Stereoselective Capture of N-Acyliminium Ions Generated from α-Hydroxy-N-Acylcarbamides: Direct Synthesis of Uracils from Barbituric Acids Enabled by SmI_2 Reduction

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Supplementary Information

Table of Contents 1

List of Known Compounds/General Methods 2
Experimental Procedures and Characterization Data 3
- Preparation of Starting Materials 3
- General Procedure and Optimization Study 8
- Addition of Nucleophiles to alpha-Hydroxy-N-Acylcarbamides 9
- Synthesis of 6-D^1-Deuterated Uracils 20
- Rearrangement of N,N-Dimethylphenobarbital 21
- Towards Library Development: Product Derivatization 22
- $H_2{}^{18}O$ Incorporation Experiments/Stability Studies 25

References 27
^{1}H and ^{13}C NMR Spectra 28

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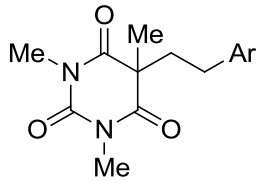
List of Known Compounds/General Methods

All starting materials reported in the manuscript have been previously described or prepared by the method reported previously.[1] *D*[1]-Enriched starting materials were prepared according to the previously reported procedure using SmI_2–D_2O.[1-3] Samarium(II) iodide was prepared by standard methods and titrated prior to use.[4-8] 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 Na/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 $CHCl_3$ and $(CH_3)_2CO$ peaks (7.27 and 77.2 ppm, 2.05 and 29.8 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.

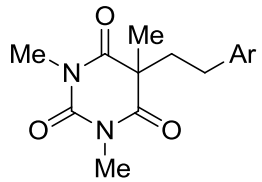
Experimental Procedures and Characterization Data

Preparation of Starting Materials



SI-1, Ar = 4-MeO-C_6H_4

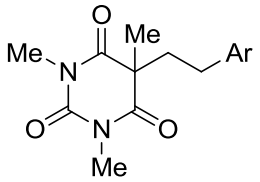
5-(4-Methoxyphenethyl)-1,3,5-trimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (SI-1). Prepared according to the procedure previously described[1] using 5-(4-methoxyphenethyl)-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (0.50 g, 1.72 mmol, 1.0 equiv), iodomethane (1.6 mL, 17.2 mmol, 10 equiv) and K_2CO_3 (0.48 g, 3.44 mmol, 2.0 equiv) in acetone (2.6 mL) at 50 °C for 24 h to give the title compound as an oil. Yield (0.52 g, 99%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.52 (s, 3 H), 2.32 (d, *J* = 10.2 Hz, 1 H), 2.33 (d, *J* = 8.8 Hz, 1 H), 2.42 (d, *J* = 8.8 Hz, 1 H), 2.43 (d, *J* = 10.2 Hz, 1 H), 3.22 (s, 6 H), 3.76 (s, 3 H), 6.77 (d, *J* = 8.6 Hz, 2 H), 6.97 (d, *J* = 8.6 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 25.7, 28.5, 30.8, 40.3, 51.0, 55.2, 113.7, 129.4, 131.3, 150.9, 158.1, 172.0; IR (neat) 749, 821, 913, 1033, 1064, 1178, 1245, 1281, 1381, 1421, 1444, 1511, 1673, 2834, 2938; HRMS calcd for $C_{16}H_{24}N_3O_4$ (M^+ + NH_4) 322.1716, found 322.1764.



SI-2, Ar = 4-CF_3-C_6H_4

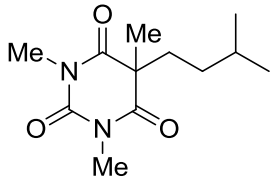
1,3,5-Trimethyl-5-(4-(trifluoromethyl)phenethyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (SI-2). Prepared according to the procedure previously described[1] using 1,3-dimethyl-5-(4-(trifluoromethyl)phenethyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (0.50 g, 1.52 mmol, 1.0 equiv), iodomethane (1.4 mL, 15.2 mmol, 10 equiv) and K_2CO_3 (0.42 g, 3.05 mmol, 2.0 equiv) in acetone (2.3 mL) at 50 °C for 24 h to give the title compound as an oil. Yield (0.52 g, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.56 (s, 3 H), 2.35 (d, *J* = 11.1 Hz, 1 H), 2.37 (d, *J* = 9.1 Hz, 1 H), 2.51 (d, *J* = 9.1 Hz, 1 H), 2.53 (d, *J* = 11.1 Hz, 1 H), 3.27 (s, 6 H), 7.22 (d, *J* = 8.1 Hz, 2 H), 7.51 (d, *J* = 8.1 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 28.6, 31.5, 39.7, 51.2, 124.1 (q, J^1=

271.3 Hz), 125.3 (q, J^3= 3.7 Hz), 128.8, 128.8 (q, J^2= 32.3 Hz), 143.8, 150.8, 171.8; ^{19}F NMR (470.6 MHz, $CDCl_3$) δ -62.5; IR (neat) 632, 753, 823, 842, 914, 1018, 1064, 1114, 1162, 1282, 1322, 1383, 1422, 1447, 1676, 2862, 2941; HRMS calcd for $C_{16}H_{21}N_3O_3F_3$ (M^+ + NH_4) 360.1530, found 360.1532.



SI-3, Ar = 4-Br-C_6H_4

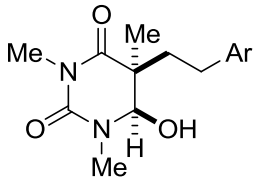
5-(4-Bromophenethyl)-1,3,5-trimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (SI-3). Prepared according to the procedure previously described[1] using 5-(4-bromophenethyl)-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (0.50 g, 1.47 mmol, 1.0 equiv), iodomethane (1.4 mL, 14.7 mmol, 10 equiv) and K_2CO_3 (0.41 g, 2.95 mmol, 2.0 equiv) in acetone (2.2 mL) at 50 °C for 24 h to give the title compound as an oil. Yield (0.52 g, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.54 (s, 3 H), 2.31 (d, *J* = 11.1 Hz, 1 H), 2.32 (d, *J* = 9.2 Hz, 1 H), 2.41 (d, *J* = 9.2 Hz, 1 H), 2.42 (d, *J* = 11.1 Hz, 1 H), 3.26 (s, 6 H), 6.96 (d, *J* = 8.3 Hz, 2 H), 7.36 (d, *J* = 8.3 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.0, 28.6, 31.1, 40.1, 51.1, 120.2, 130.2, 131.4, 138.5, 150.8, 171.9; IR (neat) 754, 809, 832, 1011, 1067, 1143, 1283, 1382, 1420, 1446, 1677, 2862, 2937; HRMS calcd for $C_{15}H_{17}N_2O_3Br$ (M^+ + H) 352.0417, found 352.0405.



SI-4

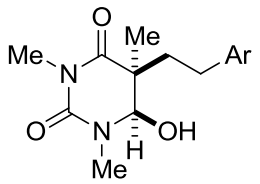
5-Isopentyl-1,3,5-trimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (SI-4). Prepared according to the procedure previously described[1] using 5-isopentyl-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (0.24 g, 1.00 mmol, 1.0 equiv), iodomethane (1.0 mL, 10.0 mmol, 10 equiv), tetrabutylammoniumbisulfate (34 mg, 0.10 mmol, 0.10 equiv) and K_2CO_3 (0.28 g, 2.00 mmol, 2.0 equiv) in DMF (2.5 mL) at 80 °C for 18 h to give the title compound after purification by chromatography on silica gel (10% EtOAc/petroleum ether) as an oil. Yield (0.0878 g, 36%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.82 (d, *J* = 6.6 Hz, 6 H), 0.88-0.97 (m, 2 H), 1.45 (dquin, *J* = 6.6,

13.2 Hz, 1 H), 1.51 (s, 3 H), 1.92-1.99 (m, 2 H), 3.30 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.2, 24.7, 28.0, 28.6, 33.9, 38.2, 51.6, 151.2, 172.4; IR (neat) 755, 1061, 1098, 1190, 1279, 1313, 1359, 1381, 1418, 1445, 1673, 2870, 2957; HRMS calcd for $C_{11}H_{17}N_2O_3$ (M^+−CH_3) 225.1243, found 225.1225.



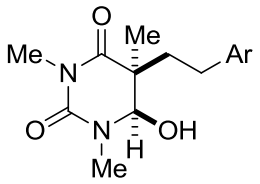
1c, Ar = 4-MeO-C_6H_4

(5*S,6*R**)-6-Hydroxy-5-(4-methoxyphenethyl)-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (1c).** Prepared according to the procedure previously described[1] using 5-(4-methoxyphenethyl)-1,3,5-trimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (0.10 mmol, 1.0 equiv), SmI_2 (0.30 mmol, 3 equiv, 3.75 mL, 0.060 M) and H_2O (1.8 mL, 1000 equiv) for 60 s at room temperature to afford after purification by chromatography (3/1 EtOAc/hexanes) the title compound as a colorless oil. Rf (1/1 EtOAc/hexanes) = 0.27. Yield 74%. ^{1}H NMR (500 MHz, CD_3Cl) (major diastereoisomer) δ 1.32 (s, 3 H), 1.59-1.66 (m, 1 H), 1.75-1.82 (m, 1 H), 2.34-2.41 (m, 1 H), 2.48-2.56 (m, 1 H), 2.92 (br, 1 H), 3.00 (s, 3 H), 3.10 (s, 3 H), 3.70 (s, 3 H), 4.45 (s, 1 H), 6.74 (d, *J* = 8.5 Hz, 2 H), 6.95 (d, *J* = 8.5 Hz, 2 H); (minor) 1.21 (s, 3 H), 1.92-1.99 (m, 1 H), 2.07-2.15 (m, 1 H), 2.48-2.56 (m, 1 H), 2.67 (td, *J* = 5.0, 12.5 Hz, 1 H), 2.94 (br, 1 H), 3.06 (s, 3 H), 3.11 (s, 3 H), 3.72 (s, 3 H), 4.49 (s, 1 H), 6.76 (d, *J* = 8.5 Hz, 2 H), 7.07 (d, *J* = 8.5 Hz, 2 H). ^{13}C NMR (75 MHz, CD_3Cl) (major diastereoisomer) δ 17.3, 27.9, 29.5, 34.7, 38.3, 47.5, 55.3, 85.9, 114.1, 129.2, 132.8, 153.0, 158.1, 173.2; (minor) 21.0, 27.9, 28.5, 34.6, 34.9, 46.2, 55.3, 85.3, 114.0, 129.2, 133.8, 152.9, 158.0, 174.3. IR (neat) 3389, 2961, 1712, 1671, 1492, 1443, 1416, 1380, 1260, 1220, 1178, 1093, 1036, 801, 772. HRMS calcd for $C_{16}H_{21}N_2O_3$ (M^+ + H – H_2O) 289.1552, found 289.1538.



1d, Ar = 4-CF_3-C_6H_4

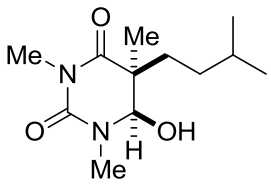
(5*S,6*R**)-6-Hydroxy-1,3,5-trimethyl-5-(4-(trifluoromethyl)phenethyl)dihydropyrimidine-2,4(1*H*,3*H*)-dione (1d).** Prepared according to the procedure previously described[1] using 1,3,5-trimethyl-5-(4-(trifluoromethyl)phenethyl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (0.10 mmol, 1.0 equiv)), SmI_2 (0.30 mmol, 3 equiv, 3.75 mL, 0.060 M) and H_2O (1.8 mL, 1000 equiv) for 60 s at room temperature to afford after purification by chromatography (3/1 EtOAc/hexanes) the title compound as a colorless oil. Rf (1/1 EtOAc/hexanes) = 0.30. Yield 71%. ^{1}H NMR (500 MHz, CD_3Cl) (major diastereoisomer) δ 1.34 (s, 3 H), 1.61-1.68 (m, 1 H), 1.81-1.88 (m, 1 H), 2.48 (td, *J* = 5.0, 12.0 Hz, 1 H), 2.61-2.69 (m, 1 H), 2.75 (br, 1 H), 3.03 (s, 3 H), 3.11 (s, 3 H), 4.46 (s, 1 H), 7.15 (d, *J* = 8.0 Hz, 2 H), 7.46 (d, *J* = 8.0 Hz, 2 H); (minor) 1.24 (s, 3 H), 1.93-2.00 (m, 1 H), 2.09-2.16 (m, 1 H), 2.60-2.69 (m, 1 H), 2.75 (br, 1 H), 2.79 (td, *J* = 4.5, 13.0 Hz, 1 H), 3.09 (s, 3 H), 3.12 (s, 3 H), 4.53 (s, 1 H), 7.27 (d, *J* = 8.0 Hz, 2 H), 7.47 (d, *J* = 8.0 Hz, 2 H). ^{13}C NMR (75 MHz, CD_3Cl) (major diastereoisomer) δ 17.3, 27.9, 30.3, 34.8, 38.2, 47.4, 86.0, 125.5 (q, J^3 = 3.8 Hz), 128.6, 144.9, 152.9, 172.8; (minor) 21.0, 27.9, 29.5, 34.6, 34.9, 46.1, 85.4, 125.5 (q, J^3 = 3.8 Hz), 128.7, 145.9, 152.8, 173.9. Aromatic CF groups were not apparent in the ^{13}C NMR spectrum despite long acquisition times. The ^{19}F spectrum clearly indicates the presence of the CF_3 group. ^{19}F NMR (470.6 MHz, $CDCl_3$) δ -62.4. IR (neat) 3400, 2961, 1716, 1672, 1421, 1326, 1260, 1219, 1067, 799, 772. HRMS calcd for $C_{16}H_{18}N_2O_2F_3$ (M^+ + H) 327.1315, found 327.1309.



1e, Ar = 4-Br-C_6H_4

(5*S,6*R**)-5-(4-Bromophenethyl)-6-hydroxy-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (1e).** Prepared according to the procedure previously described[1] using 5-(4-bromophenethyl)-1,3,5-trimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (0.10 mmol, 1.0 equiv), SmI_2 (0.30 mmol, 3 equiv, 3.75 mL, 0.060 M) and H_2O (1.8 mL, 1000 equiv) for 60 s at room temperature to afford after purification by chromatography (3/1 EtOAc/hexanes) the title compound as a colorless oil. Rf (1/1 EtOAc/hexanes) = 0.33. Yield 64%. ^{1}H NMR (500 MHz, CD_3Cl) (major diastereoisomer) δ 1.32 (s, 3 H), 1.58-1.64 (m, 1 H), 1.77-1.84 (m, 1 H), 2.34-

2.41 (m, 1 H), 2.50-2.58 (m, 1 H), 2.82 (br, 1 H), 3.02 (s, 3 H), 3.10 (s, 3 H), 4.45 (s, 1 H), 6.91 (d, *J* = 8.0 Hz, 2 H), 7.32 (d, *J* = 8.0 Hz, 2 H); (minor) 1.22 (s, 3 H), 1.90-1.97 (m, 1 H), 2.05-2.12 (m, 1 H), 2.50-2.58 (m, 1 H), 2.68 (td, *J* = 4.5, 12.5 Hz, 1 H), 2.87 (br, 1 H), 3.08 (s, 3 H), 3.11 (s, 3 H), 4.51 (s, 1 H), 7.03 (d, *J* = 8.5 Hz, 2 H), 7.33 (d, *J* = 8.5 Hz, 2 H). ^{13}C NMR (75 MHz, CD_3Cl) (major diastereoisomer) δ 17.3, 27.9, 29.8, 34.8, 38.3, 47.4, 86.0, 120.1, 130.0, 131.7, 139.7, 152.8, 172.9; (minor) 21.0, 27.9, 29.0, 34.5, 34.9, 46.1, 85.3, 119.8, 130.1, 131.6, 140.8, 152.9, 174.1. IR (neat) 73381, 2967, 1715, 1672, 1423, 1219, 1072, 772. HRMS calcd for $C_{15}H_{18}N_2O_2Br$ (M^+ + H) 337.0546, found 337.0544.



1f

(5*S,6*R**)-6-Hydroxy-5-isopentyl-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (1f).** Prepared according to the procedure previously described[1] using 5-isopentyl-1,3,5-trimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (0.10 mmol, 1.0 equiv), SmI_2 (0.40 mmol, 4 equiv) and H_2O (0.36 mL, 200 equiv) for 60 s at room temperature to afford after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a colorless oil. Yield 69%. ^{1}H NMR (400 MHz, $CD_3C(O)CD_3$) (major diastereoisomer) δ 0.90 (d, *J* = 6.8 Hz, 3 H), 0.92 (d, *J* = 6.8 Hz, 3 H), 1.14 (s, 3 H), 1.26-1.33 (m, 2 H), 1.48-1.57 (m, 1 H), 1.77 (dd, *J* = 2.6, 5.9 Hz, 1 H), 1.80 (dd, *J* = 3.1, 5.9 Hz, 1 H), 2.69 (br, 1 H), 3.05 (s, 3 H), 3.06 (s, 3 H), 4.67 (s, 1 H); (minor, diagnostic peaks) 0.84 (d, *J* = 6.8 Hz, 3 H), 0.85 (d, *J* = 6.8 Hz, 3 H), 1.05-1.13 (m, 1 H), 1.22 (s, 3 H), 1.19-1.26 (m, 1 H), 1.39-1.46 (m, 1 H), 2.69 (br, 1 H), 3.05 (s, 3 H), 3.06 (s, 3 H), 4.65 (s, 1 H); ^{13}C NMR (100 MHz, $CD_3C(O)CD_3$) (major diastereoisomer) δ 21.1, 23.0, 27.7, 29.7, 31.3, 32.1, 34.6, 46.6, 86.0, 153.6, 175.6; (minor) 17.7, 22.7, 22.9, 29.1, 33.6, 34.7, 35.3, 48.0, 84.9, 153.7, 174.5; IR (neat) 764, 789, 874, 945, 1039, 1095, 1178, 1293, 1366, 1383, 1419, 1468, 1482, 1655, 1712, 2870, 2926, 2955, 3397; HRMS calcd for $C_{12}H_{22}N_2O_3Na$ (M^+ + Na) 265.1528, found 265.1523.

General procedure for the generation and capture of N-acyliminiums. 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 (typically, BF_3•Et_2O, 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 selectivity, conversion and yield using internal standard and comparison with authentic samples. Purification by chromatography using silica gel afforded the title product.

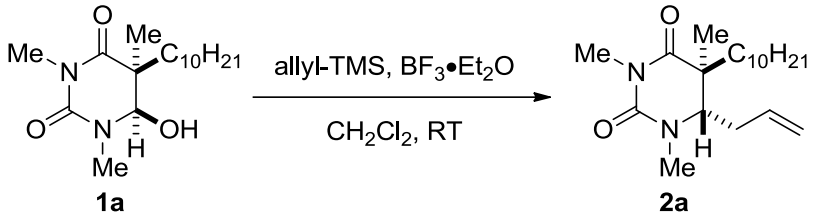
Optimization of the generation and capture of N-acyliminiums (Table 1). According to the general procedure, hemiaminal **1a** was reacted with allyltrimethylsilane (10 equiv) and a Lewis acid (typically, 3 equiv) for 2 h at room temperature. The reaction was diluted with CH_2Cl_2 (20 mL) and HCl (0.1 *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 or 500 MHz) to obtain conversion and yield using internal standard and comparison with authentic samples. Specific details are given below.

- Entries 1-8: General optimization procedure was followed using $TiCl_4$, $SnCl_4$, $AlCl_3$, Me_3Al, Me_2AlCl, TMSOTf, TFA, BF_3•Et_2O, respectively.
- Entry 7: Trifluoroacetic acid (50 equiv) was used.
- Entry 9: The reaction was carried out and quenched at -78 °C.
- Entry 10: Allylmagnesium bromide instead of allyltrimethylsilane was used.

In Entries 1-2, 6, 8-9 ($TiCl_4$, $SnCl_4$, TMSOTf, BF_3•Et_2O) clean conversion to the corresponding 5-allyl-uracil **2a** was observed. Reaction conditions from Entry 8 (BF_3•Et_2O, rt) were selected to examine the scope of the reaction based on stereoselectivity, yield and experimental convenience as determined by the optimization studies. Importantly, these results indicate that a variety of reaction conditions can be applied to intercept N-acyliminiumions generated from α-alkoxy-*N*-Ac-carbamides under acidic conditions.

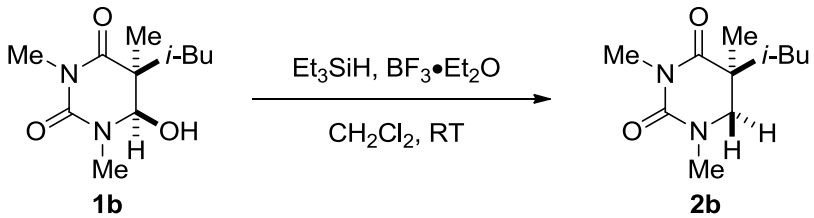
Addition of Nucleophiles to alpha-Hydroxy-N-Acylcarbamides

Table 2, Entry 1



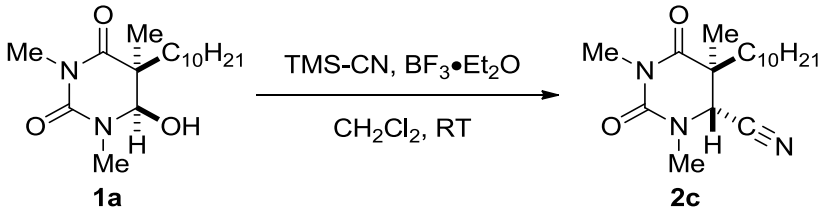
(5*S,6*S**)-6-Allyl-5-decyl-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (2a).** To a solution of hemiaminal **1a** (0.032 mmol) and allyltrimethylsilane (10 equiv) in CH_2Cl_2 (1.0 mL), BF_3•Et_2O (3 equiv) was added dropwise at rt and the reaction was stirred at rt for 2 h. The reaction was diluted with CH_2Cl_2 (20 mL)/HCl (0.1 *N*, 20 mL), extracted with CH_2Cl_2 (2 x 20 mL), dried and concentrated. Purification by chromatography (1/1 EtOAc/hexanes) afforded the title compound as a colorless oil. Yield 86%. Rf (50% EtOAc/hexanes) = 0.76. Dr > 95:5 (crude), > 95:5 (purified). Stereochemistry of the major diastereoisomer was determined by 2 D NMR experiments (NOE between Me and CH_2 (CH_2CH=CH)). Stereochemistry of other compounds was assigned by analogy. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.81 (t, *J* = 7.0 Hz, 3 H), 0.99-1.08 (m, 1 H), 1.13 (s, 3 H), 1.14-1.26 (m, 15 H), 1.33 (td, *J* = 4.0, 12.0 Hz, 1 H), 1.53 (td, *J* = 4.5, 13.0 Hz, 1 H), 2.11-2.17 (m, 1 H), 2.30-2.36 (m, 1 H), 3.00 (s, 3 H), 3.02 (dd, *J* = 4.5, 7.5 Hz, 1 H), 3.05 (s, 3 H), 4.98-5.03 (m, 2 H), 5.55-5.65 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 18.1, 22.7, 23.8, 27.7, 29.3, 29.4, 29.5, 29.5, 29.9, 31.9, 34.3, 36.7, 37.7, 44.9, 63.1, 119.1, 132.6, 153.1, 174.5. IR (neat) 2924, 2854, 1669, 1467, 1417, 1381, 1366, 1283, 1217, 1083, 917, 757 cm^{-1}. HRMS calcd for $C_{20}H_{37}N_2O_2$ (M^+ + H) 337.2850, found 337.2852. Note that uracil **2a** has been reported in our preliminary report on the reduction of cyclic 1,3-diimides using SmI_2–H_2O.

Table 2, Entry 2



5-Isobutyl-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (2b). To a solution of hemiaminal **1b** (0.050 mmol) and triethylsilane (10 equiv) in CH_2Cl_2 (1.0 mL), BF_3•Et_2O (3 equiv) was added dropwise at rt and the reaction was stirred at rt for 2 h. The reaction was diluted with CH_2Cl_2 (20 mL)/HCl (0.1 *N*, 20 mL), extracted with CH_2Cl_2 (2 x 20 mL), dried and concentrated. Purification by chromatography (1/1 EtOAc/hexanes) afforded the title compound as a colorless oil. Yield 79%. ^{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), 1.44 (d, *J* = 6.0 Hz, 1 H), 1.47 (d, *J* = 5.7 Hz, 1 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}. HRMS calcd for $C_{11}H_{20}N_2O_2Na$ (M^+ + Na) 235.1422, found 235.1422.

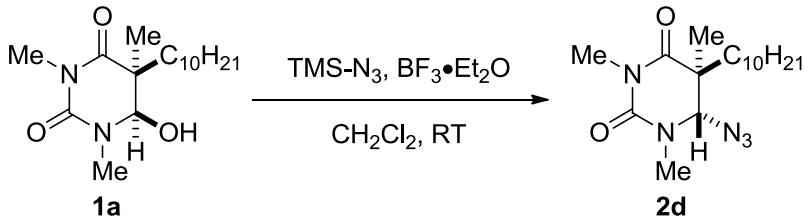
Table 2, Entry 3



(4*R,5*S**)-5-Decyl-1,3,5-trimethyl-2,6-dioxohexahydropyrimidine-4-carbonitrile (2c).** According to the general procedure, the reaction of (5*S**,6*R**)-5-decyl-6-hydroxy-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (0.032 mmol, 1 equiv), trimethylsilyl cyanide (0.320 mmol, 10 equiv), BF_3•OEt_2 (0.160 mmol, 5 equiv) in CH_2Cl_2 for 3 h afforded after purification by column chromatography (30% EtOAc/petroleum ether) the title compound as a colorless oil. Yield 99%. Dr = 81:19 (crude), 83:17 (isolated). ^{1}H NMR (500 MHz, $CD_3C(O)CD_3$) (major diastereoisomer) δ 0.88 (t, *J* = 6.9 Hz, 3 H), 1.21-1.36 (m, 16 H), 1.38 (s, 3 H), 1.57-1.64 (m, 1 H), 1.67-1.76 (m, 1 H), 3.13 (s, 3 H), 3.13 (s, 3 H), 4.69 (s, 1 H); (minor, diagnostic peaks) δ 0.87 (t, *J* = 6.9 Hz, 3 H), 1.32 (s, 3 H), 1.44-1.54 (m, 1 H), 1.64-1.70 (m, 1 H), 2.01-2.08 (m, 1 H), 3.12 (s, 3 H), 3.15 (s, 3 H), 4.68 (s, 1 H); ^{13}C NMR (125 MHz, $CD_3C(O)CD_3$) (major diastereoisomer) δ 14.4, 19.0, 23.4, 24.4, 28.4, 29.9, 30.0, 30.2, 30.3, 30.3, 32.7, 35.3, 36.1, 45.3, 55.9, 116.8, 153.3, 172.4; (minor, diagnostic peaks) δ 20.0, 23.2, 35.0, 35.3, 44.7, 55.5, 116.4, 154.0, 173.3; IR (neat) 757, 963, 1070, 1181, 1289, 1355, 1390, 1415,

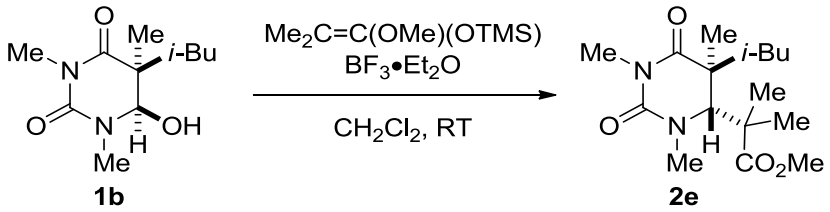
1465, 1678, 1722, 2855, 2925; LRMS calcd for $C_{18}H_{32}N_3O_2$ (M^+ + H) 322.3, found 322.4 (ES). HRMS could not be found due to instability of the title compound.

Table 2, Entry 4



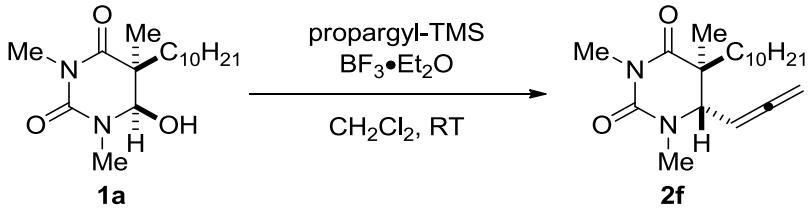
(5*S,6*S**)-6-Azido-5-decyl-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (2d).** According to the general procedure, the reaction of (5*S**,6*R**)-5-decyl-6-hydroxy-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (0.032 mmol, 1 equiv), trimethylsilylazide (0.32 mmol, 10 equiv), BF_3•OEt_2 (0.16 mmol, 5 equiv) in CH_2Cl_2 for 3 h afforded after purification by column chromatography (30% EtOAc/petroleum ether) the title compound as a colorless oil. Yield 99%. Dr = 74:26 (crude), 74:26 (isolated). ^{1}H NMR (400 MHz, $CD_3C(O)CD_3$) (major diastereoisomer) δ 0.88 (t, *J* = 6.8 Hz, 3 H), 1.27 (s, 3 H), 1.15-1.44 (m, 16 H), 1.50-1.69 (m, 2 H), 3.07 (s, 3 H), 3.21 (s, 3 H), 5.22 (s, 1 H); (minor, diagnostic peaks) δ 0.87 (t, *J* = 6.8 Hz, 3 H), 1.24 (s, 3 H), 1.83-1.93 (m, 1 H), 3.24 (s, 3 H), 5.25 (s, 1 H); ^{13}C NMR (100 MHz, $CD_3C(O)CD_3$) (major diastereoisomer) δ 14.4, 17.9, 23.4, 24.5, 27.9, 29.8, 30.0, 30.2, 30.4, 30.5, 32.7, 36.0, 37.3, 47.9, 81.2, 153.3, 173.1; (minor, diagnostic peaks) δ 20.1, 21.0, 23.1, 23.4, 28.0, 30.9, 33.7, 36.2, 46.4, 80.0, 154.0, 174.1; IR (neat) 760, 902, 949, 1072, 1237, 1295, 1379, 1420, 1466, 1676, 1720, 2102, 2855, 2924; LRMS calcd for $C_{17}H_{31}N_5O_2Na$ (M^+ + Na) 360.2, found 360.4 (ES). HRMS could not be found due to instability of the title compound.

Table 2, Entry 5



Methyl 2-((4*R,5*S**)-5-isobutyl-1,3,5-trimethyl-2,6-dioxohexahydropyrimidin-4-yl)-2-methylpropanoate (2e).** According to the general procedure, the reaction of (5*S**,6*R**)-6-hydroxy-5-isobutyl-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (0.044 mmol, 1 equiv), 1-methoxy-2-methyl-1-(trimethylsiloxy)propene (0.44 mmol, 10 equiv), BF_3•OEt_2 (0.22 mmol, 5 equiv) in CH_2Cl_2 for 3 h afforded after purification by column chromatography (30% EtOAc/petroleum ether) the title compound as a colorless oil. Yield 96%. Dr >95:5 (crude), >95:5 (isolated). ^{1}H NMR (400 MHz, $CD_3C(O)CD_3$) δ 0.74 (d, *J* = 6.7 Hz, 3 H), 0.92 (d, *J* = 6.7 Hz, 3 H), 0.99 (s, 3 H), 1.06 (s, 3 H), 1.24 (s, 3 H), 1.41-1.46 (m, 2 H), 1.64-1.76 (m, 1 H), 3.02 (s, 3 H), 3.18 (s, 3 H), 3.69 (s, 3 H), 3.75 (s, 1 H); ^{13}C NMR (100 MHz, $CD_3C(O)CD_3$) δ 17.9, 18.6, 24.1, 24.3, 25.7, 27.7, 28.1, 41.6, 45.9, 48.5, 48.9, 52.6, 69.6, 154.0, 175.0, 177.3; IR (neat) 741, 759, 981, 1038, 1089, 1138, 1181, 1220, 1258, 1290, 1391, 1420, 1475, 1666, 1708, 1725, 2870, 2955, 2989; HRMS calcd for $C_{16}H_{28}N_2O_4Na$ (M^+ + Na) 335.1947, found 335.1931.

