SUPPORTING INFORMATION FOR

Mechanosynthesis of amides in the total absence of organic solvent from reaction to product recovery

Thomas-Xavier Métro,* Julien Bonnamour, Thomas Reidon, Jordi Sarpoulet, Jean Martinez and Frédéric Lamaty*

Institut des Biomolécules Max Mousseron, UMR 5247 Université Montpellier 1 et

Université Montpellier 2-CNRS, Place Eugène Bataillon, 34095 Montpellier cedex 05, France.

E-mail: txmetro@um2.fr; frederic.lamaty@univ-montp2.fr

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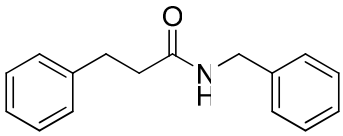
General: All reagents were purchased from Aldrich Chemical Co., Fluka and Rhône-Poulenc and used without further purification. The milling treatments were carried out in a Retsch PM100 Planetary Mill. FT-IR spectra were recorded on a Perkin-Elmer Spectrum 100 FT-IR spectrophotometer. ^{1}H NMR spectra were recorded on a Bruker Avance DPX 200 MHz spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 7.24 ppm). Data are reported as s = singlet, d = doublet, t = triplet, m = multiplet; coupling constant in Hz; integration. ^{13}C NMR spectra were recorded on a Bruker Avance AM 300 MHz spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 77.2 ppm). Analytical samples were filtrated for NMR spectra through Rotilabo®-syringe filters, PTFE, unsterile (0.20 µm pore size). Mass spectra were obtained by LC-MS with ESI using a Water Alliance 2695 as LC, coupled to a Waters ZQ spectrometer with electrospray source, a simple quadrupole analyzer and a UV Waters 2489 detector. HRMS analyse was performed on a Q-Tof (Waters, ESI, 2001) spectrometer. Enantiomeric excess was measured using a Beckman Coulter System Gold 126 Solvent Module HPLC machine and System Gold 168 Detector with 4.6 mm x 250 mm Daicel Chiralpak OD columns using *n*-hexane and 2-propanol as solvents.

General procedure: The carboxylic acid species (1.5 mmol) and CDI (243 mg, 1.5 mmol) were introduced in a 12 mL stainless steel grinding bowl with fifty stainless steel balls (5 mm diameter). The bowl was closed and placed 5 minutes within the planetary mill rotated at 500 rpm. Then, the amine species (1.35 mmol) was added. The bowl was closed and placed 10 minutes within the planetary mill

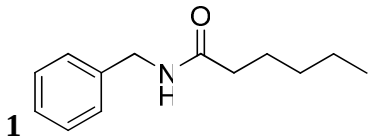
rotated at 500 rpm. 4 mL of deionised water were added and the bowl was closed and placed 5 minutes within the planetary mill rotated at 500 rpm. After this treatment, the fine suspension was filtered, washed with deionised water, and then dried under *vacuo* over P_2O_5 to obtain the final product.

***N*-Benzyl-3-phenylpropanamide**[1] Following general procedure, 3-phenylpropionic acid (0.225 g, 1.5 mmol) was used as the acid species and benzylamine hydrochloride (0.194 g, 1.35 mmol) was used as the amine species. *N*-benzyl-3-phenylpropanamide was recovered as a white solid (0.302 g, 94 %).



M.p. 79–80 °C (lit. 80 °C)[1]; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.38–7.12 (m, 10 H), 5.60 (br s, 1 H), 4.42 (d, J = 5.7 Hz, 2 H), 3.03 (t, J = 7.6 Hz, 2 H), 2.54 (t, J = 7.6 Hz, 2 H) ppm; ^{13}C NMR (300 MHz, $CDCl_3$): δ = 172.1, 140.9, 138.3, 128.7, 128.6, 128.5, 127.8, 127.5, 126.3, 43.6, 38.5, 31.8 ppm; MS (ESI): *m*/*z* 240.1 $[M+H]^+$.

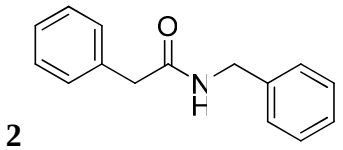
***N*-Benzylhexanamide (1)**[2] Following general procedure, hexanoic acid (0.174 g, 1.5 mmol) was used as the acid species and benzylamine hydrochloride (0.194 g, 1.35 mmol) was used as the amine species. *N*-benzyl-3-phenylacetamide was recovered as a white solid (0.273 g, 99 %).



1

M.p. 52–53 ºC (lit. 50–52 ºC)[2]; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.35–7.15 (m, 5H), 5.83 (br s, 1H), 4.38 (d, J = 5.6 Hz, 2H), 2.16 (t, J = 7.4 Hz, 2H), 1.69–1.52 (m, 2H), 1.35–1.18 (m, 4H), 0.89–0.79 (m, 3H) ppm; ^{13}C NMR (300 MHz, $CDCl_3$): δ = 173.2, 138.6, 128.9, 128.0, 127.6, 43.6, 36.9, 31.7, 25.7, 22.6, 14.1 ppm; MS (ESI): *m*/*z* 206.2 $[M+H]^+$.

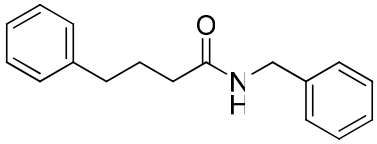
***N*-Benzyl-phenylacetamide (2)**[3] Following general procedure, phenylacetic acid (0.204 g, 1.5 mmol) was used as the acid species and benzylamine hydrochloride (0.194 g, 1.35 mmol) was used as the amine species. *N*-benzyl-3-phenylacetamide was recovered as a white solid (0.281 g, 93 %).



2

M.p. 120–121 °C (lit. 121–123 °C)[3]; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.38–7.12 (m, 10 H), 5.62 (br s, 1 H), 4.40 (d, J = 5,8 Hz, 2 H), 3.62 (s, 2 H) ppm; ^{13}C NMR (300 MHz, $CDCl_3$): δ = 171.1, 138.3, 135.0, 129.7, 129.3, 128.8, 127.7, 127.61, 127.60 , 44.0, 43.8 ppm; MS (ESI): *m*/*z* 226.2 $[M+H]^+$.

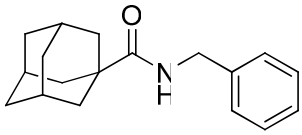
***N*-Benzyl-4-phenylbutanamide (3)**[4] Following general procedure, 4-phenylbutyric acid (0.246 g, 1.5 mmol) was used as the acid species and benzylamine hydrochloride (0.194 g, 1.35 mmol) was used as the amine species. *N*-benzyl-4-phenylbutanamide was recovered as a white solid (0.291 g, 85 %).



3

M.p. 80–81 °C (lit. 83 °C)[4]; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.38–7.10 (m, 10 H), 5.65 (br s, 1 H), 4.41 (d, J = 5.7 Hz, 2 H), 2.65 (t, J = 7.4 Hz, 2 H), 2.25–2.14 (m, 2 H), 2.07–1.90 (m, 2 H) ppm; ^{13}C NMR (300 MHz, $CDCl_3$): δ = 172.7, 141.6, 138.5, 128.8, 128.6, 128.5, 128.0, 127.6, 126.1, 43.7, 36.0, 35.3, 27.2 ppm; MS (ESI): m/z 254.2 $[M+H]^+$.

***N*-Benzyl-1-adamantanecarboxamide (4)**[4] Following general procedure, 1-adamantane carboxylic acid (0.270 g, 1.5 mmol) was used as the acid species and benzylamine hydrochloride (0.194 g, 1.35 mmol) was used as the amine species. *N*-benzyl-1-adamantanecarboxamide was recovered as a white solid (0.312 g, 77 %).



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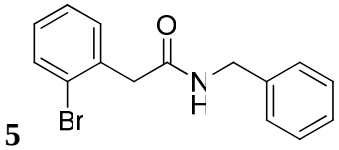
M.p. 170–171 °C (lit. 172 °C)[4]; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.38–7.18 (m, 5 H), 5.85 (br s, 1 H), 4.42 (d, J = 5.6 Hz, 2 H), 2.02 (s, 3 H), 1.93–1.58 (m, 12 H) ppm; ^{13}C NMR (300 MHz, $CDCl_3$): δ = 178.0, 138.8, 128.8, 127.7, 127.5, 43.4, 40.8, 39.4, 36.6, 28.2 ppm; MS (ESI): m/z 270.2 $[M+H]^+$.

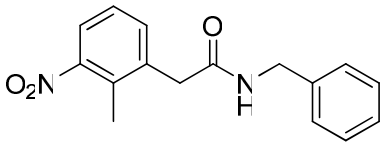
***N*-Benzyl-2-(2-bromophenyl)acetamide (5)**[3] Following general procedure, 2-(2-bromophenyl)acetic acid (0.323 g, 1.5mmol) was used as the acid species and benzyl amine hydrochloride (0.194 g, 1.35 mmol) was used as the amine species. *N*-Benzyl-2-(2-bromophenyl)acetamide was recovered as a white solid (0.411 g, 69 %).



5

M.p. 141–142 °C (lit. 144–145 °C)[3]; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.58 (dd, J = 7.8 and 1.2 Hz, 1H), 7.40–7.11 (8H), 5.71 (bs, 1H), 4.44 (d, J = 5.8 Hz, 2H), 3.78 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.6, 138.1, 134.9, 133.3, 131.9, 129.4, 128.8, 128.2, 127.7, 127.6, 125.1, 44.2, 43.8; MS (ESI): m/z 304.0 $[M(^{79}Br)+H]^+$; 306.0 $[M(^{81}Br)+H]^+$.

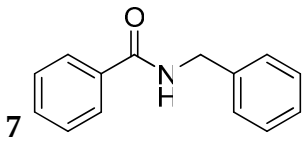
***N*–Benzyl-2-(3-nitro-2-methylphenyl)acetamide (6)** Following general procedure, 2-(3-nitro-2-methylphenyl)acetic acid (0.293 g, 1.5mmol) was used as the acid species and benzyl amine hydrochloride (0.194 g, 1.35 mmol) was used as the amine species. *N*-Benzyl-2-(3-nitro-2-methylphenyl)acetamide was recovered as a white solid (0.384 g, 91 %).



6

M.p. 142–143 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.70 (d, J = 8.1 Hz, 1H), 7.43 (d, J = 7.4 Hz, 1H), 7.33–7.27 (5H), 7.22–7.20 (2H), 5.65 (bs, 1H), 4.43 (d, J = 5.8 Hz, 2H), 3.71 (s, 2H), 2.40 (s, 3H) ; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.2, 137.9, 136.5, 134.6, 131.6, 128.9, 127.9, 127.8, 127.0, 123.6, 44.0, 42.0, 15.4; IR (neat) 3279, 1640, 1557, 1520, 1356, 731, 698 cm^{-1}, MS (ESI): m/z 285.1 $[M+H]^+$, HRMS: m/z: calcd for $C_{16}H_{17}N_2O_3$: 285.1239; found: 285.1240.

***N*-Benzyl-benzamide (7)**[4] Following general procedure, benzoic acid (0.183 g, 1.5 mmol) was used as the acid species and benzylamine hydrochloride (0.194 g, 1.35 mmol) was used as the amine species. *N*-benzyl-benzamide was recovered as a white solid (0.252 g, 88 %).



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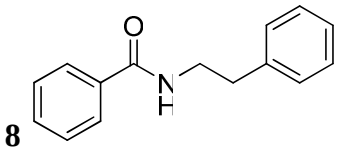
M.p. 104–105 °C (lit. 104 °C)[4]; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.82–7.23 (m, 10 H), 6.38 (br s, 1 H), 4.64 (d, J = 5.7 Hz, 2 H) ppm; ^{13}C NMR (300 MHz, $CDCl_3$): δ = 167.8, 138.4, 134.6, 131.8, 129.0, 128.8, 128.1, 127.8, 127.2, 44.3 ppm; MS (ESI): m/z 212.2 $[M+H]^+$.

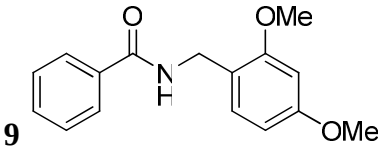
***N*-Phenethyl-benzamide (8)**[5] Following general procedure, benzoic acid (0.183 g, 1.5 mmol) was used as the acid species and phenethylamine hydrochloride (0.206 g, 1.31 mmol) was used as the amine species. *N*-phenethyl-benzamide was recovered as a white solid (0.284 g, 96 %).



8

M.p. 116–117 °C (lit. 113–116 °C)[5]; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.68–7.00 (m, 10 H), 6.05 (s, 1 H), 3.60–3.45 (m, 2 H), 2.68 (t, J = 6.5 Hz, 2 H) ppm; ^{13}C NMR (300 MHz, $CDCl_3$): δ = 167.7, 139.1, 134.8, 131.6, 129.0, 128.9, 128.8, 127.0, 126.8, 41.3, 35.9 ppm; MS (ESI): m/z 226.2 $[M+H]^+$.

***N*-2,4-Dimethoxybenzyl-benzamide (9)** Following general procedure, benzoic acid (0.183 g, 1.5 mmol) was used as the acid species and 2,4-dimethoxybenzylamine hydrochloride (0.275 g, 1.35 mmol) was used as the amine species. *N*-2,4dimethoxybenzyl-benzamide was recovered as a white solid (0.306 g, 84 %).



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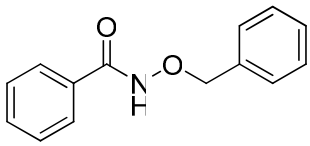
M.p. 101–102 °C; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.72–7.64 (m, 2 H), 7.46–7.16 (m, 4 H), 6.55–6.34 (m, 3 H), 4.50 (d, J = 5.7 Hz, 2 H), 3.79 (s, 3 H), 3.73 (s, 3 H) ppm; ^{13}C NMR (300 MHz, $CDCl_3$): δ = 167.3, 160.8, 158.9, 135.1, 131.5, 130.9, 128.7, 127.1, 118.9, 104.2, 98.9, 55.6, 39.8 (2 C) ppm; MS (ESI): m/z 272.2 $[M+H]^+$; HRMS: m/z: calcd for $C_{16}H_{18}NO_3$: 272.1287; found: 272.1277.

***N*-Benzyloxy-benzamide (10)**[6] Following general procedure, benzoic acid (0.183 g, 1.5 mmol) was used as the acid species and *O*-benzylhydroxylamine hydrochloride (0.216 g, 1.35 mmol) was used as the amine species. *N*-benzyloxy-benzamide was recovered as a white solid (0.195 g, 64 %).



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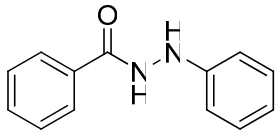
M.p. 103–104 °C (lit. 102–104 °C)[6]; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.49 (br s, 1 H), 7.70–7.22 (m, 10 H), 5.03 (s, 2 H) ppm; ^{13}C NMR (300 MHz, $CDCl_3$): δ = 166.7, 135.4, 132.2, 132.1, 129.5, 129.0, 128.9, 128.8, 127.3, 78.6 ppm; MS (ESI): *m*/*z* 228.1 $[M+H]^+$.

Benzoic acid *N´*-phenylhydrazide (11)[7] Following general procedure, benzoic acid (0.183 g, 1.5mmol) was used as the acid species and phenylhydrazine hydrochloride (0.195 g, 1.35 mmol) was used as the amine species. Benzoic acid *N´*-phenylhydrazide was recovered as a yellow solid (0.237 g, 83 %).



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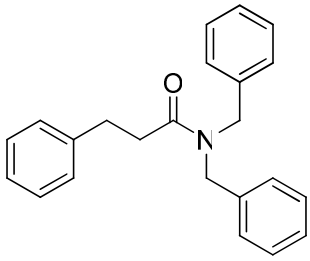
M.p. 168°C (lit. 168–169°C)[7]; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.24 (s, 1H), 7.88–7.80 (2H), 7.60–7.39 (3H), 7.28–7.17 (2H), 6.96–6.86 (3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.2, 147.3, 131.64, 131.57, 128.6, 128.2, 126.5, 120.8, 113.1; MS (ESI): m/z 213.1 $[M+H]^+$.

(*N*,*N*)-Dibenzyl-3-phenylpropanamide (12)[8] Hydrocinnamic acid (0.225 g, 1.5 mmol) and CDI (243 mg, 1.5 mmol) were introduced in a 12 mL stainless steel grinding bowl with fifty stainless steel balls (5 mm diameter). The bowl was closed and placed 5 minutes within the planetary mill rotated at 500 rpm. Then, the dibenzylamine hydrochloride (0.316 g, 1.35 mmol) was added. The bowl was closed and placed 6 h within the planetary mill rotated at 500 rpm. 4 mL of deionised water were added and the bowl was closed and placed 5 minutes within the planetary mill rotated at 500 rpm. After this treatment, the fine suspension was filtered, washed with deionised water, and then dried under *vacuo* over P_2O_5 to obtain. *N*,*N*-Dibenzyl-3-phenylpropanamide was recovered as a white solid (0.194 g, 44 %).



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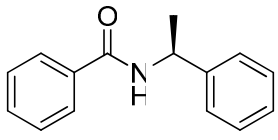
M.p. 106–107°C (lit. 104.5–105.0 °C)[8]; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.30–6.95 (15H), 4.53 (s, 2H), 4.29 (s, 2H), 2.98 (t, *J* = 7.3 Hz, 2H), 2.65 (t, *J* = 7.3 Hz, 2H) ; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.9, 141.3, 137.4, 136.5, 129.1, 128.7, 128.62, 128.59, 128.4, 127.7, 127.5, 126.4, 126.3, 50.0, 48.4, 35.1, 31.7 ; MS (ESI): m/z 330 $[M+H]^+$.

(*S*)-*N*-1-Phenylethyl-benzamide (13)[9] Following general procedure, benzoic acid (0.183 g, 1.5 mmol) was used as the acid species and (*S*)-methylbenzylamine hydrochloride (0.213 g, 1.35 mmol) was used as the amine species. (*S*)-*N*-1-phenylethyl-benzamide was recovered as a white solid (0.207 g, 68 %).



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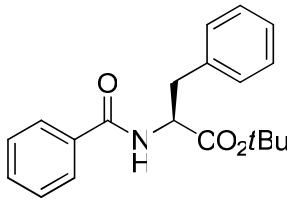
M.p. 121–122 °C (lit. 122–123 °C)[10]; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.87–7.19 (m, 10 H), 6.37 (br d, 1 H), 5.39–5.29 (m, 1 H), 1.61 (d, *J* = 6.8 Hz, 3 H) ppm; ^{13}C NMR (300 MHz, $CDCl_3$): δ = 166.8, 143.3, 134.8, 131.7, 129.0, 128.8, 127.7, 127.1, 126.5, 49.4, 21.9 ppm; MS (ESI): *m*/*z* 226.2 [*M*+H]$^+$; The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralcel OD-H, *n*-hexane/2-propanol = 90/10, Flow rate = 1 mL/min, 25 °C, λ = 230 nm, t_r = 11.9 min (*R*) and t_r = 17.4 min (*S*), 99 % ee, *S*-enantiomer).

