Electronic Supplementary Information

Chemoselective isocyanide insertion into N-H bond using iodine-DMSO: A metal-free access to substituted ureas

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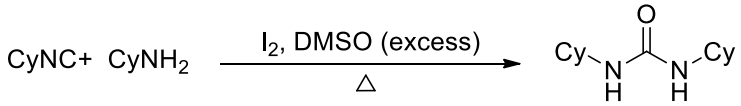
Content:

1. **General remarks:** Commercial reagents were obtained from local suppliers and used as received. DMSO was purchased from Sigma Aldrich in a septum-sealed bottle. All the products were characterized by ^{1}H NMR, ^{13}C NMR and MS spectroscopy. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were obtained on a Bruker AC-400 using $CDCl_3$ and DMSO-d_6 as solvent and solvent peaks as internal standard, unless otherwise stated. Data are reported as: (s = singlet, d = doublet, t = triplet, m = multiplet); coupling constants in Hz and chemical shift values in ppm. Infrared (IR) spectra were recorded on thin films on KBr pellets on a Perkin Elmer FT-IR spectrometer. HPLC analysis was performed on Waters M515 series equipped with a chiral column, using mixtures of *n*-hexane/isopropyl alcohol (IPA) as mobile phase. For column chromatography, we employed Merck silica gel 60-120 mesh.

2. **Table 1S: Optimization of reaction conditions**

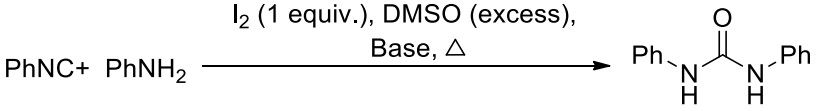


Entry	Iodine (eqv.)	Amine (eqv.)	Temperature (°C)	Time (h)	Yield (%)
1	0.5	1.0	100	6	40
2	1.0	1.0	100	1	57
3	1.5	1.0	100	1	46
4	0.8	1.0	100	1	50
5	**1.0**	**1.5**	**100**	**1**	**89**
6	1.0	2.0	100	1	72
7	1.0	1.5	110	1	64
8	1.0	1.5	120	1	54
9	1.0	1.5	90	5	75

Reaction conditions: CyNC (1 mmol), $CyNH_2$ (1.5 mmol), iodine (1 eqv.), and DMSO (2 mL)

3. Screening of additives

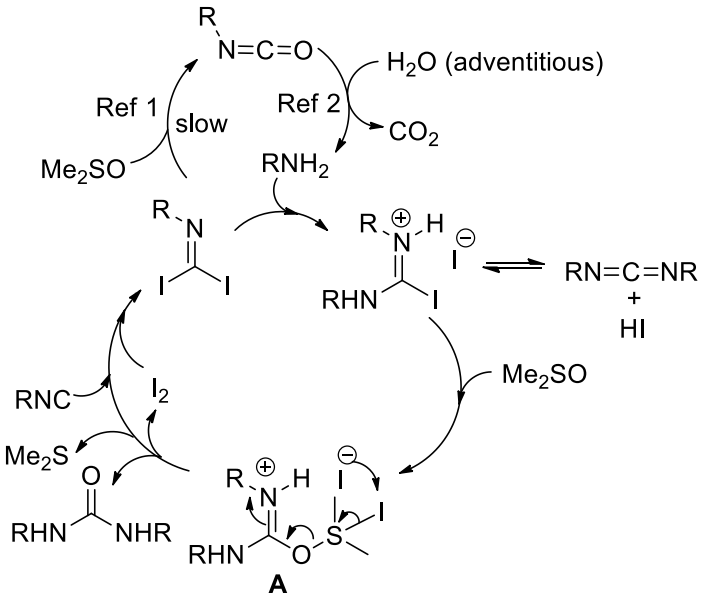
Table 2S: Screening of additives



Entry	Additives (equiv.)	Temp (°C)	Time (h)	Yield (%)
1	Et_3N (1)	100	3	0
2	Pyridine (1)	100	3	23
3	2-Chloropyridine (1)	100	3	17
4	DMAP (1)	100	3	0
5	2,6-Lutidine (1)	100	3	0
6	Imidazole (1)	100	3	52
7	Imidazole (1.5)	100	3	53
8	**DABCO (1)**	**100**	**3**	**65**
9	DABCO (1)	130	3	66
10	DABCO (1)	100	5	62
11	DABCO (1.5)	100	3	66
12	DBU (1)	100	3	45

Reaction conditions: Aniline (1 mmol), Phenylisocyanide (1 mmol), iodine (1 eqv.), and DMSO (2 mL)

4. Probable mechanism for degradative synthesis of dialkylureas from alkyl isocyanides



Scheme S1. Mechanism for degradative synthesis of dialkylureas

5. *Typical procedure* (**A**) *for synthesis of ureas from aliphatic amines*

Cyclohexyl isocyanide (1 mmol) and piperidine (1.5 mmol) in DMSO (2 mL) and iodine (1 mmol) was stirred at 100 ^{o}C for 1 h. After the completion of the reaction as monitored by TLC, 2 mL of ice-cold solution of sodium thiosulphate was added to the reaction mixture and extracted with ethyl acetate (15 mL× 3). Combined organic layers were washed successively with saturated solution of sodium thiosulphate and water and dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure yielded a off white solid which was further purified by passing through a short pad of silica gel column employing hexane: ethyl acetate (50:50) as eluent.

6. *Procedure* (**B**) *for synthesis of ureas from aromatic amines*

To a mixture of benzyl isocyanide (1 mmol), aniline (1.0 mmol) and DABCO (0.5 mmol) in 2 mL of DMSO, iodine (1 mmol) was added and stirred at 100 ^{o}C for 3 h. After the completion of the reaction as monitored by TLC, 2 mL of ice-cold solution of

sodium thiosulphate was added to the reaction mixture and extracted with ethyl acetate (15 mL× 3). Combined organic layers were washed successively with saturated solution of sodium thiosulphate and water and dried over anhydrous sodium sulfate. Solvent was evaporated under reduced pressure and the crude obtained was purified by employing silicagel column chromatography and hexane: ethyl acetate (80:20) as an eluent.

7. *Procedure* (**C**) *for amine-free synthesis of ureas from alkylisocyanides*

Alkyl isocyanide (1 mmol) in 2 mL DMSO and iodine (1 mmol) was stirred at 100 ^{o}C for 4 h. After the completion of the reaction as monitored by TLC, 2 mL of ice-cold solution of sodium thiosulphate was added to the reaction mixture and extracted with ethyl acetate (15 mL× 3). Combined organic layers were washed successively with saturated solution of sodium thiosulphate and water and dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure yielded a crude solid which was further purified by passing through a short pad of silica gel column employing hexane: ethyl acetate (50:50) as eluent.

8. Characterization and Spectral data of the urea derivatives

N-Cyclohexylpyrrolidine-1-carboxamide (**1a**):[3] White solid, m.p. 136- 137 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.01 (d, *J* = 8.0 Hz, 1 H), 3.68 – 3.59 (m, 1H), 3.31 (t, *J* = 6.8 Hz, 4 H), 1.97 – 1.86 (m, 6 H), 1.71 – 1.65 (m, 2 H), 1.62 – 1.57 (m, 1H), 1.37 – 1.30 (m, 2 H), 1.14 – 1.03 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.3, 49.0, 45.5, 34.3, 25.77, 25.6, 25.1 ppm. MS (ESI): *m*/*z* = 196.83 $[M]^+$. IR (KBr): ν = 3285, 2929, 1624, 1533, 1404, 1359 cm^{-1}.

N-Cyclohexylpiperidine-1-carboxamide (**1b**):[4] White solid, m.p. 134- 136 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.26 (d, *J* = 6.0 Hz, 1 H), 3.64 – 3.59 (m, 1 H), 3.29 – 3.26 (m, 4 H), 1.94 – 1.83 (m, 3 H), 1.69 – 1.65 (m, 2 H), 1.60 – 1.52 (m, 6H), 1.39 – 1.30 (m, 2 H), 1.17 – 1.02 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.0, 49.3, 44.7, 33.9, 25.6, 25.5, 25.1, 24.4 ppm. MS (ESI): *m*/*z* = 210.91 $[M]^+$. IR (KBr): ν = 3329, 1651, 1596, 1552, 1232 cm^{-1}.

N-Cyclohexylmorpholine-4-carboxamide (**1c**):[5] White solid, m.p. 172 - 174 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.26 (d, *J* = 6.0 Hz, 1 H), 3.67 (t, *J* = 4.8 Hz, 4 H), 3.64-3.60 (m, 1 H), 3.10 (t, *J* = 4.8 Hz, 4 H), 1.95- 1.92 (m, 2 H), 1.71 – 1.59 (m, 3 H), 1.40 – 1.30 (m, 2 H), 1.16 – 1.03 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.2, 66.5, 49.5, 44.0, 33.9, 25.6, 25.1 ppm. MS (ESI): *m*/*z* = 212.86 $[M]^+$. IR (KBr): ν = 3310, 2931, 1615, 1542, 1275, 1109 cm^{-1}.

1-Cyclohexyl-3-(1-phenylethyl)urea (**1d**):[6] White solid, m.p. 130 – 132 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 – 7.18 (m, 5 H), 4.70 – 4.63 (m, 2 H), 4.21 – 4.16 (m, 1 H), 3.44 – 3.38 (m, 1 H), 1.86 – 1.44 (m, 5 H), 1.37 (d, *J* = 6.0 Hz, 3 H), 1.25 – 0.99 (m, 5 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.5, 144.7, 128.6, 127.1, 125.9, 49.9, 48.8, 48.7, 34.0, 33.8, 33.7, 25.7, 25.6, 25.0, 24.9, 24.8, 23.5 ppm. MS (ESI): *m*/*z* = 247.02 $[M]^+$. IR (KBr): ν = 3317, 2929, 1626, 1575, 1247 cm^{-1}.

1-Benzyl-3-cyclohexylurea (**1e**):[7] White solid, m.p. 77- 78 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 – 7.16 (m, 5 H), 5.11 – 5.08 (m, 1 H), 4.72 (d, *J* = 8.8 Hz, 1 H), 4.30 (d, *J* = 5.2 Hz, 2 H), 3.52 – 3.45 (m, 1 H), 1.89 – 1.85 (m, 2 H), 1.66 – 1.61 (m, 3 H), 1.34 – 1.25 (m, 2 H), 1.09 – 1.00 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.4, 139.8, 128.5, 127.2, 127.0, 48.8, 44.0, 33.9, 25.6, 25.0 ppm. MS (ESI): *m*/*z* = 232.88 $[M]^+$. IR (KBr): ν = 3328, 2905, 1626, 1567, 1279, 1244 cm^{-1}.

3-Cyclohexyl-1,1-diethylurea (**1f**):[8] White solid, m.p. 82- 84 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.16 (d, *J* = 7.6 Hz, 1 H), 3.60 – 3.52 (m, 1 H), 3.18 (q, *J* = 6.8 Hz, 4 H), 1.87 – 1.83 (m, 2 H), 1.62 – 1.48 (m, 3 H), 1.32 – 1.22 (m, 2 H), 1.07 – 0.97 (m, 9 H) ppm. . ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.6, 49.2, 41.0, 34.0, 25.7, 25.1, 13.8 ppm. MS (ESI): *m*/*z* = 199.06 $[M]^+$. IR (KBr): ν = 3328, 1663, 1589, 1560, 1226 cm^{-1}.

N,N′-Dicyclohexylurea (**1g**):[7] White solid, m.p. 232 - 234 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.10 (d, *J* = 6.8 Hz, 2 H), 3.51 - 3.43 (m, 2 H), 1.95 – 1.91 (m, 4 H), 1.72 – 1.57 (m, 6 H), 1.40 – 1.29 (m, 4 H), 1.20 – 1.04 (m, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$ and few drops of DMSO-d_6): δ 156.6, 47.4, 33.3, 25.2, 24.4 ppm. MS (ESI): *m*/*z* = 225.06 $[M]^+$. IR (KBr): ν = 3328, 2929, 1627, 1575, 1271, 1244 cm^{-1}.

N-Benzylpyrrolidine-1-carboxamide (**1h**):[9] White solid, m.p. 122- 124 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 – 7.25(m, 5 H), 4.50 – 4.43 (m, 3 H), 3.36 (t, *J* = 6.8 Hz, 4 H), 1.92 – 1.89 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.7, 138.8, 127.4, 126.6, 126.08, 44.5, 43.5, 24.5 ppm. MS (ESI): *m*/*z* = 204.85 $[M]^+$. IR (KBr): ν = 3290, 1621, 1541, 1400, 1350, 1234 cm^{-1}.

N-Benzylpiperidine-1-carboxamide (**1i**):[7] White solid, m.p. 97- 99 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 – 7.17 (m, 5 H), 4.68 (s, 1 H), 4.35 (d, *J* = 5.2 Hz, 2 H), 3.27 (t, *J* = 5.2 Hz, 4 H), 1.52 – 1.45 (m, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.5, 139.6, 128.4, 127.5, 127.0, 44.7, 25.5, 24.2 ppm. MS (ESI): *m*/*z* = 218.83 $[M]^+$. IR (KBr): ν = 3326, 1640, 1588, 1546, 1233 cm^{-1}.

N-Benzylmorpholine-4-carboxamide (**1j**):[10] White solid, m.p. 104- 106 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 – 7.26 (m, 5 H), 4.74 (s, 1 H), 4.44 (s, 2 H), 3.70 (t, *J* = 4.0 Hz, 3 H), 3.38 (t, *J* = 4.0 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.8, 139.3, 128.6, 127.6, 127.3, 66.4, 44.8, 43.9 ppm. MS (ESI): *m*/*z* = 221.02 $[M]^+$. IR (KBr): ν = 3321, 1624, 1543, 1407, 1269, 1118 cm^{-1}.

N,N′-Dibenzylurea (**1k**):[11] White solid, m.p. 165- 167 °C, ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.34 – (m, 10 H), 4.66 (s, 2 H), 4.39 (d, *J* = 4.8 Hz, 4 H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.0, 140.9, 128.2, 126.9, 126.5, 42.9 ppm. MS (ESI): *m*/*z* = 240.80 $[M]^+$. IR (KBr): ν = 3030, 3321, 1626, 1573, 1246 cm^{-1}.

1-Benzyl-3-(1-phenylethyl)urea (**1l**):[12] White solid, m.p. 125- 126 °C, ^{1}H NMR (400 MHz,) δ 7.46 – 7.18 (m, 14H), 7.15 (d, *J* = 6.6 Hz, 3H), 4.79 (dd, *J* = 13.0, 6.4 Hz, 3H), 4.65 (s, 1H), 4.36 (d, *J* = 5.2 Hz, 2H), 4.30 (t, *J* = 6.4 Hz, 2H), 1.43 (d, *J* = 6.0 Hz, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.1, 144.4, 139.4, 128.5, 128.4, 127.2, 127.1, 127.0, 125.8, 49.8, 44.0, 23.2 ppm. MS (ESI): *m*/*z* = 218.83 $[M]^+$. IR (KBr): ν = 3335, 3320 1652, 1591, 1545, 1224 cm^{-1}.

1-Benzyl-3-butylurea (**1m**):[11] White solid, m.p. 100- 102 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21 – 7.15 (m, 5 H), 5.13 (s, 1 H), 4.79 (s, 1 H), 4.21 (d, *J* = 5.6 Hz, 2 H), 3.03 (q, *J* = 6.4 Hz, 2 H), 1.33 – 1.28 (m, 2 H), 1.24 – 1.15 (m, 2 H), 0.81 (t, *J* = 7.2 Hz, 3

H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.0, 139.6, 128.4, 127.1, 126.9, 44.0, 40.0, 32.3, 20.0, 13.8 ppm. MS (ESI): *m*/*z* = 207.05 $[M]^+$. IR (KBr): ν = 3339, 2954, 1626, 1594, 1270 cm^{-1}.

1-((3s,5s,7s)-Adamantan-1-yl)-3-benzylurea (**1n**):[13] White solid, m.p. 148- 150 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 – 7.15 (m, 5 H), 5.07 (s, 3 H), 4.65 (s, 1 H), 4.19 (d, *J* = 5.2 Hz, 2 H), 1.96 (s, 3 H), 1.84 (s, 6 H), 1.56 (s, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.7, 139.6, 128.4, 127.2, 127.1, 50.6, 43.8, 42.3, 36.4, 29.5 pmm. MS (ESI): *m*/*z* = 285.03 $[M]^+$. IR (KBr): ν = 3350, 2906, 1625, 1569, 1279, 1243, 1090 cm^{-1}.

N-(tert-Butyl)pyrrolidine-1-carboxamide (**1o**):[14] White solid, m.p. 120- 122 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.02 (s, 1 H), 3.27 (t, *J* = 6.4 Hz, 4 H), 1.87 (m, 4 H), 1.33 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.2, 50.5, 45.3, 29.5, 25.5 ppm. MS (ESI): *m*/*z* = 171.04 $[M]^+$. IR (KBr): ν = 3347, 2969, 1632, 1529, 1388, 1219 cm^{-1}.

N-(tert-Butyl)piperidine-1-carboxamide (**1p**):[15] White solid, m.p. 140- 142 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.29 (s, 1H), 3.33 – 3.14 (m, 4H), 1.60 – 1.45 (m, 6H), 1.34 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.1, 76.7, 44.8, 77.3, 50.5, 77.0, 29.5, 24.4, 25.6 ppm. MS (ESI): *m*/*z* = 184. 13 $[M]^+$. IR: ν = 3339, 2958, 1645, 1552, 1222 cm^{-1}.

N-(tert-Butyl)morpholine-4-carboxamide (**1q**):[16] White solid, m.p. 182- 184 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.29 (s,1 H), 3.66 (t, *J* = 4.8 Hz, 4 H), 3.27 (t, *J* = 4.8 Hz, 4 H), 1.37 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.0, 66.4, 50.8, 43.9, 29.3 ppm. MS (ESI): *m*/*z* = 186.82 [M]. IR (KBr): ν = 3359, 2973, 1622, 1537, 1274, 1109 cm^{-1}.

1-Benzyl-3-(tert-butyl)urea (**1r**):[17] White solid, m.p. 107- 108 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 – 7.22 (m, 5 H), 4.94 (s, 1 H), 4.63 (s, 1 H), 4.25 (s, 2 H), 1.29 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.2, 139.9, 128.3, 127.1, 126.8, 49.9, 43.7, 29.5 ppm. MS (ESI): *m*/*z* = 206.92 $[M]^+$. IR (KBr): ν = 3331, 3319, 1647, 1591, 1549, 1227 cm^{-1}.

1-Cyclohexyl-3-phenylurea (**1s**):[14] White solid, m.p. 179- 180 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (s, 1 H), 7.16 – 7.12 (m, 2 H), 7.01 – 6.96 (m, 2 H), 6.71 (t, *J* = 7.2 Hz, 1 H), 5.42 (s, 1 H), 3.52 – 3.43 (m, 1 H), 1.72 (dd, *J* = 12.4 Hz, 4.0 Hz, 2 H), 1.49 – 1.43

(m, 2 H), 1.37 – 1.34 (m, 1 H), 1.15 – 1.08 (m, 2 H), 0.95 – 0.89 (m, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.3, 140.1, 128.6, 121.4, 118.3, 48.1, 33.5, 25.5, 24.7 ppm. MS (ESI): *m*/*z* = 218.07 $[M]^+$. IR (KBr): ν = 3337, 3321, 1645, 1583, 1546, 1241 cm^{-1}.

1-Benzyl-3-phenylurea (**1t**):[9] White solid, m.p. 167- 170 ºC, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 – 7.23 (m, 9 H), 7.08 – 7.05 (m, 1 H), 6.59 (s, 1 H), 5.26 (s, 1 H), 4.40 (d, *J* = 5.6 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.4, 139.7, 139.3, 128.2, 127.9, 127.0, 126.5, 121.1, 117.7, 43.0 ppm. MS (ESI): *m*/*z* = 127.08 $[M]^+$. IR (KBr): ν = 3328, 1634, 1555, 1234 cm^{-1}.

N-phenylpiperidine-1-carboxamide (**1u**):[11] White solid, m.p. 171- 173 ºC ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.46 – 7.19 (m, 4 H), 7.02 (t, *J*=7.3 Hz, 1H), 6.39 (s, 1H), 3.80 – 2.92 (t, *J*=4.8 Hz, 4 H), 1.67 – 1.44 (m, 6 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.9, 139.2, 128.8, 122.8, 119.7, 45.2, 25.6, 24.3 ppm. MS (ESI): *m*/*z* = 205.31 $[M+H]^+$. IR: ν = 3333, 3319, 1641, 1571, 1545, 1240 cm^{-1}.

N-Phenylmorpholine-4-carboxamide (**1v**):[17] White solid, m.p. 158- 159 ºC ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 – 7.16 (m, 1H), 7.06 (t, *J*=7.2, 1H), 6.34 (s, 1H), 3.74 (t, *J*=4.8 Hz, 4 H), 3.48 (t, *J*=4.8 Hz, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.1, 138.6, 128.9, 123.3, 120.0, 66.4, 44.2 ppm. *m*/*z* = 207.21 $[M+H]^+$. IR (KBr): ν = 3331, 3323, 1642, 1569, 1546, 1239 cm^{-1}.

N-(4-Methoxyphenyl)morpholine-4-carboxamide (**1w**):[16] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (d, *J*= 8.9 Hz, 2 H), 6.83 (d, *J*=8.9 Hz, 2 H), 6.43 (s, 1 H), 3.78 (s, 3 H), 3.70 (t, *J*= 4.8 Hz, 4 H), 3.50 – 3.35 (t, *J*= 4.8 Hz, 4 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.0, 155.7, 131.6, 122.6, 114.0, 66.4, 55.4, 44.1 ppm; MS (ESI): *m*/*z* = 237.31 $[M+H]^+$; IR (KBr): ν = 3331, 3318, 1644, 1572, 1542, 1238 cm^{-1}.

1-Benzyl-3-(4-methoxyphenyl)urea (**1x**):[9] White solid, m.p. 141- 143 ºC, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 – 7.22, (m, 4 H), 7.16 – 7.13 (m, 2 H), 6.84 – 6.81 (m, 2 H), 6.45 (s, 1 H), 5.16 (s, 1 H), 4.38 (d, *J* = 5.6 Hz, 2 H), 3.76 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.0, 154.3, 139.4, 132.5, 127.9, 126.9, 126.5, 120.2, 113.5, 54.9, 43.1 ppm. MS (ESI): *m*/*z* = 257.05 $[M]^+$. IR (KBr): ν = 3307, 1628, 1608, 1564, 1244 cm^{-1}.

(S)-Methyl 2-(3-benzylureido)-3-phenylpropanoate (**2a**):[18] White solid, m.p. 96- 97 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 – 7.21 (m, 8 H), 7.07 – 7.05 (m, 2 H), 5.03 – 4.98 (m, 2 H), 4.80 – 4.76 (m, 1 H), 4.32 – 4.28 (m, 2 H), 3.66 (s, 3 H), 3.10 – 2.98 (m, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.2, 157.1, 138.9, 136.1, 136.3, 129.3, 128.4, 128.6, 127.3, 126.9, 53.9, 52.2, 44.4, 38.4 ppm. MS (ESI): *m*/*z* = 313.09 $[M]^+$. IR (KBr): ν = 3357, 3320, 1734, 1629, 1571, 1244, 1030 cm^{-1}.

(S)-Methyl 2-(3-Cyclohexylureido)-3-phenylpropanoate (**2b**):[18] White solid, m.p. 115 – 116 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (m, 3H), 7.05 (d, *J* = 7.2 Hz, 2 H), 4.71-4.67 (m, 1 H), 4.71 (d, *J* = 7.6 Hz, 1H), 4.24 (d, *J* = 7.2 Hz, 1 H), 3.65 (s, 3 H), 3.38-3.36 (m, 1 H), 3.04 – 2.98 (m, 2 H), 1.84 – 1.77 (m, 2 H), 1.61 – 1.49 (m, 3, H), 1.25 – 1.18 (m, 2 H), 1.04 – 0.99 (m, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.5, 156.6, 136.3, 129.3, 128.4, 126.9, 53.9, 52.1, 49.1, 38.5, 33.7, 33.6, 25.5, 24.9, 24.8 ppm. MS (ESI): *m*/*z* = 305.02 $[M]^+$. IR (KBr): ν = 3317, 2936, 1735, 1627, 1561, 1221 cm^{-1}.

1,3-di-tert-butylurea (**3a**):[19] White solid, m.p. 246-247 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.13 (s, 2 H), 1.30 (s, 18 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.1, 50.1, 29.6 ppm. MS (ESI): *m*/*z* = 172.20 $[M]^+$. IR (KBr): ν = 3334, 1654, 1570, 1537, 1240 cm^{-1}.

1,3-Di(1-adamentyl)urea (**3b**):[7] White solid, m.p.> 300 °C, ^{1}H NMR (400 MHz, DMSO-d_6): 3.99 (s, 2H), 2.03 (s, 6H), 1.97 (s, 12H), 1.62 (s, 12H) ppm. MS (ESI): m/z = 328.65 $[M]^+$. IR (KBr): ν = 3350, 2911, 1673, 1661, 1193 cm^{-1}.

1,3-Diphenylurea (**4a**)**:**[15] White solid, m.p. 247-248 °C, ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6): δ 8.05 (s, 2 H), 7.31 (d, *J*=7.6 Hz, 4 H), 7.13 (t, *J*=7.9 Hz, 4 H), 6.85 (t, *J*=7.4 Hz, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6): δ 153.1, 139.4, 128.7, 122.1, 118.6 ppm. *m*/*z* = 212.20 $[M]^+$. IR (KBr): ν 3338, 1644, 1566, 1541, 1241 cm^{-1}.

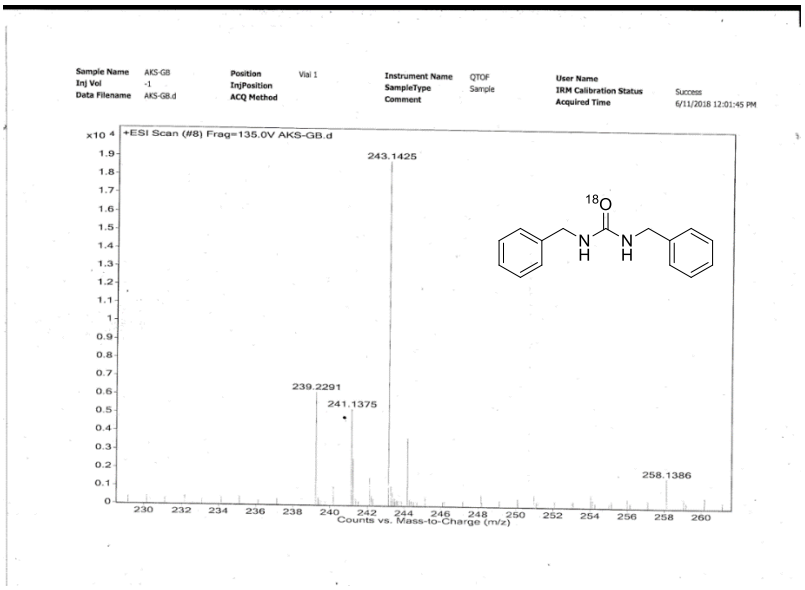
1-(4-Methoxyphenyl)-3-phenylurea (**4b**):[15] White solid, m.p. 187- 189 °C, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (s, 1 H), 7.87 (s, 1 H), 7.36 (d, *J* = 8.0 Hz, 2 H), 7.28 – 7.25 (m, 2 H), 7.20 (t, *J* = 7.6 Hz, 2 H), 6.91(t, *J* = 7.6 Hz, 1 H), 6.76 (d, *J* = 8.4 Hz, 2 H), 3.69 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.6, 153.1, 139.4, 132.3, 128.4, 121.6, 120.3, 118.2, 113.6, 55.1 ppm. MS (ESI): *m*/*z* = 242.98 $[M]^+$. IR (KBr): ν = 3336, 3321, 1645, 1550, 1231 cm^{-1}.

