.15-2.94 (m, 1H), 1.75-1.41 (m, 6H), 1.1-0.83 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.8, 154.9, 154.4, 147.8, 138.2, 135.9, 133.7, 128.3, 128.0, 127.5, 127.1, 68.0, 67.8, 67.1, 51.6, 50.8, 49.6, 45.1, 44.4, 38.8, 32.4, 29.7, 28.2, 26.5, 26.3, 26.2. LCMS (m/z): 534 (M + H^+). Anal. calcd for $C_{34}H_{35}N_3O_3$: C, 76.52; H, 6.61; N, 7.87. Found: C, 76.30; H, 6.85; N, 7.65. $[\alpha]_D^{21}$ – 41° (c 1,0, CH_3OH).

(2*S*,4*S*)-4-cyclohexyl-*N*-(quinolin-8-yl)-1-(2,2,2-trifluoroacetyl)pyrrolidine-2-carboxamide (TFA – 1)

Beige oil, yield 50%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.25, 10.10 (rotameric singlets, 1H), 8.73 (br s, 1H), 8.66 (br.s, 1H), 8.06 (d, *J* = 7.9 Hz, 1H), 7.55 – 7.32 (m, 3H), 4.95 – 4.83 (m, 1H), 4.20 – 4.04 (m, 1H), 3.40 – 3.31 (m, 1H), 2.47 – 2.30 (m, 2H), 1.88 – 1.75 (m, 1H), 1.73 –1.53 (m, 5H), 1.31 – 0.77 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.8, 168.3, 156.3 (q, *J* = 37.4 Hz), 148.6, 148.8, 138.4, 136.3, 133.8, 133.4, 127.8, 127.0, 122.3, 122.0, 121.8, 121.7, 117.5, 116.6, 115.2, 63.0, 62.5, 53.5, 52.7, 51.4, 44.1, 41.8, 41.5, 40.5, 36.6, 32.9, 31.8, 31.2, 26.1, 25.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -71.7, -72.9. (rotameric peaks) LCMS (m/z): 420 (M + H^+). Anal. calcd for $C_{22}H_{24}F_3N_3O_2$: C, 63.00; H, 5.77; N, 10.02. Found: C, 63.25; H, 5.98; N, 9.90. $[\alpha]_D^{21}$ – 61° (c 1,0, CH_3OH).

(2*S*,3*S*,4*R*)-4-cyclohexyl-3-phenyl-*N*-(quinolin-8-yl)-1-(2,2,2-trifluoroacetyl)pyrrolidine-2-carboxamide (TFA – 1a)

Light yellow oil, yield 76%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.24, 9.04 (diastereomeric singlets, 1H), 8.60 – 8.41 (m, 2H), 8.14 – 7.96 (m, 1H), 7.55 – 7.18 (m, 5H), 7.15 – 6.90 (m, 2H), 6.87 – 6.78 (m, 1H), 4.96 – 4.91 (m, 1H), 4.40 – 4.28 (m, 1H), 3.73-3.5 (m, 2H), 3.27-2.98 (m, 1H), 1.83 – 1.25 (m, 6H), 1.97-1.08 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.1, 166.7, 156.1, 155.7, 147.7, 138.0, 135.9, 135.1, 133.5, 128.5, 128.3, 127.5, 126.9, 121.9, 121.6, 121.4, 121.3, 117.7, 116.2, 68.5, 67.6, 52.5, 51.2, 49.6, 45.3, 41.9, 38.9, 38.7, 32.3, 28.5, 26.4, 26.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -71.6, -72.8 (rotameric peaks) LCMS (m/z): 496 ($M + H^+$). Anal. calcd for $C_{28}H_{28}F_3N_3O_2$: C, 67.87; H, 5.70; N, 8.48. Found: C, 67.65; H, 5.95; N, 8.70. $[\alpha]_D^{21} - 85^{\circ}$ (c 1,5, CH_3OH, 21°C).

Benzyl 4-cyclopentyl-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate(Cbz – 2)

Cream oil, yield 78%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.54, 10.37, 10.32, 10.18 (rotameric singlets, diastereomeric mixture, 1H), 8.73 (m, 2H), 8.14 (d, *J* = 6.8 Hz, 1H), 7.59 – 7.22 (m, 5H), 7.24 – 6.64 (m, 3H), 5.36 – 4.95 (m, 2H), 4.79 – 4.39 (m, 1H), 4.15 – 3.84 (m, 1H), 3.50 – 3.10 (m, 1H), 2.69 – 2.12 (m, 1H), 2.04 – 1.81 (m, 2H), 1.83 – 1.48 (m, 7H), 1.32 – 1.10 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.1, 154.9, 148.3, 138.6, 136.2, 134.3, 133.9, 128.5, 127.9, 127.7, 127.2, 121.7, 121.5, 67.3, 62.8, 62.3, 52.8, 52.3, 51.9, 44.8, 44.2, 43.9, 43.5, 42.5, 37.5, 36.5, 352, 31.6, 31.4, 31.3, 31.2, 25.3, 25.1. LCMS (m/z): 444 ($M + H^+$). Anal. calcd for $C_{27}H_{29}N_3O_3$: C, 73.11; H, 6.59; N, 9.47. Found: C, 73.00; H, 6.73; N, 9.19.

(2*S*,3*S*,4*R*)-benzyl 4-cyclopentyl-3-phenyl-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Cbz – 2a)

Beige oil, yield 40%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.42, 9.39 (rotameric singlets, 1H), 8.56 (m, 2H), 8.14 – 7.97 (m, 1H), 7.48 – 7.30 (m, 5H), 7.28 – 7.19 (m, 2H), 7.19 – 7.09 (m, 1H), 7.07 – 6.75 (m, 5H), 5.34 – 4.97 (m, 2H), 4.77 – 4.62 (m, 1H), 4.17 (m, 1H), 3.43 (m, 1H), 3.07 (m, 1H), 1.92 – 1.60 (m, 3H), 1.59 – 1.39 (s, 3H), 1.37 – 1.19 (m, 3H), 0.90 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.9, 154.4, 149.2, 138.2, 136.3, 135.9, 133.8, 128.6, 128.5, 128.2, 128.0, 127.5, 127.2, 121.4, 116.3, 68.2, 67.9, 67.1, 54.4, 53.7, 50.7, 50.3, 44.7, 44.1, 42.9, 31.7, 29.3, 25.3, 24.5. LCMS (m/z): 520 ($M + H^+$). Anal. calcd for $C_{33}H_{33}N_3O_3$: C, 76.28; H, 6.40; N, 8.09;. Found: C, 76.36; H, 6.15; N, 8.20.

(2*S*,3*aS*,6*aS*)-benzyl 2-(quinolin-8-ylcarbamoyl)hexahydrocyclopenta[b]pyrrole-1(2*H*)-carboxylate Cbz – 3)

Light yellow oil, yield 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.65 – 10.43 (rotameric singlets, 1H), 8.79 – 8.63 (m, 2H), 8.11 (d, *J* = 8.1 Hz, 1H), 7.63 – 7.22 (m, 5H), 7.20 – 6.76 (m, 3H), 5.47 – 4.96 (m, 2H), 4.76 – 4.52 (m, 1H), 4.49 –4.37 (m, 1H), 2.80 – 2.64 (m, 1H), 2.60 – 2.37 (m, 1H), 2.31 – 2.01 (m, 3H), 1.88 – 1.63 (m, 2H), 1.58 – 1.40 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.2, 155.1, 148.3, 140.8, 138.6, 136.2, 134.1, 128.5, 127.9, 127.6, 127.1, 126.5, 125.9, 121.8, 121.6, 117.4, 116.3, 110.9, 67.3, 65.8, 65.1, 64.0, 60.9, 60.3, 43.1, 42.2, 35.8, 34.1, 32.0, 24.9. LCMS

(m/z): 416 (M + H^+). Anal. calcd for $C_{25}H_{25}N_3O_3$: C, 72.27; H, 6.07; N, 10.11. Found: C, 72.46; H, 6.20; N, 9.97. $[\alpha]_D^{21}$ – 32° (c 1,0, CH_3OH, 21°C).

(2*S*,3*S*,3*aS*,6*aS*)-benzyl 3-phenyl-2-(quinolin-8-ylcarbamoyl)hexahydrocyclopenta[b]pyrrole-1(2*H*)-carboxylate (Cbz – 3a)

Yellow oil, yield 45%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.11 (s, 1H), 8.71 (d, *J* = 6.5 Hz, 1H), 8.62 (d, *J* = 3.5 Hz, 1H), 8.18 - 8.04 (m, 1H), 7.59 - 7.28 (m, 7H), 7.26 - 7.05 (m, 5H), 7.04 - 6.80 (m, 2H), 5.33 - 5.07 (m, 2H), 5.06 - 4.84 (m, 1H), 4.52 (br s, 1H), 3.02 - 2.85 (m, 1H), 2.55 - 2.23 (m, 3H), 2.17 - 2.03 (m, 1H), 1.75 - 1.62 (m, 1H), 1.61 - 1.42 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.1, 147.9, 138.5, 136.6, 136.0, 134.1, 129.5, 128.1, 127.8, 127.6, 127.2, 121.5, 116.4, 67.1, 65.3, 64.8, 49.9, 41.0, 34.9, 34.1, 28.7, 27.2. LCMS (m/z): 492 (M + H^+). Anal. calcd for $C_{31}H_{29}N_3O_3$: C, 75.74; H, 5.95; N, 8.55;. Found: C, 75.50; H, 6.21; N, 8.30. $[\alpha]_D^{21}$ +28° (c 0,5, CH_3OH, 21°C).

(2S,3aS,6aS)-*N*-(quinolin-8-yl)-1-(2,2,2-trifluoroacetyl)octahydrocyclopenta[b]pyrrole-2-carboxamide (TFA – 3)

Colorless oil, yield 70%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.25, 10.19 (rotameric singlets, 1H), 8.66 (s, 2H), 8.01 (d, *J* = 8.3 Hz, 1H), 7.51 – 7.27 (m, 3H), 4.92 – 4.81 (m, 1H), 4.70 – 4.43 (m, 1H), 2.92 – 2.53 (m, 1H), 2.52 – 2.31 (m, 1H), 2.19 – 1.96 (m, 3H), 1.89 – 1.57 (m, 2H), 1.61 – 1.44 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.4, 168.6, 156.5 (q, *J* = 37.3 Hz), 148.5, 148.3, 138.4, 136.3, 136.2, 133.9, 133.5, 127.8, 127.0, 122.2, 122.0, 121.7, 117.5, 116.5, 67.4, 64.9, 62.9, 53.5, 44.3, 41.3, 36.1, 33.4, 33.1, 32.1, 30.6, 26.2, 24.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -71.3. LCMS (m/z): 378 (M + H^+). Anal. calcd for $C_{19}H_{18}F_3N_3O_2$: C, 60.47; H, 4.81; N, 11.14. Found: C, 60.75; H, 5.03; N, 11.00. $[\alpha]_D^{21}$ -29° (c 1,0, CH_3OH, 21°C).

(2S,3S,3aS,6aS)-3-phenyl-*N*-(quinolin-8-yl)-1-(2,2,2-trifluoroacetyl)octahydrocyclopenta[b]pyrrole-2-carboxamide (TFA – 3a)

Colorless oil, yield 82%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.73, 7.37 (rotameric singlets,1H), 8.69 – 8.37 (m, 2H), 8.07 (m, 1H), 7.48 (m, 2H), 7.36 (m, 3H), 7.13 – 6.97 (m, 3H), 5.30 – 5.04 (m, 1H), 4.86 – 4.69 (m, 1H), 4.06-3.87 (m, 1H), 3.2 – 2.86 (m, 1H), 2.75 – 2.14 (m, 3H), 2.07 – 1.95 (m, 1H), 1.74 – 1.63 (m, 1H), 1.53 – 1.40 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.7, 167.2, 156.8, 156.5, 155.9, 147.9, 147.7, 138.3, 136.0, 135.5, 135.1, 133.8, 133.5, 129.7, 129.4, 128.4, 127.7, 127.3, 127.1, 121.9, 121.8, 121.5, 116.6, 68.3, 67.3, 66.9, 65.2, 51.3, 50.7, 48.5, 47.6, 35.4, 33.5, 29.7, 29.1, 28.9, 27.8, 27.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -70.8, -71.8 (rotameric peaks) LCMS (m/z): 454 (M + H^+). Anal. calcd for $C_{25}H_{22}F_3N_3O_2$: C, 66.22; H, 4.89; N, 9.27. Found: C, 66.50; H, 5.05; N, 9.39. $[\alpha]_D^{21}$ +14° (c 0,2, CH_3OH, DMF, 21°C).

(2S,3R,3aS,6aS)-*N*-(quinolin-8-yl)-3-(thiophen-2-yl)-1-(2,2,2-trifluoroacetyl)octahydrocyclopenta[b]pyrrole-2-carboxamide (TFA – 4a)

Brown oil, yield 91%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.68, 9.41 (rotameric singlets, 1H), 8.58 (m, 2H), 8.03 (t, *J* = 7.9 Hz, 1H), 7.42 (d, *J* = 6.8 Hz, 2H), 7.40 – 7.24 (m, 1H), 7.06 – 6.99 (m, 1H), 6.97 – 6.88 (m, 1H), 6.80 – 6.68 (m, 1H), (5.14 (d, *J* = 9.3 Hz), 5.00 (d, *J* = 8.9 Hz, rotameric peaks, 1H), (4.77 (q, *J* = 7.2 Hz), 4.70 (q, *J* = 7.9 Hz, rotameric peaks, 1H), (4.37 (t, *J* = 8.2 Hz), 4.24 (t, *J* = 8.6, rotameric peaks, 1H), 3.19 – 2.82 (m, 1H), 2.63 – 2.07 (m, 3H), 1.87 – 1.28 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.2, 166.8, 156.2 (q, *J* = 63.5, 37.3 Hz), 147.9, 138.3, 138.2, 137.1, 136.9, 136.1, 135.9, 133.8, 133.6, 128.0, 127.7, 127.6, 127.2, 127.1, 126.8, 125.3, 125.1, 121.9, 121.9, 121.6, 121.5, 116.5, 116.3, 68.8, 67.2, 67.0, 64.9, 60.4, 50.7, 47.4, 46.1, 43.6, 35.4, 33.6, 29.3, 27.7, 27.5, 21.0, 14.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -70.9, -71.8 (rotameric peaks) LCMS (m/z): 460 ($M + H^+$). Anal. calcd $C_{23}H_{20}F_3N_3O_2S$: C, 60.12; H, 4.39; N, 9.15. Found: C, 60.30; H, 4.05; N, 9.41. $[\alpha]_D^{21}$ +37° (c 1,0, CH_3OH, 21° C).

Benzyl 5-(quinolin-8-ylcarbamoyl)tetrahydro-2*H*-furo[3,2-b]pyrrole-4(5*H*)-carboxylate (Cbz – 5)

Colorless oil, yield 81%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.53 (s, 1H), 9.00 – 8.54 (m, 2H), 8.13 (d, *J* = 6.8 Hz, 1H), 7.64 – 7.27 (m, 5H), 7.23 – 6.81 (m, 3H), 5.58 – 5.05 (m, 2H), 4.87 – 4.66 (m, 1H), 4.57 (br. s, 1H), 4.44 (br s, 1H), 4.21 – 3.91 (m, 1H), 3.83 – 3.60 (m, 1H), 2.94 – 2.55 (m, 2H), 2.53 – 2.23 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.4, 155.1, 148.2, 138.7, 136.2, 134.1, 128.6, 128.1, 127.7, 127.4, 121.6, 116.2, 83.3, 82.4, 68.2, 67.4, 65.5, 64.8, 62.6, 35.6, 34.6, 33.8. LCMS (m/z): 418 ($M + H^+$). Anal. calcd $C_{24}H_{23}N_3O_4$: C, 69.05; H, 5.55; N, 10.07. Found: C, 69.30; H, 5.26; N, 9.82.

Benzyl 6-phenyl-5-(quinolin-8-ylcarbamoyl)tetrahydro-2*H*-furo[3,2-b]pyrrole-4(5*H*)-carboxylate (Cbz – 5a)

Yellow oil, yield 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.23, 10.00 (rotameric singlets, 1H), 8.64 (m, 2H), 8.17 – 8.03 (m, 1H) 7.65 – 7.28 (m, 7H), 7.21 – 7.01 (m, 4H), 6.99 – 6.78 (m, 2H), 5.43 – 5.03 (m, 2H), 5.07 – 4.80 (m, 1H), 4.69 – 4.43 (m, 3H), 3.91 – 3.71 (m, 2H), 3.07 – 2.72 (m, 1H), 2.65 – 2.33 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 154.9, 147.8, 138.55, 136.1, 134.3, 130.3, 128.1, 127.6, 127.4, 121.3, 116.1, 84.9, 69.0, 67.2, 65.5, 64.9, 51.2, 33.2. LCMS (m/z): 494 ($M + H^+$). Anal. calcd $C_{30}H_{27}N_3O_4$: C, 73.01; H, 5.51; N, 8.51. Found: C, 73.30; H, 5.75; N, 8.79.

5-Methyl-*N*-(quinolin-8-yl)-1-(2,2,2-trifluoroacetyl)pyrrolidine-2-carboxamide (TFA – 6)

Yellow oil, yield 61%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.38, 10.32 (rotameric singlets, 1H), 8.87 – 8.67 (m, 2H), 8.16 (t, *J* = 9.0 Hz, 1H), 7.62 – 7.38 (m, 3H), 4.93 – 4.75 (m, 1H), 4.59 – 4.24 (m, 1H), 2.59 – 2.36 (m, 1H), 2.38 – 1.81 (m, 3H), 1.70 (d, *J* = 6.1 H), 1.48 (d, *J* = 6.1 Hz) (rotameric peaks, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.9, 168.5, 156.8 (q, *J* = 37.4 Hz), 148.5, 148.4, 138.6, 136.4, 136.3, 134.0, 133.6, 127.9, 127.2, 122.3, 122.0, 121.8, 121.7, 117.5, 116.7, 116.5, 63.3, 57.9, 55.8, 32.9, 31.2, 30.7, 26.3, 20.8, 19.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -71.3, -71.8.

LCMS (m/z): 352 (M + H^+). Anal. calcd $C_{17}H_{16}F_3N_3O_2$: C, 58.12; H, 4.59; N, 11.96. Found: C, 58.39; H, 4.83; N, 11.82.

5-Methyl-3-phenyl-*N*-(quinolin-8-yl)-1-(2,2,2-trifluoroacetyl)pyrrolidine-2-carboxamide (TFA – 6a)

Yellow oil, yield 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.59, 9.25 (rotameric singlets, 1H), 8.72 – 8.47 (m, 2H), 8.08 (d, *J* = 8.1 Hz, 1H), 7.56 – 7.20 (m, 5H), 7.06 (t, *J* = 7.4 Hz, 2H), 6.89 (t, *J* = 7.2 Hz, 1H), 4.94 (d, *J* = 7.6 Hz, 1H), 4.40 (m, 1H), 3.79 (m, 1H), 2.60 – 2.36 (m, 2H), 1.81 (d, *J* = 5.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.6, 147.9, 138.1, 136.0, 135.0, 133.4, 128.6, 127.9, 127.7, 127.0, 121.9, 121.5, 116.3, 67.5, 57.1, 48.5, 34.7, 18.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -70.5, -71.8. LCMS (m/z): 428 (M + H^+). Anal. calcd $C_{23}H_{20}F_3N_3O_2$: C, 64.63; H, 4.72; N, 9.83. Found: C, 64.40; H, 5.00; N, 10.05.

Benzyl 2-cyclopropyl-5-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Cbz – 7)

Yellow oil, yield 87%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.19, 9.95 (rotameric singlets, 1H), 8.80 – 8.62 (m, 2H), 8.14 (d, *J* = 8.0 Hz, 1H), 7.60 – 7.18 (m, 5H), 7.10 – 6.98 (m, 1H), 6.82 – 6.77 (m, 1H), 6.75 – 6.68 (m, 1H), 5.31 – 4.81 (m, 2H), 4.62 (m, 1H), 3.94 – 3.63 (m, 1H), 2.61 – 2.11 (m, 3H), 1.85 (s, 1H), 1.11 – 0.11 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.3, 170.9, 155.6, 154.7, 148.2, 138.4, 136.2, 134.0, 128.3, 127.8, 127.7, 127.3, 121.6, 121.5, 116.4, 67.1, 62.9, 62.4, 30.4, 29.7, 29.1, 28.6, 15.9, 15.5, 5.8, 5.2, 1.7. LCMS (m/z): 416 (M + H^+). Anal. calcd $C_{25}H_{25}N_3O_3$: C, 72.27; H, 6.07; N, 10.11. Found: C, 72.50; H, 5.80; N, 10.40.

Benzyl 5-cyclopropyl-3-phenyl-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Cbz – 7a)

Brown oil, yield 55%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.41, 9.27 (rotameric singlets, 1H), 8.66 – 8.36 (m, 2H), 8.14 – 7.92 (m, 2H), 7.51 – 7.21 (m, 6H), 7.11 – 6.97 (m, 3H), 6.95 – 6.65 (m, 3H), 5.32 – 5.05 (m, 1H), 4.98 – 4,90 (m, 1H), 4.83 – 4.68 (m, 1H), 4.13 – 3.77 (m, 2H), 3.05 – 2,85 (m, 1H), 2.10 – 1,98 (m, 1H), 1.19 – 1.00 (m, 1H), 0.99 – 0.81 (m, 1H), 0.77 – 0.63 (m, 1H), 0.62 – 0.20 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.7, 155.7, 154.9, 147.7, 136.4, 136.1, 128.3, 127.9, 127.8, 127.3, 127.2, 121.3, 116.2, 67.8, 67.5, 67.1, 62.5, 61.9, 46.6, 45.6, 34.4, 33.3, 16.6, 16.3, 5.9, 5.2, 2.0. Anal. Calcd $C_{31}H_{29}N_3O_3$: HRMS (m/z): Calculated [M+H^+] = 492.2282; Found [M+H^+] = 492.2250 (error = 6.50 ppm). Calculated [M+Na^+] = 514.2101. Found [M+Na^+] = 514.2070 (Error = 6.03 ppm).

Benzyl 2-cyclobutyl-5-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Cbz – 8)

Beige oil, yield 56%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.54 (s), 10.14 (s), 9.91 (rotameric singlets, diastereomeric mixture, 1H), 8.84 – 8.60 (m, 2H), 8.13 (d, *J* = 7.6 Hz, 1H), 7.63 – 7.21 (m, 5H), 7.22 – 6.96 (m, 1H), 6.98 – 6.59 (m, 2H), 5.34 – 4.82 (m, 2H), 4.72 – 4.44 (m, 1H), 4.37 – 4.12 (m, 1H), 2.80 – 2.50 (m, 1H), 2.50 – 2.05 (m, 4H), 2.06 – 1.61 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ

171.4, 155.0, 154.8, 148.3, 148.1, 138.7, 138.4, 136.1, 134.2, 134.1, 128.4, 128.2, 127.9, 127.7, 127.3, 126.9, 121.6, 116.4, 67.1, 63.8, 62.8, 62.4, 40.4, 29.7, 28.6, 27.6, 27.4, 26.1, 25.5, 18.2, 18.0. LCMS (m/z): 430 (M + H^+). Anal. calcd $C_{26}H_{27}N_3O_2$: C, 72.71; H, 6.34; N, 9.78. Found: C, 72.49; H, 6.60; N, 9.52.

Benzyl 5-cyclobutyl-3-phenyl-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Cbz – 8a)

Beige oil, yield 53%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.37, 9.22 (s, 1H), 8.62 – 8.53 (m, 1H), 8.49 – 8.34 (m, 1H), 8.10 – 7.98 (m, 1H), 7.45 – 7.18 (m, 7H), 7.08 – 6.93 (m, 3H), 6.93 – 6.70 (m, 2H), 6.71 (t, *J* = 7.5 Hz, 1H), 5.23 – 4.83 (m, 2H), (4.70 (d, *J* = 8.4 Hz), 4.63 (d, *J* = 8.4 Hz, 1H), (4.44 (t, *J* = 8.1 Hz), 4.32 (t, *J* = 8.1 Hz, 1H), 3.93 – 3.64 (m, 1H), 2.95 – 2.52 (m, 2H), 2.31 – 2.04 (m, 1H), 1.99 – 1.58 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.8, 168.5, 155.78, 155.2, 147.8, 138.1, 136.4, 135.9, 133.8, 128.3, 127.9, 127.8, 127.6, 127.3, 127.2, 127.1, 121.3, 116.1, 67.9, 67.6, 67.2, 62.4, 61.9, 50.8, 46.5, 45.4, 41.3, 41.1, 31.1, 30.3, 27.8, 27.2, 25.8, 25.7, 18.2, 18.0. LCMS (m/z): 506 (M + H^+). Anal. calcd $C_{32}H_{31}N_3O_3$: C, 76.02; H, 6.18; N, 8.31. Found: C, 76.21; H, 6.40; N, 8.50.

Benzyl 2-(4-chlorophenyl)-5-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Cbz -9)

Yellow oil, yield 88%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.35, 10.12 (rotameric singltes, 1H), 8.81 – 8.77 (m, 1H), 8.75 – 8.69 (m, 1H), 8.18 (t, *J* = 6.4 Hz, 1H), 7.58 – 7.52 (m, 2H), 7.48 – 7.43 (m, 1H), 7.33 – 7.26 (m, 4H), 7.23 – 7.12 (m, 1H), 7.09 (t, *J* = 8.3 Hz, 2H), 6.92 – 6.81 (m, 1H), 6.76 (t, *J* = 7.4 Hz, 1H), 5.40 (d, *J* = 8.3), 5.29 (d, *J* = 8.3 Hz, 1H), 5.23 – 5.05 (m, 1H), 5.00 – 4.86 (m, 1H), 2.76 – 2.62 (m, 1H), 2.44 – 2.29 (m, 1H), 2.30 – 2.16 (m, 1H), 1.93 – 1.79 (m, 2H). ^{13}C NMR (126 MHz, , $CDCl_3$) δ 170.5, 148.3, 142.4, 140.9, 138.6, 136.3, 128.6, 128.5, 128.2, 127.9, 127.8, 127.6, 127.5, 127.3, 127.0, 126.8, 121.9, 121.6, 116.8, 116.5, 67.5, 67.2, 65.3, 62.8, 62.7, 61.7, 61.4, 33.8, 32.7, 28.7, 27.4. LCMS (m/z): 486 (M + H^+).

(2*S*,3*S*,5*S*)-Benzyl 5-(4-chlorophenyl)-3-phenyl-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Cbz – 9a)

White solid, mp 87-88 ^{o}C; yield 65%.^{1}H NMR (400 MHz, $CDCl_3$) δ 9.49, 9.37 (rotameric singlets, 1H), 8.69 – 8.43 (m, 2H), 8.13 8.03 – (m, 1H), 7.54 – 7.12 (m, 11H), 7.12 – 6.94 (m, 3H), 6.96 – 6.79 (m, 2H), 6.76 (t, *J* = 7.5 Hz, 1H), 5.60 – 5.47 (m, 1H), 5.22 – 5.09 (m, 1H), 5.02 – 4.88 (m, 2H), 3.98 – 3.83 (m, 1H), 3.4 – 3.22 (m, 1H), 2.08 – 2.00 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.7, 154.4, 147.3, 142.1, 141.2, 135.1, 132.2, 128.2, 128.1, 127.9, 127.7, 127.4, 127.2, 126.9, 126.4, 121.0, 120.8, 67.0, 66.6, 60.5, 60.3, 45.1, 44.0, 37.0, 36.1, 29.2. LCMS (m/z): 562 (M + H^+). Anal. calcd $C_{34}H_{28}ClN_3O_3$: C, 72.66; H, 5.02; N, 7.48. Found: C, 72.40; H, 5.30; N, 7.15.

Benzyl 2-(quinolin-8-ylcarbamoyl)-5-(thiophen-2-yl)pyrrolidine-1-carboxylate (Cbz – 10)

Beige oil, yield 69%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.31, 10.06 (rotameric singlets, 1H), 8.96 – 8.65 (m, 2H), 8.17 (t, *J* = 7.1 Hz, 1H), 7.69 – 7.15 (m, 6H), 7.13 – 6.51 (m, 5H), 5.74 – (m, 1H),

5.29 – 4.78 (m, 2H), 2.84 – 2.49 (m, 2H), 2.30 (d, *J* = 19.6 Hz, 1H), 2.19 – 1.95 (m, 1H), 1.35 – 1.24 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.7, 170.3, 148.3, 146.6, 136.25, 134.2, 133.9, 128.5, 128.2, 127.8, 127.8, 127.7, 127.4, 127.3, 126.9, 126.8, 126.7, 124.1, 123.7, 123.6, 121.8, 121.6, 116.7, 116.5, 67.4, 67.2, 65.3, 62.1, 61.9, 58.2, 57.9, 33.9, 32.6, 29.56, 28.1. LCMS (m/z): 458 (M + H^+). Anal. calcd $C_{26}H_{23}N_3O_3S$: C, 68.25; H, 5.07; N, 9.18. Found: C, 68.40; H, 5.30; N, 8.95.

Benzyl 3-phenyl-2-(quinolin-8-ylcarbamoyl)-5-(thiophen-2-yl)pyrrolidine-1-carboxylate (Cbz – 10a)

Beige oil, yield 50%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.48, 9.34 (rotameric singlets, 1H), 8.66 – 8.58 (m, 1H), 8.56 – 8.38 (m, 1H), 8.13 – 8.04 (m, 1H), 7.53 – 7.34 (m, 3H), 7.34 – 7.16 (m, 5H), 7.14 – 6.95 (m, 5H), 6.95 – 6.80 (m, 1H), 6.76 (t, *J* = 7.5 Hz, 1H), 5.86 – 5.74 (m, 1H), 5.24 – 5.13 (m, 1H), 5.08 – 4.83 (m, 2H), 4.23 – 4.12 (m, 1H), 3.40 – 3.21 (m, 1H), 2.38 – 2.10 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.4, 168.2, 154.9, 154.4, 148.2, 148.1, 147.8, 147.3, 138.2, 136.4, 135.9, 135.8, 133.7, 133.6, 128.4, 128.2, 127.9, 127.8, 127.7, 127.4, 127.2, 127.1, 126.9, 126.8, 124.1, 123.8, 123.7, 123.6, 121.5, 121.3, 116.4, 116.3, 67.5, 67.2, 67.1, 67.0, 57.7, 57.4, 46.4, 45.3, 37.7, 36.5. LCMS (m/z): 534 (M + H^+). Anal. calcd $C_{32}H_{27}N_3O_3S$: C, 72.02; H, 5.10; N, 7.87. Found: C, 72.30; H, 5.28; N, 8.00.

Benzyl 3-methyl-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Cbz – 11)

Yellow oil, yield 76%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.35 (s), 10.18 (s), 10.05 (rotameric singlets, diastereomeric mixture 1H), 8.83 – 8.63 (m, 2H), 8.10 (d, *J* = 7.9 Hz, 1H), 7.59 – 7.24 (m, 5H), 7.15 – 7.00 (m, 1H), 6.94 – 6.72 (m, 2H), 5.29 – 4.91 (m, 2H), 3.96 – 3.40 (m, 3H), 2.70 – 2.50 (m, 1H), 2.21 – 2.06 (m, 1H), 1.68 – 1.45 (m, 1H), 1.22 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7, 154.7, 148.4, 138.5, 136.2, 134.0, 128.5, 127.9, 127.6, 127.2, 121.7, 121.6, 116.4, 69.1, 67.3, 65.7, 46.7, 46.1, 39.9, 38.2, 32.3, 31.9, 31.4, 18.7, 14.8, 14.2. LCMS (m/z): 390 (M + H^+). Anal. calcd $C_{23}H_{23}N_3O_3$: C, 70.93; H, 5.95; N, 10.79. Found: C, 71.20; H, 5.78; N, 10.50.

Benzyl 3-methyl-3-phenyl-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Cbz - 11a)

Brown oil, yield 18%. ^{1}H NMR (500 MHz, $CDCl_3$) δ (9.97 (s), 9.74 (s)) (1H), (8.83 – 8.80 (m), 8.73 – 8.67 (m)) (1H), 8.41 – 8.28 (m, 1H), 8.10 (t, *J* = 9.8 Hz, 1H), 7.47 – 7.29 (m, 8H), 7.17 – 7.08 (m, 3H), 7.01 – 6.90 (m, 1H), 6.85 (t, *J* = 6.9 Hz, 1H), 5.28 – 5.01 (m, 2H), (4.68 (s), 4.55 (s)) (1H), 4.12 – 3.96 (m, 1H), 3.87 – 3.70 (m, 1H), 3.24 – 3.00 (m, 1H), 2.12 – 1.92 (m, 1H), (1.55 (s), 1.53 (s)) (3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.7, 155.0, 148.4, 138.5, 136.2, 134.0, 128.5, 127.9, 127.6, 127.2, 121.7, 116.4, 69.1, 67.3, 65.7, 60.4, 46.7, 46.1, 39.9, 38.2, 37.6, 36.8, 32.3, 31.9, 31.4, 18.7, 14.8, 14.2. LCMS (m/z): 466 (M + H^+). Anal. calcd $C_{29}H_{27}N_3O_3$: C, 74.82; H, 5.85; N, 9.03. Found: C, 74.50; H, 5.99; N, 9.30.

Benzyl 3-ethyl-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Cbz – 12)

Colorless oil, yield 88%. ^{1}H NMR (400 MHz, $CDCl_3$) δ (10.39, 10.20 (s), 10.15 (s), 10.05 (s)) (rotameric peaks, diastereomeric mixture, 1H), 8.84 – 8.62 (m, 2H), 8.12 (d, *J* = 7.6 Hz, 1H), 7.59 – 7.29 (m, 5H), 7.15 – 7.04 (m, 1H), 6.96 – 6.73 (m, 1H), 5.22 – 4.92 (m, 2H), 4.30 – 4.00 (m, 1H), 4.02 – 3.62 (m, 2H), 3.60 – 3.45 (m, 1H), 2.50 – 2.28 (m, 1H), 2.24 – 2.03 (m, 1H), 1.85 – 1.53 (m, 1H), 1.50 – 1.38 (m, 1H), 1.34 – 1.18 (m, 1H), 1.05 – 0.91 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.9, 169.6, 155.6, 154.9, 148.4, 138.54, 136.2, 134.0, 128.5, 127.9, 127.7, 127.3, 121.7, 121.6, 116.5, 116.4, 67.6, 67.3, 67.1, 65.1, 46.8, 46.7, 46.4, 46.2, 45.2, 44.5, 29.9, 29.7, 29.4, 28.9, 26.4, 23.0, 12.9, 12.2. LCMS (m/z): 404 ($M + H^+$). Anal. calcd $C_{24}H_{25}N_3O_3$: C, 71.44; H, 6.25; N, 10.41. Found: C, 71.30; H, 5.95; N, 10.16.

Benzyl 2-methyl-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Cbz – 13)

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.56, 10.33 (rotameric singlets, 1H) 8.87 – 8.48 (m, 2H), 8.11 (d, *J* = 8.2 Hz, 1H), 7.58 – 7.20 (m, 6H), 7.11 – 6.94 (m, 1H), 6.87 – 6.62 (m, 1H), 5.40 – 4.79 (m, 2H), 4.01 – 3.59 (m, 2H), 2.62 – 2.27 (m, 1H), 2.21 – 1.92 (m, 3H), (1.85 (s), 1.70 (s)) (3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 173.0, 154.4, 148.3, 136.1, 134.5, 128.4, 127.8, 127.3, 121.5, 116.3, 116.0, 67.2, 66.8, 48.7, 48.3, 41.4, 40.2, 23.1, 22.8, 22.5, 21.9. LCMS (m/z): 390 ($M + H^+$). Anal. calcd $C_{23}H_{23}N_3O_3$: C, 70.93; H, 5.95; N, 10.79. Found: C, 71.20; H, 5.67; N, 10.98.

Benzyl 2-benzhydryl-3-phenyl-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Cbz – 13c)

Brown oil, yield 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.23 (s, 1H), 8.58 (d, *J* = 7.3 Hz, 1H), 8.46 (d, *J* = 4.0 Hz, 1H), 8.00 (d, *J* = 8.2 Hz, 1H), 7.51 – 7.38 (m, 4H), 7.38 – 7.23 (m, 12H), 7.19 (t, *J* = 7.4 Hz, 2H), 7.10 (t, *J* = 7.2 Hz, 2H), 6.99 (t, *J* = 7.3 Hz, 2H), 6.88 (t, *J* = 7.4 Hz, 1H), 5.40 (s, 1H), 4.03 (m, 1H), 3.42 – 3.07 (m, 2H), 2.73 – 2.53 (m, 1H), 2.16 (m, 1H), 1.60 (s, 1H), 0.89 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.7, 156.3, 147.6, 144.1, 142.1, 140.9, 140.6, 138.8, 136.9, 135.9, 134.1, 129.3, 128.7, 128.6, 128.5, 128.4, 127.9, 127.7, 127.5, 127.0, 126.5, 121.5, 121.2, 116.5, 66.3, 45.6, 40.0, 33.6, 29.7. LCMS (m/z): 618 ($M + H^+$). Anal. calcd $C_{41}H_{35}N_3O_3$: C, 79.72; H, 5.71; N, 6.80. Found: C, 79.40; H, 5.99; N, 6.48.

Benzyl 2-ethyl-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Cbz – 14)

Beige oil, yield 60%. ^{1}H NMR (500 MHz, $CDCl_3$) δ (10.76 (s), 10.43 (s)), (1H), 8.85 – 8.64 (m, 2H), 8.14 (d, *J* = 8.1 Hz, 1H), 7.59 –7.40 (m, 3H), 7.37 – 7.22 (m, 2H), 7.18 – 6.76 (m, 2H), 5.35 – 4.93 (m, 2H), 4.00 – 3.57 (m, 2H), 2.70 – 2.16 (m, 4H), 1.98 – 1.73 (m, 2H), 1.31 – 1.20 (m, 1H), 1.00 – 0.84 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.5, 173.1, 154.7, 148.4, 140.9, 136.1, 128.6, 127.9, 127.6, 127.3, 126.9, 121.5, 116.6, 116.1, 71.6, 70.5, 67.3, 66.9, 65.3, 60.4, 49.8, 49.3, 37.3, 35.5, 27.2, 26.4, 22.8, 22.6, 14.2, 8.2, 7.8. LCMS (m/z): 404 ($M + H^+$).

(2*S*,4*R*)-4-Fluoro-*N*-(quinolin-8-yl)-1-(2,2,2-trifluoroacetyl)pyrrolidine-2-carboxamide (TFA – 15)

Colorless oil, yield 89%.^{1}H NMR (400 MHz, $CDCl_3$) δ 10.36 (s, 1H), 8.83 (m, 1H), 8.69 (d, *J* = 6.2 Hz, 1H), 8.17 (t, *J* = 7.3 Hz, 1H), 7.63 – 7.42 (m, 3H), 5.57 – 5.40 (m, 1H), 5.07 – 4.92 (m, 1H), 4.35 – 3.83 (m, 2H), 2.88 – 2.42 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.5, 148.5, 138.5, 136.3, 133.7, 127.9, 127.2, 122.4, 121.8, 116.9, 114.6, 92.7, 90.9, 61.1, 54.1, 53.9, 35.4, 35.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -72.7, -177.7. LCMS (m/z): 356 (M + H^+). Anal. calcd $C_{16}H_{13}F_4N_3O_2$: C, 54.09; H, 3.69; N, 11.83. Found: C, 54.30; H, 3.95; N, 11.46. $[\alpha]_D^{21}$ -97° (c 1,0, CH_3OH, 21°C).

(2*R*,4*R*)-Benzyl 4-fluoro-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Cbz – 16)

Yellow oil, yield 68%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.65, 10.58 (rotameric singlets, 1H), 8.82 – 8.60 (m, 2H), 8.10 (d, *J* = 8.1 Hz, 1H), 7.66 – 7.24 (m, 5H), 7.20 – 6.77 (m, 3H), 5.43 – 5.06 (m, 3H), 4.86 – 4.47 (m, 1H), 4.23 – 3.88 (m, 1H), 3.93 – 3.71 (m, 1H), 2.91 – 2.71 (m, 1H), 2.56 – 2.27 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.3, 168.4, 155.1, 154.6, 148.1, 138.2, 134.5, 133.5, 128.1, 127.6, 127.4, 126.7, 121.4, 121.0, 115.8, 92.5, 91.7, 91.1, 90.3, 67.2, 60.4, 53.7, 37.1, 35.9, 13.7. ^{19}F NMR (470 MHz, $CDCl_3$) δ -71.3, -72.4. LCMS (m/z): 394 (M + H^+). Anal. calcd $C_{22}H_{20}FN_3O_3$: C, 67.17; H, 5.12; N, 10.68. Found: C, 67.30; H, 4.95; N, 10.49. $[\alpha]_D^{21}$ -91° (c 0,2, CH_3OH, 21°C).

(*S*)-Benzyl-4,4-difluoro-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Cbz – 17)

Yellow oil, yield 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.53, 10.33 (rotameric singlets, 1H), 8.80 – 8.65 (m, 2H), 8.14 (d, *J* = 8.0 Hz, 1H), 7.53 (m, 2H), 7.48 – 7.25 (m, 4H), 7.20 – 7.03 (m, 1H), 6.99 – 6.80 (m, 1H), 5.15 – 5.05 (m, 1H), 4.92 – 4.64 (m, 2H), 4.05 – 3.87 (m,1H), 3.00 – 2.69 (m, 2H), 1.96 – 1.60 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 168.0, 148.5, 140.9, 138.5, 136.3, 133.8, 128.6, 128.0, 127.6, 127.2, 127.0, 122.3, 121.7, 116.6, 68.1, 65.3, 59.84, 54.00, 53.6, 38.5, 37.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -100.0, -101.0, -101.4, -101.7. LCMS (m/z): 412 (M + H^+). Anal. calcd $C_{22}H_{19}F_2N_3O_3$: C, 64.23; H, 4.66; N, 10.21. Found: C, 64.40; H, 4.85; N, 10.40. $[\alpha]_D^{21}$ -52° (c 1,0, CH_3OH, 21°C).

(*S*)-Benzyl 3-(quinolin-8-ylcarbamoyl)morpholine-4-carboxylate (Cbz – 18)

Beige oil, yield 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.45 (s, 1H), 8.78 (d, *J* = 4.6 Hz, 1H), 8.70 (br. s, 1H), 8.15 (d, *J* = 8.2 Hz, 1H), 7.67 – 7.08 (m, 8H), 5.42 – 5.23 (m, 2H), 4.96 – 4.60 (m, 2H), 4.33 – 3.86 (m, 2H), 3.81 – 3.47 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.4, 148.5, 138.5, 136.3, 133.9, 128.5, 128.2, 127.9, 127.3, 122.0, 121.6, 116.6, 68.0, 66.8, 66.4, 55.9, 41.6. LCMS (m/z): 392 (M + H^+). Anal. calcd $C_{22}H_{21}N_3O_4$: C, 67.51; H, 5.41; N, 10.74. Found: C, 67.28; H, 5.85; N, 11.05.

Benzyl 1-(quinolin-8-ylcarbamoyl)-2-azabicyclo[2.1.1]hexane-2-carboxylate (Cbz – 19)

Beige oil, yield 54%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.02 (s, 1H), 8.74 (m, 2H), 8.24 – 8.04 (m, 1H), 7.61 – 7.31 (m, 4H), 7.20 – 6.82 (m, 4H), 5.05 (s, 2H), 3.69 (s, 2H), 2.88 (m, 1H), 2.33 (s, 2H), 1.92 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5, 148.1, 138.4, 136.1, 134.2, 127.9, 127.6, 127.4,

121.5, 121.4, 116.5, 73.3, 67.5, 53.2, 42.7, 34.5, 29.7. LCMS (m/z): 388 ($M + H^+$). Anal. calcd $C_{23}H_{21}N_3O_3$: C, 71.30; H, 5.46; N, 10.85. Found: C, 70.98; H, 5.70; N, 11.10.

(1S,3S,5S)-Benzyl 3-(quinolin-8-ylcarbamoyl)-2-azabicyclo[3.1.0]hexane-2-carboxylate (Cbz – 20)

Beige oil, yield 78%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.43 (s, 1H), 8.82 – 8.62 (m, 2H), 8.11 (d, *J* = 8.3 Hz, 1H), 7.56 – 6.75 (m, 8H), 5.24 – 5.15 (m, 1H), 5.14 – 4.80 (m, 1H), 4.47 – 4.25 (m, 1H), 3.75 – 3.53 (m, 1H), 2.58 – 2,38 (m, 2H), 1.72 – 1.68 (m, 1H), 0.97 – 0.78 (m, 1H), 0.58 – 0.53 (br s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 148.4, 138.7, 136.2, 134.1, 128.2, 127.9, 127.7, 127.3, 67.5, 64.4, 38.0, 33.7, 16.9. LCMS (m/z): 388 ($M + H^+$). Anal. calcd $C_{23}H_{21}N_3O_3$: C, 71.30; H, 5.46; N, 10.85. Found: C, 71.65; H, 5.90; N, 11.20. $[\alpha]_D^{21}$ -100° (c 1,0, CH_3OH, 21°C).

(1*S*,3*S*,5*S*)-*N*-(Quinolin-8-yl)-2-(2,2,2-trifluoroacetyl)-2-azabicyclo[3.1.0]hexane-3-carboxamide (TFA – 20)

Cream oil, yield 45%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.33 (s, 1H), 8.79 (d, *J* = 3.5 Hz, 1H), 8.69 (br. s, 1H), 8.14 (d, *J* = 8.3 Hz, 1H), 7.51 (m, 2H), 7.47 – 7.42 (m, 1H), 4.96 – 4.73 (m, 1H), 3.78 (s, 1H), 2.76 – 2.65 (m, 1H), 2.32 (m, 1H), 2.08 – 1.92 (m, 1H), 1.18 (m, 1H), 0.75 (s, 1H).^{13}C NMR (126 MHz, $CDCl_3$) δ 167.6, 148.4, 138.5, 136.3, 133.8, 127.9, 127.2, 122.2, 121.7, 116.8, 67.4, 37.7, 31.1, 20.5, 18.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -72.6. LCMS (m/z): 350 ($M + H^+$). Anal. calcd $C_{17}H_{14}F_3N_3O_2$: C, 58.45; H, 4.04; N, 12.03. Found: C, 58.70; H, 4.25; N, 11.88. $[\alpha]_D^{21}$ -87° (c 0,3, CH_3OH, 21°C).

(*S*)-*N*-(Quinolin-8-yl)-5-(2,2,2-trifluoroacetyl)-5-azaspiro[2.4]heptane-6-carboxamide (TFA – 21)

Yellow oil, yield 53%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.39 (s, 1H), 8.93 – 8.86 (m, 1H), 8.80 – 8.66 (m, 1H), 8.33 (d, *J* = 8.2 Hz, 1H), 7.69 – 7.49 (m, 3H), 5.13 – 4.88 (m, 1H), 3.93 – 3.71 (m, 2H), 2.41 – 2.34 (m, 1H), 2.24 – 2.17 (m, 1H), 0.79 – 0.64 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.1, 146.9, 138.3, 136.4, 132.2, 127.8, 127.5, 122.2, 121.1, 119.1, 62.6, 54.6, 36.5, 20.9, 11.0, 8.8. ^{19}F NMR (470 MHz, $CDCl_3$) δ -71.3, -72.4. LCMS (m/z): 364 ($M + H^+$). Anal. $C_{18}H_{16}F_3N_3O_2$: C, 59.50; H, 4.44; N, 11.57. Found: C, 59.80; H, 4.30; N, 11.70. $[\alpha]_D^{21}$ -42°(c 0,2, CH_3OH, 21°C).

Benzyl 2-(quinolin-8-ylcarbamoyl)indoline-1-carboxylate (Cbz – 22)

Colorless solid, mp 142 – 143 °C, yield 90%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.36 (s, 1H), 8.82 – 8.60 (m, 2H), 8.14 (d, *J* = 8.2 Hz, 1H), 8.08 – 7.85 (m, 1H), 7.65 – 7.48 (m, 2H), 7.44 – 7.88 (m, 4H), 7.20 – 7.11(s, 2H), 7.10 – 6.86 (m, 3H), 5.39 – 5.11 (m, 3H), 3.79 – 3.61 (m, 1H), 3.54 – 3.40 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.8, 148.4, 138.5, 136.2, 135.7, 133.9, 128.1, 127.9, 127.3, 124.8, 123.6, 121.9, 121.6, 116.7, 115.6, 67.8, 62.9, 33.3. LCMS (m/z): 424 ($M + H^+$). Anal. calcd $C_{26}H_{21}N_3O_3$: C, 73.74; H, 5.00; N, 9.92;. Found: C, 73.60; H, 5.26; N, 9.70.

***N*-(Quinolin-8-yl)-1-(2,2,2-trifluoroacetyl)indoline-2-carboxamide (TFA – 22)**

Yellow oil, yield 42%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.27 (s, 1H), 8.78 – 8.69 (m, 1H), 8.64 (d, *J* = 6.4 Hz, 1H), 8.35 (d, *J* = 7.4 Hz, 1H), 8.14 (d, *J* = 8.2 Hz, 1H), 7.57 – 7.34 (m, 5H), 7.20 (t, *J* = 7.4 Hz, 1H), 5.46 – 5.36 (m, 1H), 3.91 – 3.73 (m, 1H), 3.59 – 3.46 (m, *J* = 16.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.1, 155.3, 154.9, 154.6, 154.2, 148.5, 141.3, 138.4, 136.2, 133.3, 129.7, 128.2, 127.8, 127.1, 126.5, 125.0, 122.3, 121.78, 118.67, 116.6, 63.0, 35.3, 29.7. ^{19}F NMR (470 MHz, $CDCl_3$) δ -71.2. LCMS (m/z): 386 (M + H^+). Anal. calcd $C_{20}H_{14}F_3N_3O_2$: C, 62.34; H, 3.66; N, 10.90;.Found: C, 62.50; H, 3.44; N, 10.68.

N-(quinolin-8-yl)-2-(2,2,2-trifluoroacetyl)-2-azaspiro[3.3]heptane-1-carboxamide (TFA-spiroAze)

Beige oil, yield 40%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.31, 10.28 (rotameric singlets, 1H), 8.85 – 8.70 (m, 2H), 8.16 (d, *J* = 8.7 Hz, 1H), 7.61 – 7.37 (m, 3H), 4.90 (s, 1H), 4.65 – 4.51 (m, 1H), 4.47 – 4.39 (m, 1H), 4.36 – 4.19 (m, 1H), 2.61 – 2.41 (m, 1H), 2.38 – 2.17 (m, 2H), 2.00 – 1.75 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.42, 164.73, 157.20, 156.82, 148.70, 148.54, 138.53, 136.29, 133.34, 127.88, 127.21, 122.52, 122.29, 121.78, 116.83, 116.68, 72.34, 63.43, 60.39, 43.02, 42.62, 34.14, 33.85, 29.11, 16.13. ^{19}F NMR (376 MHz, $CDCl_3$) δ -72.46, -73.20. LCMS (m/z): 364 (M + H^+). Anal. calcd $C_{18}H_{16}F_3N_3O_2$: C, 59.50; H, 4.44; N, 11.57;.Found: C, 59.58; H, 4.62; N, 11.65.

(*S*)-Benzyl 2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Cbz – 23)

Yellow oil, yield 85%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.40 , 10.36 (rotameric singlets, 1H), 8.93 – 8.83 (m, 1H), 8.62 (d, *J* = 7.5 Hz, 1H), 8.40 (d, *J* = 8.2 Hz, 1H), 7.74 – 7.53 (m, 3H), 7.44 – 7.26 (m, 3H), 7.19 – 7.08 (m, 1H), 7.04 – 6.82 (m, 1H), 5.19 – 4.89 (m, 2H), 4.77 – 4.58 (m, 1H), 3.65 – 3.44 (m, 2H), 2.40 – 2.15 (m, 1H), 2.09 – 2.00 (m, 1H), 1.95 – 1.79 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.73, 171.30, 155.06, 154.47, 149.47, 138.55, 137.09, 134.56, 128.87, 128.28, 127.86, 127.41, 127.30, 126.89, 122.64, 122.55, 116.97, 116.76, 66.53, 61.78, 61.22, 60.23, 47.85, 47.27, 31.70, 30.44, 24.60, 23.78, 21.23, 14.56. LCMS (m/z): 376 (M + H^+). Anal. calcd $C_{22}H_{21}N_3O_3$: C, 70.38; H, 5.64; N, 11.19. Found: C, 70.51; H, 5.40; N, 10.98. $[\alpha]_D^{21}$ -98° (c 2,5, $CHCl_3$, 21°C).

(2*S*,3*S*)-Benzyl 3-phenyl-2-(quinolin-8-ylcarbamoyl)pyrrolidine-1-carboxylate (Cbz – 23a)

White solid, mp 49 – 50 °C; yield 73%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.56 (br s, 1H), 8.63 (br s, 1H), 8.57 – 8.42 (m, 1H), 8.11 – 7.98 (m, 1H), 7.51 – 7.22 (m, 7H), 7.21 – 7.02 (m, 3H), 7.03 – 6.75 (m, 3H), 5.35 – 4.92 (m, 2H), 4.87 – 4.61 (m, 1H), 4.22 – 4.00 (m, 1H), 3.87 – 3.58 (m, 2H), 2.94 – 2.70 (m, 1H), 2.33 – 2.16 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.6, 155.0, 154.5, 147.9, 138.2, 136.5, 135.9, 133.7, 128.4, 127.9, 127.6, 127.1, 121.4, 116.3, 67.1, 66.3, 48.8, 47.9, 46.7, 46.3, 28.5, 27.8. LCMS (m/z): 452 (M + H^+). Anal. calcd $C_{28}H_{25}N_3O_3$: C, 74.48; H, 5.58; N, 9.31;. Found: C, 74.59; H, 5.34; N, 9.60. $[\alpha]_D^{21}$ +30° (c 2,5, $CHCl_3$, 21°C).

Benzyl 2-(quinolin-8-ylcarbamoyl)piperidine-1-carboxylate (Cbz – 24)

Beige solid, mp 123 – 124 ˚C, yield 84%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.44 (s, 1H), 8.77 (d, *J* = 6.6 Hz, 1H), 8.80 – 8.63 (m, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 7.64 – 7.12 (m, 8H), 5.55 – 5.00 (m, 3H), 4.43 – 4.18 (m, 1H), 3.28 – 3.03 (m, 1H), 2.59 – 2.40 (m, 1H), 1.84 – 1.34 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.4, 148.4, 138.6, 136.2, 134.1, 128.5, 128.0, 127.8, 127.2, 121.8, 121.6, 67.7, 56.1, 42.4, 25.9, 24.9, 20.5. LCMS (m/z): 390 ($M + H^+$). Anal. calcd $C_{23}H_{23}N_3O_3$: C, 70.93; H, 5.95; N, 10.79. Found: C, 70.70; H, 5.80; N, 11.00.

Benzyl 3-phenyl-2-(quinolin-8-ylcarbamoyl)piperidine-1-carboxylate (Cbz – 24a)

White solid, mp 42 – 43 ˚C, yield 75%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.53, 9.45 (rotameric singltes,1H), 8.70 – 8.46 (m, 2H), 8.11 – 8.00 (m, 1H), 7.54 – 7.27 (m, 9H), 7.26 – 7.12 (m, 3H), 7.11 – 6.99 (m, 1H), 5.40 – 5.11 (m, 3H), 4.40 – 4.17 (m, 1H), 3.83 – 3.56 (m, 1H), 3.29 – 3.15 (m, 1H), 2.75 – 2.59 (m, 1H), 2.12 – 1.95 (m, 2H), 1.84 – 1.66 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.6, 168.4, 156.5, 155.6, 147.9, 147.8, 140.8, 138.3, 136.6, 136.0, 135.8, 134.1, 133.9, 128.5, 128.4, 127.9, 127.9, 127.6, 127.1, 126.9, 126.9, 67.6, 60.9, 60.5, 44.8, 44.6, 41.4, 41.0, 25.6, 25.3, 24.0, 23.9. LCMS (m/z): 466 ($M + H^+$). Anal. calcd $C_{29}H_{27}N_3O_3$: C, 74.82; H, 5.85; N, 9.03;. Found: C, 74.69; H, 5.66; N, 9.30.

Benzyl 2-(quinolin-8-ylcarbamoyl)octahydroquinoline-1(2*H*)-carboxylate (Cbz – 25)

Cream oil, yield 70%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.55 (s, 1H), 8.84 – 8.63 (m, 2H), 8.13 (d, *J* = 7.9 Hz, 1H), 7.63 – 7.11 (m, 8H), 5.59 – 5.27 (m, 2H), 5.28 – 5.00 (m, 1H), 4.50 – 4.05 (m, 1H), 3.70 – 3.67 (m, 1H), 2.63 – 2.55 (m, 1H), 2.17 – 1.99 (m, 1H), 1.90 (m, 1H), 1.85 – 1.47 (m, 5H), 1.40 – 1.08 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 148.4, 146.8, 136.1, 128.46, 127.9, 127.3, 121.5, 116.3, 67.9, 54.4, 35.5, 31.6, 25.9, 20.7, 20.1. LCMS (m/z): 444 ($M + H^+$). Anal. calcd $C_{27}H_{29}N_3O_3$: C, 73.11; H, 6.59; N, 9.47. Found: C, 73.50; H, 6.90; N, 9.27.

Benzyl 3-phenyl-2-(quinolin-8-ylcarbamoyl)octahydroquinoline-1(2*H*)-carboxylate (Cbz – 25a)

Yellow oil, yield 60%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.28, 10.03 (rotameric singlets, 1H), 8.92 – 8.36 (m, 2H), 8.08 (m, 1H), 7.52 – 7.40 (m, 4H), 7.44 – 7.33 (m, 4H), 7.29 – 7.21 (m, 4H), 7.13 – 7.05 (m, 1H), 5.66 – 5.32 (m, 2H), 5.32 – 5.17 (m, 1H), 4.41 – 4.06 (m, 1H), 3.72 – 3.60 (m, 1H), 3.25 – 2.92 (m, 2H), 2.19 – 1.99 (m, 2H), 1.88 – 1.17 (m, 7H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.1, 168.7, 156.5, 147.8, 147.4, 140.8, 138.2, 136.3, 135.7, 135.4, 134.3, 127.9, 127.6, 127.4, 127.2, 126.7, 126.5, 126.0, 125.9, 120.9, 116.2, 116.0, 67.2, 66.7, 58.2, 57.4, 53.9, 51.3, 44.3, 43.7, 36.2, 35.0, 31.3, 31.1, 25.9, 25.4, 24.6, 20.4, 20.2. LCMS (m/z): 520 ($M + H^+$).

Benzyl 3-(quinolin-8-ylcarbamoyl)-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (Cbz – 26)

Yellowish oil, yield 51%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.42, 10.24 (rotameric singlets, 1H), 8.73 – 8.60 (m, 2H), 8.10 (d, *J* = 8.2 Hz, 1H), 7.58 – 6.96 (m, 12H), 5.56 – 5.11 (m, 2H), 5.06 – 4.64 (m,

3H), 3.6 – 3.34 (m, 1H), 3.33 – 3.11 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.8, 169.2, 155.8, 148.4, 141.0, 138.5, 136.0, 133.8, 133.0, 128.6, 128.5, 128.2, 127.9, 127.6, 127.5, 127.2, 126.9, 126.3, 126.1, 121.7, 121.5, 116.4, 116.3, 67.9, 65.3, 57.0, 55.8, 45.1, 31.7, 30.7. LCMS (m/z): 438 ($M + H^+$). Anal. calcd $C_{27}H_{23}N_3O_3$: C, 74.13; H, 5.30; N, 9.60. Found: C, 74.50; H, 5.0; N, 9.91.

Benzyl 4-phenyl-3-(quinolin-8-ylcarbamoyl)-3,4-dihydroisoquinoline-2(1*H*)-carboxylate (Cbz – 26a)

Cream oil, yield 40%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.53 (s, 1H), 8.74 – 8.45 (m, 2H), 8.06 (d, *J* = 6.9 Hz, 1H), 7.52 – 7.29 (m, 10H), 7.20 – 6.95 (m, 7H), 5.49 – 5.12 (m, 3H), 5.05 (s, 2H), 4.66 (d, *J* = 5.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 147.9, 138.2, 135.9, 133.8, 130.4, 128.4, 128.2, 127.6, 127.0, 126.7, 121.6, 121.4, 116.4, 67.8, 48.0, 45.5, 45.2. LCMS (m/z): 514 ($M + H^+$). Anal. calcd $C_{33}H_{27}N_3O_3$: C, 77.17; H, 5.30; N, 8.18. Found: C, 76.95; H, 5.62; N, 8.40.

***Tert*-butyl 2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc – 27)**

Beige solid, mp 56 – 57 °C, yield 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.51, 10.32 (rotameric singlets, 1H), 8.91 – 8.65 (m, 2H), 8.13 (t, *J* = 9.0 Hz, 1H), 7.59 – 7.34 (m, 3H), (5.04 – 4.85 (m), 4.68 – 4.52 (m)) (1H), (4.17 – 4.00 (m), 3.99 – 3.83 (m)) (1H), (3.22 – 3.10 (m), 3.05 – 2.91 (m)) (1H), 2.56 – 2.27 (m, 1H), 1.98 – 1.70 (m, 5H),(1.55 (s), 1.45 (s)) (9H), 1.43 – 1.31 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.88, 156.03, 154.78, 147.78, 147.68, 138.25, 138.08, 135.74, 135.62, 134.12, 133.82, 127.43, 126.79, 121.14, 120.98, 115.93, 80.25, 79.79, 61.20, 59.88, 59.10, 43.63, 43.34, 30.05, 29.51, 29.07, 28.90, 28.79, 28.72, 28.02, 27.80, 25.25, 24.40, 13.70. LCMS (m/z): 370 ($M + H^+$). Anal. calcd $C_{21}H_{27}N_3O_3$: C, 68.27; H, 7.37; N, 11.37. Found: C, 68.40; H, 7.60; N, 11.20.

***Tert*-butyl 3-phenyl-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc – 27a)**

Yellow oil, yield 90%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.17, 9.91, 9.87, 9.71 (rotameric singlets, diastereomeic mixture, 1H), 8.78 – 8.54 (m, 2H), 8.17 – 8.00 (m, 1H), 7.65 – 7.01 (m, 8H), (5.70 – 5.55 (m), 5.43 – 5.26 (m), 5.26 – 5.02 (m), 4.97 – 4.79 (m)) (1H), 4.23 – 4.06 (m, 1H), 4.02 – 3.77 (m, 1H), 3.76 – 3.41 (m, 1H), 3.34 – 3.06 (m, 1H), 2.81 – 2.49 (m, 1H), 2.06 – 1.84 (m, 3H), 1.83 – 1.72 (m, 1H), (1.68 (s), 1.60 (s), 1.55 (s), 1.47 (s)) (9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.1, 170.0, 168.7, 156.4, 156.2, 155.4, 154.6, 148.0, 147.7, 145.2, 143.8, 143.5, 138.4, 136.2, 136.0, 135.8, 134.2, 128.7, 128.6, 128.2, 127.9, 127.8, 127.7, 127.2, 127.0, 126.4, 126.2, 121.5, 121.3, 116.5, 116.4, 116.2, 116.0, 81.1, 80.9, 80.4, 66.2, 65.9, 64.4, 63.6, 60.4, 48.9, 48.0, 47.3, 47.2, 45.9, 45.6, 44.5, 44.1, 34.3, 34.2, 31.6, 29.5, 29.0, 28.5, 28.0, 27.3, 26.5, 22.7, 21.0, 14.2. LCMS (m/z): 446 ($M + H^+$). Anal. calcd $C_{27}H_{31}N_3O_3$: C, 72.78; H, 7.01; N, 9.43. Found: C, 72.50; H, 7.33; N, 9.17.

***N*-(Quinolin-8-yl)-1-(2,2,2-trifluoroacetyl)azepane-2-carboxamide (TFA – 27)**

Colorless oil, yield 61%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.21, 10.16 (rotameric singlets, 1H), 8.80 (br. s, 1H), 8.68 (br. s, 1H), 8.18 – 8.10 (m, 1H), 7.57 – 7.38 (m, 3H), (5.02 – 4.94 , 4.81 – 4.69) (rotameric, 1H), (4.48 – 4,39, 4.09 –3,99) (rotameric m, 1H), (3.67 – 3.52, 3.29 –3.20 (rotameric m, 1H), (2.74 –2.62, 2.54 –2.42) (rotameric m, 1H), 2.20 – 1.79 (m, 4H), 1.78 – 1.54 (m, 1H), 1.52 – 1.33 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.9, 168.6, 158.29, 148.6, 148.4, 138.5, 136.3, 133.9, 127.9, 127.2, 122.3, 122.0, 121.8, 121.7, 116.7, 61.7, 60.9, 45.2, 45.0, 31.9, 30.7, 29.9, 29.3, 28.8, 27.2, 25.5, 24.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.7, -69.1. LCMS (m/z): 366 ($M + H^+$). Anal. calcd $C_{18}H_{18}F_3N_3O_2$: C, 59.17; H, 4.97; N, 11.50. Found: C, 59.30; H, 5.25; N, 11.28.

3-Phenyl-*N*-(quinolin-8-yl)-1-(2,2,2-trifluoroacetyl)azepane-2-carboxamide (TFA – 27a)

Light yellow oil, yield 87%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.75, 9.52, 9.46 (rotameric singlets (mixture of diastereomers), 1H), 8.67 – 8.60 (m, 1H), 8.59 – 8.51 (m, 1H), 8.05 – 7.97 (m, 1H), 7.49 – 7.37 (m, 2H), 7.36 – 7.23 (m, 3H), 7.21 – 7.16 (m, 2H), 7.11 – 7.04 (m, 1H), (5.22 – 5.15, 4.79 – 4.72) (m, 1H), (4.36 – 4.27, 4.08 – 3.96) (m, 1H), 3.87 – 3.73 (m, 1H), 3.63 – 3.45 (m, 1H), 2.16 – 1.87 (m, 4H), 1.88 – 1.45 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 148.3, 143.2, 138.3, 135.9, 133.9, 129.4, 128.9, 128.6, 128.4, 127.7, 127.3, 127.1, 126.9, 122.1, 122.0, 121.5, 116.5, 66.1, 49.4, 47.1, 45.4, 34.3, 30.6, 29.6, 28.7, 26.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -67.5, -68.8. LCMS (m/z): 442. Anal. calcd $C_{24}H_{22}F_3N_3O_2$: C, 65.30; H, 5.02; N, 9.52. Found: C, 65.60; H, 5.40; N, 9.32.

Benzyl-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Cbz – 27)

Cream oil, yield 74%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.40, 10.27 (rotameric singlets, 1H), 8.83 – 8.61 (m, 2H), 8.15 – 8.02 (m, 1H), 7.58 – 7.07 (m, 7H), 7.09 – 6.96 (m, 1H), 5.35 – 5.06 (m, 2H), (4.97 – 4.85 (m), 4.77 – 4.66 (m)) (1H), 4.24 – 3.95 (m, 1H), 3.32 – 3.02 (m, 1H), 2.59 – 2.29 (m, 1H), 2.00 – 1.71 (m, 4H), 1.70 – 1.48 (m, 1H), 1.42 – 1.12 (m, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ 170.9, 170.8, 157.2, 156.0, 148.4, 138.7, 138.6, 136.8, 136.4, 136.2, 134.4, 134.1, 128.5, 128.2, 127.9, 127.7, 127.3, 121.7, 121.7, 121.6, 121.5, 116.5, 116.4, 67.5, 61.6, 60.7, 60.4, 44.5, 44.0, 30.9, 30.3, 29.7, 29.5, 29.4, 25.8, 25.2. LCMS (m/z): 404. Anal. calcd $C_{24}H_{25}N_3O_3$: C, 71.44; H, 6.25; N, 10.41. Found: C, 71.60; H, 5.97; N, 10.30.

Benzyl-3-phenyl-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Cbz – 27a)

Beige oil, yield 85%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.02, 9.86, 9.75, 9.61 (rotameric singlets, (mixture of diastereomers), 1H), 8.75 – 8.40 (m, 2H), 8.11 – 7.90 (m, 1H), 7.61 – 7.31 (m, 7H), 7.30 – 6.88 (m, 6H), 5.65 – 5.30 (m, 1H), 5.25 – 4.80 (m, 2H), 4.31 – 3.91 (m, 1H), 3.67 – 3.12 (m, 2H), 2.17 – 1.86 (m, 3H), 1.80 – 1.28 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.7, 169.3, 168.2, 157.1, 155.5, 148.3, 148.0, 144.5, 143.2, 138.5, 136.7, 136.0, 135.9, 134.5, 134.1, 128.7, 128.5, 128.3, 128.0, 127.9, 127.8, 127.7, 127.2, 127.0, 126.7, 126.4, 121.6, 121.5, 116.5, 116.2, 67.6, 66.1, 65.7, 65.1, 48.6, 47.5, 46.6, 46.0, 45.0, 44.4, 34.3, 30.9, 29.4, 28.6, 27.9, 27.5, 26.7. LCMS (m/z):

480 (M + H^+). Anal. calcd $C_{30}H_{29}N_3O_3$: C, 75.13; H, 6.10; N, 8.76. Found: C, 75.40; H, 5.95; N, 9.02.

Benzyl 2-(quinolin-8-ylcarbamoyl)azocane-1-carboxylate (Cbz – 28)

Yellow oil, yield 78%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.33, 10.23 (rotameric singlets, 1H), 8.90 – 8.58 (m, 2H), 8.09 (d, *J* = 8.3 Hz, 1H), 7.54 – 7.42 (m, 2H), 7.42 – 7.34 (m, 2H), 7.35 – 7.21 (m, 3H), 7.07 – 6.98 (m, 1H), 5.31 – 5.14 (m, 2H), (4.96 – 4.87, 4.73 – 4.55) (m, 1H), 3.97 – 3.86 (m, 1H), 3.59 – 3.17 (m, 1H), 2.32 – 2.02 (m, 2H), 1.99 – 1.66 (m, 2H), 1.68 – 1.41 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 157.2, 155.5, 148.4, 138.6, 136.8, 136.5, 136.2, 134.3, 134.1, 128.5, 128.2, 127.9, 127.7, 127.2, 126.9, 121.8, 121.7, 121.6, 121.6, 116.5, 116.3, 67.5, 61.5, 61.2, 43.5, 28.0, 27.0, 26.8, 26.6, 25.9, 24.8, 24.4. LCMS (m/z): 418 (M + H^+). Anal. calcd $C_{25}H_{27}N_3O_3$: C, 71.92; H, 6.52; N, 10.06. Found: C, 72.70; H, 6.80; N, 9.82.

Benzyl 3-phenyl-2-(quinolin-8-ylcarbamoyl)azocane-1-carboxylate (Cbz – 28a)

Yellow oil, yield 92%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.90 , 9.83, 9.77, 9.65 (rotameric singlets, diastereomeric mixture, 1H), 8.91 – 8.40 (m, 2H), 8.12 – 7.96 (m, 1H), 7.60 – 7.27 (m, 8H), 7.29 – 6.87 (m, 5H), 5.54 – 4.95 (m, 3H), 3.98 – 3.38 (m, 2H), 3.37 – 2.80 (m, 1H), 2.48 – 1.83 (m, 4H), 1.76 – 1.13 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.7, 148.2, 138.4, 136.7, 135.9, 134.0, 129.1, 128.6, 128.4, 128.7, 127.8, 127.0, 126.5, 121.5, 116.5, 67.6, 64.82 63.2, 43.8, 43.3, 36.0, 29.71, 27.6, 26.7, 25.1. LCMS (m/z): 494 (M + H^+). Anal. calcd $C_{31}H_{31}N_3O_3$: C, 75.43; H, 6.33; N, 8.51. Found: C, 75.30; H, 6.60; N, 8.80.

Benzyl-2-(quinolin-8-ylcarbamoyl)-3-(4-(trifluoromethyl)phenyl)azocane-1-carboxylate (Cbz – 29a)

Light orange oil, yield 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.95, 9.89, 9.84, 9.70 (rotameric singlets, diastereomeric mixture, 1H), 8.81 – 8.61 (m, 1H), 8.60 – 8.44 (m, 1H), 8.15 – 7.99 (m, 1H), 7.68 – 7.56 (m, 1H), 7.54 – 7.40 (m, 8H), 7.39 – 7.28 (m, 3H), 5.50 – 5.13 (m, 3H), 3.97 – 3.44 (m, 2H), (3.39 – 3.22 (m), 3.04 – 2.78 (m)) (1H), 2.33 – 2.10 (m, 1H), 1.97 – 1.41 (m, 7H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 167.6, 157.5, 155.4, 148.3, 138.3, 138.0, 136.6, 136.1, 134.2, 133.8, 129.5, 128.6, 128.4, 128.1, 127.8, 126.9, 125.6, 125.0, 121.8, 121.6, 116.6, 116.4, 67.8, 64.6, 64.3, 63.1, 46.3, 44.0, 43.1, 35.6, 27.5, 27.4, 27.0, 26.7, 25.00, 21.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.9. LCMS (m/z): 562 (M + H^+). Anal. calcd $C_{32}H_{30}F_3N_3O_3$: C, 68.44; H, 5.38; N, 7.48. Found: C, 68.31; H, 5.50; N, 7.70.

***Tert*-butyl 2-(quinolin-8-ylcarbamoyl)-3-(4-(trifluoromethyl)phenyl)azepane-1-carboxylate (Boc – 30a)**

Brown solid, mp 142 – 143 °C yield 69%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.18, 9.95, 9.91, 9.72 (rotameric singltes, diastereomeric mixture, 1H), 8.77 – 8.51 (m, 2H), 8.19 – 8.02 (m, 1H), 7.70 –

7.28 (m, 7H), (5.60 – 5.52 (m), 5.24 – 5.11 (m), 5.12 – 5.02 (m), 4.90 – 4.84 (m)) (1H), 4.20 – 3.51 (m, 2H), 3.37 – 3.01 (m, 1H), 2.74 – 2.44 (m, 1H), 2.14 – 1.98 (m, 2H), 1.97 – 1.69 (m, 2H), (1.65, 1.59, 1.55, 1.45 (s)) (9H), 1.37 – 1.12 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.36, 148.13, 136.11, 128.92, 128.32, 127.84, 127.18, 125.02, 121.58, 116.45, 116.05, 81.19, 80.74, 65.69, 64.19, 63.15, 48.94, 48.08, 46.09, 45.73, 29.47, 28.50, 28.04, 27.81, 27.21, 26.40. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.8. LCMS (m/z): 514 ($M + H^+$). Anal. calcd $C_{28}H_{30}F_3N_3O_3$: C, 65.49; H, 5.89; N, 8.18. Found: C, 65.70; H, 6.20; N, 8.40.

***Tert*-butyl (*S*)-3-(4-bromophenyl)-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc – 31a) (diastereomeric mixture)**

Light orange oil, yield 73%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.15, 9.91, 9.87, 9.68 (rotameric peaks, diastereomeric mixture, 1H), 8.76 – 8.52 (m, 2H), 8.15 – 8.01 (m, 1H), 7.55 – 7.11 (m, 7H), (5.62 – 5.40 (m), 5.19 – 5.07 (m), 5.04 – 4.95 (m), 4.84 – 4.69 (m)) (1H), 4.19 – 3.49 (m, 2H), 3.18 (m, 1H), 2.67 – 2.39 (m, 1H), 2.13 – 1.95 (m, 2H), 1.96 – 1.67 (m, 3H), (1.64 (s), 1.58 (s), 1.54 (s), 1.44 (s)) (9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.4, 156.3, 155.2, 148.2, 142.8, 142.7, 138.3, 136.1, 134.0, 131.7, 131.6, 131.3, 131.1, 130.3, 130.2, 129.7, 129.4, 127.8, 127.1, 121.6, 121.5, 120.2, 119.9, 115.9, 80.9, 80.6, 66.0, 64.2, 63.3, 48.3, 47.3, 46.8, 46.1, 45.5, 44.5, 40.4, 40.2, 40.1, 39.9, 39.7, 34.1, 29.6, 29.4, 28.8, 28.4, 28.4, 28.3, 27.8, 27.3, 27.2, 26.4. LCMS (m/z): 524, 526 ($M + H^+$). Anal. calcd $C_{27}H_{30}BrN_3O_3$: C, 61.83; H, 5.77; N, 8.01. Found: C, 62.60; H, 6.00; N, 8.20.

***Tert*-butyl-3-(4-cyanophenyl)-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc – 32a)**

Light red oil, yield 70%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.96, 9.87 (rotameric singlets, 1H), 8.68 (d, J = 2.9 Hz, 1H), 8.65 – 8.52 (m, 1H), 8.09 (d, J = 7.1 Hz, 1H), 7.91 – 7.59 (m, 2H), 7.56 – 7.30 (m, 5H), (5.60 – 5.41 (m), 5.20 – 4.98 (m)) (1H), 4.12 – 3.54 (m, 2H), 3.35 – 3.04 (m, 1H), 2.82 – 2.45 (m, 1H), 2.09 – 1.87 (m, 4H), 1.86 – 1.61 (m, 1H), (1.58 (s), 1.47 (s)) (9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.2, 156.3, 155.2, 148.3, 148.3, 145.4, 145.1, 138.4, 136.2, 133.9, 133.4, 133.1, 132.5, 130.0, 128.8, 127.9, 127.2, 121.7, 119.2, 118.9, 116.2, 112.1, 81.4, 80.9, 65.1, 62.7, 48.9, 48.3, 46.1, 28.5, 27.9, 27.5, 27.0, 26.3. LCMS (m/z): 471 ($M + H^+$). Anal. calcd $C_{28}H_{30}N_4O_3$: C, 71.47; H, 6.43; N, 11.91. Found: C, 71.20; H, 6.59; N, 11.70.

***Tert*-butyl 3-(4-(pyridin-3-ylmethoxy)phenyl)-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc -33a)**

Orange oil, yield 65%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.15, 9.88, 9.86, 9.67 (rotameric singlets, diastereomeric mixture, 1H), 8.79 – 8.46 (m, 4H), 8.15 – 8.00 (m, 1H), 7.77 – 7.61 (m, 1H), 7.53 – 7.39 (m, 3H), 7.39 – 7.19 (m, 3H), 6.94 – 6.78 (m, 2H), (5.59 – 5.46 (m), 5.19 – 5.01 (m)) (1H), 4.99 – 4.74 (m, 2H), 4.25 – 3.73 (m, 1H), 3.72 – 3.40 (m, 1H), 3.30 – 3.04 (m, 1H), (2.67 – 2.49 (m), 2.38 – 2.11 (m)) (1H), 2.07 – 1.80 (m, 4H), 1.80 – 1.68 (m, 1H), (1.64 (s), 1.58 (s), 1.53 (s), 1.43 (s)) (9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.1, 169.5, 168.8, 156.9, 156.8, 156.4, 155.4,

149.3, 148.9, 147.9, 147.8, 138.2, 138.3, 138.0, 136.7, 136.5, 136.2, 136.1, 135.9, 135.3, 134.8, 134.3, 134.2, 132.7, 129.6, 129.5, 129.0, 128.8, 127.8, 127.3, 127.0, 123.5, 121.5, 121.3, 116.4, 116.2, 115.9, 114.9, 114.8, 114.5, 81.1, 80.9, 80.4, 66.4, 66.1, 64.6, 63.61, 48.2, 47.2, 46.4, 46.4, 45.9, 45.5, 44.4, 34.4, 34.2, 29.5, 29.2, 29.0, 28.5, 28.4, 28.3, 28.0, 27.5, 27.3, 26.5. LCMS (m/z): 553 (M + H^+). Anal. calcd $C_{33}H_{36}N_4O_4$; HRMS (m/z): Calculated [M+H^+] = 553.2809; Found [M+H^+] = 553.2779 (error = 5.42 ppm). Calculated [M+Na^+] = 575.2629. Found [M+Na^+] = 575.2605 (error = 4.17 ppm).

***Tert*-butyl-3-(4-(pyridin-4-ylmethoxy)phenyl)-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc – 34a) (cis)**

Light-yellow solid, mp 75 – 76 ˚C, yield 23%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85, 9.67 (rotameric singlets, 1H), 8.73 – 8.59 (m, 2H), 8.59 – 8.52 (m, 2H), 8.08 (d, *J* = 8.0 Hz, 1H), 7.57 – 7.39 (m, 3H), 7.38 – 7.32 (m, 2H), 7.32 – 7.26 (m, 2H), 6.88 – 6.77 (m, 2H), (5.53 – 5.43 (m), 5.05 – 4.98 (m)) (1H), 4.98 – 4.88 (m, 2H), (4.12 – 3.96 (m), 3.84 – 3.73 (m)) (1H), 3.71 – 3.50 (m, 1H), 3.26 – 3.08 (m, 1H), 2.71 – 2.45 (m, 1H), 2.08 – 1.95 (m, 2H), 1.94 – 1.65 (m, 3H), (1.56 (s), 1.41 (s)) (9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.3, 156.3, 155.8, 154.9, 149.4, 147.5, 146.0, 137.9, 136.4, 136.1, 135.6, 133.8, 133.7, 129.2, 129.0, 127.3, 126.7, 120.9, 120.9, 115.7, 115.5, 113.9, 80.5, 79.9, 67.6, 65.7, 63.0, 57.9, 50.3, 47.8, 46.8, 45.4, 45.1, 28.7, 28.0, 27.8, 27.4, 26.9, 26.8, 25.9. Anal. calcd $C_{33}H_{36}N_4O_4$; HRMS (m/z): Calculated [M+H^+] = 553.2809. Found [M+H^+] = 553.2794 (error = 2.71 ppm). Calculated [M+Na^+] = 575.2629. Found [M+Na^+] = 575.2620 (error = 1.56 ppm).

***Tert*-butyl-3-(4-(pyridin-4-ylmethoxy)phenyl)-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc – 34a) (mixture of diastereomers)**

Yellow oil, yield 23%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.13, 9.86, 9.85, 9.67 (rotameric singlets, diastereomeric mixture, 1H), 8.72 – 8.59 (m, 2H), 8.59 – 8.49 (m, 2H), 8.11 – 7.99 (m, 1H), 7.49 – 7.38 (m, 3H), 7.38 – 7.22 (m, 4H), 6.87 – 6.75 (m, 2H), (5.54 – 5.43 (m), 5.11 – 4.99 (m)) (1H), (4.98 – 4.85 (m), 4.80 – 4.73 (m)) (2H), (4.13 – 4.00 (m), 3.96 – 3.70 (m)) (1H), 3.68 – 3.50 (m, 1H) , 3.29 – 3.06 (m, 1H), 2.67 – 2.44 (m, 1H), 2.08 – 1.65 (m, 5H), (1.62 (s), 1.56 (s), 1.51 (s), 1.41 (s)) (9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.4, 164.8, 163.9, 152.0, 151.8, 151.6, 150.6, 149.7, 145.2, 143.3, 143.2, 143.0, 141.6, 141.5, 133.8, 133.7, 133.5, 133.4, 132.1, 131.8, 131.5, 131.3, 131.1, 130.0, 129.7, 129.5, 129.4, 124.9, 124.8, 124.3, 124.0, 123.1, 122.5, 122.3, 116.7, 116.6, 111.8, 111.7, 111.4, 111.2, 110.2, 110.1, 109.7, 109.6, 76.3, 76.2, 75.7, 63.3, 61.5, 61.3, 59.9, 58.8, 46.0, 43.5, 42.5, 41.6, 41.19, 40.8, 39.7, 39.2, 29.6, 24.9, 24.7, 24.4, 24.2, 23.7, 22.7, 22.6, 21.7. LCMS (m/z): 553 (M + H^+). Anal. calcd $C_{33}H_{36}N_4O_4$: C, 71.72; H, 6.57; N, 10.14. Found: C, 71.40; H, 6.41; N, 10.30.

***Tert*-butyl -3-(3-(ethoxycarbonyl)phenyl)-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc – 35a)**

Yellow oil, yield 19%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81, 9.69 (rotameric peaks, 1H), 8.72 – 8.57 (m, 2H), 8.17 – 7.98 (m, 2H), 7.91 – 7.77 (m, 1H), 7.77 – 7.61 (m, 1H), 7.54 – 7.43 (m, 2H), 7.41 – 7.30 (m, 2H), (5.54 – 5.44 (m), 5.14 – 5.03 (m)) (1H), 4.38 – 4.19 (m, 2H), (4.14 – 4.00 (m), 3.91 – 3.78 (m)) (1H), 3.73 – 3.54 (m, 1H), 3.37 – 3.22 (m, 1H), 2.79 – 2.49 (m, 1H), 2.12 – 1.98 (m, 2H), 1.96 – 1.61 (m, 2H), (1.57 (s), 1.46 (s)) (9H), 1.35 – 1.24 (m, 3H), 1.21 – 0.94 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.5, 166.5, 155.4, 148.0, 144.2, 138.3, 136.0, 133.9, 133.2, 132.9, 130.4, 129.6, 128.3, 127.8, 127.2, 121.5, 116.1, 81.2, 80.6, 66.0, 63.6, 60.8, 50.9, 48.5, 47.9, 45.8, 45.6, 28.9, 28.5, 28.4, 27.9, 27.5, 26.6, 14.3. LCMS (m/z): 518 ($M + H^+$). Anal. calcd $C_{30}H_{35}N_3O_5$: C, 69.61; H, 6.82; N, 8.12. Found: C, 71.00; H, 6.90; N, 8.30.

***Tert*-butyl-2-(quinolin-8-ylcarbamoyl)-3-(3-(trifluoromethoxy)phenyl)azepane-1-carboxylate (Boc – 36a)**

Yellow solid, mp 72 – 73 ˚C; yield 59%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.19, 9.96, 9.92, 9.82 (rotameric peaks, diastereomeric mixture, 1H), 8.84 – 8.51 (m, 2H), 8.25 – 7.99 (m, 1H), 7.63 – 7.20 (m, 6H), 7.11 – 6.87 (m, 1H), (5.64 – 5.51) (m), 5.25 – 5.12 (m), 5.12 – 5.06 (m), 4.94 – 4.81 (m)) (1H), 4.20 – 3.58 (m, 2H), 3.37 – 3.05 (m, 1H), 2.82 – 2.45 (m, 1H), 2.18 – 1.77 (m, 5H), (1.66 (s), 1.60 (s), 1.49 (s)) (9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.4, 156.2, 155.3, 149.1, 148.2, 146.3, 145.9, 138.4, 136.1, 134.1, 133.9, 129.9, 129.4, 129.3, 127.8, 127.2, 126.9, 126.4, 121.5, 120.7, 119.4, 118.8, 118.5, 116.5, 116.1, 81.22, 80.7, 65.9, 65.5, 64.3, 63.1, 48.8, 48.2, 46.9, 45.8, 44.5, 29.5, 28.5, 28.4, 27.7, 27.1, 26.4. ^{19}F NMR (470 MHz, $CDCl_3$) δ -57.8. LCMS (m/z): 530 ($M + H^+$). Anal. calcd $C_{28}H_{30}F_3N_3O_4$: C, 63.51; H, 5.71; N, 7.94. Found: C, 63.20; H, 5.50; N, 7.70.

***Tert*-butyl-3-(3-acetamidophenyl)-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc – 37a)**

Light purple solid, mp 114 – 115 ˚C; yield 67%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.14, 9.92, 9.87, 9.68 (rotameric singlets, diastereomeric mixture, 1H), 8.74 – 8.47 (m, 2H), 8.14 – 7.97 (m, 1H), 7.89 – 7.66 (m, 1H), 7.65 – 7.47 (m, 1H), 7.47 – 7.30 (m, 4H), 7.24 – 6.94 (m, 2H), (5.56 – 5.47 (m), 5.20 – 5.09 (m), 5.05 – 4.93 (m), 4.90 – 4.82 (m)) (1H), 4.23 – 3.77 (m, 1H), 3.71 – 3.50 (m, 1H), 3.36 – 3.02 (m, 1H), 2.64 – 2.38 (m, 1H), 2.10 – 1.95 (m, 4H), 1.95 – 1.67 (m, 4H), (1.63 (s), 1.56 (s), 1.53 (s), 1.39 (s)) (9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.5, 168.9, 168.4, 168.0, 155.9, 155.8, 154.9, 154.1, 147.7, 147.4, 145.3, 144.1, 143.7, 137.8, 137.5, 135.5, 135.4, 134.1, 133.6, 128.9, 128.4, 127.3, 126.6, 126.5, 123.7, 123.2, 121.2, 120.9, 119.2, 118.7, 118.4, 117.9, 117.7, 115.9, 115.6, 115.4, 80.6, 80.1, 65.9, 65.2, 63.8, 63.2, 50.2, 48.1, 46.9, 46.8, 46.6, 45.71, 44.9, 44.1, 43.6, 33.8, 33.5, 28.9, 28.6, 28.4, 27.9, 27.9, 27.8, 27.1, 26.9, 26.0, 23.9. LCMS (m/z): 503 ($M + H^+$). Anal. calcd $C_{29}H_{34}N_4O_4$: C, 69.30; H, 6.82; N, 11.15. Found: C, 69.10; H, 6.70; N, 11.40.

***Tert*-butyl-3-(3-fluorophenyl)-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc – 38a)**

Yellow oil, yield 70%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.21, 9.95, 9.91, 9.77 (rotameric singlets, diastereomeric mixture, 1H), 8.74 – 8.67 (m, 2H), 8.16 – 8.04 (m, 1H), 7.62 – 7.35 (m, 3H), 7.34 – 7.06 (m, 3H), 6.90 – 6.78 (m, 1H), (5.59 (br. s), 5.14 (br. s)) (1H), 4.12 – 3.35 (m, 2H), 3.31 – 3.07 (m, 1H), 2.70 – 2.44 (m, 1H), 2.18 – 1.69 (m, 5H), (1.60 (s), 1.48 (s)) (9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.0, 163.2, 161.3, 155.8, 154.8, 147.7, 145.9, 145.7, 137.9, 135.6, 133.7, 133.5, 129.0, 127.33, 126.7, 123.8, 123.6, 121.0, 115.9, 115.7, 115.2, 114.9, 112.90, 112.7, 80.6, 80.1, 65.2, 63.7, 62.7, 48.2, 47.5, 46.5, 45.6, 45.2, 44.0, 33.6, 33.4, 28.9, 28.3, 28.0, 27.9, 27.7, 27.2, 26.7, 25.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.3, -113.6, -113.8, -114.0. LCMS (m/z): 464 ($M + H^+$). Anal. calcd $C_{27}H_{30}FN_3O_3$: C, 69.96; H, 6.52; N, 9.06. Found: C, 70.18; H, 6.79; N, 9.33.

***Tert*-butyl-3-(3,5-difluorophenyl)-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc – 39a) (cis)**

Beige oil, yield 19%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.94, 9.85 (rotameric singlets, 1H), 8.70 – 8.66 (m, 1H), 8.65 – 8.57 (m, 1H), 8.15 – 8.01 (m, 1H), 7.51 – 7.43 (m, 2H), 7.42 – 7.35 (m, 1H), 7.12 – 7.03 (m, 1H), 7.00 – 6.93 (m, 1H), 6.64 – 6.50 (m, 1H), (5.59 – 5.50 (m), 5.18 – 5.08(m)) (1H)), 4.15 – 3.53 (m, 2H), 3.22 – 3.07 (m, 1H), 2.67 – 2.39 (m, 1H), 2.09 – 1.88, (m, 3H), 1.84 – 1.65 (m, 2H), (1.63 – 1.53, 1.52 – 1.45 (br s, 9H)). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.3, 163.7, 161.7, 156.2, 155.2, 148.2, 148.1, 147.6, 138.4, 136.2, 134.1, 133.9, 127.9, 127.2, 121.6, 116.2, 111.6, 111.4, 101.9, 101.7, 81.3, 80.8, 65.1, 62.8, 48.8, 48.3, 46.1, 45.8, 29.7, 28.5, 28.4, 28.1, 27.5, 26.9, 26.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.9, -111.1. LCMS (m/z): 482 ($M + H^+$). Anal. calcd $C_{27}H_{29}F_2N_3O_3$: C, 67.35; H, 6.07; N, 8.73. Found: C, 67.10; H, 6.30; N, 8.50.

***Tert*-butyl-3-(3-bromo-4-fluorophenyl)-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc – 40a)**

Orange oil, yield 19%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.21, 9.97, 9.92, 9.77 (rotameric singlets, diastereomeric mixture, 1H), (8.74 (d, J = 4.1 Hz), 8.70 (d, J = 4.1 Hz)) (1H), 8.68 – 8.59 (m, 1H), 8.16 – 8.08 (m, 1H), 7.56 – 7.30 (m, 5H), 7.25 – 7.00 (m, 1H), (5.58 – 5.53 (br. s), 5.11 – 5.07 (br. s)) (1H), 4.19 – 3.53 (m, 2H), 3.26 – 3.08 (m, 1H), 2.66 – 2.41 (m, 1H), 2.19 – 1.68 (m, 5H), (1.60 (s), 1.48 (s)) (9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.8, 159.3, 157.3, 155.8, 154.7, 147.8, 147.7, 145.3, 145.1, 137.9, 137.7, 135.7, 133.5, 133.3, 132.5, 132.4, 127.3, 126.7, 125.1, 124.9, 121.1, 116.4, 116.2, 115.7, 106.0, 80.8, 80.3, 65.0, 62.5, 47.9, 47.2, 45.6, 45.2, 28.3, 28.0, 27.9, 27.6, 27.2, 26.6, 25.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.1, -107.4, -107.7, -108.1, -108.4. LCMS (m/z): 544, 546. Anal. calcd $C_{27}H_{29}BrFN_3O_3$: C, 59.78; H, 5.39; N, 7.75. Found: C, 59.98; H, 5.61; N, 8.00.

***Tert*-butyl-3-(4-methyl-3-nitrophenyl)-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc – 41a)**

Yellow oil, yield 73%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.94, 9.88 (rotameric singlets, 1H), 8.66 (d, J = 3.9 Hz, 1H), 8.64 – 855 (m, 1H), 8.15 – 8.00 (m, 2H), 7.70 – 7.56 (m, 1H), 7.49 – 7.43 (m, 2H),

7.20 (d, *J* = 7.8 Hz, 3H), (5.56 – 5.49 (m), 5.17 – 5.11 (m)) (1H), 4.13 – 3.56 (m, 2H), 3.32 – 3.02 (m, 1H), 2.74 – 2.56 (m, 1H), 2.49 (s, 3H), 2.12 – 1.91 (m, 3H), 1.86 – 1.64 (m, 2H), (1.58 (s), 1.48 (s)) (9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.2, 156.3, 155.2, 148.9, 148.2, 148.1, 143.3, 143.1, 138.3, 136.2, 133.9, 133.8, 133.5, 133.1, 132.6, 132.4, 131.7, 131.3, 127.9, 127.2, 124.7, 121.6, 116.2, 81.5, 80.8, 65.2, 62.8, 48.3, 47.8, 45.9, 45.8, 28.5, 28.4, 27.5, 27.1, 27.0, 26.4, 20.3. LCMS (m/z): 505 ($M + H^+$). Anal. calcd $C_{28}H_{32}N_4O_5$: C, 66.65; H, 6.39; N, 11.10. Found: C, 66.40; H, 6.60; N, 11.45.

***Tert*-butyl (S)-3-(3,4-dicyanophenyl)-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc – 42a)**

Yellow oil, yield 51%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.51, 10.33, 10.08, 10.02 (rotameric peaks, diastereomeric mixture, 1H), 8.84 – 8.69 (m, 1H), 8.63 – 8.47 (m, 1H), 8.18 – 8.08 (m, 1H), 8.05 – 7.62 (m, 3H), 7.58 – 7.34 (m, 3H), (5.63 – 5.52 (m), 5.25 – 5.10 (m), 4.98 – 4.73 (m), 4.68 – 4.48 (m)) (1H), 4.19 – 3.82 (m, 1H), 3.79 – 3.54 (m, 1H), 3.36 – 2.88 (m, 1H), 2.82 – 2.29 (m, 1H), 2.16 – 2.07 (m, 1H), 2.05 – 1.85 (m, 2H), 1.86 – 1.68 (m, 1H), (1.66 (s), 1.61 (s), 1.58 (s), 1.45 (s)) (9H), 1.38 – 1.19 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.4, 168.9, 167.7, 156.5, 150.4, 148.4, 138.4, 136.3, 136.1, 134.1, 133.7, 133.5, 133.1, 127.9, 127.2, 121.9, 121.8, 121.7, 121.5, 116.5, 116.4, 116.2, 115.7, 115.5, 113.3, 81.9, 81.3, 80.8, 80.3, 64.4, 63.9, 62.3, 61.7, 59.6, 49.2, 48.9, 47.2, 46.3, 45.9, 44.8, 44.1, 43.8, 33.3, 30.5, 30.0, 29.6, 29.4, 29.3, 28.5, 28.3, 27.6, 26.7, 26.2, 25.7, 24.9. Anal. calcd $C_{29}H_{29}N_5O_3$; HRMS (m/z): Calculated [$M+H^+$] = 496.2343. Found [$M+H^+$] = 496.2307 (error = 7.25 ppm).

***Tert*-butyl-3-(4-((tert-butoxycarbonyl)amino)-3-methoxyphenyl)-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc – 43a)**

Beige solid, mp 110 – 111 °C, yield 58%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.00, 9.80, 9.66, 9.45 (rotameric singlets, diastereomeric mixture, 1H), 8.73 – 8.50 (m, 2H), 8.12 – 8.00 (m, 1H), 7.96 – 7.82 (m, 1H), 7.54 – 7.27 (m, 3H), 7.06 – 6.67 (m, 3H), (5.42 – 5.34 (m), 5.07 – 4.95 (m), 4.92 – 4.86 (m), 4.82 – 4.69 (m)) (1H), (4.28 – 4.07 (m), 3.96 – 3.79 (m)) (1H), (3.72 (s), 3.63 (s)) (3H), 3.35 – 3.08 (m, 1H), 2.57 – 2.32 (m, 1H), 2.11 – 1.83 (m, 4H), 1.82 – 1.67 (m, 1H), (1.52 (s), 1.49 (s), 1.37 (s)) (18H), 1.27 – 1.18 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.9, 168.5, 155.7, 154.9, 152.2, 147.5, 146.8, 137.5, 135.4, 133.7, 127.3, 126.7, 120.9, 120.8, 120.5, 117.3, 115.9, 115.6, 115.4, 109.8, 109.5, 80.4, 79.9, 79.7, 66.5, 63.7, 54.7, 50.2, 47.8, 46.7, 44.8, 40.4, 28.9, 28.0, 27.9, 27.3, 26.3. LCMS (m/z): 591 ($M + H^+$). Anal. calcd $C_{33}H_{42}N_4O_6$: C, 67.10; H, 7.17; N, 9.48. Found: C, 67.30; H, 6.97; N, 9.35.