(*S*)-2-Benzoylamino-3-phenylpropionic acid *tert*-butyl ester (14)[11] Benzoic acid (0.183 g, 1.5 mmol) and CDI (243 mg, 1.5 mmol) were introduced in stainless steel grinding bowl with fifty stainless steel balls (5 mm diameter). The bowl was closed and placed 5 minutes within the planetary mill rotated at 500 rpm. Then, phenylalanine *tert*-butyl ester hydrochloride (0.348 g, 1.35 mmol) was added. The bowl was closed and placed 30 minutes within the planetary mill rotated at 500 rpm. 2.5 mL of deionised water were added and the bowl was closed and placed 5 minutes within the planetary mill rotated at 500 rpm. After this treatment, the suspension was washed with deionised water, filtered and then dried under *vacuo* over P_20_5 to obtain (*S*)-2-benzoylamino-3-phenylpropionic acid *tert*-butyl ester as a white solid (0.342 g, 78 %).



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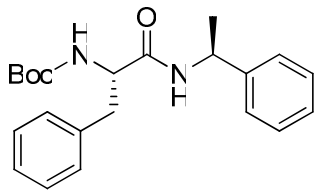
M.p. 79–80 °C (lit. 61 °C)[11]; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 7.0 Hz, 2 H), 7.61–7.20 (m, 8 H), 6.67 (br s, 1 H), 5.08–4.95 (m, 1 H), 3.29 (d, *J* = 5.2 Hz, 2 H), 1.49 (s, 9 H) ppm; ^{13}C NMR (300 MHz, $CDCl_3$): δ = 171.0, 166.9, 136.4, 134.4, 131.9, 129.9, 128.9, 128.6, 127.3, 127.2, 83.0, 54.1, 38.3, 28.3 ppm; MS (ESI): *m*/*z* 326.2 [*M*+H]$^+$; The enantioselectivity was determined by chiral HPLC analysis (DIACEL Chiralcel OD-H, n-hexane/2-propanol = 90/10, Flow rate = 1 mL/min, 25 °C, λ = 254 nm, t_r = 5.8 min (*R*) and t_r = 9.2 min (*S*), 98 % ee, *S*-enantiomer).

***tert*-Butyl *N*-((1*S*)-1-benzyl-2-oxo-2-{[(1*S*)-1-phenylethyl]amino}ethyl)carbamate (15)**[12] Following general procedure, Boc-Ph-OH (0.133 g, 0.5mmol) was used as the acid species and (*S*)-methylbenzylamine (58 µL, 0.45 mmol) was used as the amine species. *tert*-Butyl *N*-((1*S*)-1-benzyl-2-oxo-2-{[(1*S*)-1-phenylethyl]amino}ethyl)carbamate was recovered as a white solid (0.081 g, 49 %).

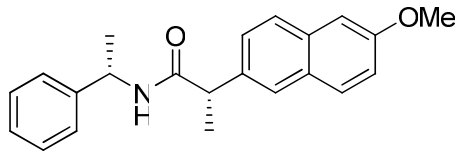


15

M.p. 136 °C (lit. 131–132 °C)[12]; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.33–7.07 (11H), 6.06 (d, *J* = 7.8 Hz, 1H), 5.17–4.96 (2H), 4.29 (q, *J* = 7.6 Hz, 1H), 3,04 (m, 2H), 1.43–1.38 (13H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.3, 142.7, 129.5, 128.8, 128.7, 127.4, 127.0, 126.2, 56.2, 48.8, 38.6, 28.4, 21.7 ppm ; MS (ESI): m/z 369.1 [*M*+H]$^+$.

(*S*,*S*)-2-(6-Methoxynaphthalen-2-yl)-*N*-(1-phenylethyl)propanamide (16)[13] (*S*)-(+)-2-(6-Methoxy-2-naphthyl)propionic acid (0.115 g, 0.5 mmol) and CDI (81 mg, 0.5 mmol) were introduced in a 12 mL stainless steel grinding bowl with fifty stainless steel balls (5 mm diameter). The bowl was closed and placed 10 minutes within the planetary mill rotated at 500 rpm. Then, the (*S*)-methylbenzylamine (122

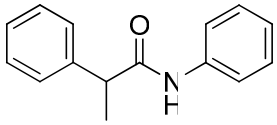
µL, 0.95 mmol) was added. The bowl was closed and placed 10 minutes within the planetary mill rotated at 500 rpm. 4 mL of deionised water were added and the bowl was closed and placed 5 minutes within the planetary mill rotated at 500 rpm. After this treatment, the fine suspension was filtered, washed with deionised water, and then dried under *vacuo* over P_2O_5 to obtain (*S*,*S*)-2-(6-methoxynaphthalen-2-yl)-*N*-(1-phenylethyl)propanamide as a white solid (0.134 g, 81 %).



16

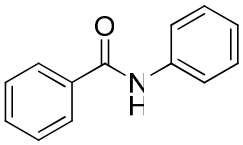
M.p. 168–169 °C (lit. 176.0–176.5 °C)[13]; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.68–7.51 (m, 3 H), 7.34–6.96 (m, 8 H), 5.60–5.47 (m, 1 H), 5.11–4.94 (m, 1 H), 3.85 (s, 3 H), 3.64 (q, *J* = 7.1 Hz, 1 H), 1.50 (d, *J* = 7.0 Hz, 3 H), 1.30 (d, *J* = 7.0 Hz, 3 H) ppm; ^{13}C NMR (300 MHz, $CDCl_3$): δ = 173.5, 157.9, 143.5, 136.7, 133.9, 129.4, 129.2, 128.7, 127.7, 127.3, 126.5, 126.3, 126.0, 119.3, 105.8, 55.5, 48.9, 47.2, 22.1, 18.8 ppm; MS (ESI): *m*/*z* 334.2 $[M+H]^+$.

***N*-Phenyl-2-phenylpropanamide**[1] Following general procedure, 2-phenylpropionic acid (0.225 g, 1.5 mmol) was used as the acid species and aniline hydrochloride (0.175 g, 1.35 mmol) was used as the amine species. *N*-phenyl-2-phenylpropanamide was recovered as a white solid (0.278 g, 91 %).



M.p. 134–135 °C (lit. 136 °C)[1]; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.43–6.95 (m, 11 H), 3.70 (q, *J* = 7.2 Hz, 1 H), 1.59 (d, *J* = 7.2 Hz, 3 H) ppm; ^{13}C NMR (300 MHz, $CDCl_3$): δ = 172.6, 141.1, 138.0, 129.3, 129.1, 127.9, 127.8, 124.5, 120.0, 48.2, 18.8 ppm; MS (ESI): *m*/*z* 226.2 $[M+H]^+$.

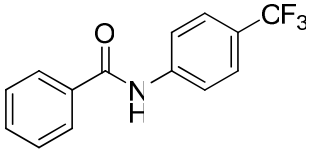
***N*-Phenyl-benzamide**[14] Following general procedure, benzoic acid (0.183 g, 1.5 mmol) was used as the acid species and aniline hydrochloride (0.175 g, 1.35 mmol) was used as the amine species. *N*-phenyl-benzamide was recovered as a white solid (0.247 g, 93 %).



M.p. 162–163°C (lit. 165–166 °C)[14]; ^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.08–7.94 (m, 11 H) ppm; ^{13}C NMR (300 MHz, $CDCl_3$): δ = 166.0, 138.1, 135.2, 132.1, 129.3, 129.0, 127.2, 124.8, 120.5 ppm; MS (ESI): *m*/*z* 198.2 $[M+H]^+$.

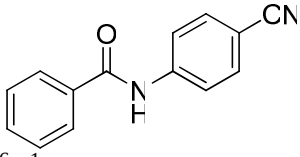
***N*-(4-Trifluoromethylphenyl)benzamide**[15] Benzoic acid (0.183 g, 1.5 mmol) and CDI (243 mg, 1.5 mmol) were introduced in a 12 mL stainless steel grinding bowl with fifty stainless steel balls (5 mm diameter). The bowl was closed and placed 5 minutes within the planetary mill rotated at 500 rpm. Then, the 4-trifluoromethylaniline hydrochloride (0.267 g, 1.35 mmol) was added. The bowl was closed and placed 30 minutes within the planetary mill rotated at 500 rpm. 4 mL of deionised water were added and

the bowl was closed and placed 5 minutes within the planetary mill rotated at 500 rpm. After this treatment, the fine suspension was filtered, washed with deionised water, and then dried under *vacuo* over P_2O_5 to obtain *N*-(4-trifluoromethylphenyl)benzamide as a grey solid (0.358 g, 82 %).



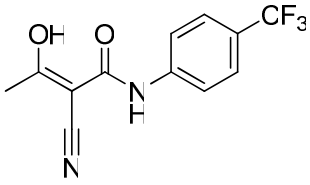
M.p. 208 °C (lit. 204–205 °C)[15]; ^{1}H NMR (200 MHz, DMSO): δ = 10.57 (s, 1H), 8.09–7.93 (4H), 7.80–7.50 (5H); ^{13}C NMR (75 MHz, DMSO): δ = 166.0, 142.8, 134.5, 131.9, 128.5, 127.8, 125.9, 120.1 ppm ; MS (ESI): m/z 266.1 $[M+H]^+$.

***N*-(4-Cyanophenyl) benzamide**[16] Benzoic acid (0.183 g, 1.5 mmol) and CDI (243 mg, 1.5 mmol) were introduced in a 12 mL stainless steel grinding bowl with fifty stainless steel balls (5 mm diameter). The bowl was closed and placed 5 minutes within the planetary mill rotated at 500 rpm. Then, 4-aminobenzonitrile (0.160 g, 1.35 mmol) was added. The bowl was closed and placed 3.5 h within the planetary mill rotated at 500 rpm. 4 mL of deionised water were added and the bowl was closed and placed 5 minutes within the planetary mill rotated at 500 rpm. After this treatment, the fine suspension was filtered, washed with deionised water, and then dried under *vacuo* over P_2O_5 to obtain *N*-(4-cyanophenyl) benzamide as a grey solid (0.300 g, 78 %).



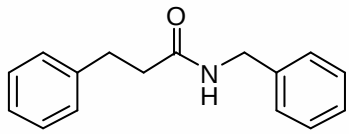
M.p. 164–166 °C (lit. 164.9–166.0 °C)[16]; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.09 (br s, 1H), 7.89–7.86 (2H), 7.80 (dt, *J* = 8.9 and 2.1 Hz, 2H), 7.65 (dt, *J* = 8.8 and 2.1 Hz, 2H), 7.59 (m, 1H), 7.53–7.48 (2H) ; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.1, 142.2, 134.2, 133.5, 132.6, 129.1, 127.3, 120.1, 119.0, 107.5 ; MS (ESI): m/z 223.1 $[M+H]^+$.

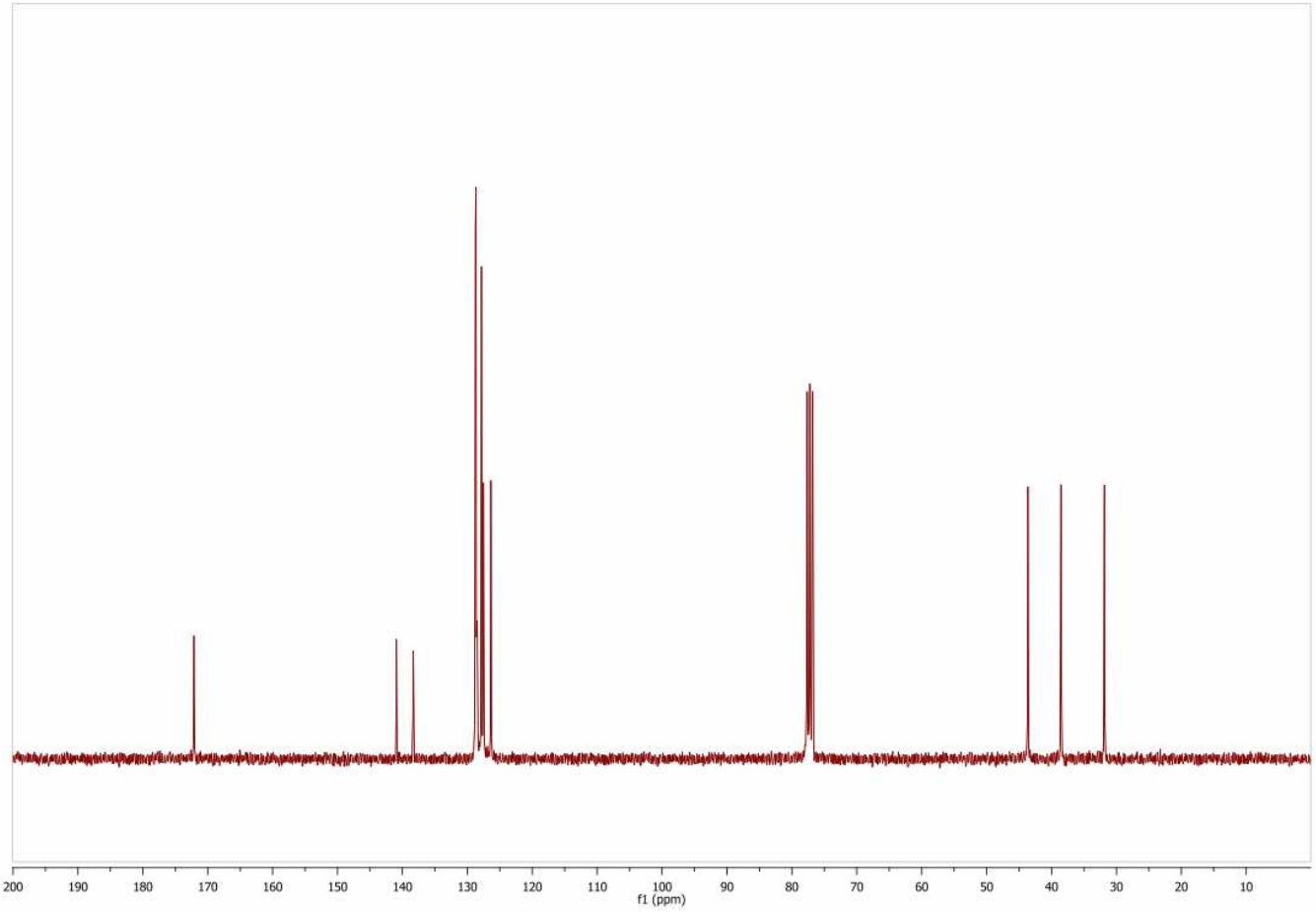
2-Cyano-3-hydroxy-*N*-[4-(trifluoromethyl)phenyl]-2-butenamide (Teriflunomide)[17] The 5-methyl-4-carboxylic acid (191 mg, 1.5 mmol) and CDI (243 mg, 1.5 mmol) were introduced in stainless steel grinding bowl with fifty stainless steel balls (5 mm diameter). The bowl was closed and placed 20 minutes within the planetary mill rotated at 500 rpm. Then, the 4-trifluoromethyl-aniline hydrochloride (267 mg, 1.35 mmol) was added. The bowl was closed and placed 5 hours within the planetary mill rotated at 500 rpm, with 1 min break every 10 min, with inversion of the rotation direction after each break. 4 mL of deionised water were added and the bowl was closed and placed 5 minutes within the planetary mill rotated at 500 rpm. After this treatment, the fine suspension was transferred into a round-bottom flask, pH was adjusted to 1 with concentrated hydrochloric acid, and the suspension was stirred during 24 hours. The suspension was then filtered and dried under *vacuo* over P_2O_5 to obtain a white solid. 2-Cyano-3-hydroxy-*N*-[4-(trifluoromethyl)phenyl]-2-butenamide as the major tautomer was recovered as a white solid (0.297 g, 81 %).



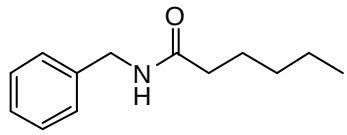
M.p. 230–232 °C; ^{1}H NMR (200 MHz, DMSO): δ = 10.97 (m, 2H), 7.75 (d, *J* = 8.5 Hz, 2H), 7.64 (d, *J* = 7.6 Hz, 2H), 2.23 (s, 3H) ; ^{13}C NMR (150 MHz, DMSO): δ = 187.3, 166.5, 142.1, 126.3, 126.0, 123.7, 123.3, 122.7, 120.7, 120.2, 119.4, 80.5, 23.9; MS (ESI): m/z 271 $[M+H]^+$.

