

Synthesis of Spirocyclic 1,2-Diamines by Dearomatising Intramolecular Diamination of Phenols

Anthony Aimon, Mark J. =. Dow, Abigail R. Hanby, Ephraim A. Okolo, Christopher M. Pask,
Adam Nelson* and Stephen P. Marsden*

Supporting Information

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General Experimental

All non-aqueous reactions were performed under an atmosphere of nitrogen unless otherwise stated. Water-sensitive reactions were performed in oven-dried glassware, cooled under nitrogen before use. Solvents were removed *in vacuo* using a Büchi rotary evaporator and a Vacuubrand PC2001 Vario diaphragm pump. A Genevac EZ-2 Elite centrifugal evaporator was used for the removal of MeOH–H₂O after Mass-Directed purification. Tetrahydrofuran (THF), CH₂Cl₂, toluene and CH₃CN were dried and purified by means of a Pure Solv MD solvent purification system (Innovative Technology Inc.). Anhydrous *N,N*-dimethylacetamide (DMA), *N,N*-dimethylformamide (DMF) and 1,4-dioxane was obtained in SureSeal bottles from Sigma-Aldrich. All other solvents used were of chromatography or analytical grade. Petrol refers to petroleum spirit (b.p. 40-60 °C). Commercially available starting materials were obtained from Sigma-Aldrich, Fluka, Acros or Alfa-Aesar and were used without purification unless stated.

Thin layer chromatography (TLC) was carried out on aluminium backed silica (Merck silica gel 60 F₂₅₄) plates supplied by Merck. Visualisation of the plates was achieved using an ultraviolet lamp ($\lambda_{\text{max}} = 254 \text{ nm}$), KMnO₄, anisaldehyde or ninhydrin. LCMS analysis was generally carried out on an Agilent 1200 series LC system comprising a Bruker HCT Ultra ion trap mass spectrometer. The solvent system used was CH₃CN/H₂O + 0.1% formic acid with a Phenomenex Luna C18 50 × 2 mm 5 micron column.

Flash chromatography was carried out using silica gel 60 (60-63 μm particles) supplied by Merck or using Biotage silica or ISOLUTE C₁₈ pre-packed cartridges on a Flashmaster II or CombiFlash Companion. Strong cation exchange solid phase extraction (SCX-SPE) was carried out using pre-packed Discovery DSC-SCX cartridges supplied by Supelco. Mass-directed HPLC purification was carried out using an Agilent 1260 Infinity HPLC system comprising an Agilent 6120 Quadrupole LC/MS and Agilent G1968D active splitter.

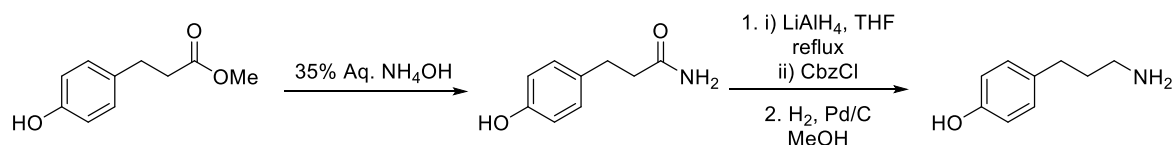
Optical rotation measurements were carried out at the sodium D-line (589 nm) on a Schmidt and Haensch H532 or an Optical Activity AA-1000 polarimeter instrument; concentrations are g/100 mL, temperatures given in °C, optical rotations are given in 10⁻¹degcm²g⁻¹ (units are omitted). Infrared spectra were recorded on a Perkin-Elmer One FT-IR spectrometer with absorption reported in wavenumbers (cm⁻¹). Chiral HPLC was carried out on either an Agilent 1100 or an Agilent Infinity 1290 series HPLC system. Racemic standards were obtained by preparing samples of both enantiomers and then combining in an approx. 1:1 ratio.

High resolution mass spectra (HRMS) were recorded on a Bruker Daltonics micrOTOF or Bruker MaXis Impact spectrometer with electrospray ionisation (ESI) source. Where EI ionisation was required, a Waters/Micromass GCT Premier spectrometer was used.

Proton (¹H) and carbon (¹³C) NMR spectral data were collected on a Bruker Advance 400, 500 or 600, Bruker DPX500 or DPX300 spectrometers. All ¹³C spectra are proton decoupled. Chemical shifts (δ) are quoted in parts per million (ppm) and referenced to the residual solvent peak. Coupling constants ($J =$) are quoted in Hertz (Hz) and splitting patterns reported in an abbreviated manner: app. (apparent), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). Assignments were made with the aid of COSY, DEPT-135, HMQC, HMBC and NOESY experiments.

Preparation of cyclisation precursors 1a-s, 3 and 5

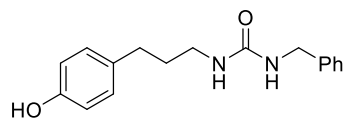
4-(3-Aminopropyl)phenol **S2**



Methyl 3-(4-hydroxyphenyl)propionate (90.0 g, 500 mmol) was dissolved in 35% ammonium hydroxide (250 mL) and stirred vigorously overnight at rt. The reaction slurry was carefully poured into ice and conc. HCl (250 mL). Additional conc. HCl was then carefully added (until pH 4-6). The solution was extracted with EtOAc (3 × 300 mL), dried (Na₂SO₄) and concentrated *in vacuo* to give a thick oil that solidified upon standing. Recrystallization from EtOAc gave the primary amide **S1** as pale yellow cuboids (71 g, 430 mmol, 86%); mp (EtOAc): 118.9-119.6 °C, {Lit.¹ 119-121 °C}; IR (ν_{\max} /cm⁻¹) 3390, 3178, 3036, 2956, 1649, 1624, 1513, 1449, 1422, 1408, 1372, 1235, 1112; ¹H NMR (500 MHz; MeOD) δ = 7.07 (2H, d, *J* = 8.5), 6.73 (2H, d, *J* = 8.5), 2.84 (2H, t, *J* = 7.5), 2.48 (2H, t, *J* = 7.5); ¹³C NMR (126 MHz; MeOD) δ = 178.4, 156.7, 132.9, 130.3, 116.1, 38.7, 31.9; HRMS (ESI⁺): Calculated for C₉H₁₂NO₂ ([M+H]⁺): 166.0862. Found: 166.0859.

To a suspension of lithium aluminum hydride (17.1 g, 450 mmol) in THF (225 mL) was added a solution of the primary amide (50.0 g, 300 mmol) in THF (150 mL) at 0 °C. The reaction mixture was warmed to rt and then refluxed for 48 h. The reaction mixture was cooled to 0 °C and the reaction was quenched drop-wise with water until effervescence ceased. Aqueous 2M NaOH (50 mL) was added followed by benzyl chloroformate (43 mL, 300 mmol). Upon consumption of the amine the reaction mixture was concentrated *in vacuo* and acidified with conc. HCl (until pH 6-7). The aqueous phase was extracted with EtOAc (3 × 250 mL), dried and concentrated *in vacuo*. The carbamate was passed through a short silica gel column eluting with EtOAc-hexanes (50:50), concentrated *in vacuo*, dissolved in MeOH (250 mL), Pd/C (2 g, 10% w/w) was added and H₂ was bubbled through using a balloon for 2 h. The solution was filtered and concentrated *in vacuo*. Dry-flash column chromatography, eluting with CH₂Cl₂/EtOH/NH₄OH (50:8:1), gave the amine **S2** (22.3 g, 147 mmol, 49%) as a pale yellow oil which solidifies upon standing. mp (CH₂Cl₂-EtOH): 91.1-91.7 °C {Lit.² 102 °C}; IR (ν_{\max} /cm⁻¹) 3328, 3279, 2850, 2500, 2206, 1600, 1483, 1247, 1230, 1169; ¹H NMR (500 MHz; MeOD) δ = 6.96 (2H, d, *J* = 8.5), 6.66 (2H, d, *J* = 8.5), 2.58 (2H, t, *J* = 7.3), 2.50 (2H, t, *J* = 7.3), 1.68 (2H, app quint, *J* = 7.4); ¹³C NMR (126 MHz; MeOD) δ = 156.8, 133.8, 130.3, 130.2, 116.3, 116.2, 42.0, 35.8, 33.3; HRMS (ESI⁺): Calculated for C₉H₁₄NO ([M+H]⁺): 152.1069. Found: 152.1069.

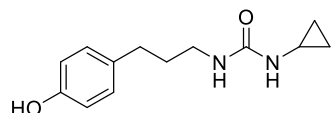
1-Benzyl-3-[3-(4-hydroxyphenyl)propyl]urea **1a**



Benzyl isocyanate (1.3 mL, 10.9 mmol, 1.1 eq) was added in one portion to the above amine **S2** (1.5 g, 9.9 mmol) in MeCN (40 mL). The reaction mixture was stirred at rt. After 16 h, the

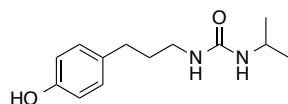
precipitate was collected and recrystallized from MeCN to give the urea as a colourless solid (2.2 g, 7.8 mmol, 79%); mp (MeCN) 104.9-106.7 °C; IR (ν_{\max} / cm^{-1}) 3427, 3337, 3032, 2924, 2479, 1608, 1558, 1514, 1491, 1440, 1429, 1360, 1254; ^1H NMR (500 MHz; MeOD) δ = 7.37 – 7.27 (4H, m), 7.27 – 7.18 (1H, m), 7.01 (2H, d, J = 8.5), 6.71 (2H, d, J = 8.5), 4.33 (2H, s), 3.16 (2H, t, J = 7.0), 2.56 (2H, t, J = 7.7 Hz), 1.76 (2H, app quint, J = 7.3); ^{13}C NMR (126 MHz; MeOD) δ = 181.7, 161.2, 156.4, 141.3, 133.9, 130.2, 130.3, 129.4, 128.2, 128.1, 127.9, 116.1, 44.7, 40.6, 33.4, 33.2; HRMS (ESI $^+$): Calculated for $\text{C}_{17}\text{H}_{21}\text{N}_2\text{O}_2$ ([M+H] $^+$): 285.1597. Found: 285.1593.

3-Cyclopropyl-1-[3-(4-hydroxyphenyl)propyl]urea 1b



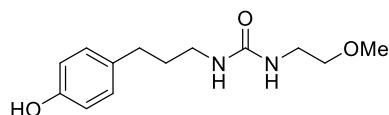
Cyclopropyl isocyanate (606 mg, 7.30 mmol, 1.1 eq) was added in one portion to the amine **S2** (1.0 g, 6.6 mmol) in MeCN (25 mL). Sodium hydroxide 2M (20 mL) was added and the reaction mixture was heated to reflux for 1 h. After concentration *in vacuo*, the reaction mixture was neutralized using aqueous hydrochloric acid (2M). The phases were separated and the aqueous phase was extracted with EtOAc (3 × 20 mL). The organic extracts were combined, dried over Na_2SO_4 and concentrated *in vacuo*. Flash column chromatography, eluting with EtOAc gave the urea as a colourless oil (1.3 g, 5.4 mmol, 83%); IR (ν_{\max} / cm^{-1}) 3327, 3011, 2929, 2856, 1639, 1554, 1514, 1453, 1231; ^1H NMR (400 MHz; MeOD) δ = 7.03 (2H, d, J = 8.5), 6.72 (2H, d, J = 8.5), 3.17 (2H, t, J = 7.0), 2.55 (2H, t, J = 7.4), 2.44 (1H, tt, J = 6.9, 3.8), 1.78 (2H, app quint, J = 7.4), 0.70 (2H, td, J = 6.9, 5.0), 0.50 – 0.43 (2H, m); ^{13}C NMR (101 MHz; MeOD) δ = 162.1, 156.4, 133.9, 130.3, 116.1, 40.6, 33.4, 33.3, 23.1, 7.5; HRMS (ESI $^+$): Calculated for $\text{C}_{13}\text{H}_{19}\text{N}_2\text{O}_2$ ([M+H] $^+$): 235.1441. Found: 235.1439.

1-[3-(4-Hydroxyphenyl)propyl]-3-isopropylurea 1c



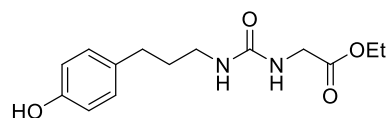
Isopropyl isocyanate (1.64 mL, 16.7 mmol, 1.01 eq.) was added to a solution of the amine **S2** (2.50 g, 16.6 mmol, 1.0 eq.) in anhydrous THF and the mixture was refluxed for 1 h. The reaction mixture was evaporated *in vacuo*. Flash chromatography with 50 – 100% EtOAc in hexane afforded the product as a colourless oil (3.24 g, 13.6 mmol, 83% yield); R_f = 0.55 (100% EtOAc). IR ν_{\max} (neat)/ cm^{-1} : 3334, 3014, 2969, 2931, 2872, 1558, 1514, 1455, 1240. ^1H NMR (500 MHz, MeOD) δ = 7.02 (2H, d, J = 8.4), 6.74 (2H, d, J = 8.4), 3.82 (1H, hept, J = 6.5), 3.13 (2H, t, J = 7.0), 2.53 (2H, t, J = 7.5), 1.76 (2H, quint, J = 7.5), 1.14 (6H, d, J = 6.6). ^{13}C NMR (125 MHz, MeOD): δ = 160.7, 156.5, 134.0, 130.4, 116.3, 43.0, 40.6, 33.6, 33.3, 23.7. HRMS (ESI): $\text{C}_{13}\text{H}_{21}\text{N}_2\text{O}_2$ [M + H] $^+$: calculated 237.1598, found 237.1592.

1-[3-(4-Hydroxyphenyl)propyl]-3-(2-methoxyethyl)urea 1d



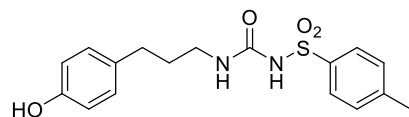
Following a procedure adapted from Padiya *et al.*,¹ to a solution of 2-methoxyethylamine (90 mg, 1.2 mmol) in water (10 mL) at 0 °C was added CDI (194 mg, 1.20 mmol, 1.0 eq). After 10 min 4-(3-aminopropyl)phenol **S2** (150 mg, 1.00 mmol) was added in a MeCN–H₂O mixture (2 mL, 50:50). The reaction mixture was stirred for 6 h then EtOAc (20 mL) was added and the phases were separated. The aqueous phase was extracted with EtOAc (3 × 10 mL). Flash column chromatography, eluting with EtOAc gave the urea (78 mg, 0.31 mmol, 31%) as a colourless oil. IR (ν_{\max} /cm⁻¹) 3336, 2929, 2865, 1627, 1613, 1557, 1512, 1449, 1363, 1233, 1108, 1090; ¹H NMR (500 MHz; MeOD) δ = 6.95 (2H, d, *J* = 8.4), 6.69 (2H, d, *J* = 8.4), 3.40 (2H, t, *J* = 5.0), 3.30 (3H, s), 3.25 (2H, t, *J* = 5.0), 3.08 (2H, t, *J* = 7.0), 2.99 (1H, br s), 2.94 (1H, br s), 2.50 (2H, t, *J* = 7.6), 1.70 (2H, app quint, *J* = 7.2); ¹³C NMR (126 MHz; MeOD) δ = 156.5, 147.7, 133.9, 130.3, 116.1, 73.1, 58.9, 40.8, 40.5, 33.4, 33.2; HRMS (ESI⁺): Calculated for C₁₃H₂₁N₂O₃ ([M+H]⁺): 253.1546. Found: 253.1546.

Ethyl 2-([3-(4-hydroxyphenyl)propyl]carbamoyl)amino)acetate **1e**



Ethyl isocyanatoacetate (462 mg, 3.6 mmol, 1.1 eq) was added in one portion to the amine **S2** (500 mg, 3.3 mmol) in MeCN (14 mL). The reaction mixture was stirred 5 h at rt. The reaction was concentrated *in vacuo*, water (10 mL) was added and the reaction was extraction with EtOAc (3 × 25 mL), dried (Na₂SO₄), filtered and concentrated *in vacuo*. Column chromatography, eluting with CH₂Cl₂–MeOH (99/1 → 95/5) have the urea as a colourless oil (610 mg, 2.17 mmol, 66%); IR (ν_{\max} /cm⁻¹) 2921, 1741, 1613, 1532, 1514, 1263, 1217, 731, 703; ¹H NMR (300 MHz; MeOD) δ = 7.04 (2H, d, *J* = 8.5), 6.72 (2H, d, *J* = 8.5), 4.20 (2H, q, *J* = 7.1), 3.89 (2H, s), 3.15 (2H, t, *J* = 7.9), 2.57 (2H, t, *J* = 6.7), 1.77 (2H, tt, *J* = 7.5, 6.5), 1.29 (3H, t, *J* = 7.1); ¹³C NMR (75 MHz, MeOD) δ = 172.8, 161.1, 156.4, 133.9, 130.3, 116.1, 62.1, 42.8, 40.6, 33.4, 33.2, 14.5; HRMS (ESI⁺): Calculated for C₁₄H₂₀N₂NaO₄ ([M+Na]⁺): 303.1315. Found: 303.1309.

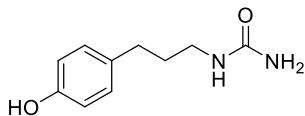
3-[3-(4-Hydroxyphenyl)propyl]-1-(4-methylbenzenesulfonyl)urea **1f**



Tosyl isocyanate (1.44 g, 7.3 mmol, 1.1 eq) was added in one portion to the amine **S2** (1.00 g, 6.6 mmol) in MeCN (33 mL). The reaction mixture was stirred 5 h at rt. Water (5 mL) was added and the reaction was concentrated *in vacuo*, extracted with EtOAc (3 × 25 mL), dried (Na₂SO₄), filtered and concentrated *in vacuo*. Column chromatography, eluting with EtOAc–hexanes (50:50) gave the sulfonyl urea as a pale yellow oil (2.04 g, 5.9 mmol, 89%); IR (ν_{\max} /cm⁻¹) 3436, 3333, 3099, 2921, 1667, 1614, 1595, 1548, 1515, 1451, 1439, 1327, 1154, 1086; ¹H NMR δ (400 MHz, MeOD) δ = 7.87–7.83 (2H, d, *J* = 8.4), 7.37 (2H, d, *J* = 8.4), 6.90 (2H, d, *J* = 8.5), 6.66 (2H, d, *J* = 8.5), 3.08 (2H, t, *J* = 6.9), 2.42–2.37 (5H, m (includes 3H, s at 2.40)), 1.70–1.60 (2H, m); ¹³C NMR (101 MHz, MeOD) δ = 156.4, 153.8, 145.7, 138.6, 133.5, 130.6,

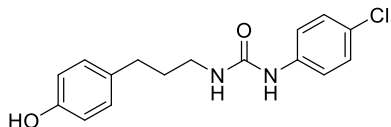
130.2, 128.5, 116.1, 40.3, 32.9, 32.6, 21.5; HRMS (ESI⁺): Calculated for C₁₇H₂₁N₂O₄S ([M+H]⁺): 349.1216. Found: 349.1212.

[3-(4-Hydroxyphenyl)propyl]urea **1g**



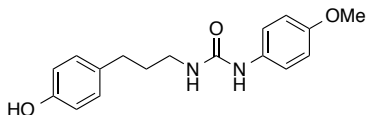
Potassium cyanate (324 mg, 4 mmol) was added to a solution of the phenol **S2** (500 mg, 3.3 mmol) in HCl 2M (5 mL), the reaction was stirred for 16h. The reaction was extracted with EtOAc (3 × 25 mL), dried (Na₂SO₄), filtered and concentrated *in vacuo*. Column chromatography, eluting with CH₂Cl₂—MeOH (95/5) gave the urea as a colourless solid (582 mg, 2.99 mmol, 90%); IR (ν_{max}/cm⁻¹) 3198, 1651, 1591, 1545, 1509, 1451, 1374, 1348; ¹H NMR δ (400 MHz, MeOD) δ = 7.00 (2H, d, *J* = 8.5), 6.69 (2H, d, *J* = 8.5), 3.09 (2H, t, *J* = 7.0), 2.54 (2H, t, *J* = 7.7), 1.78 – 1.69 (2H, m); ¹³C NMR (101 MHz, MeOD) δ = 162.3, 156.4, 133.8, 130.2, 116.1, 40.5, 33.3, 33.1; HRMS (ESI⁺): Calculated for C₁₀H₁₅N₂O₂ ([M+H]⁺): 195.1128. Found: 195.1123.

1-(4-Chlorophenyl)-3-[3-(4-hydroxyphenyl)propyl]urea **1h**



4-Chlorophenyl isocyanate (447 mg, 2.91 mmol, 1.1 eq) was added in one portion to the amine **S2** (400 mg, 2.64 mmol) in MeCN (14 mL). The reaction mixture was stirred 5 h at rt. The precipitated solid was filtered using vacuum filtration and washed with MeCN. The solid was dried under vacuum to give the urea as a colourless solid (412 mg, 1.35 mmol, 51%). m.p. (MeCN) 140.8–141.6 °C; IR (ν_{max}/cm⁻¹) 3321, 2941, 2865, 2466, 1617, 1513, 1495, 1469, 1245, 1089; ¹H NMR (400 MHz; MeOD) δ = 7.33 (2H, d, *J* = 8.9), 7.21 (2H, d, *J* = 8.9), 7.00 (2H, d, *J* = 8.5), 6.70 (2H, d, *J* = 8.5), 3.17 (2H, t, *J* = 7.0), 2.56 (2H, app t, *J* = 7.7), 1.77 (2H, app quint, *J* = 7.3); ¹³C NMR (101 MHz; MeOD) δ = 158.0, 156.4, 139.9, 133.7, 130.2, 129.6, 128.0, 121.2, 116.1, 40.3, 33.2 (2 signals); HRMS (ESI⁺): Calculated for C₁₆H₁₈³⁵ClN₂O₂ ([M+H]⁺): 305.1051. Found: 305.1053.

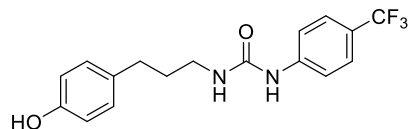
1-(3-(4-Hydroxyphenyl)propyl)-3-(4-methoxyphenyl)urea **1i**



4-Methoxyphenyl isocyanate (0.30 mL, 2.30 mmol, 1.01 eq.) was added to a solution of the amine **S2** (345 mg, 2.28 mmol, 1.0 eq.) in anhydrous THF and the mixture was refluxed for 1 h. The reaction mixture was evaporated *in vacuo*. Flash chromatography with 50 – 100% EtOAc in hexane afforded the title compound as a brown oil (497 mg, 1.66 mmol, 73% yield); R_f = 0.41 (70% EtOAc in hexane). IR ν_{max} (neat)/cm⁻¹: 3308, 3053, 2935, 2837, 1647, 1554,

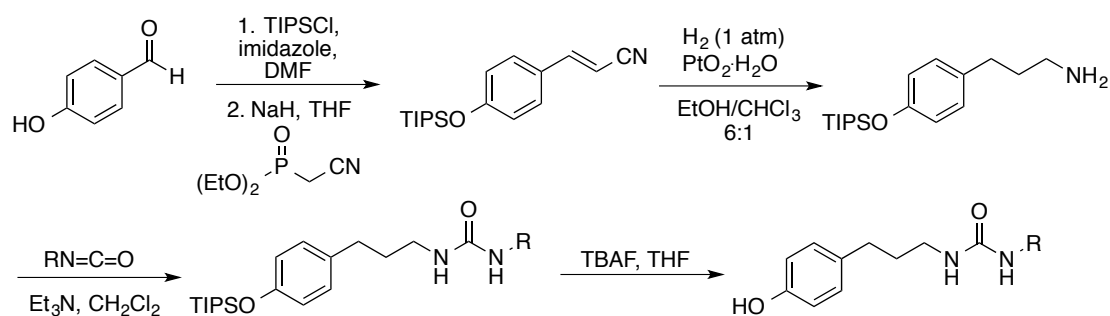
1509, 1441, 1228. ^1H NMR δ (300 MHz, MeOD) δ = 7.10 (2H, d, J = 9.0), 6.90 (2H, d, J = 8.4), 6.72 (2H, d, J = 9.0), 6.59 (2H, d, J = 8.7), 3.63 (3H, s), 3.07 (2H, t, J = 6.9), 2.45 (2H, t, J = 7.2), 1.67 (2H, quint, J = 7.3). ^{13}C NMR (75 MHz, MeOD) δ = 158.8, 157.0, 156.4, 133.8, 133.6, 130.2, 122.8, 116.1, 115.0, 55.8, 40.4, 33.3, 33.2. HRMS (ESI): $\text{C}_{17}\text{H}_{21}\text{N}_2\text{O}_3$ [$\text{M} + \text{H}^+$]: calculated 301.1547, found 301.1543.

3-[3-(4-Hydroxyphenyl)propyl]-1-[4-(trifluoromethyl)phenyl]urea **1j**

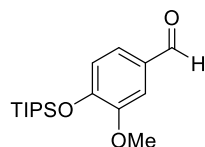


4-(Trifluoromethyl)phenyl isocyanate (1.44 g, 7.30 mmol, 1.1 eq) was added in one portion to the amine **S2** (1.0 g, 6.6 mmol) in MeCN (33 mL). The reaction mixture was stirred overnight at rt and concentrated *in vacuo* to give the crude sulfonyl urea. Flash column chromatography, eluting with EtOAc gave the urea as a colourless oil (1.8 g, 5.2 mmol, 78%); IR (ν_{max} / cm^{-1}) 3336, 2937, 1657, 1600, 1546, 1512, 1409, 1318, 1231, 1161, 1107, 1065, 1014; ^1H NMR δ (400 MHz; MeOD) 7.57 – 7.51 (4H, m), 7.04 (2H, d, J = 8.5), 6.72 (2H, d, J = 8.5), 3.22 (2H, t, J = 7.0), 2.60 (2H, app t, J = 7.0), 1.22 (2H, app quint, J = 7.0); ^{13}C NMR (101 MHz; MeOD) δ = 157.7, 156.4, 144.7, 133.7, 130.3, 126.9 (q, J = 4), 125.9 (q, J = 270), 124.5 (q, J = 32), 119.1, 116.2, 40.3, 33.2, 33.1; HRMS (ESI $^+$): Calculated for $\text{C}_{17}\text{H}_{18}\text{F}_3\text{N}_2\text{O}_2$ ([$\text{M} + \text{H}^+$]): 339.1310. Found: 339.1314.

Preparation of 2-methoxy-substituted substrates **1k-n**



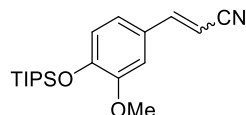
3-Methoxy-4-[[tris(propan-2-yl)silyl]oxy]benzaldehyde **S3**



Vanillin (10.0 g, 65.7 mmol) was dissolved in DMF (35 mL). Triisopropylsilyl chloride (17 mL, 79.4 mmol, 1.21 eq) was added and the reaction mixture was cooled down to 0 °C before the addition of imidazole (5.37 g, 78.9 mmol, 1.20 eq). The reaction mixture was warmed to rt and stirred overnight. EtOAc (250 mL) and H₂O (100 mL) were added. The phases were separated and the organic phase was successively washed with H₂O (2 × 100 mL), aqueous HCl (1M, 100 mL), aqueous saturated NaHCO₃ (100 mL) and brine (100 mL). The organic

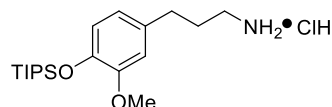
phase was then dried over Na_2SO_4 , filtered and concentrated *in vacuo*. Flash column chromatography (SiO_2 , hexane–EtOAc, 95:5) gave the title compound (19.5 g, 63.2 mmol, 96%) as a colourless oil. IR ($\nu_{\text{max}}/\text{cm}^{-1}$) 2943, 2866, 1696, 1591, 1505, 1462, 1284, 1192, 1123, 1070; ^1H NMR (400 MHz, CDCl_3) δ = 9.83 (1H, d, J = 0.6), 7.39 (1H, d, J = 1.8), 7.35 (1H, ddd, J = 8.0, 1.8, 0.6), 6.97 (1H, d, J = 8.0), 3.86 (3H, s), 1.34 – 1.20 (3H, m), 1.09 (18H, d, J = 7.5); ^{13}C NMR (101 MHz, CDCl_3) δ = 191.1, 151.9, 151.7, 130.7, 126.3, 120.2, 110.2, 55.5, 17.9, 13.0; HRMS (ESI^+): Calculated for $\text{C}_{17}\text{H}_{29}\text{O}_3\text{Si}$ ($[\text{M}+\text{H}]^+$): 309.1880. Found: 309.1880.

(2E/Z)-3-(3-Methoxy-4-{{tris(propan-2-yl)silyl}oxy}phenyl)prop-2-enenitrile S4



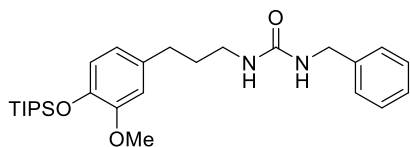
Following a procedure adapted from Pouységu *et al.*,² to a solution of THF (150 mL) at 0 °C was added NaH (60% in mineral oil, 2.90 g, 72.5 mmol, 1.15 eq) portionwise and the suspension was stirred for 10 min. Diethylcyanophosphonate (11.8 mL, 72.9 mmol, 1.16 eq) was added dropwise at 0 °C and the reaction mixture was stirred 10 min before the addition of the above aldehyde **S3** (19.4 g, 62.9 mmol) in THF (46 mL). The reaction mixture was stirred for 2 h at 0 °C, and MTBE was added (300 mL) before filtration of the reaction mixture directly over a pad of silica washed with MTBE. The nitrile (20.5 g, 61.8 mmol, 98%) was taken to the next step without further purification required. Alternatively the nitriles could be purified by flash column chromatography (SiO_2 , hexane–EtOAc; 95:5). IR ($\nu_{\text{max}}/\text{cm}^{-1}$) 2940, 2864, 2208, 1593, 1509, 1464, 1280, 1163; **Major E isomer** ^1H NMR (400 MHz, CDCl_3) δ = 7.30 (1H, d, J = 16.6, propene 3-H), 6.93 (1H, dd, J = 8.1, 2.1, Ar 6-H), 6.90 (1H, d, J = 2.1, Ar 2-H), 6.86 (1H, d, J = 8.1, Ar 5-H), 5.70 (1H, d, J = 16.5, propene 2-H), 3.83 (3H, s, OMe), 1.30 – 1.20 (3H, m, 3 × TIPS-H), 1.09 (18H, d, J = 7.3, 6 × TIPS- H_3); ^{13}C NMR (101 MHz, CDCl_3) δ = 151.3, 150.4, 148.9, 127.1, 121.5, 120.6, 118.7, 110.1, 93.4, 55.5, 17.8, 12.9; **Minor E isomer** (400 MHz, CDCl_3) δ = 7.58 (1H, d, J = 2.2), 7.14 (1H, dd, J = 8.2, 2.2), 7.00 (1H, d, J = 12.1), 6.95 – 6.85 (1H, m (massif with maj = or isomer)), 5.26 (1H, d, J = 12.1), 3.86 (3H, s), 1.33 – 1.20 (3H, m), 1.09 (18H, d, J = 7.2); ^{13}C NMR (101 MHz, CDCl_3) δ = (1 peak missing, most probably hidden behind carbon peak of the major isomer) 151.0, 148.5, 127.3, 123.9, 120.3, 118.2, 111.3, 91.5, 17.7, 12.3; HRMS (ESI^+): Calculated for $\text{C}_{19}\text{H}_{30}\text{NO}_2\text{Si}$ ($[\text{M}+\text{H}]^+$): 332.2040. Found: 332.2038.

Amine salt S5

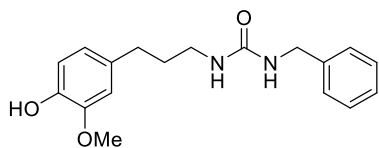


Following a procedure adapted from Pouységu *et al.*,² to a mixture of EtOH– CHCl_3 (6:1, 56 mL) was added the above unsaturated nitrile (3.89 g, 11.8 mmol). $\text{PtO}_2 \cdot \text{H}_2\text{O}$ (187 mg, 0.823 mmol, 0.07 eq) was added and the reaction mixture was stirred under an atmosphere (balloon) of H_2 overnight. MeOH (100 mL) was added and the stirring was stopped. After 30 min the reaction mixture was removed from the reaction flask without the solid platinum residue. After concentration *in vacuo* the amine salt was used directly without further purification.

1-Benzyl-3-[3-(4-hydroxy-3-methoxyphenyl)propyl]urea 1k

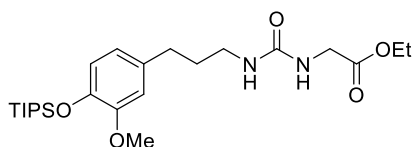


To a solution of the crude amine salt **S5** (1.79 g, ≤ 4.80 mmol) in CH_2Cl_2 (20 mL) at 0°C was successively added Et_3N (940 μL , 6.74 mmol, ≥ 1.40 eq) and benzyl isocyanate (600 μL , 4.86 mmol, ≥ 1.01 eq). The reaction mixture was stirred for 30 min at rt. Saturated aqueous NH_4Cl (20 mL) and H_2O (20 mL) were added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (2×30 mL). The organic extracts were washed with brine (20 mL), dried over Na_2SO_4 , filtered and concentrated *in vacuo*. Flash column chromatography (SiO_2 , hexane– EtOAc , 8:2 to 6:4) afforded the desired urea **S6** as a colourless oil (1.37 g, 2.90 mmol, 60% over two steps). IR ($\nu_{\text{max}}/\text{cm}^{-1}$) 3331, 2942, 2865, 1625, 1580, 1513, 1453, 1316, 1272, 1156; ^1H NMR (400 MHz; CDCl_3) δ = 7.32 – 7.17 (5H, m), 6.75 (1H, d, J = 8.0), 6.60 (1H, d, J = 1.6), 6.60 (1H, dd, J = 8.0, 1.6), 5.31 – 5.05 (1H, m), 5.01 – 4.74 (1H, m), 4.27 – 4.24 (2H, m), 3.74 (3H, s), 3.15 – 3.06 (2H, m), 2.54 – 2.45 (2H, m), 1.76 – 1.65 (2H, m), 1.30 – 1.18 (3H, m), 1.08 (18H, d, J = 7.2); ^{13}C NMR (101 MHz; CDCl_3) δ = 158.7, 150.8, 143.7, 139.5, 134.8, 128.6, 127.4, 127.2, 120.3, 120.3, 112.6, 55.6, 44.4, 40.2, 32.9, 32.1, 18.0, 14.3; HRMS (ESI^+): Calculated for $\text{C}_{27}\text{H}_{43}\text{N}_2\text{O}_3\text{Si}$ ($[\text{M}+\text{H}]^+$): 471.3037. Found: 471.3036.

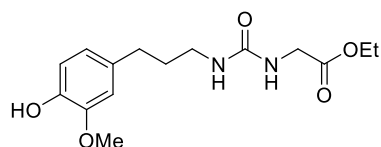


To a solution of the above urea (1.22 g, 2.58 mmol) in THF (5 mL) at 0°C was added $n\text{Bu}_4\text{NF}$ (1M in THF, 2.8 mL, 2.8 mmol, 1.1 eq) dropwise. The reaction mixture warmed to rt and stirred for 2 h. After concentration *in vacuo* the residue was purified by flash column chromatography (SiO_2 , CH_2Cl_2 then CH_2Cl_2 – MeOH , 98:2 to 96:4) to afford the desired phenol as a colourless solid (803 mg, 2.55 mmol, 99%). m.p. (CH_2Cl_2) 93.2 – 93.9°C ; IR ($\nu_{\text{max}}/\text{cm}^{-1}$) 3506, 3305, 3030, 2928, 2858, 1621, 1570, 1515, 1437, 1311, 1231, 1275, 1231, 1120, 1026; ^1H NMR (400 MHz; CDCl_3) δ = 7.31–7.18 (5H, m), 6.80 (1H, d, J = 8.0), 6.62 (1H, d, J = 1.7), 6.58 (1H, dd, J = 8.0, 1.7), 5.88 (1H, s), 5.42 (1H, br. s), 5.14 (1H, br. s), 4.26 (2H, d, J = 5.8), 3.81 (3H, s), 3.11 (2H, app q, J = 6.7), 2.49 (2H, t, J = 7.7), 1.70 (2H, app tt, J = 7.4, 7.4); ^{13}C NMR (101 MHz; CDCl_3) δ = 158.9, 146.6, 143.9, 139.5, 133.6, 128.6, 127.3, 127.3, 120.9, 114.4, 111.2, 55.9, 44.3, 40.0, 32.9, 32.1; HRMS (ESI^+): Calculated for $\text{C}_{18}\text{H}_{23}\text{N}_2\text{O}_3$ ($[\text{M}+\text{H}]^+$): 315.1703. Found: 315.1699.

Ethyl 2-([3-(4-hydroxy-3-methoxyphenyl)propyl]carbamoyl)amino)acetate 1l

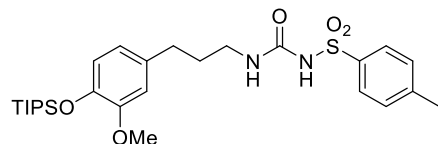


To a solution of the crude amine salt **S5** (840 mg, ≤ 2.25 mmol) in CH_2Cl_2 (15 mL) at 0°C was successively added Et_3N (470 μL , 3.37 mmol, ≥ 1.50 eq) and ethyl isocyanatoacetate (275 μL , 2.45 mmol, ≥ 1.09 eq). The reaction mixture was stirred for 2 h at rt. Saturated aqueous NH_4Cl (15 mL) and H_2O (10 mL) were added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (2×20 mL). The organic extracts were washed with brine (20 mL), dried over Na_2SO_4 , filtered and concentrated *in vacuo*. Flash column chromatography (SiO_2 , hexane– EtOAc , 7:3 to 5:5) afforded the desired urea **S7** as a colourless oil (627 mg, 1.40 mmol, 62% over two steps). IR ($\nu_{\text{max}}/\text{cm}^{-1}$) 3368, 2941, 2865, 1741, 1625, 1574, 1511, 1416, 1278, 1191, 1156, 1030; ^1H NMR (400 MHz; CDCl_3) δ = 6.76 (1H, d, J = 8.0), 6.65 (1H, d, J = 1.9), 6.58 (1H, dd, J = 8.0 and 1.9), 4.97 (1H, t, J = 5.2), 4.72 (1H, t, J = 5.5), 4.18 (2H, q, J = 7.1), 3.97 (2H, d, J = 5.4), 3.77 (3H, s), 3.19 (2H, td, J = 6.8, 5.5), 2.56 (2H, t, J = 7.7), 1.84 – 1.75 (2H, m), 1.31 – 1.19 (6H, m), 1.08 (18H, d, J = 7.2); ^{13}C NMR (101 MHz; CDCl_3) δ = 171.5, 157.9, 150.8, 143.7, 134.7, 120.3, 120.3, 112.6, 61.4, 55.6, 42.3, 40.3, 32.9, 32.0, 18.0, 14.3, 13.0; HRMS (ESI^+): Calculated for $\text{C}_{24}\text{H}_{43}\text{N}_2\text{O}_4\text{Si}$ ($[\text{M}+\text{H}]^+$): 467.2935. Found: 467.2934.



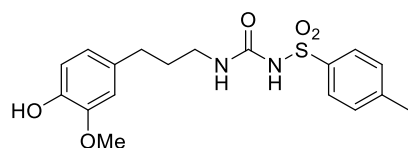
To a solution of the above urea (627 mg, 1.40 mmol) in THF (2 mL) at 0°C was added $n\text{Bu}_4\text{NF}$ (1M in THF, 1.6 mL, 1.6 mmol, 1.1 eq) dropwise. The reaction mixture warmed to rt and stirred for 2 h. After concentration *in vacuo* the residue was purified by flash column chromatography (SiO_2 , CH_2Cl_2 then CH_2Cl_2 – MeOH , 98:2 to 96:4) to afford the desired phenol as a colourless oil (397 mg, 1.28 mmol, 91%). IR ($\nu_{\text{max}}/\text{cm}^{-1}$) 3365, 2859, 1737, 1637, 1562, 1513, 1451, 1374, 1268, 1192, 1027; ^1H NMR (400 MHz; CDCl_3) δ = 6.81 (1H, d, J = 8.0), 6.67 (1H, d, J = 1.7), 6.64 (1H, dd, J = 8.0, 1.7), 5.60 (1H, s), 5.08 (1H, t, J = 5.2), 4.82 (1H, t, J = 5.6), 4.18 (2H, q, J = 7.1), 3.97 (2H, d, J = 5.4), 3.85 (3H, s), 3.19 (2H, td, J = 6.8, 5.5), 2.56 (2H, t, J = 7.7), 1.82 – 1.73 (2H, m), 1.26 (3H, t, J = 7.1); ^{13}C NMR (101 MHz; CDCl_3) δ = 171.6, 158.1, 146.6, 143.9, 133.6, 120.9, 114.4, 111.1, 61.5, 56.0, 42.3, 40.2, 32.9, 32.1, 14.2; HRMS (ESI^+): Calculated for $\text{C}_{15}\text{H}_{23}\text{N}_2\text{O}_5$ ($[\text{M}+\text{H}]^+$): 311.1601. Found: 311.1599.

3-[3-(4-Hydroxy-3-methoxyphenyl)propyl]-1-(4-methylbenzenesulfonyl)urea **1m**



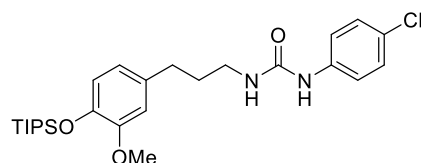
To a solution of the crude amine salt **S5** (827 mg, ≤ 2.22 mmol) in CH_2Cl_2 (15 mL) at 0°C was successively added Et_3N (470 μL , 3.37 mmol, ≥ 1.52 eq) and *p*-toluenesulfonylisocyanate (370 μL , 2.42 mmol, ≥ 1.09 eq). The reaction mixture was stirred for 2 h at rt. Saturated aqueous NH_4Cl (15 mL) and H_2O (10 mL) were added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (2×20 mL). The organic extracts were washed with Brine

(20 mL), dried over Na₂SO₄, filtered and concentrated *in vacuo*. Flash column chromatography (SiO₂, hexane–EtOAc, 7:3 to 5:5) afforded the desired urea **58** as a colourless oil (554 mg, 1.03 mmol, 47% over two steps). IR (ν_{\max} /cm⁻¹) 3346, 2942, 2865, 1662, 1544, 1513, 1417, 1342, 1274, 1232, 1159, 1090; ¹H NMR (400 MHz; CDCl₃) δ = 8.51 (1H, br s), 7.76 (2H, d, *J* = 8.3), 7.28 (2H, d, *J* = 8.3), 6.78 (1H, d, *J* = 8.0), 6.62 (1H, d, *J* = 1.9), 6.55 (1H, dd, *J* = 8.0 and 1.9), 3.78 (3H, s), 3.22 (2H, dt, *J* = 7.0, 6.2), 2.50 (2H, app t, *J* = 7.6), 2.41 (3H, s), 1.83 – 1.73 (2H, m), 1.30 – 1.19 (3H, m), 1.09 (18H, d, *J* = 7.2); ¹³C NMR (101 MHz; CDCl₃) δ = 151.8, 150.8, 144.8, 143.9, 136.9, 134.7, 130.1, 127.0, 120.4, 120.3, 112.6, 55.6, 39.8, 32.6, 31.3, 21.7, 18.0, 13.0; HRMS (ESI⁺): Calculated for C₂₇H₄₃N₂O₅SSi ([M+H]⁺): 535.2656. Found: 535.2653.



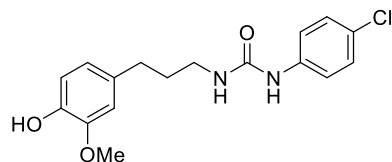
To a solution of the above urea (554 mg, 1.04 mmol) in THF (2 mL) at 0 °C was added *n*Bu₄NF (1M in THF, 1.2 mL, 1.2 mmol, 1.15 eq) dropwise. The reaction mixture warmed to rt and stirred for 2 h. After concentration *in vacuo* the residue was purified by flash column chromatography (SiO₂, CH₂Cl₂ then CH₂Cl₂–MeOH, 98:2 to 96:4) to afford the desired phenol as a colourless solid (332 mg, 0.88 mmol, 84%). m.p. (CH₂Cl₂) 128.4–129.0 °C; IR (ν_{\max} /cm⁻¹) 3353, 2937, 2945, 1699, 1598, 1514, 1514, 1451, 1337, 1269, 1233, 1157, 1089; ¹H NMR (400 MHz; CD₃OD) δ = 7.85 (2H, d, *J* = 8.3), 7.36 (2H, d, *J* = 8.3), 6.69 – 6.65 (2H, m), 6.52 (1H, dd, *J* = 8.0 and 1.7), 3.79 (3H, s), 3.08 (2H, t, *J* = 6.9), 2.45 – 2.38 (5H, m includes 2.40, s), 1.68 (2H, app quint, *J* = 7.1); ¹³C NMR (101 MHz; CD₃OD) δ = 153.9, 148.8, 145.7, 145.6, 138.7, 134.2, 130.6, 128.5, 121.7, 116.1, 113.0, 56.3, 40.3, 33.4, 32.5, 21.5; HRMS (ESI⁺): Calculated for C₁₈H₂₃N₂O₅S ([M+H]⁺): 379.1322. Found: 379.1313.

1-(4-Chlorophenyl)-3-[3-(4-hydroxy-3-methoxyphenyl)propyl]urea **1n**



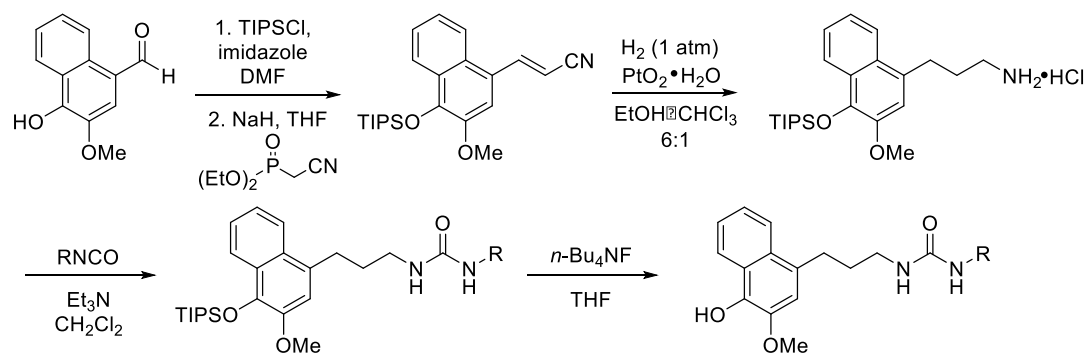
To a solution of the crude amine salt **55** (345 mg, ≤0.925 mmol) in CH₂Cl₂ (8 mL) at 0 °C was successively added Et₃N (170 μL, 1.22 mmol, ≥1.32 eq) and 4-chlorophenyl isocyanate (156 mg, 1.02 mmol, ≥1.10 eq). The reaction mixture was stirred overnight at rt. Saturated aqueous NH₄Cl (10 mL) and H₂O (10 mL) were added and the phases were separated. The aqueous phase was extracted with CH₂Cl₂ (2 × 20 mL). The organic extracts were washed with brine (20 mL), dried over Na₂SO₄, filtered and concentrated *in vacuo*. Flash column chromatography (SiO₂, hexane–EtOAc, 8:2 to 7:3) afforded the desired urea **59** as a colourless oil (305 mg, 0.621 mmol, 67% over two steps). IR (ν_{\max} /cm⁻¹) 3330, 2941, 2865, 1645, 1594, 1552, 1512, 1491, 1272, 1229, 1157; ¹H NMR (400 MHz; CDCl₃) δ = 7.18 (4H, s), 7.09 (1H, s), 6.75 (1H, d, *J* = 8.0), 6.60 (1H, d, *J* = 1.9), 6.54 (1H, dd, *J* = 8.0, 1.9), 5.27 (1H, t, *J*

= 5.6), 3.73 (3H, s), 3.19 (2H, td, $J = 6.7, 5.6$), 2.52 (2H, dd, $J = 8.0, 7.2$), 1.80 – 1.70 (2H, m), 1.29 – 1.17 (3H, m), 1.08 (18H, d, $J = 7.2$); ^{13}C NMR (101 MHz; CDCl_3) $\delta = 156.1, 150.8, 143.8, 137.5, 134.6, 129.1, 128.4, 121.6, 120.3, 120.3, 112.5, 55.6, 40.1, 32.9, 31.9, 18.0, 12.9$; HRMS (ESI⁺): Calculated for $\text{C}_{26}\text{H}_{39}\text{ClN}_2\text{NaO}_3\text{Si}$ ($[\text{M}+\text{Na}]^+$): 513.2310. Found: 513.2311.

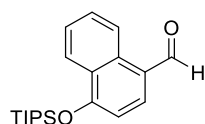


To a solution of the above urea (304 mg, 0.620 mmol) in THF (5 mL) at 0 °C was added $n\text{Bu}_4\text{NF}$ (1M in THF, 0.70 mL, 0.70 mmol, 1.1 eq) dropwise. The reaction mixture warmed to rt and stirred overnight. After concentration *in vacuo* the residue was purified by flash column chromatography (SiO_2 , CH_2Cl_2 then CH_2Cl_2 -MeOH, 98:2) to afford the desired phenol as a colourless solid (190 mg, 0.569 mmol, 91%). m.p. (CH_2Cl_2 -MeOH) 157.6–158.6 °C; IR ($\nu_{\text{max}}/\text{cm}^{-1}$) 3547, 3330, 2936, 2861, 2838, 1630, 1592, 1563, 1514, 1488, 1252, 1242, 1206, 1118, 1033; ^1H NMR (400 MHz; MeOD) $\delta = 7.34$ (2H, d, $J = 8.9$), 7.21 (2H, d, $J = 8.9$), 6.77 (1H, d, $J = 1.8$), 6.70 (1H, d, $J = 8.0$), 6.63 (1H, dd, $J = 8.0, 1.8$), 3.82 (3H, s), 3.19 (2H, t, $J = 7.0$), 2.58 (2H, dd, $J = 8.2, 7.1$), 1.80 (2H, app dq, $J = 8.6, 7.2$); ^{13}C NMR (101 MHz; MeOD) $\delta = 158.0, 148.9, 145.6, 139.9, 134.5, 129.6, 128.0, 121.7, 121.3, 116.1, 113.1, 56.3, 40.3, 33.6, 33.1$; HRMS (ESI⁺): Calculated for $\text{C}_{17}\text{H}_{20}\text{ClN}_2\text{O}_3$ ($[\text{M}+\text{H}]^+$): 335.1156. Found: 335.1154.

Preparation of naphthol-derived substrates 1o-r



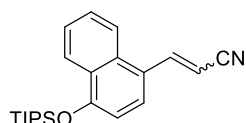
4-[[Tris(propan-2-yl)silyl]oxy]naphthalene-1-carbaldehyde S10



4-Hydroxy-1-naphthaldehyde (3.00 g, 17.4 mmol) was dissolved in DMF (9 mL). Triisopropylsilyl chloride (4.5 mL, 21.0 mmol, 1.21 eq) was added and the reaction mixture was cooled down to 0 °C before the addition of imidazole (1.42 g, 20.9 mmol, 1.20 eq). The reaction mixture was warmed to rt and stirred overnight. EtOAc (150 mL) and H_2O (50 mL) were added. The phases were separated and the organic phase was successively washed

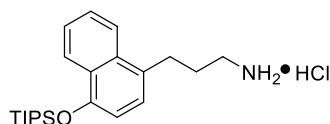
with H₂O (2 × 50 mL), aqueous HCl (1M, 50 mL), aqueous saturated NaHCO₃ (50 mL) and Brine (100 mL). The organic phase was then dried over Na₂SO₄, filtered and concentrated *in vacuo*. Flash column chromatography (SiO₂, hexane–EtOAc, 95:5) gave the title compound (5.43 g, 16.5 mmol, 95%) as a colourless oil. IR (ν_{\max} /cm⁻¹) 2938, 2863, 2732, 1616, 1566, 1507, 1460, 1428, 1393, 1166, 1055; ¹H NMR (400 MHz; CDCl₃) δ = 10.2 (1H, s), 9.33 (1H, d, *J* = 8.5), 8.36 (1H, d, *J* = 8.4), 7.86 (1H, d, *J* = 7.9), 7.70 (1H, ddd, *J* = 8.4, 7.3, 0.9), 7.59 (1H, ddd, *J* = 8.5, 7.3, 0.9), 6.97 (1H, d, *J* = 7.9), 1.47 (3H, sept, *J* = 7.5), 1.47 (18H, d, *J* = 7.5); ¹³C NMR (101 MHz; CDCl₃) δ = 192.2, 158.5, 139.3, 132.7, 129.5, 127.7, 126.4, 125.2, 125.0, 123.1, 111.1, 18.1, 13.2; HRMS (ESI⁺): Calculated for C₂₀H₂₉O₂Si ([M+H]⁺): 329.1931. Found: 329.1928.

(2E/2Z)-3-(4-{{Tris(propan-2-yl)silyl}oxy)naphthalen-1-yl}prop-2-enitrile S11



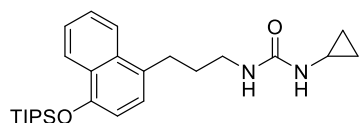
Following a procedure adapted from Pouységu *et al.*,² to a solution of THF (26 mL) at 0 °C was added NaH (60% in mineral oil, 475 mg, 11.8 mmol, 1.15 eq) portionwise and the suspension was stirred for 10 min. Diethylcyanophosphonate (2.0 mL, 12 mmol, 1.16 eq) was added dropwise at 0 °C and the reaction mixture was stirred 10 min before the addition of the above aldehyde **S10** (3.38 g, 10.3 mmol) in THF (8 mL). The reaction mixture was stirred for 7 h at 0 °C, and Et₂O was added (100 mL) before filtration of the reaction mixture directly over a pad of silica washed with Et₂O. After concentration *in vacuo*, the residue was purified by flash column chromatography (SiO₂, hexane–EtOAc, 95:5 to 9:1) to give the desired nitriles as an inseparable mixture of isomers (2.27 g, 6.47 mmol, 63%, *E/Z* 5.3:1). IR (ν_{\max} /cm⁻¹) 2943, 2865, 2214, 1509, 1458, 1427, 1369, 1264, 1218, 1068; **Major isomer peaks reported only** ¹H NMR (400 MHz, CDCl₃) δ = 8.21 (1H, dd, *J* = 8.2, 1.1), 8.03 (1H, d, *J* = 16.4), 7.89 (1H, d, *J* = 8.2), 7.50 – 7.39 (3H, m), 6.75 (1H, d, *J* = 8.2), 5.72 (1H, d, *J* = 16.4), 1.36 – 1.25 (3H, m), 1.04 (18H, d, *J* = 7.5); ¹³C NMR (101 MHz, CDCl₃) δ = 155.6, 147.6, 132.5, 127.9, 127.8, 125.9, 125.8, 123.7, 123.6, 122.7, 119.1, 111.9, 95.8, 18.2, 13.2; HRMS (ESI⁺): Calculated for C₂₂H₃₀NOSi ([M+H]⁺): 352.2091. Found: 352.2085.

Amine salt S12

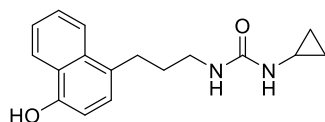


Following a procedure adapted from Pouységu *et al.*,² to a mixture of EtOH–CHCl₃ (6:1, 56 mL) was added the unsaturated nitrile **S11** (4.02 g, 12.1 mmol). PtO₂·H₂O (200 mg, 0.816 mmol, 0.067 eq) was added and the reaction mixture was stirred under an atmosphere of H₂ (balloon) overnight. MeOH (100 mL) was added and the stirring was stopped. After 30 min the reaction mixture was removed from the reaction flask without the solid platinum residue. After concentration *in vacuo* the amine salt was used directly without further purification.

3-Cyclopropyl-1-[3-(4-hydroxynaphthalen-1-yl)propyl]urea **1o**

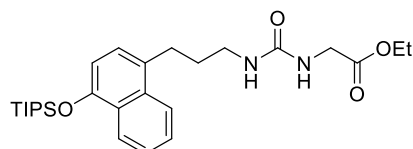


To a solution of the crude amine salt **S12** (400 mg, ≤ 1.01 mmol) in CH_2Cl_2 (10 mL) at 0°C was successively added Et_3N (150 μL , 1.07 mmol, ≥ 1.06 eq) and cyclopropyl isocyanate (95 μL , 1.12 mmol, ≥ 1.11 eq). The reaction mixture was stirred for 2 h at rt. Saturated aqueous NH_4Cl (15 mL) and H_2O (10 mL) were added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (2 \times 20 mL). The organic extracts were washed with brine (20 mL), dried over Na_2SO_4 , filtered and concentrated *in vacuo*. Flash column chromatography (SiO_2 , hexane–EtOAc, 5:5) afforded the desired urea **S13** as a colourless solid (317 mg, 0.714 mmol, 71% over two steps). mp (hexane–EtOAc): $92\text{--}93^\circ\text{C}$; IR ($\nu_{\text{max}}/\text{cm}^{-1}$) 2945, 2867, 1632, 1584, 1461, 1392, 1273, 1157, 1069; ^1H NMR (400 MHz, CDCl_3) δ = 8.31 (1H, dd, J = 7.9, 1.5), 7.95 (1H, d, J = 8.5), 7.53 – 7.44 (2H, m), 7.15 (1H, d, J = 7.7), 6.79 (1H, d, J = 7.7), 4.93 (1H, br s), 4.60 (1H, s), 3.36 (2H, dd, J = 13.1, 6.8), 3.05 (2H, t, J = 7.5), 2.34 – 2.27 (1H, m), 2.03 – 1.94 (2H, m), 1.47 – 1.35 (3H, m), 1.15 (18H, d, J = 7.4, 6 \times TIPS- H_3), 0.69 – 0.64 (2H, m), 0.54 – 0.49 (2H, m); ^{13}C NMR (101 MHz, CDCl_3) δ = 159.1, 150.9, 133.0, 129.9, 128.1, 126.2, 126.0, 124.8, 123.7, 123.6, 111.4, 40.3, 31.4, 30.1, 22.4, 18.2, 13.2, 7.6; HRMS (ESI^+): Calculated for $\text{C}_{26}\text{H}_{41}\text{N}_2\text{O}_2\text{Si}$ ($[\text{M}+\text{H}]^+$): 441.2931. Found: 441.2931.

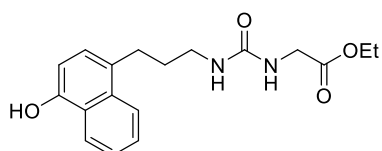


To a solution of the above urea **S13** (153 mg, 0.348 mmol) in THF (2 mL) at 0°C was added $n\text{Bu}_4\text{NF}$ (1M in THF, 370 μL , 0.370 mmol, 1.06 eq) dropwise. The reaction mixture warmed to rt and stirred for 2 h. After concentration *in vacuo* the residue was purified by flash column chromatography (SiO_2 , CH_2Cl_2 –MeOH, 98:2 to 96:4) to afford the desired phenol as a colourless solid (76 mg, 0.267 mmol, 77%). mp (CH_2Cl_2 –MeOH): $167\text{--}169^\circ\text{C}$; IR ($\nu_{\text{max}}/\text{cm}^{-1}$) 3434, 3280, 3126, 2932, 1643, 1620, 1543, 1515, 1457, 1333, 1280, 1249, 1138; ^1H NMR (400 MHz; MeOD) δ = 8.22 (1H, d, J = 8.1), 7.95 (1H, d, J = 8.3), 7.49 – 7.43 (1H, m), 7.43 – 7.37 (1H, m), 7.12 (1H, d, J = 7.6), 6.73 (1H, d, J = 7.6), 3.23 (2H, t, J = 6.6), 2.99 (2H, t, J = 7.5), 2.44 – 2.36 (1H, m), 1.87 (2H, app quint, J = 6.7), 0.66 (2H, app q, J = 5.8), 0.47 – 0.40 (2H, m); ^{13}C NMR (101 MHz; MeOD) δ = 162.1, 153.1, 134.0, 129.7, 127.1, 126.9, 126.8, 125.1, 124.5, 123.8, 108.4, 40.9, 32.6, 30.8, 23.1, 7.4; HRMS (ESI^+): Calculated for $\text{C}_{17}\text{H}_{21}\text{N}_2\text{O}_2$ ($[\text{M}+\text{H}]^+$): 285.1597. Found: 285.1594.

Ethyl 2-([3-(4-(TIPSO)naphthalen-1-yl)propyl]carbamoyl)amino)acetate **1p**

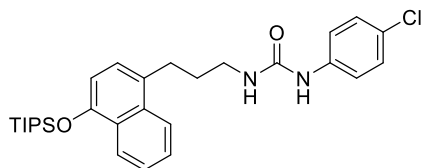


To a solution of the crude amine salt (599 mg, ≤ 1.52 mmol) in CH_2Cl_2 (20 mL) at 0 °C was successively added Et_3N (300 μL , 2.15 mmol, ≥ 1.41 eq) and ethyl isocyanatoacetate (175 μL , 1.56 mmol, ≥ 1.02 eq). The reaction mixture was stirred for 2 h at rt. Saturated aqueous NH_4Cl (15 mL) and H_2O (10 mL) were added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (2 \times 20 mL). The organic extracts were washed with brine (20 mL), dried over Na_2SO_4 , filtered and concentrated *in vacuo*. Flash column chromatography (SiO_2 , hexane–EtOAc, 6:4 to 5:5) afforded the desired urea **S14** as a colourless oil (246 mg, 0.50 mmol, 32% over two steps). IR ($\nu_{\text{max}}/\text{cm}^{-1}$) 3350, 2944, 2866, 2247, 1743, 1634, 1573, 1460, 1391, 1273, 1197, 1156, 1068; ^1H NMR (400 MHz; CDCl_3) δ = 8.32 – 8.29 (1H, m), 7.92 (1H, dd, J = 7.1, 2.3), 7.50 – 7.42 (2H, m), 7.11 (1H, d, J = 7.8), 6.77 (1H, d, J = 7.8), 5.44 (1H, t, J = 5.3), 5.28 (1H, t, J = 5.5), 4.12 (2H, q, J = 7.1), 3.97 (2H, d, J = 5.5), 3.29 – 3.24 (2H, m), 3.02 – 2.96 (2H, m), 1.95 – 1.86 (2H, m), 1.46 – 1.34 (3H, m), 1.21 (3H, t, J = 7.1), 1.15 (18H, d, J = 7.5); ^{13}C NMR (101 MHz, CDCl_3) δ = 171.6, 158.4, 150.7, 133.0, 129.9, 128.0, 126.1, 125.8, 124.7, 123.7, 123.4, 111.4, 61.3, 42.3, 40.4, 31.1, 29.8, 18.2, 14.1, 13.1; HRMS (ESI^+): Calculated for $\text{C}_{27}\text{H}_{43}\text{N}_2\text{O}_4\text{Si}$ ($[\text{M}+\text{H}]^+$): 487.2986. Found: 487.2984.



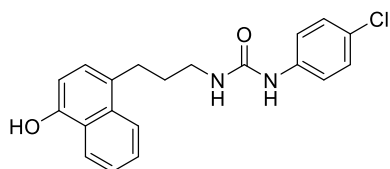
To a solution of the above urea **S14** (246 mg, 0.50 mmol) in THF (10 mL) at 0 °C was added $n\text{Bu}_4\text{NF}$ (1M in THF, 600 μL , 0.600 mmol, 1.1 eq) dropwise. The reaction mixture warmed to rt and stirred for 2 h. After concentration *in vacuo* the residue was purified by flash column chromatography (SiO_2 , EtOAc then CH_2Cl_2 –MeOH, 97:3) to afford the desired phenol as a colourless oil (145 mg, 0.44 mmol, 88%). IR ($\nu_{\text{max}}/\text{cm}^{-1}$) 3410, 2950, 2821, 1850, 1635, 1515, 1377, 1460, 1353, 1201, 1151; ^1H NMR (300 MHz; MeOD) δ = 8.22 (1H, dd, J = 8.3, 1.0), 7.97 (1H, d, J = 8.4), 7.47 (1H, ddd, J = 8.4, 6.8, 1.5), 7.39 (1H, ddd, J = 8.1, 6.8, 1.3), 7.13 (1H, d, J = 7.7), 6.73 (1H, d, J = 7.7), 4.17 (2H, q, J = 7.1), 3.87 (2H, s), 3.21 (2H, t, J = 6.9), 3.00 (2H, dd, J = 8.7, 6.9), 1.86 (2H, dq, J = 8.7, 6.9), 1.25 (3H, t, J = 7.1); ^{13}C NMR (75 MHz; MeOD) δ = 172.7, 161.1, 153.0, 134.1, 129.7, 127.2, 126.9, 126.8, 125.1, 124.6, 123.8, 108.4, 62.0, 42.8, 40.9, 32.6, 30.7, 14.4; HRMS (ESI^+): Calculated for $\text{C}_{18}\text{H}_{23}\text{N}_2\text{O}_4$ ($[\text{M}+\text{H}]^+$): 331.1652. Found: 331.1647.

1-(4-Chlorophenyl)-3-[3-(4-hydroxynaphthalen-1-yl)propyl]urea **1q**



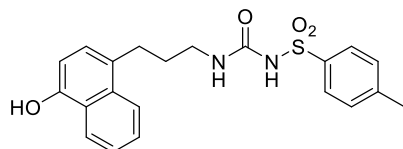
To a solution of the crude amine salt (361 mg, ≤ 0.916 mmol) in CH_2Cl_2 (10 mL) at 0 °C was successively added Et_3N (150 μL , 1.07 mmol, ≥ 1.17 eq) and 4-chlorophenyl isocyanate (155

mg, 1.01 mmol, ≥ 1.10 eq). The reaction mixture was stirred for 2 h at rt. Saturated aqueous NH_4Cl (15 mL) and H_2O (10 mL) were added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (2 \times 20 mL). The organic extracts were washed with brine (20 mL), dried over Na_2SO_4 , filtered and concentrated *in vacuo*. Flash column chromatography (SiO_2 , hexane–EtOAc, 7:3) followed by crystallisation with CH_2Cl_2 afforded the desired urea **S15** as a colourless solid (243 mg, 0.476 mmol, 52% over two steps). m.p. (CH_2Cl_2): 135–136 °C; IR ($\nu_{\text{max}}/\text{cm}^{-1}$) 2942, 2865, 1646, 1590, 1552, 1491, 1462, 1393, 1276, 1237, 1091; ^1H NMR (400 MHz, CDCl_3) δ = 8.33 – 8.29 (1H, m), 7.91 – 7.87 (1H, m), 7.49 – 7.42 (2H, m), 7.21 (2H, d, J = 8.9), 7.16 (2H, d, J = 8.9), 7.09 (1H, d, J = 7.7), 6.76 (1H, d, J = 7.7), 6.49 (1H, br s), 4.85 (1H, app t, J = 5.5), 3.34 – 3.27 (2H, m), 3.00 (2H, app t, J = 7.5), 1.97 – 1.88 (2H, m), 1.46 – 1.34 (3H, m), 1.14 (18H, d, J = 7.5); ^{13}C NMR (101 MHz, CDCl_3) δ = 155.7, 150.9, 137.3, 133.0, 129.6, 129.3, 128.8, 128.1, 126.2, 126.0, 124.9, 123.6, 123.6, 122.0, 111.4, 40.4, 30.9, 30.0, 18.2, 13.2; HRMS (ESI $^+$): Calculated for $\text{C}_{29}\text{H}_{39}\text{N}_2^{35}\text{ClNaO}_2\text{Si}$ ($[\text{M}+\text{Na}]^+$): 533.2361. Found: 533.2359.



To a solution of the above urea **S15** (239 mg, 0.460 mmol) in THF (2 mL) at 0 °C was added $n\text{Bu}_4\text{NF}$ (1M in THF, 540 μL , 0.54 mmol, 1.17 eq) dropwise. The reaction mixture warmed to rt and stirred for 2 h. After concentration *in vacuo* the residue was purified by flash column chromatography (SiO_2 , hexane–EtOAc, 6:4 to 5:5) to afford the desired phenol as a colourless solid (105 mg, 0.297 mmol, 65%). mp (hexane–EtOAc): 170–171 °C; IR ($\nu_{\text{max}}/\text{cm}^{-1}$) 3334, 3287, 2936, 2861, 1632, 1589, 1565, 1490, 1381, 1352, 1280, 1224, 1120; ^1H NMR (400 MHz, MeOD) δ = 8.22 (1H, d, J = 8.2), 7.96 (1H, d, J = 8.3), 7.49 – 7.43 (1H, m), 7.42 – 7.37 (1H, m), 7.34 (2H, d, J = 8.7), 7.21 (2H, d, J = 8.7), 7.13 (1H, d, J = 7.6), 6.73 (1H, d, J = 7.6), 3.26 (2H, t, J = 6.9), 3.02 (2H, t, J = 7.6), 1.90 (2H, tt, J = 7.6, 6.9); ^{13}C NMR (101 MHz, MeOD) δ = 158.1, 153.1, 139.9, 134.0, 129.6, 129.5, 128.0, 127.2, 126.9, 126.8, 125.1, 124.5, 123.8, 121.3, 108.4, 40.7, 32.4, 30.7; HRMS (ESI $^+$): Calculated for $\text{C}_{20}\text{H}_{20}^{35}\text{ClN}_2\text{O}_2$ ($[\text{M}+\text{H}]^+$): 355.1207. Found: 355.1204.

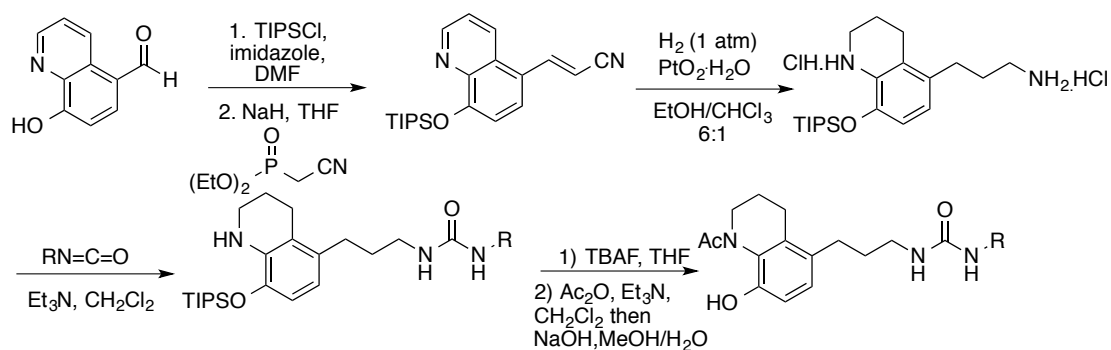
3-[3-(4-Hydroxynaphthalen-1-yl)propyl]-1-(4-methylbenzenesulfonyl)urea 1r



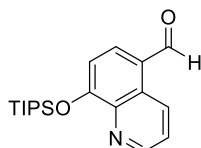
To a solution of the crude amine salt (430 mg, ≤ 1.09 mmol) in CH_2Cl_2 (10 mL) at 0 °C was successively added Et_3N (160 μL , 1.15 mmol, ≥ 1.05 eq) and *p*-toluenesulfonyl isocyanate (185 μL , 1.21 mmol, ≥ 1.11 eq). The reaction mixture was stirred for 2 h at rt. Saturated aqueous NH_4Cl (15 mL) and H_2O (10 mL) were added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (2 \times 20 mL). The organic extracts were washed

with brine (20 mL), dried over Na_2SO_4 , filtered and concentrated *in vacuo*. Flash column chromatography (SiO_2 , hexane–EtOAc, 8:2) afforded an amorphous solid (416 mg, ≤ 0.752 mmol) that was used straight without further purification. The solid was dissolved in THF (4 mL) and $n\text{Bu}_4\text{NF}$ (1M in THF, 840 μL , 0.840 mmol, ≥ 1.12 eq) was added dropwise at 0 °C. The reaction mixture warmed to rt and stirred overnight. After concentration *in vacuo* the residue was purified by flash column chromatography (SiO_2 , CH_2Cl_2 then CH_2Cl_2 –MeOH, 98:2) to afford the desired phenol as a colourless solid (258 mg, 0.648 mmol, 59%, 3 steps). m.p. (hexane–EtOAc) 144.0–144.4 °C; IR ($\nu_{\text{max}}/\text{cm}^{-1}$) 3310, 2958, 2884, 1670, 1588, 1542, 1380, 1276, 1245, 1186, 1160, 1052; ^1H NMR (400 MHz, MeOD) δ = 8.21 (1H, dd, J = 7.9, 1.5), 7.86 – 7.80 (3H, m including d, J = 8.1 at 7.84), 7.45 – 7.36 (2H, m), 7.30 (2H, d, J = 8.1), 7.01 (1H, d, J = 7.7), 6.70 (1H, d, J = 7.7), 3.17 (2H, t, J = 6.8), 2.86 – 2.80 (2H, m), 2.31 (3H, s), 1.81 – 1.73 (2H, m); ^{13}C NMR (101 MHz, MeOD) δ = 154.2, 153.1, 145.6, 138.7, 134.0, 130.6, 129.3, 128.4, 127.0, 126.9, 126.7, 125.1, 124.4, 123.8, 108.3, 40.7, 31.8, 30.4, 21.4; HRMS (ESI $^+$): Calculated for $\text{C}_{21}\text{H}_{23}\text{N}_2\text{O}_4\text{S}$ ($[\text{M}+\text{H}]^+$): 399.1373. Found: 399.1369.

Preparation of the tetrahydroquinoliny urea 1s



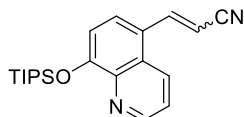
8-[[Tris(propan-2-yl)silyl]oxy]quinoline-5-carbaldehyde S16



8-Hydroxyquinoline-5-carbaldehyde (250 mg, 1.44 mmol) was dissolved in DMF (2 mL). Triisopropylsilyl chloride (370 μL , 1.73 mmol, 1.20 eq) was added and the reaction mixture was cooled down to 0 °C before the addition of imidazole (118 mg, 1.73 mmol, 1.20 eq). The reaction mixture was warmed to rt and stirred overnight. More triisopropylsilyl chloride (1.2 eq) and imidazole (1.2 eq) were added and the reaction mixture was stirred for 24 h. EtOAc (30 mL) and H_2O (10 mL) were added. The phases were separated and the organic phase was successively washed with H_2O (2×10 mL), aqueous HCl (1M, 10 mL), aqueous saturated NaHCO_3 (10 mL) and brine (20 mL). The organic phase was then dried over Na_2SO_4 , filtered and concentrated *in vacuo*. Flash column chromatography (SiO_2 , hexane–EtOAc, 9:1) gave the title compound (353 mg, 1.07 mmol, 74%) as a colourless oil. IR ($\nu_{\text{max}}/\text{cm}^{-1}$) 2942, 2891, 2864, 2723, 1684, 1600, 1560, 1500, 1474, 1377, 1319, 1249, 1169, 1089; ^1H NMR (400 MHz, CDCl_3) δ = 10.15 (1H, s), 9.65 (1H, dd, J = 8.6, 1.7), 8.90 (1H, dd, J = 4.1, 1.7), 7.93 (1H, d, J =

8.0), 7.56 (1H, dd, $J = 8.6, 4.1$), 7.26 (1H, d, $J = 8.0$), 1.51 – 1.40 (3H, m), 1.12 (18H, d, $J = 7.5$); ^{13}C NMR (101 MHz, CDCl_3) $\delta = 192.0, 159.5, 149.1, 141.4, 139.7, 133.6, 127.9, 124.6, 124.0, 115.9, 18.2, 13.9$; HRMS (ESI $^+$): Calculated for $\text{C}_{19}\text{H}_{28}\text{NO}_2\text{Si}$ ($[\text{M}+\text{H}]^+$): 330.1883. Found: 330.1881.

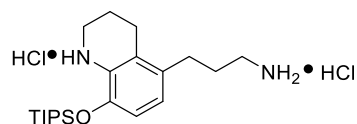
(2E/Z)-3-(8-{{Tris(propan-2-yl)silyl}oxy}quinolin-5-yl)prop-2-enenitrile S17



Following a procedure adapted from Pouységu *et al.*,² to a solution of THF (4 mL) at 0 °C was added NaH (60% in mineral oil, 50 mg, 1.25 mmol, 1.17 eq) portionwise and the suspension was stirred for 10 min. Diethylcyanophosphonate (220 μL , 1.36 mmol, 1.27 eq) was added dropwise at 0 °C and the reaction mixture was stirred 10 min before the addition of aldehyde **S16** (352 mg, 1.07 mmol) in THF (2 mL). The reaction mixture was stirred for 7 h at 0 °C, and Et_2O was added (20 mL) before the reaction mixture was filtered directly over a pad of silica washed with Et_2O . After concentration *in vacuo* the residue was purified by flash column chromatography (hexane– EtOAc , 95:5) to provide the desired nitriles as a (Z/E, 1:5) mixture of diastereomers (328 mg, 0.934 mmol, 87%). For characterization purposes the isomers could be separated.

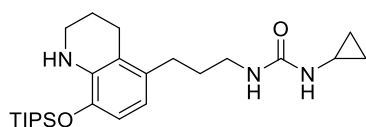
IR (ν_{max} / cm^{-1}) 2942, 2864, 2214, 1612, 1564, 1470, 1400, 1387, 1313, 1269, 1091; **Major E isomer** ^1H NMR (400 MHz, CDCl_3) $\delta = 8.90$ (1H, dd, $J = 4.0, 1.3$), 8.35 (1H, dd, $J = 8.6, 1.3$), 8.06 (1H, d, $J = 16.3$), 7.69 (1H, d, $J = 8.2$), 7.49 (1H, dd, $J = 8.6, 4.0$), 7.19 (1H, d, $J = 8.2$), 5.89 (1H, d, $J = 16.3$), 1.49 – 1.37 (3H, m), 1.12 (19 H, d, $J = 7.5$); ^{13}C NMR (101 MHz, CDCl_3) $\delta = 156.5, 148.9, 146.0, 141.7, 130.8, 127.4, 126.2, 122.8, 122.3, 118.7, 117.0, 96.3, 18.2, 13.7$; **Minor Z isomer** ^1H NMR (400 MHz, CDCl_3) $\delta = 8.91$ (1H, dd, $J = 4.1, 1.5$), 8.25 (1H, dd, $J = 8.6, 1.5$), 8.20 (1H, d, $J = 8.2$), 7.77 (1H, d, $J = 11.8$), 7.47 (1H, dd, $J = 8.6, 4.1$), 7.25 (1H, d, $J = 8.2$), 5.59 (1H, d, $J = 11.9$), 1.51 – 1.39 (3H, m), 1.13 (18H, d, $J = 7.5$); ^{13}C NMR (101 MHz, CDCl_3) $\delta = 156.0, 148.7, 144.8, 141.8, 131.0, 128.4, 127.9, 122.6, 122.1, 117.6, 116.8, 96.1, 18.2, 13.7$; HRMS (ESI $^+$): Calculated for $\text{C}_{21}\text{H}_{28}\text{N}_2\text{NaOSi}$ ($[\text{M}+\text{H}]^+$): 375.1863. Found: 375.1856.