***Tert*-butyl-3-(9*H*-fluoren-3-yl)-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc – 44a) (cis)**

Bright yellow oil, yield 47%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66, 9.38 (rotameric singlets, 1H), 8.73 – 8.57 (m, 1H), (8.37 – 8.27 (m), 8.19 – 8.07 (m)) (1H), 7.96 (d, *J* = 8.1 Hz, 1H), 7.71 – 7.56 (m, 3H), 7.55 – 7.28 (m, 6H), 7.18 – 6.98 (m, 1H), (5.58 – 5.45 (m), 5.02 – 4.92 (m)) (1H), 4.38 – 3.86 (m, 1H), 3.81 – 3.56 (m, 2H), 3.55 – 3.36 (m, 2H), 3.36 – 3.10 (m, 1H), 2.77 – 2.36 (m, 1H), 2.22 – 1.74 (m, 4H), (1.56 (s), 1.40 (s)) (9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.5, 147.2, 142.9, 142.0, 141.7, 141.0, 139.7, 135.3, 133.6, 127.2, 126.6, 126.1, 125.9, 124.4, 120.7, 119.1, 115.7, 115.4, 80.4, 79.9, 66.8, 63.9, 48.2, 46.9, 45.3, 44.9, 36.2, 28.8, 28.0, 27.6, 26.9, 26.3. LCMS (m/z): 534 ($M + H^+$). Anal. calcd $C_{34}H_{35}N_3O_3$: C, 76.52; H, 6.61; N, 7.87. Found: C, 76.30; H, 6.33; N, 7.98.

***Tert*-butyl (2S,3S)-3-(9*H*-fluoren-3-yl)-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc – 44a) (diastereomeric mixture)**

Bright yellow oil, yield 47%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.01, 9.81, 9.66, 9.37 (rotameric singlets, diastereomeric mixture, 1H), 8.78 – 8.07 (m, 2H), 7.95 (d, *J* = 6.1 Hz, 1H), 7.74 – 7.54 (m, 3H), 7.55 – 7.35 (m, 5H), 7.34 – 7.28 (m, 1H), 7.19 – 6.98 (m, 1H), (5.54 – 5.43 (m), 5.20 – 5.10 (m), 5.01 – 4.94 (m), 4.92 – 4.82 (m)) (1H), 4.34 – 3.85 (m, 1H), 3.82 – 3.08 (m, 5H), 2.80 – 2.27 (m, 1H), 2.24 – 1.81 (m, 4H), (1.63 (s), 1.56 (s), 1.53 (s), 1.39 (s)) (9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.9, 147.7, 146.9, 143.7, 143.3, 142.5, 142.2, 141.5, 140.2, 139.9, 139.2, 138.2, 135.8, 134.1, 127.7, 127.1, 126.6, 126.3, 126.1, 124.9, 121.3, 119.6, 116.4, 116.1, 115.9, 81.1, 80.4, 67.3, 64.8, 64.4, 48.7, 47.8, 47.5, 45.8, 45.5, 44.6, 36.7, 34.6, 29.7, 29.6, 29.3, 29.1, 28.6, 28.3, 27.5, 26.8. LCMS (m/z): 534 ($M + H^+$). Anal. calcd $C_{34}H_{35}N_3O_3$: C, 76.52; H, 6.61; N, 7.87. Found: C, 76.81; H, 6.83; N, 7.68.

***Tert*-butyl-3-(6-iodo-9-oxo-9*H*-fluoren-3-yl)-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc – 45a) (cis)**

Bright yellow oil, yield 53%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.93, 9.80 (rotameric singlets, 1H), 8.76 – 8.49 (m, 2H), 8.07 (d, *J* = 8.0, 1H), 7.94 (s, 1H), 7.82 (d, *J* = 7.6 Hz, 1H), 7.79 – 7.73 (m, 1H), 7.72 – 7.64 (m, 1H), 7.59 – 7.43 (m, 2H), 7.41 – 7.35 (m, 1H), 7.35 – 7.27 (m, 1H), 7.18 (d, *J* = 7.8 Hz, 1H), (5.58 – 5.45 (m), 5.15 – 5.01 (m)) (1H), (4.18 – 4.02 (m), 3.84 – 3.73 (m)) (1H), 3.73 – 3.55 (m, 1H), 3.34 – 3.14 (m, 1H), 2.76 – 2.51 (m, 1H), 2.13 – 2.01 (m, 1H), 1.98 – 1.81 (m, 1H), 1.80 – 1.67 (m, 1H), (1.60 (s), 1.48 (s)) (9H), 1.32 – 1.22 (m, 1H), 0.95 – 0.80 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.4, 190.9, 168.3, 156.2, 155.3, 148.0, 146.1, 145.8, 143.7, 143.4, 142.9, 141.9, 141.8, 138.3, 138.2, 136.1, 135.4, 134.9, 134.8, 134.0, 133.9, 133.5, 133.1, 127.8, 127.2, 124.8, 122.1, 121.8, 121.5, 120.3, 120.2, 116.2, 116.1, 94.4, 93.5, 93.3, 81.4, 80.7, 65.8, 63.2, 48.9, 48.1, 45.9, 45.7, 41.0, 29.7, 28.8, 28.5, 28.3, 28.1, 27.9, 27.4, 27.1, 26.5. LCMS (m/z): 674 ($M + H^+$). Anal. calcd $C_{34}H_{32}IN_3O_4$: C, 60.63; H, 4.79; N, 6.24. Found: C, 60.81; H, 4.50; N, 6.48.

***Tert*-butyl-3-(2-methylbenzofuran-5-yl)-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc – 46a)**

Yellow oil, yield 83%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.00, 9.79, 9.66, 9.38 (rotameric singlets, diastereomeric mixture, 1H), 8.75 – 8.57 (m, 1H), 8.56 – 8.26 (m, 1H), 8.08 – 7.94 (m, 1H), 7.61 – 7.35 (m, 3H), 7.35 – 7.23 (m, 2H), 7.25 – 7.09 (m, 1H), (6.29 – 6.14 (m), 6.09 – 6.02 (m)) (1H), (5.57 – 5.50 (m), 5.23 – 5.12 (m), 5.05 – 4.97 (m), 4.93 – 4.82 (m)) (1H), (4.27 – 4.13 (m), 3.95 – 3.79 (m)) (1H), 3.71 – 3.48 (m, 1H), 3.43 – 3.21 (m, 1H), 2.73 – 2.46 (m, 1H), 2.35 (s, 3H), 2.16 – 1.64 (m, 5H), (1.62 (s), 1.52 (s), 1.40 (s)) (9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.2, 168.5, 155.7, 154.9, 153.1, 147.2, 137.6, 137.5, 137.1, 135.3, 133.8, 133.5, 128.8, 128.7, 127.2, 126.7, 123.3, 123.1, 120.8, 120.7, 119.2, 115.6, 115.4, 109.6, 102.1, 80.4, 79.9, 66.7, 63.9, 50.3, 48.1, 46.9, 45.4, 44.9, 40.5, 29.1, 28.3, 28.0, 27.8, 27.3, 26.9, 26.2, 13.5 . LCMS (m/z): 500 ($M + H^+$). Anal. calcd $C_{30}H_{33}N_3O_4$: C, 72.12; H, 6.66; N, 8.41. Found: C, 72.41; H, 6.80; N, 8.60.

***Tert*-butyl-3-(2,3-dihydrobenzofuran-5-yl)-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc – 47a)**

Cream oil, yield 70%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.74, 9.50 (rotameric singlets, 1H), 8.80 – 8.57 (m, 2H), 8.17 – 8.03 (m, 1H), 7.55 – 7.33 (m, 3H), 7.33 – 7.21 (m, 1H), 7.17 – 7.09 (m, 1H), 6.70 (d, *J* = 8.3 Hz, 1H), (5.51 – 5.35 (m), 4.99 – 4.83 (m)) (1H), 4.50 – 4.33 (m, 1H), 4.33 – 4.17 (m, 1H), 3.97 – 3.56 (m, 1H), 3.56 – 3.42 (m, 1H), 3.34 – 3.12 (m, 1H), 3.10 – 2.76 (m, 1H), 2.69 – 2.43 (m, 1H), 2.13 – 1.98 (m, 3H), 1.94 – 1.67 (m, 2H), (1.58 (s), 1.42 (s)) (9H), 1.34 – 1.23 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.0, 158.7, 156.2, 155.4, 147.9, 138.4, 135.9, 135.6, 134.2, 127.9, 127.8, 127.3, 127.2, 126.9, 126.8, 124.9, 124.7, 121.5, 121.2, 116.1, 115.9, 108.9, 80.9, 80.3, 71.1, 67.2, 64.3, 48.1, 46.9, 45.9, 45.4, 29.7, 29.5, 28.7, 28.5, 28.3, 27.9, 27.5, 26.7. LCMS (m/z): 488 ($M + H^+$). Anal. calcd $C_{29}H_{33}N_3O_4$: C, 71.44; H, 6.82; N, 8.62. Found: C, 71.70; H, 6.53; N, 8.88.

***Tert*-butyl-3-(benzo[d][1,3]dioxol-5-yl)-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc – 48a)**

Light-yellow oil, yield 83%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.83, 9.64 (rotameric singlets, 1H), 8.73 – 8.64 (m, 2H), 8.14 – 8.06 (m, 1H), 7.54 – 7.43 (m, 2H), 7.31 – 7.36 (s, 1H), 7.11 – 6.93 (m, 1H), 6.93 – 6.85 (m, 1H), 6.71 (d, *J* = 7.6 Hz, 1H), 5.86 (br. s, 1H), 5.80 – 5.71 (m, 1H), (5.50 – 5.48 (m), 5.04 – 4.98 (m)) (1H) (4.18 – 4.11 (m), 3.88 – 3.81 (m)) (1H), 3.76 – 3.57 (m, 1H), 3.57– 3.52 (m, 1H), (3.26 – 3.21 (m), 3.17 – 3.11 (m,)) (1H), (2.61 – 2.54 (m), 2.50 – 2.4 (m)) (1H), 2.08 – 1.95 (m, 2H), 1.95 – 1.70 (m, 2H), (1.58 (s), 1.44 (s)) (9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.8, 156.2, 155.4, 147.9, 147.5, 146.0, 145.8, 138.4, 138.3, 137.8, 137.5, 136.1, 134.3, 134.1, 127.8, 127.3, 121.6, 121.5, 121.4, 116.2, 116.0, 109.2, 109.0, 107.9, 100.8, 80.9, 80.4, 71.7, 71.0, 66.7, 63.9, 61.9, 48.5, 47.4, 45.9, 45.5, 31.7, 29.3, 28.5, 28.3, 28.0, 27.6, 27.3, 26.5, 19.3, 13.9. LCMS

(m/z): 490 (M + H^+). Anal. Calcd $C_{28}H_{31}N_3O_5$: C, 68.69; H, 6.38; N, 8.58. Found: C, 68.50; H, 6.50; N, 8.80.

***Tert*-butyl-3-(8-nitroquinolin-3-yl)-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc – 49a)**

Orange oil, yield 40%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.01, 9.82 (s, 1H), (9.31 – 9.25 (m), 9.15 – 9.08 (m)) (1H), 8.64 – 8.43 (m, 2H), 8.37 – 8.25 (m, 1H), 8.10 – 8.04 (m, 1H) 7.99 – 7.81 (m, 2H), 7.56 – 7.39 (m, 3H), 7.39 – 7.30 (m, 1H), (5.71 – 5.55 (m), 5.25 – 5.16(m)) (1H), 4.19 – 3.56 (m, 2H), 3.52 – 3.32 (m, 1H), 2.88 – 2.68 (m, 1H), 2.16 – 2.04 (m, 2H), 2.00 – 1.64 (m, 3H), (1.59 (s), 1.46 (s), (9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.6, 155.8, 154.0, 153.6, 147.6, 138.1, 137.7, 135.7, 134.8, 131.6, 128.4, 127.3, 126.7, 124.6, 124.4, 122.7, 121.1, 115.8, 81.1, 80.5, 64.2, 62.1, 46.7, 45.7, 45.1, 27.9, 27.6, 26.7, 25.9. LCMS (m/z): 542 (M + H^+). Anal. calcd $C_{30}H_{31}N_5O_5$: C, 66.53; H, 5.77; N, 12.93. Found: C, 66.20; H, 5.98; N, 12.59.

***Tert*-butyl-2-(quinolin-8-ylcarbamoyl)-3-(thiophen-2-yl)azepane-1-carboxylate (cis) (Boc - 50a)**

Yellow oil, yield 70%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.05, 9.98 (rotameric singlets, 1H), 8.74 – 8.59 (m, 2H), 8.17 – 8.02 (m, 1H), 7.55 – 7.45 (m, 2H), 7.46 – 7.35 (m, 1H), 7.22 – 7.13 (m, 1H), 7.11 – 7.04 (m, 1H), 6.96 – 6.88 (m, 1H), (5.72 – 5.64 (m), 5.40 – 5.35 (m)) (1H), 3.89 – 3.63 (m, 2H), 3.57 – 3.46 (m, 1H), 2.69 – 2.44 (m, 1H), 2.27 – 2.10 (m, 1H), 2.07 – 1.68 (m, 4H), (1.58 (s), 1.51 (s)) (9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.6, 168.3, 156.3, 155.4, 148.1, 147.3, 136.3, 134.3, 134.1, 127.9, 127.3, 126.7, 126.56, 124.8, 123.6, 121.6, 116.5, 81.1, 80.6, 65.1, 63.0, 46.1, 45.7, 44.5, 44.0, 30.9, 30.6, 28.5, 28.4, 27.1, 26.9, 26.7, 26.4. LCMS (m/z): 452 (M + H^+). Anal. calcd $C_{25}H_{29}N_3O_3S$: C, 66.49; H, 6.47; N, 9.31. Found: C, 66.57; H, 6.68; N, 9.50.

***Tert*-butyl-2-(quinolin-8-ylcarbamoyl)-3-(thiophen-2-yl)azepane-1-carboxylate (diastereomeric mixture) (Boc - 50a)**

Yellow oil, yield 70%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.34, 10.05, 9.97 (rotameric singlets, diastereomeric mixture, 1H), 8.80 – 8.64 (m, 2H), 8.16 – 8.03 (m, 1H), 7.58 – 7.42 (m, 2H), 7.41 – 7.33 (m, 1H), (7.20 – 7.15 (m), 7.14 – 7.06 (m), 7.02 – 6.93 (m), 6.90 – 6.81 (m)) (3H), (5.77 – 5.67 (m), 5.45 – 5.33 (m), 5.24 – 5.14 (m), 4.97 – 4.86 (m)) (1H), 4.07 – 3.82 (m, 1H), 3.79 – 3.65 (m, 1H), (3.60 – 3.46 (m), 3.23 – 3.05 (m)) (1H), (2.67 – 2.45 (m), 2.30 – 2.14 (m)) (2H), 2.12 – 1.69 (m, 4H), (1.67 (s,), 1.60 (s), 1.54 (s), 1.52 (s)) (9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.8, 169.2, 168.5, 168.2, 156.3, 155.3, 154.4, 148.2, 148.1, 147.8, 147.2, 138.6, 138.4, 136.2, 136.2, 135.9, 134.8, 134.5, 134.2, 127.9, 127.3, 127.0, 126.7, 126.6, 124.8, 124.2, 124.1, 123.6, 123.4, 121.7, 121.5, 116.6, 116.4, 81.3, 81.1, 80.6, 65.9, 65.2, 64.4, 63.0, 46.0, 45.8, 44.5, 44.4, 44.0, 42.2, 35.2, 35.1, 30.9, 30.6, 29.2, 28.9, 28.5, 28.4, 28.1, 27.1, 26.9, 26.7, 26.4. LCMS (m/z): 452 (M + H^+). Anal. calcd $C_{25}H_{29}N_3O_3S$: C, 66.49; H, 6.47; N, 9.31. Found: C, 66.63; H, 6.37; N, 9.20.

***Tert*-butyl-3-(pyridin-2-yl)-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Boc – 51a)**

Brown oil, yield 83%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.00, 9.79, 9.66, 9.38 (rotameric peaks, diastereomeric mixture, 1H), 8.73 – 8.57 (m, 1H), 8.56 – 8.25 (m, 1H), 8.02 (d, *J* = 7.9 Hz, 1H), 7.60 – 7.35 (m, 4H), 7.32 – 7.12 (m, 3H), (6.25 – 6.19 (m), 6.20 – 6.15 (m), 6.10 – 6.02 (m)) (1H), (5.54 – 5.48 (m), 5.21 – 5.11 (m), 5.05 – 4.99 (m), 4.91 – 4.83 (m)) (1H), (4.26 – 4.16 (m), 3.98 – 3.77 (m)) (1H), (3.70 – 3.59 (m), 3.57 – 3.48 (m)) (1H), 3.43 – 3.14 (m, 1H), 2.73 – 2.45 (m, 1H), 2.15 – 1.88 (m, 3H), 1.86 – 1.64 (m, 1H), (1.62 (s), 1.52 (s), 1.40 (s)) (9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.2, 168.5, 155.9, 154.9, 154.7, 153.1, 147.2, 137.5, 137.1, 135.3, 133.7, 128.9, 128.8, 128.7, 127.2, 126.6, 126.5, 123.3, 123.1, 120.8, 120.7, 119.4, 119.2, 118.7, 115.6, 115.4, 109.7, 109.6, 102.2, 102.1, 80.4, 79.9, 66.7, 64.5, 63.8, 50.3, 48.1, 46.9, 45.4, 44.9, 44.0, 40.5, 29.1, 28.3, 28.0, 27.8, 27.3, 26.9, 26.2, 13.5. LCMS (m/z): 447 ($M + H^+$). Anal. calcd $C_{26}H_{30}N_4O_3$: C, 69.93; H, 6.77; N, 12.55. Found: C, 69.60; H, 6.90; N, 12.80.

Benzyl-3-(pyridin-3-yl)-2-(quinolin-8-ylcarbamoyl)azepane-1-carboxylate (Cbz – 52a)

Light brown oil, yield 60%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.11, 9.96, 9.92, 9.83 (rotameric singlets, diastereomeric mixture, 1H), 8.79 – 8.68 (m, 1H), 8.66 – 8.46 (m, 2H), 8.43 – 8.29 (m, 1H), 8.12 – 7.98 (m, 1H), (7.68 (d, *J* = 7.9 Hz), 7.58 (d, *J* = 7.9 Hz) (1H), 7.48 – 7.39 (m, 3H), 7.39 – 7.30 (m, 3H), 7.29 – 7.04 (m, 3H), 5.46 – 5.18 (m, 2H), (5.05 (d, *J* = 10.8 Hz), 4.86 (d, *J* = 10.5 Hz) (1H), 4.17 – 3.87 (m, 1H), 3.64 – 3.45 (m, 1H), 3.40 – 3.14 (m, 1H), 2.08 – 1.83 (m, 3H), 1.82 – 1.44 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 157.1, 155.3, 149.8, 149.5, 149.2, 148.4, 147.9, 140.1, 138.5, 136.5, 136.1, 135.9, 135.5, 134.3, 128.5, 128.1, 127.8, 127.1, 127.0, 123.7, 123.2, 121.8, 121.5, 116.6, 116.3, 67.8, 65.7, 65.3, 45.0, 44.9, 44.7, 44.3, 33.7, 29.3, 29.1, 28.3, 27.4. Anal. Calcd: $C_{29}H_{28}N_4O_3$; HRMS (m/z): Calculated [$M+H^+$] = 481.2234. Found [$M+H^+$] = 481.2201 (error = 6.86 ppm). Calculated [$M+Na^+$] = 503.2054; Found [$M+Na^+$] = 503.2008 (error = 9.14 ppm).

1-(*Tert*-butoxycarbonyl)-3-phenylazepane-2-carboxylic acid (Boc – 53)

White solid, m.p 89 – 88 ^{o}C, yield 51%. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.33 (m, 1H), 7.33 – 7.27 (m, 3H), 7.23 – 7.15 (m, 1H), (5.33 – 5.24 (m), 4.88 – 4.84 (m)) (1H), (4.03 – 3.88 (m), 3.71 – 3.58 (m)) (1H), 3.55 – 3.38 (m, 1H), 3.26 – 3.04 (m, 1H), 2.38 – 2.12 (m, 1H), 2.08 – 1.85 (m, 3H), 1.72 – 1.54 (m, 1H), (1.50 (s), 1.45 (s)) (9H), 1.42 – 1.36 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.3, 175.6, 156.1, 155.0, 143.1, 142.7, 128.3, 128.2, 128.0, 126.6, 126.3, 80.9, 80.6, 64.4, 62.6, 48.1, 47.0, 45.9, 45.1, 29.5, 28.7, 28.4, 27.5, 27.0, 26.8. LCMS (m/z): 318 ($M-H^-$). Anal. calcd $C_{18}H_{25}NO_4$: C, 67.69; H, 7.89; N, 4.39. Found: C, 67.40; H, 7.99; N, 4.55.

Comments on determination of cis/trans ratio for derivatives of 7-, 8-membered cyclic amino acids in diastereomeric mixtures:

The cis/trans assignment was based on the integration of 2-CH proton (α-CH) as a diagnostic signal in ^{1}H NMR. The signal is usually shifted to the lower field - 4.5-5.5 ppm - compared to other aliphatic protons and is easily recognized therefore. Due to the presence of NCbz rotamers, it is commonly found as 2 signals in a case of a single diastereomer.

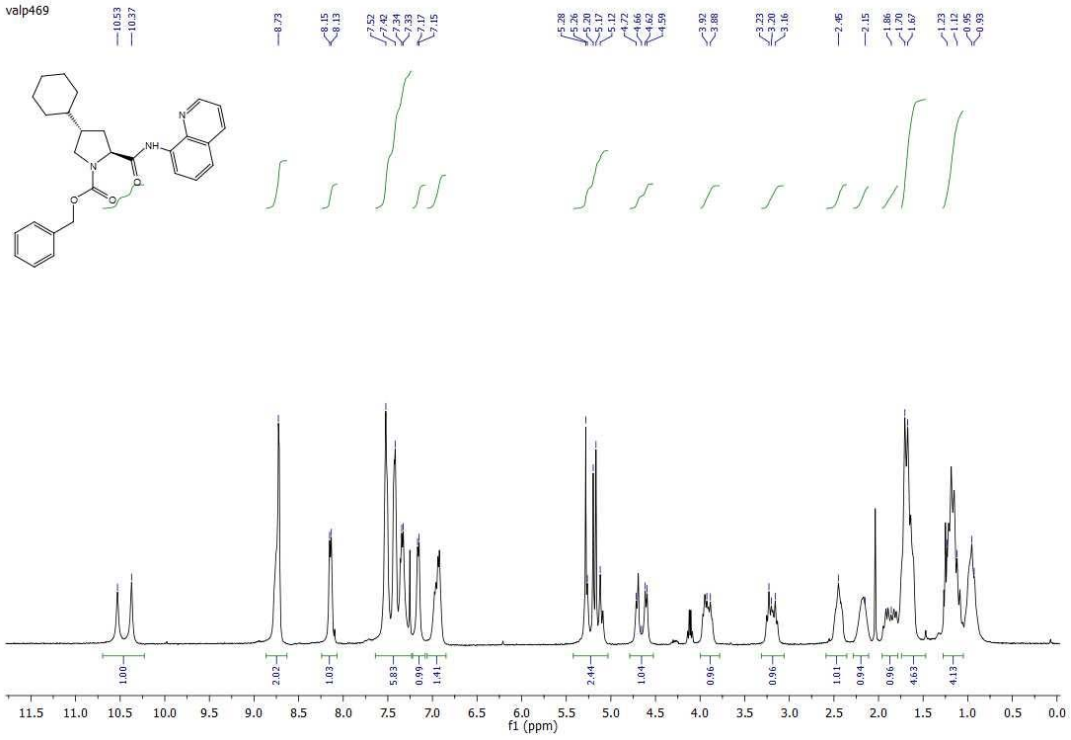
Cis-isomers: 2 broad singlets;

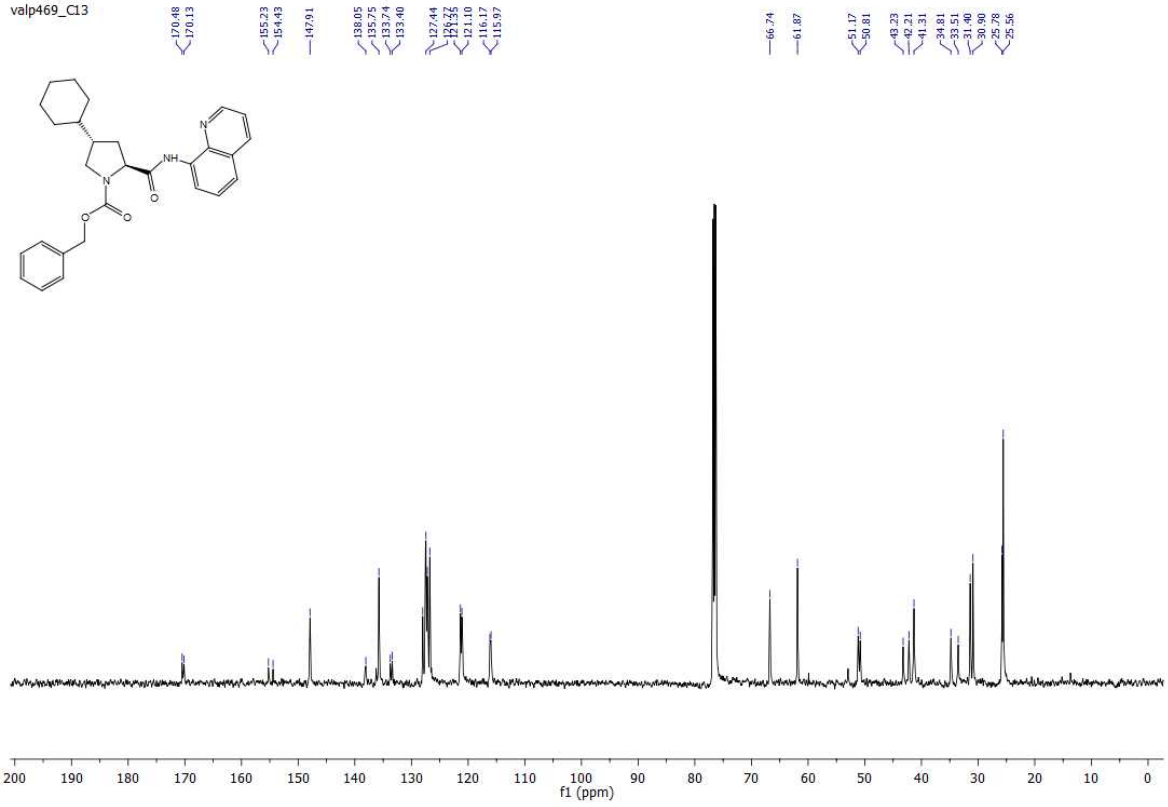
Trans-isomers: 2 doublets, J = 11 Hz.

For representative compounds **Cbz-29a**, **Boc-35a**, **Boc-37a**, **Boc-47a**, additional 2D-NMR experiments were measured to prove the assignment.

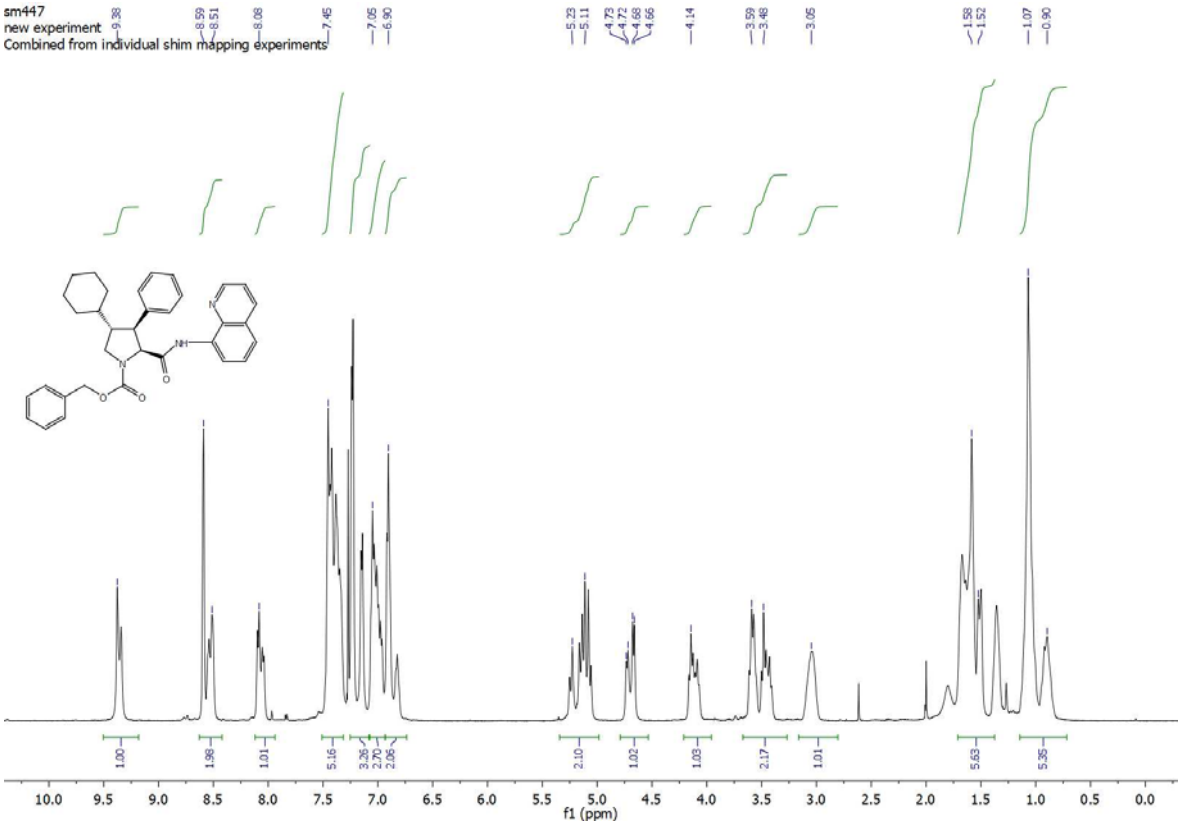
(C) Copies of ^{1}H and ^{13}C NMR spectra

Compound Cbz - 1





Compound 1a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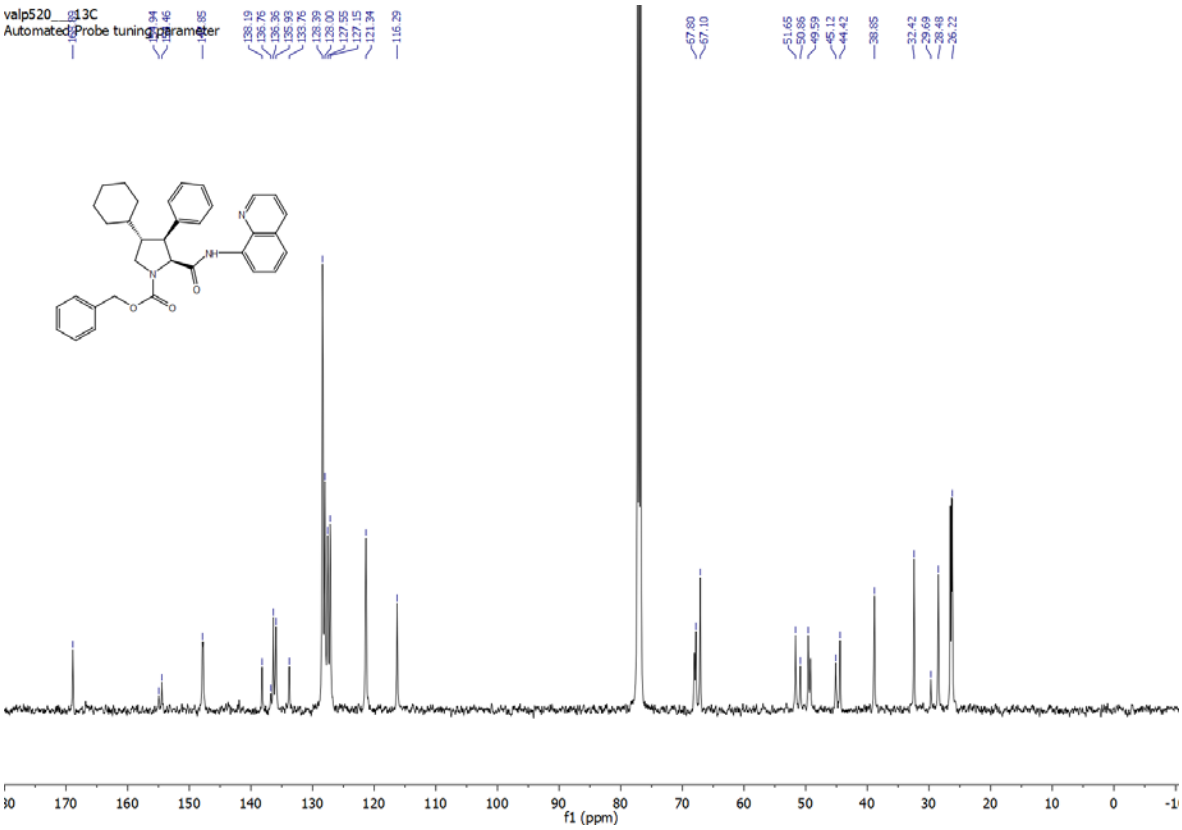
Combined from individual shim mapping experiments
f1 (ppm)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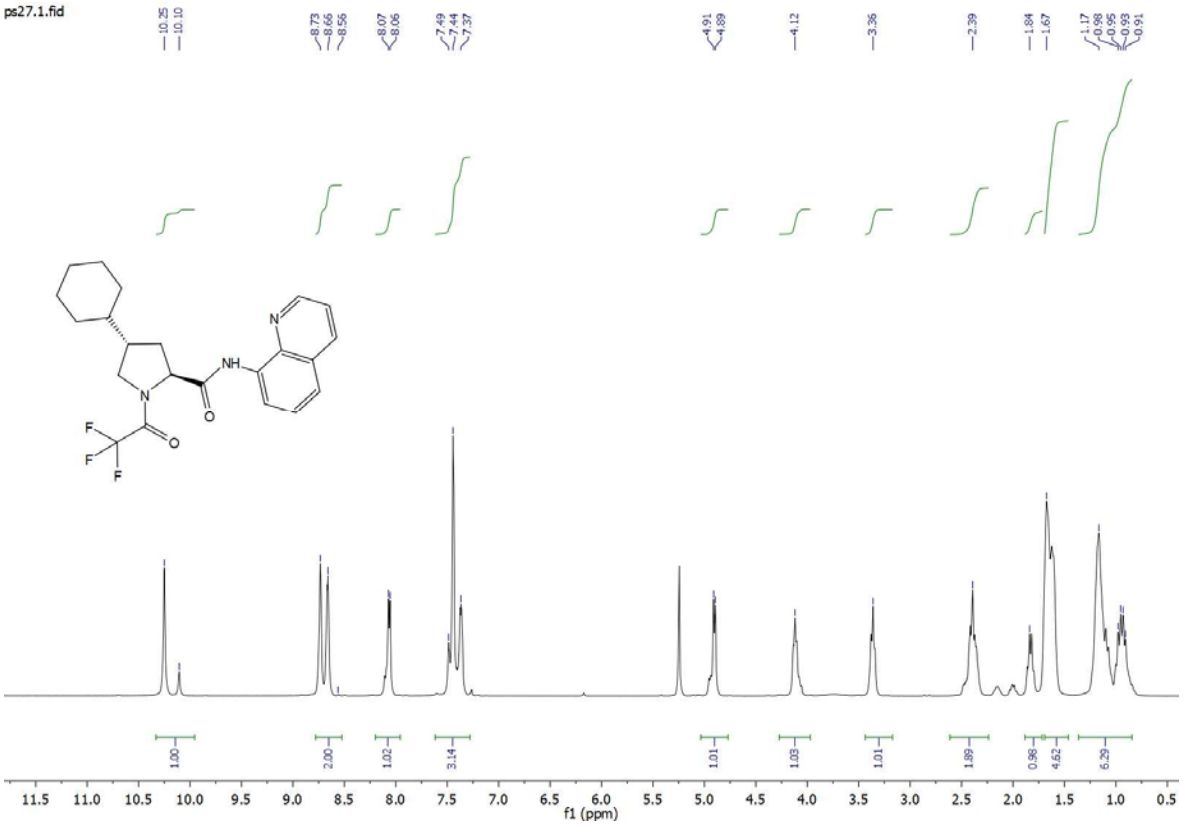
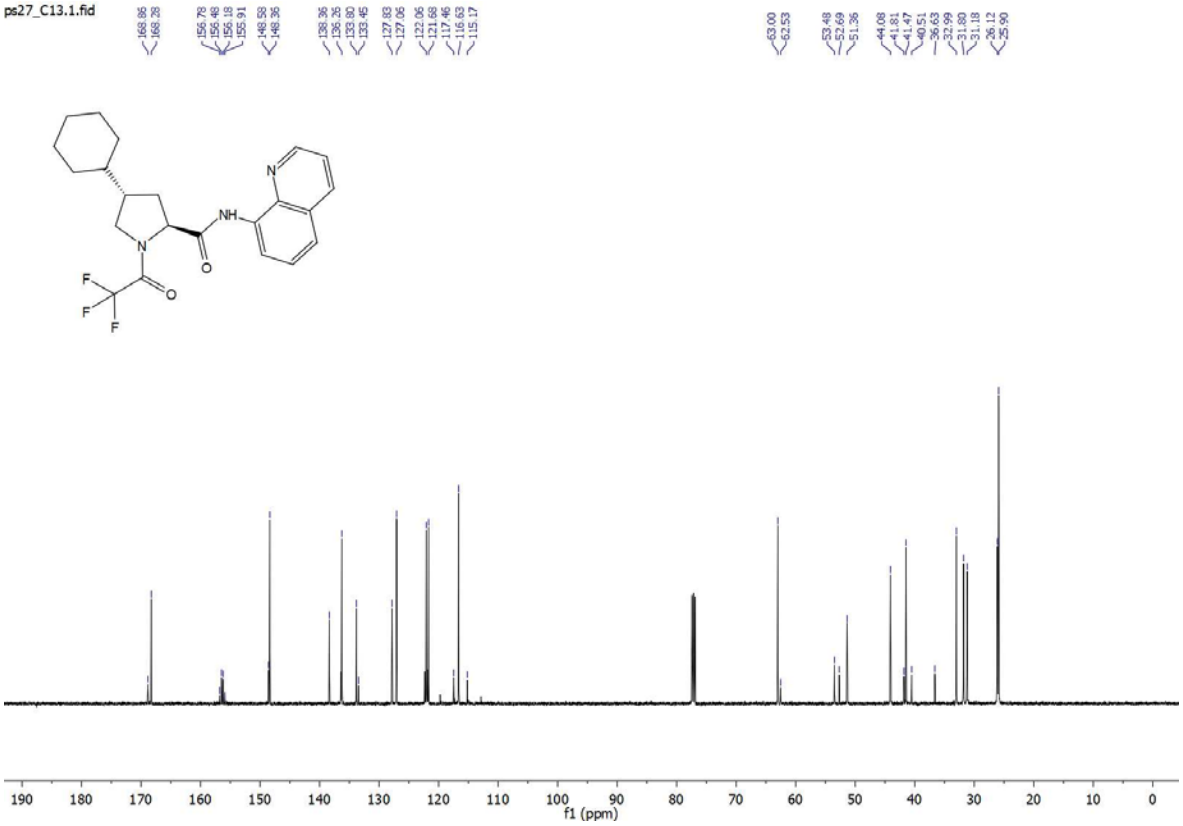
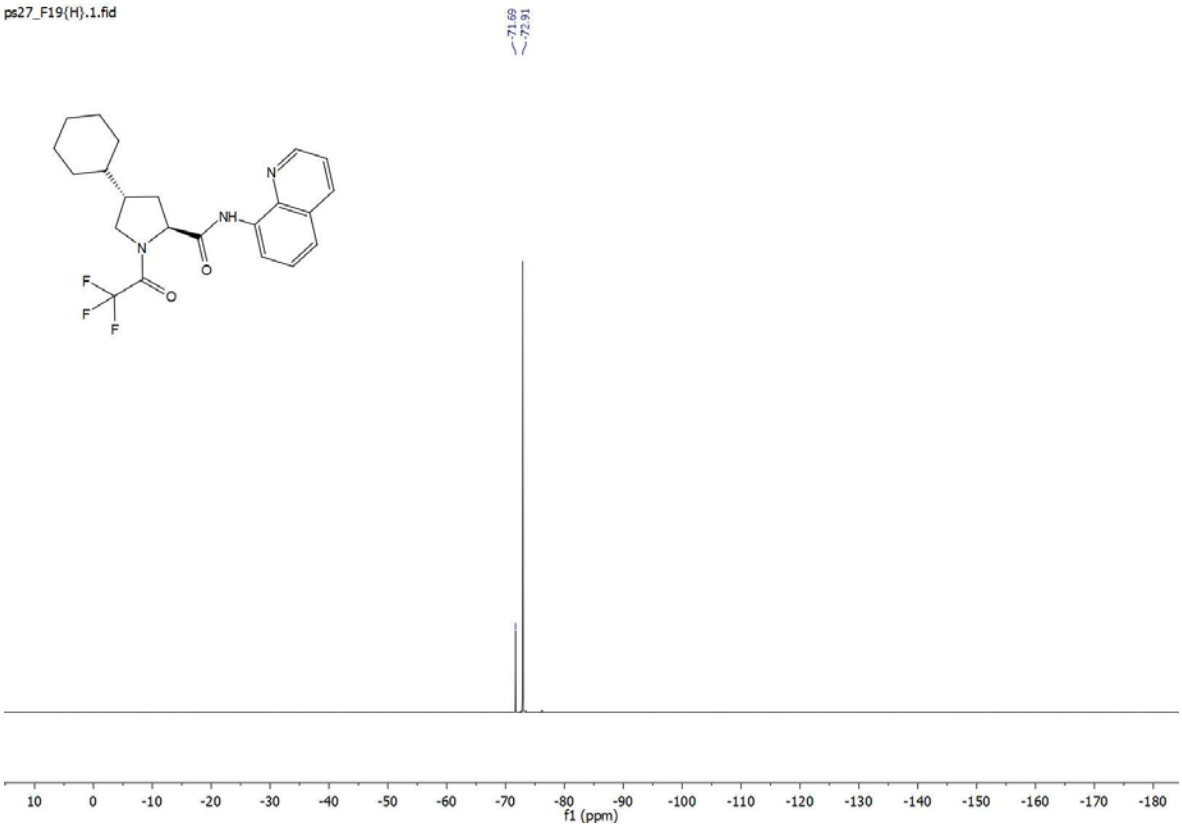
Compound TFA – 1



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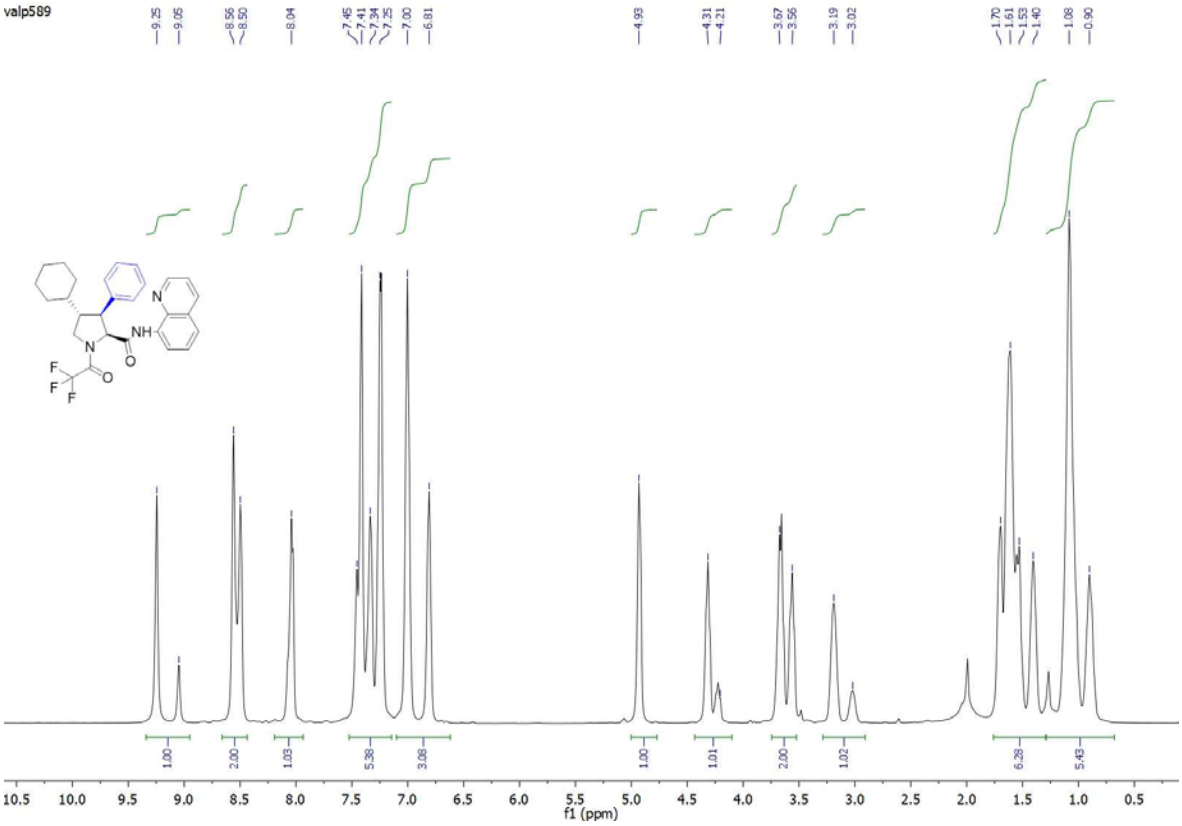
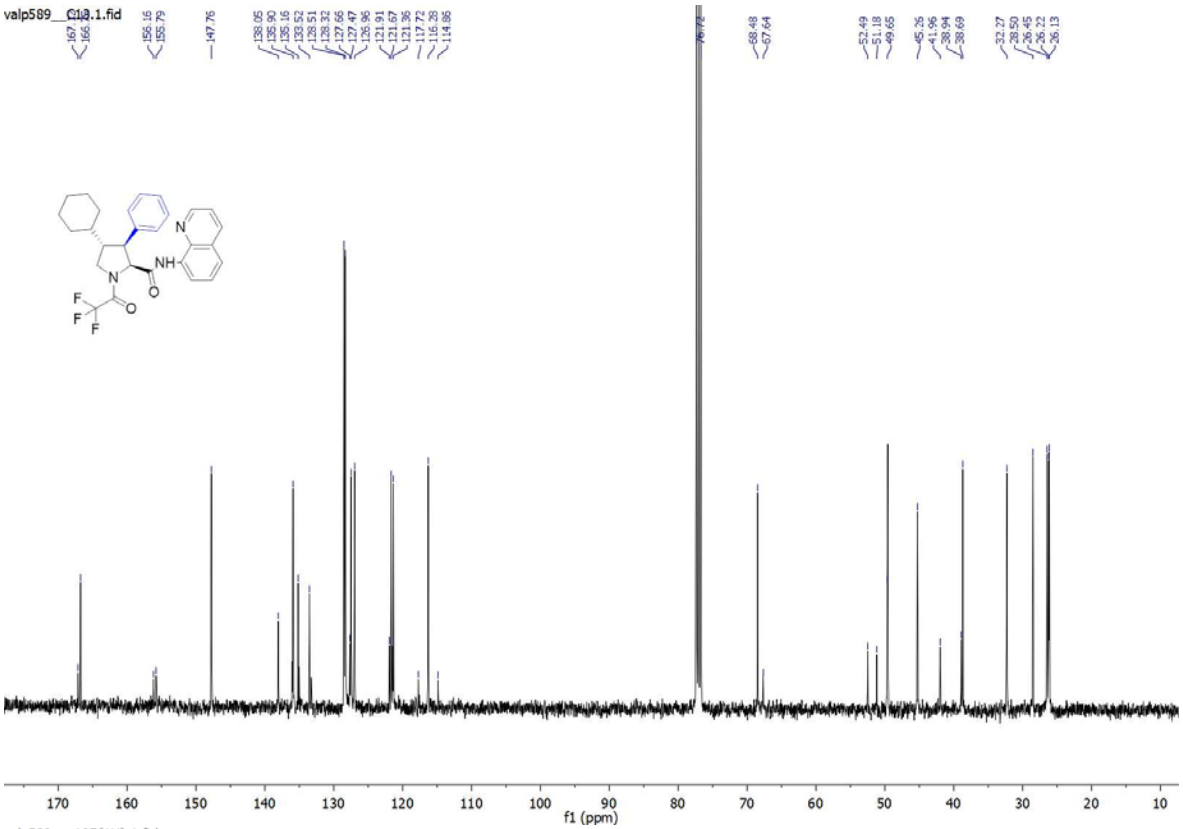
f1 (ppm)

Compound TFA - 1a

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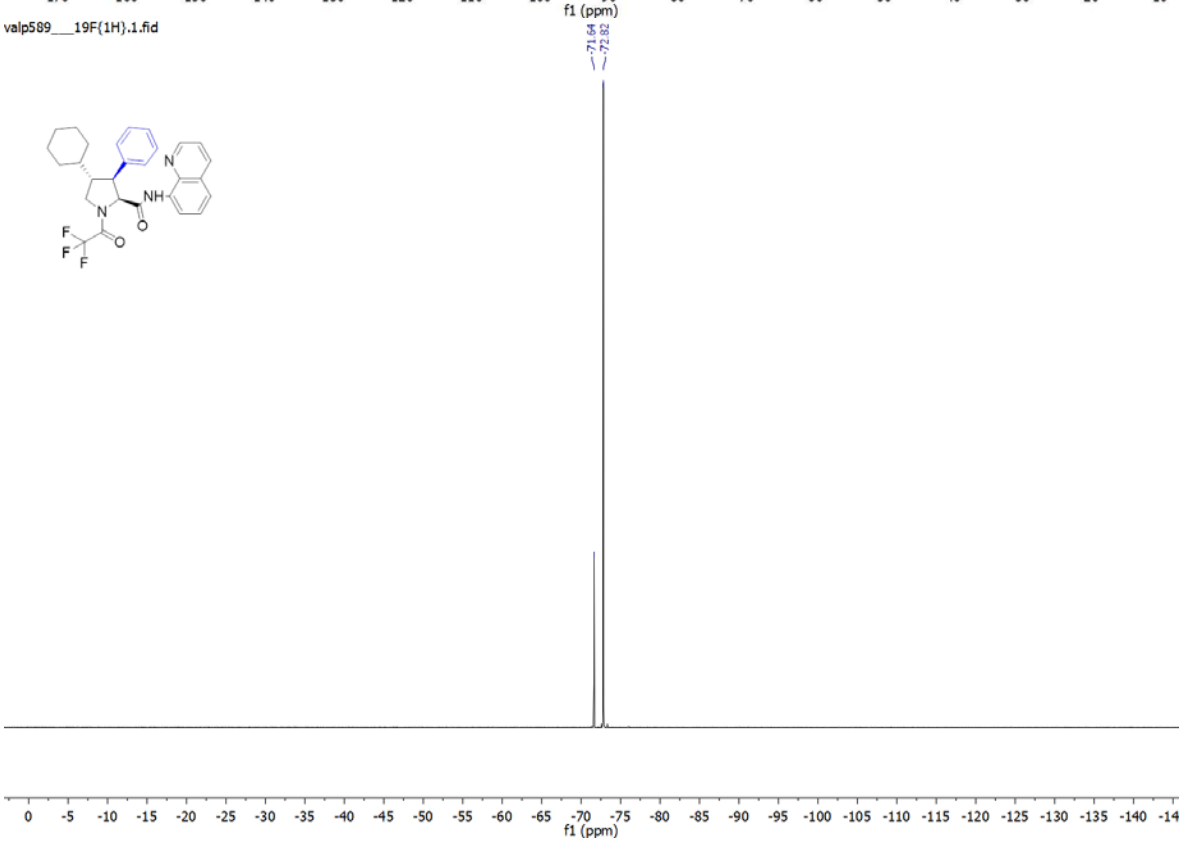
f1 (ppm)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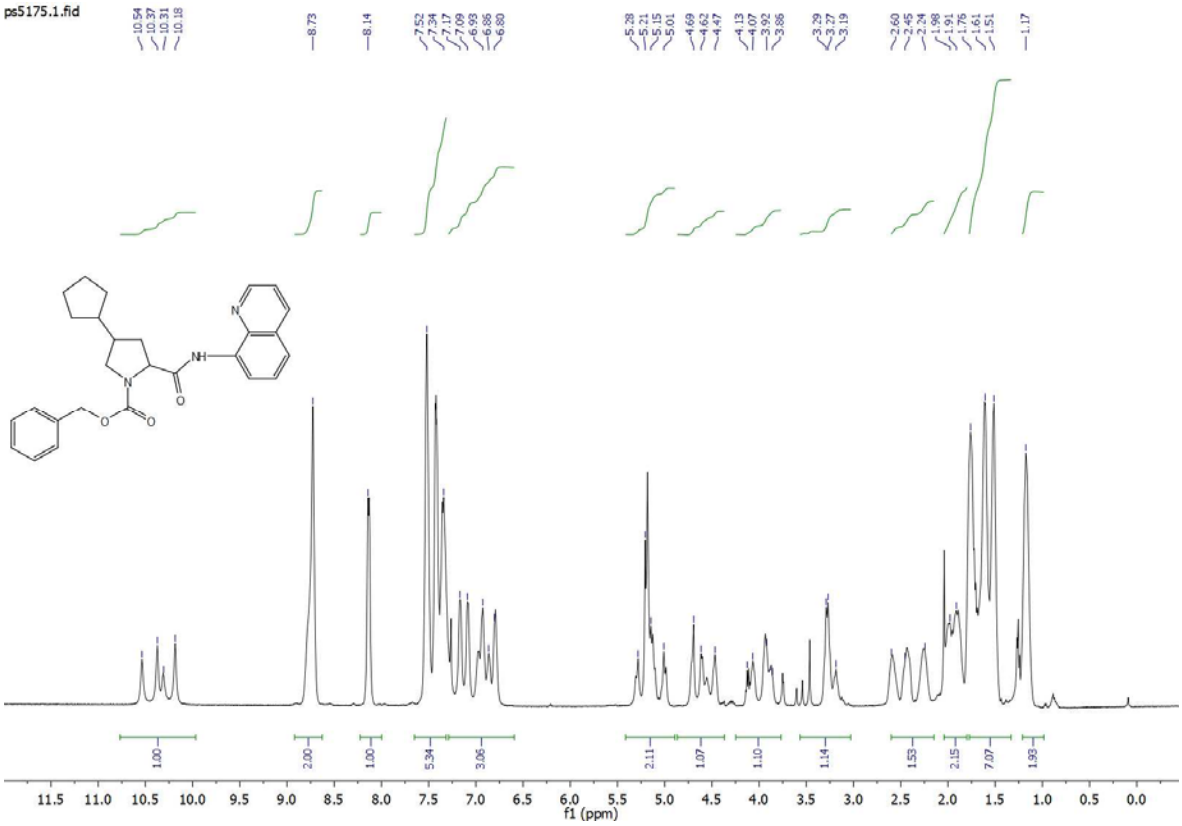
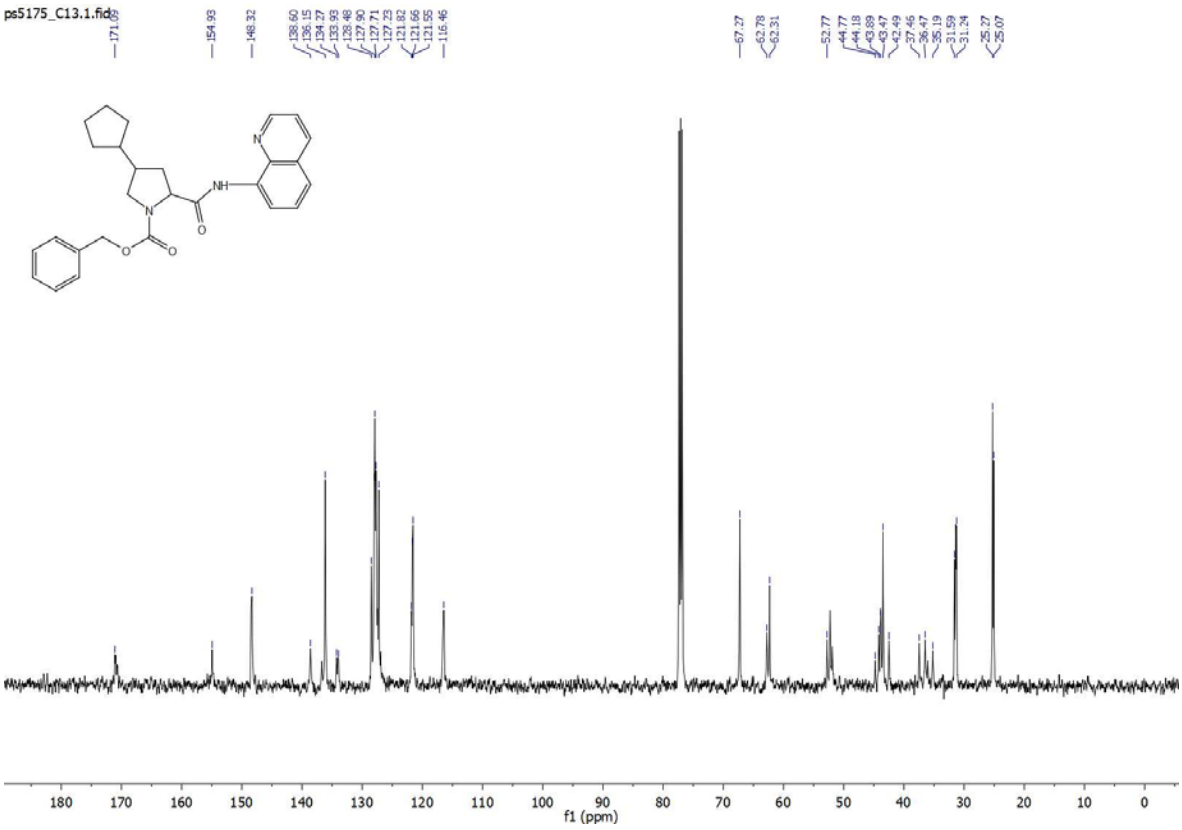
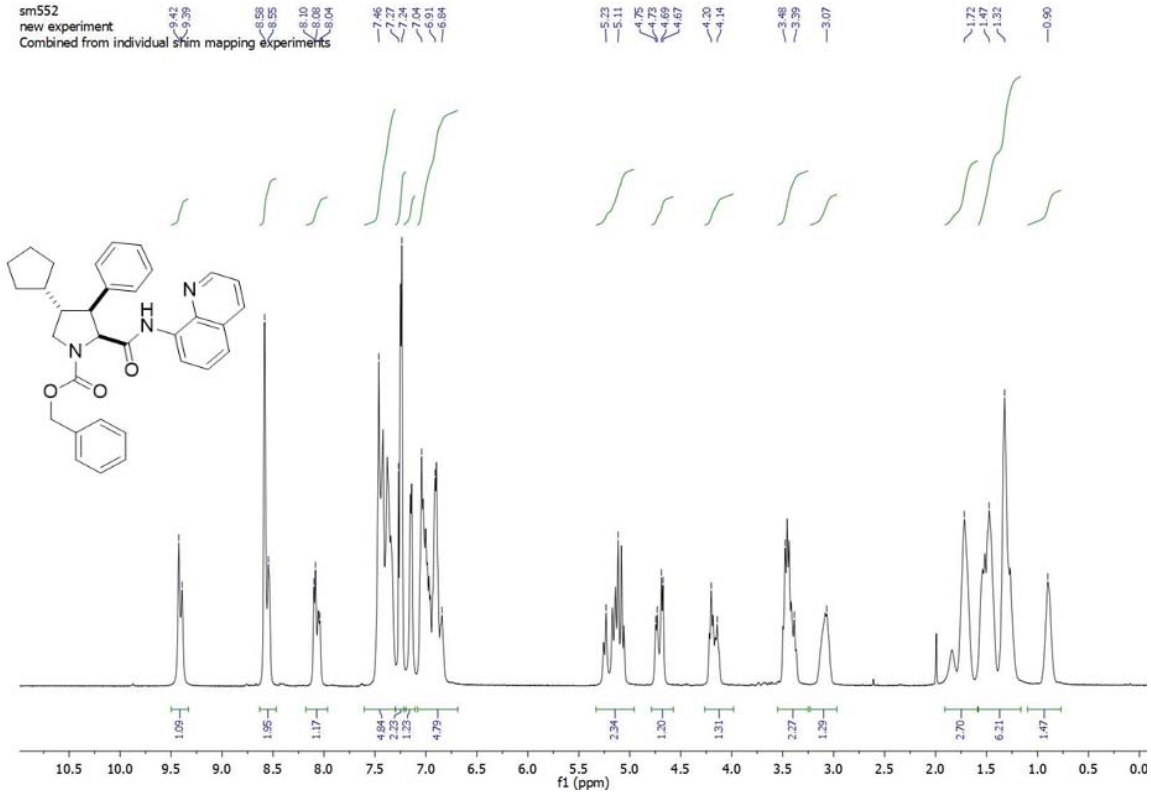
f1 (ppm)

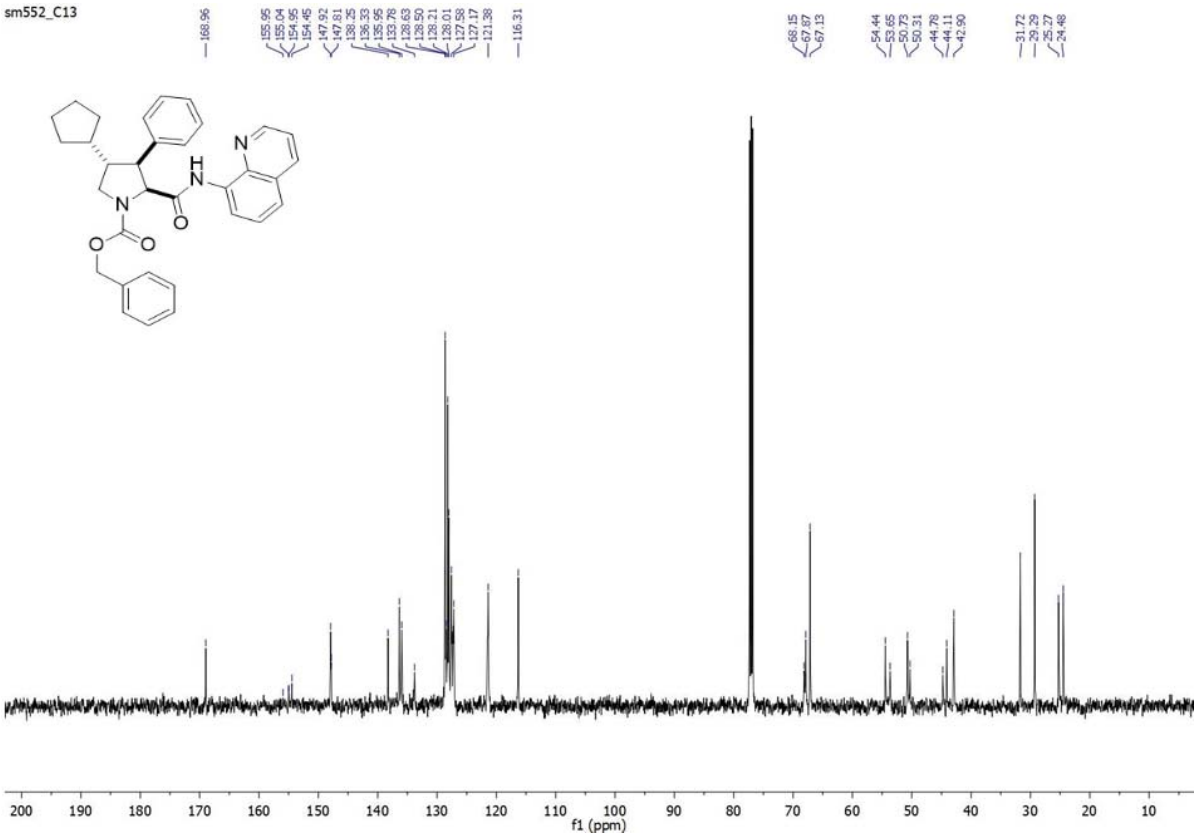
Compound Cbz – 2



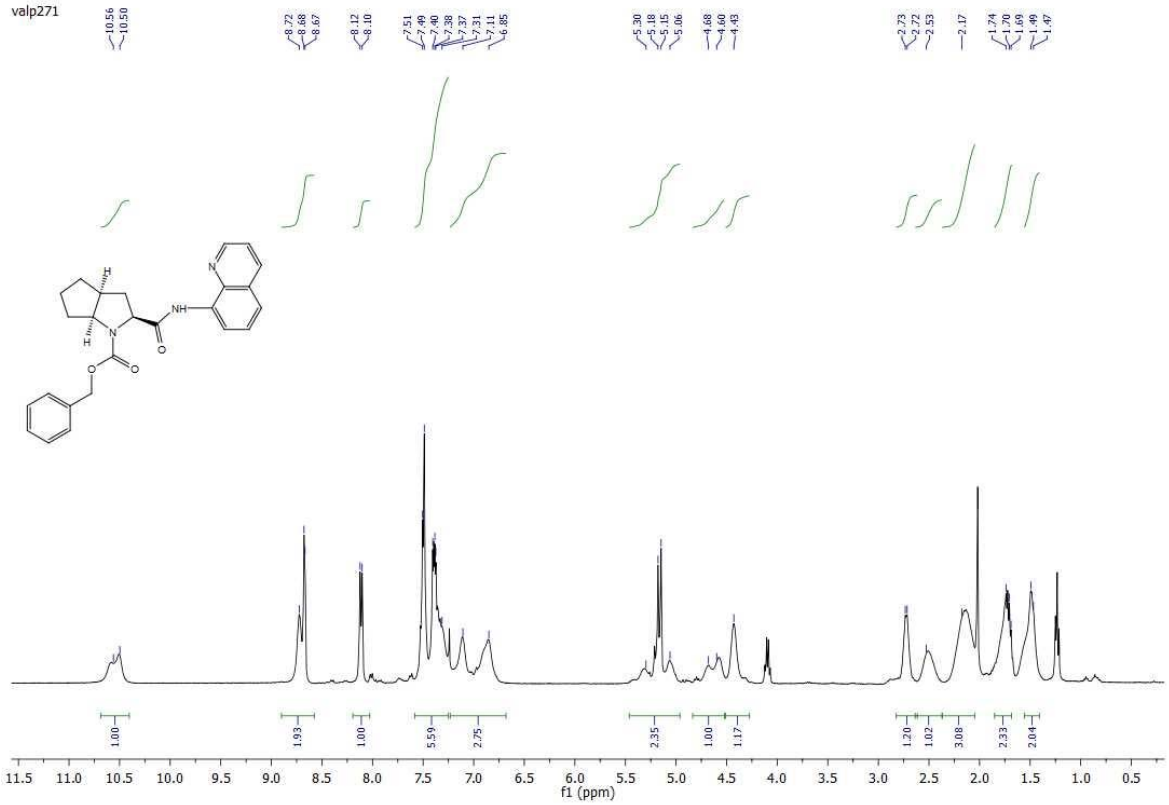


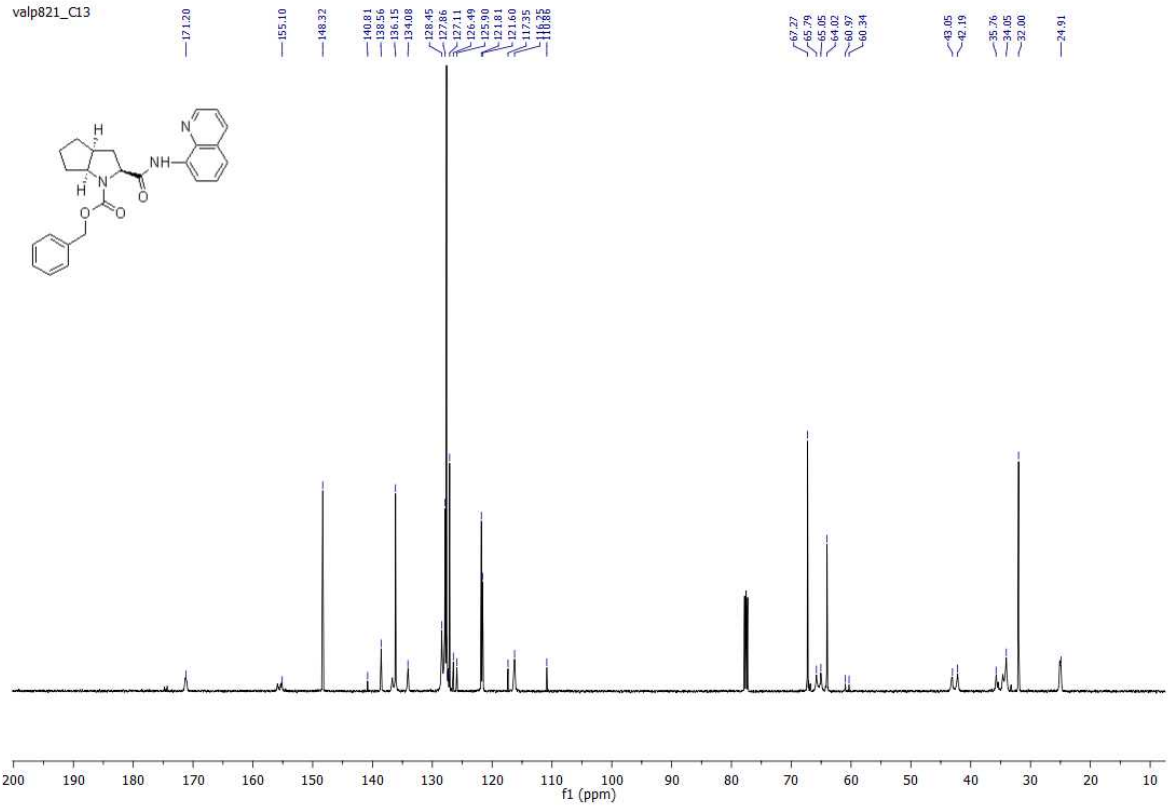
Compound Cbz – 2a



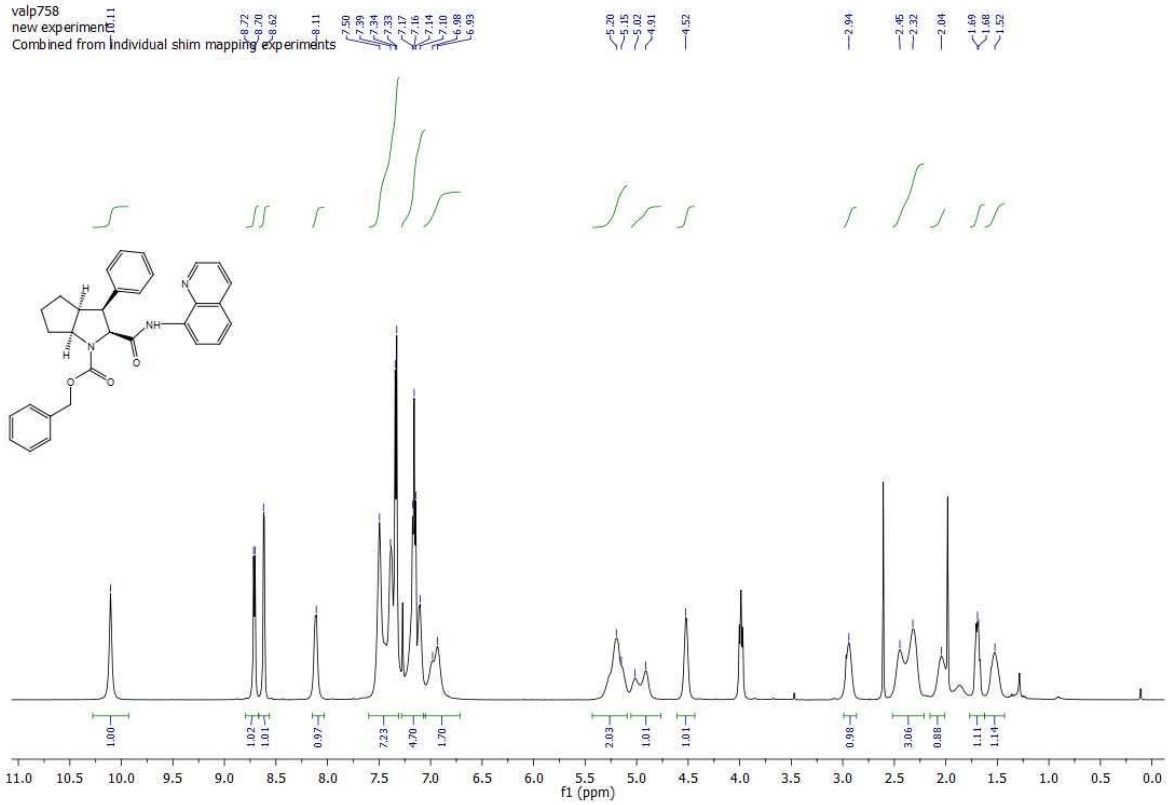


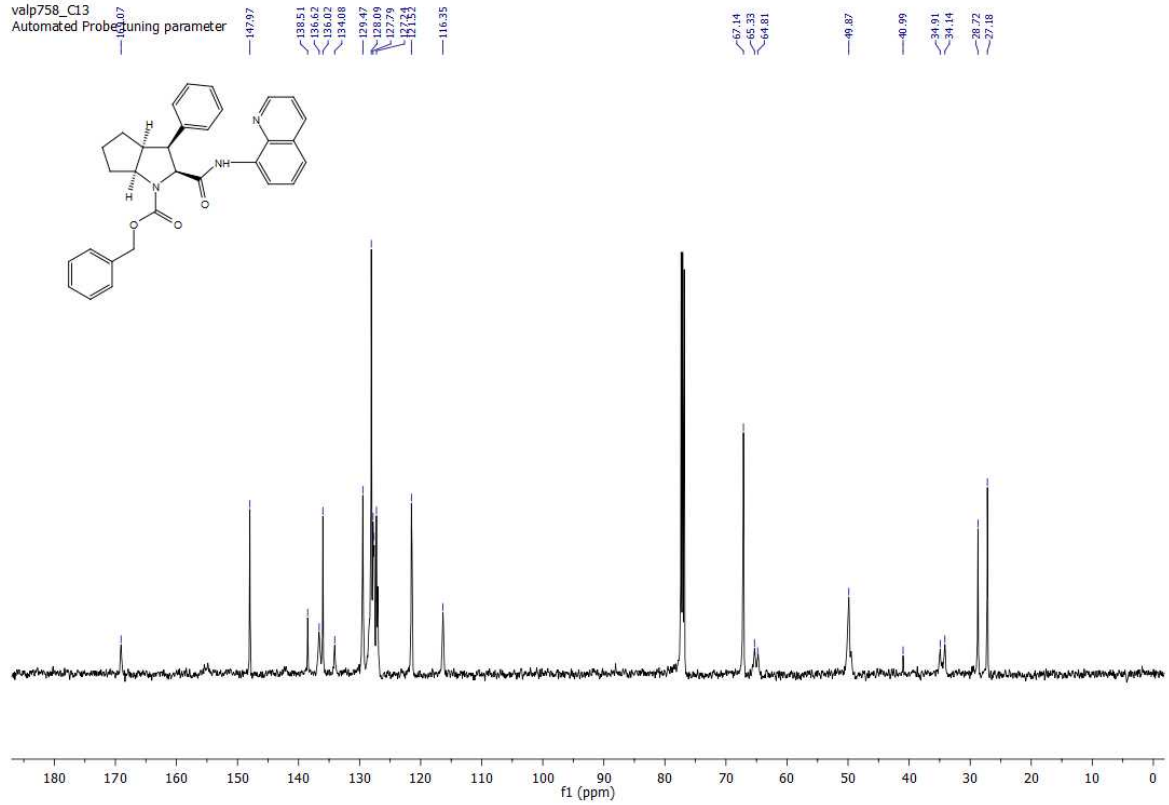
Compound Cbz– 3



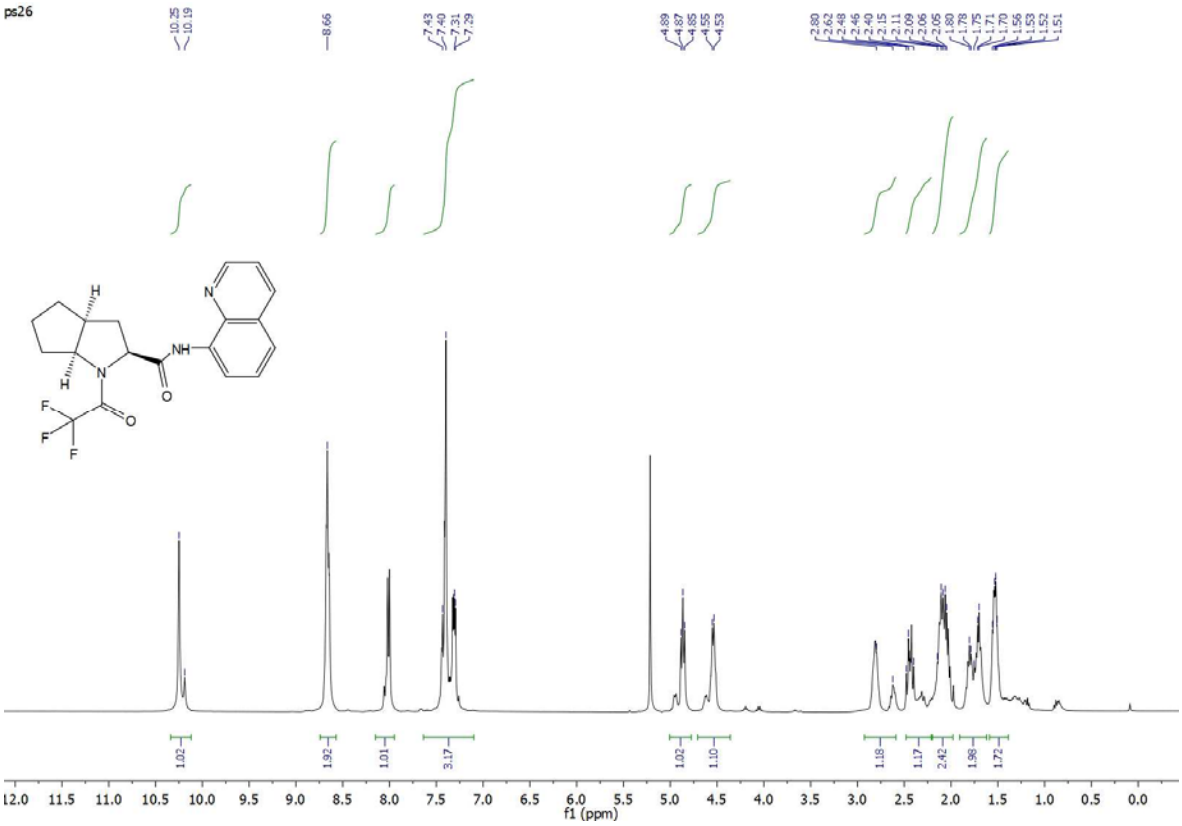


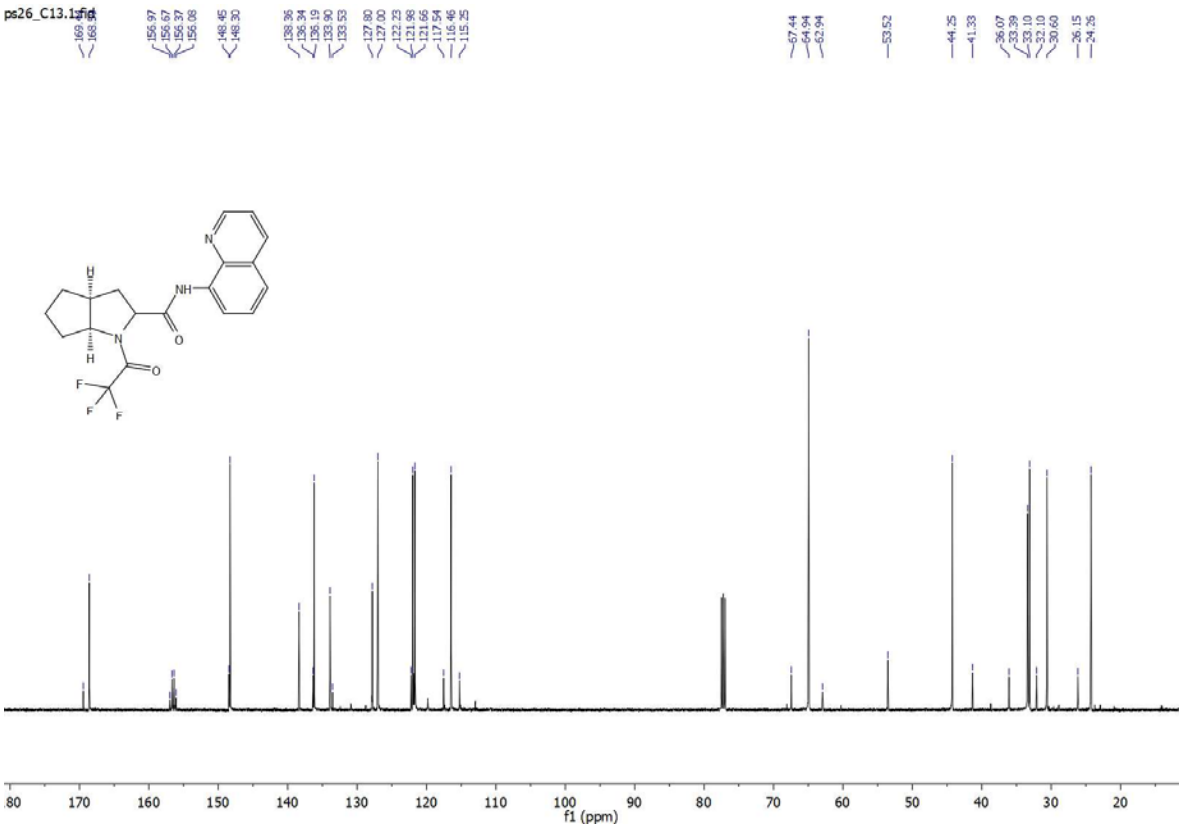
Compound Cbz – 3a

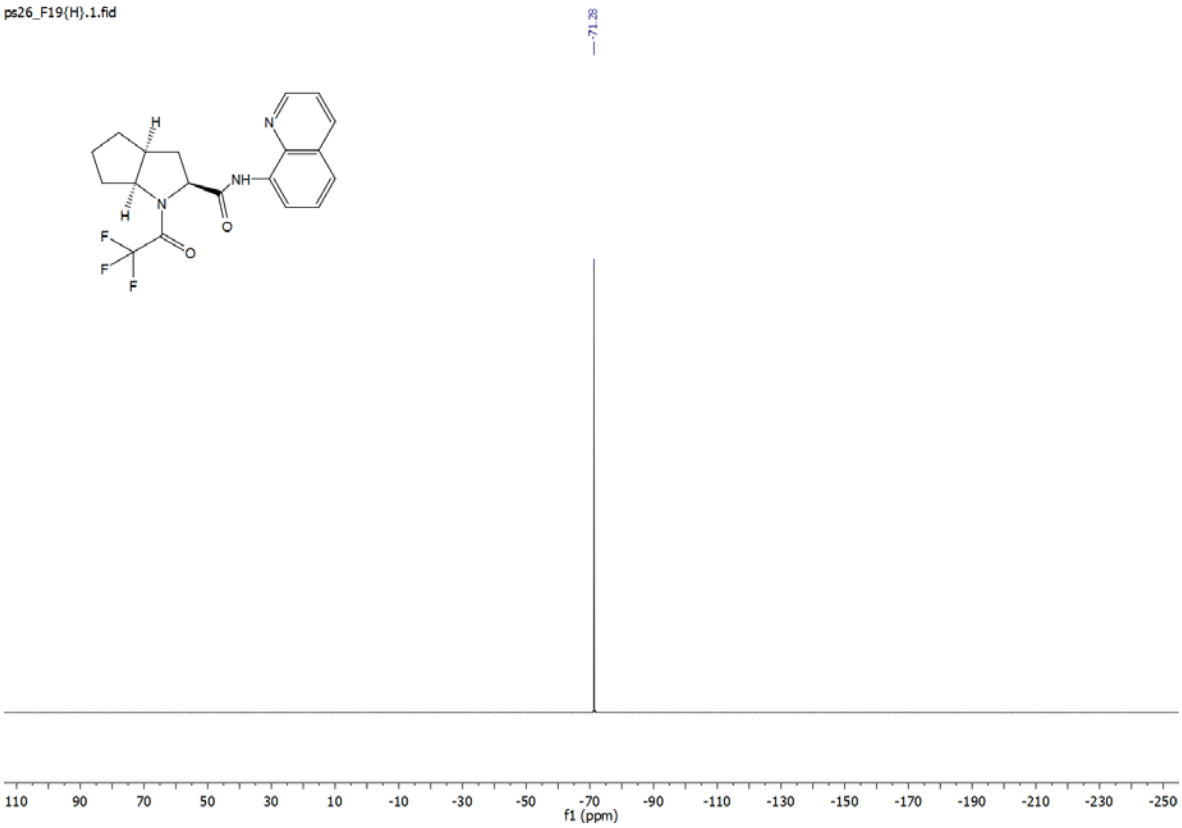




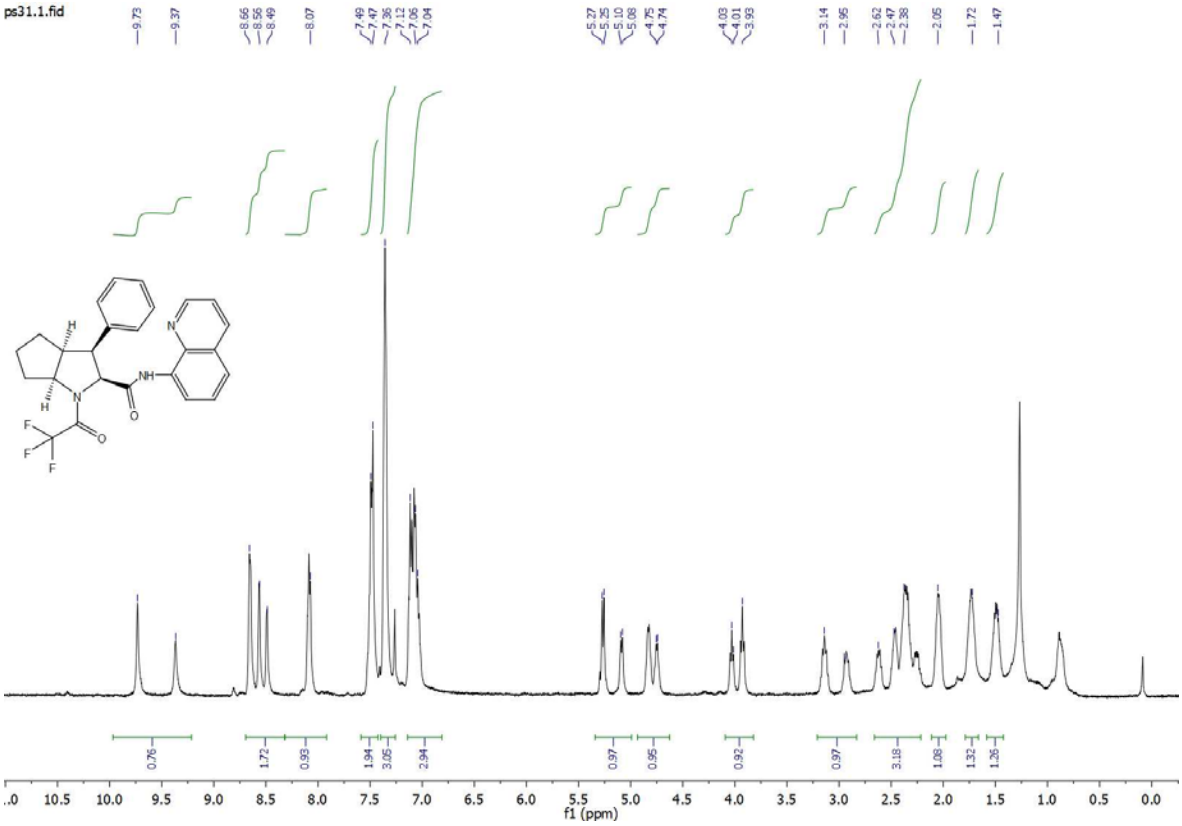
Compound TFA– 3

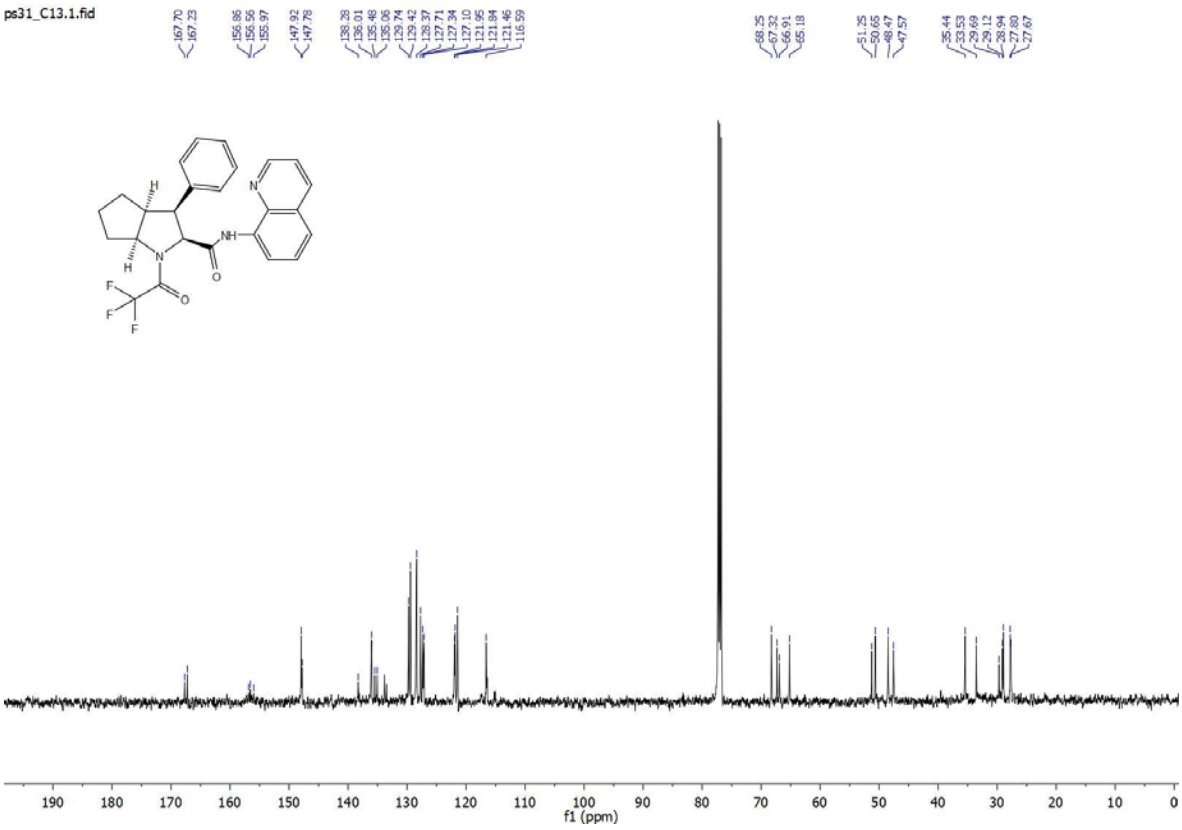




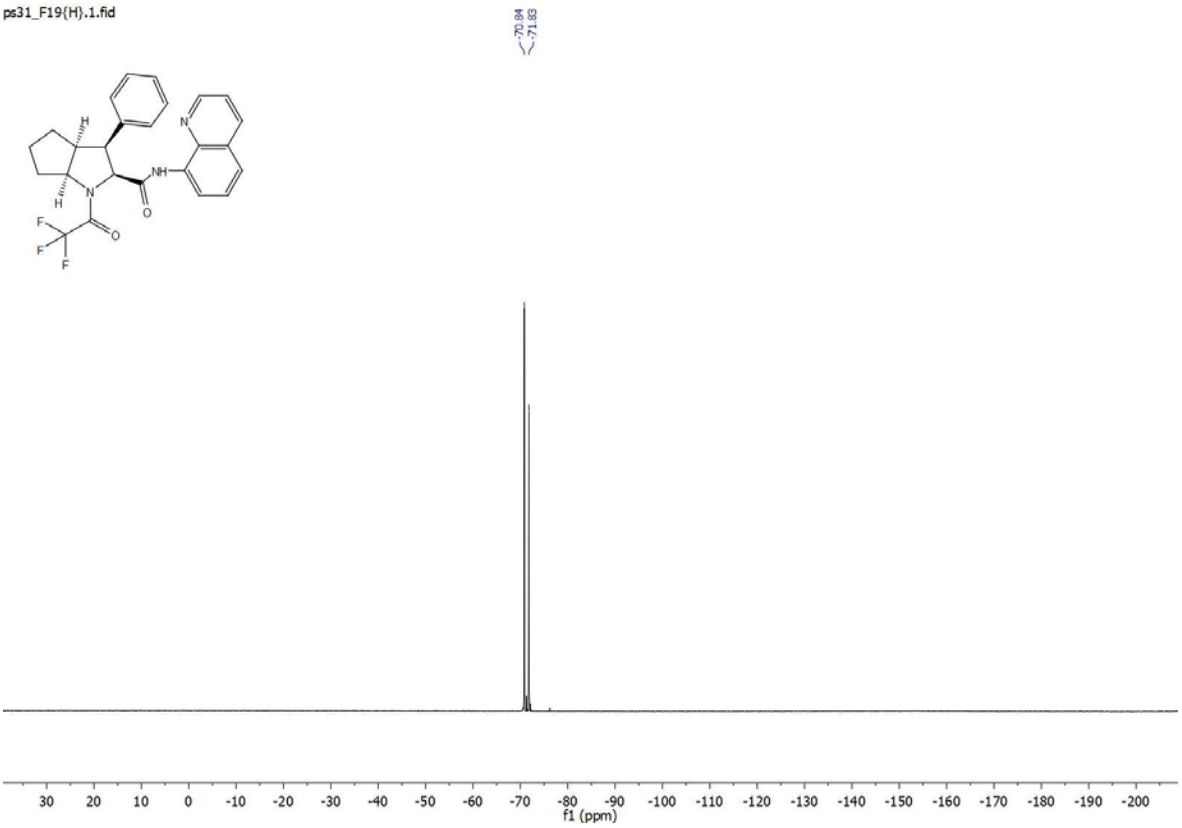

ps26_F19{H}.1.fid
-71.28
H
N
NH
O
H
N
F
F
F
O
110
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
-230
-250
f1 (ppm)

