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Binary reducing agents containing dichloroindium hydride for the selective, partial, or tandem reductions of bifunctional compounds consisting of halo-nitriles, halo-esters, and halo-carboxylic acids

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SUPPORTING INFORMATION

Table of Contents

General Methods

All reactions were carried out under an argon atmosphere. All glassware, needles, and cannula were oven-dried at 120 °C and all glassware was cooled to 25 °C under argon atmosphere prior to use. All reactions were equipped with magnetic stirring. All air and moisture sensitive compounds were introduced via argon-purged syringe or cannula through a rubber septum. All of the reagents were purchased from Fisher Scientific or Aldrich Chemical Co., and stored under argon without further purification before use. Acetonitrile (MeCN) and tetrahydrofuran (THF) were transferred from a solvent purification system to an ampule under an argon atmosphere and stored for no more than 4 weeks. All products were isolated through simple acid-base extraction and no further purification was utilized. Products were analyzed through nuclear magnetic resonance (NMR) spectroscopy and measured in ppm. Data obtained on a 500 MHz spectrometer using $CDCl_3$ (δ=7.26) as an internal standard for ^{1}H NMR and 125 MHz using $CDCl_3$ (δ=77.0) as an internal standard for ^{13}C spectra. Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad; coupling constants (*J*) are given in Hertz (Hz). Powder X-ray diffraction (PXRD) data was collected on a Rigaku SmartLab X-ray diffractometer equipped with a copper X-ray tube [λ (Cu Kα) = 1.54056 Å, tube energy 44 mA / 40 kV]. Analysis was carried out at room temperature with a scan rate of 3.0 °/min and with a step size of 0.02 °.

General Procedures for Selective, Partial, and Tandem Reductions using Binary Hydrides

Selective reduction of 6-bromohexanoic acid using DIBAL-H to produce 6-bromohexanol (known) [1]

The following procedure is for the selective reduction of 6-bromohexanoic acid using DIBAL-H (Scheme 1, b). An oven-dried round bottom flask (RBF) (50-mL) was cooled under argon and charged with a stir bar, 6-bromohexanoic acid (0.585 g, 3 mmol) and re-flushed with argon. Anhydrous THF (10 mL) was added at 25 °C followed by DIBAL-H (1.2 M in hexanes, 7.5 mL, 9 mmol) dropwise over 5 minutes and the mixture stirred for 4 hours (*Caution: Hydrogen evolution!*). Thin layer chromatography (TLC) analysis indicated completion of the reaction. The reaction mixture was quenched with 3M NaOH (15 mL) (*Caution: Hydrogen evolution!)* and the mixture was extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated under reduced pressure (25 °C, 1 Torr) to afford 6-bromohexanol as a colorless oil (0.511g, 2.82 mmol, 94%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.60 (t, *J* = 6.5; 2H) δ 3.38 (t, *J* = 6.5; 2H), δ 2.60 (s br, 1H), δ 1.83 (m, 2H), δ 1.54 (m, 2H), δ 1.42 (m, 2H), δ 1.36 (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 62.68, 33.95, 32.73, 32.44, 27.96, 24.96 ppm.

Selective reduction of 6-bromohexanoic acid using BH_3:THF to produce 6-bromohexanol (known)[1]

The following procedure is for the selective reduction of 6-bromohexanoic acid using BH_3:THF (Scheme 1, c). 6-bromohexanoic acid (0.585 g, 3 mmol) was added to an oven-dried RBF (50-mL) and charged with argon and a stir bar. Anhydrous THF (10 mL) followed by BH_3:THF (1.0 M in THF, 3.0 mL, 3 mmol) dropwise over 5 minutes at 25 °C (*Caution: Hydrogen evolution!*). The mixture was stirred for 4 hours at 25 °C under argon. TLC analysis indicated completion of the reaction. The reaction mixture was quenched with 3M NaOH (10 mL) (*Caution: Hydrogen evolution!)* and the mixture was extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated under reduced pressure (25 °C, 1 Torr) to afford the 6-bromohexanol product as a colorless oil (0.532 g, 2.94 mmol, 98%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.60 (t, *J* = 6.5; 2H), δ 3.38 (t, *J* = 6.5; 2H), δ 2.60 (s br, 1H), δ 1.83 (m, 2H), δ 1.54 (m, 2H), δ 1.42 (m, 2H), δ 1.36 (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 62.68, 33.95, 32.73, 32.44, 27.96, 24.96 ppm.

