Capture-Collapse Heterocyclization: 1,3-Diazepanes by C-N Reductive Elimination from Rhodacyclopentanones

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Supporting Information

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General Experimental Details. Starting materials sourced from commercial suppliers were used as received unless otherwise stated. Dry solvents, where necessary, were obtained by distillation using standard procedures or by passage through a column of anhydrous alumina using equipment from Anhydrous Engineering based on the Grubb's design.[1] The removal of solvents *in vacuo* was achieved using both a Büchi rotary evaporator (bath temperatures up to 40 °C) at a pressure of either 15 mmHg (diaphragm pump) or 0.1 mmHg (oil pump), as appropriate, and a high vacuum line at r.t.. Reactions requiring anhydrous conditions were run under an atmosphere of dry nitrogen or argon; glassware was either flame dried immediately prior to use or placed in an oven (200 °C) for at least 2 h and allowed to cool either in a desiccator or under an atmosphere of nitrogen or argon; liquid reagents, solutions or solvents were added *via* syringe through rubber septa. Commercially available Merck Kieselgel $60F_{254}$ aluminium backed plates were used for TLC analysis. Visualization was achieved by either UV fluorescence or basic $KMnO_4$ solution and heat. Flash column chromatography (FCC) was performed using silica gel (Aldrich 40-63 μm, 230-400 mesh). The crude material was applied to the column as a solution in the corresponding solvent system, CH_2Cl_2, or by pre-adsorption onto silica, as appropriate. Melting points were determined using a Reichert melting point table and temperature controller and are uncorrected. Infra-red spectra were recorded in the range 4000-600 cm^{-1} on a Perkin Elmer Spectrum either as neat films or solids compressed onto a diamond window. Abbreviations used are: w (weak), m (medium) or s (strong). NMR spectra were recorded using either a Varian 400 MHz or JOEL ECS 400 MHz spectrometer. Chemical shifts (δ) are quoted in parts per million (ppm), coupling constants (*J*) are given in Hz to the nearest 0.5 Hz. Other abbreviations used are s (singlet), d (doublet), t (triplet), m (multiplet) and br (broad). ^1H and ^{13}C NMR spectra were referenced to the appropriate residual solvent peak. Assignments of ^1H NMR and ^{13}C NMR signals were made, where possible, using COSY, $DEPT^{135}$, HSQC, HMBC and NOE experiments. Where mixtures of products (*e.g.* diastereomers, regioisomers or 8 vs 9) have been isolated together, they have been characterized separately where possible. *Numbering systems for NMR signal assignments are specified on the structure and are not related to those used for the compound names.* Mass spectra were determined by the University of Bristol mass spectrometry service by either electron impact (EI^+) or chemical ionization (CI^+) using a Fisons VG Analytical Autospec spectrometer, or by electrospray ionization (ESI^+) using a Brüker Daltonics Apex IV spectrometer. Chiral SFC was performed using the racemate as a standard on an Agilent 1290 Infinity system equipped with a quaternary pump, diode array detector and column thermostat under the conditions specified in each case.

General procedure A for the formation of ureas from isocyanates

To a solution of amine (110 mol%) and NEt_3 (200 mol%) in CH_2Cl_2 (0.3 M) at 0 °C was added the specified isocyanate (100 mol%). The reaction mixture was warmed to r.t. and stirred for the specified time (1-18 h). The solution was diluted with CH_2Cl_2 (3 mL/mmol) and washed with water (5 mL/mmol), aq. 1 M HCl (5 mL/mmol), sat. aq. $NaHCO_3$ (5 mL/mmol) and brine (5 mL/mmol). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The product was purified by flash column chromatography, under the conditions noted, to afford the title compound.

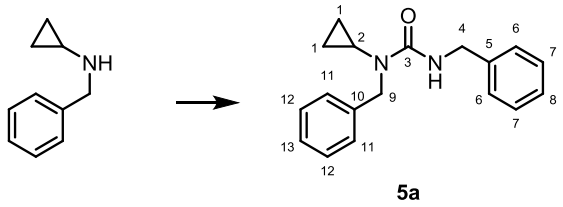
General procedure B for the carbonylative cyclization of cyclopropylureas

An oven dried reaction tube, fitted with a magnetic stirrer, was charged with benzoic acid (15 mol%), the specified Rh pre-catalyst (3.5-10 mol%), PPh_3 (7.0-20 mol%) and urea substrate (100 mol%). The tube was fitted with a rubber septum and purged with argon. Argon sparged anhydrous 1,2-dichlorobenzene (0.2 M) was added *via* syringe before aging the catalyst for *ca.* 5 minutes. The reaction tube was purged with CO and the reaction mixture was sparged for 10 seconds. The reaction was heated at the specified temperature (90-100 °C) under a CO atmosphere until complete consumption of the starting material was observed by thin layer chromatography (23-92 h). The mixture was cooled to r.t., concentrated *in vacuo* and purified by flash column chromatography, under the conditions noted, to afford the target heterocycle.

General procedure C for the deprotection/urea formation of Boc-protected cyclopropylamines

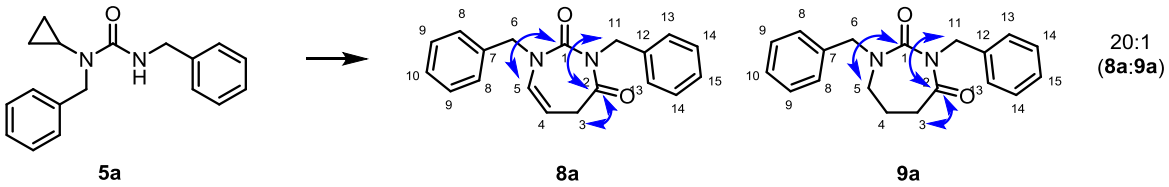
To a solution of Boc-protected cyclopropylamine (100 mol%) in CH_2Cl_2 (1 M) was added trifluoroacetic acid (1000 mol%) and the reaction was stirred at r.t. for 30 minutes. The reaction mixture was concentrated *in vacuo*. The resulting trifluoroacetate salt and NEt_3 (250 mol%) were dissolved in CH_2Cl_2 (0.3 M) before adding benzyl isocyanate (95 mol%). The reaction was stirred at r.t. for the specified time before being diluted with CH_2Cl_2 (5 mL/mmol). The solution was washed with water (5 mL/mmol), aq. 1 M HCl (5 mL/mmol), sat. aq. $NaHCO_3$ (5 mL/mmol) and brine (5 mL/mmol), dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash column chromatography, under the conditions noted, provided the target compound.

1,3-Dibenzyl-1-cyclopropylurea (5a)



General procedure A: *N*-Benzylcyclopropanamine[2] (1.77 g, 11.0 mmol) and benzyl isocyanate (1.24 mL, 10.0 mmol) were employed. The crude mixture was purified by silica gel column chromatography (50% EtOAc/hexane) to yield the title compound **5a** (2.26 g, 81%) as a colorless solid; m.p.: 80-82 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 3369 (s), 1635 (s), 1504 (s), 1285 (m), 1230 (m); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35-7.21 (10H, m, 2 × C**6**-H, 2 × C**7**-H, C**8**-H, 2 × C**11**-H, 2 × C**12**-H and C**13**-H), 5.61 (1H, t, *J* = 5.5 Hz, NH), 4.58 (2H, s, C**9**-H_2), 4.50 (2H, d, *J* = 5.5 , Hz, C**4**-H_2), 2.35 (1H, tt, *J* = 7.0, 4.0 Hz, C**2**-H), 0.78-0.74 (4H, m, C**1**-H_2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.1 (C**3**), 139.8 (C**5**), 139.1 (C**10**), 128.7, 128.5, 128.0, 127.5, 127.3, 127.0 (C**6**, C**7**, C**8**, C**11**, C**12** and C**13**), 50.6 (C**9**), 44.9 (C**4**), 27.8 (C**2**), 8.8 (C**1**); HRMS: (ESI^+) Calculated for $C_{18}H_{21}N_2O$: 281.1648. Found $[M + H]^+$: 281.1662.

1,3-Dibenzyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8a) *and* 1,3-Dibenzyl-1,3-diazepane-2,4-dione (9a)



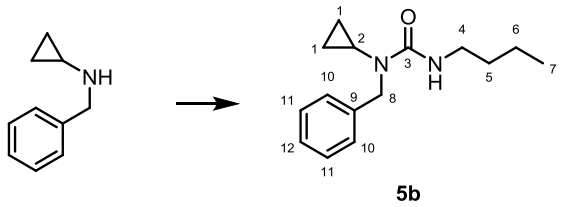
General Procedure B: Urea **5a** (53.2 mg, 0.15 mmol) and $[Rh(cod)_2]BARF$ (3.5 mol%) were employed and the reaction was stirred for 24 h at 100 °C. The crude mixture was purified by silica gel column chromatography (25% EtOAc/hexane) to yield the title compound **8a** (37.5 mg, 82%) as a yellow oil. Analysis of the crude reaction mixture by ^{1}H NMR revealed a 20:1 (**8a**:**9a**) mixture of products. An analytical sample of **9a** was also isolated for characterisation.

Data for major compound **8a**; ν_{max} / cm^{-1}: 1699 (s), 1647 (s), 1406 (s), 1395 (s), 1212 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.30-7.21 (8H, m, 2 × C**9**-H, C**10**-H, 2 × C**13**-H, 2 × C**14**-H, C**15**-H), 7.05-7.03 (2H, m, 2 × C**8**-H), 6.03 (1H, d, *J* = 7.0 Hz, C**5**-H), 5.54 (1H, dt, *J* = 7.0, 7.0 Hz, C**4**-H), 5.05 (2H, s, C**11**-H_2), 4.73 (2H, s, C**6**-H_2), 3.08 (2H, d, *J* = 7.0 Hz, C**3**-H_2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.0 (C**2**), 153.9 (C**1**), 137.6 (C**12**), 136.1 (C**7**), 130.3 (C**5**), 128.7.

128.4, 128.1, 127.8, 127.6, 127.3 (C**8**, C**9**, C**10**, C**13**, C**14**, C**15**), 112.7 (C**4**), 53.0 (C**6**), 47.9 (C**11**), 35.0 (C**3**); HRMS: (ESI$^+$) Calculated for $C_{19}H_{18}N_2NaO_2$: 329.1260. Found $[M + Na]^+$: 329.1249. *The structure of this compound was confirmed by 2D NMR. Key HMBC correlations are included on the compound structure above.*

Data for minor compound **9a**; ν_{max} / cm^{-1}: 1694 (s), 1656 (s), 1421 (s), 1214 (s), 1158 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38-7.23 (8H, m, 2 × C**9**-H, C**10**-H, 2 × C**13**-H, 2 × C**14**-H, C**15**-H), 7.09-7.06 (2H, m, 2 × C**8**-H), 4.94 (2H, s, C**11**-H_2), 4.60 (2H, s, C**6**-H_2), 3.18 (2H, t, *J* = 7.0 Hz, C**5**-H_2), 2.54 (2H, t, *J* = 7.0 Hz, C**3**-H_2), 1.86 (2H, tt, *J* = 7.0, 7.0 Hz, C**4**-H_2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.3 (C**2**), 157.6 (C**1**), 137.8 (C**12**), 136.7 (C**7**), 128.8, 128.7, 128.5, 127.8, 127.5 (C**8**, C**9**, C**10**, C**13**, C**14**, C**15**), 51.8 (C**6**), 46.8 (C**11**), 45.6 (C**5**), 33.7 (C**3**), 25.7 (C**4**); HRMS: (ESI$^+$) Calculated for $C_{19}H_{20}N_2NaO_2$: 331.1417. Found $[M + Na]^+$: 331.1416. *The structure of this compound was confirmed by 2D NMR. Key HMBC correlations are included on the compound structure above.*

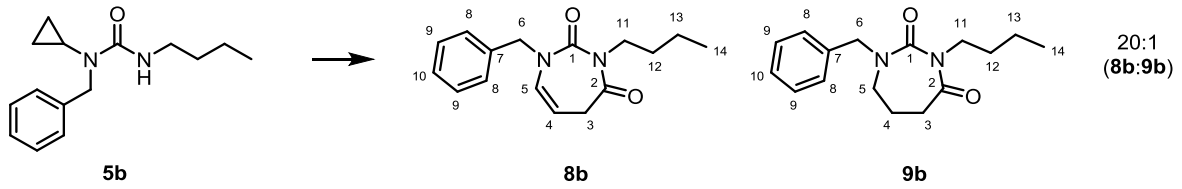
1-Benzyl-3-butyl-1-cyclopropylurea (5b)



5b

General procedure A: *N*-Benzylcyclopropanamine[2] (1.77 g, 11.0 mmol) and butyl isocyanate (1.12 mL, 10.0 mmol) were employed. This crude mixture was purified by silica gel column chromatography (30% EtOAc/hexane) to yield the title compound **5b** (2.43 g, 99%) as a colorless oil; ν_{max} / cm^{-1}: 3377 (m), 1638 (s), 1513 (s), 1283 (s), 1269 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.27-7.16 (5H, m, 2 × C**10**-H, 2 × C**11**-H, C**12**-H), 5.31 (1H, t, *J* = 5.5 Hz, NH), 4.51 (2H, s, C**8**-H_2), 3.26 (2H, td, *J* = 7.0, 5.5 Hz, C**4**-H_2), 2.28 (1H, tt, *J* = 6.5, 4.0 Hz, C**2**-H), 1.53-1.46 (2H, m, C**5**-H_2), 1.38-1.29 (2H, m, C**6**-H_2), 0.91 (3H, t, *J* = 7.5 Hz, C**7**-H_3), 0.76-0.67 (4H, m, 4 × C**1**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.0 (C**3**), 139.2 (C**9**), 128.3, 128.8, 126.8 (C**10**, C**11**, C**12**), 50.3 (C**8**), 40.4 (C**4**), 32.5 (C**5**), 27.7 (C**2**), 20.1 (C**6**), 13.8 (C**7**), 8.6 (C**1**); HRMS: (ESI$^+$) Calculated for $C_{15}H_{22}N_2NaO$: 269.1624. Found $[M + Na]^+$: 269.1629.

3-Benzyl-1-butyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8b) *and* 1-Benzyl-3-butyl-1,3-diazepane-2,4-dione (9b)



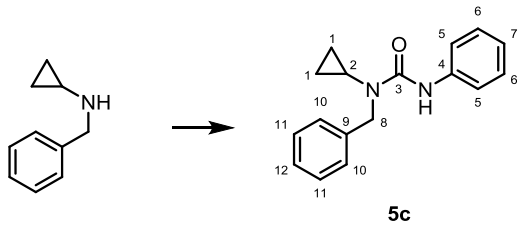
5b **8b** **9b**

General Procedure B: Urea **5b** (37.0 mg, 0.15 mmol) and [Rh(cod)$_2$]BARF (5.0 mol%) were employed and the reaction was stirred for 24 h at 100 °C. The crude mixture was purified by silica gel column chromatography (20% EtOAc/hexane) to yield the title compound **8b** (35.2 mg, 85%) as a yellow oil. Analysis of the crude reaction mixture by ^{1}H NMR revealed a 20:1 (**8b**:**9b**) mixture of products. The minor product **9b** was not isolated.

Data for major compound **8b**: ν_{max} / cm^{-1}: 2958 (m), 1698 (s), 1645 (s), 1407 (s), 1214 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36-7.26 (5H, m, 2 × C**8**-H, 2 × C**9**-H, C**10**-H), 6.10 (1H, d, *J* = 7.0 Hz, C**5**-H), 5.52 (1H, dt, *J* = 7.0, 7.0 Hz, C**4**-H), 4.79 (2H, s, C**6**-H$_2$), 3.80 (2H, t, *J* = 7.0 Hz, C**11**-H$_2$), 2.99 (2H, d, *J* = 7.0 Hz, C**3**-H$_2$), 1.55 (2H, tt, *J* = 7.0, 7.0 Hz, C**12**-H$_2$), 1.27 (2H, tq, *J* = 7.0, 7.0 Hz, C**13**-H$_2$), 0.90 (3H, t, *J* = 7.0 Hz, C**14**-H$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.1 (C**2**), 154.4 (C**1**), 136.6 (C**7**), 130.5 (C**5**), 128.8, 127.9, 127.8 (C**8**, C**9**, C**10**), 113.0 (C**4**), 53.2 (C**6**), 45.4 (C**11**), 35.2 (C**3**), 30.4 (C**12**), 20.1 (C**13**), 13.8 (C**14**); HRMS: (ESI$^+$) Calculated for $C_{16}H_{20}N_2NaO_2$: 295.1417. Found [M + Na]$^+$: 295.1421.

Data for minor compound **9b**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.66 (2H, s, C**6**-H$_2$), 3.75 (2H, t, *J* = 7.0 Hz, C**11**-H$_2$), 3.36 (2H, t, *J* = 7.0 Hz, C**5**-H$_2$), 2.50 (2H, t, *J* = 7.0 Hz, C**3**-H$_2$); HRMS: (ESI$^+$) Calculated for $C_{16}H_{22}N_2NaO_2$: 297.1573. Found [M + Na]$^+$: 297.1575.

1-Benzyl-1-cyclopropyl-3-phenylurea (5c)

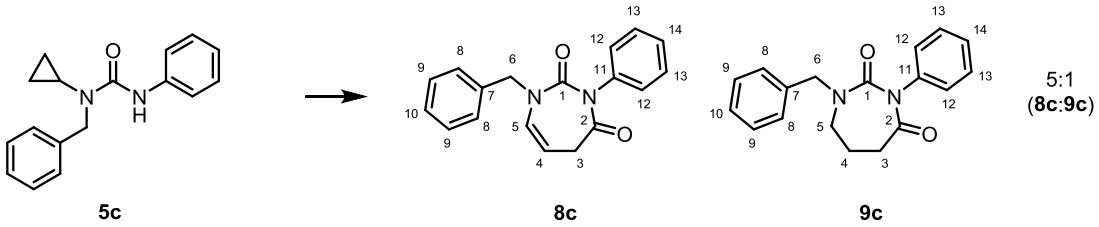


5c

General procedure A: *N*-Benzylcyclopropanamine[2] (1.77 g, 11.0 mmol) and phenyl isocyanate (1.09 mL, 10.0 mmol) were employed. The crude mixture was purified by column chromatography (30% EtOAc/hexane) to yield the title compound **5c** (2.54 g, 95%) as a colorless oil; ν_{max} / cm^{-1}: 3431 (m), 3355 (m), 1659 (s), 1595 (s), 1522 (s), 1499 (s), 1440 (s),

1237 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.49 (2H, d, *J* = 7.5 Hz, 2 × C**5**-H), 7.37-7.24 (8H, m, NH, 2 × C**6**-H, 2 × C**10**-H, 2 × C**11**-H, C**12**-H), 7.05 (1H, t, *J* = 7.5 Hz, C**7**-H), 4.64 (2H, s, C**8**-H_2), 2.53 (1H, tt, *J* = 7.0, 4.0 Hz, C**2**-H), 0.97-0.88 (4H, m, 4 × C**1**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.1 (C**3**), 139.0 (C**9**), 138.6 (C**10**), 128.9 (C**6**), 128.5, 127.9, 127.1 (C**10**, C**11**, C**12**), 123.0 (C**7**), 119.5 (C**5**), 50.4 (C**8**), 28.1 (C**2**), 9.0 (C**1**); HRMS: (ESI$^+$) Calculated for $C_{17}H_{18}N_2NaO$: 289.1311. Found [M + Na]$^+$: 289.1306.

3-Benzyl-1-phenyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8c) *and* 1-Benzyl-3-phenyl-1,3-diazepane-2,4-dione (9c)



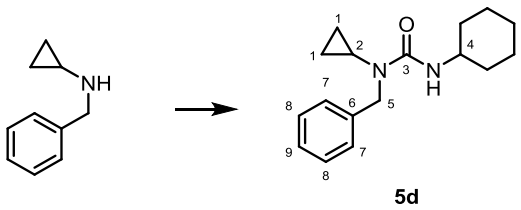
5c **8c** **9c**

General Procedure B: Urea **5c** (40.0 mg, 0.15 mmol) and [Rh(cod)$_2$]BARF (7.5 mol%) were employed and the reaction was stirred for 70 h at 100 °C. The crude mixture was purified by column chromatography (15-25% EtOAc/hexane) to yield the title compound **8c** (12.2 mg, 28%) as a yellow oil. Analysis of the crude reaction mixture by ^{1}H NMR revealed a 5:1 (**8c**:**9c**) mixture of products. The minor product **9c** was not isolated.

Data for major compound **8c**: ν_{max} / cm^{-1}: 2987 (s), 1705 (s), 1652 (s), 1403 (s), 1392 (s), 1226 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.45-7.19 (10H, m, 2 × C**8**-H, 2 × C**9**-H, C**10**-H, 2 × C**12**-H, 2 × C**13**-H, C**14**-H), 6.26 (1H, d, *J* = 7.0 Hz, C**5**-H), 5.66 (1H, dt, *J* = 7.0, 7.0 Hz, C**4**-H), 4.81 (2H, s, C**6**-H_2), 3.17 (2H, d, *J* = 7.0 Hz, C**3**-H_2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.5 (C**2**), 153.7 (C**1**), 138.8 (C**11**), 136.4 (C**7**), 130.8 (C**5**), 129.1, 128.8, 128.5, 128.3, 128.1, 128.0 (C**8**, C**9**, C**10**, C**12**, C**13**, C**14**), 113.3 (C**4**), 53.5 (C**6**), 35.2 (C**3**); HRMS: (ESI$^+$) Calculated for $C_{18}H_{16}N_2NaO_2$: 315.1104. Found [M + Na]$^+$: 315.1092.

Data for minor compound **9c**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.26 (2H, t, *J* = 7.0 Hz, C**5**-H_2).

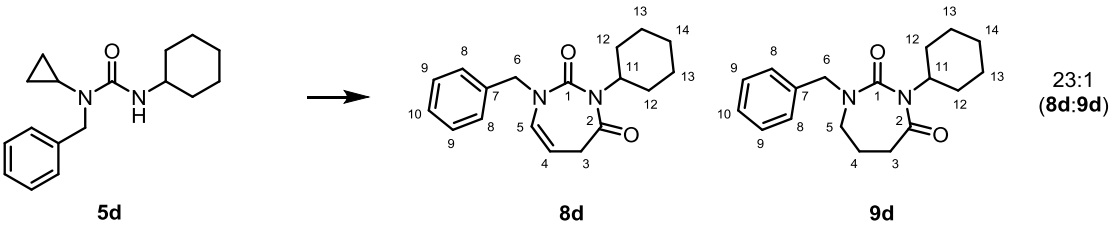
1-Benzyl-3-cyclohexyl-1-cyclopropylurea (5d)



5d

General procedure A: *N*-Benzylcyclopropanamine[2] (1.77 g, 11.0 mmol) and cyclohexyl isocyanate (1.28 mL, 10.0 mmol) were employed. The crude mixture was purified by column chromatography (30% EtOAc/hexane) to yield the title compound **5d** (2.15 g, 79%) as a colorless solid: m.p. 60-63 °C ($CHCl_3$); ν_{max} / cm^{-1}: 3366 (m), 1643 (s), 1506 (s), 1452 (s), 1256 (s); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.23-7.13 (5H, m, 2 × C**7**-H, 2 × C**8**-H, C**9**-H), 5.18 (1H, d, *J* = 8.0 Hz, NH), 4.48 (2H, s, C**5**-H_2), 3.67 (1H, m, C**4**-H), 2.25 (1H, tt, *J* = 6.5, 4.0 Hz, C**2**-H), 1.94-1.90 (2H, m, 2 × cyclohexyl CH), 1.68-1.62 (2H, m, 2 × cyclohexyl CH), 1.55 (1H, m, 1 × cyclohexyl CH), 1.39-1.28 (2H, m, 2 × cyclohexyl CH), 1.19-1.08 (3H, m, 3 × cyclohexyl CH), 0.73-0.64 (4H, m, 4 × C**1**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.2 (C**3**), 139.2 (C**6**), 128.3, 127.8, 126.8 (C**7**, C**8**, C**9**), 50.3 (C**5**), 49.1 (C**4**), 33.8 (cyclohexyl CH_2), 27.6 (C**2**), 25.7 (cyclohexyl CH_2), 24.9 (cyclohexyl CH_2), 8.6 (C**1**); HRMS: (ESI^+) Calculated for $C_{17}H_{24}N_2NaO$: 295.1781. Found $[M + Na]^+$: 295.1779.

3-Benzyl-1-cyclohexyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8d) *and* 1-Benzyl-3-cyclohexyl-1,3-diazepane-2,4-dione (9d)



5d **8d** **9d**

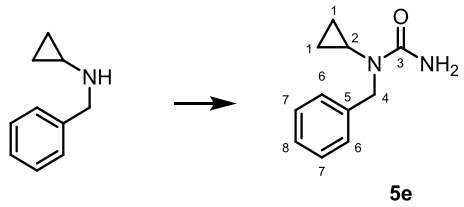
General Procedure B: Urea **5d** (40.9 mg, 0.15 mmol) and $[Rh(cod)_2]BARF$ (7.5 mol%) were employed and the reaction was stirred for 24 h at 100 °C. The crude mixture was purified by column chromatography (20% EtOAc/hexane) to yield the title compound **8d** (31.0 mg, 69%) as a yellow oil. Analysis of the crude reaction mixture by ^1H NMR revealed a 23:1 (**8d**:**9d**) mixture of products. The minor product **9d** was not isolated.

Data for major compound **8d**: ν_{max} / cm^{-1}: 2928 (s), 1695 (s), 1648 (s), 1406 (s), 1394 (s), 1223 (s), 1049 (s); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.36-7.24 (5H, m, 2 × C**8**-H, 2 × C**9**-H, C**10**-H), 6.09 (1H, d, *J* = 7.0 Hz, C**5**-H), 5.55 (1H, dt, *J* = 7.0, 7.0 Hz, C**4**-H), 4.77 (2H, s, C**6**-H_2), 4.14

(1H, tt, *J* = 12.0, 3.5 Hz, C**11**-H), 2.93 (2H, d, *J* = 7.0 Hz, C**3**-H$_2$), 2.08-1.98 (2H, m, 2 × C**12**-H), 1.81 1.63 (5H, m, 2 × C**12**-H, 2 × C**13**-H, 1 × C**14**-H), 1.38-1.11 (3H, m, 2 × C**13**-H, 1 × C**14**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 17.5 (C**2**), 153.9 (C**1**), 136.5 (C**7**), 130.3 (C**5**), 128.8, 127.9, 127.8 (C**8**, C**9**, C**10**), 114.3 (C**4**), 57.5 (C**11**), 52.7 (C**6**), 35.4 (C**3**), 29.9 (C**12**), 26.3 (C**13**), 25.4 (C**14**); HRMS: (ESI$^+$) Calculated for $C_{18}H_{22}N_2NaO_2$: 321.1573. Found [M + Na]$^+$: 321.1568.

Data for minor compound **9d**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.64 (2H, s, C**6**-H$_2$).

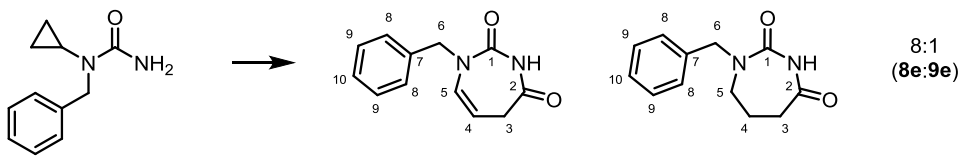
1-Benzyl-1-cyclopropylurea (5e)



5e

The title compound was prepared following the literature procedure.[3] In a round bottom flask containing a stirrer bar, *N*-benzylcyclopropanamine[2] (1.47 g, 10.0 mmol) was suspended in water (40 mL) and conc. HCl (0.84 mL, 10.0 mmol) was added. Upon stirring, a solution of KOCN (1.22 g, 15.0 mmol) in water (40 mL) was added. The mixture was stirred at r.t. for 36 h, during which time a colorless precipitate was formed. The precipitate was collected by suction filtration and the cake was purified by recystallization (CH_2Cl_2/hexane) to yield the title compound **5e** (712 mg, 37%) as colorless needles; m.p. 96-98 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 3484 (m), 3455 (m), 3150 (m), 1646 (s), 1591 (s), 1413 (s), 1028 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.33-7.22 (5H, m, 2 × C**6**-H, 2 × C**7**-H, C**8**-H), 5.24 (2H, br. s, NH$_2$), 4.55 (2H, s, C**4**-H$_2$), 2.44 (1H, m, C**2**-H), 0.83-0.75 (4H, m, 4 × C**1**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 160.1 (C**3**), 138.7 (C**5**), 128.4, 127.7, 127.0 (C**6**, C**7**, C**8**), 50.1 (C**4**), 28.6 (C**2**), 8.5 (C**1**); HRMS: (ESI$^+$) Calculated for $C_{11}H_{14}N_2NaO$: 213.0998. Found [M + Na]$^+$: 213.1006.

3-Benzyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8e) ***and*** **1-Benzyl-1,3- diazepane-2,4-dione (9e)**



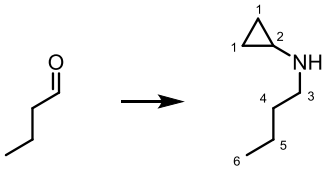
5e **8e** **9e**

General Procedure B: Urea **5e** (28.5 mg, 0.15 mmol) and [Rh(cod)$_2$]BARF (5.0 mol%) were employed and the reaction was stirred for 72 h at 100 °C. The crude mixture was purified by column chromatography (45% EtOAc/hexane) to yield the title compound **8e** (17.5 mg, 54%) as a beige oil. Analysis of the crude reaction mixture by ^{1}H NMR revealed an 8:1 (**8e**:**9e**) mixture of products. The minor product **9e** was not isolated.

Data for major compound **8e**: ν_{max} / cm^{-1}: 3215 (m), 2987 (s), 1653 (s), 1412 (s), 1388 (s), 1260 (s), 1075 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.50 (1H, br. s, N<u>H</u>), 7.38-7.24 (5H, m, 2 × C**8**-<u>H</u>, 2 × C**9**-<u>H</u>, C**10**-<u>H</u>), 6.09 (1H, d, *J* = 7.5 Hz, C**5**-<u>H</u>), 5.42 (1H, dt, *J* = 7.5, 7.0 Hz, C**4**-<u>H</u>), 4.78 (2H, s, C**6**-<u>H$_2$</u>), 3.06 (2H, d, *J* = 7.0 Hz, C**3**-<u>H$_2$</u>); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.1 (C**2**), 151.2 (C**1**), 136.2 (C**7**), 130.8 (C**5**), 128.9, 128.0, 127.9 (C**8**, C**9**, C**10**), 110.4 (C**4**), 52.6 (C**6**), 34.3 (C**3**); HRMS: (ESI$^+$) Calculated for $C_{12}H_{12}N_2NaO_2$: 239.0790. Found [M + Na]$^+$: 239.0787.

Data for minor compound **9e**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.41 (2H, t, *J* = 7.0 Hz, C**5**-<u>H$_2$</u>).

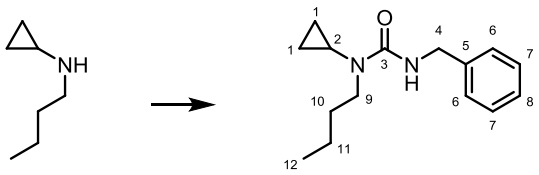
***N*-Butylcyclopropanamine**



A solution of cyclopropylamine (8.31 mL, 120 mmol), butyraldehyde (9.01 mL, 100 mmol) and $NaHCO_3$ (12.6 g, 150 mmol) in MeOH (100 mL) was heated at reflux for 24 h. The reaction mixture was cooled to 0 °C and $NaBH_4$ (4.73 g, 125 mmol) was added portionwise over 5 minutes. The solution was warmed r.t. and stirred for 18 h. The reaction mixture was concentrated *in vacuo* and then sat. aq. $NaHCO_3$ (100 mL) was added. The solution was extracted with CH_2Cl_2 (3 × 75 mL) and then the organic extracts were combined, washed with brine (75 mL), dried over Na_2SO_4 and concentrated *in vacuo* to yield *N*-butylcyclopropylamine (7.20 g, 63%) as a yellow oil, *N.B. Due to volatility issues a cold water bath was used when concentrating in vacuo*; ν_{max} / cm^{-1}: 3087 (w), 2957 (s), 2930 (s), 1457 (s), 1214 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.63 (2H, t, *J* = 7.0 Hz, C**3**-<u>H$_2$</u>), 2.06 (1H, tt, *J* = 7.0, 4.0 Hz, C**2**-<u>H</u>), 1.55 (1H, br. s, N<u>H</u>), 1.45-1.38 (2H, m, C**4**-<u>H$_2$</u>), 1.34-1.24 (2H, m, C**5**-<u>H$_2$</u>), 0.87 (3H, t, *J* = 7.5 Hz, C**6**-<u>H$_3$</u>), 0.39-0.35 (2H, m, 2 × C**1**-<u>H</u>), 0.29-0.25 (2H, m, 2 × C**1**-<u>H</u>); ^{13}C NMR ($CDCl_3$, 100

MHz): δ 49.4 (C**3**), 32.3 (C**4**), 30.4 (C**2**), 20.6 (C**5**), 14.0 (C**6**), 6.3 (C**1**); HRMS: (ESI^+) Calculated for $C_7H_{16}N$: 114.1277. Found $[M + H]^+$: 114.1280.

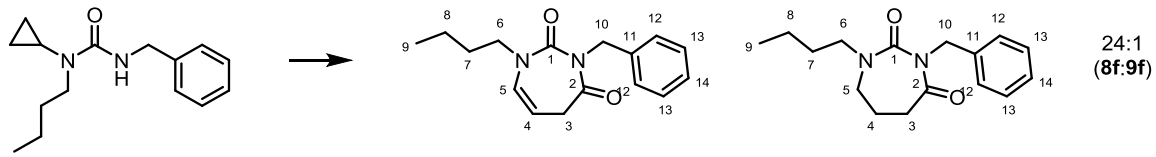
3-Benzyl-1-butyl-1-cyclopropylurea (5f)



5f

General procedure A: *N*-Butylcyclopropanamine (1.25 g, 11.0 mmol) and benzyl isocyanate (1.24 mL, 10.0 mmol) were employed. This crude mixture was purified by column chromatography (40% EtOAc/hexane) to yield the title compound **5f** (1.33 g, 54%) as a colorless solid; m.p. 39-40 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 3327 (m), 1635 (s), 1517 (s), 1372 (m), 1292 (s), 1026 (m); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.37-7.24 (5H, m, 2 × C**6**-H, 2 × C**7**-H, C**8**-H), 5.52 (1H, t, *J* = 6.0 Hz, NH), 4.47 (2H, d, *J* = 6.0 Hz, C**4**-H_2), 3.35 (2H, t, *J* = 7.0 Hz, C**9**-H_2), 2.46 (1H, tt, *J* = 6.5, 4.0 Hz, C**2**-H), 1.60-1.52 (2H, m, C**10**-H_2), 1.37-1.28 (2H, m, C**11**-H_2), 0.94 (3H, t, *J* = 7.5 Hz, C**12**-H_3), 0.83-0.79 (2H, m, 2 × C**1**-H), 0.73-0.69 (2H, m, 2 × C**1**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.8 (C**3**), 139.9 (C**5**), 128.6, 127.4, 127.1 (C**6**, C**7**, C**8**), 46.6 (C**9**), 44.6 (C**4**), 30.5 (C**10**), 27.5 (C**2**), 20.2 (C**11**), 14.0 (C**12**), 8.6 (C**1**); HRMS: (ESI^+) Calculated for $C_{15}H_{22}N_2NaO$: 269.1624. Found $[M + Na]^+$: 269.1620.

1-Benzyl-3-butyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8f) ***and*** **3-Benzyl-1-butyl-1,3-diazepane-2,4-dione (9f)**



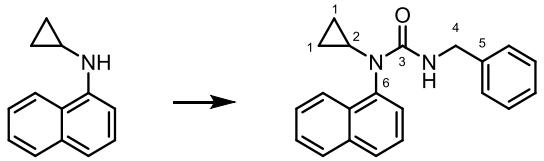
5f **8f** **9f**

General Procedure B: Urea **5f** (37.0 mg, 0.150 mmol) and $[Rh(cod)_2]BARF$ (3.5 mol%) were employed and the reaction was stirred for 25 h at 100 °C. The crude mixture was purified by column chromatography (30% EtOAc/hexane) to yield the title compound **8f** (33.3 mg, 82%) as a yellow oil. Analysis of the crude reaction mixture by ^1H NMR revealed a 24:1 (**8f**:**9f**) mixture of products. The minor product **9f** was not isolated.

Data for major compound **8f**: ν_{max} / cm^{-1}: 2958 (m), 1699 (s), 1647 (s), 1408 (s), 1212 (s); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.29-7.20 (5H, m, 2 × C**12**-H, 2 × C**13**-H, C**14**-H), 6.04 (1H, d, *J* = 7.0 Hz, C**5**-H), 5.56 (1H, dt, *J* = 7.0, 7.0 Hz, C**4**-H), 5.00 (2H, s, C**10**-H_2), 3.55 (2H, t, *J* = 7.0 Hz, C**6**-H_2), 3.09 (2H, d, *J* = 7.0 Hz, C**3**-H_2), 1.56-1.48 (2H, m, C**7**-H_2), 1.31-1.22 (2H, m, C**8**-H_2), 0.90 (3H, t, *J* = 7.0 Hz, C**9**-H_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.1 (C**2**), 153.6 (C**1**), 137.7 (C**11**), 130.7 (C**5**), 128.3, 127.8, 127.1 (C**12**, C**13**, C**14**), 112.4 (C**4**), 49.9 (C**6**), 48.0 (C**10**), 34.9 (C**3**), 30.2 (C**7**), 19.9 (C**8**), 13.7 (C**9**); HRMS: (ESI^+) Calculated for $C_{16}H_{20}N_2NaO_2$: 295.1417. Found $[M + Na]^+$: 295.1419.

Data for minor compound **9f**: *Characteristic signals only*: ^1H NMR ($CDCl_3$, 400 MHz): δ 2.60 (2H, t, *J* = 7.0 Hz, C**3**-H_2).

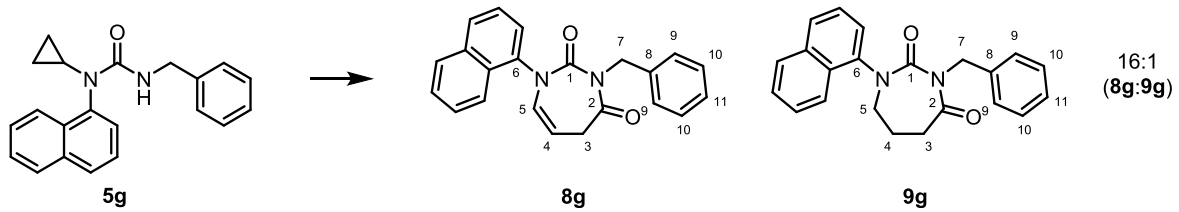
3-Benzyl-1-cyclopropyl-1-(naphthalen-1-yl)urea (5g)



5g

General procedure A: *N*-Cyclopropylnaphthalen-1-amine[4] (1.83 g, 10.0 mmol) and benzyl isocyanate (1.09 mL, 10.0 mmol) were employed. The crude mixture was purified by column chromatography (10-30% EtOAc/hexane) to yield the title compound **5g** (1.15 g, 36%) as a yellow solid; m.p. 109-111 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 3357 (m), 1650 (s), 1504 (s), 1311 (s), 1220 (m); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.88-7.81 (3H, m, 3 × ArCH), 7.54-7.45 (3H, m, 3 × ArCH), 7.30-7.14 (6H, m, 6 × ArCH), 4.79 (1H, br. s, NH), 4.38 (2H, d, *J* = 6.0 Hz, C**4**-H_2), 3.26 (1H, tt, *J* = 7.0, 4.0 Hz, C**2**-H), 0.77-0.69 (2H, m, 2 × C**1**-H), 0.62-0.47 (2H, m, 2 × C**1**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.5 (C**3**), 139.6 (C**5**), 138.0 (C**6**), 134.8 (ArC), 131.6 (ArC), 128.5, 128.4, 127.4, 127.2, 127.1, 126.7, 126.6, 125.9, 123.1 (10 × ArCH), 44.6 (C**4**), 31.2 (C**2**), 7.6 (C**1**); HRMS: (ESI^+) Calculated for $C_{21}H_{20}N_2NaO$: 339.1468. Found $[M + Na]^+$: 339.1479.

1-Benzyl-3-(naphthalen-1-yl)-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8g) *and* 3-Benzyl-1-(naphthalen-1-yl)-1,3-diazepane-2,4-dione (9g)



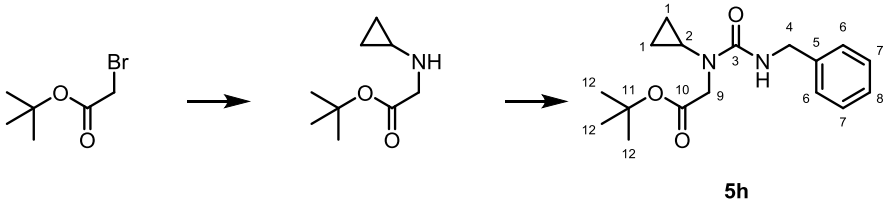
5g **8g** **9g**

General Procedure B: Urea **5g** (47.5 mg, 0.150 mmol) and $[Rh(cod)_2]BARF$ (5.0 mol%) were employed and the reaction was stirred for 72 h at 100 °C. The crude mixture was purified by column chromatography (30% EtOAc/hexane) to yield the title compound **8g** (31.0 mg, 60%) as a yellow oil. Analysis of the crude reaction mixture by ^{1}H NMR revealed a 16:1 (**8g**:**9g**) mixture of products. The minor product **9g** was not isolated.

Data for major compound **8g**: ν_{max} / cm^{-1}: 2960 (s), 1701 (s), 1652 (s), 1394 (s), 1201 (s), 1141 (m); 1H NMR ($CDCl_3$, 400 MHz): δ 7.88-7.86 (2H, m, 2 × ArC<u>H</u>), 7.49-7.45 (2H, m, 2 × ArC<u>H</u>), 7.40-7.35 (5H, m, 2 × C**9**-H, 2 × C**10**-<u>H</u>, C**11**-<u>H</u>), 7.28-7.24 (2H, m, 2 × ArC<u>H</u>), 6.93 (1H, d, *J* = 8.5 Hz, 1 × ArC<u>H</u>), 6.11 (1H, dd, *J* = 7.0, 1.0 Hz, C**5**-<u>H</u>), 5.65 (1H, dt, *J* = 7.0, 7.0 Hz, C**4**-<u>H</u>), 5.36 (1H, d, *J* = 14.5 Hz, 1 × C**7**-<u>H</u>), 4.90 (1H, d, *J* = 14.5 Hz, 1 × C**7**-<u>H</u>), 3.50-3.40 (2H, m, C**3**-<u>H_2</u>); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.9 (C**2**), 153.6 (C**1**), 137.4 (C**8**), 137.3 (C**6**), 134.6 (Ar<u>C</u>), 131.6 (C**5**), 129.4 128.8, 128.7, 128.5, 128.5, 127.5 (C**9**, C**10**, C**11**, 3 × Ar<u>C</u>), 127.3, 126.5, 126.0, 125.5, 121.8 (5 × Ar<u>C</u>H), 111.1 (C**4**), 48.0 (C**7**), 35.0 (C**3**); HRMS: (ESI^+) Calculated for $C_{22}H_{18}N_2NaO_2$: 365.1260. Found $[M + Na]^+$: 365.1265.

Data for minor compound **9g**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.26 (2H, t, *J* = 7.0 Hz, C**5**-<u>H_2</u>).

***tert*-Butyl *N*-(benzylcarbamoyl)-*N*-cyclopropylglycinate (5h)**

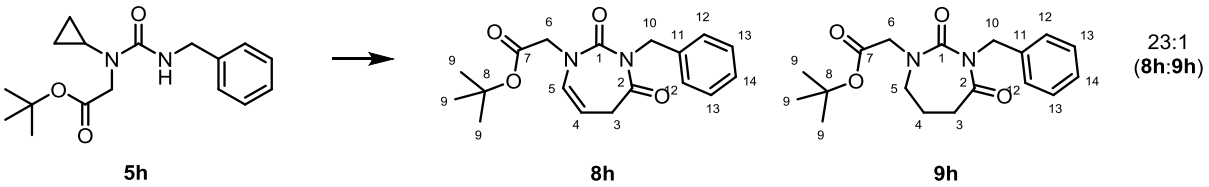


5h

To a solution of cyclopropylamine (1.04 mL, 15.0 mmol) and NEt_3 (2.79 mL, 20.0 mmol), in CH_2Cl_2 (20 mL), was added *t*-butyl bromoacetate (1.48 mL, 10.0 mmol) at r.t.. The reaction mixture was stirred for 7 h before cooling to 0 °C. Benzyl isocyanate (1.84 mL, 20.0 mmol) was added and the reaction mixture was warmed to r.t. and stirred for a further 17 h. The resulting solution was diluted with CH_2Cl_2 (25 mL), and washed with water (30 mL), aq. 1 M

HCl (30 mL), sat. aq. $NaHCO_3$ (30 mL) and brine (30 mL) before being dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by column chromatography (40-50% EtOAc/hexane) to yield the title compound **5h** (1.50 g, 49%) as a colorless solid; m.p. 70-72 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 3359 (s), 2973 (w), 1749 (s), 1639 (s), 1526 (s), 1220 (s), 1151 (s); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.36-7.31 (4H, m, 2 × C**6**-H, 2 × C**7**-H), 7.26 (1H, m, C**8**-H), 5.67 (1H, br. s, NH), 4.49 (2H, d, *J* = 5.5 Hz, C**4**-H_2), 3.99 (2H, s, C**9**-H_2), 2.71 (1H, m, C**2**-H), 1.47 (9H, s, C**12**-H_3), 0.80 (2H, m, 2 × C**1**-H), 0.73 (2H, m, 2 × C**1**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.1 (C**10**), 158.9 (C**3**), 139.7 (C**5**), 128.7 (C**6**), 127.6 (C**7**), 127.3 (C**8**), 81.5 (C**11**), 50.1 (C**9**), 44.8 (C**4**), 28.7 (C**2**), 28.3 (C**12**), 8.8 (C**1**); HRMS: (ESI^+) Calculated for $C_{17}H_{24}N_2NaO_3$: 327.1679. Found $[M + H]^+$: 327.1684.

***tert*-Butyl 2-(3-benzyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-1,3-diazepin-1-yl)acetate (8h) *and* *tert*-Butyl 2-(3-benzyl-2,4-dioxo-1,3-diazepan-1-yl)acetate (9h)**



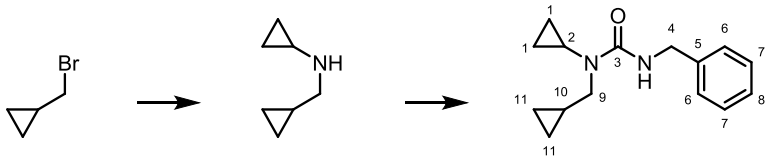
5h **8h** **9h**

General Procedure B: Urea **5h** (45.7 mg, 0.15 mmol) and $[Rh(cod)_2]BARF$ (5.0 mol%) were employed and the reaction was stirred for 48 h at 100 °C. The crude mixture was purified by column chromatography (20% EtOAc/hexane) to yield the title compound **8h** (32.4 mg, 65%) as a colorless oil. Analysis of the crude reaction mixture by ^1H NMR revealed a 23:1 (**8h**:**9h**) mixture of products. The minor product **9h** was not isolated.

Data for major compound **8h**: m.p. 113-116 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 2976 (w), 1747 (s), 1696 (s), 1647 (s), 1438 (s), 1219 (s), 1152 (s); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.30-7.19 (5H, m, 2 × C**12**-H, 2 × C**13**-H, C**14**-H), 6.02 (1H, d, *J* = 7.0 Hz, C**5**-H), 5.61 (1H, dt, *J* = 7.0, 7.0 Hz, C**4**-H), 5.00 (2H, s, C**10**-H_2), 4.14 (2H, s, C**6**-H_2), 3.29 (2H, d, *J* = 7.0 Hz, C**3**-H_2), 1.44 (9H, s, C**9**-H_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.5 (C**2**), 167.3 (C**7**), 154.3 (C**1**), 137.7 (C**11**), 130.9 (C**5**), 128.5, 127.9, 127.3 (C**12**, C**13**, C**14**), 113.7 (C**4**), 82.7 (C**8**), 52.0 (C**6**), 48.2 (C**10**), 35.1 (C**3**), 28.2 (C**9**); HRMS: (ESI^+) Calculated for $C_{18}H_{22}N_2NaO_4$: 353.1472. Found $[M + Na]^+$: 353.1476.

Data for minor compound **9h**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.83 (2H, t, *J* = 7.0 Hz, C**5**-$\underline{H}_2$).

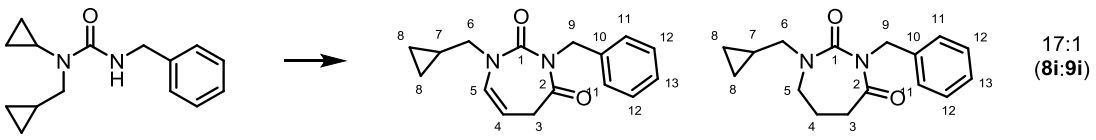
3-Benzyl-1-cyclopropyl-1-(cyclopropylmethyl)urea (5i)



5i

(Bromomethyl)cyclopropane (0.97 mL, 10.0 mmol) was added to a stirred solution of cyclopropylamine (2.08 mL, 30.0 mmol) in DMSO (25 mL) at room temperature. The reaction was stirred for 20 h before being diluted with CH_2Cl_2 (200 mL), washed with water (2 × 200 mL) and brine (200 mL). The organics were dried over Na_2SO_4 and carefully concentrated *in vacuo*. The crude amine was dissolved in CH_2Cl_2 (33 mL) and cooled to 0 °C before adding benzyl isocyanate (1.12 mL, 9.09 mmol). The reaction mixture was warmed to r.t. and stirred for 16 h. The reaction mixture was concentrated *in vacuo* to yield a crude mixture which was purified by column chromatography (25% EtOAc/hexane) to yield the title compound **5i** (1.10 g, 45%) as a colorless solid. m.p. 74-75 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 3375 (s), 2922 (w), 1640 (s), 1628 (s), 1509 (s), 1274 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.30-7.18 (5H, m, 2 × C**6**-$\underline{H}$, 2 × C**7**-$\underline{H}$, C**8**-$\underline{H}$), 5.54 (1H, br. s, N$\underline{H}$), 4.42 (2H, d, *J* = 6.0 Hz, C**4**-$\underline{H}_2$), 3.18 (2H, d, *J* = 7.0 Hz, C**9**-$\underline{H}_2$), 2.54 (1H, m, C**2**-$\underline{H}$), 1.00 (1H, m, C**10**-$\underline{H}$), 0.76 (2H, m, C**1**-$\underline{H}_2$), 0.65 (2H, m, C**1**-$\underline{H}_2$), 0.41 (2H, m, C**11**-$\underline{H}_2$), 0.20 (2H, m, C**11**-$\underline{H}_2$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.1 (C**3**), 140.0 (C**5**), 128.7 (C**7**), 127.6 (C**6**), 127.2 (C**8**), 51.4 (C**9**), 44.8 (C**4**), 27.7 (C**2**), 10.1 (C**10**), 9.1 (C**1**), 3.5 (C**11**); HRMS: (ESI$^+$) Calculated for $C_{15}H_{20}N_2NaO$: 267.1468. Found [M + Na]$^+$: 267.1470.

1-Benzyl-3-(cyclopropylmethyl)-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8i) ***and*** **3-benzyl-1-(cyclopropylmethyl)-1,3-diazepane-2,4-dione (9i)**



5i **8i** **9i**

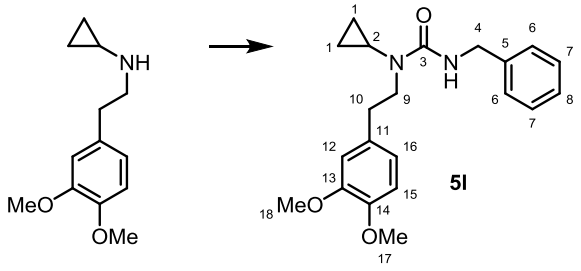
General Procedure B: Urea **5i** (36.7 mg, 0.15 mmol) and [Rh(cod)$_2$]BARF (3.5 mol%) were employed and the reaction was stirred for 24 h at 100 °C. The crude mixture was purified by

column chromatography (20% EtOAc/hexane) to yield the title compound **8i** (35.0 mg**,** 86%) as a brown oil. Analysis of the crude reaction mixture by ^{1}H NMR revealed a 20:1 (**8i**:**9i**) mixture of products. The minor product **9i** was not isolated.

Data for major compound **8i**: ν_{max} / cm^{-1}: 3003 (w), 1699 (s), 1648 (s), 1409 (s), 1214 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.31-7.19 (5H, m, 2 × C**11**-H, 2 × C**12**-H, C**13**-H), 6.13 (1H, d, *J* = 7.0 Hz, C**5**-H), 5.59 (1H, dt, *J* = 7.0, 7.0 Hz, C**4**-H), 5.01 (2H, s, C**9**-H_2), 3.46 (2H, d, *J* = 7.0 Hz, C**6**-H_2), 3.14 (2H, d, *J* = 7.0 Hz, C**3**-H_2), 1.04 (1H, m, C**7**-H), 0.49 (2H, m, 2 × C**8**-H), 0.26 (2H, m, C**8**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.4 (C**2**), 153.9 (C**1**), 137.9 (C**10**), 130.9 (C**5**), 128.4, 127.9, 127.2 (C**11**, C**12**, C**13**), 112.7 (C**4**), 54.5 (C**6**), 48.1 (C**9**), 35.1 (C**3**), 10.2 (C**7**), 3.6 (C**8**); HRMS: (ESI$^+$) Calculated for $C_{16}H_{18}N_2NaO_2$: 293.1260. Found [M + Na]$^+$: 293.1270.

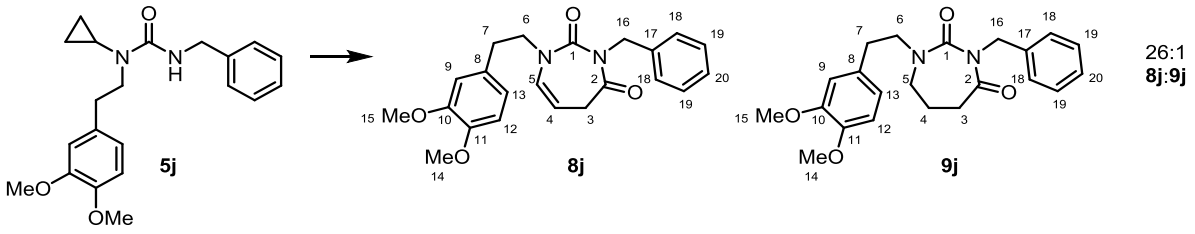
Data for minor compound **9i**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.65 (2H, t, *J* = 7.5 Hz, C**3**-H_2).

3-Benzyl-1-cyclopropyl-1-(3,4-dimethoxyphenethyl)urea (5l)



General procedure A: *N*-(3,4-Dimethoxyphenethyl)cyclopropanamine[5] (664 mg, 3.00 mmol) and benzyl isocyanate (0.370 mL, 3.00 mmol) were employed. The crude mixture was purified by column chromatography (60-80% EtOAc/hexane) to yield the title compound **5l** (978 mg, 92%) as a yellow oil; ν_{max} / cm^{-1}: 3373 (m), 1644 (s), 1510 (s), 1453 (s), 1259 (s), 1235 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34-7.22 (5H, m, 2 × C**6**-H, 2 × C**7**-H, C**8**-H), 6.79-6.75 (3H, m, C**12**-H, C**15**-H, C**16**-H), 5.56 (1H, t, *J* = 5.0 Hz, NH), 4.45 (2H, d, *J* = 5.0 Hz, C**4**-H_2), 3.84 (3H, s, C**17**/**18**-H_3), 3.83 (3H, s, C**17**/**18**-H_3), 3.56 (2H, t, *J* = 7.0 Hz, C**9**-H_2), 2.84 (2H, t, *J* = 7.0 Hz, C**10**-H_2), 2.32 (1H, tt, *J* = 7.0, 4.0 Hz, C**2**-H), 0.76-0.72 (2H, m, 2 × C**1**-H), 0.66-0.58 (2H, m, 2 × C**1**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.7 (C**3**), 148.8, 147.4 (C**14**, C**15**), 139.8 (C**5**), 132.4 (C**11**), 128.6, 127.3, 127.1 (C**6**, C**7**, C**8**), 120.8 (C**16**), 112.2, 111.2 (C**12**, C**15**), 55.9, 55.8 (C**17**, C**18**), 49.1 (C**9**), 44.5 (C**4**), 34.4 (C**10**), 28.0 (C**2**), 8.8 (C**1**); HRMS: (ESI$^+$) Calculated for $C_{21}H_{26}N_2NaO_3$: 377.1836. Found [M + Na]$^+$: 377.1833.

1-Benzyl-3-(3,4-dimethoxyphenethyl)-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8j) *and* 3-Benzyl-1-(3,4-dimethoxyphenethyl)-1,3-diazepane-2,4-dione (9j)

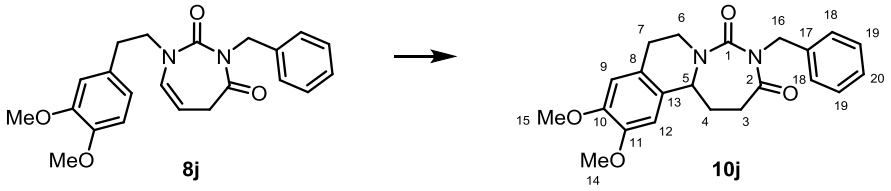


General Procedure B: Urea **5j** (53.2 mg, 0.150 mmol) and $[Rh(cod)_2]OTf$ (2.5 mol%) were employed and the reaction was stirred for 30 h at 100 °C. The crude mixture was purified by column chromatography (50% EtOAc/hexane) to yield the title compound **8j** (43.9 mg, 77%) as a yellow oil. Analysis of the crude reaction mixture by ^{1}H NMR revealed a 26:1 (**8j**:**9j**) mixture of products. The minor product **9j** was not isolated.

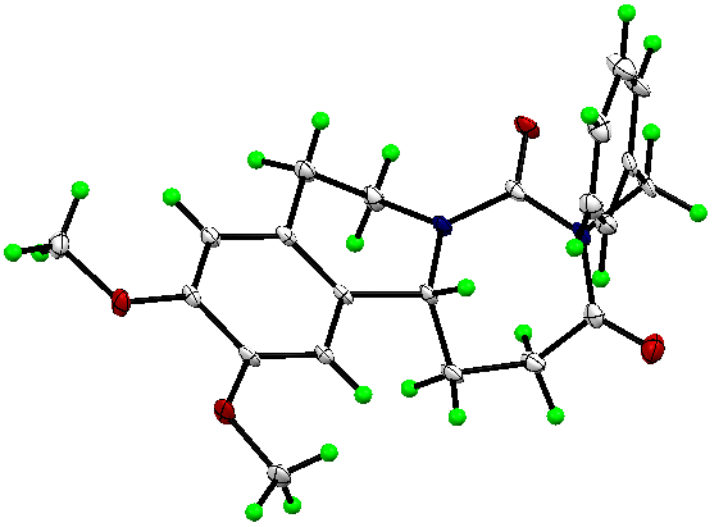
Data for major compound **8j**: ν_{max} / cm^{-1}: 2936 (m), 1699 (s), 1649 (s), 1515 (s), 1410 (s), 1263 (s), 1214 (s), 1028 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.32-7.21 (5H, m, 2 × C**18**-H, 2 × C**19**-H, C**20**-H), 6.74 (1H, d, *J* = 8.0 Hz, C**12**-H), 6.69 (1h, d, *J* = 2.0 Hz, C**9**-H), 6.60 (1H, dd, *J* = 8.0, 2.0 Hz, C**13**-H), 5.87 (1H, d, *J* = 7.0 Hz, C**5**-H), 5.46 (dt, *J* = 7.0, 7.0 Hz, C**4**-H), 5.01 (2H, s, C**16**-H_2), 3.85-3.78 (8H, m, C**6**-H_2, C**14**-H_3, C**15**-H_3), 2.93 (2H, d, *J* = 7.0 Hz, C**3**-H_2), 2.82 (2H, t, *J* = 7.0 Hz, C**7**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.1 (C**2**), 153.6 (C**1**), 149.0 (C**10**), 147.8 (C**11**), 137.7 (C**17**), 130.8 (C**5**), 130.4 (C**8**), 128.4, 127.8, 127.2 (C**18**, C**19**, C**20**), 120.9 (C**13**), 112.5 (C**4**), 111.9 (C**9**), 111.2 (C**12**), 55.9, 55.9 (C**14**, C**15**), 51.5 (C**6**), 48.0 (C**16**), 34.8 (C**3**), 33.9 (C**7**); HRMS: (ESI$^+$) Calculated for $C_{22}H_{24}N_2NaO_4$: 403.1628. Found $[M + Na]^+$: 403.1635.

Data for minor compound **9j**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.47 (2H, t, *J* = 7.0 Hz, C**3**-H_2).

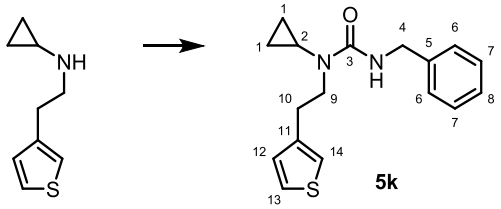
4-Benzyl-10,11-dimethoxy-1,7,8,12*b*-tetrahydro-[1,3]diazepino[7,1-*a*]isoquinoline-3,5(2*H*,4*H*)-dione (10j)



A solution of urea **8j** (43.1 mg, 0.113 mmol) and TFA (87.0 μL, 1.13 mmol) in CH_2Cl_2 (1 mL) was heated in a sealed tube at 60 °C for 24 h. The reaction mixture was cooled to r.t. and sat. aq. $NaHCO_3$ (20 mL) was added. The solution was extracted with CH_2Cl_2 (3 × 15 mL) and the organic extracts were combined, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (60% EtOAc/hexane) to yield the title compound **10j** (39.2 mg, 91%) as a colorless solid; m.p. 176-178 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 1693 (s), 1651 (s), 1519 (s), 1430 (s), 1259 (s), 1230 (s), 1163 (s); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.39 (2H, dd, *J* = 7.5, 1.5 Hz, 2 × C**18**-H), 7.30-7.21 (3H, m, 2 × C**19**-H, C**20**-H), 6.67 (1H, s, C**9**-H), 6.50 (1H, s, C**12**-H), 4.98 (1H, d, *J* = 14.5 Hz, 1 × C**16**-H), 4.86 (1H, d, *J* = 14.5 Hz, 1 × C**16**-H), 4.65 (1H, dd, *J* = 13.0, 5.5 Hz, C**5**-H), 3.94 (1H, ddd, *J* = 12.5, 7.5, 4.5 Hz, 1 × C**6**-H), 3.87 (3H, s, C**14**/**15**-H_3), 3.83 (3H, s, C**14**/**15**-H_3), 3.62 (1H, ddd, *J* = 12.5, 7.5, 4.5 Hz, 1 × C**6**-H), 2.89-2.73 (3H, m, 1 × C**3**-H, 2 × C**7**-H), 2.65 (1H, ddd, *J* = 12.5, 6.5, 1.0 Hz, 1 × C**3**-H), 2.45 (1H, dddd, *J* = 13.5, 12.0, 6.5, 5.5 Hz, 1 × C**4**-H), 2.04 (1H, m, 1 × C**4**-H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.7 (C**2**), 157.3 (C**1**), 148.2, 148.0 (C**10**, C**11**), 137.8 (C**17**) 128.5, 128.5, 127.4 (C**18**, C**19**, C**20**), 126.7 (C**13**), 126.4 (C**8**), 111.3 (C**9**), 109.0 (C**12**), 50.1, 56.0 (C**14**, C**15**), 55.3 (C**5**), 47.1 (C**16**), 41.1 (C**6**), 35.2 (C**4**), 34.4 (C**3**), 28.3 (C**7**); HRMS: (ESI^+) Calculated for $C_{22}H_{24}N_2NaO_4$: 403.1628. Found $[M + Na]^+$: 403.1615. *The structure of this compound was determined unambiguously by X-ray crystallography.*

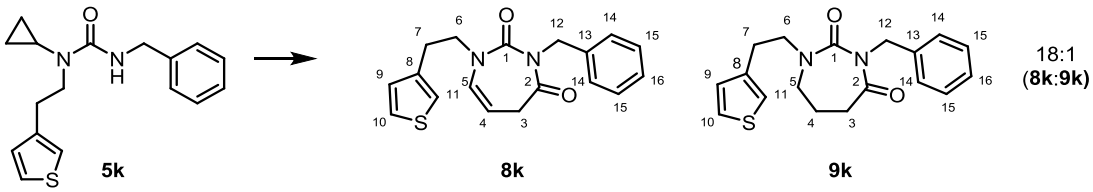


3-Benzyl-1-cyclopropyl-1-(2-(thiophen-3-yl)ethyl)urea (5k)



General procedure A: *N*-(2-(Thiophen-3-yl)ethyl)cyclopropanamine[5] (418 mg, 2.50 mmol) and benzyl isocyanate (309 μL, 2.50 mmol) were employed. The crude mixture was purified by column chromatography (25% EtOAc/hexane) to yield the title compound **5k** (640 mg, 85%) as a colorless solid; m.p. 77-79 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 3380 (m), 1643 (s), 1504 (s), 1344 (m), 1304 (s); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.35-7.21 (6H, m, 2 × C**6**-H, 2 × C**7**-H, C**8**-H, C**13**-H), 7.03-6.97 (2H, m, C**12**-H, C**14**-H), 5.52 (1H, br. s, NH), 4.47 (2H, d, *J* = 5.5 Hz, C**4**-H_2), 3.60 (2H, t, *J* = 7.0 Hz, C**9**-H_2), 2.93 (2H, t, *J* = 7.0 Hz, C**10**-H_2), 2.33 (1H, tt, *J* = 6.5, 4.0 Hz, C**2**-H), 0.81-0.70 (2H, m, 2 × C**1**-H), 0.67-0.60 (2H, m, 2 × C**1**-H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 158.6 (C**3**), 140.0, 139.8 (C**5**, C**11**), 128.6, 128.5, 127.4, 127.1 (C**6**, C**7**, C**8**, C**12**), 125.3 (C**13**), 121.1 (C**14**), 48.1 (C**9**), 44.6 (C**4**), 29.2 (C**10**), 27.9 (C**2**), 8.7 (C**1**); HRMS: (ESI^+) Calculated for $C_{17}H_{20}N_2NaOS$ 323.1189. Found $[M + Na]^+$: 323.1190.

1-Benzyl-3-(2-(thiophen-3-yl)ethyl)-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8k) *and* 3-Benzyl-1-(2-(thiophen-3-yl)ethyl)-1,3-diazepane-2,4-dione (9k)



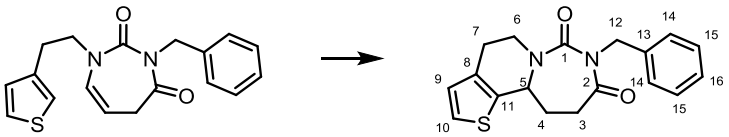
General Procedure B: Urea **5k** (53.2 mg, 0.150 mmol) and $[Rh(cod)_2]OTf$ (2.5 mol%) were employed and the reaction was stirred for 30 h at 100 °C. The crude mixture was purified by column chromatography (40% EtOAc/hexane) to yield the title compound **8k** (45.0 mg, 92%) as a yellow oil. Analysis of the crude reaction mixture by ^{1}H NMR revealed an 18:1 (**8k**:**9k**) mixture of products. The minor product **9k** was not isolated.

Data for major compound **8k**: ν_{max} / cm^{-1}: 2956 (m), 1698 (s), 1647 (s), 1409 (s), 1265 (s), 1213 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.32-7.23 (6H, m, C**10**-H, 2 × C**14**-H, 2 × C**15**-H, C**16**-H), 6.87 (1H, dd, *J* = 5.0, 1.5 Hz, C**9**-H), 6.79 (1H, dd, *J* = 3.0, 1.5 Hz, C**11**-H), 5.79 (1H, d, *J* = 7.0 Hz, C**5**-H), 5.45 (1H, dt, *J* = 7.0, 7.0 Hz, C**4**-H), 5.02 (2H, s, C**12**-H_2), 3.81 (2H, t, *J* = 7.0 Hz, C**6**-H_2), 2.94-2.89 (4H, m, C**3**-H_2, C**7**-H_2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.1 (C**2**),

153.5 (C**1**), 138.2 (C**8**), 137.7 (C**13**), 130.7 (C**5**), 128.4, 128.0, 127.9, 127.2 (C**9**, C**14**, C**15**, C**16**), 126.0 (C**10**), 121.8 (C**11**), 112.5 (C**4**), 50.7 (C**6**), 47.9 (C**12**), 34.7 (C**3**), 28.6 (C**7**); HRMS: (ESI$^+$) Calculated for $C_{18}H_{18}N_2NaO_2S$: 349.0981. Found $[M + Na]^+$: 349.0994.

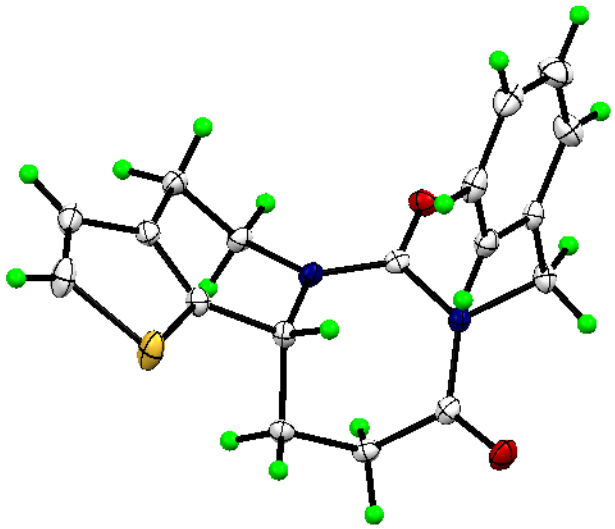
Data for minor compound **9k**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.02 (2H, t, *J* = 7.0 Hz, C**5**-$\underline{H}_2$).

8-Benzyl-4,10,11,11*a*-tetrahydrothieno[2',3':3,4]pyrido[1,2-*c*][1,3]diazepine- 7,9(5*H*,8*H*)-dione (10k)

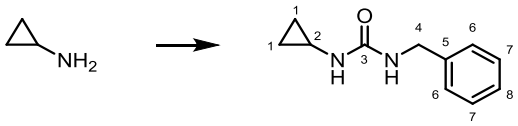


10k **10k**

A solution of **10k** (44.0 mg, 0.135 mmol) and TFA (103 μL, 1.35 mmol) in CH_2Cl_2 (1.5 mL) was heated in a sealed tube at 60 °C for 24 h. The reaction mixture was cooled to r.t. and sat. aq. $NaHCO_3$ (20 mL) was added. The solution was extracted with CH_2Cl_2 (3 × 15 mL) and the organic extracts were combined, dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography (50% EtOAc/hexane) to yield the title compound **10k** (33.4 mg, 76%) as a colorless solid; m.p.: 114-116 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 1695 (s), 1655 (s), 1417 (s), 1336 (s), 1254 (s), 1163 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36-7.34 (2H, m, 2 × C**14**-$\underline{H}$), 7.28-7.19 (3H, m, 2 × C**15**-$\underline{H}$, C**16**-$\underline{H}$), 7.16 (1H, d, *J* = 5.0 Hz, C**10**-$\underline{H}$), 6.78 (1H, d, *J* = 5.0 Hz, C**9**-$\underline{H}$), 4.94 (1H, d, *J* = 14.5 Hz, 1 × C**12**-$\underline{H}$), 4.88 (1H, dd, *J* = 13.0, 5.5 Hz, C**5**-$\underline{H}$), 4.82 (1H, d, *J* = 14.5 Hz, 1 × C**12**-$\underline{H}$), 4.64 (1H, dt, *J* = 13.0, 4.0 Hz, 1 × C**6**-$\underline{H}$), 3.12 (1H, m, 1 × C**6**-$\underline{H}$), 2.76-2.60 (4H, m, C**3**-$\underline{H}_2$, 2 × C**7**-$\underline{H}$), 2.45 (1H, m, 1 × C**4**-$\underline{H}$), 2.25 (1H, m, 1 × C**4**-$\underline{H}$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.3 (C**2**), 157.0 (C**1**), 137.7 (C**13**), 134.5 (C**8**), 133.4 (C**11**), 128.6, 128.5, 127.5 (C**14**, C**15**, C**16**), 126.9 (C**9**), 123.8 (C**10**), 53.6 (C**5**), 47.3 (C**12**), 39.3 (C**6**), 34.0 (C**7**), 33.9 (C**4**), 25.5 (C**3**); HRMS: (ESI$^+$) Calculated for $C_{18}H_{18}N_2NaO_2S$: 349.0981. Found $[M + Na]^+$: 349.0985. *The structure of this compound was determined unambiguously by X-ray crystallography.*

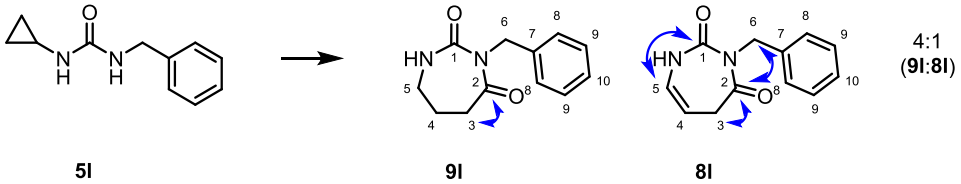


1-Benzyl-3-cyclopropylurea (5l)



General procedure A: Cyclopropylamine (0.762 mL, 11.0 mmol) and benzyl isocyanate (1.09 mL, 10.0 mmol) were employed. The crude mixture was purified by recrystallization (CH_2Cl_2/hexane) to yield the title compound **5l** (1.58 g, 83%) as a colorless solid; m.p.: 139-140 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 3309 (s), 1623 (s), 1574 (s), 1453 (m), 1255 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37-7.25 (2 × C**6**-H, 2 × C**7**-H, C**8**-H), 5.31 (1H, br. s, NH), 4.79 (1H, br. s, NH), 4.47 (2H, d, *J* = 6.0 Hz, C**4**-H_2), 2.46 (1H, tt, *J* = 7.0, 3.5 Hz, C**2**-H), 0.76-0.71 (2H, m, 2 × C**1**-H), 0.60-0.57 (2H, m, 2 × C**1**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.9 (C**3**), 139.4 (C**5**), 128.6, 127.4, 127.3 (C**6**, C**7**, C**8**), 44.2 (C**4**), 22.4 (C**2**), 7.6 (C**1**); HRMS: (ESI^+) Calculated for $C_{11}H_{14}N_2NaO$: 213.0998. Found $[M + Na]^+$: 213.0997. *The spectroscopic properties of this compound were consistent with the data available in the literature.*[6]

3-Benzyl-1,3-diazepane-2,4-dione (9l) ***and*** **1-Benzyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8l)**



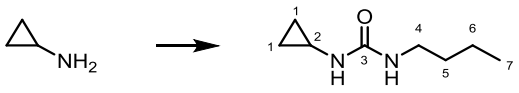
General Procedure B: Urea **5l** (28.5 mg, 0.150 mmol) and [Rh(cod)$_2$]BARF (5.0 mol%) were employed and the reaction was stirred for 23 h at 90 °C. The crude mixture was purified by column chromatography (30% EtOAc/hexane) to yield the title compound **9l** (20.3 mg**,** 62%, 4:1, **9l**:**8l**) as a yellow oil. Analysis of the crude reaction mixture by ^{1}H NMR revealed a 4:1 (**9l**:**8l**) mixture of products.

Data for the mixture of compounds: ν_{max} / cm^{-1}: 3300 (m), 2987 (s), 1705 (s), 1537 (s), 1381 (s), 1255 (s).

Data for major compound **9l**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.79 (1H, br. s, N<u>H</u>), 7.35-7.21 (5H, m, 2 × C**8**-<u>H</u>, 2 × C**9**-<u>H</u>, C**10**-<u>H</u>), 4.50 (2H, d, *J* = 6.0 Hz, C**6**-<u>H$_2$</u>), 3.89 (2H, t, *J* = 7.0 Hz, C**5**-<u>H$_2$</u>), 2.61 (2H, t, *J* = 7.0 Hz, C**3**-<u>H$_2$</u>), 2.04 (2H, tt, *J* = 7.0, 7.0 Hz, C**4**-<u>H$_2$</u>); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 177.1 (C**2**), 153.0 (C**1**), 138.3 (C**7**), 128.6, 127.4, 127.3 (C**8**, C**9**, C**10**), 45.7 (C**5**), 43.8 (C**6**), 33.4 (C**3**), 17.1 (C**4**); HRMS: (ESI$^+$) Calculated for $C_{12}H_{14}N_2NaO_2$: 241.0947. Found [M + Na]$^+$: 241.0963. *The structure of this compound was confirmed by 2D NMR. Key HMBC correlations are included on the compound structure above.*

Data for minor compound **8l**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.79 (1H, br. s, N<u>H</u>), 7.35-7.21 (5H, m, 2 × C**8**-<u>H</u>, 2 × C**9**-<u>H</u>, C**10**-<u>H</u>), 6.12 (1H, dd, *J* = 7.0, 4.0 Hz, C**5**-<u>H</u>), 5.44 (1H, dt, *J* = 7.0, 7.0 Hz, C**4**-<u>H</u>), 5.01 (2H, s, C**6**-<u>H$_2$</u>), 3.20 (2H, d, *J* = 7.0 Hz, C**3**-<u>H$_2$</u>); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.0 (C**2**), 154.2 (C**1**), 137.5 (C**7**), 128.3, 127.9, 127.3 (C**8**, C**9**, C**10**), 126.0 (C**5**), 110.1 (C**4**), 48.0 (C**6**), 35.2 (C**3**); HRMS: (ESI$^+$) Calculated for $C_{12}H_{12}N_2O_2$: 216.0899. Found [M]$^+$: 216.0898. *The structure of this compound was confirmed by 2D NMR. Key HMBC correlations are included on the compound structure above.*

1-Butyl-3-cyclopropylurea (5m)

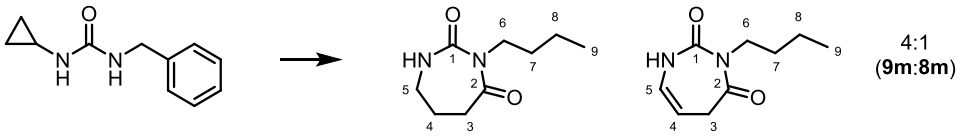


5m

General procedure A: Cyclopropylamine (0.76 mL, 11.0 mmol) and *n*-butyl isocyanate (1.13 mL, 10.0 mmol) were employed. The crude mixture was purified by column chromatography (75% EtOAc/hexane) to yield the title compound **5m** (1.29 g, 83%) as a colorless solid; m.p. 73-74 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 3305 (m), 2931 (m), 1626 (s), 1564 (s), 1250 (m), 1224 (m); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.00 (1H, br. s, N<u>H</u>), 4.86 (1H, br. s, N<u>H</u>), 3.22 (2H, m, C**4**-<u>H$_2$</u>), 2.41 (1H, m, C**2**-<u>H</u>), 1.49 (2H, m, C**5**-<u>H$_2$</u>), 1.35 (2H, m, C**6**-<u>H$_2$</u>), 0.92 (3H, t, *J* = 7.0

Hz, C**7**-H$_3$), 0.73-0.52 (4H, m, C**1**-H$_2$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.3 (C**3**), 40.1 (C**4**), 32.5 (C**5**), 22.5 (C**2**), 20.2 (C**6**), 13.9 (C**7**), 7.6 (C**1**); HRMS: (ESI$^+$) Calculated for $C_8H_{16}N_2NaO$: 179.1155. Found [M + H]$^+$: 179.1160.

3-Butyl-1,3-diazepane-2,4-dione (9m) ***and*** **1-Butyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8m)**



5m **9m** **8m**

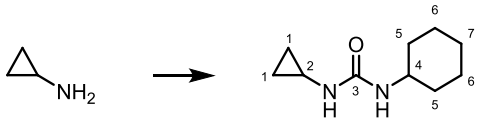
General Procedure B: Urea **5m** (23.4 mg, 0.150 mmol) and [Rh(cod)$_2$]BARF (5.0 mol%) were employed and the reaction was stirred for 47 h at 90 °C. The crude mixture was purified by column chromatography (40% EtOAc/hexane) to yield the title compound **9m** (19.8 mg**,** 72%, 5:1, **9m**:**8m**) as a yellow oil. Analysis of the crude reaction mixture by ^{1}H NMR revealed a 4:1 (**9m**:**8m**) mixture of products.

Data for the mixture of compounds: ν_{max} / cm^{-1}: 3307 (w), 2958 (w), 1708 (s), 1541 (s), 1381 (s), 1255 (s).

Data for the major product **9m**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.38 (1H, br. s, NH), 3.85 (2H, t, *J* = 7.0 Hz, C**5**-H$_2$), 3.29 (2H, m, C**6**-H$_2$), 2.59 (2H, t, *J* = 8.0 Hz, C**3**-H$_2$), 2.02 (2H, m, C**4**-H$_2$), 1.52 (2H, m, C**7**-H$_2$), 1.36 (2H, m, C**8**-H$_2$), 0.92 (3H, t, *J* = 7.0 Hz, C**9**-H$_2$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 177.1 (C**2**), 153.1 (C**1**), 45.8 (C**5**), 39.7 (C**6**), 33.6 (C**3**), 30.5 (C**7**), 20.2 (C**8**), 17.2 (C**4**), 13.9 (C**9**); HRMS: (ESI$^+$) Calculated for $C_9H_{16}N_2NaO_2$: 207.1104. Found [M + Na]$^+$: 207.1100.

Data for the minor product **8m**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.49 (1H, br. s, NH), 6.15 (1H, dd, *J* = 7.0, 7.0 Hz, C**5**-H), 5.42 (1H, m, C**4**-H), 3.77 (2H, t, *J* = 7.5 Hz, C**6**-H$_2$), 3.14 (2H, d, *J* = 7.0 Hz, C**3**-H$_2$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.3 (C**2**), 154.9 (C**1**), 126.1 (C**5**), 110.4 (C**4**), 45.3 (C**6**), 35.5 (C**3**), 31.8 (C**7**), 20.2 (C**8**), 13.9 (C**9**).

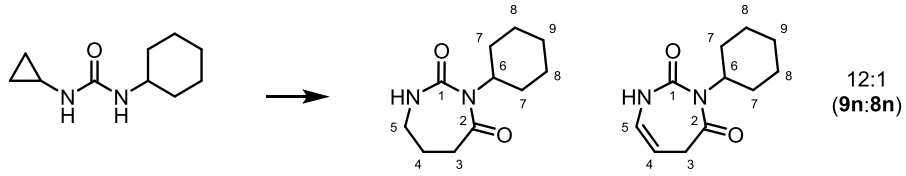
1-Cyclohexyl-3-cyclopropylurea (5n)



5n

General Procedure A: Cyclopropylamine (0.76 mL, 11.0 mmol) and cyclohexyl isocyanate (1.28 mL, 10.0 mmol) were employed to yield the title compound **5n** (1.67 g, 92%) as a colorless solid; m.p.: 125-126 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 3325 (s), 2926 (w), 1629 (s), 1568 (s), 1253 (w); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.84 (1H, br. s, N<u>H</u>), 4.60 (1H, br. s, N<u>H</u>), 3.64 (1H, m, C**4**-<u>H</u>), 2.41 (1H, m, C**2**-<u>H</u>), 1.95 (2H, m, C**5**-<u>H_2</u>), 1.74-1.66 (2H, m, C**6**-<u>H_2</u>), 1.64-1.57 (2H, m, C**7**-<u>H_2</u>), 1.43-1.33 (2H, m, C**6**-<u>H_2</u>), 1.23-1.10 (2H, m, C**5**-<u>H_2</u>), 0.73 (2H, m, 2 × C**1**-<u>H</u>), 0.56 (2H, m, 2 × C**1**-<u>H</u>); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.5 (C**3**), 48.8 (C**4**), 34.0 (C**5**), 25.8 (C**7**), 25.1 (C**6**), 22.5 (C**2**), 7.7 (C**1**); HRMS: (ESI^+) Calculated for $C_{10}H_{18}N_2NaO$: 205.1317. Found $[M + Na]^+$: 205.1311.

3-Cyclohexyl-1,3-diazepane-2,4-dione (9n) ***and*** **1-Cyclohexyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8n)**



5n **9n** **8n**

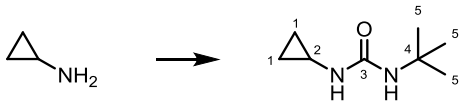
General Procedure B: Urea **5n** (27.3 mg, 0.15 mmol) and $[Rh(cod)_2]$BARF (5.0 mol%) were employed and the reaction was stirred for 51 h at 90 °C. The crude mixture was purified by column chromatography (25% EtOAc/hexane) to yield the title compound **9n** (21.2 mg, 67%) as a pale yellow oil. Analysis of the crude reaction mixture by ^{1}H NMR revealed a 12:1 (**9n**:**8n**) mixture of products. The minor product **8n** was not isolated.

Data for the major product **9n**: ν_{max} / cm^{-1}: 3291 (br.), 2929 (br.), 2854 (br.), 17.6 (s), 1534 (s), 1380 (m), 1243 (m), 1219 (m); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.35 (1H, br. m, N<u>H</u>), 3.84 (2H, t, *J* = 7.0 Hz, C**5**-<u>H_2</u>), 3.71 (1H, m, C**6**-<u>H</u>), 2.58 (2H, t, *J* = 8.0 Hz, C**3**-<u>H_2</u>), 2.00 (2H, tt, *J* = 8.0, 7.0 Hz, C**4**-<u>H_2</u>), 1.92-1.88 (2H, m, 2 × C**7**-<u>H</u>), 1.72-1.67 (2H, m, 2 × C**8**-<u>H</u>), 1.60-1.55 (1H, m, 1 × C**9**-<u>H</u>), 1.41-1.31 (2H, m, 2 × C**8**-<u>H</u>), 1.29-1.15 (3H, m, 2 × C**7**-<u>H</u>, 1 × C**9**-<u>H</u>); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 177.1 (C**2**), 152.2 (C**1**), 48.7 (C**6**), 45.8 (C**5**), 33.7 (C**3**), 33.1 (C**7**),

25.7 (C**9**), 24.8 (C**8**), 17.1 (C**4**); HRMS: (ESI$^+$) Calculated for $C_{11}H_{18}N_2NaO_2$: 233.1260. Found $[M + Na]^+$: 233.1256.

Data for the minor product **8n**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.16 (1H, dt, *J* = 6.0, 2.0 Hz, C**4**-H).

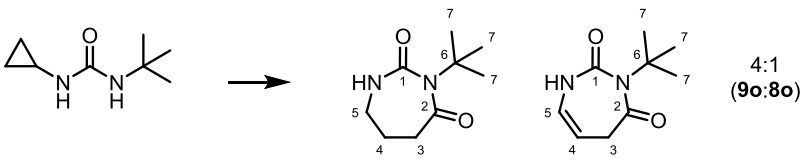
1-(*tert*-Butyl)-3-cyclopropylurea (5o)



5o

General Procedure A: Cyclopropylamine (0.38 mL, 5.50 mmol) and *tert*-butyl isocyanate (0.43 mL, 5.0 mmol) were employed to yield the title compound **5o** (461 mg, 59%) as a colorless solid; ν_{max} / cm^{-1}: 3323 (br.), 2965 (m), 1635 (s), 1557 (s), 1453 (m), 1360 (m), 1276 (m), 1218 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.86 (1H, br. s, NH), 4.54 (1H, br. s, NH), 2.38 (1H, m, C**2**-H), 1.35 (9H, s, C**5**-H$_3$), 0.70 (2H, m, 2 × C**1**-H), 0.53 (2H, m, 2 × C**1**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.4 (C**3**), 50.5 (C**4**), 29.6 (C**5**), 22.7 (C**2**), 7.6 (C**1**); HRMS: (ESI+) Calculated for $C_8H_{16}N_2NaO$: 179.1155. Found $[M + Na]^+$: 179.1155.

3-(*tert*-Butyl)-1,3-diazepane-2,4-dione (9o) *and* 1-(*tert*-Butyl)-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8o)



5o **9o** **8o**

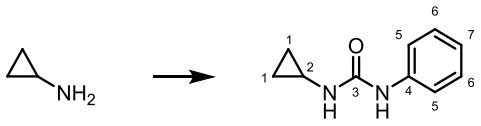
General Procedure B: Urea **5o** (23.4 mg, 0.15 mmol) and $[Rh(cod)_2]$BARF (5.0 mol%) were employed and the reaction was stirred for 48 h at 90 °C. The crude mixture was purified by column chromatography (50% EtOAc/hexane) to yield the title compound **9o** (21.2 mg, 53%, 5:1, **9o**:**8o**) as a pale yellow oil. Analysis of the crude reaction mixture by ^{1}H NMR revealed a 4:1 (**9o**:**8o**) mixture of products.

Data for the mixture of compounds: ν_{max} / cm^{-1}:3288 (br.), 2966 (br.), 1710 (s), 1547 (s), 1383 (m), 1364 (m), 1263 9m), 1201 (m).

Data for the major product **9o**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.41 (1H, br. s, N<u>H</u>), 3.82 (2H, t, *J* = 7.0 Hz, C**5**-<u>H</u>$_2$), 2.58 (2H, t, *J* = 8.0 Hz, C**3**-<u>H</u>$_2$), 1.99 (2H, tt, *J* = 8.0, 7.0 Hz, C**4**-<u>H</u>$_2$), 1.37 (9H, s, C**7**-<u>H</u>$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 177.0 (C**2**), 151.6 (C**1**), 50.9 (C**6**), 45.6 (C**6**), 33.8 (C**3**), 29.0 (C**7**), 17.0 (C**4**); HRMS: (ESI^+) Calculated for $C_9H_{16}N_2NaO_2$: 207.1104. Found $[M + Na]^+$: 207.1114.

Data for the minor product **8o**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ; ^{13}C NMR ($CDCl_3$, 100 MHz): δ; 8.34 (1H, br. s, N<u>H</u>), 6.18 (1H, dt, *J* = 6.0, 2.0 Hz, C**5**-<u>H</u>), 4.42 (1H, t, *J* = 2.0 Hz, C**4**-<u>H</u>), 1.40 (9H, s, C**7**-<u>H</u>$_3$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 146.1 (C**5**), 51.0 (C**3**), 29.1 (C**7**).

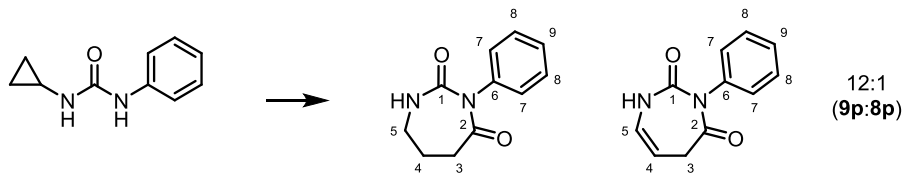
1-Cyclopropyl-3-phenylurea (5p)



5p

General procedure A: Cyclopropylamine (0.76 mL, 11.0 mmol) and phenyl isocyanate (0.90 mL, 10.0 mmol) were employed to yield the title compound **5p** (1.30 g, 74%) as a colorless solid; m.p. 160-161 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 3341 (w), 1642 (s), 1594 (s), 1547 (s), 1242 (s), 741 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38 (2H, m, 2 × C**5**-<u>H</u>), 7.29 (2H, m, 2 × C**6**-<u>H</u>), 7.07 (1H, br. s, N<u>H</u>), 7.05 (1H, m, C**7**-<u>H</u>), 5.17 (1H, br. s, N<u>H</u>), 2.59 (1H, m, C**2**-<u>H</u>), 0.81 (2H, m, 2 × C**1**-<u>H</u>), 0.62 (2H, m, 2 × C**1**-<u>H</u>); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.8 (C**3**), 138.7 (C**4**), 129.2 (C**6**), 123.5 (C**7**), 120.2 (C**5**), 22.7 (C**2**), 7.6 (C**1**); HRMS: (ESI^+) Calculated for $C_{10}H_{12}N_2NaO$: 199.0842. Found $[M + Na]^+$: 199.0847.

3-Phenyl-1,3-diazepane-2,4-dione (9p) ***and*** **1-Phenyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8p)**



5p **9p** **8p**

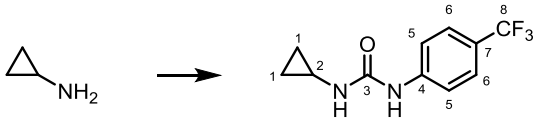
General Procedure B: Urea **5p** (26.4 mg, 0.15 mmol) and $[Rh(cod)_2]$BARF (5.0 mol%) were employed with 1,4-dioxane as solvent and the reaction was stirred for 49 h at 90 °C. The crude

mixture was purified by column chromatography (25% EtOAc/hexane) to yield the title compound **9p** (20.5 mg**,** 67%, 25:1, **9p**:**8p**) as a beige solid. Analysis of the crude reaction mixture by ^{1}H NMR revealed a 12:1 (**9p**:**8p**) mixture of products. The minor product **8p** was not isolated.

Data for the major product **9p**: m.p. 89-92 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 3088 (m), 1719 (s), 1599 (s), 1556 (s), 1379 (s), 1210 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.54 (1H, br. s, N<u>H</u>), 7.53 (2H, m, 2 × C**8**-<u>H</u>), 7.33 (2H, m, 2 × C**7**-<u>H</u>), 7.10 (1H, t, C**9**-<u>H</u>), 3.95 (2H, t, *J* = 7.2 Hz, C**5**-<u>H_2</u>), 2.69 (2H, t, *J* = 8.0 Hz, C**3**-<u>H_2</u>), 2.09 (2H, dt, *J* = 8.0, 7.0 Hz, C**4**-<u>H_2</u>); ^{13}C ($CDCl_3$, 100 MHz): δ 177.3 (C**2**), 150.1 (C**1**), 137.4 (C**7**), 129.0 (C**8**), 124.0 (C**10**), 120.0 (C**9**), 45.7, 33.5 (C**3**, C**5**), 16.8 (C**4**). HRMS: (ESI^+) Calculated for $C_{11}H_{12}N_2NaO_2$: 227.0791. Found $[M + Na]^+$: 227.0791.

Data for the minor product **8p**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.25 (1H, dt, *J* = 6.0, 2.0 Hz, C**4**-<u>H</u>).

