

Supplementary Material

Generation of Mixed Anhydrides via Oxidative Fragmentation of Tertiary Cyclopropanols with Phenyliodine(III) Dicarboxylates

Dzmitry M. Zubrytski ¹, Gábor Zoltán Elek ², Margus Lopp ² and Dzmitry G. Kananovich ^{2,*}

¹ Belarusian State University, Department of Organic Chemistry, Leningradskaya 14, Minsk 220050, Belarus; zubrytski_dzmitry@rambler.ru (D.M.Z.)

² Tallinn University of Technology, School of Science, Department of Chemistry and Biotechnology, Akadeemia tee 15, Tallinn 12618, Estonia; gabor.elek@taltech.ee (G.Z.E.); margus.lopp@taltech.ee (M.L.)

* Correspondence: dzmitry.kananovich@taltech.ee; Tel.: +372-6204382

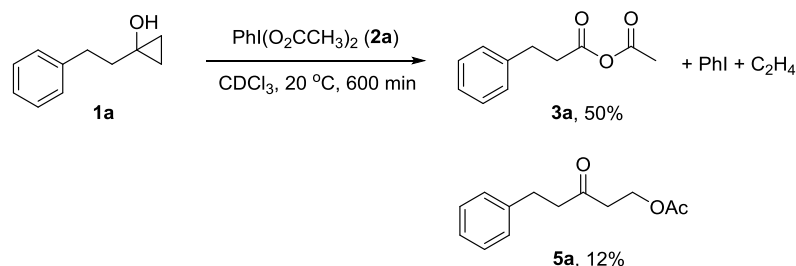
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1. Oxidative fragmentation of cyclopropanols with phenyliodine(III) dicarboxylates: characterization of mixed anhydrides

Selected experiments from **Table 1**:

Table 1, Entry 3: Reaction of **1a** with PIDA reagent (**2a**) in CDCl₃.



A solution of cyclopropanol **1a** (6.1 mg, 0.0375 mmol) in anhydrous CDCl₃ (0.37 mL) was mixed with solution of PIDA reagent **2a** (12.1 mg, 0.0375 mmol, 1.05 equiv.) in anhydrous CDCl₃ (0.37 mL) and progress of the reaction was monitored by ¹H NMR spectroscopy. Initial concentrations of both reactants nearly equal to 0.05 M. Conversion of starting materials **1a**, **2a** and accumulation of product **3a** were calculated from the integral intensities of the corresponding signals. Thus, consumption of **1a** was followed by its characteristic signals at 1.88, 0.77, 0.46 ppm, consumption of **2a** – by the signal at 8.09 ppm, accumulation of product **3a** – by its signal at 2.19 ppm. Approximately 90% consumption of the starting materials was observed after 600 min.

Characteristic NMR resonances of mixed acetic acid anhydride **3a**: ¹H NMR (400 MHz, CDCl₃) δ = 2.99 (t, *J* = 7.7 Hz, 2H, PhCH₂), 2.78 (t, *J* = 7.7 Hz, 2H, CH₂CO), 2.19 (s, 3H, CH₃CO). ¹³C NMR (100.6 MHz, CDCl₃) δ = 168.7 (CH₂CO), 166.5 (CH₃CO), 36.9 (CH₂CO), 30.3 (PhCH₂), 22.4 (CH₃CO). Signal assignment is based on HSQC and HMBC data. Aromatic regions of NMR spectra have not been analyzed due to overlap with PhI signals.

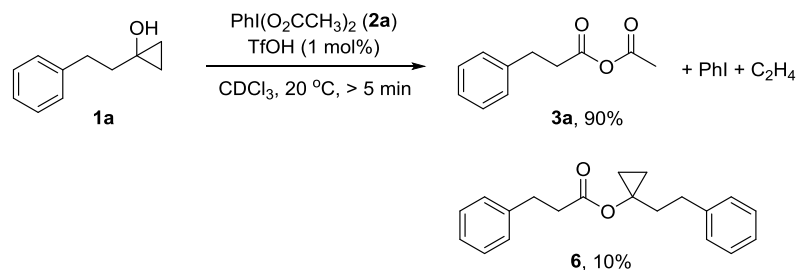
HRMS (ESI): calcd. for C₁₁H₁₂O₃Na⁺ [M+Na]⁺ 215.0679, found *m/z* 215.0670.

Characteristic NMR resonance of β-acetyloxyketone by-product **5a**: ¹H NMR (400 MHz, CDCl₃) δ = 4.32 (t, *J* = 6.2 Hz, 2H, CH₂COAc), 2.01 (s, 3H, CH₃CO₂). ¹³C NMR (100.6 MHz, CDCl₃) δ = 59.4 (CH₂COAc).

HRMS (ESI): calcd. for C₁₃H₁₆O₃Na⁺ [M+Na]⁺ 243.0992, found *m/z* 243.0983.

The corresponding β-acetyloxyketone by-product was also isolated in the oxidation of 1-octylcyclopropanol **1b** with PIDA reagent, see section 2 below.

Table 1, Entry 4: Reaction of cyclopropanol **1a** with PIDA reagent (**2a**) in CDCl₃ in the presence of catalytic amounts of TfOH (1 mol%).



A solution of TfOH (40 μ L, ca. 0.01 M in CDCl_3 , 1 mol%) was added to solution of reagent **2a** (12.9 mg, 0.04 mmol, 1.1 equiv.) in anhydrous CDCl_3 (0.37 mL) and then mixed with a solution of cyclopropanol **1a** (6.1 mg, 0.0375 mmol) in anhydrous CDCl_3 (0.37 mL). Progress of the reaction was monitored by ^1H NMR spectroscopy. Full consumption of the starting material **1a** was observed immediately after acquisition of the first ^1H NMR spectrum (less than in 5 min). Yields of products **3a** and **6** were calculated from the integral intensities of the corresponding ^1H NMR signals.

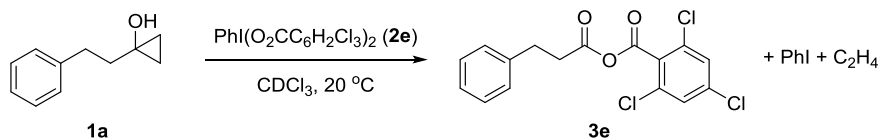
Characteristic NMR resonances of mixed acetic acid anhydride **3a**: ^1H NMR (400 MHz, CDCl_3) δ = 2.99 (t, J = 7.7 Hz, 2H, PhCH_2), 2.78 (t, J = 7.7 Hz, 2H, CH_2CO), 2.19 (s, 3H, CH_3CO). ^{13}C NMR (100.6 MHz, CDCl_3) δ = 168.7 (CH_2CO), 166.5 (CH_3CO), 36.9 (CH_2CO), 30.3 (PhCH_2), 22.4 (CH_3CO). Signal assignment is based on HSQC and HMBC data. Aromatic regions of NMR spectra have not been analyzed due to overlap with PhI signals.

HRMS (ESI): calcd. for $\text{C}_{11}\text{H}_{12}\text{O}_3\text{Na}^+$ [$\text{M}+\text{Na}$] $^+$ 215.0679, found m/z 215.0670.

Characteristic NMR signals for by-product **6** (aromatic region of NMR spectra has not been analyzed): ^1H NMR (400 MHz, CDCl_3) δ = 2.89 (t, J = 7.7 Hz, 2H), 2.67 (m, 2H), 2.49 (t, J = 7.7 Hz, 2H), 2.05 (m, 2H), 0.76 (m, 2H), 0.62 (m, 2H). ^{13}C NMR (100.6 MHz, CDCl_3) δ = 173.0 (CO), 36.3 (CH_2), 36.1 (CH_2), 32.4 (CH_2), 31.1 (CH_2), 12.0 (2 CH_2 cp).

HRMS (ESI): calcd. for $\text{C}_{20}\text{H}_{22}\text{O}_2\text{Na}^+$ [$\text{M}+\text{Na}$] $^+$ 317.1512, found m/z 317.1515.

Table 1, Entry 9: Reaction of **1a** with **2e** in CDCl_3 .



A solution of cyclopropanol **1a** (6.1 mg, 0.0375 mmol) in anhydrous CDCl_3 (0.37 mL) was mixed with solution of reagent **2e** (26 mg, 0.04 mmol, 1.05 equiv.) in anhydrous CDCl_3 (0.37 mL) and progress of the reaction was monitored by ^1H NMR spectroscopy. Initial concentrations of both reactants nearly equal to 0.05 M. Conversion of starting materials **1a**, **2e** and accumulation of product **3e** were calculated from the integral intensities of the corresponding signals. Thus, consumption of **1a** was followed by its characteristic signals at 1.88, 0.77, 0.46 ppm, consumption of **2e** – by the signal at 8.26 ppm, accumulation of product **3e** – by its signal at 3.04 ppm. Full consumption of the starting material **1a** was observed within 100 min.

According to ^1H and ^{13}C NMR analysis (see Figures S1 and S2 below), the reaction mixture after the completion of reaction contained mixed anhydride **3e**, 2,4,6-trichlorobenzoic acid, iodobenzene and ethylene as reaction products (see copies of NMR spectra below). By integration of ^1H NMR spectrum, yield of **3e** can be estimated as 98%. The corresponding β -acyloxy ketone by-product **5e** has a characteristic signal of $\text{CH}_2\text{OCO}_2\text{Ar}$ protons at 4.65 ppm (t, J = 6.2 Hz, 1H) in ^1H NMR spectra and its yield does not exceed 2%. Characteristic NMR resonances of mixed anhydride **3e**: ^1H NMR (400 MHz, CDCl_3) δ = 7.37 (s, 2H, $\text{C}_6\text{H}_2\text{Cl}_3$), 3.04 (m, 2H, PhCH_2), 2.91 (m, 2H, CH_2CO). ^{13}C NMR (100.6 MHz, CDCl_3) δ = 167.2 (CH_2CO), 159.2 (ArCO), 37.11 (CH_2CO), 30.22 (PhCH_2). Signal assignment is based on HSQC and HMBC data (see Figure S3 below). HRMS (ESI): calcd. for $\text{C}_{16}\text{H}_{11}\text{Cl}_3\text{O}_3\text{Na}^+$ [$\text{M}+\text{Na}$] $^+$ 378.9666, found m/z 378.9655.

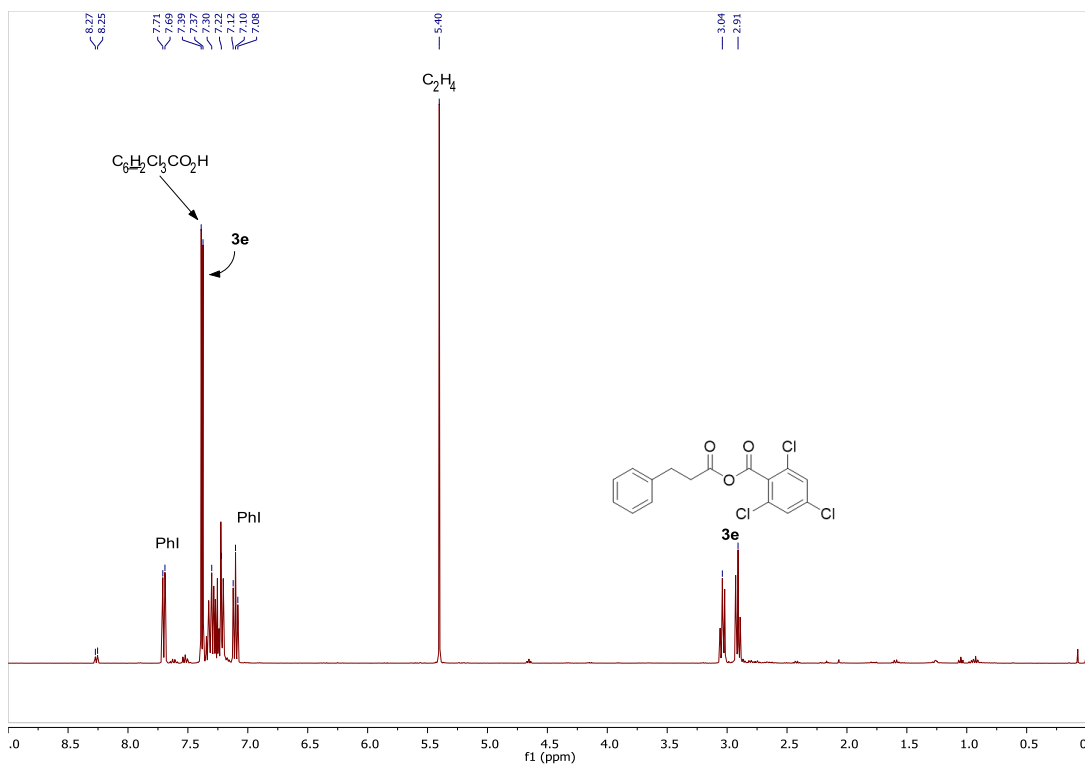


Figure S1. ^1H NMR of the reaction mixture after completion of the reaction with the assignment of the key signals.

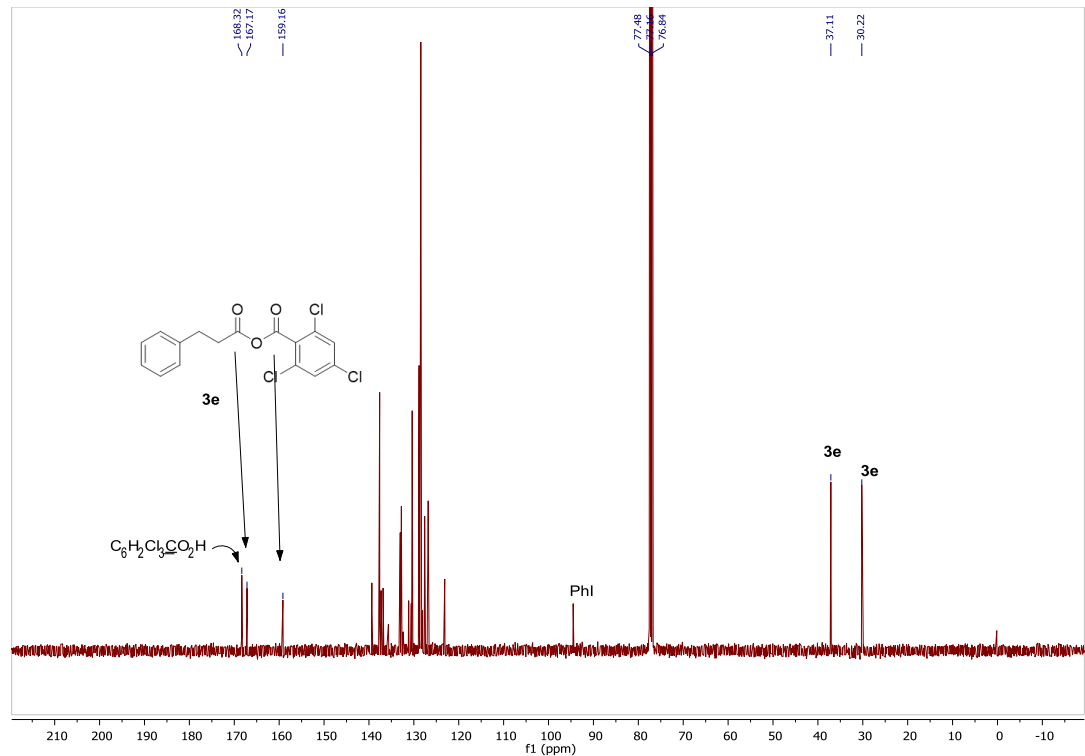
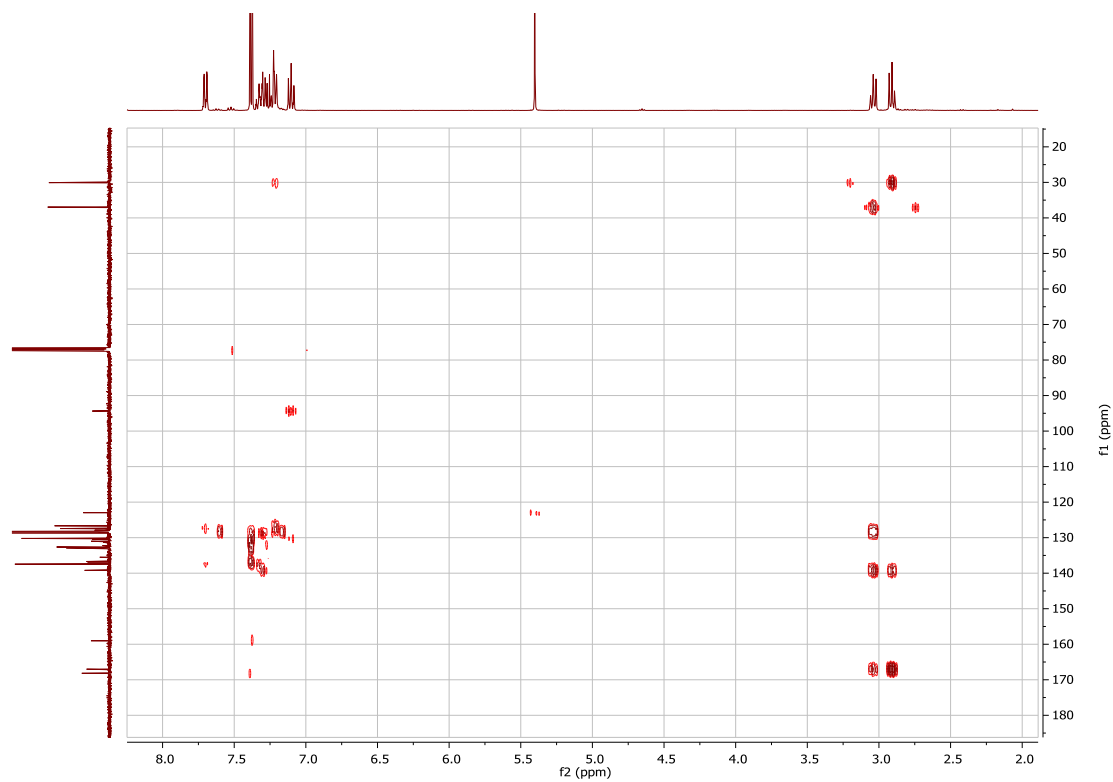


Figure S2. ^{13}C NMR of the reaction mixture after completion of the reaction with the assignment of the key signals.



Expansion:

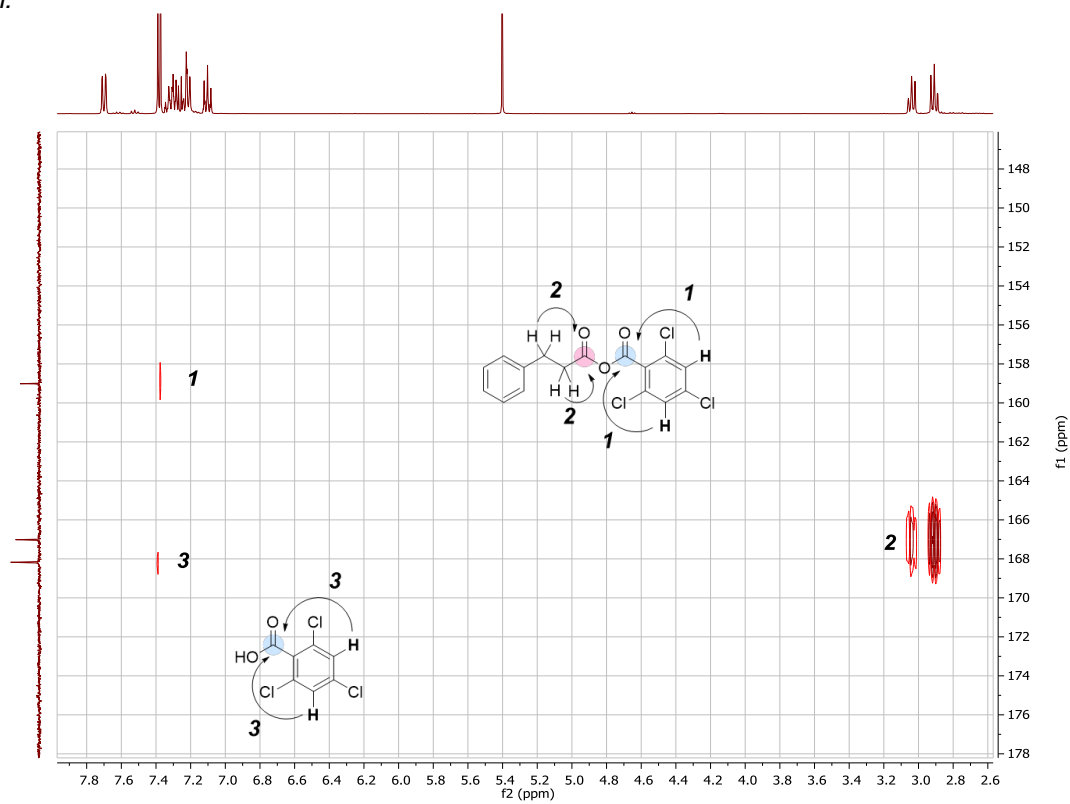


Figure S3. HMBC spectrum of the reaction mixture after completion of the reaction with the assignment of the key correlations.