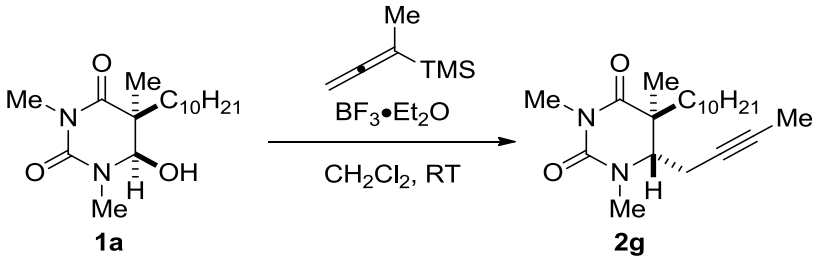
Table 2, Entry 6



(5*S,6*S**)-5-Decyl-1,3,5-trimethyl-6-(propa-1,2-dien-1-yl)dihydropyrimidine-2,4(1*H*,3*H*)-dione (2f).** According to the general procedure, the reaction of (5*S**,6*R**)-5-decyl-6-hydroxy-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (0.032 mmol, 1 equiv), trimethyl(propargyl)silane (0.32 mmol, 10 equiv), BF_3•OEt_2 (0.16 mmol, 5 equiv) in CH_2Cl_2 for 3 h afforded the title compound as a colorless oil. Yield 77% (determined by ^{1}H NMR analysis). Analytical sample was purified for characterization purposes (30% EtOAc/petroleum ether). Dr = 87:13 (crude), 89:11 (isolated). ^{1}H NMR (500 MHz, $CD_3C(O)CD_3$) (major diastereoisomer) δ 0.88 (t, *J* = 6.6 Hz, 3 H), 1.17 (s, 3 H), 1.21-1.35 (m, 14 H), 1.38-1.43 (m, 1 H), 1.53 (ddd, *J* = 4.7, 12.1, 13.4 Hz, 1 H), 1.60-1.71 (m, 2 H), 2.99 (s, 3 H), 3.04 (s, 3 H), 3.71 (dt, *J* = 2.1, 7.0 Hz, 1 H), 4.82 - 4.94 (m, 2 H), 5.15 (q, *J* = 6.6 Hz, 1 H); ^{13}C NMR (125 MHz, $CD_3C(O)CD_3$) (major diastereoisomer) δ 14.4, 18.7, 23.4, 24.6, 27.8, 28.0, 30.2, 30.3, 30.7, 32.7, 34.6, 35.0, 37.8, 46.6, 63.0, 77.7, 87.6, 153.7, 174.0, 209.1; IR (neat) 722, 757, 847, 1061, 1075, 1096, 1186, 1230,

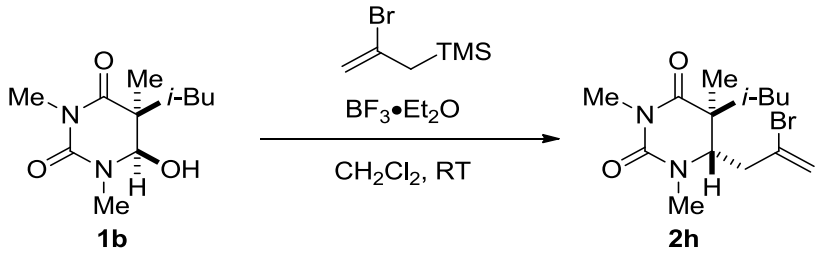
1287, 1381, 1396, 1416, 1466, 1674, 1709, 1736, 1955, 2853, 2923; HRMS calcd for $C_{20}H_{35}N_2O_2$ (M^+ + H) 335.2693, found 335.2690.

Table 2, Entry 7



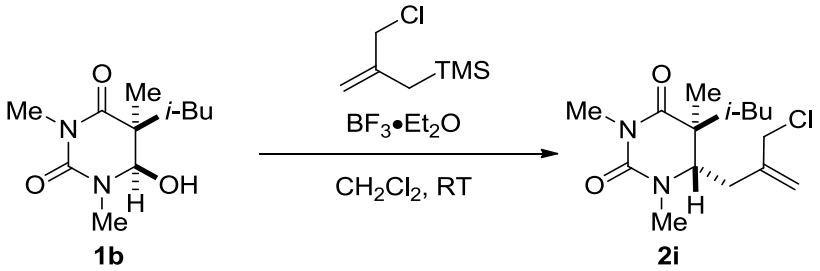
(5*S,6*S**)-6-(But-2-yn-1-yl)-5-decyl-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (2g).** According to the general procedure, the reaction of (5*S**,6*R**)-5-decyl-6-hydroxy-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (0.032 mmol, 1 equiv), 3-(trimethylsilyl)-1,2-butadiene (0.32 mmol, 10 equiv), BF_3•OEt_2 (0.16 mmol, 5 equiv) in CH_2Cl_2 for 3 h afforded after purification by column chromatography (30% EtOAc/petroleum ether) the title compound as a colorless oil. Yield 96%. Dr = 91:9 (crude), 90:10 (isolated). ^{1}H NMR (500 MHz, $CD_3C(O)CD_3$) (major diastereoisomer) δ 0.87 (t, *J* = 6.9 Hz, 3 H), 1.11-1.18 (m, 1 H), 1.19 (s, 3 H), 1.22-1.33 (m, 14 H), 1.33-1.41 (m, 1 H), 1.47 (ddd, *J* = 4.4, 12.0, 13.5 Hz, 1 H), 1.62 (ddd, *J* = 4.7, 12.3, 13.5 Hz, 1 H), 1.67 (t, *J* = 2.5 Hz, 3 H), 2.32 (ddq, *J* = 2.5, 5.1, 17.3 Hz, 1 H), 2.56 (ddq, *J* = 2.5, 4.1, 17.3 Hz, 1 H), 3.04 (s, 3 H), 3.07 (s, 3 H), 3.32 (dd, *J* = 4.1, 5.1 Hz, 1 H); ^{13}C NMR (125 MHz, $CD_3C(O)CD_3$) (major diastereoisomer) δ 3.3, 14.4, 18.2, 19.9, 23.4, 24.4, 27.8, 30.1, 30.2, 30.3, 30.4, 30.7, 32.7, 35.7, 38.9, 45.0, 62.4, 75.0, 79.4, 153.6, 174.3; IR (neat) 722, 756, 1063, 1097, 1191, 1285, 1382, 1398, 1417, 1467, 1665, 1710, 2853, 2922; HRMS calcd for $C_{21}H_{36}N_2O_2Na$ (M^+ + Na) 371.2669, found 371.2663.

Table 2, Entry 8



(5*S,6*S**)-6-(2-Bromoallyl)-5-isobutyl-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (2h).** According to the general procedure, the reaction of (5*S**,6*R**)-6-hydroxy-5-isobutyl-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (0.044 mmol, 1 equiv), 2-bromoallyl trimethylsilane (0.44 mmol, 10 equiv), BF_3•OEt_2 (0.22 mmol, 5 equiv) in CH_2Cl_2 for 3 h afforded after purification by column chromatography (30% EtOAc/petroleum ether) the title compound as a colorless oil. Yield 86%. Dr = 88:12 (crude), >95:5 (isolated). ^{1}H NMR (500 MHz, $CD_3C(O)CD_3$) δ 0.76 (d, *J* = 6.8 Hz, 3 H), 0.93 (d, *J* = 6.8 Hz, 3 H), 1.18 (s, 3 H), 1.46 (dd, *J* = 3.8, 14.0 Hz, 1 H), 1.56 (dd, *J* = 7.3, 14.0 Hz, 1 H), 1.70-1.80 (m, 1 H), 2.62 (dd, *J* = 9.8, 14.2 Hz, 1 H), 2.74 (ddd, *J* = 0.9, 4.0, 14.2 Hz, 1 H), 3.04 (s, 3 H), 3.10 (s, 3 H), 3.51 (dd, *J* = 4.0, 9.8 Hz, 1 H), 5.55 (d, *J* = 1.9 Hz, 1 H), 5.82 (m, 1 H); ^{13}C NMR (125 MHz, $CD_3C(O)CD_3$) δ 19.0, 24.0, 24.5, 25.6, 27.9, 37.8, 43.0, 46.1, 47.0, 63.2, 121.8, 131.4, 153.0, 174.5; IR (neat) 758, 895, 1037, 1090, 1178, 1217, 1284, 1398, 1418, 1471, 1631, 1668, 1710, 2866, 2928, 2956; HRMS calcd for $C_{14}H_{24}N_2O_2Br$ (M^+ + H) 331.1016, found 331.1017.

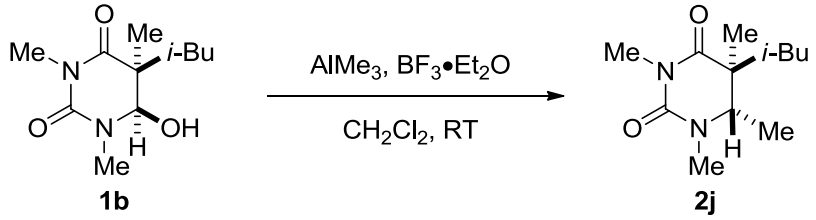
Table 2, Entry 9



(5*S,6*S**)-6-(2-(Chloromethyl)allyl)-5-isobutyl-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (2i).** According to the general procedure, the reaction of (5*S**,6*R**)-6-hydroxy-5-isobutyl-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (0.044 mmol, 1 equiv), 2-(chloromethyl)allyl-trimethylsilane (0.44 mmol, 10 equiv), BF_3•OEt_2 (0.22 mmol, 5 equiv) in CH_2Cl_2 for 3 h afforded after purification by column chromatography (30% EtOAc/petroleum ether) the title compound as a colorless oil. Yield 85%. Dr >95:5 (crude), >95:5 (isolated). ^{1}H NMR (500 MHz, $CD_3C(O)CD_3$) δ 0.75 (d, *J* = 6.5 Hz, 3 H), 0.91 (d, *J* = 6.5 Hz, 3 H), 1.20 (s, 3 H), 1.42 (dd, *J* = 3.8, 14.2 Hz, 1 H), 1.55 (dd, *J* = 7.6, 14.2 Hz, 1 H), 1.71-1.79 (m, 1 H), 2.19 (ddd, *J* = 0.9, 10.1, 14.0 Hz, 1 H), 2.59 (ddd, *J* = 0.9, 4.2, 14.0 Hz, 1 H), 3.00 (s, 3 H), 3.06 (s, 3 H), 3.48 (dd, *J* = 4.2, 10.1 Hz, 1 H), 4.23 (dd, *J* = 0.9, 12.3 Hz, 1 H), 4.30 (dd, *J* = 0.9, 12.3 Hz, 1

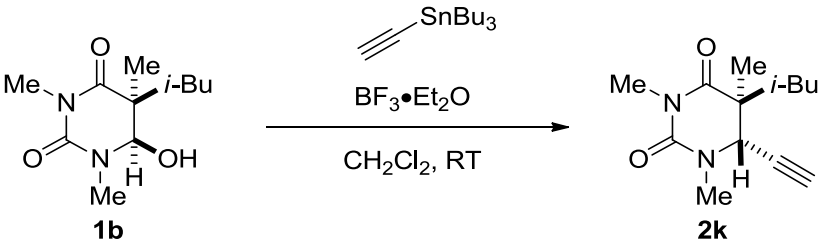
H), 5.09 (d, J = 0.9 Hz, 1 H), 5.33 (d, J = 0.9 Hz, 1 H); ^{13}C NMR (125 MHz, $CD_3C(O)CD_3$) δ 19.1, 24.0, 24.5, 25.7, 27.9, 34.3, 37.7, 46.6, 47.0, 48.6, 63.4, 119.4, 143.0, 153.1, 174.8; IR (neat) 759, 919, 1037, 1091, 1178, 1200, 1226, 1283, 1398, 1417, 1471, 1663, 1707, 2873, 2926, 2955; HRMS calcd for $C_{15}H_{26}N_2O_2Cl$ (M^+ + H) 301.1683, found 301.1680.

Table 2, Entry 10



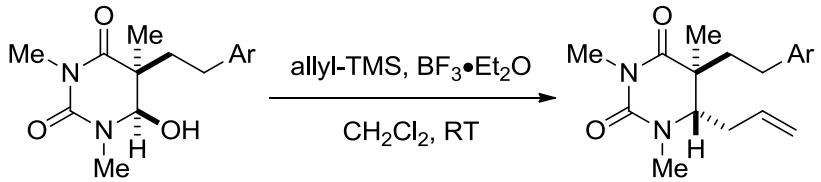
(5*S,6*S**)-5-Isobutyl-1,3,5,6-tetramethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (2j).** To a solution of (5*S**,6*R**)-6-hydroxy-5-isobutyl-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (0.05 mmol) in CH_2Cl_2 (1.0 mL), trimethylaluminum (2.0 M, hexanes, 10 equiv), followed by BF_3•Et_2O (5 equiv) was added dropwise at rt and the reaction was stirred at rt for 2 h. The reaction was diluted with CH_2Cl_2 (20 mL)/NH_4Cl (aq, sat., 20 mL), extracted with CH_2Cl_2 (2 x 20 mL), dried and concentrated. Purification by chromatography (1/1 EtOAc/hexanes) afforded the title compound as a colorless oil. Yield 88%. Dr > 95:5 (crude), >95:5 (purified). Rf (20% EtOAc/hexanes) = 0.74. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.73 (d, J = 6.4 Hz, 3 H), 0.85 (d, J = 6.4 Hz, 3 H), 1.02 (d, J = 6.8 Hz, 3 H), 1.11 (s, 3 H), 1.27 (dd, J = 4.0, 13.6 Hz, 1 H), 1.56 (dd, J = 7.2, 14.0 Hz, 1 H), 1.61-1.72 (m, 1 H), 2.96 (q, J = 6.4 Hz, 1 H), 2.98 (s, 3 H), 3.09 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 18.5, 23.9, 23.9, 25.3, 27.5, 34.7, 45.6, 46.2, 59.8, 152.7, 174.4; IR (neat) 2956, 1709, 1667, 1484, 1416, 1399, 1285, 1209, 1181, 1103, 1051, 1035, 998, 758 cm^{-1}. HRMS calcd for $C_{12}H_{23}N_2O_2$ (M^+ + H) 227.1754, found 227.1745.

Table 2, Entry 11



(5*S,6*S**)-6-Ethynyl-5-isobutyl-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (2k).** According to the general procedure, the reaction of (5*S**,6*R**)-6-hydroxy-5-isobutyl-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (0.044 mmol, 1 equiv), ethynyltributylstannane (0.44 mmol, 10 equiv), BF_3•OEt_2 (0.22 mmol, 5 equiv) in CH_2Cl_2 for 3 h afforded after purification by column chromatography (30% EtOAc/petroleum ether) the title compound as a colorless oil. Yield 99%. Dr >85:15 (crude), 88:12 (isolated). ^{1}H NMR (400 MHz, $CD_3C(O)CD_3$) (major diastereoisomer) δ 0.79 (d, *J* = 6.4 Hz, 3 H), 0.92 (d, *J* = 6.4 Hz, 3 H), 1.34 (s, 3 H), 1.46 (dd, *J* = 4.4, 13.9 Hz, 1 H), 1.63-1.70 (m, 1 H), 1.71-1.80 (m, 1 H), 3.04 (d, *J* = 2.0 Hz, 1 H), 3.05 (s, 3 H), 3.08 (s, 3 H), 4.08 (d, *J* = 2.4 Hz, 1 H); ^{13}C NMR (100 MHz, $CD_3C(O)CD_3$) (major diastereoisomer) δ 24.1, 24.7, 25.3, 28.0, 34.8, 45.5, 46.0, 56.7, 76.3, 79.3, 153.7, 173.7; IR (neat) 667, 749, 761, 872, 1038, 1090, 1175, 1286, 1393, 1415, 1464, 1670, 1714, 2852, 2871, 2925, 2956; HRMS calcd for $C_{13}H_{21}N_2O_2$ (M^+ + H) 237.1598, found 237.1593.

Table 2, Entry 12

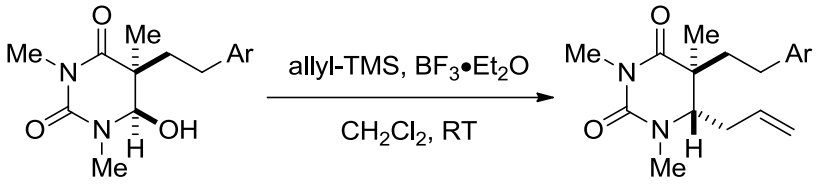


1c, Ar = 4-MeO-C_6H_4 **2l**, Ar = 4-MeO-C_6H_4

(5*S,6*S**)-6-Allyl-5-(4-methoxyphenethyl)-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (2l).** According to the general procedure, the reaction of hemiaminal **1c** (0.050 mmol, 1 equiv), allyltrimethylsilane (0.50 mmol, 10 equiv), BF_3•OEt_2 (0.15 mmol, 3 equiv) in CH_2Cl_2 for 2 h at room temperature afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a colorless oil. Yield 75%. Dr > 95:5 (crude), > 95:5 (purified). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.24 (s, 3 H), 1.58-1.64 (m, 1 H), 1.85 (td, *J* = 5.0, 12.0 Hz, 1 H), 2.14-2.21 (m, 1 H), 2.28-2.39 (m, 2 H), 2.53 (td, *J* = 5.5, 13.0 Hz, 1 H), 2.98 (s, 3 H), 3.05 (s, 3 H), 3.05 (dd, *J* = 4.5, 7.0 Hz, 1 H), 3.71 (s, 3 H), 4.99-5.04 (m, 2 H), 5.56-5.65 (m, 1 H), 6.74 (d, *J* = 9.0 Hz, 2 H), 6.95 (d, *J* = 9.0 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.1, 27.7, 29.4, 34.3, 36.6, 39.8, 45.0, 55.3, 63.2, 114.0, 119.3, 129.2, 132.4, 133.0, 153.0, 158.1, 174.0. IR (neat) 2947, 1708,

1667, 1513, 1478, 1417, 1285, 1247, 1050, 757 cm^{-1}. HRMS calcd for $C_{19}H_{26}N_2O_3Na$ (M^+ + Na) 353.1841, found 353.1825.

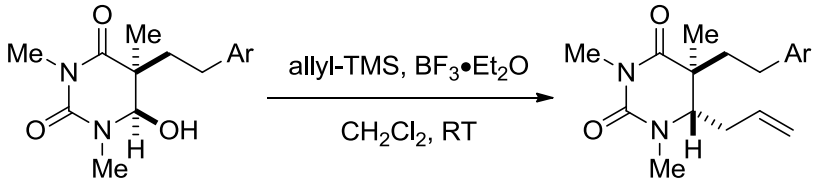
Table 2, Entry 13



1d, Ar = 4-CF_3-C_6H_4 **2m**, Ar = 4-CF_3-C_6H_4

(5*S,6*S**)-6-Allyl-1,3,5-trimethyl-5-(4-(trifluoromethyl)phenethyl)dihydropyrimidine-2,4(1*H*,3*H*)-dione (2m).** According to the general procedure, the reaction of hemiaminal **1d** (0.050 mmol, 1 equiv), allyltrimethylsilane (0.50 mmol, 10 equiv), BF_3•OEt_2 (0.15 mmol, 3 equiv) in CH_2Cl_2 for 2 h at room temperature afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a colorless oil. Yield 92%. Dr > 95:5 (crude), > 95:5 (purified). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.25 (s, 3 H), 1.58-1.66 (m, 1 H), 1.92 (td, *J* = 5.5, 12.5 Hz, 1 H), 2.16-2.22 (m, 1 H), 2.34-2.45 (m, 2 H), 2.65 (td, *J* = 5.0, 12.5 Hz, 1 H), 3.00 (s, 3 H), 3.04-3.07 (m, 1 H), 3.05 (s, 3 H), 5.01-5.05 (m, 2 H), 5.56-5.65 (m, 1 H), 7.15 (d, *J* = 8.0 Hz, 2 H), 7.46 (d, J = 8.5 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.2, 27.8, 30.3, 34.3, 36.6, 39.2, 45.0, 63.5, 119.5, 125.5 (q, J^3 = 3.8 Hz), 128.5, 128.6, 132.2, 145.0, 152.9, 173.5; ^{19}F NMR (470.6 MHz, $CDCl_3$) δ -62.5. IR (neat) 2938, 1708, 1668, 1478, 1418, 1325, 1286, 1163, 1122, 1067, 920, 825 cm^{-1}. HRMS calcd for $C_{19}H_{24}N_2O_2F_3$ (M^+ + H) 369.1784, found 369.1785.

Table 2, Entry 14

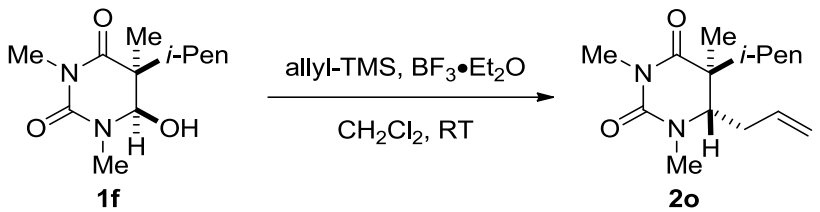


1e, Ar = 4-Br-C_6H_4 **2n**, Ar = 4-Br-C_6H_4

(5*S,6*S**)-6-Allyl-5-(4-bromophenethyl)-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (2n).** According to the general procedure, the reaction of hemiaminal **1e** (0.050 mmol, 1 equiv), allyltrimethylsilane (0.50 mmol, 10 equiv), BF_3•OEt_2 (0.15 mmol, 3 equiv) in CH_2Cl_2 for 2 h at room temperature afforded after purification by chromatography (1/1 EtOAc/hexanes) the

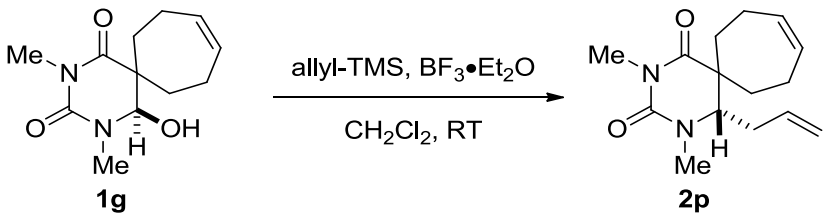
title compound as a colorless oil. Yield 77%. Dr > 95:5 (crude), > 95:5 (purified). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.23 (s, 3 H), 1.56-1.63 (m, 1 H), 1.88 (td, *J* = 5.0, 12.5 Hz, 1 H), 2.15-2.21 (m, 1 H), 2.28-2.39 (m, 2 H), 2.54 (td, *J* = 5.0, 12.5 Hz, 1 H), 2.99 (s, 3 H), 3.04 (dd, *J* = 4.0, 7.0 Hz, 1 H), 3.05 (s, 3 H), 5.00-5.04 (m, 2 H), 5.55-5.64 (m, 1 H), 6.91 (d, *J* = 8.5 Hz, 2 H), 7.32 (d, *J* = 8.5 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.2, 27.7, 29.8, 34.3, 36.6, 39.4, 45.0, 63.4, 119.4, 120.0, 130.0, 131.6, 132.3, 139.9, 153.0, 173.7. IR (neat) 2937, 1707, 1667, 1513, 1474, 1418, 1285, 1247, 1179, 1179, 1050, 918, 823 cm^{-1}. HRMS calcd for $C_{18}H_{24}N_2O_2Br_1$ (M^+ + H) 379.1016, found 379.1018.

Table 2, Entry 15



(5*S,6*S**)-6-Allyl-5-isopentyl-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (2o).** According to the general procedure, the reaction of hemiaminal **1f** (0.041 mmol, 1.0 equiv), allyltrimethylsilane (0.41 mmol, 10 equiv) and BF_3•OEt_2 (0.21 mmol, 5.0 equiv) in CH_2Cl_2 (1.0 mL) for 3 h afforded after purification by chromatography (40% EtOAc/petroleum ether) the title compound as a colorless oil. Yield 76%. Dr = 91:9 (crude), 92:8 (isolated). ^{1}H NMR (400 MHz, $CD_3C(O)CD_3$) δ 0.84 (d, *J* = 6.6 Hz, 3 H), 0.85 (d, *J* = 6.6 Hz, 3 H), 0.99-1.09 (m, 1 H), 1.16 (s, 3 H), 1.19-1.28 (m, 1 H), 1.39-1.52 (m, 2 H), 1.53-1.63 (m, 1 H), 2.17-2.25 (m, 1 H), 2.47 (dddt, *J* = 1.3, 4.3, 7.3, 14.2 Hz, 1 H), 3.00 (s, 3 H), 3.04 (s, 3 H), 3.35 (dd, *J* = 4.4, 6.9 Hz, 1 H), 4.99-5.09 (m, 2 H), 5.72 (ddt, *J* = 7.4, 9.9, 17.2 Hz, 1 H); ^{13}C NMR (100 MHz, $CD_3C(O)CD_3$) δ 18.4, 22.7, 22.9, 27.7, 29.1, 33.4, 35.1, 36.1, 36.6, 45.6, 63.1, 118.7, 134.6, 153.5, 174.9; IR (neat) 758, 917, 1039, 1093, 1178, 1196, 1217, 1283, 1366, 1383, 1398, 1417, 1469, 1665, 1708, 2870, 2929, 2953; HRMS calcd for $C_{15}H_{27}N_2O_2$ (M^+ + H) 267.2073, found 267.2067.

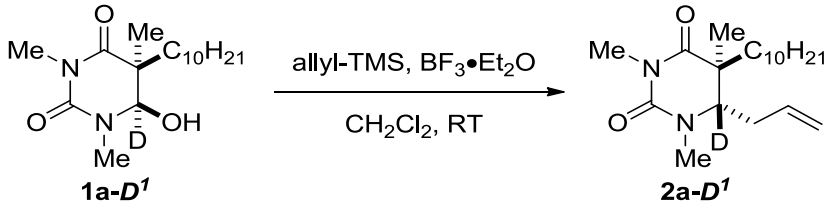
Table 2, Entry 16



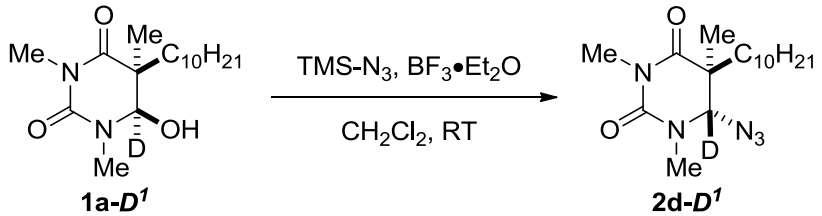
5-Allyl-2,4-dimethyl-2,4-diazaspiro[5.6]dodec-9-ene-1,3-dione (2p). According to the general procedure, the reaction of 5-hydroxy-2,4-dimethyl-2,4-diazaspiro[5.6]dodec-9-ene-1,3-dione (0.042 mmol, 1 equiv), allyltrimethylsilane (0.42 mmol, 10 equiv), BF_3•OEt_2 (0.21 mmol, 5 equiv) in CH_2Cl_2 for 3 h afforded after purification by column chromatography (30% EtOAc/petroleum ether) the title compound as a colorless oil. Yield 83%. ^{1}H NMR (400 MHz, $CD_3C(O)CD_3$) δ 1.63-1.72 (m, 1 H), 1.77-1.94 (m, 2 H), 2.10-2.31 (m, 5 H), 2.43-2.55 (m, 2 H), 3.00 (s, 3 H), 3.05 (s, 3 H), 3.60 (dd, *J* = 4.3, 7.3 Hz, 1 H), 5.00-5.11 (m, 2 H), 5.57-5.82 (m, 1 H), 5.57-5.82 (m, 1 H), 5.75 (ddt, *J* = 7.4, 10.0, 17.1 Hz, 1 H); ^{13}C NMR (100 MHz, $CD_3C(O)CD_3$) δ 24.4, 24.8, 27.7, 30.8, 34.8, 35.0, 36.8, 48.3, 61.5, 118.7, 130.9, 132.1, 134.7, 153.4, 175.6; IR (neat) 632, 727, 756, 917, 1001, 1028, 1052, 1093, 1135, 1219, 1282, 1373, 1398, 1416, 1436, 1475, 1663, 1706, 2847, 2929, 3017; HRMS calcd for $C_{15}H_{23}N_2O_2$ (M^+ + H) 263.1754, found 263.1753.

Synthesis of 6-*D*[1]-Deuterated Uracils

Scheme 1



(5*S,6*S**)-6-*D*[1]-6-Allyl-5-decyl-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (2a-*D*[1]).** According to the general procedure, reaction of (5*S**,6*R**)-6-*D*[1]-5-decyl-6-hydroxy-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (0.032 mmol, 1 equiv), allyltrimethylsilane (0.32 mmol, 10 equiv), BF_3•OEt_2 (0.21 mmol, 5 equiv) in CH_2Cl_2 for 3 h afforded after purification by column chromatography (30% EtOAc/petroleum ether) the title compound as a colorless oil. Yield 99%, >98% *D*[1]. Dr = 91:9 (crude), >95:5 (isolated). ^{1}H NMR (500 MHz, $CD_3C(O)CD_3$) δ 0.87 (t, *J* = 6.9 Hz, 3 H), 1.09-1.15 (m, 1 H), 1.16 (s, 3 H), 1.21-1.33 (m, 14 H), 1.34-1.41 (m, 1 H), 1.46 (ddd, *J* = 4.4, 12.2, 13.3 Hz, 1 H), 1.54-1.62 (m, 1 H), 2.21 (dd, *J* = 7.4, 14.2 Hz, 1 H), 2.46 (dd, *J* = 7.4, 14.2 Hz, 1 H), 3.00 (s, 3 H), 3.03 (s, 3 H), 5.01 (dt, *J* = 1.1, 9.9 Hz, 1 H), 5.05 (dq, *J* = 1.6, 17.1 Hz, 1 H), 5.71 (ddt, *J* = 7.4, 9.9, 17.1 Hz, 1 H); ^{13}C NMR (125 MHz, $CD_3C(O)CD_3$) δ 14.4, 18.4, 23.4, 24.5, 27.6, 30.1, 30.2, 30.3, 30.4, 30.7, 32.7, 34.9, 36.5, 38.4, 45.6, 62.8 (t, *J* = 20.9 Hz), 118.7, 134.5, 153.5, 174.8; IR (neat) 758, 917, 1028, 1093, 1336, 1387, 1414, 1456, 1669, 1710, 2853, 2923; HRMS calcd for $C_{20}H_{36}D_1N_2O_2$ (M^+ + H) 338.2912, found 338.2899.

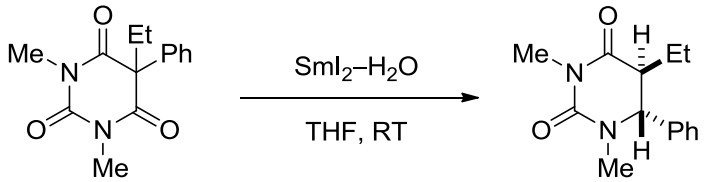


(5*S,6*S**)-6-*D*[1]-6-Azido-5-decyl-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (2d-*D*[1]).** According to the general procedure, reaction of (5*S**,6*R**)-6-*D*[1]-5-decyl-6-hydroxy-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (0.050 mmol, 1 equiv), allyltrimethylsilane (0.50 mmol, 10 equiv), BF_3•OEt_2 (0.15 mmol, 3 equiv) in CH_2Cl_2 for 2 h at room temperature afforded after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a

colorless oil. Yield 91%, >98% D^1. Dr = 75:25 (crude), 74:26 (purified). Minor diastereoisomer was partially separable by careful chromatography. Rf (20% EtOAc/hexanes) = 0.65. ^{1}H NMR (400 MHz, $CD_3C(O)CD_3$) (major diastereoisomer) δ 0.89 (t, *J* = 6.8 Hz, 3 H), 1.21-1.34 (m, 15 H), 1.30 (s, 3 H), 1.36-1.45 (m, 1 H), 1.53-1.67 (m, 2 H), 3.10 (s, 3 H), 3.23 (s, 3 H); (minor) 0.89 (t, *J* = 6.4 Hz, 3 H), 1.25 (s, 3 H), 1.27-1.42 (m, 15 H), 1.44-1.55 (m, 1 H), 1.66 (td, *J* = 4.0, 12.4 Hz, 1 H), 1.85-1.95 (m, 1 H), 3.09 (s, 3 H), 3.25 (s, 3 H); ^{13}C NMR (100 MHz, $CD_3C(O)CD_3$) (major diastereoisomer) δ 14.4, 17.8, 23.4, 24.5, 27.9, 28.6, 29.9, 30.2, 30.3, 30.5, 32.6, 36.0, 37.2, 47.7, 80.7 (t, J^1 = 24.1 Hz), 153.2, 173.1; (minor) 14.2, 21.0, 23.1, 23.2, 27.8, 30.2, 30.3, 30.9, 32.6, 33.7, 36.0, 46.4, 79.8 (t, J^1 = 24.0 Hz), 153.2, 174.0. IR (neat) 2924, 2854, 2098, 1720, 1674, 1461, 1418, 1384, 1325, 1241, 1076, 1038, 1002, 885, 763 cm^{-1}. HRMS calcd for $C_{17}H_{31}N_5O_2D_1$ (M^+ + H) 339.2613, found 339.2617.

Rearrangement of N,N-Dimethylphenobarbital

Scheme 2



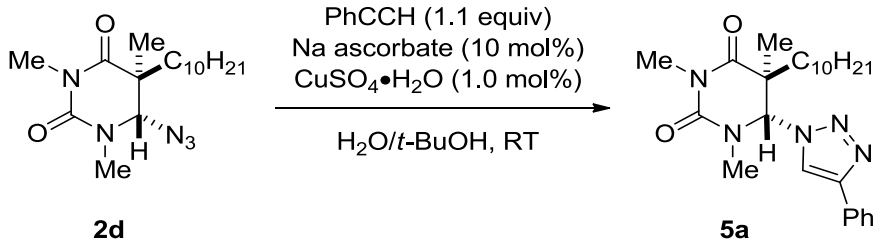
3 **4**

(5*S,6*R**)-5-Ethyl-1,3-dimethyl-6-phenyldihydropyrimidine-2,4(1*H*,3*H*)-dione (4).** According to the general procedure for reactions involving SmI_2,[1-3] cyclic 1,3-diimide **3** (0.10 mmol) was reacted with SmI_2 (0.80 mmol, 8 equiv, 10.0 mL, 0.080 M) and H_2O (1.8 mL, 1000 equiv) for 30 min at rt, followed by work-up with CH_2Cl_2/HCl (1.0 *N*) to afford after purification by chromatography (1/1 EtOAc/hexanes) the title compound as a colorless oil. Yield 84%. Dr = 72:28 (crude), 71:29 (purified. Rf (50% EtOAc/hexanes) = 0.44. Stereochemistry of the major diastereoisomer was determined by 2 D NMR experiments. ^{1}H NMR (500 MHz, $CDCl_3$) δ (major diastereoisomer) 0.85 (t, *J* = 8.0 Hz, 3 H), 1.82-1.91 (m, 1 H), 2.11-2.20 (m, 1 H), 2.72 (s, 3 H), 2.85 (s, 3 H), 2.99-3.03 (m, 1 H), 3.92 (d, *J* = 3.5 Hz, 1 H), 7.05 (dd, *J* = 1.5, 7.0 Hz, 2 H), 7.13-7.24 (m, 3 H); (minor) 0.82 (t, *J* = 7.0 Hz, 3 H), 1.82-1.91 (m, 2 H), 2.68 (s, 3 H), 2.96 (s, 3 H), 3.05-3.09 (m, 1 H), 3.93 (d, *J* = 3.0 Hz, 1 H), 7.10 (dd, *J* = 1.0, 7.0 Hz, 2 H), 7.13-7.23 (m, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (major diastereoisomer) 12.5, 22.6, 24.5, 28.3, 47.4, 66.0,

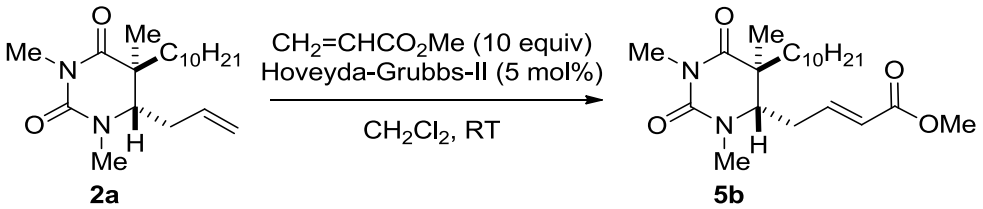
127.5, 128.2, 128.5, 137.9, 156.6, 172.0; (minor) 12.5, 24.6, 25.0, 30.6, 49.5, 66.5, 127.5, 128.4, 128.6, 137.6, 157.2, 172.2. IR (neat) 2965, 2876, 1767, 1705, 1452, 1421, 1396, 1273, 1216, 1023, 757, 703 cm^{-1}. HRMS calcd for $C_{14}H_{18}N_2O_2Na$ (M^+ + Na) 269.1260, found 269.1255.

