Electronic Supplementary Material (ESI) for Chemical Communications

Structural analysis and reactivity of unusual tetrahedral intermediates enabled by SmI_2-mediated reduction of barbituric acids: vinylogous N-acyliminium additions to α-alkoxy-N-Ac-carbamides

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Supplementary Information

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List of Known Compounds/General Methods

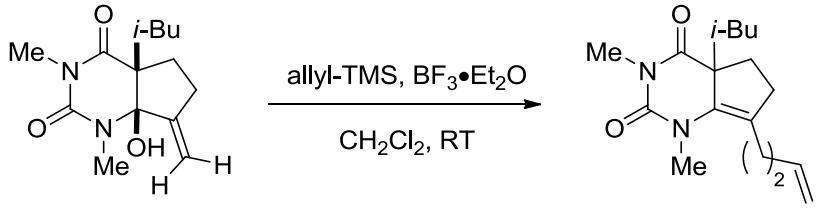
All starting materials reported in the manuscript have been previously described.[1-2] Samarium(II) iodide was prepared by standard methods and titrated prior to use.[3-7] All experiments involving SmI_2 were performed using standard techniques under argon or nitrogen atmosphere unless stated otherwise. All solvents were purchased at the highest commercial grade and used as received or after purification by passing through activated alumina columns or distillation from sodium/benzophenone (tetrahydrofuran) or calcium hydride (dichloromethane) under nitrogen. All solvents were deoxygenated prior to use. All other chemicals were purchased at the highest commercial grade and used as received. Reaction glassware was oven-dried at 140 °C for at least 24 h or flame-dried prior to use, allowed to cool under vacuum and purged with argon (three cycles). All yields refer to isolated yields unless stated otherwise. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on Bruker spectrometers at 300, 400 and 500 MHz (^{1}H NMR) and 75, 100 and 125 MHz (^{13}C NMR). All shifts are reported in parts per million (ppm) relative to residual $CHCl_3$ peak (7.27 and 77.2 ppm, ^{1}H NMR and ^{13}C NMR, respectively). All coupling constants (J) are reported in hertz (Hz). Abbreviations are: s, singlet; d, doublet; t, triplet; q, quartet; br s, broad singlet. GC-MS chromatography was performed using Agilent 7890A GC System and Agilent 5975C inert XL EI/CI MSD with Triple Axis Detector equipped with Agilent HP-5MS column (19091S-433) (length 30 m, internal diameter 0.25 mm, film 0.25 μm) using helium as the carrier gas at a flow rate of 1 mL/min and an initial oven temperature of 40 °C or 50 °C. The injector temperature was 250 °C. The detector temperature was 250 °C. For runs with the initial oven temperature of 50 °C, temperature was increased with a 25 °C/min ramp after 50 °C hold for 3 min to a final temperature of 300 °C, then hold at 300 °C for 5 min (splitlesss mode of injection, total run time of 18 min). All flash chromatography was performed using silica gel, 60 Å, 230−400 mesh. TLC analysis was carried out on aluminium sheets coated with silica gel 60 F254, 0.2 mm thickness. The plates were visualized using a 254 nm ultraviolet lamp or aqueous potassium permanganate solutions. ^{1}H NMR and ^{13}C NMR data are given for all compounds in the Supporting Experimental for characterization purposes. ^{1}H NMR, ^{13}C NMR, IR and HRMS data are reported for all new compounds. All compounds have been prepared as racemates.

Experimental Procedures and Characterization Data

General procedure for the vinylogous N-acyliminium additions. An oven-dried vial equipped with a stir bar was charged with hemiaminal substrate (neat), placed under a positive pressure of argon, and subjected to three evacuation/backfilling cycles under high vacuum. Dichloromethane was added, followed by silicon-based nucleophile (neat, typically, 10 equiv) and the mixture was stirred vigorously under argon. Lewis acid (BF_3•Et_2O, typically, 3 equiv) was added at room temperature, and the reaction mixture was stirred for the indicated time. The reaction was diluted with CH_2Cl_2 (20 mL) and HCl (0.1 *N*, 20 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL), the organic layers were combined, dried over Na_2SO_4, filtered, and concentrated. The sample was analyzed by ^{1}H NMR ($CDCl_3$, 400 and 500 MHz) to obtain 1,4/1,2 selectivity, conversion and yield using internal standard and comparison with authentic samples. Purification by chromatography using silica gel afforded the title product.

Vinylogous N-Acyliminium Addition to alpha-Alkoxy-N-Acylcarbamides

Table 2, Entry 1

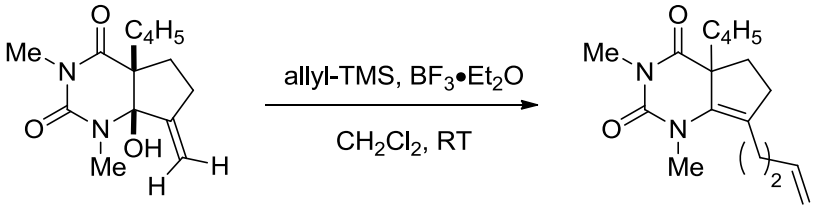


6a **7a**

7-(But-3-en-1-yl)-4a-isobutyl-1,3-dimethyl-5,6-dihydro-1*H*-cyclopenta[d]pyrimidine-2,4(3*H*,4a*H*)-dione (7a). To a solution of allylic hemiaminal (4a*S*,7a*R*)-7a-hydroxy-4a-isobutyl-1,3-dimethyl-7-methylenetetrahydro-1*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*,4a*H*)-dione **6a** (37.6 µmol, 1.0 equiv) and allyltrimethylsilane (0.38 mmol, 10 equiv) in CH_2Cl_2 (1.0 mL), BF_3•OEt_2 (24 µL, 0.19 mmol, 5.0 equiv) was added dropwise at room temperature and the reaction mixture was stirred for 3 hours. The reaction was diluted with NH_4Cl (aq, sat., 2.0 mL), extracted with CH_2Cl_2 (3 × 2.0 mL), dried and concentrated. Purification by chromatography on silica gel (20% EtOAc/petroleum ether) afforded the title compound as a colorless oil. Yield 89%. 1,4/1,2 selectivity >95:5. ^{1}H NMR (500 MHz, $CD_3C(O)CD_3$) δ 0.83 (d, *J* = 6.6 Hz, 3 H), 0.91 (d, *J* = 6.6 Hz, 3 H), 1.41 (dd, *J* = 14.0, 6.6 Hz, 1 H), 1.51 (dd, *J* = 14.0, 5.0 Hz, 1 H), 1.60-1.69 (m , 1 H),

2.01 (ddd, *J* = 13.3, 8.5, 1.6 Hz, 1 H), 2.15 (dt, *J* = 13.3, 9.4 Hz, 1 H), 2.19-2.33 (m, 4 H), 2.40-2.48 (m, 1 H), 2.48-2.55 (m, 1 H), 3.07 (s, 3 H), 3.32 (s, 3 H), 4.95 (ddt, *J* = 10.2, 2.0, 0.9 Hz, 1 H), 5.05 (dq, *J* = 17.1, 1.6 Hz, 1 H), 5.84 (ddt, *J* = 17.1, 10.2, 6.6 Hz, 1 H). ^{13}C NMR (125 MHz, $CD_3C(O)CD_3$) δ 24.5, 24.9, 25.9, 28.5, 28.9, 30.1, 32.7, 32.9, 35.7, 45.6, 57.1, 115.6, 125.8, 133.7, 138.9, 153.2, 175.3. IR (neat) 754, 912, 995, 1031, 1090, 1162, 1281, 1310, 1374, 1414, 1447, 1668, 1718, 2847, 2866, 2917, 2955. HRMS calcd for $C_{17}H_{27}N_2O_2$ (M^+ + H) 291.2073, found 291.2080.

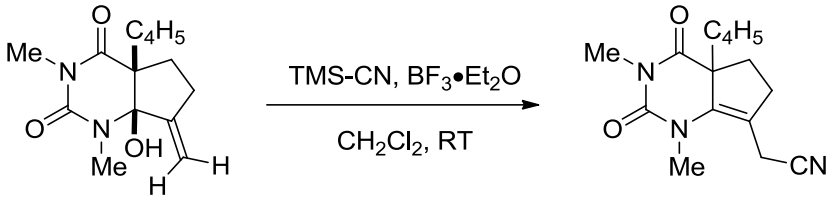
Table 2, Entry 2



6b **7b**

7-(But-3-en-1-yl)-4a-(but-3-yn-1-yl)-1,3-dimethyl-1,4a,5,6-tetrahydro-2*H*-cyclopenta[*d*] pyrimidine-2,4(3*H*)-dione (7b). According to the general procedure, the reaction of allylic hemiaminal (4a*R*,7a*R*)-4a-(but-3-yn-1-yl)-7a-hydroxy-1,3-dimethyl-7-methylenetetrahydro-1*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*,4a*H*)-dione **6b** (38.1 μmol, 1.0 equiv), allyltrimethysilane (0.38 μmol, 10 equiv) and BF_3•OEt_2 (0.19 mmol, 5.0 equiv) in CH_2Cl_2 (1.0 mL) at room temperature for 3 h, afforded after purification by chromatography (40% EtOAc/petroleum ether) the title compound as a colorless oil. Yield 82%. 1,4/1,2 selectivity >95:5. ^{1}H NMR (400 MHz, $CD_3C(O)CD_3$) δ 1.75-1.83 (m, 2 H), 2.06-2.11 (m, 1 H), 2.13-2.21 (m, 3 H), 2.23-2.33 (m, 4 H), 2.36 (t, *J* = 2.6 Hz, 1 H), 2.43-2.59 (m, 2 H), 3.08 (s, 3 H), 3.34 (s, 3 H), 4.96 (ddt, *J* = 1.1, 2.0, 10.2 Hz, 1 H), 5.06 (dq, *J* = 1.6, 17.1 Hz, 1 H), 5.86 (ddt, *J* = 6.5, 10.2, 17.1 Hz, 1 H). ^{13}C NMR (100 MHz, $CD_3C(O)CD_3$) δ 14.6, 28.5, 28.9, 29.6, 32.8, 33.0, 35.6, 36.1, 56.9, 70.3, 84.3, 115.7, 126.3, 132.3, 138.9, 152.8, 174.7. IR (neat) 638, 751, 914, 964, 997, 1050, 1073, 1142, 1281, 1374, 1415, 1450, 1665, 1716, 2851, 2925, 2953, 3269. HRMS calcd for $C_{17}H_{23}N_2O_2$ (M^+ + H) 287.1760, found 287.1754.

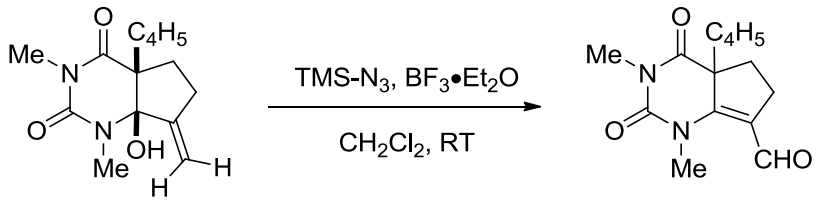
Table 2, Entry 3



6b **7c**

2-(4a-(But-3-yn-1-yl)-1,3-dimethyl-2,4-dioxo-2,3,4,4a,5,6-hexahydro-1*H*-cyclopenta[*d*] pyrimidin-7-yl)acetonitrile (7c). According to the general procedure, the reaction of allylic hemiaminal (4a*R*,7a*R*)-4a-(but-3-yn-1-yl)-7a-hydroxy-1,3-dimethyl-7-methylenetetrahydro-1*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*,4a*H*)-dione **6b** (38.1 µmol, 1.0 equiv), trimethylsilyl cyanide (0.38 µmol, 10 equiv) and BF_3•OEt_2 (0.19 mmol, 5.0 equiv) in CH_2Cl_2 (1.0 mL) at room temperature for 3 h afforded after purification by chromatography (40% EtOAc/petroleum ether) the title compound as a colorless oil. Yield 74%. 1,4/1,2 selectivity >95:5. Note that the title compound is unstable. ^{1}H NMR (400 MHz, $CD_3C(O)CD_3$) δ 1.70-1.76 (m, 2 H), 2.00-2.13 (m, 4 H), 2.24 (t, *J* = 2.6 Hz, 1 H), 2.29-2.38 (m, 1 H), 2.46-2.59 (m, 1 H), 2.97 (s, 3 H), 3.29 (s, 3 H), 3.43-3.62 (m, 2 H). ^{13}C NMR (100 MHz, $CD_3C(O)CD_3$) δ 14.6, 17.8, 28.6, 29.5, 33.0, 35.2, 36.1, 57.2, 70.4, 84.1, 114.0, 117.8, 136.3, 152.7, 173.9. IR (neat) 645, 751, 1051, 1075, 1148, 1279, 1303, 1324, 1375, 1416, 1450, 1664, 1719, 2852, 2921, 3284. HRMS (EI) calcd for $C_{15}H_{17}N_3O_2$ (M^+) 271.1315, found 271.1313.

Table 2, Entry 4

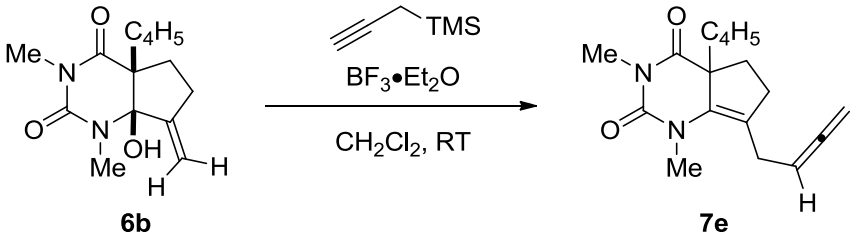


6b **7d**

4a-(But-3-yn-1-yl)-1,3-dimethyl-2,4-dioxo-2,3,4,4a,5,6-hexahydro-1*H*-cyclopenta[*d*] pyrimidine-7-carbaldehyde (7d). According to the general procedure, the reaction of allylic hemiaminal (4a*R*,7a*R*)-4a-(but-3-yn-1-yl)-7a-hydroxy-1,3-dimethyl-7-methylenetetrahydro-1*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*,4a*H*)-dione **6b** (38.1 µmol, 1.0 equiv), trimethylsilylazide (0.38 µmol, 10 equiv) and BF_3•OEt_2 (0.19 mmol, 5.0 equiv) in CH_2Cl_2 (1.0 mL) at room temperature for 3 h afforded after purification by chromatography (40% EtOAc/petroleum ether) the title

compound as a colorless oil. Yield 51%. 1,4/1,2 selectivity >95:5. Note that the title compound is unstable. ^{1}H NMR (400 MHz, $CD_3C(O)CD_3$) δ 1.95-2.02 (m, 2 H), 2.06-2.10 (m, 1 H), 2.13-2.35 (m, 3 H), 2.39 (t, *J* = 2.8 Hz, 1 H), 2.50 (ddd, *J* = 7.5, 10.3, 15.8 Hz, 1 H), 2.62-2.71 (m, 1 H), 3.17 (s, 3 H), 3.66 (s, 3 H), 10.16 (s, 1 H). ^{13}C NMR (100 MHz, $CD_3C(O)CD_3$) δ 14.9, 26.9, 28.9, 29.3, 37.0, 38.2, 58.5, 70.6, 83.8, 122.9, 151.9, 152.0, 172.5, 187.0. IR (neat) 644, 721, 750, 914, 962, 1054, 1073, 1137, 1244, 1286, 1322, 1372, 1426, 1600, 1676, 1728, 2854, 2924, 2952, 3269. HRMS calcd for $C_{14}H_{17}N_2O_3$ (M^+ + H) 261.1239, found 261.1235.

