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Design, synthesis, and biological evaluation of oxazolidone derivatives as highly potent *N*-Acylethanolamine acid amidase (NAAA) inhibitors

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Supplemental Experimental Procedures

1–Pentadecanyl–carbonyl pyrrolidine (1a)

Following the **General Procedure A** (eluent: EtOAc/PE 1: 5), the amidation of palmitoyl chloride with pyrrolidine afford **1a** (83 mg; yield: 89%) as white crystals: mp 84.0–84.6°C; IR (film)ν_{max}: 2923, 2852, 1648, 1426 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 7.2 Hz, 3 H), 1.25–1.30 (m, 24 H), 1.60–1.67 (m, 2 H), 1.81–1.88 (m, 2 H), 1.91–1.98 (m, 2 H), 2.25 (t, J = 8 Hz, 2 H), 3.39–3.47 (m, 4 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.6, 24.4, 24.9, 26.1, 29.3, 29.43, 29.49, 29.52, 29.62, 29.64, 31.9, 34.8, 45.5, 46.6, 171.8 ppm; MS (ESI, m/z): 310 $(M + H)^+$.

(R)–tert–butyl 1–palmitoylpyrrolidin–3–ylcarbamate (1c–1)

Following the **General Procedure A** (eluent: EtOAc/PE 1: 3), the amidation of palmitoyl chloride with (R)–tert–butyl pyrrolidin–3–ylcarbamate afford **1c–1** (108 mg; yield: 85%) as white crystals: mp: 47.3–49.0 °C; $[\alpha]_D^{20}$ 41 (c 0.5, $CHCl_3$); IR (film)ν_{max}: 3329, 2955, 2918, 2849, 1684, 1631, 1566, 1541, 1446, 1309, 1249 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 7.2 Hz, 3 H), 1.25–1.30 (m, 24 H), 1.45 (S, 9 H), 1.58–1.65 (m, 2 H), 1.76–1.98 (m, 1 H), 2.10–2.26 (m, 3 H), 3.27–3.37 (m, 1 H), 3.47–3.58 (m, 2 H), 3.65–3.73 (m, 1 H), 4.22 (br, 1 H), 4.74–4.82 (m, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.6, 24.8, 24.9, 28.3, 29.3, 29.4, 29.5, 29.6, 30.3, 31.9, 32.4, 34.3, 34.8, 43.6, 44.6, 49.3, 50.8, 51.1, 52.6, 79.9, 155.2, 155.3, 172.1 ppm; MS (ESI, m/z): 425 $(M + H)^+$; Anal. calcd for $C_{25}H_{48}N_2O_3$: C, 70.71; H, 11.39; N, 6.60; Found: C, 70.97; H, 11.41; N, 6.58.

(R)–1–(3–aminopyrrolidin–1–yl)hexadecan–1–one (1c)

Following the **General Procedure C** (eluent: MeOH: CH_2Cl_2 = 1:15), the reaction of **1c–1** afford **1c** (41 mg, 90%) as white crystals, mp: 39.6–41.1 °C; $[\alpha]_D^{20}$ –12.5 (c 0.2, CH_3OH); IR (film)ν_{max}: 3120, 2923, 2857, 1634, 1454, 1371, 1329, 1222, 1190, 1108 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 0.94 (t,J = 6.4 Hz, 3 H), 1.33–1.37 (m, 24 H), 1.62–1.67 (m, 2 H), 1.95–2.08 (m, 1 H), 2.22–2.39 (m, 3 H), 3.43–3.82 (m, 5 H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ 13.1, 22.3, 24.5, 24.6, 29.1, 29.2, 29.3, 29.4, 30.1, 31.2, 31.7, 33.7, 34.1, 43.5, 44.4, 49.1, 50.6, 50.7, 51.9, 173.0, 173.3 ppm; MS (ESI, m/z): 325 $(M + H)^+$; Anal. calcd for $C_{20}H_{40}N_2O$: C, 74.02; H, 12.42; N, 8.63; Found: C, 74.06; H, 12.45; N, 8.62.

(S)–tert–butyl 1–palmitoylpyrrolidin–3–ylcarbamate (1d–1)

Following the **General Procedure A** (eluent: EtOAc/PE 1: 3), the amidation of palmitoyl chloride with (S)–tert–butyl pyrrolidin–3–ylcarbamate afford **1d–1** (117 mg; yield: 92%) as white crystals, mp: 42.0–43.0 °C; $[\alpha]_D^{20}$ –39 (c 0.4, $CHCl_3$); IR (film)ν_{max}: 3330, 2955, 2918, 2850, 1684, 1630, 1566, 1541, 1446, 1309, 1249 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t,J = 7.2 Hz, 3 H), 1.25–1.30 (m, 24 H), 1.45 (S, 9 H), 1.58–1.65 (m, 2 H), 1.76–1.98 (m, 1 H), 2.10–2.26 (m, 3 H), 3.27–3.37 (m, 1 H), 3.47–3.58 (m, 2 H), 3.65–3.73 (m, 1 H), 4.22 (br, 1 H), 4.74–4.82 (m, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.6, 24.8, 24.9, 28.3, 29.3, 29.4, 29.5, 29.6, 30.3, 31.9, 32.4, 34.3, 34.8, 43.6, 44.6, 49.3, 50.8, 51.1, 52.6, 79.9, 155.2, 155.3, 172.1 ppm; MS (ESI, m/z): 425 $(M + H)^+$;Anal. calcd for $C_{25}H_{48}N_2O_3$: C, 70.71; H, 11.39; N, 6.60; Found: C, 70.99; H, 11.40; N, 6.59.

(S)–1–(3–aminopyrrolidin–1–yl)hexadecan–1–one (1d)
Following the **General Procedure C** (eluent: MeOH: CH_2Cl_2 = 1:15), the reaction of **1d–1** with CF_3COOH afford **1d** (34 mg, 74%) as white wax; $[\alpha]_D^{20}$ 12.5 (c 0.1, CH_3OH); IR (film)ν_{max}: 3120, 2923, 2857, 1634, 1454, 1371, 1329, 1222, 1190, 1108 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 0.94 (t, J = 6.4 Hz, 3 H), 1.33–1.37 (m, 24 H), 1.62–1.67 (m, 2 H), 1.95–2.08 (m, 1 H), 2.22–2.39 (m, 3 H), 3.43–3.82 (m, 5 H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ 13.0, 22.3, 24.5, 24.6, 29.1, 29.2, 29.3, 29.4, 30.1, 31.2, 31.7, 33.7, 34.1, 43.5, 44.4, 49.1, 50.6, 50.7, 51.9, 173.0, 173.3 ppm; MS (ESI, m/z): 325 $(M + H)^+$; Anal. calcd for $C_{20}H_{40}N_2O$: C, 74.02; H, 12.42; N, 8.63; Found: C, 74.02; H, 12.43; N, 8.64.

(R)–1–(2–methylpyrrolidin–1–yl)hexadecan–1–one (1e)
Following the **General Procedure D** (eluent: EtOAc/PE 1: 5), the reaction starting from **1q** afford **1e** (35 mg, 52%) as white wax; $[\alpha]_D^{20}$ −27.9 (c 0.1, $CDCl_3$); IR (film)ν_{max}: 2956, 2921, 2850, 1649, 1460, 1418 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 7.2 Hz, 3 H), 1.18 (d, J = 6.3 Hz, 3 H), 1.25–1.30 (m, 24 H), 1.55–1.70 (m, 3 H), 1.84–2.07 (m, 3 H), 2.20–2.33 (m, 2 H), 3.34–3.50 (m,2 H), 3.96–4.24 (m, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 19.5, 21.2, 21.8, 22.6, 23.9, 24.8, 25.5, 29.3, 29.4, 29.5, 29.6, 29.6, 31.9, 33.2, 34.2, 35.0, 45.3, 46.8, 52.5, 53.0, 171.5, 171.7 ppm; MS (ESI, m/z): 324 $(M + H)^+$; Anal. calcd for $C_{21}H_{41}NO$: C, 77.95; H, 12.77; N, 4.33; Found: C, 77.93; H, 12.79; N, 4.34.

(S)–1–(2–methylpyrrolidin–1–yl)hexadecan–1–one (1f)
Following the **General Procedure D** (eluent: EtOAc/PE 1: 5), the reaction starting from **1r** afford compound **1f** (41 mg, 63%) as yellow wax; $[\alpha]_D^{20}$ 27.9 (c 0.1, $CDCl_3$); IR (film)ν_{max}: 2949, 2919, 2850, 1620, 1578, 1544, 1466 cm^{-1};^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 7.2 Hz, 3 H), 1.18 (d, J = 6.3 Hz, 3 H), 1.25–1.30 (m, 24 H), 1.55–1.70 (m, 3 H), 1.84–2.07 (m, 3 H), 2.20–2.33 (m, 2 H), 3.34–3.50 (m,2 H), 3.96–4.24 (m, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 19.5, 21.2, 21.8, 22.6, 23.9, 24.8, 25.5, 29.3, 29.4, 29.5, 29.6, 29.6, 31.9, 33.2, 34.2, 35.0, 45.3, 46.8, 52.5, 53.0, 171.5, 171.7 ppm; MS (ESI, m/z): 324 $(M + H)^+$; Anal. calcd for $C_{21}H_{41}NO$: C, 77.95; H, 12.77; N, 4.33; Found: C, 77.94; H, 12.79; N, 4.34.

1–palmitoylpyrrolidin–2–one (1g)
To a solution ofpyrrolidin–2–one (44 mg, 0.5 mmol) in THF (5 mL) was added slowly a solution of 2.5 M n–BuLi (0.55 mmol, 0.2 mL hexane) under nitrogen atmosphere at –78°C. After being stirred at the same temperature for 10 min, a solution of palmitoyl chloride (151 mg, 0.55 mmol) in THF (2 mL) was slowly added. The reaction mixture was stirred at –78°C for 0.5 hours, and allowed to warm slowly to room temperature in 5 hours. The reaction was quenched with 1.0 mL a sat. aqueous solution of NH_4Cl and extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (eluent: EtOAc/PE 1: 5) to afford **1g** (92 mg; yield: 57%) as white crystals, mp: 71.9–72.6 °C; IR (film)ν_{max}: 2916, 2841, 1728, 1682, 1465, 1398, 1256 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 3 H), 1.26–1.31 (m, 24 H), 1.59–1.66 (m, 2 H), 1.99–2.07 (m, 2 H), 2.59 (t, J = 8.0 Hz, 2 H), 2.88 (t, J = 8.0 Hz, 2 H), 3.80 (t, J = 8.0 Hz, 2 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 17.1, 22.5, 24.1, 29.1, 29.2, 29.3, 29.4, 29.5, 29.5, 29.5, 31.8, 33.6, 36.7, 45.3, 174.3, 175.1 ppm; MS (ESI, m/z): 324 $(M + H)^+$; Anal. calcd for $C_{20}H_{37}NO_2$: C, 74.25; H, 11.53; N, 4.33. Found: C, 75.44;

H, 11.47; N, 8.33.

1–palmitoylimidazolidin–2–one (1h)

To a suspension of NaH (60% in mineral oil, 60 mg) in anhydrous THF (5 mL), was added slowly a solution of 2–Imidazolidinone hemihydrates (48 mg, 0.5 mmol) in THF (5 mL) under nitrogen atmosphere at –20°C. After being stirred at the same temperature for 10 min, a solution of palmitoyl chloride (151 mg, 0.55 mmol) in THF (2 mL) was slowly added. The reaction mixture was stirred at –20°C for 0.5 hours, and allowed to warm slowly to room temperature in 5 hours. The reaction was quenched with 1.0 mL a sat. aqueous solution of NH_4Cl and extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (eluent: EtOAc/PE 1: 2) to afford **1h** (71 mg; yield: 44%) as white crystals, mp: 114.5–116.8 °C; IR (film)ν_{max}: 3249, 2916, 2841,1738, 1677 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 3 H), 1.25–1.33 (m, 24 H), 1.61–1.68 (m, 2 H), 2.91 (t, J = 6.8 Hz, 2 H), 3.48 (t, J = 8.0 Hz, 2 H), 3.95 (t, J = 8.0 Hz, 2 H), 5.28 (s, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 22.7, 24.7, 29.2, 29.3, 29.4, 29.5, 29.7, 31.9, 35.2, 36.5, 42.3, 156.7, 174.0 ppm; MS (ESI, m/z): 325 $(M + H)^+$; Anal. calcd for $C_{19}H_{36}N_2O_2$: C, 70.32; H, 11.18; N, 8.63. Found: C, 70.52; H, 11.16; N, 8.64.

3–palmitoyloxazolidin–2–one (1i)

Following the **General Procedure E** (eluent: EtOAc/PE 1: 5), the imidation of palmitoyl chloride with oxazolidin–2–one afford **1i** (83 mg; yield: 51%) as white crystals, mp: 92.2–93.8 °C; IR (film)ν_{max}: 2914, 2846, 1765, 1699, 1386 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 7.2 Hz, 3 H), 1.26–1.32 (m, 24 H), 1.62–1.69 (m, 2 H), 2.91 (t, J = 7.6 Hz, 2 H), 4.02 (t, J = 8.0 Hz, 2 H), 4.41 (t, J = 8.0 Hz, 2 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 22.6, 24.2, 29.1, 29.3, 29.4, 29.5, 29.6, 29.6, 31.8, 35.0, 42.5, 61.9, 153.5, 173.5 ppm; MS (ESI, m/z): 326 $(M + H)^+$; Anal. calcd for $C_{19}H_{35}NO_3$: C, 70.11; H, 10.84; N, 4.30. Found: C, 70.13; H, 10.86; N, 4.32.

(R)–1–(3–hydroxypyrrolidin–1–yl)hexadecan–1–one (1j)

Following the **General Procedure A** (eluent: EtOAc/PE 1: 2), the amidation of palmitoyl chloride with (R)–pyrrolidin–3–ol afford **1j** (64 mg; yield: 66%) as white crystals, mp: 58.8–59.5 °C; $[\alpha]_D^{20}$ –10.3 (c 0.7, $CHCl_3$); IR (film)ν_{max}: 3380, 2923, 2847, 1622, 1462, 1377, 1338, 1226 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.4 Hz, 3 H), 1.26–1.30 (m, 24 H), 1.69–1.77 (m, 2 H), 1.93–1.98 (m, 1 H), 2.00–2.05 (m, 1 H), 2.19–2.28 (m, 2 H), 3.36–3.45 (m, 5 H), 4.49 (d, J = 20.8 Hz, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 22.6, 24.8, 29.2, 29.4, 29.4, 29.5, 29.6, 31.9, 32.9, 34.2, 34.6, 34.8, 43.5, 44.6, 54.1, 54.8, 69.2, 70.8, 172.3, 172.5 ppm; MS (ESI, m/z): 326 $(M + H)^+$; Anal. calcd for $C_{20}H_{39}NO_2$: C, 73.79; H, 12.08; N, 4.30; Found: C, 73.92; H, 12.11; N, 4.29.

(S)–1–(3–hydroxypyrrolidin–1–yl)hexadecan–1–one (1k)

Following the **General Procedure A** (eluent: EtOAc/PE 1: 2), the amidation of palmitoyl chloride with (S)–pyrrolidin–3–ol afford **1k** (77 mg; yield: 79%) as white crystals, mp: 51.5–53.8 °C; $[\alpha]_D^{20}$ 10.3 (c 0.7, $CHCl_3$); IR (film)ν_{max}: 3379, 2923, 2847, 1622, 1463, 1376, 1338, 1226 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.4 Hz, 3 H), 1.25–1.29 (m, 24 H), 1.62–1.66 (m, 2 H), 1.93–1.98 (m, 1 H), 2.00–2.05 (m, 1 H), 2.21–2.28 (m, 2 H), 3.41–3.68 (m, 5 H), 4.48 (d, J = 12.8 Hz, 1 H) ppm; ^{13}C

NMR (100 MHz, $CDCl_3$) δ 14.0, 22.6, 24.8, 29.3, 29.4, 29.4, 29.5, 29.6, 31.8, 32.9, 34.2, 34.6, 34.8, 43.5, 44.6, 54.2, 54.8, 69.3, 70.9, 172.3, 172.5 ppm; MS (ESI, m/z): 326 $(M + H)^+$; Anal. calcd for $C_{20}H_{39}NO_2$: C, 73.79; H, 12.08; N, 4.30; Found: C, 73.84; H, 12.10; N, 4.31.

(R)–1–(3–methoxypyrrolidin–1–yl)hexadecan–1–one (1l)
Following the **General Procedure B** (eluent: EtOAc/PE 1: 10), the reaction of **1j** with CH_3I afford **1l** (17 mg; yield: 81%) as colorless oil; $[\alpha]_D^{20}$ –45.1 (c 0.2, $CHCl_3$); IR (film)ν_{max}: 2950, 2919, 2850, 1646, 1459, 1429, 1371, 1102 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 3 H), 1.25–1.29 (m, 24 H), 1.60–1.66 (m, 2 H), 1.85–2.09 (m, 2 H), 2.21–2.28 (m, 2 H), 3.33 (d, J = 8.0 Hz, 3 H), 3.42–3.69 (m, 4 H), 3.97 (dd, J = 26.0, 2.8 Hz, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.6, 24.8, 29.3, 29.3, 29.4, 29.5, 29.6, 29.7, 31.5, 31.8, 34.6, 34.8, 43.4, 44.5, 50.2, 51.7, 56.4, 56.5, 78.4, 79.9, 171.9, 172.1 ppm; MS (ESI, m/z): 340 $(M + H)^+$; Anal. calcd for $C_{21}H_{41}NO_2$: C, 74.28; H, 12.17; N, 4.13; Found: C, 74.43; H, 12.20; N, 4.13.

(S)–1–(3–methoxypyrrolidin–1–yl)hexadecan–1–one (1m)
Following the **General Procedure B** (eluent: EtOAc/PE 1: 10), the reaction of **1k** with CH_3I afford **1m** (20 mg; yield: 95%) as colorless oil; $[\alpha]_D^{20}$ 45.0 (c 0.3, $CHCl_3$); IR (film)ν_{max}: 2956, 2924, 2851, 1642, 1464, 1431, 1374 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 7.2 Hz, 3 H), 1.25–1.33 (m, 24 H), 1.60–1.66 (m, 2 H), 1.87–2.10 (m, 2 H), 2.21–2.27 (m, 2 H), 3.33 (d, J = 8.0 Hz, 3 H), 3.42–3.69 (m, 4 H), 3.94 (dd, J = 28.0, 2.0 Hz, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.6, 24.8, 29.3, 29.4, 29.5, 29.6, 29.7, 31.5, 31.8, 34.6, 34.8, 43.4, 44.5, 50.2, 51.7, 56.4, 56.5, 78.4, 79.9, 171.9, 172.1 ppm; MS (ESI, m/z): 340 $(M + H)^+$; Anal. calcd for $C_{21}H_{41}NO_2$: C, 74.28; H, 12.17; N, 4.13; Found: C, 74.38; H, 12.15; N, 4.12.

1–palmitoylpyrrolidine–3–carbonitrile (1n)
Following the **General Procedure A** (eluent: EtOAc/PE 1: 5), the amidation of palmitoyl chloride with pyrrolidine–3–carbonitrile afford **1n** (92 mg; yield: 92%) as white solid, mp: 57.5–59.3 ^oC; IR (film)ν_{max}: 2914, 2849, 2250, 1637, 1430 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.4 Hz, 3 H), 1.26–1.30 (m, 24 H), 1.63–1.66 (m, 2 H), 2.18–2.38 (m, 4 H), 3.09–3.24 (m, 1 H), 3.52–3.58(m, 1 H), 3.63–3.82 (m, 3 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 22.6, 24.6, 24.7, 27.1, 28.6, 28.7, 29.2, 29.3, 29.4, 29.5, 29.5, 29.6, 30.4, 31.8, 34.5, 34.7, 44.3, 44.9, 48.5, 49.2, 119.3, 119.7, 171.5, 171.9 ppm; MS (ESI, m/z): 335 $(M + H)^+$; Anal. calcd for $C_{21}H_{38}N_2O$: C, 75.39; H, 11.45; N, 8.37. Found: C, 75.44; H, 11.47; N, 8.33.

1–palmitoylpyrrolidine–3–carboxamide (1o)
Following the **General Procedure A** (eluent: EtOAc/PE 1: 5), the amidation of palmitoyl chloride with pyrrolidine-3-carboxamide afford **1o** (93 mg; yield: 88%) as white solid, mp: 121.2–122.4 ^oC; IR (film)ν_{max}: 3374, 2917, 2849, 1650, 1632, 1469, 1440 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 3 H), 1.25–1.30 (m, 24 H), 1.57–1.60 (m, 2 H), 2.12–2.30 (m, 4 H), 2.93–3.11 (m, 1 H), 3.36–3.48 (m, 1 H), 3.55–3.80 (m, 3 H), 6.18 (br, 1 H) , 6.51 (br, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 22.6, 24.7, 28.5, 29.2, 29.3, 29.4, 29.4, 29.5, 29.6, 31.8, 34.5, 34.6, 42.3, 44.3, 45.3, 46.1, 48.5, 48.8, 171.9, 172.0, 174.5, 174.9 ppm; MS (ESI, m/z): 353 $(M + H)^+$; Anal. calcd for $C_{21}H_{40}N_2O_2$: C, 71.61; H, 11.46; N, 7.95; Found: C, 71.54; H, 11.44; N, 7.95.

1–palmitoylpyrrolidin–3–one (1p)

To a solution of DMP (212 mg, 0.5 mmol) in CH_2Cl_2 (5 mL), was added dropwise **1j** or **1k** (65 mg, 0.2 mmol) in CH_2Cl_2 (5 mL) under nitrogen atmosphere, the mixture was stirred at the room temperature for 3 hours, filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (eluent: EtOAc/PE 1: 5) to afford compound **2i** (42 mg, 64%) as white crystals, mp: 77.3–78.6 ^oC; IR (film)ν_{max}: 2955, 2923, 2852, 1730, 1648, 1466, 1422 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 3 H), 1.26–1.30 (m, 24 H), 1.65–1.69 (m, 3 H), 2.24 (t, J = 8.0 Hz, 1 H), 2.34 (t, J = 8.0 Hz, 1 H), 2.62 (t, J = 8.0 Hz, 1 H), 2.70 (t, J = 8.0 Hz, 1 H), 3.88–3.93 (m, 4 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.7, 24.6, 24.7, 29.3, 29.4, 29.5, 29.6, 29.6, 29.7, 31.9, 33.3, 35.0, 36.2, 37.4, 41.8, 43.3, 52.3, 53.1, 172.4, 172.6, 209.7, 209.9 ppm; MS (ESI, m/z): 324 $(M + H)^+$; Anal. calcd for $C_{20}H_{37}NO_2$: C, 74.25; H, 11.53; N, 4.33; Found: C, 74.11; H, 11.50; N, 4.34.

(R)–1–(2–(hydroxymethyl)pyrrolidin–1–yl)hexadecan–1–one (1q)

Following the **General Procedure A** (eluent: EtOAc/PE 1: 2), the amidation of palmitoyl chloride with (R)–pyrrolidin–2–ylmethanol afford **1q** (66 mg; yield: 65%) as white crystals, mp: 38.1–40.0 ^oC; $[\alpha]_D^{20}$ 25.5 (c 0.1, $CDCl_3$); IR (film)ν_{max}: 3415, 2918, 2850, 1620, 1462, 1050 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 7.1 Hz, 3 H), 1.26–1.31 (m, 24 H), 1.55–1.68 (m, 3 H), 1.83–2.08 (m, 3 H), 2.30 (t, J = 7.8 Hz, 2 H), 3.43–3.67 (m, 4 H) , 4.18–4.25 (m, 1 H), 5.22(s, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 22.6, 24.3, 24.7, 28.2, 29.3, 29.3, 29.4, 29.4, 29.5, 29.6, 29.6, 31.9, 35.0, 48.0, 61.0, 67.4, 174.6 ppm; MS (ESI, m/z): 340 $(M + H)^+$; Anal. calcd for $C_{21}H_{41}NO_2$: C, 74.28; H, 12.17; N, 4.13; Found: C, 74.31; H, 12.15; N, 4.12.

(S)–1–(2–(hydroxymethyl)pyrrolidin–1–yl)hexadecan–1–one (1r)

Following the **General Procedure A** (eluent: EtOAc/PE 1: 2), the amidation of palmitoyl chloride with (S)–pyrrolidin–2–ylmethanol afford **1r** (64 mg; yield: 63%) as white crystals, mp: 45.0–45.5 ^oC; $[\alpha]_D^{20}$ −25.5 (c 0.1, $CDCl_3$); IR (film)ν_{max}: 3414, 2916, 2849, 1619, 1463, 1051 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.9 Hz, 3 H), 1.26–1.31 (m, 24 H), 1.56–1.68 (m, 3 H), 1.83–2.08 (m, 3 H), 2.30 (t, J = 7.8 Hz, 2 H), 3.43–3.66 (m, 4 H), 4.18–4.24 (m, 1 H), 5.21 (s, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 22.6, 24.3, 24.7, 28.2, 29.3, 29.3, 29.4, 29.4, 29.6, 29.6, 29.6, 31.8, 35.0, 48.0, 61.0, 67.4, 76.7, 174.6 ppm; MS (ESI, m/z): 340 $(M + H)^+$; Anal. calcd for $C_{21}H_{41}NO_2$: C, 74.28; H, 12.17; N, 4.13; Found: C, 74.33; H, 12.18; N, 4.13.

(R)–1–(2–(methoxymethyl)pyrrolidin–1–yl)hexadecan–1–one (1s)

Following the **General Procedure A** (eluent: EtOAc/PE 1: 5), the amidation of palmitoyl chloride with (R)–pyrrolidin–2–ylmethanol afford **1s** (89 mg; yield: 84%) as colorless oil; $[\alpha]_D^{20}$ 37.1 (c 0.1, $CDCl_3$); IR (film)ν_{max}: 2919, 2849, 1642, 1574, 1537, 1466, 1413, 1113 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 3 H), 1.26–1.30 (m, 24 H), 1.62–1.65 (m, 2 H), 1.86–2.05 (m, 4 H), 2.17–2.36 (m, 2 H), 3.21–3.47 (m, 6 H), 3.52–3.58 (m, 1 H), 4.02–4.25 (m, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ14.0, 21.8, 22.6, 24.1, 24.7, 25.1, 25.4, 27.4, 28.7, 29.3, 29.4, 29.4, 29.5, 29.6, 29.6, 31.8, 33.3, 34.2, 35.0, 45.4, 47.2, 56.2, 56.9, 58.9, 59.1, 72.3, 74.0, 172.1, 172.4 ppm; MS (ESI, m/z): 354 $(M + H)^+$; Anal. calcd for $C_{22}H_{43}NO_2$: C, 74.73; H, 12.26; N, 3.96; Found: C, 74.70; H, 12.27; N, 3.97.

(S)–1–(2–(methoxymethyl)pyrrolidin–1–yl)hexadecan–1–one (1t)

Following the **General Procedure A** (eluent: EtOAc/PE 1: 5), the amidation of

palmitoyl chloride with (S)–2–(methoxymethyl)pyrrolidine afford **1t** (95 mg; yield: 89%) as colorless oil; $[\alpha]_D^{20}$ −37.1 (c 0.1, $CDCl_3$); IR (film)ν_{max}: 2919, 2850, 1650, 1458, 1415, 1114 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 7.2 Hz, 3 H), 1.26–1.30 (m, 24 H), 1.61–1.65 (m, 2 H), 1.86–2.03 (m, 4 H), 2.23–2.36 (m, 2 H), 3.21–3.47 (m, 6 H), 3.52–3.56 (m, 1 H), 4.02–4.26 (m, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 21.9, 22.7, 24.1, 24.8, 25.5, 27.4, 28.7, 29.3, 29.4, 29.4, 29.5, 29.6, 29.7, 31.9, 34.2, 35.0, 45.5, 47.3, 56.2, 56.9, 58.9, 59.1, 72.3, 74.1, 172.1, 172.5 ppm; MS (ESI, m/z): 354 $(M + H)^+$; Anal. calcd for $C_{22}H_{43}NO_2$: C, 74.73; H, 12.26; N, 3.96; Found: C, 74.74; H, 12.27; N, 3.95.

3–benzoyloxazolidin–2–one (2a)[1]

Following the **General Procedure E** (eluent: EtOAc/PE 1: 3), the imidation of benzoic acid with oxazolidin–2–one afford **2a** (52 mg; yield: 54%) as white crystals, mp: 194.2–196.3 °C; IR (film)ν_{max}: 2917, 2894, 1774, 1677, 1380, 1338, 1201, 1108 cm^{-1};^1H NMR (400 MHz, $CDCl_3$) δ 4.16 (t, J = 8.0 Hz, 2 H), 4.48 (t, J = 8.0 Hz, 2 H), 7.44 (dd, J = 7.2, 7.2 Hz, 2 H),7.55 (dd, J = 8.0, 7.2 Hz, 1 H), 7.65 (d, J = 8.0 Hz, 2 H) ppm;^{13}C NMR (100 MHz, $CDCl_3$) δ 43.1, 62.3, 127.88, 129.1, 132.4, 132.6, 153.2, 169.8 ppm; MS (ESI, m/z): 192 $(M + H)^+$; Anal. calcd for $C_{10}H_9NO_3$: C, 62.82; H, 4.74; N, 7.33. Found: C, 62.60; H, 4.73; N, 7.33.

3–(2–phenylacetyl)oxazolidin–2–one (2b)[2]

Following the **General Procedure E** (eluent: EtOAc/PE 1: 3), the imidation of 2–phenylacetic acid with oxazolidin–2–one afford **2b** (32 mg; yield: 31%) as white crystals, mp: 67.0–67.5°C; IR (film)ν_{max}: 2917, 2856, 1770, 1683, 1385, 1217, 1084 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.96 (t, J = 8.0 Hz, 2 H), 4.26 (s, 1 H), 4.31 (t, J = 8.0 Hz, 2 H), 7.24–7.33 (m, 5 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.9, 42.5, 61.9, 127.0, 128.4, 129.6, 133.5, 153.4, 171.1 ppm; MS (ESI, m/z): 206 $(M + H)^+$; Anal. calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.42; H, 5.41; N, 6.83.

3–(3–phenylpropanoyl)oxazolidin–2–one (2c)

Following the **General Procedure E** (eluent: EtOAc/PE 1: 3), the imidation of 3–phenylpropanoic acid with oxazolidin–2–one afford **2c** (41 mg; yield: 37%) as white crystals, mp: 114.3–116.6 °C; IR (film)ν_{max}: 2917, 2856, 1766, 1692, 1390, 1317, 1227, 1043 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.99 (t, J = 7.6 Hz, 2 H), 3.25 (t, J = 7.6 Hz, 2 H), 3.99 (d, J = 8.0 Hz, 2 H), 4.37 (t, J = 8.0 Hz, 2 H), 7.18–7.30 (m, 5 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.1, 36.7, 42.4, 62.0, 126.2, 128.4, 128.5, 153.5, 172.5 ppm; MS (ESI, m/z): 220 $(M + H)^+$; Anal. calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.81; H, 5.97; N, 6.39.

3–(4–phenylbutanoyl)oxazolidin–2–one (2d)

Following the **General Procedure E** (eluent: EtOAc/PE 1: 4), the imidation of 4–phenylbutanoic acid with oxazolidin–2–one afford **2d** (52 mg; yield: 45%) as white crystals, mp: 72.9–74.4 °C; IR (film)ν_{max}: 2919, 2850, 1779, 1737, 1702, 1496, 1478, 1386, 1240, 1041 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.95–2.04 (m, 2 H), 2.69 (t, J = 7.6 Hz, 2 H), 2.96 (t, J = 7.6 Hz, 2 H), 3.96 (t, J = 8.4 Hz, 2 H), 4.36 (t, J = 8.4 Hz, 2 H), 7.19–7.20 (m, 3 H), 7.26–7.29 (m, 2 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.8, 34.5, 35.1, 42.4, 62.0, 125.9, 128.3, 128.4, 141.4, 153.5, 173.2 ppm; MS (ESI, m/z): 234 $(M + H)^+$; Anal. calcd for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.78; H, 6.48; N, 5.99.

3–(5–phenylpentanoyl)oxazolidin–2–one (2e)[3]
Following the **General Procedure E** (eluent: EtOAc/PE 1: 4), the imidation of 5–phenylpentanoic acid with oxazolidin–2–one afford **2e** (69 mg; yield: 56%) as white crystals, mp: 62.6–65.3 °C; IR (film)ν_{max}: 2924, 2858, 1780, 1700, 1497, 1478, 1453, 1388, 1225, 1111, 1040 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.69–1.71 (m, 4 H), 2.64 (t, J = 7.2 Hz, 2 H), 2.94 (t, J = 7.2 Hz, 2 H), 3.98 (t, J = 8.4 Hz, 2 H), 4.37 (t, J = 8.4 Hz, 2 H), 7.17–7.19 (m, 3 H), 7.25–7.29 (m, 2 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ23.8, 30.7, 34.8, 35.5, 42.4, 61.9, 125.7, 128.2, 128.3, 142.1, 153.5, 173.3 ppm; MS (ESI, m/z): 248 $(M + H)^+$; Anal. calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 68.20; H, 6.91; N, 5.67.

3–(6–phenylhexanoyl)oxazolidin–2–one (2f)
Following the **General Procedure E** (eluent: EtOAc/PE 1: 4), the imidation of 6–phenylhexanoic acid with oxazolidin–2–one afford **2f** (41 mg; yield: 31%) as white crystals, mp: 65.3–66.9 °C; IR (film)ν_{max}: 2920, 2858, 1780, 1700, 1388, 1225, 1111, 1039 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.36–1.44 (m, 2 H), 1.61–1.73 (m, 4 H), 2.61 (t, J = 7.6 Hz, 2 H), 2.90 (t, J = 7.6 Hz, 2 H), 3.97 (t, J = 8.4 Hz, 2 H), 4.36 (t, J = 8.4 Hz, 2 H), 7.16–7.18 (m, 3 H), 7.24–7.28 (m, 2 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.0, 28.6, 31.1, 34.9, 35.6, 42.4, 61.9, 125.5, 128.2, 128.3, 142.4, 153.4, 173.3 ppm; MS (ESI, m/z): 262 $(M + H)^+$; HRMS (ESI) calcd for $[C_{15}H_{20}NO_3]^+$ $(M + H)^+$: 262.1443; found: 262.1438; Anal. calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.70; H, 7.31; N, 5.38.

3–(7–phenylheptanoyl)oxazolidin–2–one (2g)
Following the **General Procedure E** (eluent: EtOAc/PE 1: 5), the imidation of 7–phenylheptanoic acid with oxazolidin–2–one afford **2g** (61 mg; yield: 44%) as white wax; IR (film)ν_{max}: 2918, 2850, 1781, 1703, 1386, 1225, 1039 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.35–1.42 (m, 4 H), 1.58–1.69 (m, 4 H), 2.60 (t, J = 7.6 Hz, 2 H), 2.90 (t, J = 7.6 Hz, 2 H), 3.98 (t, J = 8.4 Hz, 2 H), 4.36 (t, J = 8.4 Hz, 2 H), 7.16–7.17 (m, 3 H), 7.24–7.28 (m, 2 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.1, 28.9, 28.9, 31.2, 35.0, 35.8, 42.4, 61.9, 125.5, 128.1, 128.3, 142.6, 153.5, 173.4 ppm; MS (ESI, m/z): 276 $(M + H)^+$; Anal. calcd for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09. Found: C, 69.83; H, 7.68; N, 5.10.

3–(8–phenyloctanoyl)oxazolidin–2–one (2h)
Following the **General Procedure E** (eluent: EtOAc/PE 1: 5), the imidation of 8–phenyloctanoic acid with oxazolidin–2–one afford **2h** (64 mg; yield: 44%) as white crystals, mp: 71.5–72.3 °C; IR (film)ν_{max}: 2920, 2848, 1780, 1703, 1386, 1225, 1020 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.35–1.42 (m, 4 H), 1.58–1.69 (m, 4 H), 2.60 (t, J = 7.6 Hz, 2 H), 2.90 (t, J = 7.6 Hz, 2 H), 3.98 (t, J = 8.4 Hz, 2 H), 4.36 (t, J = 8.4 Hz, 2 H), 7.16–7.17 (m, 3 H), 7.24–7.28 (m, 2 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.1, 28.9, 28.9, 31.2, 35.0, 35.8, 42.4, 61.9, 125.5, 128.1, 128.3, 142.6, 153.5, 173.4 ppm; MS (ESI, m/z): 290 $(M + H)^+$; Anal. calcd for $C_{17}H_{23}NO_3$: C, 70.56; H, 8.01; N, 4.84. Found: C, 70.61; H, 7.99; N, 4.85.

Biphenyl–4–yl–carbonyl oxazolidin–2–one (3a)[1]
Following the **General Procedure E** (eluent: EtOAc/PE 1: 2), the imidation of 4–phenylbenzoic acid with oxazolidin–2–one afford **3a** (71 mg; yield: 53%) as white crystals, mp: 251.6–253.7 °C; IR (film)ν_{max}: 2917, 2849, 1761, 1676, 1579, 1384,

1332, 1204, 1099, 1032 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.20 (t, J = 8.0 Hz, 2 H), 4.52 (t, J = 8.0 Hz, 2 H), 7.39 (t, J = 7.6 Hz, 1 H), 7.46 (t, J = 7.6 Hz, 2 H), 7.61–7.66 (m, 4 H), 7.76 (d, J = 8.0 Hz, 2 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.8, 62.3, 126.6, 127.3, 128.1, 128.9, 129.8, 131.1, 140.0, 145.3, 153.3, 169.5 ppm; MS (ESI, m/z): 268 $(M + H)^+$; Anal. calcd for $C_{16}H_{13}NO_3$: C, 71.90; H, 4.90; N, 5.24. Found: C, 72.10; H, 4.91; N, 5.23.

3–(4–phenoxybenzoyl)oxazolidin–2–one (3b)[1]
Following the **General Procedure E** (eluent: EtOAc/PE 1: 2), the imidation of 4–phenoxybenzoic acid with oxazolidin–2–one afford **3b** (77 mg; yield: 55%) as white crystals, mp: 149.0–151.5 °C; IR (film)ν_{max}: 2915, 2844, 1779, 1681, 1575, 1482, 1445, 1382, 1322 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.17 (t, J = 8.0 Hz, 2 H), 4.50 (t, J = 8.0 Hz, 2 H), 6.97 (ddd, J = 8.4, 2.8, 2.0 Hz, 2 H), 7.08 (dd, J = 8.4, 0.8 Hz, 2 H), 7.19 (dd, J = 7.6 Hz, 1 H), 7.40 (ddd, J = 8.4, 7.6, 2.0 Hz 2 H), 7.67 (ddd, J = 8.4, 2.8, 2.0 Hz, 2 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.9, 62.2, 116.7, 120.3, 124.6, 126.4, 130.0, 131.7, 153.4, 155.5, 161.7, 168.9 ppm; MS (ESI, m/z): 284 $(M + H)^+$; Anal. calcd for $C_{16}H_{13}NO_4$: C, 67.84; H, 4.63; N, 4.94. Found: C, 67.75; H, 4.63; N, 4.95.