2. Characterization of by-products

3-Oxoundecyl acetate: isolated in 12% yield in the reaction of 1-octylcyclopropanol **1b** with PhI(OAc)₂ without subsequent treatment of the reaction mixture with benzylamine (Table 2, Entry 1). IR (liquid film) cm⁻¹ 1746, 1719, 1238. ¹H NMR (400 MHz, CDCl₃) δ = 4.31 (t, *J* = 6.3 Hz, 2H), 2.71 (t, *J* = 6.3 Hz, 2H), 2.41 (t, *J* = 7.4 Hz, 2H), 2.01 (s, 3H), 1.44-1.06 (m, 12H), 0.86 (t, *J* = 6.8 Hz, 3H). ¹³C NMR (100.6 MHz, CDCl₃) δ = 208.2, 171.0, 59.6, 43.4, 41.4, 31.9, 29.4, 29.3, 29.2, 23.7, 22.7, 20.9, 14.2.

12-Hydroxydodecan-3-one (27): was obtained in 81% yield in reaction of 1-(9-hydroxynonyl)cyclopropan-1-ol **1g** with scandium(III) triflate (Table 3, Entry 1) in a mixture of acetonitrile and tetrahydrofuran (17 : 1 by volume). M.p. 48.1-48.5 °C; IR (KBr) cm⁻¹ 3339, 3236, 1711, 1701. ¹H NMR (400 MHz, CDCl₃) δ = 3.61 (t, *J* = 6.6 Hz, 2H), 2.44-2.33 (m, 4H), 1.68 (br.s, 1H), 1.60-1.48 (m, 4H), 1.37-1.19 (m, 10H), 1.02 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (100.6 MHz, CDCl₃) δ = 212.0, 63.1, 42.5, 36.0, 32.9, 29.5, 29.4, 29.4, 29.4, 25.8, 24.0, 8.0. HRMS (ESI) *m/z* calcd for C₁₂H₂₅O₂⁺ [M+H]⁺ 201.1849, found 201.1881.

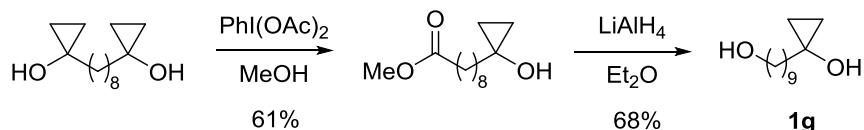
1,12-Dioxacyclodocosane-2,13-dione (26a). White solid. IR (liquid film) cm⁻¹ 1735. ¹H NMR (400 MHz, CDCl₃) δ = 4.10 (t, *J* = 5.8 Hz, 4H), 2.31 (t, *J* = 6.9 Hz, 4H), 1.70-1.55 (m, 8H), 1.43-1.19 (m, 20H). ¹³C NMR (100.6 MHz, CDCl₃) δ = 174.0, 64.2, 35.0, 29.5, 29.2, 29.2, 29.1, 28.8, 26.2, 25.6. HRMS (ESI) *m/z* calcd for C₂₀H₃₇O₄⁺ [M+H]⁺ 341.2686, found 341.2663. Spectral data are in accordance with those reported [1, 2].

1,14-Dioxacyclohexacosane-2,15-dione (26b). White solid. IR (liquid film) cm⁻¹ 1735. ¹H NMR (400 MHz, CDCl₃) δ = 4.10 (t, *J* = 5.8 Hz, 4H), 2.31 (t, *J* = 7.1 Hz, 4H), 1.73-1.54 (m, 8H), 1.48-1.16 (m, 28H). ¹³C NMR (100.6 MHz, CDCl₃) δ = 174.2, 64.3, 34.9, 29.7, 29.6, 29.6, 29.3, 29.1, 28.7, 26.2, 25.5. Spectral data are in accordance with those reported [1].

3. Preparation of cyclopropanols

Cyclopropanols **1a-d** have been prepared by Kulinkovich cyclopropanation of the corresponding carboxylic esters [3] and previously reported [4, 5]. Peptide cyclopropanol **1e** and bicyclic cyclopropanols **1f,i** were prepared by following the published protocols [6, 7]. Preparation of cyclopropanols **1g** and **1h** is described below.

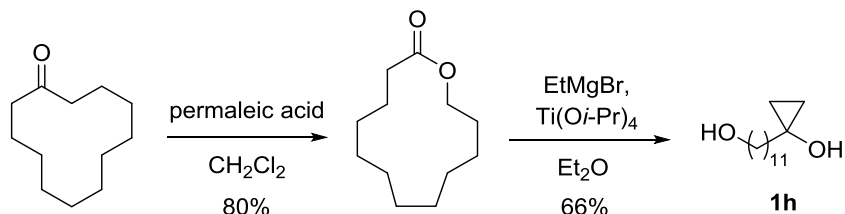
1-(9-Hydroxynonyl)cyclopropan-1-ol (**1g**)



To a solution of 1,1'-(octane-1,8-diyl)bis(cyclopropan-1-ol) (0.946 g, 4.2 mmol) in anhydrous methanol (53 mL) a solution of (diacetoxyiodo)benzene (1.348 g, 4.2 mmol) in methanol (19 mL) was added dropwise within 1 h. After reaction finished (TLC control) the reaction mixture was diluted with water (30 mL), extracted with dichloromethane (5×20 mL). Combined organic extracts were washed with brine (2×10 mL) and dried with Na_2SO_4 . After removing the solvents under reduced pressure and purifying the residue by silica gel column chromatography (eluent: PE, then PE / EtOAc), methyl 9-(1-hydroxycyclopropyl)nonanoate was obtained as white solid (0.434 g, 61% yield, 74% conversion). M.p. 38.7-39.4 °C. IR (KBr) cm^{-1} 3338, 3255, 1727. ^1H NMR (400 MHz, CDCl_3) δ = 3.66 (s, 3H), 2.29 (t, J = 7.5 Hz, 2H), 1.86 (br.s, 1H), 1.69-1.56 (m, 2H), 1.56-1.43 (m, 4H), 1.37-1.26 (m, 8H), 0.72 (dd, J = 6.2, 5.2 Hz, 2H), 0.42 (dd, J = 6.2, 5.2 Hz, 2H). ^{13}C NMR (100.6 MHz, CDCl_3) δ = 174.5, 56.0, 51.6, 38.4, 34.2, 29.7, 29.6, 29.3, 29.2, 26.0, 25.1, 13.6.

To a cooled to 0 °C suspension of lithium aluminium hydride (81 mg, 2.1 mmol) in anhydrous diethyl ether (7 mL) a solution of methyl 9-(1-hydroxycyclopropyl)nonanoate (433 mg, 1.9 mmol) in diethyl ether (5 mL) was added dropwise. After reaction finished (TLC control) the reaction mixture was quenched with an excess of ethyl acetate and washed with 10% sulfuric acid. The aqueous layer was extracted with diethyl ether (3×15 mL). The combined organic extracts were washed successively with saturated aqueous solutions of NaHCO_3 , NaCl and dried with Na_2SO_4 . After removal of the solvents under reduced pressure and purification of the residue by silica gel column chromatography, the target product was obtained as white solid (260 mg, 68% yield). M.p. 55.5-56.1 °C. IR (KBr) cm^{-1} 3332, 3219. ^1H NMR (400 MHz, CDCl_3) δ = 3.63 (t, J = 6.6 Hz, 2H), 1.62-1.43 (m, 7H), 1.39-1.25 (m, 11H), 0.72 (dd, J = 6.4, 5.0 Hz, 2H), 0.43 (dd, J = 6.4, 5.0 Hz, 2H). ^{13}C NMR (100.6 MHz, CDCl_3) δ = 63.2, 56.0, 38.4, 32.9, 29.8, 29.7, 29.7, 29.5, 26.0, 25.9, 13.6.

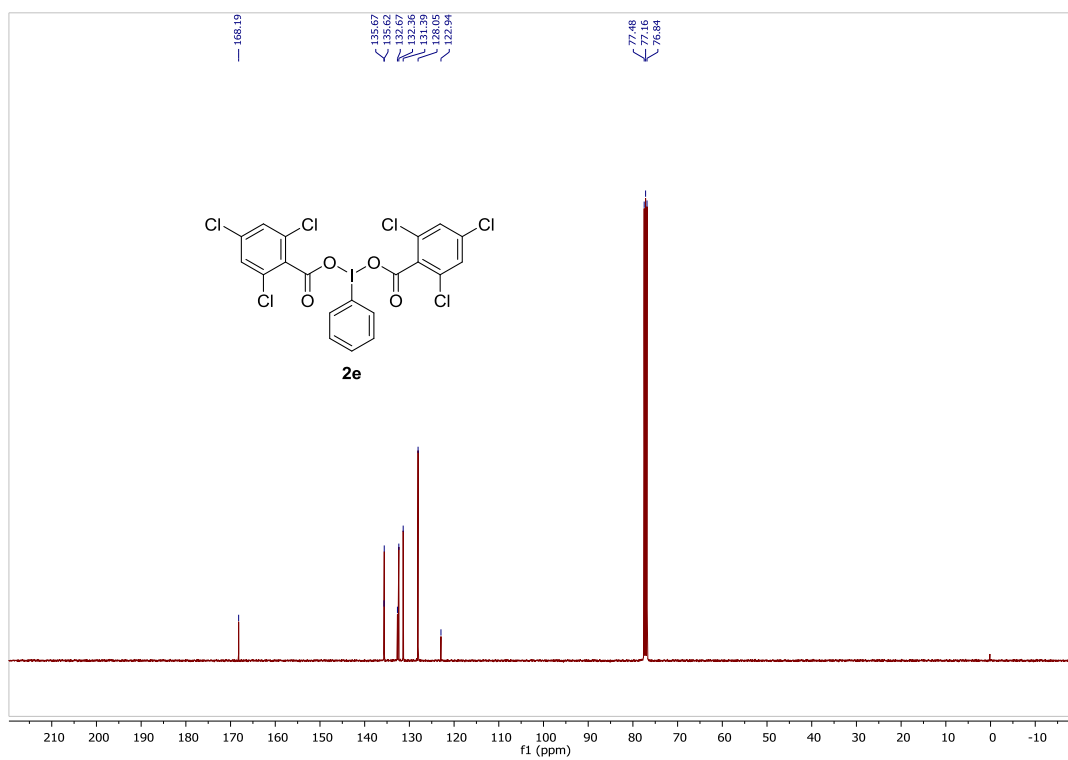
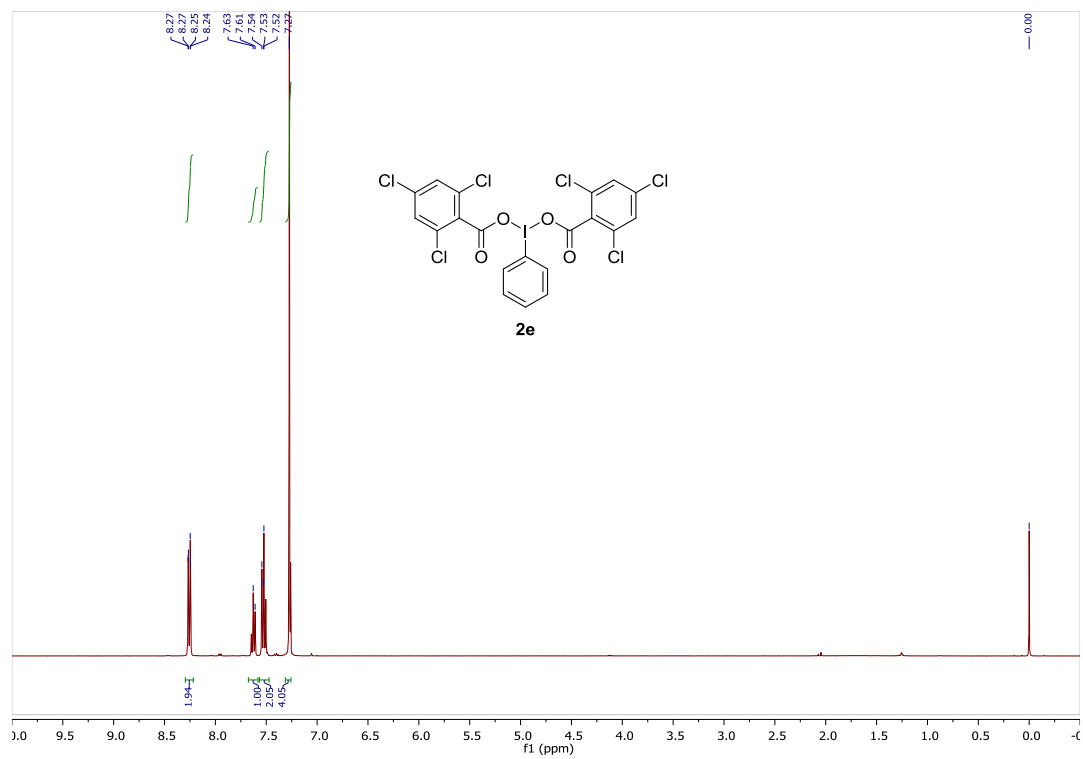
1-(11-Hydroxyundecyl)cyclopropan-1-ol (**1h**)

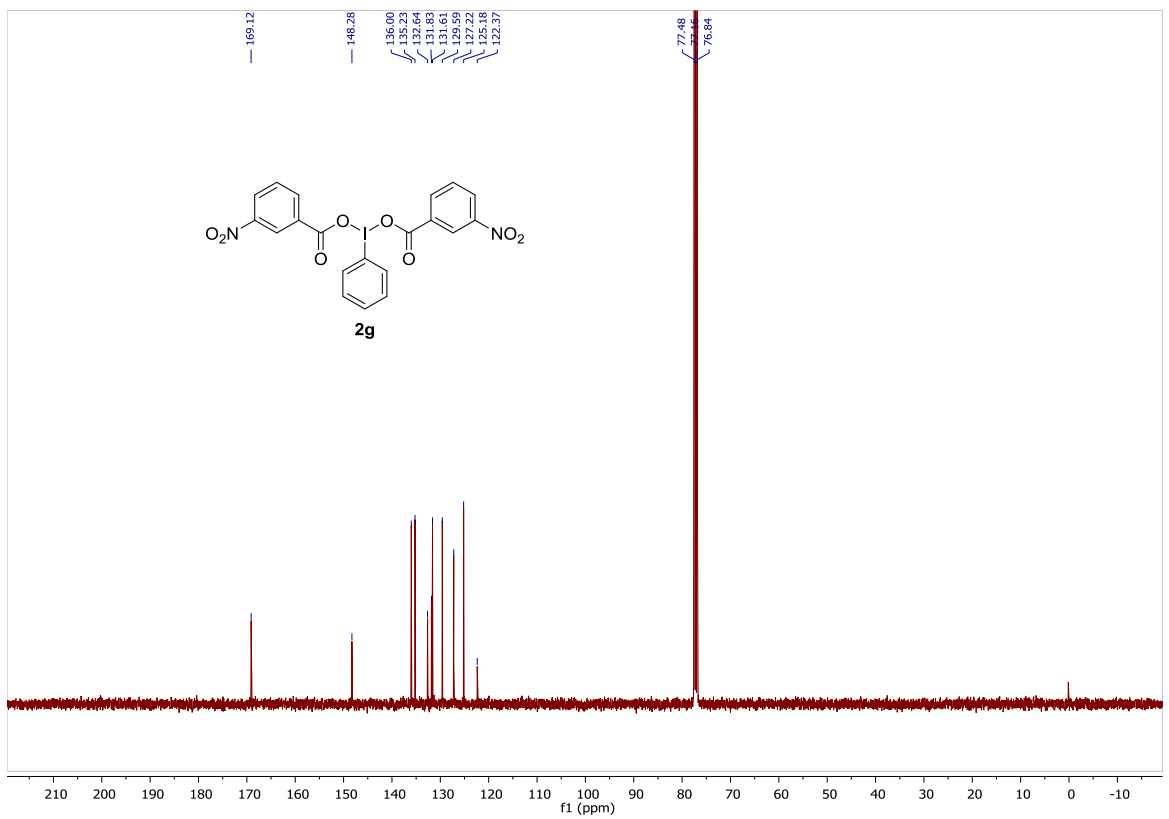
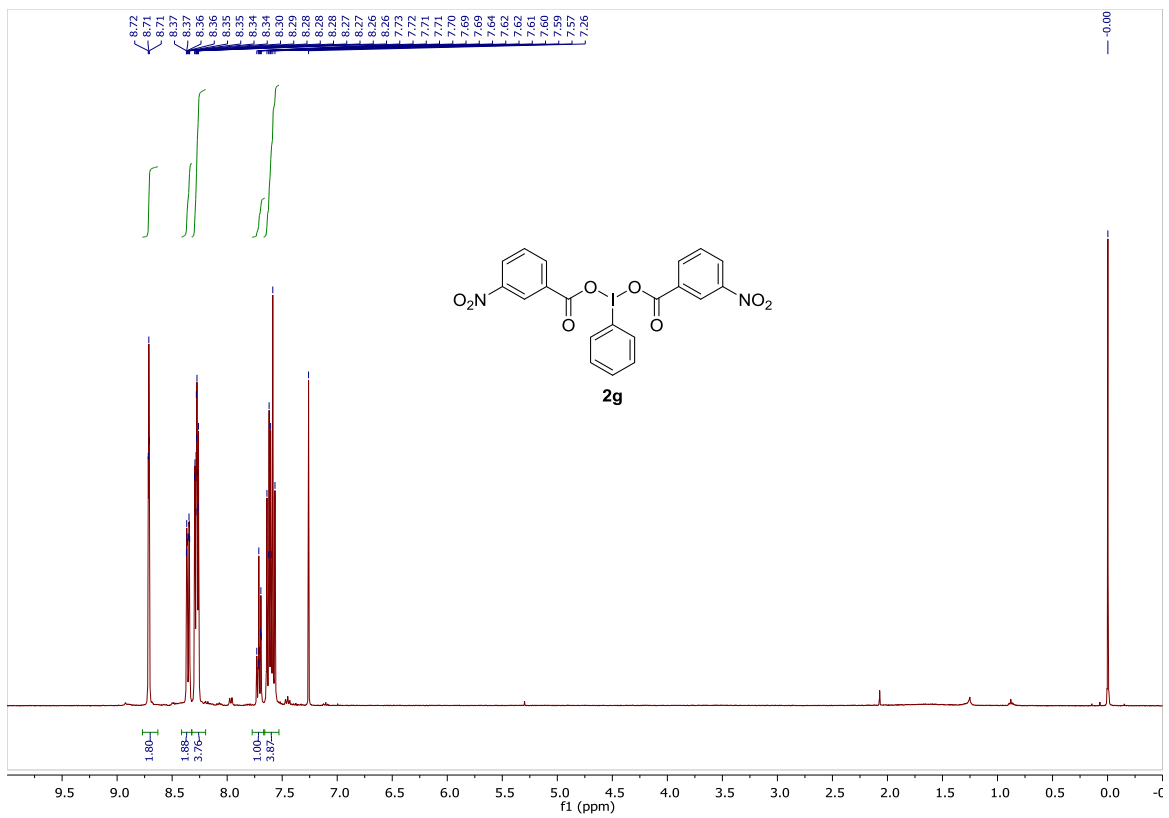