Compound TFA– 3a

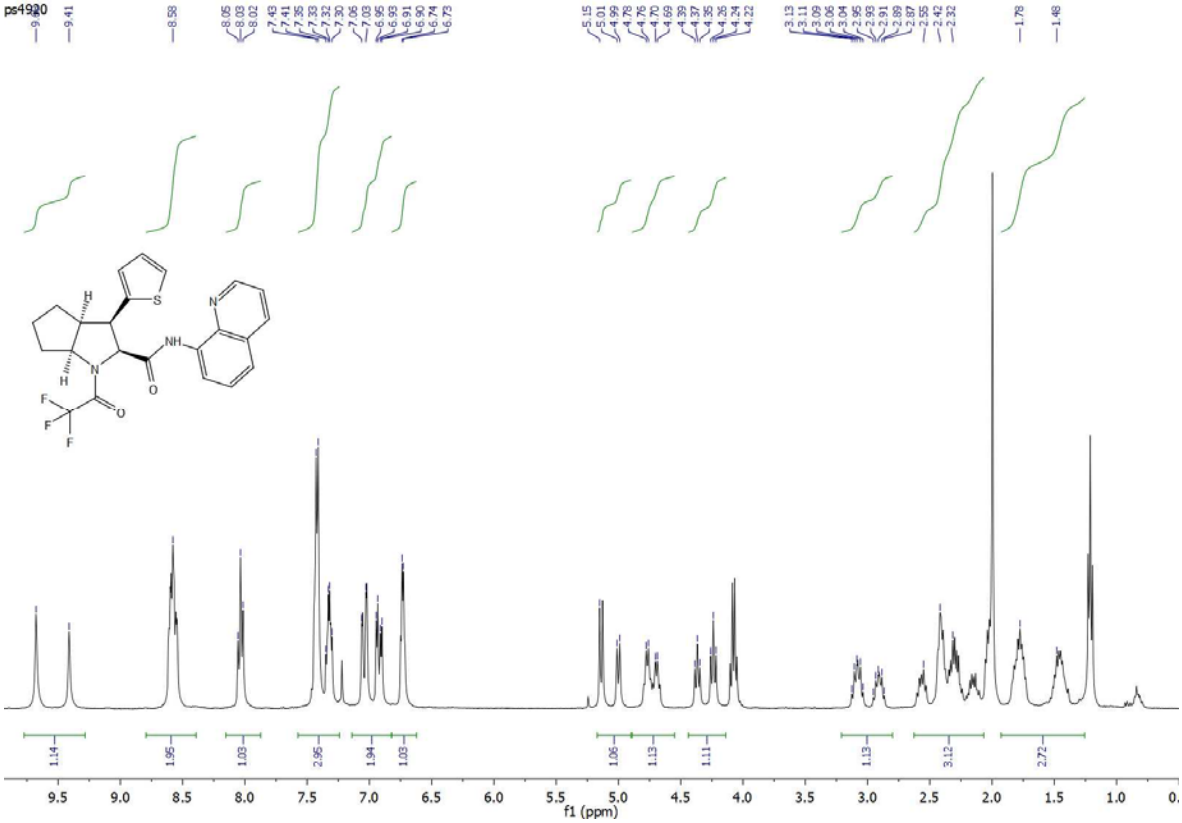


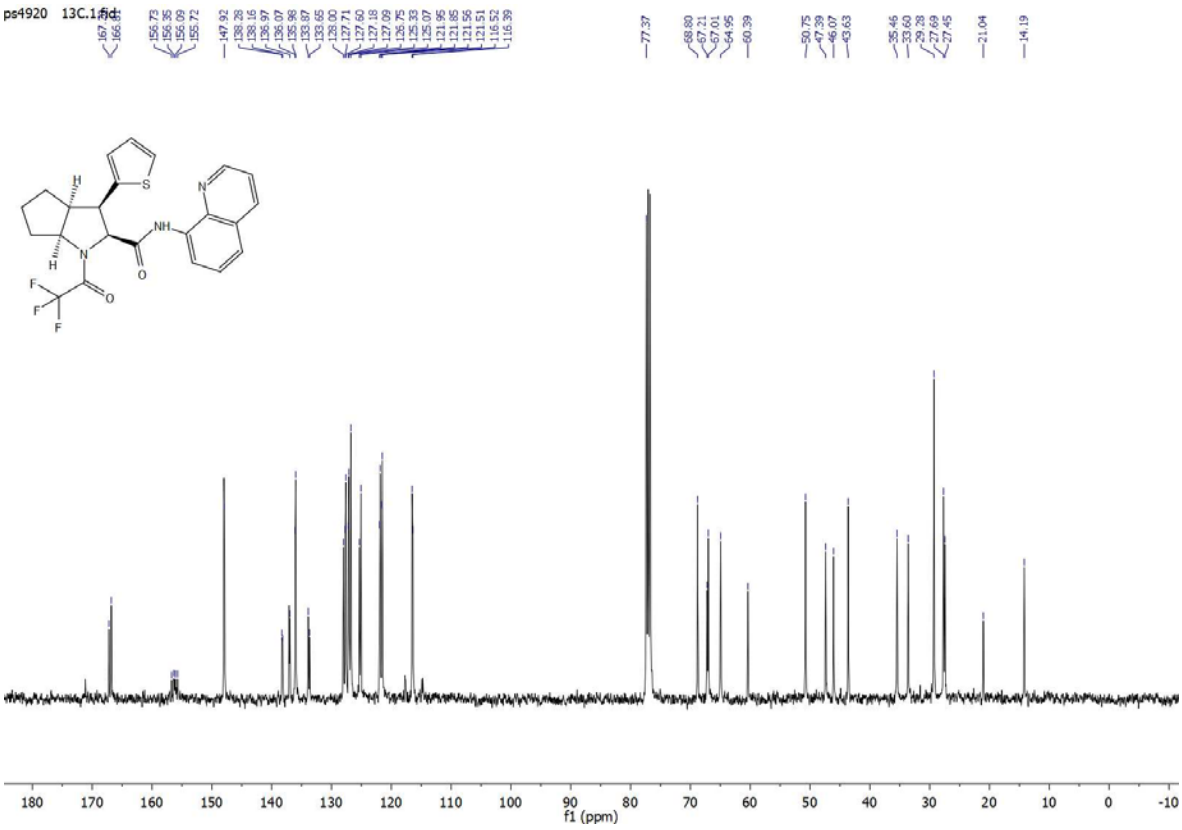


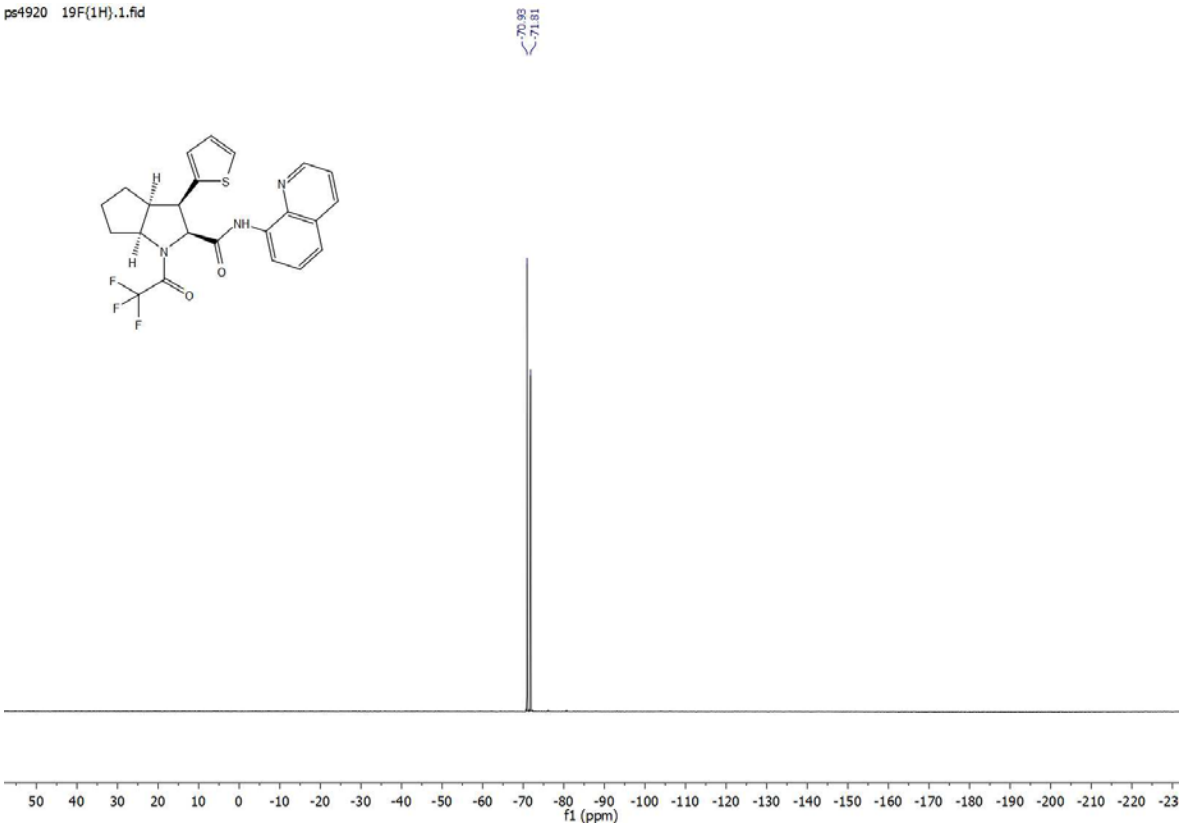
ps31_F19{H}.1.fid



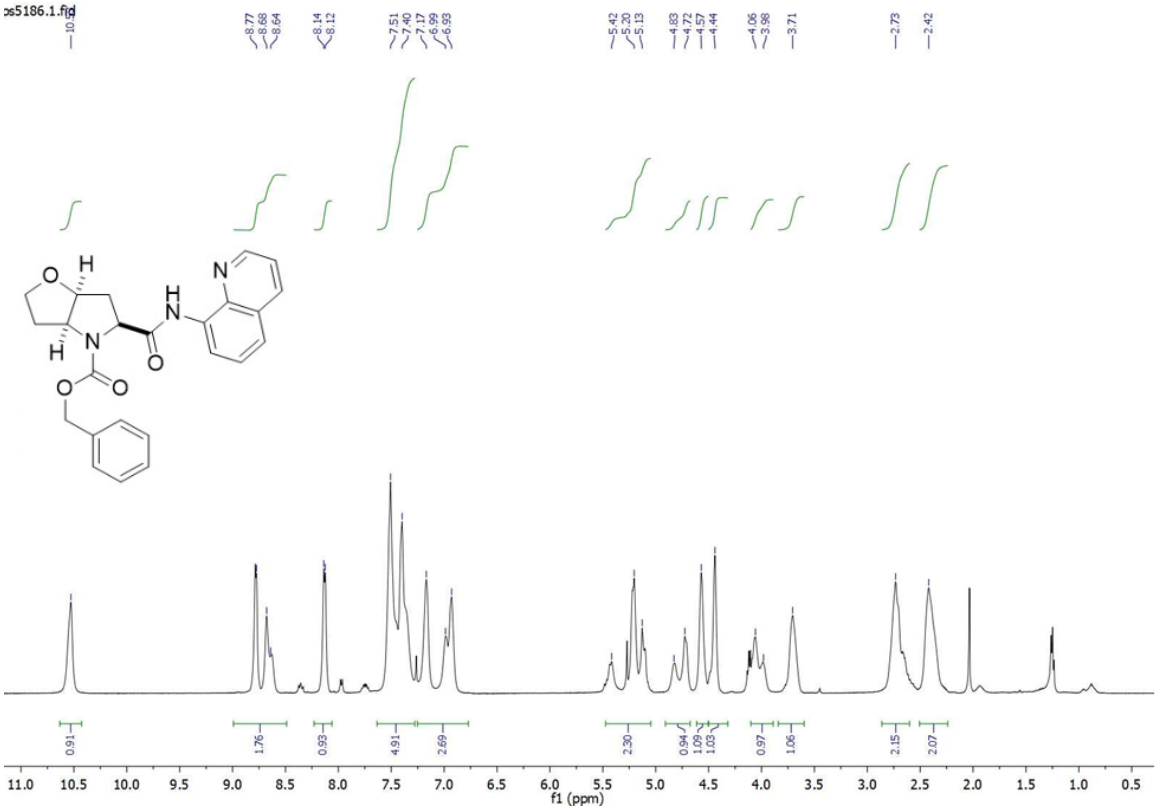
Compound TFA– 4a

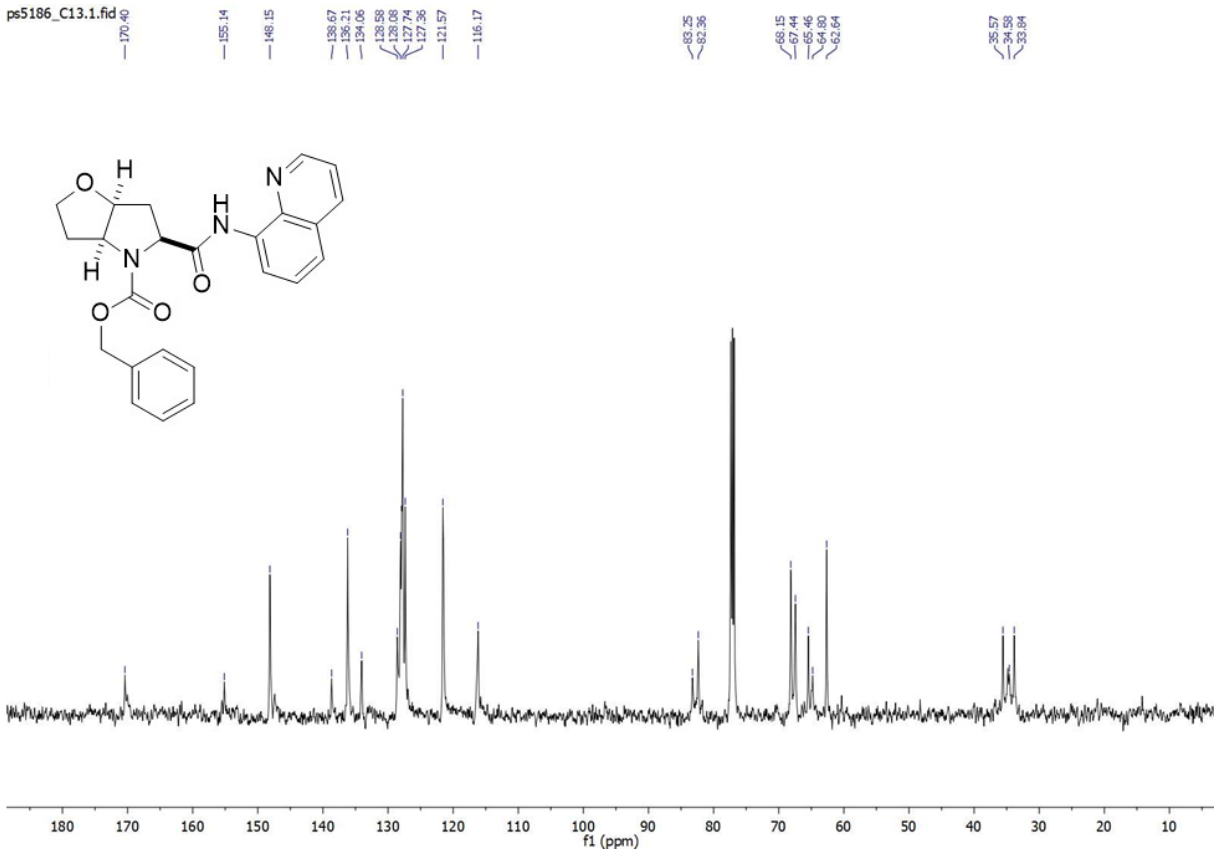




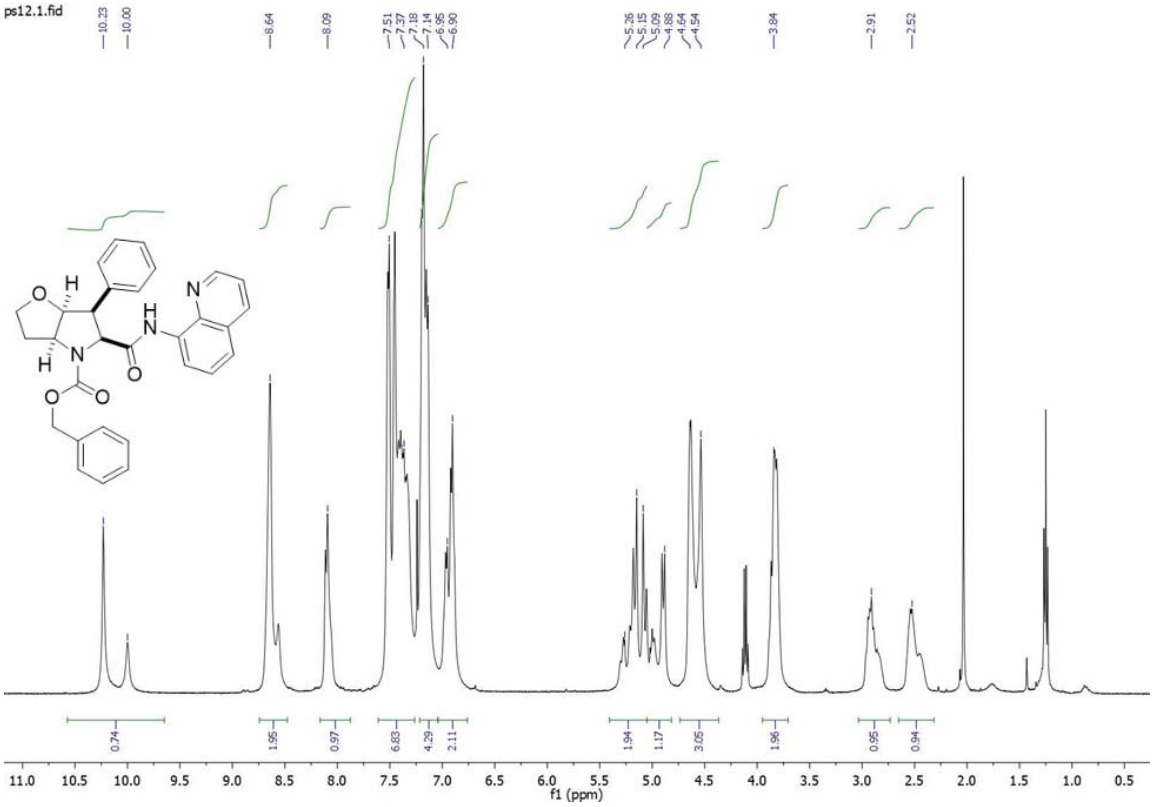

ps4920 19F{1H}.1.fid
-70.93
-71.81
H
S
N
NH
O
H
N
O
F
F
F
50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -23
f1 (ppm)

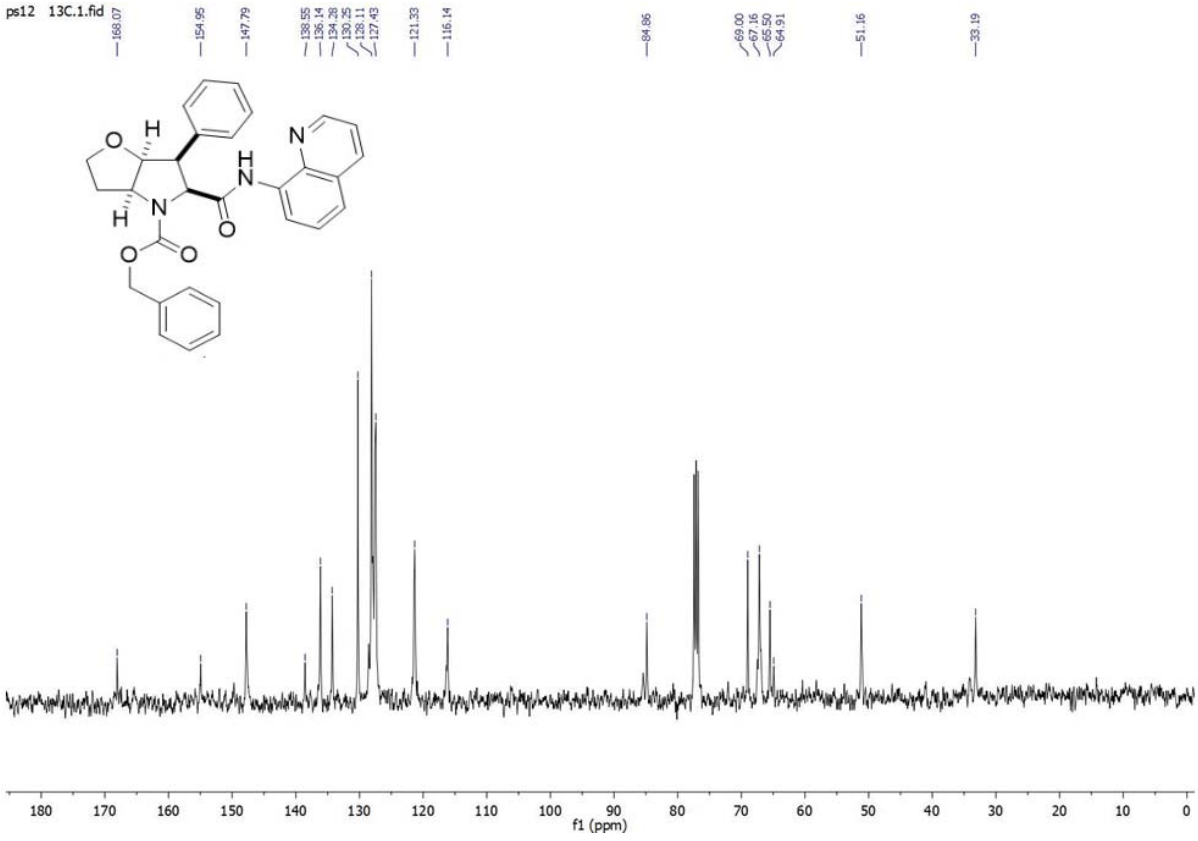
Compound Cbz – 5



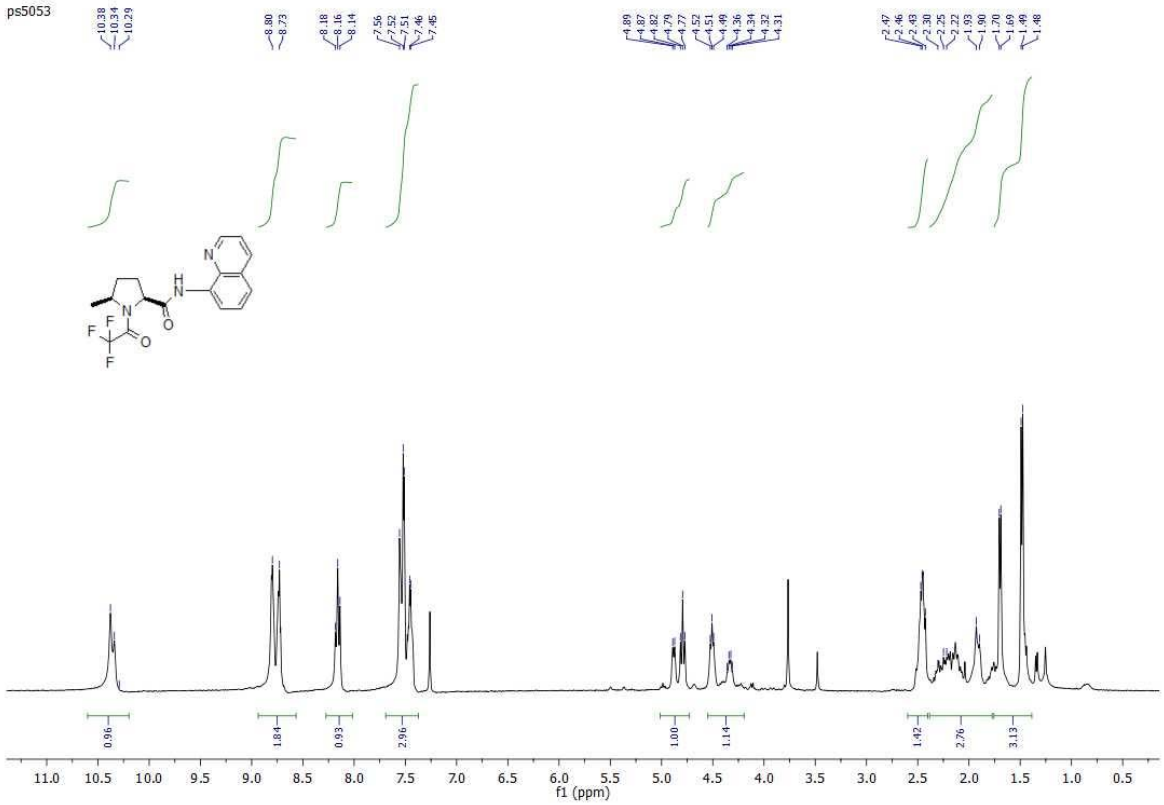


Compound Cbz – 5a

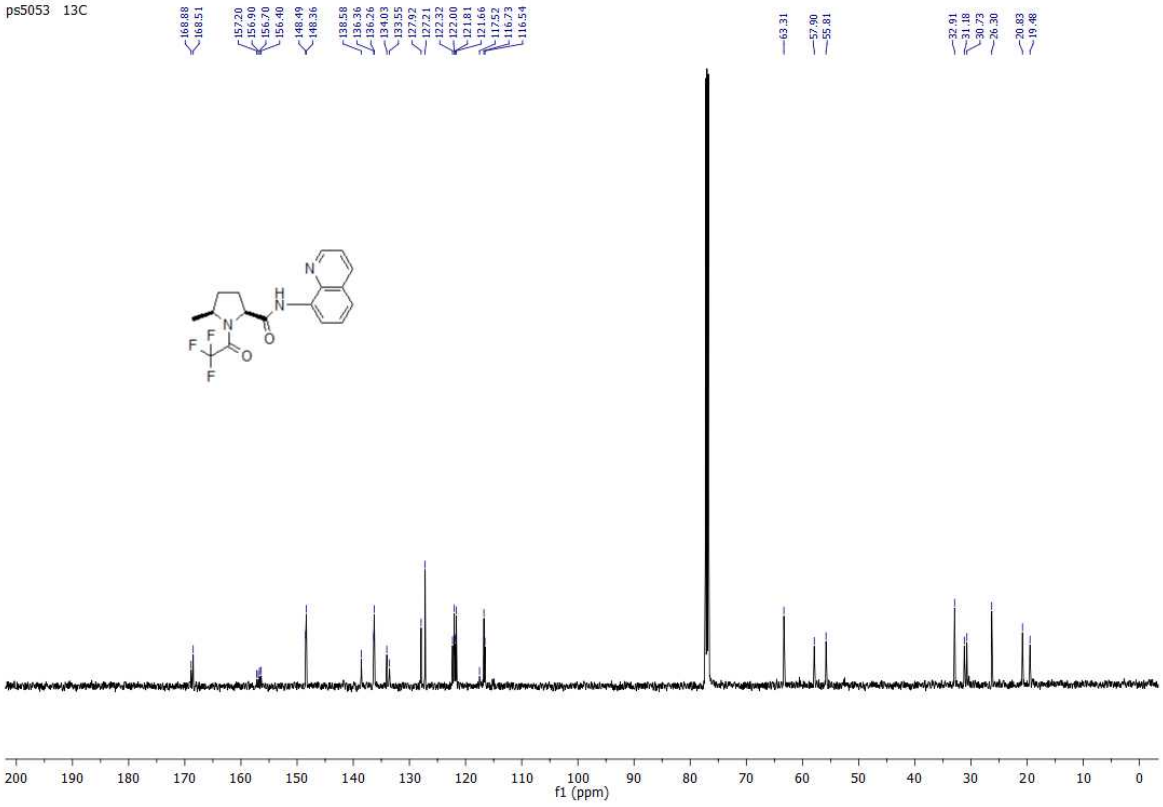




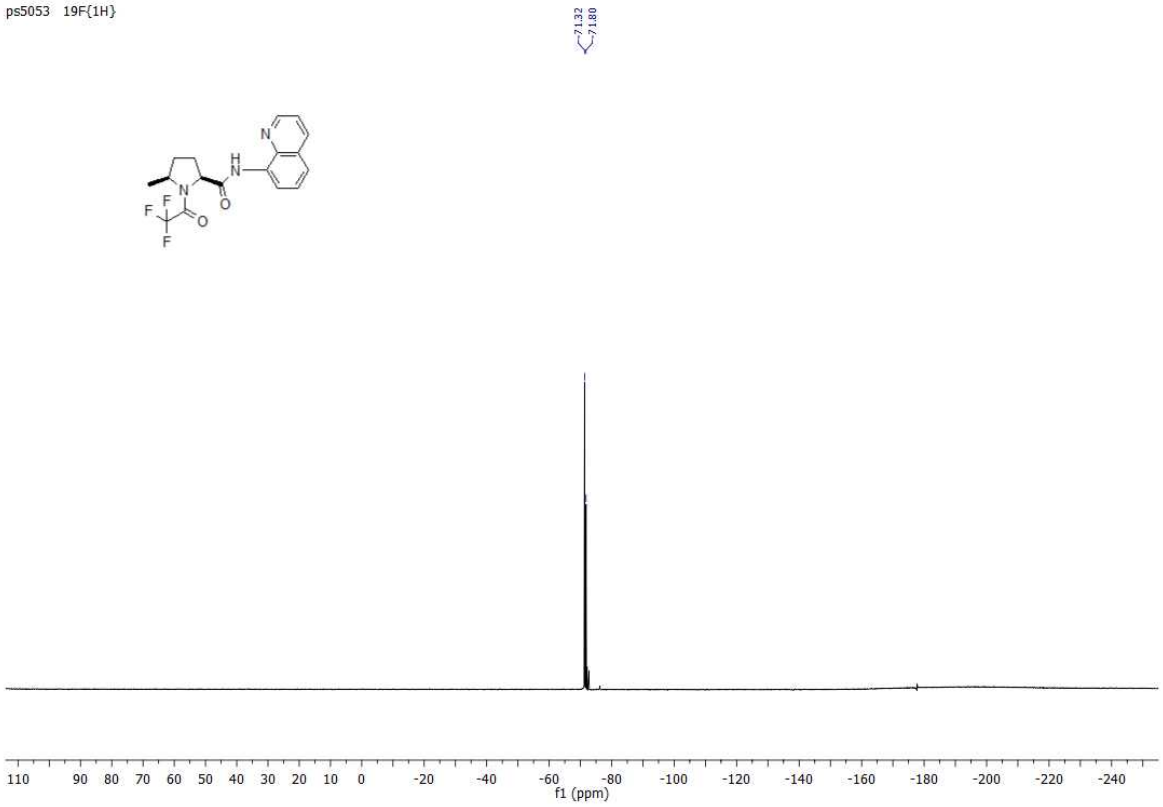
Compound TFA - 6



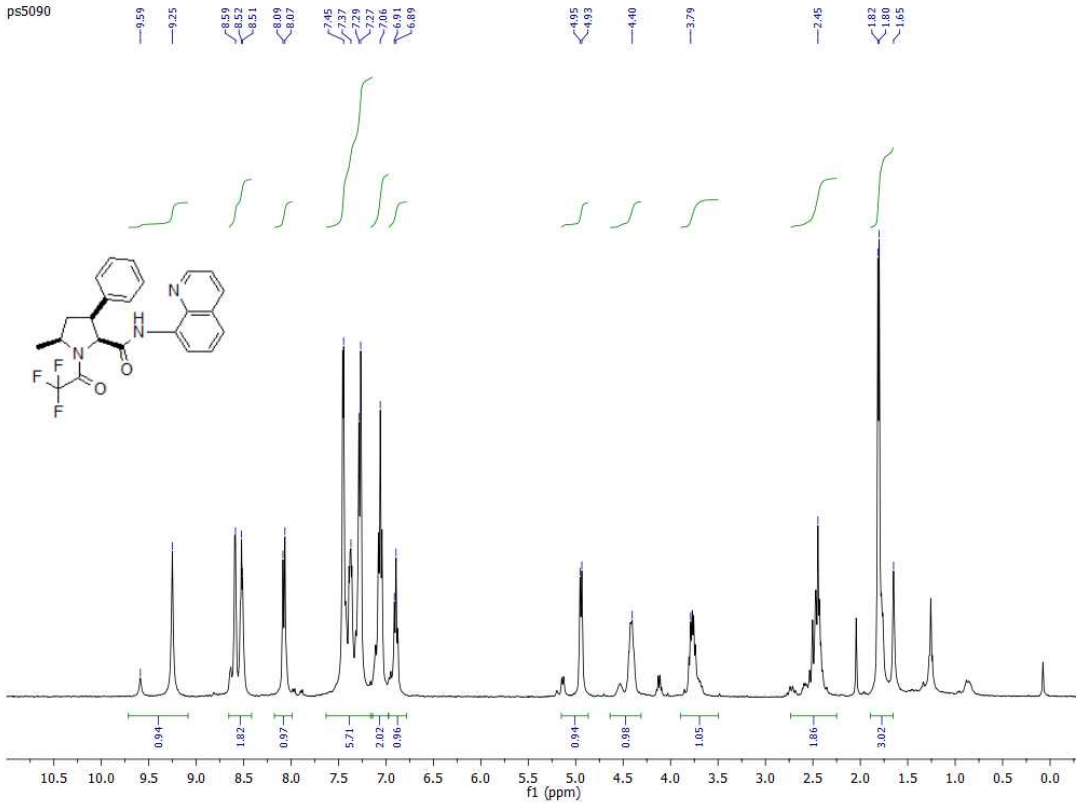
ps5053 13C

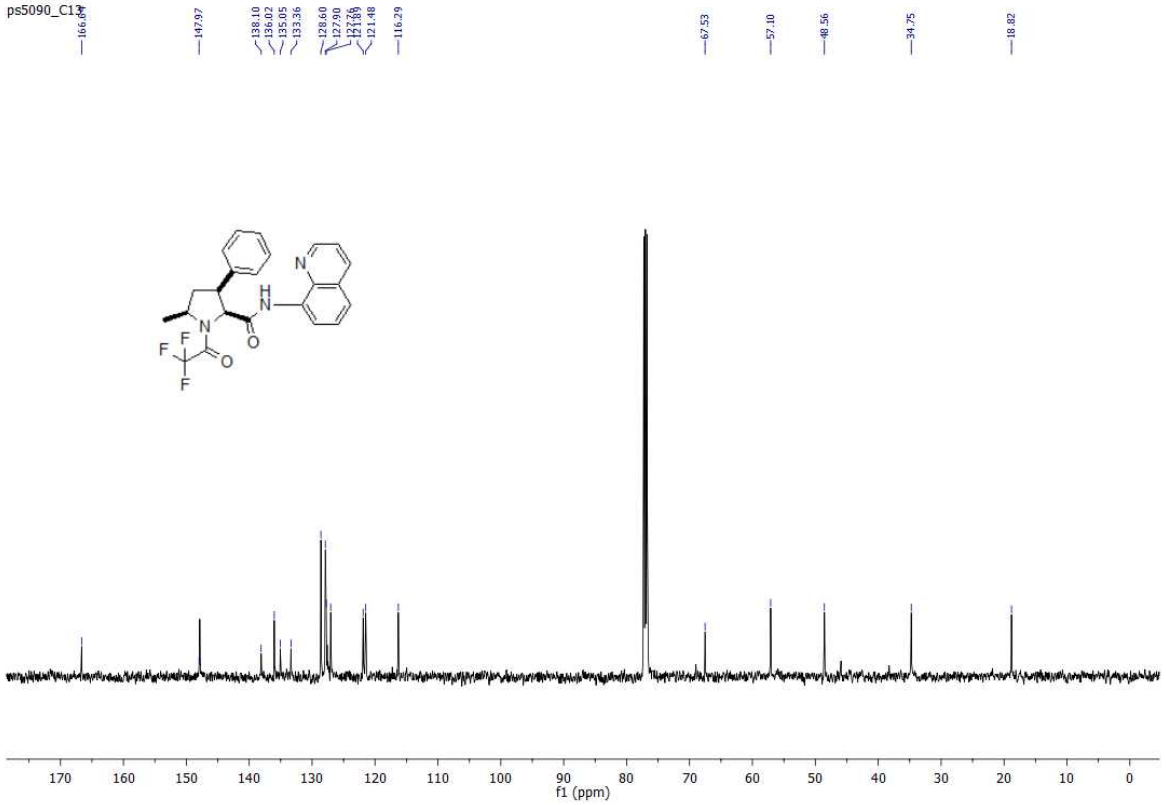


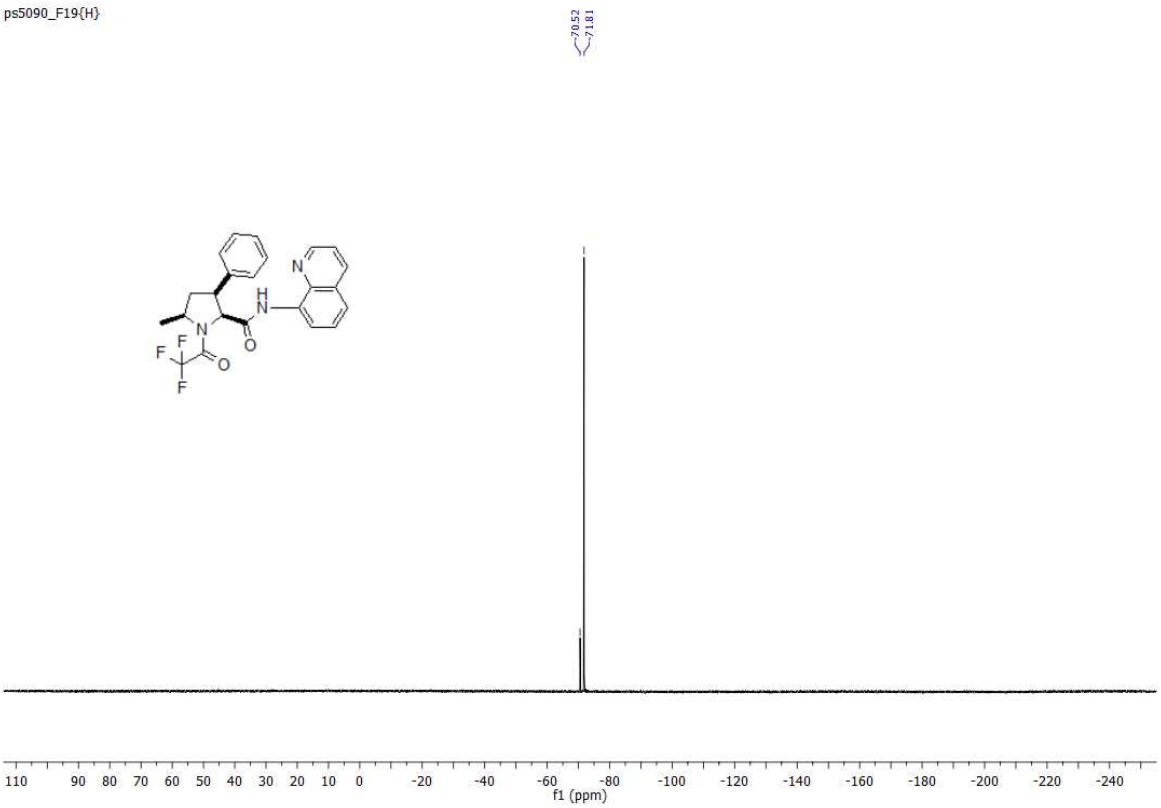
ps5053 19F{1H}



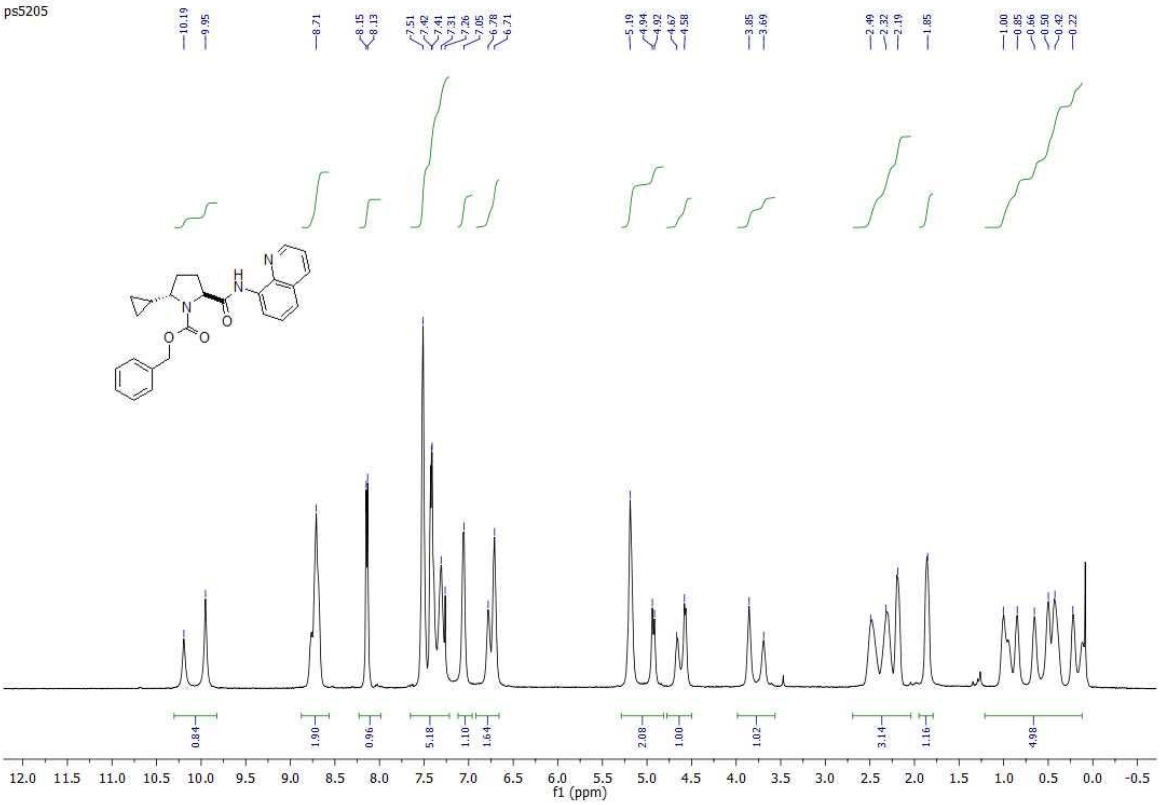
Compound TFA – 6a

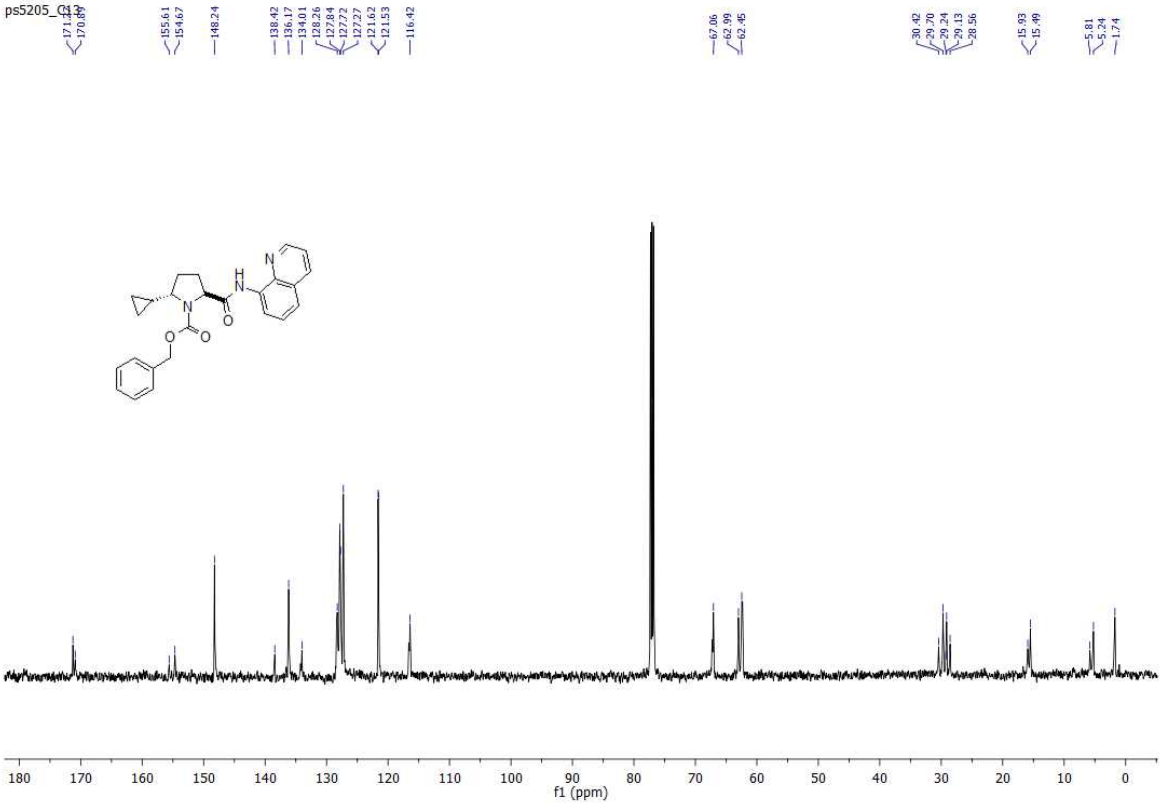




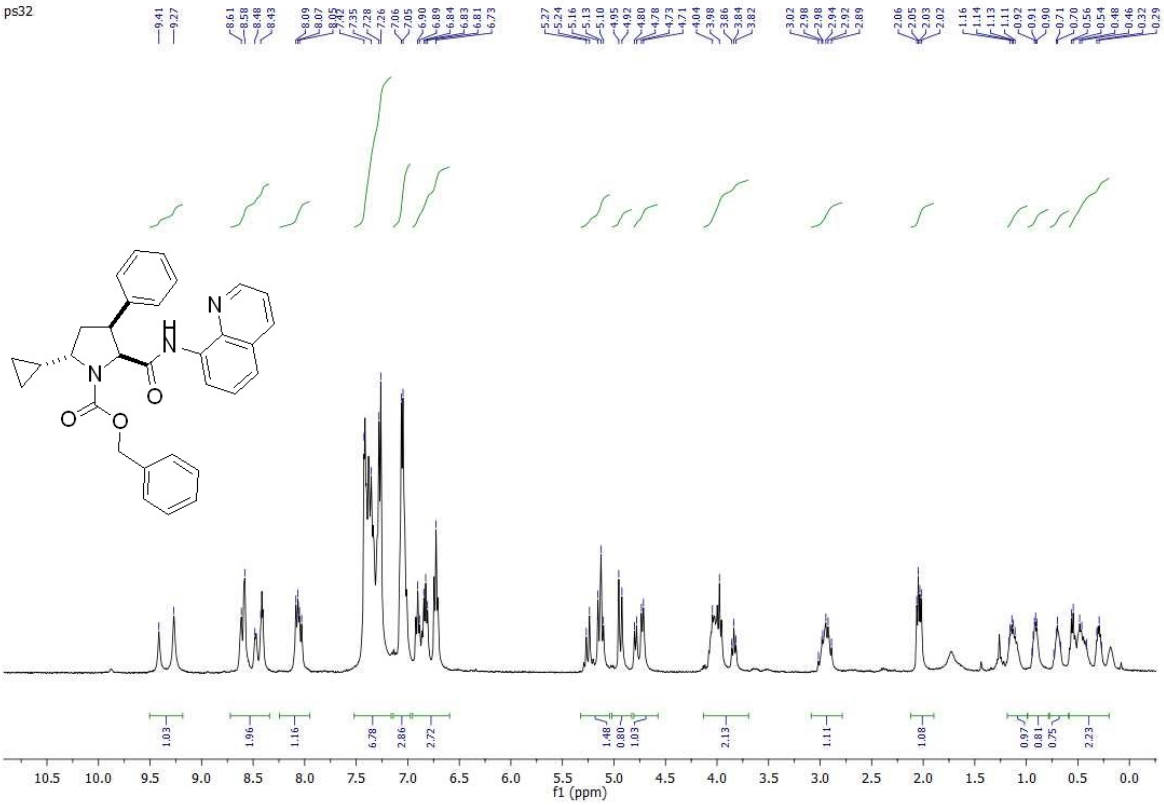

ps5090_F19{H}
-70.52
-71.81
N
H
N
O
F
F
F
N
O
110
90
80
70
60
50
40
30
20
10
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
f1 (ppm)