Reactivity of 6-DH-Uracils – Rapid Generation of Diversity

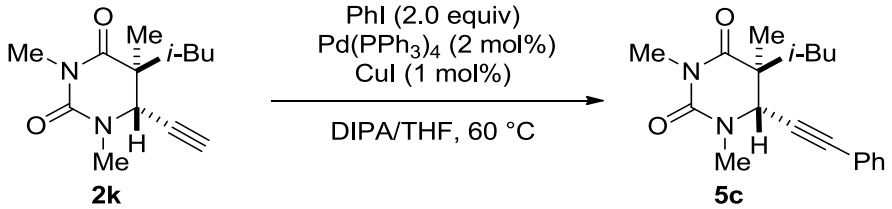
Scheme 3



(5*S,6*S**)-5-Decyl-1,3,5-trimethyl-6-(4-phenyl-1*H*-1,2,3-triazol-1-yl)dihydropyrimidine-2,4(1*H*,3*H*)-dione (5a).** A 10 mL vial was charged with uracil **2d** (0.030 mmol, 1.0 equiv, dr = 74:26), phenylacetylene (0.033 mmol, 1.1 equiv), sodium ascorbate (10 mol%), $CuSO_4$•$5H_2O$ (1 mol%), H_2O (0.25 mL) and *t*-BuOH (0.25 mL) and stirred for 24 h at room temperature. The reaction mixture was diluted with water and extracted with CH_2Cl_2 to give the title compound as an oil after purification by chromatography. Yield 59%. Dr = 72:28 (crude), 77:23 (isolated). ^{1}H NMR (500 MHz, $CD_3C(O)CD_3$) δ (major diastereoisomer) 0.88 (t, *J* = 6.8 Hz, 3 H), 1.18 (s, 3 H), 1.21-1.36 (m, 15 H), 1.45-1.51 (m, 1 H), 1.76-1.86 (m, 1 H), 1.87-1.95 (m, 1 H), 3.05 (s, 3 H), 3.22 (s, 3 H), 6.01 (s, 1 H), 7.31-7.37 (m, 1 H), 7.41-7.46 (m, 2 H), 7.86-7.90 (m, 2 H), 8.46 (s, 1 H); (minor, diagnostic peaks) 0.84 (t, *J* = 7.2 Hz, 3 H), 0.91 (s, 3 H), 0.93-1.00 (m, 1 H), 1.39-1.45 (m, 1 H), 3.05 (s, 3 H), 3.22 (s, 3 H), 6.07 (s, 1 H), 8.48 (s, 1 H); ^{13}C NMR (125 MHz, $CD_3C(O)CD_3$) δ (major diastereoisomer) 14.4, 23.4, 24.6, 28.2, 30.0, 30.1, 30.2, 30.3, 30.5, 31.7, 32.7, 34.7, 38.9, 47.3, 78.0, 121.8, 126.5, 129.1, 129.8, 131.7, 147.9, 153.6, 172.7; (minor, diagnostic peaks) 17.5, 23.1, 23.4, 28.3, 32.7, 33.1, 34.8, 46.1, 77.2, 121.5, 126.5, 129.1, 131.6, 147.9, 153.4, 173.8; IR (neat) 694, 764, 810, 942, 972, 1026, 1036, 1073, 1159, 1273, 1299, 1395, 1419, 1467, 1481, 1674, 1720, 2853, 2923; HRMS calcd for $C_{25}H_{37}N_5O_2Na$ (M^+ + Na) 462.2839, found 462.2850.

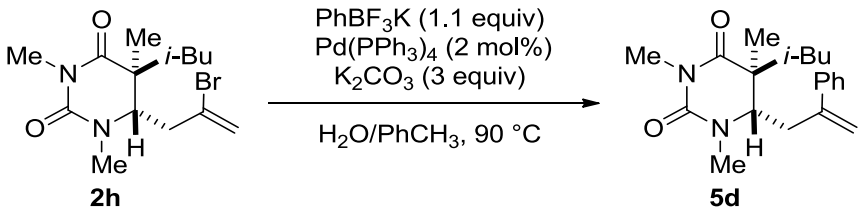


(*E*)-Methyl 4-((4*S,5*S**)-5-decyl-1,3,5-trimethyl-2,6-dioxohexahydropyrimidin-4-yl)but-2-enoate (5b).** A 10 mL vial was charged with uracil **1a** (0.030 mmol, 1.0 equiv, dr = 90:10), methyl acrylate (0.300 mmol, 10 equiv), Hoveyda-Grubbs II catalyst (5 mol%) and CH_2Cl_2 (0.5 mL) and stirred overnight at room temperature to afford after column chromatography (30% EtOAc/petroleum ether) the title compound as a colorless oil. Yield 79%. Dr = 92:8 (crude), 89:11 (isolated). ^{1}H NMR (400 MHz, $CD_3C(O)CD_3$) δ (major diastereoisomer) 0.86 (s, 3 H), 1.08-1.16 (m, 1 H), 1.19 (s, 3 H), 1.22-1.33 (m, 14 H), 1.34-1.42 (m, 1 H), 1.48 (ddd, *J* = 4.2, 12.1, 13.4 Hz, 1 H), 1.59 (ddd, *J* = 4.8, 12.1, 13.4 Hz, 1 H), 2.43 (dddd, *J* = 1.5, 6.7, 8.3, 14.2 Hz, 1 H), 2.67 (dddd, *J* = 1.5, 4.5, 7.3, 14.2 Hz, 1 H), 3.00 (s, 3 H), 3.04 (s, 3 H), 3.51 (dd, *J* = 4.5, 6.7 Hz, 1 H), 3.66 (s, 3 H), 5.90 (dt, *J* = 1.3, 15.6 Hz, 1 H), 6.81 (dt, *J* = 7.8, 15.6 Hz, 1 H); ^{13}C NMR (100 MHz, $CD_3C(O)CD_3$) δ (major diastereoisomer) 14.4, 18.4, 23.4, 24.5, 27.7, 30.1, 30.2, 30.3, 30.4, 30.6, 32.7, 33.3, 36.3, 38.2, 45.7, 51.7, 62.8, 124.8, 144.7, 153.4, 166.6, 174.5; IR (neat) 722, 758, 855, 981, 1041, 1096, 1168, 1219, 1270, 1324, 1399, 1418, 1436, 1467, 1667, 1710, 1726, 2853, 2924; HRMS calcd for $C_{22}H_{38}N_2O_4Na$ (M^+ + Na) 417.2724, found 417.2728.



(5*S,6*S**)-5-Isobutyl-1,3,5-trimethyl-6-(phenylethynyl)dihydropyrimidine-2,4(1*H*,3*H*)-dione (5c).** A 10 mL vial was charged with uracil **2k** (0.042 mmol, 1 equiv, dr = 88:12), iodobenzene (0.084 mmol, 2.0 equiv), tetrakis(triphenylphosphine)palladium (2 mol%), CuI (1 mol%), diisopropylamine (0.2 mL) and THF (1.0 mL) and stirred overnight at 60 °C. The reaction mixture was filtered through a plug of celite and purified by chromatography (20% EtOAc/petroleum ether) to afford the title compound as a colorless oil. Yield 65%. dr = 89:11

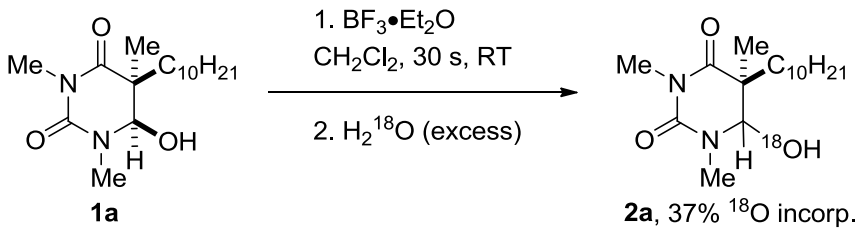
(crude), 88:12 (isolated). ^{1}H NMR (400 MHz, $CD_3C(O)CD_3$) δ (major diastereoisomer) 0.81 (d, *J* = 6.7 Hz, 3 H), 0.94 (d, *J* = 6.7 Hz, 3 H), 1.41 (s, 3 H), 1.52 (dd, *J* = 4.3, 13.9 Hz, 1 H), 1.64-1.75 (m, 1 H), 1.75-1.83 (m, 1 H), 3.11 (s, 3 H), 3.12 (s, 3 H), 4.31 (s, 1 H), 7.34-7.44 (m, 5 H); ^{13}C NMR (100 MHz, $CD_3C(O)CD_3$) δ (major diastereoisomer) 20.0, 24.2, 24.8, 25.4, 28.2, 35.0, 45.7, 46.5, 57.4, 84.7, 86.9, 122.9, 129.5, 129.9, 132.6, 153.9, 174.0; IR (neat) 691, 757, 1037, 1070, 1090, 1174, 1285, 1392, 1414, 1443, 1465, 1670, 1713, 2869, 2928, 2956; HRMS calcd for $C_{19}H_{25}N_2O_2$ (M^+ + H) 313.1911, found 313.1914.



(5*S,6*S**)-5-Isobutyl-1,3,5-trimethyl-6-(2-phenylallyl)dihydropyrimidine-2,4(1*H*,3*H*)-dione (5d).** Literature procedure was followed: G. A. Molander and T. Fumagalli, *J. Org. Chem.*, **2006**, *71*, 5743. A 10 mL vial was charged with uracil **2h** (0.030 mmol, 1.0 equiv), potassium phenyltrifluoroborate (0.037 mmol, 1.1 equiv), K_2CO_3 (0.100 mmol, 3.0 equiv), tetrakis(triphenylphosphine)palladium (2 mol%), toluene (0.5 mL) and H_2O (0.2 mL) and stirred for 3 h at 90 °C. The reaction mixture was cooled to room temperature, $MgSO_4$ was added and the reaction mixture filtered through a short plug of silica. Purification by chromatography (20% EtOAc/petroleum ether) afforded the title compound as a colorless oil. Yield 75%. Dr >95:5 (crude), >95:5 (isolated). ^{1}H NMR (400 MHz, $CD_3C(O)CD_3$) δ 0.71 (d, *J* = 6.7 Hz, 3 H), 0.85 (d, *J* = 6.7 Hz, 3 H), 1.26 (s, 3 H), 1.34 (dd, *J* = 3.8, 14.1 Hz, 1 H), 1.48 (dd, *J* = 7.6, 14.1 Hz, 1 H), 1.64-1.77 (m, 1 H), 2.46 (ddd, *J* = 0.5, 10.5, 14.1 Hz, 1 H), 2.77 (s, 3 H), 3.05 (s, 3 H), 3.06-3.12 (m, 1 H), 3.21 (dd, *J* = 3.9, 10.5 Hz, 1 H), 5.14 (m, 1 H), 5.44 (d, *J* = 1.3 Hz, 1 H), 7.29-7.35 (m, 1 H), 7.36-7.43 (m, 2 H), 7.48-7.54 (m, 2 H); ^{13}C NMR (100 MHz, $CD_3C(O)CD_3$) δ 19.1, 24.0, 24.5, 25.6, 27.9, 36.5, 37.9, 46.6, 46.9, 63.9, 116.8, 127.0, 128.8, 129.6, 140.7, 146.0, 152.9, 174.8; IR (neat) 707, 758, 779, 902, 1037, 1090, 1178, 1282, 1397, 1416, 1467, 1667, 1708, 2866, 2929, 2955; HRMS calcd for $C_{20}H_{29}N_2O_2$ (M^+ + H) 329.2224, found 329.2214.

$H_2{}^{18}O$ Incorporation Experiments/Stability Studies

Scheme 4



$H_2{}^{18}O$ Incorporation. According to the general procedure for generation of N-acyliminiums, an oven-dried vial was charged with (5*S*,6*R*)-5-decyl-6-hydroxy-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (0.060 mmol, 1.0 equiv) and CD_2Cl_2 (0.50 mL), and BF_3•Et_2O (3 equiv) was added under a strong flow of argon with vigorous stirring. After 30 s, the reaction mixture was quenched by rapid addition of $H_2{}^{18}O$ (97 atom %, 0.10 mL). $H_2{}^{18}O$ incorporation = 37% (determined by HRMS analysis). HRMS calcd for $C_{17}H_{32}N_2O_3Na$ (M^+ + Na) 335.2305, found 335.2300. HRMS calcd for $C_{17}H_{32}N_2O_2{}^{18}O_1Na$ (M^+ + Na) 337.2348, found 337.2342.

Acidic Conditions. In a separate experiment, an oven-dried vial was charged with (5*S*,6*R*)-5-decyl-6-hydroxy-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (0.032 mmol, 1.0 equiv) and CD_3CN (0.50 mL), and DCl (0.10 mL, 35% wt in D_2O) was added under strong flow of argon with vigorous stirring. Analysis of the reaction mixture by ^1H NMR (500 MHz) indicated disappearance of the hemiaminal peaks, CD_3CN, 4.49 ppm (d, J = 5.4 Hz, minor) and 4.54 ppm (d, J = 5.4 Hz, major), and presence of a new broad peak at 8.89 ppm, consistent with the formation of an N-acyliminium ion.[9] Rapid decomposition of the reaction mixture was observed by NMR analysis.

Basic Conditions. In a separate experiment, an oven-dried vial was charged with (5*S*,6*R*)-5-decyl-6-hydroxy-1,3,5-trimethyldihydropyrimidine-2,4(1*H*,3*H*)-dione (0.032 mmol, 1.0 equiv) and CD_3CN (0.50 mL), and NaOD (0.10 mL, 40% wt in D_2O) was added under strong flow of argon with vigorous stirring. Analysis of the reaction mixture by ^1H NMR (500 MHz) indicated decomposition of the reaction mixture.

We thank Malcolm Spain (University of Manchester) for assistance with stability studies.

Additional Discussion. The stability studies are consistent with a rapid formation of N-acyliminiums upon exposure of the corresponding alpha-hydroxy-N-acylcarbamides to acidic conditions. In the presence of external nucleophiles opening of hemiaminals and/or N-acyliminiums to form alicyclic ureids is not observed as the nucleophilic capture outcompetes the N-acyliminium degradation. However, in the absence of external nucleophiles, these N-acyliminium ions undergo slow decomposition (several unidentified products are formed). Additionally, under basic conditions a rapid decomposition of alpha-hydroxy-N-acylcarbamides is observed. Overall, these studies are consistent with the presence of equilibria between the open and closed form of cyclic hemiaminals and/or N-acyliminiums as previously suggested by the X-ray crystallographic analysis.[1] These studies suggest that the equilibrium favors cyclic N-acyliminiums under mildly Lewis acidic conditions, which allows for the efficient, highly stereoselective nucleophilic addition.

We postulate that the excellent stereoselectivity of the nucleophilic capture arises from a rigid planar structure of the cyclic N-acyliminium intermediate, in which the steric influence of substituents at the 5-position is enhanced due to non-bonding interactions compared to the traditional chair-conformation of six-membered rings.[10] Further studies on the application of N-acyliminium ions are ongoing in our laboratories and these results will be reported shortly.