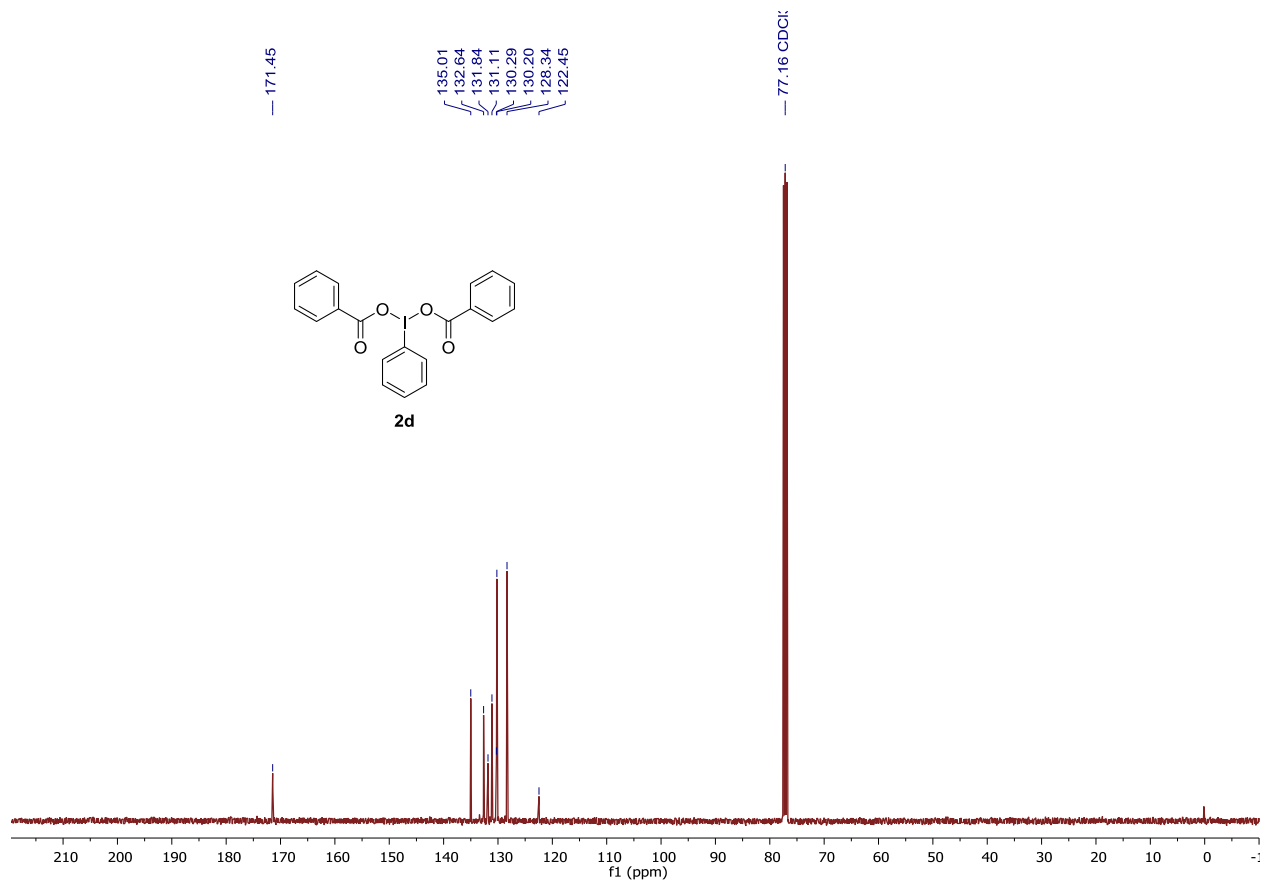
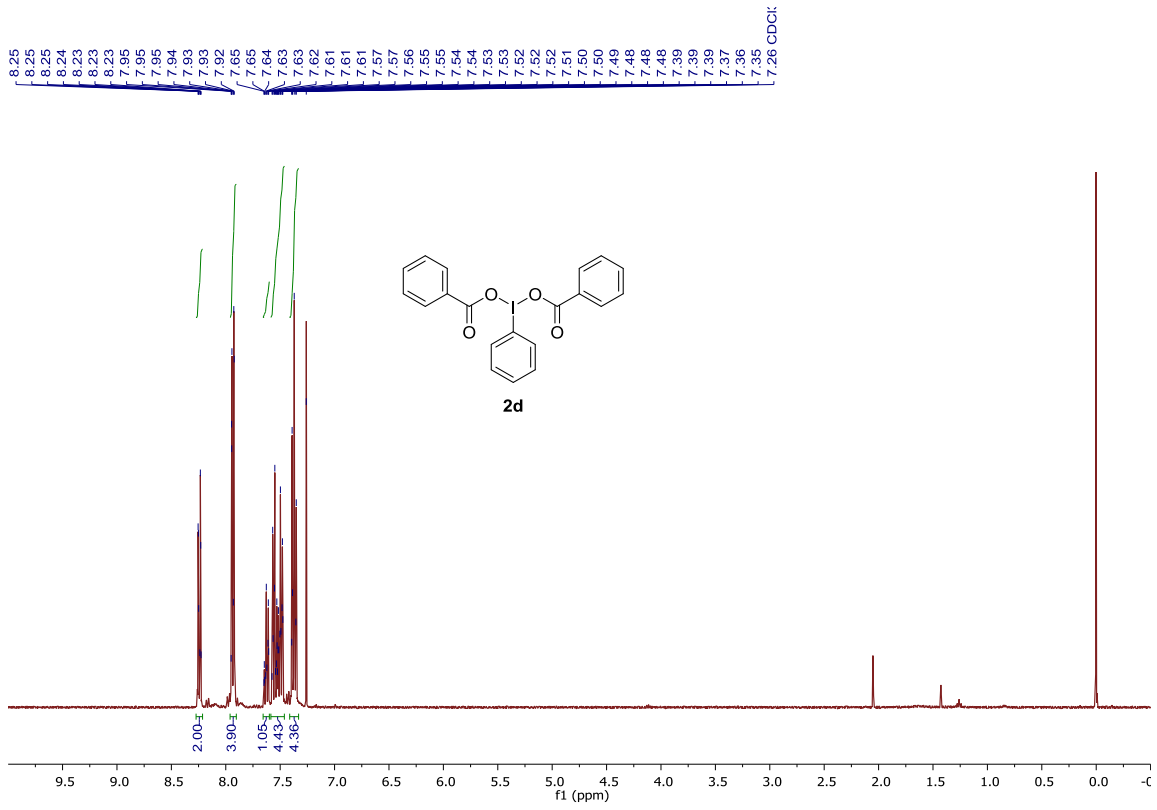
The title compound was prepared in two steps: 1) oxidation of cyclododecanone with permaleic acid by the Baeyer-Villiger reaction to oxacyclotridecan-2-one (80% yield) according to the literature procedure [8]; 2) Kulinkovich hydroxycyclopropanation of oxacyclotridecan-2-one. The procedure of the Kulinkovich hydroxycyclopropanation is as follows: to a solution of oxacyclotridecan-2-one (2.23 g, 11.3 mmol) and titanium (IV) isopropoxide (3.20 g, 11.3 mmol) in anhydrous tetrahydrofuran (13 mL) a solution of

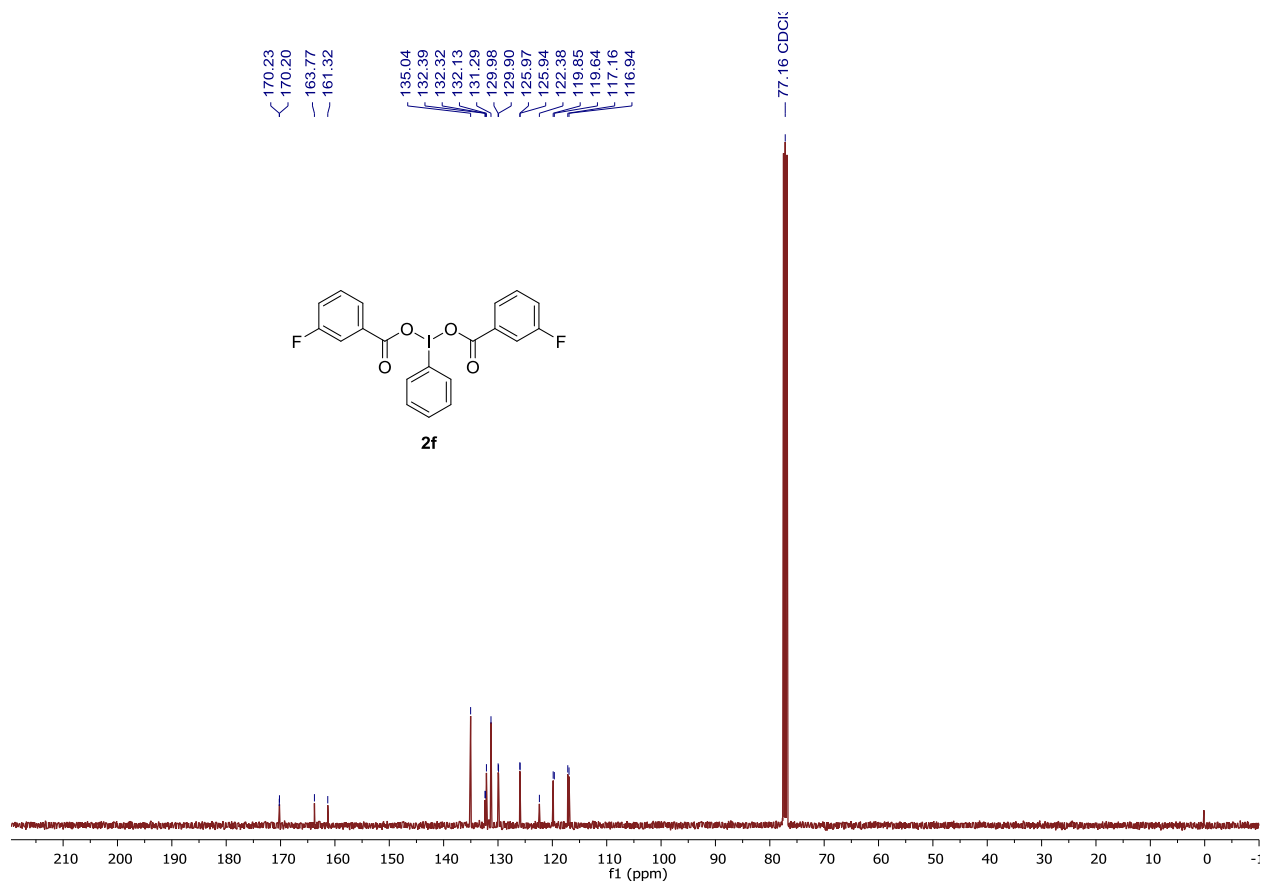
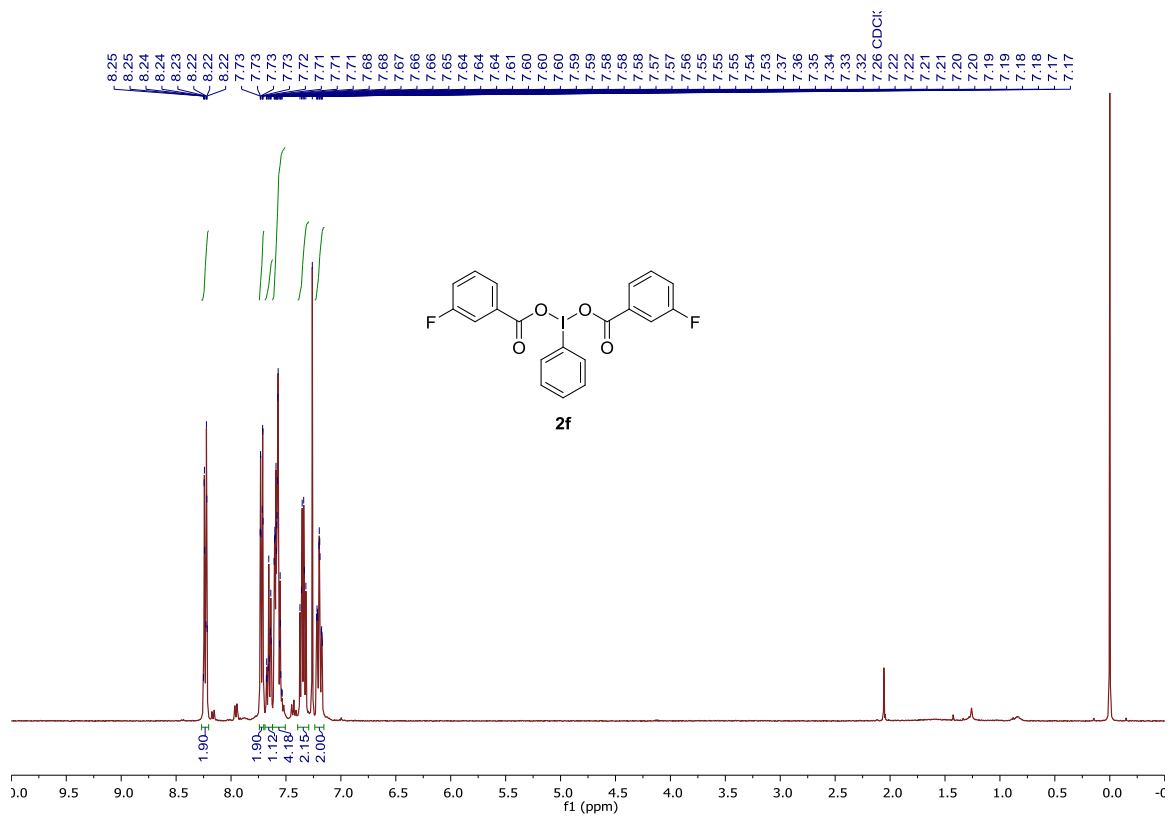
ethylmagnesium bromide (32.4 ml, 1.5 M) was added dropwise at room temperature. After completion of the reaction (TLC control), the mixture was treated with 10% sulfuric acid, the aqueous layer was separated and extracted with diethyl ether (3 × 30 ml). The combined organic extracts were washed sequentially with saturated aqueous NaHCO₃, NaCl and dried over Na₂SO₄. After evaporation of the solvents under reduced pressure and purification of the residue by recrystallization from benzene target product (1.69 g, 66% yield) was obtained. White solid, m.p. 66.7-67.6°C (benzene). IR (KBr) cm⁻¹ 3326, 3219. ¹H NMR (400 MHz, CDCl₃) δ = 3.62 (t, *J* = 6.3 Hz, 2H), 1.64-1.42 (m, 7H), 1.40-1.18 (m, 15H), 0.78-0.63 (m, 2H), 0.47-0.37 (m, 2H). ¹³C NMR (100.6 MHz, CDCl₃) δ = 63.2, 55.9, 38.4, 32.9, 29.8, 29.7, 29.7, 29.5, 26.0, 25.8, 13.6.

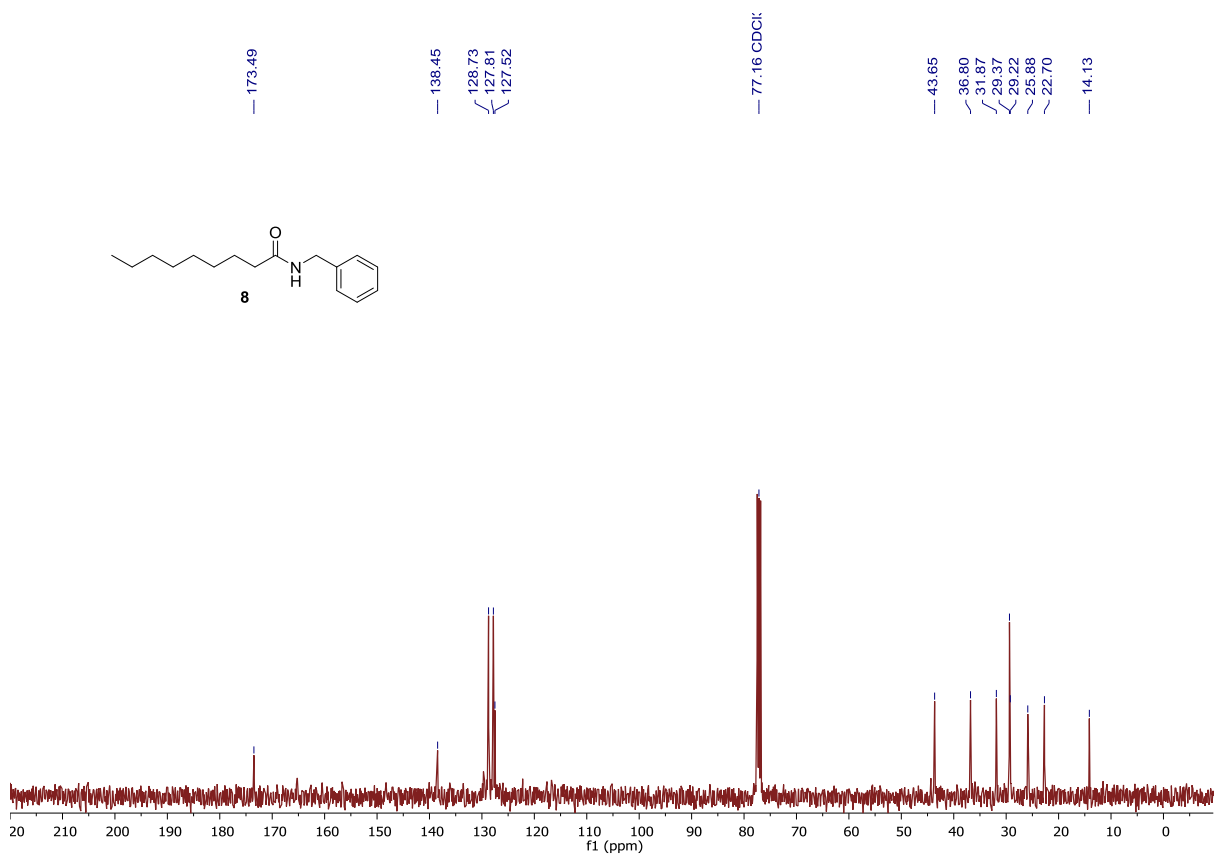
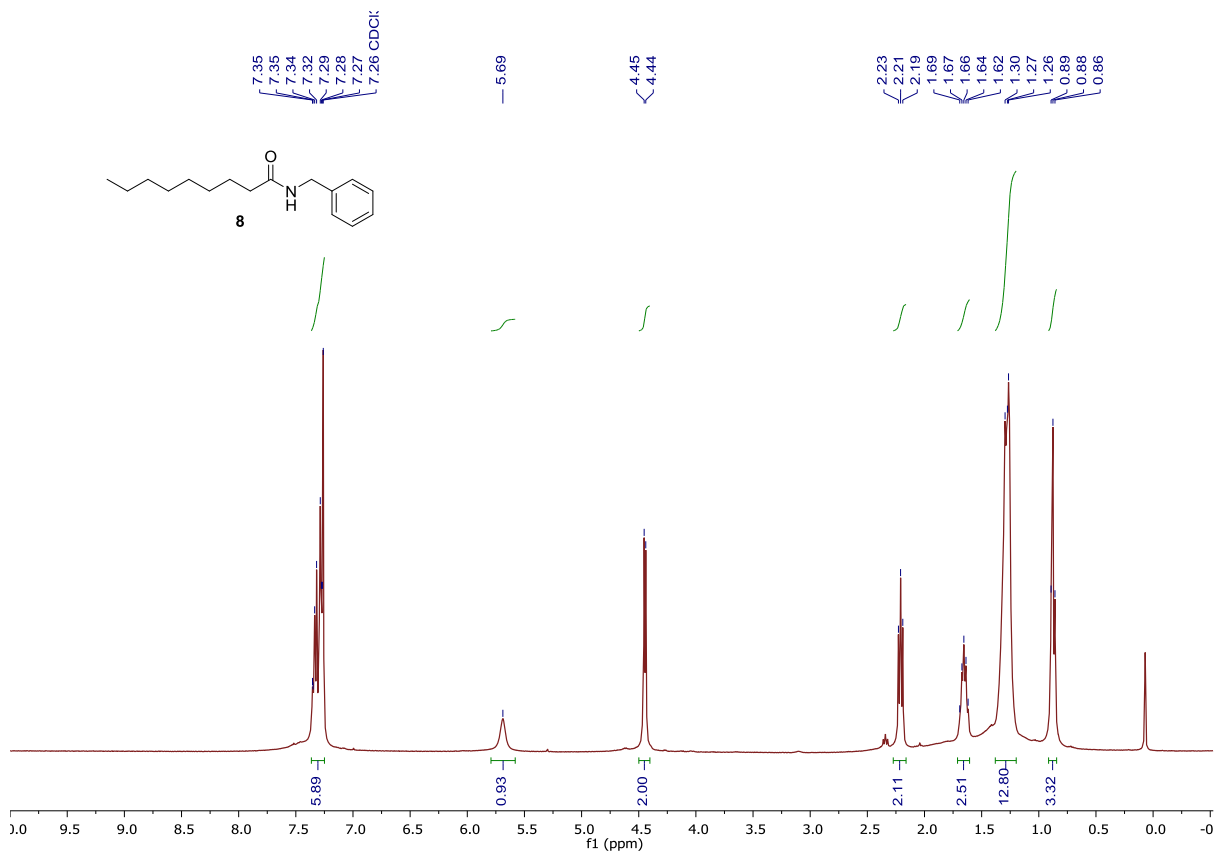
4. Copies of ^1H and ^{13}C NMR spectra