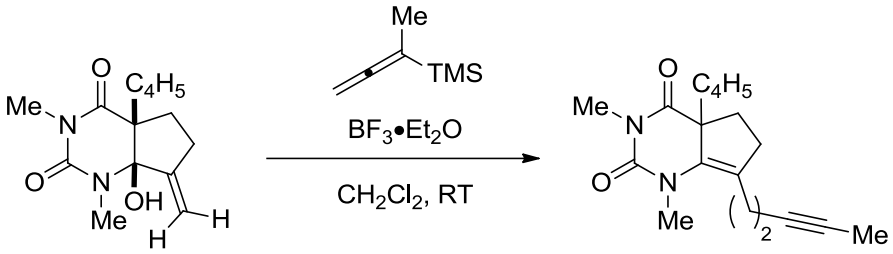
Table 2, Entry 5



6b **7e**

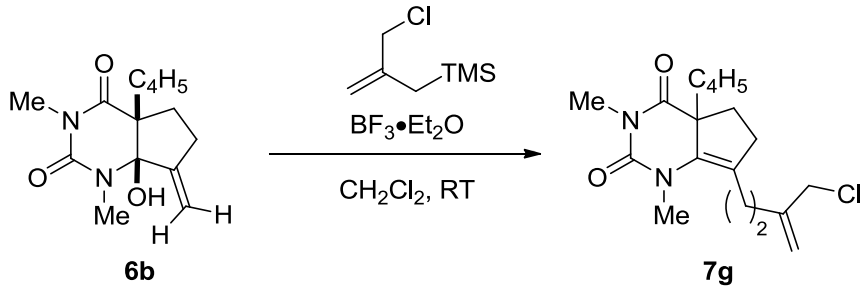
4a-(But-3-yn-1-yl)-7-(buta-2,3-dien-1-yl)-1,3-dimethyl-5,6-dihydro-1*H*-cyclopenta [*d*]pyrimidine-2,4(3*H*,4a*H*)-dione (7e). According to the general procedure, the reaction of allylic hemiaminal (4a*R*,7a*R*)-4a-(but-3-yn-1-yl)-7a-hydroxy-1,3-dimethyl-7-methylene tetrahydro-1*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*,4a*H*)-dione **6b** (38.1 μmol, 1.0 equiv), trimethyl(propargyl)silane (0.38 μmol, 10 equiv) and BF_3•OEt_2 (0.19 mmol, 5.0 equiv) in CH_2Cl_2 (1.0 mL) at room temperature for 3 h afforded the title compound in 77% yield (determined by ^{1}H NMR analysis). Note that the title compound is unstable. Analytical sample was obtained after careful purification by chromatography (40% EtOAc/petroleum ether) to give the title compound as a colorless oil. 1,4/1,2 selectivity >95:5. ^{1}H NMR (400 MHz, $CD_3C(O)CD_3$) δ 1.76 - 1.83 (m, 2 H), 2.07-2.12 (m, 1 H), 2.12-2.29 (m, 4 H), 2.35 (t, *J* = 2.8 Hz, 1 H), 2.52-2.64 (m, 1 H), 2.76-2.90 (m, 1 H), 3.08 (s, 3 H), 3.09-3.17 (m, 1 H), 3.35 (s, 3 H), 4.78 (dt, *J* = 3.5, 7.0 Hz, 2 H), 5.26 (quin, *J* = 6.5 Hz, 1 H). ^{13}C NMR (100 MHz, $CD_3C(O)CD_3$) δ 14.6, 28.4, 28.5, 29.6, 33.3, 35.3, 36.2, 57.1, 70.3, 76.3, 84.1, 88.4, 124.1, 133.0, 152.8, 174.6, 210.1. IR (neat) 638, 751, 848, 1050, 1074, 1146, 1285, 1374, 1415, 1449, 1664, 1717, 2851, 2923, 2953, 3290. HRMS calcd for $C_{17}H_{21}N_2O_2$ (M^+ + H) 285.1603, found 285.1591.

Table 2, Entry 6



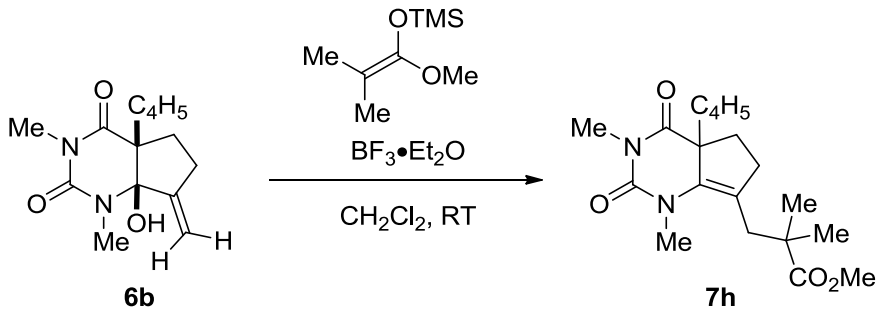
4a-(But-3-yn-1-yl)-1,3-dimethyl-7-(pent-3-yn-1-yl)-1,4a,5,6-tetrahydro-2*H*-cyclopenta[*d*] pyrimidine-2,4(3*H*)-dione (7f). According to the general procedure, the reaction of allylic hemiaminal (4a*R*,7a*R*)-4a-(but-3-yn-1-yl)-7a-hydroxy-1,3-dimethyl-7-methylenetetrahydro-1*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*,4a*H*)-dione **6b** (38.1 µmol, 1.0 equiv), 3-(trimethylsilyl)-1,2-butadiene (0.38 µmol, 10 equiv) and BF_3•OEt_2 (0.19 mmol, 5.0 equiv) in CH_2Cl_2 (1.0 mL) at room temperature for 3 h afforded the title compound in 64% yield (determined by ^{1}H NMR analysis). Careful purification by chromatography (40% EtOAc/petroleum ether) afforded the title compound as a colorless oil. The title compound was inseparable from an unidentified impurity. 1,4/1,2 selectivity >95:5. Assigned through a combination of 1D and 2D NMR experiments: ^{1}H NMR (500 MHz, $CD_3C(O)CD_3$) δ 1.73 (t, *J* = 2.4 Hz, 3 H), 1.78-1.84 (m, 2 H), 2.06-2.11 (m, 1 H), 2.12-2.29 (m, 4 H), 2.29-2.35 (m, 3 H), 2.36 (t, *J* = 2.8 Hz, 1 H), 2.49-2.57 (m, 1 H), 2.57-2.64 (m, 1 H), 3.08 (s, 3 H), 3.41 (s, 3 H). ^{13}C NMR (125 MHz, $CD_3C(O)CD_3$) δ 3.0, 14.4, 17.9, 28.5, 28.5, 29.6, 32.5, 35.6, 36.2, 57.1, 70.3, 77.4, 78.9, 84.3, 125.7, 132.7, 153.0, 175.2. IR (neat) 638, 752, 836, 1051, 1072, 1129, 1148, 1247, 1282, 1375, 1415, 1451, 1662, 1716, 2851, 2918, 2950, 3279. HRMS calcd for $C_{18}H_{23}N_2O_2$ (M^+ + H) 299.1754, found 299.1758.

Table 2, Entry 7



4a-(But-3-yn-1-yl)-7-(3-(chloromethyl)but-3-en-1-yl)-1,3-dimethyl-1,4a,5,6-tetrahydro-2*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*)-dione (7g). According to the general procedure, the reaction of allylic hemiaminal (4a*R*,7a*R*)-4a-(but-3-yn-1-yl)-7a-hydroxy-1,3-dimethyl-7-methylene tetrahydro-1*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*,4a*H*)-dione **6b** (38.1 µmol, 1.0 equiv), 2-(chloromethyl)allyl-trimethylsilane (0.38 µmol, 10 equiv) and BF_3•OEt_2 (0.19 mmol, 5.0 equiv) in CH_2Cl_2 (1.0 mL) at room temperature for 3 h afforded after purification by chromatography (40% EtOAc/petroleum ether) the title compound as a colorless oil. Yield 76%. 1,4/1,2 selectivity >95:5. ^{1}H NMR (500 MHz, $CD_3C(O)CD_3$) δ 1.77-1.83 (m, 2 H), 2.06-2.11 (m, 1 H), 2.11-2.22 (m, 3 H), 2.29-2.35 (m, 1 H), 2.36 (t, *J* = 2.7 Hz, 1 H), 2.37-2.48 (m, 3 H), 2.51-2.61 (m, 2 H), 3.07-3.09 (m, 3 H), 3.37 (s, 3 H), 4.20 (br. d, *J* = 0.9 Hz, 2 H), 5.05 (d, *J* = 1.3 Hz, 1 H), 5.20 (br. s, 1 H). ^{13}C NMR (125 MHz, $CD_3C(O)CD_3$) δ 14.6, 27.7, 28.6, 29.6, 32.1, 32.8, 35.5, 36.1, 48.8, 57.0, 70.3, 84.0, 115.3, 126.1, 132.8, 146.0, 153.4, 174.2. IR (neat) 637, 750, 857, 909, 965, 1051, 1075, 1126, 1144, 1280, 1376, 1415, 1448, 1664, 1715, 2851, 2925, 2950, 3291. HRMS calcd for $C_{18}H_{24}N_2O_2Cl$ (M^+ + H) 335.1526, found 335.1513.

Table 2, Entry 8



Methyl 3-(4a-(but-3-yn-1-yl)-1,3-dimethyl-2,4-dioxo-2,3,4,4a,5,6-hexahydro-1*H*-cyclopenta[*d*]pyrimidin-7-yl)-2,2-dimethylpropanoate (7h). According to the general procedure, the reaction of allylic hemiaminal (4a*R*,7a*R*)-4a-(but-3-yn-1-yl)-7a-hydroxy-1,3-dimethyl-7-methylenetetrahydro-1*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*,4a*H*)-dione **6b** (38.1 µmol, 1.0 equiv), 1-methoxy-2-methyl-1-(trimethylsiloxy)propene (0.38 µmol, 10 equiv) and BF_3•OEt_2 (0.19 mmol, 5.0 equiv) in CH_2Cl_2 (1.0 mL) at room temperature for 3 h afforded after purification by chromatography (40% EtOAc/petroleum ether) the title compound as a colorless oil. Yield 81%. 1,4/1,2 selectivity >95:5. ^{1}H NMR (400 MHz, $CD_3C(O)CD_3$) δ 1.17 (s, 3 H), 1.23 (s, 3 H), 1.79 (ddd, *J* = 4.0, 7.2, 8.7 Hz, 2 H), 2.06-2.09 (m, 2 H), 2.13-2.21 (m, 3 H), 2.38 (t, *J* = 2.8 Hz, 1 H),

2.33-2.42 (m, 1 H), 2.55 (d, *J* = 14.5 Hz, 1 H), 2.65 (d, *J* = 14.5 Hz, 1 H), 3.07 (s, 3 H), 3.34 (s, 3 H), 3.61 (s, 3 H). ^{13}C NMR (100 MHz, $CD_3C(O)CD_3$) δ 14.6, 26.0, 26.2, 28.5, 29.6, 33.4, 35.6, 35.6, 39.3, 43.2, 52.1, 56.5, 70.4, 84.1, 124.8, 134.8, 153.1, 174.7, 178.1. IR (neat) 643, 752, 857, 959, 982, 998, 1050, 1075, 1140, 1192, 1281, 1367, 1415, 1450, 1666, 1716, 2846, 2923, 2952, 3270. HRMS calcd for $C_{19}H_{26}N_2O_4Na$ (M^+ + Na) 369.1785, found 369.1785.

Table SI-1. Crystal Data and Structure Refinement Summaries for **1**-**4**.

Compound	**1**	**2**	**3**	**4**
Empirical Formula	$[C_{12}H_{18}N_2O_3]$	$[C_{17}H_{30}N_2O_3Si]$	$[C_{15}H_{20}N_2O_4]$	$[C_{14}H_{24}N_2O_3]$
Fw	238.28	338.52	292.33	268.35
T (K)	100(2)	100(2)	100(2)	100(2)
λ (Å)	1.54178	1.54178	1.54178	1.54178
Cryst. Syst.	Monoclinic	Monoclinic	Monoclinic	Triclinic
Space Group	P2(1) /c	P2(1) /c	P2(1) /c	P-1
a (Å)	8.3649(4)	24.0386(14)	9.9234(8)	10.6950(4)
b (Å)	6.9926(4)	17.4493(11)	11.5741(8)	11.6833(4)
c (Å)	19.9506 (10)	18.3975(13)	25.7812(19)	13.3792(5)
α (deg)	90	90	90	81.732
β (deg)	93.726(3)	90	92.474	67.685
γ (deg)	90	90	90	66.432
V ($Å^3$)	1164.49(10)	7717.0(9)	2958.3	1417.50(9)
Z	4	16	8	4
d_{calcd} (mg/m^3)	1.359	1.165	1.313	1.257
Abs coeff (mm^{-1})	0.807	1.198	0.791	0.715
F(000)	512	2944	1248	584
Crystal size (mm)	0.18 x 0.16 x 0.03	0.18 x 0.13 x 0.07	0.22 x 0.19 x 0.06	0.12 x 0.04 x 0.02
θ range (deg)	5.30-72.96	1.84-69.89	3.43-70.11	4.13-68.21
limiting indices	-10<=h<=8 -8<=k<=6 -23<=l<=24	-28<=h<=27 -21<=k<=21 -22<=l<=22	-11<=h<=11 -13<=k<=14 -31<=l<=27	-12<=h<=12 -14<=k<=14 -16<=l<=16
Reflns collected	7587	13438	11362	15959
Independent reflections/R_{int}	2266/0.0537	13438/0.0000	5181/0.0514	4999/0.0616
Completeness [%]	98.8	94.4	94.6	96.8
Absorption correction	Semi-empirical from equivalents	Semi-empirical from equivalents	Semi-empirical from equivalents	Semi-empirical from equivalents
Max, Min Transm.	0.9762, 0.660645	0.9209, 0.628481	0.9541, 0.623021	0.9859, 0.761355
Refinement method	Full-matrix least squares on F^2	Full-matrix least squares on F^2	Full-matrix least squares on F^2	Full-matrix least squares on F^2
Data/Restraints/ Params	2266/0/157	13438/0/862	5181/0/387	4999/0/355
GOF (F^2)	1.059	0.977	1.033	1.016
Final R indices (R1, wR2)	0.1005, 0.2615	0.0912, 0.2155	0.0545, 0.1413	0.0487, 0.1220
R indices (all data)	0.1118, 0.2736	0.1642, 0.2779	0.0664, 0.1491	0.0622, 0.1313
Largest diff. peak and hole ($e.Å^{-3}$)	1.520 and -0.384	0.554 and -0.625	0.323 and -0.369	0.311 and -0.261

Figure SI-1. ORTEP Structure of **1 (CCDC 972705)**.