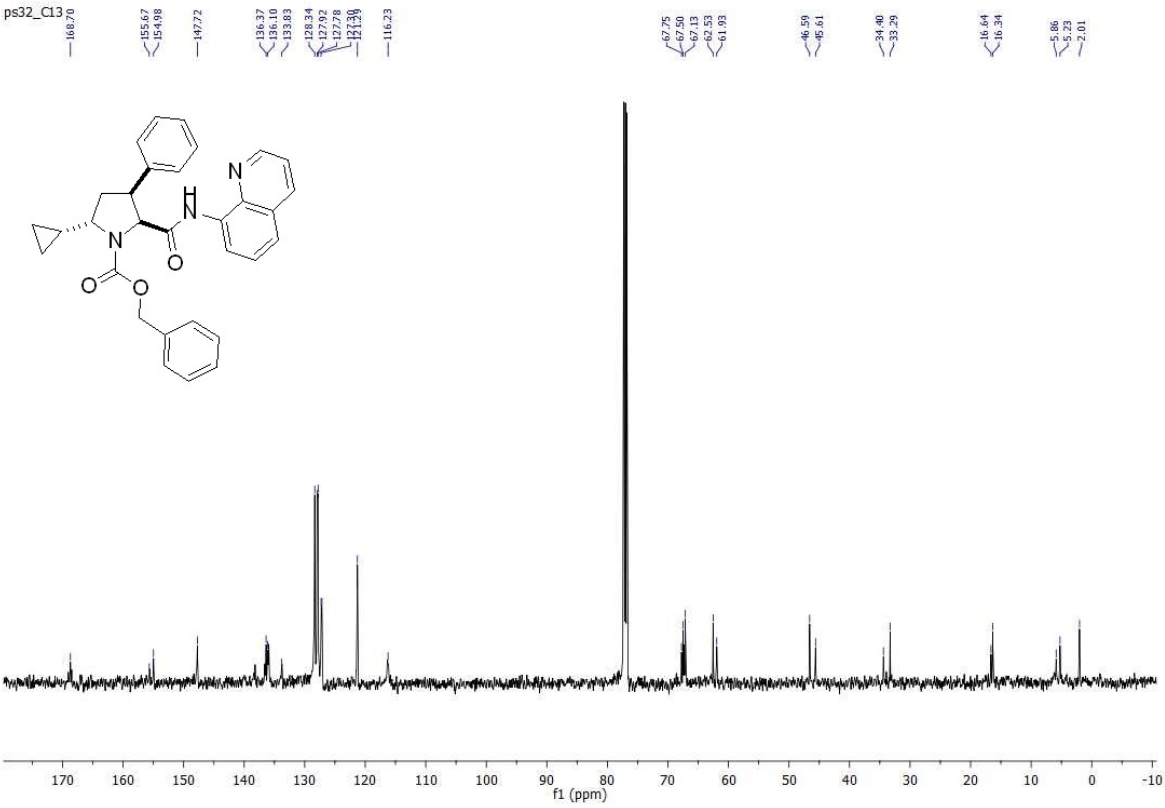
Compound Cbz 7



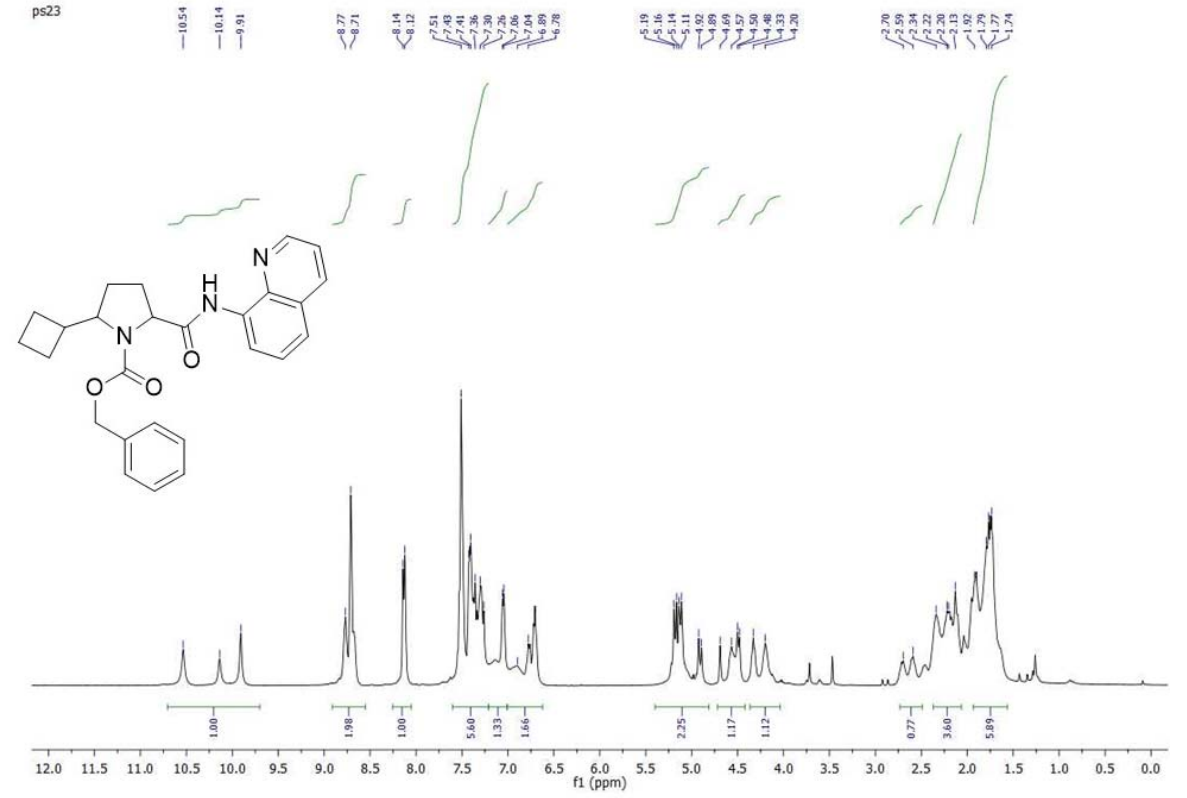


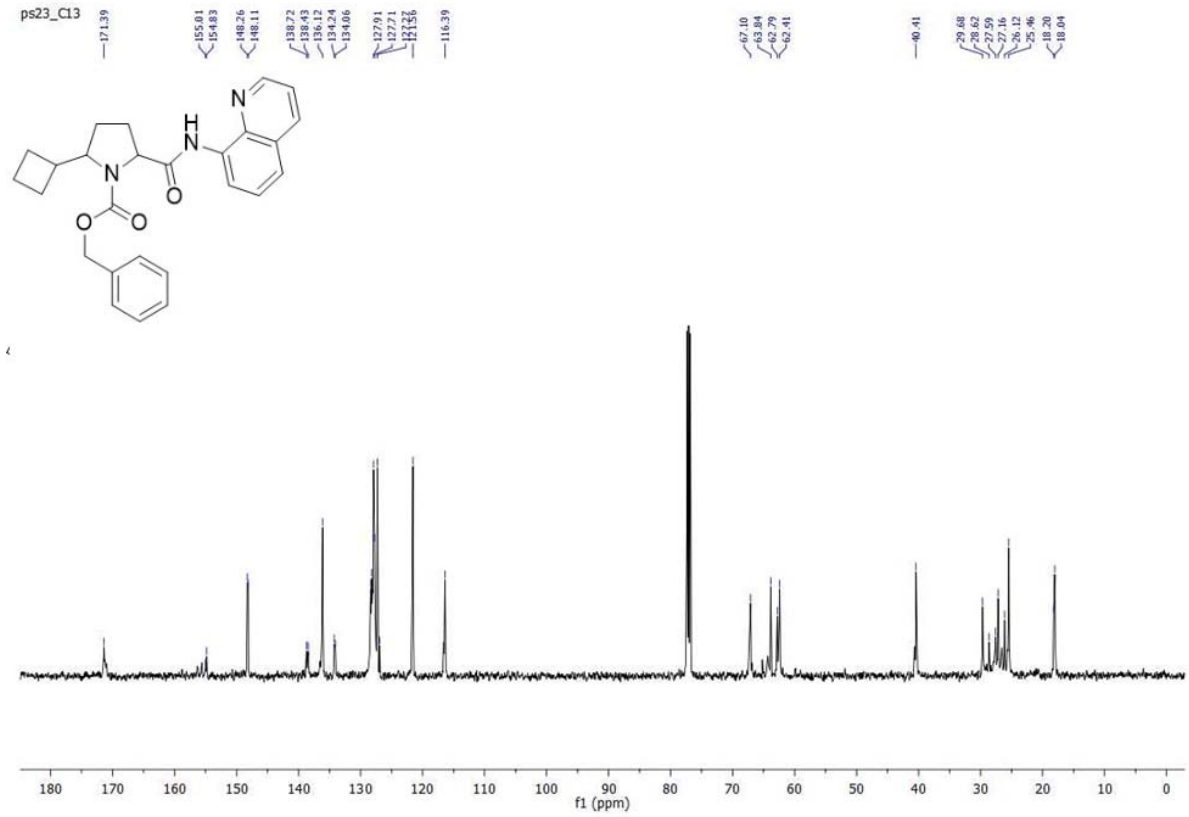
Compound Cbz – 7a



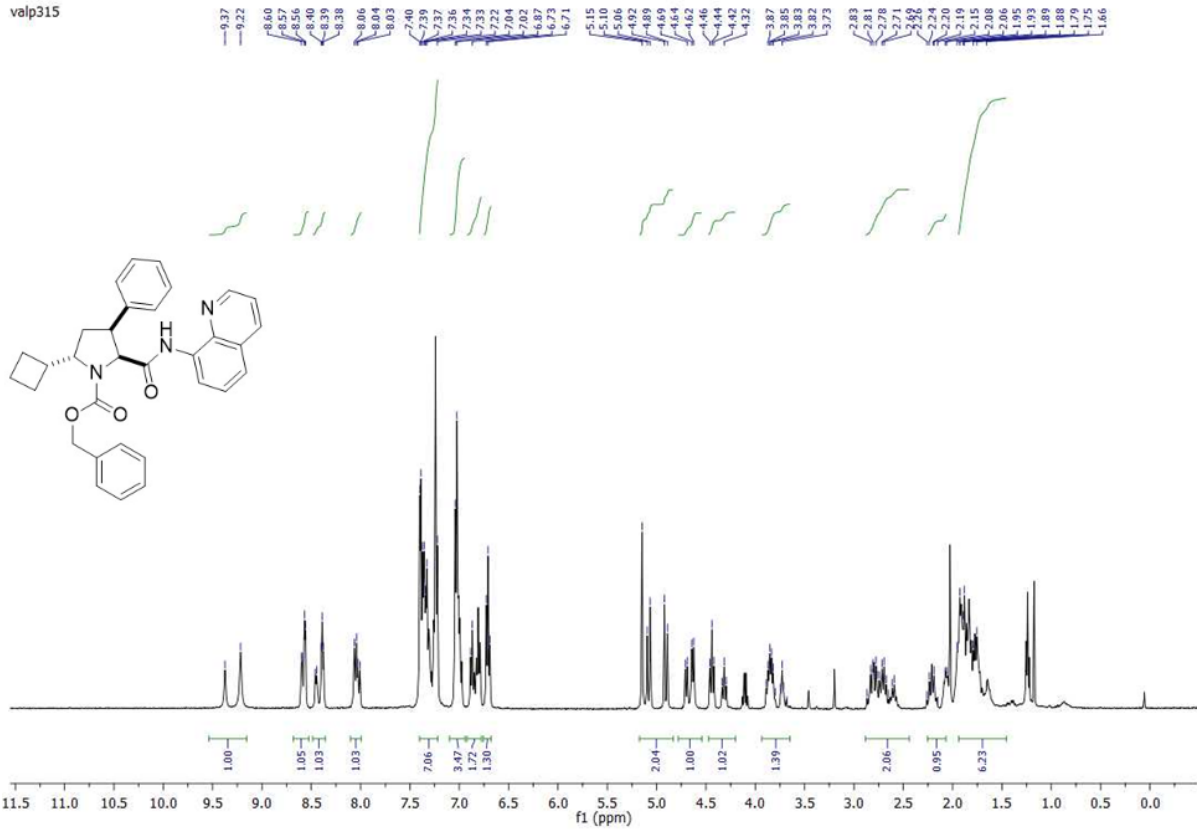


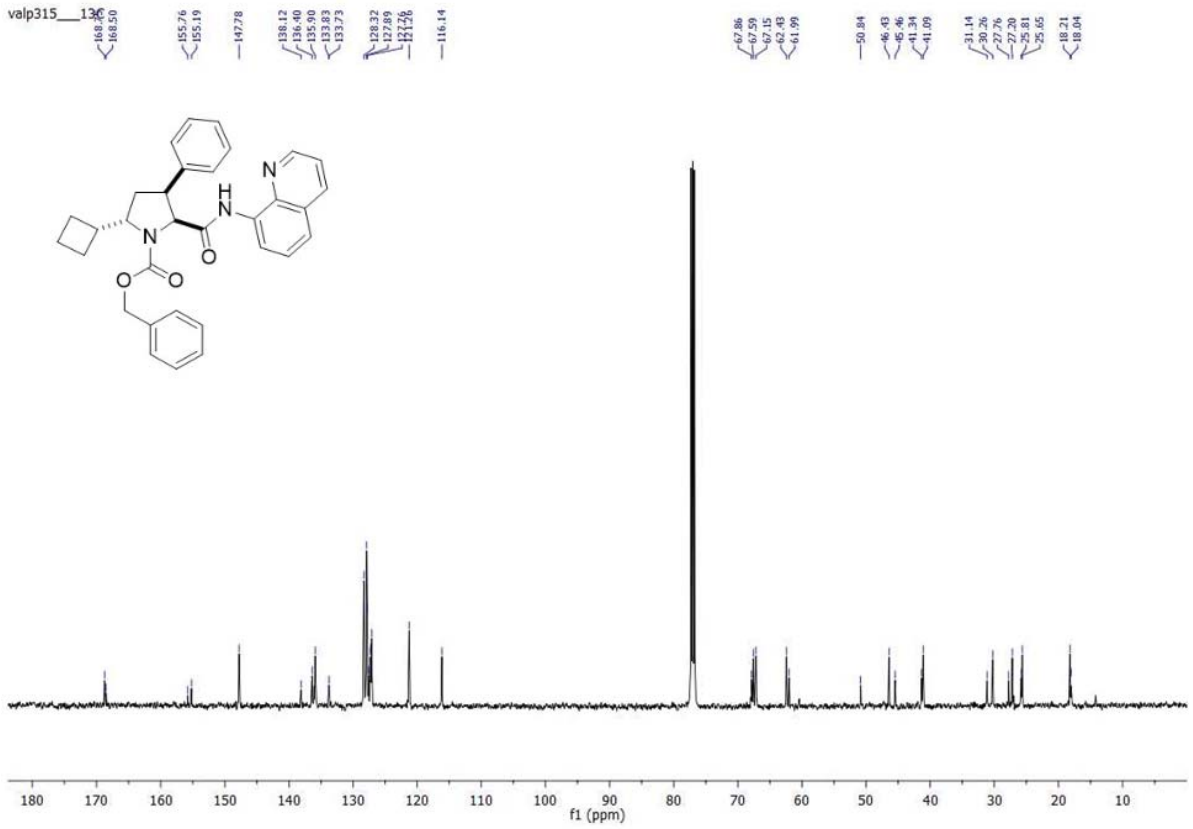
Compound Cbz - 8



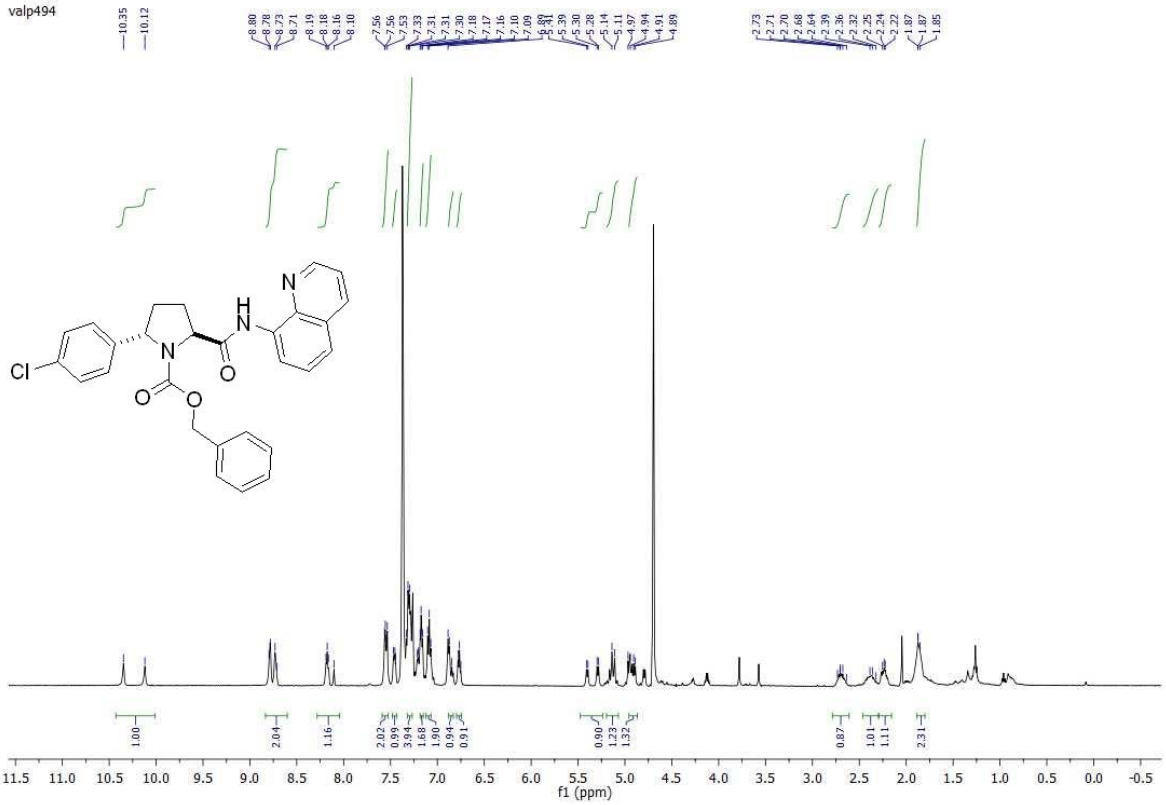


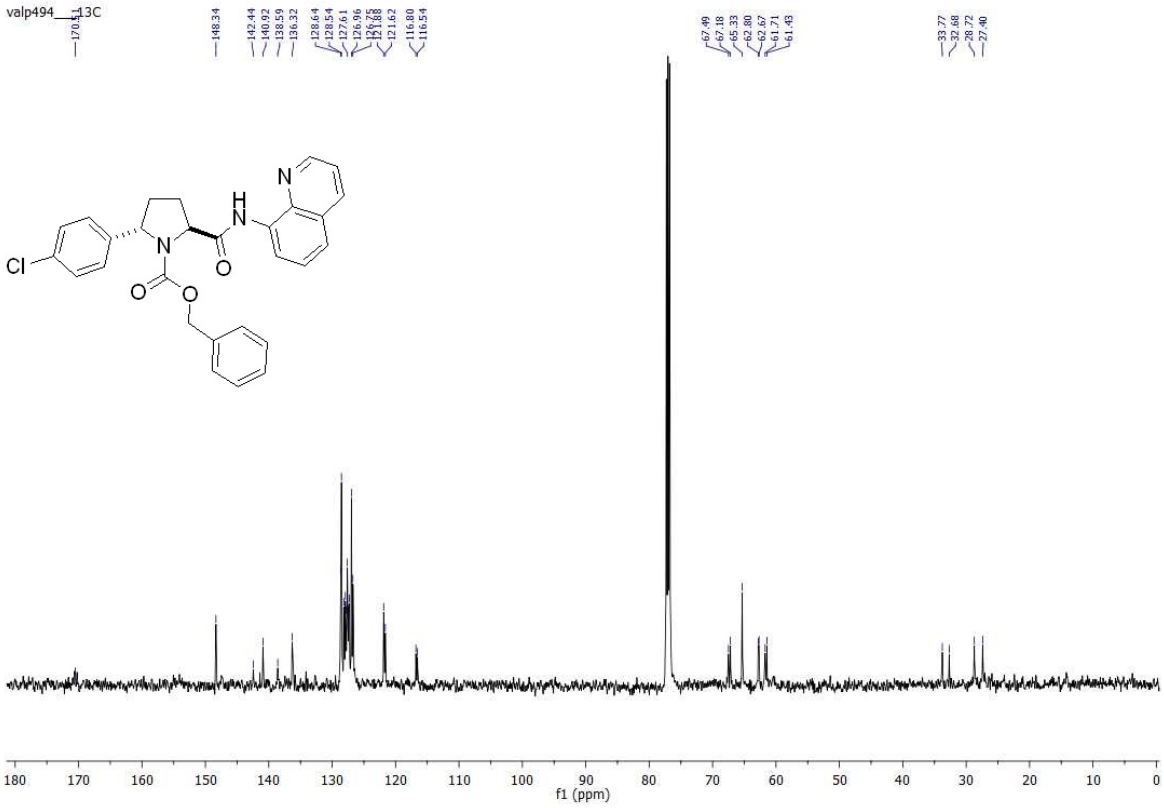
Compound Cbz - 8a



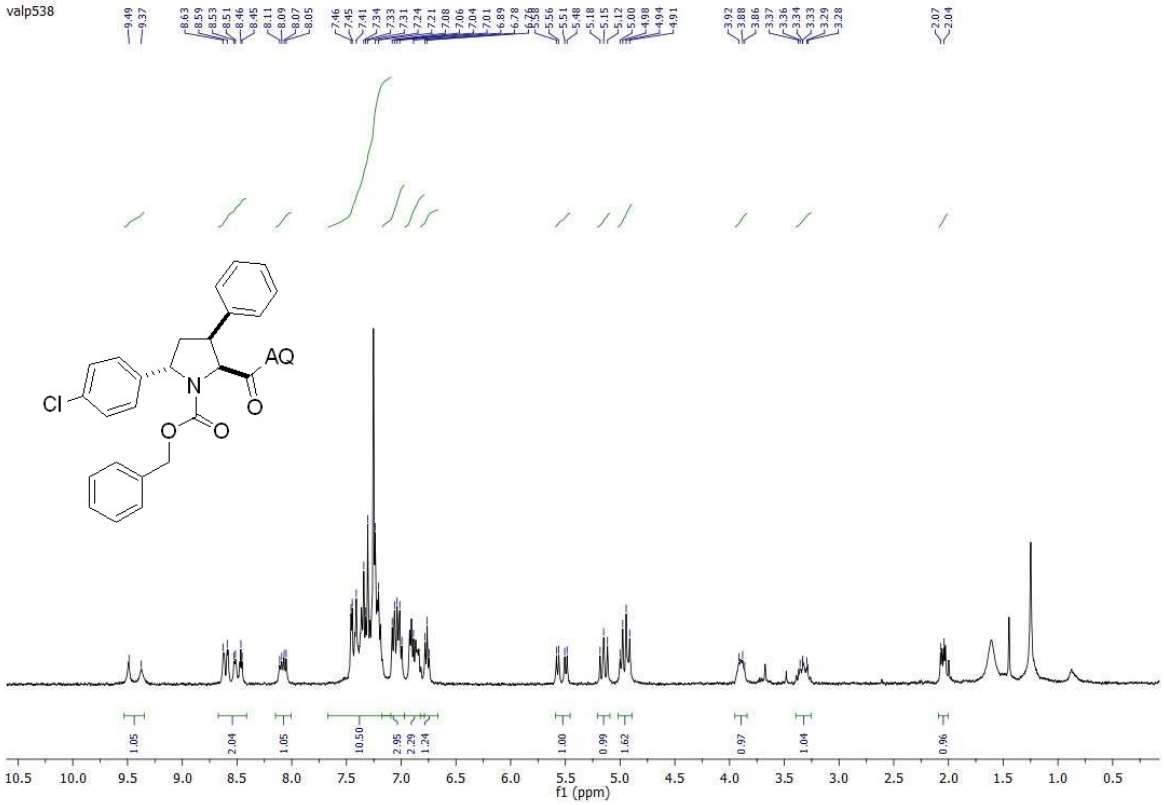


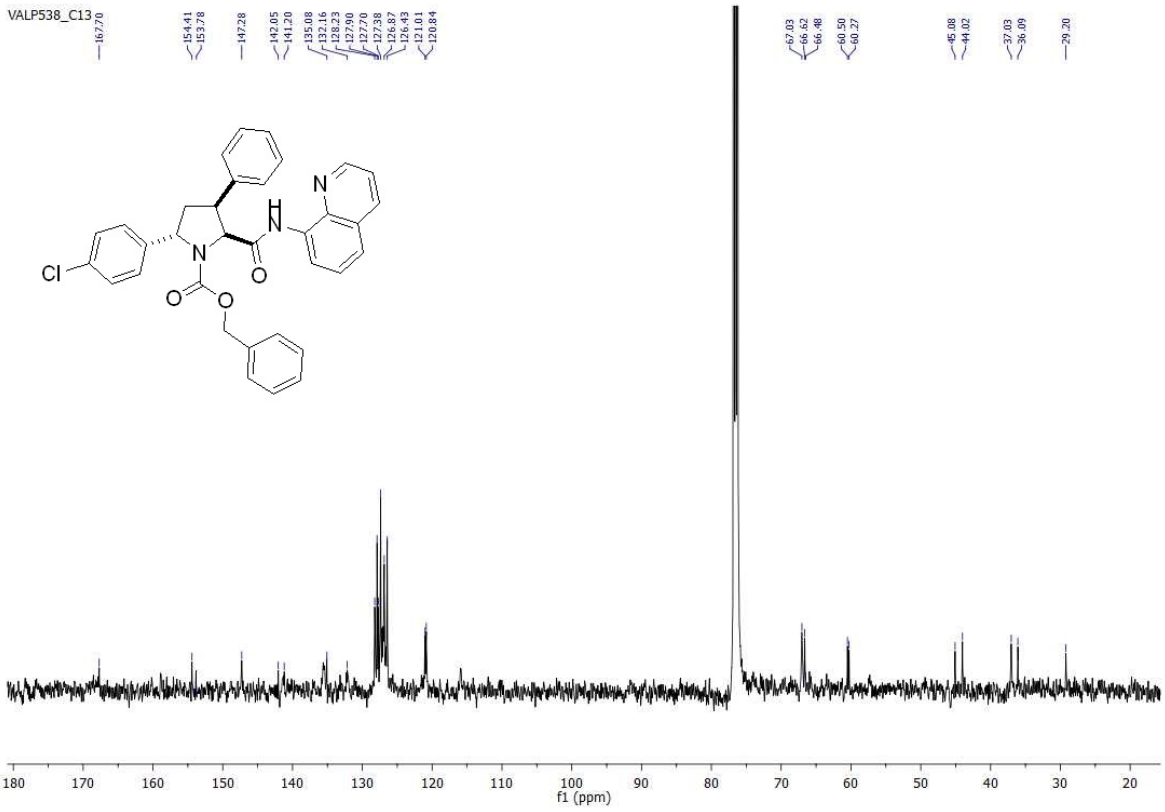
Compound Cbz -9



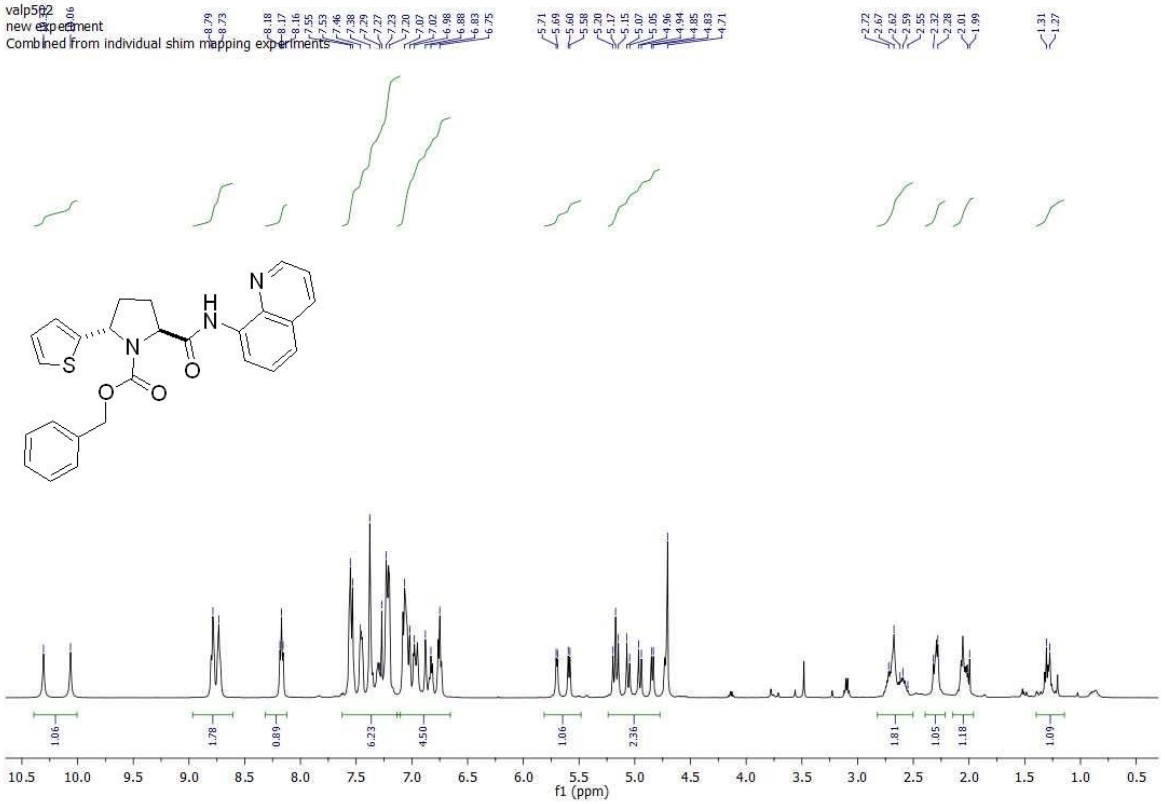


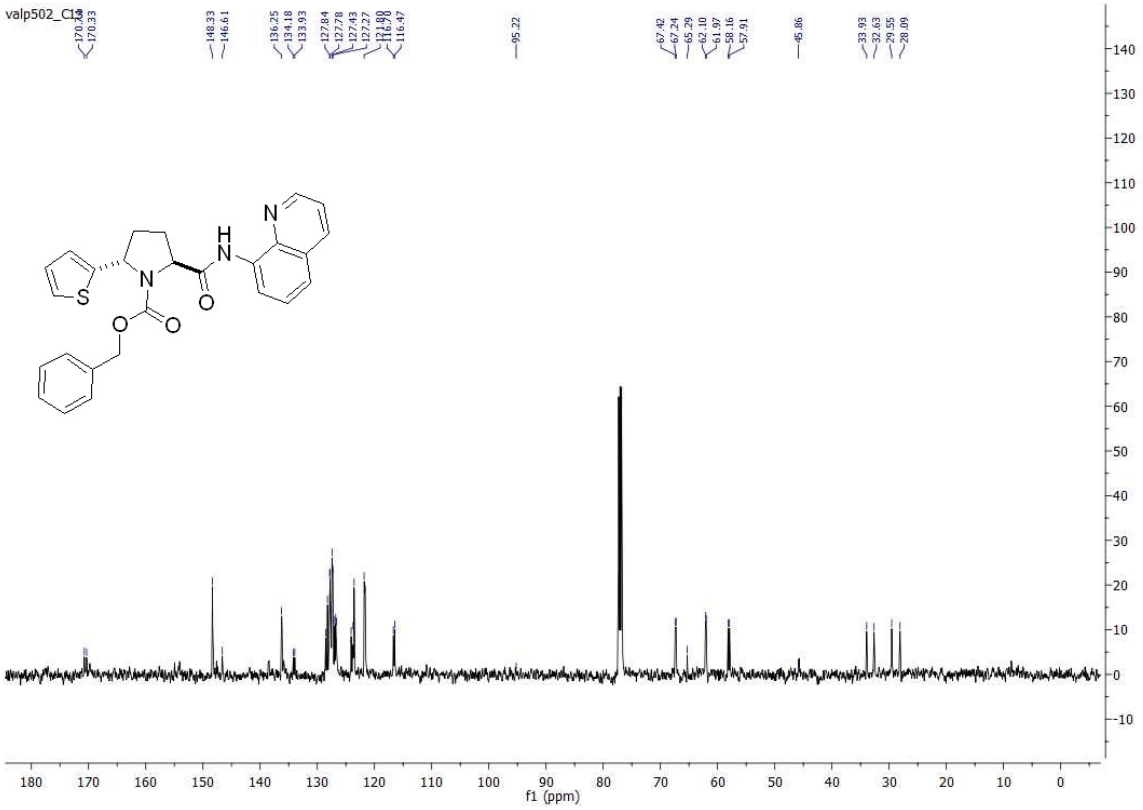
Compound Cbz-9a



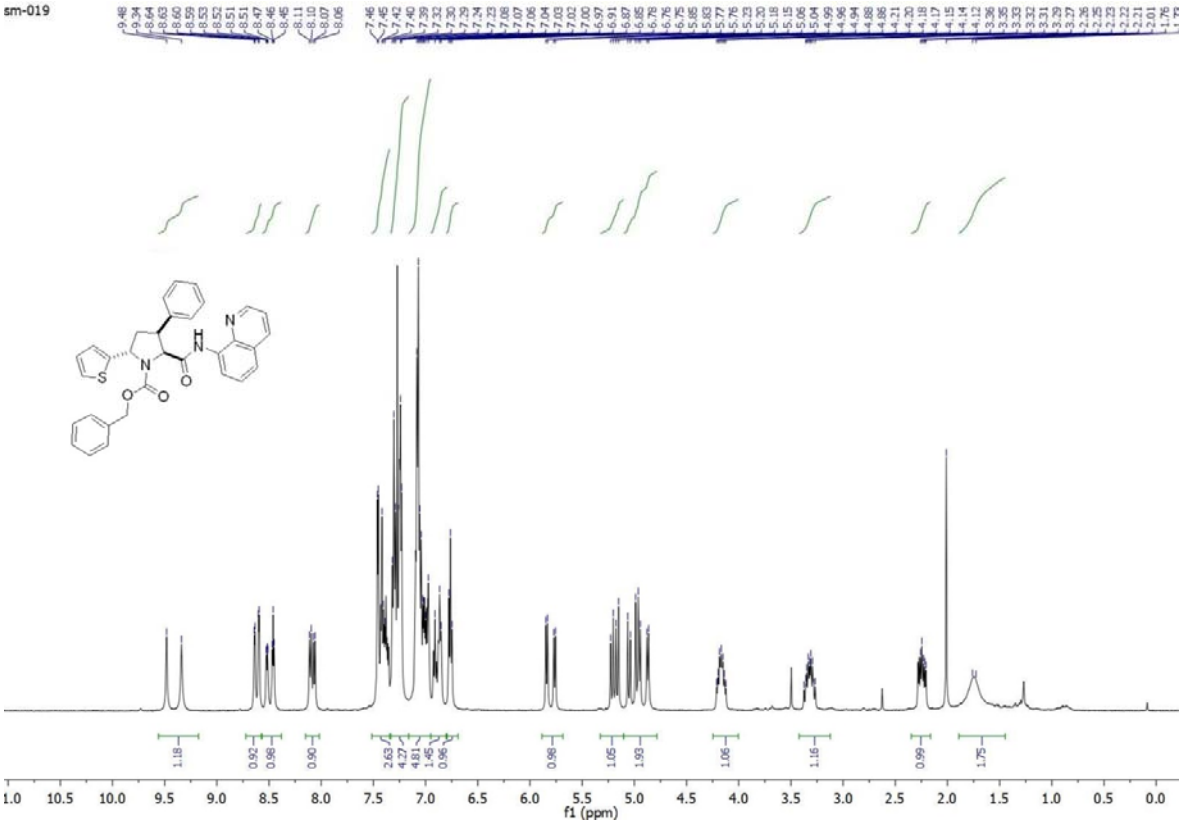


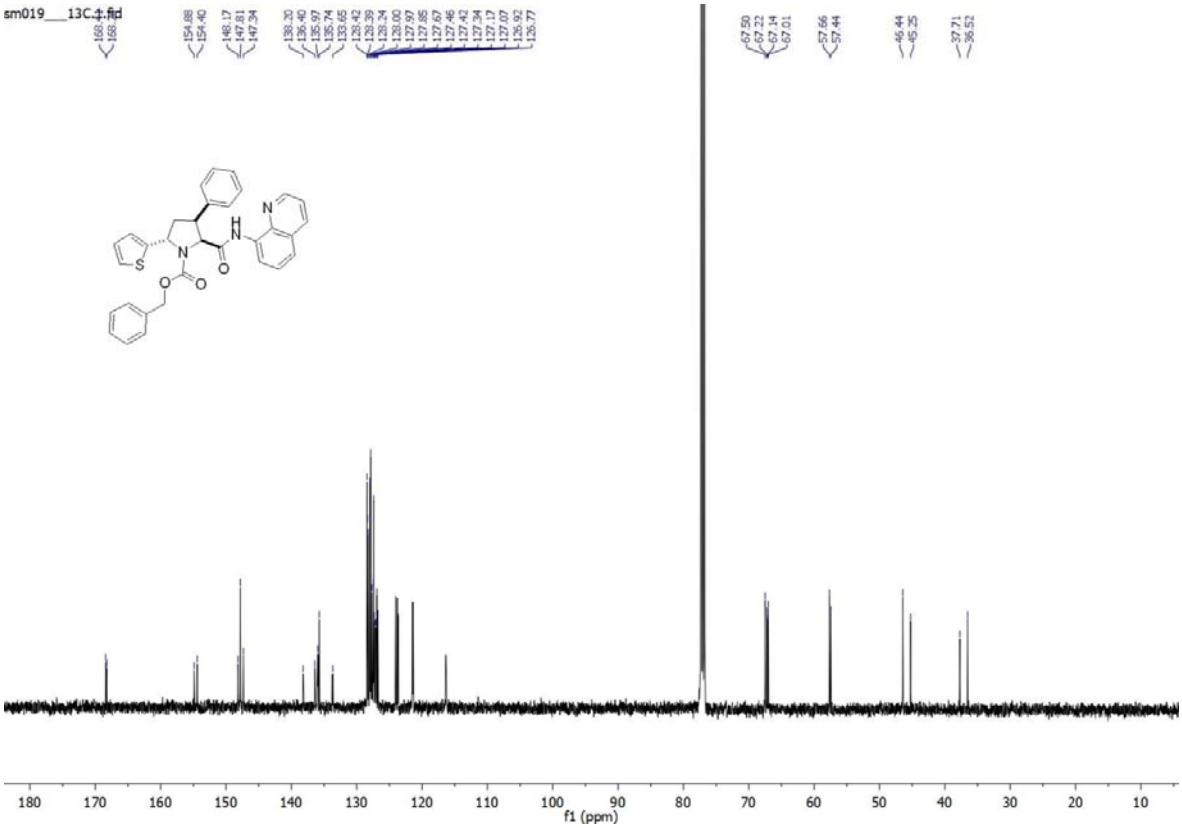
Compound Cbz -10



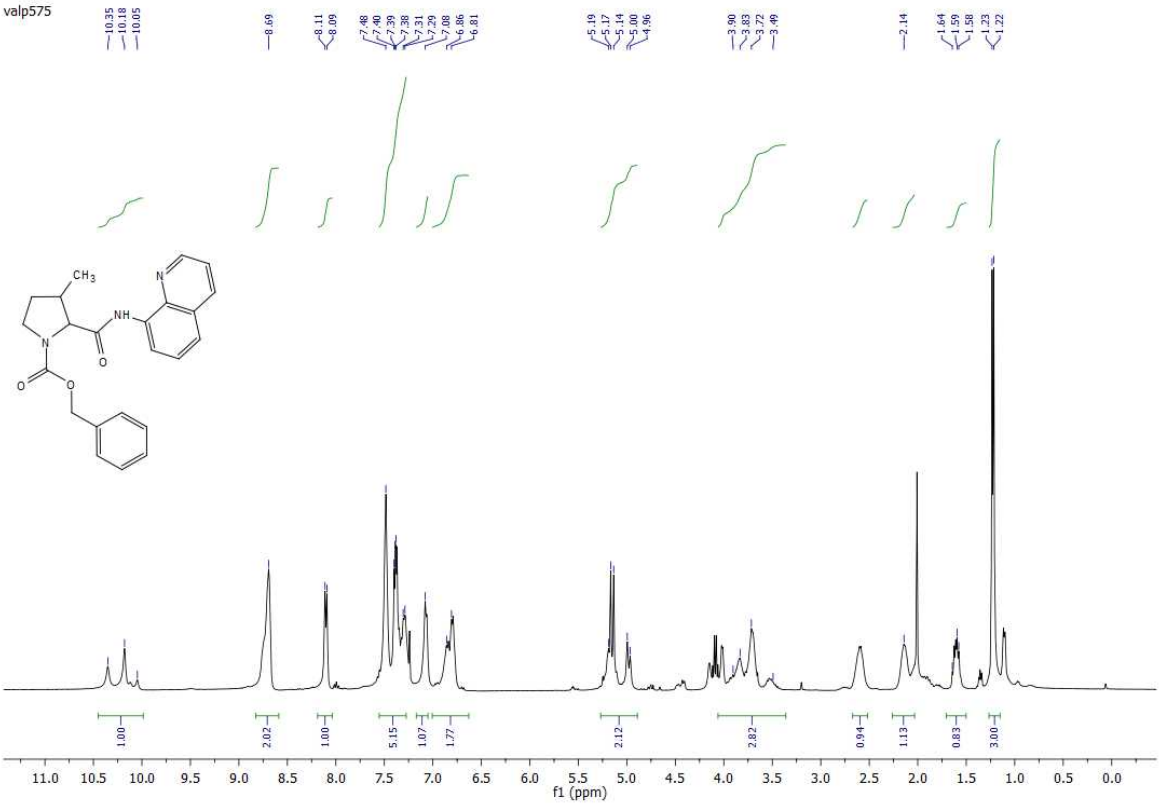


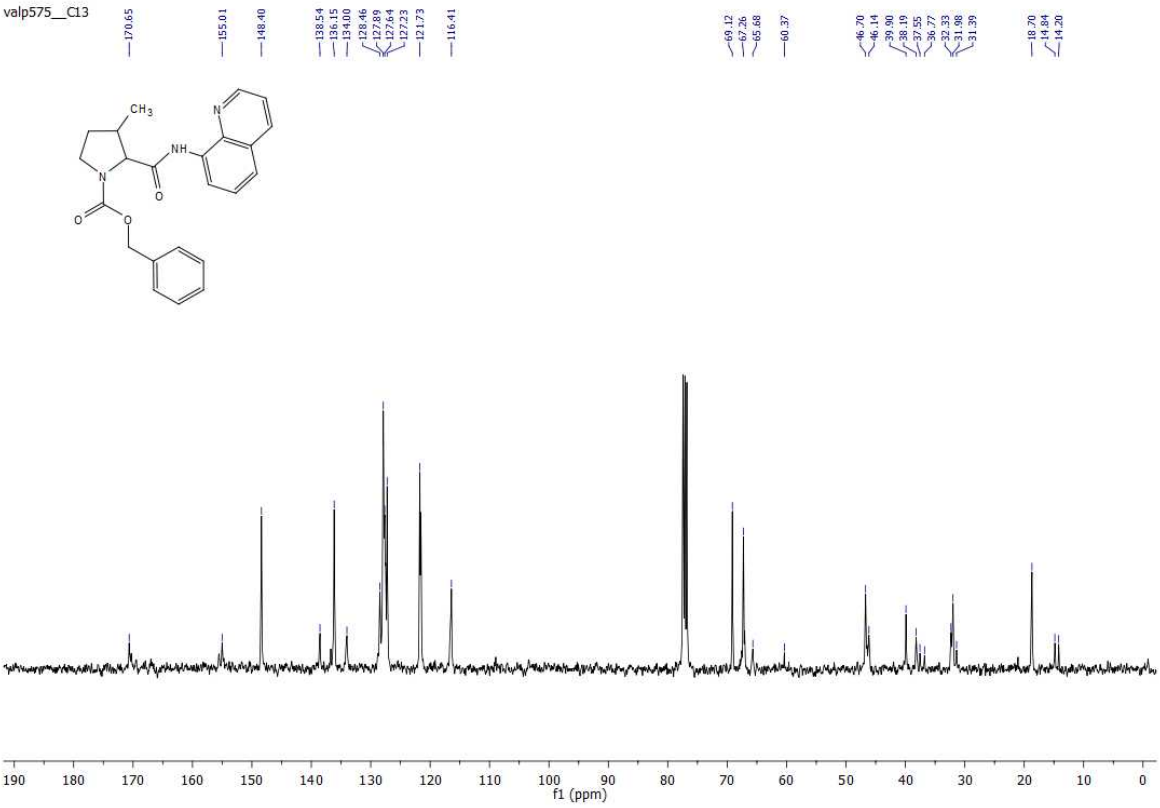
Compoud Cbz – 10a



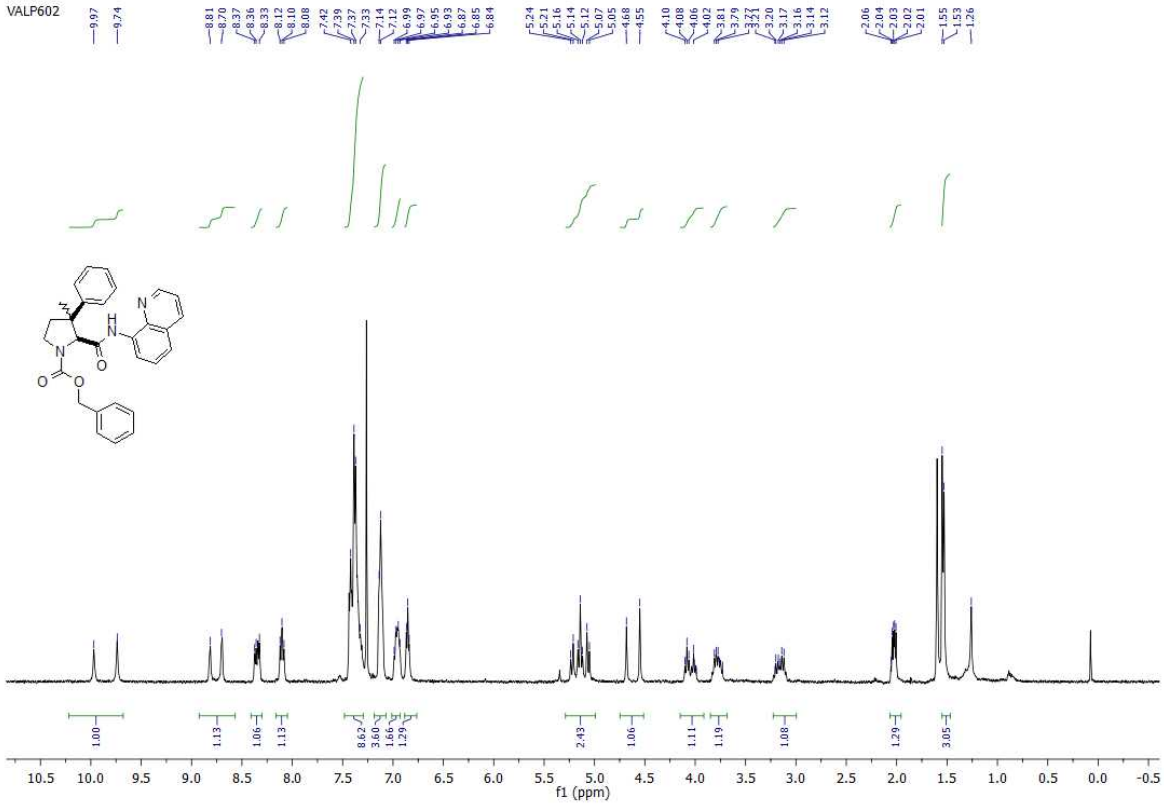


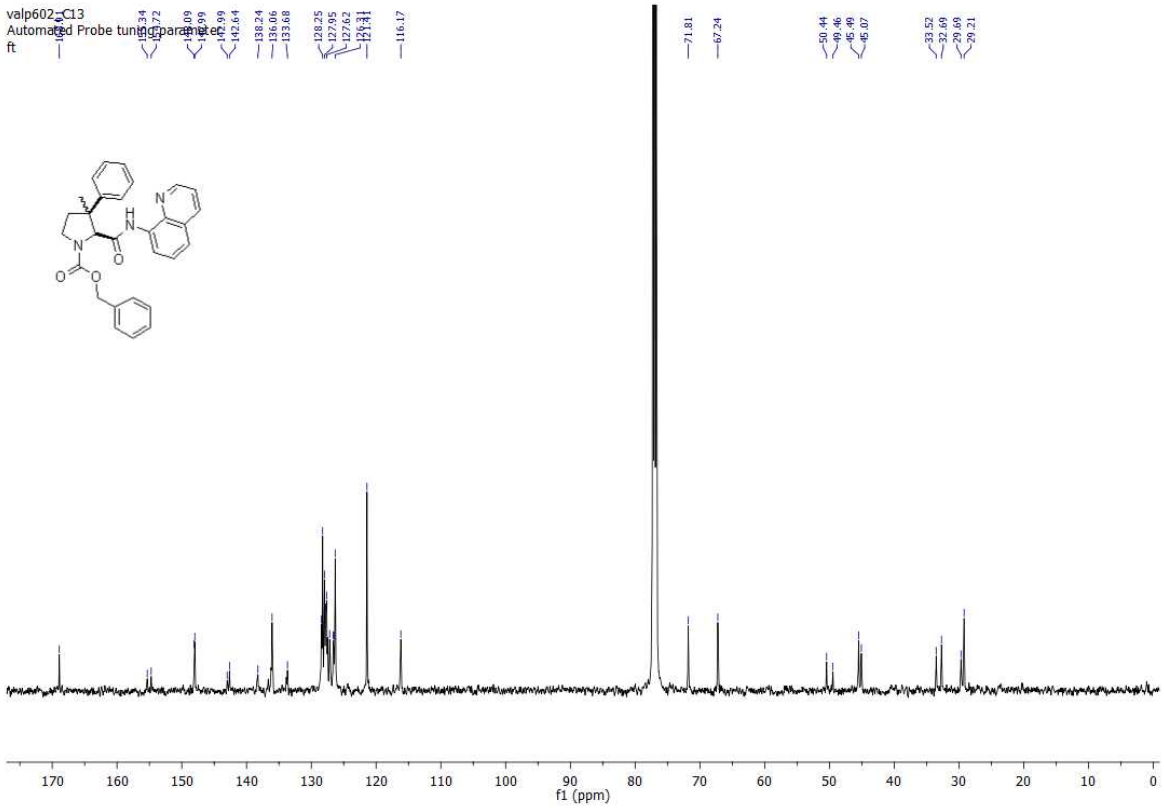
Compound Cbz – 11



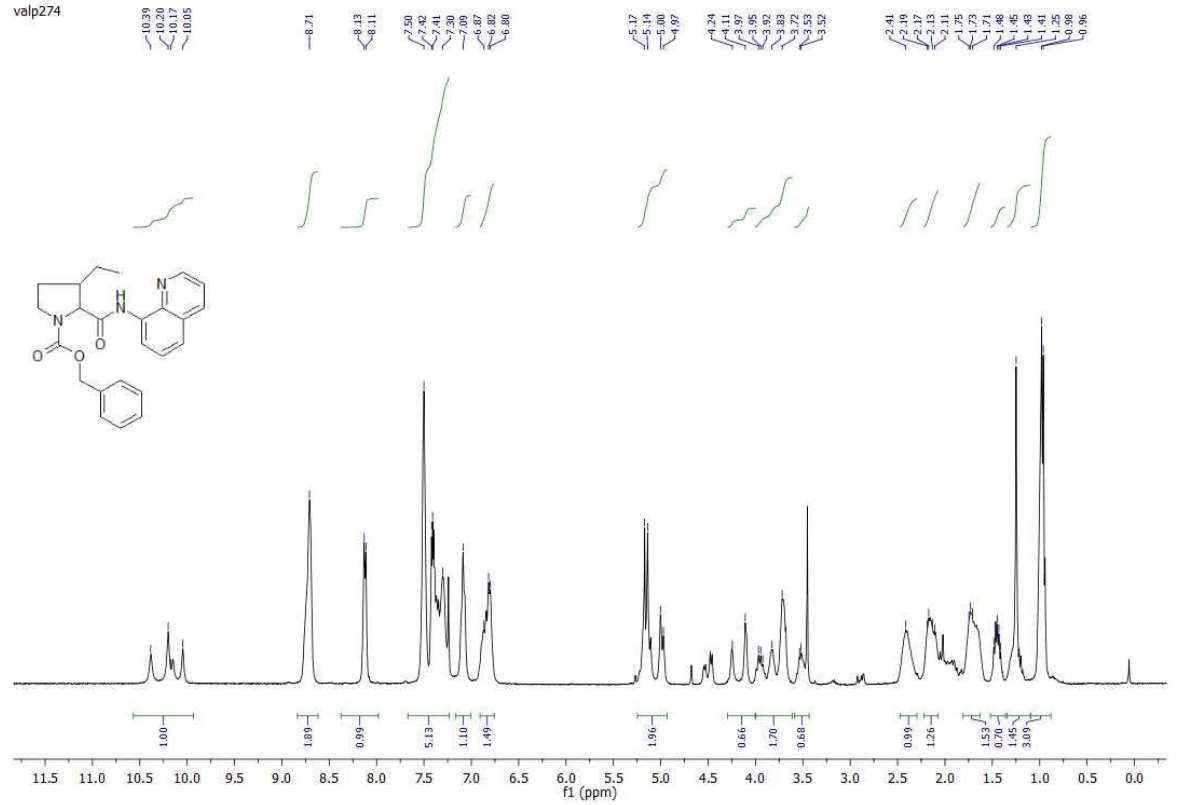


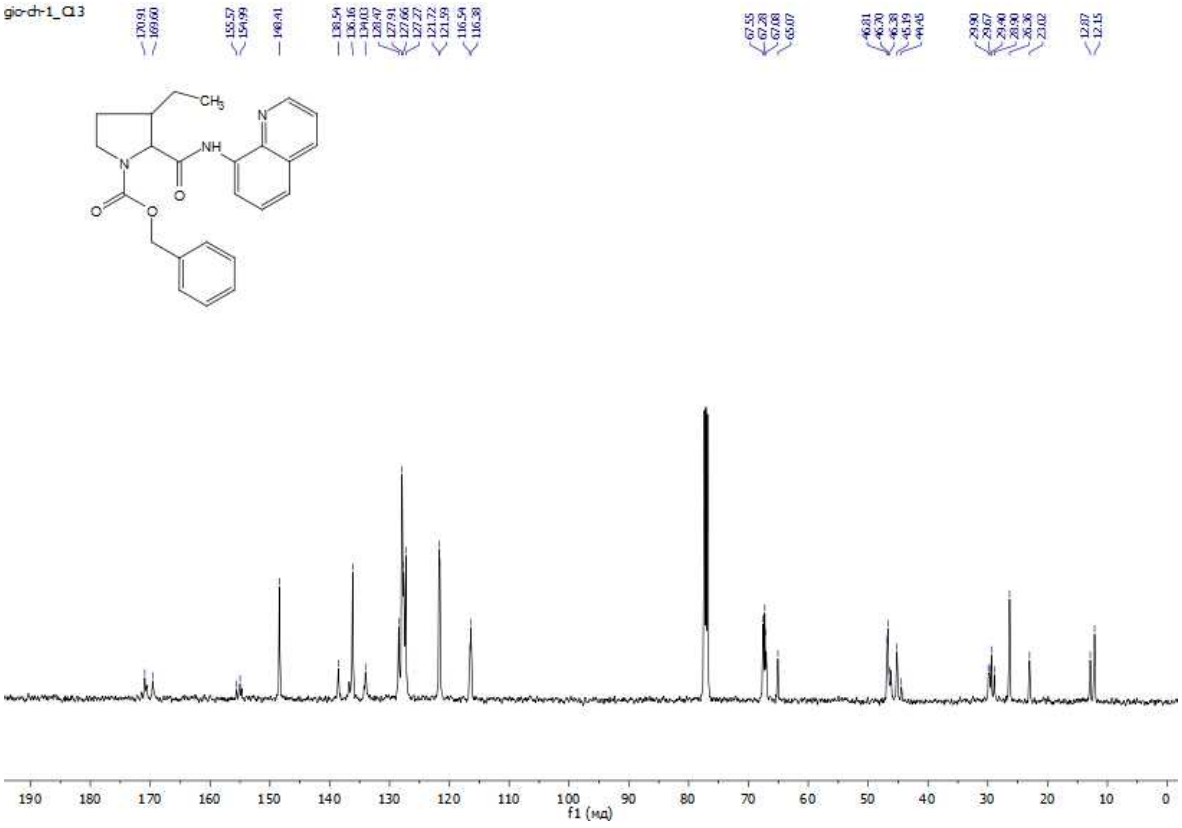
Compound Cbz – 11a





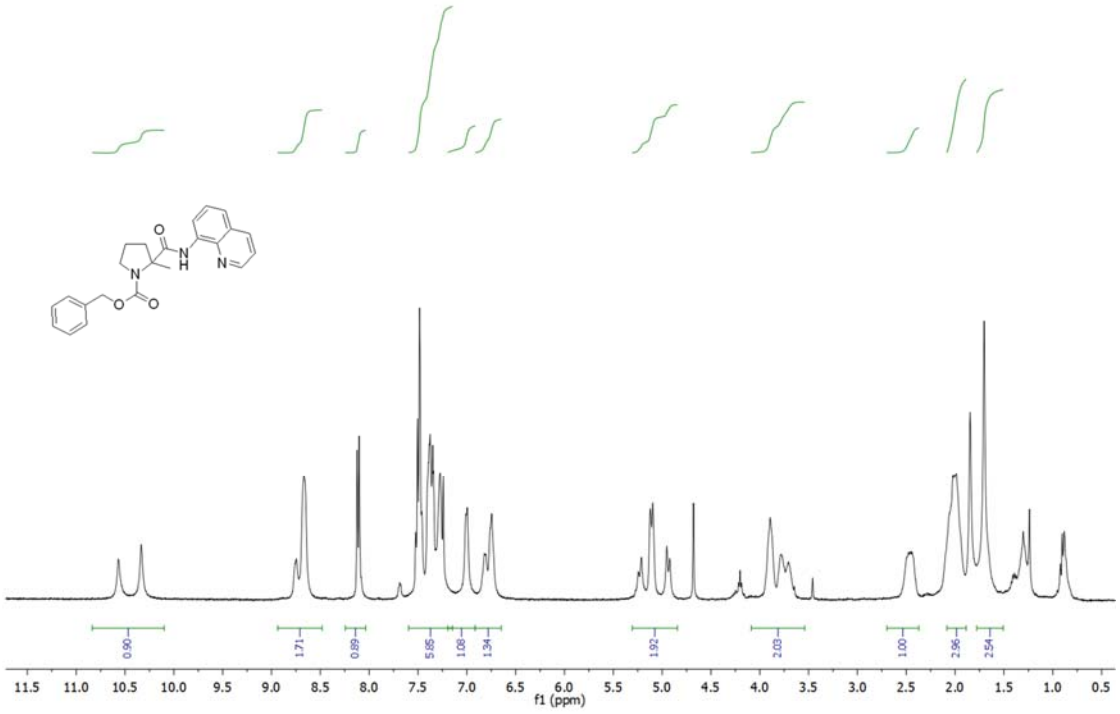
Compound Cbz – 12



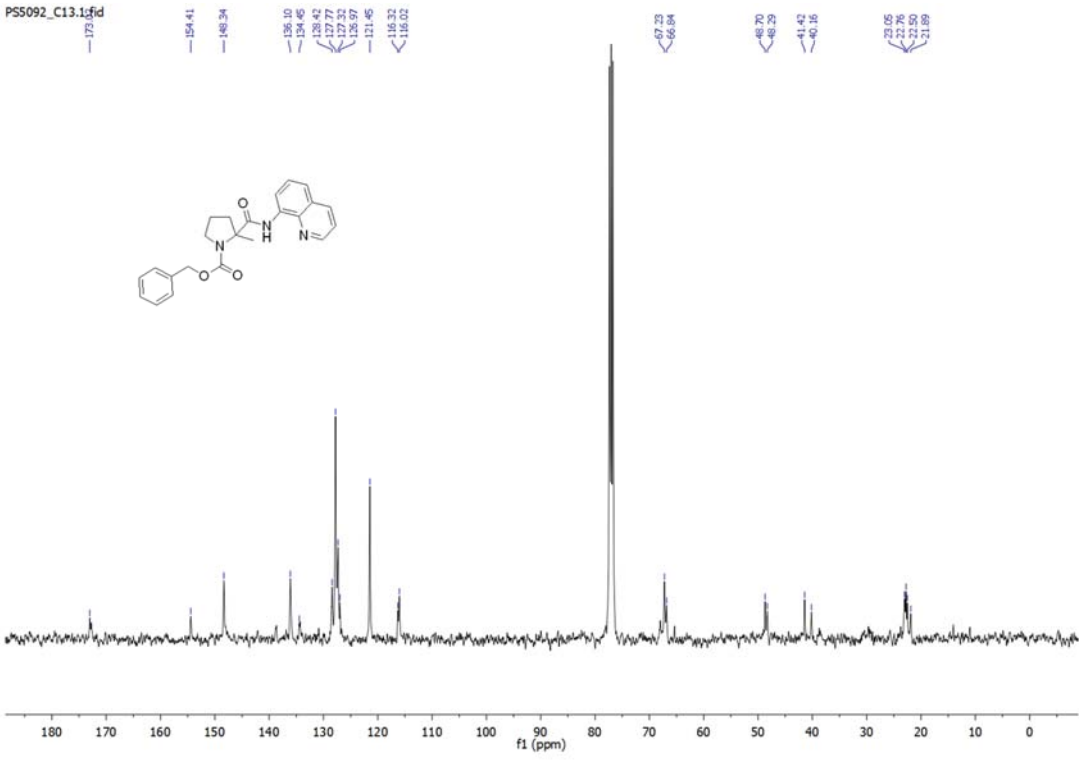


Compound Cbz – 13

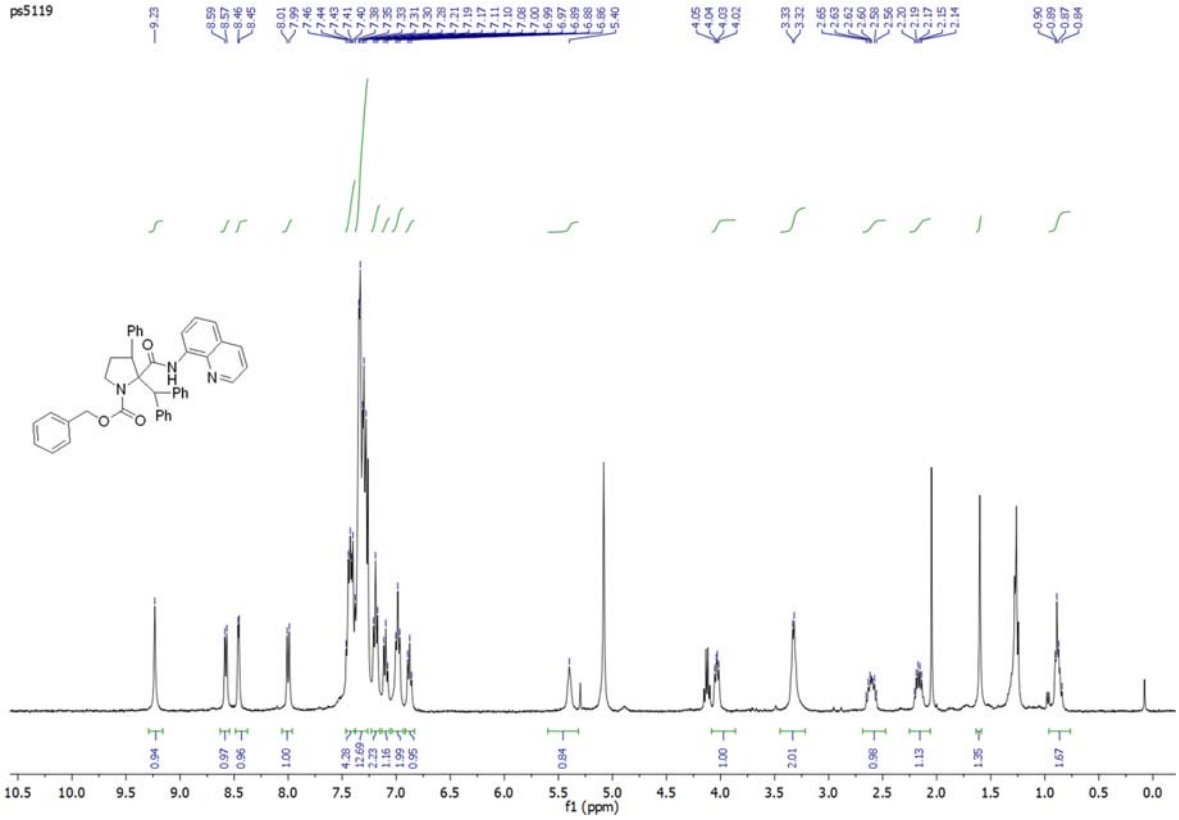
ps5092.1.fid

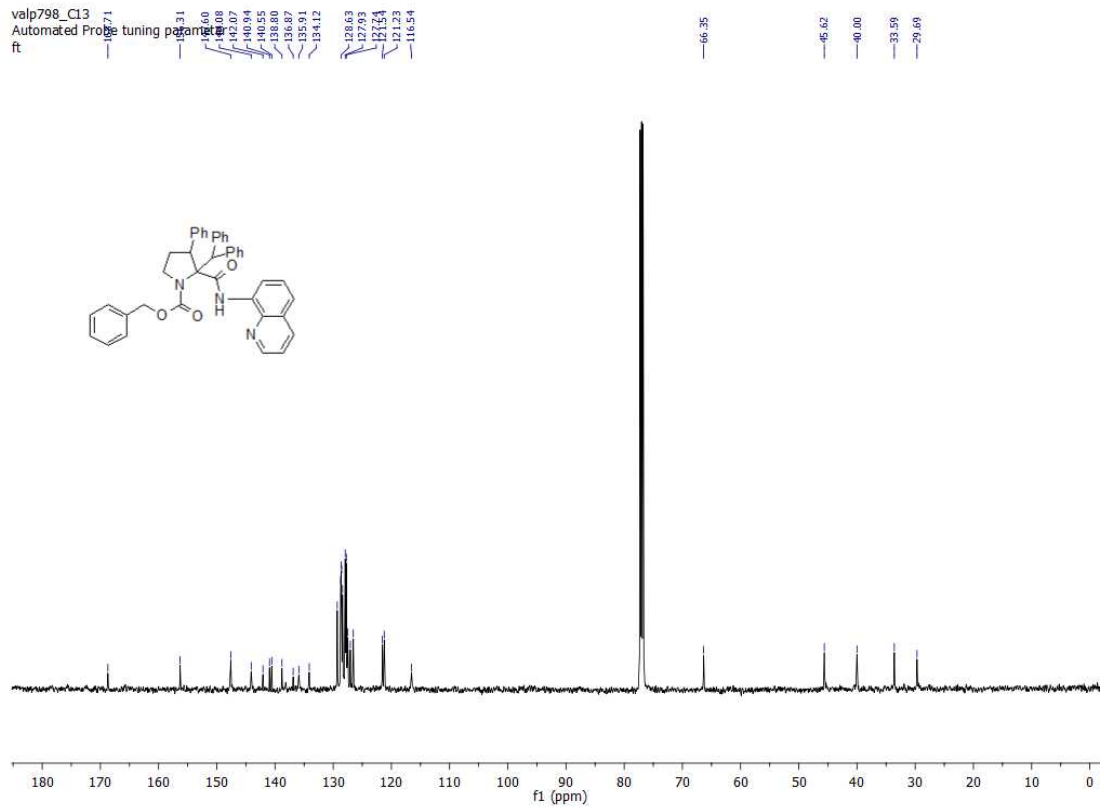


PS5092_C13.1.fid

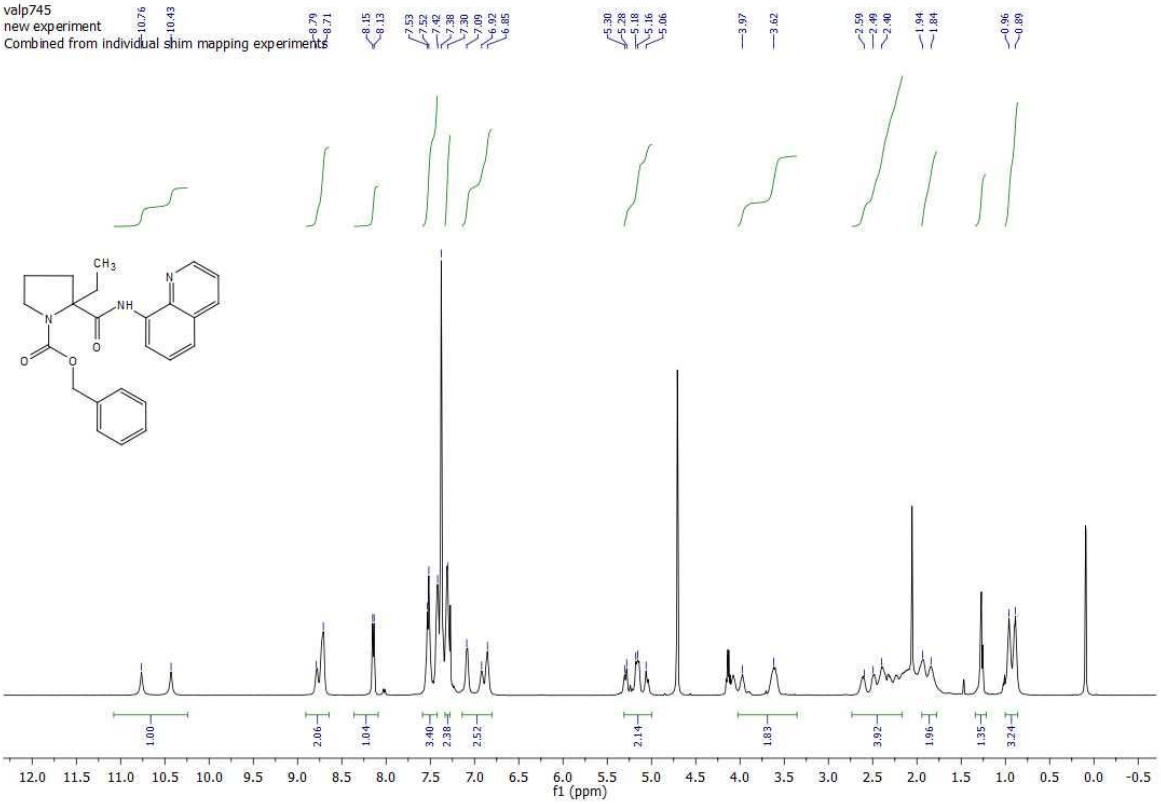


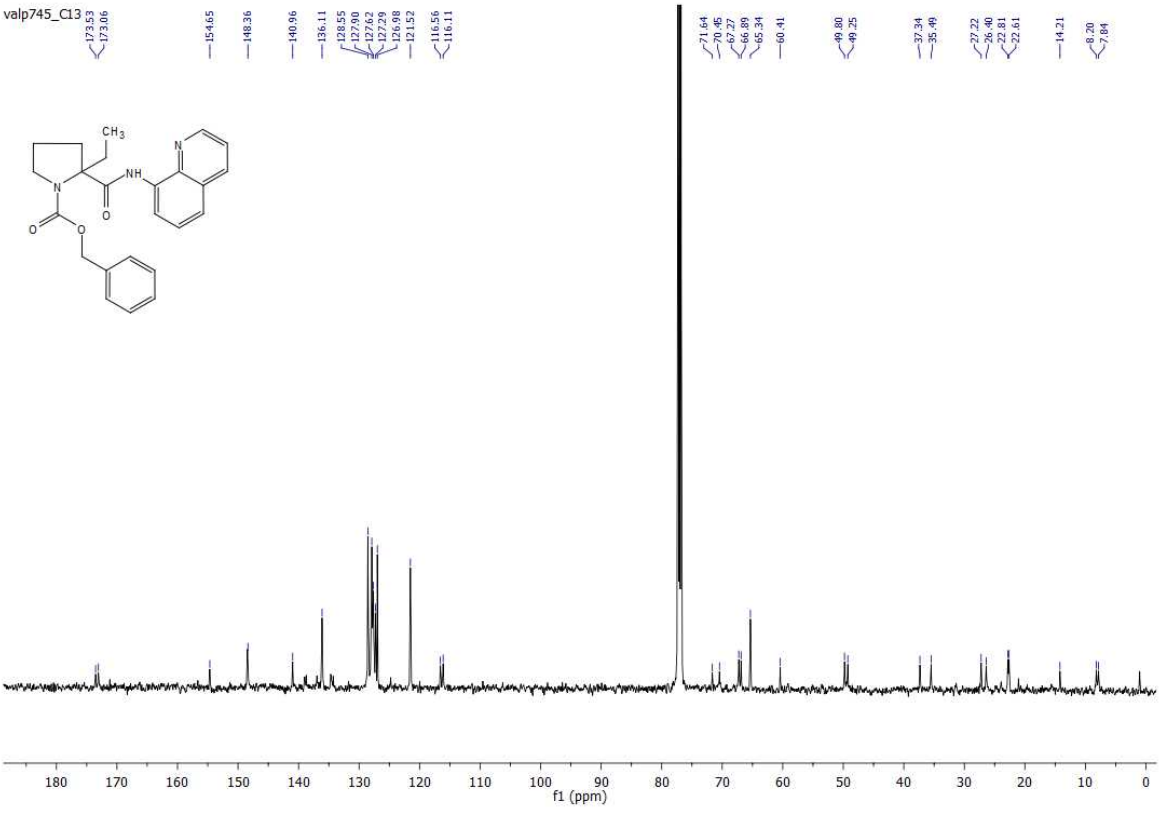
Compound Cbz – 13c



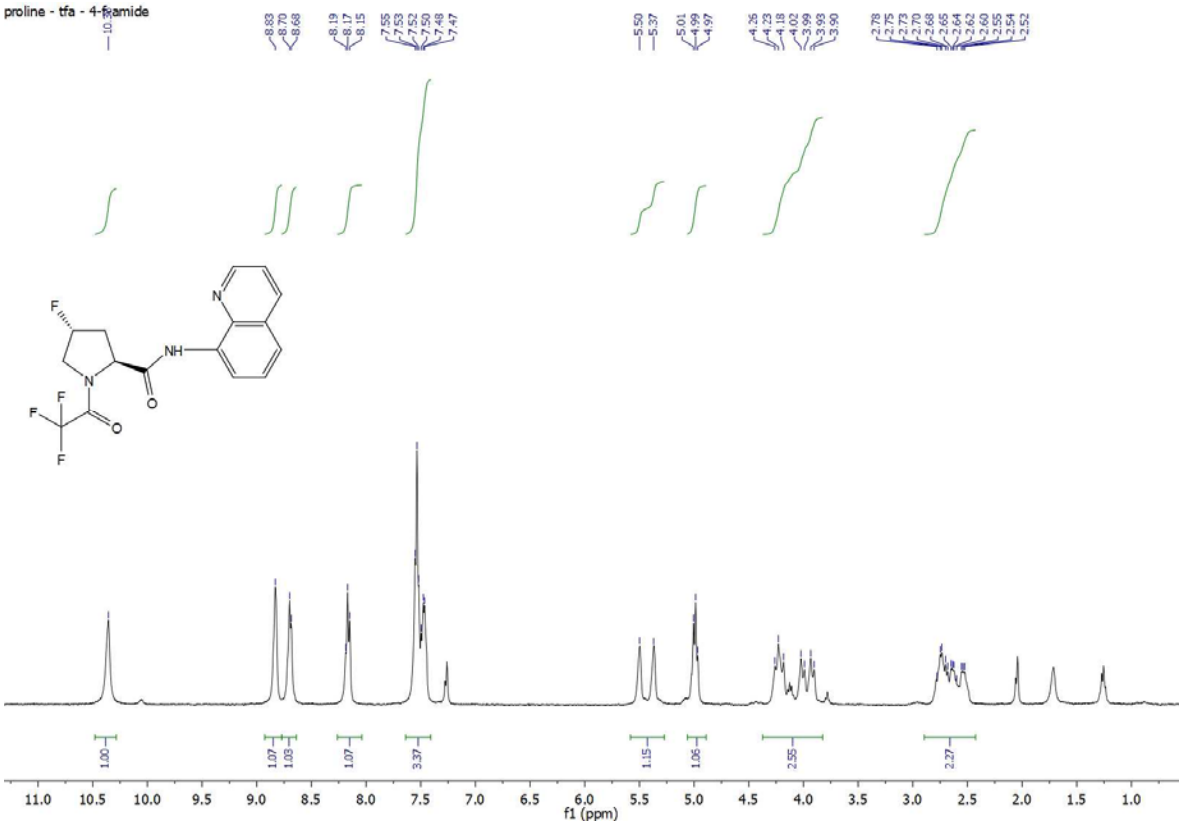


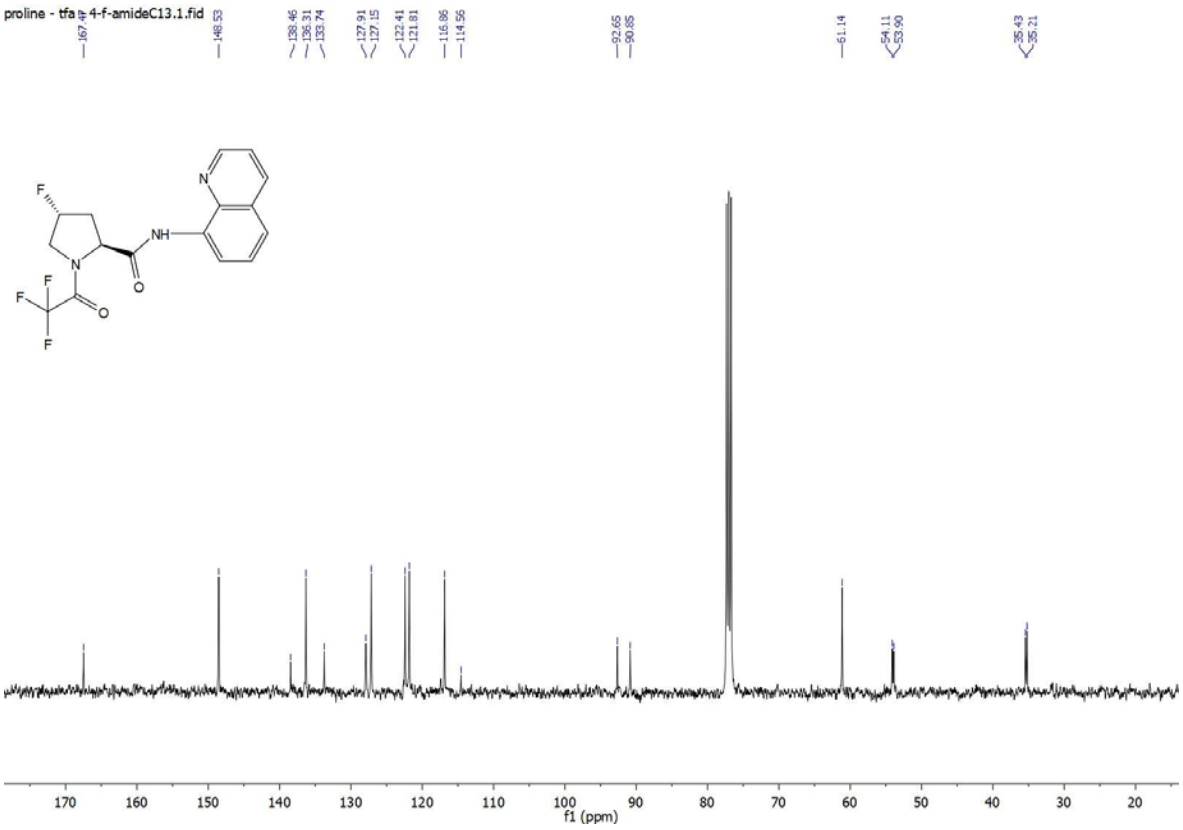
Compound Cbz – 14

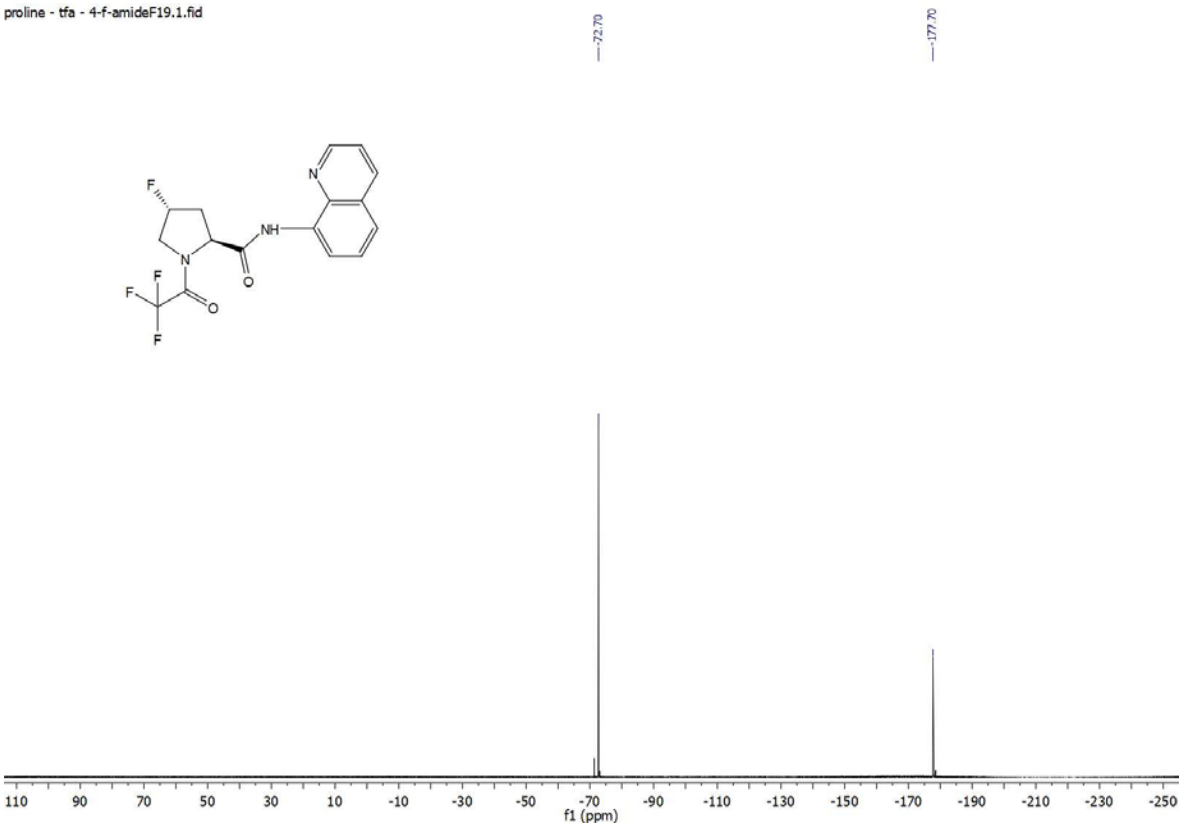




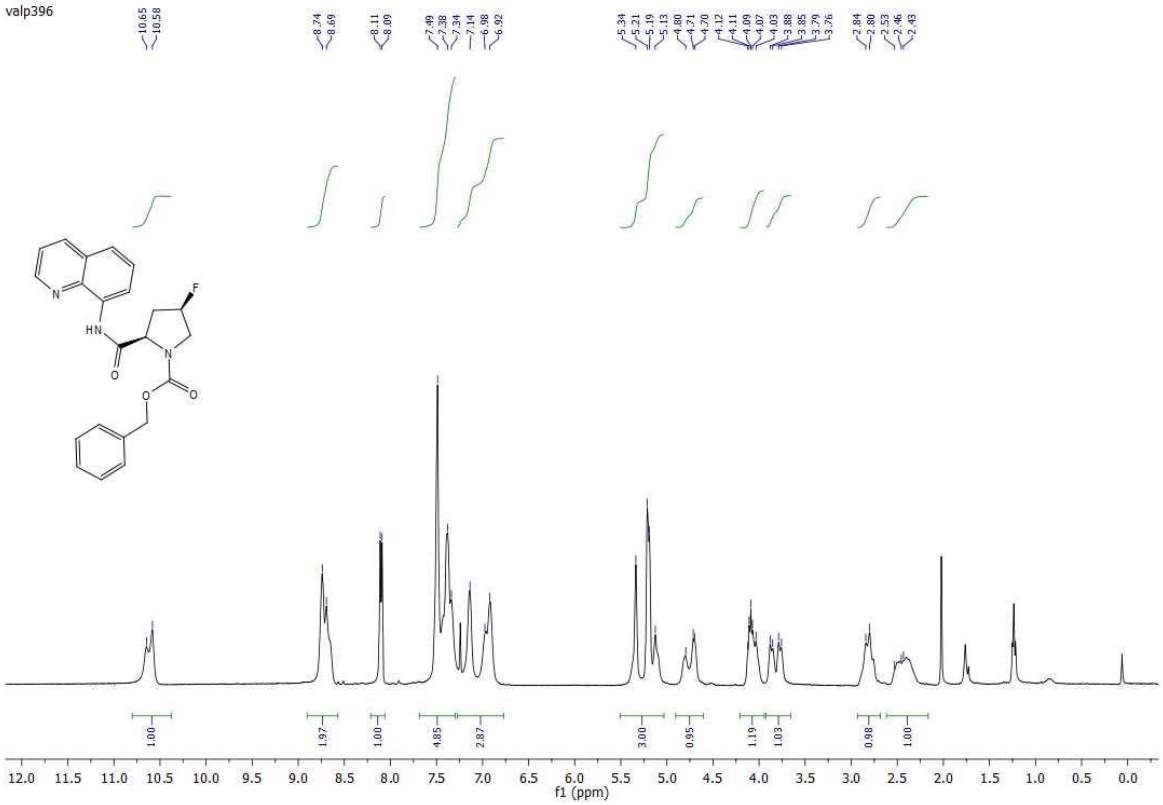
Compound TFA – 15

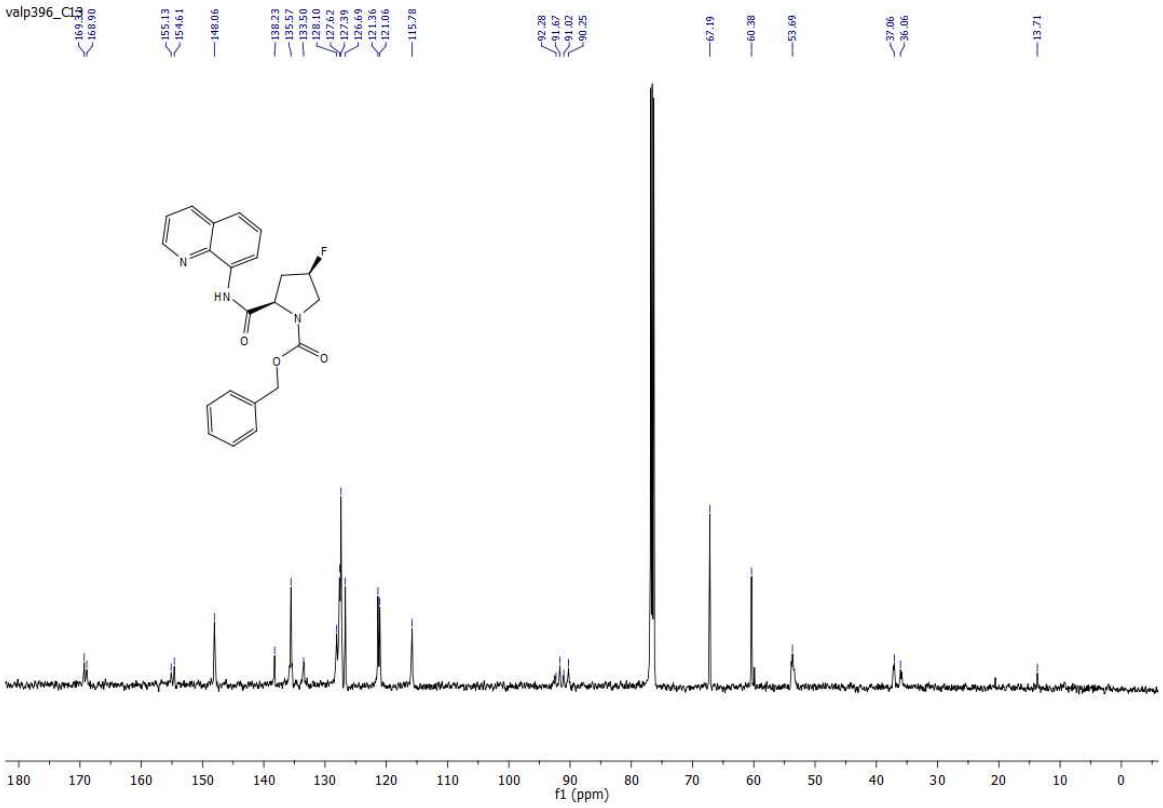


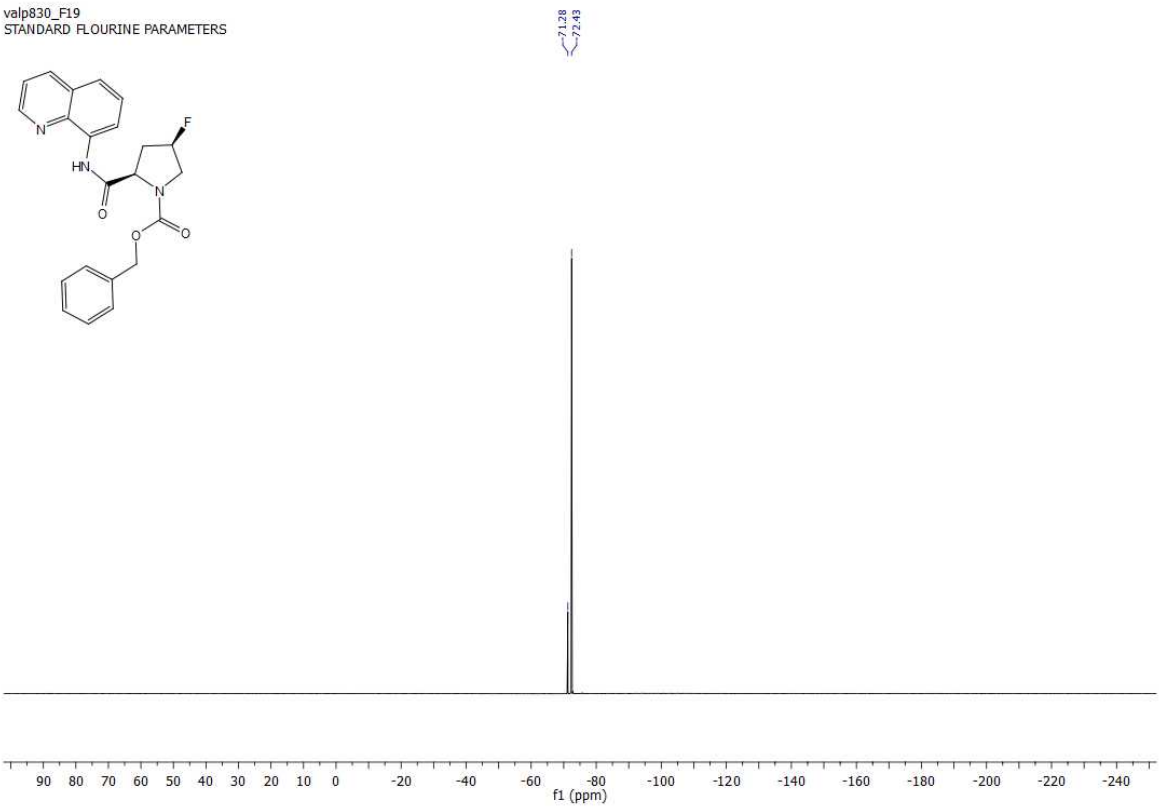



proline - tfa - 4-f-amideF19.1.fid
-72.70
-177.70
F
N
NH
O
F
F
F
O
110
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
-230
-250
f1 (ppm)

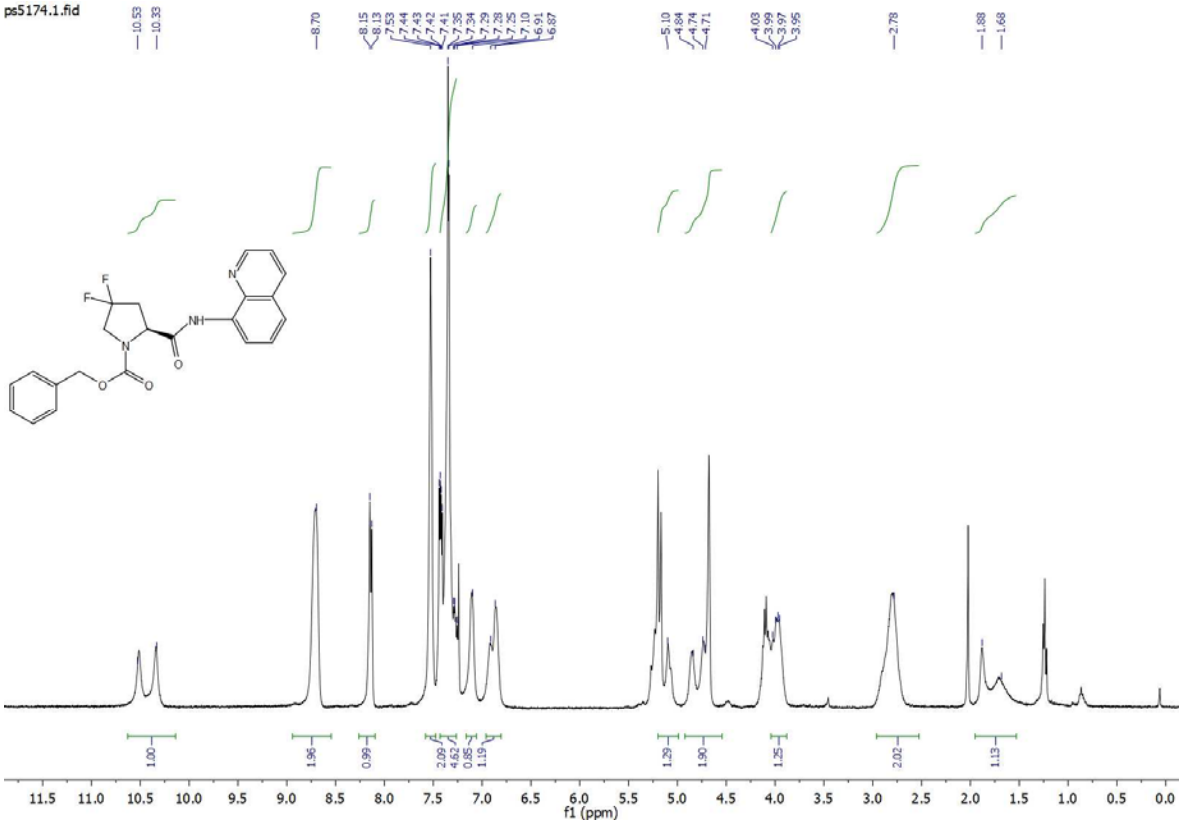
Compound Cbz – 16

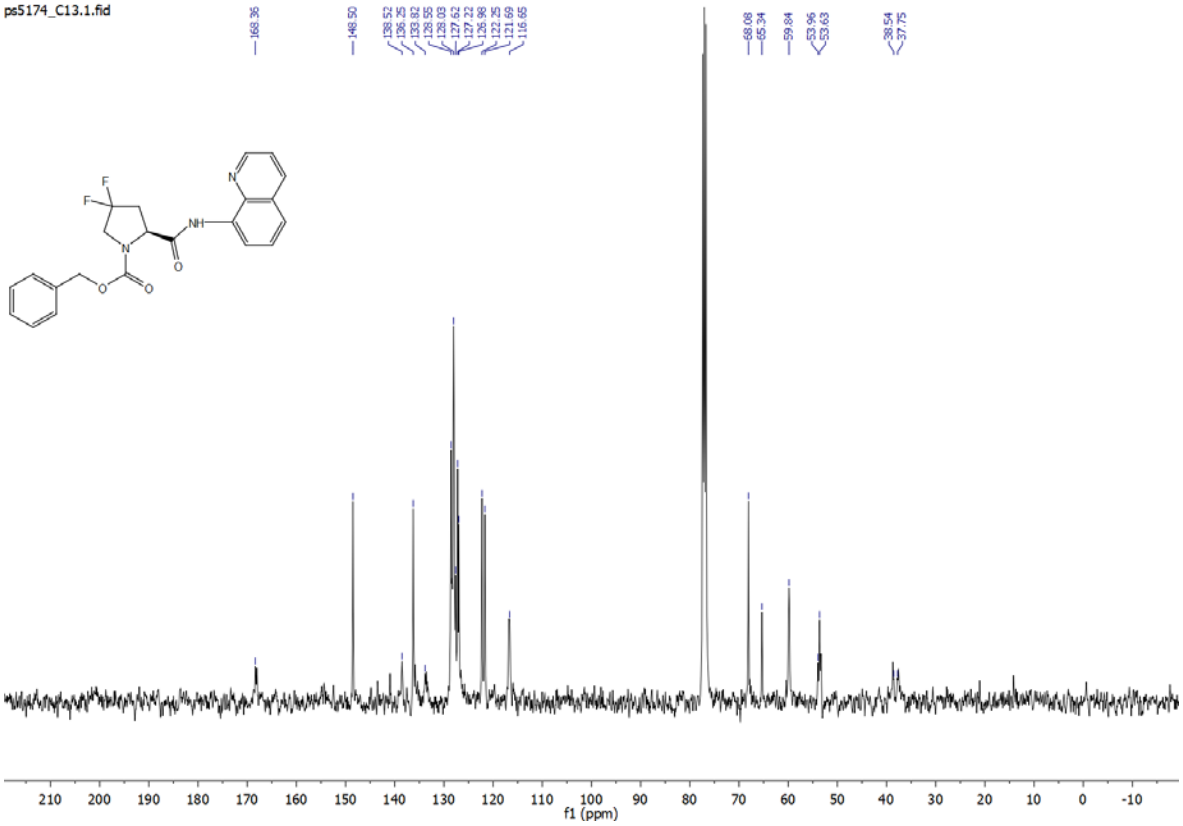


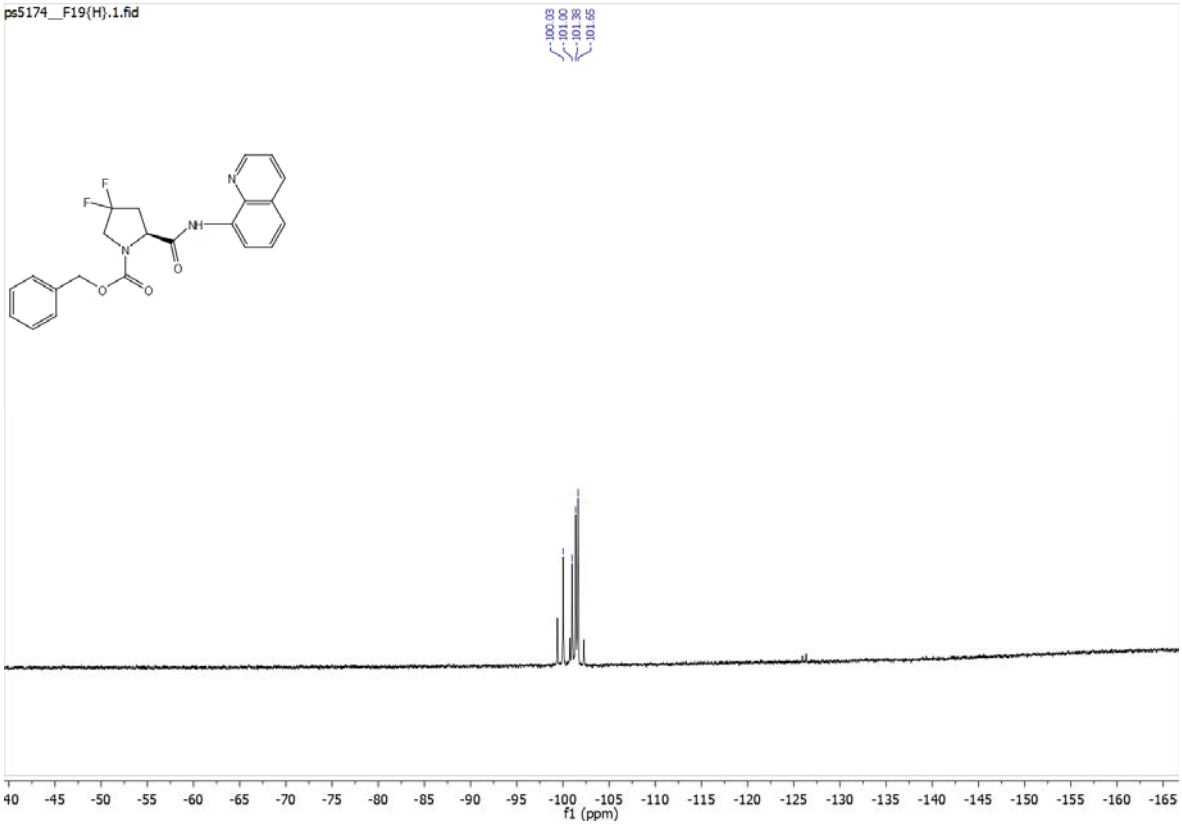



valp830_F19
STANDARD FLOURINE PARAMETERS
-71.28
-72.43
N
HN
O
N
F
O
O
90 80 70 60 50 40 30 20 10 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -240
f1 (ppm)

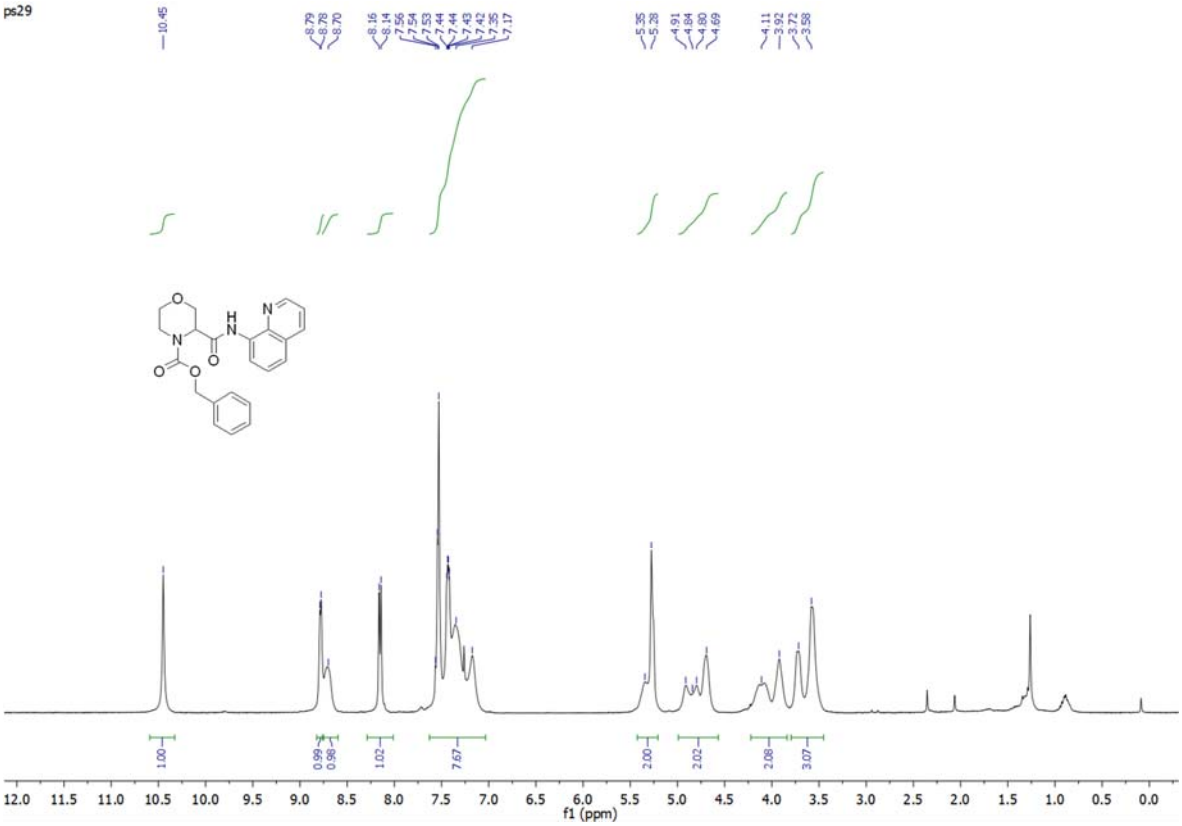
Compound Cbz – 17

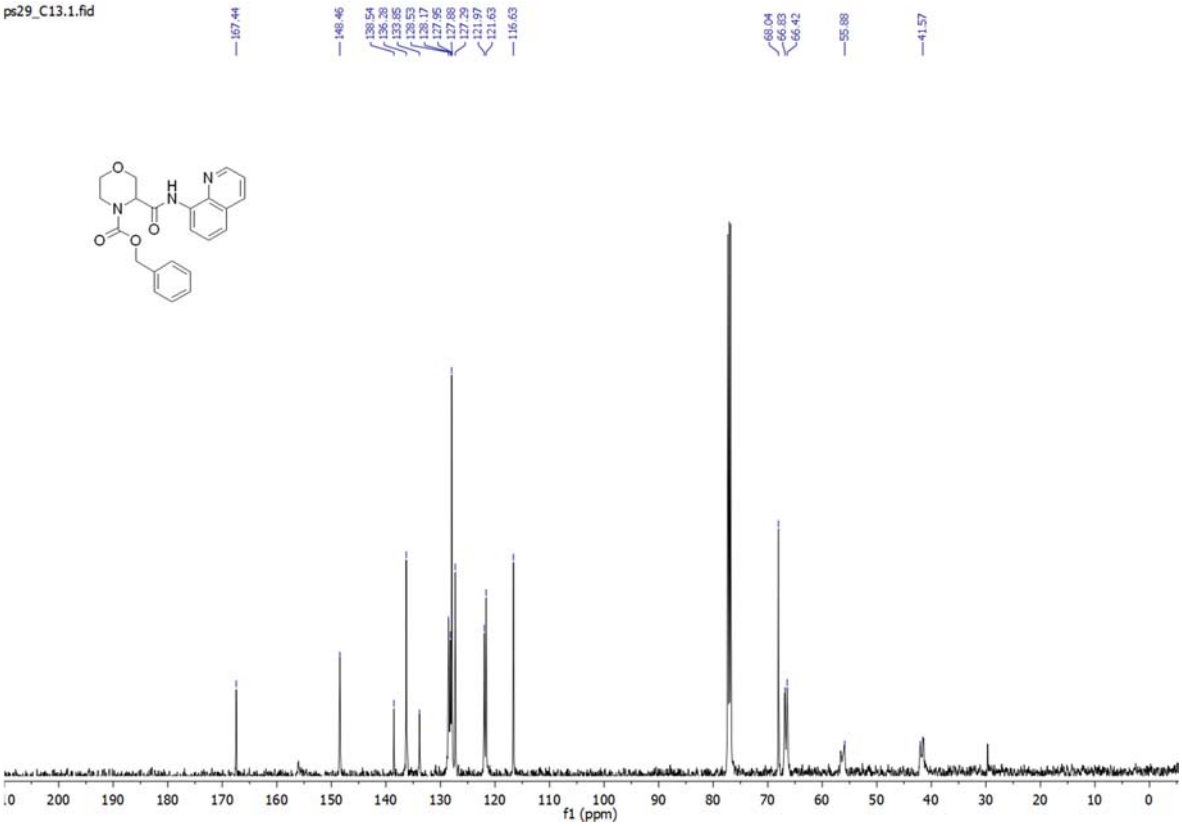




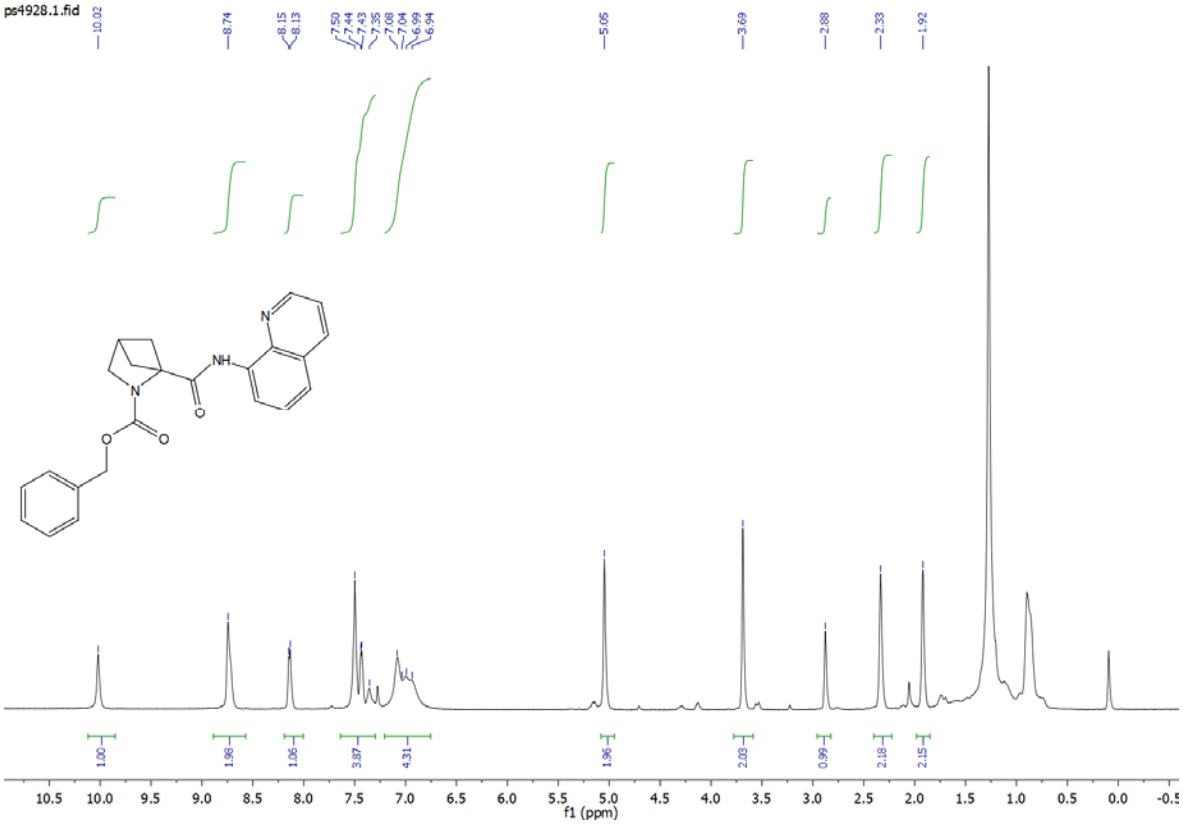

ps5174__F19(H).1.fid
-100.03
-101.00
-101.38
-101.65
F
F
N
NH
O
N
O
O
40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165
f1 (ppm)

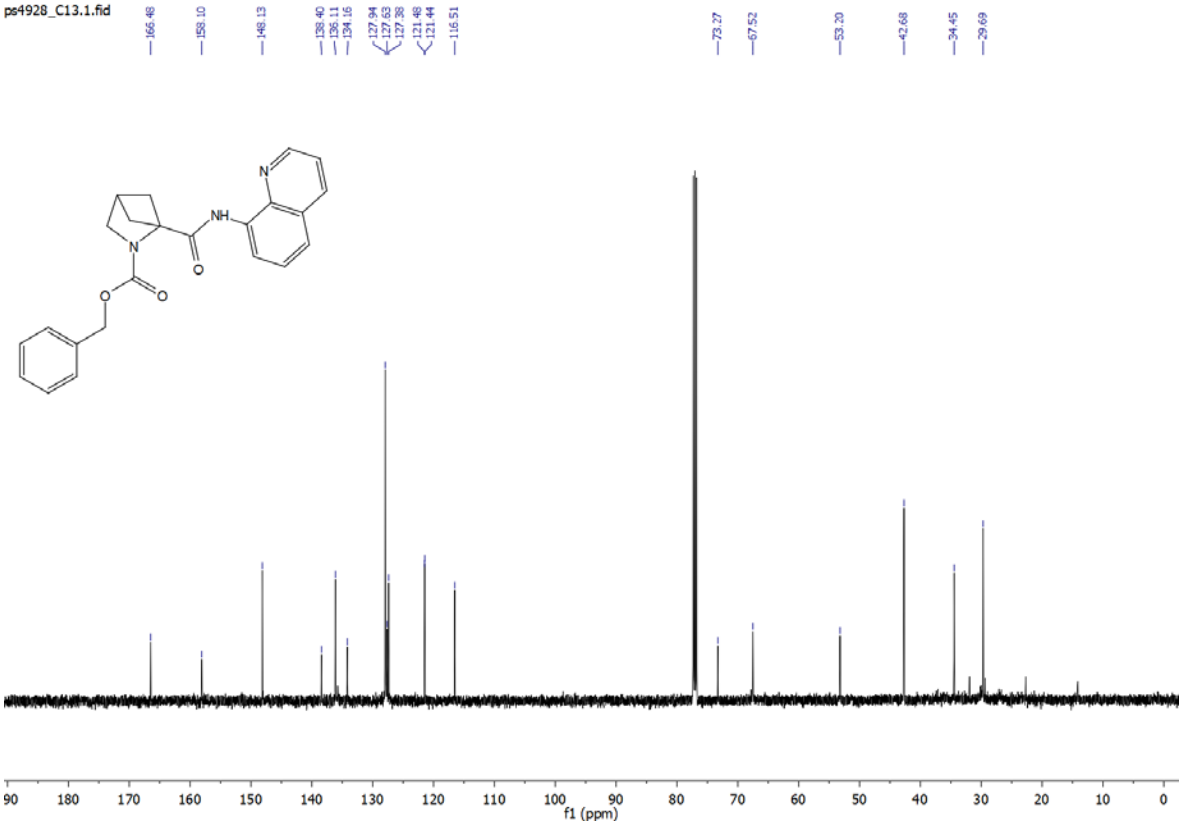
Compound Cbz – 18



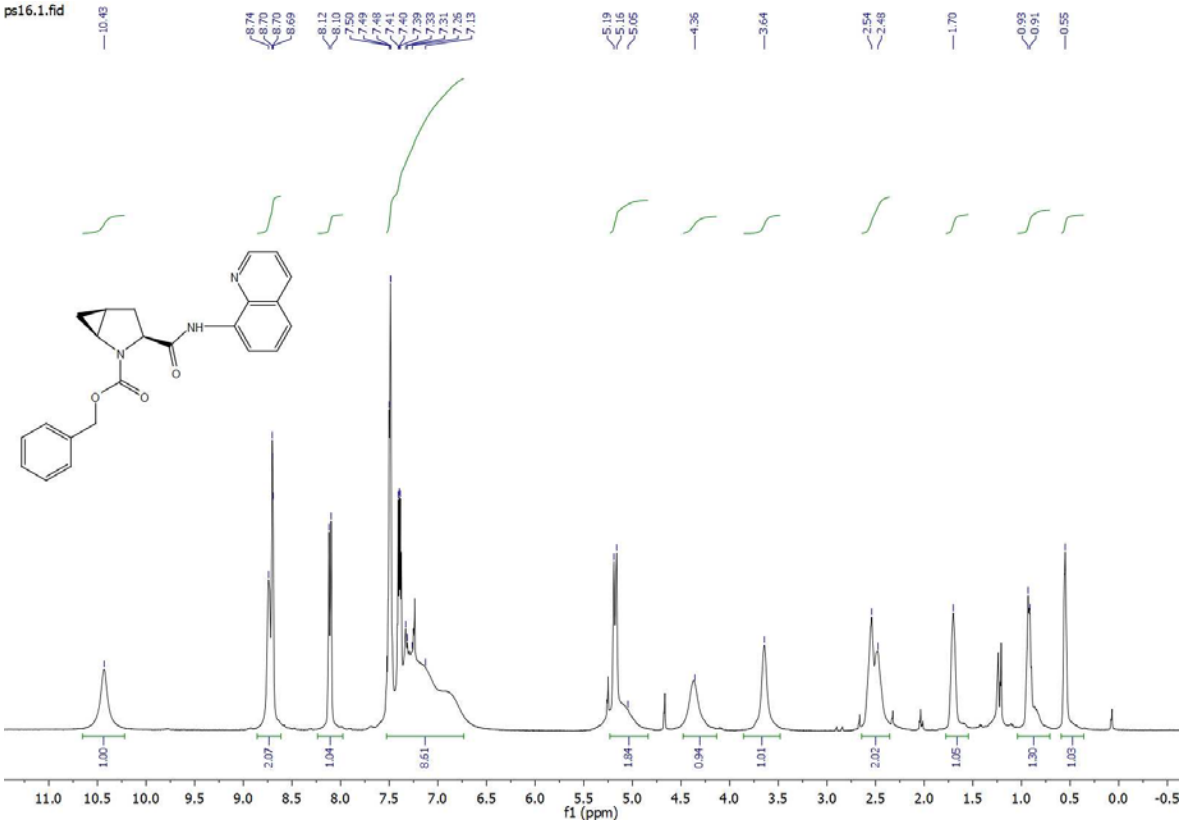


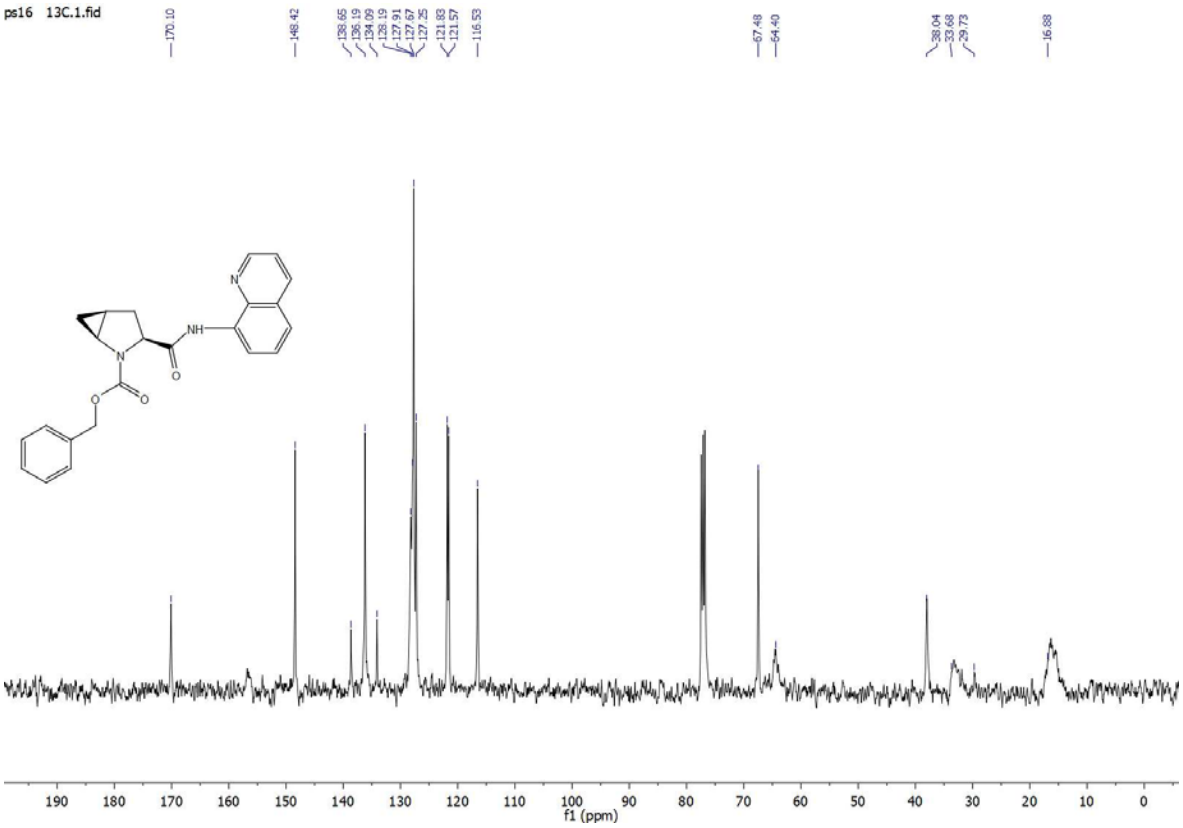
Compound Cbz – 19



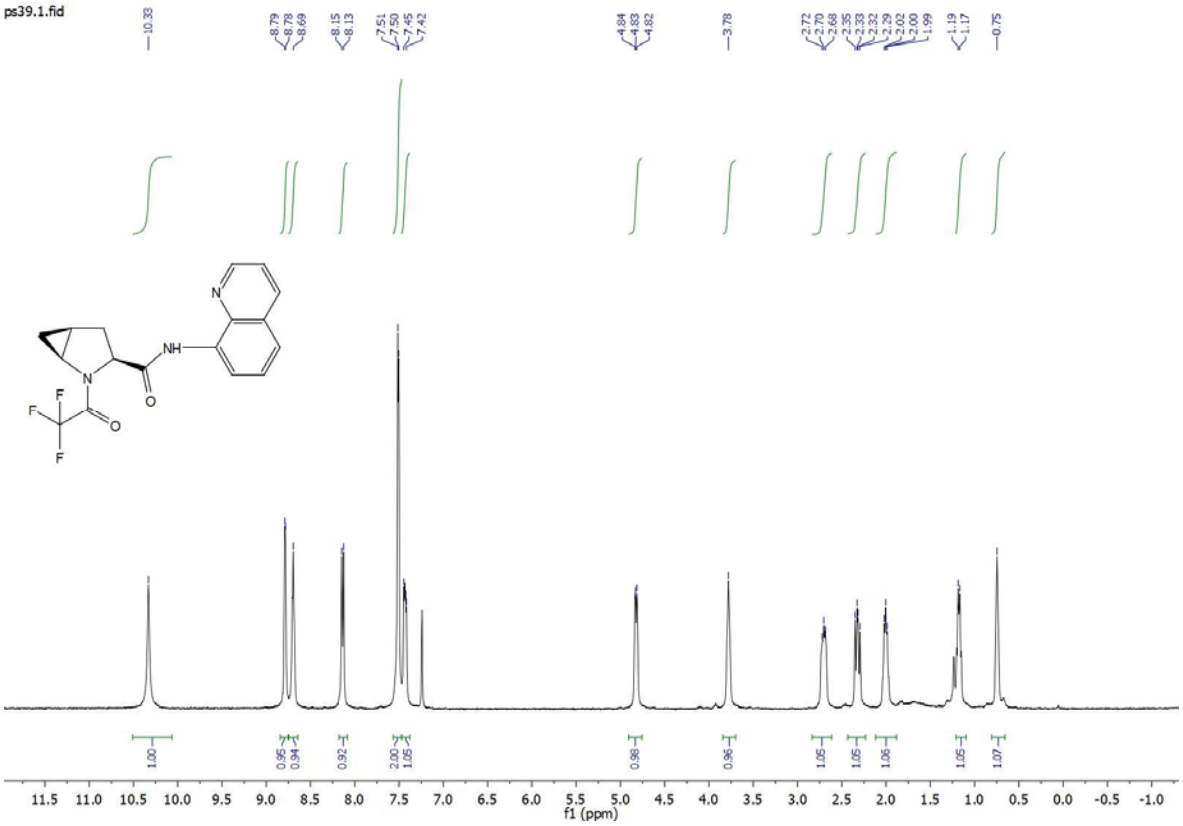


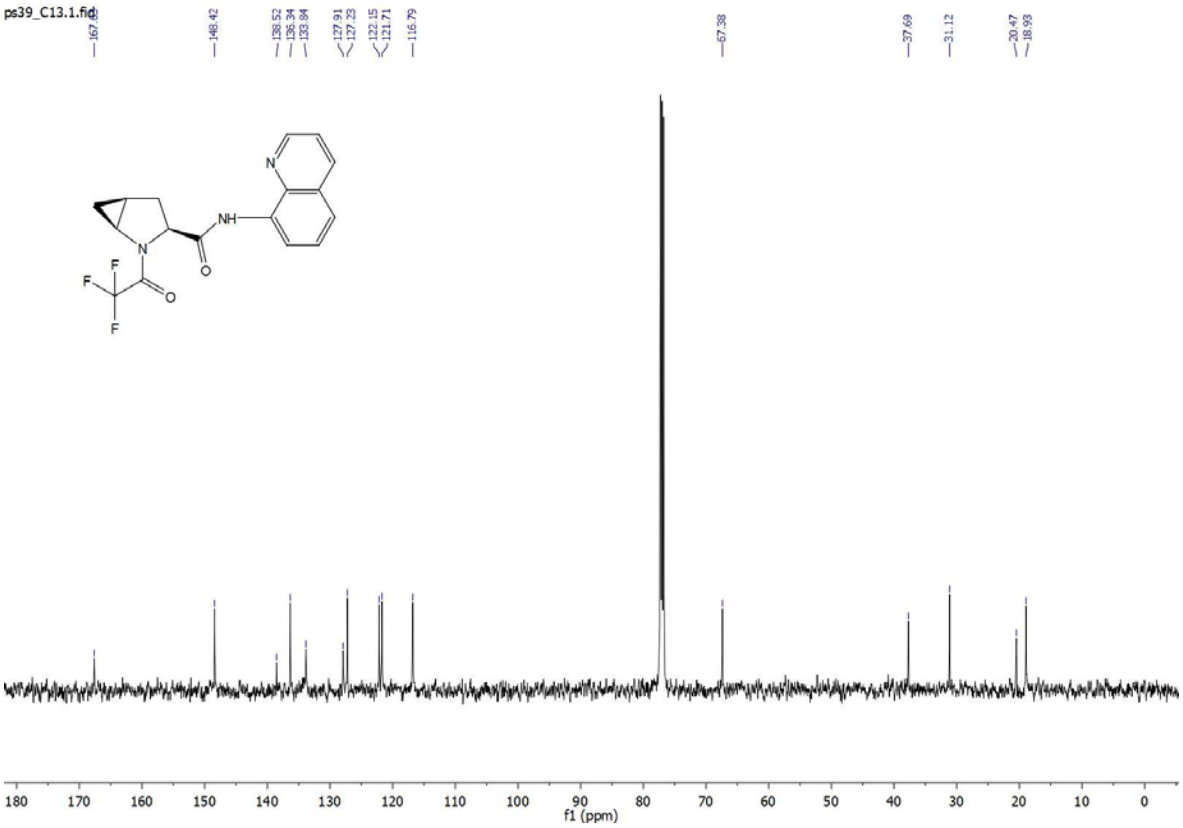
Compound Cbz – 20

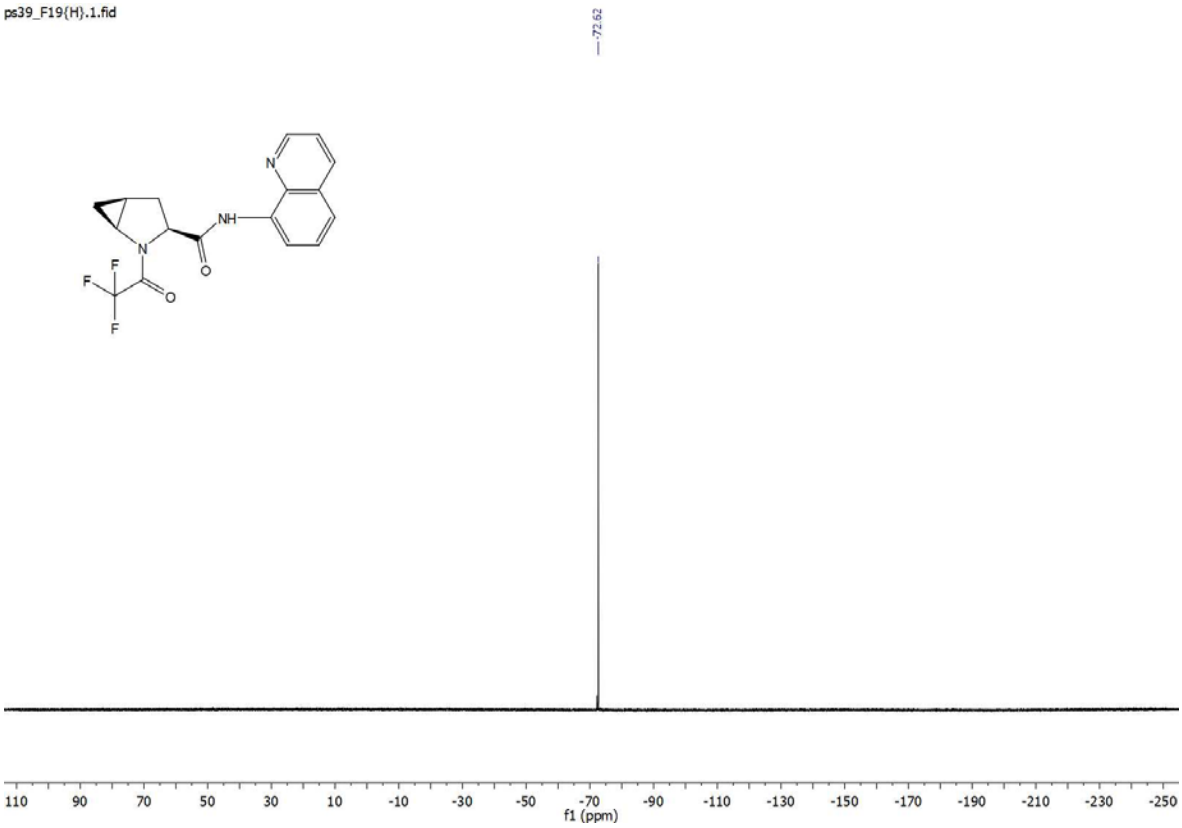




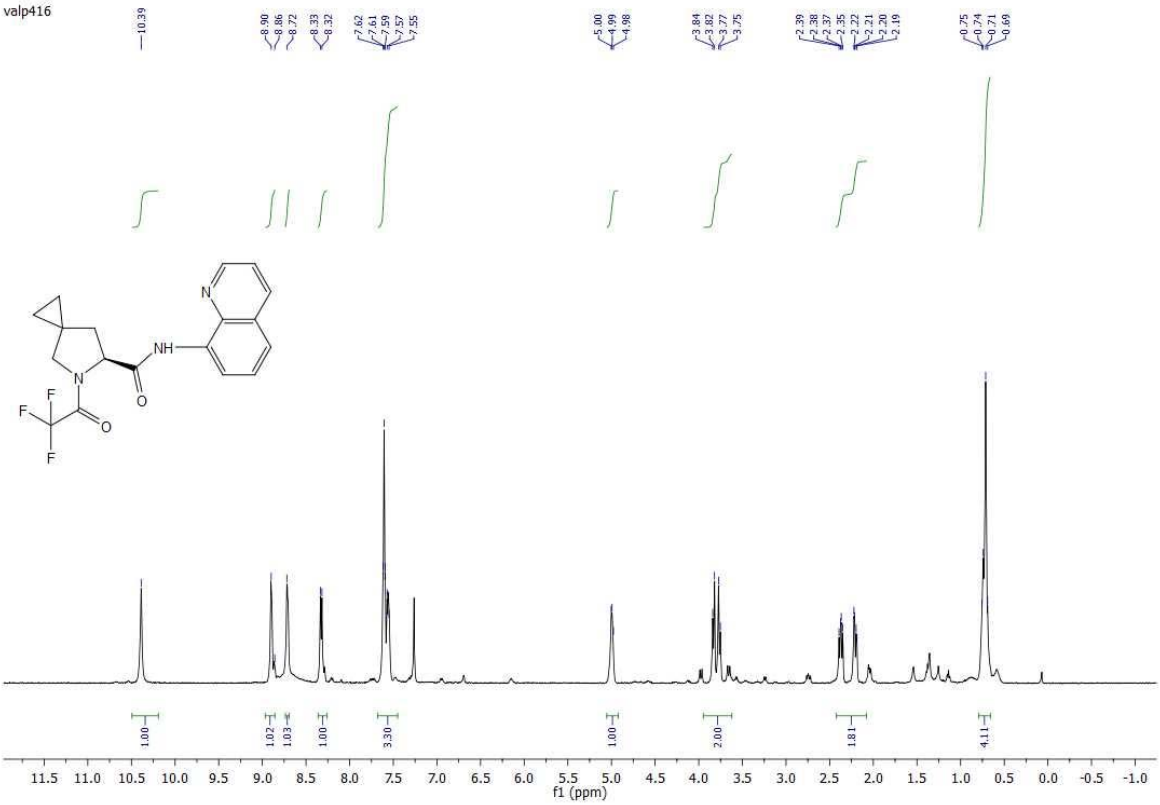
Compound TFA – 20

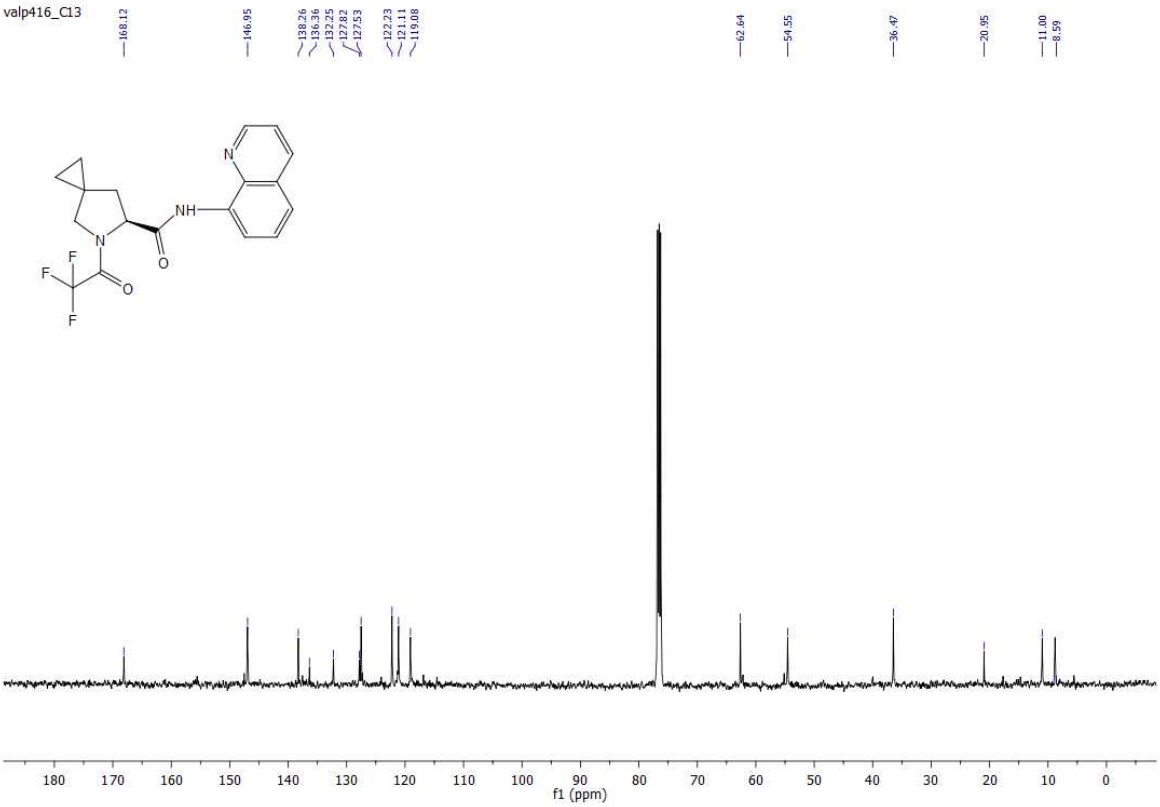


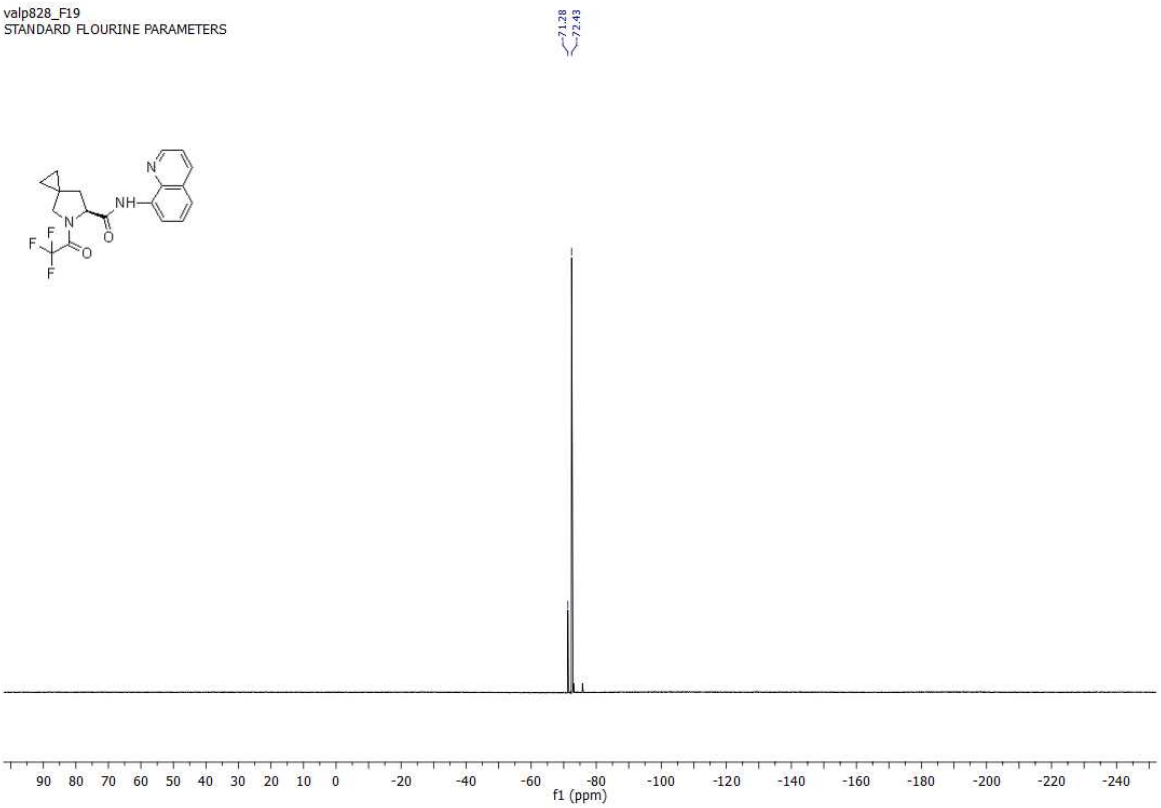



ps39_F19{H}.1.fid
-72.62
N
NH
O
N
F
F
F
O
110
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
-230
-250
f1 (ppm)

Compound TFA-21






valp828_F19
STANDARD FLOURINE PARAMETERS
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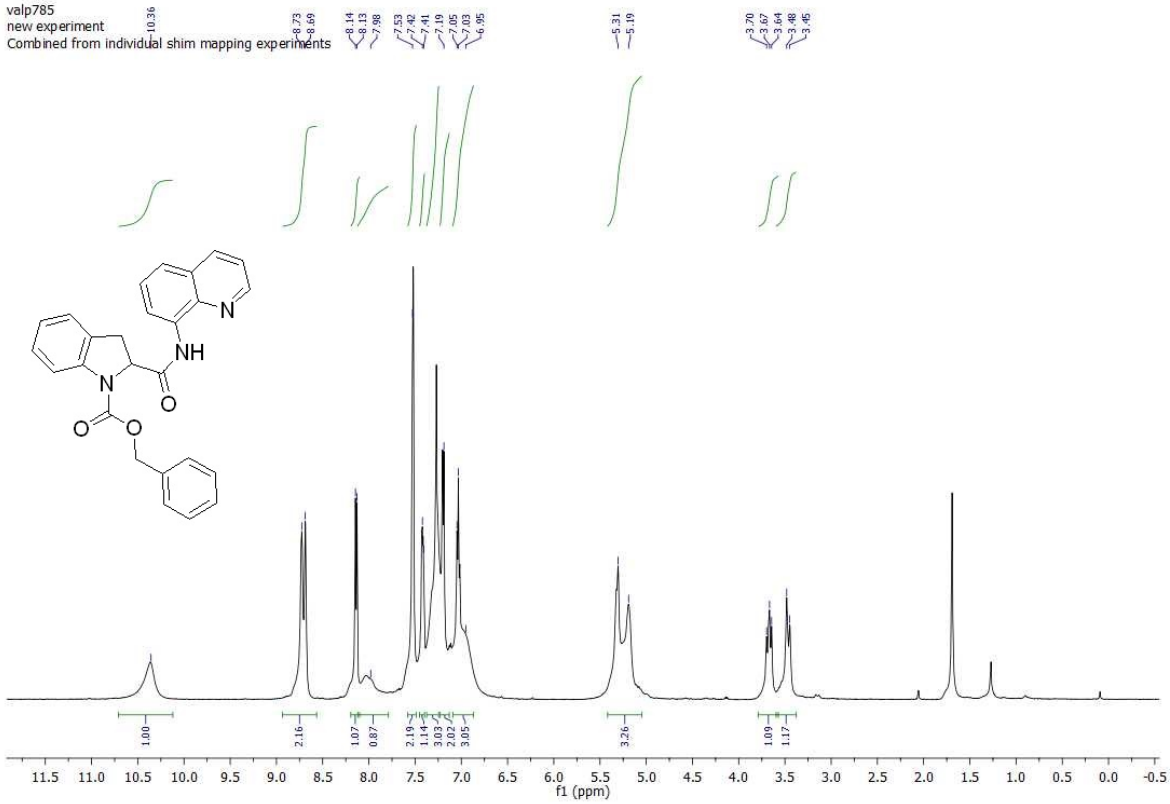
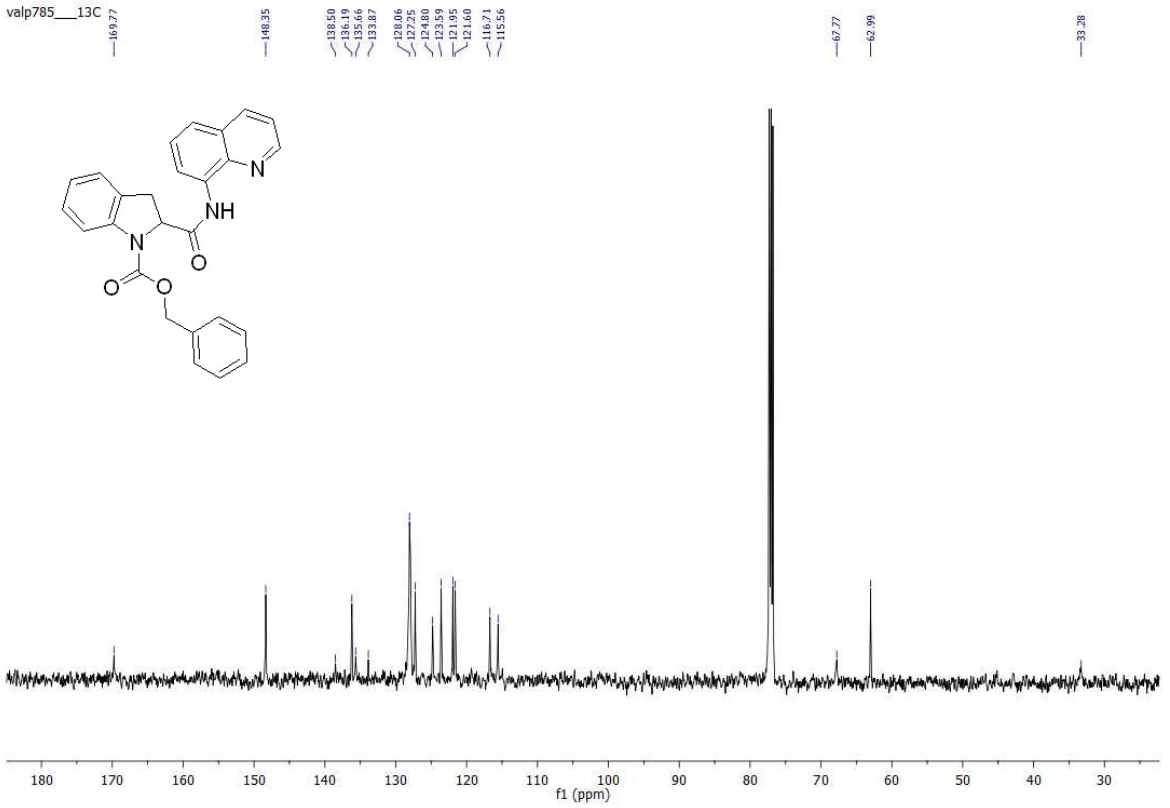
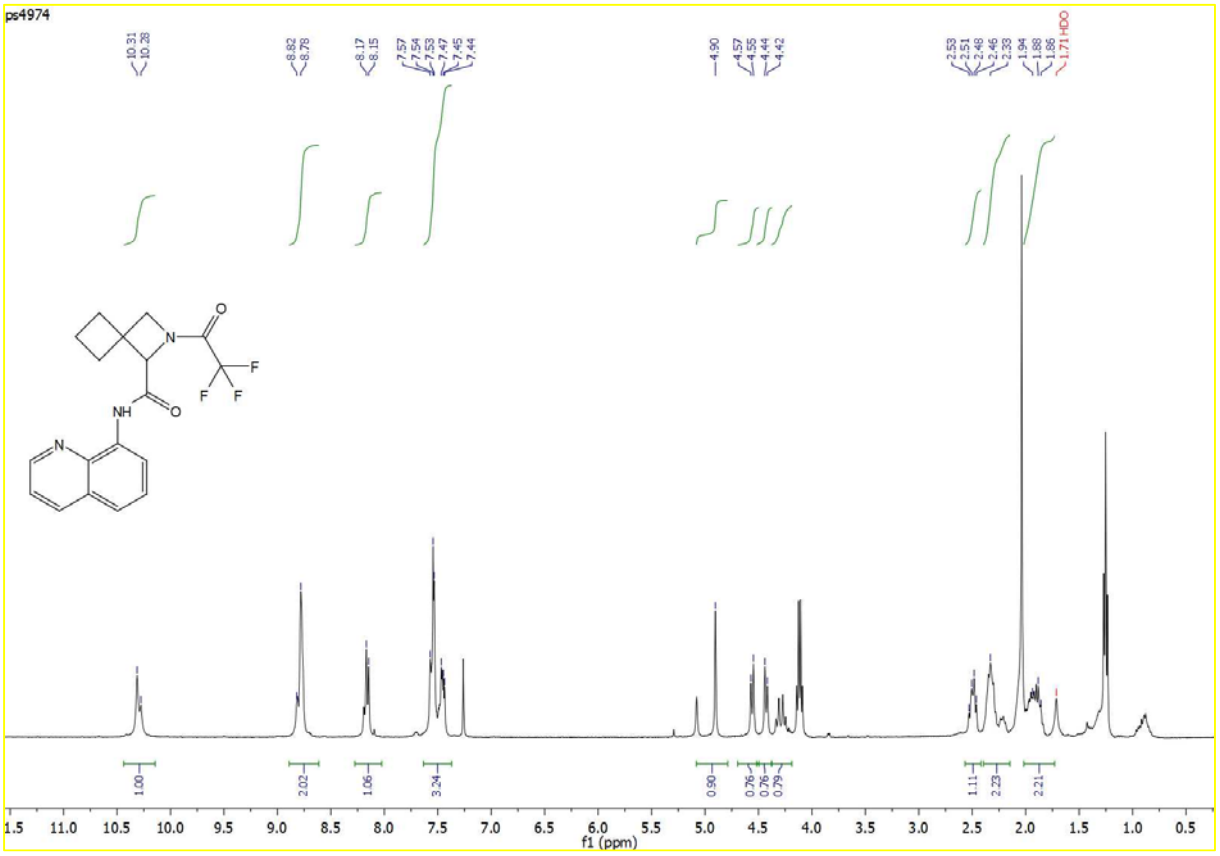
72.43
N
NH
O
N
F
F
F
O
90 80 70 60 50 40 30 20 10 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -240
f1 (ppm)