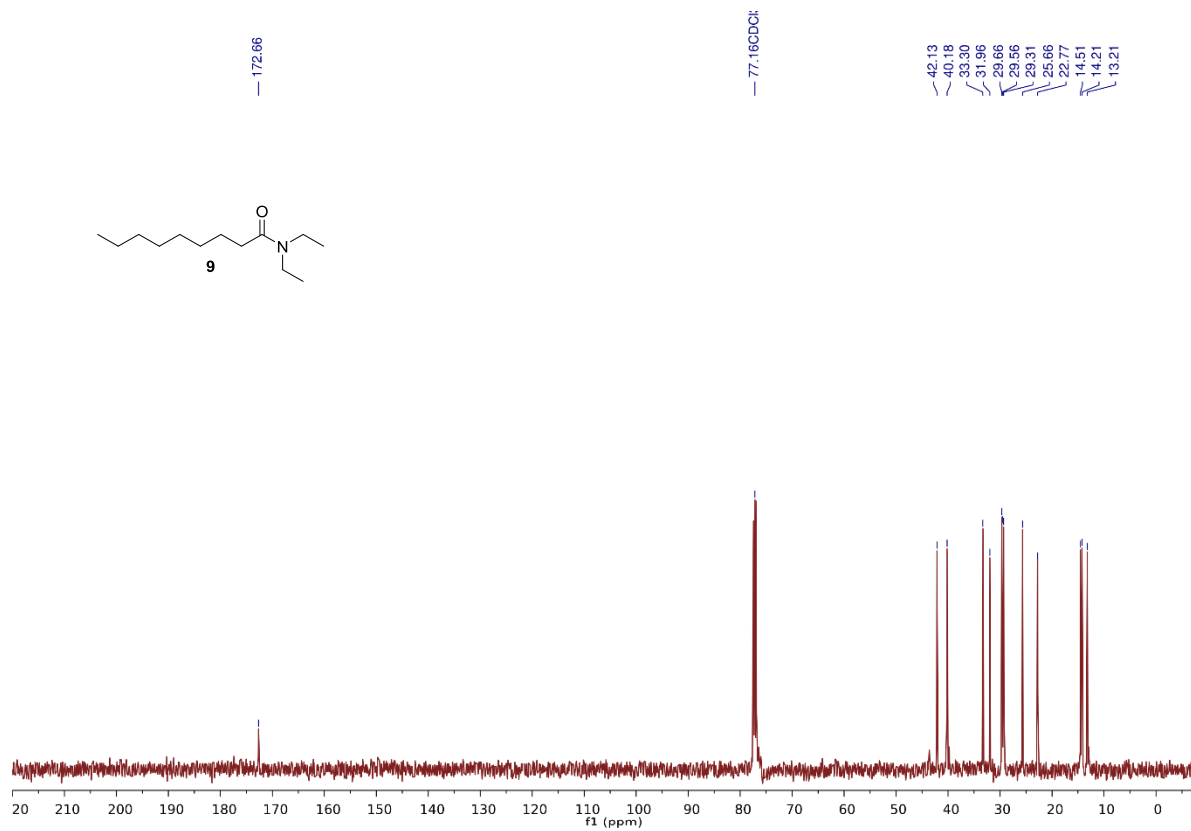
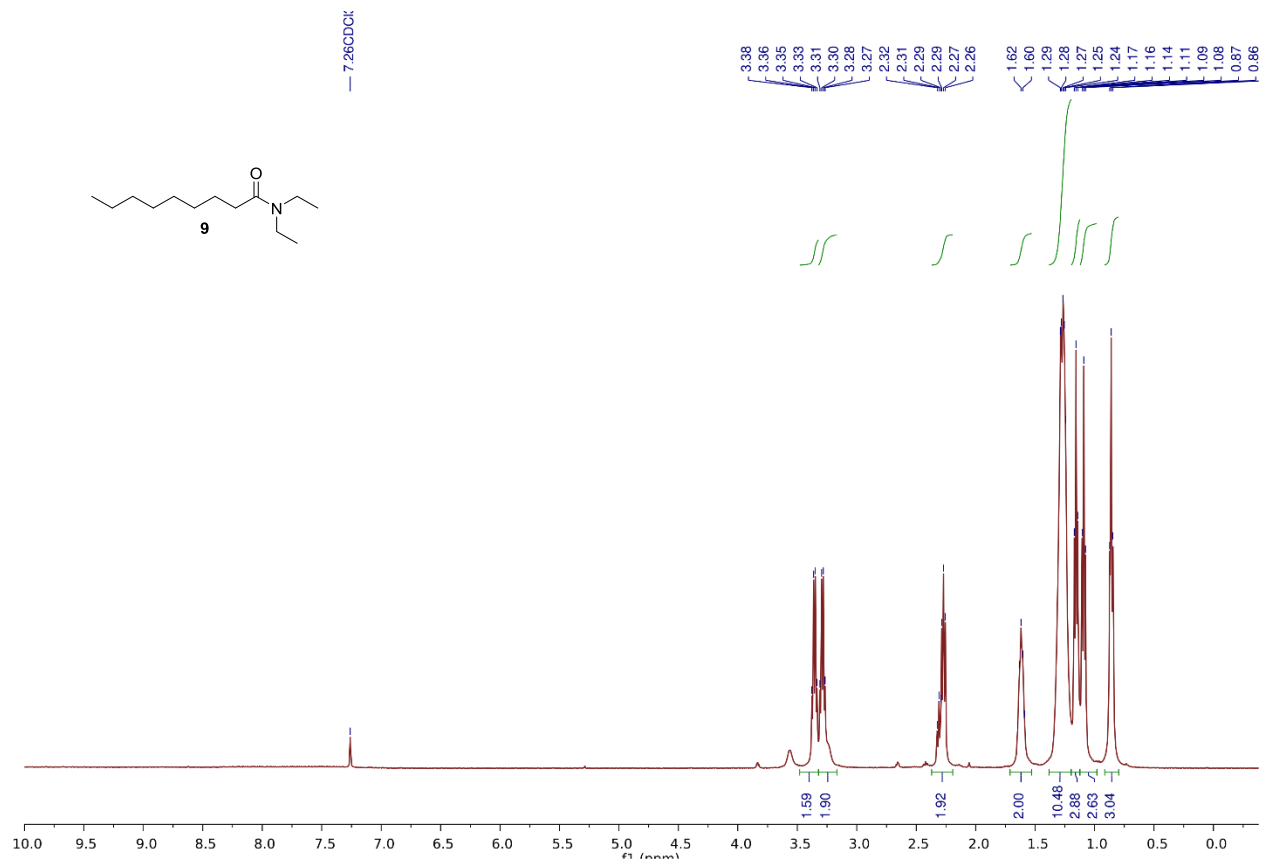


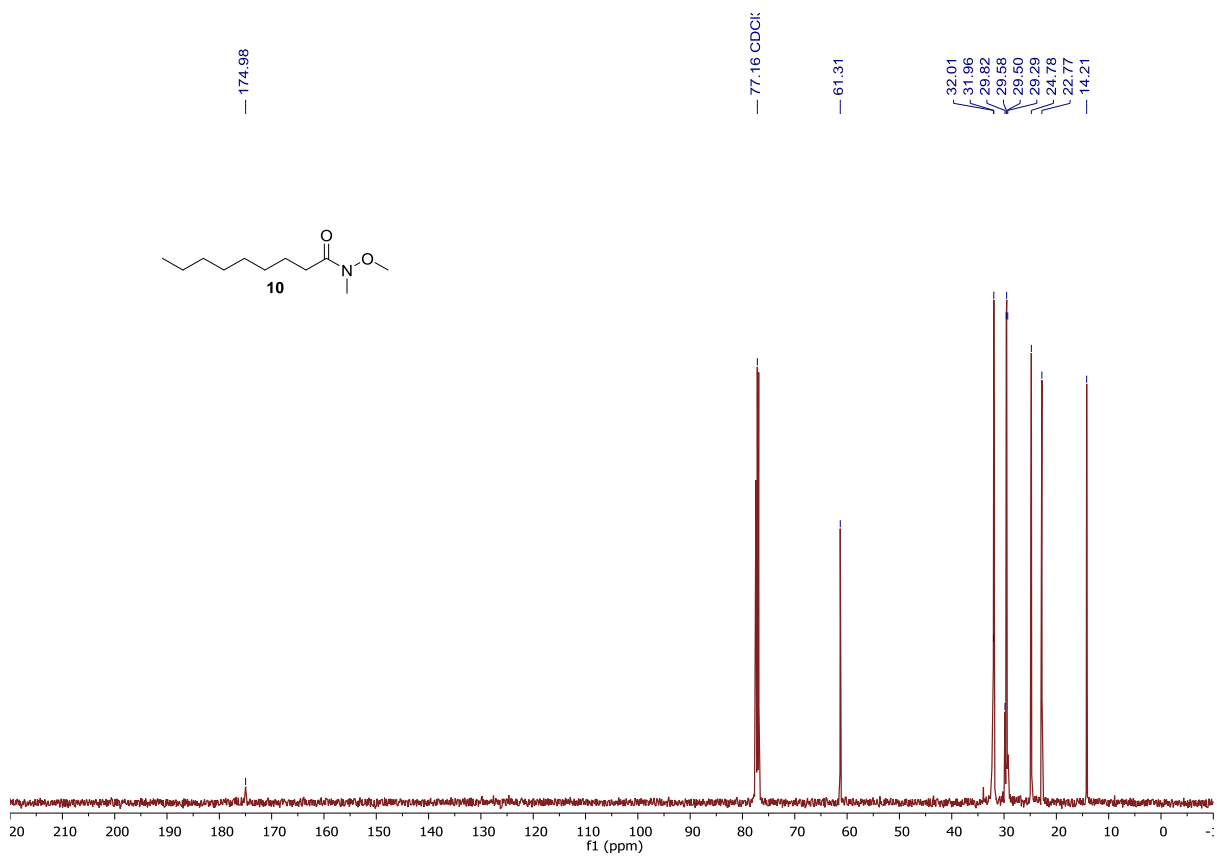
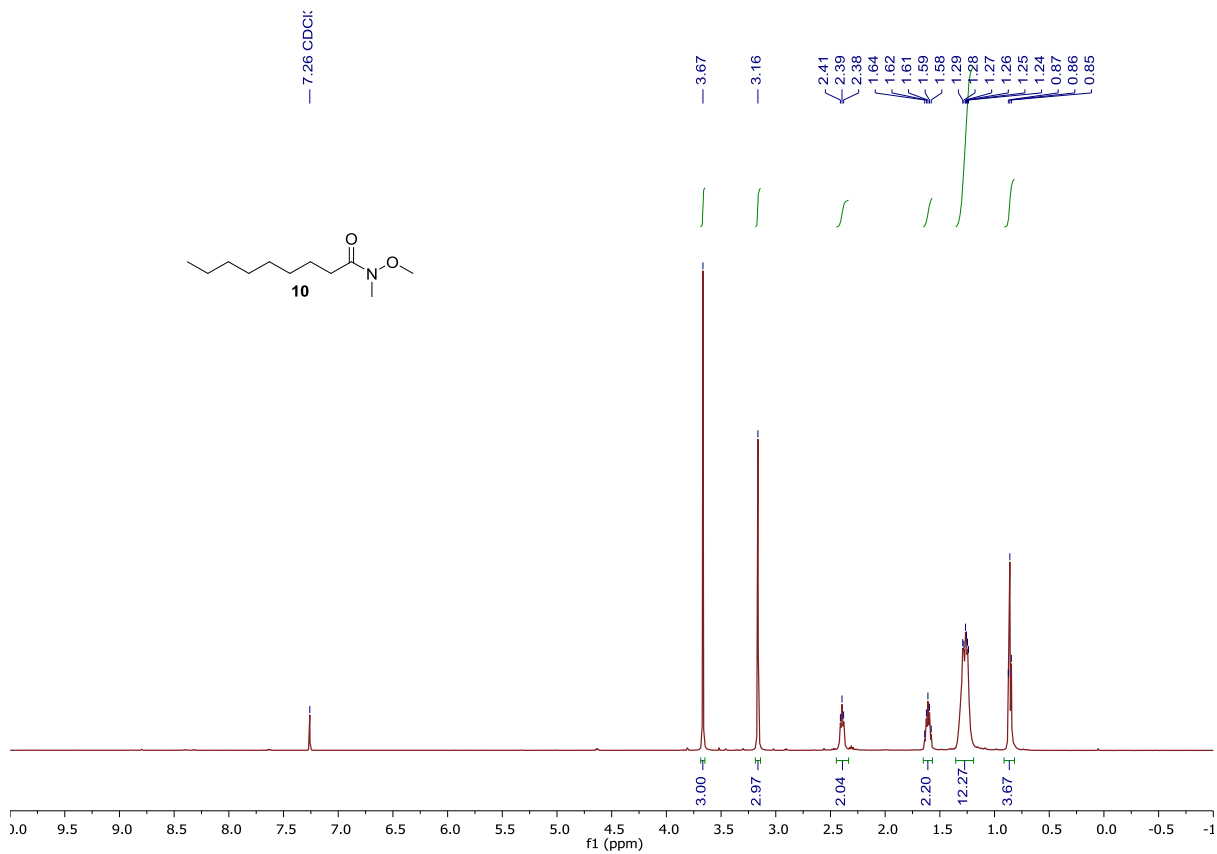


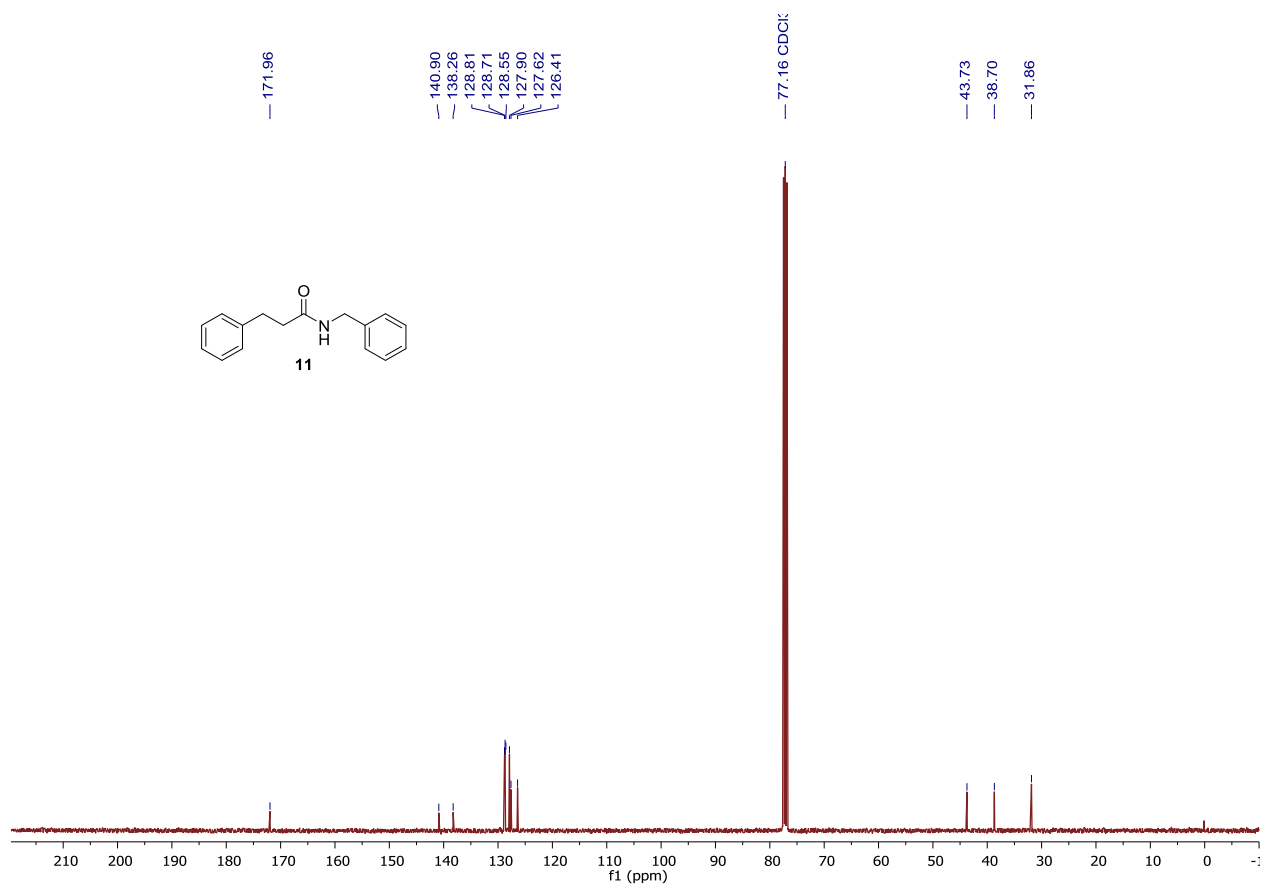
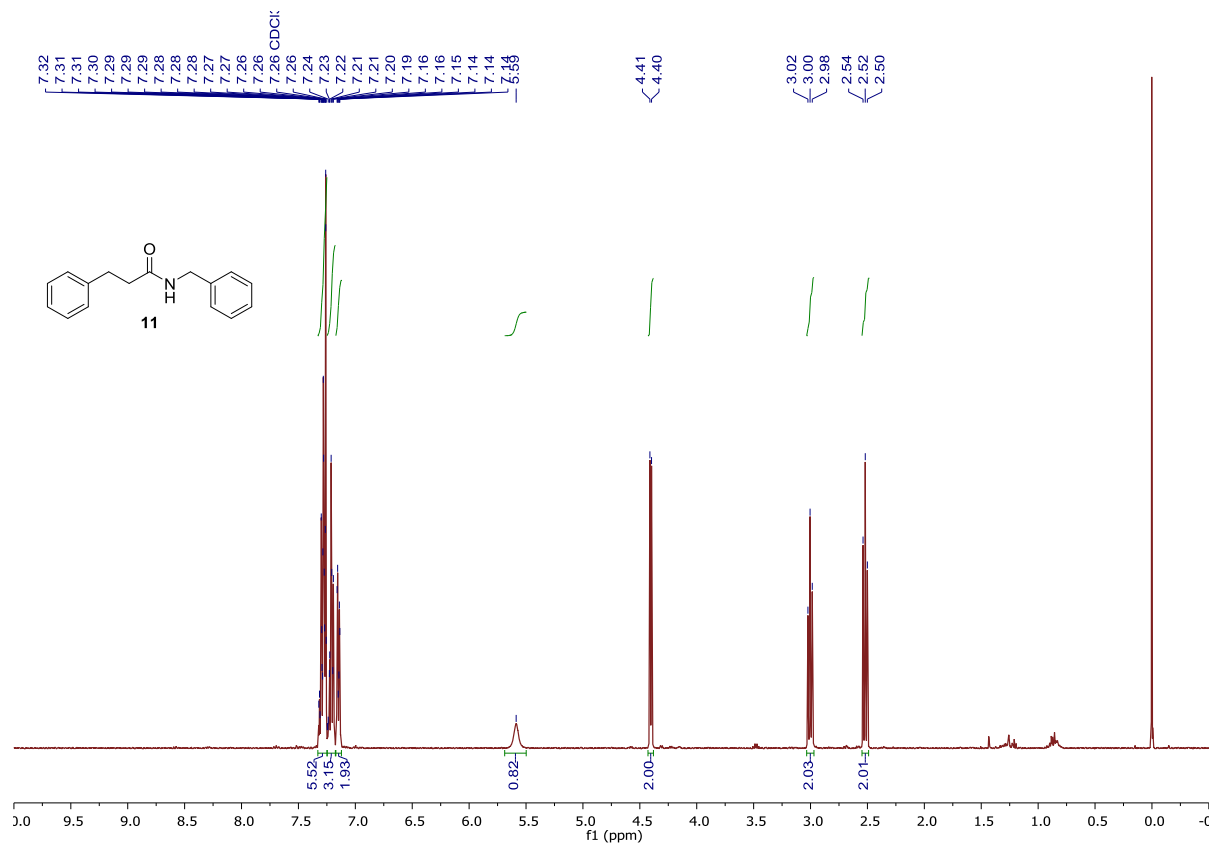