3–(4–(benzyloxy)benzoyl)oxazolidin–2–one (3c)
Following the **General Procedure E** (eluent: EtOAc/PE 1: 5), the imidation of 4–(benzyloxy)benzoic acid with oxazolidin–2–one afford **3c** (108 mg; yield: 73%) as white crystals, mp: 198.0–201.3 °C; IR (film)ν_{max}: 2916, 2849, 1774, 1670, 1607, 1512, 1378, 1338, 1249, 1194, 1108, 1024 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.14 (t, J = 8.0 Hz, 2 H), 4.47 (t, J = 8.0 Hz, 2 H), 5.11 (s, 2 H), 6.99 (d, J = 8.8 Hz, 2 H), 7.34–7.43 (m, 5 H), 7.69 (d, J = 8.8 Hz, 2 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.9, 62.2, 70.1, 114.0, 124.7, 127.5, 128.2, 128.6, 131.8, 136.2, 153.5, 162.4, 169.0 ppm; MS (ESI, m/z): 298 $(M + H)^+$; Anal. calcd for $C_{17}H_{15}NO_4$: C, 68.68; H, 5.09; N, 4.71. Found: C, 68.90; H, 5.11; N, 4.69.

4–phenethoxybenzoic acid (3d–1)
Following the **General Procedure F** (eluent: EtOAc/PE 1: 5), the reaction starting from 4–hydroxybenzoic acid afford **3d–1** (315 mg; yield: 65%) as white wax; IR (film)ν_{max}: 3415, 2949, 2917, 2848, 1677, 1608, 1254 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.13 (d, J = 7.0 Hz, 2 H), 4.24 (d, J = 7.0 Hz, 2 H), 6.93 (d, J = 8.8 Hz, 2 H), 7.23–7.35 (m, 5 H), 7.33–7.40 (m, 4 H), 8.04 (dd, J = 7.1 Hz, 1.8 Hz, 2 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.6, 68.9, 114.2, 121.7, 126.7, 128.6, 128.9, 132.3, 137.8, 163.3, 171.5 ppm; MS (ESI, m/z): 243 $(M + H)^+$; Anal. calcd for $C_{17}H_{15}NO_4$: C, 74.36; H, 5.82. Found: C, 74.21; H, 5.82.

3–(4–phenethoxybenzoyl)oxazolidin–2–one (3d)
Following the **General Procedure E** (eluent: EtOAc/PE 1: 5), the imidation of **3d-1** with oxazolidin–2–one afford **3d** (84 mg; yield: 54%) as white crystals, mp: 127.3–129.7 °C; IR (film)ν_{max}: 2916, 2849, 1777, 1672, 1605, 1508, 1384, 1324, 1307, 1254, 1168, 1094, 1029 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.11 (t, J = 7.2 Hz, 2 H), 4.14 (t, J = 8.0 Hz, 2 H), 4.22 (t, J = 7.2 Hz, 2 H), 4.46 (t, J = 8.0 Hz, 2 H), 6.90 (d, J = 8.4 Hz, 2 H), 7.23–7.34 (m, 5 H), 7.67 (d, J = 8.4 Hz, 2 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 35.6, 43.9, 62.2, 68.8, 113.7, 124.4, 126.6, 128.5, 129.0, 131.8, 137.8, 153.5, 162.5, 169.0 ppm; MS (ESI, m/z): 312 $(M + H)^+$; Anal. calcd for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.53; H, 5.51; N, 4.49

3–(4–benzylidenepiperidine–1–carbonyl)oxazolidin–2–one (3e)
Following the **General Procedure G** (eluent: EtOAc/PE 1: 4), the reaction starting from 4–benzylidenepiperidine afford **3e** (18 mg; yield: 16%) as yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.47 (t, J = 5.7 Hz, 2 H), 2.60 (t, J = 5.7 Hz, 2 H), 3.50–3.58 (m, 2 H), 3.62–3.67 (m, 2 H), 3.99 (t, J = 7.8 Hz, 2 H), 4.42 (t, J = 7.8 Hz, 2 H), 6.4 (s, 1 H), 7.18–7.24 (m, 3 H), 7.33 (dd, J = 7.4, 7.4 Hz, 2 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ31.2, 36.7, 42.4, 44.3, 44.4, 62.4, 123.3, 126.0, 128.1, 128.9, 129.9, 140.6, 152.5, 154.1 ppm; MS (ESI, m/z): 287 $(M + H)^+$; HRMS (ESI) calcd for $[C_{16}H_{19}N_2O_3]^+$ $(M + H)^+$: 287.1396; found: 287.1389.

3–(4–benzylpiperidine–1–carbonyl)oxazolidin–2–one (3f)
Following the **General Procedure G** (eluent: EtOAc/PE 1: 4), the reaction starting from 4–benzylpiperidine afford **3f** (15 mg; yield: 13%) as corless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23–1.37 (m, 2 H), 1.67–1.79 (m, 3 H), 2.55 (d, J = 7.1 Hz, 2 H), 2.88 (br, 2 H), 3.93 (t, J = 7.8 Hz, 2 H), 4.37 (t, J = 7.8 Hz, 2 H), 6.8 (d, J = 6.8 Hz, 2 H), 7.19 (dd, J = 7.2, 7.2 Hz, 1 H), 7.25–7.29 (m, 2 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.7, 37.8, 42.7, 44.3, 62.6, 125.9, 128.1, 128.9, 139.8, 152.4, 154.2 ppm; MS (ESI, m/z): 289 $(M + H)^+$; HRMS (ESI) calcd for $[C_{16}H_{21}N_2O_3]^+$ $(M + H)^+$: 289.1552; found: 289.1541.

3–(1–benzylpiperazine–4–carbonyl)oxazolidin–2–one (3g)
Following the **General Procedure G** (eluent: EtOAc/PE 1: 1), the reaction starting from 1–benzylpiperazine afford **3g** (14 mg; yield: 12%) as corless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.51 (d, J = 5.1 Hz, 4 H), 3.52–3.57 (m, 6 H), 3.94 (t, J = 7.8 Hz, 2 H), 4.38 (t, J = 7.8 Hz, 2 H), 7.24–7.34 (m, 5 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.6, 44.3, 52.5, 62.6, 62.7, 127.2, 128.2, 129.0, 137.3, 152.4, 154.1 ppm; MS (ESI, m/z): 290 $(M + H)^+$; HRMS (ESI) calcd for $[C_{15}H_{20}N_3O_3]^+$ $(M + H)^+$: 290.1505; found: 290.1517.

4–benzylidenecyclohexanecarboxylic acid (3h–1)[5]
To a solution of Benzyltriphenylphosphonium chloride (389 mg, 1.0 mmol) in THF (15 mL) was added slowly a solution of 2 M LiHMDS (2.5 mmol, 1.25 mL THF) under nitrogen atmosphere at –78°C. The reaction mixture was stirred at –78°C for 15 min, and allowed to warm slowly to 0°C in 0.5 hour. After being stirred at 0°C for 1 hour, a solution of 4-Oxocyclohexanecarboxylic acid (150 mg, 1.05 mmol) in THF (2 mL) was slowly added at –78°C. The reaction mixture was allowed to warm slowly to 0°C and stirred at the same temperature for 18 hour. The reaction was quenched with 15 mL aqueous 4 M HCl and extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (eluent: EtOAc/PE 1: 5) to afford **3h–1** (60 mg; yield: 28%) as colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.54–1.76 (m, 2 H), 1.99–2.12 (m, 3 H), 2.21–2.27 (m, 1 H), 2.42–2.45 (m, 1 H), 2.54–2.59 (m, 1 H), 2.84–2.87 (m, 1 H), 6.29 (s, 1 H), 7.17–7.23 (m, 3 H), 7.30 (dd, J = 7.6, 7.6 Hz, 2 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.6, 29.3, 30.0, 25.6, 42.6, 123.4, 126.0, 128.0, 128.8, 137.8, 140.4, 181.9 ppm; MS (ESI, m/z): 217 $(M + H)^+$; Anal. calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.88; H, 7.47.

3–(4–benzylidenecyclohexanecarbonyl)oxazolidin–2–one (3h)

Following the **General Procedure E** (eluent: EtOAc/PE 1: 5), the imidation of **3h–1** afford **3h** (78 mg; yield: 55%) as colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.50–1.72 (m, 3 H), 1.93–1.99 (m, 1 H), 2.01–2.08 (m, 2 H), 2.30–2.38 (m, 1 H), 2.43–2.47 (m, 1 H), 2.93–2.97 (m, 1 H), 3.70–3.78 (m, 1 H), 4.00 (t, J = 7.8 Hz, 2 H), 4.40 (t, J = 7.8 Hz, 2 H), 6.32 (s, 1 H), 7.71–7.21 (m, 3 H), 7.29–7.32 (m, 2 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.8, 29.6, 30.3, 35.7, 41.7, 42.7, 61.9, 123.3, 126.0, 128.0, 128.9, 137.9, 140.6, 153.1, 175.9 ppm; MS (ESI, m/z): 286 $(M + H)^+$; Anal. calcd for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71; N, 4.91. Found: C, 71.37; H, 6.72; N, 4.91.

3–(4–benzylcyclohexanecarbonyl)oxazolidin–2–one (3i)

Compound **3h** (28 mg, 0.1 mmol) in EtOAc (10 mL) was treated with 10% Pd/C (200 mg) and purged with H_2. After stirring for 12 hours at room temperature, the reaction mixture was filtered through celite and concentrated under reduced pressure to afford the product as white wax (28 mg; yield: 98%); ^{1}H NMR (400 MHz, $CDCl_3$) δ1.53–1.68 (m, 6 H), 1.77–1.90 (m, 3 H), 2.62 (t, J = 7.6 Hz, 2 H), 3.60-3.66 (m, 1 H), 4.01 (t, J = 8.0 Hz, 2 H), 4.38 (t, J = 8.0 Hz, 2 H), 6.32 (s, 1 H), 7.12–7.19 (m, 3 H), 7.25–7.29 (m, 2 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.2, 28.6, 36.4, 39.8, 40.1, 42.8, 61.8, 125.7, 128.1, 129.0, 141.3, 153.1, 176.6 ppm; MS (ESI, m/z): 288 $(M + H)^+$; Anal. calcd for $C_{17}H_{21}NO_3$: C, 71.06; H, 7.37; N, 4.87. Found: C, 71.19; H, 7.38; N, 4.86.

6–cyclohexylhexanoic acid (3j–1) [4]

To a solution of (4–Carboxybutyl)triphenylphosphonium bromide (443 mg, 1.0 mmol) in THF (15 mL) was added slowly a solution of 2 M LiHMDS (2.5 mmol, 1.25 mL THF) under nitrogen atmosphere at –78°C. The reaction mixture was stirred at –78°C for 15 min, and allowed to warm slowly to 0°C in 0.5 hour. After being stirred at 0°C for 1 hour, a solution of cyclohexanecarbaldehyde (112 mg, 1.05 mmol) in THF (2 mL) was slowly added at –78°C. The reaction mixture was allowed to warm slowly to 0°C and stirred at the same temperature for 18 hour. The reaction was quenched with 15 mL aqueous 4 M HCl and extracted with EtOAc (3 × 5 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue in EtOAc (10 mL) was treated with 10% Pd/C (200 mg) and purged with H_2. After stirring for 12 hours at room temperature, the reaction mixture was filtered through celite and concentrated under reduced pressure to afford the product **3j–1** (139 mg; yield: 70%) as colorless oil, IR (film)ν_{max}: 3404, 2918, 2850, 1709, 1445, 1025 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84–0.92 (m, 2 H), 1.14–1.34 (m, 10 H), 1.64–1.72 (m, 7 H), 2.36 (t, J = 7.5 Hz, 2 H) ppm;^{13}C NMR (100 MHz, $CDCl_3$) δ 24.7, 26.4, 26.4, 26.7, 29.4, 33.4, 34.1, 37.2, 37.6, 180.1 ppm; MS (ESI, m/z): 199 $(M + H)^+$; Anal. calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.55; H, 11.17.

3–(6–cyclohexylhexanoyl)oxazolidin–2–one (3j)

Following the **General Procedure E** (eluent: EtOAc/PE 1: 5), the imidation of **3j-1** with oxazolidin–2–one afford **3j** (57 mg; yield: 43%) as white crystals, mp: 65.0–66.6 ^{o}C; IR (film)ν_{max}: 2917, 2849, 1577, 1541, 1468, 1384, 1068, 1023 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82–0.90 (m, 2 H), 1.15–1.23 (m, 6 H), 1.32–1.34 (m, 4 H), 1.63–1.70 (m, 7 H), 2.92 (t, J = 7.6 Hz, 2 H), 4.03 (t, J = 8.0 Hz, 2 H), 4.42 (t, J = 8.0 Hz, 2 H) ppm;^{13}C NMR (100 MHz, $CDCl_3$) δ 24.3, 26.4, 26.5, 26.7, 29.4, 33.4, 35.0, 37.3, 37.6, 42.5, 61.9, 153.5, 173.6 ppm; MS (ESI, m/z): 268 $(M + H)^+$; Anal. calcd for $C_{15}H_{25}NO_3$: C, 67.38; H, 9.42; N, 5.24. Found: C, 67.15; H, 9.41; N, 5.25.

Biphenyl–3–yl–carbonyl oxazolidin–2–one (3k)
Following the **General Procedure E** (eluent: EtOAc/PE 1: 2), the imidation of 3–phenylbenzoic acid with oxazolidin–2–one afford **3k** (81 mg; yield: 61%) as white crystals, mp: 205.6–208.8 ^{o}C; IR (film)ν_{max}: 2916, 2848, 1633, 1565, 1406, 1107, 1037 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.19–4.20 (m, 2 H), 4.52 (br, 2 H), 7.36–7.38 (m, 1 H), 7.44 (br, 2 H), 7.50–7.52 (m, 1 H), 7.59–7.61 (m, 3 H), 7.77–7.78 (br, 1 H), 7.87 (s, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.7, 48.0, 48.2, 48.4, 48.6, 48.9, 62.6, 127.0, 127.6, 128.3, 128.7, 130.8, 140.0, 140.9, 153.9, 170.0 ppm; MS (ESI, m/z): 268 $(M + H)^+$; Anal. calcd for $C_{16}H_{13}NO_3$: C, 71.90; H, 4.90; N, 5.24. Found: C, 71.74; H, 4.89; N, 5.25.

Biphenyl–3–yl–methylcarbonyl oxazolidin–2–one (3l)
Following the **General Procedure E** (eluent: EtOAc/PE 1: 3), the imidation of 3–phenylphenylacetic acid with oxazolidin–2–one afford **3l** (63 mg; yield: 45%) as white wax; IR (film)ν_{max}: 2916, 2848, 1776, 1697, 1598, 1478, 1387, 1366, 1223, 1180, 1109 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.02 (t, J = 8.0 Hz, 2 H), 4.35 (s, 2 H), 4.39 (t, J = 8.0 Hz, 2 H), 7.31 (d, J = 7.2 Hz, 1 H), 7.34 (d, J = 7.2 Hz, 1 H), 7.38–7.44 (m, 3 H), 7.50 (d, J = 7.6 Hz, 1 H), 7.55–7.60 (m, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 41.1, 42.7, 61.9, 126.0, 127.2, 127.3, 128.6, 128.6, 128.7, 128.9, 134.0, 140.8, 141.5, 153.5, 171.2 ppm; MS (ESI, m/z): 282 $(M + H)^+$; Anal. calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.71; H, 5.39; N, 4.96.

Biphenyl–4–yl–methylcarbonyl oxazolidin–2–one (3m)
Following the **General Procedure E** (eluent: EtOAc/PE 1: 3), the imidation of 4–phenylphenylacetic acid with oxazolidin–2–one afford **3m** (65 mg; yield: 46%) as white crystals, mp: 197.6–200 ^{o}C; IR (film)ν_{max}: 2914, 2844, 1776, 1697, 1578, 1386, 1366, 1025 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.00 (t, J = 8.4 Hz, 2 H), 4.31 (s, 2 H), 4.36 (t, J = 8.4 Hz, 2 H), 7.33 (t, J = 7.6 Hz, 1 H), 7.37–7.44 (m, 4 H), 7.54–7.58 (m, 4 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.7, 42.6, 61.9, 126.9, 127.0, 127.2, 128.7, 130.1, 132.5, 140.0, 140.7, 153.4, 171.1 ppm; MS (ESI, m/z): 282 $(M + H)^+$; Anal. calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.67; H, 5.38; N, 4.97.

3–(3–phenoxybenzoyl)oxazolidin–2–one (3n)
Following the **General Procedure E** (eluent: EtOAc/PE 1: 2), the imidation of 3–phenoxybenzoic acid with oxazolidin–2–one afford **3n** (68 mg; yield: 48%) as white crystals, mp: 140.3–141.4 ^{o}C; IR (film)ν_{max}: 2917, 2845, 1783, 1682, 1577, 1483, 1436, 1322, 1200 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.14 (t, J = 8.0 Hz, 2 H), 4.46 (t, J = 8.0 Hz, 2 H), 7.04 (dd, J = 8.6, 1.0 Hz, 2 H), 7.12 (dd, J = 7.4, 0.9 Hz, 1 H), 7.18 (dddd, J = 7.2, 7.2, 2.0, 2.0 Hz, 1 H), 7.26 (br, 1 H), 7.33–7.39 (m, 4 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.6, 62.2, 119.1, 119.1, 122.6, 123.6, 123.7, 129.4, 129.9, 134.3, 153.0, 156.6, 156.8, 169.1 ppm; MS (ESI, m/z): 284 $(M + H)^+$; Anal. calcd for $C_{16}H_{13}NO_4$: C, 67.84; H, 4.63; N, 4.94. Found: C, 68.01; H, 4.64; N, 4.93.

3–(2–(3–phenoxyphenyl)acetyl)oxazolidin–2–one (3o)
Following the **General Procedure E** (eluent: EtOAc/PE 1: 5), the imidation of 2–(3–phenoxyphenyl)acetic acid with oxazolidin–2–one afford **3o** (78 mg; yield: 53%) as white wax; IR (film)ν_{max}: 2914, 2844, 1777, 1701, 1583, 1486, 1387, 1366, 1269, 1246, 1211 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.99 (t, J = 8.0 Hz, 2 H), 4.24 (s, 1

H), 4.37 (t, J = 8.0 Hz, 2 H), 6.89 (d, J = 7.8 Hz, 1 H), 6.96 (s, 1 H), 7.01 (dd, J = 8.4, 8.4 Hz, 3 H), 7.09 (dd, J = 7.8 Hz, 1 H), 7.25 (d, J = 7.8 Hz, 1 H), 7.31 (dd, J = 8.4, 8.4 Hz, 2 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.9, 42.6, 61.9, 117.4, 118.9, 120.1, 123.2, 124.5, 129.6, 129.7, 135.3, 153.4, 156.9, 157.2, 170.8 ppm; MS (ESI, m/z): 298 $(M + H)^+$; Anal. calcd for $C_{17}H_{15}NO_4$: C, 68.68; H, 5.09; N, 4.71. Found: C, 68.51; H, 5.08; N, 4.72.

3–(2–(4–phenoxyphenyl)acetyl)oxazolidin–2–one (3p)
Following the **General Procedure E** (eluent: EtOAc/PE 1: 5), the imidation of 2–(4–phenoxyphenyl)acetic acid with oxazolidin–2–one afford **3p** (88 mg; yield: 59%) as white crystals, mp: 122.3–124.9 °C; IR (film)ν_{max}: 2916, 2848, 1777, 1577, 1537, 1486, 1467, 1385, 1237, 1108, 1040 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.02 (t, J = 8.0 Hz, 2 H), 4.25 (s, 2 H), 4.39 (t, J = 8.0 Hz, 2 H), 6.95-7.00 (m, 4 H), 7.09 (t, J = 7.6 Hz, 1 H), 7.27-7.32 (m, 4 H)ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.3, 42.6, 62.0, 118.8, 118.9, 123.3, 128.2, 129.7, 131.0, 153.4, 156.4, 157.0, 171.3 ppm; MS (ESI, m/z): 298 $(M + H)^+$; Anal. calcd for $C_{17}H_{15}NO_4$: C, 68.68; H, 5.09; N, 4.71. Found: C, 68.73; H, 5.10; N, 4.72.

3–(benzyloxy)benzoic acid (3q–1)
Following the **General Procedure F** (eluent: EtOAc/PE 1: 5), the reaction starting from 3–hydroxybenzoic acid afford **3q–1** (342 mg; yield: 75%) as white crystals, mp: 131.2–133.5 °C; IR (film)ν_{max}: 3087, 2917, 2849, 1681, 1603, 1587, 1452 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.11 (s, 2 H), 7.21–7.24 (m, 1 H), 7.33–7.36 (m, 1 H), 7.38–7.41 (m, 3 H), 7.44 (d, J = 7.2 Hz, 2 H), 7.73 (d, J = 7.2 Hz, 2 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 70.2, 115.5, 121.2, 122.9, 127.5, 128.1, 128.6, 129.6, 130.6, 136.4, 158.8, 172.1 ppm; MS (ESI, m/z): 229 $(M + H)^+$; Anal. calcd for $C_{17}H_{15}NO_4$: C, 73.67; H, 5.30. Found: C, 73.90; H, 5.29.

3–(3–(benzyloxy)benzoyl)oxazolidin–2–one (3q)
Following the **General Procedure E** (eluent: EtOAc/PE 1: 5), the imidation of 3–(benzyloxy)benzoic acid with oxazolidin–2–one afford **3q** (82 mg; yield: 55%) as white crystals, mp: 142.1–143.3 °C; IR (film)ν_{max}: 2916, 2849, 1785, 1679, 1634, 1579, 1436, 1383, 1325, 1244, 1217, 1196, 1145, 1098, 1037 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$) δ 4.16 (t, J = 7.6 Hz, 2 H), 4.48 (t, J = 7.6 Hz, 2 H), 5.08 (s, 2 H), 7.14–7.44 (m, 9 H)ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.7, 62.2, 70.3, 115.1, 119.3, 121.7, 127.6, 128.1, 128.6, 129.0, 133.9, 136.5, 153.1, 158.3, 169.5 ppm; MS (ESI, m/z): 298 $(M + H)^+$; Anal. calcd for $C_{17}H_{15}NO_4$: C, 68.68; H, 5.09; N, 4.71. Found: C, 68.81; H, 5.11; N, 4.71.

3–(2–(3–(benzyloxy)phenyl) acetyl)oxazolidin–2–one (3r)
Following the **General Procedure E** (eluent: EtOAc/PE 1: 5), the imidation of 2–(3–(benzyloxy)phenyl)acetic acid with oxazolidin–2–one afford **3r** (76 mg; yield: 49%) as white wax; IR (film)ν_{max}: 2916, 2849, 1777, 1698, 1583, 1489, 1449, 1387, 1365, 1272, 1224, 1158, 1109, 1039 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.97 (t, J = 8.1 Hz, 2 H), 4.25 (s, 2 H), 4.35 (t, J = 8.1 Hz, 2 H), 5.04 (s, 2 H), 6.88 (d, J = 7.9 Hz, 1 H), 6.91 (d, J = 7.9 Hz, 1 H), 6.96 (s, 1H), 7.22 (dd, J = 7.9, 7.9 Hz, 1 H), 7.30 (dd, J = 7.2, 7.2 Hz, 1 H), 7.37 (dd, J = 7.2, 7.2 Hz, 2 H), 7.42 (d, J = 7.2 Hz,2 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 41.0, 42.6, 61.9, 69.9, 113.7, 116.2, 122.3, 127.5, 127.9, 128.5, 129.5, 135.0, 137.0, 153.4, 158.9, 171.0 ppm; MS (ESI, m/z): 312 $(M + H)^+$; Anal. calcd for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.20; H, 5.49; N, 4.51.

2–(4–(benzyloxy)phenyl) acetic acid (3s–1)

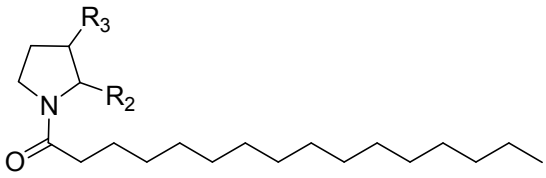
Following the **General Procedure F** (eluent: EtOAc/PE 1: 5), the reaction starting from 2–(4–hydroxyphenyl)acetic acid afford **3s–1** (300 mg; yield: 62%) as white crystals, mp: 123.6–124.2^{o}C; IR (film)ν_{max}: 3087, 2917, 2849, 1688, 1513, 1452, 1249, 1014 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.54 (s, 2 H), 5.00 (s, 2 H), 6.91 (d, J = 8.4 Hz, 2 H), 7.14 (d, J = 8.4 Hz, 2 H), 7.27–7.31 (m, 1 H), 7.33–7.40 (m, 4 H), 10.99 (s, 1 H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 40.1, 69.9, 114.9, 125.5, 127.4, 127.9, 128.5, 130.4, 136.9, 158.0, 178.4 ppm; MS (ESI, m/z): 243 $(M + H)^{+}$; Anal. calcd for $C_{17}H_{15}NO_4$: C, 74.36; H, 5.82. Found: C, 74.62; H, 5.81.

3–(2–(4–(benzyloxy)phenyl)acetyl)oxazolidin–2–one (3s)

Following the **General Procedure E** (eluent: EtOAc/PE 1: 5), the imidation of 2–(4–(benzyloxy)phenyl)acetic acid with oxazolidin–2–one afford **3s** (77 mg; yield: 50%) as white crystals, mp: 108.4–110.5 ^{o}C; IR (film)ν_{max}: 2916, 2849, 1777, 1698, 1607, 1511, 1387, 1365, 1240, 1177, 1111, 1040, 1016 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$) δ 3.96 (t, J = 8.0 Hz, 2 H), 4.20 (s, 2 H), 4.33 (t, J = 8.0 Hz, 2 H), 5.03 (s, 2 H), 6.92 (d, J = 8.4 Hz, 2 H), 7.22 (d, J = 8.4 Hz, 2 H), 7.30 (t, J = 7.2 Hz, 1 H), 7.35–7.42 (m, 4 H)ppm;^{13}C NMR (100 MHz, $CDCl_3$) δ 40.1, 42.6, 61.9, 69.9, 114.8, 125.8, 127.4, 127.9, 128.5, 130.7, 136.9, 153.4, 157.9, 171.5 ppm; MS (ESI, m/z): 312 $(M + H)^{+}$; Anal. calcd for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.65; H, 5.51; N, 4.50.

Supplementary Tables

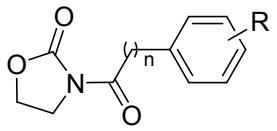
Table S1. Inhibitory activities of compounds **1k–1u** towards NAAA and FAAH[a]



Compound	R_2	R_3	IC_{50} of NAAA (μM)	IC_{50} of FAAH (μM)
1j	-H	(R)-OH	> 100	> 100
1k	-H	(S)-OH	> 100	> 100
1l	-H	(R)-OMe	> 100	> 100
1m	-H	(S)-OMe	> 100	> 100
1n	-H	(R)/(S)-CN	> 100	> 100
1o	-H	(R)/(S)-$CONH_2$	> 100	> 100
1p	-H	= O	> 100	> 100
1q	(R)-CH_2OH	-H	> 100	> 100
1r	(S)-CH_2OH	-H	> 100	> 100
1s	(R)-CH_2OMe	-H	> 100	> 100
1t	(S)-CH_2OMe	-H	> 100	> 100

[a]Data are presented as IC_{50} ± standard error of the mean. All experiments were performed in triplicate.

Table S2. Inhibitory activities of compounds **3k–3s** towards NAAA and FAAH[a]



Compound	n	R	IC_{50} of NAAA (μM)	IC_{50} of FAAH (μM)
3k	0	3-Ph	>20	>20
3l	1	3-Ph	>20	>20
3m	1	4-Ph	>20	>20
3n	0	3-OPh	>20	>20
3o	1	3-OPh	>20	>20
3p	1	4-OPh	>20	>20
3q	0	3-OBn	>20	>20
3r	1	3-OBn	>20	>20
3s	1	4-OBn	>20	>20

[a]Data are presented as IC_{50} ± standard error of the mean. All experiments were performed in triplicate.

Table S3. Purity of the new synthesized compounds

Compounds	HPLC purity	Compounds	HPLC purity
1c	98.3%	**3a**	98.5%
1d	98.7%	**3b**	98.8%
1e	99.1%	**3c**	99.0%
1f	98.6%	**3d**	97.8%
1g	99.5%	**3e**	99.4%
1h	99.4%	**3f**	98.2%
1i	99.1%	**3g**	98.6%
2a	98.6%	**3h**	98.5%
2b	99.0%	**3i**	98.8%
2c	97.9%	**3j**	99.3%
2d	99.2%		
2e	98.8%		
2f	99.3%		
2g	99.5%		
2h	99.4%		

Purity of each compound was determined on an Agilent 1200-HPLC system. Column: Hypersil Gold C18 column, 250 × 4.6 mm, 5 μm; flow rate: 0.75 mL/min, detection: UV at 220 and 254 nm; mobile phase: 10–98% acetonitrile/water and a 50–98% acetonitrile/water.

Supplementary Figures

Figure S1. Characterization of 2f as a reversible and noncompetitive NAAA inhibitor. (A) Concentration-dependent inhibitory effects of **2f** on the human NAAA (closed circles); (B) Concentration-dependent inhibitory effects of **2f** on the recombinant rat NAAA-transfected HEK293 cells (open triangles).

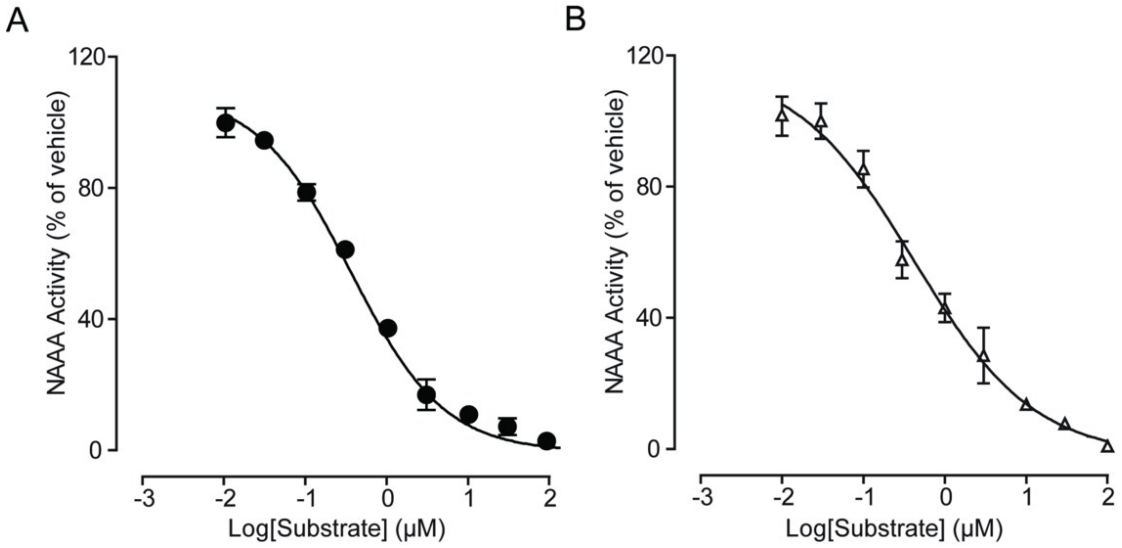


Figure S2. Effects of NAAA inhibitor on body weight and food intake. C57 mice were treated a single introgastric administration of vehicle (5% Tween 80 and 5% PEG 400 in saline, circle) or **2f** at 30 mg/kg/day (square), 100 mg/kg/day (triangle) for 30 and 10 days, respectively. Mice were housed in metabolic cages and monitored for body weight (A) and food intake (B). Body weight was expressed by Mean ± SEM, and total food intake per day were recored.

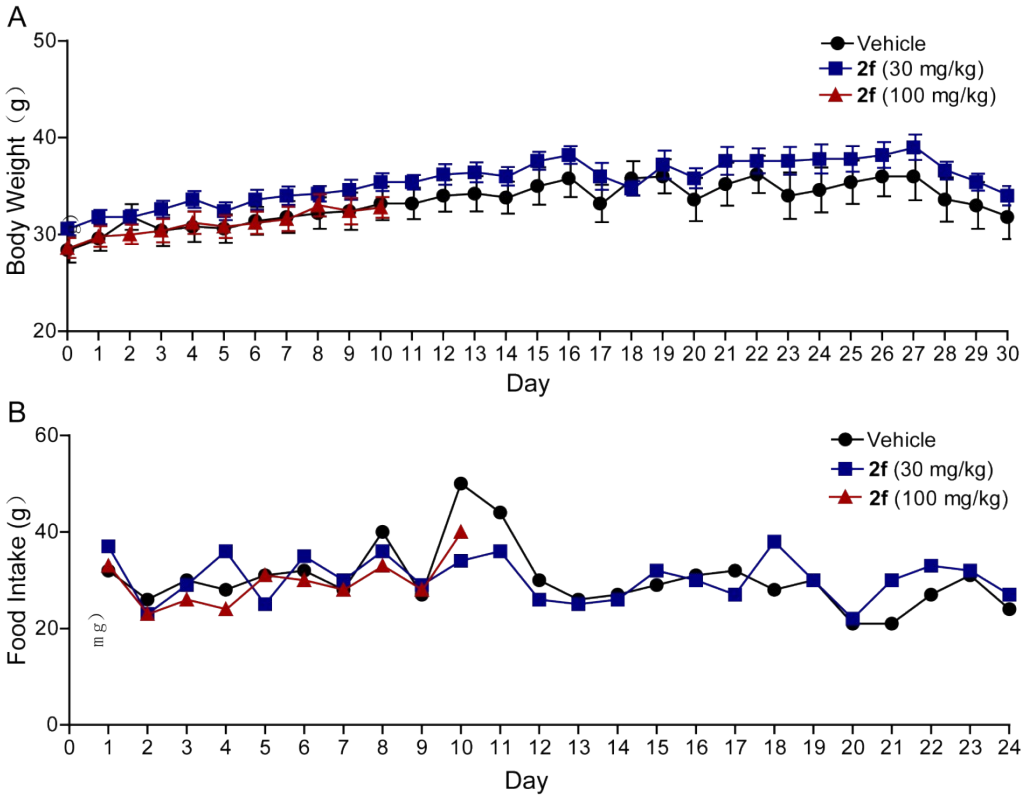


Figure S3. Assessment of gastric mucosa injury caused by NAAA and COX inhibitors. The dual COX1/2 inhibitor indomethacin (20 mg/kg for 3 days) produced significant gastric distension (B), ulcer and hemorrhages (G), while the NAAA inhibitor **2f** (30 mg/kg for 30 days and 100 mg/kg for 10 days) did not induce the similar gastric toxicity (C, D, F). All compounds were administered introgastrically in saline containing 5% Tween 80 and 5% PEG 400.

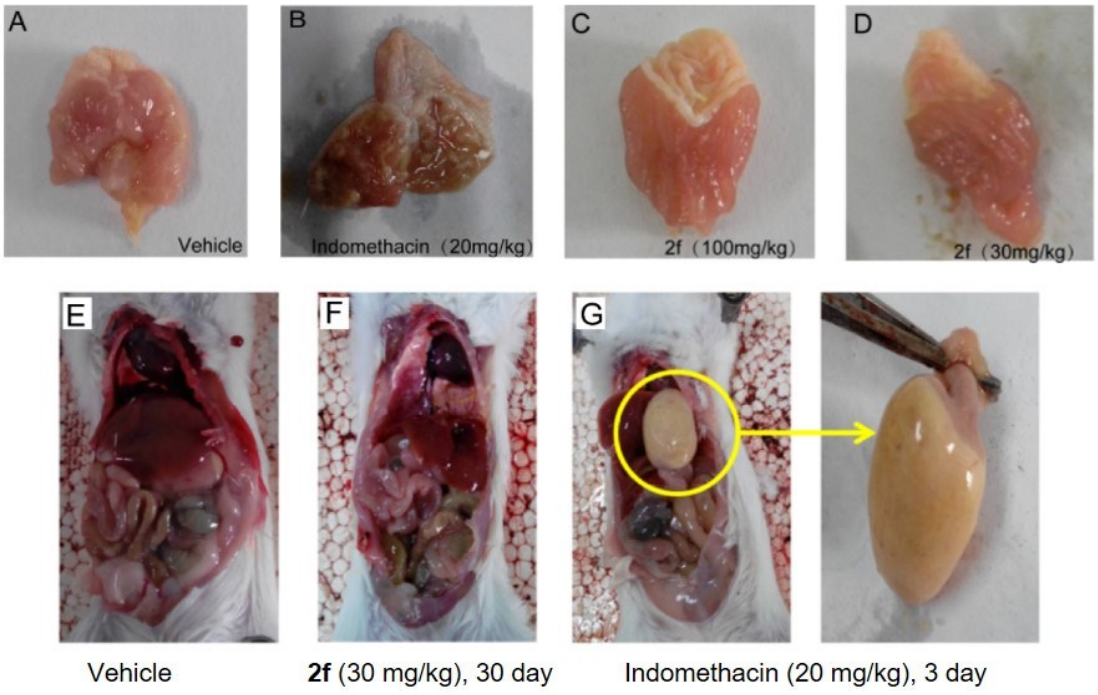


Figure S4. The inhibition of hERG channels in CHO cells by 2f (A) and cisapride (B).