Amine salt S18



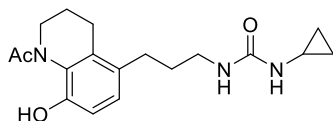
Following a procedure adapted from Pouységu *et al.*,² to a mixture of $\text{EtOH}-\text{CHCl}_3$ (6:1, 7 mL) was added unsaturated nitrile (328 mg, 0.932 mmol). $\text{PtO}_2 \cdot \text{H}_2\text{O}$ (15 mg, 0.066 mmol, 0.07 eq) was added and the reaction mixture was stirred under an atmosphere of H_2 (balloon) overnight. MeOH (50 mL) was added and the stirring was stopped. After 30 min the reaction mixture was removed from the reaction flask without the solid platinum residue. After concentration *in vacuo* the amine salt **S18** was used directly without further purification.

3-Cyclopropyl-1-[3-(8-{{tris(propan-2-yl)silyl}oxy)-1,2,3,4-tetrahydroquinolin-5-yl)propyl]urea S19



To a solution of the crude amine salt (≤ 0.932 mmol) in CH_2Cl_2 (5 mL) at 0°C was successively added Et_3N (390 μL , 2.78 mmol, ≥ 2.98 eq) and cyclopropyl isocyanate (83 μL , 0.98 mmol, ≥ 1.05 eq). The reaction mixture was stirred for 2 h at rt. Saturated aqueous NaHCO_3 (10 mL) and H_2O (10 mL) were added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (2×10 mL). The organic extracts were washed with brine (10 mL), dried over Na_2SO_4 , filtered and concentrated *in vacuo*. Flash column chromatography (SiO_2 , hexane–EtOAc, 5:5 2:8) provided the desired urea as a colourless oil (186 mg, 0.418 mmol, 45% over two steps). IR ($\nu_{\text{max}}/\text{cm}^{-1}$) 3330, 2941, 2865, 1633, 1566, 1501, 1433, 1258, 1194; ^1H NMR (400 MHz; CDCl_3) δ = 6.51 (1H, d, J = 8.1), 6.29 (1H, d, J = 8.1), 4.98 (1H, t, J = 5.2), 4.81 (1H, s), 4.22 (1H, s), 3.32 – 3.26 (4H, m), 2.68 (2H, t, J = 6.5), 2.51 (2H, dd, J = 8.3, 7.0), 2.39 – 2.32 (1H, m), 1.99 – 1.91 (2H, m), 1.77 (2H, app dq, J = 8.6, 7.1), 1.34 – 1.22 (3H, m), 1.10 (18H, d, J = 7.4), 0.68 (2H, td, J = 6.7, 4.7), 0.54 – 0.49 (2H, m); ^{13}C NMR (101 MHz; CDCl_3) δ = 159.2, 140.6, 136.6, 132.5, 119.6, 115.8, 114.4, 41.2, 40.3, 30.8, 30.0, 23.9, 22.4, 22.4, 18.1, 13.0, 7.5; HRMS (ESI $^+$): Calculated for $\text{C}_{25}\text{H}_{43}\text{N}_3\text{O}_2\text{Si}$ ($[\text{M}+\text{H}]^+$): 446.3197. Found: 446.3205.

1-[3-(1-Acetyl-8-hydroxy-1,2,3,4-tetrahydroquinolin-5-yl)propyl]-3-cyclopropylurea **1s**

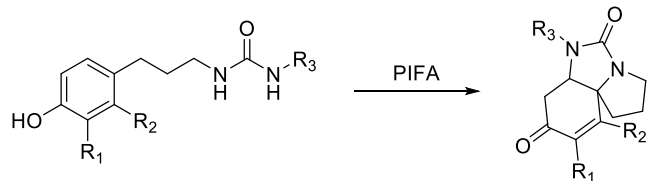


To a solution of the urea **S19** (140 mg, 0.314 mmol) in THF (2 mL) at 0°C was added $n\text{Bu}_4\text{NF}$ (1M in THF, 350 μL , 0.350 mmol, 1.11 eq) dropwise. The reaction mixture warmed to rt and stirred for 15 min. After concentration *in vacuo* the residue was purified by flash column chromatography (SiO_2 , hexane–EtOAc, 1:9 then 0:10 then EtOAc–MeOH 97:3) to afford the desired phenol as a colourless oil (74 mg, 0.256 mmol, 82%). The compound was diluted in CH_2Cl_2 (2 mL) and the solution was cooled to 0°C . Et_3N (79 μL , 0.566 mmol, 2.21 eq) and acetic anhydride (54 μL , 0.571 mmol, 2.23 eq) were successively added. The reaction mixture was stirred at rt overnight. Saturated aqueous NH_4Cl (20 mL) and H_2O (20 mL) were added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (2×40 mL). The organic extracts were washed with brine (50 mL), dried over Na_2SO_4 , filtered and concentrated *in vacuo*. The residue was next diluted in MeOH (3 mL) and H_2O (1 mL). At 0°C NaOH (100 mg, 2.50 mmol, 9.77 eq) was added. The reaction mixture was stirred at rt for 2 h. After removal of MeOH under *vacuo*, the residue was diluted with H_2O (5 mL) and CH_2Cl_2 (5 mL). Aqueous HCl (1N) was added until the aqueous phase reached an acidic pH (*ca* 4) and after vigorous stirring for 15 min the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (2×10 mL). The combined organic extracts were washed with saturated NaHCO_3 (10 mL) and brine (10 mL), dried over Na_2SO_4 , filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2 , CH_2Cl_2 then CH_2Cl_2 –MeOH, 97:3) to afford the desired phenol as a colourless solid (78 mg, 0.235 mmol, 75%

over 3 steps). m.p. (CH₂Cl₂-MeOH): 131-132 °C; IR (ν_{max} /cm⁻¹) 3300, 3019, 2933, 1619, 1573, 1504, 1462, 1412, 1282, 1092; ¹H NMR (400 MHz; MeOD) δ = 6.95 (1H, d, *J* = 8.3), 6.71 (1H, d, *J* = 8.3), 4.59 – 4.49 (1H, m), 3.17 (2H, t, *J* = 6.9), 2.92 – 2.83 (2H, m), 2.59 (2H, t, *J* = 8.4, 6.9), 2.47 – 2.40 (1H, m), 2.35 – 2.16 (2H, m), 2.01 (3H, br s), 1.70 (2H, app quint, *J* = 7.2), 1.64 – 1.53 (1H, m), 0.72 – 0.66 (2H, m), 0.48 – 0.42 (2H, m); ¹³C NMR (101 MHz; MeOD) δ = 174.0, 162.1, 150.2, 136.7, 131.2, 129.1, 128.5, 114.9, 42.6, 40.7, 33.0, 30.5, 25.3, 23.7, 23.1, 23.1, 21.8, 7.5; HRMS (ESI⁺): Calculated for C₁₈H₂₆N₃O₃ ([M+H]⁺): 332.1968. Found: 332.1963.

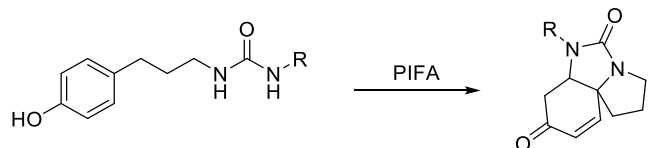
Oxidative dearomatisations (Tables 1, 2)

General procedure A for oxidative dearomatisation:



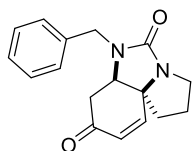
To a solution of the urea in a hexafluoroisopropanol–CH₂Cl₂ mixture (50:50, 0.2 M) at 0 °C was added a solution of [bis(trifluoroacetoxy)iodo]benzene (1.10 eq) in hexafluoroisopropanol–CH₂Cl₂ (50:50, 1 M) dropwise. The reaction mixture was kept at 0 °C for 2 h and then allowed to warm to rt. Upon completion, the reaction mixture was concentrated *in vacuo* and the residue was purified by flash column chromatography to give the desired product.

General procedure B for oxidative dearomatisation:



To a solution of the urea in a hexafluoroisopropanol (0.1 M) at 0 °C was added a solution of [bis(trifluoroacetoxy)iodo]benzene (1.10 eq) in hexafluoroisopropanol (1.0 M) dropwise. The reaction mixture was kept at 0 °C for 2 h and then allowed to warm to rt. Upon completion, the reaction mixture was concentrated *in vacuo* and the residue was purified by flash column chromatography to give the desired product.

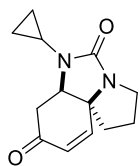
7-Benzyl-5,7-diazatricyclo[6.4.0.0^{1,5}]dodec-11-ene-6,10-dione **2a**



General Procedure A was followed starting with urea **1a** (2.00 g, 7.03 mmol). Flash column chromatography eluting with EtOAc–hexanes (80:20) gave the desired enone (1.34 g, 4.75 mmol, 68%) as a colourless oil.

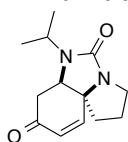
IR (ν_{\max} /cm⁻¹) 2966, 1687, 1416, 779, 728, 587; ¹H NMR (500 MHz; MeOD) δ = 7.36 – 7.22 (5H, m), 6.48 (1H, dd, J = 10.2, 0.8), 6.05 (1H, J = 10.2), 4.81 (1H, d, J = 15.3), 3.99 (1H, d, J = 15.3), 3.90 (1H, ddd, J = 12.0, 7.8, 4.2), 3.65 (1H, dd, J = 5.6, 5.4), 3.18 (1H, app dt, J = 12.0, 7.4), 2.64 (1H, d, J = 5.4), 2.63 (1H, d, J = 5.6), 2.10 – 2.00 (1H, m), 1.94 – 1.76 (3H, m); ¹³C NMR (126 MHz; MeOD) δ = 195.5, 162.5, 146.4, 136.2, 128.9, 128.2, 127.9, 127.5, 63.1, 58.5, 46.3, 45.4, 38.2, 35.4, 25.7; HRMS (ESI⁺): Calculated for C₁₇H₁₉N₂O₂ ([M+H]⁺): 283.1441. Found: 283.1434.

7-Cyclopropyl-5,7-diaztricyclo[6.4.0.0^{1,5}]dodec-11-ene-6,10-dione **2b**



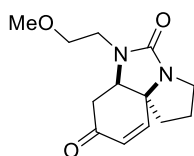
General Procedure A was followed starting with urea **1b** (1.06 g, 4.53 mmol). Flash column chromatography eluting with EtOAc–hexanes (80:20) gave the desired enone (547 mg, 2.36 mmol, 52%) as a colourless oil. IR (ν_{\max} / cm^{-1}) 3487, 2971, 2889, 1682, 1410, 1379, 1364, 1225; ^1H NMR (500 MHz; MeOD) δ = 6.62 (1H, dd, J = 10.2, 1.3), 6.04 (1H, dd, J = 10.2, 0.8), 4.02 (1H, app td, J = 4.5, 1.3), 3.72 (1H, ddd, J = 11.9, 7.3, 4.1), 3.17 (1H, dt, J = 11.9), 2.98 (1H, ddd, J = 16.7, 4.3, 0.9), 2.90 (1H, dd, J = 16.7, 4.6), 2.17 (1H, tt, J = 7.2, 3.7), 2.15 – 1.92 (4H, m), 0.79 (1H, app dtd, J = 9.7, 7.2 and 5.0), 0.73 (1H, app dtd, J = 9.7, 7.2 and 4.8), 0.61 (1H, dddd, J = 10.1, 6.4, 5.0 and 3.7), 0.45 (1H, dddd, J = 10.1, 6.7, 4.8 and 3.7); ^{13}C NMR (126 MHz; MeOD) δ = 198.4, 165.5, 148.6, 128.1, 65.2, 64.2, 46.9, 38.5, 35.5, 26.9, 25.1, 7.0, 5.0; HRMS (ESI⁺): Calculated for $\text{C}_{13}\text{H}_{17}\text{N}_2\text{O}_2$ ($[\text{M}+\text{H}]^+$): 233.1284. Found: 233.1281.

6-Isopropyl-2,3,6a,7-tetrahydro-1H,5H-benzo[d]pyrrolo[1,2-c]imidazole-5,8(6H)-dione **2c**



General Procedure A was followed starting with urea **1c** (603 mg, 2.55 mmol). Flash column chromatography eluting with 1% MeOH in DCM gave the desired enone (222 mg, 0.95 mmol, 37%) as a colourless oil. ^1H NMR (300 MHz, MeOD) δ = 6.58 (1H, d, J = 10.2), 5.96 (1H, d, J = 10.2), 4.04 (1H, dd, J = 6.9, 5.3), 3.82 (1H, hept, J = 6.9), 3.65 (1H, ddd, J = 15.6, 7.8, 3.9), 3.02 (1H, m), 2.81 (1H, dd, J = 16.1, 5.2), 2.61 (1H, dd, J = 16.1, 6.9), 2.05 - 1.90 (1H, m), 1.90 – 1.82 (1H, m), 1.82 – 1.72 (2H, m), 1.14 (3H, d, J = 6.9), 1.11 (3H, d, J = 6.9). ^{13}C NMR (75 MHz, MeOD) δ = 198.2, 164.2, 147.8, 128.2, 64.7, 59.1, 46.7, 46.0, 41.9, 35.8, 25.5, 21.4, 19.5. IR ν_{\max} (neat)/ cm^{-1} : 2966, 2938, 2876 (C-H), 1681 (C=O), 1456 (C=C). HRMS (ESI): $\text{C}_{13}\text{H}_{19}\text{N}_2\text{O}_2$ [$\text{M} + \text{H}^+$]: calculated 235.1441, found 235.1437.

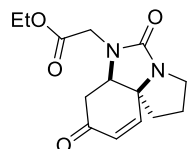
7-[2-Methoxyethyl]-5,7-diaztricyclo[6.4.0.0^{1,5}]dodecane-6,10-dione **2d**



General Procedure A was followed starting with urea **1d** (155 mg, 0.614 mmol). Flash column chromatography eluting with EtOAc–hexanes (8:2 to 10:0) gave the desired enone (57.6 mg, 0.228 mmol, 37%) as a colourless oil. IR (ν_{\max} / cm^{-1}) 2928, 2885, 1677, 1410, 1392, 1311, 1114, 1028; ^1H NMR (500 MHz; MeOD) δ = 6.47 (1H, dd, J = 10.2 and 0.9, 12-H), 6.06 (1H, d, J = 10.2), 4.03 (1H, app t, J = 5.4), 3.87 – 3.80 (1H, m), 3.53 – 3.39 (3H, m), 3.30 (3H, s, OMe), 3.26 – 3.20 (1H, m), 3.19 – 3.11 (1H, m), 2.78 (1H, dd, J = 16.4 and 5.2), 2.75 (1H, dd, J

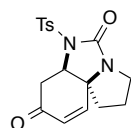
= 16.4 and 5.8), 2.12 – 2.02 (1H, m), 1.99 – 1.87 (3H, m); ^{13}C NMR (126 MHz; MeOD) δ = 195.8, 162.3, 146.2, 127.6, 71.5, 63.2, 60.5, 58.8, 46.1, 41.1, 38.4, 35.2, 25.5; HRMS (ESI⁺): Calculated for $\text{C}_{13}\text{H}_{19}\text{N}_2\text{O}_3$ ([M+H]⁺): 251.1390. Found: 251.1396.

Ethyl 2-{6,10-dioxo-5,7-diazatricyclo[6.4.0.0^{1,5}]dodec-11-en-7-yl}acetate **2e**



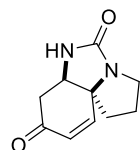
General Procedure A was followed starting with urea **1e** (610 mg, 2.18 mmol). Flash column chromatography eluting with CH_2Cl_2 –MeOH (99:1) gave the desired enone (482 mg, 1.73 mmol, 79%) as a colourless oil. IR (ν_{max} / cm^{-1}) 2977, 1739, 1687, 1428, 1394, 1314, 1246, 1205, 1094, 1028, 977, 778; ^1H NMR (500 MHz, CDCl_3) δ = 6.46 (1H, d, J = 10.2, 12-H), 6.04 (1H, d, J = 10.2), 4.18 (1H, d, J = 18.2), 4.20–4.07 (3H, m), 3.82 (1H, dd, J = 11.3, 7.8 and 3.3), 3.58 (1H, d, J = 18.2), 3.18–3.11 (1H, m), 2.73 (1H, dd, J = 16.8 and 4.9), 2.61 (1H, dd, J = 16.8 and 4.2), 2.11–1.88 (4H, m), 1.24 (3H, t, J = 7.2); ^{13}C NMR (125 MHz, CDCl_3) δ = 195.0, 169.1, 162.5, 146.9, 127.3, 63.2, 61.3, 60.5, 46.6, 42.6, 37.4, 35.3, 26.2, 14.1; HRMS (ESI⁺): Calculated for $\text{C}_{14}\text{H}_{18}\text{N}_2\text{NaO}_4$ ([M+Na]⁺): 301.1158. Found: 301.1159.

(6aR*,10aS*)-6-(4-Toluenesulfonyl)-2,3,6a,7-tetrahydro-1H,5H-benzo[d]pyrrolo[1,2-c]imidazole-5,8(6H)-dione **2f**



General Procedure A was followed starting with urea **1f** (518 mg, 1.49 mmol). Flash column chromatography eluting with 40% EtOAc/hexanes gave the desired enone (118 mg, 0.34 mmol, 23%) as a white solid. IR ν_{max} (neat)/ cm^{-1} : 2958, 2930, 1736, 1685, 1597, 1494, 1458, 1369. ^1H NMR (300 MHz, CDCl_3) δ = 7.85 (2H, d, J = 8.3), 7.26 (2H, d, J = 8.2), 6.40 (1H, d, J = 10.3), 6.05 (1H, d, J = 10.3), 4.54 (1H, dd, J = 8.8, 5.8), 3.84 – 3.70 (1H, m), 3.12 (1H, dd, J = 15.9, 5.7), 3.05 (1H, ddd, J = 12.9, 5.7, 1.2), 2.86 (1H, dd, J = 15.9, 8.8), 2.36 (3H, s), 2.04 – 1.82 (3H, m), 1.63 (1H, dt, J = 12.8, 9.5). ^{13}C NMR (75 MHz, CDCl_3) δ = 194.5, 156.3, 145.2, 142.8, 135.5, 129.7, 129.0, 128.3, 63.2, 58.3, 44.7, 41.3, 35.1, 23.5, 21.7. HRMS (ESI): $\text{C}_{17}\text{H}_{19}\text{N}_2\text{O}_4\text{S}$ [M + H]⁺: calculated 347.1060, found 347.1060.

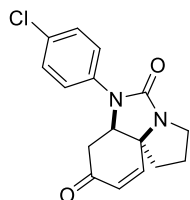
5,7-Diazatricyclo[6.4.0.0^{1,5}]dodec-11-ene-6,10-dione **2g**



General Procedure A was followed starting with urea **1g** (250 mg, 1.29 mmol). Flash column chromatography eluting with EtOAc–MeOH (90:10) gave the desired enone (157 mg, 0.82 mmol, 64%) as a colourless foam. IR (ν_{max} / cm^{-1}) 3291, 2972, 2890, 1675, 1396, 1313, 1241,

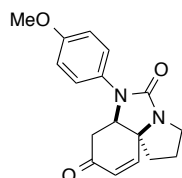
1183, 1127; ^1H NMR (400 MHz, CDCl_3) δ = 6.46 (1H, d, J = 10.3), 6.09 (1H, d, J = 10.3), 5.11 (1H, s), 4.07 (1H, app t, J = 4.6), 3.80 (1H, dt, J = 7.7, 5.0), 3.17 – 3.09 (1H, m), 2.72 (1H, dd, J = 16.7, 4.8), 2.66 (1H, dd, J = 16.7, 4.6), 2.13 – 2.06 (1H, m), 2.03 – 1.89 (3H, m); ^{13}C NMR (101 MHz, CDCl_3) δ = 195.4, 163.4, 146.2, 127.7, 65.1, 57.4, 45.6, 40.0, 35.3, 26.3; HRMS (ESI $^+$): Calculated for $\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}_2$ ($[\text{M}+\text{H}]^+$): 193.0972. Found: 193.0966.

7-(4-Chlorophenyl)-5,7-diazatricyclo[6.4.0.0 1 , 5]dodec-11-ene-6,10-dione **2h**



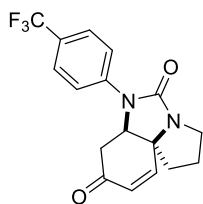
General Procedure A was followed starting with urea **1h** (100 mg, 0.328 mmol). Flash column chromatography eluting with EtOAc–hexanes (5:5) gave the desired enone (46.8 mg, 0.155 mmol, 47%) as a colourless oil. IR (ν_{max} / cm^{-1}) 2967, 2887, 1686, 1493, 1414, 1381, 1314, 1044; ^1H NMR (400 MHz, CDCl_3) δ = 7.32 (2H, d, J = 8.8), 7.19 (2H, d, J = 8.8), 6.55 (1H, d, J = 10.2), 6.12 (1H, d, J = 10.2), 4.46 (1H, dd, J = 5.8, 5.2), 3.96 – 3.88 (1H, m), 3.29 – 3.20 (1H, m), 2.79 (1H, dd, J = 16.6, 5.2), 2.68 (1 H, dd, J = 16.6, 5.8), 2.20 – 1.99 (4H, m); ^{13}C NMR (101 MHz, CDCl_3) δ = 194.7, 159.9, 145.7, 135.7, 130.7, 129.4, 127.9, 124.0, 62.8, 60.2, 45.8, 38.2, 35.8, 25.4; HRMS (ESI $^+$): Calculated for $\text{C}_{16}\text{H}_{16}^{35}\text{ClN}_2\text{O}_2$ ($[\text{M}+\text{H}]^+$): 303.0894. Found: 303.0892.

6-(4-Methoxyphenyl)-2,3,6a,7-tetrahydro-1H,5H-benzo[*d*]pyrrolo[1,2-*c*]imidazole-5,8(6*H*)-dione **2i**



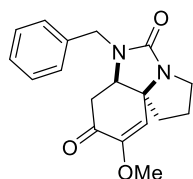
General Procedure A was followed starting with urea **1i** (250 mg, 0.83 mmol). Flash column chromatography eluting with 1% MeOH in DCM gave the desired enone (104 mg, 0.35 mmol, 42%) as a white solid. IR ν_{max} (neat)/ cm^{-1} : 2957, 2900, 2834, 1686, 1582, 1510, 1443, 1390. ^1H NMR (300 MHz, CDCl_3) δ = 7.13 (2H, d, J = 9.0), 6.91 (2H, d, J = 9.0), 6.56 (1H, d, J = 10.2), 6.13 (1H, d, J = 10.3), 4.36 (1H, t, J = 5.1), 3.99 – 3.88 (1H, m), 3.80 (3H, s), 3.30 - 3.19 (1H, m), 2.74 (1H, dd, J = 16.6, 5.0), 2.66 (1H, dd, J = 16.6, 5.2), 2.30 – 2.12 (1H, m), 2.12 – 2.07 (1H, m), 2.06 – 1.99 (2H, m). ^{13}C NMR (75 MHz, CDCl_3) δ = 195.1, 160.6, 157.7, 146.2, 129.8, 127.6, 125.8, 114.6, 62.8, 61.7, 55.5, 45.9, 38.1, 35.5, 25.7. HRMS (ESI): $\text{C}_{17}\text{H}_{19}\text{N}_2\text{O}_3$ [$\text{M} + \text{H}^+$]: calculated 299.1390, found 299.1390.

7-[4-(Trifluoromethyl)phenyl]-5,7-diazatricyclo[6.4.0.0^{1,5}]dodec-11-ene-6,10-dione **2j**



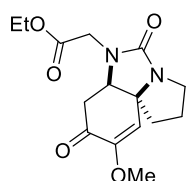
General Procedure A was followed starting with urea **1j** (1.93 g, 5.69 mmol). Flash column chromatography eluting with MeOH–CH₂Cl₂ (1:99) gave the desired enone (1.51 g, 4.49 mmol, 79%) as a colourless oil. IR (ν_{\max} /cm⁻¹) 2973, 2896, 1686, 1614, 1522, 1425, 1323, 1313, 1072; ¹H NMR (500 MHz; MeOD) δ = 6.62 (1H, dd, J = 10.2, 1.3), 6.04 (1H, dd, J = 10.2, 0.8), 4.02 (1H, app td, J = 4.5, 1.3), 3.72 (1H, ddd, J = 11.9, 7.3, 4.1), 3.17 (1H, dt, J = 11.9, 7.2), 2.98 (1H, ddd, J = 16.7, 4.3, 0.9), 2.90 (1H, dd, J = 16.7, 4.6), 2.17 (1H, tt, J = 7.2, 3.7), 2.15 – 1.92 (4H, m), 0.79 (1H, app dtd, J = 9.7, 7.2 and 5.0), 0.73 (1H, app dtd, J = 9.7, 7.2 and 4.8), 0.61 (1H, dddd, J = 10.1, 6.4, 5.0 and 3.7), 0.45 (1H, dddd, J = 10.1, 6.7, 4.8 and 3.7); ¹³C NMR (126 MHz; MeOD) δ = 198.4, 165.5, 148.6, 128.1, 65.2, 64.2, 46.9, 38.5, 35.5, 26.9, 25.1, 7.0, 5.0; HRMS (ESI⁺): Calculated for C₁₇H₁₆F₃N₂O₂ ([M+H]⁺): 337.1158. Found: 337.1152.

7-Benzyl-11-methoxy-5,7-diazatricyclo[6.4.0.0^{1,5}]dodec-11-ene-6,10-dione **2k**



General Procedure B was followed starting with urea **1k** (87 mg, 0.28 mmol). Flash column chromatography (SiO₂, hexane–EtOAc, 2:8 to 1:9) gave the desired enone (47 mg, 0.15 mmol, 54%) as a colourless oil. IR (ν_{\max} /cm⁻¹) 2956, 2908, 1692, 1494, 1360, 1317, 1283, 1081; ¹H NMR (400 MHz; CDCl₃) δ = 7.28 – 7.15 (5H, m), 5.31 (1H, s), 4.76 (1H, d, J = 15.2), 3.91 (1H, d, J = 15.2), 3.83 (1H, ddd, J = 12.0, 7.8, 4.2), 3.57 (3H, s), 3.52 (1H, t, J = 5.6), 3.13 (1H, dt, J = 12.0, 7.1), 2.72 – 2.62 (2H, m), 2.06 – 1.93 (1H, m), 1.89 – 1.70 (3H, m); ¹³C NMR (101 MHz; CDCl₃) δ = 190.4, 162.5, 150.1, 136.1, 128.9, 128.4, 127.9, 113.8, 64.7, 57.6, 55.1, 45.9, 45.4, 38.9, 36.6, 25.5; HRMS (ESI⁺): Calculated for C₁₈H₂₁N₂O₃ ([M+H]⁺): 313.1546. Found: 313.1545.

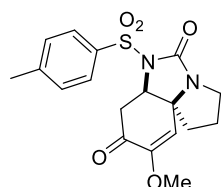
Ethyl 2-{11-methoxy-6,10-dioxo-5,7-diazatricyclo[6.4.0.0^{1,5}]dodec-11-en-7-yl}acetate **2l**



General Procedure B was followed starting with urea **1l** (190 mg, 0.612 mmol). Flash column chromatography (SiO₂, hexane–EtOAc, 2:8 to 0:10) gave the desired enone (157 mg, 0.510 mmol, 83%) as a colourless oil. IR (ν_{\max} /cm⁻¹) 3469, 2975, 1687, 1631, 1416, 1389, 1318, 1199, 1150, 1085; ¹H NMR (400 MHz; CDCl₃) δ = 5.35 (1H, s), 4.21 (1H, d, J = 18.24.19 – 4.08

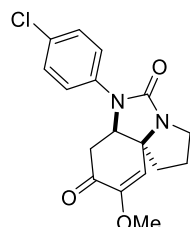
(3H, m), 3.82 (1H, ddd, $J = 11.7, 7.3, 3.6$), 3.61 (3H, s), 3.57 (1H, d, $J = 18.2$), 3.16 (1H, ddd, $J = 11.7, 7.9, 6.8$), 2.81 (1H, dd, $J = 16.7, 4.7$), 2.72 (1H, dd, $J = 16.7, 4.6$), 2.14 – 1.87 (4H, m), 1.24 (3H, t, $J = 7.1$); ^{13}C NMR (101 MHz; CDCl_3) $\delta = 190.1, 169.2, 162.5, 149.8, 114.5, 64.9, 61.4, 59.9, 55.1, 46.3, 42.6, 38.1, 36.7, 26.1, 14.2$; HRMS (ESI^+): Calculated for $\text{C}_{15}\text{H}_{21}\text{N}_2\text{O}_5$ ($[\text{M}+\text{H}]^+$): 309.1444. Found: 309.1444.

11-Methoxy-7-(4-methylbenzenesulfonyl)-5,7-diazatricyclo[6.4.0.0^{1,5}]dodec-11-ene-6,10-dione **2m**



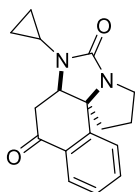
General Procedure B was followed starting with urea **1m** (140 mg, 0.371 mmol). Flash column chromatography (SiO_2 , hexane–EtOAc, 2:8 to 0:10) gave the desired enone (102 mg, 0.271 mmol, 73%) as a colourless solid. m.p. (hexane–EtOAc) 205.2–208.6 °C; IR ($\nu_{\text{max}}/\text{cm}^{-1}$) 2974, 2907, 2255, 1736, 1633, 1595, 1337, 1203, 1149, 1063; ^1H NMR (400 MHz; CDCl_3) $\delta = 7.91$ (2H, d, $J = 8.3$), 7.31 (2H, d, $J = 8.3$), 5.30 (1H, s), 4.57 (1H, dd, $J = 9.2, 5.7$), 3.84 (1H, ddd, $J = 12.4, 8.4, 6.1$), 3.62 (3H, s), 3.28 (1H, dd, $J = 15.9, 5.7$), 3.11 (1H, ddd, $J = 12.4, 8.5, 6.5$), 2.99 (1H, dd, $J = 15.9, 9.2$), 2.42 (3H, s), 2.10 – 1.98 (2H, m), 1.92 (1H, ddd, $J = 12.4, 7.2, 3.4$), 1.68 (1H, app dt, $J = 12.4, 9.8$); ^{13}C NMR (101 MHz; CDCl_3) $\delta = 189.4, 156.6, 151.1, 145.3, 135.6, 129.8, 128.3, 110.2, 65.1, 57.6, 55.3, 44.3, 42.0, 36.4, 23.5, 21.8$; HRMS (ESI^+): Calculated for $\text{C}_{18}\text{H}_{21}\text{N}_2\text{O}_5\text{S}$ ($[\text{M}+\text{H}]^+$): 377.1165. Found: 377.1162.

7-(4-Chlorophenyl)-11-methoxy-5,7-diazatricyclo[6.4.0.0^{1,5}]dodec-11-ene-6,10-dione **2n**



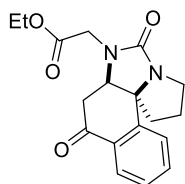
General Procedure A was followed starting with urea **1n** (80.5 mg, 0.241 mmol). Flash column chromatography (SiO_2 , hexane–EtOAc, 3:7 to 2:8) gave the desired enone (51.4 mg, 0.155 mmol, 64%) as a colourless oil. IR ($\nu_{\text{max}}/\text{cm}^{-1}$) 2964, 2897, 1696, 1633, 1494, 1386, 1320, 1092; ^1H NMR (400 MHz, CDCl_3) $\delta = 7.31$ (2H, d, $J = 8.8$), 7.21 (2H, d, $J = 8.8$), 5.43 (1H, s), 4.41 (1H, dd, $J = 6.0, 5.3$), 3.92 (1H, ddd, $J = 12.2, 7.7, 4.5$), 3.67 (3H, s), 3.30 – 3.20 (1H, m), 2.90 (1H, dd, $J = 16.4, 5.1$), 2.80 (1H, dd, $J = 16.4, 6.3$), 2.29 – 1.95 (4H, m); ^{13}C NMR (101 MHz, CDCl_3) $\delta = 189.7, 160.0, 150.3, 135.9, 130.6, 129.4, 123.7, 113.0, 64.4, 59.5, 55.2, 45.4, 38.9, 37.1, 25.2$; HRMS (ESI^+): Calculated for $\text{C}_{17}\text{H}_{18}^{35}\text{ClN}_2\text{O}_3$ ($[\text{M}+\text{H}]^+$): 333.1000. Found: 333.0997.

11-Cyclopropyl-11,13-diazatetracyclo[8.6.0.0^{1,13}.0^{2,7}]hexadeca-2(7),3,5-triene-8,12-dione
2o



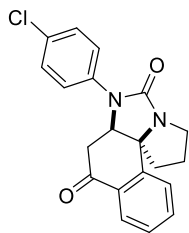
General Procedure A was followed starting with urea **1o** (76.6 mg, 0.270 mmol). Flash column chromatography (SiO₂, CH₂Cl₂ then CH₂Cl₂–MeOH, 95:5) gave the desired product (20.5 mg, 0.072 mmol, 27%) as a colourless solid. m.p. 163.1–163.2°C; IR (ν_{\max} /cm⁻¹) 2968, 2881, 1686, 1601, 1396, 1376, 1323, 1292, 1174; ¹H NMR (400 MHz, CDCl₃) δ = 7.92 (1H, dd, *J* = 8.1, 1.4), 7.61 (1H, ddd, *J* = 8.1, 7.7, 1.4), 7.40 – 7.35 (2H, m), 4.04 (1H, dd, *J* = 12.1, 7.9), 3.86 (1H, dd, *J* = 4.1, 3.6), 3.39 (1H, app td, *J* = 11.5, 5.4), 3.32 (1H, dd, *J* = 16.7, 3.6), 2.94 (1H, dd, *J* = 16.7, 4.1), 2.36 – 2.17 (3H, m), 2.11 – 2.04 (1H, m), 2.01 – 1.87 (1H, m), 0.85 – 0.76 (1H, m), 0.72 – 0.57 (2H, m), 0.51 – 0.43 (1 H, m); ¹³C NMR (101 MHz, CDCl₃) δ = 194.9, 164.8, 146.6, 134.8, 131.2, 128.3, 127.8, 125.4, 66.3, 64.8, 48.8, 39.0, 37.8, 27.5, 24.9, 5.9, 4.6; HRMS (ESI⁺): Calculated for C₁₇H₁₉N₂O₂ ([M+H]⁺): 283.1441. Found: 283.1441.

Ethyl 2-{8,12-dioxo-11,13-diazatetracyclo[8.6.0.0^{1,13}.0^{2,7}]hexadeca-2(7),3,5-trien-11-yl}acetate 2p



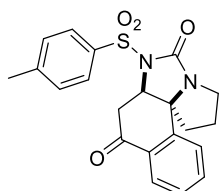
General Procedure B was followed starting with urea **1p** (95 mg, 0.29 mmol). Flash column chromatography (SiO₂, hexane–EtOAc, 9:1) gave the desired product (60 mg, 0.18 mmol, 62%) as a colourless solid. mp (hexane–EtOAc): 115.7–116.3 °C; IR (ν_{\max} /cm⁻¹) 2975, 2890, 1739, 1691, 1601, 1408, 1389, 1324, 1294, 1204; ¹H NMR (400 MHz; CDCl₃) δ = 7.91 (1H, dd, *J* = 7.9, 1.2), 7.62 (1H, td, *J* = 7.9, 1.3), 7.43 – 7.35 (2H, m), 4.31 (1H, app t, *J* = 3.7), 4.23 – 4.13 (3H, m), 4.03 (1H, app dd, *J* = 11.7, 7.5), 3.60 (1H, d, *J* = 18.2), 3.42 (1H, app td, *J* = 11.5, 5.5), 2.97 (1H, dd, *J* = 16.9, 4.1), 2.90 (1H, dd, *J* = 16.9, 3.4), 2.43 – 2.19 (3H, m), 2.14 – 1.98 (1H, m), 1.26 (3H, t, *J* = 7.1); ¹³C NMR (101 MHz; CDCl₃) δ = 194.5, 169.4, 163.7, 146.4, 134.9, 131.3, 128.3, 127.9, 125.4, 65.6, 62.6, 61.4, 49.4, 42.7, 39.1, 37.4, 27.7, 14.2; HRMS (ESI⁺): Calculated for C₁₈H₂₁N₂O₄ ([M+H]⁺): 329.1495. Found: 329.1491.

11-(4-Chlorophenyl)-11,13-diazatetracyclo[8.6.0.0¹,¹³.0²,⁷]hexadeca-2(7),3,5-triene-8,12-dione **2q**



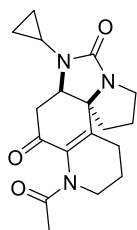
General Procedure A was followed starting with urea **1q** (105 mg, 0.296 mmol). Flash column chromatography (SiO₂, hexane–EtOAc, 7:3 to 5:5) gave the desired product (63.3 mg, 0.179 mmol, 60%) as a colourless solid. mp (hexane–EtOAc): 187–188 °C; IR (ν_{\max} /cm⁻¹) 2951, 2885, 1690, 1598, 1531, 1493, 1374, 1325, 1175, 1132, 1089; ¹H NMR (400 MHz, MeOD) δ = 7.87 (1H, dd, *J* = 7.9, 1.2), 7.75 (1H, ddd, *J* = 8.1, 7.4, 1.4), 7.63 (1H, d, *J* = 7.9), 7.46 (1H, ddd, *J* = 8.1, 7.4, 1.1), 7.39 (2H, d, *J* = 8.8), 7.12 (2H, d, *J* = 8.8), 4.71 (1H, dd, *J* = 4.0, 3.5), 3.95 (1H, app dd, *J* = 11.6, 7.7), 3.54 (1H, app td, *J* = 11.4, 5.9), 3.17 (1H, dd, *J* = 16.9, 4.2), 2.89 (1H, dd, *J* = 16.9, 3.3), 2.58 (1H, ddd, *J* = 13.3, 8.4, 1.7), 2.43 (1H, ddd, *J* = 13.3, 10.9, 7.4), 2.37 – 2.28 (1H, m), 2.20 – 2.08 (1H, m); ¹³C NMR (101 MHz, MeOD) δ = 196.2, 163.5, 147.6, 137.2, 136.2, 132.5, 132.3, 130.1, 129.6, 129.0, 127.2, 126.1, 66.9, 65.0, 39.5, 37.9, 28.2 (one signal under solvent peak, at 48.6 in CDCl₃); HRMS (ESI⁺): Calculated for C₂₀H₁₈³⁵ClN₂O₂ ([M+H]⁺): 353.1051. Found: 353.1045.

11-(4-Methylbenzenesulfonyl)-11,13-diazatetracyclo[8.6.0.0¹,¹³.0²,⁷]hexadeca-2(7),3,5-triene-8,12-dione **2r**



General Procedure A was followed starting with urea **1r** (99.6 mg, 0.250 mmol). Flash column chromatography (SiO₂, hexane–EtOAc, 2:8 then CH₂Cl₂–MeOH 95:5) gave the desired product (28.7 mg, 0.0720 mmol, 29%) as a colourless oil. IR (ν_{\max} /cm⁻¹) 2927, 2892, 1732, 1692, 1599, 1328, 1293, 1167, 1087; ¹H NMR (400 MHz, CDCl₃) δ = 7.97 (1H, dd, *J* = 7.8, 1.2), 7.90 (2H, d, *J* = 8.3), 7.61 (1H, app td, *J* = 7.7, 1.4), 7.43 (1H, app td, *J* = 7.3, 0.8), 7.33 – 7.28 (3H, m), 4.50 (1H, app t, *J* = 5.1), 3.97 (1H, ddd, *J* = 10.5, 8.4, 1.7), 3.62 (1H, dd, *J* = 16.4, 5.5), 3.38 – 3.30 (1H, m), 3.15 (1H, dd, *J* = 16.4, 4.7), 2.41 (3H, s), 2.28 – 2.16 (3H, m), 2.01 – 1.95 (1H, m); ¹³C NMR (101 MHz, CDCl₃) δ = 193.4, 156.9, 145.2, 143.8, 135.1, 134.9, 131.4, 129.7, 128.6, 127.4, 126.2, 65.8, 63.2, 47.4, 40.2, 38.2, 26.2, 21.8; HRMS (ESI⁺): Calculated for C₂₁H₂₁N₂O₄S ([M+H]⁺): 397.1216. Found: 397.1219.

6-Acetyl-11-cyclopropyl-6,11,13-triazatetracyclo[8.6.0.0¹,¹³.0²,⁷]hexadec-2(7)-ene-8,12-dione 2s

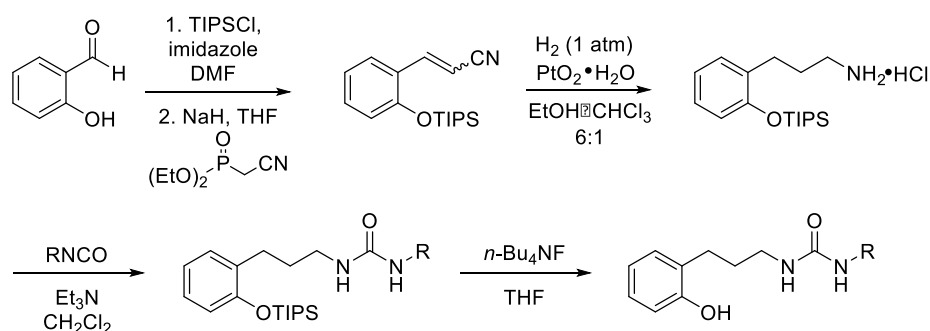


General Procedure B was followed starting with urea **1s** (76 mg, 0.23 mmol). Flash column chromatography (SiO₂, CH₂Cl₂ then CH₂Cl₂-MeOH, 97:3) gave the desired product (59 mg, 0.18 mmol, 78%) as a colourless oil. The product is rotameric leading to complex NMRs – spectra (CDCl₃) were recorded at rt and 50 °C without significant clarification; switching to MeOD did not result in clarification.

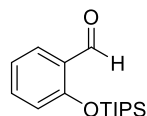
IR (ν_{\max} /cm⁻¹) 2957, 2883, 2237, 1687, 1655, 1386, 1315, 1230, 1027; ¹H NMR (501 MHz, CDCl₃, 50 °C) δ = 3.93 (1H, dd, J = 11.9, 8.3), 3.86 – 3.67 (2H, br m, includes at 3.73, dd, J = 4.1, 3.0), 3.41 – 3.16 (1H, br m), 3.16 (1H, dd, J = 15.6, 2.9), 3.10 – 3.03 (1H, m), 2.86 (1H, dd, J = 15.6, 4.0), 2.34 and 2.30 (1H, 2 × t, J = 6.8), 2.16 – 1.73 (11H, m), 0.84 – 0.78 (1H, m), 0.71 – 0.60 (2H, m), 0.60 – 0.53 (1H, m); ¹³C NMR (126 MHz, CDCl₃, 50 °C) δ = 188.2, 169.2, 163.6, 145.9 (*very broad and faint*), 134.4, 66.1, 65.1, 48.4, 42.5, 36.1, 33.7, 26.1, 23.9, 23.3, 22.2, 21.7, 4.8, 3.6; HRMS (ESI⁺): Calculated for C₁₈H₂₄N₃O₃ ([M+H]⁺): 330.1812. Found: 330.1807.

Preparation of compounds 3-6 (Scheme 1)

Preparation of 3a

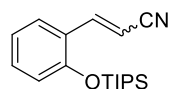


2-[[Tris(propan-2-yl)silyl]oxy]benzaldehyde **S20**



Salicylaldehyde (3 mL, 28.2 mmol) was dissolved in DMF (14 mL). Triisopropylsilyl chloride (7.3 mL, 34 mmol, 1.2 eq) was added and the reaction mixture was cooled down to 0 °C before the addition of imidazole (2.31 g, 33.9 mmol, 1.20 eq). The reaction mixture was warmed to rt and stirred overnight. EtOAc (50 mL) and H₂O (20 mL) were added. The phases were separated and the organic phase was successively washed with H₂O (2 × 20 mL), aqueous HCl (1M, 20 mL), aqueous saturated NaHCO₃ (20 mL) and brine (50 mL). The organic phase was then dried over Na₂SO₄, filtered and concentrated *in vacuo*. Flash column chromatography (SiO₂, hexane–EtOAc, 95:5) gave the title compound **S20** (6.85 g, 24.6 mmol, 87%) as a colourless oil. IR ($\nu_{\text{max}}/\text{cm}^{-1}$) 2945, 2866, 1597, 1575, 1388, 1368, 1476, 1456, 1306, 1275, 1117; ¹H NMR (300 MHz; CDCl₃) δ = 10.5 (1H, s), 7.81 (1H, dd, J = 7.8, 1.9), 7.44 (1H, ddd, J = 8.3, 7.3, 1.9), 7.04 – 6.97 (1H, m), 6.89 (1H, dd, J = 8.3, 0.6), 1.42 – 1.28 (3H, m), 1.13 (18H, d, J = 7.2); ¹³C NMR (75 MHz; CDCl₃) δ = 190.4, 159.6, 135.8, 128.4, 126.9, 121.2, 119.9, 18.1, 13.2; HRMS (ESI⁺): Calculated for C₁₆H₂₇O₂Si ([M+H]⁺): 279.1774. Found: 279.1766.

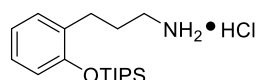
(2E/2Z)-3-(2-[[Tris(propan-2-yl)silyl]oxy]phenyl)prop-2-enitrile **S21**



Following a procedure adapted from Pouységu *et al.*,² to a solution of THF (60 mL) at 0 °C was added NaH (60% in mineral oil, 1.13 g, 28.1 mmol, 1.15 eq) portionwise and the suspension was stirred for 10 min. Diethylcyanophosphonate (4.6 mL, 28.4 mmol, 1.16 eq) was added dropwise at 0 °C and the reaction mixture was stirred 10 min before the addition of aldehyde **S20** (6.8 g, 24.4 mmol) in THF (19 mL). The reaction mixture was stirred for 2 h at 0 °C, and Et₂O was added (100 mL) before filtration of the reaction mixture directly over a pad of silica washed with Et₂O. After concentration *in vacuo*, the residue was purified

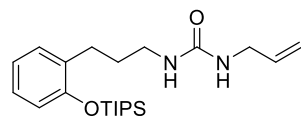
by flash column chromatography (SiO₂, hexane–EtOAc, 9:1) to give the desired nitriles **S21** as an inseparable mixture of isomers (7.22 g, 23.9 mmol, 97%, *E/Z* 3.3:1). IR (ν_{\max} /cm⁻¹) 2945, 2867, 2216, 1611, 1598, 1481, 1454, 1263, 1103; **Major E isomer** ¹H NMR (300 MHz; CDCl₃) δ = 7.78 (1H, d, *J* = 16.8), 7.41 (1H, dd, *J* = 7.8, 1.7), 1.42 – 1.28 (1H, m), 6.95 (1H, t, *J* = 7.5), 6.86 (1H, d, *J* = 8.3), 5.89 (1H, d, *J* = 16.8), 1.40 – 1.25 (3H, m), 1.12 (18H, d, *J* = 7.2); ¹³C NMR (75 MHz; CDCl₃) δ = 154.9, 146.4, 132.4, 127.2, 124.7, 121.4, 119.5, 118.9, 95.7, 18.0, 13.1; **Minor Z isomer** ¹H NMR (300 MHz; CDCl₃) δ = 8.12 (1H, dd, *J* = 7.9, 1.6), 7.61 (1H, d, *J* = 12.2), 1.42 – 1.28 (1H, m), 7.01 (1H, t, *J* = 7.8), 6.86 (1H, d, *J* = 8.3), 5.42 (1H, d, *J* = 12.2), 1.40 – 1.25 (3H, m), 1.12 (18H, d, *J* = 7.1); ¹³C NMR (75 MHz; CDCl₃) δ = 154.8, 144.4, 132.2, 128.5, 125.0, 121.3, 118.9, 117.7, 94.4, 18.0, 13.0; HRMS (ESI⁺): Calculated for C₁₈H₂₈NOSi ([M+H]⁺): 302.1934. Found: 302.1925.

Amine salt **S22**



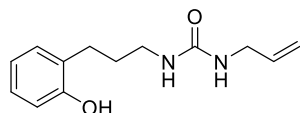
Following a procedure adapted from Pouységu *et al.*,² to a mixture of EtOH–CHCl₃ (6:1, 53 mL) was added unsaturated nitrile (3.50 g, 11.6 mmol). PtO₂·H₂O (184 mg, 0.810 mmol, 0.07 eq) was added and the reaction mixture was stirred under an atmosphere of H₂ (balloon) overnight. MeOH (100 mL) was added and the stirring was stopped. After 30 min the reaction mixture was removed from the reaction flask without the solid platinum residue. After concentration *in vacuo* the amine salt **S22** was used directly without further purification.

3-(Prop-2-en-1-yl)-1-[3-(2-{[tris(propan-2-yl)silyl]oxy}phenyl)propyl]urea **S23**



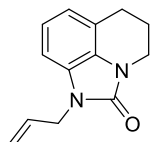
To a solution of the crude amine salt **S22** (1.04 g, \leq 3.03 mmol) in CH₂Cl₂ (20 mL) at 0 °C was successively added Et₃N (450 μ L, 3.22 mmol, \geq 1.06 eq) and allyl isocyanate (270 μ L, 3.05 mmol, \geq 1.01 eq). The reaction mixture was stirred for 2 h at rt. Saturated aqueous NH₄Cl (20 mL) and H₂O (20 mL) were added and the phases were separated. The aqueous phase was extracted with CH₂Cl₂ (2 \times 40 mL). The organic extracts were washed with Brine (50 mL), dried over Na₂SO₄, filtered and concentrated *in vacuo*. Flash column chromatography (SiO₂, hexane–EtOAc, 6:4) provided the desired urea **S23** as a colourless oil (826 mg, 2.12 mmol, 70% over two steps). IR (ν_{\max} /cm⁻¹) 3334, 2943, 2865, 1629, 1570, 1489, 1452, 1256, 1014; ¹H NMR (300 MHz, CDCl₃) δ = 7.10 (1H, dd, *J* = 7.4, 1.7), 7.04 (1H, td, *J* = 7.7, 1.8), 6.84 (1H, td, *J* = 7.4, 1.1), 6.78 (1H, dd, *J* = 8.0, 0.9), 5.84 (1H, ddt, *J* = 17.1, 10.4, 5.5), 5.17 (1H, app dq, *J* = 17.2, 1.6), 5.10 (1H, ddt, *J* = 10.2, 1.6, 1.4), 4.49 – 4.40 (1H, m), 3.76 (2H, app tt, *J* = 5.7, 1.5), 3.48 (1H, s), 3.20 (2H, app dt, *J* = 7.0, 6.0), 2.66 (2H, dd, *J* = 8.2, 6.9), 1.86 – 1.74 (2H, m), 1.37 – 1.23 (3H, m), 1.10 (18 H, d, *J* = 7.2); ¹³C NMR (75 MHz, CDCl₃) δ = 158.2, 154.0, 135.5, 131.7, 130.2, 127.0, 120.9, 118.1, 115.8, 43.2, 40.6, 30.4, 28.2, 18.2, 13.2; HRMS (ESI⁺): Calculated for C₂₂H₃₉N₂O₂Si ([M+H]⁺): 391.2775. Found: 391.2778.

1-[3-(2-Hydroxyphenyl)propyl]-3-(prop-2-en-1-yl)urea **3**



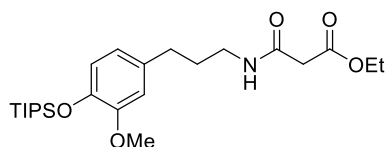
To a solution of the above urea **S23** (769 mg, 1.97 mmol) in THF (20 mL) at 0 °C was added *n*Bu₄NF (1M in THF, 2.6 mL, 2.6 mmol, 1.3 eq) dropwise. The reaction mixture warmed to rt and stirred for 2 h. After concentration *in vacuo* the residue was purified by flash column chromatography (SiO₂, hexane–EtOAc, 4:6 to 2:8) to afford the desired phenol as a colourless solid (333 mg, 1.42 mmol, 72%). m.p. 95.7–96.3 °C; IR (ν_{\max} /cm⁻¹) 3376, 3328, 2948, 2864, 1602, 1571, 1504, 1457, 1417, 1350, 1267, 1232, 1180, 1113; ¹H NMR (400 MHz, MeOD) δ = 7.04 (1H, d, *J* = 7.3), 6.98 (1H, t, *J* = 7.6), 6.76 – 6.70 (2H, t, *J* = 7.5), 5.85 (1H, ddt, *J* = 16.8, 10.2, 4.8), 5.17 (1H, d, *J* = 16.8), 5.06 (1H, d, *J* = 10.2), 3.73 (2H, d, *J* = 4.8), 3.13 (2H, t, *J* = 6.9), 2.62 (2H, t, *J* = 7.5), 1.81 – 1.71 (2H, m); ¹³C NMR (101 MHz, MeOD) δ = 161.1, 156.2, 136.9, 131.0, 129.2, 127.9, 120.5, 115.8, 115.2, 43.3, 40.7, 31.5, 28.3; HRMS (ESI⁺): Calculated for C₁₃H₁₉N₂O₂ ([M+H]⁺): 235.1441. Found: 235.1438.

3-(Prop-2-en-1-yl)-1,3-diazatricyclo[6.3.1.0^{4,12}]dodeca-4(12),5,7-trien-2-one **4**



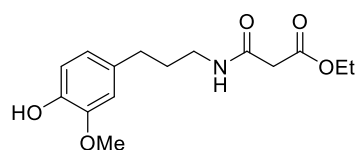
General Procedure B was followed starting with urea **3** (51.2 mg, 0.219 mmol). Flash column chromatography (SiO₂, hexane–EtOAc, 9:1) gave the tetrahydroquinoline (9.5 mg, 0.041 mmol, 19%) as a colourless oil. A minor side product (containing two carbon *sp*²: CH at 7.74 (d, *J* = 8.3) in ¹H NMR and 137.4 in ¹³C NMR; CH at 7.11 (d, *J* = 8.3) in ¹H NMR and 131.2 in ¹³C NMR) could not be separated from the product; IR (ν_{\max} /cm⁻¹) 3484, 2935, 1699, 1498, 1409, 1352; ¹H NMR (400 MHz, CDCl₃) δ = 6.95 (1H, t, *J* = 7.7), 6.85 (1H, d, *J* = 7.6), 6.80 (1H, d, *J* = 7.7), 5.91 (1H, ddt, *J* = 16.9, 10.6, 5.5), 5.27 – 5.19 (2H, m), 4.51 – 4.48 (2H, m), 3.90 – 3.86 (2H, m), 2.86 (2H, t, *J* = 6.1), 2.18 – 2.07 (2H, m); ¹³C NMR (101 MHz, CDCl₃) δ = 153.4, 132.5, 127.9, 126.7, 120.8, 119.5, 119.4, 117.6, 106.0, 43.7, 39.2, 24.0, 22.0; HRMS (ESI⁺): Calculated for C₁₃H₁₅N₂O ([M+H]⁺): 215.1178. Found: 215.1176.

Ethyl 2-([3-(4-hydroxy-3-methoxyphenyl)propyl]carbamoyl)acetate **5**



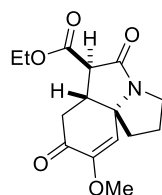
To a solution of the crude amine salt **S5** (3.22 g, \leq 8.64 mmol) in CH₂Cl₂ (60 mL) at 0 °C was successively added Et₃N (2.8 mL, 20 mmol, \geq 2.4 eq) and ethyl malonyl chloride (1.2 mL, 9.3 mmol, \geq 1.1 eq). The reaction mixture was stirred for 2 h at rt. Saturated aqueous NH₄Cl (30 mL) and H₂O (20 mL) were added and the phases were separated. The aqueous phase was

extracted with CH₂Cl₂ (2 × 40 mL). The organic extracts were washed with brine (40 mL), dried over Na₂SO₄, filtered and concentrated *in vacuo*. Flash column chromatography (SiO₂, hexane–EtOAc, 6:4) afforded the urea **S24** as a colourless oil (2.87 g, 6.36 mmol, 74% over two steps). IR (ν_{\max} /cm⁻¹) 3292, 2942, 2865, 1740, 1649, 1556, 1513, 1464, 1274, 1232, 1157, 1072; ¹H NMR (400 MHz; CDCl₃) δ = 7.10 (1H, s), 6.71 (1H, d, *J* = 8.0), 6.60 (1H, d, *J* = 1.9), 6.54 (1H, dd, *J* = 8.0 and 1.9), 4.14 (2H, q, *J* = 7.1), 3.73 (3H, s), 3.27 – 3.21 (4H, m, includes 2H, 3.22, s), 2.52 (2H, dd, *J* = 8.1, 7.2), 1.78 (2H, app dq, *J* = 8.1, 7.2), 1.23 (3H, t, *J* = 7.1), 1.27 – 1.12 (3H, m), 1.02 (18H, d, *J* = 7.2); ¹³C NMR (101 MHz; CDCl₃) δ = 169.9, 165.0, 150.8, 143.8, 134.5, 120.3, 120.3, 112.6, 61.6, 55.6, 41.1, 39.2, 32.9, 31.2, 18.0, 14.2, 13.0; HRMS (ESI⁺): Calculated for C₂₄H₄₂NO₅Si ([M+H]⁺): 452.2826. Found: 452.2822.



To a solution of the above malonate half-ester/half-amide **S24** (2.81 g, 6.23 mmol) in THF (20 mL) at 0 °C was added *n*Bu₄NF (1M in THF, 8.2 mL, 8.2 mmol, 1.3 eq) dropwise. The reaction mixture warmed to rt and stirred for 2 h. After concentration *in vacuo* the residue was purified by flash column chromatography (SiO₂, hexane–EtOAc, 2:8 to 1:9) to afford the desired phenol as a colourless oil (1.64 g, 5.56 mmol, 89%). IR (ν_{\max} /cm⁻¹) 3305, 2937, 1732, 1647, 1553, 1514, 1451, 1429, 1268, 1186, 1151, 1123, 1028; ¹H NMR (400 MHz; CDCl₃) δ = 7.19 (1H, s), 6.80 (1H, d, *J* = 8.0), 6.68 – 6.62 (2H, m), 5.74 (1H, s), 4.18 (2H, q, *J* = 7.1), 3.85 (3H, s), 3.33 – 3.26 (4H, m (includes 3.27, s)), 2.60 – 2.54 (2H, m), 1.86 – 1.77 (2H, m), 1.27 (3H, t, *J* = 7.1); ¹³C NMR (101 MHz, CDCl₃) δ = 169.8, 165.1, 146.6, 143.9, 133.2, 120.9, 114.4, 111.1, 61.6, 55.9, 41.1, 39.1, 32.8, 31.2, 14.1; HRMS (ESI⁺): Calculated for C₁₅H₂₂NO₅ ([M+H]⁺): 296.1492. Found: 296.1488.

Ethyl 2-methoxy-3,6-dioxo-3*H*,4*H*,5*H*,6*H*,8*H*,9*H*,10*H*,10*bH*-cyclohexa[*h*]pyrrolizine-5-carboxylate **6**

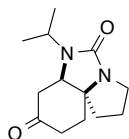


To a solution of [bis(trifluoroacetoxy)iodo]benzene (1.95 g, 4.53 mmol, 1.1 eq) in MeCN (40 mL) and H₂O (50 μ L) at 0 °C was added a solution of phenol **5** (1.22 g, 4.14 mmol) in MeCN (13 mL) dropwise. The reaction mixture was stirred at 0 °C for 20 min before the addition of Et₃N (1.5 mL, 10.8 mmol, 2.6 eq). The reaction mixture was concentrated *in vacuo* and the residue was partitioned between EtOAc (20 mL) and H₂O (20 mL). The phases were separated and the aqueous phase was extracted with EtOAc (2 × 20 mL). The combined organic extracts were washed with brine (30 mL), dried over Na₂SO₄, filtered and concentrated *in vacuo*. The residue was then diluted with MeCN (20 mL) and the solution cooled to 0 °C. Cs₂CO₃ (2.8 g, 8.5 mmol, 2.0 eq) was added and the reaction mixture was

stirred 40 min. After concentration *in vacuo*, the residue was purified by flash column chromatography (SiO₂, hexane–EtOAc, 1:9) gave the desired product (596 mg, 2.03 mmol, 49%) as a colourless solid. A suitable crystal was obtained for X-Ray crystallography. mp (hexane–EtOAc): 168–170 °C; IR ($\nu_{\text{max}}/\text{cm}^{-1}$) 2939, 1736, 1686, 1626, 1463, 1351, 1324, 1304, 1179, 1146, 1076; ¹H NMR (400 MHz, CDCl₃) δ = 5.45 (1H, d, J = 1.3), 4.23 – 4.14 (2H, m), 3.80 – 3.72 (1H, m), 3.58 (3H, s), 3.51 (1H, d, J = 12.4), 3.17 – 3.03 (2H, m), 2.76 (1H, dd, J = 17.6, 5.8), 2.59 (1H, dd, J = 17.6, 1.9), 2.25 – 1.97 (4H, m), 1.24 (3H, t, J = 7.1); ¹³C NMR (101 MHz, CDCl₃) δ = 190.1 (COOEt), 168.4, 168.1, 149.6, 114.6, 66.9, 61.8, 55.9, 55.0, 44.9, 42.5, 36.9, 36.5, 26.1, 14.1; HRMS (ESI⁺): Calculated for C₁₅H₂₀NO₅ ([M+H]⁺): 294.1335. Found: 294.1331.

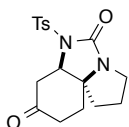
Functional group manipulations on dearomatised products: Scheme 2

6-Isopropylhexahydro-1*H*,5*H*-benzo[*d*]pyrrolo[1,2-*c*]imidazole-5,8(6*H*)-dione **7**



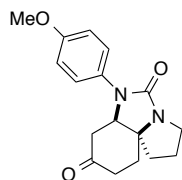
To a solution of the enone **2c** (197 mg, 0.84 mmol, 1.0 eq.) and tris(triphenyl)rhodium(I) chloride (15.6 mg, 16.9 μ mol, 2.0 mol%) in 5 mL THF, 6 mL of TES was added. The mixture was stirred at room temperature for 24 h. 0.05 mL of 1M HCl was then added and the mixture was stirred at room temperature for 1 h and evaporated *in vacuo*. Flash chromatography eluting with 50 – 100% EtOAc in hexane afforded the product **7** (167 mg, 0.71 mmol, 85%). IR ν_{\max} (neat)/ cm^{-1} : 2967, 1682. ^1H NMR (300 MHz, MeOD) δ = 4.03 (1H, dd, J = 5.1, 3.2), 3.71 (1H, hept, J = 6.9), 3.53 (1H, ddd, J = 12.0, 6.0, 3.3), 2.92 (1H, ddd, J = 12.0, 5.7, 3.6), 2.83 (1H, dd, J = 15.5, 5.3), 2.50 (1H, dd, J = 15.5, 3.1), 2.31 – 2.22 (2H, m), 2.03 (1H, ddd, J = 14.5, 10.1, 6.5), 1.95 – 1.78 (4H, m), 1.65 – 1.52 (1H, m), 1.14 (3H, d, J = 6.9), 1.12 (3H, d, J = 6.9). ^{13}C NMR (75 MHz, MeOD) δ = 213.1, 164.9, 66.6, 60.0, 46.3, 45.3, 43.6, 38.0, 36.1, 29.5, 24.6, 21.4, 19.5. HRMS (ESI): $\text{C}_{13}\text{H}_{21}\text{N}_2\text{O}_2$ [$\text{M} + \text{H}^+$]: calculated 237.1598, found 237.1595.

6-(4-Toluenesulfonyl)hexahydro-1*H*,5*H*-benzo[*d*]pyrrolo[1,2-*c*]imidazole-5,8(6*H*)-dione **8**



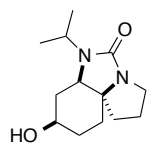
To a mixture of $\text{Pd}(\text{OH})_2/\text{C}$ (27.0 mg, 20% w/w) and enone **2f** (133 mg, 0.38 mmol, 1.0 eq.) under an atmosphere of nitrogen, 10 mL of HPLC grade EtOAc was added gently. The reaction mixture was degassed and hydrogen gas was bubbled through it with the aid of a balloon, and this procedure was repeated twice. The mixture was then allowed to stir under a balloon of hydrogen for 27 h at room temperature. The reaction mixture was filtered through a plug of Celite washing with 100 mL EtOAc. The filtrate was evaporated *in vacuo*. Flash chromatography eluting with 50 - 90% EtOAc in hexane afforded the product **8** as a white solid (111 mg, 0.32 mmol, 83%); IR ν_{\max} (neat)/ cm^{-1} : 2959, 1718, 1596, 1494, 1455, 1352. ^1H NMR δ (400 MHz, CDCl_3) δ = 7.83 (2H, d, J = 8.4), 7.32 (2H, d, J = 8.8), 4.56 (1H, dd, J = 5.2, 3.8), 3.66 (1H, ddd, J = 12.0, 5.6, 3.2), 3.13 (1H, dd, J = 16.3, 3.7), 2.94 (1H, ddd, J = 12.1, 9.2, 4.9), 2.84 (1H, dd, J = 16.3, 5.3), 2.35 (3H, s), 2.34 - 2.18 (2H, m), 2.03 – 1.79 (5H, m), 1.59-1.50 (1H, m). ^{13}C NMR (100 MHz, CDCl_3) δ = 208.1, 156.6, 145.0, 135.4, 129.6, 128.4, 65.1, 59.4, 43.6, 42.9, 37.1, 34.8, 28.4, 23.5, 21.7. HRMS (ESI): $\text{C}_{17}\text{H}_{21}\text{N}_2\text{O}_4\text{S}$ [$\text{M} + \text{H}^+$]: calculated 349.1217, found 349.1217.

6-(4-Methoxyphenyl)hexahydro-1*H*,5*H*-benzo[*d*]pyrrolo[1,2-*c*]imidazole-5,8(6*H*)-dione **9**



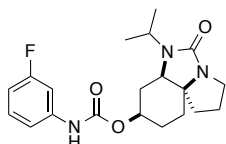
To a mixture of Pd(OH)₂/C (20.8 mg, 20% w/w) and enone **2i** (104 mg, 0.35 mmol, 1.0 eq.) under an atmosphere of nitrogen, 10 mL of HPLC grade EtOAc was added gently. The reaction mixture was degassed and hydrogen gas was bubbled through it with the aid of a balloon, and this procedure was repeated twice. The mixture was then allowed to stir under a balloon of hydrogen for 23 h at room temperature. The reaction mixture was filtered through a plug of Celite washing with 100 mL EtOAc. The filtrate was evaporated *in vacuo*. Flash chromatography eluting with 2 - 4% MeOH in DCM afforded the product **9** as a brown solid (72 mg, 0.24 mmol, 69%); IR ν_{\max} (neat)/cm⁻¹: 2998, 2953, 2891, 1710, 1617, 1586, 1516, 1406. ¹H NMR (500 MHz, CDCl₃) δ = 7.04 (2H, d, *J* = 9.0), 6.81 (2H, d, *J* = 9.0), 4.35 (1H, t, *J* = 4.0), 3.76 (1H, ddd, *J* = 11.5, 5.5, 3.5), 3.71 (3H, s), 3.07 (1H, ddd, *J* = 11.5, 6.0, 3.5), 2.60 – 2.54 (2H, m), 2.54 -2.49 (1H, m), 2.31 (1H, dt, *J* = 19.0, 3.9), 2.03 – 1.89 (5H, m), 1.80 (1H, ddd, *J* = 16.0, 9.5, 3.5). ¹³C NMR (125 MHz, CDCl₃) δ = 208.2, 160.0, 156.3, 128.9, 124.3, 113.6, 63.2, 60.0, 54.5, 43.5, 39.4, 37.4, 34.2, 28.7, 23.4. HRMS (ESI): C₁₇H₂₁N₂O₃ [M + H⁺]: calculated 301.1547, found 301.1544.

8-Hydroxy-6-isopropyloctahydro-1*H*,5*H*-benzo[*d*]pyrrolo[1,2-*c*]imidazol-5-one **10**



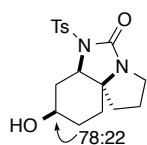
A mixture of the ketone **7** (24.0 mg, 0.10 mmol, 1.0 eq.) and CeCl₃·7H₂O (45.5 mg, 0.12 mmol, 1.2 eq.) in 3 mL of HPLC grade MeOH and it was allowed to stir at -78 °C for 30 min. NaBH₄ (4.62 mg, 0.12 mmol, 1.2 eq.) was then added and the mixture was left to warm up to room temperature for another 30 min. The reaction mixture was evaporated *in vacuo*. It was then taken up in 1 mL H₂O, diluted with 50 mL EtOAc, dried over Na₂SO₄ and evaporated *in vacuo*. Flash chromatography with 1 – 4% MeOH in DCM afforded the product **10** as a single diastereomer (22.0 mg, 0.09 mmol, 92% yield). IR ν_{\max} (neat)/cm⁻¹: 3399, 2937, 1666, 1056. ¹H NMR (500 MHz, CDCl₃) δ = 3.99 (1H, hept, *J* = 7.0), 3.78 (1H, ddd, *J* = 12.4, 9.2, 5.2), 3.57 (1H, tt, *J* = 10.5, 4.0), 3.44 (1H, dd, *J* = 10.1, 6.5), 2.85 (1H, ddd, *J* = 12.0, 6.0, 3.0), 2.33 (1H, dddd, *J* = 12.7, 6.5, 4.3, 2.2), 2.13 (1H, s), 1.85 (1H, dt, *J* = 14.5, 4.0), 1.80 – 1.63 (3H, m), 1.50 – 1.34 (4H, m), 1.31 – 1.23 (1H, m), 1.14 (3H, d, *J* = 7.0), 1.11 (3H, d, *J* = 6.5). ¹³C NMR (125 MHz, CDCl₃) δ = 162.6, 66.2, 64.5, 53.6, 43.2, 43.0, 40.8, 33.6, 29.6, 28.1, 21.9, 21.4, 18.8. HRMS (ESI): C₁₃H₂₃N₂O₂ [M + H⁺]: calculated 239.1754, found 239.1750.

Preparation of crystalline derivative of **10**: 6-isopropyl-5-oxooctahydro-1*H*,5*H*-benzo[*d*]pyrrolo[1,2-*c*]imidazol-8-yl (3-fluorophenyl)carbamate **S25**



A mixture of the ketone **7** (27.0 mg, 0.11 mmol, 1.0 eq.) and $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ (51.0 mg, 0.14 mmol, 1.2 eq.) in 3 mL of HPLC grade MeOH was allowed to stir at -78°C for 30 min. NaBH_4 (5.18 mg, 0.14 mmol, 1.2 eq.) was then added and the mixture was left to warm up to room temperature for another 30 min. The reaction mixture was evaporated *in vacuo*. It was then taken up in 1 mL H_2O , diluted with 50 mL EtOAc, dried over Na_2SO_4 and evaporated *in vacuo*. To a solution of the crude product in 5 mL DCM, 3-fluorophenylisocyanate (13 μL , 0.11 mmol, 1.0 eq.) and TEA (0.05 mL, 0.34 mmol, 3.0 eq.) were added and the mixture was stirred at room temperature overnight. The reaction mixture was evaporated *in vacuo*. Flash chromatography with 1 – 4% MeOH in DCM afforded the carbamate as a diastereomeric mixture in the ratio of 93:7 (36 mg, 0.10 mmol, 84% yield). Crystals of the major diastereomer were grown for X-ray analysis. IR ν_{max} (neat)/ cm^{-1} : 3254 (N-H); 3076, 2968 (C-H); 1723, 1671 (C=O); 1606, 1546, 1495 (C=C); 1221 (C-O). ^1H NMR (Major diastereomer, 500 MHz, CDCl_3) δ = 7.30 (1H, d, J = 10.6), 7.17 (1H, td, J = 8.2, 6.6), 7.00 (1H, d, J = 8.0), 6.68 (1H, td, J = 8.3, 2.3), 4.69 (1H, tt, J = 10.8, 4.0), 3.99 (1H, hept, J = 6.9), 3.79 (1H, ddd, J = 12.4, 9.3, 5.2), 3.52 (1H, dd, J = 9.9, 6.5), 2.86 (1H, ddd, J = 12.5, 7.0, 4.0), 2.43 – 2.36 (1H, m), 1.88 (1H, dt, J = 15.0, 4.0), 1.85 – 1.80 (1H, m), 1.77 (1H, ddd, J = 12.5, 6.0, 3.0), 1.75 – 1.66 (1H, m), 1.62 – 1.40 (4H, m), 1.37 (1H, ddd, J = 14.6, 10.8, 4.7), 1.14 (3H, d, J = 6.9), 1.12 (3H, d, J = 6.9). Signals for minor isomer visible at: 5.06 (0.07H, quint, J = 4.5), 3.70 (0.07H, dd, J = 8.2, 5.7). ^{13}C NMR (Major diastereomer, 125 MHz, CDCl_3) δ = 162.6, 162.2 (d, J = 243.0), 151.8, 138.7 (d, J = 13.2), 129.1 (d, J = 9.5), 112.8, 108.9, 104.9 (d, J = 26.8), 69.3, 64.4, 53.2, 43.3, 43.0, 36.9, 33.6, 27.6, 26.0, 21.9, 21.4, 18.7. Signals for minor isomer visible at: 52.1, 34.4, 25.1, 24.1, 22.2, 21.2. HRMS (ESI): $\text{C}_{20}\text{H}_{27}\text{FN}_3\text{O}_3$ [$\text{M} + \text{H}^+$]: calculated 376.2031, found 376.2028.

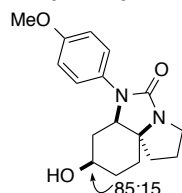
8-Hydroxy-6-(4-toluenesulfonyl)octahydro-1H,5H-benzo[d]pyrrolo[1,2-c]imidazol-5-one **11**



A mixture of the ketone **8** (18.0 mg, 0.05 mmol, 1.0 eq.) and $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ (23.2 mg, 0.06 mmol, 1.2 eq.) in 3 mL of HPLC grade MeOH was allowed to stir at -78°C for 30 min. NaBH_4 (2.40 mg, 0.06 mmol, 1.2 eq.) was then added and the mixture was left to warm up to room temperature for another 30 min. The reaction mixture was evaporated *in vacuo*. It was then taken up in 1 mL H_2O , diluted with 50 mL EtOAc, dried over Na_2SO_4 and evaporated *in vacuo*. Flash chromatography with 1 – 2% MeOH in DCM afforded the product **11** as a 78:22 mixture of diastereomers (15.0 mg, 0.04 mmol, 83% yield). IR ν_{max} (neat)/ cm^{-1} : 3388, 2922, 2852, 1727, 1658, 1597, 1161. ^1H NMR (Major diastereomer, 500 MHz, CDCl_3) δ = 7.87 (2H, d, J = 8.5), 7.24 (2H, d, J = 8.5), 4.17 (1H, dd, J = 10.0, 6.4), 3.74 – 3.61 (2H, m, 8-H), 2.89 (1H, ddd, J = 12.1, 9.4, 5.7), 2.67 (1H, dddd, J = 12.8, 6.4, 4.5, 1.9), 2.35 (3H, s), 1.86 – 1.70 (4H, m), 1.60 – 1.24 (6H, m). Signals for minor isomer visible at: 4.29 (0.29H, dd, J = 8.0, 5.5), 4.09

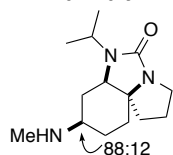
(0.29H, quint, $J = 5.0$). ^{13}C NMR (Major diastereomer, 125 MHz, CDCl_3) $\delta = 158.4, 144.8, 136.2, 129.6, 128.2, 66.4, 65.1, 57.7, 44.0, 39.4, 34.4, 30.0, 28.2, 22.9, 21.7$. Signals for minor isomer visible at: 158.1, 144.7, 136.1, 129.5, 128.1, 65.4, 63.9, 57.3, 43.8, 36.7, 35.2, 27.6, 25.3, 23.0. HRMS (ESI): $\text{C}_{17}\text{H}_{23}\text{N}_2\text{O}_4\text{S}$ [$\text{M} + \text{H}^+$]: calculated 351.1373, found 351.1369.

8-Hydroxy-6-(4-methoxyphenyl)octahydro-1*H*,5*H*-benzo[*d*]pyrrolo[1,2-*c*]imidazol-5-one **12**



A mixture of the ketone **9** (30.0 mg, 0.10 mmol, 1.0 eq.) and $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ (44.7 mg, 0.12 mmol, 1.2 eq.) in 3 mL of HPLC grade MeOH was allowed to stir at -78°C for 30 min. NaBH_4 (4.54 mg, 0.12 mmol, 1.2 eq.) was then added and the mixture was left to warm up to room temperature for another 30 min. The reaction mixture was evaporated *in vacuo*. It was then taken up in 1 mL H_2O , diluted with 50 mL EtOAc, dried over Na_2SO_4 and evaporated *in vacuo*. Flash chromatography with 1 – 3% MeOH in DCM afforded the product **12** as an 85:15 mixture of diastereomers (29.0 mg, 0.10 mmol, 96% yield). IR ν_{max} (neat)/ cm^{-1} : 3398, 2934, 1674, 1582, 1510, 1462, 1244. ^1H NMR (Major diastereomer, 500 MHz, CDCl_3) $\delta = 7.27$ (2H, d, $J = 9.0$), 6.80 (2H, d, $J = 9.5$), 3.96 (1H, dd, $J = 9.5, 6.2$), 3.85 (1H, ddd, $J = 12.3, 9.0, 5.5$), 3.72 (3H, s), 3.65 (1H, qd, $J = 9.0, 4.3$), 2.99 (1H, ddd, $J = 12.0, 6.0, 3.0$), 2.24 (1H, dddd, $J = 12.7, 6.2, 4.5, 1.9$), 1.91 (1H, dt, $J = 14.5, 4.0$), 1.89 – 1.73 (6H, m), 1.49 (1H, tdd, $J = 12.9, 9.4, 3.6$), 1.41 – 1.36 (1H, m), 1.36 – 1.31 (1H, m). Signals for minor isomer visible at: 4.15 (0.17H, dd, $J = 6.5, 5.5$), 4.03 (0.18H, quint, $J = 5.5$). ^{13}C NMR (Major diastereomer, 125 MHz, CDCl_3) $\delta = 162.0, 156.4, 131.4, 123.4, 114.4, 69.9, 64.4, 58.4, 55.5, 44.3, 38.0, 35.4, 30.5, 29.0, 23.2$. Signals for minor isomer visible at: 64.6, 64.0, 57.7, 36.3, 33.9, 28.4, 26.6, 23.7. HRMS (ESI): $\text{C}_{17}\text{H}_{23}\text{N}_2\text{O}_3$ [$\text{M} + \text{H}^+$]: calculated 303.1703, found 303.1698.