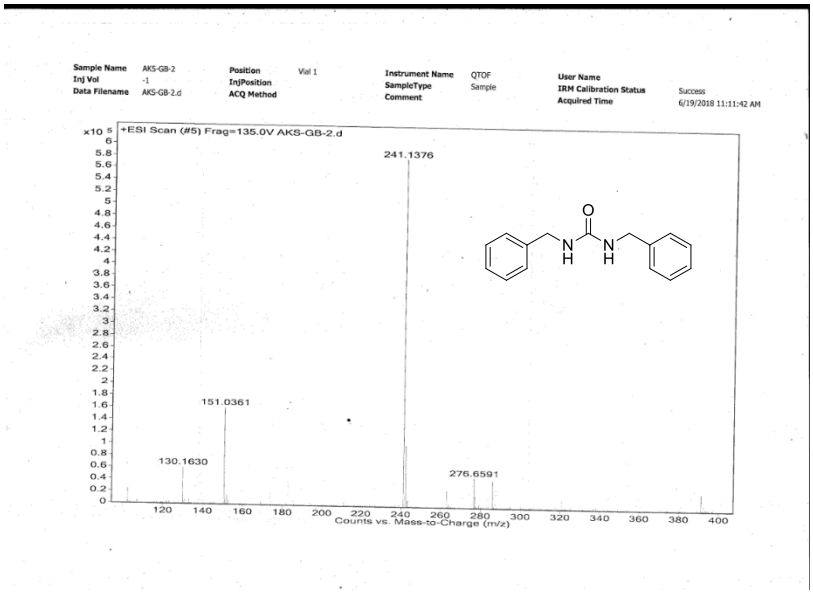
1-Benzyl-3-(2-(4-chlorophenyl)-2-hydroxyethyl)urea (**5**)**:** White solid, m.p. 178-180 ^{o}C, ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.51 – 7.26 (m, 5 H), 7.21-7.18 (m, 2 H), 6.49 (t, *J*=6.0, 1 H), 6.01 (t, *J*=5.5, 1 H), 5.64 (d, *J*=4.2, 1 H), 4.85 – 4.34 (m, 1 H), 4.17 (d, *J*=5.6 Hz, 2 H), 3.37 – 3.18 (m, 1 H), 3.12- 3.08 (m, 1 H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 158.1, 142.7, 140.7, 131.3, 128.1, 127.8, 127.8, 126.8, 126.4, 71.3, 47.1, 42.7 ppm. MS (ESI): *m*/*z* = 304.44 $[M]^+$. IR (KBr): ν = 3562, 3364, 3296, 1615, 1193 cm^{-1}.

9. Method for preparation of ^{18}O-labeled dibenzylurea

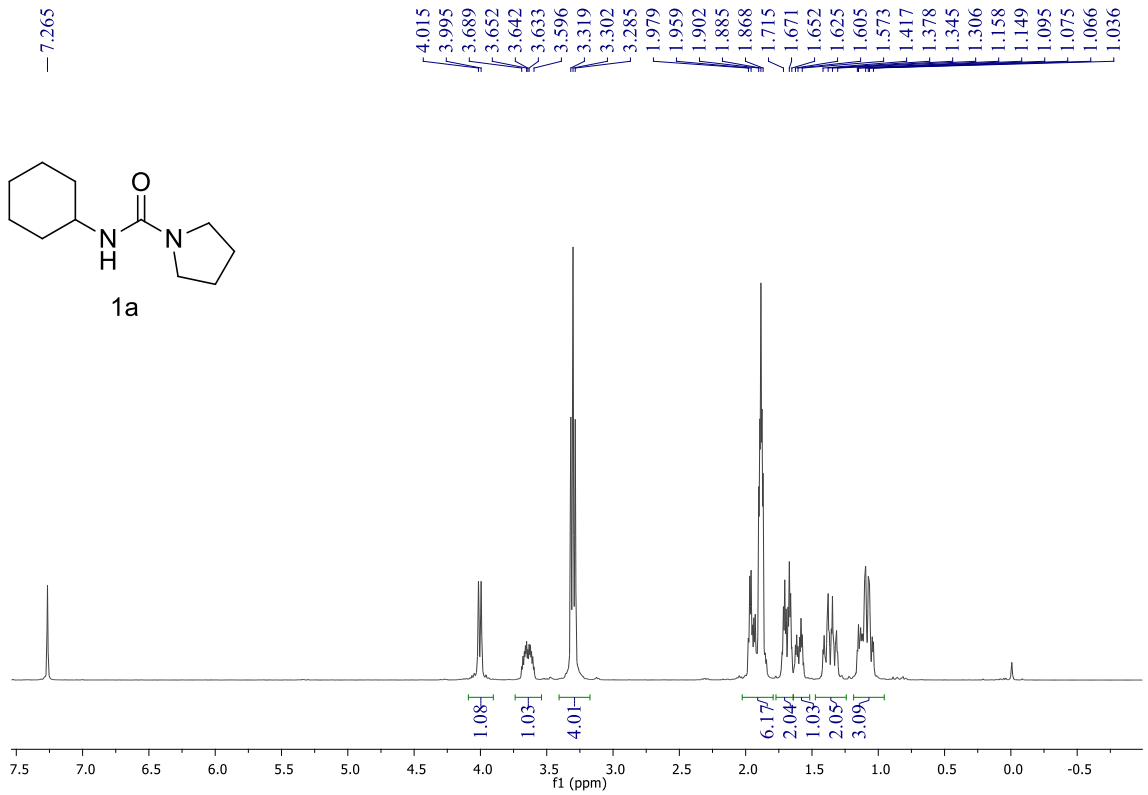
Me_2SO^{18} was synthesized following literature procedure.[20] The solid dimethylsulfur dibromide (5.0 g, 22.5 mmoles) prepared was added portion-wise over a period of 15 min to a vigorously stirred solution of freshly distilled triethylamine (6.3 ml, 45 mmoles) and ^{18}O-labeled water (0.20 ml, 11 mmoles) in 15 mL of anhydrous THF. The temperature of the reaction was maintained below 50 ^{o}C by occasional cooling in ice. The precipitate of triethylamine hydrobromide was removed by centrifugation and washed twice with ether. The combined yellow supernatant and washings were distilled at room temperature at reduced pressure (15 mm) to remove the solvent and the tan residue was distilled in a short-path apparatus (60-70 ^{o}C at 0.3 mm) giving 1.03 g of a pale yellow liquid. Without further purification the reaction was performed between benzyl isocyanide (57 mg, 0.5 mmol) and benzyl amine (80 mg, 0.75 mmol) as per optimized procedure. After the completion of the reaction as monitored by TLC, 2 mL of ice-cold solution of sodium thiosulphate was added to the reaction mixture and extracted with ethyl acetate (15 mL× 3). Combined organic layers were washed successively with saturated solution of sodium thiosulphate and water and dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure yielded the corresponding ^{18}O-derivative of dibenzylurea as an off-white solid which was further purified by passing through a short pad of silica gel column employing hexane: ethyl acetate (50:50) as eluent. ESI-MS analysis result clearly showed $[M+H]^+$ peak at 243.1425 corresponding to ^{18}O-derivative of dibenzylurea.

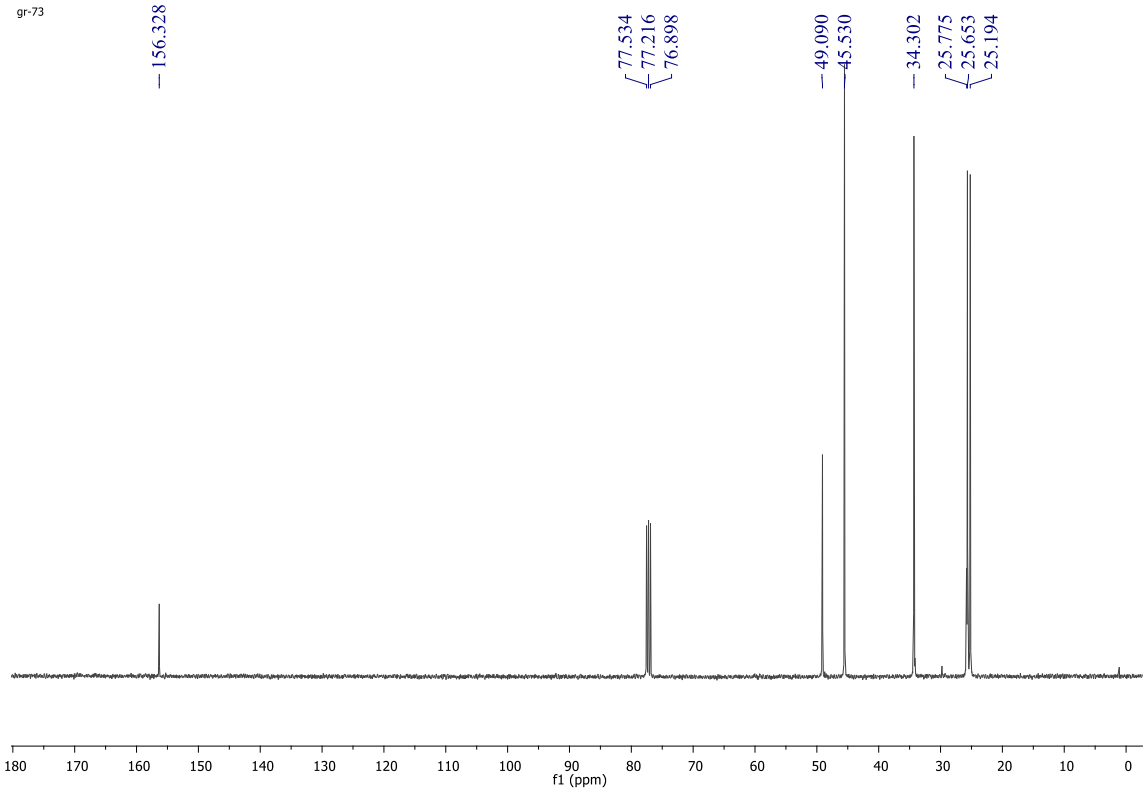
10. HRMS specrat of ^{18}O-labeled dibenzylurea and ^{16}O-dibenzylurea