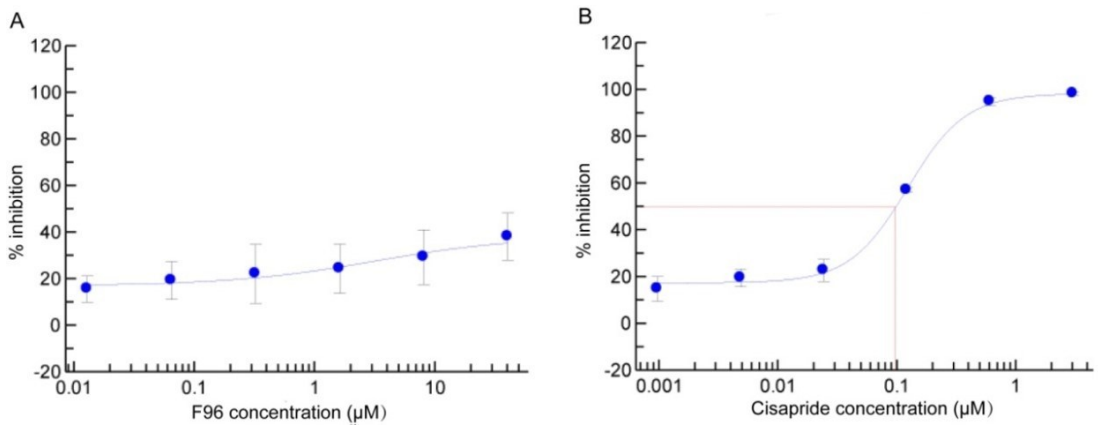
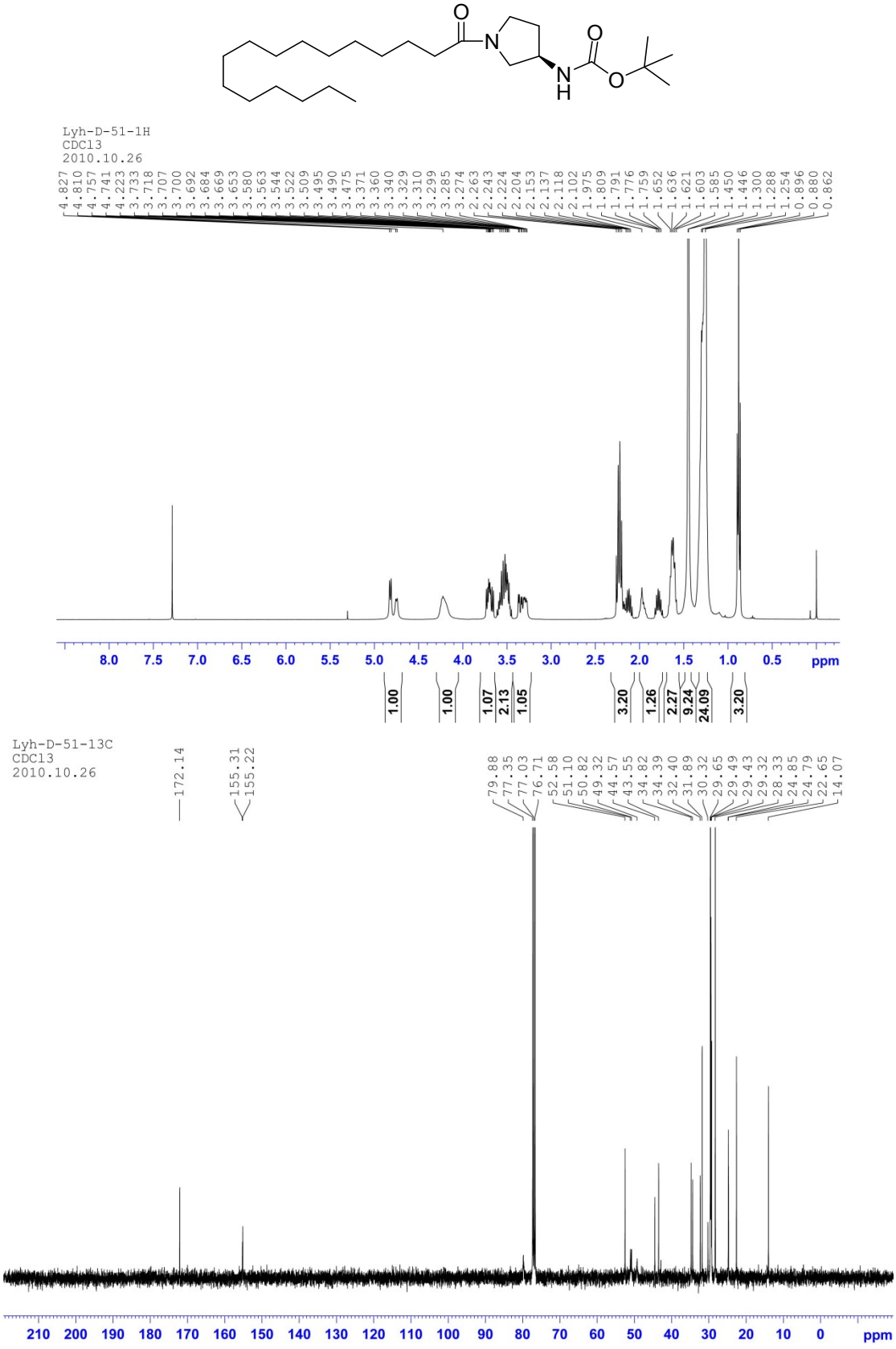
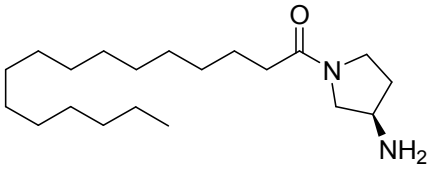


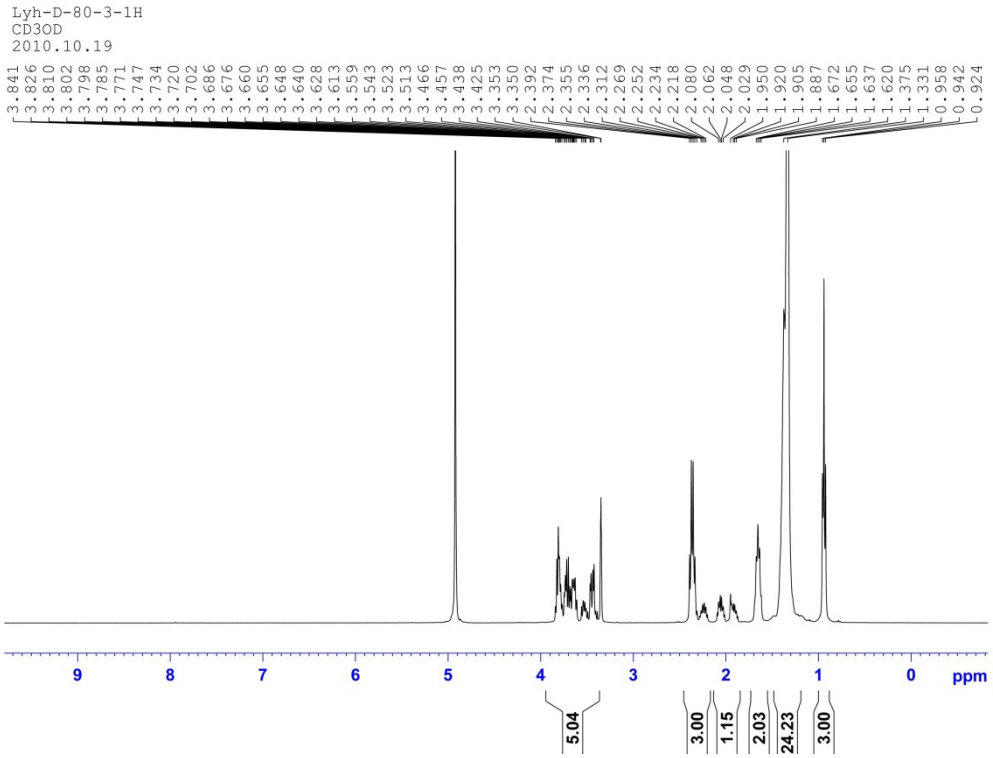
Figure S5. ^{1}H and ^{13}C NMR spectra of compounds

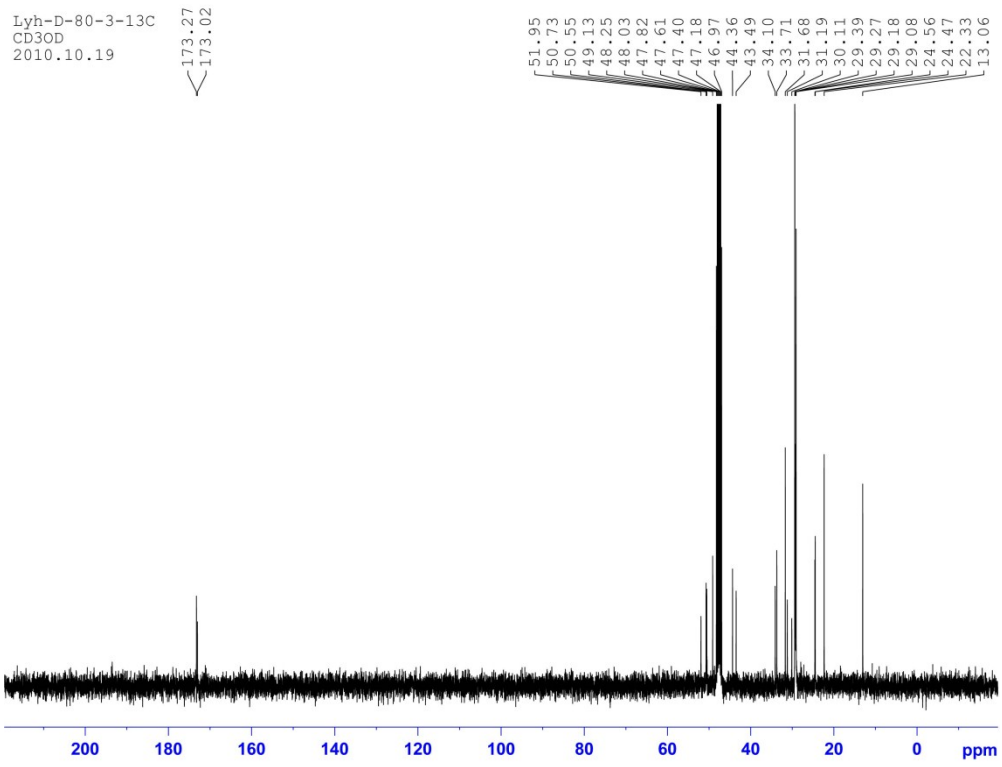
(R)-tert-butyl 1-palmitoylpyrrolidin-3-ylcarbamate (1c-1)



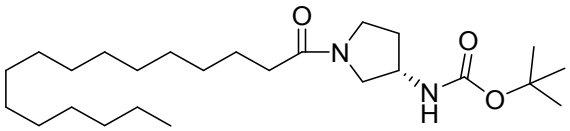
(R)-1-(3-aminopyrrolidin-1-yl)hexadecan-1-one (1c)

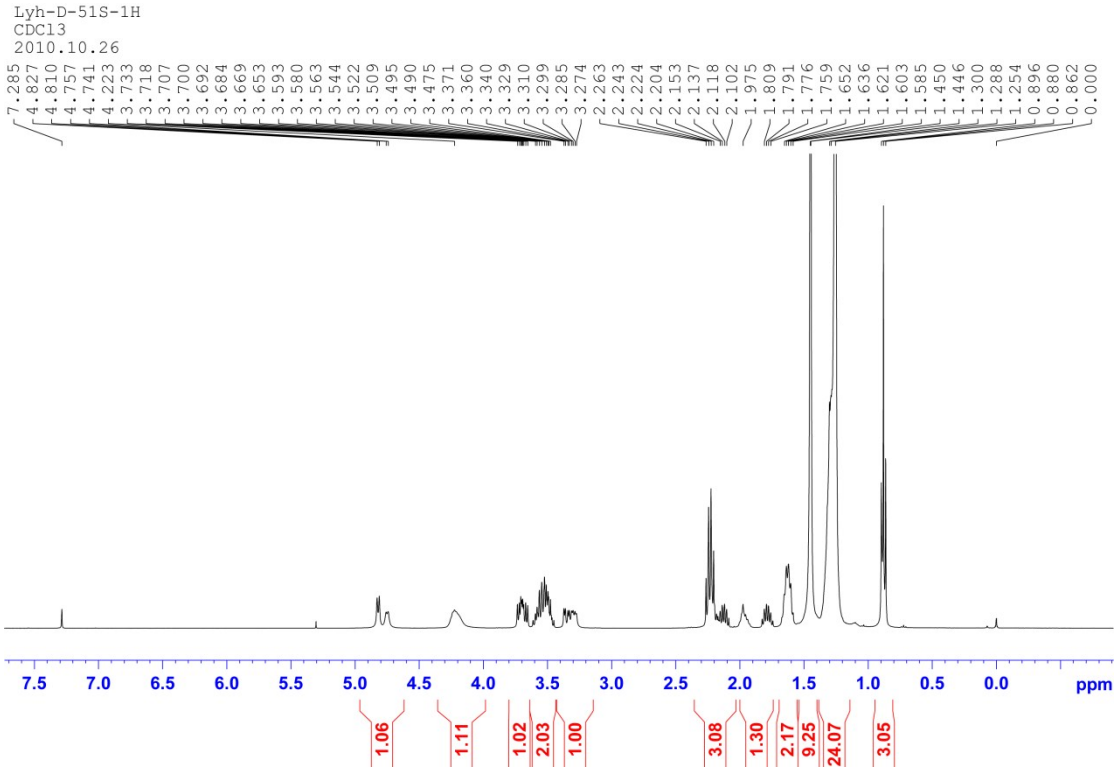


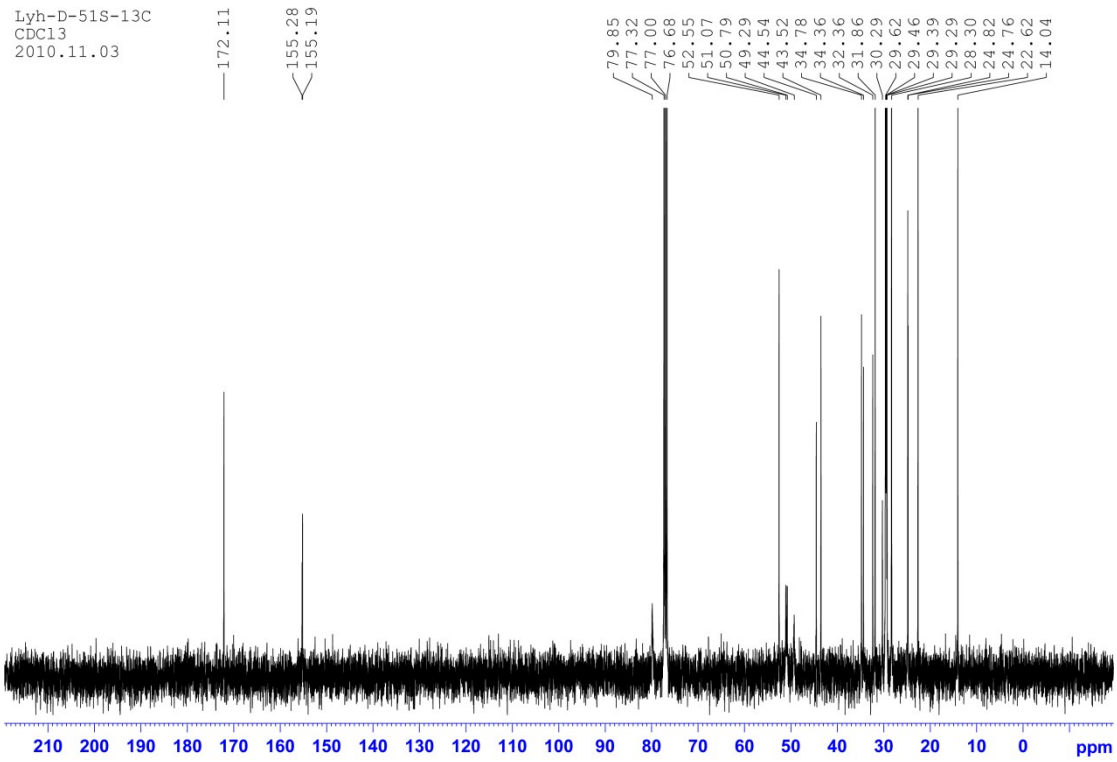




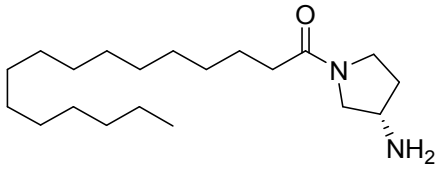
(S)-tert-butyl 1-palmitoylpyrrolidin-3-ylcarbamate (1d-1)

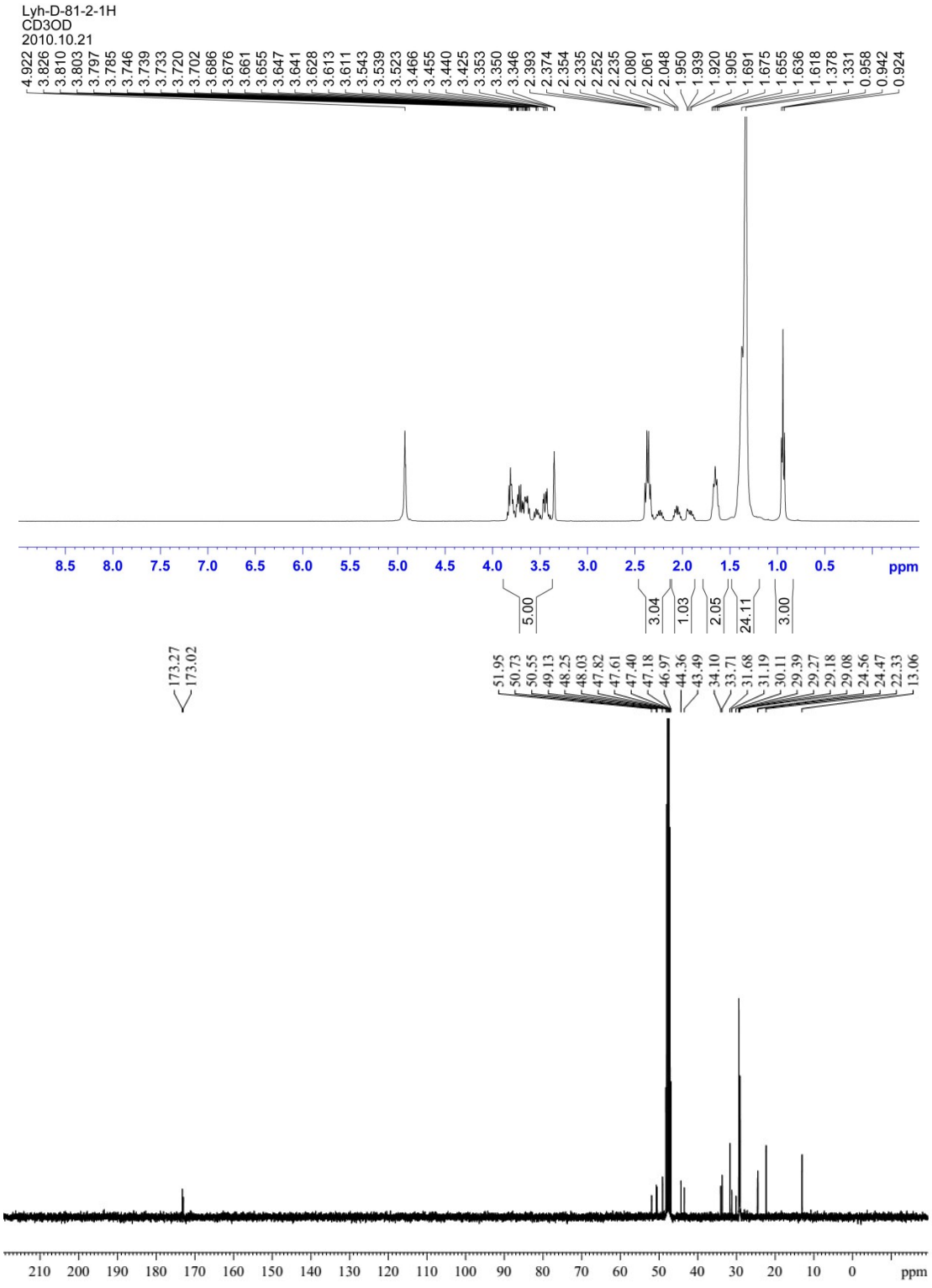




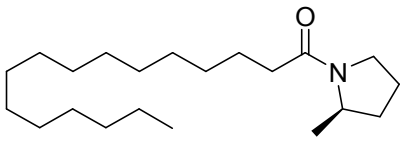


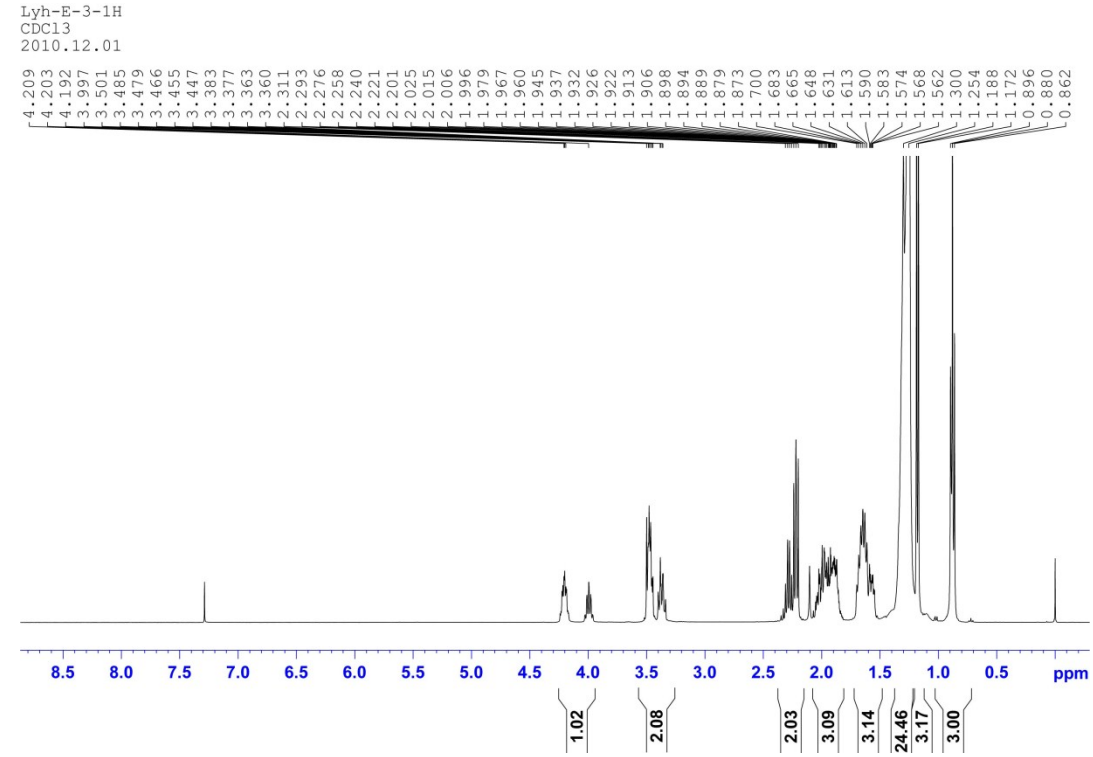
(S)-1-(3-aminopyrrolidin-1-yl)hexadecan-1-one (1d)

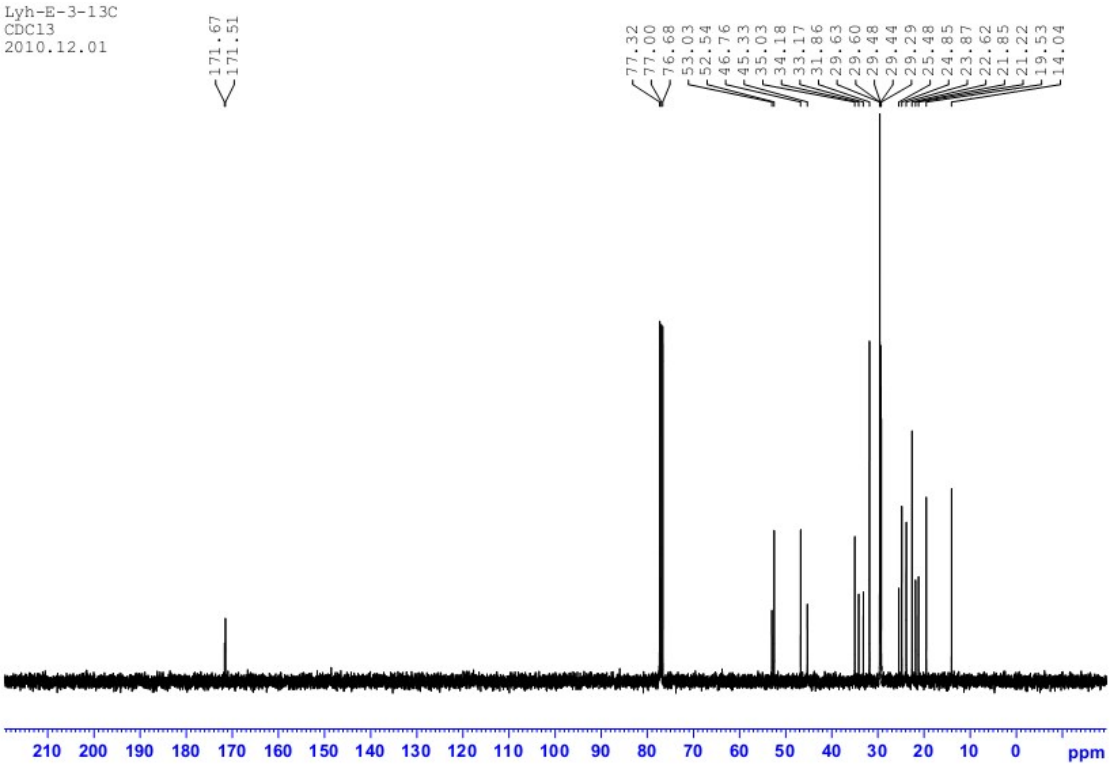




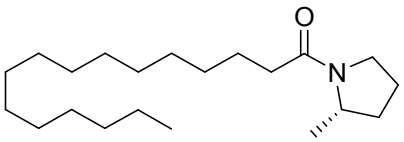
(R)-1-(2-methylpyrrolidin-1-yl)hexadecan-1-one (1e)

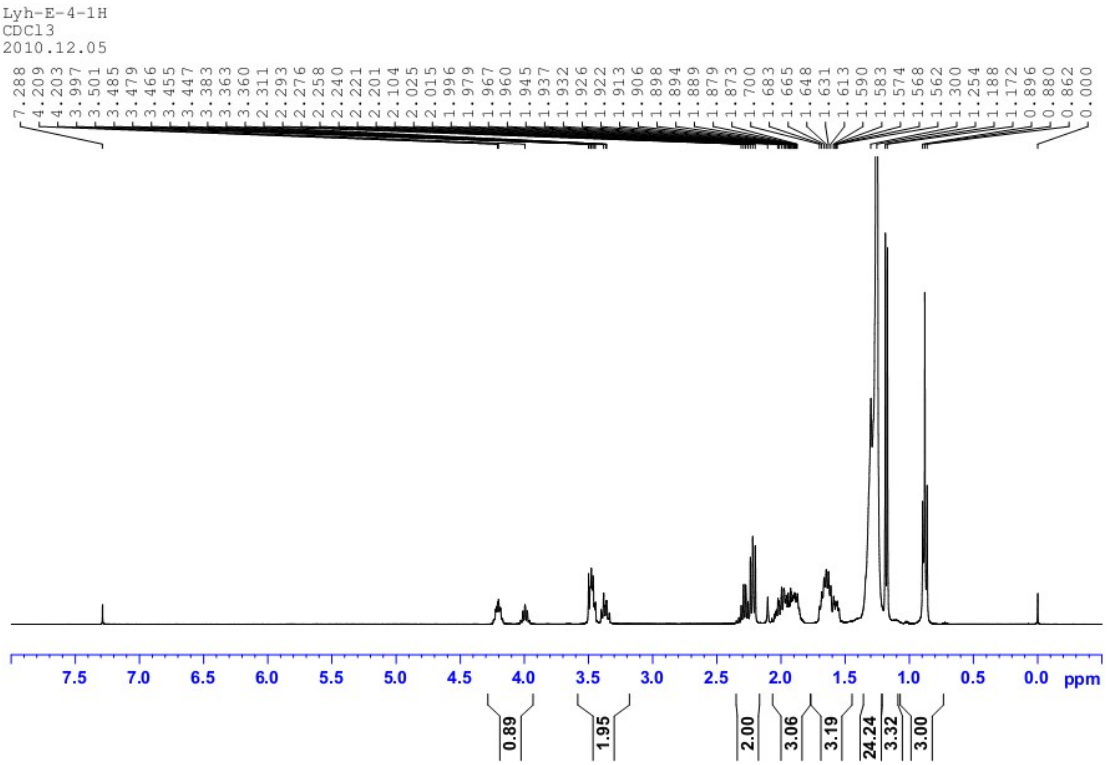


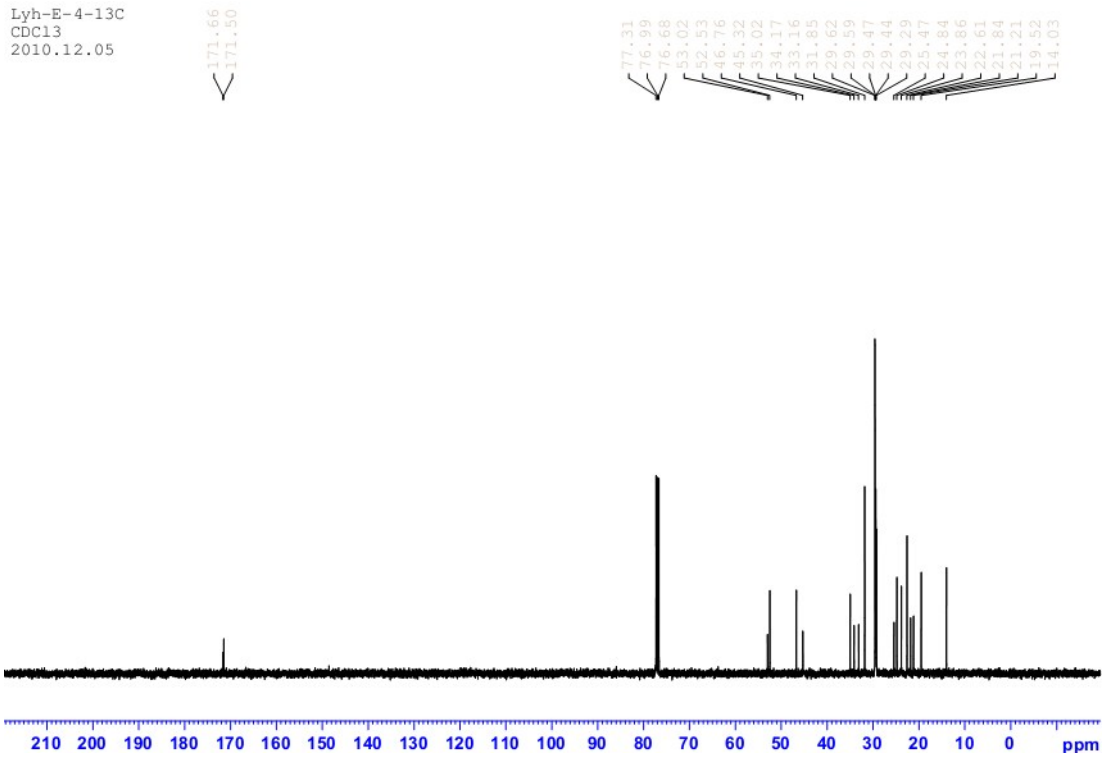




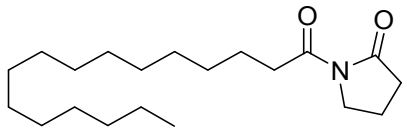
(S)-1-(2-methylpyrrolidin-1-yl)hexadecan-1-one (1f)

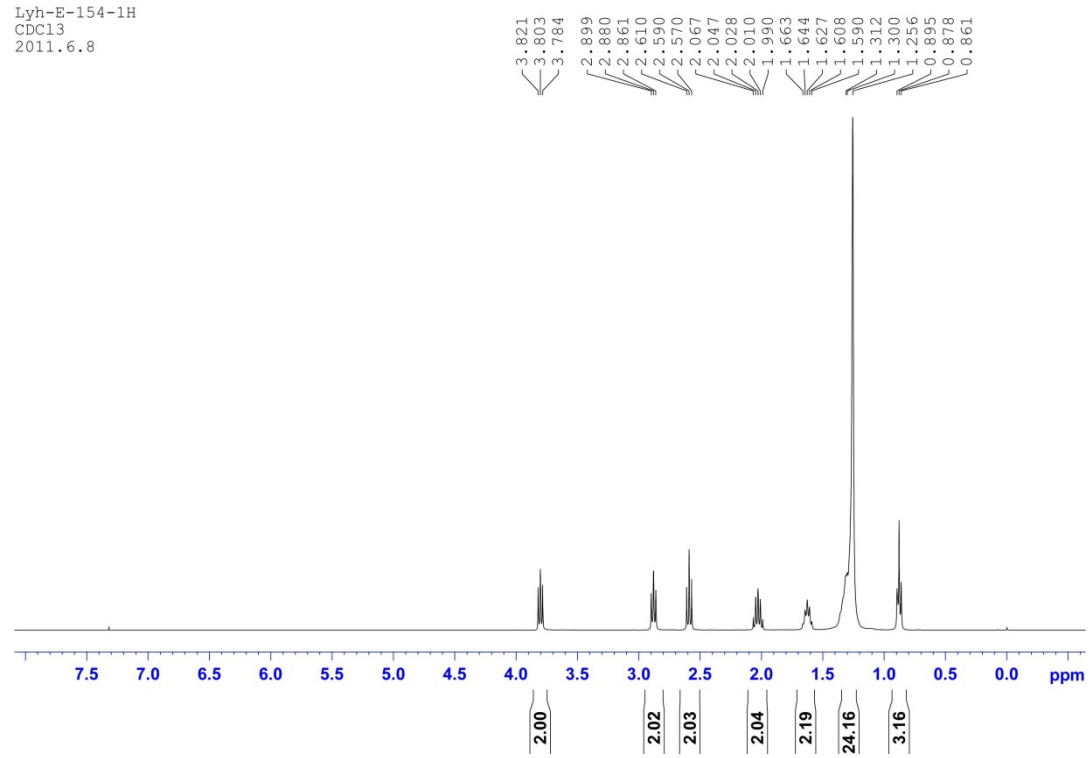


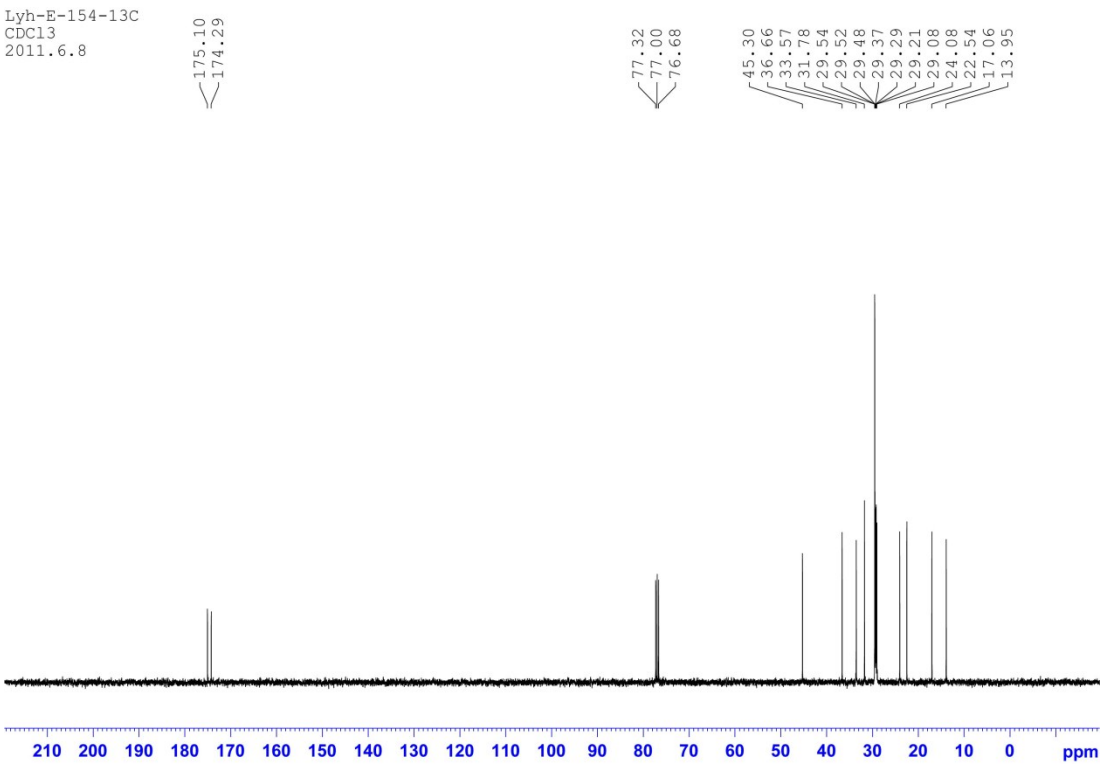




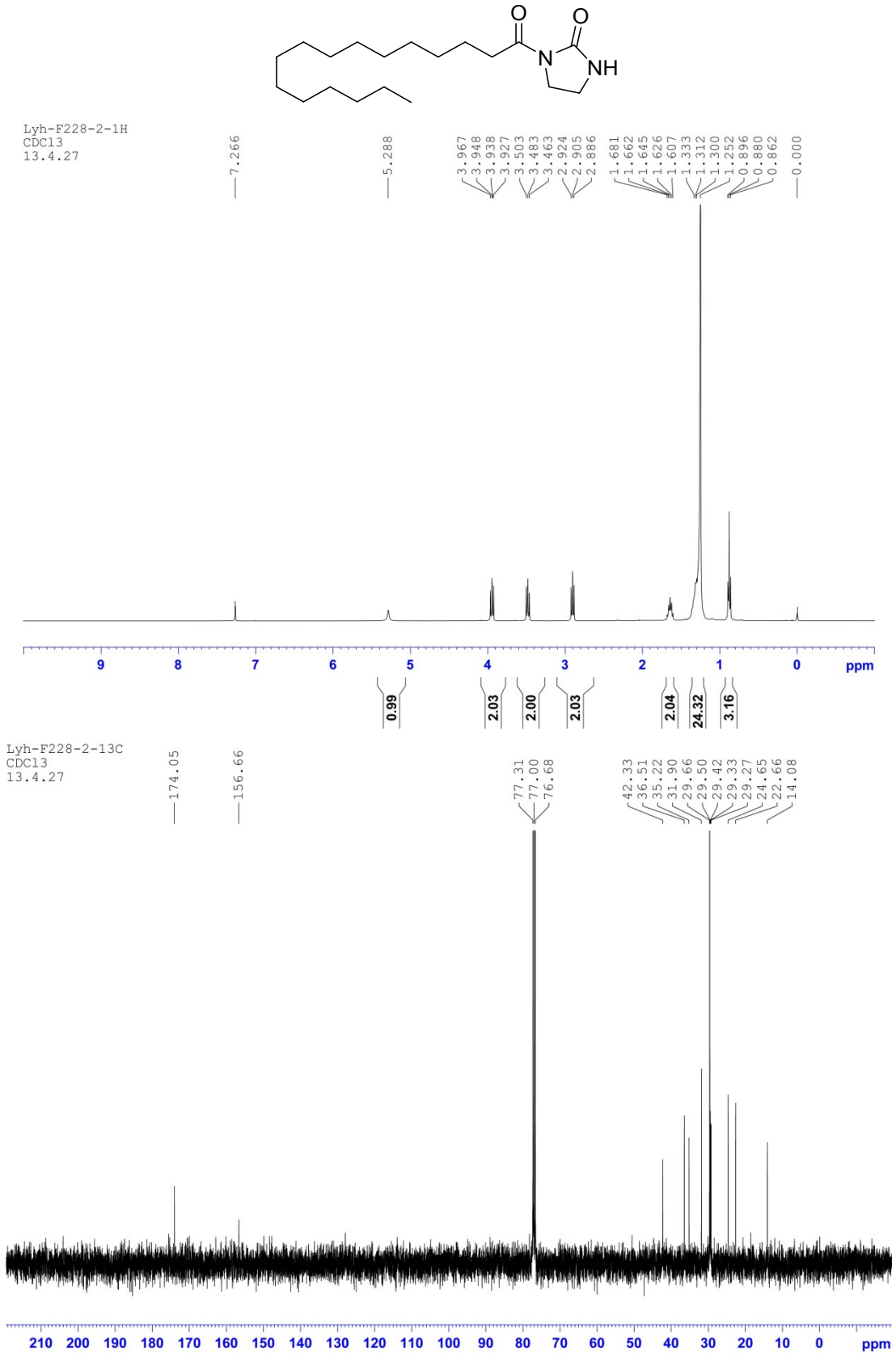
1-palmitoylpyrrolidin-2-one (1g)