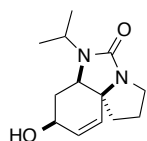
6-Isopropyl-8-(methylamino)octahydro-1*H*,5*H*-benzo[*d*]pyrrolo[1,2-*c*]imidazol-5-one **13**



To a solution of the ketone **7** (22.0 mg, 0.09 mmol, 1.0 eq.) in 6 mL THF, 33 wt% methylamine in EtOH (0.10 mL, 0.93 mmol, 10.0 eq.) and titanium isopropoxide (0.06 mL, 0.19 mmol, 2.0 eq.) were added and the mixture was left to stir at room temperature overnight. NaBH_4 (5.30 mg, 0.14 mmol, 1.5 eq.) was added to the reaction mixture at -78°C and it was stirred at the same temperature for 30 min. It was then allowed to warm up to room temperature for another 30 min. The reaction mixture was evaporated *in vacuo*. It was then taken up in 1 mL H_2O , diluted with 50 mL EtOAc, dried over MgSO_4 and evaporated *in vacuo*. Flash chromatography with 5% MeOH in DCM, followed by 99:9:1 of DCM/MeOH/aq. NH_3 respectively, afforded the product **13** as a diastereomeric mixture in the ratio of 88:12 (21.0 mg, 0.08 mmol, 90% yield). IR ν_{max} (neat)/ cm^{-1} : 3306, 2966, 2936, 2791, 1686. ^1H NMR

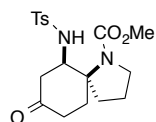
(Major diastereomer, 500 MHz, CDCl₃) δ = 3.98 (1H, hept, J = 7.0), 3.77 (1H, ddd, J = 12.4, 9.2, 5.3), 3.41 (1H, dd, J = 10.4, 6.5), 2.84 (1H, ddd, J = 12.4, 9.3, 5.9), 2.37 – 2.31 (4H, m, 8-H), 2.26 (1H, dddd, J = 12.5, 6.1, 3.7, 2.2), 1.88 – 1.82 (1H, m), 1.77 – 1.65 (4H, m), 1.44 – 1.34 (2H, m), 1.29 – 1.15 (3H, m), 1.14 (3H, d, J = 7.0), 1.11 (3H, d, J = 7.0). Signals for minor isomer visible at: 3.69 (0.14H, ddd, J = 12.1, 8.8, 6.0), 3.61 (0.13H, t, J = 5.5). ¹³C NMR (Major diastereomer, 125 MHz, CDCl₃) δ = 162.6, 64.9, 54.0, 53.7, 43.2, 43.0, 38.4, 33.8, 32.3, 28.8, 26.4, 21.9, 21.5, 18.7. Signals for minor isomer visible at: 162.4, 64.8, 53.8, 43.3, 34.8, 32.8, 25.3, 24.4, 22.2, 21.2, 18.5. HRMS (ESI): C₁₄H₂₆N₃O [M + H⁺]: calculated 252.2070, found 252.2079.

8-Hydroxy-6-isopropyl-2,3,6,6a,7,8-hexahydro-1H,5H-benzo[d]pyrrolo[1,2-c]imidazol-5-one 14



A mixture of enone **2c** (186 mg, 0.79 mmol, 1.0 eq.) and CeCl₃·7H₂O (354 mg, 0.95 mmol, 1.2 eq.) in 4 mL of HPLC grade methanol was allowed to stir for 30 min at -78 °C after which NaBH₄ (35.9 mg, 0.95 mmol, 1.2 eq.) was added and the mixture was further stirred at the same temperature for 40 min. The reaction mixture was then allowed to warm up to room temperature for 1 h. It was extracted with EtOAc (5 × 20mL), dried over MgSO₄ and evaporated *in vacuo*. Silica gel chromatography eluting with 70 – 90% EtOAc in hexane afforded the compound **14** as a white solid (173 mg, 0.73 mmol, 92% yield); IR ν_{\max} (neat)/cm⁻¹: 3369, 2971, 2937, 1666, 1416, 1223. ¹H NMR (300 MHz, MeOD) δ = 5.87 (1H, dt, J = 10.2, 1.3), 5.67 (1H, dd, J = 10.2, 2.2), 4.21 (1H, ddd, J = 10.8, 4.5, 2.4), 3.96 (1H, hept, J = 6.9), 3.79 (1H, dd, J = 12.0, 5.1), 3.71 (1H, ddd, J = 12.3, 5.7, 3.0), 3.04 (1H, ddd, J = 12.2, 9.2, 5.7), 2.44 (1H, dtd, J = 11.2, 4.8, 1.4), 2.04 – 1.79 (2H, m), 1.69 (1H, ddd, J = 12.3, 7.8, 2.6), 1.61 – 1.40 (2H, m), 1.28 (3H, d, J = 6.9), 1.26 (3H, d, J = 6.6). ¹³C NMR (75 MHz, MeOD) δ = 164.5, 134.7, 127.0, 65.8, 65.5, 56.0, 46.1, 45.3, 39.8, 36.3, 23.6, 22.4, 19.6. HRMS (ESI): C₁₃H₂₁N₂O₂ [M + H⁺]: calculated 237.1598, found 237.1598.

Methyl (5S',6R')-6-(4-methylbenzenesulfonamido)-8-oxo-1-azaspiro[4.5]decane-1-carboxylate 15



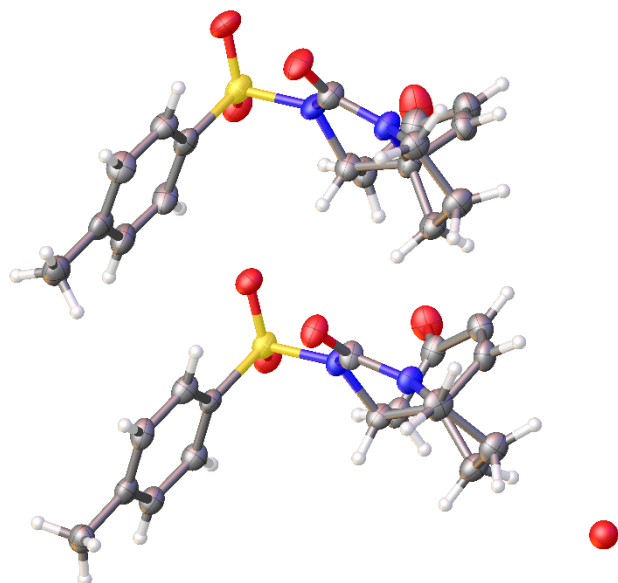
The enone **2f** (1.2 g, 3.5 mmol) was hydrogenated using palladium on carbon (10%, 120 mg) in methanol (40 mL), this gave the ketone **8** (1.21 g) as a foam which was not purified further. Sodium methoxide (100 mg, 1.85 mmol) was added to a solution of ketone (80 mg, <0.23 mmol) in toluene (2 mL); the solution was stirred at room temperature for 30 mins and then heated to 80 °C for 1 h. The reaction was cooled to room temperature, HCl (1M aq., 2 mL) was added and the reaction extracted with EtOAc (5 × 5 mL), dried, filtered and concentrated *in vacuo*. Column chromatography, eluting with EtOAc-hexanes (50:50) gave

the ketone **15** (74 mg, 0.184 mmol, 80%) as a colourless glass; ^1H NMR (500 MHz; DMSO) δ = 7.65 (2H, d, J = 8.3), 7.56 (1H, d, J = 5.3), 7.40 (2H, d, J = 8.3), 3.59 (3H, s), 3.55 (1H, dd, J = 10.6 and 4.9), 3.29 (1H, dt, J = 10.0 and 8.0), 2.85 (1H, td, J = 13.6, 13.2, 4.8), 2.73 (1H, br s), 2.60 (1H, dd, J = 15.9, 4.9), 2.55-2.49 (1H, m), 2.45–2.25 (3H, m), 2.41 (3H, s), 1.83 (1H, ddd, J = 12.8, 9.8, 6.9), 1.75 – 1.56 (3H, m); ^{13}C NMR (126 MHz; DMSO) δ = 207.9, 156.3, 143.0, 136.6, 129.5, 126.5, 65.2, 57.6, 52.4, 48.1, 45.8, 37.9, 37.1, 29.3, 20.9; IR (ν_{max} / cm^{-1}) 3319, 2943, 2831, 1667, 1450, 1378, 1325, 1021, 736, 564; HRMS (ESI $^+$): Calculated for $\text{C}_{18}\text{H}_{22}\text{N}_2\text{NaO}_5\text{S}$ ($[\text{M}+\text{Na}]^+$): 403.1304. Found: 403.1305.

References

- (1) Padiya, K. J.; Gavade, S.; Kardile, B.; Tiwari, M.; Bajare, S.; Mane, M.; Gaware, V.; Varghese, S.; Harel, D.; Kurhade, S. Unprecedented "In Water" Imidazole Carbonylation: Paradigm Shift for Preparation of Urea and Carbamate. *Org. Lett.* **2012**, *14*, 2814-2817.
- (2) Pouységu, L.; Avellan, A.-V.; Quideau, S. Iodine(III)-Mediated Generation of Nitrogen-Tethered Orthoquinolyl Acetates for the Construction of Oxygenated Indole, Quinoline, and Phenanthridine Alkaloid Motifs. *J. Org. Chem.* **2002**, *67*, 3425-3436.

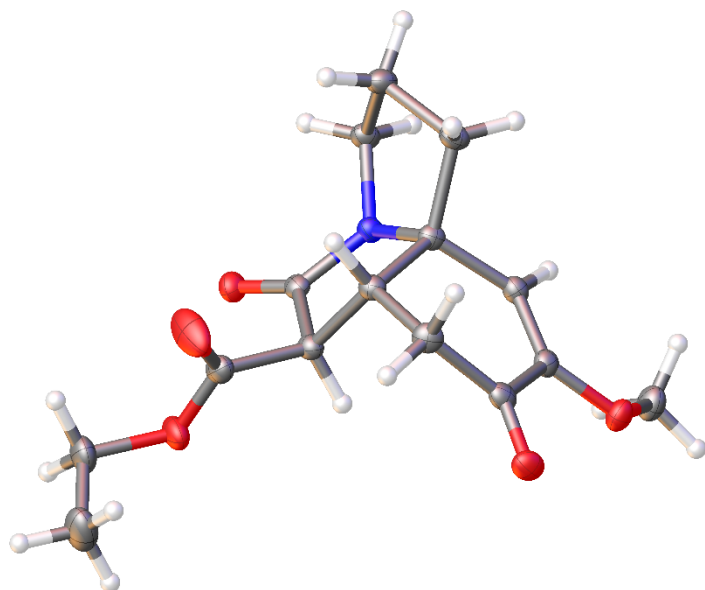
X-ray structure of compound 2f



CCDC deposition number: 2174965

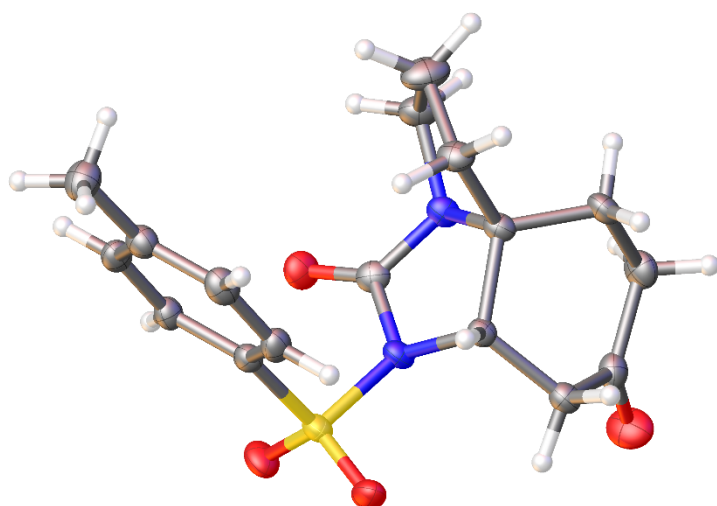
Empirical formula	C ₁₇ H _{18.13} N ₂ O _{4.06} S
Formula weight	347.52
Temperature/K	125.01(10)
Crystal system	monoclinic
Space group	C2/c
a/Å	21.9810(18)
b/Å	8.5032(5)
c/Å	34.011(3)
α/°	90
β/°	91.007(7)
γ/°	90
Volume/Å ³	6355.9(8)
Z	16
ρ _{calc} /cm ³	1.453
μ/mm ²	2.037
F(000)	2922.0
Crystal size/mm ³	0.22 × 0.04 × 0.04
Radiation	CuKα (λ = 1.54184)
2θ range for data collection/°	8.046 to 147.086
Index ranges	-27 ≤ h ≤ 25, -10 ≤ k ≤ 8, -31 ≤ l ≤ 42
Reflections collected	12352
Independent reflections	6240 [R _{int} = 0.0862, R _{sigma} = 0.1321]
Data/restraints/parameters	6240/0/436
Goodness-of-fit on F ²	1.038
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0771, wR ₂ = 0.1679
Final R indexes [all data]	R ₁ = 0.1395, wR ₂ = 0.2158
Largest diff. peak/hole / e Å ⁻³	0.45/-0.58

X-ray structure of compound 6



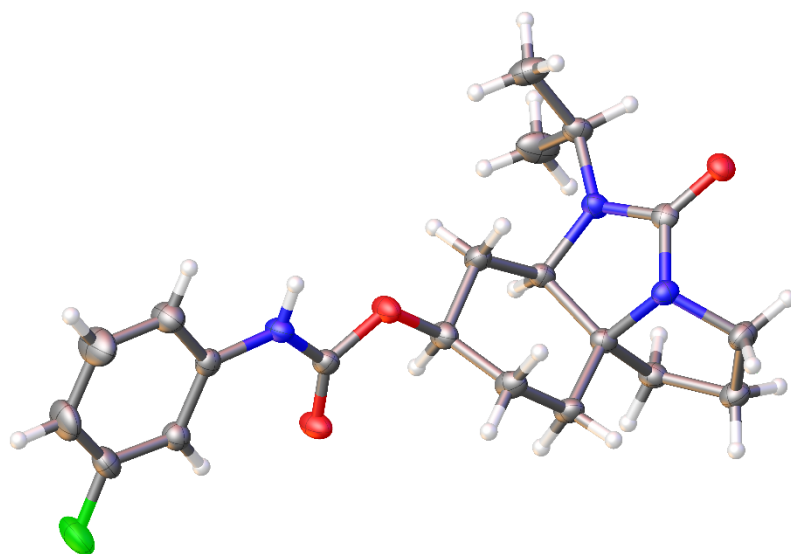
CCDC deposition number:	2174962
Empirical formula	C ₁₅ H ₁₉ NO ₅
Formula weight	293.31
Temperature/K	120.00(15)
Crystal system	monoclinic
Space group	P2 ₁ /c
a/Å	10.1141(4)
b/Å	7.4519(4)
c/Å	18.8419(8)
α/°	90
β/°	96.346(4)
γ/°	90
Volume/Å ³	1411.40(11)
Z	4
ρ _{calc} /cm ³	1.380
μ/mm ²	0.104
F(000)	624.0
Crystal size/mm ³	0.29 × 0.26 × 0.18
Radiation	Kα (λ = 0.71073)
2θ range for data collection/°	5.884 to 62.456
Index ranges	-13 ≤ h ≤ 14, -10 ≤ k ≤ 10, -24 ≤ l ≤ 27
Reflections collected	19778
Independent reflections	4269 [R _{int} = 0.0521, R _{sigma} = 0.0420]
Data/restraints/parameters	4269/0/192
Goodness-of-fit on F ²	1.068
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0521, wR ₂ = 0.1222
Final R indexes [all data]	R ₁ = 0.0652, wR ₂ = 0.1309
Largest diff. peak/hole / e Å ⁻³	0.50/-0.30

X-ray structure of compound 8



CCDC deposition number:	2174967
Empirical formula	C ₁₇ H ₂₀ N ₂ O ₄ S
Formula weight	348.41
Temperature/K	25.01(10)
Crystal system	tetragonal
Space group	P4 ₁
a/Å	8.51937(12)
b/Å	8.51937(12)
c/Å	22.6198(5)
α/°	90
β/°	90
γ/°	90
Volume/Å ³	1641.74(6)
Z	4
ρ _{calc} /cm ³	1.410
μ/mm ²	1.967
F(000)	736.0
Crystal size/mm ³	0.17 × 0.08 × 0.06
Radiation	CuKα (λ = 1.54184)
2θ range for data collection/°	10.384 to 146.892
Index ranges	-10 ≤ h ≤ 10, -7 ≤ k ≤ 9, -27 ≤ l ≤ 27
Reflections collected	6158
Independent reflections	3188 [R _{int} = 0.0412, R _{sigma} = 0.0545]
Data/restraints/parameters	3188/1/218
Goodness-of-fit on F ²	1.014
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0378, wR ₂ = 0.0852
Final R indexes [all data]	R ₁ = 0.0440, wR ₂ = 0.0892
Largest diff. peak/hole / e Å ⁻³	0.22/-0.21
Flack parameter	0.004(19)

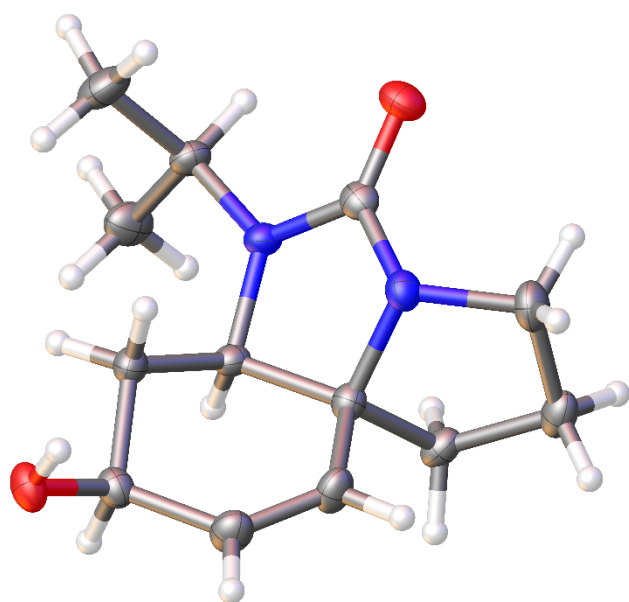
X-ray structure of S25 (urea derivative of compound 10)



CCDC deposition number: 2175094

Empirical formula	C ₂₀ H ₂₆ FN ₃ O ₃
Formula weight	375.44
Temperature/K	120.00(18)
Crystal system	monoclinic
Space group	P21/c
a/Å	11.6465(3)
b/Å	19.7846(5)
c/Å	8.73330(19)
α/°	90
β/°	103.566(2)
γ/°	90
Volume/Å ³	1956.20(8)
Z	4
ρ _{calc} /cm ³	1.275
μ/mm ²	0.766
F(000)	800.0
Crystal size/mm ³	0.14 × 0.11 × 0.06
Radiation	CuKα (λ = 1.54184)
2θ range for data collection/°	7.808 to 146.908
Index ranges	-10 ≤ h ≤ 13, -20 ≤ k ≤ 24, -10 ≤ l ≤ 9
Reflections collected	8404
Independent reflections	3763 [R _{int} = 0.0327, R _{sigma} = 0.0390]
Data/restraints/parameters	3763/0/250
Goodness-of-fit on F ²	1.047
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0402, wR ₂ = 0.0945
Final R indexes [all data]	R ₁ = 0.0520, wR ₂ = 0.1021
Largest diff. peak/hole / e Å ⁻³	0.24/-0.20

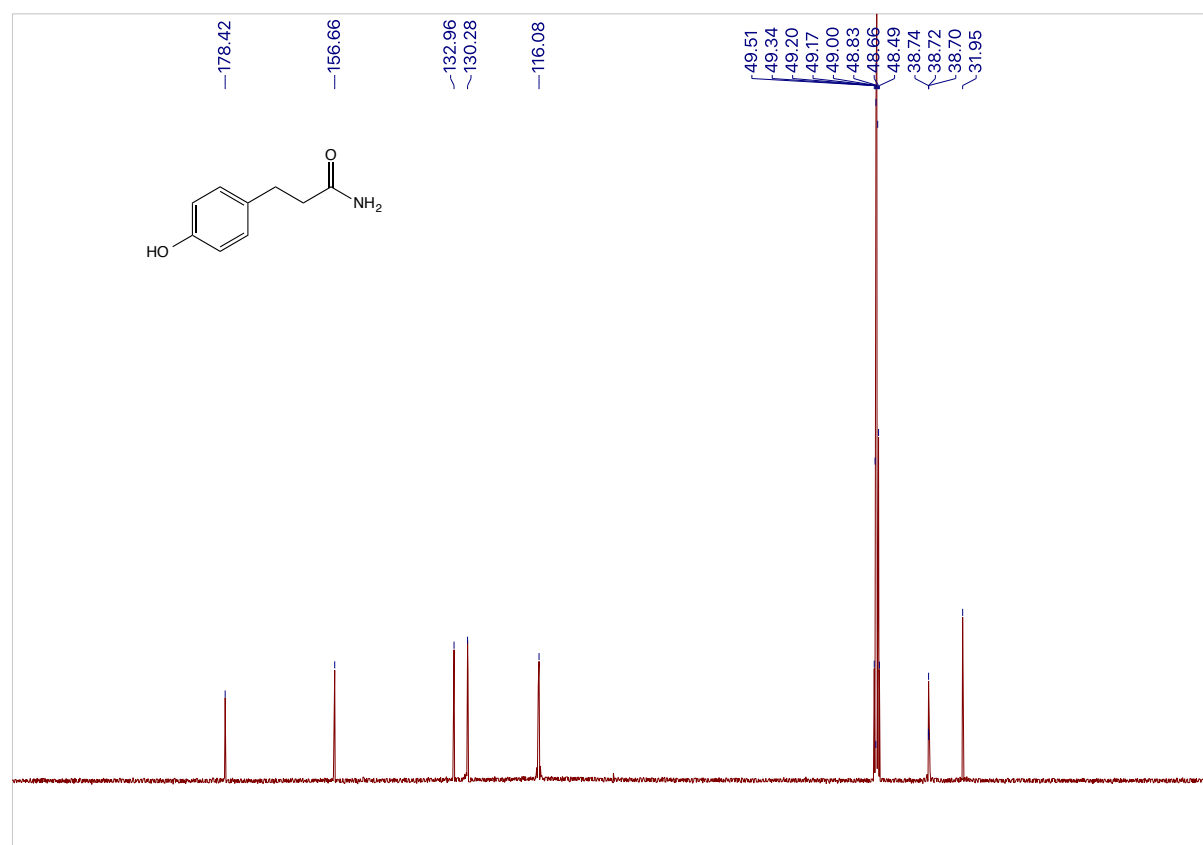
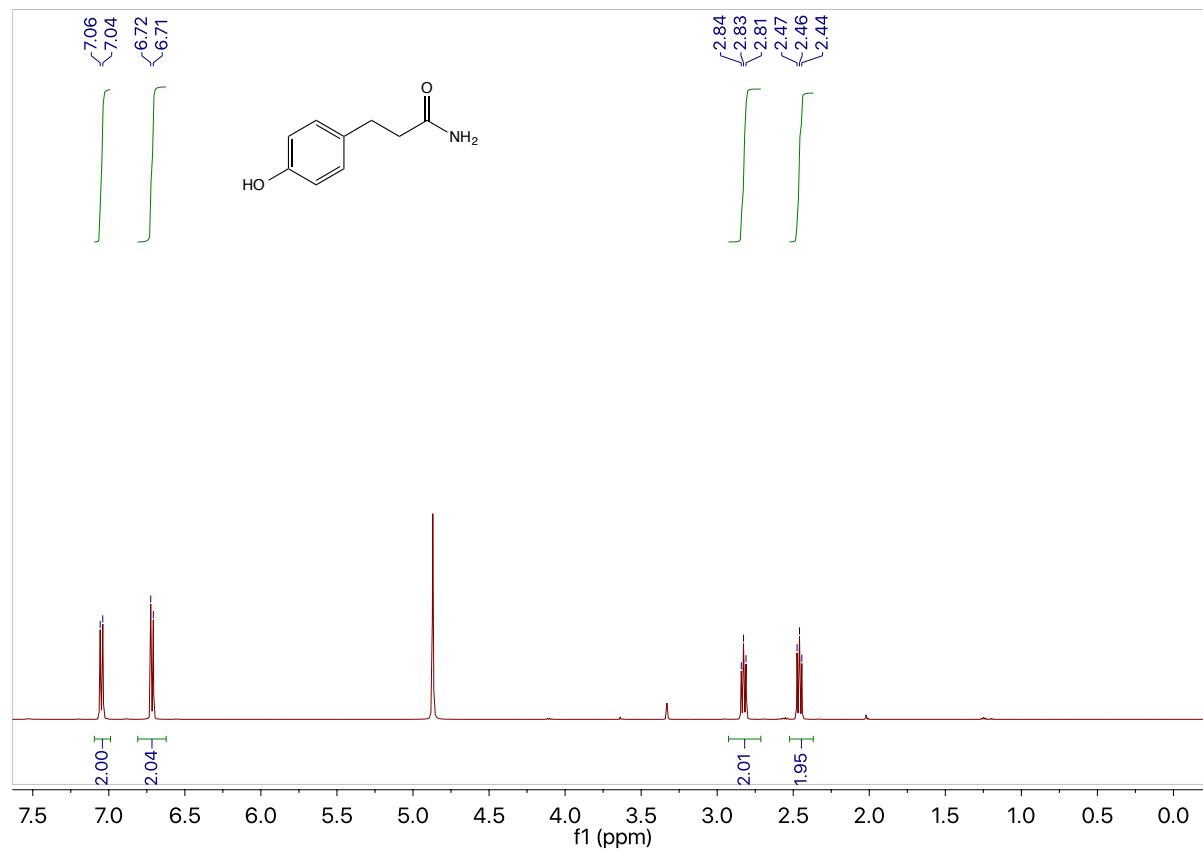
X-ray structure of compound 14



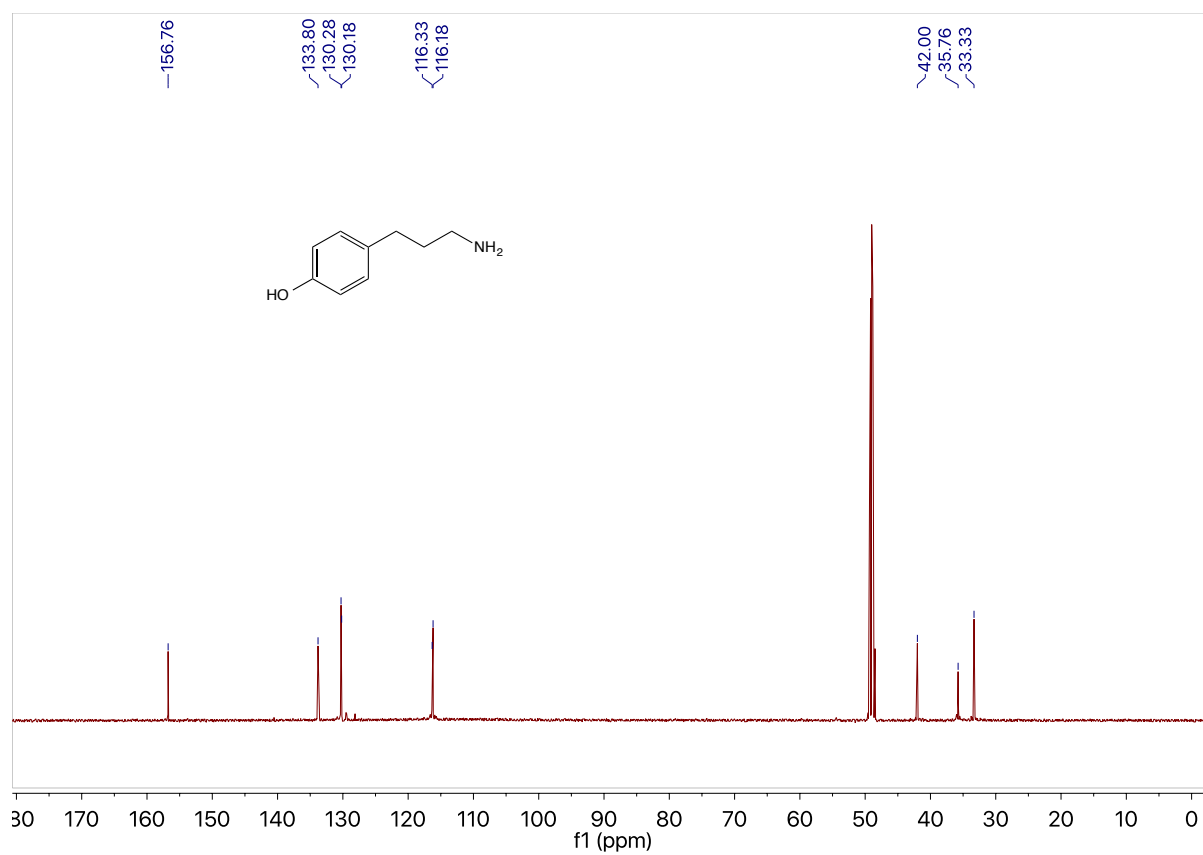
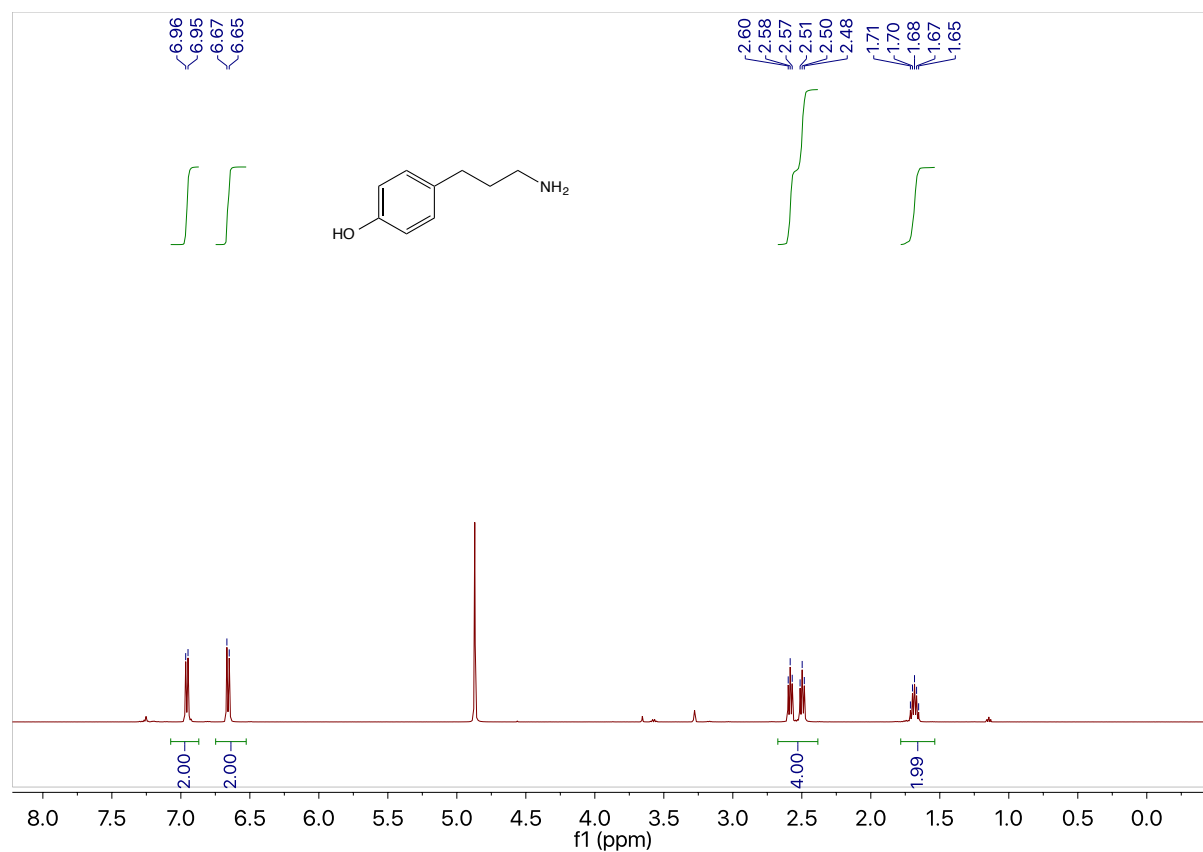
CCDC deposition number:	2174963
Empirical formula	C ₁₃ H ₂₀ N ₂ O ₂
Formula weight	236.31
Temperature/K	125.01(10)
Crystal system	monoclinic
Space group	P2 ₁ /n
a/Å	9.3232(2)
b/Å	15.4039(3)
c/Å	9.4930(2)
α/°	90
β/°	114.951(3)
γ/°	90
Volume/Å ³	1236.08(5)
Z	4
ρ _{calc} /cm ³	1.270
μ/mm ²	0.691
F(000)	512.0
Crystal size/mm ³	0.29 × 0.21 × 0.11
Radiation	CuKα (λ = 1.54184)
2θ range for data collection/°	11.49 to 147.082
Index ranges	-11 ≤ h ≤ 11, -18 ≤ k ≤ 19, -11 ≤ l ≤ 11
Reflections collected	9586
Independent reflections	2433 [R _{int} = 0.0241, R _{sigma} = 0.0188]
Data/restraints/parameters	2433/0/160
Goodness-of-fit on F ²	1.037
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0379, wR ₂ = 0.0934
Final R indexes [all data]	R ₁ = 0.0420, wR ₂ = 0.0964
Largest diff. peak/hole / e Å ⁻³	0.28/-0.19

^1H and ^{13}C NMR Spectra

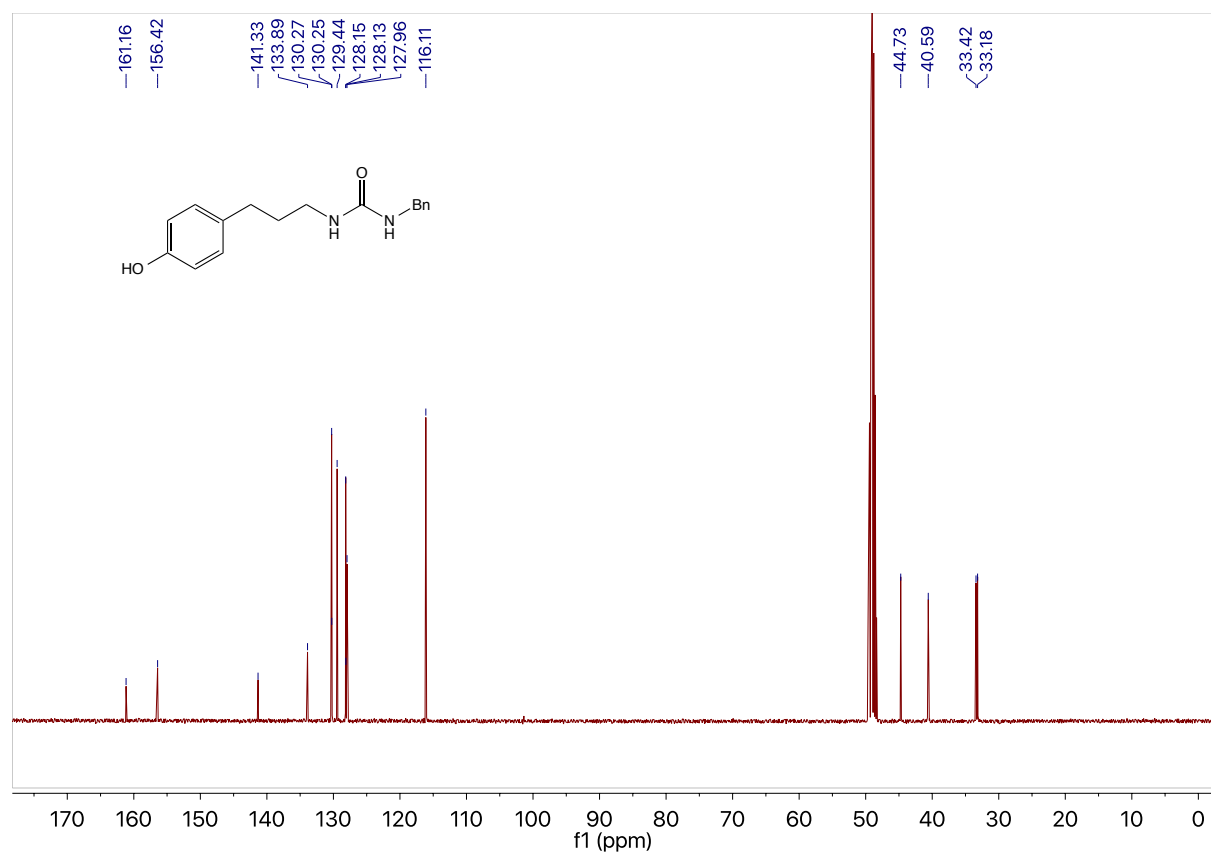
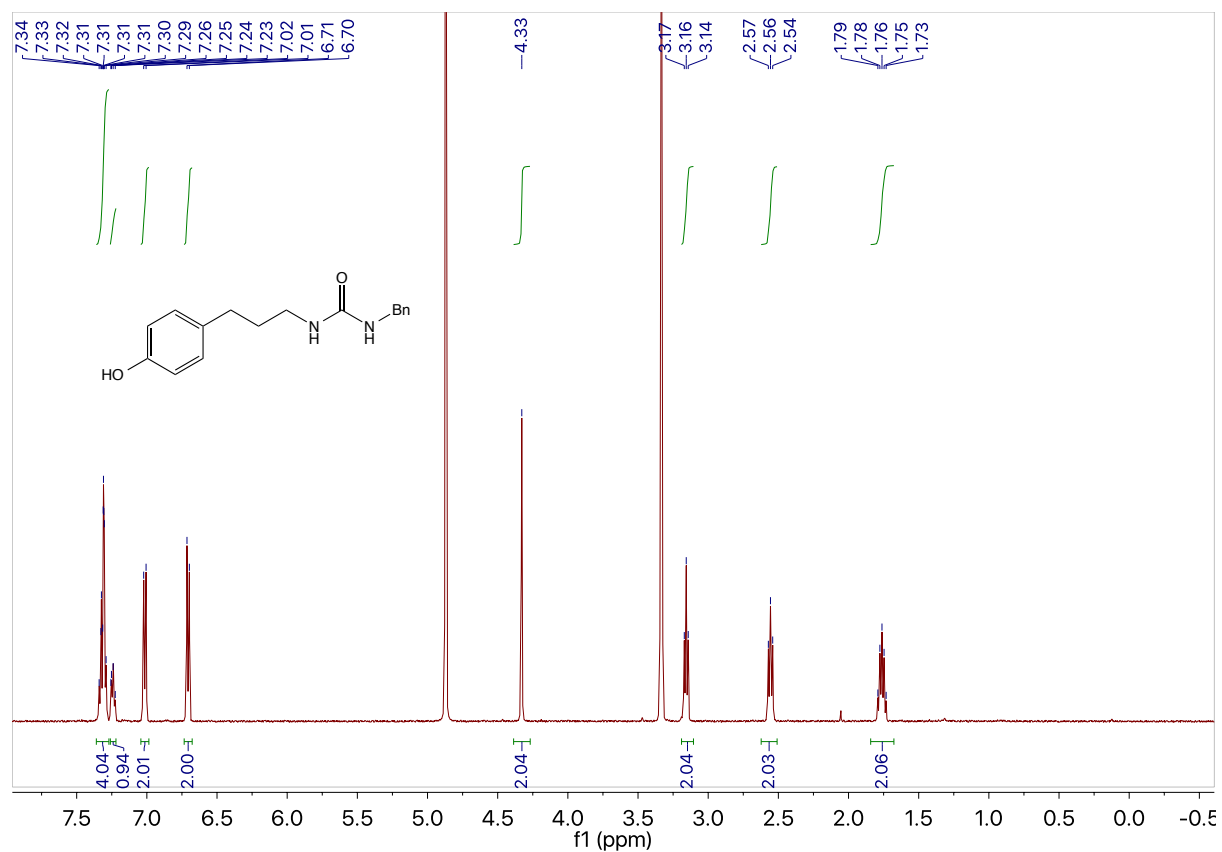
3,4-Hydroxypropanamide S1



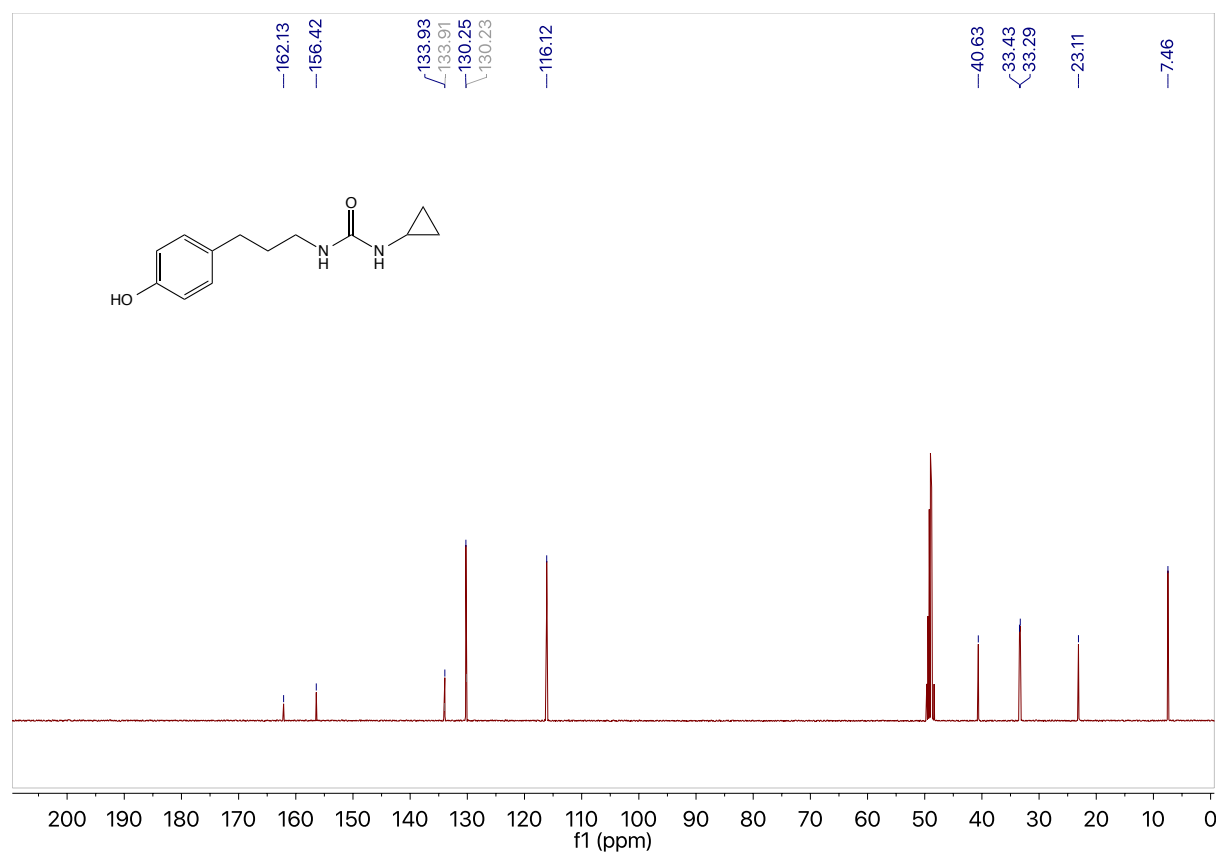
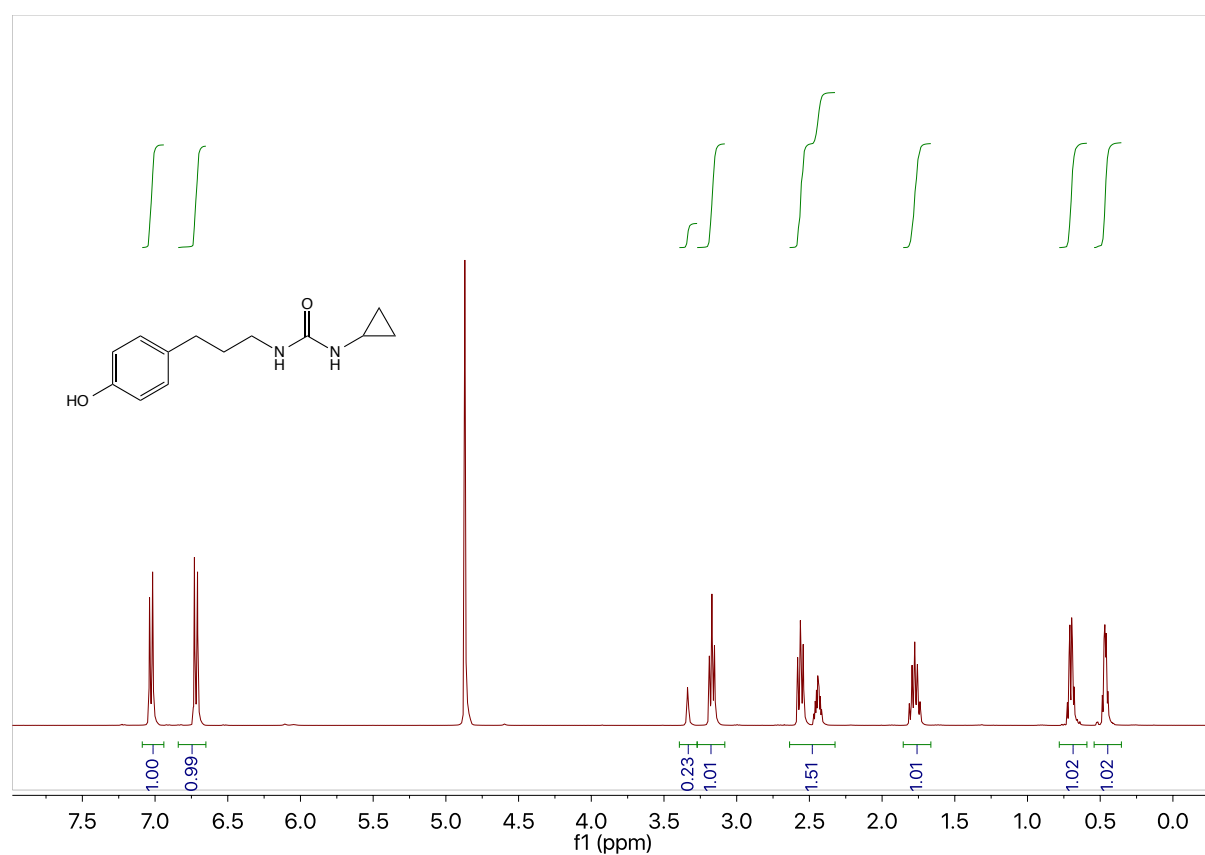
4-(3-Aminopropyl)phenol S2



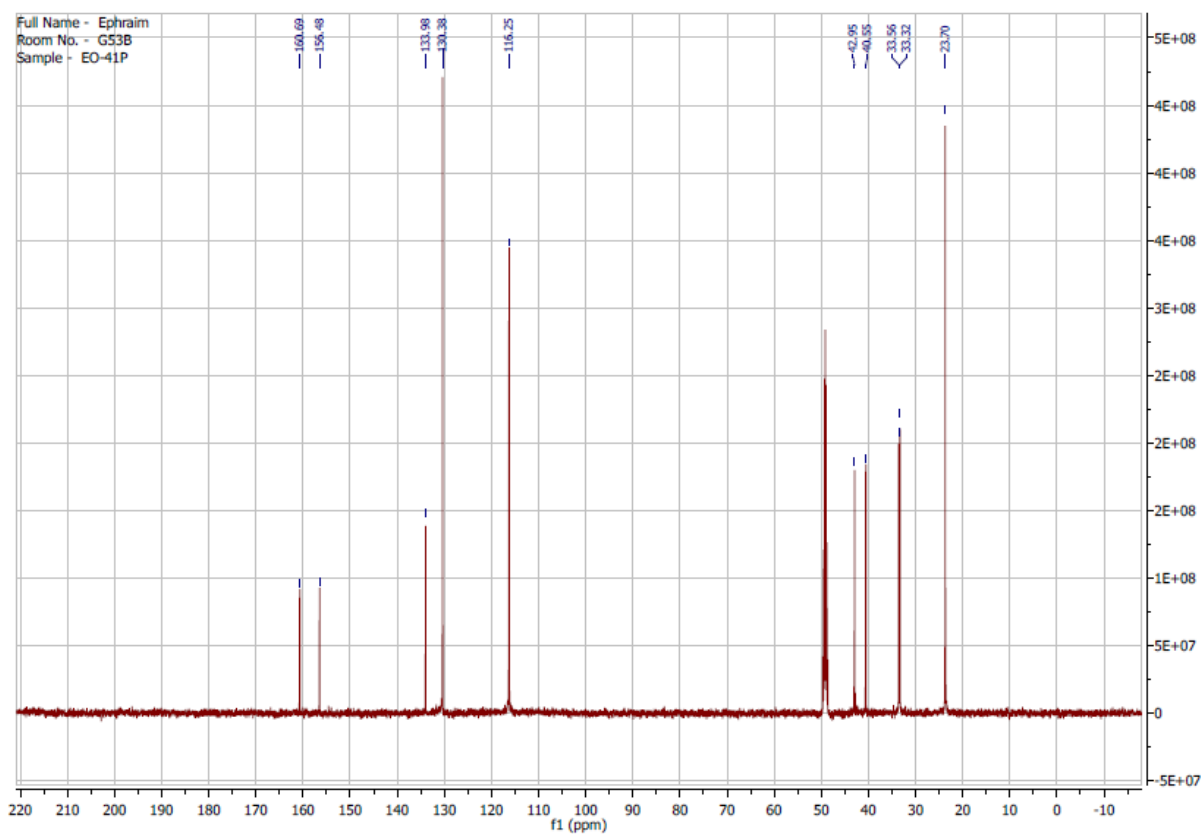
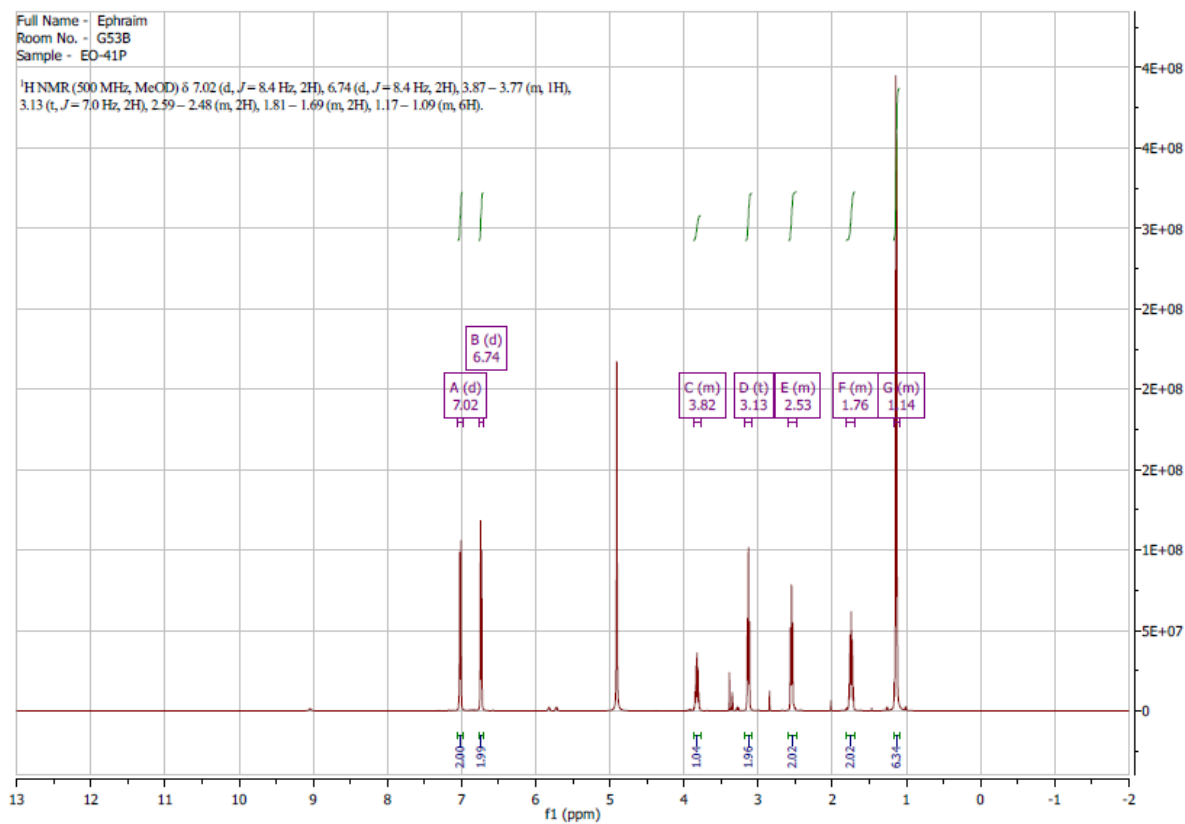
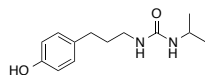
1-Benzyl-3-[3-(4-hydroxyphenyl)propyl]urea 1a



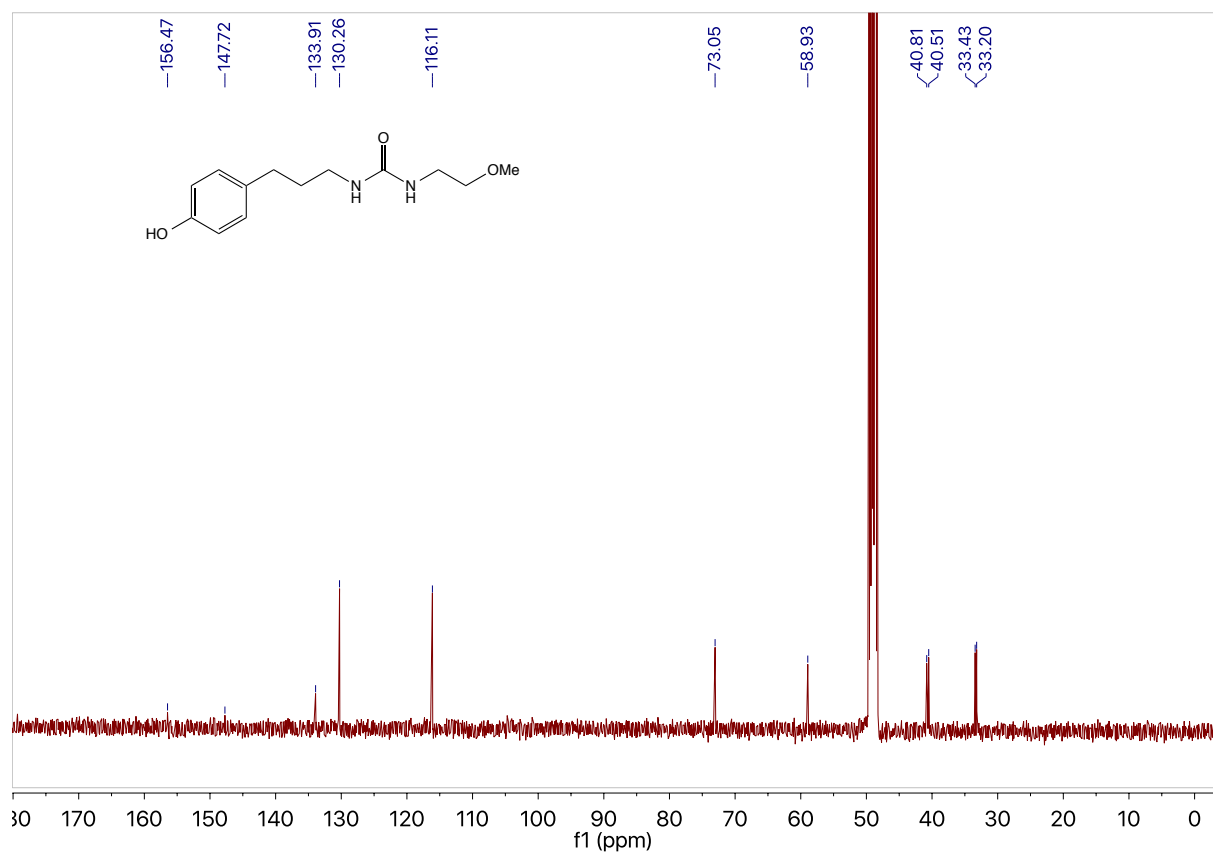
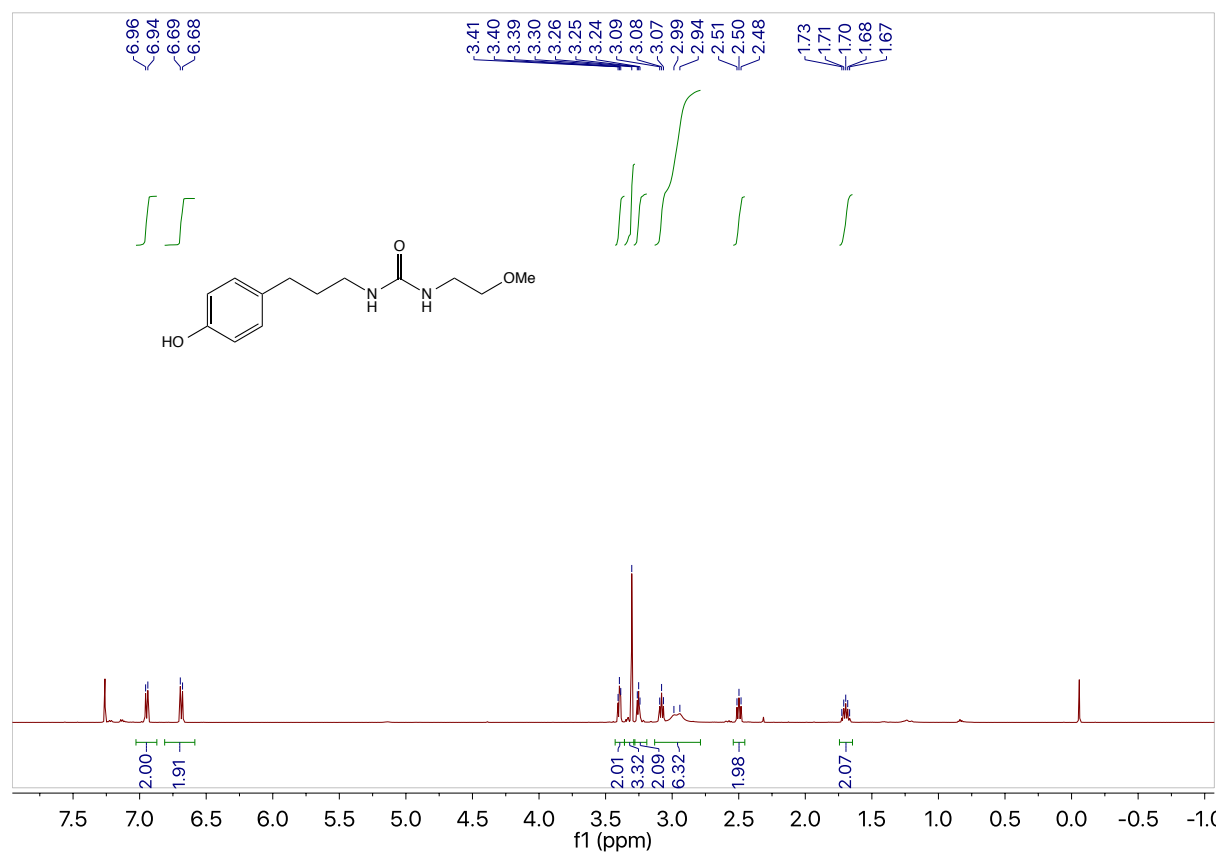
3-Cyclopropyl-1-[3-(4-hydroxyphenyl)propyl]urea 1b



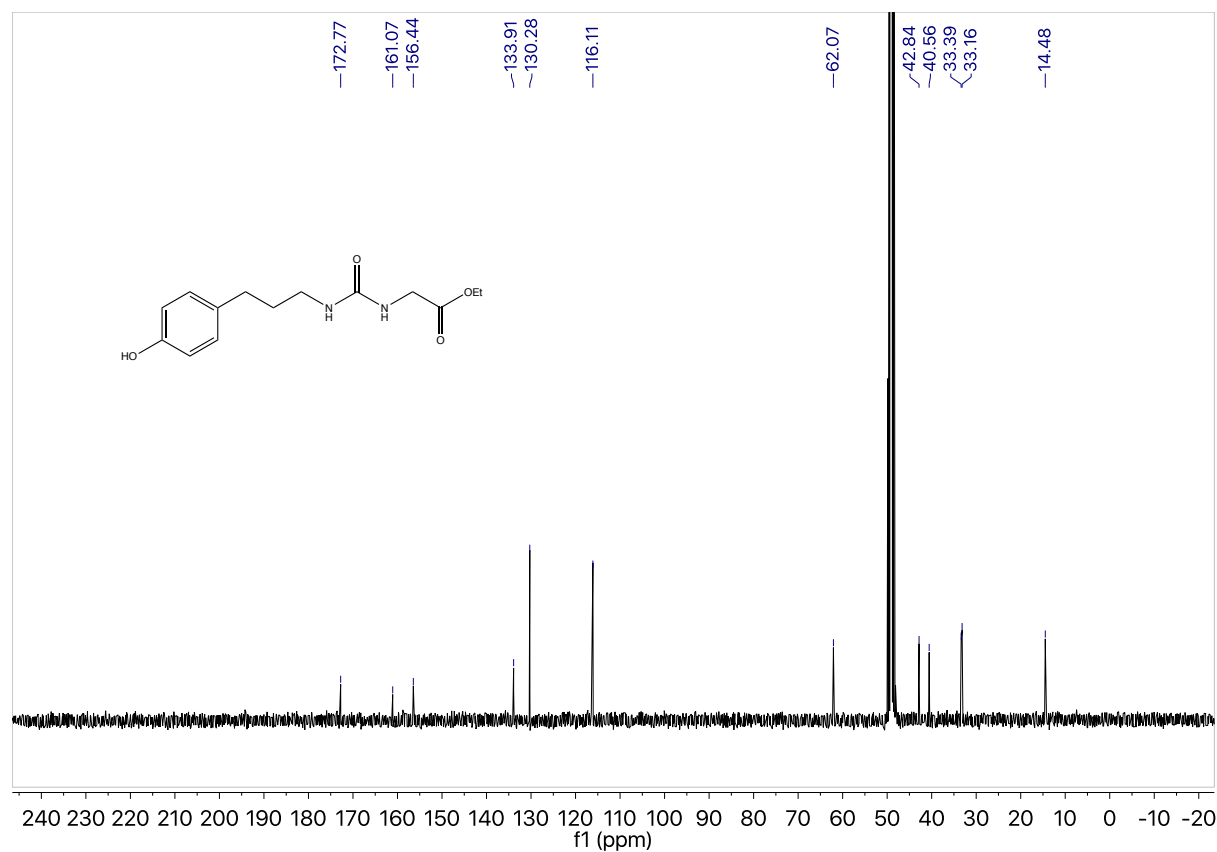
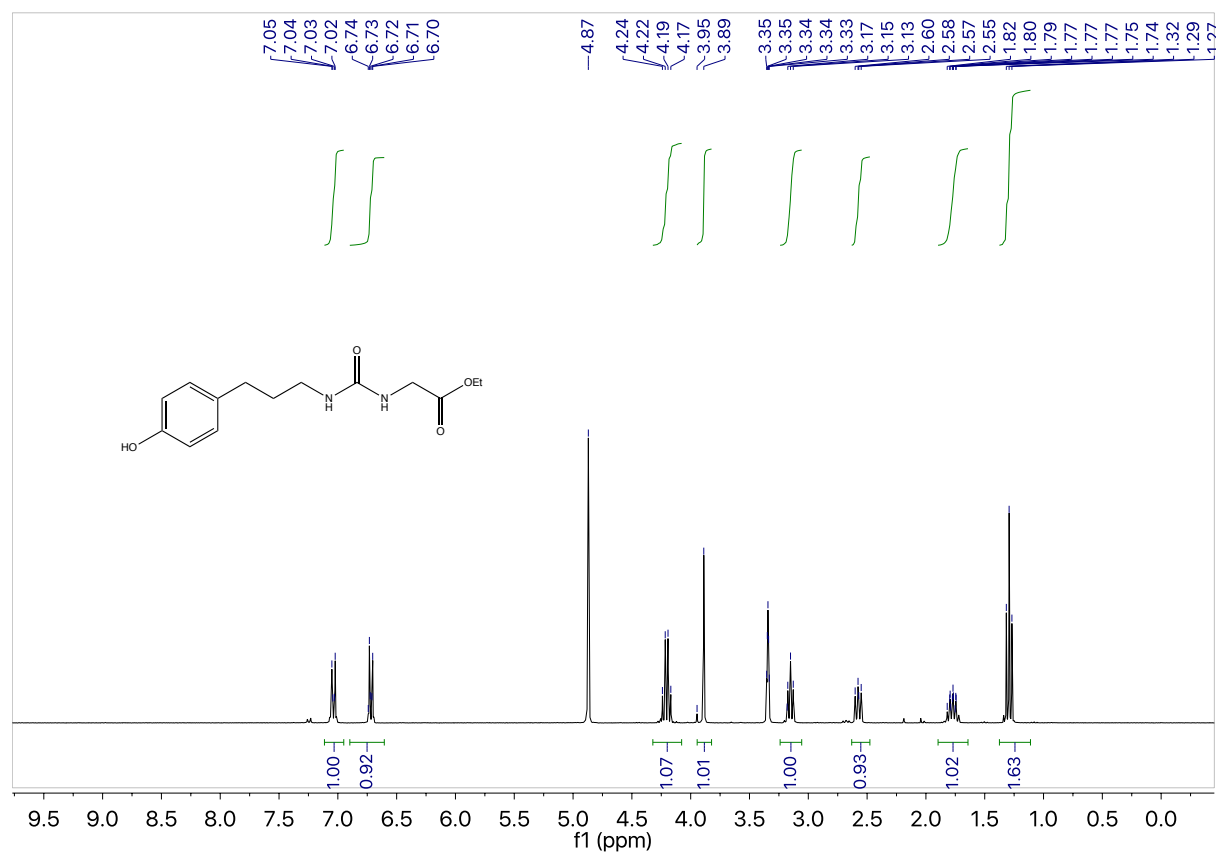
1-[3-(4-Hydroxyphenyl)propyl]-3-isopropylurea 1c



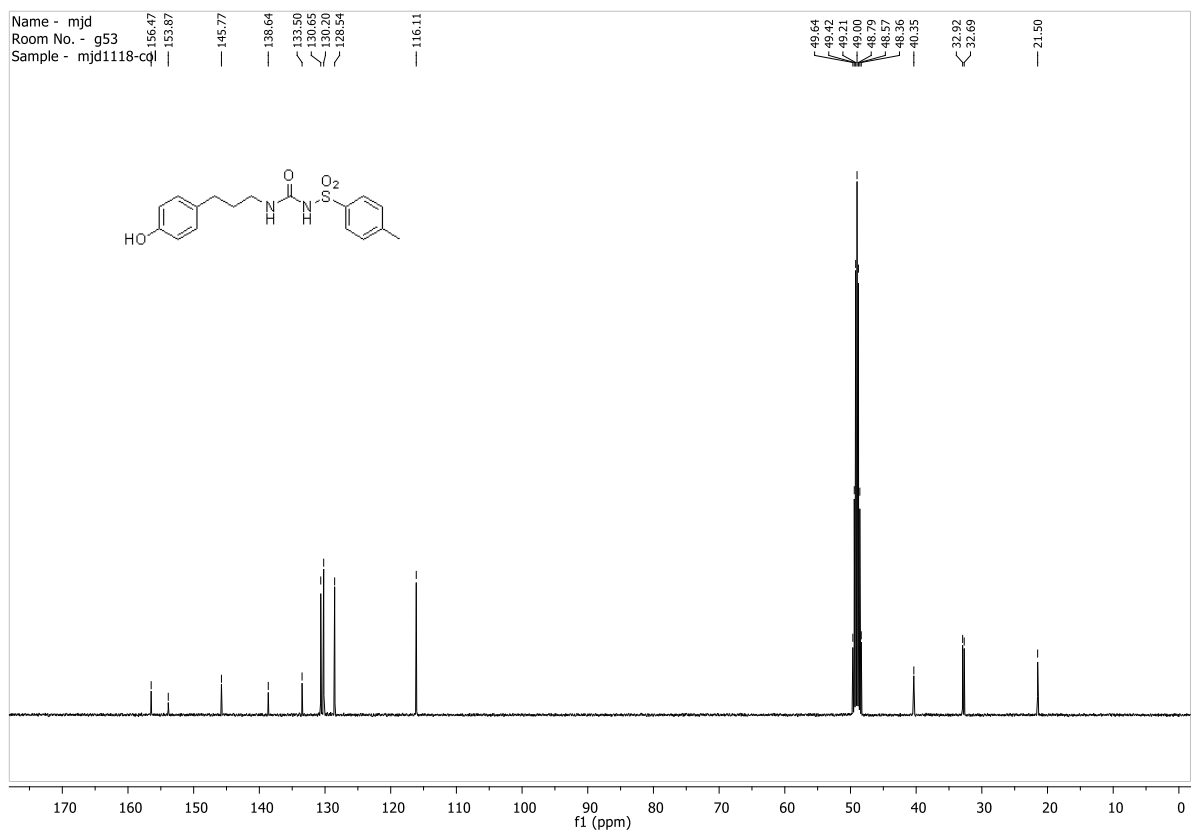
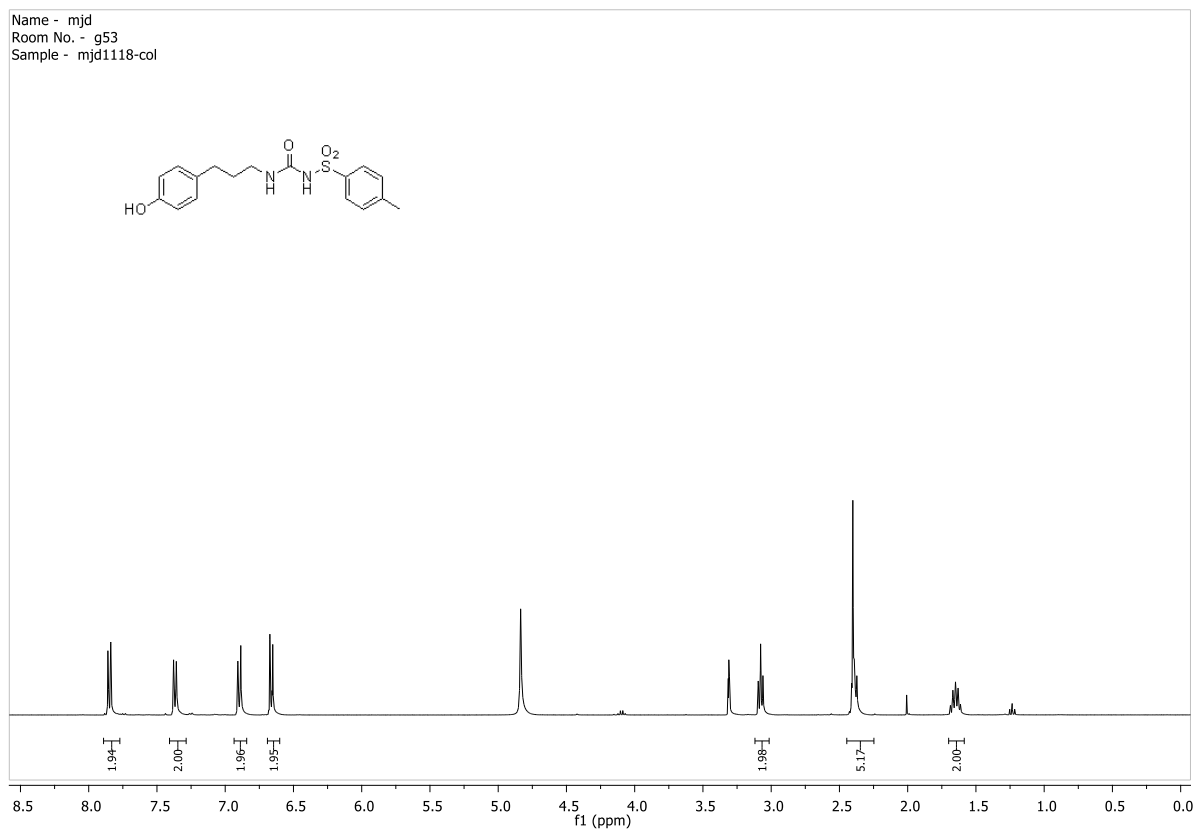
1-[3-(4-Hydroxyphenyl)propyl]-3-(2-methoxyethyl)urea 1d



Ethyl 2-({[3-(4-hydroxyphenyl)propyl]carbamoyl}amino)acetate 1e

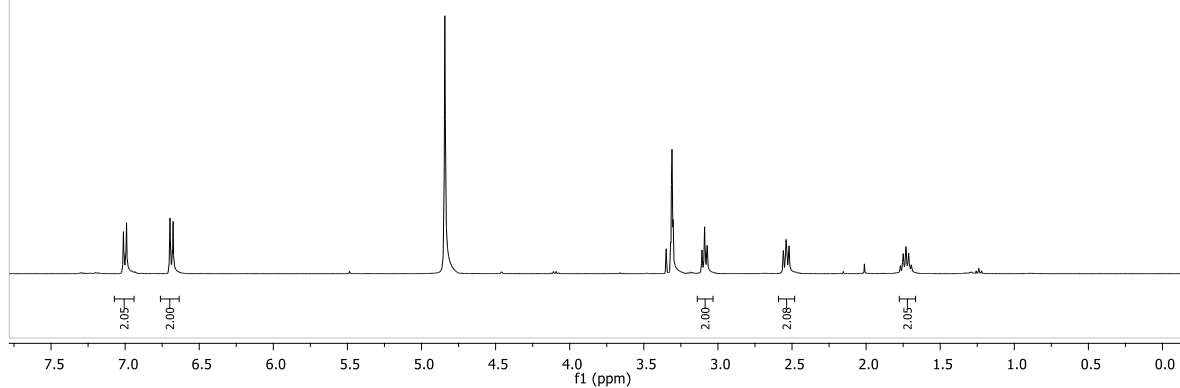
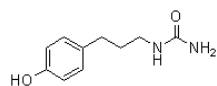


3-[3-(4-Hydroxyphenyl)propyl]-1-(4-methylbenzenesulfonyl)urea 1f

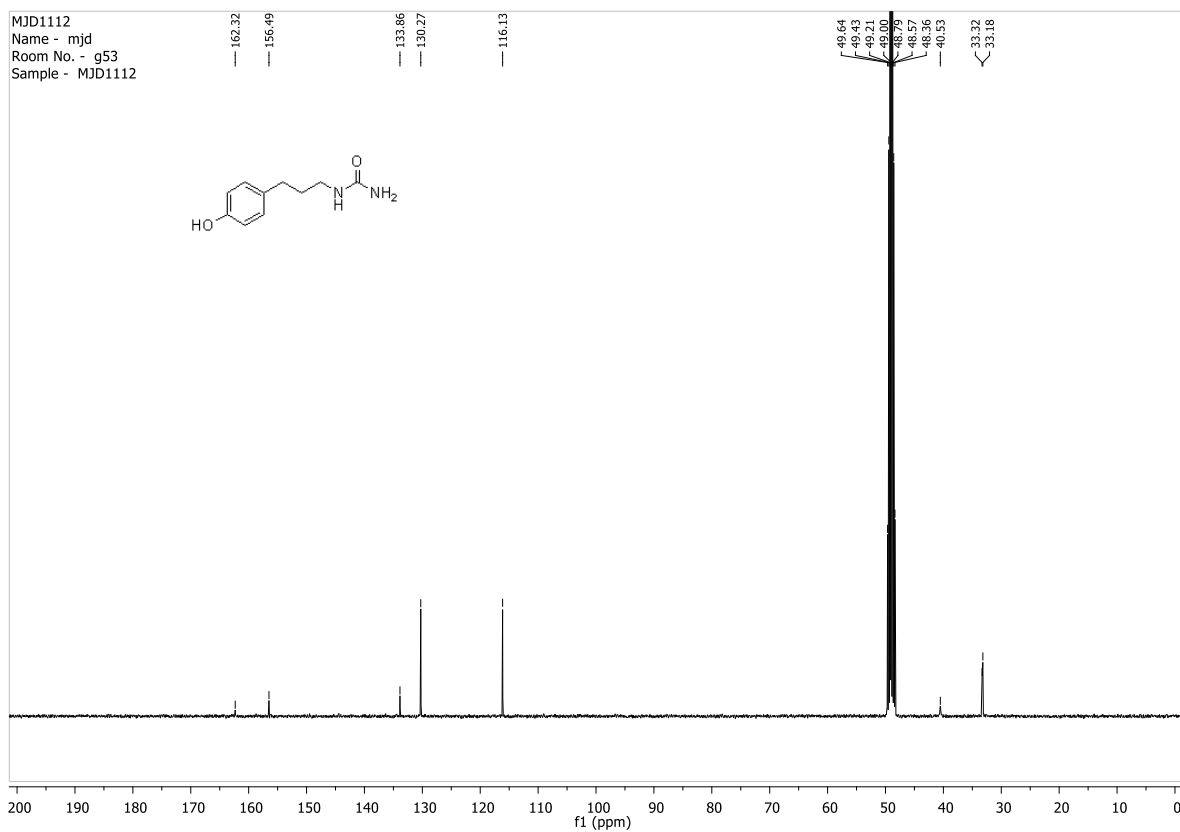
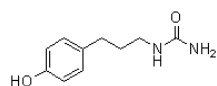