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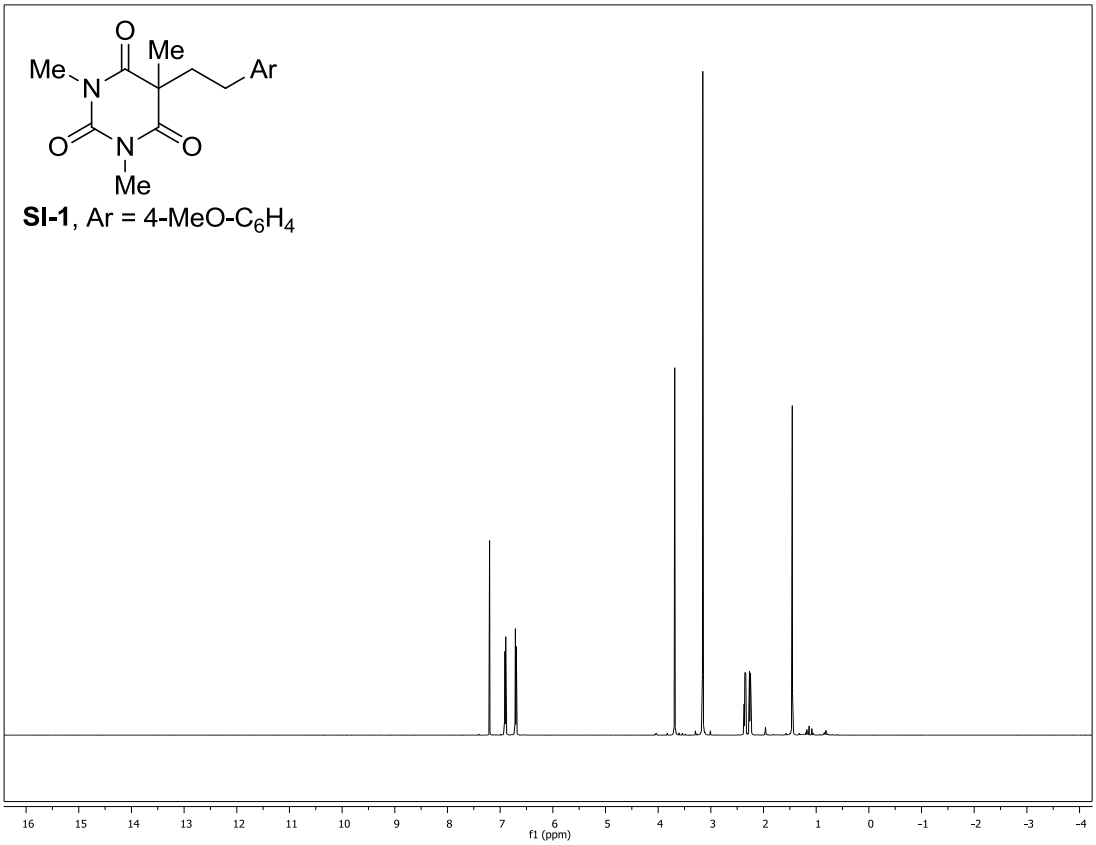
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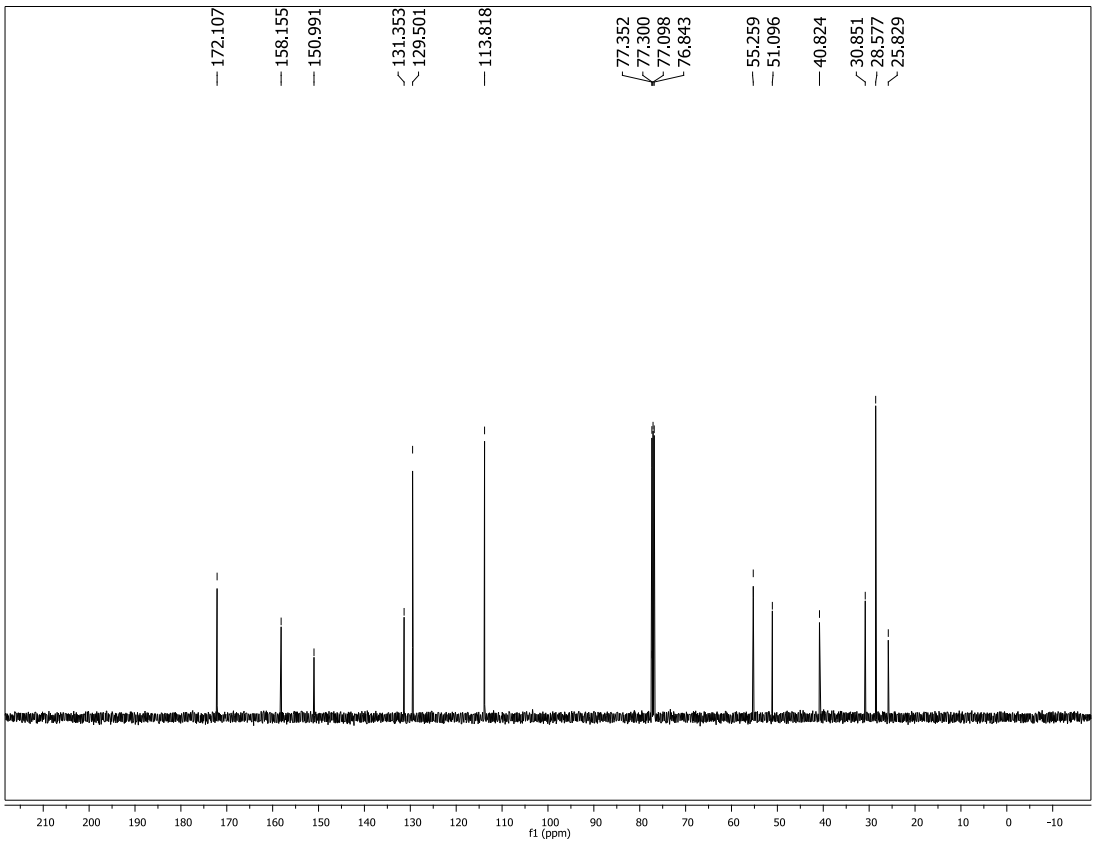
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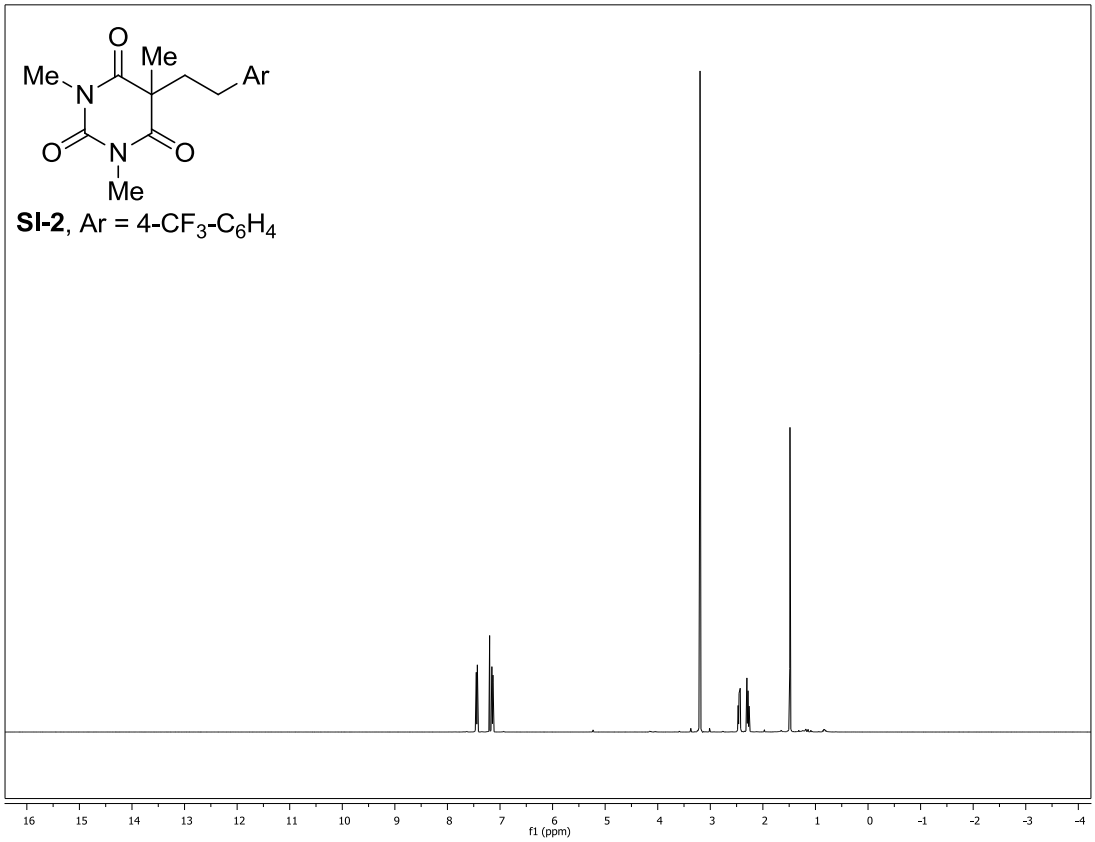
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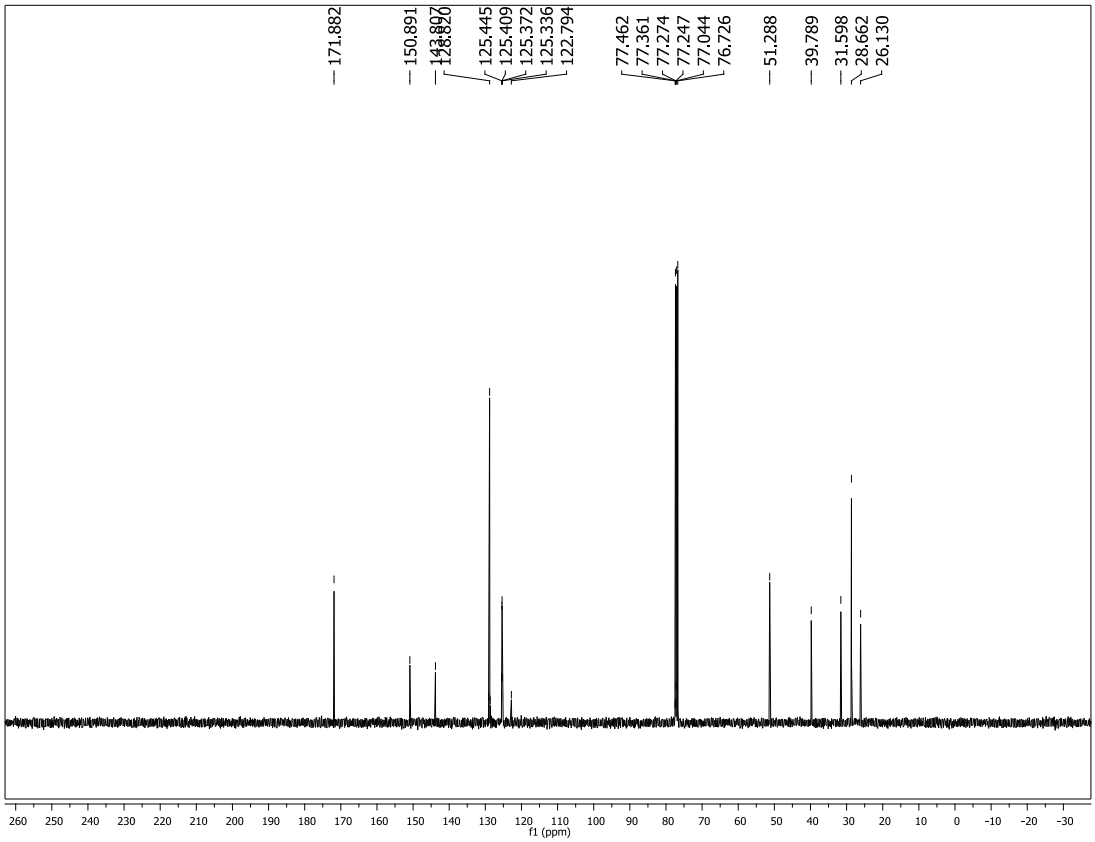
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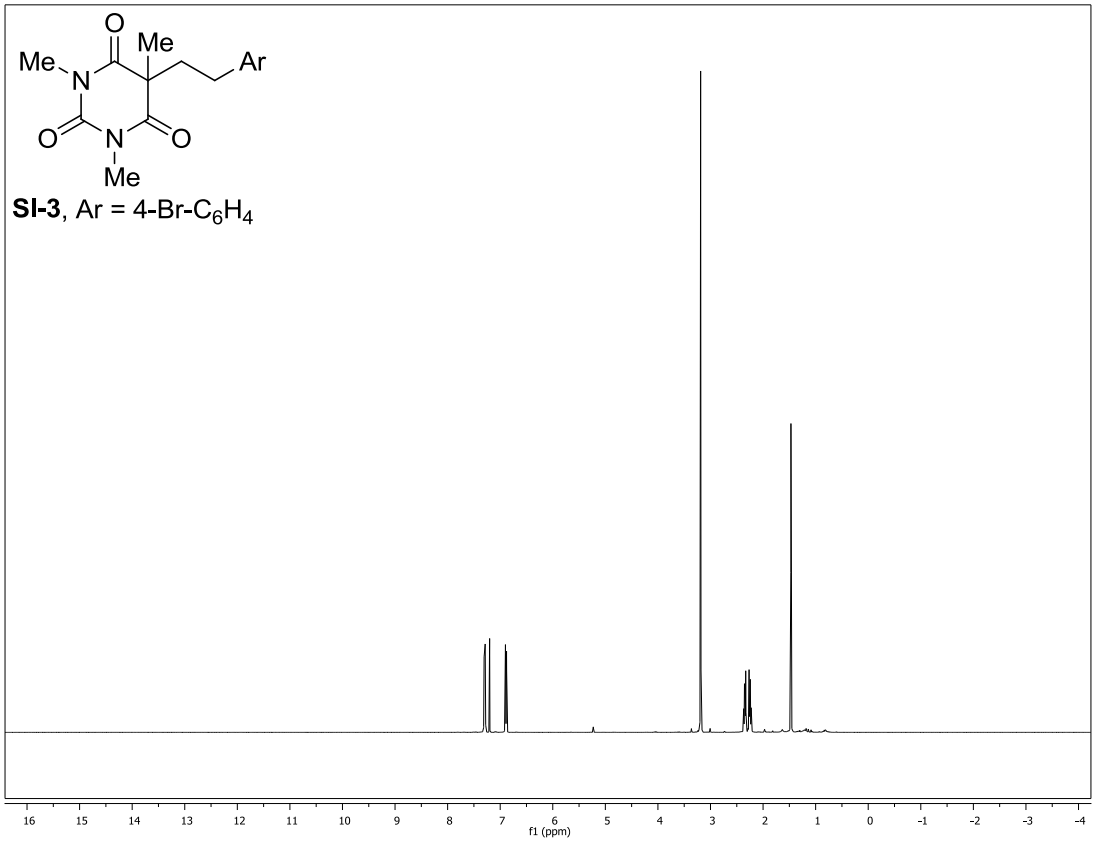
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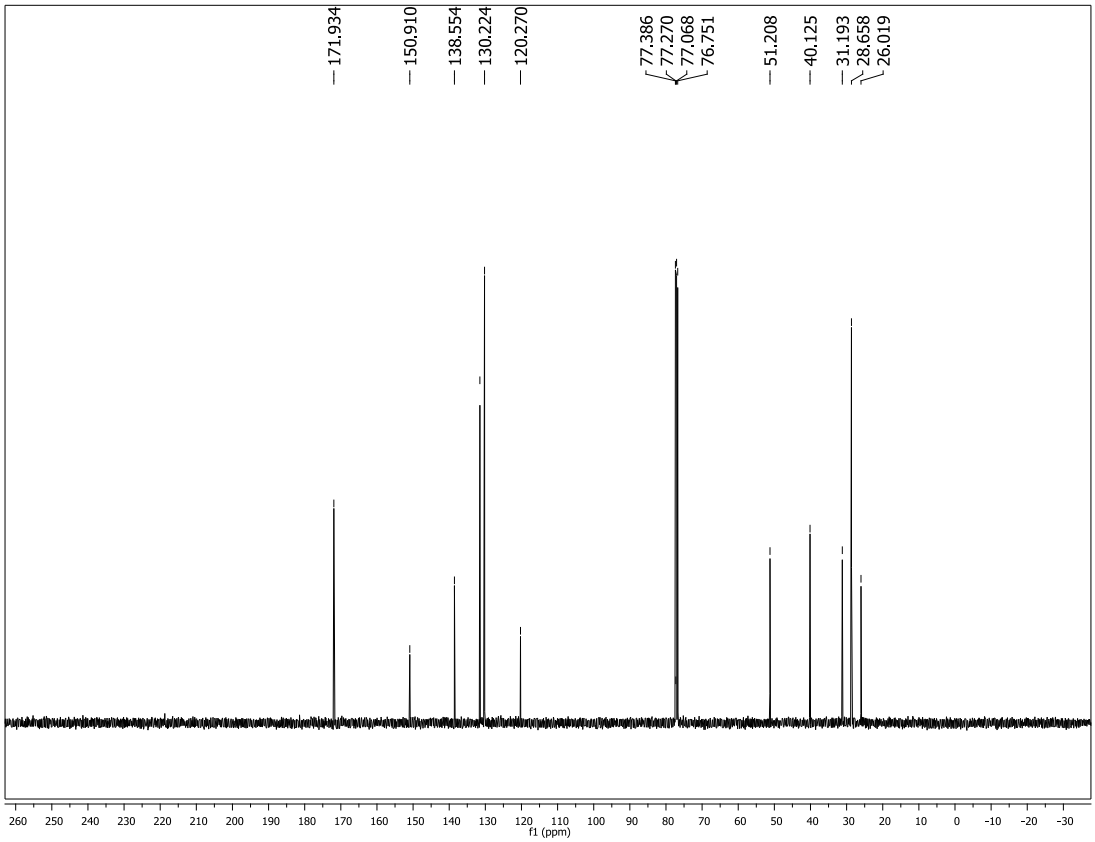
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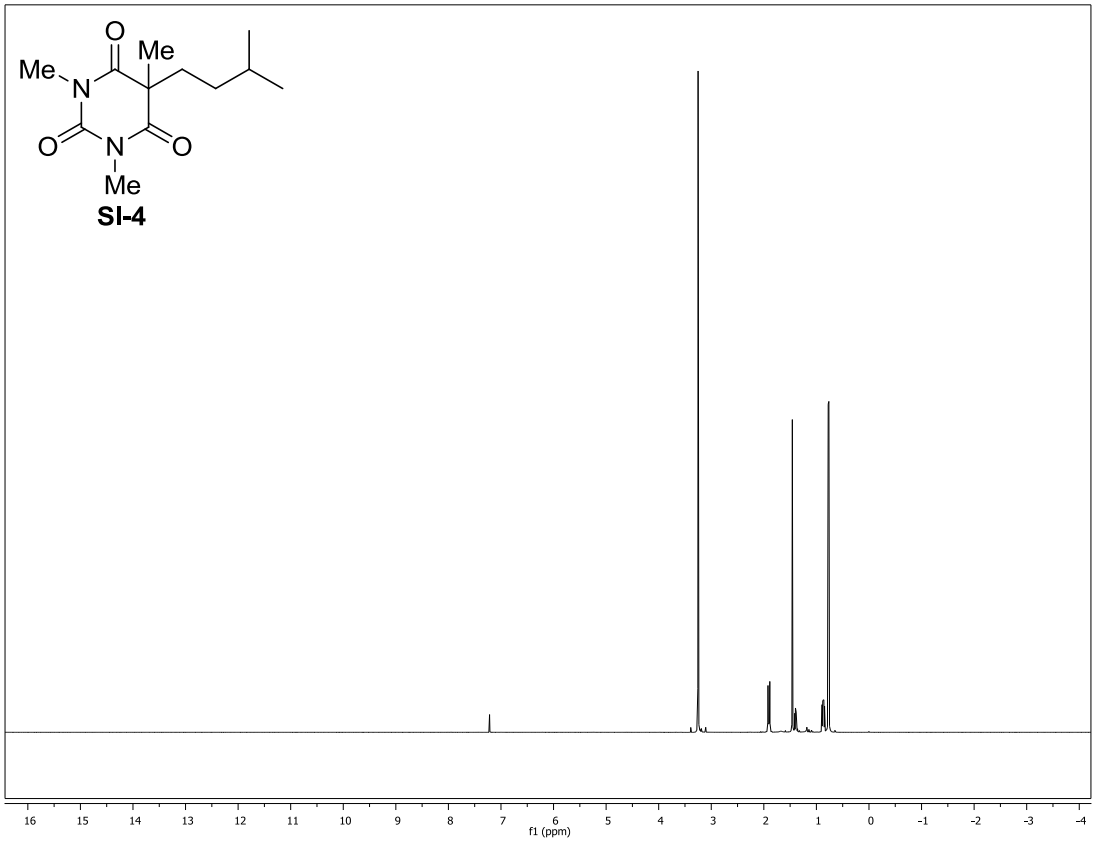
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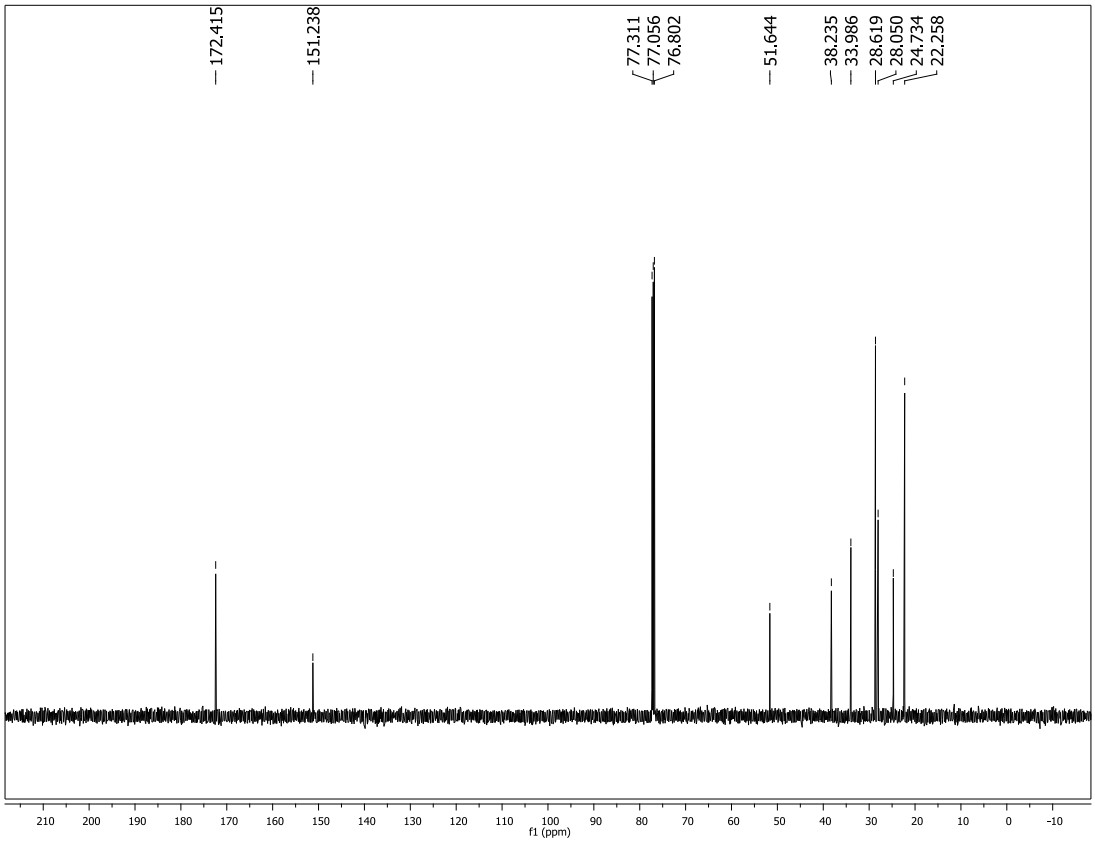
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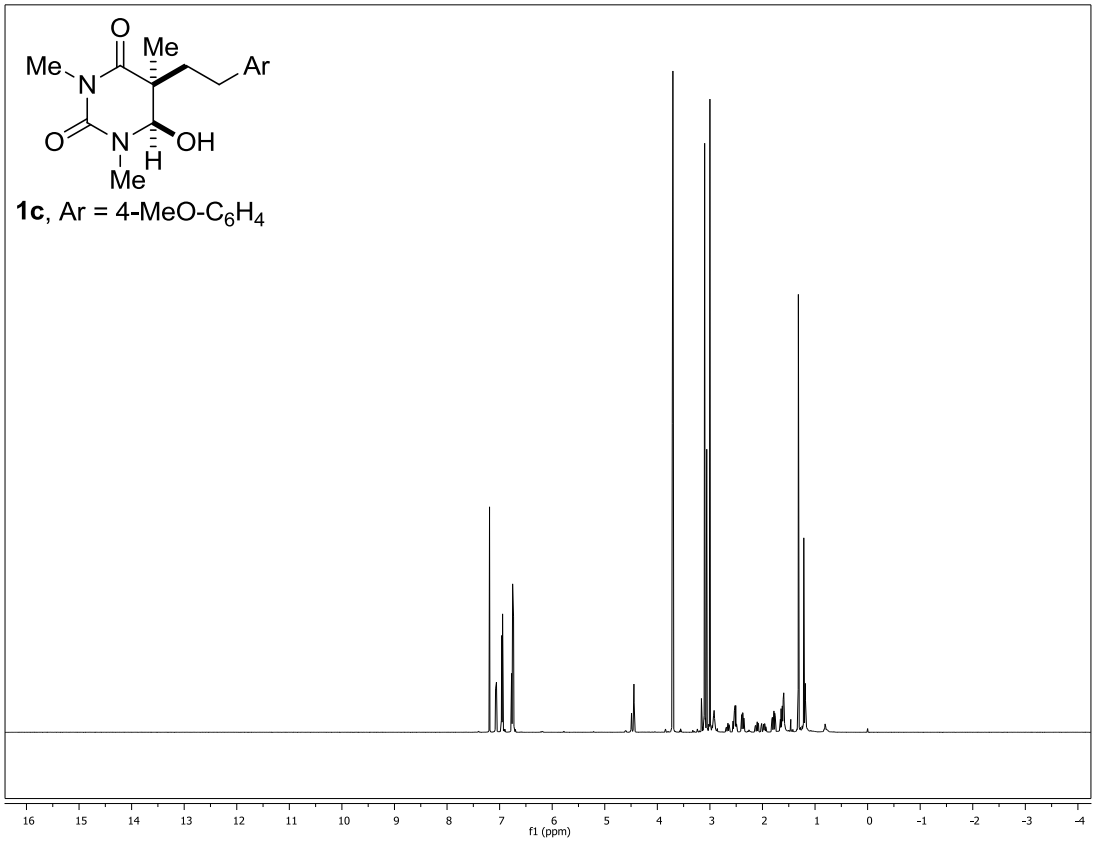
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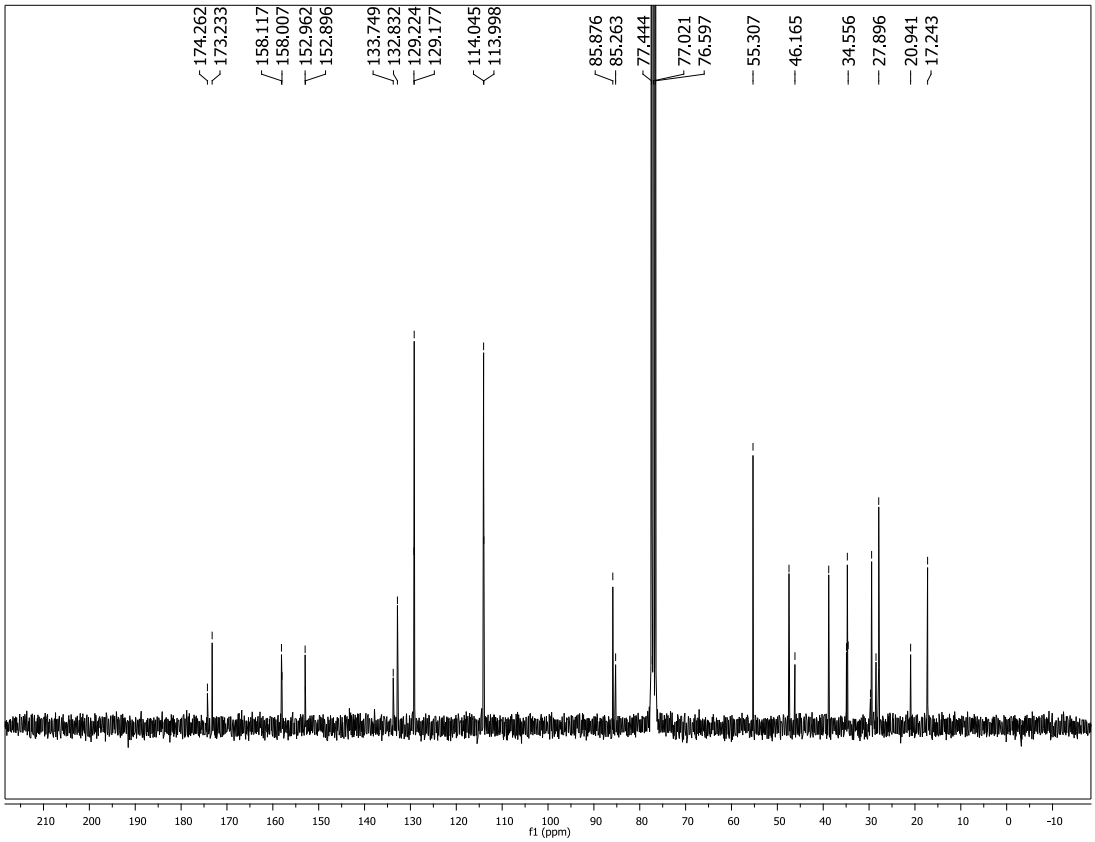
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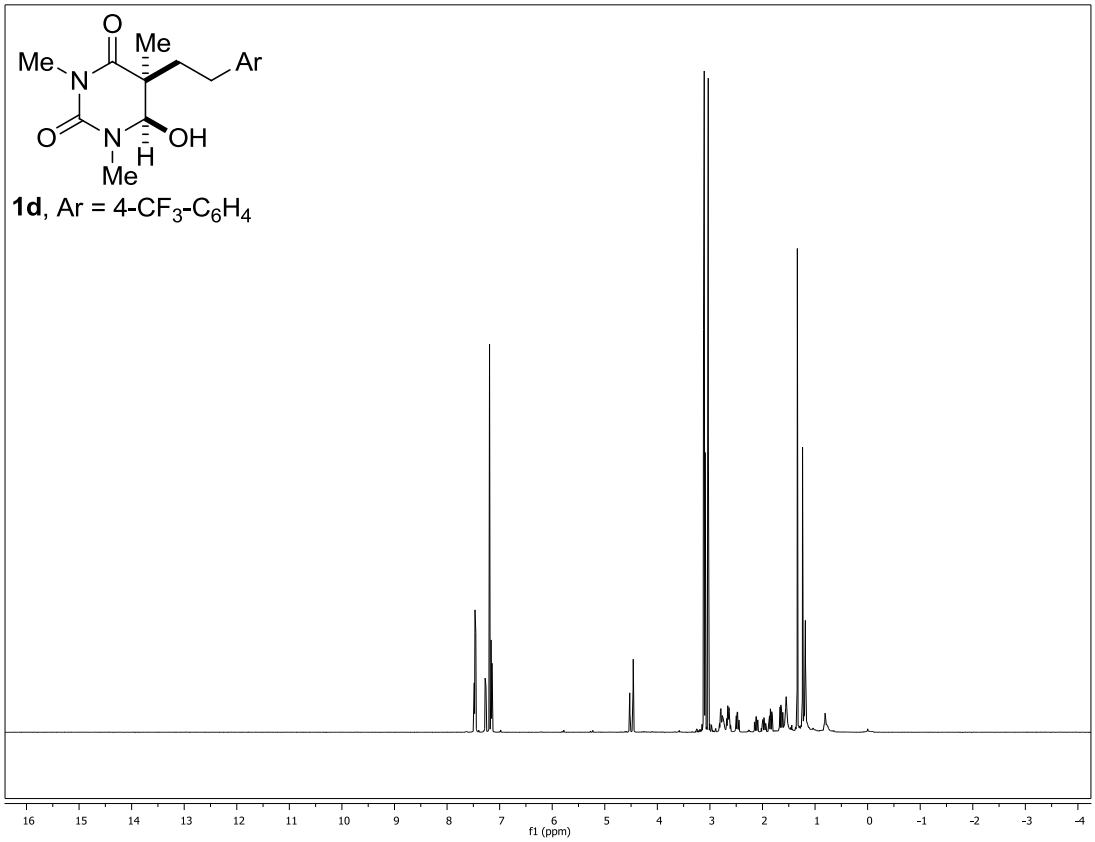
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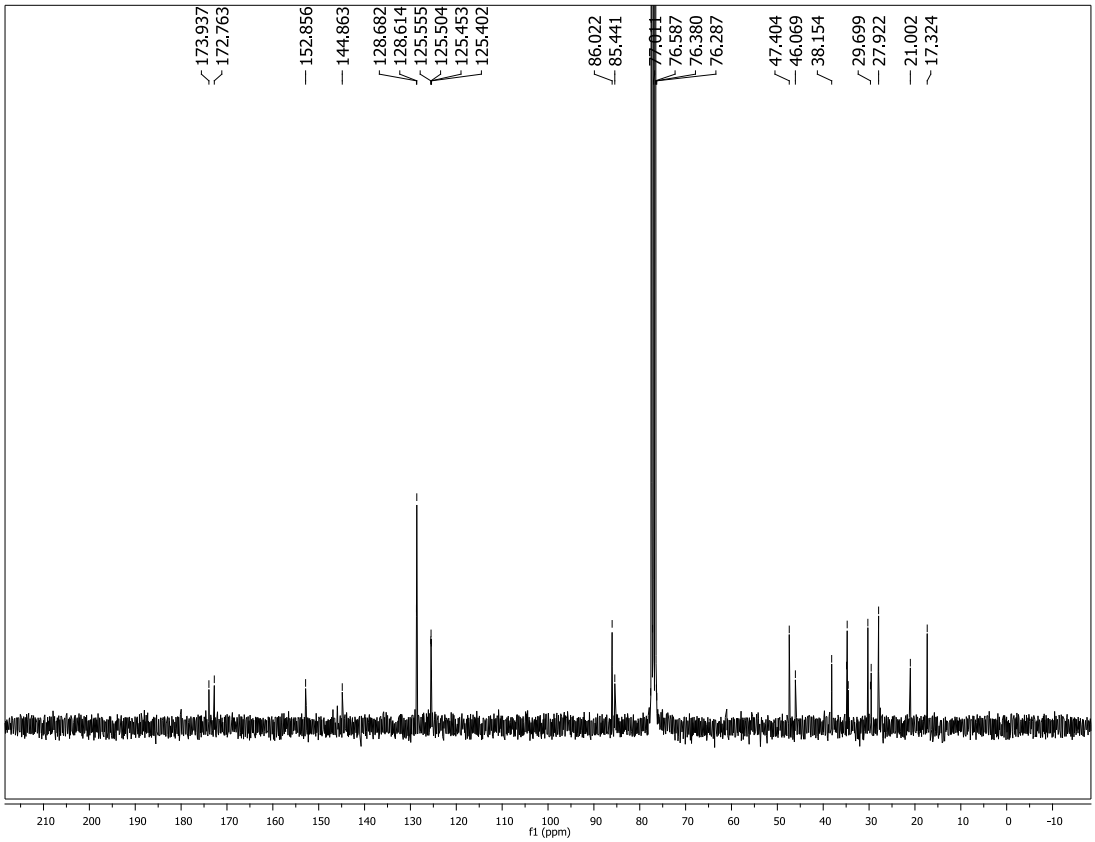
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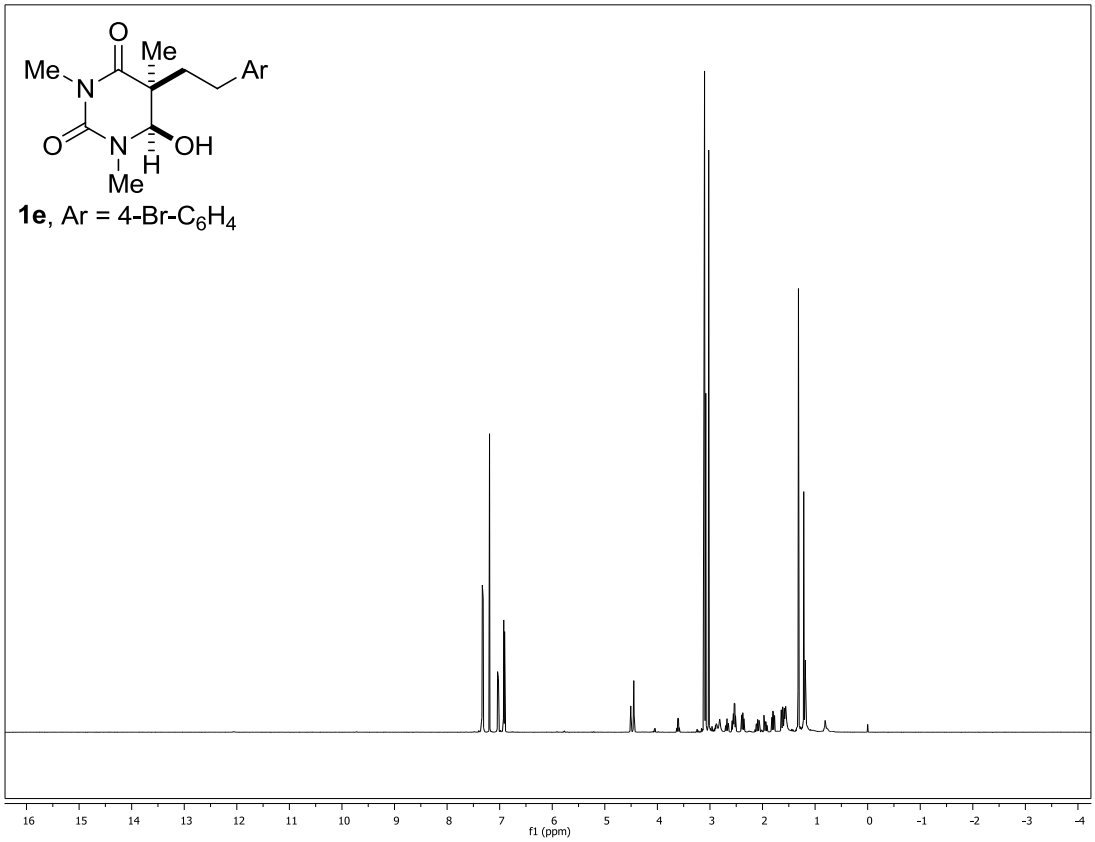
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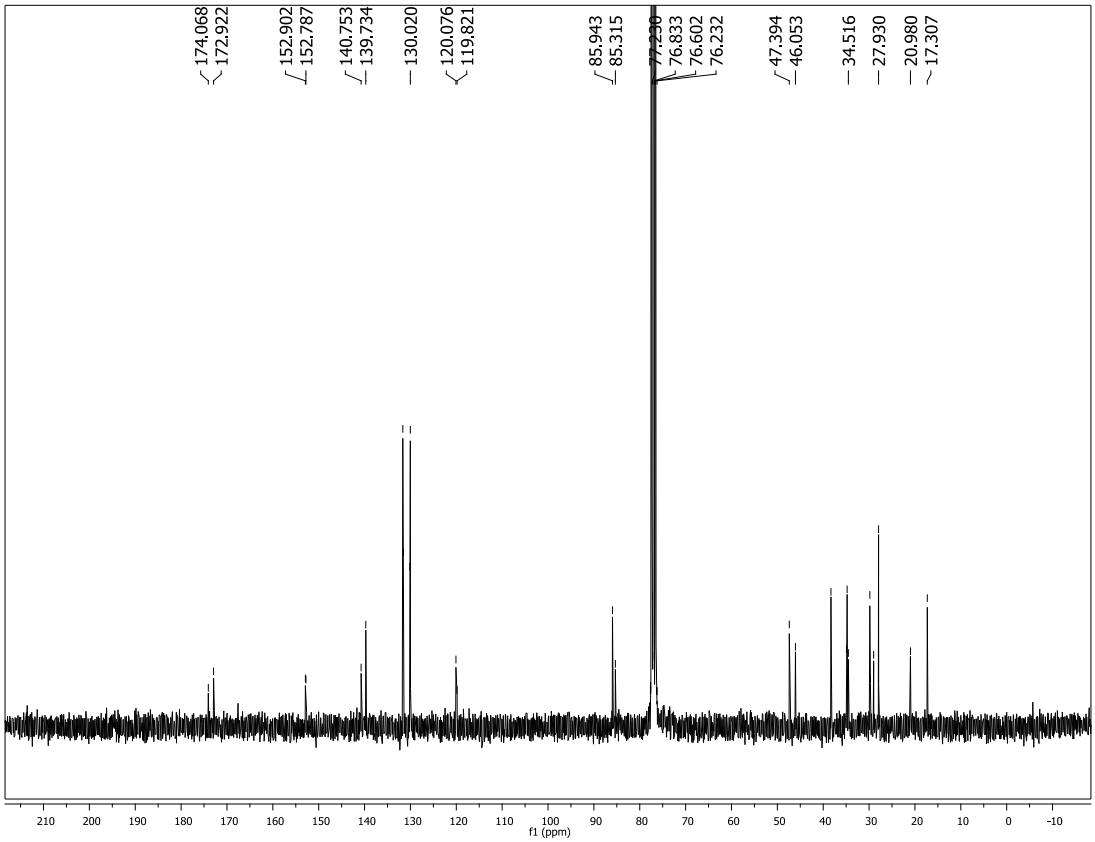
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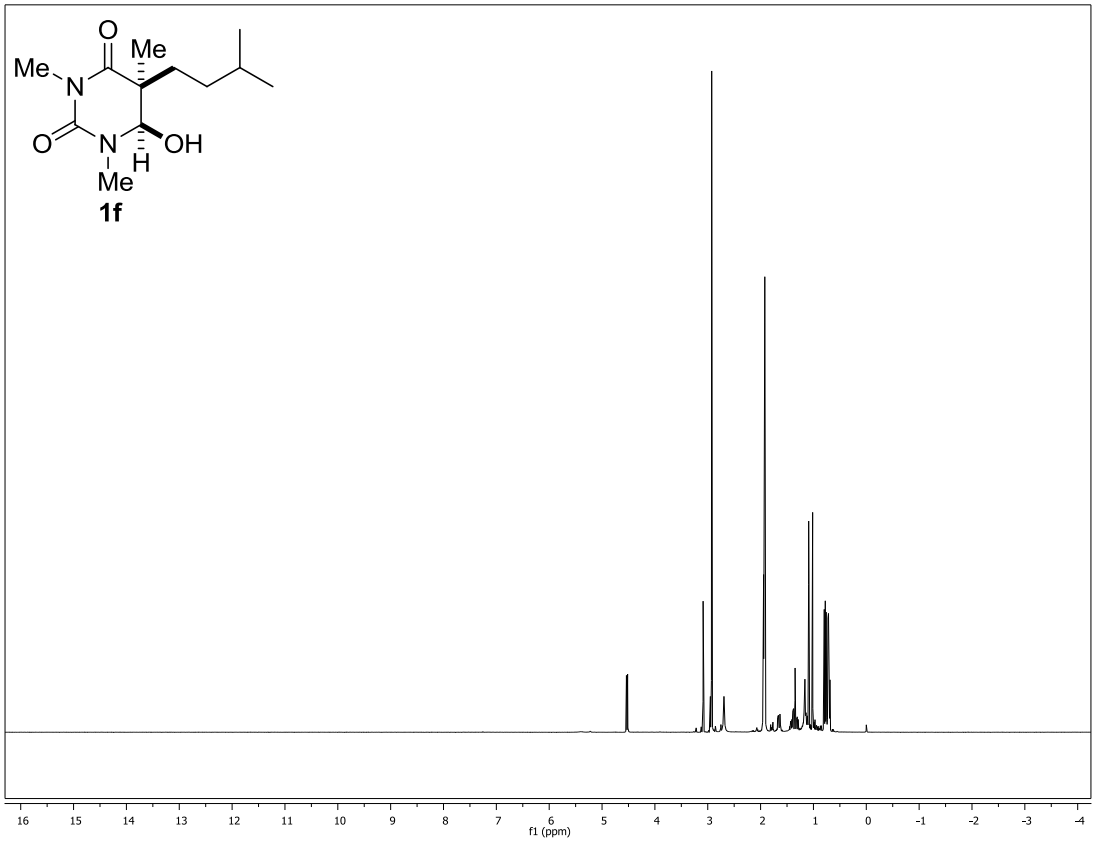
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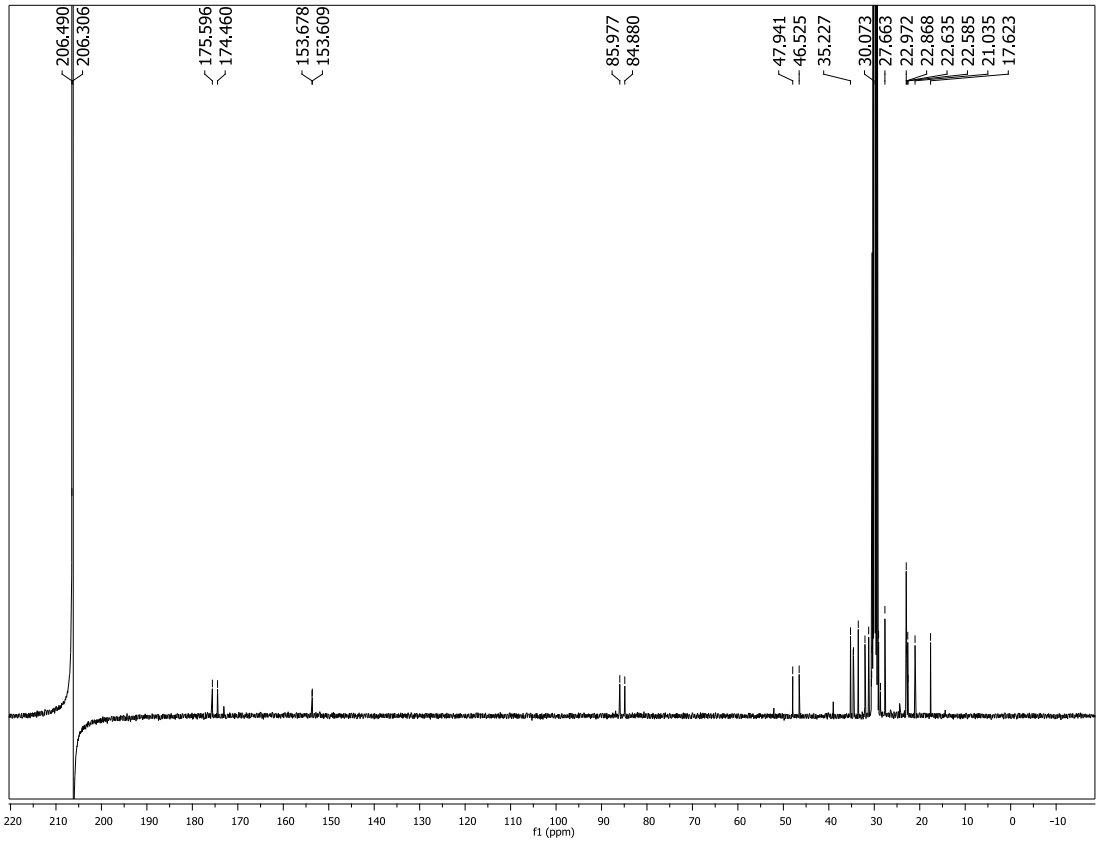
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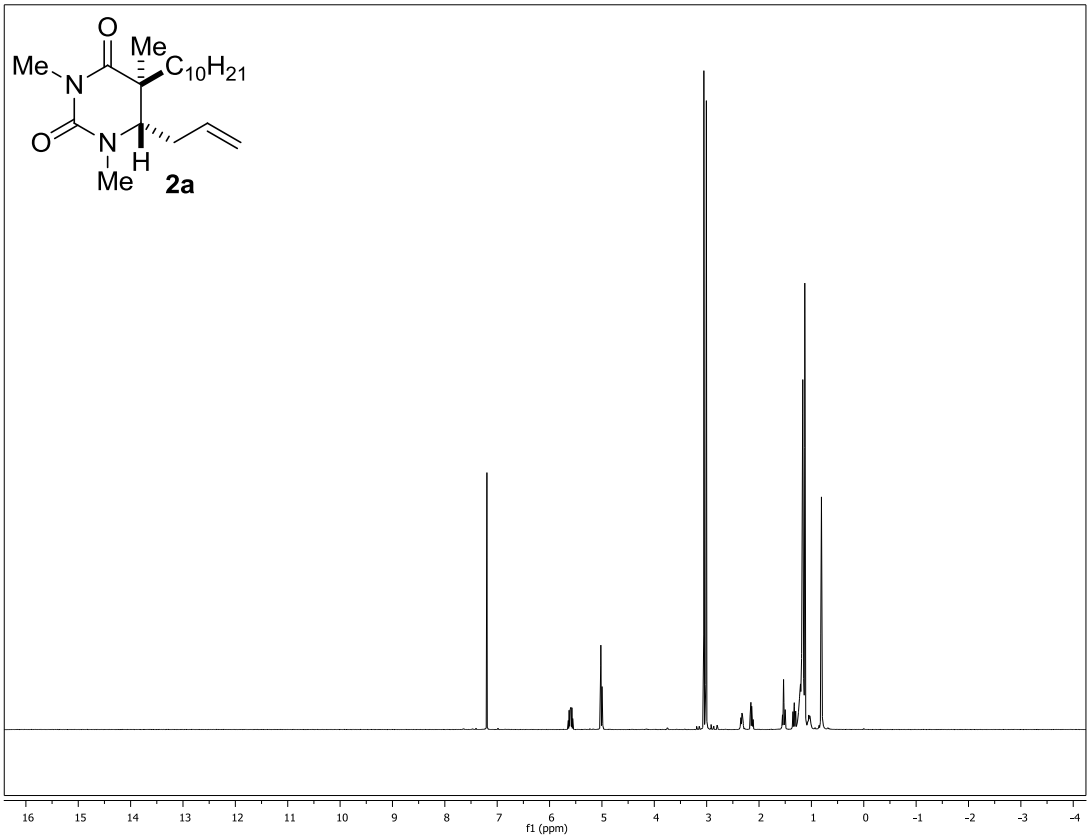
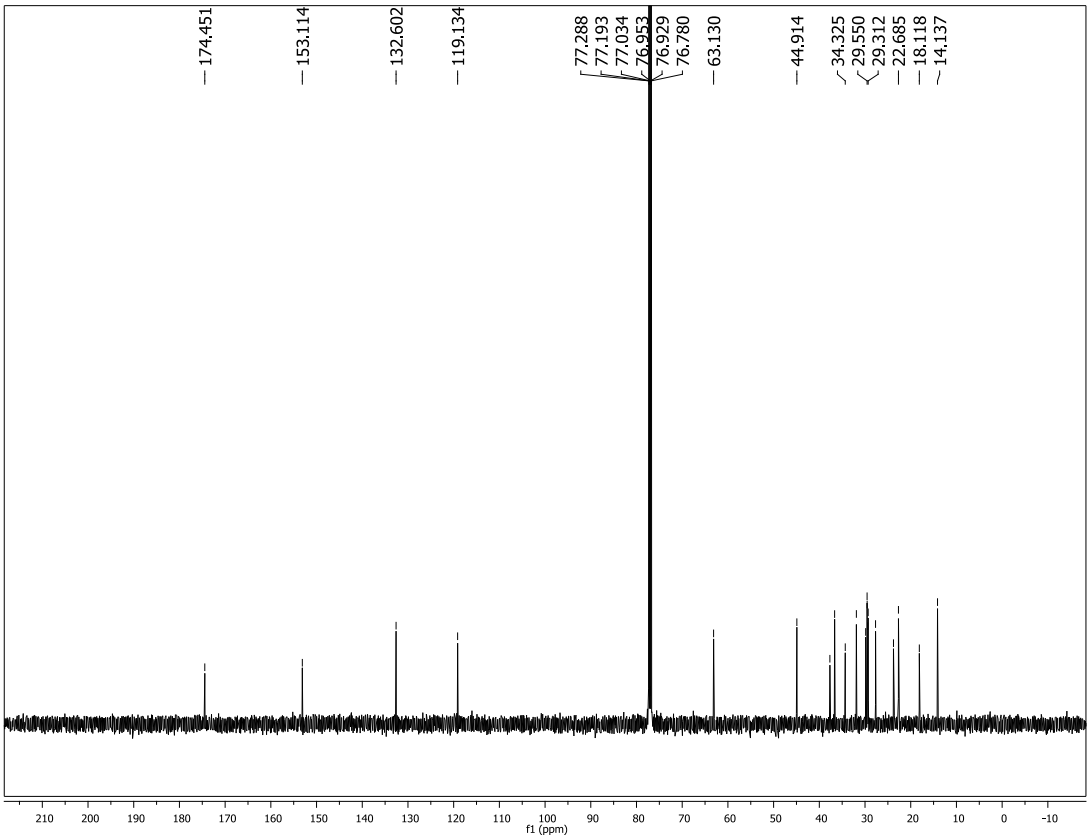
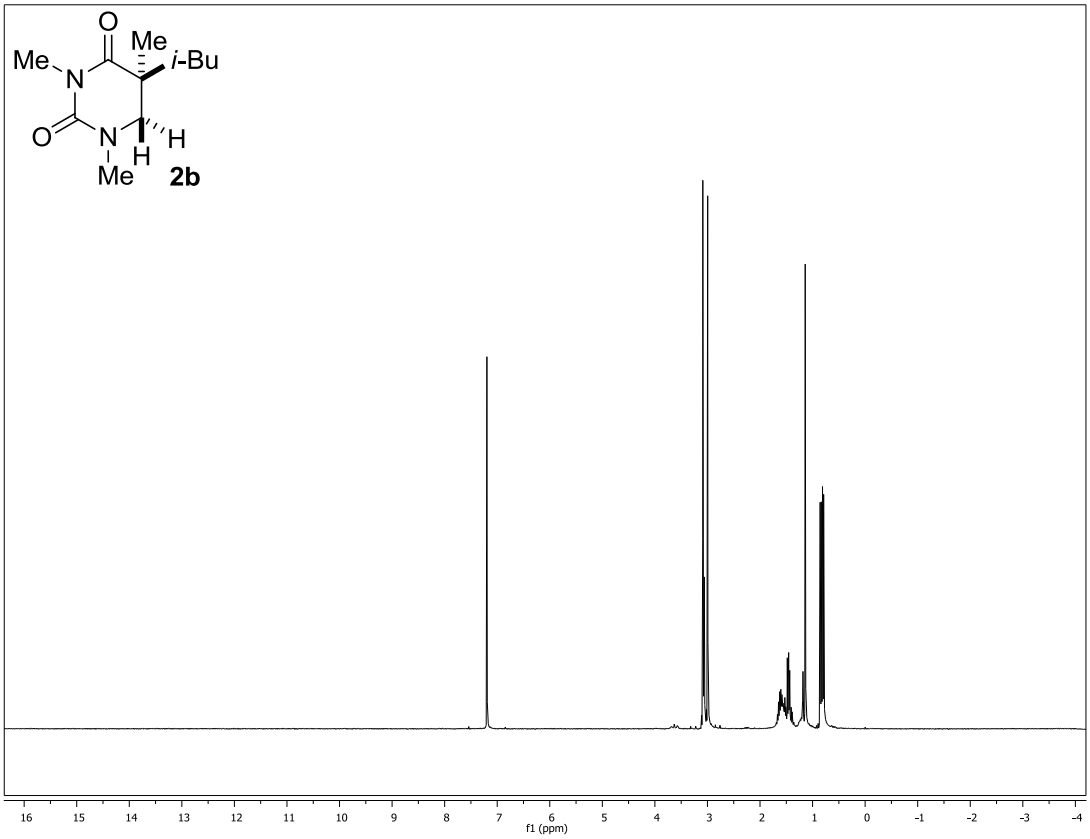
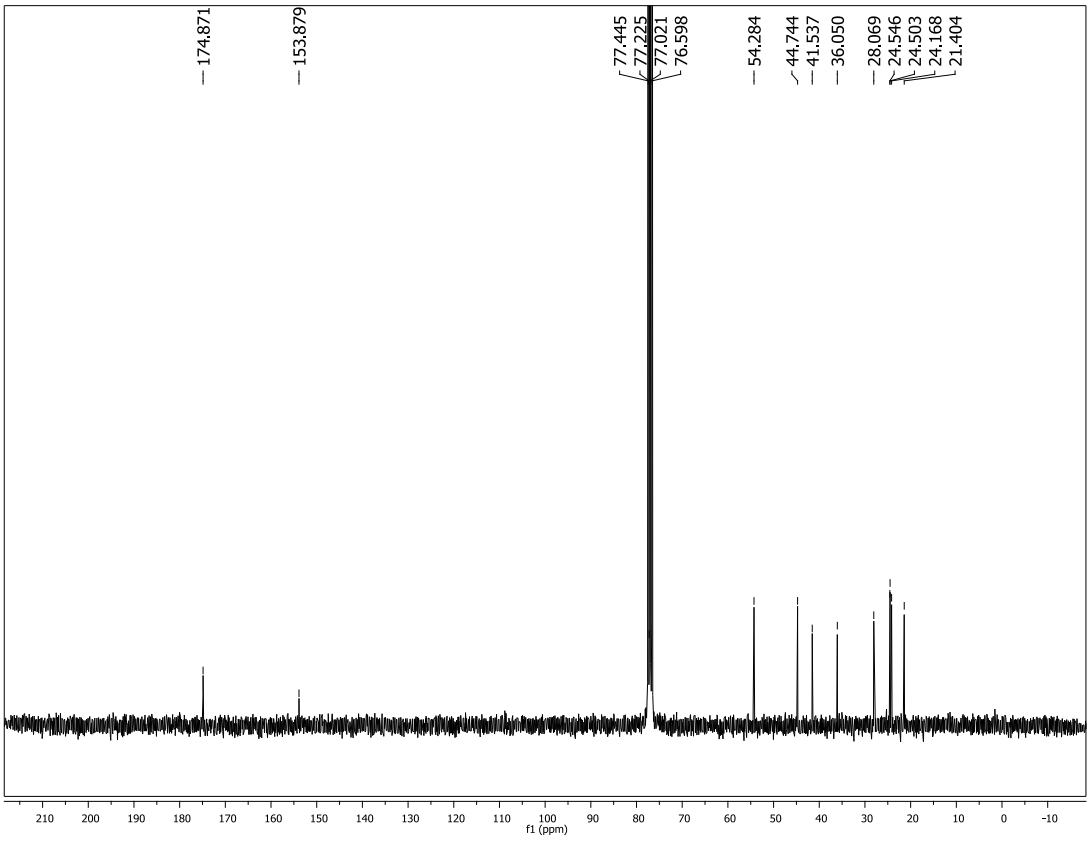
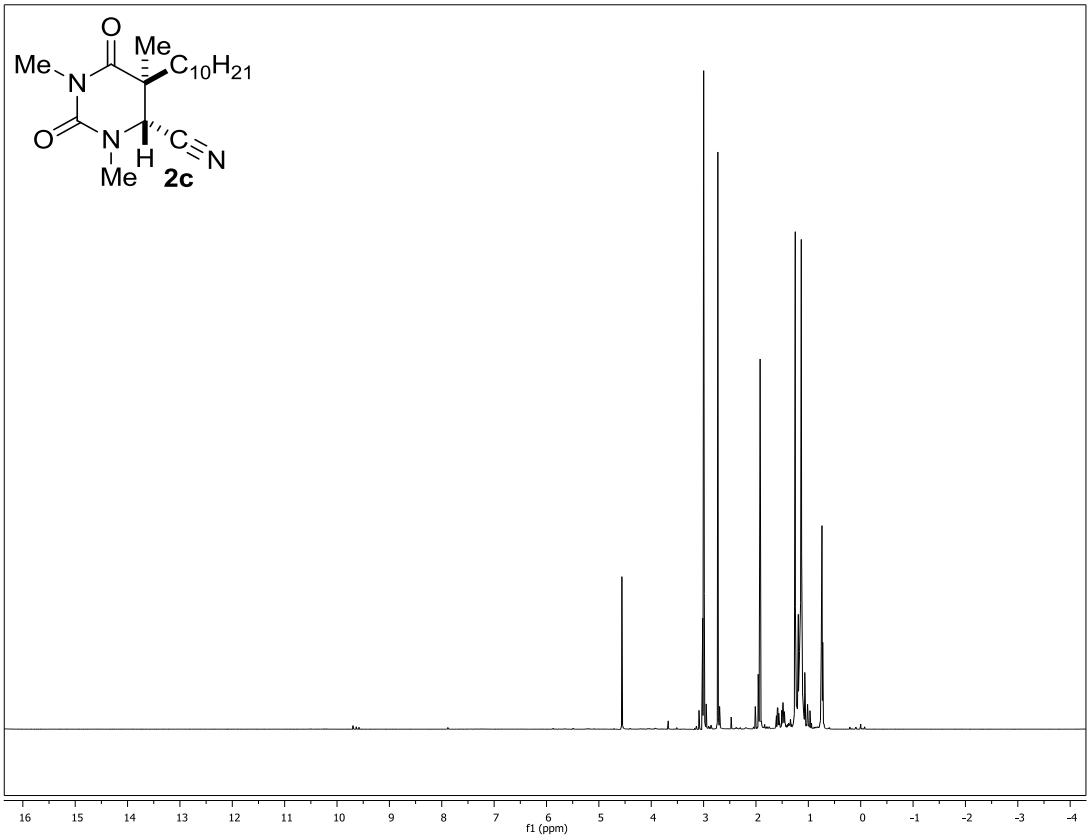
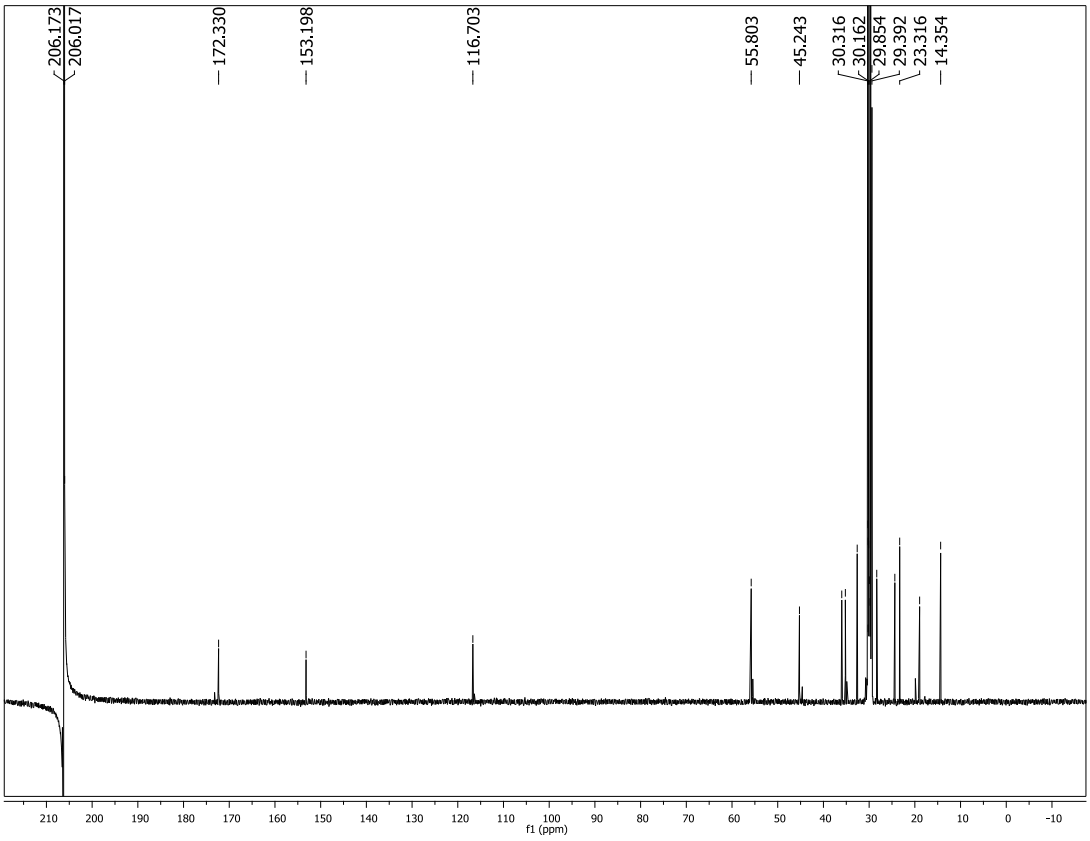