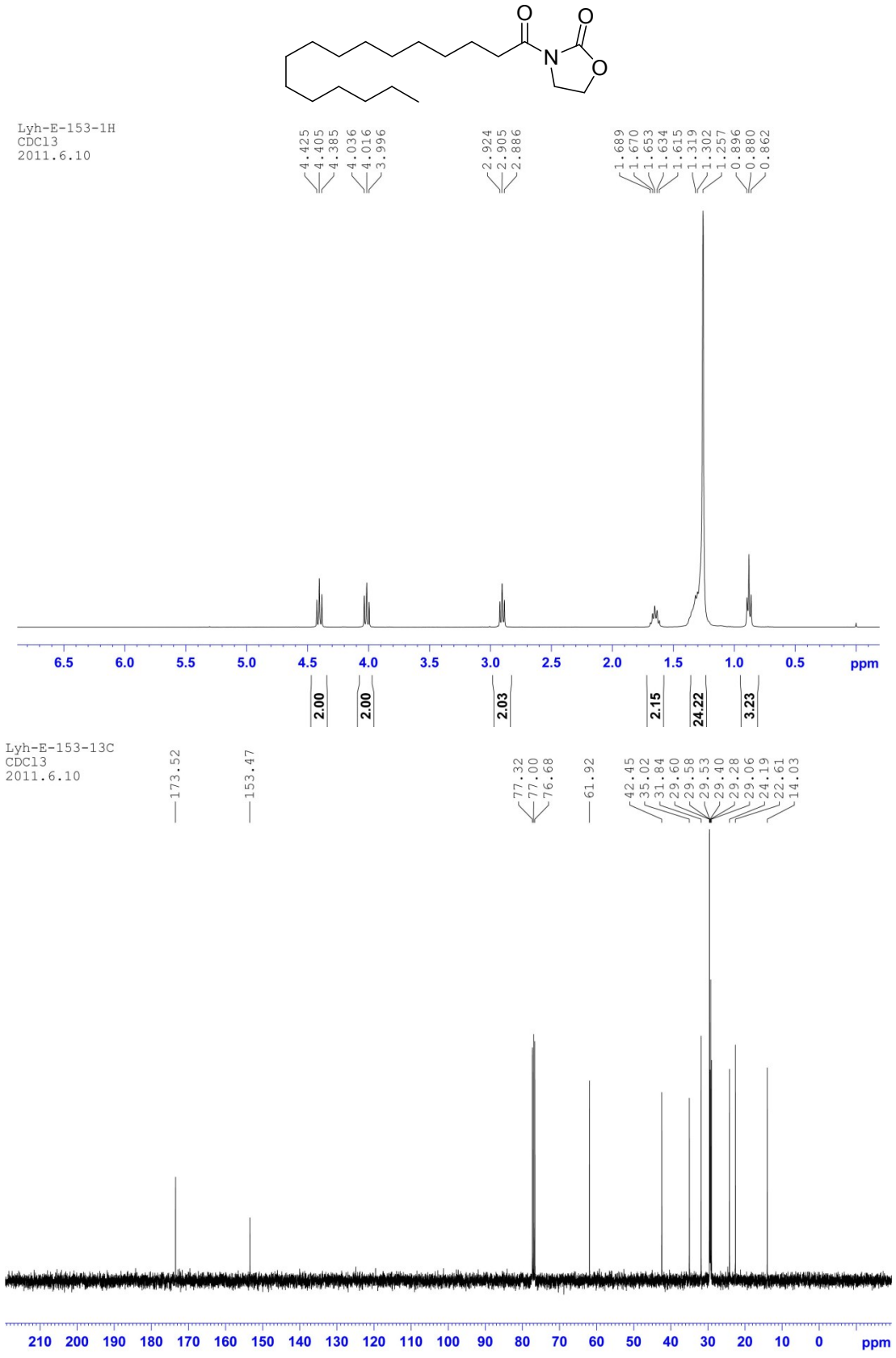




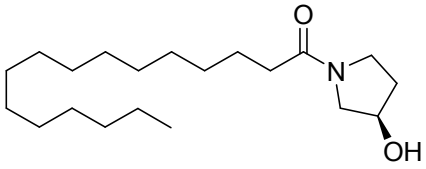
1-palmitoylimidazolidin-2-one (1h)

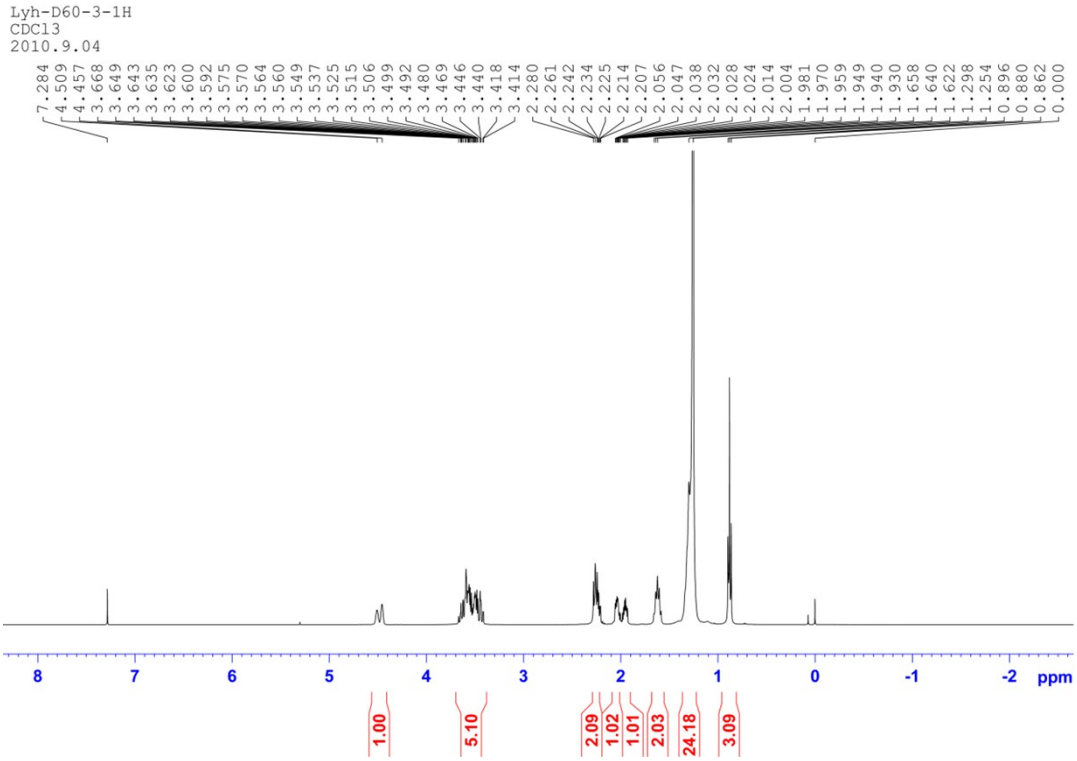


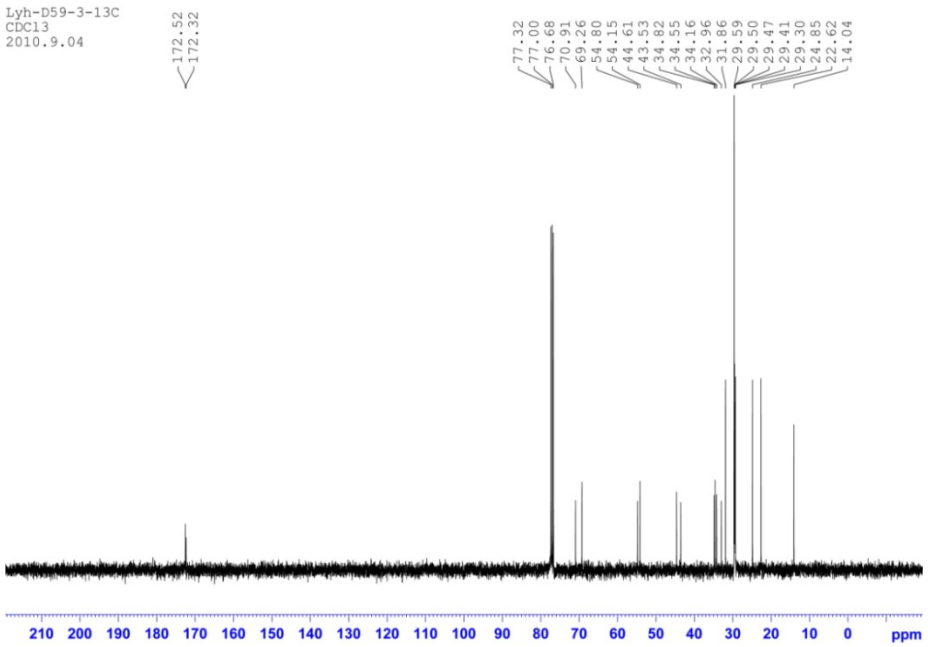
3-palmitoyloxazolidin-2-one (1i)



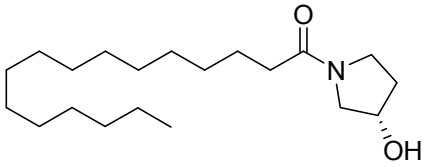
(R)-1-(3-hydroxypyrrolidin-1-yl)hexadecan-1-one (1j)

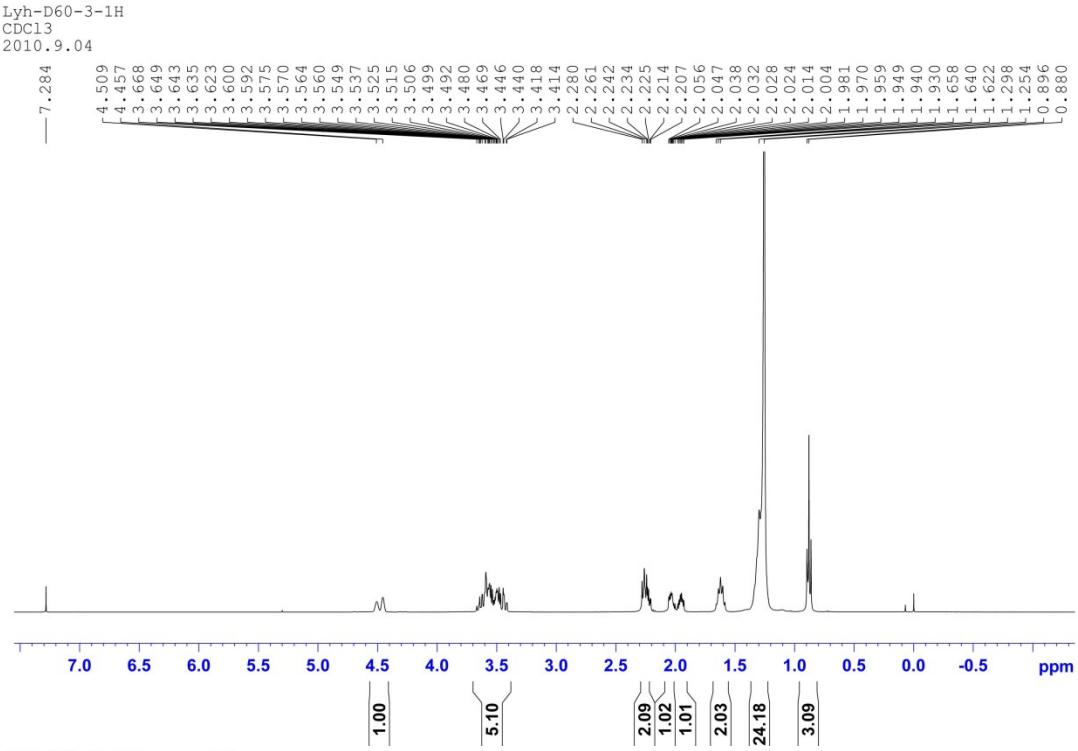


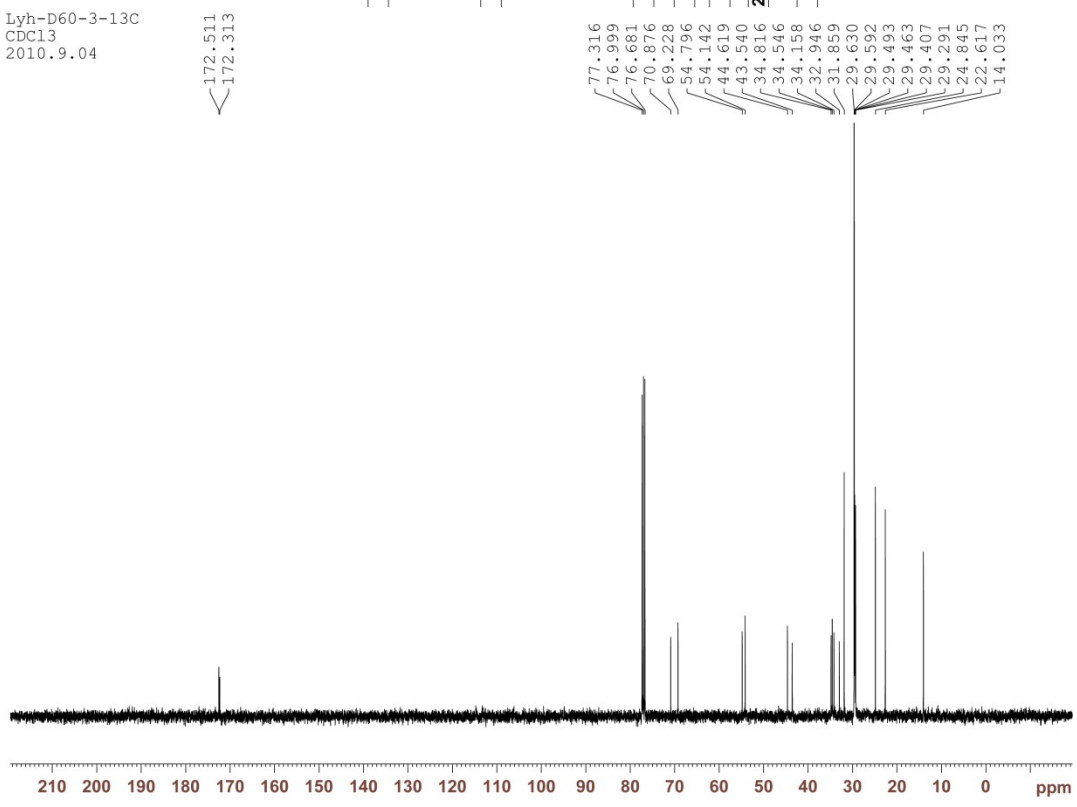




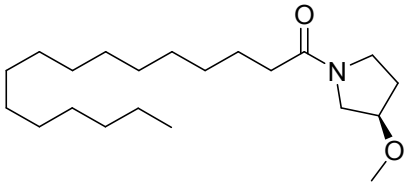
(S)-1-(3-hydroxypyrrolidin-1-yl)hexadecan-1-one (1k)

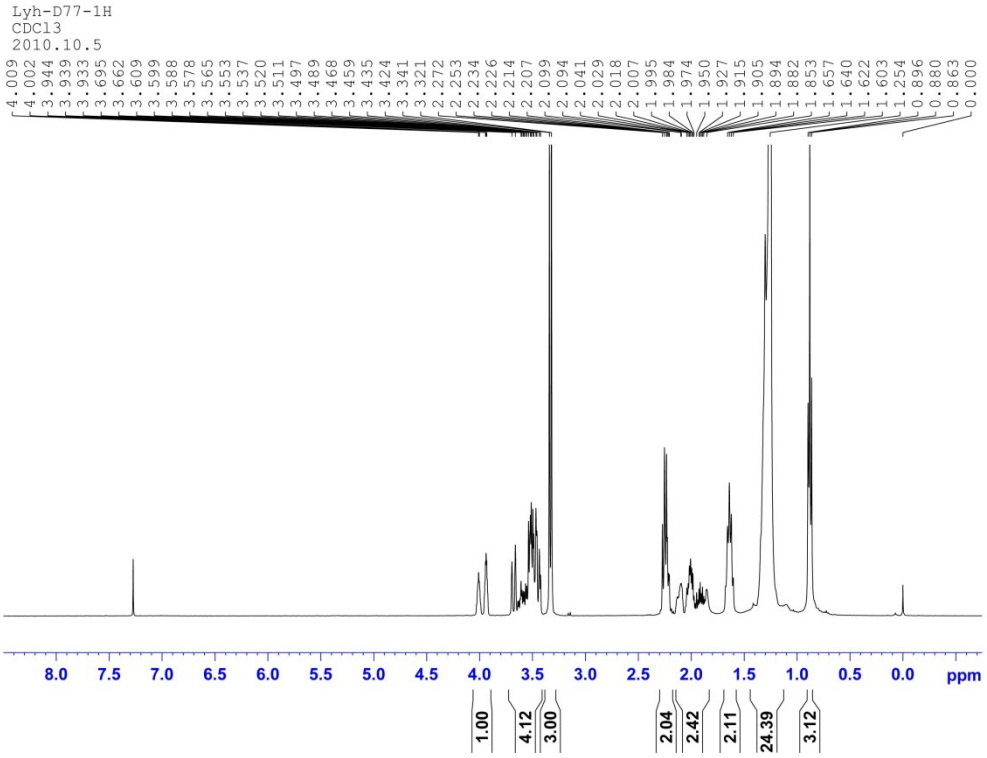


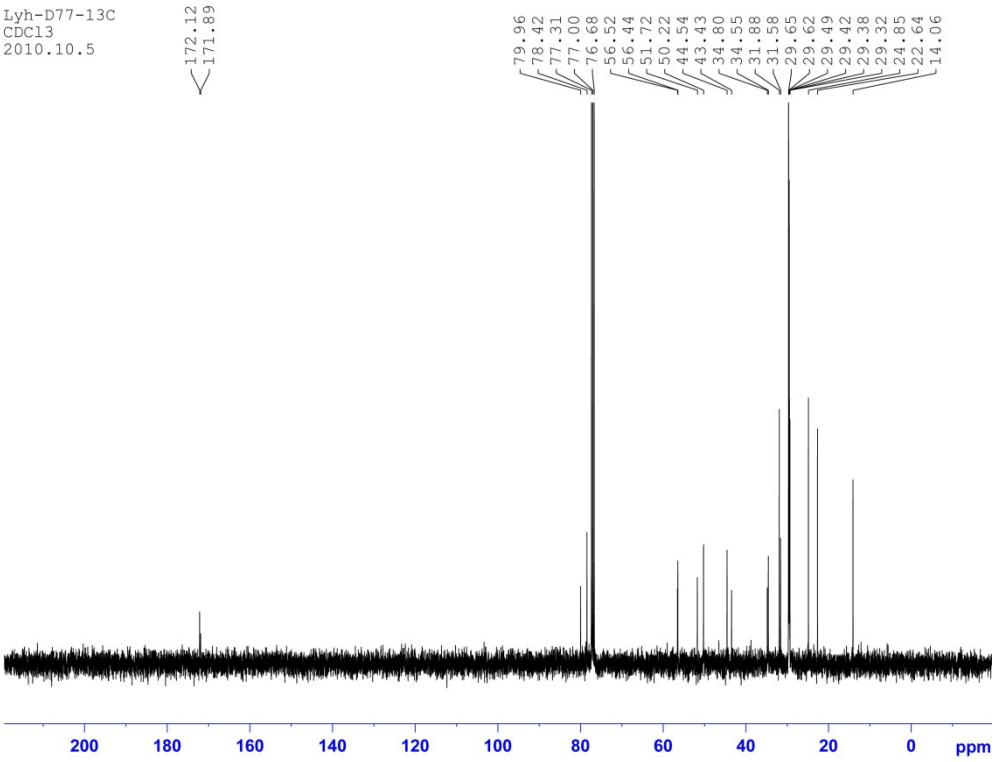




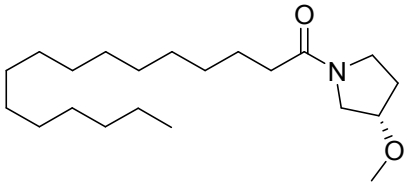
(R)-1-(3-methoxypyrrolidin-1-yl)hexadecan-1-one (1l)

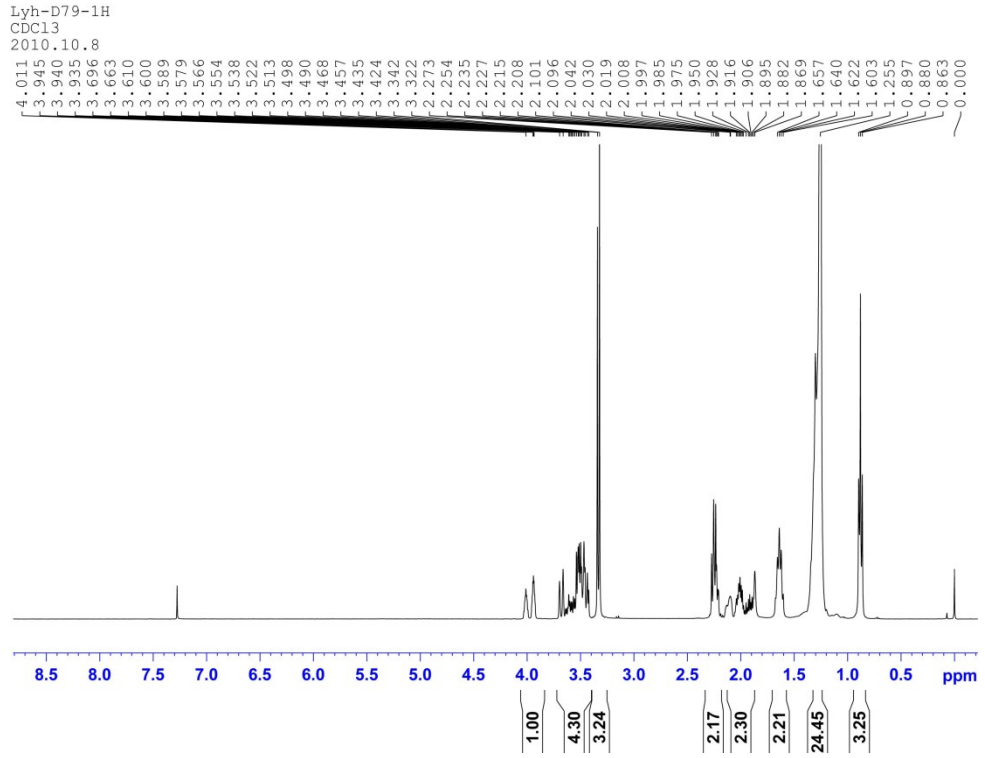


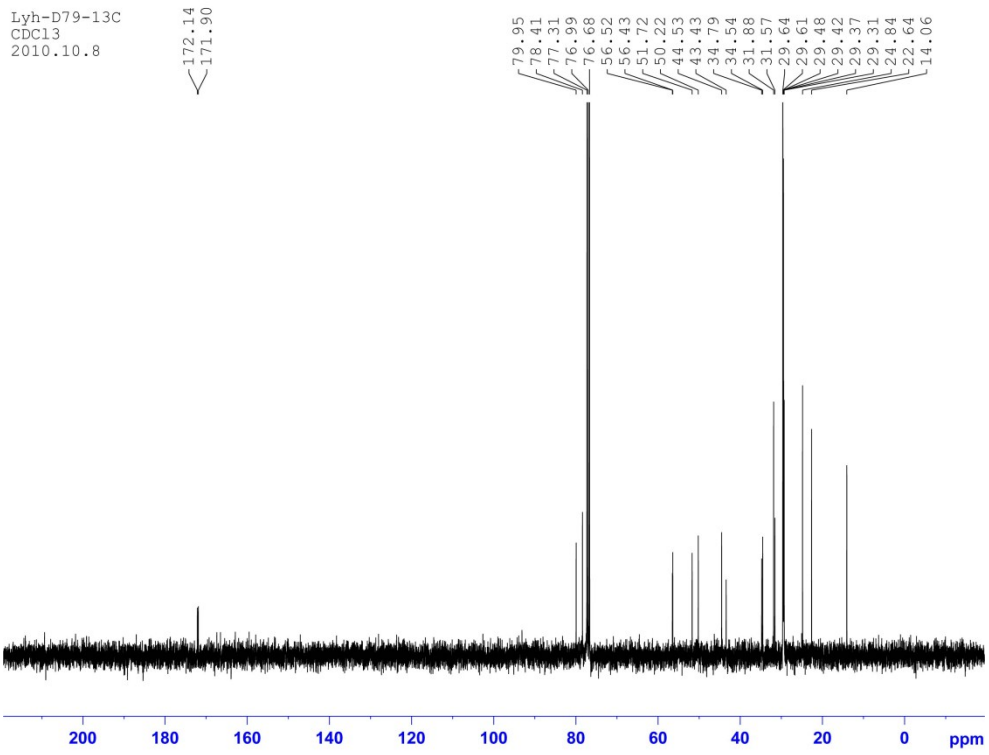




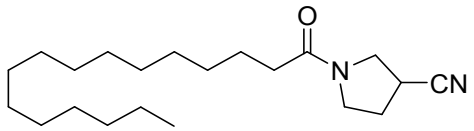
(S)-1-(3-methoxypyrrolidin-1-yl)hexadecan-1-one (1m)

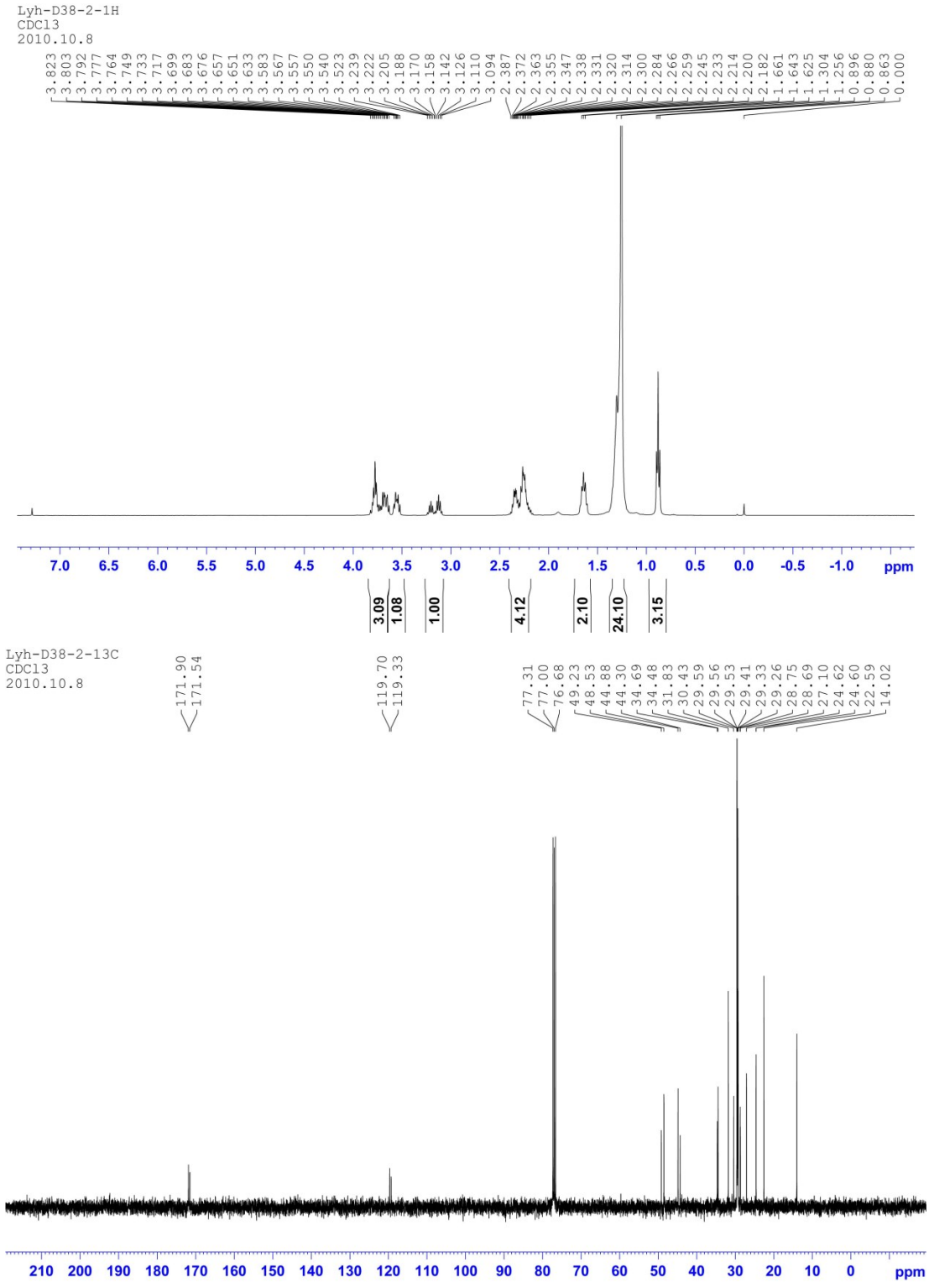




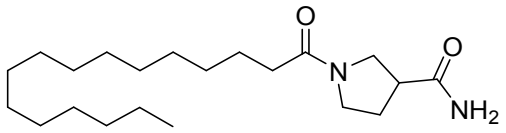


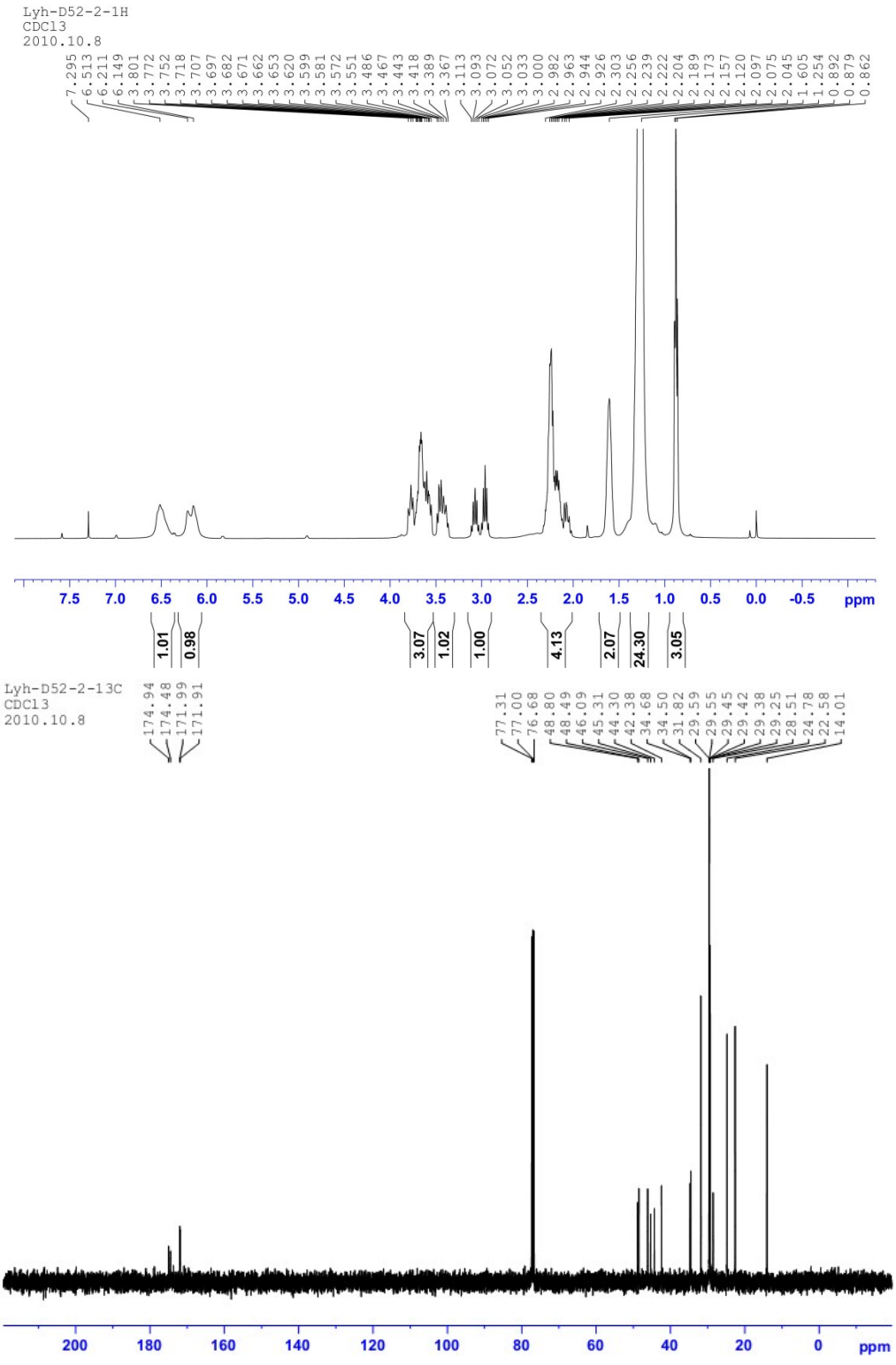
1-palmitoylpyrrolidine-3-carbonitrile (1n)



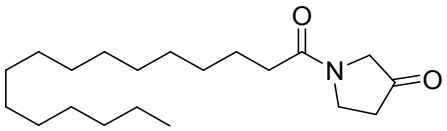


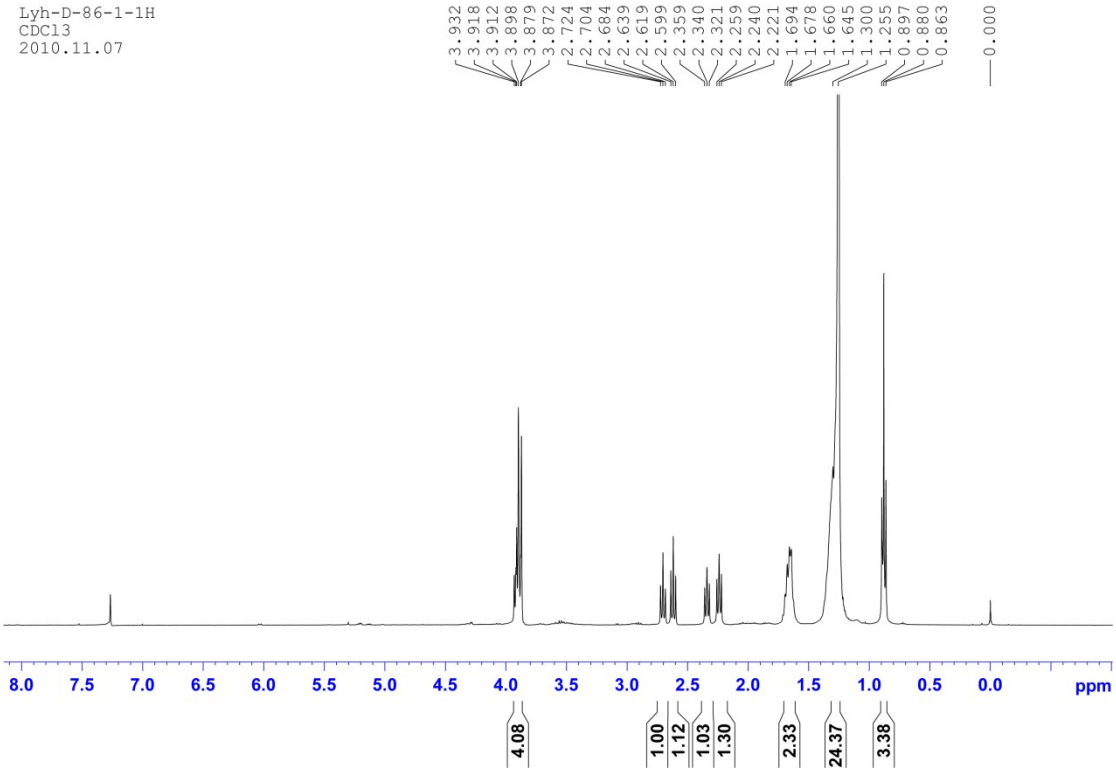
1-palmitoylpyrrolidine-3-carboxamide (1o)

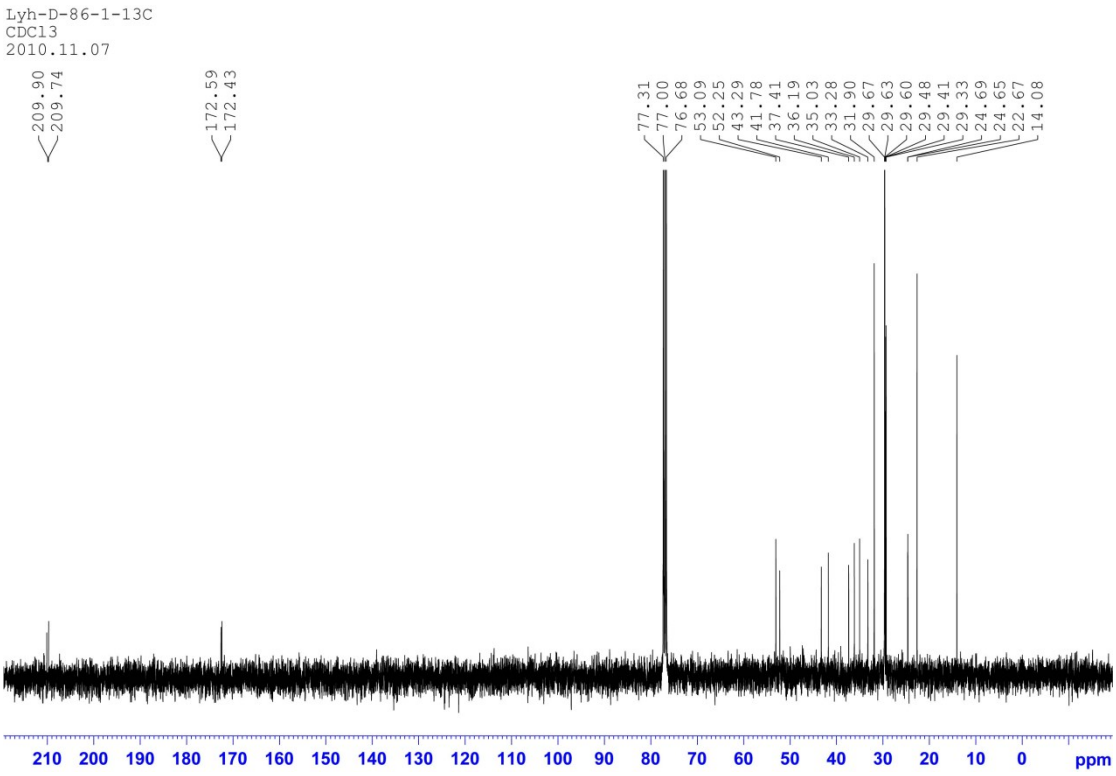




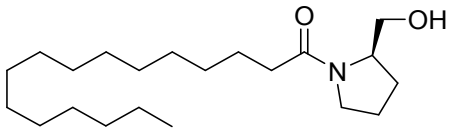
1-palmitoylpyrrolidin-3-one (1p)