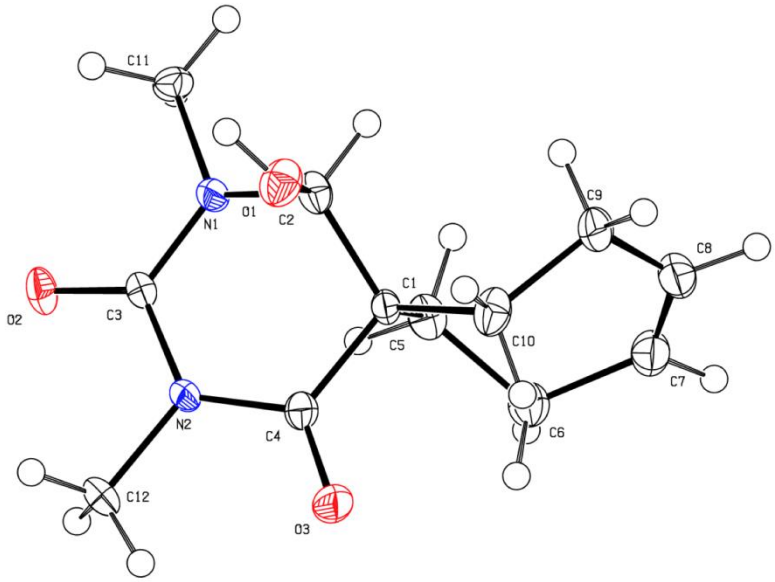


Figure SI-2. ORTEP Structure of **2 (CCDC 972704)**.

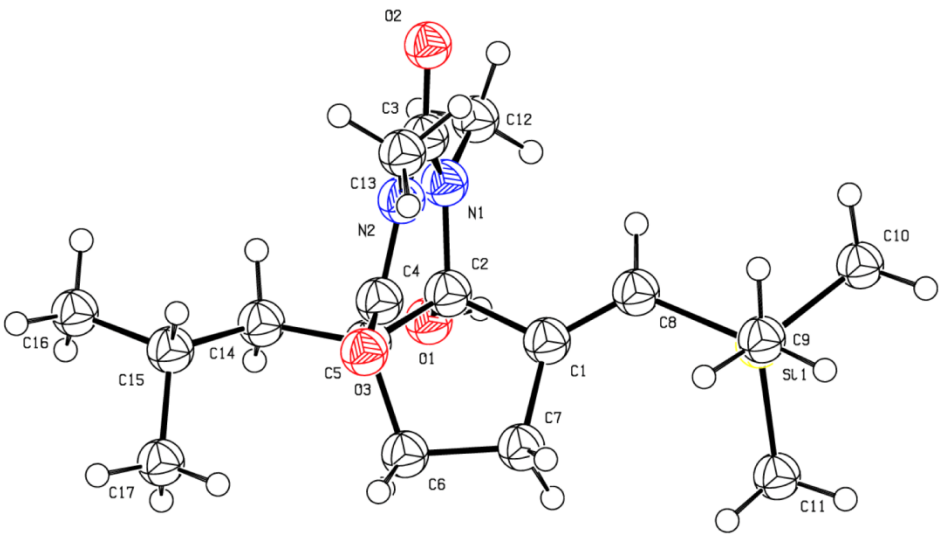


Figure SI-3. ORTEP Structure of **3 (CCDC 948381)**.

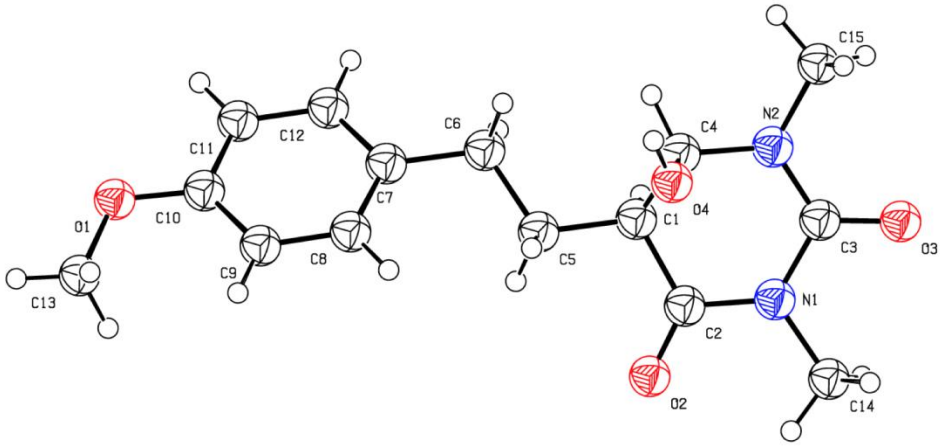


Figure SI-4. ORTEP Structure of **4 (CCDC 948382)**.

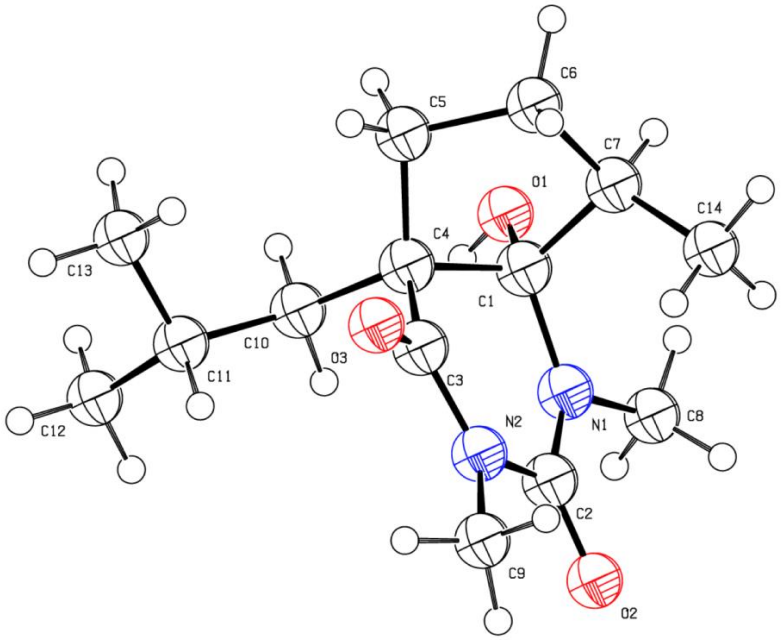


Table SI-2. Selected bond lengths and angles of **1**.

bond	[Å]	angle	[Å]
C1–C2	1.522	N1–C2–O1–H1	-43.5
C2–O1	1.407	H2–C2–O1–H1	77.4
C2–H2	1.000	C1–C2–O1–H1	-164.1
N1–C2	1.463	C11–N1–C2–O1	95.1
O1–H1	0.839	C3–N1–C2–O1	-70.8
N1–C3	1.338	C5–C1–C2–H2	-59.8
C3–O2	1.224	C5–C1–C2–O1	-178.3
N1–C11	1.464	C10–C1–C2–H2	63.6
N2–C3	1.413	C10–C1–C2–O1	-54.9
N2–C12	1.477	C10–C1–C2–N1	-177.7
N2–C4	1.389	H2–C2–C1–C4	-175.8
C4–O3	1.215	N1–C3–N2–C4	-9.5
C1–C4	1.528	C3–N2–C4–C1	-3.6

Table SI-3A. Selected bond lengths of **2**.[a]

bond[a]	[Å]	bond[b]	[Å]
C2–C5	1.53	C2–C5	1.530
C2–C1	1.52	C2–C1	1.524
C2–O1	1.422	C2–O1	1.409
N1–C2	1.47	N1–C2	1.470
O1–H1	0.840	O1–H1	0.840
N1–C3	1.37	N1–C3	1.344
C3–O2	1.231	C3–O2	1.230
N1–C12	1.465	N1–C12	1.458
N2–C3	1.386	N2–C3	1.399
N2–C13	1.48	N2–C13	1.472
N2–C4	1.36	N2–C4	1.381

C4–O3	1.21	C4–O3	1.206
C5–C4	1.53	C5–C4	1.524
C1–C8	1.34	C1–C8	1.331
C8–H8	0.948	C8–H8	0.949
C8–Si1	1.862	C8–Si1	1.868

[a]Four molecules in the unit cell (representative bond lengths and angles are shown). [b]Refers to an independent determination of crystallographic structure of **2**.

Table SI-3B. Selected angles of **2**.[a]

angle[a]	[deg]	angle[b]	[deg]
N1–C2–O1–H1	74.9	N1–C2–O1–H1	-100.6
C1–C2–O1–H1	-51.0	C1–C2–O1–H1	26.2
C5–C2–O1–H1	-163.9	C5–C2–O1–H1	139.2
C12–N1–C2–O1	-31.5	C12–N1–C2–O1	32.8
C3–N1–C2–O1	156.9	C3–N1–C2–O1	-155.5
C14–C5–C2–O1	-50.1	C14–C5–C2–O1	49.7
C14–C5–C2–C1	-166.7	C14–C5–C2–C1	167.5
C6–C5–C2–O1	74.6	C6–C5–C2–O1	-75.1
C6–C5–C2–C1	-42.4	C6–C5–C2–C1	42.7
C6–C5–C2–N1	-166.5	C6–C5–C2–N1	166.2
O1–C2–C5–C4	-172.0	O1–C2–C5–C4	170.6
N1–C3–N2–C4	-11	N1–C3–N2–C4	11.4
C3–N2–C4–C5	-8	C3–N2–C4–C5	8.2
N2–C4–C5–C2	39.3	N2–C4–C5–C2	-39.2
C4–C5–C2–N1	-52.7	C4–C5–C2–N1	51.9
C5–C2–N1–C3	37.9	C5–C2–N1–C3	-37.1
C2–N1–C3–N2	-5	C2–N1–C3–N2	4.6
C8–C1–C7–C6	169.3	C8–C1–C7–C6	-167.5
C8–C1–C2–N1	-23	C8–C1–C2–N1	23.5
C8–C1–C2–O1	99.8	C8–C1–C2–O1	99.8
C8–C1–C2–C5	-144.8	C8–C1–C2–C5	144.4

H8–C8–C1–C2	-1	H8–C8–C1–C2	-0.3
H8–C8–C1–C7	-176.5	H8–C8–C1–C7	177.3
Si1–C8–C1–C2	178.7	Si1–C8–C1–C2	179.6
Si1–C8–C1–C7	4	Si1–C8–C1–C7	-2.8

[a]Four molecules in the unit cell (representative bond lengths and angles are shown). [b]Refers to an independent determination of crystallographic structure of **2** ($N_{lp}\rightarrow\sigma^*_{C-O}$ = 61.4°; $O_{lp1}\rightarrow\sigma^*_{C-N}$ = 139.4°; $O_{lp2}\rightarrow\sigma^*_{C-C(ext)}$ = 146.2°; $O_{lp2}\rightarrow\sigma^*_{C-C(int)}$ = 100.8°)

Table SI-4A. Selected bond lengths of **3**.[a]

bond	[Å]	bond	[Å]
C1–C4	1.518	C16–C19	1.519
C4–H4A	1.00	C19–H19	1.00
C4–O4	1.413	C19–O8	1.411
N2–C4	1.461	N4–C19	1.458
O4–H4	0.840	O8–H8	0.840
N2–C3	1.343	N4–C18	1.352
C3–O3	1.229	C18–O7	1.236
N2–C15	1.467	N4–C30	1.463
N1–C3	1.401	N3–C18	1.395
N1–C14	1.471	N3–C29	1.469
N1–C2	1.390	N3–C17	1.392
C2–O2	1.210	C17–O6	1.214
C2–C1	1.514	C17–C16	1.511

[a]Two molecules in the unit cell.

Table SI-4B. Selected angles of **3**.[a]

angle	[deg]	angle	[deg]
N2–C4–O4–H4	109.5	N4–C19–O8–H8	103.0
H4A–C4–O4–H4	-10.7	H19–C19–O8–H8	-17.4
C1–C4–O4–H4	-130.8	C16–C19–O8–H8	-136.9
C15–N2–C4–O4	-87.6	C30–N4–C19–O8	-81.8
C3–N2–C4–O4	72.9	C18–N4–C19–O8	72.5

H1–C1–C4–H4A	57.0	H16–C16–C19–H19	60.9
H1–C1–C4–O4	177.2	H16–C16–C19–O8	-179.7
C5–C1–C4–H4A	-61.1	C20–C16–C19–H19	-58.0
C5–C1–C4–O4	59.1	C20–C16–C19–O8	61.4
C5–C1–C4–N2	179.6	C20–C16–C19–N4	-177.6
H4A–C4–C1–C2	173.8	H19–C19–C16–C17	177.4
N2–C3–N1–C2	9.5	N4–C18–N3–C17	7.0
C3–N1–C2–C1	1.4	C18–N3–C17–C16	7.7
N1–C2–C1–C4	-33.7	N3–C17–C16–C19	-39.6
C2–C1–C4–N2	54.5	C17–C16–C19–N4	57.8
C1–C4–N2–C3	-47.5	C16–C19–N4–C18	-47.5
C4–N2–C3–N1	15.6	C19–N4–C18–N3	14.4

[a]Two molecules in the unit cell.

Table SI-5A. Selected bond lengths of **4**.[a]

bond	[Å]	bond	[Å]
C1–C4	1.549	C15–C18	1.552
C1–C7	1.561	C15–C21	1.553
C1–O1	1.407	C15–O4	1.407
N1–C1	1.466	N3–C15	1.466
O1–H1	0.840	O4–H4	0.840
N1–C2	1.350	N3–C16	1.354
C2–O2	1.222	C16–O5	1.218
N1–C8	1.471	N3–C22	1.469
N2–C2	1.423	N4–C16	1.421
N2–C9	1.465	N4–C23	1.468
N2–C3	1.366	N4–C17	1.370
C3–O3	1.227	C17–O6	1.225
C4–C3	1.514	C18–C17	1.514

[a]Two molecules in the unit cell.

Table SI-5B. Selected angles of **4**.[a]

angle	[deg]	angle	[deg]
N1–C1–O1–H1	51.0	N3–C15–O4–H4	-52.1
C7–C1–O1–H1	175.1	C21–C15–O4–H4	-176.3
C4–C1–O1–H1	-71.5	C18–C15–O4–H4	70.8
C8–N1–C1–O1	40.1	C22–N3–C15–O4	-40.6
C2–N1–C1–O1	-154.8	C16–N3–C15–O4	155.1
C10–C4–C1–O1	48.6	C24–C18–C15–O4	-48.9
C10–C4–C1–C7	161.9	C24–C18–C15–C21	-161.9
C5–C4–C1–O1	-75.5	C19–C18–C15–O4	74.6
C5–C4–C1–C7	37.7	C19–C18–C15–C21	-38.4
C5–C4–C1–N1	163.5	C19–C18–C15–N3	-163.9
O1–C1–C4–C3	167.8	O4–C15–C18–C17	-167.8
N1–C2–N2–C3	4.6	N3–C16–N4–C17	-3.6
C2–N2–C3–C4	14.2	C16–N4–C17–C18	-14.6
N2–C3–C4–C1	-39.2	N4–C17–C18–C15	39.0
C3–C4–C1–N1	46.8	C17–C18–C15–N3	-46.2
C4–C1–N1–C2	-32.9	C18–C15–N3–C16	32.9
C1–N1–C2–N2	6.2	C15–N3–C16–N4	-6.9

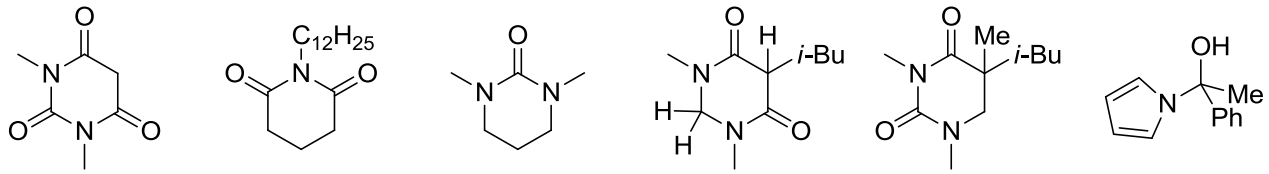
[a]Two molecules in the unit cell.