[3-(4-Hydroxyphenyl)propyl]urea 1g

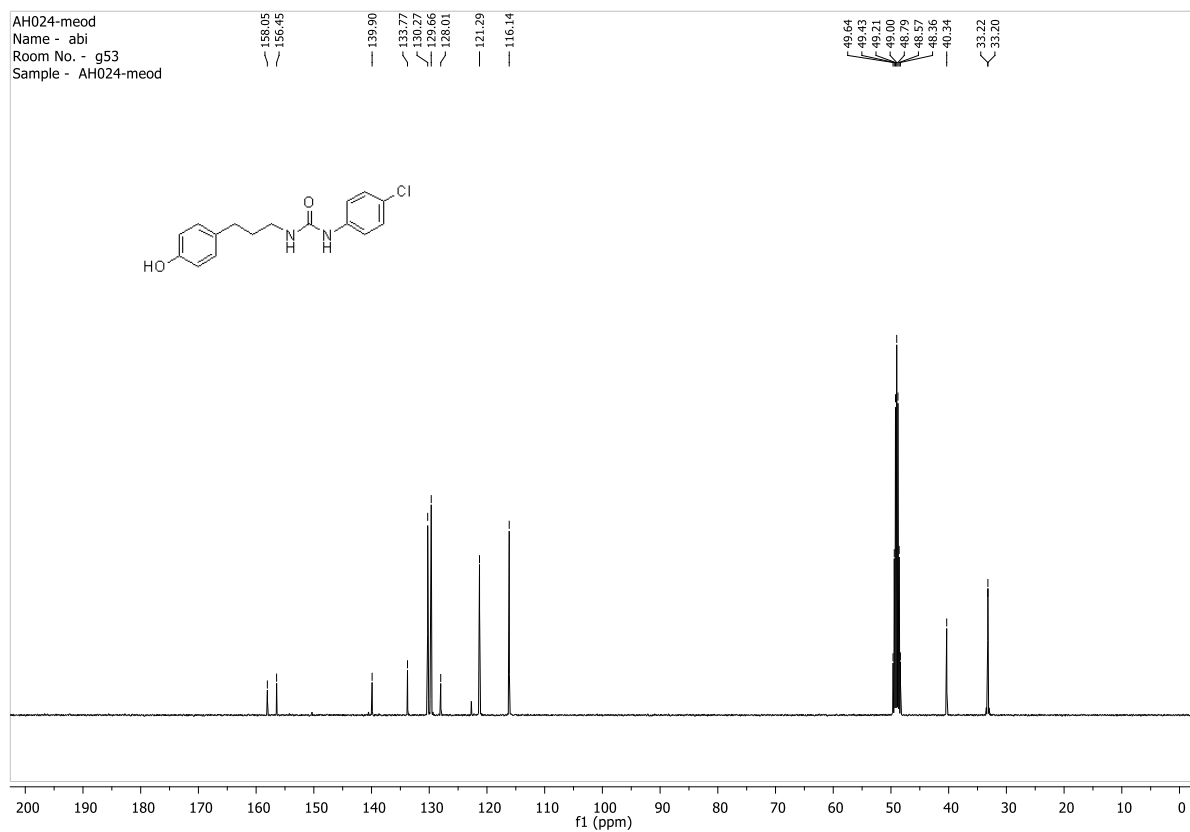
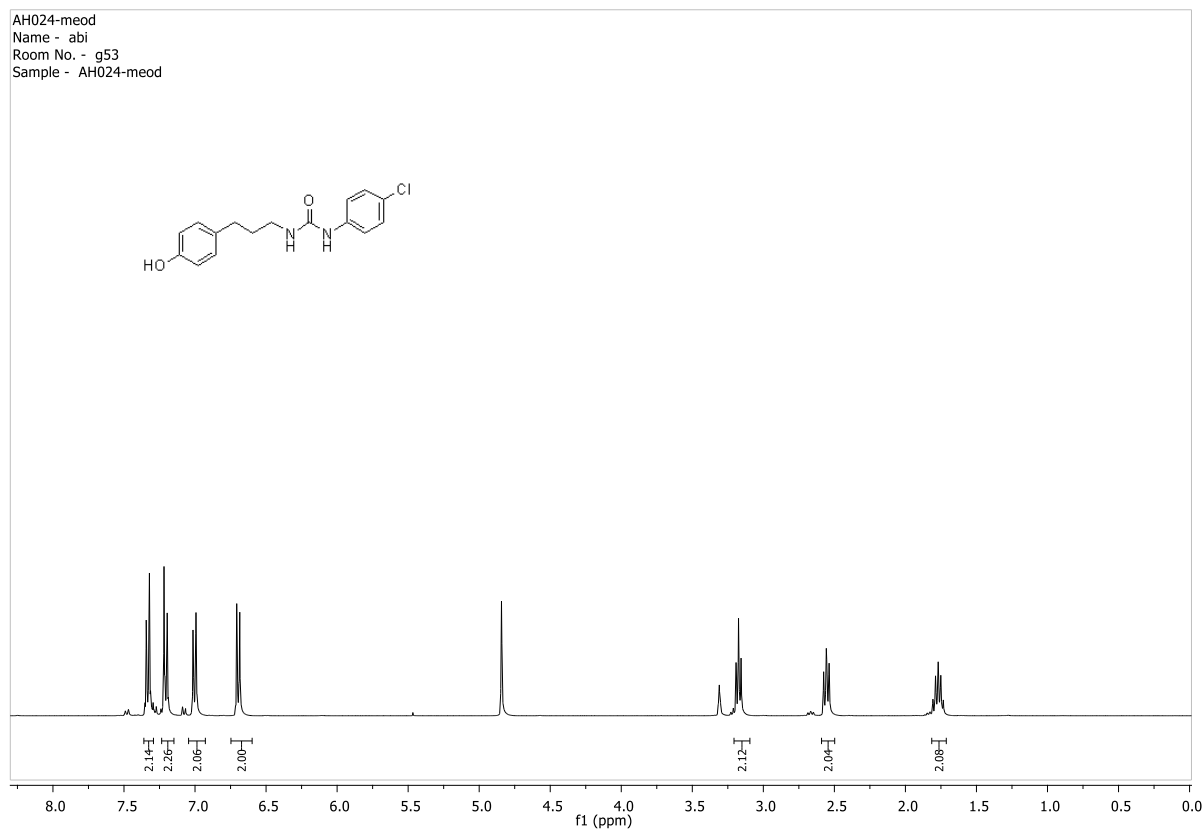
MJD1112
Name - mjd
Room No. - g53
Sample - MJD1112



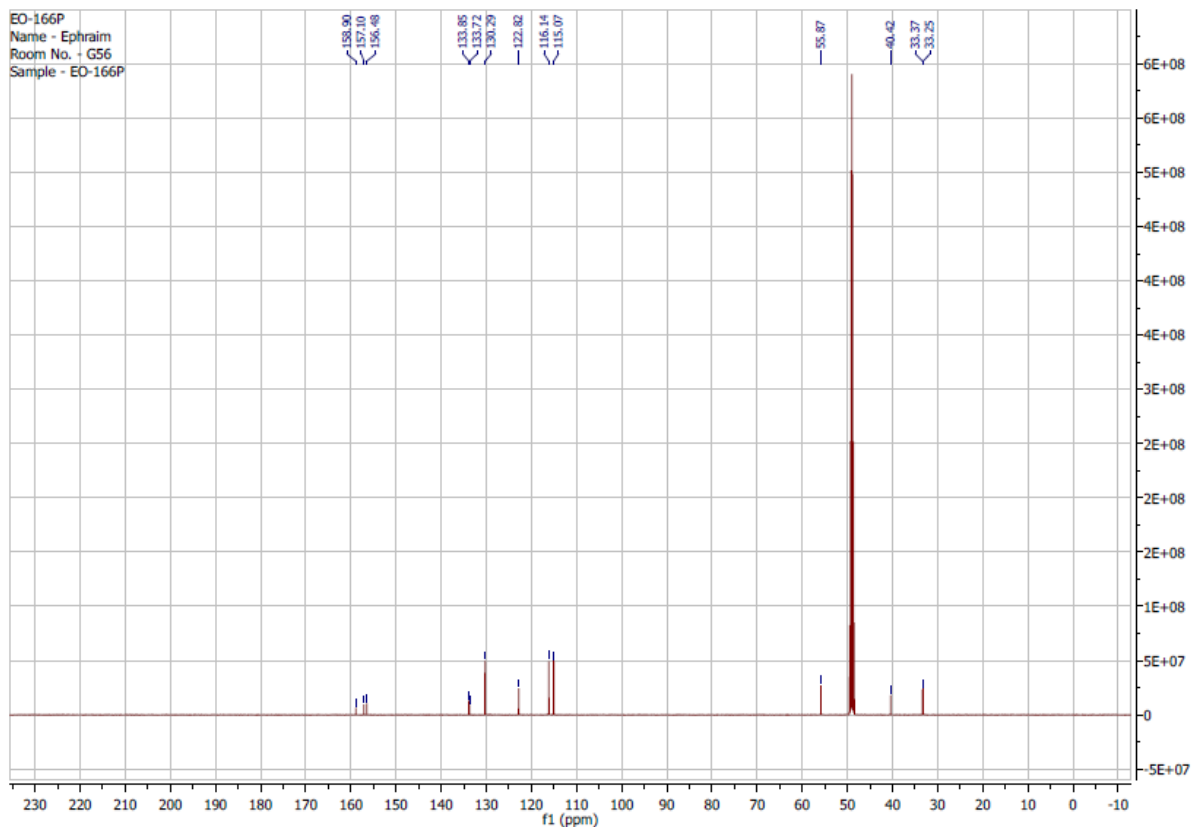
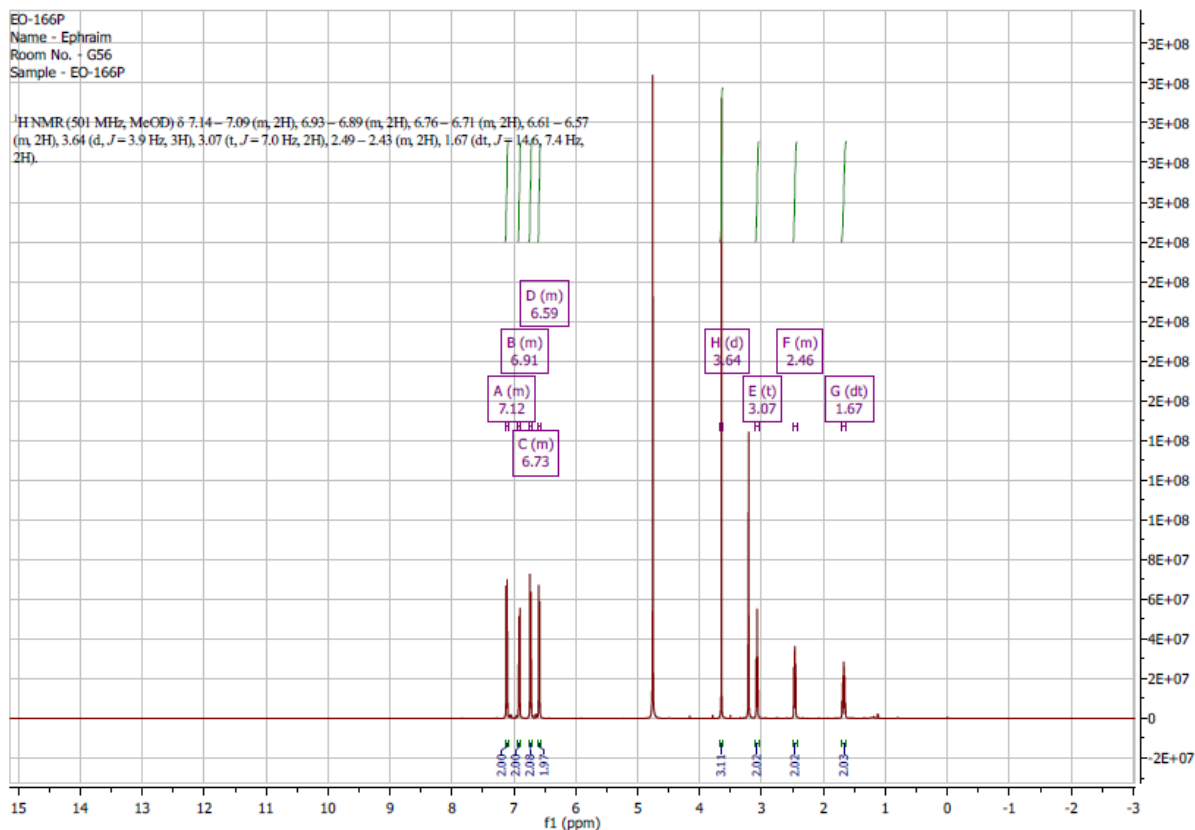
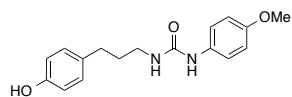
MJD1112
Name - mjd
Room No. - g53
Sample - MJD1112



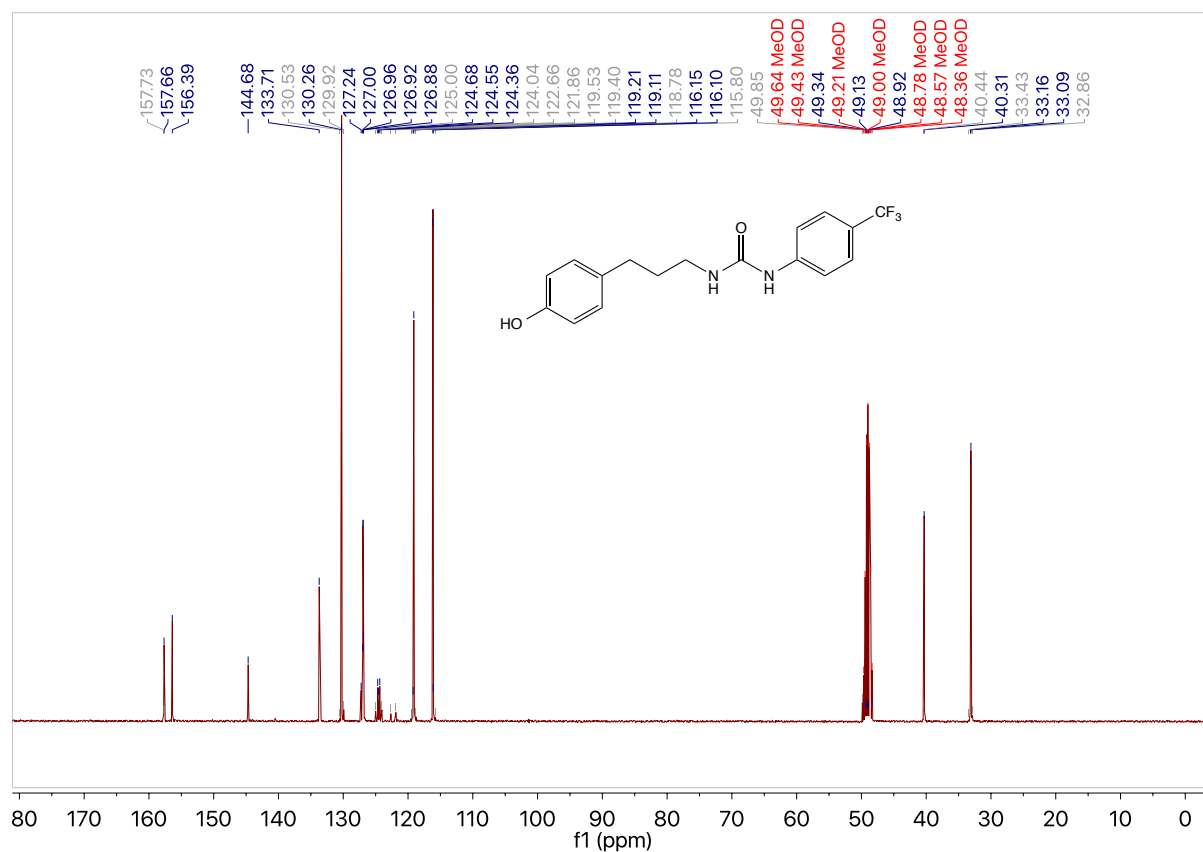
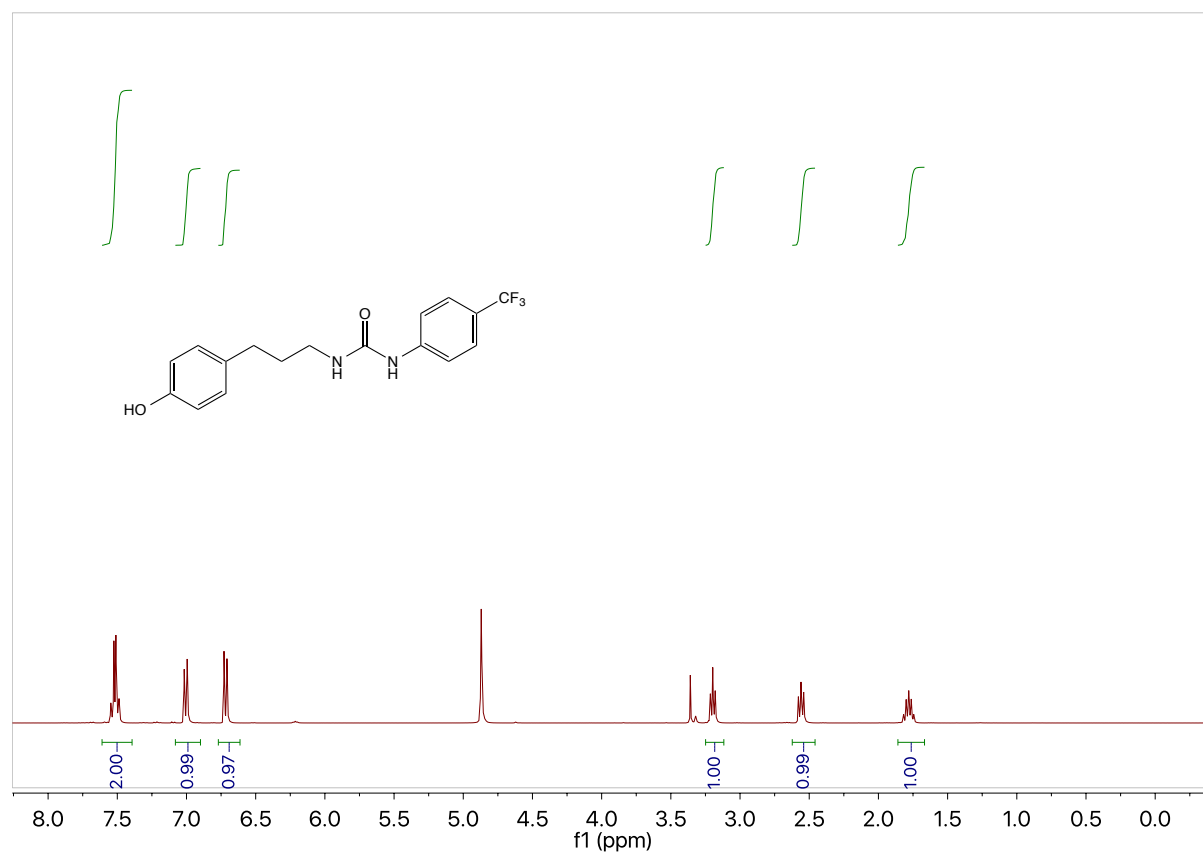
1-(4-Chlorophenyl)-3-[3-(4-hydroxyphenyl)propyl]urea 1h



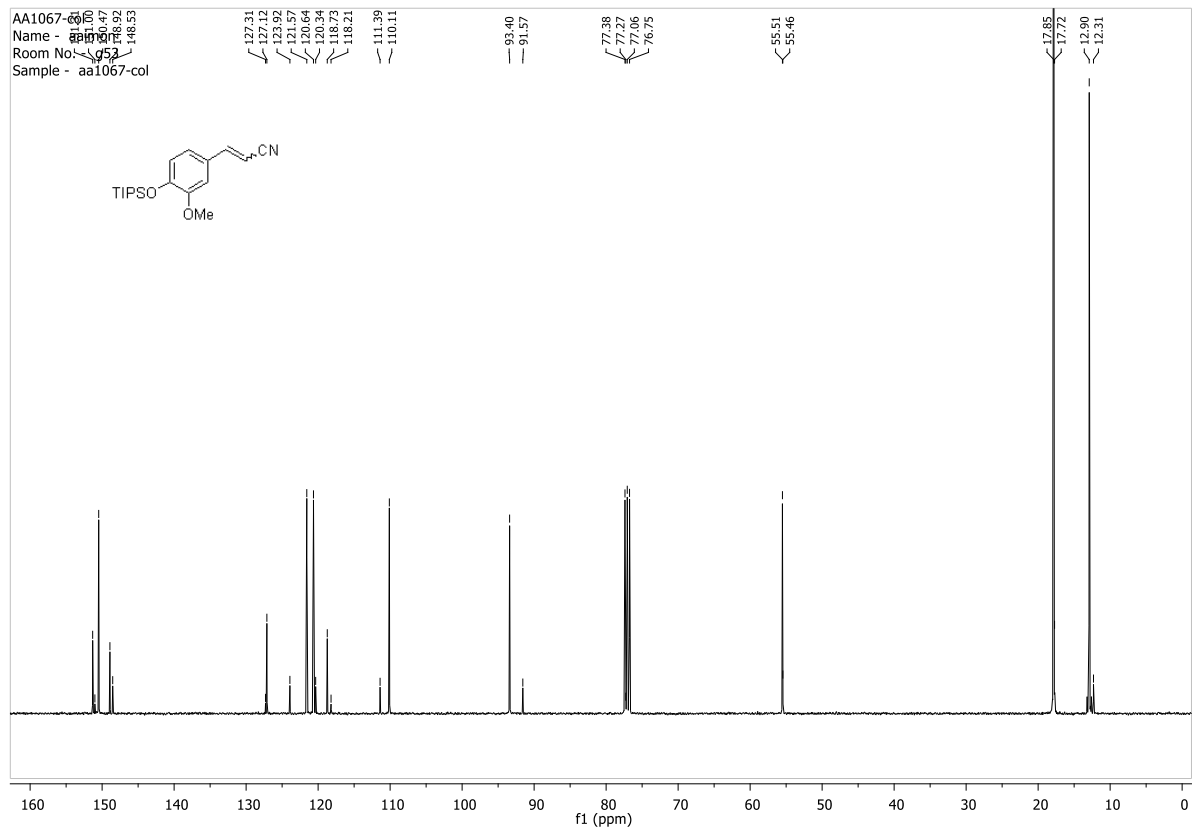
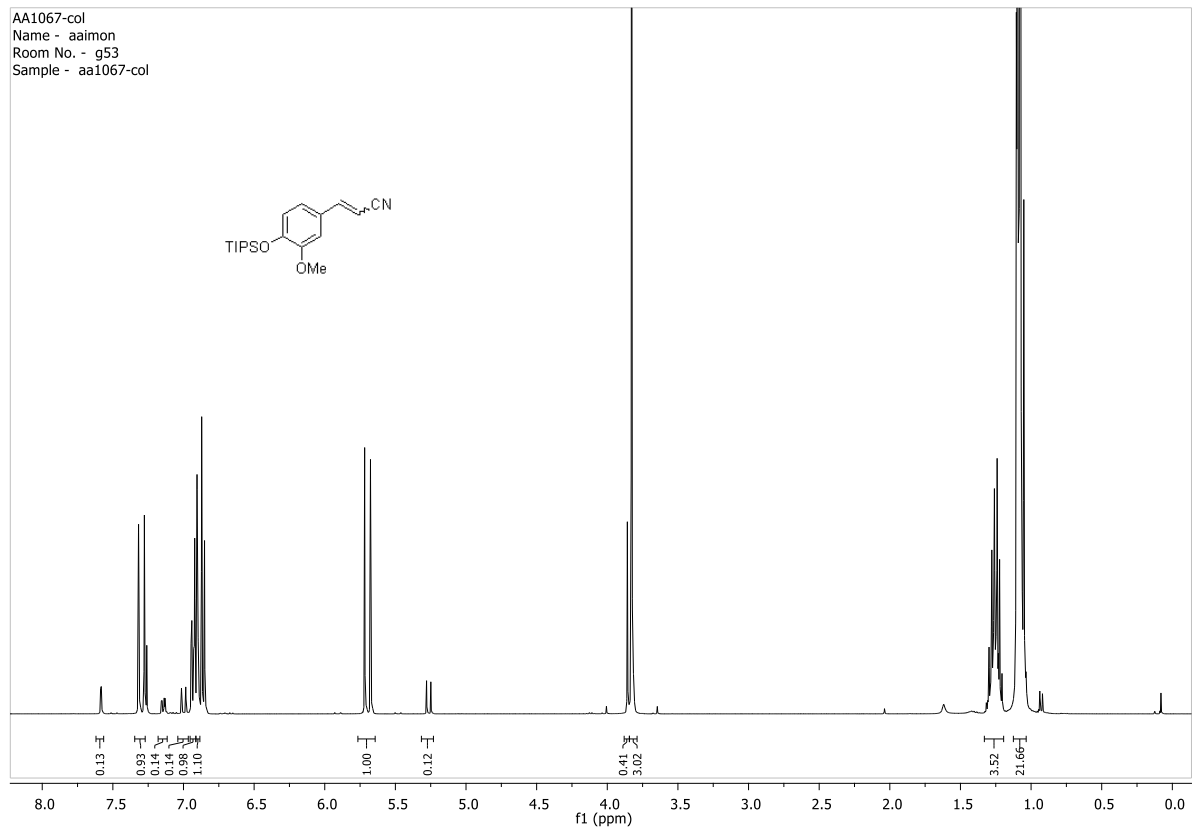
1-(3-(4-Hydroxyphenyl)propyl)-3-(4-methoxyphenyl)urea 1i



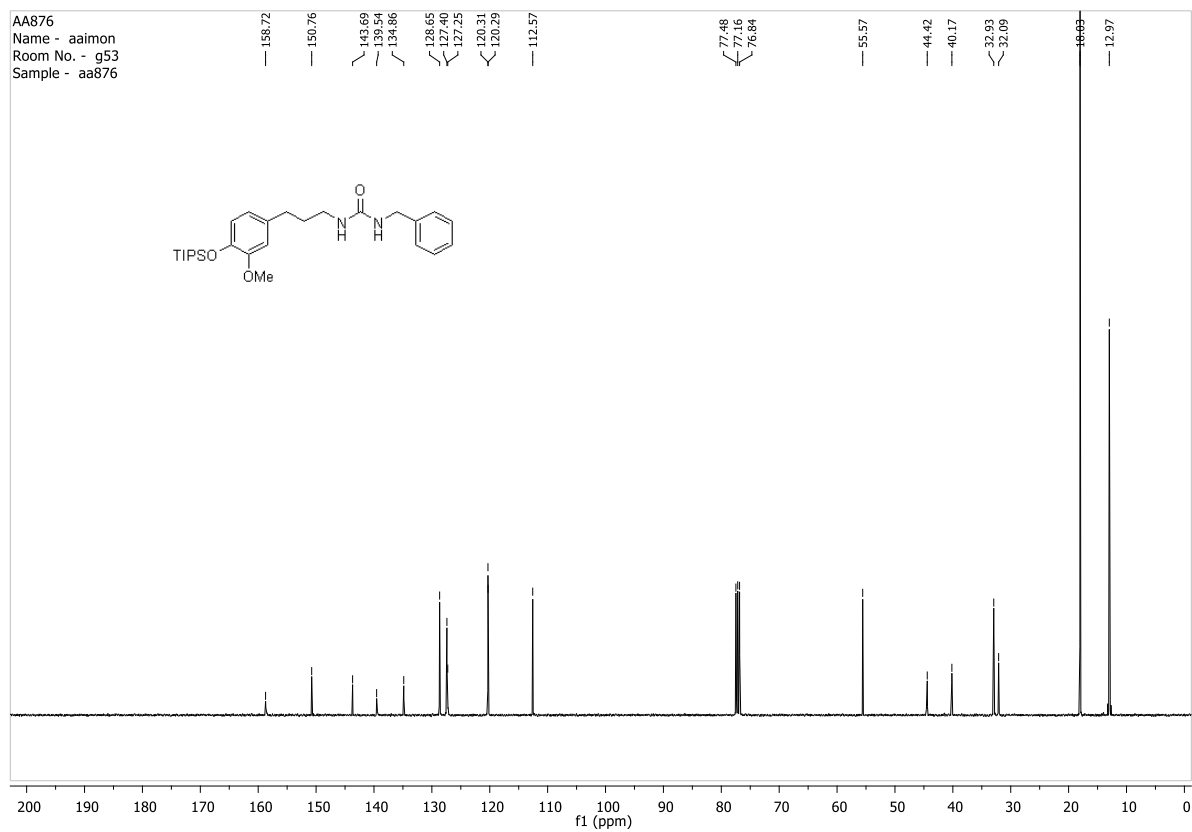
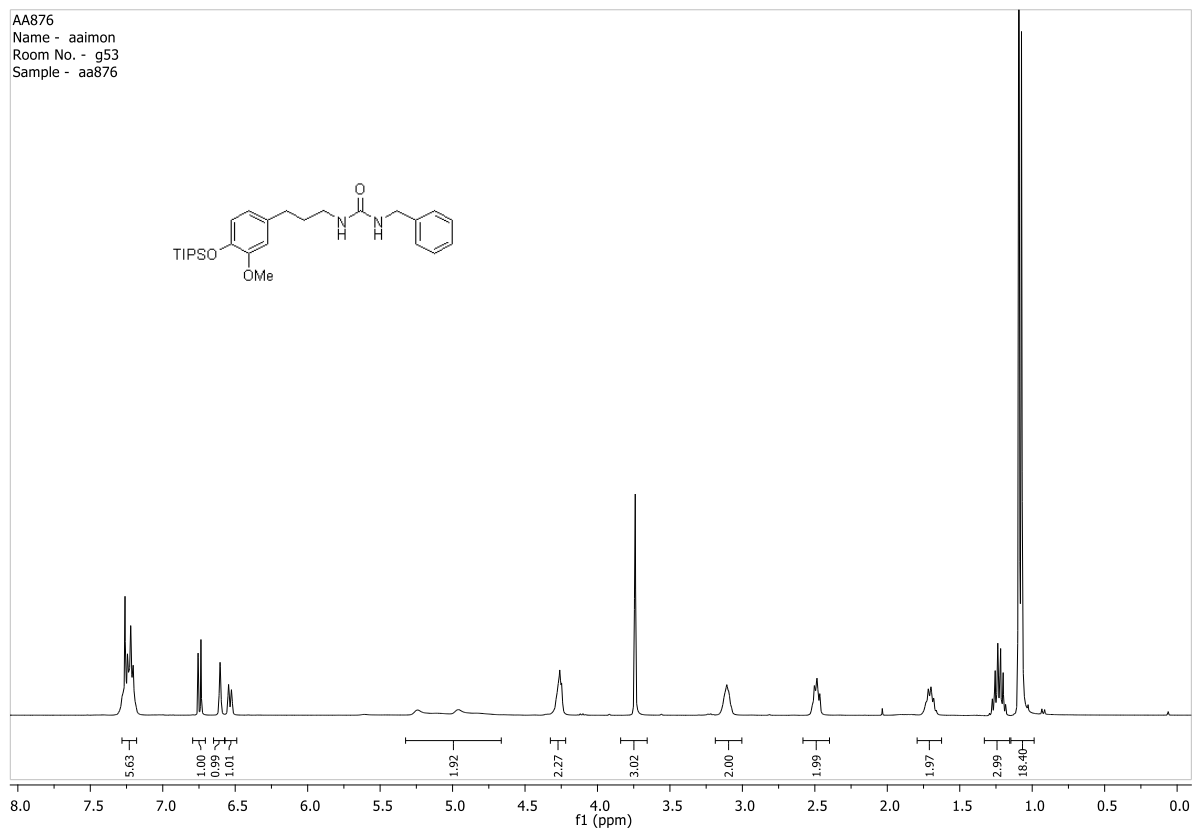
3-[3-(4-Hydroxyphenyl)propyl]-1-[4-(trifluoromethyl)phenyl]urea 1j



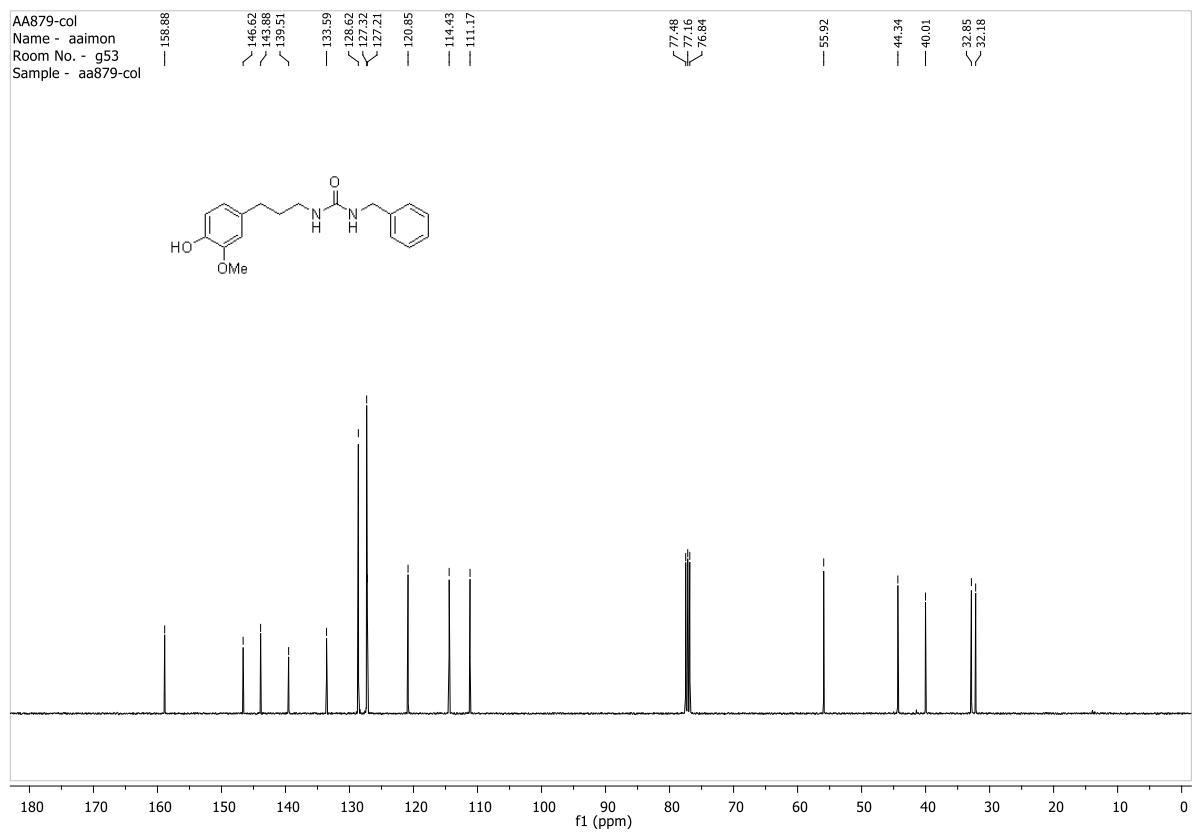
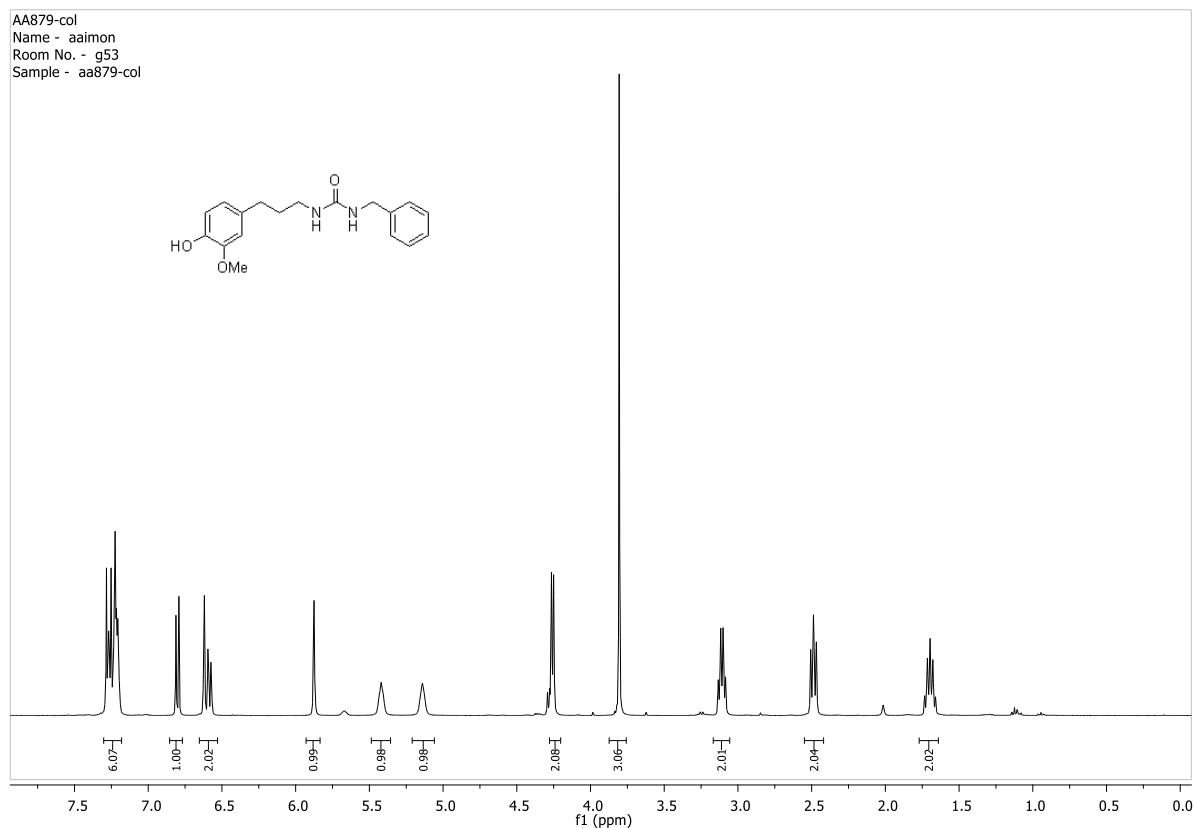
(2E/Z)-3-(3-Methoxy-4-[[tris(propan-2-yl)silyl]oxy]phenyl)prop-2-enitriles S4



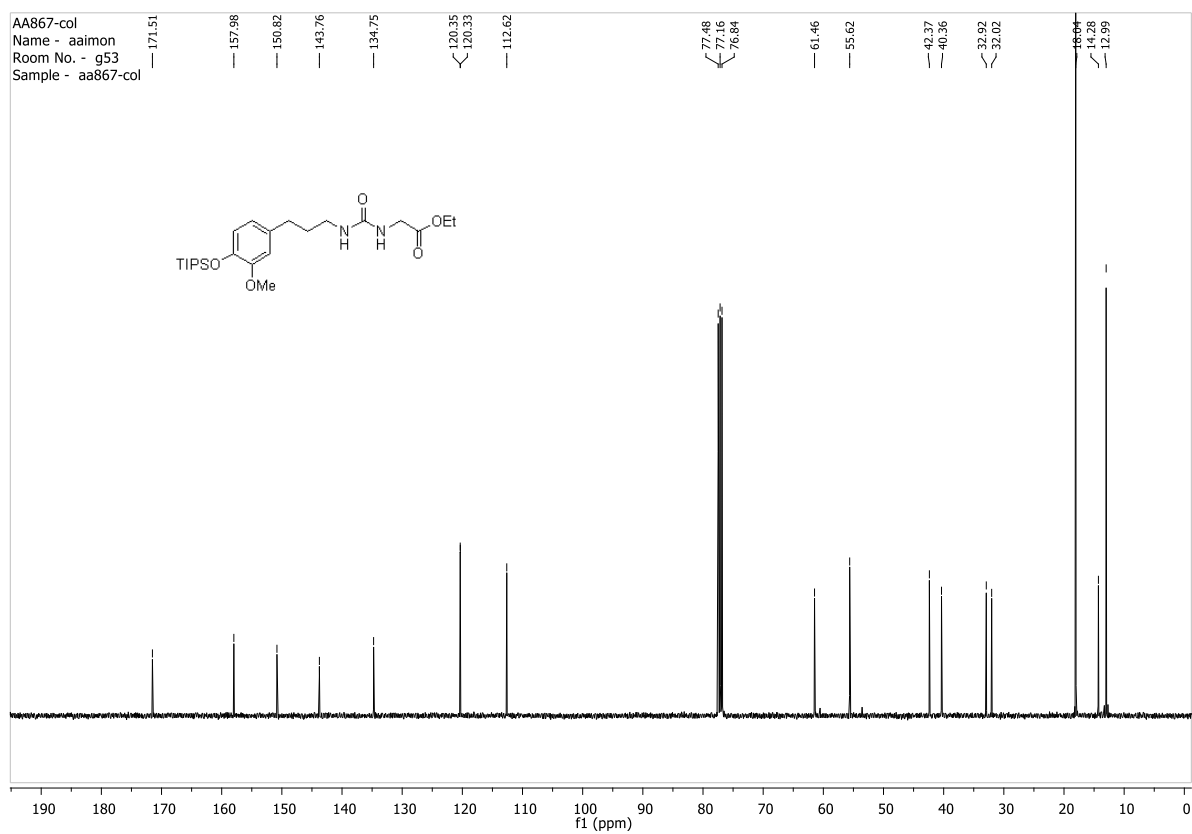
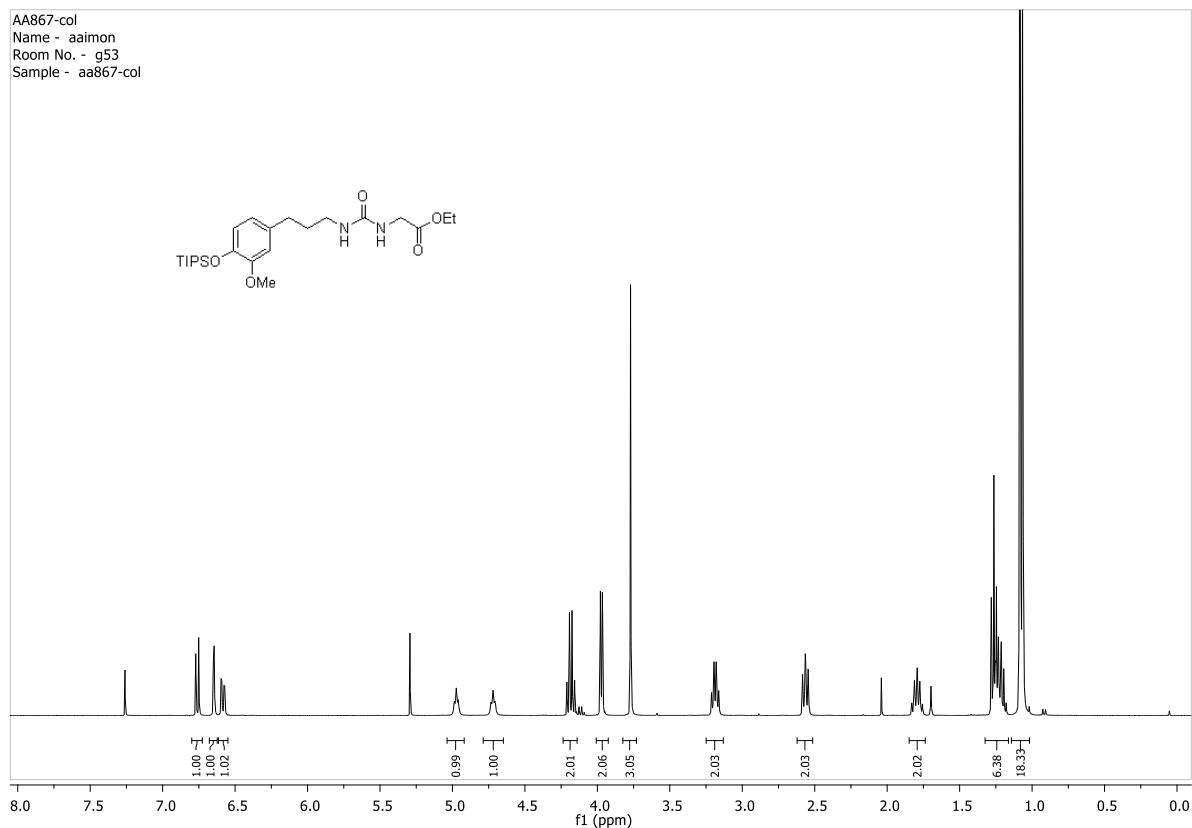
1-Benzyl-3-[3-(3-methoxy-4-[[tris(propan-2-yl)silyl]oxy]phenyl)propyl]urea S6



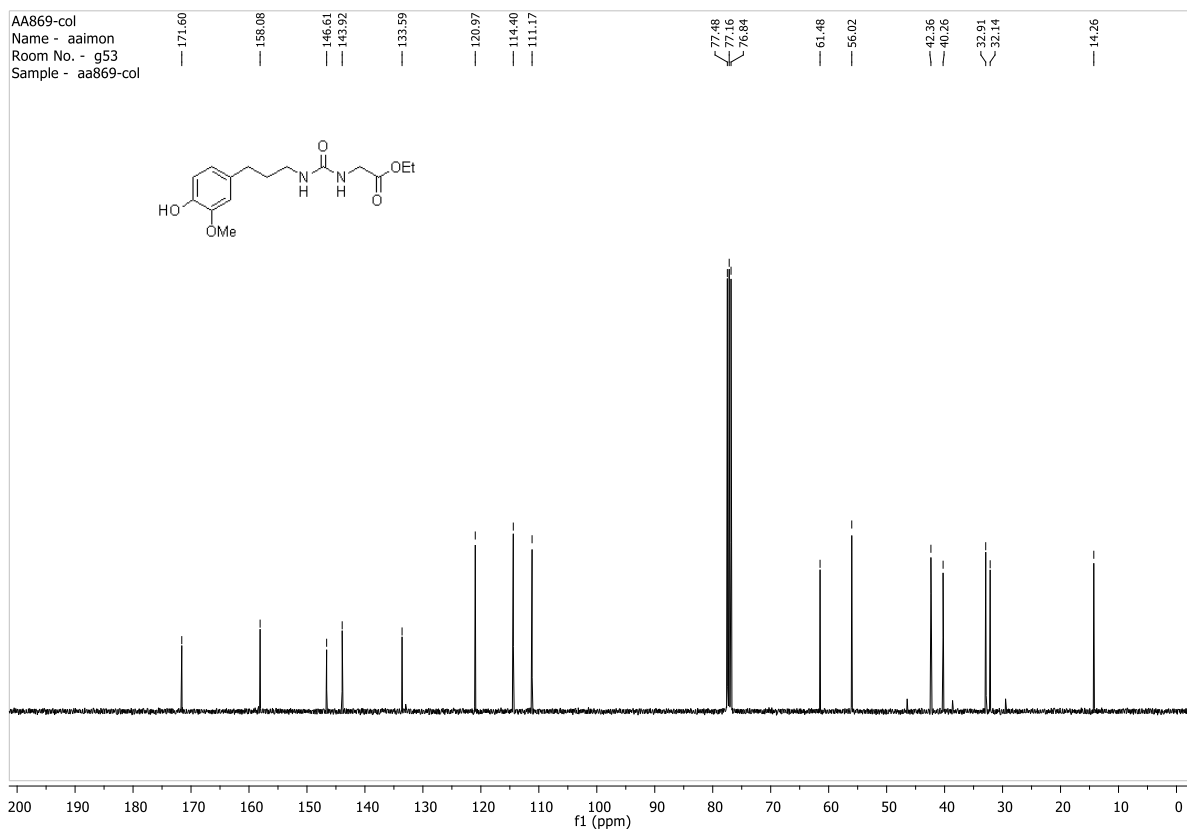
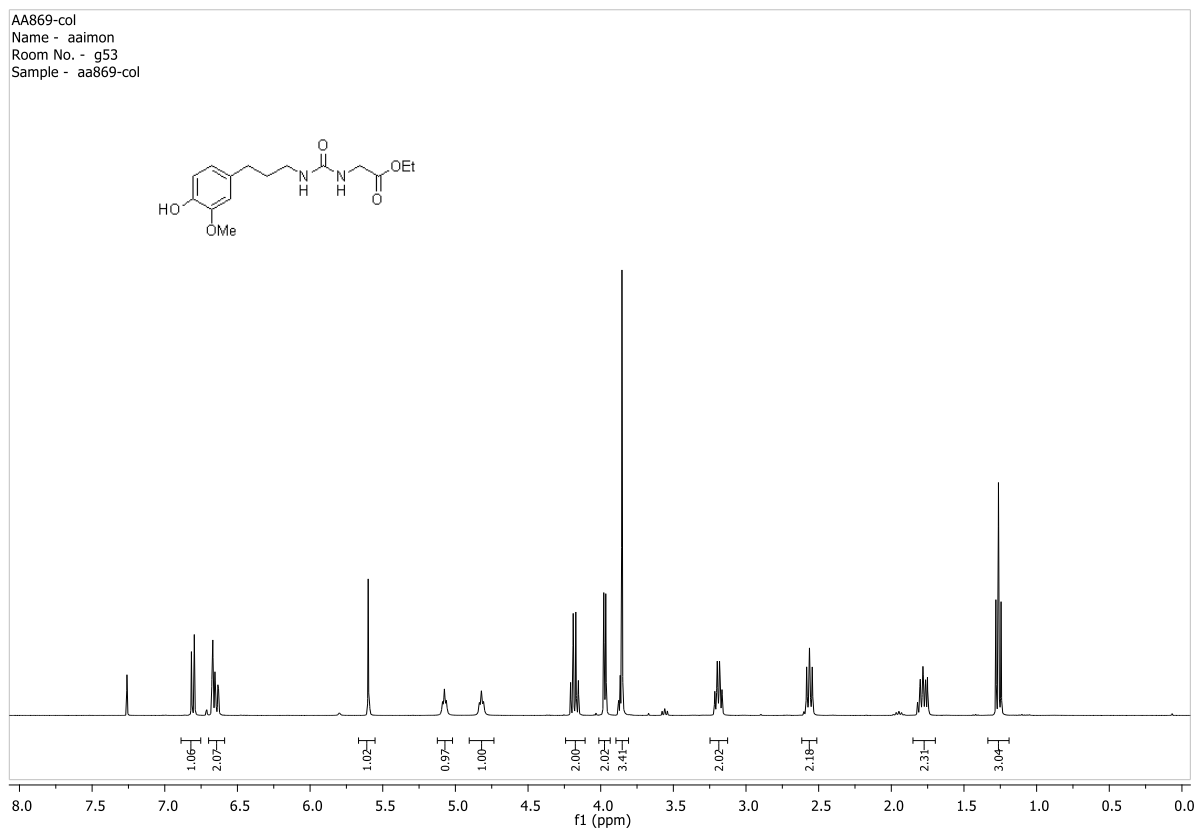
1-Benzyl-3-[3-(4-hydroxy-3-methoxyphenyl)propyl]urea 1k



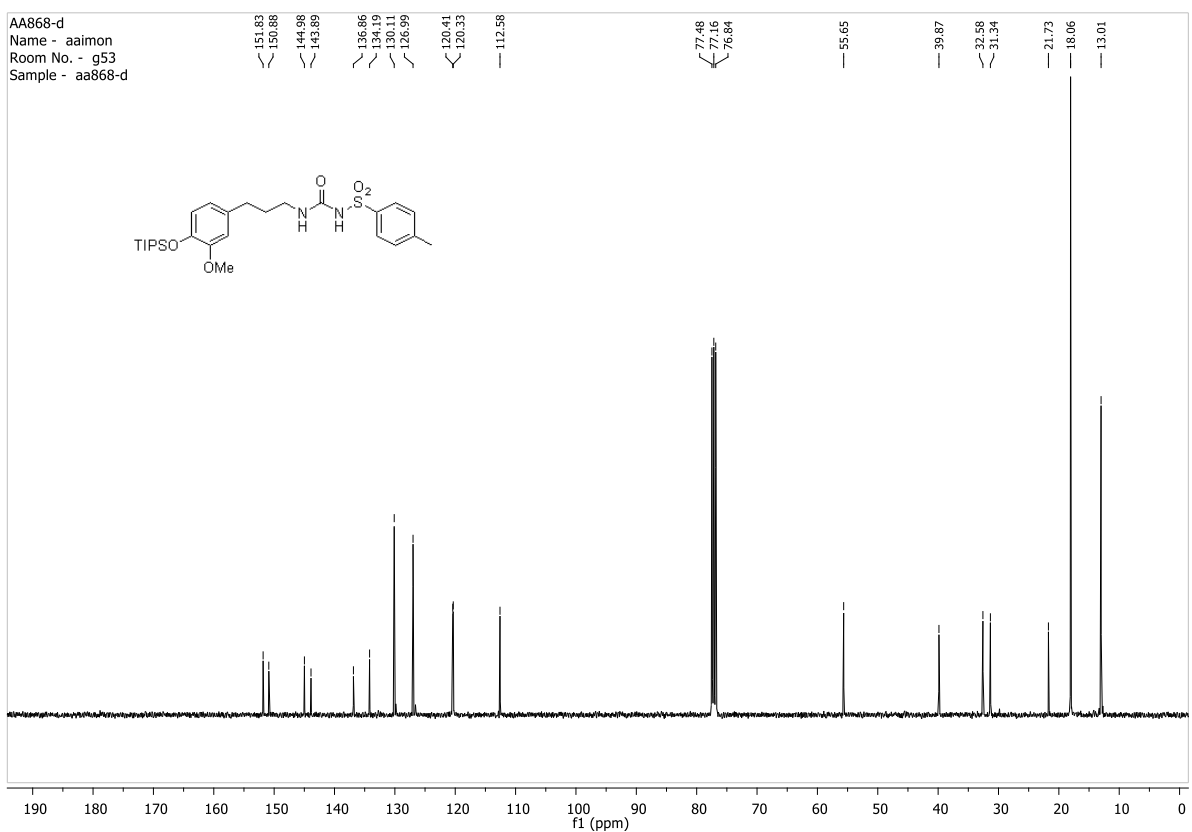
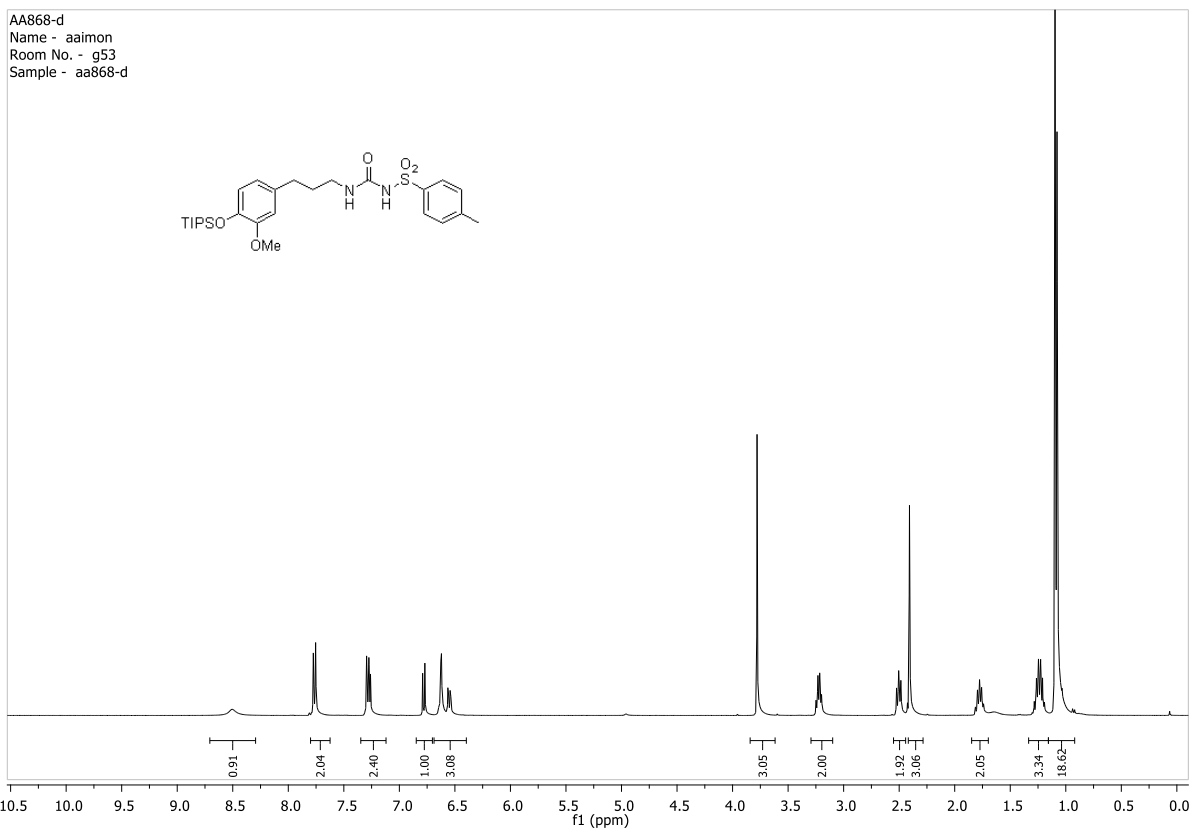
Ethyl 2-({[3-(3-methoxy-4-{[tris(propan-2-yl)silyl]oxy}phenyl)propyl]carbamoyl}amino)-acetate S7



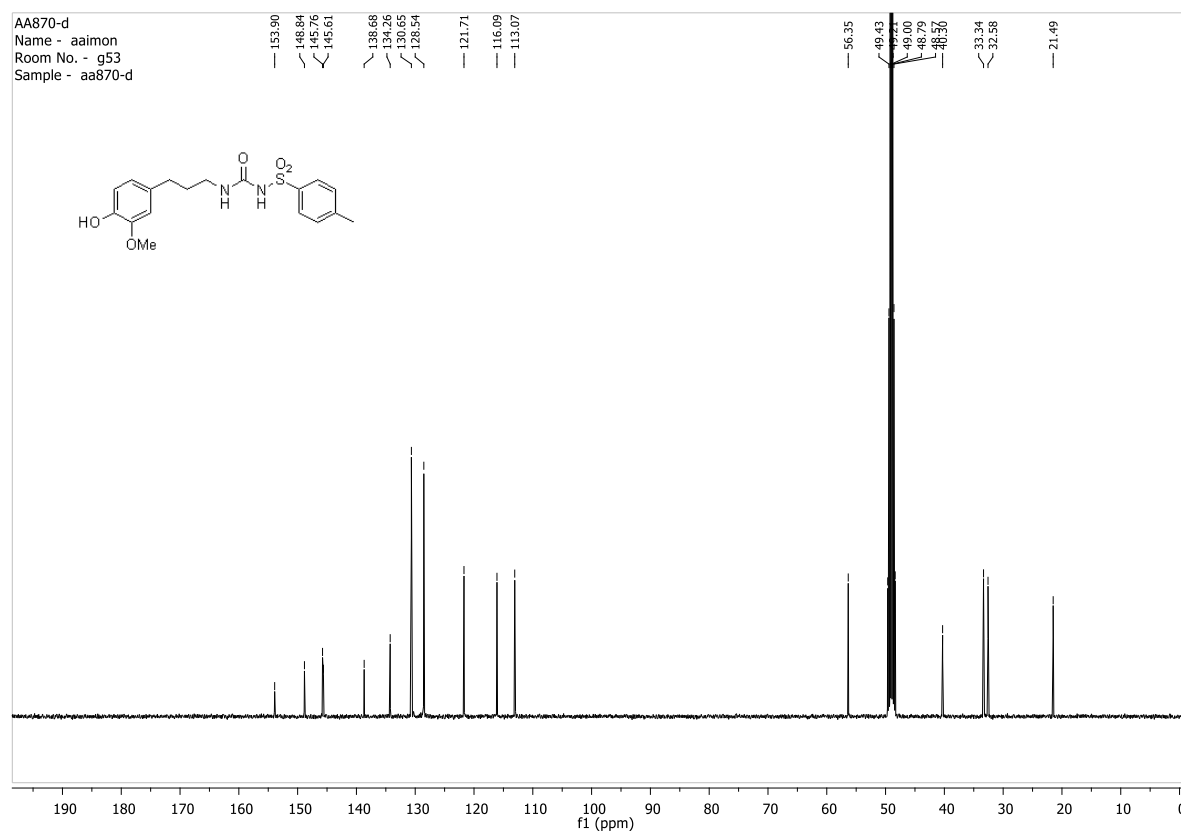
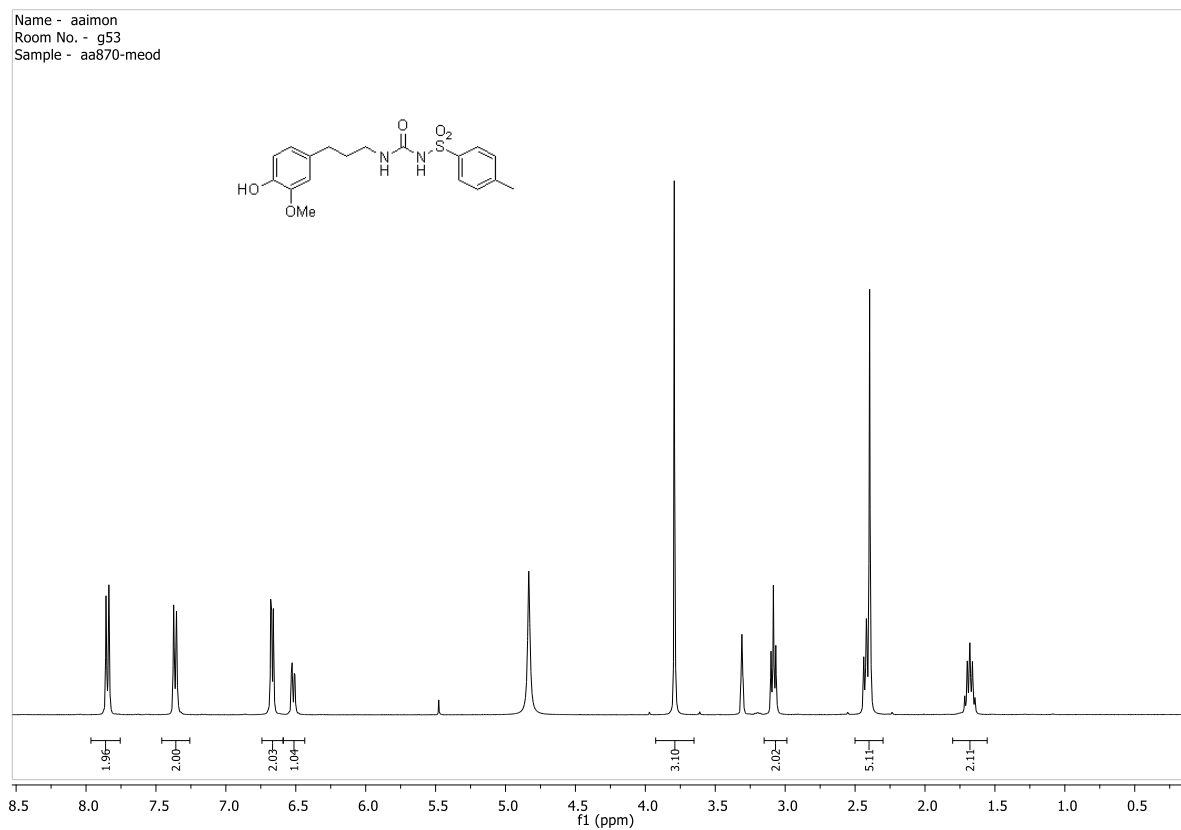
Ethyl 2-({[3-(4-hydroxy-3-methoxyphenyl)propyl]carbamoyl}amino)acetate 11



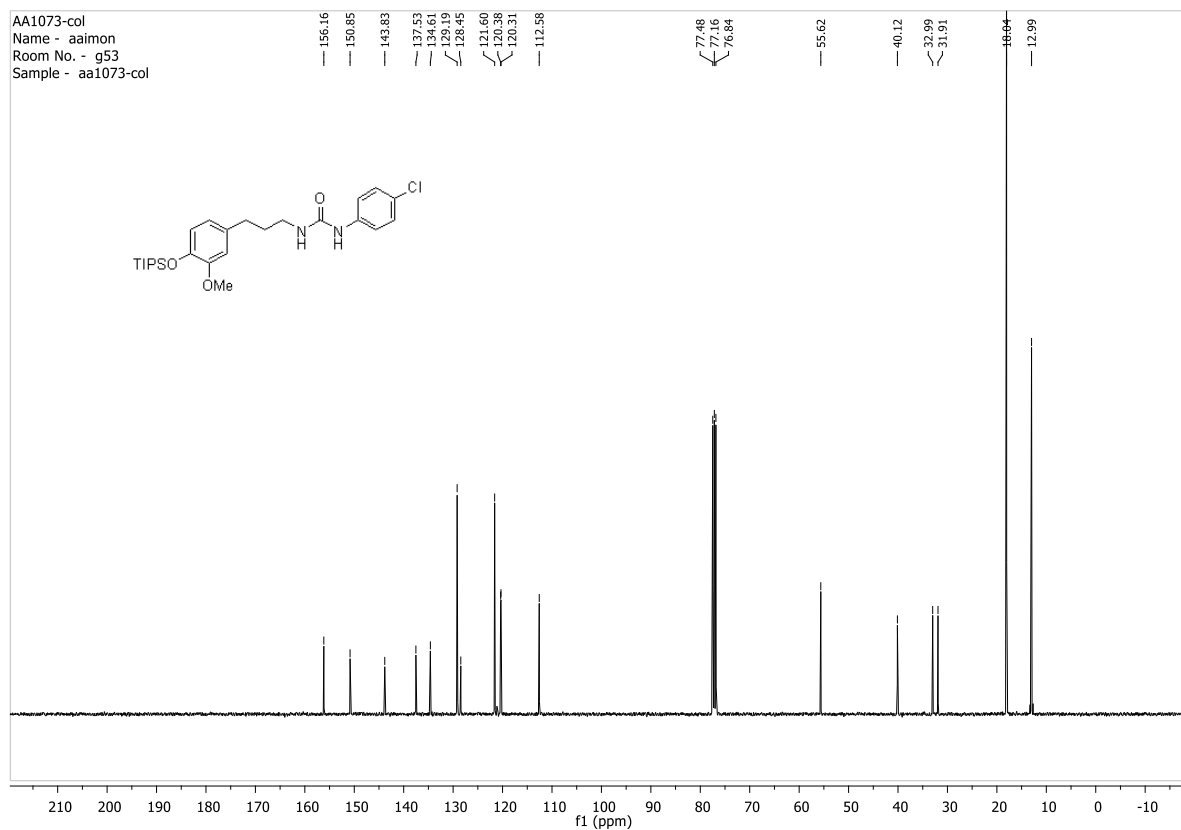
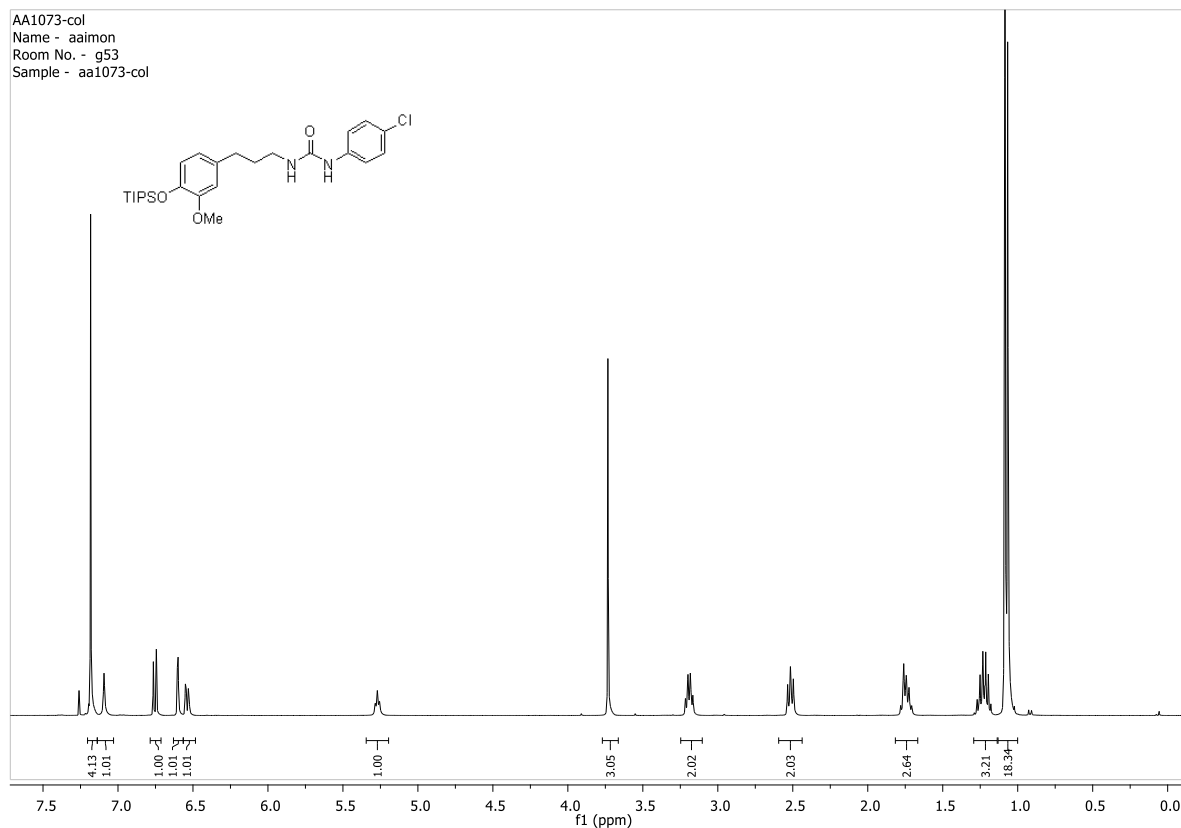
3-[3-(3-Methoxy-4-{*tris*(propan-2-yl)silyl]oxy}phenyl)propyl]-1-(4-methylbenzenesulfonyl)urea S8



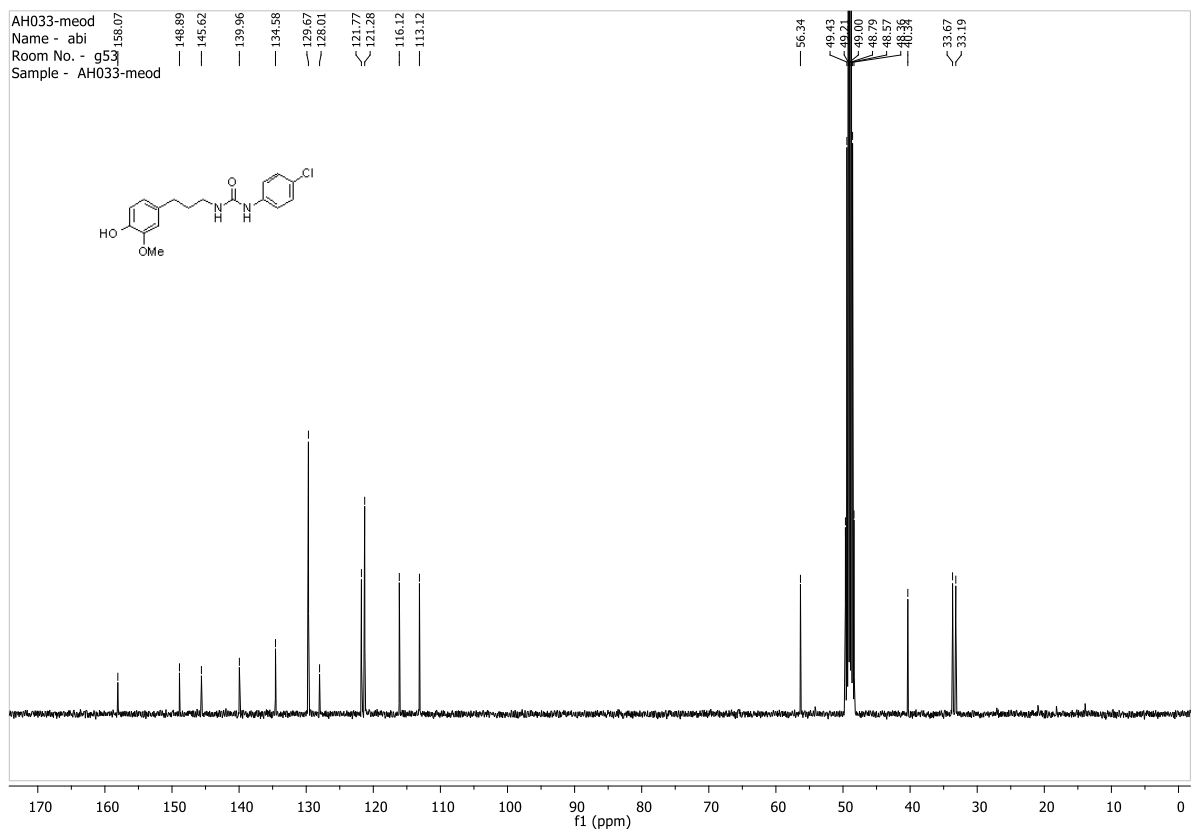
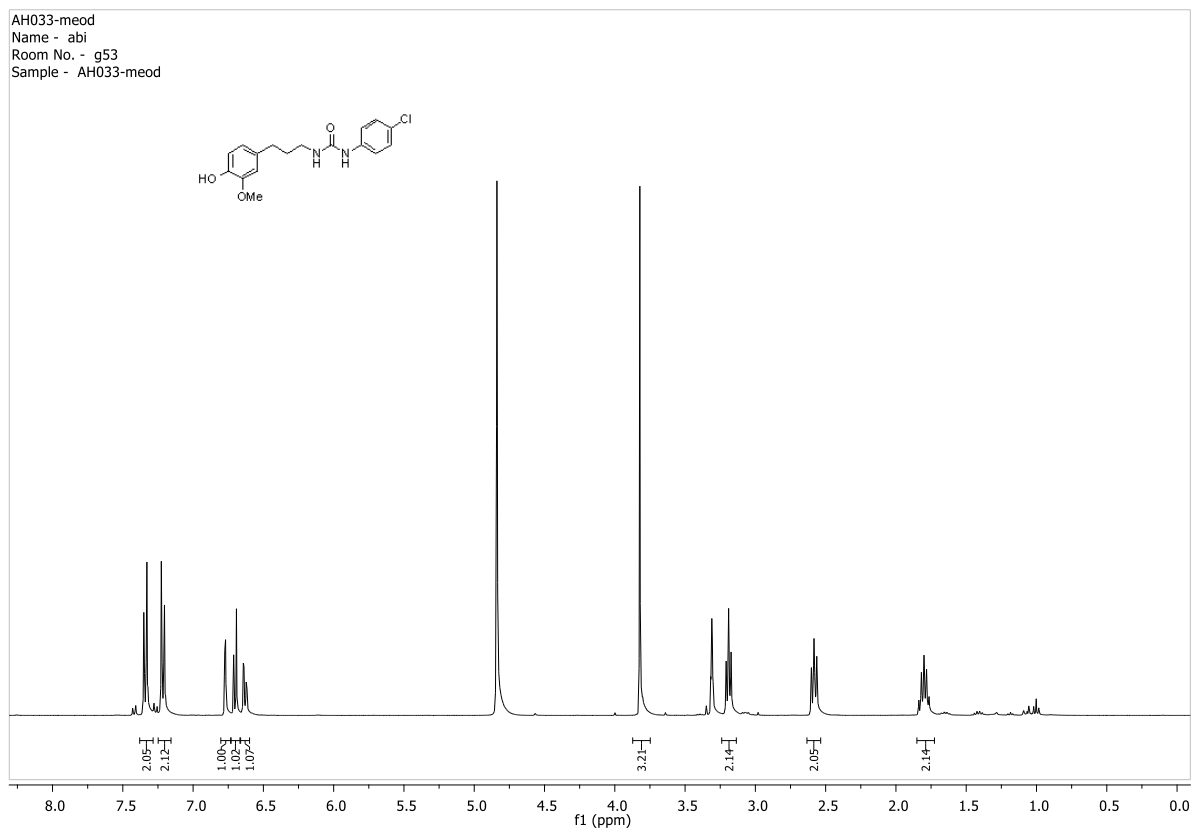
3-[3-(4-Hydroxy-3-methoxyphenyl)propyl]-1-(4-methylbenzenesulfonyl)urea 1m



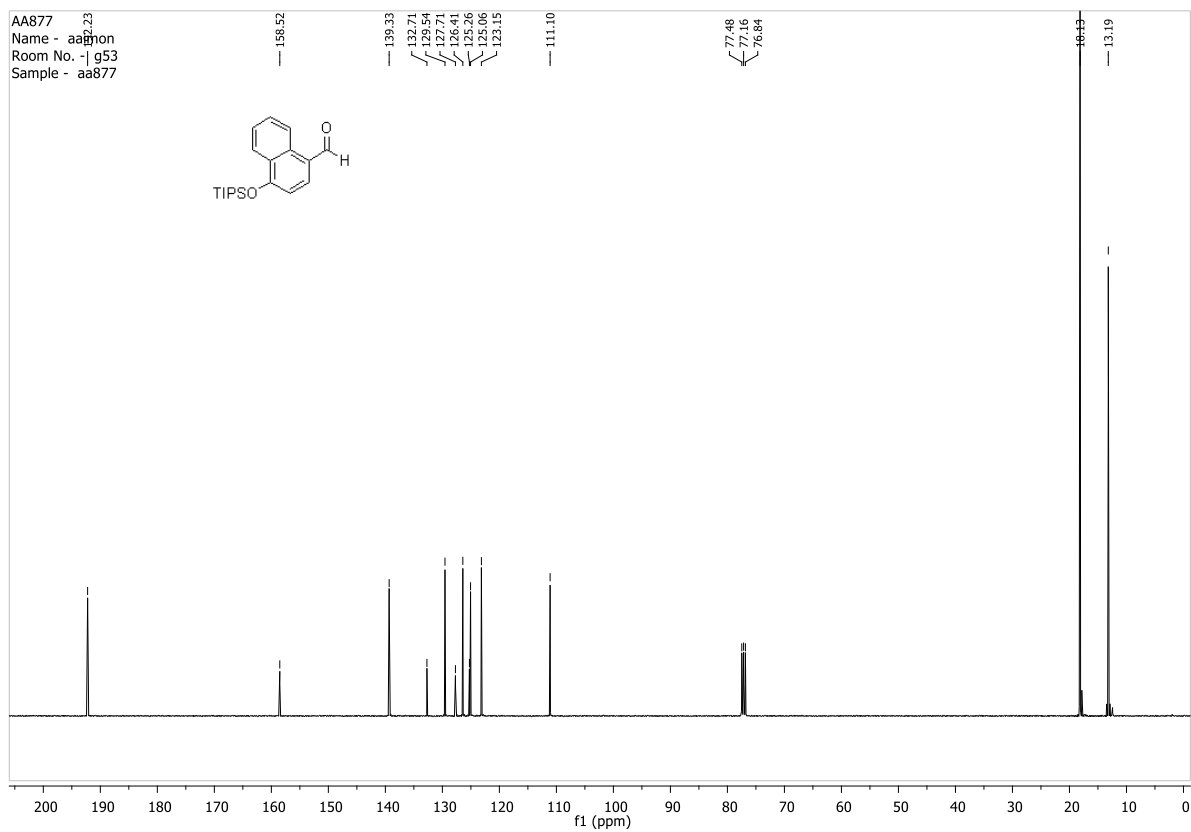
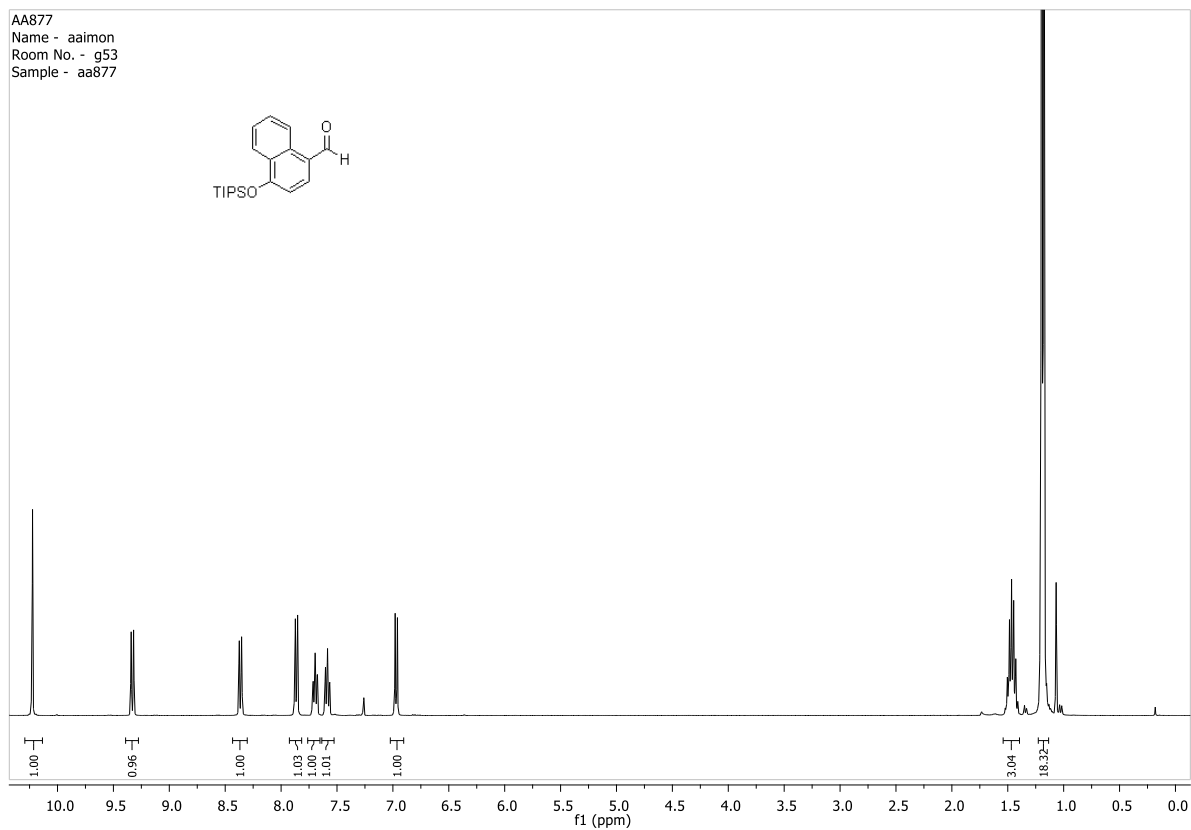
1-(4-Chlorophenyl)-3-[3-(3-methoxy-4-[[tris(propan-2-yl)silyl]oxy)phenyl)propyl]urea S9