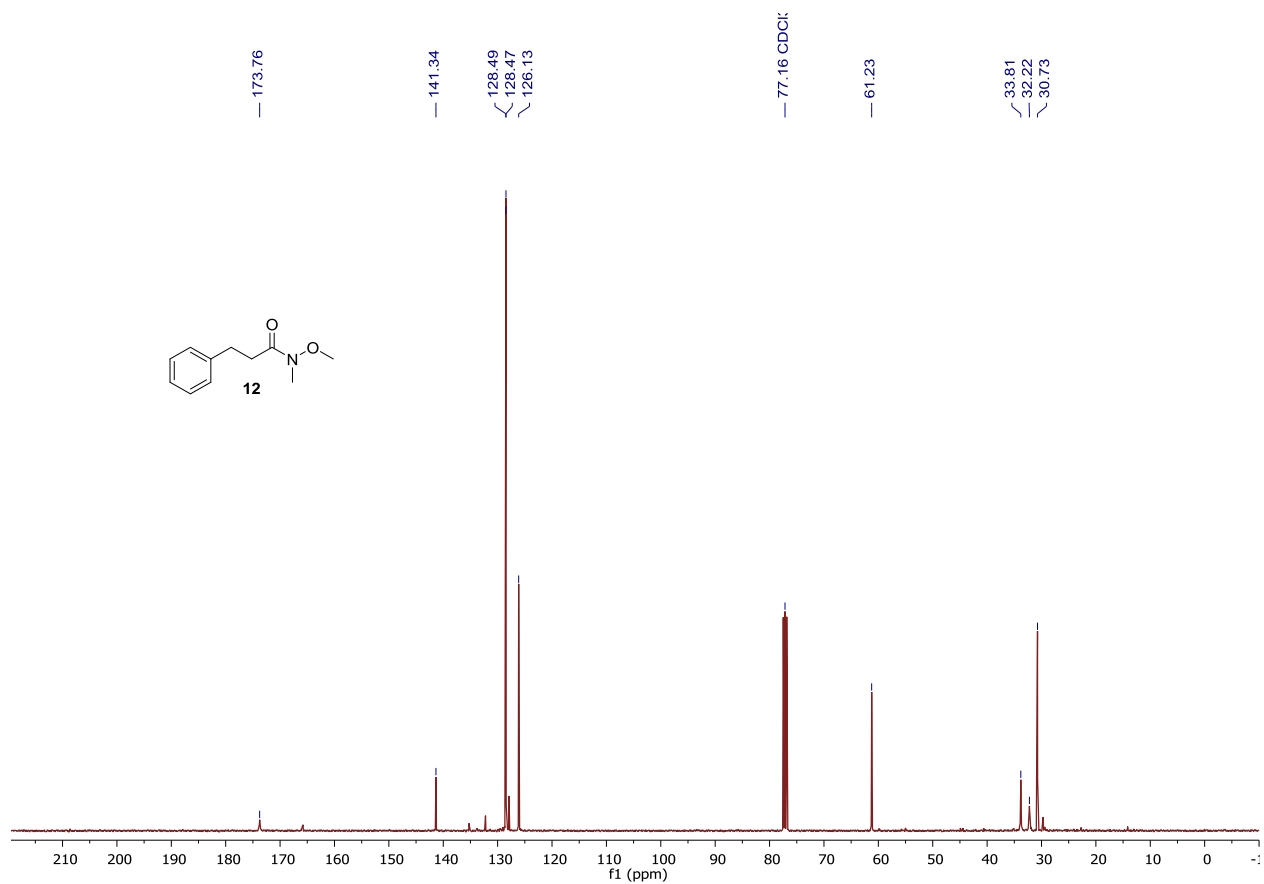
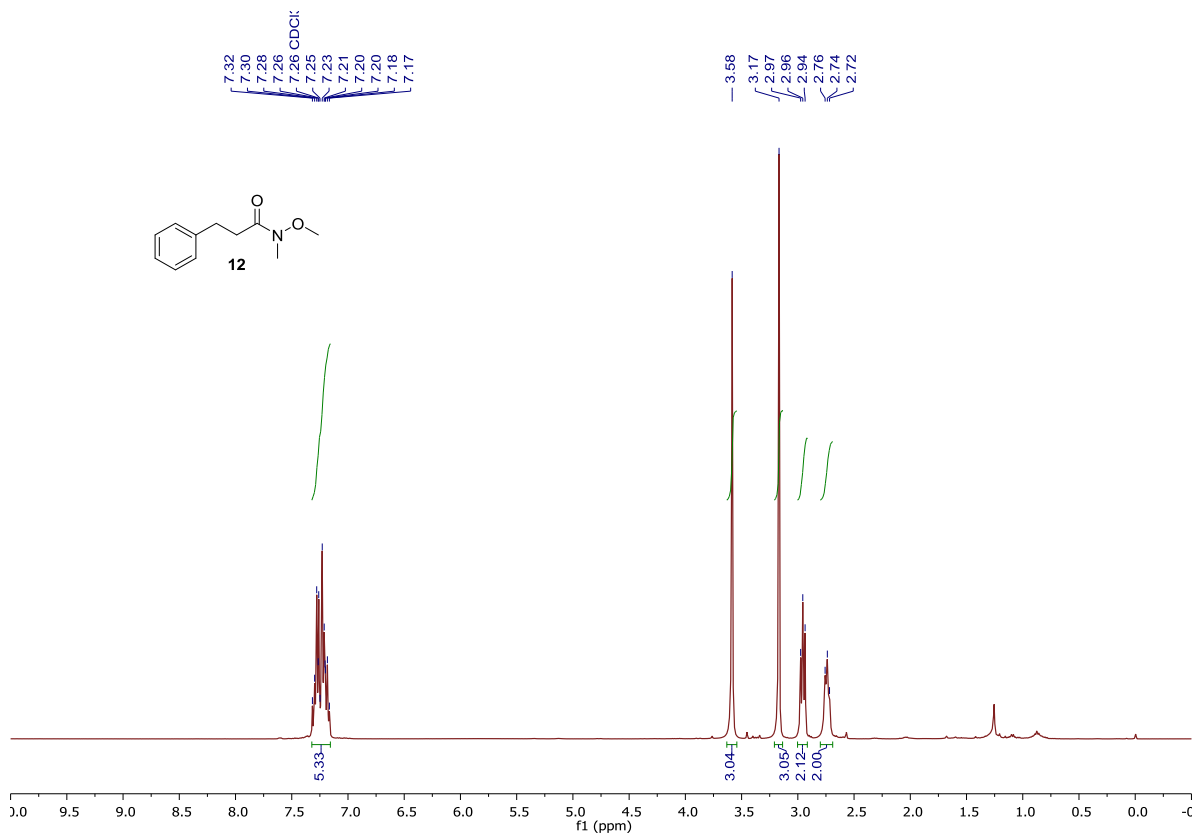


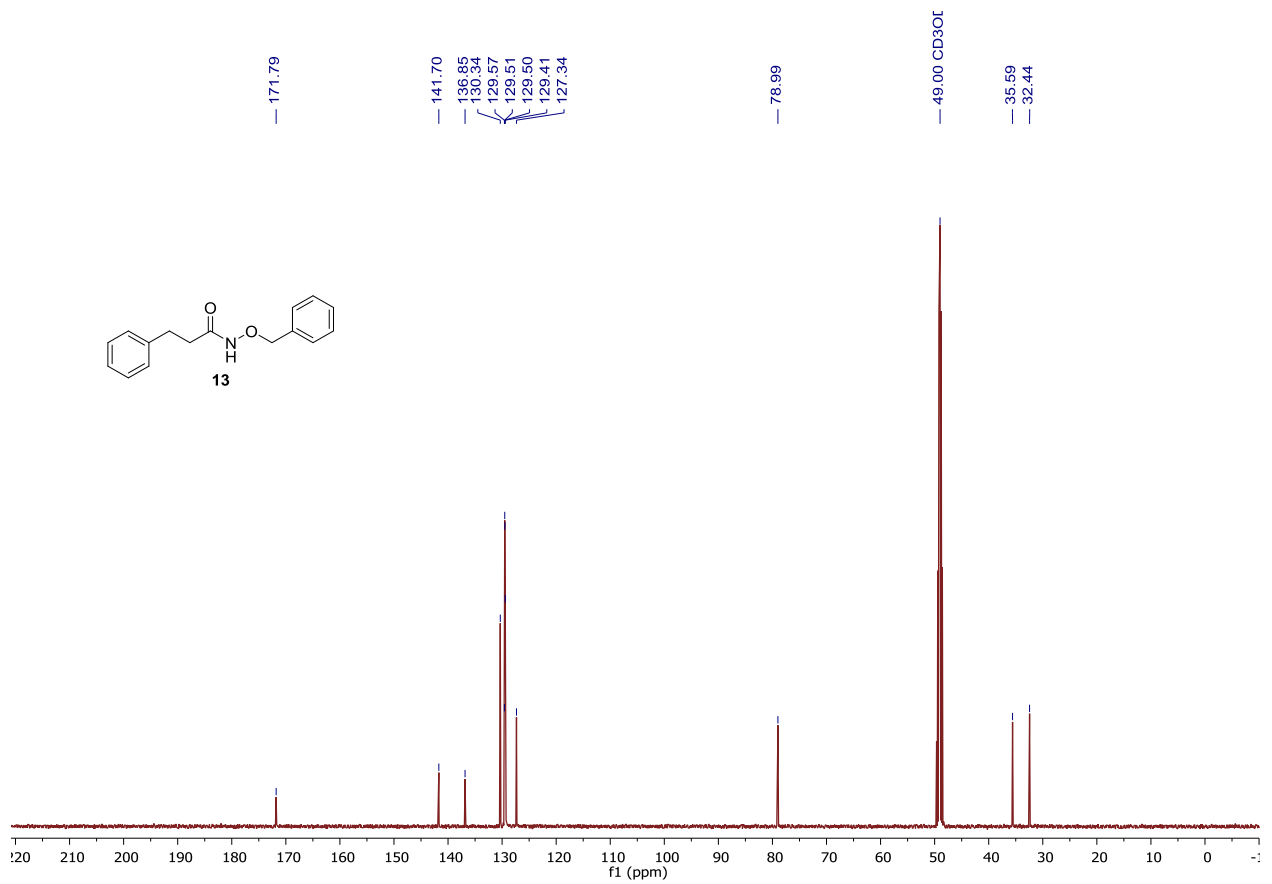
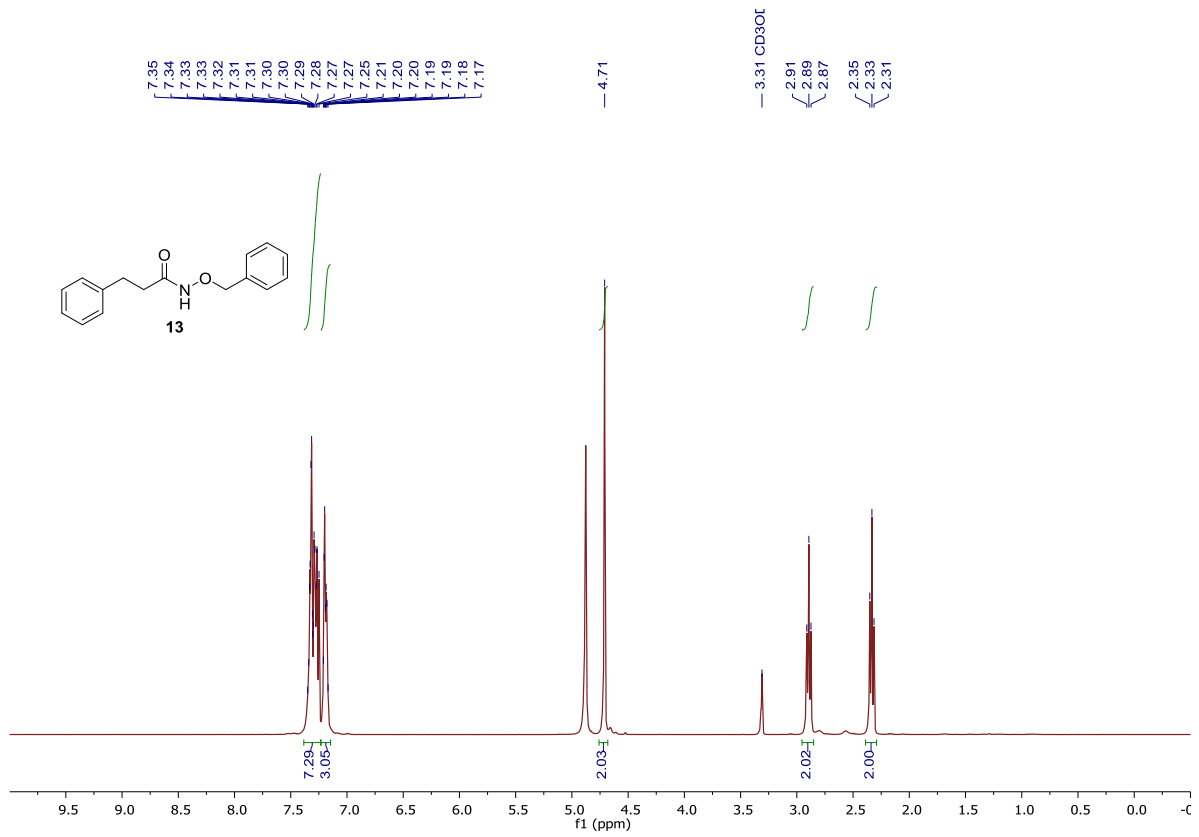


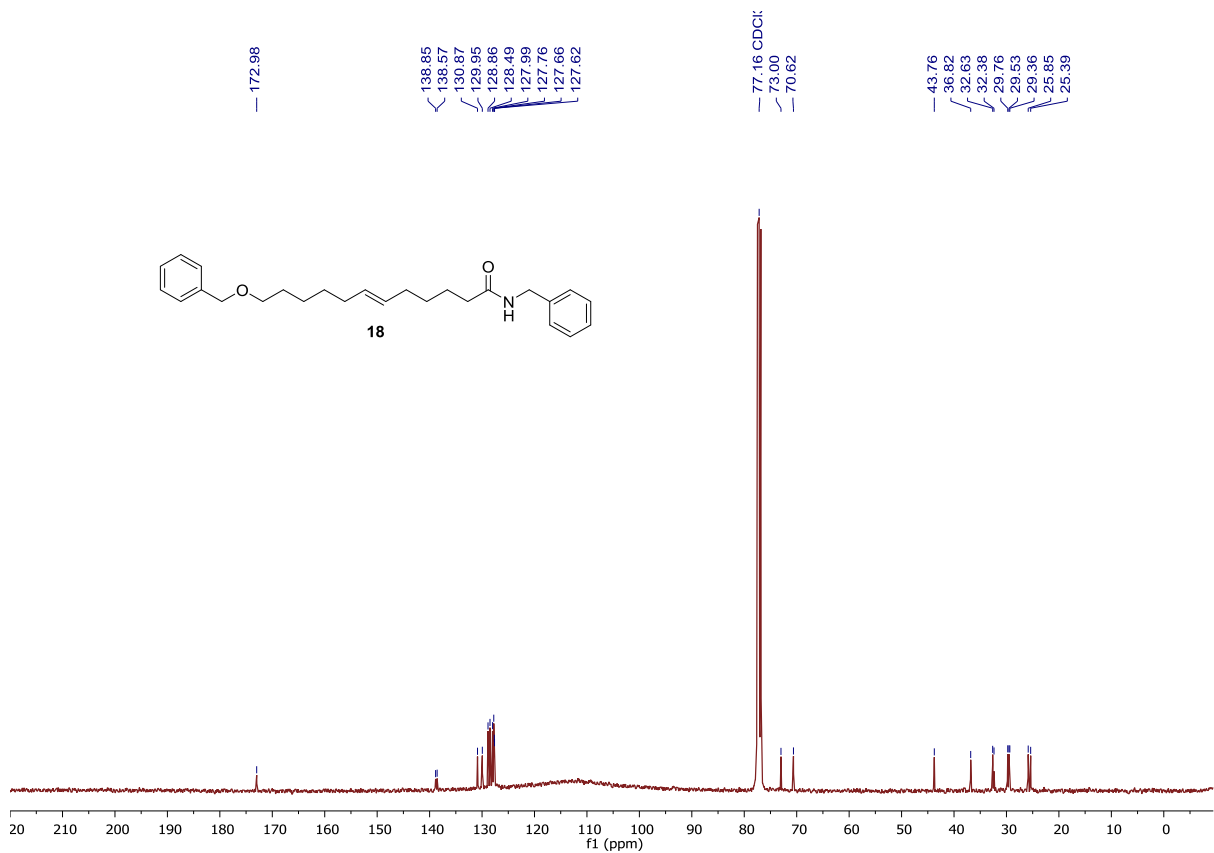
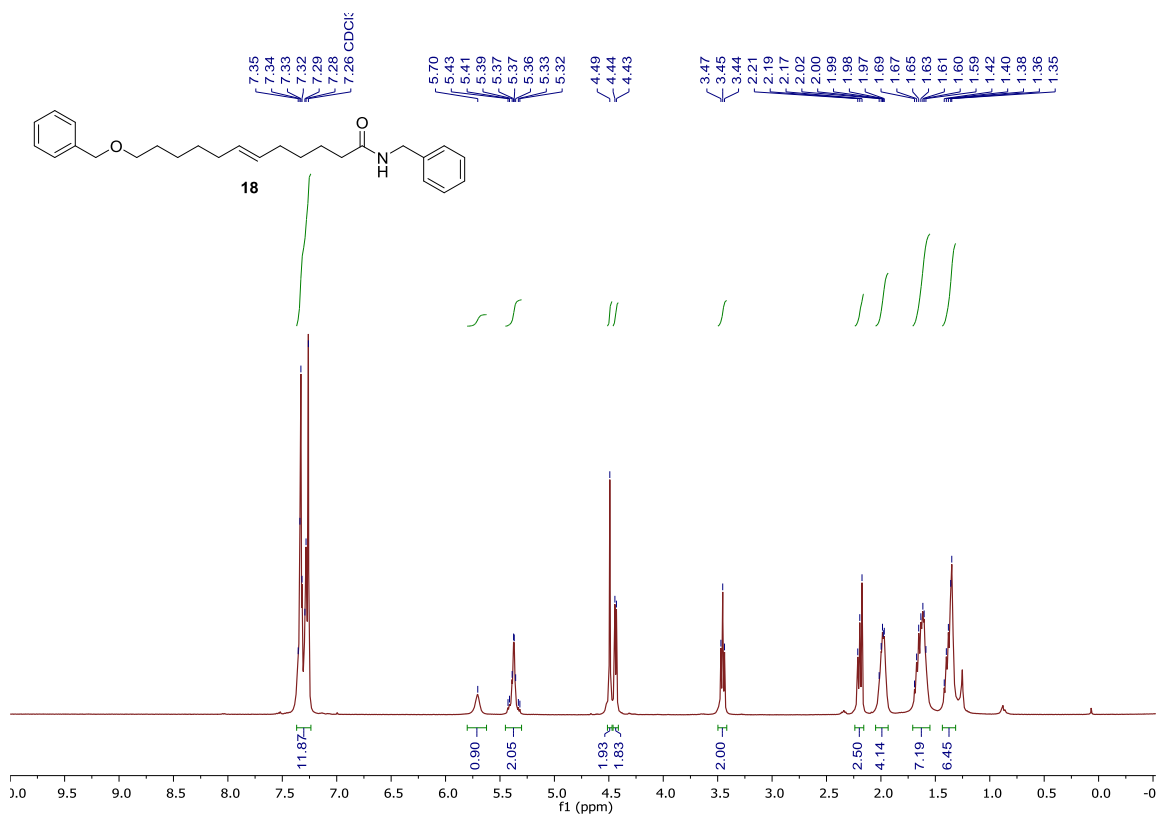