Table SI-6. Selected Spectroscopic Properties of **1-4** and Related Carbonyl Derivatives.

entry	aminal or derivative	δ^{13}_{C-OH} [a]	$\delta^{13}_{C=O1}$ [a]	$\delta^{13}_{C=O2}$ [a]	$\Delta\delta_{C-OH}$ [b]	$\nu_{C=O1}$ [c]	$\nu_{C=O2}$ [c]
1	**1**	84.6	153.7	175.0	4.0	1658	1709
2	**2**	93.2	153.6	174.2	12.6	1645	1709
3	**3**	80.6	154.1	171.5	-	1657	1711
4	**4**	95.4	153.1	173.9	14.8	1644	1704
5	**SI-A**	-	153.4	166.5	-	1659.1	1690.1
6	**SI-B**	-	-	173.0	-	1671.5	1725.8
7	**SI-C**	-	157.0	-	-	1623.7	-
8	**SI-D**	-	-	169.1	-	1655.2	1678.7
9	**SI-E**	-	153.9	174.9	-	1672.3	1712.4
10[8]	**5**	86.1	-	-	-	-	-

[a] δ ^{13}C NMR C–OH and δ ^{13}C NMR C=O [ppm]; entries 1-4: measured at 100 MHz in $CD_3C(O)CD_3$; entries 5-9: measured at 75 MHz in $CD_3C(O)CD_3$. Entry 9: in $CDCl_3$. For α-Me/α-$C_{10}H_{21}$ analogue of **SI-E**: δ^{13}C=O 154.2 and 175.3 in $CD_3C(O)CD_3$. Entry 10: measured in $CDCl_3$ at 100 MHz. [b] $\Delta\delta^{13}$C–OH = [δ^{13}C–OH - 80.6]. [c] $\nu_{C=O}$ [cm^{-1}].

Figure SI-5. Reference Carbonyl and α-Amino Alcohol Derivatives **A-E** and **5**.



1,3-Dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (SI-A). Table SI-6, Entry 5. ^{1}H NMR (300 MHz, $CD_3C(O)CD_3$) δ 3.19 (s, 6 H), 3.70 (s, 2 H); ^{13}C NMR (75 MHz, $CD_3C(O)CD_3$) δ 28.3, 40.2, 153.4, 166.5; IR (neat) 2967, 1690, 1659, 1526, 1463, 1442, 1419, 1386, 1359, 1312, 1277, 1213, 1150, 1115, 1031, 985, 934, 730.

1-Dodecylpiperidine-2,6-dione (SI-B). Table SI-6, Entry 6. ^{1}H NMR (300 MHz, $CD_3C(O)CD_3$) δ 0.89 (t, J = 6.6 Hz, 3 H), 1.21-1.37 (m, 18 H), 1.39-1.51 (m, 2 H), 1.89-1.98 (m, 2 H), 2.63 (t, J = 6.6 Hz, 4 H), 3.77 (t, J = 7.5 Hz. 2 H); ^{13}C NMR (75 MHz, $CD_3C(O)CD_3$) δ

14.4, 18.0, 23.4, 27.7, 28.8, 30.1, 30.1, 30.3, 30.4, 30.4, 30.4, 32.7, 33.3, 39.7, 173.0; IR (neat) 2922, 2853, 1726, 1672, 1464, 1435, 1389, 1353, 1261, 1165, 1120, 1055, 926, 722.

1,3-Dimethyltetrahydropyrimidin-2(1*H*)-one (SI-C). Table SI-6, Entry 7. ^{1}H NMR (300 MHz, $CD_3C(O)CD_3$) δ 1.89-2.00 (m, 2 H), 2.82 (s, 6 H), 3.24 (t, *J* = 6.0 Hz, 4 H); ^{13}C NMR (75 MHz, $CD_3C(O)CD_3$) δ 23.1, 35.7, 48.6, 157.0; IR (neat) 2935, 2860, 1624, 1522, 1445, 1401, 1362, 1316, 1251, 1215, 1105, 1057, 925, 726.

5-Isobutyl-1,3-dimethyldihydropyrimidine-4,6(1*H*,5*H*)-dione (SI-D). Table SI-6, Entry 8. ^{1}H NMR (300 MHz, $CD_3C(O)CD_3$) δ 0.90 (d, *J* = 6.3 Hz, 6 H), 1.73 (t, *J* = 6.6 Hz, 2 H), 1.76-1.88 (m, 1 H), 2.99 (s, 6 H), 3.07 (t, *J* = 6.6 Hz, 1 H), 4.68 (d, *J* = 12.0 Hz, 1 H), 4.88 (d, *J* = 12.3 Hz, 1 H); ^{13}C NMR (75 MHz, $CD_3C(O)CD_3$) δ 22.8, 26.8, 32.6, 35.2, 49.2, 63.2, 169.1; IR (neat) 2955, 2869, 1679, 1655, 1498, 1465, 1406, 1266, 1227, 1171, 1130, 1105, 1067, 909, 727.

5-Isobutyl-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (SI-E). Table SI-6, Entry 9. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.80 (d, *J* = 6.6 Hz, 3 H), 0.84 (d, *J* = 6.6 Hz, 3 H), 1.14 (s, 3 H), 1.46 (dd, *J* = 6.0, 8.1 Hz, 2 H), 1.52-1.67 (m, 1 H), 3.00 (s, 3 H), 3.04 (d, *J* = 12.3 Hz, 1 H), 3.09 (d, *J* = 12.6 Hz, 1 H), 3.09 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.4, 24.2, 24.5, 24.6, 28.1, 36.1, 41.5, 44.8, 54.3, 153.9, 174.9. IR (neat) 2957, 1712, 1672, 1493, 1442, 1380, 1289, 1178, 1094, 1038 cm^{-1}.

Spectroscopic properties of α-hydroxy amines **1-4** (**1-3**: $CD_3C(O)CD_3$, **4**: $CDCl_3$) have been previously reported.[1-2] Characterization data of **4** in $CD_3C(O)CD_3$ is listed below for comparison purposes. **(4a*S*,7*S*,7a*R*)-7a-Hydroxy-4a-isobutyl-1,3,7-trimethyltetrahydro-1*H*-cyclopenta[*d*]pyrimidine-2,4(3*H*,4a*H*)-dione (4). Table SI-6, Entry 4.** ^{1}H NMR (400 MHz, $CD_3C(O)CD_3$) δ 0.55 (d, *J* = 7.6 Hz, 3 H), 0.68 (d, *J* = 6.0 Hz, 3 H), 0.76 (d, *J* = 6.0 Hz, 3 H), 1.00-1.10 (m, 1 H), 1.36-1.44 (m, 2 H), 1.48-1.56 (m, 2 H), 1.86-1.97 (m, 1 H), 2.18-2.27 (m, 1 H), 2.50-2.58 (m, 1 H), 2.88 (s, 3 H), 2.94 (s, 3 H), 4.84 (s, 1 H); ^{13}C NMR (100 MHz, $CD_3C(O)CD_3$) δ 18.0, 23.9, 25.0, 25.6, 28.3, 29.3, 29.4, 32.0, 43.8, 44.0, 56.1, 95.4, 153.1, 173.9. IR (neat) 3418, 2957, 1704, 1644, 1455, 1414, 1385, 1326, 1122, 1086, 1044, 913, 754 cm^{-1}.

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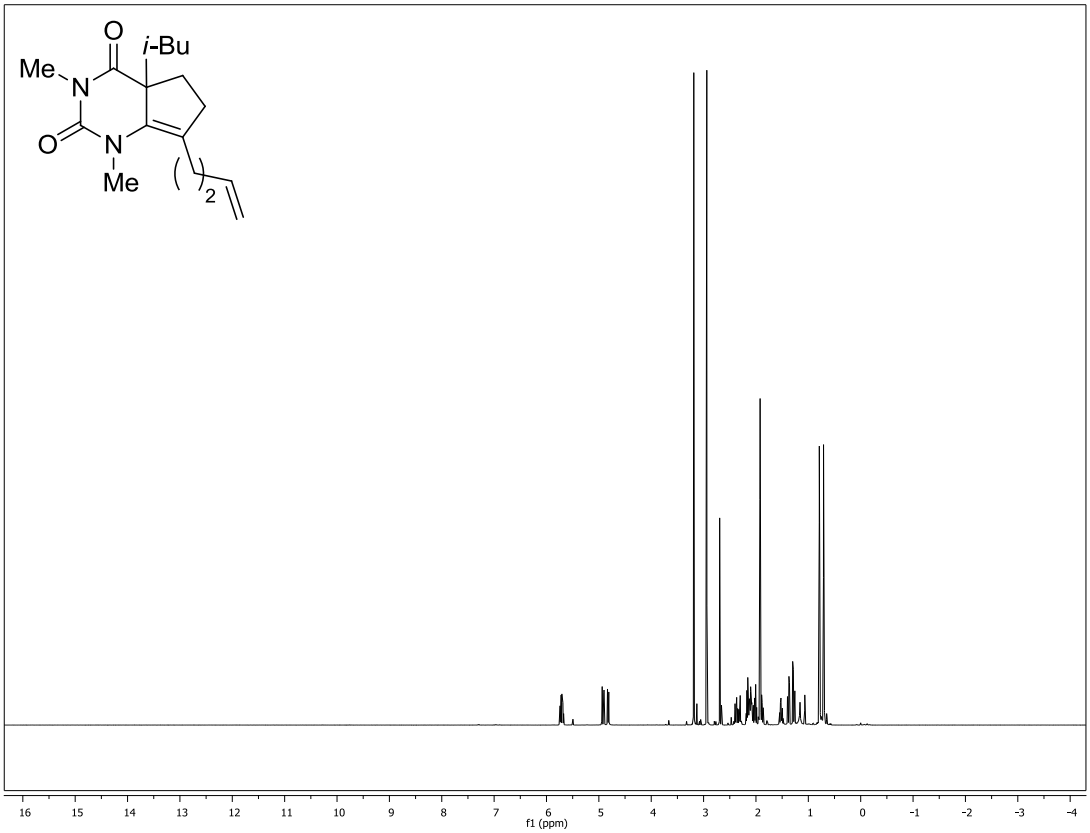