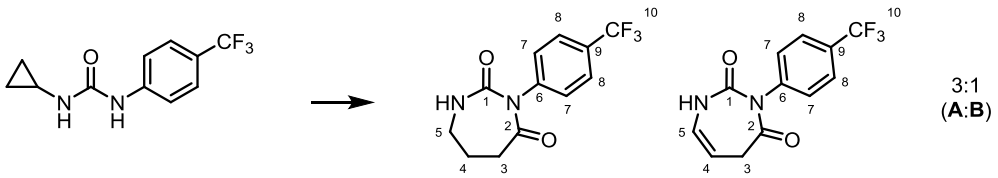
1-Cyclopropyl-3-(4-(trifluoromethyl)phenyl)urea (5q)



5q

General procedure A: Cyclopropylamine (0.38 mL, 5.50 mmol) and 4-(trifluoromethyl)phenyl isocyanate (0.71 mL, 5.00 mmol) were employed to yield the title compound **5q** (1.00 g, 82%) as a colorless solid; m.p. 180-181 °C ($CHCl_3$); ν_{max} / cm^{-1}: 3313 (br.), 1651 (s), 1603 (m), 1544 (s), 1326 (s), 1161 (s), 1107 (s), 1062 (s); ^{1}H NMR (MeOD-d_4, 400 MHz): δ 7.58-7.51 (4H, m, 2 × C**5**-<u>H</u>, 2 × C**6**-<u>H</u>), 2.60 (1H, m, C**2**-<u>H</u>), 0.75 (2H, m, 2 × C**1**-<u>H</u>), 0.51 (2H, m, 2 × C**1**-<u>H</u>); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.9 (C**3**), 144.6 (C**8**), 127.0, 119.4 (C**5**, C**6**), 23.3 (C**2**), 7.3 (C**1**); HRMS: (ESI^+) Calculated for $C_{11}H_{11}F_3N_2NaO$: 267.0716. Found $[M + Na]^+$: 267.0714.

3-(4-(Trifluoromethyl)phenyl)-1,3-diazepane-2,4-dione (9q) ***and*** **1-(4-(Trifluoromethyl) phenyl)-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8q)**



5q **9q** **8q**

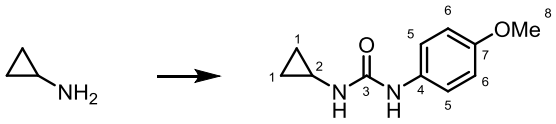
General Procedure B: Urea **5q** (36.6 mg, 0.15 mmol) and [Rh(cod)$_2$]BARF (5.0 mol%) were employed and the reaction was stirred for 42 h at 90 °C. The crude mixture was purified by column chromatography (30% EtOAc/hexane) to yield the title compound **9q** (29.1 mg, 71%, 3:1, **9q**:**8q**) as a yellow solid. Analysis of the crude reaction mixture by ^{1}H NMR revealed a 3:1 (**9q**:**8q**) mixture of products.

Data for the mixture of compounds: ν_{max} / cm^{-1}: 3131 (br.), 3075 (br.), 1707 (s), 1692 (s), 1602 (m), 1557 (m), 1325 (m), 1112 (s).

Data for major compound **9q**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.80 (1H, br. s, N<u>H</u>), 7.72-7.54 (4H, m, 2 × C**7**-<u>H</u>, 2 × C**8**-<u>H</u>), 3.96 (2H, t, *J* = 7.0 Hz, C**5**-<u>H</u>$_2$), 2.71 (2H, t, *J* = 8.0 Hz, C**3**-<u>H</u>$_2$), 2.11 (2H, tt, *J* = 8.0, 7.0 Hz, C**4**-<u>H</u>$_2$); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 177.7 (C**2**), 126.4, 119.7 (C**7**, C**8**), 45.8 (C**5**), 33.6 (C**3**), 16.9 (C**4**); HRMS: (ESI$^+$) Calculated for $C_{12}H_{11}F_3N_2NaO_2$: 295.0665. Found [M + Na]$^+$: 295.0659.

Data for minor compound **8q**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.70 (1H, br. s, N<u>H</u>), 7.72 -7.54 (4H, m, 2 × C**7**-<u>H</u>, 2 × C**8**-<u>H</u>), 7.40 (1H, dt, *J* = 6.0, 2.0 Hz, C**5**-<u>H</u>), 6.29 (1H, dt, *J* = 6.0, 2.0 Hz, C**4**-<u>H</u>), 4.56 (2H, dd, *J* = 2.0, 2.0 Hz, C**3**-<u>H</u>$_2$); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 172.0 (C**2**), 147.3 (C**5**), 127.2 (C**4**), 126.4, 119.7 (C**7**, C**8**), 51.4 (C**3**).

1-Cyclopropyl-3-(4-methoxyphenyl)urea (5q)

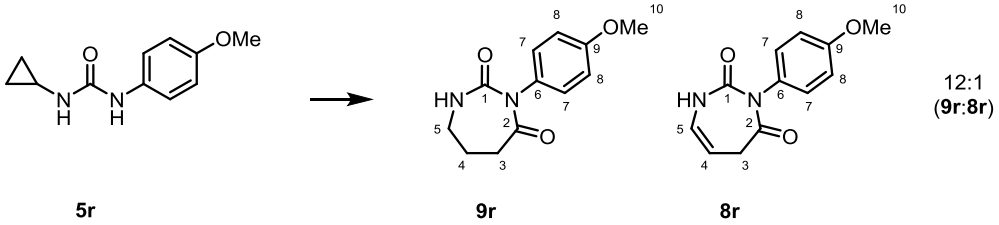


5q

General procedure A: Cyclopropylamine (0.76 mL, 11.0 mmol) and 1-isocyanato-4-methoxybenzene (1.09 mL, 10.0 mmol) were employed to yield the title compound **5q** (1.98 g, 96%) as a colorless solid; m.p. 146-149 °C (CH_2Cl_2); ν_{max} / cm^{-1}: 3289 (m), 1637 (s), 1561 (s), 1508 (s), 1243 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.28 (2H, m, 2 × C**6**-<u>H</u>), 6.86 (2H, m, 2 × C**5**-<u>H</u>), 6.68 (1H, br. s, N<u>H</u>), 3.79 (3H, s, C**8**-<u>H</u>$_3$), 2.58 (1H, m, C**2**-<u>H</u>), 0.81 (2H, m, 2 × C**1**-

H), 0.63 (2H, m, 2 × C**1**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.5 (C**7**), 131.3 (C**4**), 123.3 (C**6**), 114.5 (C**5**), 55.6 (C**8**), 22.8 (C**2**), 7.78 (C**1**); HRMS: (ESI$^+$) Calculated for $C_{11}H_{14}N_2NaO$: 229.0953. Found $[M + Na]^+$: 229.0947.

3-(4-Methoxyphenyl)-1,3-diazepane-2,4-dione (9r) ***and*** **1-(4-Methoxyphenyl)-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8r)**



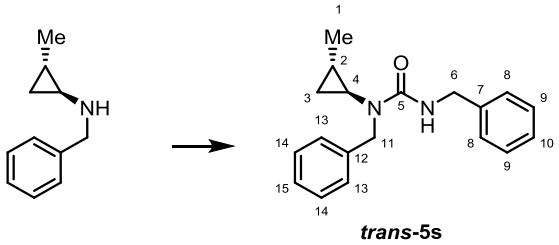
5r **9r** **8r**

General Procedure B: Urea **5r** (30.9 mg, 0.15 mmol) and $[Rh(cod)_2]BARF$ (5.0 mol%) were employed and the reaction was stirred for 25 h at 90 °C. The crude mixture was purified by column chromatography (30% EtOAc/hexane) to yield the title compound **9r** (22.0 mg**,** 63%) as a colorless solid. Analysis of the crude reaction mixture by ^{1}H NMR revealed a 12:1 (**9r**:**8r**) mixture of products. The minor product **8r** was not isolated.

Data for major compound **9r**: m.p. 114-116 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 2918 (m), 1702 (s), 1552 (s), 1511 (s), 1382 (s), 1212 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 10.4 (1H, br. s, NH), 7.42 (2H, m, 2 × C**8**-H), 6.86 (2H, m, 2 × C**7**-H), 3.94 (2H, t, *J* = 7.0 Hz, C**5**-H_2), 3.78 (3H, s, C**10**-H_3), 2.68 (2H, t, *J* = 8.0 Hz, C**3**-H_2), 2.07 (2H, tt, *J* = 8.0, 7.0 Hz, C**4**-H_2); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 177.3 (C**2**), 156.4 (C**9**), 150.5 (C**1**), 130.6 (C**6**), 121.9 (C**8**), 114.3 (C**7**), 55.6 (C**10**), 45.8 (C**5**), 33.7 (C**3**), 16.9 (C**4**); HRMS: (ESI$^+$) Calculated for $C_{12}H_{14}N_2NaO_3$: 257.0902. Found $[M + Na]^+$: 257.08967.

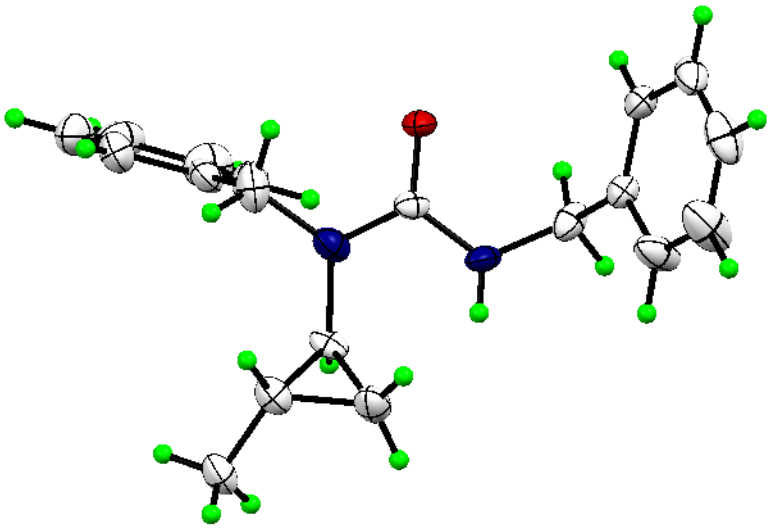
Data for the minor product **8r**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.25 (1H, d, *J* = 6.0 Hz, C**4**-H).

1,3-Dibenzyl-1-((1*S,2*S**)-2-methylcyclopropyl)urea (*trans*-5s)**

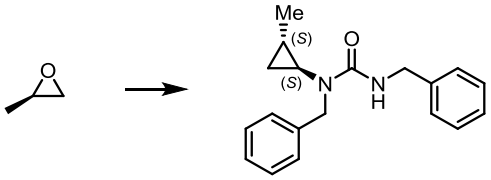


***trans*-5s**

General procedure A: (1*S**,2*S**)-*N*-Benzyl-2-methylcyclopropan-1-amine[5] (968 mg, 6.00 mmol) and benzyl isocyanate (0.74 μL, 6.00 mmol) were employed. The crude mixture was purified by column chromatography (30% EtOAc/hexane) to yield the title compound ***trans*-5s** (1.58 g, 89%) as a colorless oil; m.p. 49-51 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 3363 (m), 2957 (m), 1631 (s), 1504 (s), 1454 (s), 1221 (s); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.36-7.22 (10H, m, 2 × C**8**-H, 2 × C**9**-H, C**10**-H, 2 × C**13**-H, 2 × C**14**-H, C**15**-H), 5.48 (1H, t, *J* = 5.5 Hz, NH), 4.62-4.49 (4H, m, C**6**-H_2, C**11**-H_2), 2.02 (1H, ddd, *J* = 7.0, 7.0, 3.5 Hz, C**4**-H), 1.11 (1H, m, C**2**-H), 0.97 (3H, d, *J* = 6.0 Hz, C**1**-H_3), 0.91 (1H, m, 1 × C**3**-H), 0.55 (1H, m, 1 × C**3**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.0 (C**5**), 139.8, 139.0 (C**7**, C**12**), 128.7, 128.5, 128.1, 127.5, 127.3, 127.1 (C**8**, C**9**, C**10**, C**13**, C**14**, C**15**), 50.3 (C**11**), 45.0 (C**6**), 35.3 (C**4**), 16.9 (C**1**), 16.8 (C**3**), 16.6 (C**2**); HRMS: (ESI^+) Calculated for $C_{19}H_{22}N_2NaO$: 317.1624. Found $[M + Na]^+$: 317.1632. *The structure and relative stereochemistry of this compound was determined unambiguously by X-ray crystallography.*



1,3-Dibenzyl-1-((1*S*,2*S*)-2-methylcyclopropyl)urea ((*S*,*S*)-*trans*-5s)



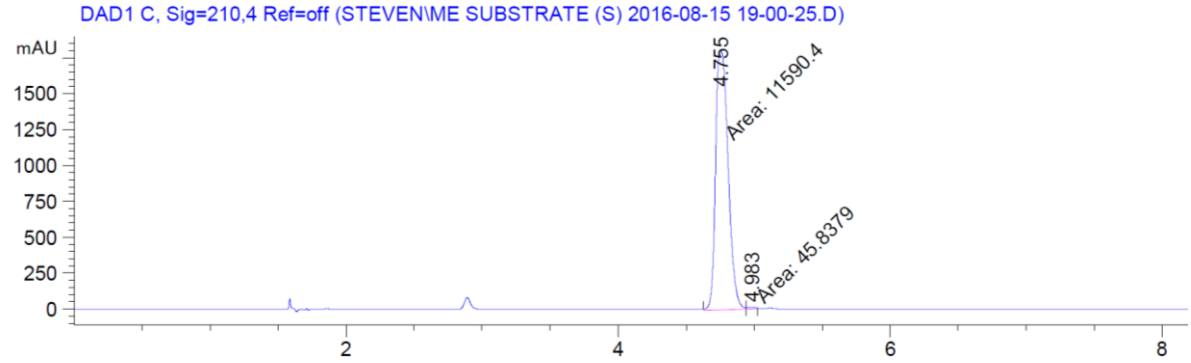
(*R*)-propylene oxide
commercially available

(*S*,*S*)-trans-5s
99% ee

Enantiopure substrate **(*S*,*S*)-*trans*-5s** (99% e.e.)was synthesised starting from commercially available (*R*)-propylene oxide according to the literature procedure.[5,7]

$[\alpha]_D^{27}$ +41.1 (c = 1.2, $CHCl_3$).

The enantiopurity of this compound was determined by chiral SFC (Chiralpak IB, isocratic CO_2-MeOH 88:12, 2.0 mL/min, 40 °C) against a racemic standard; t_R (major) – 4.8 min and t_R (minor) – 5.0 min.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
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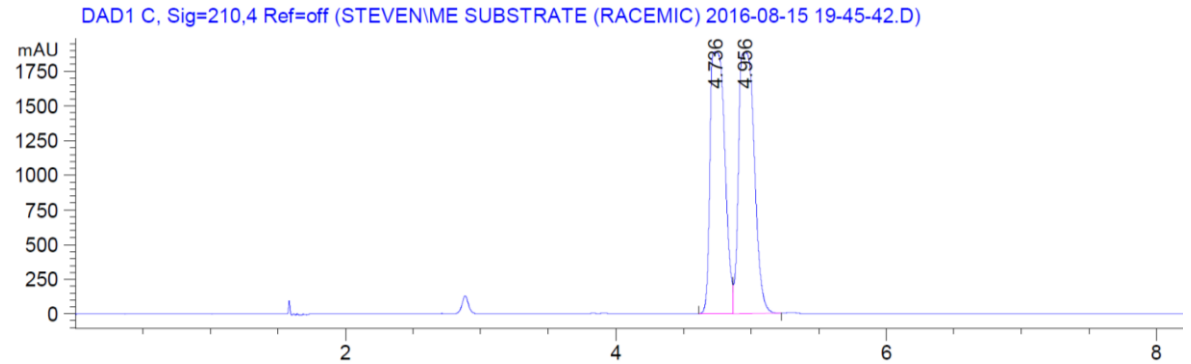
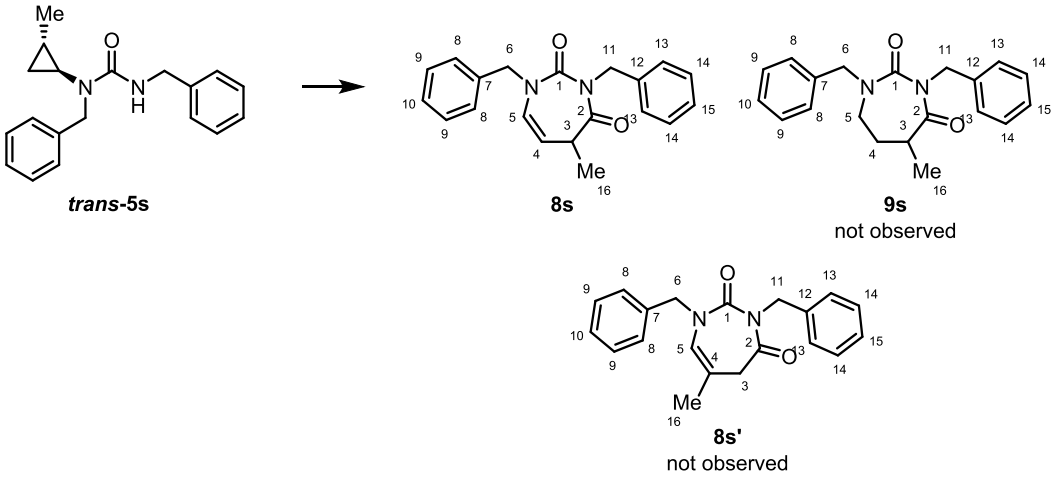
2	4.983	FM	0.0680	45.83789	11.22983	0.3939



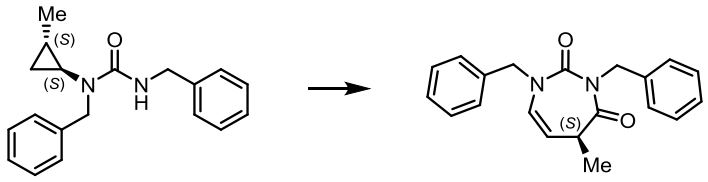
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.736	BV	0.0902	1.43725e4	1889.92505	48.4774
2	4.956	VB	0.0965	1.52754e4	1885.69458	51.5226

1,3-Dibenzyl-6-methyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8s)



General Procedure B: Urea ***trans*-5s** (44.2 mg, 0.15 mmol) and $[Rh(cod)_2]BARF$ (7.5 mol%) were employed and the reaction was stirred for 73 h at 100 °C. The crude mixture was purified by column chromatography (10% EtOAc/hexane) to yield the title compound **8s** (33.5 mg, 70%) as a yellow oil. Analysis of the crude reaction mixture by ^{1}H NMR revealed complete selectivity for **8s** over the corresponding saturated product **9s** and C4-substituted regioisomer **8s'**; ν_{max} / cm^{-1}: 2987 (m), 1699 (s), 1649 (s), 1402 (s), 1265 (s), 1183 (s), 1076 (s), 1046 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.31-7.22 (8H, m, 2 × C**9**-H, C**10**-H, 2 × C**13**-H, 2 × C**14**-H, C**15**-H), 7.07-7.02 (2H, m, 2 × C**8**-H), 5.99 (1H, dd, *J* = 7.0 Hz, 2.0 Hz, C**5**-H), 5.27 (1H, d, *J* = 14.5 Hz, 1 × C**11**-H), 5.21 (1H, dd, *J* = 7.0, 6.0 Hz, C**4**-H), 4.90 (1H, d, *J* = 14.5 Hz, 1 × C**11**-H), 4.83 (1H, d, *J* = 15.0 Hz, 1 × C**6**-H), 4.66 (1H, d, *J* = 15.0 Hz, 1 × C**6**-H), 3.06 (1H, qdd, *J* = 7.0, 6.0, 2.0 Hz, C**3**-H), 1.35 (3H, d, *J* = 7.0 Hz, C**16**-H_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.3 (C**2**), 154.0 (C**1**), 137.7 (C**12**), 136.1 (C**7**), 128.7, 128.5, 128.4, 128.1, 127.7, 127.6, 127.2 (C**5**, C**8**, C**9**, C**10**, C**13**, C**14**, C**15**), 120.2 (C**4**), 52.9 (C**6**), 48.2 (C**11**), 38.0 (C**3**), 13.7 (C**16**); HRMS: (ESI$^+$) Calculated for $C_{20}H_{20}N_2NaO_2$: 343.1417. Found $[M + Na]^+$: 343.1413.

(*S*)-1,3-Dibenzyl-6-methyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione ((*S*)-8s)



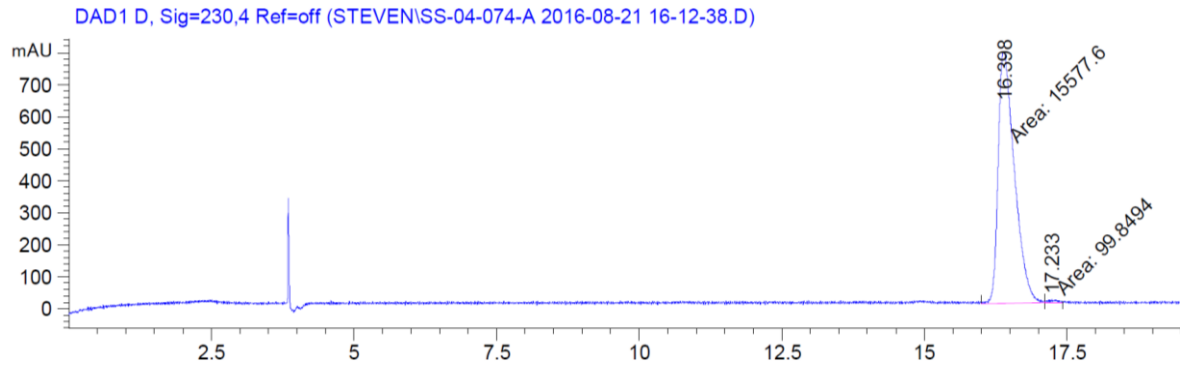
(*S*,*S*)-trans-5s
99% ee

(*S*)-8s
99% ee

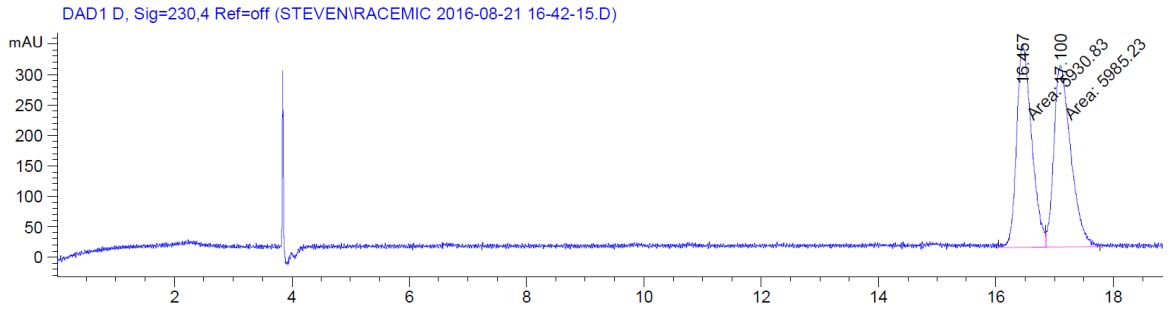
General Procedure B: Urea **(*S*,*S*)-*trans*-5s** (44.2 mg, 0.15 mmol) and [Rh(cod)$_2$]BARF (7.5 mol%) were employed and the reaction was stirred for 74 h at 100 °C. The crude mixture was purified by column chromatography (10% EtOAc/hexane) to yield the title compound **(*S*)-8s** (21.1 mg, 65%, 99% e.e.) as a yellow oil.

$[\alpha]_D^{27}$ +205.2 (c = 1.2, $CHCl_3$).

The enantiopurity of this compound was determined by chiral SFC (Chiralpak IB, isocratic CO_2-MeOH 95:5, 1.0 mL/min, 8 °C) against a racemic standard; t_R (major – 16.4 min and t_R (minor) – 17.2 min.

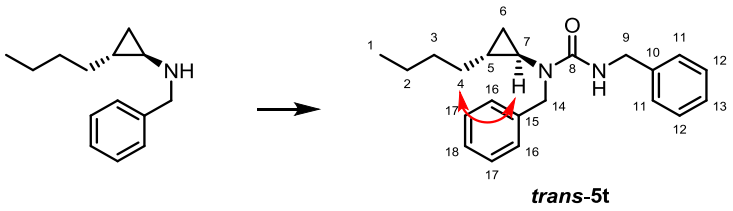


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.398	MF	0.3310	1.55776e4	784.31073	99.3631
2	17.233	FM	0.1726	99.84943	9.64204	0.6369



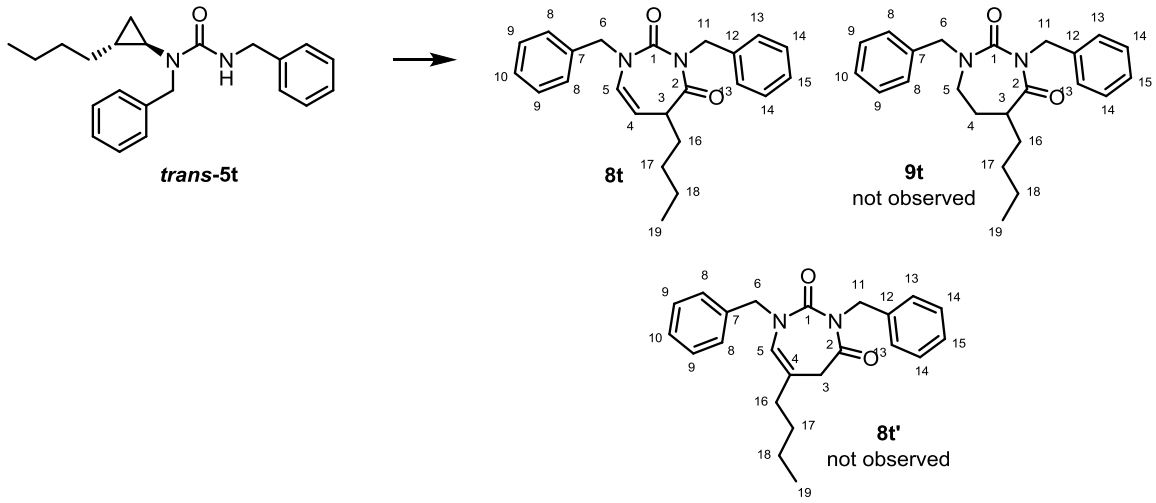
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.457	MF	0.2961	5930.83105	333.84116	49.7717
2	17.100	FM	0.3346	5985.22900	298.11276	50.2283

1,3-Dibenzyl-1-((1*R,2*R**)-2-butylcyclopropyl)urea (*trans*-5t)**



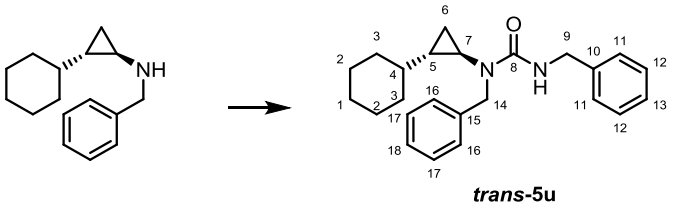
General procedure A: (1*R**,2*R**)-*N*-Benzyl-2-butylcyclopropan-1-amine[5] (497 mg, 2.44 mmol) was employed and the residue was purified by column chromatography (20% EtOAc/hexane) to provide the title compound ***trans*-5t** (677 mg, 82%) as a colorless oil; ν_{max} / cm^{-1}: 2956 (m), 2923 (m), 1644 (s), 1513 (s), 1453 (m), 1352 (m), 1267 (m); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37-7.21 (10H, m, 2 x C**11**-H, 2 x C**12**-H, C**13**-H, 2 x C**16**-H, 2 x C**17**-H, C**18**-H), 5.52 (1H, m, NH), 4.57 (2H, s, C**14**-H_2), 4.50 (2H, t, *J* = 5.0 Hz, C**9**-H_2), 2.08 (1H, m, C**7**-H), 1.26-1.17 (5H, m, 2 x C**2**-H, 2 x C**3**-H, 1 × C**4**-H), 1.12-1.01 (2H, m, 1 × C**4**-H, 1 × C**5**-H), 0.87 (1H, m, 1 × C**6**-H), 0.81 (3H, m, C**1**-H_3), 0.55 (1H, m, 1 × C**6**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.0 (C**8**), 139.8 (C**10**), 139.2 (C**15**), 128.8, 128.5, 127.9, 127.7, 127.4, 127.0 (C**11**, C**12**, C**13**, C**16**, C**17**, C**18**), 50.5 (C**14**), 45.0 (C**9**), 34.5 (C**7**), 32.1 (C**4**), 31.1, 22.6 (C**2**, C**3**), 22.4 (C**5**), 15.8 (C**6**), 14.0 (C**1**); HRMS: (ESI^+) Calculated for $C_{22}H_{28}N_2NaO$: 359.2094. Found $[M + Na]^+$: 359.2094. *The relative stereochemistry of this compound was corroborated by nOe experiments (as indicated on the compound structure). A strong nOe was observed between C7-H and C4-H_2. No significant nOe was observed between C7-H and C5-H.*

1,3-Dibenzyl-6-butyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8t)



General Procedure B: Urea ***trans*-5t** (50.5 mg, 0.15 mmol) and $[Rh(cod)_2]BF_4$ (10 mol%) were employed and the reaction was stirred for 45 h at 100 °C. The crude mixture was purified by column chromatography (7.5% EtOAc/hexane) to yield the title compound **8t** (32.2 mg, 59%) as a yellow solid. Analysis of the crude reaction mixture by ^{1}H NMR revealed complete selectivity for **8t** over the corresponding saturated product **9t** and C4-substituted regioisomer **8t'**; m.p. 88-89 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 2954 (m), 1688 (s), 1646 (s), 1446 (m), 1405 (s), 1332 (m), 1272 (m), 1181 (m); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.31-7.21 (8H, m, 2 × C**9**-H, C**10**-H, 2 × C**13**-H, 2 × C**14**-H, C**15**-H), 7.06-7.03 (2H, m, 2 × C**8**-H), 6.01 (1H, dd, *J* = 7.0, 2.0 Hz, C**5**-H), 5.26-5.23 (2H, m, C**4**-H, 1 × C**11**-H), 4.90 (1H, d, *J* = 14.5 Hz, 1 × C**11**-H), 4.81 (1H, d, *J* = 15.0 Hz, 1 × C**6**-H), 4.68 (1H, d, *J* = 15.0 Hz, 1 × C**6**-H), 2.89 (1H, m, C**3**-H), 1.96 (1H, m, 1 × C**16**-H), 1.64 (1H, m, 1 × C**16**-H), 1.33-1.25 (4H, m, 2 × C**17**-H, 2 × C**18**-H), 0.89 (3H, m, C**19**-H_3); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 171.8 (C**2**), 154.2 (C**1**), 137.9 (C**12**), 136.3 (C**7**), 129.0, 128.8, 128.5, 128.2, 127.9, 127.7, 127.3 (C**5**, C**8**, C**9**, C**10**, C**13**, C**14**, C**15**), 119.7 (C**4**), 22.9 (C**6**), 48.2 (C**11**), 43.7 (C**3**), 29.3 (C**17**), 27.9 (C**16**), 22.5 (C**18**), 14.1 (C**9**); HRMS: (ESI$^+$) Calculated for $C_{23}H_{26}N_2NaO_2$: 385.1886. Found $[M + Na]^+$: 385.1891.

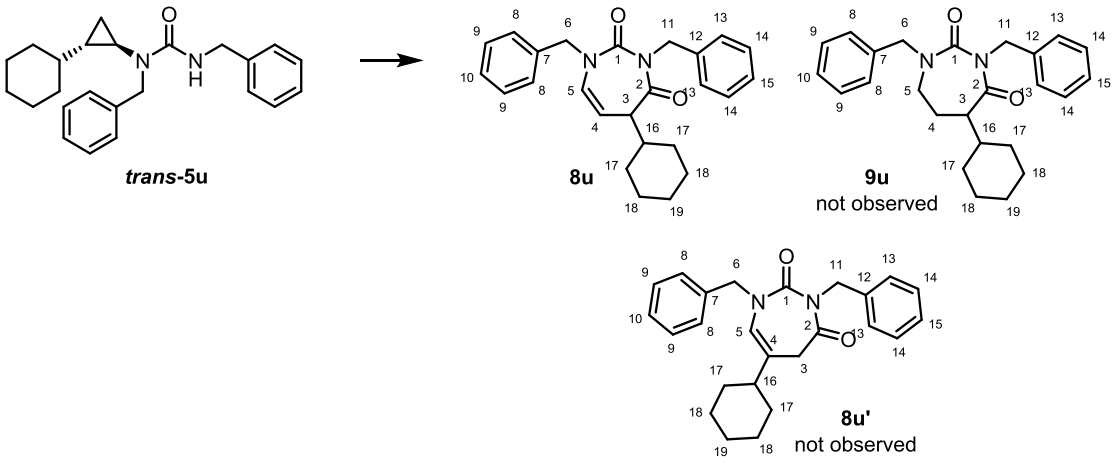
1,3-Dibenzyl-1-((1*R,2*S**)-2-cyclohexylcyclopropyl)urea (*trans*-5u)**



General procedure A: (1*R**,2*S**)-*N*-Benzyl-2-cyclohexylcyclopropan-1-amine[5] (355 mg, 1.55 mmol) was employed and the residue was purified by column chromatography (15-20%

EtOAc/hexane) to provide the title compound ***trans*-5u** (500 mg, 89%) as a colorless oil; m.p. 73-74 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 3346 (m), 2922 (m), 1630 (s), 1518 (s), 1349 (m), 1221 (m), 696 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37-7.21 (10H, m, 2 × C**11**-H, 2 × C**12**-H, C**13**-H, 2 × C**16**-H, 2 × C**17**-H, C**18**-H,), 5.63 (1H, t, *J* = 5.0 Hz, NH), 4.64 (1H, d, *J* = 15.5 Hz, 1 × C**14**-H), 4.51 (1H, d, *J* = 15.5 Hz, 1 × C**14**-H), 4.49 (2H, m, C**9**-H_2), 2.20 (1H, m, C**7**-H), 1.68-1.50 (5H, m, 5 × cyclohexyl CH), 1.13-0.88 (6H, m, C**4**-H, 5 × cyclohexyl CH), 0.82 (1H, m, 1 × C**6**-H), 0.64-0.47 (2H, m, C**5**-H, 1 × C**6**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.0 (C**8**), 139.7 (C**10**), 139.4 (C**15**), 128.7, 128.5, 127.9, 127.7, 127.4, 126.9 (C**11**, C**12**, C**13**, C**16**, C**17**, C**18**), 50.7 (C**14**), 45.1 (C**9**), 41.0 (C**5**), 33.7 (C**7**), 32.7, 32.1 (2 × cyclohexyl CH_2), 28.7 (C**4**), 26.3, 26.1, 26.1 (3 × cyclohexyl CH_2), 14.7 (C**6**); HRMS: (ESI^+) Calculated for $C_{24}H_{30}N_2NaO$: 385.2256. Found $[M + Na]^+$: 385.2342.

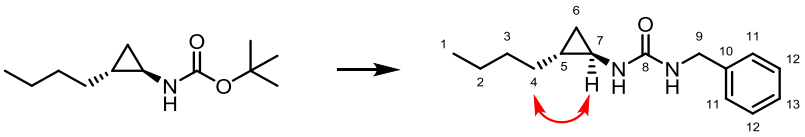
1,3-Dibenzyl-6-cyclohexyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8u)



General Procedure B: Urea ***trans*-5u** (54.4 mg, 0.15 mmol) and $[Rh(cod)_2]BF_4$ (7.5 mol%) were employed and the reaction was stirred for 73 h at 100 °C. The crude mixture was purified by column chromatography (7.5% EtOAc/hexane) to yield the title compound **8u** (16.9 mg, 29%) as a yellow oil. Analysis of the crude reaction mixture by ^{1}H NMR revealed complete selectivity for **8u** over the corresponding saturated product **9u** and C4-substituted regioisomer **8u'**; ν_{max} / cm^{-1}: 2923 (m), 2850 (m), 1698 (m), 1646 (s), 1401 (s), 1178 (m); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.30-7.21 (8H, m, 2 × C**9**-H, C**10**-H, 2 × C**13**-H, 2 × C**14**-H, C**15**-H), 7.07-7.03 (2H, m, 2 × C**8**-H), 6.01 (1H, dd, *J* = 7.0, 1.5 Hz, C**5**-H), 5.38 (1H, dd, *J* = 7.0, 7.0 Hz, C**4**-H), 5.18 (1H, d, *J* = 14.5 Hz, 1 × C**11**-H), 4.92 (1H, d, *J* = 14.5 Hz, 1 × C**11**-H), 4.84 (1H, d, *J* = 15.0 Hz, 1 × C**6**-H), 4.63 (1H, d, *J* = 15.0 Hz, 1 × C**6**-H), 2.67 (1H, m, C**3**-H), 1.96-1.86 (2H, m, C**16**-H, 1 × C**17**-H), 1.79 (1H, m, 1 × cyclohexyl CH), 1.70-1.63 (3H, m, 3 × cyclohexyl

C<u>H</u>), 1.34-1.08 (3H, m, 3 × cyclohexyl C<u>H</u>), 0.91-0.79 (2H, m, 1 × C**17**-<u>H</u>, 1 × cyclohexyl C<u>H</u>); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 170.7 (C**2**), 154.2 (C**1**), 137.9 (C**12**), 136.2 (C**7**), 129.1 (C**5**), 128.8, 128.5, 128.2, 127.9, 127.8, 127.3 (C**8**, C**9**, C**10**, C**13**, C**14**, C**15**), 117.8 (C**4**), 52.9 (C**6**), 50.2 (C**3**), 48.3 (C**11**), 35.7 (C**16**), 31.9 (C**17**), 30.3, 26.5, 26.1, 25.9 (C**17**, 2 × C**18**, C**19**); HRMS: (ESI$^+$) Calculated for $C_{25}H_{28}N_2NaO_2$: 411.2043. Found [M + Na]$^+$: 411.2050.

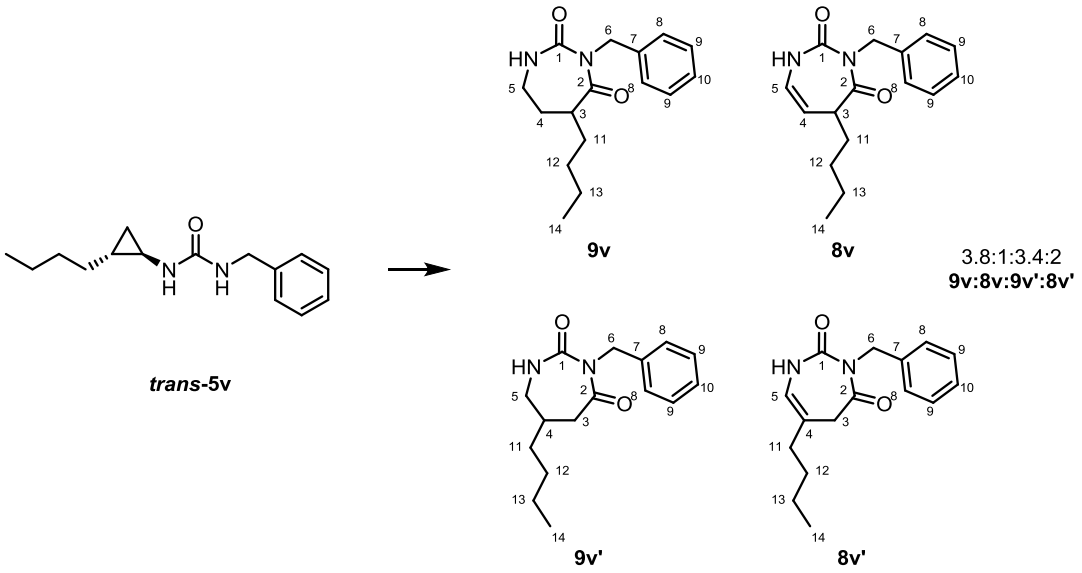
1-Benzyl-3-((1*R,2*R**)-2-butylcyclopropyl)urea (*trans*-5v)**



***trans*-5v**

General procedure C: *tert*-Butyl ((1*R**,2*R**)-2-butylcyclopropyl)carbamate[5] (427 mg, 2.00 mmol) was employed and the residue was purified by column chromatography (40% EtOAc/hexane) to provide the title compound ***trans*-5v** (463 mg, 94%) as a colorless solid; m.p. 80-83 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 3318 (m), 2915 (m), 1625 (s), 1570 (s), 1454 (m), 1242 (s), 1067 (m), 696 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35-7.23 (5H, m, 2 x C**11**-<u>H</u>, 2 x C**12**-<u>H</u>, C**13**-<u>H</u>), 5.23 (1H, br. m, N<u>H</u>), 4.74 (1H, br. s, N<u>H</u>), 4.43 (2H, m, C**9**-<u>H_2</u>), 2.14 (1H, m, C**7**-<u>H</u>), 1.35-1.16 (6H, m, 2 x C**2**-<u>H</u>, 2 x C**3**-<u>H</u>, 2 x C**4**-<u>H</u>), 0.94-0.82 (4H, m, C**1**-<u>H_3</u>, C**5**-<u>H</u>), 0.69 (1H, m, 1 x C**6**-<u>H</u>), 0.51 (1H, m, 1 x C**6**-<u>H</u>); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 159.0 (C**8**), 139.4 (C**10**), 128.8, 127.7, 127.4 (C**11**, C**12**), 127.4 (C**13**), 44.4 (C**9**), 32.0 (C**4**), 31.3 (C**3**), 29.1 (C**7**), 22.5 (C**2**), 21.5 (C**5**), 14.9 (C**6**), 14.1 (C**1**); HRMS: (ESI$^+$) Calculated for $C_{15}H_{22}N_2NaO$: 269.1624. Found [M + Na]$^+$: 269.1618. *The relative stereochemistry of this compound was corroborated by nOe experiments (as indicated on the compound structure). A strong nOe was observed between C7-<u>H</u> to C4-<u>H_2</u>. No significant nOe was observed between C7-<u>H</u> and C5-<u>H</u>.*

3-Benzyl-5-butyl-1,3-diazepane-2,4-dione (9v), 1-Benzyl-6-butyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8v), 3-Benzyl-6-butyl-1,3-diazepane-2,4-dione (9v') *and* 1-Benzyl-5-butyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8v')



General Procedure B: Urea ***trans*-5v** (36.9 mg, 0.15 mmol) and $[Rh(cod)_2]BARF$ (5.0 mol%) were employed and the reaction was stirred for 38 h at 100 °C. The crude mixture was purified by column chromatography (20% EtOAc/hexane) to yield the title compounds (28.8 mg, 70%, 3.8:1:3.4:1.9, **9v**:**8v**:**9v'**:**8v'**) as a brown oil. *Repeated column chromatography allowed the partial separation of the products into two mixtures **A** (15.5 mg, 38%, 4.8:1:6.0, **9v**:**8v**:**9v'**) and **B** (10.5 mg, 26%, 1.1:1:2, **9v**:**8v**:**8v'**). The products were assigned by analogy to **9y**, **8y**, **9y'** and **8y'** and by 2D NMR (HSQC, HMBC).*

Data for the mixture of compounds: ν_{max} / cm^{-1}: 3298 (m), 2928 (m), 1705 (s), 1541 (s), 1361 (m), 1272 (m).

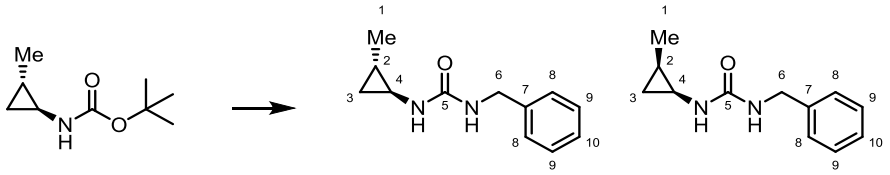
Data for product **9v**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.81 (1H, br. s, NH), 7.33-7.24 (5H, m, 2 × C**8**-H, 2 × C**9**-H, C**10**-H), 4.50 (2H, m, C**6**-H_2), 3.93 (1H, m, 1 × C**5**-H), 3.66 (1H, m, 1 × C**5**-H), 2.60 (1H, m, C**3**-H), 2.20 (1H, m, 1 × C**4**-H), 1.68 (1H, m, 1 × C**4**-H), 1.50-1.24 (6H, m, C**11**-H_2, C**12**-H_2, C**13**-H_2), 0.93-0.89 (3H, m, C**14**-H_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 179.2 (C**2**), 44.4 (C**3**), 43.9, 43.9 (C**5**, C**6**), 24.1 (C**4**), 14.1 (C**14**); HRMS: (ESI^+) Calculated for $C_{16}H_{22}N_2NaO_2$: 297.1573. Found $[M + Na]^+$: 297.1583.

Data for product **8v**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36-7.22 (5H, m, 2 × C**8**-H, 2 × C**9**-H, C**10**-H), 6.10 (1H, m, C**5**-H), 5.14 (1H, dd, *J* = 6.5, 6.5 Hz, C**4**-H), 5.07 (1H, d, J = 14.5 Hz, 1 × C**6**-H), 4.97 (1H, d, J = 14.5 Hz, 1 × C**6**-H), 3.05 (1H, m, C**3**-H), 2.00 (1H, m, 1 × C**11**-H), 0.96-0.89 (3H, m, C**14**-H_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 124.6 (C**5**), 117.0 (C**4**), 48.3 (C**6**), 43.9 (C**3**), 28.4 (C**11**).

Data for product **9v'**: *Full characterization data for compound **9v'** is presented on S42.*

Data for product **8v'**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.79 (1H, br. s, N<u>H</u>), 7.36-7.22 (5H, m, 2 × C**8**-<u>H</u>, 2 × C**9**-<u>H</u>, C**10**-<u>H</u>), 6.87 (1H, m, C**5**-<u>H</u>), 4.55 (2H, m, C**6**-<u>H_2</u>), 4.34 (2H, m, C**3**-<u>H_2</u>), 2.27 (2H, m, C**11**-<u>H_2</u>), 1.53 (2H, m, C**12**-<u>H_2</u>), 1.41-1.28 (2H, m, C**13**-<u>H_2</u>), 0.93 (3H, m, C**14**-<u>H_3</u>); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 138.3 (C**5**), 49.2 (C**3**), 43.9 (C**6**), 25.2 (C**11**).

1-Benzyl-3-((1*S,2*S**)-2-methylcyclopropyl)urea (*trans*-5y) *and* 1-Benzyl-3-((1*R**,2*S**)-2-methylcyclopropyl)urea (*cis*-5y)**



***trans*-5y** ***cis*-5y**

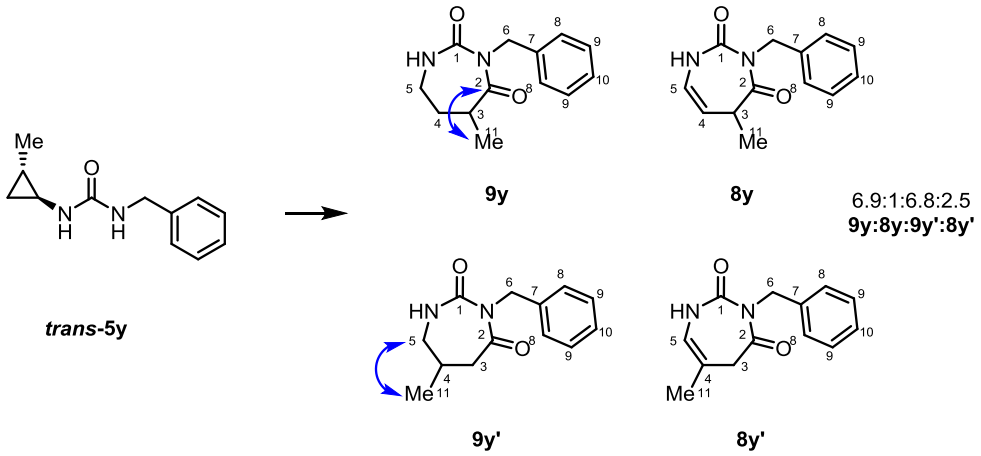
General procedure C: 1-Benzyl-3-((1*S**,2*S**)-2-methylcyclopropyl)urea[5] (700 mg, 4.09 mmol, 5:1 d.r.) was employed and the residue was purified by column chromatography (50% EtOAc/hexane) to provide the title compound (751 mg, 90%, 8:1 d.r., ***trans*-5y**:***cis*-5y**) as a pale brown solid. *The product diastereomers were inseparable by column chromatography.*

Data for the mixture of compounds: m.p. 102-104 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 3314 (br.), 2956 (m), 1625 (s), 1561 (s), 1246 (s), 1071 (m), 1025 (m).

Data for major product ***trans*-5y**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37-7.25 (5H, m, 2 × C**8**-<u>H</u>, 2 × C**9**-<u>H</u>, C**10**-<u>H</u>), 5.16 (1H, br. s, N<u>H</u>), 4.68 (1H, br. s, N<u>H</u>), 4.46 (2H, dd, *J* = 5.5, 3.5 Hz, C**6**-<u>H_2</u>), 2.13 (1H, m, C**4**-<u>H</u>), 1.04 (3H, d, *J* = 6.0, C**1**-<u>H_3</u>), 0.99-0.91 (1H, m, C**2**-<u>H</u>), 0.73 (1H, m, 1 × C**3**-<u>H</u>), 0.51 (1H, m, 1 × C**3**-<u>H</u>); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.9 (C**5**), 139.5 (C**6**), 128.8, 127.5, 127.5 (C**8**, C**9**, C**10**), 30.1 (C**4**), 17.1 (C**1**), 16.1, 15.8 (C**2**, C**3**); HRMS: (ESI^+) Calculated for $C_{12}H_{16}N_2NaO$: 227.1155. Found $[M + Na]^+$: 227.1148.

Data for minor product ***cis*-5y**: *Characteristic signals only*: ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.23 (1H, br. s, N<u>H</u>), 4.58 (1H, br. s, N<u>H</u>), 2.44 (1H, m, C**4**-<u>H</u>), 1.10 (3H, d, *J* = 6.0, C**1**-<u>H_3</u>), 0.17 (1H, m, 1 × C**3**-<u>H_2</u>).

3-Benzyl-5-methyl-1,3-diazepane-2,4-dione (9y), 1-Benzyl-6-methyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8y), 3-Benzyl-6-methyl-1,3-diazepane-2,4-dione (9y') *and* 1-Benzyl-5-methyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8y')



General Procedure B: Compound ***trans*-5y** (30.6 mg, 0.15 mmol, 8:1 d.r.) and $[Rh(cod)_2]BARF$ (5.0 mol%) were employed and the reaction was stirred for 69 h at 90 °C. The crude mixture was purified by column chromatography (25% EtOAc/hexane) to yield the title compounds as two separate mixtures, **A** (22.3 mg, 64%, 6.3:1:6.3, **9y**:**8y**:**9y'**) and **B** (6.2 mg, 18%, 1.3:1:5.6, **9y**:**9y':8y'**) as colorless oils. *Combined yields and product distribution (28.5 mg, 81%, 6.9:1:6.8:2.5, **9y**:8y:**9y':8y'**). The compounds could not be separated by column chromatography.*

Data for the mixture of compounds: ν_{max} / cm^{-1}: 3301 (br.), 2964 (br.), 1708 (s), 1535 (s), 1454 (m), 1358 (m), 1258 (m).

Data for product **9y**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.79-8.74 (1H, br. s, N<u>H</u>), 7.35-7.23 (5H, m, 2 × C**8**-<u>H</u>, 2 × C**9**-<u>H</u>, C**10**-<u>H</u>), 4.49 (2H, d, *J* = 6.0 Hz, C**6**-<u>H_2</u>), 3.93 (1H, m, 1 × C**5**-<u>H</u>), 3.66 (1H, m, 1 × C**5**-<u>H</u>), 2.75-2.63 (1H, m, C**3**-<u>H</u>), 2.29-2.21 (1H, m, 1 × C**4**-<u>H</u>), 1.64 (1H, m, 1 × C**4**-<u>H</u>), 1.23 (3H, d, *J* = 7.0 Hz, C**11**-<u>H_3</u>); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 179.6 (C**2**), 43.9 (C**5**), 38.3 (C**3**), 26.3 (C**4**), 15.5 (C**11**); HRMS: (ESI^+) Calculated for $C_{13}H_{16}N_2NaO_2$: 255.1104. Found $[M + Na]^+$: 255.1099. *The regiochemistry of this compound was elucidated by HMBC experiments (as indicated on the compound structure.). A strong HMBC signal was observed between C**11**-<u>H_3</u> and <u>C**2**</u>. No measureable HMBC signal was observed between C**11**-<u>H_3</u> and <u>C**5**</u> or between C**5**-<u>H</u> and <u>C**11**</u>.*

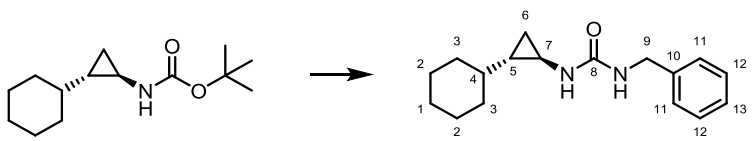
Data for product **8y**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35-7.23 (5H, m, 2 × C**8**-<u>H</u>, 2 × C**9**-<u>H</u>, C**10**-<u>H</u>), 6.06 (1H, m, C**5**-<u>H</u>), 5.09 (1H, m, C**4**-<u>H</u>), 5.08 (1H, d, *J*

= 14.5 Hz, 1 × C**6**-H), 4.96 (1H, d, *J* = 14.5 Hz, 1 × C**6**-H), 3.20 (1H, m, C**3**-H), 1.37 (3H, d, *J* = 7.0 Hz, C**11**-H_3); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 124.3 (C**5**), 117.8 (C**4**), 48.3 (C**6**), 38.3 (C**3**), 14.2 (C**11**); HRMS: (ESI^+) Calculated for $C_{13}H_{14}N_2NaO_2$: 253.0953. Found $[M + Na]^+$: 253.0948. *The structure of this compound was assigned by the similarity of the ^{1}H NMR signals of the C4 and C5 positions to related structures reported herein. The assignment was supported by 2D NMR experiments (HSQC, HMBC).*

Data for product **9y'**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.79-8.74 (1H, br. s, NH), 7.35-7.23 (5H, m, 2 × C**8**-H, 2 × C**9**-H, C**10**-H), 4.50-4.48 (2H, m, C**6**-H_2), 4.03 (1H, dd, *J* = 11.0, 7.5 Hz, 1 × C**5**-H), 3.42 (1H, dd, *J* = 11.0, 6.5 Hz, 1 × C**5**-H), 2.72 (1H, m, 1 × C**3**-H), 2.43 (1H, m, C**4**-H), 2.25 (1H, m, 1 × C**3**-H), 1.15 (3H, d, *J* = 7.0 Hz, C**11**-H_3); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 176.8 (C**2**), 52.7 (C**5**), 41.6 (C**3**), 25.6 (C**4**), 19.2 (C**11**); HRMS: (ESI^+) Calculated for $C_{13}H_{16}N_2NaO_2$: 255.1104. Found $[M + Na]^+$: 255.1099. *The regiochemistry of this compound was elucidated by HMBC experiments (as indicated on the compound structure.). A strong HMBC signal was observed between C**11**-H_3 and C**5** and between C**5**-H and C**11**. No measureable HMBC signal was observed between C**11**-H_3 and C**2**.*

Data for product **8y'**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.78 (1H, br. s, NH), 7.35-7.24 (5H, m, 2 × C**8**-H, 2 × C**9**-H, C**10**-H), 6.91 (1H, m, C**5**-H), 4.55 (2H, d, J = 6.0 Hz, C**6**-H_2), 4.33 (2H, m, C**3**-H_2), 1.91 (3H, m, C**11**-H_3); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 139.3 (C**5**), 128.8, 127.8 (C**8**, C**9**), 127.5 (C**10**), 49.1 (C**3**), 43.8 (C**6**), 11.0 (C**11**); HRMS: (ESI^+) Calculated for $C_{13}H_{14}N_2NaO_2$: 253.0953. Found $[M + Na]^+$: 253.0948. *The structure of this compound was assigned using 2D NMR experiments (HSQC, HMBC).*

1-Benzyl-3-((1*R,2*S**)-2-cyclohexylcyclopropyl)urea (*trans*-5z)**

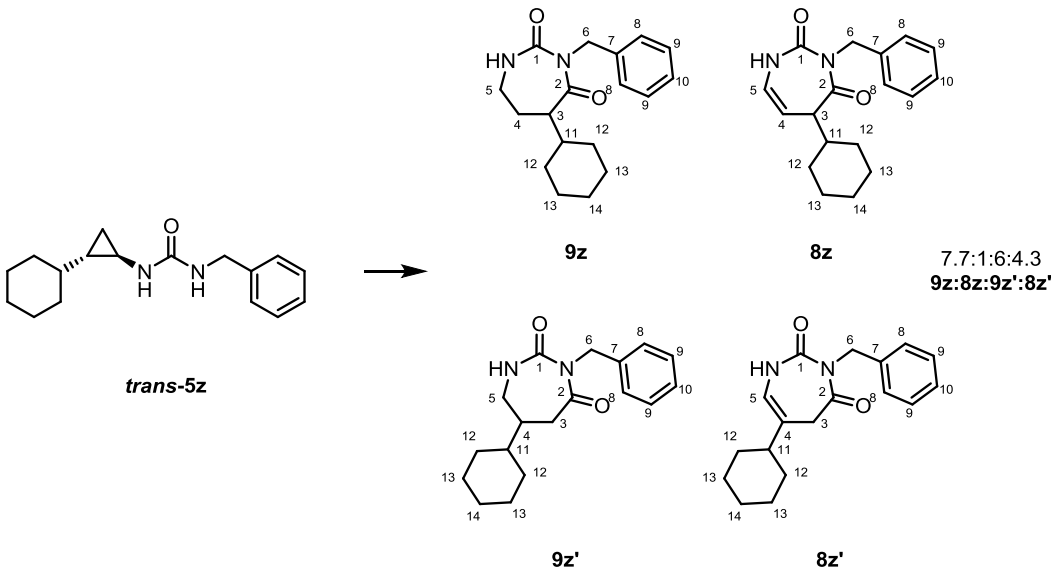


***trans*-5z**

General procedure C: *tert*-Butyl ((1*R**,2*S**)-2-cyclohexylcyclopropyl)carbamate[5] (350 mg, 1.46 mmol) was employed and the residue was purified by column chromatography (40% EtOAc/hexane) to provide the title compound ***trans*-5z** (345 mg, 87%) as a colorless solid; m.p. 80-83 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}:3319 (br.), 2919 (m), 2847 (m), 1626 (s), 1589 (s), 1577 (s), 1446 (m), 1255 (m), 1235 (m); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35-7.22 (5H, m, 2 × C**11**-

H, 2 × C**12**-H, C**13**-H), 5.27 (1H, br. m, NH), 4.68 (1H, br. m, NH), 4.42 (2H, m, C**9**-H_2), 2.19 (1H, m, C**7**-H), 1.73-1.60 (5H, m, 5 × cyclohexyl CH), 1.18-0.94 (5H, m, 5 × cyclohexyl CH), 0.75 (1H, m, C**4**-H), 0.64 (1H, m, 1 × C**6**-H), 0.61-0.51 (2H, m, C**5**-H, 1 × C**6**-H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 158.9 (C**8**), 139.3 (C**10**), 128.7, 127.8, 127.5 (C**11**, C**12**, C**13**), 44.5 (C**9**), 40.8 (C**5**), 32.9, 32.3 (2 × cyclohexyl CH_2), 28.2 (C**4**), 27.9 (C**7**), 26.4, 26.2, 26.1 (3 × cyclohexyl CH_2), 13.7 (C**6**); HRMS: (ESI^+) Calculated for $C_{17}H_{24}N_2NaO$: 295.1786. Found $[M + Na]^+$: 295.1775.

3-Benzyl-5-cyclohexyl-1,3-diazepane-2,4-dione (9z), 1-Benzyl-6-cyclohexyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8z), 3-Benzyl-6-cyclohexyl-1,3-diazepane-2,4-dione (9z') *and* 1-Benzyl-5-cyclohexyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8z')



General Procedure B: Compound ***trans*-5z** (40.8 mg, 0.15 mmol) and $[Rh(cod)_2]BARF$ (7.5 mol%) were employed and the reaction was stirred for 72 h at 100 °C. The crude mixture was purified by column chromatography (25% EtOAc/hexane) to yield the title compounds (25.6 mg, 57%, 7.7:1:6:4.3, **9z**:**8z**:**9z'**:**8z'**) as a brown oil; *The compounds could not be separated by column chromatography. The products were assigned by analogy to **9y**, **8y**, **9y'** and **8y'**.*

Data for the mixture of compounds: ν_{max} / cm^{-1}: 3305 (br.), 2923 (m), 2853 (m), 1707 (s), 1537 (s), 1449 (m), 1360 (m), 1259 (m).

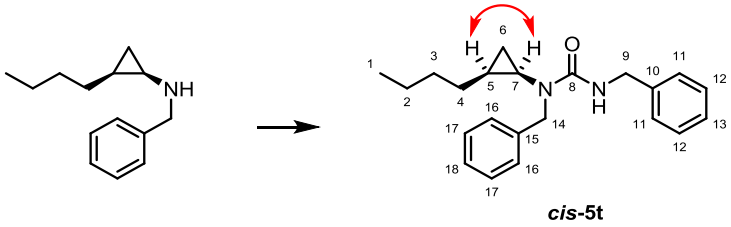
Data for product **9z**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 3.87 (1H, m, 1 × C**5**-H), 3.66 (1H, m, 1 × C**5**-H); HRMS: (ESI^+) Calculated for $C_{18}H_{24}N_2NaO_2$: 323.1730. Found $[M + Na]^+$: 323.1739.

Data for product **8z**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.09 (1H, m, C**5**-H), 5.27 (1H, t, *J* = 7.0 Hz, C**4**-H).

Data for product **9z'**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.05 (1H, dd, *J* = 11.0, 8.0 Hz, 1 × C**5**-H), 3.43 (1H, dd, *J* = 11.0, 9.0 Hz, 1 × C**5**-H), 2.62 (1H, m, 1 × C**3**-H), 2.35 (1H, m, 1 × C**3**-H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 49.8 (C**5**), 38.2 (C**3**).

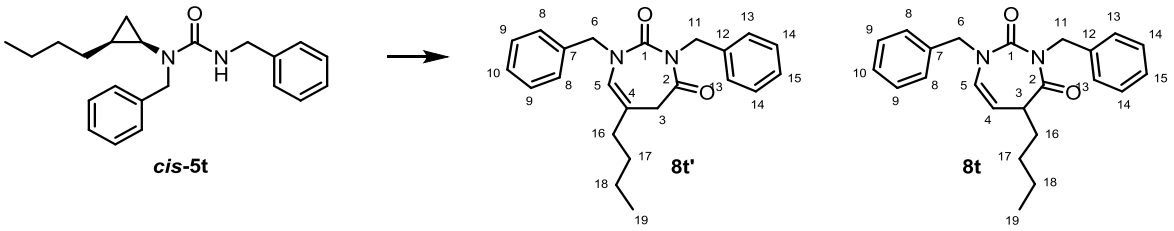
Data for product **8z'**: *Characteristic signals only*: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.81 (1H, s, C**5**-H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 136.8 (C**5**).

(1*R,2*S**)-1,3-Dibenzyl-1-(2-butylcyclopropyl)urea (*cis*-5t)**



General procedure A: (1*R**,2*S**)-*N*-Benzyl-2-butylcyclopropan-1-amine[8] (508 mg, 2.50 mmol) and benzyl isocyanate (309 μL, 2.50 mmol) were employed. The crude mixture was purified by column chromatography (20% EtOAc/hexane) to yield the title compound ***cis*-5t** (814 mg, 97%) as a colorless solid; m.p.: 44-46 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 3356 (m), 2927 (s), 1639 (s), 1512 (s), 1495 (s), 1453 (s), 1229 (m); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36-7.22 (10H, m, 2 × C**11**-H, 2 × C**12**-H, C**13**-H, 2 × C**16**-H, 2 × C**17**-H, C**18**-H), 5.54 (1H, t, *J* = 5.5 Hz, NH), 4.86 (1H, d, *J* = 15.0 Hz, 1 × C**14**-H), 4.56-4.46 (2H, m, C**9**-H_2), 4.33 (1H, d, *J* = 15.0 Hz, 1 × C**14**-H), 2.39 (1H, ddd, *J* = 7.5, 6.0, 4.5 Hz, C**7**-H), 1.63 (1H, m, 1 × C**4**-H), 1.37-1.23 (4H, m, C**2**-H_2, C**3**-H_2), 1.02-0.81 (6H, m, C**1**-H_3, 1 × C**4**-H, C**5**-H, 1 × C**6**-H), 0.42 (1H, m, 1 × C**6**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.5 (C**8**), 139.6 (C**10**), 139.0 (C**15**), 128.6, 128.4, 128.1, 127.7, 127.2, 126.9 (C**11**, C**12**, C**13**, C**16**, C**17**, C**18**), 50.6 (C**14**), 44.9 (C**9**), 32.7 (C**7**), 31.7 (C**3**), 27.1 (C**4**), 22.5 (C**2**), 20.7 (C**5**), 14.0 (C**1**), 12.6 (C**6**); HRMS: (ESI^+) Calculated for $C_{22}H_{29}N_2O$: 337.2274. Found $[M + H]^+$: 337.2275. *The relative stereochemistry of this compound was corroborated by nOe experiments (as indicated on the compound structure). A strong nOe was observed between C**7**-H to C**5**-H. No significant nOe was observed between C**4**-H_2 and C**7**-H.*

1,3-Dibenzyl-5-butyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8t') *and* 1,3- Dibenzyl-6-butyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8t)

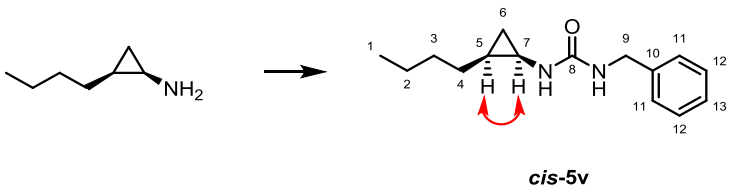


General Procedure B: Urea ***cis*-5t** (50.5 mg, 0.15 mmol) and $[Rh(cod)_2]OTf$ (7.5 mol%) were employed and the reaction was stirred for 73 h at 100 °C. The crude mixture was purified by column chromatography (50% EtOAc/hexane) to yield the title compound **8t'** (34.6 mg, 64%) as a yellow oil. Analysis of the crude reaction mixture by ^{1}H NMR revealed a 6:1 (**8t'**:**8t**) mixture of products.

Data for major compound **8t'**: ν_{max} / cm^{-1}: 1697 (m), 1647 (s), 1412 (m), 1215 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34-7.24 (8H, m, 2 × C**9**-H, C**10**-H, 2 × C**13**-H, 2 × C**14**-H, C**15**-H), 7.08-7.06 (2H, m, 2 × C**8**-H), 5.75 (1H, t, *J* = 1.0 Hz, C**5**-H), 5.05 (2H, s, C**11**-H_2), 4.72 (2H, s, C**6**-H_2), 3.04 (2H, s, C**3**-H_2), 2.14 (2H, td, *J* = 7.0, 1.0 Hz, C**16**-H_2), 1.45-1.39 (2H, m, C**17**-H_2), 1.27-1.18 (2H, m, C**18**-H_2), 0.87 (3H, t, *J* = 7.5 Hz, C**19**-H_3); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 169.7 (C**2**), 154.1 (C**1**), 137.7 (C**12**), 136.3 (C**7**), 128.7, 128.3, 128.1, 128.0, 127.7, 127.6, 127.2 (C**4**, C**8**, C**9**, C**10**, C**13**, C**14**, C**15**), 124.1 (C**5**), 53.0 (C**6**), 47.5 (C**11**), 39.4 (C**3**), 33.7 (C**16**), 29.0 (C**17**), 21.9 (C**18**), 13.7 (C**19**); HRMS: (ESI$^+$) Calculated for $C_{23}H_{27}N_2O_2$: 363.2067. Found $[M + H]^+$: 363.2078.

Data for product **8t**: *Full characterization data for compound **8t** is presented on S31-S32.*

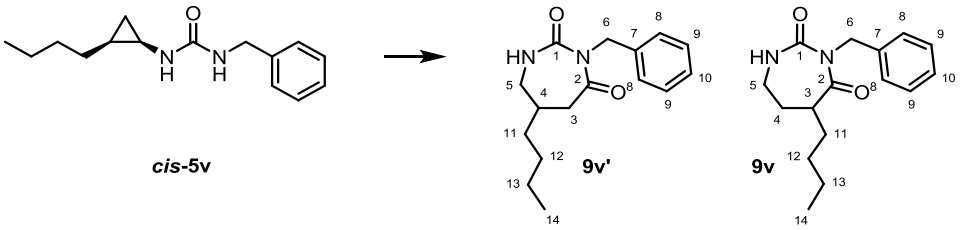
(1*R,2*S**)-1-Benzyl-3-(2-butylcyclopropyl)urea (*cis*-5v)**



General procedure A: (1*R**,2*S**)-2-Butylcyclopropan-1-amine[8] (283 mg, 2.50 mmol) and benzyl isocyanate (309 μL, 2.50 mmol) were employed. The crude mixture was purified by column chromatography (75% EtOAc/hexane) to yield the title compound ***cis*-5v** (430 mg, 70%) as a colorless solid; m.p.: 66-68 °C (CH_2Cl_2/hexane); ν_{max} / cm^{-1}: 3319 (s), 2927 (s), 1625 (s), 1572 (s), 1267 (s), 1240 (s); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.31-7.22 (5H, m, 2 × C**11**-H, 2 × C**12**-H, C**13**-H), 5.44 (1H, br. s, NH), 4.92 (1H, br. s, NH), 4.40 (2H, d, *J* = 6.0 Hz, C**9**-

H_2), 2.45 (1H, m, C**7**-H), 1.45 (1H, m, 1 × C**4**-H), 1.37-1.28 (4H, m, C**2**-H_2, C**3**-H_2), 1.19 (1H, m, 1 × C**4**-H), 0.89-0.84 (4H, m, C**1**-H_3, 1 × C**6**-H), 0.13 (1H, m, 1 × C**6**-H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 159.5 (C**8**), 139.5 (C**10**), 128.5, 127.4, 127.2 (C**11**, C**12**, C**13**), 44.2 (C**9**), 31.7 (C**3**), 27.0 (C**4**), 26.7 (C**7**), 22.6 (C**2**), 18.1 (C**5**), 14.0 (C**1**), 12.8 (C**6**); HRMS: (ESI+) Calculated for $C_{15}H_{23}N_2O$: 247.1805. Found $[M + H]^+$: 247.1804. *The relative stereochemistry of this compound was corroborated by nOe experiments (as indicated on the compound structure). A strong nOe was observed between C7-H to C5-H. No significant nOe was observed between C7-H and C4-H_2.*

3-Benzyl-6-butyl-1,3-diazepane-2,4-dione (9v') *and* 3-Benzyl-5-butyl-1,3-diazepane-2,4-dione (9v)

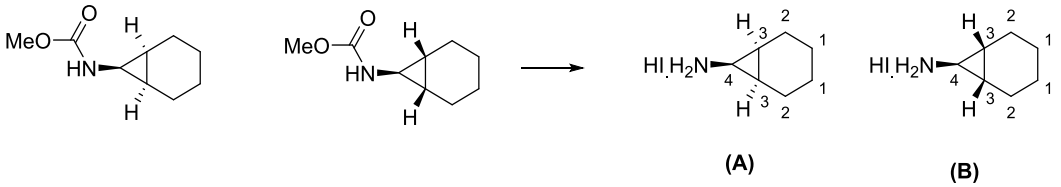


General Procedure B: Urea ***cis*-5v** (37.0 mg, 0.15 mmol) and $[Rh(cod)_2]BARF$ (7.5 mol%) were employed and the reaction was stirred for 38 h at 90 °C. The crude mixture was purified by column chromatography (20% EtOAc/hexane) to yield the title compound **9v'** and **9v** (24.0 mg, 58%, 10:1, **9v'**:**9v**) as a yellow oil. Analysis of the crude reaction mixture by ^{1}H NMR revealed a 5:1 (**9v'**:**9v**) mixture of products.

Data for product **9v'**: ν_{max} / cm^{-1}: 3304 (m), 2925 (m), 1709 (s), 1537 (s), 1260 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.75 (1H, br. s, NH), 7.39-7.20 (5H, m, 2 × C**8**-H, 2 × C**9**-H, C**10**-H), 4.50 (2H, d, *J* = 6.0 Hz, C**6**-H_2), 4.04 (1H, dd, *J* = 11.0, 7.5 Hz, 1 × C**5**-H), 3.44 (1H, dd, *J* = 11.0, 7.0 Hz, 1 × C**5**-H), 2.69 (1H, m, 1 × C**3**-H), 2.35-2.26 (2H, m, 1 × C**3**-H, C**4**-H), 1.52-1.26 (6H, m, C**11**-H_2, C**12**-H_2, C**13**-H_2), 0.91 (3H, t, *J* = 7.0 Hz, C**14**-H_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.7 (C**2**), 153.0 (C**1**), 138.3 (C**7**), 128.6, 127.6, 127.3 (C**8**, C**9**, C**10**), 51.2 (C**5**), 43.8 (C**6**), 39.9 (C**3**), 33.8 (C**11**), 30.7 (C**4**), 29.5 (C**12**), 22.6 (C**13**), 13.9 (C**14**); HRMS: (ESI^+) Calculated for $C_{16}H_{22}N_2NaO_2$: 297.1573. Found $[M + Na]^+$: 297.1572.

Data for product **9v**: *Partial characterization data for compound **9v** is presented on S34-35.*

(1*R,6*S**,7*S**)-Bicyclo[4.1.0]heptan-7-amine hydroiodide (A) *and* (1*R**,6*S**,7*R**)-Bicyclo[4.1.0]heptan-7-amine hydroiodide (B)**



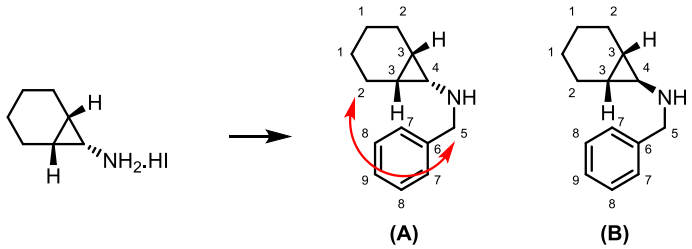
Iodotrimethylsilane (2.45 mL, 17.2 mmol) was added to a stirred solution of methyl ((1*R**,6*S**,7*S**)-bicyclo[4.1.0]heptan-7-yl)carbamate[9] (1.46 g, 8.61 mmol), in CH_2Cl_2 (86 mL) at r.t.. The reaction mixture was heated at reflux for 1 h before cooling to r.t.. MeOH (17 mL) was added and the reaction mixture was heated at reflux for 30 minutes before cooling to r.t. and concentrated *in vacuo*. The resulting orange solid was suspended in Et_2O (20 mL) and filtered, washing with Et_2O, to yield the title compounds (1.79 g, 87%, 3:1 d.r., **A**:**B**) as a brown solid. *The product diastereomers were not separable at this point.*

Data for the mixture of compounds: ν_{max} / cm^{-1}: 2922 (s), 1571 (m), 1352 (m), 1066 (s); HRMS: (ESI^+) Calculated for $C_7H_{14}N$: 112.1121. Found $[M+H]^+$: 112.1123.

Data for major compound **A**: ^{1}H NMR (MeOD-d_4, 400 MHz): δ 2.53 (1H, t, *J* = 8.0 Hz, C**4**-H), 2.13-2.03 (2H, m, 2 × C**2**-H), 1.56-1.46 (2H, m, 2 × C**2**-H), 1.46-1.36 (2H, m, 2 × C**1**-H), 1.33-1.13 (4H, m, 2 × C**1**-H, 2 × C**3**-H); ^{13}C NMR (MeOD-d_4, 100 MHz): δ 31.1 (C**4**), 22.0 (C**1**), 17.7 (C**2**), 11.4 (C**3**).

Data for major compound **B**: ^{1}H NMR (MeOD-d_4, 400 MHz): δ 2.36 (1H, t, *J* = 8.0 Hz, C**4**-H), 1.98-1.85 (2H, m, 2 × C**2**-H), 1.76-1.67 (2H, m, 2 × C**2**-H), 1.35-1.07 (6H, m, 4 × C**1**-H, 2 × C**3**-H); ^{13}C NMR (MeOD-d_4, 100 MHz): δ 34.1 (C**4**), 22.4 (C**2**), 21.8 (C**1**), 17.0 (C**3**).

(1*R,6*S**,7*S**)-*N*-Benzylbicyclo[4.1.0]heptan-7-amine (A)** ***and*** **(1*R**,6*S**,7*R**)-*N*-Benzylbicyclo[4.1.0]heptan-7-amine (B)**



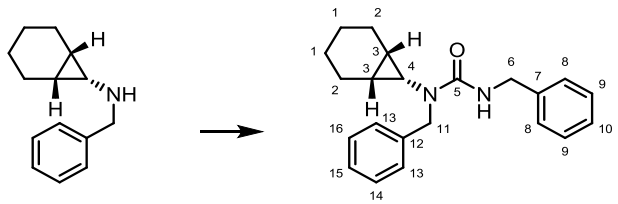
To a stirred solution of (1*R**,6*S**,7*S**)-bicyclo[4.1.0]heptan-7-amine hydroiodide (1.50 g, 6.3 mmol, 3:1 d.r.) in MeOH (14 mL) was added $NaHCO_3$ (2.11 g, 25.1 mmol) and benzaldehyde (0.58 mL, 5.65 mmol) before the reaction mixture was heated at reflux for 8 h. The reaction

mixture was cooled to 0 °C before $NaBH_4$ (285 mg, 7.52 mmol) was added portionwise. The reaction mixture was warmed to r.t. and stirred for 16 h. The reaction mixture was concentrated *in vacuo* before adding water (80 mL) and extracting with CH_2Cl_2 (3 × 30 mL). The combined organics were dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography (30% EtOAc/hexane) to afford diastereomer **A** (807 mg, 71%) as a pale yellow oil, and diastereomer **B** (267 mg, 23%) as a pale yellow oil.

Data for product **A**: ν_{max} / cm^{-1}: 3290 (br.), 2927 (s), 1642 (s), 1542 (m), 1495 (m), 1452 (m); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.40-7.21 (5H, m, 2 × C**7**-H, 2 × C**8**-H, C**9**-H), 3.81 (2H, s, C**5**-H_2), 2.03 (1H, t, *J* = 7.5 Hz, C**4**-H), 1.85-1.73 (2H, m, 2 × C**2**-H), 1.59-1.49 (2H, m, 2 × C**2**-H), 1.47-1.31 (2H, m, 2 × C**1**-H), 1.30-1.17 (2H, m, 2 × C**1**-H), 0.86-0.83 (2H, m, 2 × C**3**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 141.4 (C**6**), 128.4, 128.3, 126.9 (C**7**, C**8**, C**9**), 54.0 (C**5**), 36.4 (C**4**), 22.8 (C**1**), 18.5 (C**2**), 12.3 (C**3**); HRMS: (ESI^+) Calculated for $C_{14}H_{20}N$: 202.1590. Found $[M+H]^+$: 202.1596. *The relative stereochemistry of this compound was corroborated by nOe experiments (as indicated on the compound structure). An nOe was observed between C**5**-H_2 and C**2**-H_2. No significant nOe was observed between C**5**-H_2 and C**3**-H.*

Data for product **B**: ν_{max} / cm^{-1}: 2923 (s), 2850 (s), 1449 (s), 1295 (m); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.35-7.23 (5H, m, 2 × C**7**-H, 2 × C**8**-H, C**9**-H), 3.81 (2H, s, C**5**-H_2), 1.89 – 1.80 (3H, m, 2 × C**2**-H, C**4**-H), 1.72 (1H, br. s, NH), 1.62-1.55 (2H, m, 2 × C**2**-H), 1.25-1.16 (2H, m, 2 × C**1**-H), 1.09-1.01 (2H, m, 2 × C**2**-H), 0.94-0.87 (2H, m, 2 × C**3**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 140.7 (C**6**), 128.3, 128.3, 126.8 (C**7**, C**8**, C**9**), 53.6 (C**5**), 42.3 (C**4**), 23.0 (C**2**), 21.8 (C**1**), 18.8 (C**3**); HRMS: (ESI^+) Calculated for $C_{14}H_{20}N$: 202.1590. Found $[M + H]^+$: 202.1589.

1,3-Dibenzyl-1-((1*R,6*S**,7*S**)-bicyclo[4.1.0]heptan-7-yl)urea (5w)**

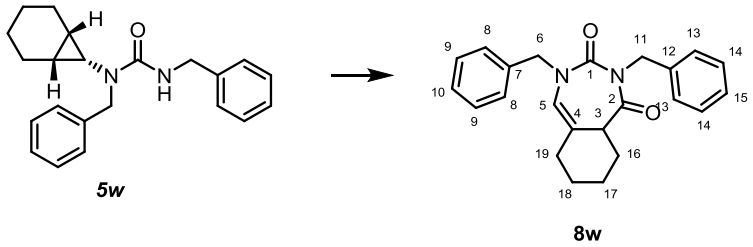


5w

General procedure A: (1*R**,6*S**,7*S**)-*N*-Benzylbicyclo[4.1.0]heptan-7-amine (750 mg, 3.73 mmol) was employed and the residue was purified by column chromatography (15-20% EtOAc/hexane) to provide the title compound **5w** (1.16 g, 93%) as a colorless solid; m.p.: 105-107 °C (CH_3Cl/hexane); ν_{max} / cm^{-1}: 2924 (w), 1632 (s), 1504 (s), 1278 (m), 1231 (m); ^1H NMR (DMSO-d_6, 500 MHz, 70 °C): δ 7.32-7.19 (10H, m, 2 × C**8**-H, 2 × C**9**-H, C**10**-H, 2 ×

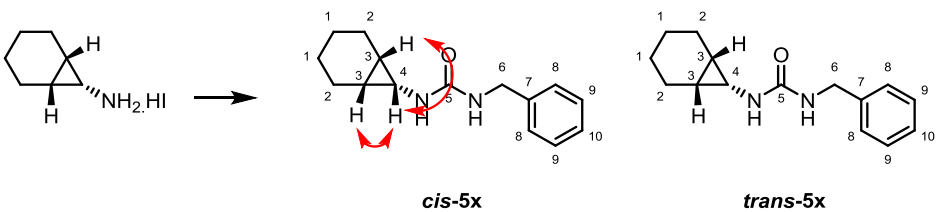
C**13**-H, 2 × C**14**-H, 2 × C**15**-H), 6.63 (1H, m, NH), 4.53 (2H, br. s, C**11**-H_2), 4.33 (2H, d, *J* = 5.9 Hz, C**6**-H_2), 2.23 (1H, t, *J* = 7.4 Hz, C**4**-H), 1.82 (2H, m, 2 × C**2**-H), 1.56 (2H, m, 2 × C**2**-H), 1.30-1.17 (4H, m, C**1**-H), 1.10 (2H, m, C**3**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.2 (C**5**), 140.2 (C**7**), 138.5 (C**12**), 127.6, 127.5, 127.3, 126.8, 126.2, 125.9 (C**8**, C**9**, C**10**, C**13**, C**14**, C**15**), 49.8 (C**11**), 43.5 (C**6**), 34.1 (C**4**), 20.7 (C**1**), 18.5 (C**2**), 13.9 (C**3**); HRMS: (ESI$^+$) Calculated for $C_{22}H_{26}N_2NaO$: 357.1937. Found [M + Na]$^+$: 357.1937.

2,4-Dibenzyl-4,6,7,8,9,9a-hexahydro-1*H*-benzo[e][1,3]diazepine-1,3(2*H*)-dione (8w)



General Procedure B: Urea **5w** (50.2 mg, 0.15 mmol) and [Rh(cod)$_2$]BARF (10.0 mol%) were employed and the reaction was stirred for 96 h at 90 °C. The crude mixture was purified by column chromatography (10% EtOAc/hexane) to yield the title compound **8w** (28.2 mg, 54%) as a colorless oil; ν_{max} / cm^{-1}: 2934 (w), 2863 (w), 1697 (s), 1645 (s), 1404 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.33-7.24 (8H, m, 2 × C**9**-H, C**10**-H, 2 × C**13**-H, 2 × C**14**-H, C**15**-H), 7.07-7.05 (2H, m, C**8**-H), 5.82 (1H, s, C**5**-H), 5.24 (1H, d, *J* = 14.5 Hz, C**11**-H), 4.92-4.84 (2H, m, 1 × C**6**-H, 1 × C**11**-H), 4.59 (1H, d, *J* = 15.0 Hz, C**6**-H), 3.16 (1H, m, C**3**-H), 2.39 (1H, m, C**16**-H), 2.27 (1H, m, C**18**-H), 2.13 (1H, m, C**16**-H), 1.81-1.67 (3H, m, 1 × C**17**-H, C**18**-H, C**19**-H), 1.50 (1H, m, C**19**-H), 1.33 (1H, m, C**17**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.7 (C**2**), 154.5 (C**1**), 138.0 (C**12**), 136.4 (C**7**), 128.8, 128.5, 128.4, 128.2, 127.7, 127.2 (C**8**, C**9**, C**10**, C**13**, C**14**, C**15**), 123.2 (C**5**), 52.8 (C**6**), 47.7 (C**11**), 41.2 (C**3**), 27.0 (C**16**), 23.1 (C**17**), 22.7 (C**19**), 22.1 (C**18**); HRMS: (ESI$^+$) Calculated for $C_{23}H_{24}N_2NaO_2$: 383.1730. Found [M + Na]$^+$: 383.1739.

1-Benzyl-3-((1*R,6*S**,7*S**)-bicyclo[4.1.0]heptan-7-yl)urea (*cis*-5x) *and* 1-Benzyl-3-((1*R**,6*S**,7*S**)-bicyclo[4.1.0]heptan-7-yl)urea (*trans*-5x)**



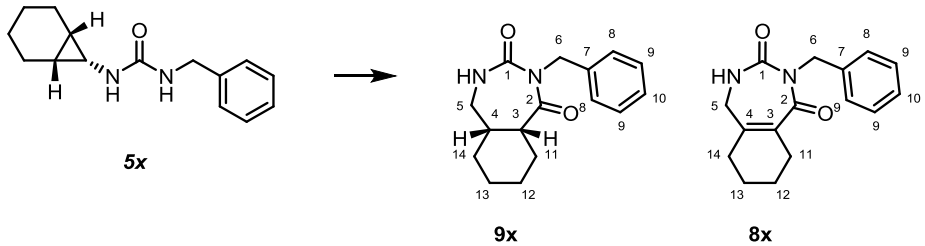
General procedure A: (1*R**,6*S**,7*S**)-Bicyclo[4.1.0]heptan-7-amine hydroiodide (480 mg, 3.73 mmol, 3:1 d.r.) was employed and the residue was purified by column chromatography (50% EtOAc/hexane) to provide the title compound ***cis*-5x** (378 mg, 77%, 4:1 d.r., ***cis*-5x**:***trans*-5x**) as a colorless solid.

Data for the mixture of diastereomers: ν_{max} / cm^{-1}: 3316 (s), 2924 (s), 2850 (s), 1629 (s), 1565 (s), 1249 (s); *m/z* (ESI^+) HRMS: Calculated for $C_{15}H_{21}N_2O$: 245.1648. Found $[M + H]^+$: 245.1646.

Data for major diastereomer ***cis*-5x**: ^1H NMR ($CDCl_3$, 400 MHz): δ 7.36-7.25 (5H, m, 2 × C**8**-H, 2 × C**9**-H, C**10**-H), 5.23 (1H, br. s, NH), 4.47 (2H, d, *J* = 6.0 Hz, C**6**-H_2) 2.33 (1H, t, *J* = 7.0 Hz, C**4**-H), 1.87 (2H, m, 2 × C**2**-H), 1.44-1.34 (2H, m, 2 × C**2**-H), 1.27-1.18 (4H, m, 4 × C**1**-H), 1.08-1.03 (2H, m, 2 × C**3**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.3 (C**5**), 139.5 (C**7**), 128.7, 127.6, 127.3 (C**8**, C**9**, C**10**), 44.4 (C**6**), 29.0 (C**4**), 21.8 (C**1**), 18.0 (C**2**), 12.2 (C**3**). *The relative stereochemistry of this compound was corroborated by nOe experiments (as indicated on the compound structure). A strong nOe was observed between C**4**-H to C**3**-H.*

Data for minor diastereomer ***trans*-5x**: *Characteristic signals only*: ^1H NMR ($CDCl_3$, 400 MHz): δ 5.05 (1H, br. s, NH), 4.66 (1H, br. s, NH), 2.11 (1H, m, C**4**-H), 1.66 – 1.58 (2H, m, 2 × C**2**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.3 (C**5**), 139.6 (C**7**), 128.7, 127.2, (ArCH), 44.1 (C**6**), 34.0 (C**4**), 22.3 (C**2**), 21.3 (C**1**), 19.7 (C**3**).

(5a*S,9a*R**)-2-Benzyloctahydro-1*H*-benzo[e][1,3]diazepine-1,3(2*H*)-dione (9x)** ***and*** **2-Benzyl-4,5,6,7,8,9-hexahydro-1*H*-benzo[e][1,3]diazepine-1,3(2*H*)-dione (8x)**

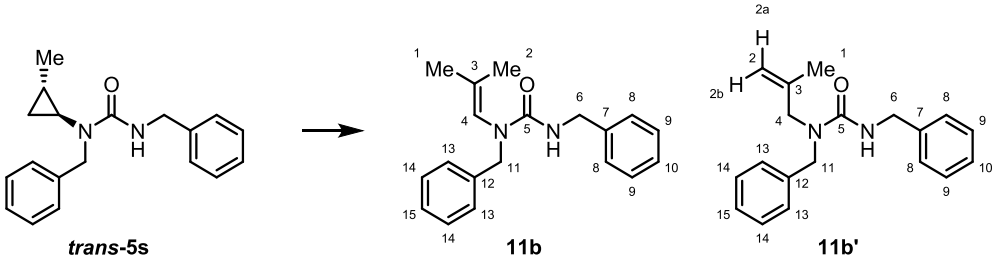


General Procedure B: Urea **5x** (36.7 mg, 0.15 mmol) and $[Rh(cod)_2]BARF$ (7.5 mol%) were employed and the reaction was stirred for 48 h at 110 °C. The crude mixture was purified by column chromatography (15-25% EtOAc/hexane) to yield the title compound **9x** (20.7 mg, 51%) as a pale brown oil and **8x** (6.8 mg, 17%) as a colorless oil. Analysis of the crude reaction mixture by ^1H NMR revealed a 3:1 (**9x**:**8x**) mixture of products.

Data for major product **9x**: ν_{max} / cm^{-1}: 3304 (m), 2929 (m), 1707 (s), 1536 (s), 1380 (s), 1247 (s); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.76 (1H, br. s, NH), 7.35-7.24 (5H, m, 2 × C**8**-H, 2 × C**9**-H, C**10**-H), 4.53 (1H, ddd, *J* = 15.0 Hz, 5.5 Hz, 1 × C**6**-H), 4.47 (1H, dd, *J* = 15.0 Hz, 5.5 Hz, 1 × C**6**-H), 3.67 (1H, dd, *J* = 11.0 Hz, 6.0 Hz, 1 × C**5**-H), 3.61 (1H, dd, *J* = 11.0 Hz, 2.0 Hz, 1 × C**5**-H), 2.69 (1H, td, *J* = 7.0, 4.0 Hz, C**3**-H), 2.33 (1H, m, C**4**-H), 2.04 (1H, m, 1 × C**14**-H), 1.76 (1H, m, 1 × C**11**-H), 1.64-1.50 (3H, m, 1 × C**12**-H, 1 × C**13**-H, 1 × C**14**-H), 1.27-1.13 (3H, m, 1 × C**11**-H, 1 × C**12**-H, 1 × C**13**-H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 178.1 (C**2**), 153.5 (C**1**), 138.2 (C**7**), 128.6, 127.6, 127.3 (C**8**, C**9**, C**10**), 49.3 (C**5**), 44.2 (C**3**), 43.8 (C**6**), 31.2 (C**4**), 27.7 (C**11**), 23.4 (C**12**), 22.9 (C**14**), 22.6 (C**13**); HRMS: (ESI^+) Calculated for $C_{16}H_{20}N_2NaO_2$: 295.1417. Found $[M + Na]^+$: 295.1424.

Data for minor product **8x**: ν_{max} / cm^{-1}: 3298 (m), 2930 (m), 1699 (s), 1679 (m), 1537 (s), 1356 (s), 1250 (s); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.75 (1H, br. s, NH), 7.35-7.22 (5H, m, 2 × C**8**-H, 2 × C**9**-H, C**10**-H), 4.53 (2H, d, *J* = 6.0 Hz, C**6**-H_2), 4.26 (2H, s, C**5**-H_2), 2.35-2.32 (2H, m, C**14**-H_2), 2.21-2.17 (2H, m, C**11**-H_2), 1.79-1.70 (4H, m, C**12**-H_3, C**13**-H_3); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 172.2 (C**2**), 154.8 (C**4**), 152.7 (C**1**), 138.5 (C**7**), 131.3 (C**3**), 128.6, 127.5, 127.2 (C**8**, C**9**, C**10**), 51.5 (C**5**), 43.6 (C**6**), 24.4 (C**14**), 21.7, 21.5 (C**12**, C**13**), 19.8 (C**11**); HRMS: (ESI^+) Calculated for $C_{16}H_{18}N_2NaO_2$: 293.1260. Found $[M + Na]^+$: 293.1264.

1,3-Dibenzyl-1-(2-methylprop-1-en-1-yl)urea (11b) ***and*** **1,3-Dibenzyl-1-(2-methylallyl)urea (11b')**



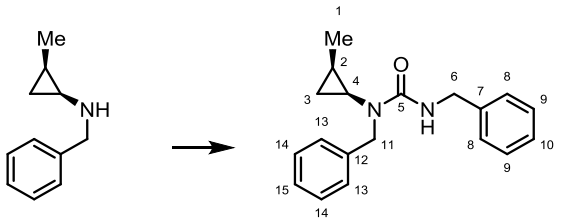
To a resealable tube containing $[Rh(cod)_2]BF_4$ (4.00 mg, 0.01 mmol) and PPh_3 (7.90 mg, 0.03 mmol) under an atmosphere of argon was added urea ***trans*-5s** (58.9 mg, 0.20 mmol) in anhydrous toluene (2 mL). The tube was sealed and heated at 100 °C and stirred for 2 h. The mixture was cooled to r.t. and concentrated *in vacuo*. The crude mixture was purified by column chromatography (25% EtOAc/hexane) to yield the title compounds **11b** and **11b'** (50.7 mg, 86%, 2:1, **11b**:**11b'**) as a colorless oil. *The isomers could not be separated by silica gel column chromatography*. Analysis of the crude reaction mixture by ^{1}H NMR revealed a 2:1 (**11b**:**11b'**) mixture of products.

Data for the mixture of compounds: ν_{max} / cm^{-1}: 3355 (m), 1643 (s), 1510 (s), 1496 (s), 1434 (m), 1264 (s); HRMS: (ESI^+) Calculated for $C_{19}H_{23}N_2O$: 295.1805. Found $[M + H]^+$: 295.1804.

Data for compound **11b**: ^1H NMR ($CDCl_3$, 400 MHz): δ 7.37-7.23 (10H, m, 2 × C**8**-H, 2 × C**9**-H, C**10**-H, 2 × C**13**-H, 2 × C**14**-H, C**15**-H), 5.67 (1H, s, C**4**-H), 5.11 (1H, t, *J* = 6.0 Hz, NH), 4.62 (2H, s, C**11**-H_2), 4.47 (2H, d, *J* = 6.0 Hz, C**6**-H_2), 1.66 (3H, s, C**1**/**2**-H_3), 1.50 (3H, s, C**1**/**2**-H_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 157.0 (C**5**), 139.8 (C**7**), 138.4 (C**12**), 137.9 (C**3**), 128.6, 128.5. 128.3. 127.5, 127.4, 127.0 (C**8**, C**9**, C**10**, C**13**, C**14**, C**15**), 122.3 (C**4**), 51.1 (C**11**), 44.8 (C**6**), 21.9, 17.6 (C**1**, C**2**).