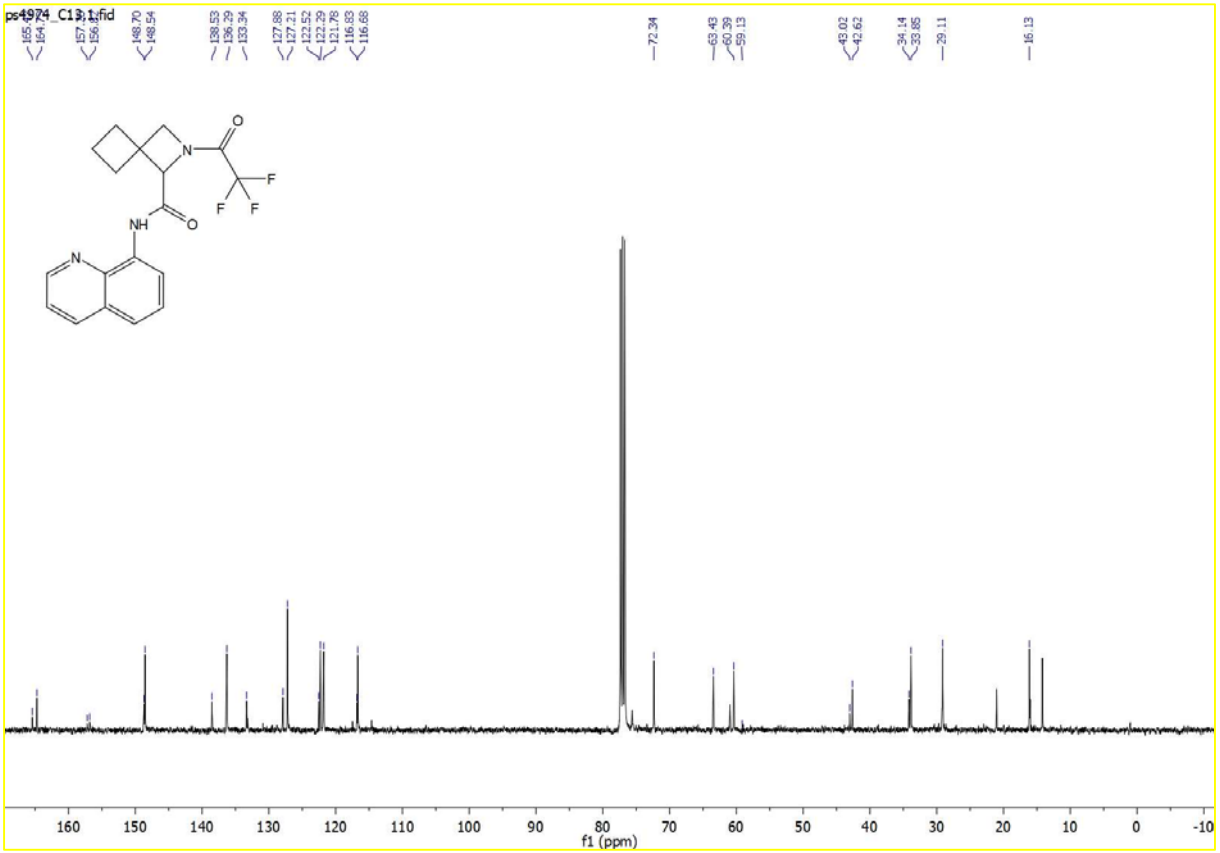
Compound Cbz-22

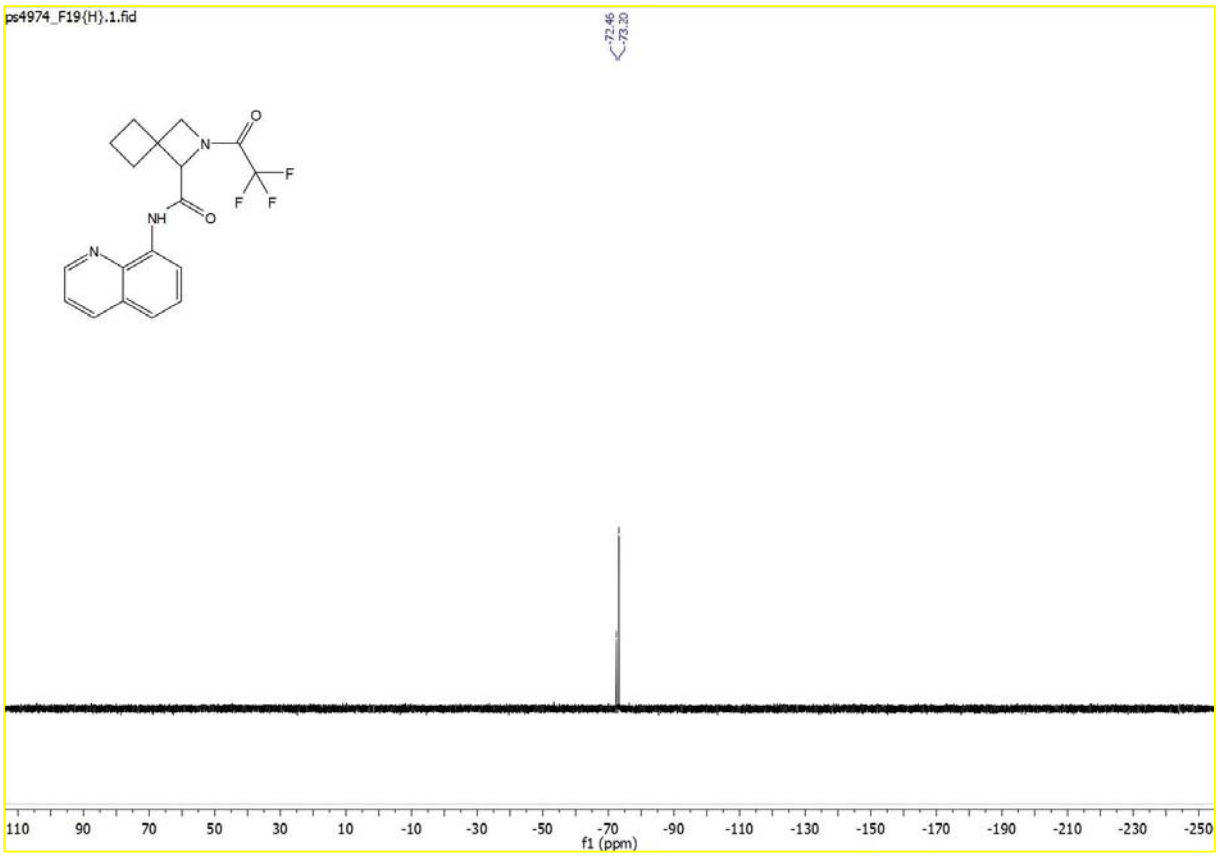




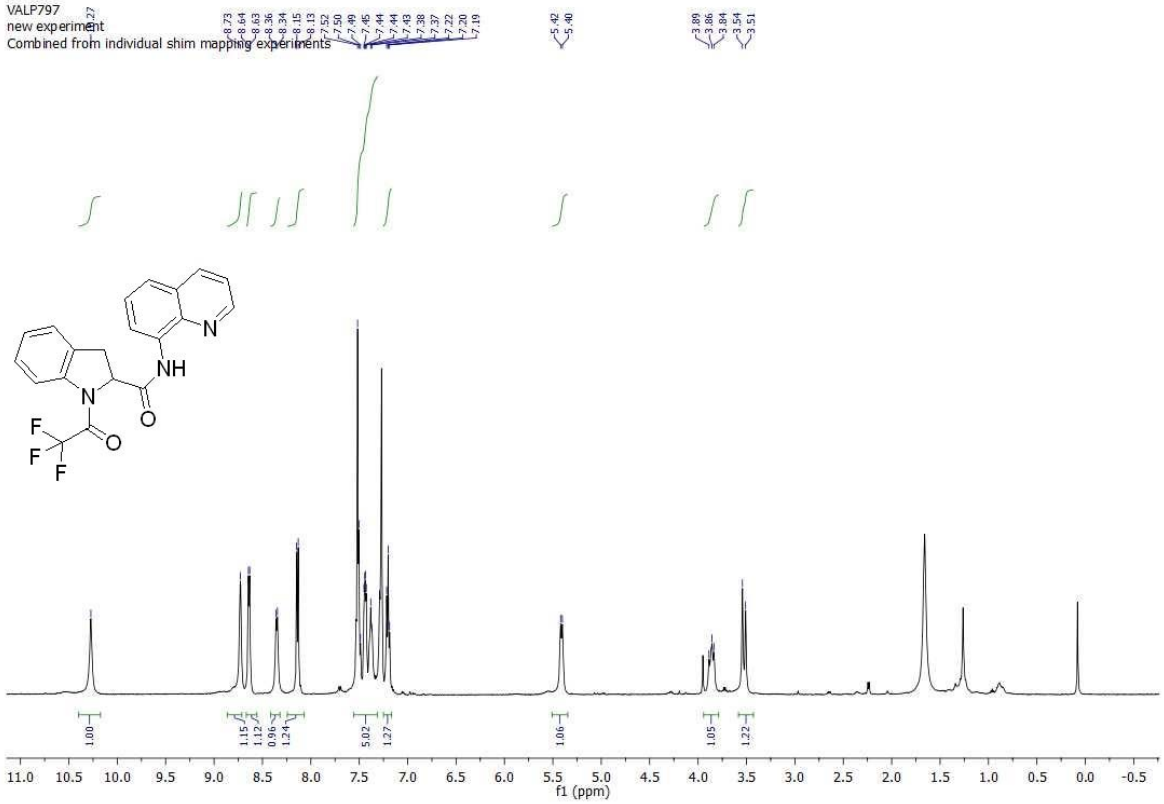
TFA-spiroAze

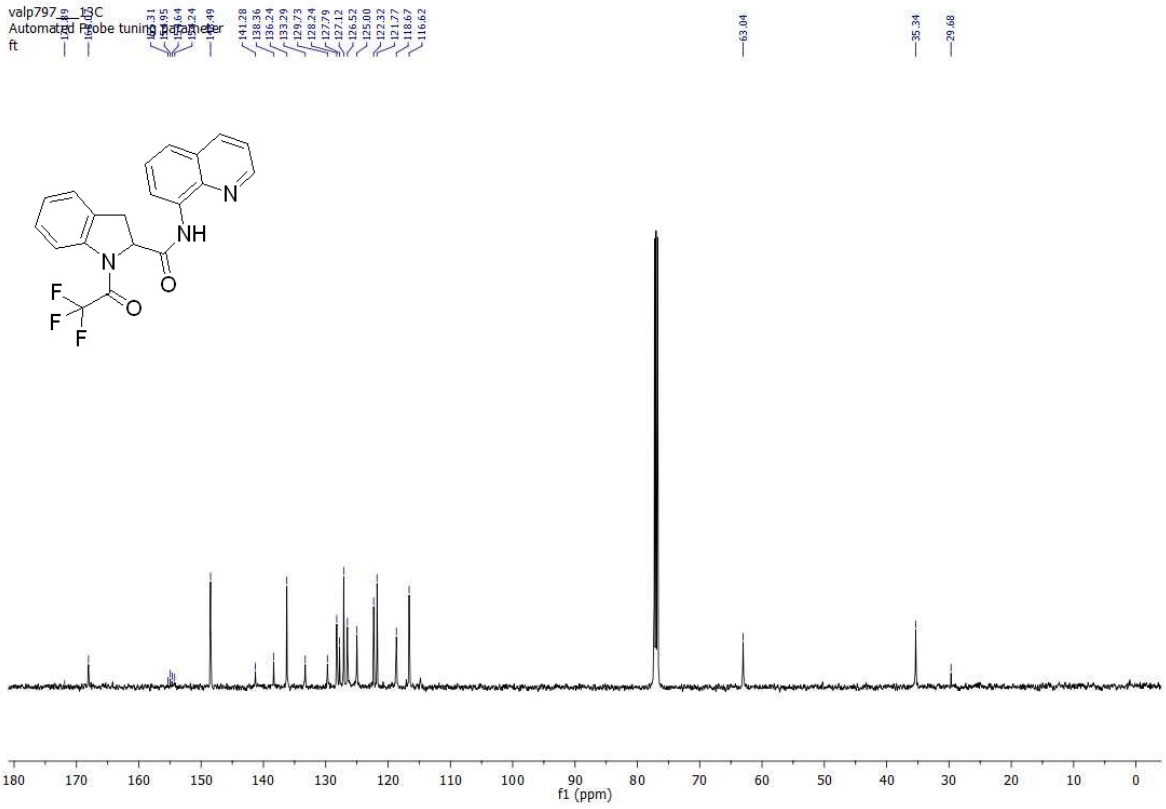




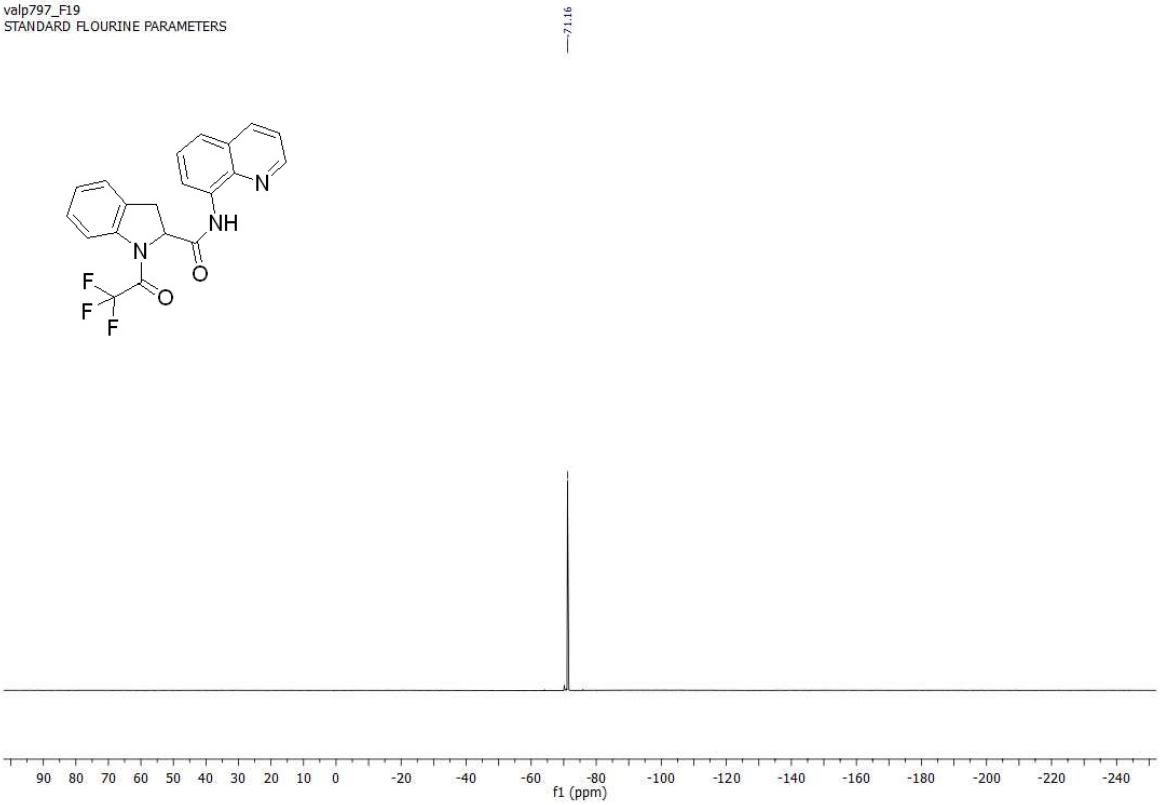

ps4974_F19{H}.1.fid
-72.46
-73.20
O
N
F
F
F
NH
O
N
110
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
-230
-250
f1 (ppm)

Compound TFA – 22

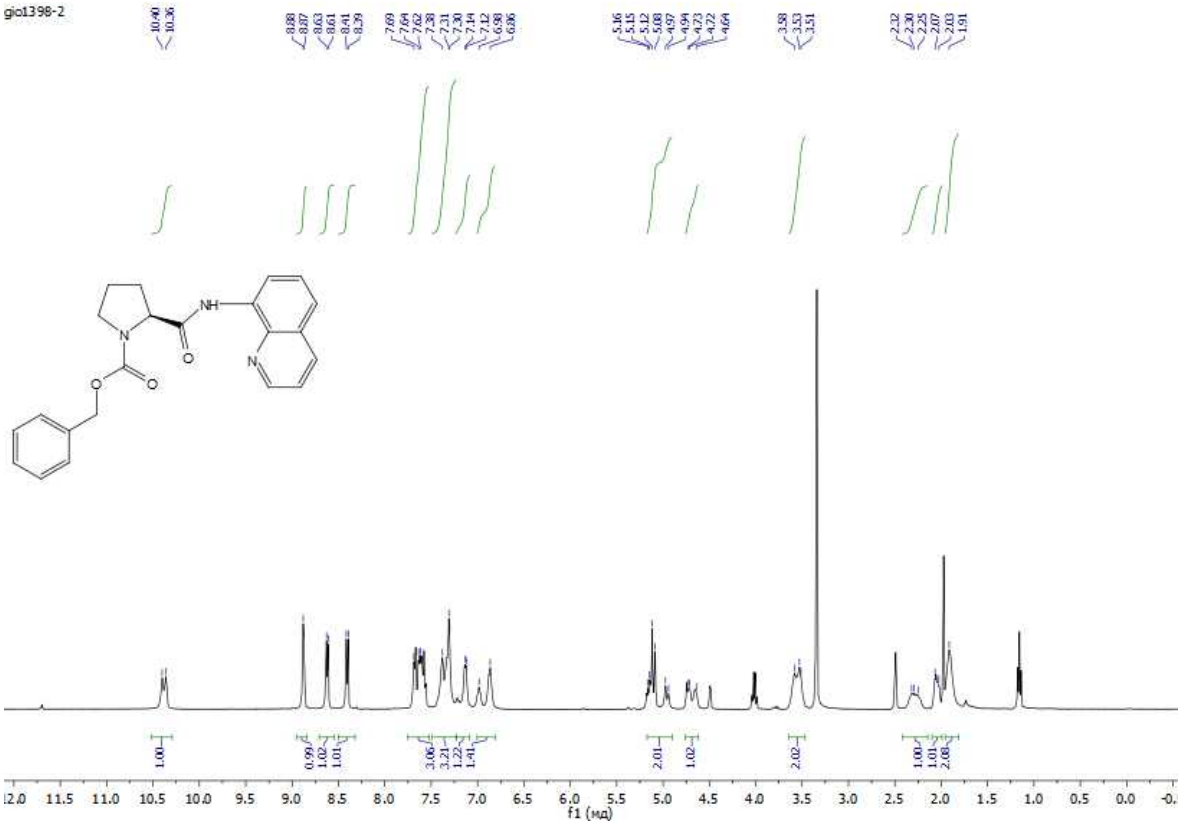


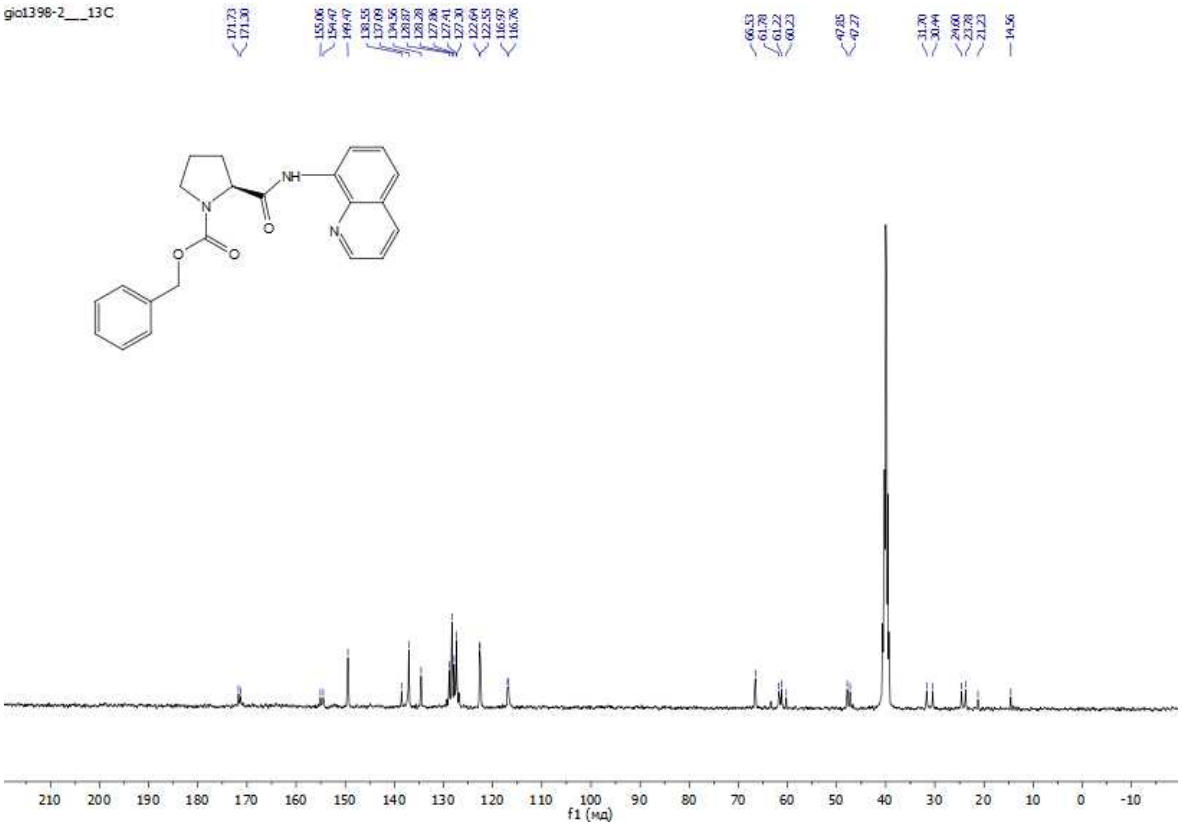


valp797_F19
STANDARD FLOURINE PARAMETERS

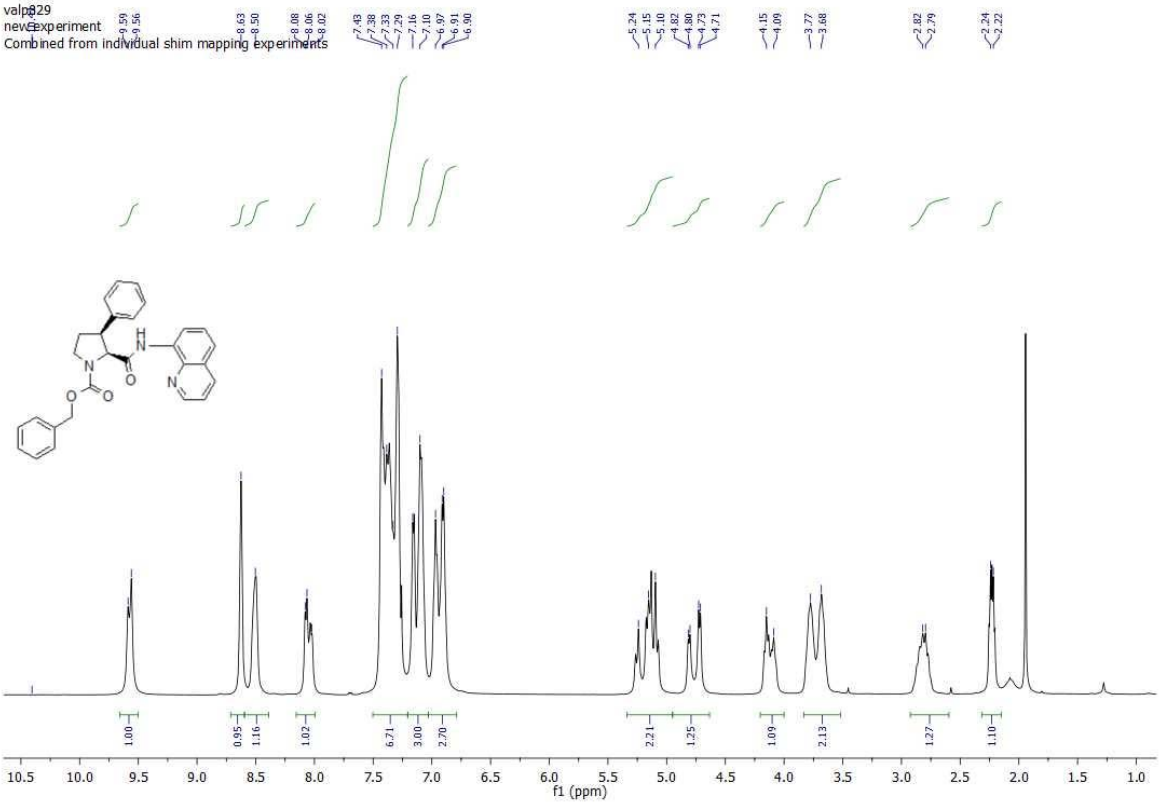


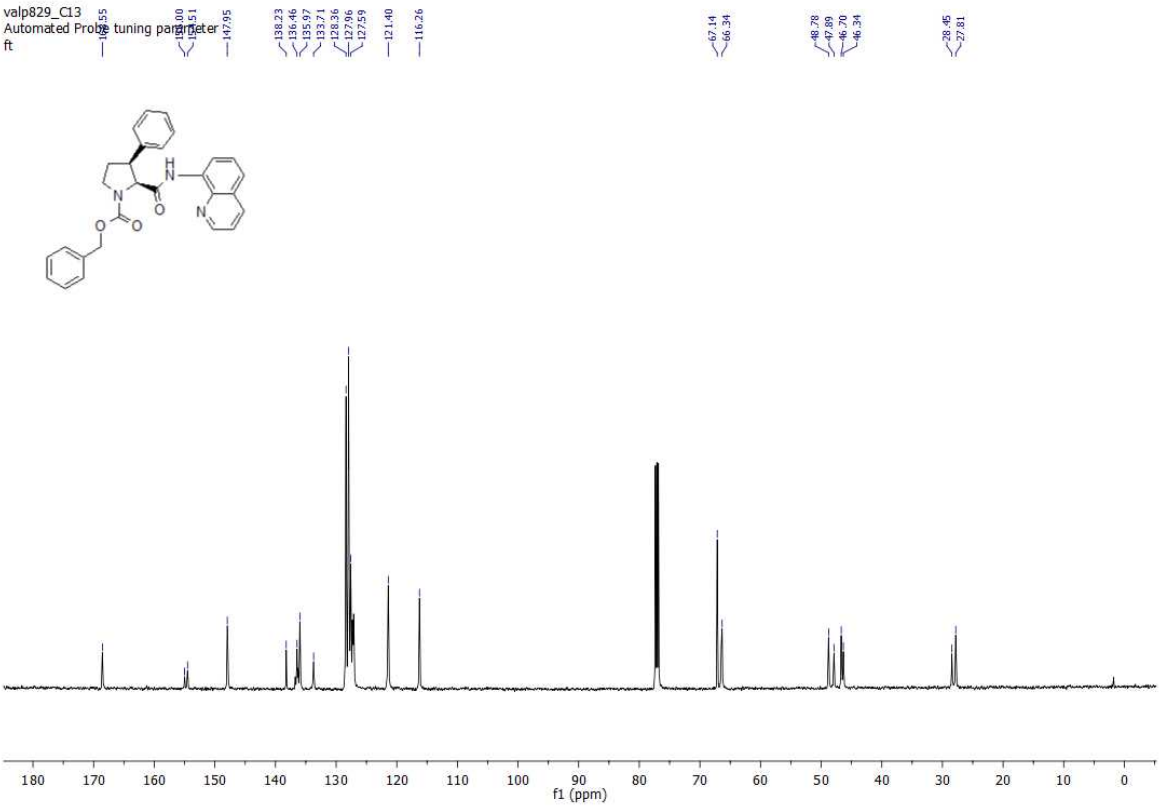
Compound Cbz – 23



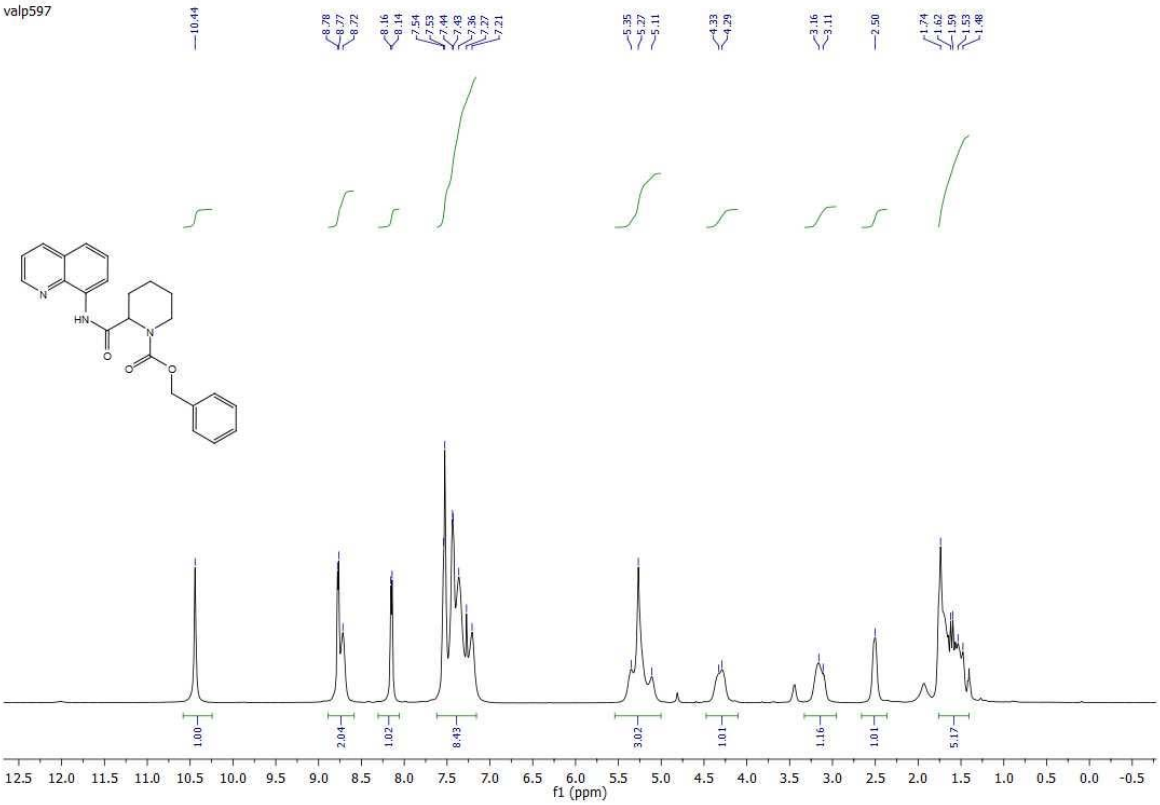


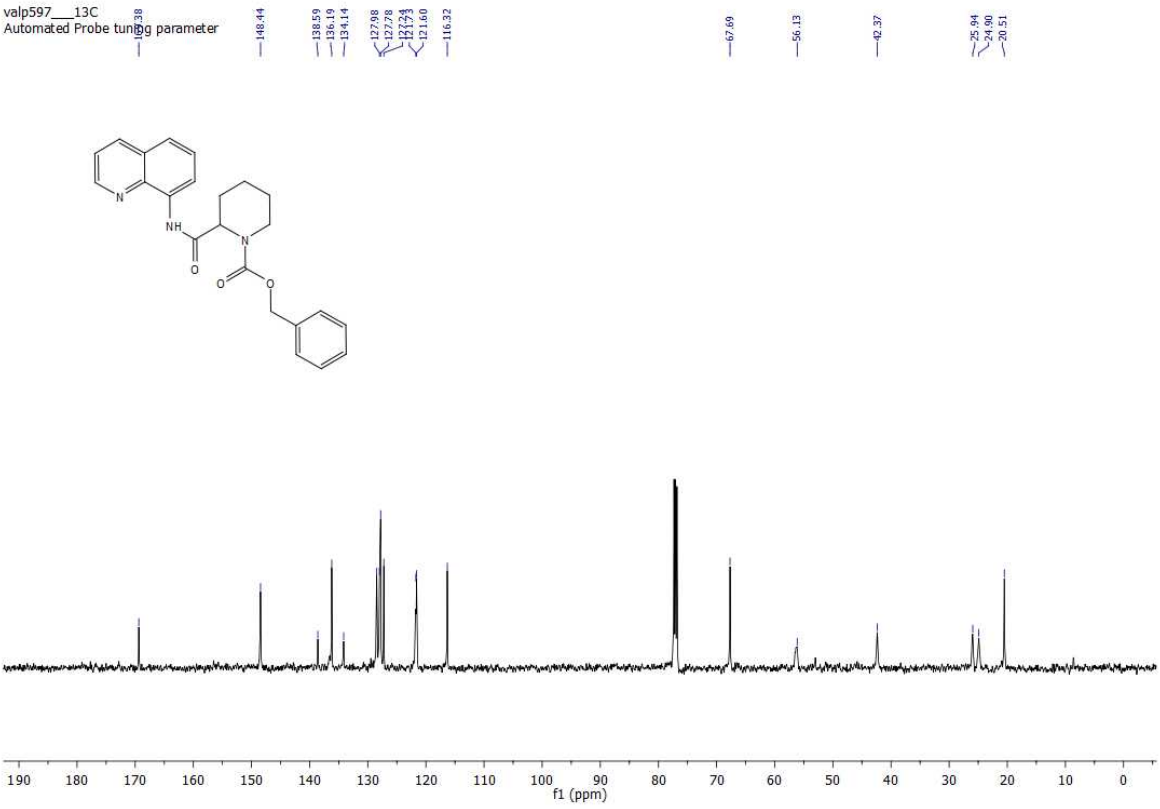
Compound Cbz – 23a



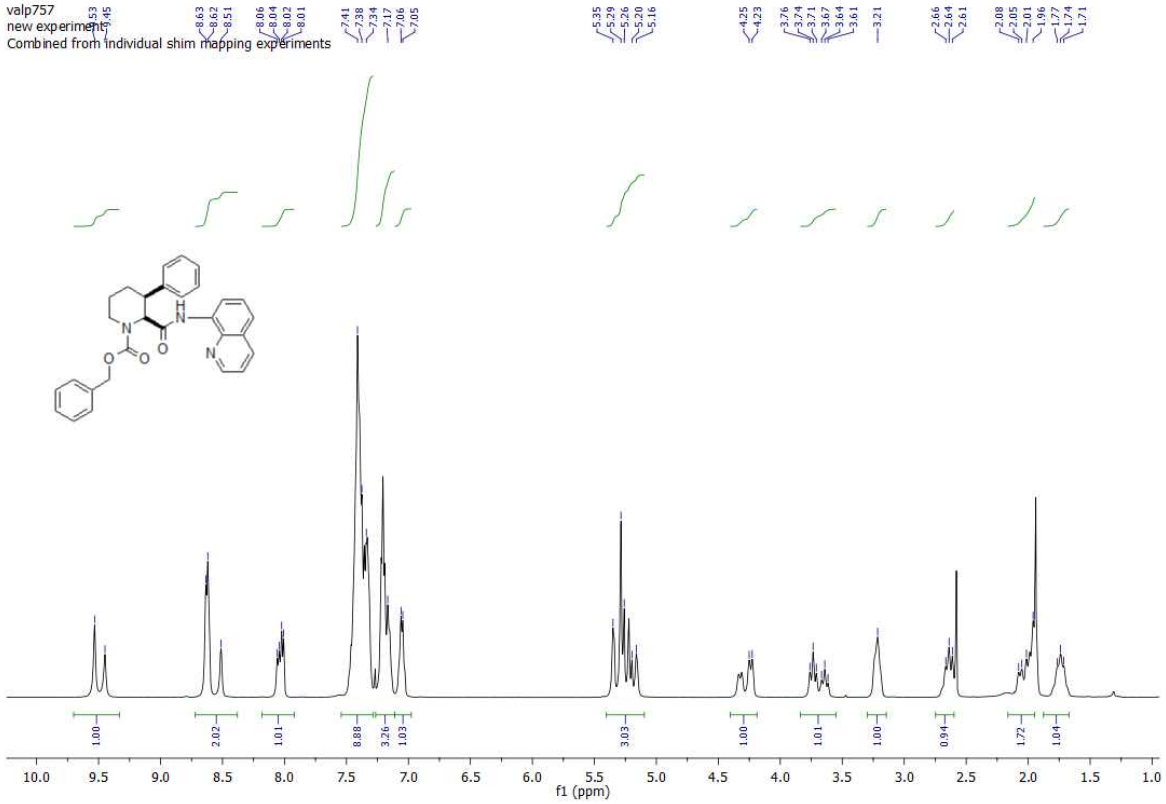


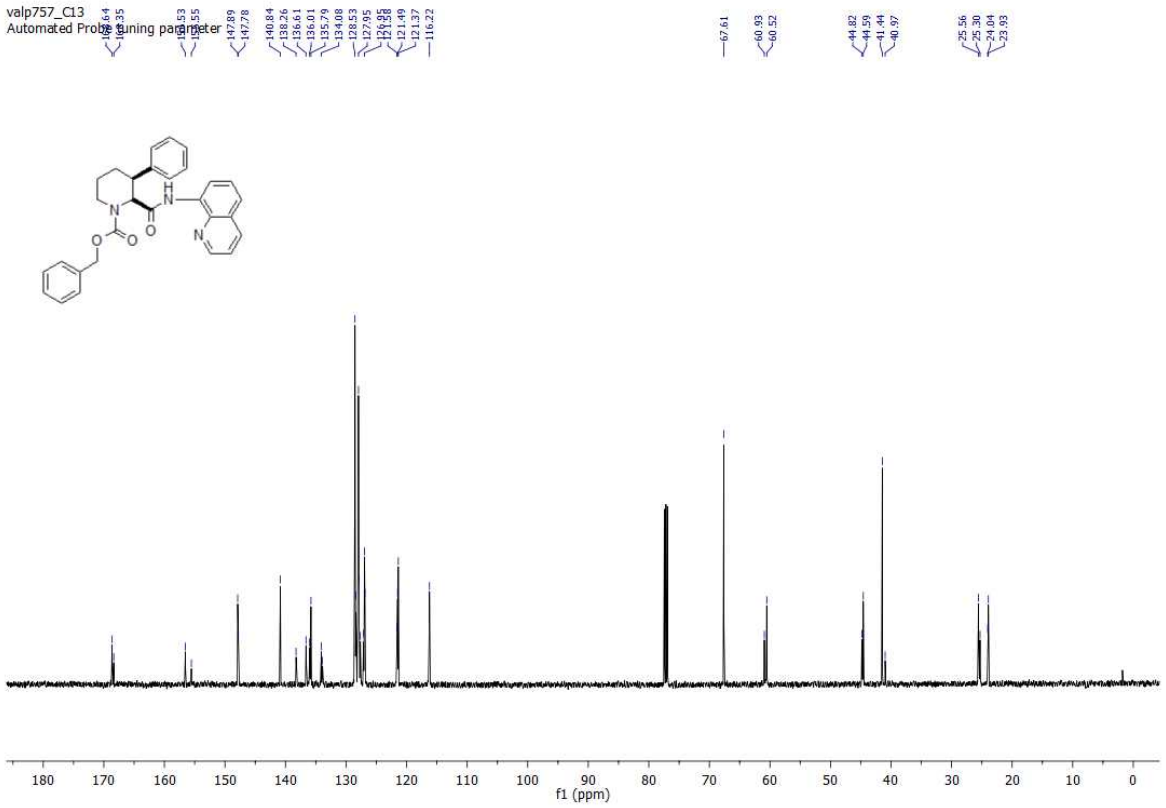
Compound Cbz – 24



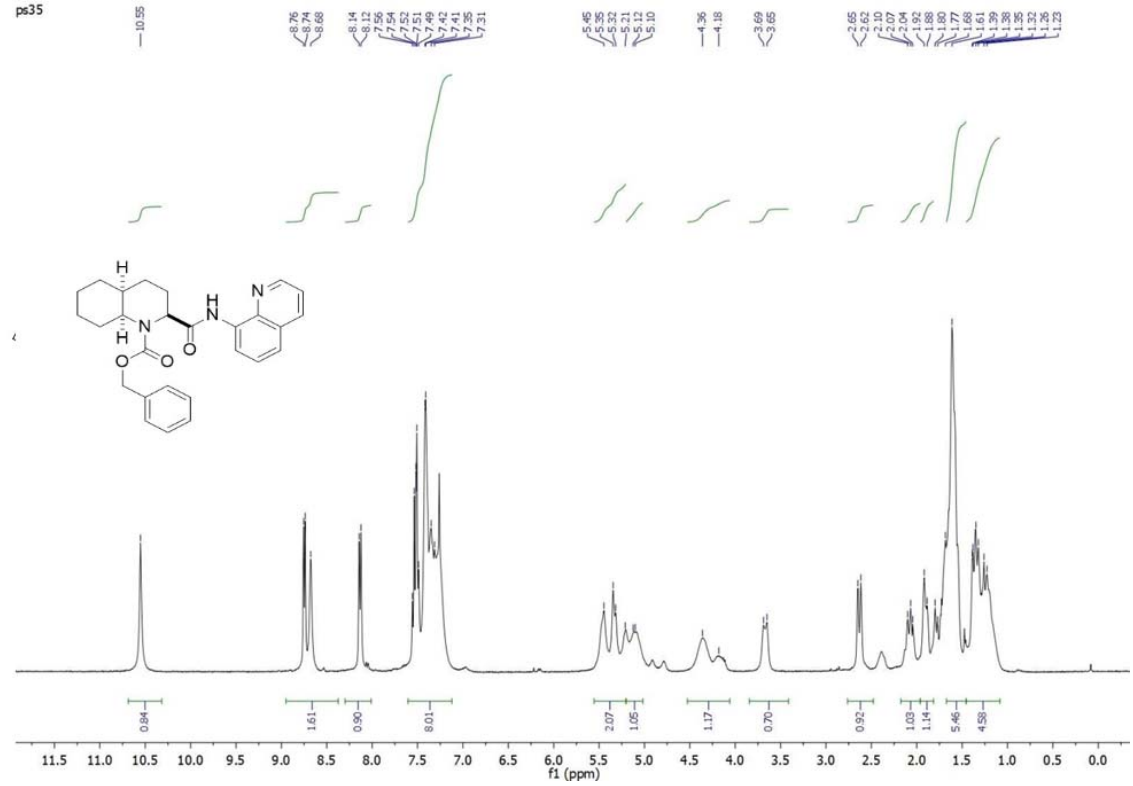


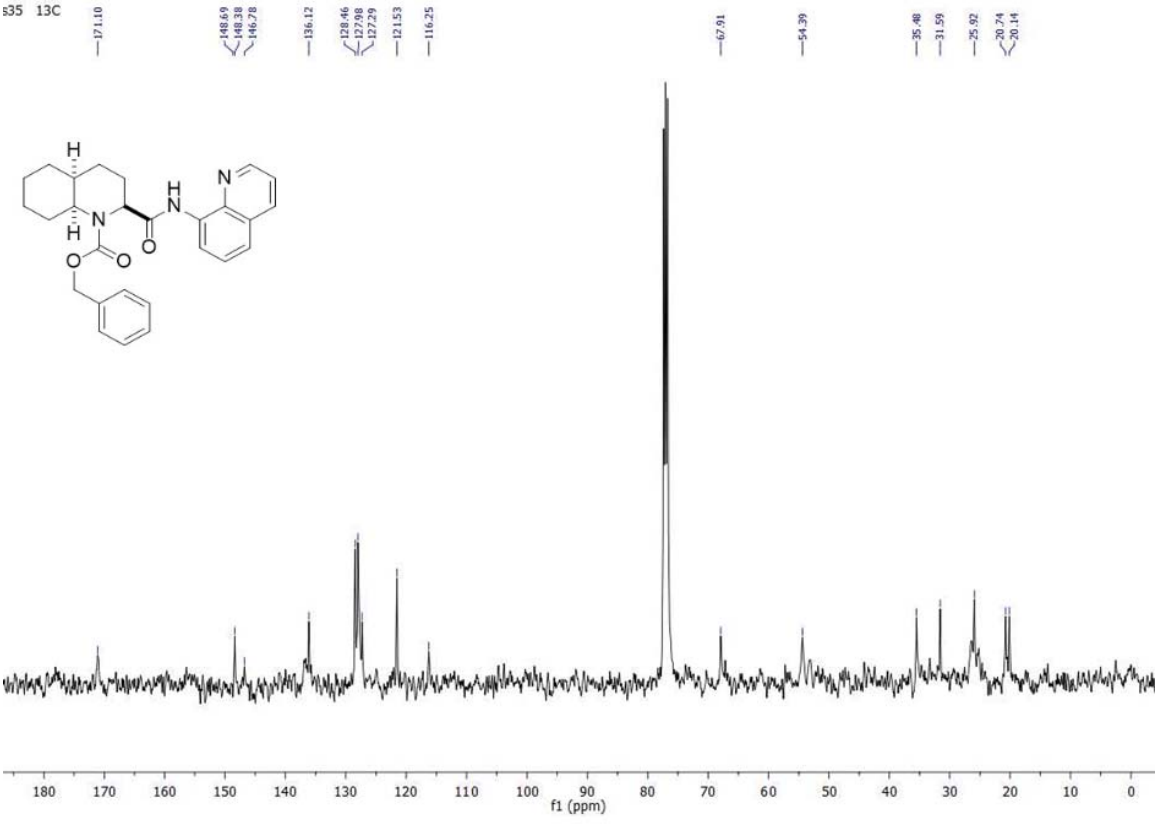
Compound Cbz – 24a



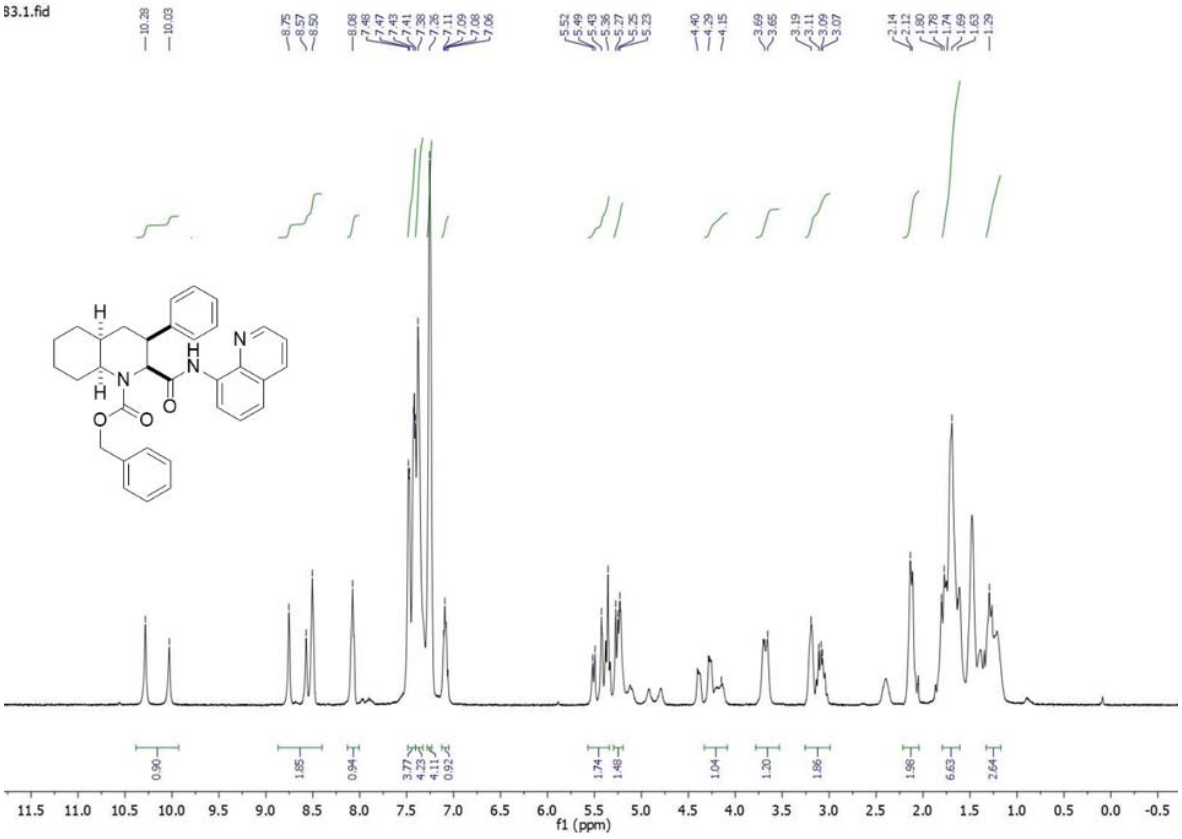


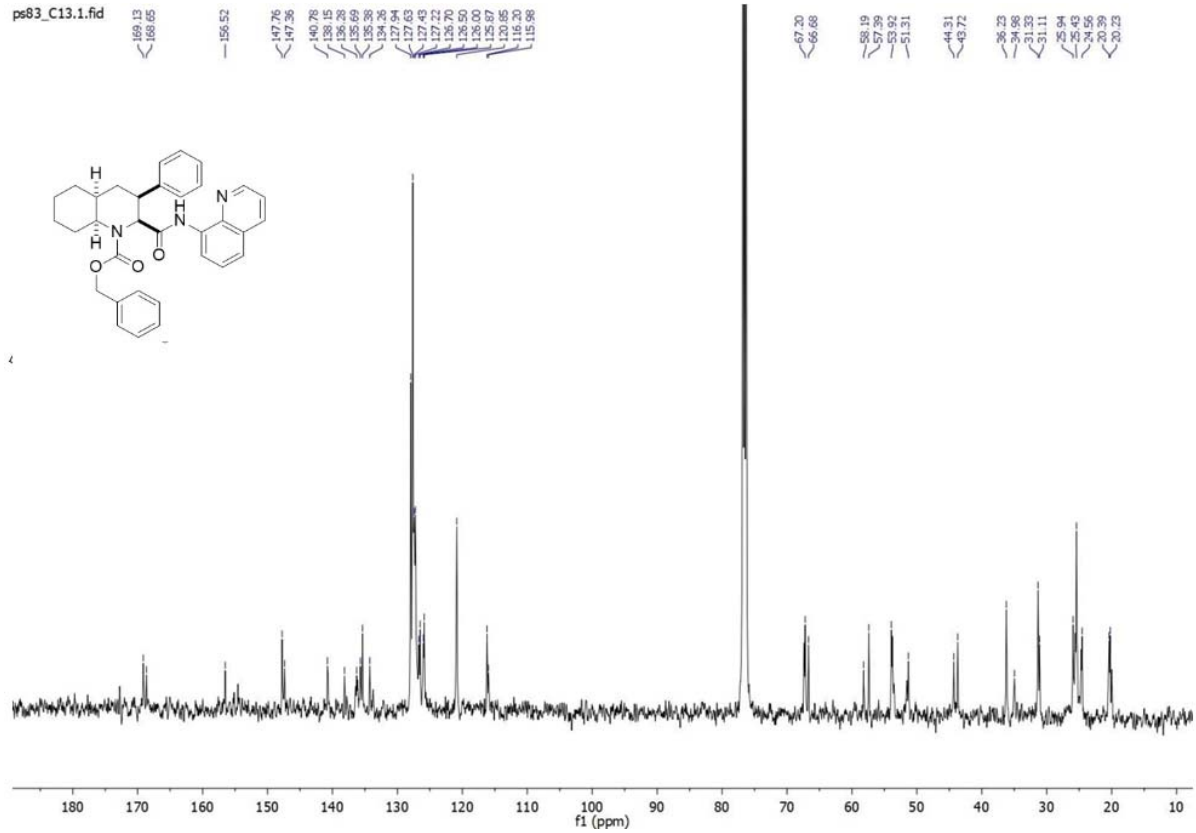
Compound Cbz – 25



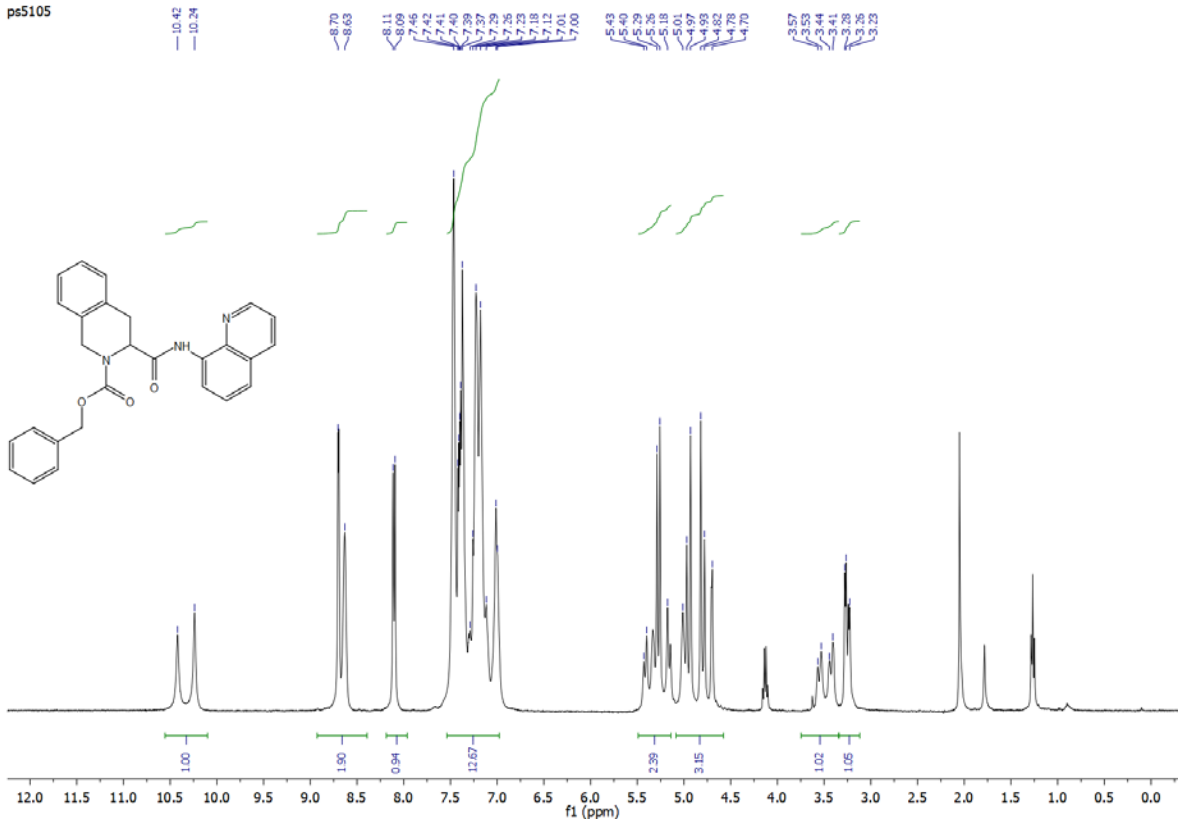


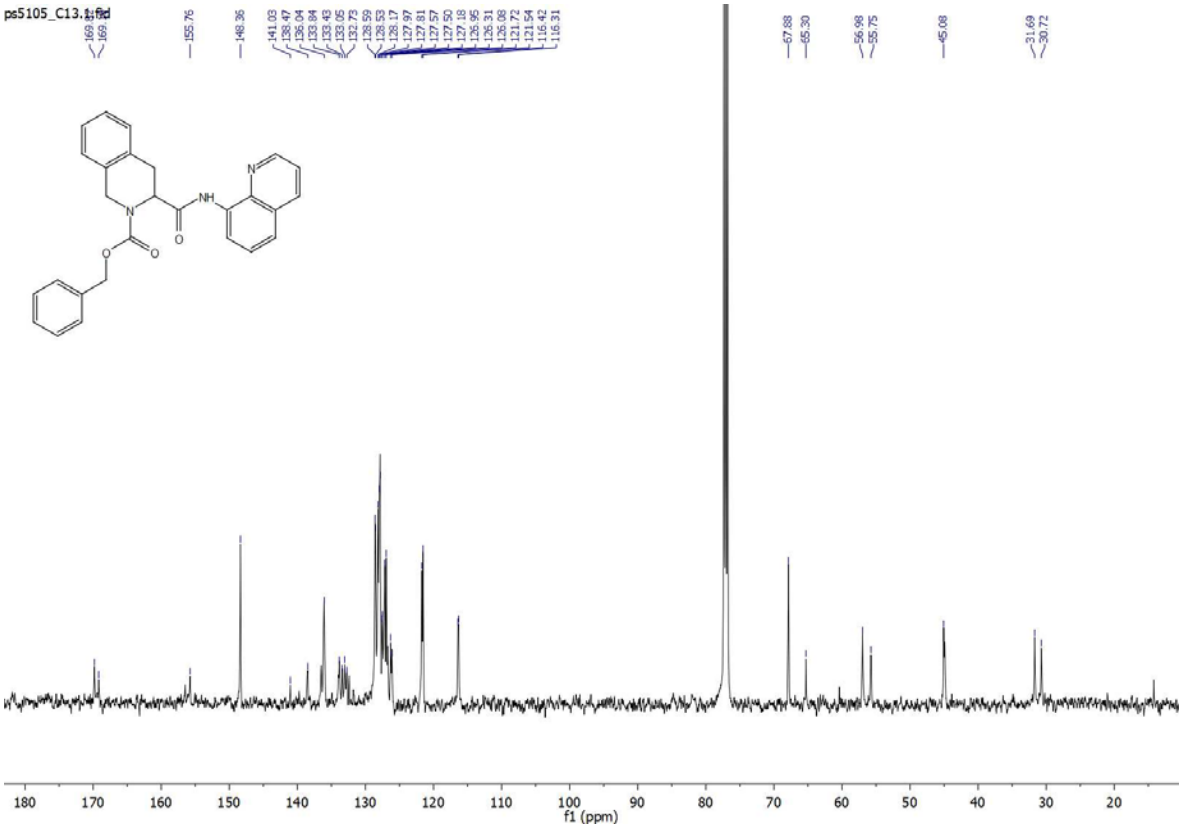
Compound Cbz – 25a



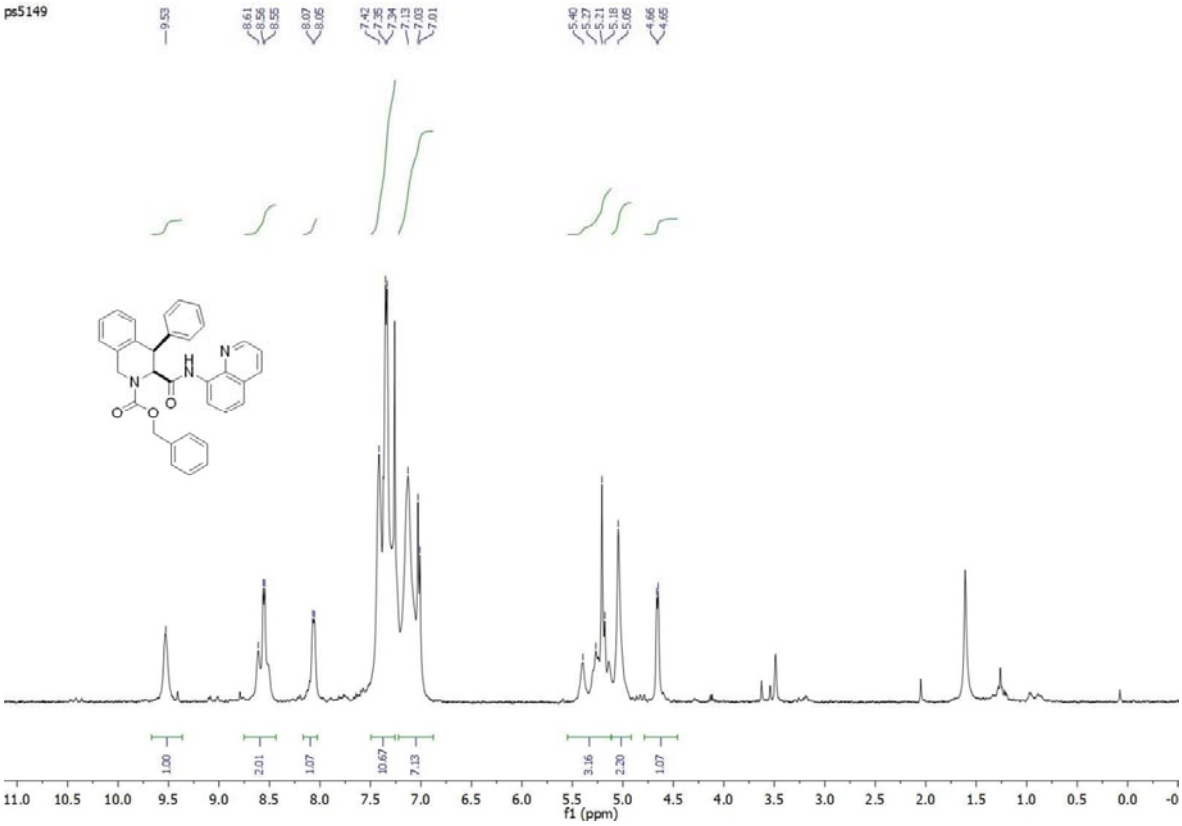


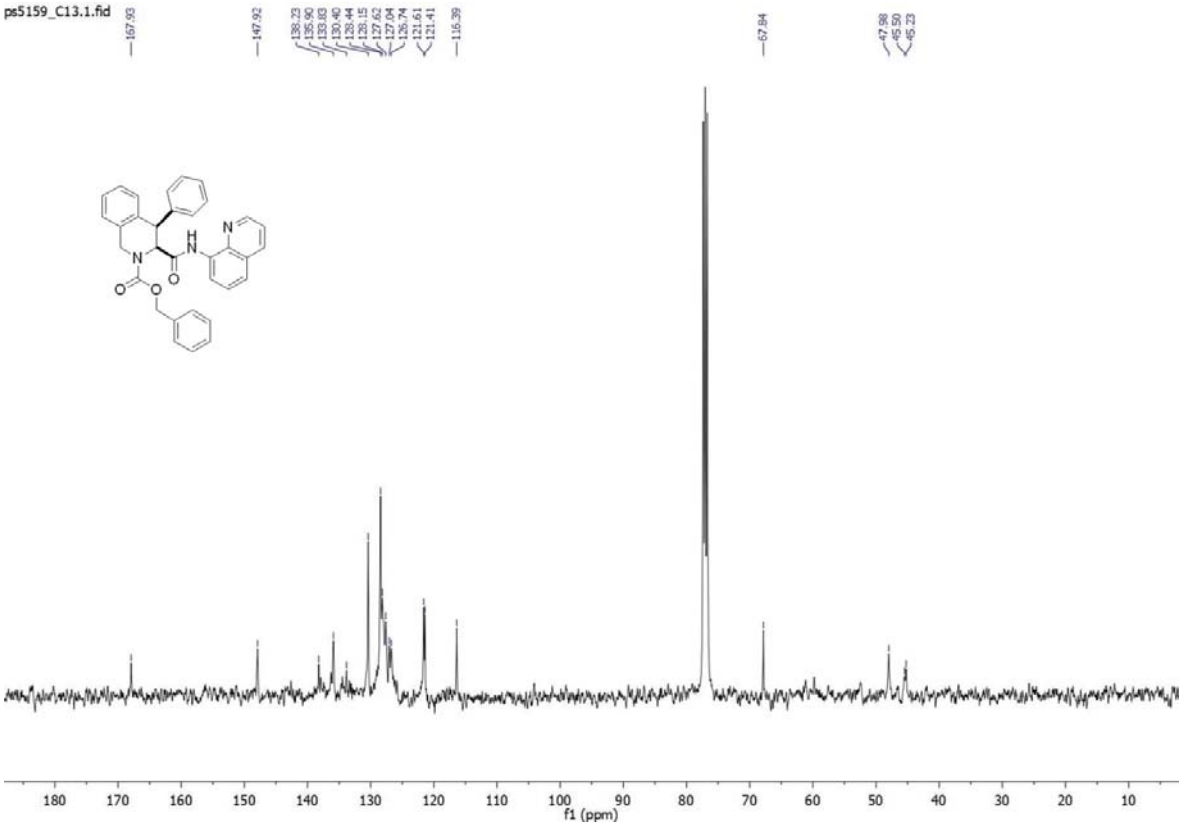
Compound Cbz – 26



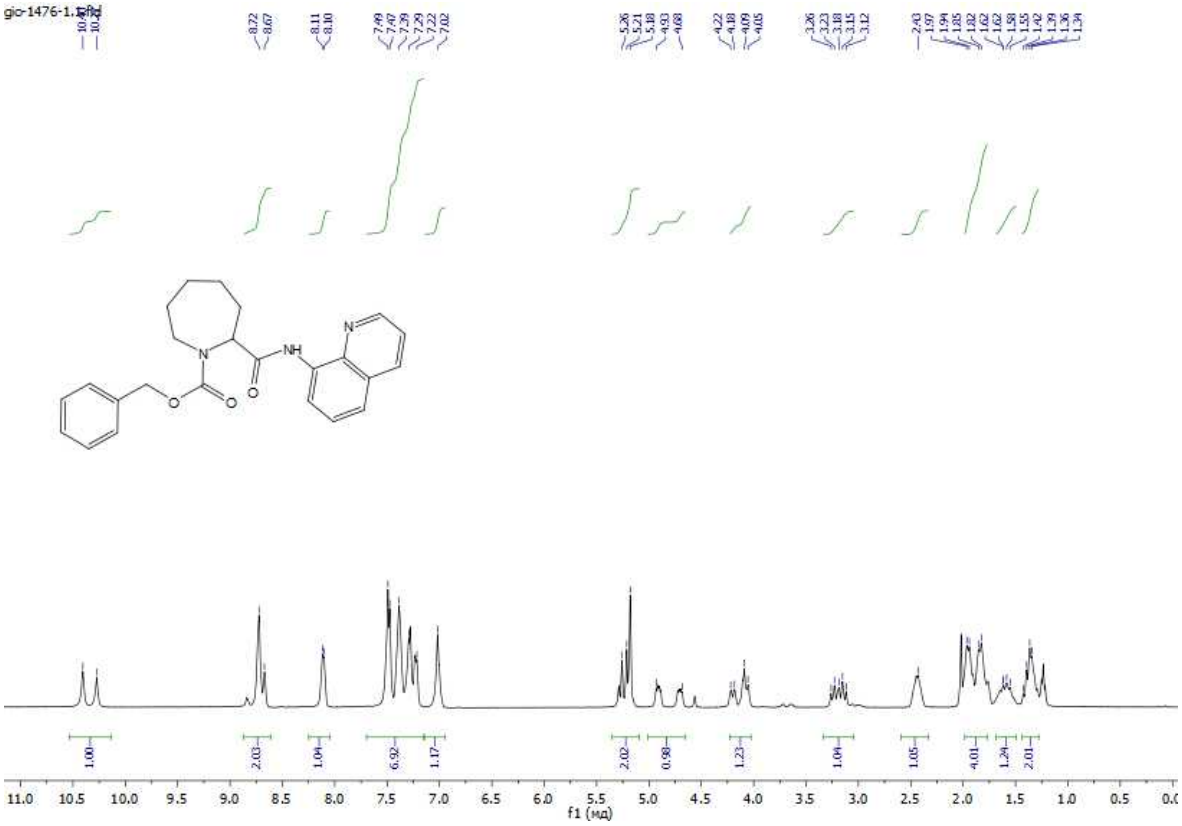


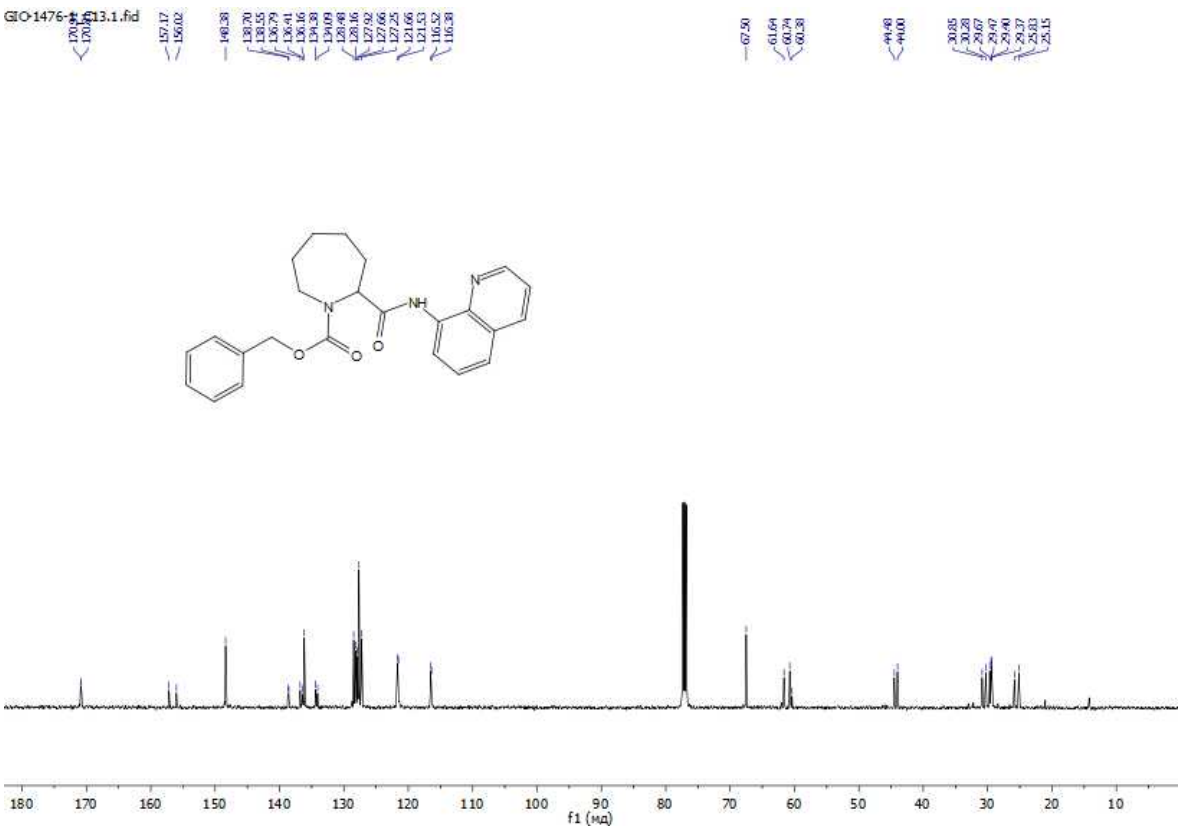
Compound Cbz – 26a





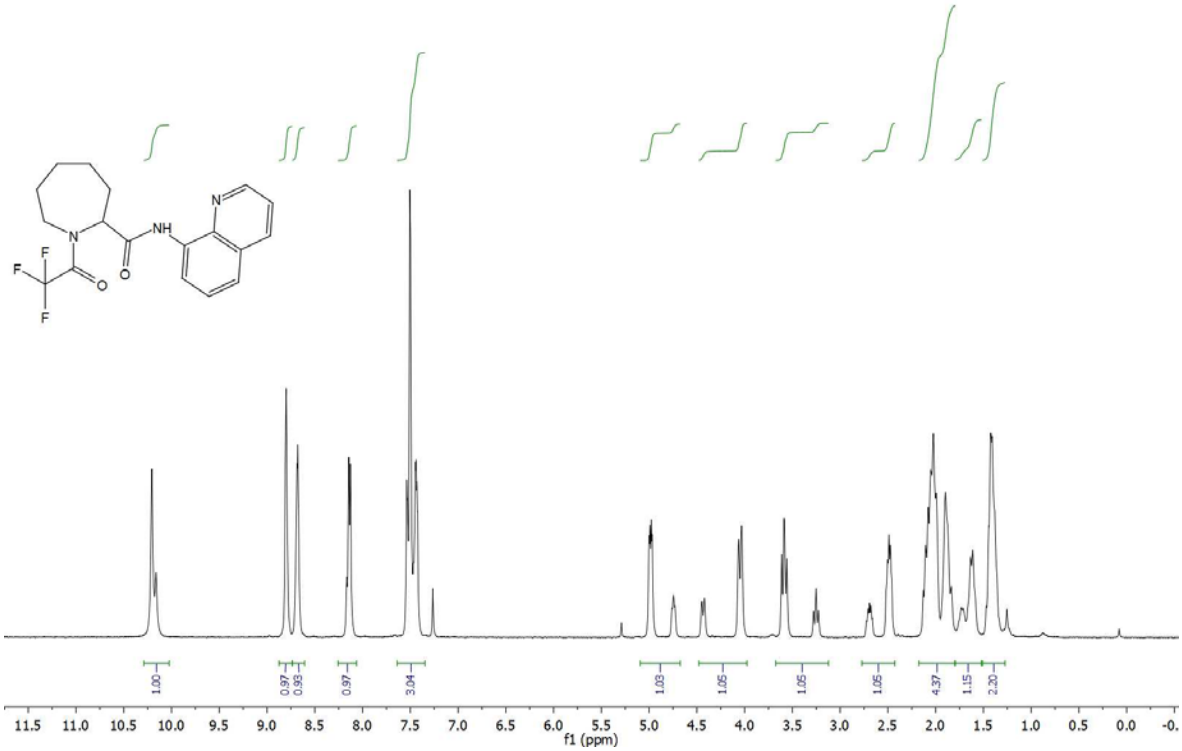
Compound Cbz – 27



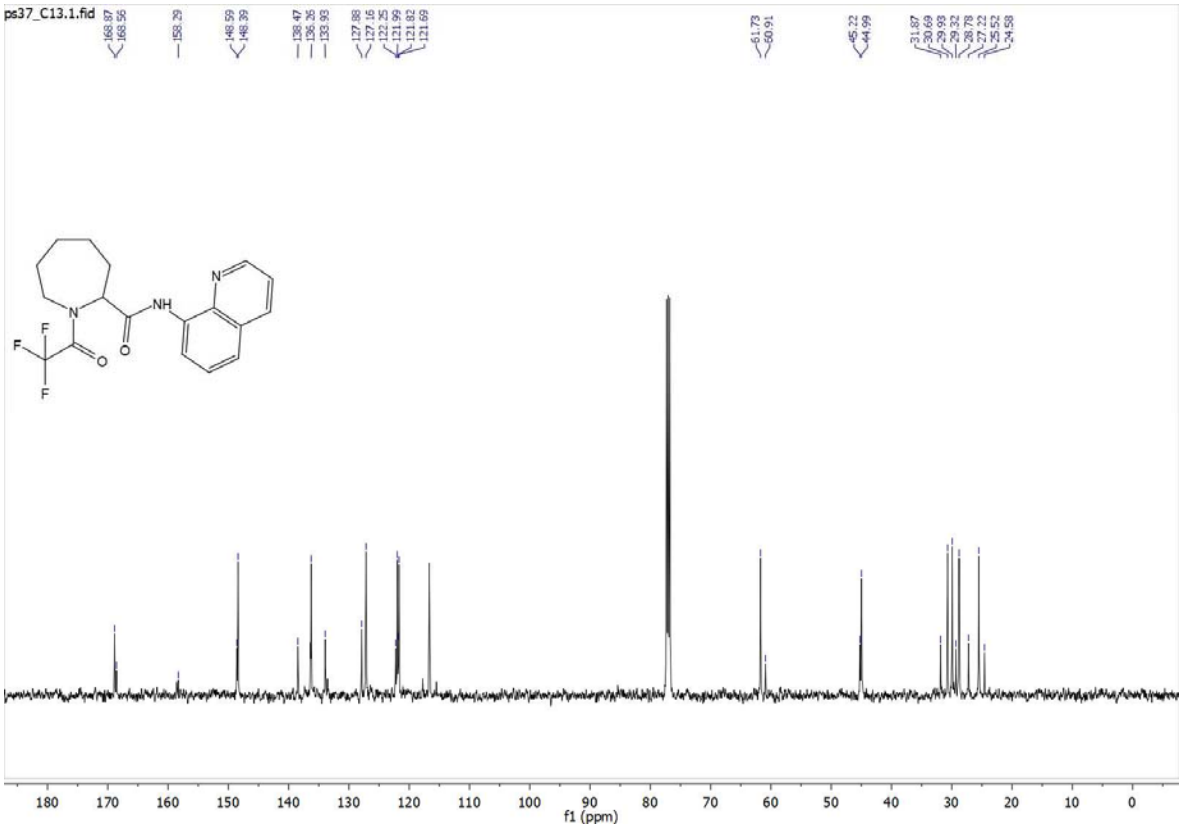


Compound TFA – 27

ps37 (CDCL3).1.fid

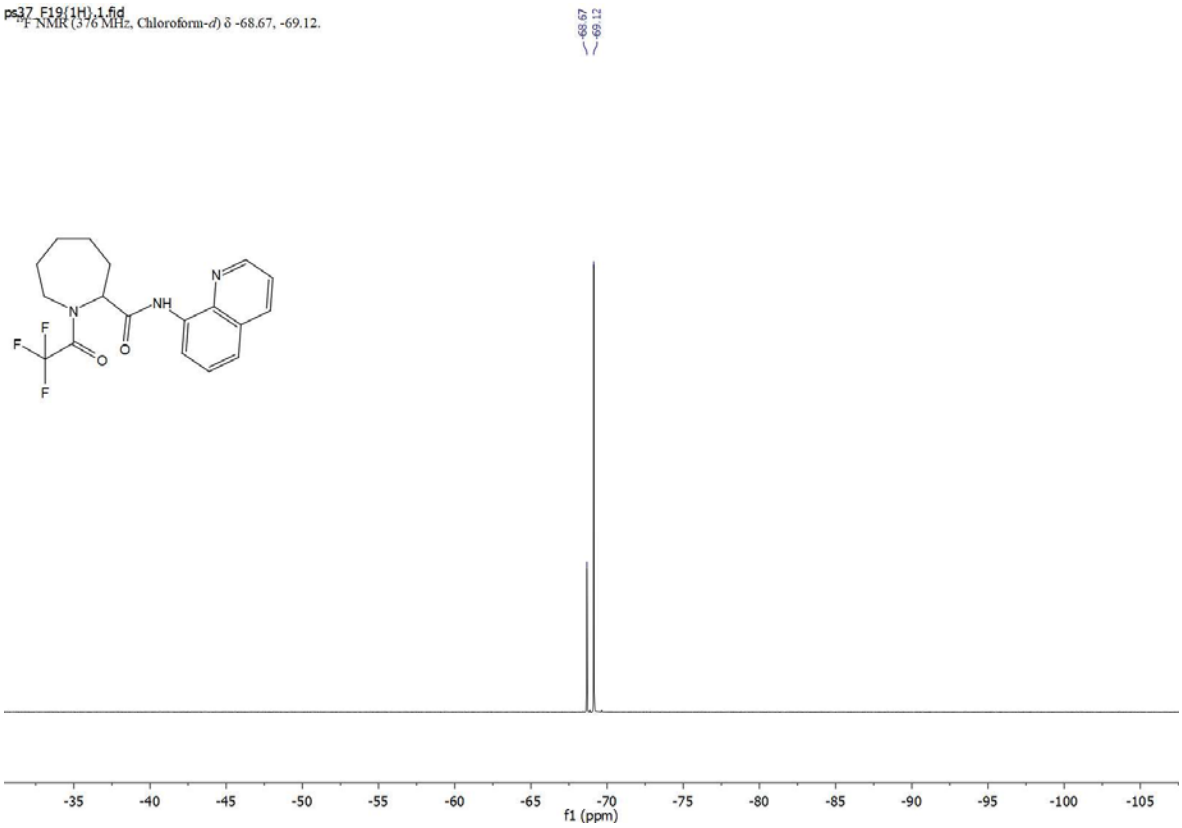


ps37_C13.1.fid

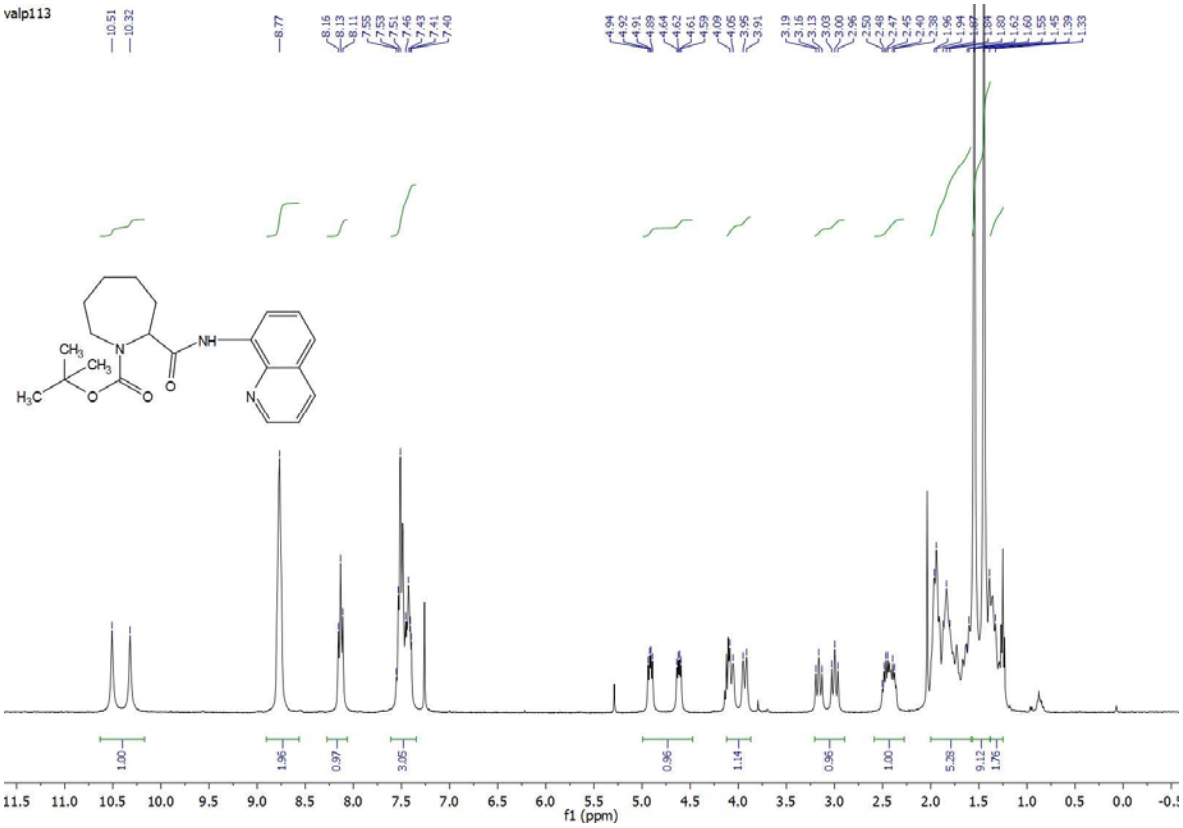


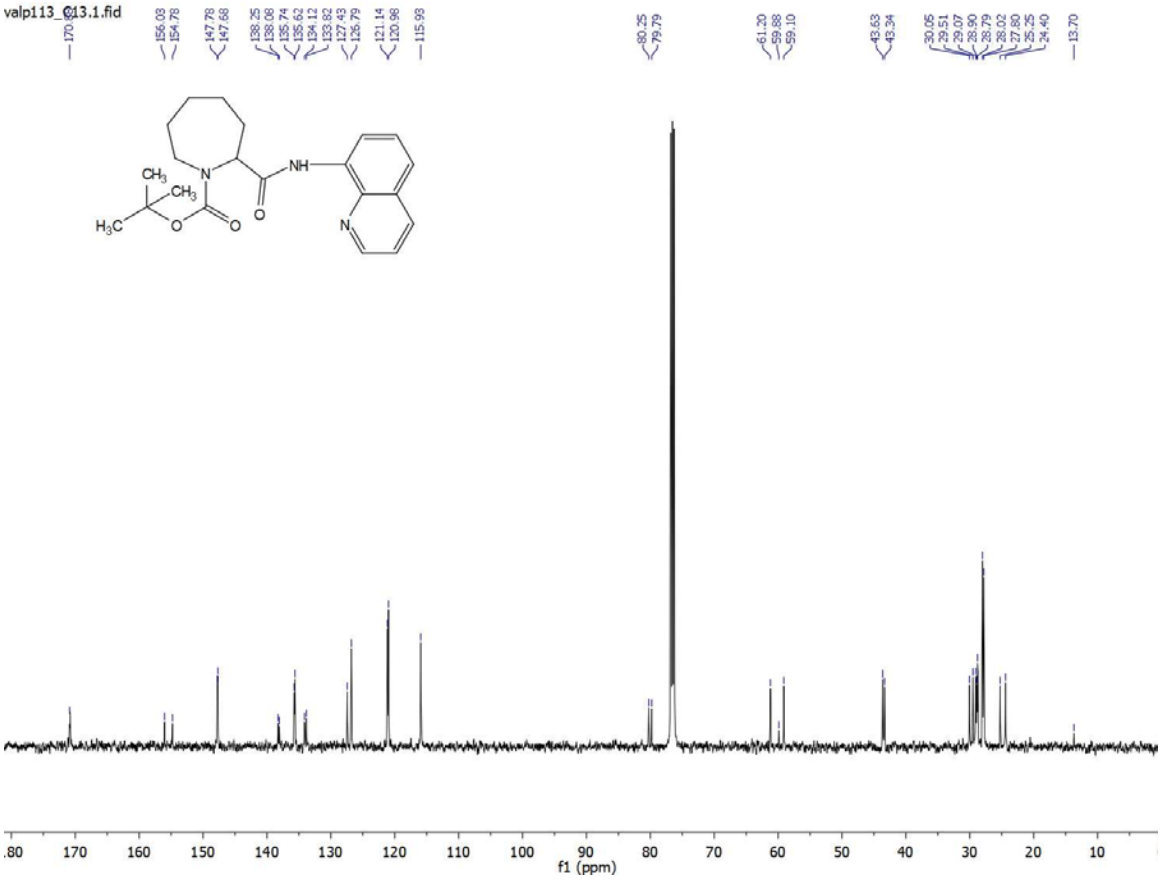
ps37_F19{1H}.1.fid

^{19}F NMR (376 MHz, Chloroform-*d*) δ -68.67, -69.12.