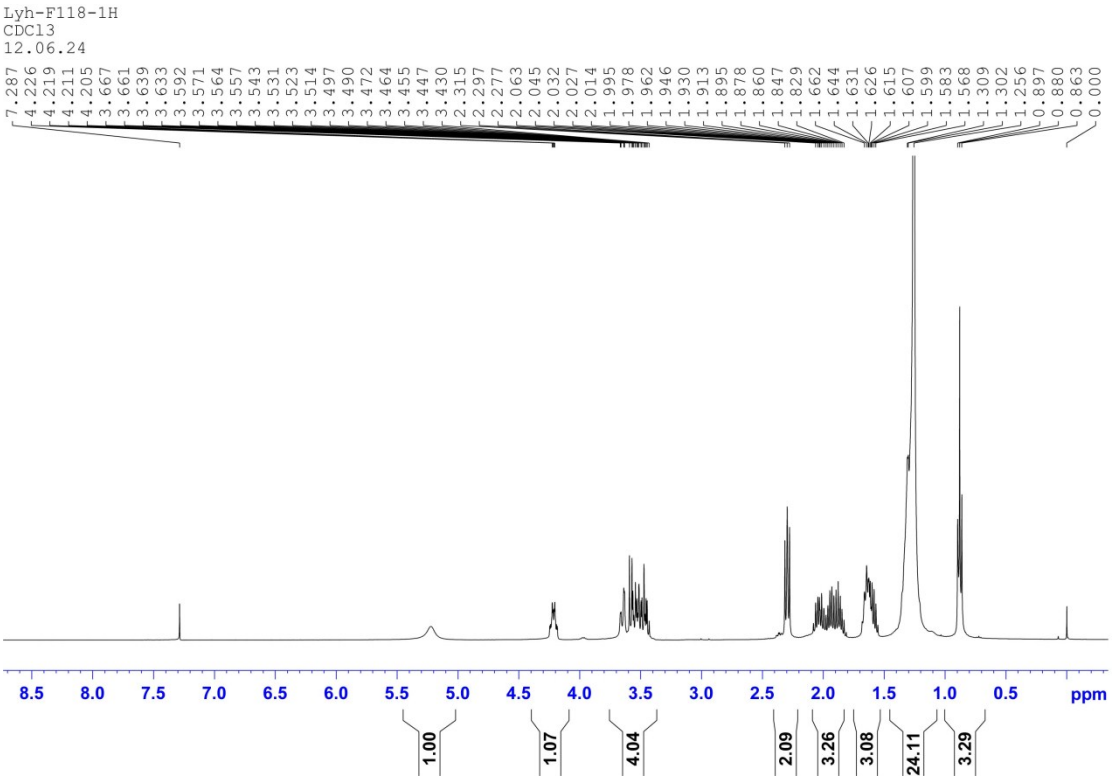


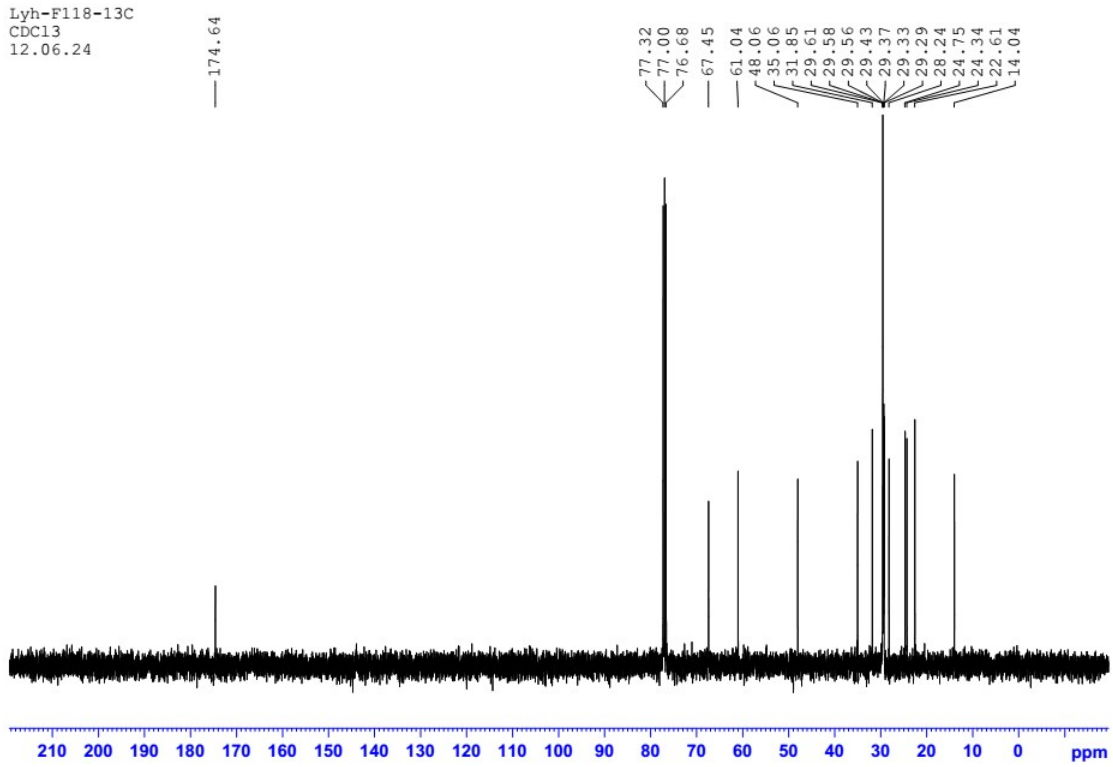




(R)–1–(2–(hydroxymethyl)pyrrolidin–1–yl)hexadecan–1–one (1q)







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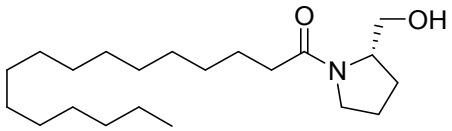
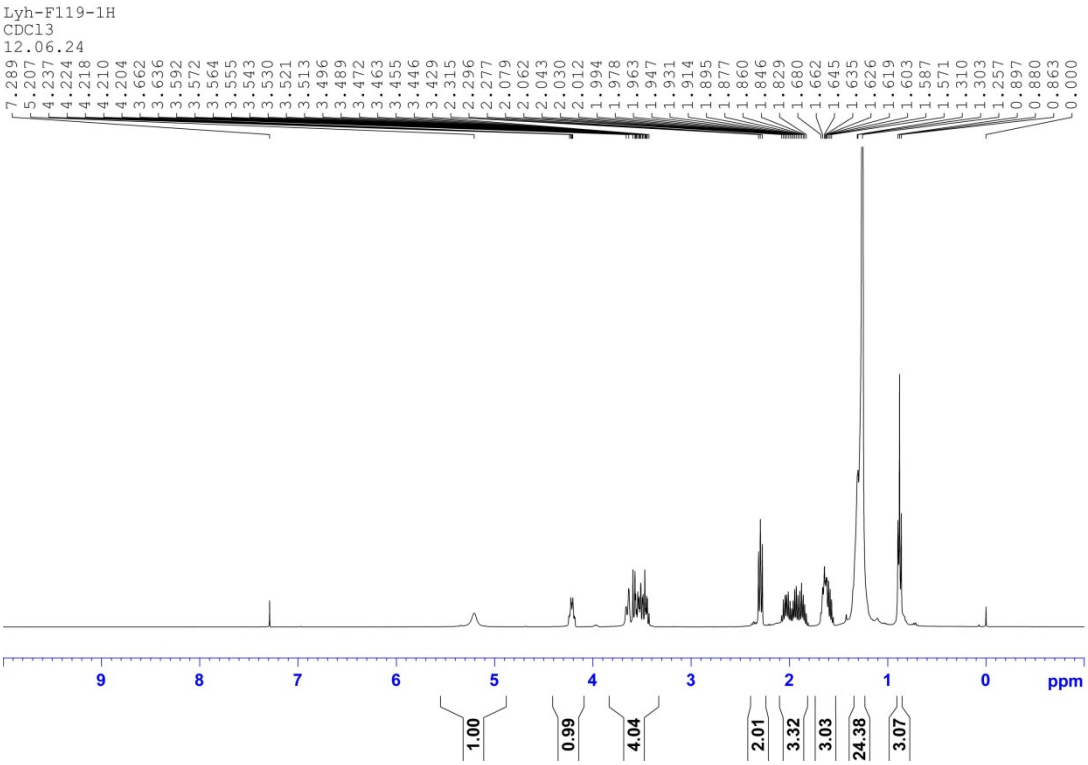
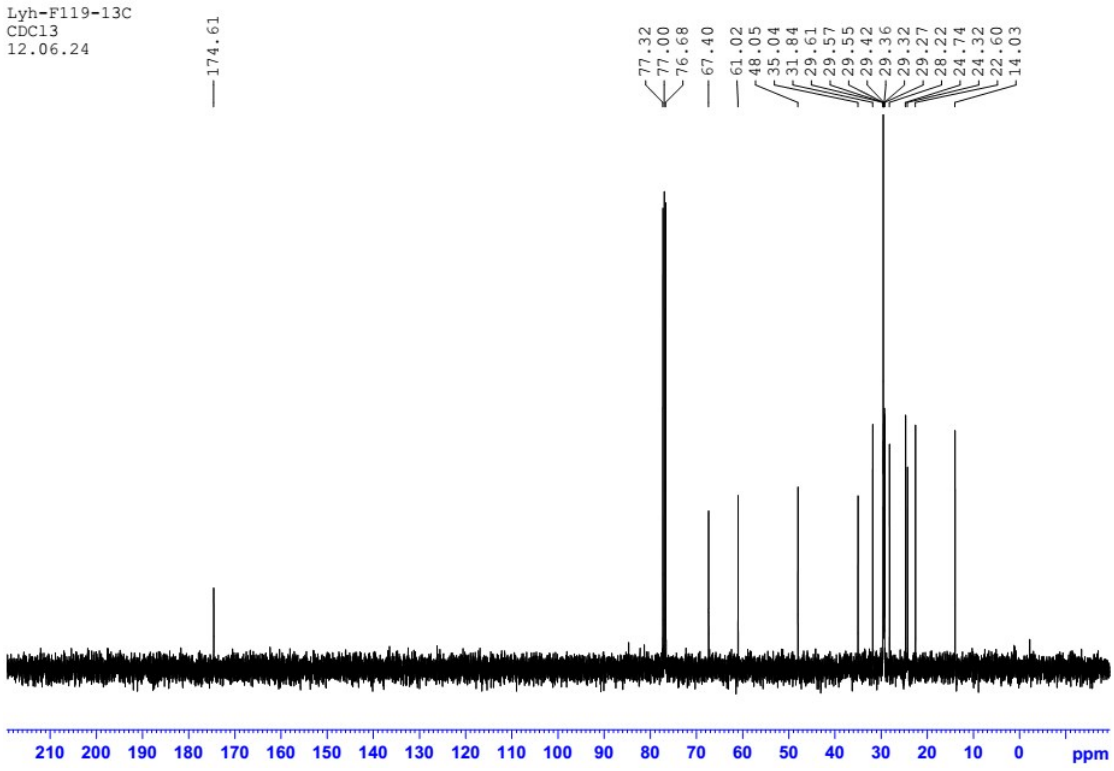
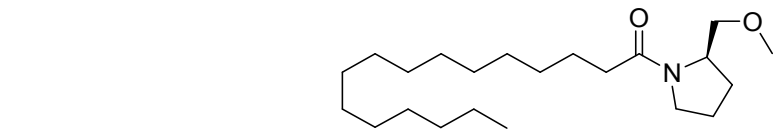
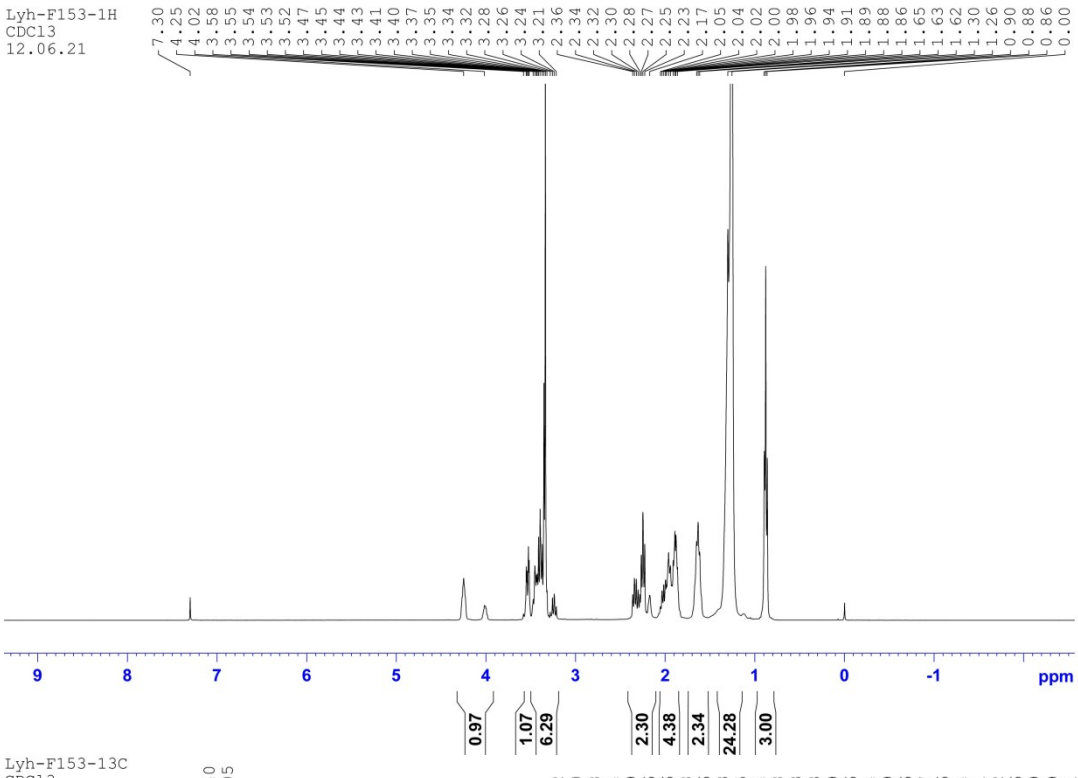


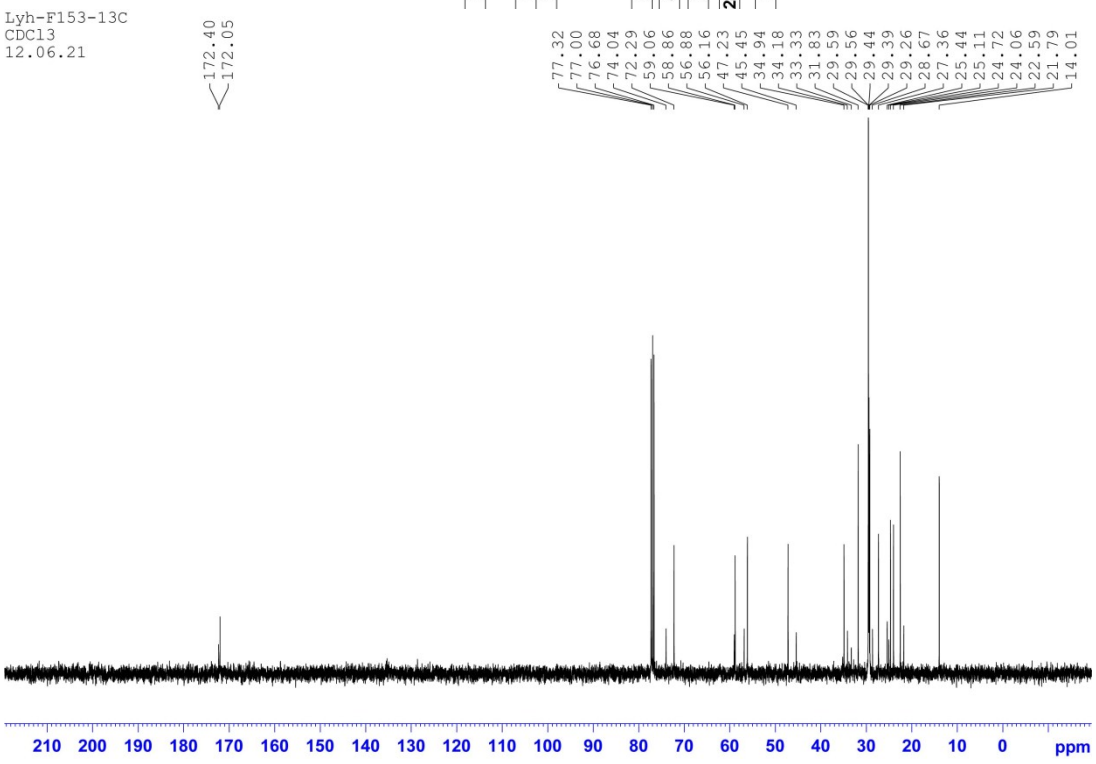




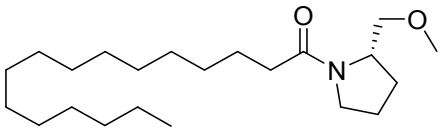
(R)–1–(2–(methoxymethyl)pyrrolidin–1–yl)hexadecan–1–one (1s)

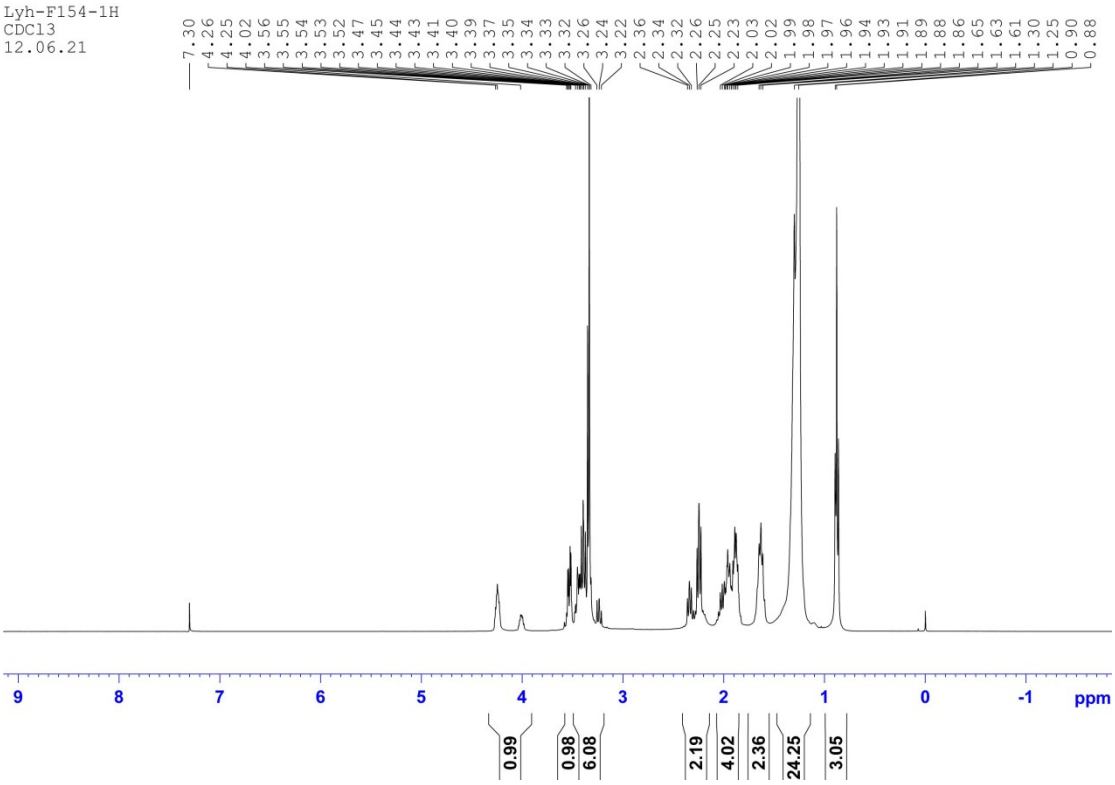


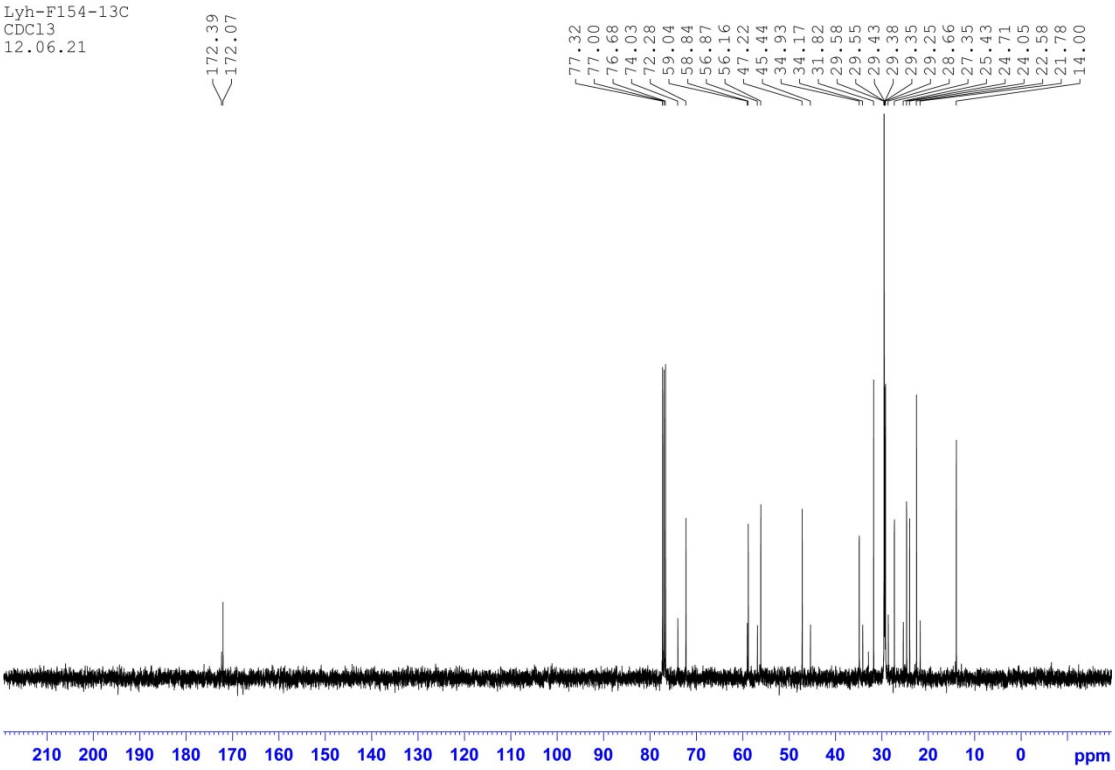




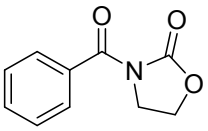
(S)–1–(2–(methoxymethyl)pyrrolidin–1–yl)hexadecan–1–one (1t)

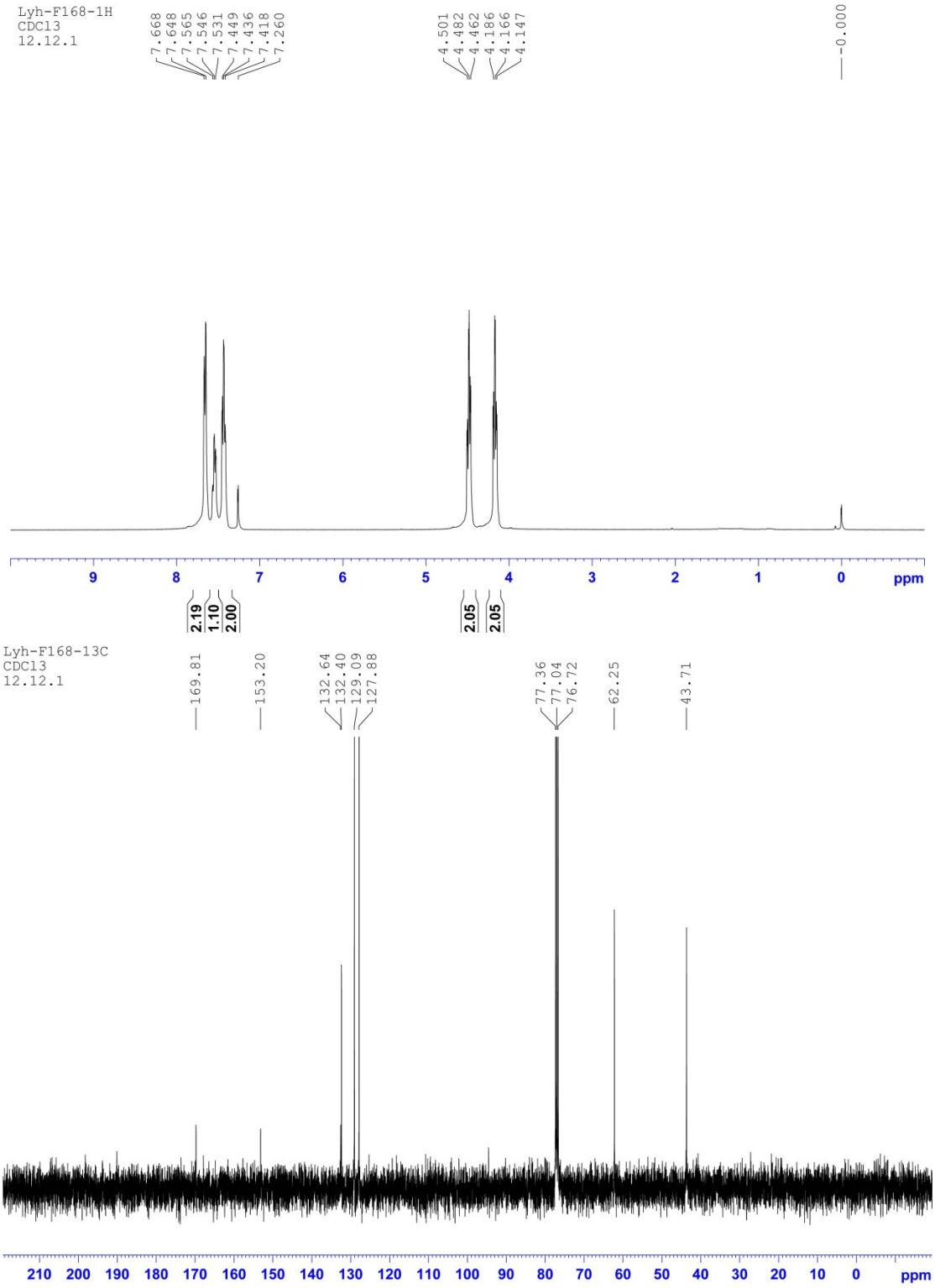




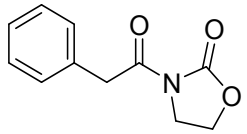


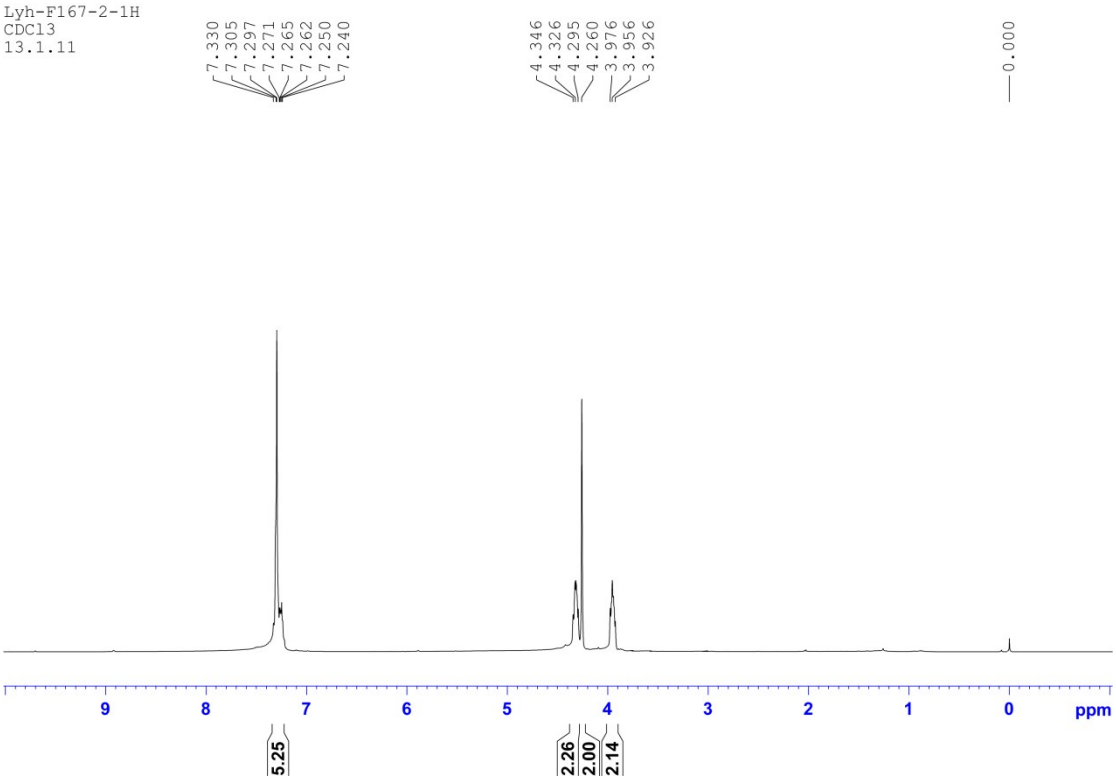
3-benzoyloxazolidin-2-one (2a)

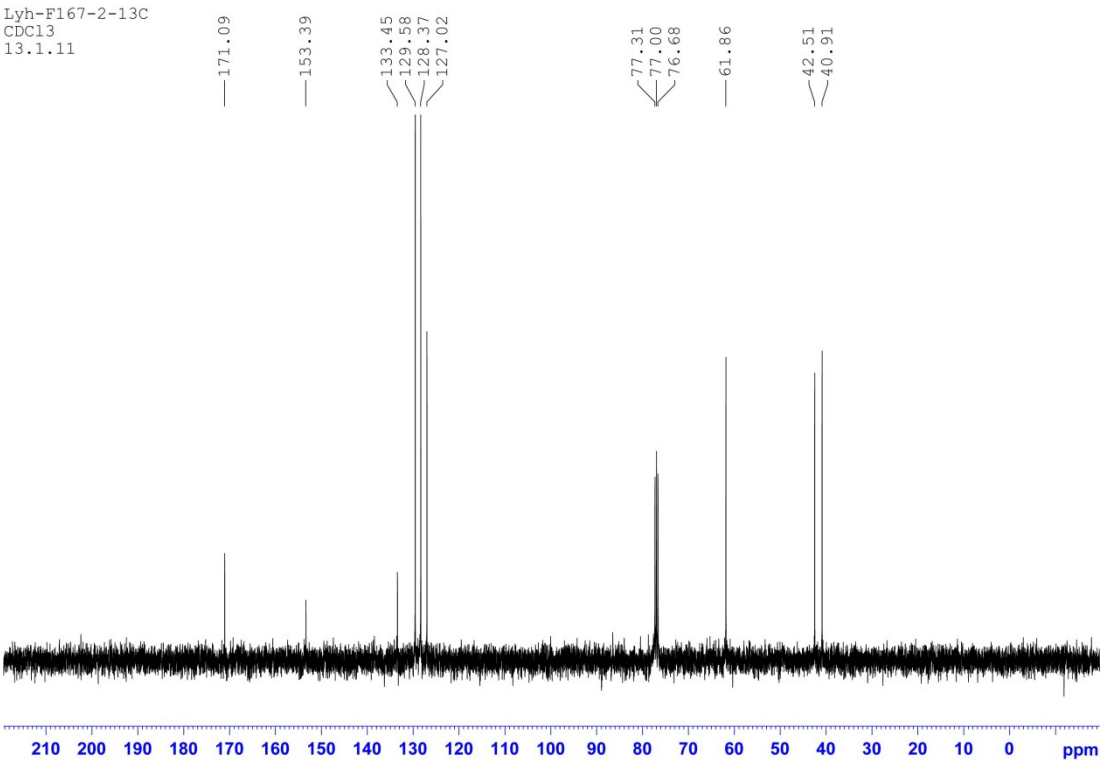




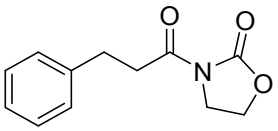
3-(2-phenylacetyl)oxazolidin-2-one (2b)

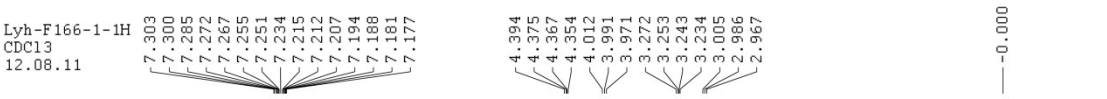


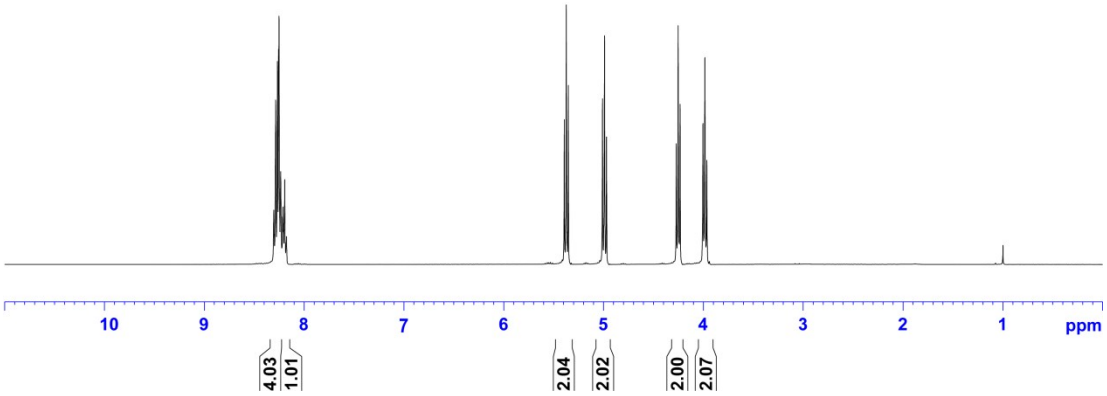


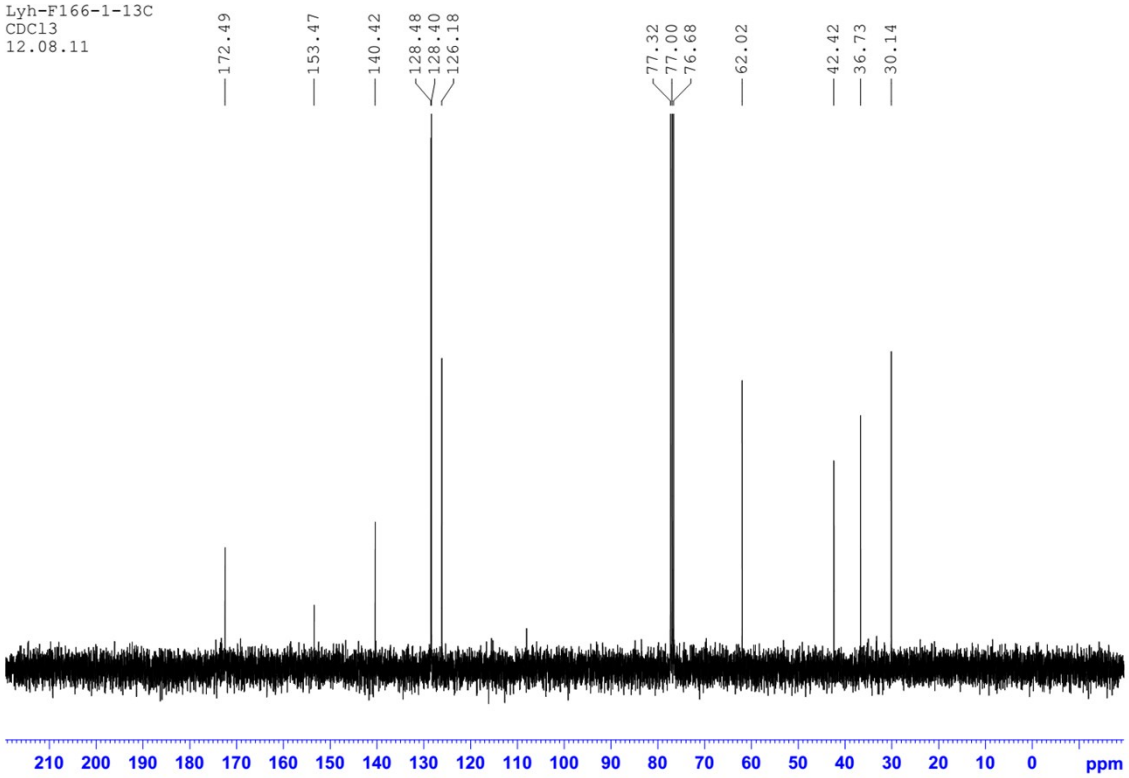


3-(3-phenylpropanoyl)oxazolidin-2-one (2c)

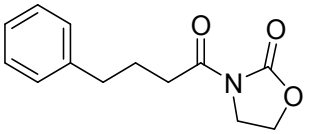


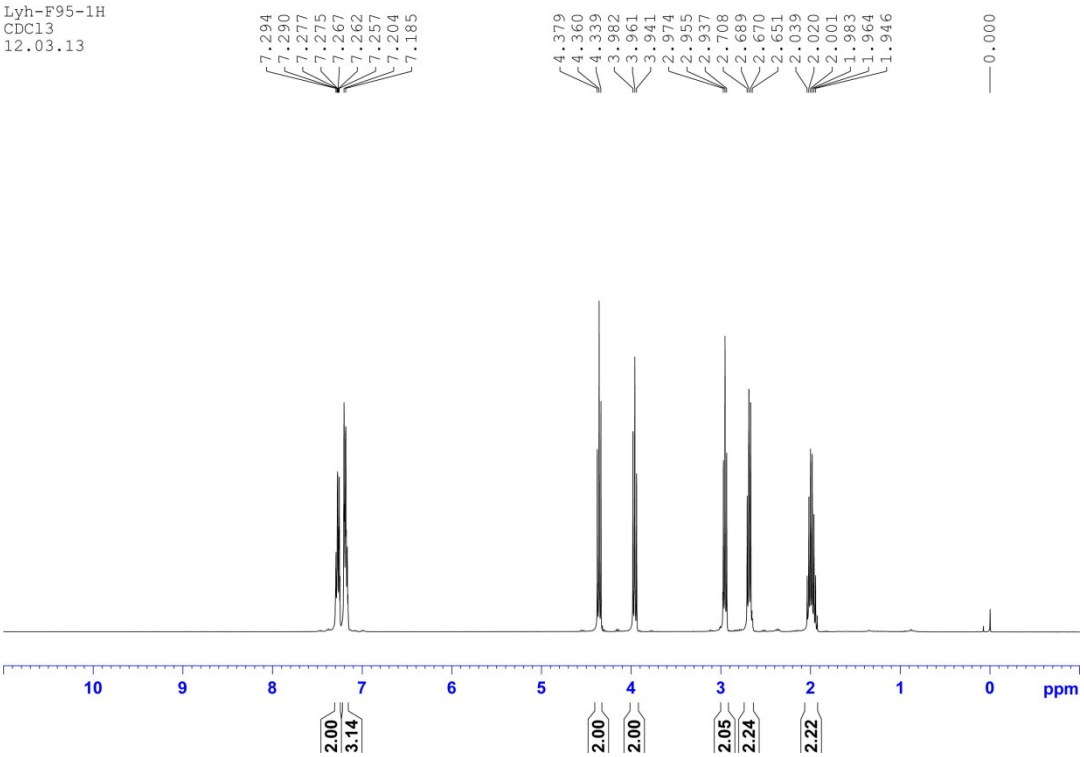


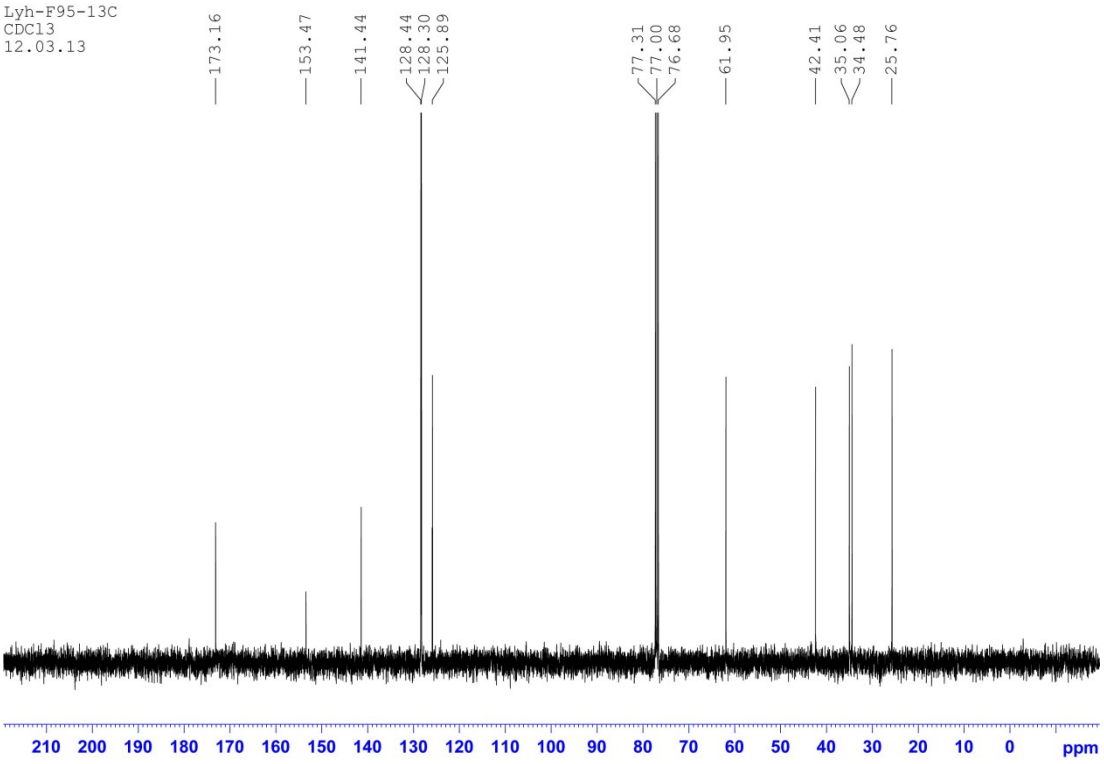




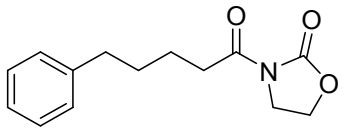
3-(4-phenylbutanoyl)oxazolidin-2-one (2d)