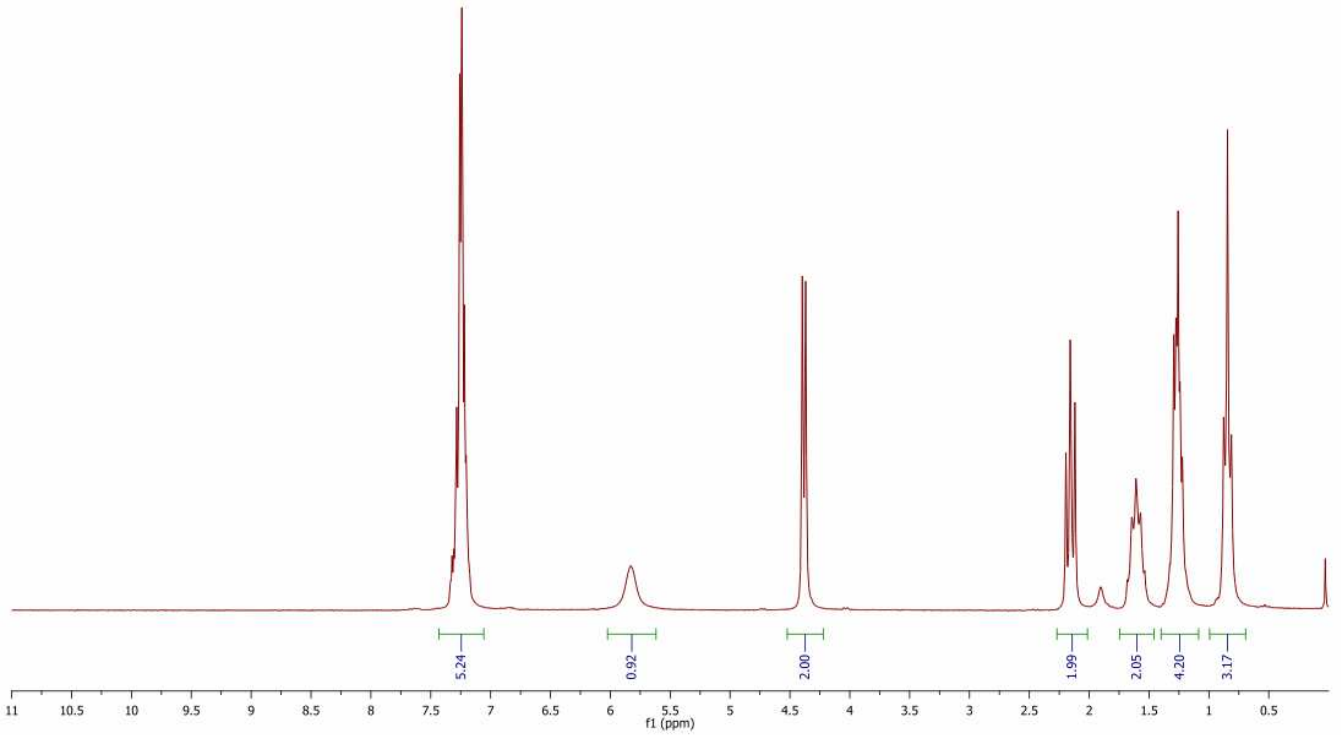
_N_-Benzyl-3-phenylpropanamide

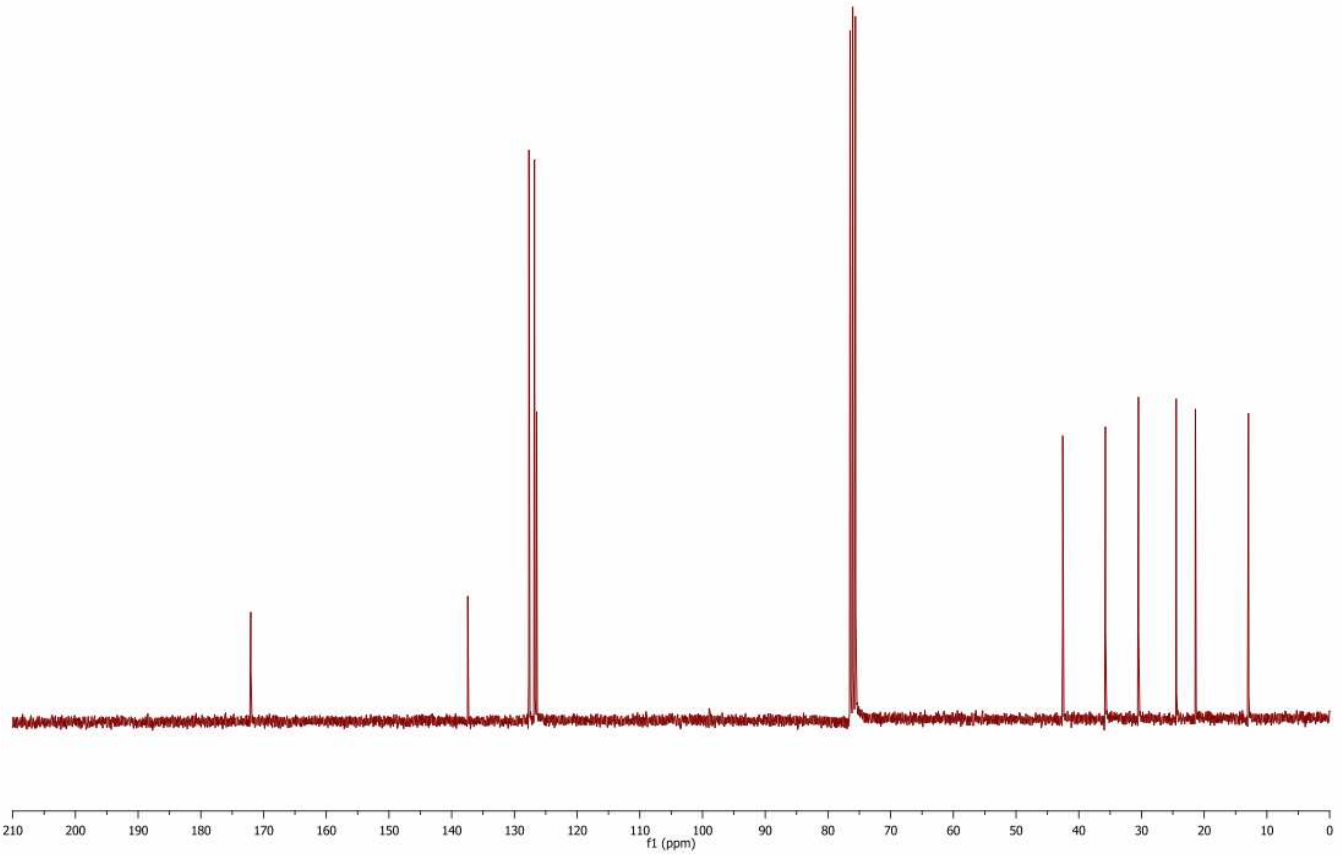




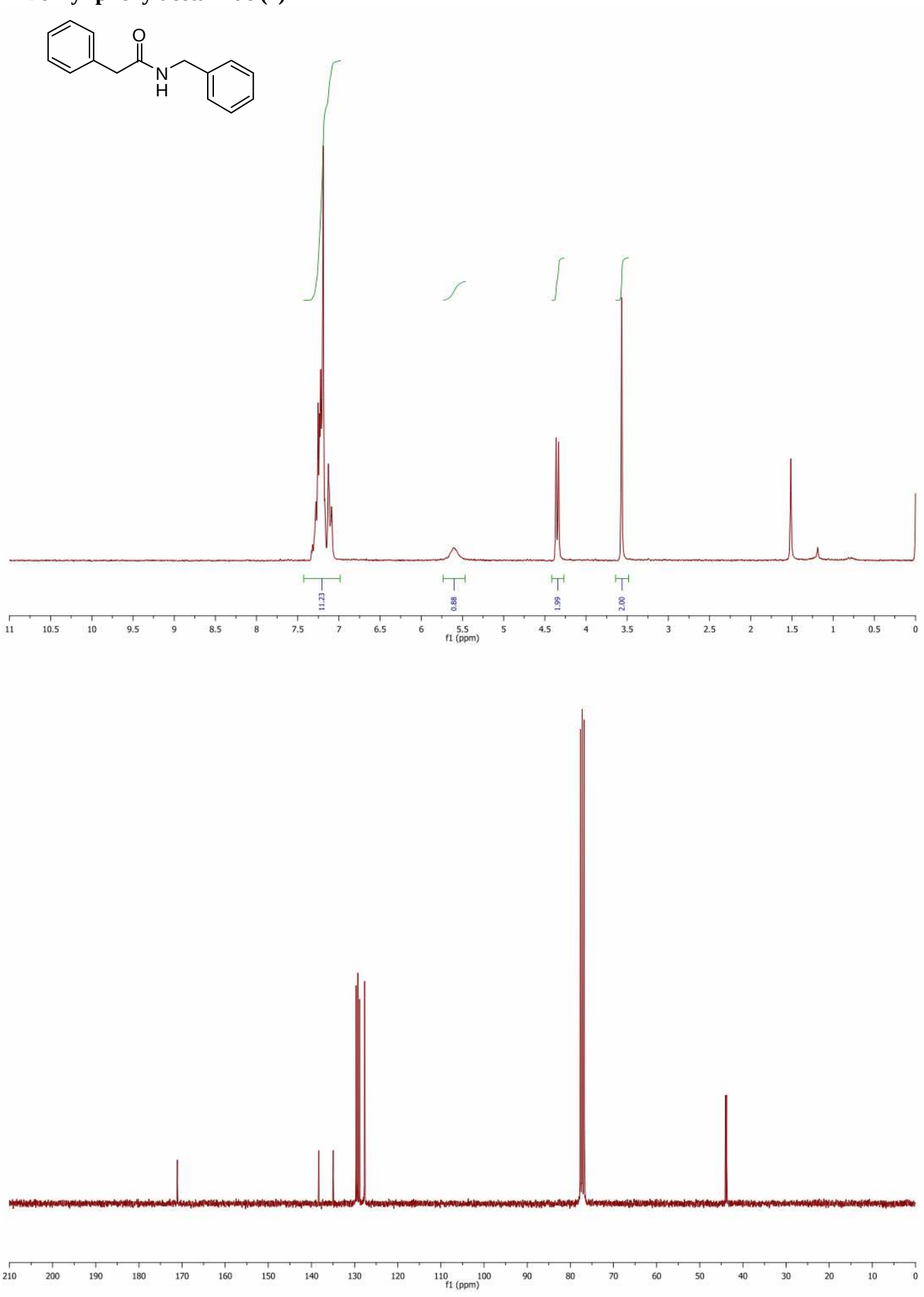
N-Benzylhexanamide (1)



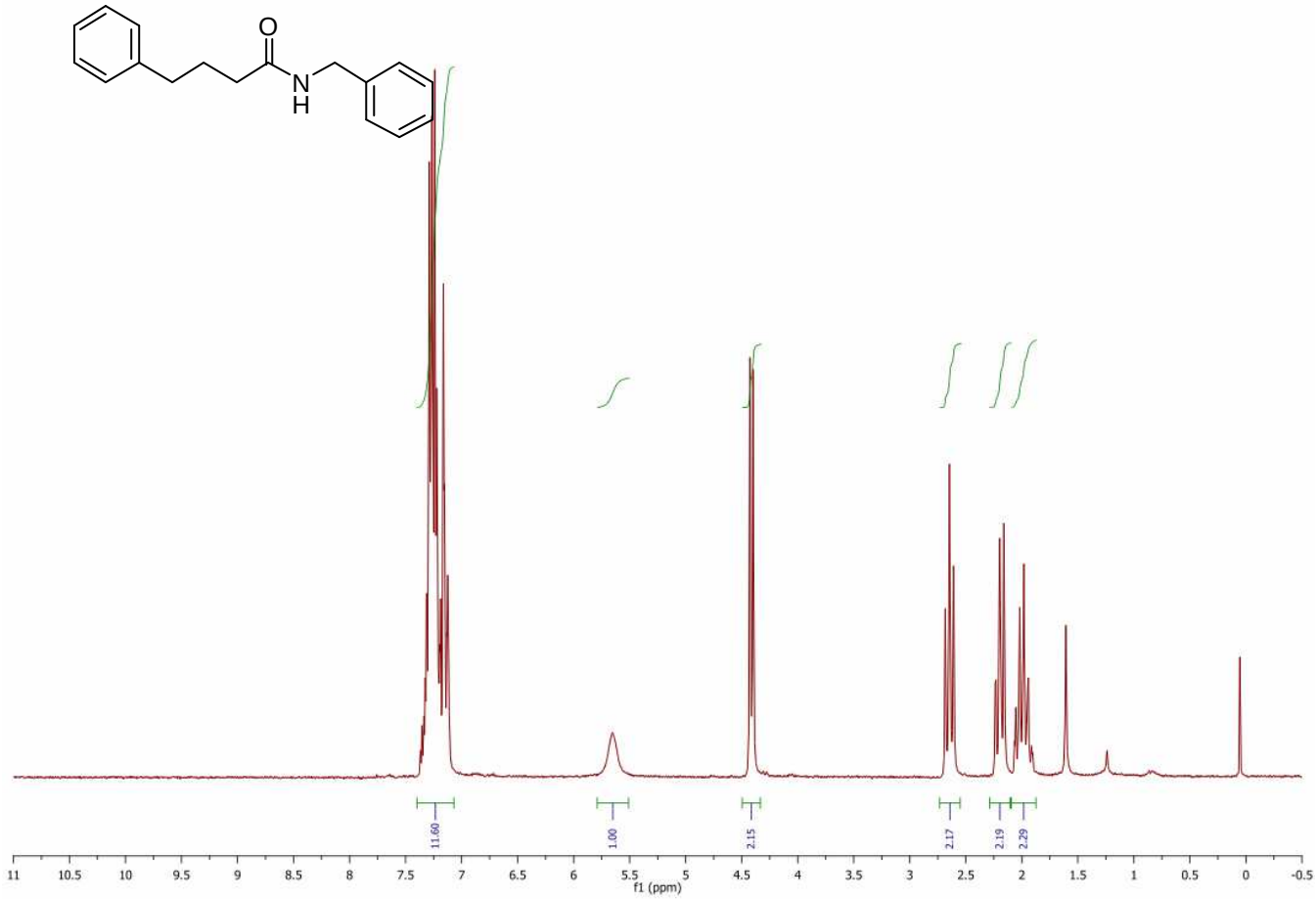


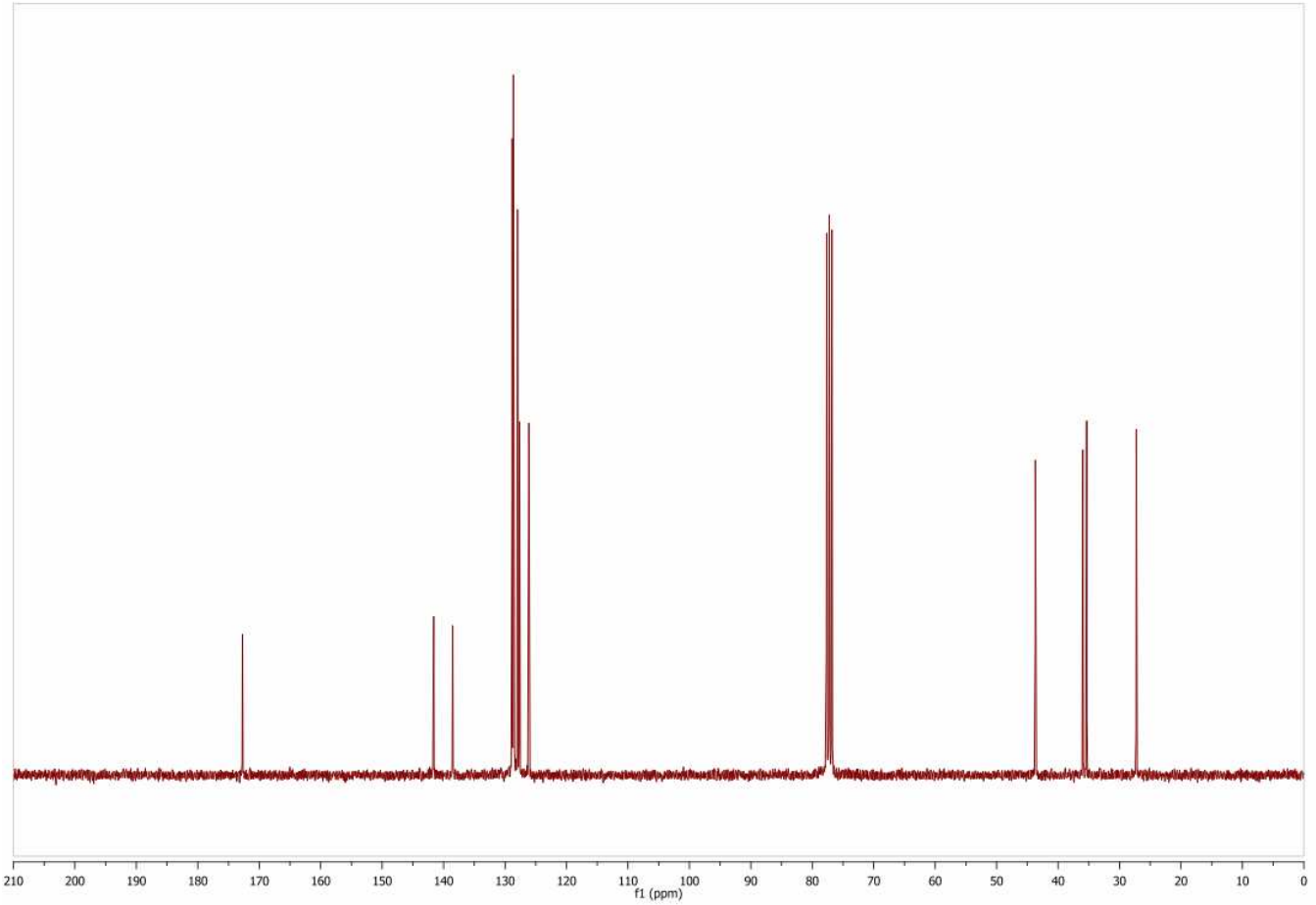


N-Benzyl-phenylacetamide (2)

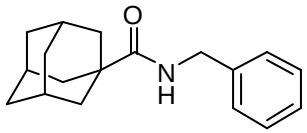


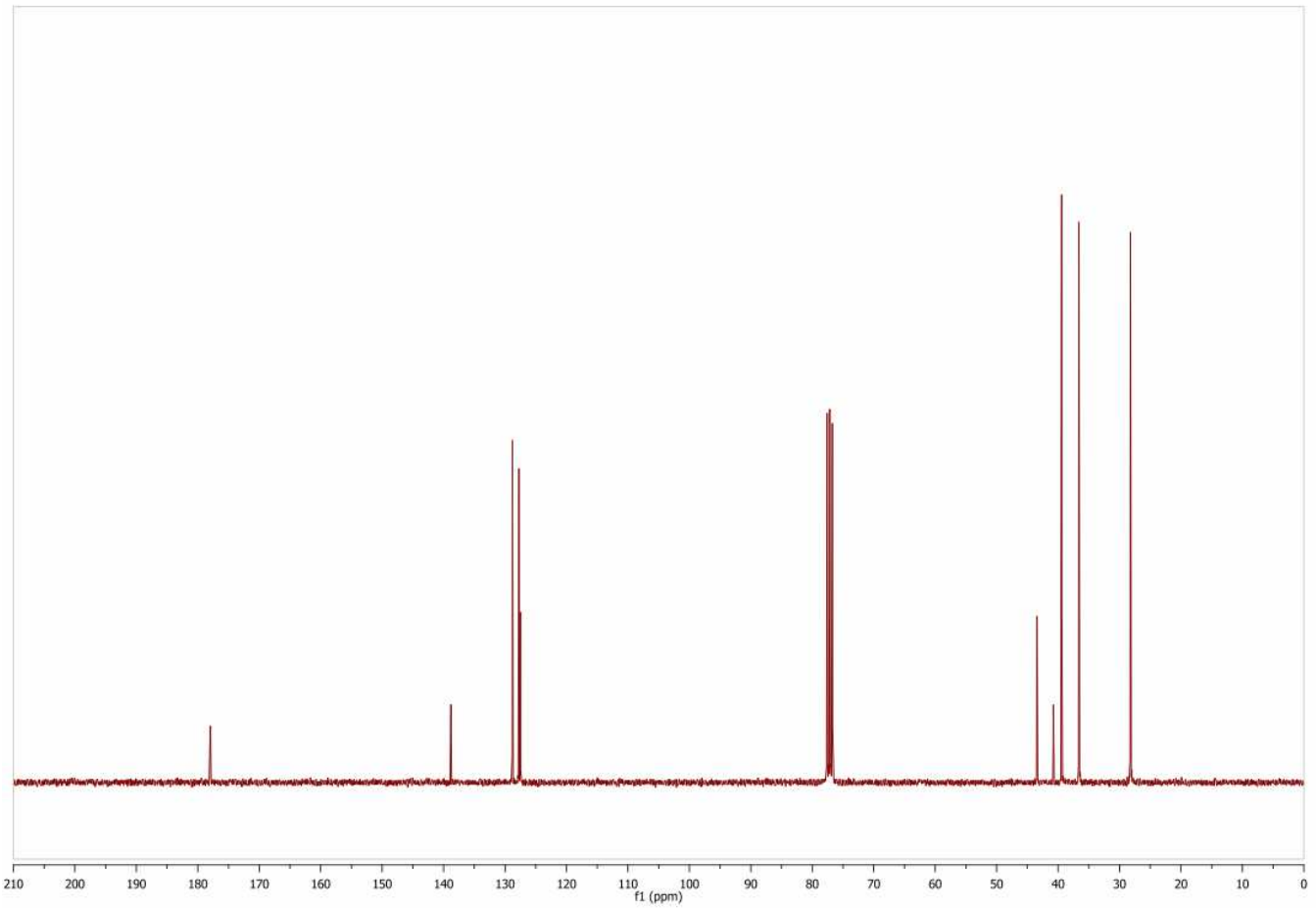
_N_-Benzyl-4-phenylbutanamide (3)