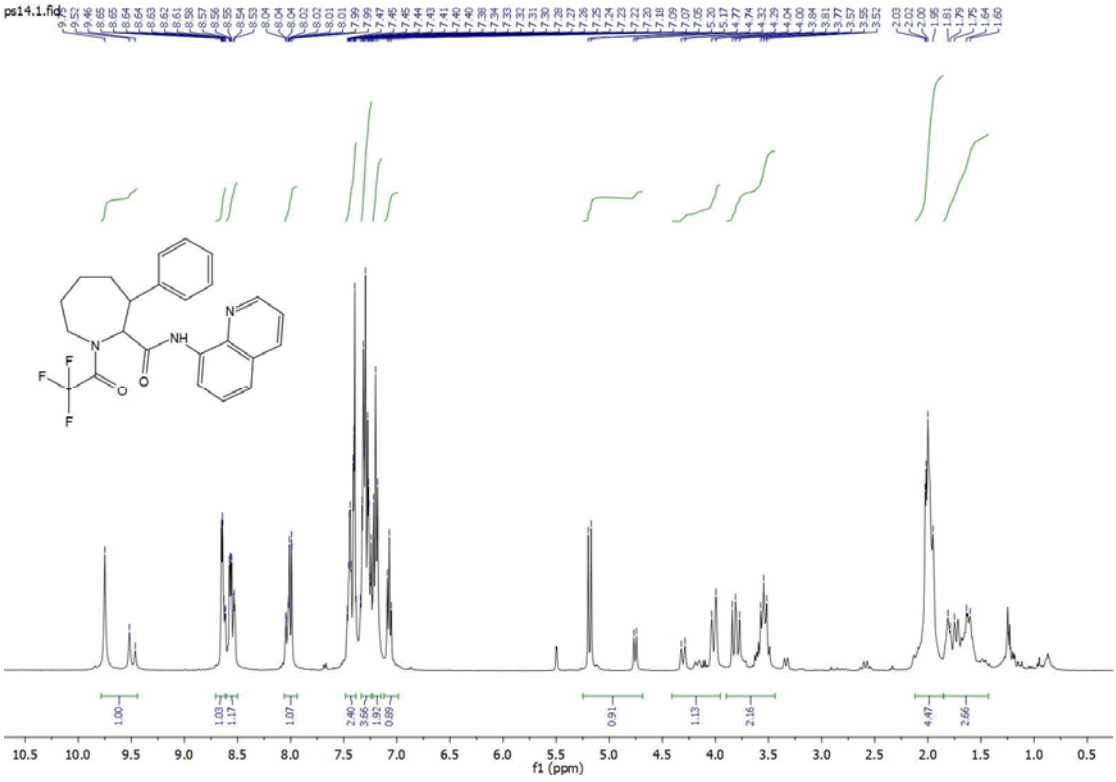


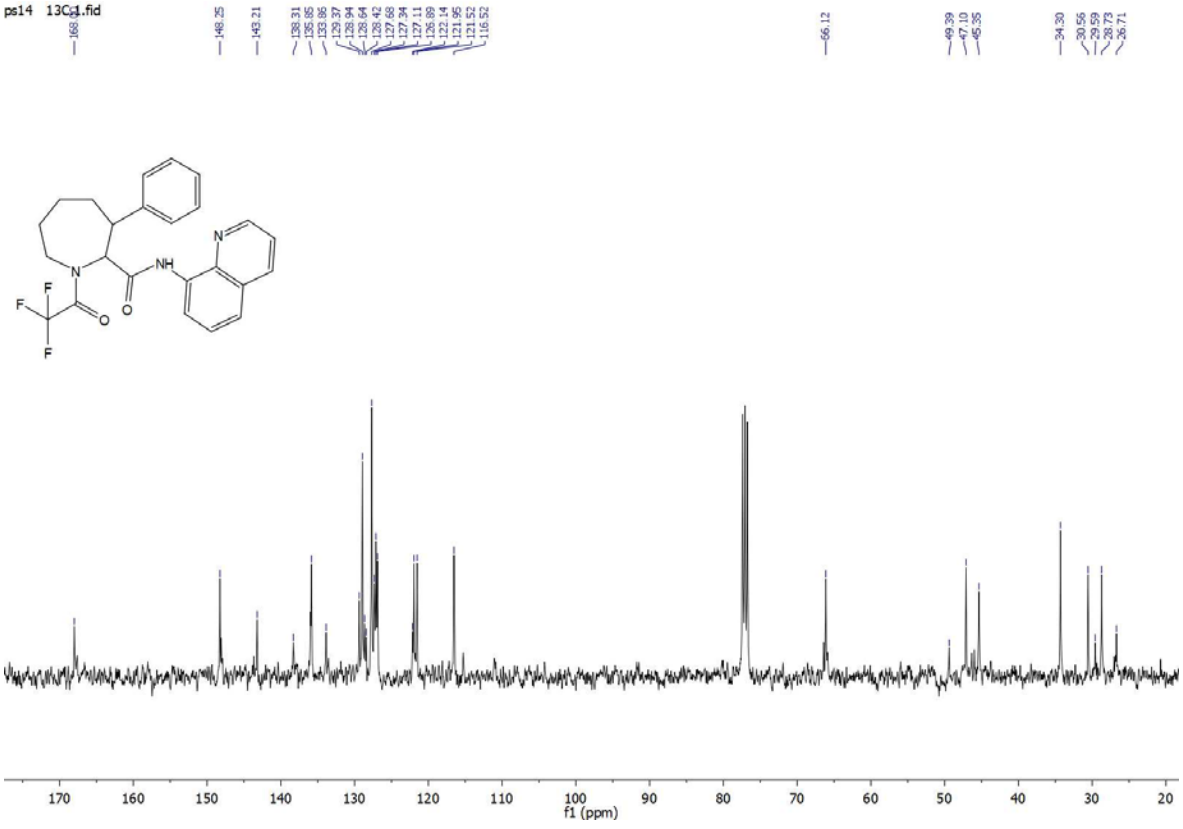
Compound Boc – 27

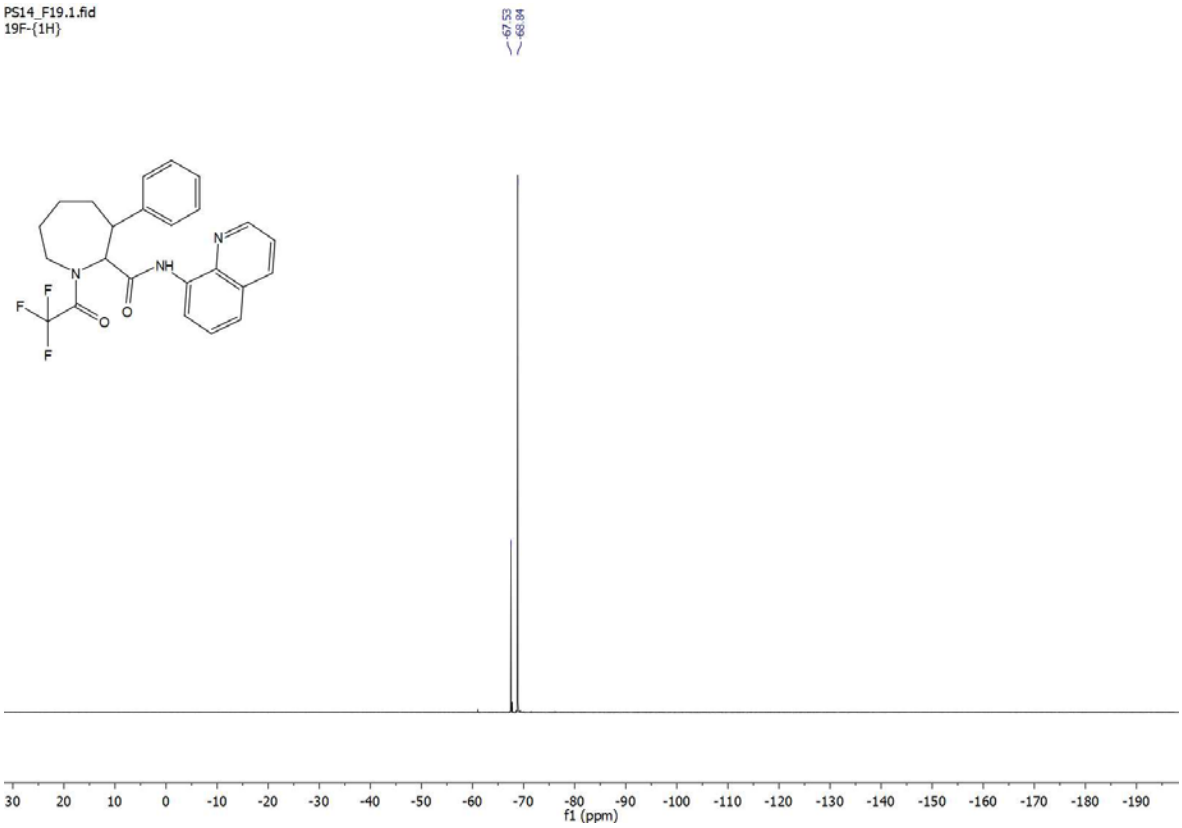




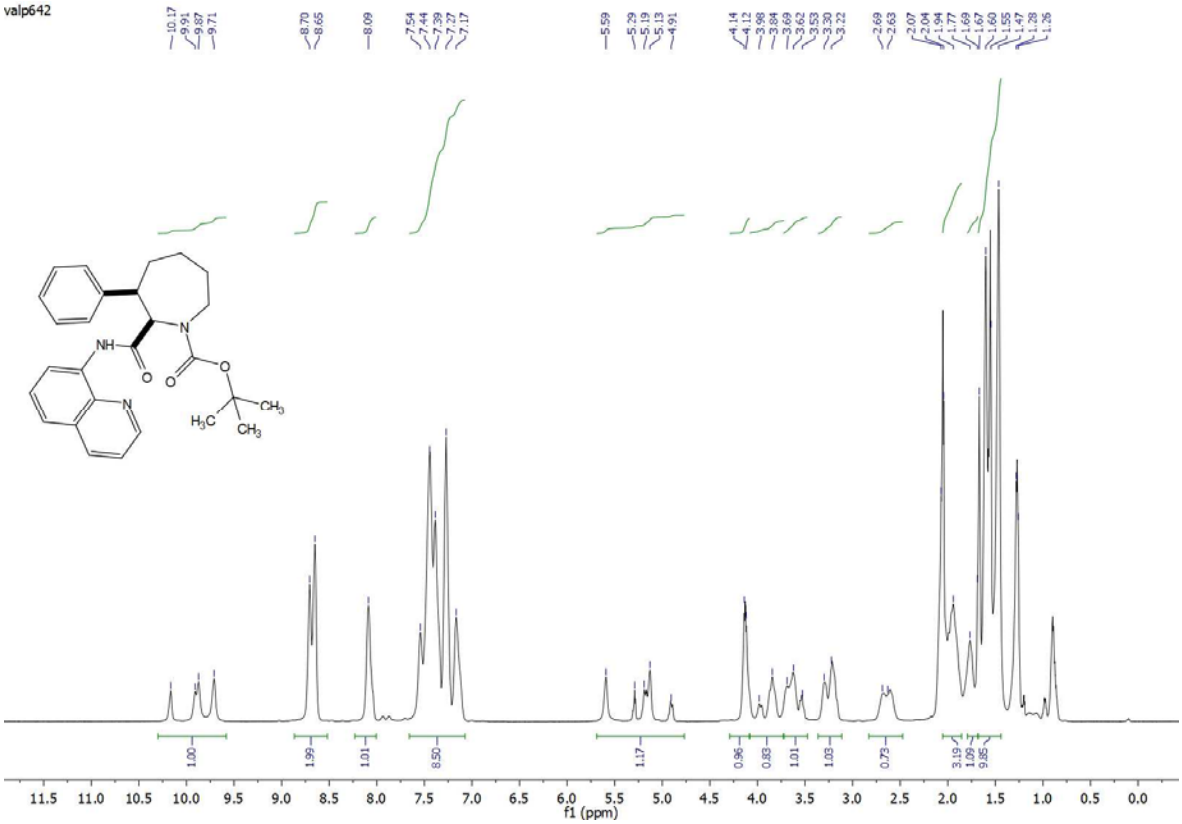
Compound TFA – 27a

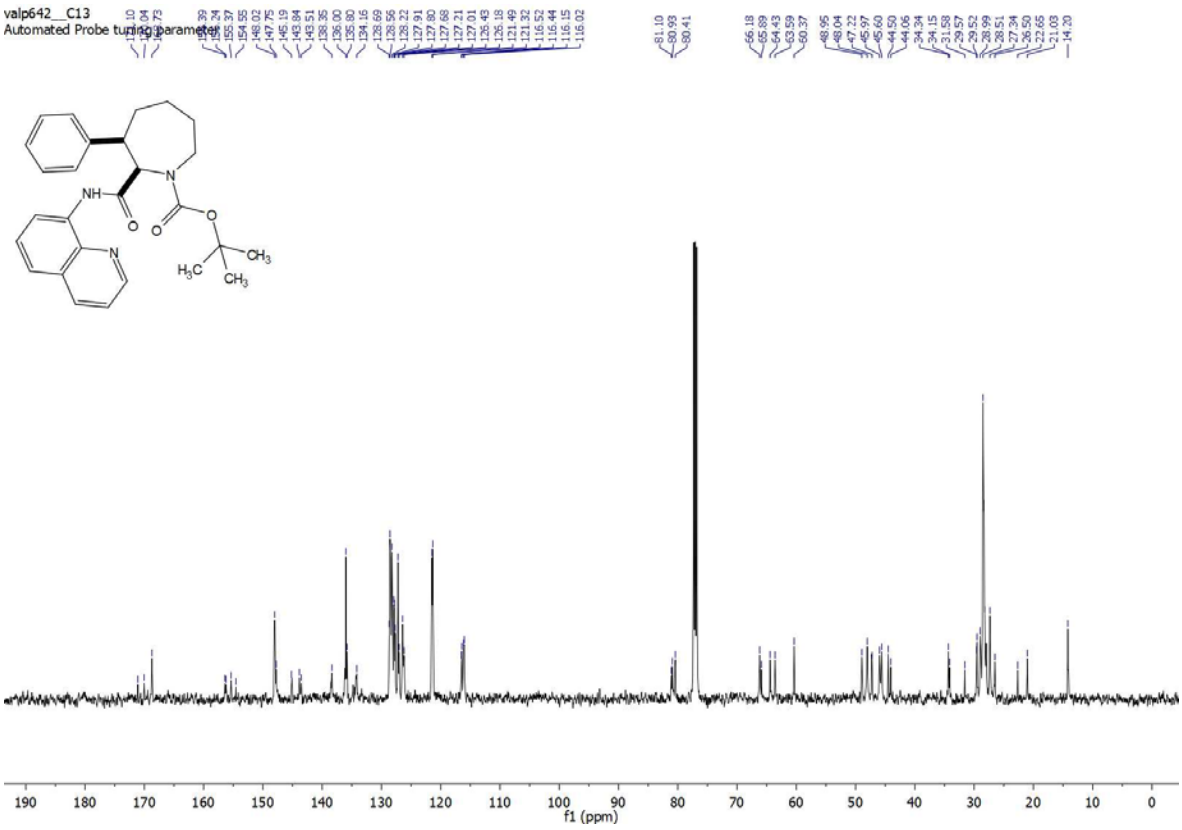




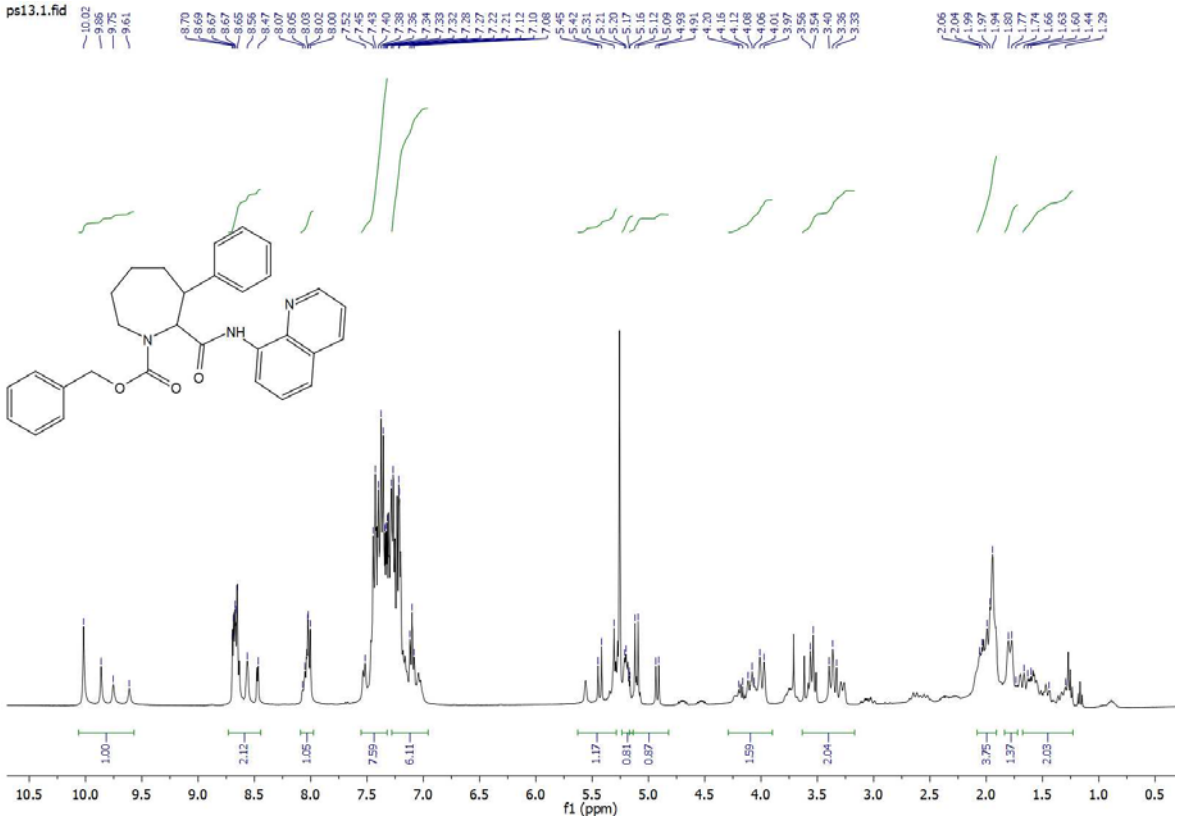

PS14_F19.1.fid
19F-{1H}
-67.53
-68.84
N
NH
O
O
F
F
F
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

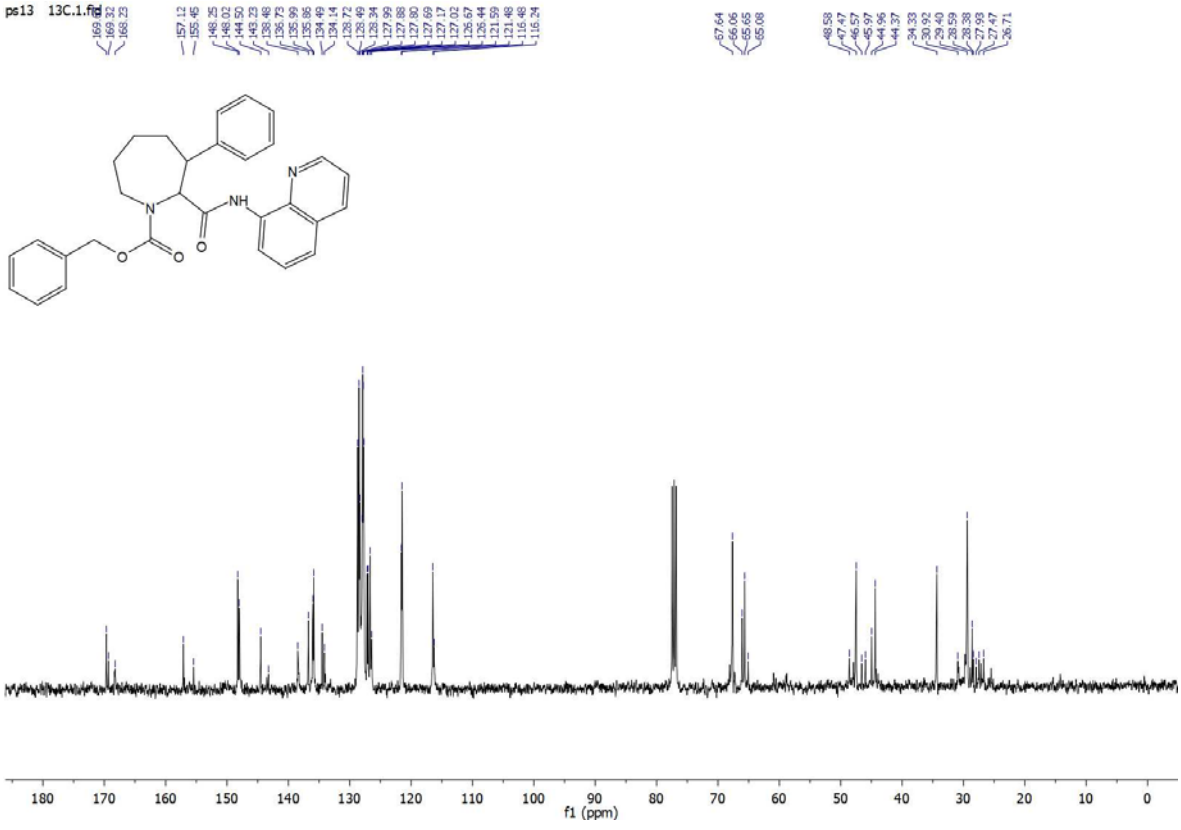
Compound Boc – 27a



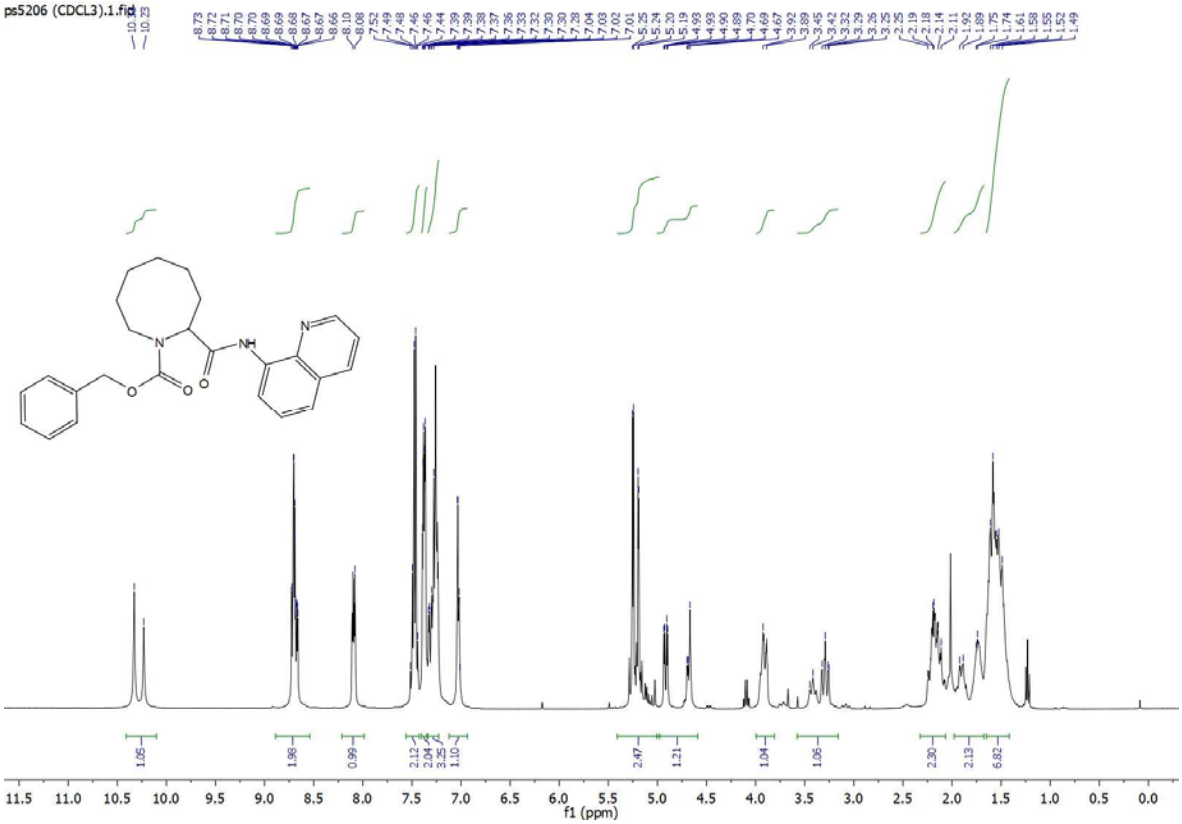


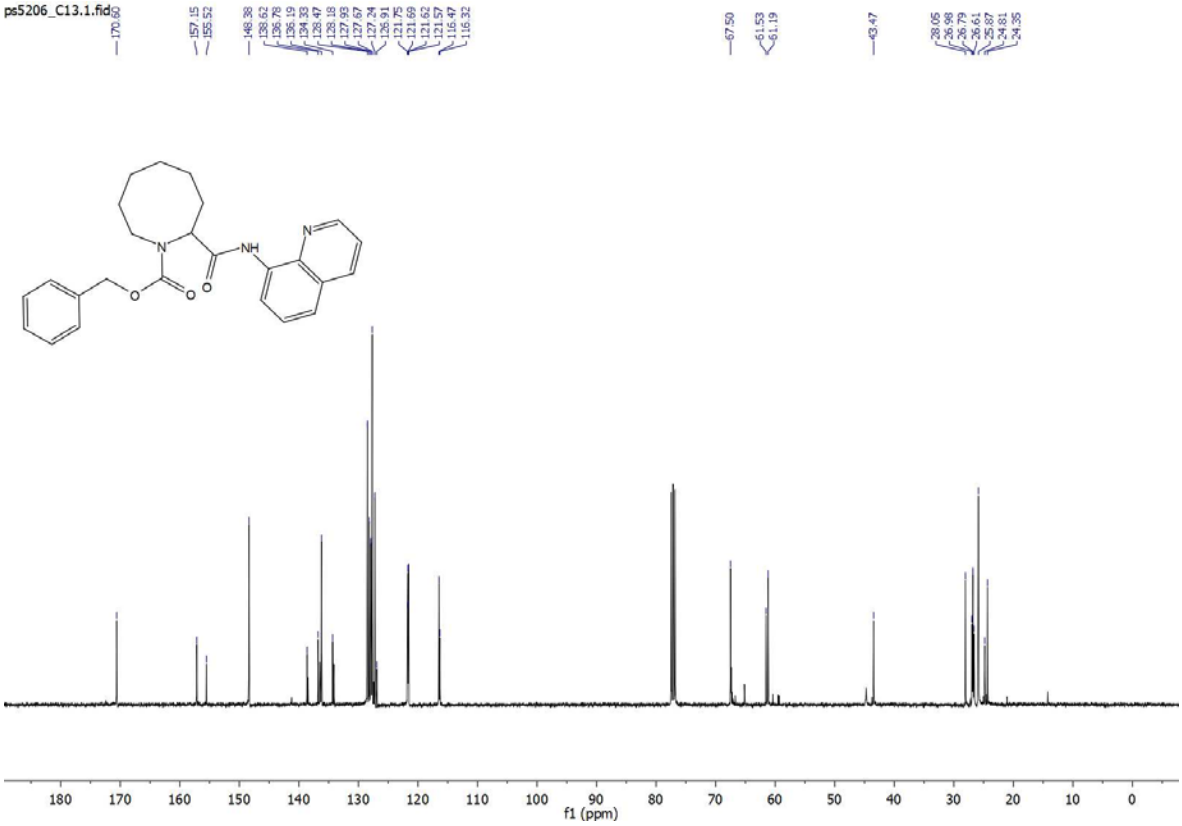
Compound Cbz – 27a



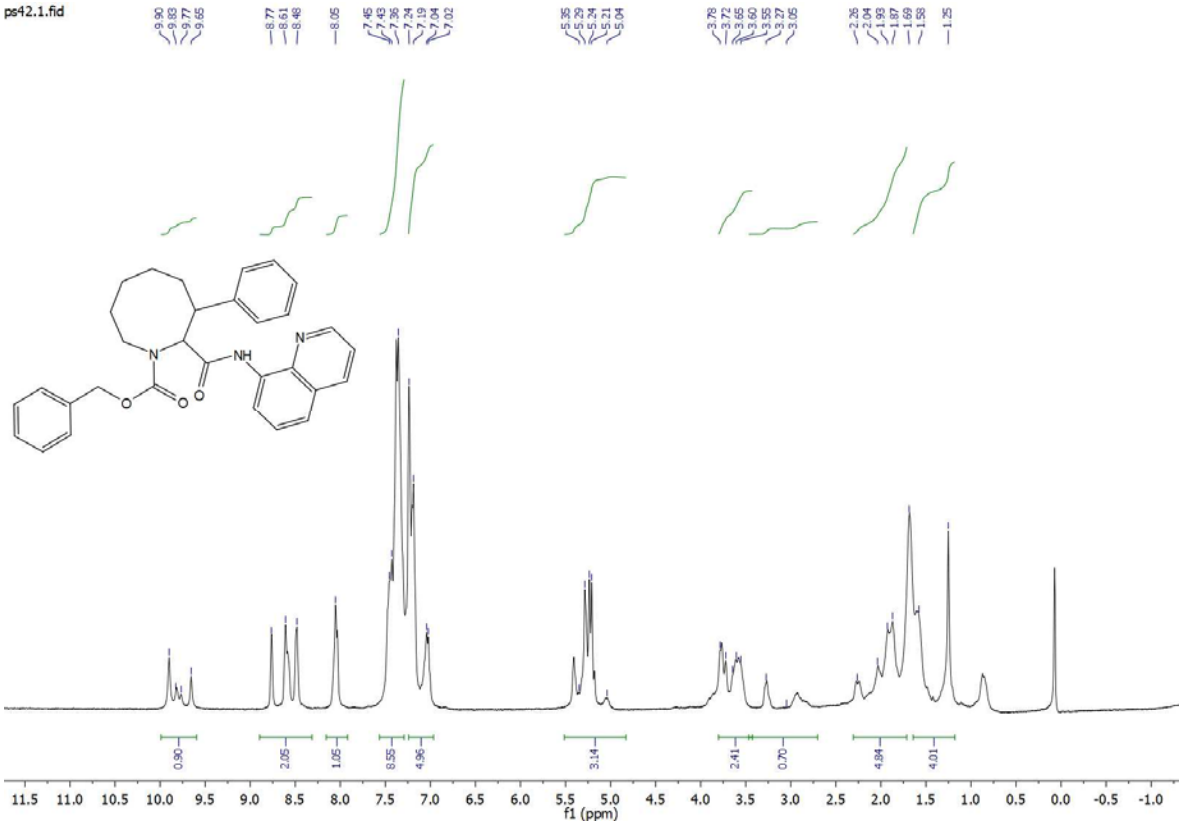


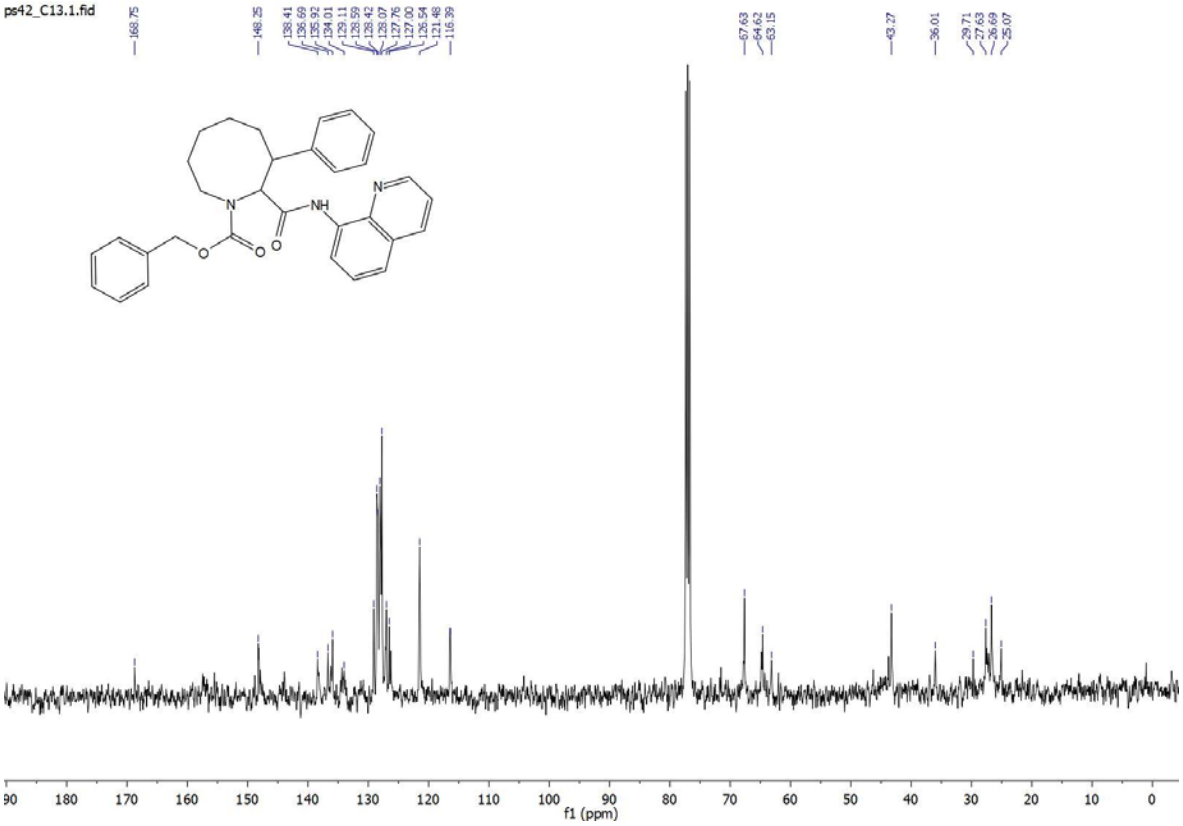
Compound Cbz – 28



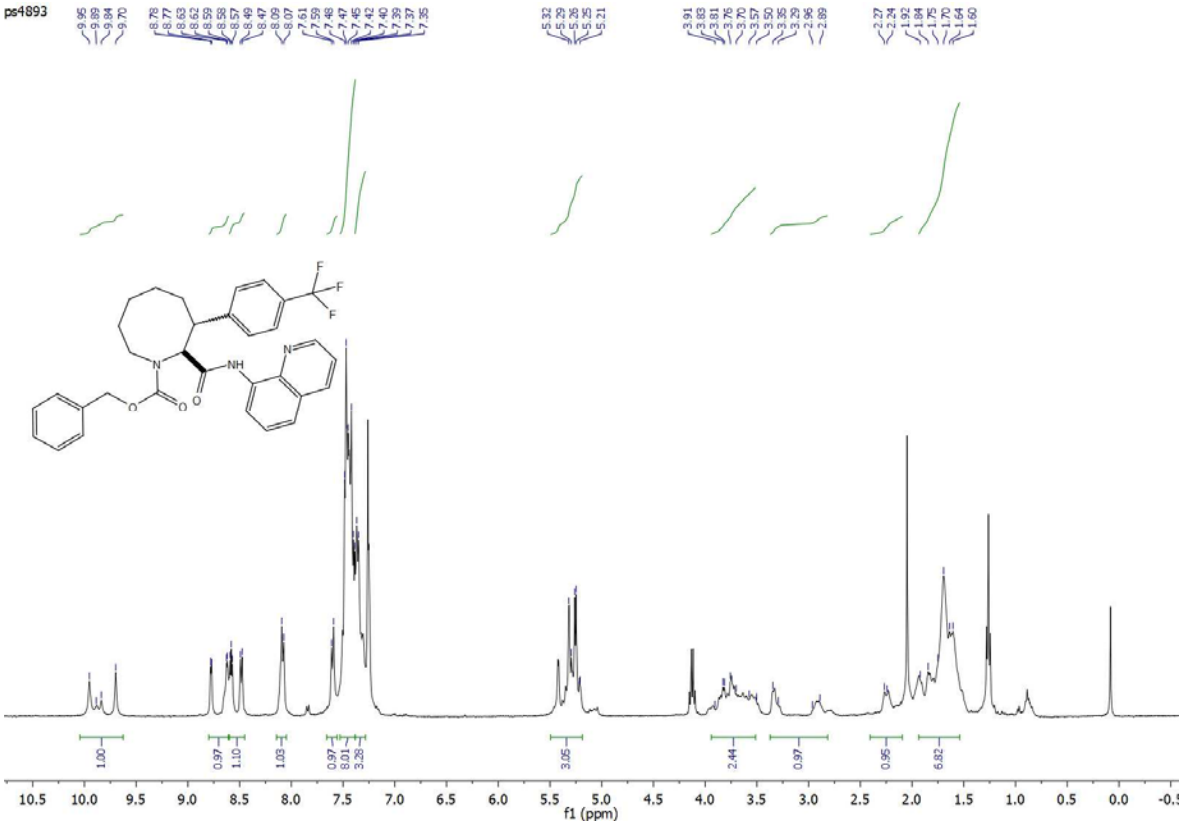


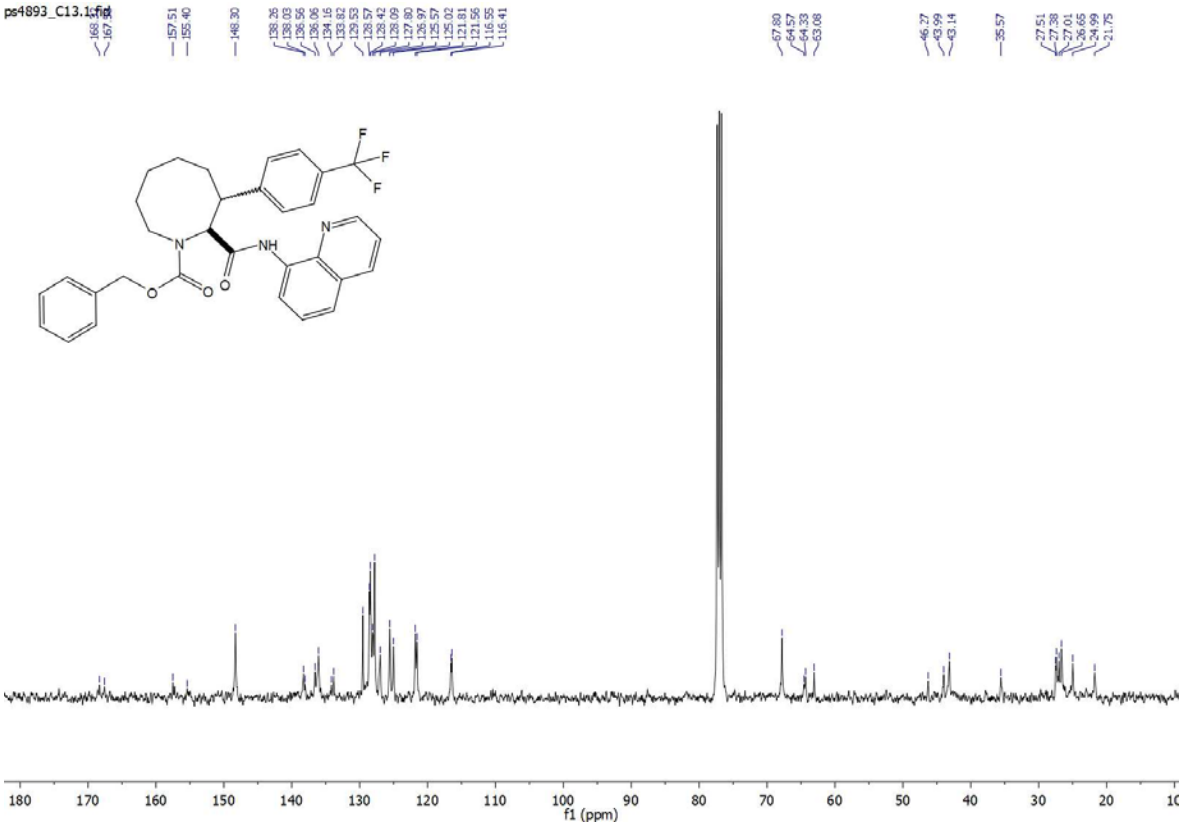
Compound Cbz – 28a



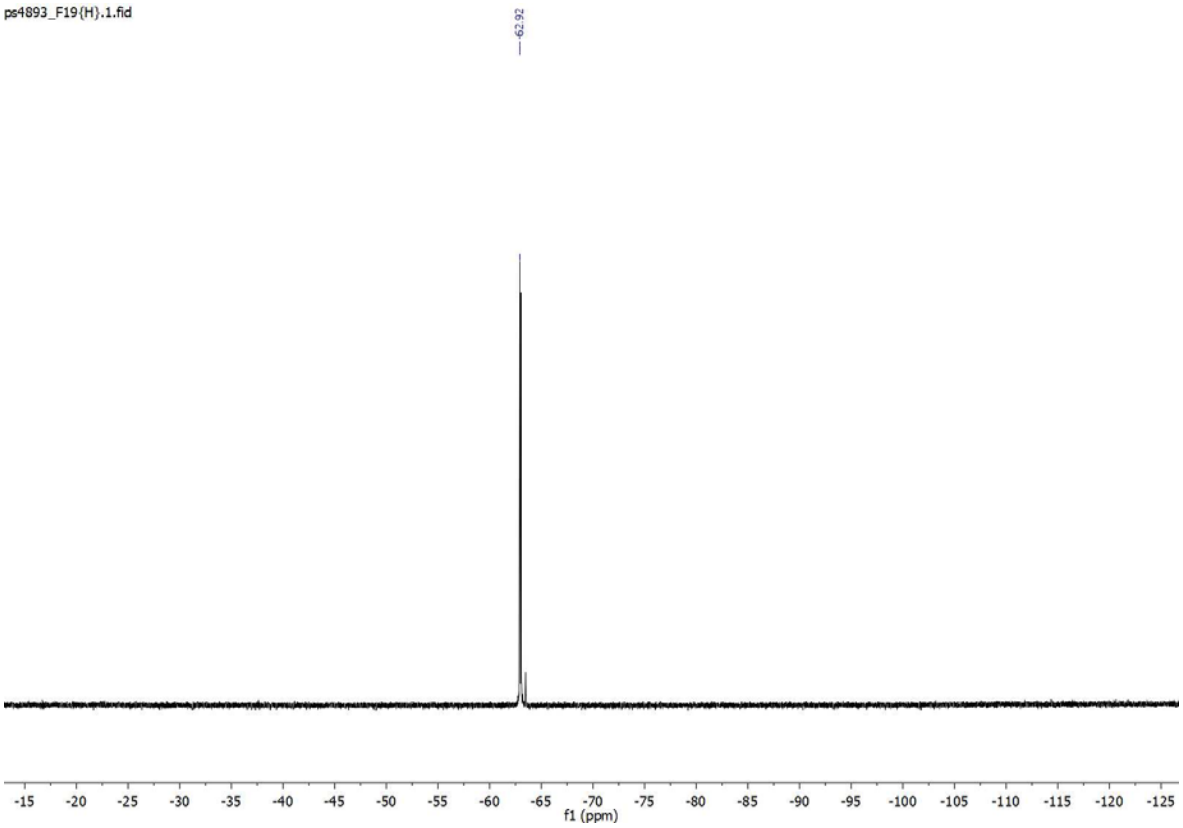


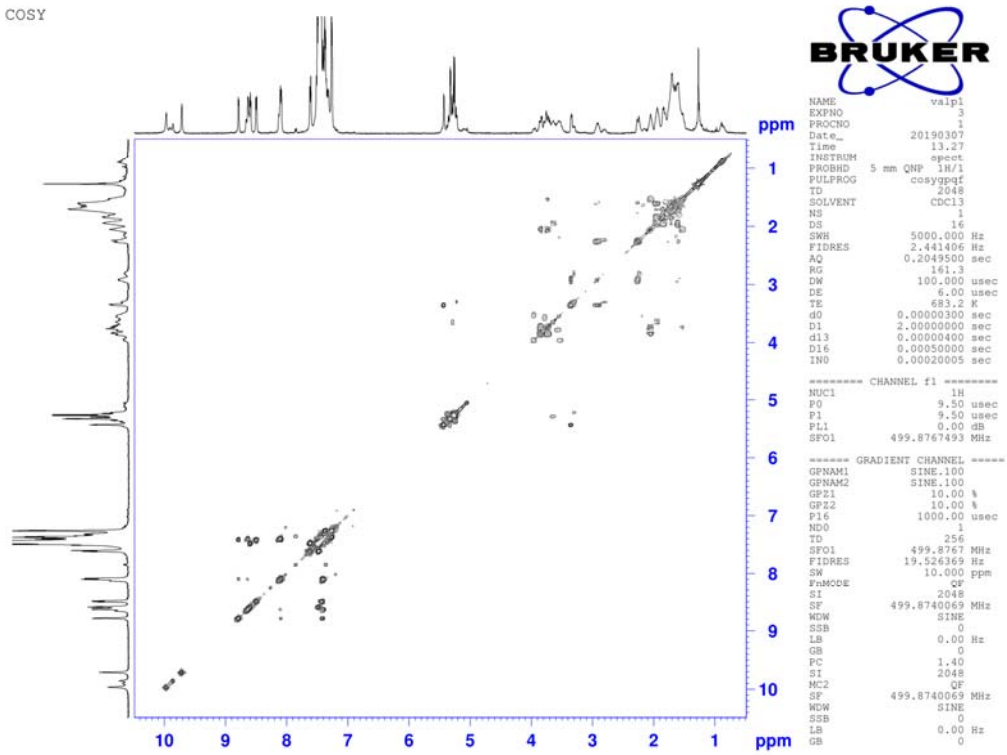
Compound Cbz – 29a





ps4893_F19{H}.1.fid

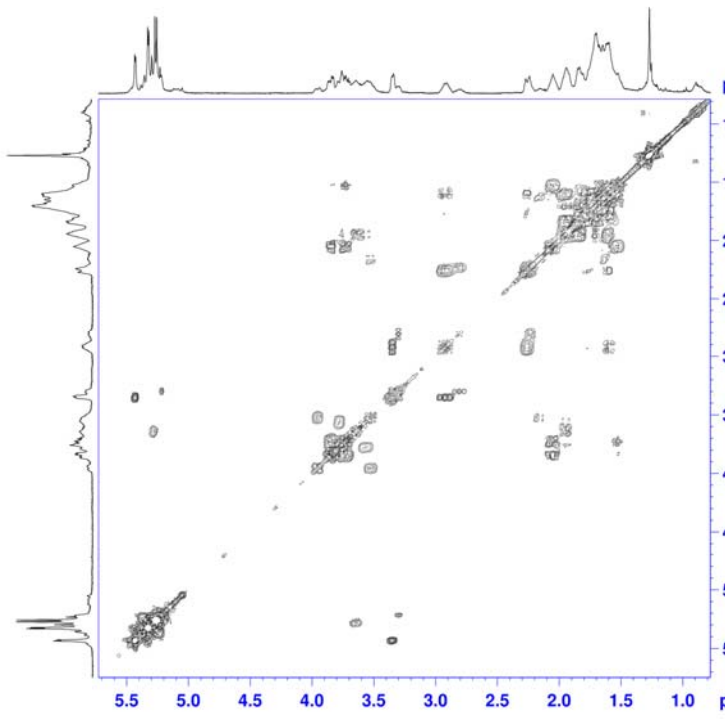




BRUKER

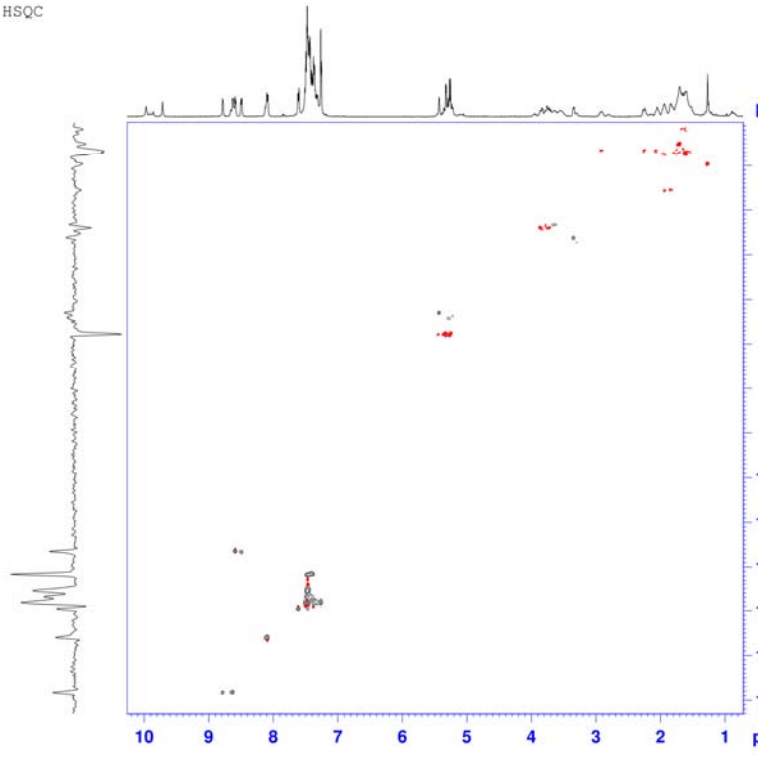
NAME	valp1
EXPNO	3
PROCNO	1
Date_	20190307
Time	13.27
INSTRUM	spect
PROBHD	5 mm QNP 1H/1
PULPROG	cosygpqf
TD	2048
SOLVENT	CDCl3
NS	1
DS	16
SWH	5000.000 Hz
FIDRES	2.441406 Hz
AQ	0.2049500 sec
RG	161.3
DW	100.000 usec
DE	6.00 usec
TE	683.2 K
d0	0.00000300 sec
D1	2.00000000 sec
d13	0.00000400 sec
D16	0.00050000 sec
IN0	0.00020005 sec
======== CHANNEL f1 ========	
NUC1	1H
P0	9.50 usec
P1	9.50 usec
PL1	0.00 dB
SFO1	499.8767493 MHz
====== GRADIENT CHANNEL =====	
GPNAM1	SINE.100
GPNAM2	SINE.100
GPZ1	10.00 %
GPZ2	10.00 %
P16	1000.00 usec
ND0	1
TD	256
SFO1	499.8767 MHz
FIDRES	19.526369 Hz
SW	10.000 ppm
FnMODE	QF
SI	2048
SF	499.8740069 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0
PC	1.40
SI	2048
MC2	QF
SF	499.8740069 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0

COSY

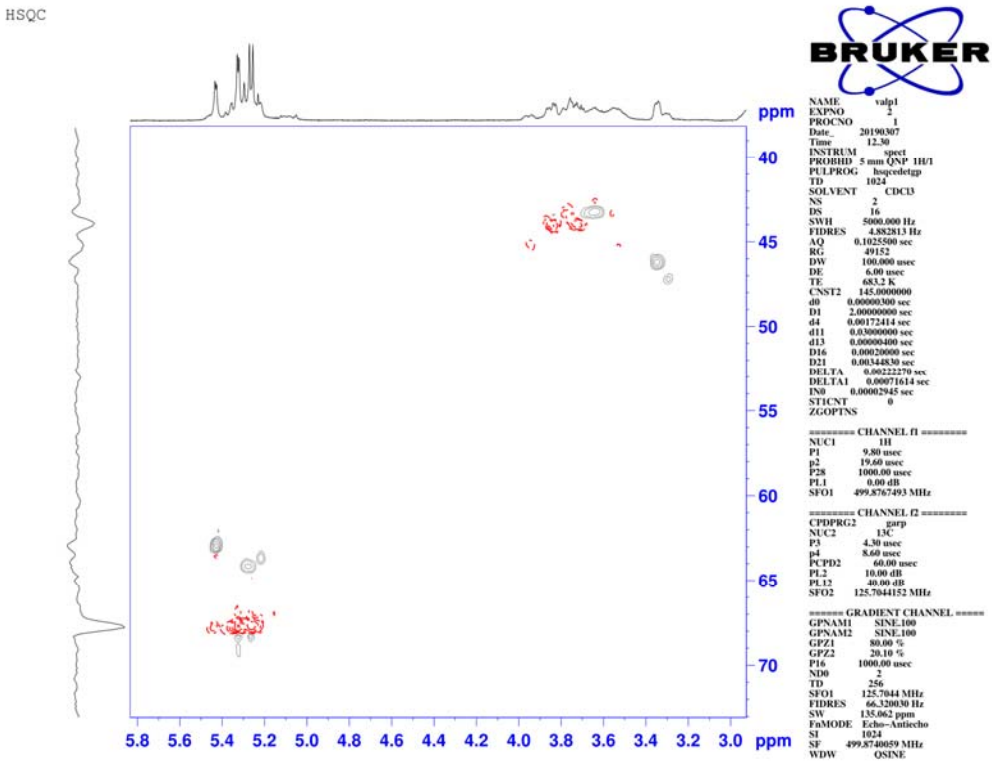


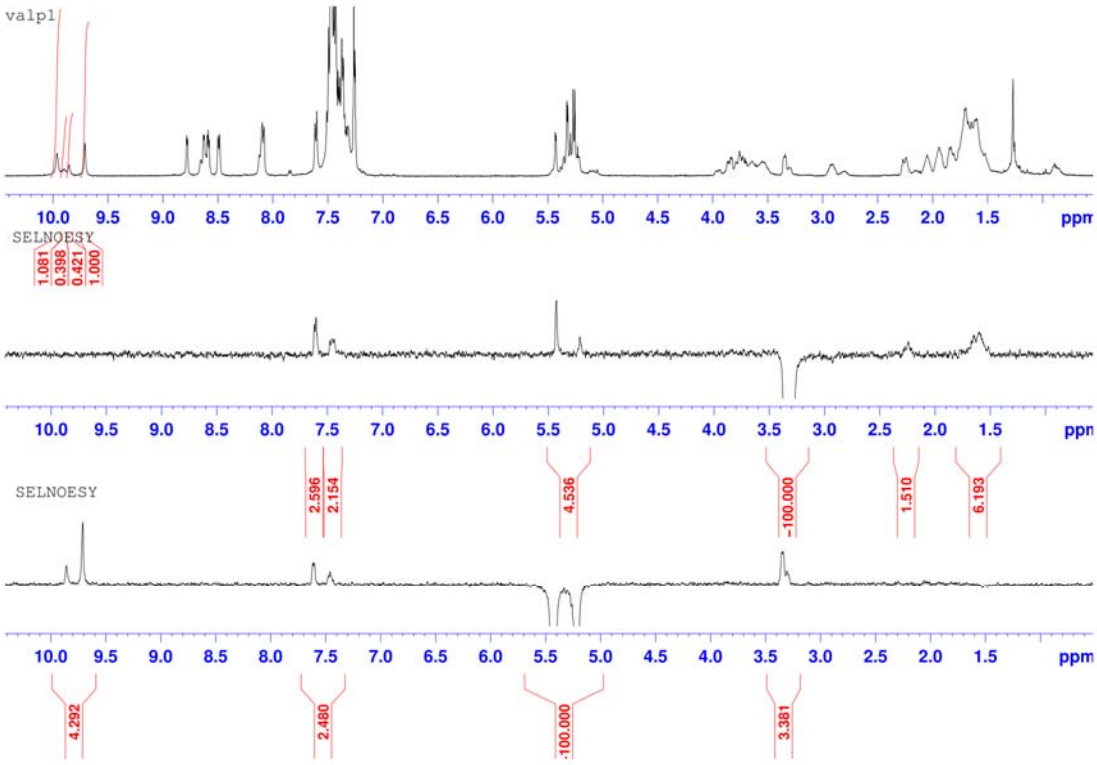

```
NAME                valp1
EXPNO                   3
PROCNO                  1
Date_            20190307
Time                13.27
INSTRUM             spect
PROBHD    5 mm QNP  1H/1
PULPROG         cosygpqf
TD                  2048
SOLVENT             CDCl3
NS                      1
DS                     16
SWH              5000.000 Hz
FIDRES           2.441406 Hz
AQ               0.2049500 sec
RG                 161.3
DW               100.000 usec
DE                 6.00 usec
TE                 683.2 K
d0               0.00000300 sec
D1               2.00000000 sec
d13              0.00000400 sec
D16              0.00050000 sec
IN0              0.00020005 sec

======== CHANNEL f1 ========
NUC1                    1H
P0                   9.50 usec
P1                   9.50 usec
PL1                  0.00 dB
SFO1          499.8767493 MHz

====== GRADIENT CHANNEL =====
GPNAM1           SINE.100
GPNAM2           SINE.100
GPZ1                10.00 %
GPZ2                10.00 %
P16               1000.00 usec
ND0                     1
TD                    256
SFO1           499.8767 MHz
FIDRES        19.526369 Hz
SW               10.000 ppm
FnMODE                QF
SI                  2048
SF            499.8740069 MHz
WDW                 SINE
SSB                    0
LB                  0.00 Hz
GB                     0
PC                  1.40
SI                  2048
MC2                   QF
SF            499.8740069 MHz
WDW                 SINE
SSB                    0
LB                  0.00 Hz
GB                     0
```

HSQC

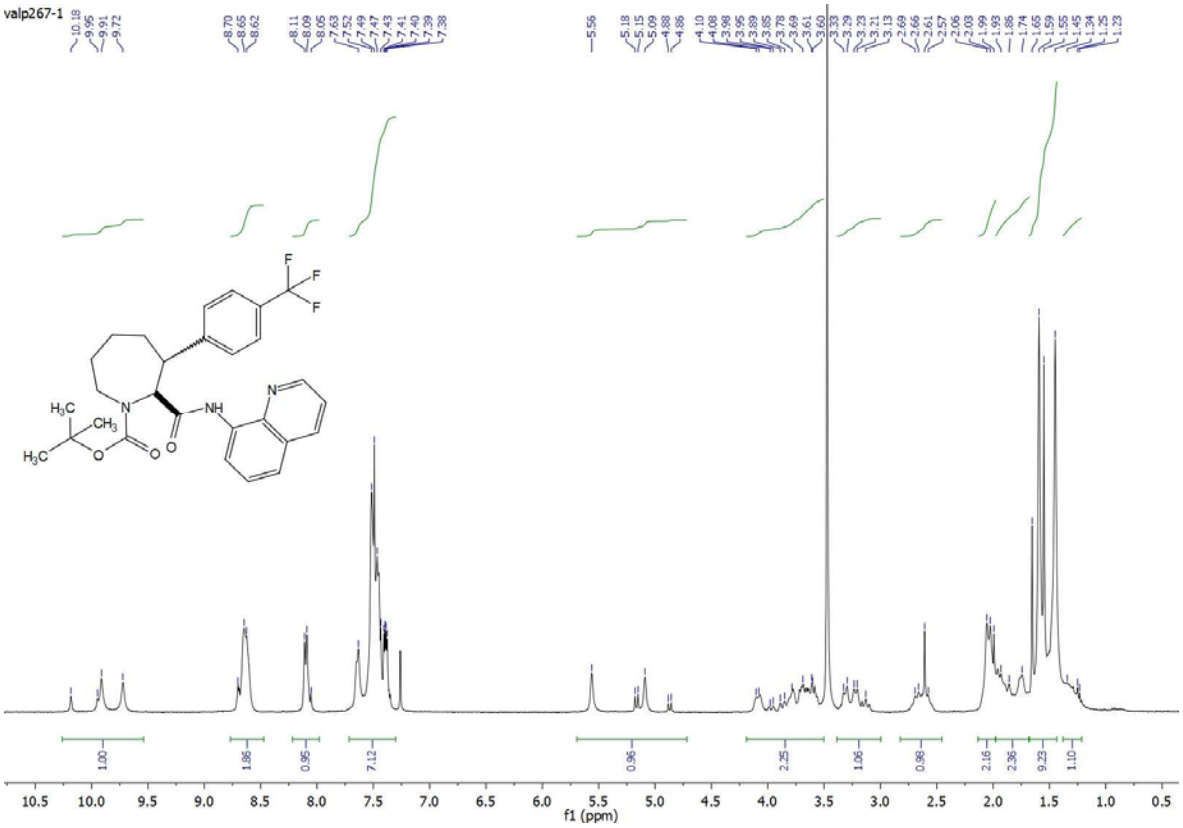


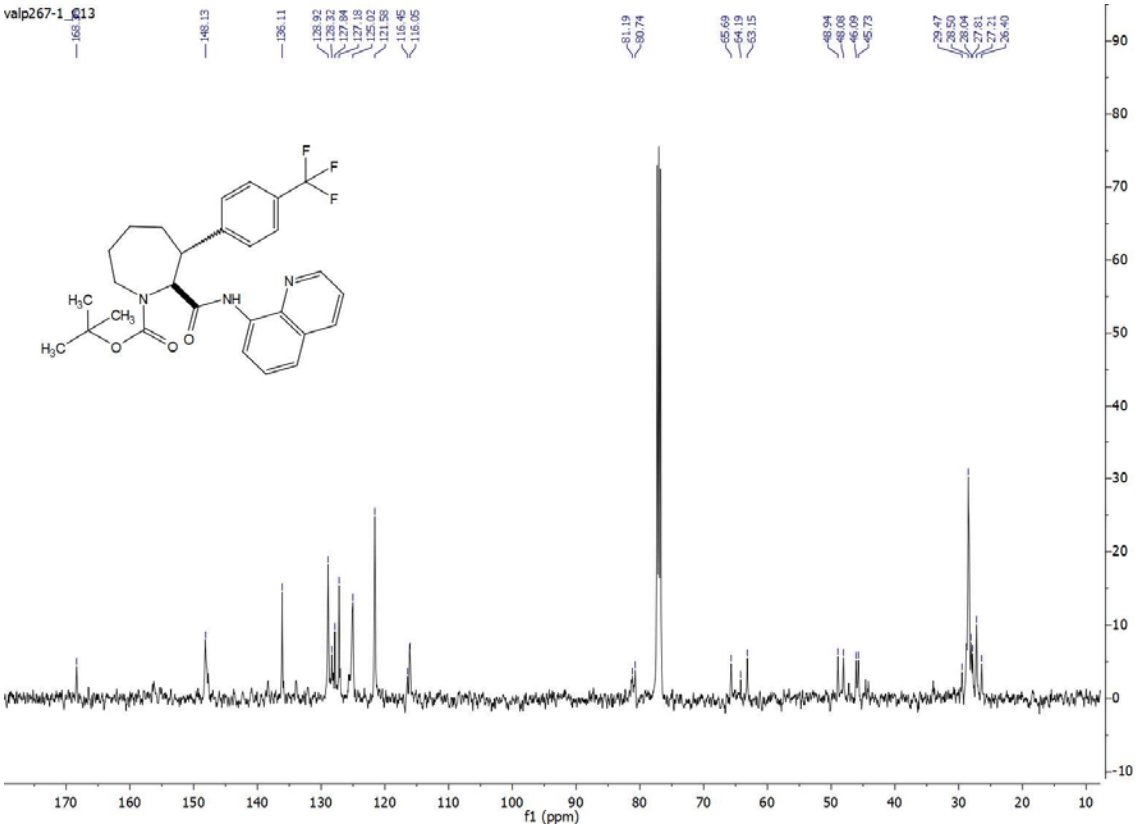

```
NAME            valp1
EXPNO               2
PROCNO              1
Date_        20190307
Time            12.30
INSTRUM         spect
PROBHD  5 mm QNP 1H/1
PULPROG     hsqcedetgp
TD                1024
SOLVENT          CDCl3
NS                  2
DS                 16
SWH          5000.000 Hz
FIDRES       4.882813 Hz
AQ           0.1025500 sec
RG                49152
DW           100.000 usec
DE             6.00 usec
TE             683.2 K
CNST2        145.0000000
d0           0.00000300 sec
D1           2.00000000 sec
d4           0.00172414 sec
d11          0.03000000 sec
d13          0.00000400 sec
D16          0.00020000 sec
D21          0.00344830 sec
DELTA        0.00222270 sec
DELTA1       0.00071614 sec
IN0          0.00002945 sec
STSICNT             0
ZGOPTNS

======== CHANNEL f1 ========
NUC1               1H
P1              9.80 usec
p2             19.60 usec
P28          1000.00 usec
PL1             0.00 dB
SFO1     499.8767493 MHz

======== CHANNEL f2 ========
CPDPRG2         garp
NUC2              13C
P3              4.30 usec
p4              8.60 usec
PCPD2          60.00 usec
PL2            10.00 dB
PL12           40.00 dB
SFO2     125.7044152 MHz

====== GRADIENT CHANNEL =====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPZ1             80.00 %
GPZ2             20.10 %
P16            1000.00 usec
ND0                 2
TD                256
SFO1     125.7044 MHz
FIDRES    66.320030 Hz
SW        135.062 ppm
FnMODE    Echo-Antiecho
SI              1024
SF       499.8740059 MHz
WDW             QSINE
```

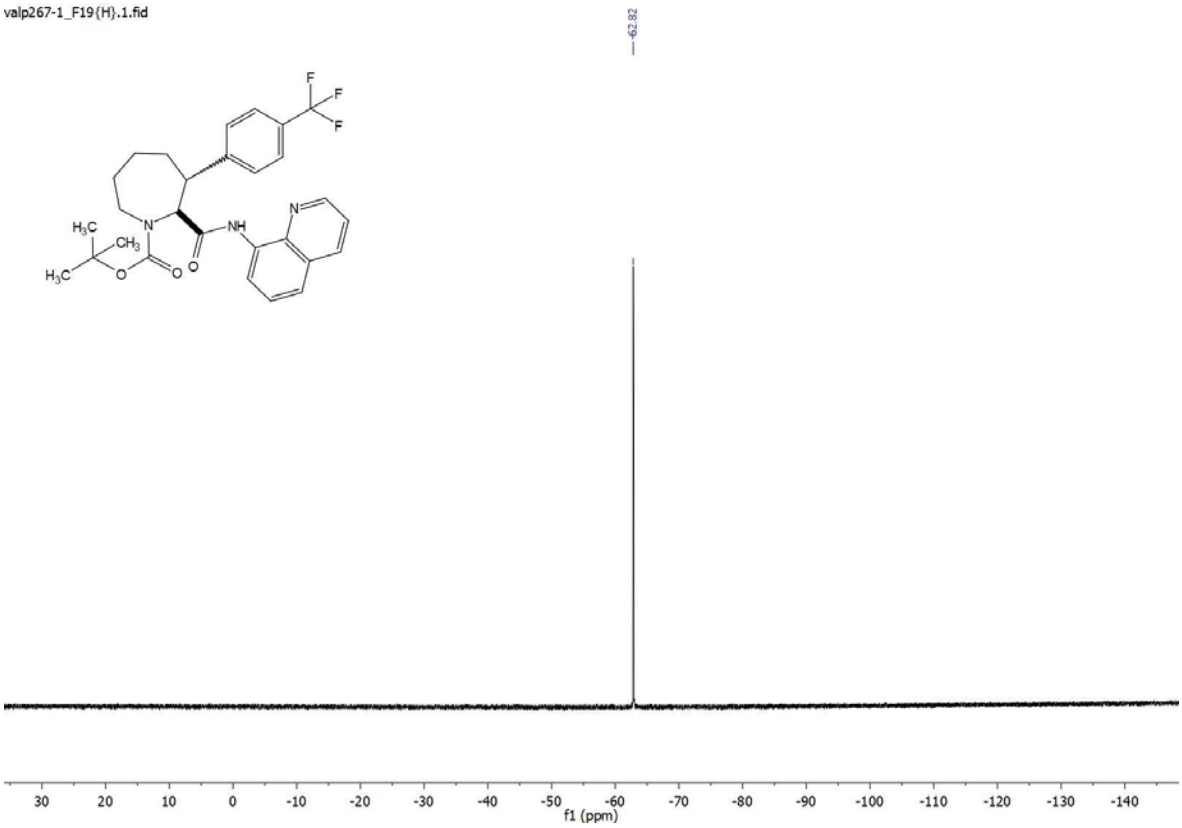

HSQC
BRUKER
ppm
40
45
50
55
60
65
70
5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 ppm
NAME valp1
EXPNO 2
PROCNO 1
Date_ 20190307
Time 12.30
INSTRUM spect
PROBHD 5 mm QNP 1H/1
PULPROG hsqcedetgp
TD 1024
SOLVENT CDCl3
NS 2
DS 16
SWH 5000.000 Hz
FIDRES 4.882813 Hz
AQ 0.1025500 sec
RG 49152
DW 100.000 usec
DE 6.00 usec
TE 683.2 K
CNST2 145.0000000
d0 0.00000300 sec
D1 2.00000000 sec
d4 0.00172414 sec
d11 0.03000000 sec
d13 0.00000400 sec
D16 0.00020000 sec
D21 0.00344830 sec
DELTA 0.00222270 sec
DELTA1 0.00071614 sec
IN0 0.00002945 sec
ST1CNT 0
ZGOPTNS
======== CHANNEL f1 ========
NUC1 1H
P1 9.80 usec
p2 19.60 usec
P28 1000.00 usec
PL1 0.00 dB
SFO1 499.8767493 MHz
======== CHANNEL f2 ========
CPDPRG2 garp
NUC2 13C
P3 4.30 usec
p4 8.60 usec
PCPD2 60.00 usec
PL2 10.00 dB
PL12 40.00 dB
SFO2 125.7044152 MHz
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPZ1 80.00 %
GPZ2 20.10 %
P16 1000.00 usec
ND0 2
TD 256
SFO1 125.7044 MHz
FIDRES 66.320030 Hz
SW 135.062 ppm
FnMODE Echo-Antiecho
SI 1024
SF 499.8740059 MHz
WDW QSINE


valp1
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 ppm
SELNOESY
1.061
0.398
0.421
1.000
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 ppm
SELNOESY
2.596
2.154
4.536
-100.000
1.510
6.193
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 ppm
4.292
2.480
-100.000
3.381

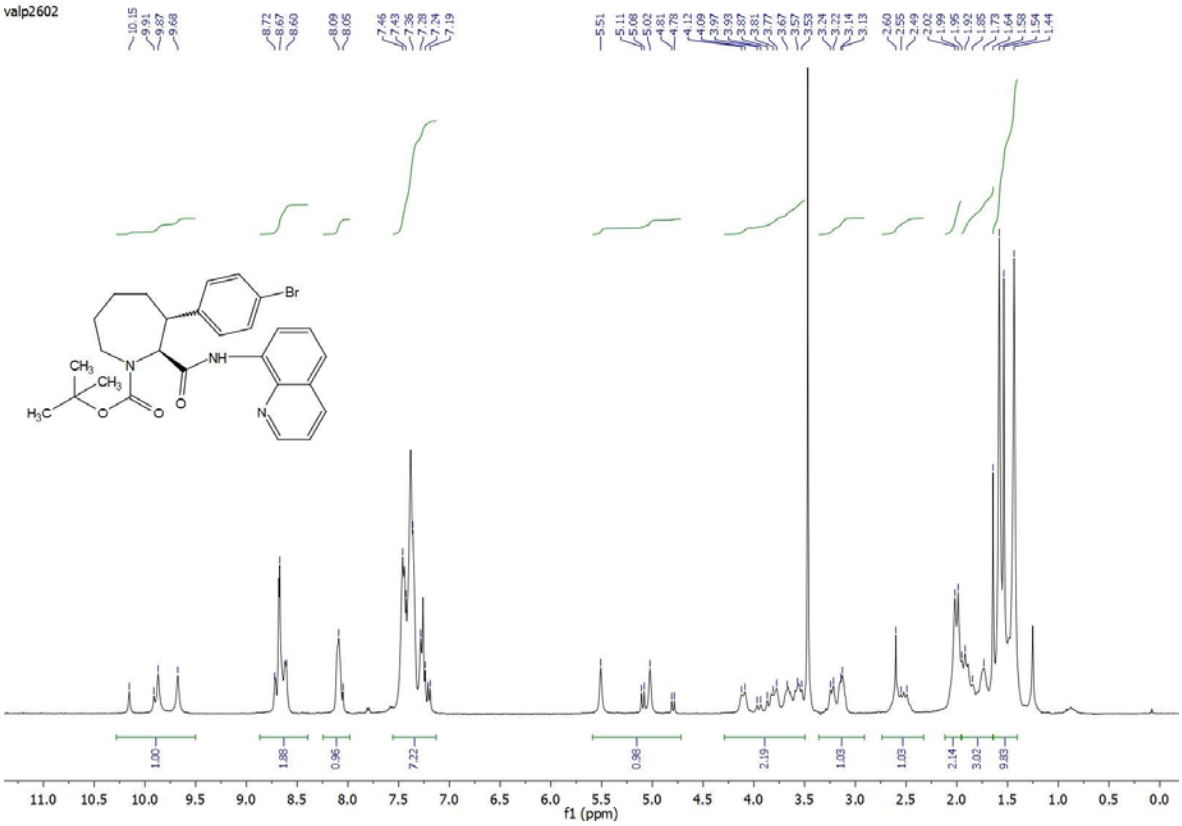
Compound Boc – 30a

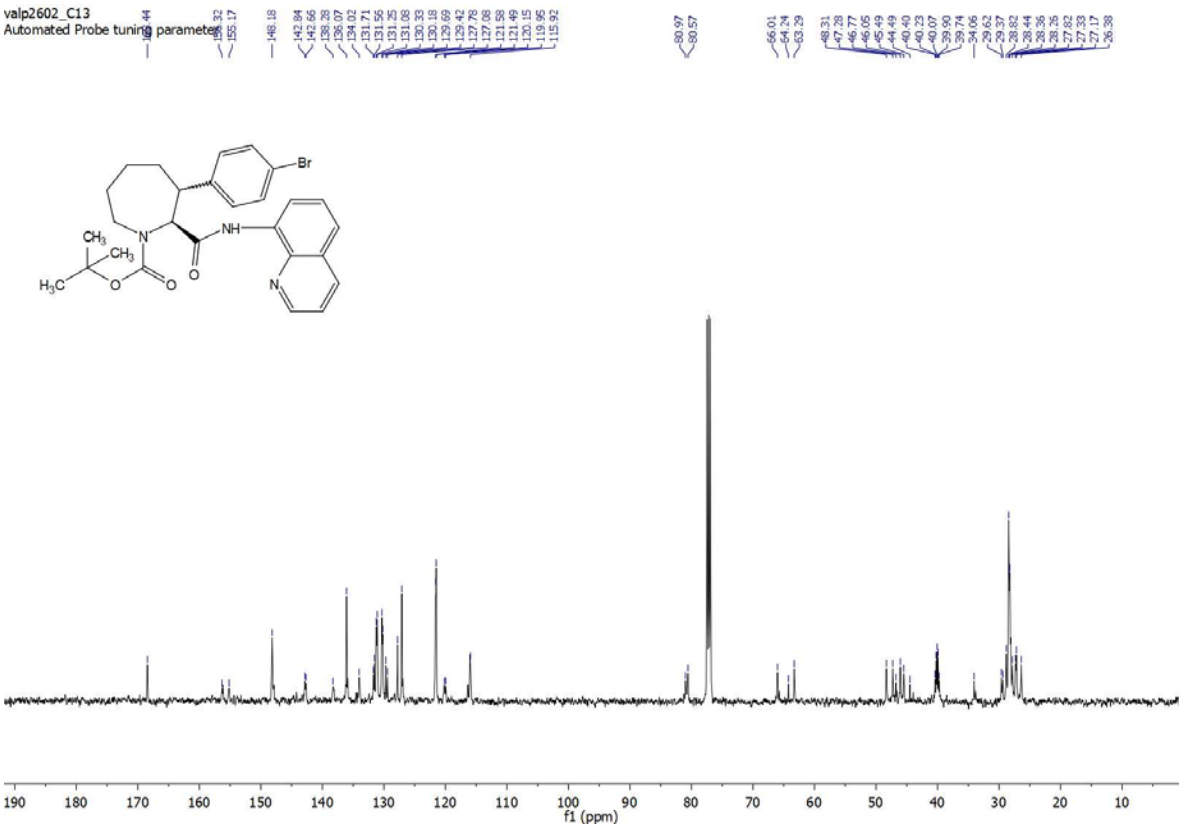




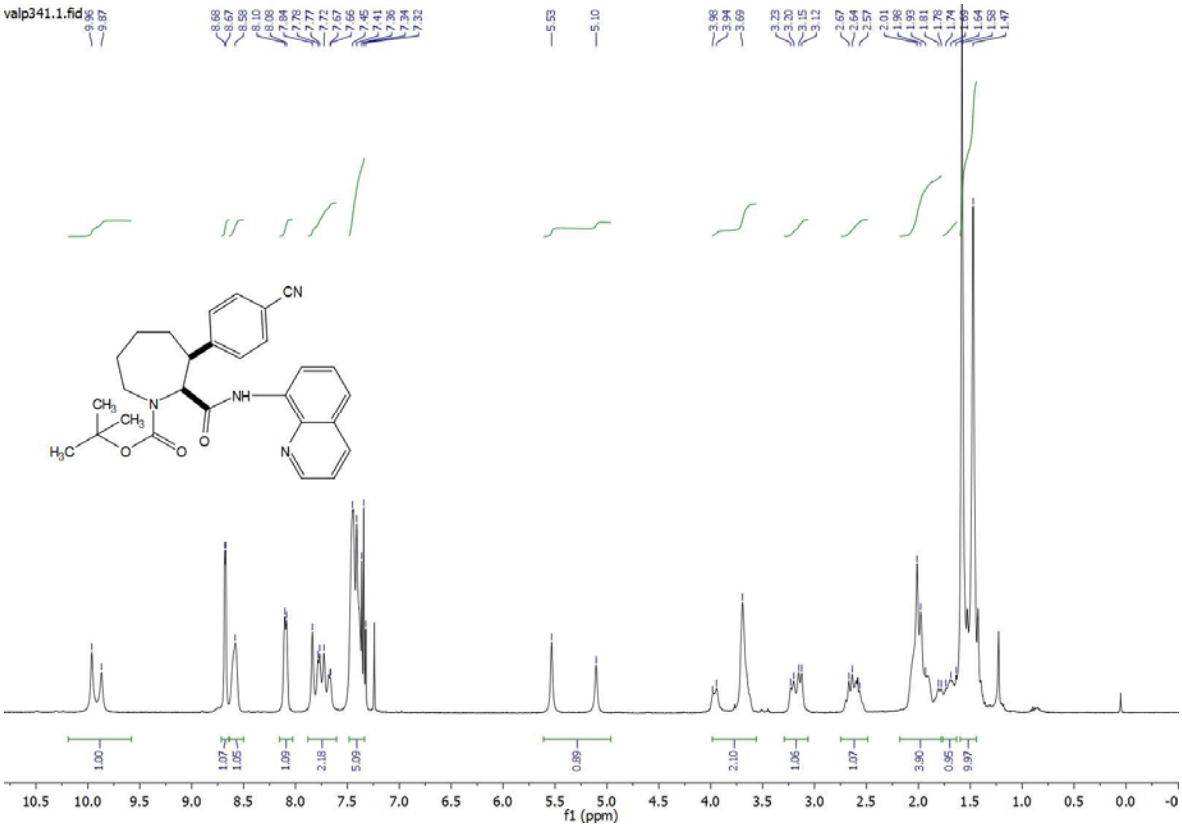

valp267-1_F19{H}.1.fid
-62.82
F
F
F
N
NH
N
O
O
O
H3C
CH3
H3C
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
f1 (ppm)

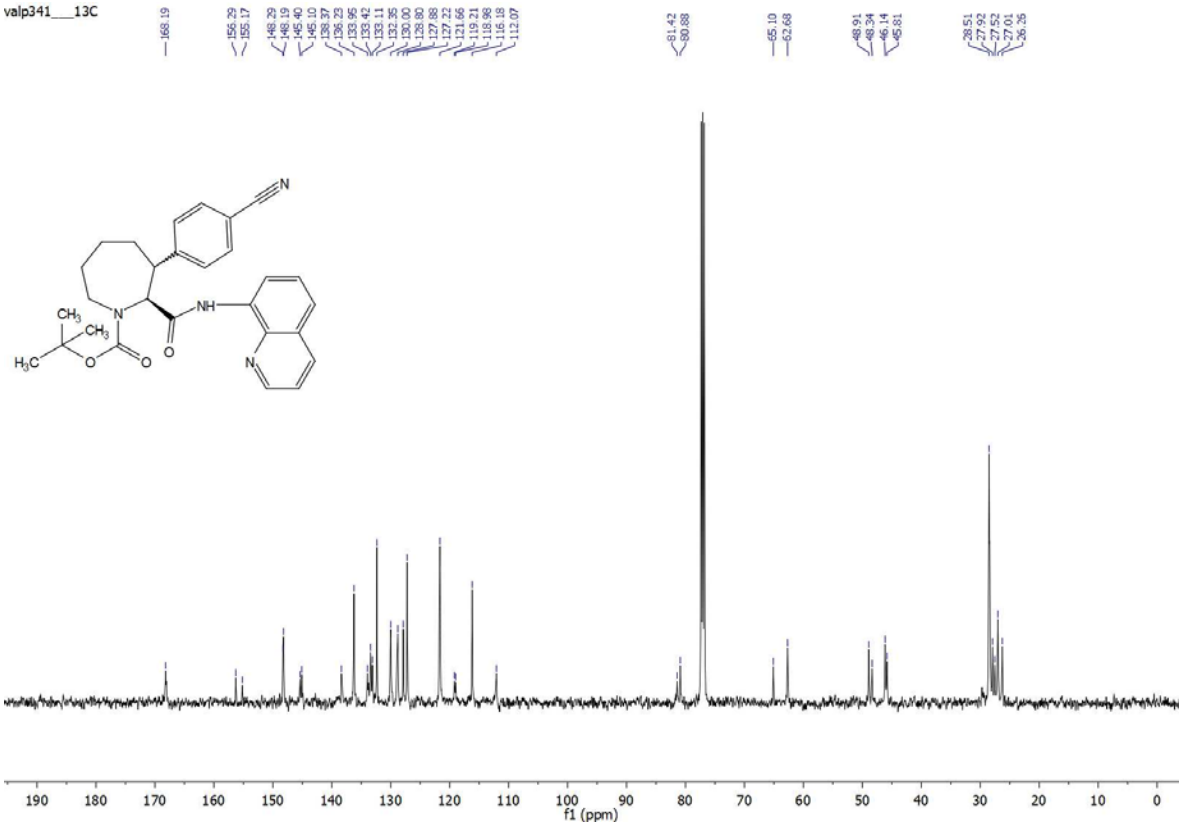
Compound Boc – 31a



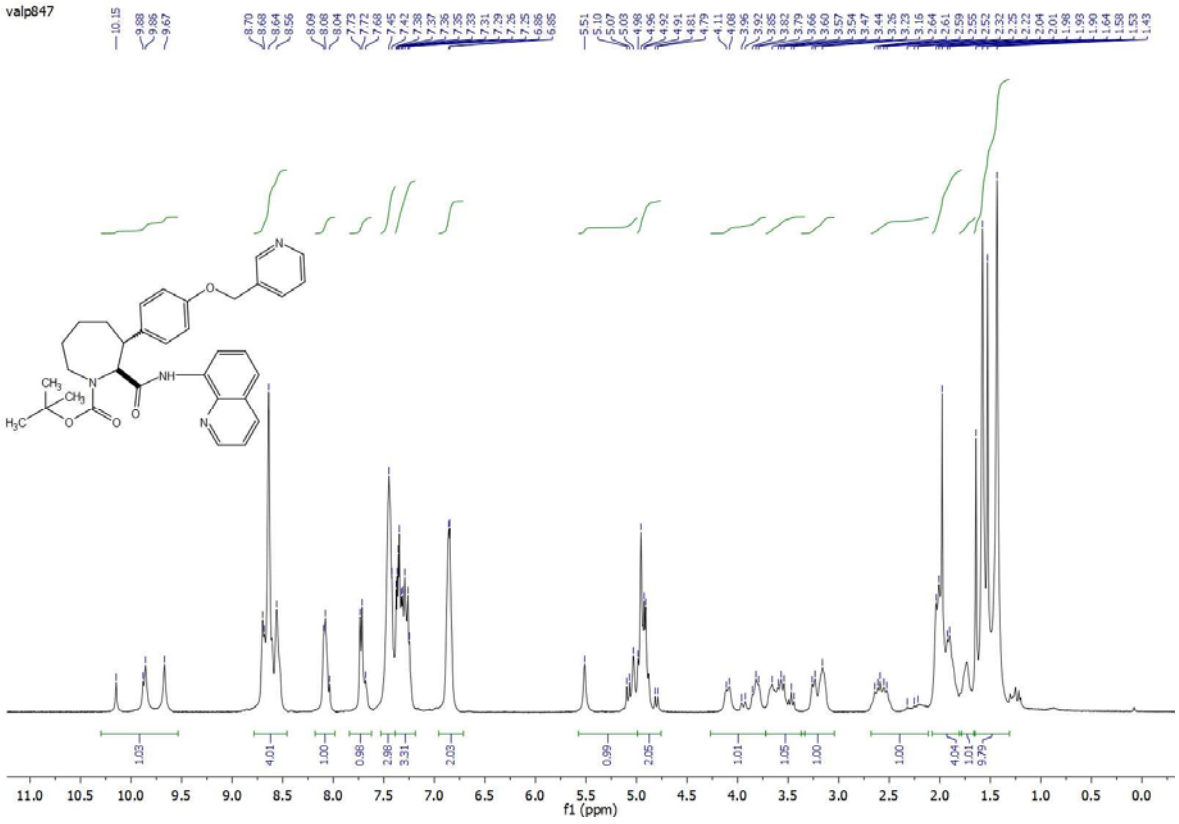


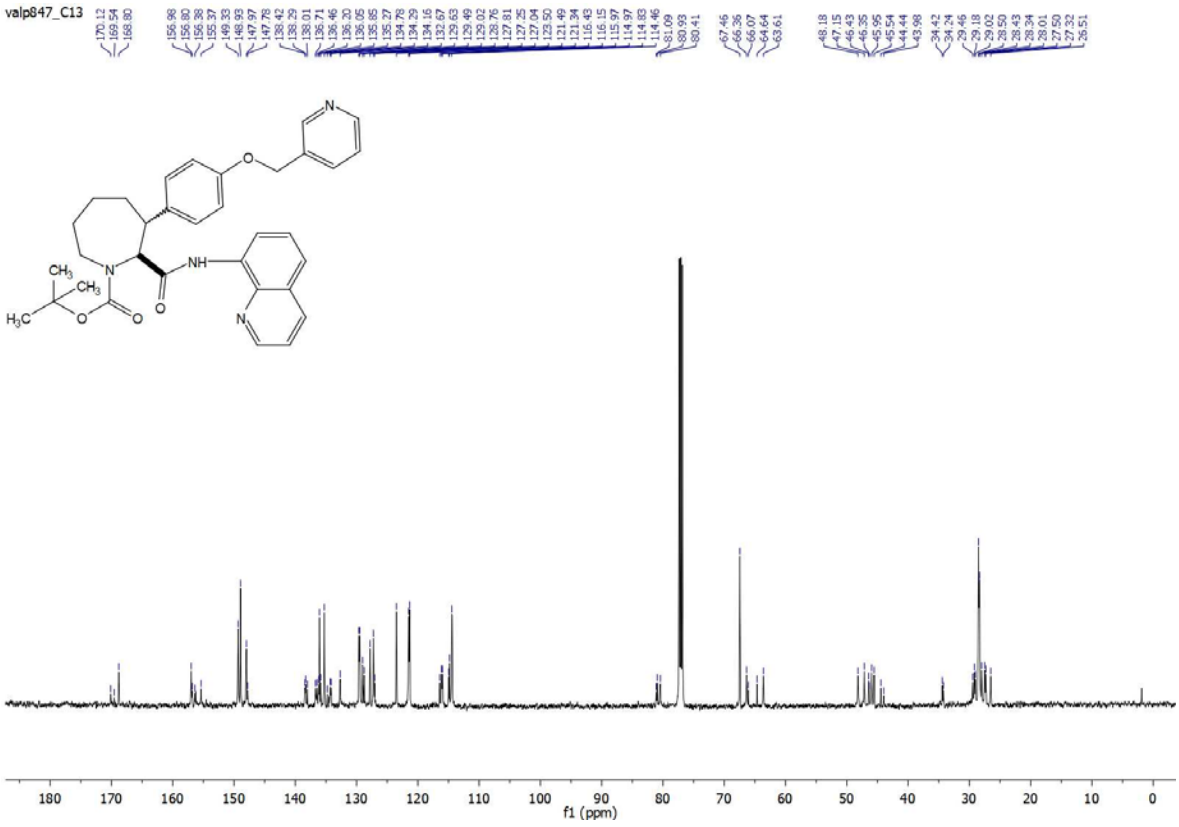
Compound Boc – 32a



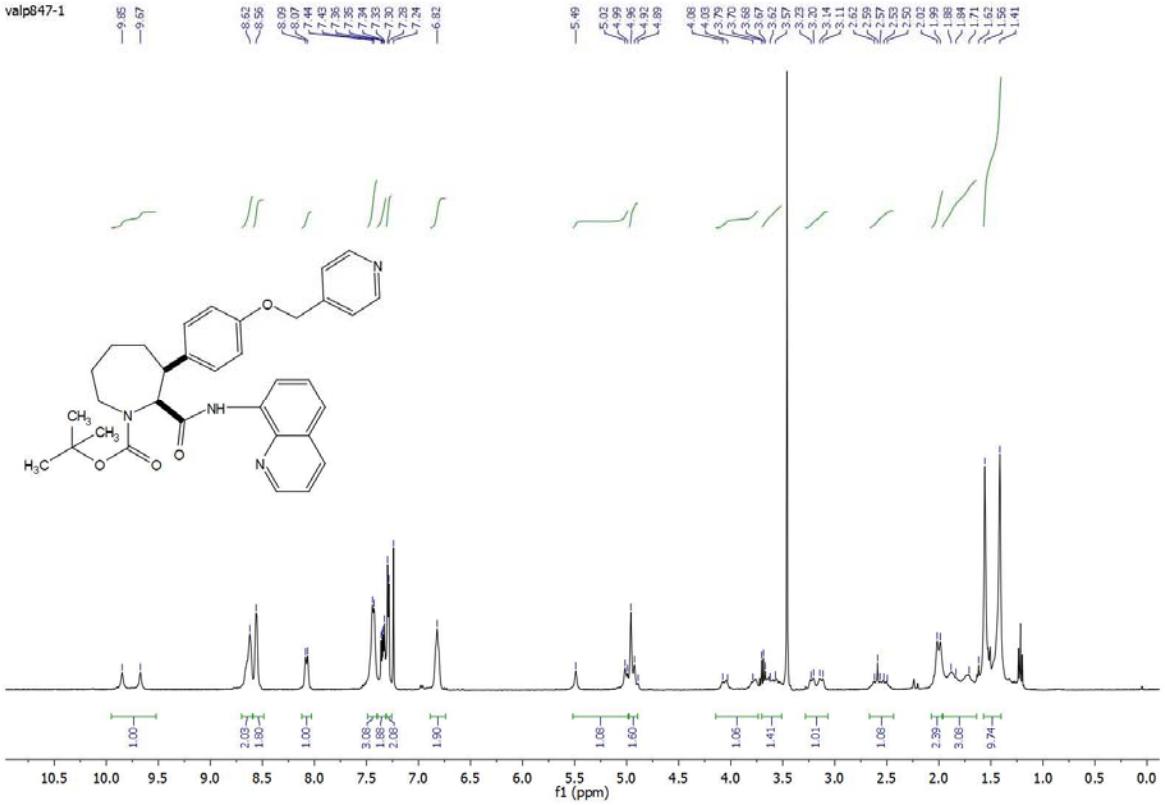


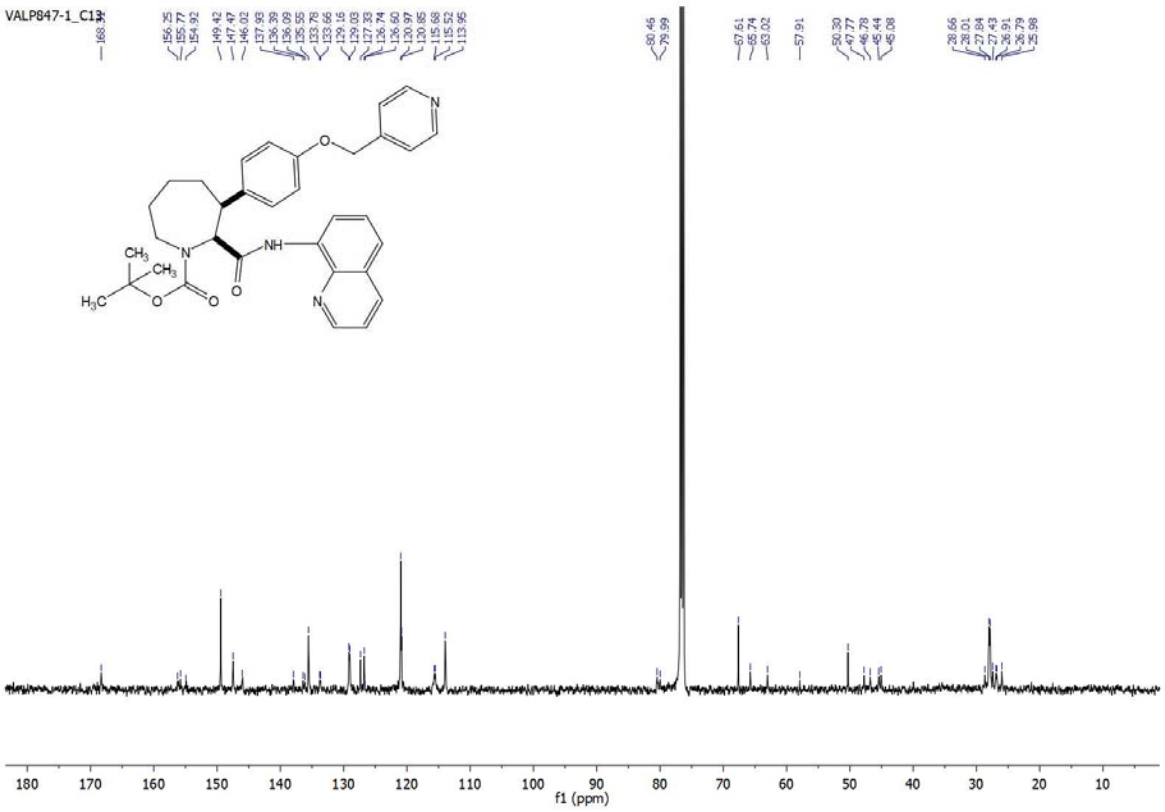
Compound Boc – 33a



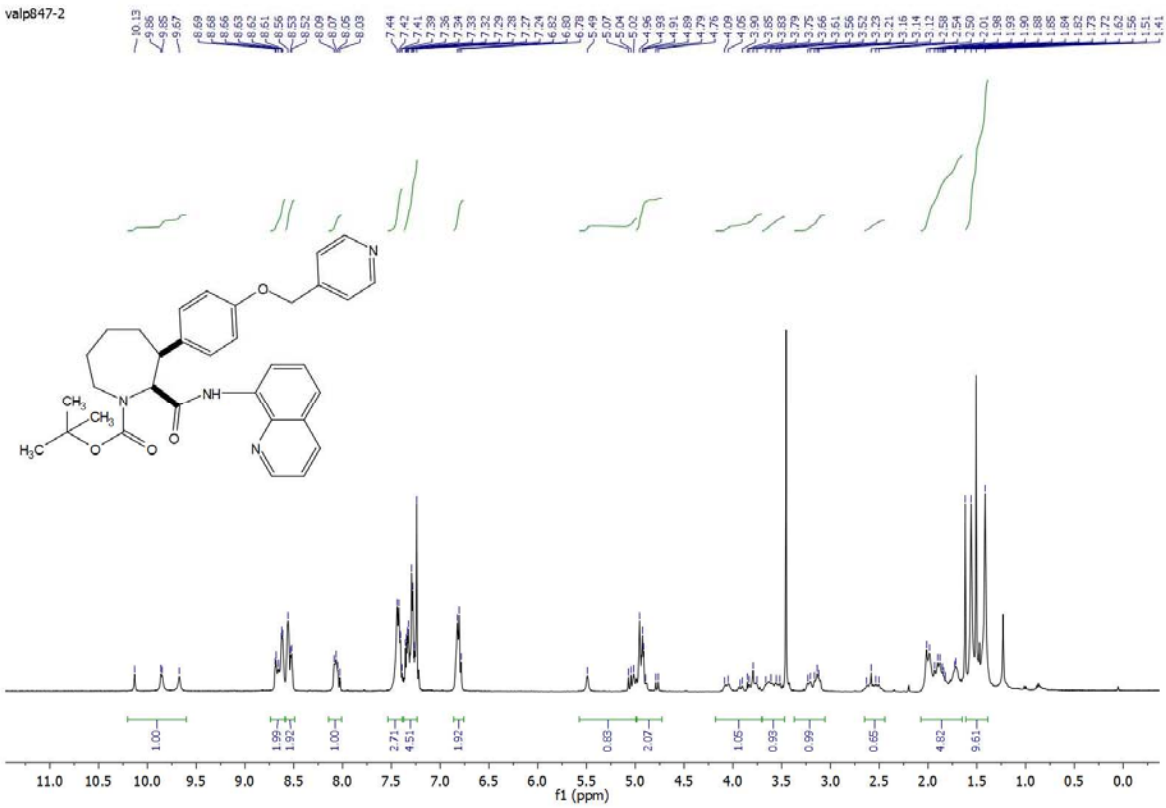


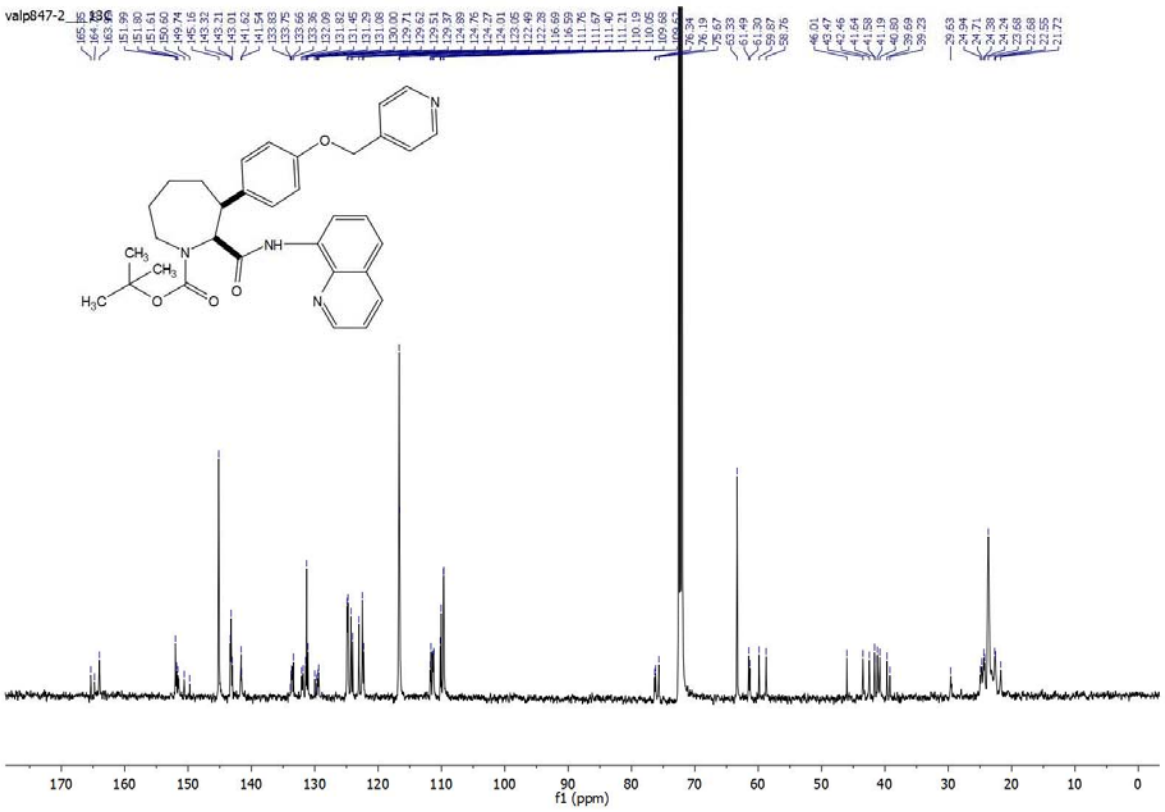
Compound Boc – 34a (cis)



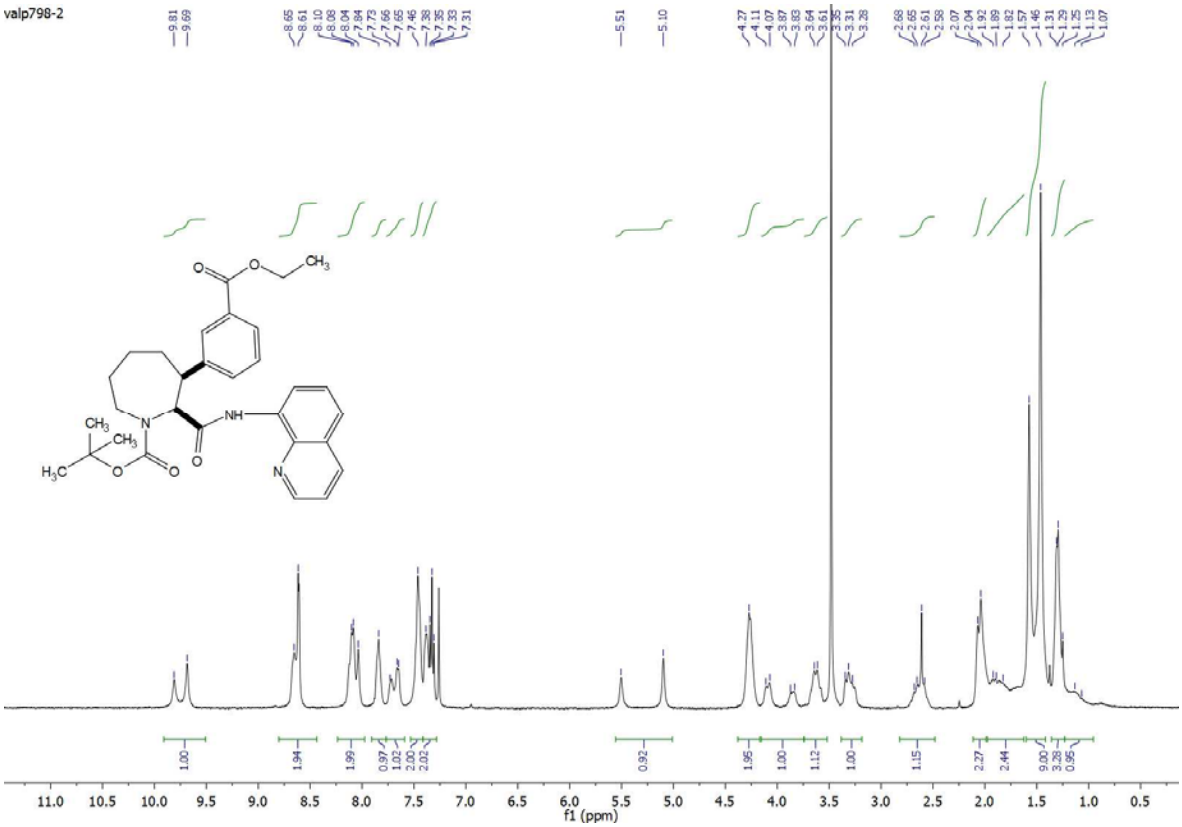


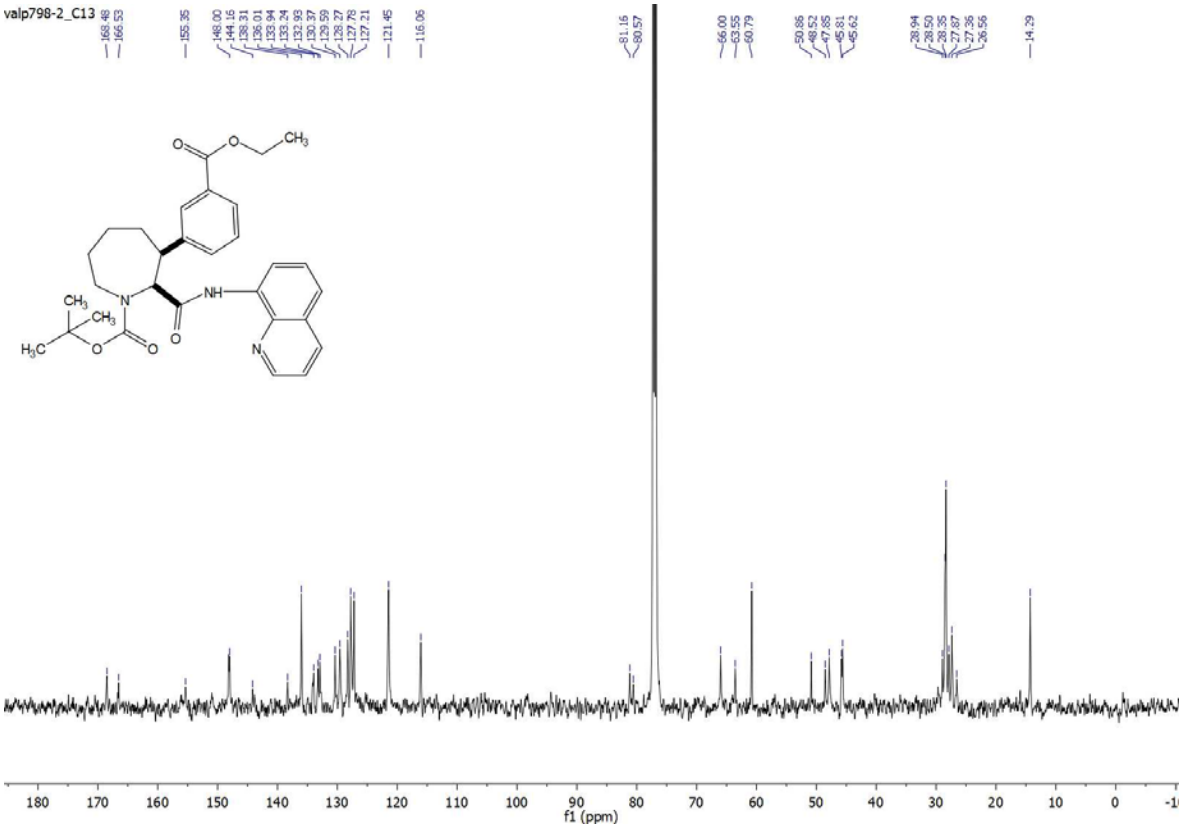
Compound Boc – 34a (a mixture of diastereomers)

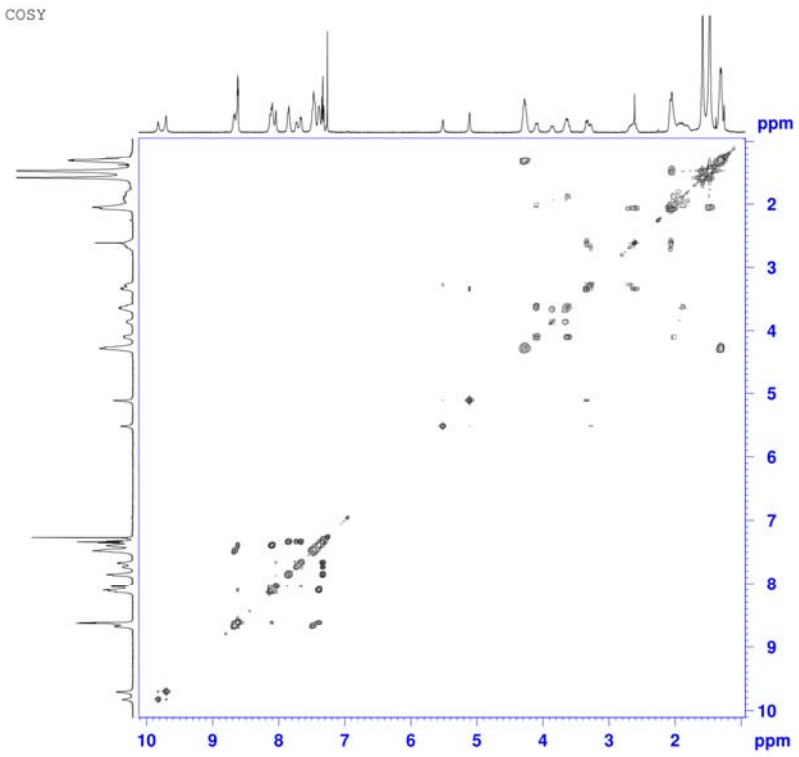




Compound Boc – 35a

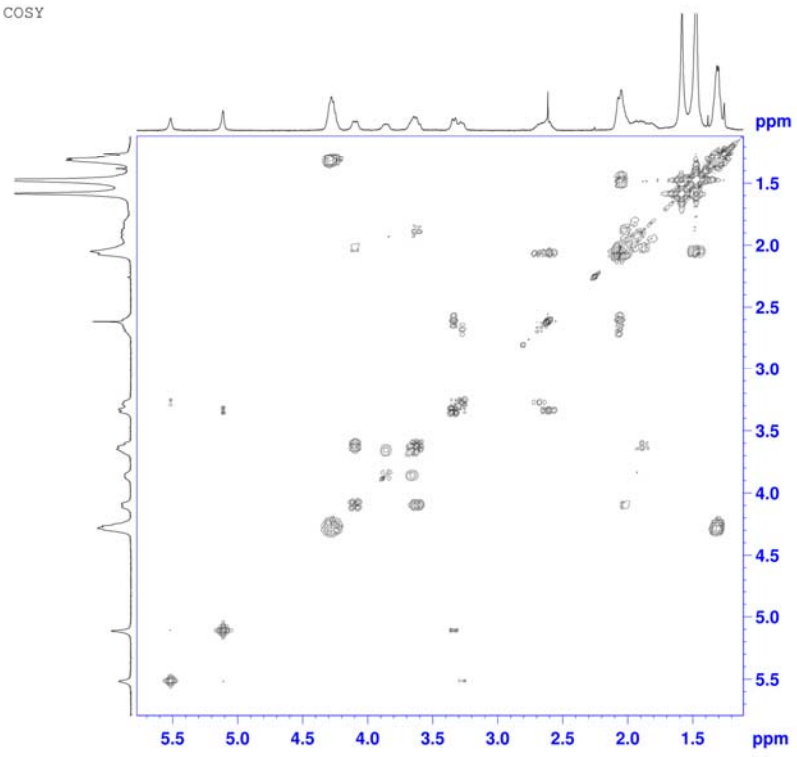







```
NAME                  valp3
EXPNO                     3
PROCNO                    1
Date_              20190308
Time                 21.44
INSTRUM              spect
PROBHD    5 mm QNP  1H/1
PULPROG          cosygpqf
TD                    2048
SOLVENT               CDCl3
NS                        1
DS                       16
SWH               5000.000 Hz
FIDRES               2.441406 Hz
AQ                0.2049500 sec
RG                    161.3
DW                  100.000 usec
DE                     6.00 usec
TE                   683.2 K
d0                0.00000300 sec
D1                2.00000000 sec
d13               0.00000400 sec
D16               0.00050000 sec
IN0               0.00020005 sec

======== CHANNEL f1 ========
NUC1                      1H
P0                     9.50 usec
P1                     9.50 usec
PL1                    0.00 dB
SFO1            499.8767493 MHz

====== GRADIENT CHANNEL =====
GPNAM1              SINE.100
GPNAM2              SINE.100
GPZ1                  10.00 %
GPZ2                  10.00 %
P16                 1000.00 usec
ND0                       1
TD                      256
SFO1              499.8767 MHz
FIDRES           19.526369 Hz
SW                    10.000 ppm
FnMODE                   QF
SI                      2048
SF              499.8740069 MHz
WDW                    SINE
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.40
SI                      2048
MC2                      QF
SF              499.8740069 MHz
WDW                    SINE
SSB                       0
LB                     0.00 Hz
GB                        0
```