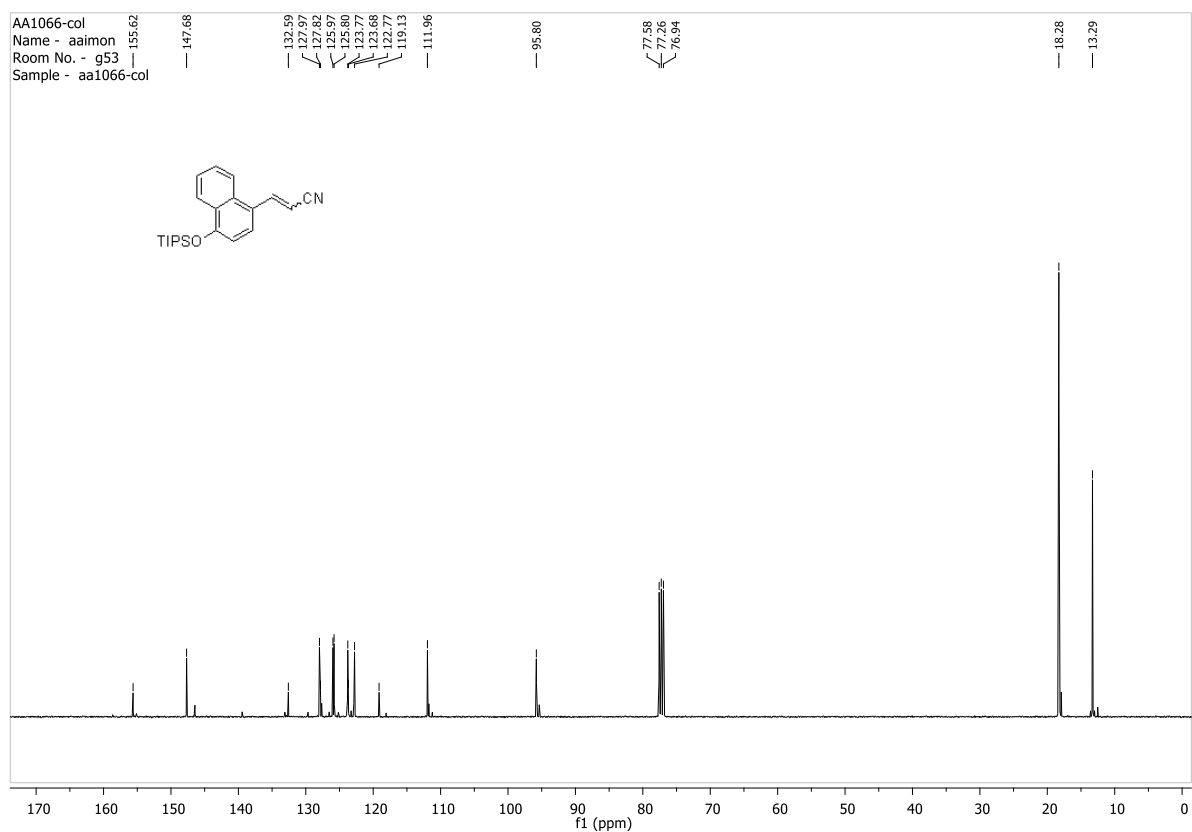
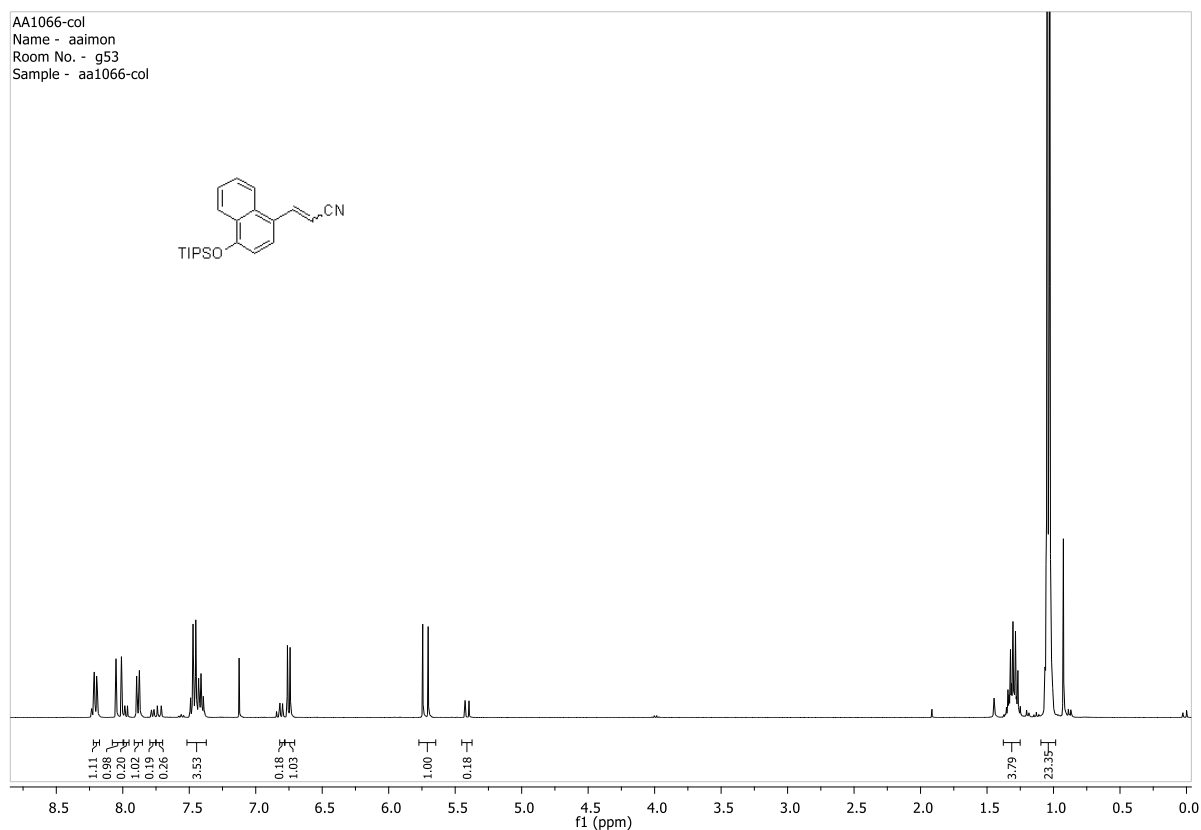
1-(4-Chlorophenyl)-3-[3-(4-hydroxy-3-methoxyphenyl)propyl]urea 1n



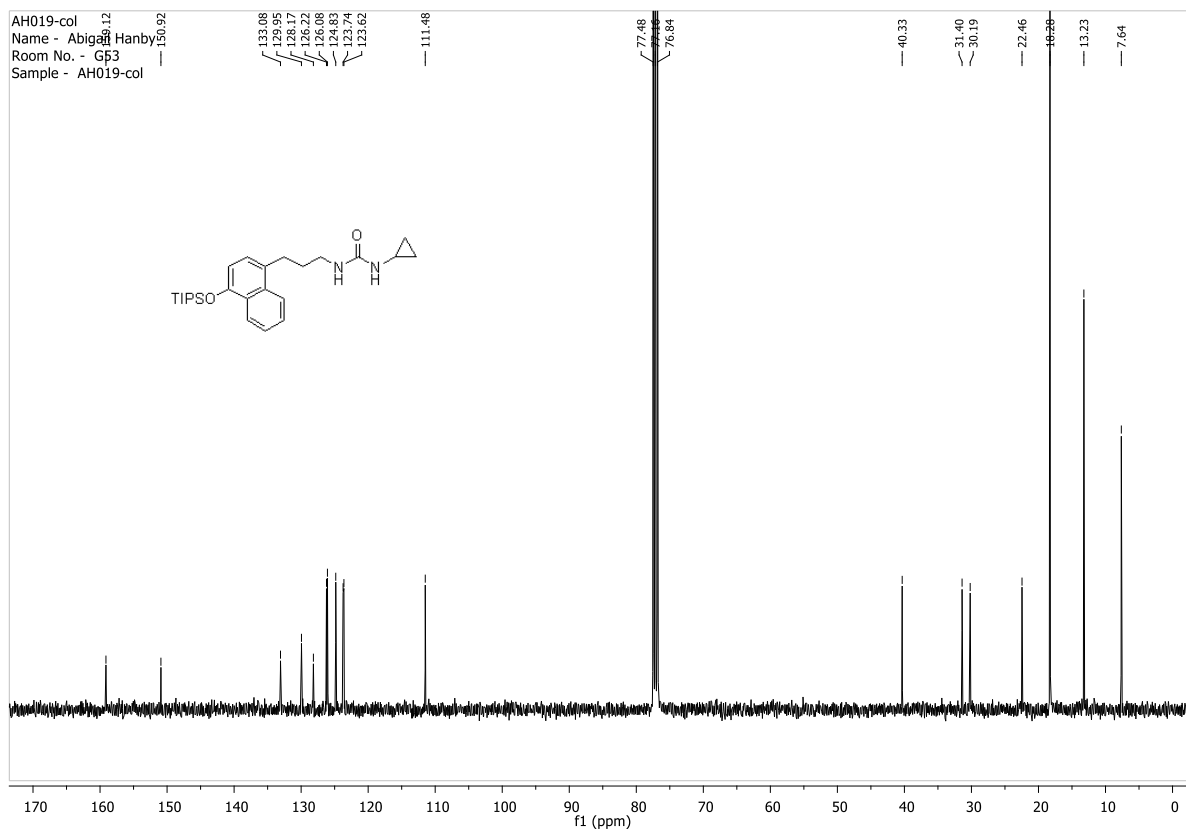
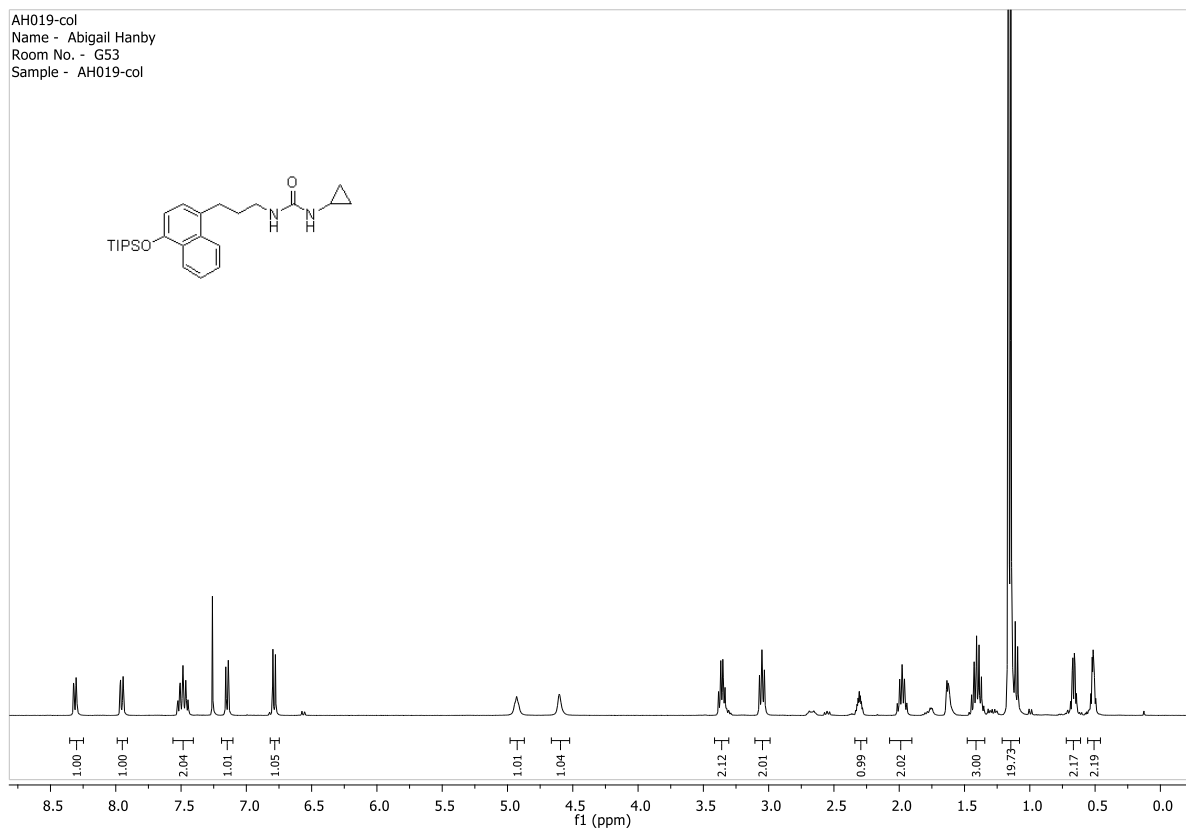
4-[[Tris(propan-2-yl)silyl]oxy]naphthalene-1-carbaldehyde S10



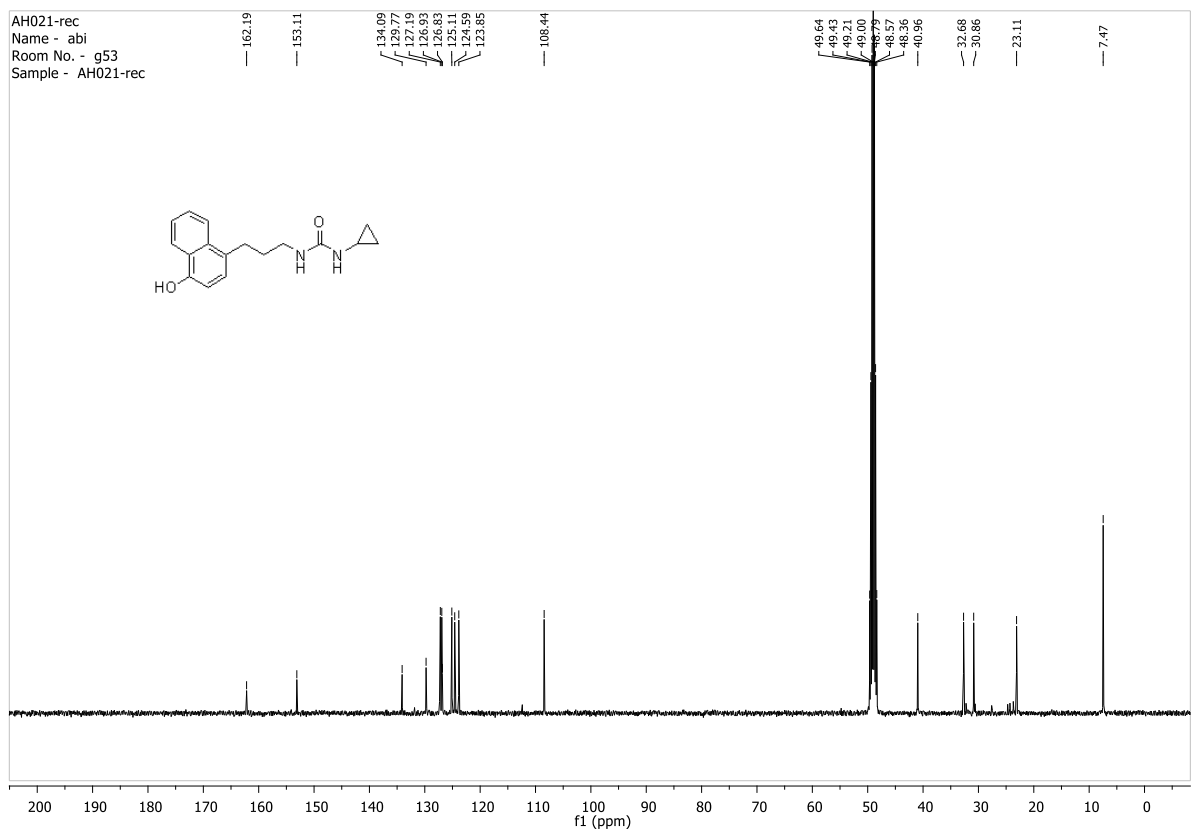
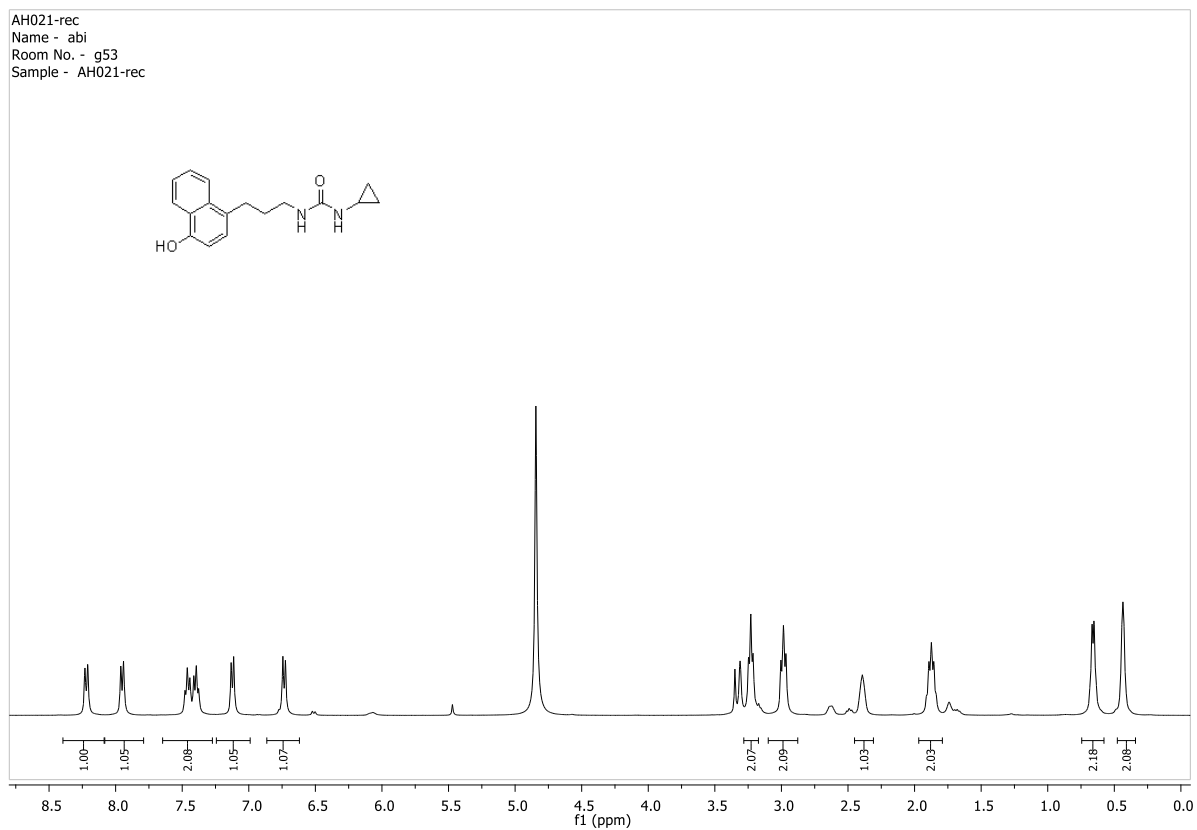
(2E/2Z)-3-(4-{[Tris(propan-2-yl)silyl]oxy}naphthalen-1-yl)prop-2-enitrile S11



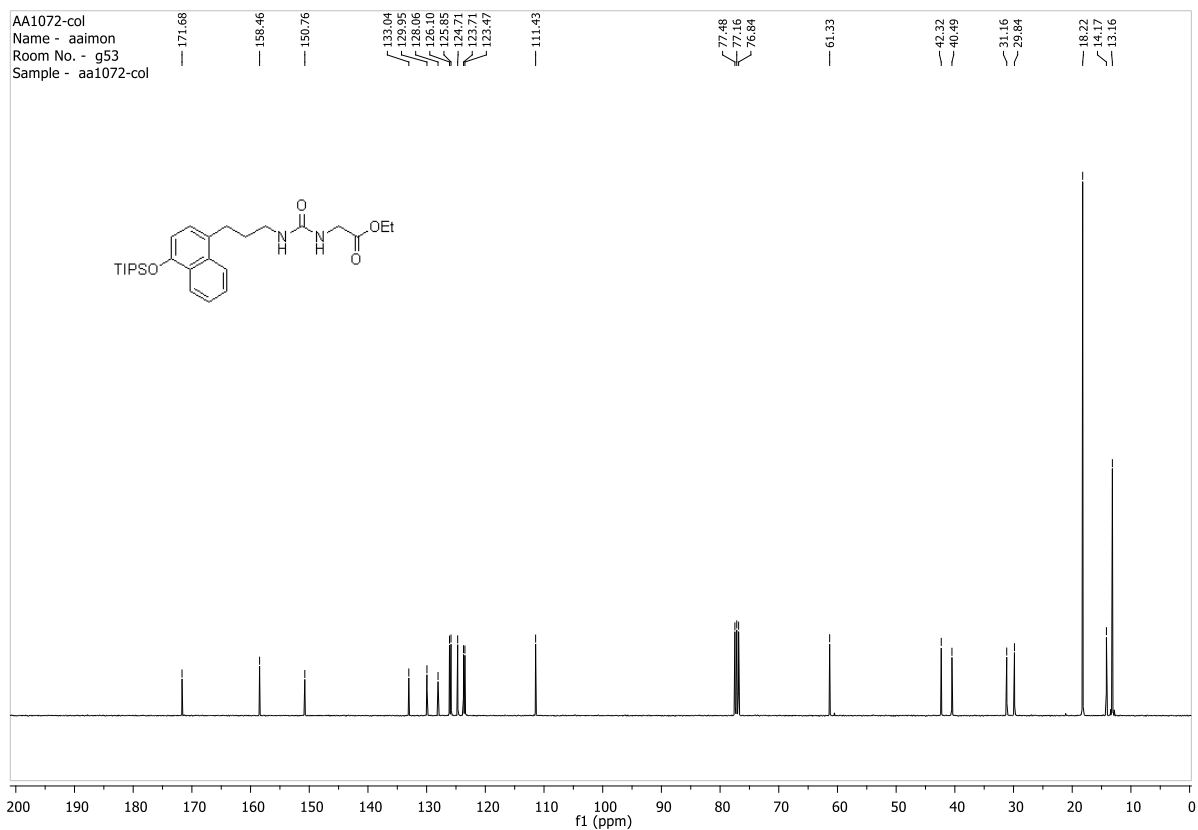
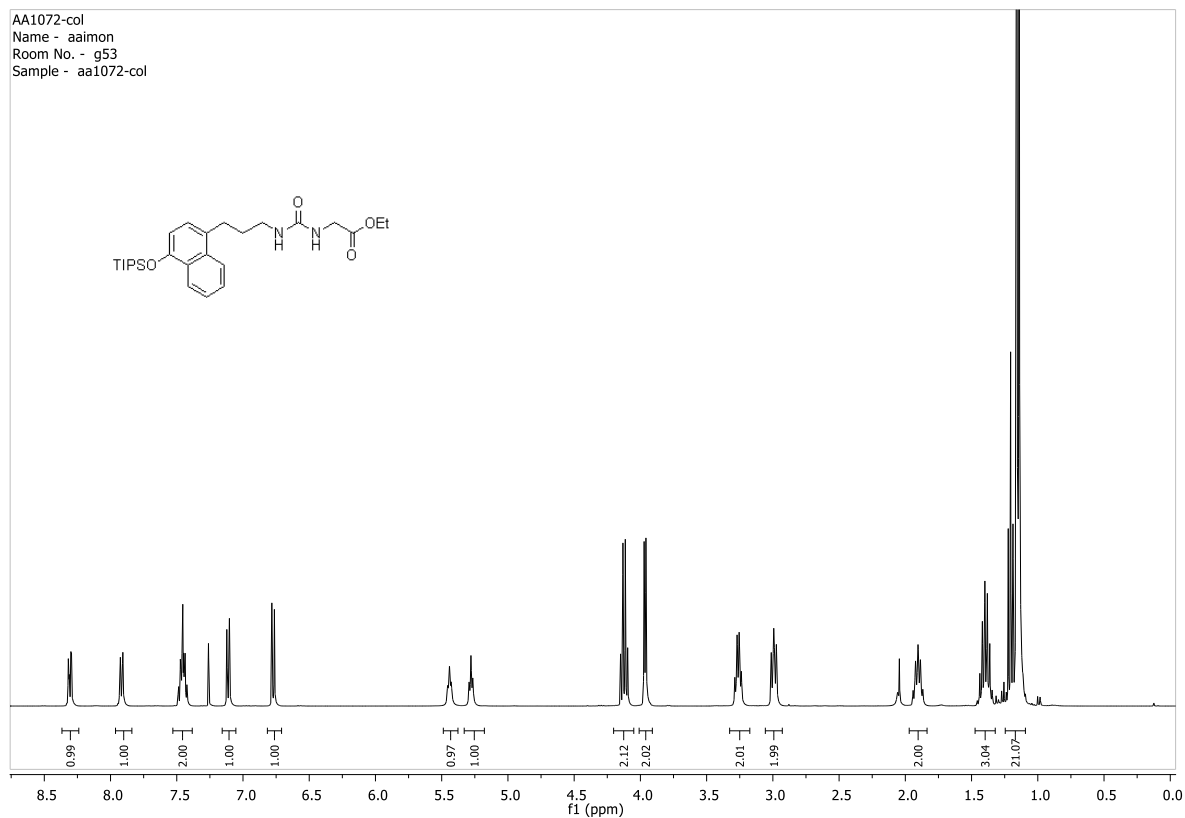
3-Cyclopropyl-1-[3-(4-[[tris(propan-2-yl)silyl]oxy)naphthalen-1-yl]propyl]urea S13



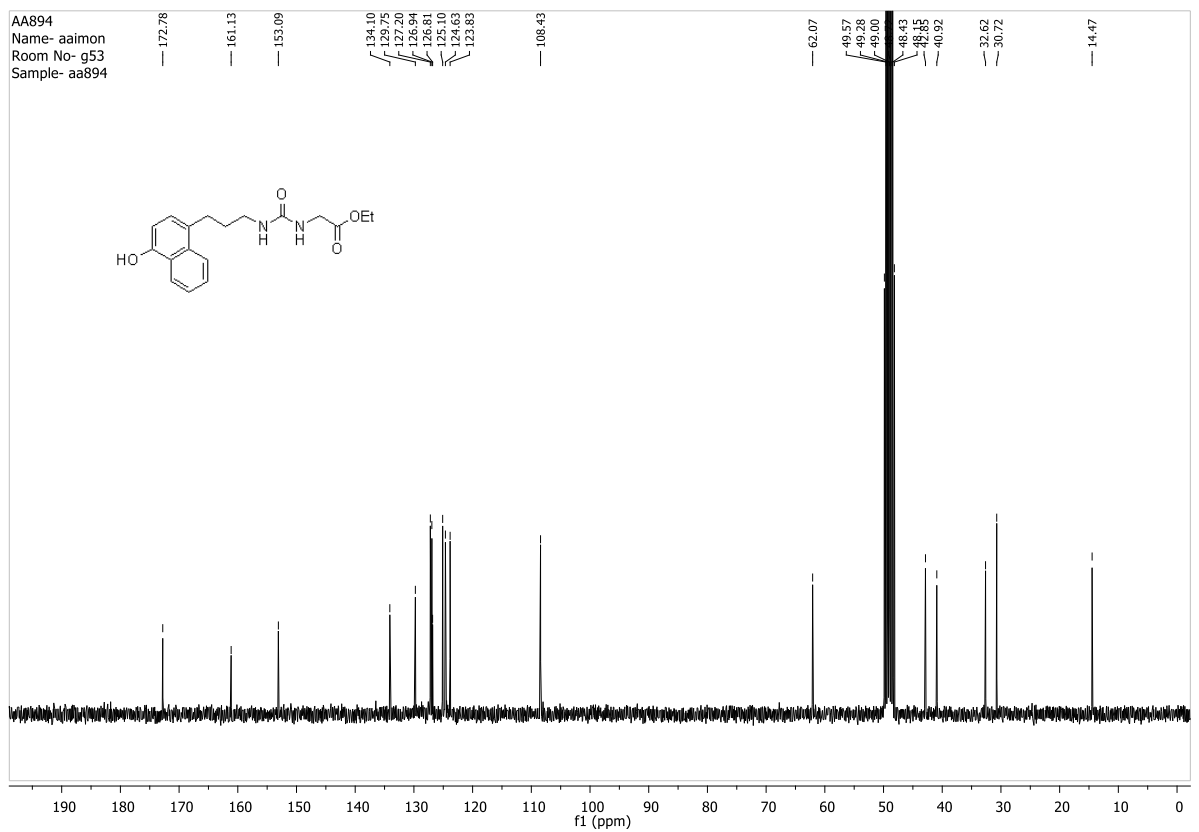
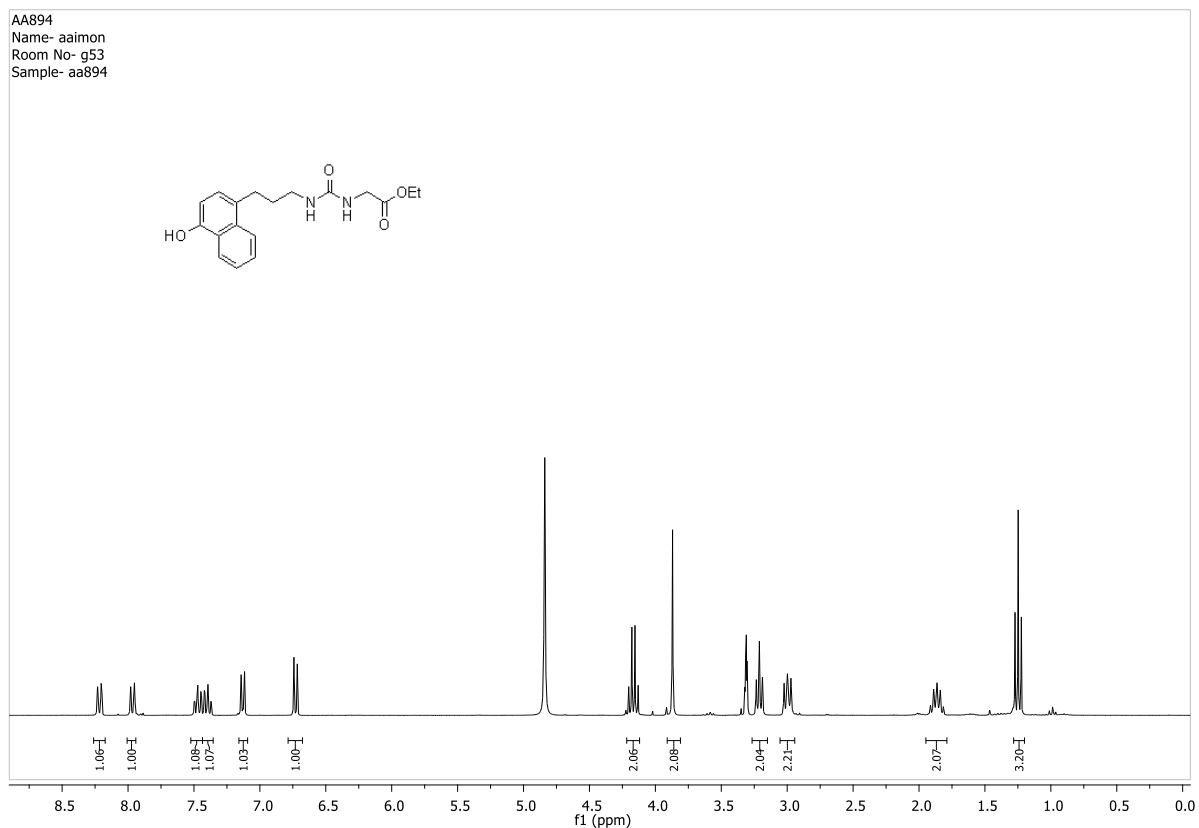
3-Cyclopropyl-1-[3-(4-hydroxynaphthalen-1-yl)propyl]urea 1o



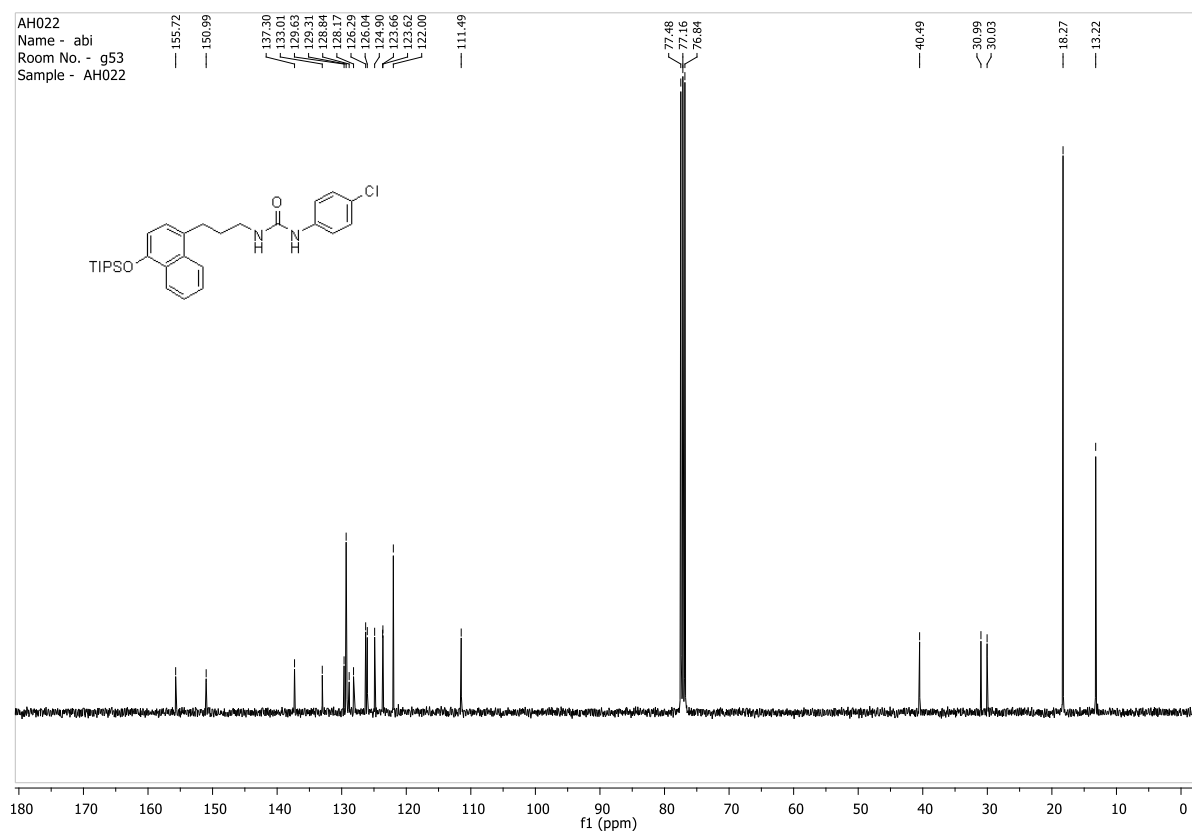
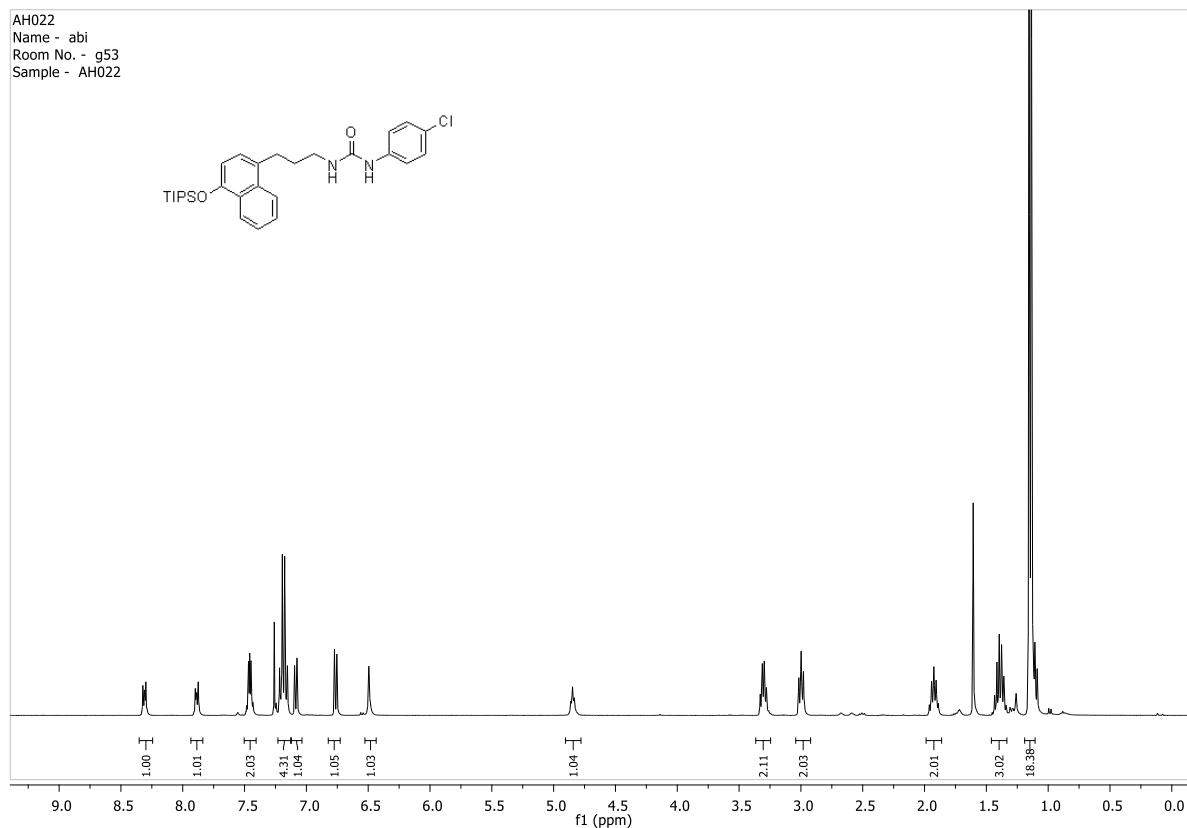
Ethyl 2-({3-(4-{[tris(propan-2-yl)silyl]oxy)naphthalen-1-yl}propyl)carbamoyl}amino)-acetate S14



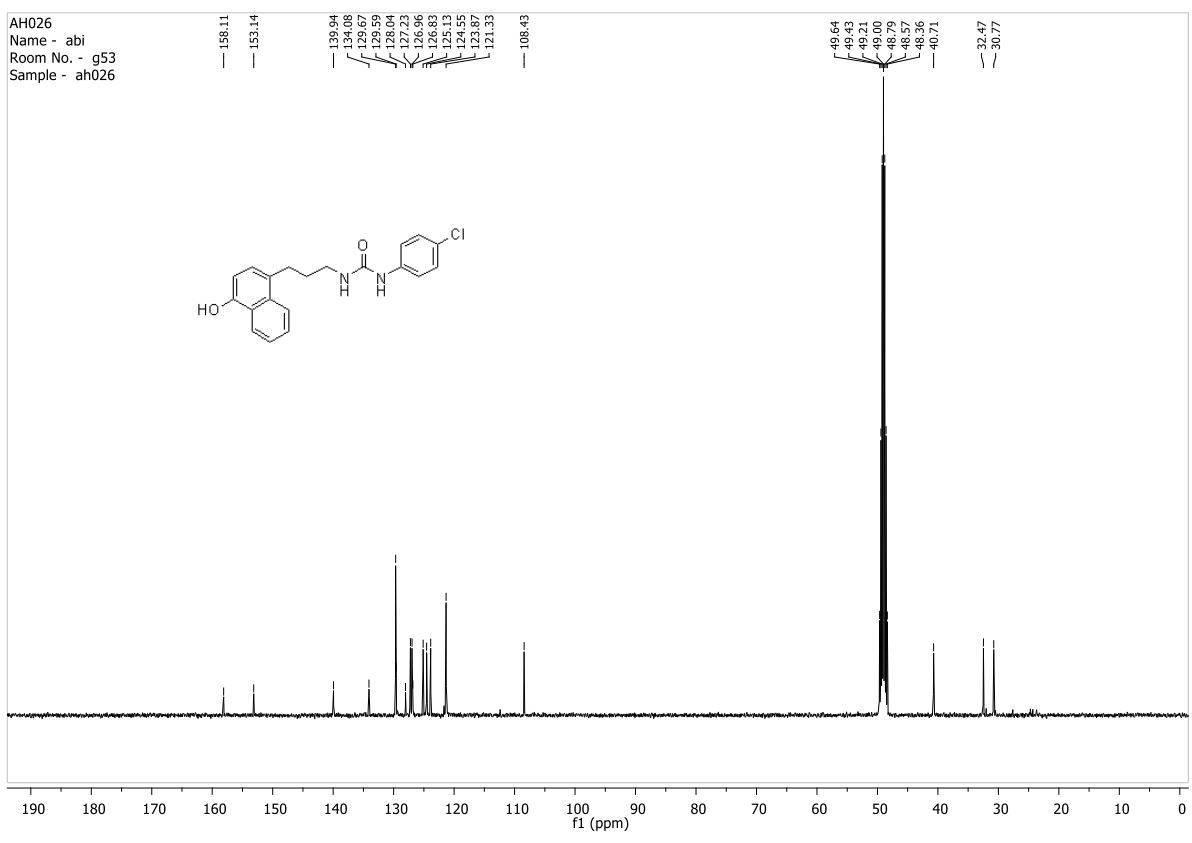
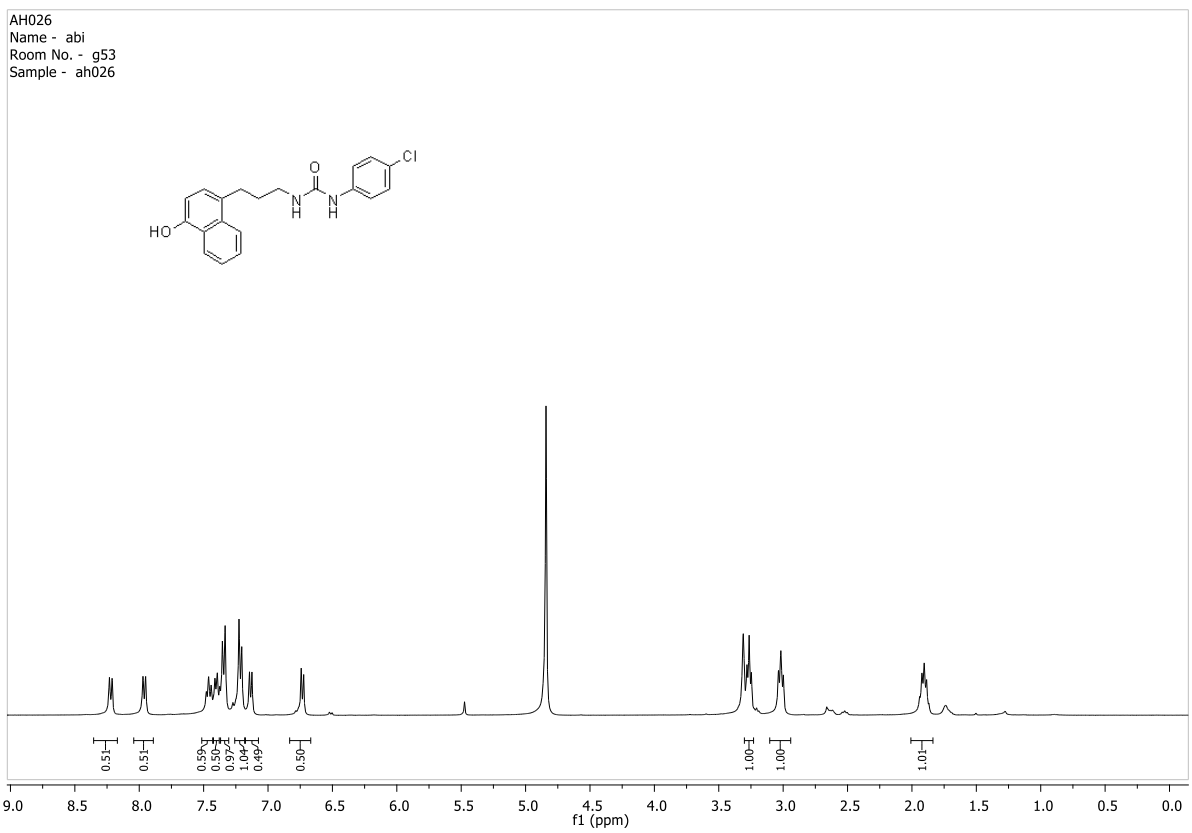
Ethyl 2-([3-(4-hydroxynaphthalen-1-yl)propyl]carbamoyl)amino)acetate 1p



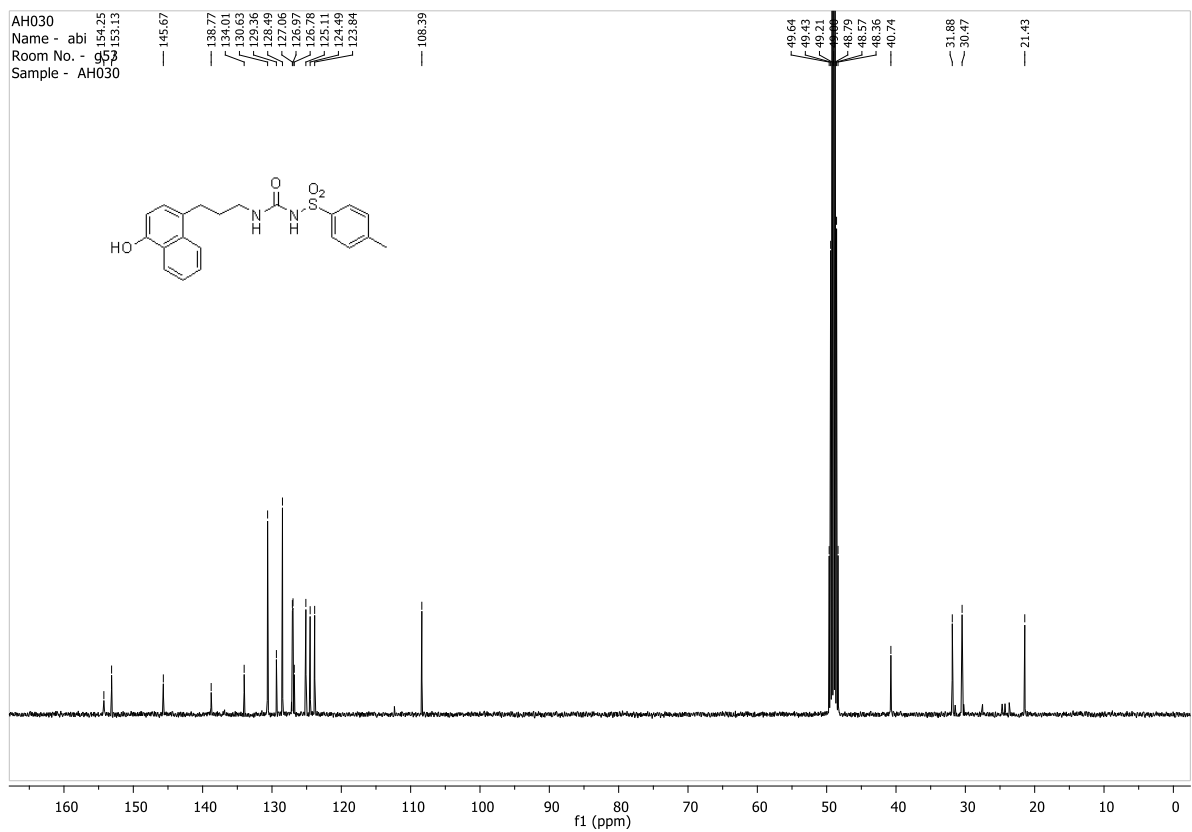
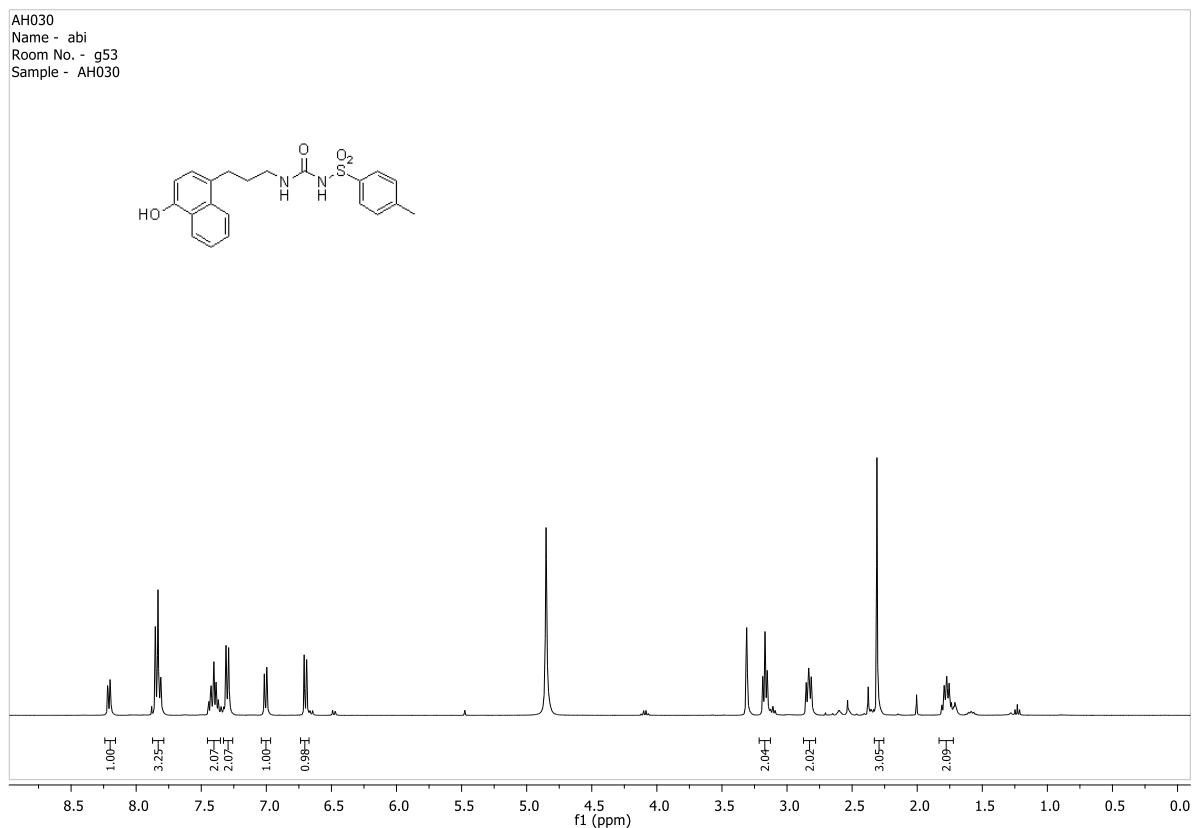
1-(4-Chlorophenyl)-3-[3-(4-{[tris(propan-2-yl)silyl]oxy}naphthalen-1-yl)propyl]urea S15



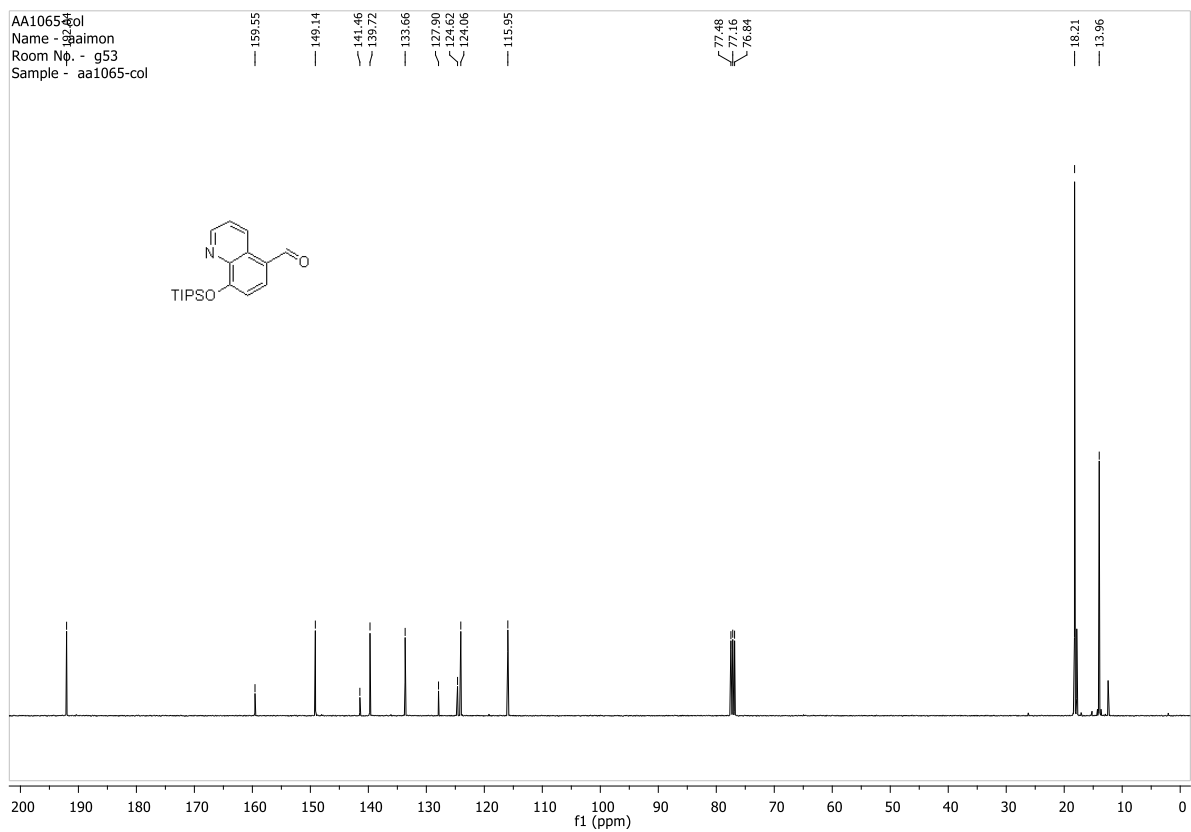
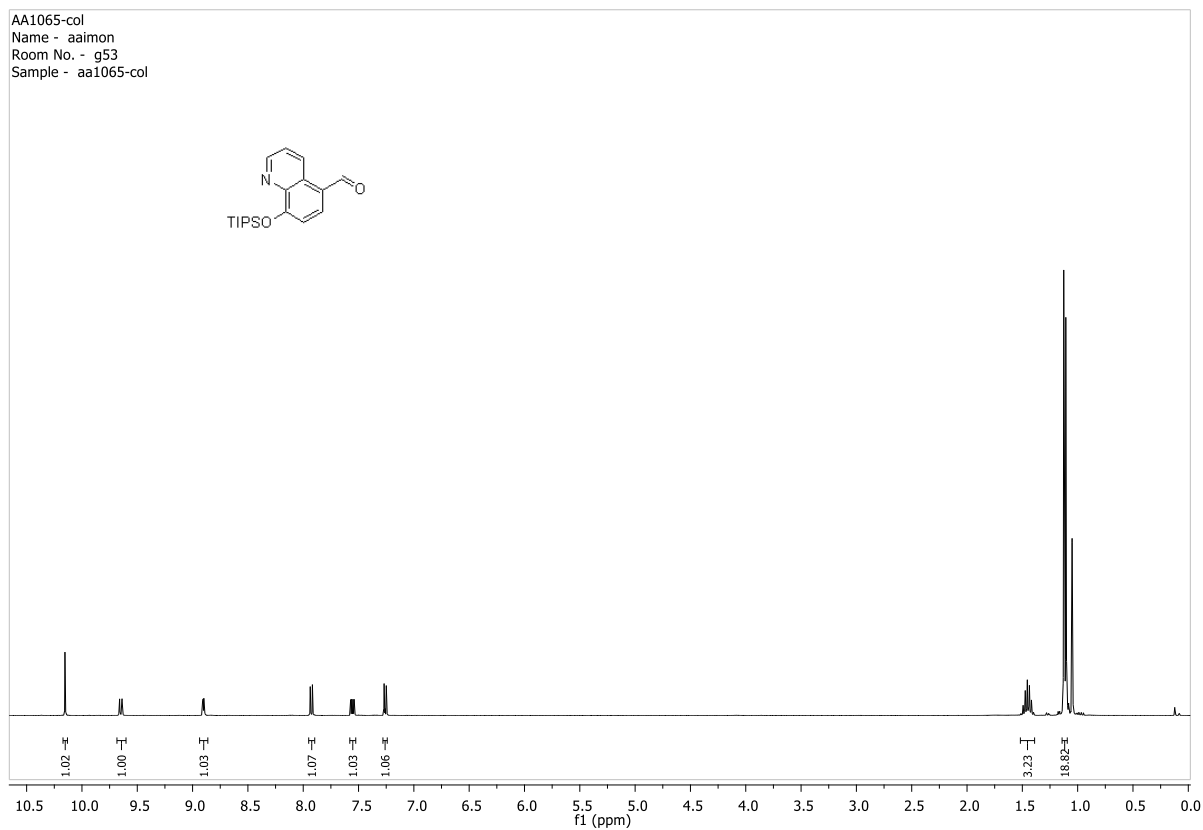
1-(4-Chlorophenyl)-3-[3-(4-hydroxynaphthalen-1-yl)propyl]urea 1q



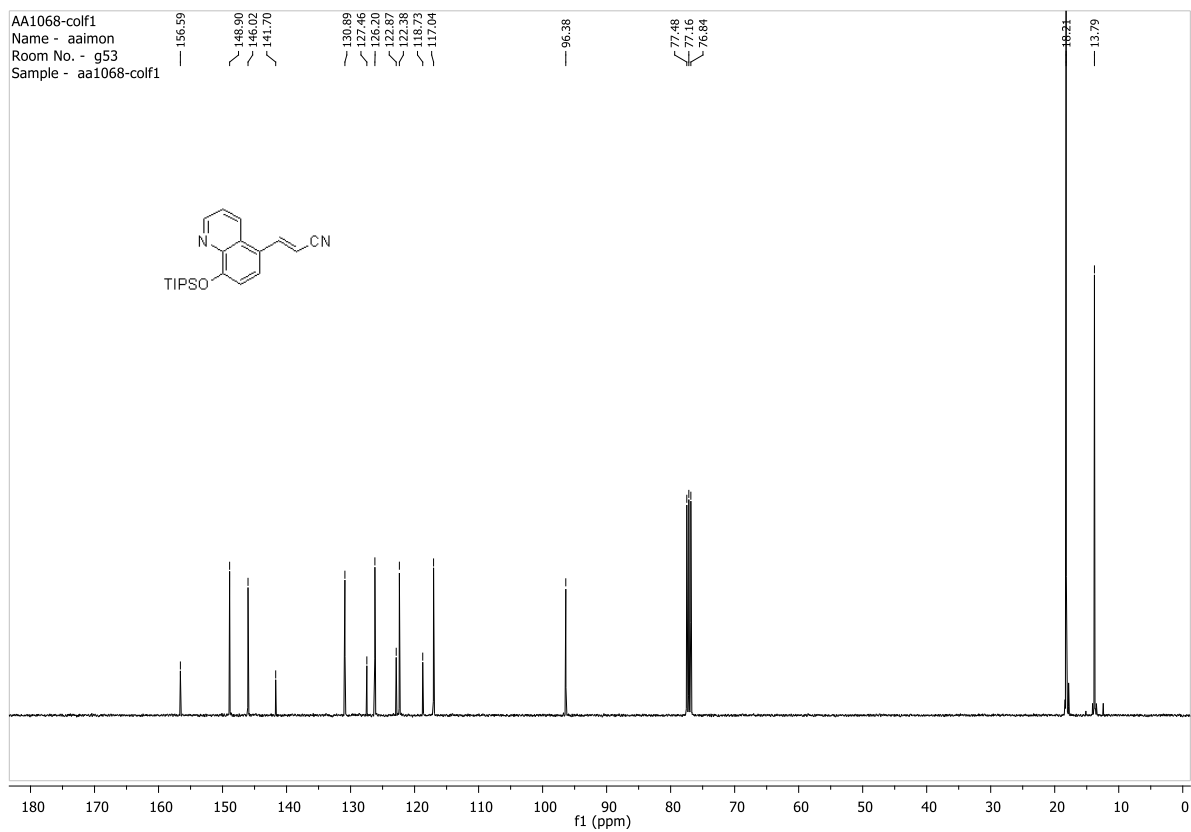
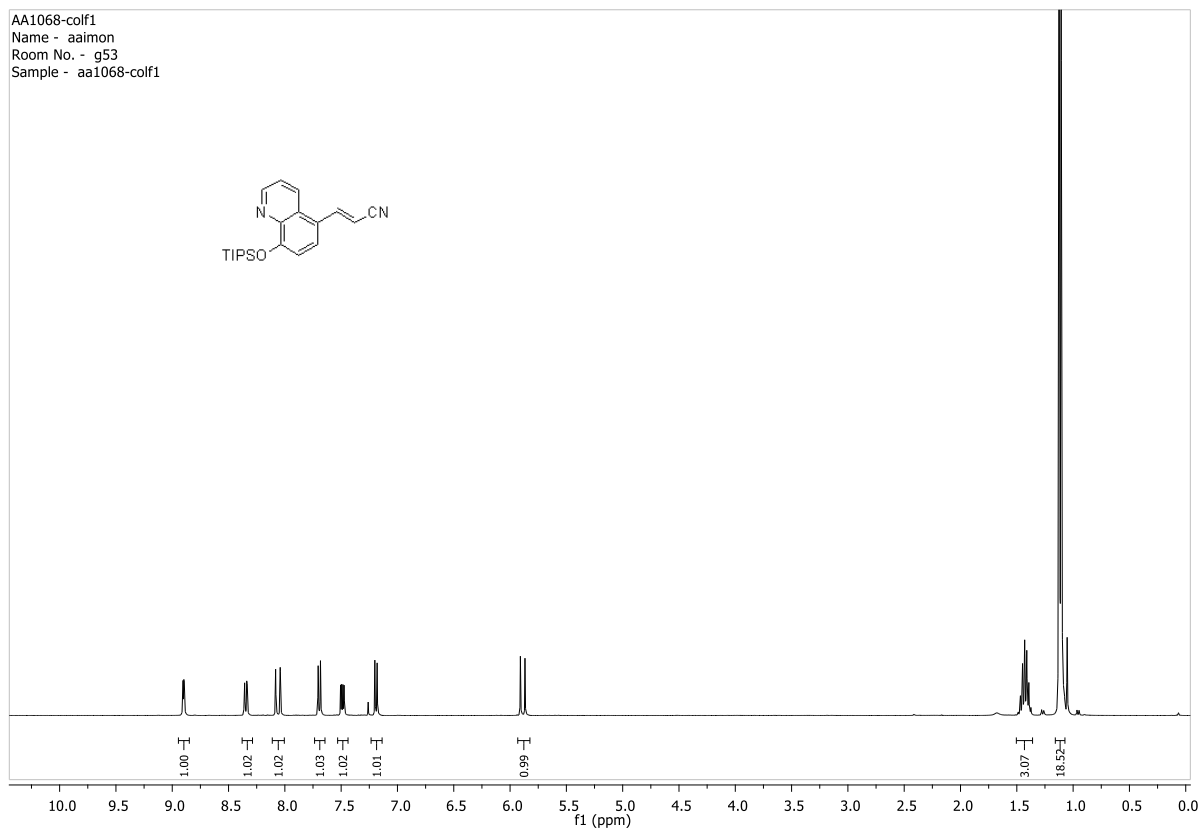
3-[3-(4-Hydroxynaphthalen-1-yl)propyl]-1-(4-methylbenzenesulfonyl)urea 1r



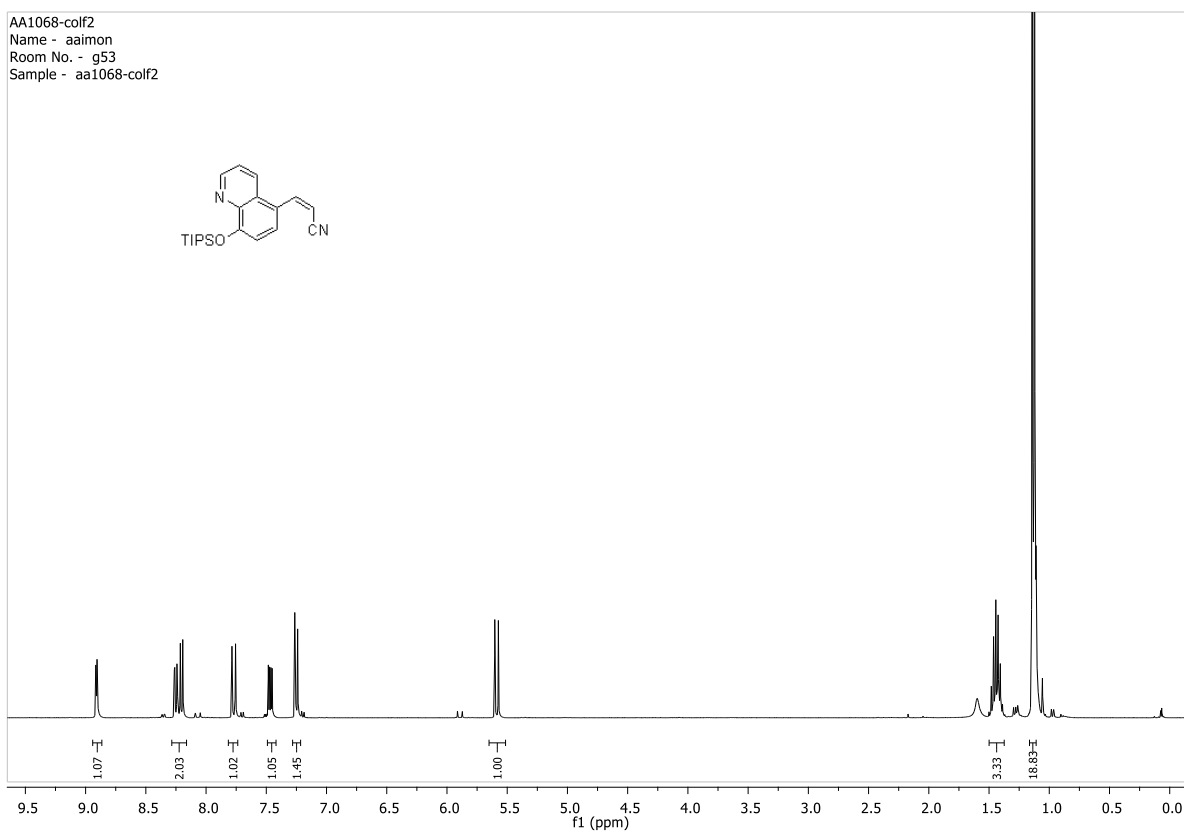
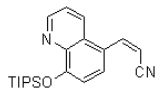
8-[[Tris(propan-2-yl)silyl]oxy]quinoline-5-carbaldehyde S16



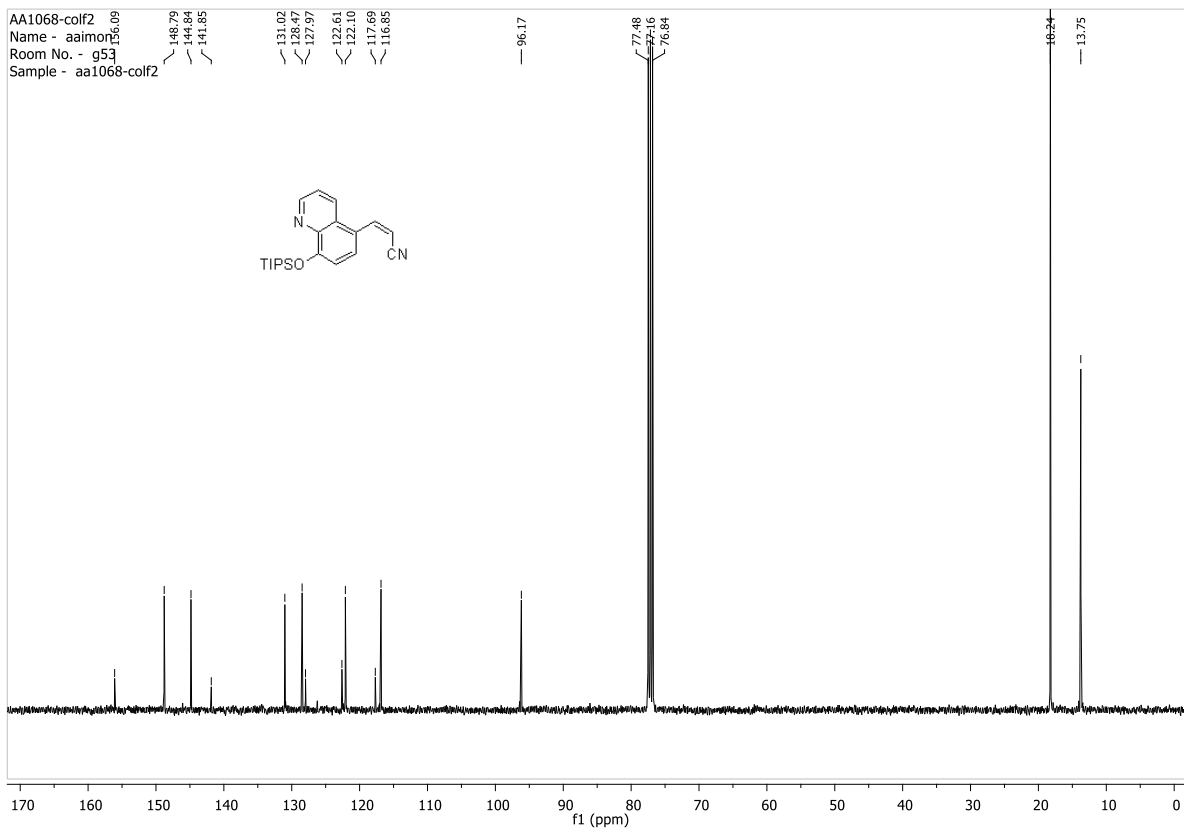
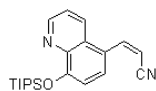
(2E/Z)-3-(8-{[Tris(propan-2-yl)silyl]oxy}quinolin-5-yl)prop-2-enitrile S17



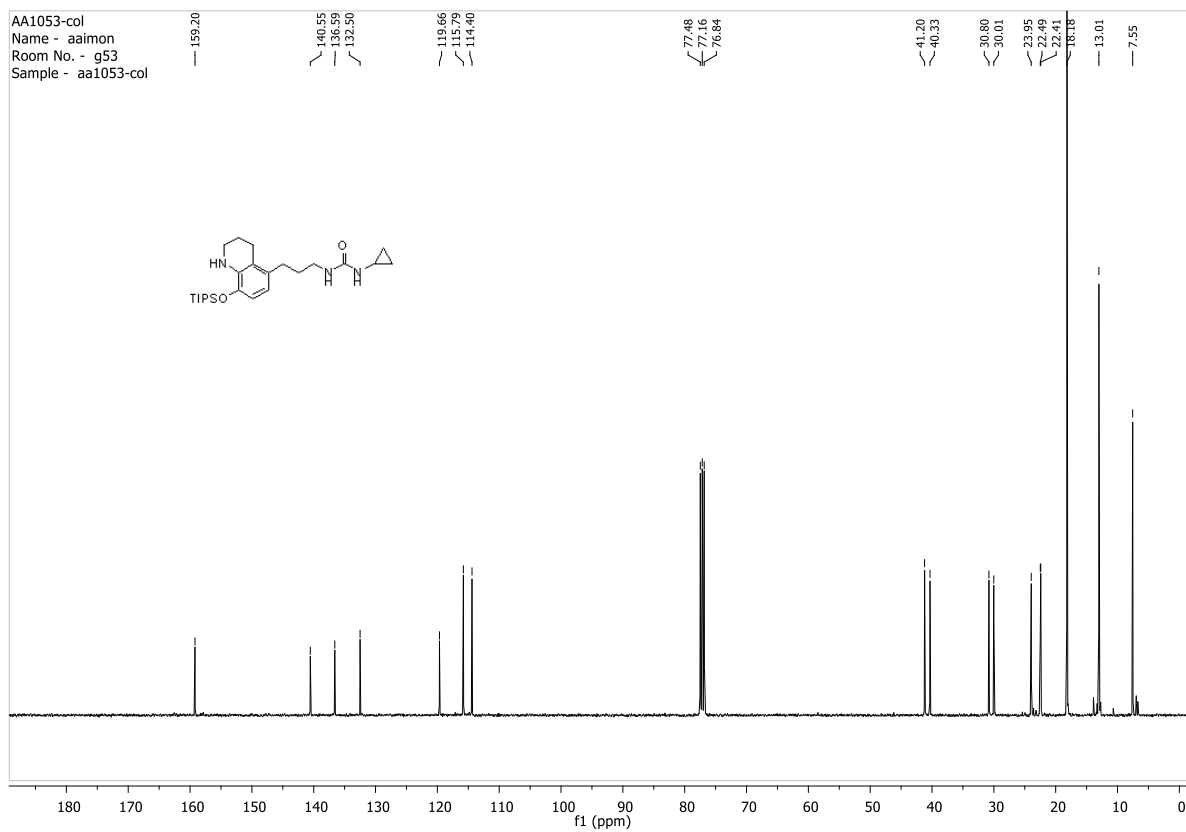
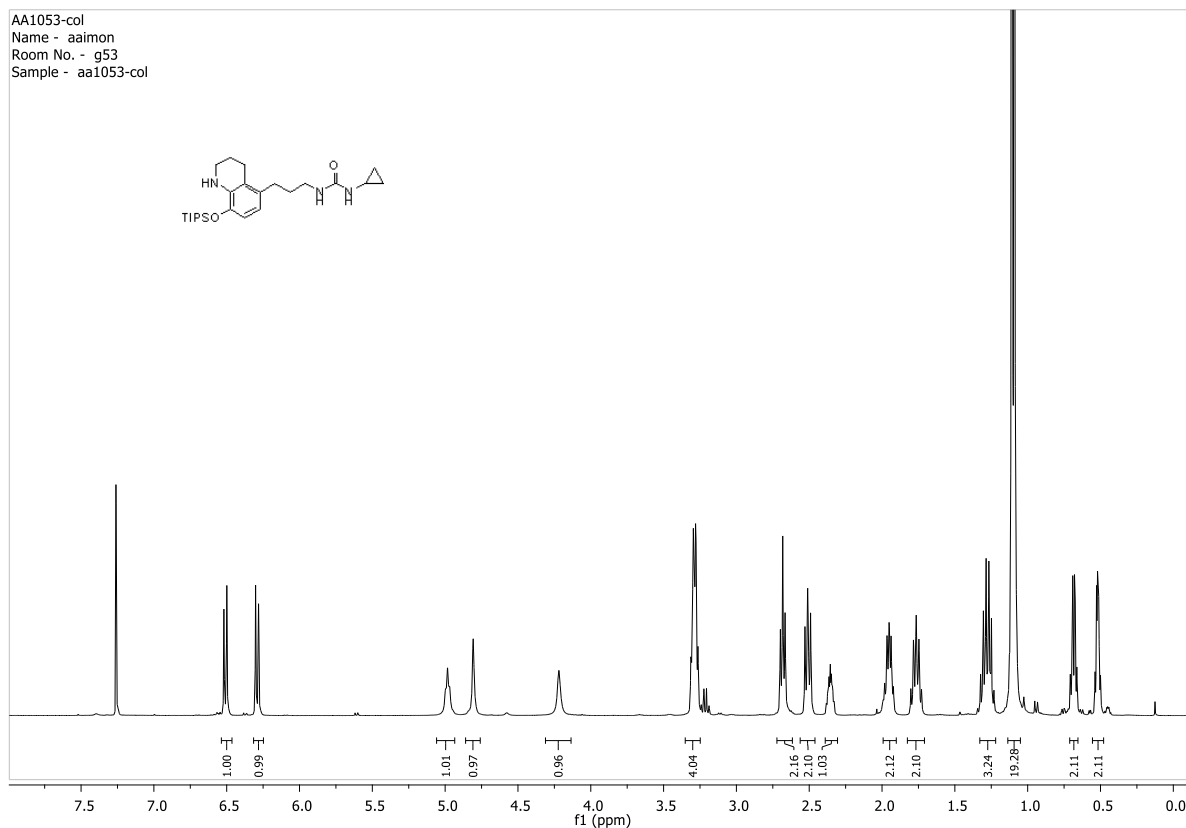
AA1068-colf2
Name - aaimon
Room No. - g53
Sample - aa1068-colf2