Data for compound **11b'**: ^1H NMR ($CDCl_3$, 400 MHz): δ 7.37-7.23 (10H, m, 2 × C**8**-H, 2 × C**9**-H, C**10**-H, 2 × C**13**-H, 2 × C**14**-H, C**15**-H), 4.92 (1H, s, C**2**-H), 4.89 (1H, s, C**2**-H), 4.86 (1H, br. s, NH), 4.54 (2H, s, C**11**-H_2), 4.46 (2H, d, *J* = 6.0 Hz, C**6**-H_2), 3.79 (2H, s, C**4**-H_2), 1.70 (3H, s, C**1**-H_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.5 (C**5**), 141.3 (C**3**), 139.6 (C**7**), 138.0 (C**12**), 128.7, 128.5, 128.4, 127.5, 127.3, 127.1 (C**8**, C**9**, C**10**, C**13**, C**14**, C**15**), 111.9 (C**1**), 52.7 (C**4**), 50.4 (C**11**), 44.9 (C**6**), 19.9 (C**1**).

(1*S,2*R**)-1,3-Dibenzyl-1-(2-methylcyclopropyl)urea (*cis*-5s)**

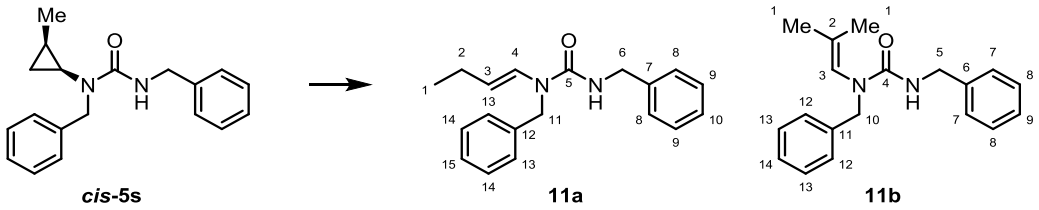


***cis*-5s**

General procedure A: (1*S**,2*R**)-*N*-Benzyl-2-methylcyclopropan-1-amine[5] (484 mg, 3.00 mmol) and benzyl isocyanate (371 μL, 3.00 mmol) were employed. The crude mixture was purified by column chromatography (30% EtOAc/hexane) to yield the title compound ***cis*-5s** (744 mg, 84%) as a colorless oil; ν_{max} / cm^{-1}: 3326 (m), 2969 (s), 1639 (s), 1511 (s), 1453 (s), 1229 (m), 1056 (m); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.37-7.23 (10H, m, 2 × C**8**-H, 2 × C**9**-H, C**10**-H, 2 × C**13**-H, 2 × C**14**-H, C**15**-H), 5.53 (1H, t, *J* = 5.5 Hz, NH), 4.88 (1H, d, *J* = 15.0 Hz, 1 × C**11**-H), 4.58-4.46 (2H, m, C**6**-H_2), 4.33 (1H, d, *J* = 15.0 Hz, 1 × C**11**-H), 2.37 (1H, ddd, *J* = 8.0, 6.0, 4.5 Hz, C**4**-H), 1.09-0.96 (4H, m, C**1**-H_3, C**2**-H), 0.89 (1H, m, 1 × C**3**-H), 0.40 (1H, m, 1 × C**3**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 159.5 (C**5**), 139.6 (C**7**), 139.0 (C**11**), 128.6, 128.4, 128.2, 127.7, 127.2, 126.9 (C**8**, C**9**, C**10**, C**13**, C**14**, C**15**), 51.7 (C**11**), 45.0 (C**6**), 32.6 (C**4**), 14.7 (C**2**), 13.6 (C**3**), 12.7 (C**1**); HRMS: (ESI^+) Calculated for $C_{19}H_{22}N_2NaO$: 317.1624.

Found [M + Na]$^+$: 317.1613. *The relative stereochemistry was assigned as the opposite diastereomer of* ***trans-5s***.

(*E*)-1,3-Dibenzyl-1-(but-1-en-1-yl)urea (11a) ***and*** **1,3-Dibenzyl-1-(2-methylprop-1-en-1-yl)urea (11b)**

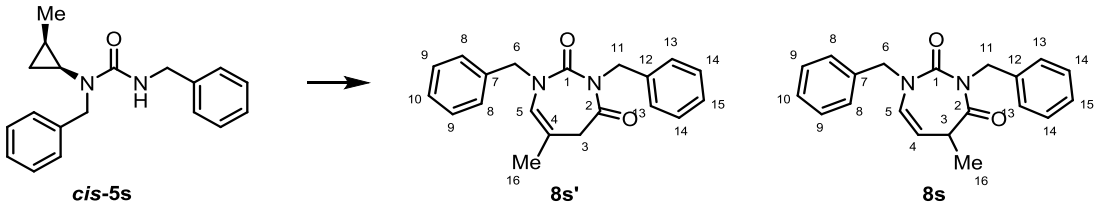


To a resealable tube containing $[Rh(cod)_2]BF_4$ (4.00 mg, 0.01 mmol) and PPh_3 (7.90 mg, 0.03 mmol) under an atmosphere of argon was added urea ***cis*****-5s** (58.9 mg, 0.20 mmol) in anhydrous toluene (2 mL). The tube was sealed and heated at 100 °C and stirred for 2 h. The mixture was cooled to r.t. and concentrated *in vacuo*. The crude mixture was purified by column chromatography (25% EtOAc/hexane) to yield the title compound **11a** (21.8 mg, 37%) as a colorless oil. Analysis of the crude reaction mixture by ^{1}H NMR revealed an 11:1 (**11a**:**11b**) mixture of products.

Data for compound **11a**: ν_{max} / cm^{-1}: 3322 (s), 1628 (s), 1531 (s), 1452 (s), 1248 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.35-7.21 (10H, m, 2 × C**8**-H, 2× C**9**-H, C**10**-H, 2 × C**13**-H, 2 × C**14**-H, C**15**-H), 6.81 (1H, d, *J* = 14.0 Hz, C**4**-H), 5.03-4.93 (2H, m, C**3**-H, NH), 4.73 (2H, s, C**11**-H_2), 4.44 (2H, d, *J* = 5.5 Hz, C**6**-H_2), 2.02 (2H, dq, *J* = 7.0, 7.0 Hz, C**2**-H_2), 0.95 (3H, t, *J* = 7.0 Hz, C**1**-H_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 156.0 (C**5**), 139.1 (C**7**), 137.3 (C**12**), 128.7, 128.6, 127.5, 127.3, 127.2, 126.8, 126.5 (C**4**, C**8**, C**9**, C**10**, C**13**, C**14**, C**15**), 114.8 (C**3**), 48.7 (C**11**), 44.9 (C**6**), 23.5 (C**2**), 14.7 (C**1**); HRMS: (ESI$^+$) Calculated for $C_{19}H_{23}N_2O$: 295.1805. Found [M + H]$^+$: 295.1808.

Data for compound **11b**: *Full characterization data for compound* ***11b*** *is presented on S47-S48.*

1,3-Dibenzyl-5-methyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8s') and 1,3- Dibenzyl-6-methyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8s)

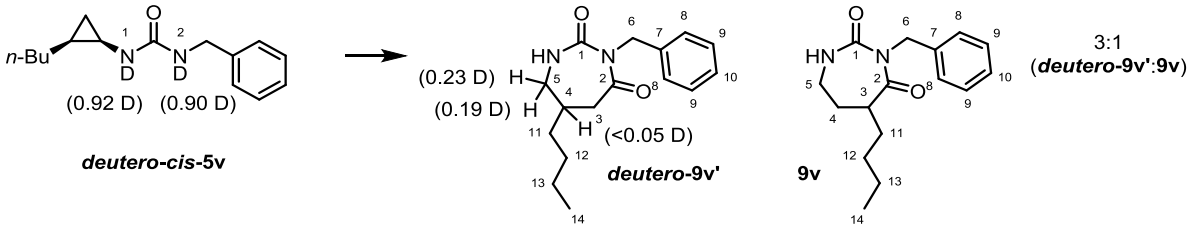


General Procedure B: Urea ***cis*-5s** (44.2 mg, 0.15 mmol) and $[Rh(cod)_2]BARF$ (7.5 mol%) were employed and the reaction was stirred for 72 h at 100 °C. The crude mixture was purified by column chromatography (25% EtOAc/hexane) to yield the title compound **8s'** (32.6 mg, 68%) as a pale yellow oil. Analysis of the crude reaction mixture by ^1H NMR revealed a 5:1 (**8s'**:**8s**) mixture of products.

Data for major regioisomer **8s'**: ν_{max} / cm^{-1}: 2971 (s), 1698 (s), 1646 (s), 1408 (s), 1214 (s); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.35-7.21 (8H, m, 2 × C**9**-H, C**10**-H, 2 × C**13**-H, 2 × C**14**-H, C**15**-H), 7.08-7.04 (2H, m, 2 × C**8**-H), 5.78 (1H, q, *J* = 1.5 Hz, C**5**-H), 5.04 (2H, s, C**11**-H_2), 4.71 (2H, s, C**6**-H_2), 3.04 (2H, s, C**3**-H_2), 1.86 (3H, s, C**16**-H_3); ^{13}C NMR ($CDCl_3$, 100 MHz,): δ 169.2 (C**2**), 154.1 (C**1**), 137.6 (C**12**), 136.3 (C**7**), 128.7, 128.4, 128.1, 127.7, 127.6, 127.2 (C**8**, C**9**, C**10**, C**13**, C**14**, C**15**), 124.5 (C**5**), 124.0 (C**4**), 52.9 (C**6**), 47.6 (C**11**), 40.8 (C**3**), 19.6 (C**16**); HRMS: (ESI^+) Calculated for $C_{20}H_{20}N_2NaO_2$: 343.1417. Found $[M + Na]^+$: 343.1408.

Data for minor regioisomer **8s**: *Full characterization data for compound **8s** is presented on S30-S31.*

3-Benzyl-6-butyl-1,3-diazepane-2,4-dione (*deutero*-9v') *and* 3-Benzyl-5-butyl-1,3-diazepane-2,4-dione (9v)



***Deutero-cis*-5v** was initially prepared by repeatedly dissolving ***cis*-5v** in MeOD-d_4 and concentrating the resulting solution *in-vacuo*. *92% deuterium incorporation at N**1** and 90% deuterium incorporation at N**2** was measured by ^1H NMR.*

Data for ***deutero-cis*-5v**: ^1H NMR ($CDCl_3$, 500 MHz): δ 7.31-7.22 (5H, m, 2 × C**11**-H, 2 × C**12**-H, C**13**-H), 5.44 (0.08H, br. s, NH), 4.92 (0.10H, br. s, NH), 4.40 (2H, d, *J* = 6.0 Hz, C**9**-

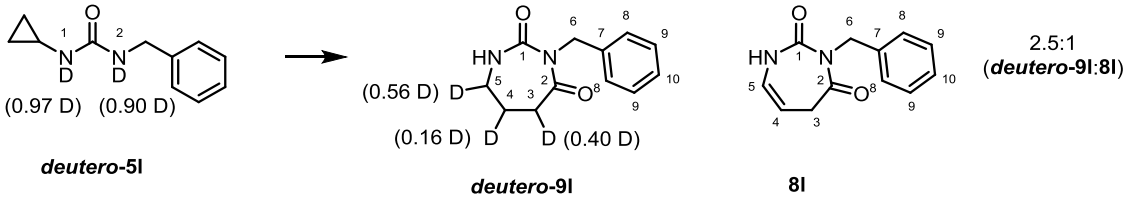
H_2), 2.45 (1H, m, C**7**-H), 1.45 (1H, m, 1 × C**4**-H), 1.37-1.28 (4H, m, C**2**-H_2, C**3**-H_2), 1.19 (1H, m, 1 × C**4**-H), 0.89-0.84 (4H, m, C**1**-H_3, 1 × C**6**-H), 0.13 (1H, m, 1 × C**6**-H). *$CDCl_3$ was base filtered (K_2CO_3 plug) prior to use.*

General Procedure B: Urea ***deutero-cis*-5v** (37.0 mg, 0.150 mmol) and $[Rh(cod)_2]$BARF (7.5 mol%) were employed and the reaction was stirred for 43 h at 90 °C. The crude mixture was purified by column chromatography (20% EtOAc/hexane) to yield the title compound ***deutero*-9v'** (19.2 mg**,** 47%) as a yellow oil. *Analysis of the product revealed 23% and 16% deuterium incorporation at the diastereotopic C**5** positions. <5% deuterium incorporation was measured at C**4**. **9v** could not be isolated in a pure form and therefor deuterium incorporation could not be confirmed.*

Data for product ***deutero*-9v'**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.75 (1H, br. s, NH), 7.39-7.20 (5H, m, 2 × C**8**-H, 2 × C**9**-H, C**10**-H), 4.50 (2H, d, *J* = 6.0 Hz, C**6**-H_2), 4.04 (0.81H, dd, *J* = 11.0, 7.5 Hz, 1 × C**5**-H), 3.44 (0.77H, dd, *J* = 11.0, 7.0 Hz, 1 × C**5**-H), 2.69 (1H, m, 1 × C**3**-H), 2.35-2.26 (1.96H, m, 1 × C**3**-H, C**4**-H), 1.52-1.26 (6H, m, C**11**-H_2, C**12**-H_2, C**13**-H_2), 0.91 (3H, t, *J* = 7.0 Hz, C**14**-H_3). ^{2}H NMR ($CHCl_3$, 500 MHz): δ 8.74 (0.34 D, br. s, ND), 4.05 (0.71D, br. s, 1 × C**5**-D), 3.44 (1D, br. s, 1 × C**5**-D), 2.28 (0.04D, br. m, C**4**-D).

Data for minor compound **9v**: *Partial characterization data for compound **9v** is presented on S34-35.*

3-Benzyl-1,3-diazepane-2,4-dione (*deutero*-9l) *and* 1-Benzyl-3,6-dihydro-1*H*-1,3-diazepine-2,7-dione (8l)



***deutero*-5l** ***deutero*-9l** **8l**

***Deutero*-5l** was initially prepared by repeatedly dissolving **5l** in MeOD-d_4 and concentrating the resulting solution *in-vacuo*. *97% deuterium incorporation at N**1** and 90% deuterium incorporation at N**2** was measured by ^{1}H NMR.*

Data for ***deutero*-5l**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37-7.25 (2 × C**6**-H, 2 × C**7**-H, C**8**-H), 5.31 (0.03H, br. s, NH), 4.79 (0.10H, br. s, NH), 4.47 (2H, d, *J* = 6.0 Hz, C**4**-H_2), 2.46 (1H, tt,

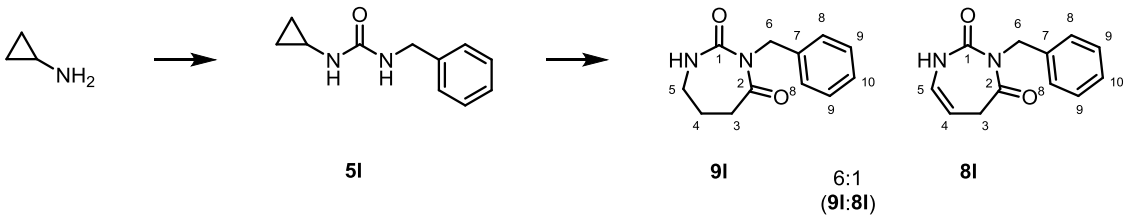
J = 7.0, 3.5 Hz, C**2**-H), 0.76-0.71 (2H, m, 2 × C**1**-H), 0.60-0.57 (2H, m, 2 × C**1**-H). *$CDCl_3$ was base filtered (K_2CO_3 plug) prior to use.*

General Procedure B: Urea ***deutero*-5l** (28.5 mg, 0.150 mmol) and [Rh(cod)$_2$]BARF (5.0 mol%) were employed and the reaction was stirred for 24 h at 90 °C. The crude mixture was purified by column chromatography (30% EtOAc/hexane) to yield the title compound (20.5 mg**,** 63%, 2.5:1, ***deutero*-9l**:**8l**) as a yellow oil. *Analysis of the product revealed 56% deuterium incorporation at C**5**, 16% at C**4** and 40% at C**3**. No deuterium incorporation was observed in **8l**.*

Data for product ***deutero*-9l**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.79 (1H, br. s, NH), 7.35-7.21 (5H, m, 2 × C**8**-H, 2 × C**9**-H, C**10**-H), 4.50 (2H, d, *J* = 6.0 Hz, C**6**-H$_2$), 3.89 (1.44H, t, *J* = 7.0 Hz, C**5**-H$_2$), 2.61 (1.60H, t, *J* = 7.0 Hz, C**3**-H$_2$), 2.04 (1.84H, tt, *J* = 7.0, 7.0 Hz, C**4**-H$_2$); ^{2}H NMR ($CHCl_3$, 500 MHz): δ 3.89 (0.56D, br. s, C**5**-D), 2.60 (0.49D, br. s, C**3**-D), 2.02 (0.06D, br. s, C**4**-D).

Data for minor compound **8l**: *Full characterization data for compound **8l** is presented on S34-35.*

Procedure for the one-step urea formation/carbonylative cyclization sequence

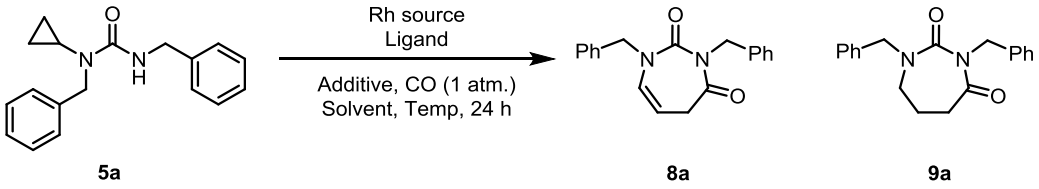


To a flame-dried flask, fitted with a magnetic stirrer under an atmosphere of nitrogen, was charged cyclopropylamine (0.069 mL, 1.0 mmol) and argon sparged 1,2-DCB (5 mL, 0.2 M) followed by benzyl isocyanate (0.124 mL, 1.00 mmol). The reaction mixture was heated to 80 ^{o}C to allow complete solvation of intermediate urea **5l**. Meanwhile, an oven dried reaction tube, fitted with a magnetic stirrer, was charged with [Rh(cod)$_2$]BARF (8.87 mg, 0.0075 mmol), and PPh_3 (3.93 mg, 0.015 mmol). The reaction tube was fitted with a rubber septum and purged with argon before the addition of the urea solution (0.75 mL, 0.015 mmol) by syringe. The resulting mixture was stirred for *ca.* 5 minutes at r.t.. The reaction tube was purged with CO and the reaction mixture was sparged with CO for 10 seconds before being heated to 100 ^{o}C for 24 h. The mixture was cooled to r.t., concentrated *in vacuo* and purified by flash column

chromatography (40% EtOAc/hexane) to yield the title compounds (18.7 mg, 57%, 6:1, **9l**:**8l**) as a yellow oil.

Selected Reaction Optimization Tables:

Initial optimization of parent substrate 5a;

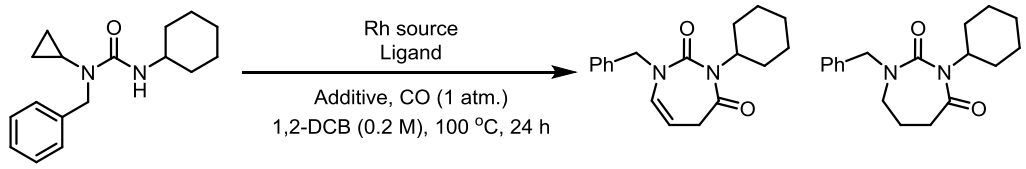


5a **8a** **9a**

Entry	Rh source	Ligand[a]	Solvent	Additive	T	Yield[b]	8a:9a
1	$[Rh(cod_2)]OTf$ (7.5 mol%)	$P(3,4,5\text{-}(F)_3C_6H_2)_3$	1,2-DCB (0.15 M)	-	130 °C	57%	4:1
2	$[Rh(cod)Cl]_2$ (3.75 mol%)	$P(3,4,5\text{-}(F)_3C_6H_2)_3$	1,2-DCB (0.15 M)	-	130 °C	16%	3:1
3	$[Rh(cod_2)]OTf$ (7.5 mol%)	PPh_3	1,2-DCB (0.15 M)	-	115 °C	70%	9:1
4	$[Rh(cod_2)]OTf$ (7.5 mol%)	PPh_3	1,2-DCB (0.15 M)	-	100 °C	65%	27:1
5	$[Rh(cod_2)]OTf$ (7.5 mol%)	PPh_3	1,2-DCB (0.15 M)	$PhCO_2H$ (100 mol%)	100 °C	77%	13:1
6	$[Rh(cod_2)]OTf$ (7.5 mol%)	PPh_3	1,2-DCB (0.15 M)	$PhCO_2H$ (10 mol%)	100 °C	76%	19:1
7	$[Rh(cod_2)]OTf$ (2.5 mol%)	PPh_3	1,2-DCB (0.2 M)	$PhCO_2H$ (10 mol%)	100 °C	76%[c]	19:1
8	$[Rh(cod_2)]BARF$ (3.5 mol%)	PPh_3	1,2-DCB (0.2 M)	$PhCO_2H$ (15 mol%)	100 °C	82%[c]	20:1

[a]2 eq. of ligand were employed relative to Rh loading. [b]*In-situ* yields are quoted. [c]Isolated yield.

Optimization of "challenging" substrate 5d;

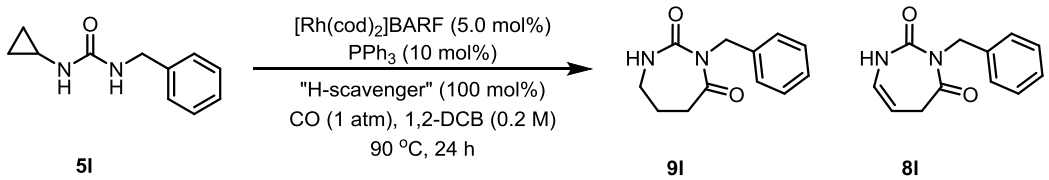


5d **8d** **9d**

Entry	Rh source	Ligand[a]	Additive	time	Yield[b]	8d:9d
1	[Rh(cod$_2$)]OTf (2.5 mol%)	PPh_3	$PhCO_2H$ (10 mol%)	24 h	23%	>15:1
2	[Rh(cod$_2$)]OTf (7.5 mol%)	PPh_3	$PhCO_2H$ (10 mol%)	24 h	45%	19:1
3	[Rh(cod$_2$)]BARF (3.5 mol%)	PPh_3	$PhCO_2H$ (10 mol%)	24 h	44%	17:1
4	[Rh(cod$_2$)]BARF (7.5 mol%)	PPh_3	$PhCO_2H$ (10 mol%)	24 h	53%	20:1
5	[Rh(cod$_2$)]BARF (7.5 mol%)	PPh_3	$PhCO_2H$ (10 mol%)	48 h	62%	18:1
6	[Rh(cod$_2$)]BARF (7.5 mol%)	PPh_3	$PhCO_2H$ (15 mol%)	72 h	69%[c]	23:1

[a]2 eq. of ligand were employed relative to Rh loading. [b]*In-situ* yields are quoted. [c]Isolated yield.

The effect of hydrogen scavengers on saturated/unsaturated product ratios;



5l **9l** **8l**

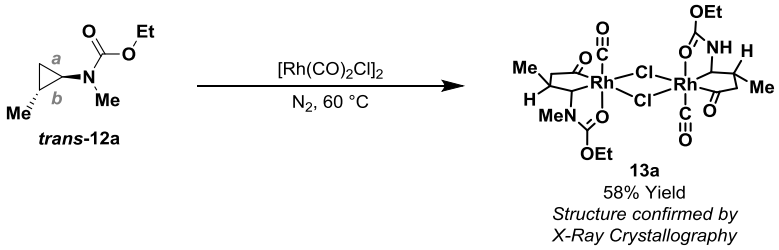
Entry	"H-Scavenger"	Yield[a]	Product ratio (9l:8l)[c]
1	No Additive	62%[b]	4:1
2	Diphenylacetylene	28%	2:1
3	Norbornene	39%	1:1.5

[a]*In-situ* yields are quoted. [b]Isolated yield. [c]Product ratios were determined by ^{1}H NMR analysis against an internal standard.

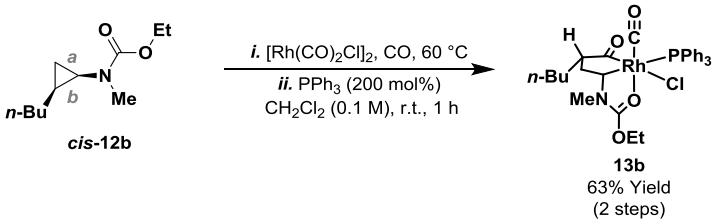
*The presence of hydrogen scavengers was found to alter the reaction selectivity towards the unsaturated product (**8l**).*

Further Oxidative Insertion Regioselectivity Experiments

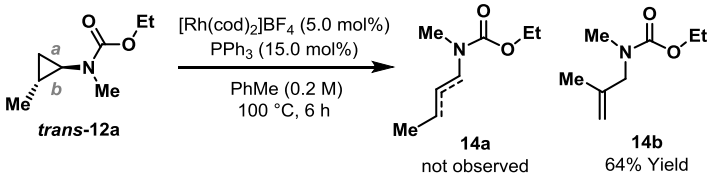
(A) Rhodacycle derived from *trans*-substituted cyclopropyl carbamate. Preferential insertion into bond a in the presence of CO ligands.[5]



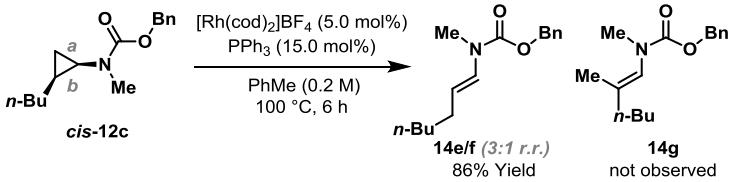
(B) Rhodacycle derived from *cis*-substituted cyclopropyl carbamate. Preferential insertion into bond b in the presence of CO ligands.[8]



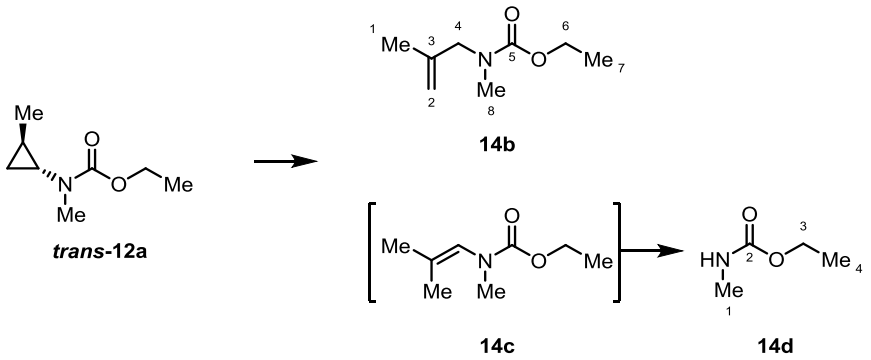
(C) β-Hydride elimination experiment on *trans*-substituted cyclopropyl carbamate. Preferential insertion into bond a in the absence of CO ligands (procedures and data are given below).



(D) β-Hydride elimination experiment on *cis*-substituted cyclopropyl carbamate. Preferential insertion into bond b in the absence of CO ligands (procedures and data are given below).



Ethyl methyl(2-methylprop-1-en-1-yl)carbamate (14b), Ethyl methyl(2-methylallyl)carbamate (14c) *and* Ethyl methylcarbamate (14d)



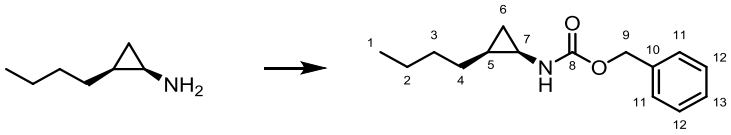
An oven dried reaction tube, fitted with a magnetic stirrer, was charged with $[Rh(cod)_2]BF_4$ (3.1 mg, 0.0075 mmol) and PPh_3 (5.9 mg, 0.0225 mmol). The tube was fitted with a rubber septum and purged with argon. ***trans*-12a**[5] (23.6 mg, 0.15 mmol, single diastereomer) in argon sparged anhydrous toluene (0.75 mL) was added *via* syringe before aging the catalyst for *ca.* 5 minutes. The reaction was heated at 100 °C with stirring for 6 h. The mixture was cooled to r.t., concentrated *in vacuo* and purified by column chromatography (5% EtOAc/hexane) to yield the title compounds (15.1 mg, 64%, 5:1, **14b**:**14d**) as a colorless oil. *The presence of **14d** is attributed to hydrolysis of enamine **14c** under the reaction conditions. No linear β-hydride elimination products resulting from insertion into bond b were observed by NMR analysis of the crude reaction mixture.*

Data for the mixture of compounds: ν_{max} / cm^{-1}: 2978 (w), 1698 (s), 1447 (m), 1382 (m), 1147 (s); HRMS: (ESI^+) Calculated for $C_8H_{15}NNaO_2$: 180.1000. Found $[M + Na]^+$: 180.0988.

Data for major compound **14b:** ^1H NMR ($CDCl_3$, 400 MHz): δ 4.86 (1H, br. s, C**2**-H), 4.77 (1H, br. s, C**2**-H), 4.14 (2H, q, J = 7.0 Hz, C**6**-H_2), 3.80 (2H, m, C**4**-H_2), 2.82 (3H, m, C**8**-H_3), 1.67 (3H, s, C**1**-H_3), 1.26 (3H, m, C**7**-H_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 111.9 (C**2**), 61.4 (C**6**), 54.7 (C**4**), 33.3 (C**8**), 19.9 (C**1**), 14.9 (C**7**).

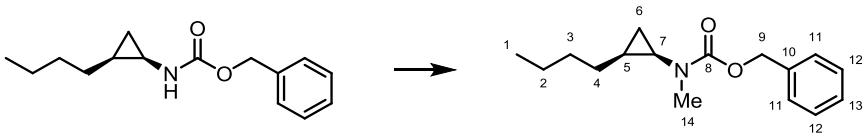
Data for major compound **14d:** *Characteristic signals only*: ^1H NMR ($CDCl_3$, 400 MHz): δ 2.98 (3H, s, C**1**-H_3). *Proton signals corresponding to C**3** and C**4** closely overlap C**6** and C**7** of compound **14b**.*

Benzyl ((1*R,2*S**)-2-butylcyclopropyl)carbamate**



To a stirring solution of (1*R**,2*S**)-2-butylcyclopropan-1-amine[8] (100 mg, 0.88 mmol) and NEt_3 (0.15 mL, 1.06 mmol) in CH_2Cl_2 (4.4 mL) was added benzyl chloroformate (150 μL, 1.06 mmol) dropwise at 0 °C over 10 minutes under an atmosphere of nitrogen. The mixture was warmed to r.t. and stirred overnight. The mixture was diluted with water (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The organic extracts were combined, washed with brine (10 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The crude mixture was purified by column chromatography (20% EtOAc/hexane) to yield the title compound (145 mg, 67%) as a colorless oil; ν_{max} / cm^{-1}: 3324 (m), 1700 (s), 1525 (s), 1453 (m), 1259 (s), 1075 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36-7.27 (5H, m, 2 × C**11**-H, 2 × C**12**-H, C**13**-H), 5.16-5.09 (2H, m, C**9**-H_2), 4.73 (1H, m, NH), 2.69 (1H, m, C**7**-H), 1.49-1.18 (6H, m, C**2**-H_2, C**3**-H_2, C**4**-H_2), 0.98-0.83 (5H, m, C**1**-H_3, C**5**-H, 1 × C**6**-H), 0.16 (1H, m, 1 × C**6**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 157.3 (C**8**), 136.7 (C**10**), 128.4, 128.0 (C**11**, C**12**, C**13**), 66.7 (C**9**), 31.7 (C**3**), 27.6 (C**7**), 27.3 (C**4**), 22.5 (C**2**), 17.4 (C**5**), 13.9 (C**1**), 12.3 (C**6**); HRMS: (ESI^+) Calculated for $C_{15}H_{22}NO_2$: 248.1645. Found $[M + H]^+$: 248.1642.

Benzyl ((1*R,2*S**)-2-butylcyclopropyl)(methyl)carbamate (*cis*-12c)**

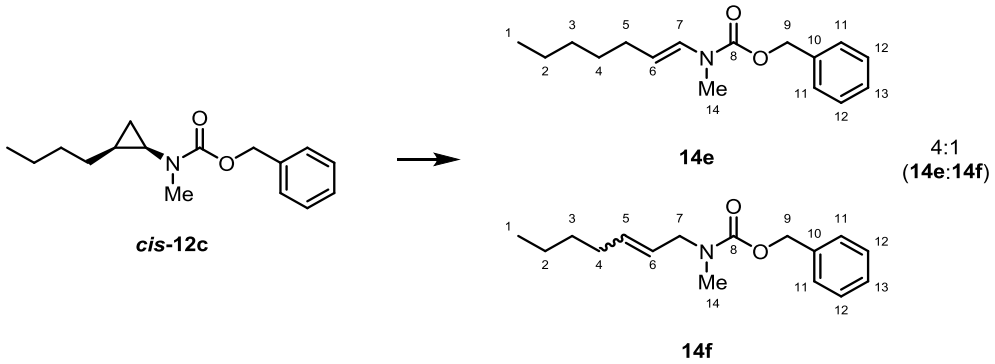


***cis*-12c**

To a solution of NaH (58 mg, 2.4 mmol) in THF (1.6 mL) was added a solution of benzyl ((1*R**,2*S**)-2-butylcyclopropyl)carbamate (120 mg, 0.485 mmol) in THF (0.25 mL) and the reaction was stirred at 0 °C for 1 h. Methyl iodide (150 μL, 2.4 mmol) was added dropwise at 0 °C and the reaction was stirred at r.t. for 18 h. Water (5 mL) was added to the reaction mixture and the solution was extracted with Et_2O (3 × 5 mL). The organic extracts were combined, washed with brine (5 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The crude mixture was purified by column chromatography (10% EtOAc/hexane) to yield the title compound ***cis*-12c** (99.2 mg, 78%) as a colorless oil; ν_{max} / cm^{-1}: 2927 (s), 1701 (s), 1455 (m), 1391 (s), 1344 (s), 1150 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.39-7.28 (5H, m, 2 × C**11**-H, 2 × C**12**-H, C**13**-

H), 5.19 -5.09 (2H, m, C**9**-H$_2$), 2.91 (3H, s, C**14**-H$_3$), 2.68 (1H, ddd, *J* = 7.5, 7.0, 4.5 Hz, C**7**-H), 1.58 (1H, m, 1 × C**4**-H), 1.37 – 1.25 (4H, m, C**2**-H$_2$, C**3**-H$_2$), 0.99 – 0.81 (6H, m, C**1**-H$_3$, 1 × C**4**-H, C**5**-H, 1 × C**6**-H), 0.32 (1H, m, 1 × C**6**-H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.0 (C**8**), 136.9 (C**10**), 128.4, 127.9 (C**11**, C**12**, C**13**), 67.0 (C**9**), 35.8 (C**14**), 35.4 (C**7**), 31.7 (C**3**), 27.6 (C**4**), 22.6 (C**2**), 19.7 (C**5**), 14.1 (C**1**), 11.9 (C**6**); HRMS: (ESI$^+$) Calculated for $C_{16}H_{23}NNaO_2$: 284.1621. Found [M + Na]$^+$: 284.1623.

Benzyl (*E*)-hept-1-en-1-yl(methyl)carbamate (14e) *and* Benzyl hept-2-en-1-yl(methyl)carbamate (14f)

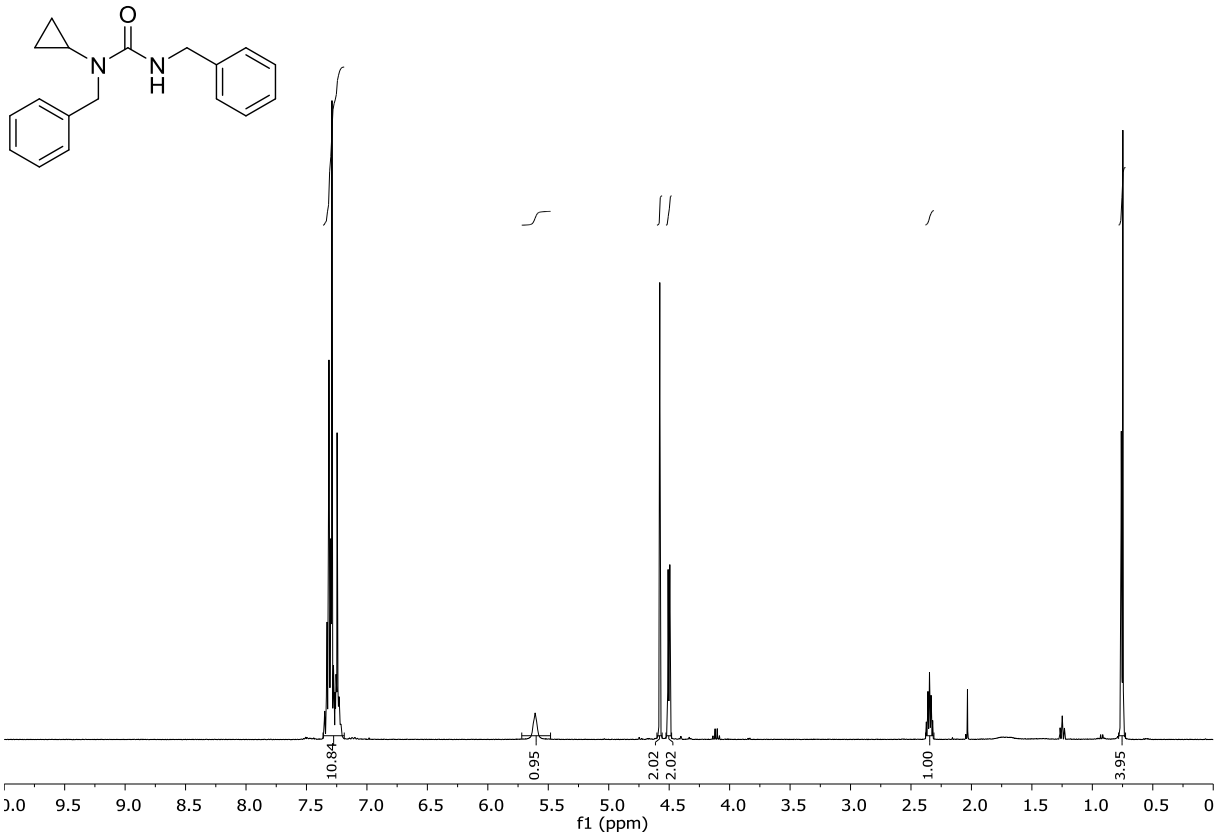


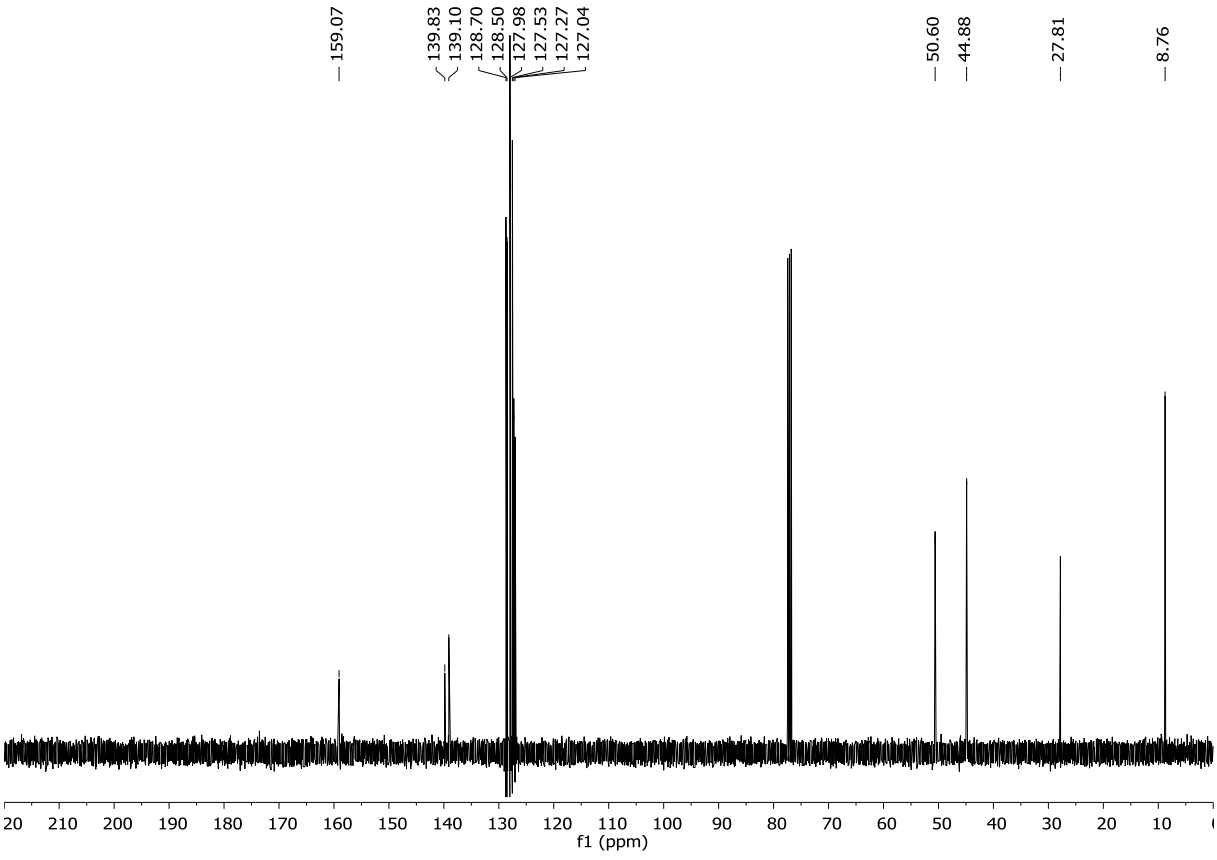
An oven dried reaction tube, fitted with a magnetic stirrer, was charged with $[Rh(cod)_2]BF_4$ (3.7 mg, 0.009 mmol) and PPh_3 (7.1 mg, 0.027 mmol). The tube was fitted with a rubber septum and purged with argon. Benzyl ((1*R**,2*S**)-2-butylcyclopropyl)(methyl)carbamate (47 mg, 0.18 mmol) in argon sparged anhydrous toluene (2 mL) was added *via* syringe before aging the catalyst for *ca.* 5 minutes. The reaction was heated at 100 °C with stirring for 3 h. The mixture was cooled to r.t., concentrated *in vacuo* and purified by column chromatography (5% EtOAc/hexane) to yield regioisomer **14e** (31.1 mg, 66%, 1:1, mixture of rotamers *A:B*) as a colorless oil and regioisomer **14f** (9.4 mg, 20%, tentatively assigned mixture of *E*/*Z* diastereomers) as a colorless oil.

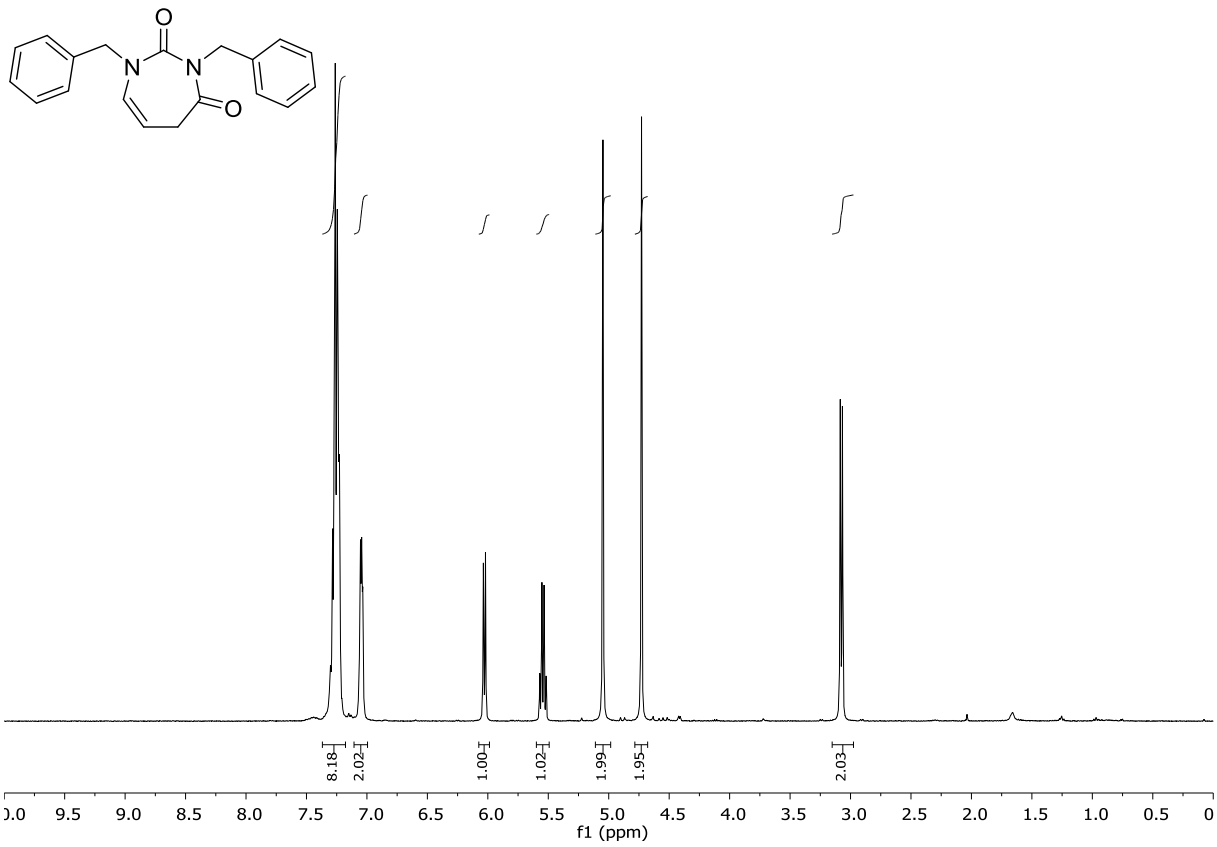
Data for the major regioisomer **14e**: ν_{max} / cm^{-1}: 2928 (m), 1693 (s), 1403 (m), 1214 (m), 1153 (s); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38-7.30 (5H, m, 2 × C**11**-H, *A*+*B*, 2 × C**12**-H, *A*+*B*, C**13**-H, *A*+*B*), 7.01 (0.50H, d, *J* = 14.0 Hz, C**7**-H, *A*), 6.89 (0.50H, d, *J* = 14.0 Hz, C**7**-H, *B*), 5.19 (2H, s, C**9**-H$_2$, *A*+*B*), 4.85 (1H, dt, *J* = 14.0, 7.5 Hz, C**6**-H, *A*+*B*), 3.07-3.05 (3H, m, C**14**-H$_3$, *A*+*B*), 2.08-1.99 (2H, m, C**5**-H$_2$, *A*+*B*), 1.40-1.25 (6H, m, C**2**-H$_2$, *A*+*B*, C**3**-H$_2$, *A*+*B*, C**4**-H$_2$, *A*+*B*), 0.89 (3H, t, J = 7.0 Hz, C**1**-H$_3$, *A*+*B*); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 154.3, 153.9 (C**8**, *A*+*B*), 136.4 (C**10**, *A*+*B*), 128.5, 128.2, 128.0 (C**11**, *A*+*B*, C12, *A*+*B*, C13, *A*+*B*), 127.5 (C**7**, *A*+*B*), 110.0 (C**6**, *A*+*B*), 67.8, 67.6 (C**9**, *A*+*B*), 31.5 (CH$_2$, *A*+*B*), 31.0 (C**14**, *A*+*B*), 30.2 (CH$_2$,

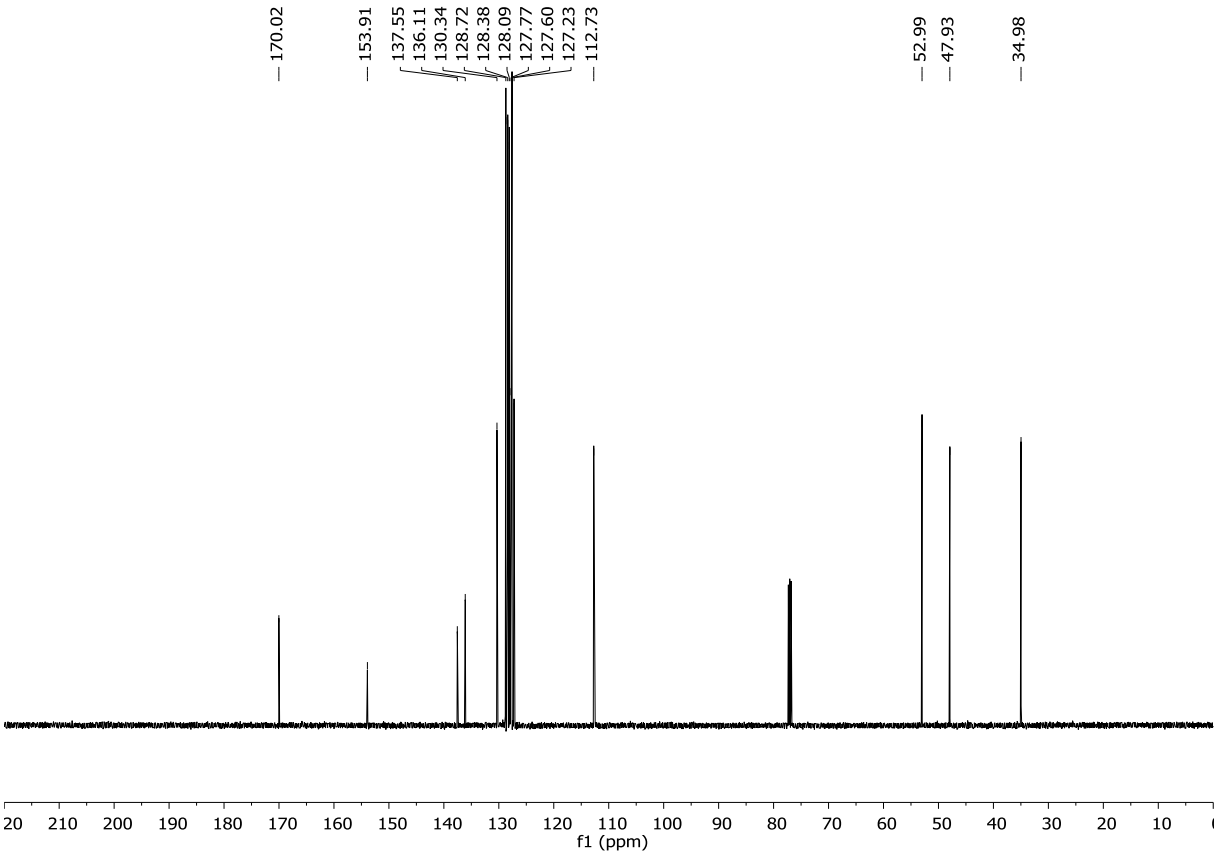
A+B, C**5**, *A+B*), 22.5 (CH_2, *A+B*), 14.1 (C**1**, *A+B*). ***C2***, ***C3*** *and* ***C4*** *could not be assigned. Aldehyde peaks appear due to decomposition of the product*; HRMS: (ESI^+) Calculated for $C_{16}H_{23}NNaO_2$: 284.1621. Found $[M + Na]^+$: 284.1618.

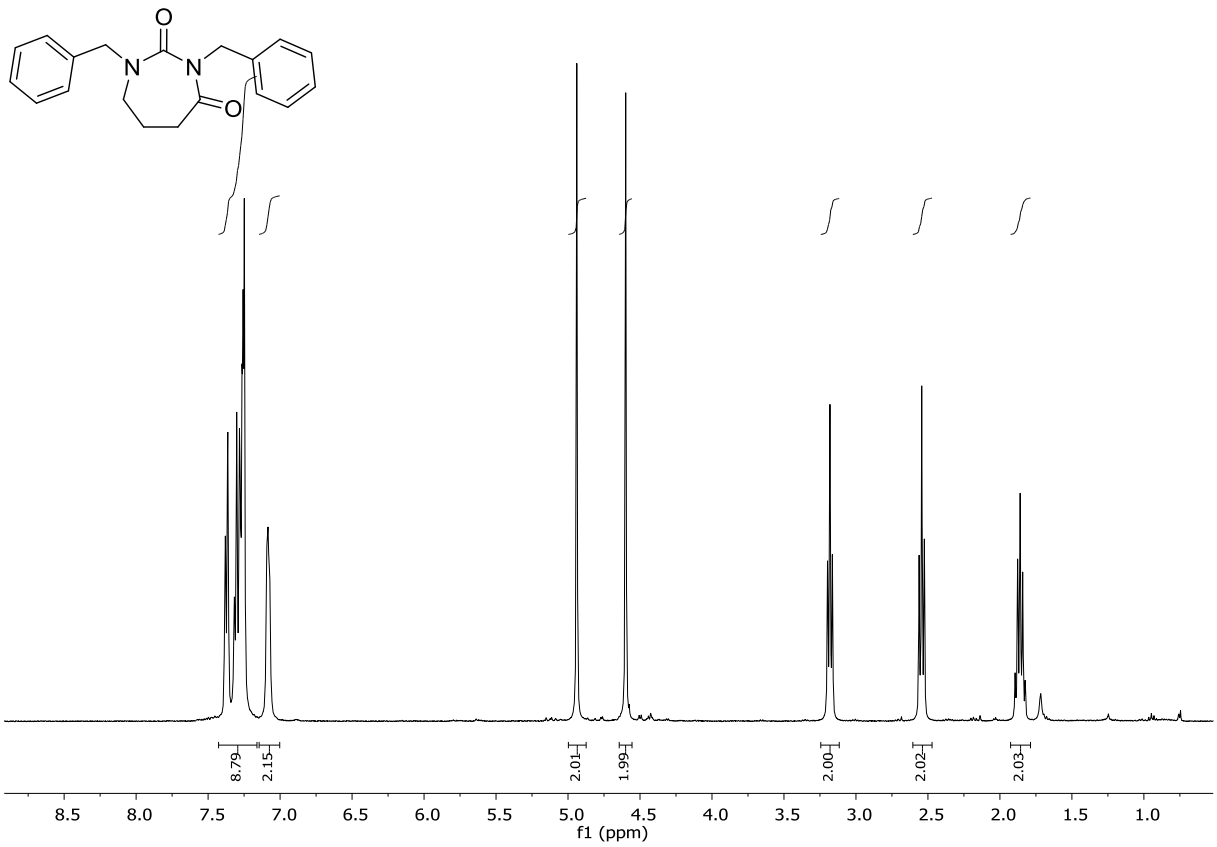
Data for the minor regioisomer **14f**: ν_{max} / cm^{-1}: 2929 (m), 1705 (s), 1397 (m), 1324 (m), 1256 (s), 1136 (s); ^1H NMR (400 MHz, $CDCl_3$): δ 7.38-7.28 (5H, m, 2 × C**11**-H, 2 × C**12**-H, C**13**-H), 5.55 (1H, m, C**5**-H), 5.39 (1H, m, C**6**-H), 5.13 (2H, s, C**9**-H_2), 3.87-3.79 (2H, m, C**7**-H_2), 2.88-2.82 (3H, m, C**14**-H_3), 2.06-1.97 (2H, m, C**4**-H_2), 1.37-1.23 (4H, m, C**2**-H_2, C**3**-H_2), 0.90 (3H, t, *J* = C**1**-H_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.2 (C**8**), 137.0 (C**10**), 133.9 (C**5**), 128.4, 127.8, 127.8 (C**11**, C**12**, C**13**), 124.6 (C**6**), 67.0 (C**9**), 50.6 (C**7**), 33.1 (C**14**), 31.8 (C**4**), 31.3 (CH_2), 22.2 (CH_2), 13.9 (C**1**). ***C2*** *and* ***C3*** *could not be assigned*; HRMS: (ESI^+) Calculated for $C_{16}H_{23}NNaO_2$: 284.1621. Found $[M + Na]^+$: 284.1619.

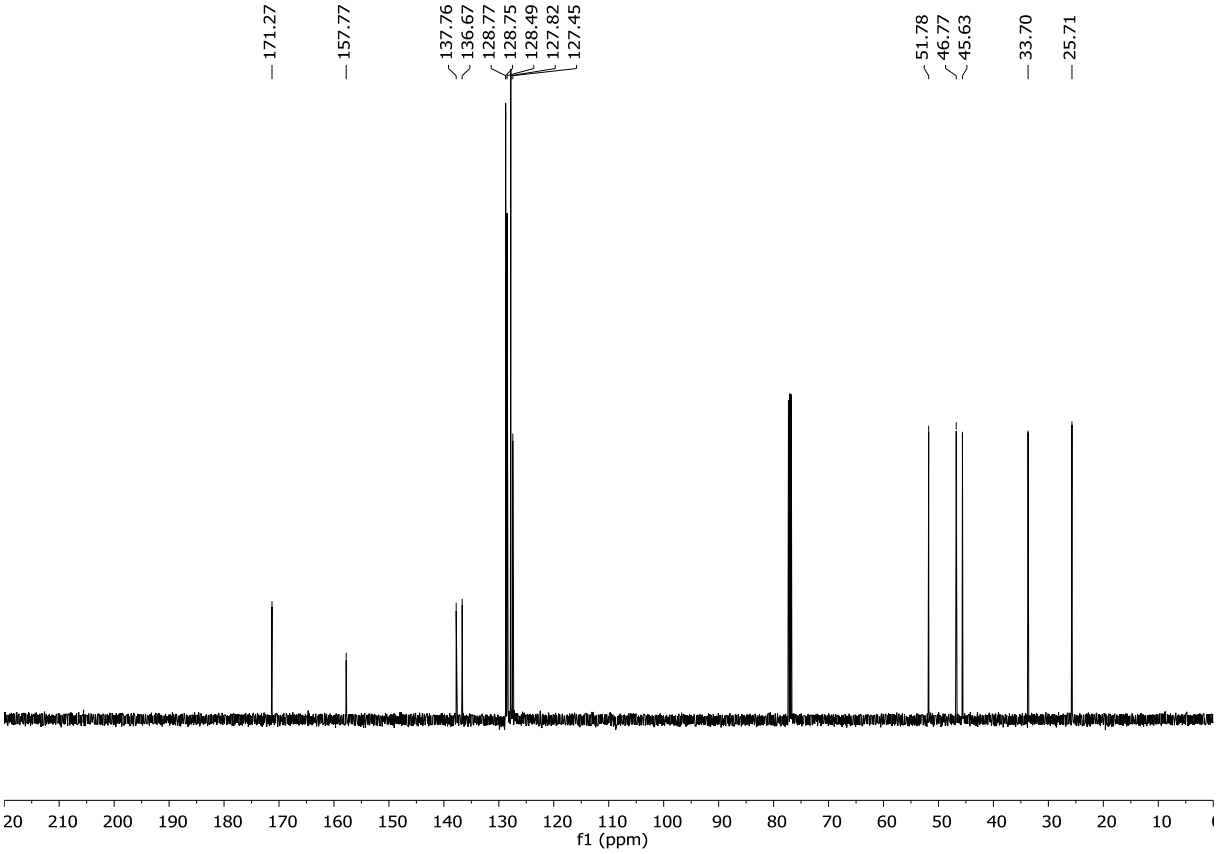

O
N
N
H
10.84
0.95
2.02
2.02
1.00
3.95
f1 (ppm)

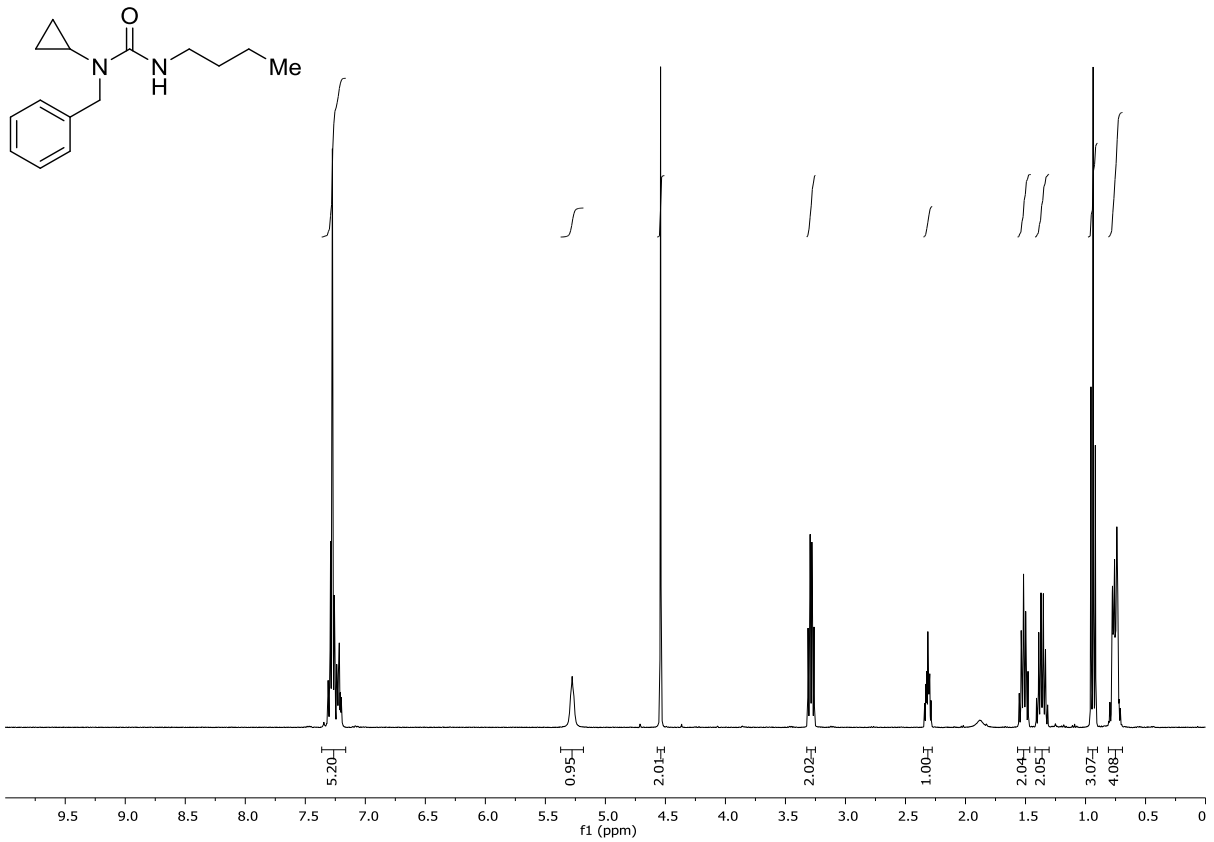

159.07
139.83
139.10
128.70
128.50
127.98
127.53
127.27
127.04
50.60
44.88
27.81
8.76
f1 (ppm)

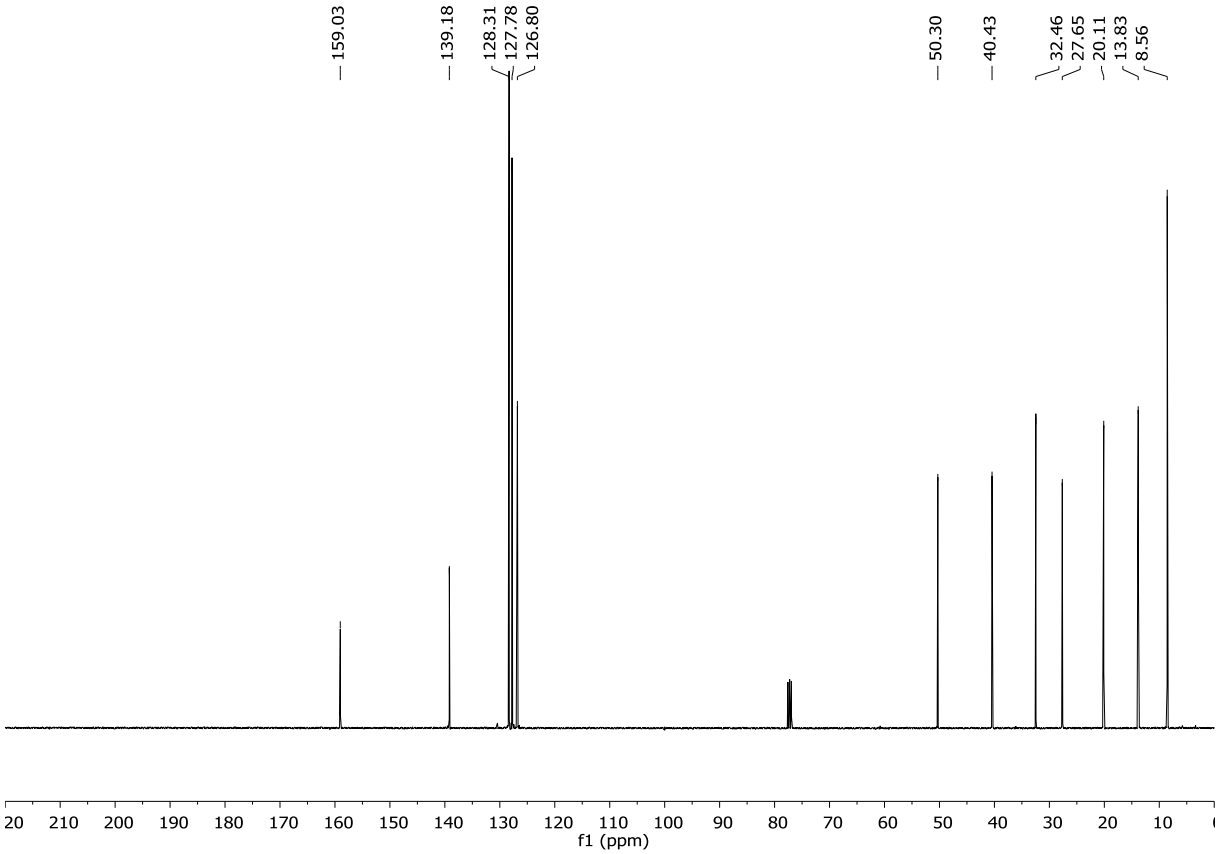

O
N
N
O
8.18
2.02
1.00
1.02
1.99
1.95
2.03
f1 (ppm)

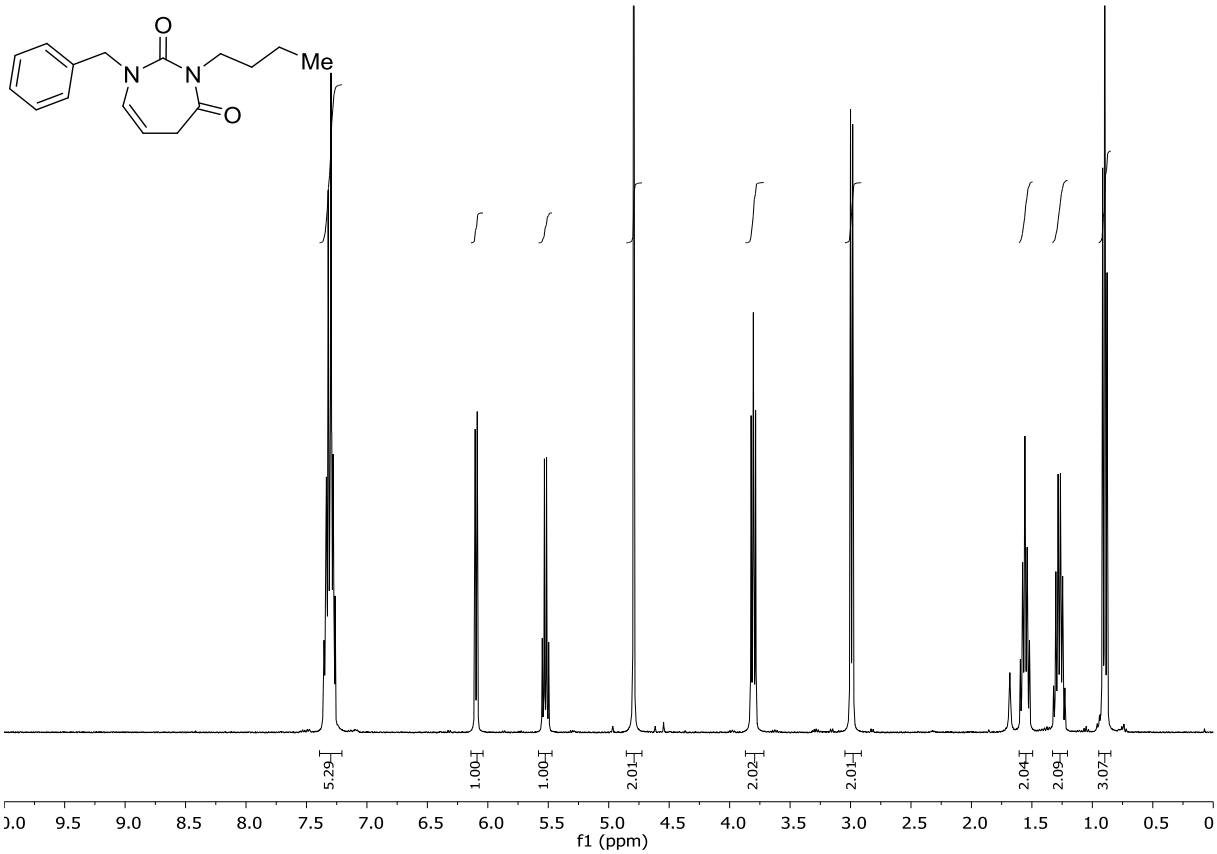

170.02
153.91
137.55
136.11
130.34
128.72
128.38
128.09
127.77
127.60
127.23
112.73
52.99
47.93
34.98
f1 (ppm)

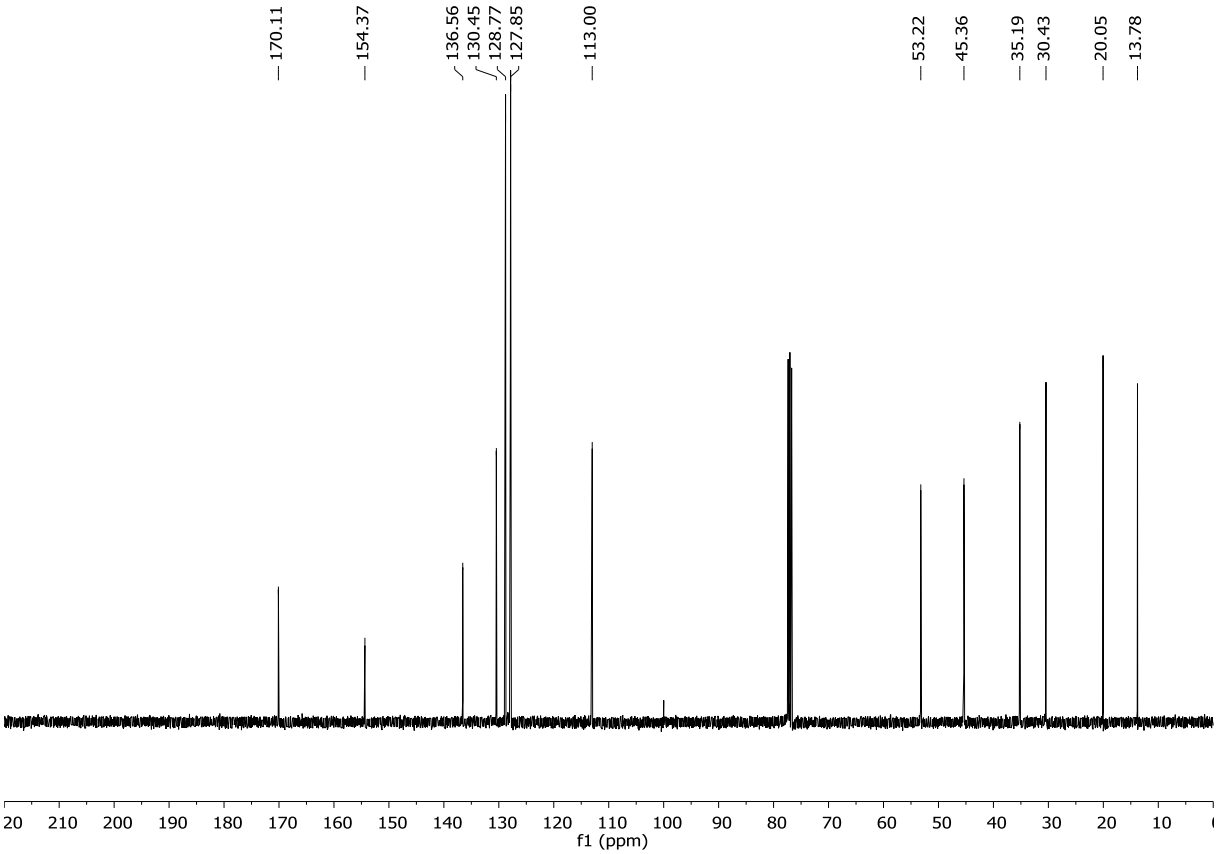

O
N
N
O
8.79
2.15
2.01
1.99
2.00
2.02
2.03
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

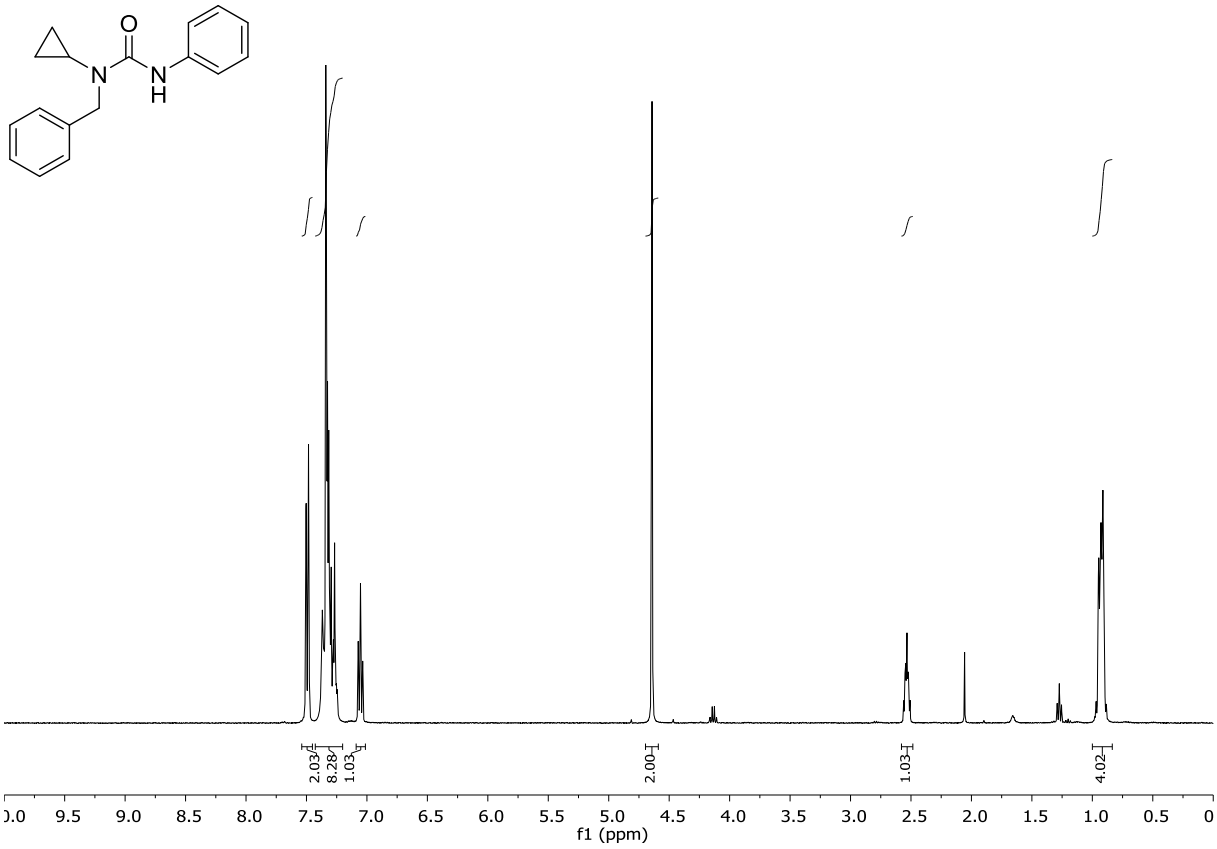

171.27
157.77
137.76
136.67
128.77
128.75
128.49
127.82
127.45
51.78
46.77
45.63
33.70
25.71
20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

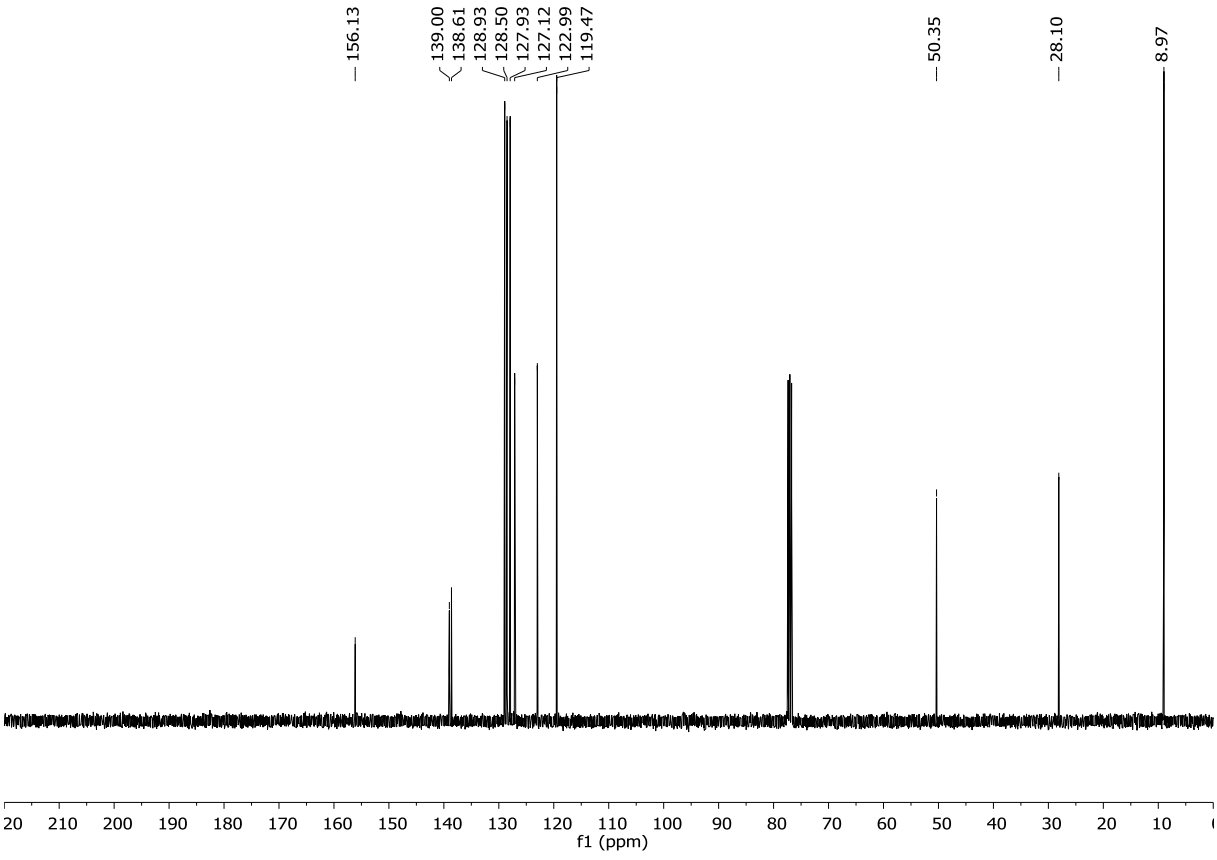

O
N
N
H
Me
5.20
0.95
2.01
2.02
1.00
2.04
2.05
3.07
4.08
f1 (ppm)

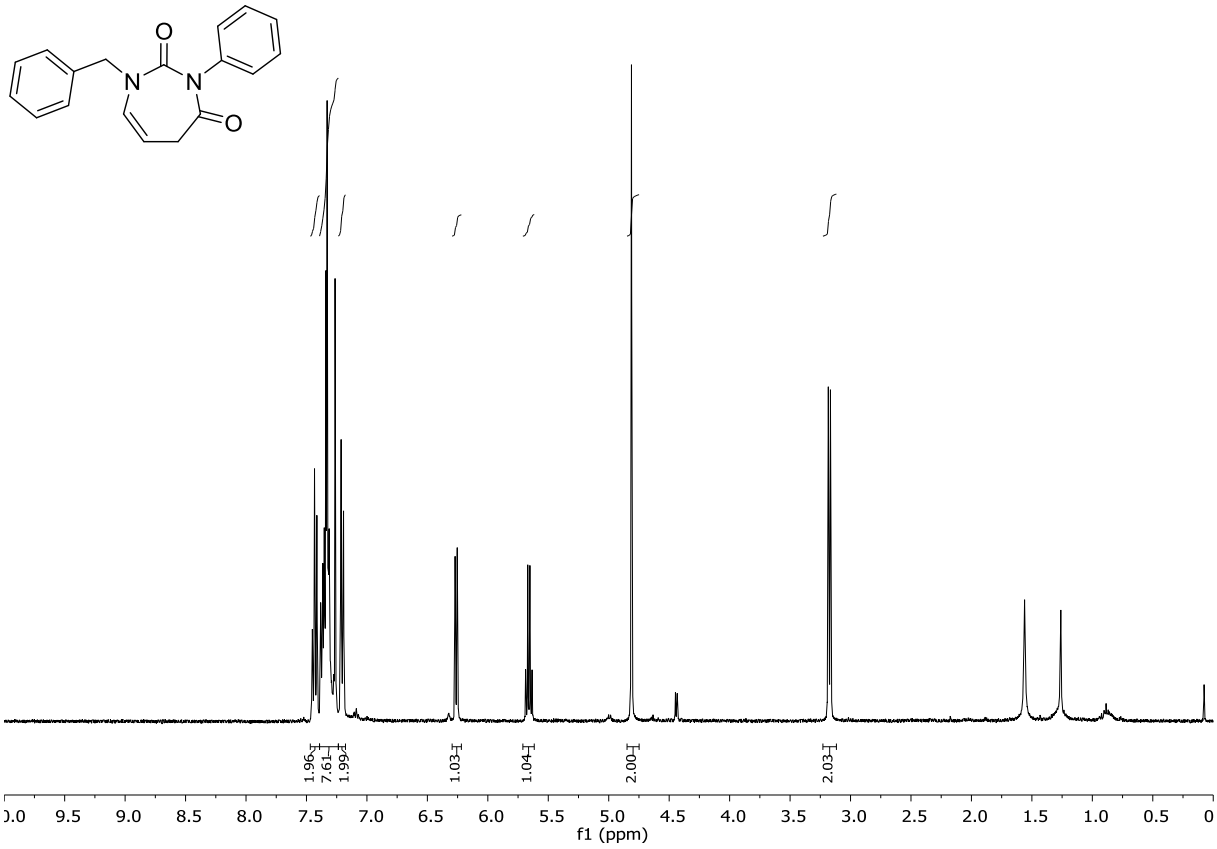

159.03
139.18
128.31
127.78
126.80
50.30
40.43
32.46
27.65
20.11
13.83
8.56
f1 (ppm)

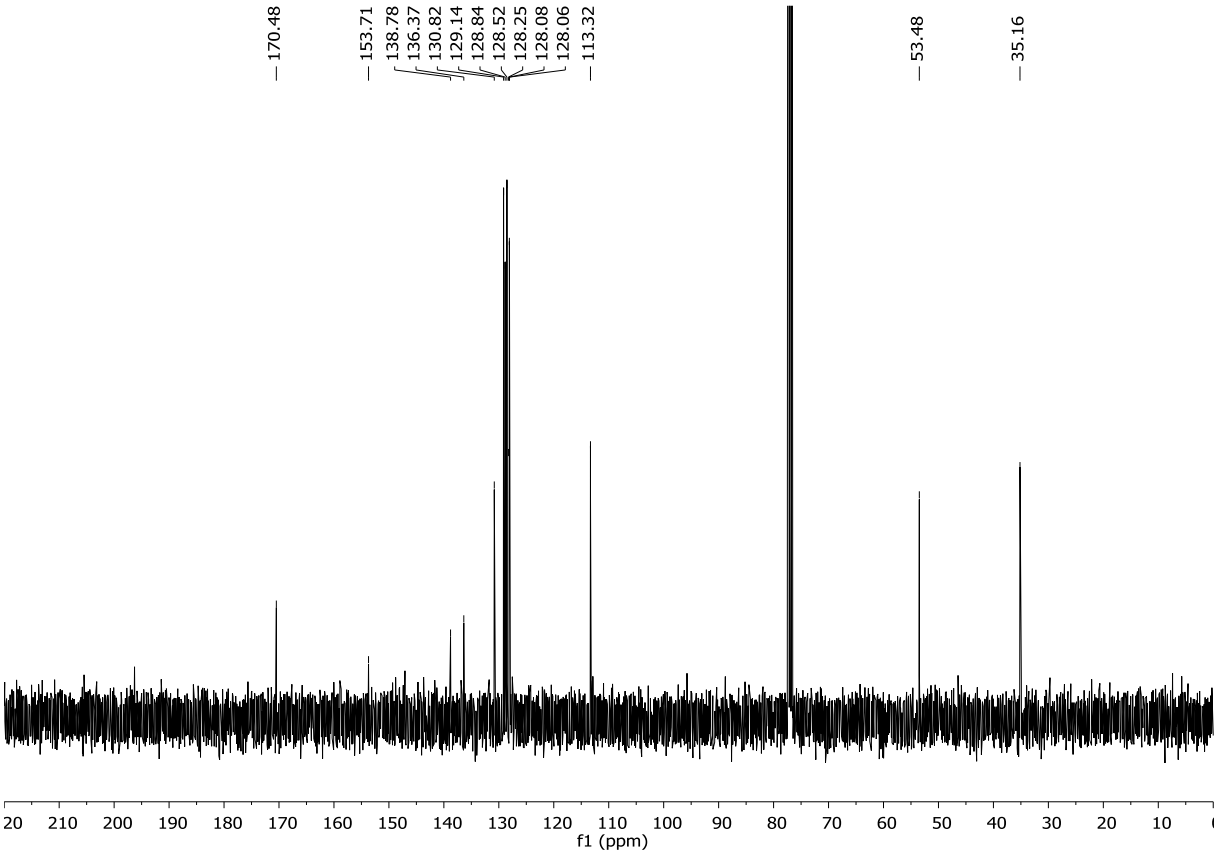

O
N
N
Me
O
5.29
1.00
1.00
2.01
2.02
2.01
2.04
2.09
3.07
f1 (ppm)

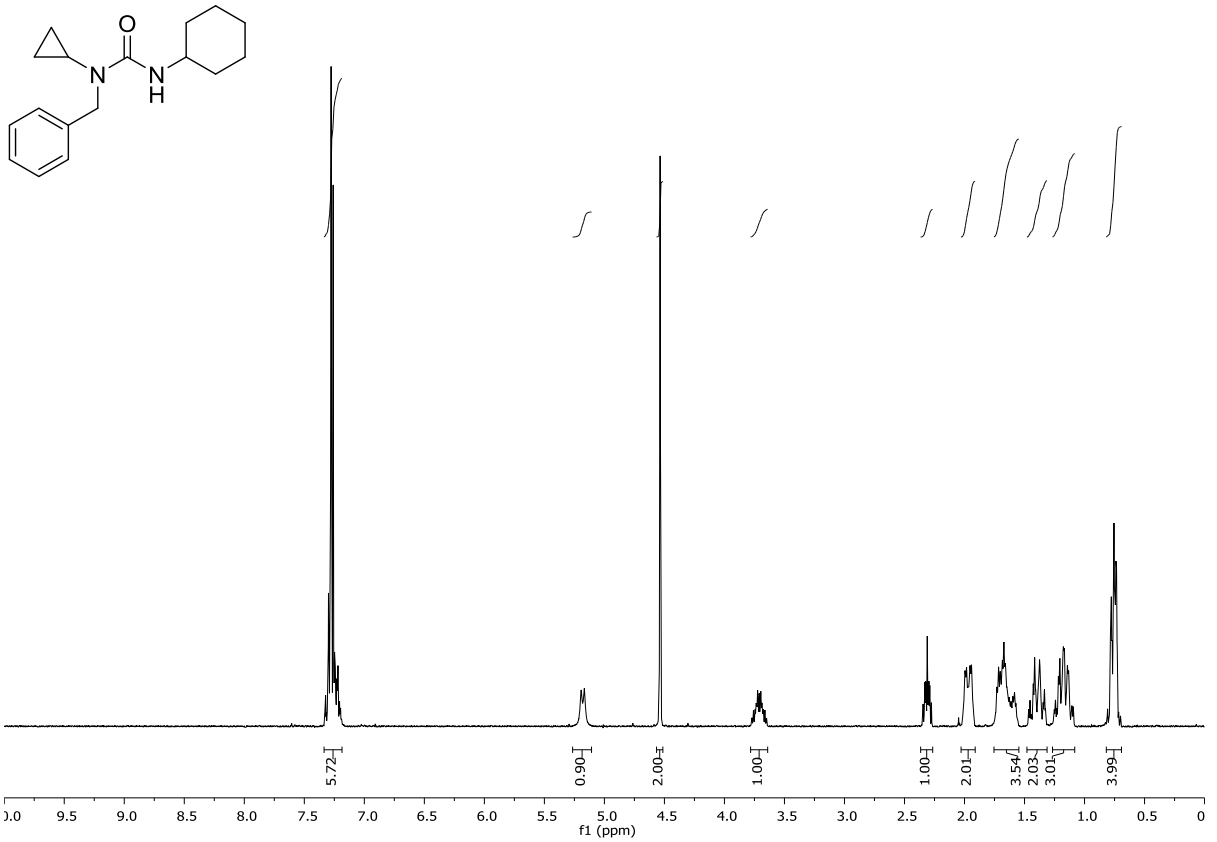

170.11
154.37
136.56
130.45
128.77
127.85
113.00
53.22
45.36
35.19
30.43
20.05
13.78
f1 (ppm)

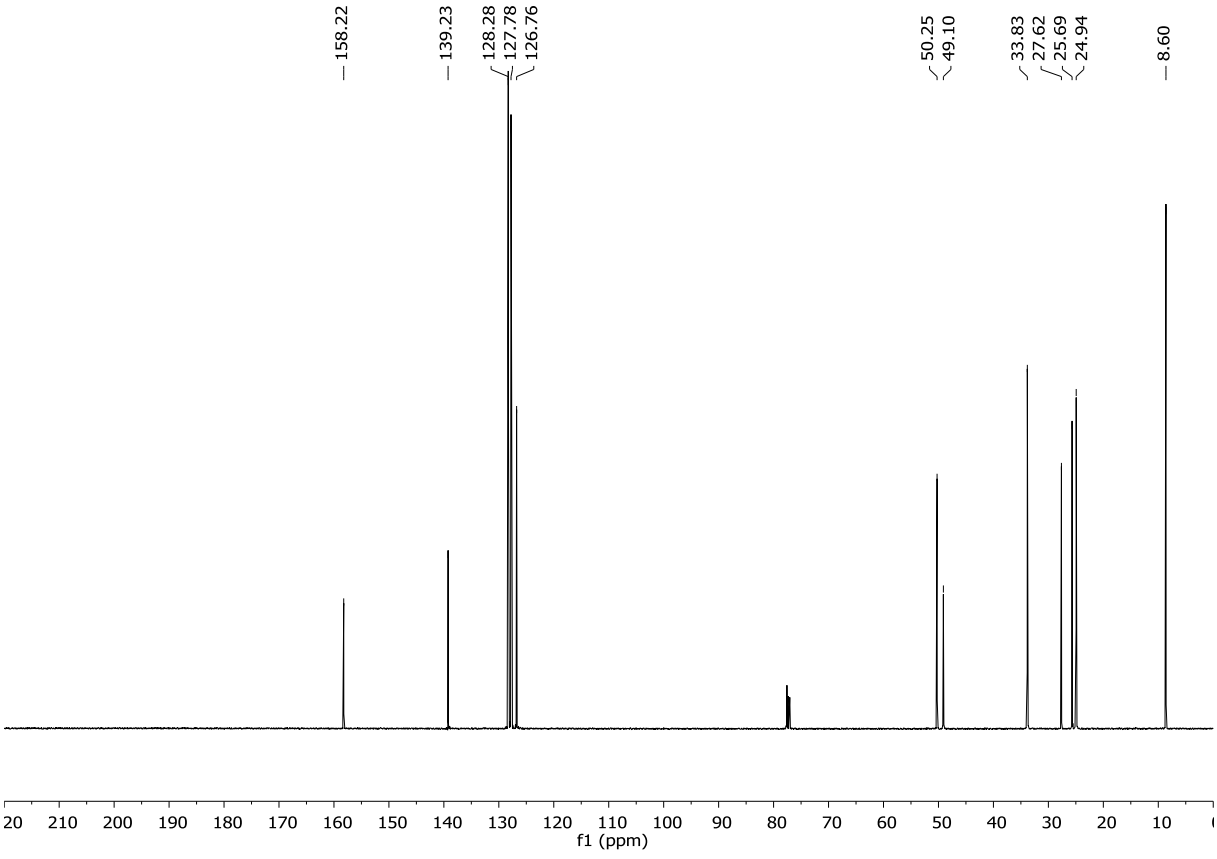

O
N
N
H
2.03
8.28
1.03
2.00
1.03
4.02
f1 (ppm)