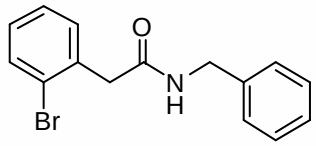


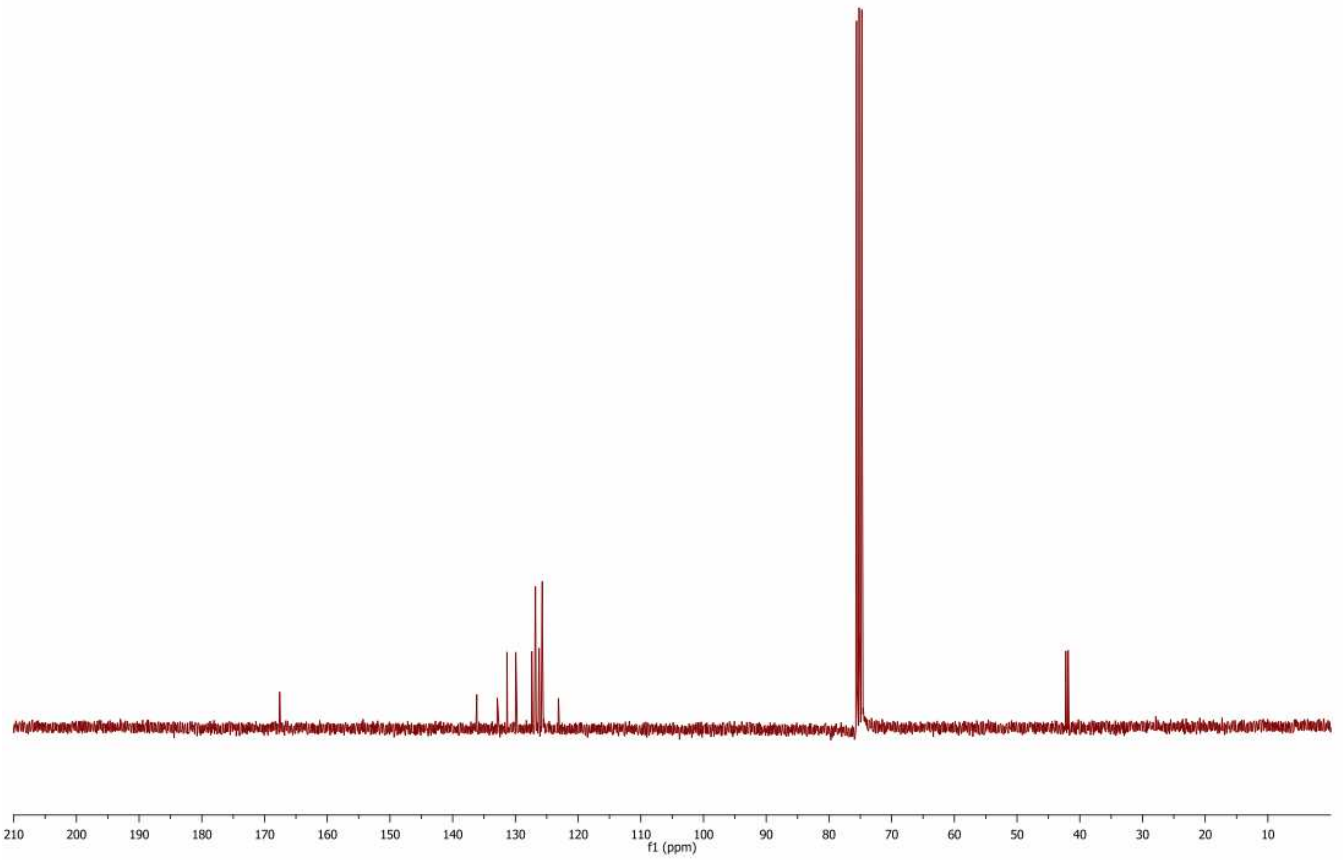
N-Benzyl-1-adamantanecarboxamide (4)



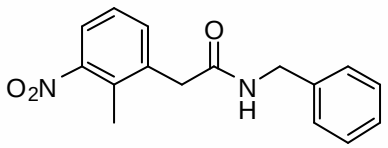


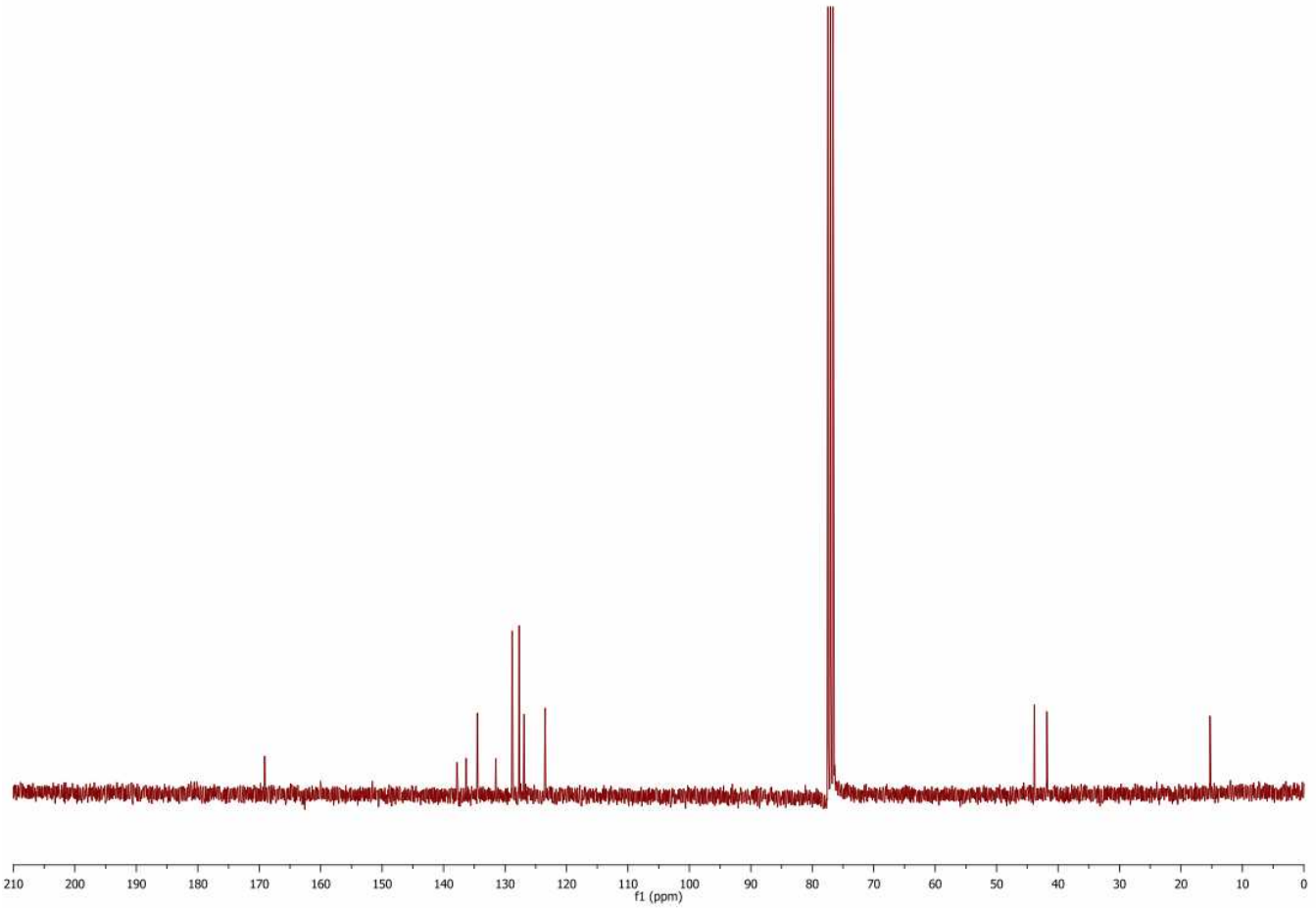
_N_-Benzyl-2-(2-bromophenyl)acetamide (5)



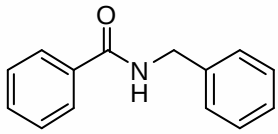


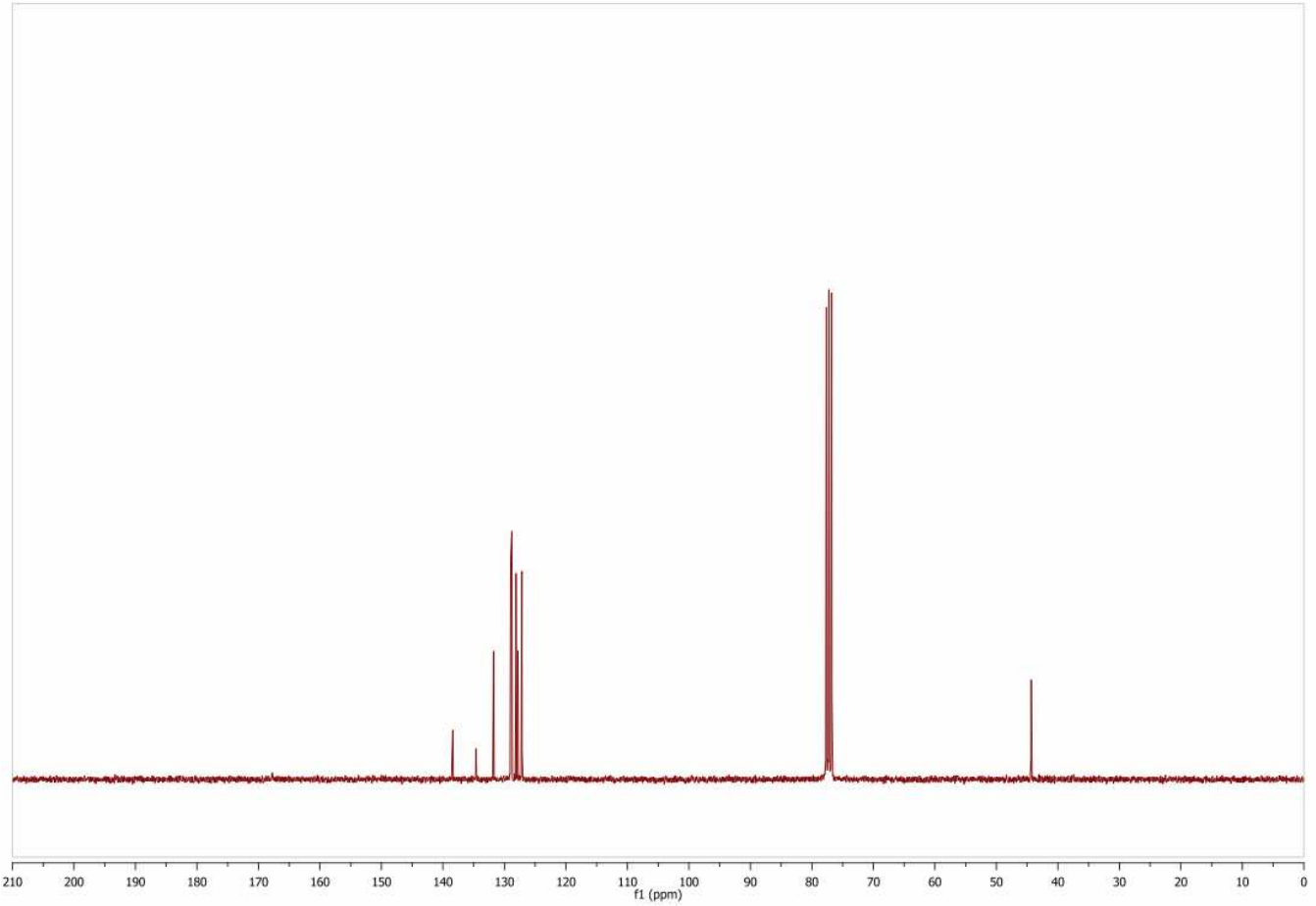
_N_–Benzyl-2-(3-nitro-2-methylphenyl)acetamide (6)



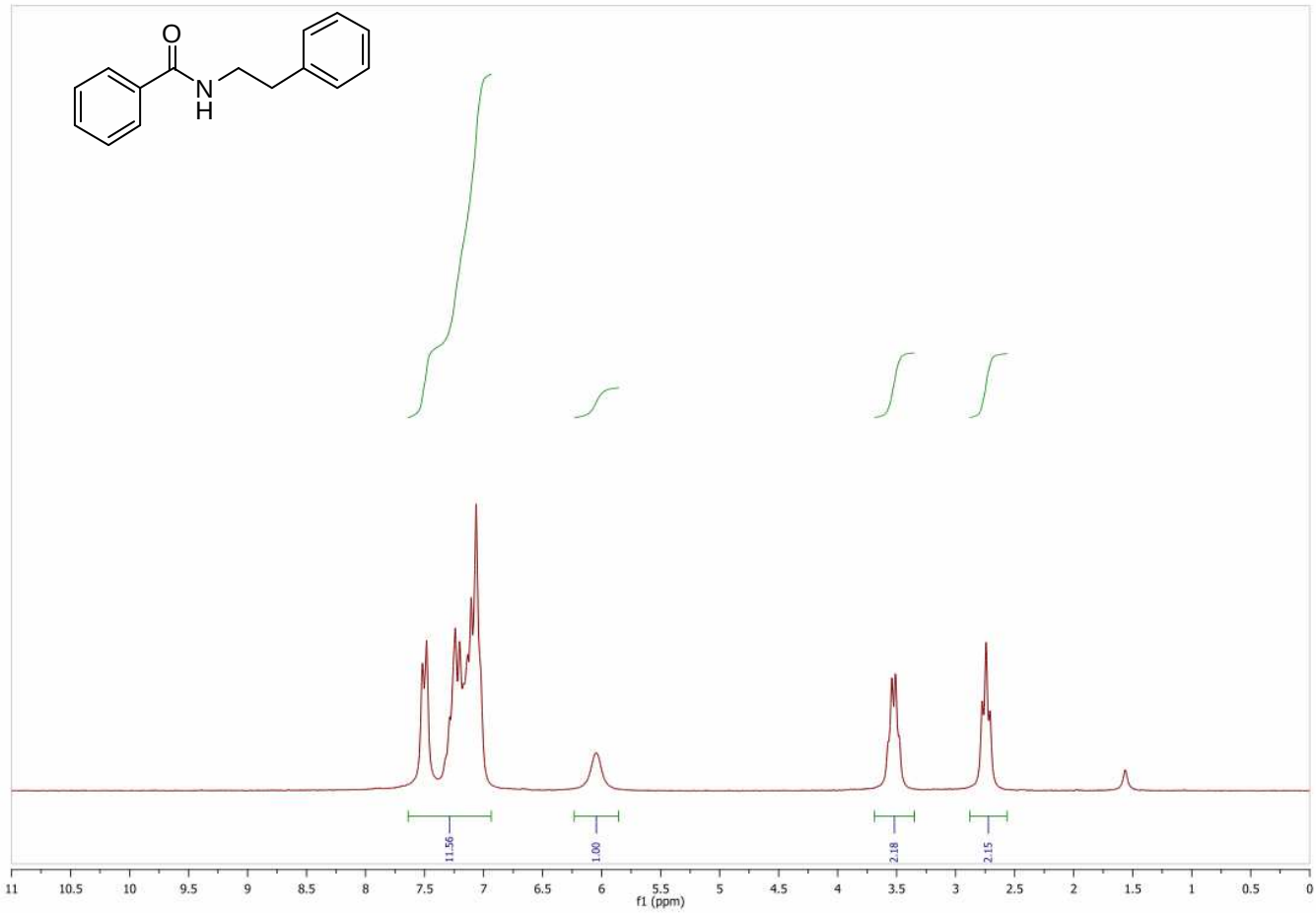


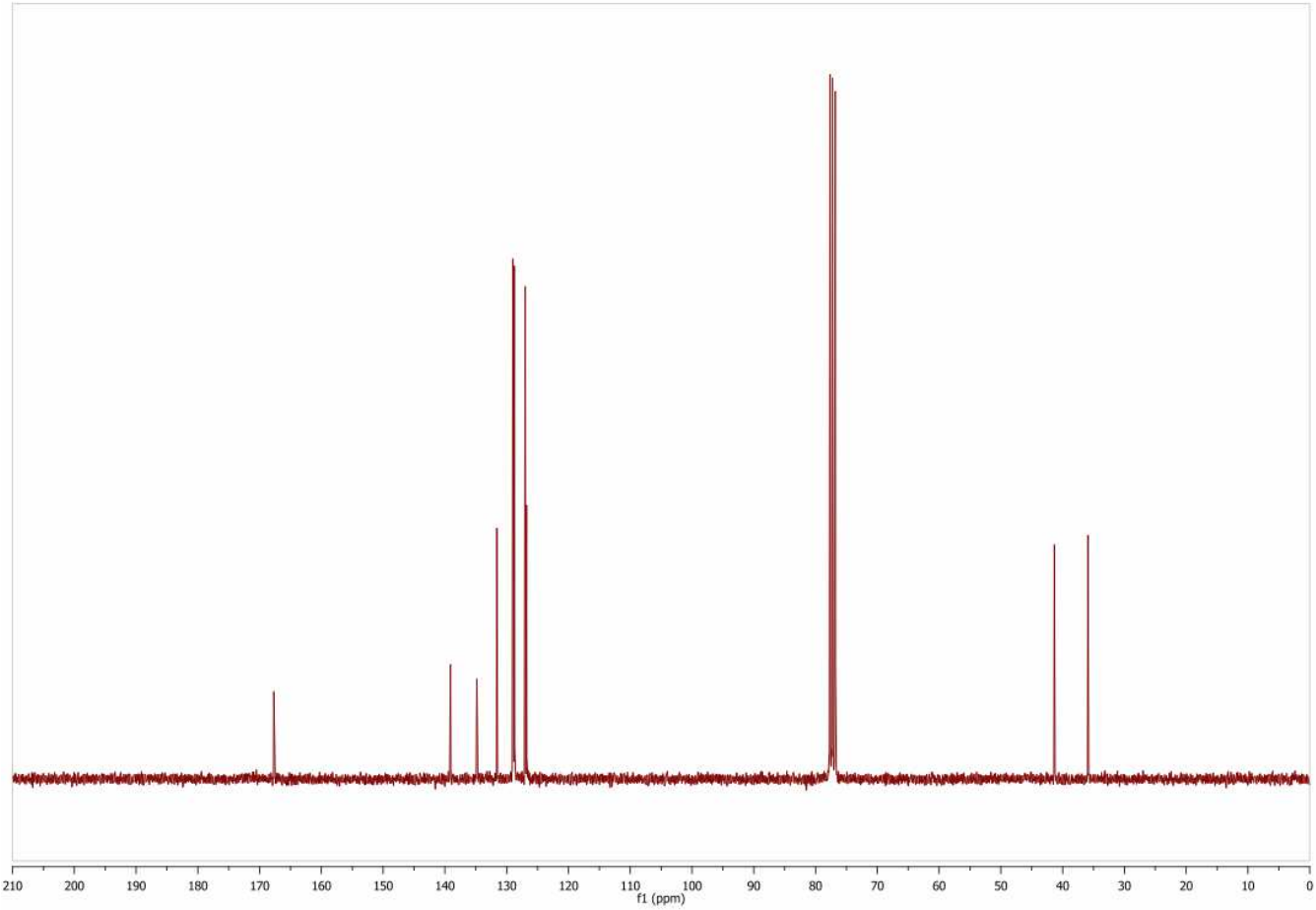
_N_-benzyl-benzamide (7)