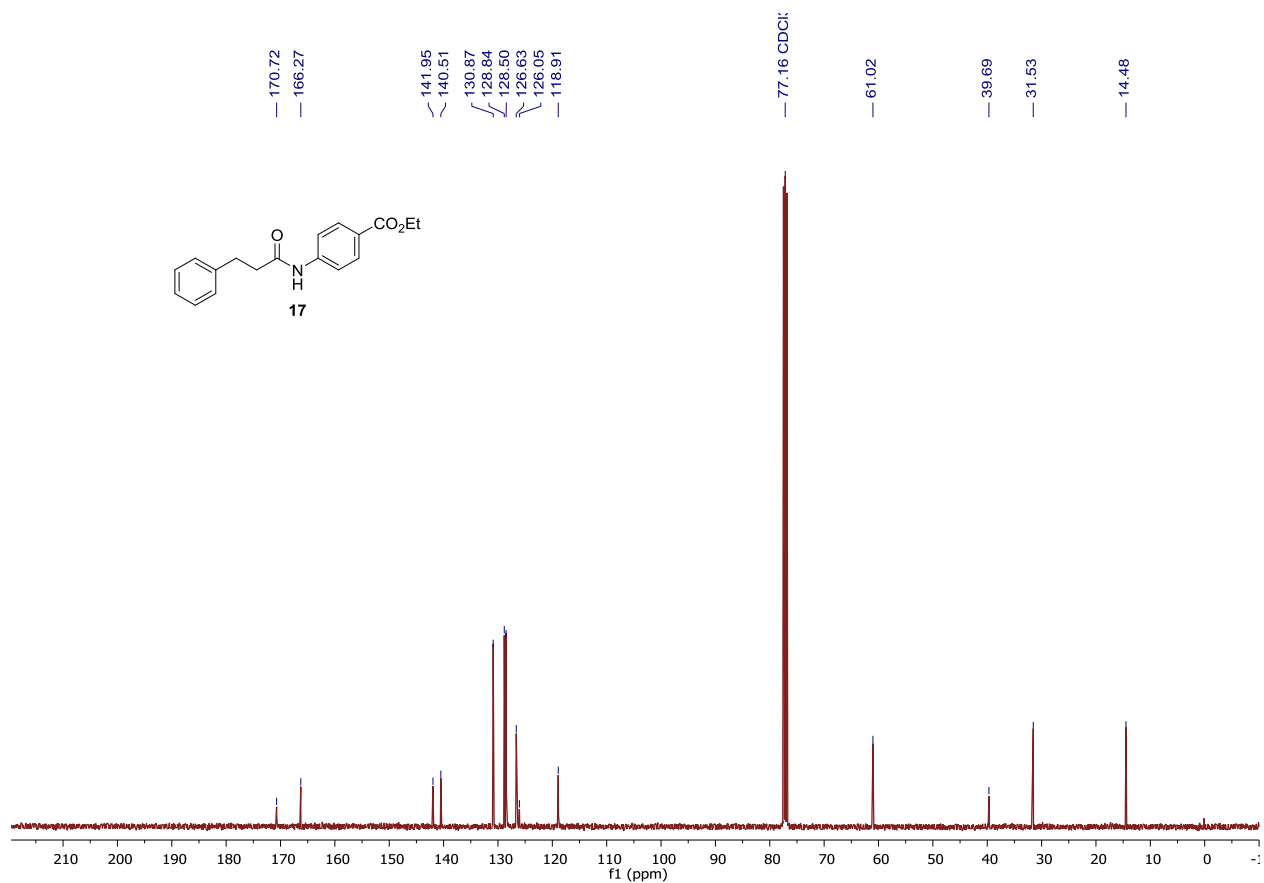
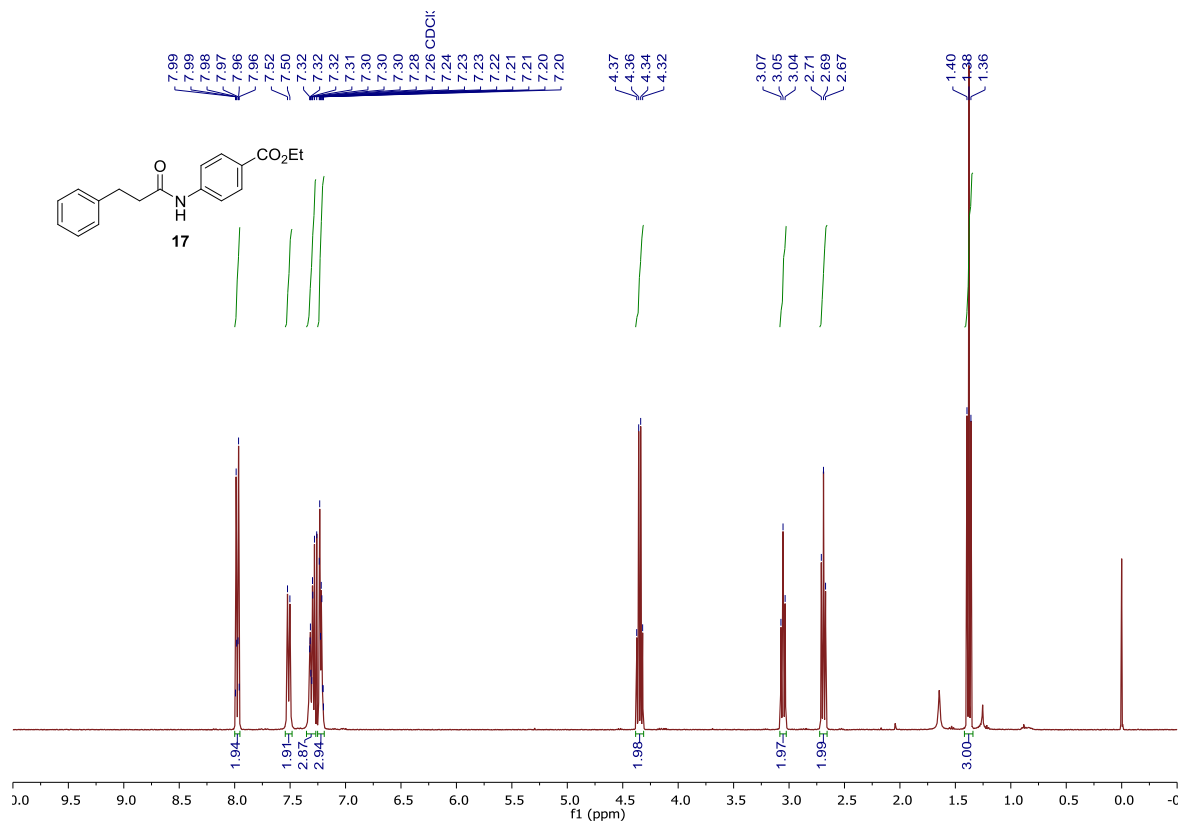


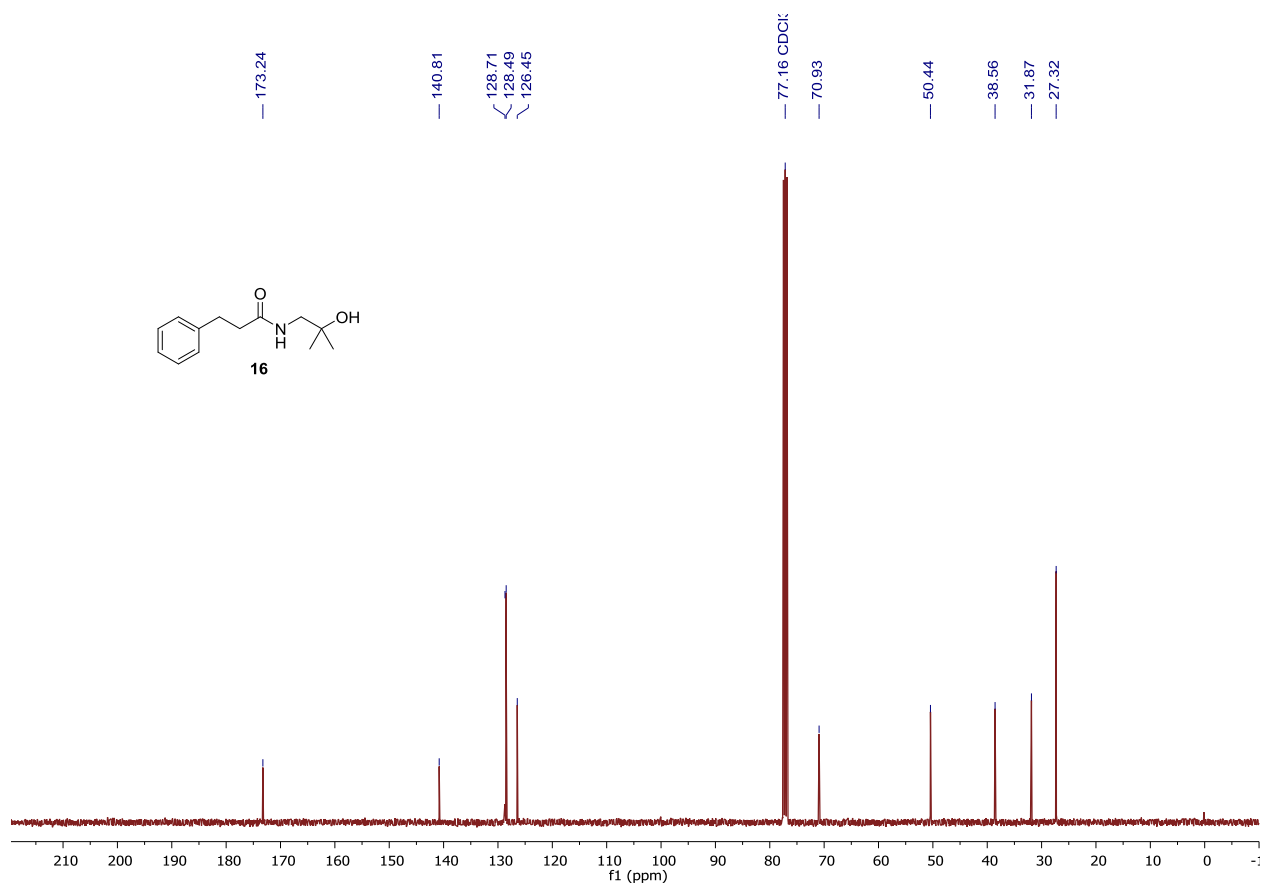
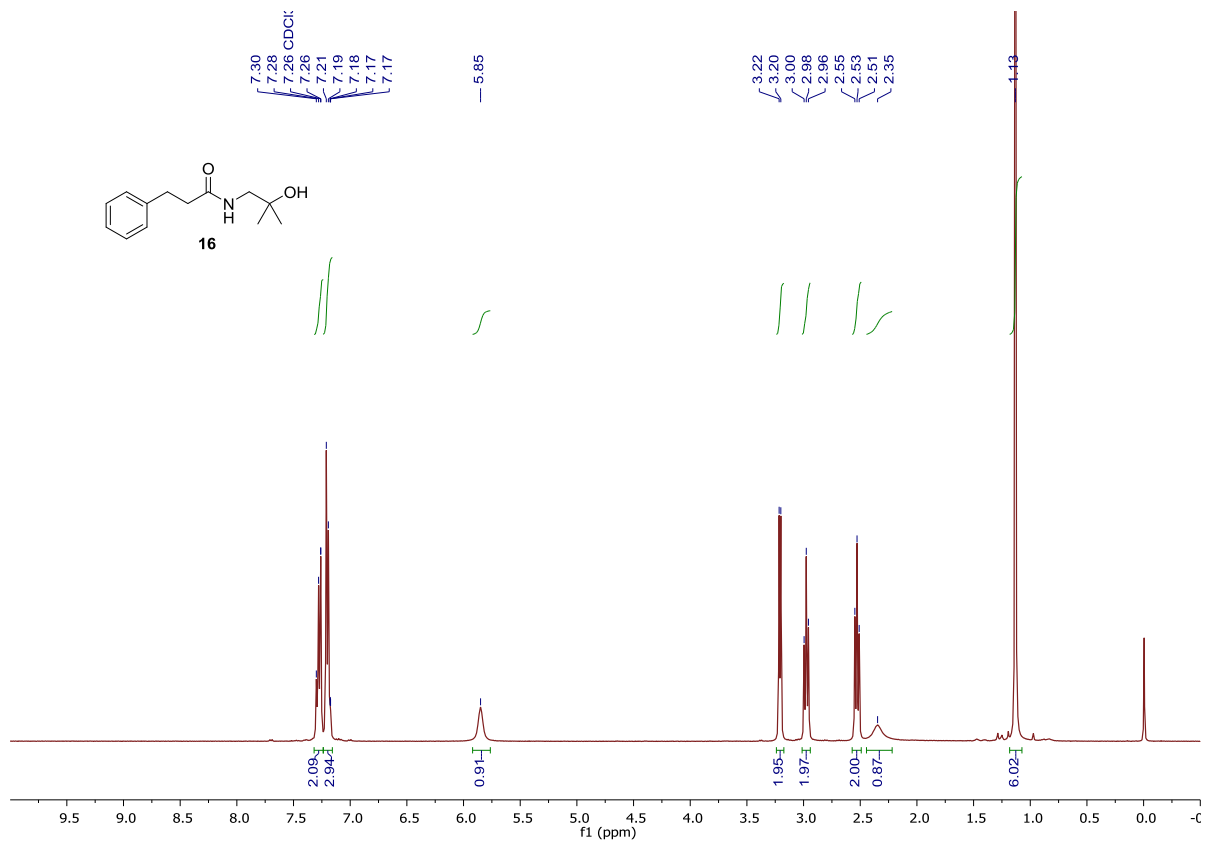


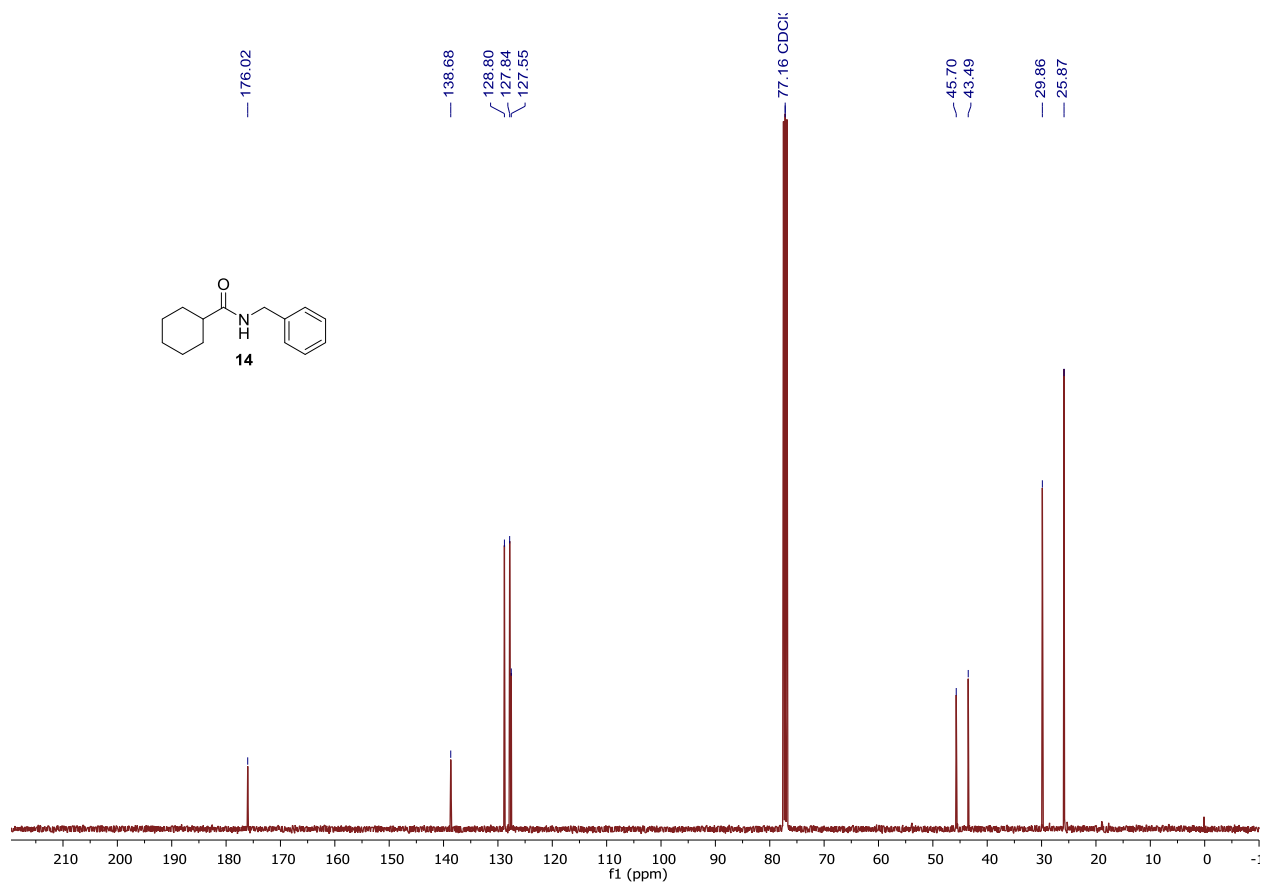
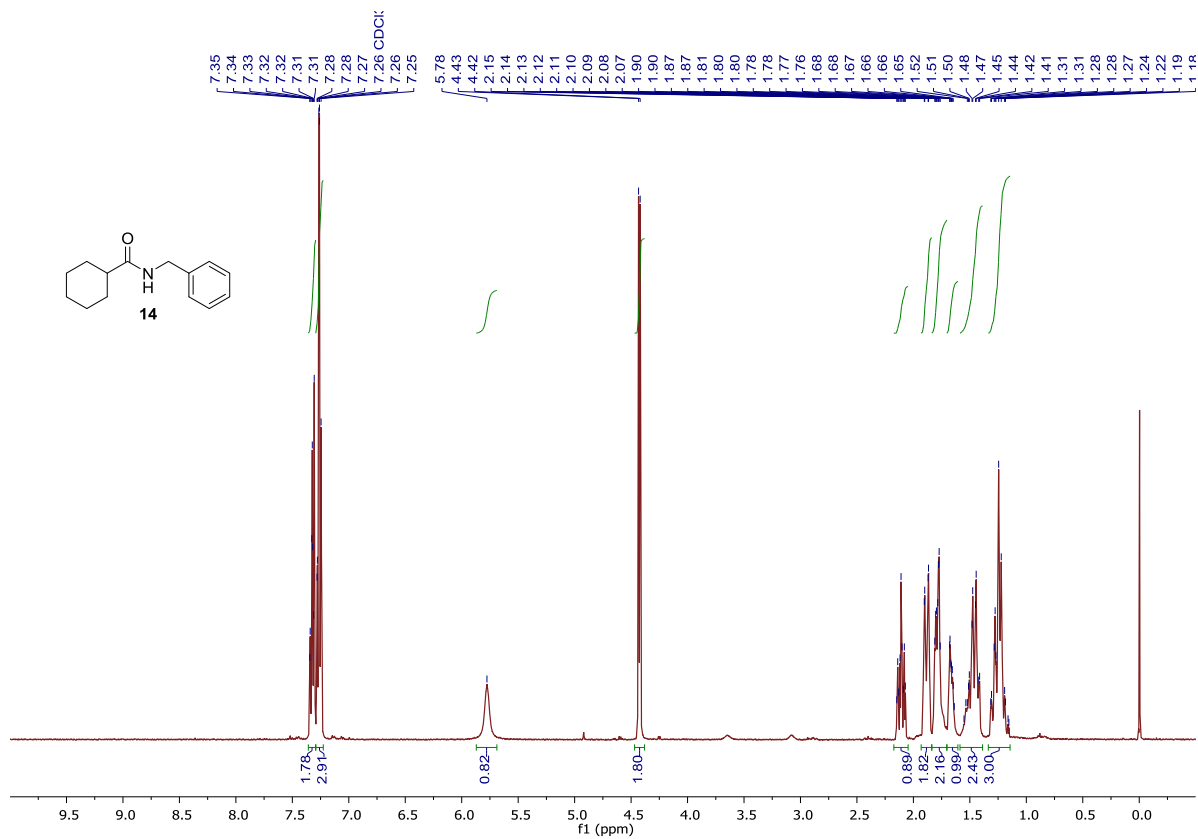