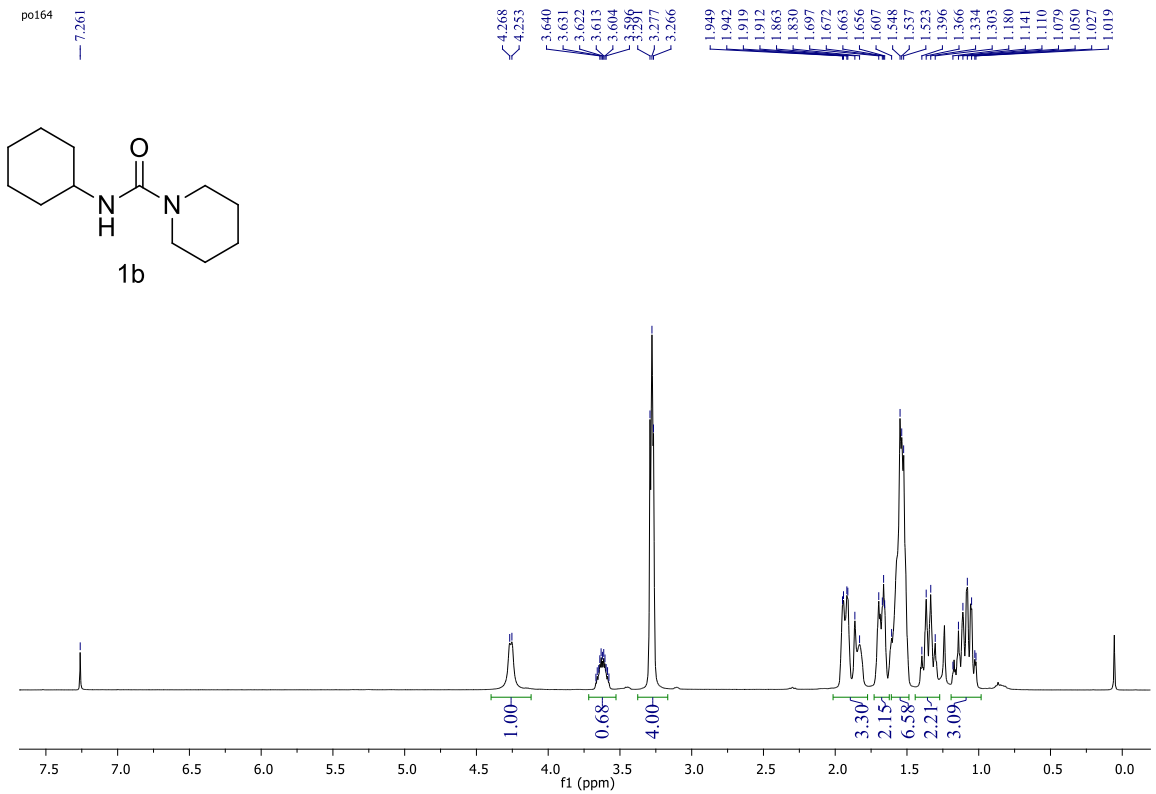




11. ^{1}H NMR and ^{13}C NMR spectra for the ureas



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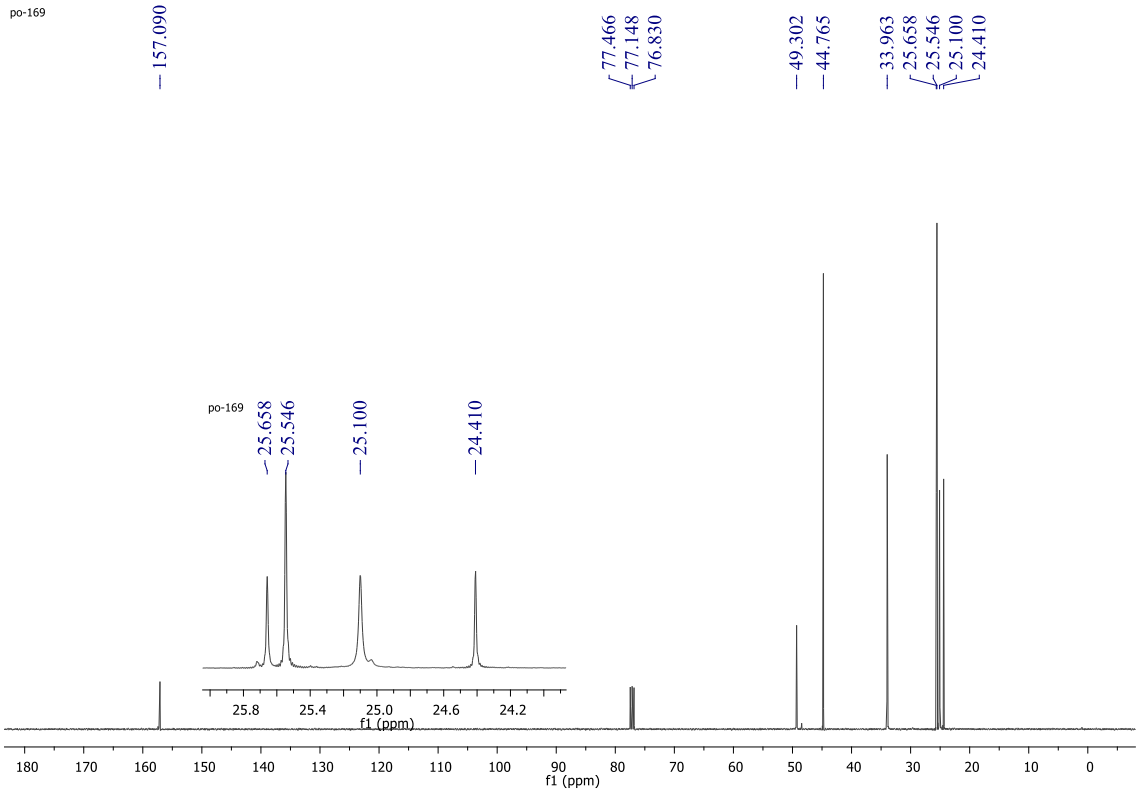
3.640
3.631
3.622
3.613
3.604
3.586
3.291
3.277
3.266
1.949
1.942
1.919
1.912
1.863
1.830
1.697
1.672
1.663
1.656
1.607
1.548
1.537
1.523
1.396
1.366
1.334
1.303
1.180
1.141
1.110
1.079
1.050
1.027
1.019
O
N
H
N
1b
1.00
0.68
4.00
3.30
2.15
6.58
2.21
3.09
f1 (ppm)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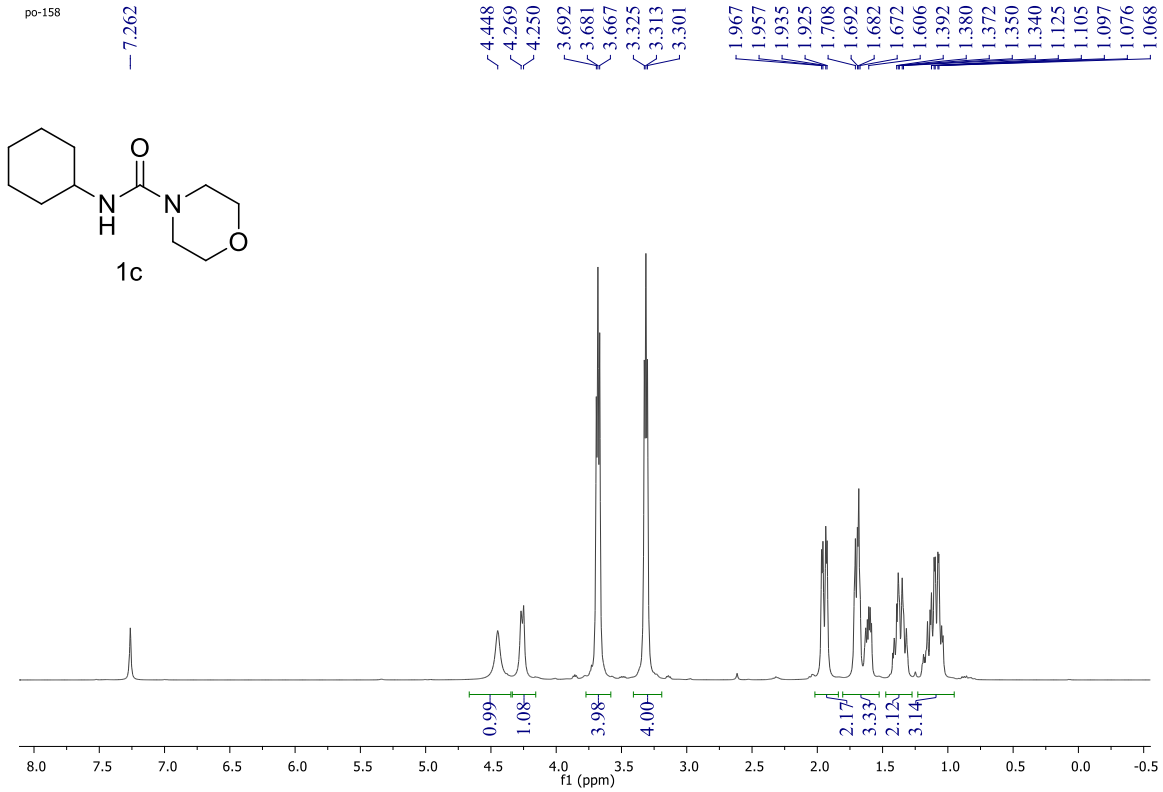
77.148
76.830
49.302
44.765
33.963
25.658
25.546
25.100
24.410
f1 (ppm)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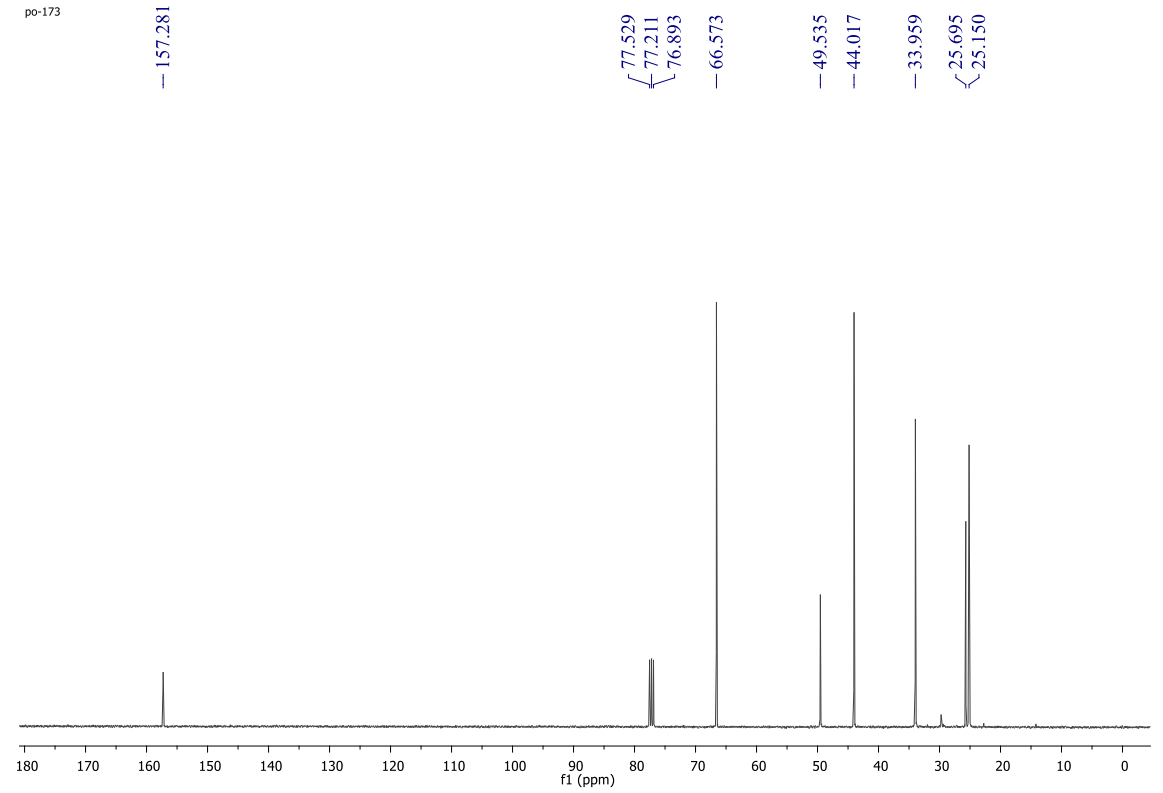
3.681
3.667
3.325
3.313
3.301
1.967
1.957
1.935
1.925
1.708
1.692
1.682
1.672
1.606
1.392
1.380
1.372
1.350
1.340
1.125
1.105
1.097
1.076
1.068
O
N
H
N
O
1c
0.99
1.08
3.98
4.00
2.17
3.33
2.12
3.14
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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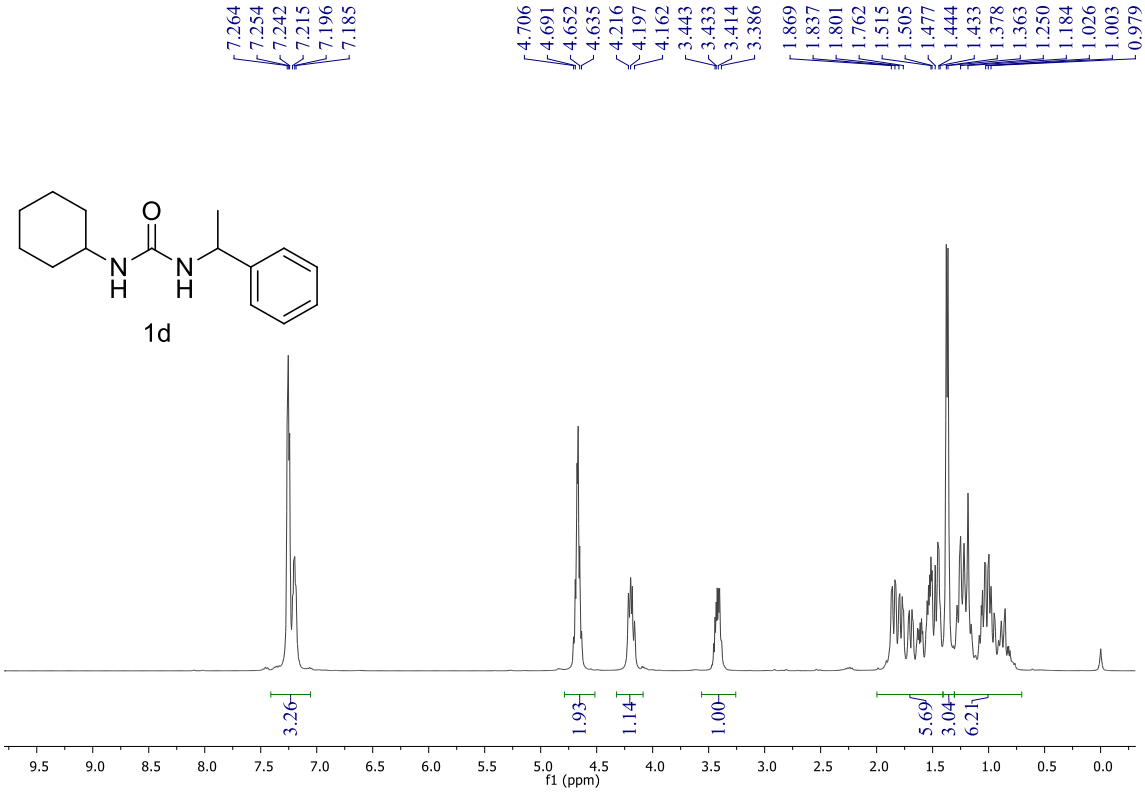
77.211
76.893
66.573
49.535
44.017
33.959
25.695
25.150
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.254
7.242
7.215
7.196
7.185
4.706
4.691
4.652
4.635
4.216
4.197
4.162
3.443
3.433
3.414
3.386
1.869
1.837
1.801
1.762
1.515
1.505
1.477
1.444
1.433
1.378
1.363
1.250
1.184
1.026
1.003
0.979
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H
N
H
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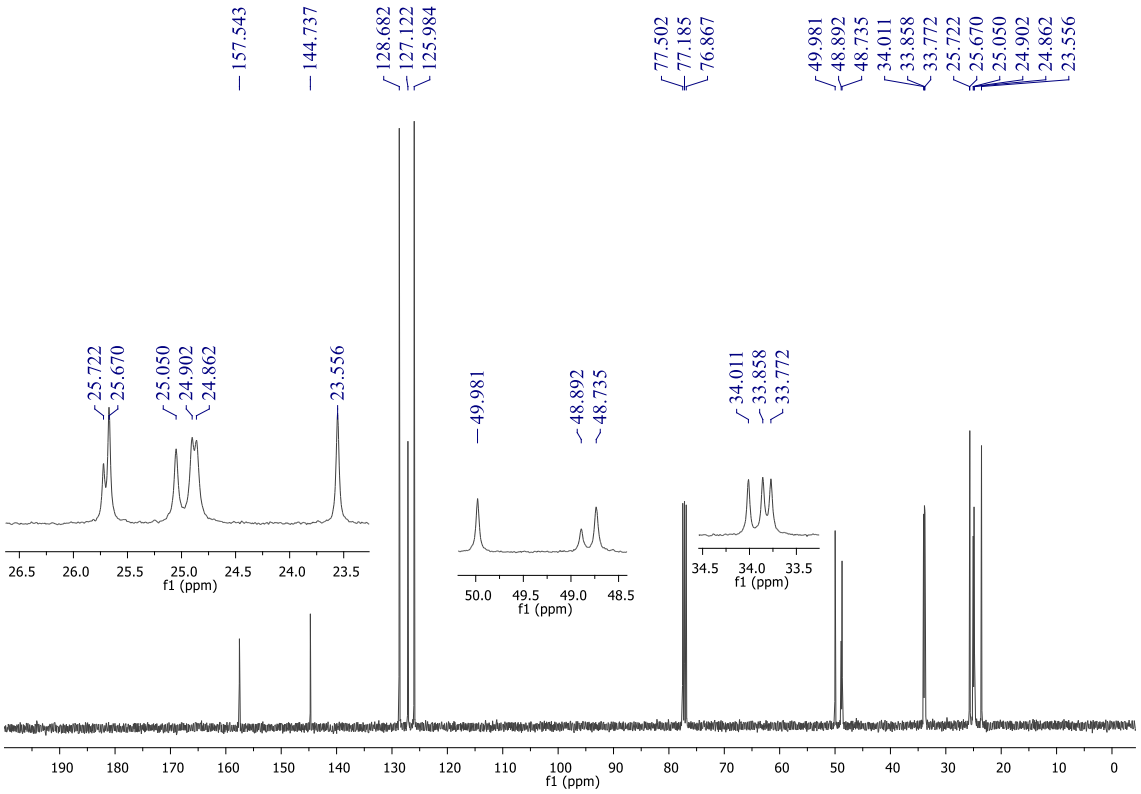
3.26
1.93
1.14
1.00
5.69
3.04
6.21
f1 (ppm)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127.122
125.984
77.502
77.185
76.867
49.981
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48.735
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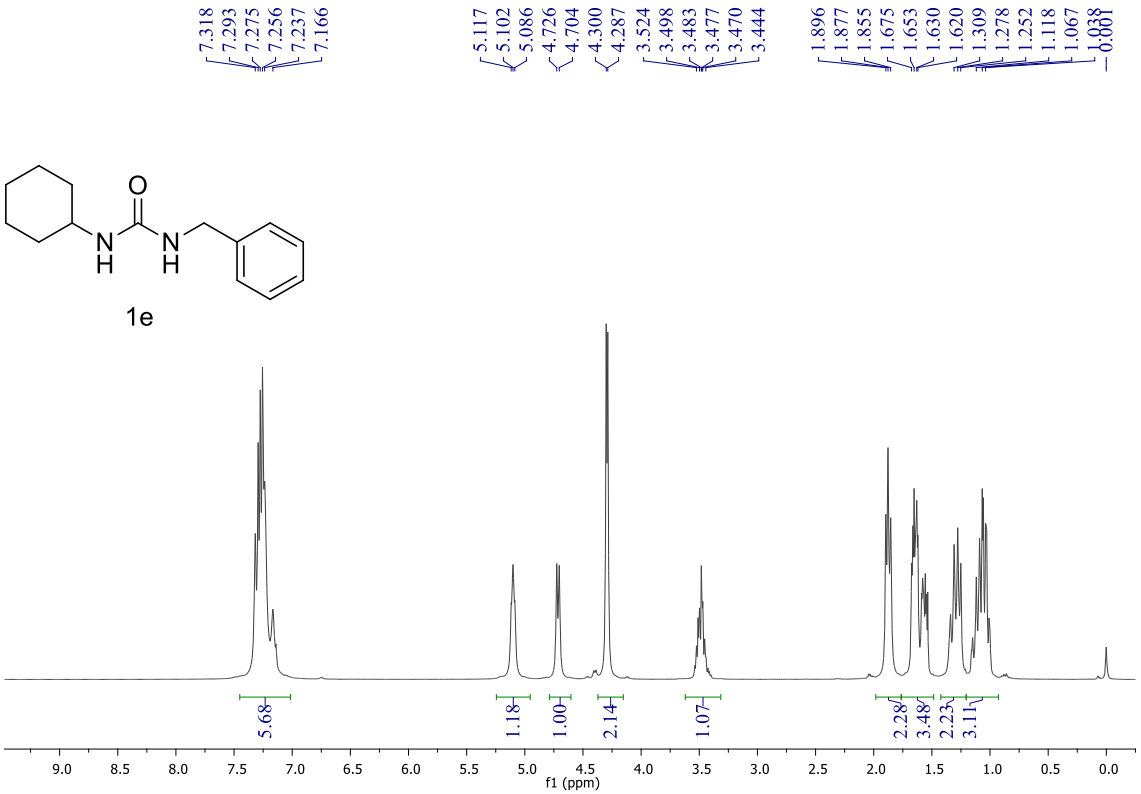
33.858
33.772
25.722
25.670
25.050
24.902
24.862
23.556
f1 (ppm)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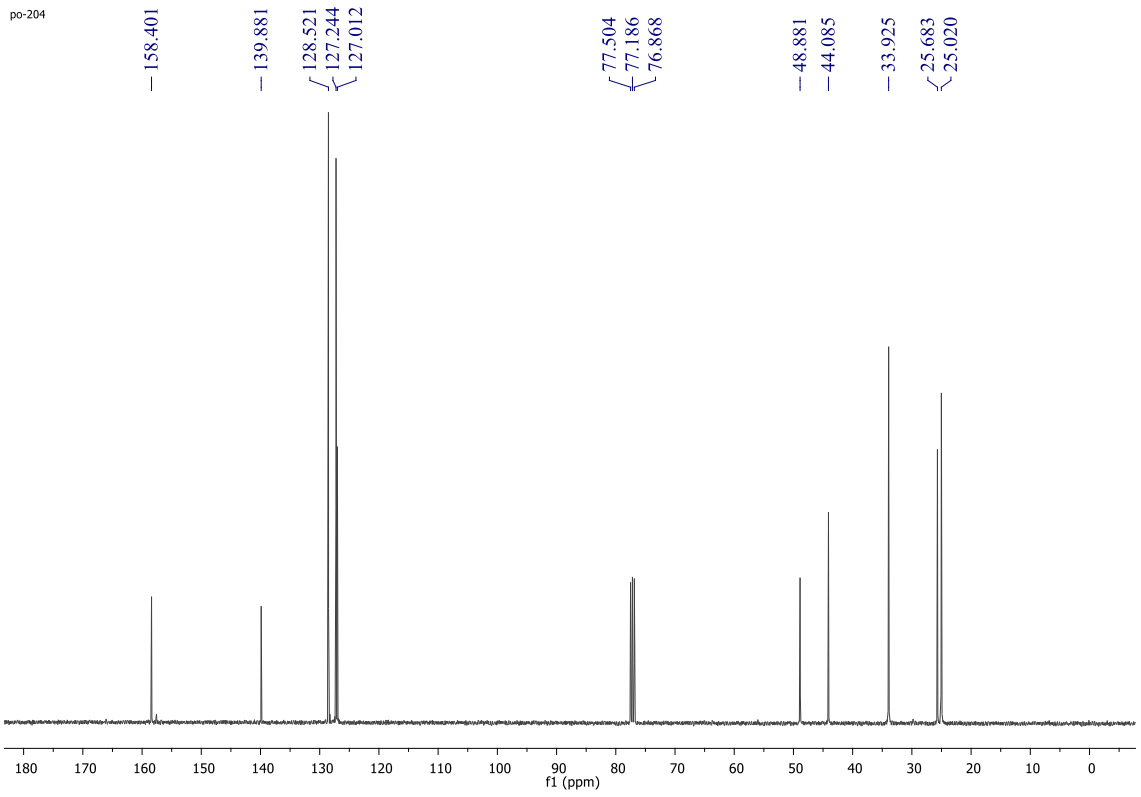
7.293
7.275
7.256
7.237
7.166
5.117
5.102
5.086
4.726
4.704
4.300
4.287
3.524
3.498
3.483
3.477
3.470
3.444
1.896
1.877
1.855
1.675
1.653
1.630
1.620
1.309
1.278
1.252
1.118
1.067
1.038
0.001
O
N
H
N
H
1e
5.68
1.18
1.00
2.14
1.07
2.28
3.48
2.23
3.11
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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128.521
127.244
127.012
77.504
77.186
76.868
48.881
44.085
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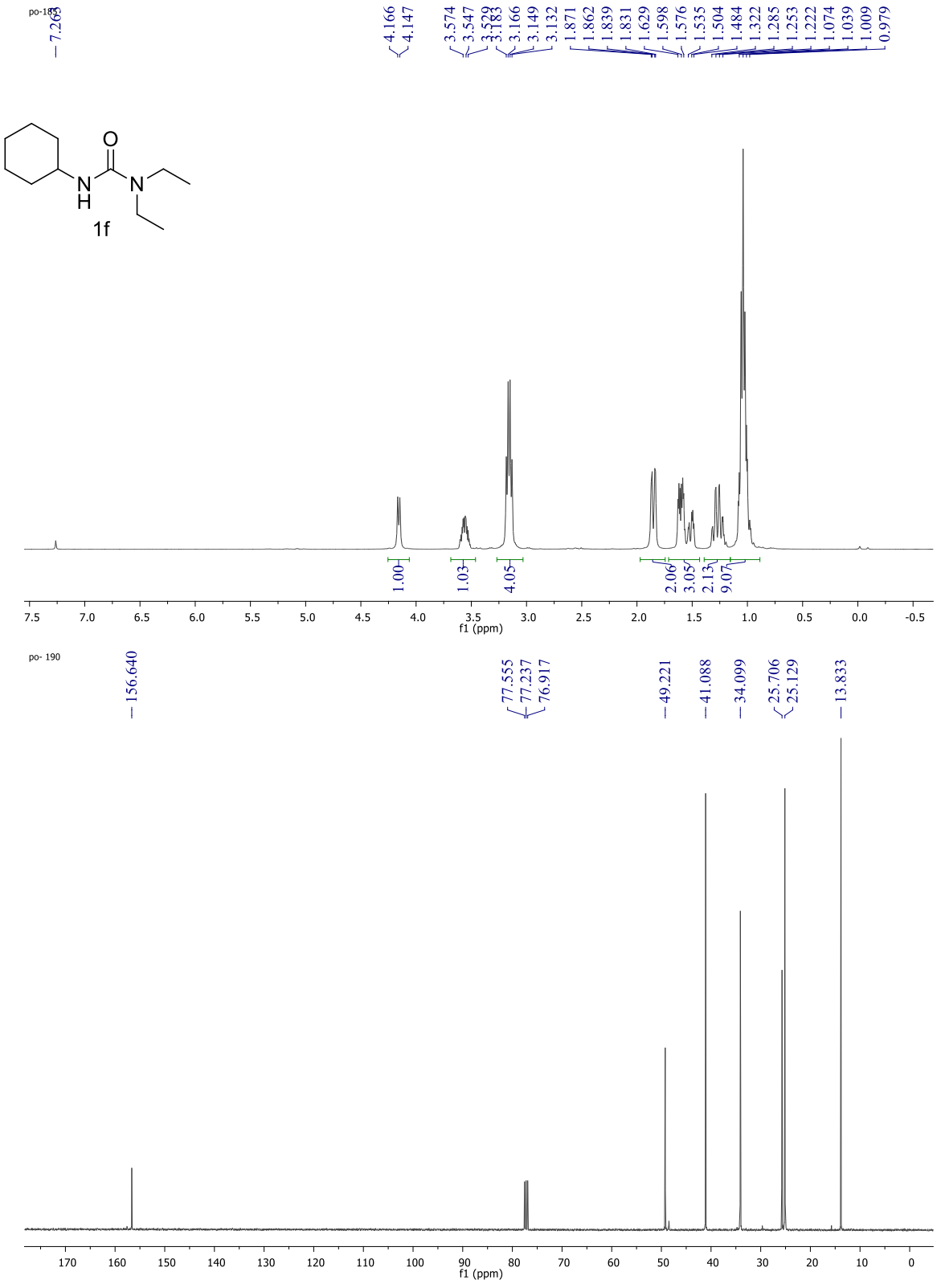
25.683
25.020
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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3.574
3.547
3.529
3.183
3.166
3.149
3.132
1.871
1.862
1.839
1.831
1.629
1.598
1.576
1.535
1.504
1.484
1.322
1.285
1.253
1.222
1.074
1.039
1.009
0.979
O
N
H
N
1f
1.00
1.03
4.05
2.06
3.05
2.13
9.07
f1 (ppm)
po- 190
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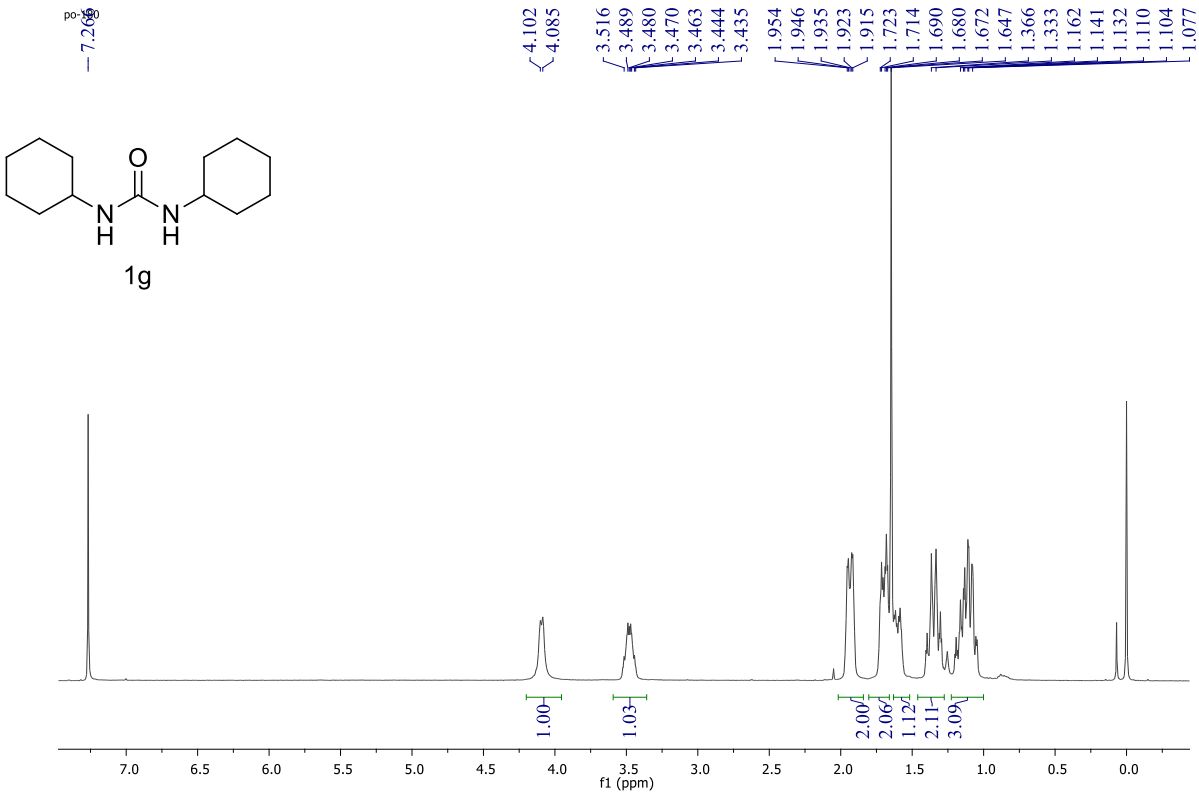
77.237
76.917
49.221
41.088
34.099
25.706
25.129
13.833
f1 (ppm)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3.435
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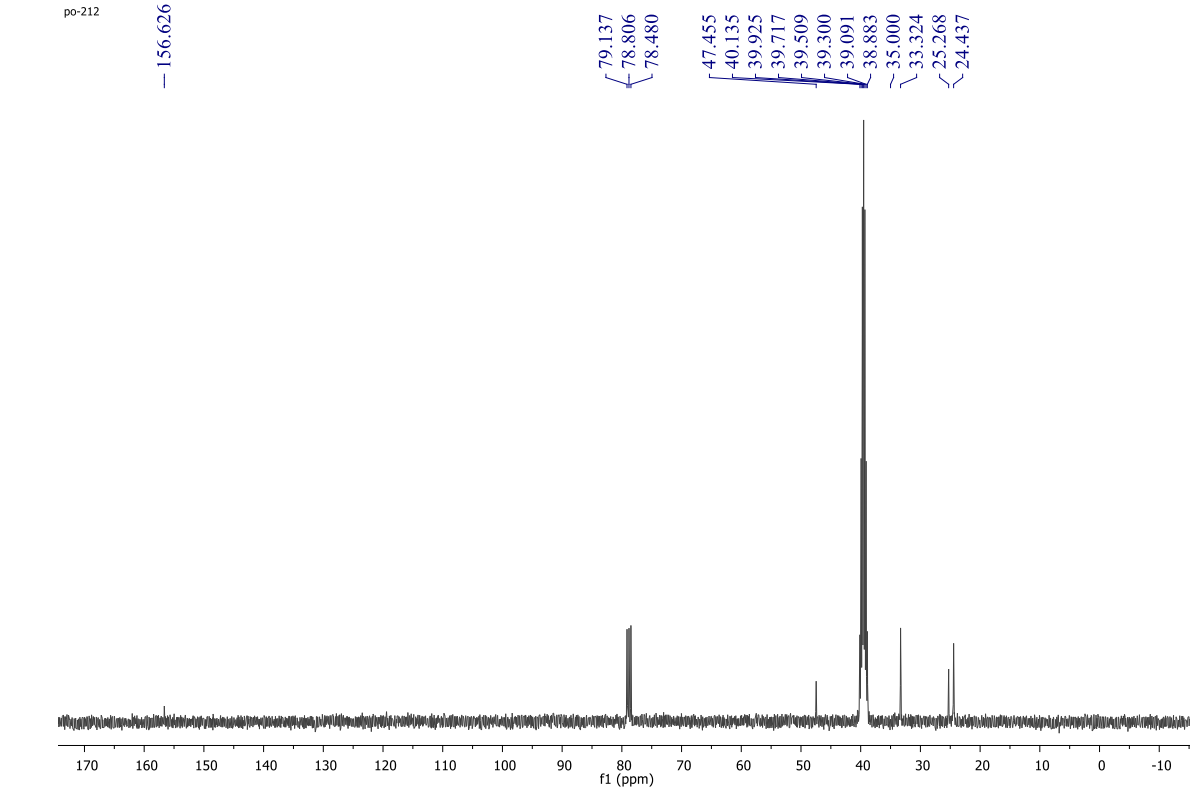
1.935
1.923
1.915
1.723
1.714
1.690
1.680
1.672
1.647
1.366
1.333
1.162
1.141
1.132
1.110
1.104
1.077
O
N
H
N
H
1g
1.00
1.03
2.00
2.06
1.12
2.11
3.09
f1 (ppm)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78.480
47.455
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39.925
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39.509
39.300
39.091
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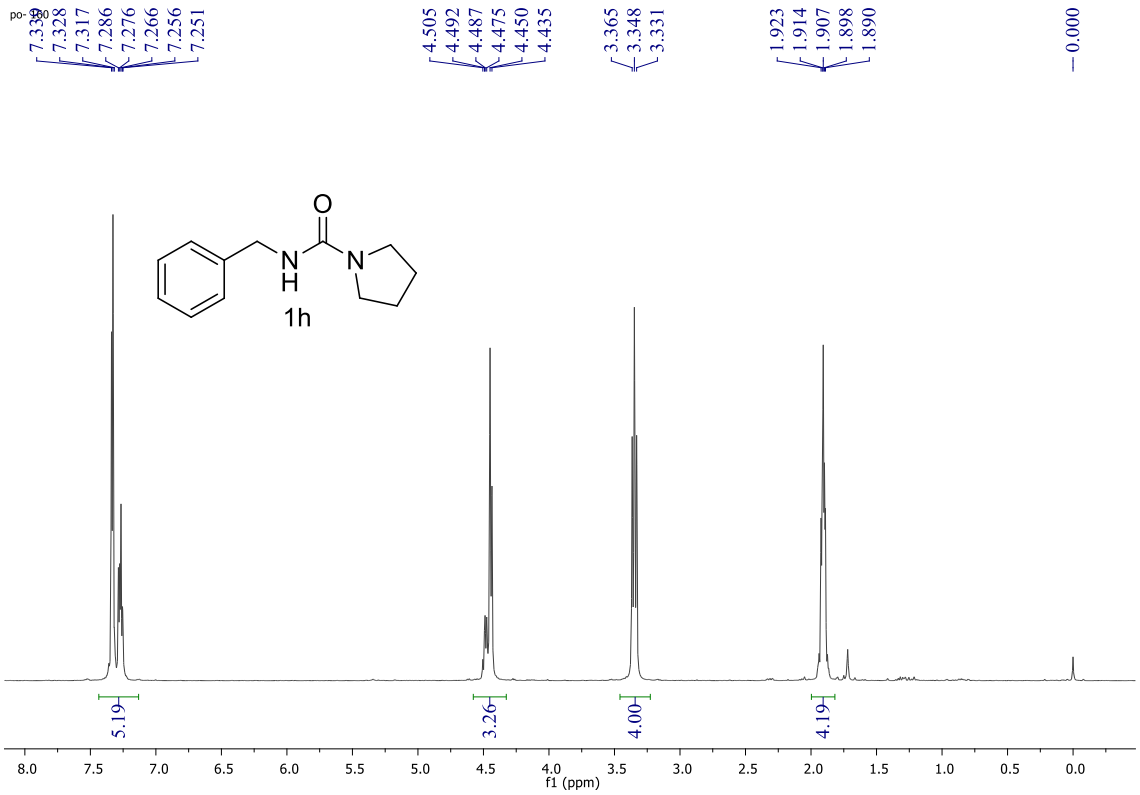
35.000
33.324
25.268
24.437
f1 (ppm)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7.276
7.266
7.256
7.251
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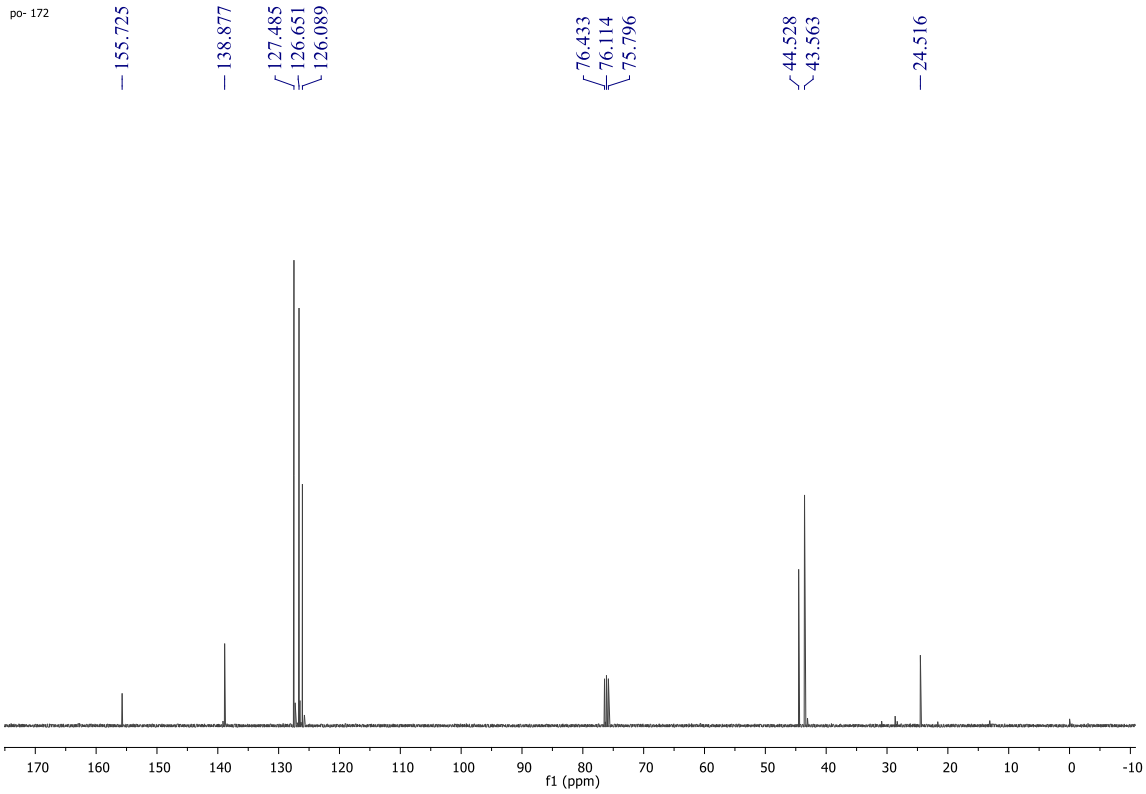
4.492
4.487
4.475
4.450
4.435
3.365
3.348
3.331
1.923
1.914
1.907
1.898
1.890
0.000
O
N
H
N
1h
5.19
3.26
4.00
4.19
f1 (ppm)


po- 172
155.725
138.877
127.485
126.651
126.089
76.433
76.114
75.796
44.528
43.563
24.516
f1 (ppm)

PO- 156

7.256
7.240
7.226
7.203
7.190
7.181
7.172
4.684
4.354
4.341
3.275
3.262
3.249
1.526
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1.500
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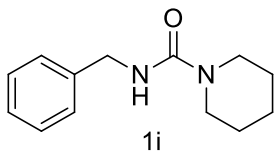
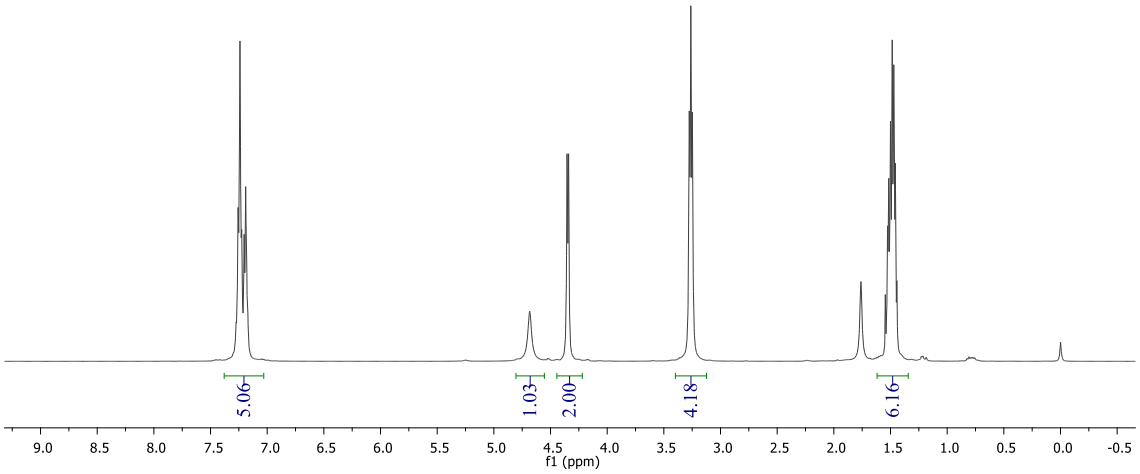
1.471
1.458
-0.001