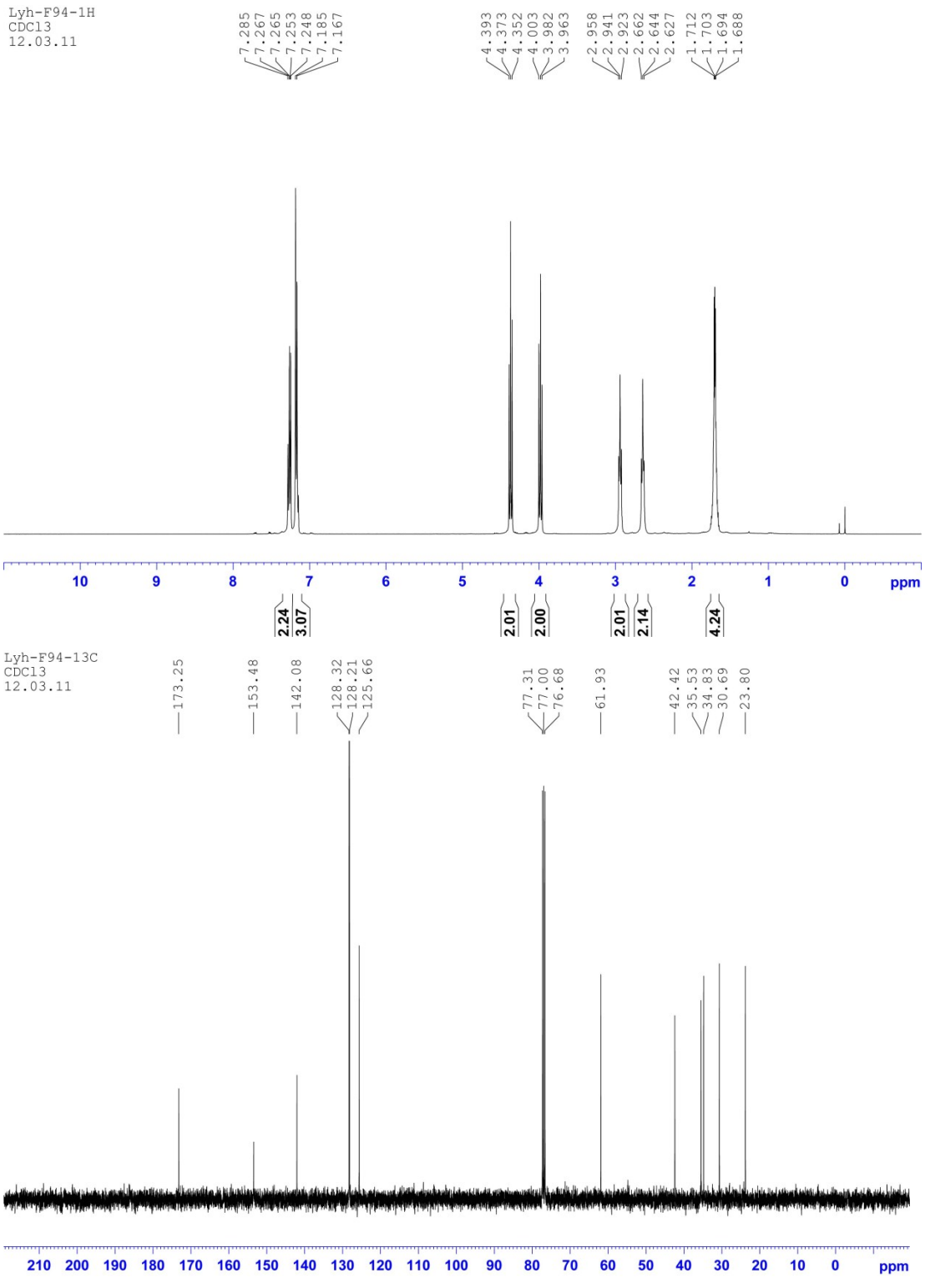




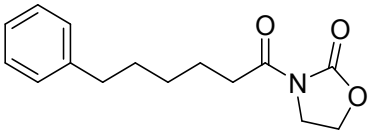


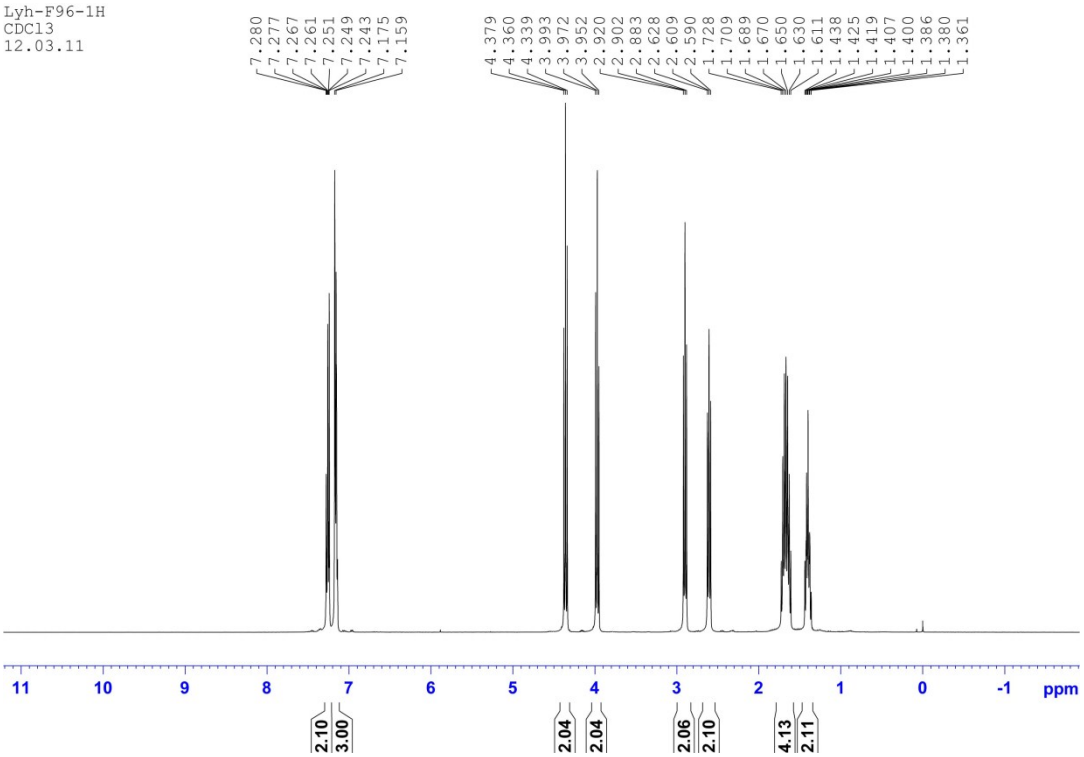
3-(5-phenylpentanoyl)oxazolidin-2-one (2e)

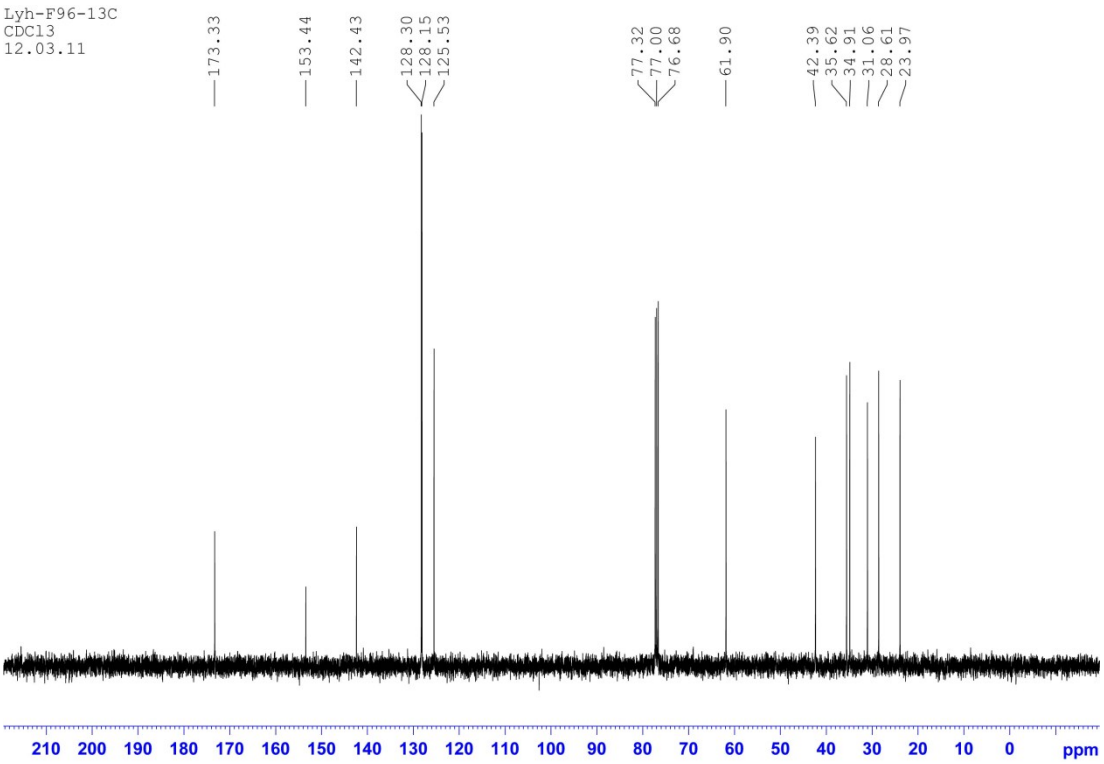




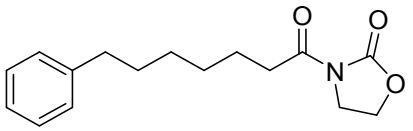
3-(6-phenylhexanoyl)oxazolidin-2-one (2f)

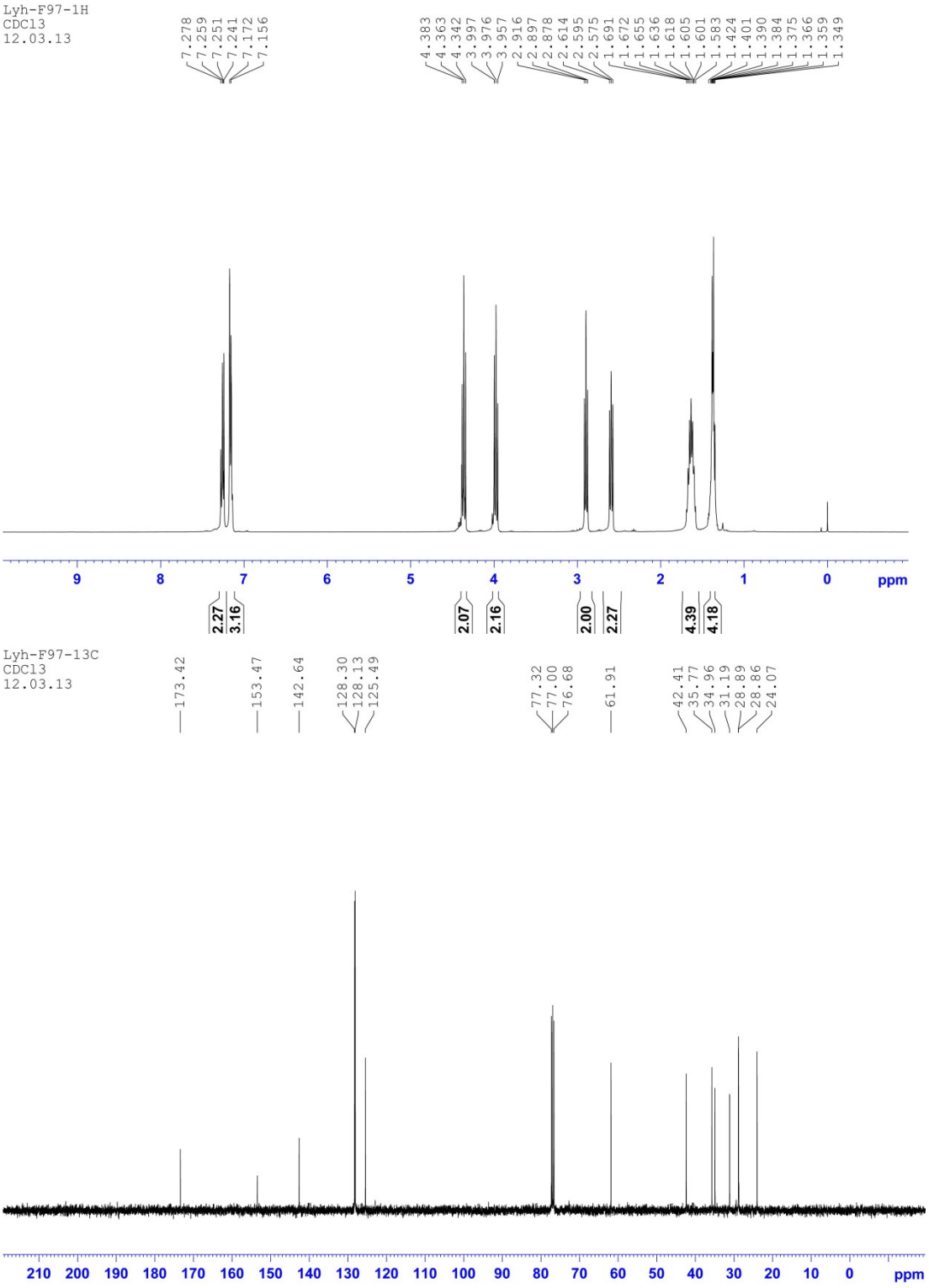




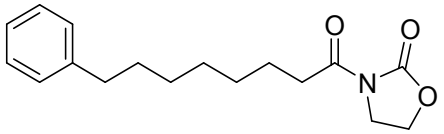


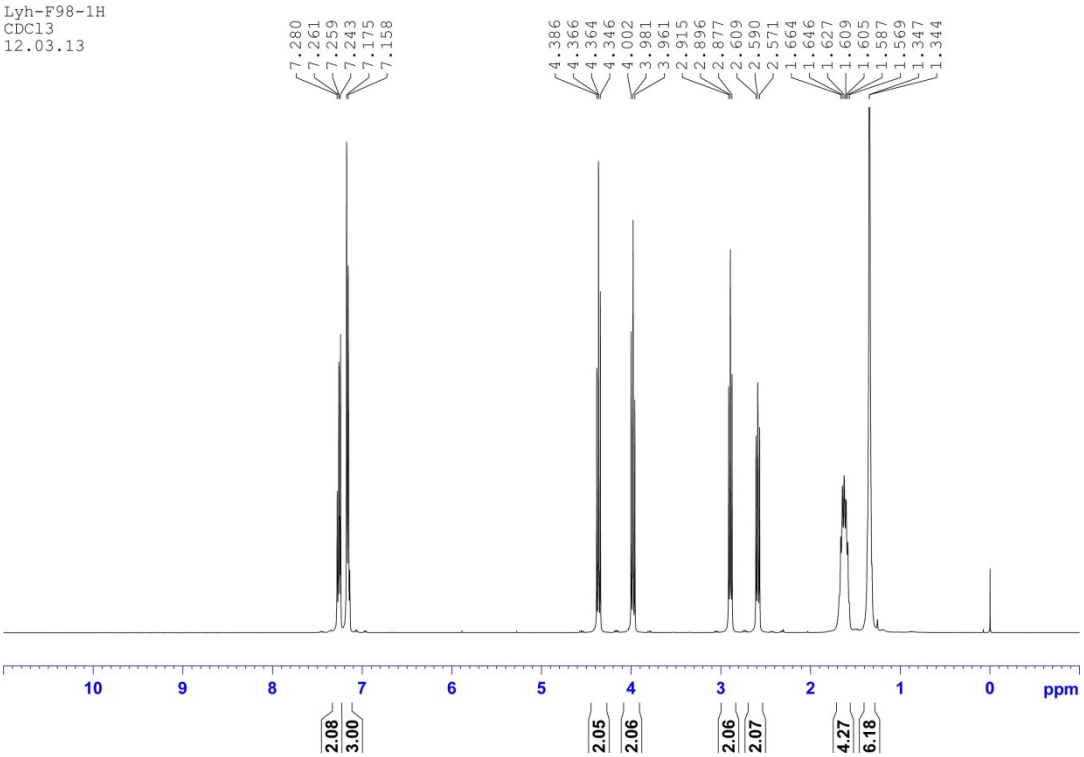
3-(7-phenylheptanoyl)oxazolidin-2-one (2g)

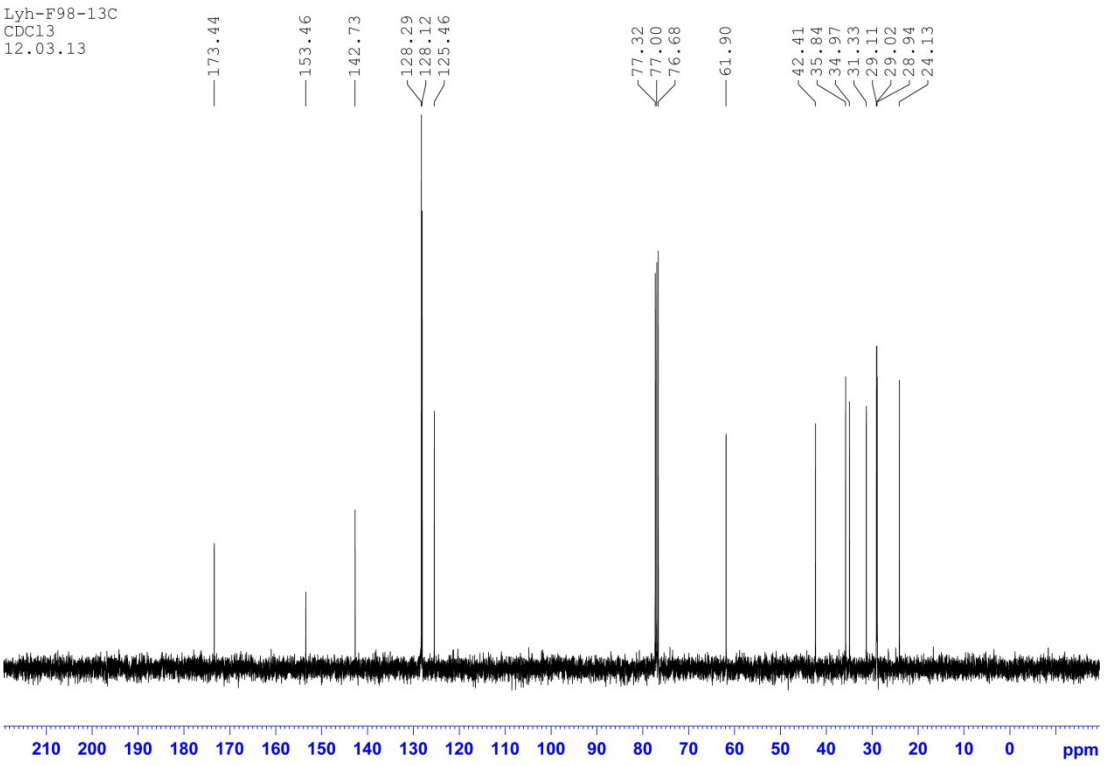




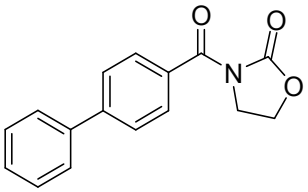
3-(8-phenyloctanoyl)oxazolidin-2-one (2h)

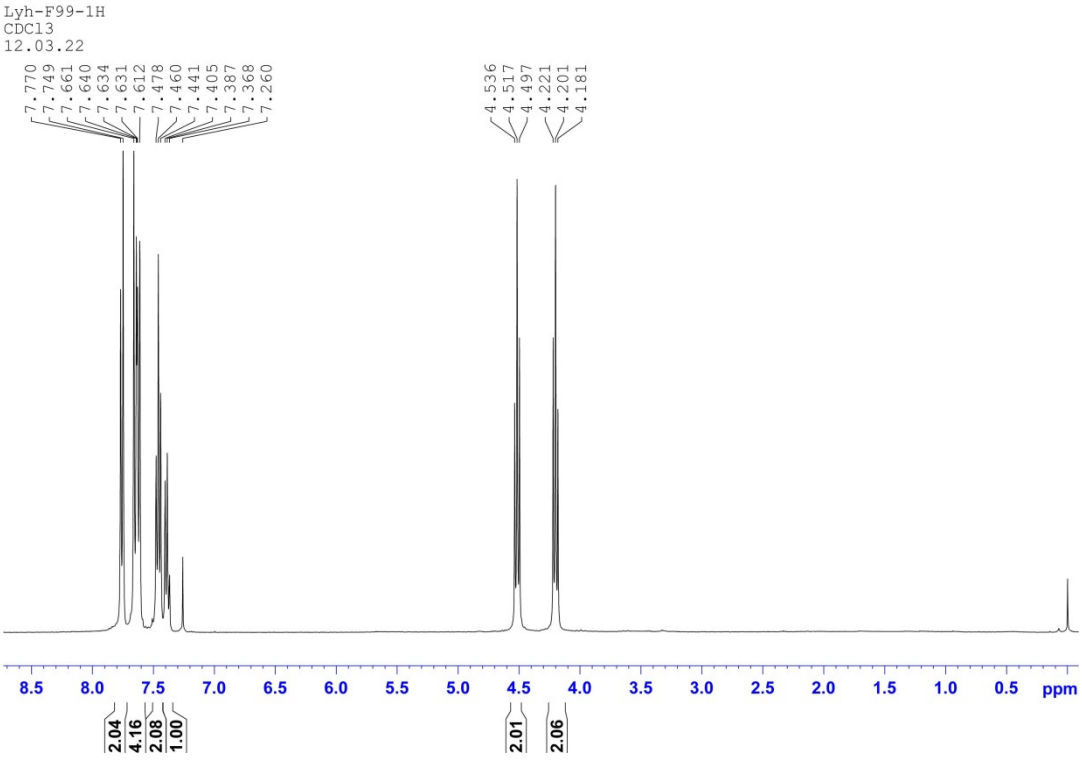


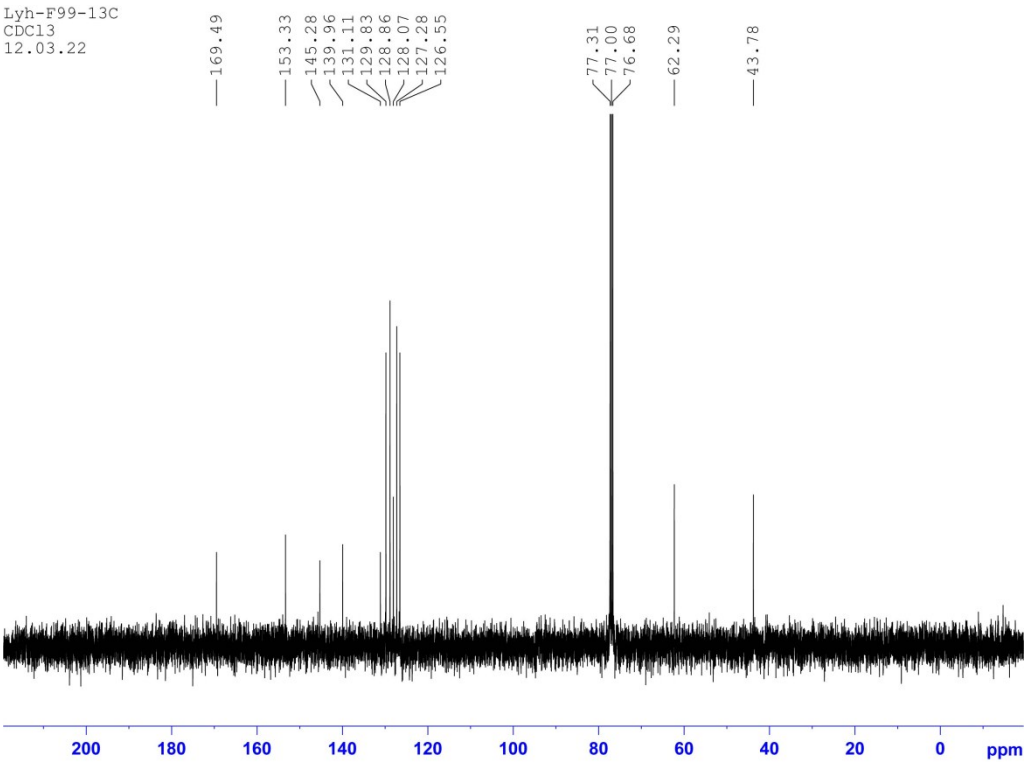




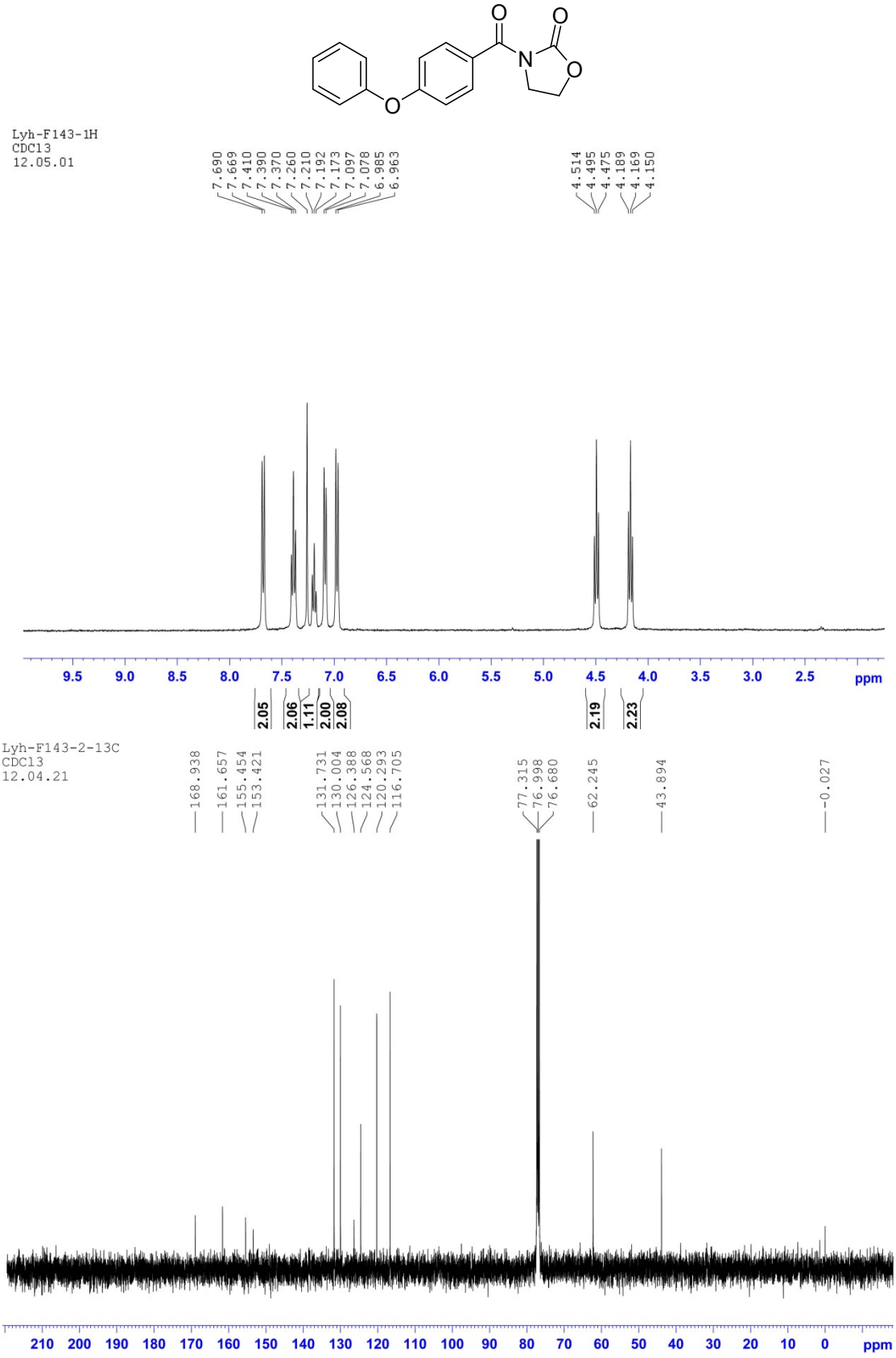
Biphenyl-4-yl-carbonyl oxazolidin-2-one (3a)



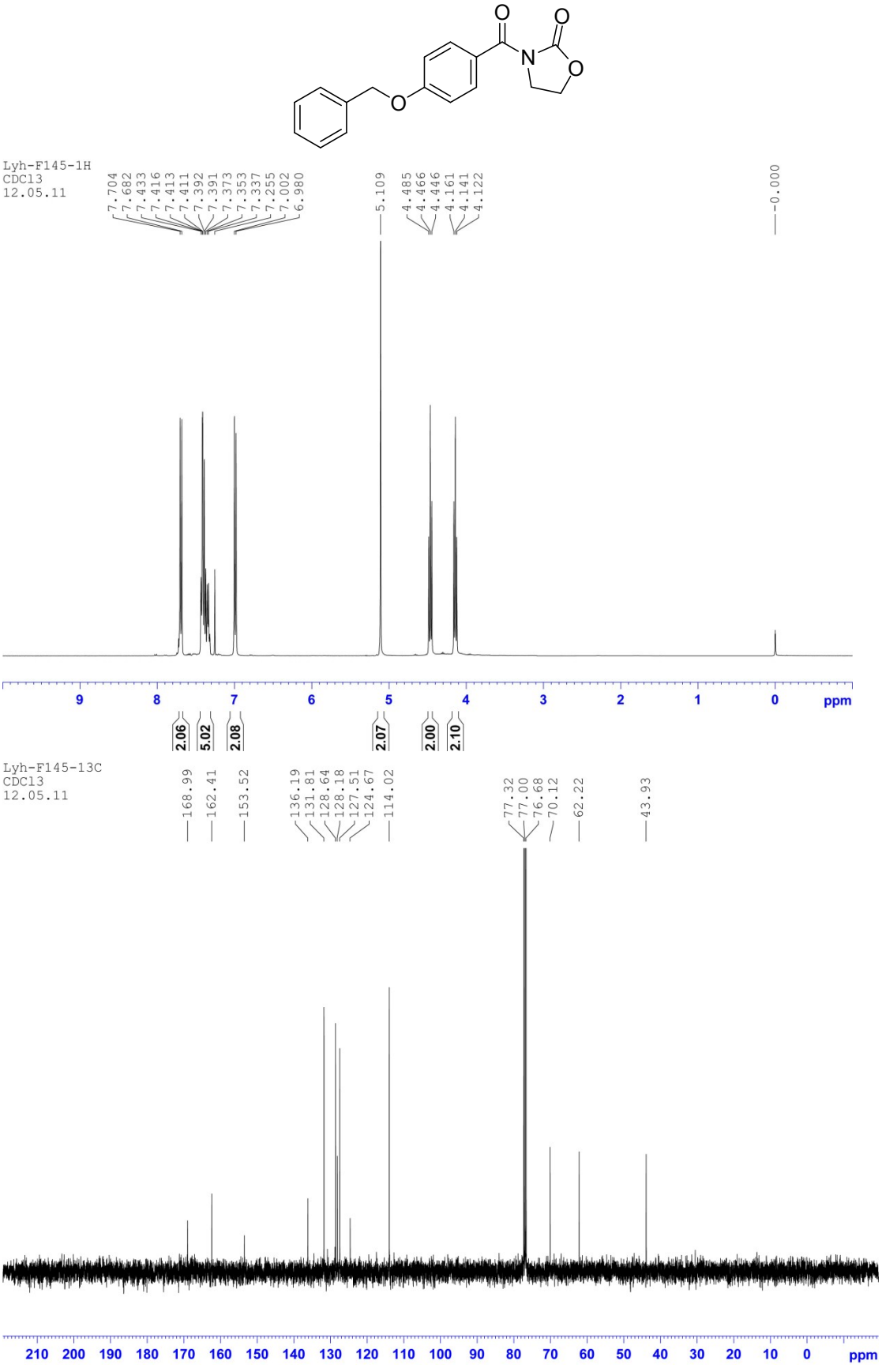




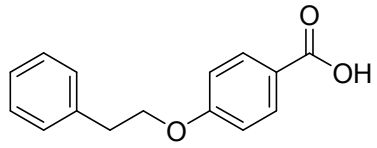
3-(4-phenoxybenzoyl)oxazolidin-2-one (3b)

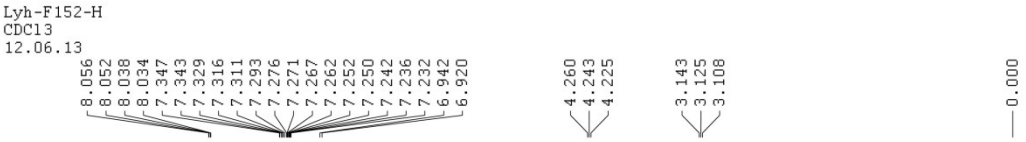


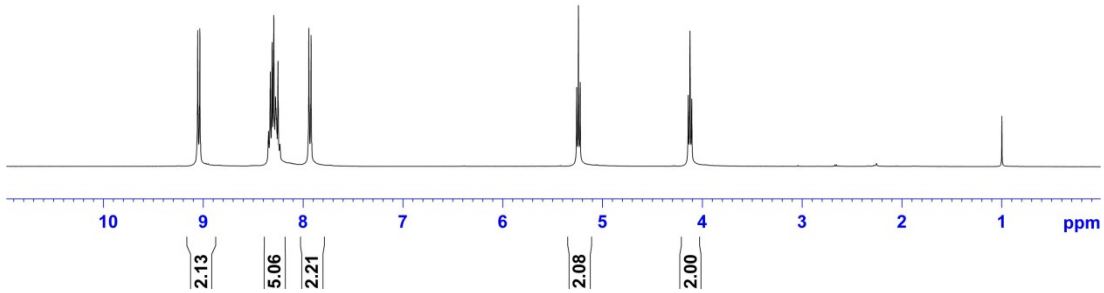
3-(4-(benzyloxy)benzoyl)oxazolidin-2-one (3c)

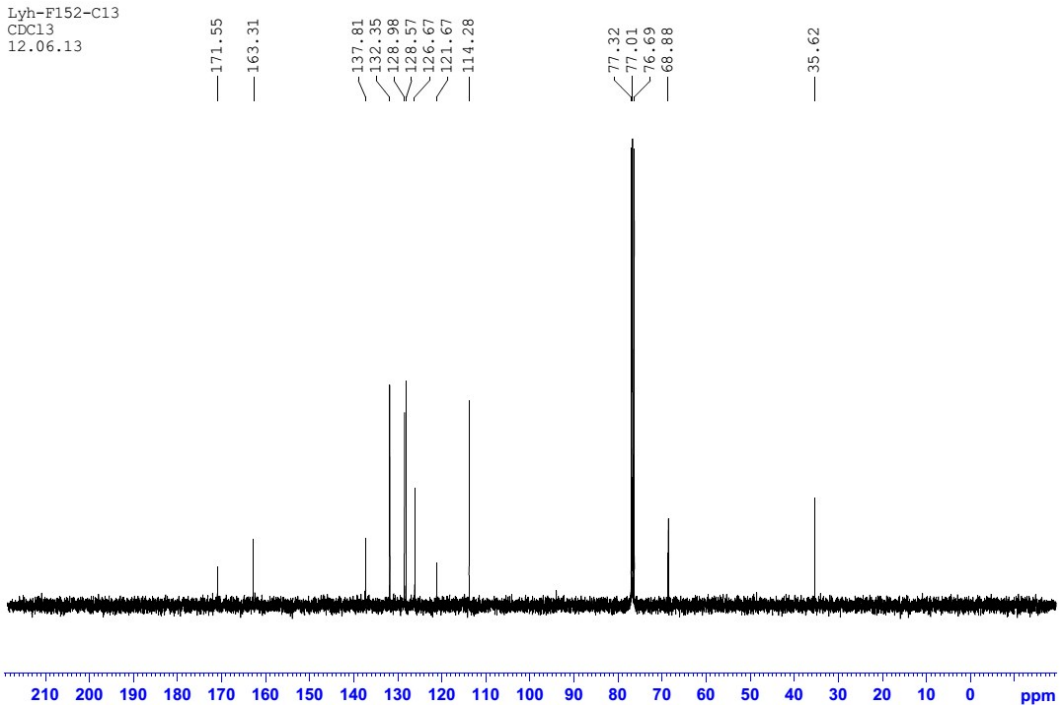


4-phenethoxybenzoic acid (3d-1)