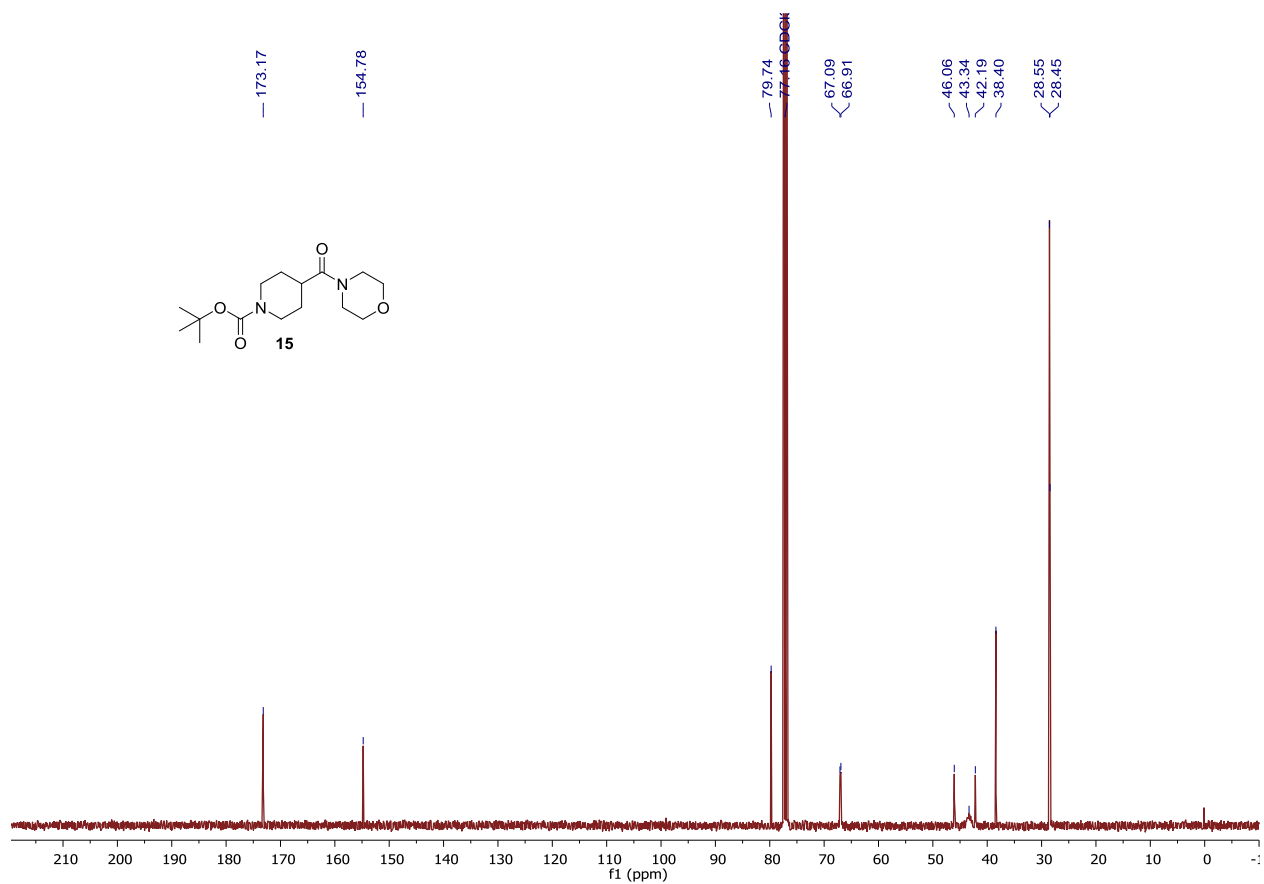
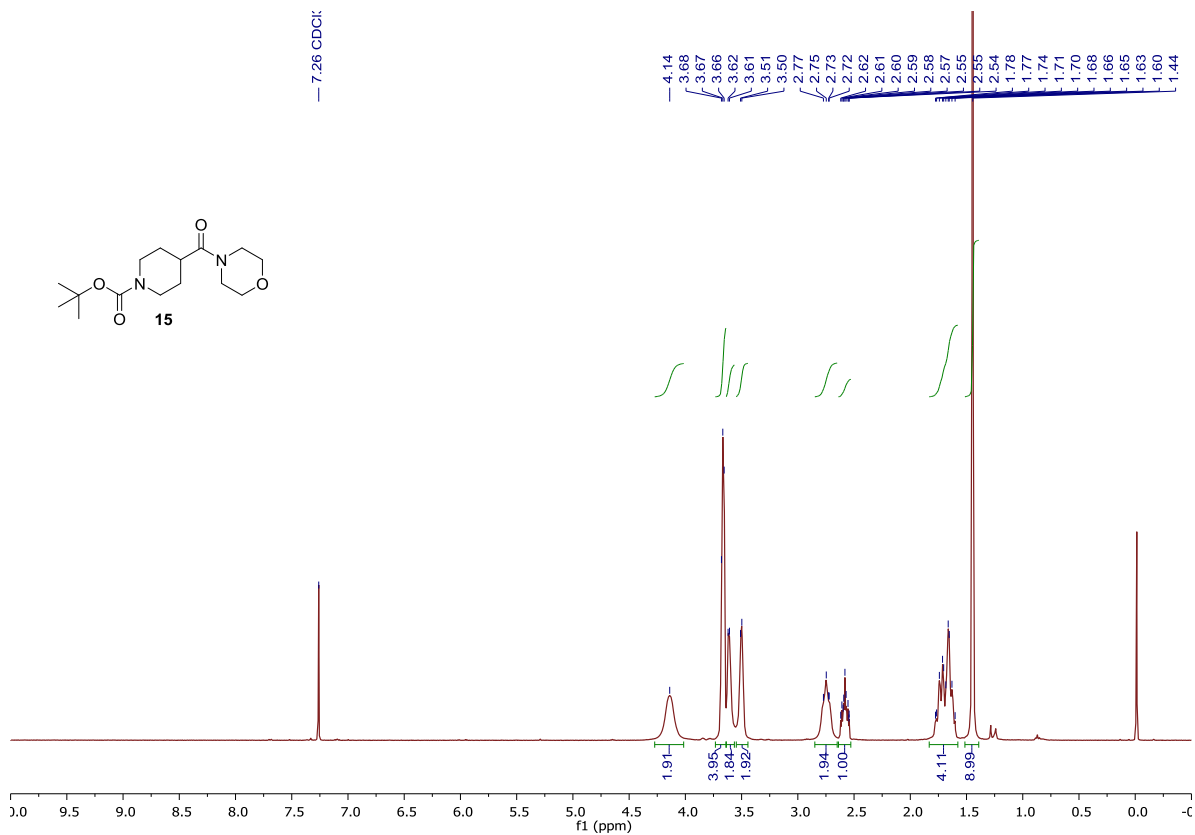


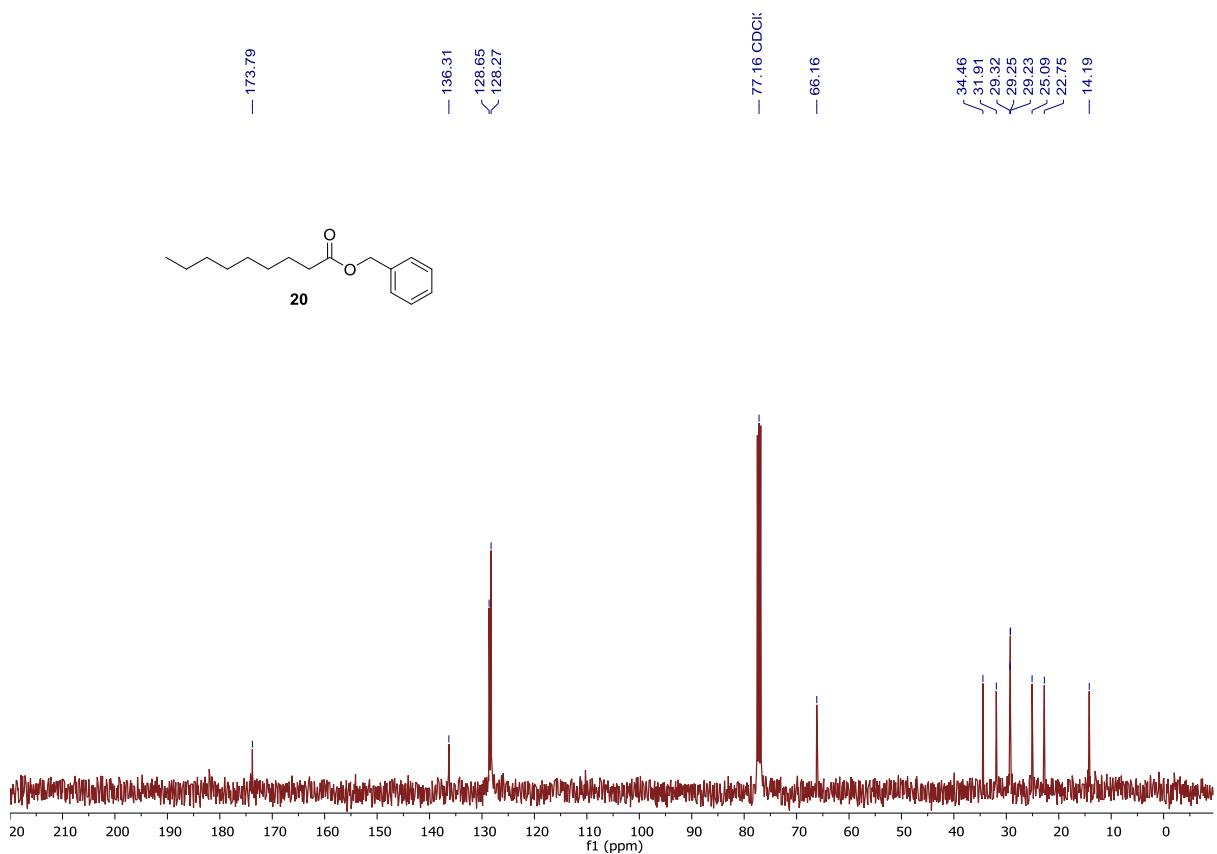
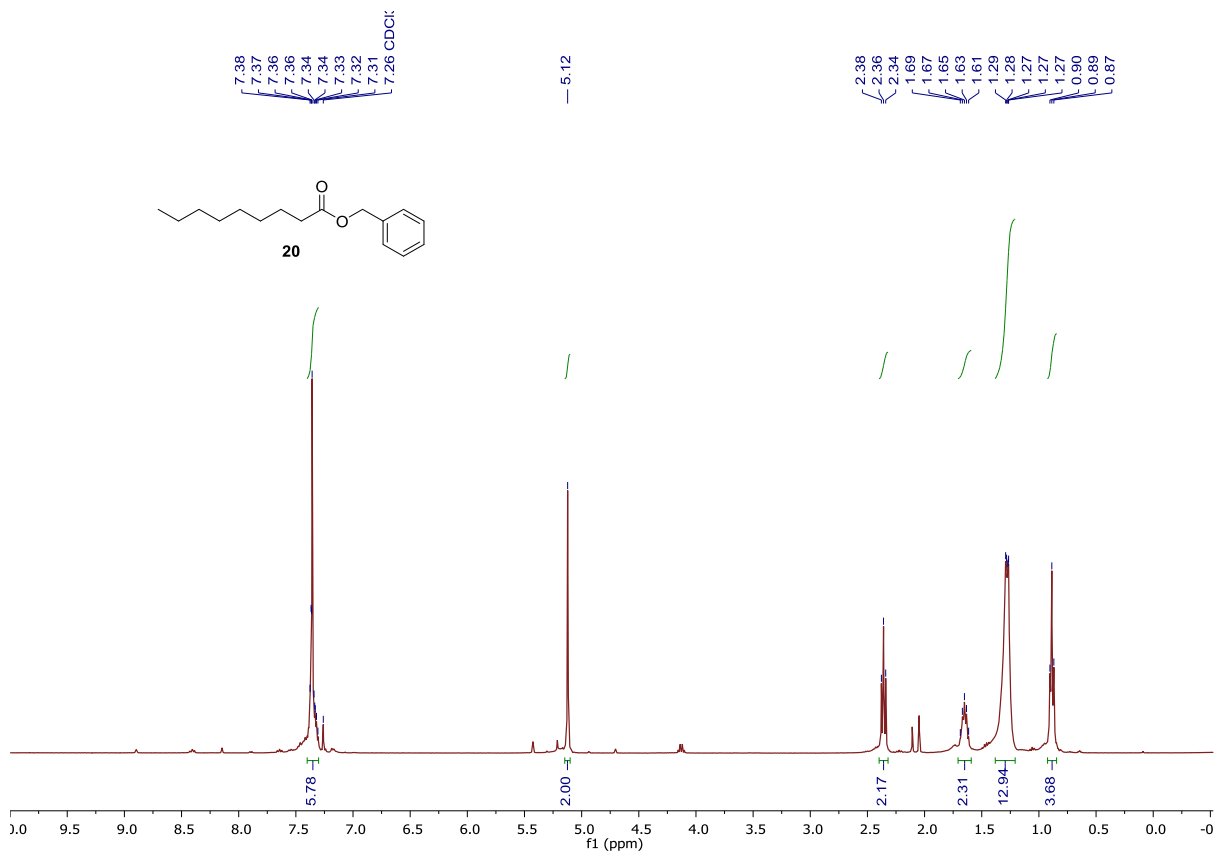


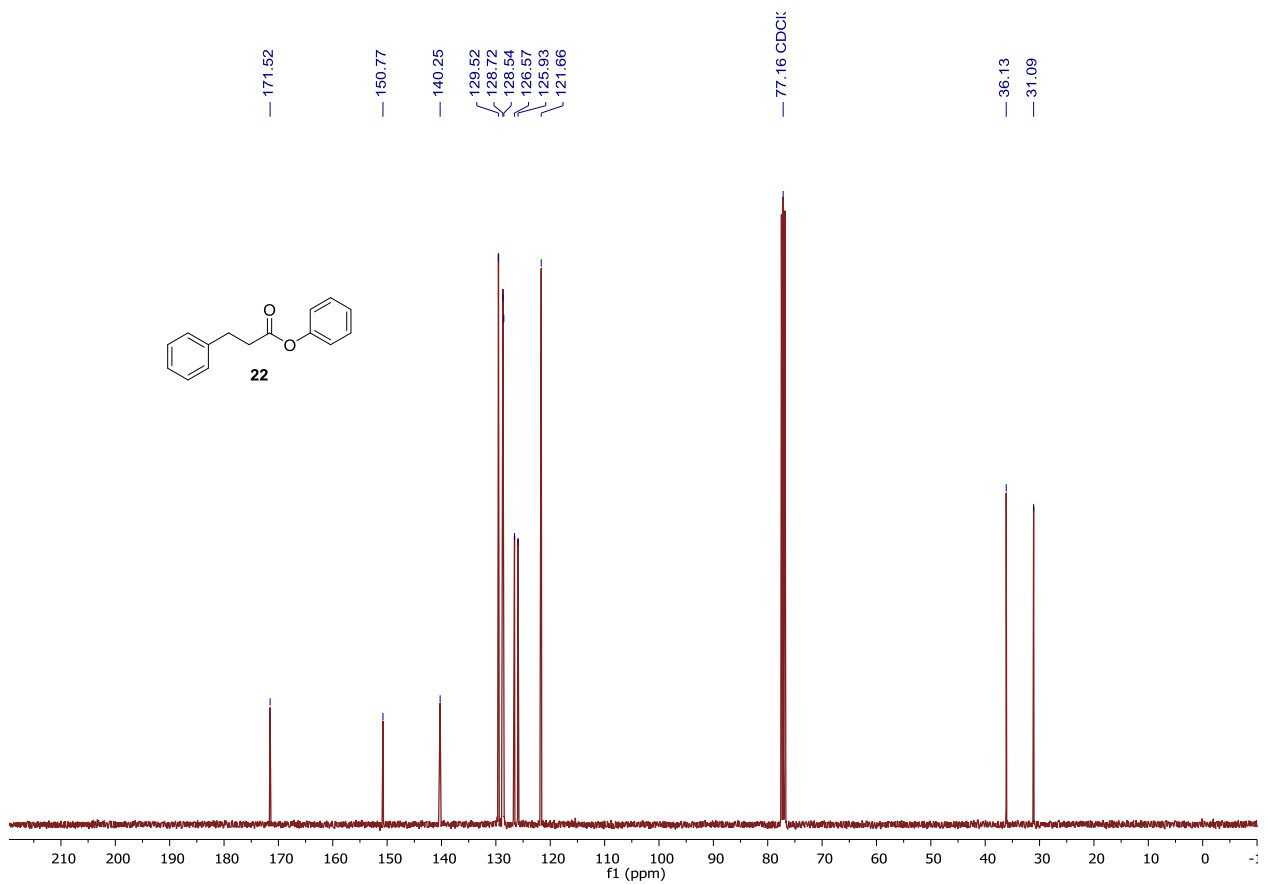
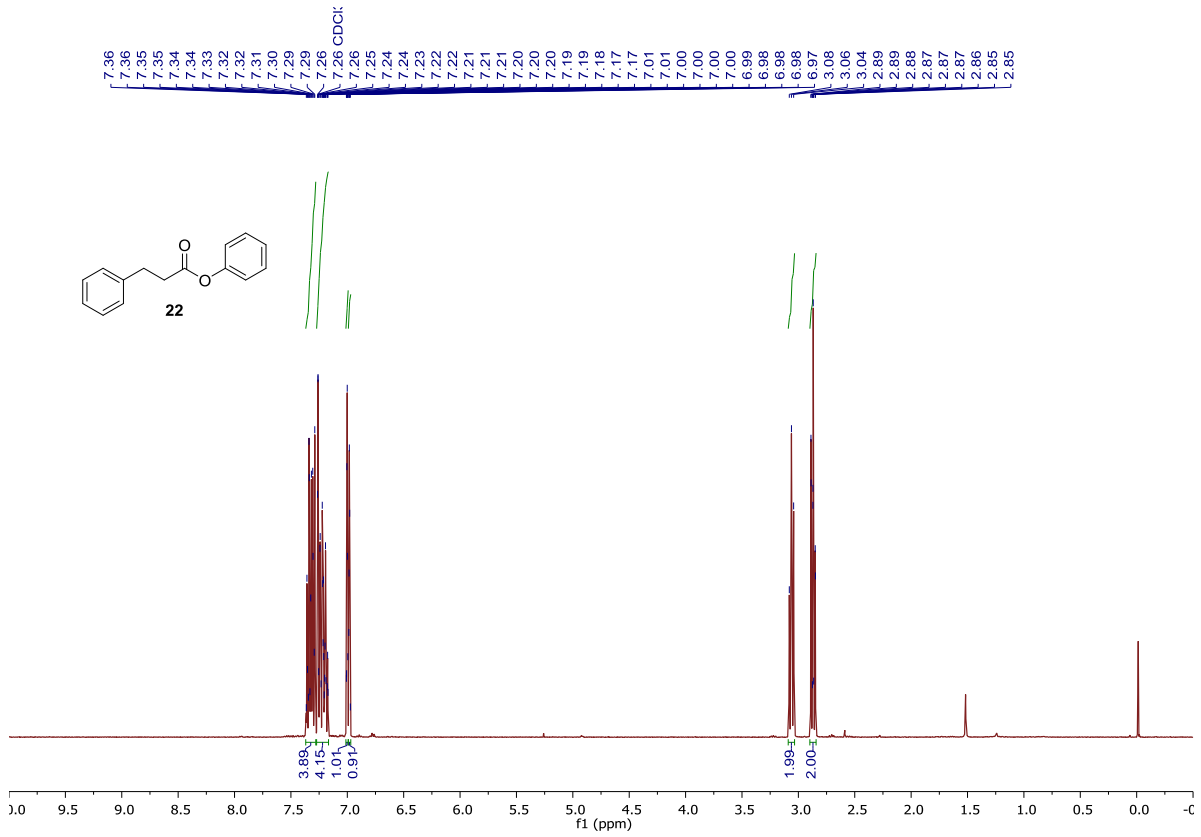


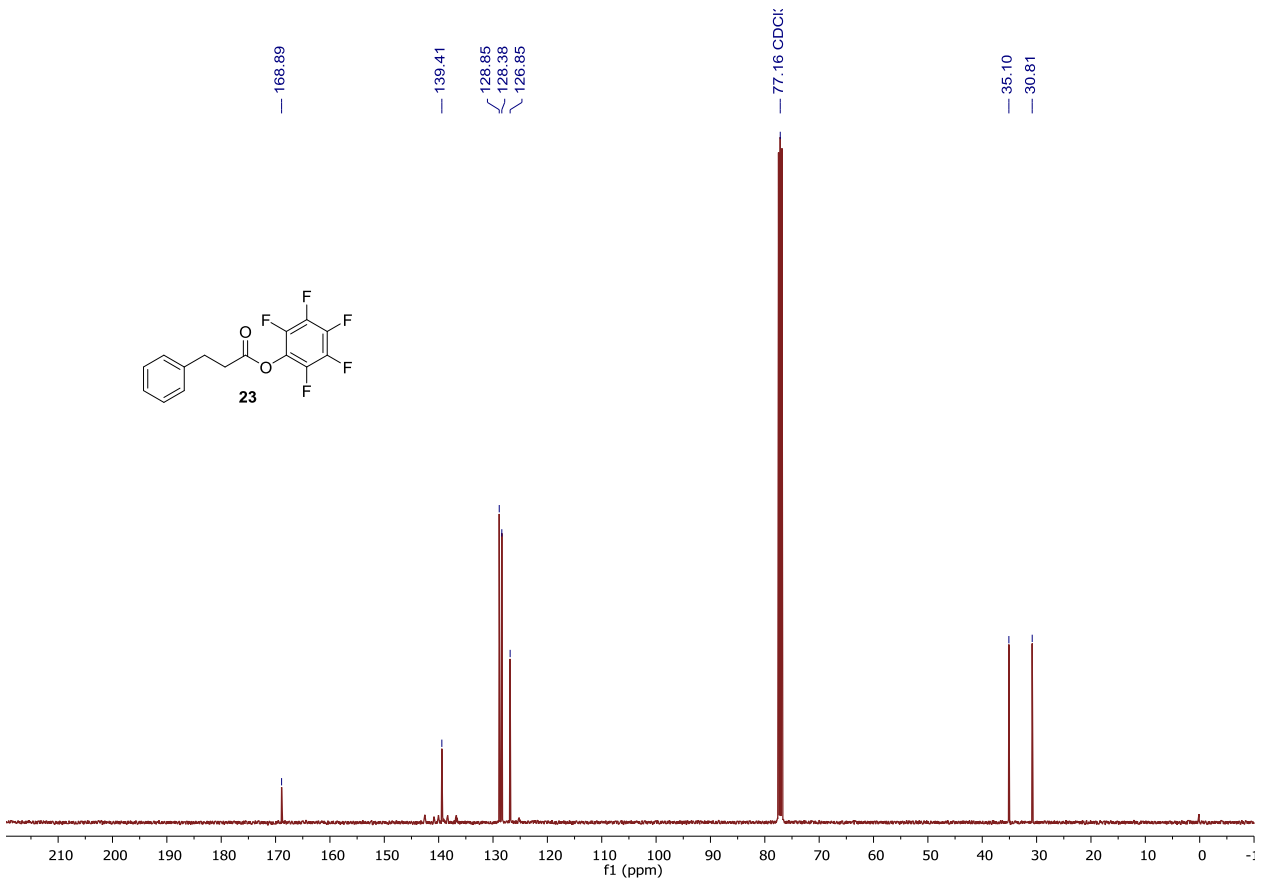
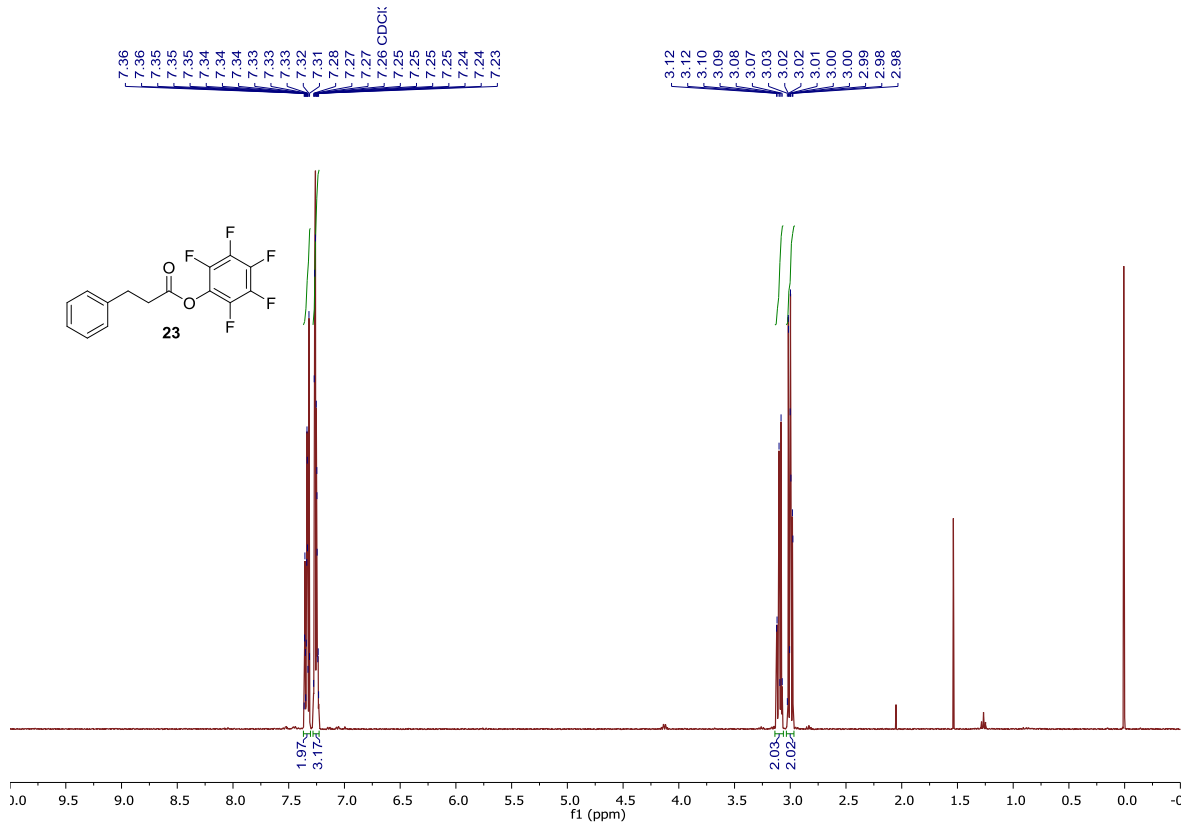