1i



PO- 167

157.519
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128.409
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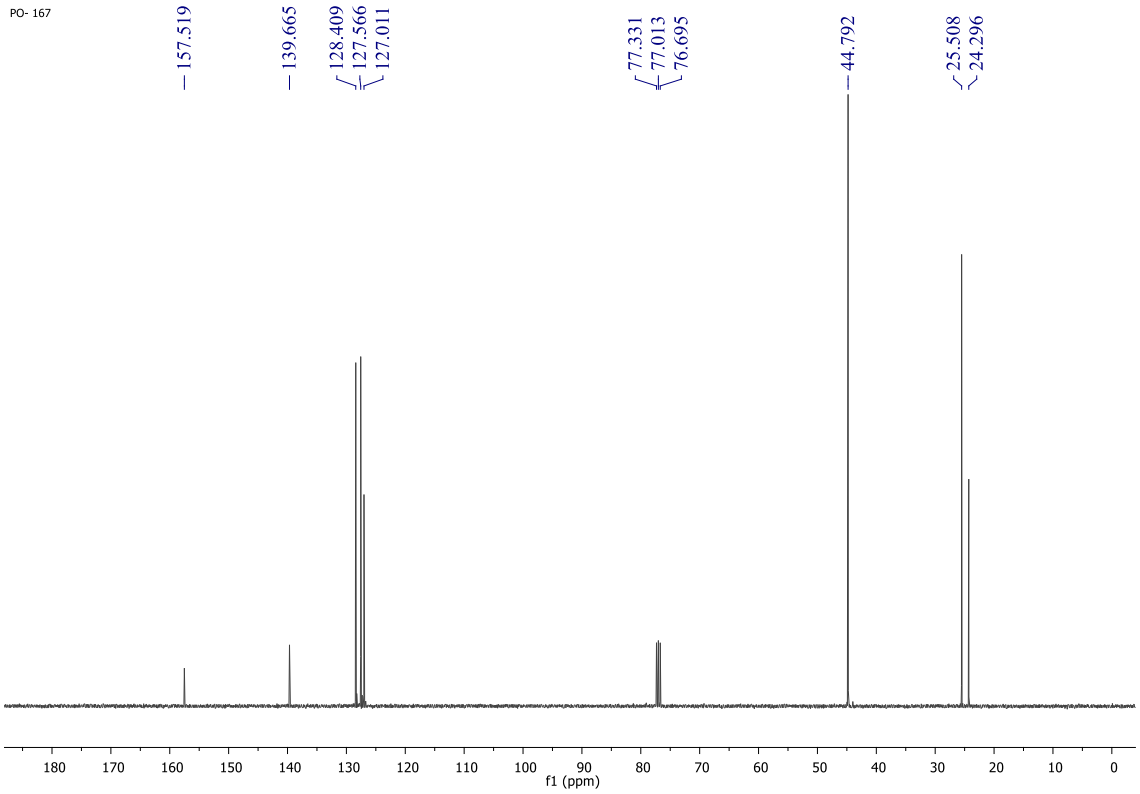
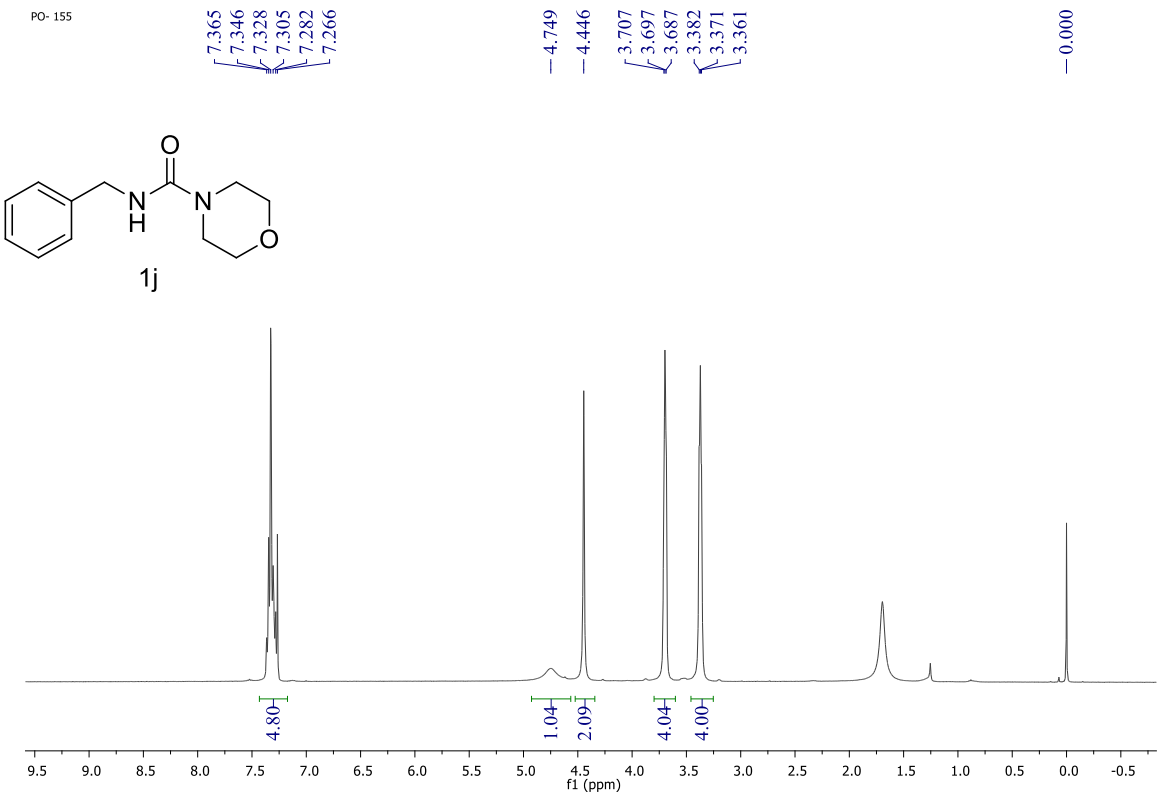
127.011
77.331
77.013
76.695
44.792
25.508
24.296

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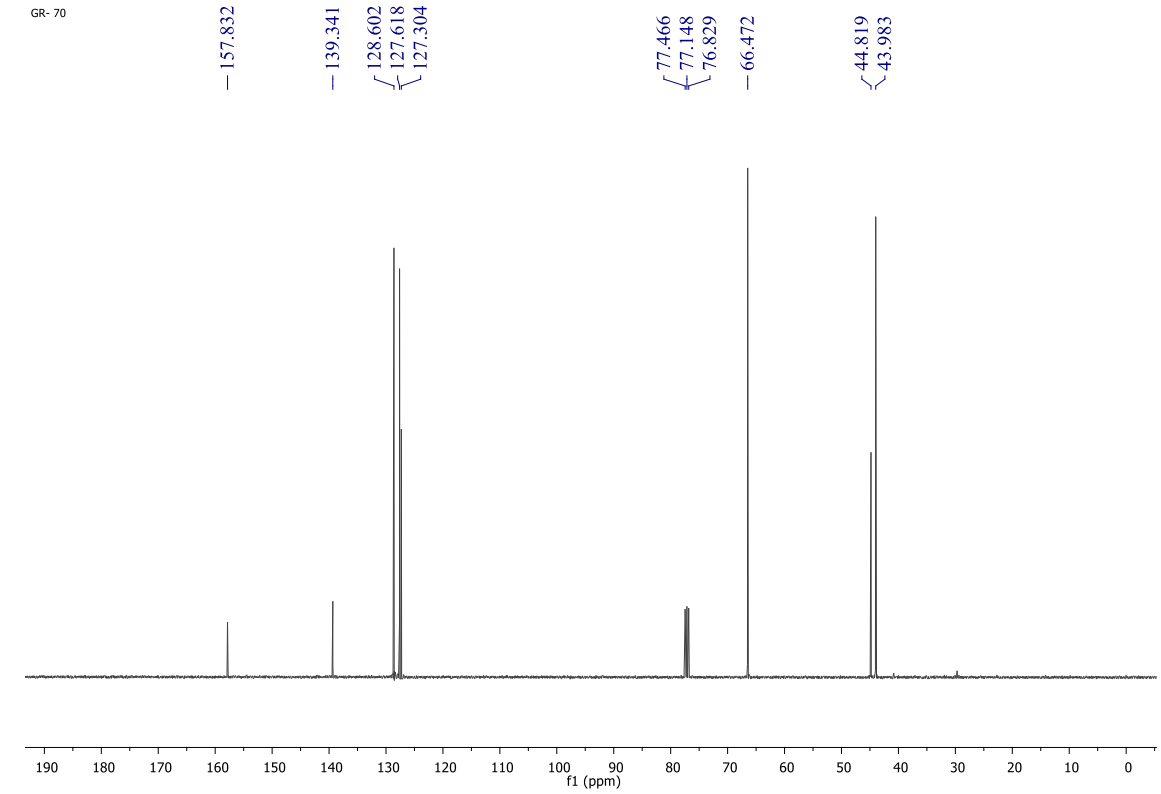
7.328
7.305
7.282
7.266
4.749
4.446
3.707
3.697
3.687
3.382
3.371
3.361
0.000
O
N
H
N
O
1j
4.80
1.04
2.09
4.04
4.00
f1 (ppm)


GR- 70
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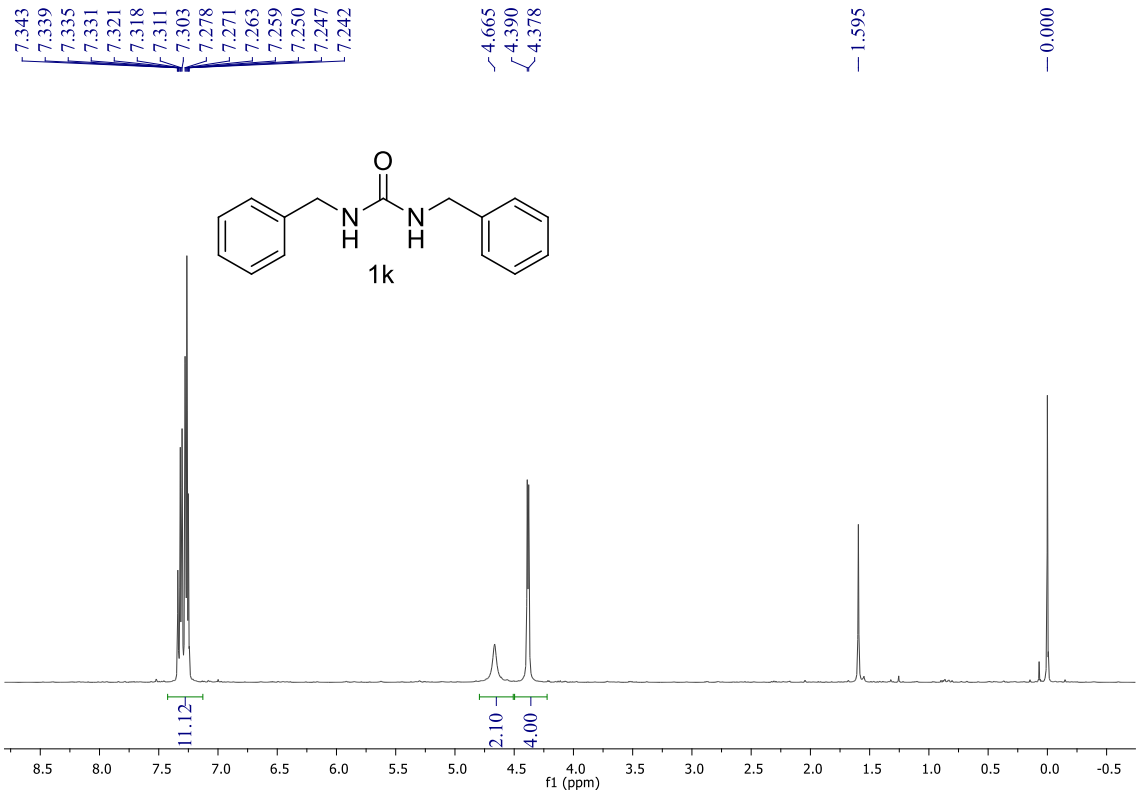
127.304
77.466
77.148
76.829
66.472
44.819
43.983
f1 (ppm)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7.335
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7.321
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7.311
7.303
7.278
7.271
7.263
7.259
7.250
7.247
7.242
4.665
4.390
4.378
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0.000
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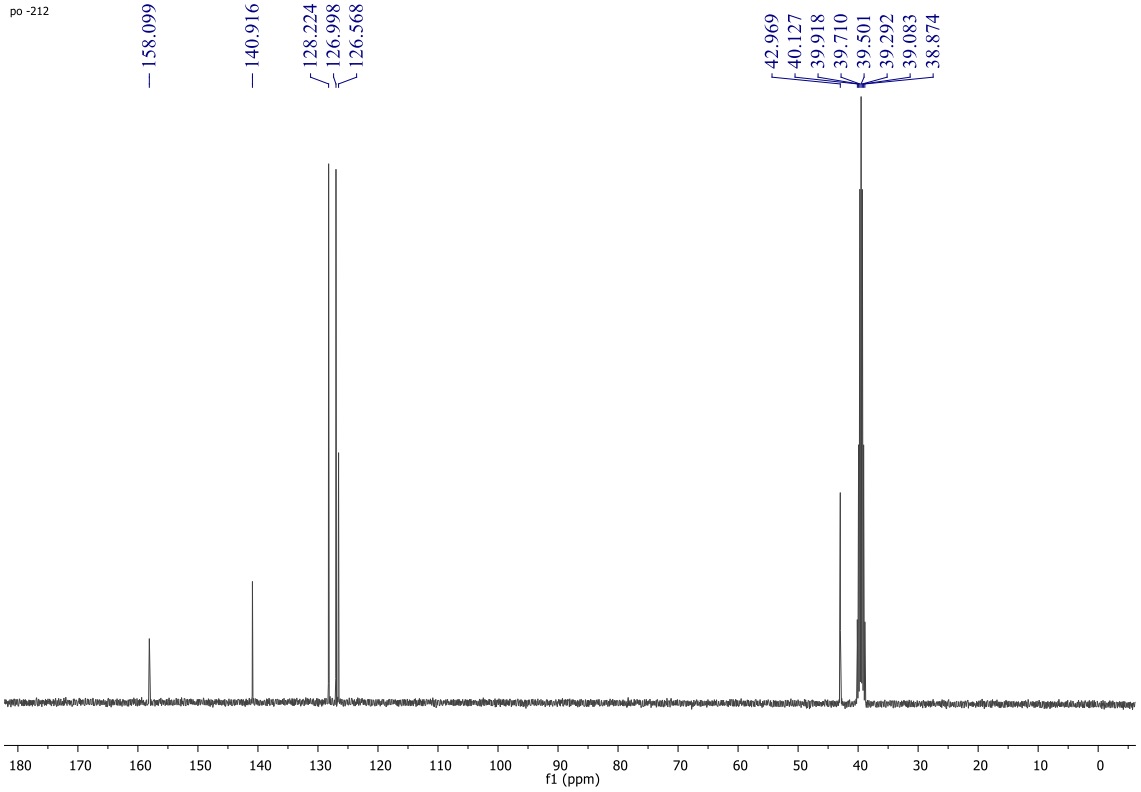
N
H
N
H
1k
11.12
2.10
4.00
f1 (ppm)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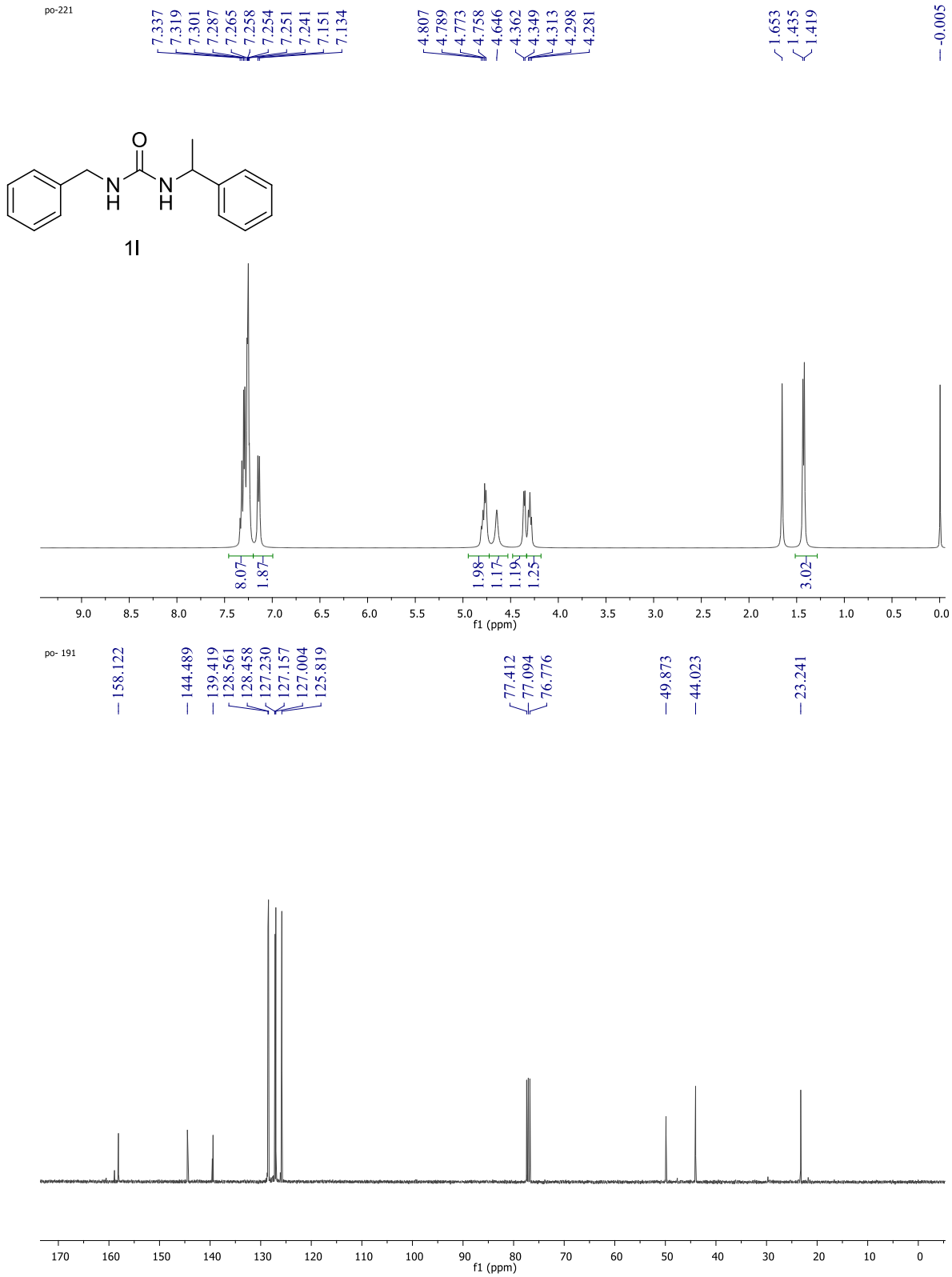
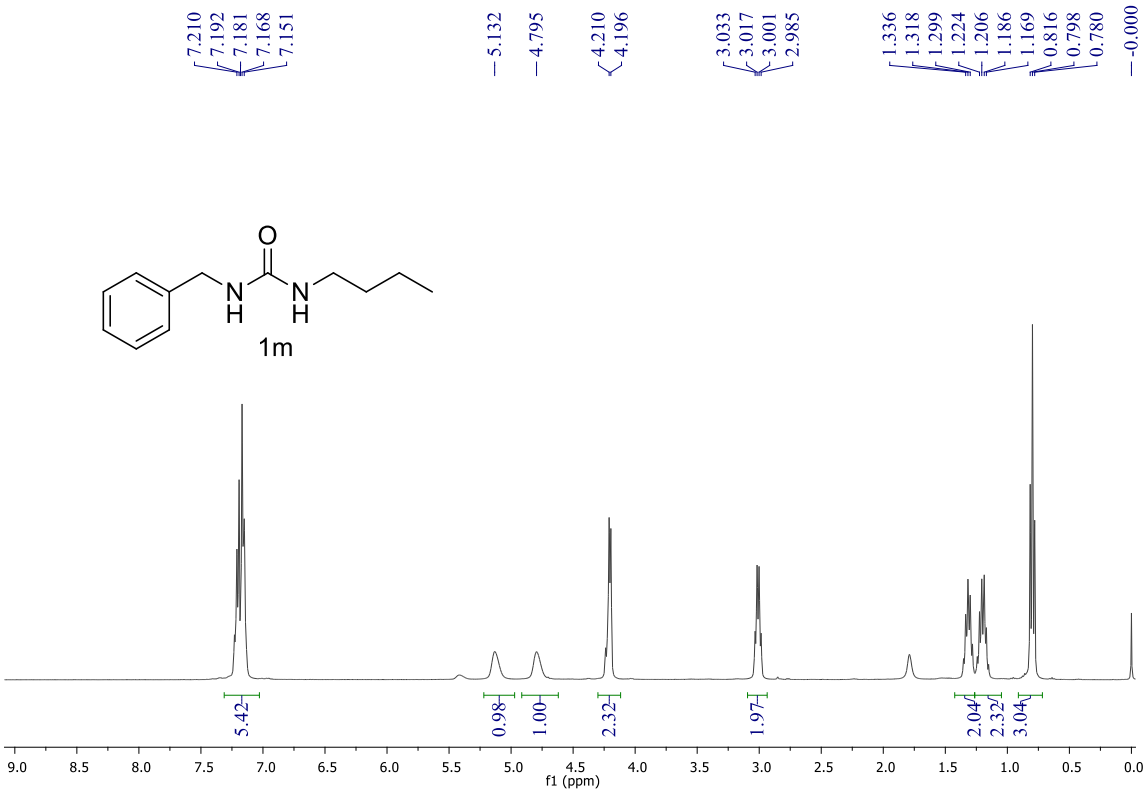
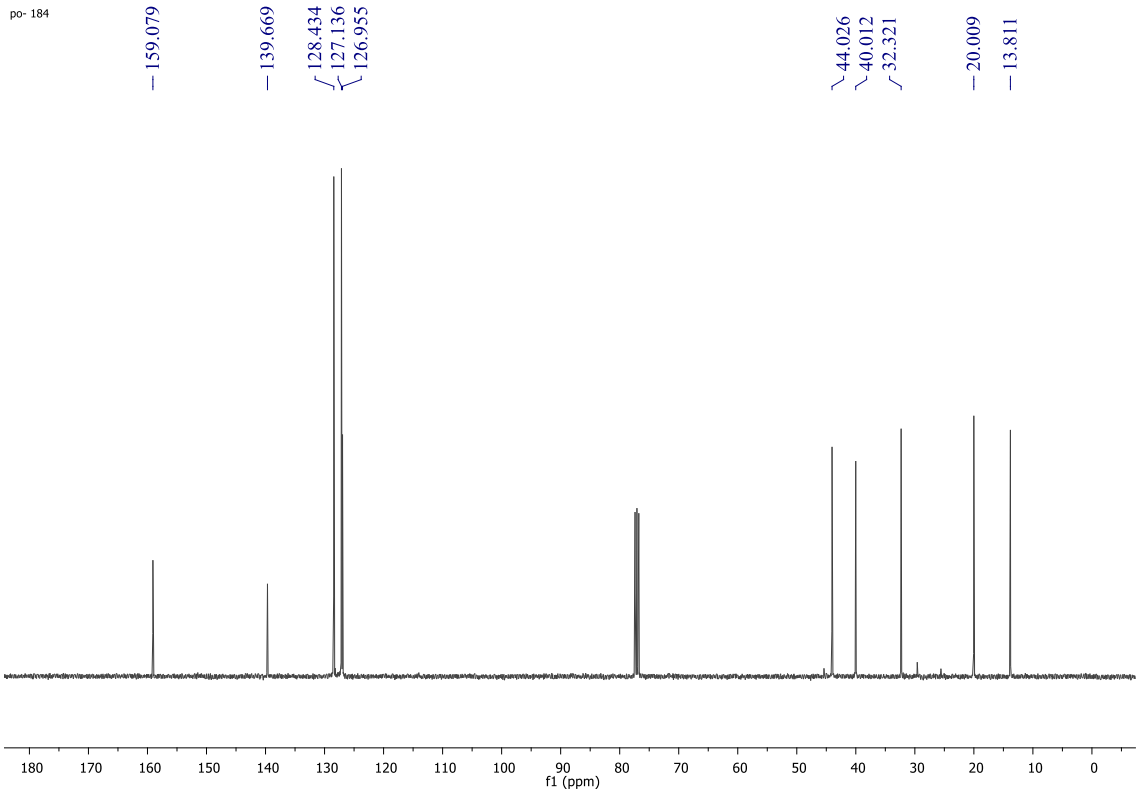
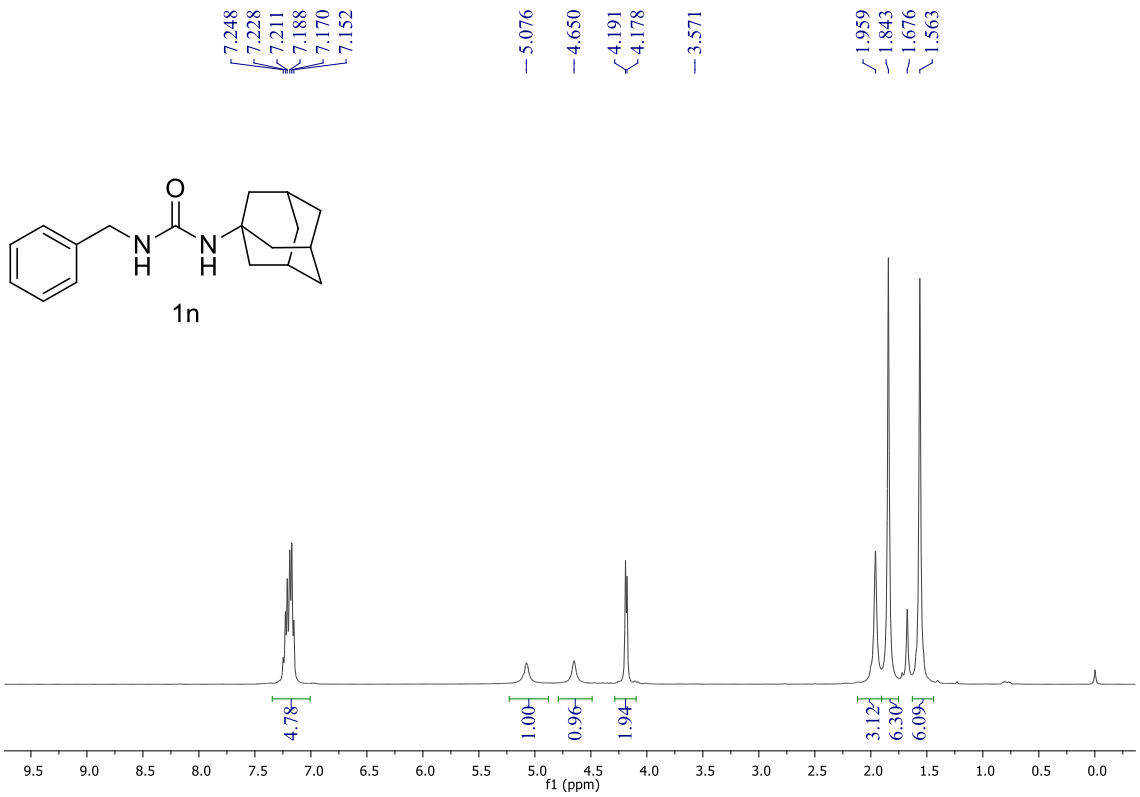
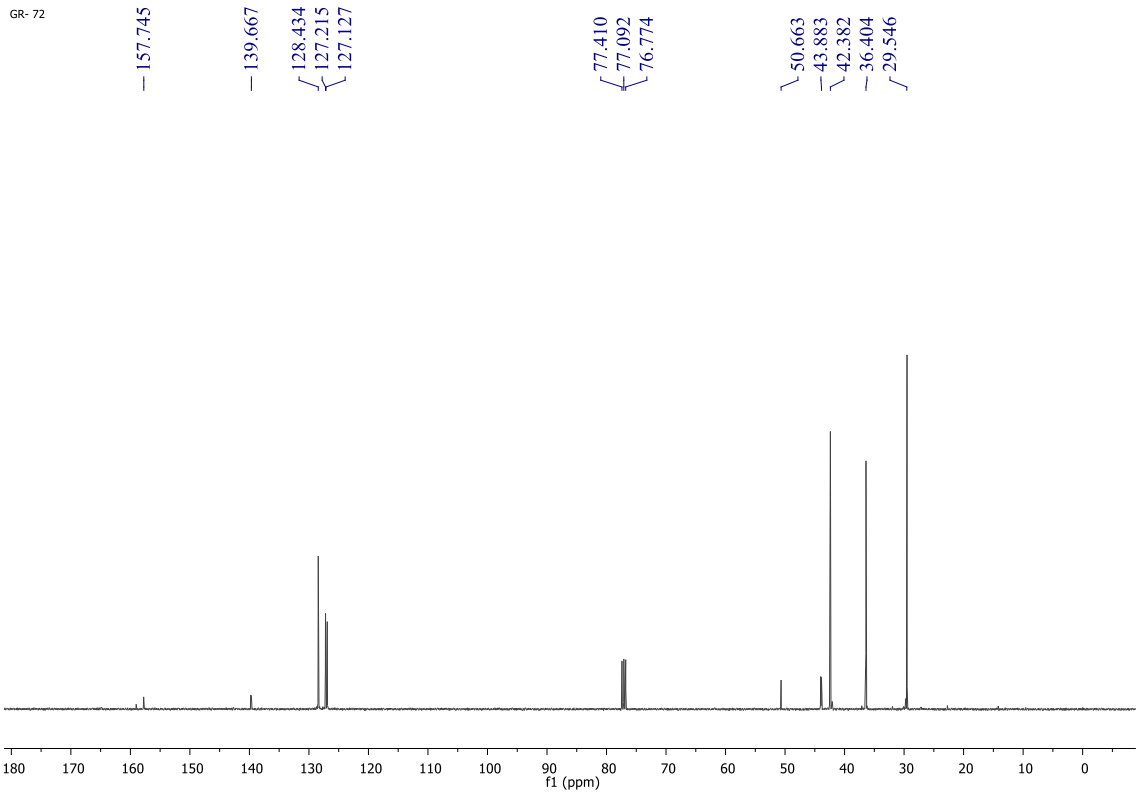
140.916
128.224
126.998
126.568
42.969
40.127
39.918
39.710
39.501
39.292
39.083
38.874
f1 (ppm)