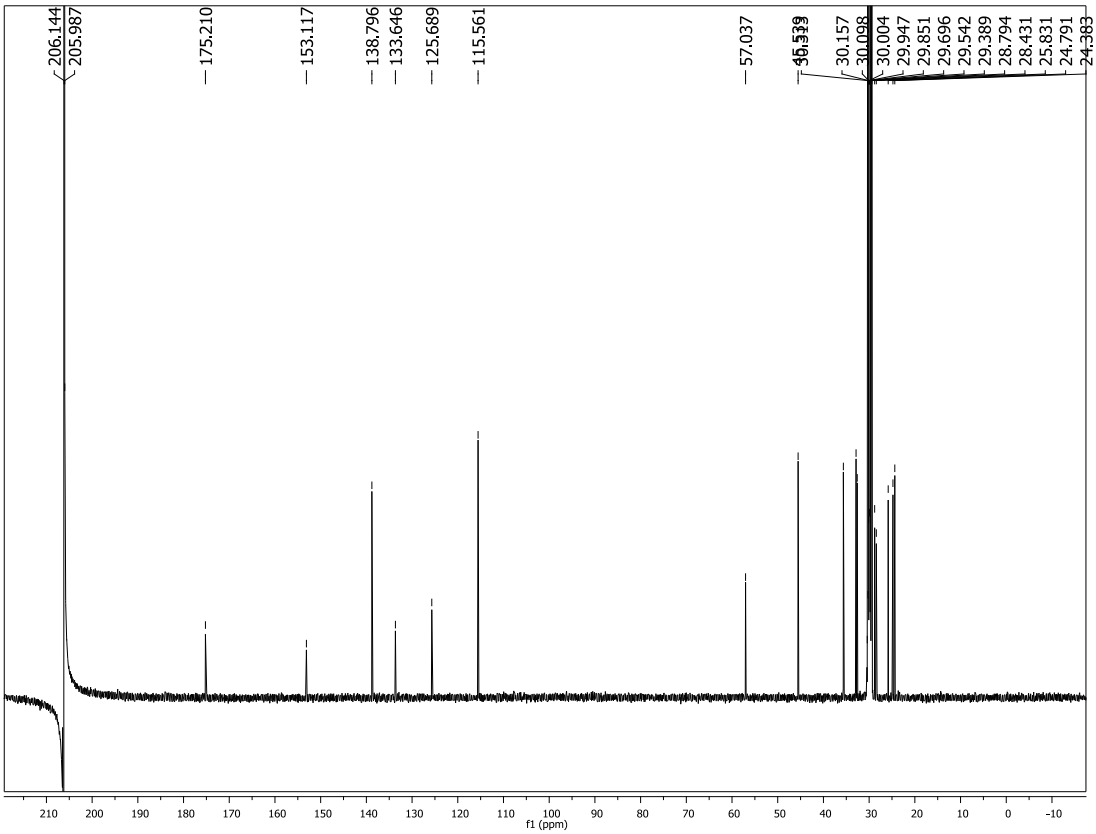

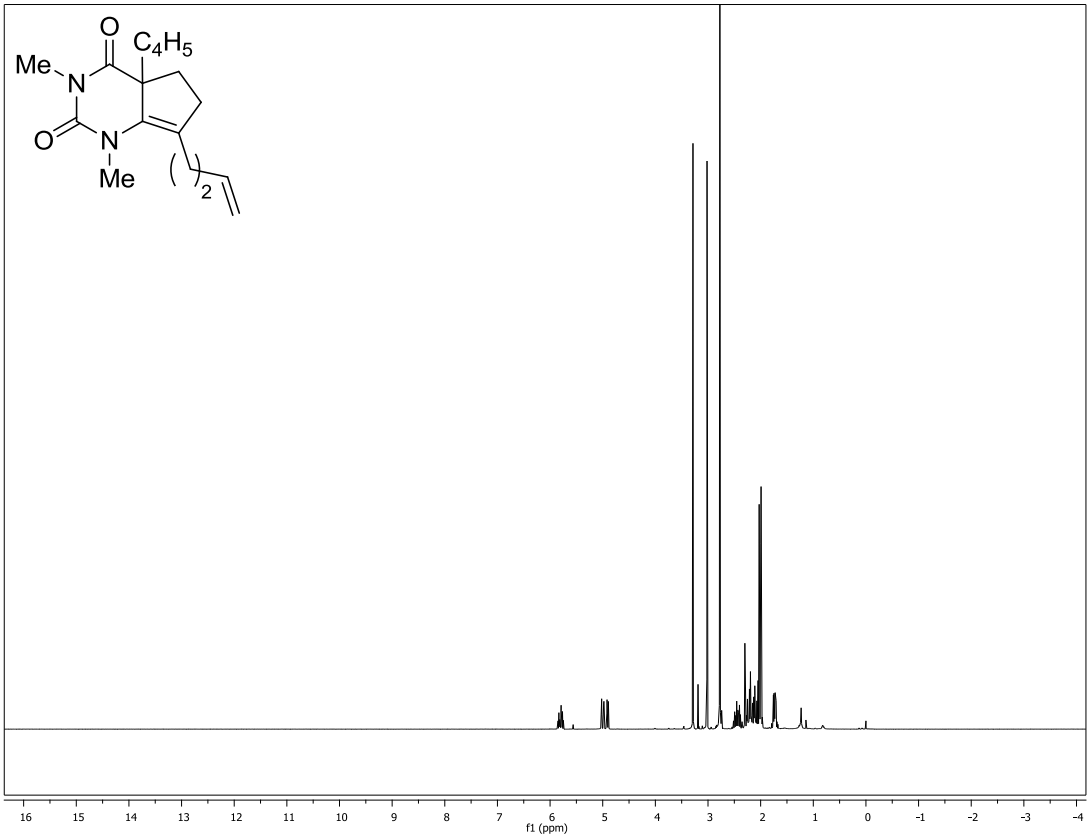
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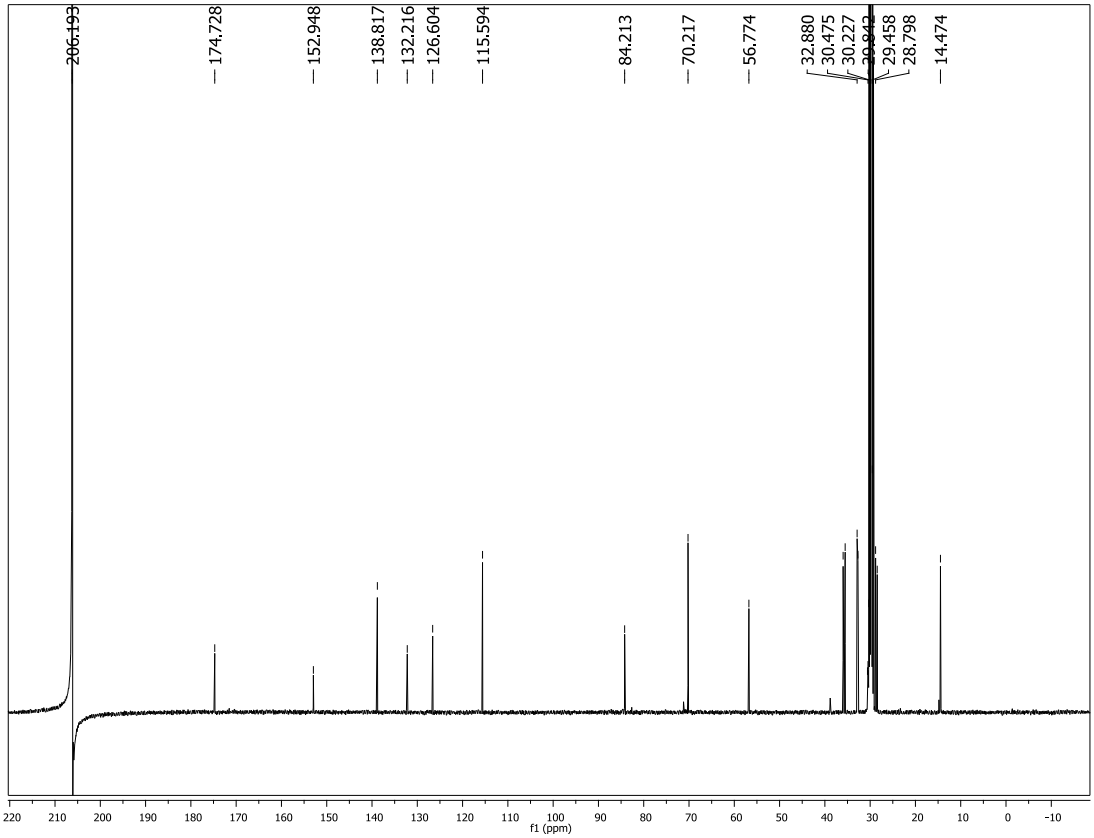
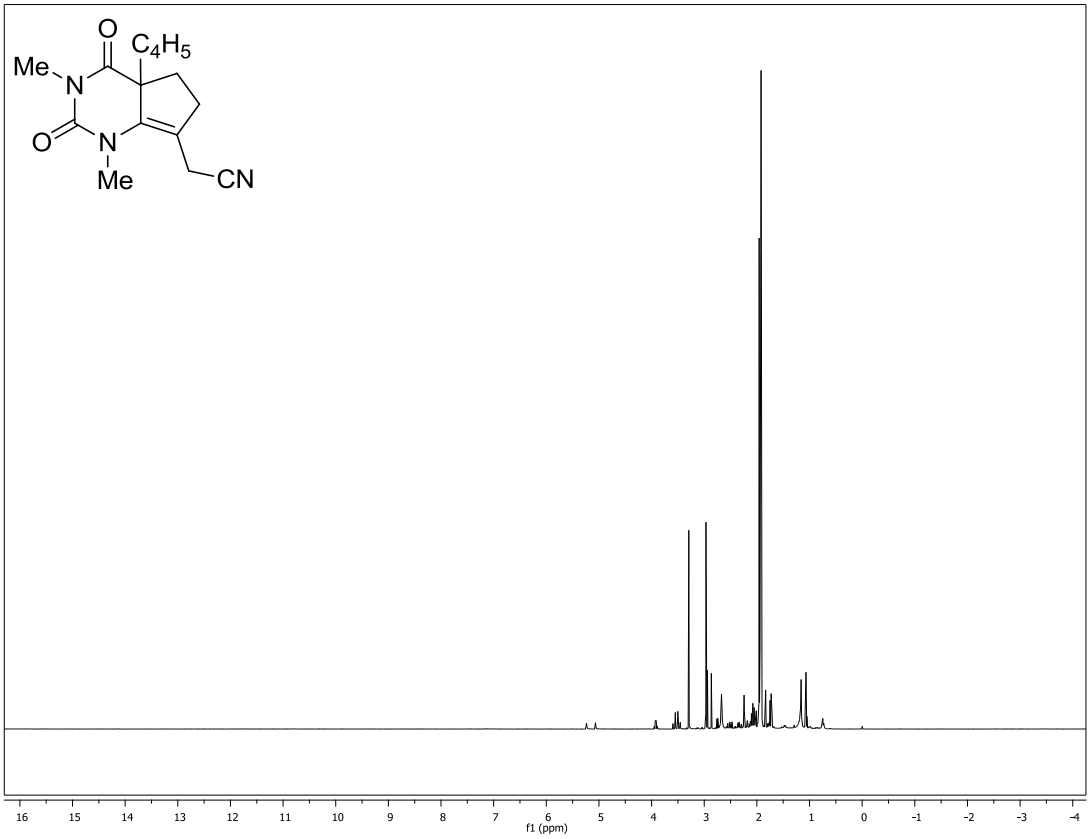
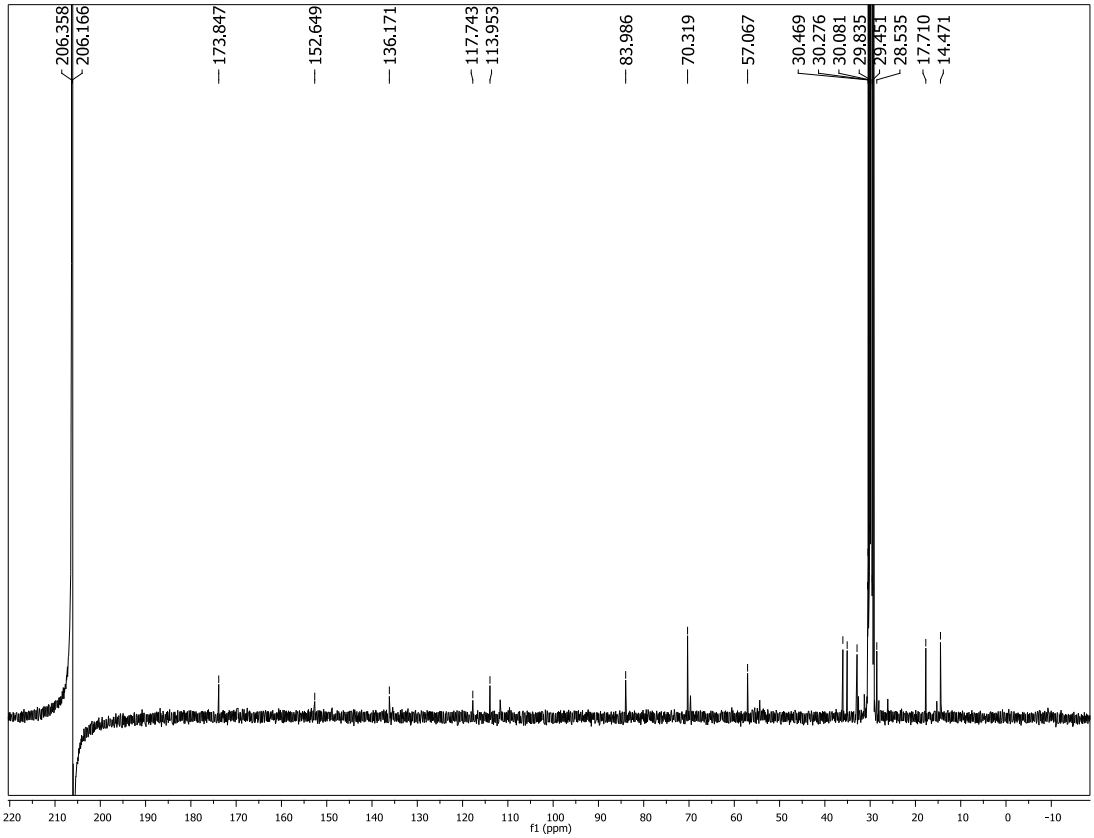
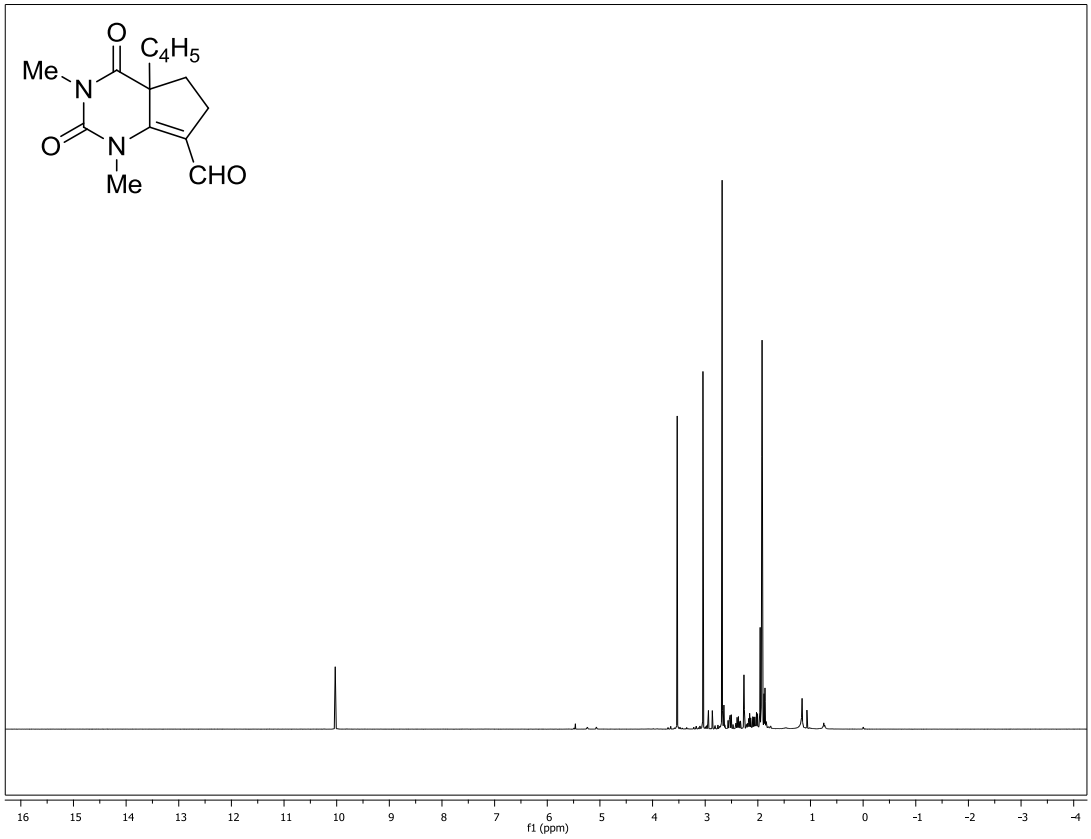
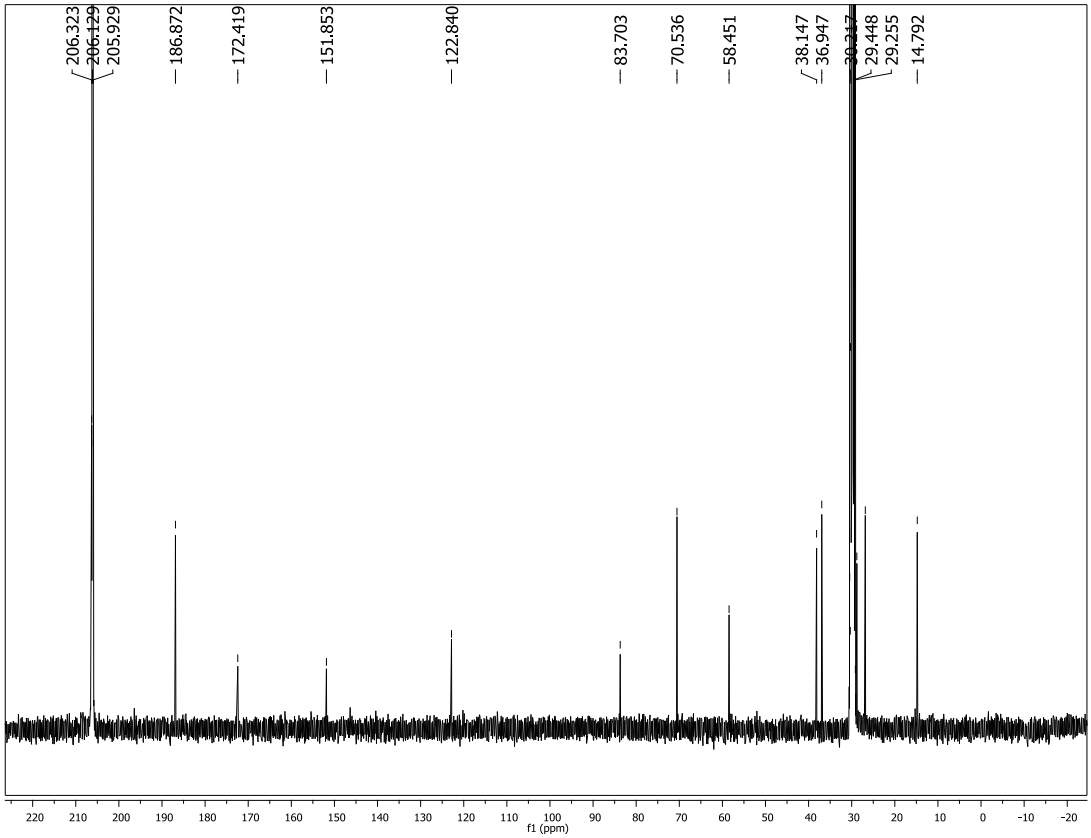
Me
2
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