O
Me
Me
N
C10H21
O
N
H
Me
2a
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

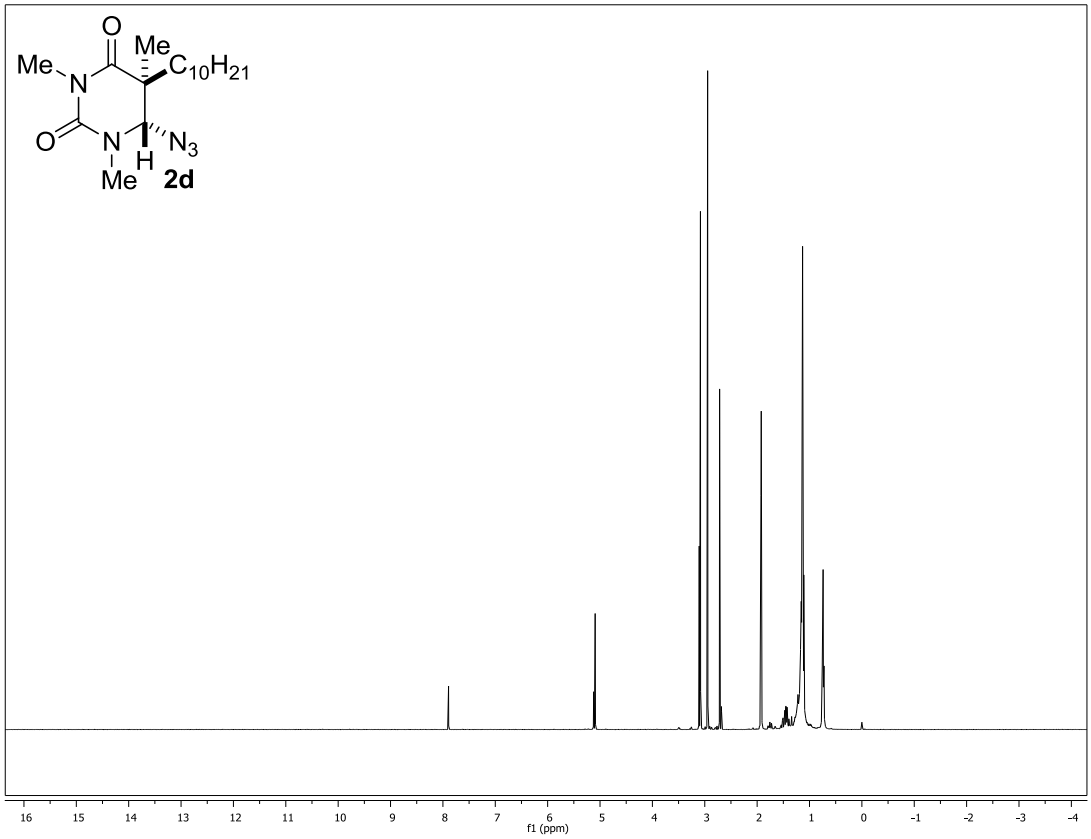

174.451
153.114
132.602
119.134
77.288
77.193
77.034
76.953
76.929
76.780
63.130
44.914
34.325
29.550
29.312
22.685
18.118
14.137
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

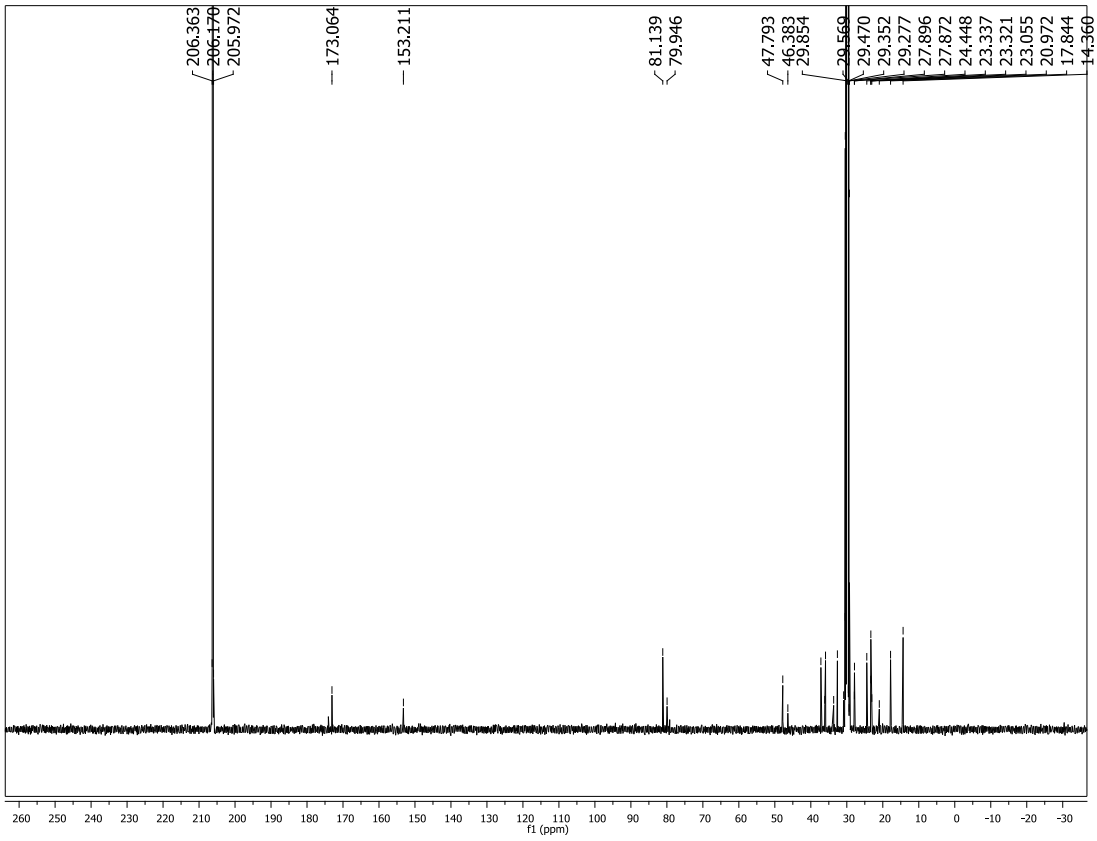

Me
i-Bu
H
Me
2b
f1 (ppm)

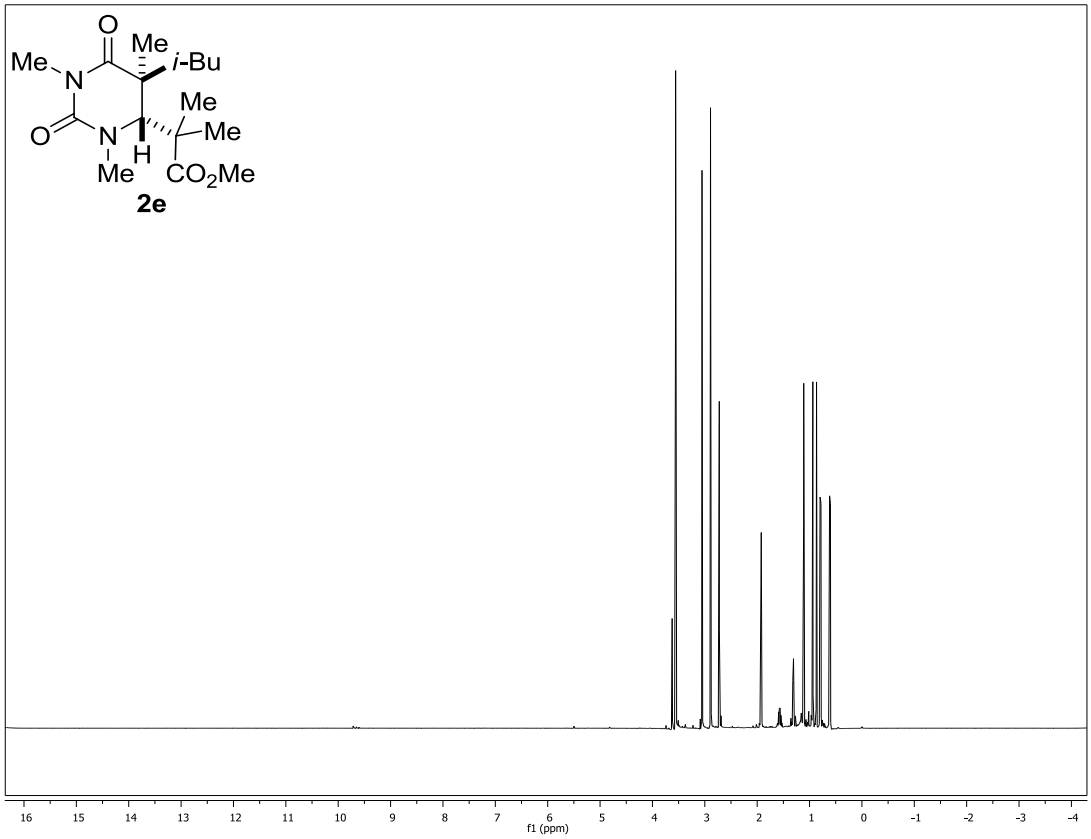

174.871
153.879
77.445
77.225
77.021
76.598
54.284
44.744
41.537
36.050
28.069
24.546
24.503
24.168
21.404
f1 (ppm)

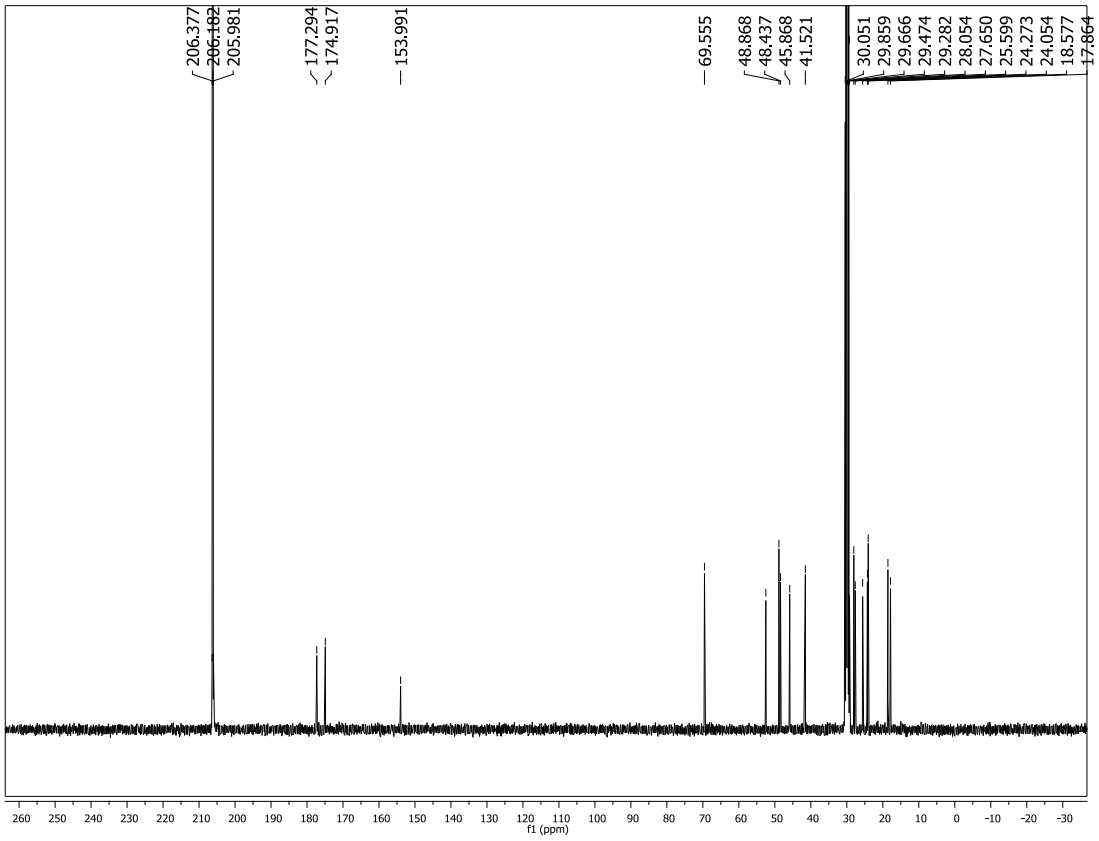

Me
N
O
Me
$C_{10}H_{21}$
O
N
H
C
N
Me
2c
f1 (ppm)

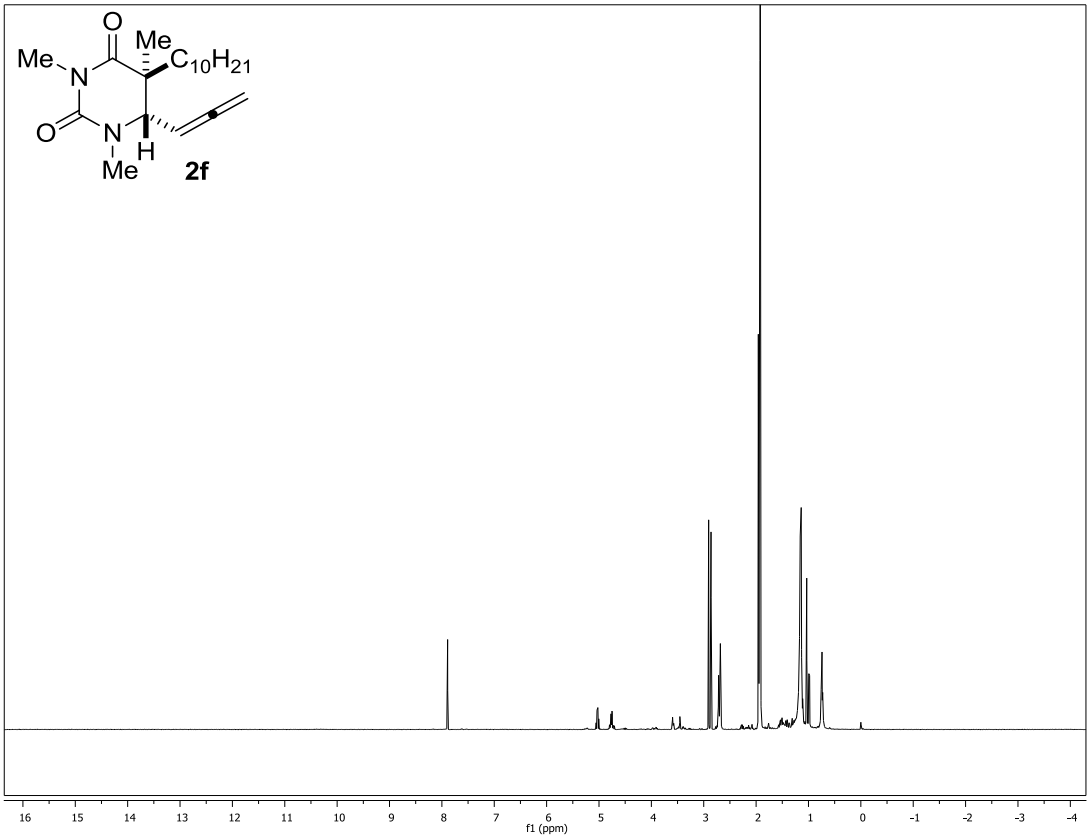

206.173
206.017
172.330
153.198
116.703
55.803
45.243
30.316
30.162
29.854
29.392
23.316
14.354
f1 (ppm)

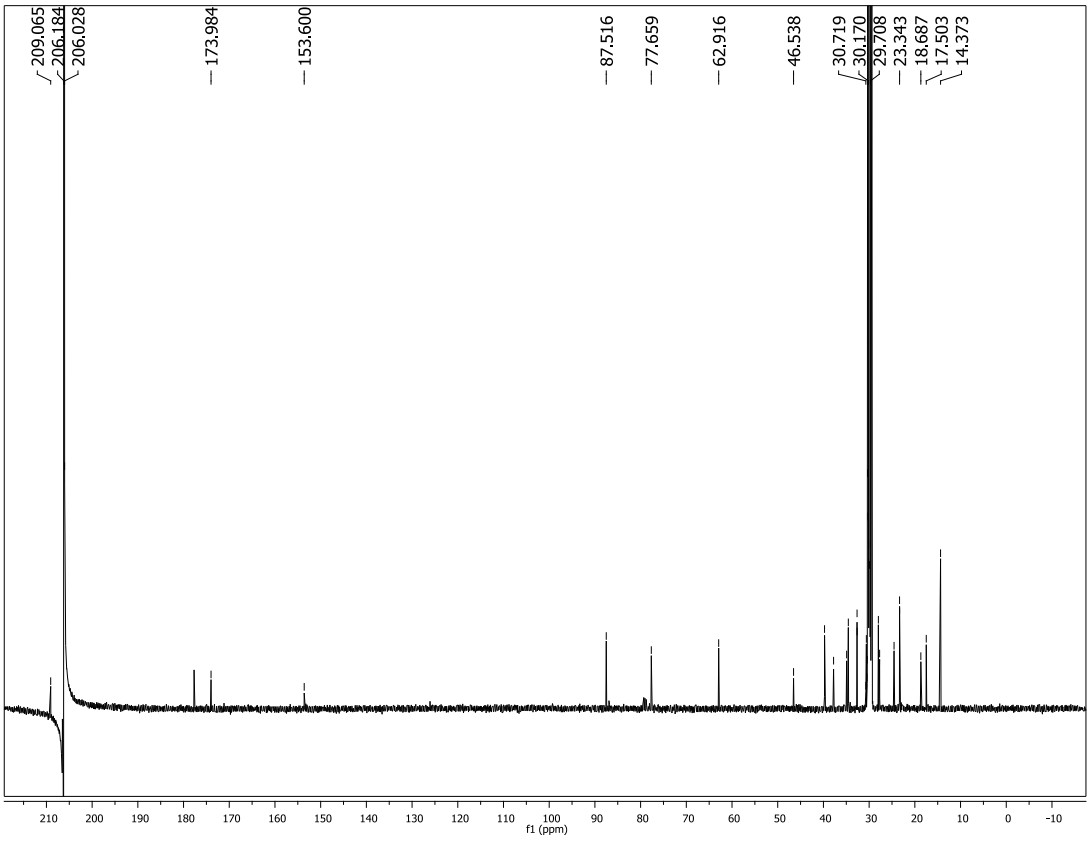

Me
N
O
Me
$C_{10}H_{21}$
O
N
H
N_3
Me
2d
f1 (ppm)

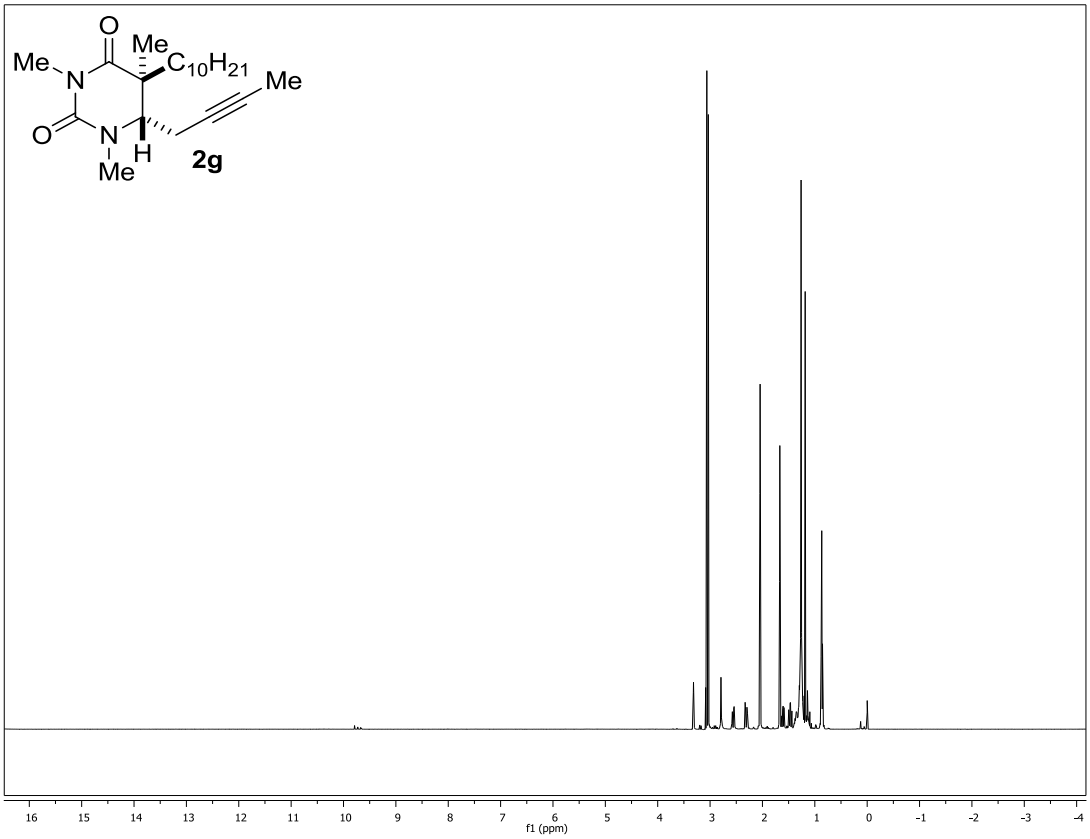

206.363
206.170
205.972
173.064
153.211
81.139
79.946
47.793
46.383
29.854
29.560
29.470
29.352
29.277
27.896
27.872
24.448
23.337
23.321
23.055
20.972
17.844
14.360
f1 (ppm)