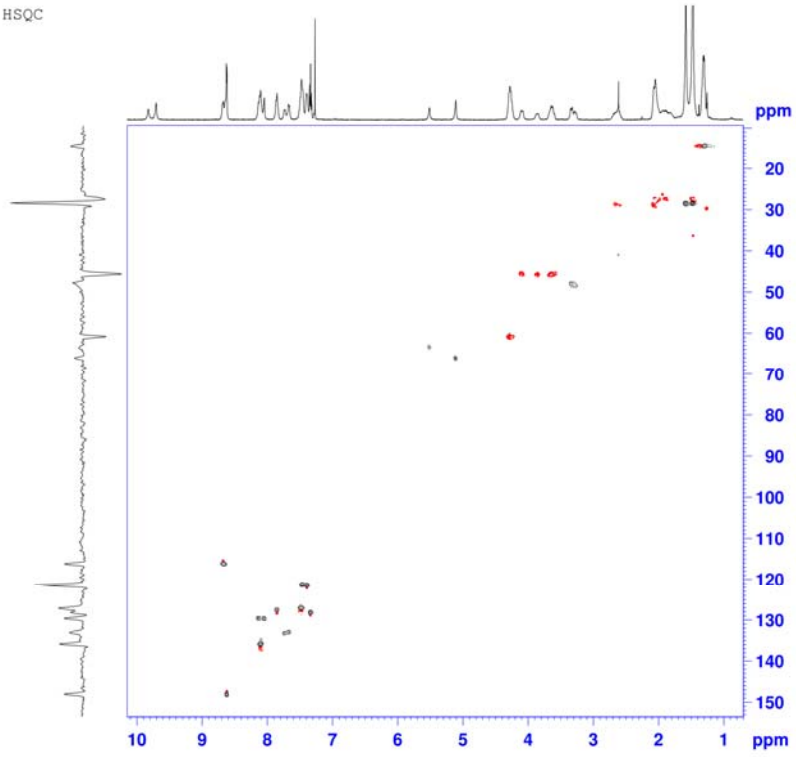
COSY



BRUKER

```
NAME                valp3
EXPNO                   3
PROCNO                  1
Date_            20190308
Time                21.44
INSTRUM             spect
PROBHD    5 mm QNP  1H/1
PULPROG          cosygpqf
TD                   2048
SOLVENT              CDCl3
NS                      1
DS                     16
SWH              5000.000 Hz
FIDRES           2.441406 Hz
AQ               0.2049500 sec
RG                   161.3
DW                 100.000 usec
DE                   6.00 usec
TE                  683.2 K
d0               0.00000300 sec
D1               2.00000000 sec
d13              0.00000400 sec
D16              0.00050000 sec
IN0              0.00020005 sec

======== CHANNEL f1 ========
NUC1                   1H
P0                   9.50 usec
P1                   9.50 usec
PL1                  0.00 dB
SFO1          499.8767493 MHz

====== GRADIENT CHANNEL =====
GPNAM1            SINE.100
GPNAM2            SINE.100
GPZ1                10.00 %
GPZ2                10.00 %
P16               1000.00 usec
ND0                     1
TD                    256
SFO1           499.8767 MHz
FIDRES         19.526369 Hz
SW                10.000 ppm
FnMODE                 QF
SI                   2048
SF            499.8740069 MHz
WDW                 SINE
SSB                    0
LB                  0.00 Hz
GB                     0
PC                  1.40
SI                   2048
MC2                    QF
SF            499.8740069 MHz
WDW                 SINE
SSB                    0
LB                  0.00 Hz
GB                     0
```

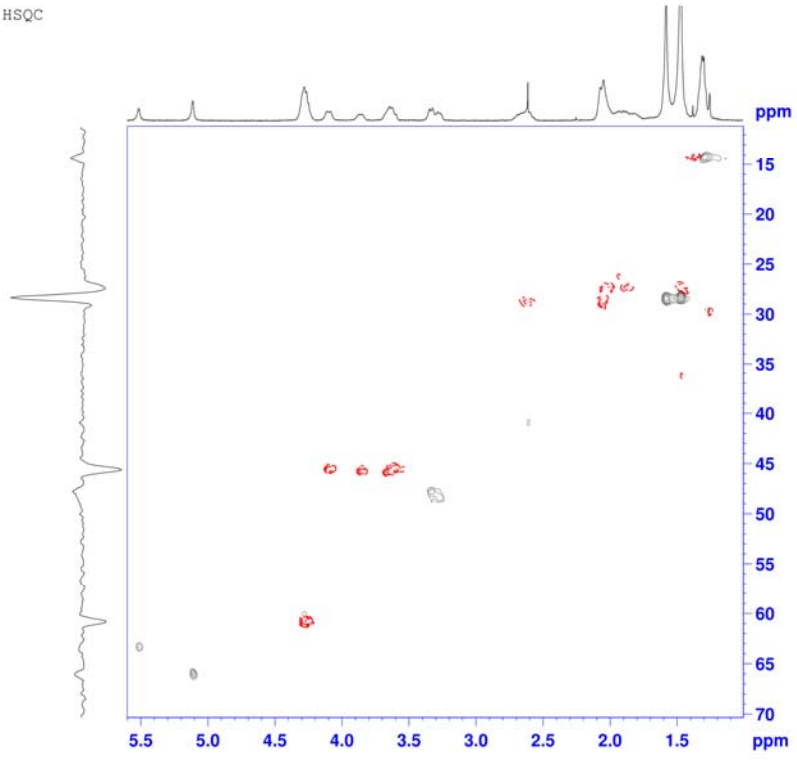
HSQC



BRUKER

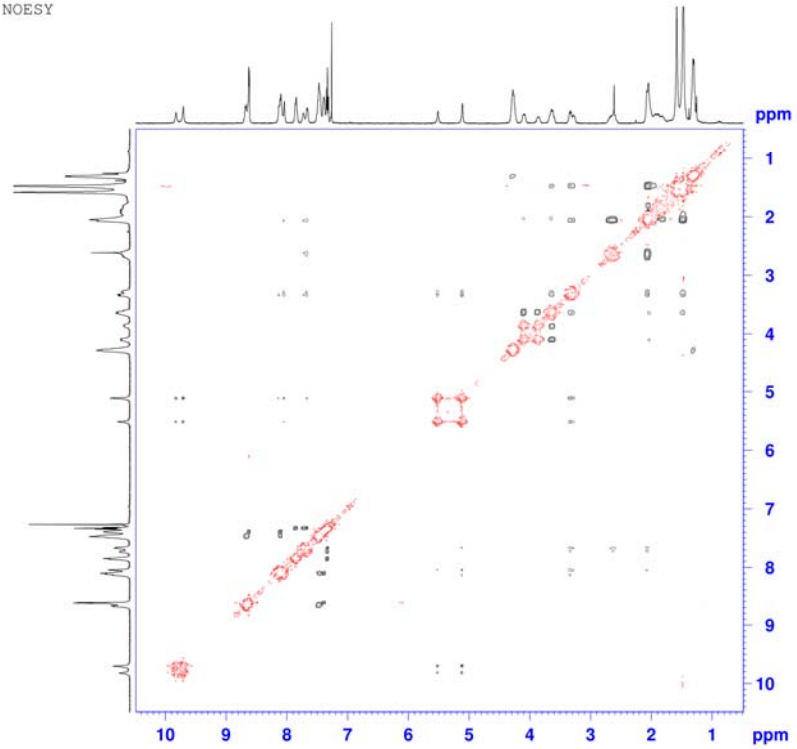
```
NAME                valp3
EXPNO                   2
PROCNO                  1
Date_            20190308
Time                21.25
INSTRUM             spect
PROBHD    5 mm QNP  1H/1
PULPROG          hsqcedetgp
TD                   1024
SOLVENT              CDCl3
NS                      2
DS                     16
SWH              5000.000 Hz
FIDRES           4.882813 Hz
AQ               0.1025500 sec
RG                   49152
DW                 100.000 usec
DE                   6.00 usec
TE                  683.2 K
CNST2              145.0000000
d0               0.00000300 sec
D1               2.00000000 sec
d4               0.00172414 sec
d11              0.03000000 sec
d13              0.00000400 sec
D16              0.00020000 sec
D21              0.00344830 sec
DELTA            0.00222270 sec
DELTA1           0.00071614 sec
IN0              0.00002565 sec
ST1CNT                  0
ZGOPTNS

======== CHANNEL f1 ========
NUC1                   1H
P1                   9.80 usec
p2                  19.60 usec
P28                1000.00 usec
PL1                  0.00 dB
SFO1          499.8767493 MHz

======== CHANNEL f2 ========
CPDPRG2               garp
NUC2                  13C
P3                   4.30 usec
p4                   8.60 usec
PCPD2               60.00 usec
PL2                 10.00 dB
PL12                40.00 dB
SFO2          125.7037867 MHz

====== GRADIENT CHANNEL =====
GPNAM1            SINE.100
GPNAM2            SINE.100
GPZ1                80.00 %
GPZ2                20.10 %
P16               1000.00 usec
ND0                     2
TD                    256
SFO1          125.7038 MHz
FIDRES         76.145226 Hz
SW             155.072 ppm
FnMODE    Echo-Antiecho
SI                   1024
SF            499.8740059 MHz
WDW                 QSINE
```

HSQC

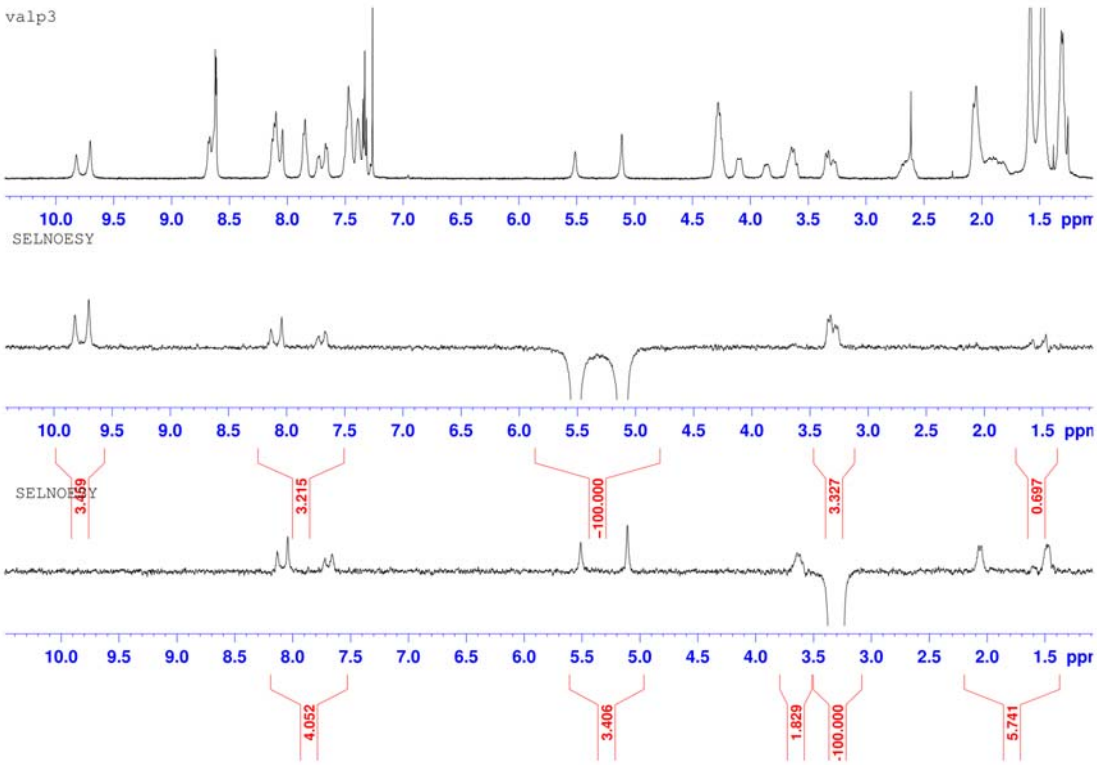



```
NAME          valp3
EXPNO             2
PROCNO            1
Date_      20190308
Time          21.25
INSTRUM        spect
PROBHD  5 mm QNP 1H/1
PULPROG     hsqcedetgp
TD              1024
SOLVENT         CDCl3
NS                2
DS               16
SWH         5000.000 Hz
FIDRES      4.882813 Hz
AQ          0.1025500 sec
RG              49152
DW          100.000 usec
DE            6.00 usec
TE            683.2 K
CNST2       145.0000000
d0          0.00000300 sec
D1          2.00000000 sec
d4          0.00172414 sec
d11         0.03000000 sec
d13         0.00000400 sec
D16         0.00020000 sec
D21         0.00344830 sec
DELTA       0.00222270 sec
DELTA1      0.00071614 sec
IN0         0.00002565 sec
ST1CNT             0
ZGOPTNS

======== CHANNEL f1 ========
NUC1              1H
P1             9.80 usec
p2            19.60 usec
P28         1000.00 usec
PL1            0.00 dB
SFO1    499.8767493 MHz

======== CHANNEL f2 ========
CPDPRG2         garp
NUC2              13C
P3             4.30 usec
p4             8.60 usec
PCPD2         60.00 usec
PL2           10.00 dB
PL12          40.00 dB
SFO2    125.7037867 MHz

====== GRADIENT CHANNEL =====
GPNAM1       SINE.100
GPNAM2       SINE.100
GPZ1          80.00 %
GPZ2          20.10 %
P16         1000.00 usec
ND0               2
TD              256
SFO1    125.7038 MHz
FIDRES     76.145226 Hz
SW         155.072 ppm
FnMODE   Echo-Antiecho
SI              1024
SF      499.8740059 MHz
WDW           QSINE
```

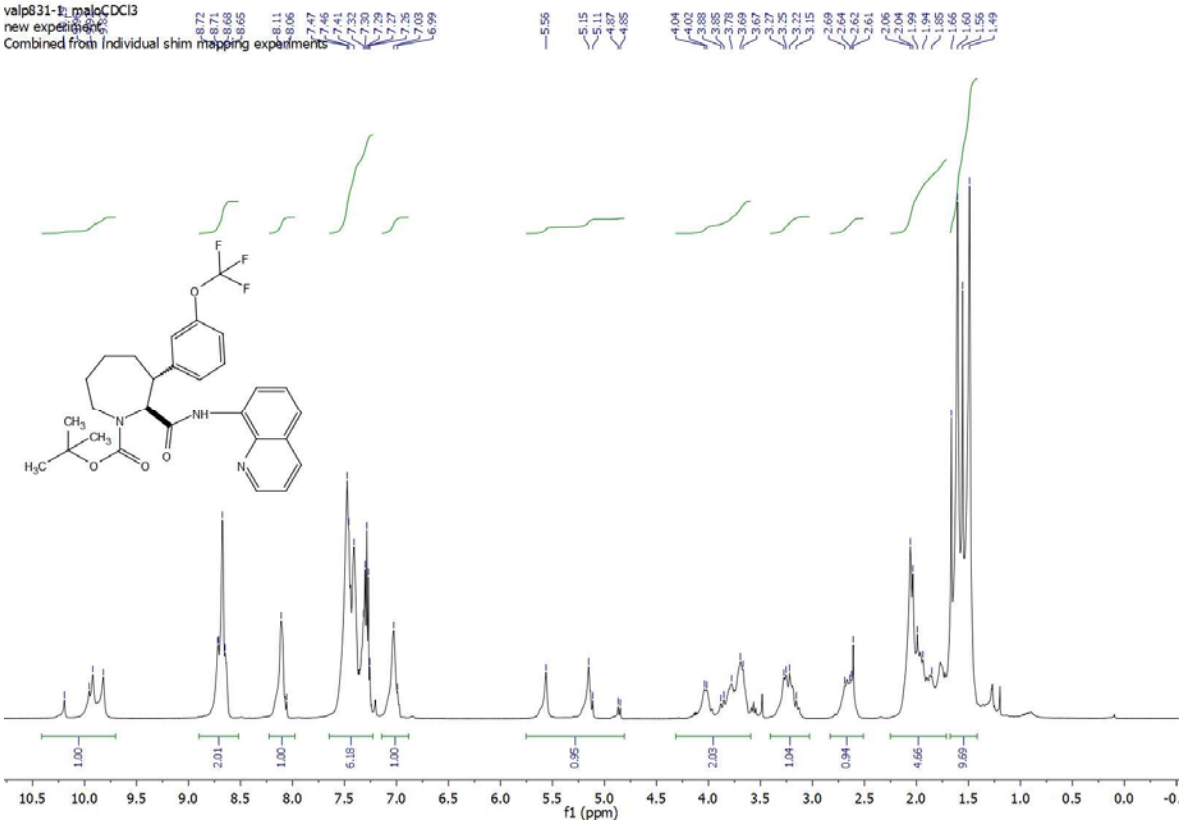
NOESY

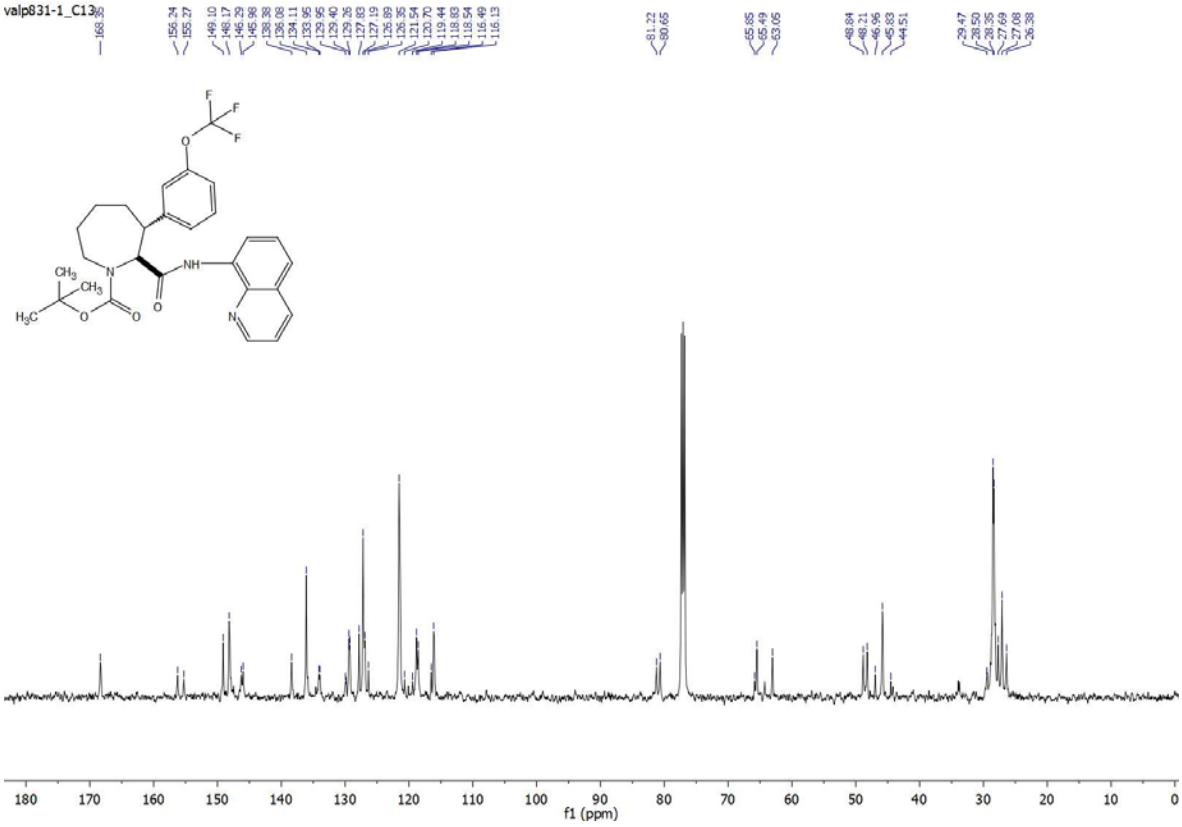


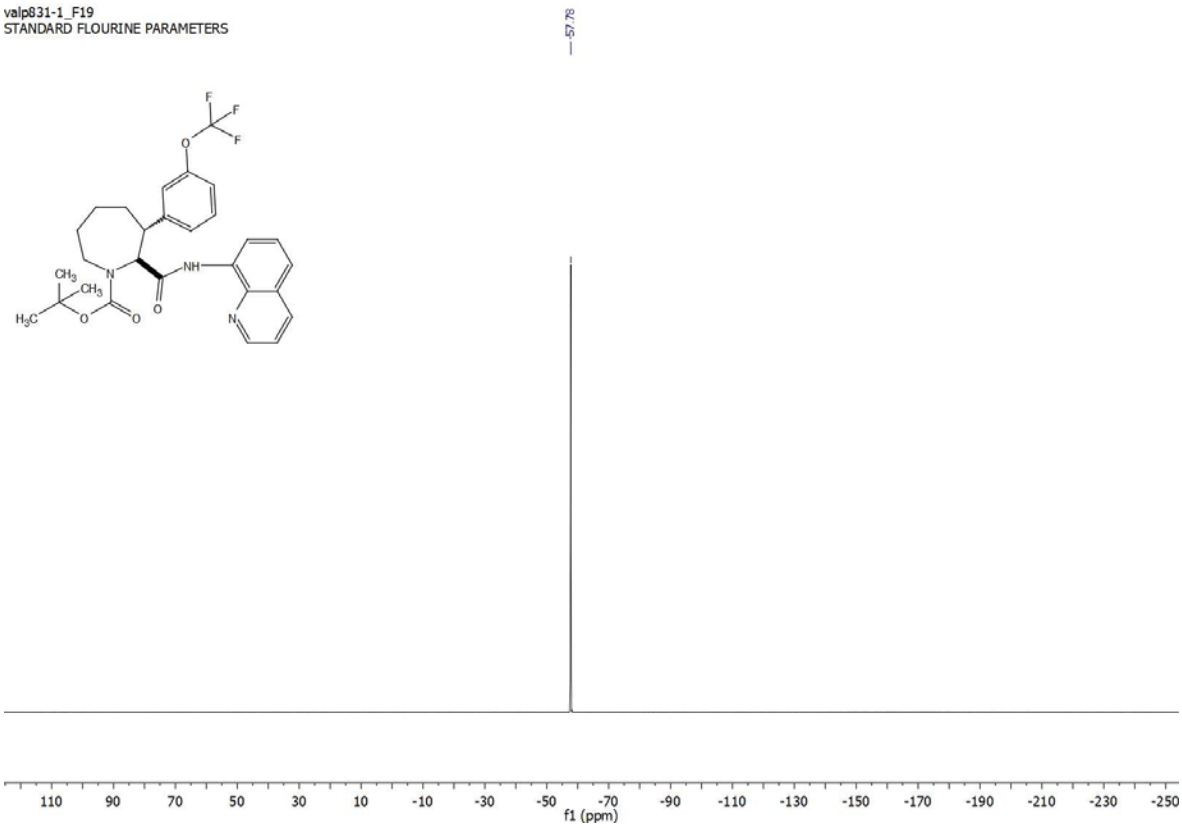

```
NAME                  valp3
EXPNO                     6
PROCNO                    1
Date_              20190308
Time                  22.33
INSTRUM                spect
PROBHD  5 mm QNP  1H/1
PULPROG      noesygpphzs
TD                     2048
SOLVENT             CDCl3
NS                       48
DS                       16
SWH                5000.000 Hz
FIDRES                2.441406 Hz
AQ                0.2049500 sec
RG                     101.6
DW                   100.000 usec
DE                      6.00 usec
TE                     683.2 K
d0                0.00008755 sec
D1                2.00000000 sec
D8                0.50000000 sec
D16               0.00020000 sec
IN0               0.00020005 sec
ST1CNT                    0
TAU               0.47471601 sec

======== CHANNEL f1 ========
NUC1                     1H
P1                     9.80 usec
P32                20000.00 usec
PL1                    0.00 dB
SFO1          499.8767493 MHz
SP29                  28.00 dB
SPNAM29   Crp(40,20,20.10)
SPOAL29                0.500
SPOFFS29               0.00 Hz

====== GRADIENT CHANNEL =====
GPNAM1               SINE.100
GPZ0                    10.00 %
GPZ1                    40.00 %
P31                   5000.00 usec
ND0                        1
TD                       128
SFO1                499.8767 MHz
FIDRES             39.052738 Hz
SW                    10.000 ppm
FnMODE          States-TPPI
SI                       2048
SF                499.8740069 MHz
WDW                    QSINE
SSB                        2
LB                      0.00 Hz
GB                         0
PC                      1.40
SI                       2048
MC2             States-TPPI
SF                499.8740069 MHz
WDW                    QSINE
SSB                        2
LB                      0.00 Hz
GB                         0
```


valp3
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 ppm
SELNOESY
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 ppm
SELNOESY
3.459
3.215
-100.000
3.327
0.697
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 ppm
4.052
3.406
1.829
-100.000
5.741

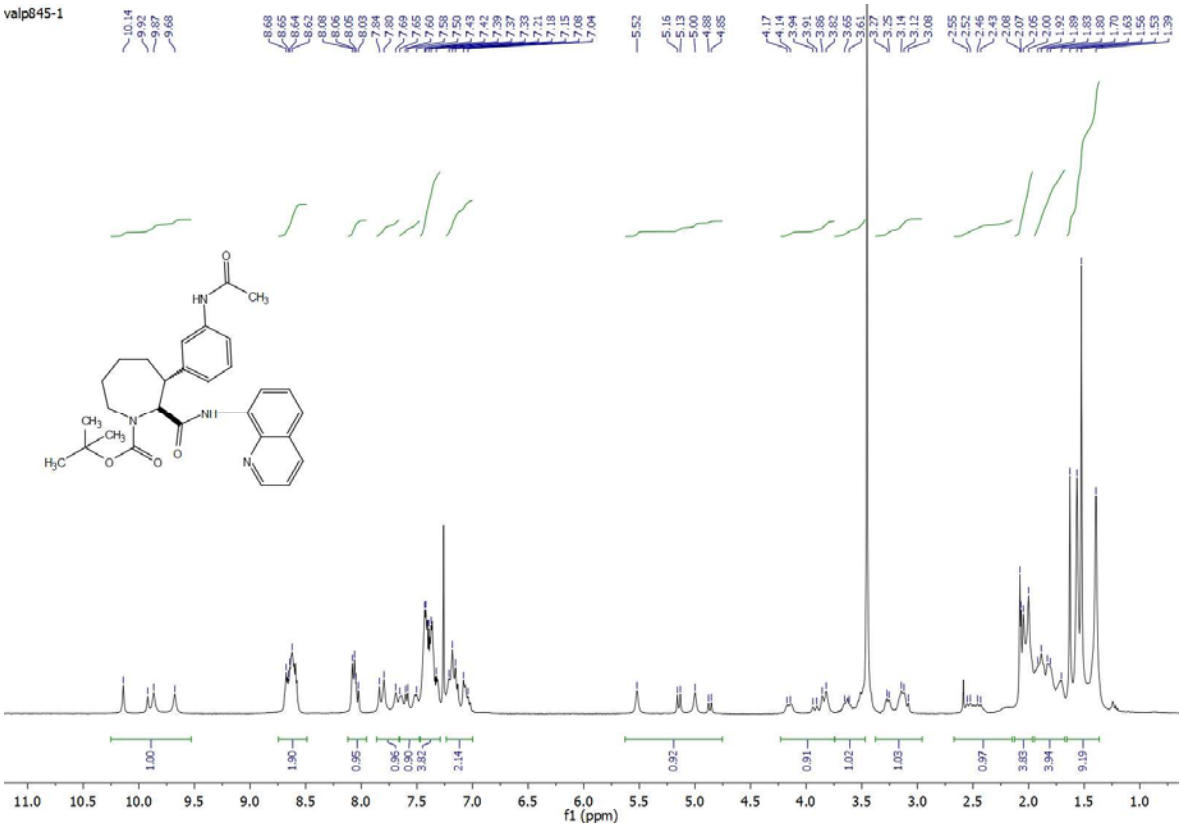
Compound Boc – 36a

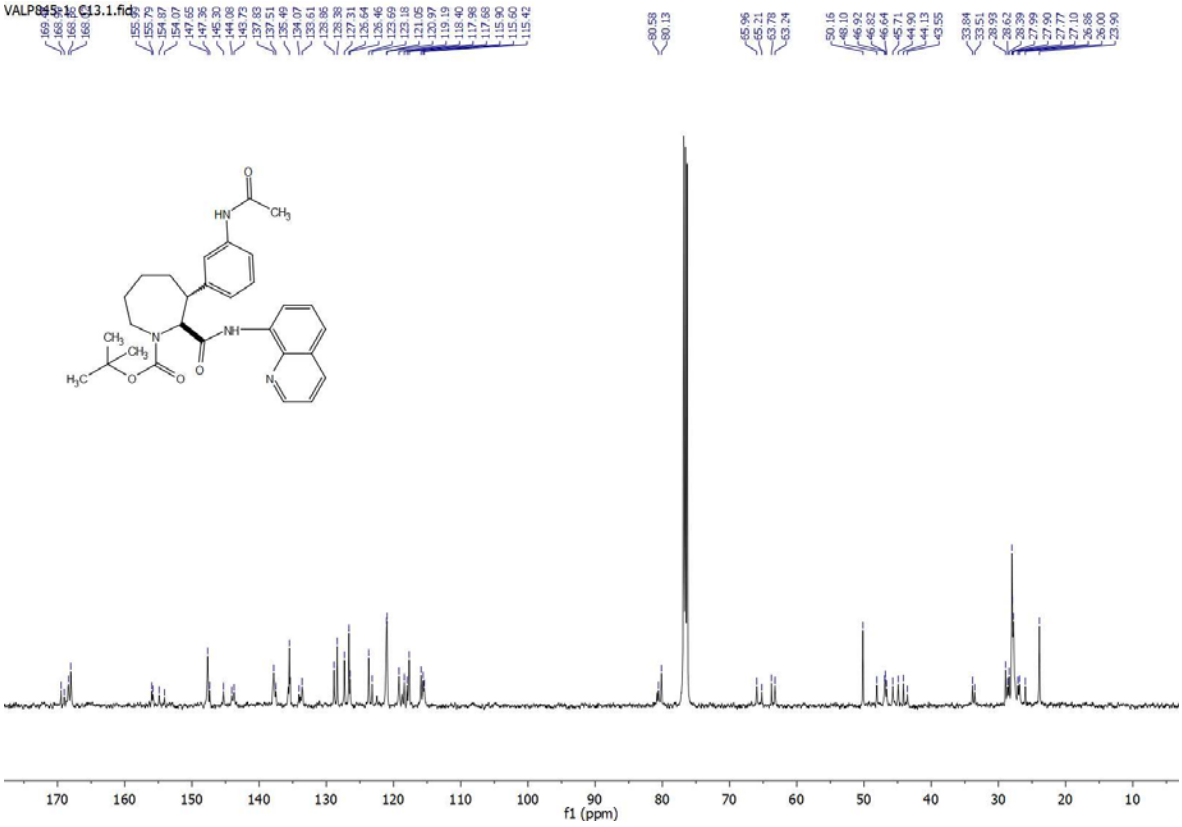


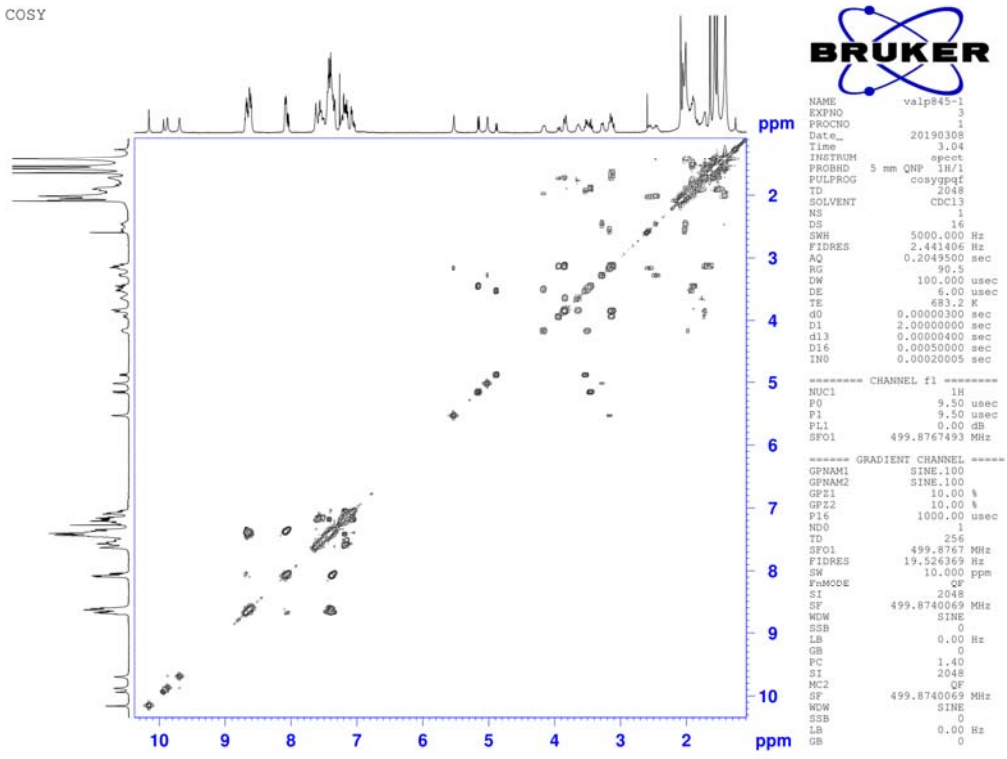



valp831-1_F19
STANDARD FLOURINE PARAMETERS
-57.78
F
F
F
O
N
NH
O
CH3
CH3
H3C
O
O
N
110
90
70
50
30
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
-230
-250
f1 (ppm)

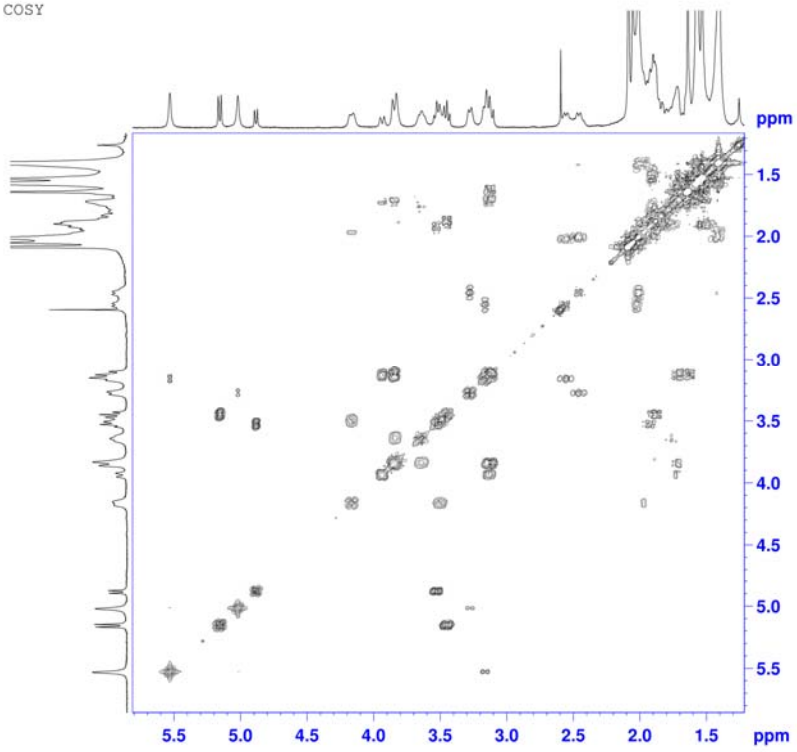
Compound Boc – 37a






COSY
ppm
10 9 8 7 6 5 4 3 2 ppm
BRUKER
NAME valp845-1
EXPNO 3
PROCNO 1
Date_ 20190308
Time 3.04
INSTRUM spect
PROBHD 5 mm QNP 1H/1
PULPROG cosygpqf
TD 2048
SOLVENT CDCl3
NS 1
DS 16
SWH 5000.000 Hz
FIDRES 2.441406 Hz
AQ 0.2049500 sec
RG 90.5
DW 100.000 usec
DE 6.00 usec
TE 683.2 K
d0 0.00000300 sec
D1 2.00000000 sec
d13 0.00000400 sec
D16 0.00050000 sec
IN0 0.00020005 sec
======== CHANNEL f1 ========
NUC1 1H
P0 9.50 usec
P1 9.50 usec
PL1 0.00 dB
SFO1 499.8767493 MHz
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPZ1 10.00 %
GPZ2 10.00 %
P16 1000.00 usec
ND0 1
TD 256
SFO1 499.8767 MHz
FIDRES 19.526369 Hz
SW 10.000 ppm
FnMODE QF
SI 2048
SF 499.8740069 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0
PC 1.40
SI 2048
MC2 QF
SF 499.8740069 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0

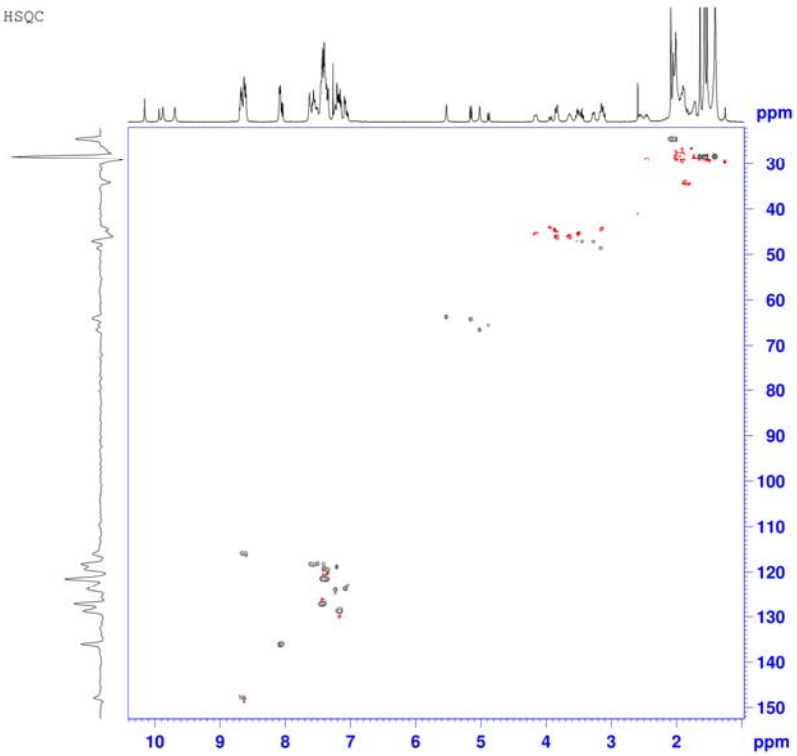
COSY



BRUKER

```
NAME                valp845-1
EXPNO                       3
PROCNO                      1
Date_                20190308
Time                     3.04
INSTRUM                 spect
PROBHD    5 mm QNP  1H/1
PULPROG          cosygpqf
TD                       2048
SOLVENT                 CDCl3
NS                          1
DS                         16
SWH                5000.000 Hz
FIDRES             2.441406 Hz
AQ                 0.2049500 sec
RG                      90.5
DW                  100.000 usec
DE                    6.00 usec
TE                    683.2 K
d0                 0.00000300 sec
D1                 2.00000000 sec
d13                0.00000400 sec
D16                0.00050000 sec
IN0                0.00020005 sec

======== CHANNEL f1 ========
NUC1                       1H
P0                      9.50 usec
P1                      9.50 usec
PL1                     0.00 dB
SFO1             499.8767493 MHz

====== GRADIENT CHANNEL =====
GPNAM1                SINE.100
GPNAM2                SINE.100
GPZ1                     10.00 %
GPZ2                     10.00 %
P16                    1000.00 usec
ND0                         1
TD                        256
SFO1             499.8767 MHz
FIDRES           19.526369 Hz
SW                    10.000 ppm
FnMODE                    QF
SI                        2048
SF               499.8740069 MHz
WDW                     SINE
SSB                        0
LB                      0.00 Hz
GB                         0
PC                      1.40
SI                        2048
MC2                       QF
SF               499.8740069 MHz
WDW                     SINE
SSB                        0
LB                      0.00 Hz
GB                         0
```

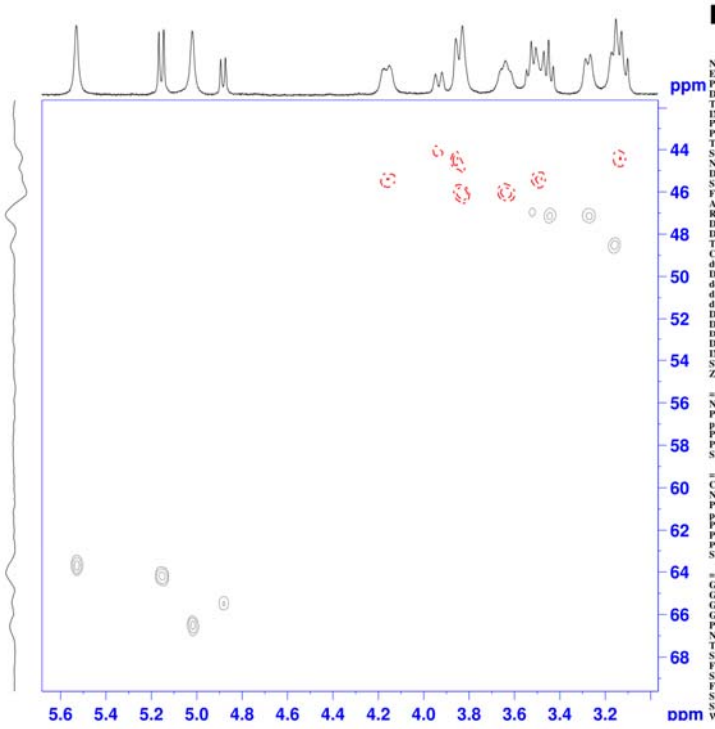
HSQC



BRUKER

```
NAME          valp845-1
EXPNO                 2
PROCNO                1
Date_          20190311
Time              11.41
INSTRUM           spect
PROBHD  5 mm QNP 1H/1
PULPROG       hsqcedetgp
TD                 1024
SOLVENT           CDCl3
NS                    2
DS                   16
SWH           5000.000 Hz
FIDRES        4.882813 Hz
AQ            0.1025500 sec
RG                49152
DW            100.000 usec
DE              6.00 usec
TE              683.2 K
CNST2         145.0000000
d0            0.00000300 sec
D1            2.00000000 sec
d4            0.00172414 sec
d11           0.03000000 sec
d13           0.00000400 sec
D16           0.00020000 sec
D21           0.00344830 sec
DELTA         0.00222270 sec
DELTA1        0.00071614 sec
IN0           0.00002485 sec
ST1CNT                0
ZGOPTNS

======== CHANNEL f1 ========
NUC1                 1H
P1                9.80 usec
p2               19.60 usec
P28            1000.00 usec
PL1               0.00 dB
SFO1       499.8767493 MHz

======== CHANNEL f2 ========
CPDPRG2           garp
NUC2                13C
P3               4.30 usec
p4               8.60 usec
PCPD2           60.00 usec
PL2              10.00 dB
PL12             40.00 dB
SFO2       125.7034725 MHz

====== GRADIENT CHANNEL =====
GPNAM1          SINE.100
GPNAM2          SINE.100
GPZ1               80.00 %
GPZ2               20.10 %
P16             1000.00 usec
ND0                    2
TD                   256
SFO1       125.7035 MHz
FIDRES     78.596581 Hz
SW             160.065 ppm
FnMODE    Echo-Antiecho
SI                  1024
SF         499.8740059 MHz
WDW               QSINE
```

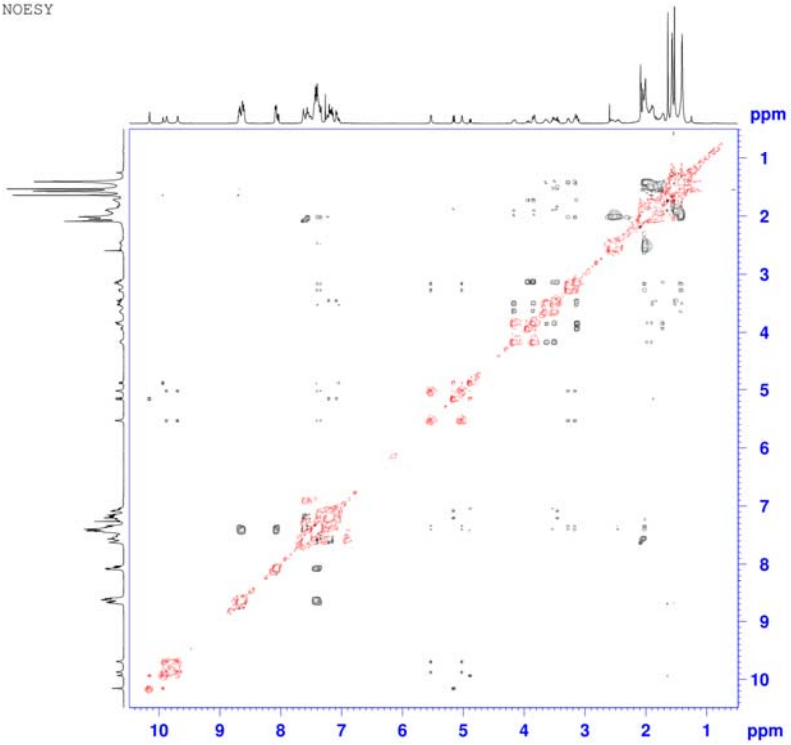
HSQC



BRUKER

NAME	valp845-1
EXPNO	2
PROCNO	1
Date_	20190311
Time	11.41
INSTRUM	spect
PROBHD	5 mm QNP 1H/1
PULPROG	hsqcedetgp
TD	1024
SOLVENT	CDCl3
NS	2
DS	16
SWH	5000.000 Hz
FIDRES	4.882813 Hz
AQ	0.1025500 sec
RG	49152
DW	100.000 usec
DE	6.00 usec
TE	683.2 K
CNST2	145.0000000
d0	0.00000300 sec
D1	2.00000000 sec
d4	0.00172414 sec
d11	0.03000000 sec
d13	0.00000400 sec
D16	0.00020000 sec
D21	0.00344830 sec
DELTA	0.00222270 sec
DELTA1	0.00071614 sec
IN0	0.00002485 sec
ST1CNT	0
ZGOPTNS	
======== CHANNEL f1 ========	
NUC1	1H
P1	9.80 usec
p2	19.60 usec
P28	1000.00 usec
PL1	0.00 dB
SFO1	499.8767493 MHz
======== CHANNEL f2 ========	
CPDPRG2	garp
NUC2	13C
P3	4.30 usec
p4	8.60 usec
PCPD2	60.00 usec
PL2	10.00 dB
PL12	40.00 dB
SFO2	125.7034725 MHz
====== GRADIENT CHANNEL =====	
GPNAM1	SINE.100
GPNAM2	SINE.100
GPZ1	80.00 %
GPZ2	20.10 %
P16	1000.00 usec
ND0	2
TD	256
SFO1	125.7035 MHz
FIDRES	78.596581 Hz
SW	160.065 ppm
FnMODE	Echo-Antiecho
SI	1024
SF	499.8740059 MHz
WDW	QSINE

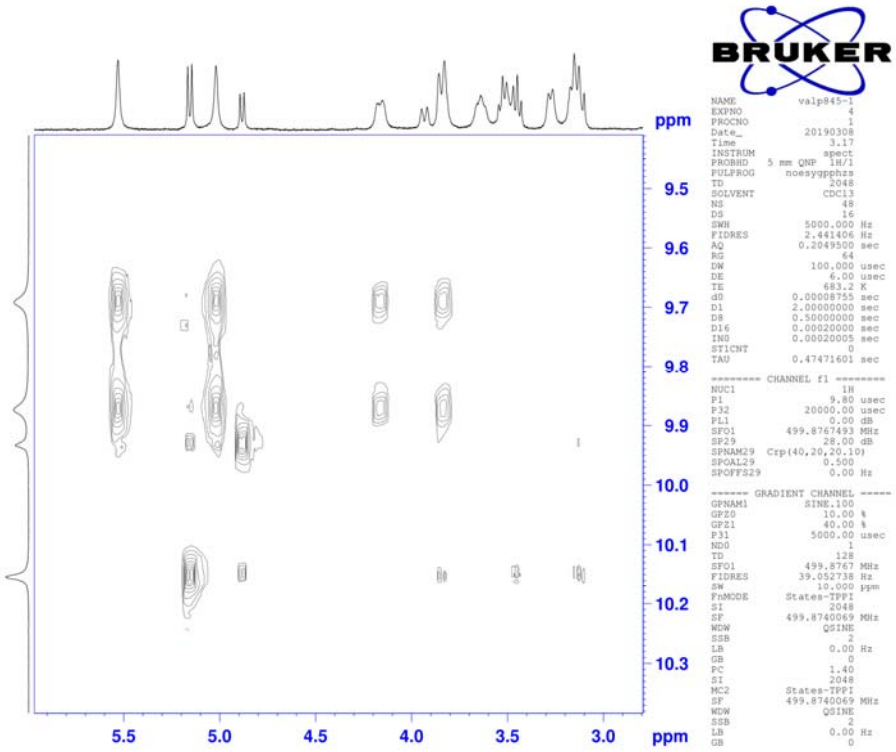
NOESY



BRUKER

NAME	valp845-1
EXPNO	4
PROCNO	1
Date_	20190308
Time	3.17
INSTRUM	spect
PROBHD	5 mm QNP 1H/1
PULPROG	noesygpphzs
TD	2048
SOLVENT	CDCl3
NS	48
DS	16
SWH	5000.000 Hz
FIDRES	2.441406 Hz
AQ	0.2049500 sec
RG	64
DW	100.000 usec
DE	6.00 usec
TE	683.2 K
d0	0.00008755 sec
D1	2.00000000 sec
D8	0.50000000 sec
D16	0.00020000 sec
IN0	0.00020005 sec
ST1CNT	0
TAU	0.47471601 sec
======== CHANNEL f1 ========	
NUC1	1H
P1	9.80 usec
P32	20000.00 usec
PL1	0.00 dB
SFO1	499.8767493 MHz
SP29	28.00 dB
SPNAM29	Crp(40,20,20.10)
SPOAL29	0.500
SPOFFS29	0.00 Hz
====== GRADIENT CHANNEL =====	
GPNAM1	SINE.100
GPZ0	10.00 %
GPZ1	40.00 %
P31	5000.00 usec
ND0	1
TD	128
SFO1	499.8767 MHz
FIDRES	39.052738 Hz
SW	10.000 ppm
FnMODE	States-TPPI
SI	2048
SF	499.8740069 MHz
WDW	QSINE
SSB	2
LB	0.00 Hz
GB	0
PC	1.40
SI	2048
MC2	States-TPPI
SF	499.8740069 MHz
WDW	QSINE
SSB	2
LB	0.00 Hz
GB	0

NOESY

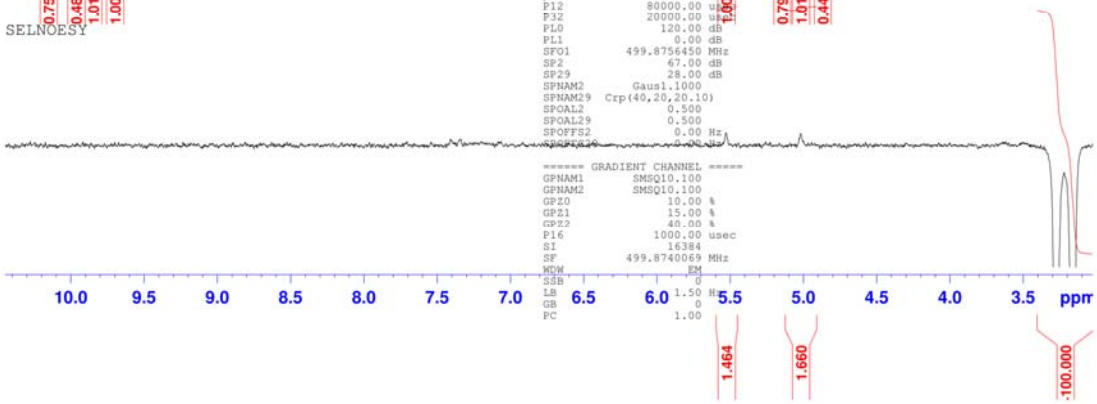



```
NAME                valp845-1
EXPNO                       4
PROCNO                      1
Date_                20190308
Time                     3.17
INSTRUM                 spect
PROBHD     5 mm QNP  1H/1
PULPROG          noesygpphzs
TD                       2048
SOLVENT                 CDCl3
NS                         48
DS                         16
SWH                5000.000 Hz
FIDRES             2.441406 Hz
AQ                 0.2049500 sec
RG                        64
DW                  100.000 usec
DE                    6.00 usec
TE                   683.2 K
d0                 0.00008755 sec
D1                 2.00000000 sec
D8                 0.50000000 sec
D16                0.00020000 sec
IN0                0.00020005 sec
ST1CNT                     0
TAU                0.47471601 sec

======== CHANNEL f1 ========
NUC1                       1H
P1                       9.80 usec
P32                  20000.00 usec
PL1                      0.00 dB
SFO1               499.8767493 MHz
SP29                    28.00 dB
SPNAM29   Crp(40,20,20.10)
SPOAL29                 0.500
SPOFFS29                0.00 Hz

====== GRADIENT CHANNEL =====
GPNAM1               SINE.100
GPZ0                    10.00 %
GPZ1                    40.00 %
P31                   5000.00 usec
ND0                        1
TD                       128
SFO1               499.8767 MHz
FIDRES              39.052738 Hz
SW                     10.000 ppm
FnMODE          States-TPPI
SI                       2048
SF                 499.8740069 MHz
WDW                      QSINE
SSB                        2
LB                      0.00 Hz
GB                         0
PC                      1.40
SI                       2048
MC2             States-TPPI
SF                 499.8740069 MHz
WDW                      QSINE
SSB                        2
LB                      0.00 Hz
GB                         0
```

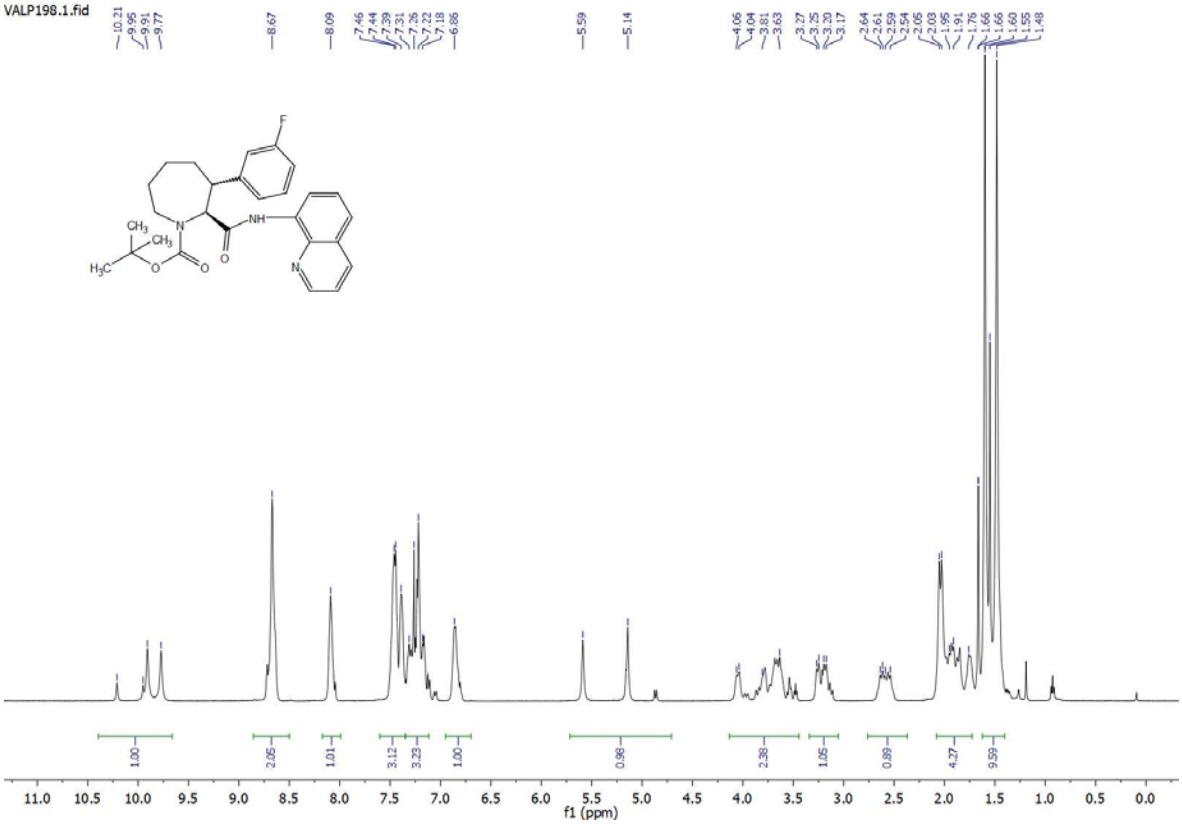
valp845-1

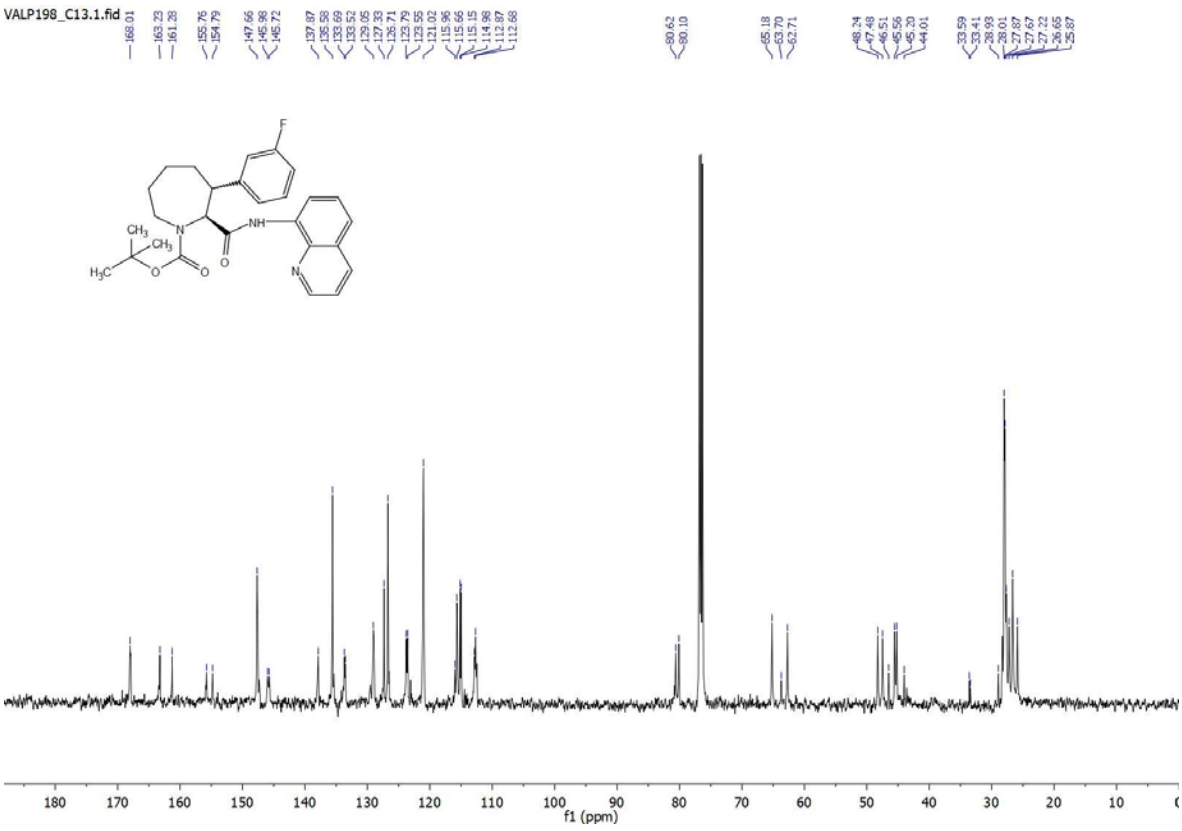

```
NAME                valp845-1
EXPNO                       5
PROCNO                      1
Date_                20190311
Time                    12.05
INSTRUM                 spect
PROBHD     5 mm QNP  1H/1
PULPROG          selnogpzs
TD                      32768
SOLVENT                 CDCl3
NS                        128
DS                          4
SWH                10000.000 Hz
FIDRES             0.305176 Hz
AQ                 1.6385000 sec
RG                      645.1
DW                   50.000 usec
DE                    6.00 usec
TE                   683.2 K
D1                 2.00000000 sec
D8                 0.50000000 sec
D16                0.00020000 sec
DELTA1             0.24879999 sec
DELTA2             0.22856601 sec
ID0                        1

======== CHANNEL f1 ========
NUC1                       1H
P1                       9.80 usec
p2                      19.60 us
P12                  80000.00 us
P32                  20000.00 us
PL0                    120.00 dB
PL1                      0.00 dB
SFO1               499.8756450 MHz
SP2                     67.00 dB
SP29                    28.00 dB
SPNAM2               Gaus1.1000
SPNAM29   Crp(40,20,20.10)
SPOAL2                  0.500
SPOAL29                 0.500
SPOFFS2                 0.00 Hz
SPOFFS29                0.00 Hz

====== GRADIENT CHANNEL =====
GPNAM1              SMSQ10.100
GPNAM2              SMSQ10.100
GPZ0                    10.00 %
GPZ1                    15.00 %
GPZ2                    40.00 %
P16                   1000.00 usec
SI                       16384
SF                 499.8740069 MHz
WDW                        EM
SSB                        0
LB                      1.50 Hz
GB                         0
PC                      1.00
```

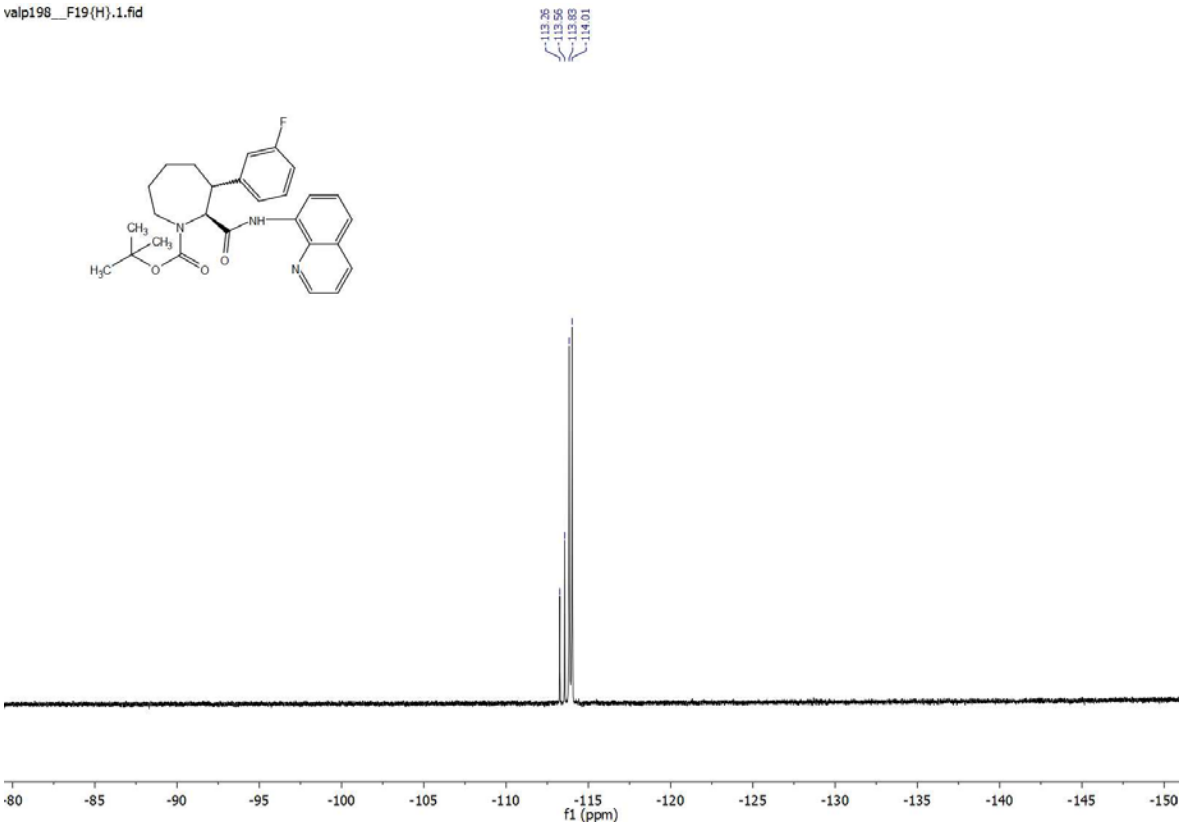
SELNOESY



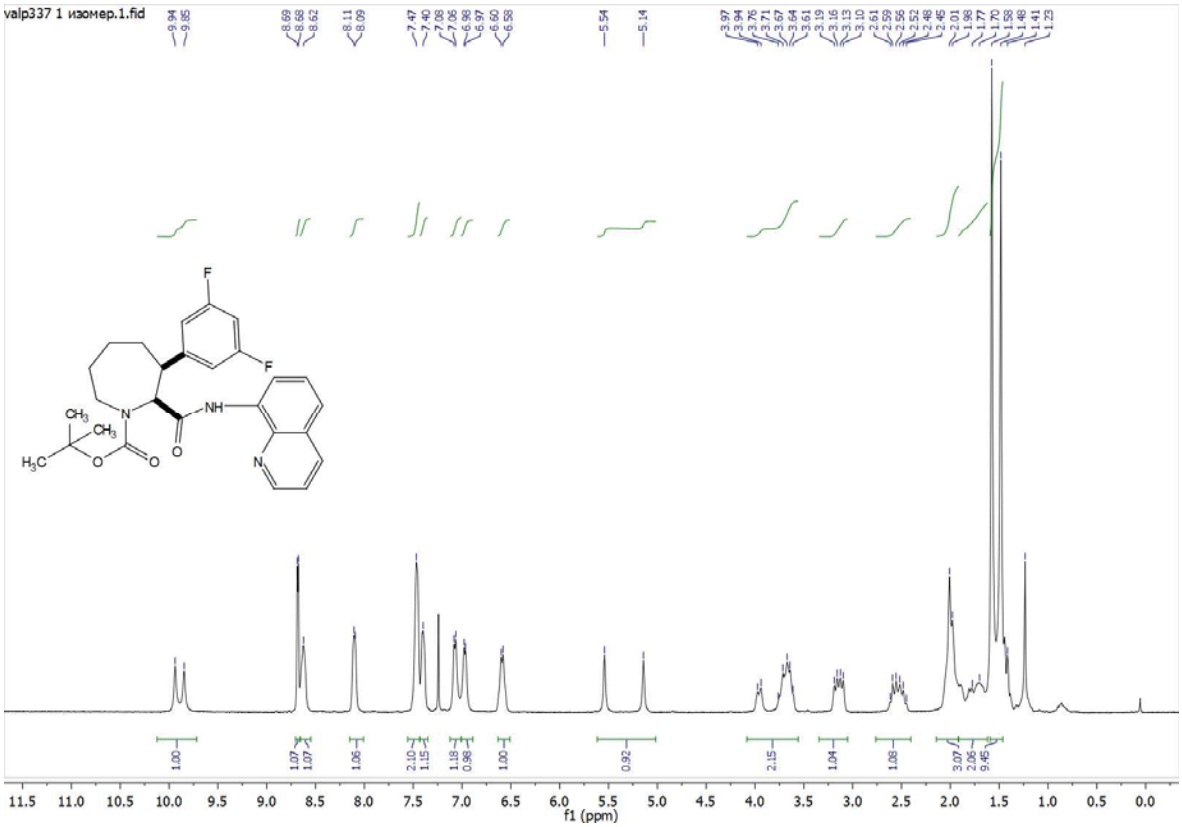
Compound Boc – 38a

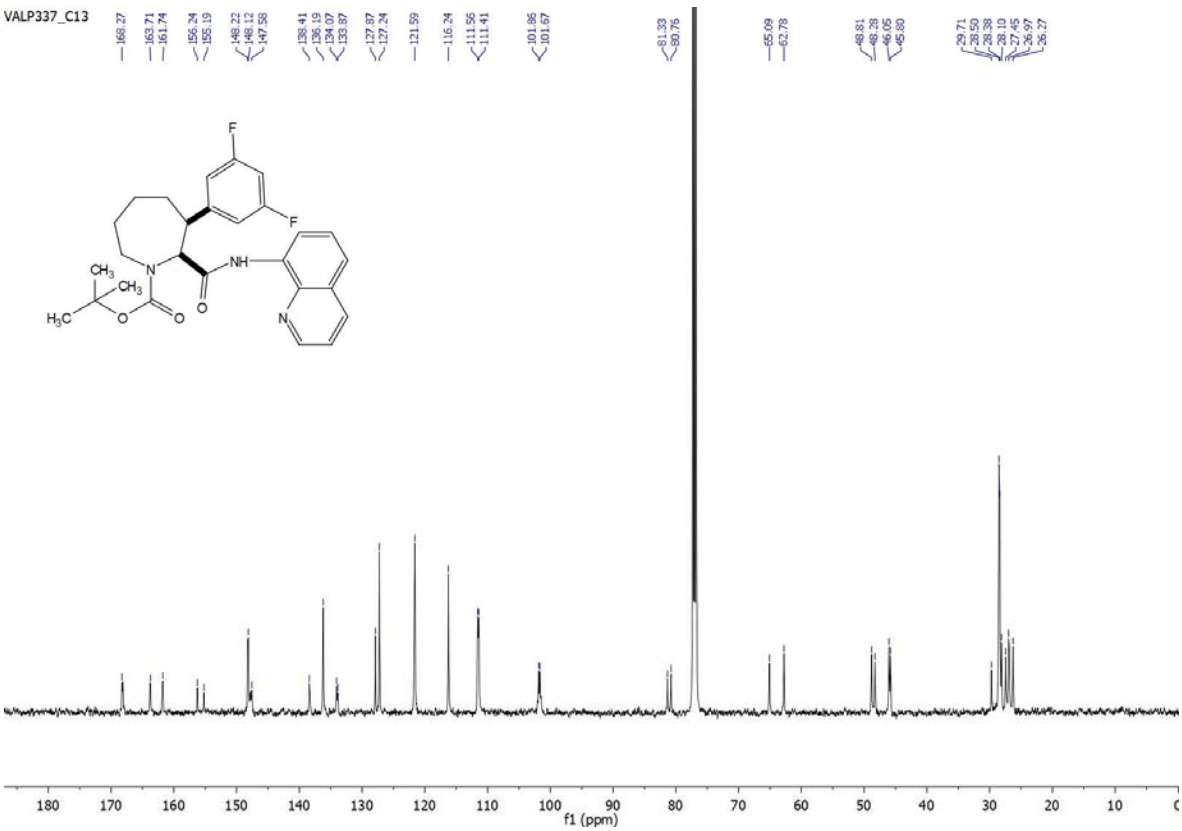





valp198__F19{H}.1.fid
-113.26
-113.56
-113.83
-114.01
F
N
NH
O
O
O
N
CH3
CH3
H3C
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
-150
f1 (ppm)

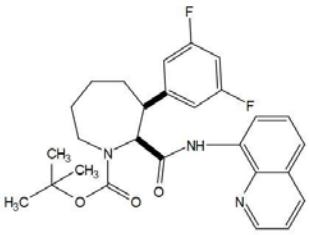
Compound – 39a



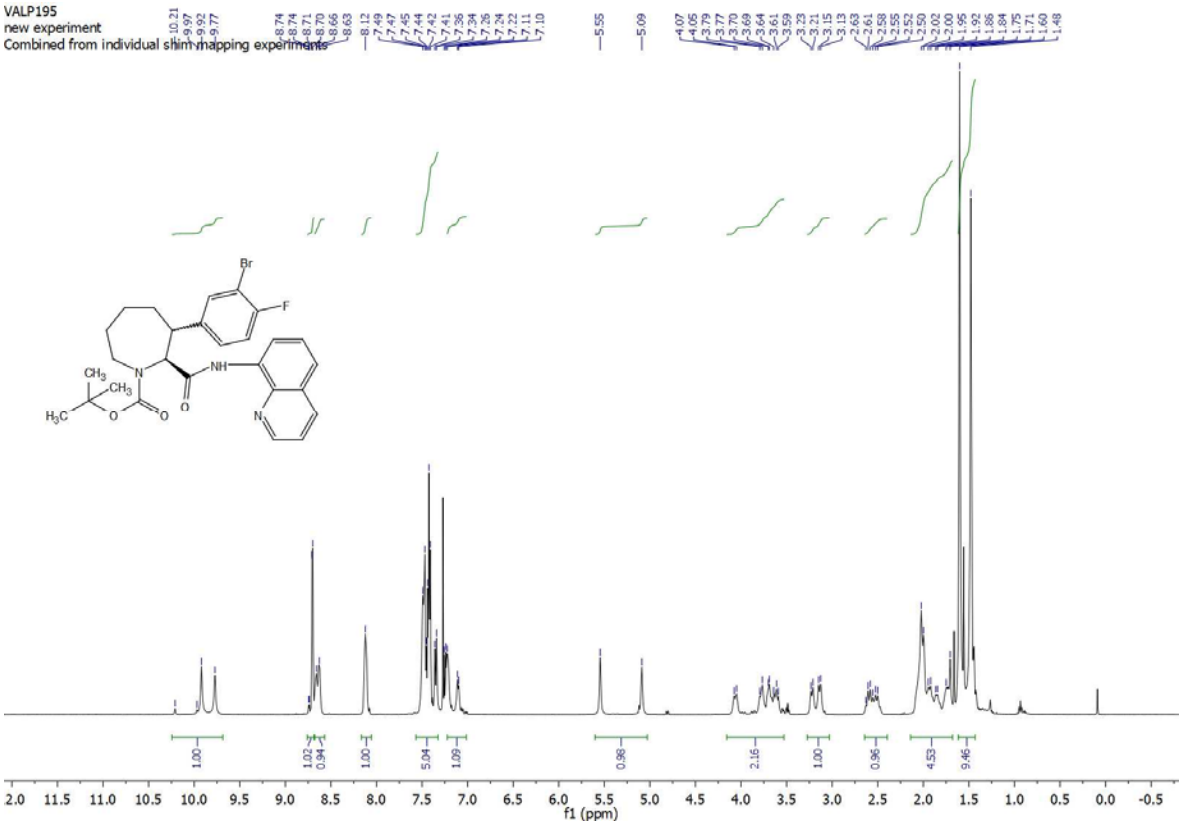


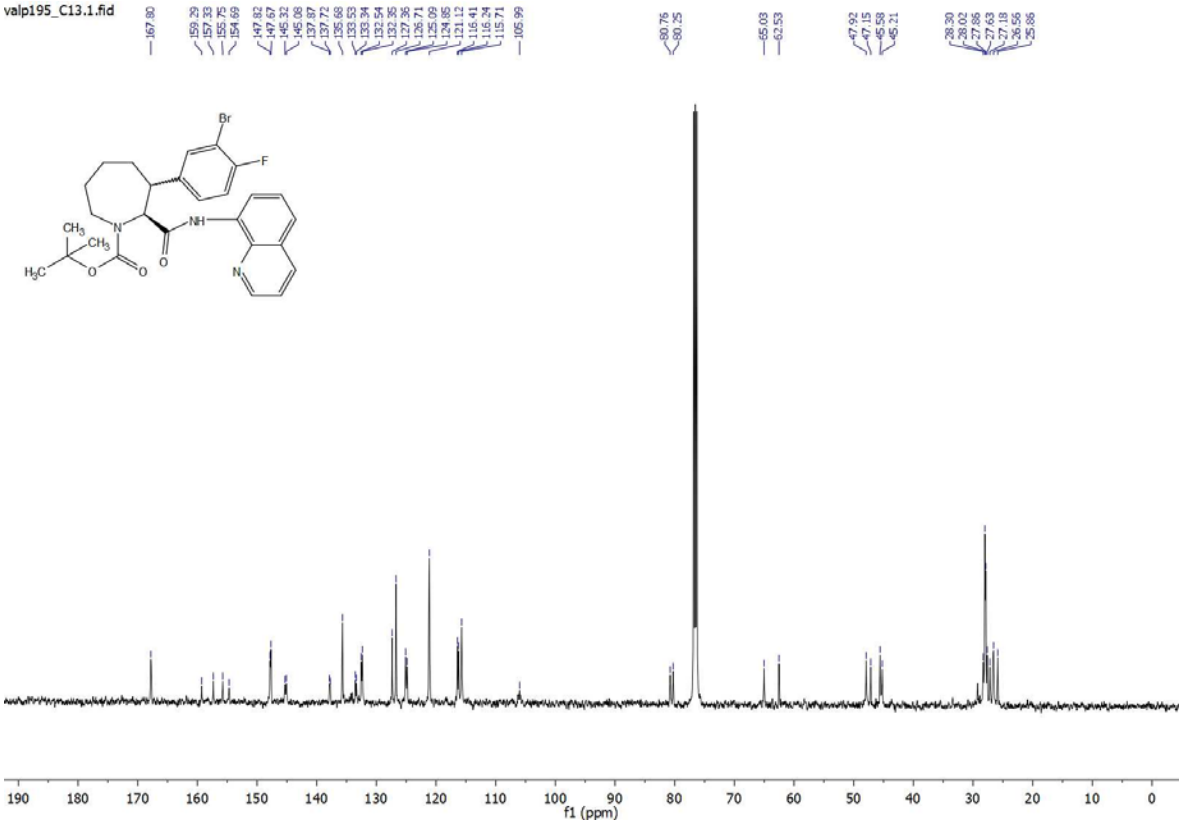
valp337_F19(H),1.fid

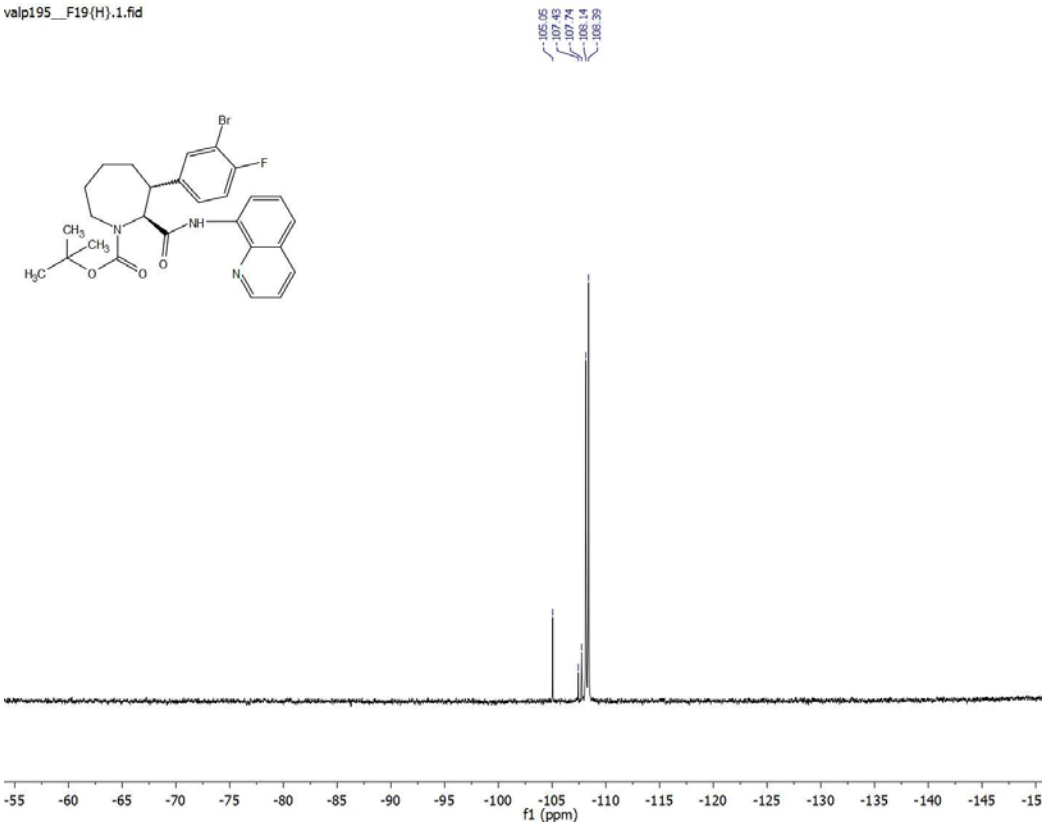
^{19}F NMR (376 MHz, Chloroform-*d*) δ -110.89, -111.14.



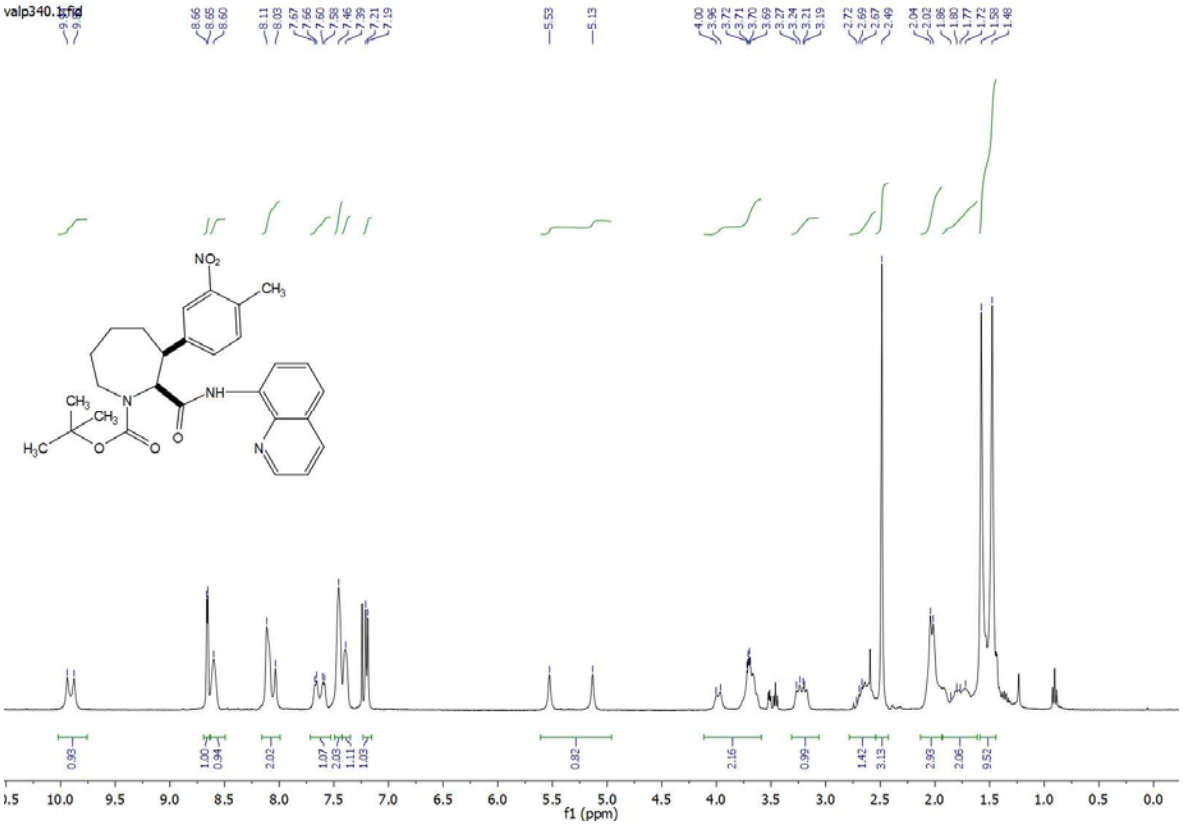
Compound Boc – 40a

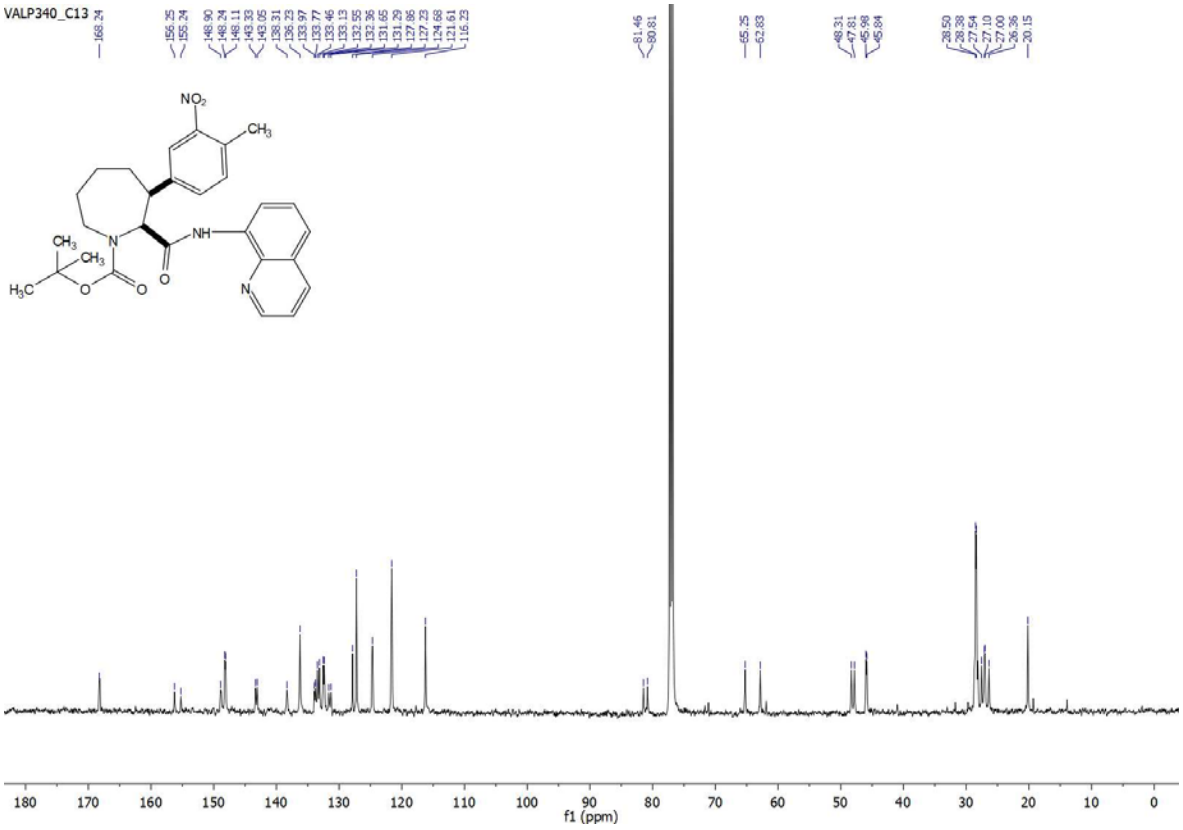




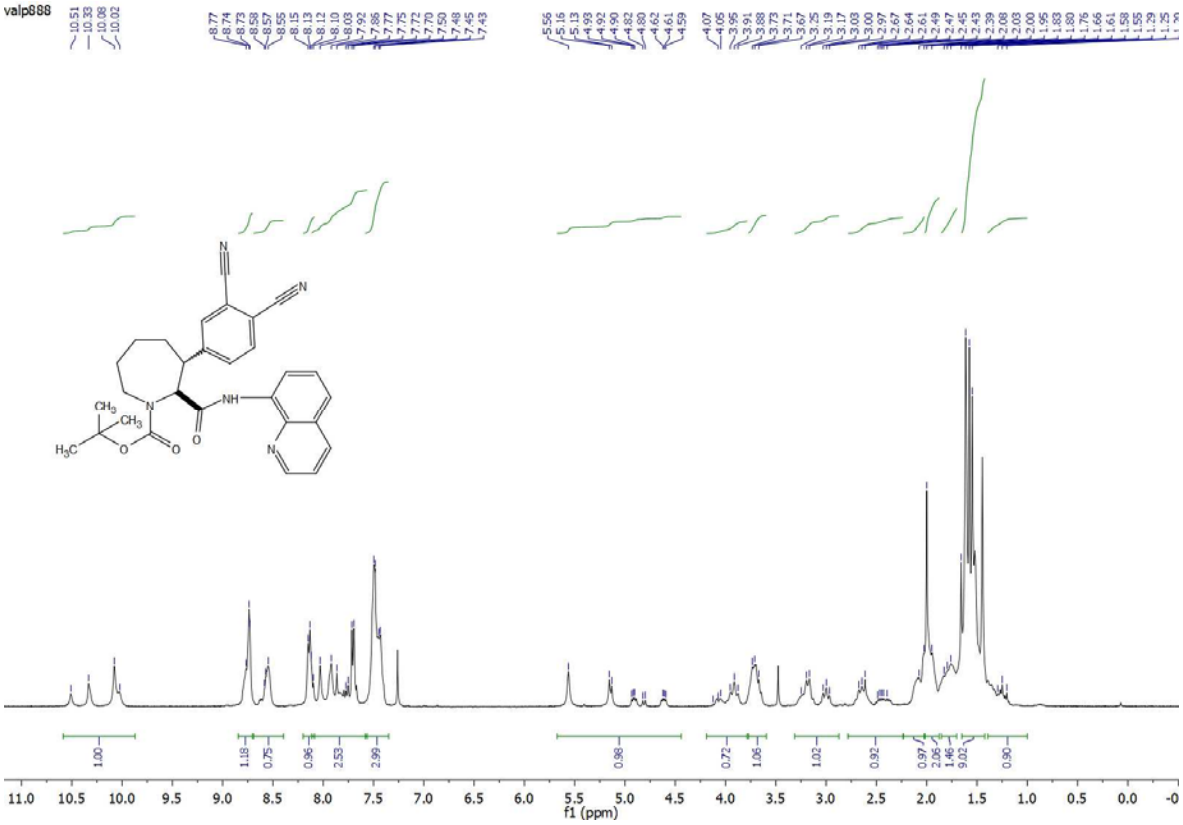

valp195__F19{H}.1.fid
-105.05
-107.43
-107.74
-108.14
-108.39
Br
F
NH
N
O
O
O
CH3
CH3
H3C
-55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -15
f1 (ppm)