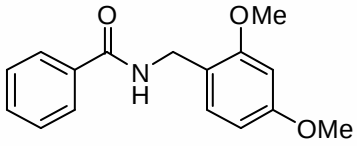


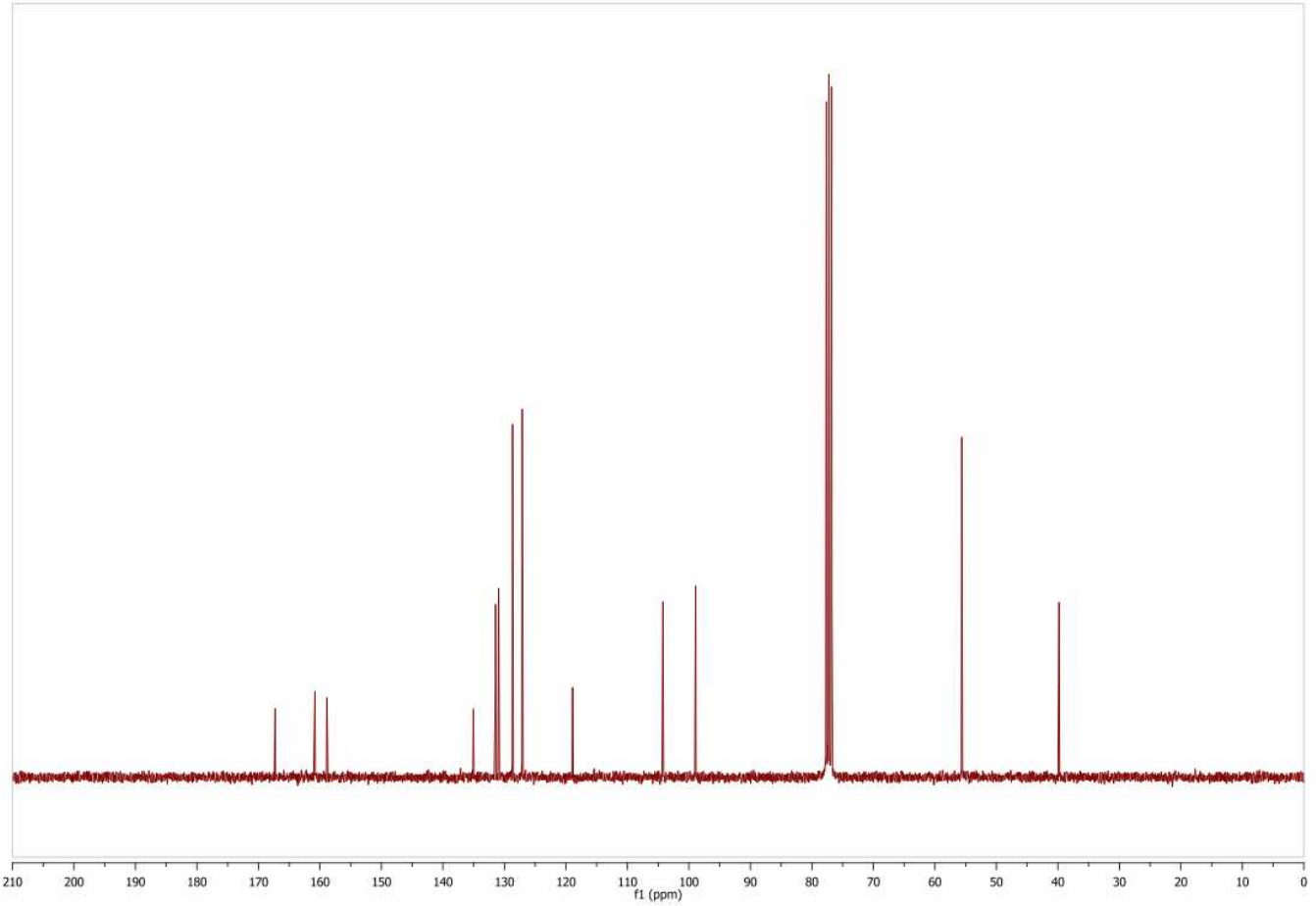
_N_-phenethyl-benzamide (8)



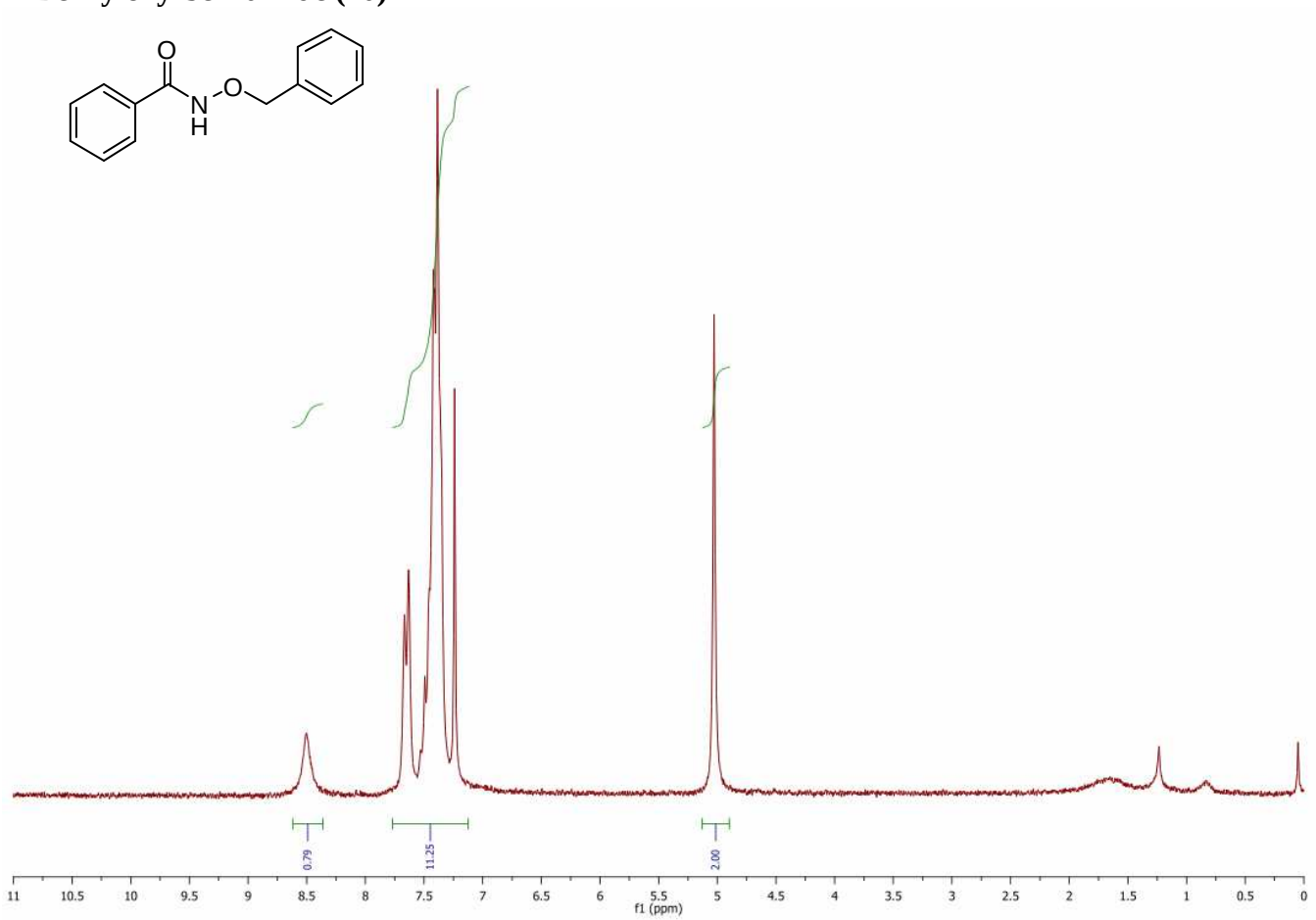


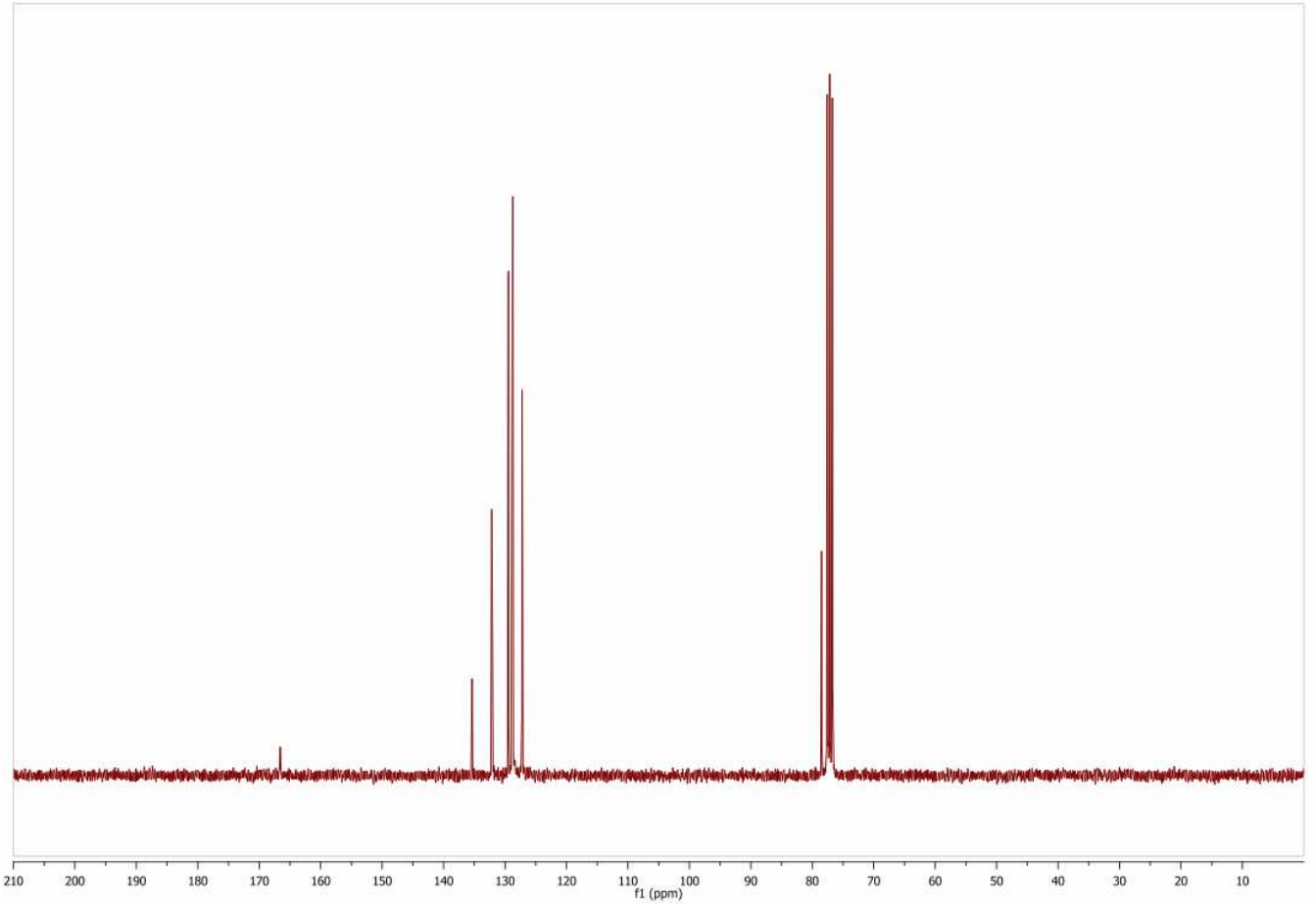
_N_-2,4-Dimethoxybenzyl-benzamide (9)



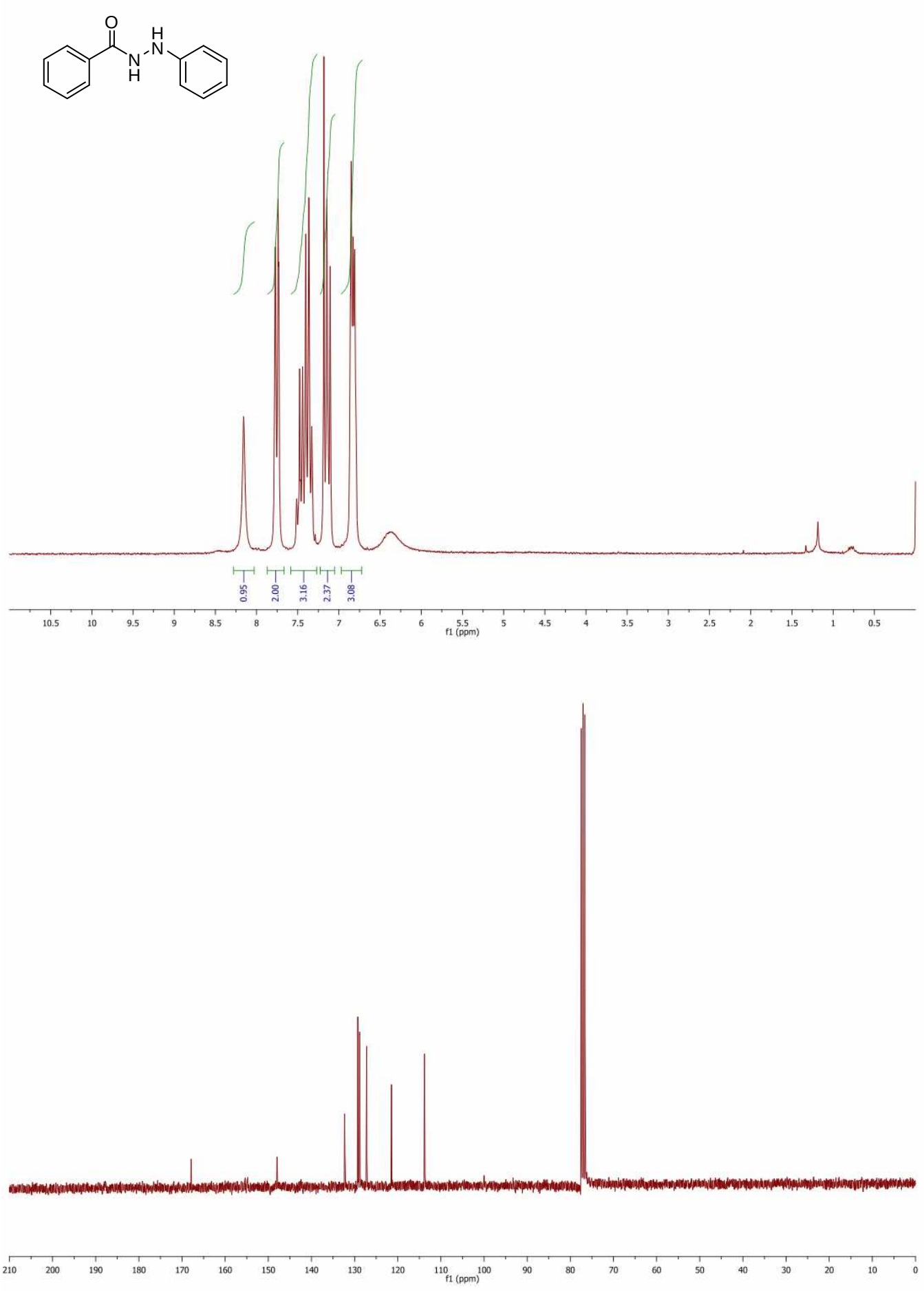


_N_-Benzyloxy-benzamide (10)