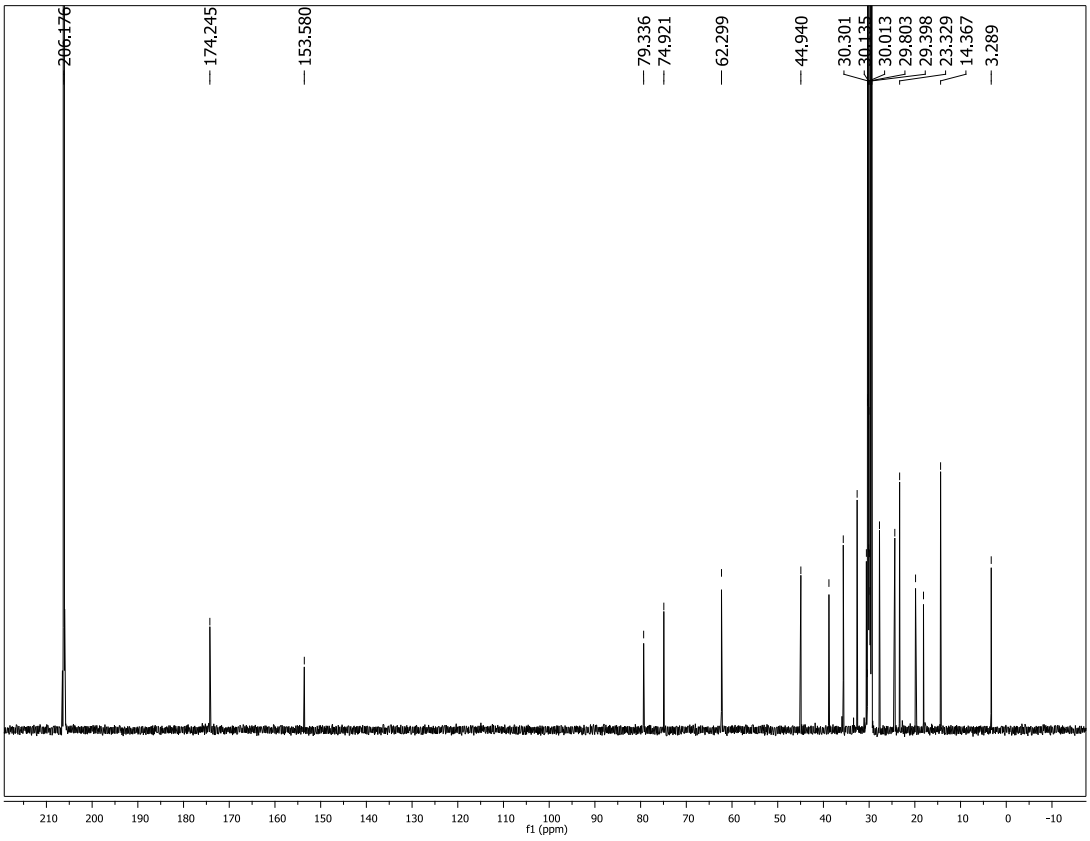

Me
i-Bu
Me
Me
Me
CO2Me
2e
f1 (ppm)

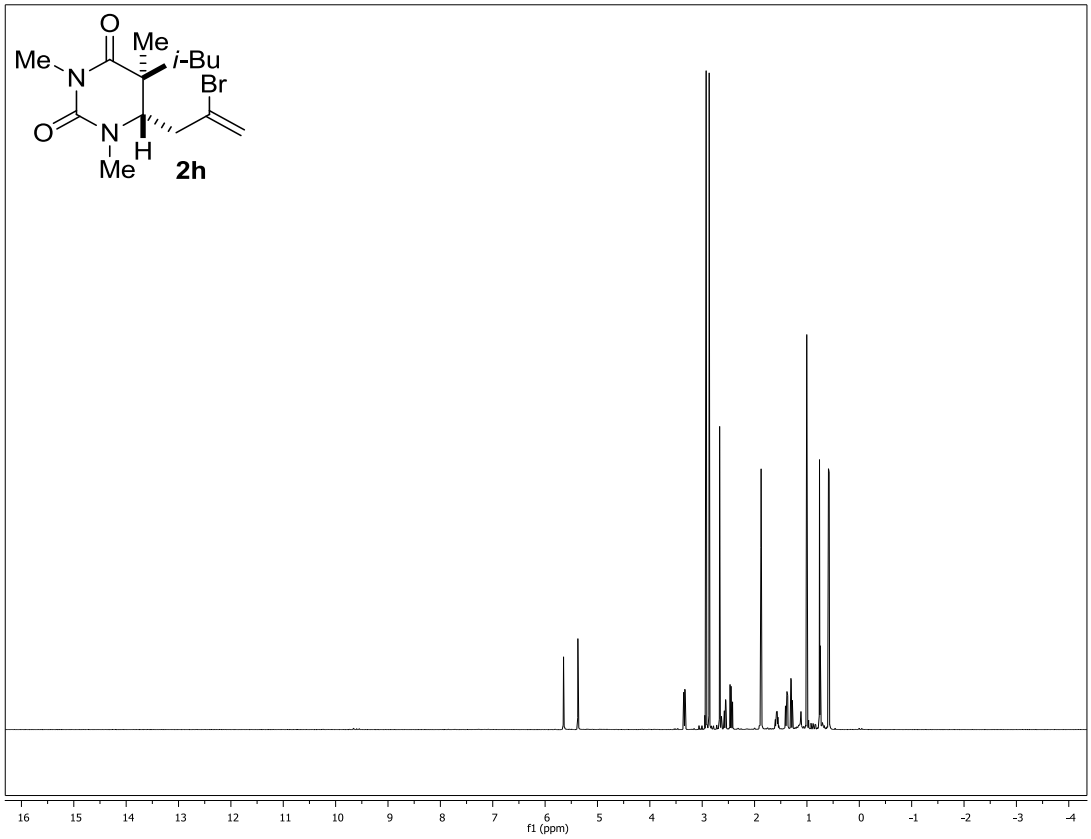

206.377
206.182
205.981
177.294
174.917
153.991
69.555
48.868
48.437
45.868
41.521
30.051
29.859
29.666
29.474
29.282
28.054
27.650
25.599
24.273
24.054
18.577
17.864
f1 (ppm)

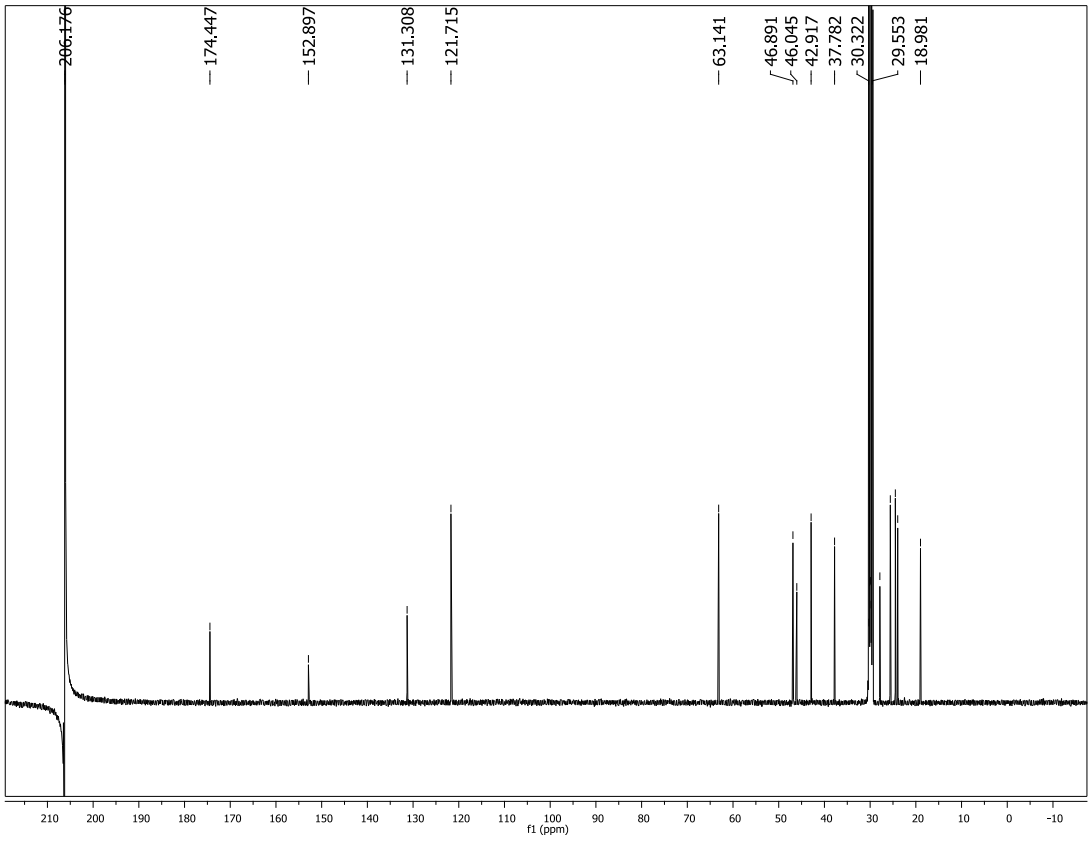

Me
N
O
Me
$C_{10}H_{21}$
O
N
H
Me
2f
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

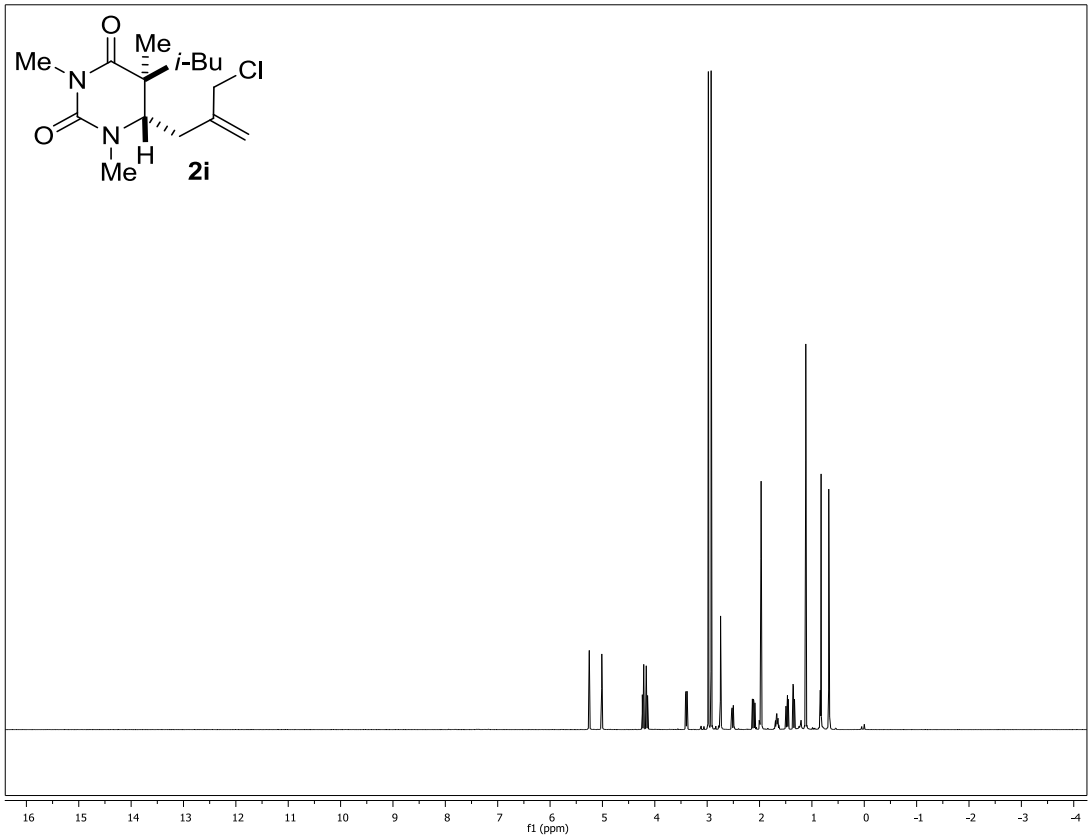

209.065
206.184
206.028
173.984
153.600
87.516
77.659
62.916
46.538
30.719
30.170
29.708
23.343
18.687
17.503
14.373
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

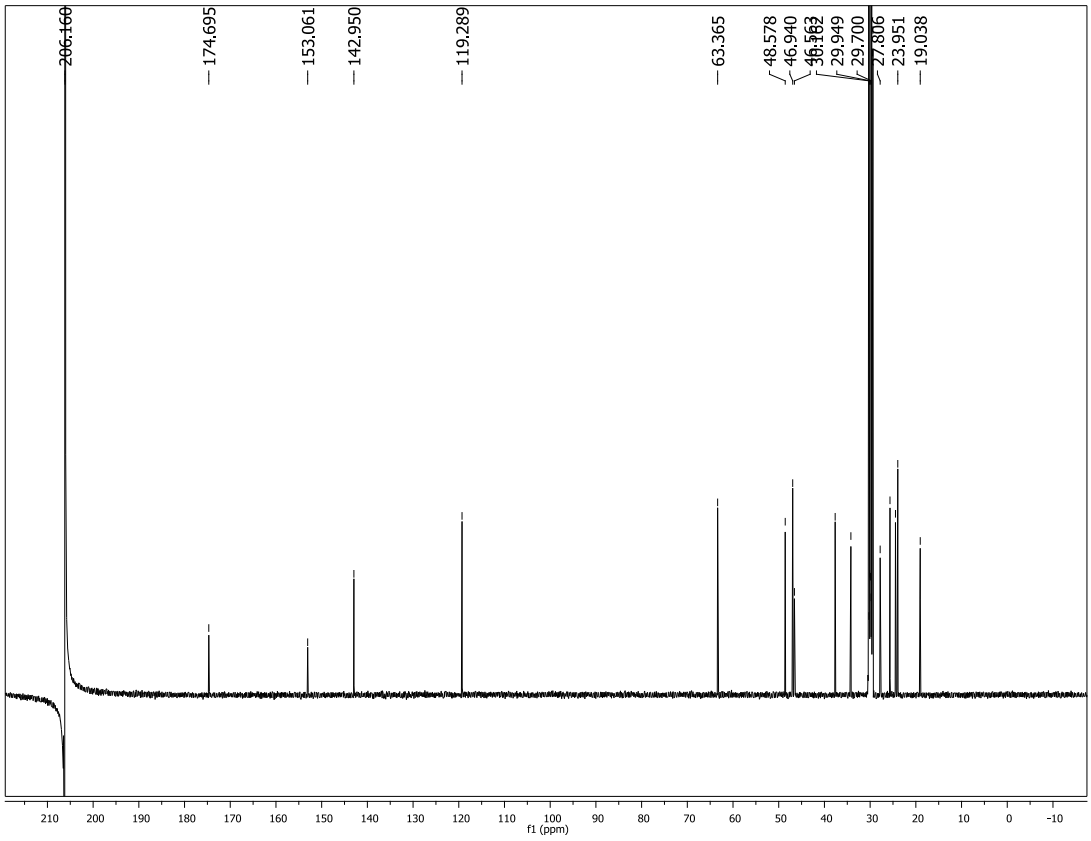

Me
N
O
Me
$C_{10}H_{21}$
Me
O
N
H
Me
2g
f1 (ppm)

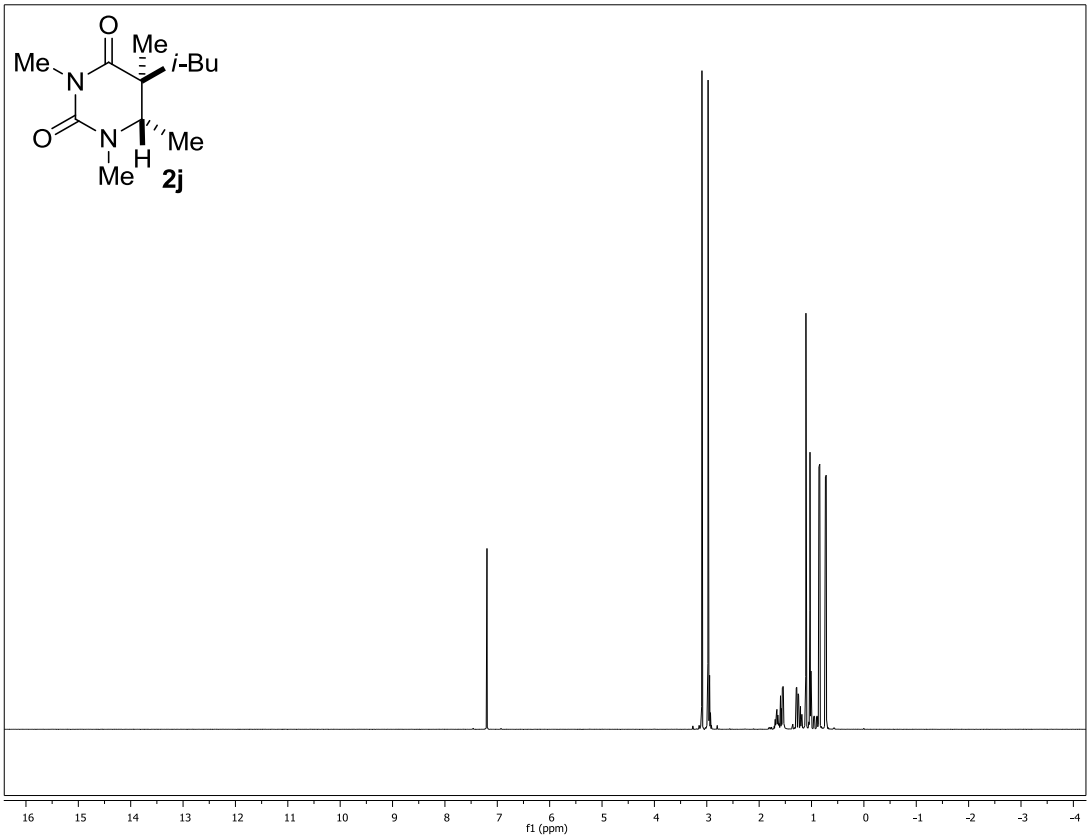

206.176
174.245
153.580
79.336
74.921
62.299
44.940
30.301
30.135
30.013
29.803
29.398
23.329
14.367
3.289
f1 (ppm)

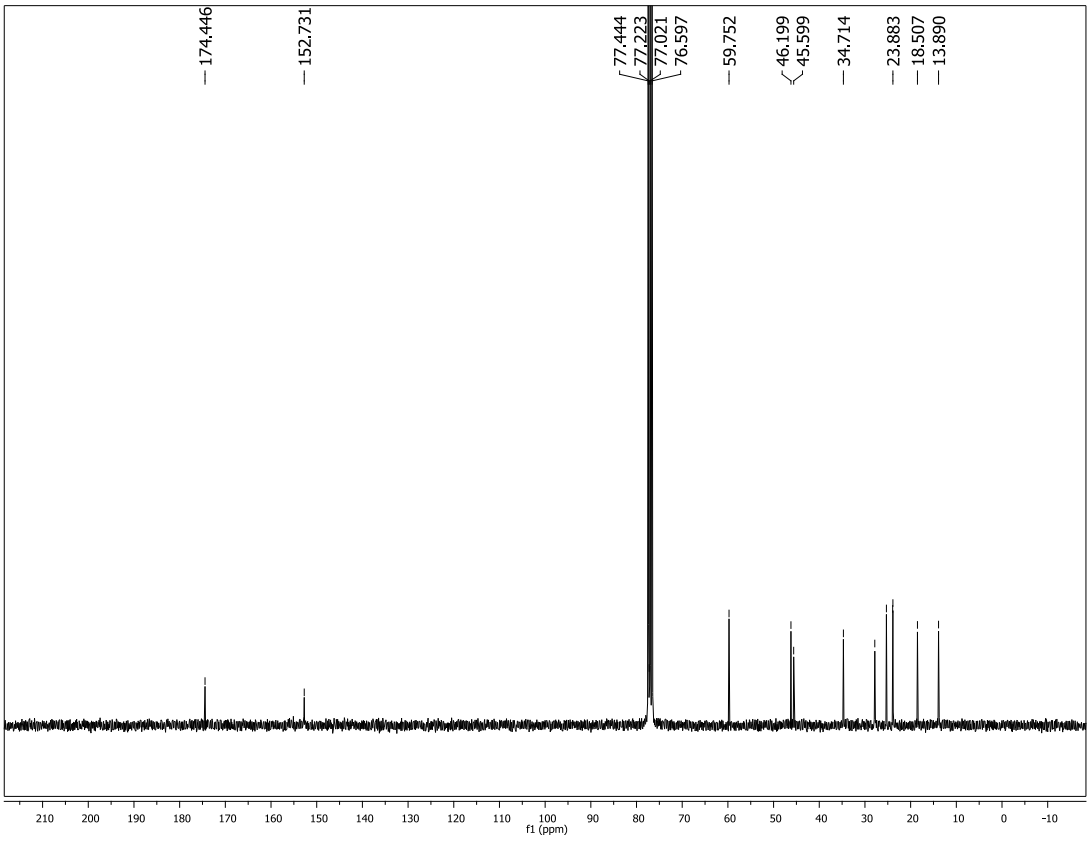

Me
N
O
Me
i-Bu
Br
O
N
H
Me
2h
f1 (ppm)

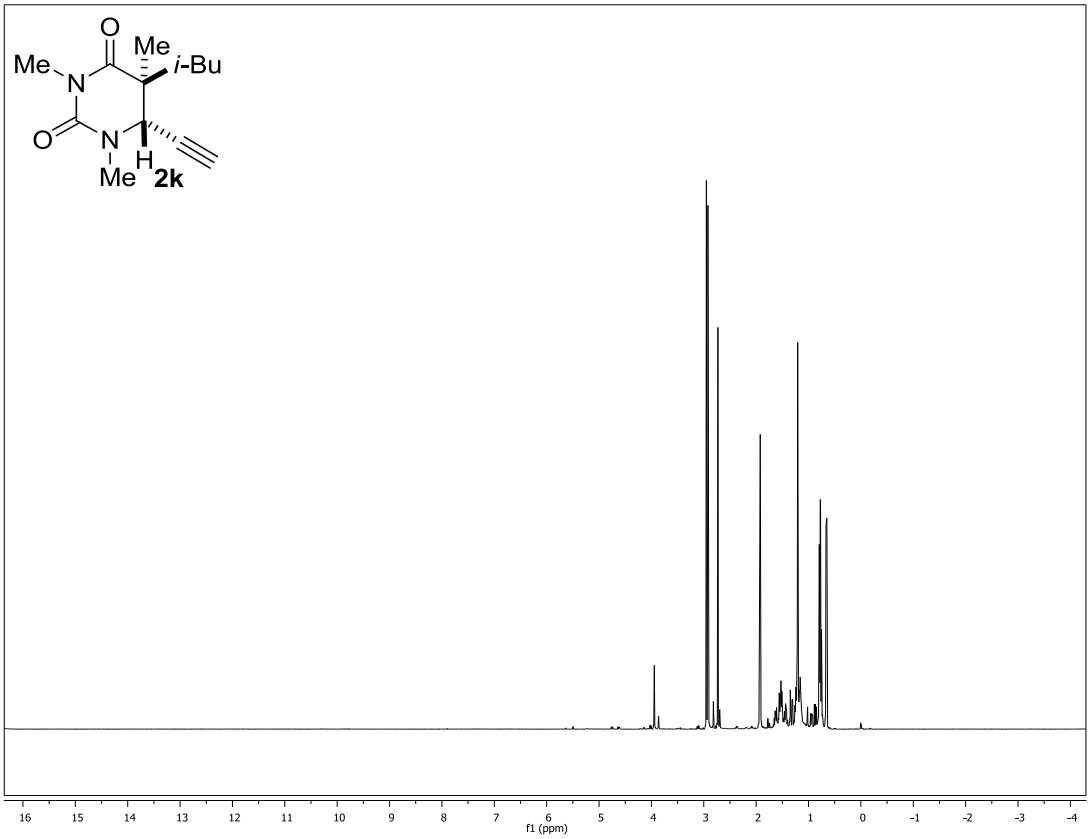

206.176
174.447
152.897
131.308
121.715
63.141
46.891
46.045
42.917
37.782
30.322
29.553
18.981
f1 (ppm)

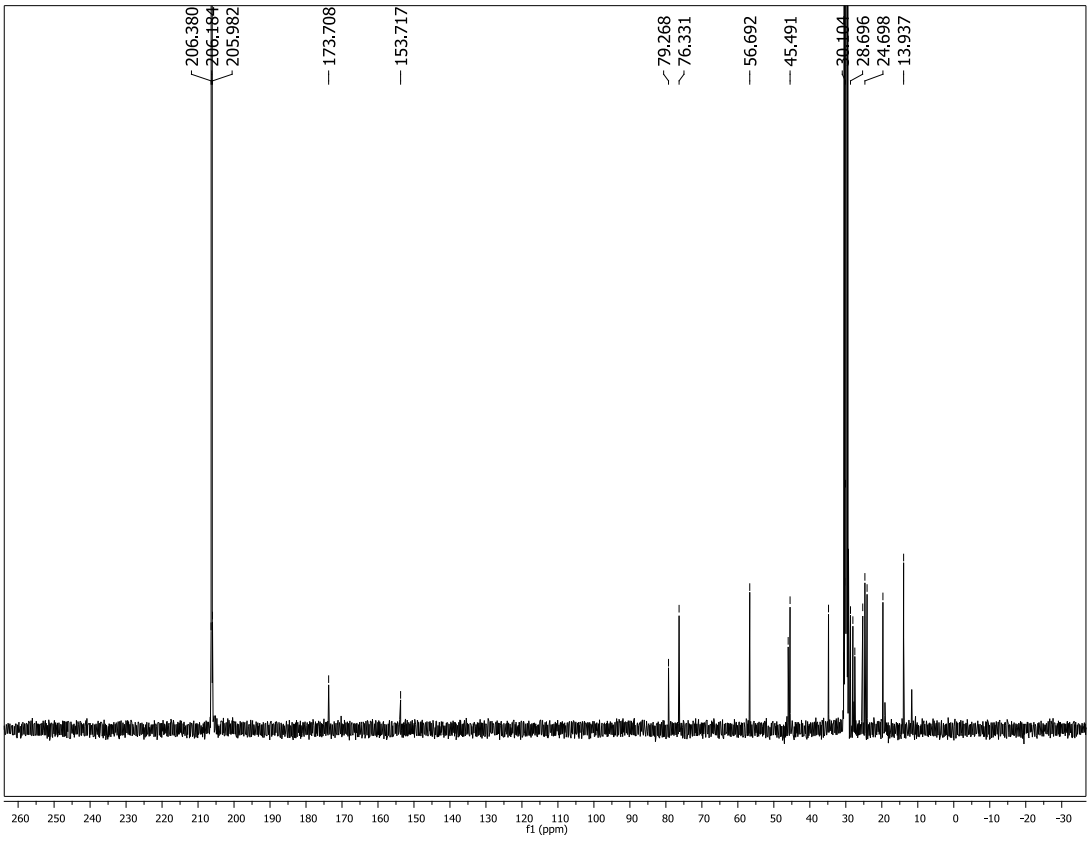

Me
O
Me
i-Bu
Cl
N
O
N
H
Me
2i
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

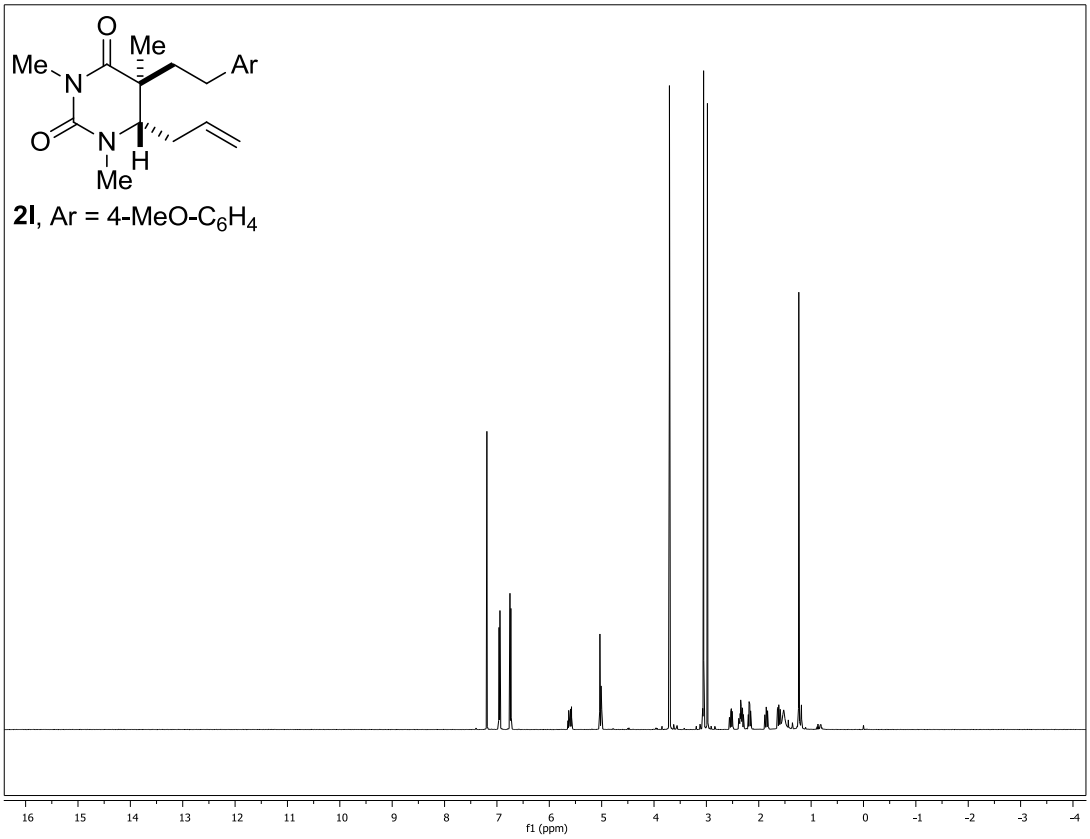

206.160
174.695
153.061
142.950
119.289
63.365
48.578
46.940
29.949
29.700
27.806
23.951
19.038
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

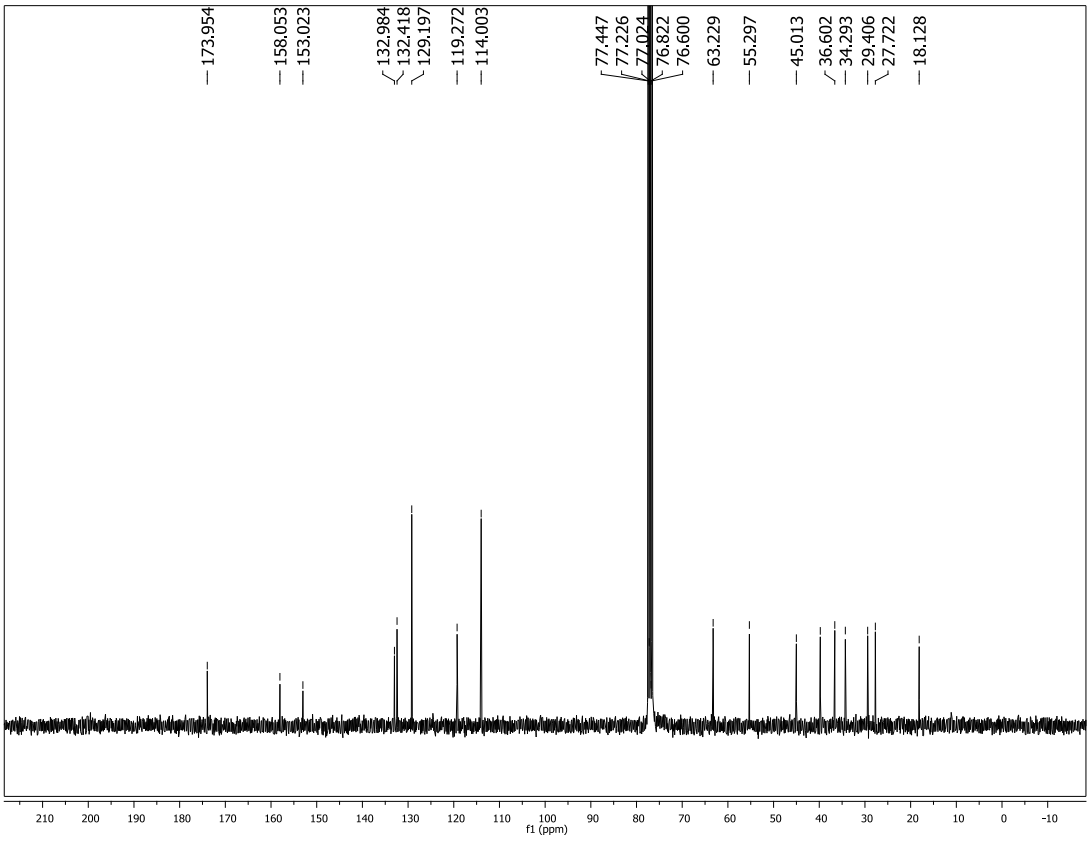

Me
i-Bu
Me
Me
H
Me
2j
f1 (ppm)