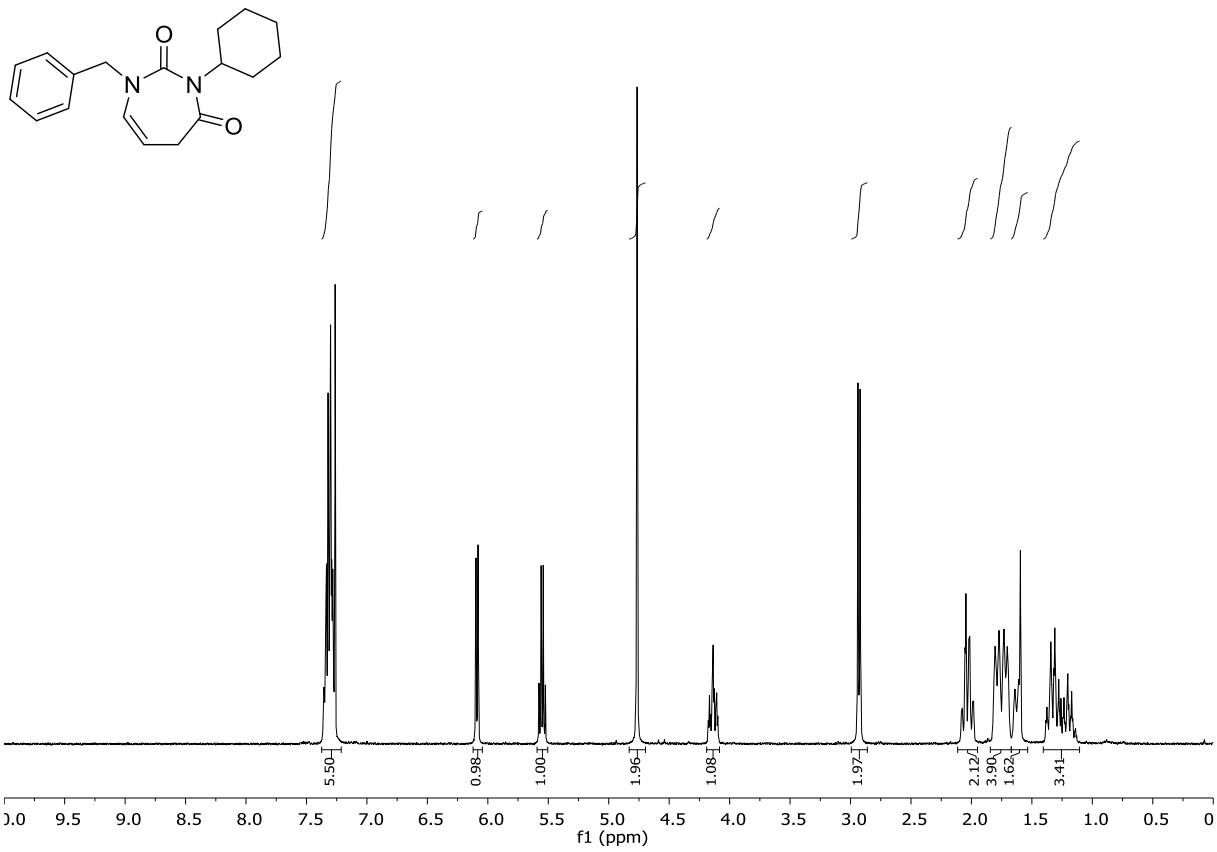

156.13
139.00
138.61
128.93
128.50
127.93
127.12
122.99
119.47
50.35
28.10
8.97
f1 (ppm)

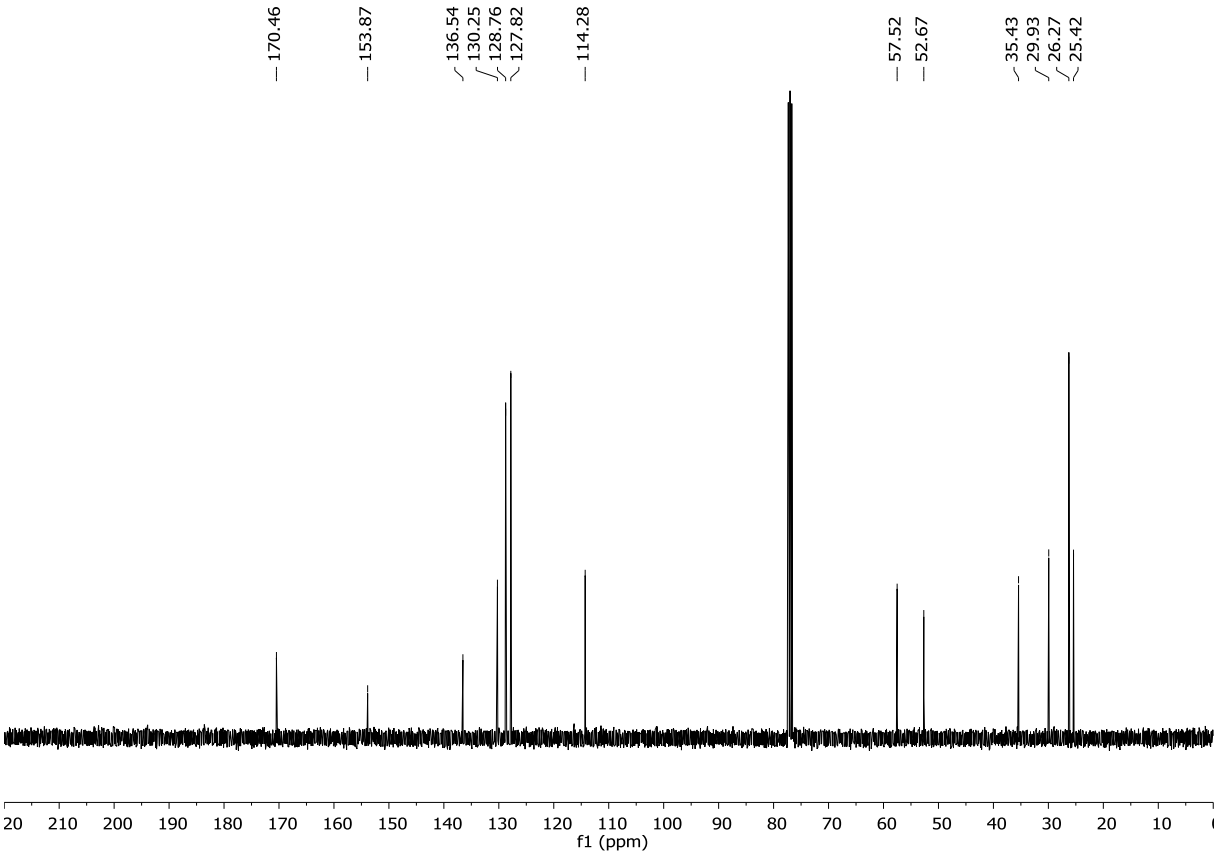

O
N
N
O
1.96
7.61
1.99
1.03
1.04
2.00
2.03
f1 (ppm)

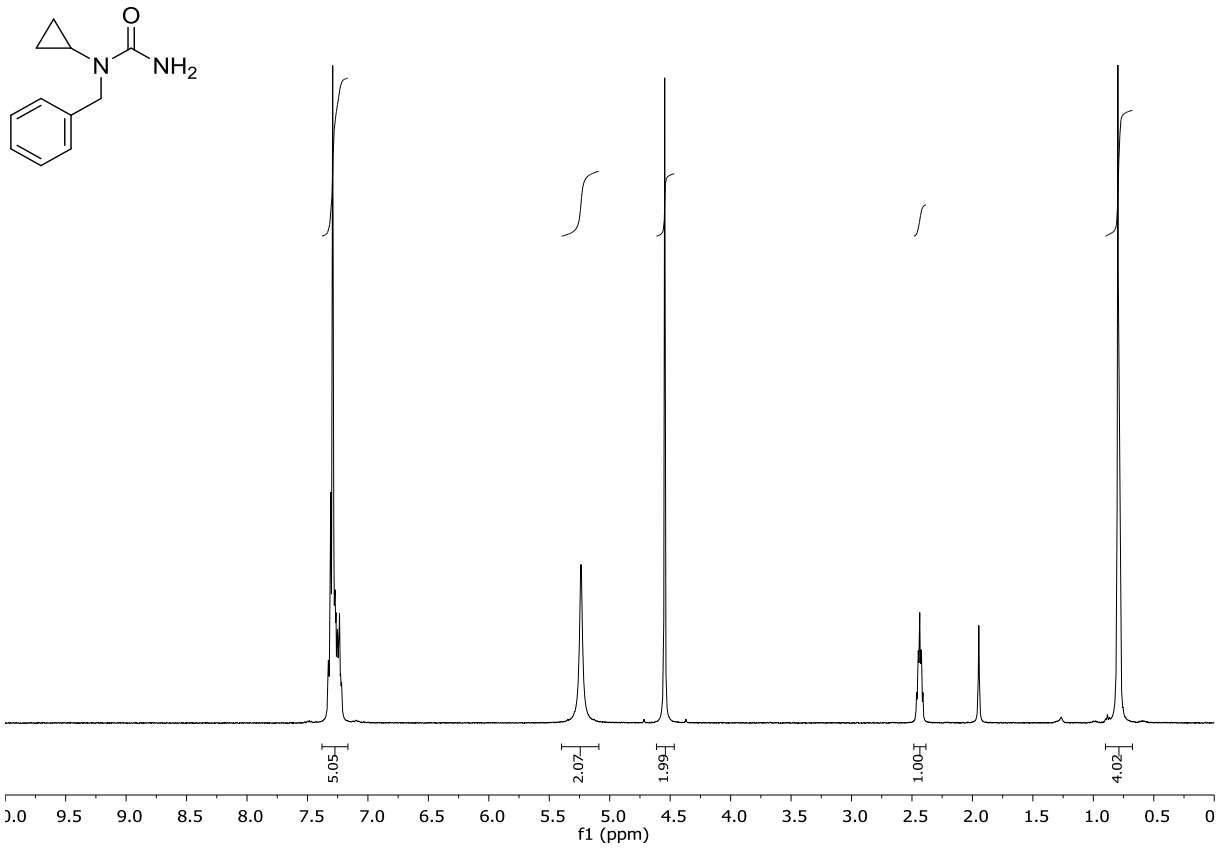

170.48
153.71
138.78
136.37
130.82
129.14
128.84
128.52
128.25
128.08
128.06
113.32
53.48
35.16
f1 (ppm)

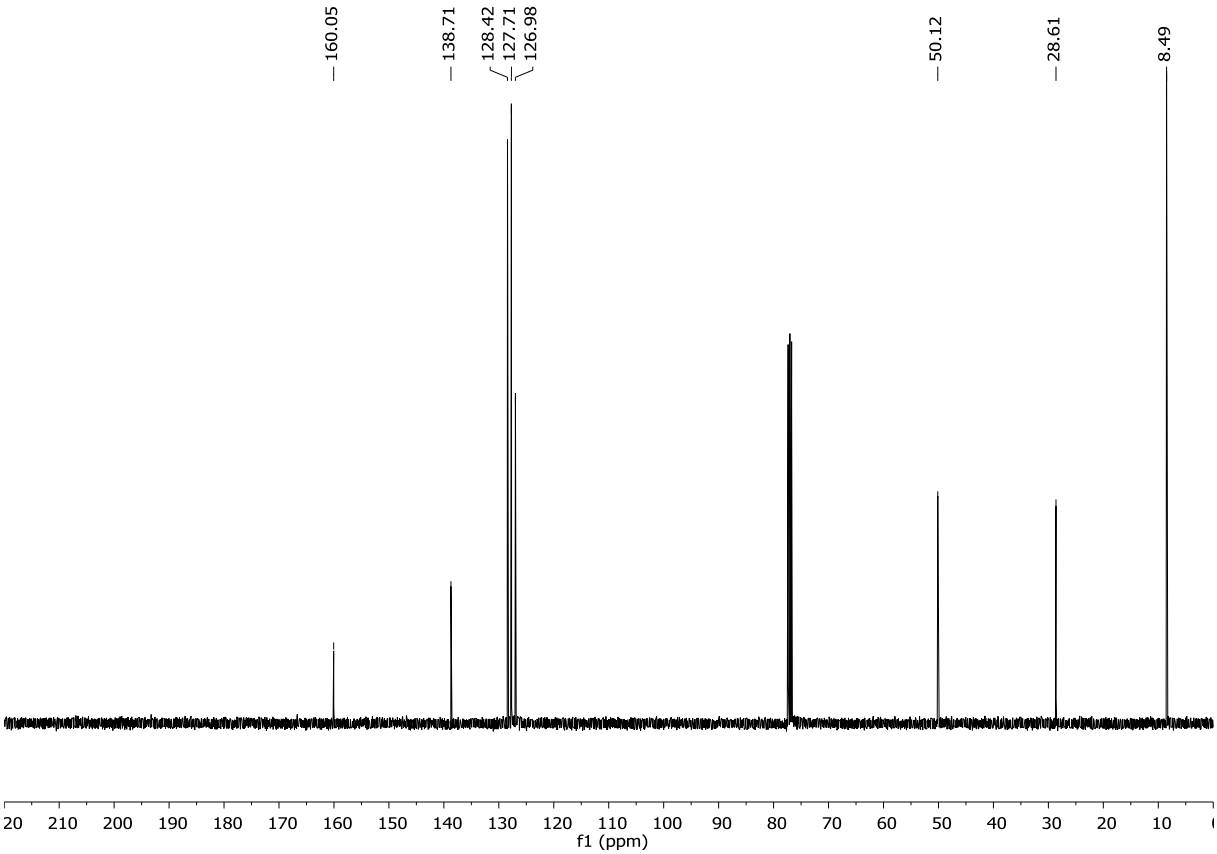

O
N
N
H
5.72
0.90
2.00
1.00
1.00
2.01
3.54
2.03
3.01
3.99
f1 (ppm)

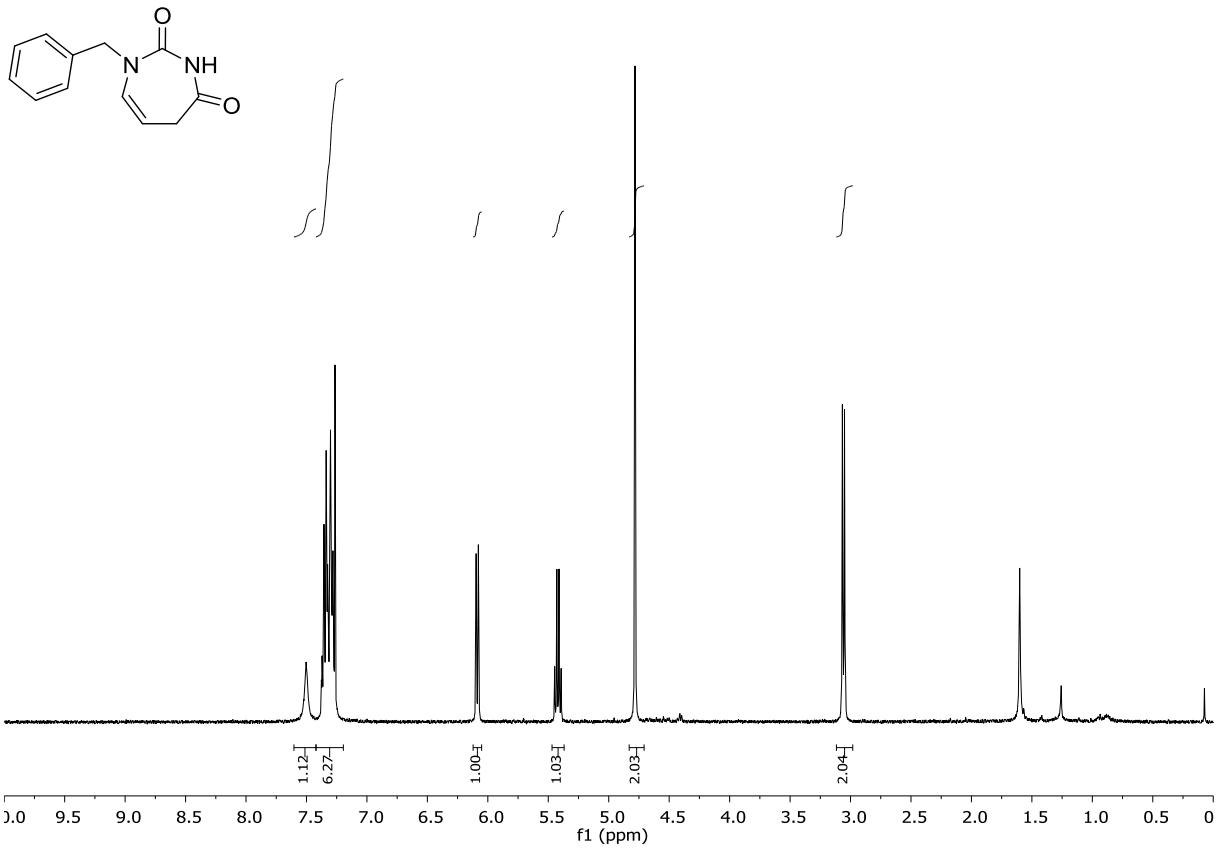

158.22
139.23
128.28
127.78
126.76
50.25
49.10
33.83
27.62
25.69
24.94
8.60
f1 (ppm)

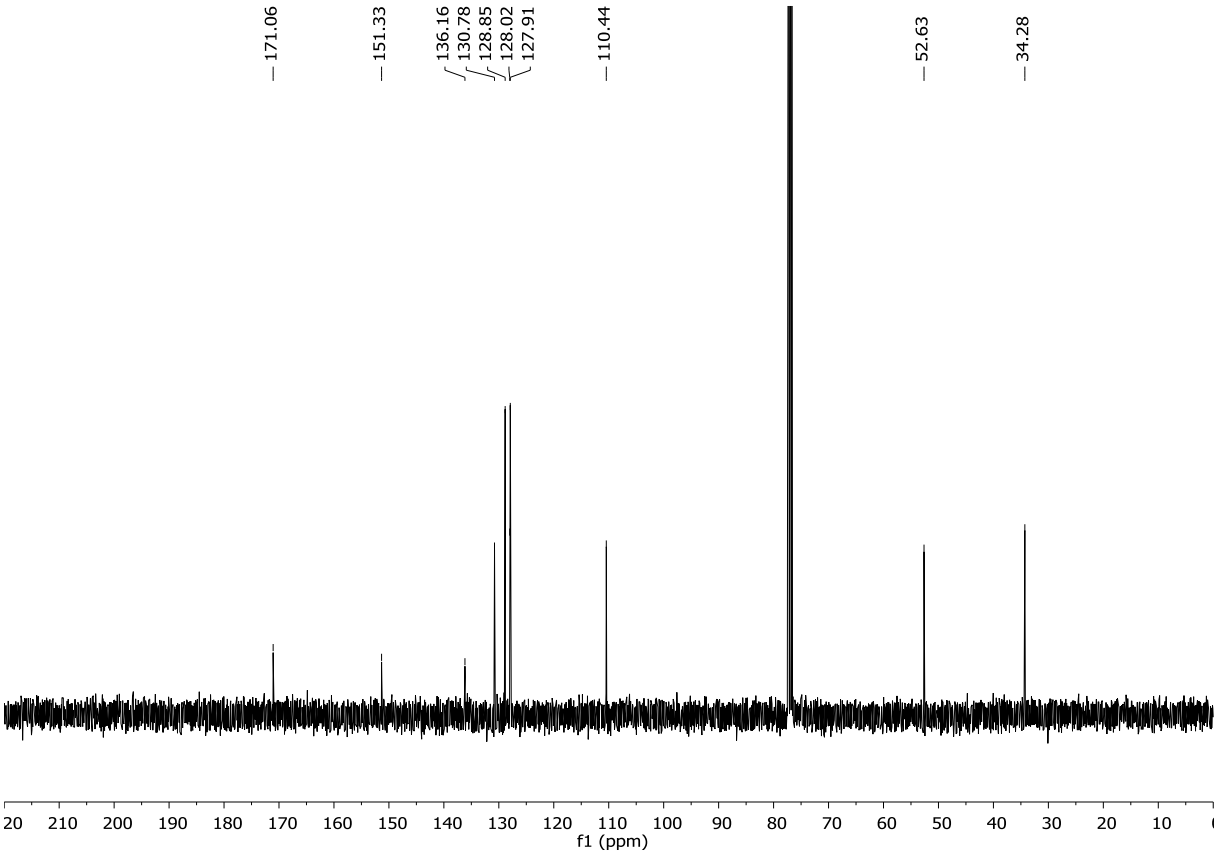

O
N
N
O
5.50
0.98
1.00
1.96
1.08
1.97
2.12
3.90
1.62
3.41
f1 (ppm)

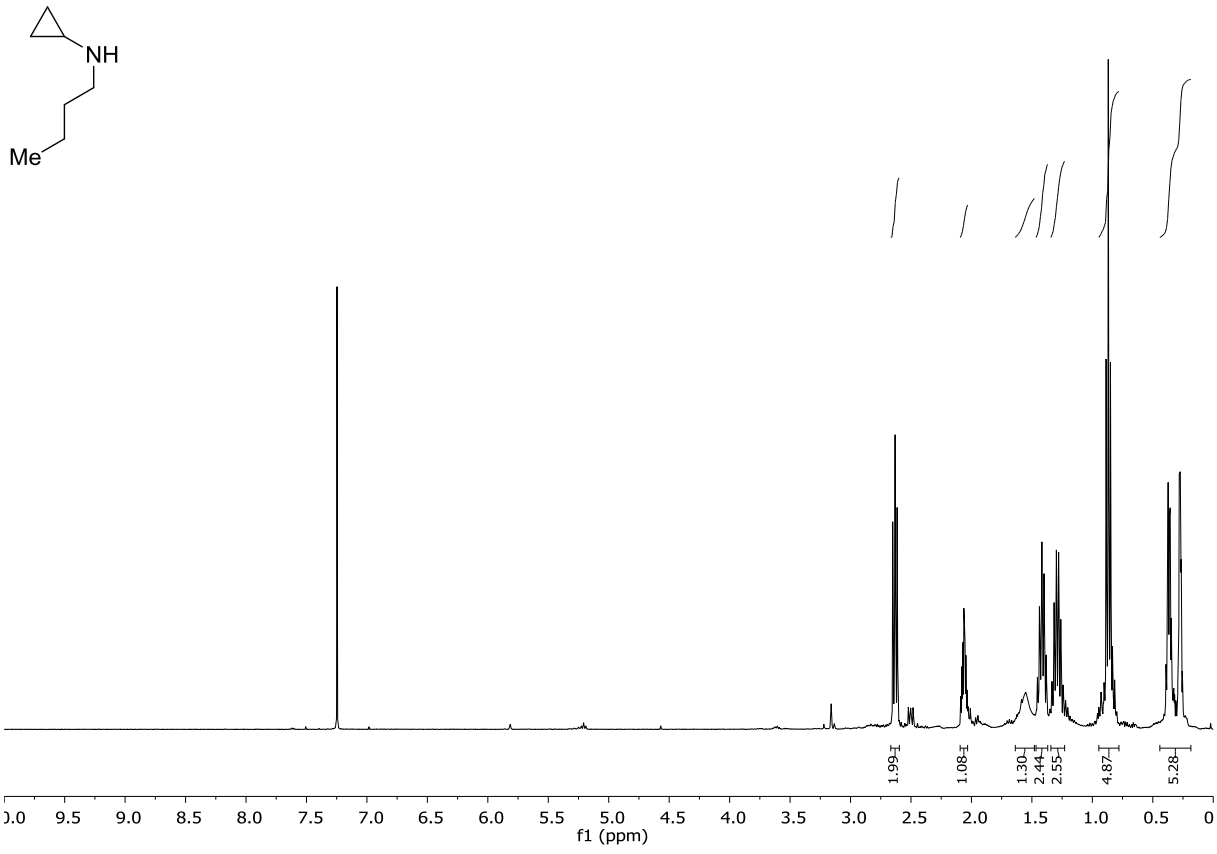

170.46
153.87
136.54
130.25
128.76
127.82
114.28
57.52
52.67
35.43
29.93
26.27
25.42
f1 (ppm)

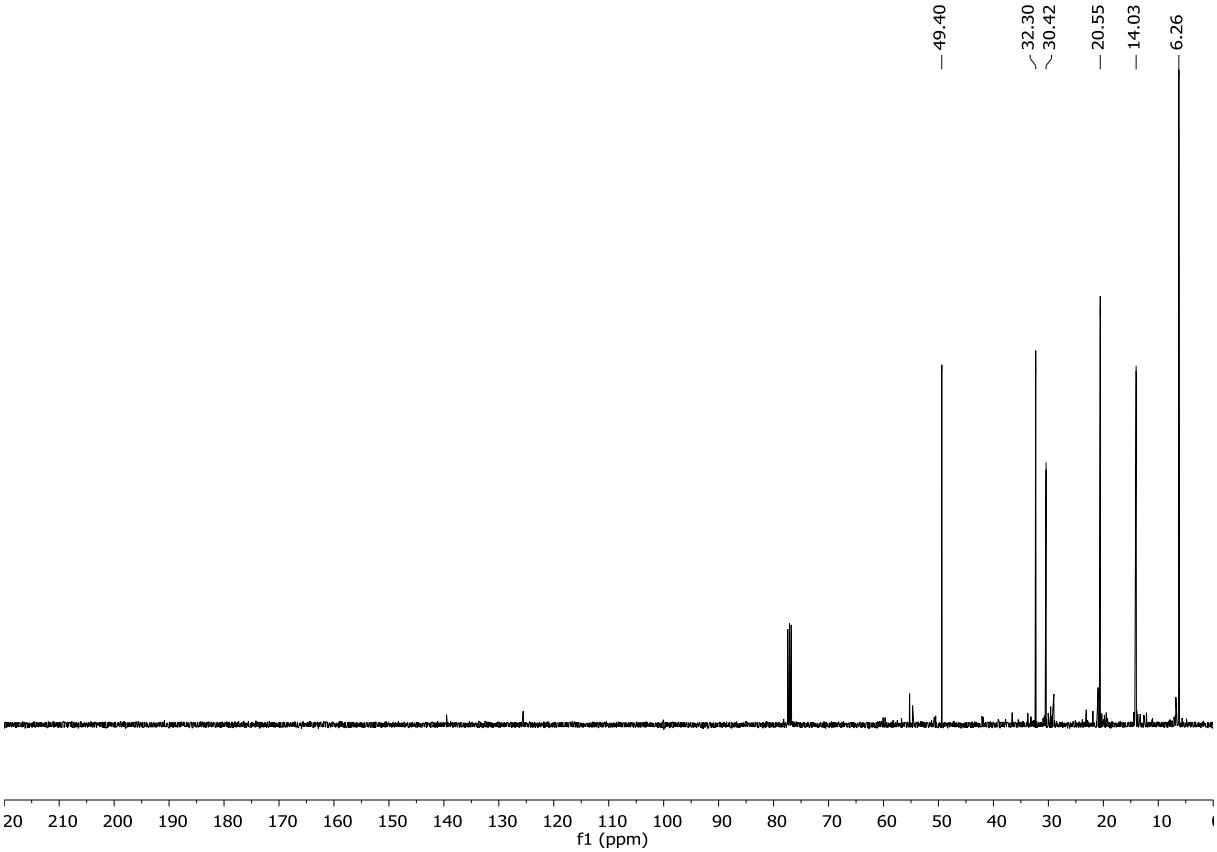

O
N
NH2
5.05
2.07
1.99
1.00
4.02
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)

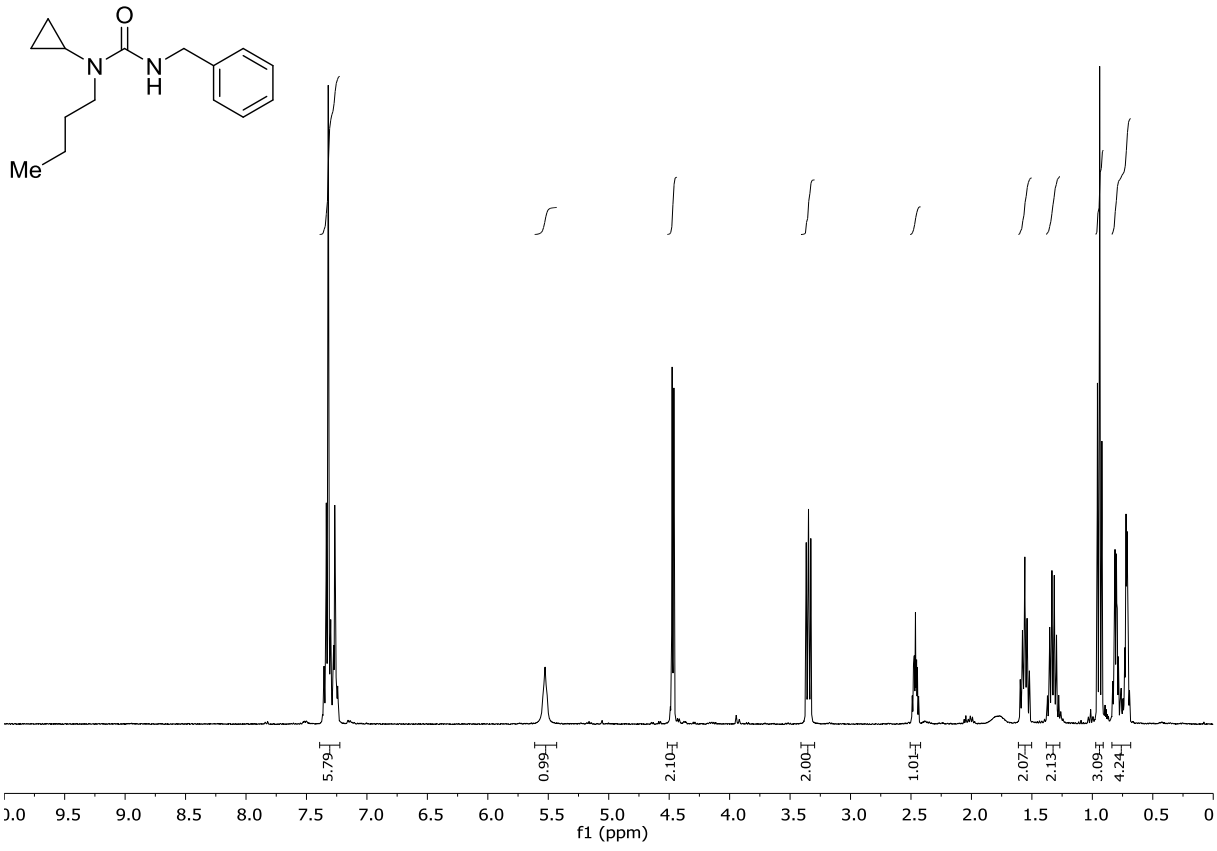

160.05
138.71
128.42
127.71
126.98
50.12
28.61
8.49
f1 (ppm)

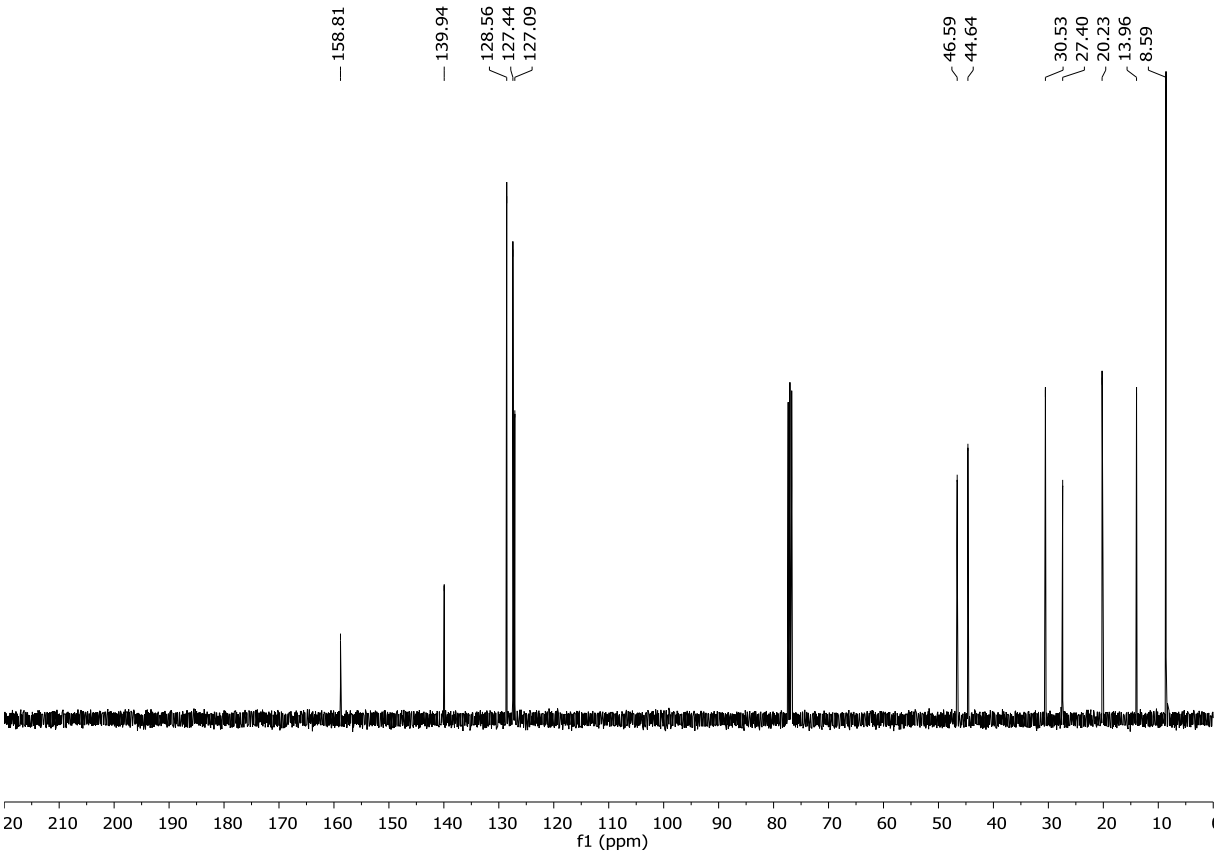

O
N
NH
O
1.12
6.27
1.00
1.03
2.03
2.04
f1 (ppm)

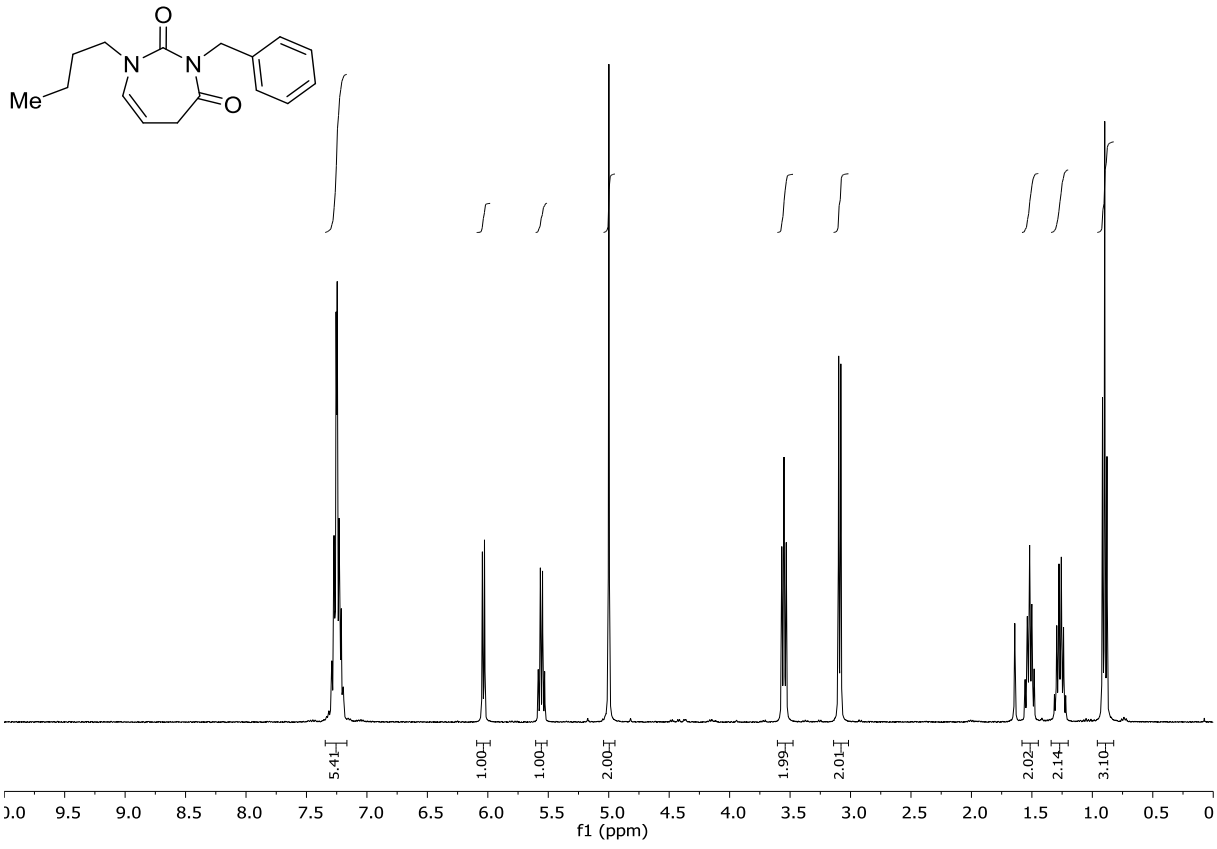

171.06
151.33
136.16
130.78
128.85
128.02
127.91
110.44
52.63
34.28
f1 (ppm)

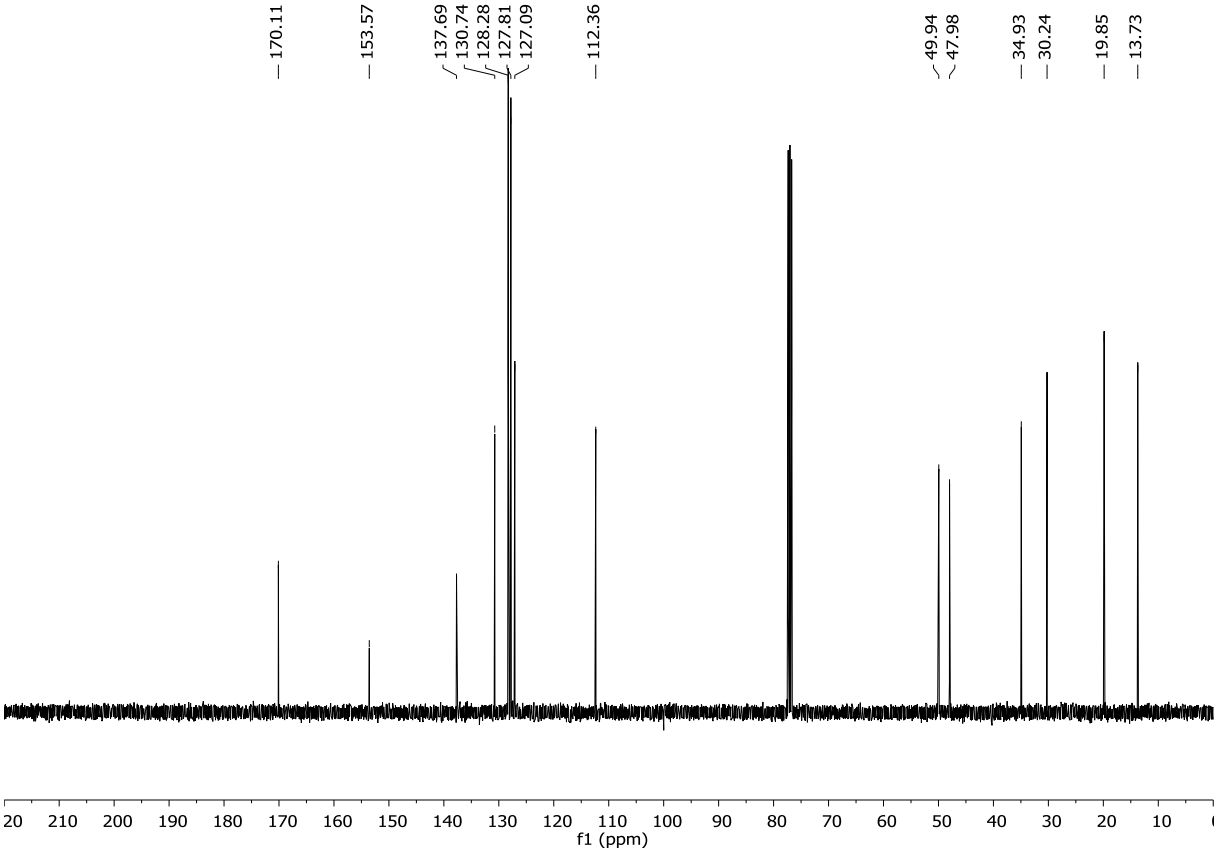

NH
Me
1.99
1.08
1.30
2.44
2.55
4.87
5.28
f1 (ppm)

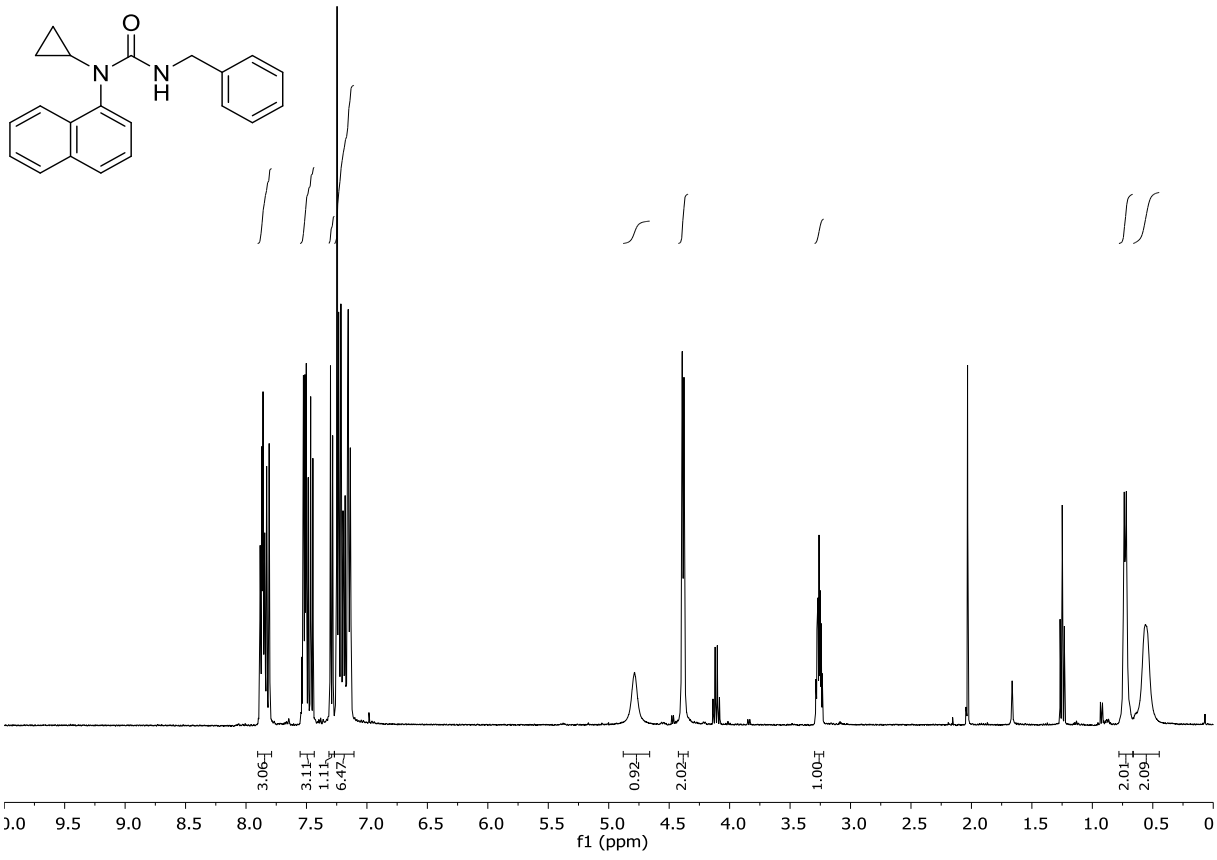

49.40
32.30
30.42
20.55
14.03
6.26
f1 (ppm)

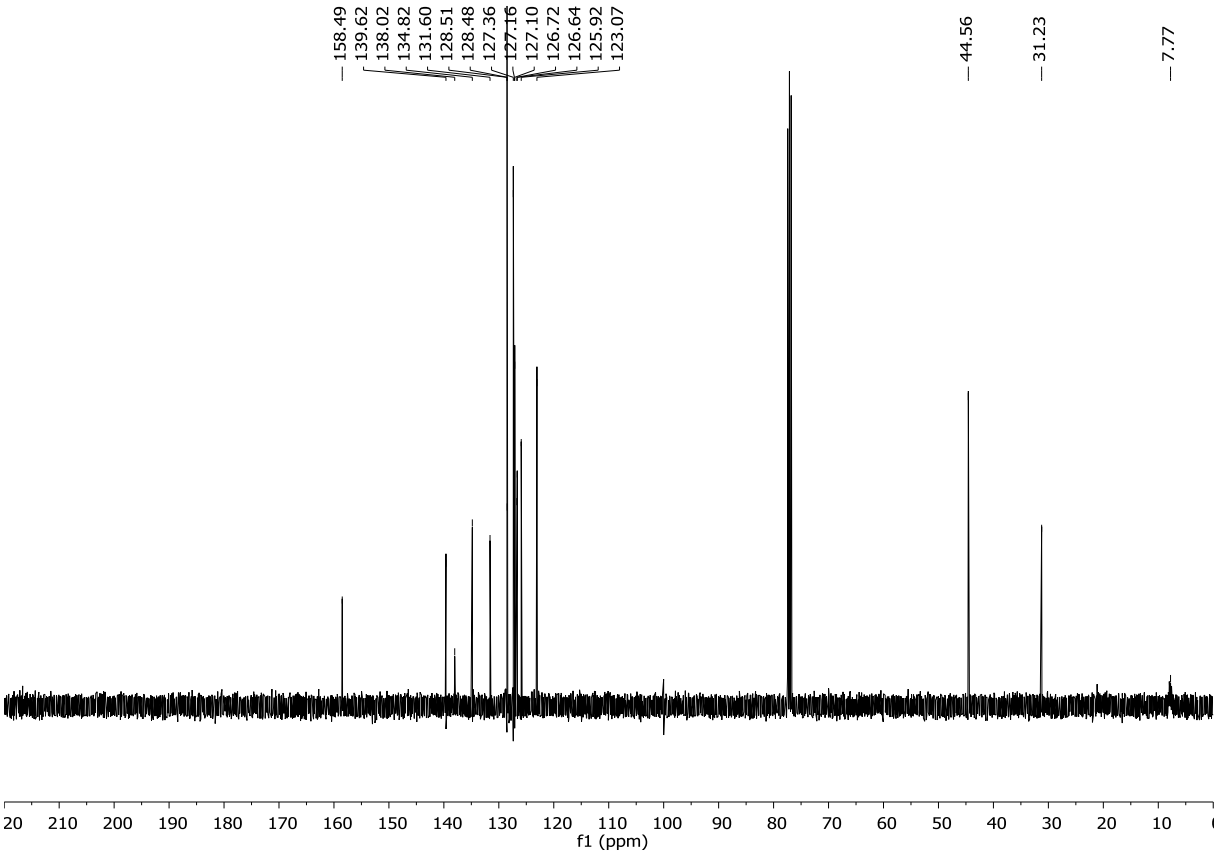

O
N
N
H
Me
5.79
0.99
2.10
2.00
1.01
2.07
2.13
3.09
4.24
f1 (ppm)

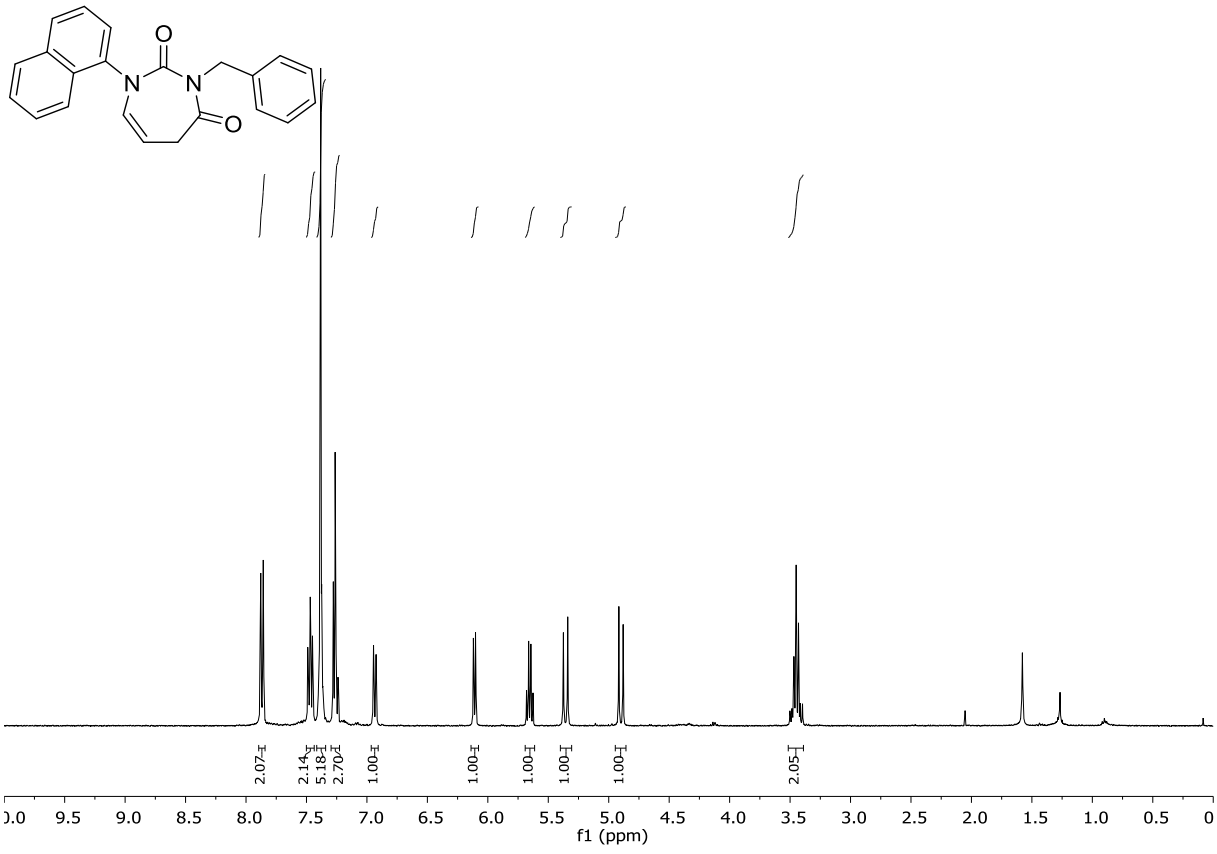

158.81
139.94
128.56
127.44
127.09
46.59
44.64
30.53
27.40
20.23
13.96
8.59
f1 (ppm)

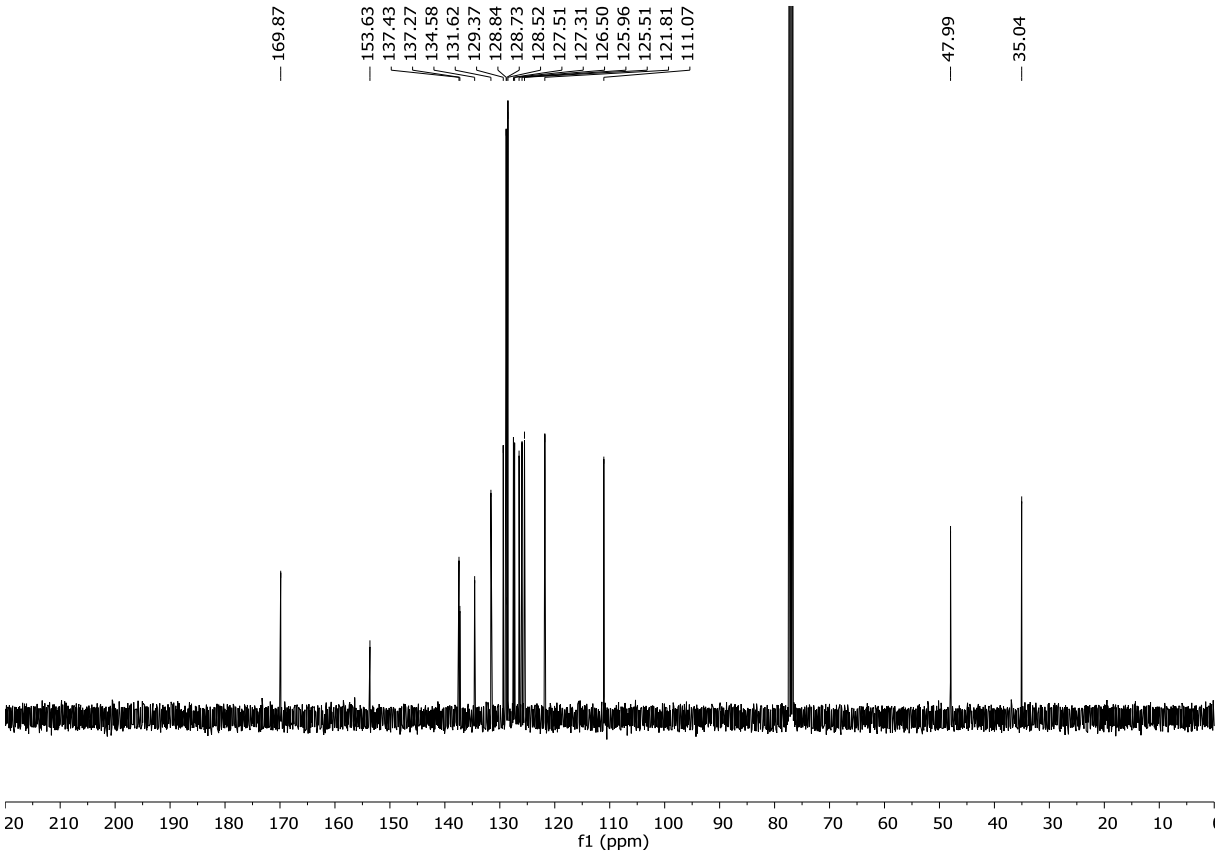

O
N
N
O
Me
5.41
1.00
1.00
2.00
1.99
2.01
2.02
2.14
3.10
f1 (ppm)

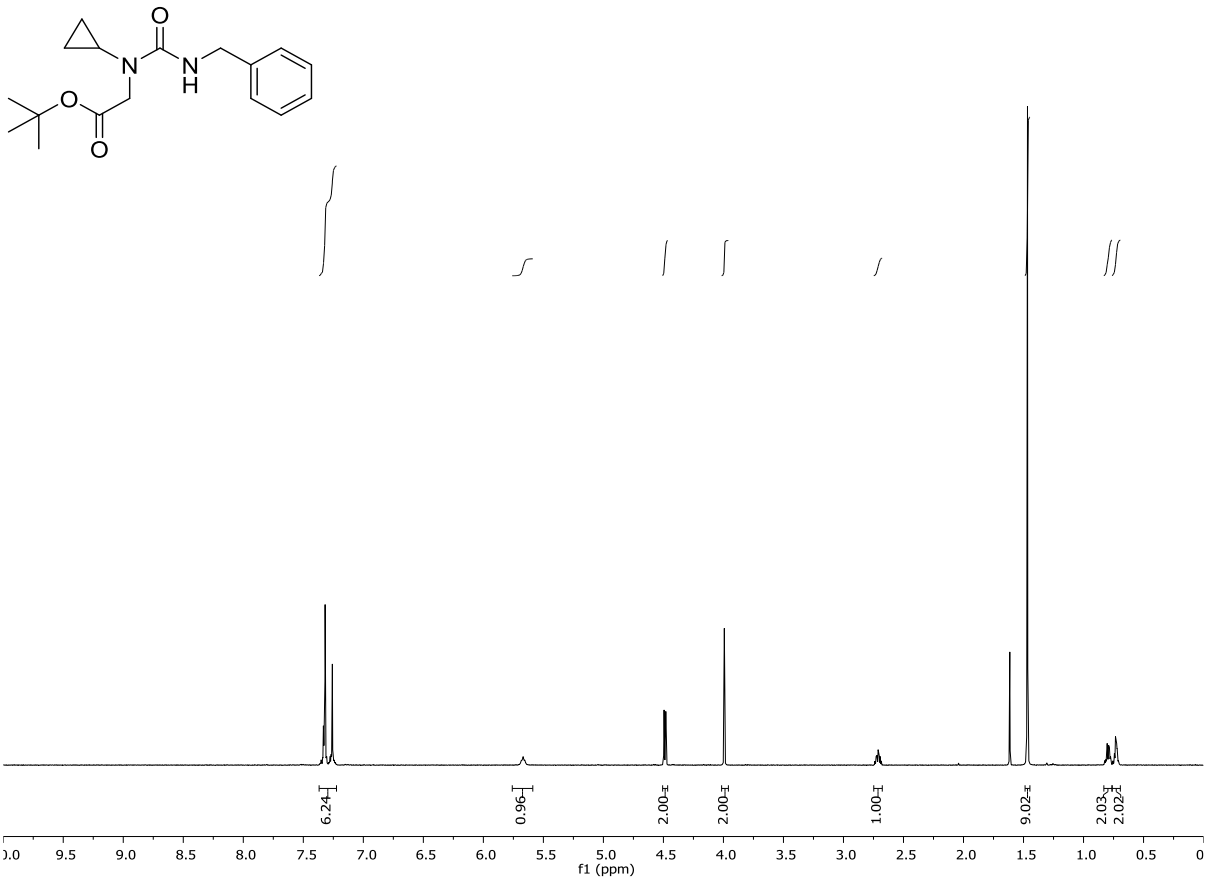

170.11
153.57
137.69
130.74
128.28
127.81
127.09
112.36
49.94
47.98
34.93
30.24
19.85
13.73
f1 (ppm)

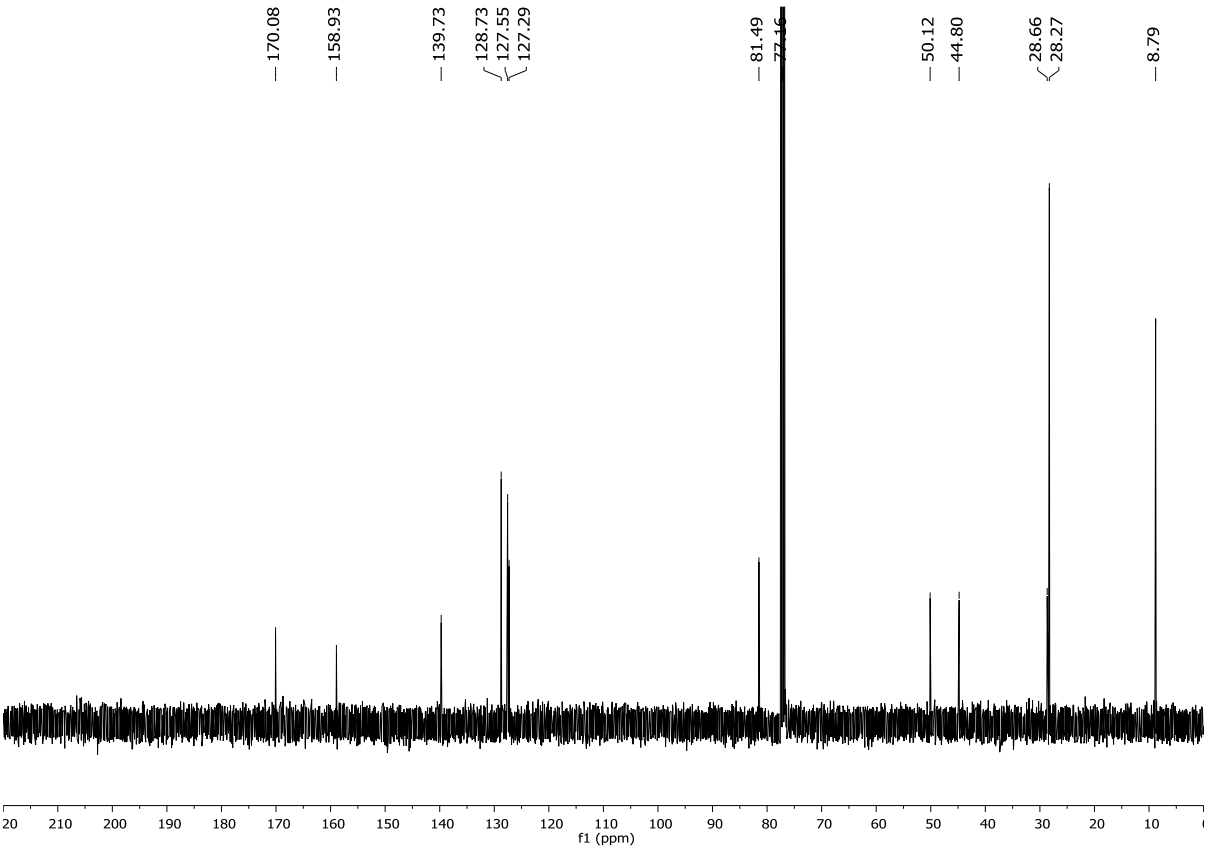

O
N
N
H
3.06
3.11
1.11
6.47
0.92
2.02
1.00
2.01
2.09
f1 (ppm)

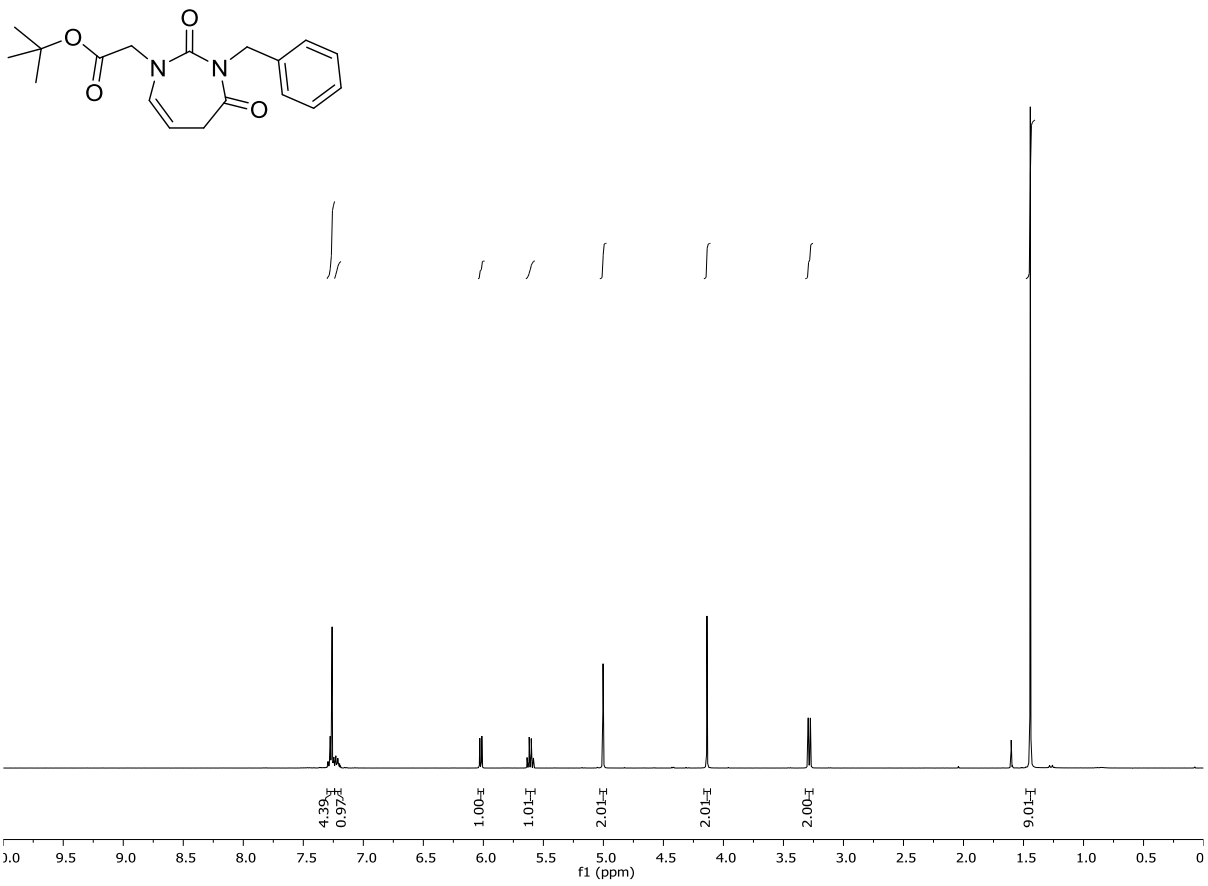

158.49
139.62
138.02
134.82
131.60
128.51
128.48
127.36
127.16
127.10
126.72
126.64
125.92
123.07
44.56
31.23
7.77
f1 (ppm)

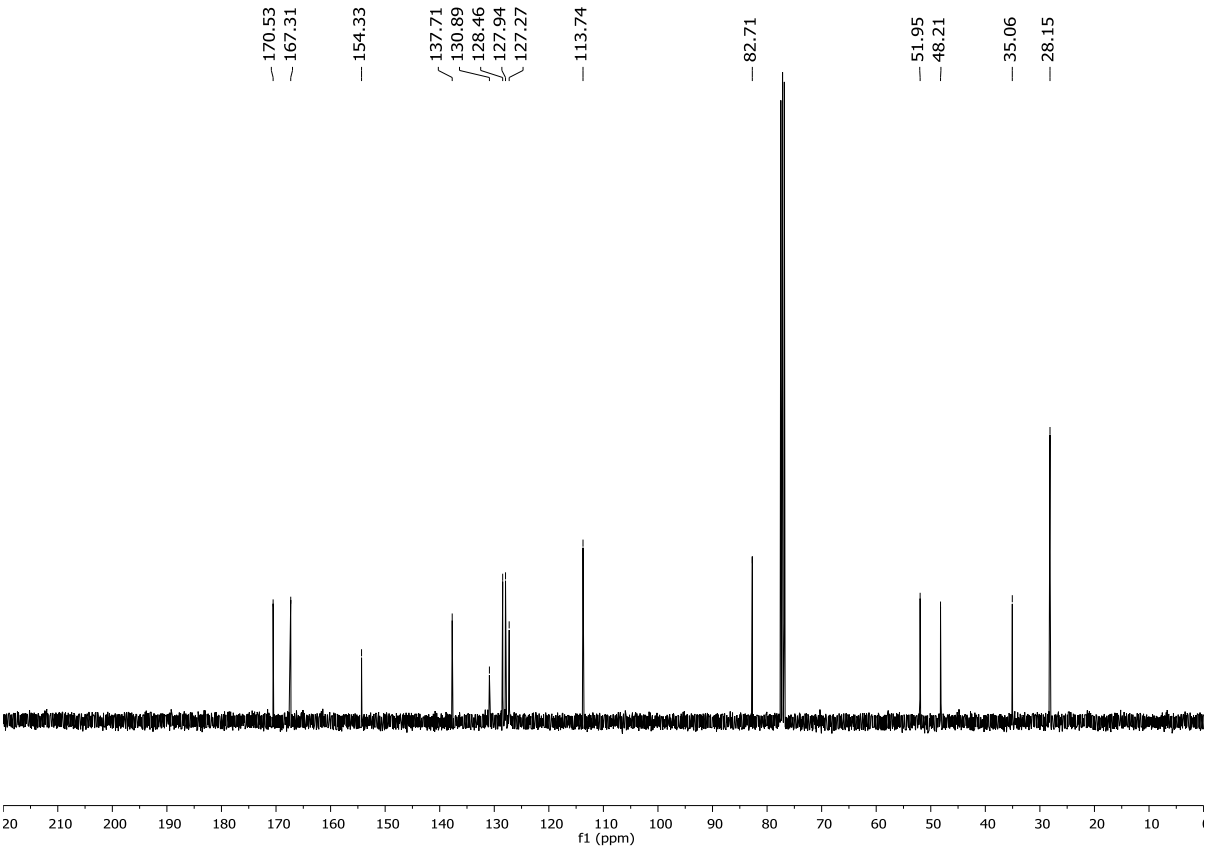

O
N
N
O
2.07
2.14
5.18
2.70
1.00
1.00
1.00
1.00
1.00
2.05
f1 (ppm)

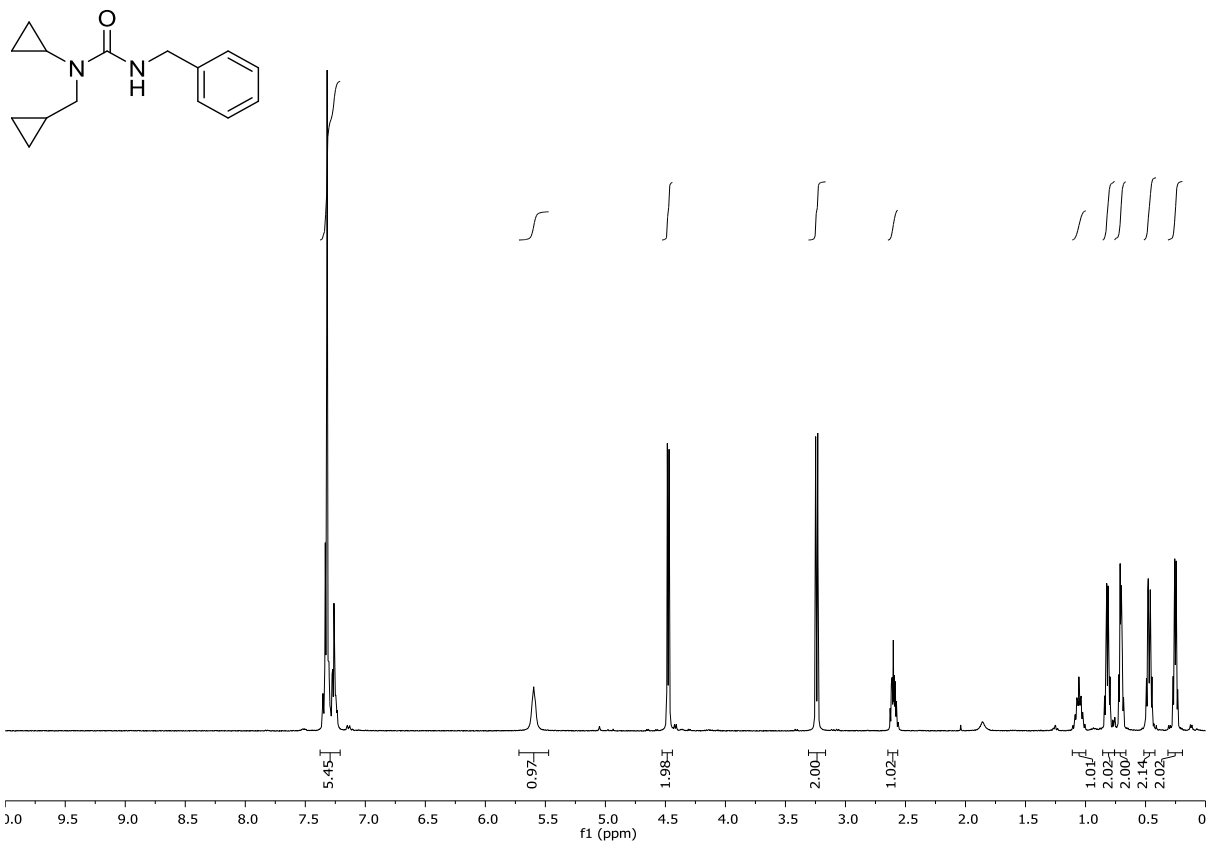

169.87
153.63
137.43
137.27
134.58
131.62
129.37
128.84
128.73
128.52
127.51
127.31
126.50
125.96
125.51
121.81
111.07
47.99
35.04
f1 (ppm)

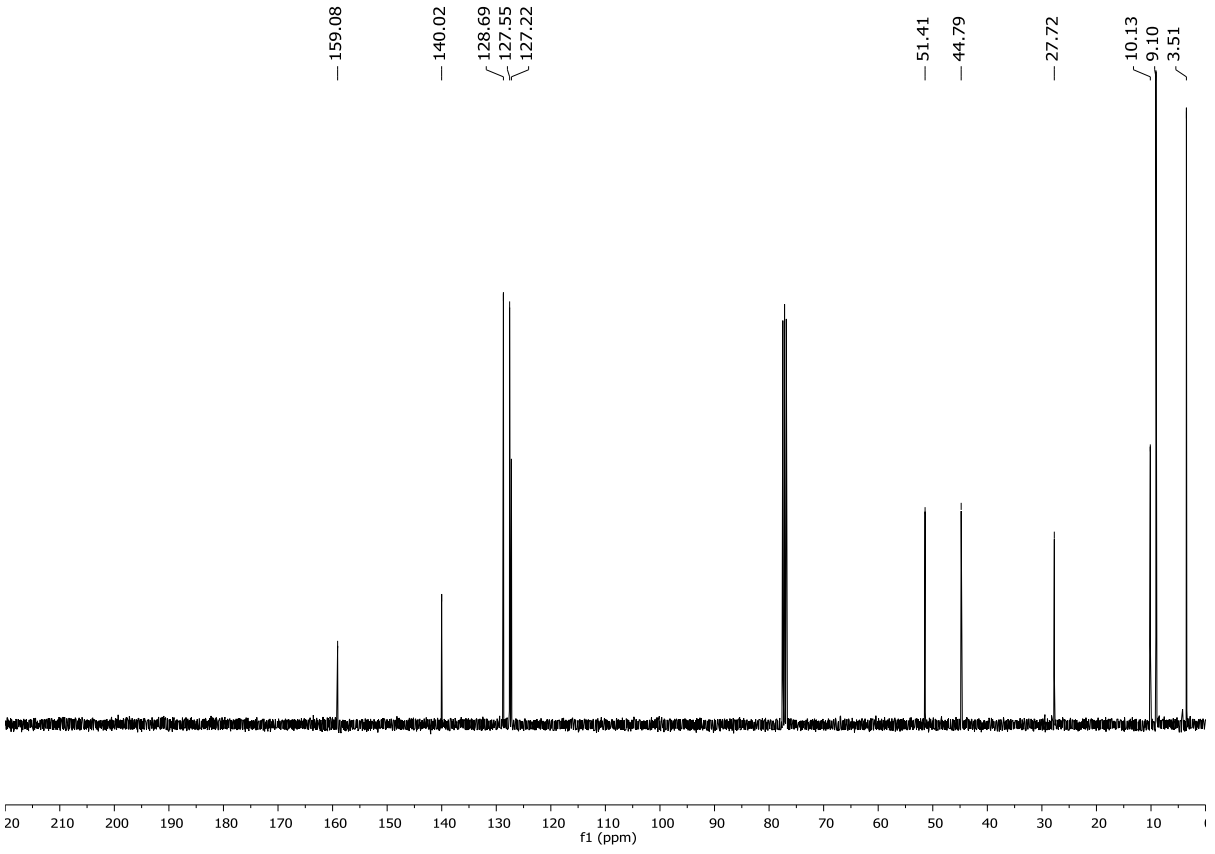

O
N
N
H
O
O
6.24
0.96
2.00
2.00
1.00
9.02
2.03
2.02
f1 (ppm)

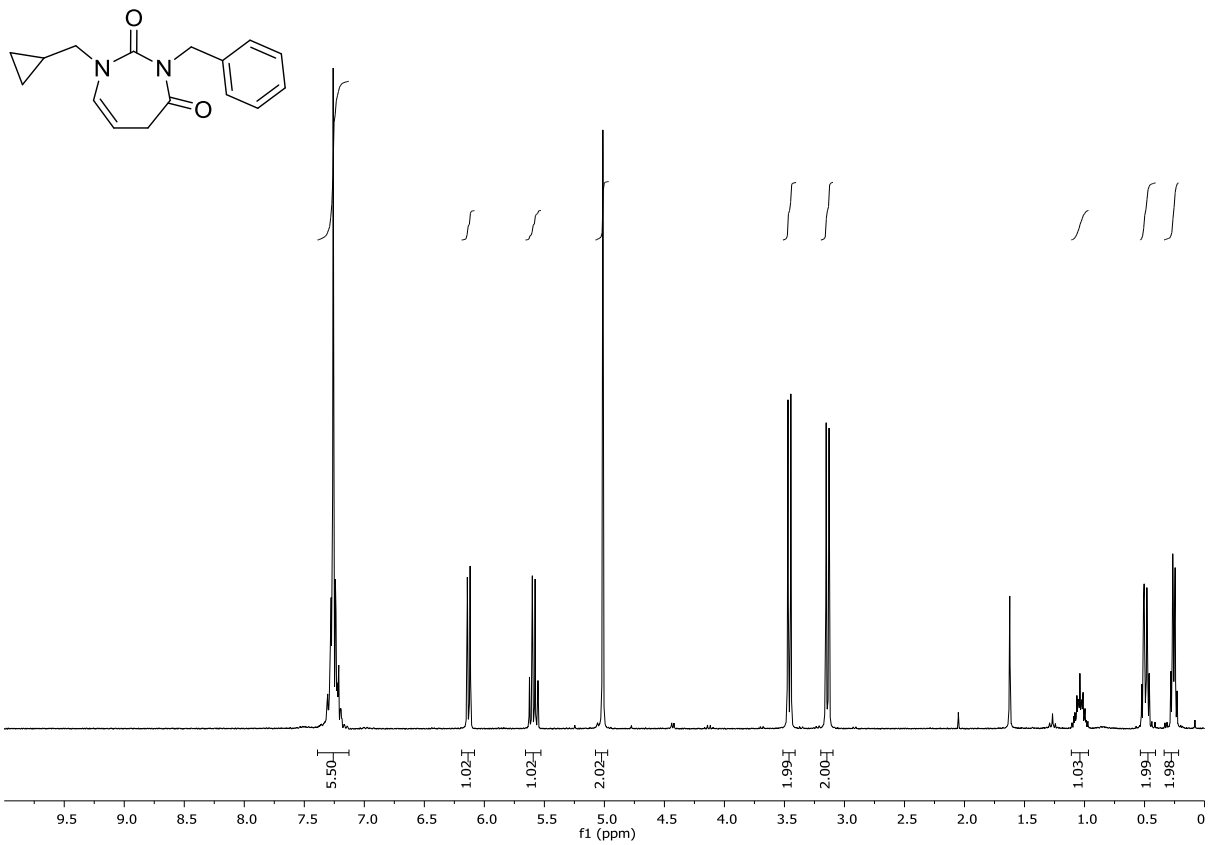

170.08
158.93
139.73
128.73
127.55
127.29
81.49
77.16
50.12
44.80
28.66
28.27
8.79
f1 (ppm)

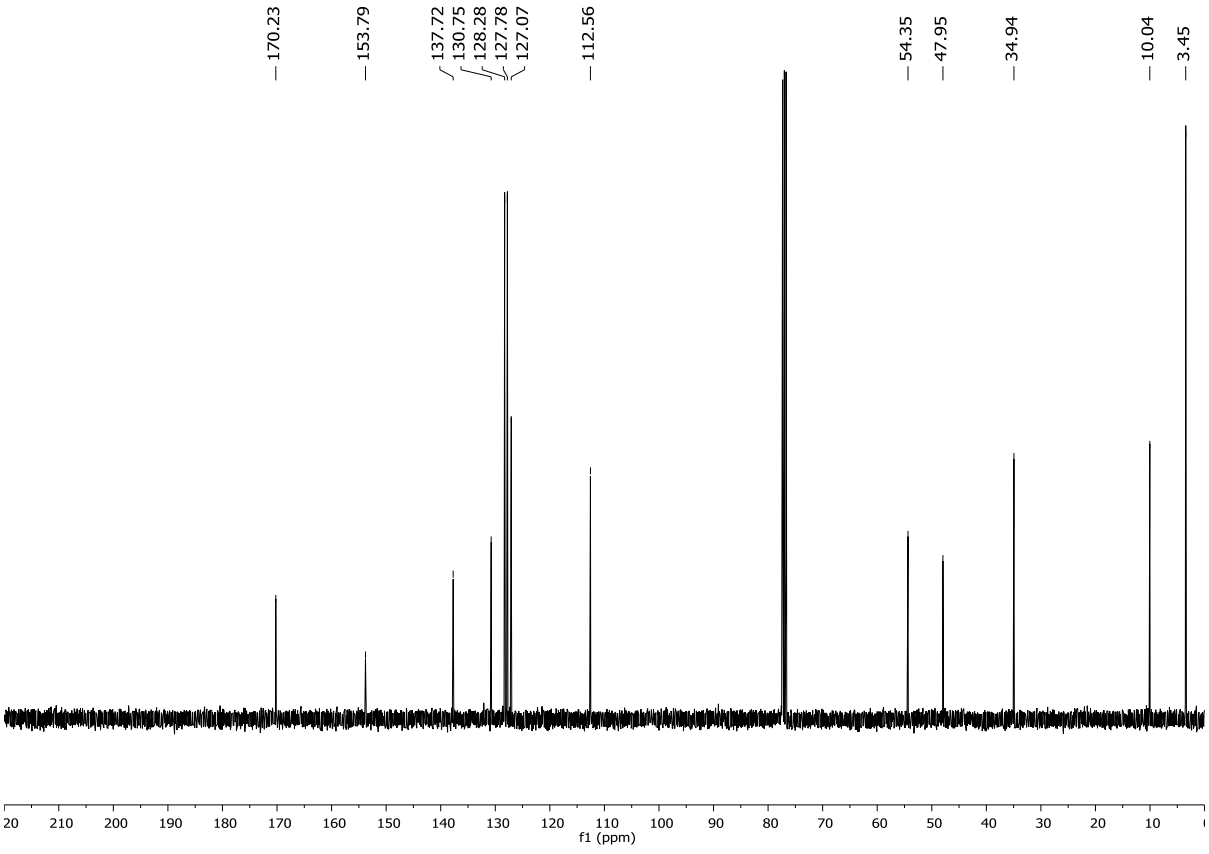

4.39
0.97
1.00
1.01
2.01
2.01
2.00
9.01
f1 (ppm)

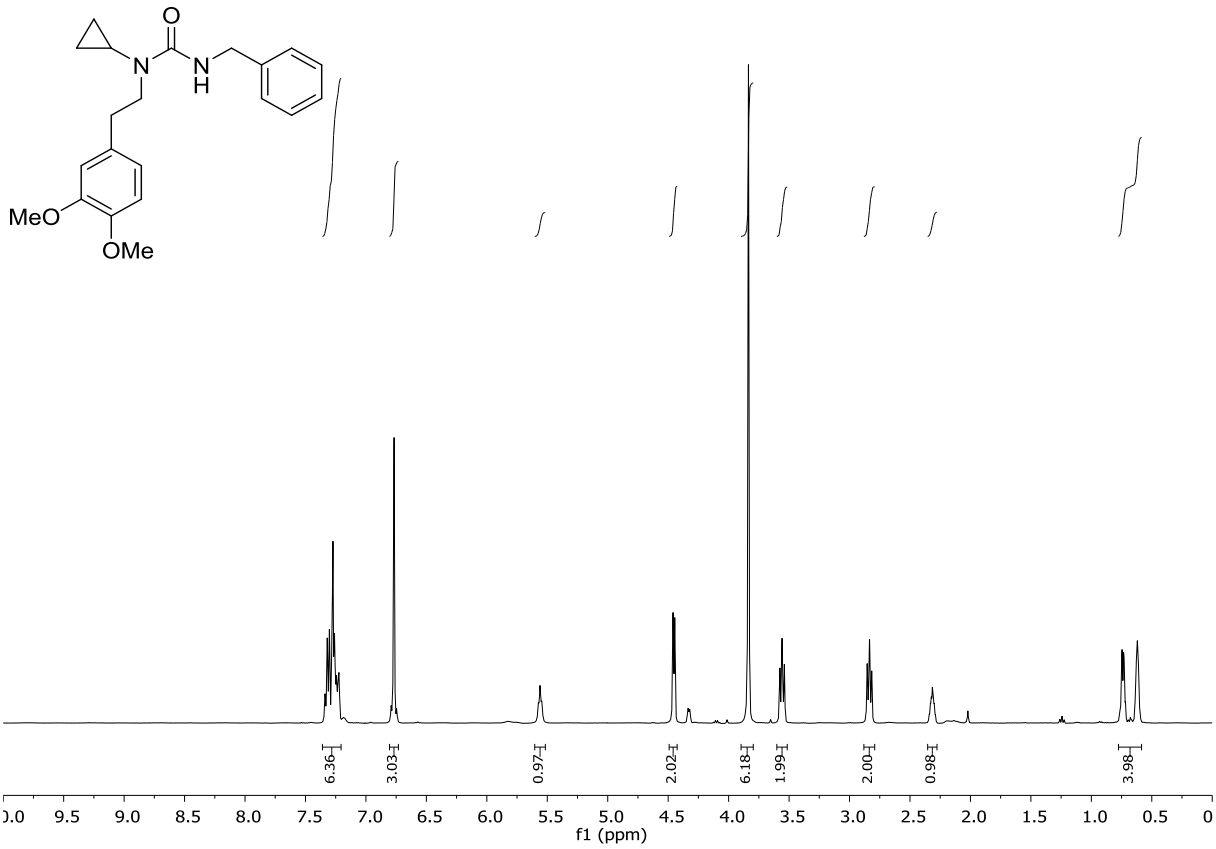

170.53
167.31
154.33
137.71
130.89
128.46
127.94
127.27
113.74
82.71
51.95
48.21
35.06
28.15
f1 (ppm)

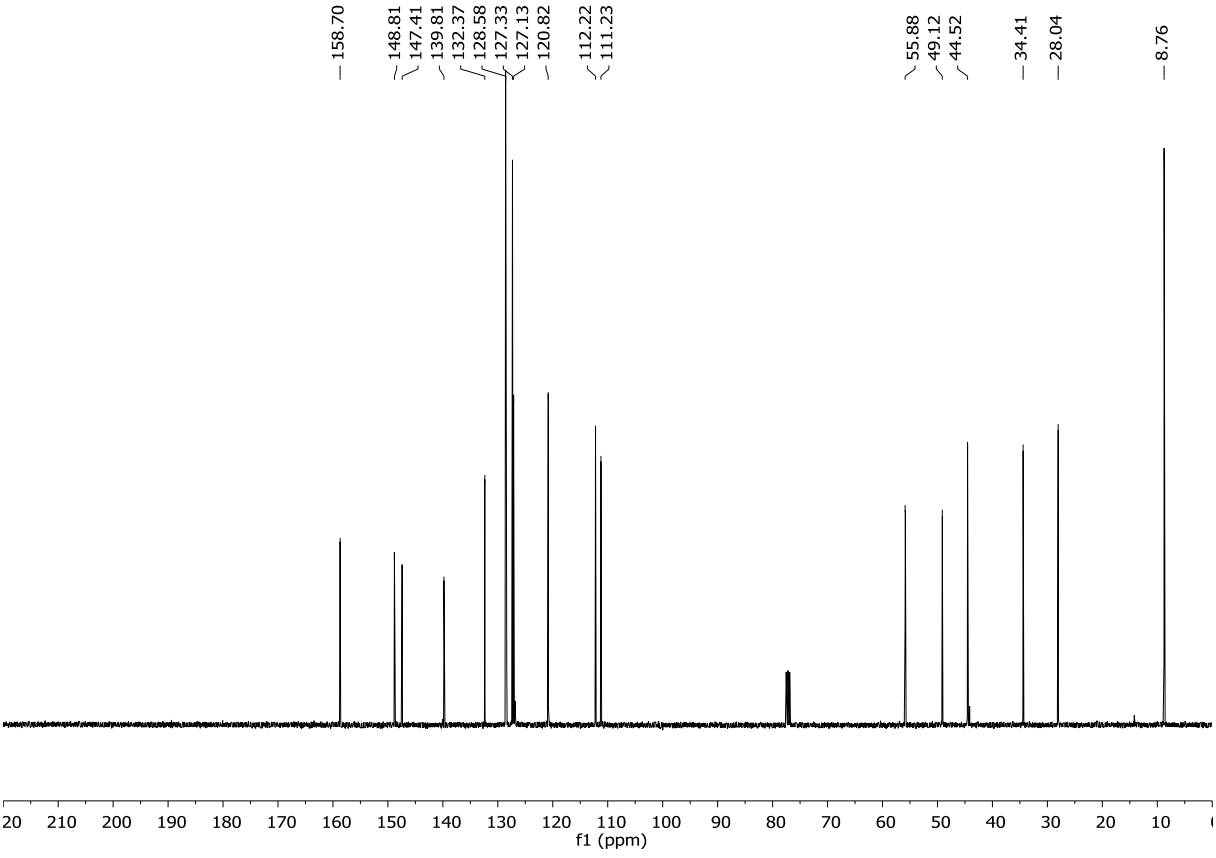

O
N
N
H
5.45
0.97
1.98
2.00
1.02
1.01
2.02
2.00
2.14
2.02
f1 (ppm)


159.08
140.02
128.69
127.55
127.22
51.41
44.79
27.72
10.13
9.10
3.51
f1 (ppm)


O
N
N
O
5.50
1.02
1.02
2.02
1.99
2.00
1.03
1.99
1.98
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)


170.23
153.79
137.72
130.75
128.28
127.78
127.07
112.56
54.35
47.95
34.94
10.04
3.45
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


O
N
N
H
MeO
OMe
6.36
3.03
0.97
2.02
6.18
1.99
2.00
0.98
3.98
f1 (ppm)