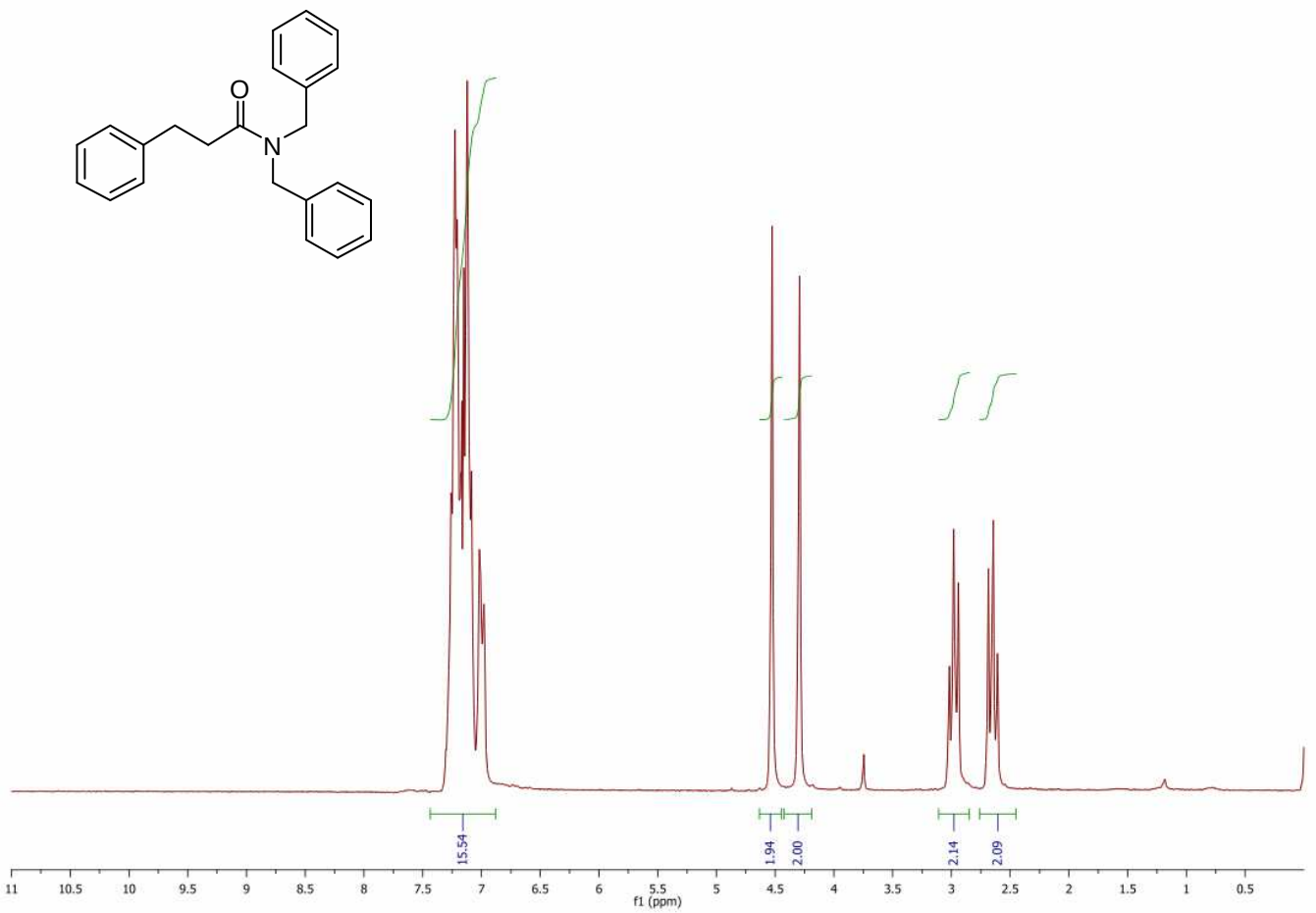


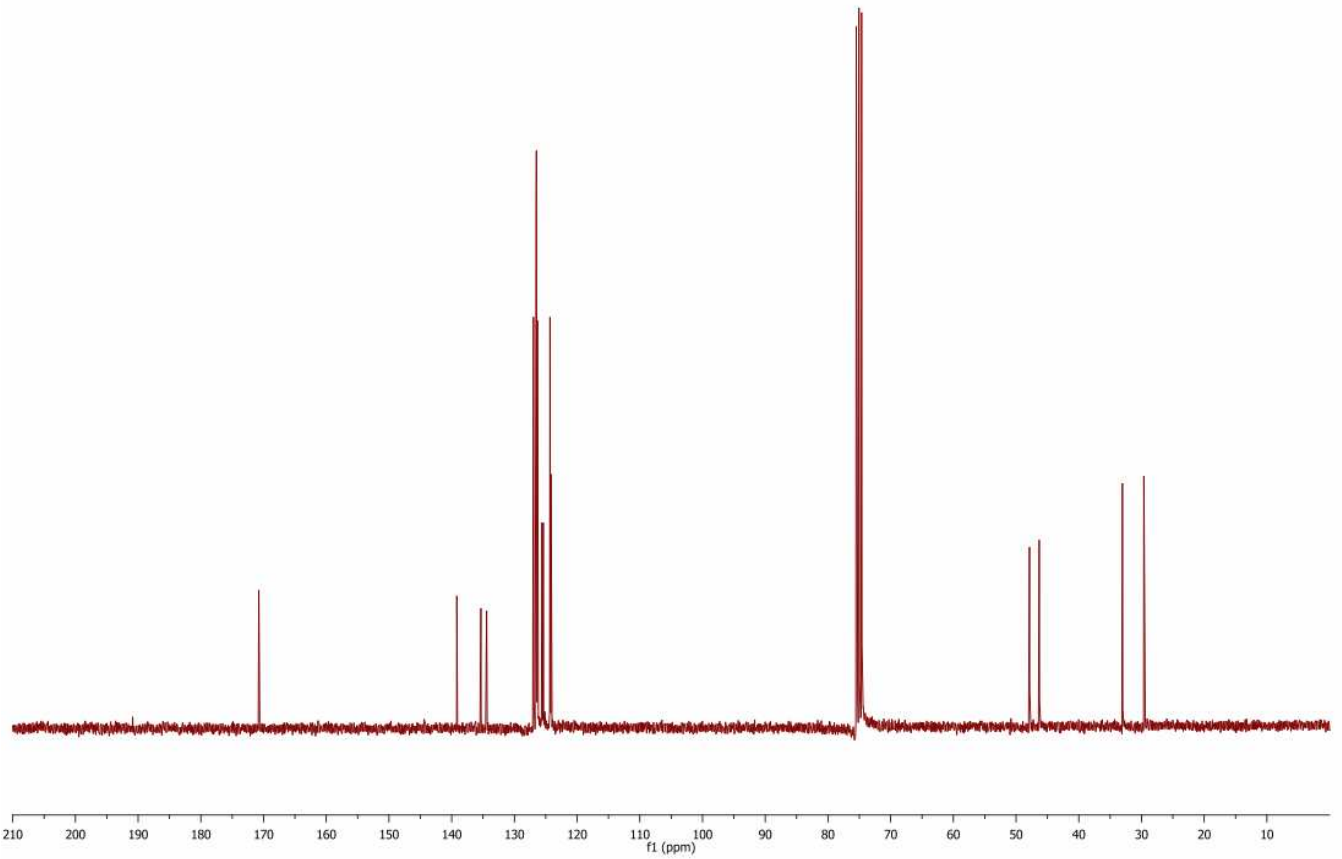


Benzoic acid *N´*-phenylhydrazide (11)

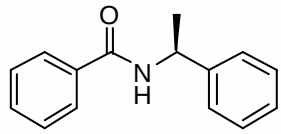


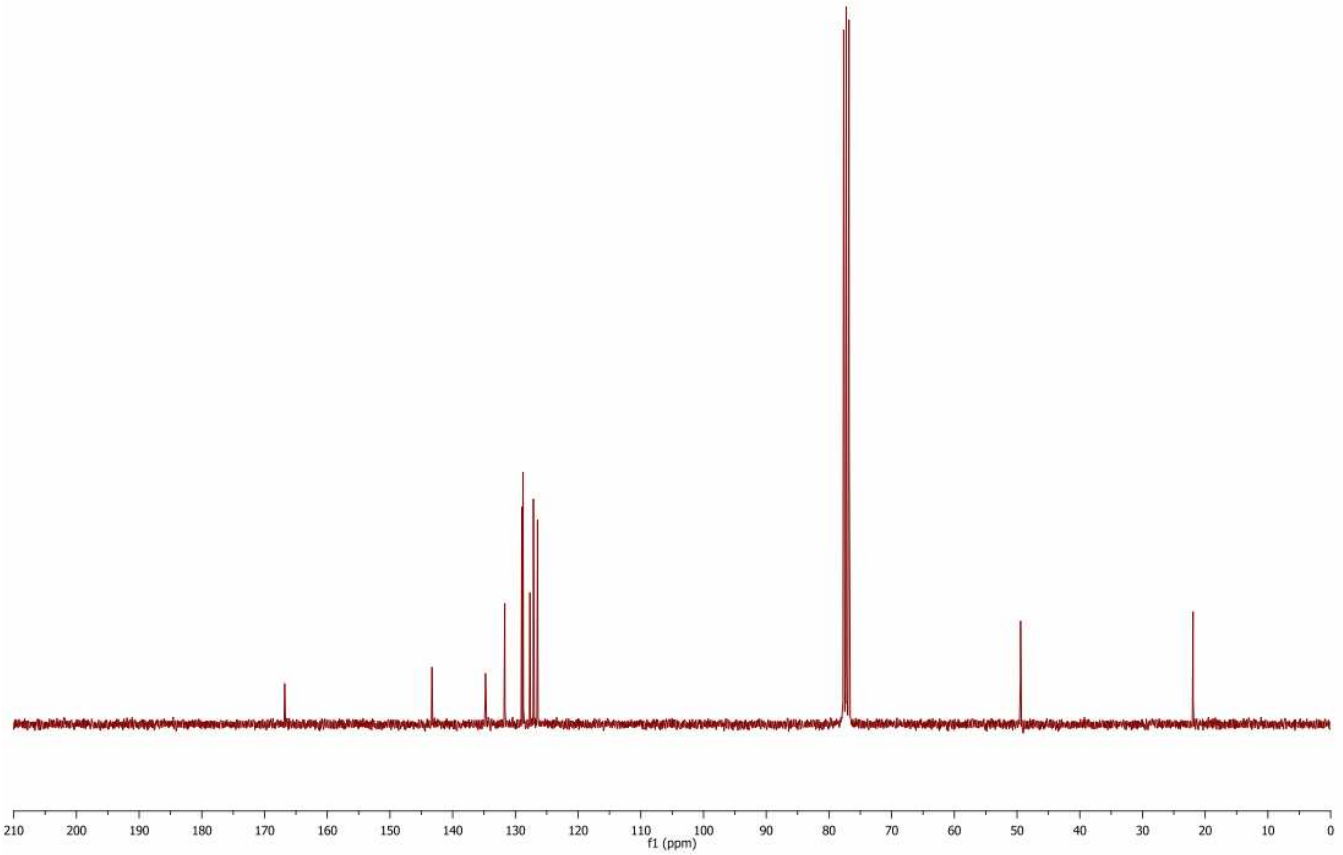
_N,N_-Dibenzyl-3-phenylpropanamide (12)



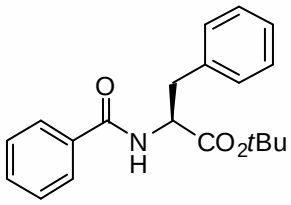


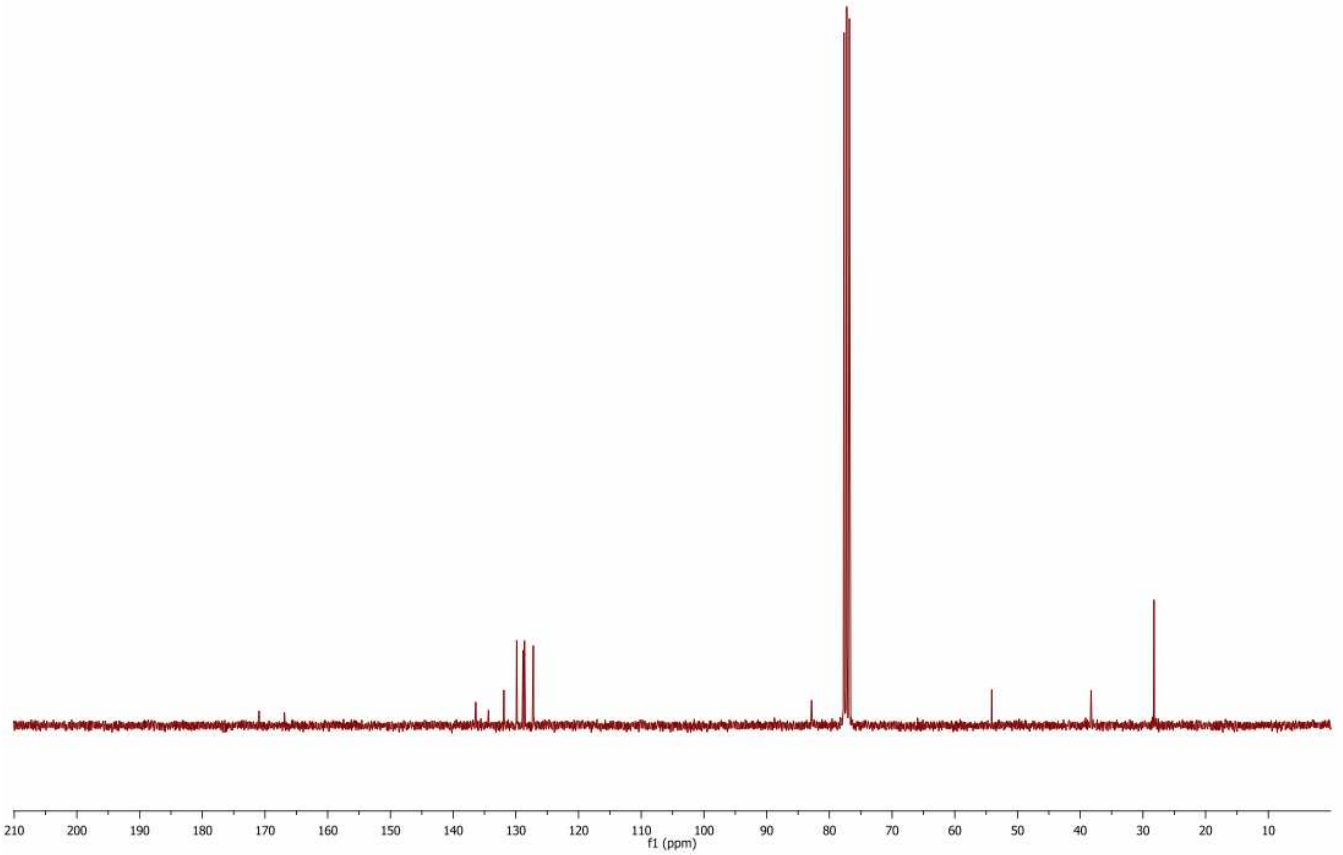
(*S*)-*N*-1-Phenylethyl-benzamide (13)



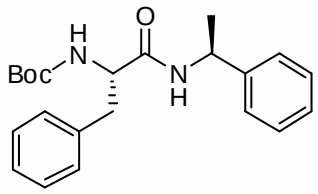


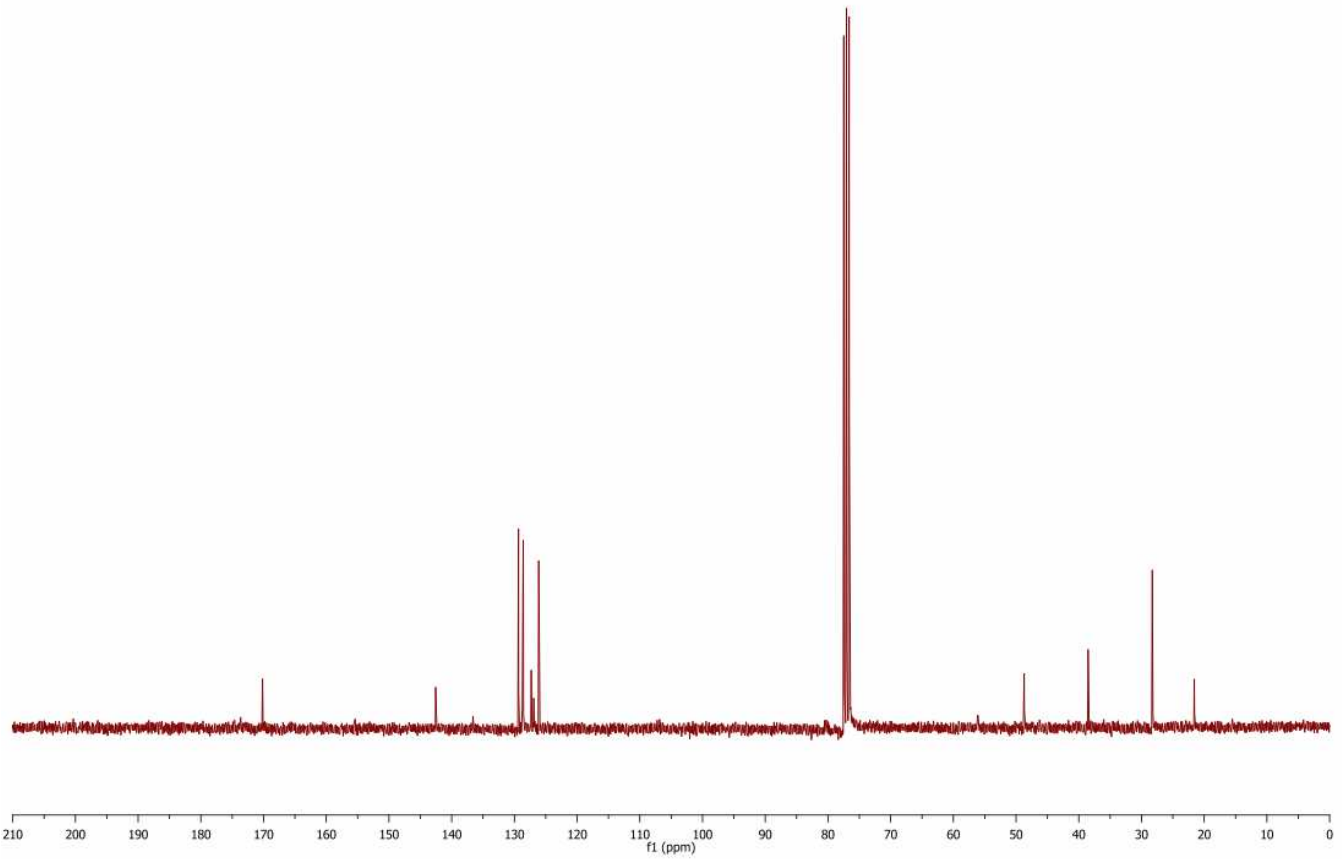
(*S*)-2-Benzoylamino-3-phenylpropionic acid tert-butyl ester (14)