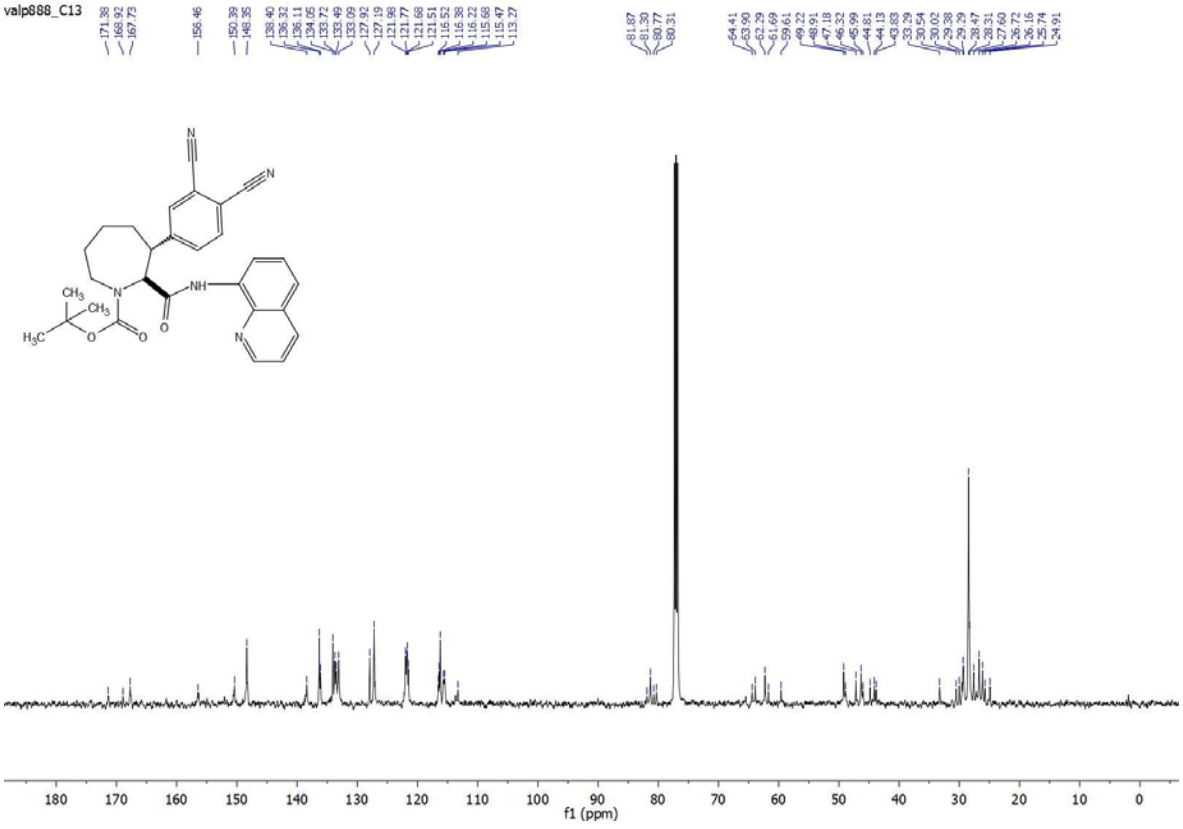
Compound Boc – 41a



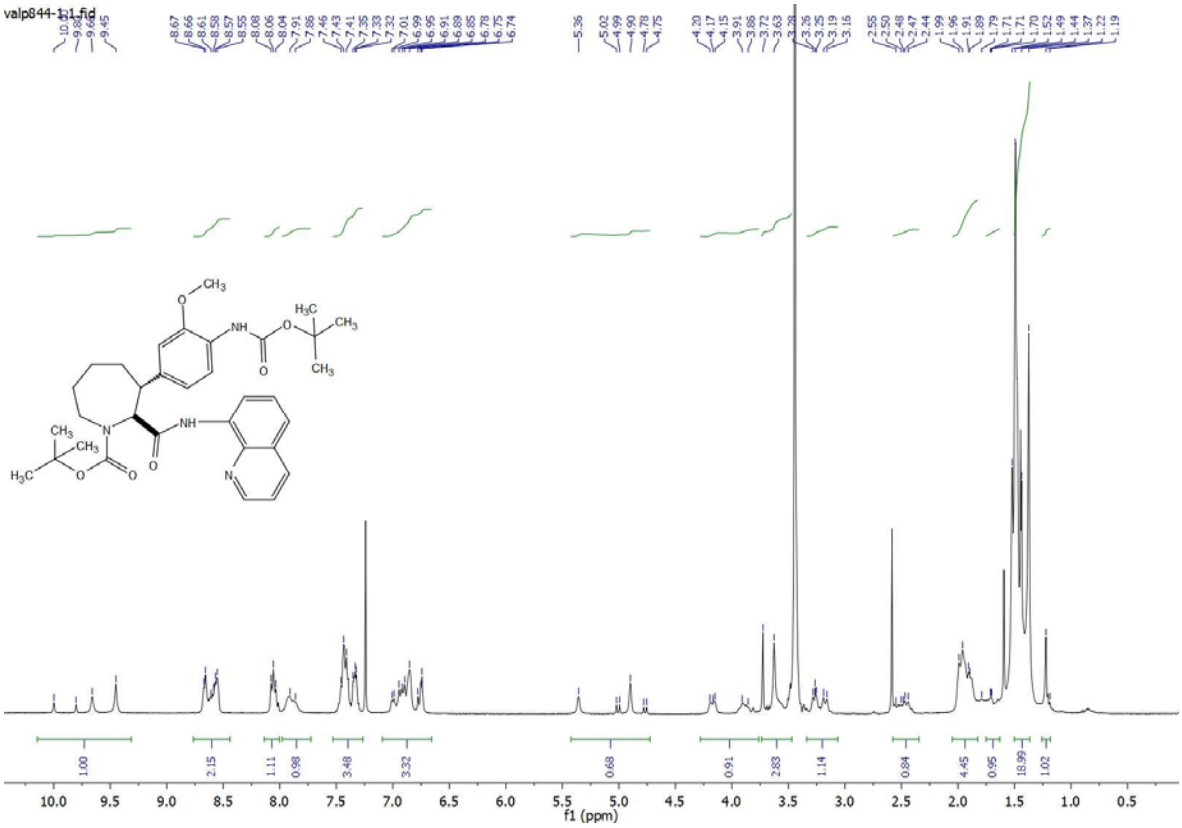


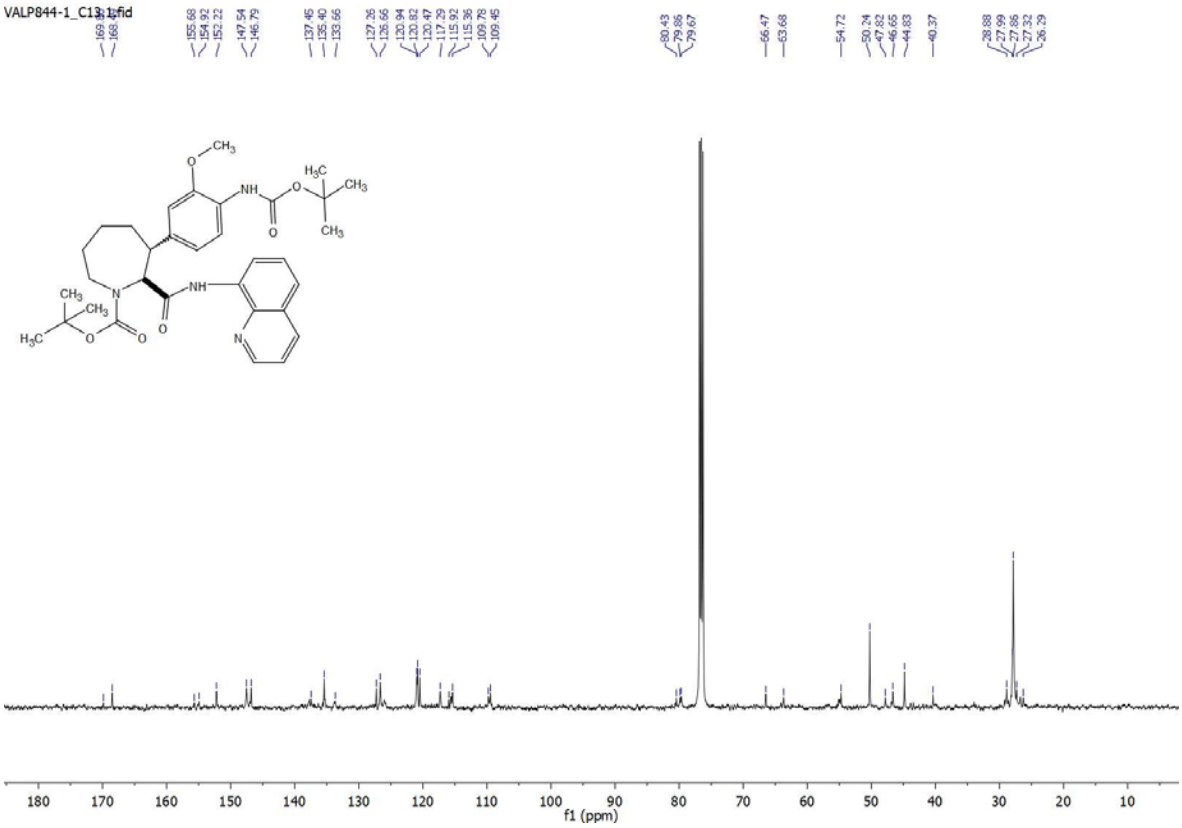
Compound Boc – 42a



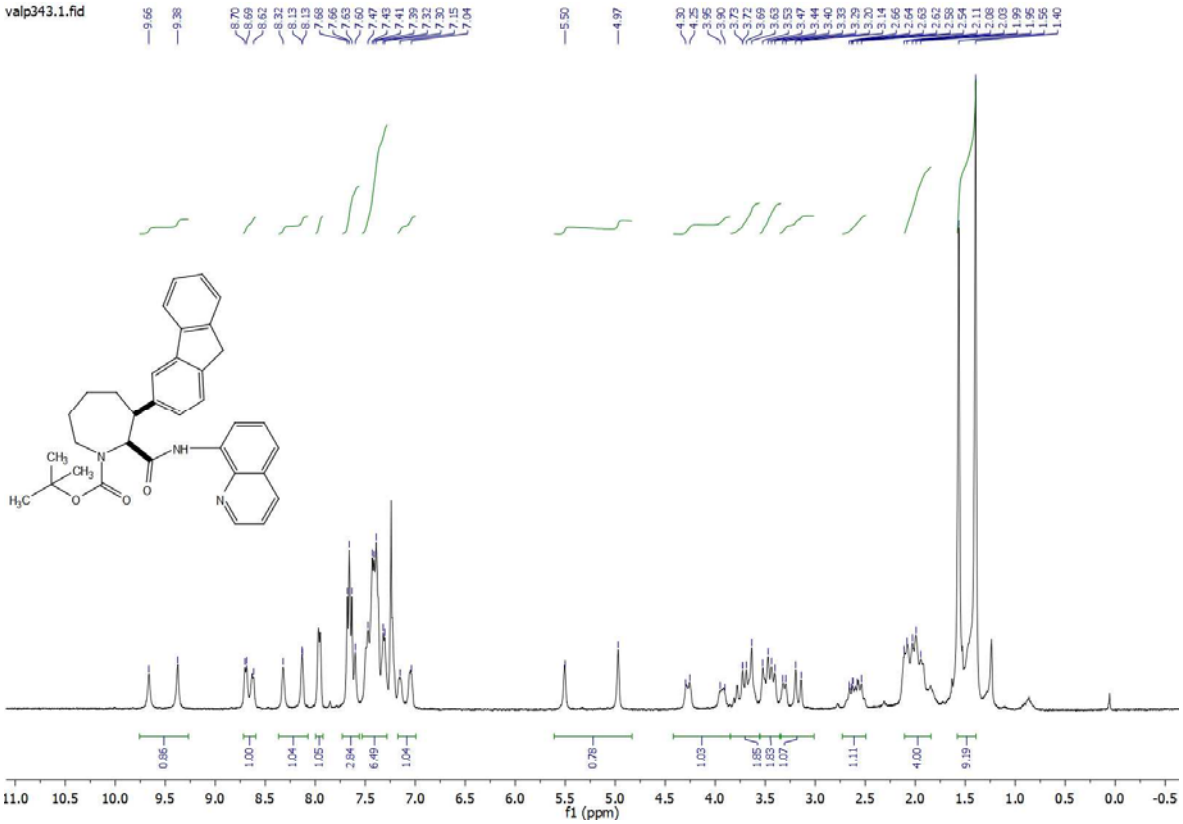


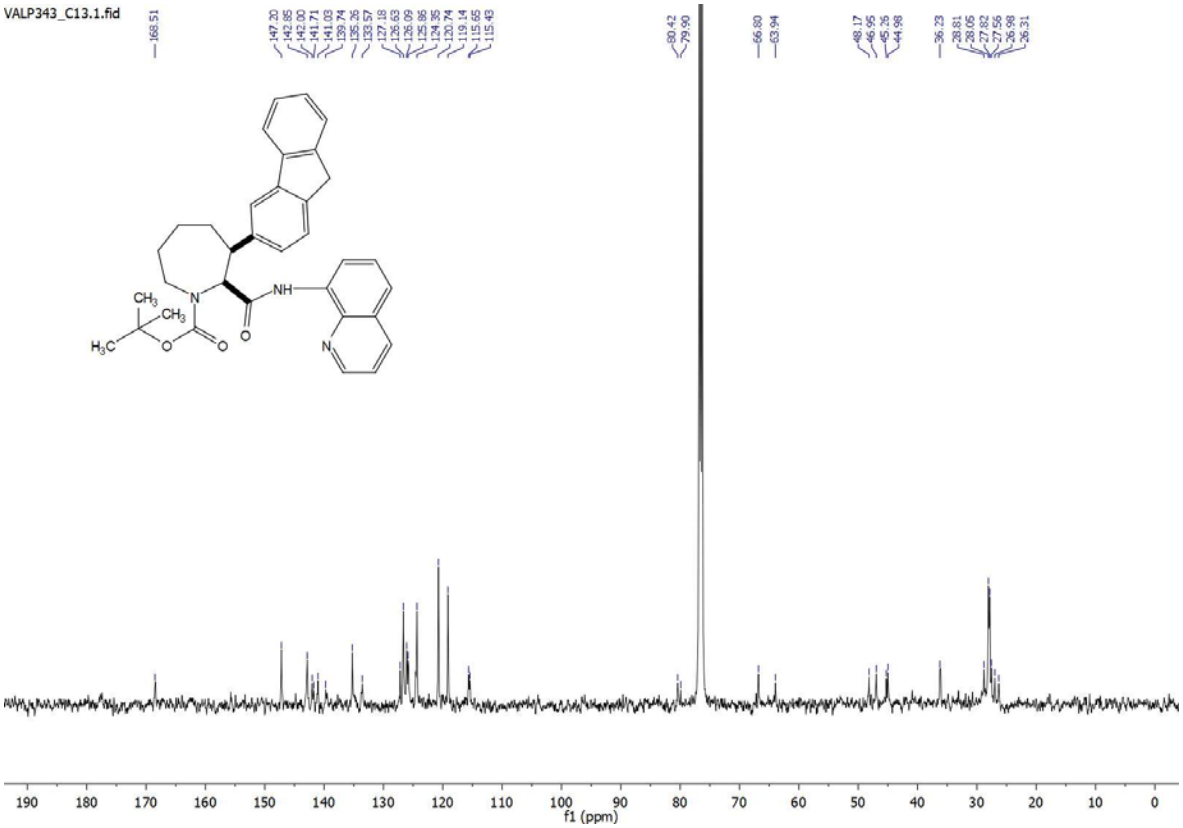
Compound Boc – 43a



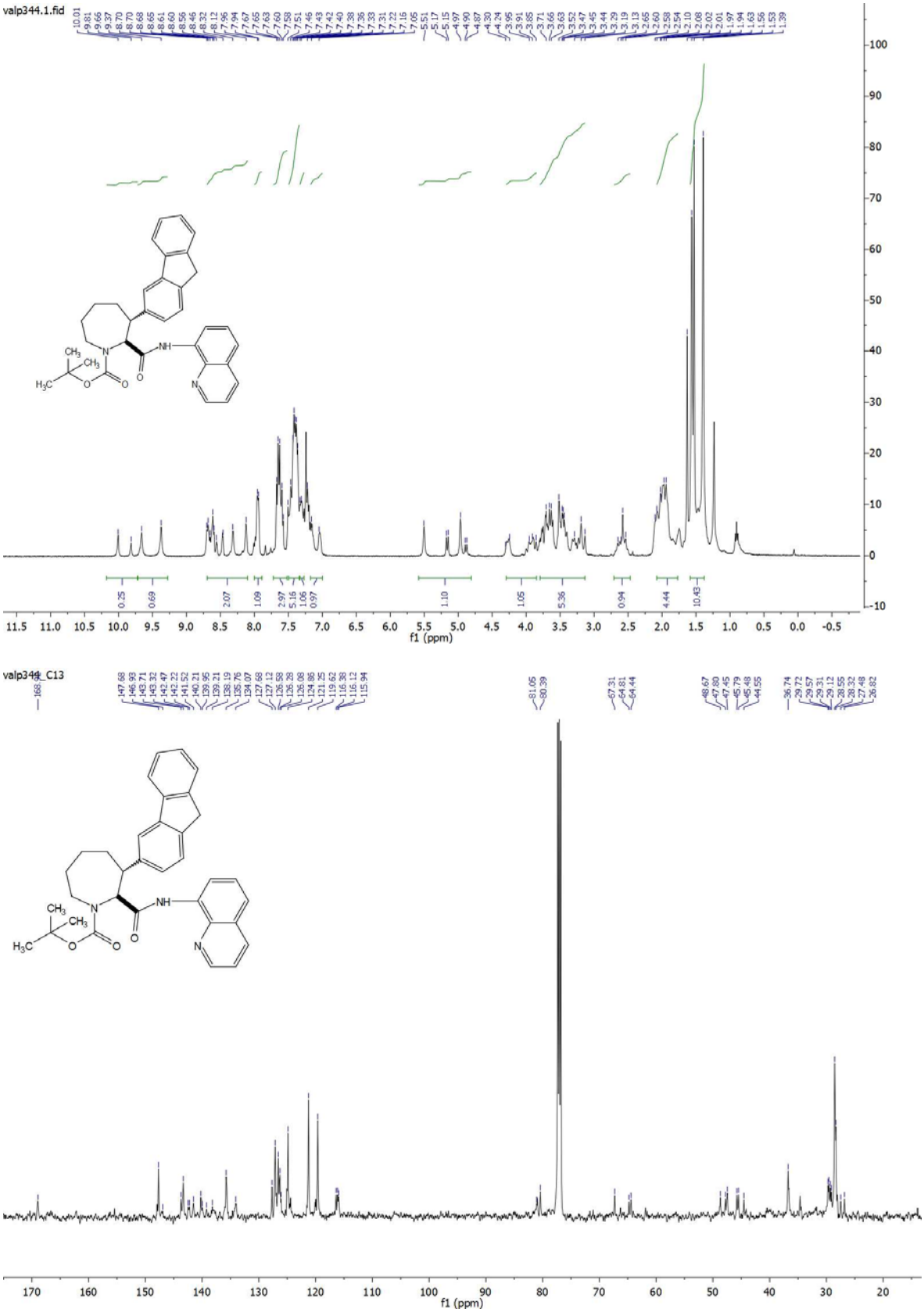


Compound Boc – 44a (cis only)

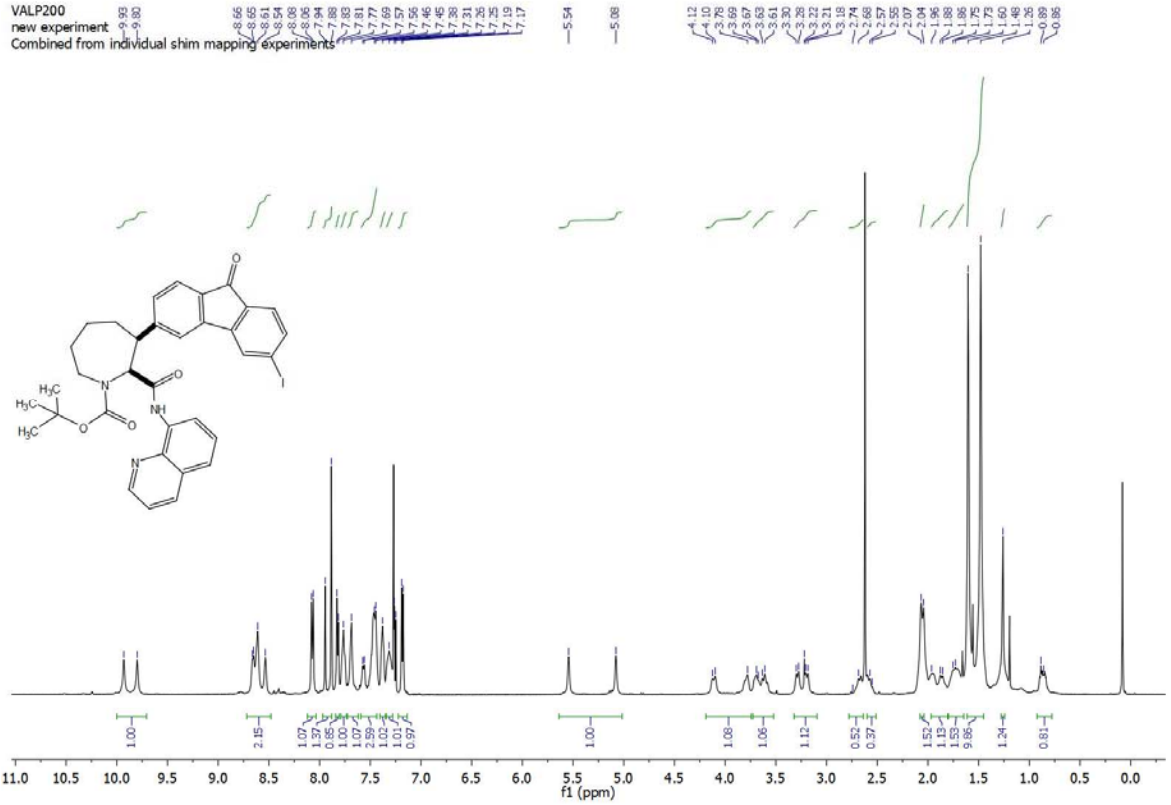


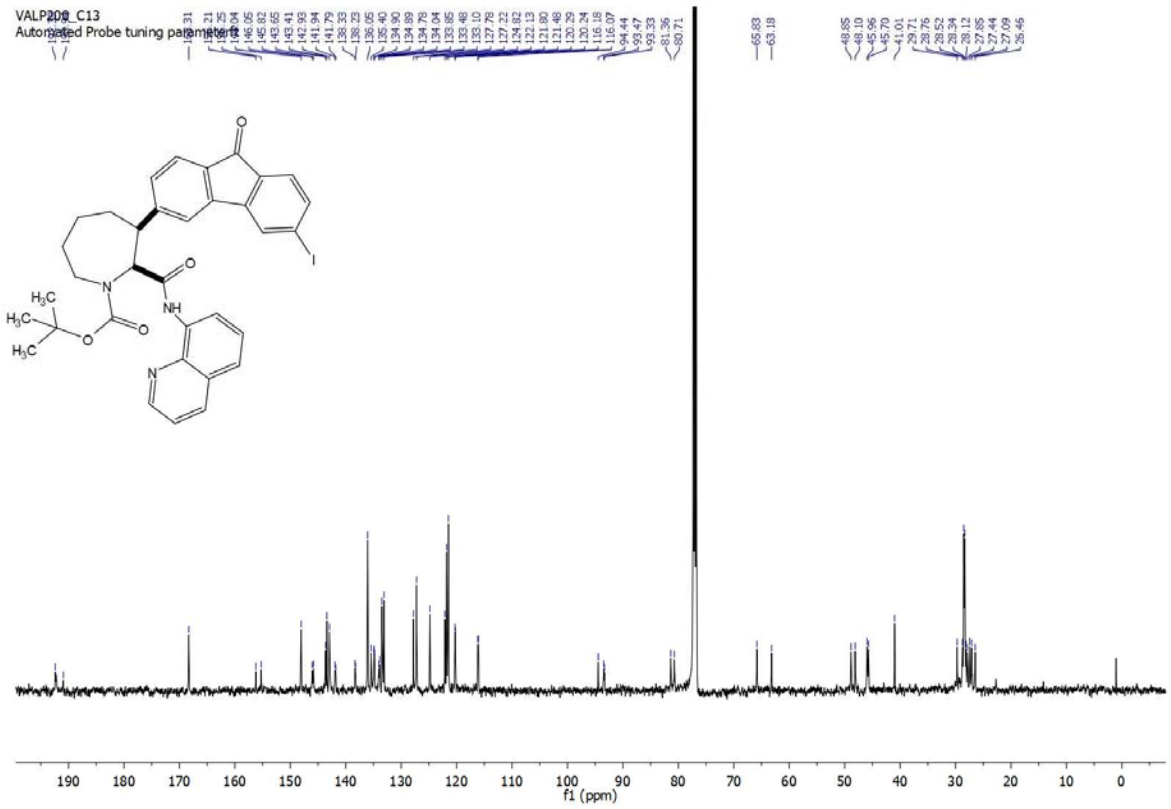


Compound Boc – 44a (diasteriomeric mixture)

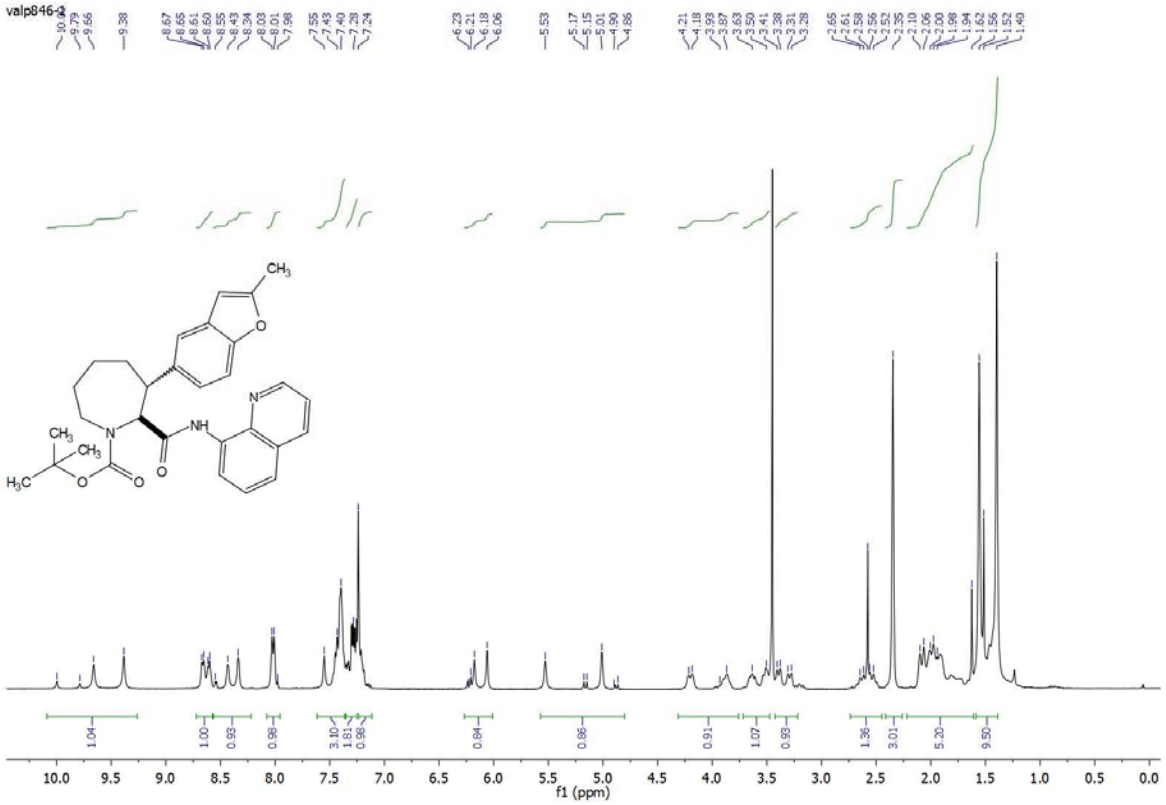


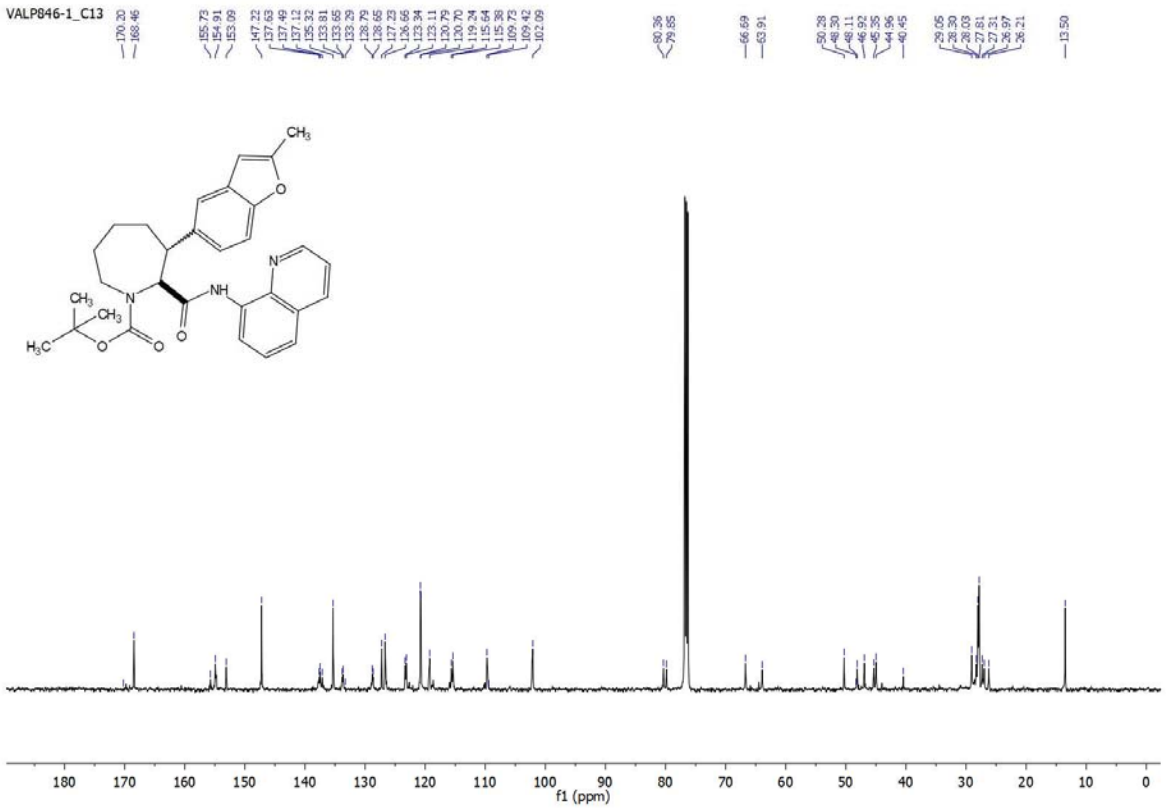
Compound Boc – 45a (cis)



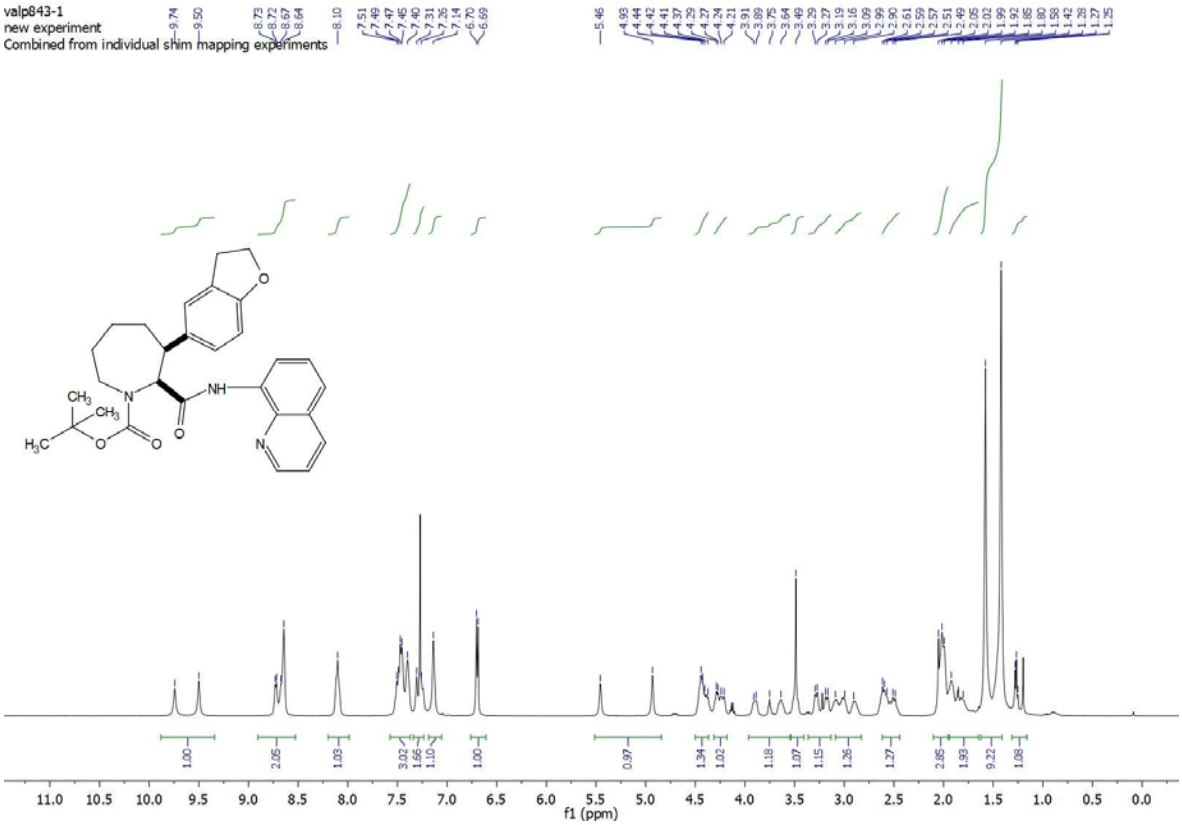


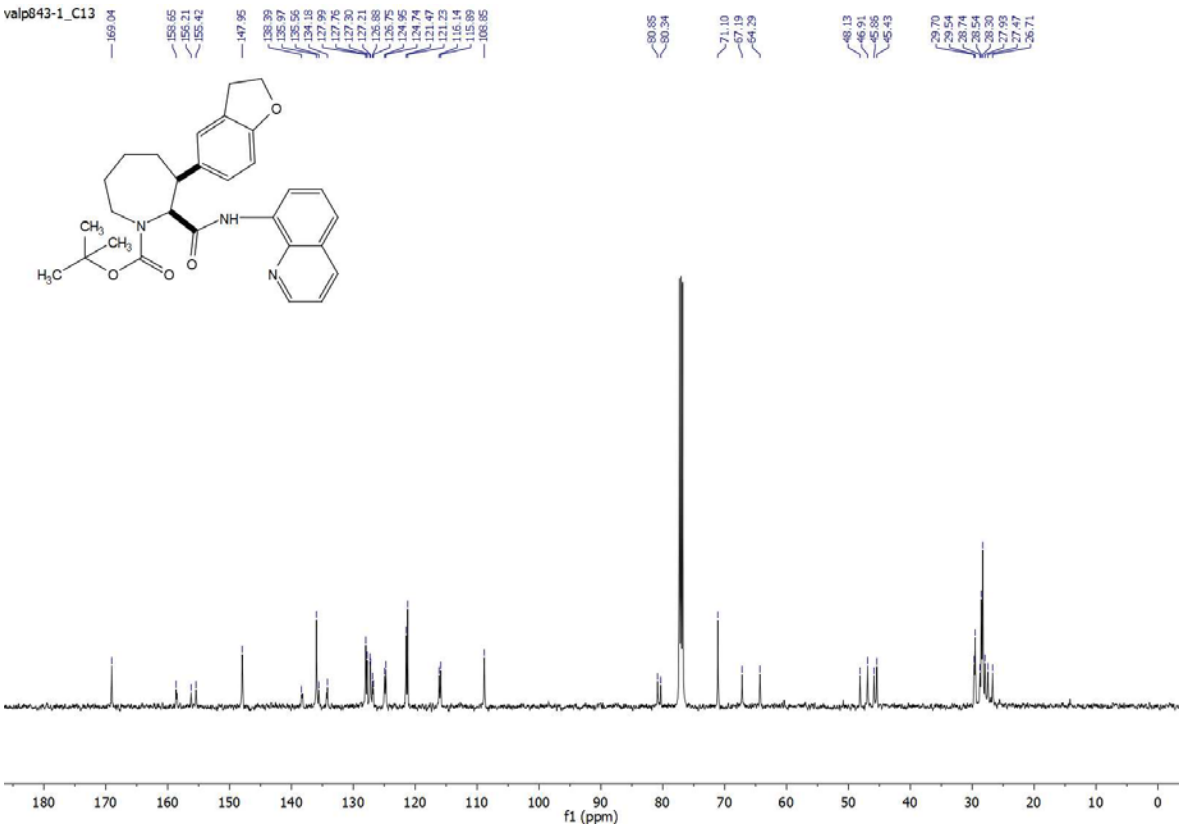
Compound Boc – 46a

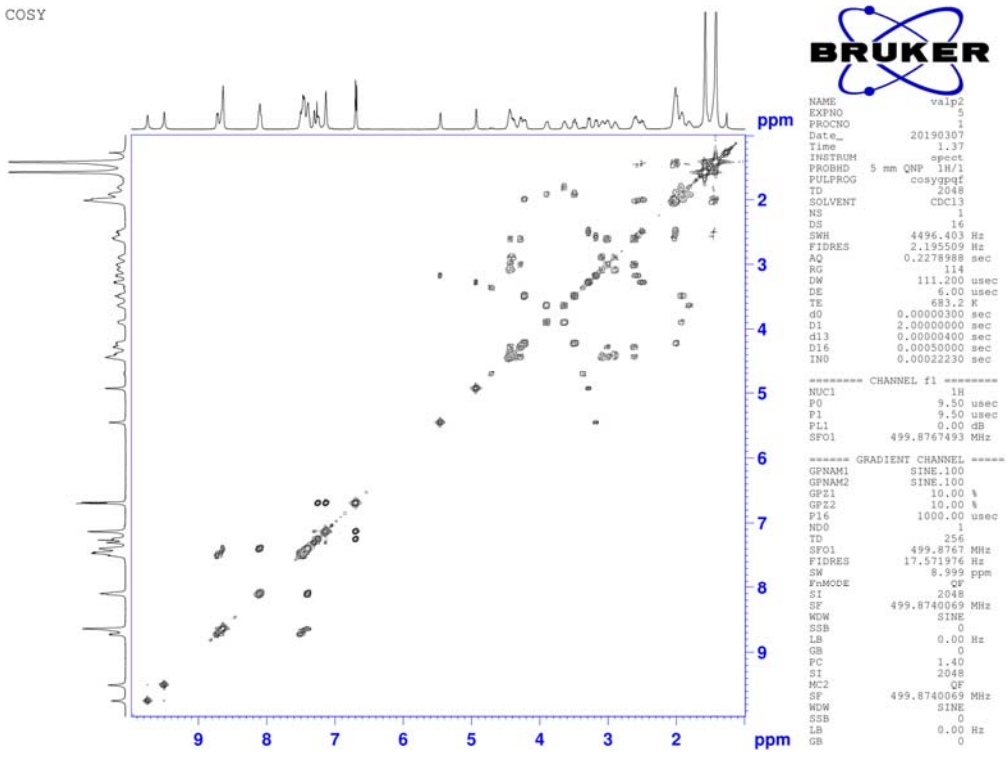


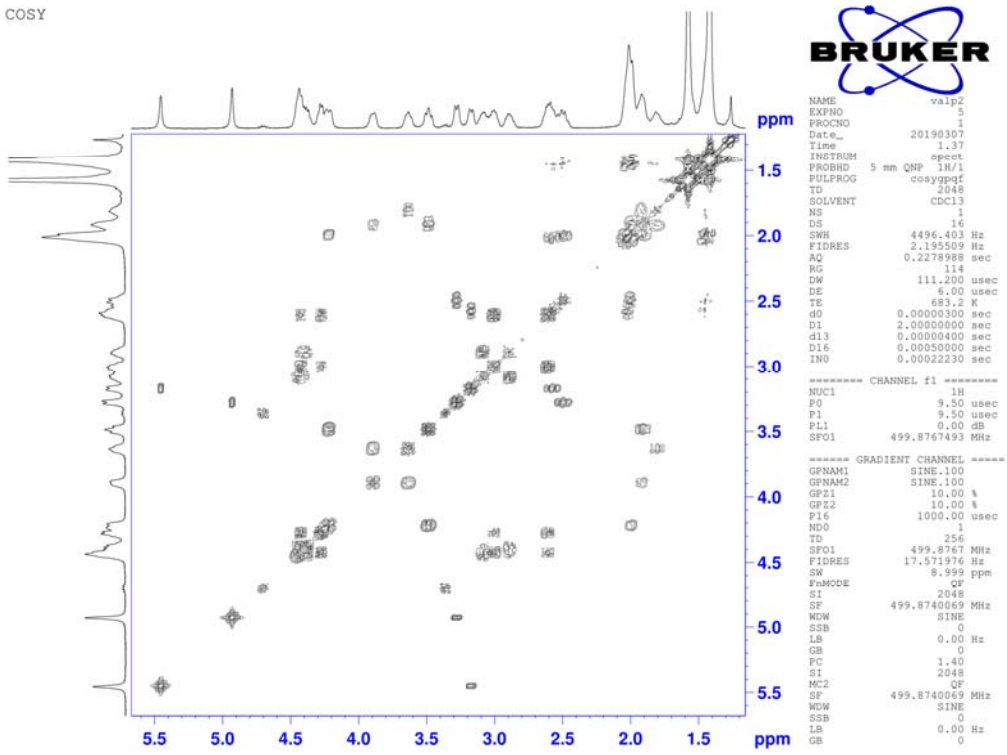


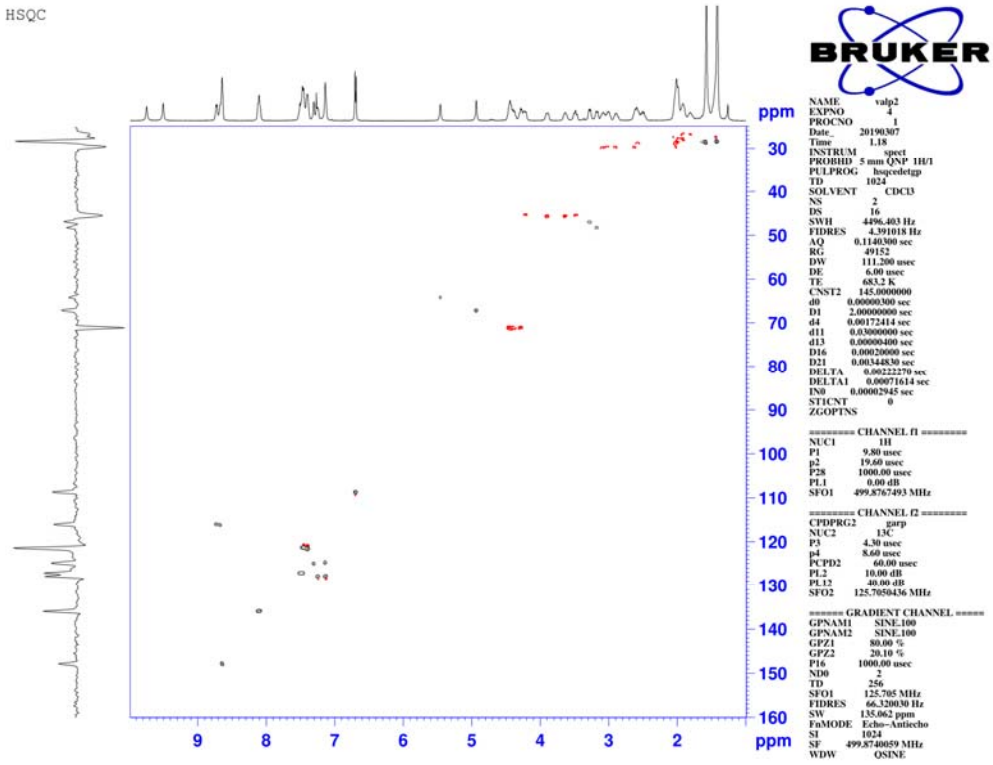
Compound Boc – 47a






COSY
ppm
9 8 7 6 5 4 3 2
ppm
BRUKER
NAME valp2
EXPNO 5
PROCNO 1
Date_ 20190307
Time 1.37
INSTRUM spect
PROBHD 5 mm QNP 1H/1
PULPROG cosygpqf
TD 2048
SOLVENT CDCl3
NS 1
DS 16
SWH 4496.403 Hz
FIDRES 2.195509 Hz
AQ 0.2278988 sec
RG 114
DW 111.200 usec
DE 6.00 usec
TE 683.2 K
d0 0.00000300 sec
D1 2.00000000 sec
d13 0.00000400 sec
D16 0.00050000 sec
IN0 0.00022230 sec
======== CHANNEL f1 ========
NUC1 1H
P0 9.50 usec
P1 9.50 usec
PL1 0.00 dB
SFO1 499.8767493 MHz
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPZ1 10.00 %
GPZ2 10.00 %
P16 1000.00 usec
ND0 1
TD 256
SFO1 499.8767 MHz
FIDRES 17.571976 Hz
SW 8.999 ppm
FnMODE QF
SI 2048
SF 499.8740069 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0
PC 1.40
SI 2048
MC2 QF
SF 499.8740069 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0


COSY
ppm
5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5
ppm
BRUKER
NAME valp2
EXPNO 5
PROCNO 1
Date_ 20190307
Time 1.37
INSTRUM spect
PROBHD 5 mm QNP 1H/1
PULPROG cosygpqf
TD 2048
SOLVENT CDCl3
NS 1
DS 16
SWH 4496.403 Hz
FIDRES 2.195509 Hz
AQ 0.2278988 sec
RG 114
DW 111.200 usec
DE 6.00 usec
TE 683.2 K
d0 0.00000300 sec
D1 2.00000000 sec
d13 0.00000400 sec
D16 0.00050000 sec
IN0 0.00022230 sec
======== CHANNEL f1 ========
NUC1 1H
P0 9.50 usec
P1 9.50 usec
PL1 0.00 dB
SFO1 499.8767493 MHz
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPZ1 10.00 %
GPZ2 10.00 %
P16 1000.00 usec
ND0 1
TD 256
SFO1 499.8767 MHz
FIDRES 17.571976 Hz
SW 8.999 ppm
FnMODE QF
SI 2048
SF 499.8740069 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0
PC 1.40
SI 2048
MC2 QF
SF 499.8740069 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0

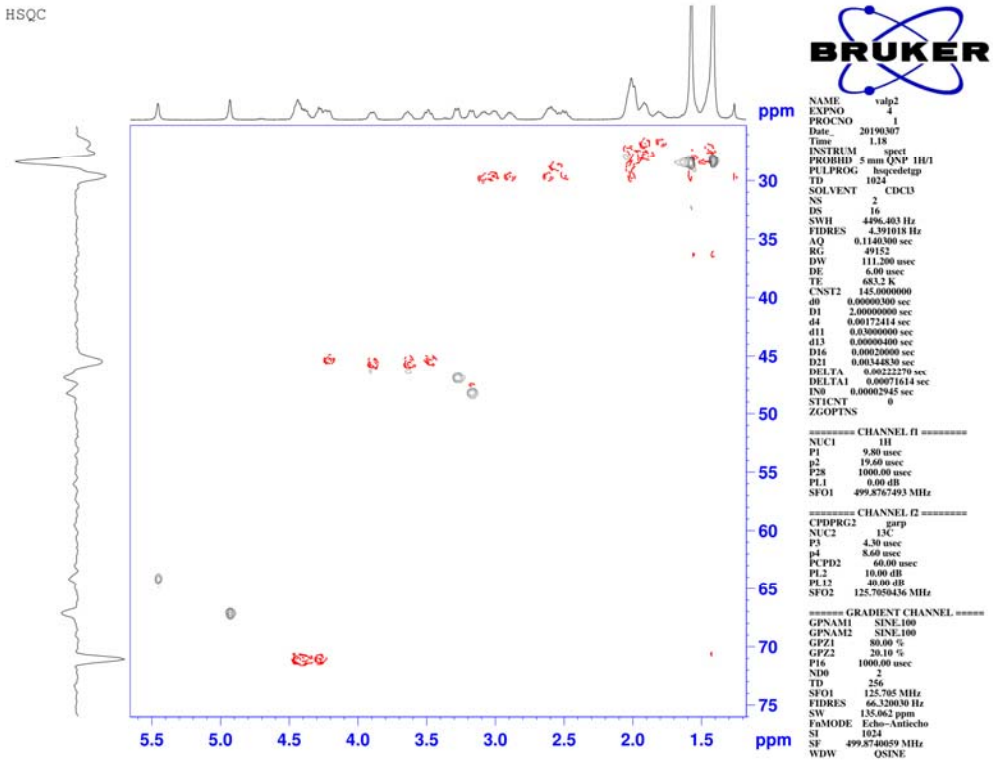


NAME valp2
EXPNO 4
PROCNO 1
Date_ 20190307
Time 1.18
INSTRUM spect
PROBHD 5 mm QNP 1H/1
PULPROG hsqcedetgp
TD 1024
SOLVENT CDCl3
NS 2
DS 16
SWH 4496.403 Hz
FIDRES 4.391018 Hz
AQ 0.1140300 sec
RG 49152
DW 111.200 usec
DE 6.00 usec
TE 683.2 K
CNST2 145.0000000
d0 0.00000300 sec
D1 2.00000000 sec
d4 0.00172414 sec
d11 0.03000000 sec
d13 0.00000400 sec
D16 0.00020000 sec
D21 0.00344830 sec
DELTA 0.00222270 sec
DELTA1 0.00071614 sec
IN0 0.00002945 sec
ST1CNT 0
ZGOPTNS

======== CHANNEL f1 ========
NUC1 1H
P1 9.80 usec
p2 19.60 usec
P28 1000.00 usec
PL1 0.00 dB
SFO1 499.8767493 MHz

======== CHANNEL f2 ========
CPDPRG2 garp
NUC2 13C
P3 4.30 usec
p4 8.60 usec
PCPD2 60.00 usec
PL2 10.00 dB
PL12 40.00 dB
SFO2 125.7050436 MHz

====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPZ1 80.00 %
GPZ2 20.10 %
P16 1000.00 usec
ND0 2
TD 256
SFO1 125.705 MHz
FIDRES 66.320030 Hz
SW 135.062 ppm
FnMODE Echo-Antiecho
SI 1024
SF 499.8740059 MHz
WDW QSINE

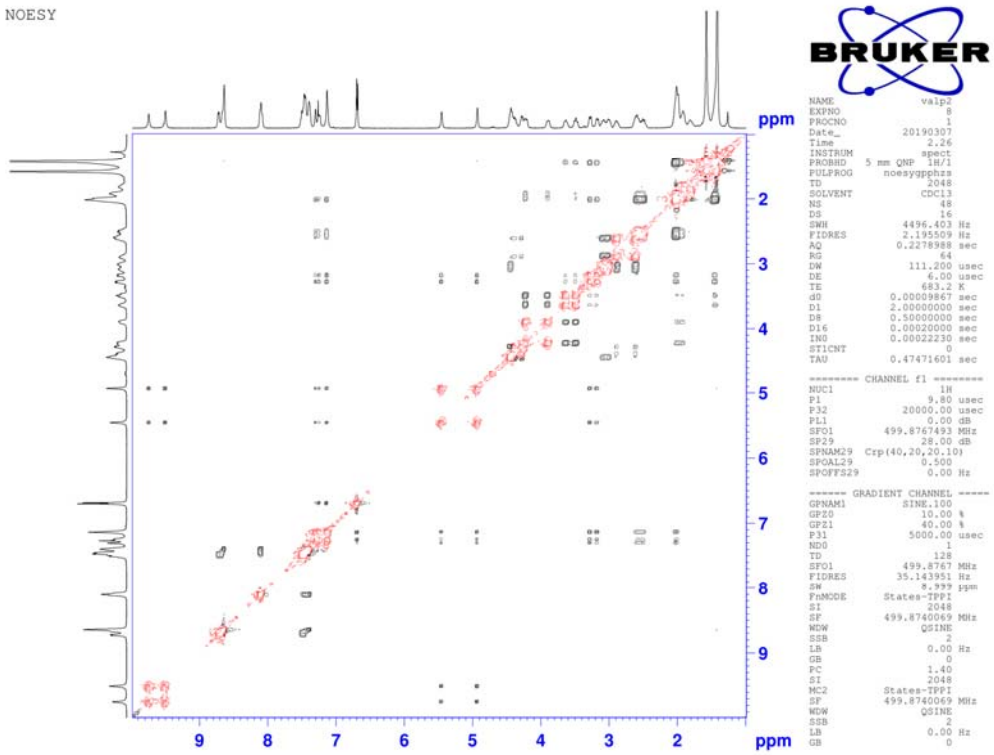


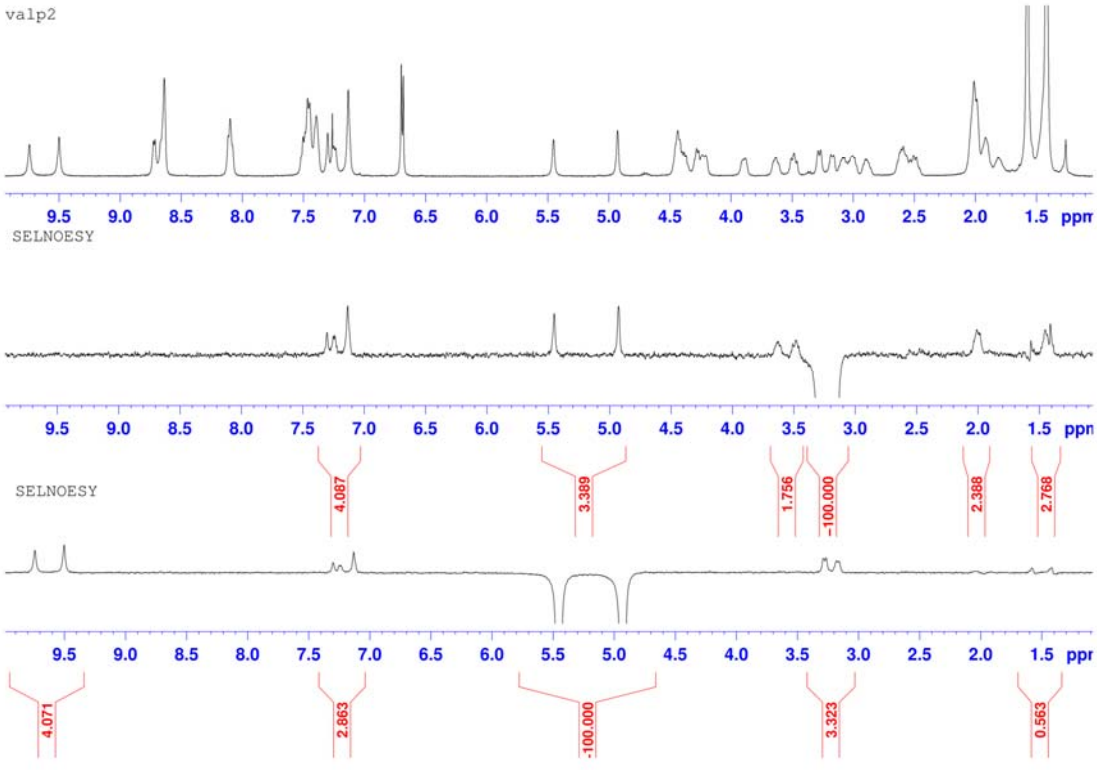
NAME valp2
EXPNO 4
PROCNO 1
Date_ 20190307
Time 1.18
INSTRUM spect
PROBHD 5 mm QNP 1H/1
PULPROG hsqcedetgp
TD 1024
SOLVENT CDCl3
NS 2
DS 16
SWH 4496.403 Hz
FIDRES 4.391018 Hz
AQ 0.1140300 sec
RG 49152
DW 111.200 usec
DE 6.00 usec
TE 683.2 K
CNST2 145.0000000
d0 0.00000300 sec
D1 2.00000000 sec
d4 0.00172414 sec
d11 0.03000000 sec
d13 0.00000400 sec
D16 0.00020000 sec
D21 0.00344830 sec
DELTA 0.00222270 sec
DELTA1 0.00071614 sec
IN0 0.00002945 sec
ST1CNT 0
ZGOPTNS

======== CHANNEL f1 ========
NUC1 1H
P1 9.80 usec
p2 19.60 usec
P28 1000.00 usec
PL1 0.00 dB
SFO1 499.8767493 MHz

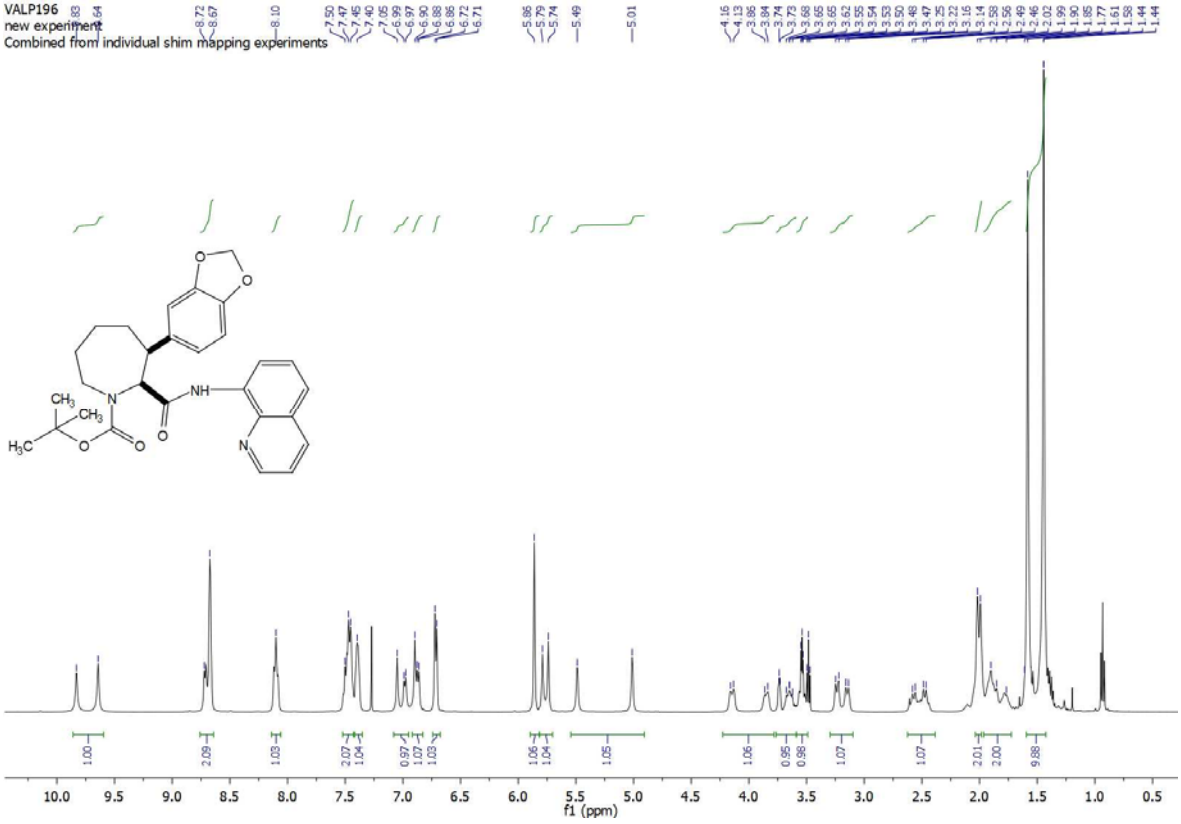
======== CHANNEL f2 ========
CPDPRG2 garp
NUC2 13C
P3 4.30 usec
p4 8.60 usec
PCPD2 60.00 usec
PL2 10.00 dB
PL12 40.00 dB
SFO2 125.7050436 MHz

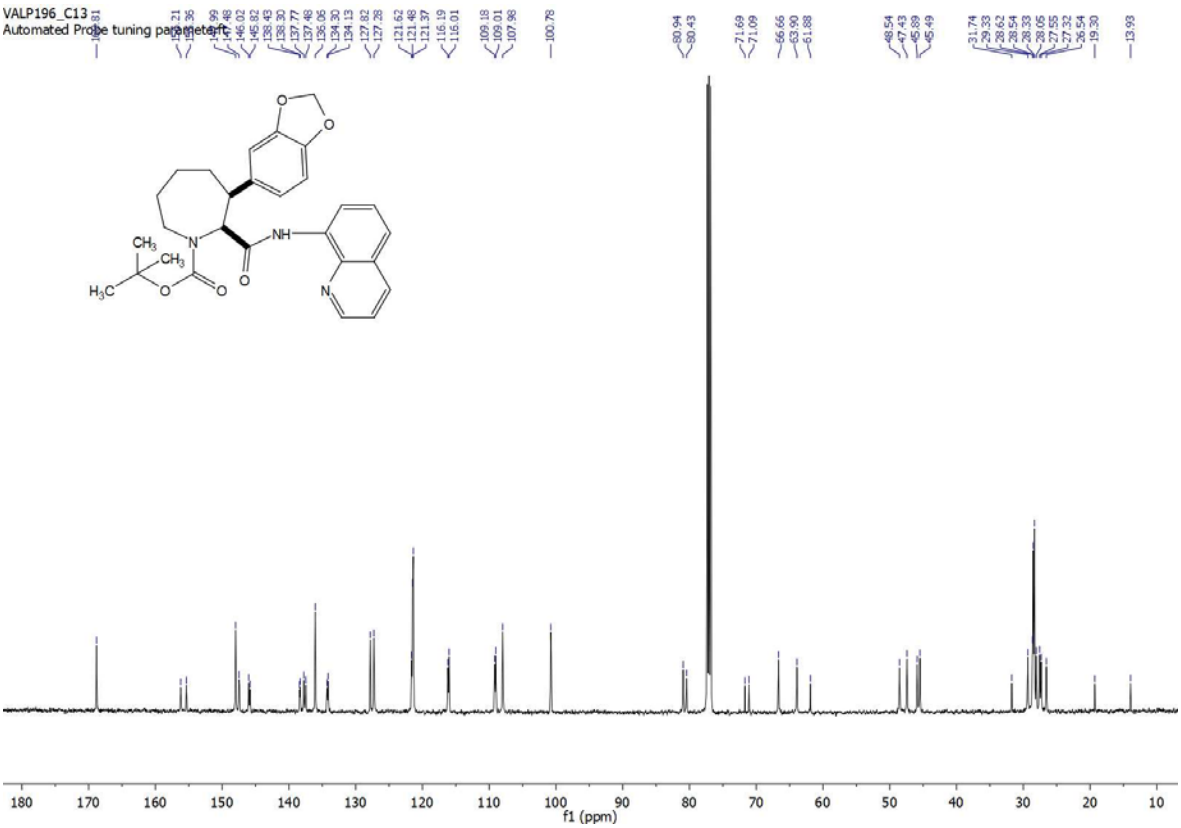
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPNAM2 SINE.100
GPZ1 80.00 %
GPZ2 20.10 %
P16 1000.00 usec
ND0 2
TD 256
SFO1 125.705 MHz
FIDRES 66.320030 Hz
SW 135.062 ppm
FnMODE Echo-Antiecho
SI 1024
SF 499.8740059 MHz
WDW QSINE


NOESY
BRUKER
ppm
9 8 7 6 5 4 3 2 ppm
NAME valp2
EXPNO 8
PROCNO 1
Date_ 20190307
Time 2.26
INSTRUM spect
PROBHD 5 mm QNP 1H/1
PULPROG noesygpphzs
TD 2048
SOLVENT CDCl3
NS 48
DS 16
SWH 4496.403 Hz
FIDRES 2.195509 Hz
AQ 0.2278988 sec
RG 64
DW 111.200 usec
DE 6.00 usec
TE 683.2 K
d0 0.00009867 sec
D1 2.00000000 sec
D8 0.50000000 sec
D16 0.00020000 sec
IN0 0.00022230 sec
ST1CNT 0
TAU 0.47471601 sec
======== CHANNEL f1 ========
NUC1 1H
P1 9.80 usec
P32 20000.00 usec
PL1 0.00 dB
SFO1 499.8767493 MHz
SF29 28.00 dB
SPNAM29 Crp(40,20,20.10)
SPOAL29 0.500
SPOFFS29 0.00 Hz
====== GRADIENT CHANNEL =====
GPNAM1 SINE.100
GPZ0 10.00 %
GPZ1 40.00 %
P31 5000.00 usec
ND0 1
TD 128
SFO1 499.8767 MHz
FIDRES 35.143951 Hz
SW 8.999 ppm
FnMODE States-TPPI
SI 2048
SF 499.8740069 MHz
WDW QSINE
SSB 2
LB 0.00 Hz
GB 0
PC 1.40
SI 2048
MC2 States-TPPI
SF 499.8740069 MHz
WDW QSINE
SSB 2
LB 0.00 Hz
GB 0

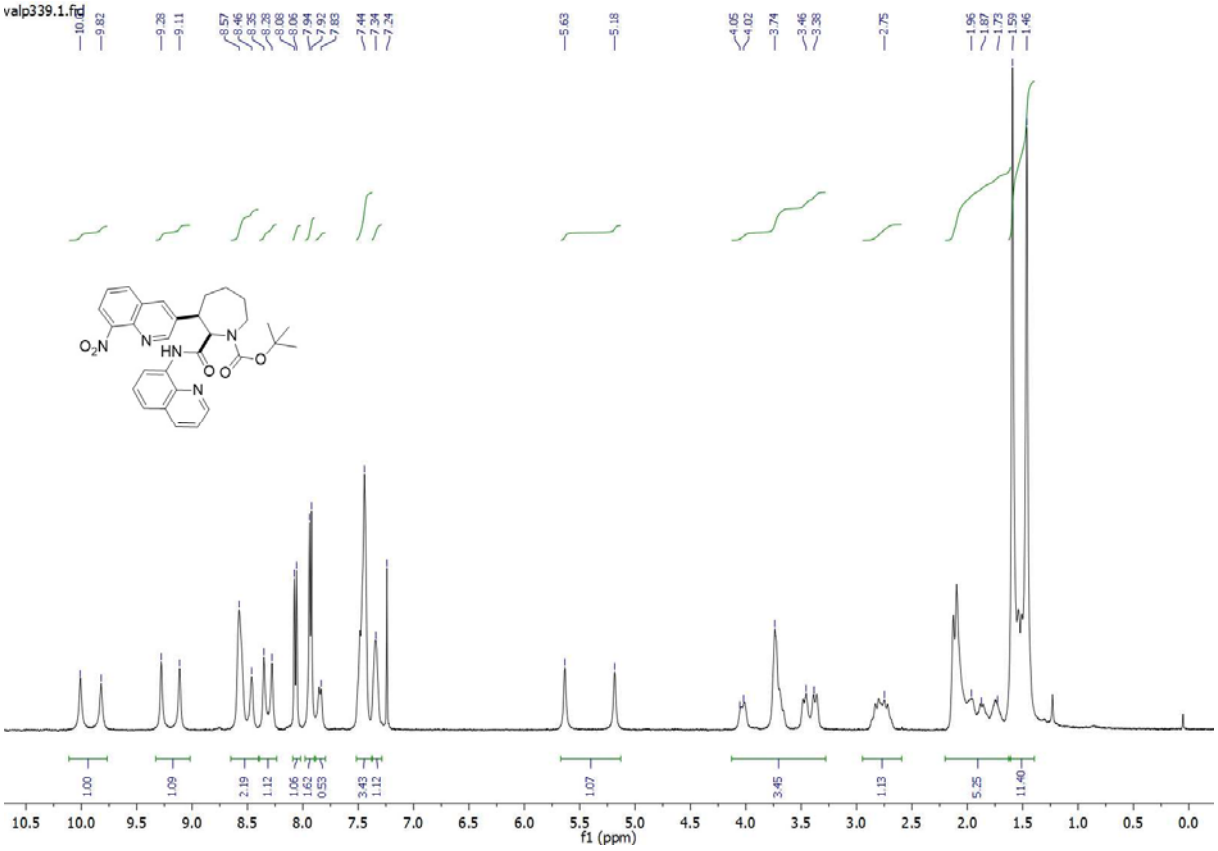

valp2
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 ppm
SELNOESY
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 ppm
4.087
3.389
1.756
-100.000
2.388
2.768
SELNOESY
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 ppm
4.071
2.863
-100.000
3.323
0.563

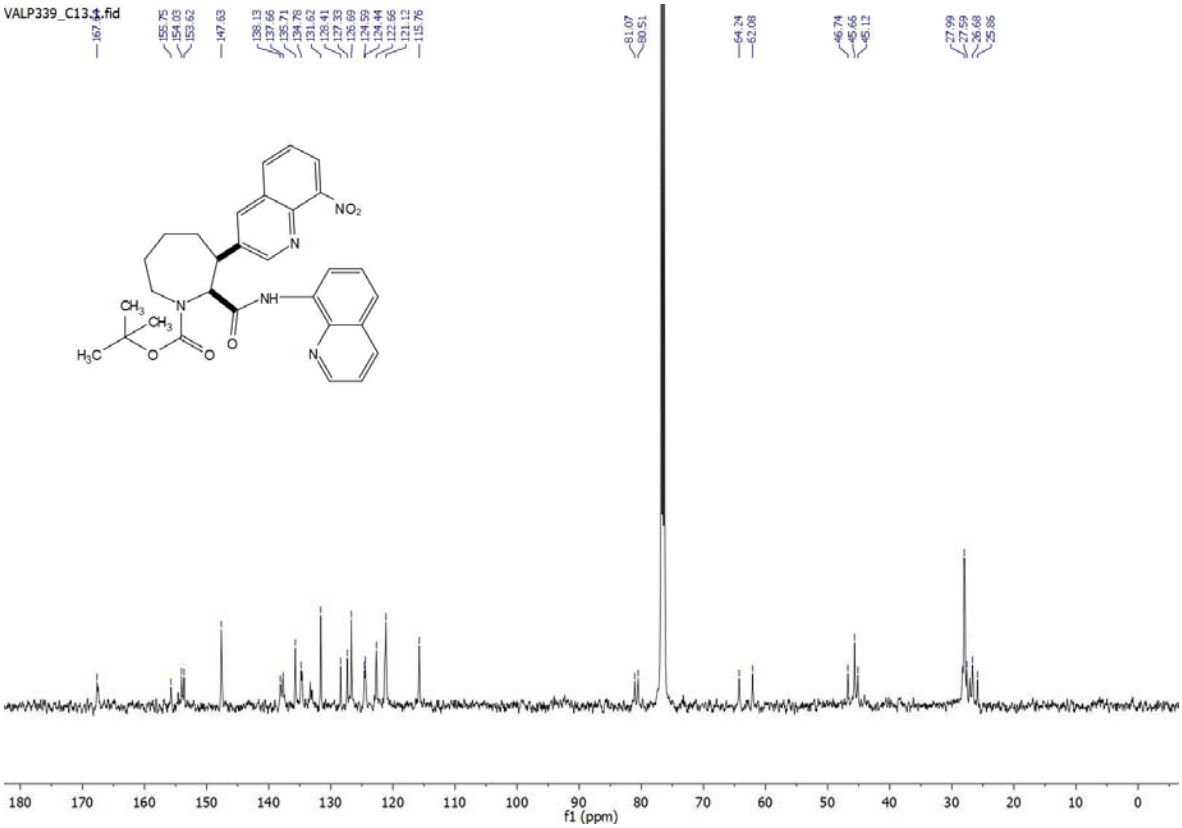
Compound Boc – 48a



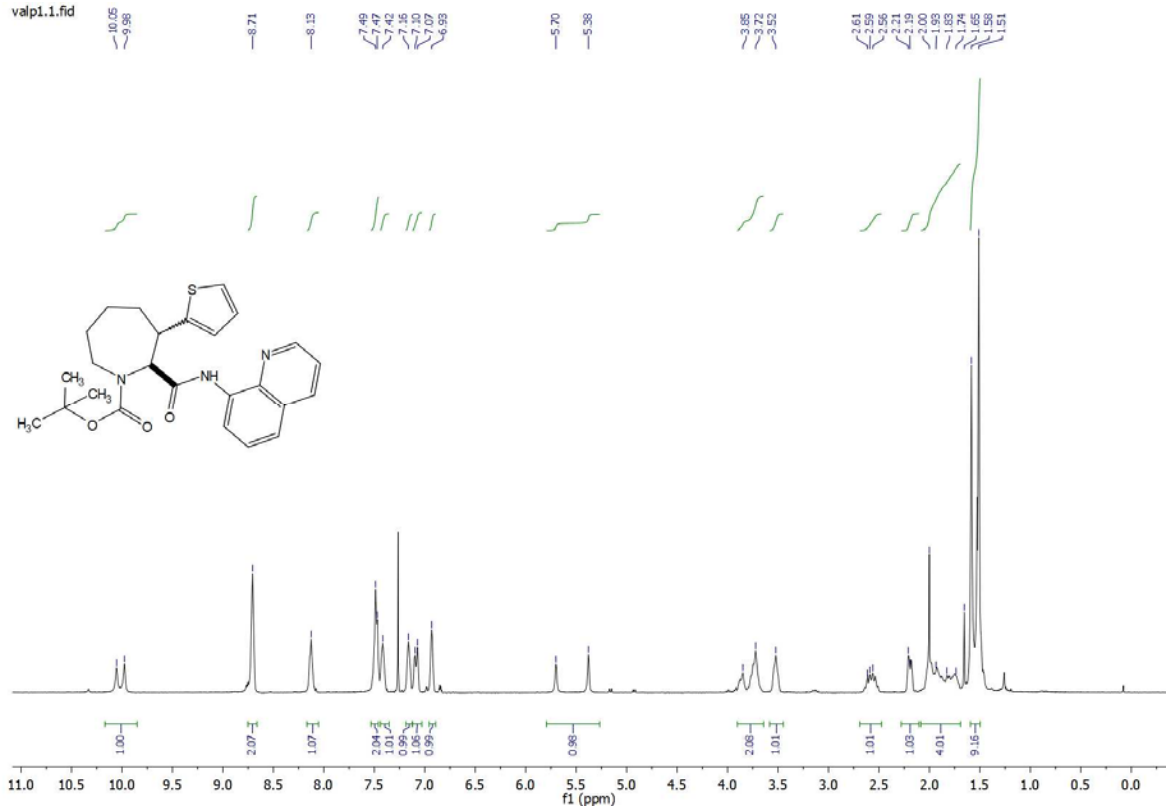


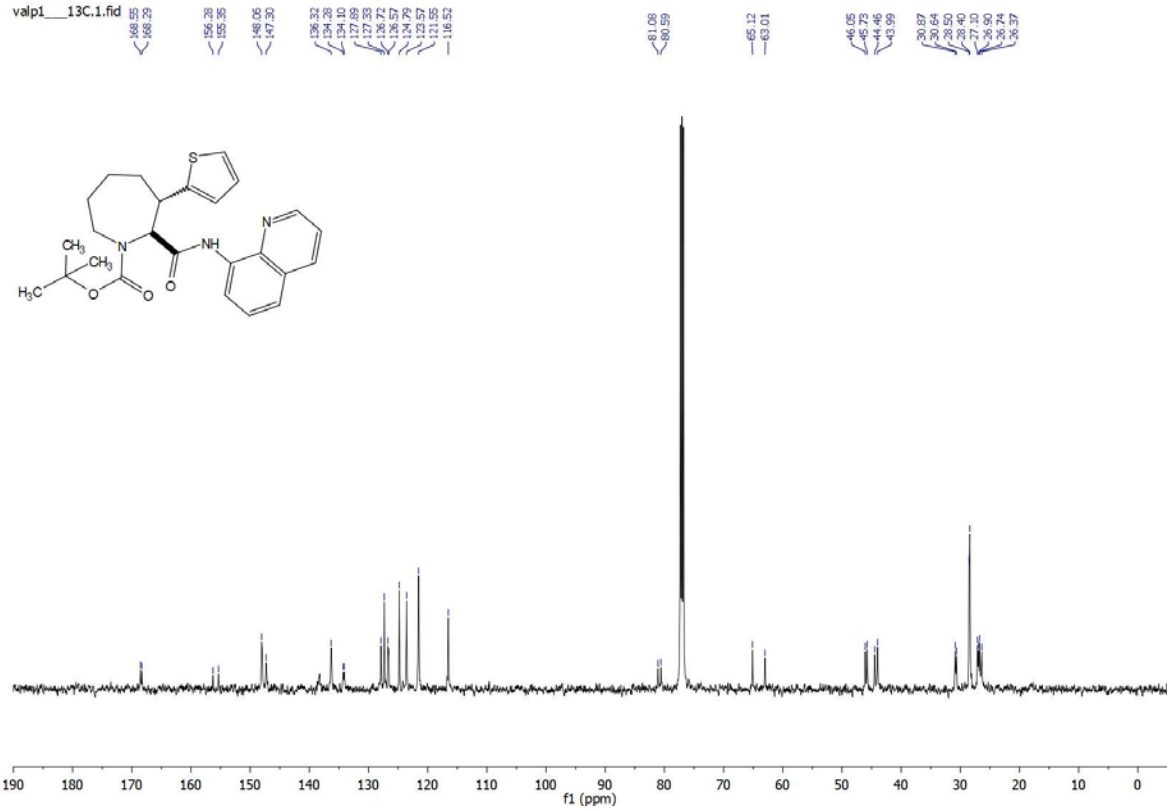
Compound Boc – 49a



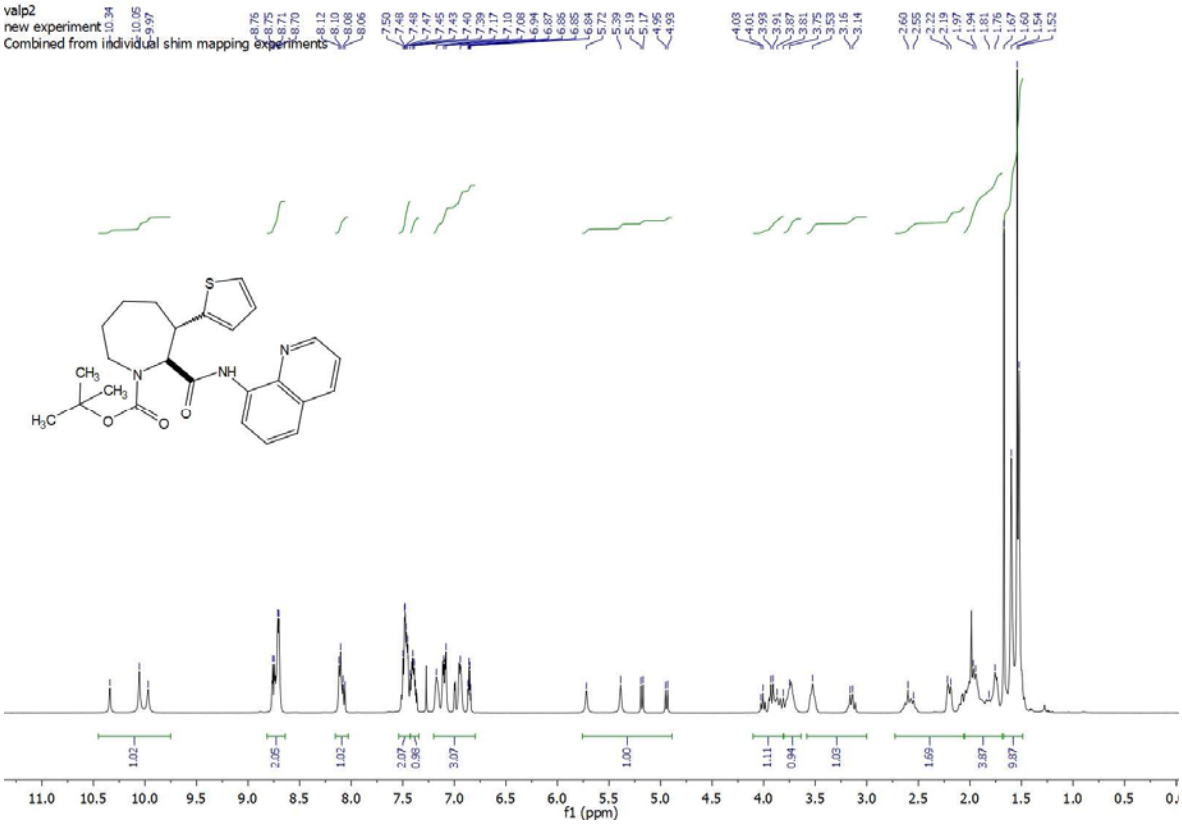


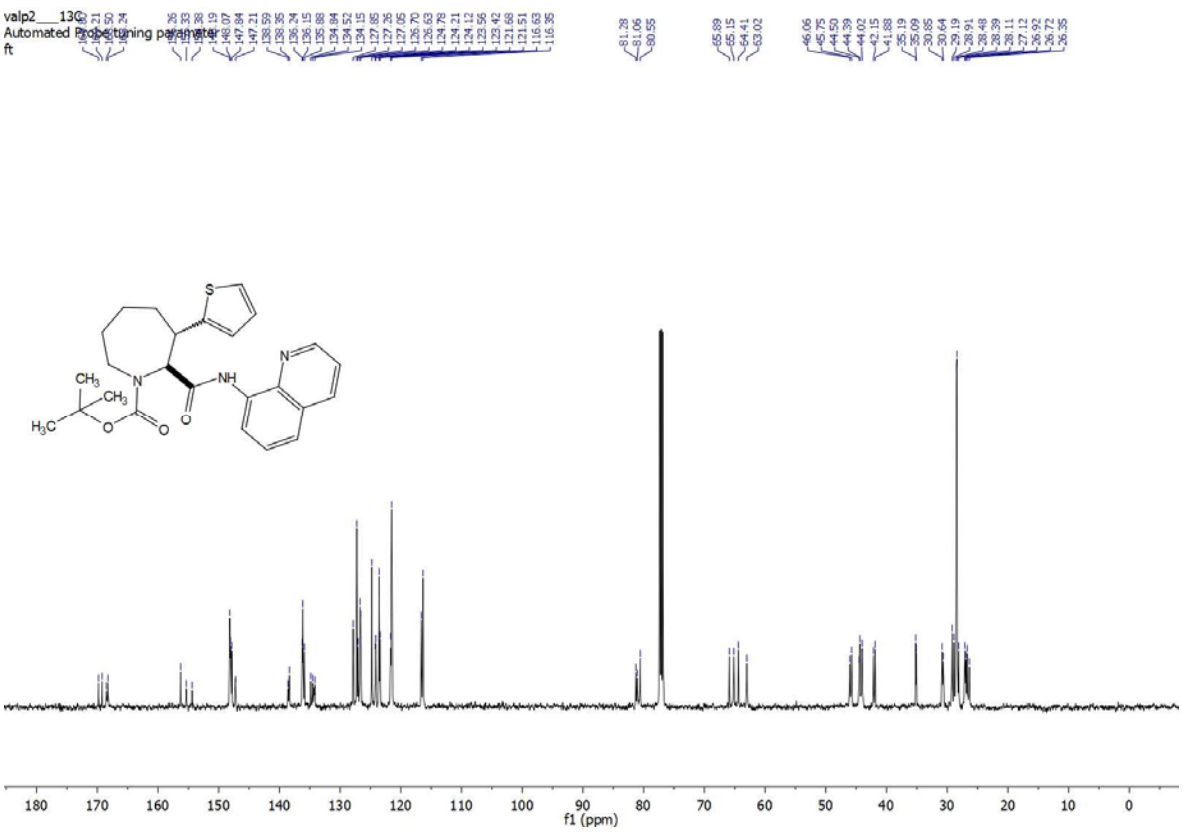
Compound Boc – 50a (cis)



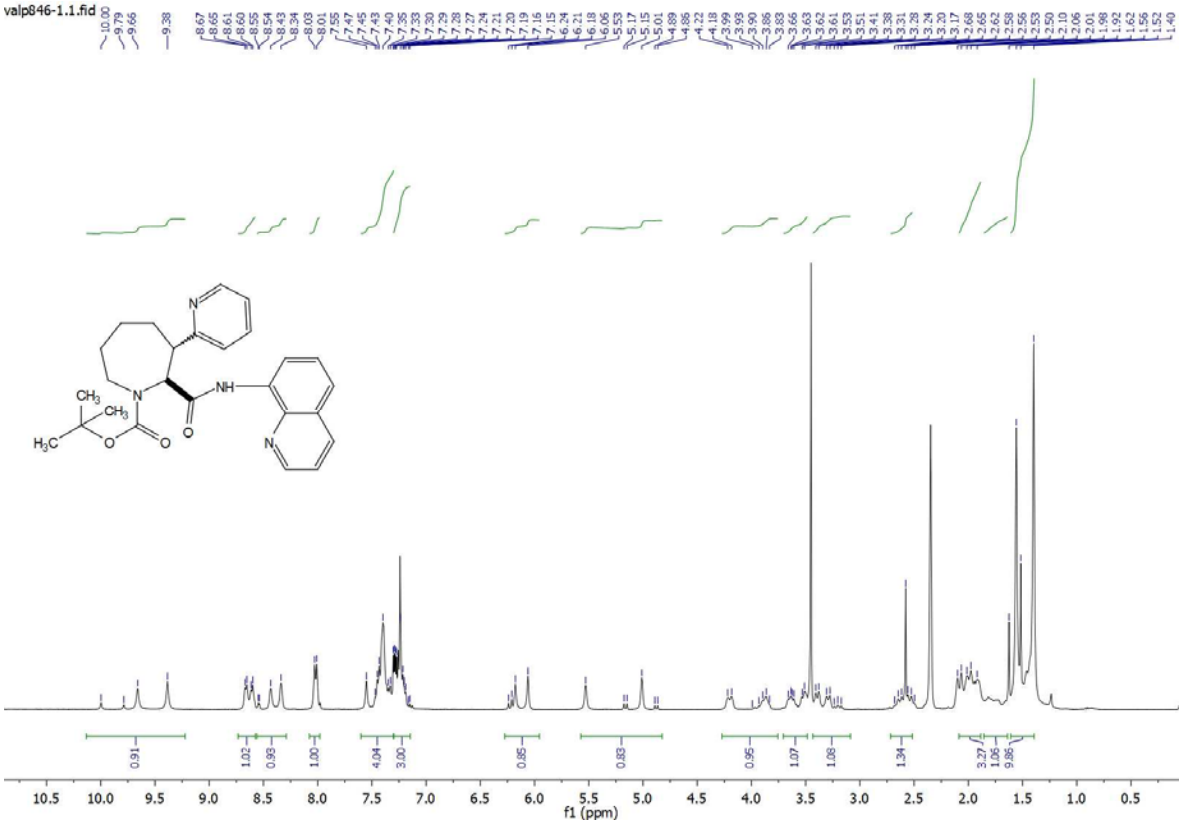


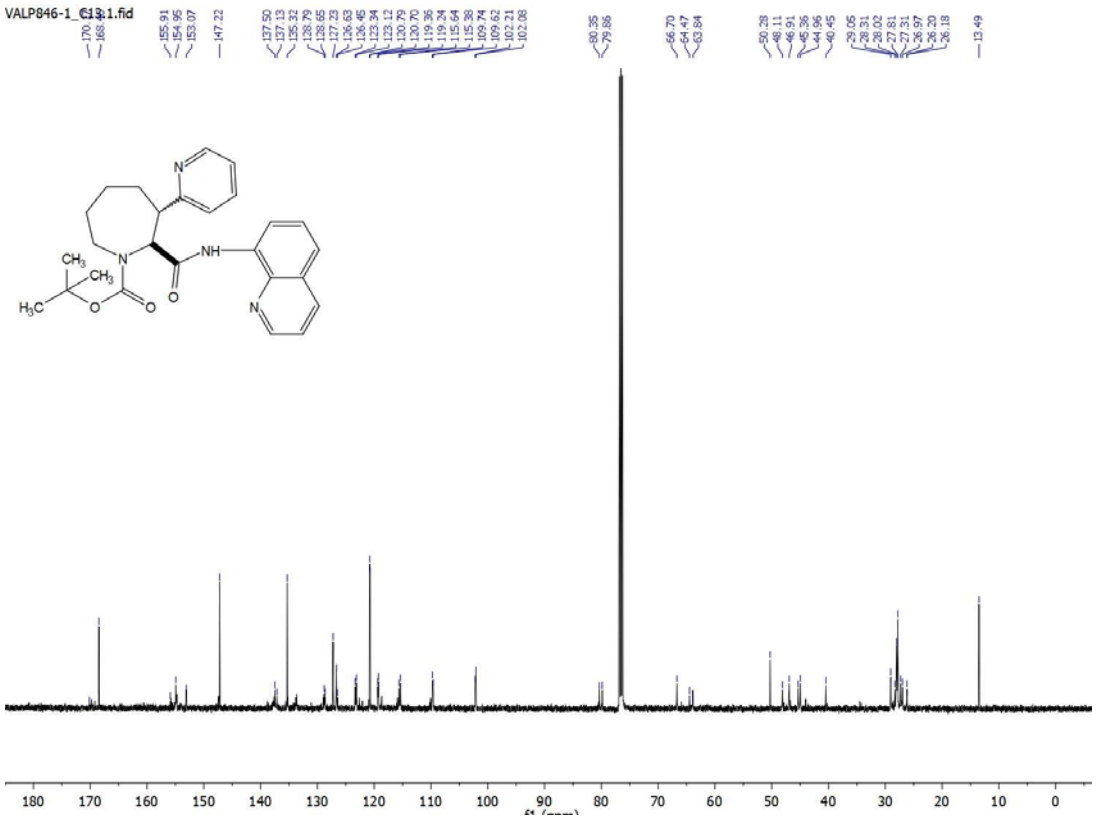
Compound Boc – 50a (diastereomeric mixture)



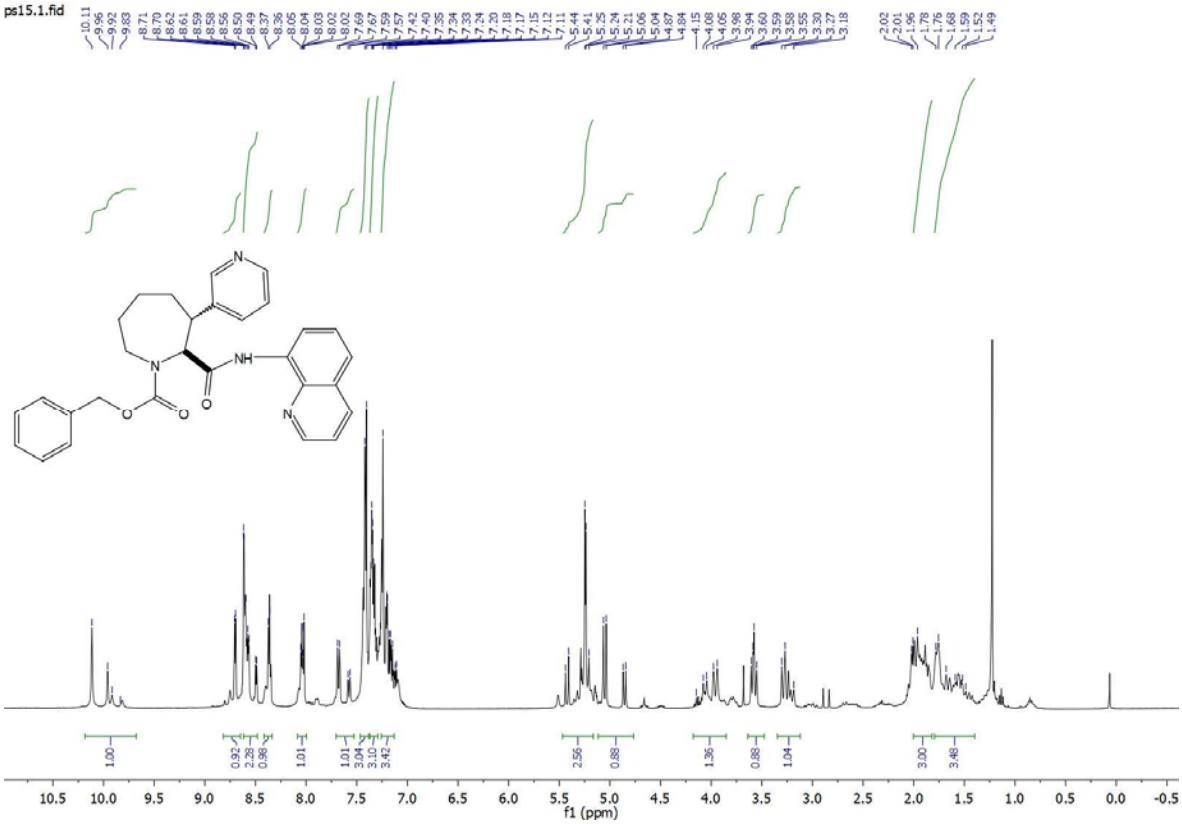


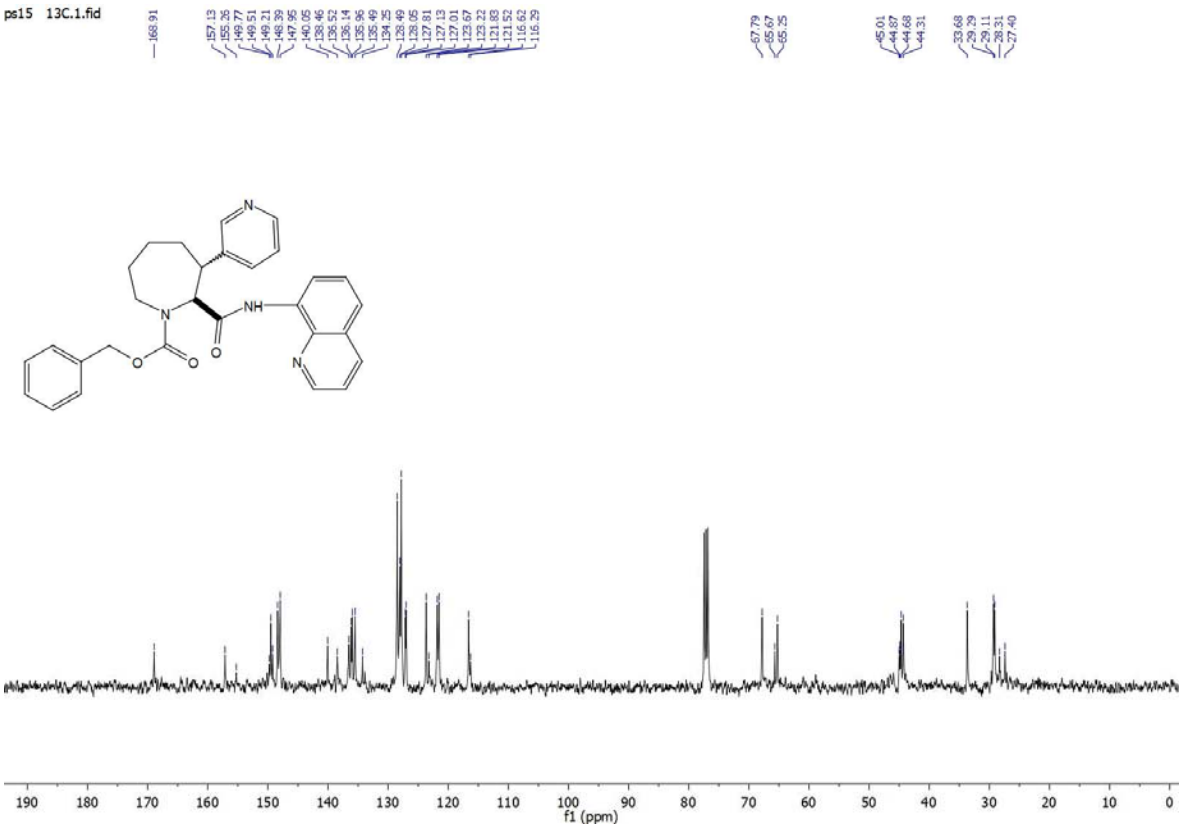
Compound Boc – 51a



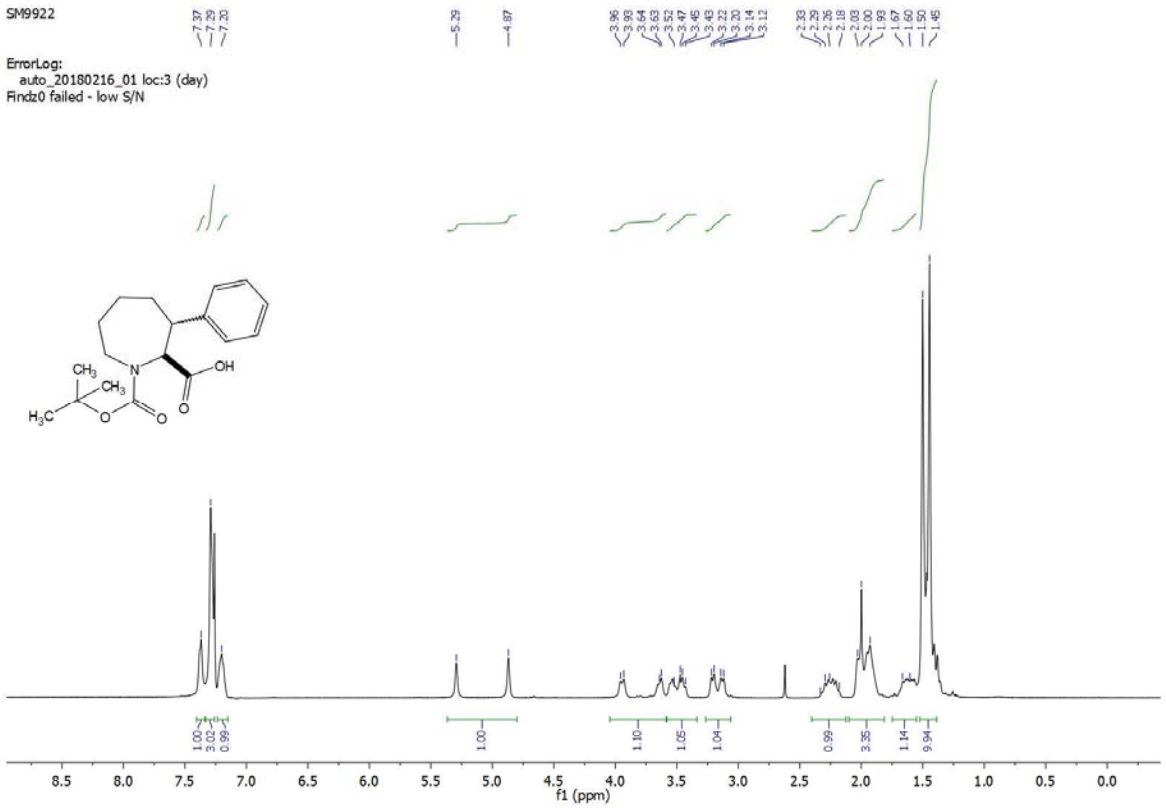


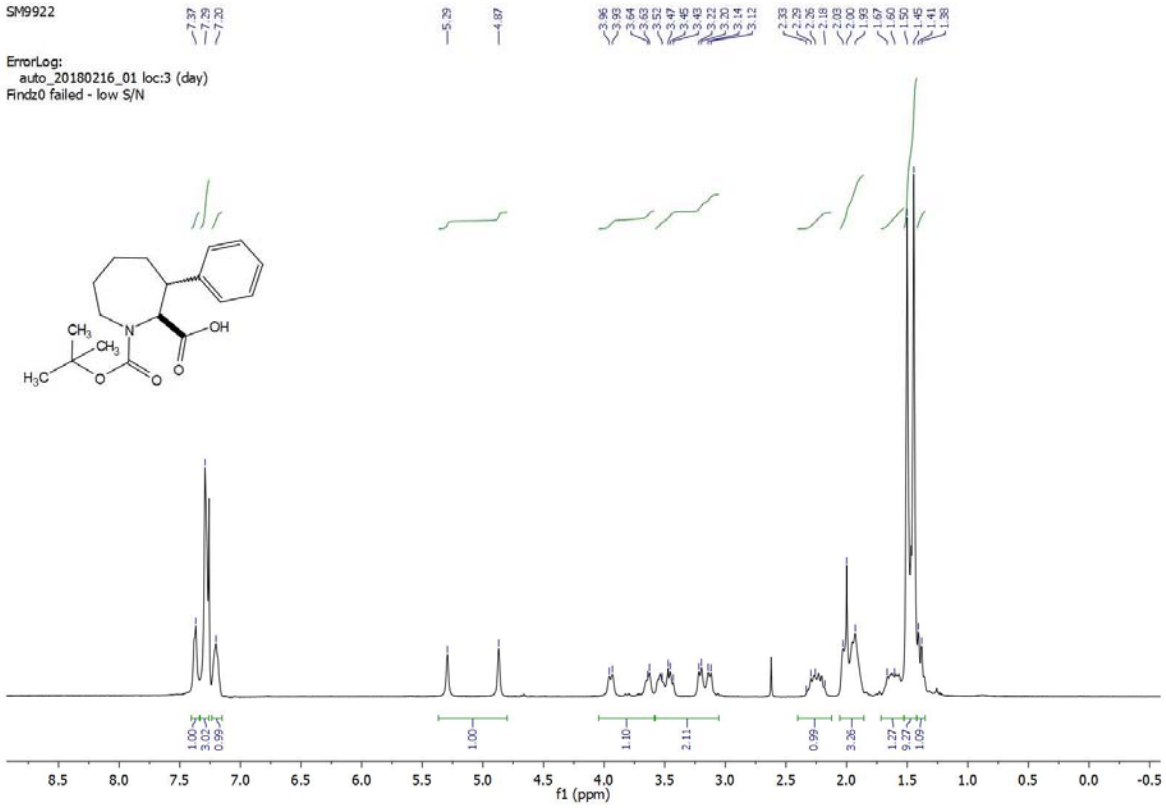
Compound Cbz – 52a





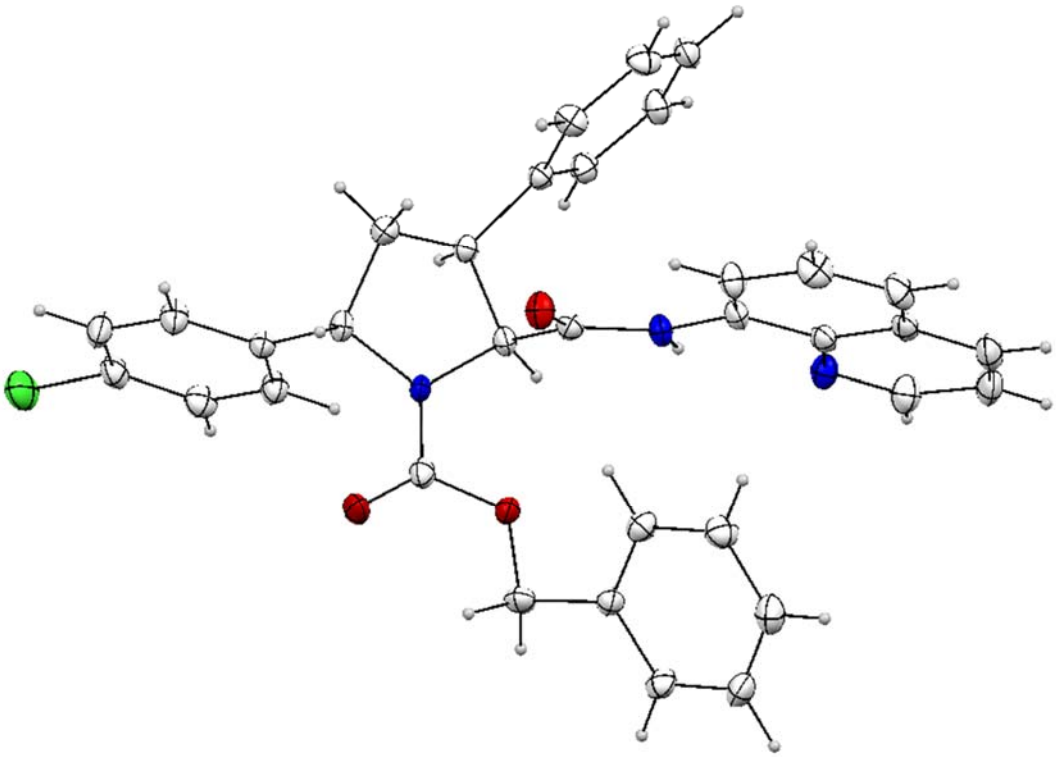
Compound Boc – 53





X-Ray

Compound 9a



Compound Cbz-2a*$HClO_4$