158.70
148.81
147.41
139.81
132.37
128.58
127.33
127.13
120.82
112.22
111.23
55.88
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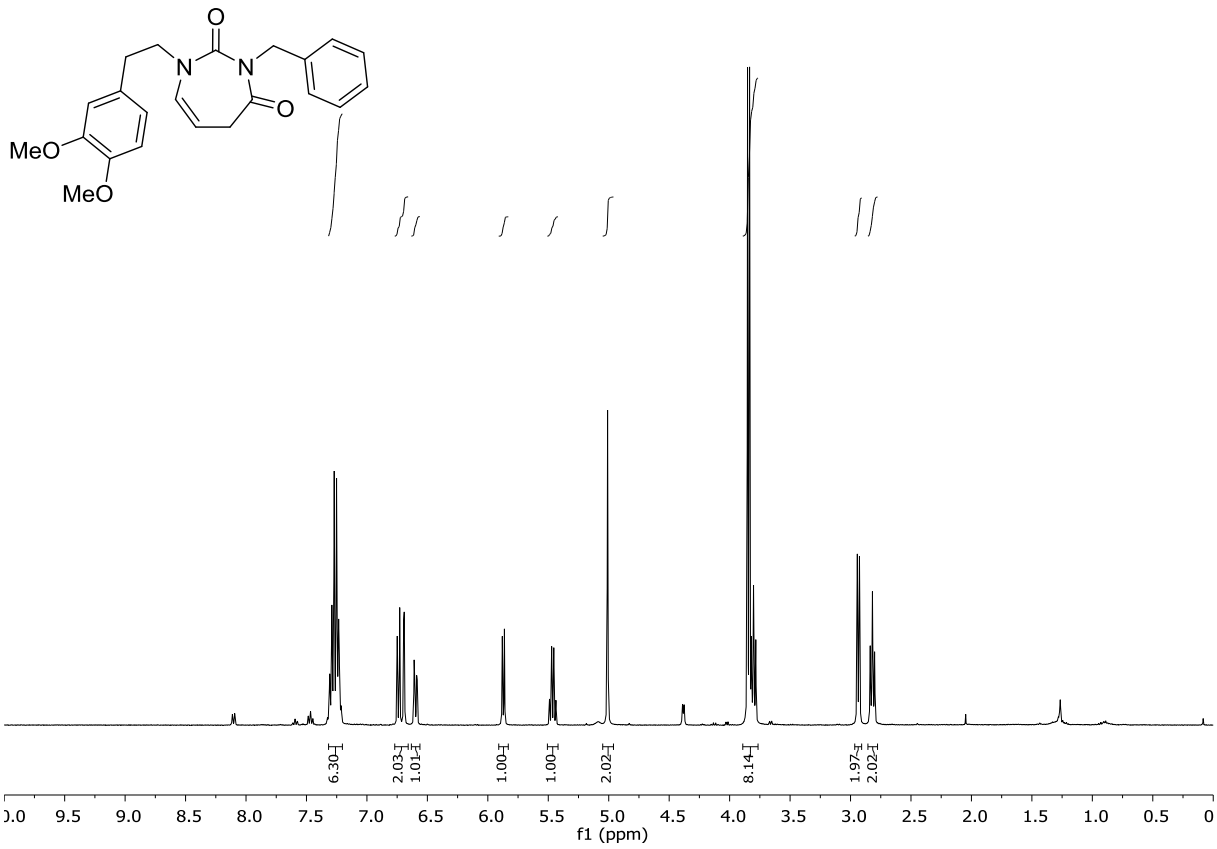
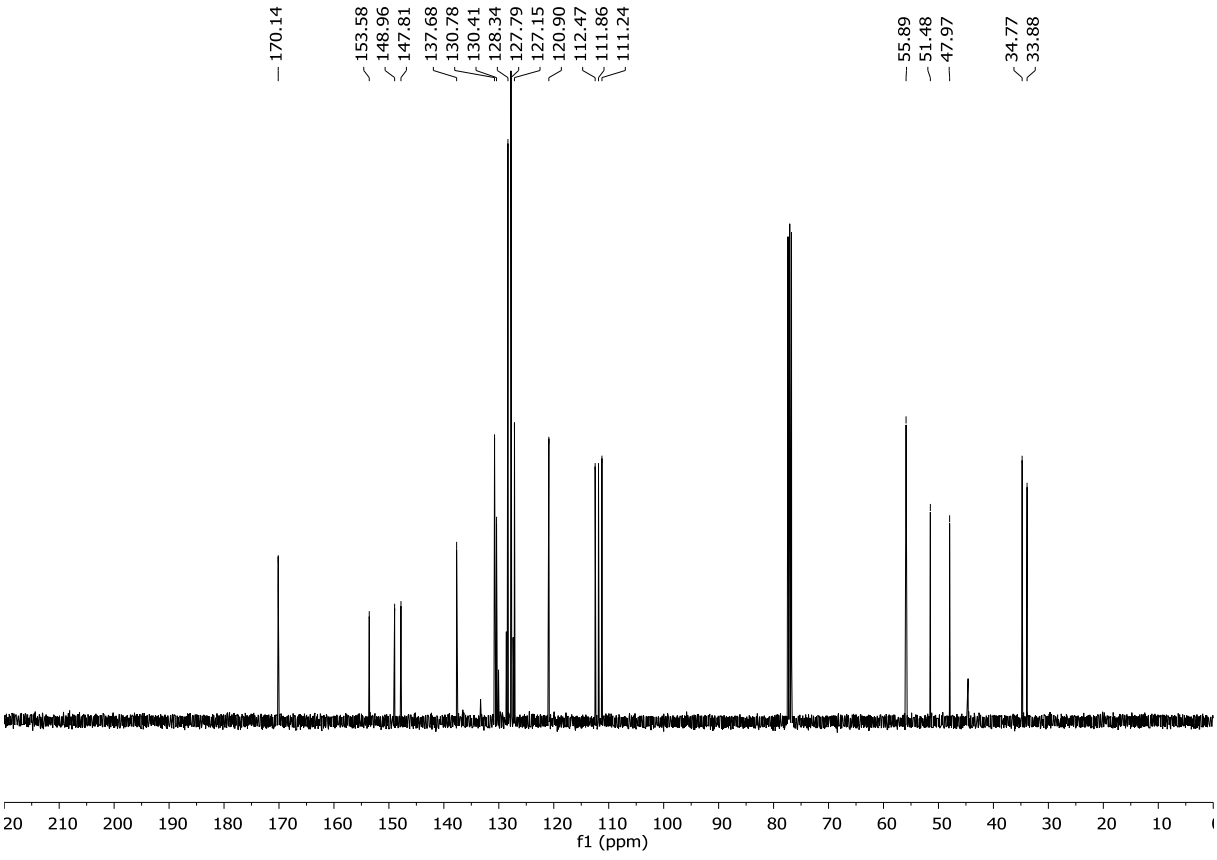
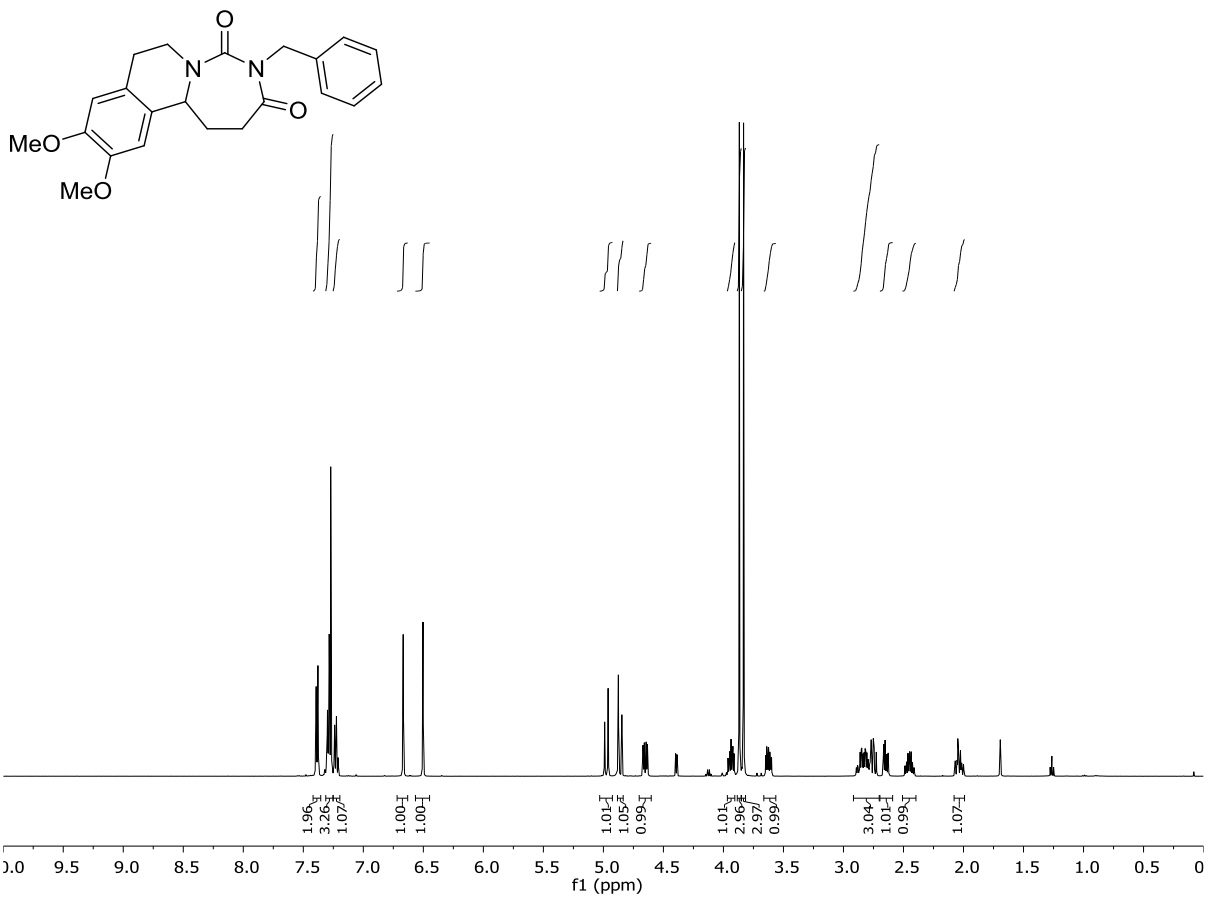
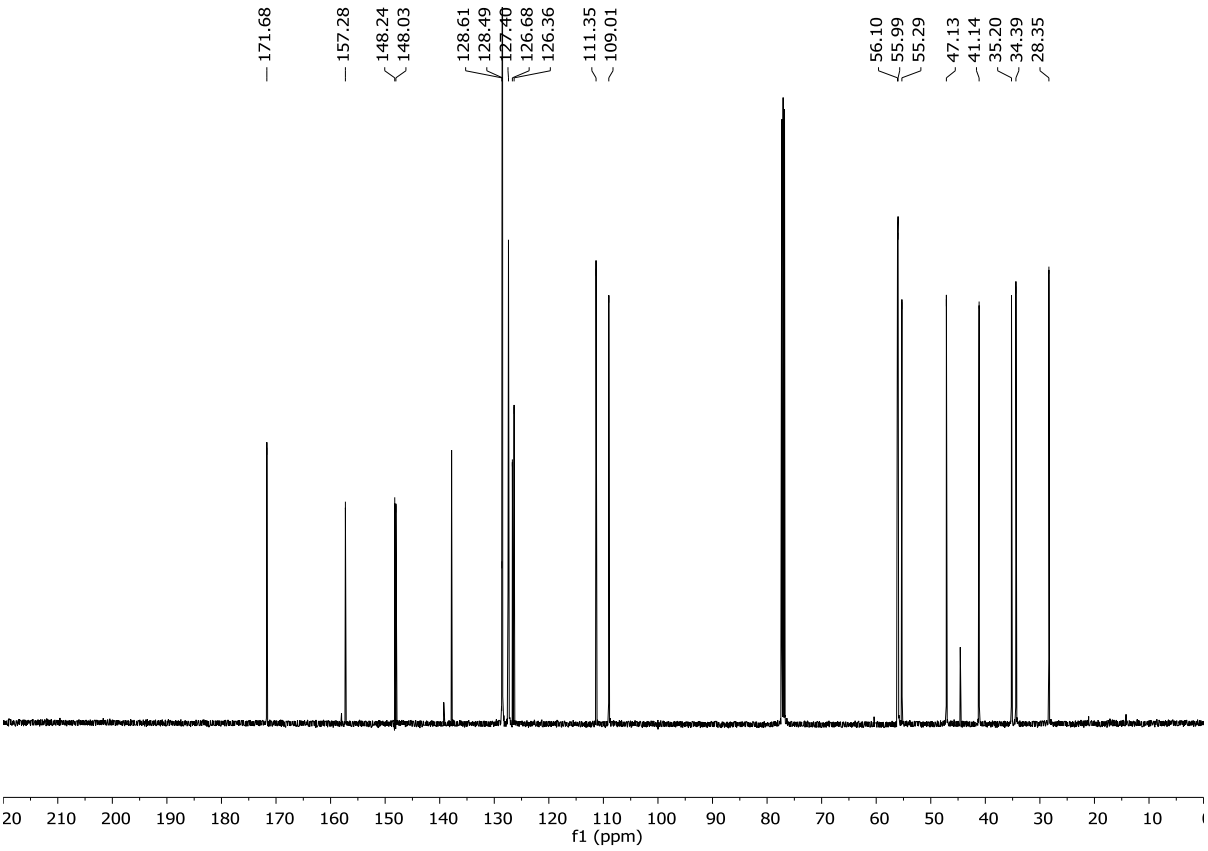
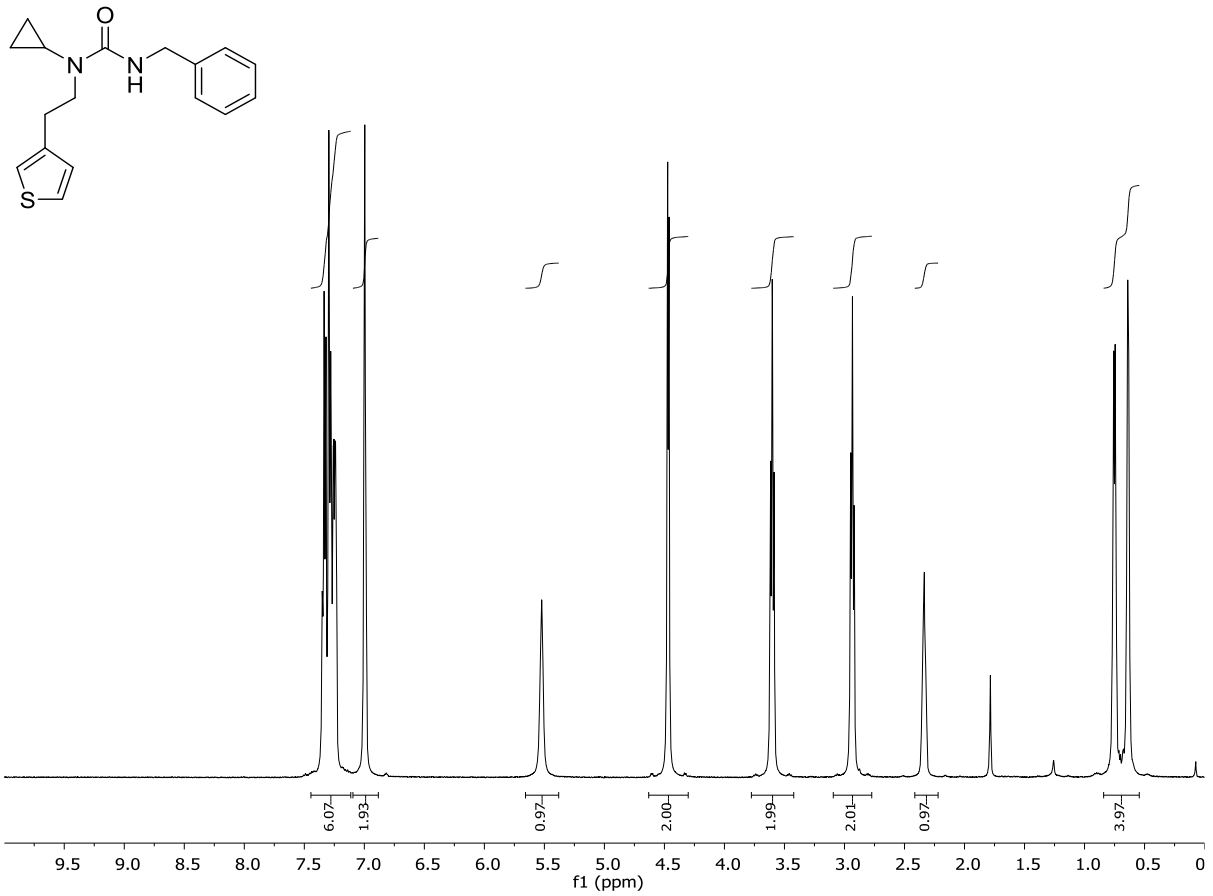
44.52
34.41
28.04
8.76
f1 (ppm)

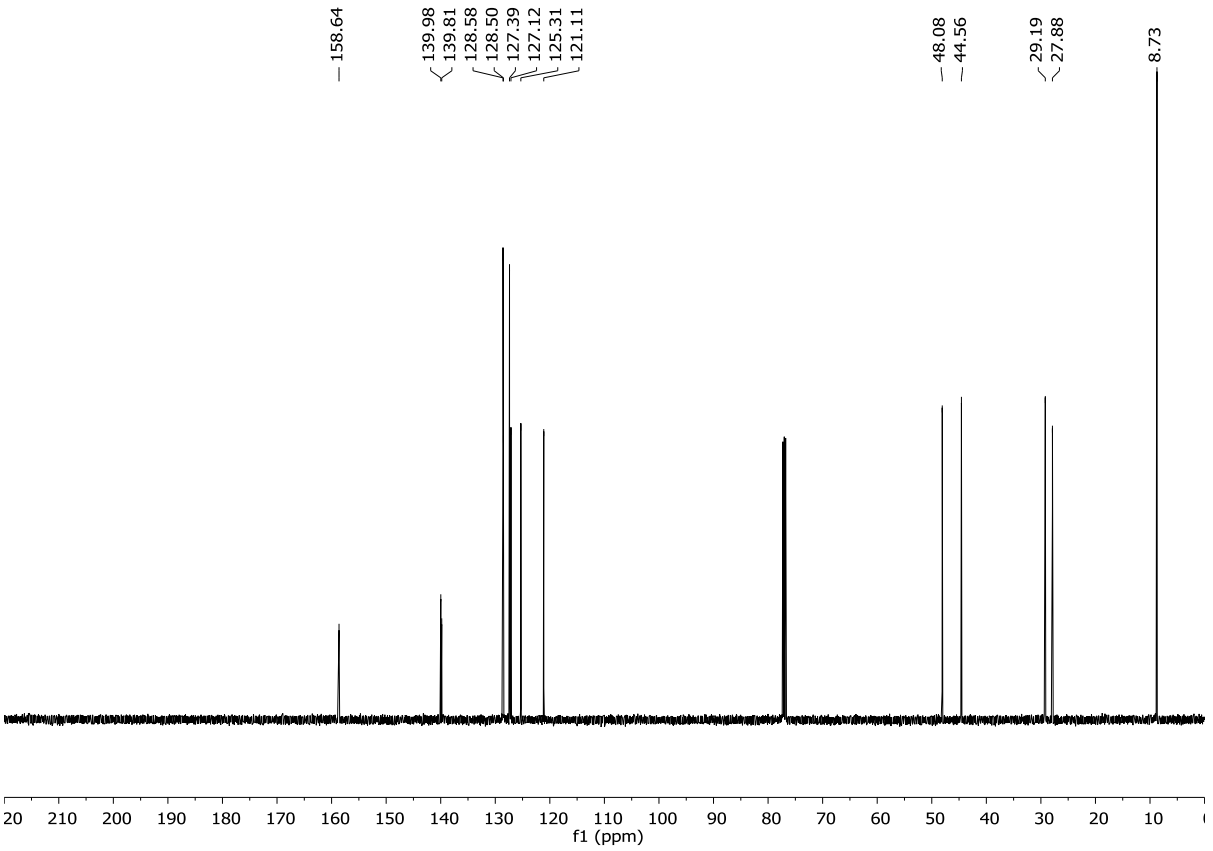

O
N
N
O
MeO
MeO
6.30
2.03
1.01
1.00
1.00
2.02
8.14
1.97
2.02
f1 (ppm)

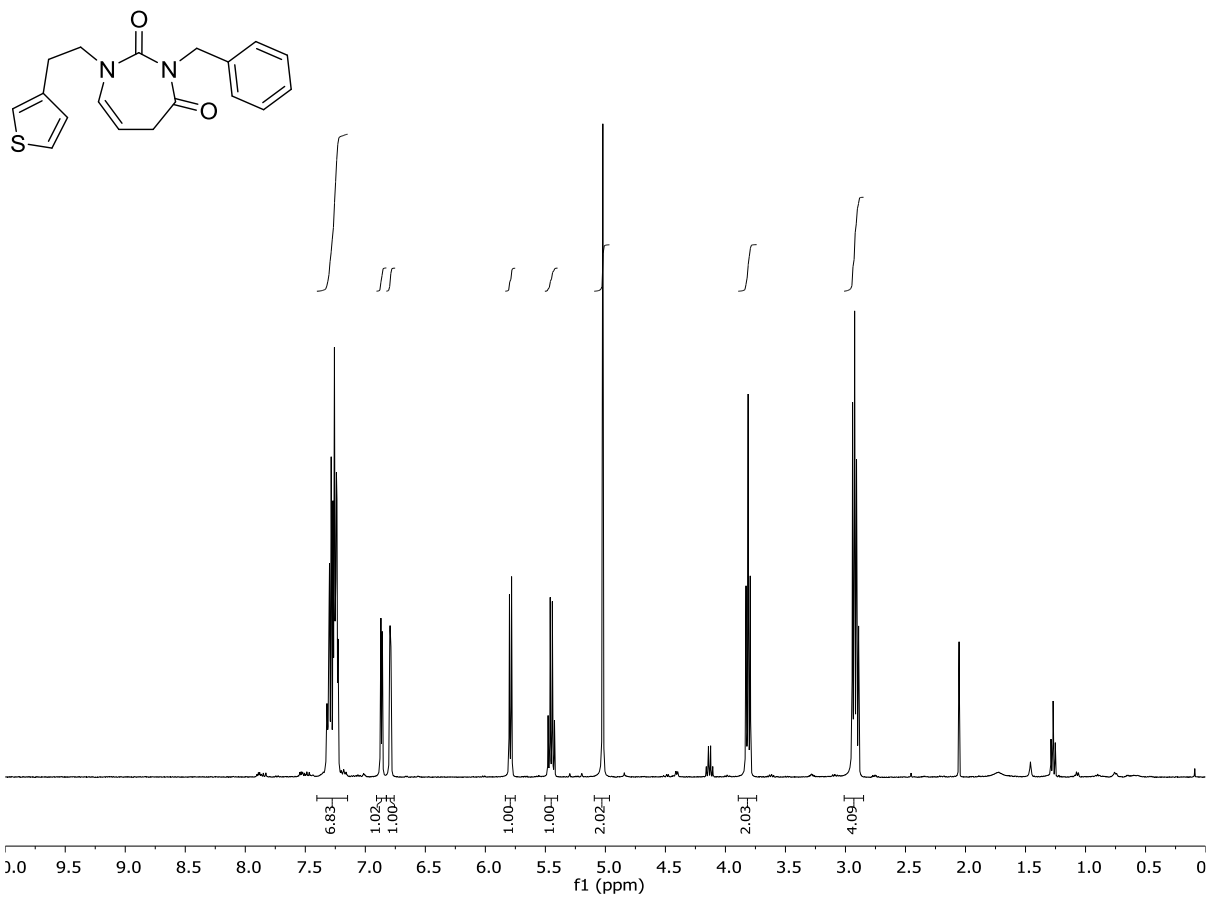

170.14
153.58
148.96
147.81
137.68
130.78
130.41
128.34
127.79
127.15
120.90
112.47
111.86
111.24
55.89
51.48
47.97
34.77
33.88
f1 (ppm)

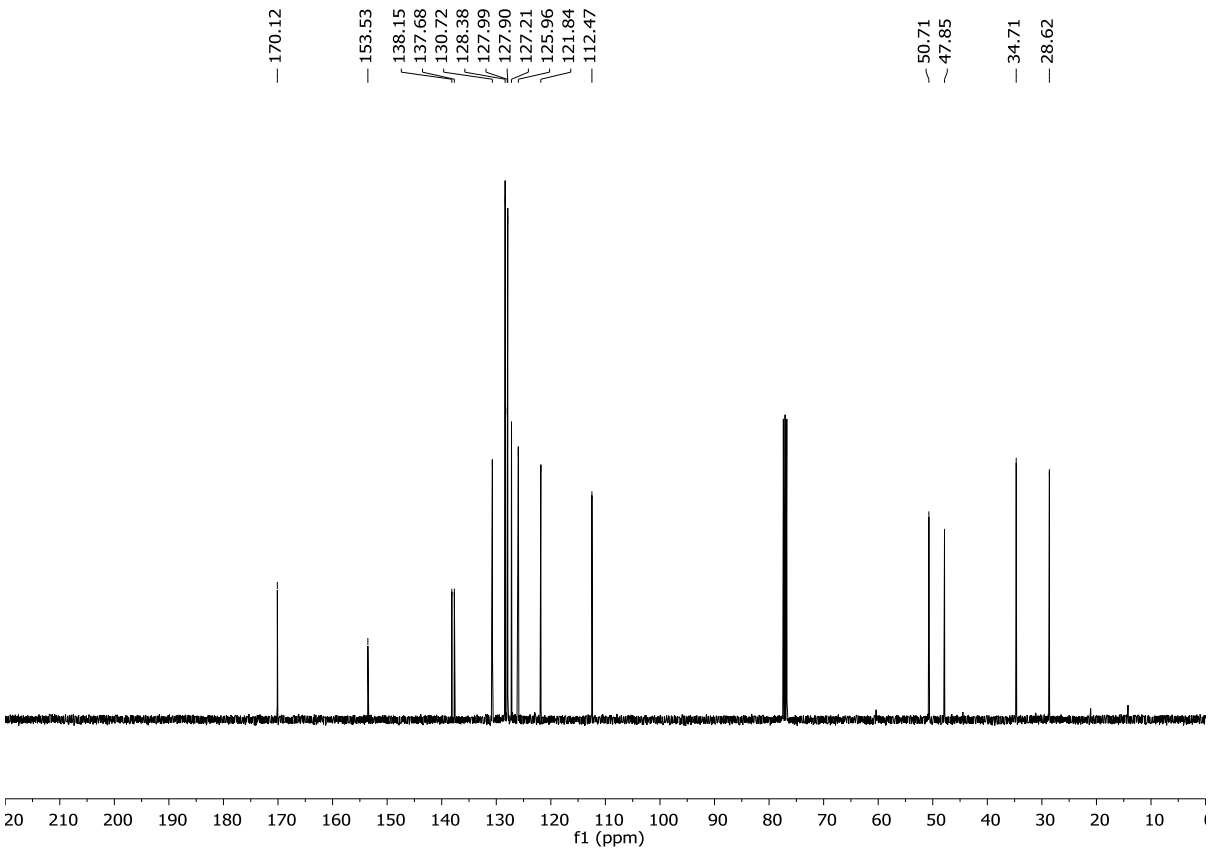

O
N
N
O
MeO
MeO
1.96
3.26
1.07
1.00
1.00
1.01
1.05
0.99
1.01
2.96
2.97
0.99
3.04
1.01
0.99
1.07
f1 (ppm)

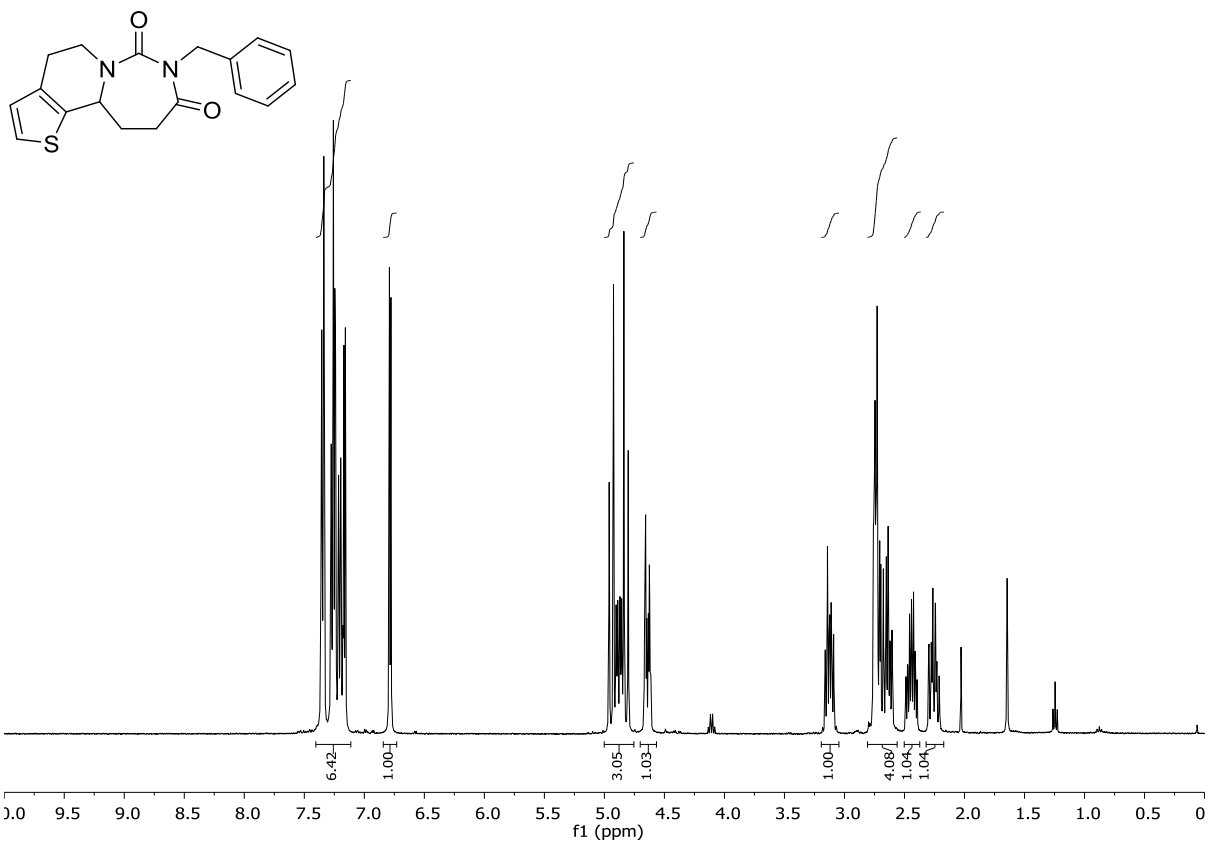

171.68
157.28
148.24
148.03
128.61
128.49
127.40
126.68
126.36
111.35
109.01
56.10
55.99
55.29
47.13
41.14
35.20
34.39
28.35
f1 (ppm)

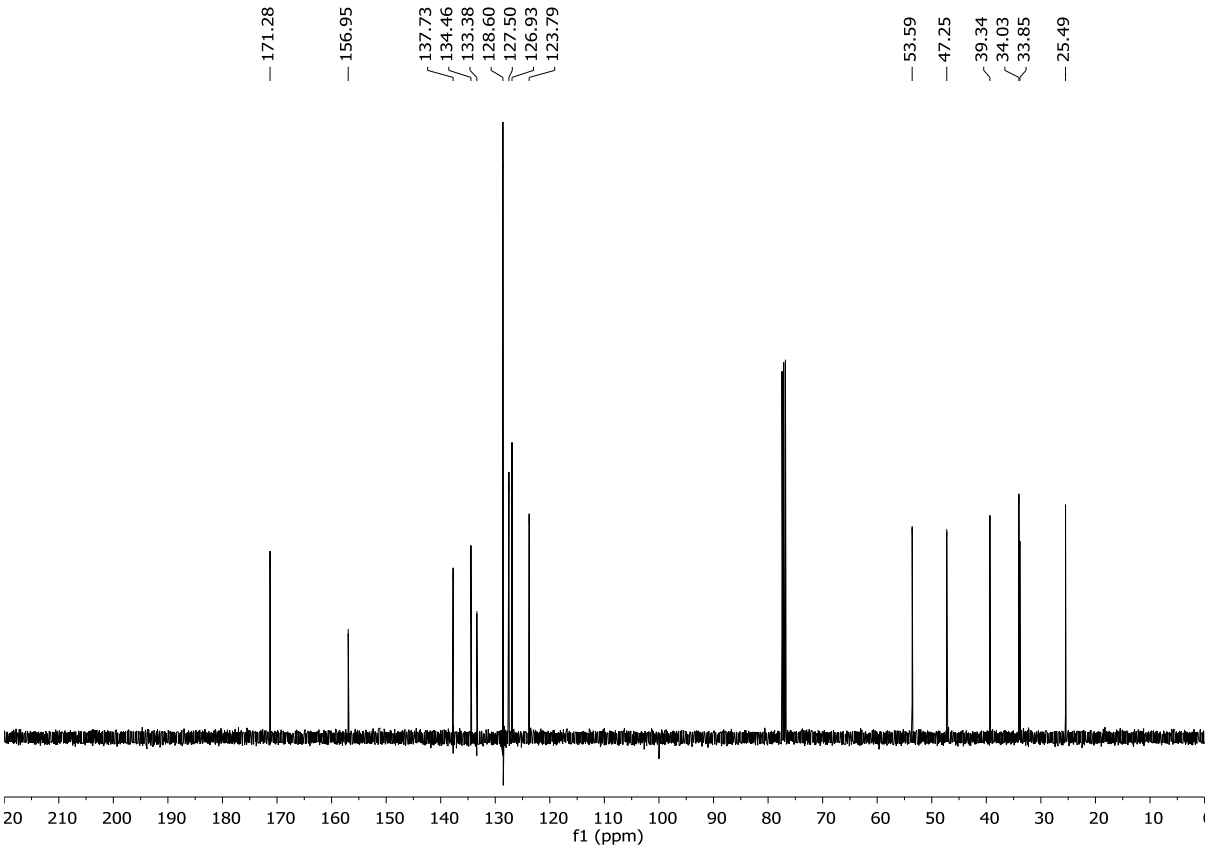

O
N
N
H
S
6.07
1.93
0.97
2.00
1.99
2.01
0.97
3.97
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)

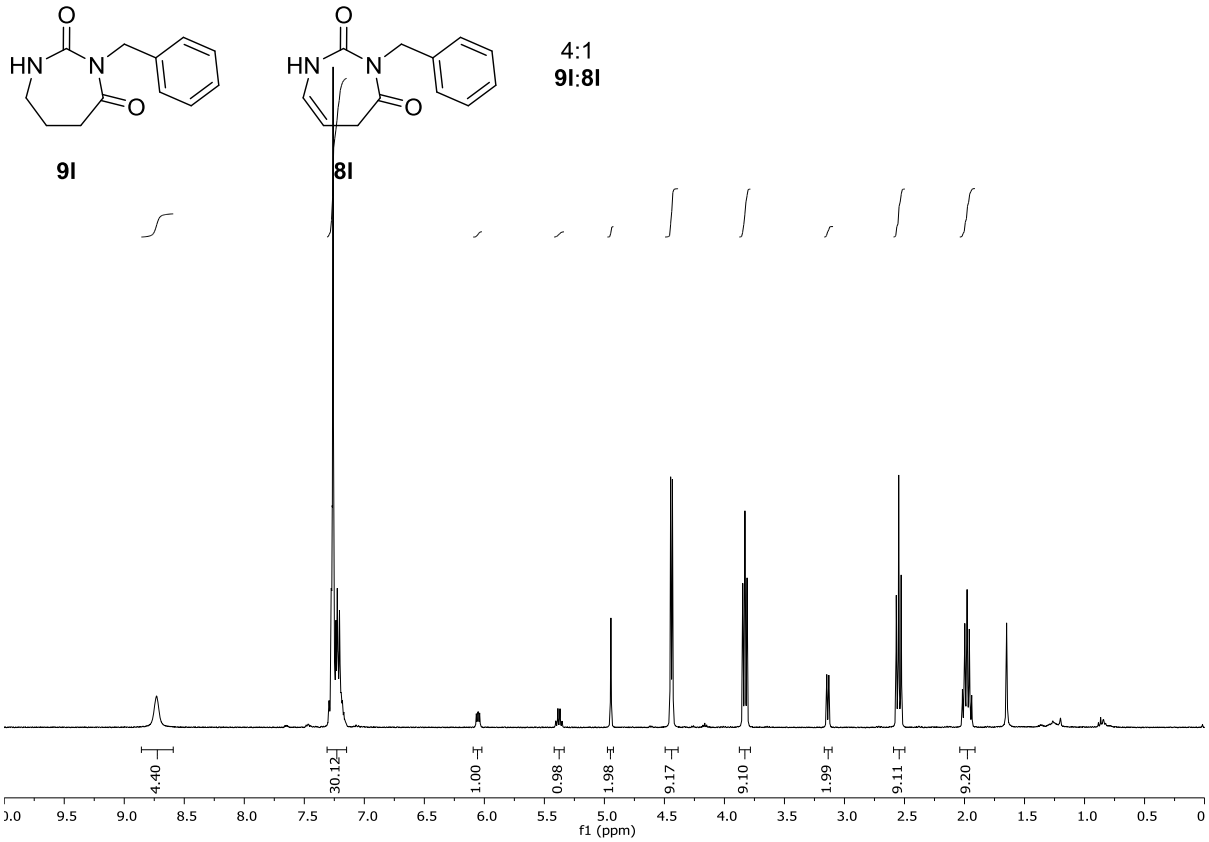

158.64
139.98
139.81
128.58
128.50
127.39
127.12
125.31
121.11
48.08
44.56
29.19
27.88
8.73
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

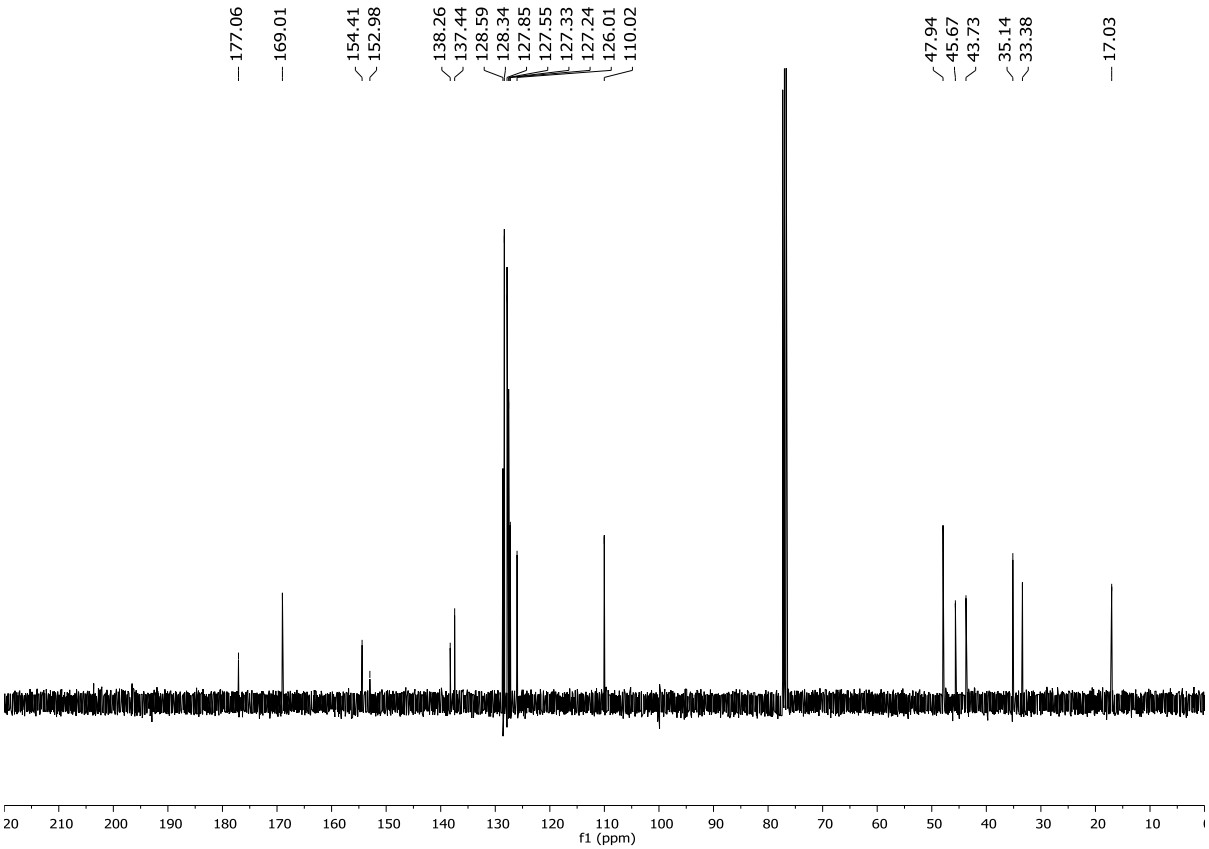

O
N
N
O
S
6.83
1.02
1.00
1.00
1.00
2.02
2.03
4.09
f1 (ppm)

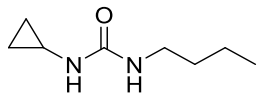

170.12
153.53
138.15
137.68
130.72
128.38
127.99
127.90
127.21
125.96
121.84
112.47
50.71
47.85
34.71
28.62
f1 (ppm)

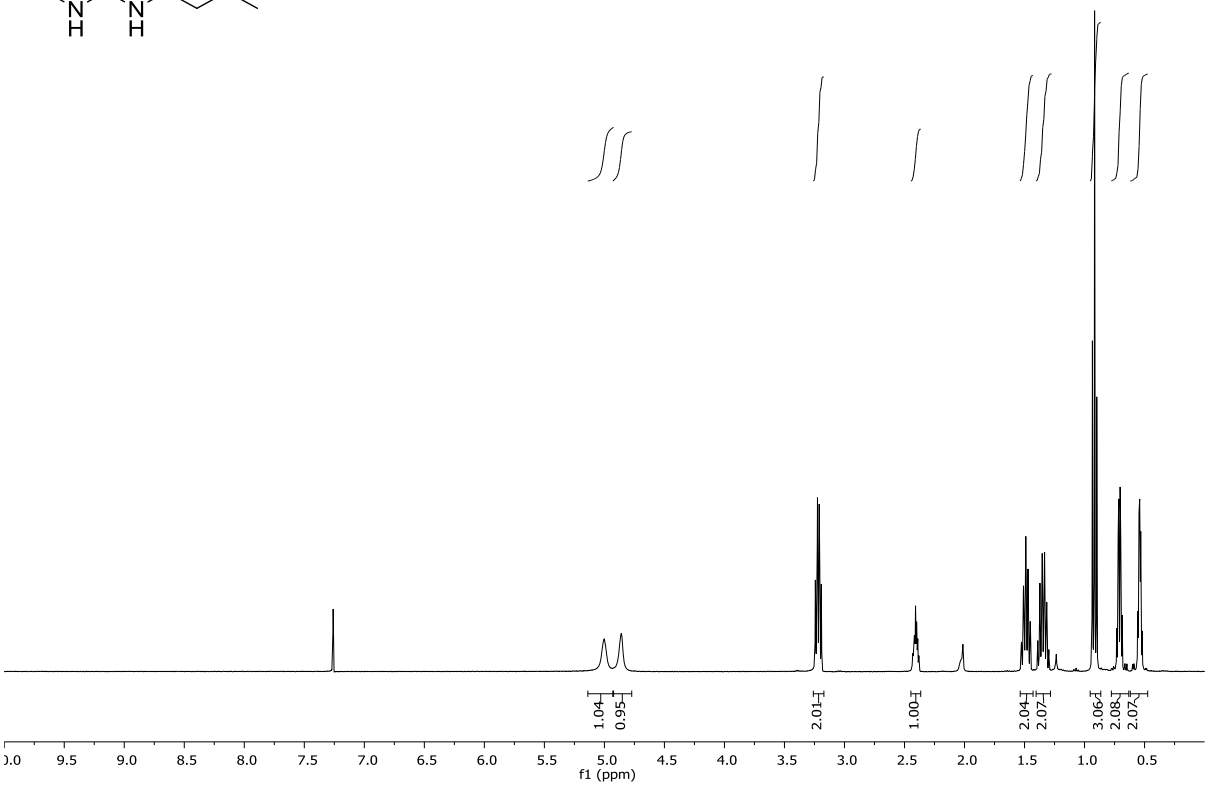

O
N
N
O
S
6.42
1.00
3.05
1.03
1.00
4.08
1.04
1.04
f1 (ppm)

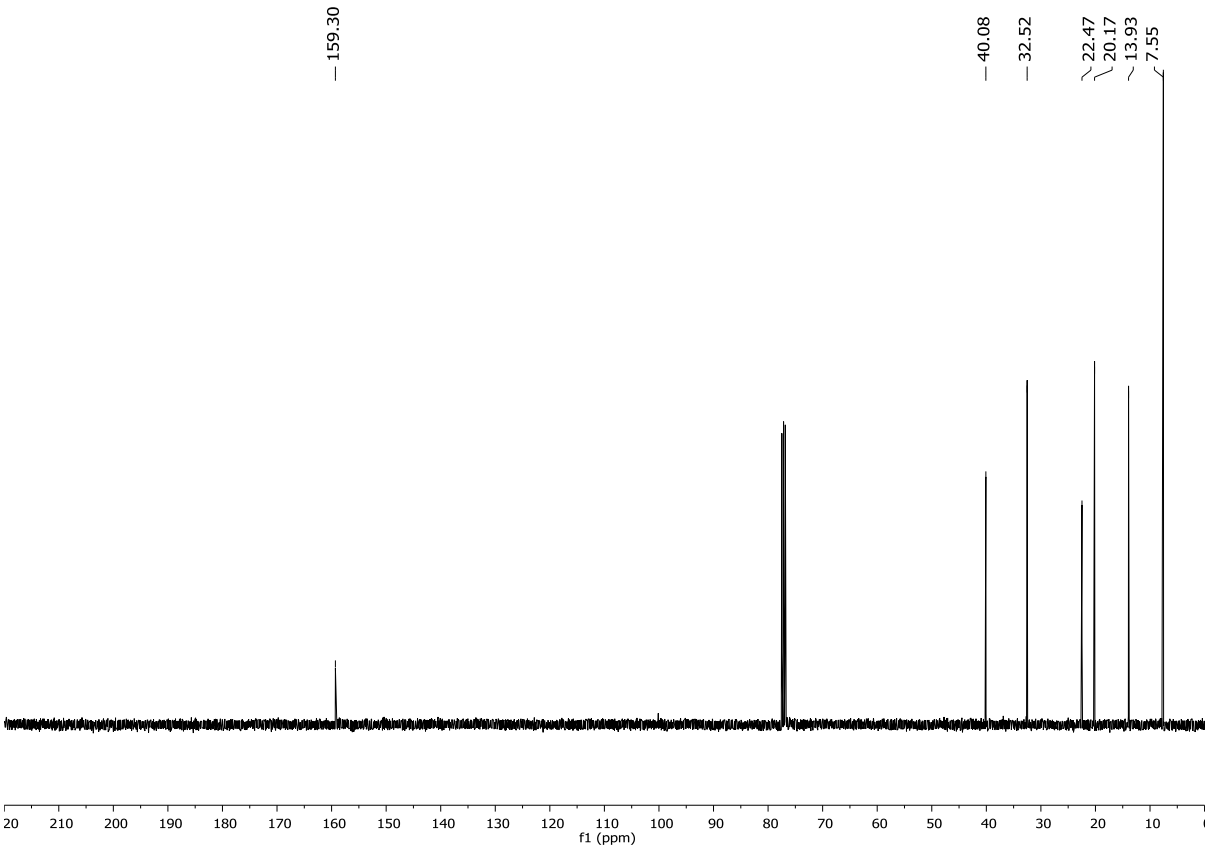

171.28
156.95
137.73
134.46
133.38
128.60
127.50
126.93
123.79
53.59
47.25
39.34
34.03
33.85
25.49
f1 (ppm)

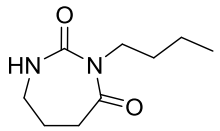

9l
8l
4:1
9l:8l
4.40
30.12
1.00
0.98
1.98
9.17
9.10
1.99
9.11
9.20
f1 (ppm)


177.06
169.01
154.41
152.98
138.26
137.44
128.59
128.34
127.85
127.55
127.33
127.24
126.01
110.02
47.94
45.67
43.73
35.14
33.38
17.03
f1 (ppm)

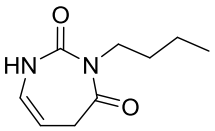



1.04
0.95
2.01
1.00
2.04
2.07
3.06
2.08
2.07
f1 (ppm)


159.30
40.08
32.52
22.47
20.17
13.93
7.55
f1 (ppm)

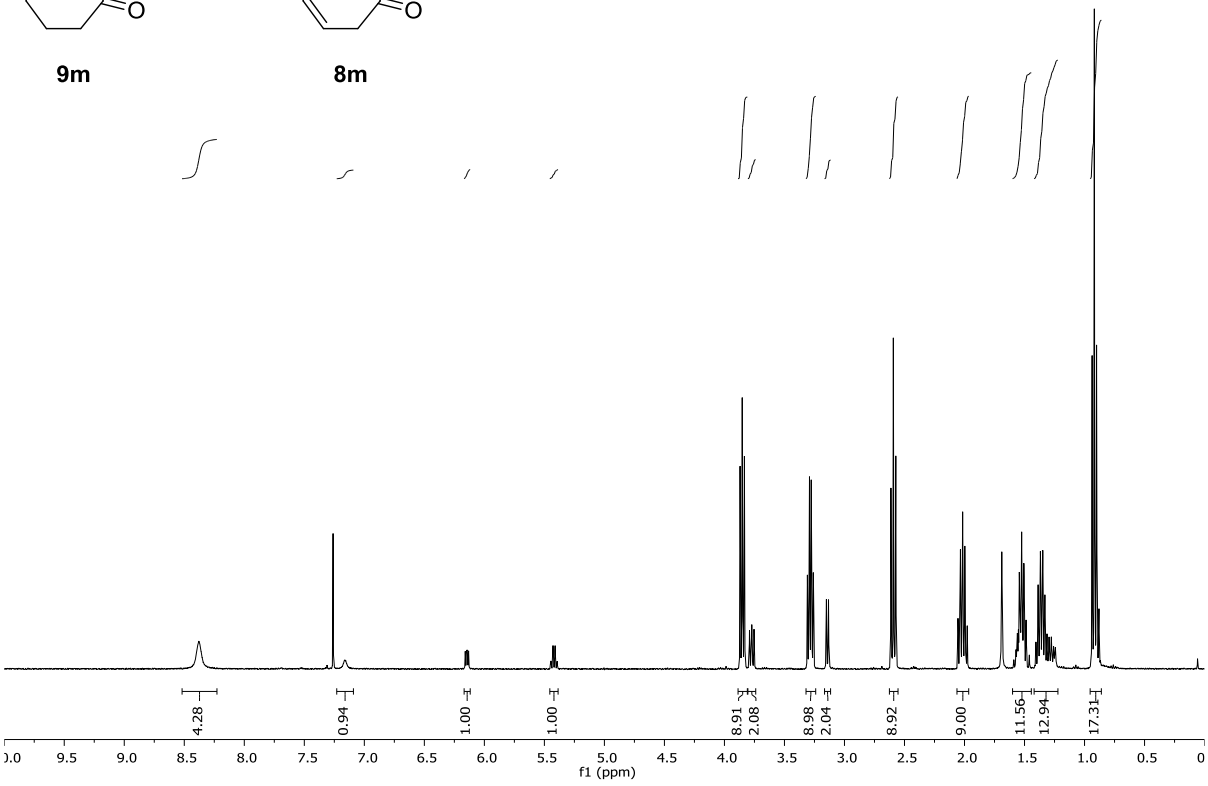


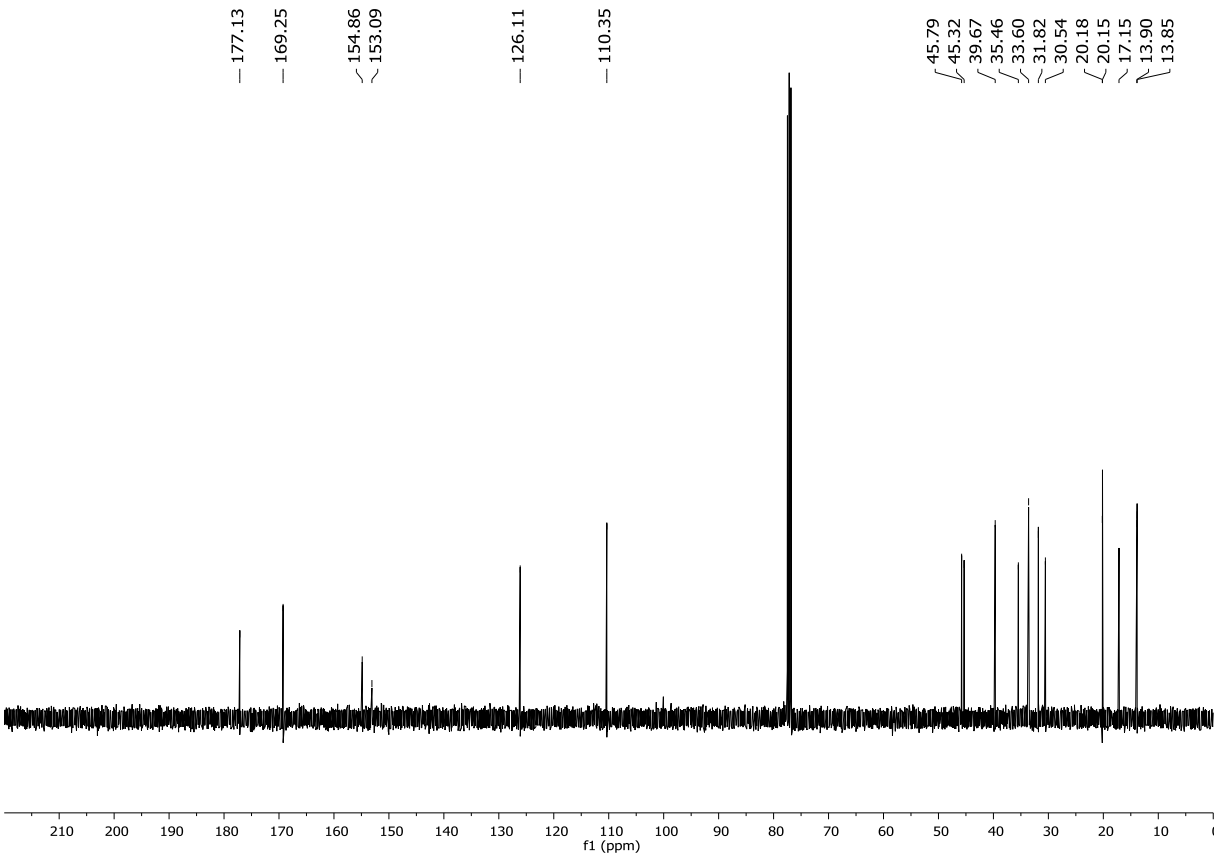
9m

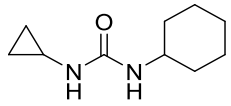


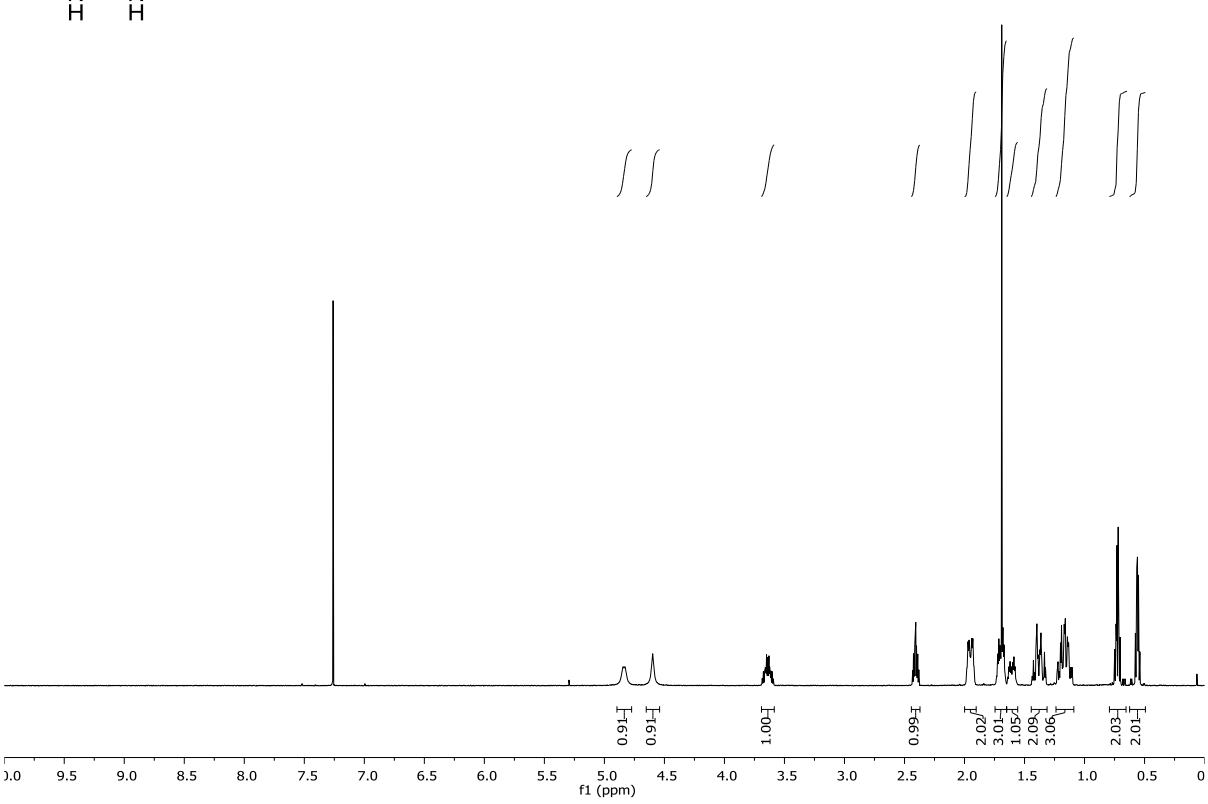
8m

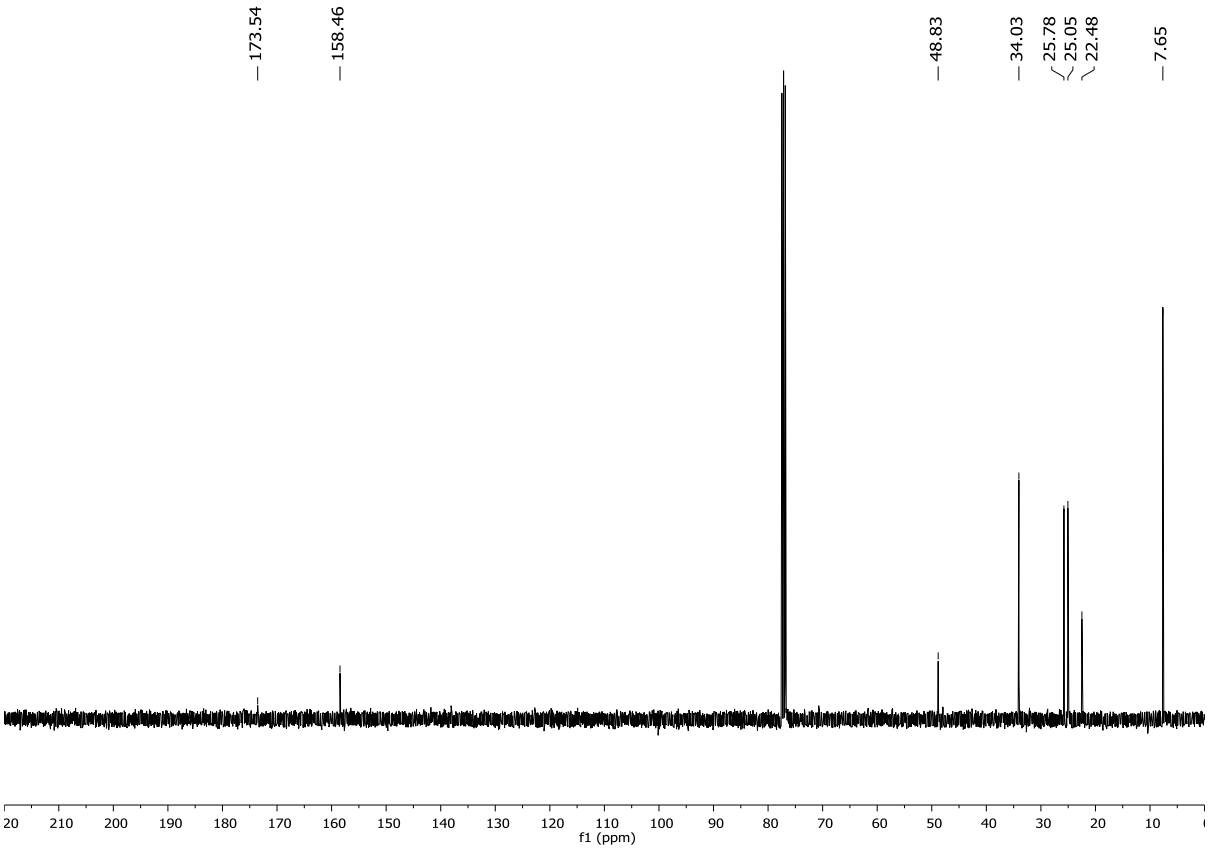
5:1
9m:**8m**

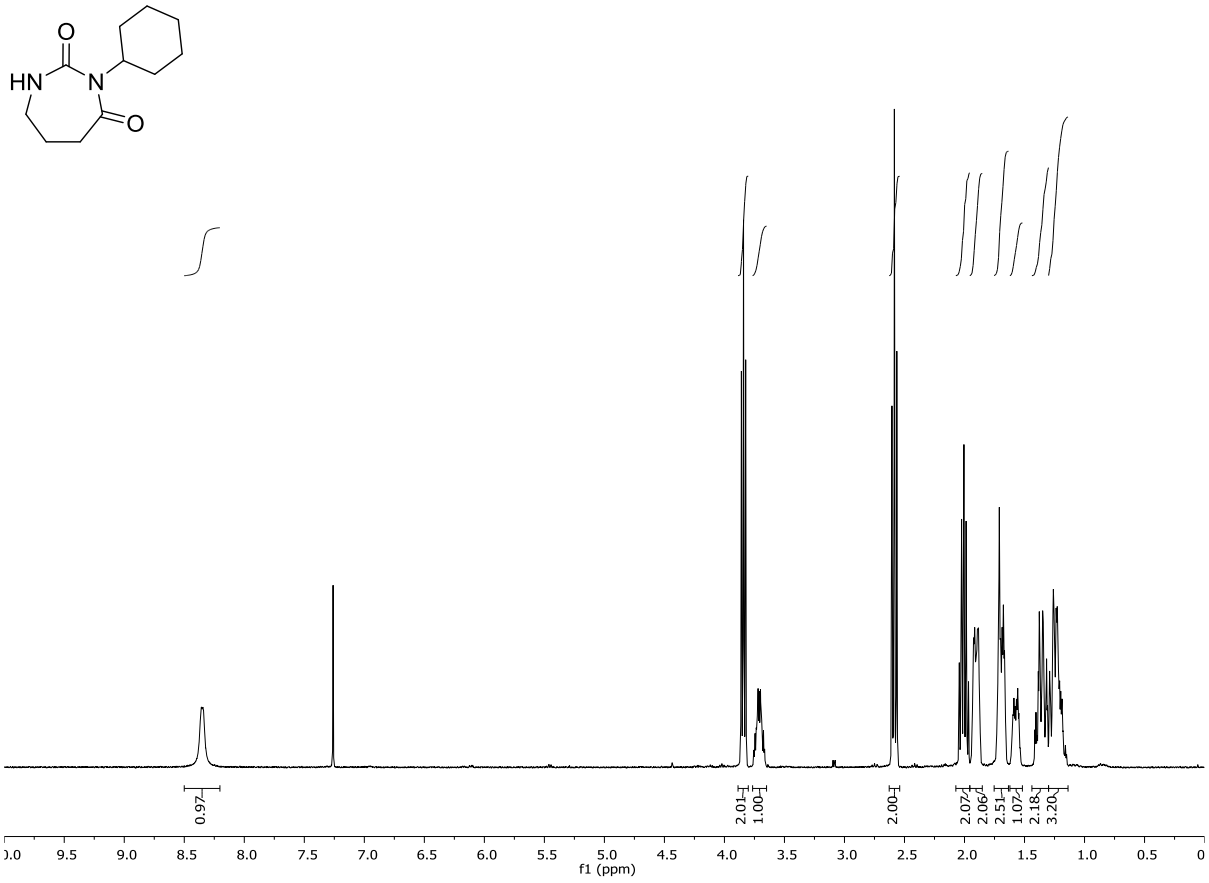

4.28
0.94
1.00
1.00
8.91
2.08
8.98
2.04
8.92
9.00
11.56
12.94
17.31
f1 (ppm)

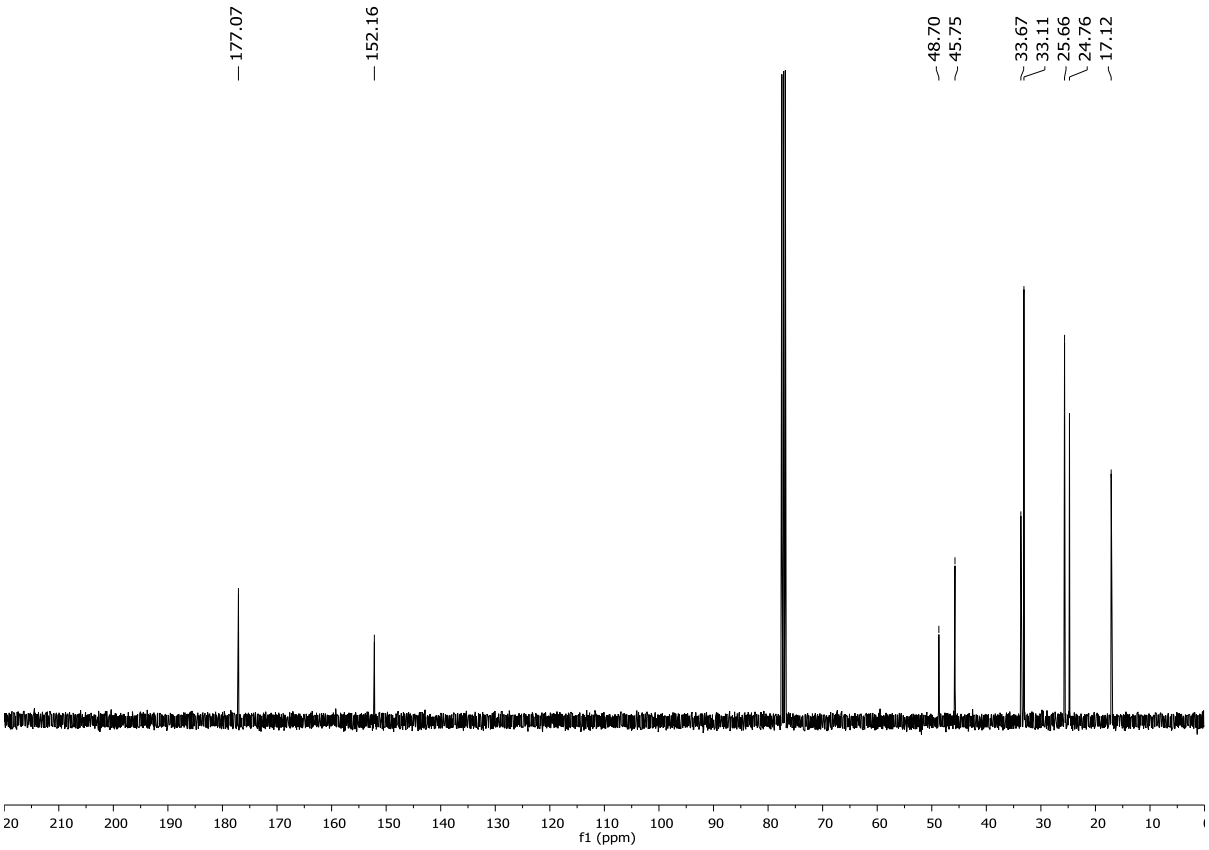

177.13
169.25
154.86
153.09
126.11
110.35
45.79
45.32
39.67
35.46
33.60
31.82
30.54
20.18
20.15
17.15
13.90
13.85
f1 (ppm)

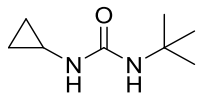

O
N
H
N
H

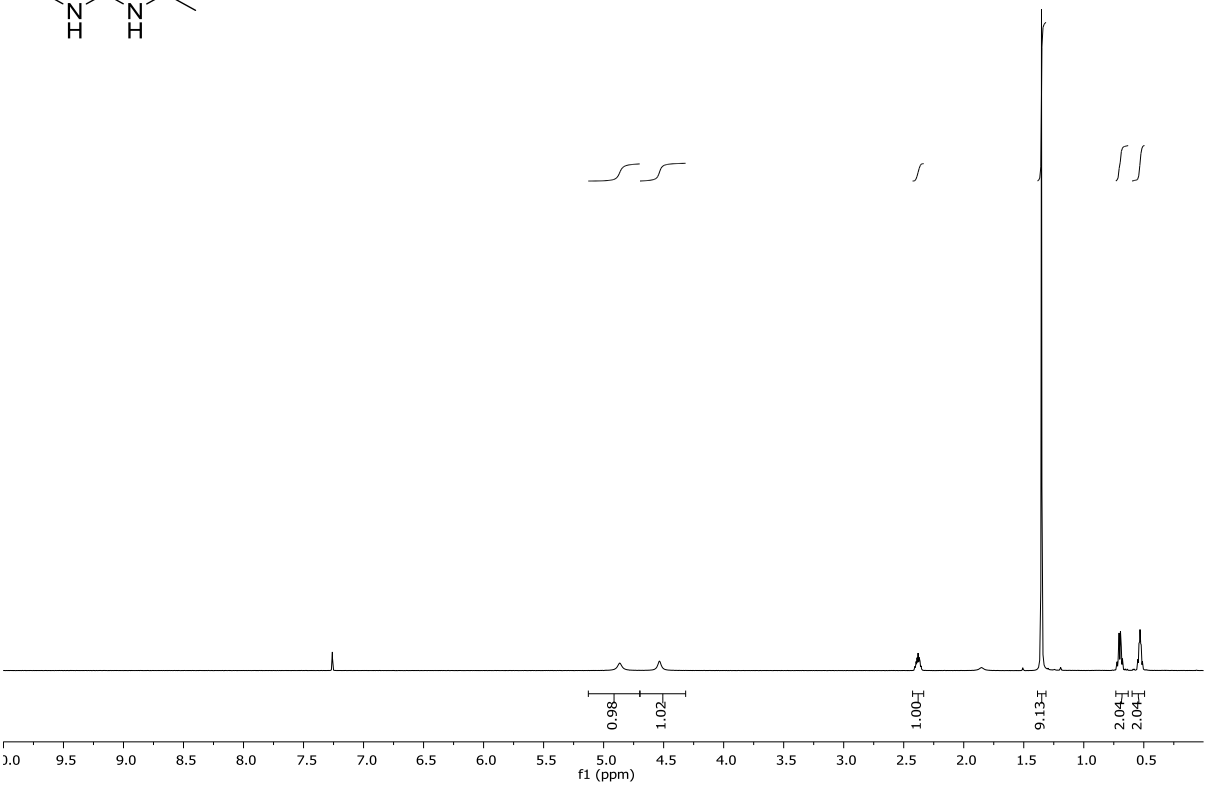

0.91
0.91
1.00
0.99
2.02
3.01
1.05
2.09
3.06
2.03
2.01
f1 (ppm)

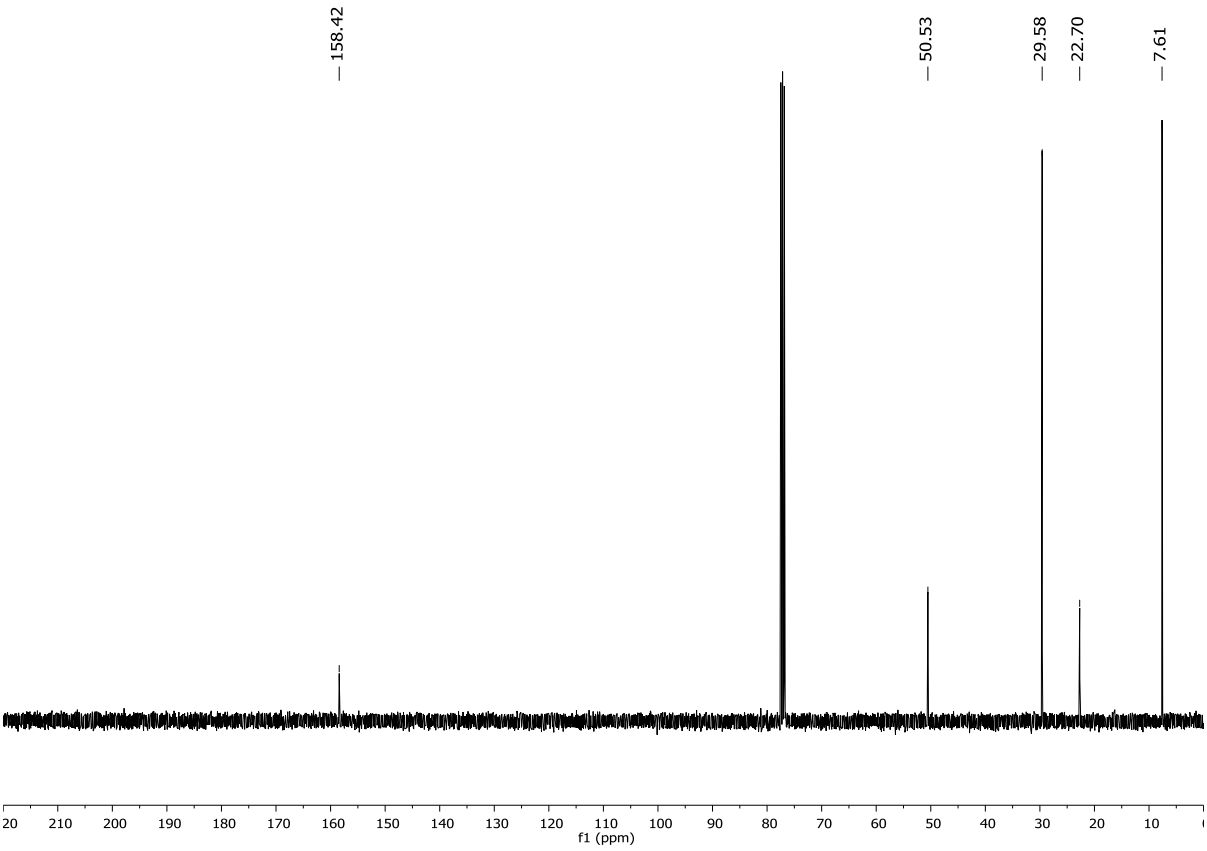

173.54
158.46
48.83
34.03
25.78
25.05
22.48
7.65
f1 (ppm)

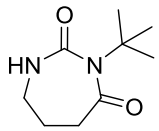

O
HN
N
O
0.97
2.01
1.00
2.00
2.07
2.06
2.51
1.07
2.18
3.20
f1 (ppm)


177.07
152.16
48.70
45.75
33.67
33.11
25.66
24.76
17.12
f1 (ppm)

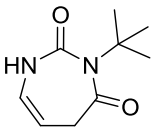



0.98
1.02
1.00
9.13
2.04
2.04
f1 (ppm)


158.42
50.53
29.58
22.70
7.61
f1 (ppm)



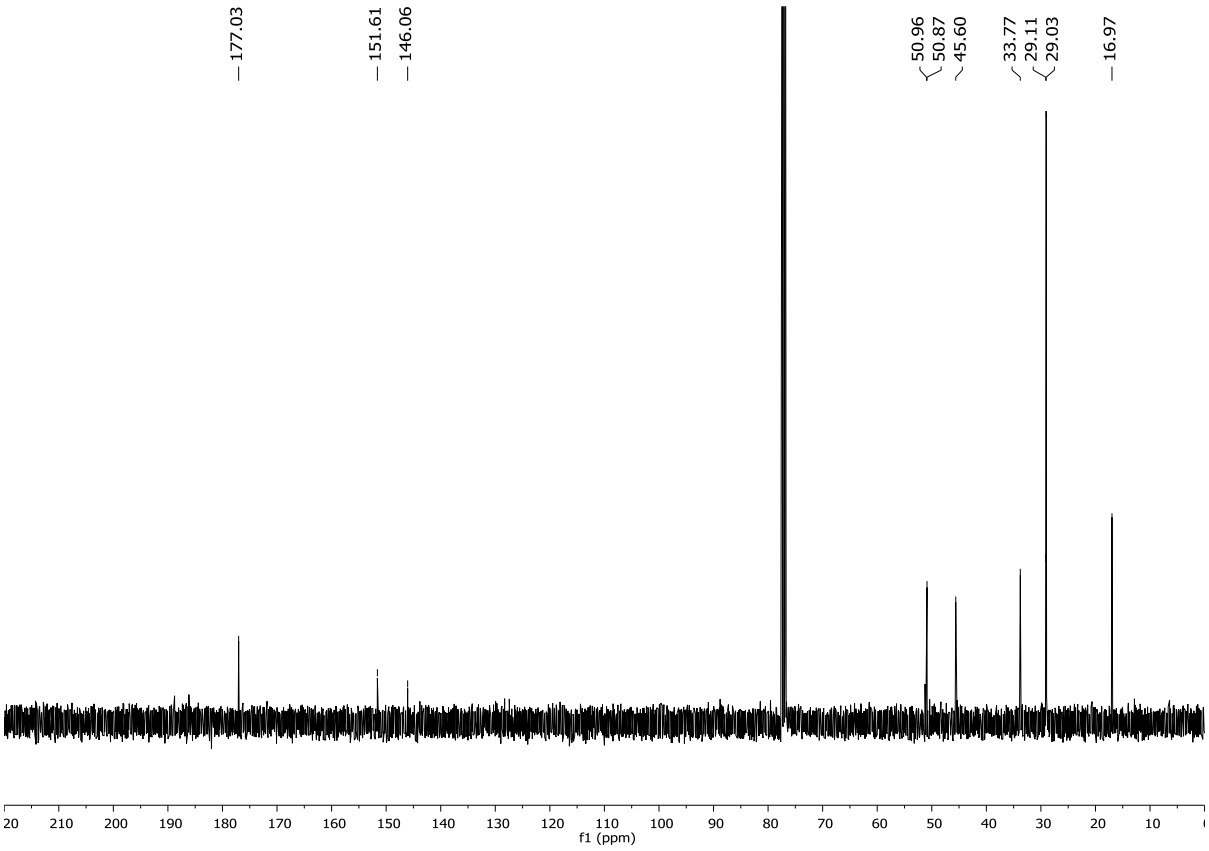
9o

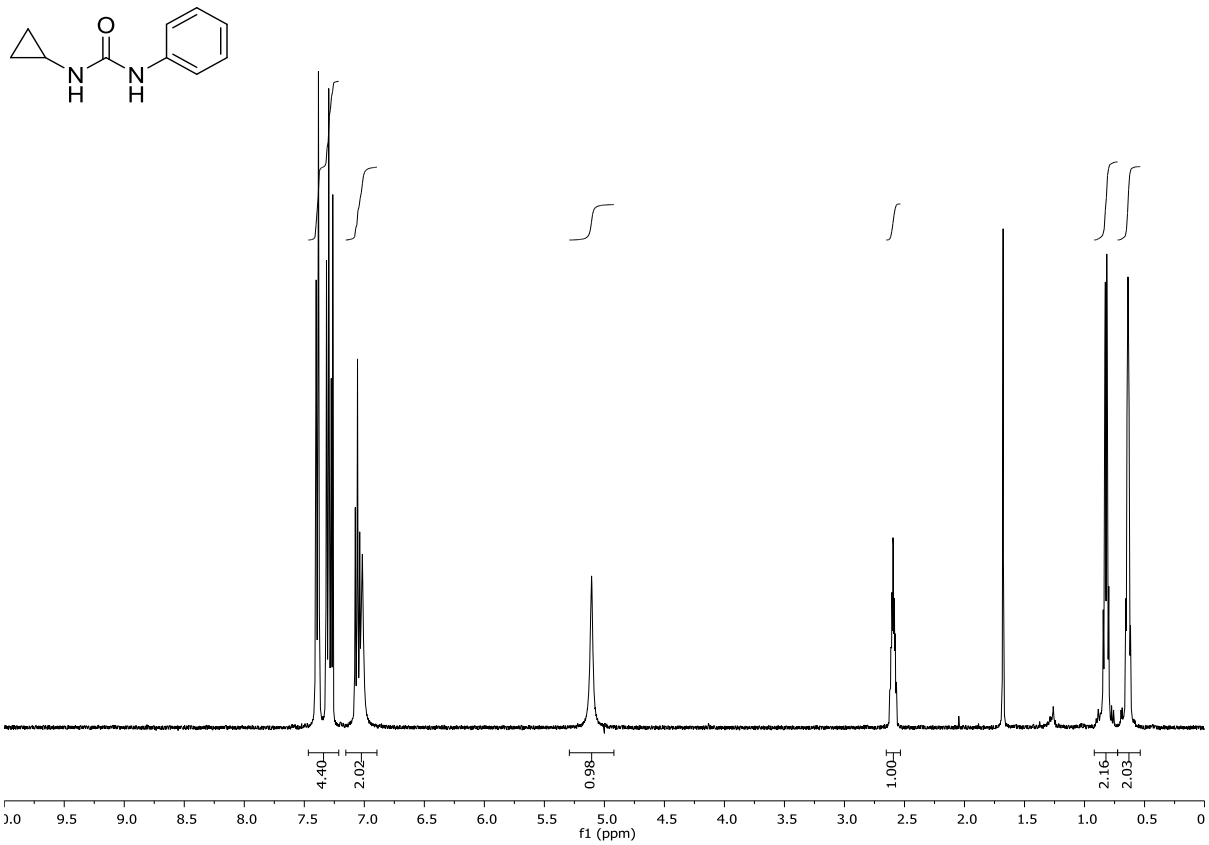


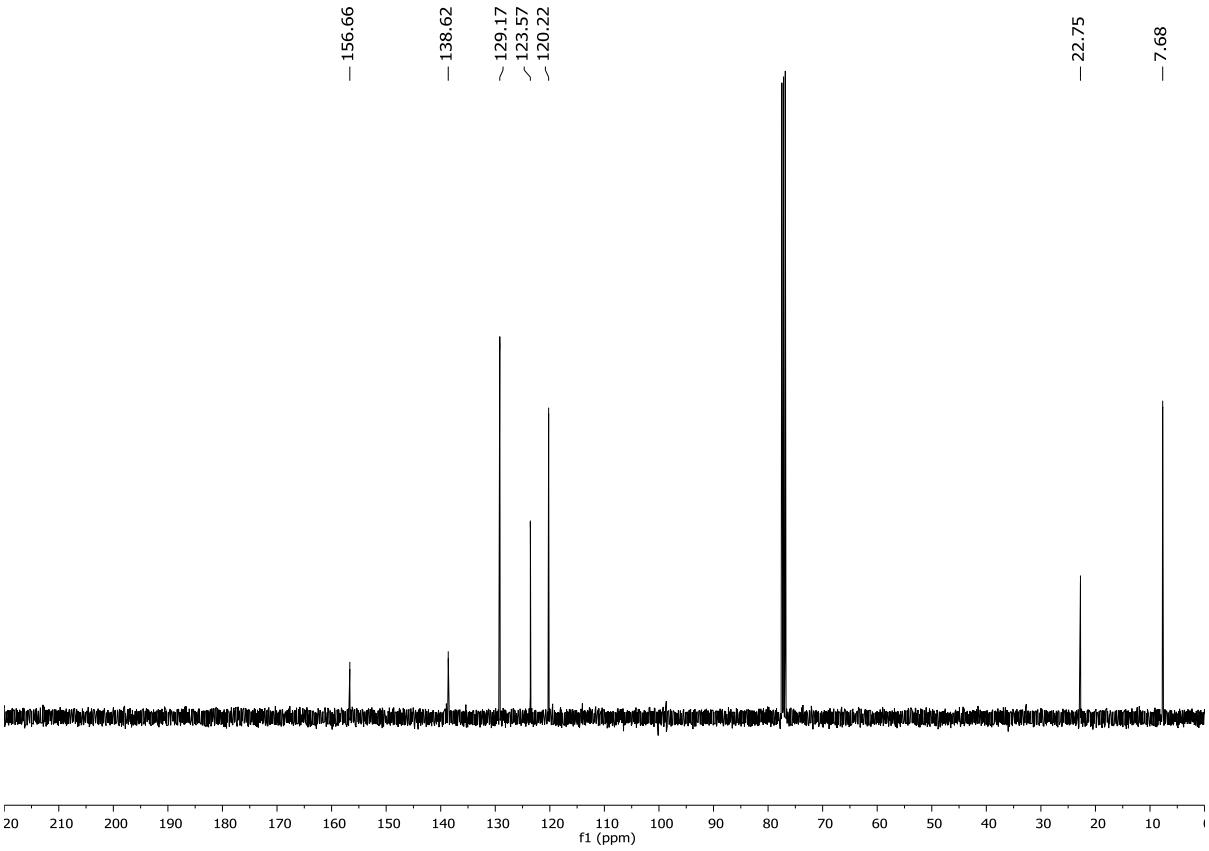
8o

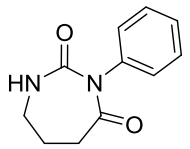
5:1
9o:**8o**

5.09
1.00
2.04
8.37
8.41
8.52
10.00
40.43
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)

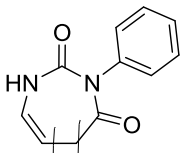

177.03
151.61
146.06
50.96
50.87
45.60
33.77
29.11
29.03
16.97
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


4.40
2.02
0.98
1.00
2.16
2.03
f1 (ppm)


156.66
138.62
129.17
123.57
120.22
22.75
7.68
f1 (ppm)

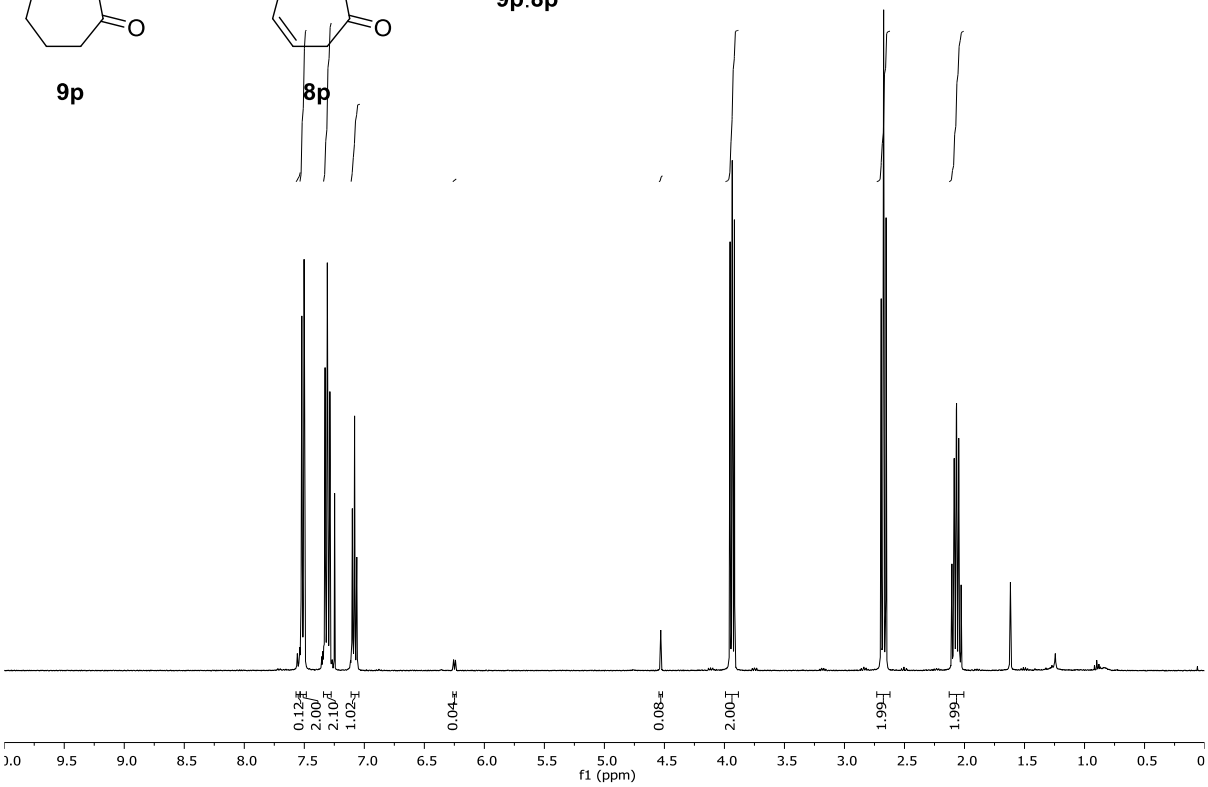


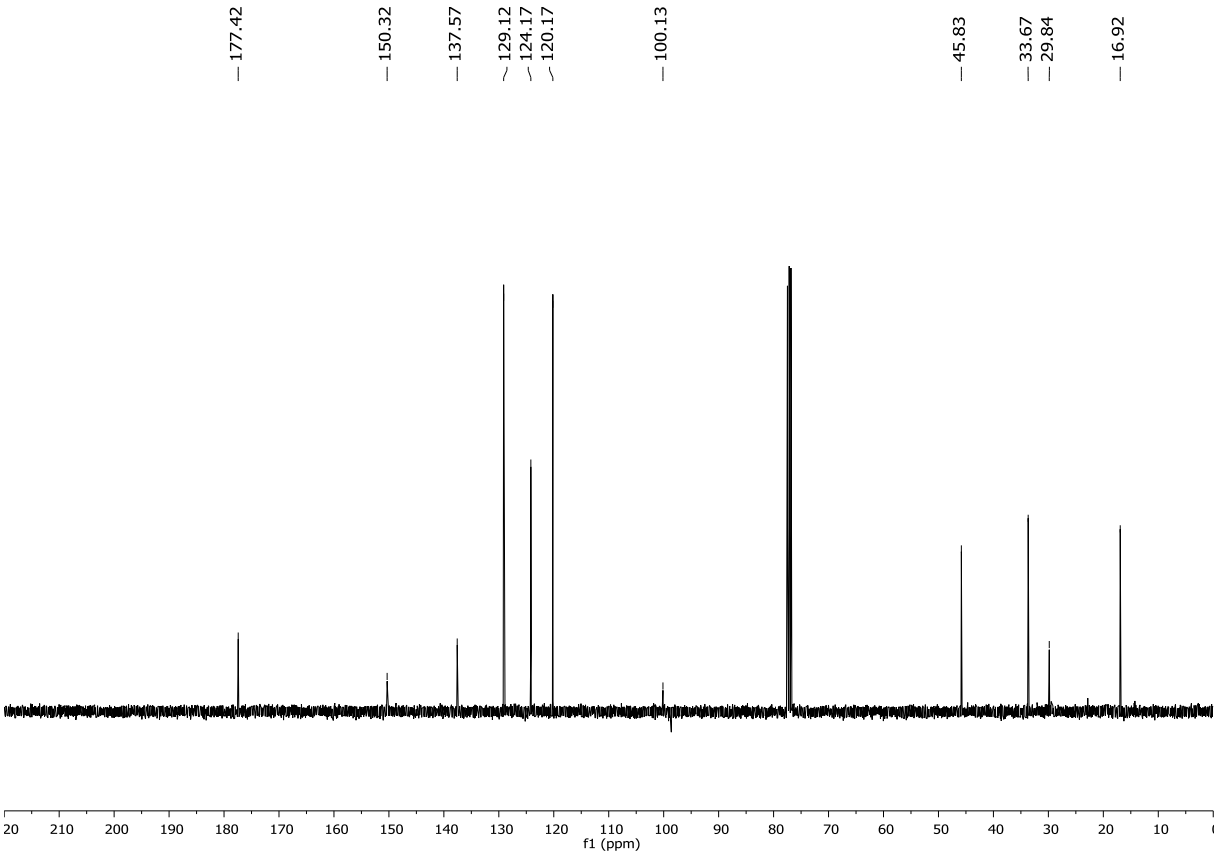
9p

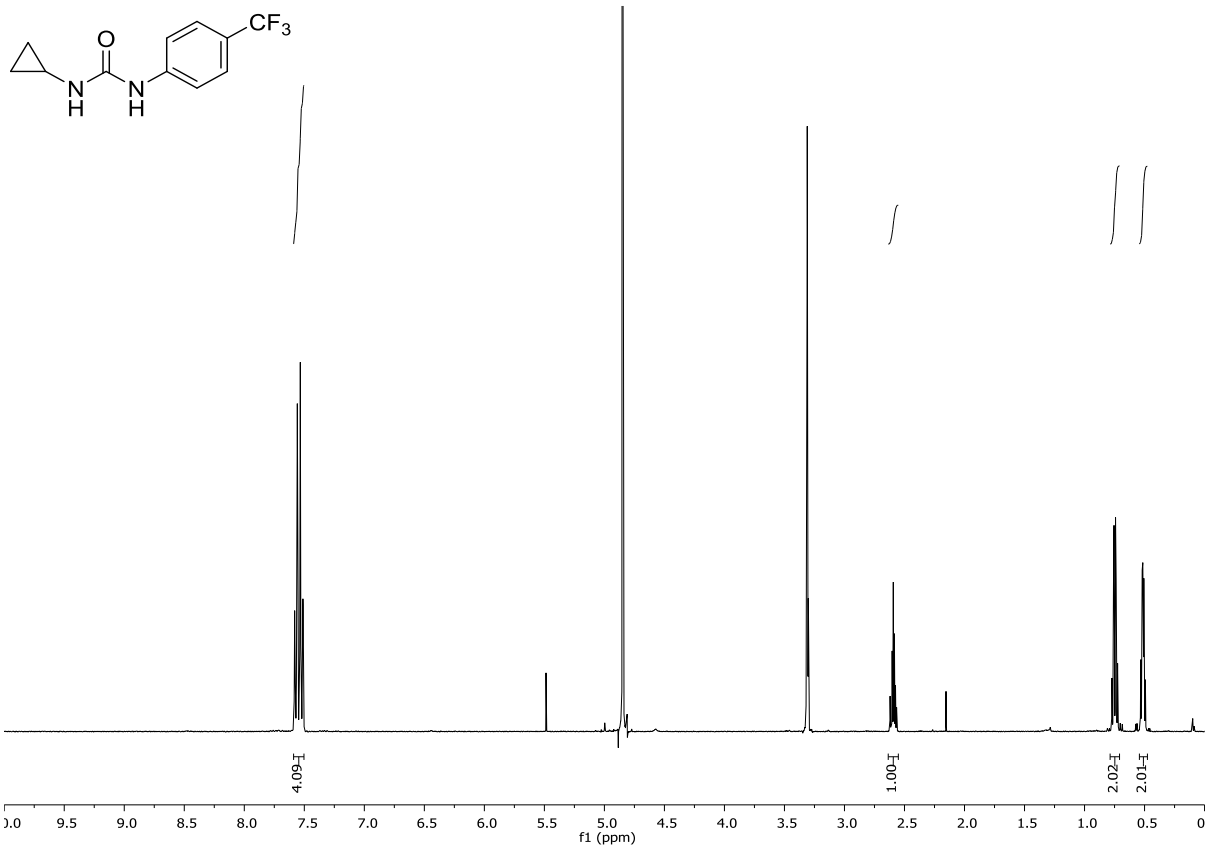


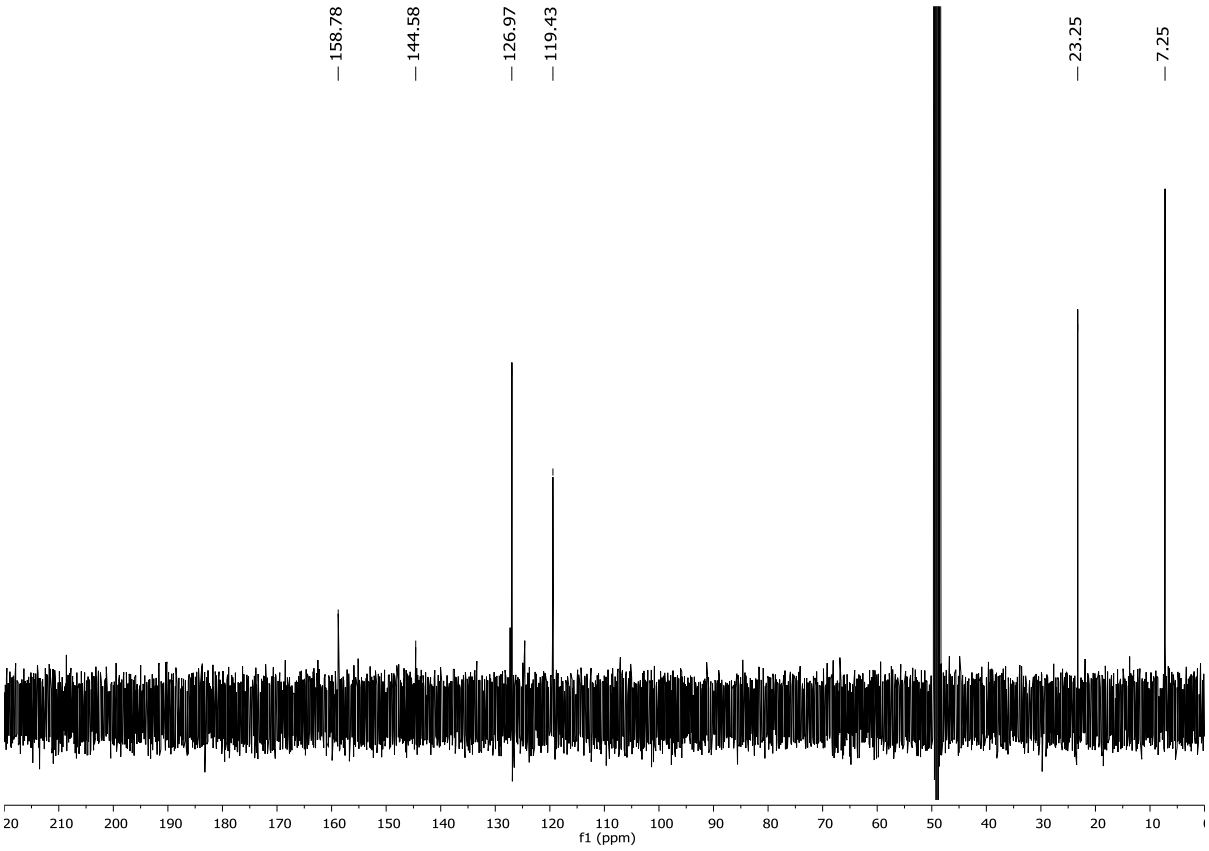
8p

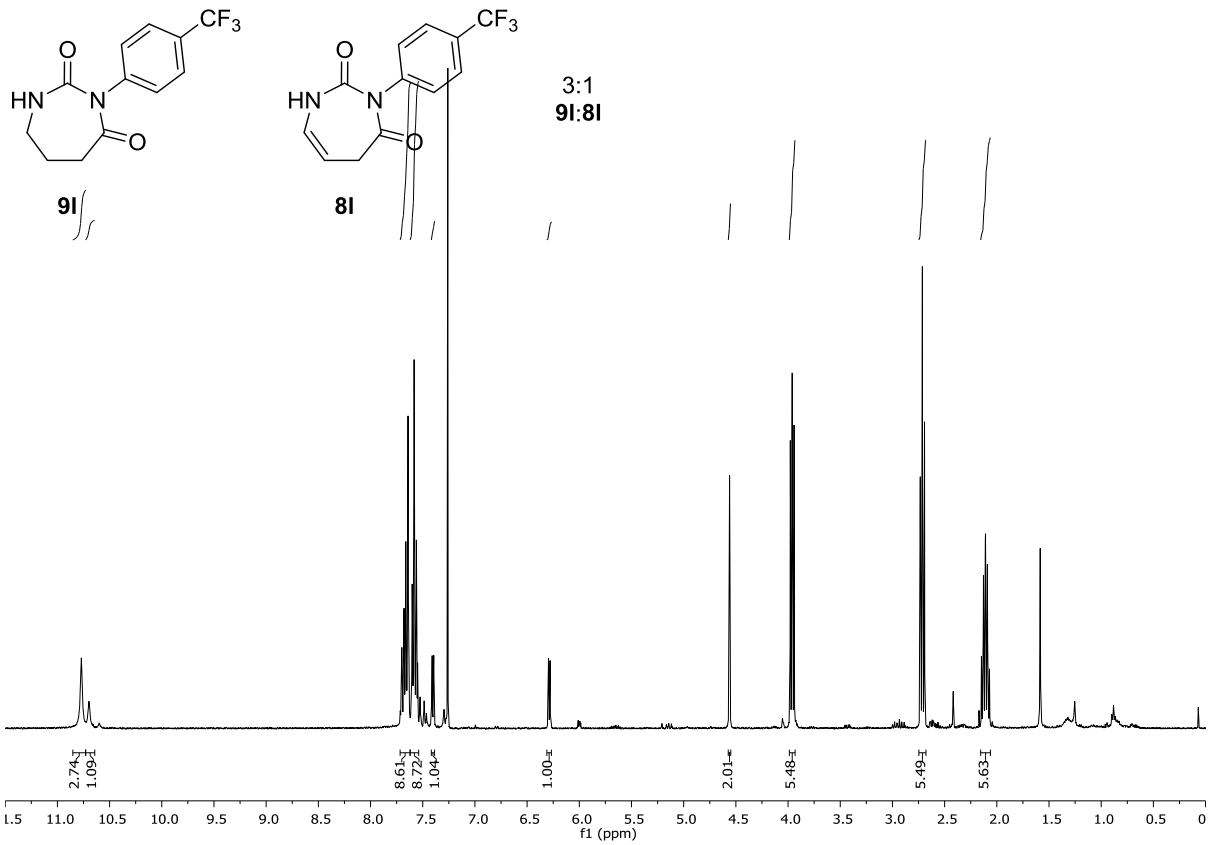
25:1
9p:**8p**

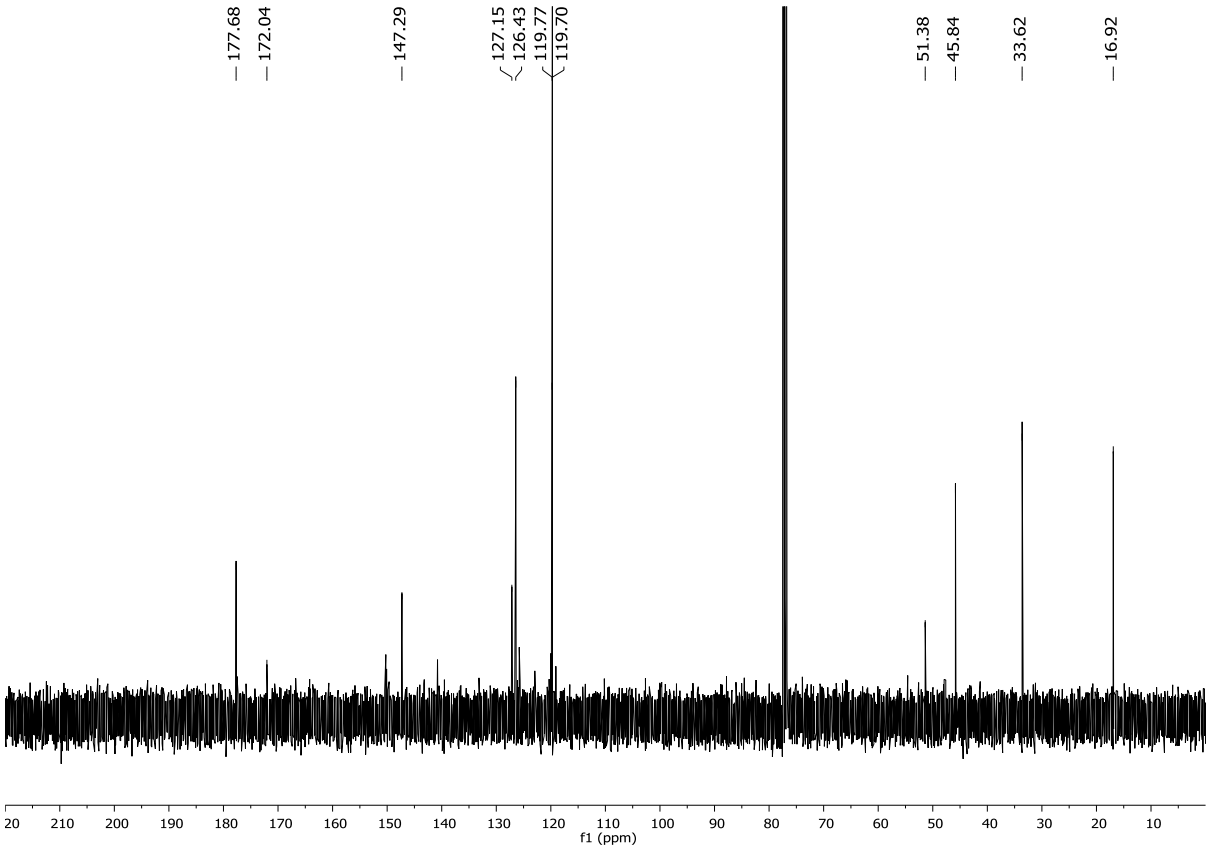


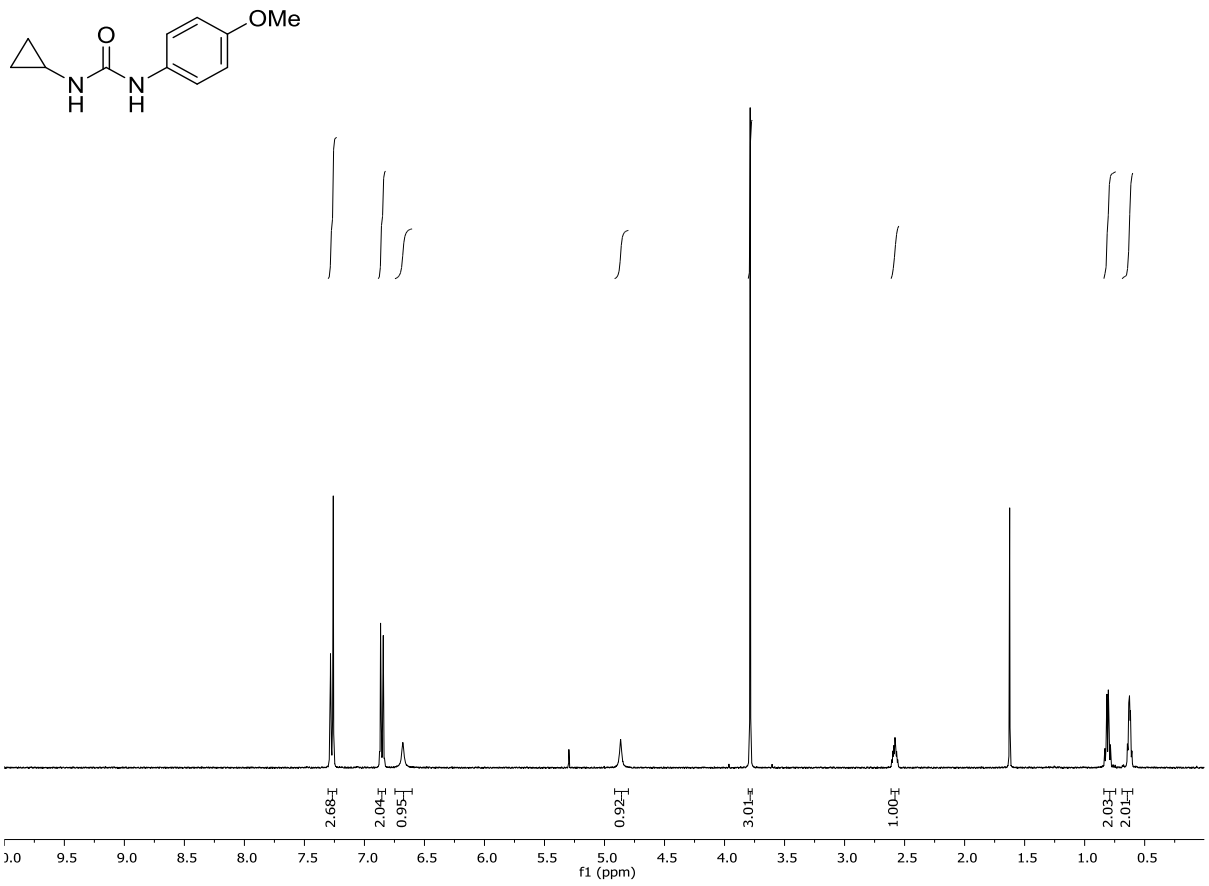


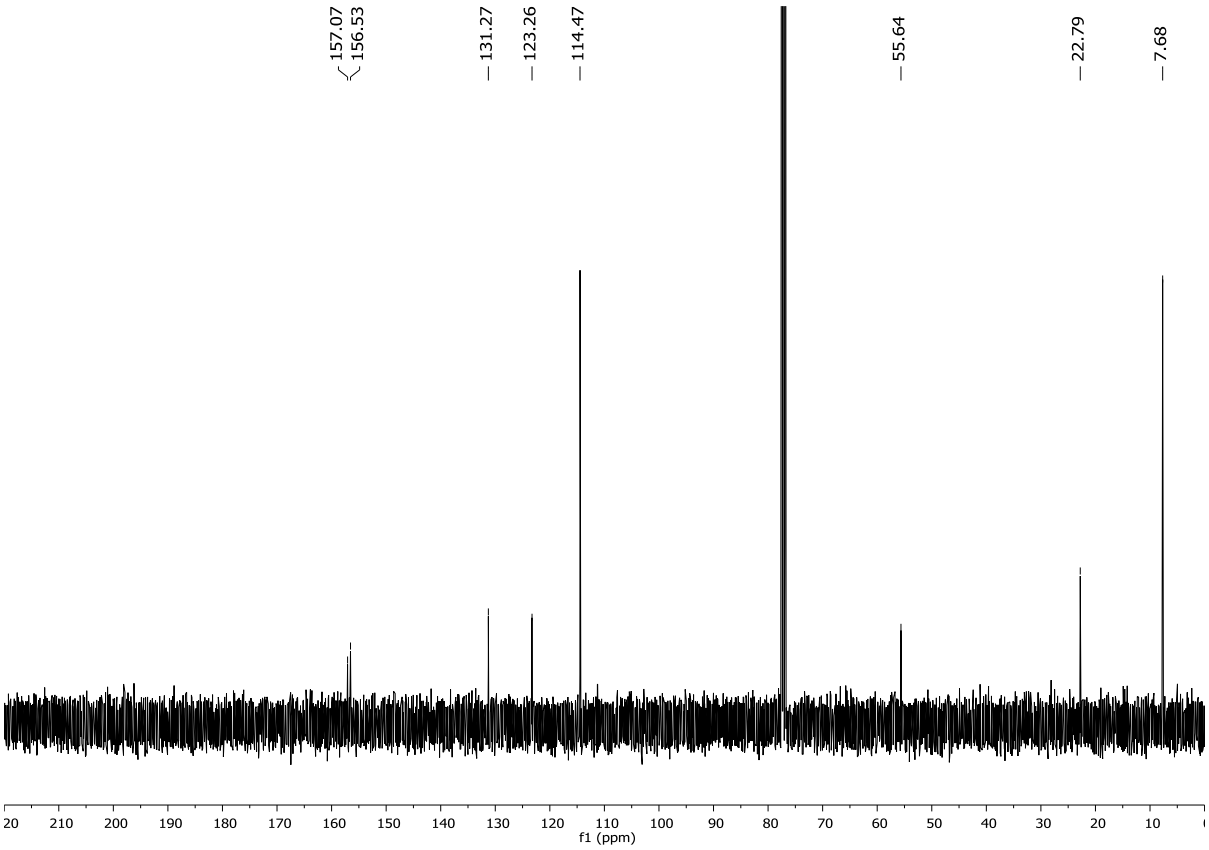

CF3
O
N
H
N
H
4.09
1.00
2.02
2.01
f1 (ppm)