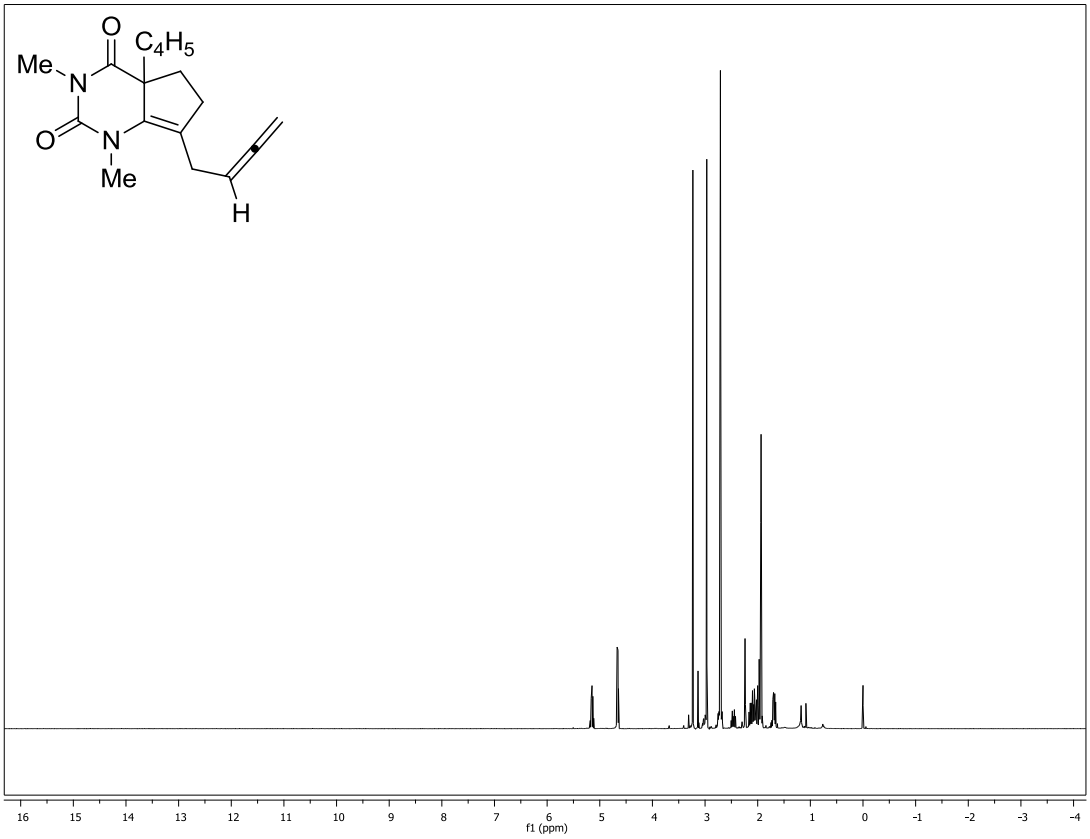

206.193
174.728
152.948
138.817
132.216
126.604
115.594
84.213
70.217
56.774
32.880
30.475
30.227
29.458
28.798
14.474
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

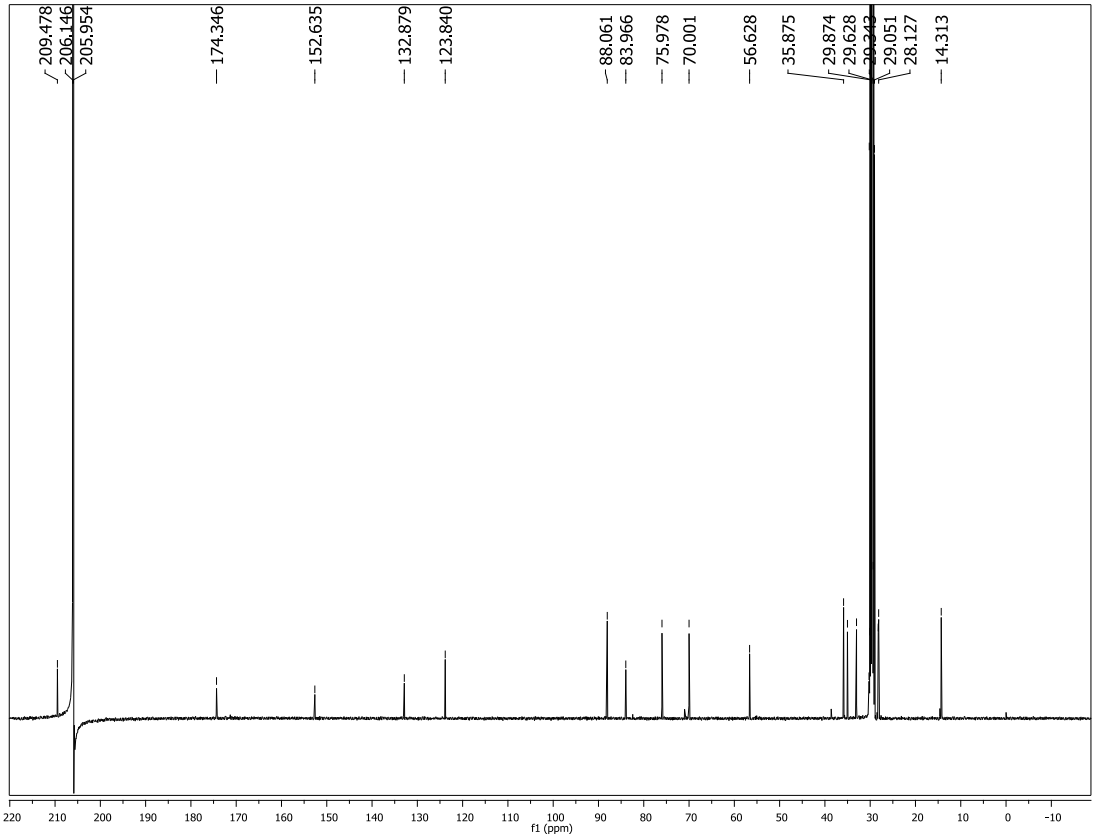

O
C4H5
Me
N
O
N
Me
CN
f1 (ppm)

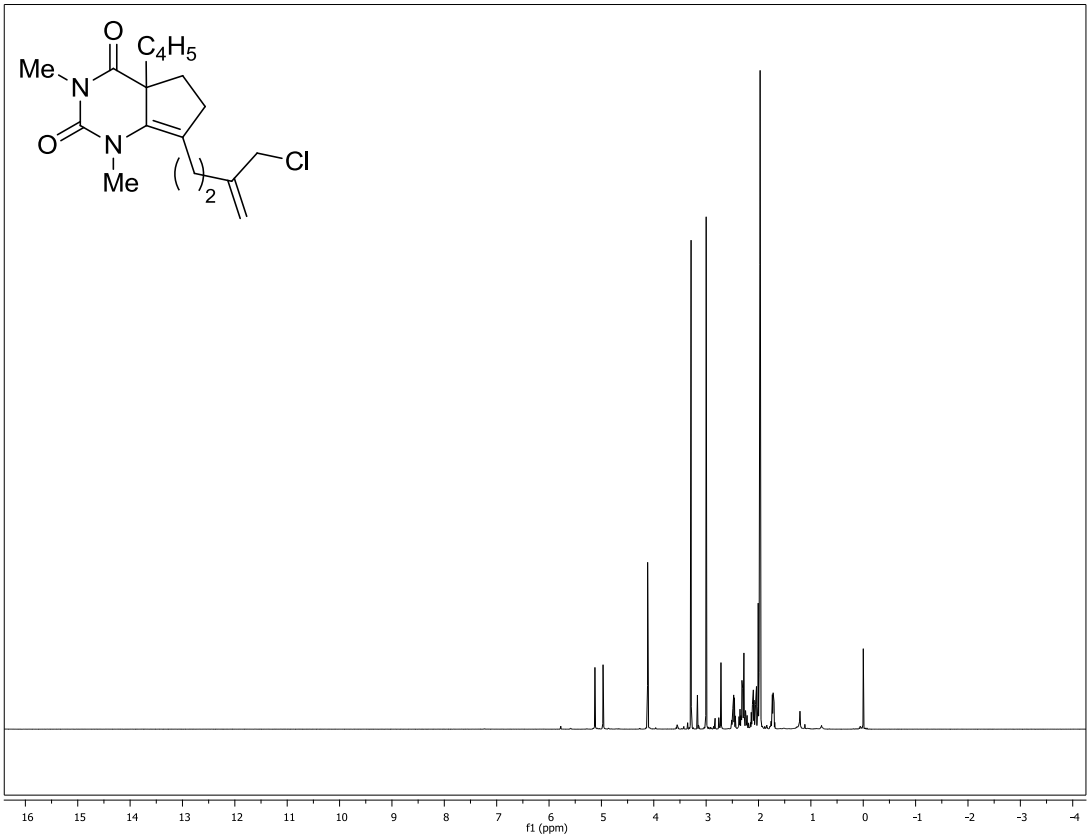

206.358
206.166
173.847
152.649
136.171
117.743
113.953
83.986
70.319
57.067
30.469
30.276
30.081
29.835
29.451
28.535
17.710
14.471
f1 (ppm)

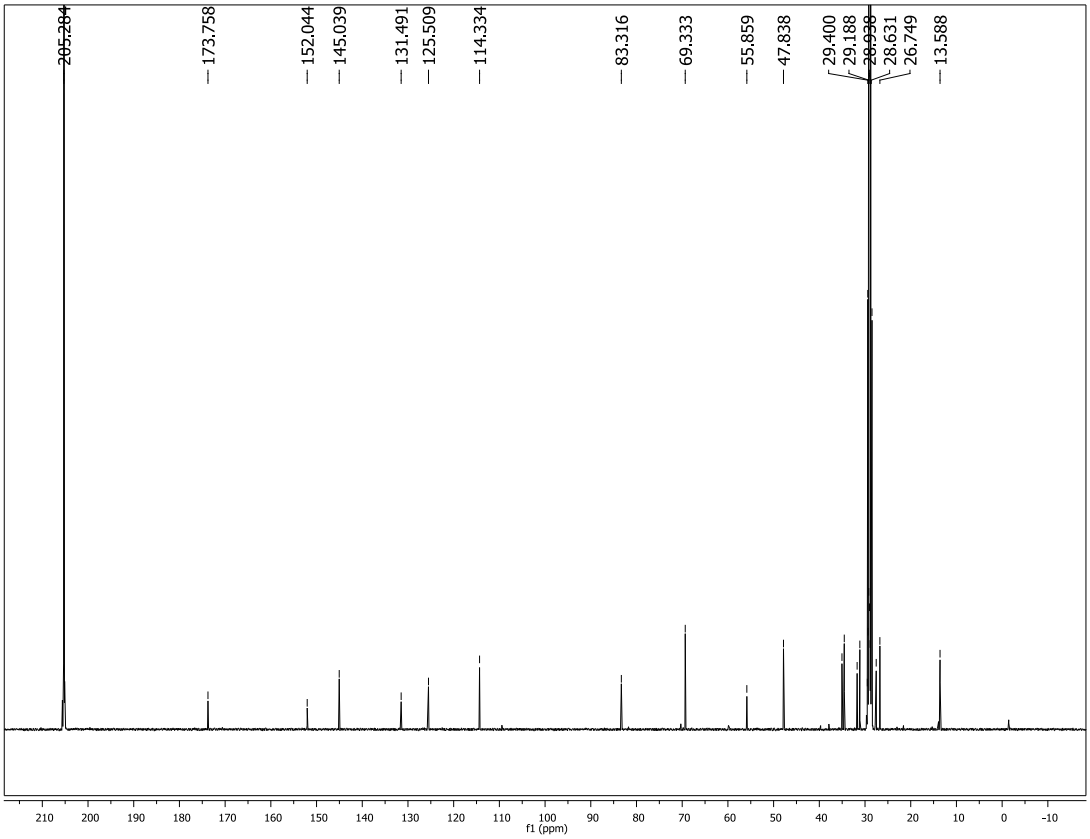


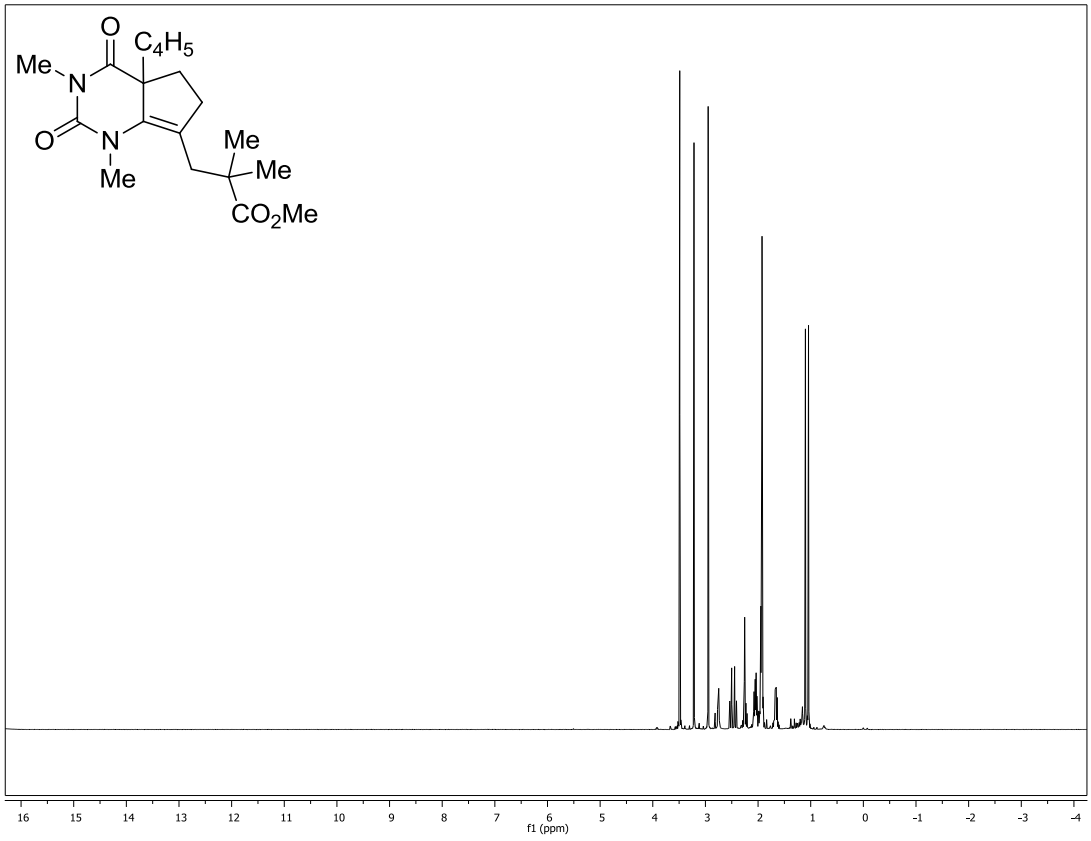


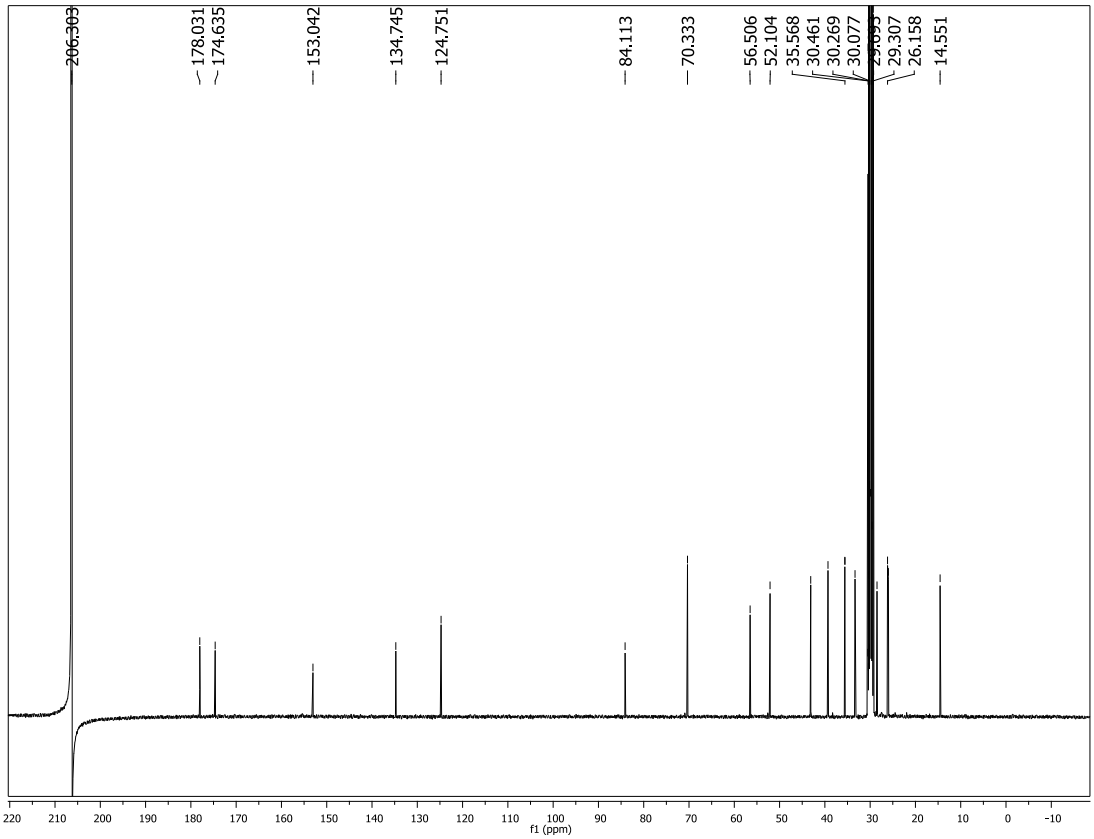

O
C4H5
Me
N
O
N
Me
H
f1 (ppm)