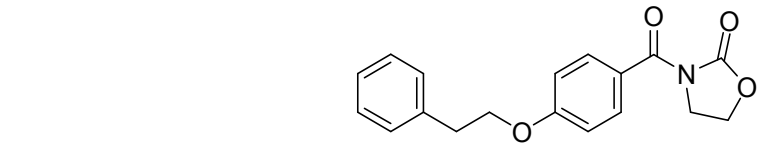


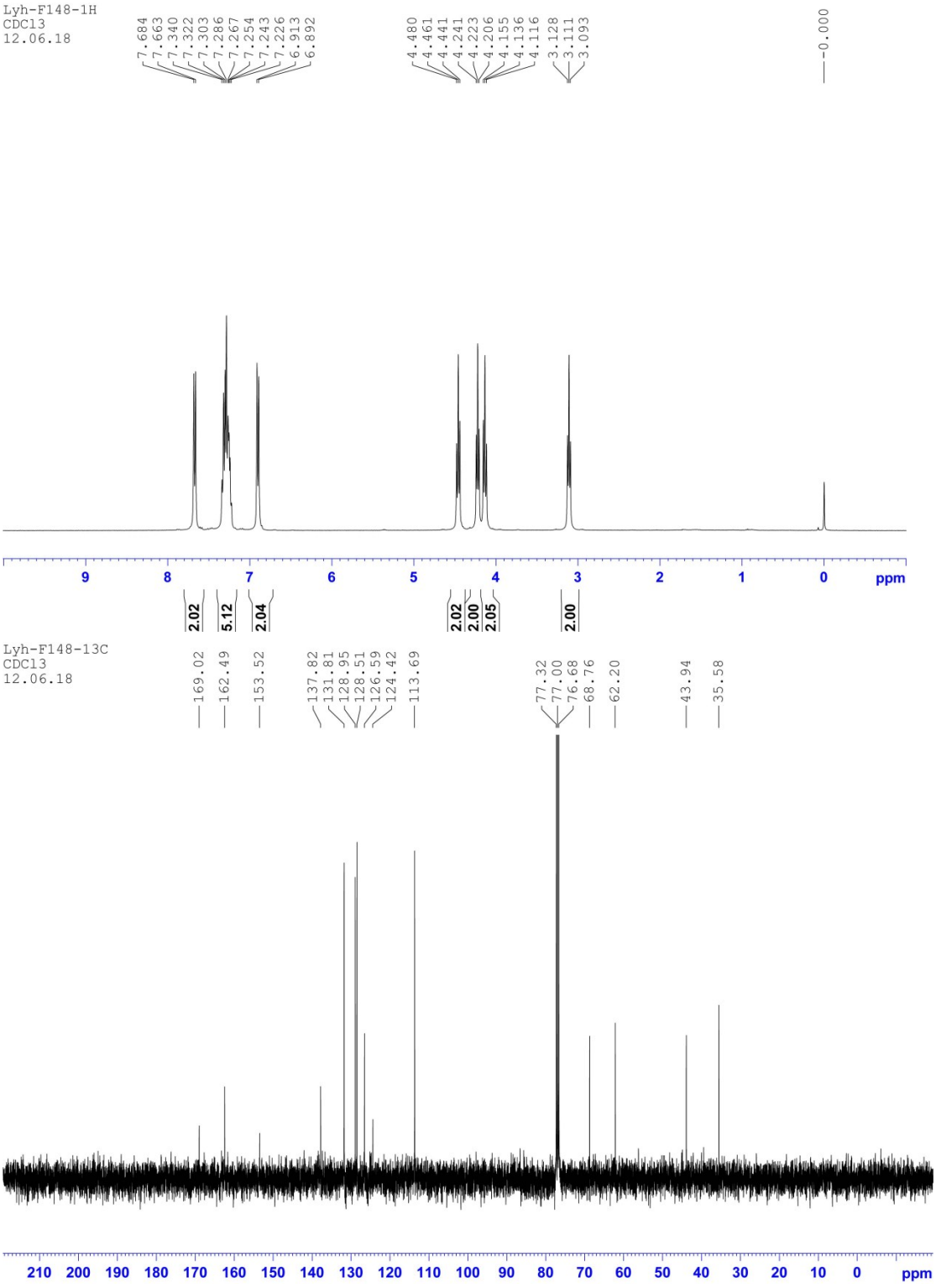




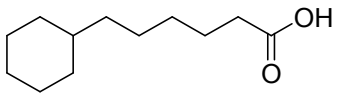


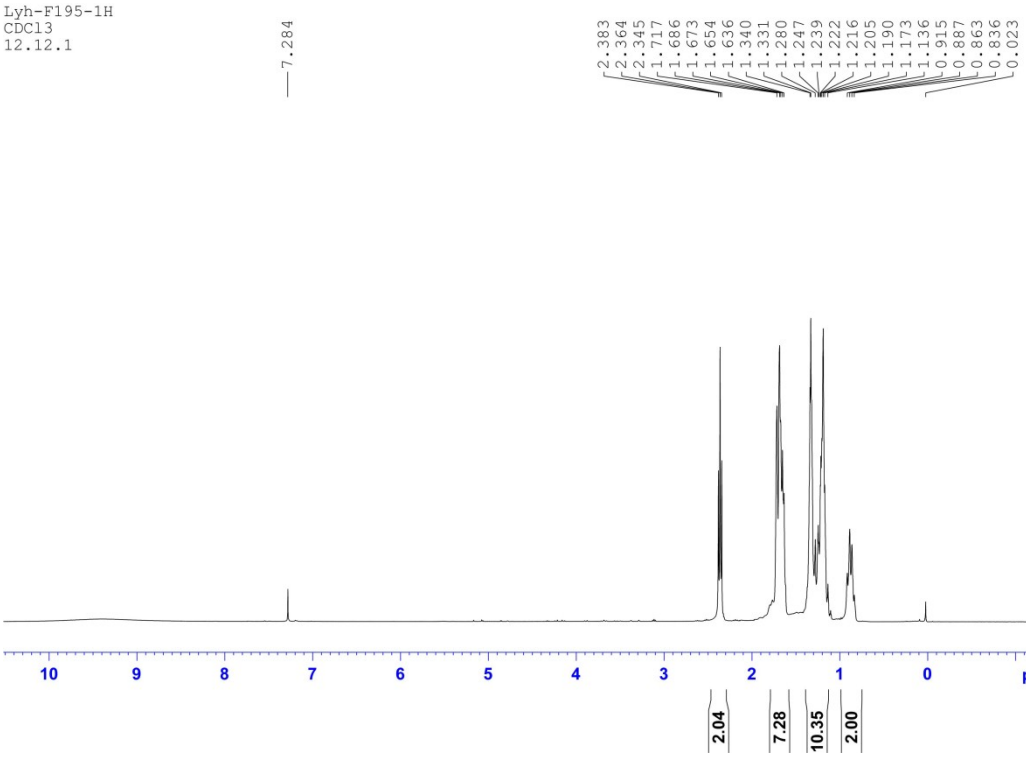
3-(4-phenethoxybenzoyl)oxazolidin-2-one (3d)

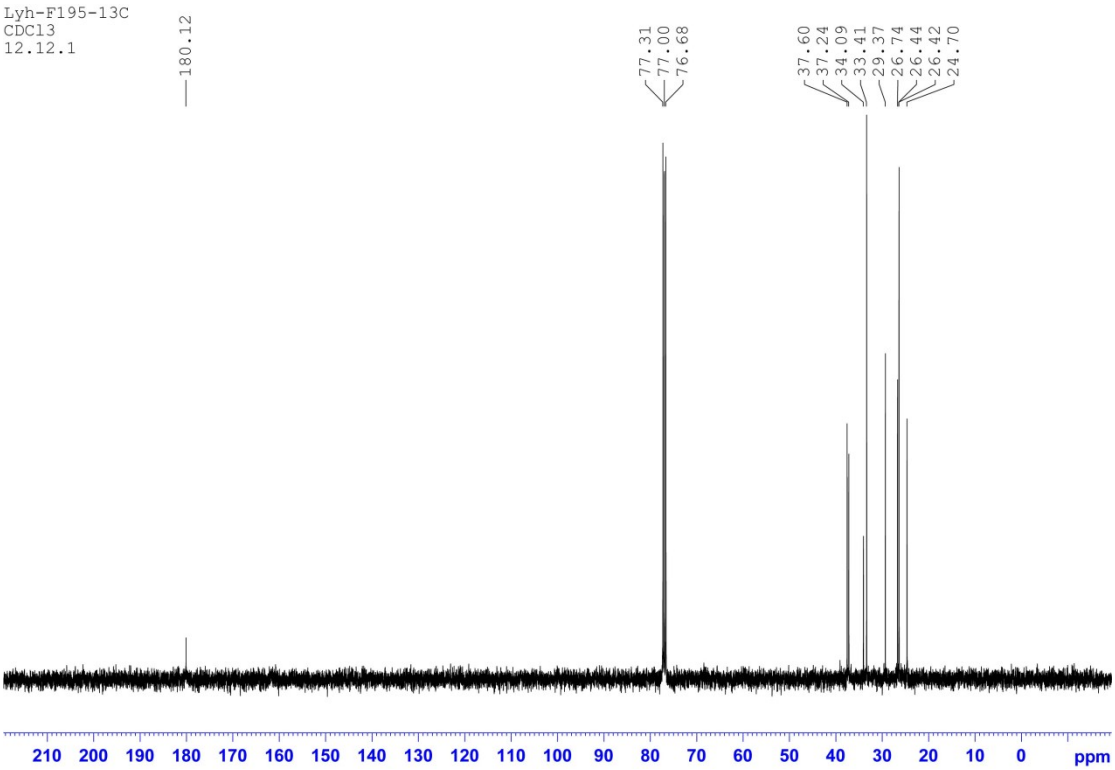




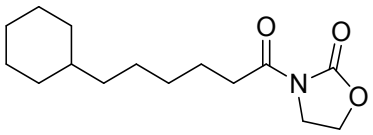
6-cyclohexylhexanoic acid (3j-1)

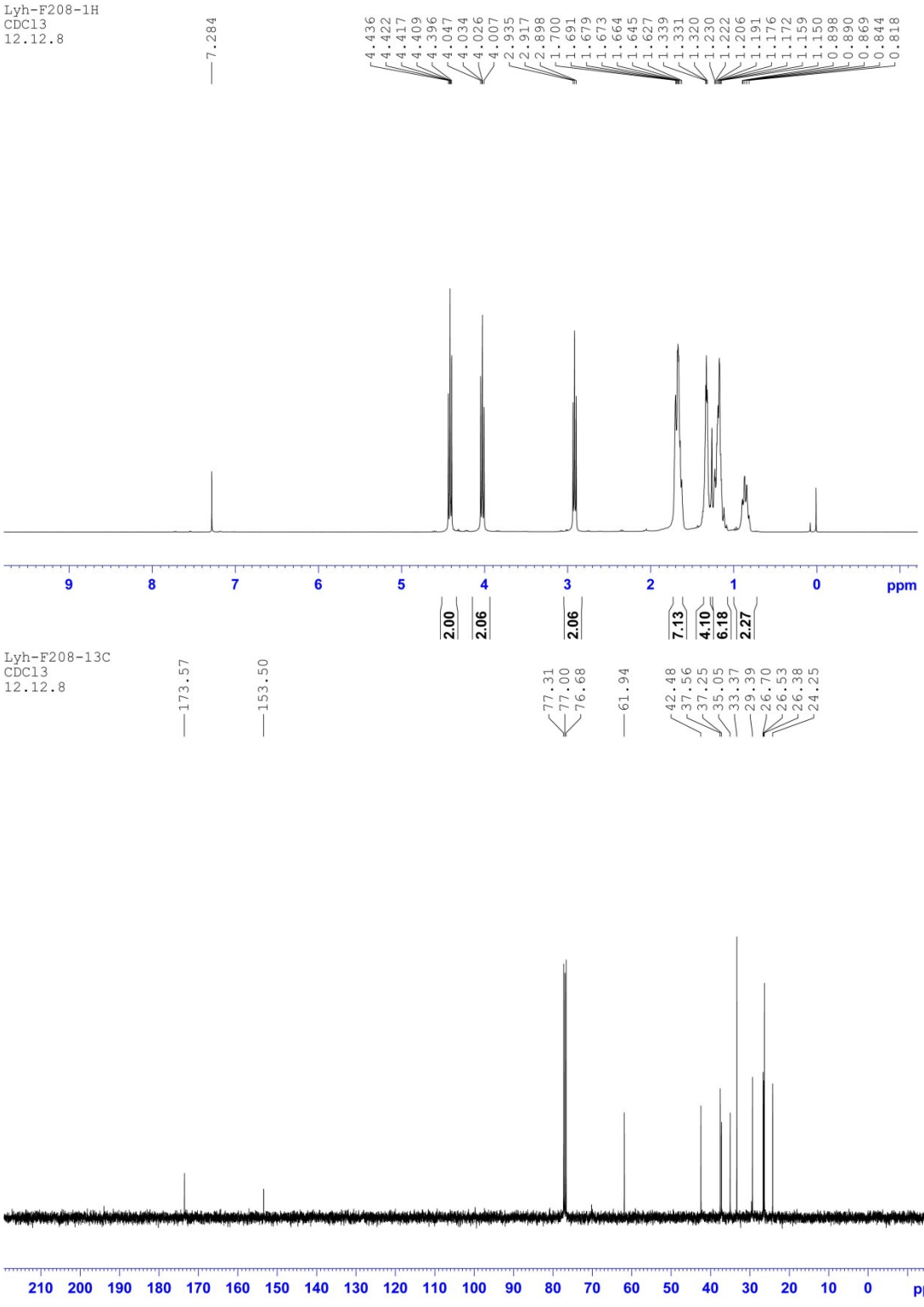




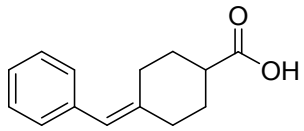


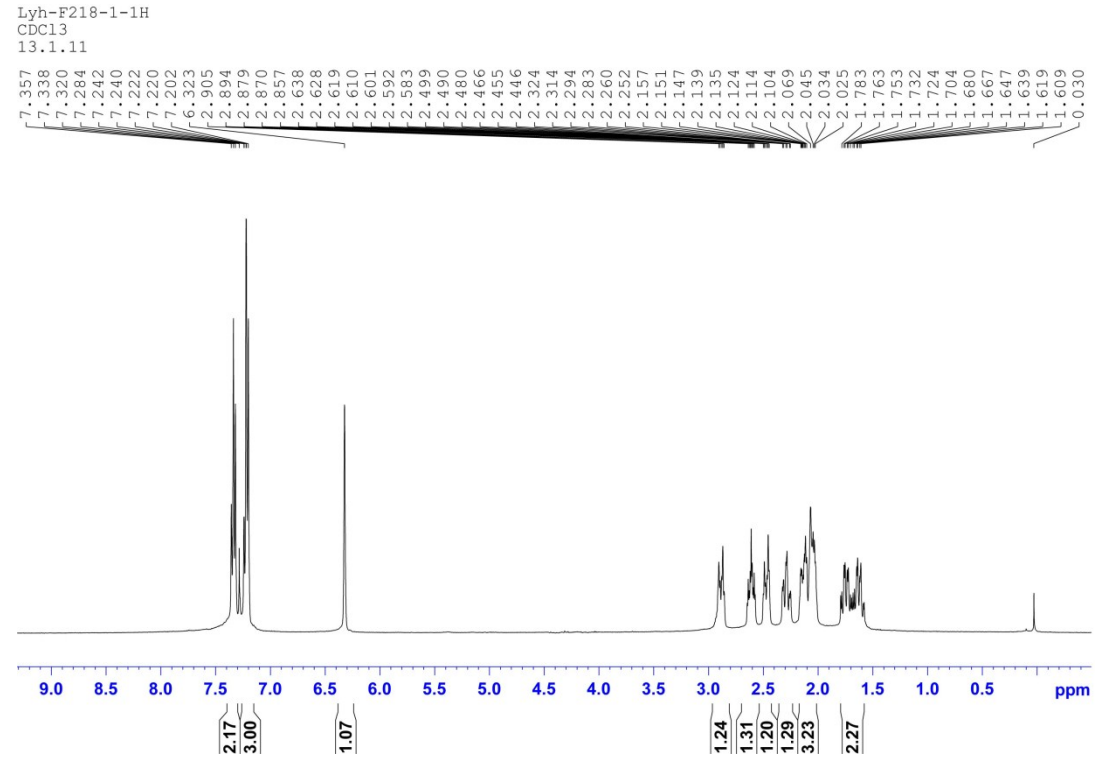
3-(6-cyclohexylhexanoyl)oxazolidin-2-one (3j)

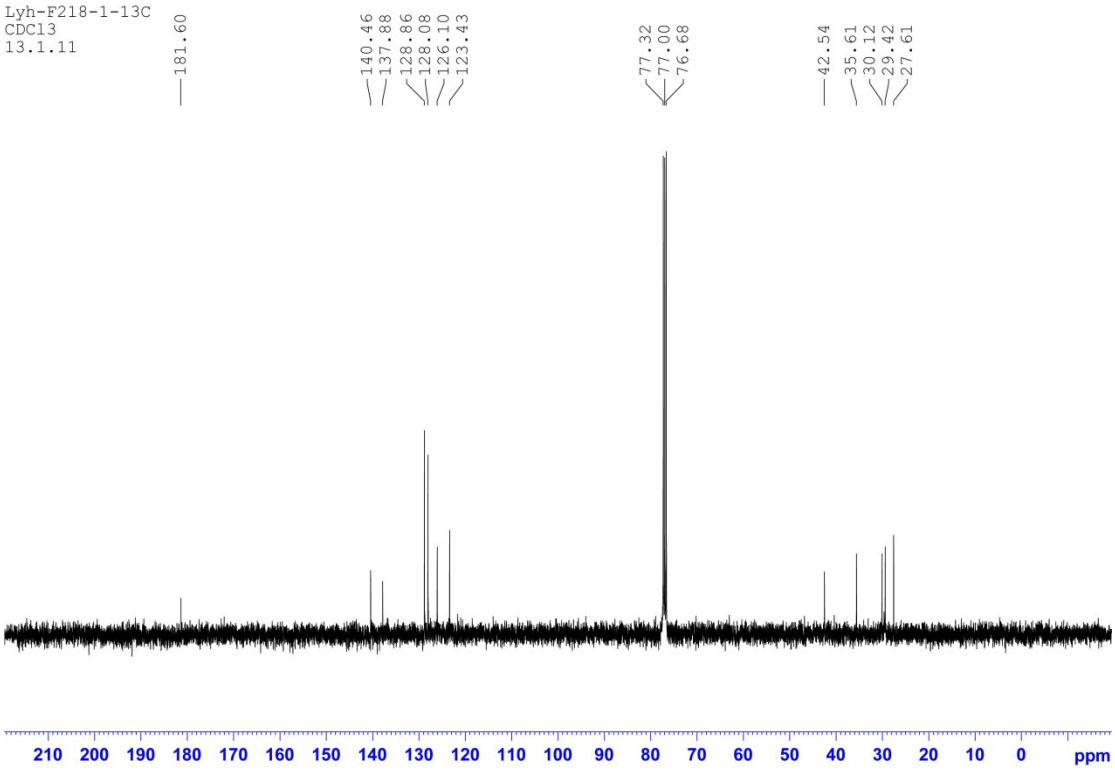




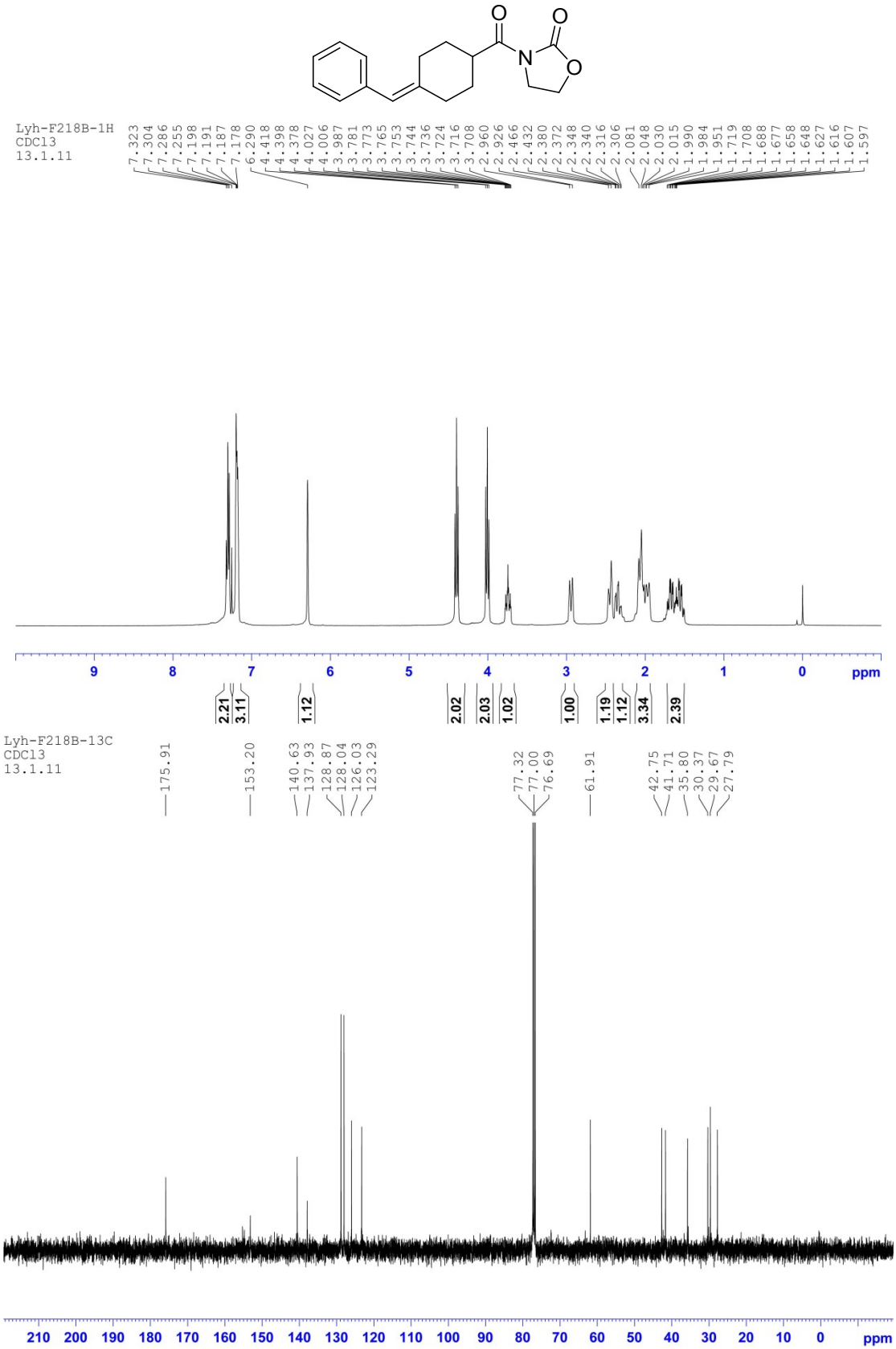
4-benzylidenecyclohexanecarboxylic acid (3h-1)



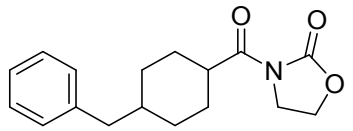


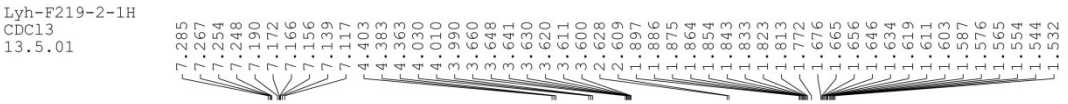


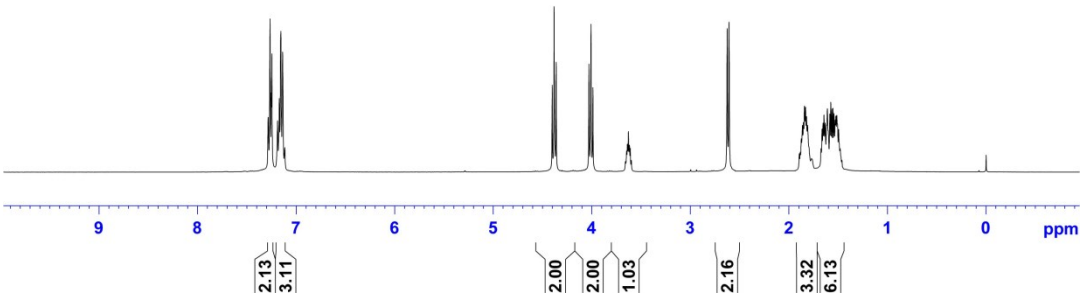
(-)-3-(4-benzylidenecyclohexanecarbonyl)oxazolidin-2-one (3h)

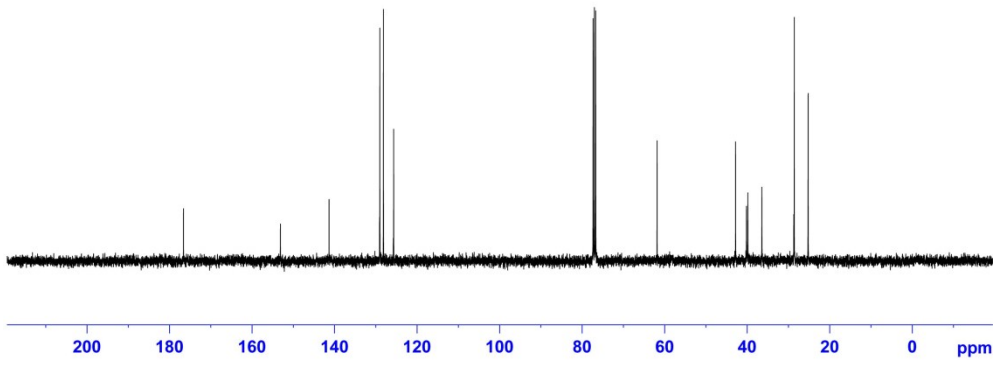


3-(4-benzylcyclohexanecarbonyl)oxazolidin-2-one (3i)

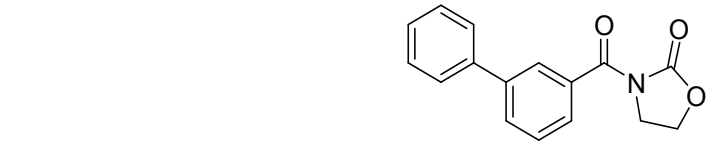


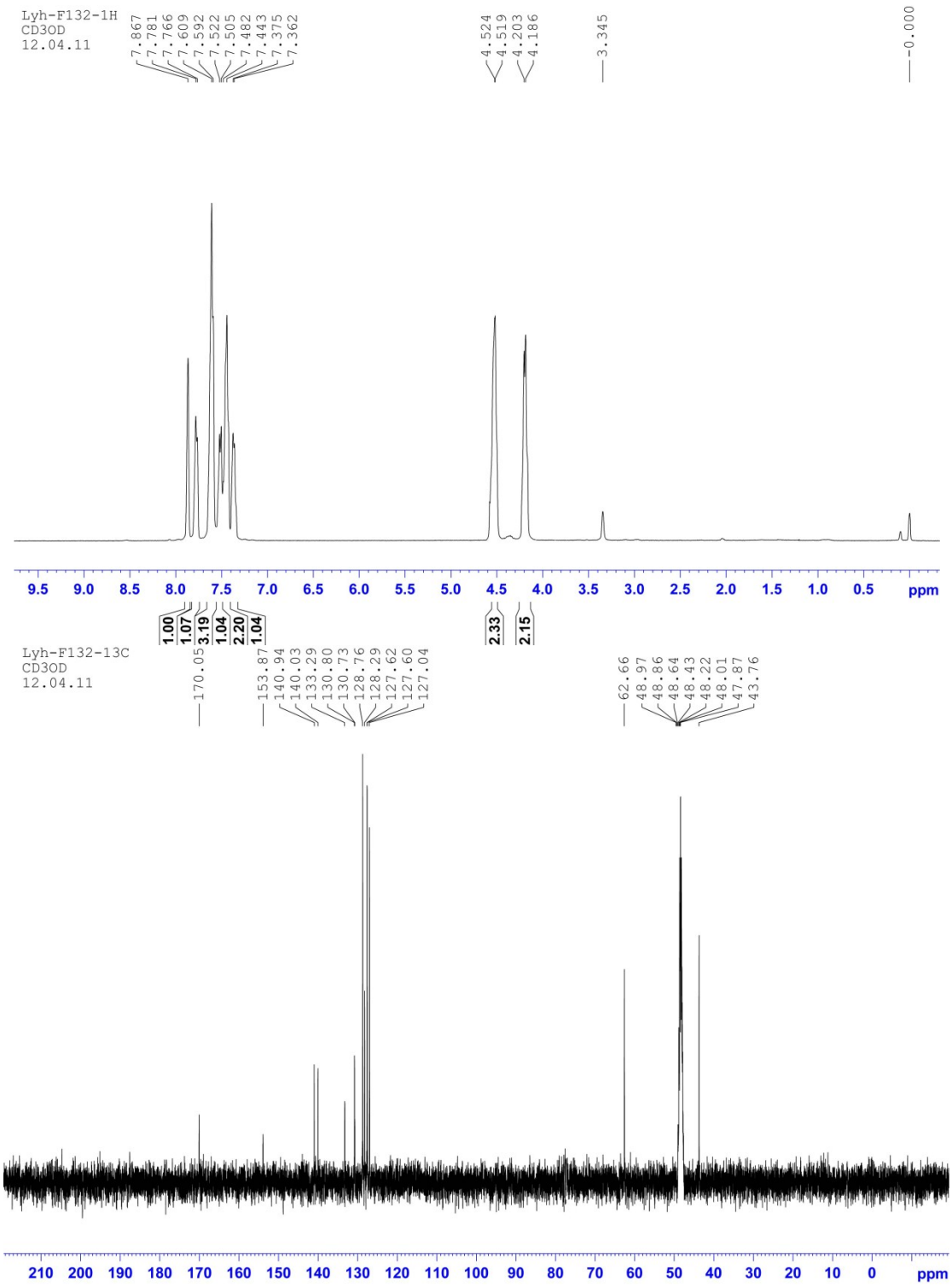




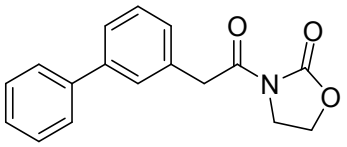


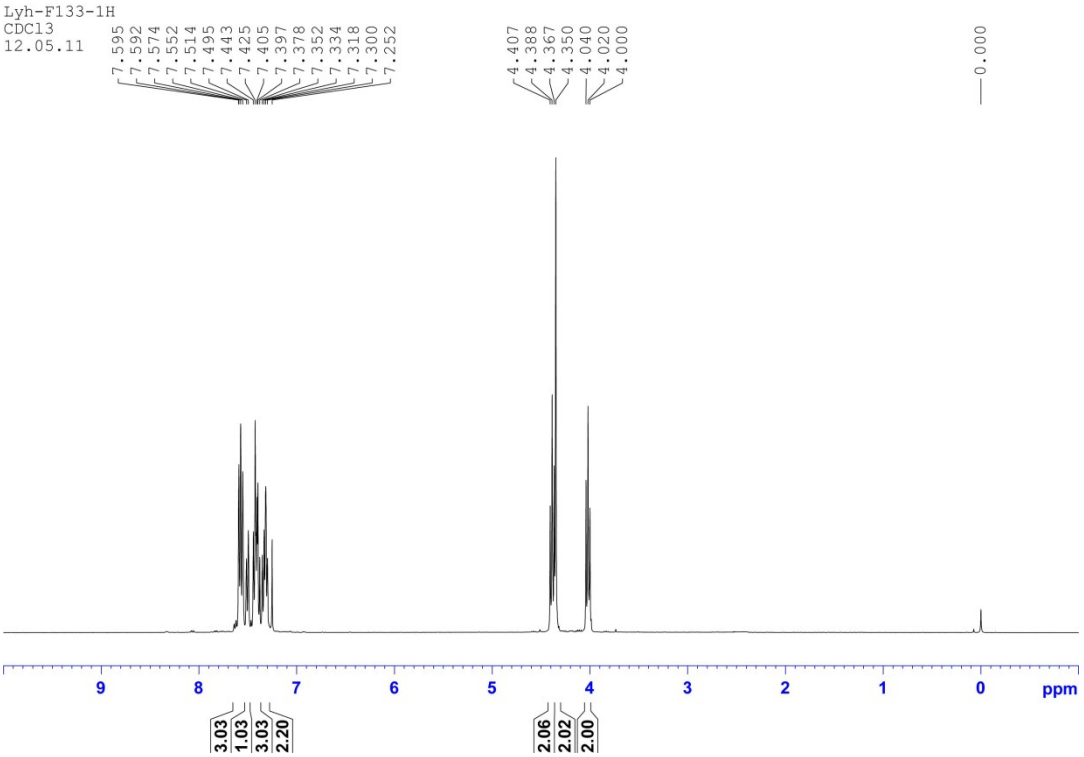
Biphenyl-3-yl-carbonyl oxazolidin-2-one (3k)

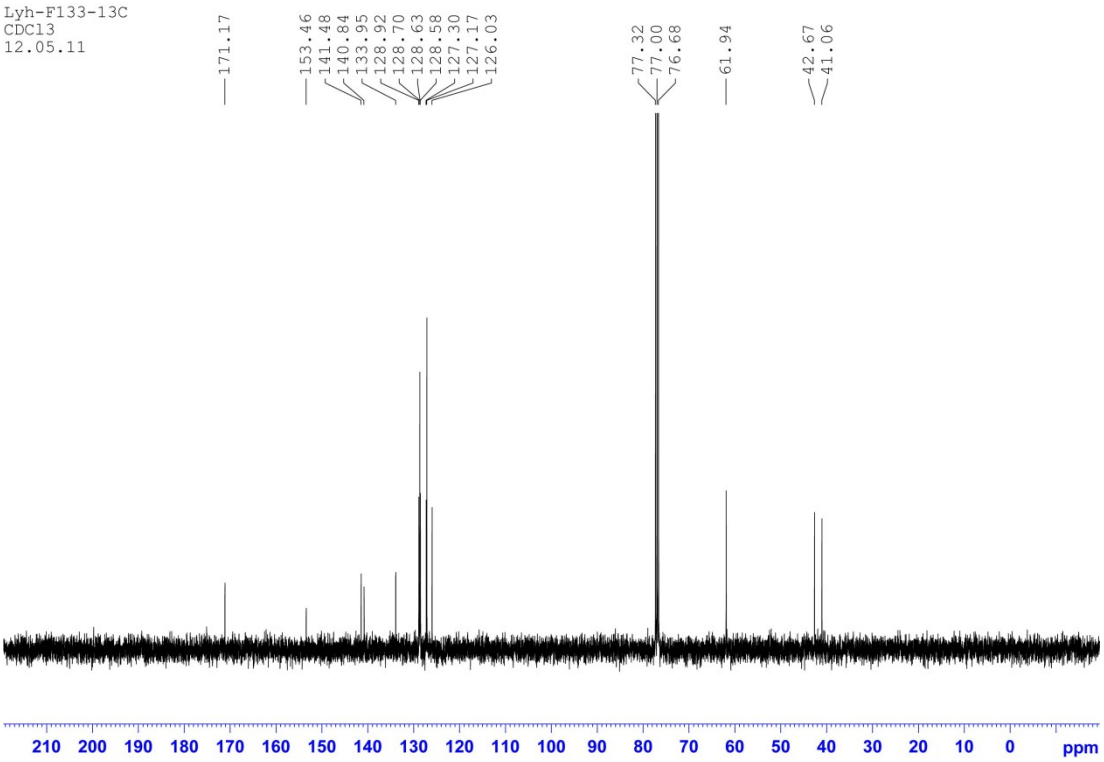




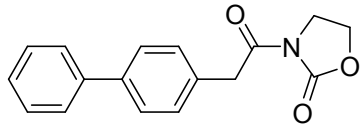
Biphenyl-3-yl-methylcarbonyl oxazolidin-2-one (3l)

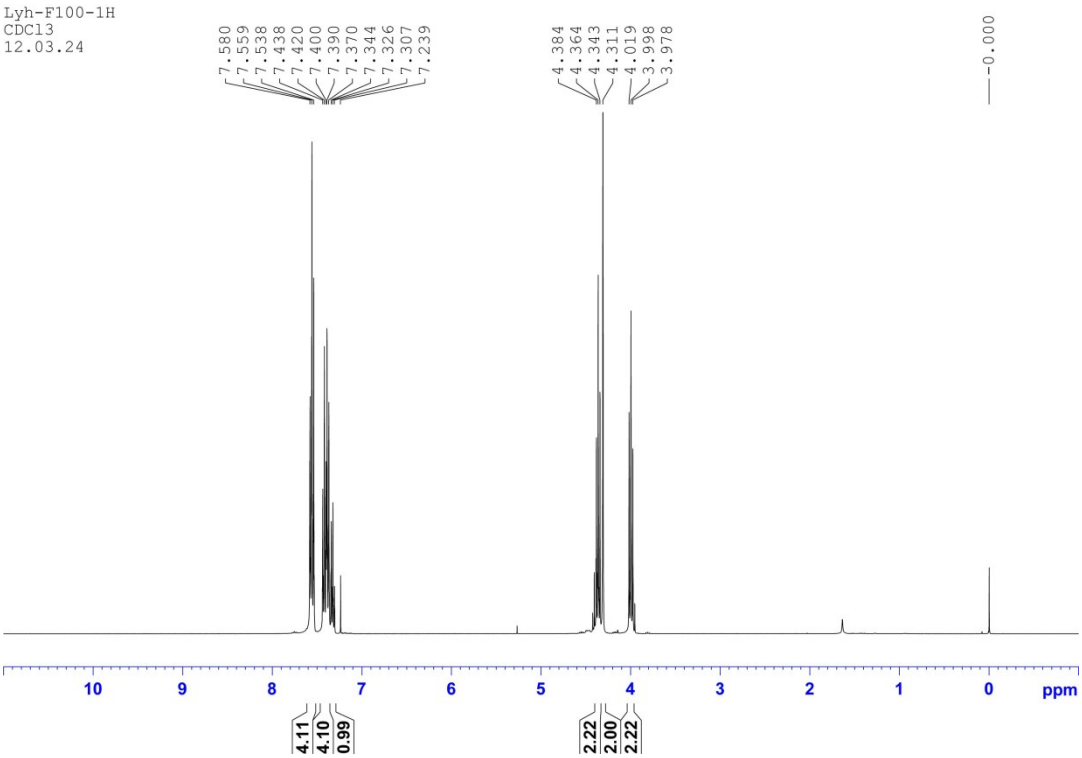


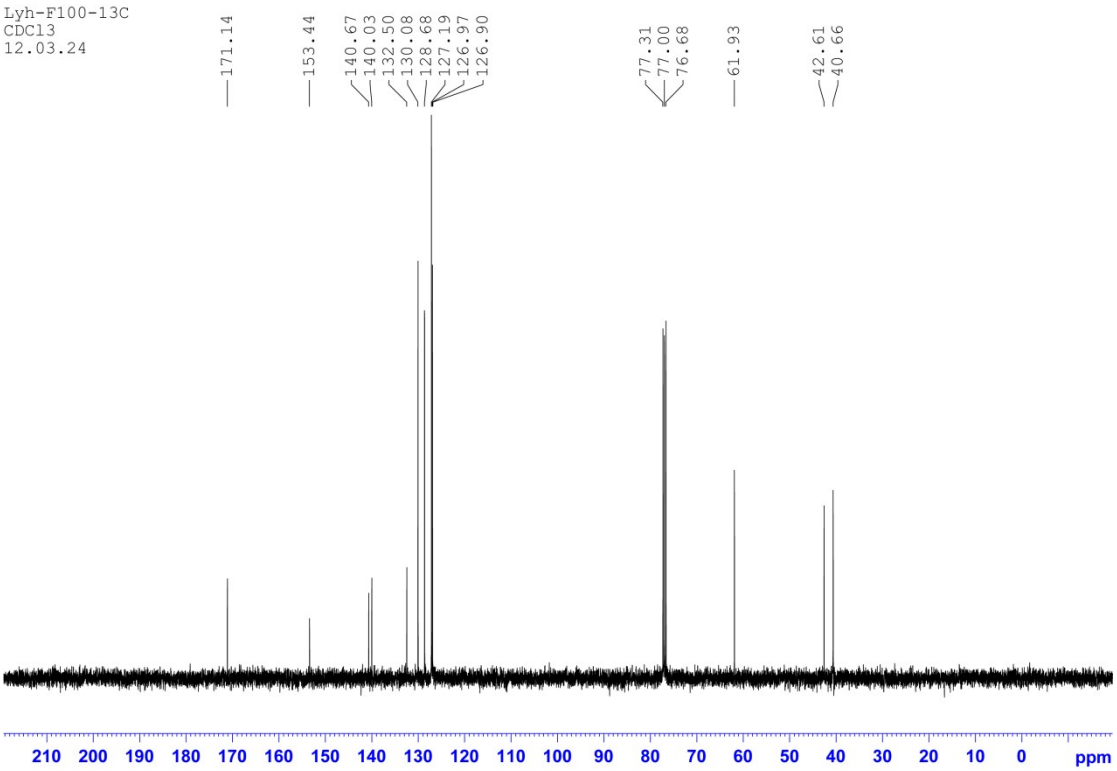




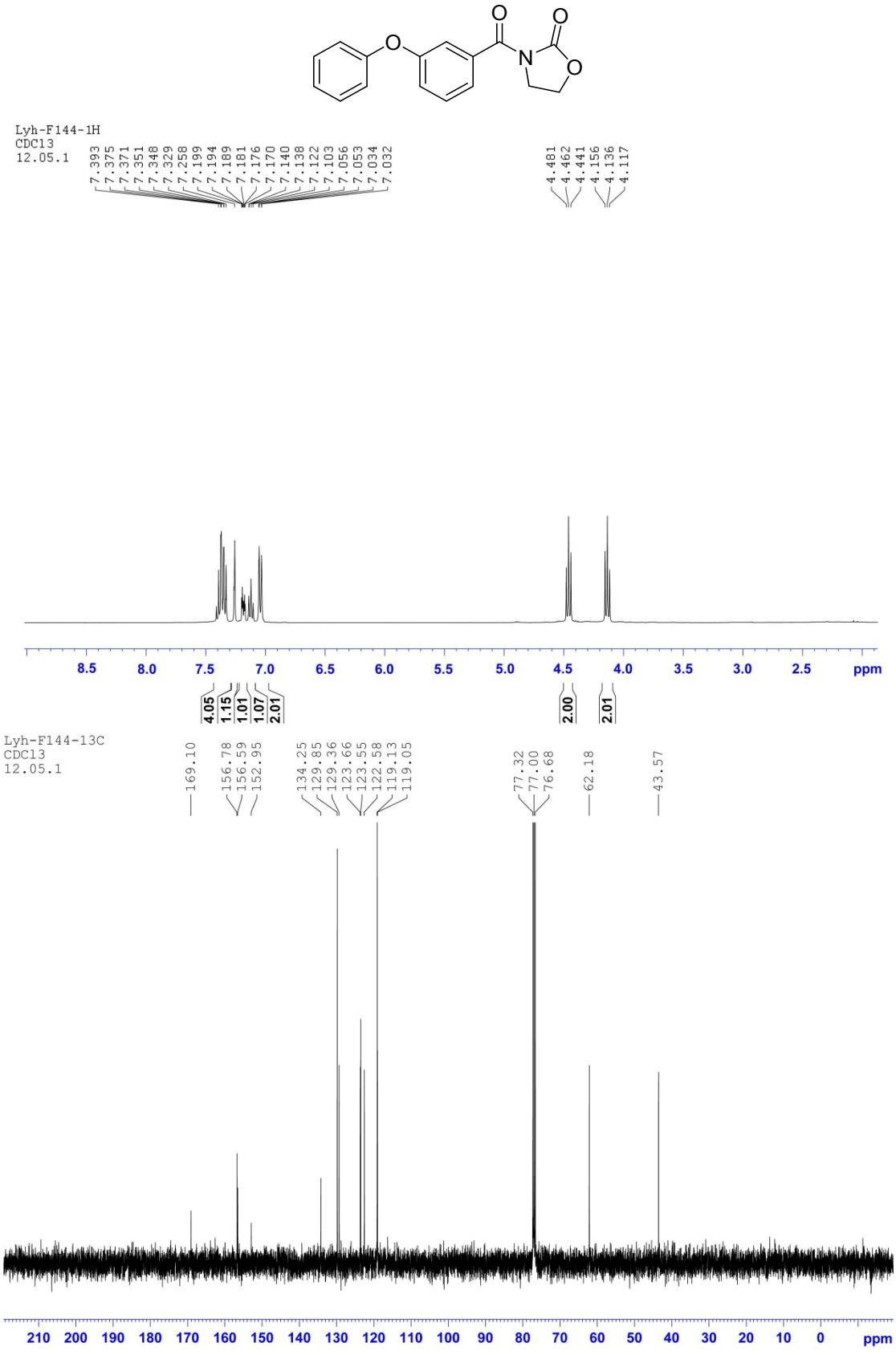
Biphenyl-4-yl-methylcarbonyl oxazolidin-2-one (3m)