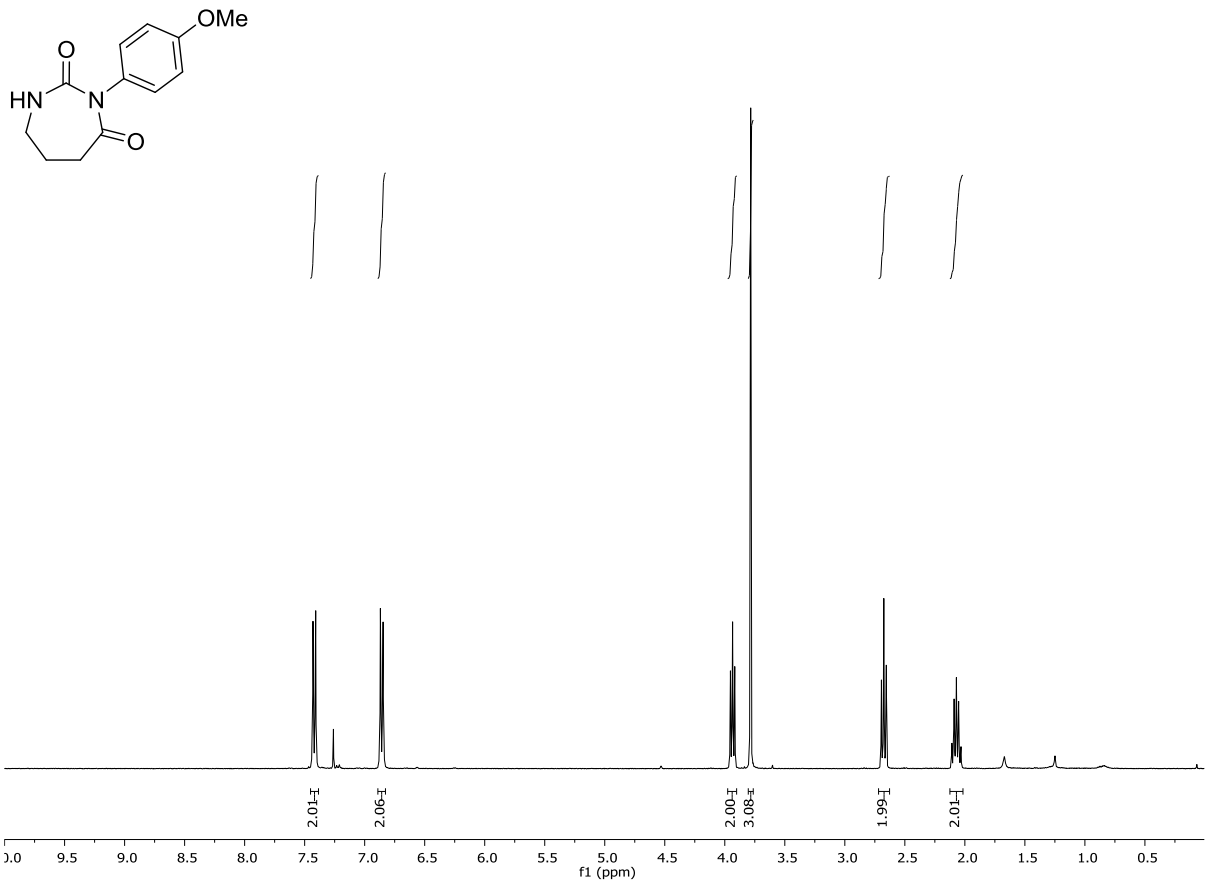

158.78
144.58
126.97
119.43
23.25
7.25
f1 (ppm)

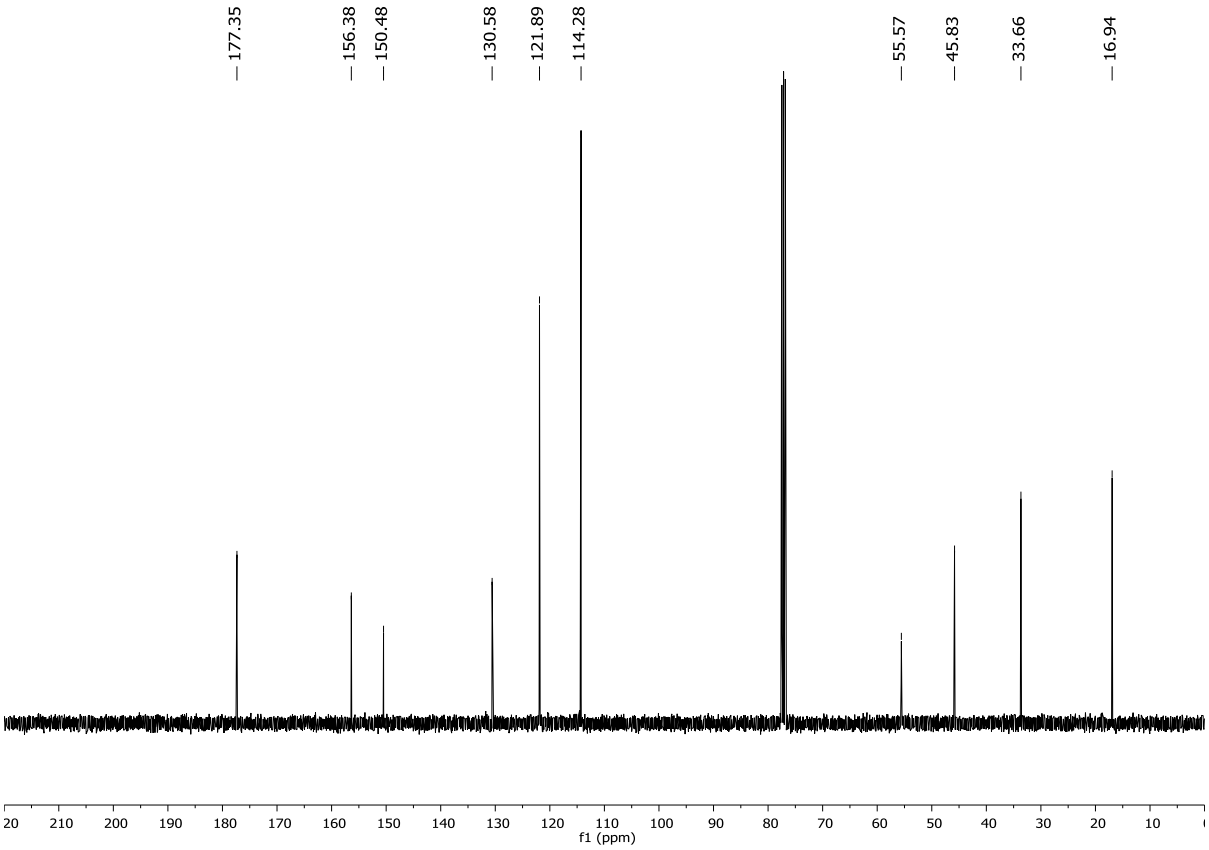

CF3
O
HN
N
O
9l
8l
3:1
9l:8l
2.74
1.09
8.61
8.72
1.04
1.00
2.01
5.48
5.49
5.63
f1 (ppm)

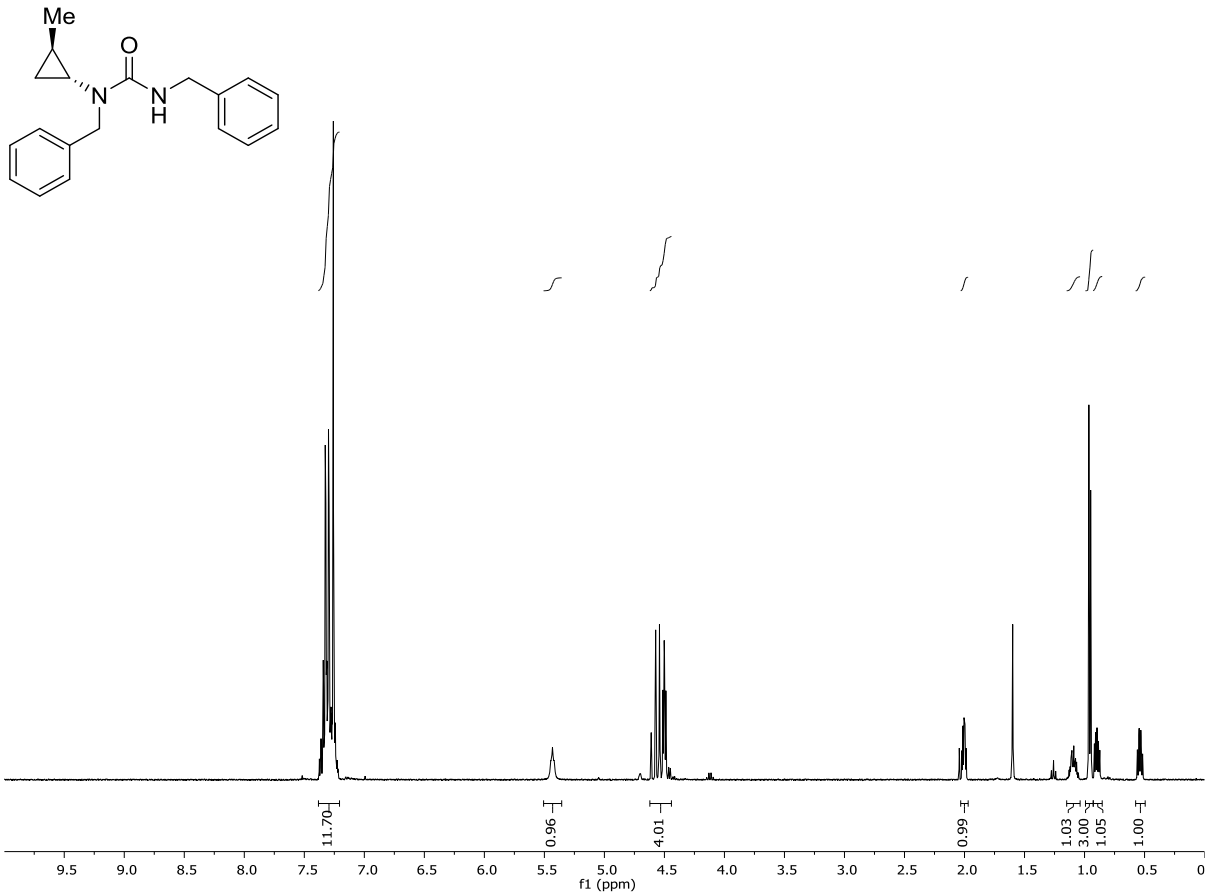

177.68
172.04
147.29
127.15
126.43
119.77
119.70
51.38
45.84
33.62
16.92
f1 (ppm)

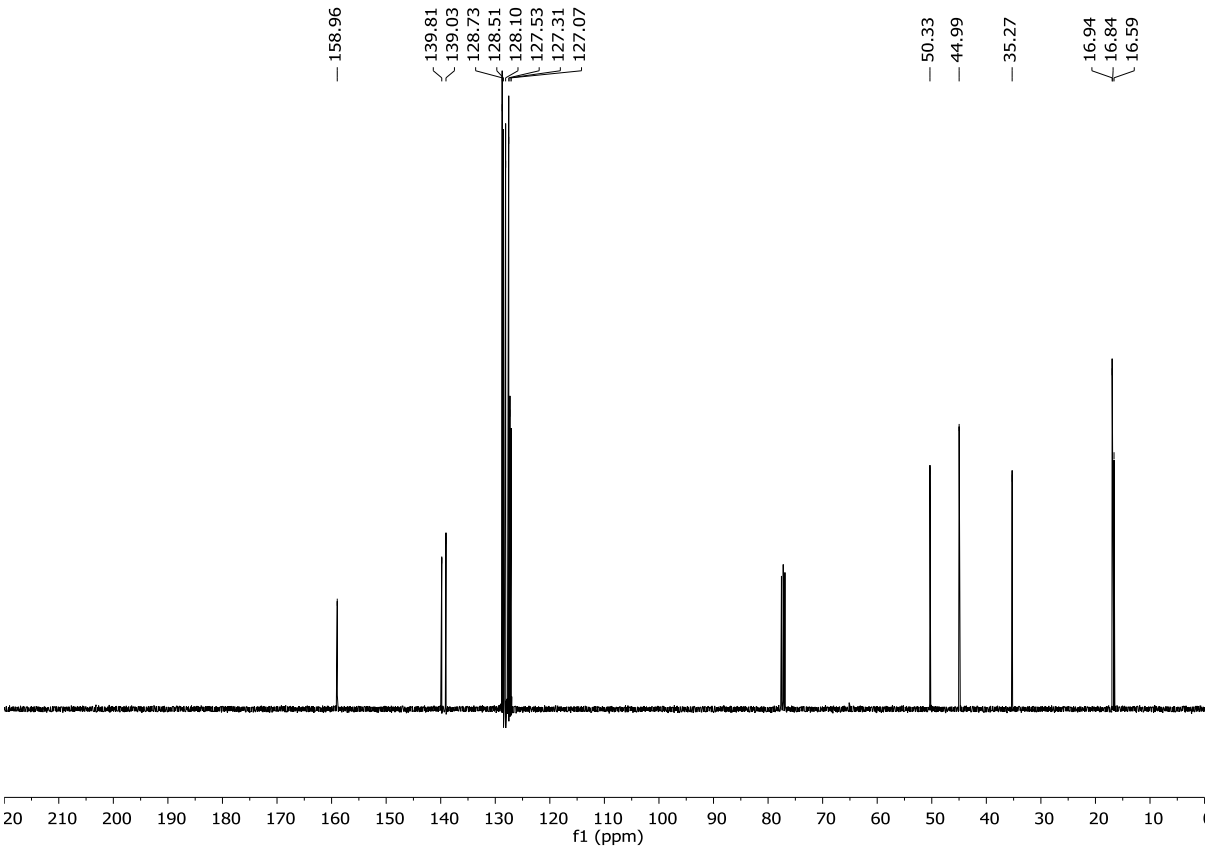

OMe
O
N
H
N
H
2.68
2.04
0.95
0.92
3.01
1.00
2.03
2.01
f1 (ppm)

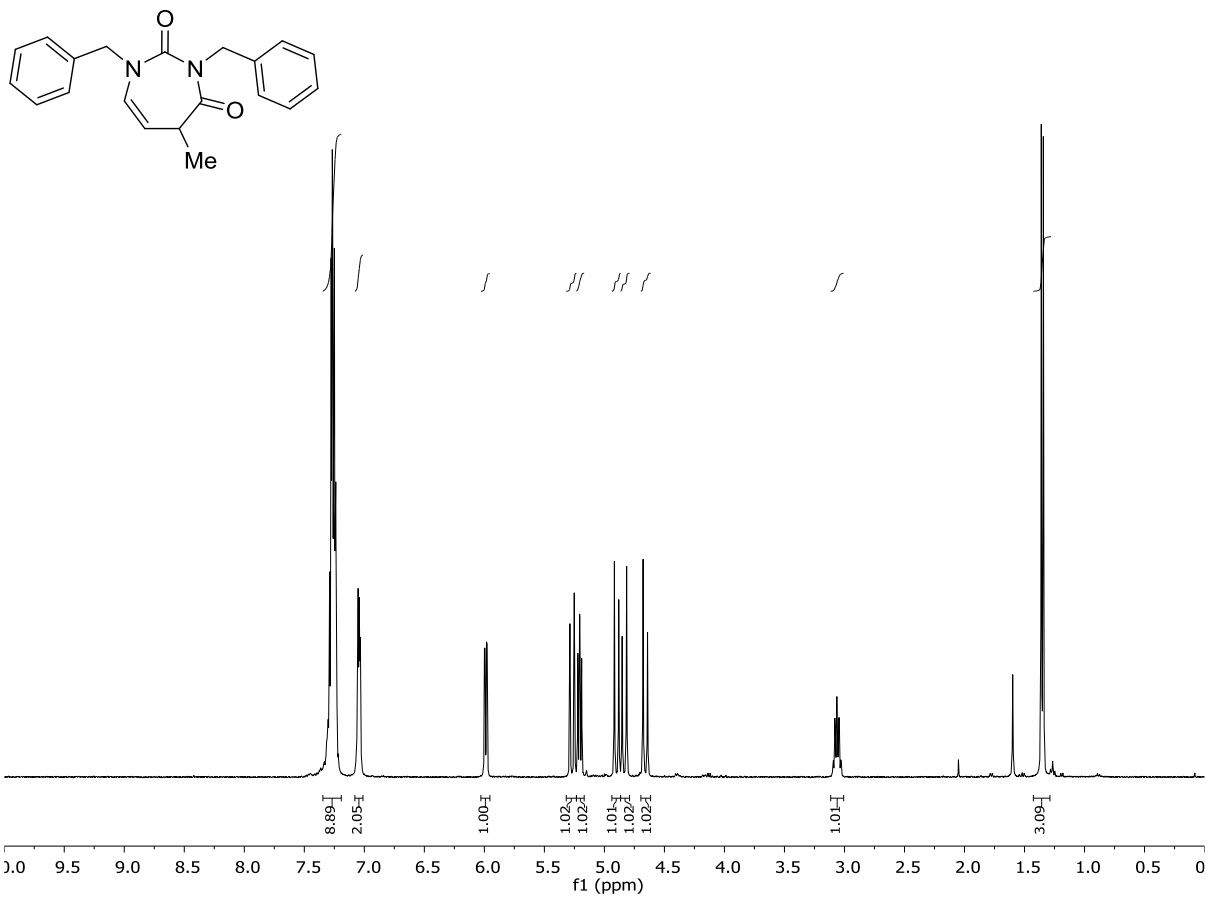

157.07
156.53
131.27
123.26
114.47
55.64
22.79
7.68
f1 (ppm)

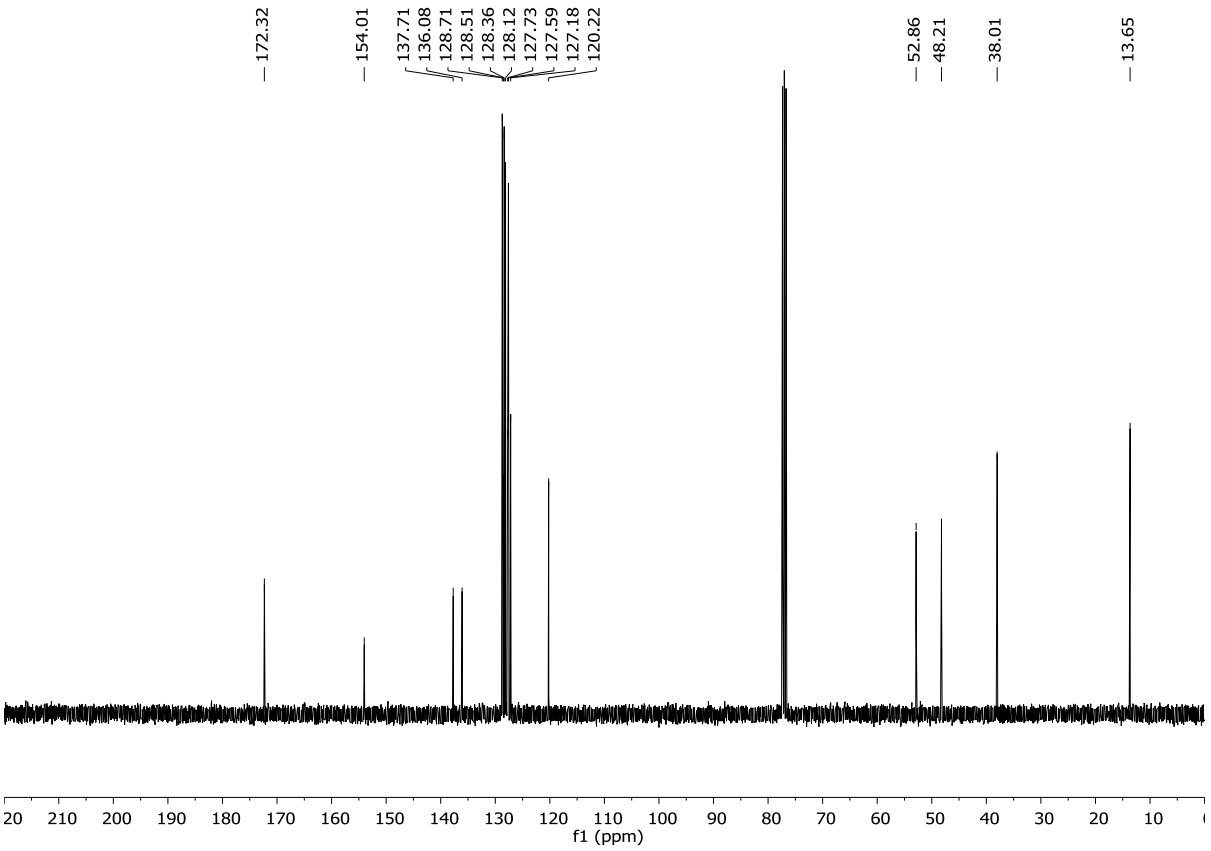

OMe
O
HN
N
O
2.01
2.06
2.00
3.08
1.99
2.01
f1 (ppm)

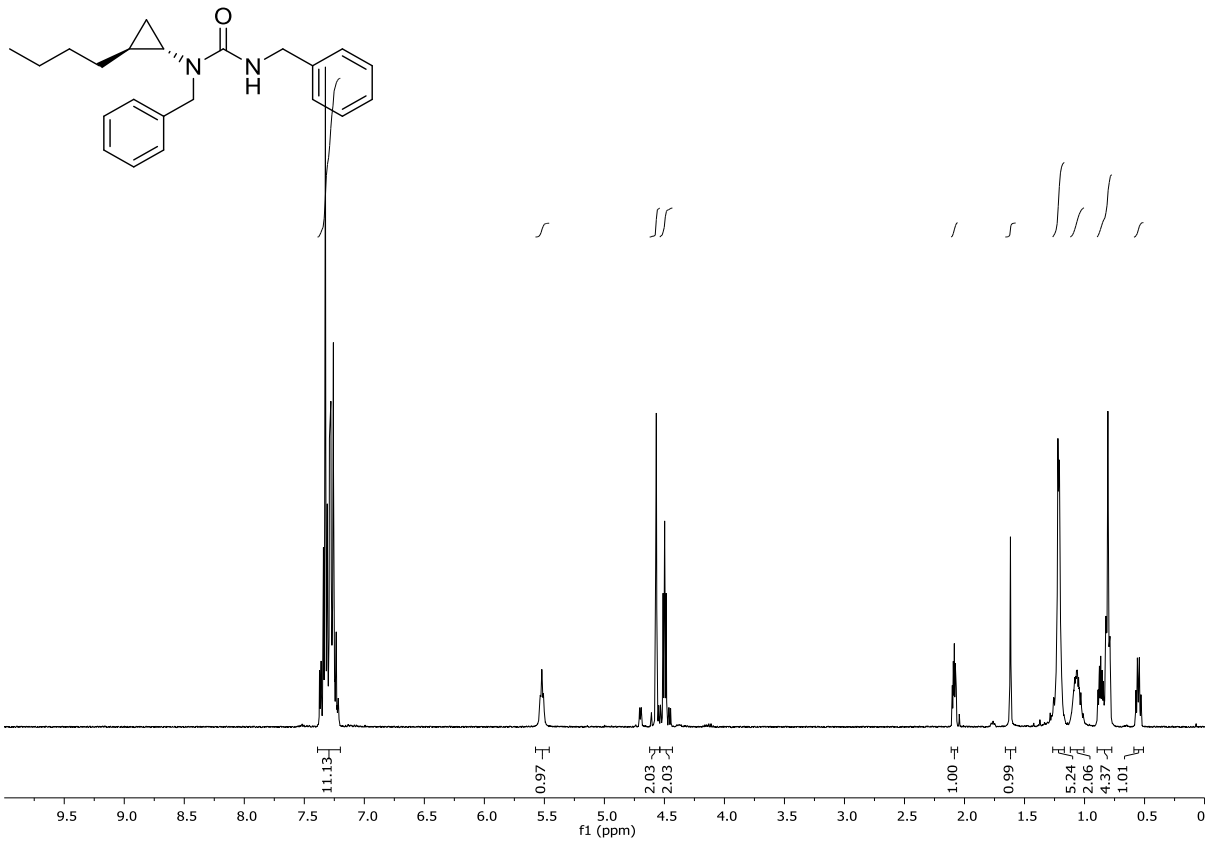

177.35
156.38
150.48
130.58
121.89
114.28
55.57
45.83
33.66
16.94
f1 (ppm)

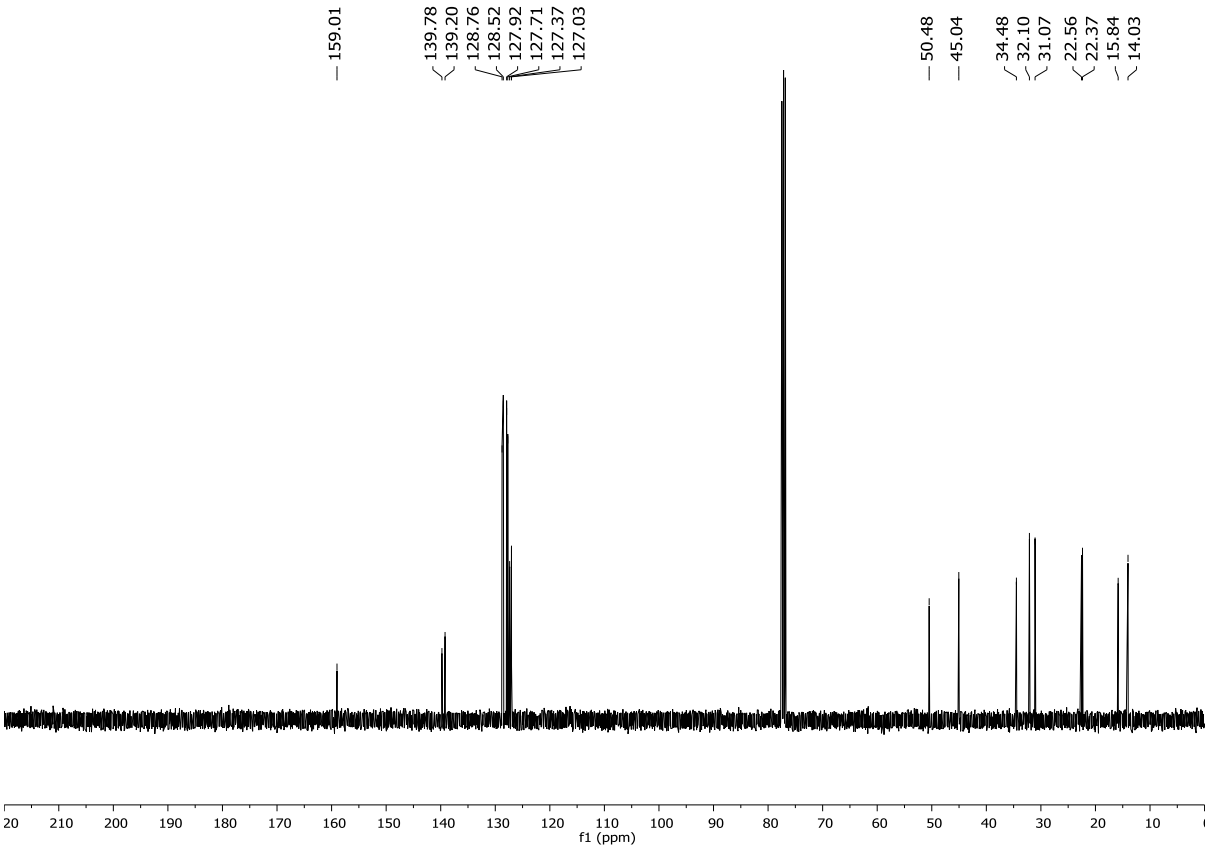

Me
O
N
N
H
11.70
0.96
4.01
0.99
1.03
3.00
1.05
1.00
f1 (ppm)

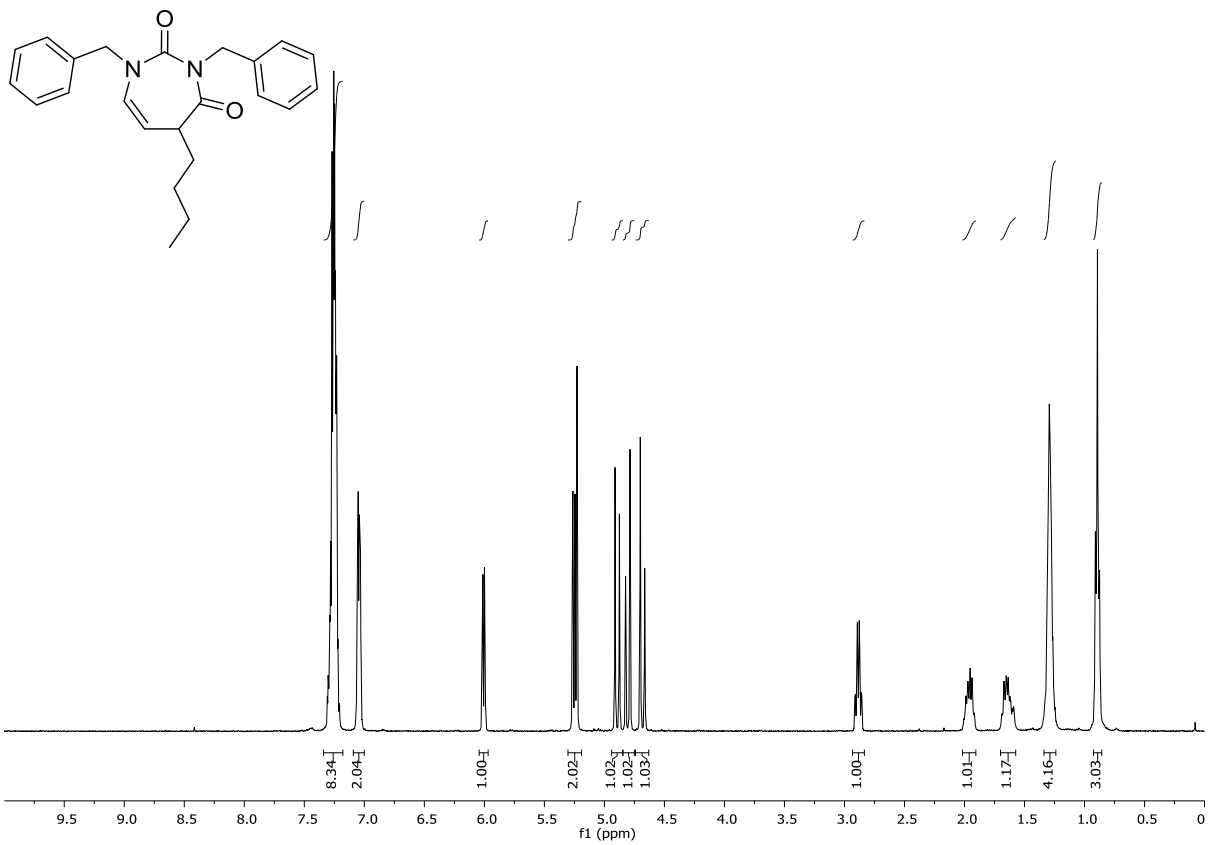

158.96
139.81
139.03
128.73
128.51
128.10
127.53
127.31
127.07
50.33
44.99
35.27
16.94
16.84
16.59
f1 (ppm)

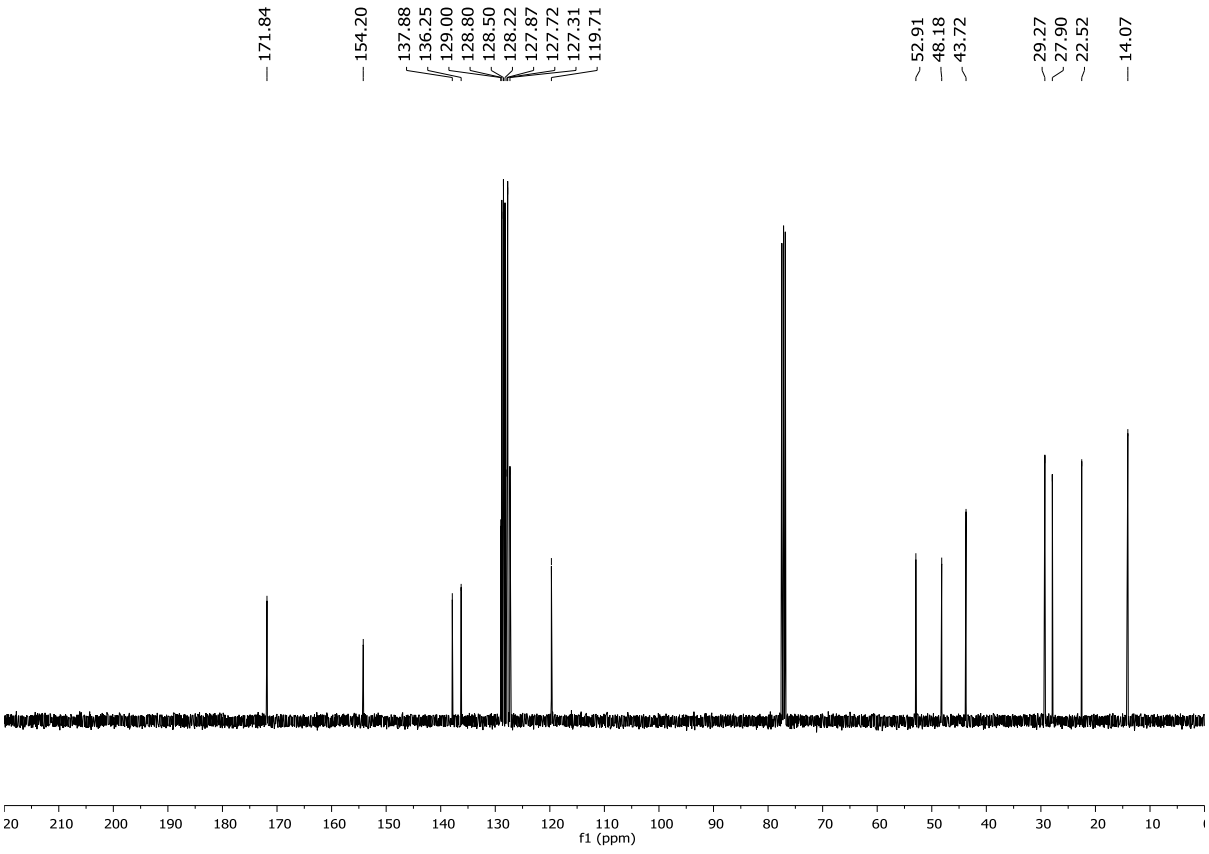

O
N
N
O
Me
8.89
2.05
1.00
1.02
1.02
1.01
1.02
1.02
1.01
3.09
f1 (ppm)

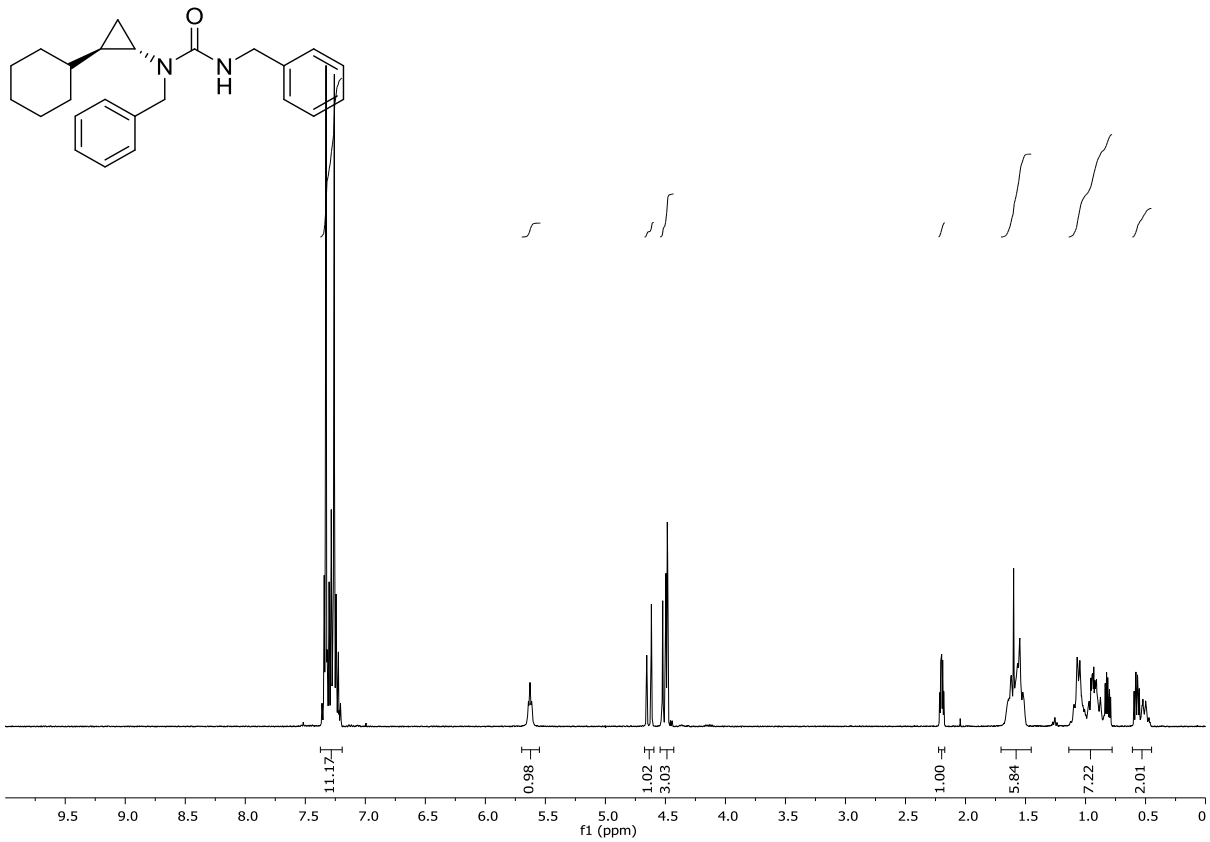

172.32
154.01
137.71
136.08
128.71
128.51
128.36
128.12
127.73
127.59
127.18
120.22
52.86
48.21
38.01
13.65
f1 (ppm)

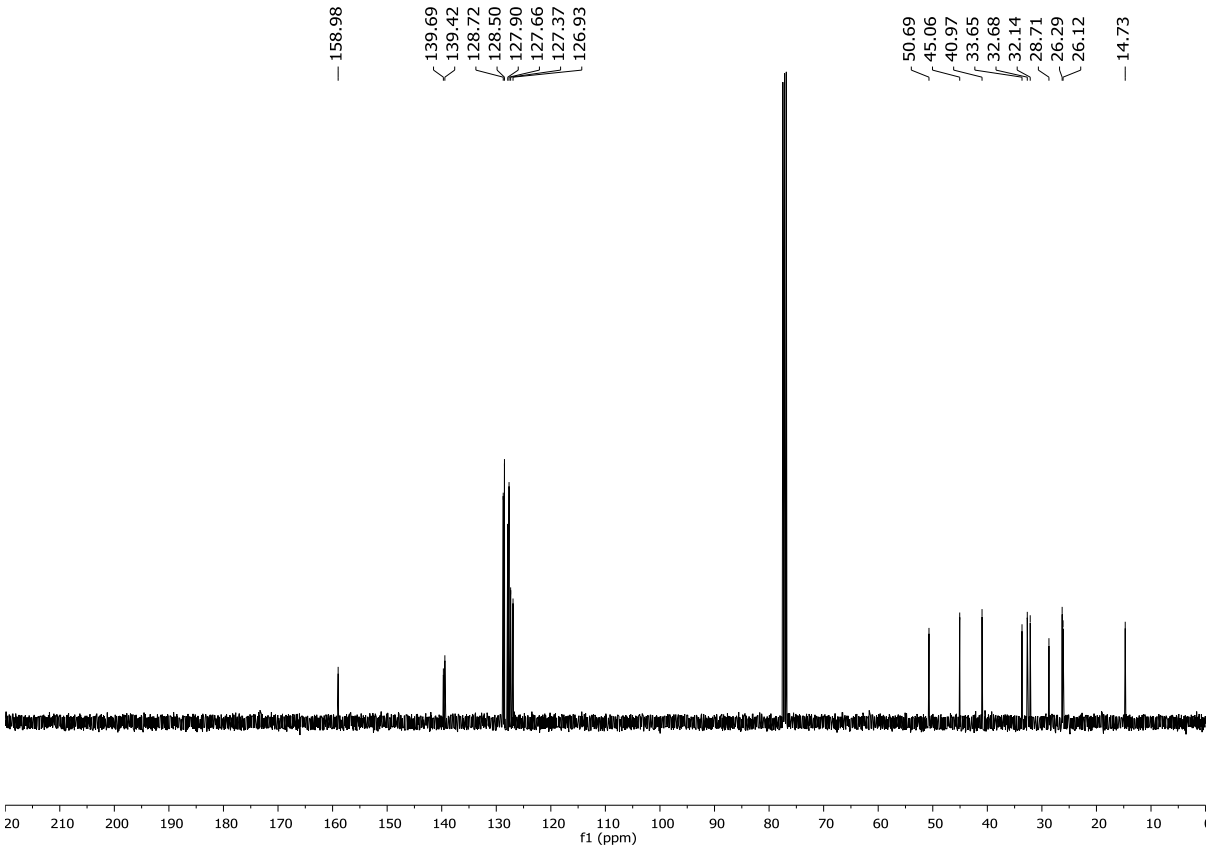

O
N
N
H
11.13
0.97
2.03
2.03
1.00
0.99
5.24
2.06
4.37
1.01
f1 (ppm)

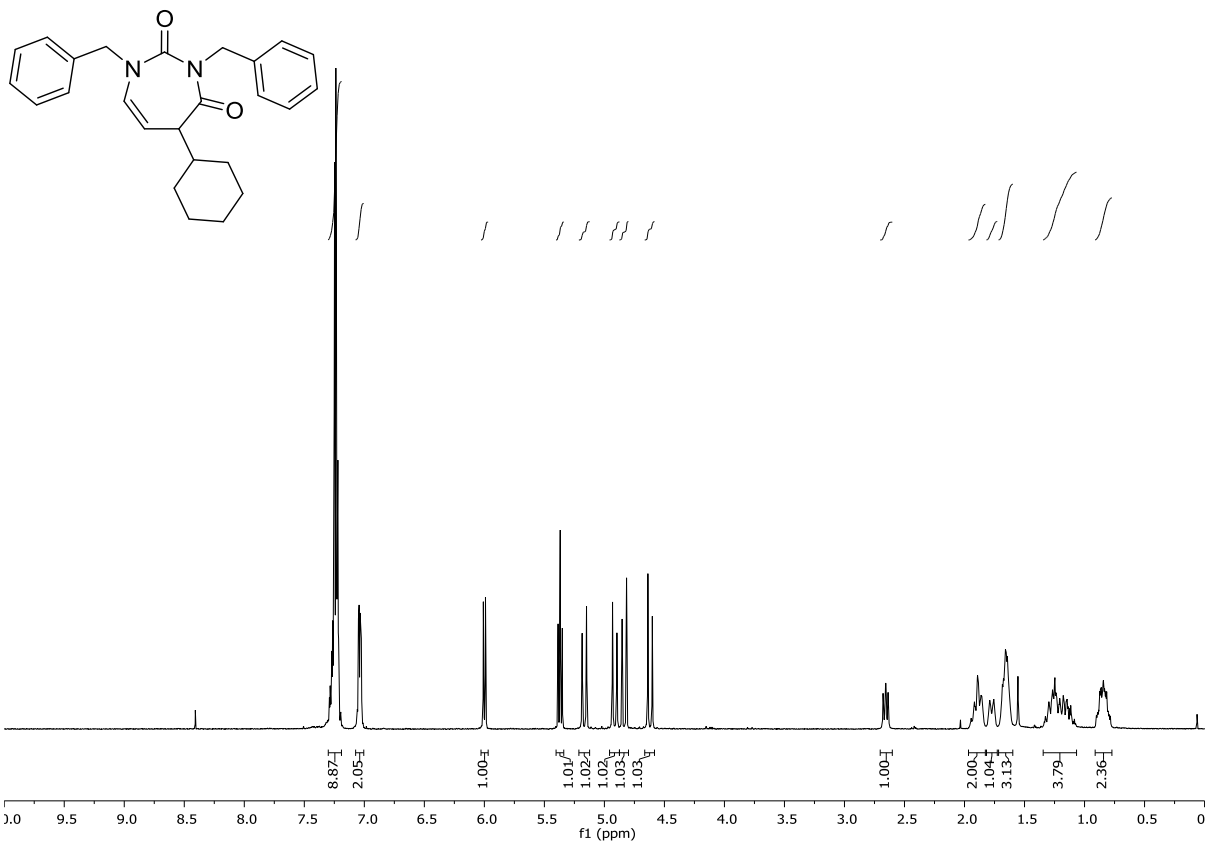

159.01
139.78
139.20
128.76
128.52
127.92
127.71
127.37
127.03
50.48
45.04
34.48
32.10
31.07
22.56
22.37
15.84
14.03
f1 (ppm)

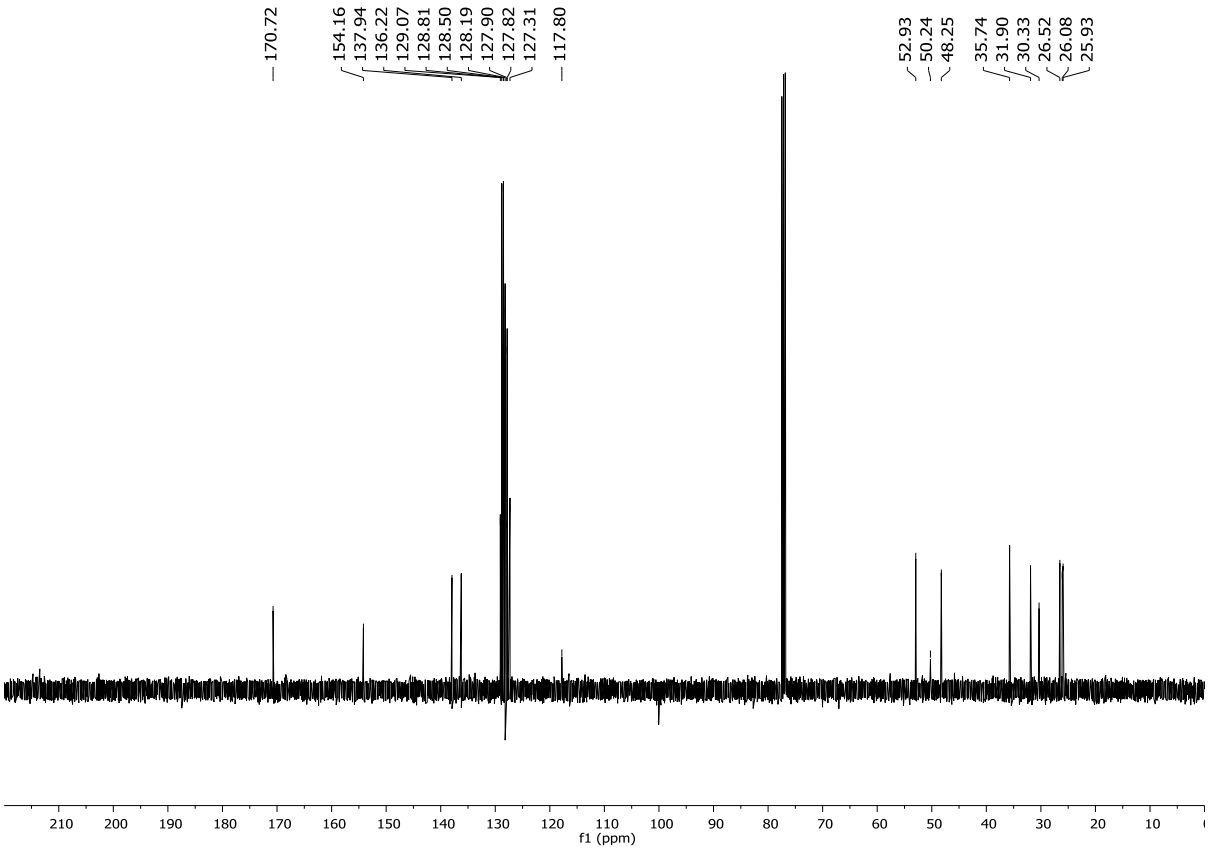

O
N
N
O
8.34
2.04
1.00
2.02
1.02
1.02
1.03
1.00
1.01
1.17
4.16
3.03
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)

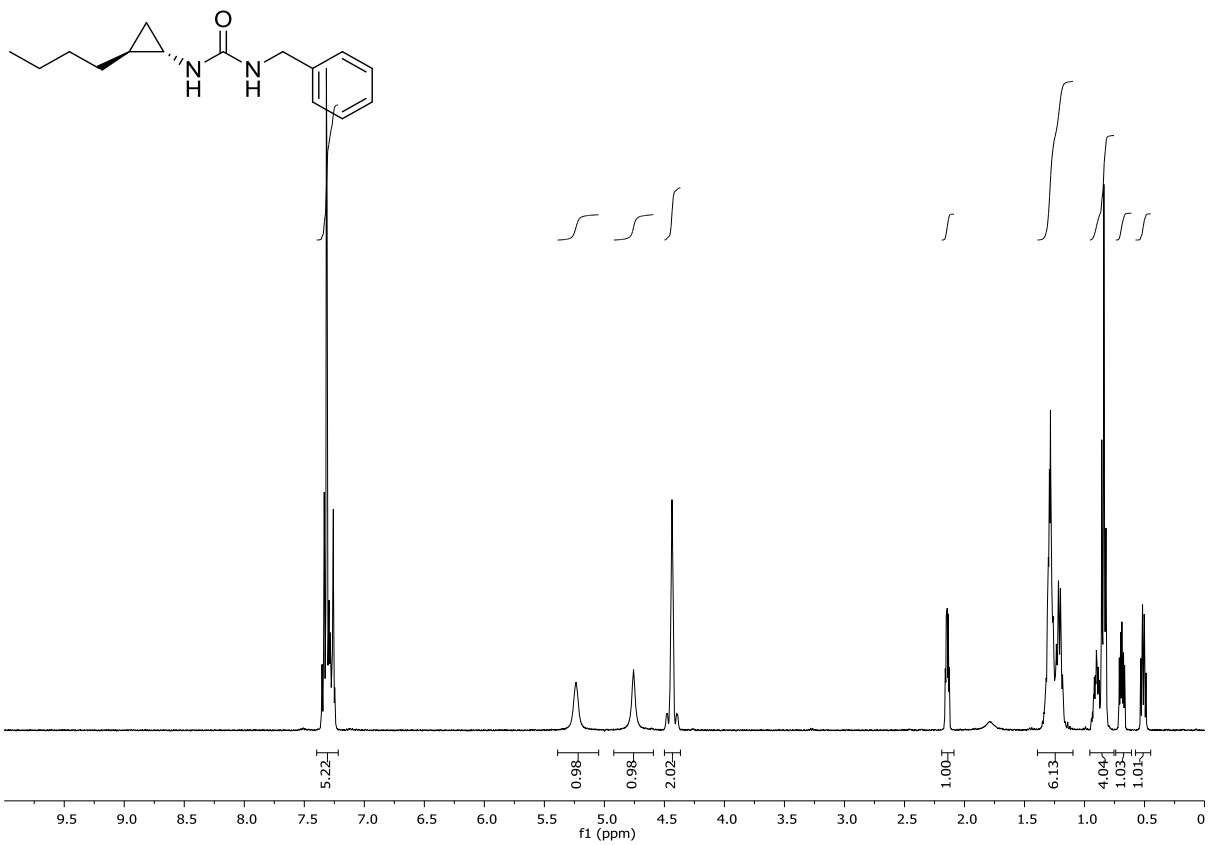

171.84
154.20
137.88
136.25
129.00
128.80
128.50
128.22
127.87
127.72
127.31
119.71
52.91
48.18
43.72
29.27
27.90
22.52
14.07
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

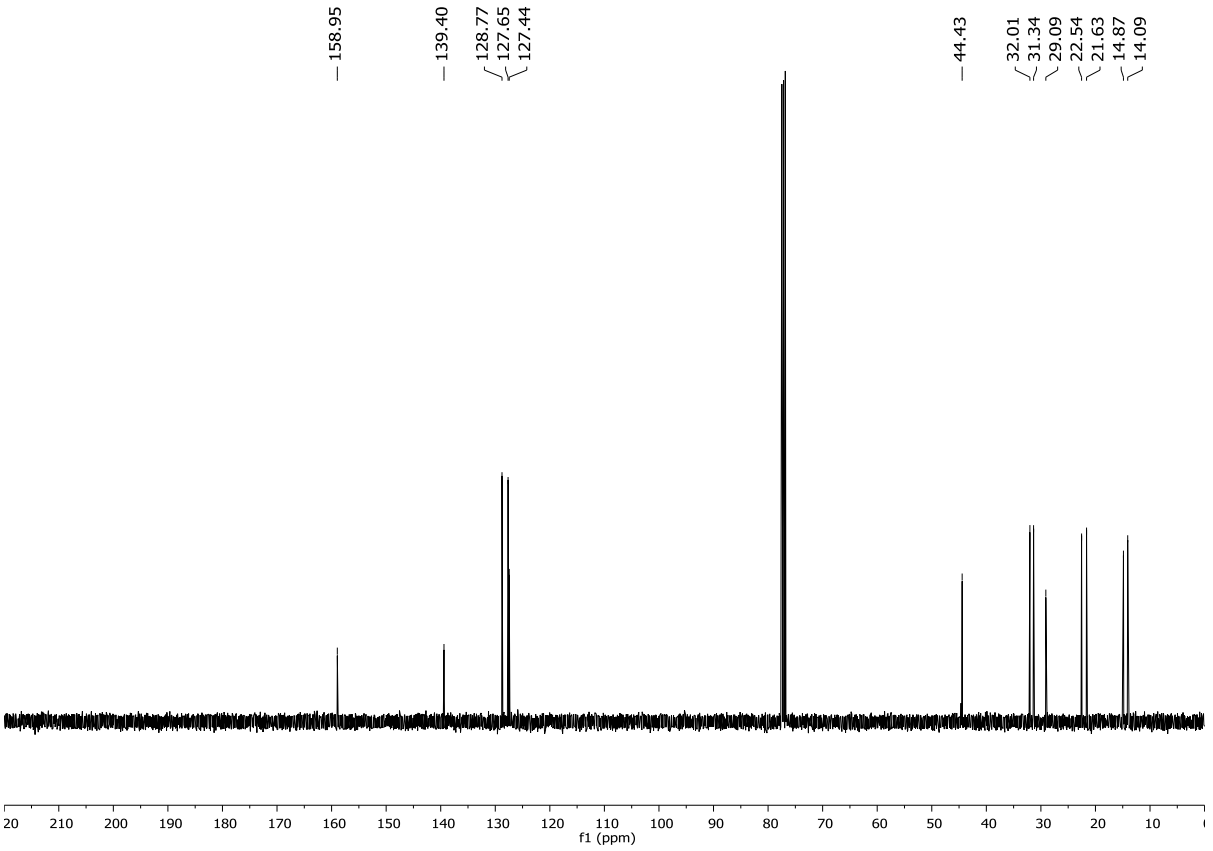

O
N
N
H
11.17
0.98
1.02
3.03
1.00
5.84
7.22
2.01
f1 (ppm)

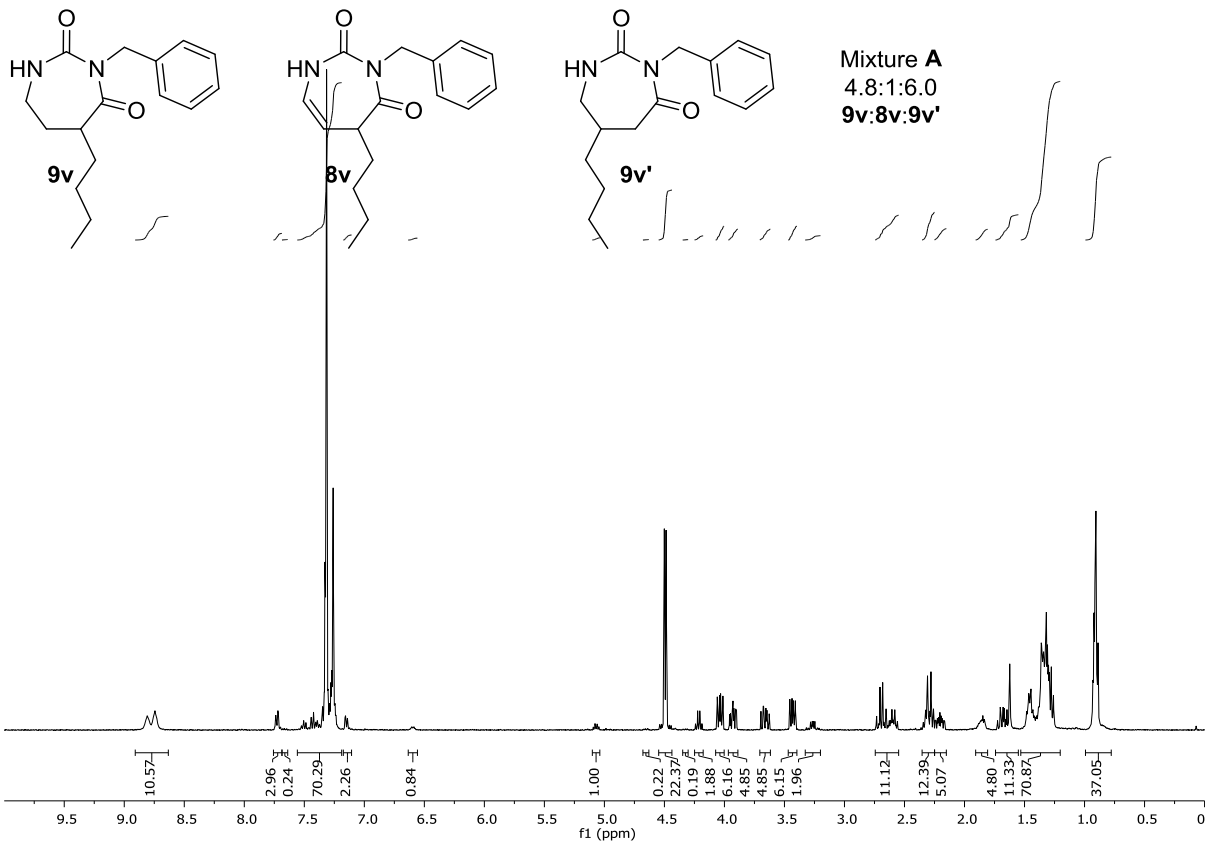

158.98
139.69
139.42
128.72
128.50
127.90
127.66
127.37
126.93
50.69
45.06
40.97
33.65
32.68
32.14
28.71
26.29
26.12
14.73
f1 (ppm)

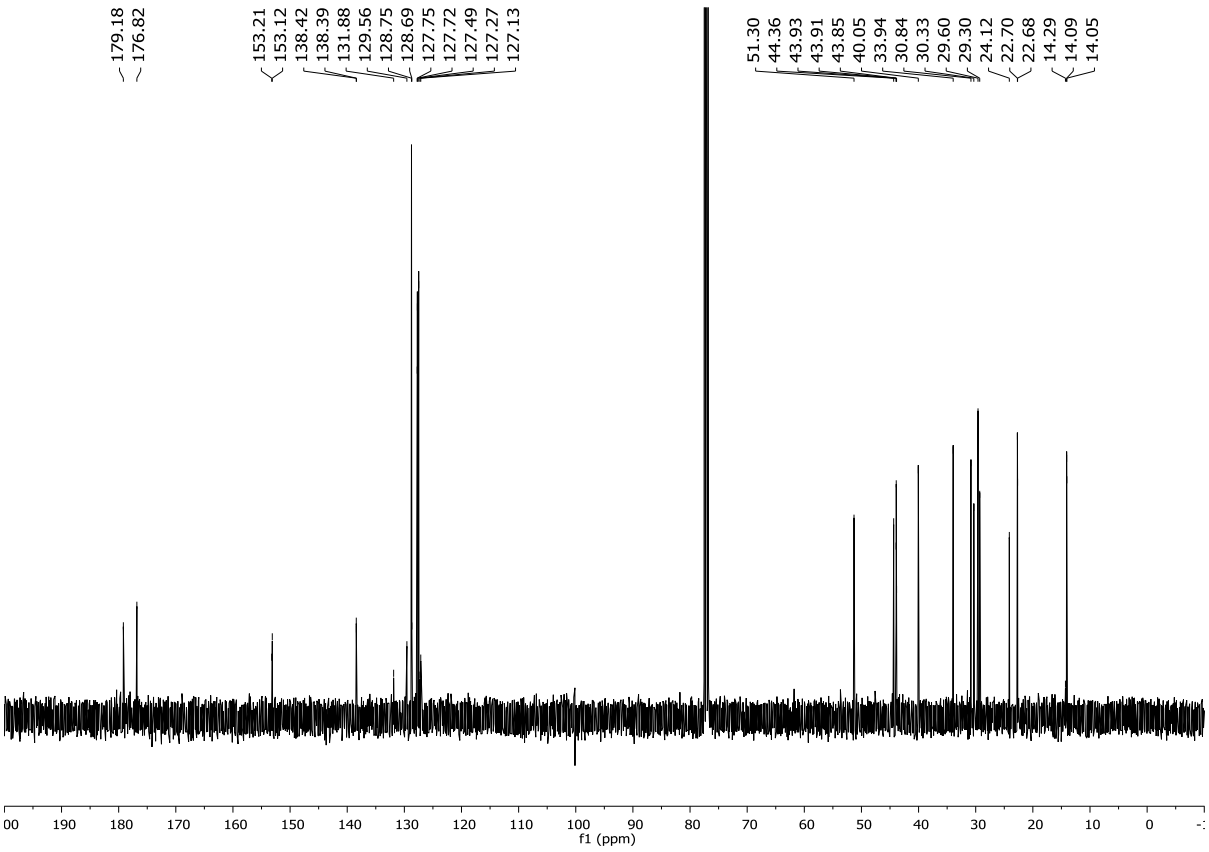

O
N
N
O
8.87
2.05
1.00
1.01
1.02
1.03
1.03
1.00
2.00
1.04
3.13
3.79
2.36
f1 (ppm)

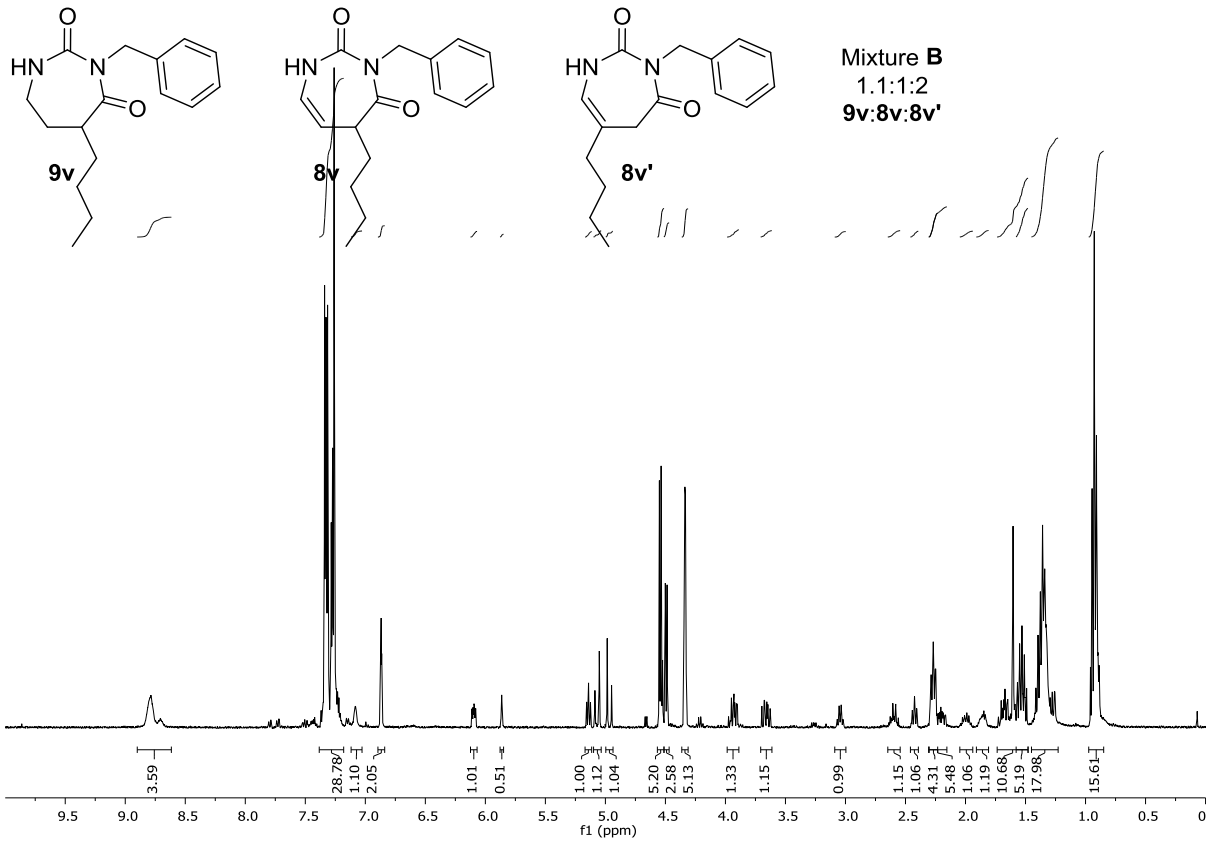

170.72
154.16
137.94
136.22
129.07
128.81
128.50
128.19
127.90
127.82
127.31
117.80
52.93
50.24
48.25
35.74
31.90
30.33
26.52
26.08
25.93
f1 (ppm)

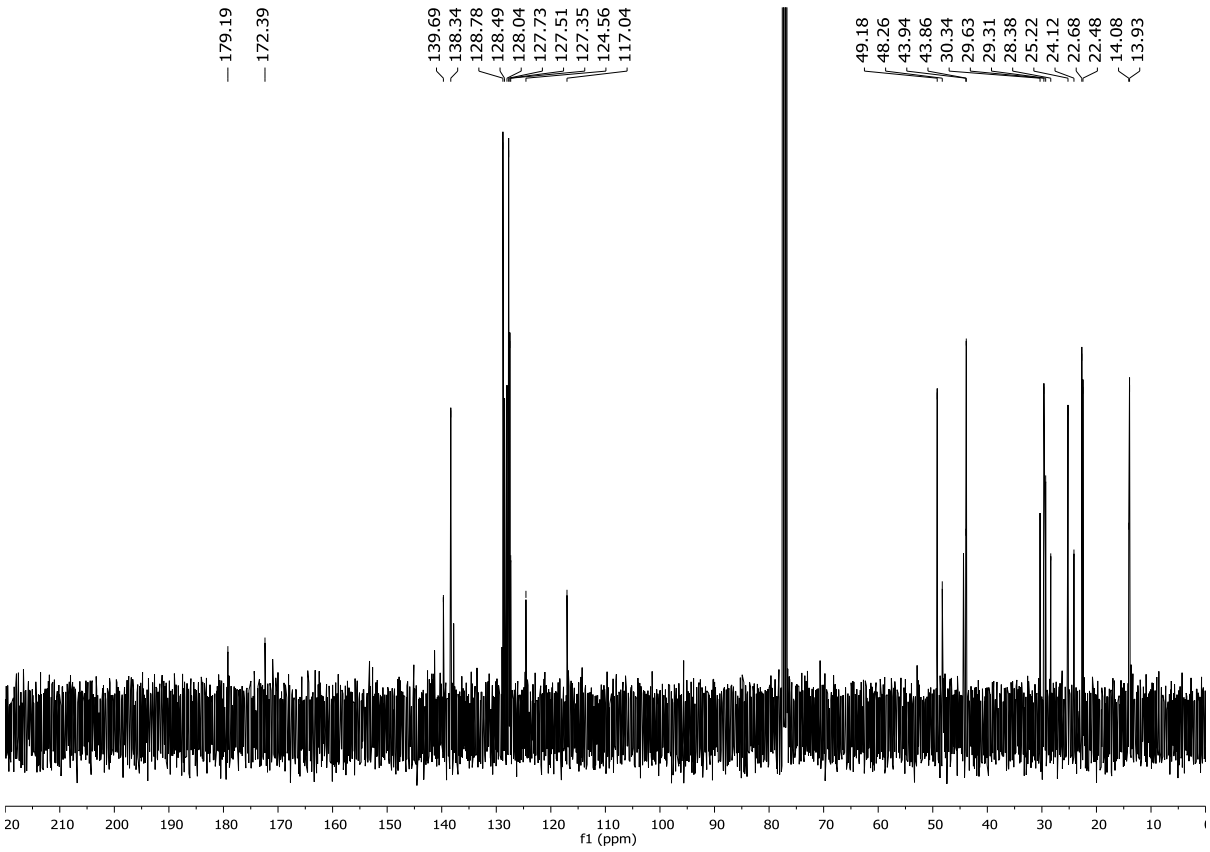

O
N
H
N
H
5.22
0.98
0.98
2.02
1.00
6.13
4.04
1.03
1.01
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)

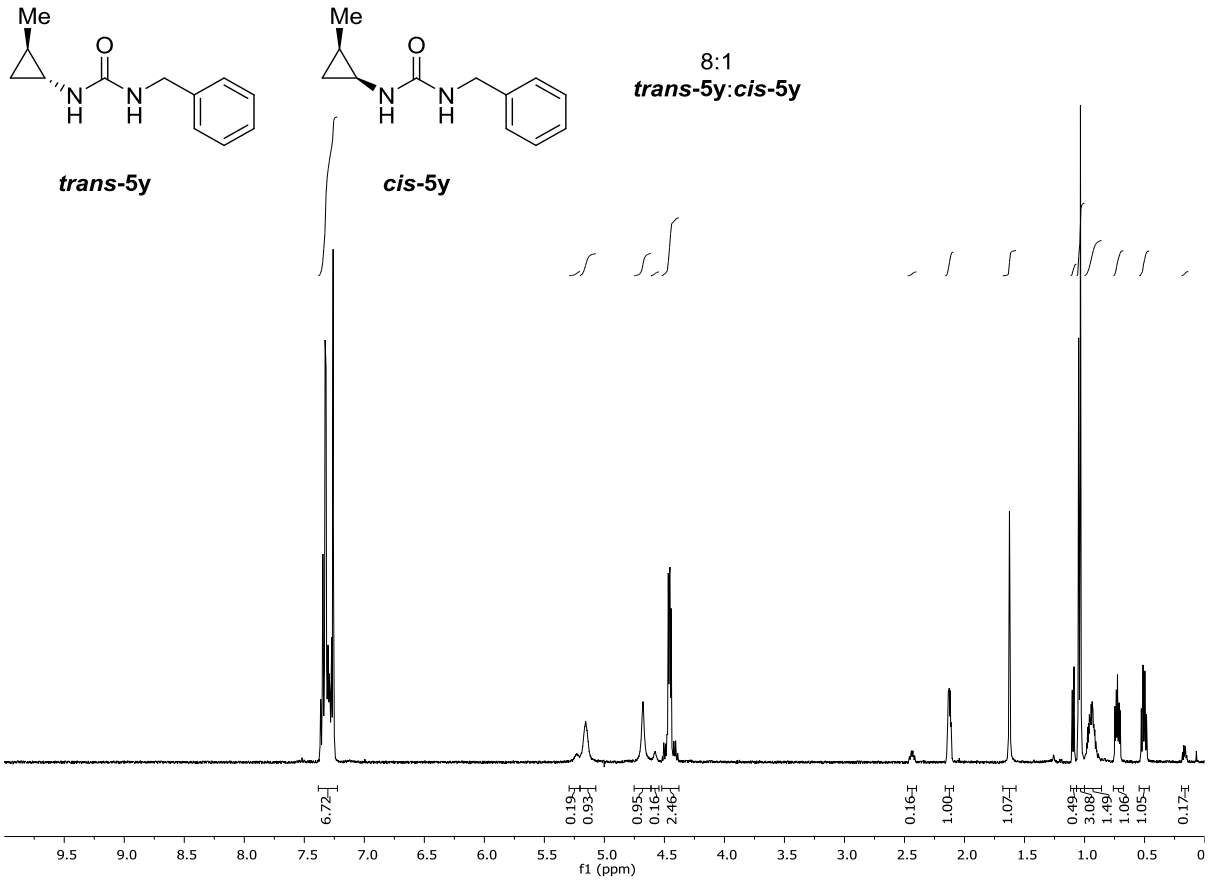

158.95
139.40
128.77
127.65
127.44
44.43
32.01
31.34
29.09
22.54
21.63
14.87
14.09
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

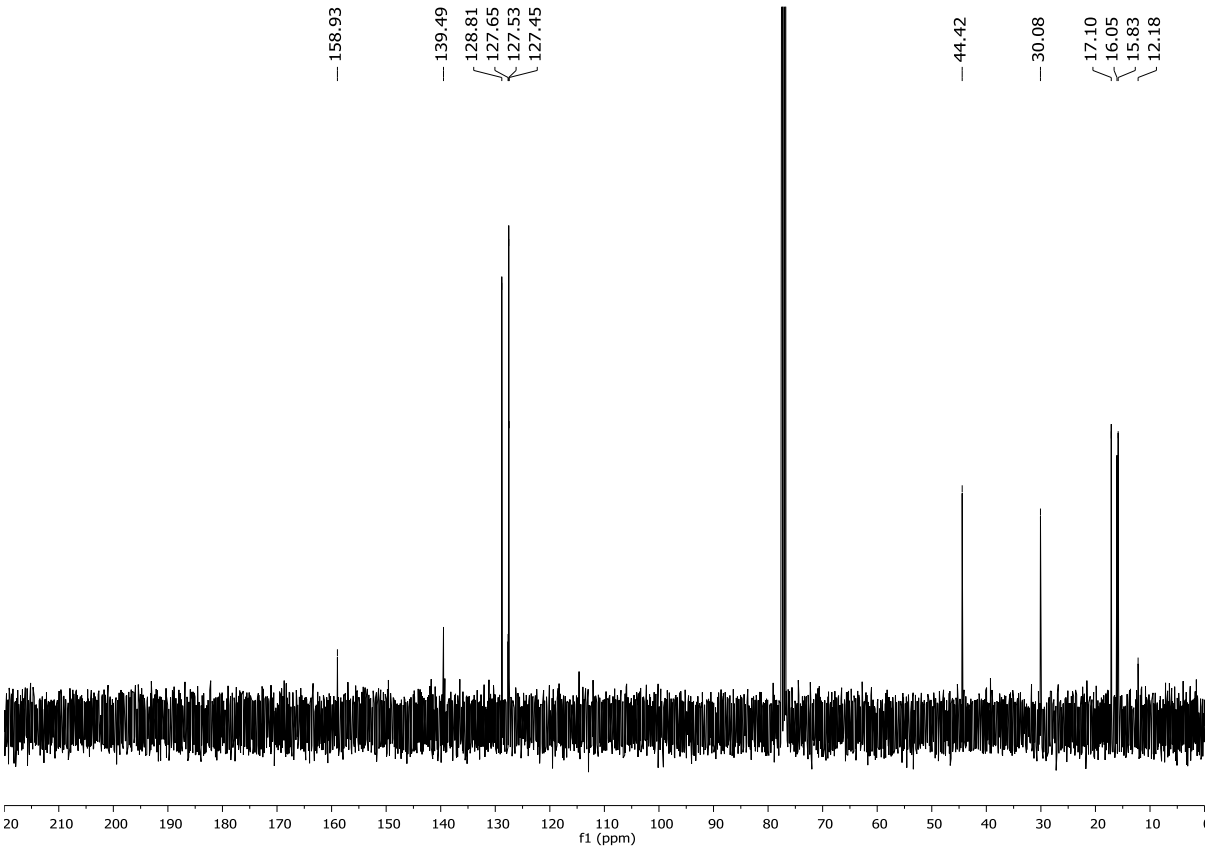

9v
8v
9v'
Mixture A
4.8:1:6.0
9v:8v:9v'
10.57
2.96
0.24
70.29
2.26
0.84
1.00
0.22
22.37
0.19
1.88
6.16
4.85
4.85
6.15
1.96
11.12
12.39
5.07
4.80
11.33
70.87
37.05
f1 (ppm)

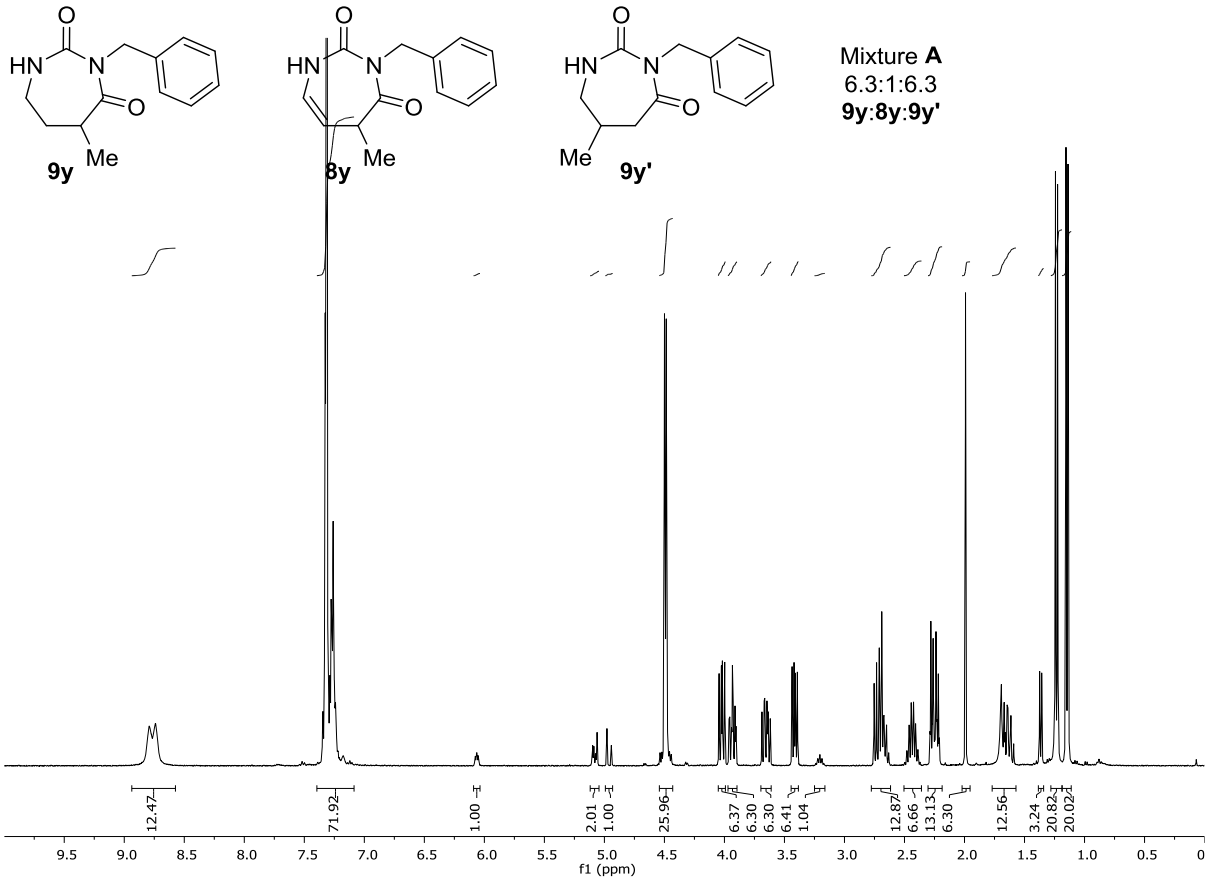

179.18
176.82
153.21
153.12
138.42
138.39
131.88
129.56
128.75
128.69
127.75
127.72
127.49
127.27
127.13
51.30
44.36
43.93
43.91
43.85
40.05
33.94
30.84
30.33
29.60
29.30
24.12
22.70
22.68
14.29
14.09
14.05
f1 (ppm)

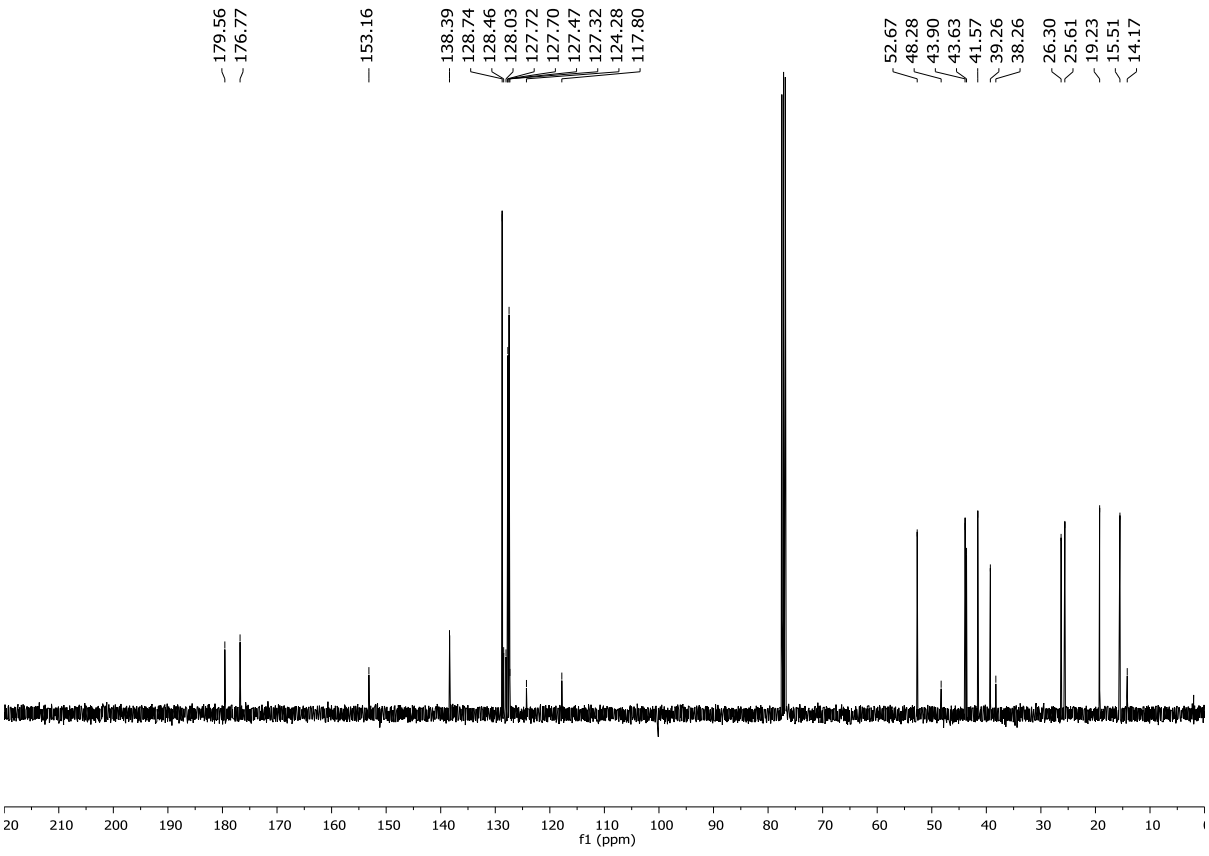

9v
8v
8v'
Mixture **B**
1.1:1:2
9v:**8v**:**8v'**
f1 (ppm)

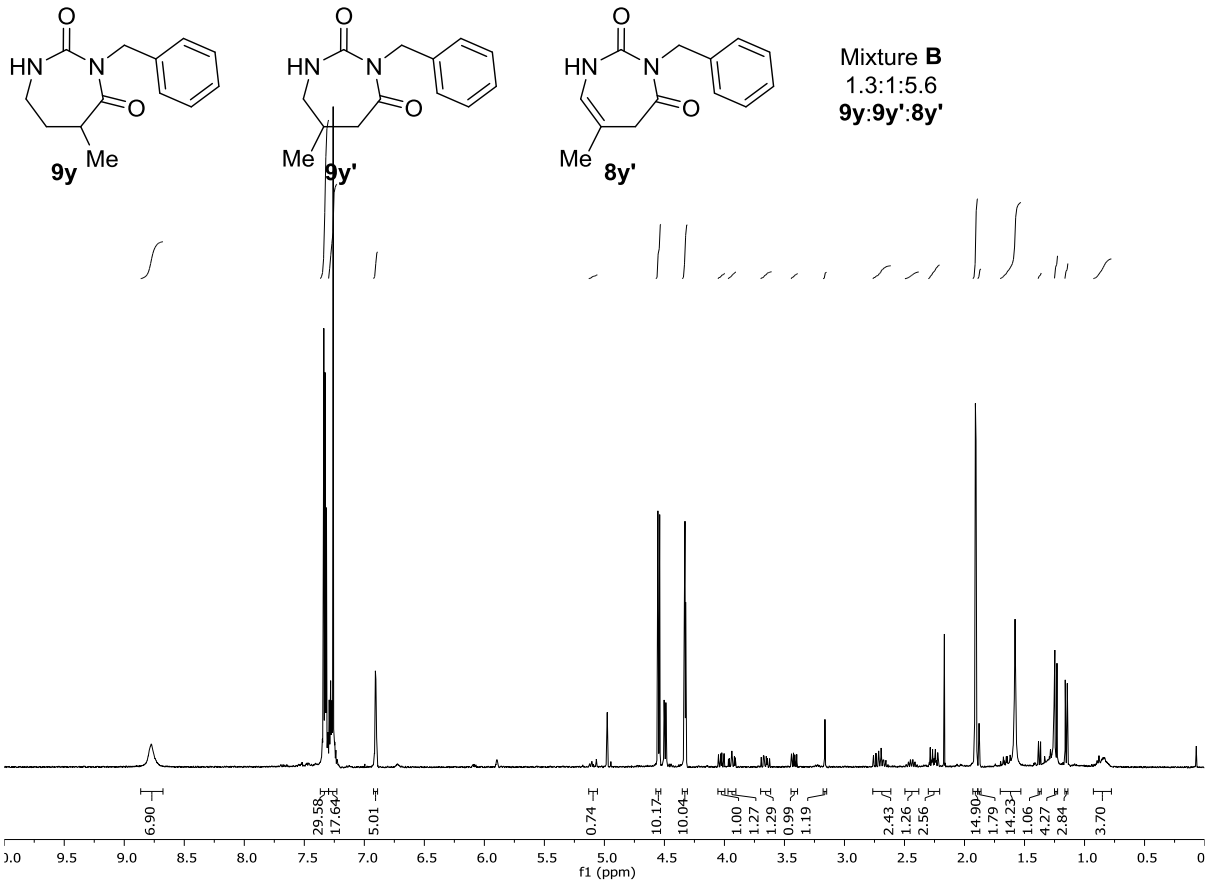

179.19
172.39
139.69
138.34
128.78
128.49
128.04
127.73
127.51
127.35
124.56
117.04
49.18
48.26
43.94
43.86
30.34
29.63
29.31
28.38
25.22
24.12
22.68
22.48
14.08
13.93
f1 (ppm)