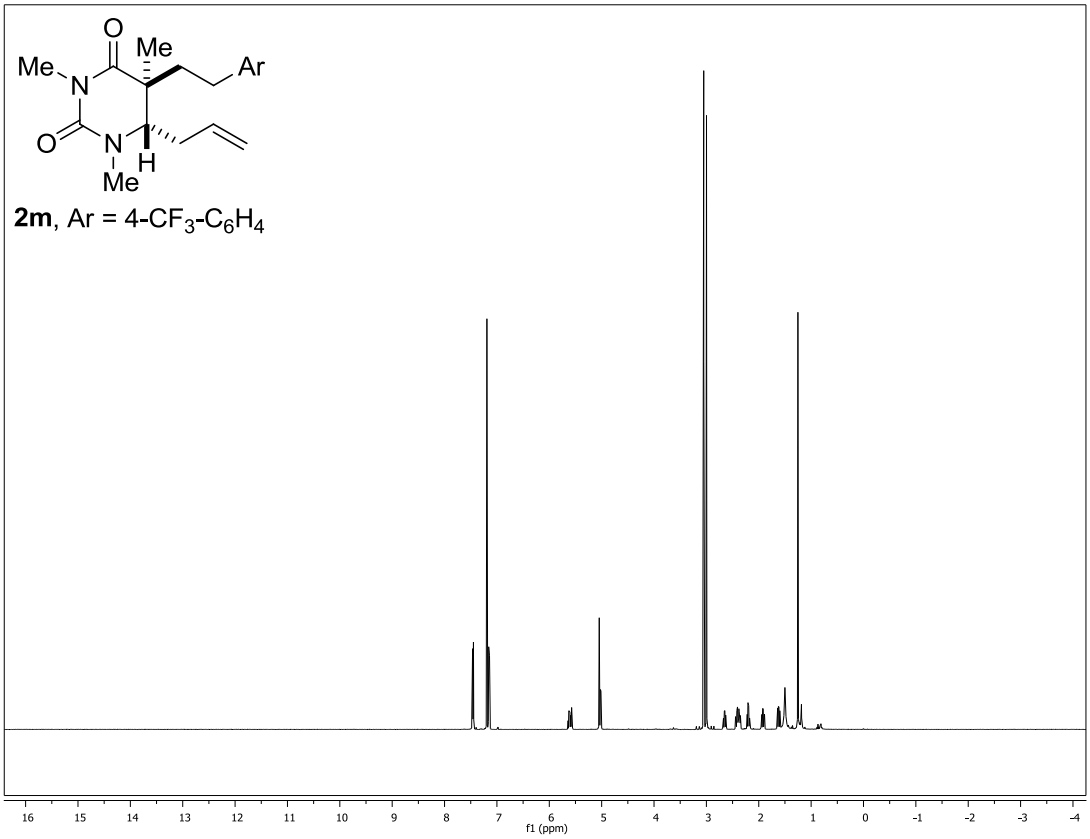

174.446
152.731
77.444
77.223
77.021
76.597
59.752
46.199
45.599
34.714
23.883
18.507
13.890
f1 (ppm)

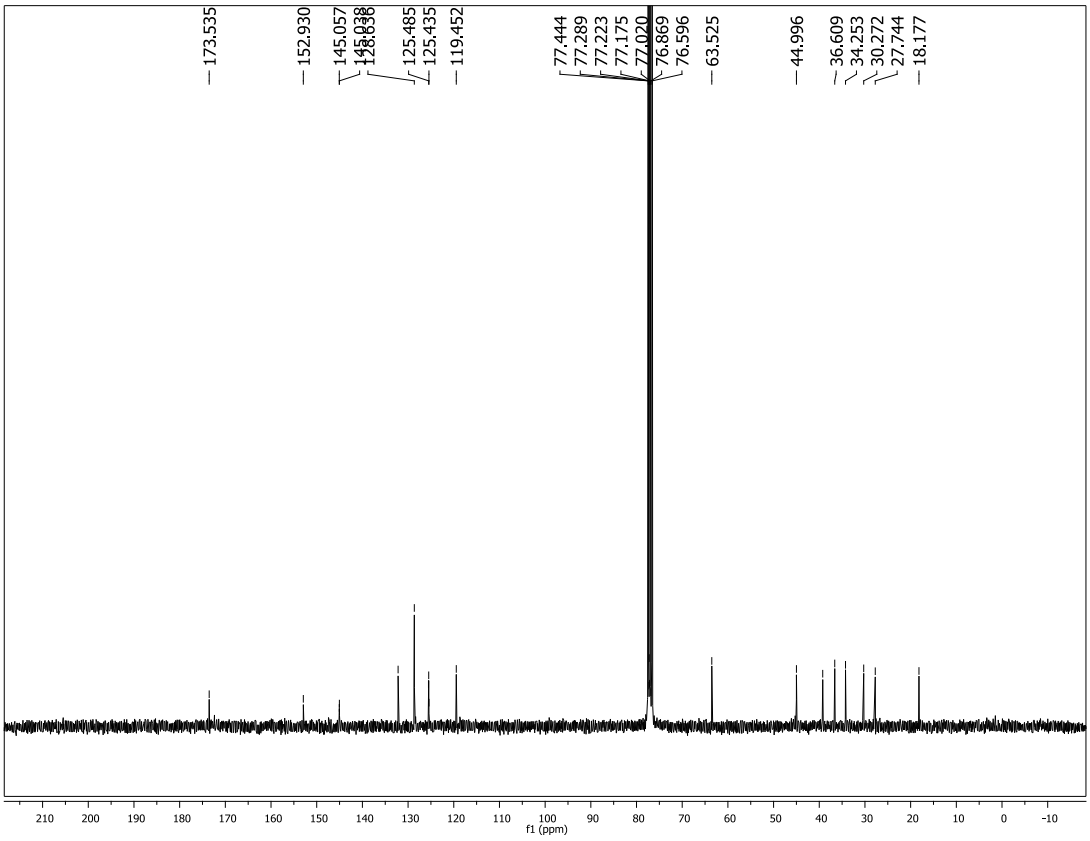

Me
i-Bu
2k
f1 (ppm)

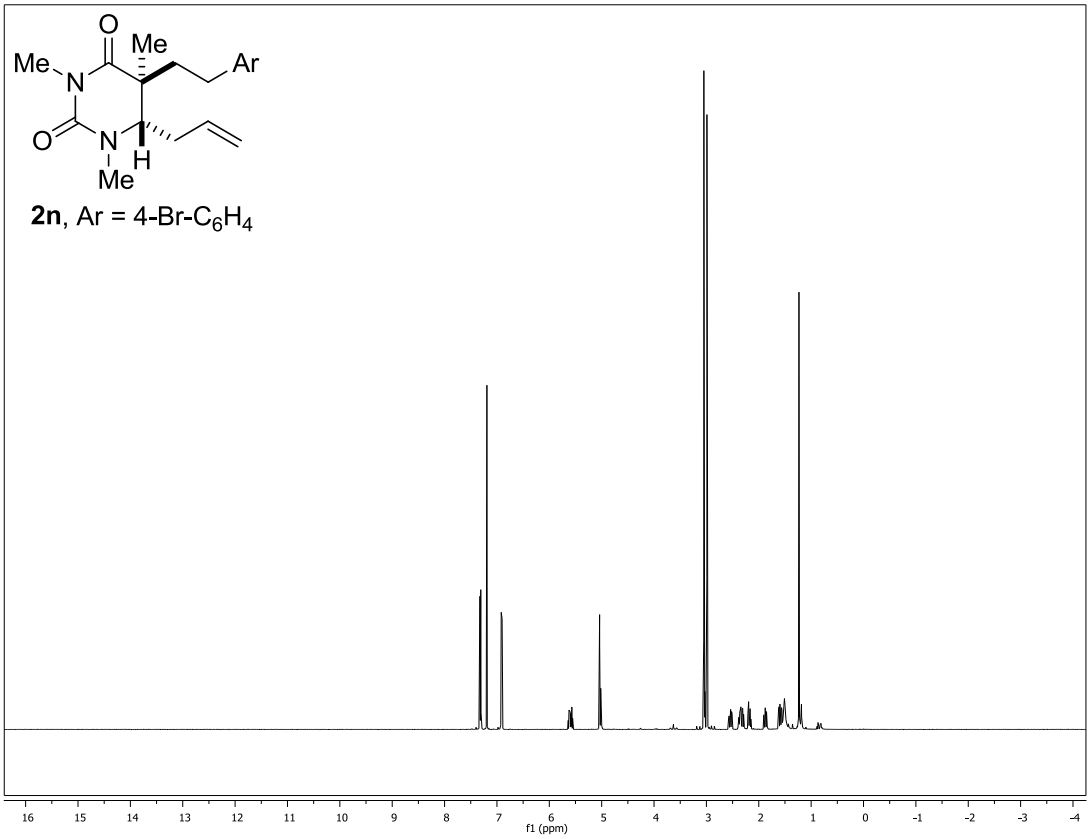

206.380
206.184
205.982
173.708
153.717
79.268
76.331
56.692
45.491
30.104
28.696
24.698
13.937
f1 (ppm)

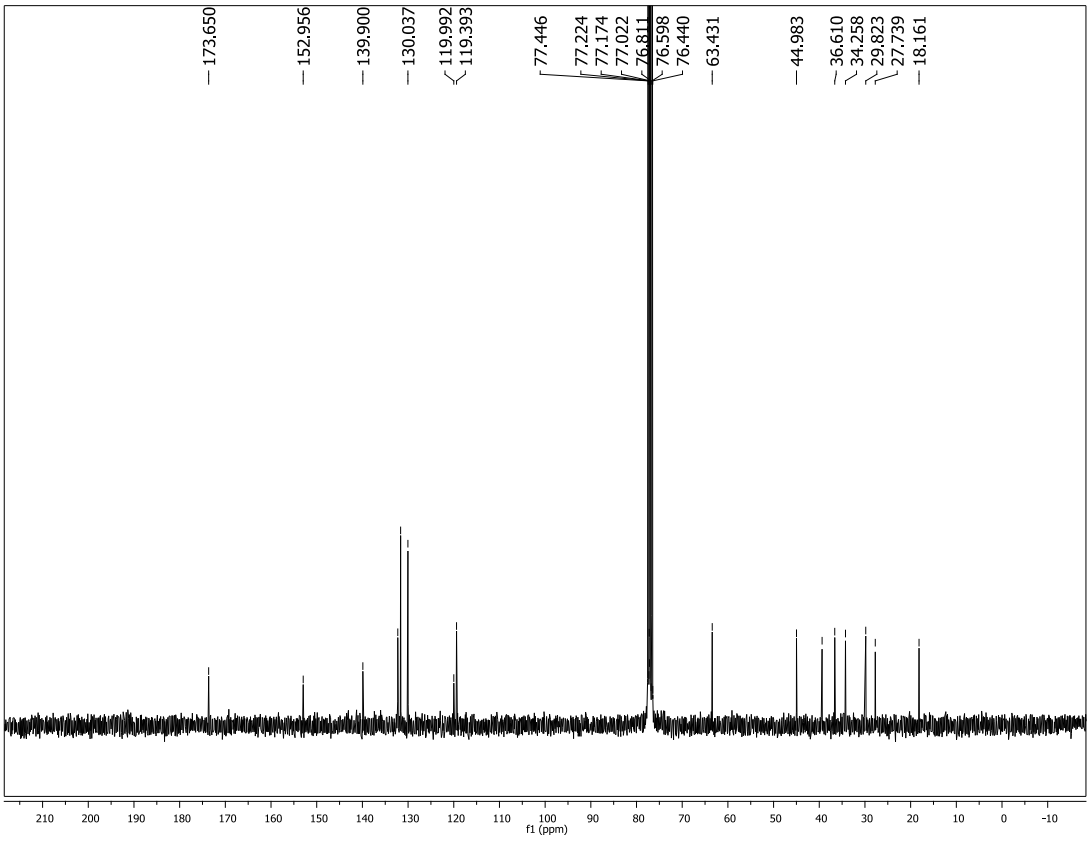

Me
Ar
Me
N
O
N
H
Me
O
2l, Ar = 4-MeO-C_6H_4
f1 (ppm)


173.954
158.053
153.023
132.984
132.418
129.197
119.272
114.003
77.447
77.226
77.024
76.822
76.600
63.229
55.297
45.013
36.602
34.293
29.406
27.722
18.128
f1 (ppm)


Me
Me
Ar
N
N
O
O
H
Me
2m, Ar = 4-CF$_3$-C$_6$H$_4$
f1 (ppm)


173.535
152.930
145.057
125.485
125.435
119.452
77.444
77.289
77.223
77.175
77.020
76.869
76.596
63.525
44.996
36.609
34.253
30.272
27.744
18.177
f1 (ppm)


Me
Me
Ar
N
O
N
H
O
Me
2n, Ar = 4-Br-C_6H_4
f1 (ppm)


173.650
152.956
139.900
130.037
119.992
119.393
77.446
77.224
77.174
77.022
76.811
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76.440
63.431
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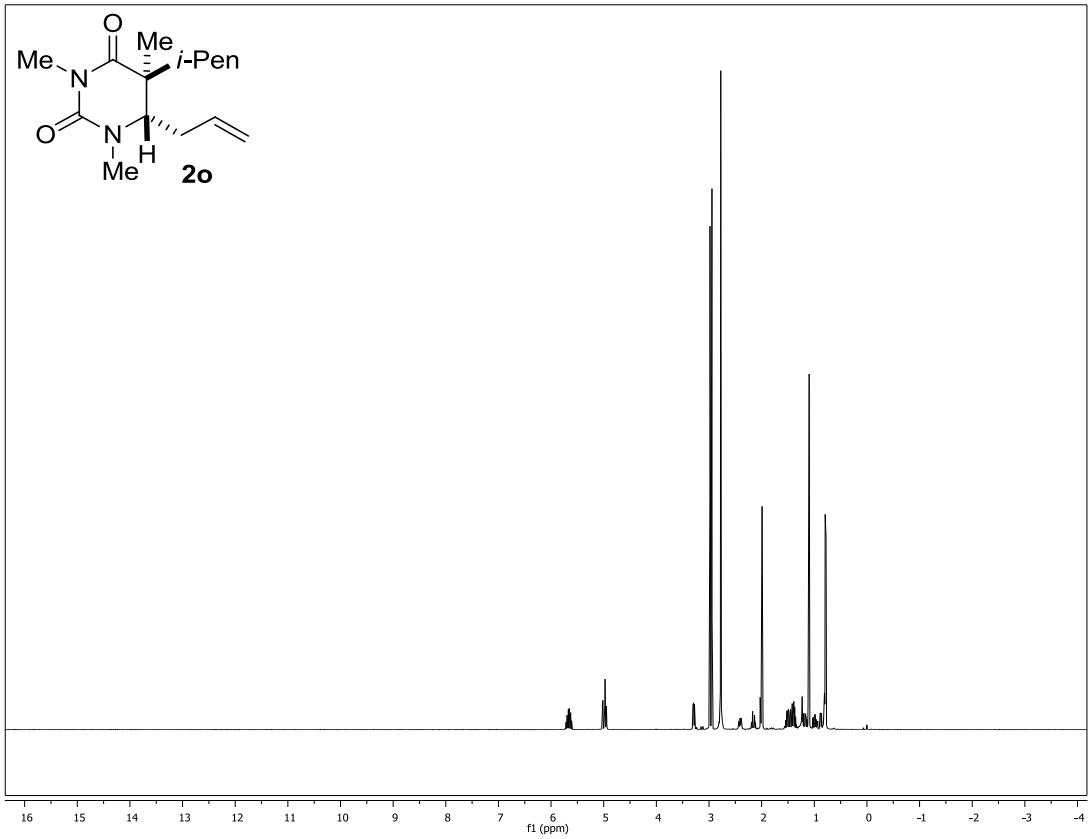
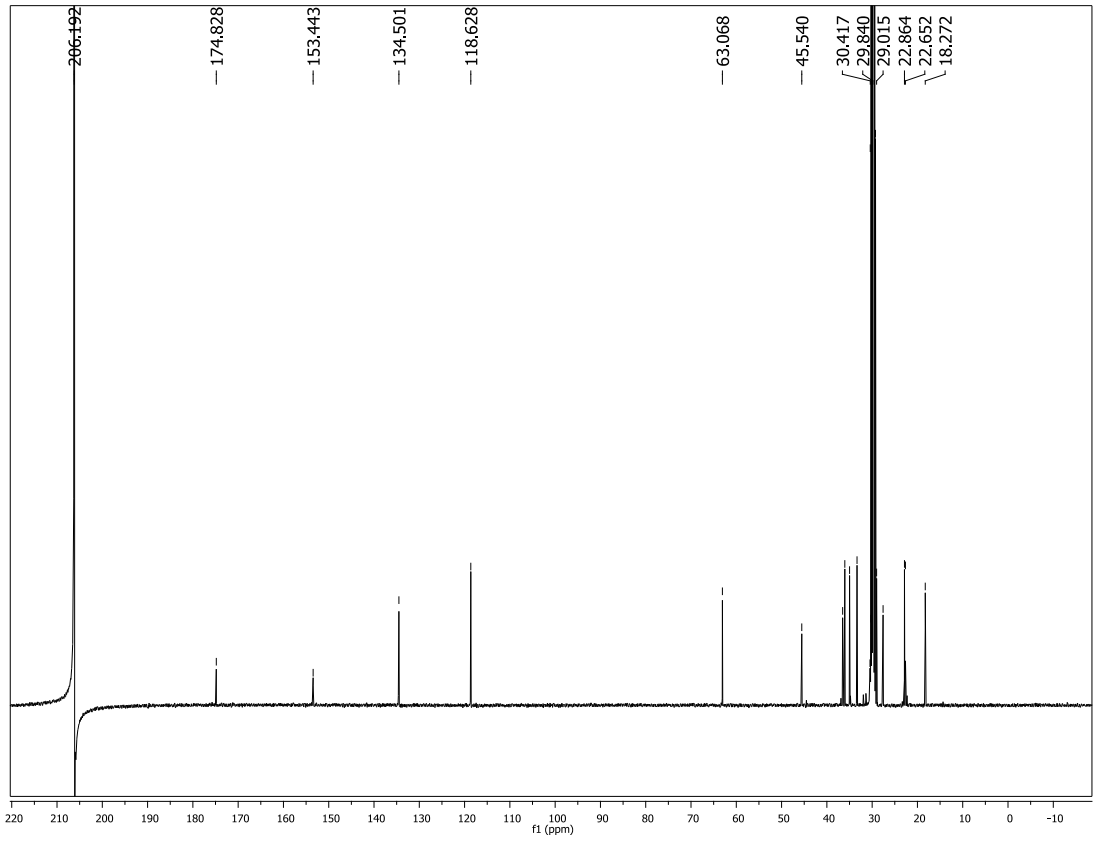
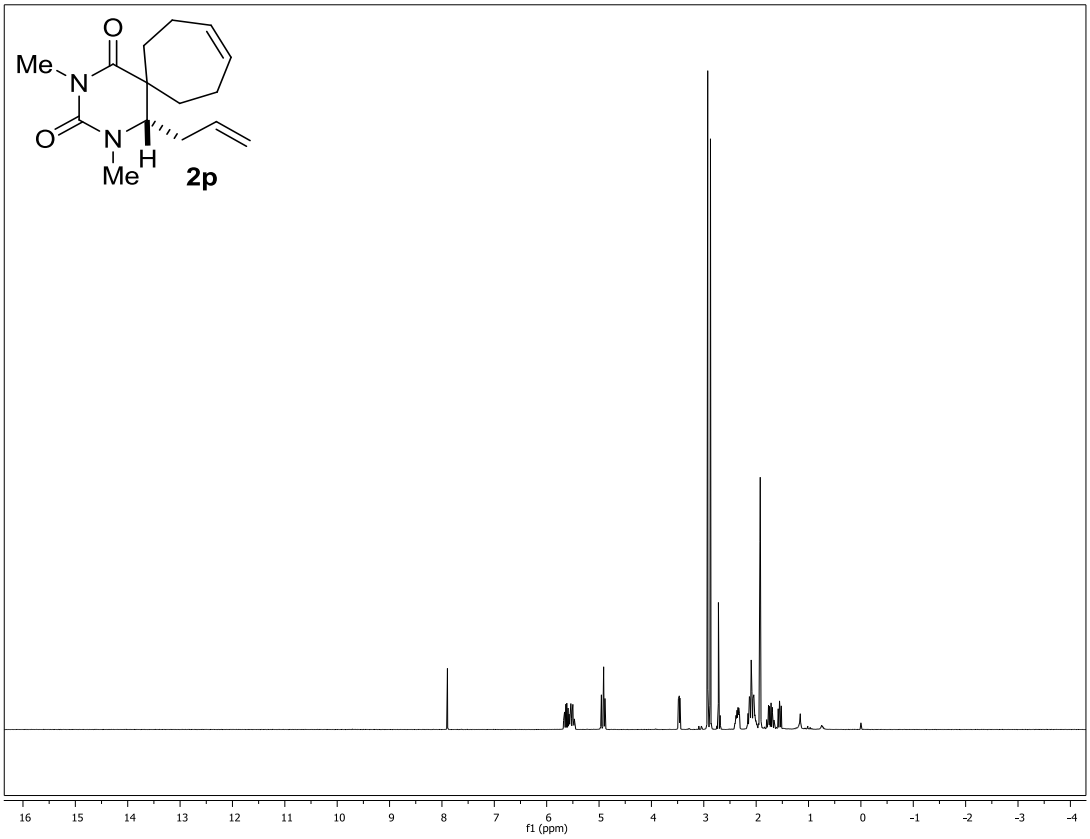
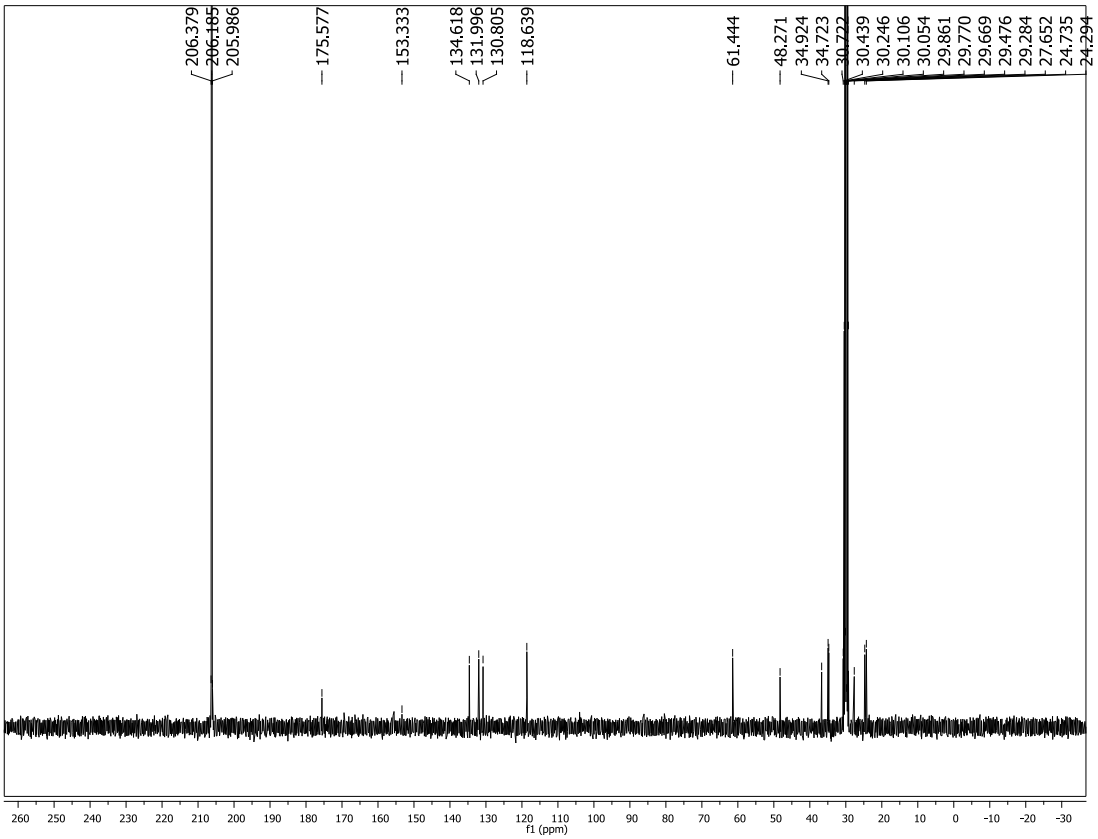
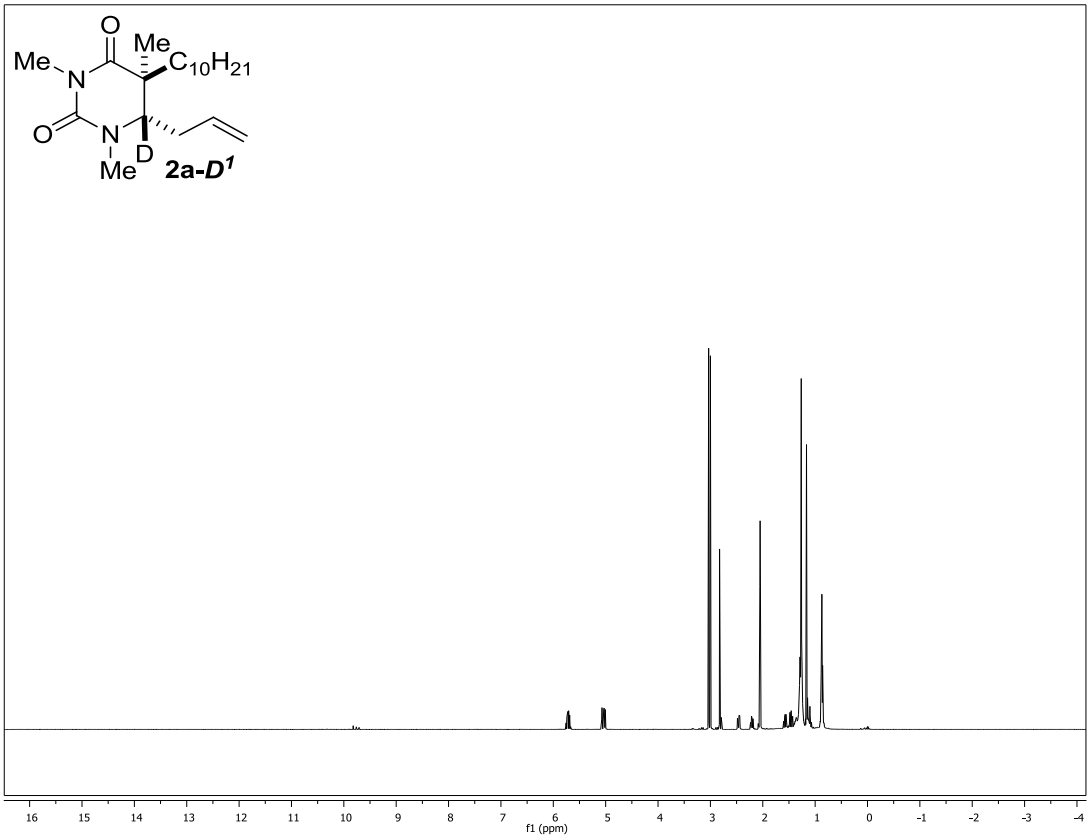
36.610
34.258
29.823
27.739
18.161
f1 (ppm)

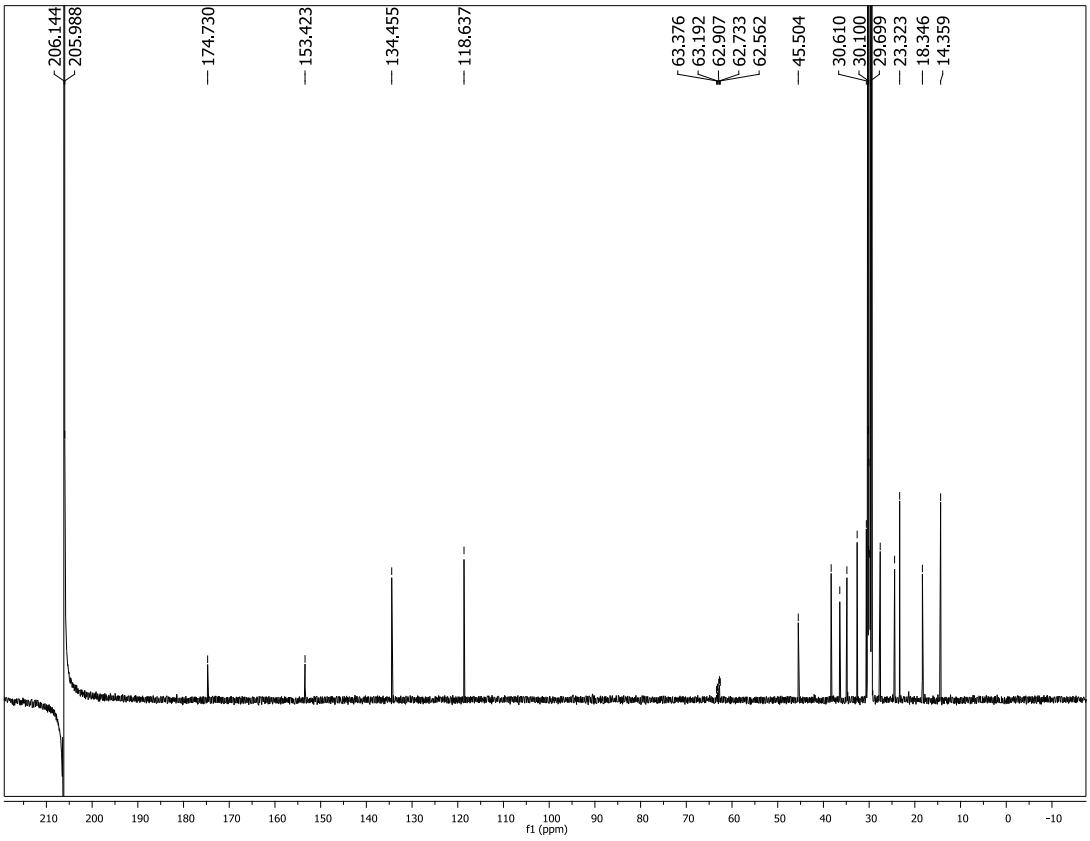

Me
O
Me
i-Pen
N
O
N
H
Me
2o
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

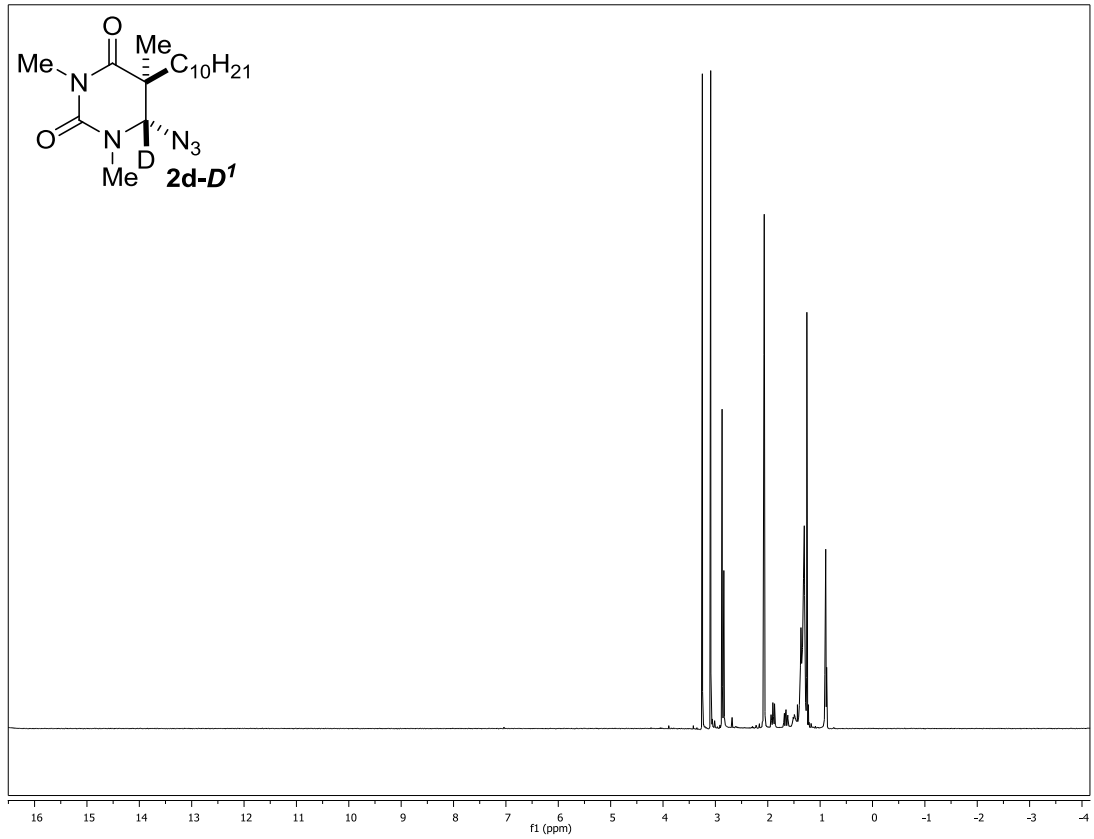

206.192
174.828
153.443
134.501
118.628
63.068
45.540
30.417
29.840
29.015
22.864
22.652
18.272
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