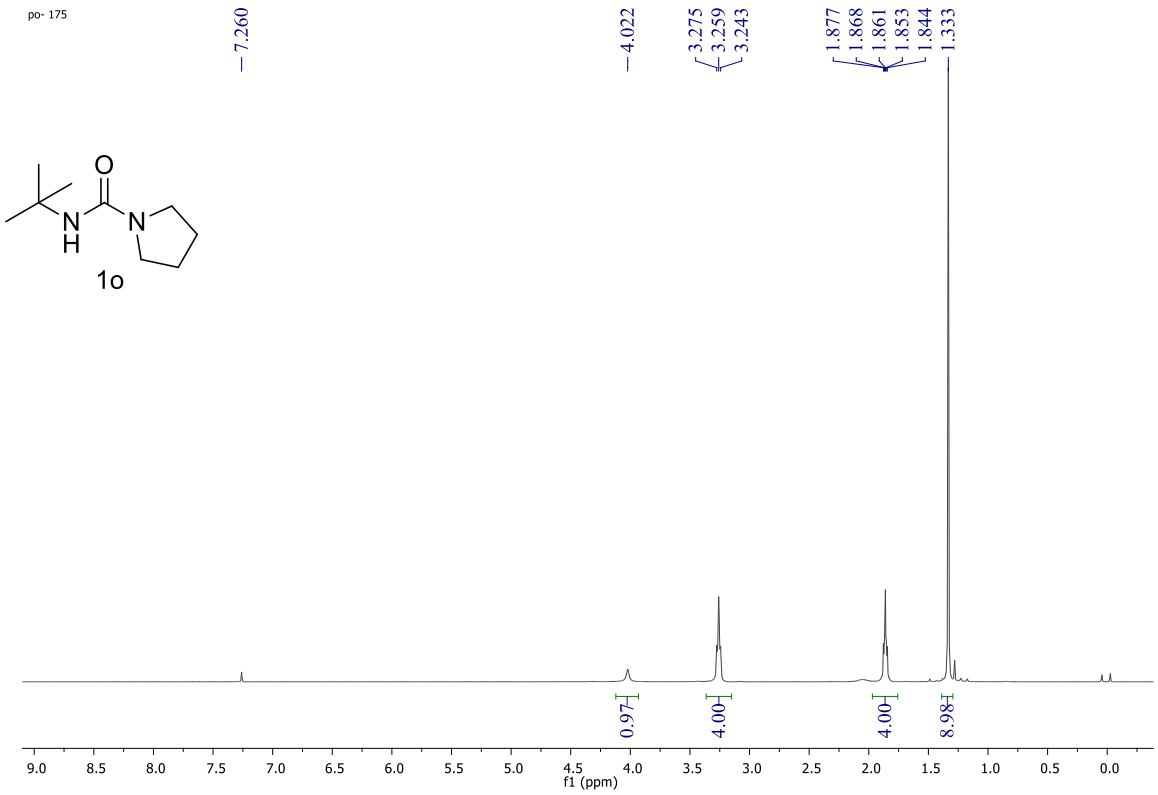

po-221
7.337
7.319
7.301
7.287
7.265
7.258
7.254
7.251
7.241
7.151
7.134
4.807
4.789
4.773
4.758
4.646
4.362
4.349
4.313
4.298
4.281
1.653
1.435
1.419
-0.005
O
N
H
N
H
1l
8.07
1.87
1.98
1.17
1.19
1.25
3.02
f1 (ppm)
po- 191
158.122
144.489
139.419
128.561
128.458
127.230
127.157
127.004
125.819
77.412
77.094
76.776
49.873
44.023
23.241
f1 (ppm)

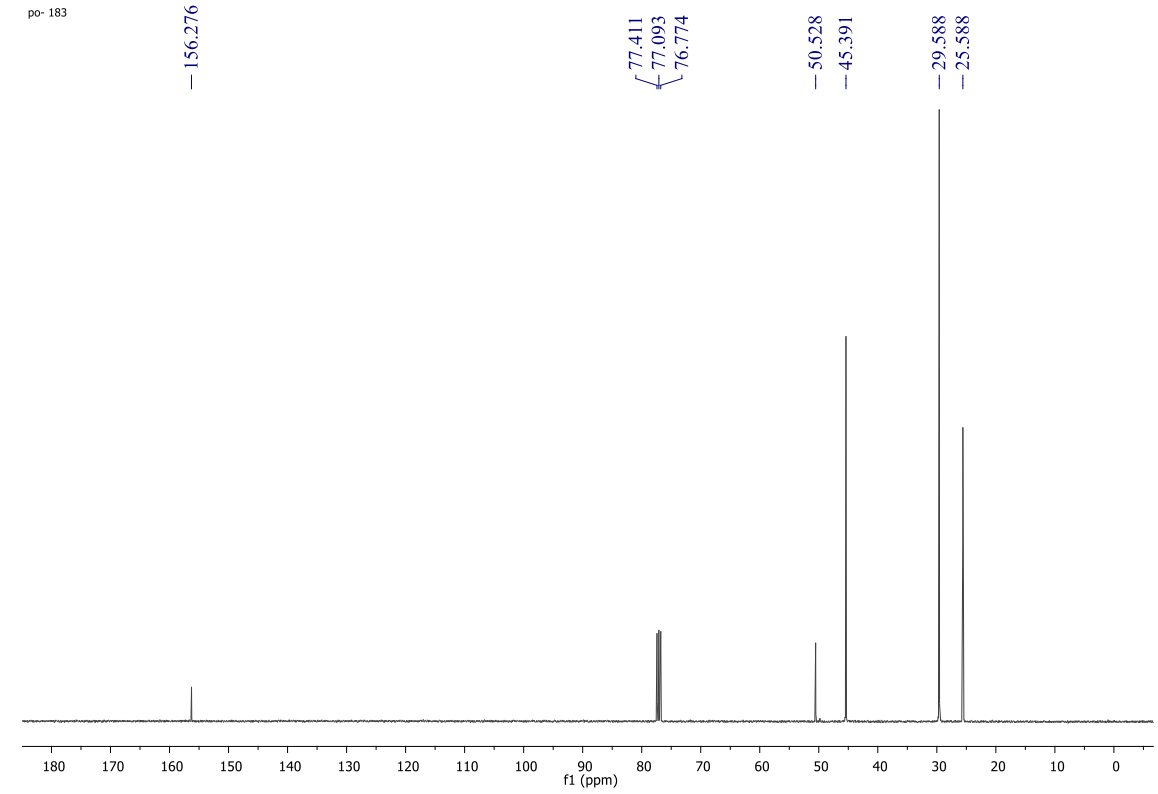

7.210
7.192
7.181
7.168
7.151
5.132
4.795
4.210
4.196
3.033
3.017
3.001
2.985
1.336
1.318
1.299
1.224
1.206
1.186
1.169
0.816
0.798
0.780
-0.000
O
N
H
N
H
1m
5.42
0.98
1.00
2.32
1.97
2.04
2.32
3.04
f1 (ppm)

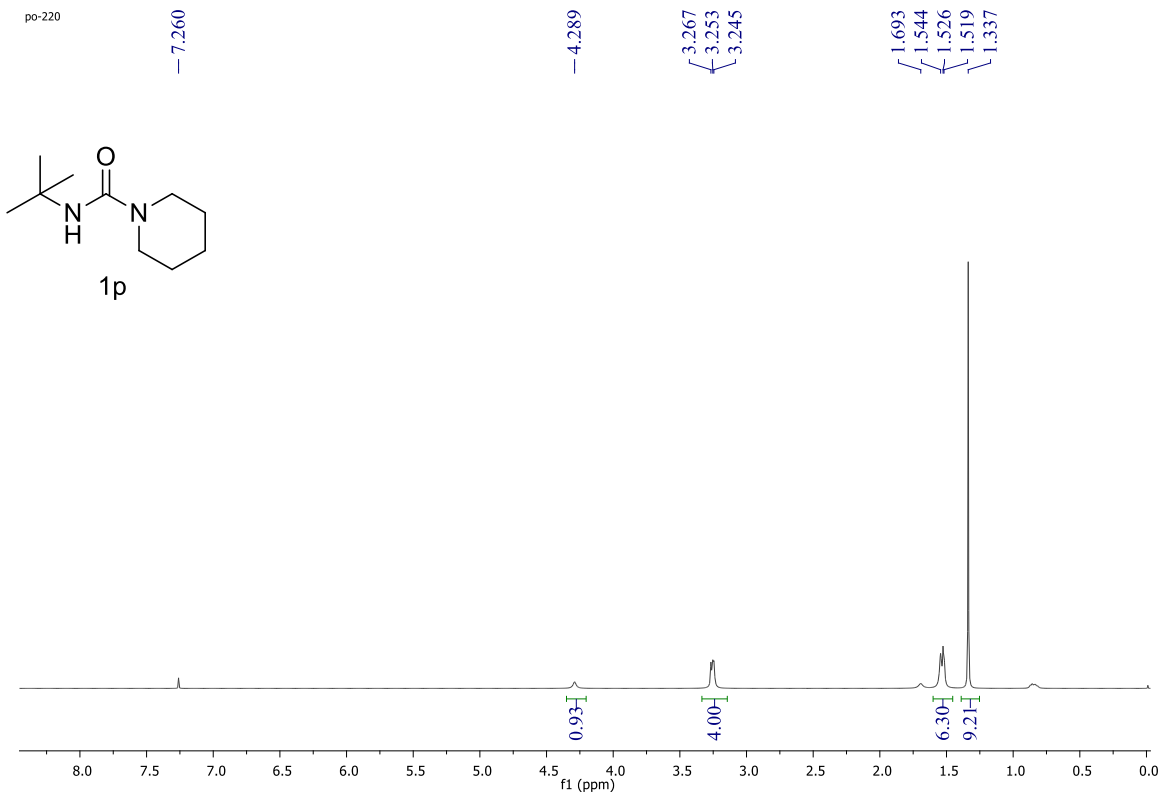

po- 184
159.079
139.669
128.434
127.136
126.955
44.026
40.012
32.321
20.009
13.811
f1 (ppm)

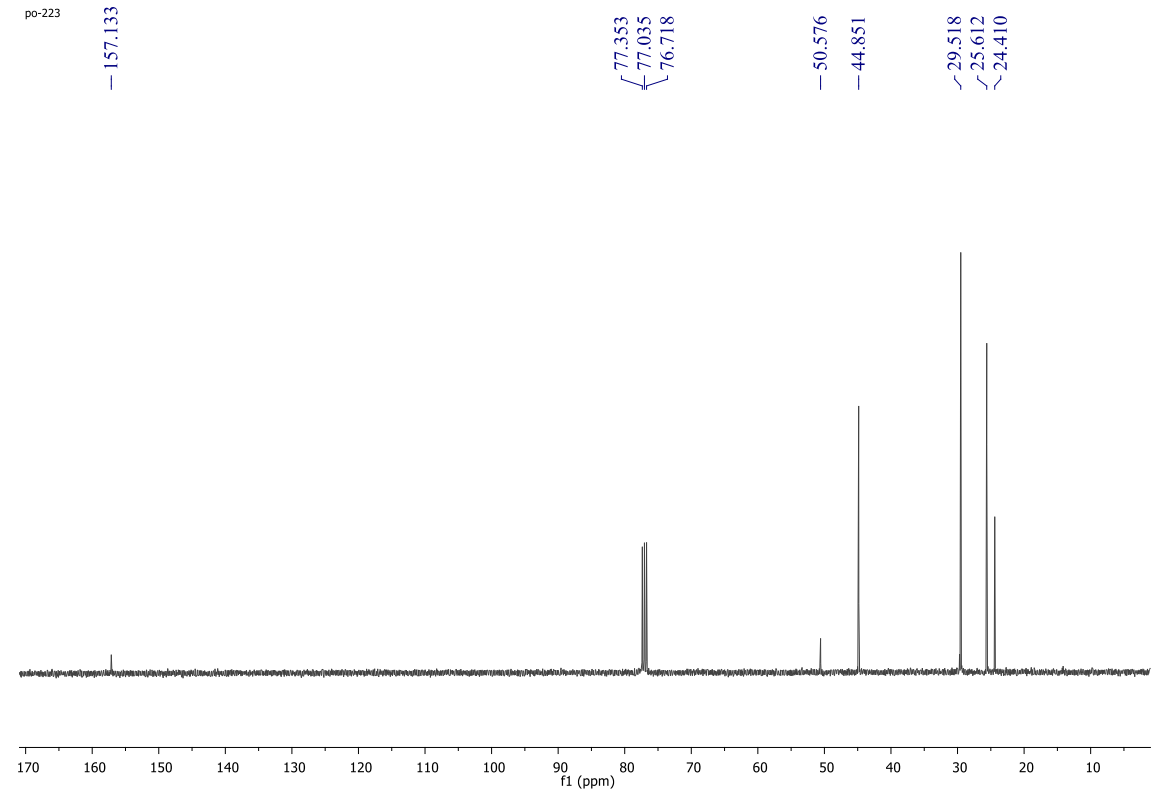

7.248
7.228
7.211
7.188
7.170
7.152
5.076
4.650
4.191
4.178
3.571
1.959
1.843
1.676
1.563
O
N
H
N
H
1n
4.78
1.00
0.96
1.94
3.12
6.30
6.09
f1 (ppm)

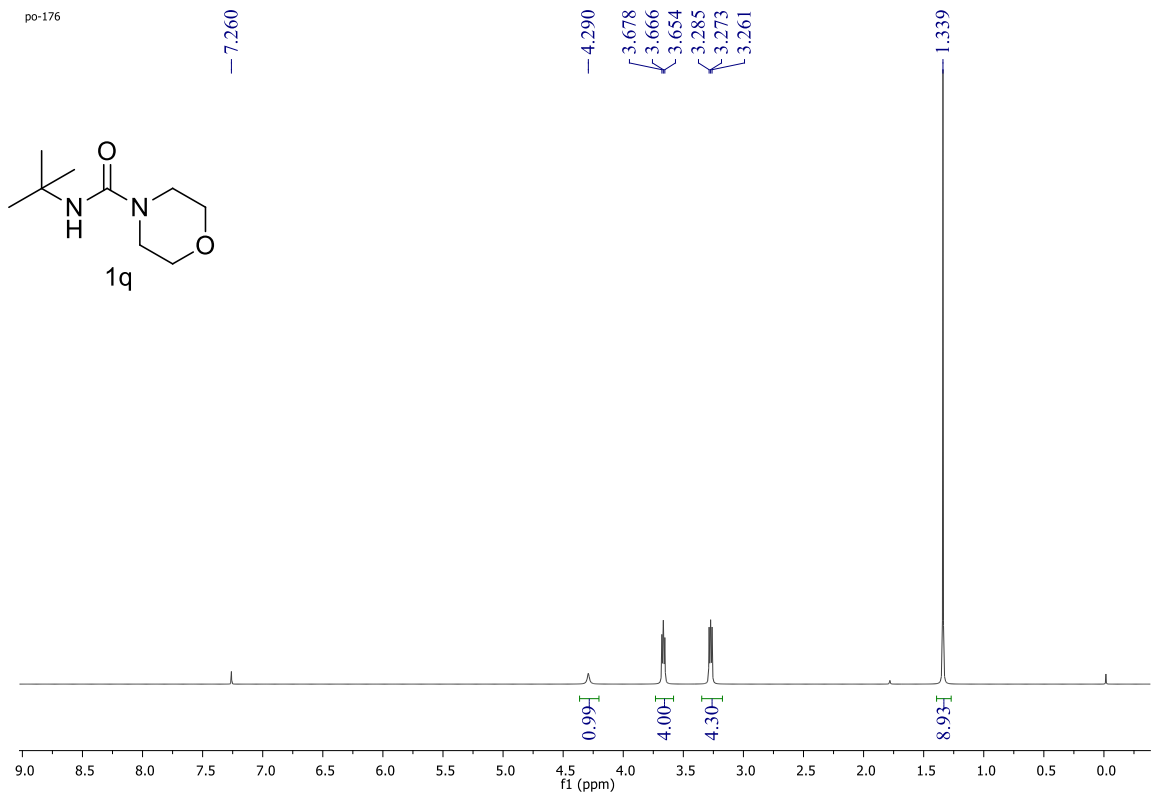

GR- 72
157.745
139.667
128.434
127.215
127.127
77.410
77.092
76.774
50.663
43.883
42.382
36.404
29.546
f1 (ppm)

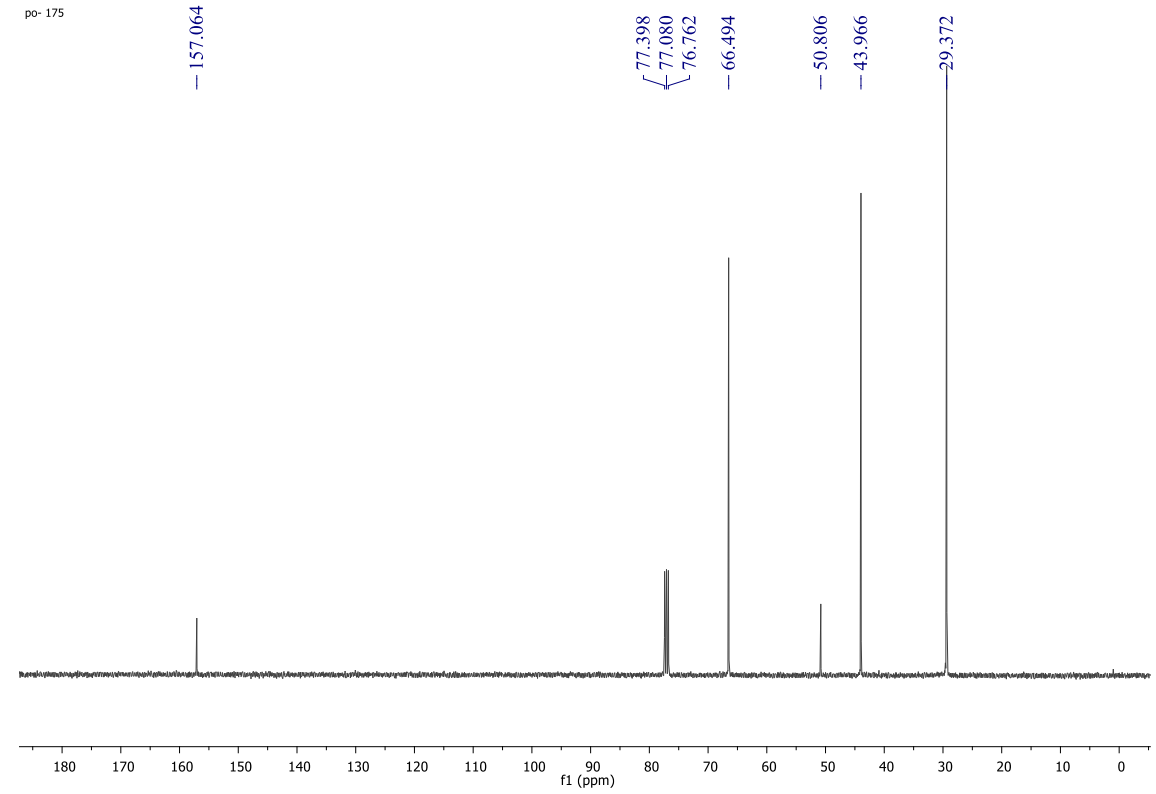

po- 175
7.260
4.022
3.275
3.259
3.243
1.877
1.868
1.861
1.853
1.844
1.333
O
N
H
N
1o
0.97
4.00
4.00
8.98
f1 (ppm)

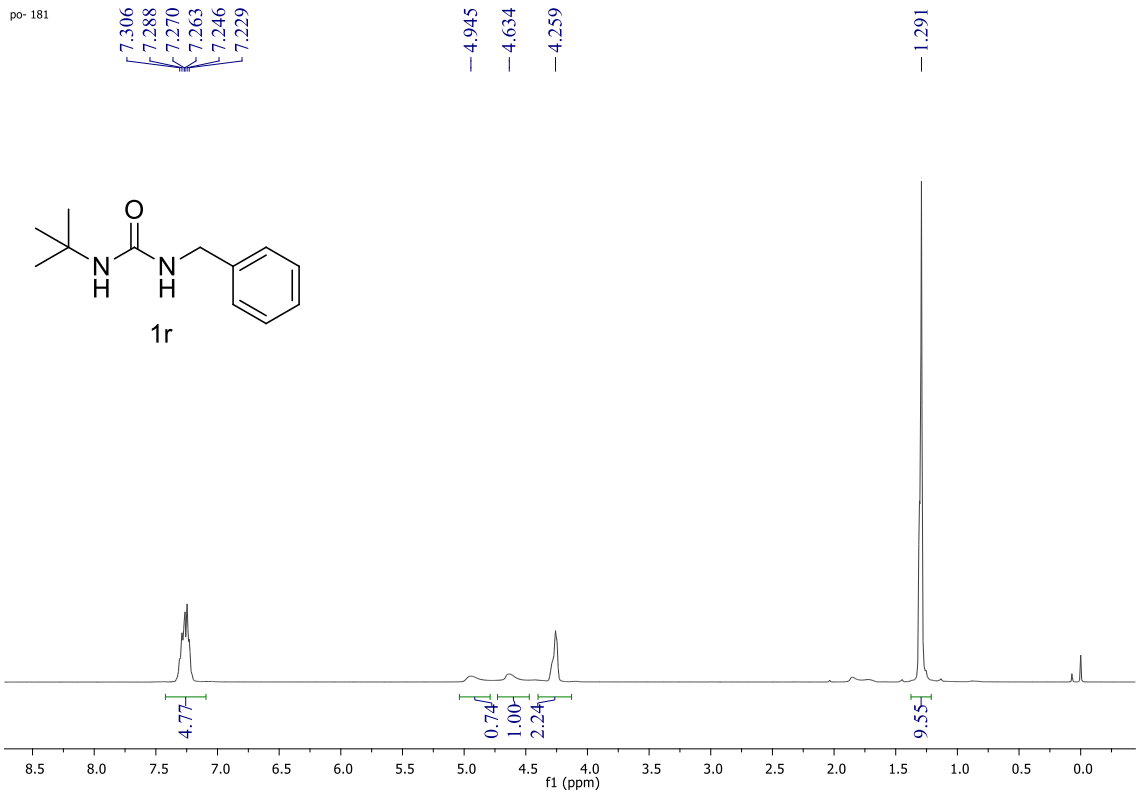

po- 183
156.276
77.411
77.093
76.774
50.528
45.391
29.588
25.588
f1 (ppm)

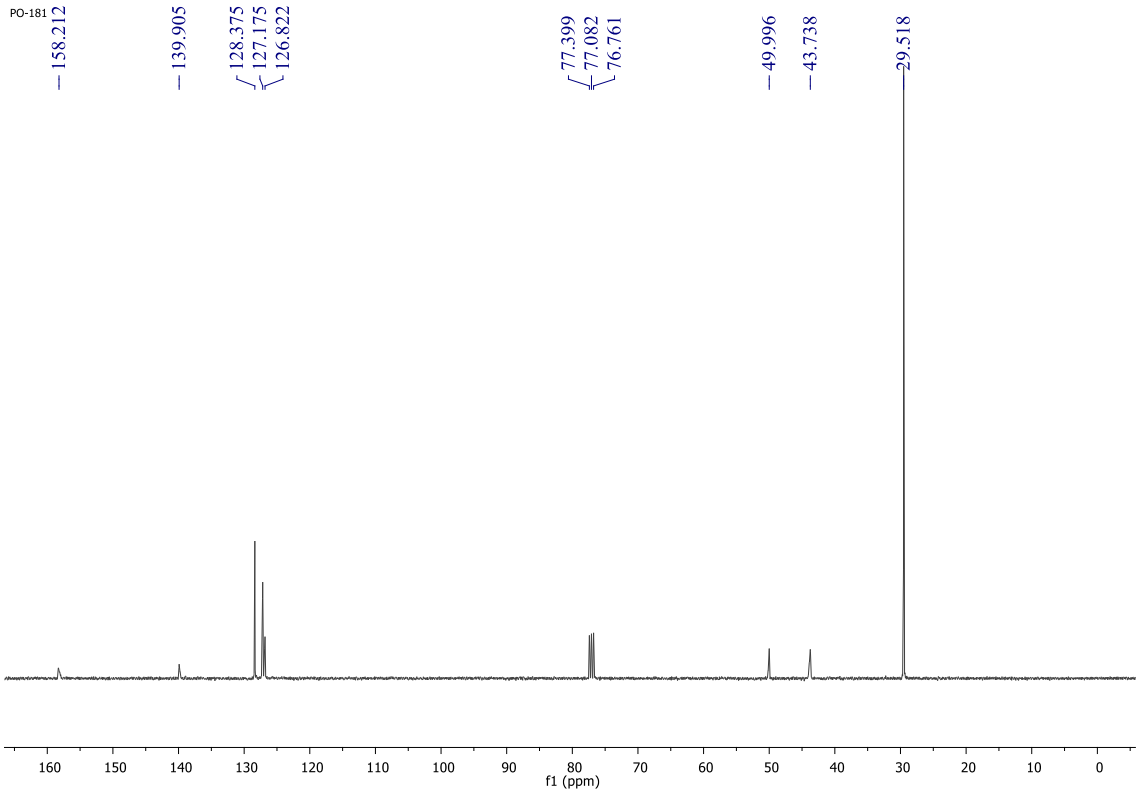

po-220
7.260
4.289
3.267
3.253
3.245
1.693
1.544
1.526
1.519
1.337
O
N
H
N
1p
0.93
4.00
6.30
9.21
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


po-223
157.133
77.353
77.035
76.718
50.576
44.851
29.518
25.612
24.410
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