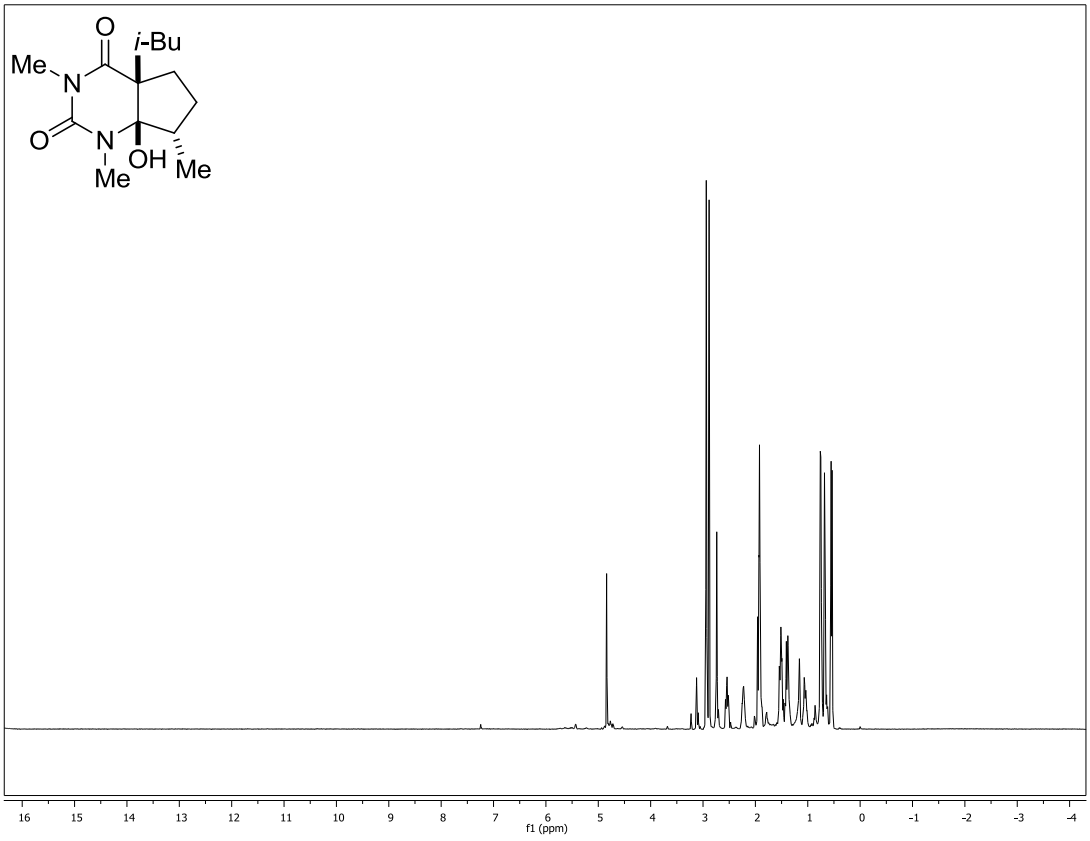

209.478
206.146
205.954
174.346
152.635
132.879
123.840
88.061
83.966
75.978
70.001
56.628
35.875
29.874
29.628
29.343
29.051
28.127
14.313
f1 (ppm)