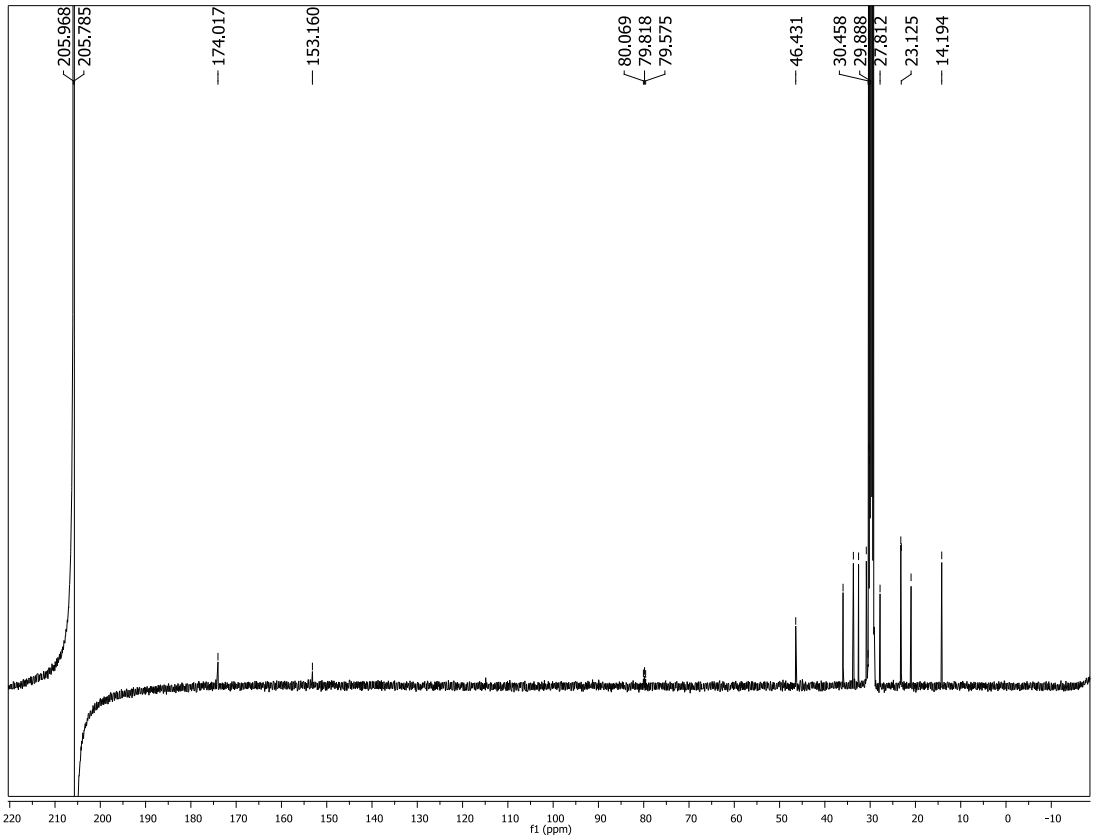

Me
N
O
O
N
H
Me
2p
f1 (ppm)

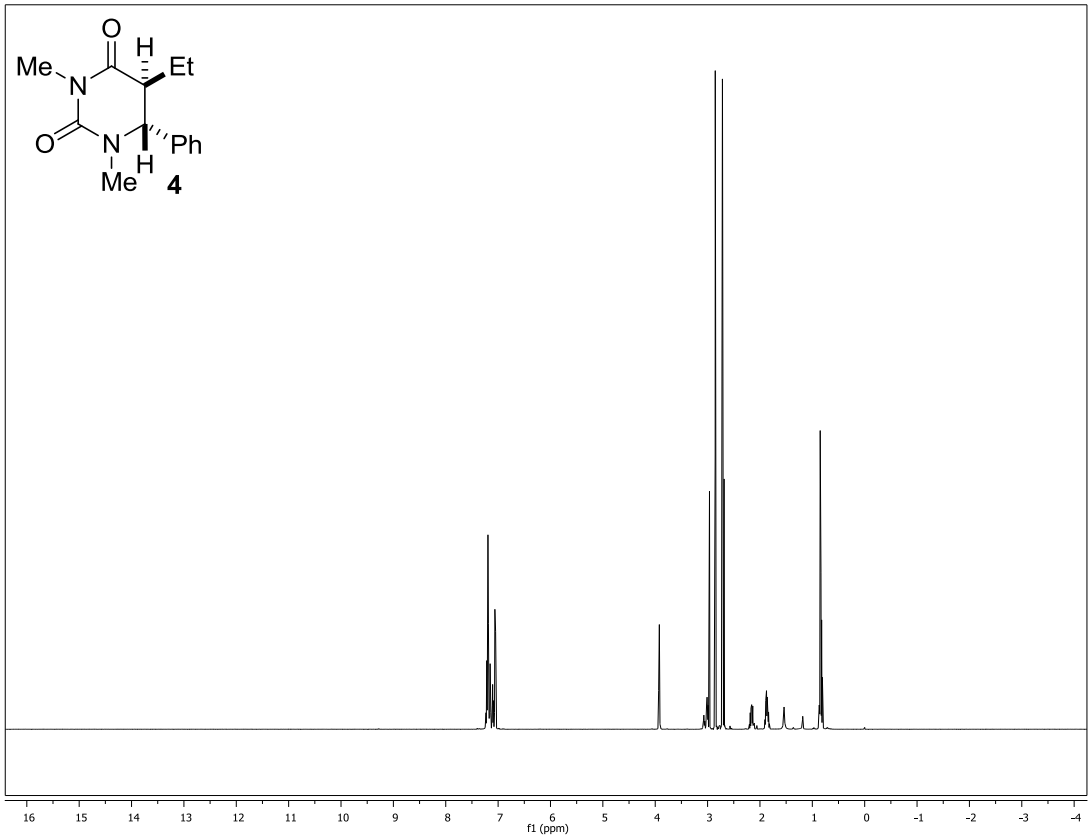

206.379
206.185
205.986
175.577
153.333
134.618
131.996
130.805
118.639
61.444
48.271
34.924
34.723
30.722
30.439
30.246
30.106
30.054
29.861
29.770
29.669
29.476
29.284
27.652
24.735
24.294
f1 (ppm)

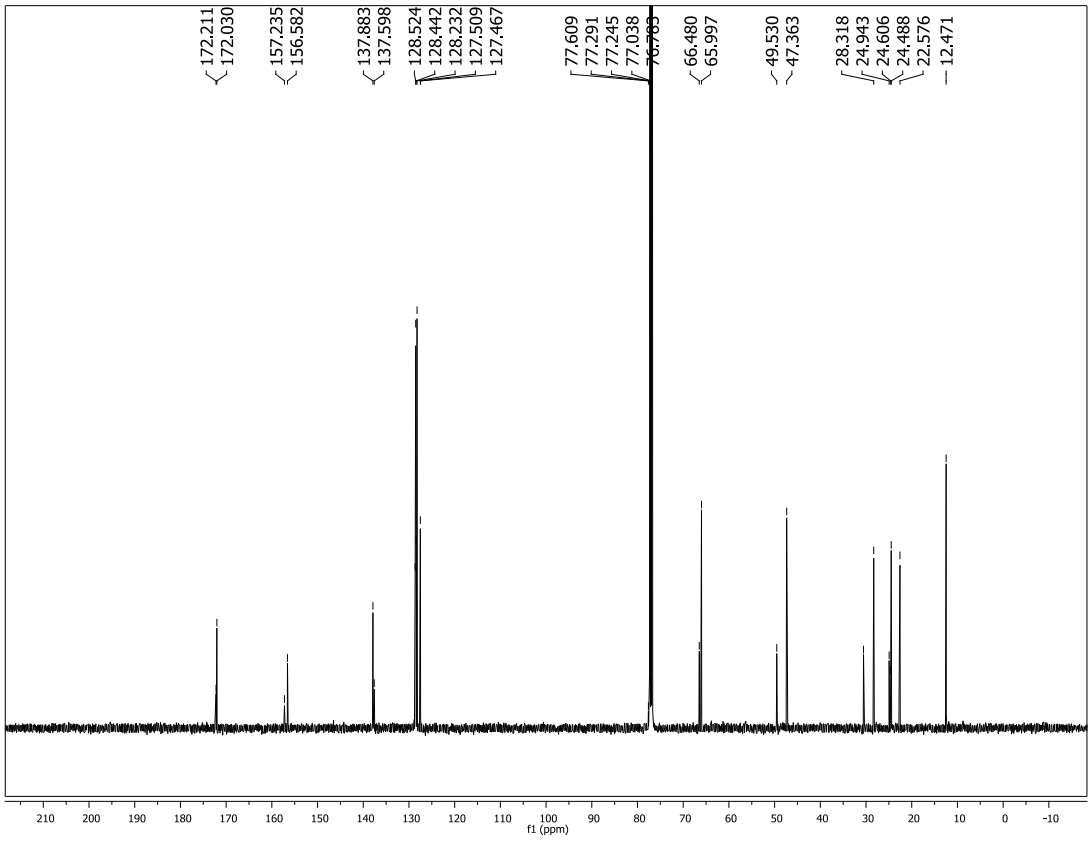

Me
N
O
Me
C10H21
O
N
D
Me
2a-D1
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

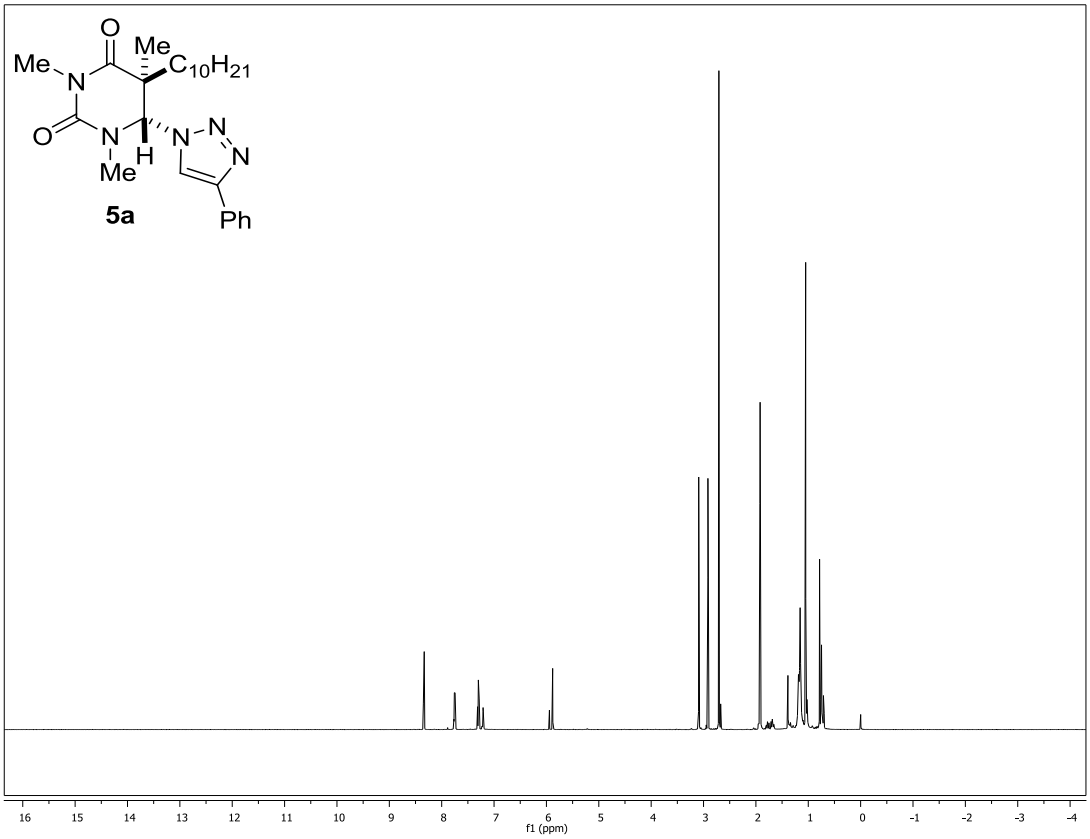

206.144
205.988
174.730
153.423
134.455
118.637
63.376
63.192
62.907
62.733
62.562
45.504
30.610
30.100
29.699
23.323
18.346
14.359
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

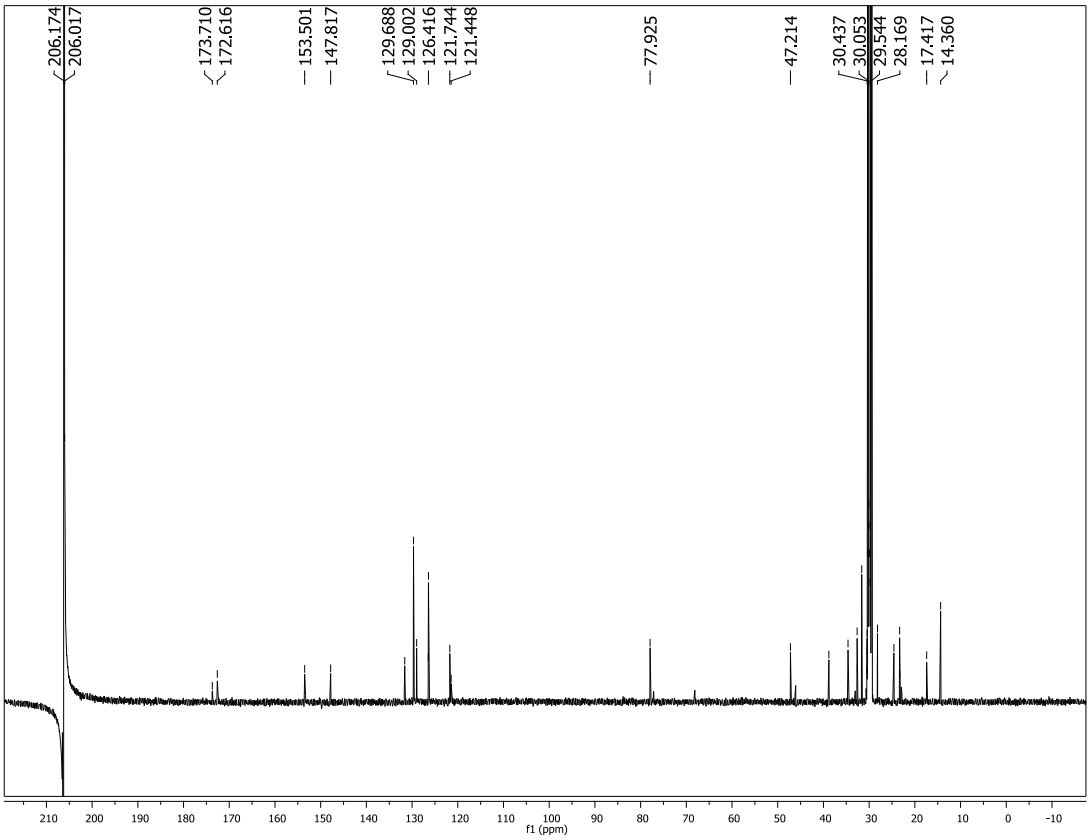

Me
N
O
Me
$C_{10}H_{21}$
O
N
D
N_3
Me
2d-*D*[1]
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

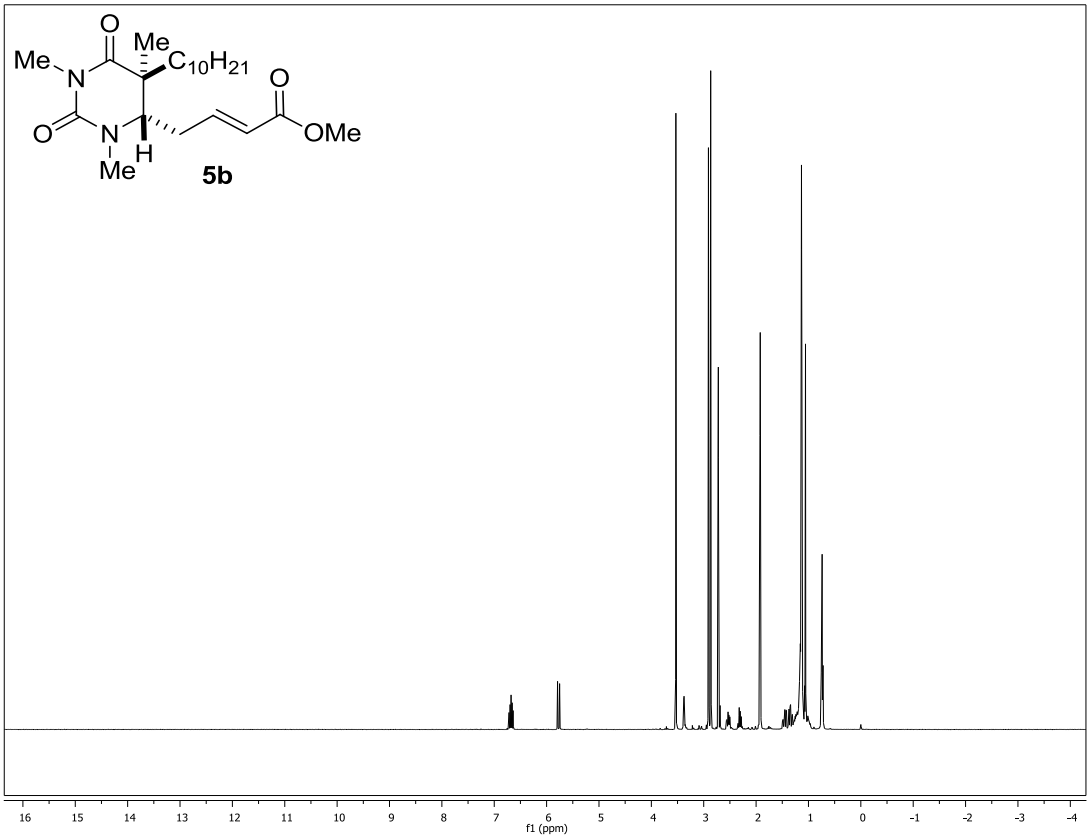

205.968
205.785
174.017
153.160
80.069
79.818
79.575
46.431
30.458
29.888
27.812
23.125
14.194
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

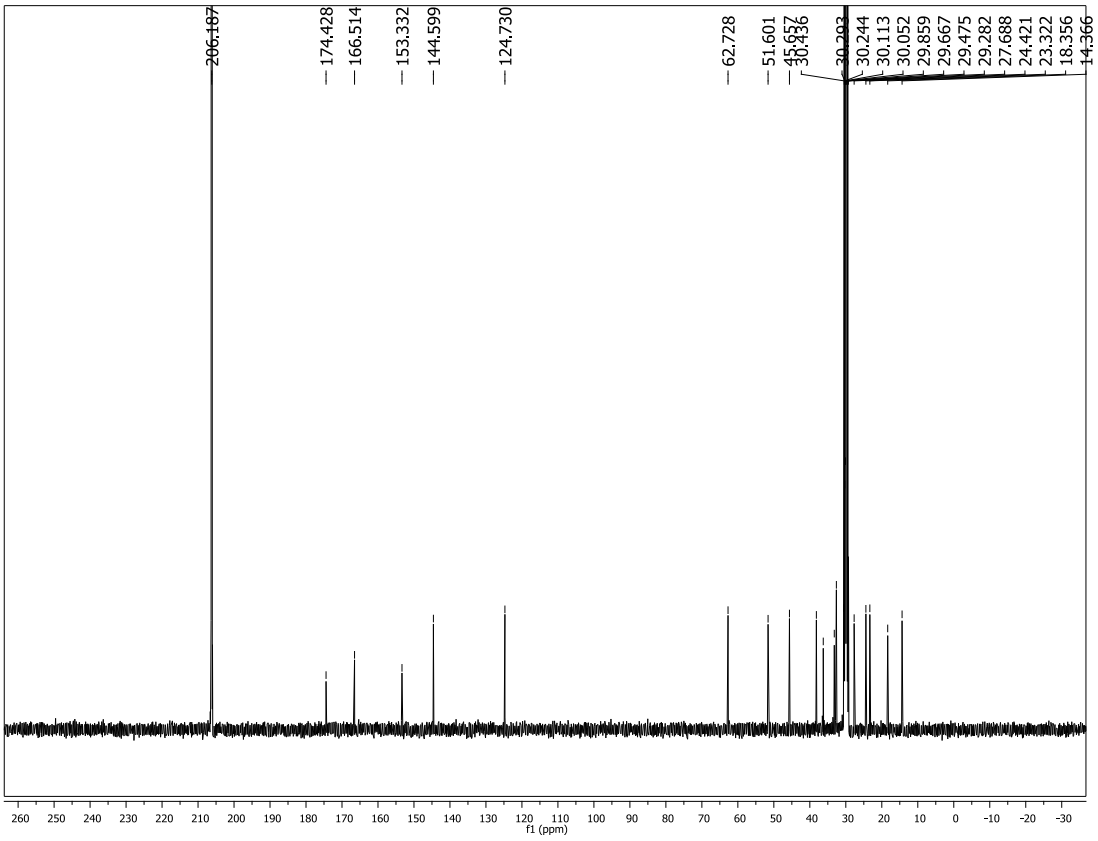

Me
N
O
H
Et
O
N
Ph
H
Me
4
f1 (ppm)

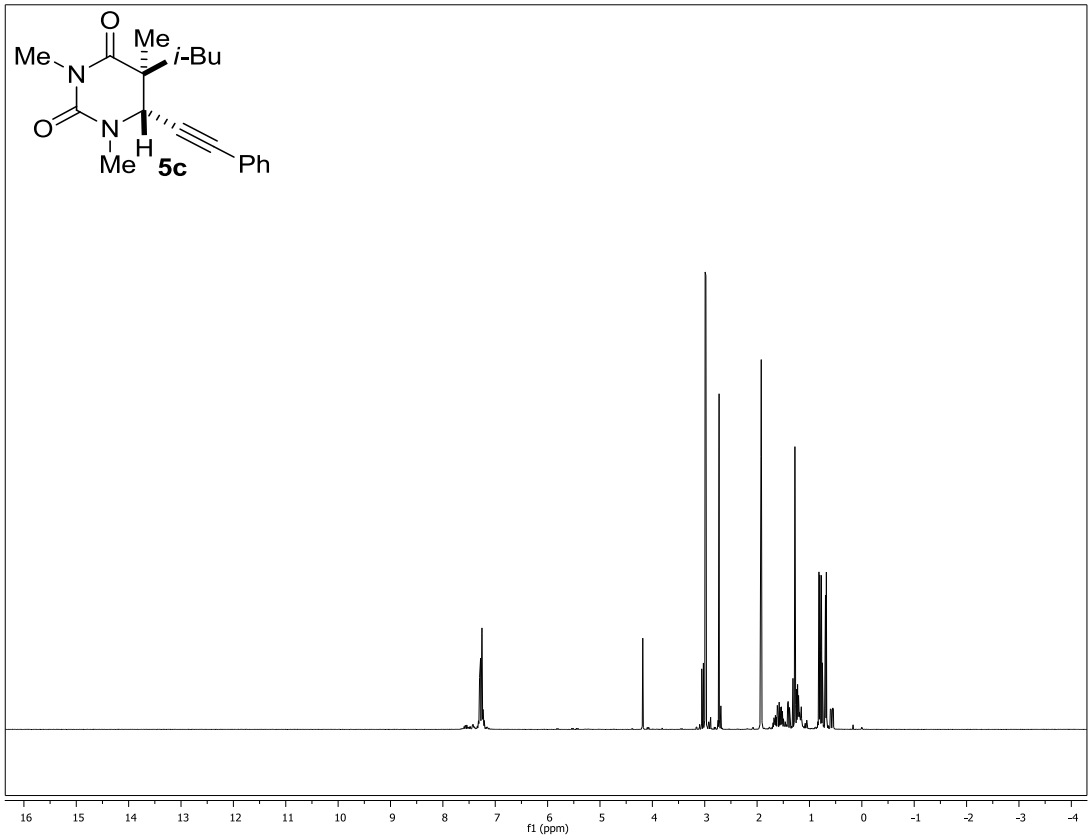

172.211
172.030
157.235
156.582
137.883
137.598
128.524
128.442
128.232
127.509
127.467
77.609
77.291
77.245
77.038
76.783
66.480
65.997
49.530
47.363
28.318
24.943
24.606
24.488
22.576
12.471
f1 (ppm)

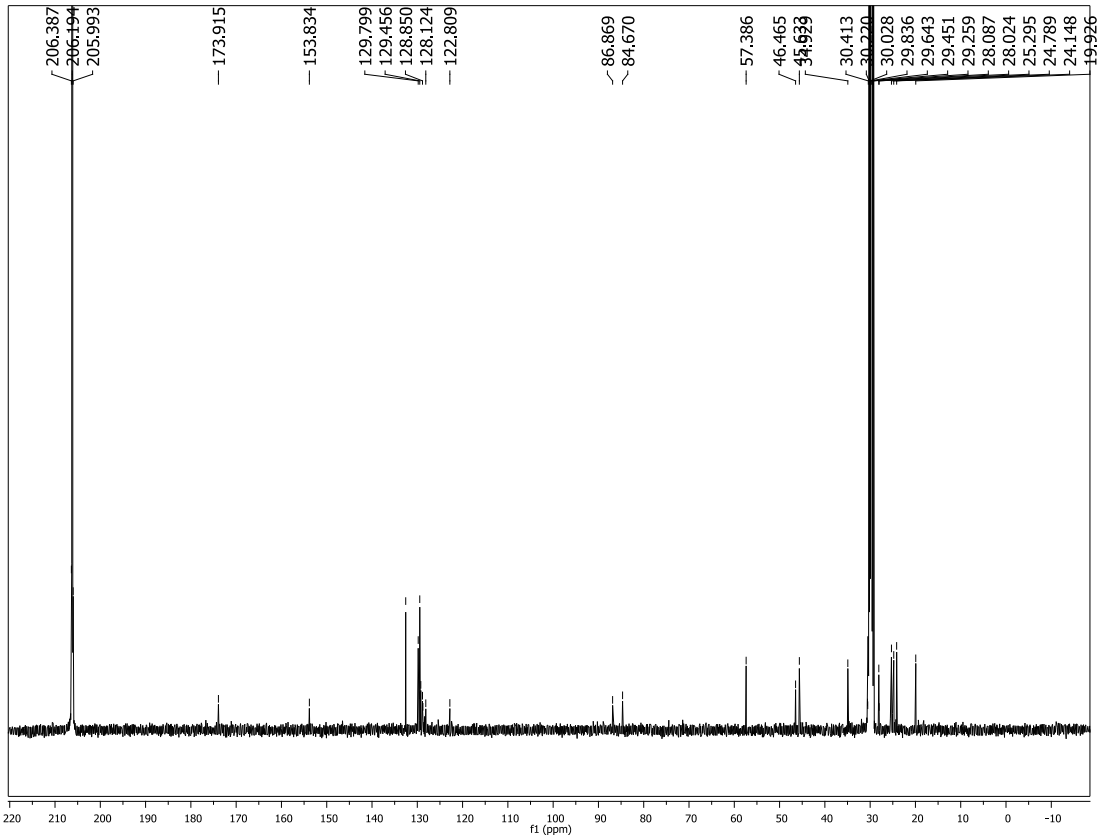

Me
N
O
Me
C10H21
O
N
H
N
N
N
Me
Ph
5a
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

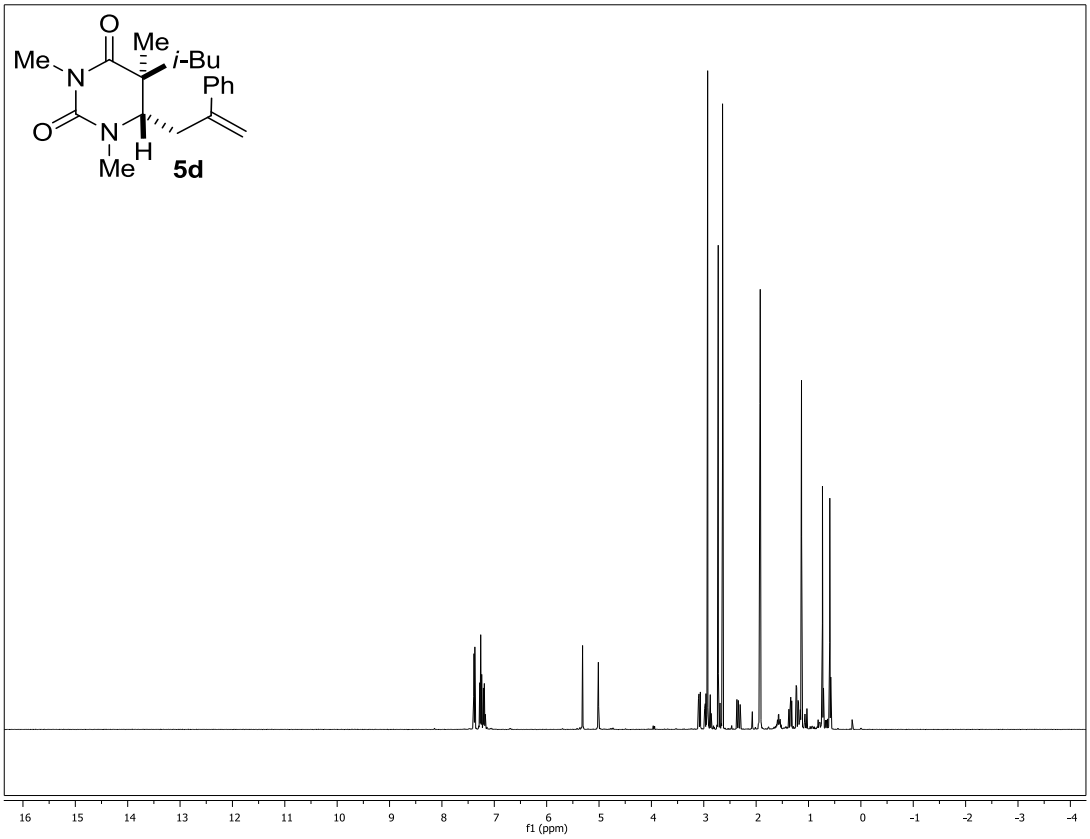

206.174
206.017
173.710
172.616
153.501
147.817
129.688
129.002
126.416
121.744
121.448
77.925
47.214
30.437
30.053
29.544
28.169
17.417
14.360
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

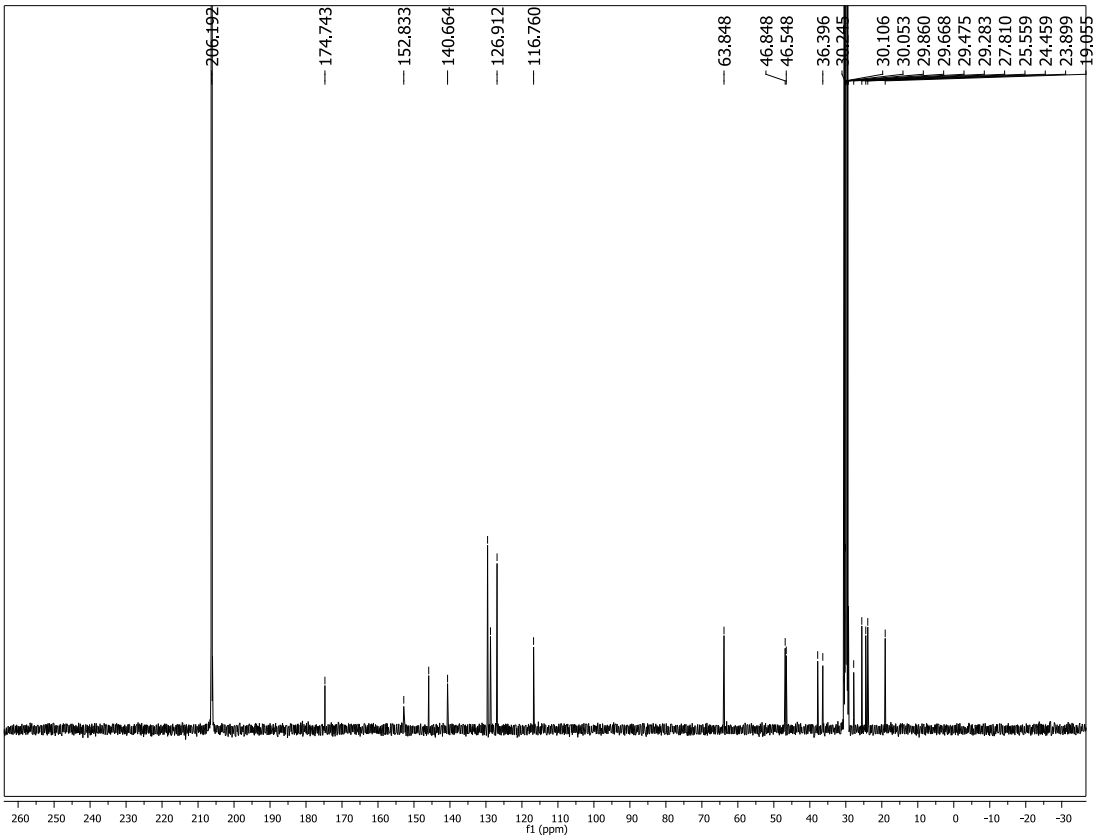

Me
N
O
Me
$C_{10}H_{21}$
O
N
H
Me
O
OMe
5b
f1 (ppm)


206.187
174.428
166.514
153.332
144.599
124.730
62.728
51.601
45.657
30.436
30.203
30.244
30.113
30.052
29.859
29.667
29.475
29.282
27.688
24.421
23.322
18.356
14.366
f1 (ppm)


Me
i-Bu
Me
N
O
O
N
H
Me
5c
Ph
f1 (ppm)


206.387
206.194
205.993
173.915
153.834
129.799
129.456
128.850
128.124
122.809
86.869
84.670
57.386
46.465
30.413
30.028
29.836
29.643
29.451
29.259
28.087
28.024
25.295
24.789
24.148
19.926
f1 (ppm)


Me
N
O
Me
i-Bu
Ph
O
N
H
Me
5d
f1 (ppm)


206.192
174.743
152.833
140.664
126.912
116.760
63.848
46.848
46.548
36.396
30.245
30.106
30.053
29.860
29.668
29.475
29.283
27.810
25.559
24.459
23.899
19.055
f1 (ppm)