Selective reduction of 6-bromohexanoic acid to hexanoic acid using $HInCl_2$ (known) [2]

The following method is used for the selective reduction of 6-bromohexanoic acid using $HInCl_2$ (Scheme 1, e). An oven-dried RBF (100-mL) was equipped with a stir bar, rubber septum and cooled under argon to 25 °C. Anhydrous $InCl_3$ (1.326 g, 6 mmol) was added and the flask was re-flushed with argon. Anhydrous THF (20 mL) was added and the mixture stirred vigorously for 5 minutes at 25 °C. The RBF was then placed in a water bath and DIBAL-H (1.2 M in hexanes, 5.0 mL, 6 mmol) was added dropwise over 5 minutes. The reaction was allowed to stir for 1 hour at 25 °C. To the reaction flask was added solid 6-bromohexanoic acid (0.585 g, 3 mmol) and re-flushed with argon (*Caution: Hydrogen evolution!)*. The mixture was stirred for 4 hours at 25 °C. TLC analysis indicated completion of the reaction and was quenched with 3M NaOH (15 mL) (*Caution: Hydrogen evolution!)* and acidified to pH 4 with acetic acid. The mixture was extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated under reduced pressure (25 °C, 1 Torr) to afford the hexanoic acid as a colorless oil (0.272 g, 2.34 mmol, 78%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 11.30 (s br; 1H), δ 2.34 (t, *J* = 7; 2H), δ 1.64 (m, 2H), δ 1.32 (m, 4H), δ 0.89 (m, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 180.89, 34.15, 31.24, 24.39, 22.31, 13.85 ppm.

Stepwise reduction of 6-bromohexanoic acid using binary hydrides DIBAL-H and $HInCl_2$ to produce 1-hexanol (known) [3]

The following procedure was used for the tandem reduction of 6-bromohexanoic acid using binary hydride system DIBAL-H and $HInCl_2$ (Scheme 1, f). An oven-dried 100-mL RBF was cooled under argon to 25 °C and charged with a stir bar and rubber septum. 6-bromohexanoic acid (0.585 g, 3 mmol) was added and the flask was re-flushed with argon. To this was added anhydrous THF (10 mL), followed by the dropwise addition of DIBAL-H (1.2 M in hexanes, 7.5 mL, 9 mmol) over 5 minutes (*Caution: Hydrogen evolution!*). The mixture was stirred for 4 hours at 25 °C under argon. The reaction was quenched with 3M NaOH (15 mL) and the mixture was extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to afford crude 6-bromohexanol. A separate 100-mL oven-dried RBF, cooled under argon to 25 °C and was fit with a rubber septum and stir bar. Anhydrous $InCl_3$ (1.326 g, 6 mmol) was added and re-flushed with argon followed by anhydrous THF (20 mL) and the mixture stirred vigorously for 5 minutes at 25 °C. The RBF was then placed in a water bath and DIBAL-H (1.2 M in hexanes, 5.0 mL, 6 mmol) was added dropwise over 5 minutes. The reaction was allowed to stir for 1 hour at 25 °C. 6-bromohexanol (0.39 mL, 3 mmol) was added (*Caution: Hydrogen evolution!)* and the mixture was stirred for 4 hours at 25 °C under argon. Thin layer chromatography analysis indicated completion of the reaction. The reaction mixture was quenched with 3M NaOH (15 mL) (*Caution: Hydrogen evolution!)* and the mixture was extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to afford 1-hexanol product as a colorless oil (0.281 g, 2.76 mmol, 92%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.60 (t, *J* = 6.5, 2H), δ 1.53 (m, 2H), δ 1.27 (m, 7H), δ 0.87 (t, *J* = 7, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 63.11, 32.98, 31.69, 27.97, 25.47, 22.65, 14.01.

Selective reduction of 6-bromohexanoic acid using binary hydrides $HInCl_2$ and BH_3:THF to produce 6-bromohexanol (known) [1]