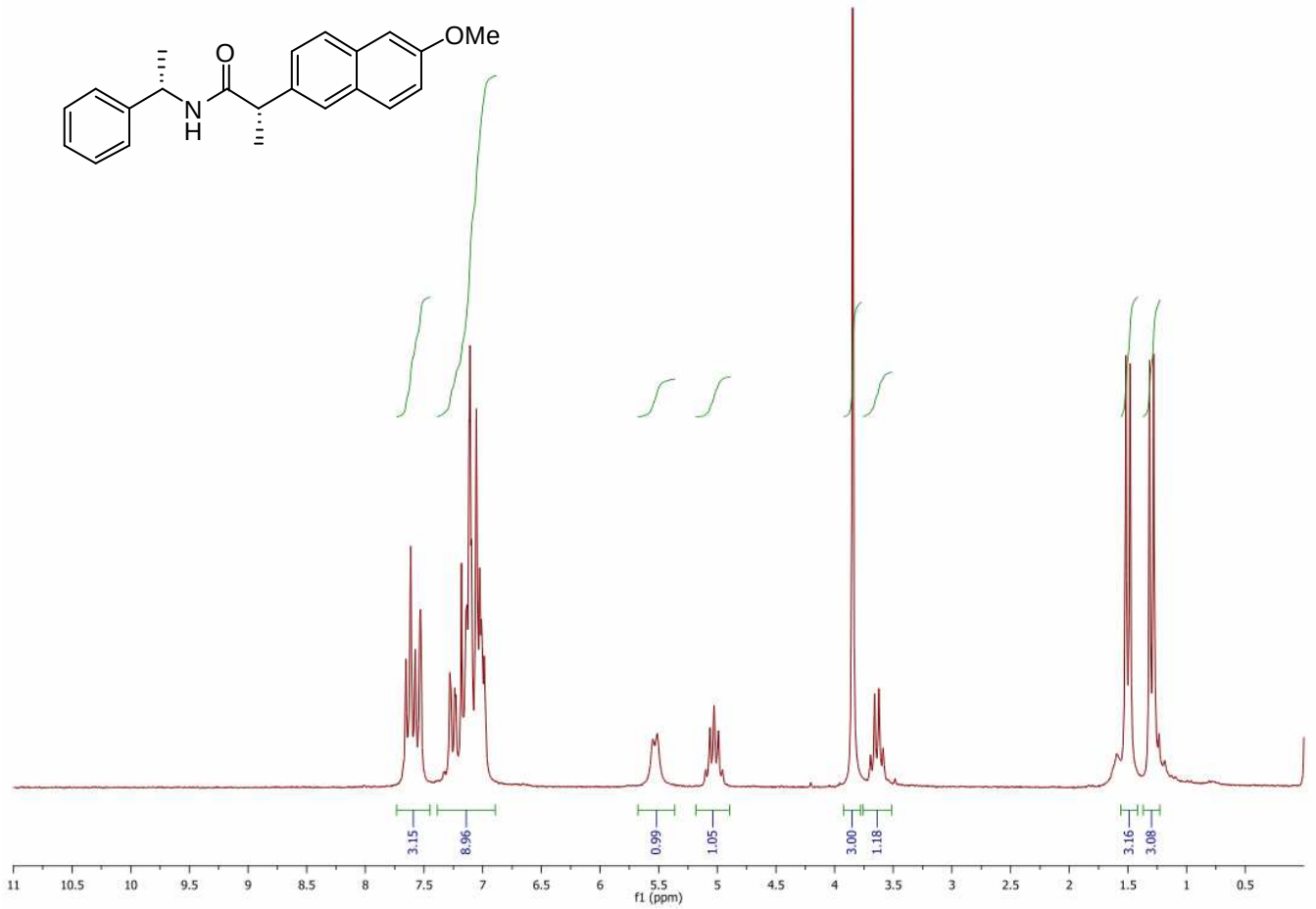


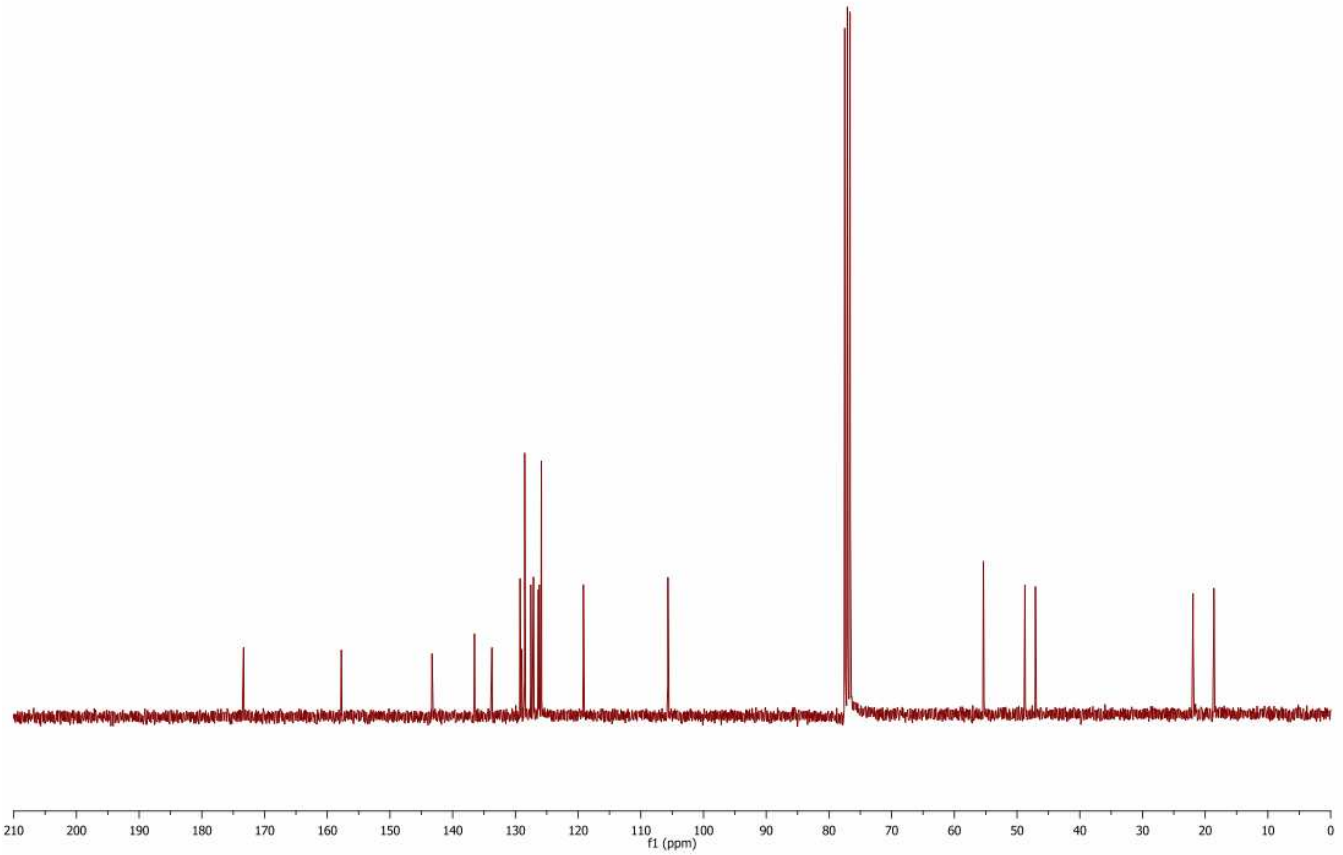
tert-Butyl _N_-((1_S_)-1-benzyl-2-oxo-2-{[(1_S_)-1-phenylethyl]amino}ethyl)carbamate (15)



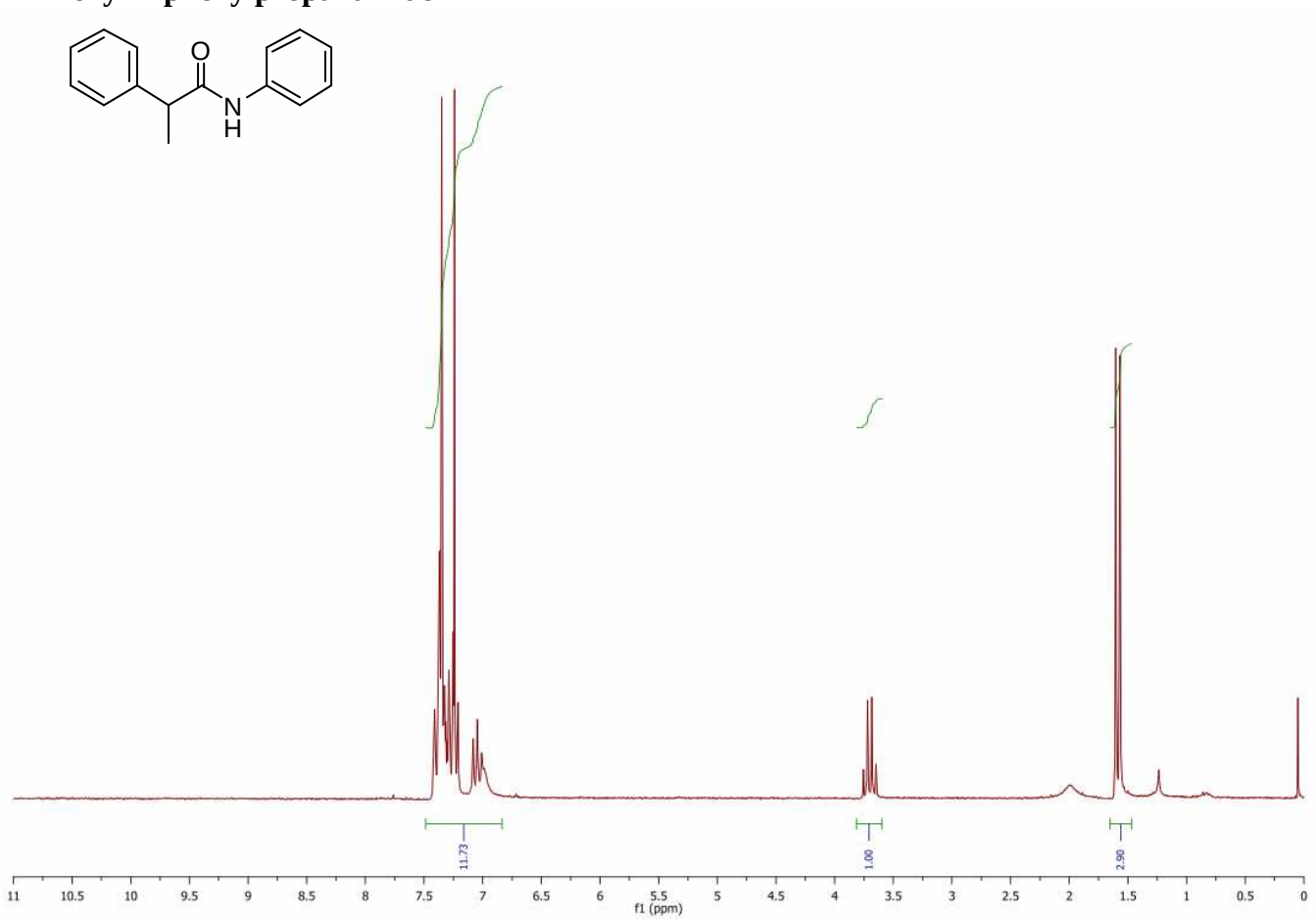


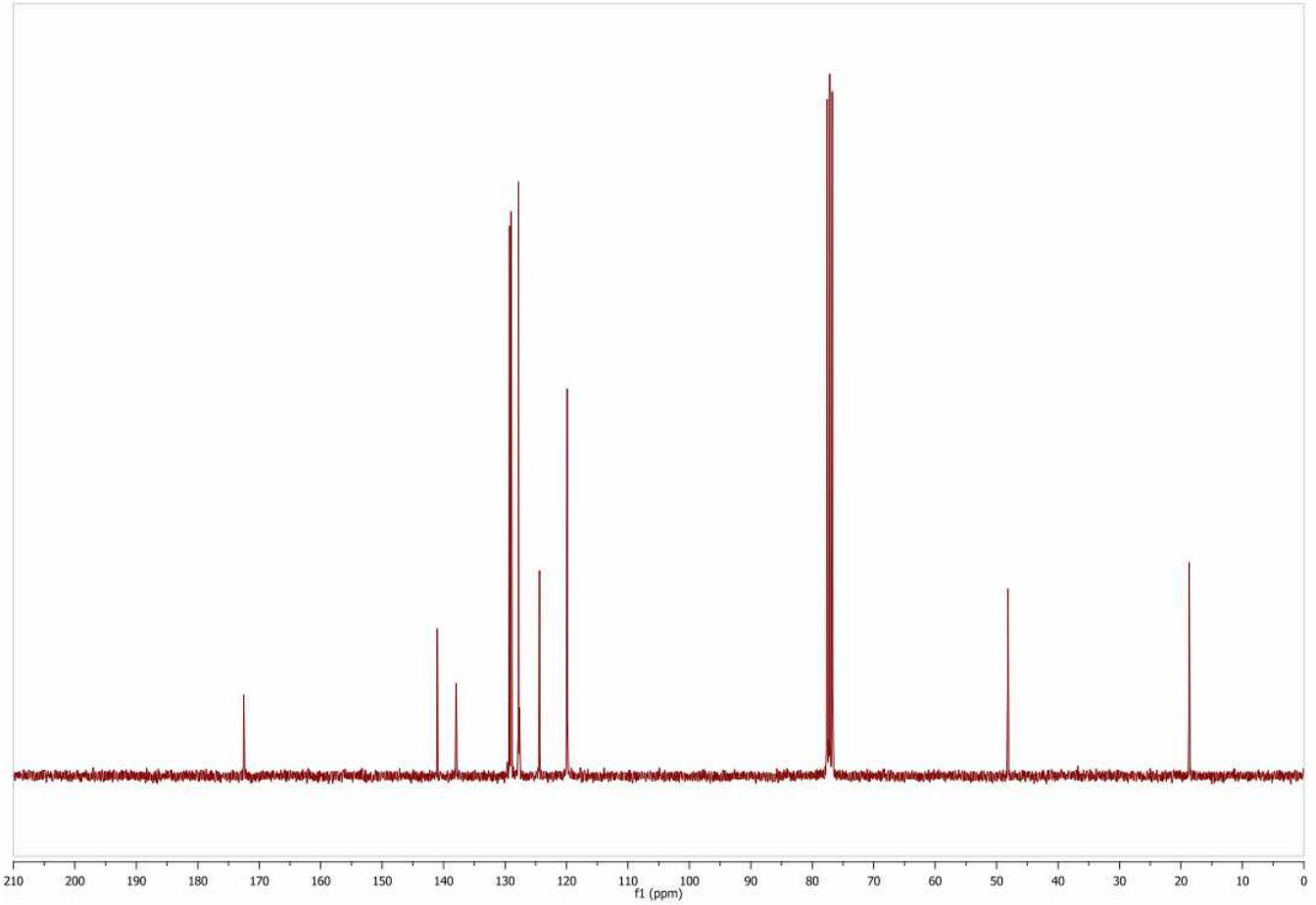
(*S,S*)-2-(6-Methoxynaphthalen-2-yl)-N-(1-phenylethyl)propanamide (16)