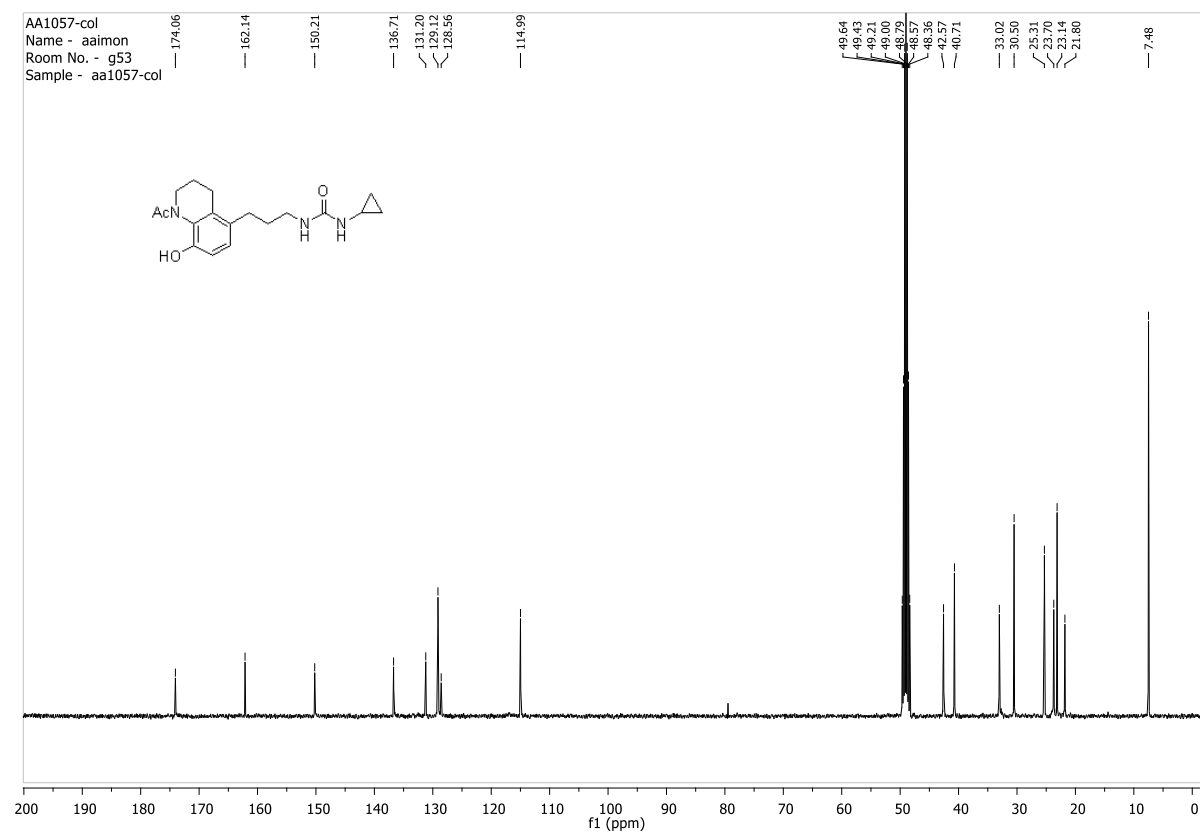
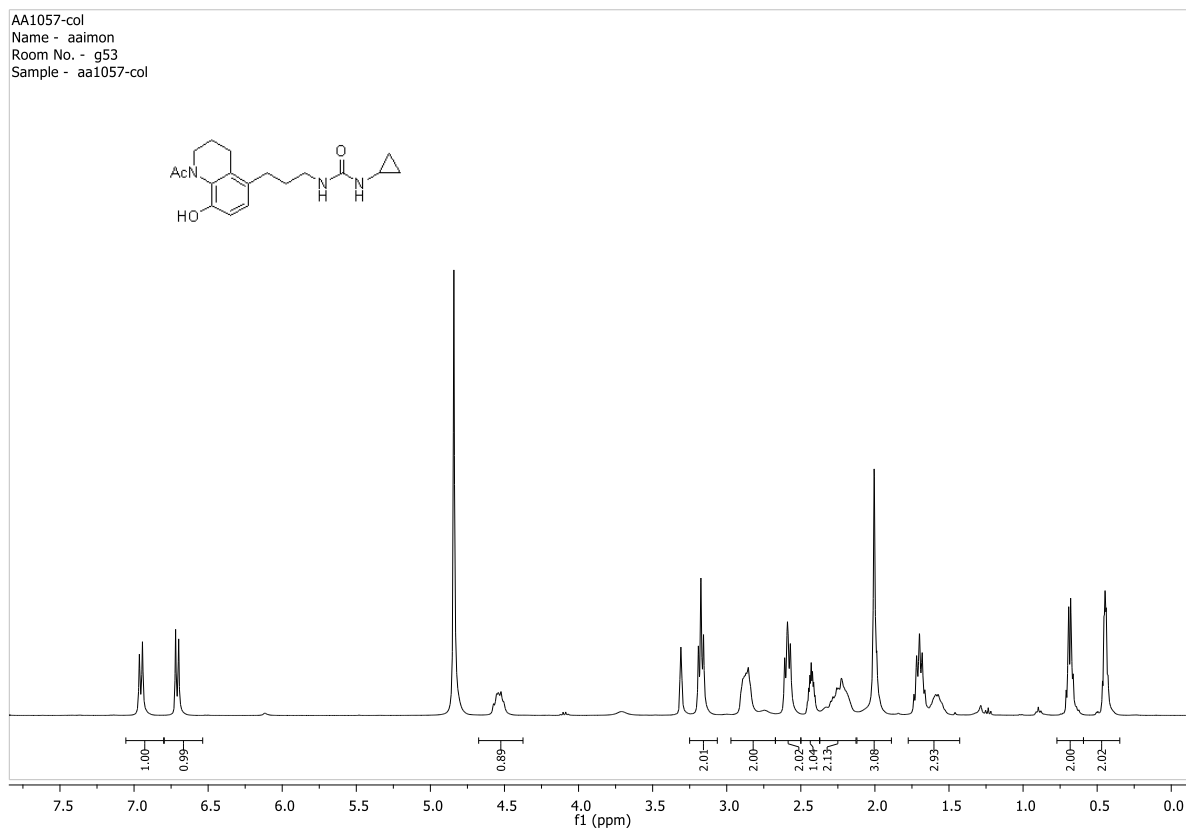
AA1068-colf2
Name - aaimon
Room No. - g53
Sample - aa1068-colf2



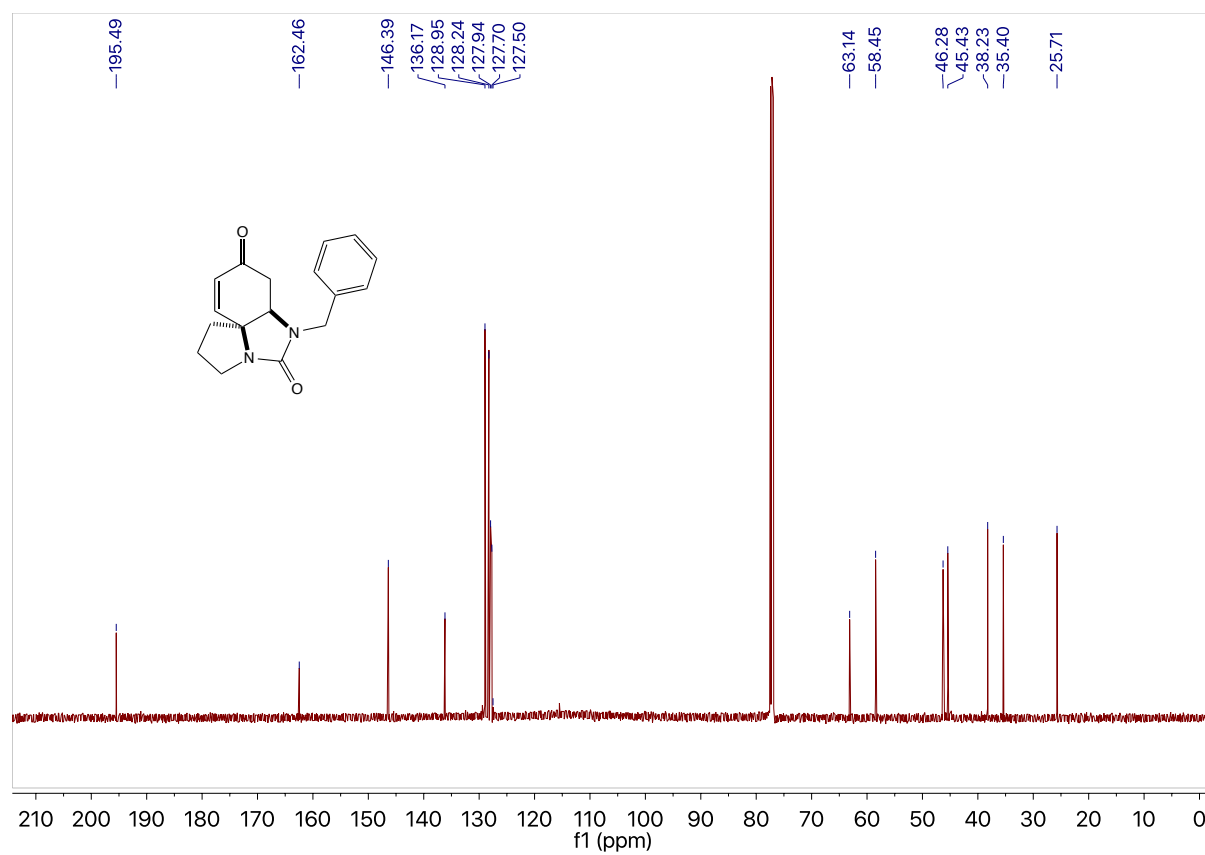
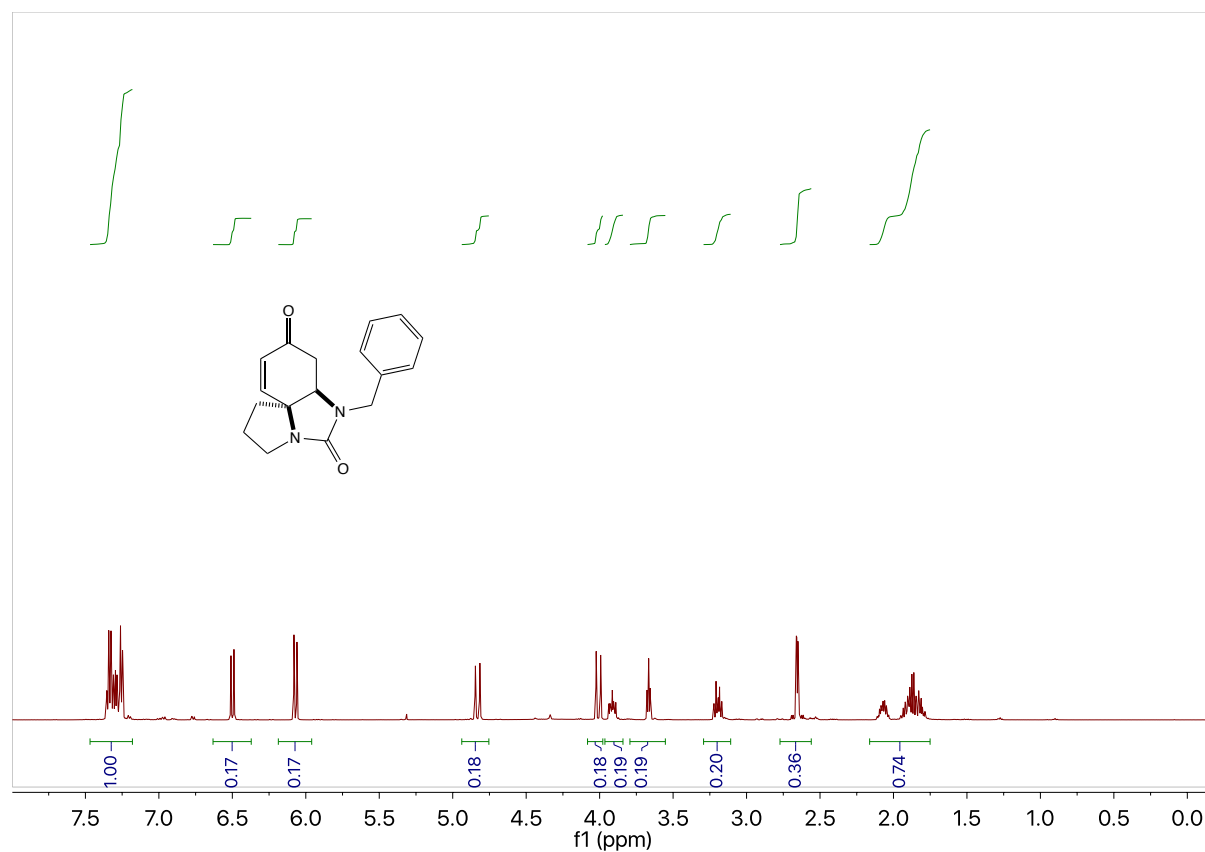
3-Cyclopropyl-1-[3-(8-{[tris(propan-2-yl)silyl]oxy}-1,2,3,4-tetrahydroquinolin-5-yl)propyl]urea S19



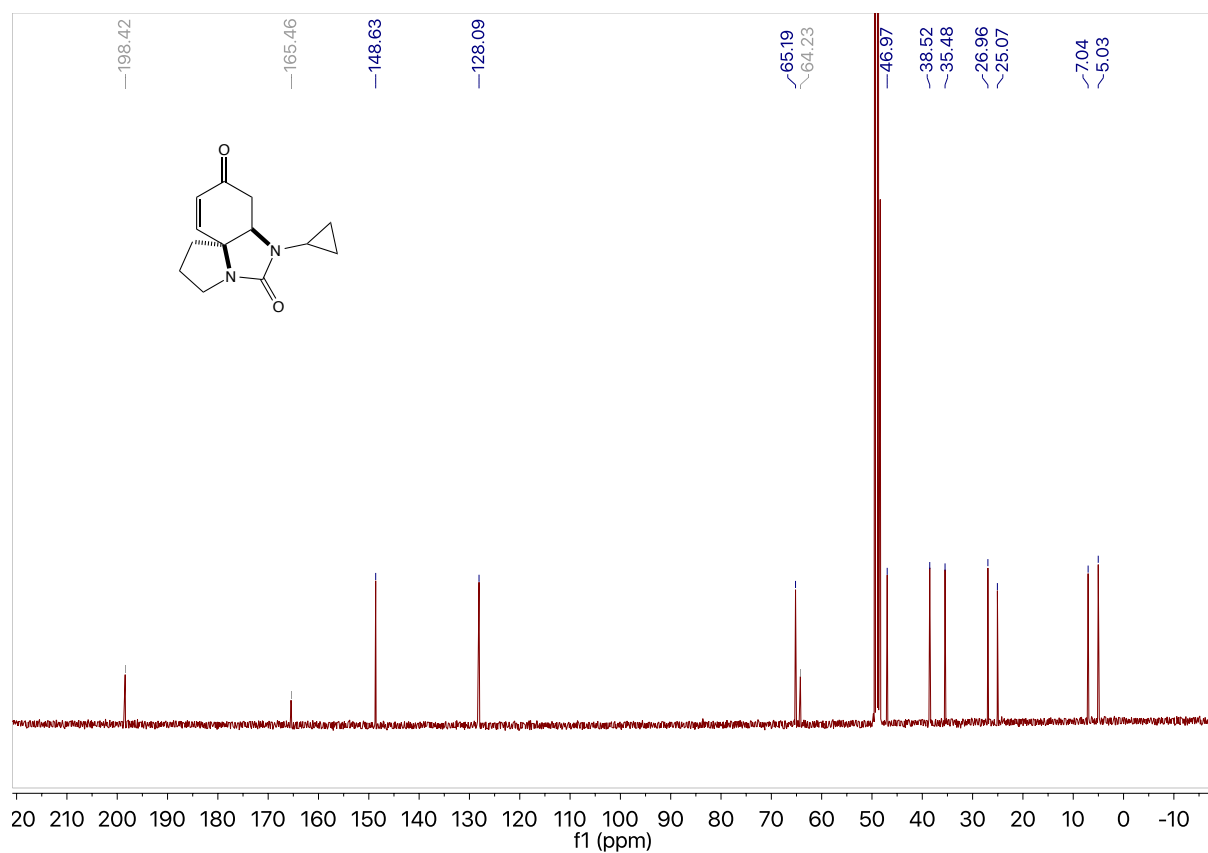
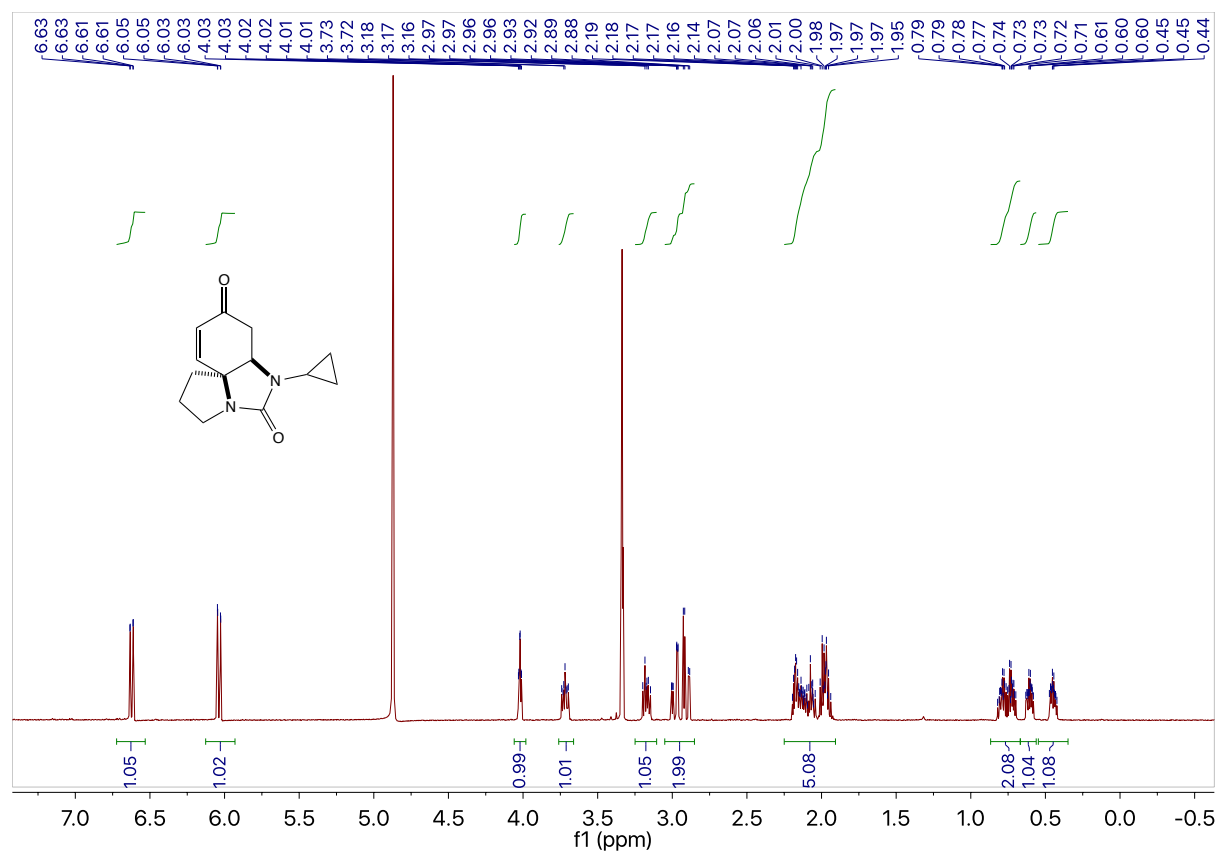
1-[3-(1-Acetyl-8-hydroxy-1,2,3,4-tetrahydroquinolin-5-yl)propyl]-3-cyclopropylurea 1s



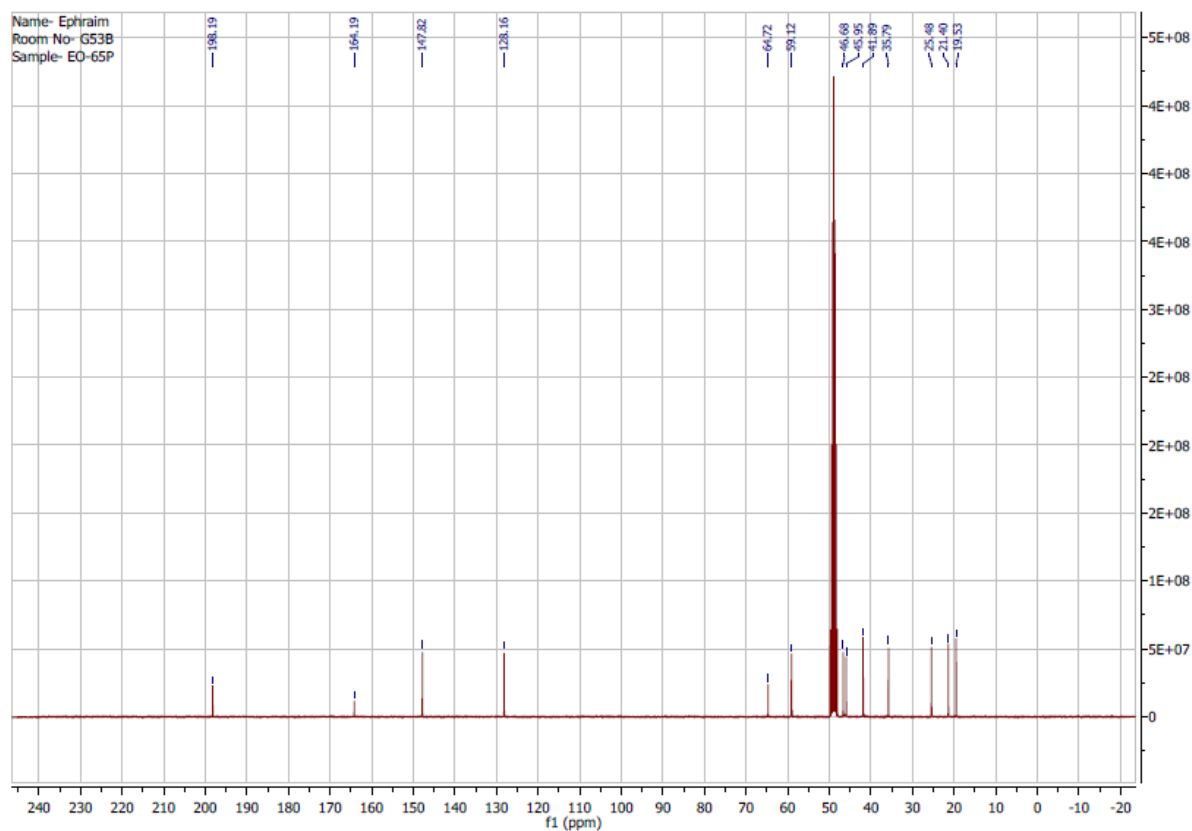
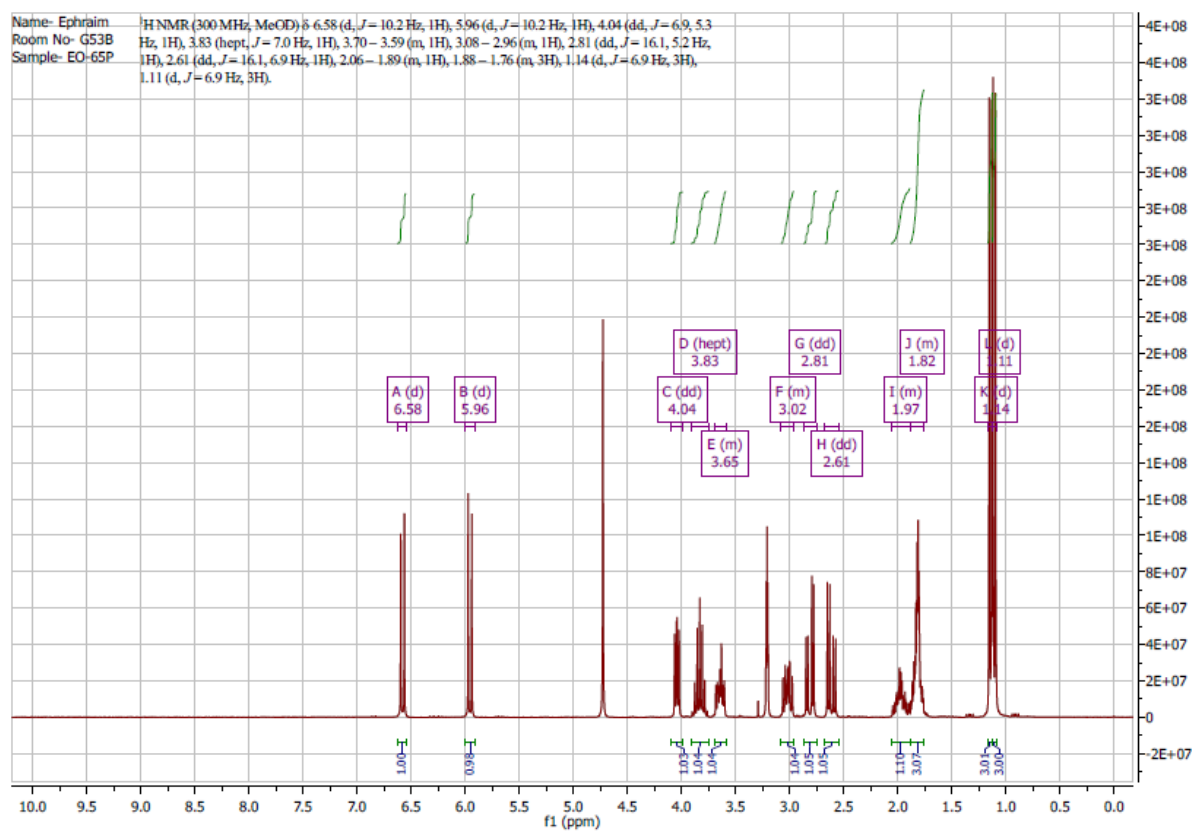
7-Benzyl-5,7-diaztricyclo[6.4.0.0^{1,5}]dodec-11-ene-6,10-dione 2a



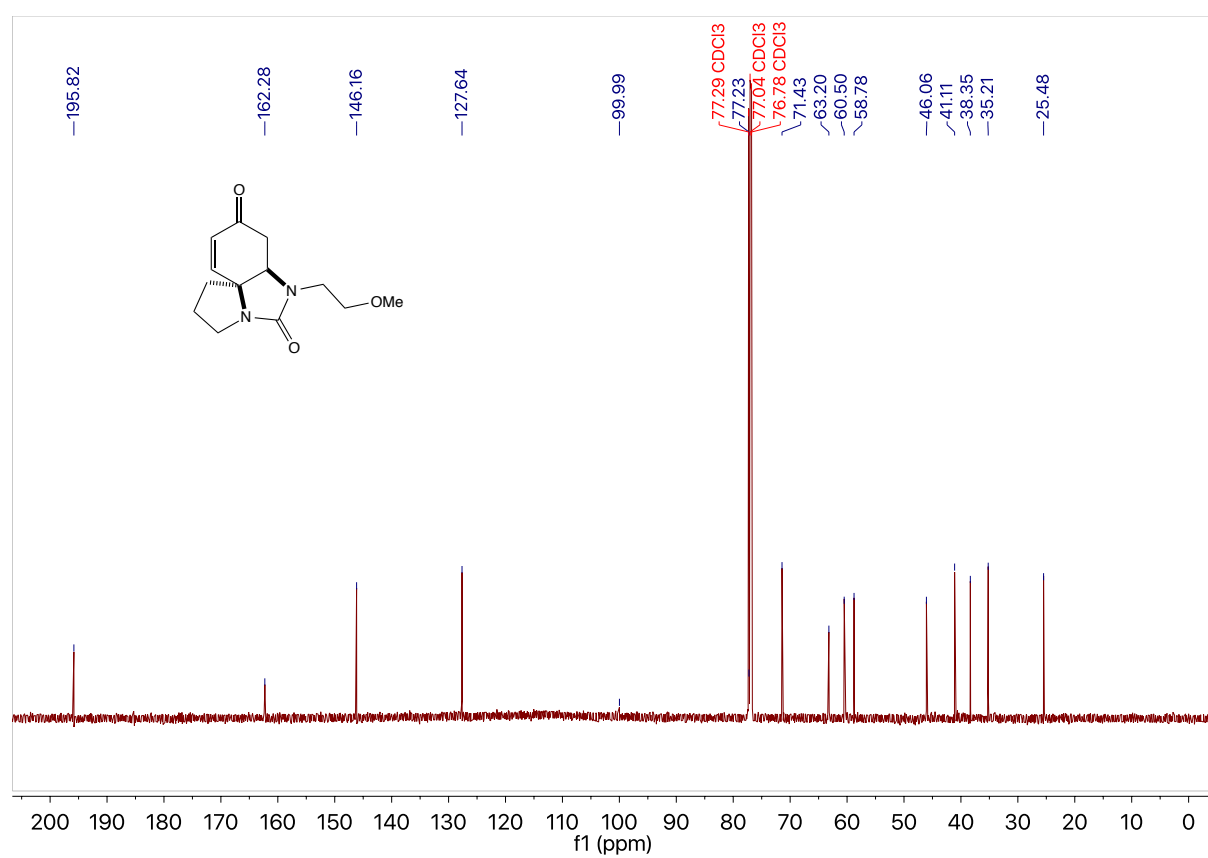
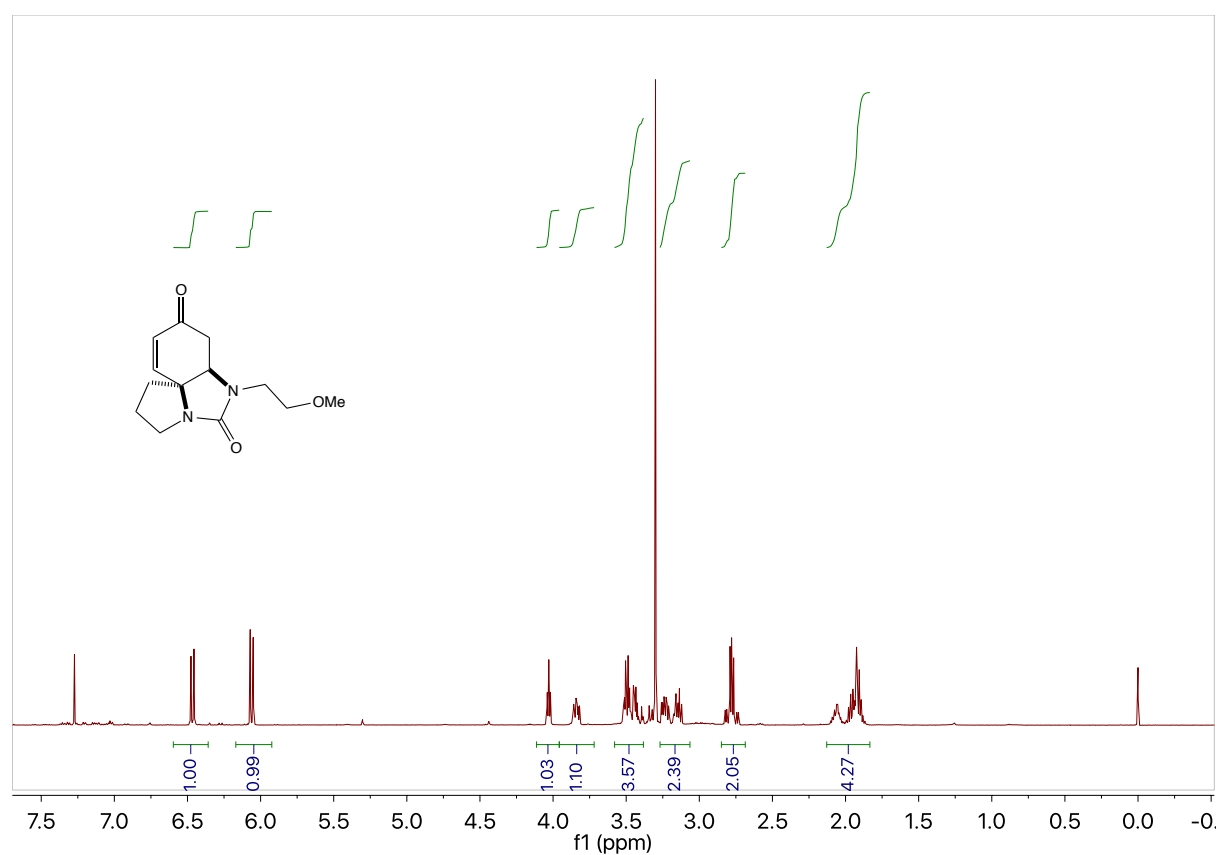
7-Cyclopropyl-5,7-diaztricyclo[6.4.0.0^{1,5}]dodec-11-ene-6,10-dione 2b



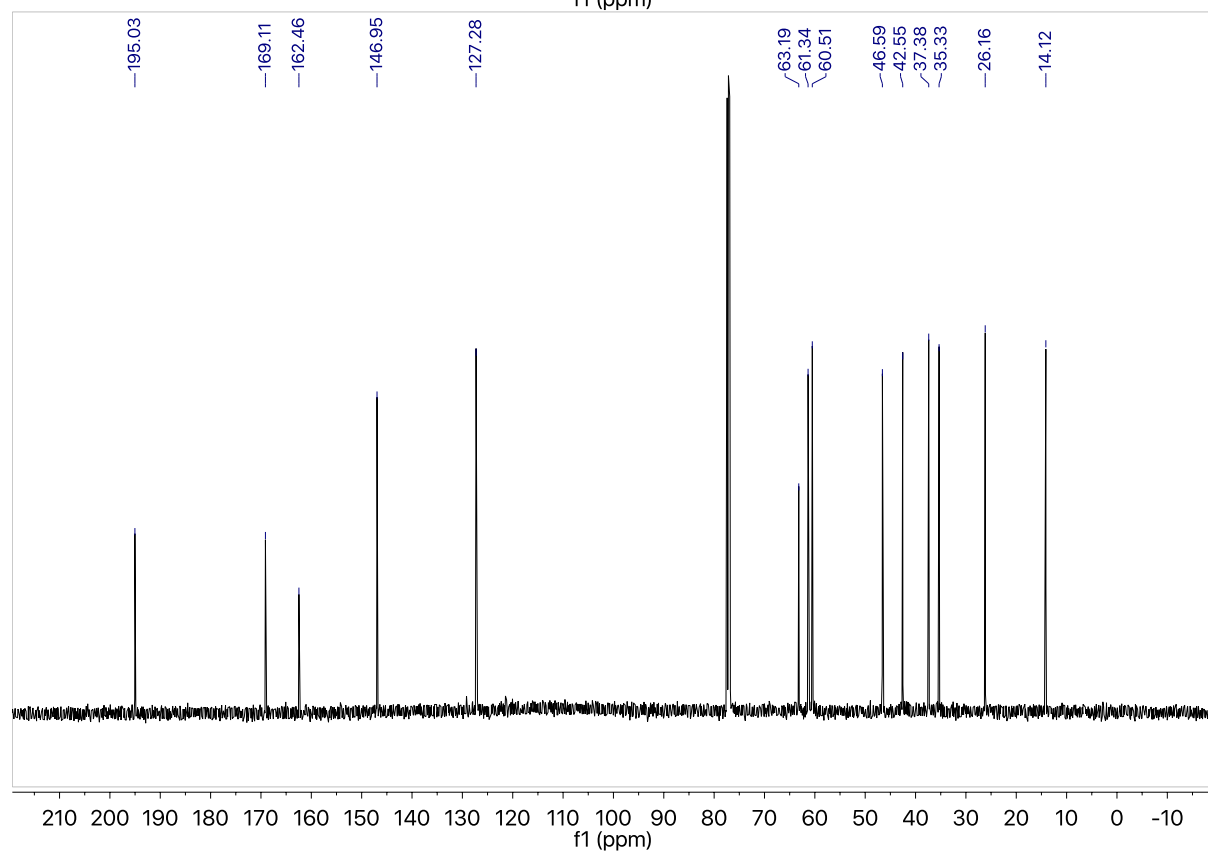
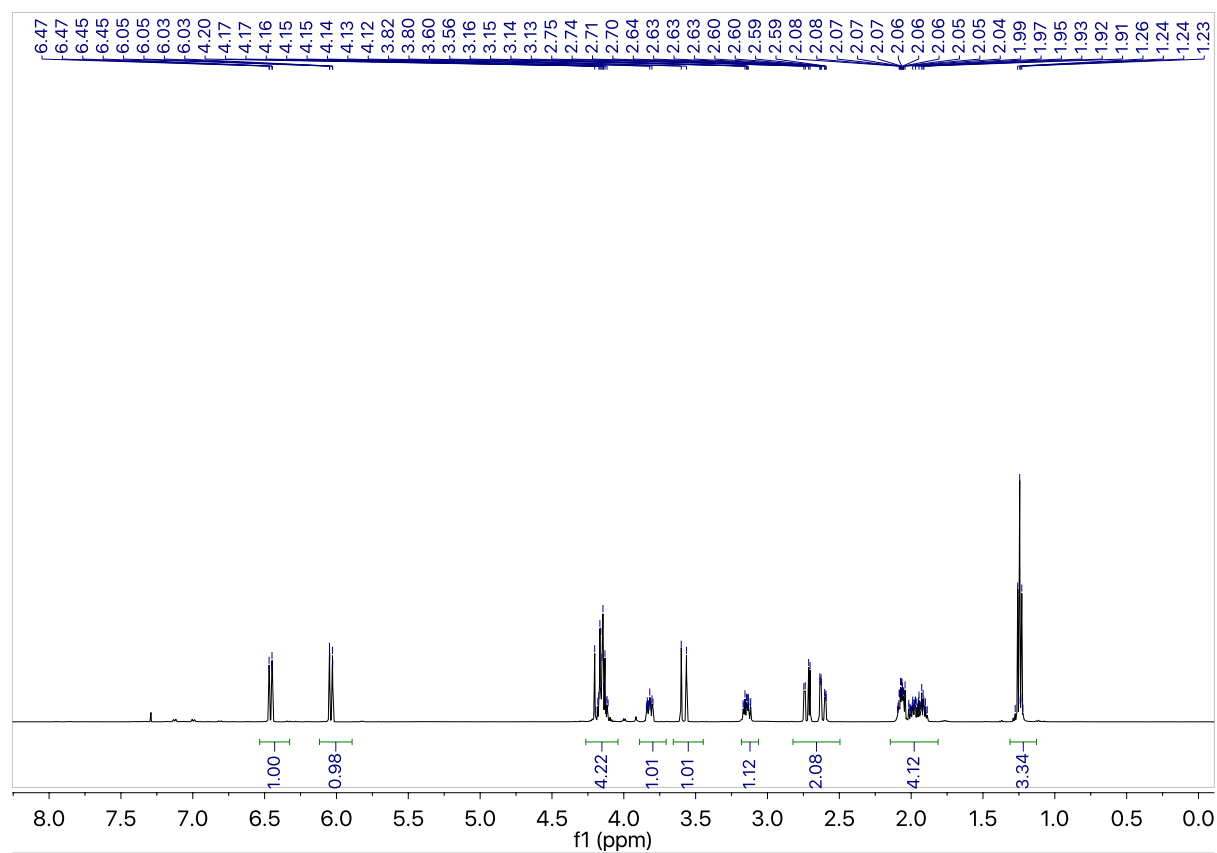
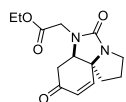
6-Isopropyl-2,3,6a,7-tetrahydro-1*H*,5*H*-benzo[*d*]pyrrolo[1,2-*c*]imidazole-5,8(6*H*)-dione 2c



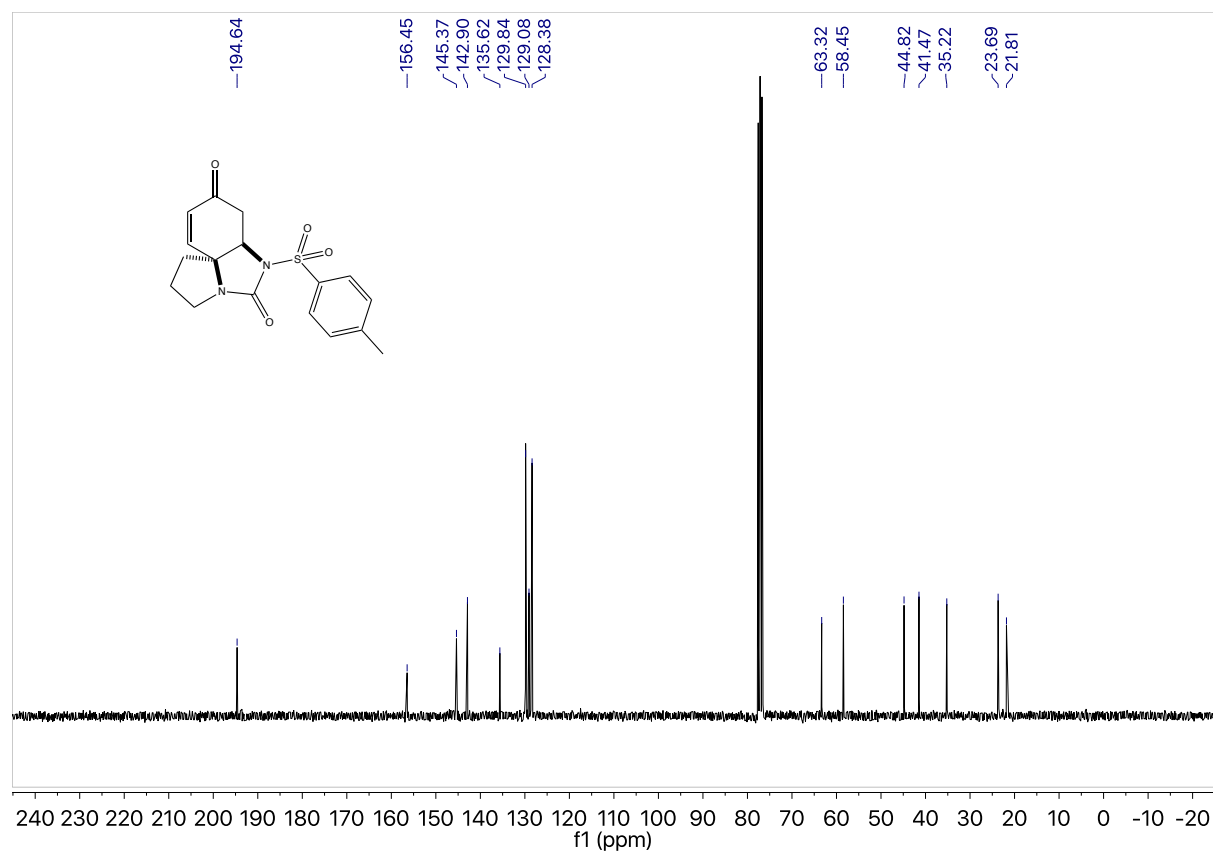
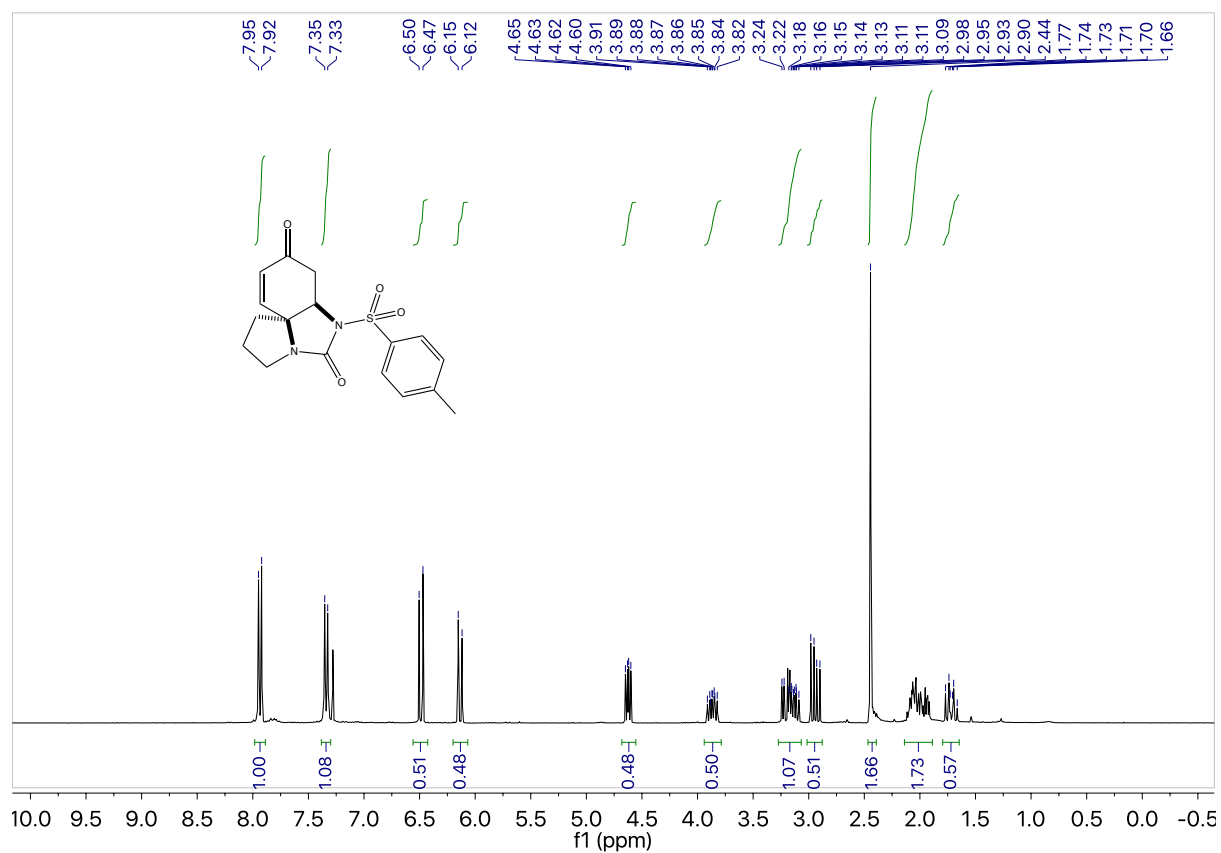
7-[2-Methoxyethyl]-5,7-diazatricyclo[6.4.0.0^{1,5}]dodecane-6,10-dione 2d



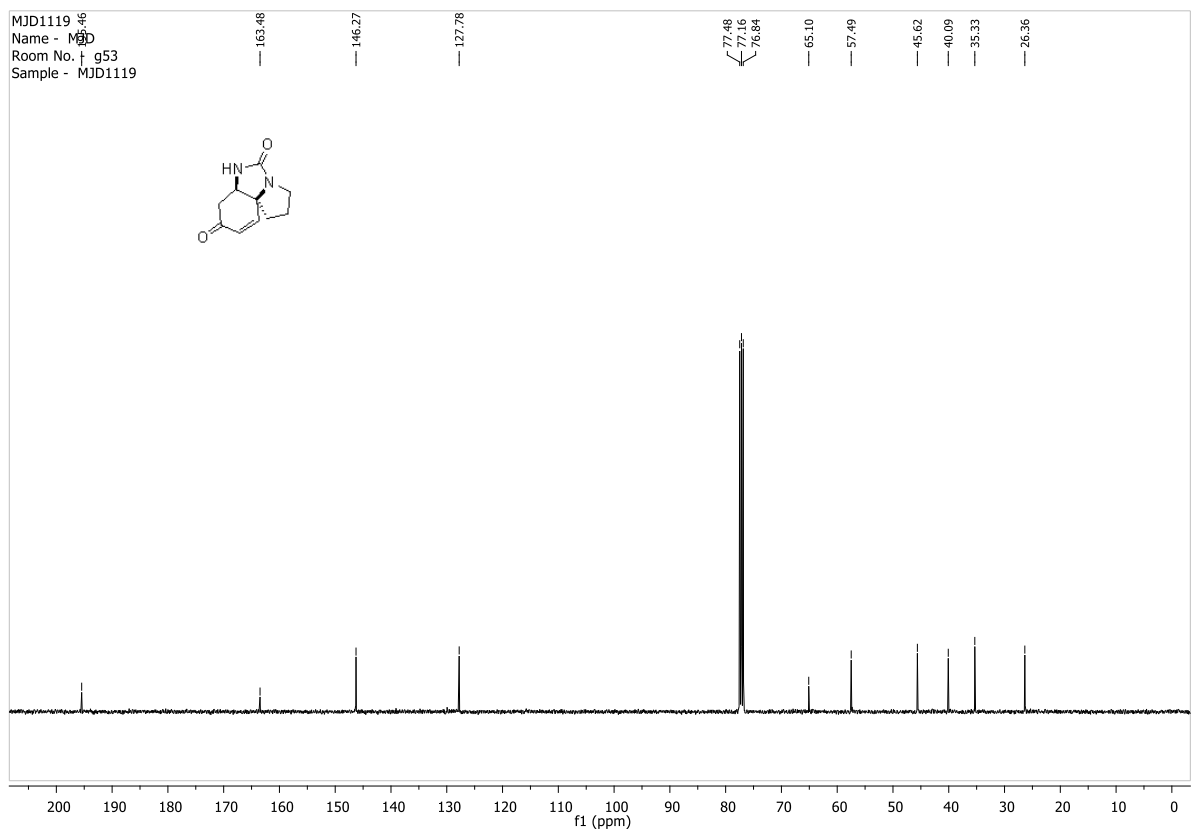
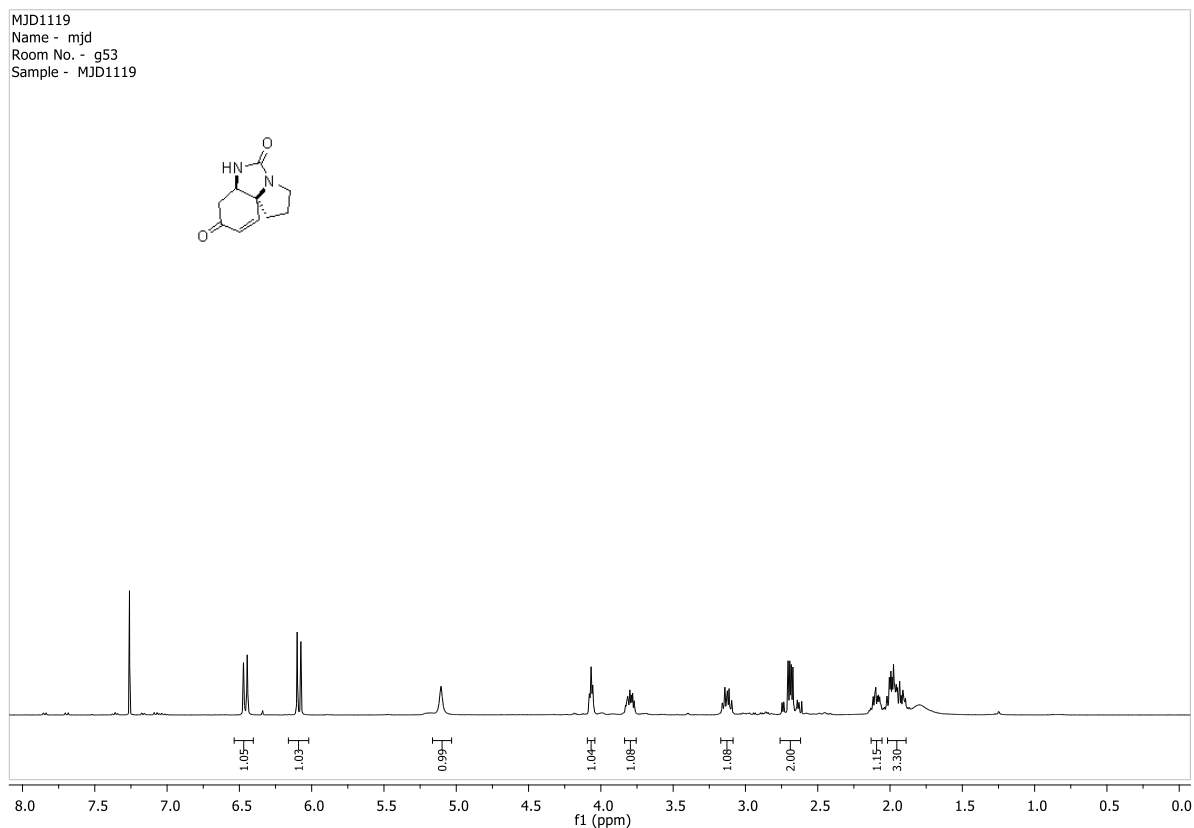
Ethyl 2-{6,10-dioxo-5,7-diazatricyclo[6.4.0.0^{1,5}]dodec-11-en-7-yl}acetate 2e



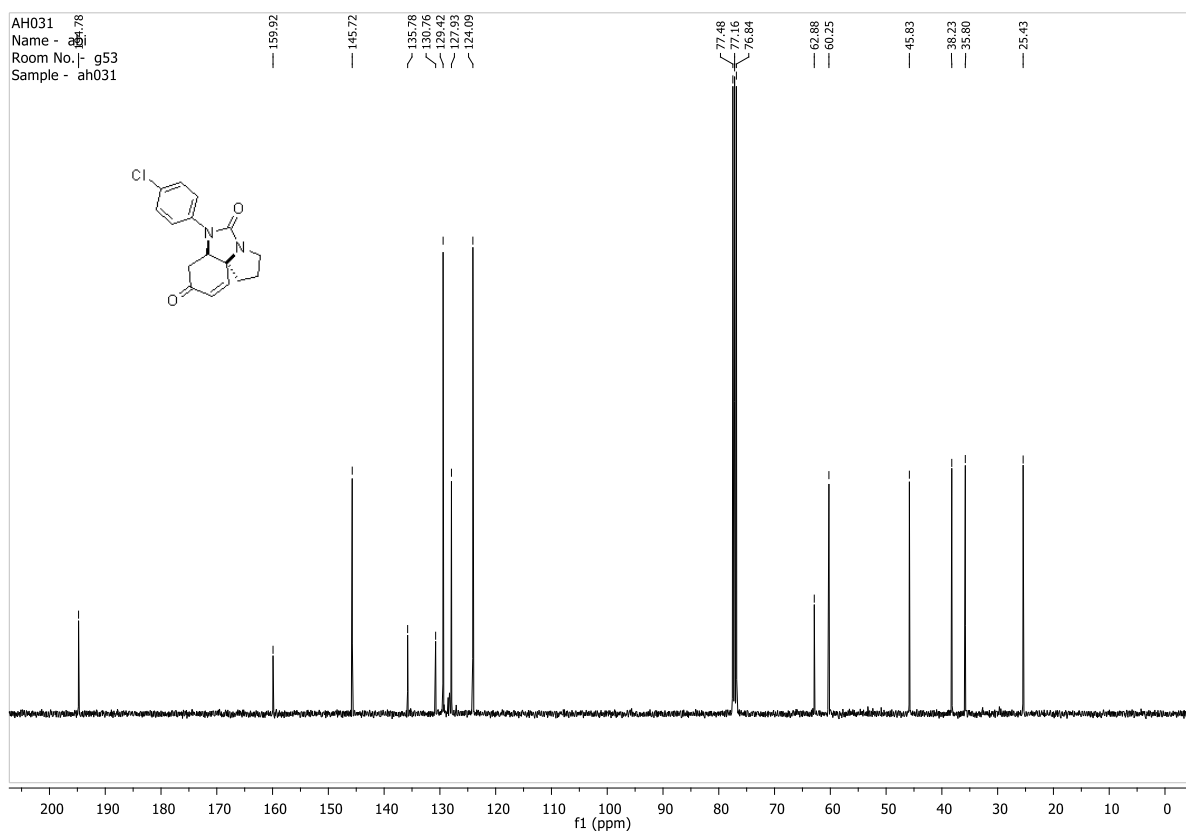
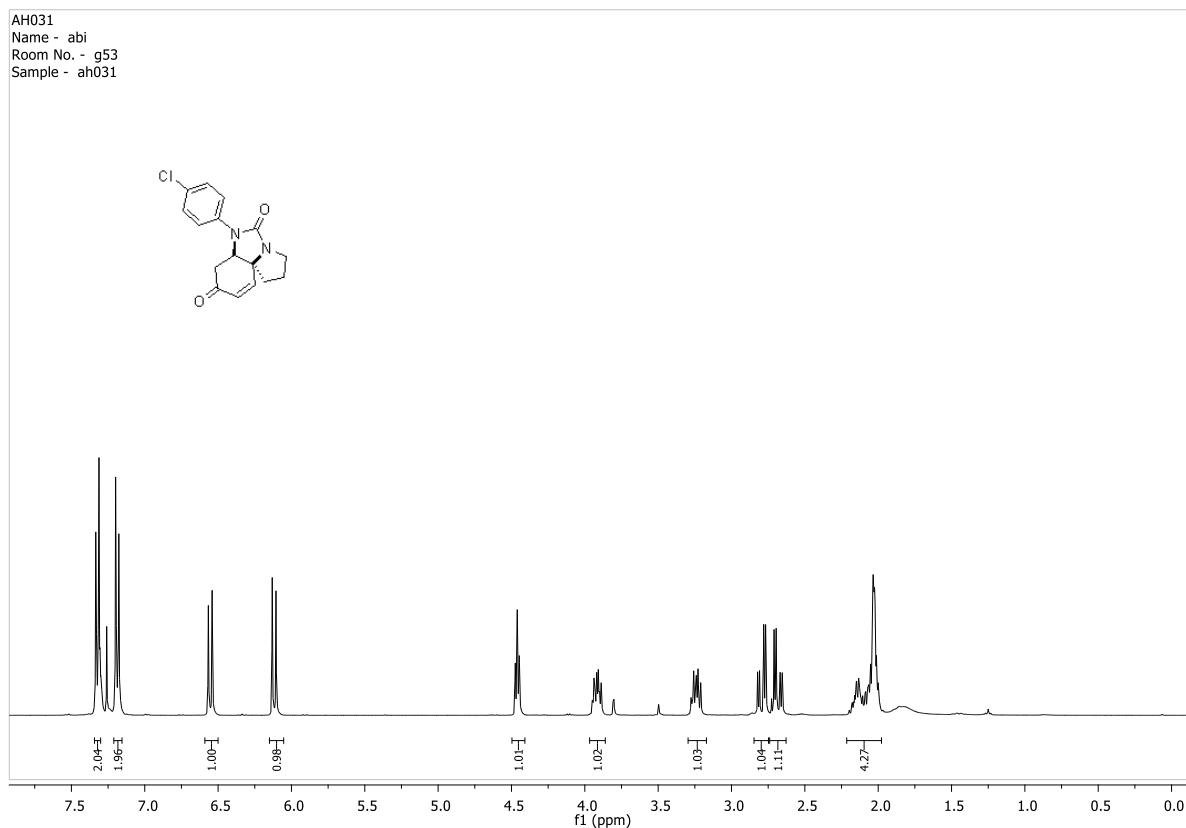
7-(4-Methylbenzenesulfonyl)-5,7-diazatricyclo[6.4.0.0^{1,5}]dodec-11-ene-6,10-dione 2f



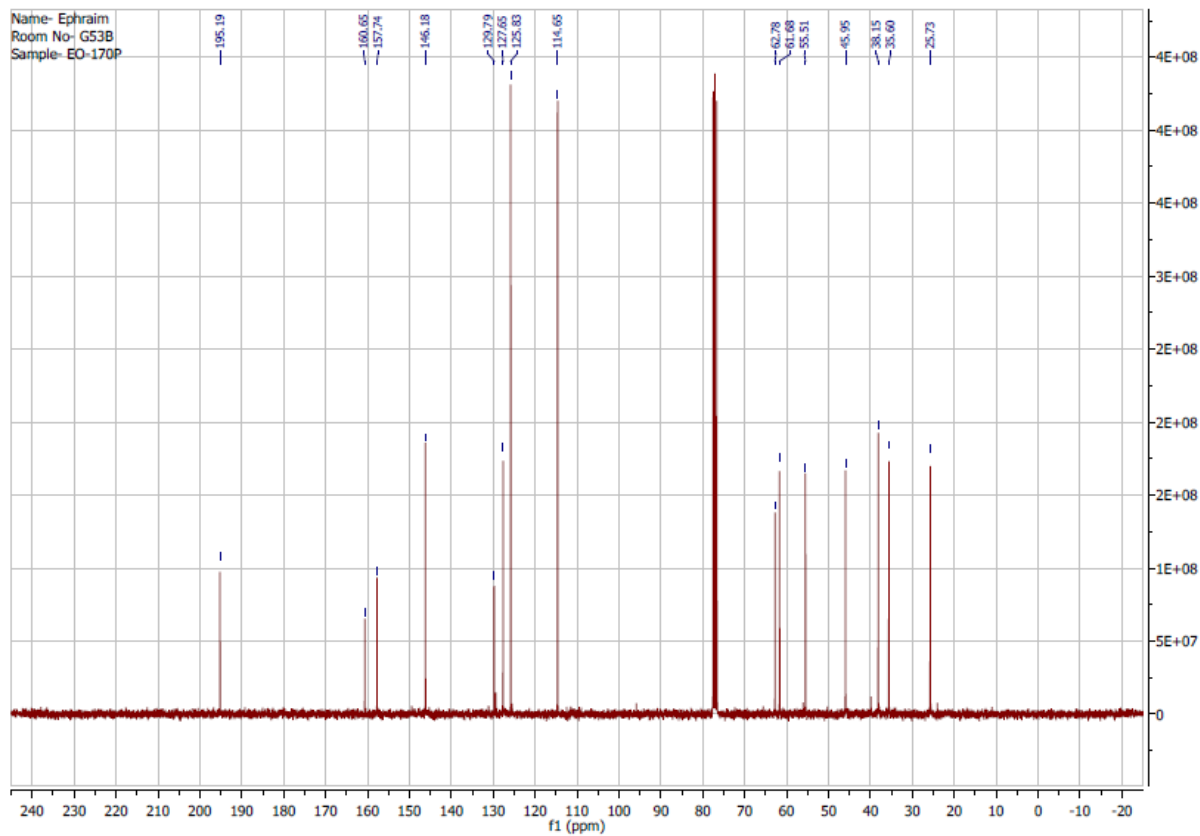
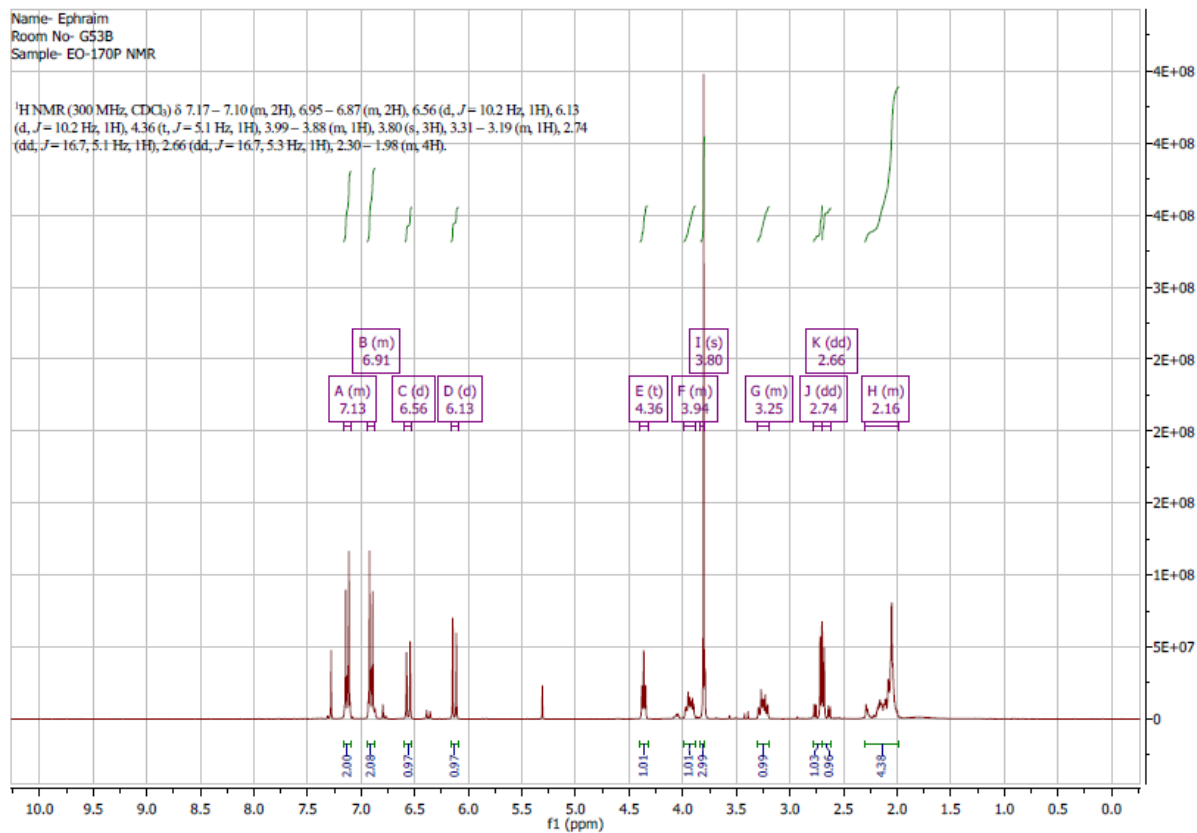
5,7-Diazatricyclo[6.4.0.0^{1,5}]dodec-11-ene-6,10-dione 2g



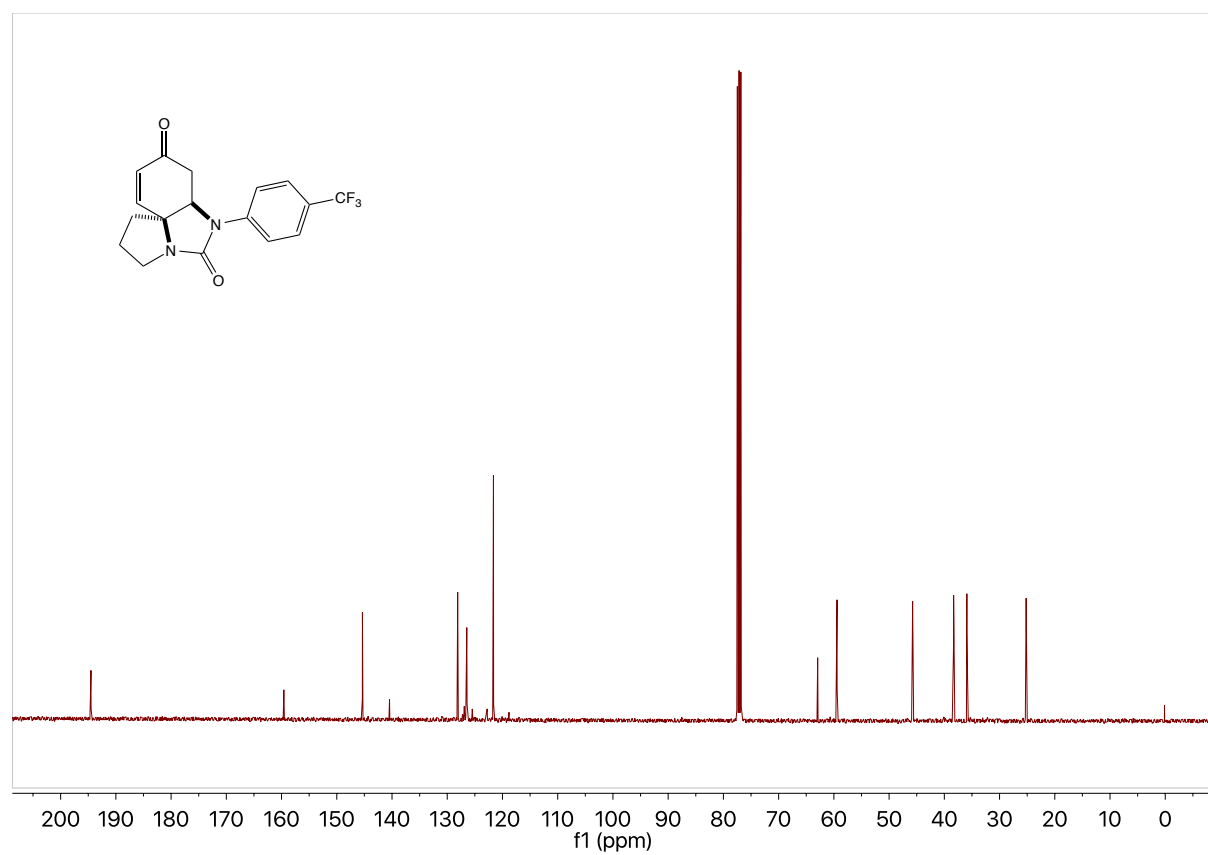
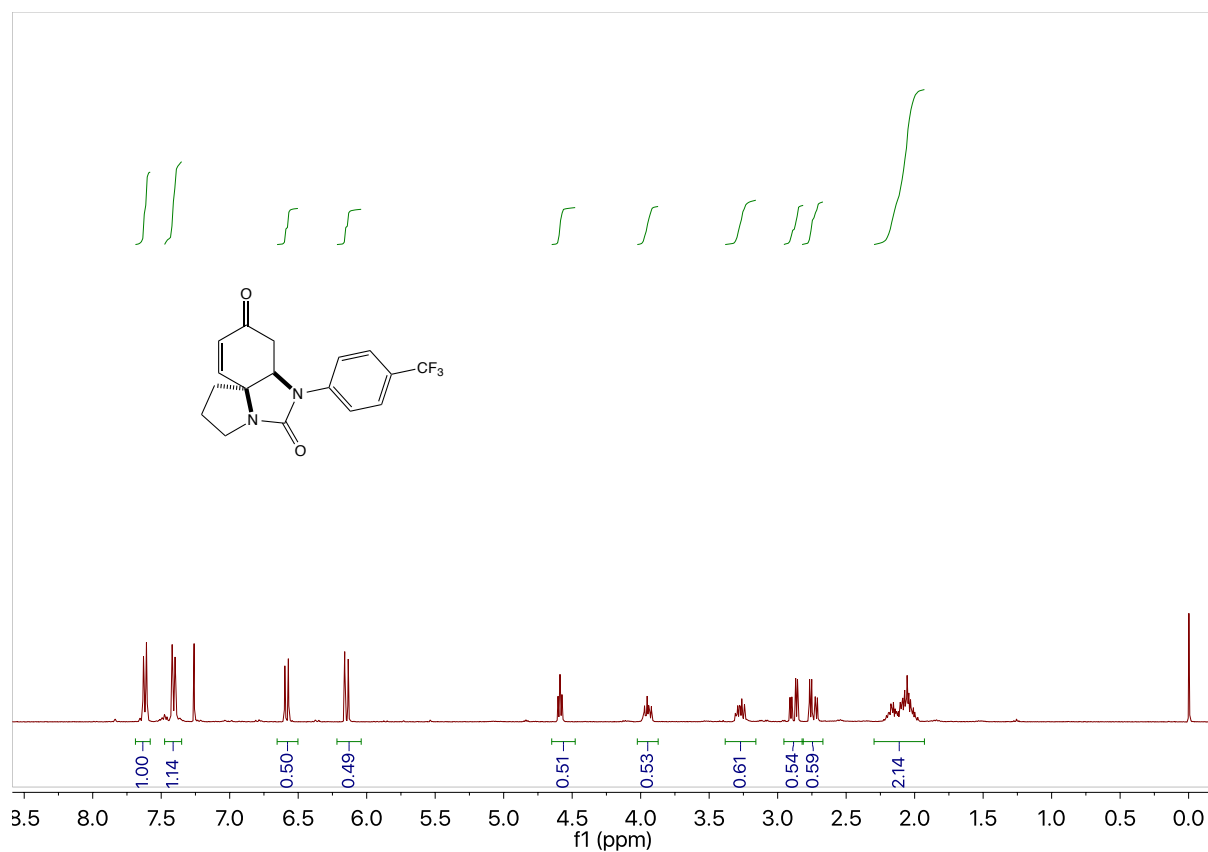
7-(4-Chlorophenyl)-5,7-diazatricyclo[6.4.0.0^{1,5}]dodec-11-ene-6,10-dione 2h



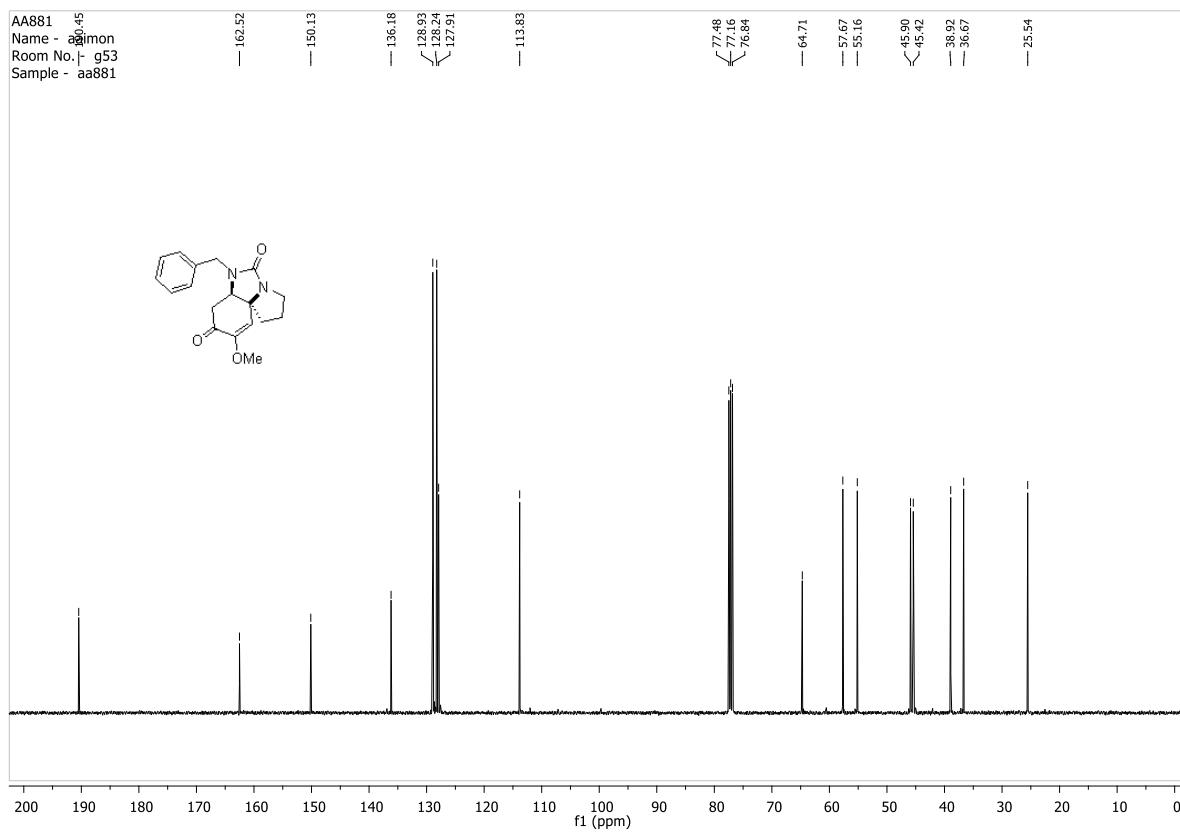
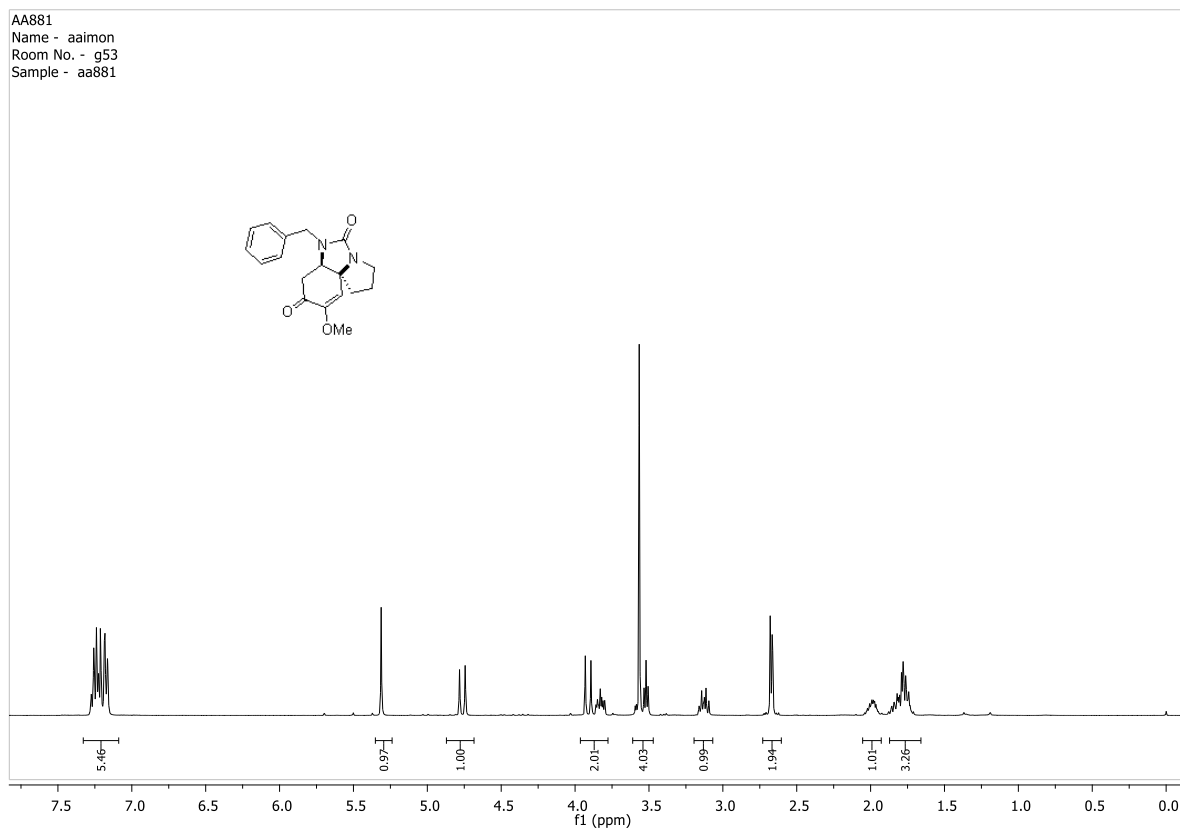
6-(4-Methoxyphenyl)-2,3,6a,7-tetrahydro-1H,5H-benzo[d]pyrrolo[1,2-c]imidazole-5,8(6H)-dione 2i