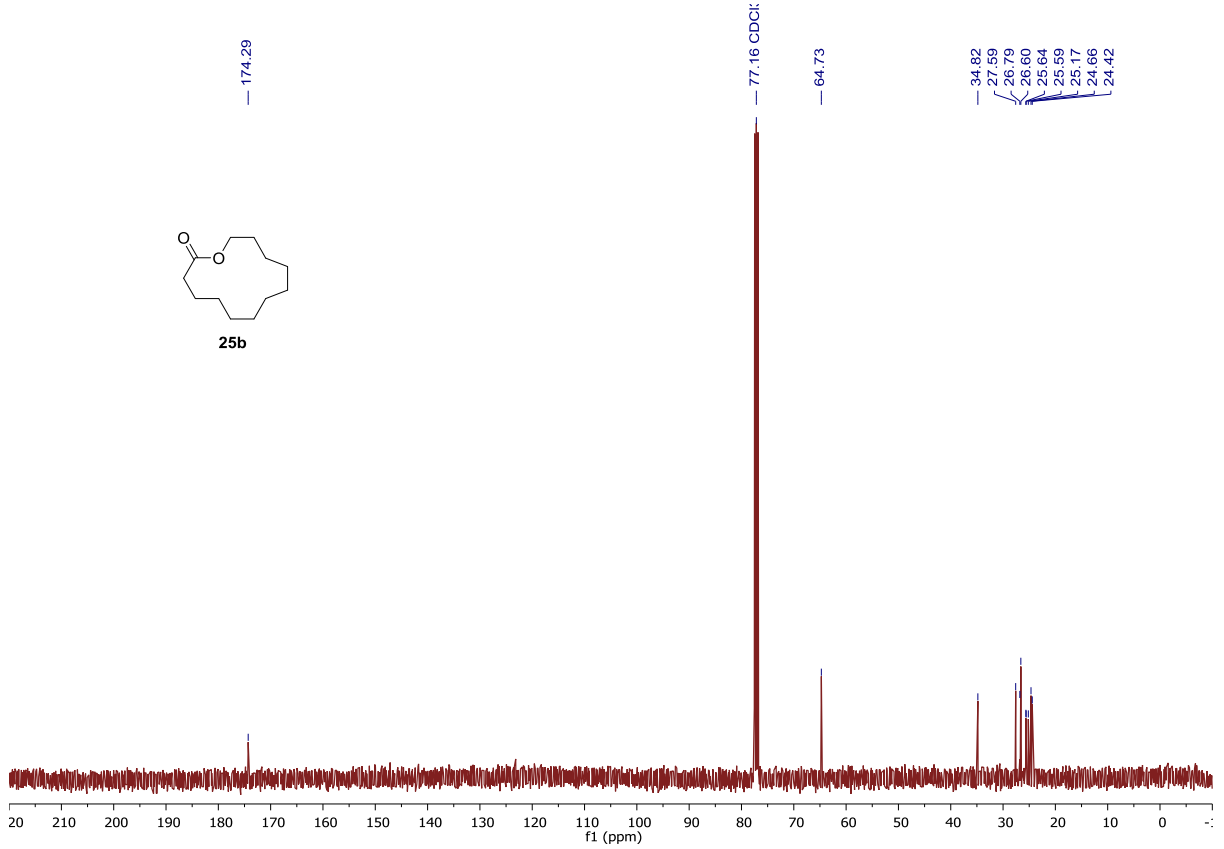
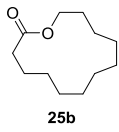
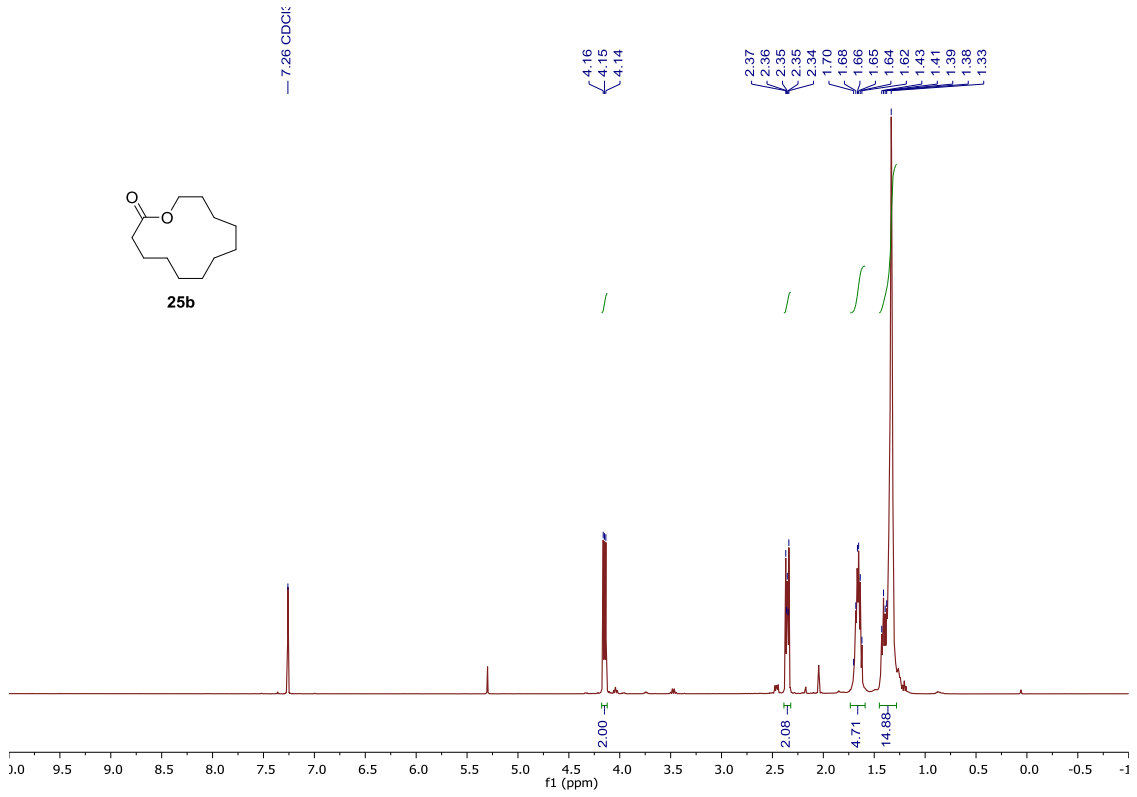
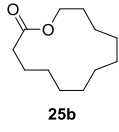


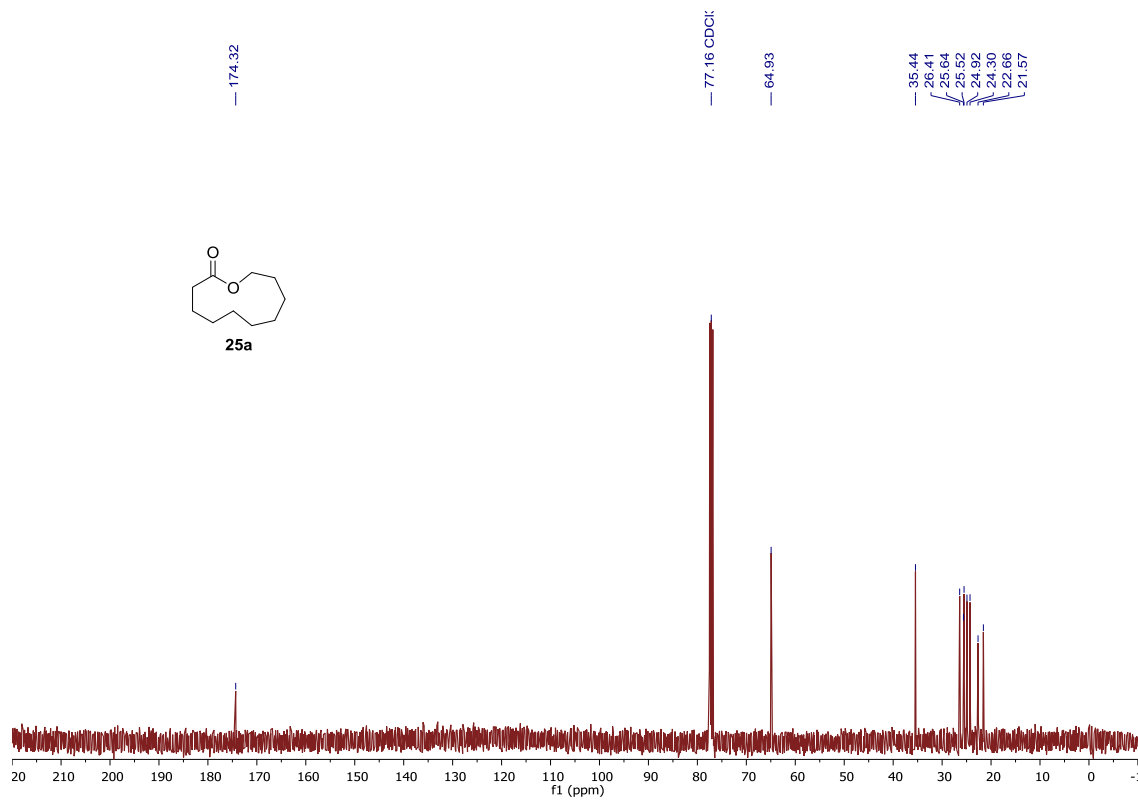
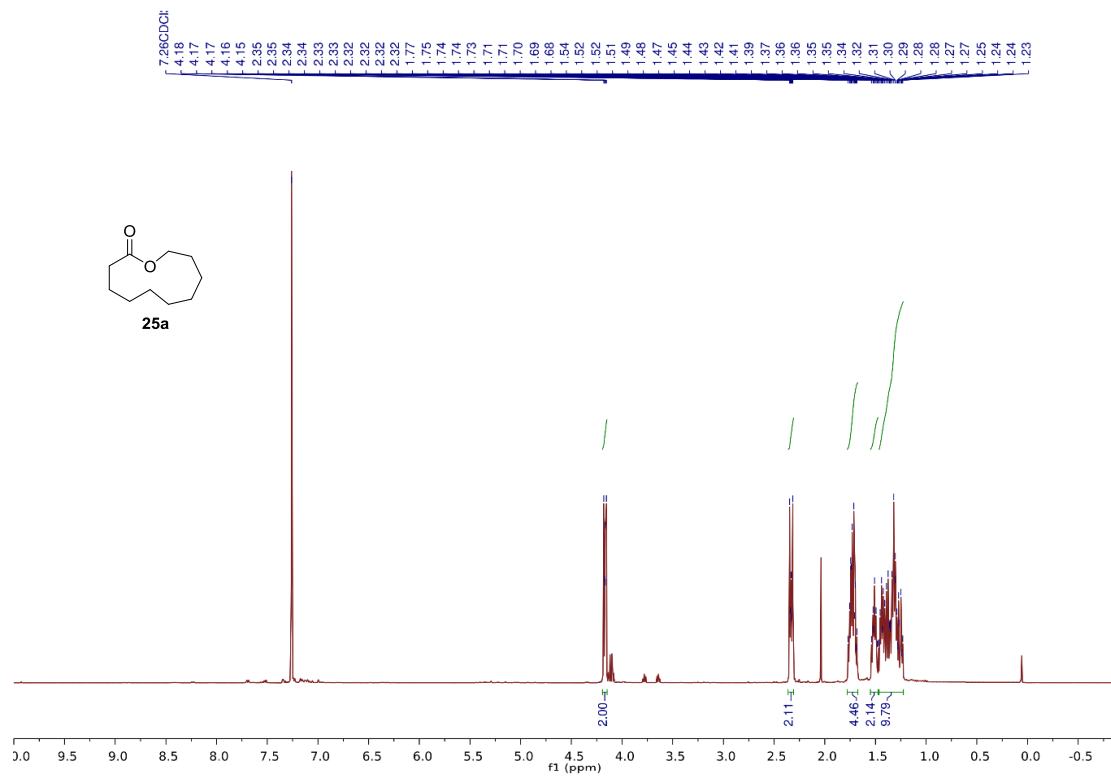


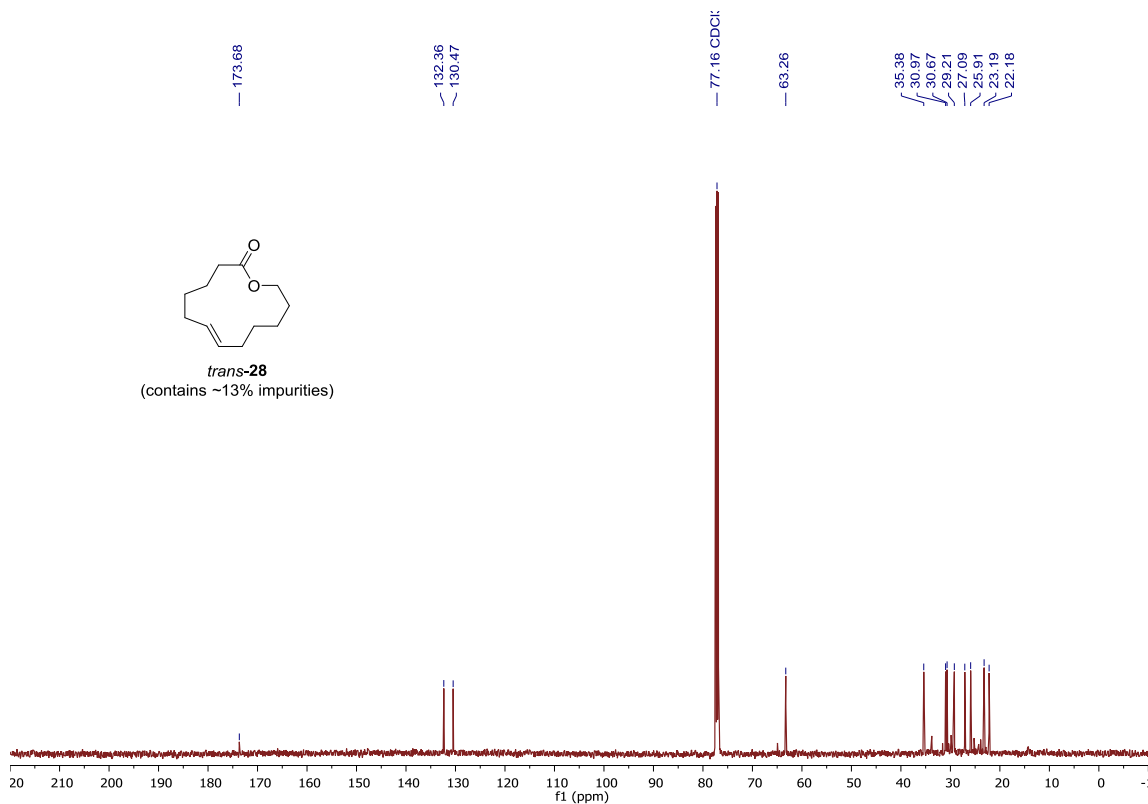
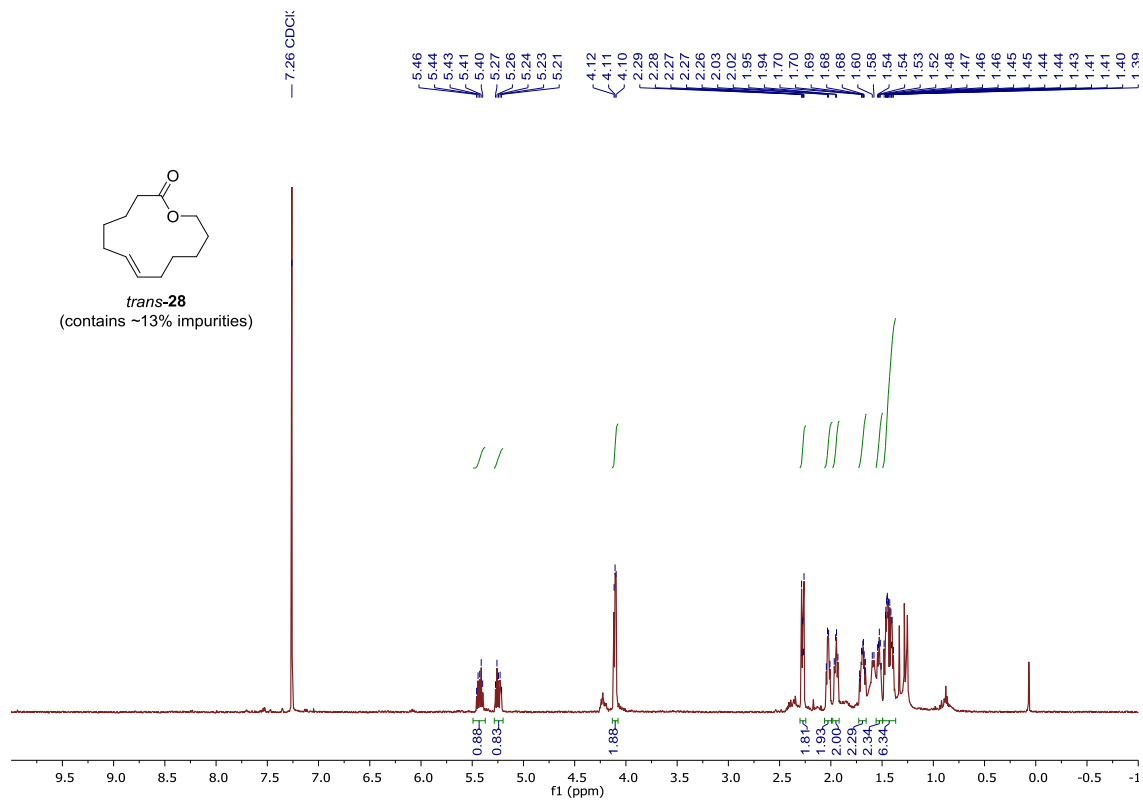












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