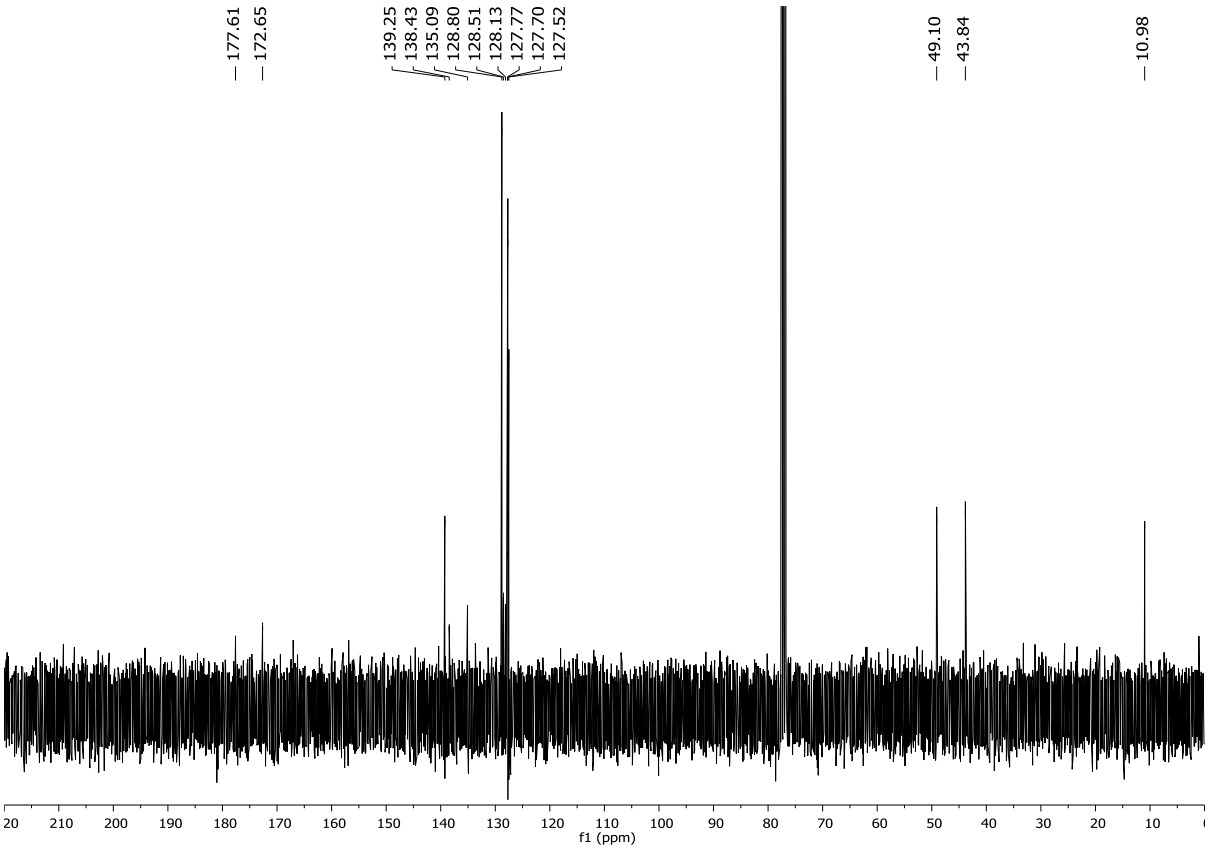

Me
O
N
H
N
H
trans-5y
Me
O
N
H
N
H
cis-5y
8:1
trans-5y:cis-5y
6.72
0.19
0.93
0.95
0.16
2.46
0.16
1.00
1.07
0.49
3.08
1.49
1.06
1.05
0.17
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)

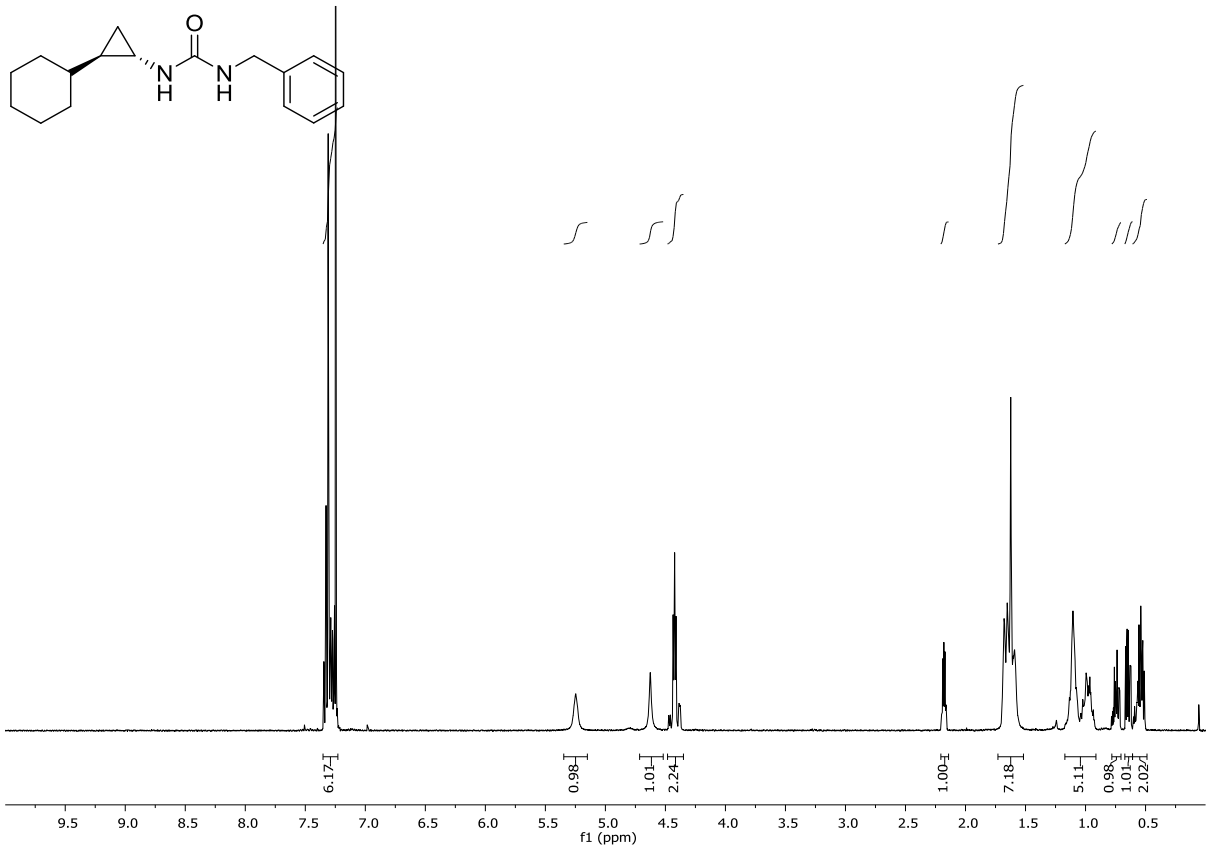

158.93
139.49
128.81
127.65
127.53
127.45
44.42
30.08
17.10
16.05
15.83
12.18
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

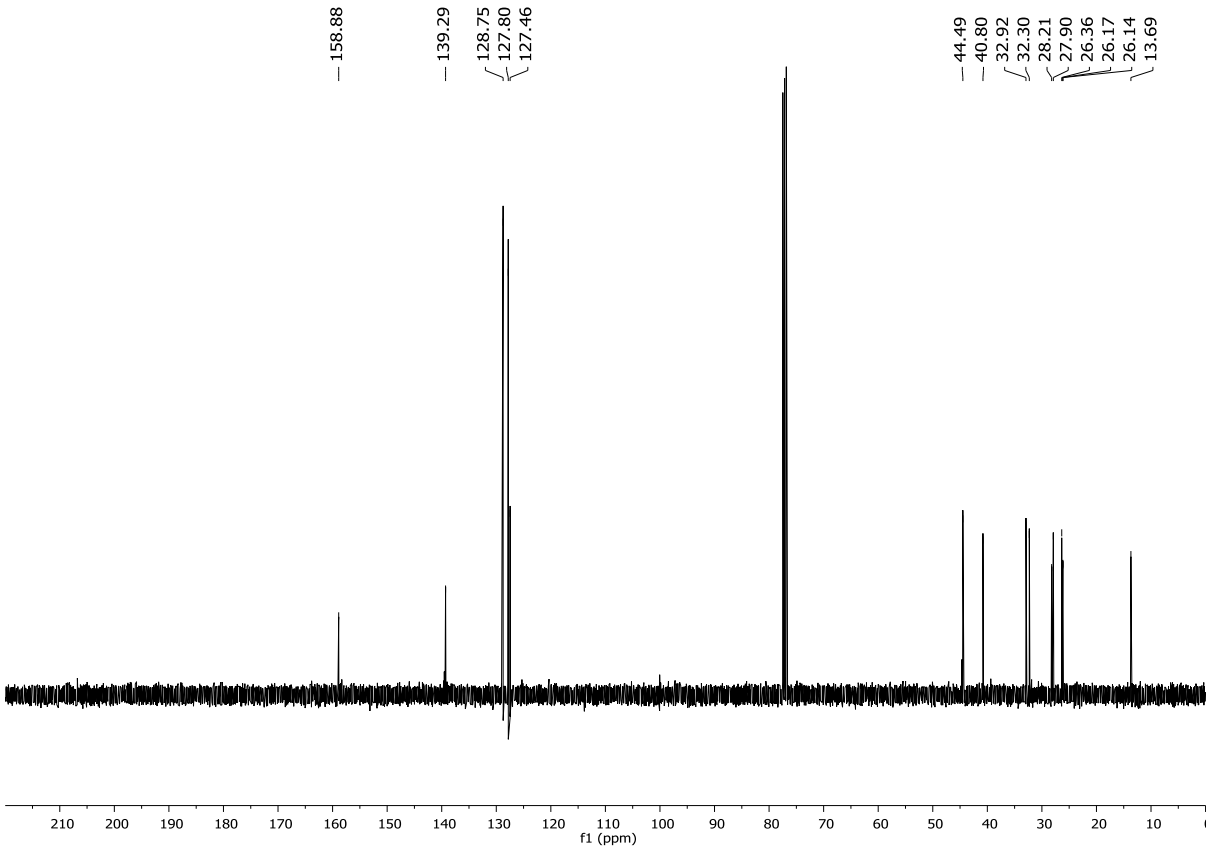

9y
8y
9y'
Mixture A
6.3:1:6.3
9y:8y:9y'
12.47
71.92
1.00
2.01
1.00
25.96
6.37
6.30
6.30
6.41
1.04
12.87
6.66
13.13
6.30
12.56
3.24
20.82
20.02
f1 (ppm)

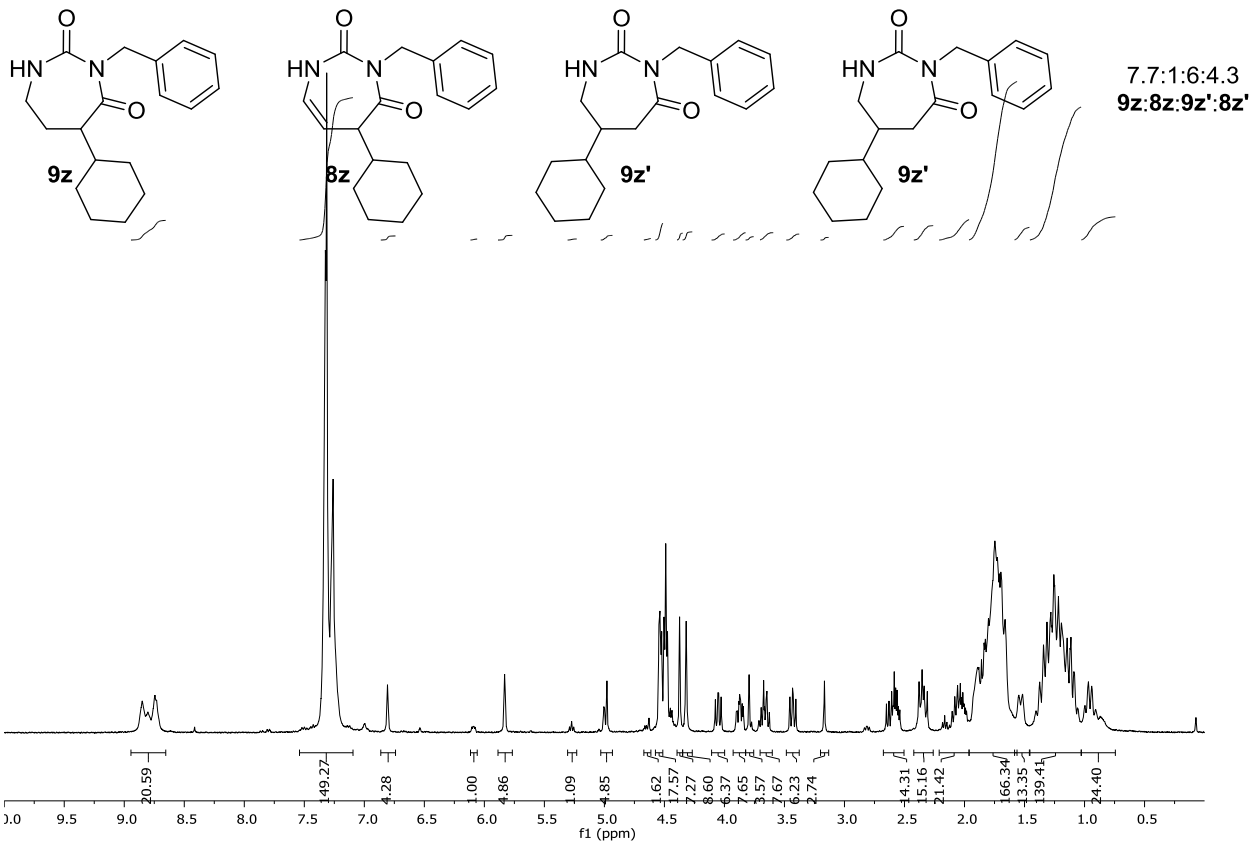

179.56
176.77
153.16
138.39
128.74
128.46
128.03
127.72
127.70
127.47
127.32
124.28
117.80
52.67
48.28
43.90
43.63
41.57
39.26
38.26
26.30
25.61
19.23
15.51
14.17
f1 (ppm)

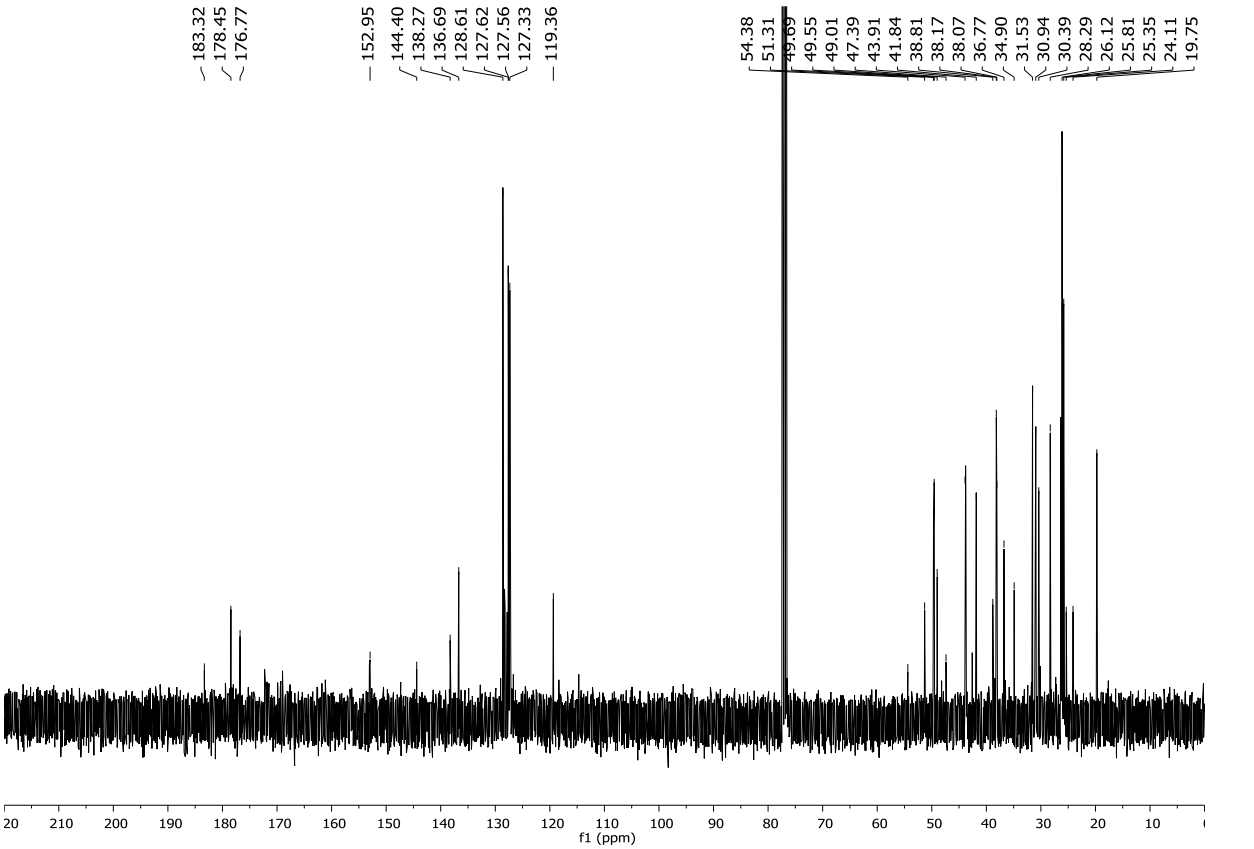

9y
9y'
8y'
Mixture B
1.3:1:5.6
9y:9y':8y'
f1 (ppm)

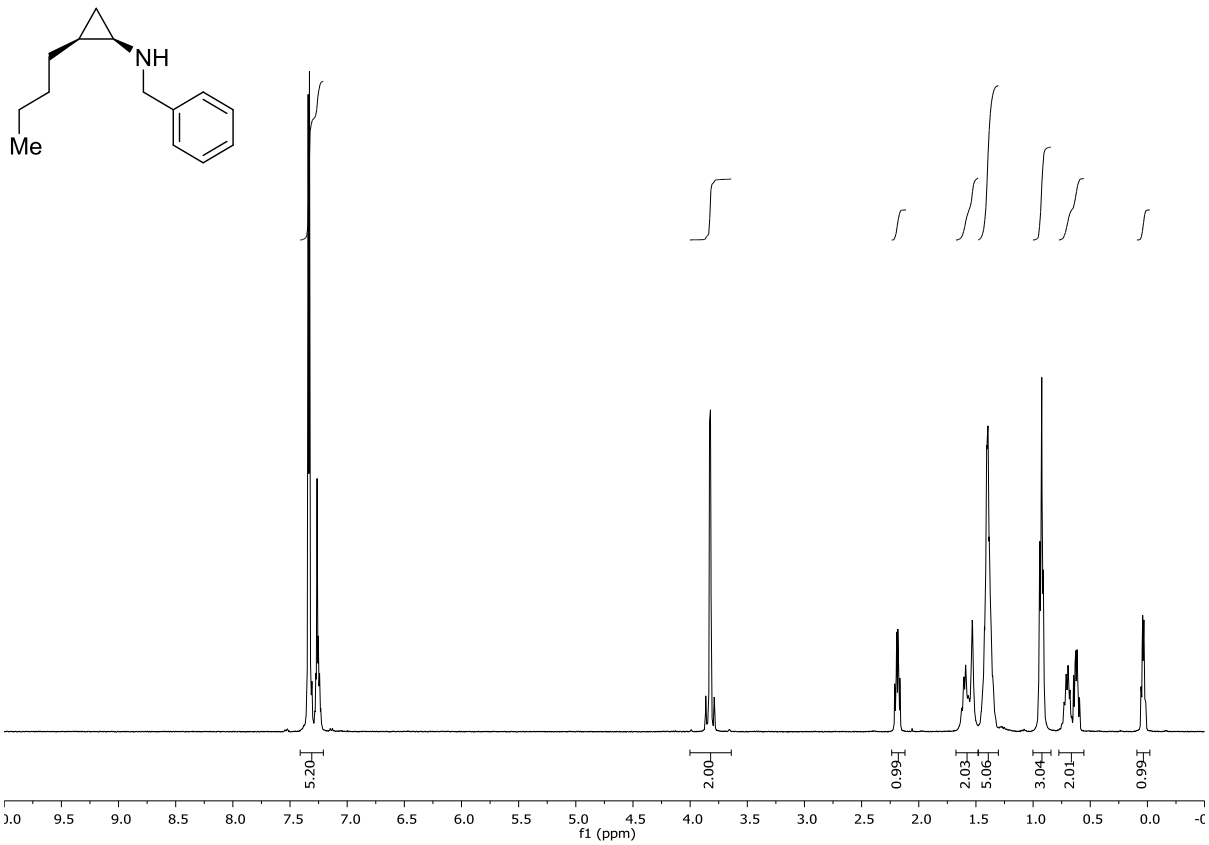

177.61
172.65
139.25
138.43
135.09
128.80
128.51
128.13
127.77
127.70
127.52
49.10
43.84
10.98
f1 (ppm)

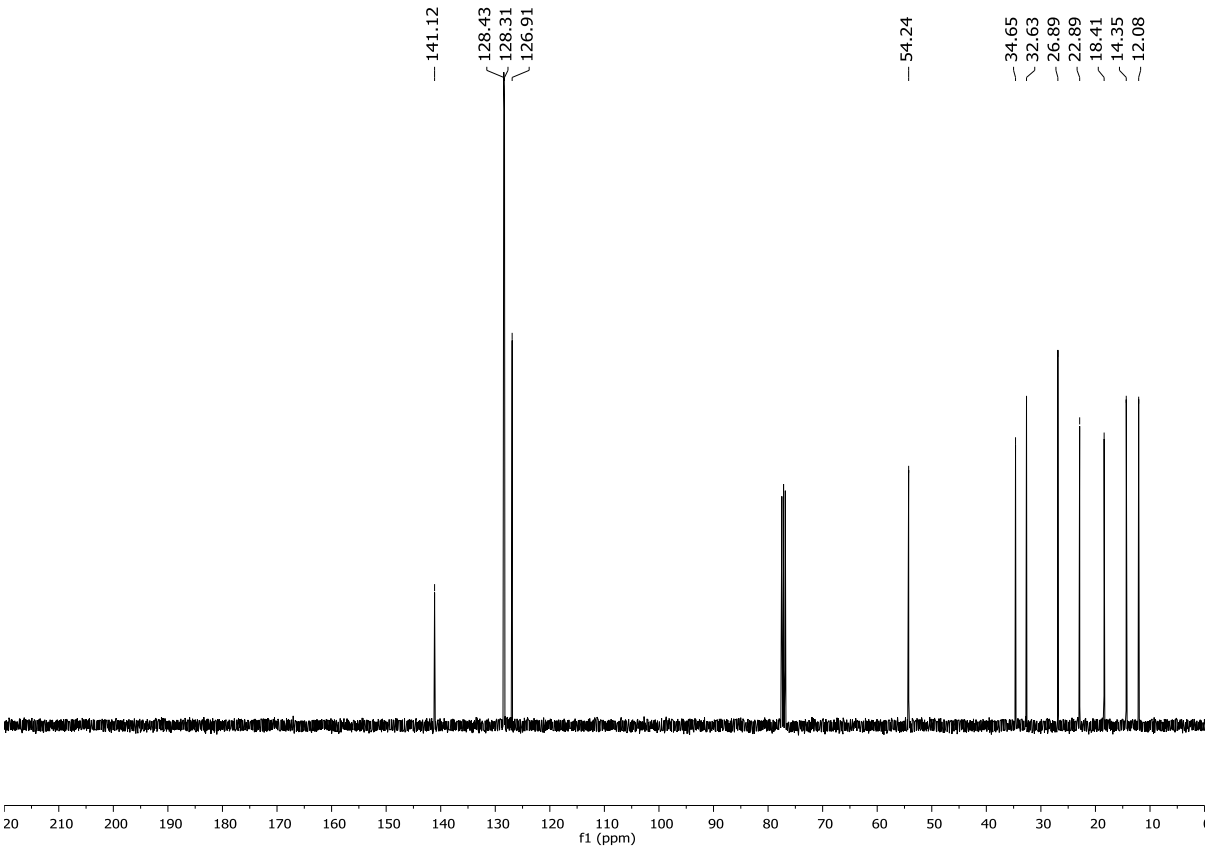

O
N
H
N
H
6.17
0.98
1.01
2.24
1.00
7.18
5.11
0.98
1.01
2.02
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

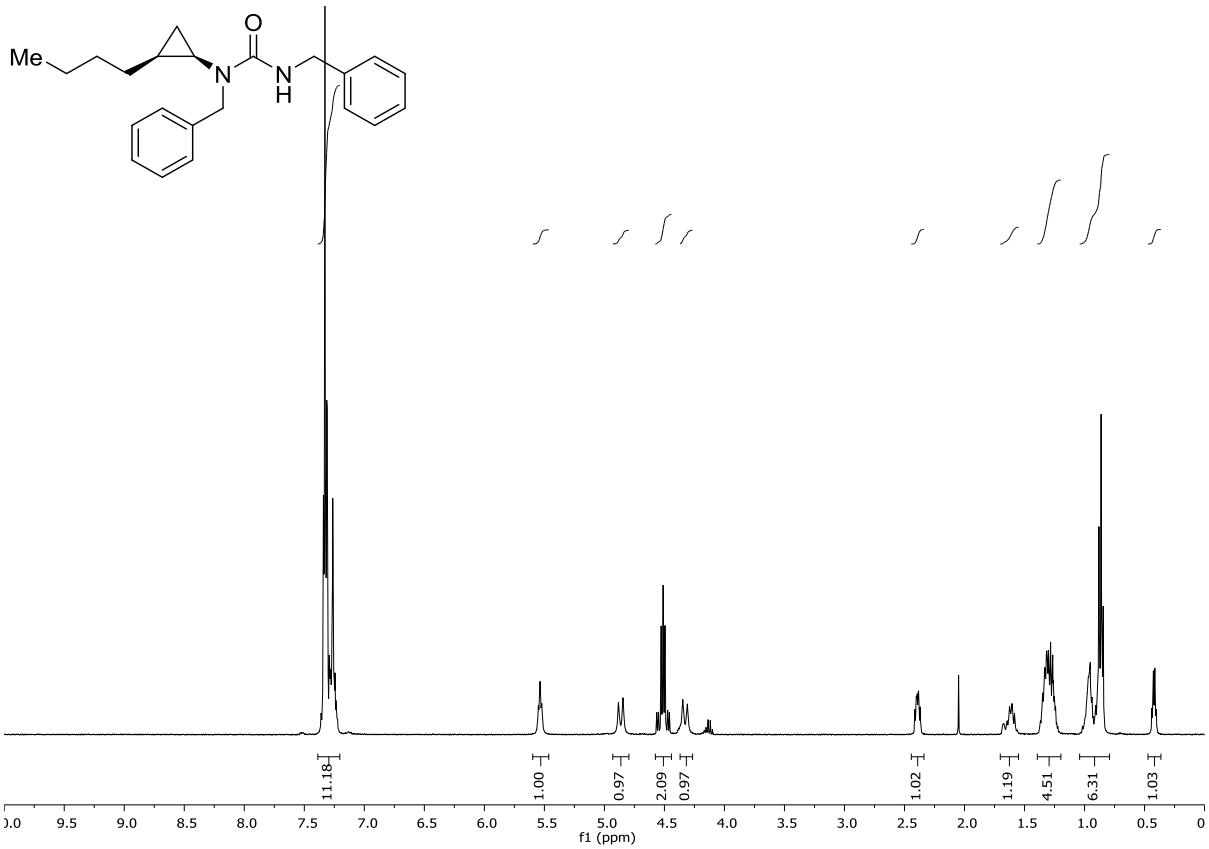

158.88
139.29
128.75
127.80
127.46
44.49
40.80
32.92
32.30
28.21
27.90
26.36
26.17
26.14
13.69
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

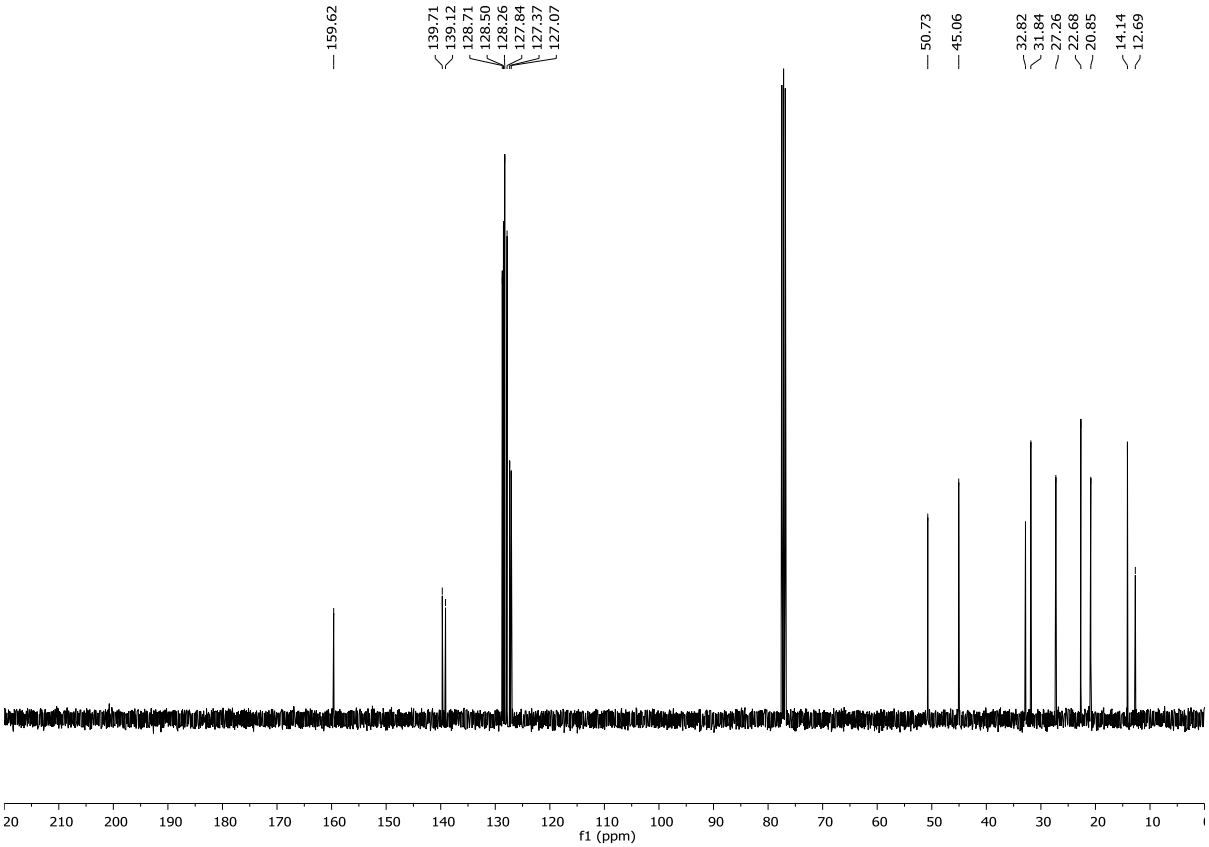

9z
8z
9z'
9z'
7.7:1:6:4.3
9z:8z:9z':8z'
20.59
49.27
4.28
1.00
4.86
1.09
4.85
1.62
17.57
7.27
8.60
6.37
7.65
3.57
7.67
6.23
2.74
14.31
15.16
21.42
166.34
13.35
139.41
24.40
f1 (ppm)

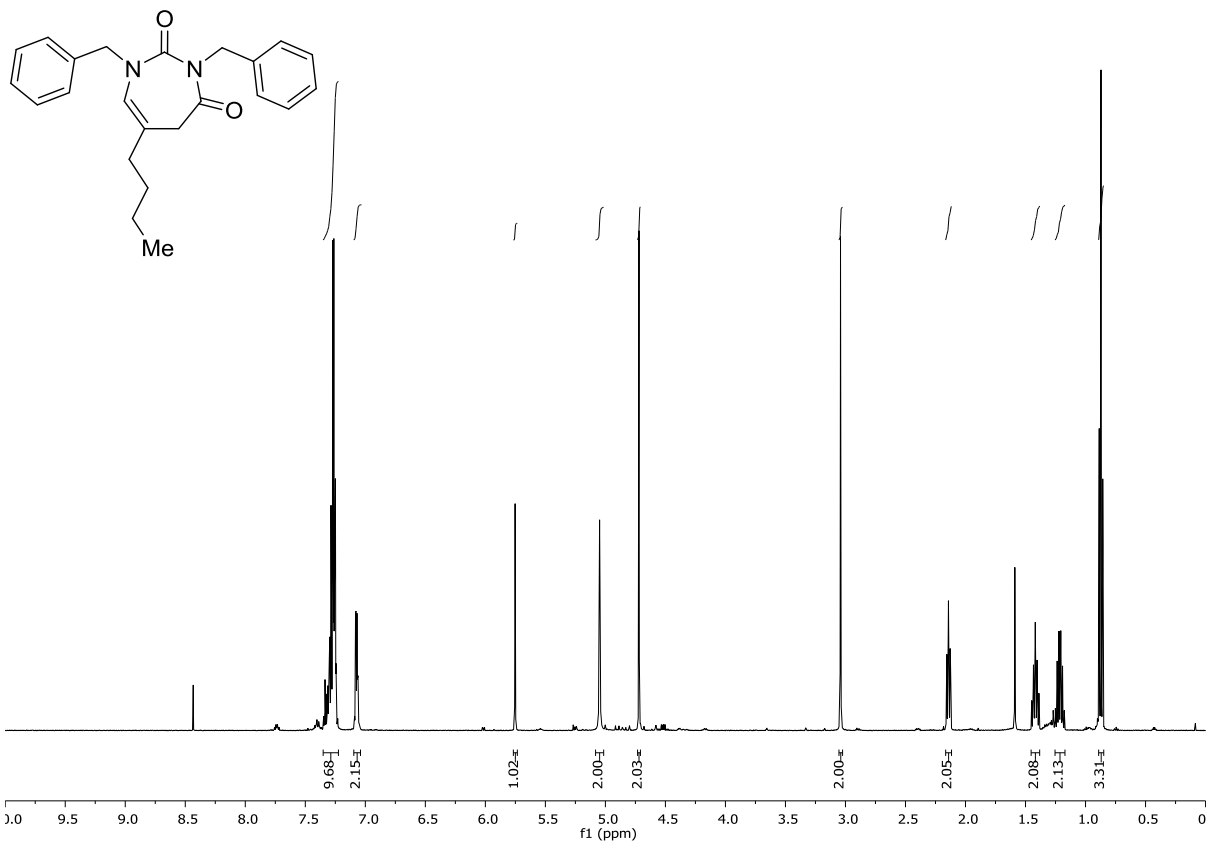

183.32
178.45
176.77
152.95
144.40
138.27
136.69
128.61
127.62
127.56
127.33
119.36
54.38
51.31
49.69
49.55
49.01
47.39
43.91
41.84
38.81
38.17
38.07
36.77
34.90
31.53
30.94
30.39
28.29
26.12
25.81
25.35
24.11
19.75
f1 (ppm)

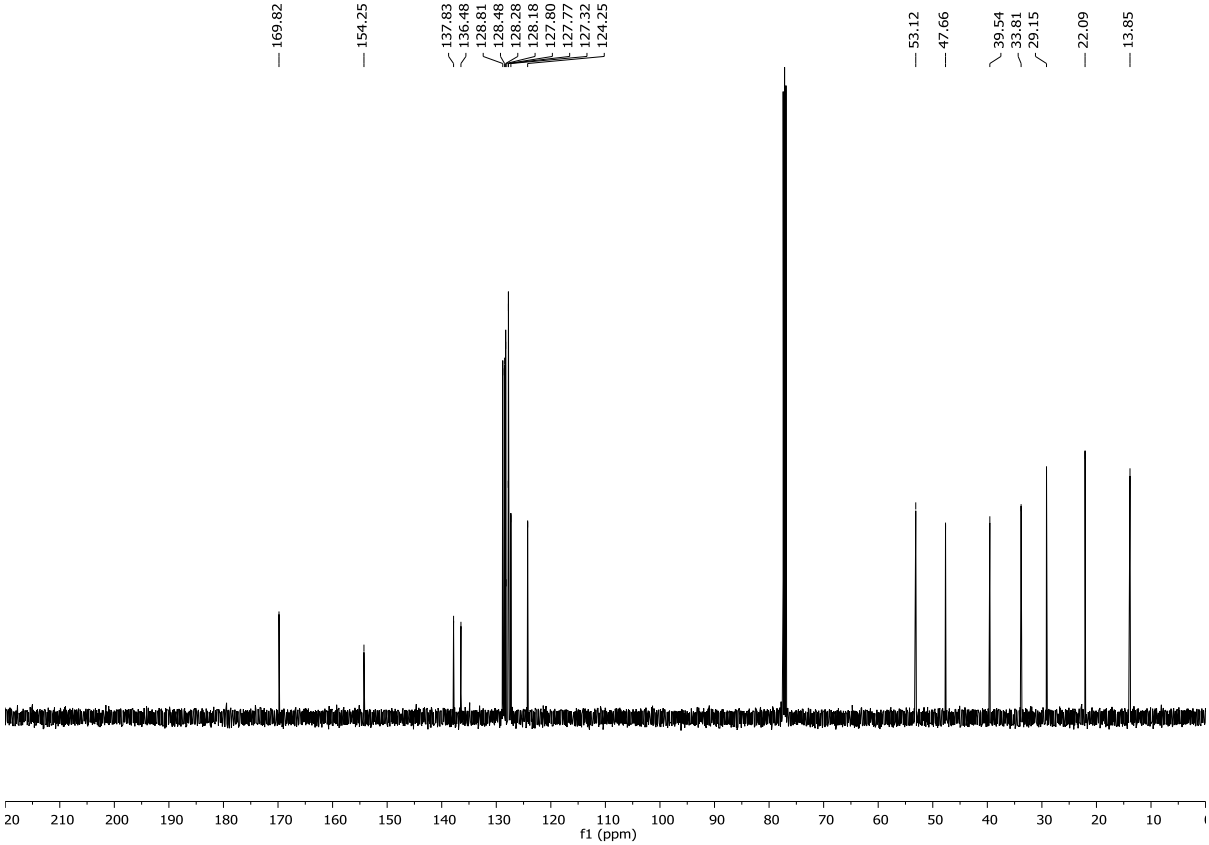

NH
Me
5.20
2.00
0.99
2.03
5.06
3.04
2.01
0.99
f1 (ppm)

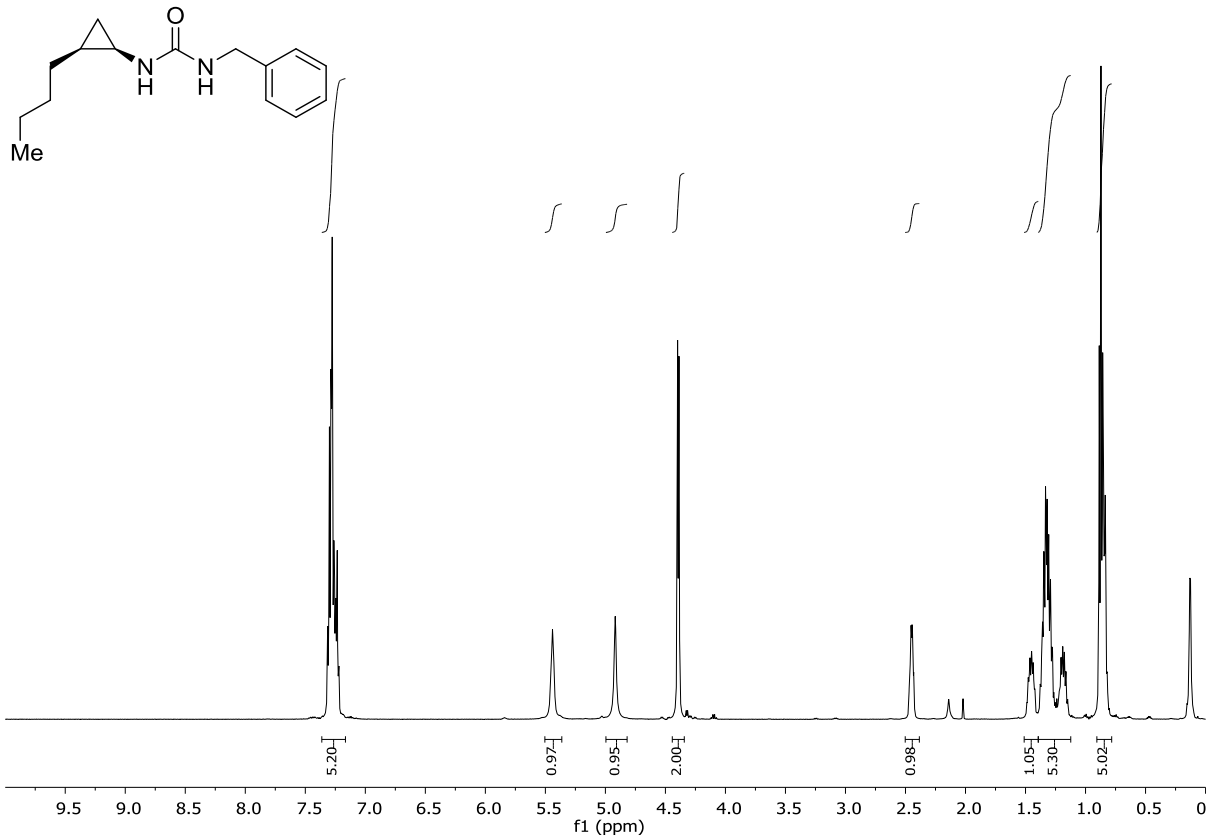

141.12
128.43
128.31
126.91
54.24
34.65
32.63
26.89
22.89
18.41
14.35
12.08
f1 (ppm)

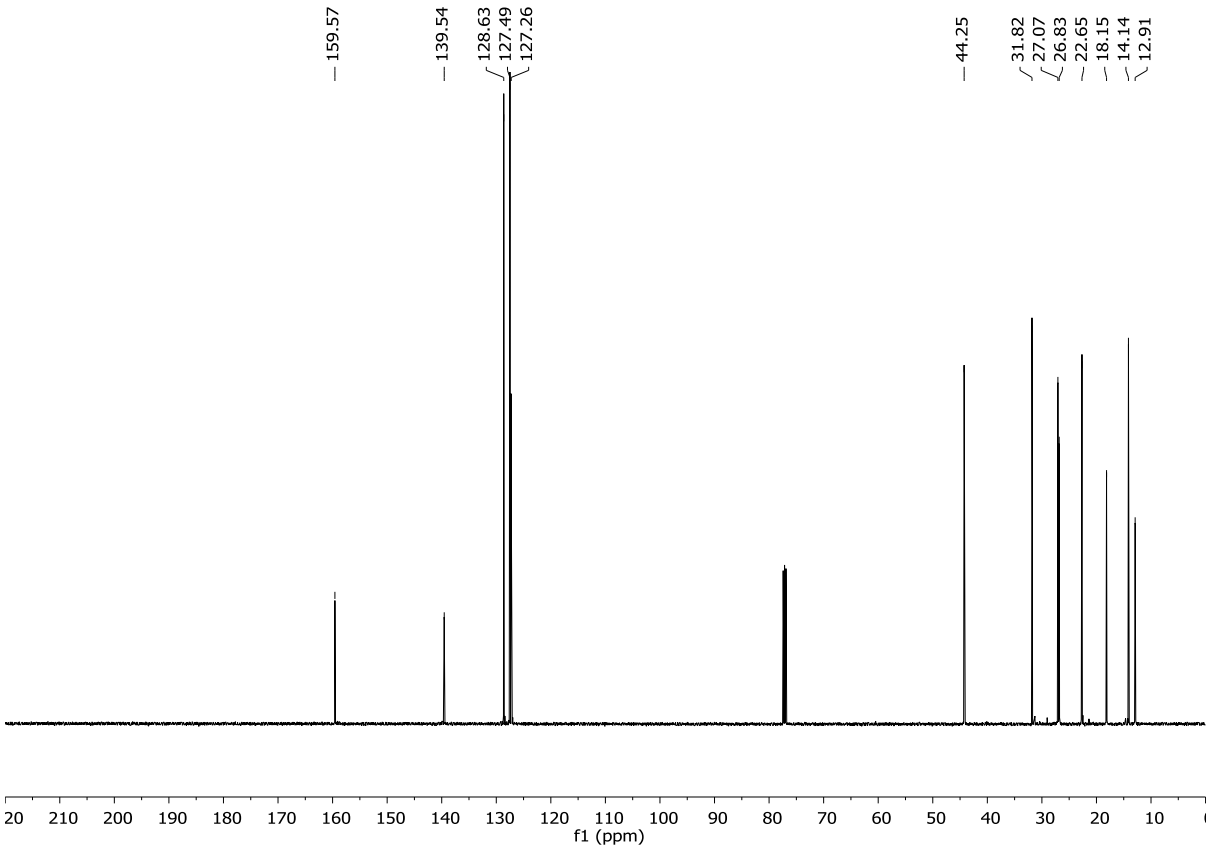

Me
O
N
N
H
11.18
1.00
0.97
2.09
0.97
1.02
1.19
4.51
6.31
1.03
f1 (ppm)

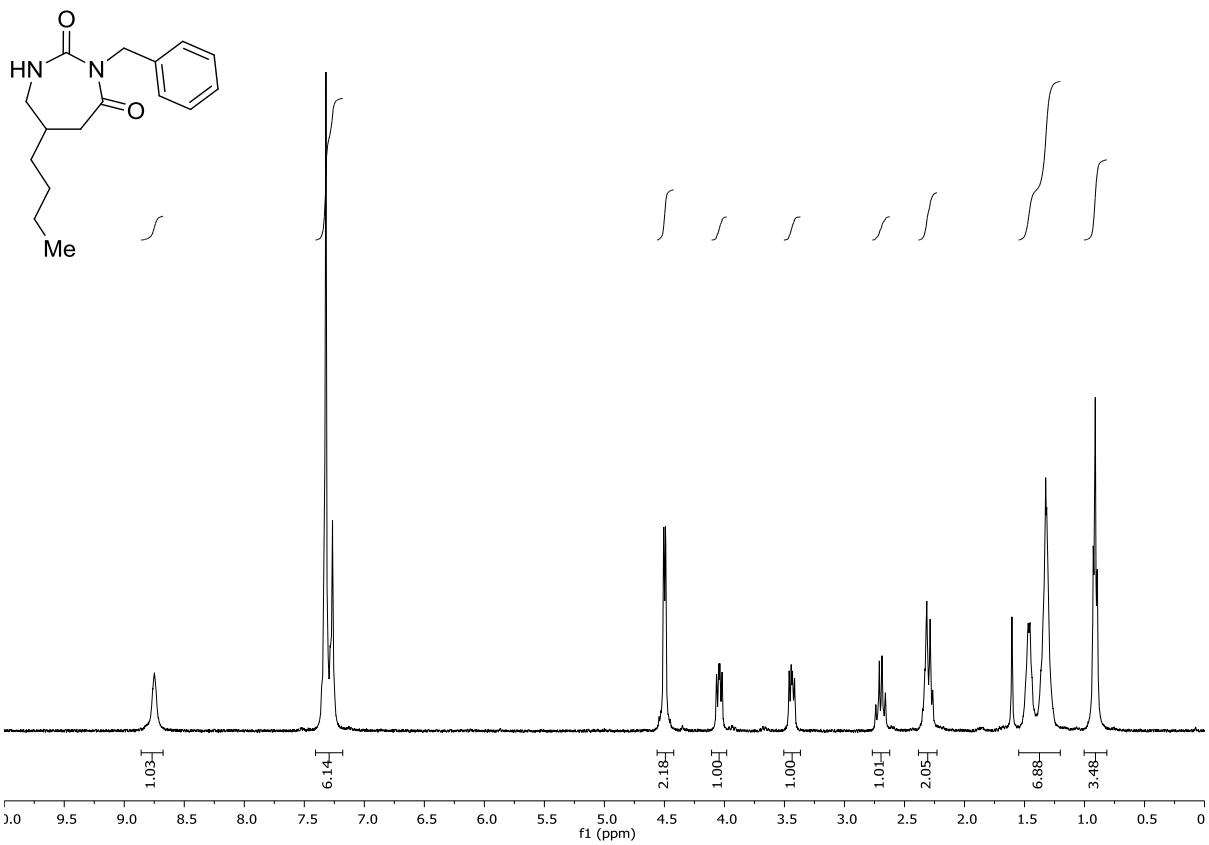

159.62
139.71
139.12
128.71
128.50
128.26
127.84
127.37
127.07
50.73
45.06
32.82
31.84
27.26
22.68
20.85
14.14
12.69
f1 (ppm)

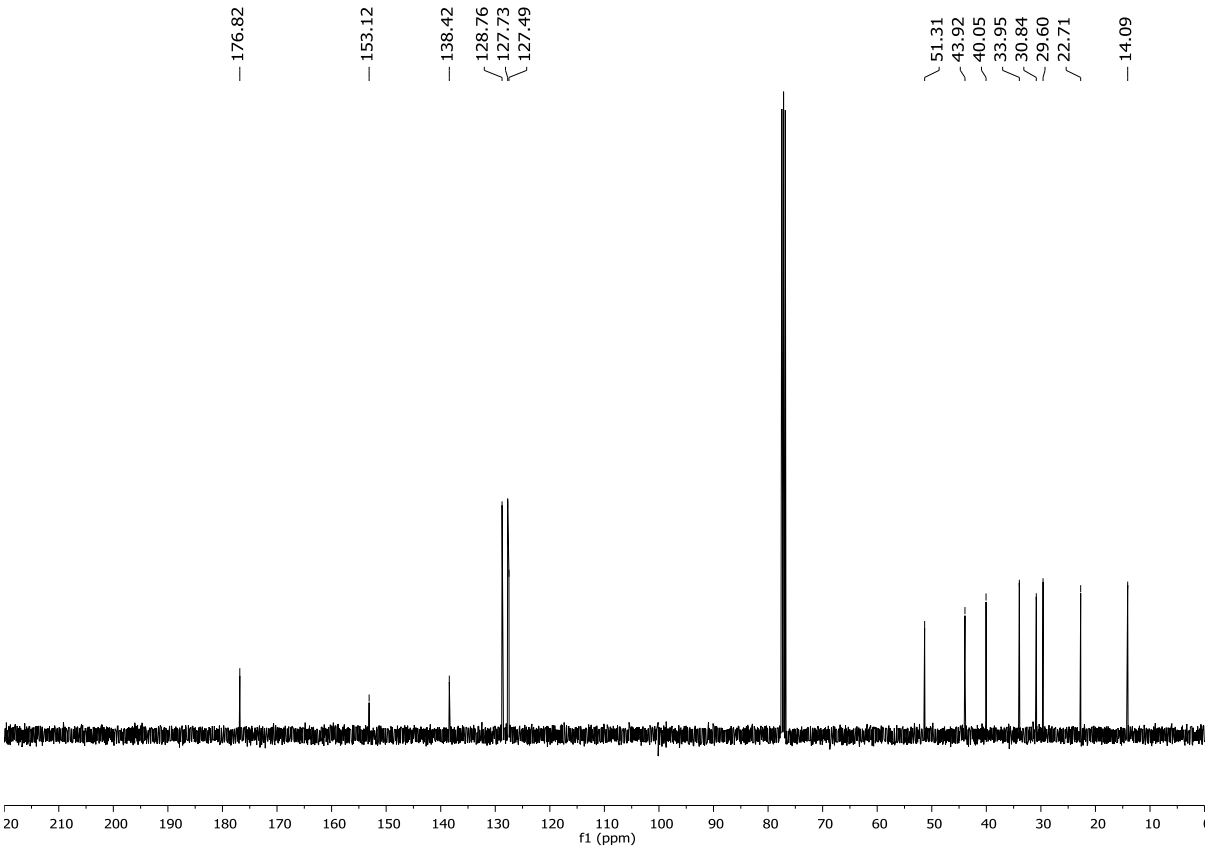

O
N
N
O
Me
9.68
2.15
1.02
2.00
2.03
2.00
2.05
2.08
2.13
3.31
f1 (ppm)

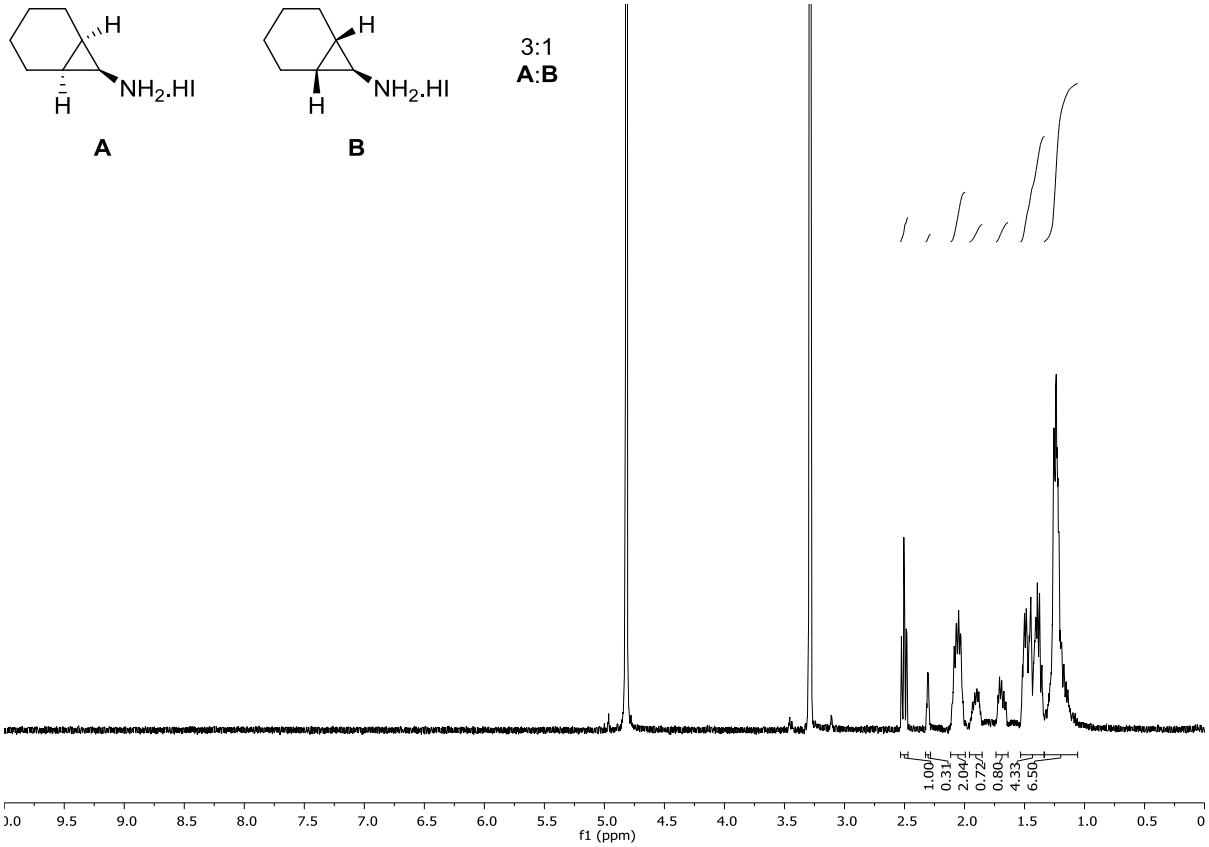

169.82
154.25
137.83
136.48
128.81
128.48
128.28
128.18
127.80
127.77
127.32
124.25
53.12
47.66
39.54
33.81
29.15
22.09
13.85
f1 (ppm)

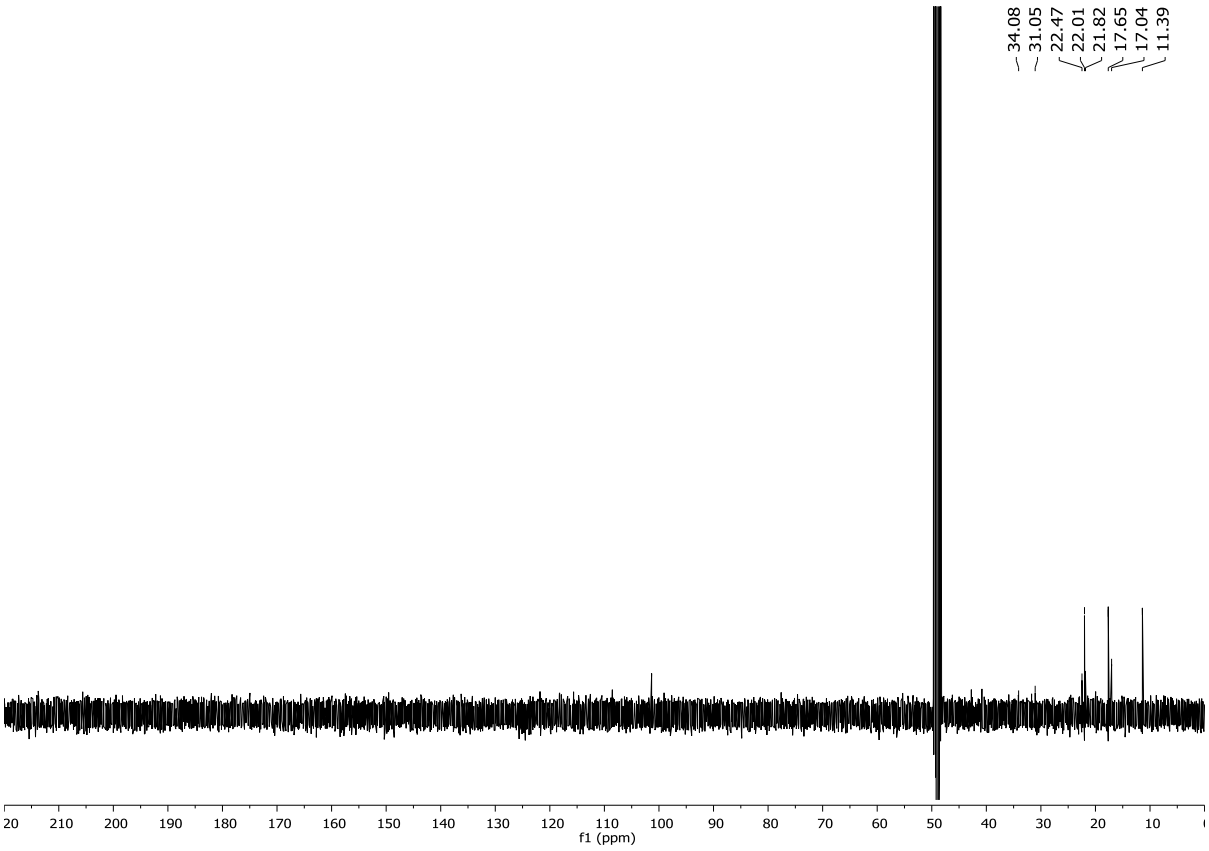

O
N
H
N
H
Me
5.20
0.97
0.95
2.00
0.98
1.05
5.30
5.02
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)

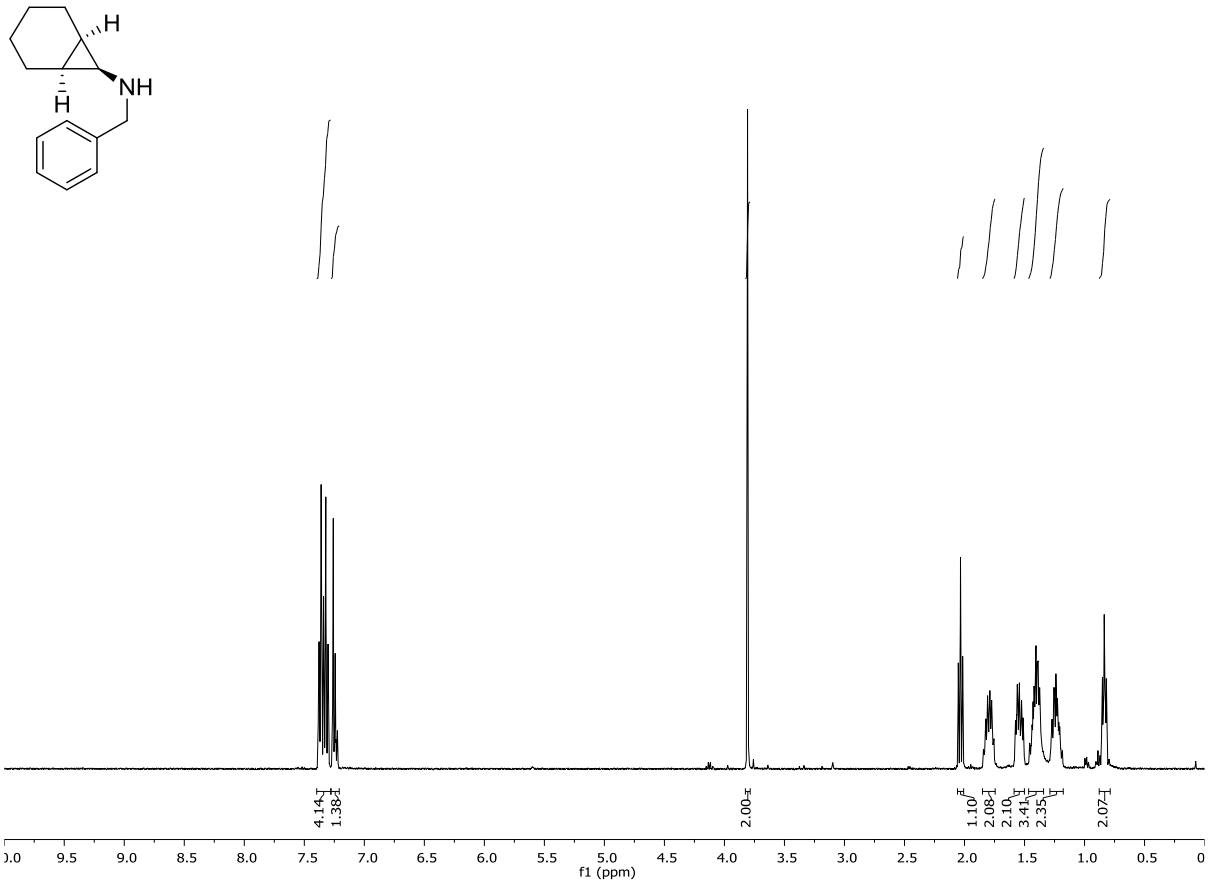

159.57
139.54
128.63
127.49
127.26
44.25
31.82
27.07
26.83
22.65
18.15
14.14
12.91
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

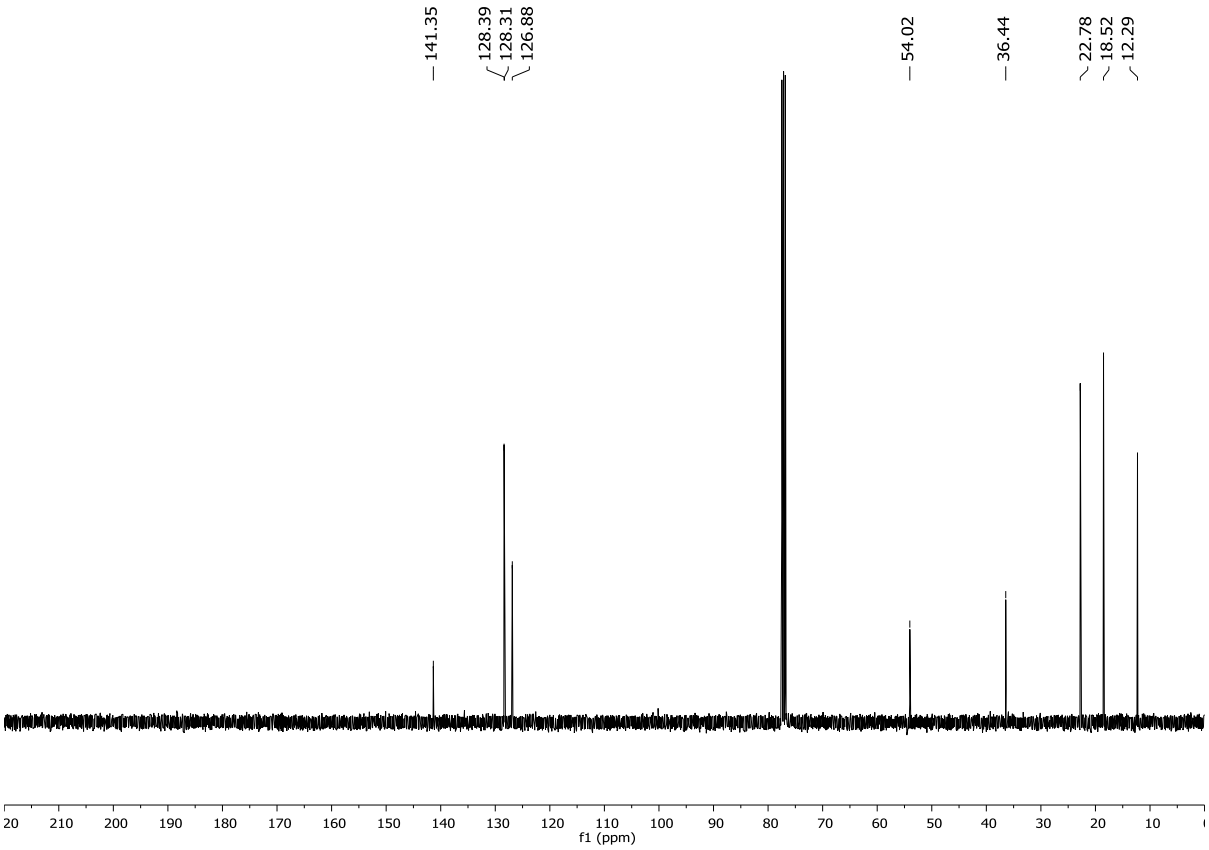

O
HN
N
O
Me
1.03
6.14
2.18
1.00
1.00
1.01
2.05
6.88
3.48
f1 (ppm)

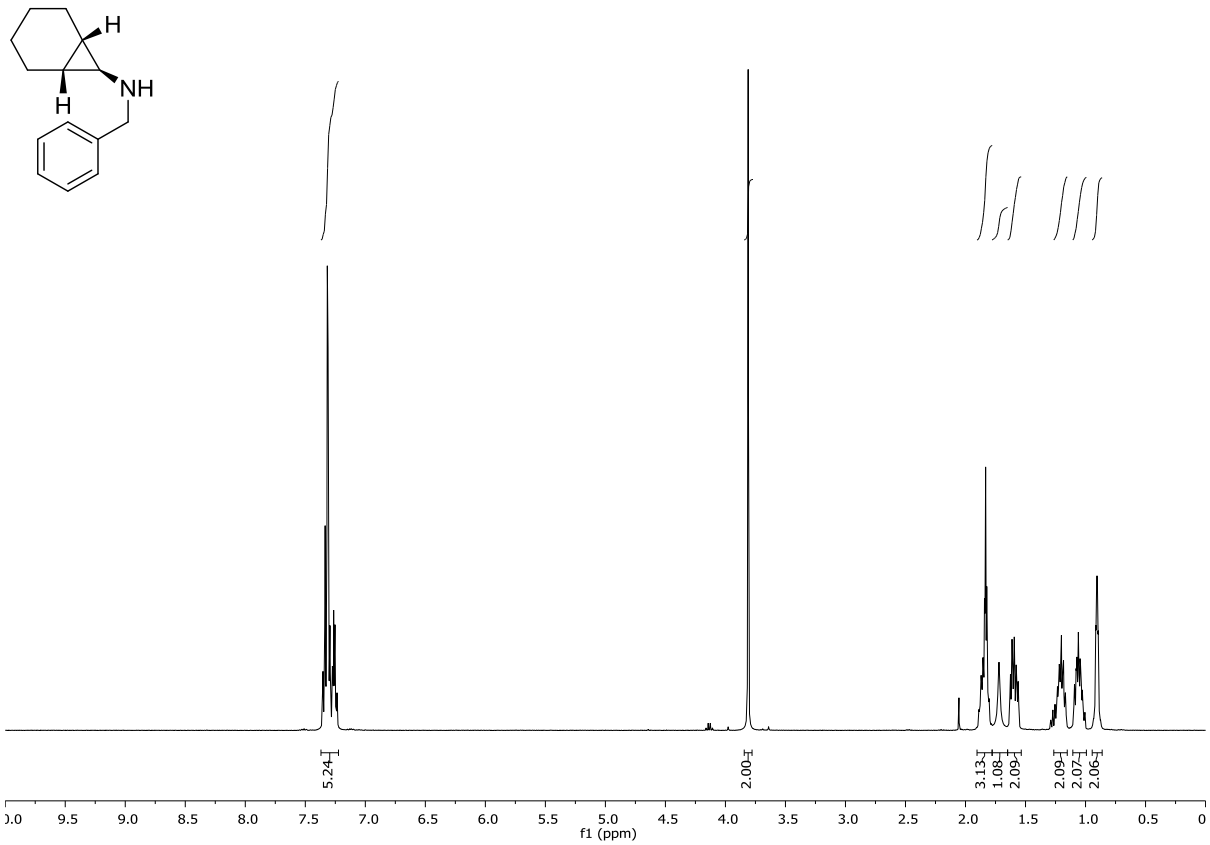

176.82
153.12
138.42
128.76
127.73
127.49
51.31
43.92
40.05
33.95
30.84
29.60
22.71
14.09
f1 (ppm)

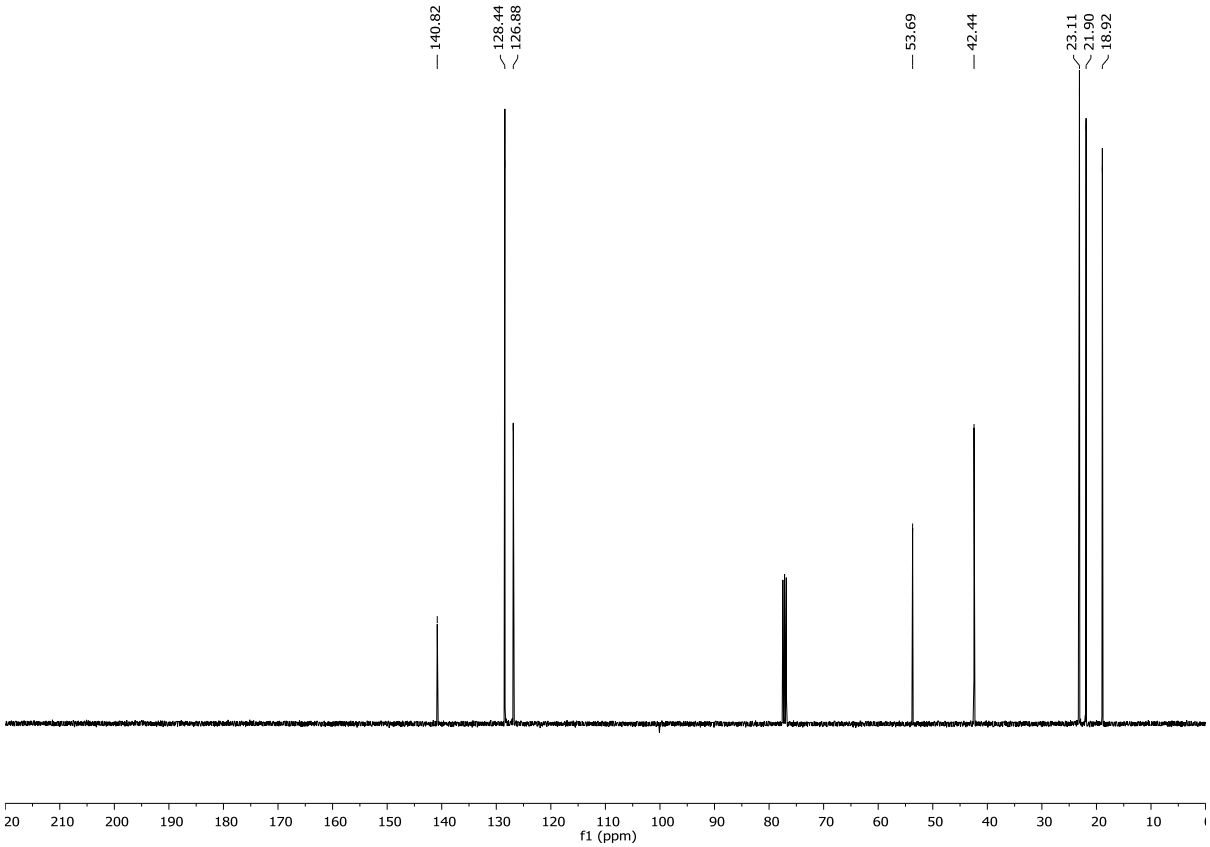

H
NH2.HI
H
A
H
NH2.HI
H
B
3:1
A:B
1.00
0.31
2.04
0.72
0.80
4.33
6.50
f1 (ppm)

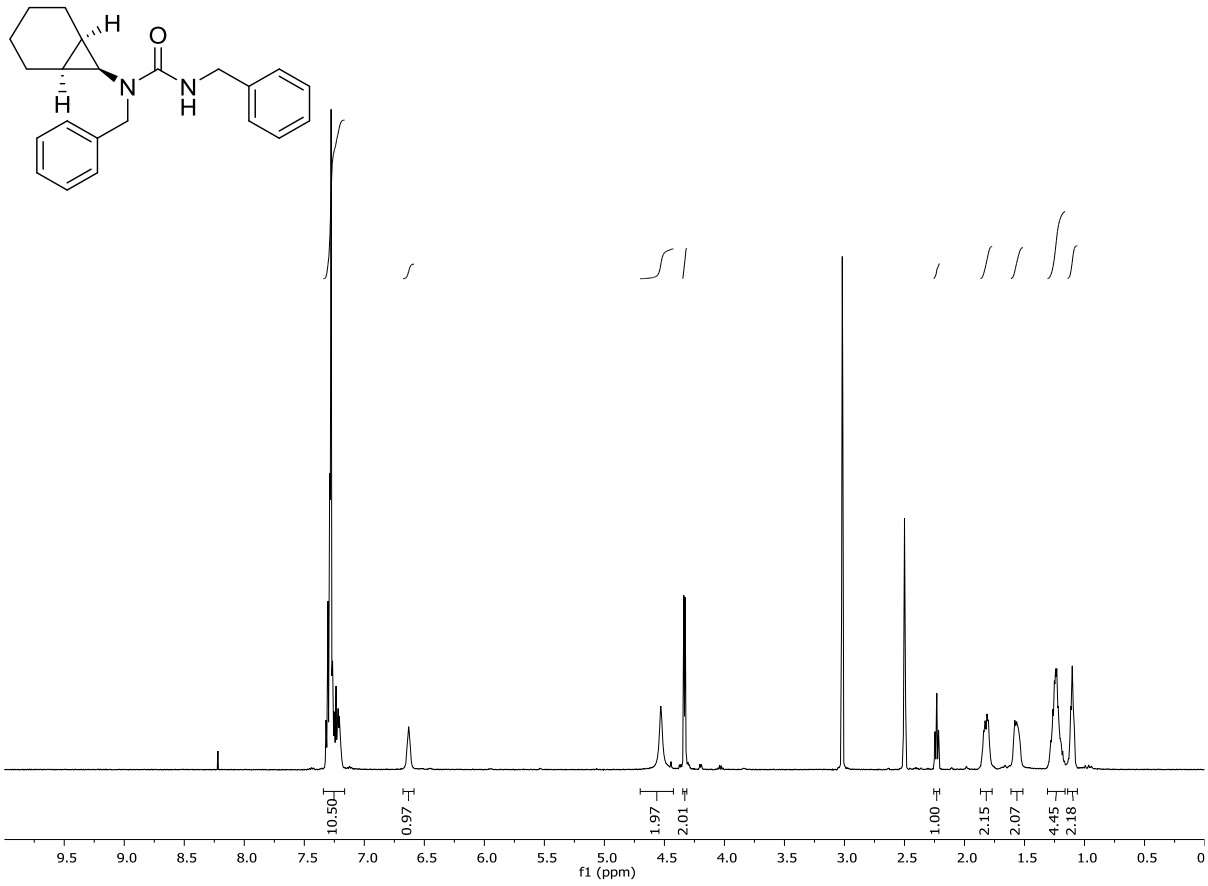

34.08
31.05
22.47
22.01
21.82
17.65
17.04
11.39
f1 (ppm)

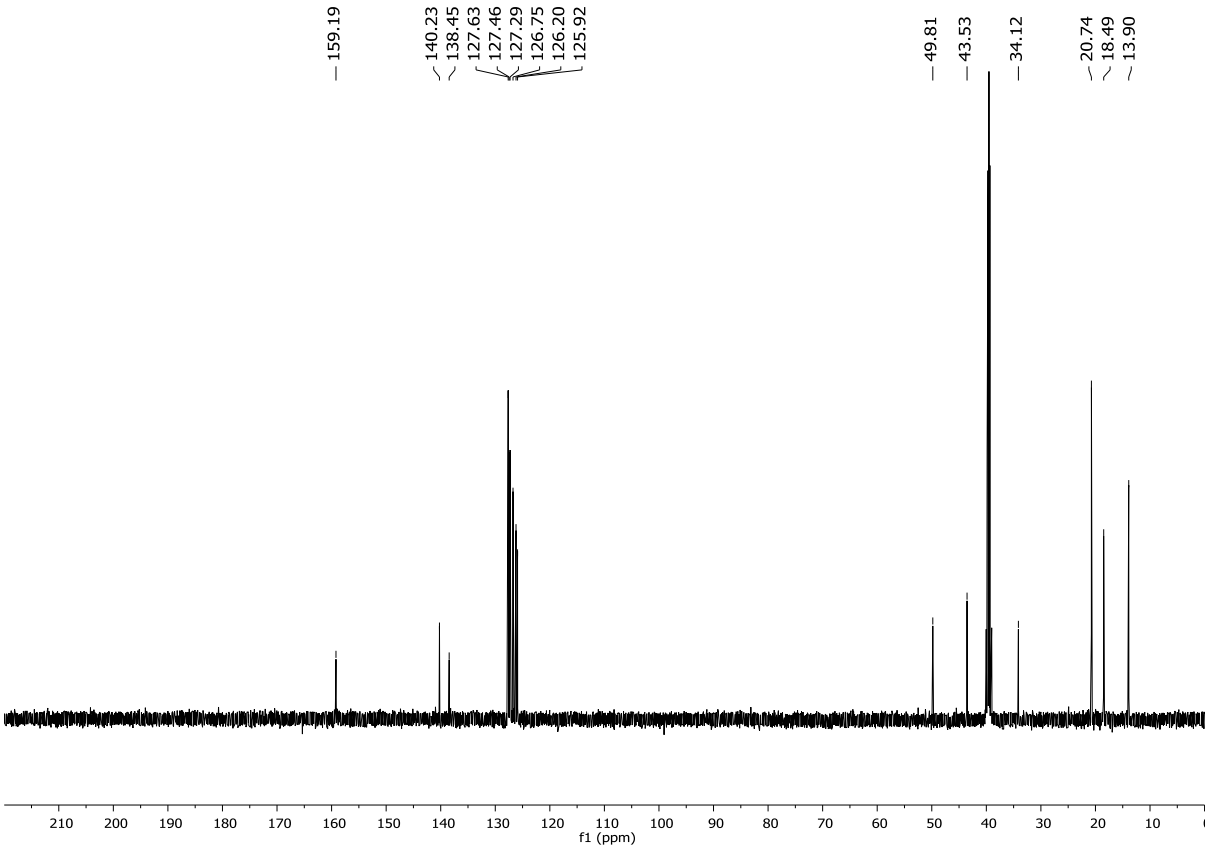

H
NH
H
4.14
1.38
2.00
1.10
2.08
2.10
3.41
2.35
2.07
f1 (ppm)

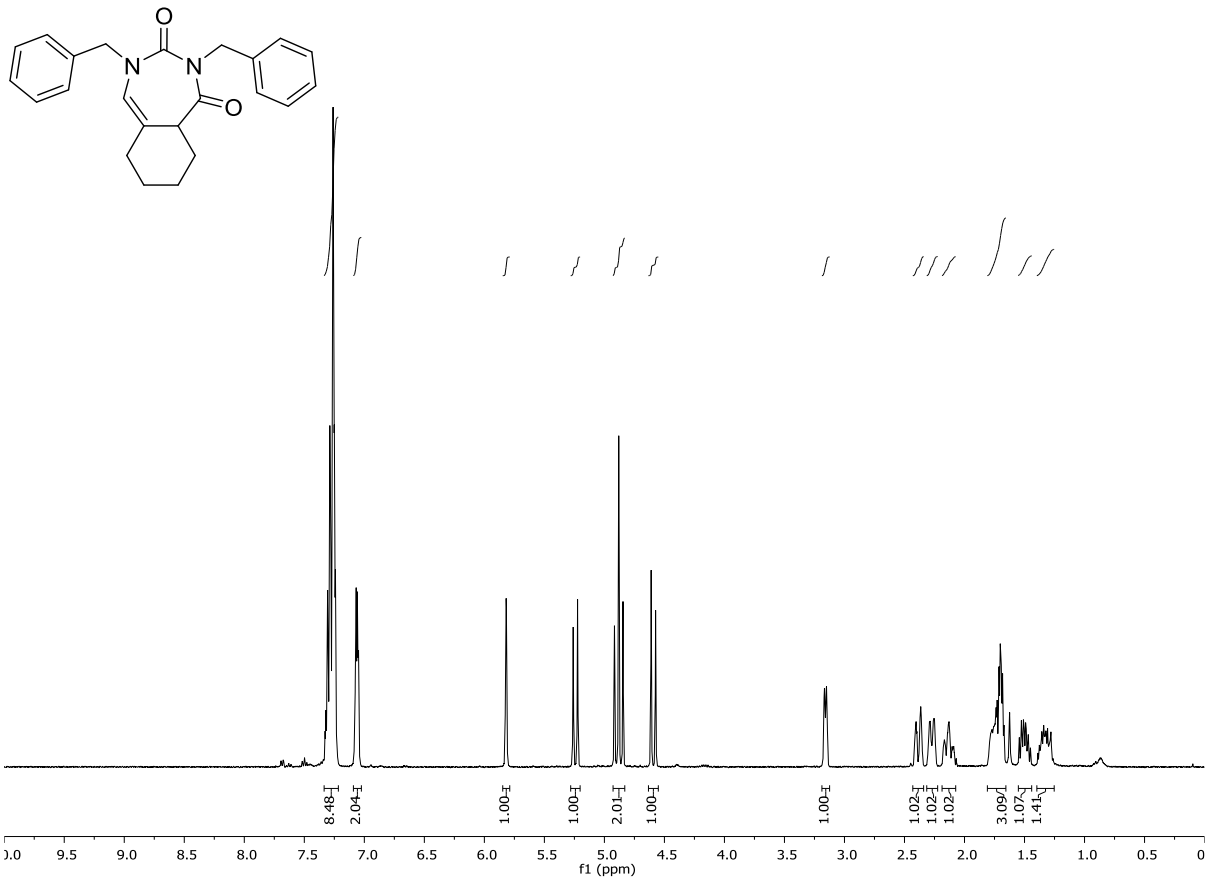

141.35
128.39
128.31
126.88
54.02
36.44
22.78
18.52
12.29
f1 (ppm)

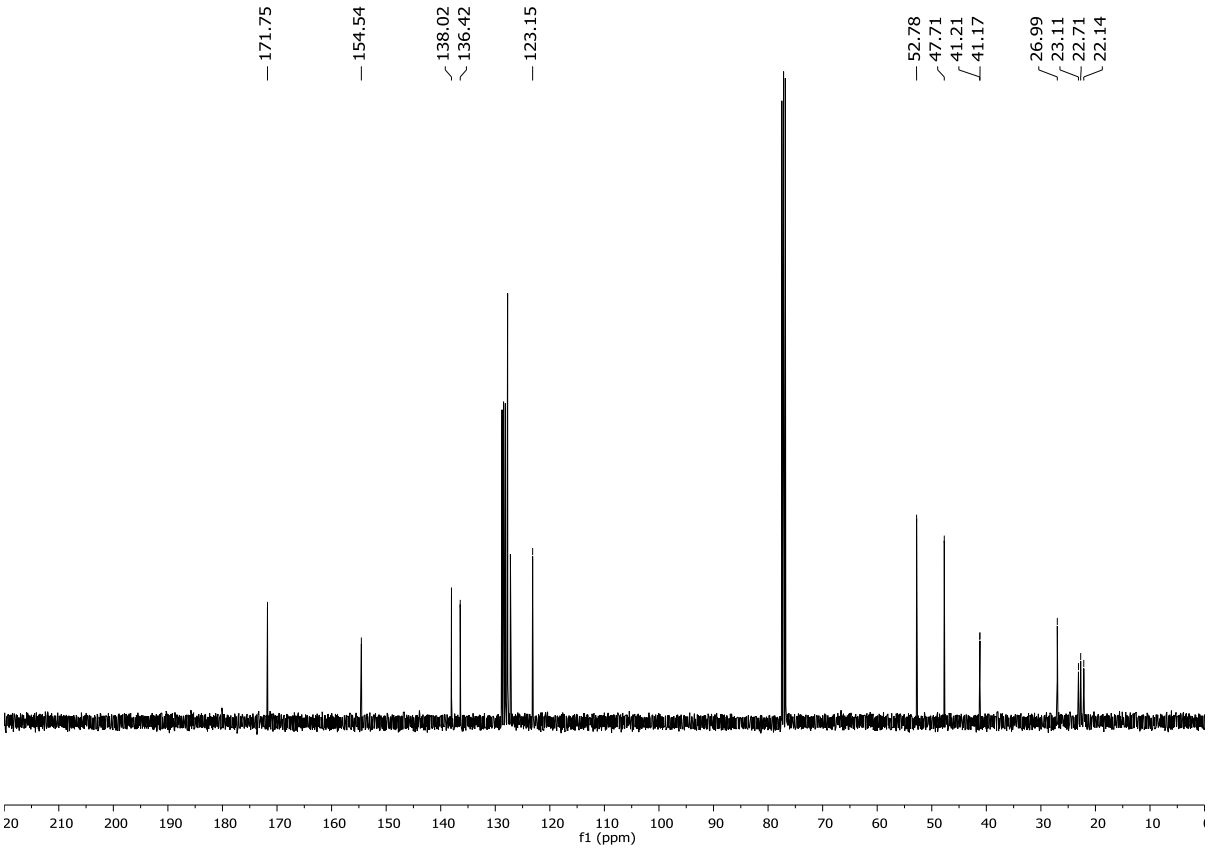

H
NH
H
5.24
2.00
3.13
1.08
2.09
2.09
2.07
2.06
f1 (ppm)

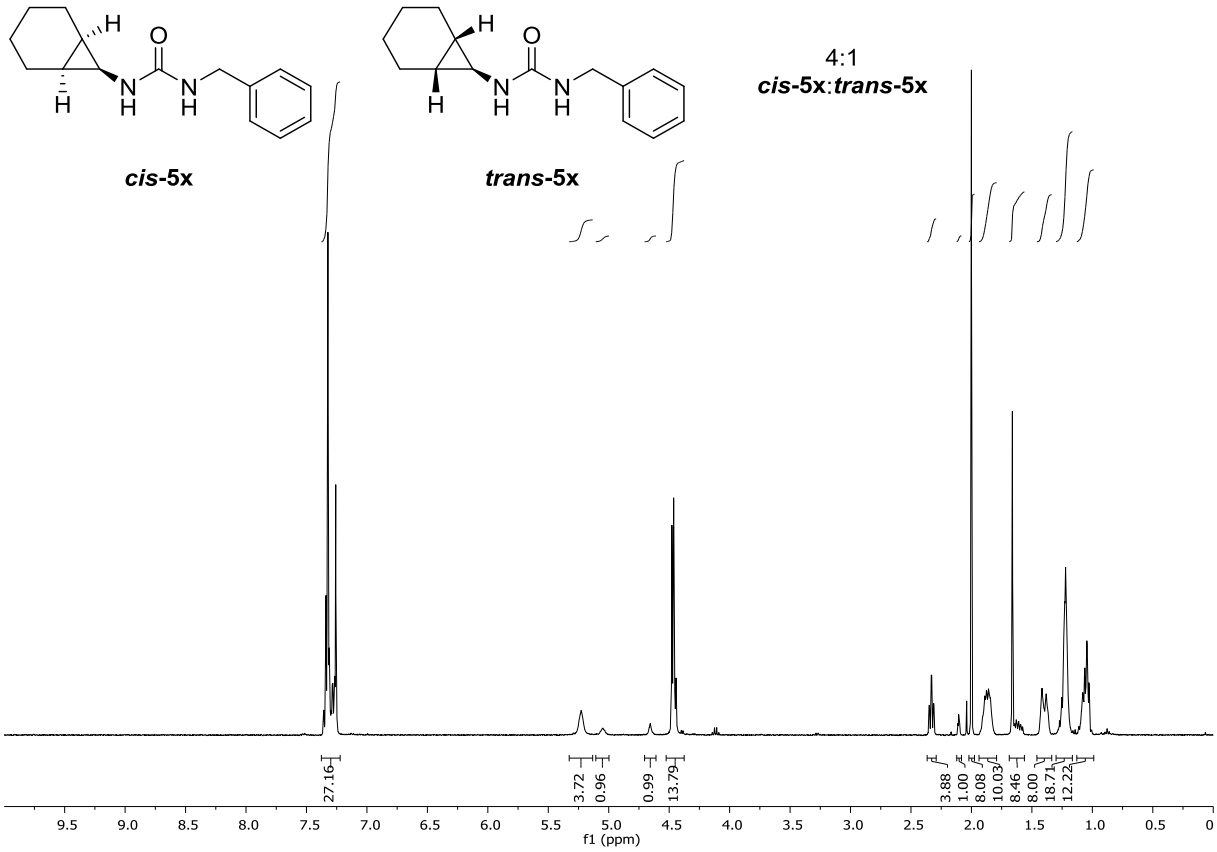

140.82
128.44
126.88
53.69
42.44
23.11
21.90
18.92
f1 (ppm)

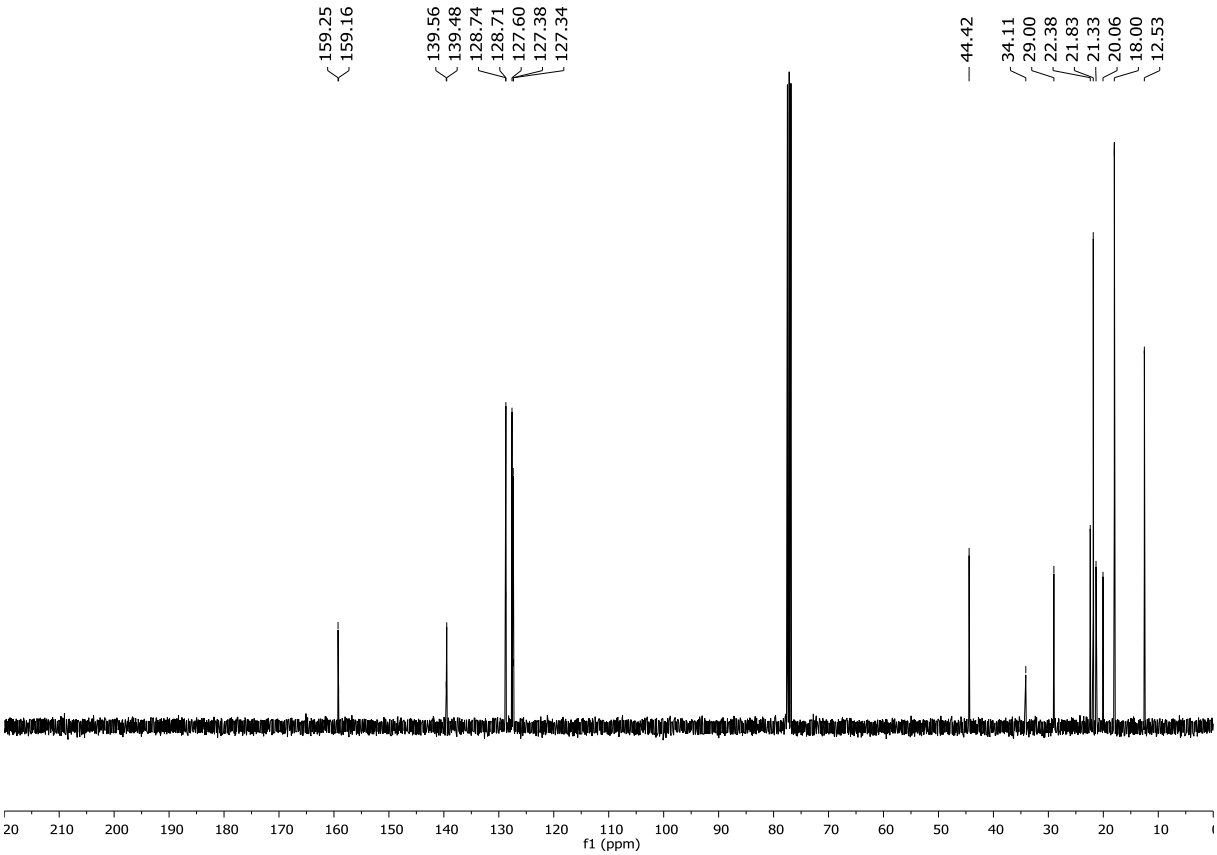

H
O
N
N
H
H
10.50
0.97
1.97
2.01
1.00
2.15
2.07
4.45
2.18
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)