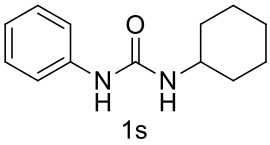

po-176
7.260
4.290
3.678
3.666
3.654
3.285
3.273
3.261
1.339
O
N
H
N
O
1q
0.99
4.00
4.30
8.93
f1 (ppm)


po- 175
157.064
77.398
77.080
76.762
66.494
50.806
43.966
29.372
f1 (ppm)

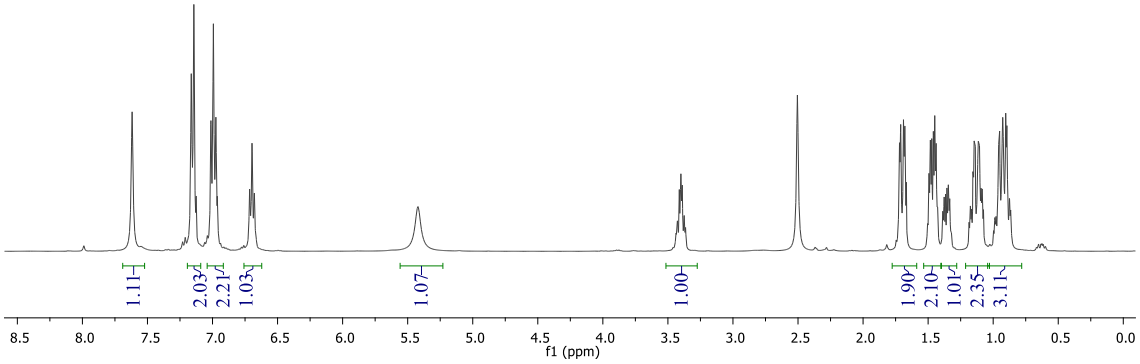

po- 181
7.306
7.288
7.270
7.263
7.246
7.229
4.945
4.634
4.259
1.291
O
N
H
N
H
1r
4.77
0.74
1.00
2.24
9.55
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

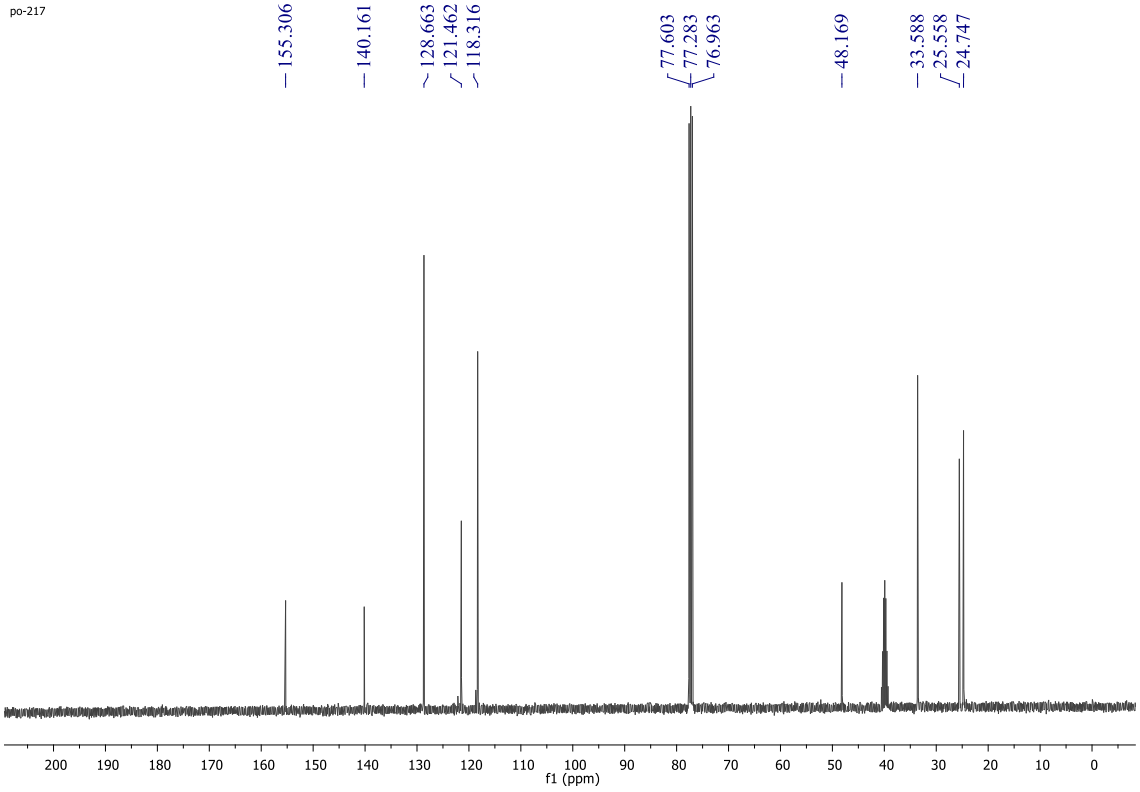

PO-181
158.212
139.905
128.375
127.175
126.822
77.399
77.082
76.761
49.996
43.738
29.518
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

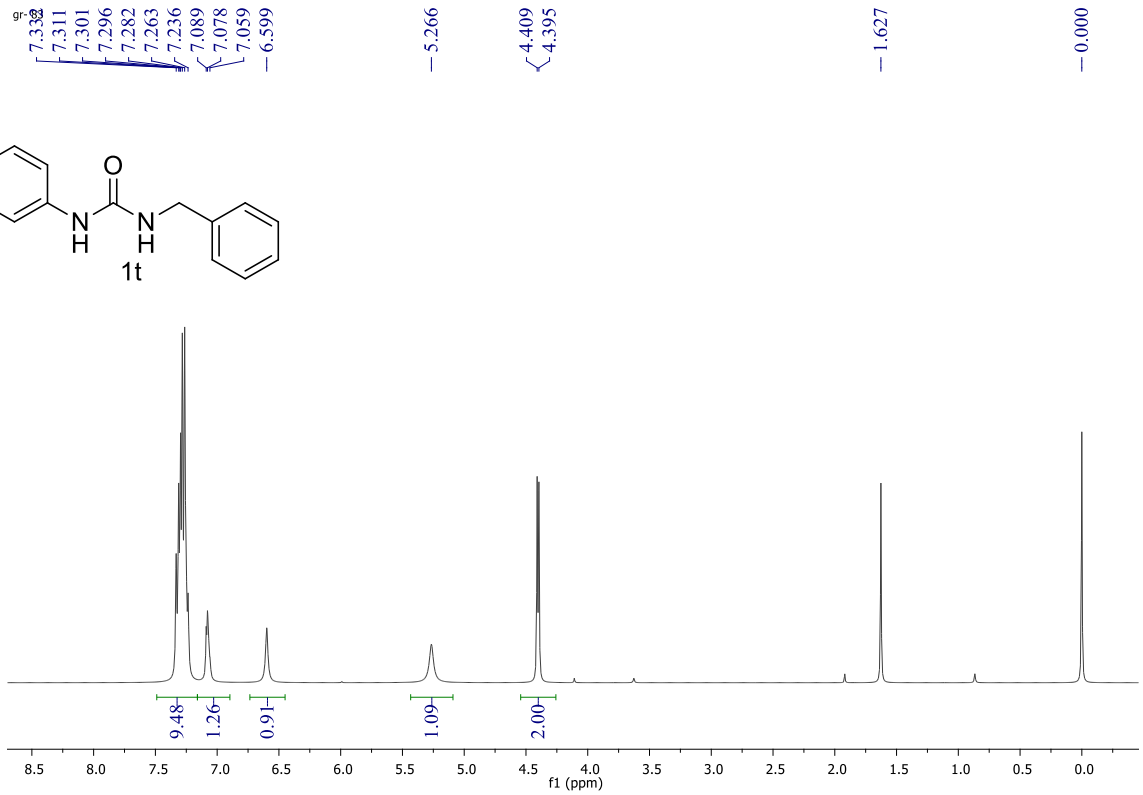

7.618
7.163
7.144
7.126
7.012
6.993
6.974
6.964
6.715
6.697
6.678
5.421
3.412
3.400
3.390
2.505
1.720
1.711
1.689
1.679
1.667
1.493
1.483
1.472
1.460
1.449
1.439
1.428
1.377
1.366
1.355
1.345
1.334
1.175
1.166
1.156
1.146
1.137
1.114
1.105
1.094
1.085
1.075
0.958
0.951
0.927
0.904
0.895
0.875

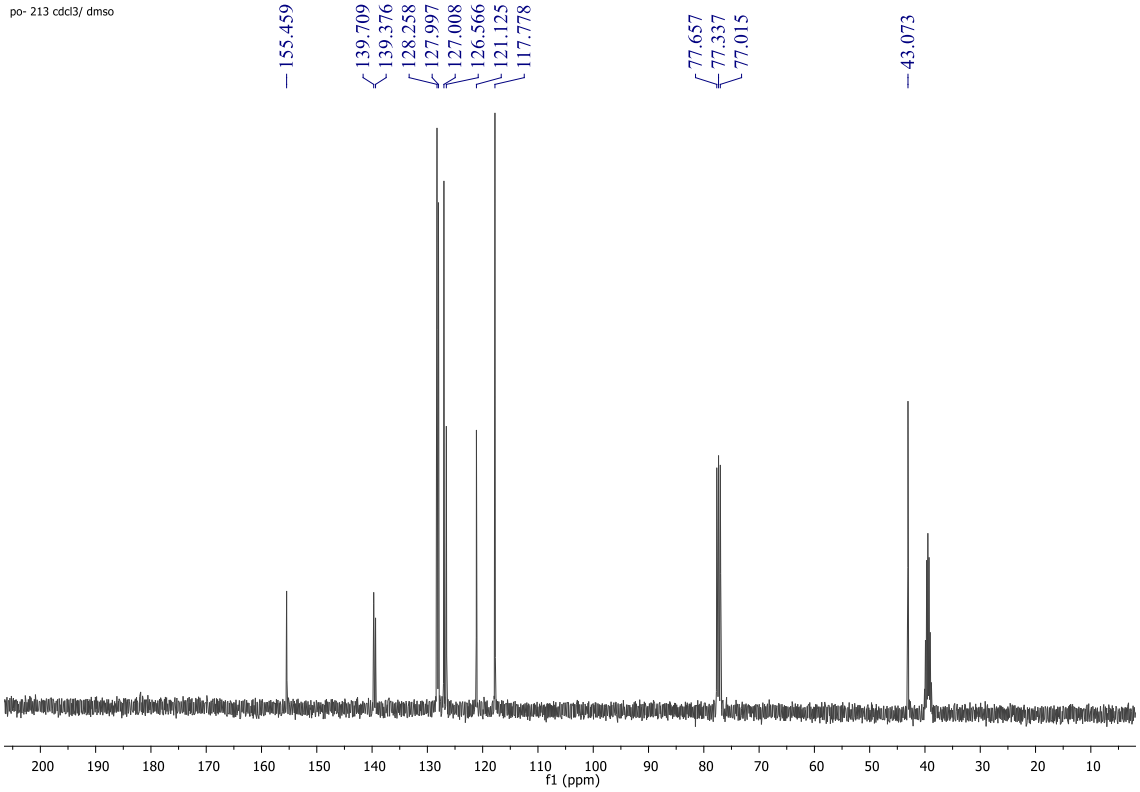

O
N
H
N
H

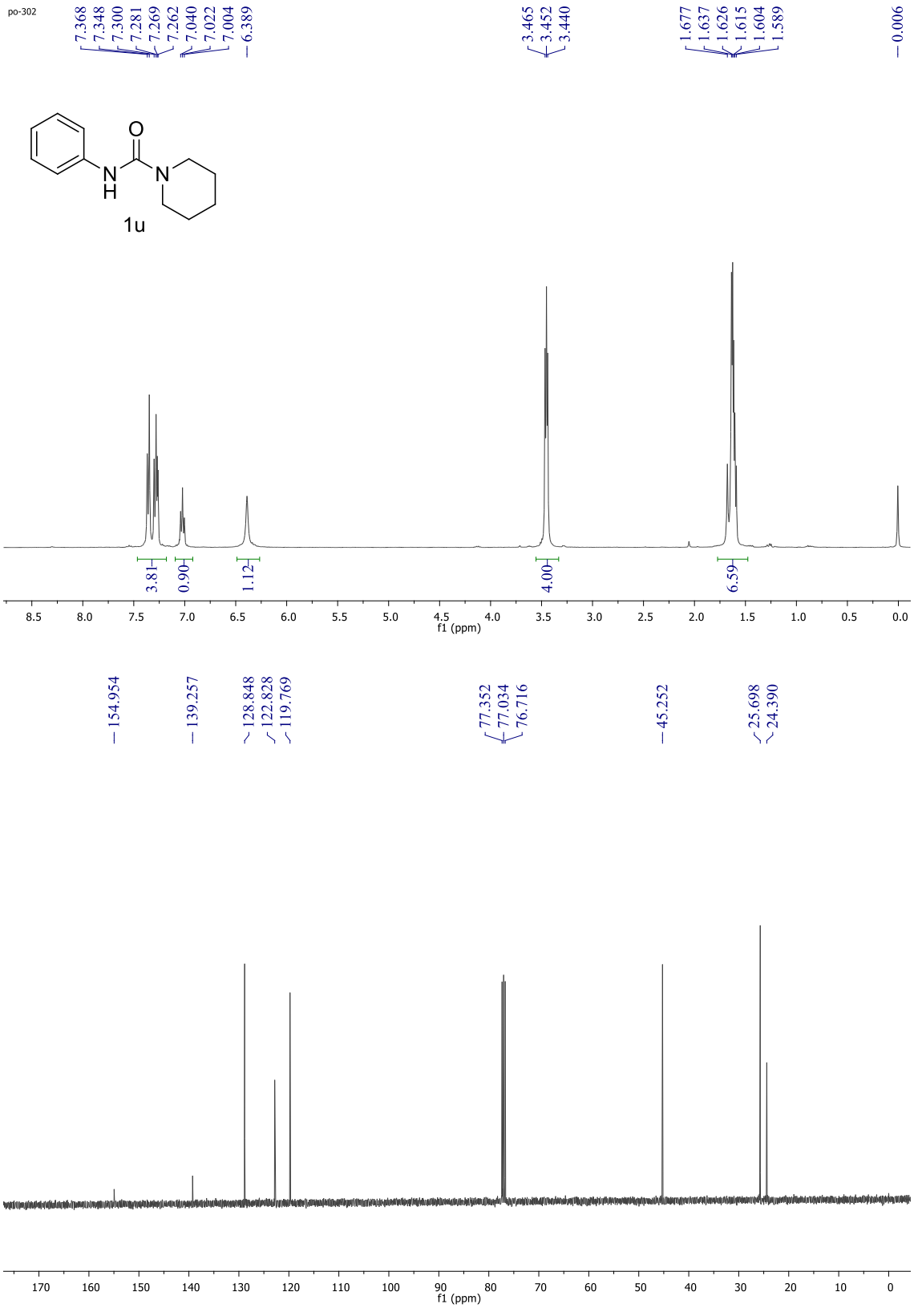
1s

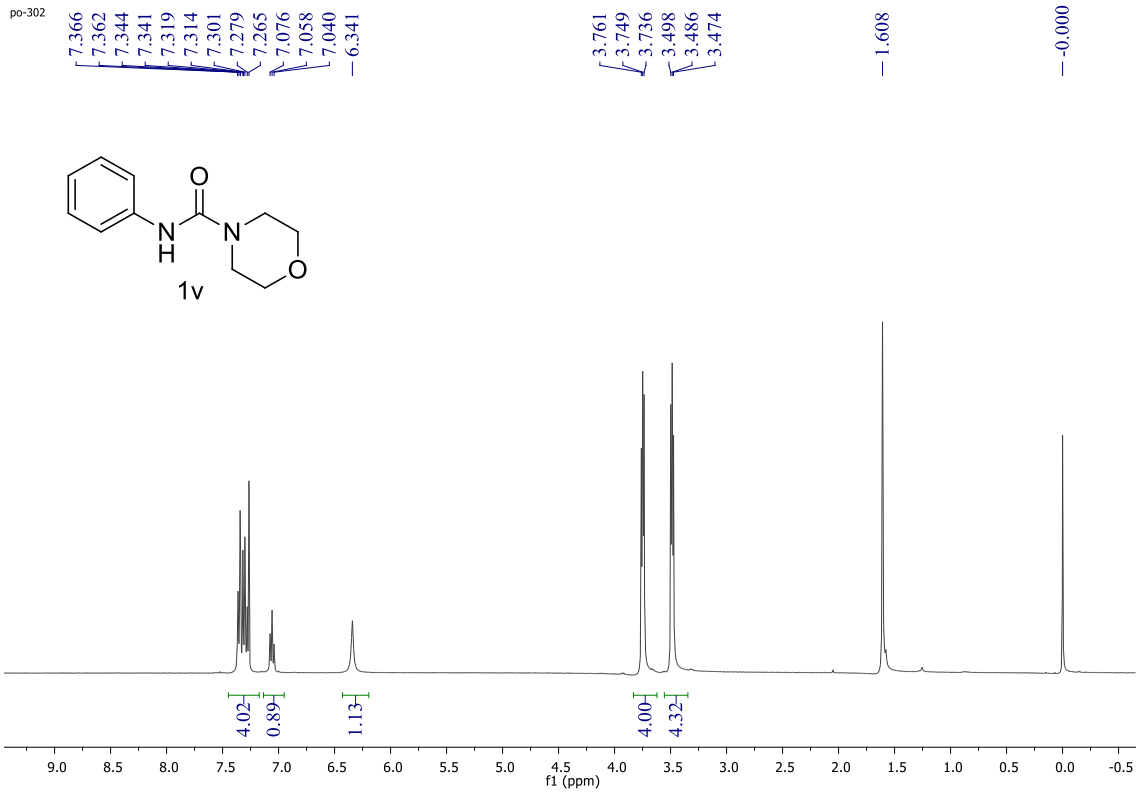

1.11
2.03
2.21
1.03
1.07
1.00
1.90
2.10
1.01
2.35
3.11
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

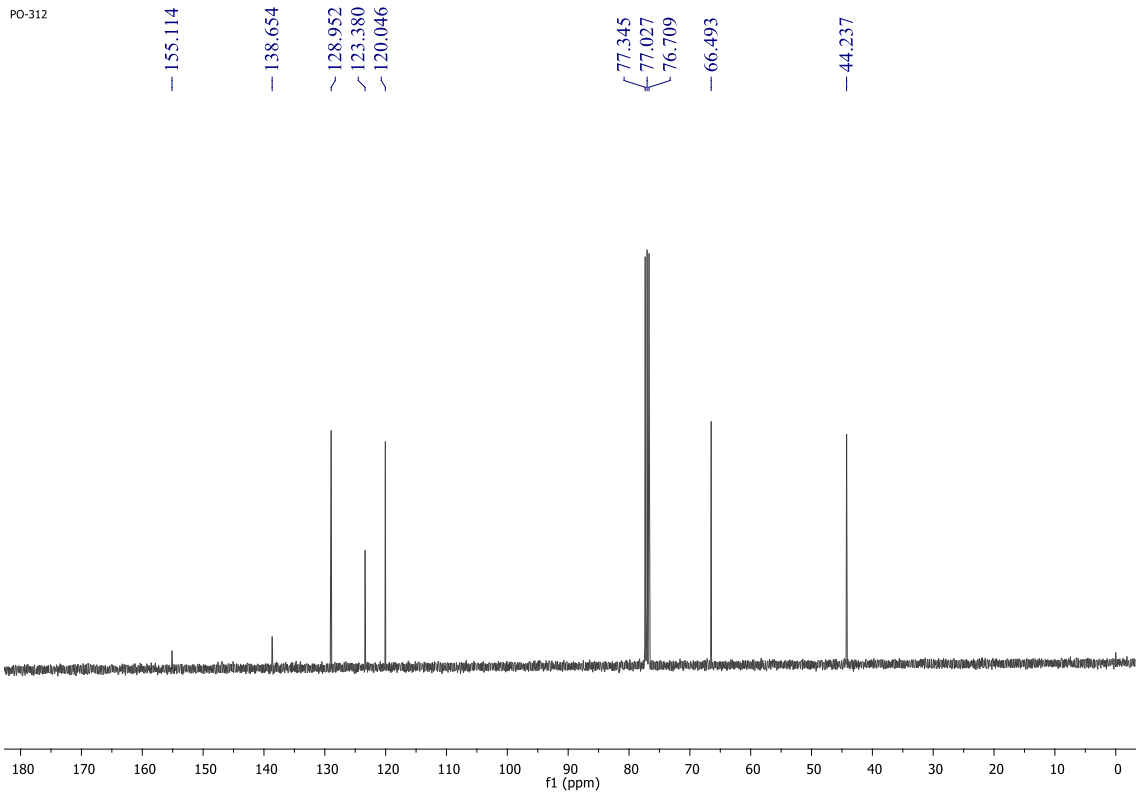

po-217
155.306
140.161
128.663
121.462
118.316
77.603
77.283
76.963
48.169
33.588
25.558
24.747
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

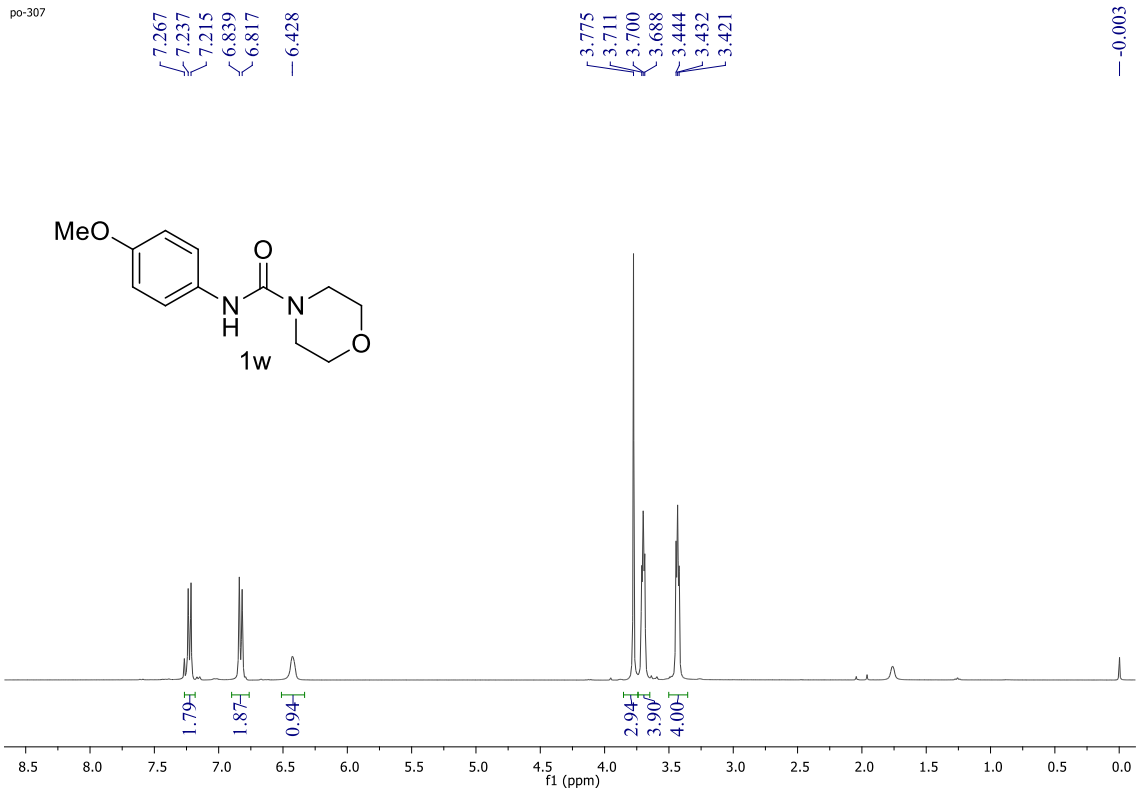

7.332
7.311
7.301
7.296
7.282
7.263
7.236
7.089
7.078
7.059
6.599
5.266
4.409
4.395
1.627
0.000
O
N
H
N
H
1t
9.48
1.26
0.91
1.09
2.00
f1 (ppm)

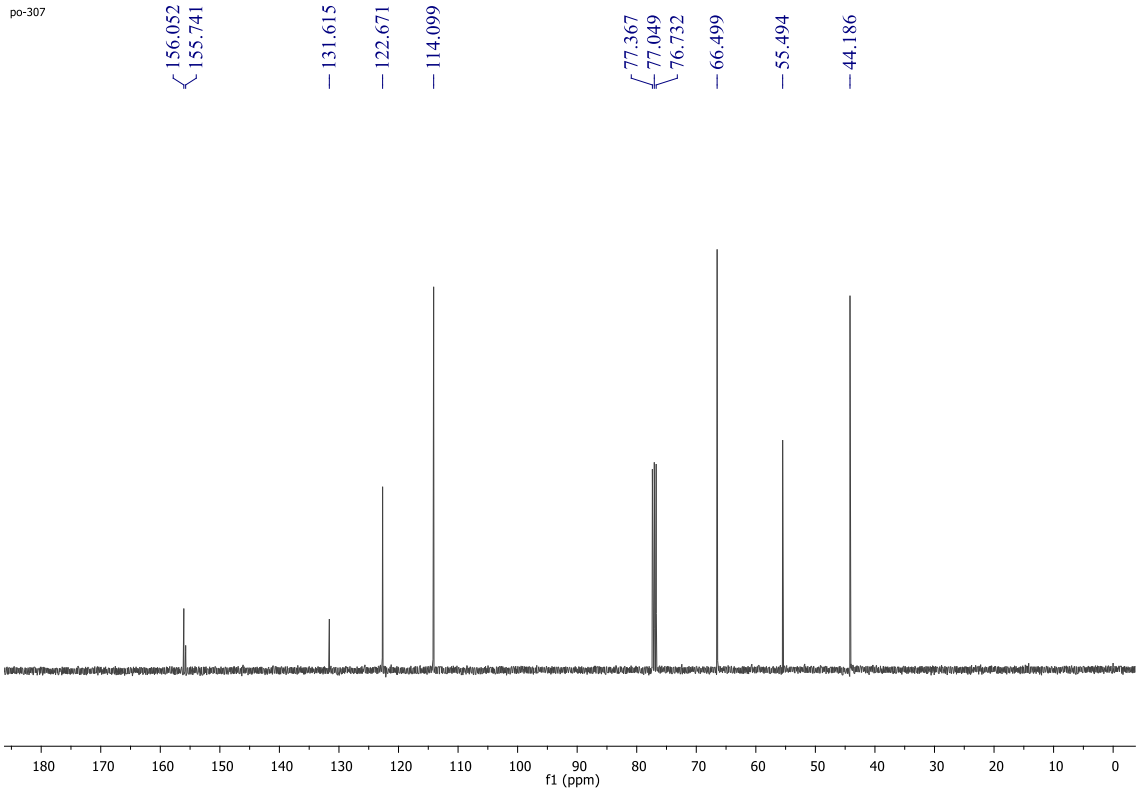

po- 213 cdcl3/ dmso
155.459
139.709
139.376
128.258
127.997
127.008
126.566
121.125
117.778
77.657
77.337
77.015
43.073
f1 (ppm)