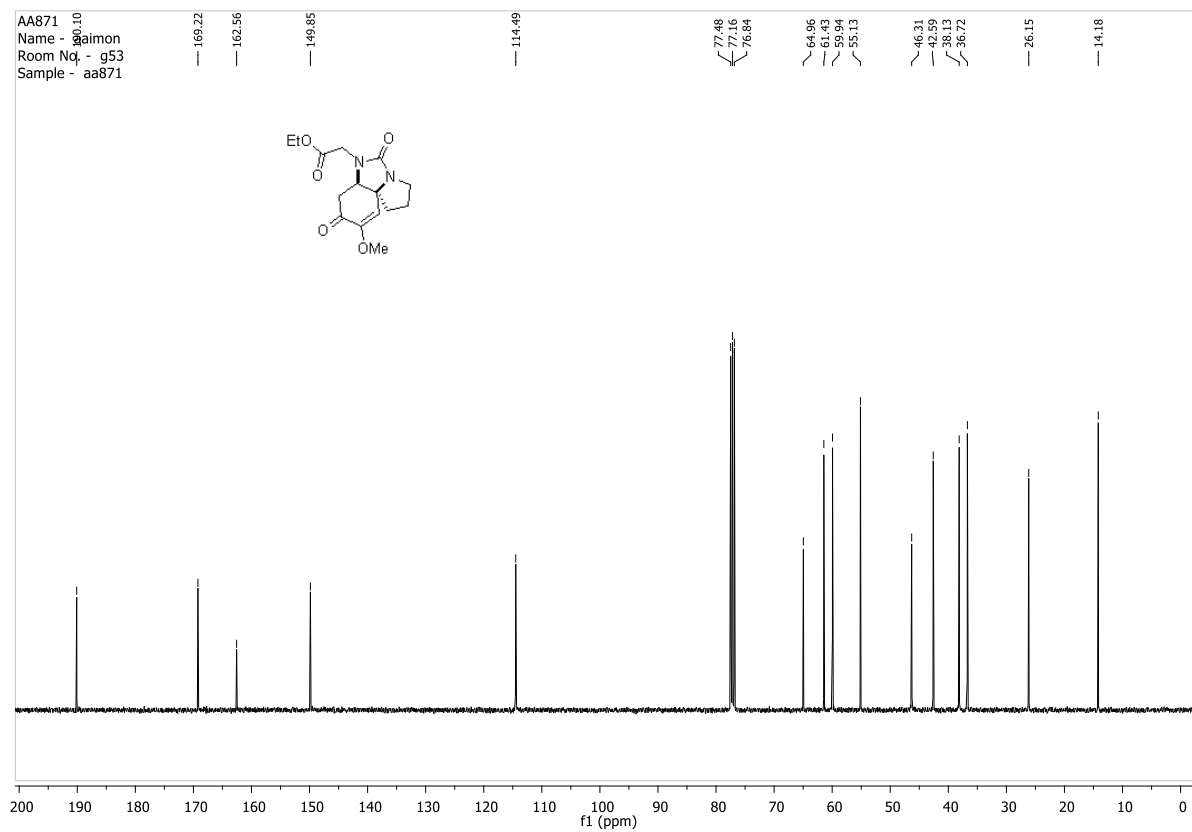
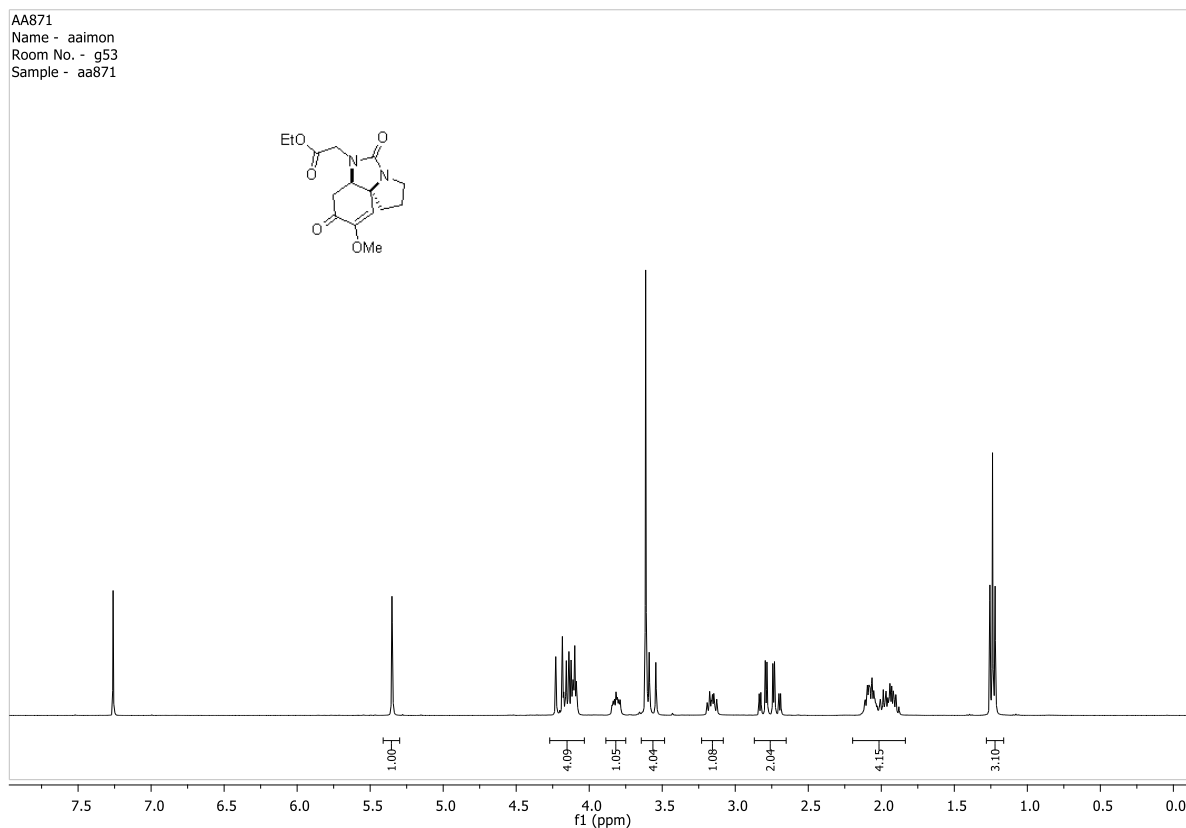
7-[4-(Trifluoromethyl)phenyl]-5,7-diaztricyclo[6.4.0.0^{1,5}]dodec-11-ene-6,10-dione 2J =



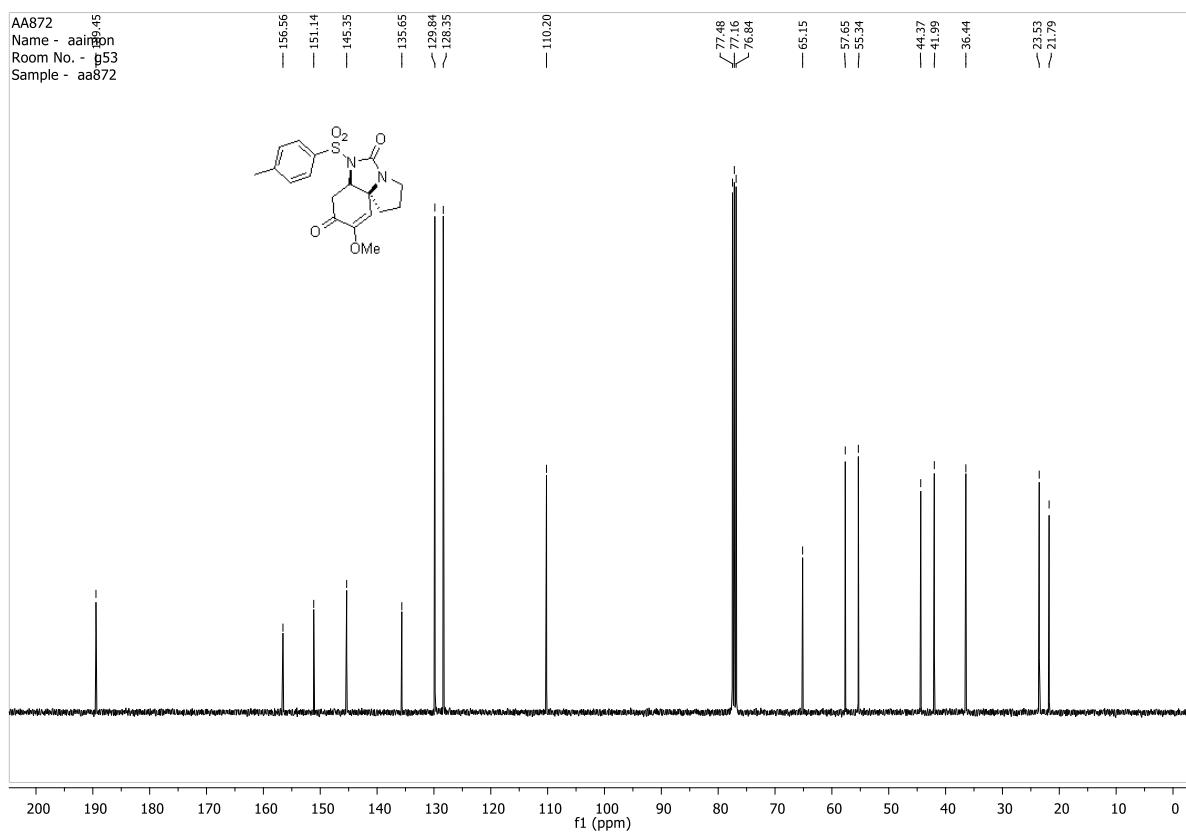
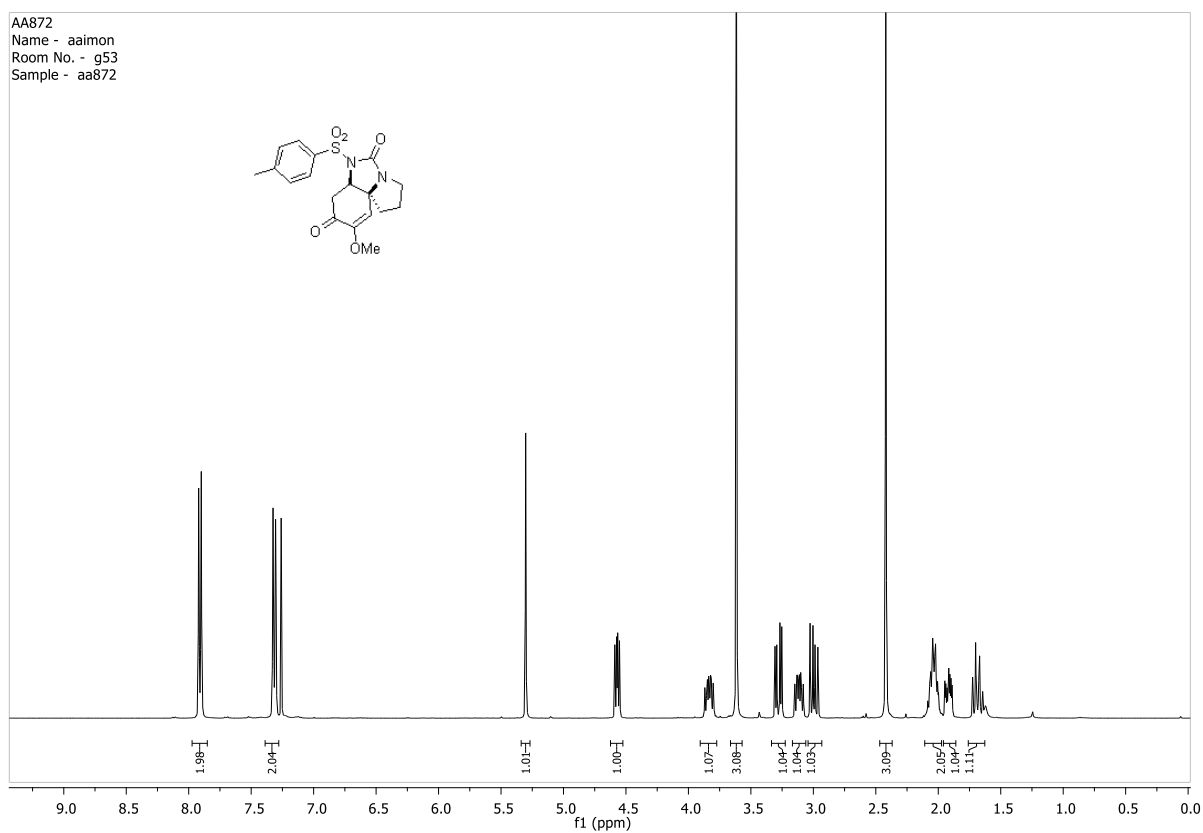
7-Benzyl-11-methoxy-5,7-diazatricyclo[6.4.0.0^{1,5}]dodec-11-ene-6,10-dione 2k



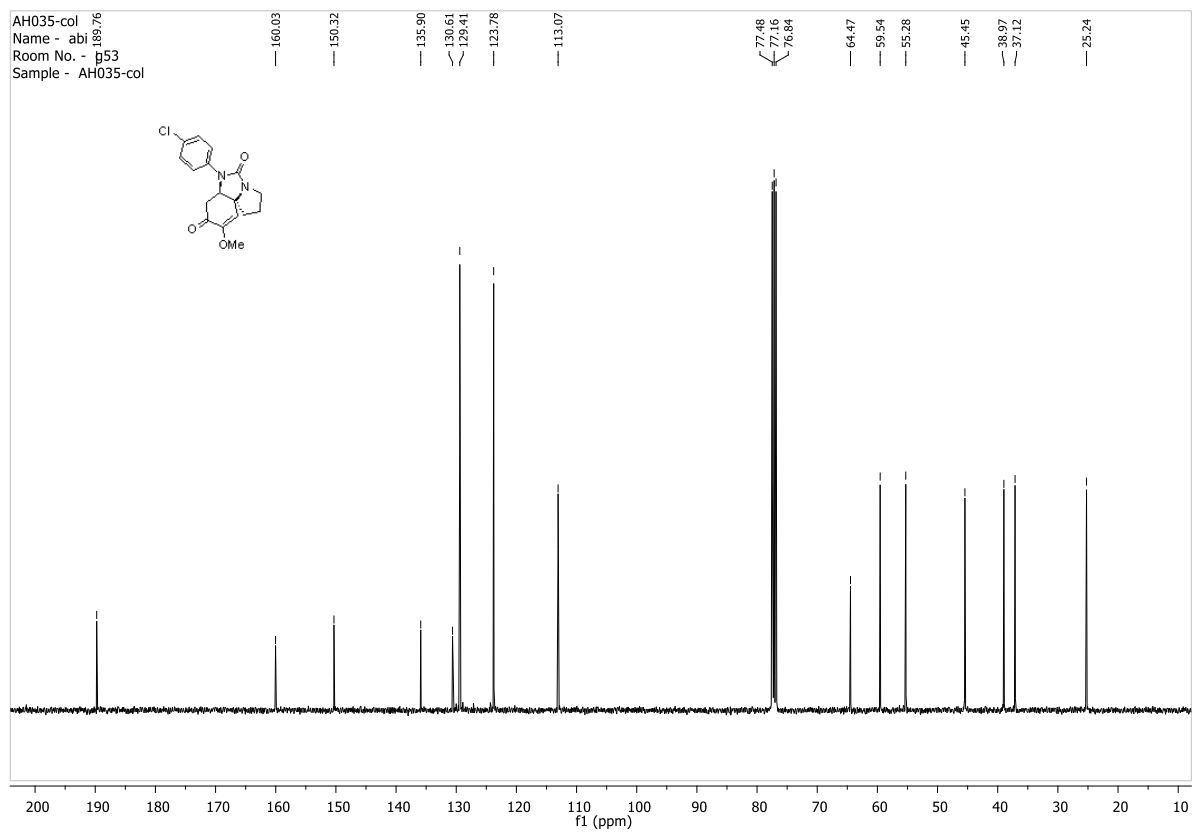
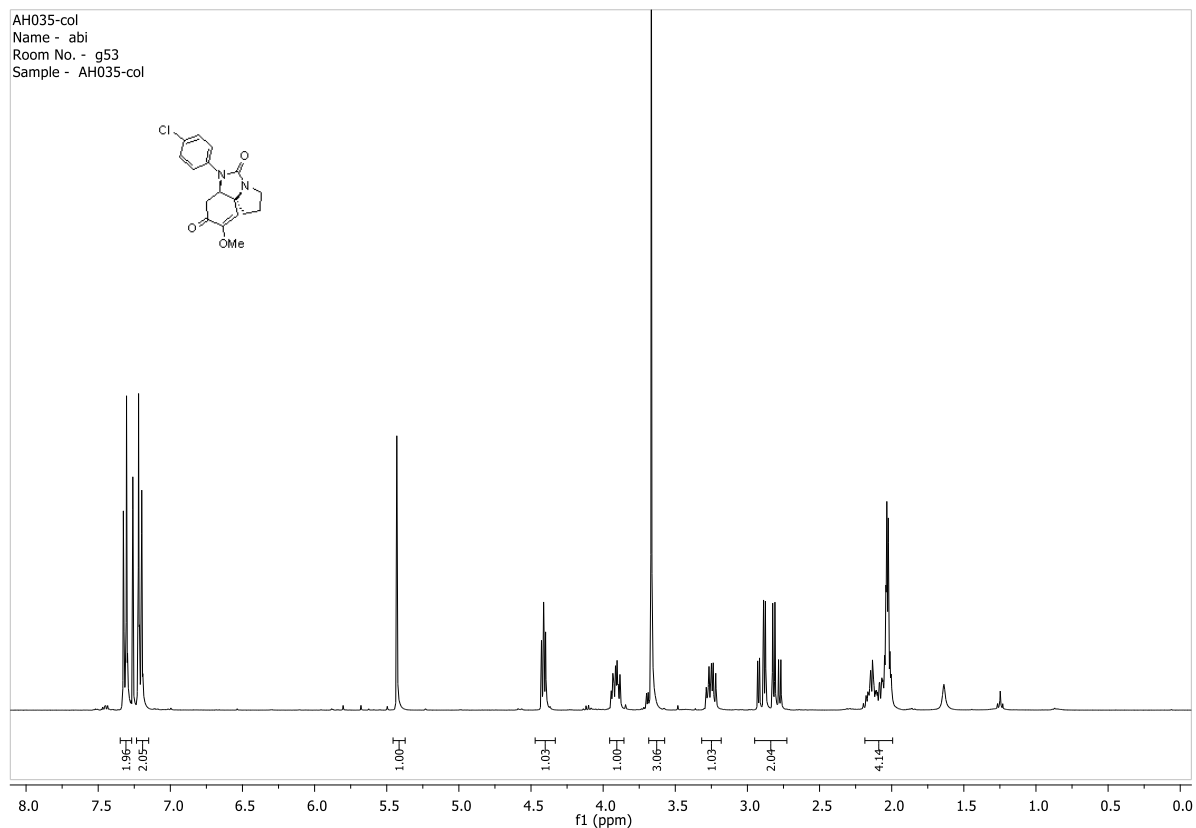
Ethyl 2-{11-methoxy-6,10-dioxo-5,7-diazatricyclo[6.4.0.0^{1,5}]dodec-11-en-7-yl}acetate 2I



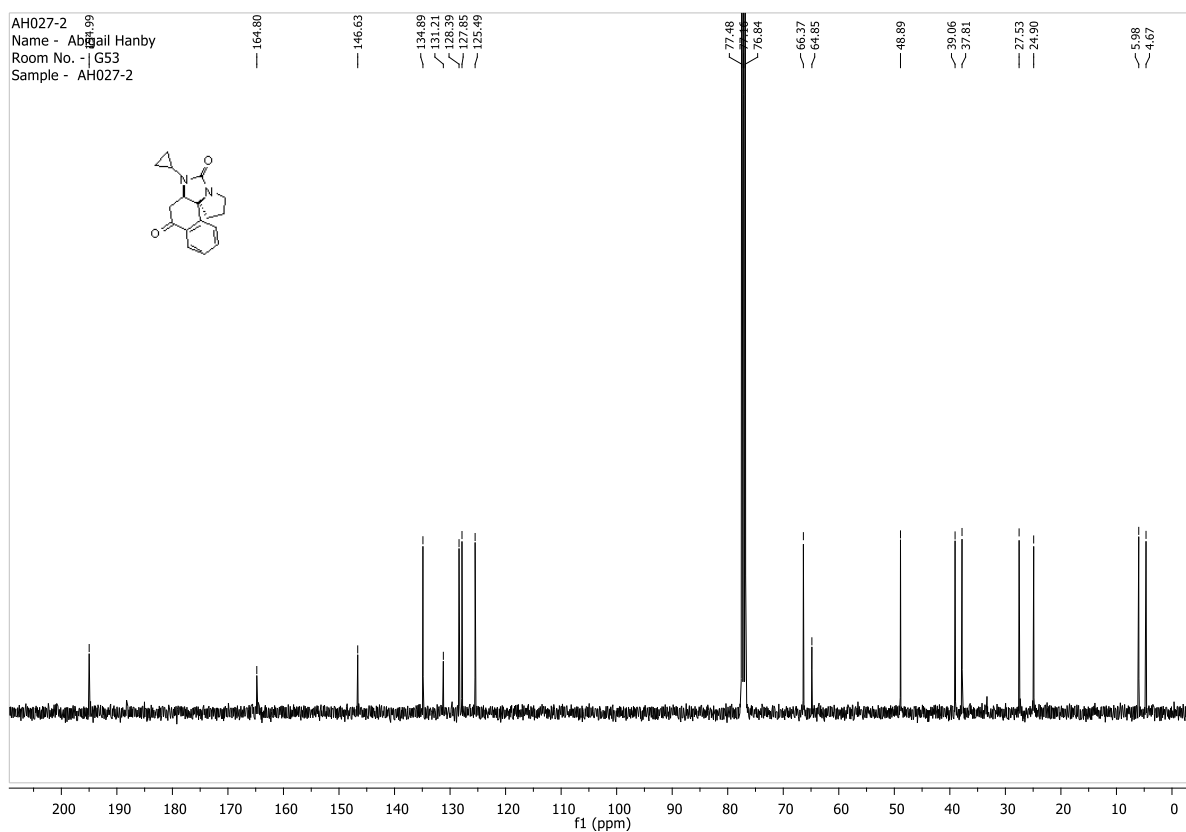
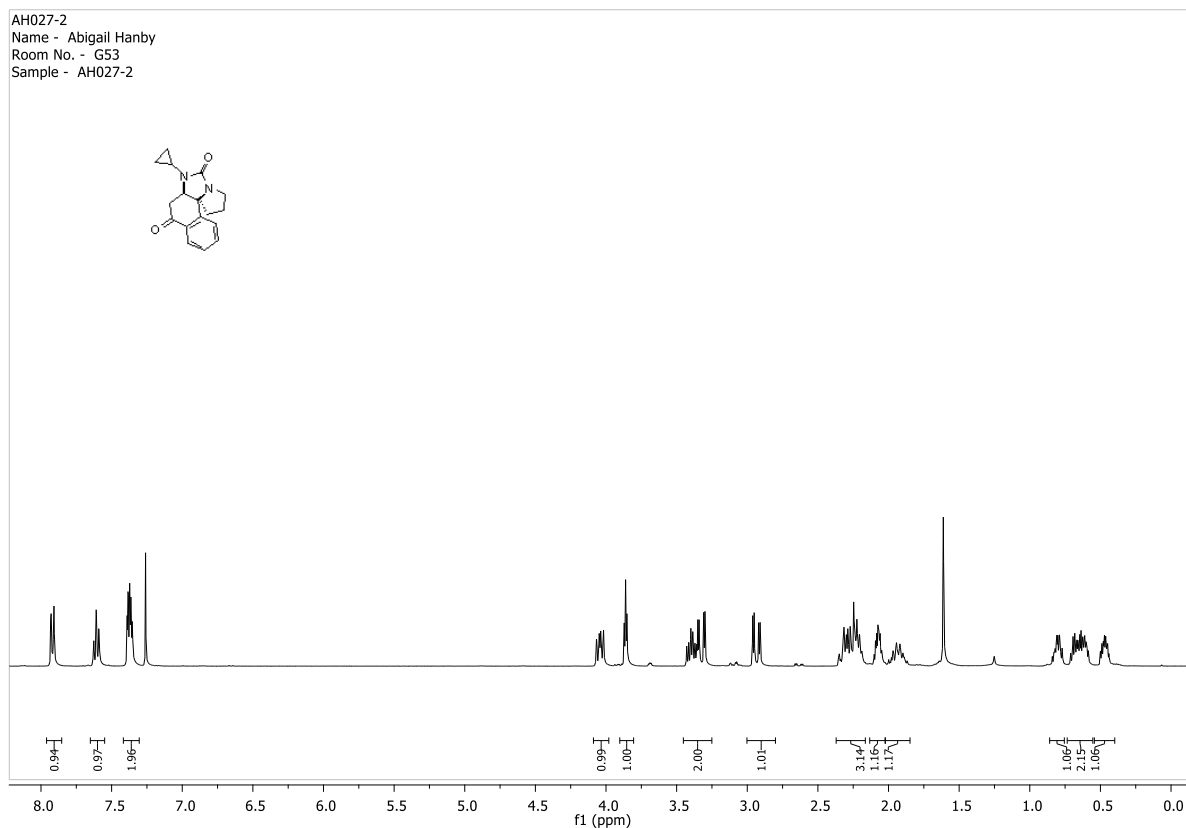
11-Methoxy-7-(4-methylbenzenesulfonyl)-5,7-diazatricyclo[6.4.0.0^{1,5}]dodec-11-ene-6,10-dione 2m



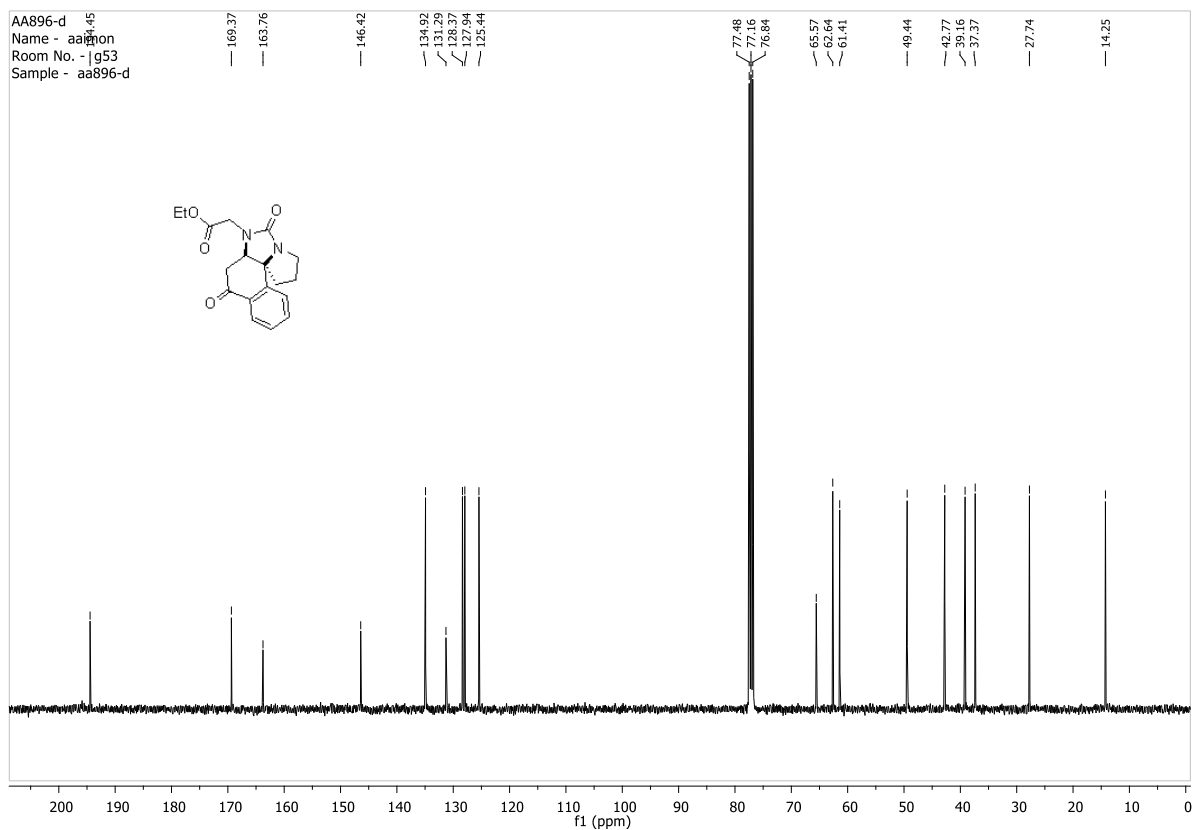
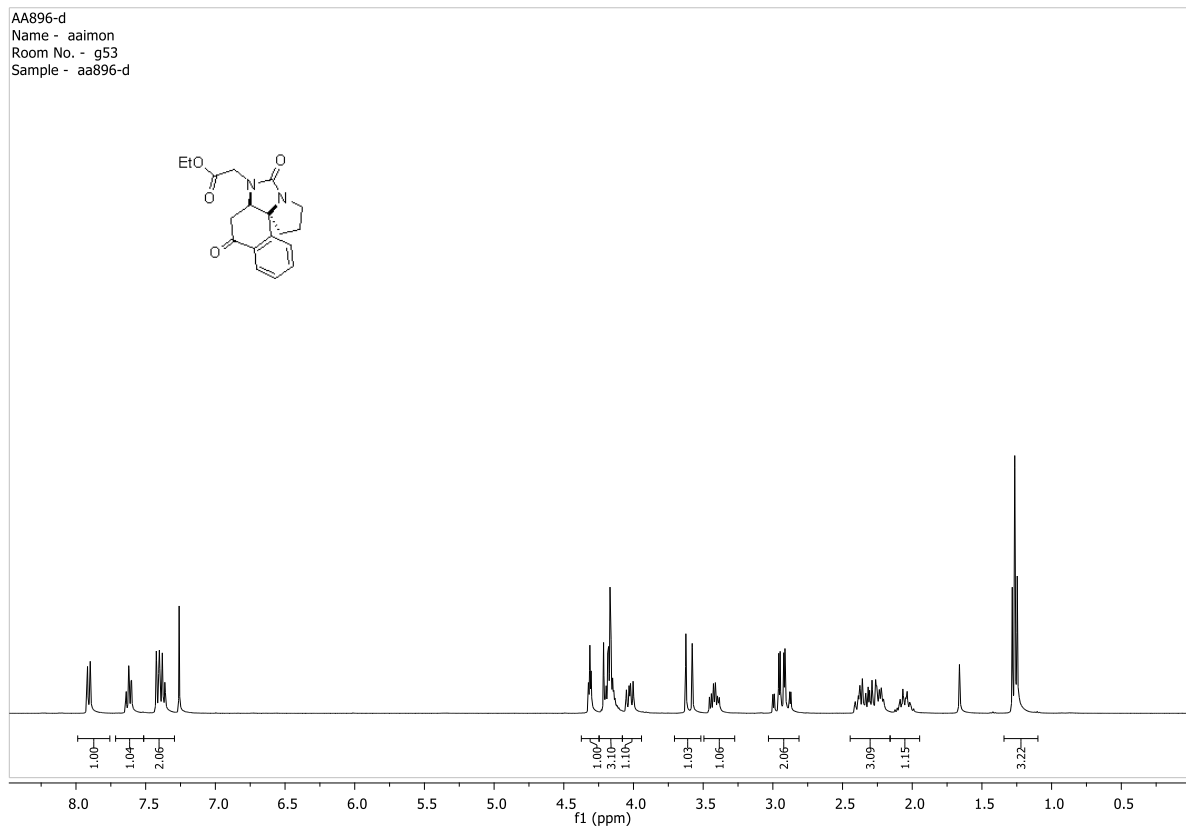
7-(4-Chlorophenyl)-11-methoxy-5,7-diazatricyclo[6.4.0.0^{1,5}]dodec-11-ene-6,10-dione 2n



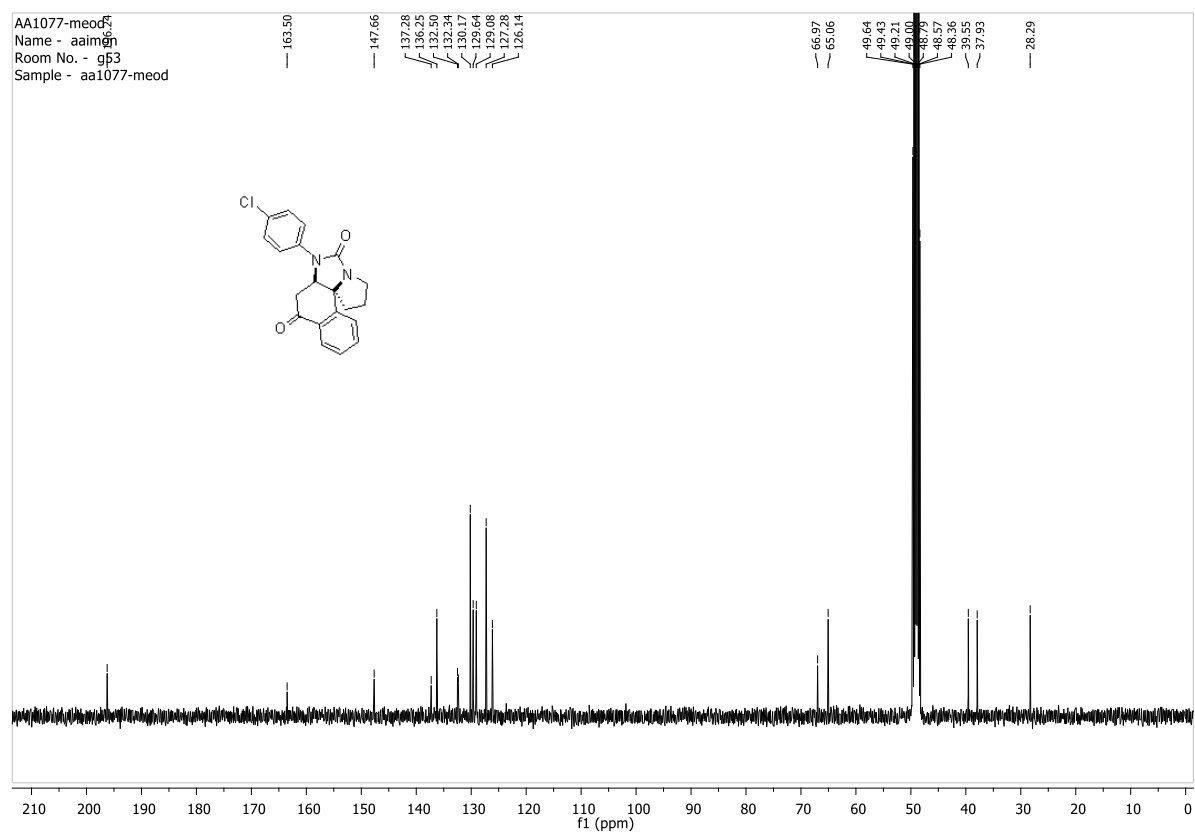
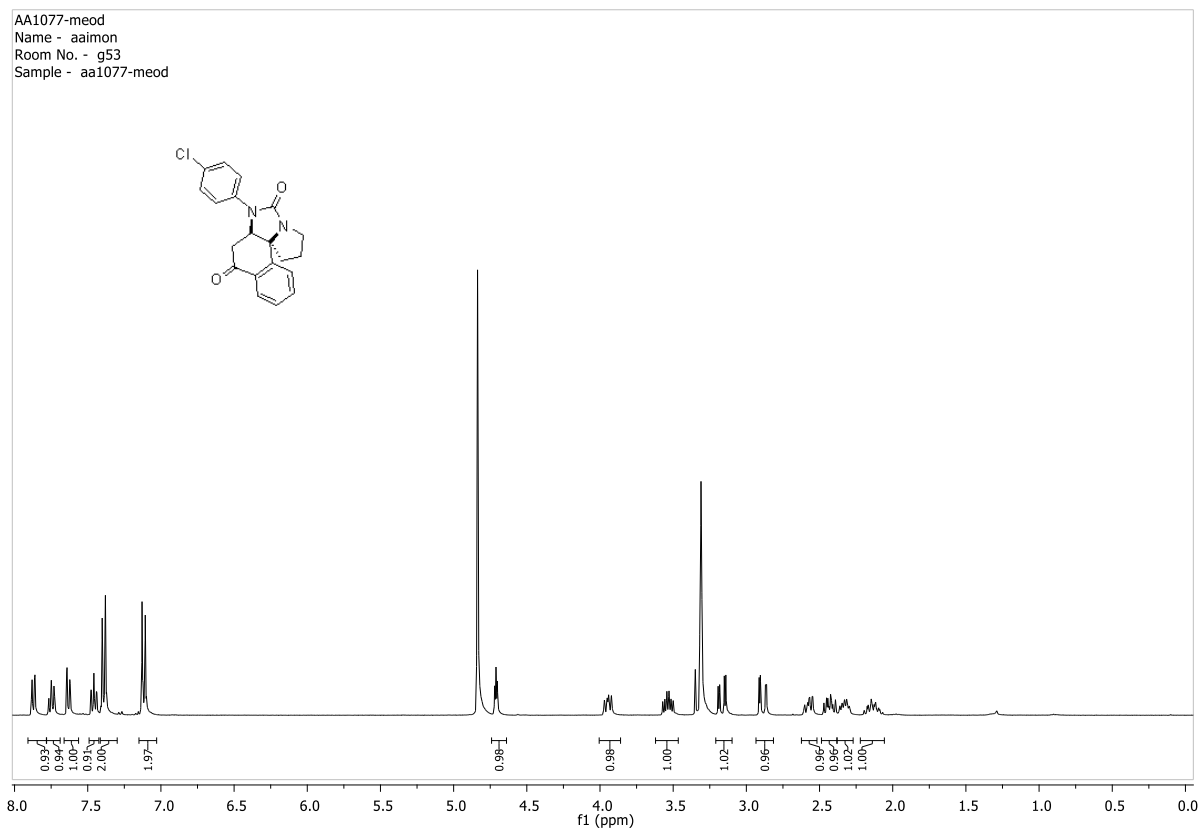
11-Cyclopropyl-11,13-diazatetracyclo[8.6.0.0^{1,13}.0^{2,7}]hexadeca-2(7),3,5-triene-8,12-dione
2o



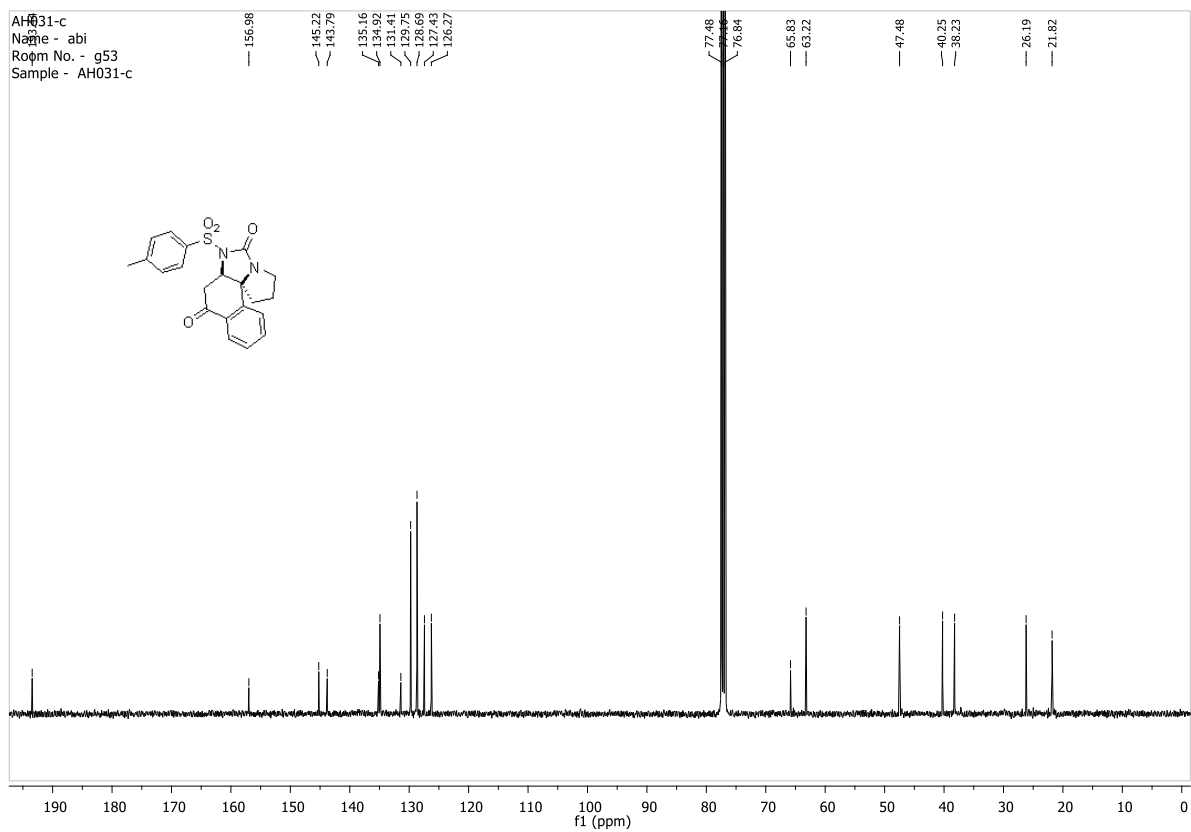
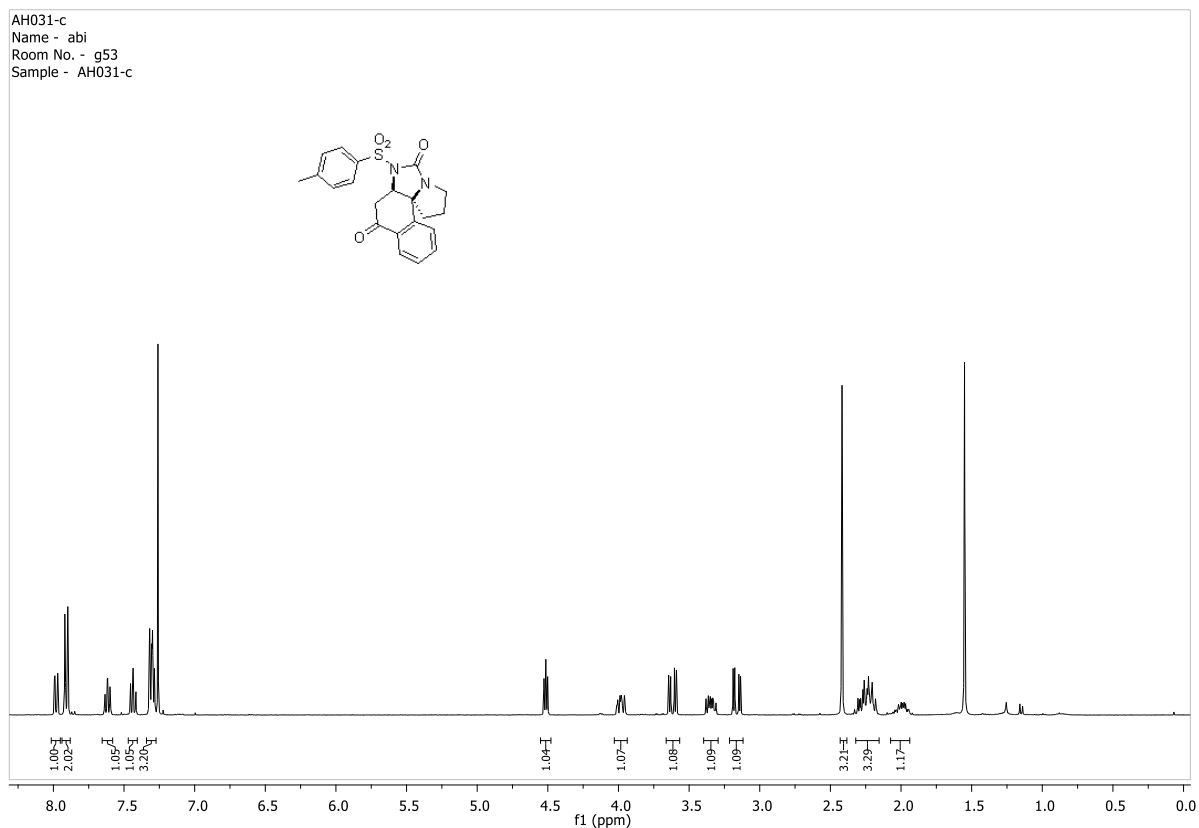
Ethyl 2-{8,12-dioxo-11,13-diazatetracyclo[8.6.0.0^{1,13}.0^{2,7}]hexadeca-2(7),3,5-trien-11-yl}acetate 2p



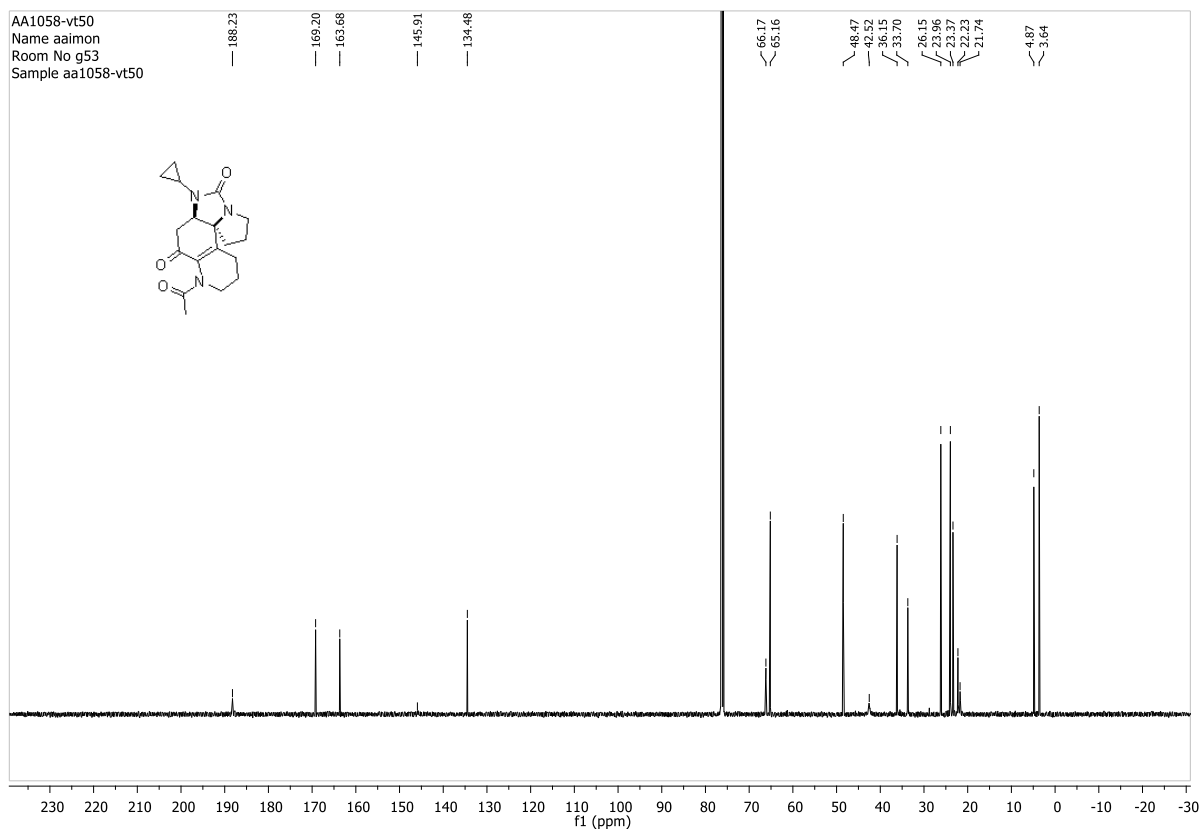
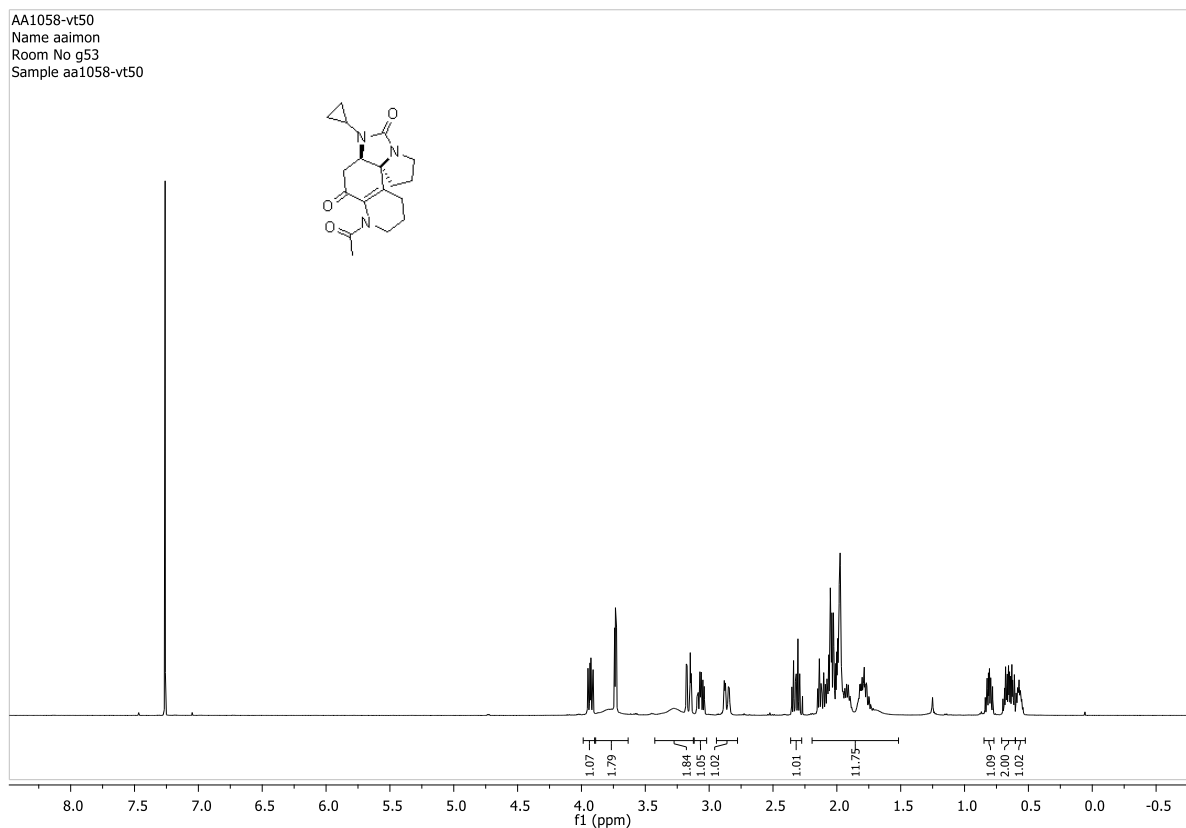
11-(4-Chlorophenyl)-11,13-diazatetracyclo[8.6.0.0^{1,13}.0^{2,7}]hexadeca-2(7),3,5-triene-8,12-dione 2q



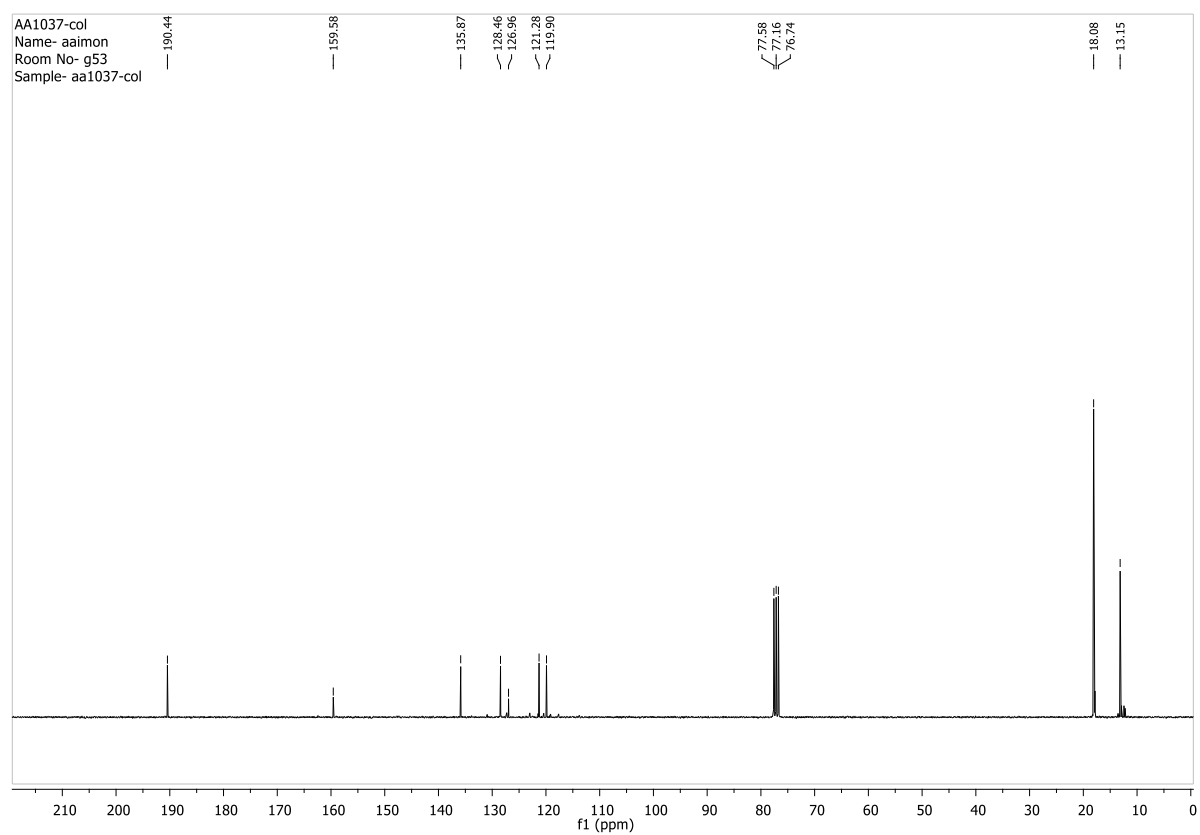
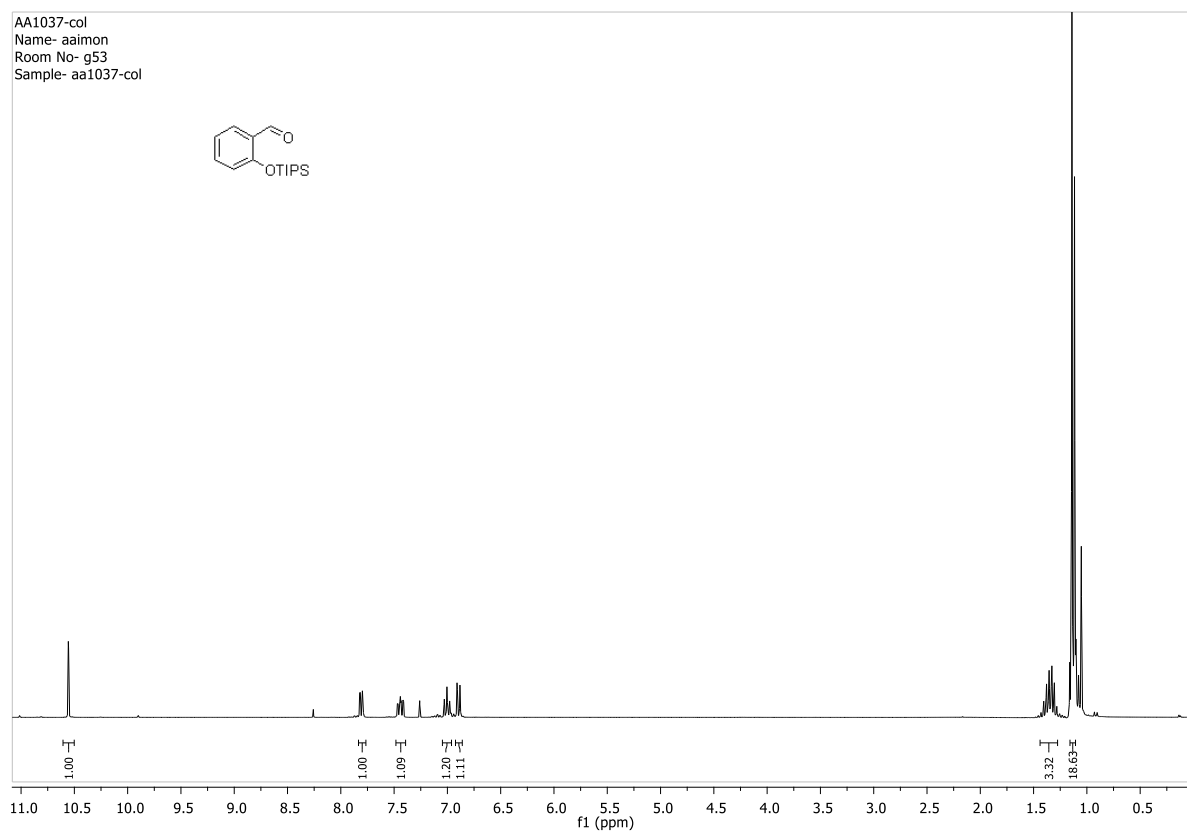
11-(4-Methylbenzenesulfonyl)-11,13-diazatetracyclo[8.6.0.0^{1,13}.0^{2,7}]hexadeca-2(7),3,5-triene-8,12-dione 2r



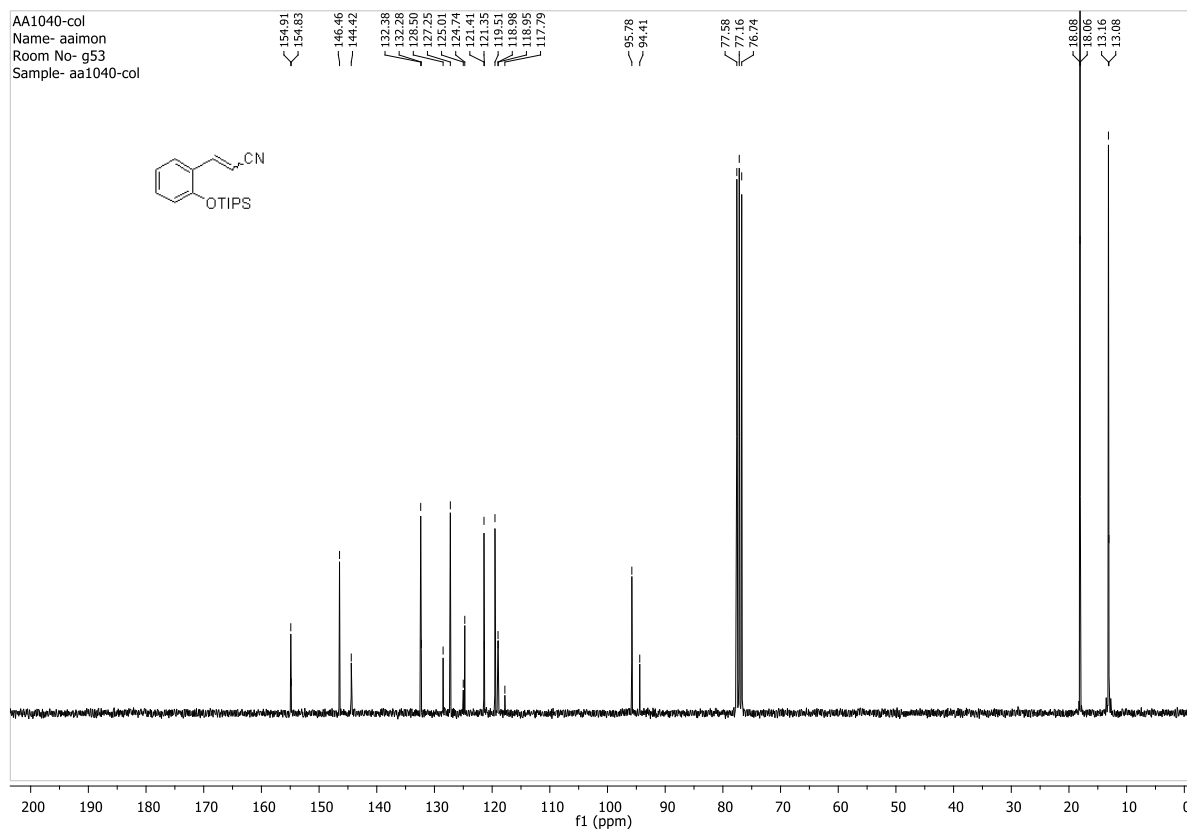
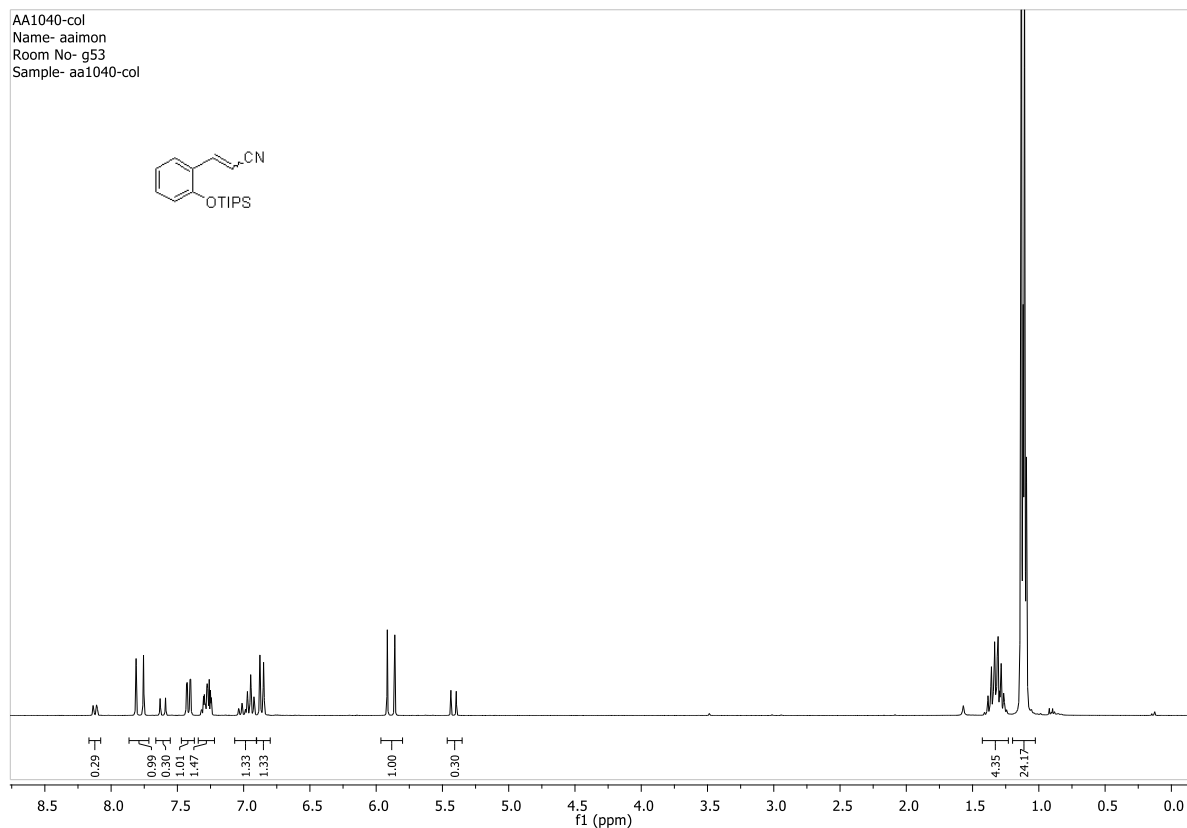
6-Acetyl-11-cyclopropyl-6,11,13-triazatetracyclo[8.6.0.0¹,¹³.0²,⁷]hexadec-2(7)-ene-8,12-dione 2s



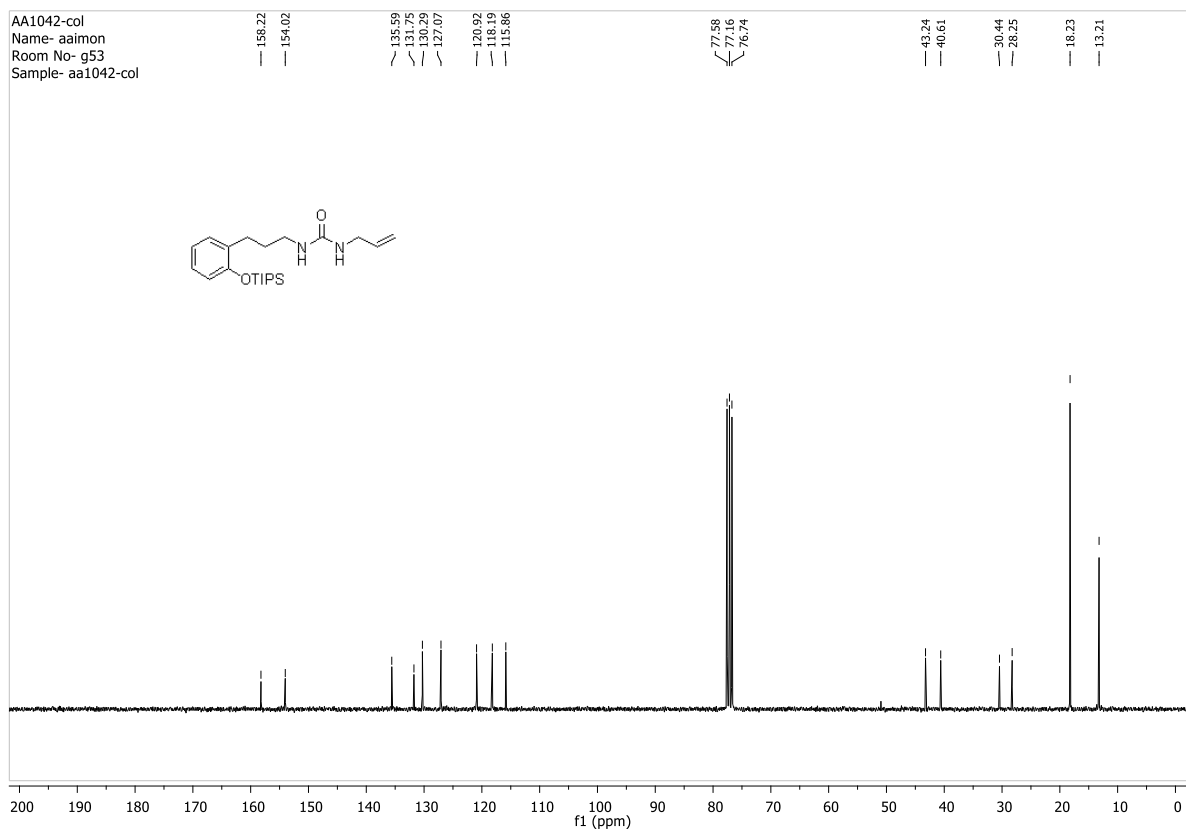
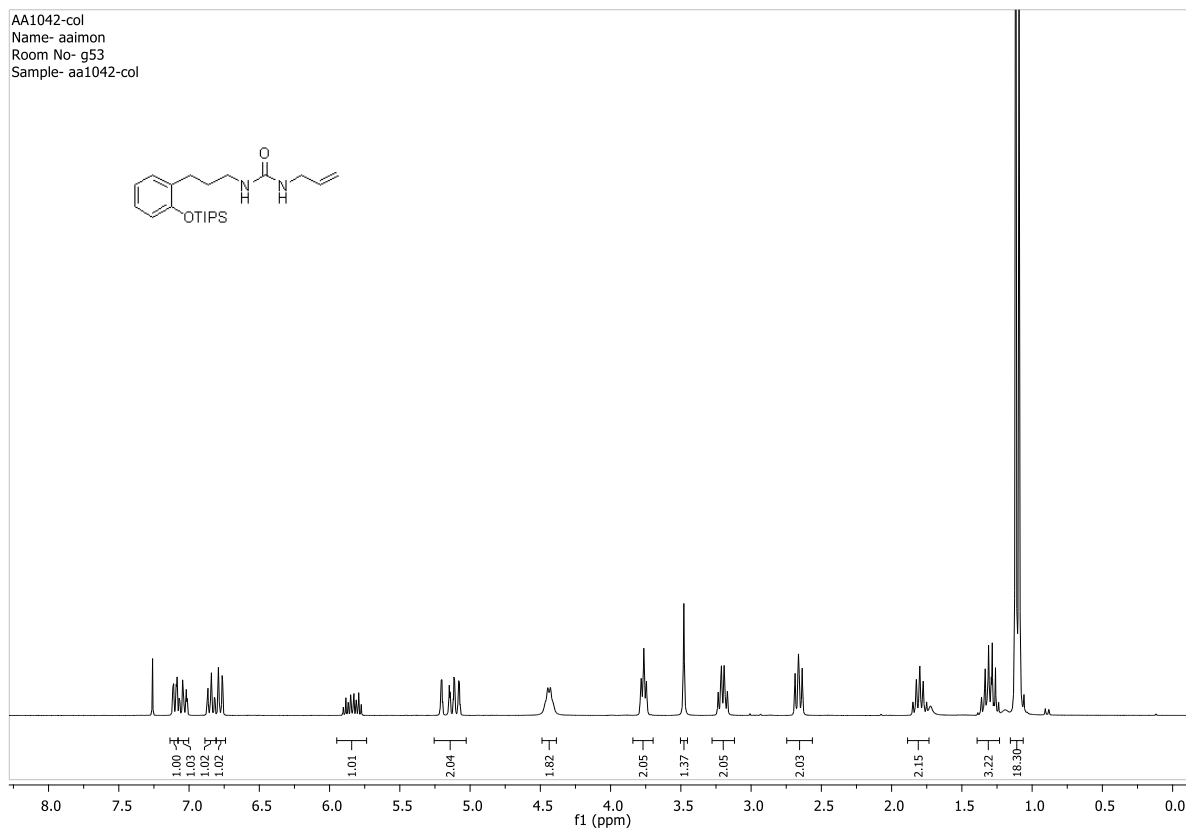
2-[[Tris(propan-2-yl)silyl]oxy]benzaldehyde S20



(2E/2Z)-3-(2-{{Tris(propan-2-yl)silyl}oxy}phenyl)prop-2-enitrile S21

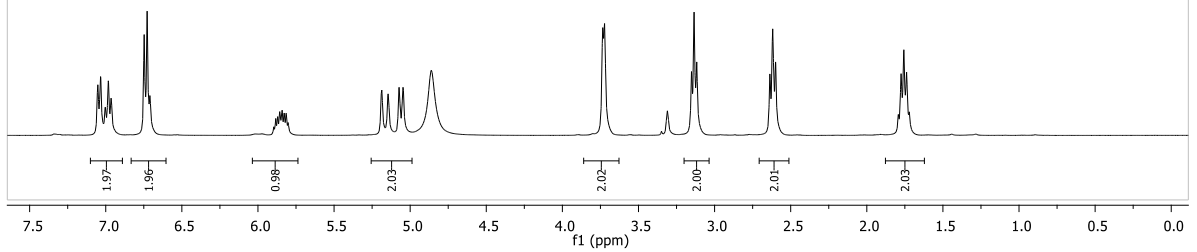
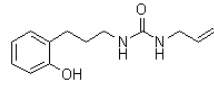


3-(Prop-2-en-1-yl)-1-[3-(2-[[tris(propan-2-yl)silyl]oxy}phenyl)propyl]urea S23

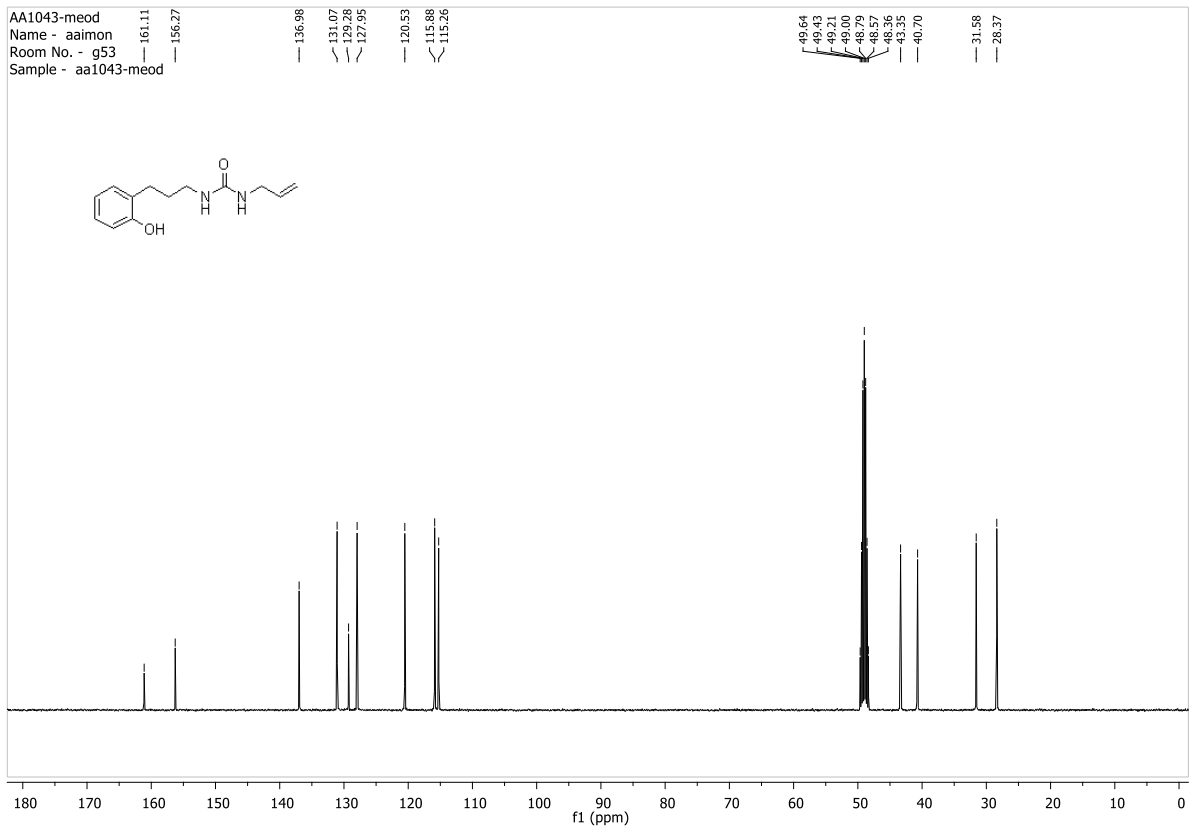
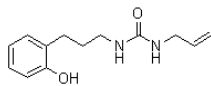


1-[3-(2-Hydroxyphenyl)propyl]-3-(prop-2-en-1-yl)urea 3

AA1043-meod
 Name - aaimon
 Room No. - g53
 Sample - aa1043-meod

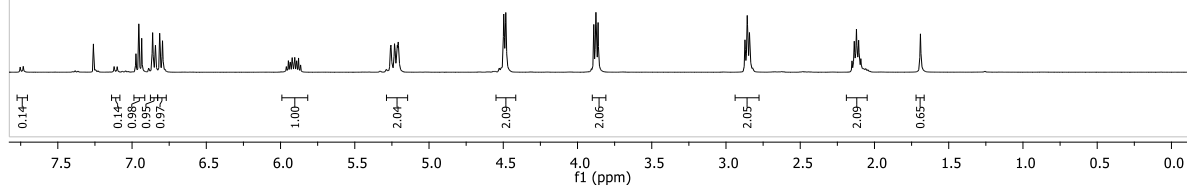
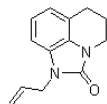


AA1043-meod
 Name - aaimon
 Room No. - g53
 Sample - aa1043-meod

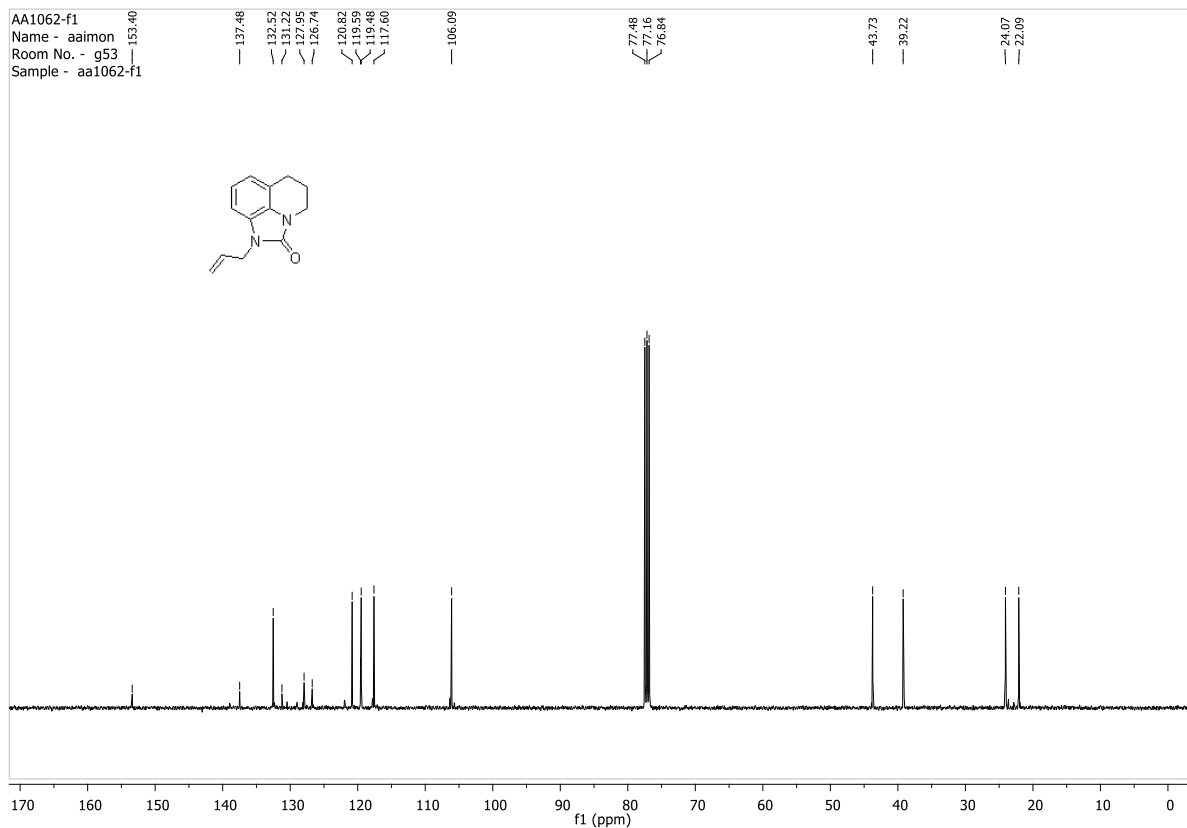
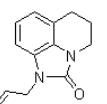