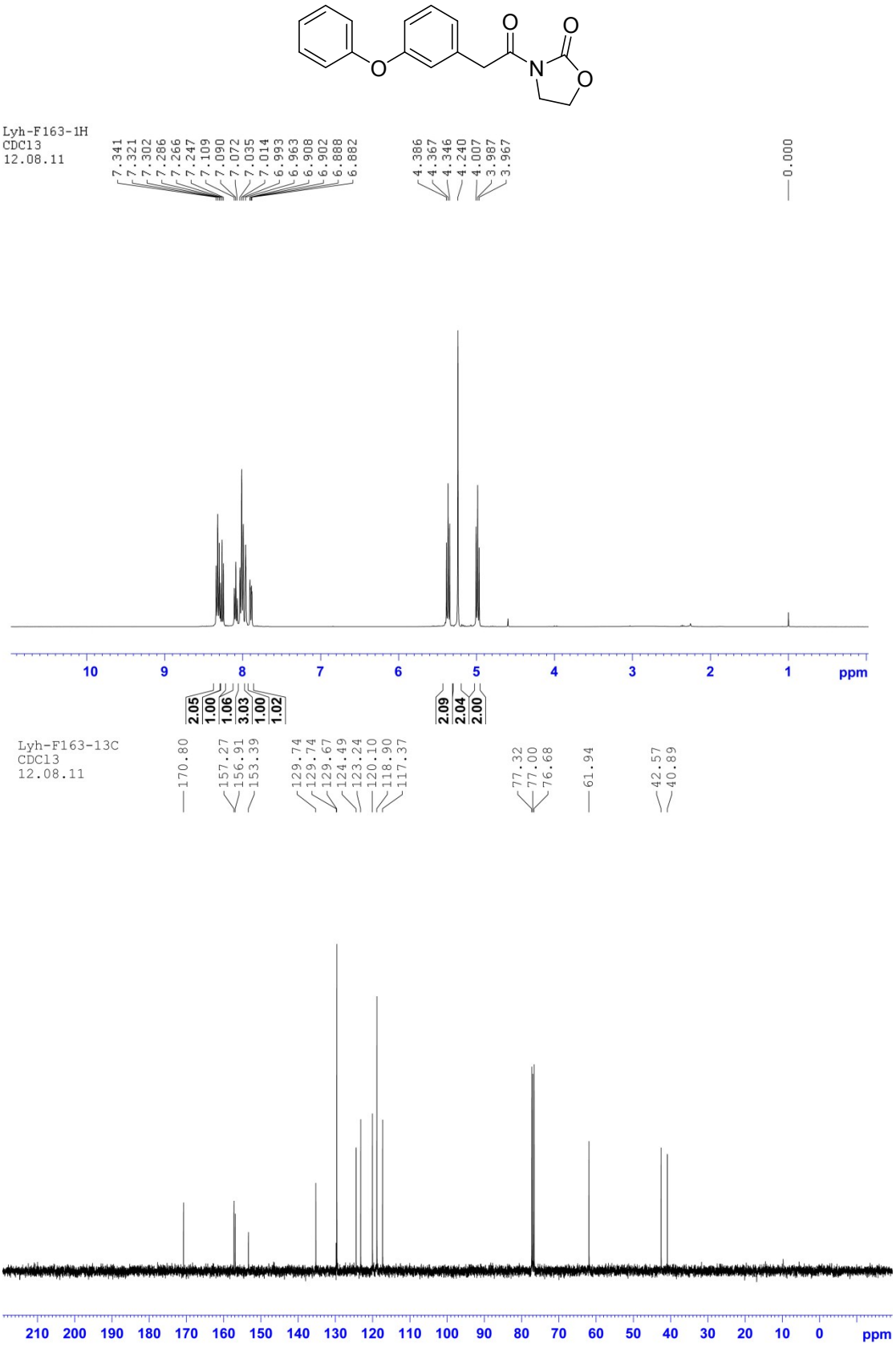




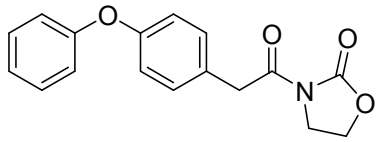
3-(3-phenoxybenzoyl)oxazolidin-2-one (3n)

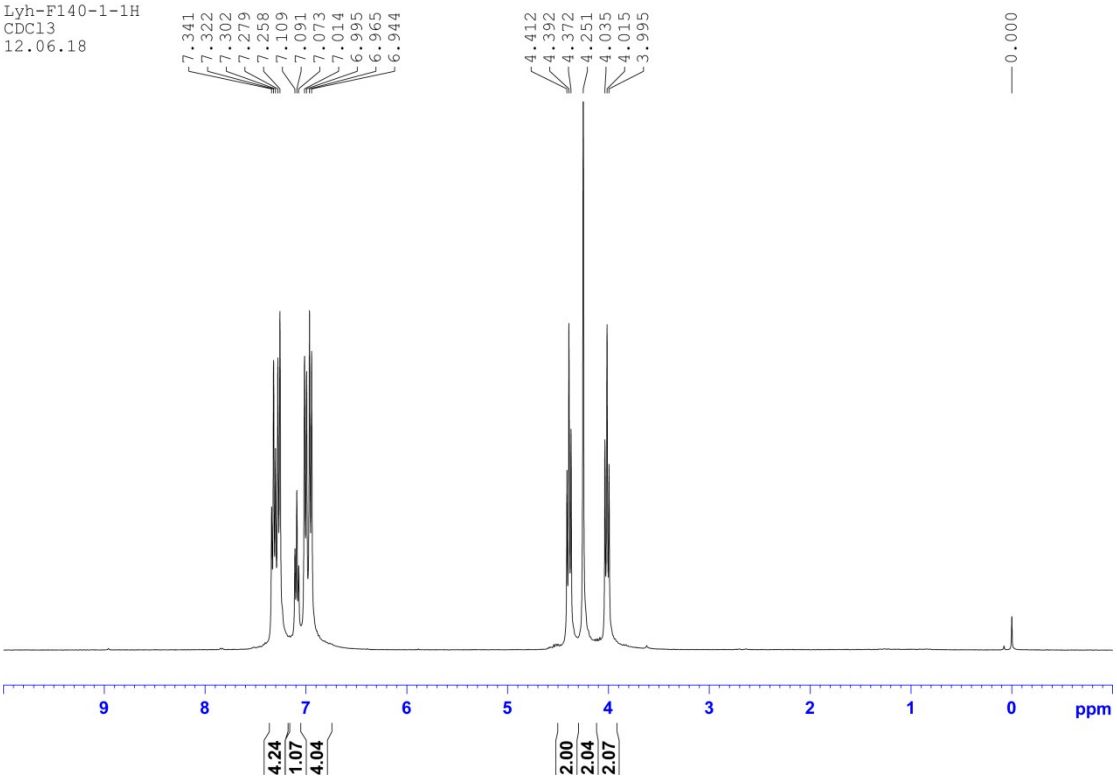


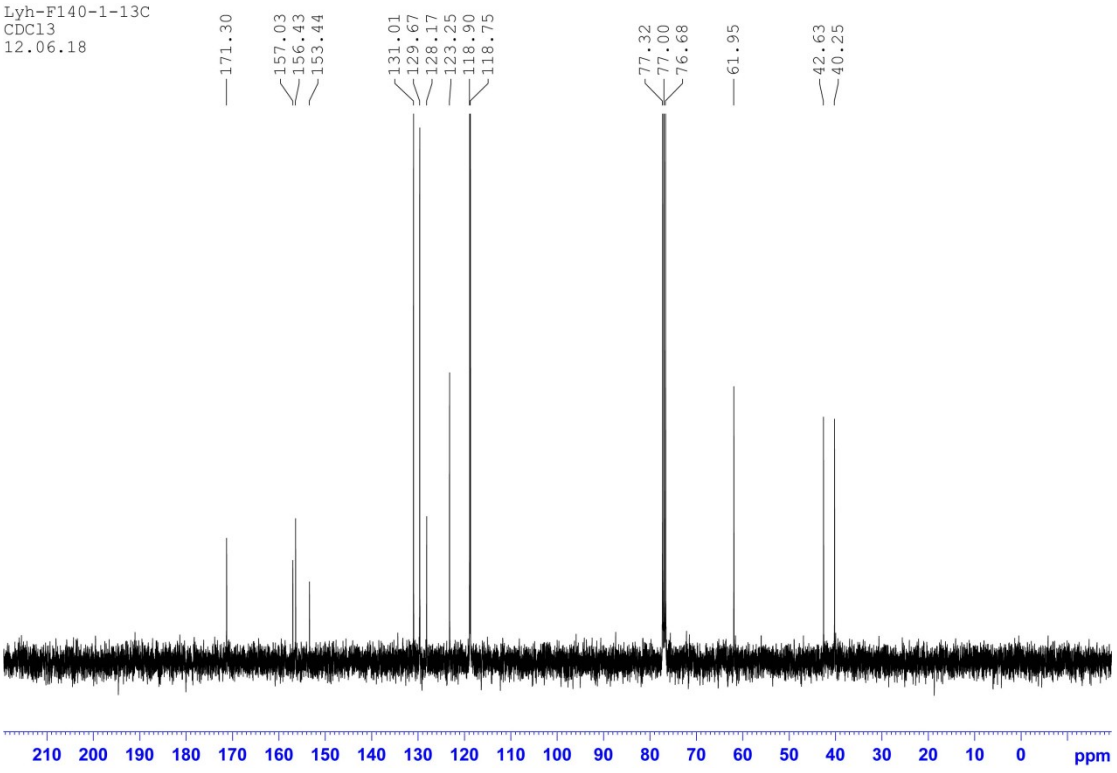
3-(2-(3-phenoxyphenyl)acetyl)oxazolidin-2-one (3o)



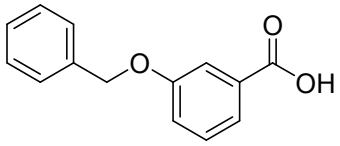
3-(2-(3-phenoxyphenyl)acetyl)oxazolidin-2-one (3p)

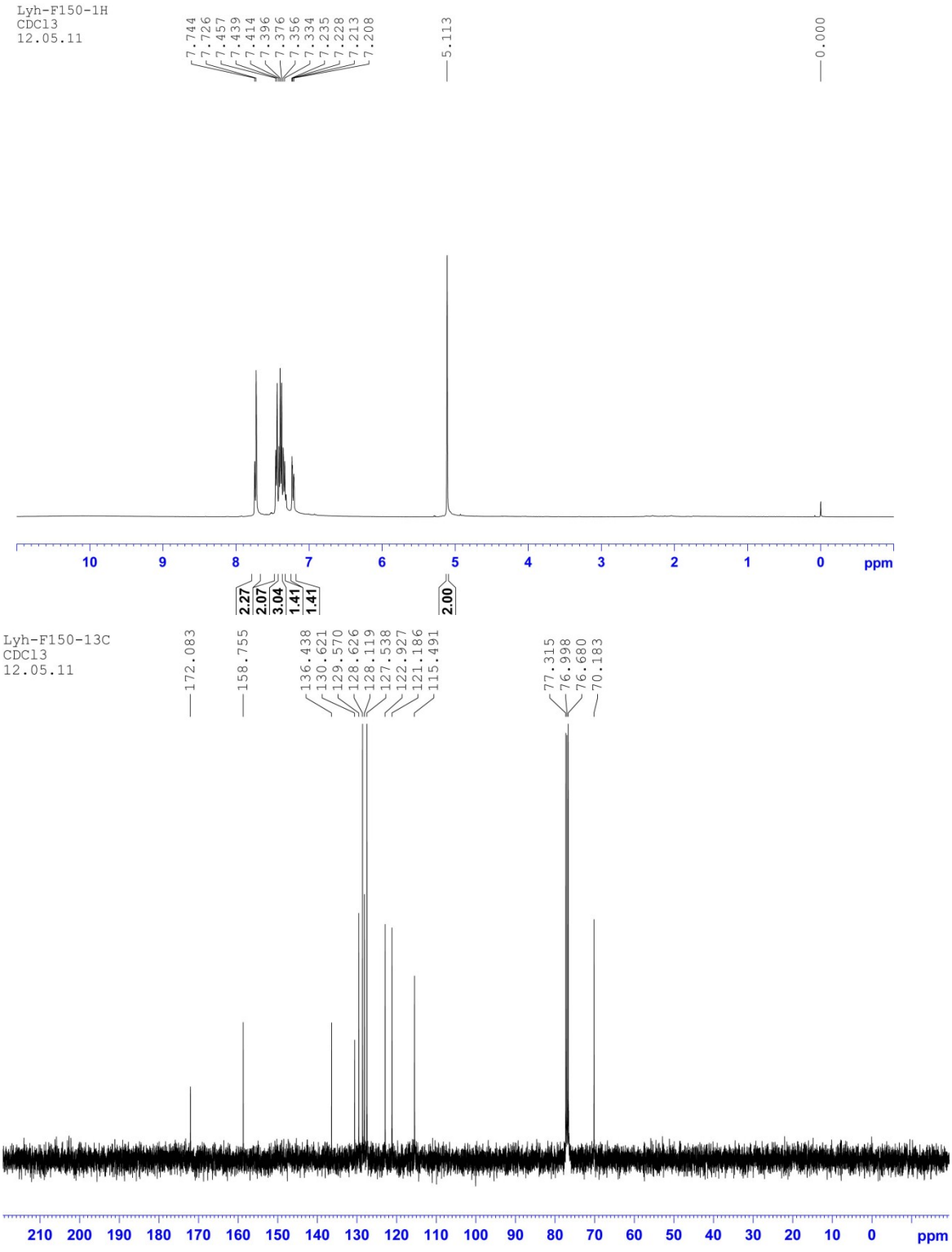




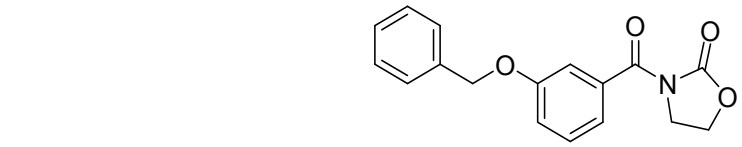


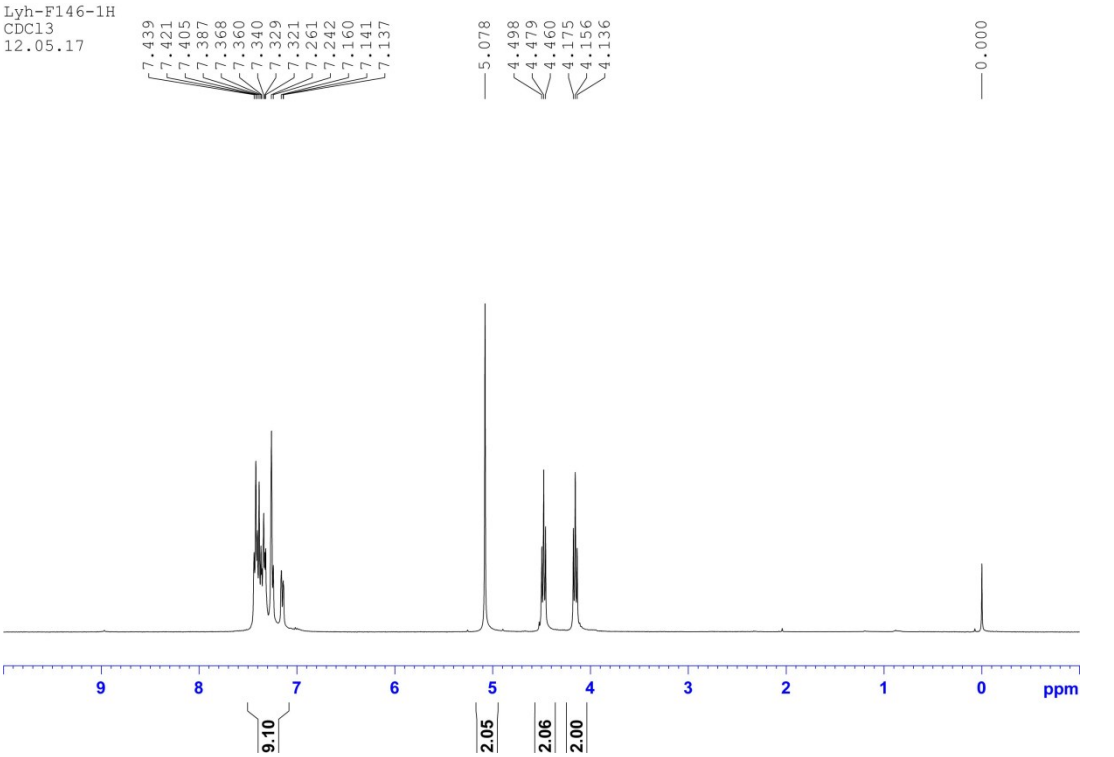
3-(benzyloxy)benzoic acid (3q-1)

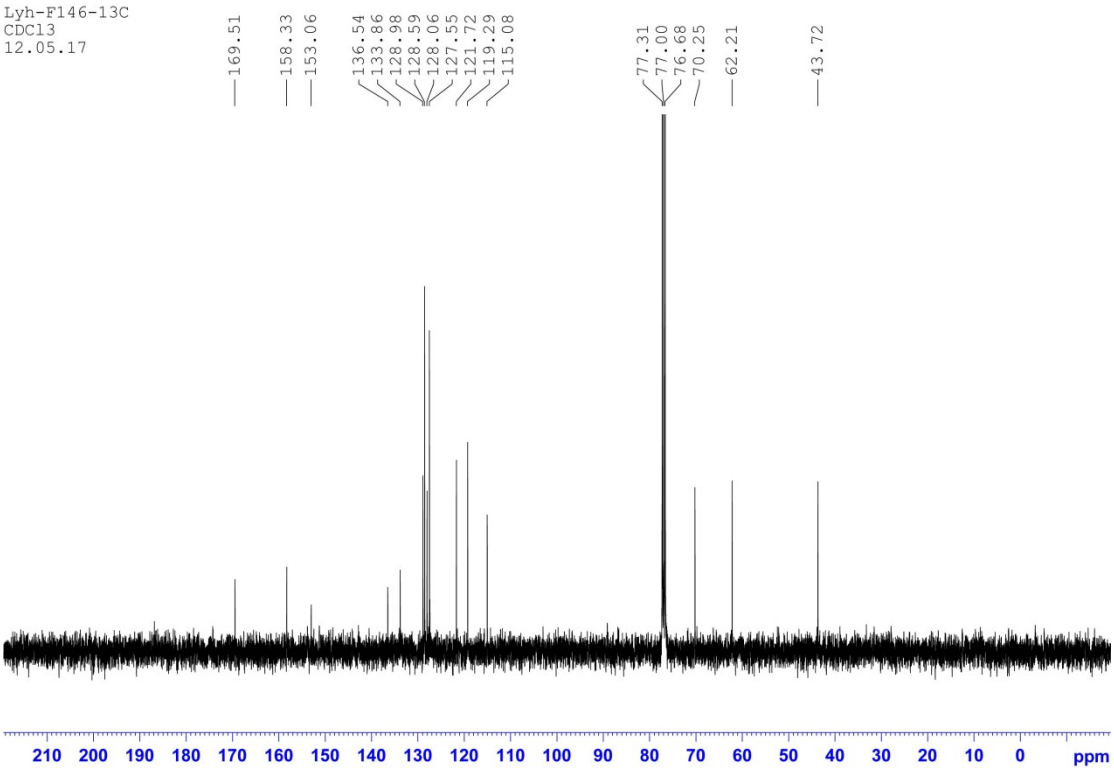




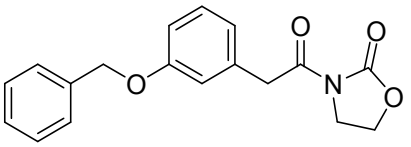
3-(3-(benzyloxy)benzoyl)oxazolidin-2-one (3q)

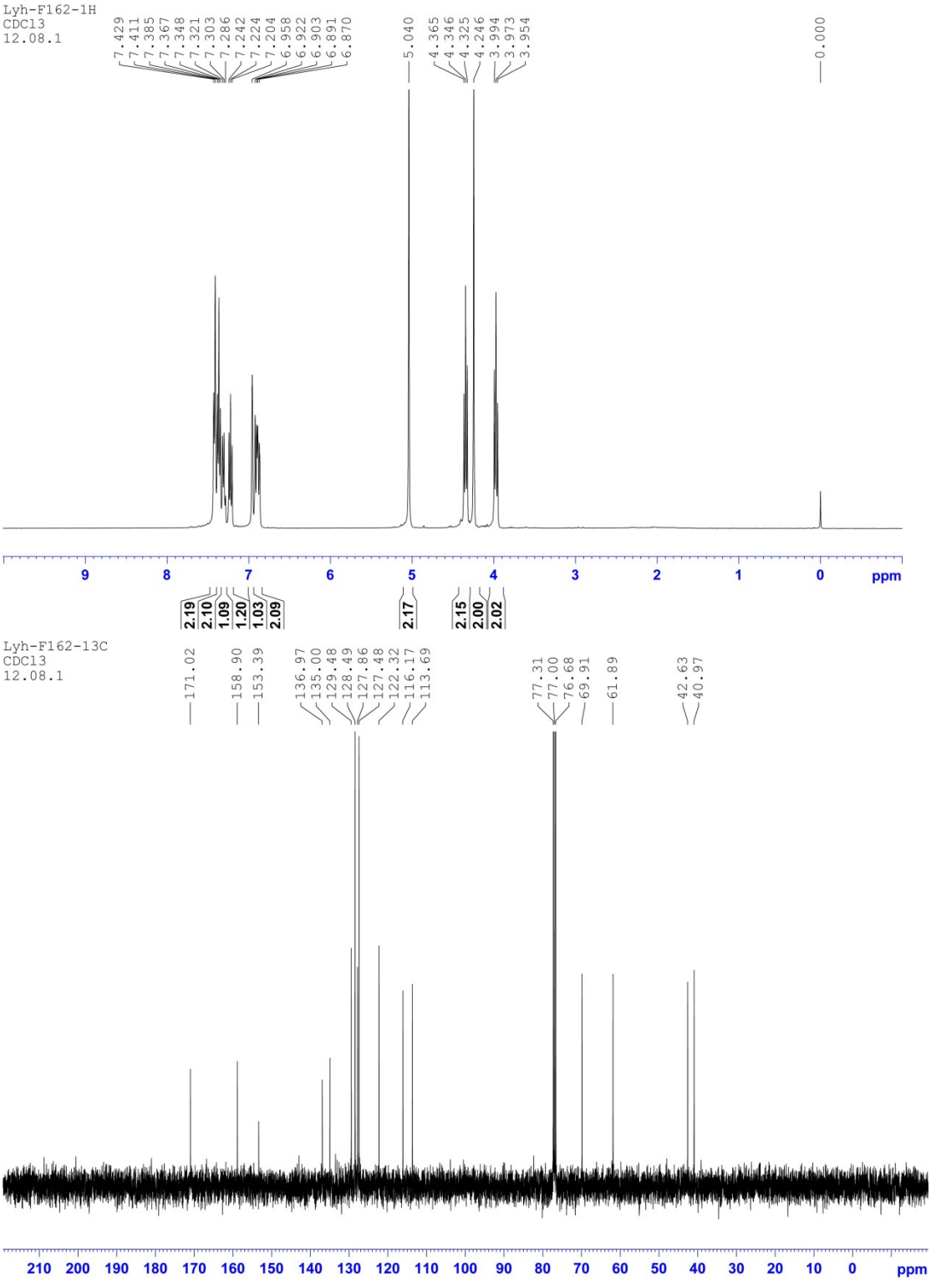




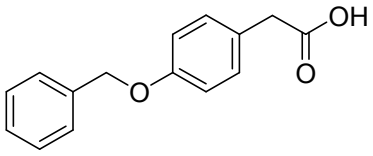


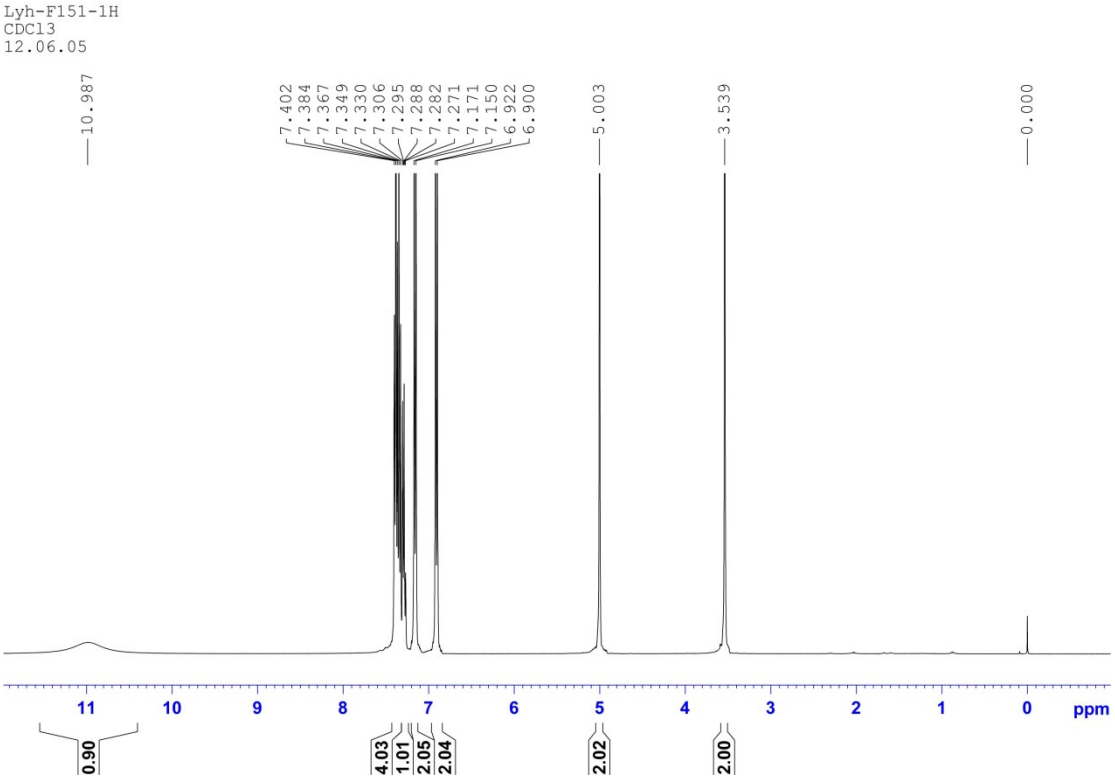
3-(2-(3-(benzyloxy)phenyl)acetyl)oxazolidin-2-one (3r)

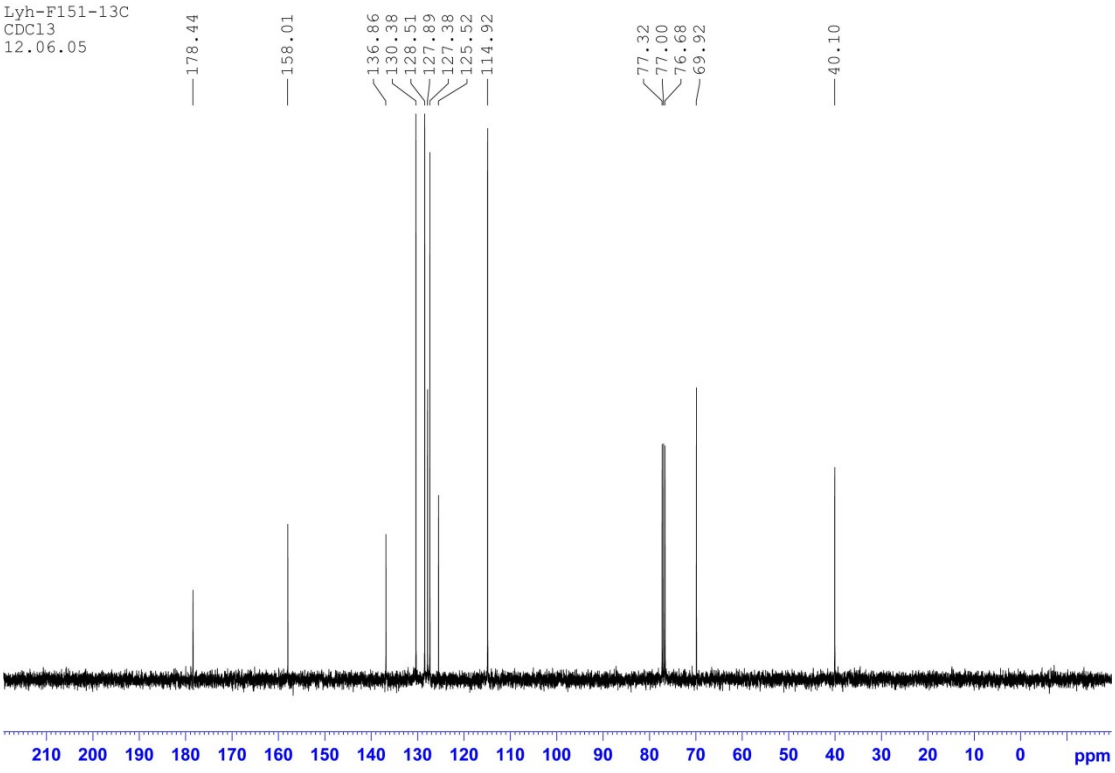




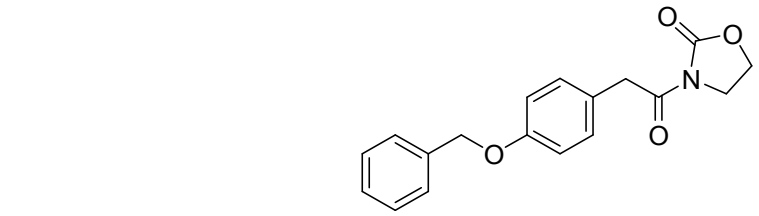
2-(4-(benzyloxy)phenyl)acetic acid (3s-1)

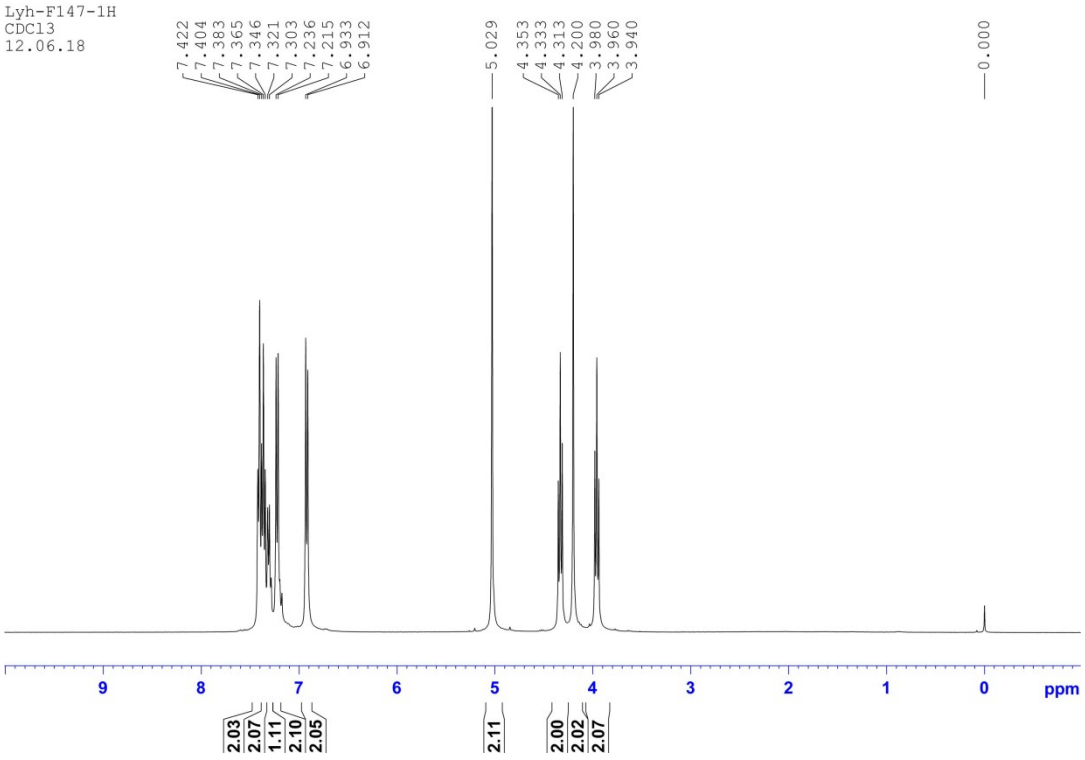


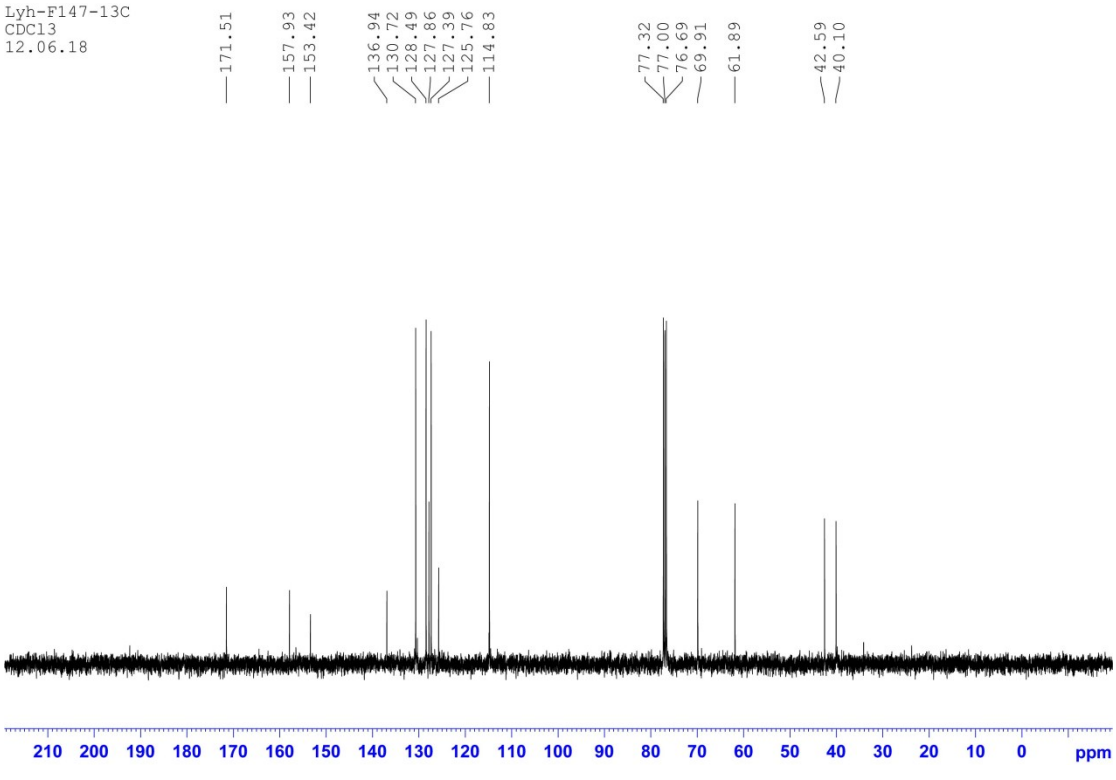




3-(2-(4-(benzyloxy)phenyl)acetyl)oxazolidin-2-one (3s)







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