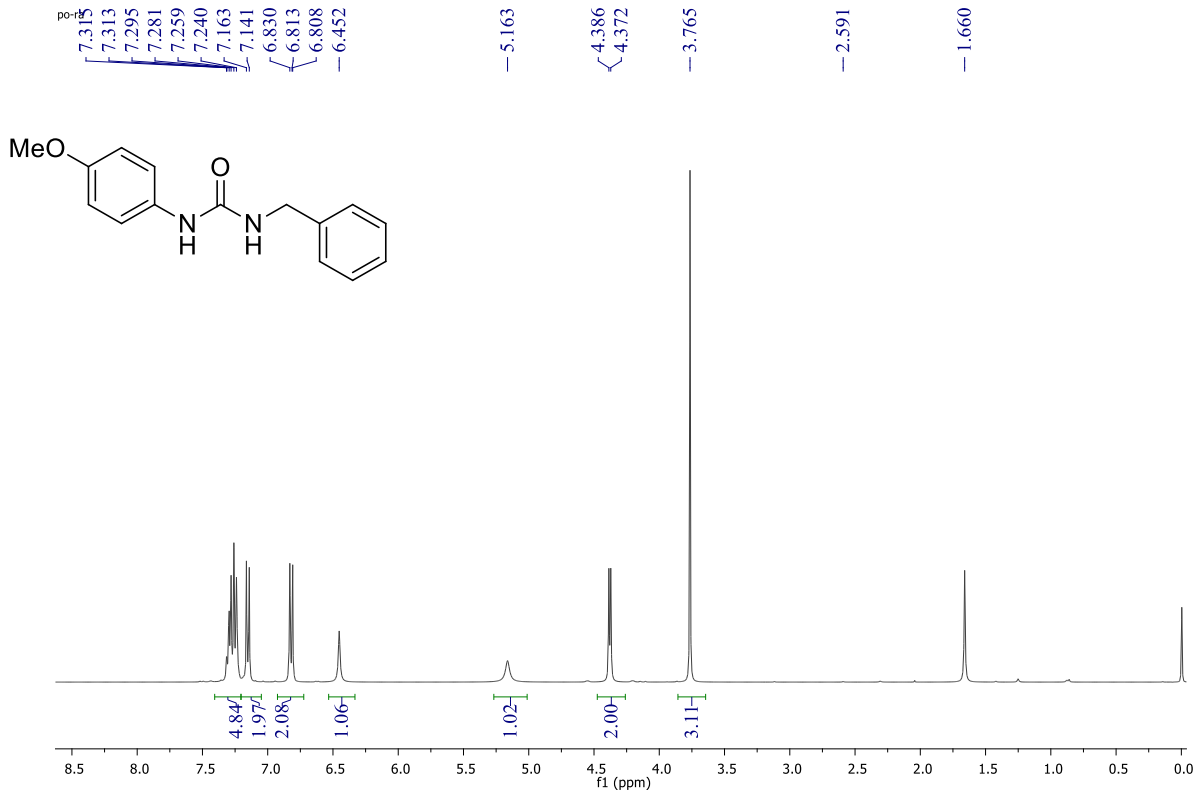

po-302
7.368
7.348
7.300
7.281
7.269
7.262
7.040
7.022
7.004
6.389
3.465
3.452
3.440
1.677
1.637
1.626
1.615
1.604
1.589
0.006
O
N
H
N
1u
3.81
0.90
1.12
4.00
6.59
f1 (ppm)
154.954
139.257
128.848
122.828
119.769
77.352
77.034
76.716
45.252
25.698
24.390
f1 (ppm)

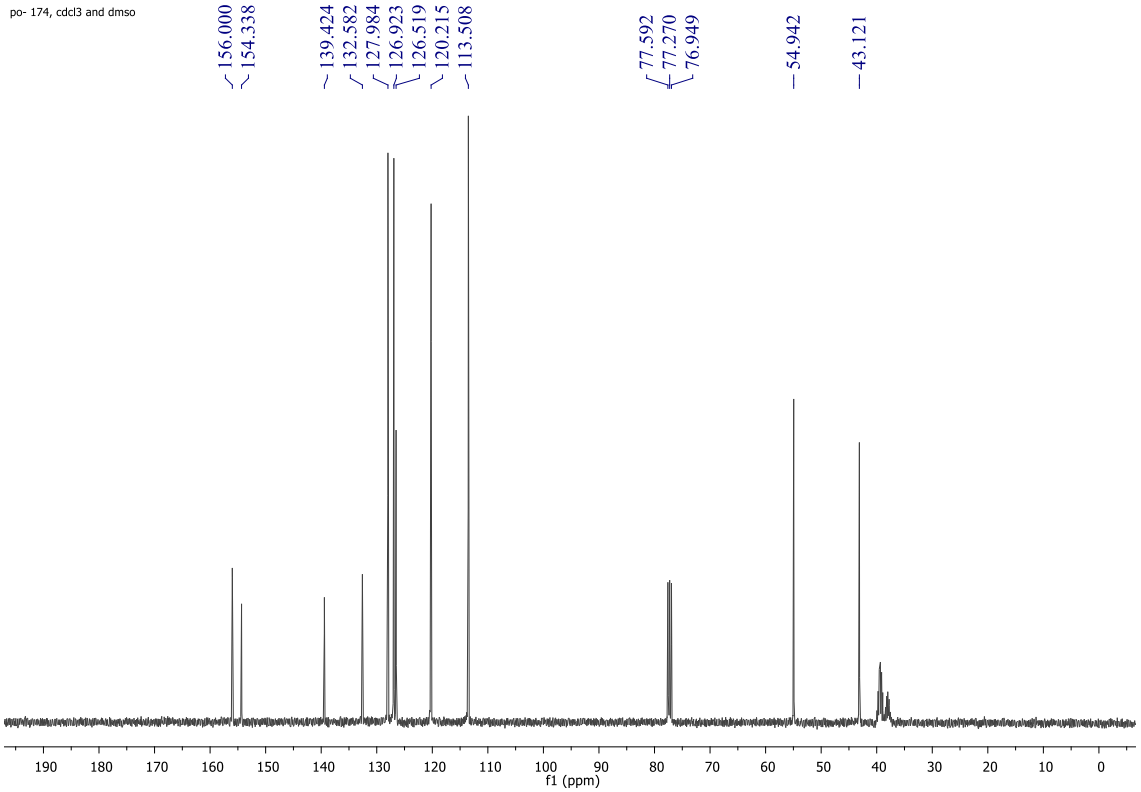

po-302
7.366
7.362
7.344
7.341
7.319
7.314
7.301
7.279
7.265
7.076
7.058
7.040
6.341
3.761
3.749
3.736
3.498
3.486
3.474
1.608
-0.000
O
N
H
N
O
1v
4.02
0.89
1.13
4.00
4.32
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

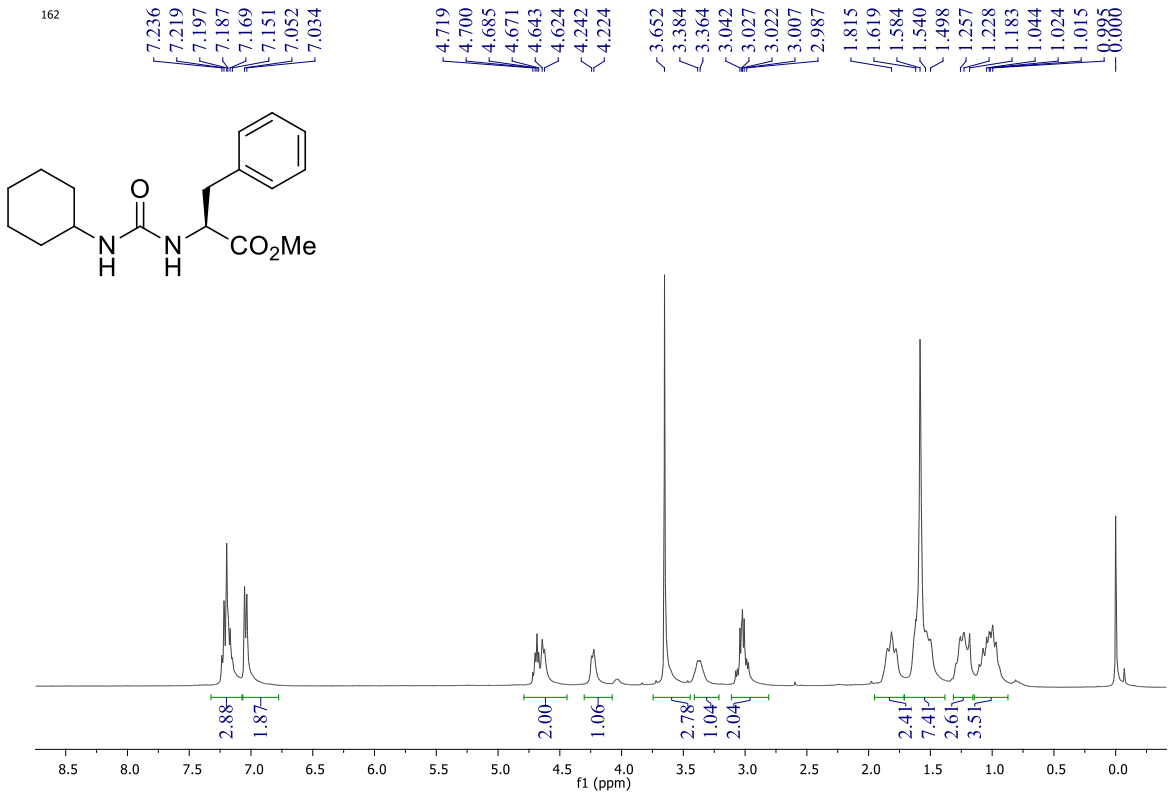

PO-312
155.114
138.654
128.952
123.380
120.046
77.345
77.027
76.709
66.493
44.237
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

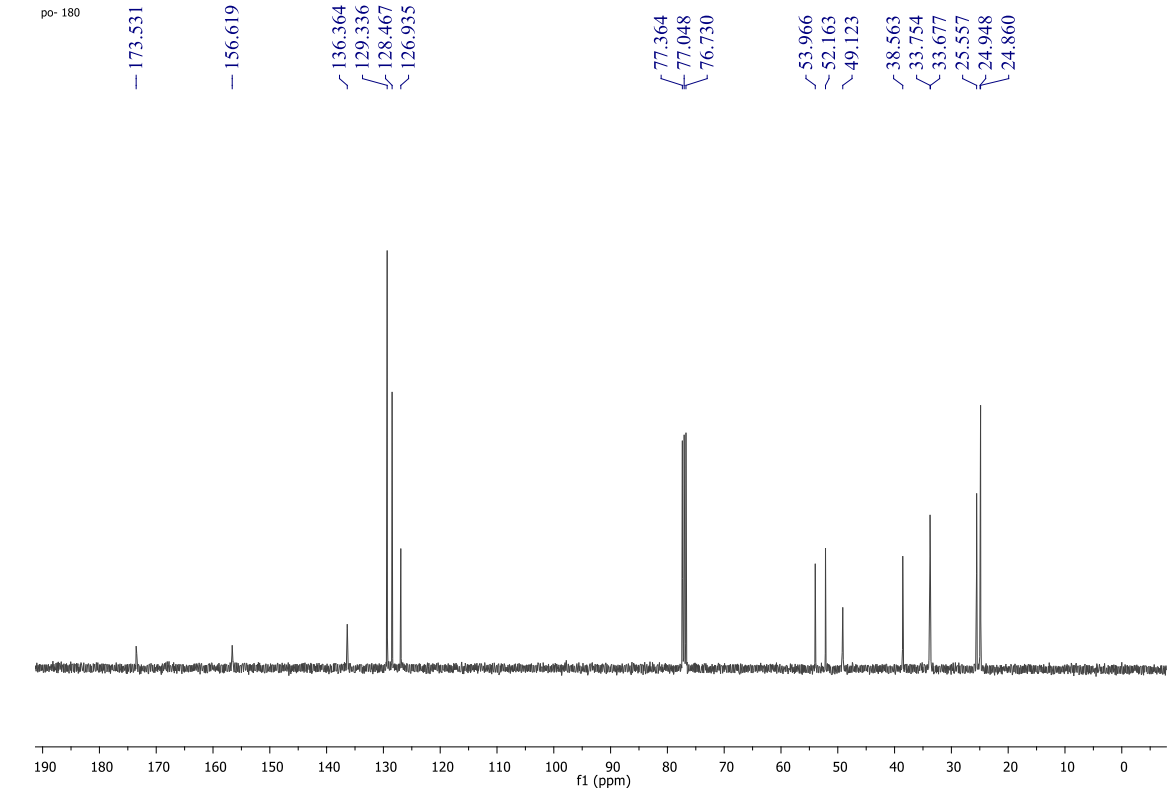

po-307
7.267
7.237
7.215
6.839
6.817
6.428
3.775
3.711
3.700
3.688
3.444
3.432
3.421
-0.003
MeO
O
N
H
N
O
1w
1.79
1.87
0.94
2.94
3.90
4.00
f1 (ppm)

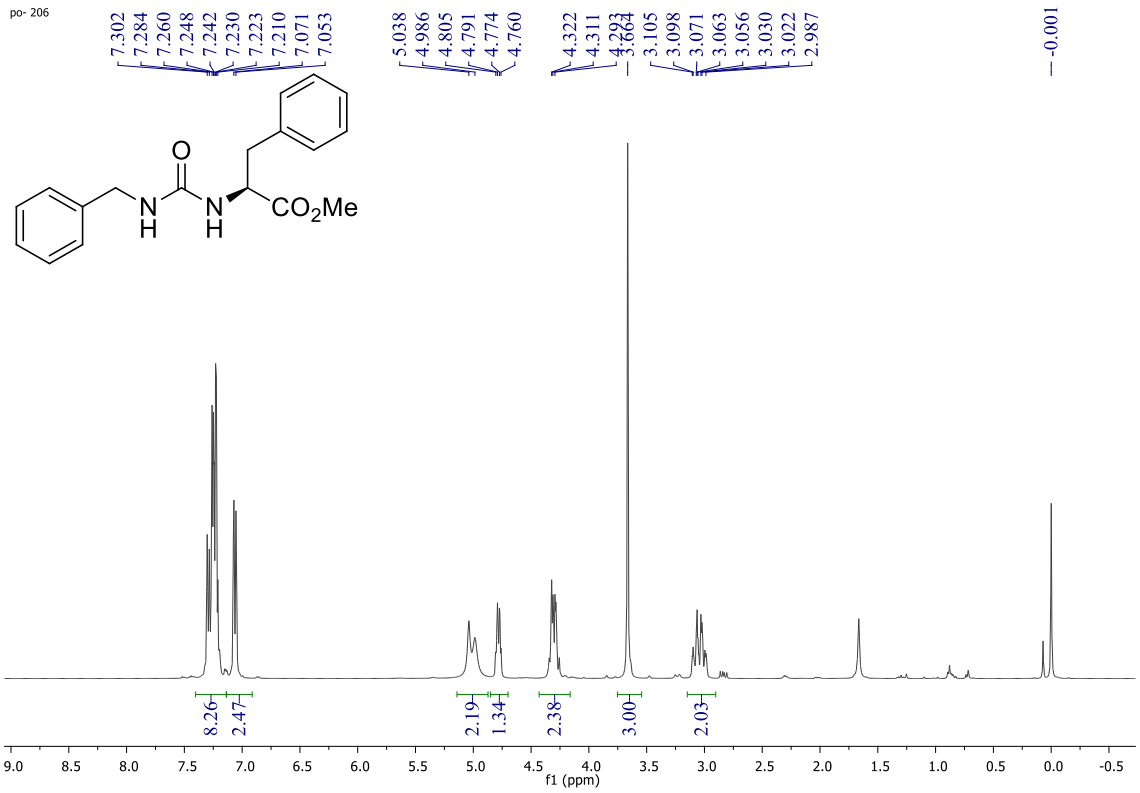

po-307
156.052
155.741
131.615
122.671
114.099
77.367
77.049
76.732
66.499
55.494
44.186
f1 (ppm)

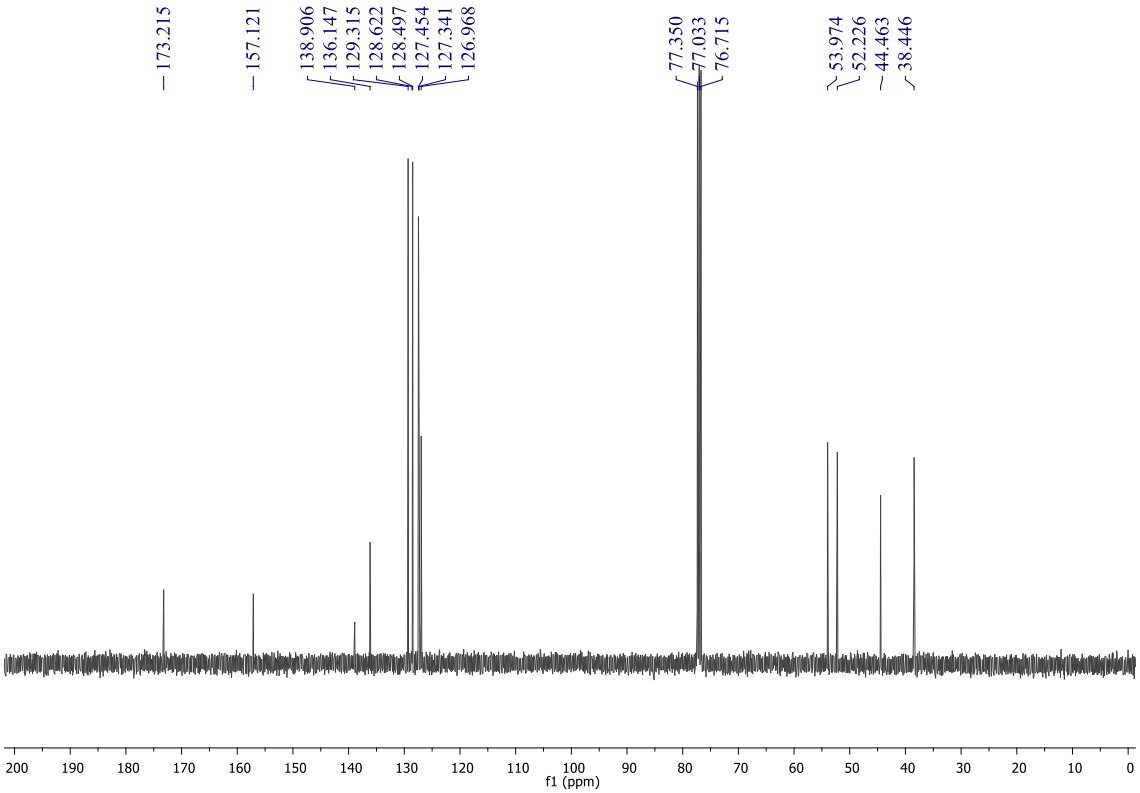

po-174
7.315
7.313
7.295
7.281
7.259
7.240
7.163
7.141
6.830
6.813
6.808
6.452
5.163
4.386
4.372
3.765
2.591
1.660
MeO
O
N
H
N
H
4.84
1.97
2.08
1.06
1.02
2.00
3.11
f1 (ppm)

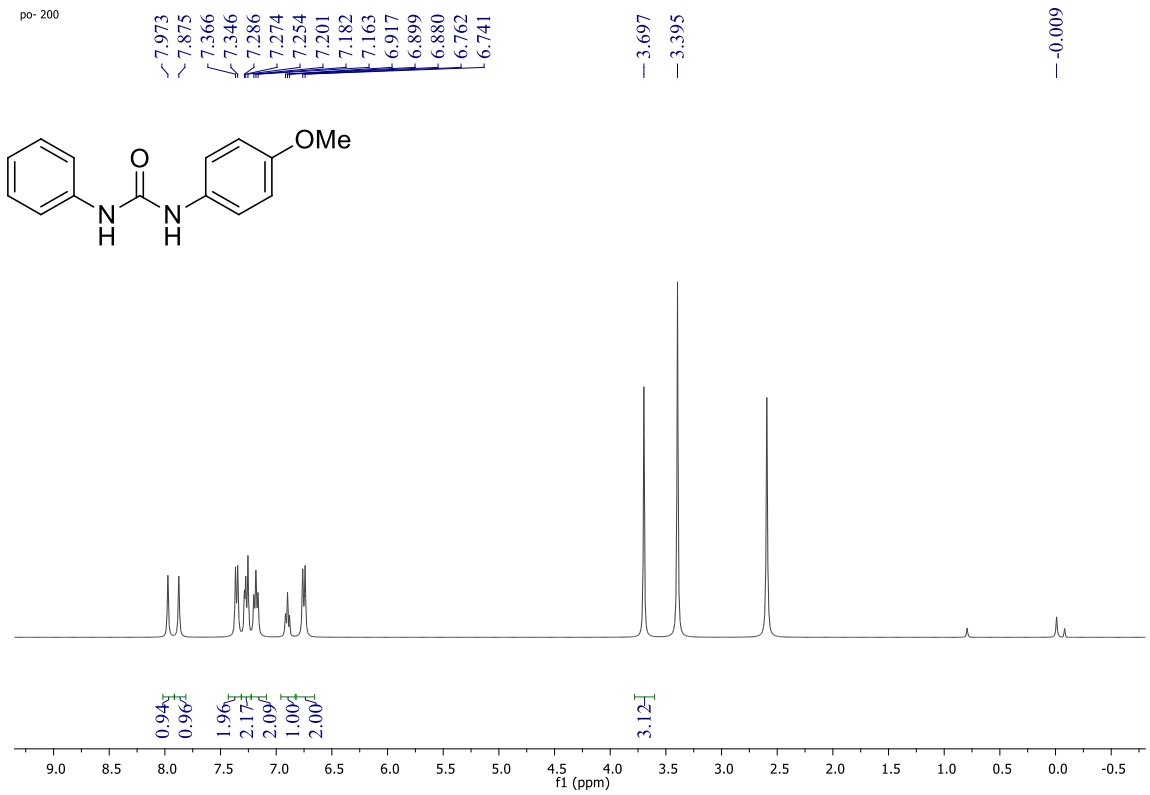

po- 174, cdcl3 and dmso
156.000
154.338
139.424
132.582
127.984
126.923
126.519
120.215
113.508
77.592
77.270
76.949
54.942
43.121
f1 (ppm)

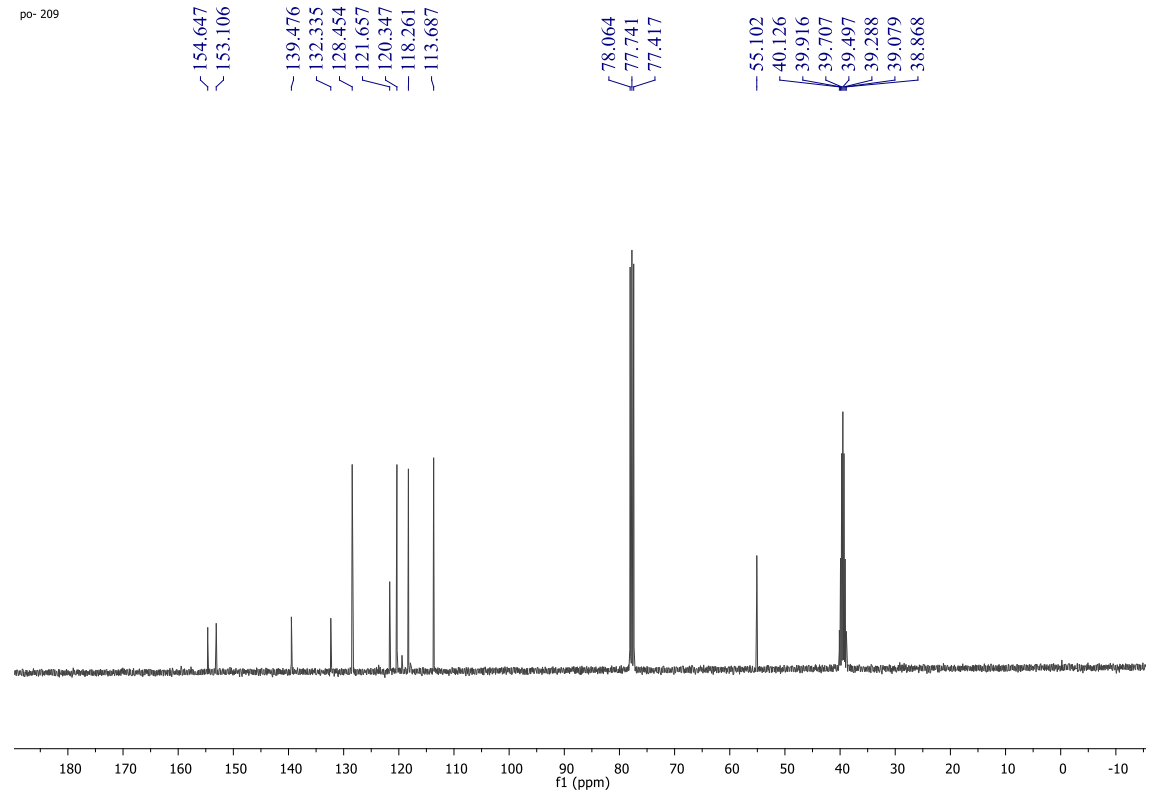

162
7.236
7.219
7.197
7.187
7.169
7.151
7.052
7.034
4.719
4.700
4.685
4.671
4.643
4.624
4.242
4.224
3.652
3.384
3.364
3.042
3.027
3.022
3.007
2.987
1.815
1.619
1.584
1.540
1.498
1.257
1.228
1.183
1.044
1.024
1.015
0.885
0.000
O
N
H
N
H
CO2Me
2.88
1.87
2.00
1.06
2.78
1.04
2.04
2.41
7.41
2.61
3.51
8.5
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
0.0
f1 (ppm)

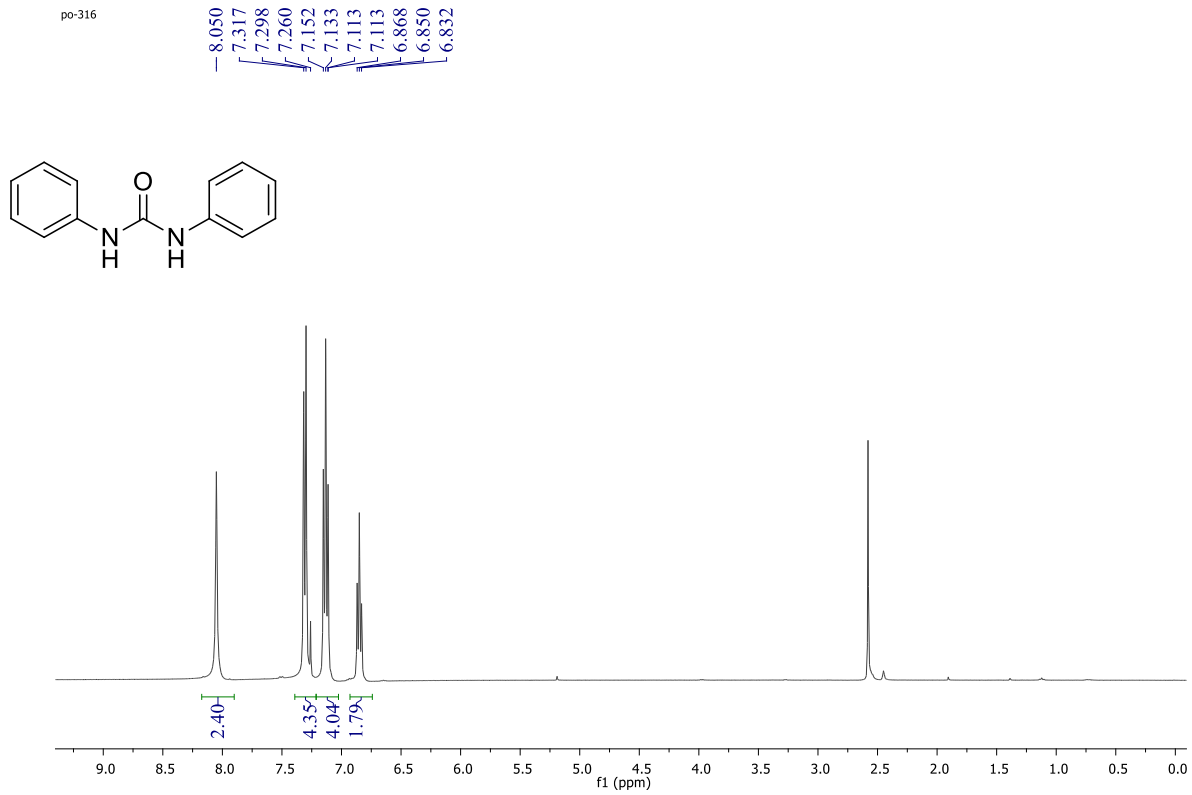

po- 180
173.531
156.619
136.364
129.336
128.467
126.935
77.364
77.048
76.730
53.966
52.163
49.123
38.563
33.754
33.677
25.557
24.948
24.860
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