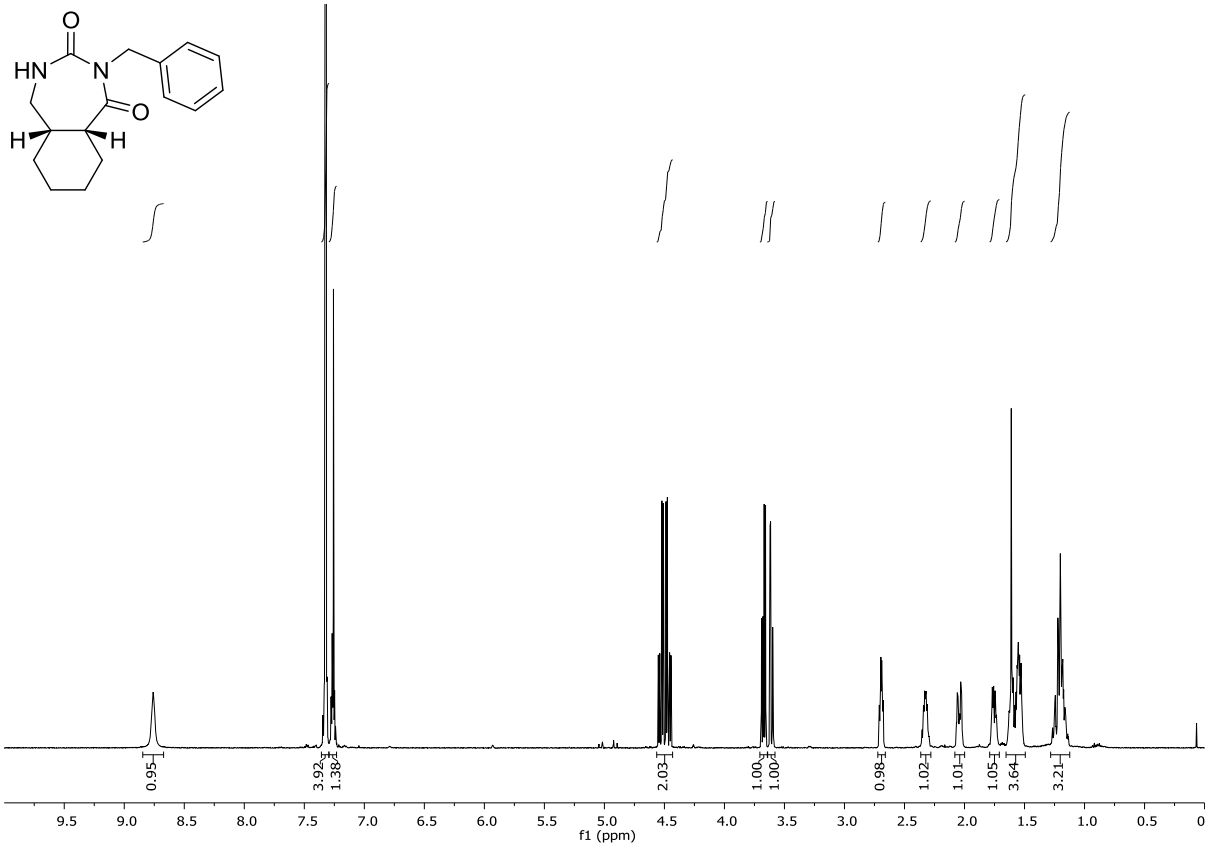

159.19
140.23
138.45
127.63
127.46
127.29
126.75
126.20
125.92
49.81
43.53
34.12
20.74
18.49
13.90
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

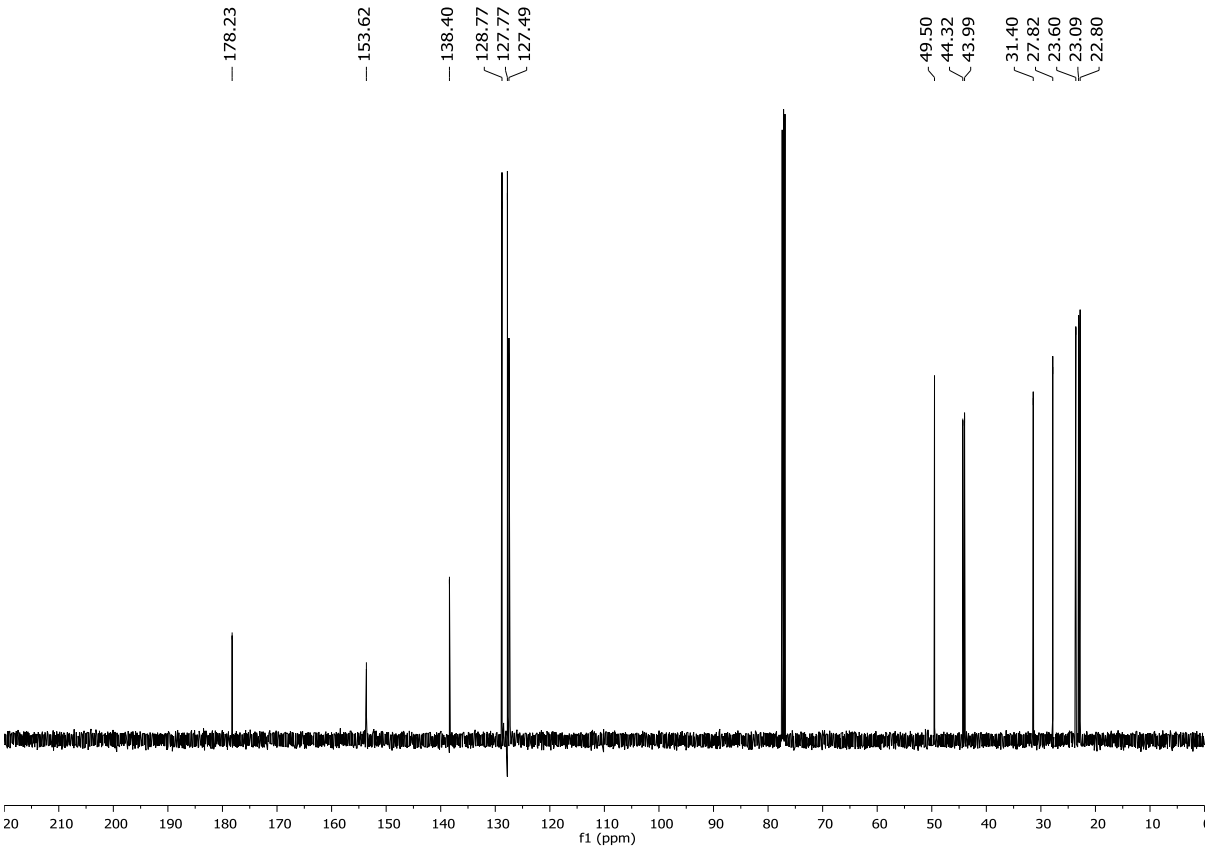

O
N
N
O
8.48
2.04
1.00
1.00
2.01
1.00
1.00
1.02
1.02
1.02
3.09
1.07
1.41
f1 (ppm)

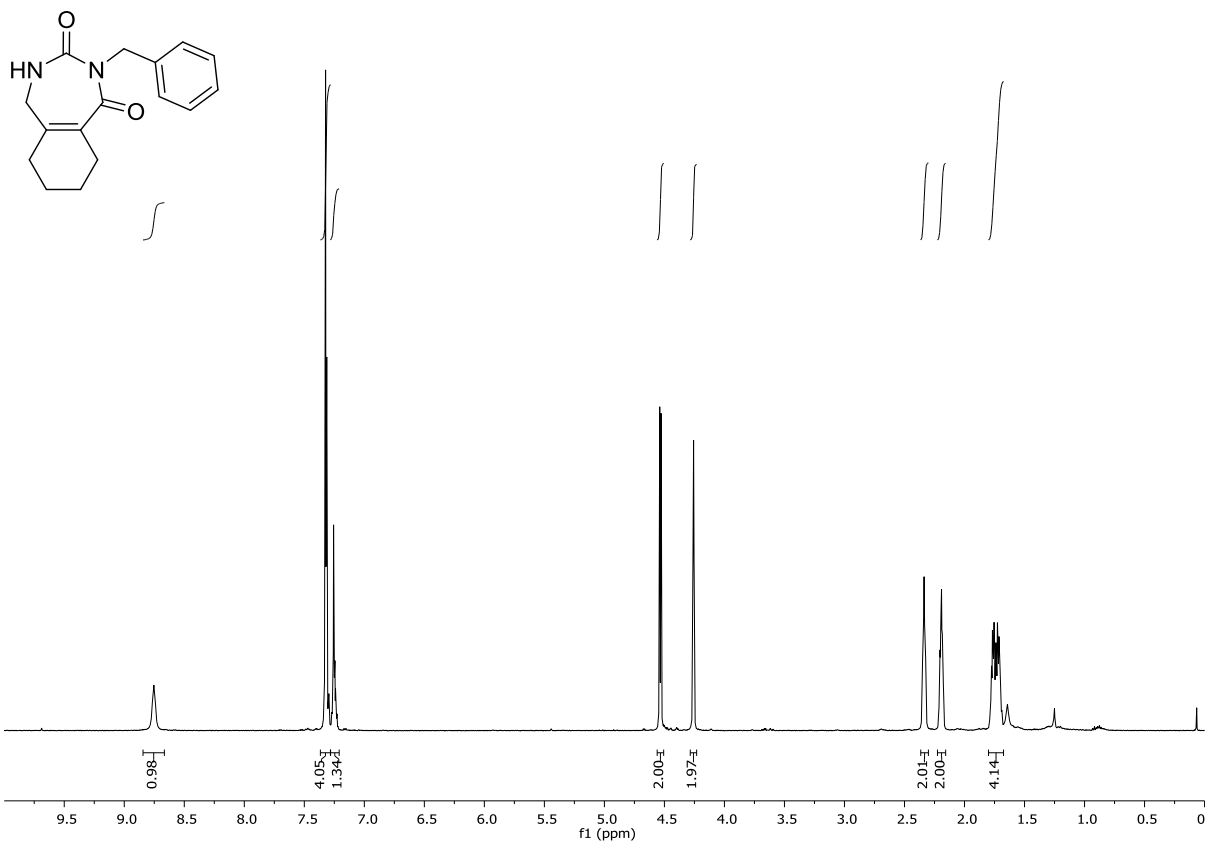

171.75
154.54
138.02
136.42
123.15
52.78
47.71
41.21
41.17
26.99
23.11
22.71
22.14
f1 (ppm)

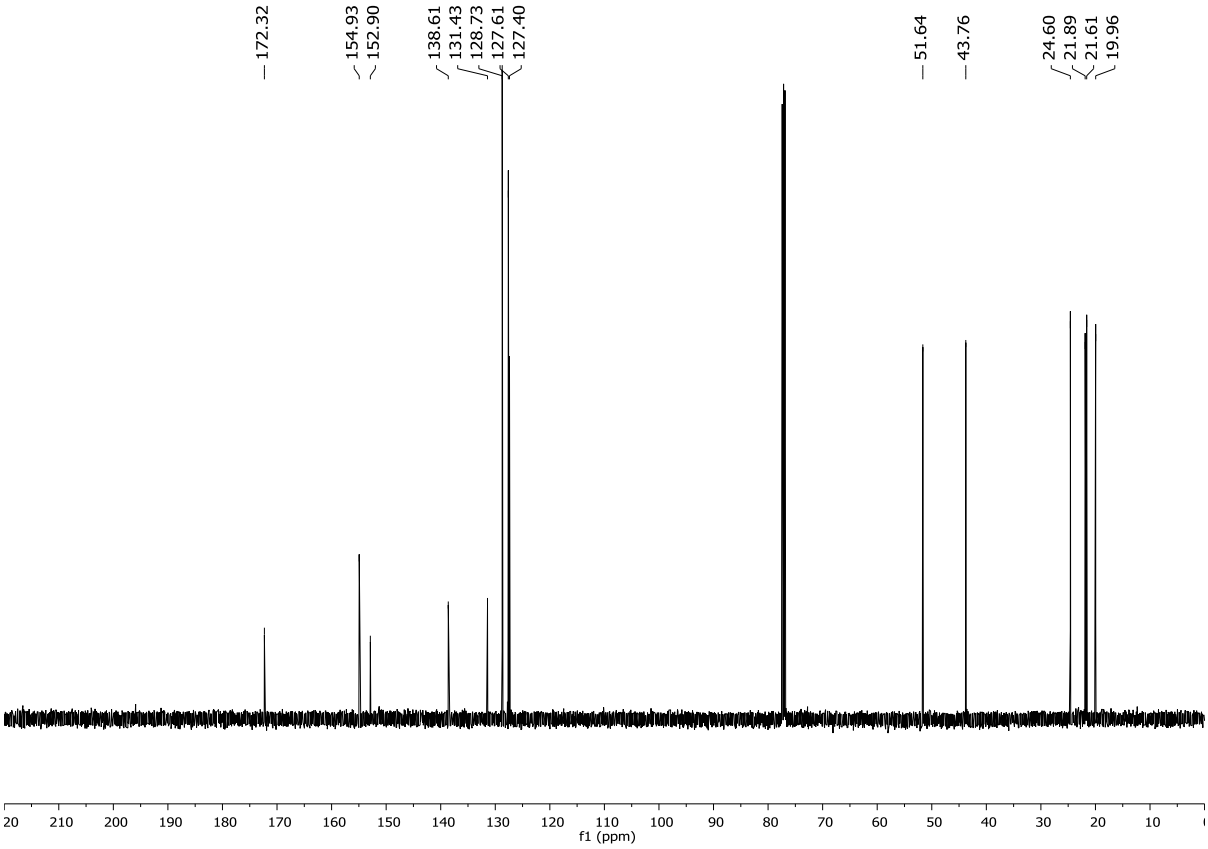

cis-5x
trans-5x
4:1
cis-5x:trans-5x
27.16
3.72
0.96
0.99
13.79
3.88
1.00
8.08
10.03
8.46
8.00
18.71
12.22
f1 (ppm)

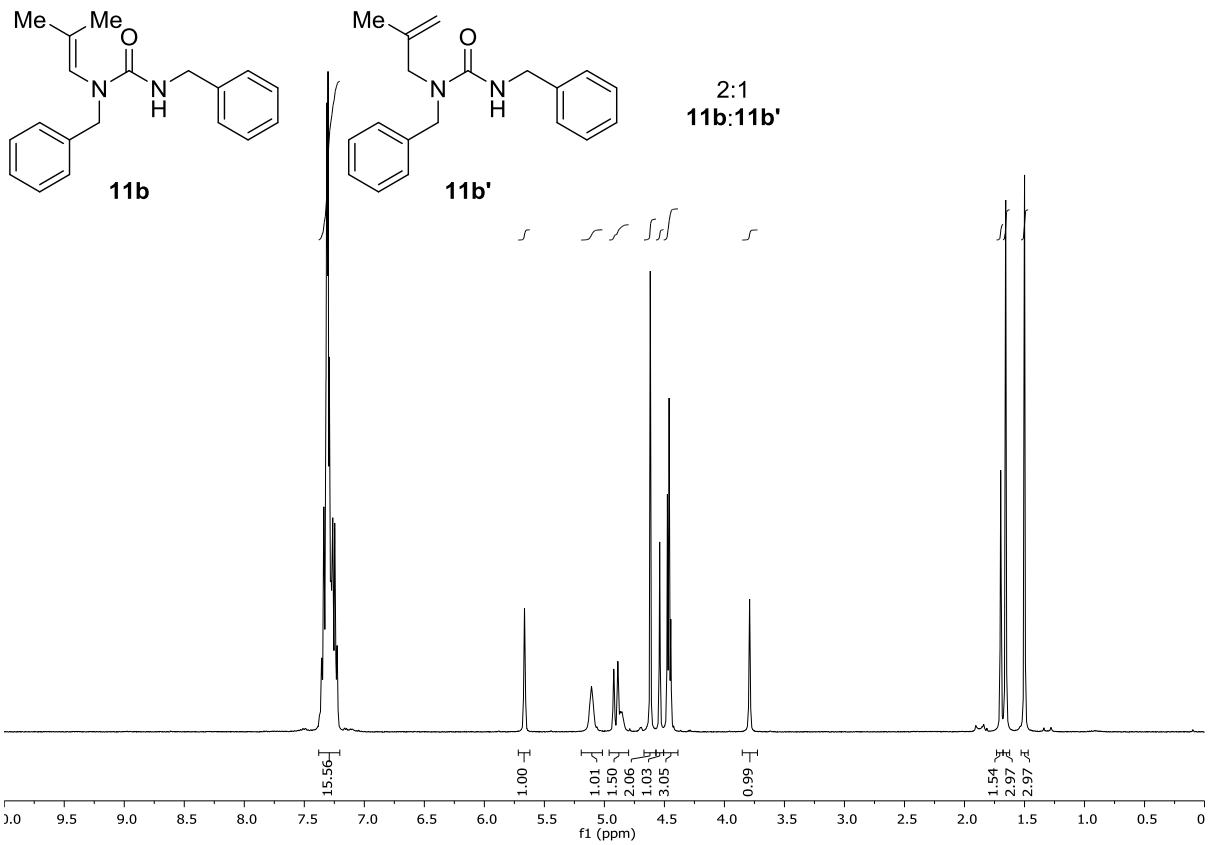

159.25
159.16
139.56
139.48
128.74
128.71
127.60
127.38
127.34
44.42
34.11
29.00
22.38
21.83
21.33
20.06
18.00
12.53
f1 (ppm)

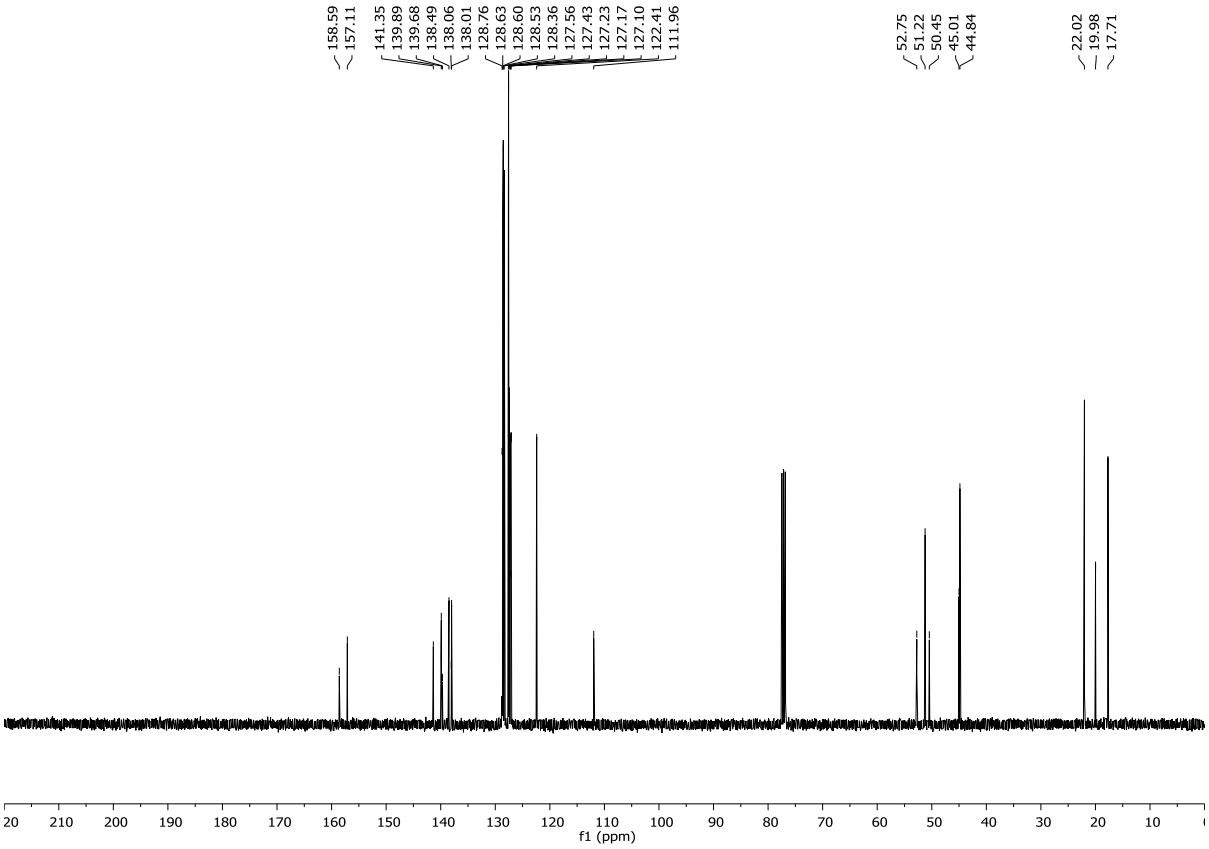

O
HN
N
O
H
H
0.95
3.92
1.38
2.03
1.00
1.00
0.98
1.02
1.01
1.05
3.64
3.21
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)

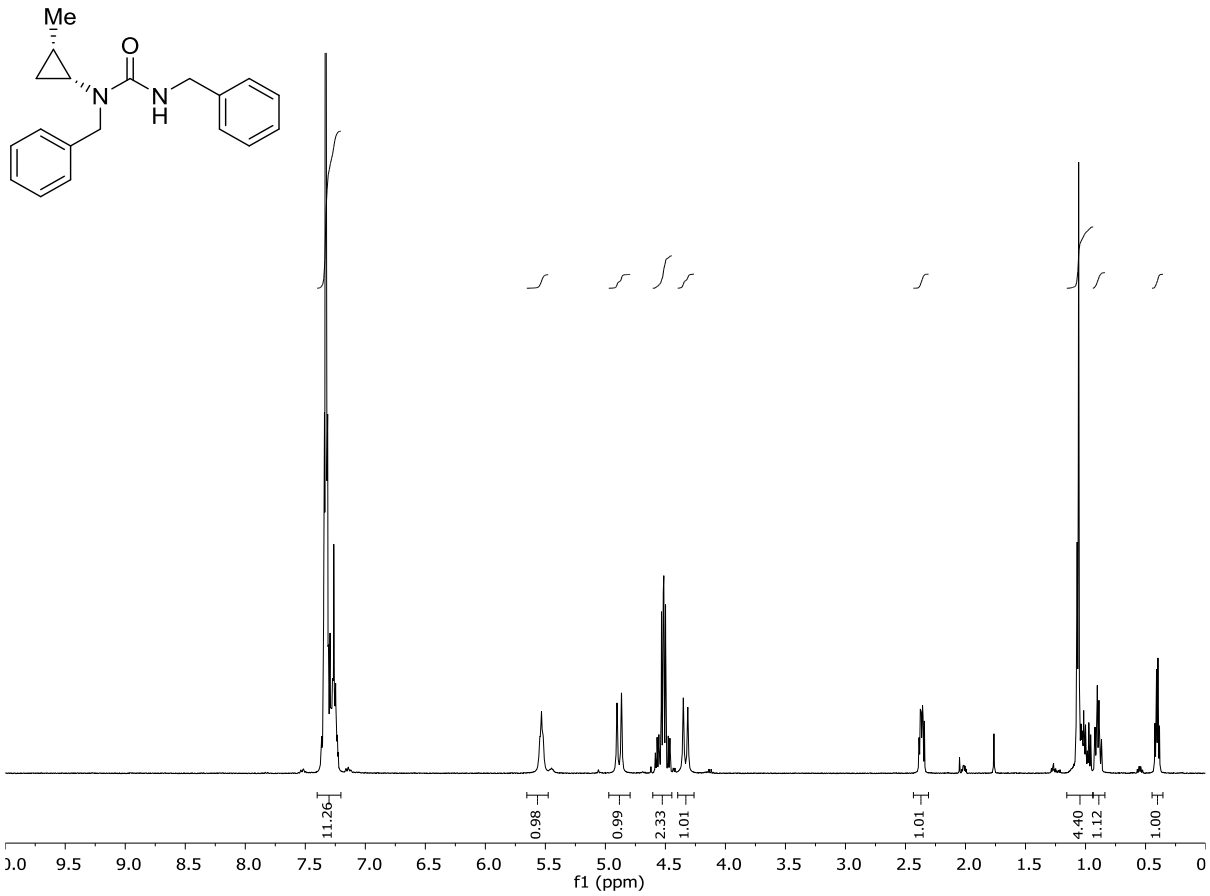

178.23
153.62
138.40
128.77
127.77
127.49
49.50
44.32
43.99
31.40
27.82
23.60
23.09
22.80
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

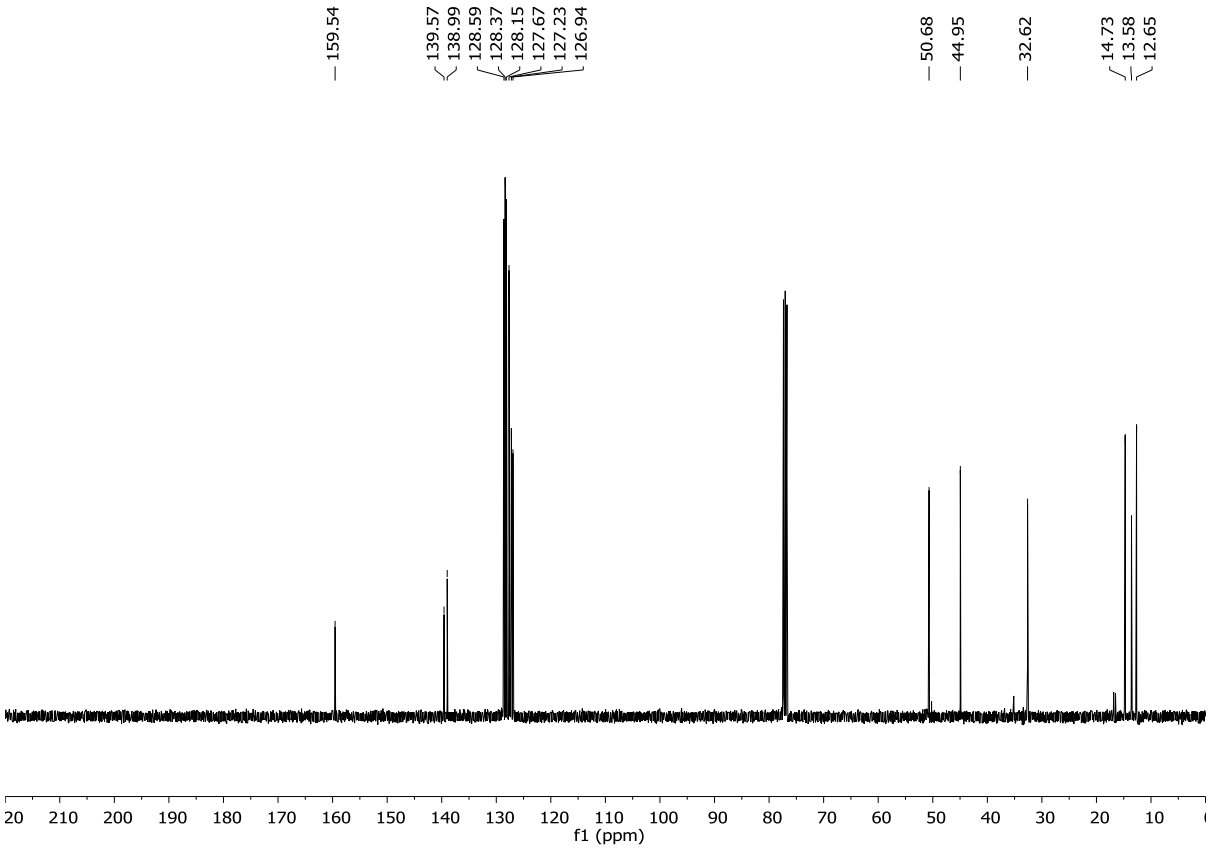

O
HN
N
O
0.98
4.05
1.34
2.00
1.97
2.01
2.00
4.14
f1 (ppm)

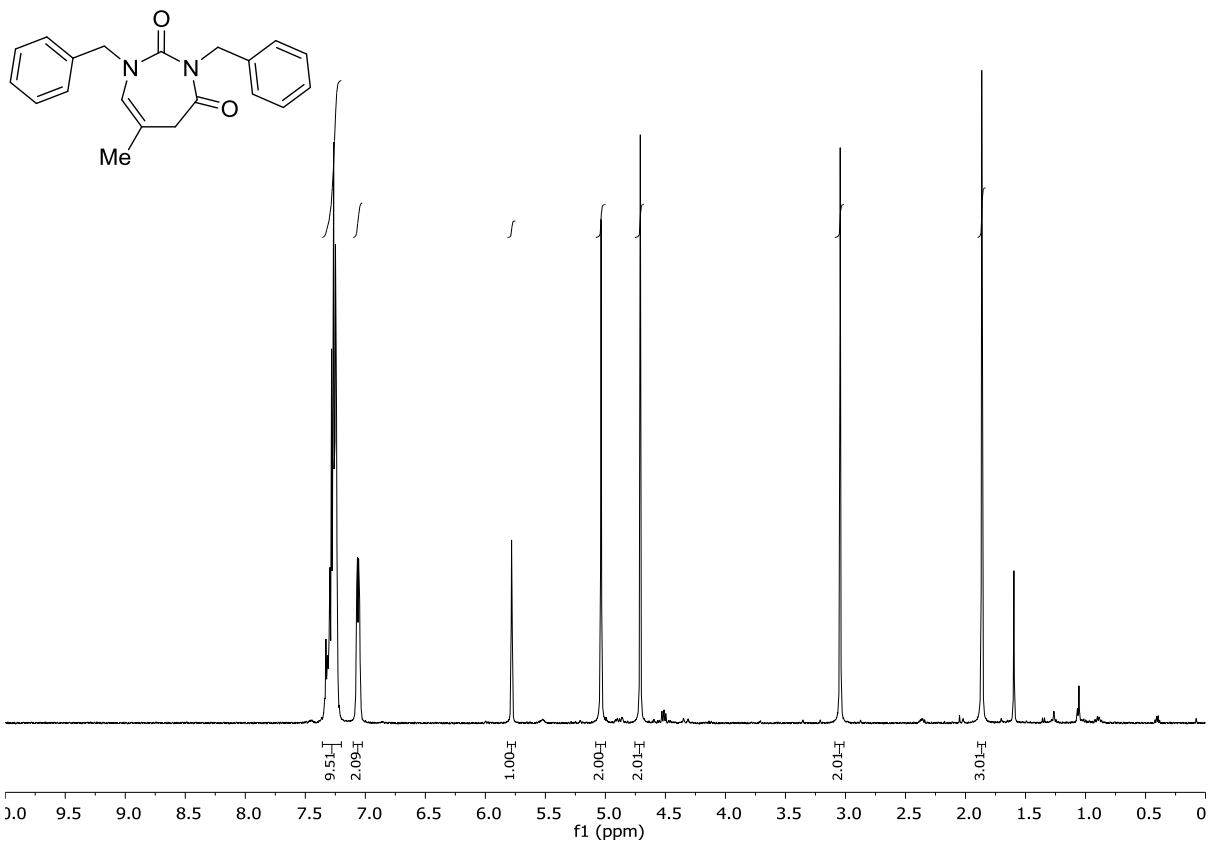

172.32
154.93
152.90
138.61
131.43
128.73
127.61
127.40
51.64
43.76
24.60
21.89
21.61
19.96
f1 (ppm)

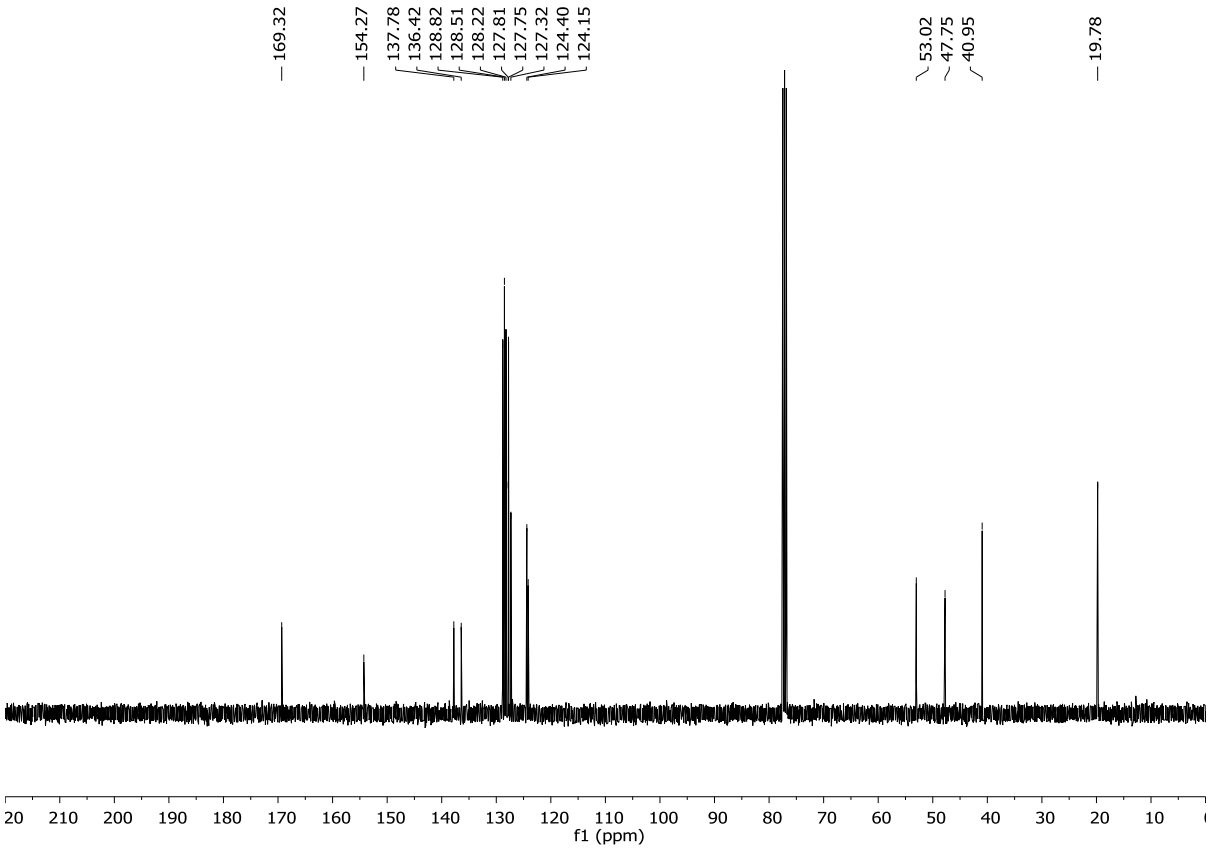

Me
Me
O
N
N
H
11b
Me
O
N
N
H
11b'
2:1
11b:11b'
15.56
1.00
1.01
1.50
2.06
1.03
3.05
0.99
1.54
2.97
2.97
f1 (ppm)

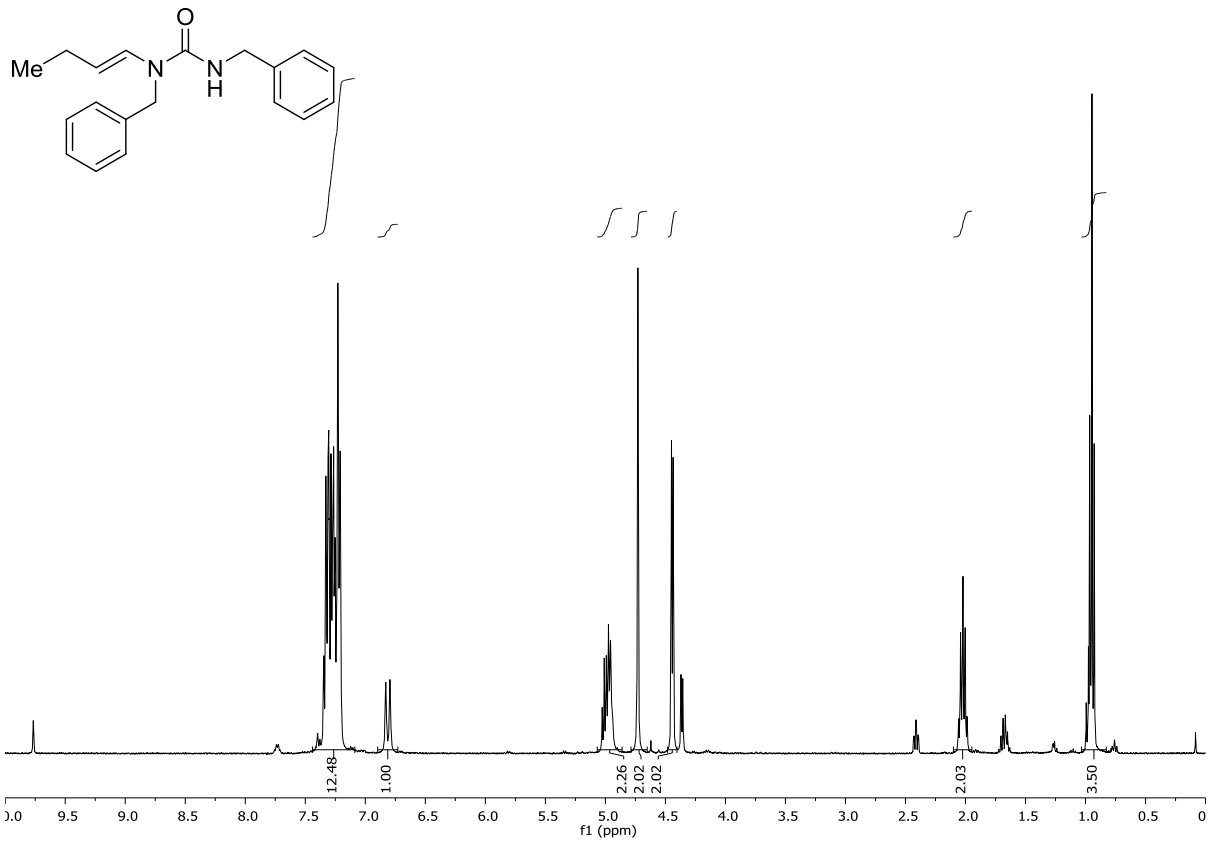

158.59
157.11
141.35
139.89
139.68
138.49
138.06
138.01
128.76
128.63
128.60
128.53
128.36
127.56
127.43
127.23
127.17
127.10
122.41
111.96
52.75
51.22
50.45
45.01
44.84
22.02
19.98
17.71
f1 (ppm)

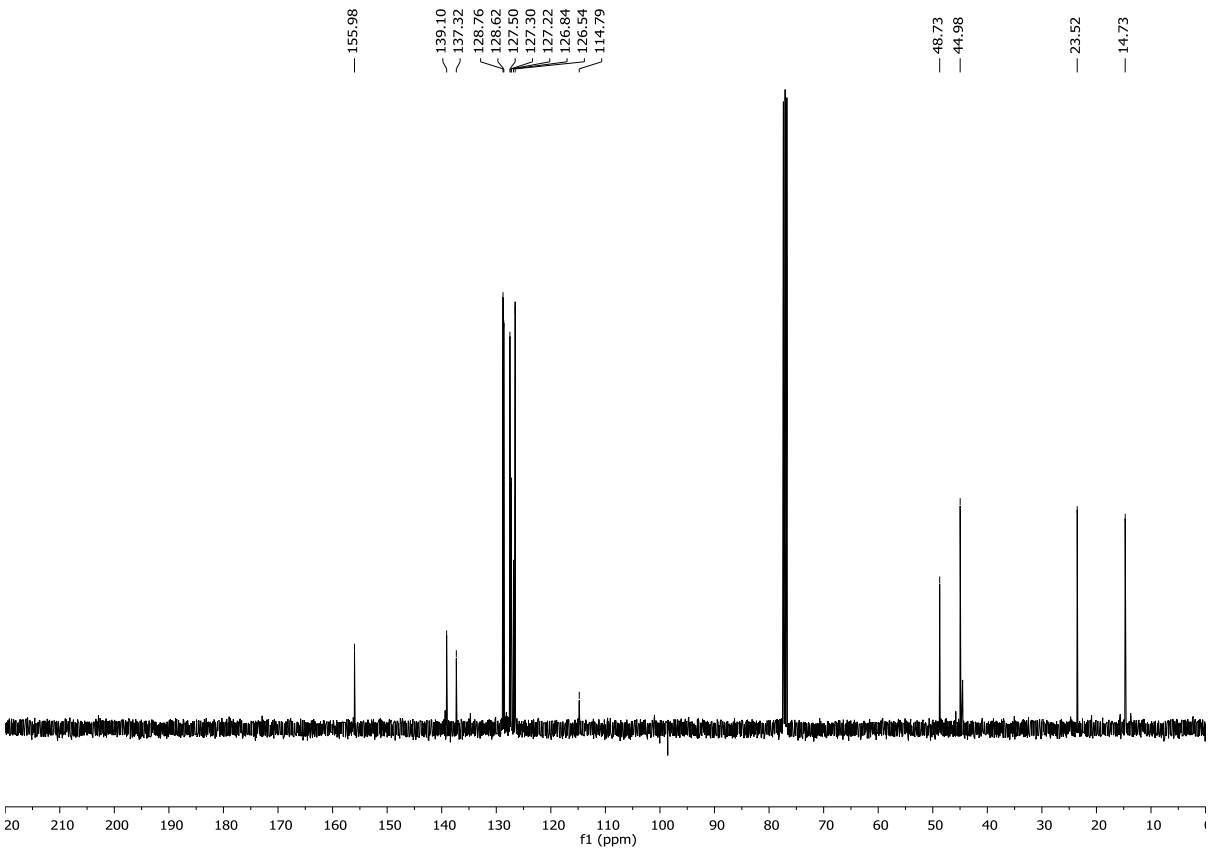

Me
O
N
N
H
11.26
0.98
0.99
2.33
1.01
1.01
4.40
1.12
1.00
f1 (ppm)

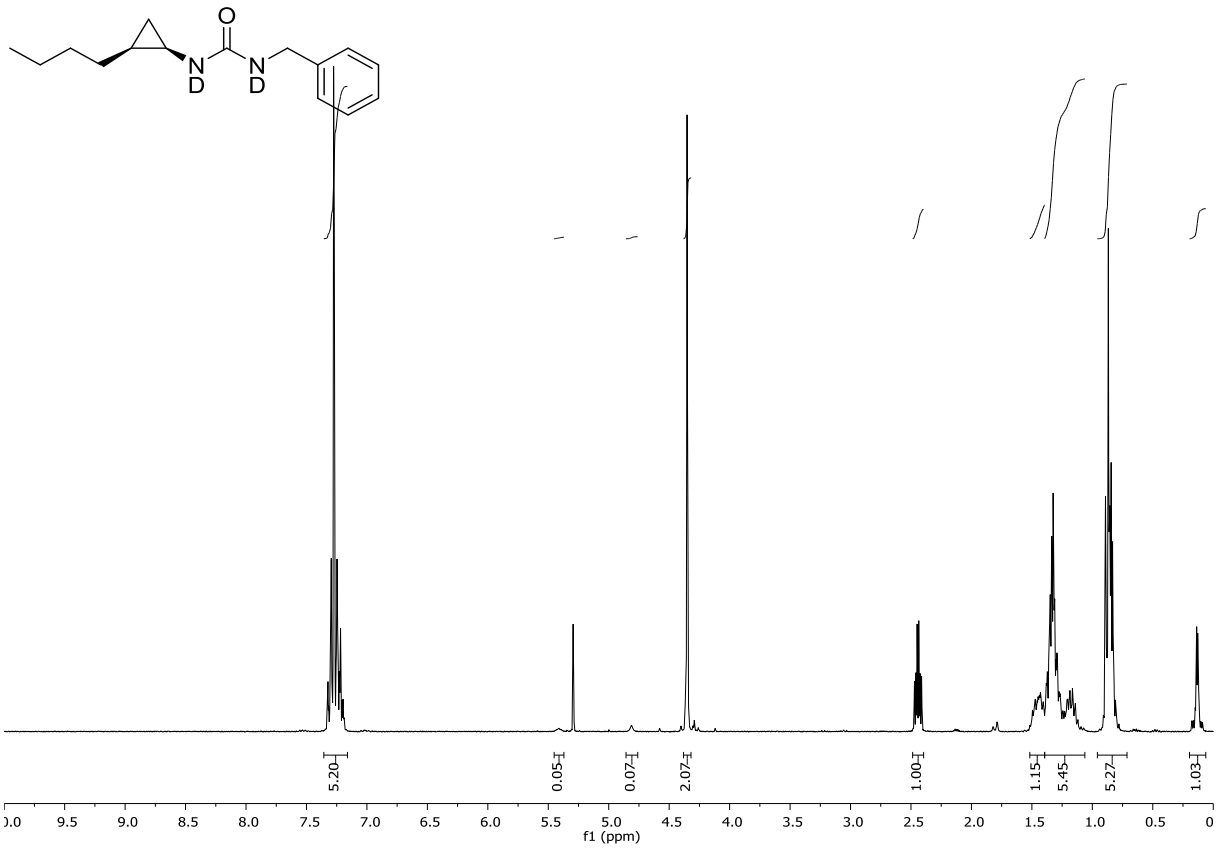

159.54
139.57
138.99
128.59
128.37
128.15
127.67
127.23
126.94
50.68
44.95
32.62
14.73
13.58
12.65
f1 (ppm)

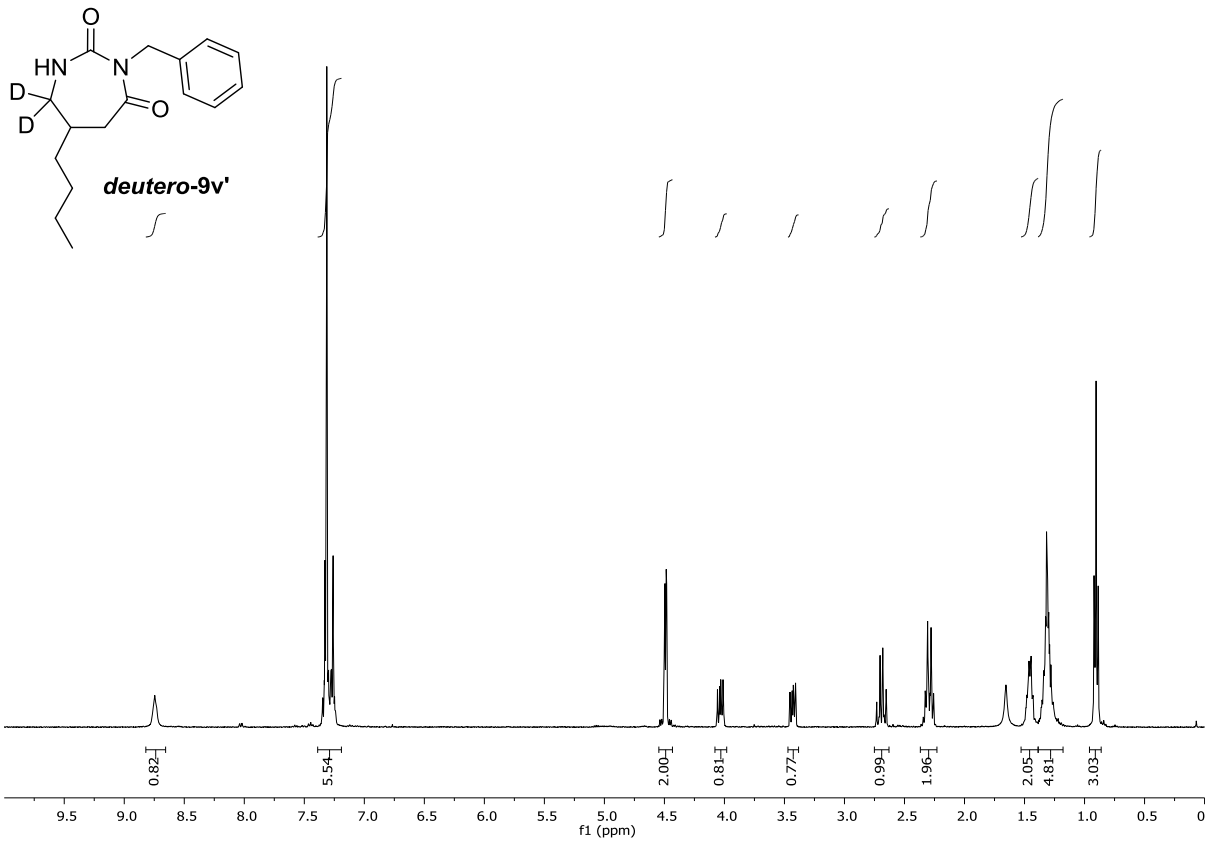

O
N
N
O
Me
9.51
2.09
1.00
2.00
2.01
2.01
3.01
f1 (ppm)

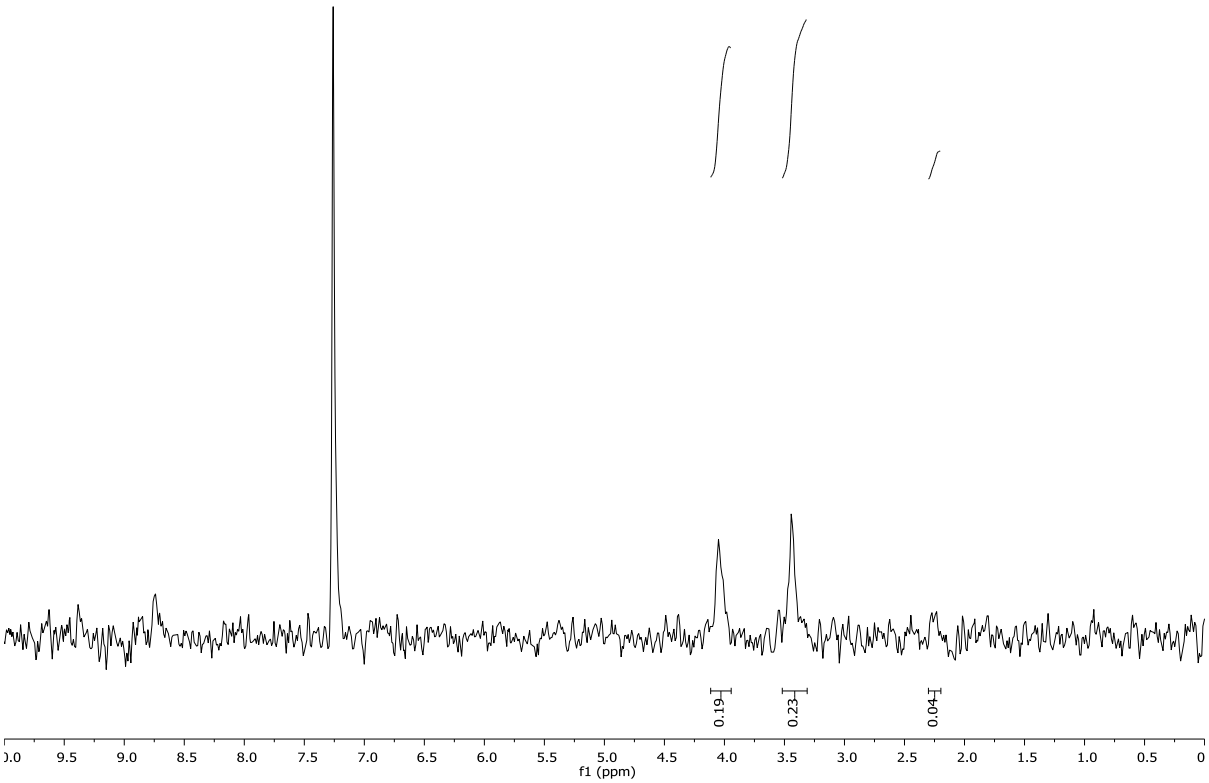

169.32
154.27
137.78
136.42
128.82
128.51
128.22
127.81
127.75
127.32
124.40
124.15
53.02
47.75
40.95
19.78
f1 (ppm)

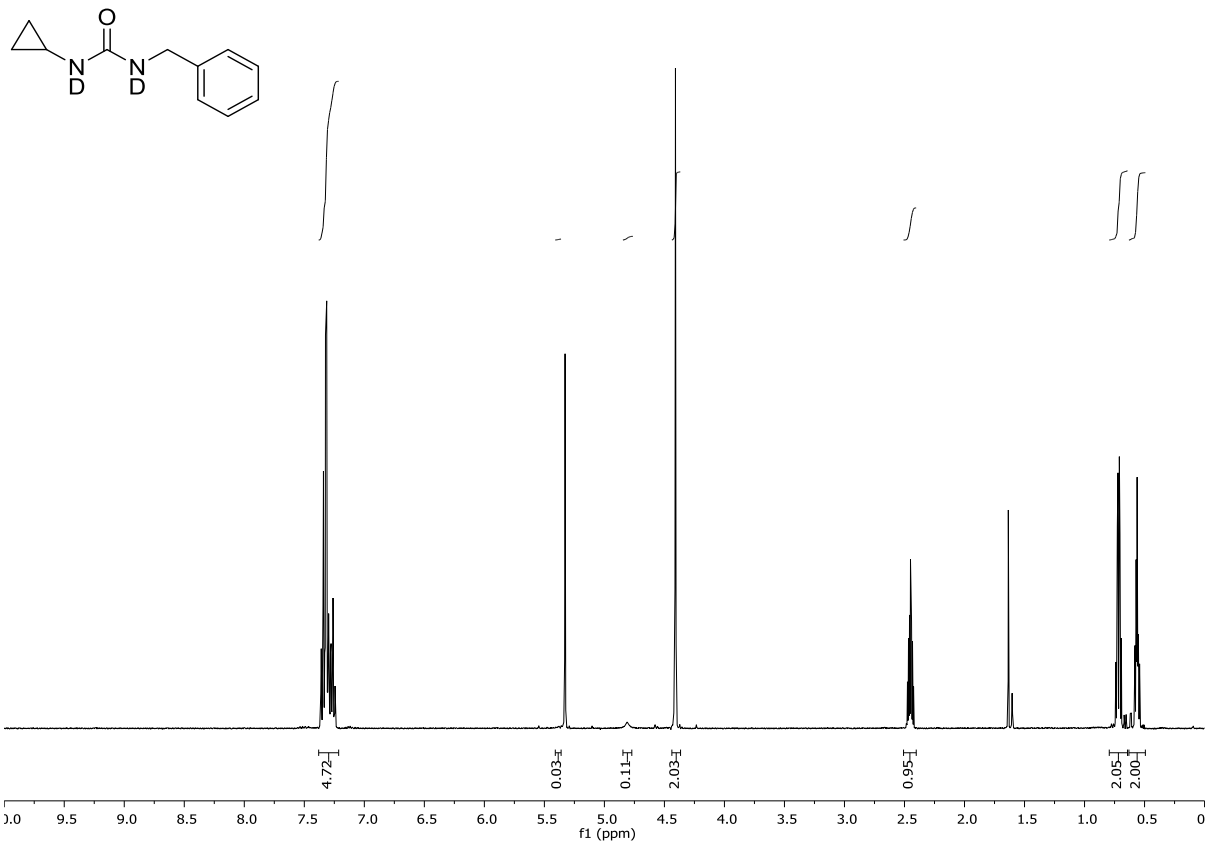

Me
O
N
N
H
12.48
1.00
2.26
2.02
2.02
2.03
3.50
f1 (ppm)

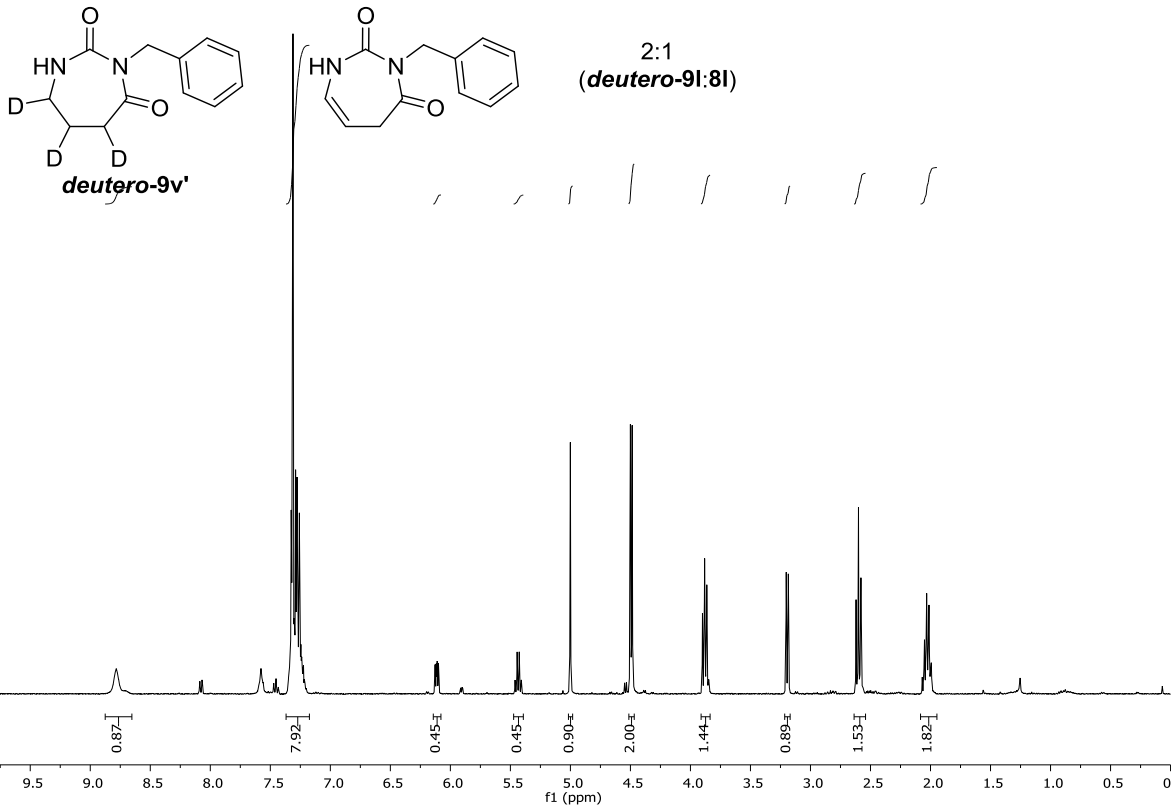

155.98
139.10
137.32
128.76
128.62
127.50
127.30
127.22
126.84
126.54
114.79
48.73
44.98
23.52
14.73
f1 (ppm)

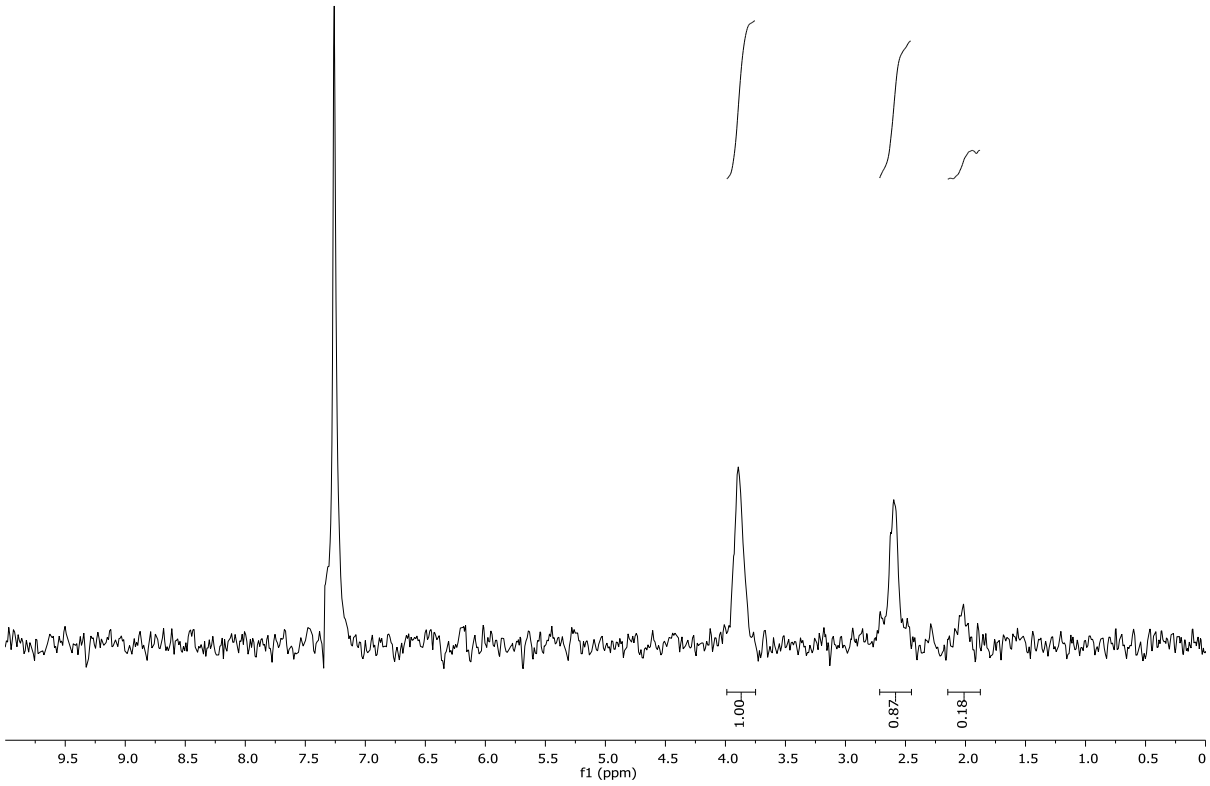

O
N
D
N
D
5.20
0.05
0.07
2.07
1.00
1.15
5.45
5.27
1.03
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)

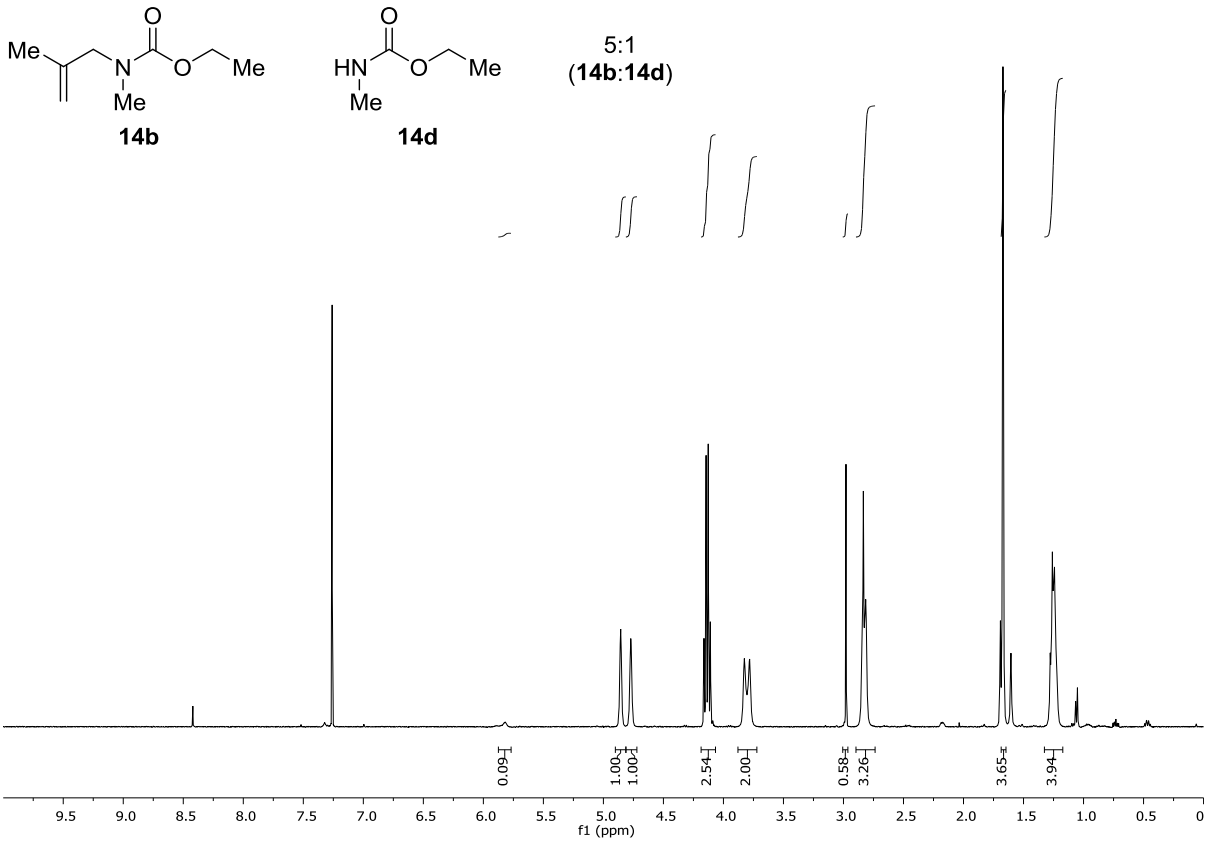

O
HN
N
O
D
D
deutero-9v'
0.82
5.54
2.00
0.81
0.77
0.99
1.96
2.05
4.81
3.03
f1 (ppm)

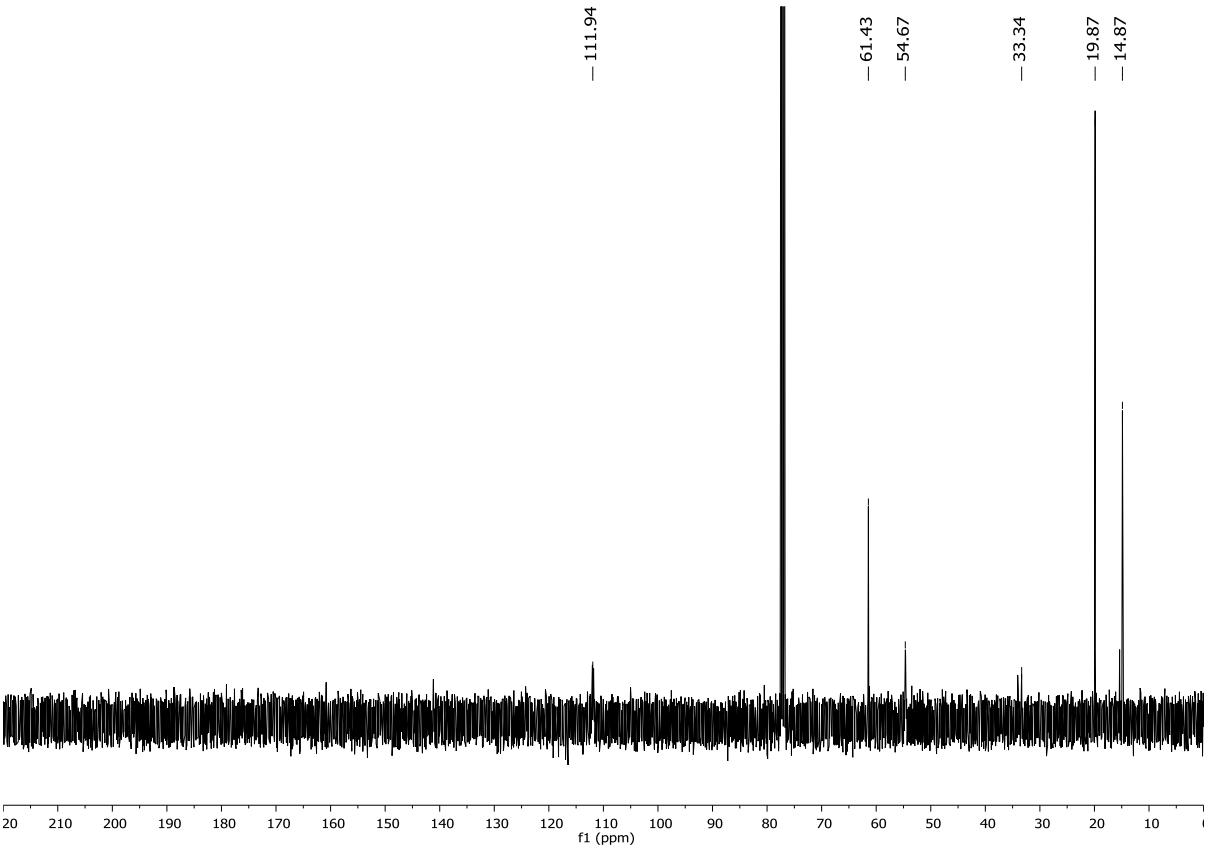

0.19
0.23
0.04
f1 (ppm)

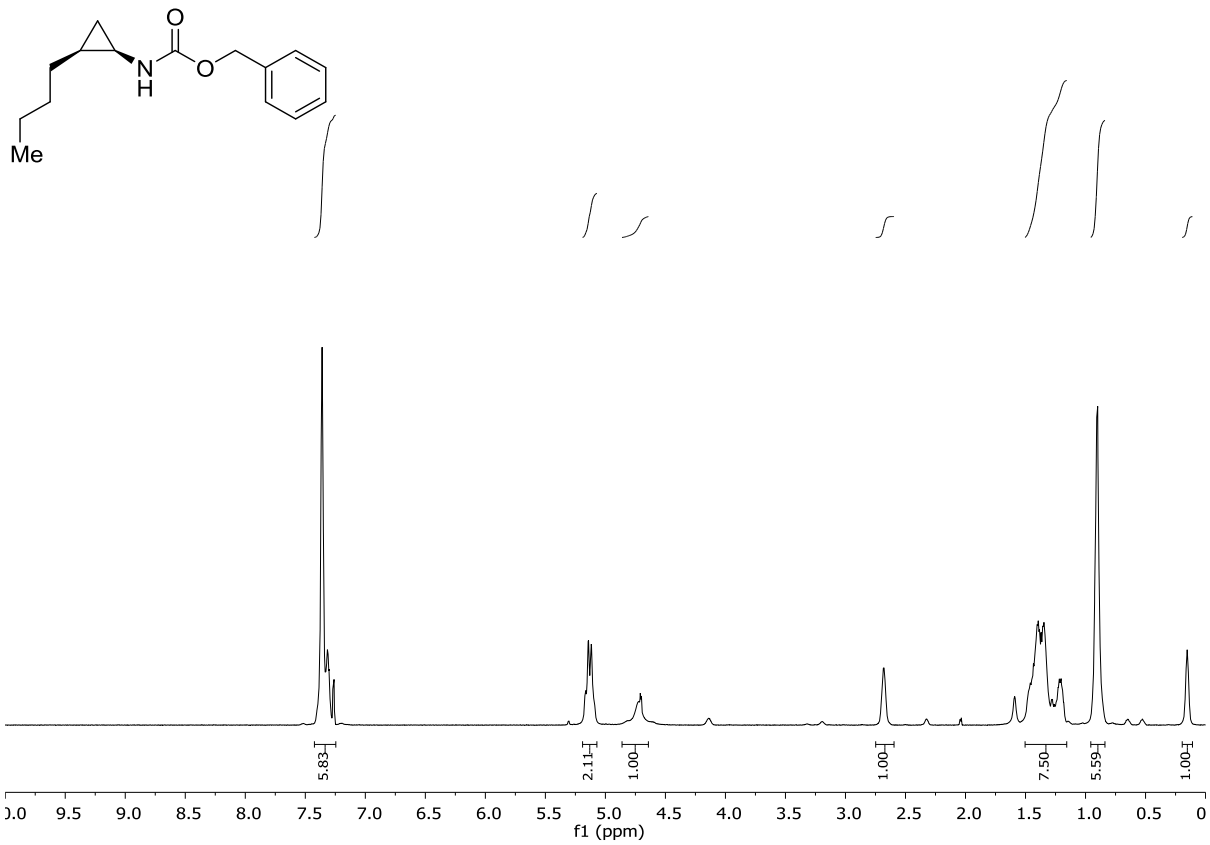

O
N
D
N
D
4.72
0.03
0.11
2.03
0.95
2.05
2.00
f1 (ppm)

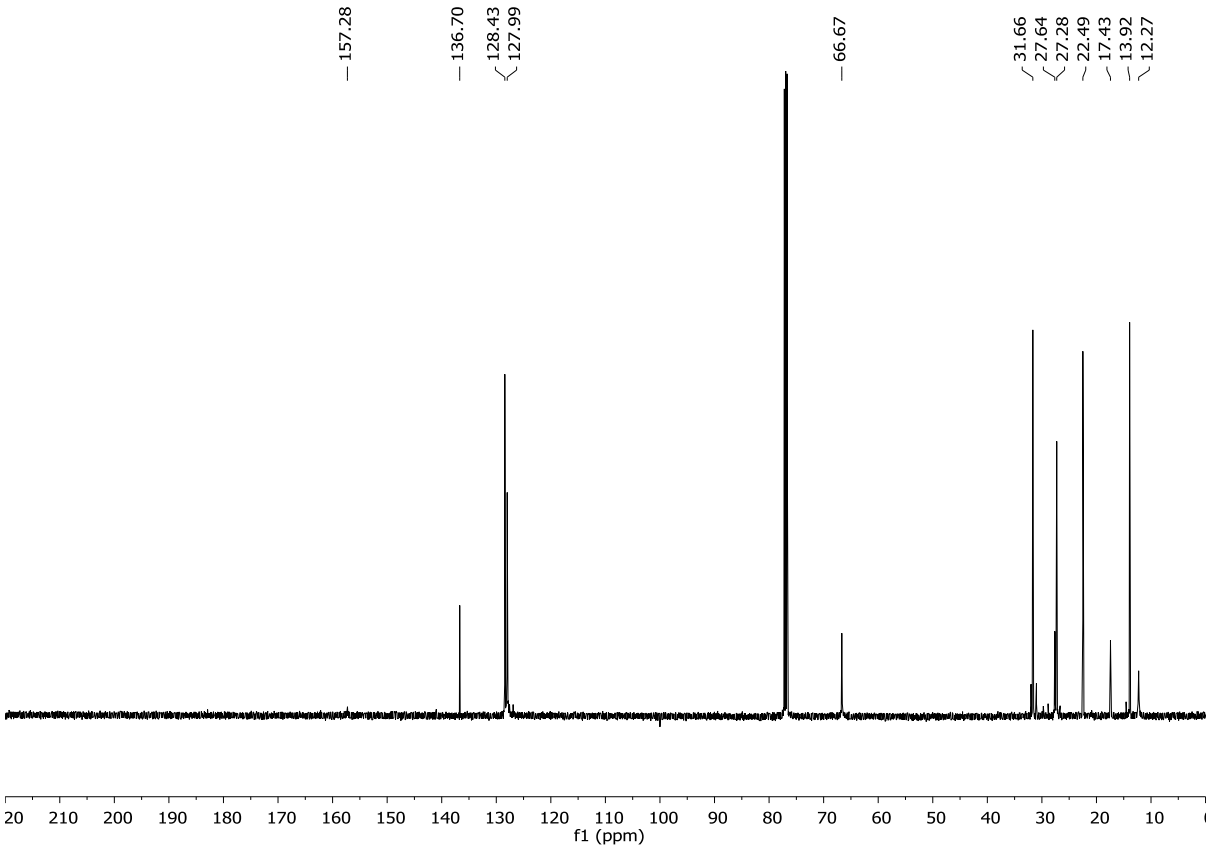

HN
N
O
O
D
D
D
deutero-9v'
2:1
(deutero-9l:8l)
0.87
7.92
0.45
0.45
0.90
2.00
1.44
0.89
1.53
1.82
f1 (ppm)

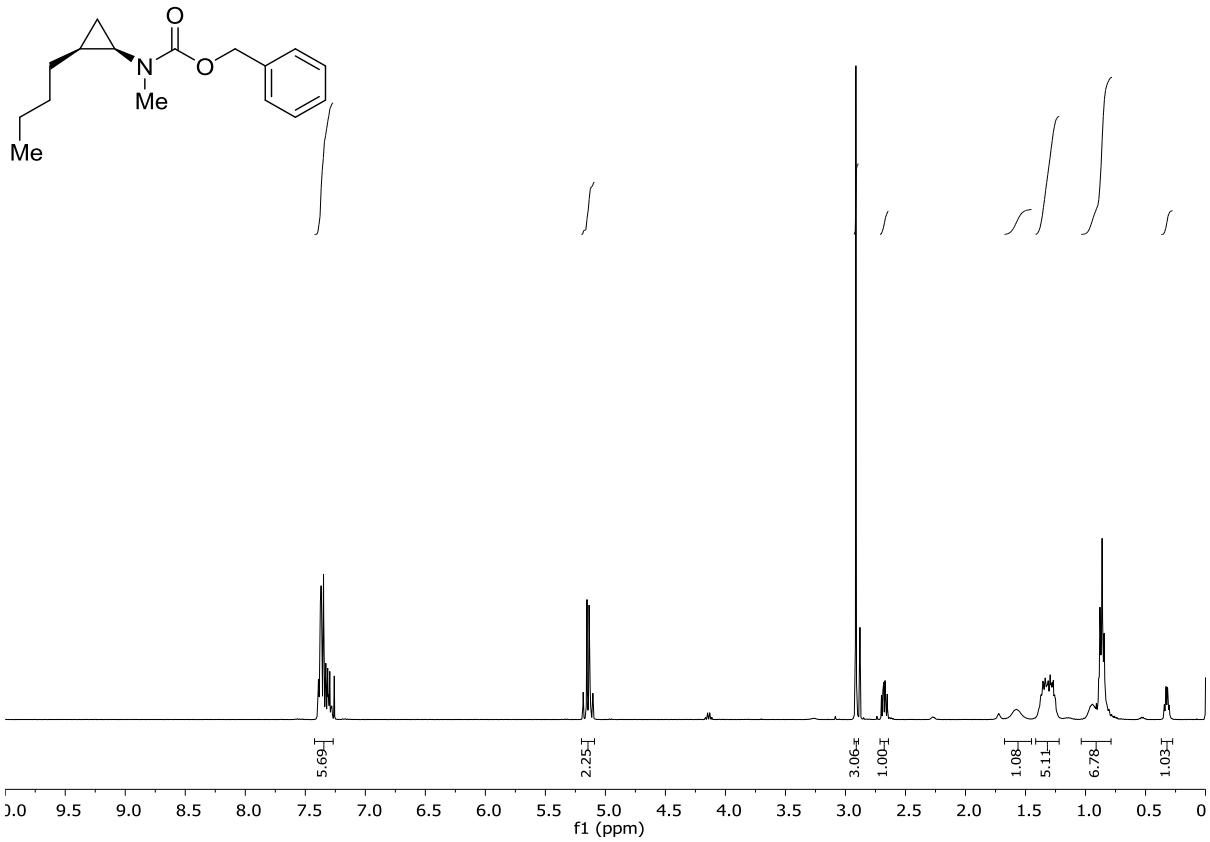

1.00
0.87
0.18
f1 (ppm)

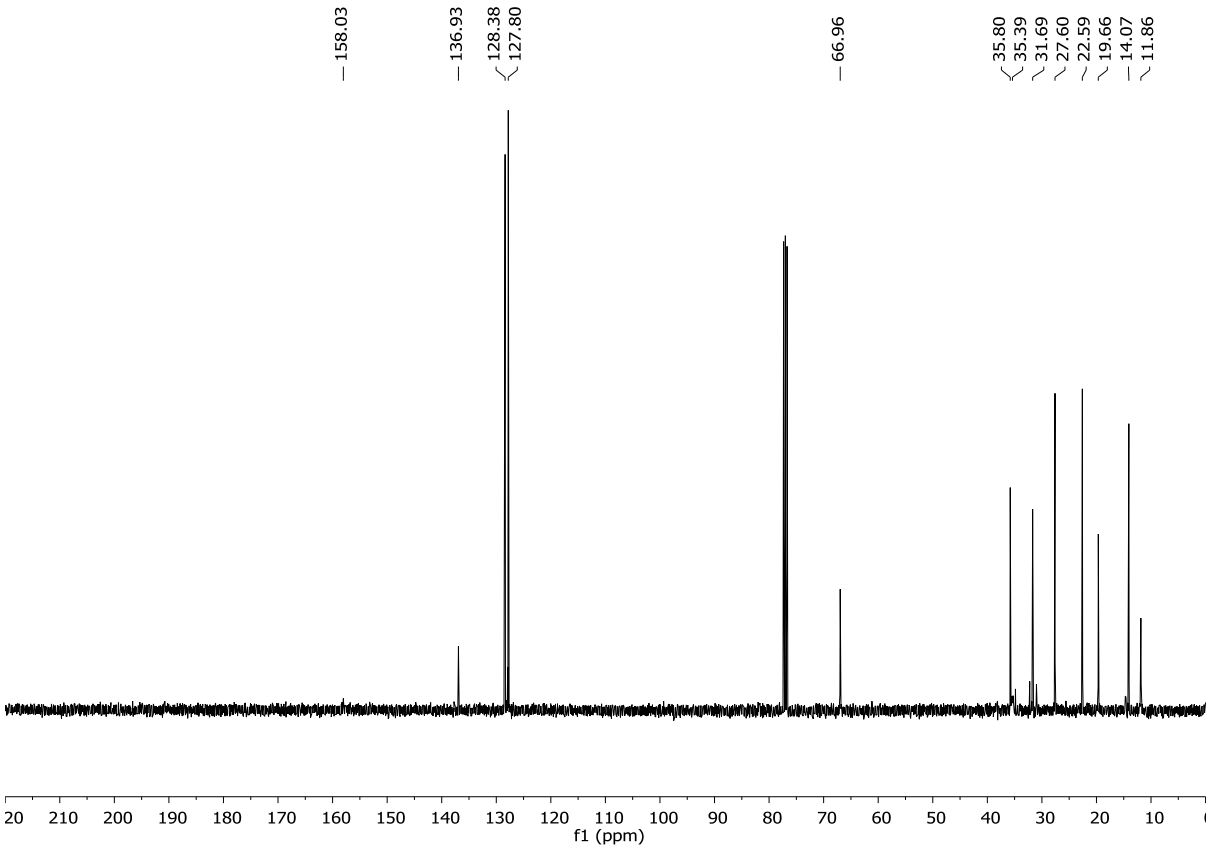

Me
O
N
O
Me
Me
14b
HN
O
Me
Me
14d
5:1
(14b:14d)
0.09
1.00
1.00
2.54
2.00
0.58
3.26
3.65
3.94
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)

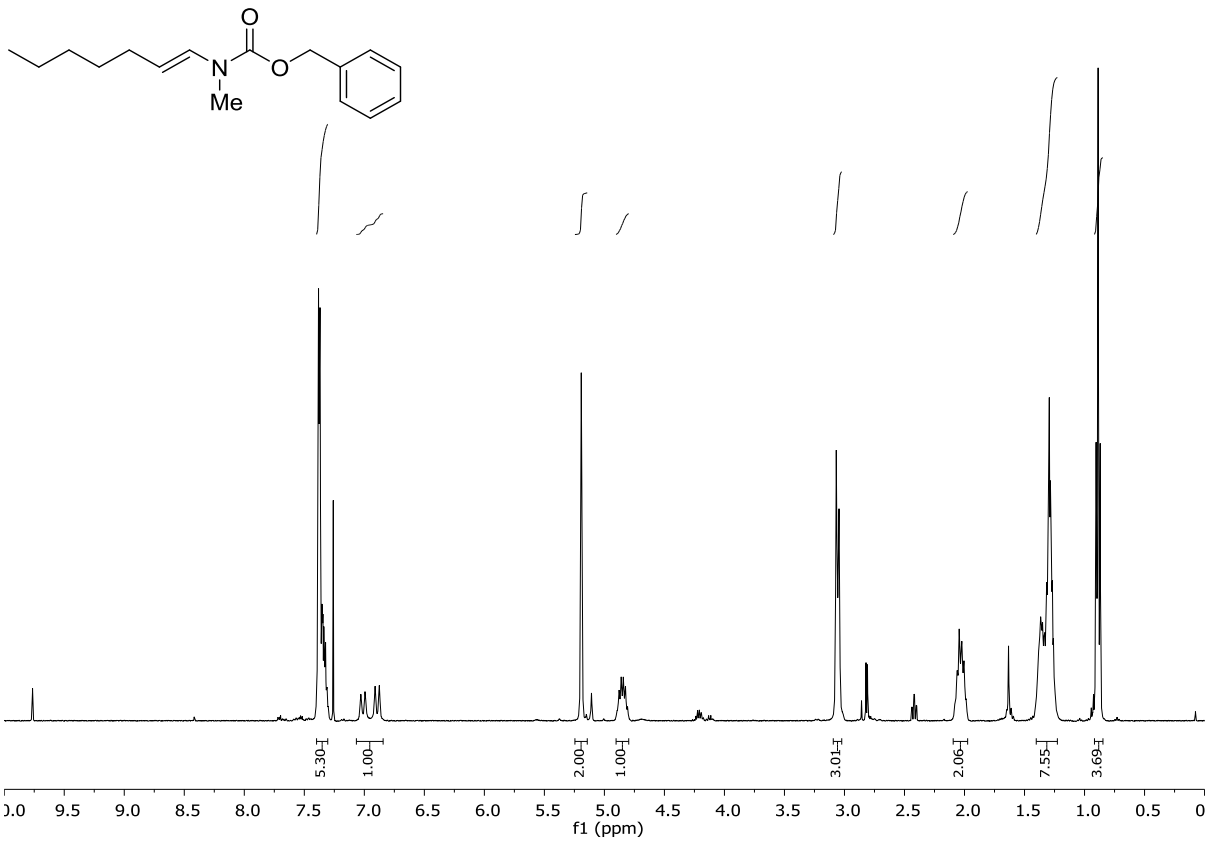

111.94
61.43
54.67
33.34
19.87
14.87
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

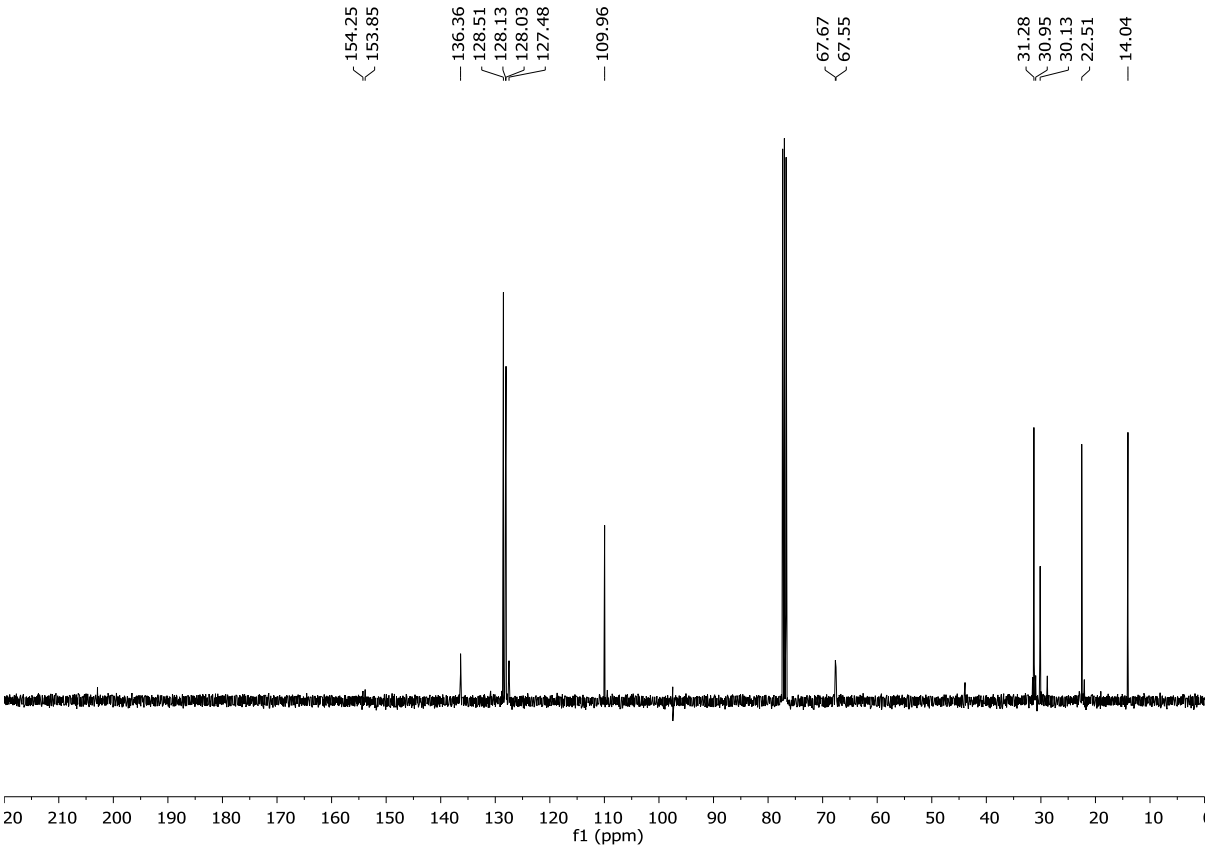

O
N
H
O
Me
5.83
2.11
1.00
1.00
7.50
5.59
1.00
f1 (ppm)

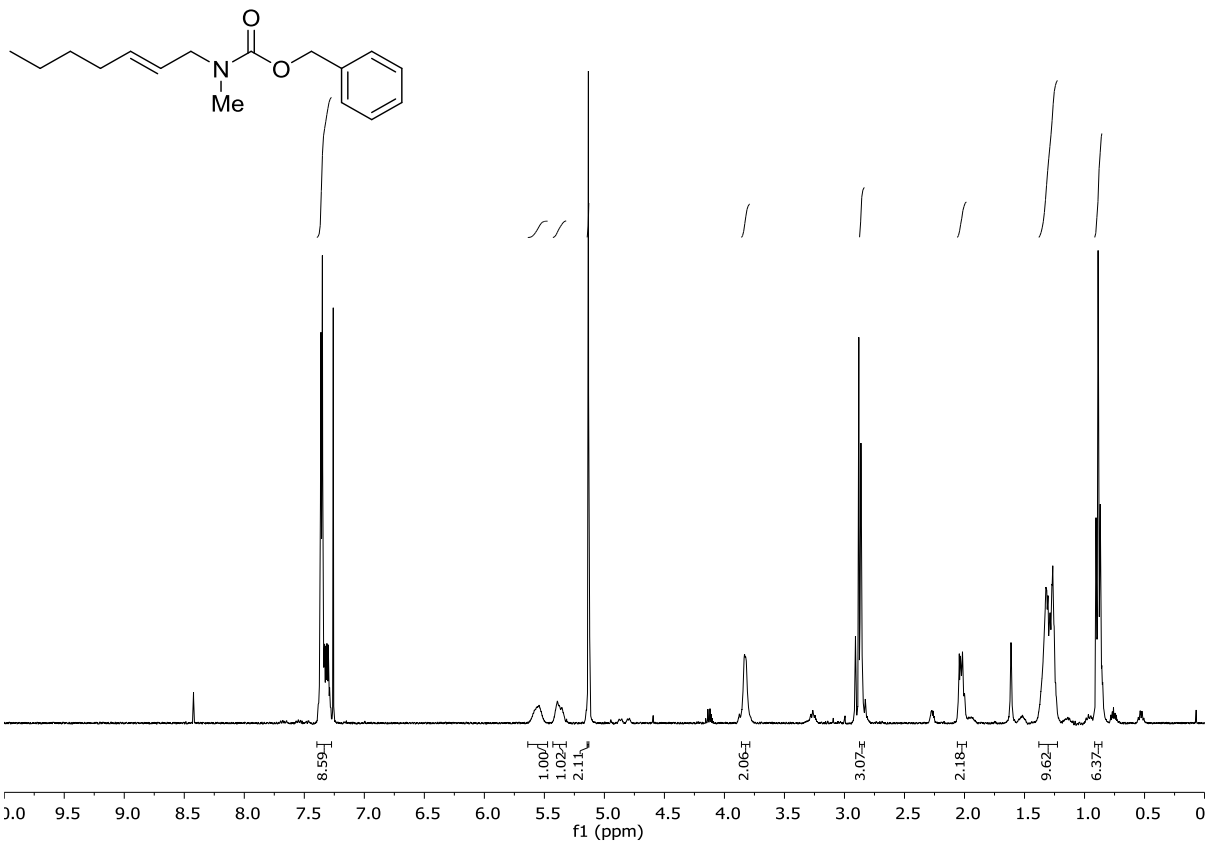

157.28
136.70
128.43
127.99
66.67
31.66
27.64
27.28
22.49
17.43
13.92
12.27
f1 (ppm)

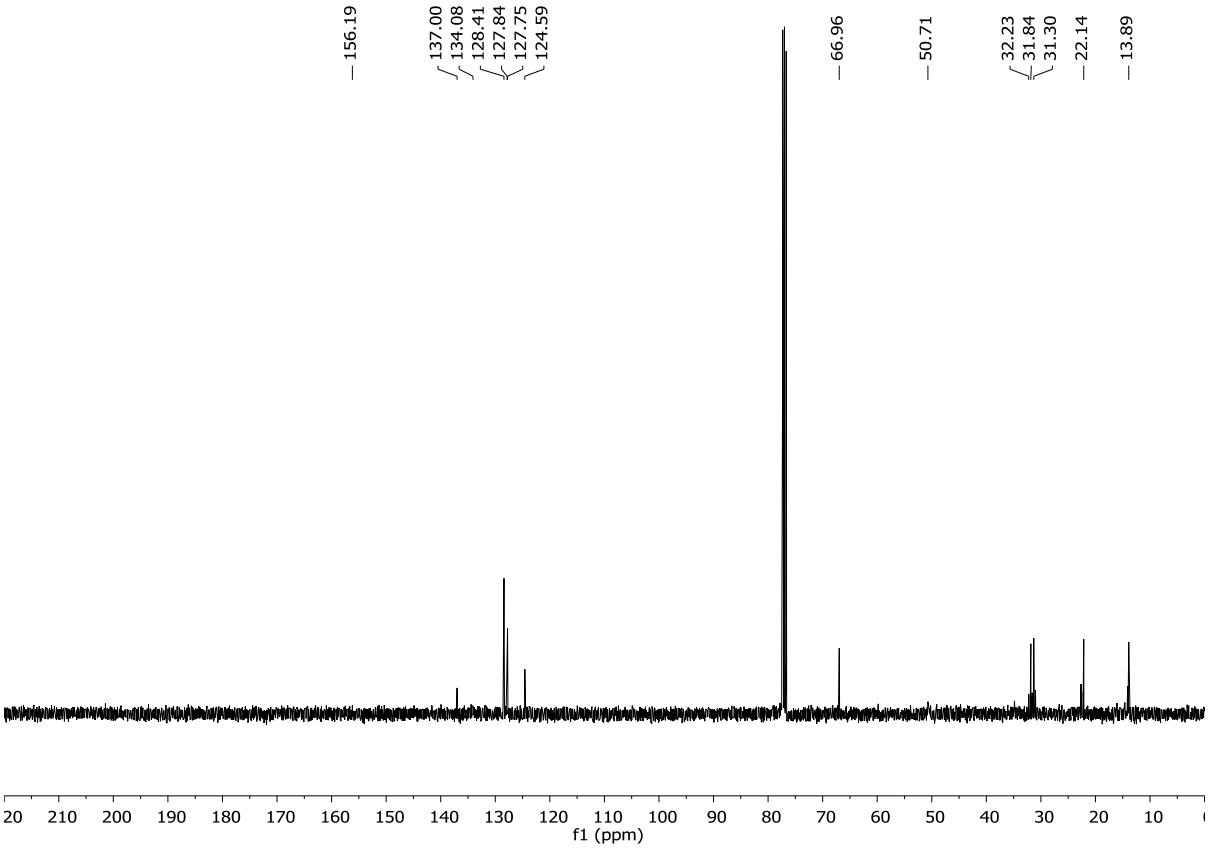

O
N
Me
O
Me
5.69
2.25
3.06
1.00
1.08
5.11
6.78
1.03
f1 (ppm)


158.03
136.93
128.38
127.80
66.96
35.80
35.39
31.69
27.60
22.59
19.66
14.07
11.86
f1 (ppm)


O
N
Me
O
5.30
1.00
2.00
1.00
3.01
2.06
7.55
3.69
f1 (ppm)


154.25
153.85
136.36
128.51
128.13
128.03
127.48
109.96
67.67
67.55
31.28
30.95
30.13
22.51
14.04
f1 (ppm)


O
N
Me
O
8.59
1.00
1.02
2.11
2.06
3.07
2.18
9.62
6.37
f1 (ppm)


156.19
137.00
134.08
128.41
127.84
127.75
124.59
66.96
50.71
32.23
31.84
31.30
22.14
13.89
f1 (ppm)

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