8-Hydroxy-*N*-(prop-2-en-1-yl)-1,2,3,4-tetrahydroquinoline-1-carboxamide 4

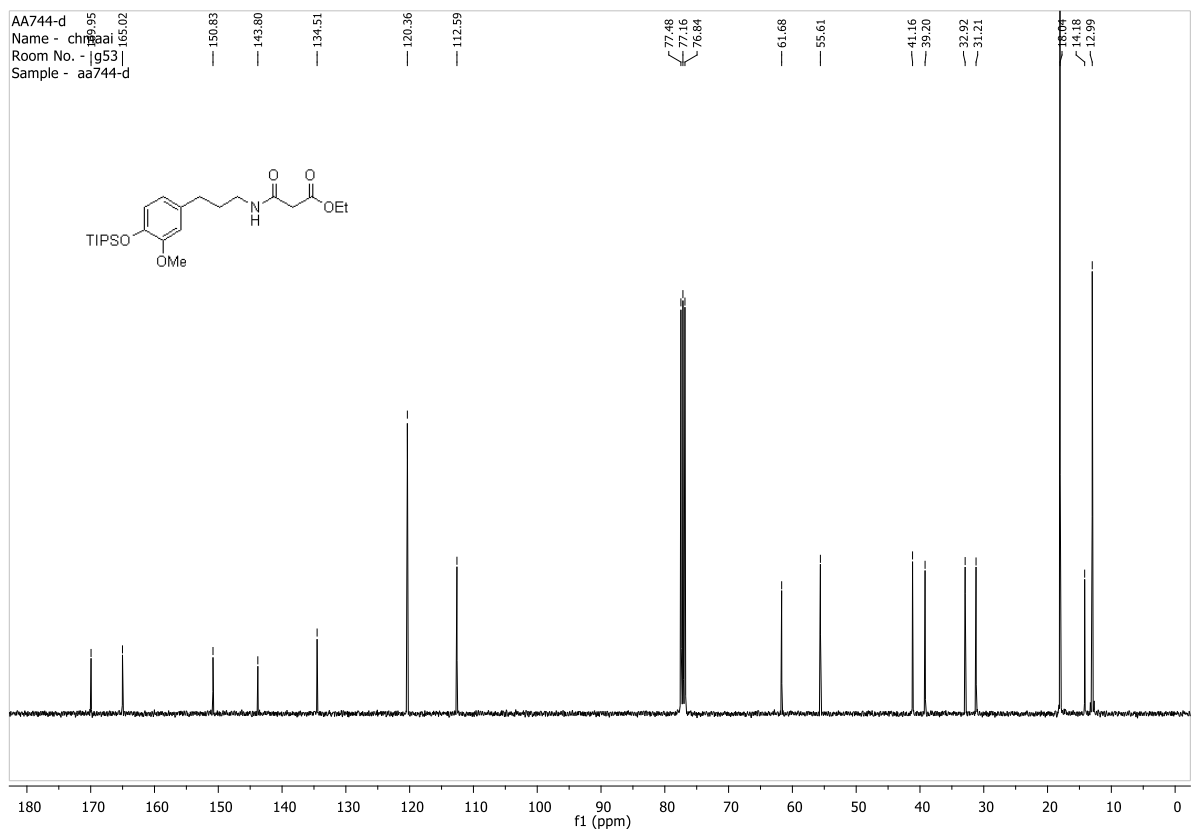
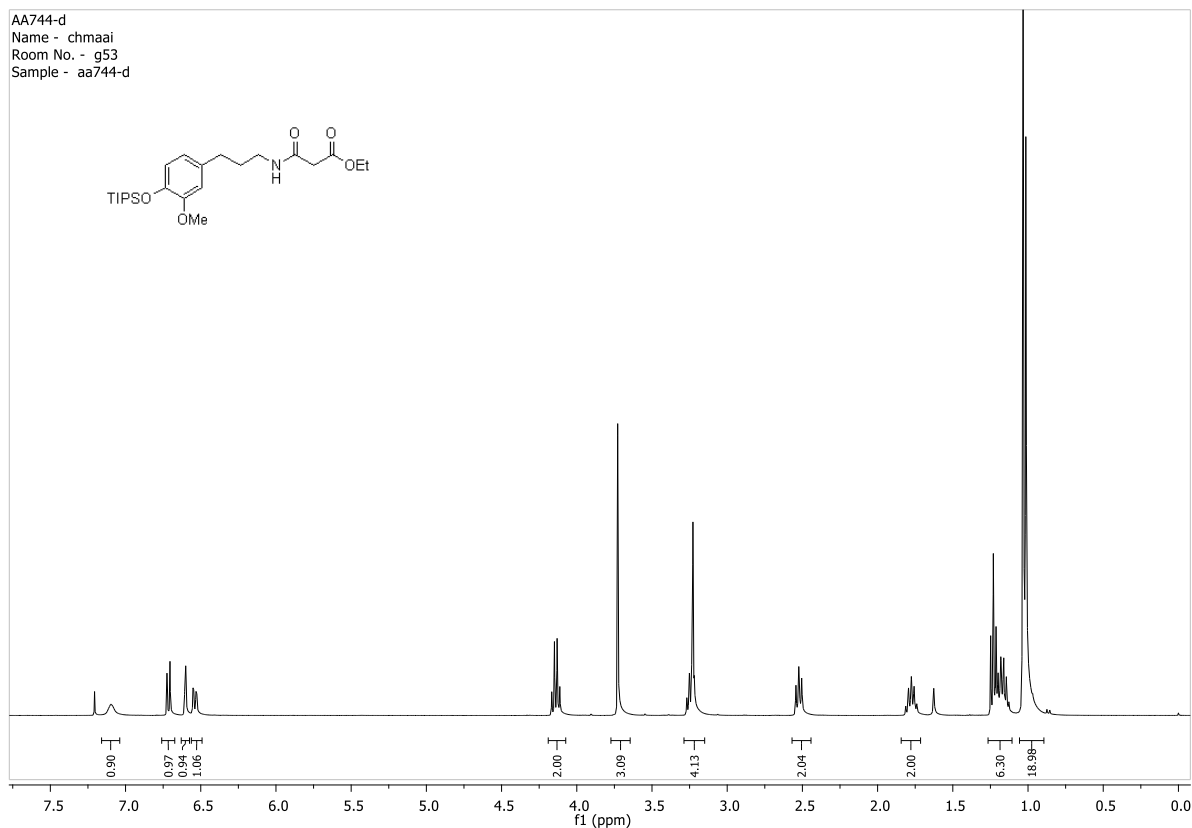
AA1062-f1
 Name - aaimon
 Room No. - g53
 Sample - aa1062-f1



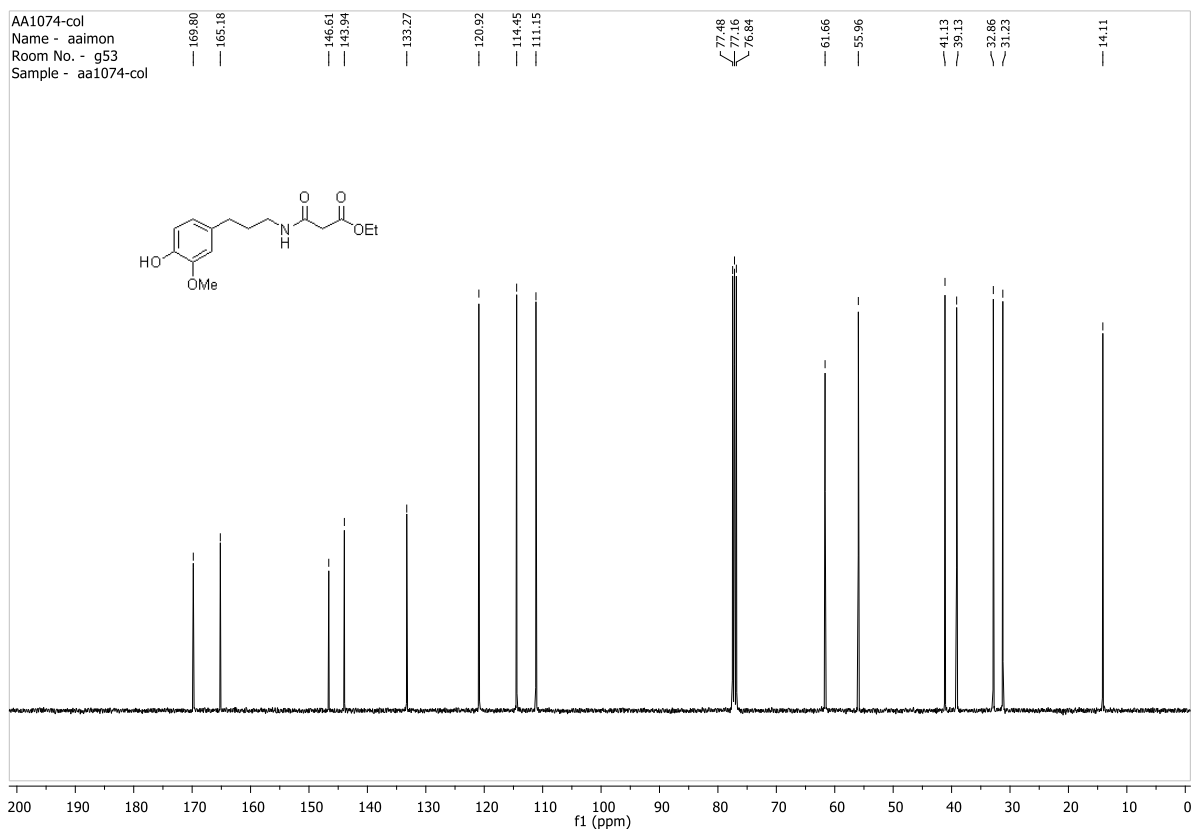
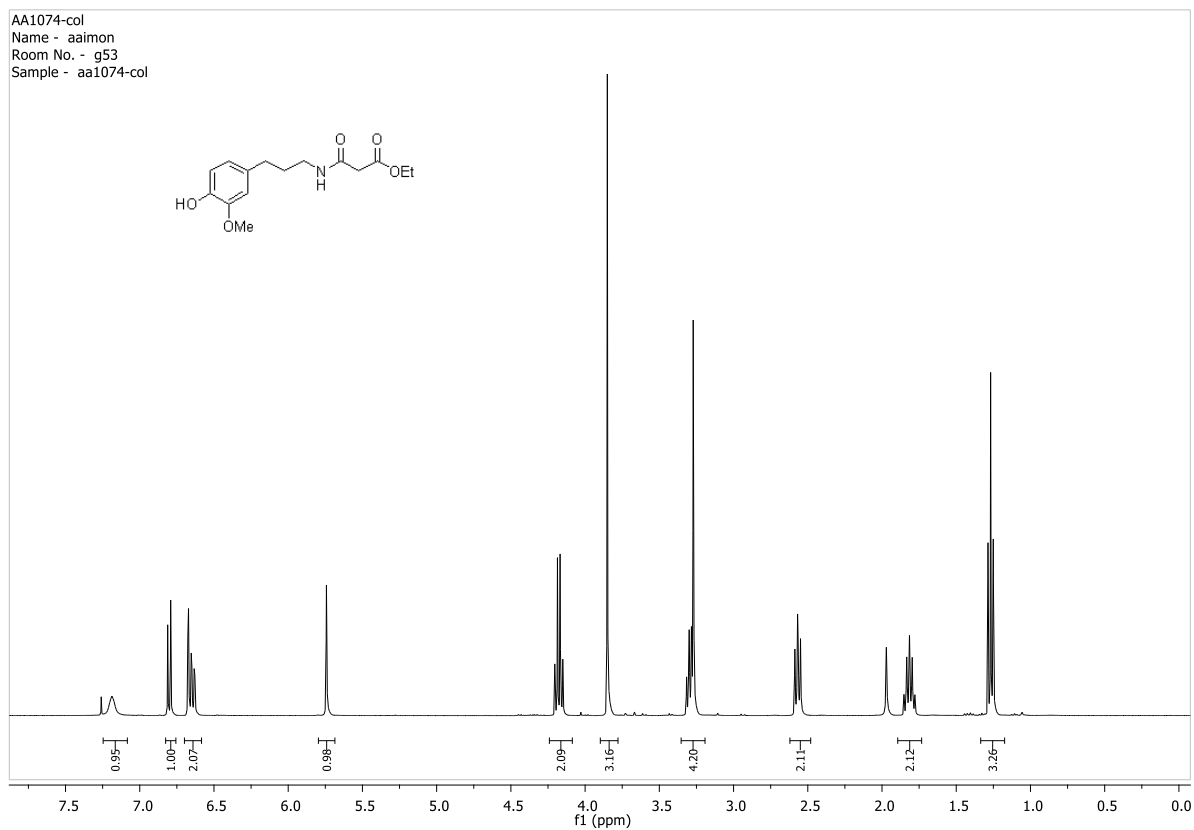
AA1062-f1
 Name - aaimon
 Room No. - g53
 Sample - aa1062-f1



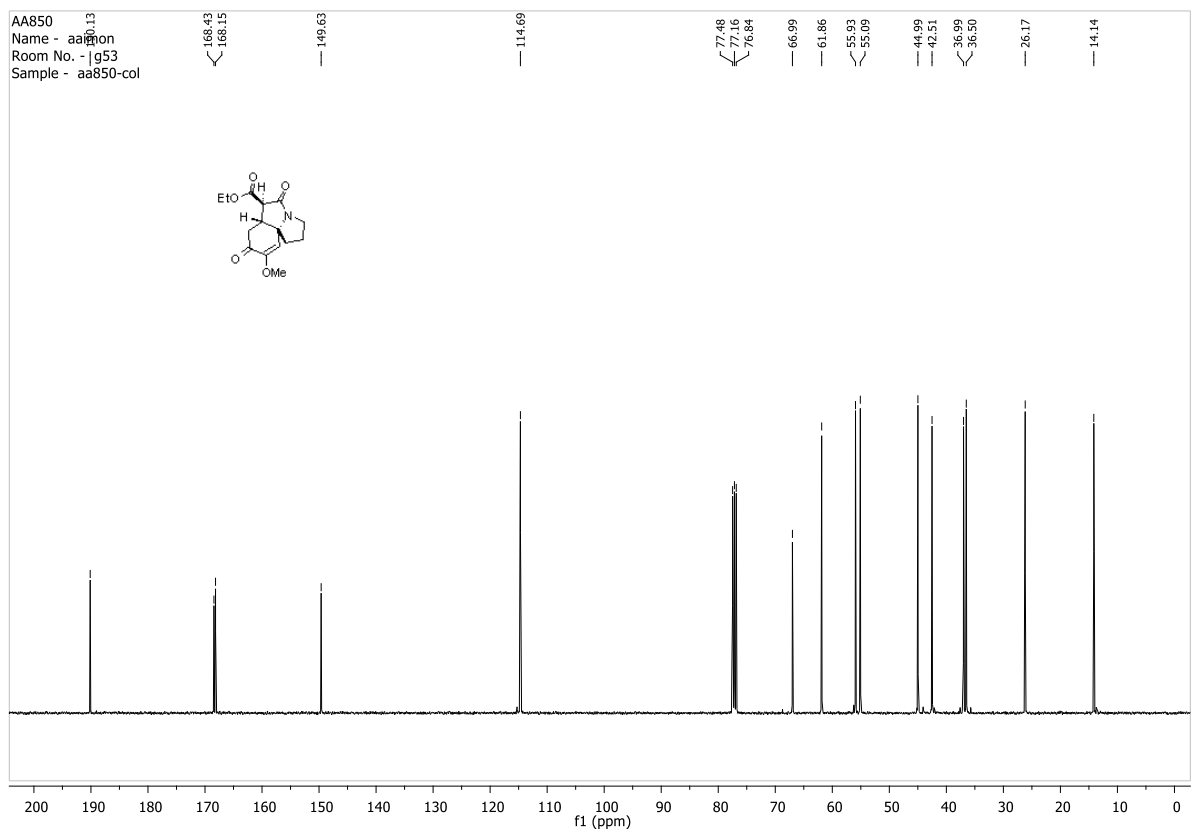
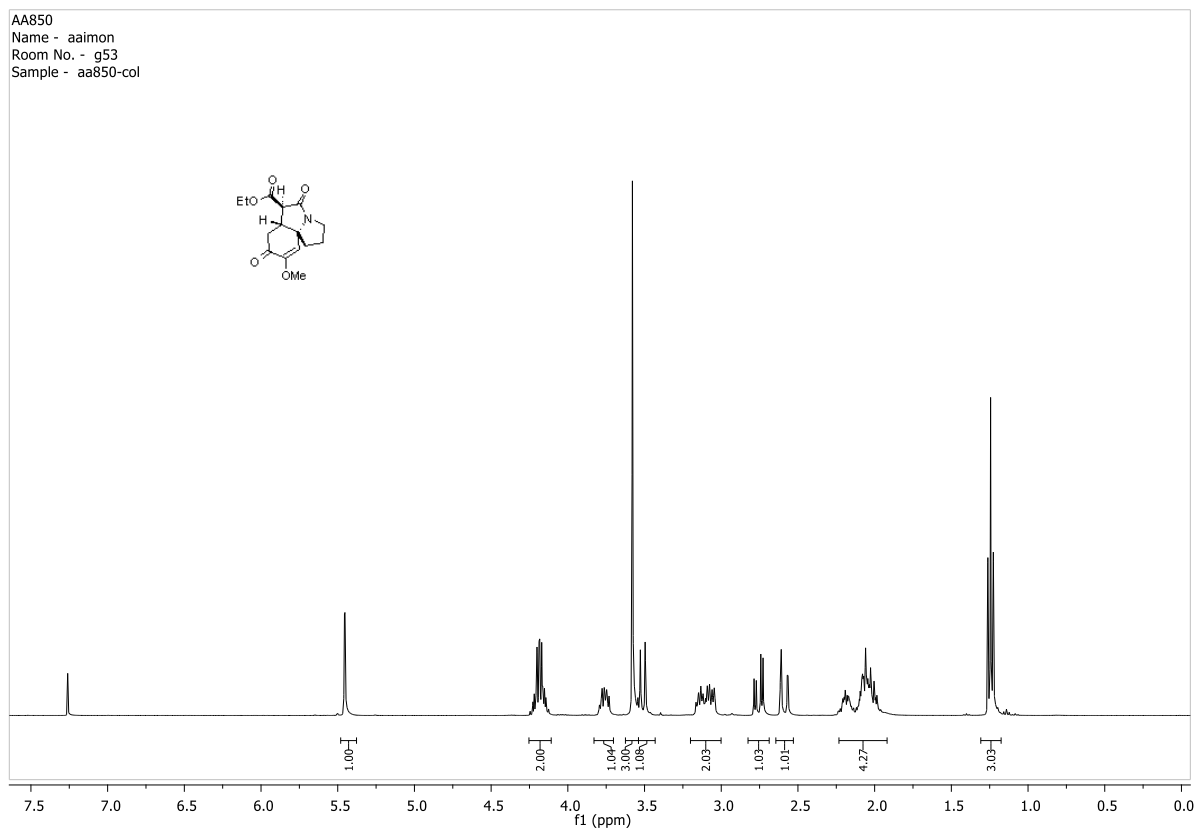
Ethyl 2-([3-(3-methoxy-4-[[tris(propan-2-yl)silyl]oxy]phenyl)propyl]carbamoyl)acetate S24



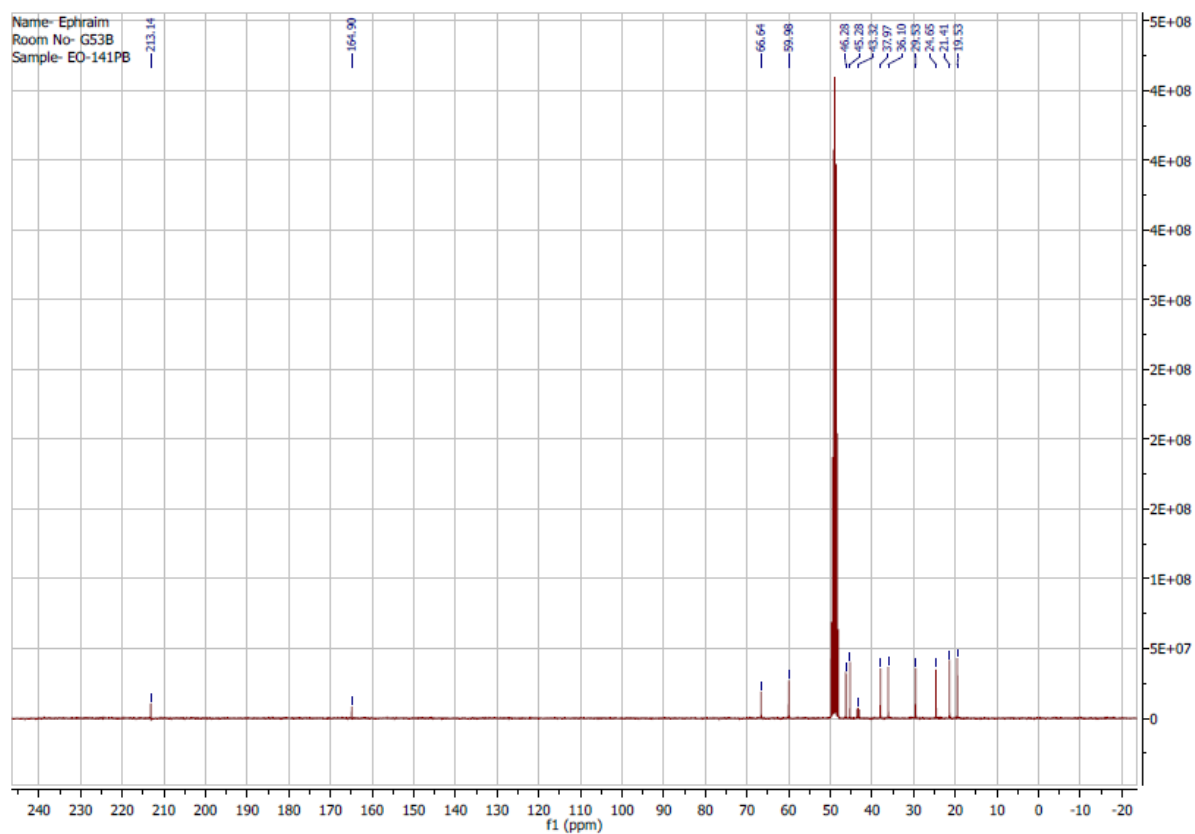
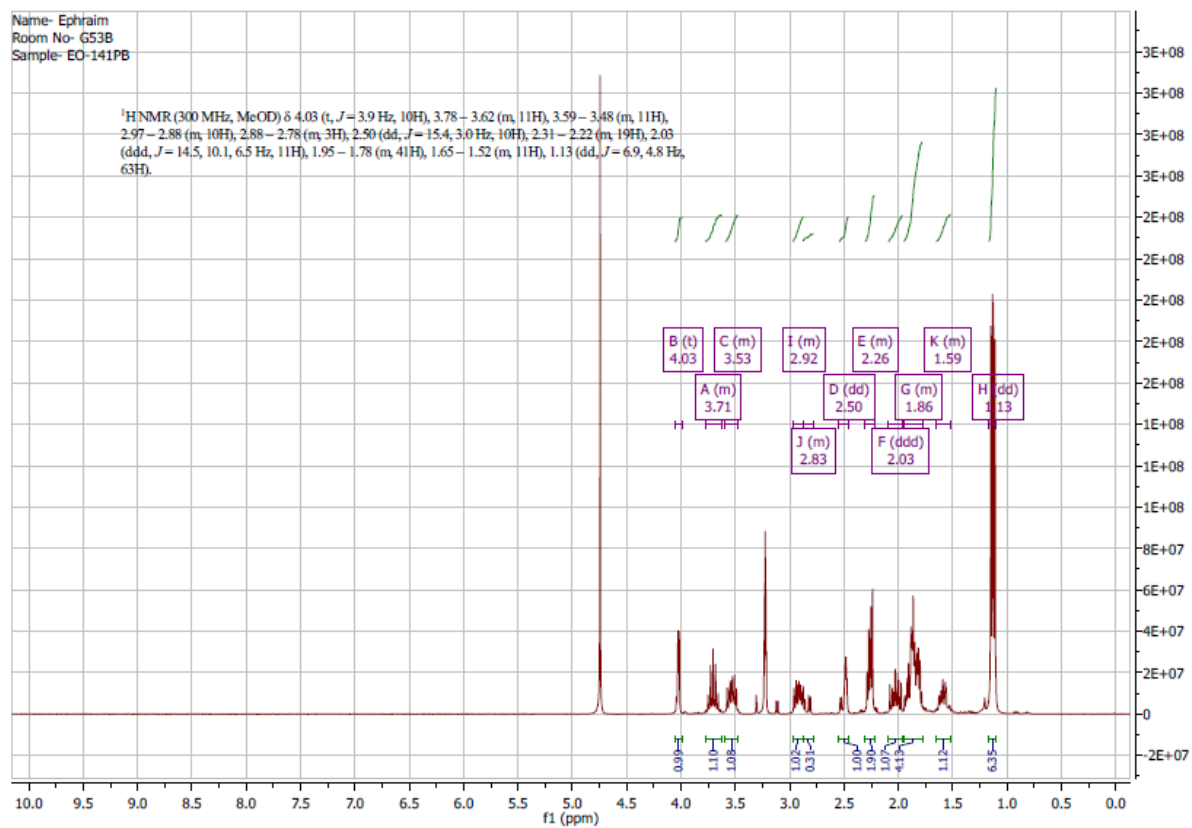
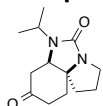
Ethyl 2-([3-(4-hydroxy-3-methoxyphenyl)propyl]carbamoyl)acetate 5



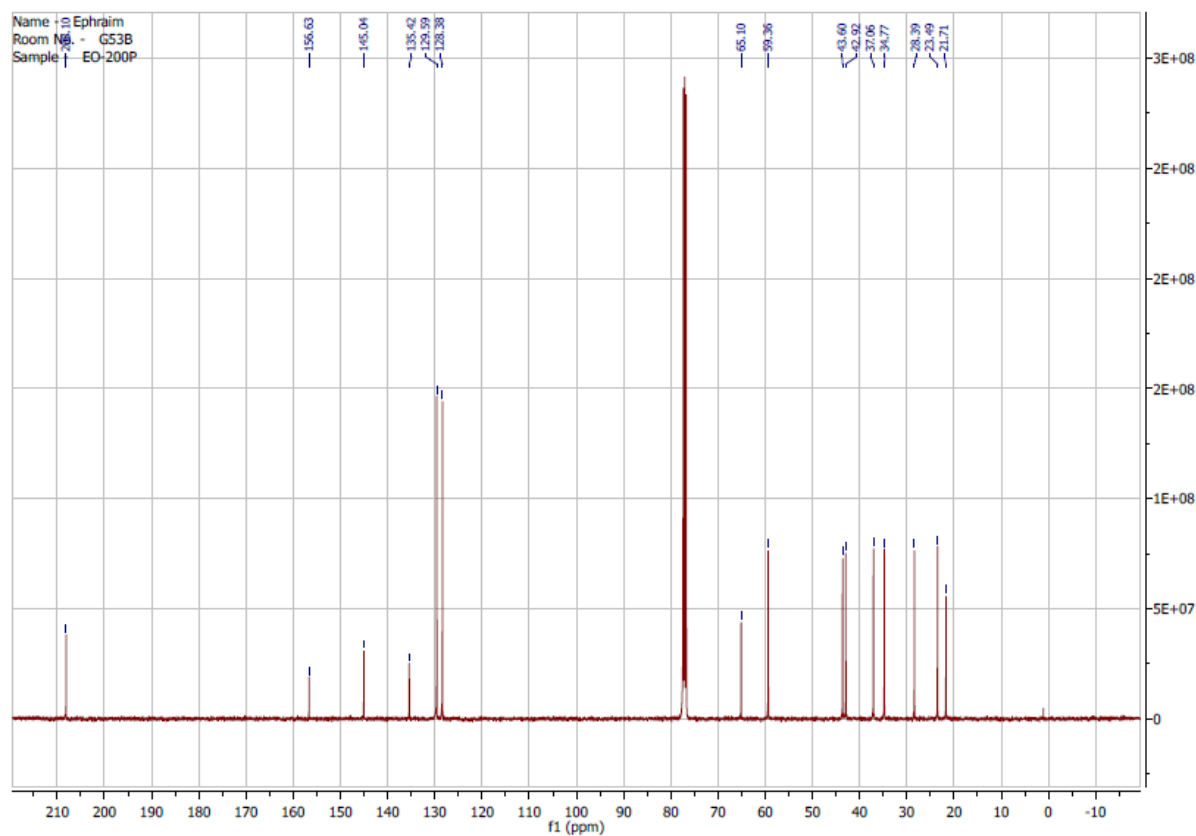
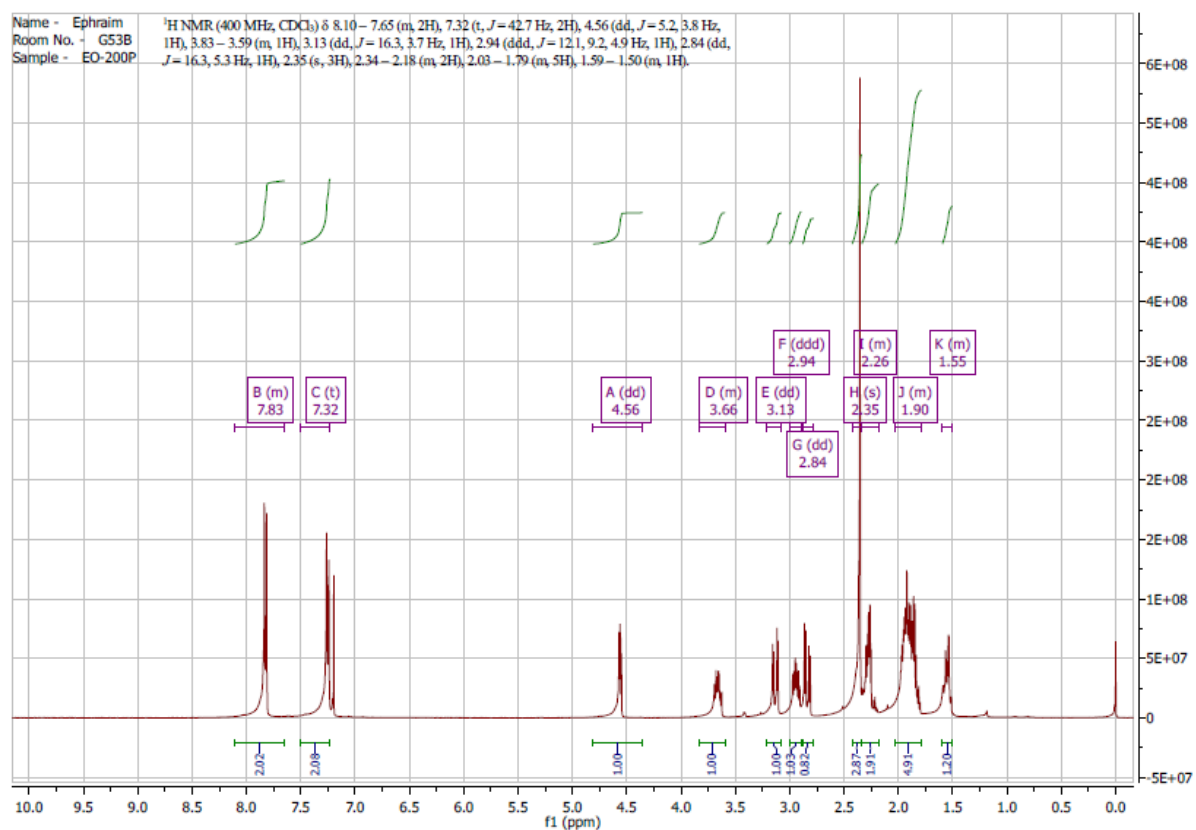
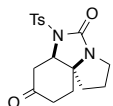
Ethyl 2-methoxy-3,6-dioxo-3*H*,4*H*,5*H*,6*H*,8*H*,9*H*,10*H*,10*bH*-cyclohexa[*h*]pyrrolizine-5-carboxylate 6



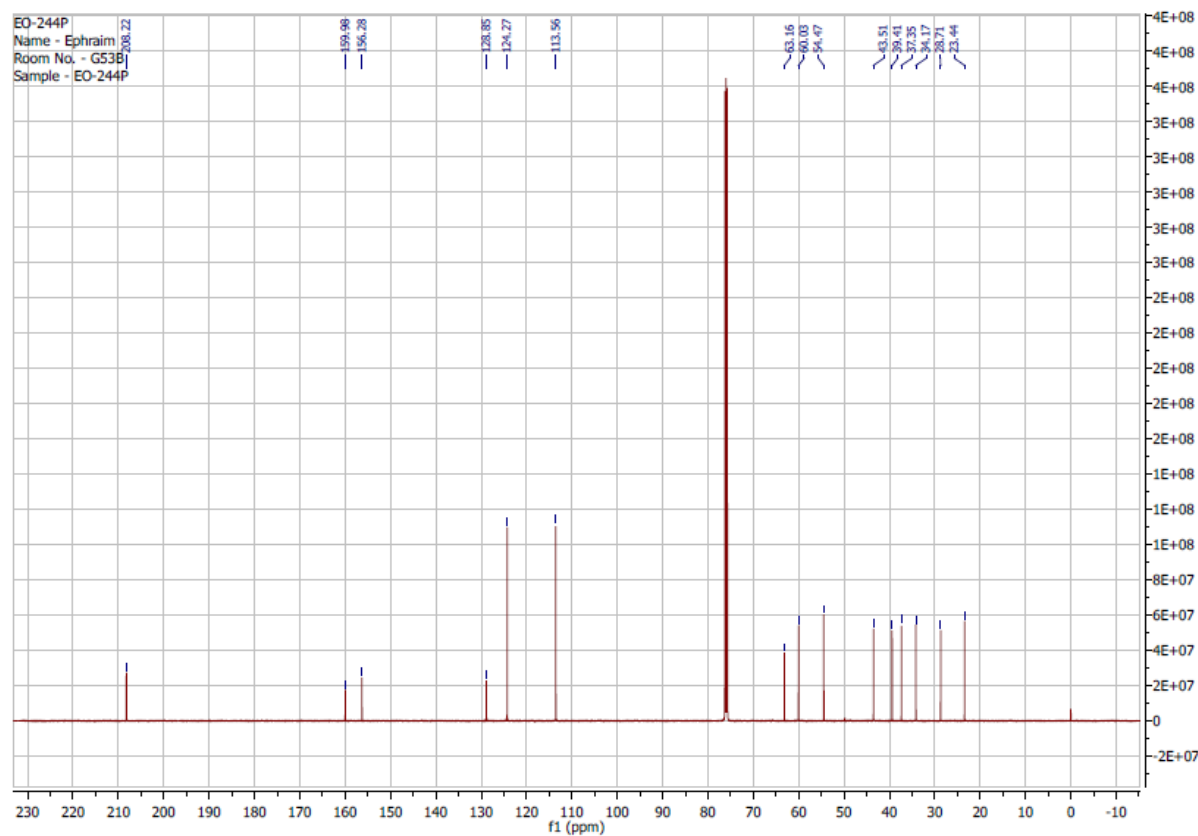
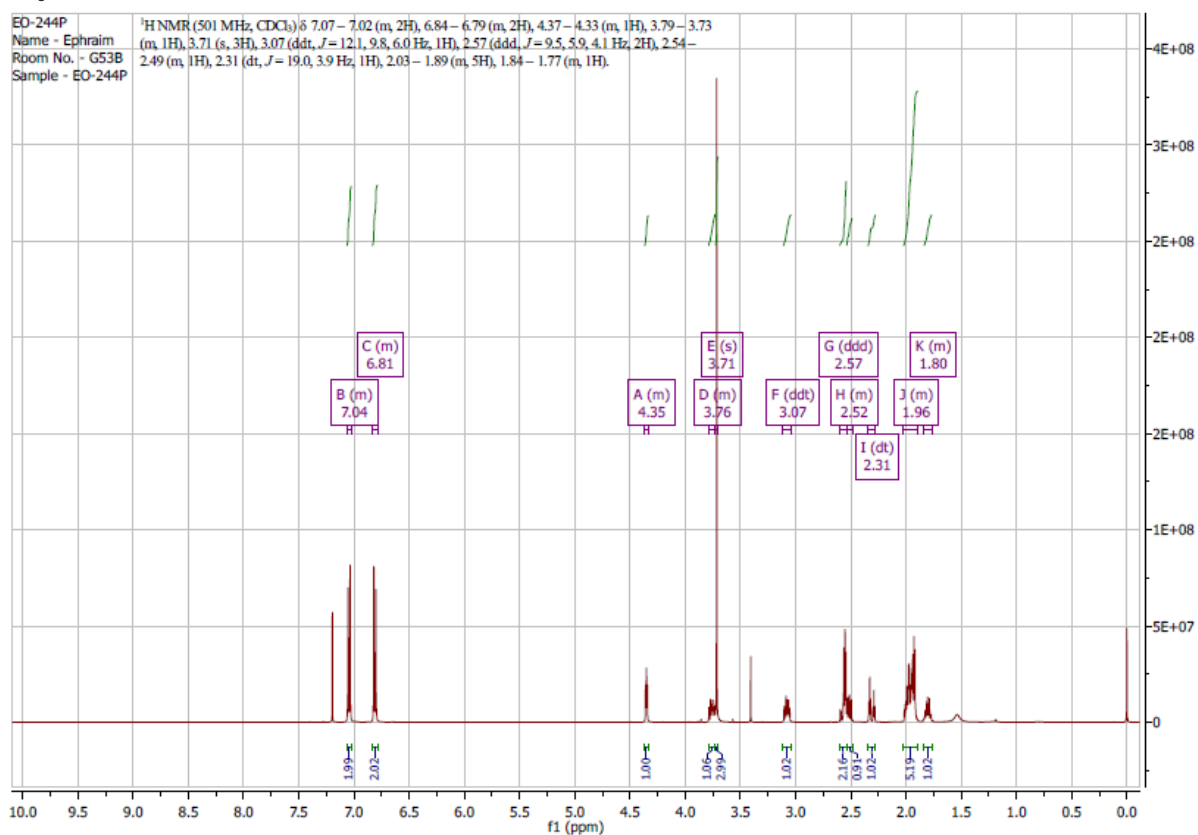
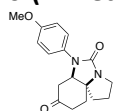
6-Isopropylhexahydro-1*H*,5*H*-benzo[*d*]pyrrolo[1,2-*c*]imidazole-5,8(6*H*)-dione 7



6-(4-Toluenesulfonyl)hexahydro-1*H*,5*H*-benzo[*d*]pyrrolo[1,2-*c*]imidazole-5,8(6*H*)-dione **8**



6-(4-Methoxyphenyl)hexahydro-1*H*,5*H*-benzo[*d*]pyrrolo[1,2-*c*]imidazole-5,8(6*H*)-dione 9

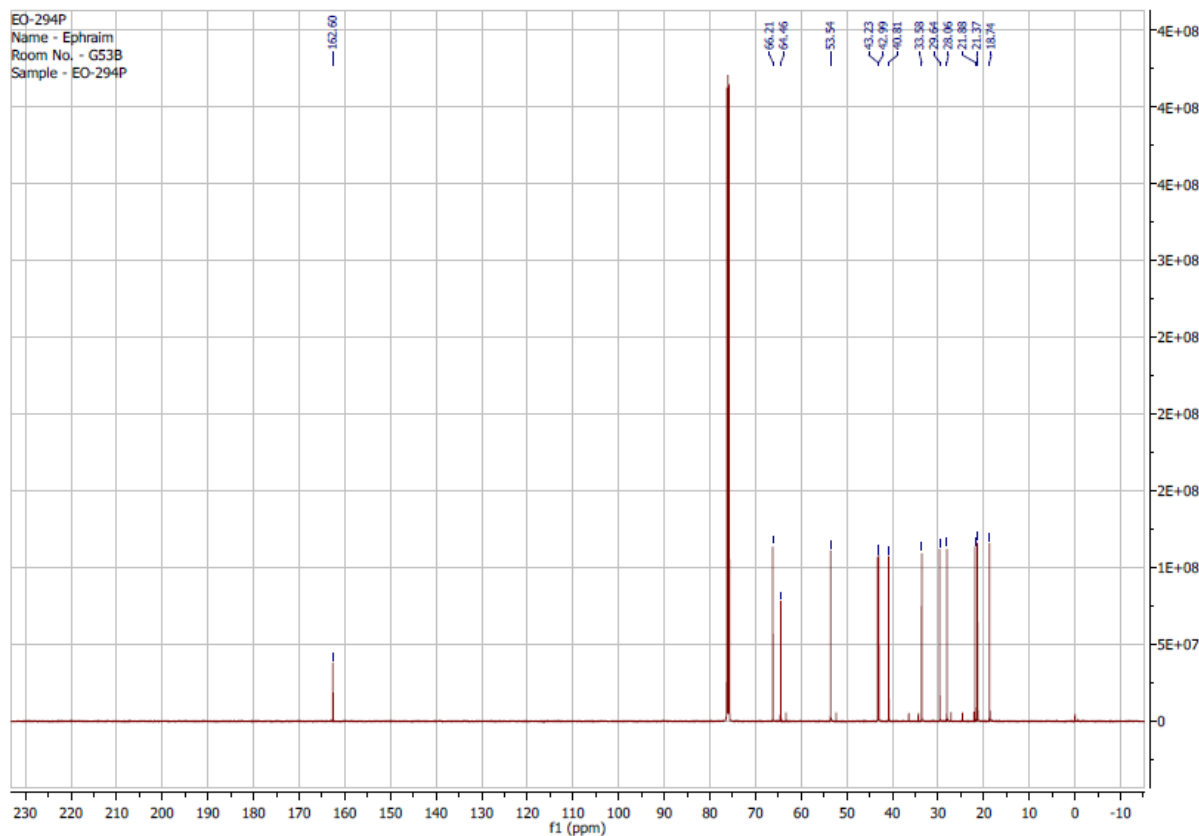
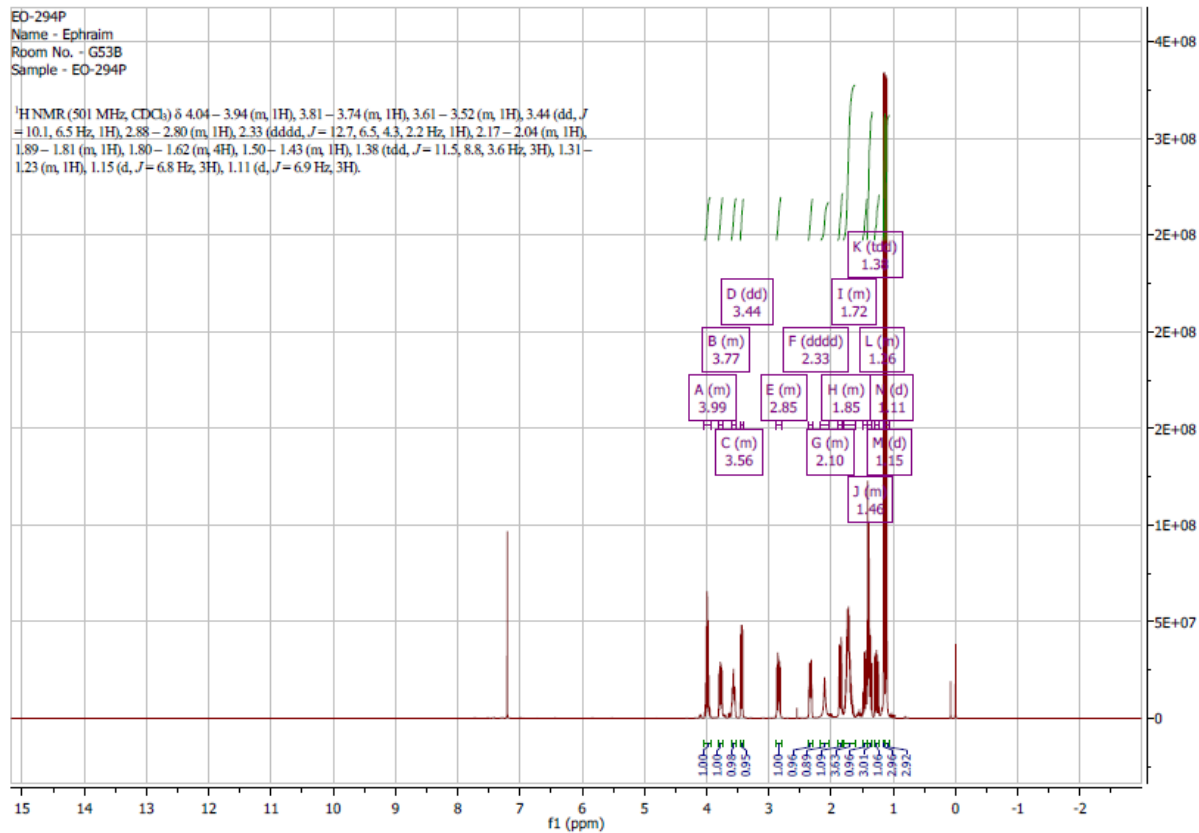


8-Hydroxy-6-isopropyloctahydro-1*H*,5*H*-benzo[*d*]pyrrolo[1,2-*c*]imidazol-5-one 10



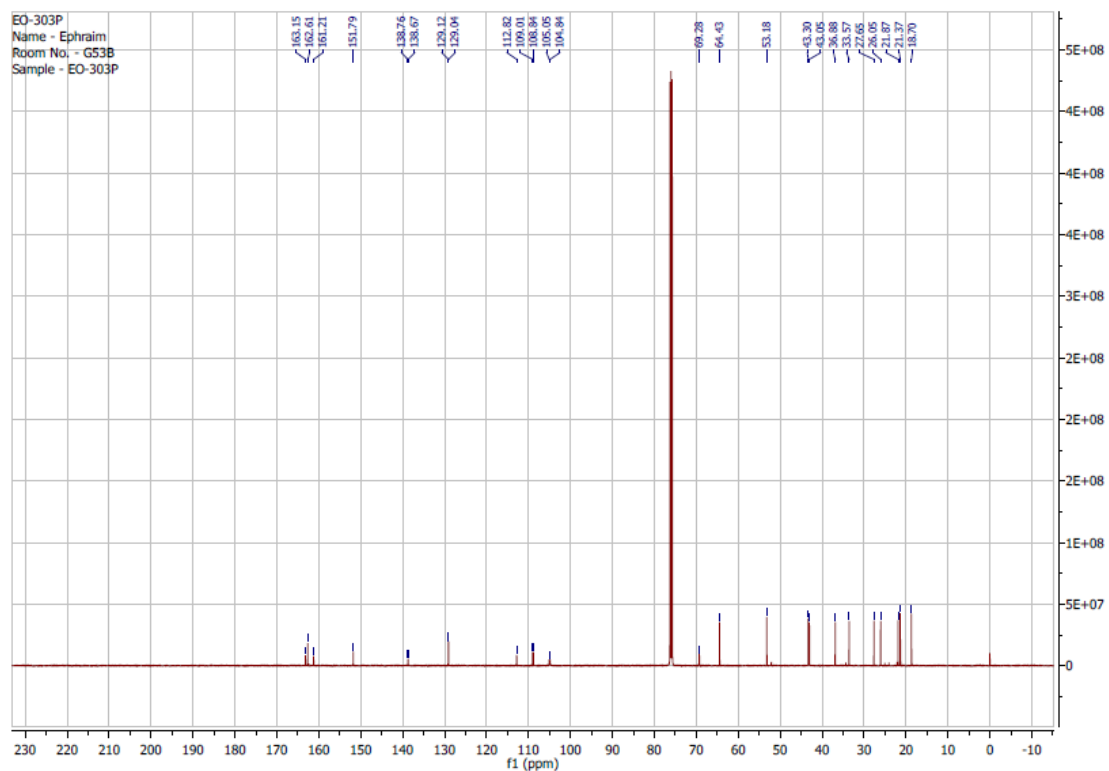
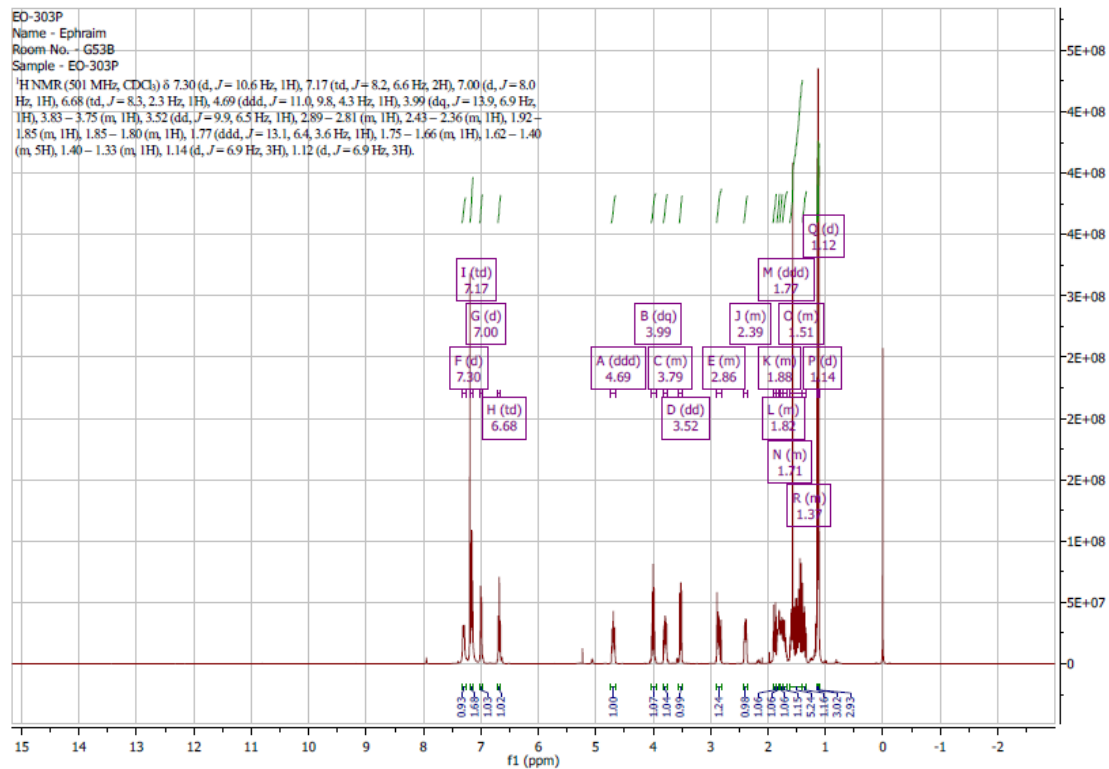
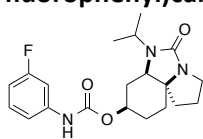
EO-294P
Name - Ephraim
Room No. - G53B
Sample - EO-294P

¹H NMR (501 MHz, CDCl₃) δ 4.04 – 3.94 (m, 1H), 3.81 – 3.74 (m, 1H), 3.61 – 3.52 (m, 1H), 3.44 (dd, *J* = 10.1, 6.5 Hz, 1H), 2.88 – 2.80 (m, 1H), 2.33 (dddd, *J* = 12.7, 6.5, 4.3, 2.2 Hz, 1H), 2.17 – 2.04 (m, 1H), 1.89 – 1.81 (m, 1H), 1.80 – 1.62 (m, 4H), 1.50 – 1.43 (m, 1H), 1.38 (tdd, *J* = 11.5, 8.8, 3.6 Hz, 3H), 1.31 – 1.23 (m, 1H), 1.15 (d, *J* = 6.8 Hz, 3H), 1.11 (d, *J* = 6.9 Hz, 3H).

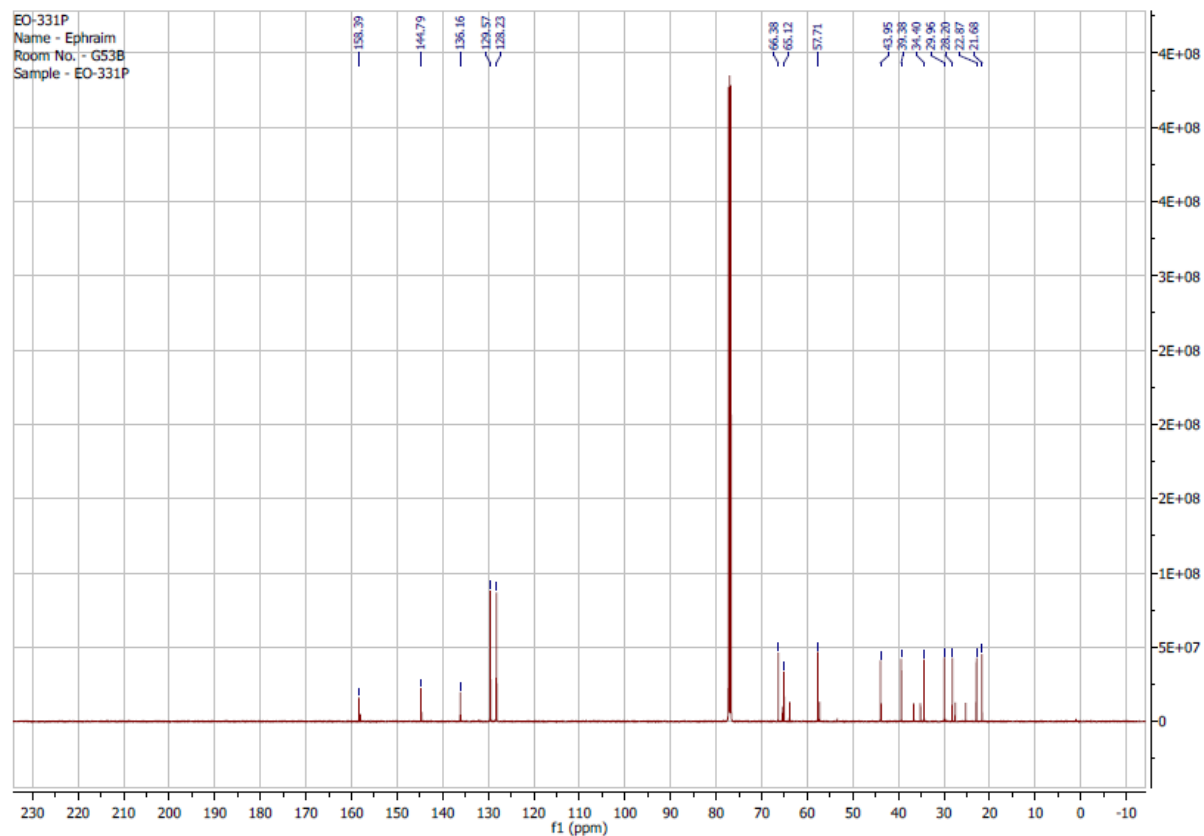
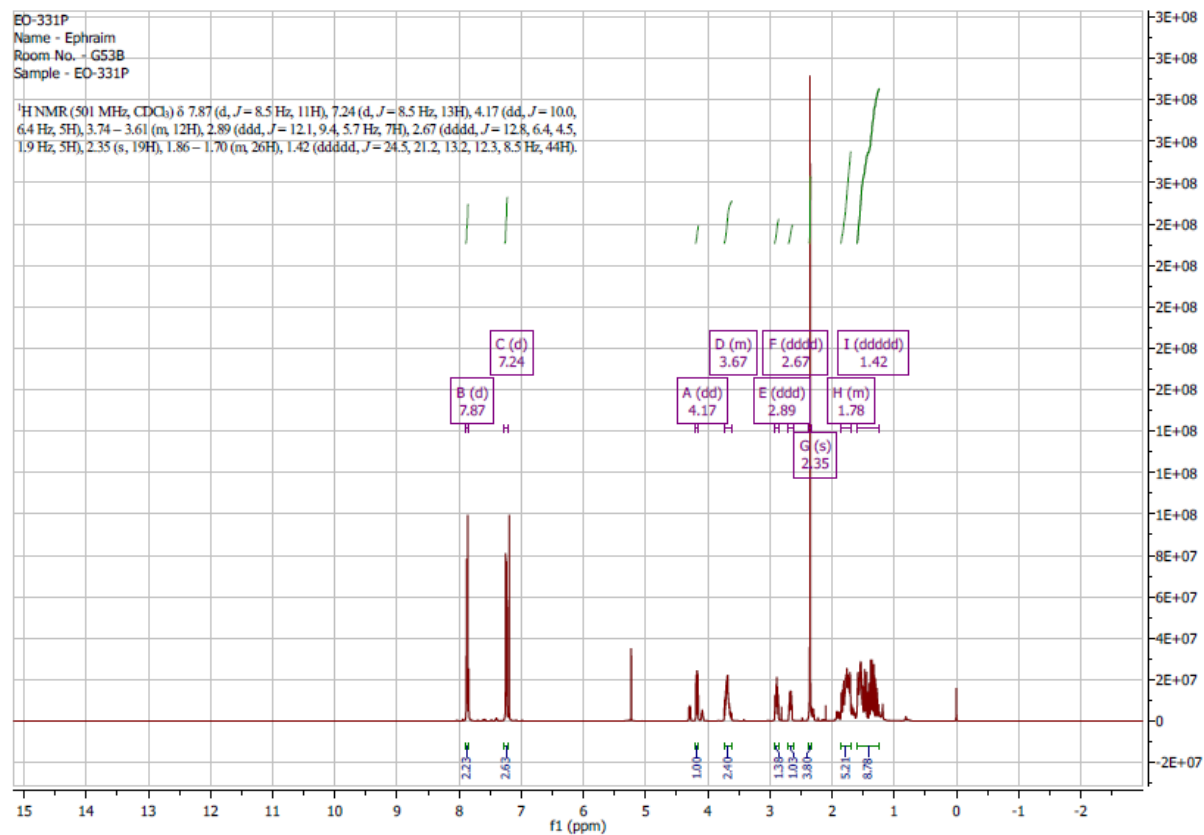


**6-Isopropyl-5-oxooctahydro-1*H*,5*H*-benzo[*d*]pyrrolo[1,2-*c*]imidazol-8-yl
fluorophenyl)carbamate S25**

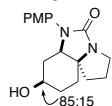
(3-



8-Hydroxy-6-(4-toluenesulfonyl)octahydro-1*H*,5*H*-benzo[*d*]pyrrolo[1,2-*c*]imidazol-5-one 11

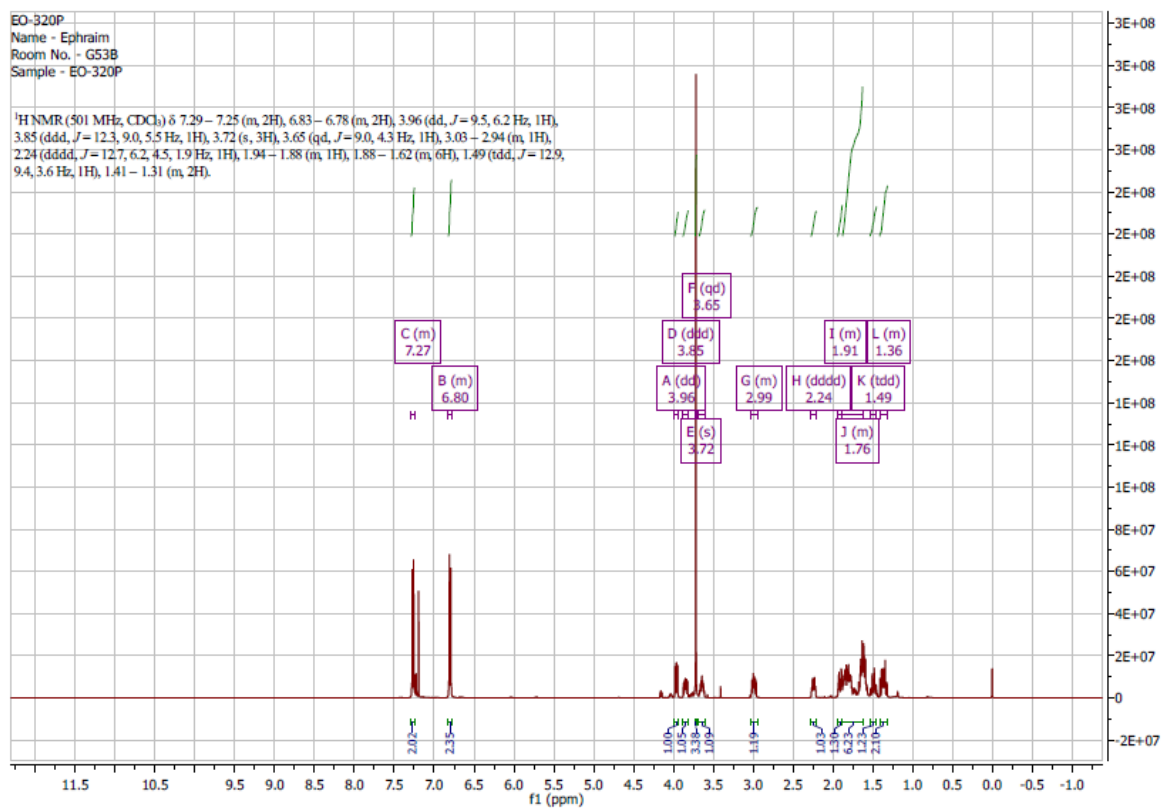


8-Hydroxy-6-(4-methoxyphenyl)octahydro-1*H*,5*H*-benzo[*d*]pyrrolo[1,2-*c*]imidazol-5-one 12



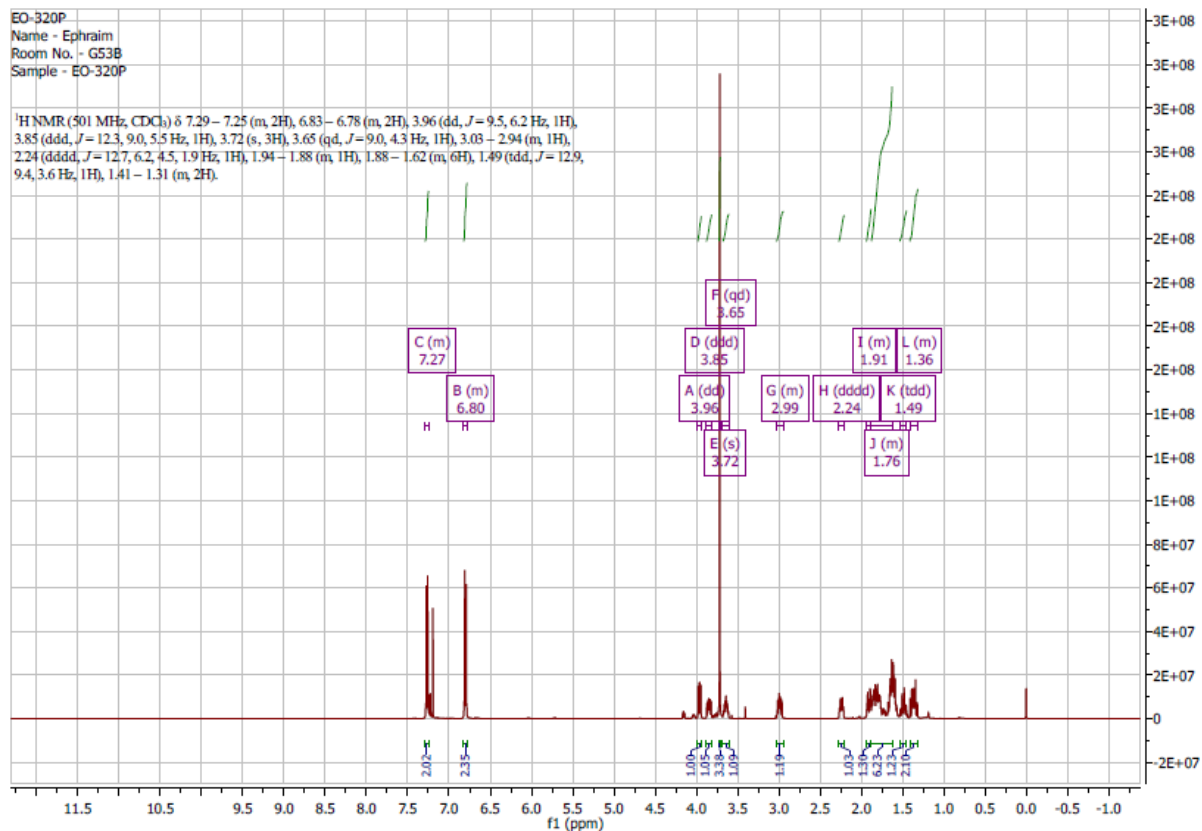
EO-320P
Name - Ephraim
Room No. - G53B
Sample - EO-320P

¹H NMR (501 MHz, CDCl₃) δ 7.29 – 7.25 (m, 2H), 6.83 – 6.78 (m, 2H), 3.96 (dd, *J* = 9.5, 6.2 Hz, 1H), 3.85 (ddd, *J* = 12.3, 9.0, 5.5 Hz, 1H), 3.72 (s, 3H), 3.65 (qd, *J* = 9.0, 4.3 Hz, 1H), 3.03 – 2.94 (m, 1H), 2.24 (dddd, *J* = 12.7, 6.2, 4.5, 1.9 Hz, 1H), 1.94 – 1.88 (m, 1H), 1.88 – 1.62 (m, 6H), 1.49 (tdd, *J* = 12.9, 9.4, 3.6 Hz, 1H), 1.41 – 1.31 (m, 2H).

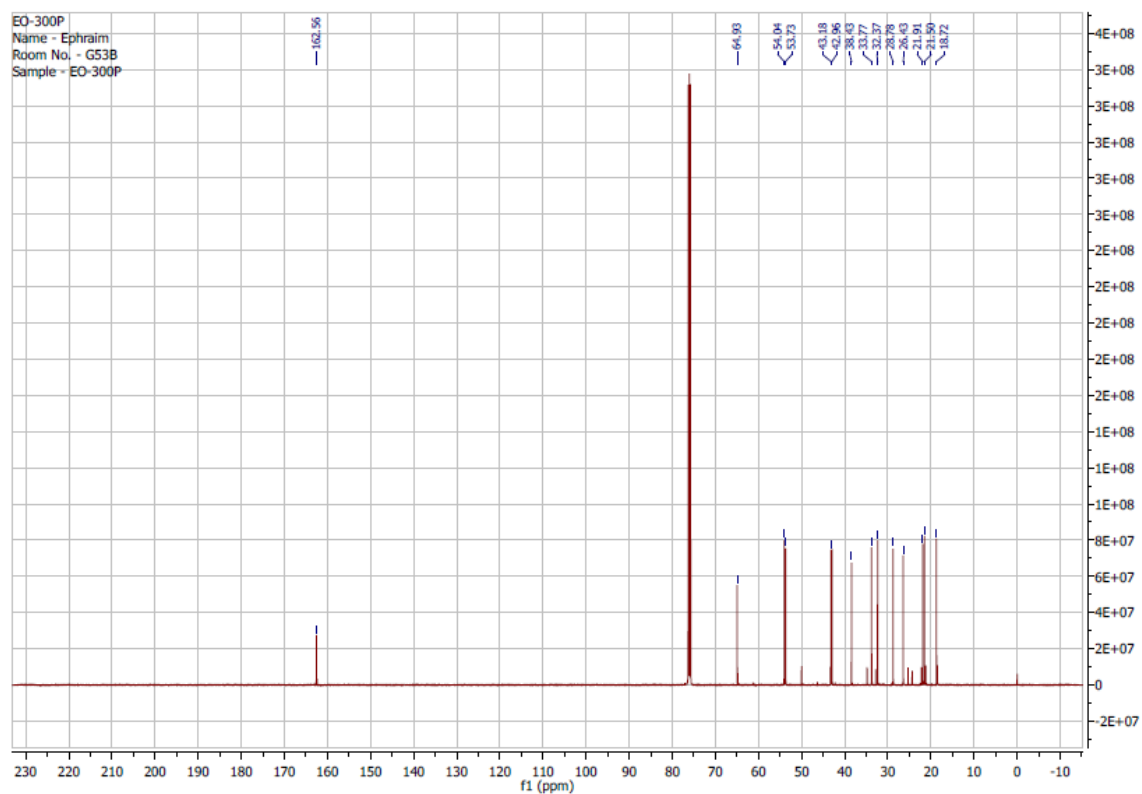
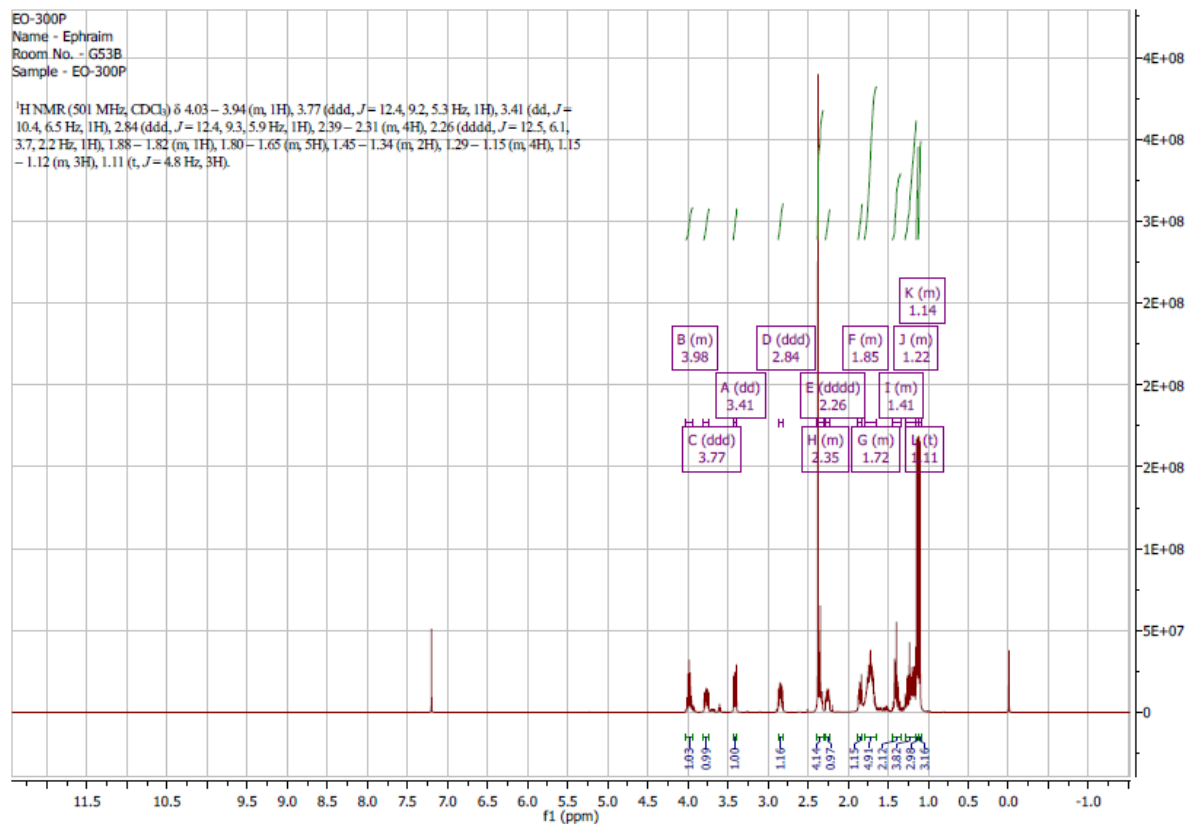
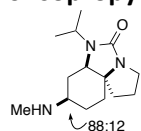


EO-320P
Name - Ephraim
Room No. - G53B
Sample - EO-320P

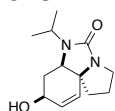
¹H NMR (501 MHz, CDCl₃) δ 7.29 – 7.25 (m, 2H), 6.83 – 6.78 (m, 2H), 3.96 (dd, *J* = 9.5, 6.2 Hz, 1H), 3.85 (ddd, *J* = 12.3, 9.0, 5.5 Hz, 1H), 3.72 (s, 3H), 3.65 (qd, *J* = 9.0, 4.3 Hz, 1H), 3.03 – 2.94 (m, 1H), 2.24 (dddd, *J* = 12.7, 6.2, 4.5, 1.9 Hz, 1H), 1.94 – 1.88 (m, 1H), 1.88 – 1.62 (m, 6H), 1.49 (tdd, *J* = 12.9, 9.4, 3.6 Hz, 1H), 1.41 – 1.31 (m, 2H).



6-Isopropyl-8-(methylamino)octahydro-1*H*,5*H*-benzo[*d*]pyrrolo[1,2-*c*]imidazol-5-one 13

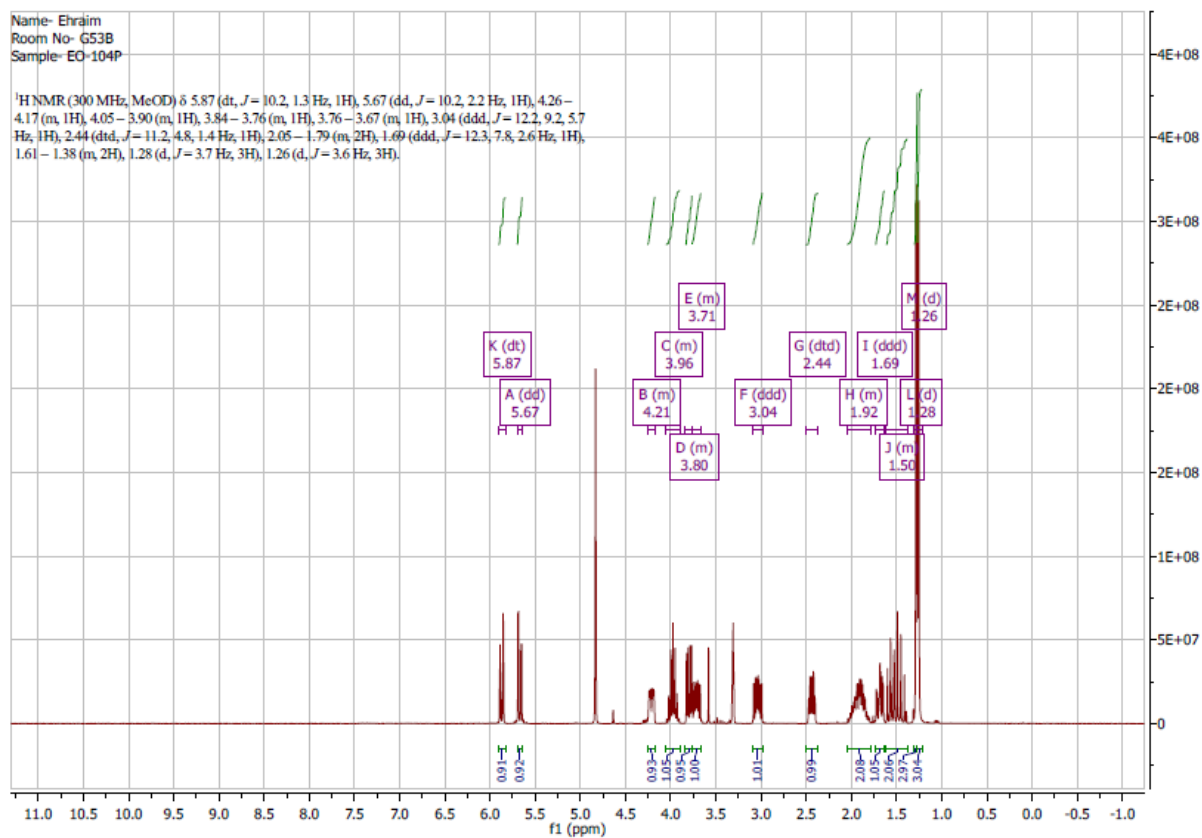


8-Hydroxy-6-isopropyl-2,3,6,6a,7,8-hexahydro-1*H*,5*H*-benzo[*d*]pyrrolo[1,2-*c*]imidazol-5-one 14

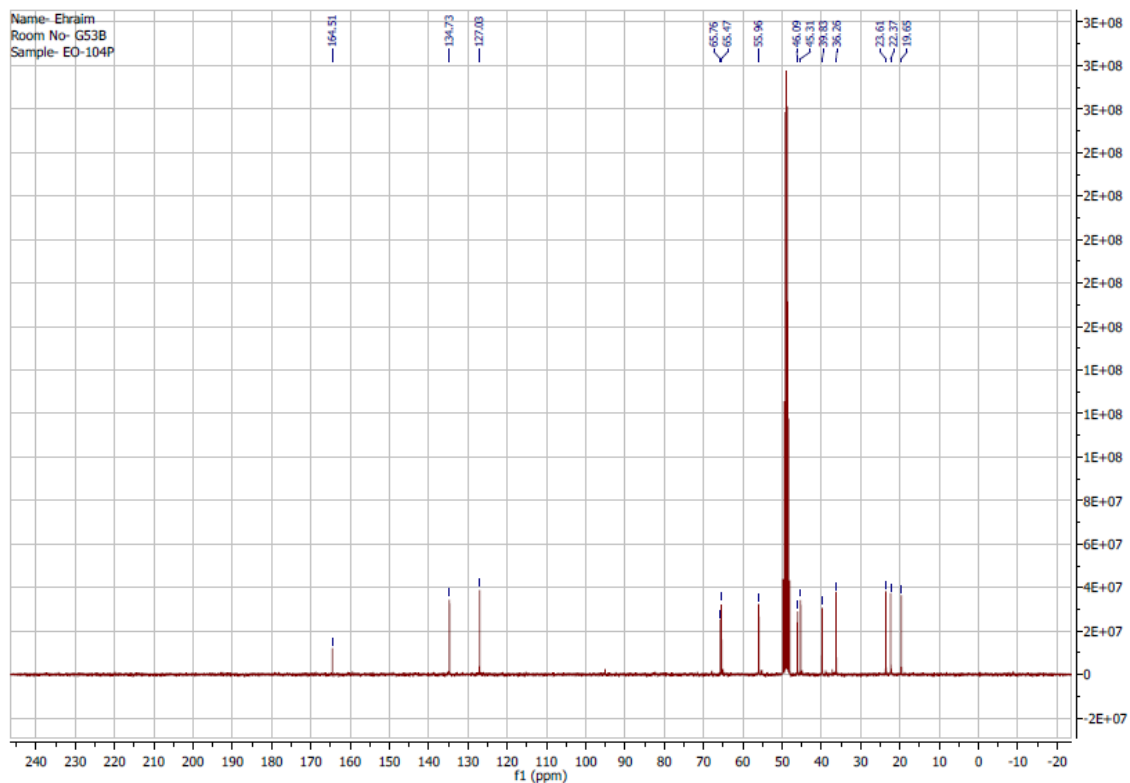


Name- Ehrain
Room No- G53B
Sample- EO-104P

¹H NMR (300 MHz, MeOD) δ 5.87 (dt, $J = 10.2, 1.3$ Hz, 1H), 5.67 (dd, $J = 10.2, 2.2$ Hz, 1H), 4.26 – 4.17 (m, 1H), 4.05 – 3.90 (m, 1H), 3.84 – 3.76 (m, 1H), 3.76 – 3.67 (m, 1H), 3.04 (ddd, $J = 12.2, 9.2, 5.7$ Hz, 1H), 2.44 (dtd, $J = 11.2, 4.8, 1.4$ Hz, 1H), 2.05 – 1.79 (m, 2H), 1.69 (ddd, $J = 12.3, 7.8, 2.6$ Hz, 1H), 1.61 – 1.38 (m, 2H), 1.28 (d, $J = 3.7$ Hz, 3H), 1.26 (d, $J = 3.6$ Hz, 3H).



Name- Ehrain
Room No- G53B
Sample- EO-104P



Methyl 6-(4-methylbenzenesulfonamido)-8-oxo-1-azaspiro[4.5]decane-1-carboxylate 15