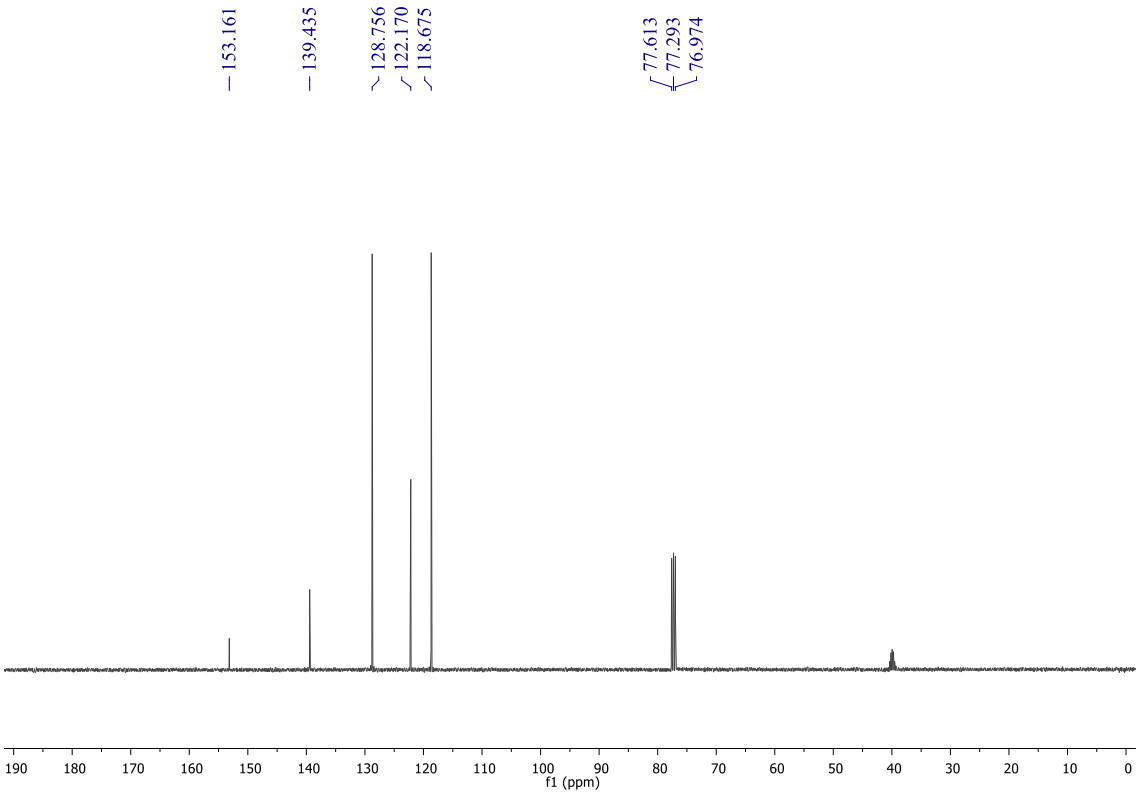

po- 206
7.302
7.284
7.260
7.248
7.242
7.230
7.223
7.210
7.071
7.053
5.038
4.986
4.805
4.791
4.774
4.760
4.322
4.311
4.293
3.664
3.105
3.098
3.071
3.063
3.056
3.030
3.022
2.987
-0.001
O
N
H
N
H
CO2Me
8.26
2.47
2.19
1.34
2.38
3.00
2.03
f1 (ppm)

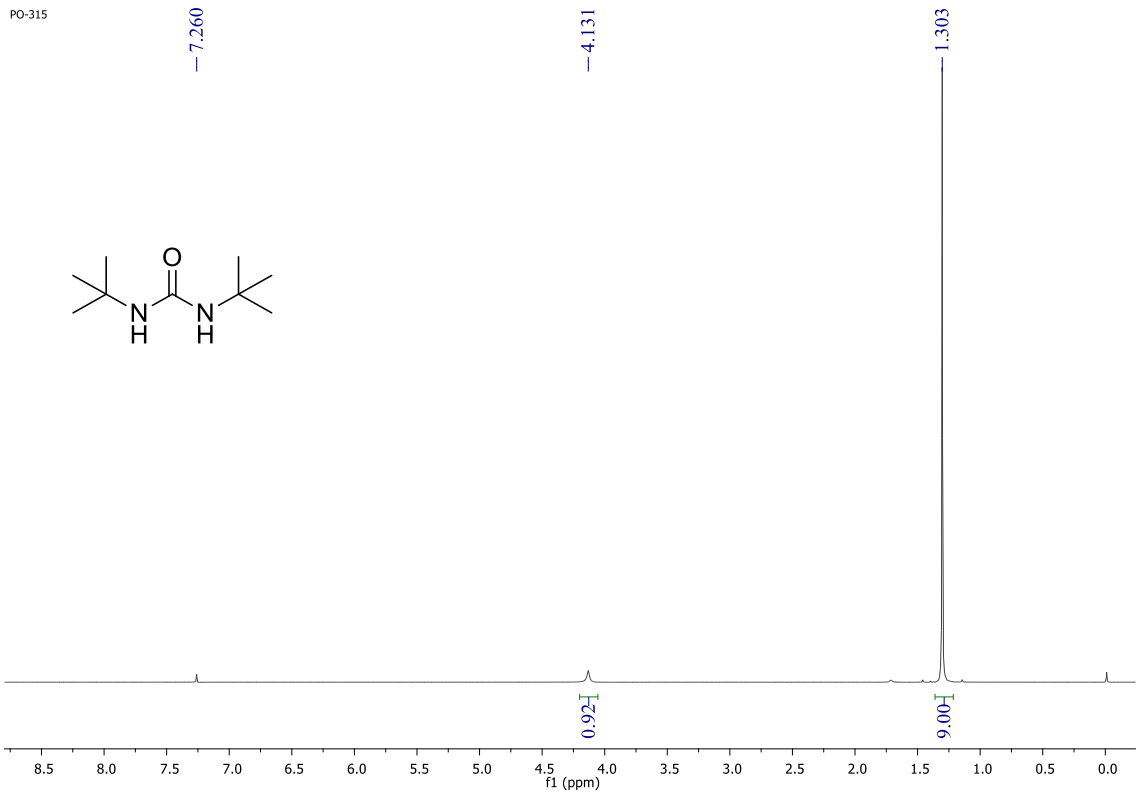

173.215
157.121
138.906
136.147
129.315
128.622
128.497
127.454
127.341
126.968
77.350
77.033
76.715
53.974
52.226
44.463
38.446
f1 (ppm)

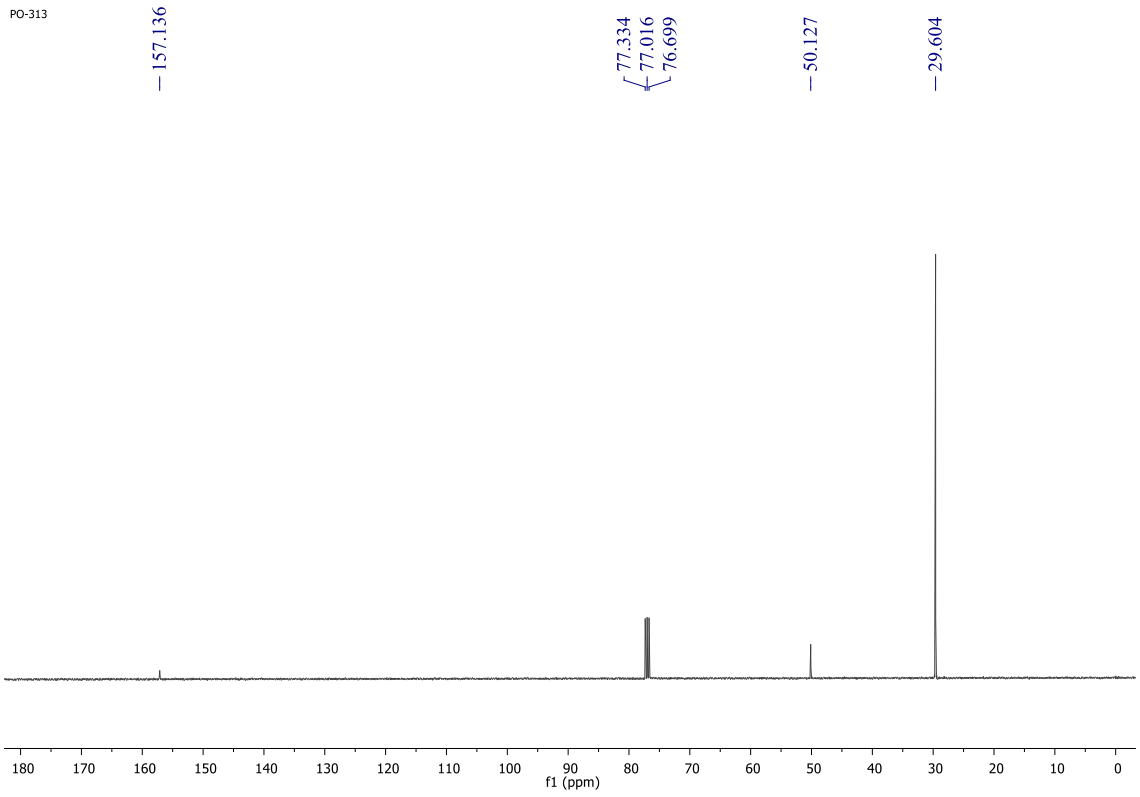

po- 200
7.973
7.875
7.366
7.346
7.286
7.274
7.254
7.201
7.182
7.163
6.917
6.899
6.880
6.762
6.741
3.697
3.395
-0.009
OMe
O
N
H
N
H
0.94
0.96
1.96
2.17
2.09
1.00
2.00
3.12
f1 (ppm)

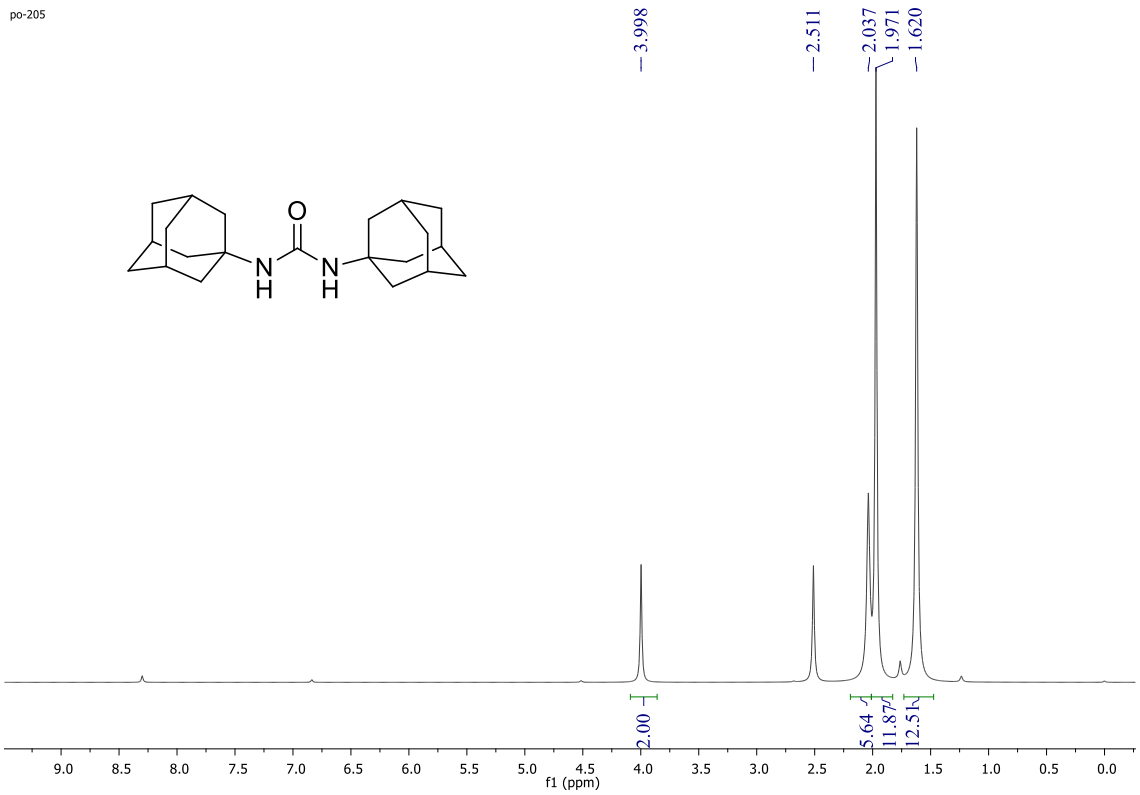

po- 209
154.647
153.106
139.476
132.335
128.454
121.657
120.347
118.261
113.687
78.064
77.741
77.417
55.102
40.126
39.916
39.707
39.497
39.288
39.079
38.868
f1 (ppm)

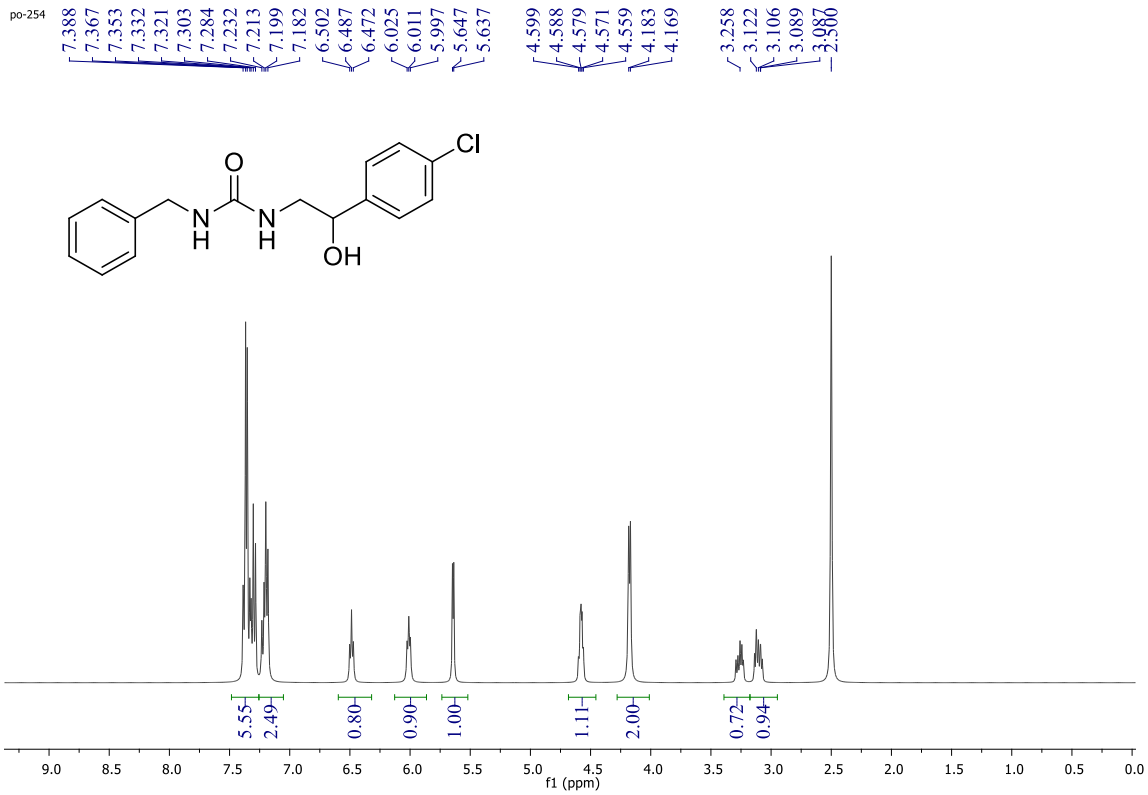

po-316
8.050
7.317
7.298
7.260
7.152
7.133
7.113
7.113
6.868
6.850
6.832
2.40
4.35
4.04
1.79
f1 (ppm)

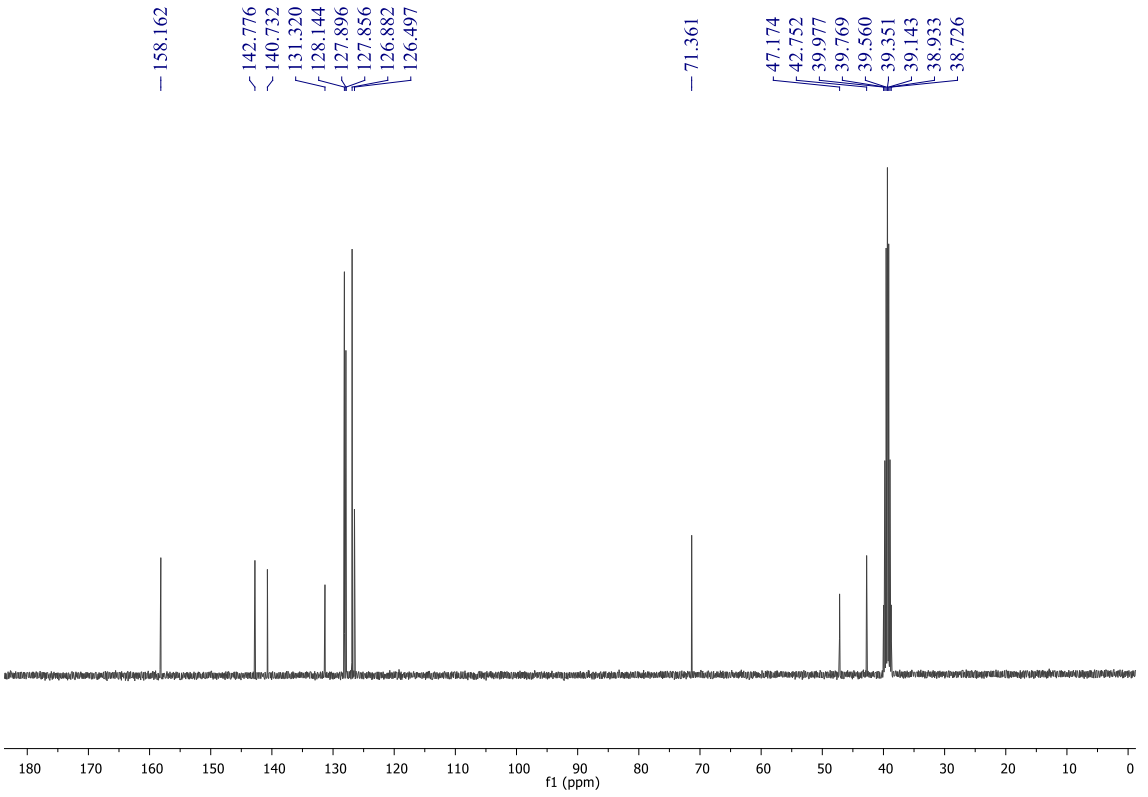

153.161
139.435
128.756
122.170
118.675
77.613
77.293
76.974
f1 (ppm)


PO-315
7.260
4.131
1.303
O
N
H
N
H
0.92
9.00
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
0.0
f1 (ppm)


PO-313
157.136
77.334
77.016
76.699
50.127
29.604
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

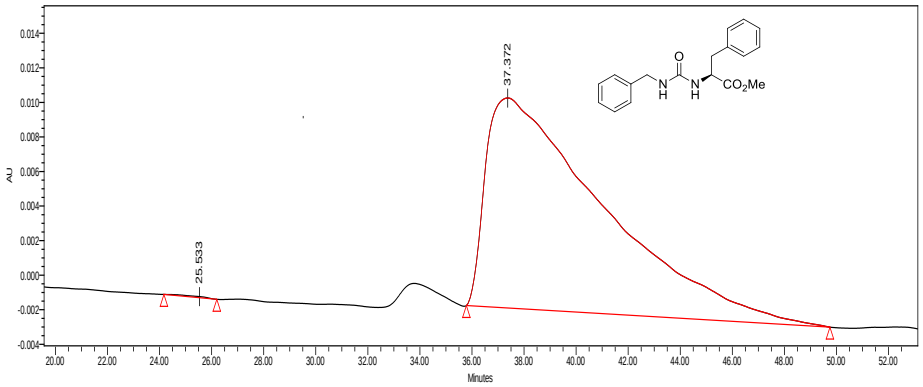

po-205
3.998
2.511
2.037
1.971
1.620
O
N
H
N
H
2.00
5.64
11.87
12.51
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


po-254
7.388
7.367
7.353
7.332
7.321
7.303
7.284
7.232
7.213
7.199
7.182
6.502
6.487
6.472
6.025
6.011
5.997
5.647
5.637
4.599
4.588
4.579
4.571
4.559
4.183
4.169
3.258
3.122
3.106
3.089
3.087
2.500
Cl
O
N
H
N
H
OH
5.55
2.49
0.80
0.90
1.00
1.11
2.00
0.72
0.94
f1 (ppm)

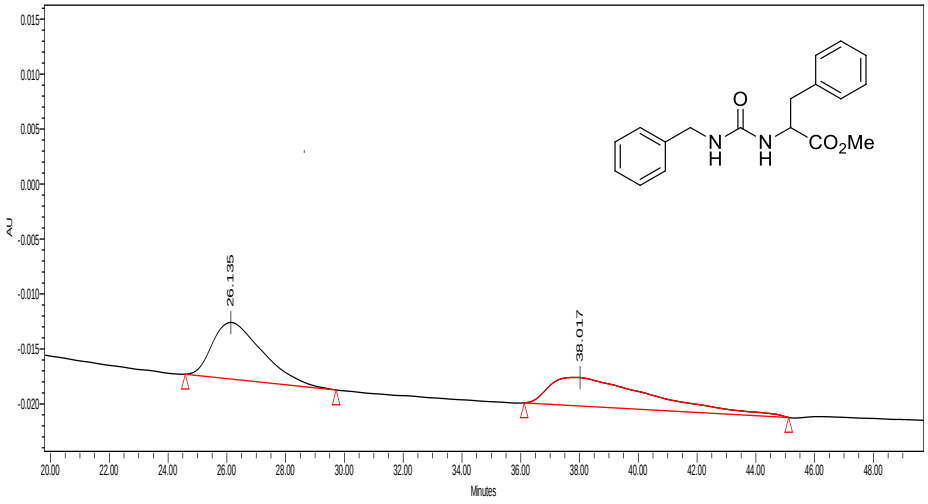

158.162
142.776
140.732
131.320
128.144
127.896
127.856
126.882
126.497
71.361
47.174
42.752
39.977
39.769
39.560
39.351
39.143
38.933
38.726
f1 (ppm)

12. HPLC traces of chiral urea derivative

(S)-methyl 2-(3-benzylureido)-3-phenylpropanoate 2a: HPLC analysis was performed by using CHIRALCEL AS column, hexane/2-propanol 90:10, flow rate 1.0 mL/min, UV 210 nm, minor 25.5 and major 37.37 min.

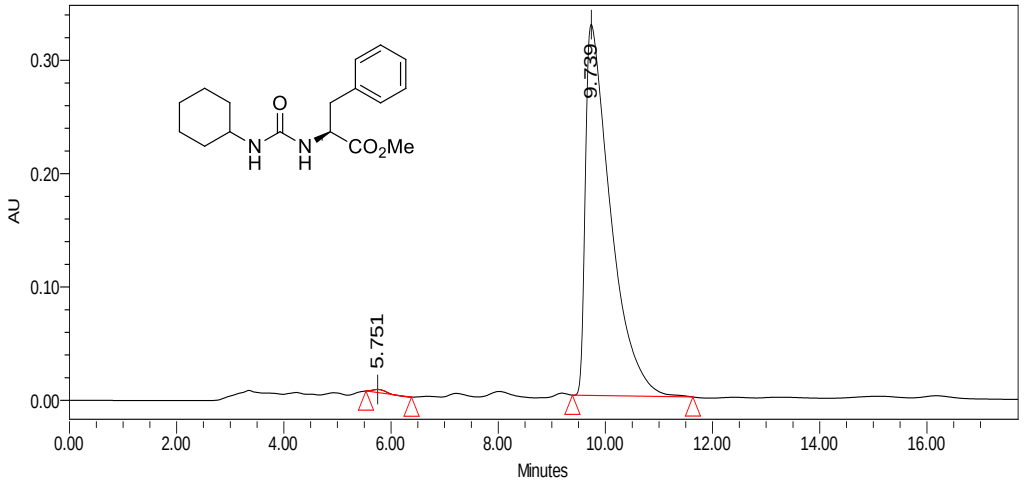


	Retention Time	Area	% Area	Height
2	37.372	3832182	99.87	12155
1	25.533	5176	0.13	65

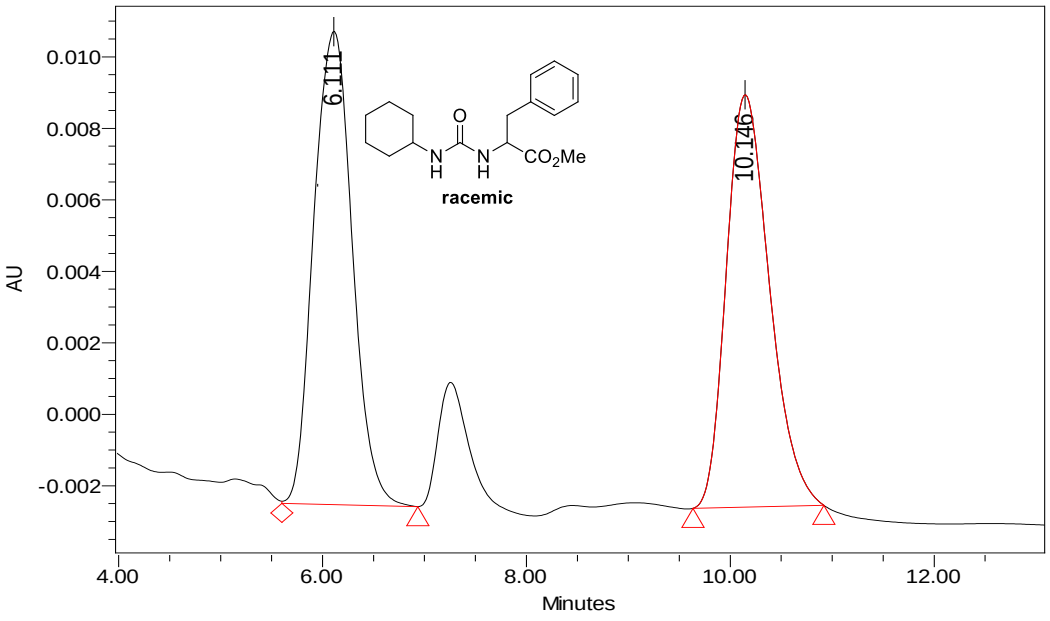


	Retention Time	Area	% Area	Height
2	38.017	634571	50.79	2584
1	26.135	614897	49.21	5144

(*S*)-Methyl 2-(3-Cyclohexylureido)-3-phenylpropanoate 2b: HPLC analysis was performed by using CHIRALCEL AD-H column, hexane/2-propanol 85:15, flow rate 1.0 mL/min, UV 210 nm, minor 5.7 and major 9.7 min.



	Name	Retention Time	Area	% Area	Height
1		5.751	71610	0.67	3422
2		9.739	10685514	99.33	327838



	Name	Retention Time	Area	% Area	Height
1		6.111	346525	49.27	13205
2		10.146	356799	50.73	11687

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