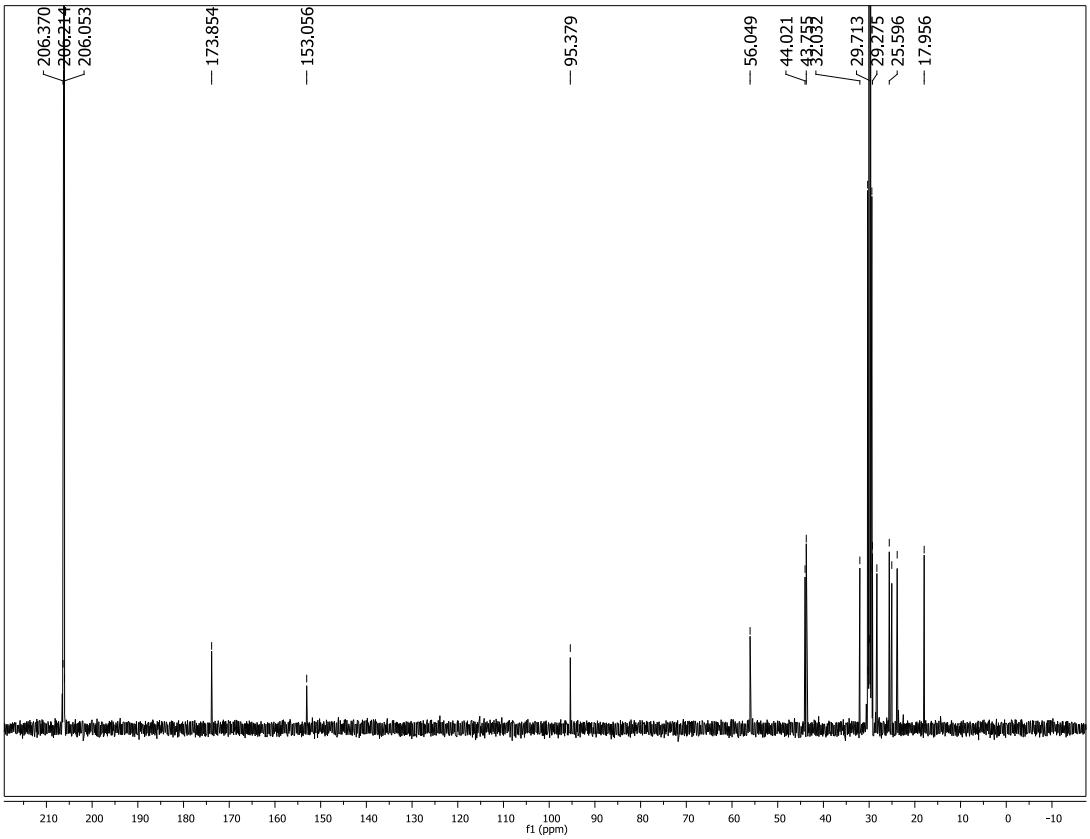


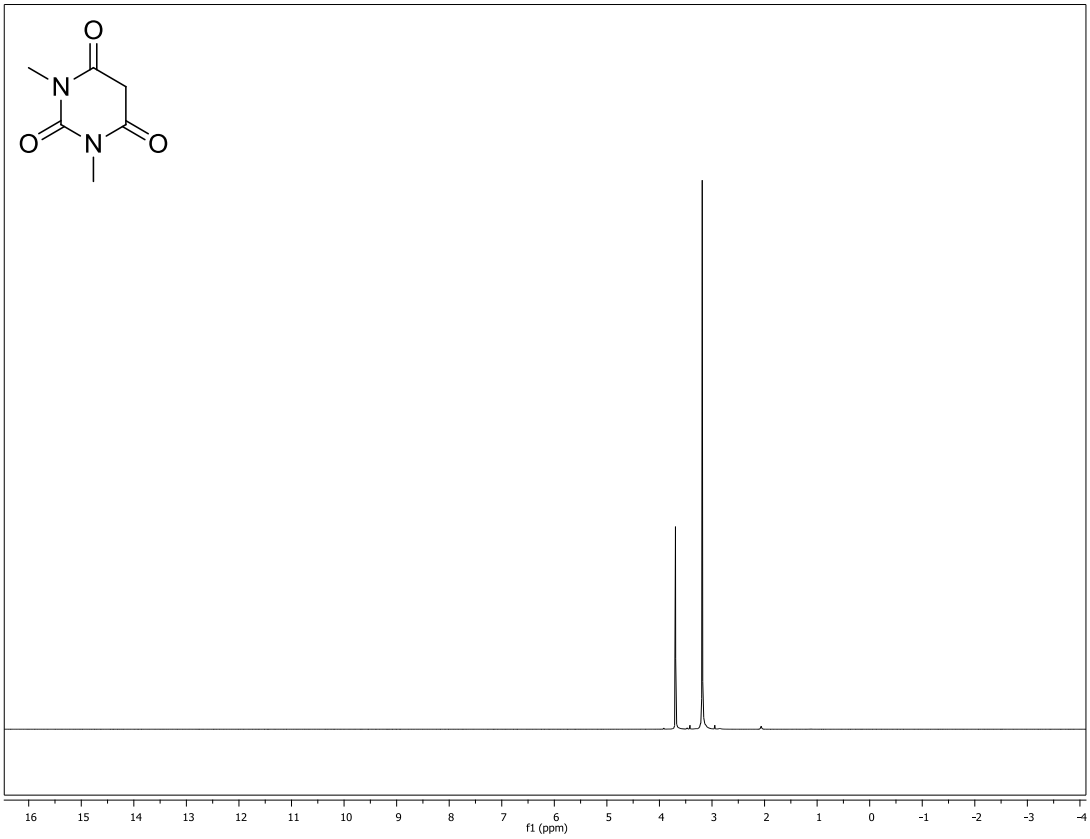


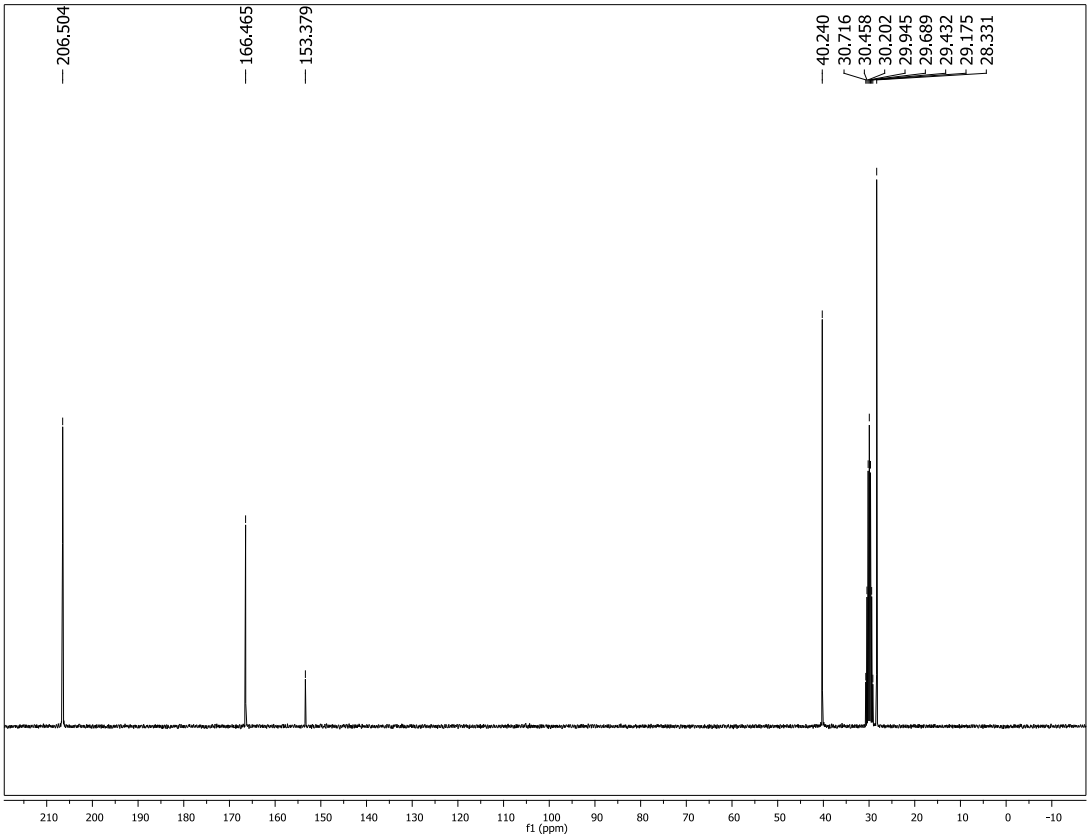


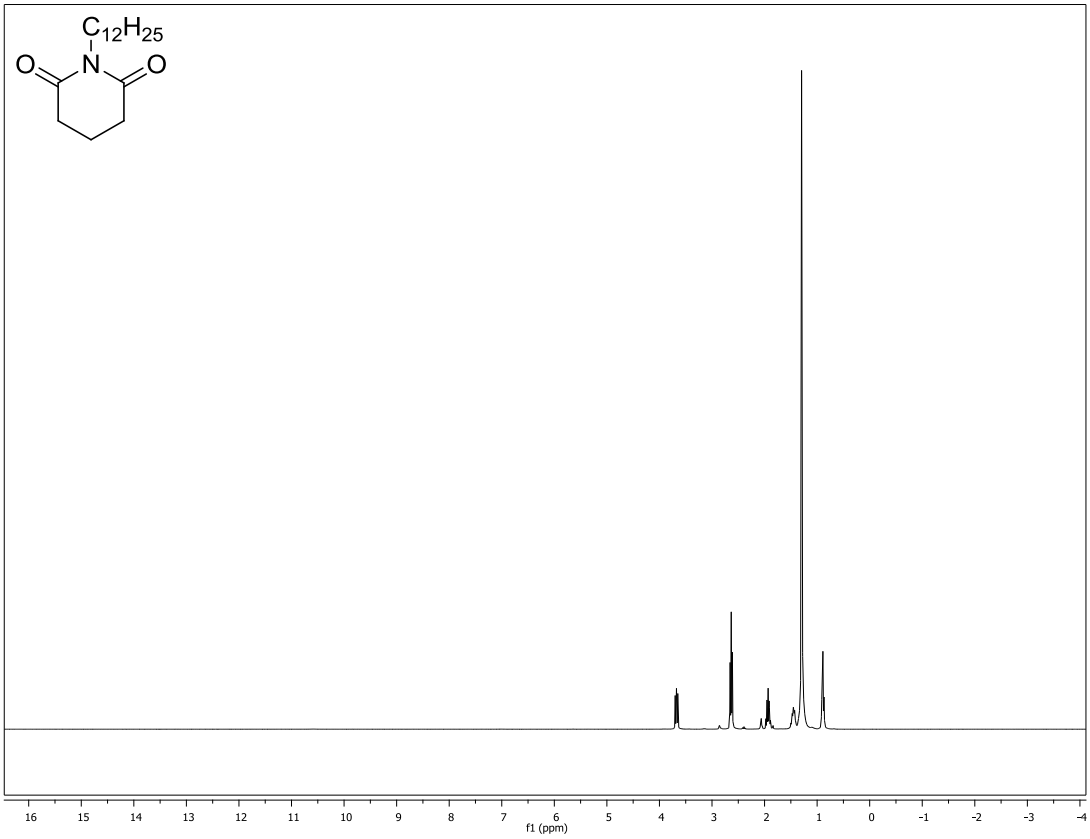


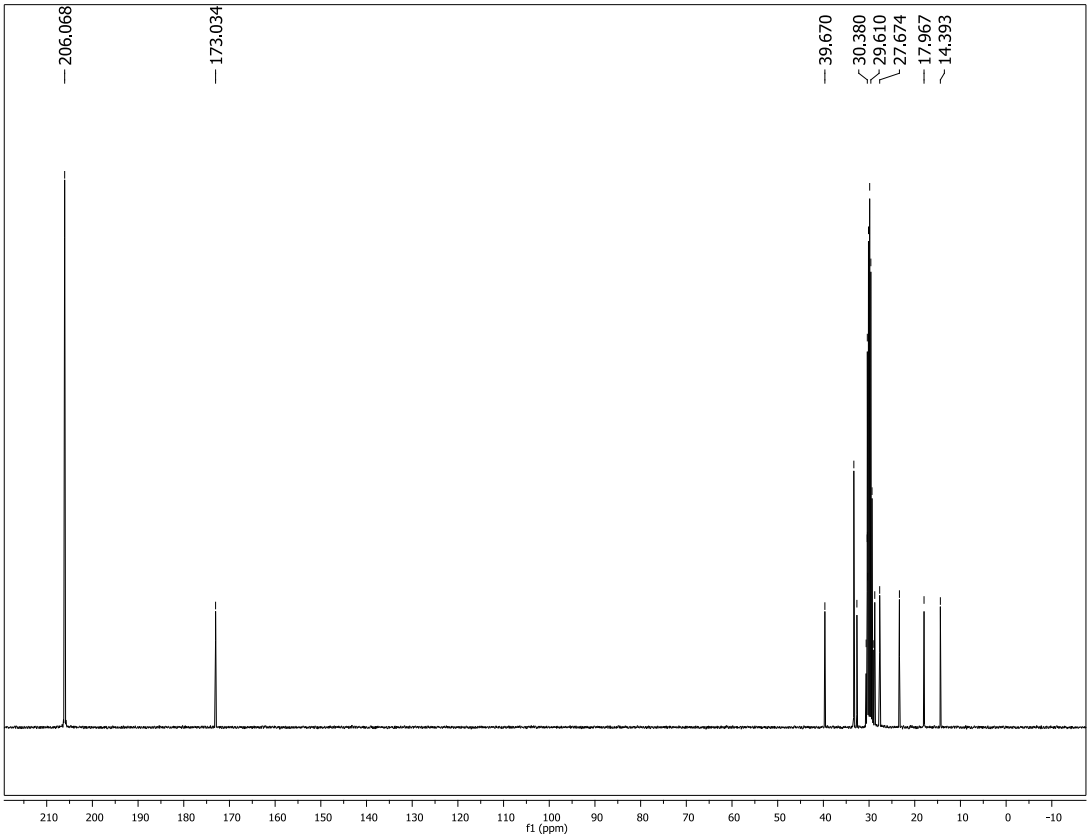

O
i-Bu
Me
N
O
N
OH
Me
Me
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

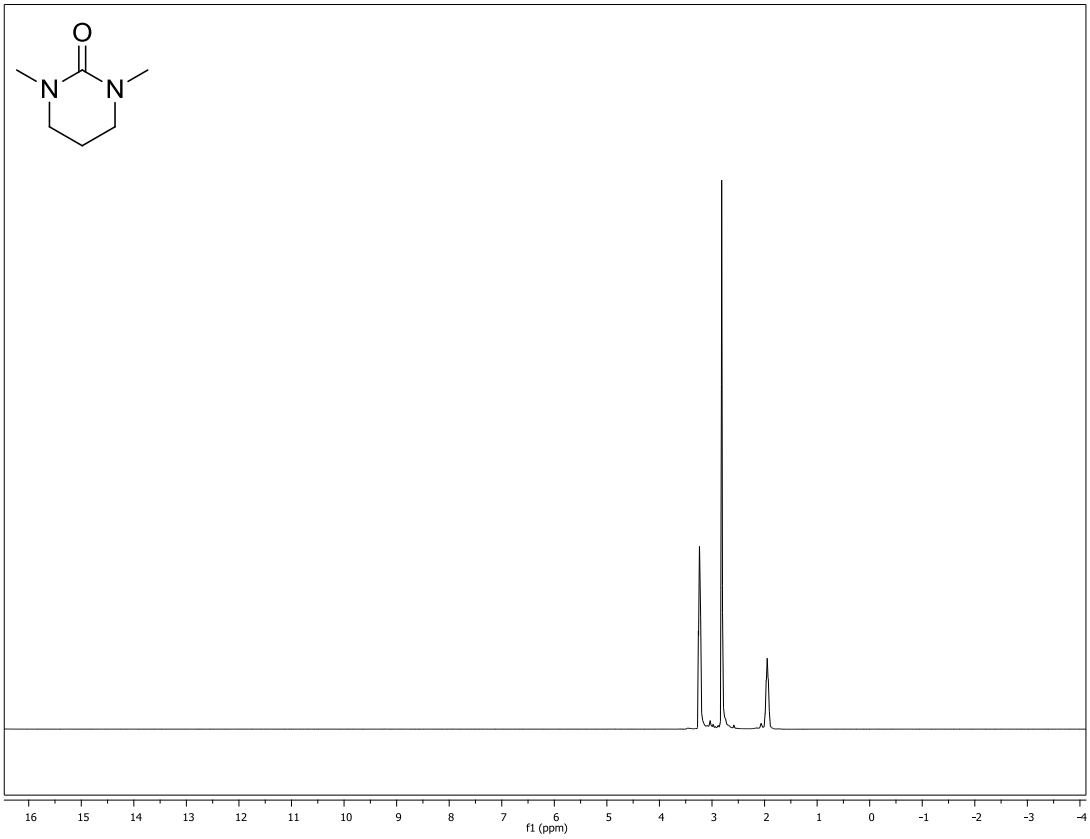

206.370
206.214
206.053
173.854
153.056
95.379
56.049
44.021
43.755
43.032
32.032
29.713
29.275
25.596
17.956
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

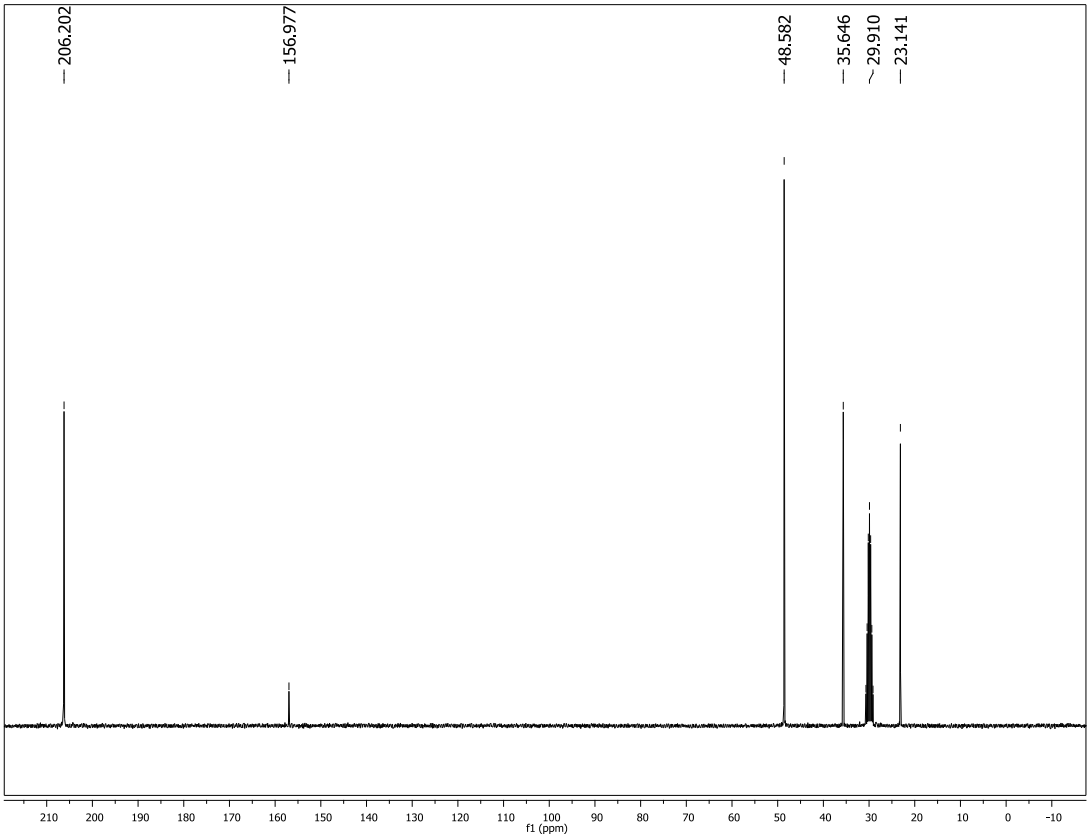

O
N
O
N
O
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

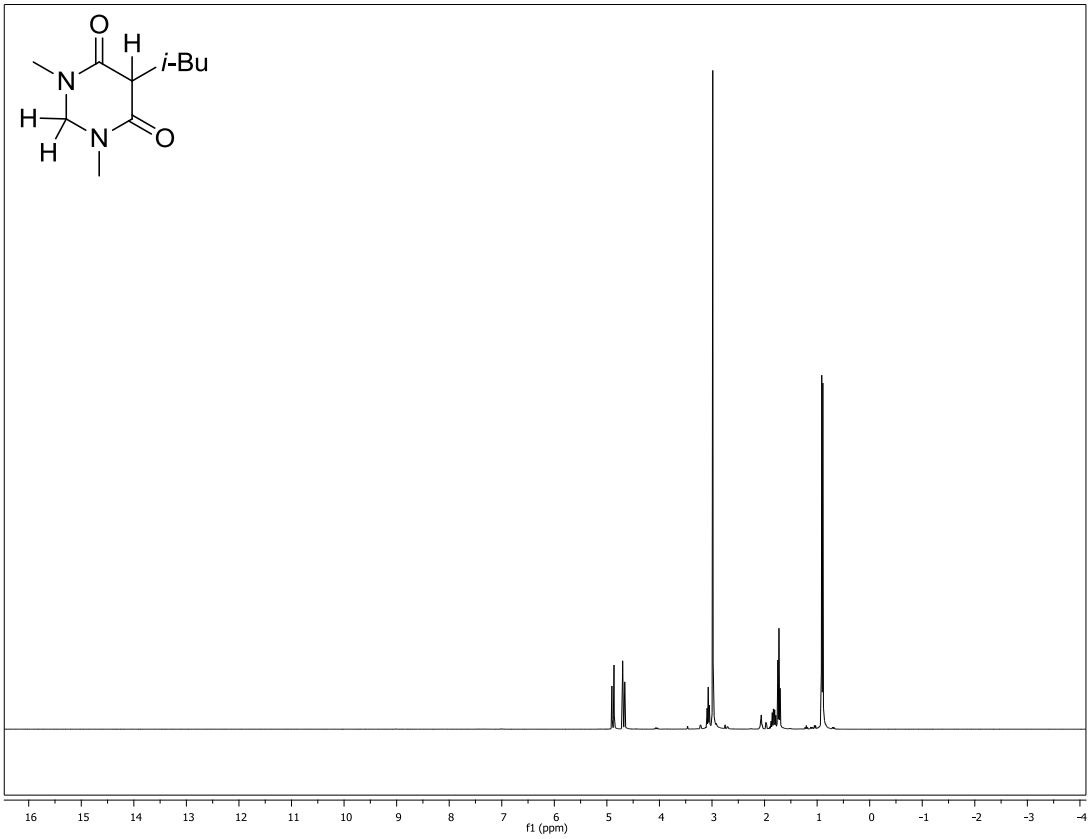

206.504
166.465
153.379
40.240
30.716
30.458
30.202
29.945
29.689
29.432
29.175
28.331
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

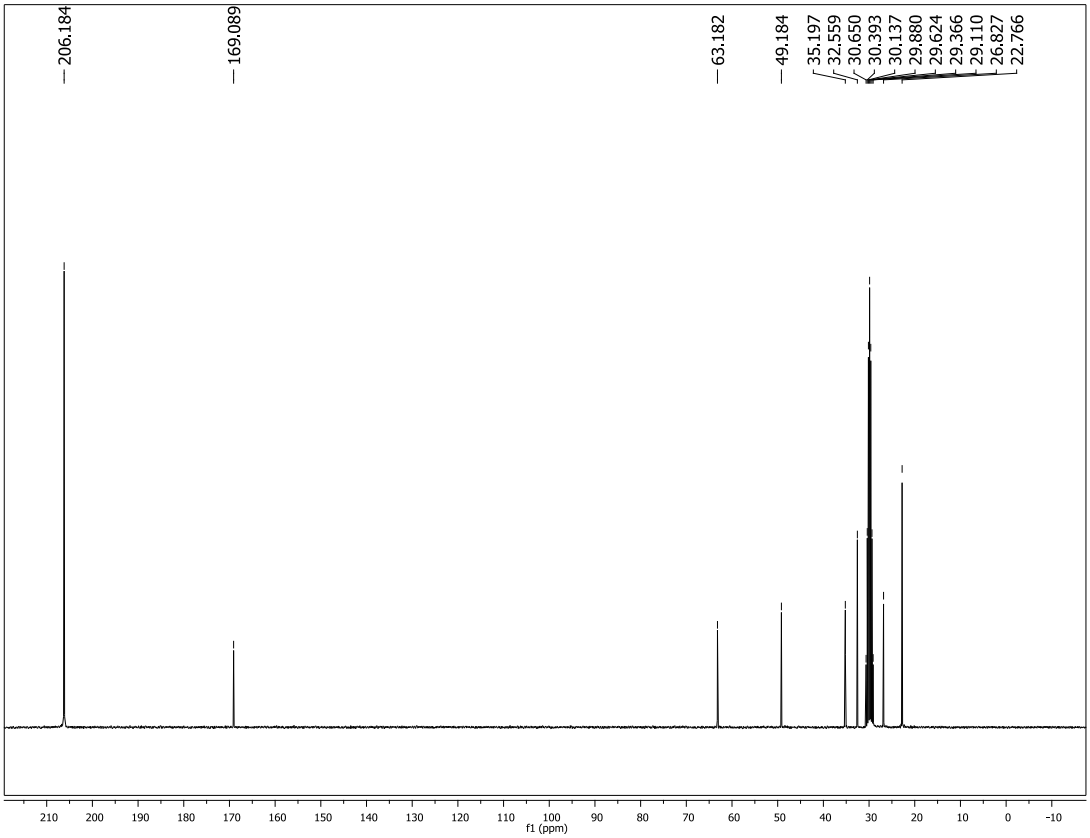





O
N
N
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)


206.202
156.977
48.582
35.646
29.910
23.141
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


O
H
i-Bu
N
H
H
N
O
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)


206.184
169.089
63.182
49.184
35.197
32.559
30.650
30.393
30.137
29.880
29.624
29.366
29.110
26.827
22.766
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)