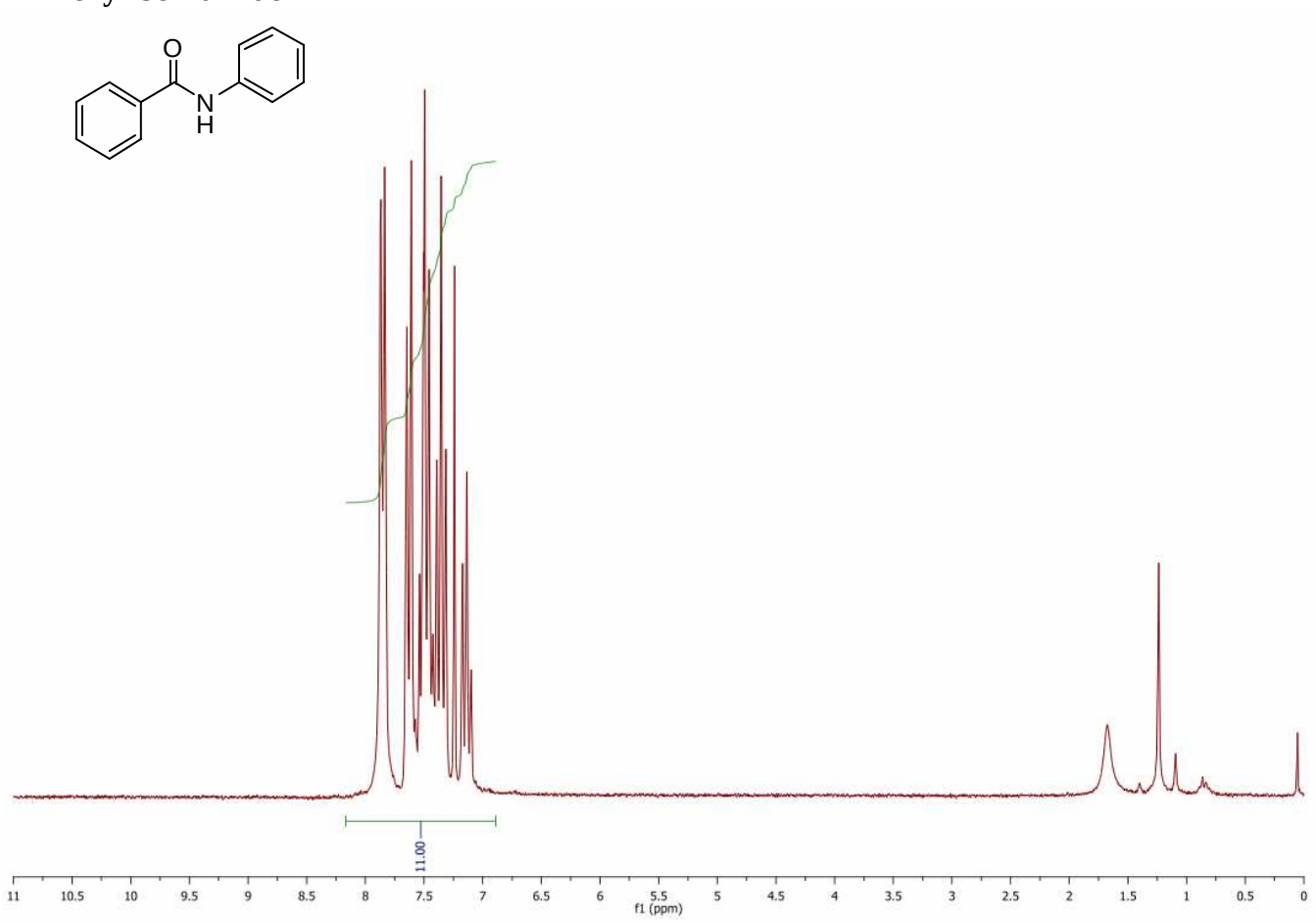


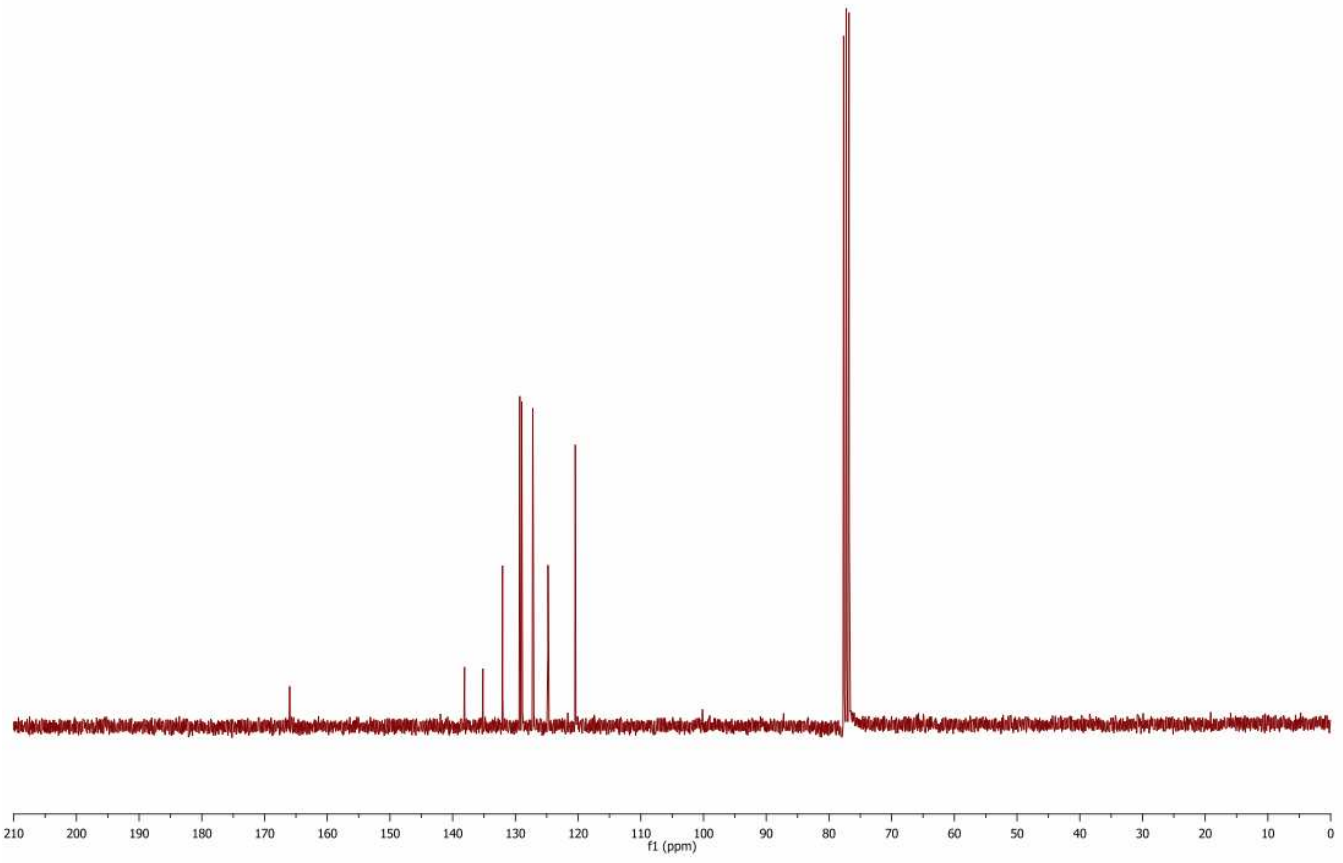
_N_-Phenyl-2-phenylpropanamide



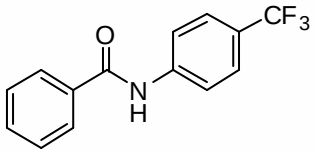


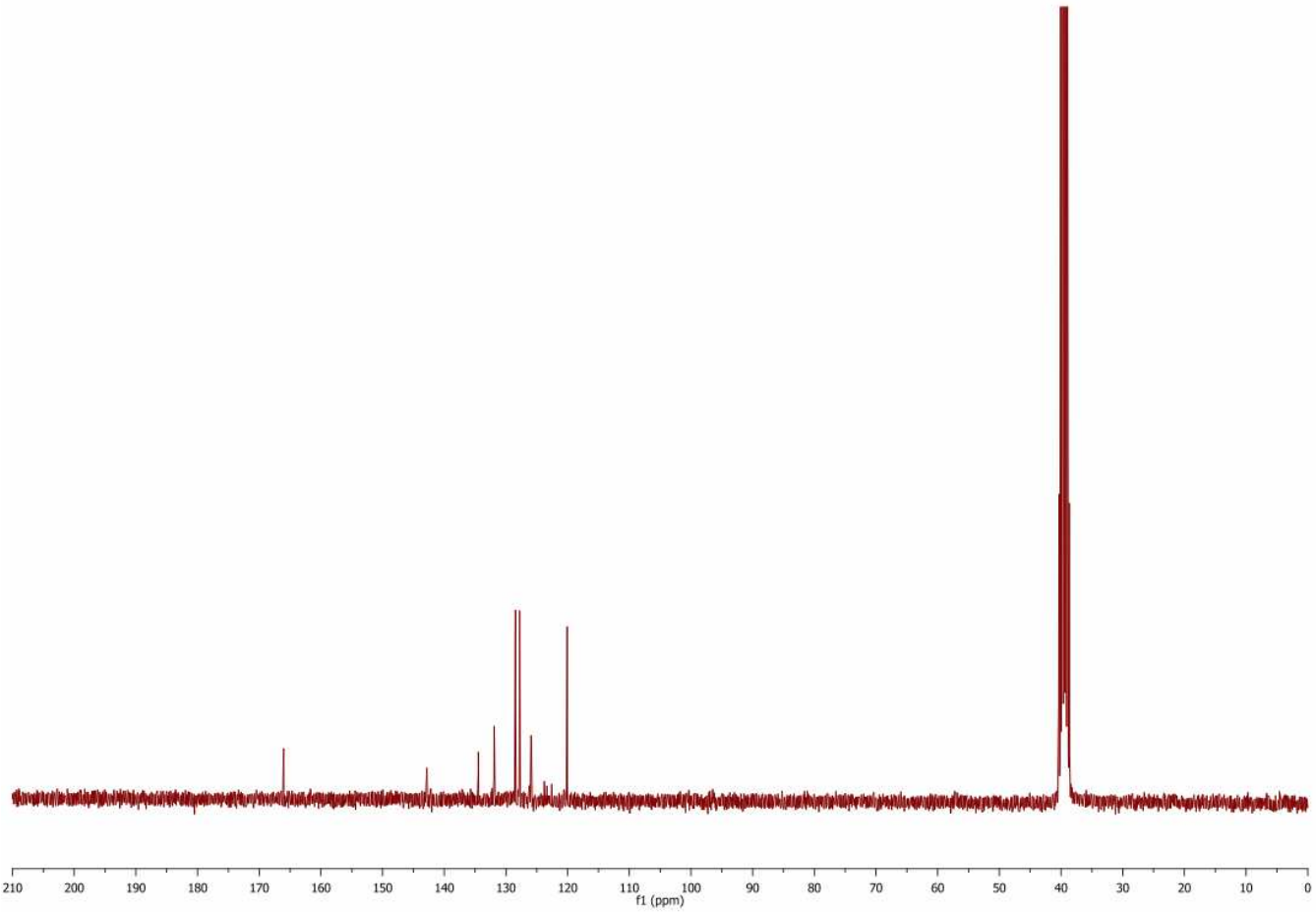
_N_-Phenyl-benzamide



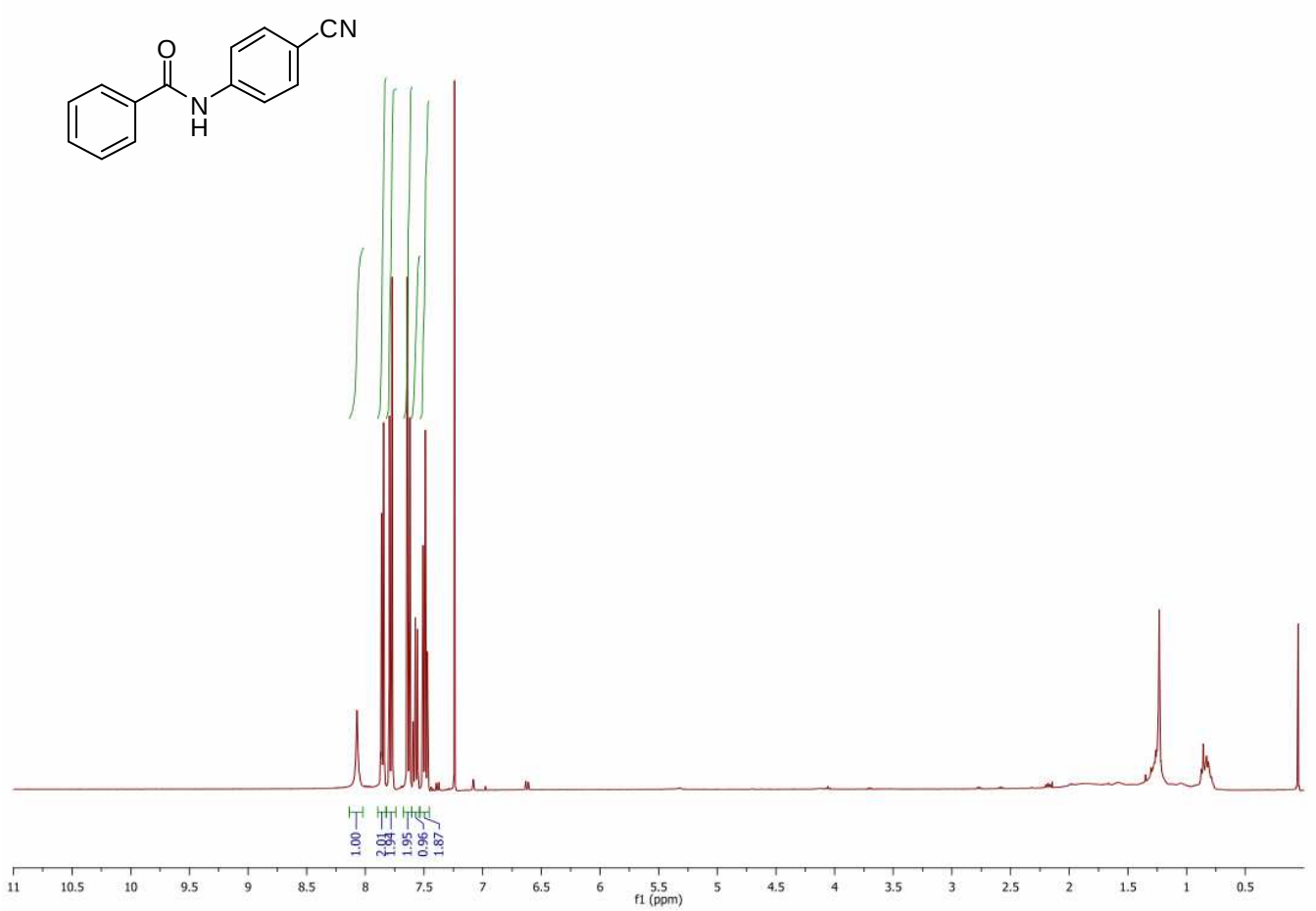


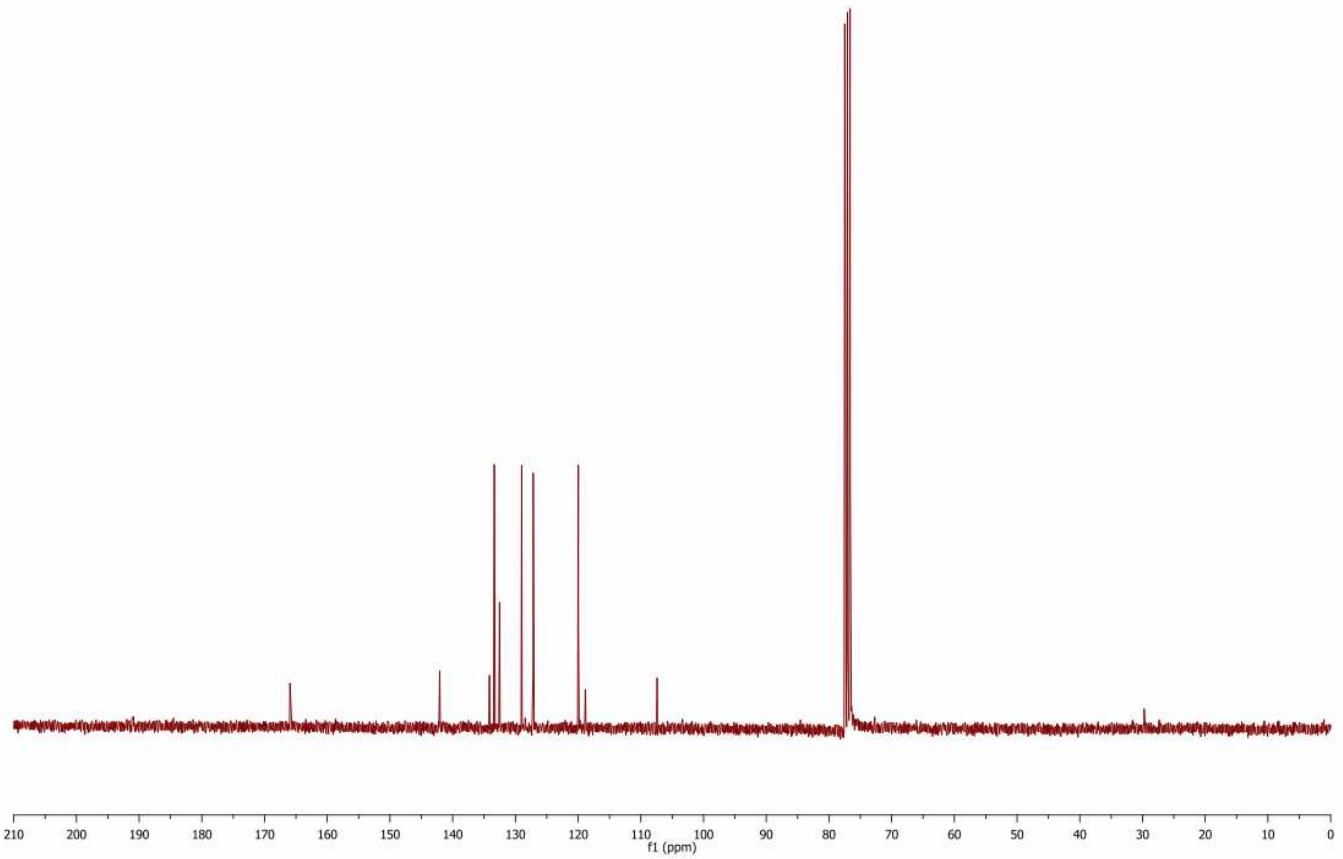
_N_-(4-Trifluoromethylphenyl)benzamide



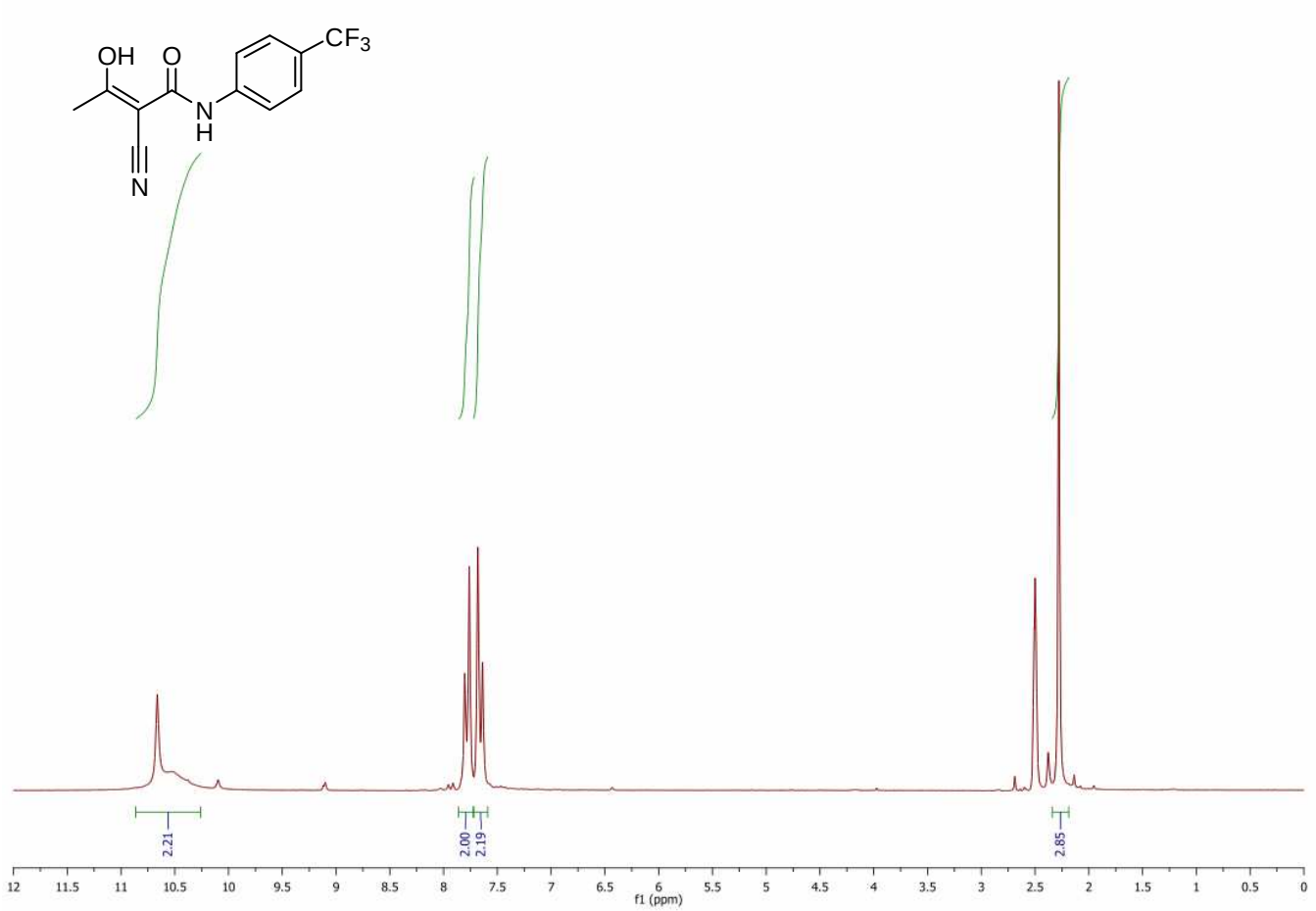


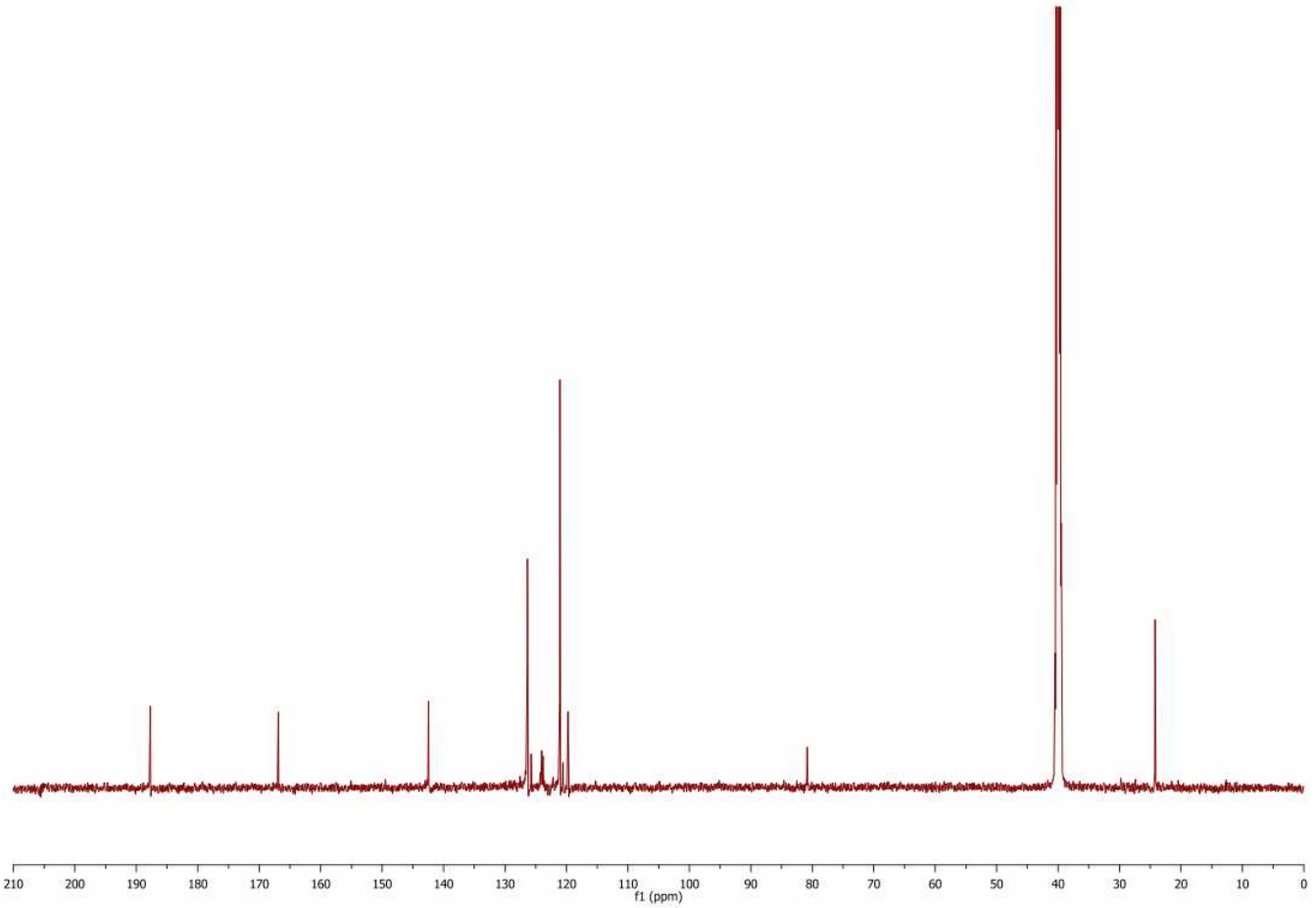
_N_-(4-Cyanophenyl) benzamide





2-Cyano-3-hydroxy-*N*-[4-(trifluoromethyl)phenyl]-2-butenamide (Teriflunomide)





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