Binary hydrides $HInCl_2$ and BH_3:THF (Scheme 1, d) are used for the selective reduction of 6-bromohexanoic acid to produce 6-bromohexanol. A 50-mL oven dried RBF was fitted with a stir bar and rubber septum was allowed to cool to 25 °C using argon. Anhydrous $InCl_3$ (0.663 g, 3 mmol) was quickly added and the RBF was again flushed with argon. Anhydrous THF (10 mL) was added and the mixture stirred vigorously for 5 minutes while the indium dissolved. Sodium borohydride ($NaBH_4$, 0.340 g, 9 mmol) was added and the reaction flask was re-purged with argon. The reaction mixture stirred at 25 °C for 1 hour and the reaction flask became and opaque silver color. 6-bromohexanoic acid (0.585 g, 3 mmol) was then added and the reaction flask was purged with argon (*Caution: Hydrogen evolution!*). The mixture stirred for 4 hours at 25 °C under argon. Thin layer chromatography analysis indicated completion of the reaction. The reaction mixture was quenched with 3M NaOH (10 mL) (*Caution: Hydrogen evolution!)*. The mixture was filtered using a Büchner funnel, and the solid was discarded. The filtrate was extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to isolate 6-bromohexanol as a colorless oil (0.511g, 2.82 mmol, 94%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.60 (t, *J* = 6.5; 2H), δ 3.38 (t, *J* = 6.5; 2H), δ 2.60 (s br, 1H), δ 1.83 (m, 2H), δ 1.54 (m, 2H), δ 1.42 (m, 2H), δ 1.36 (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 62.68, 33.95, 32.73, 32.44, 27.96, 24.96 ppm.

Selective reduction of Ethyl 6-bromohexanoate using DIBAL-H to produce 6-bromohexanol (known) [1]

The following procedure is used for the selective reduction of ethyl 6-bromohexanoate using DIBAL-H (Table 1, entry 1). A 50-mL oven-dried RBF was cooled under argon and charged with a stir bar and fit with a rubber septum. Ethyl 6-bromohexanoate (0.53 mL, 3 mmol) was added followed by anhydrous THF (10 mL). DIBAL-H (1.2 M in hexanes, 5.0 mL, 6 mmol) was added dropwise over 5 minutes at 25 °C. The mixture was stirred for 4 hours at 25 °C under argon. Thin layer chromatography analysis indicated completion of the reaction. The reaction mixture was quenched with 3M NaOH (15 mL) (*Caution: Hydrogen evolution!)* and the mixture was extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to afford the 6-bromohexanol product as a colorless oil (0.537 g, 2.97 mmol, 99%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.60 (t, *J* = 6.5; 2H), δ 3.38 (t, *J* = 6.5; 2H), δ 2.60 (s br, 1H), δ 1.83 (m, 2H), δ 1.54 (m, 2H), δ 1.42 (m, 2H), δ 1.36 (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 62.68, 33.95, 32.73, 32.44, 27.96, 24.96 ppm.

Attempted Reduction of Ethyl 6-bromohexanoate using BH_3:THF

An oven-dried RBF (50-mL) fit with a rubber septum, was cooled under argon and charged with a stir bar. Ethyl 6-bromohexanoate (0.53 mL, 3 mmol) was added, followed by anhydrous THF (10 mL) at 25 °C. Next, BH_3:THF (stabilized with $NaBH_4$, 1.0 M in THF, 3.0 mL, 3 mmol), was added dropwise over 5 minutes at 25 °C (Table 1, entry 2). The mixture was stirred for 4 hours at 25 °C under argon. To avoid hydrolyzing the ester group, the reaction mixture was quenched with 3M NH_4OH (10 mL) (*Caution: Hydrogen evolution!)* and the mixture extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to afford a mixture (66:34) of 6-bromohexanol and ethyl 6-bromohexanoate products respectively (based on ^{1}H NMR integration).

Selective reduction of Ethyl 6-bromohexanoate to ethyl hexanoate using $HInCl_2$ (known)[4]

The following procedure was employed for the selective reduction of ethyl 6-bromohexanoate using $HInCl_2$ (Table 1, entry 3). An oven-dried RBF (100-mL) with stir bar and fitted with a rubber septum was cooled under argon. When the flask reached 25 °C, anhydrous $InCl_3$ (1.326 g, 6 mmol) was added and the flask was re-purged with argon. Anhydrous THF (20 mL) was then added and the mixture stirred vigorously for 5 minutes and 25 °C. The RBF was immersed in a water bath and DIBAL-H (1.2 M in hexanes, 5.0 mL, 6 mmol) was added dropwise over 10 minutes at 25 °C. The reaction stirred for 1 hour at 25 °C. Ethyl 6-bromohexanoate (0.53 mL, 3 mmol) was added and the mixture stirred under argon at 25 °C for 4 more hours. Thin layer chromatography analysis indicated completion of the reaction and the reaction mixture was quenched with 3M NH_4OH (10 mL) (*Caution: Hydrogen evolution!)*. The mixture was extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated under reduced pressure (25 °C, 1 Torr) to give the ethyl hexanoate as colorless oil. (0.337 g, 2.34 mmol, 78%) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.12 (q, *J* = 7, 2H), δ 2.27 (t, *J* = 7.5, 2H), δ 1.61 (m, 2H) δ 1.30 (m, 4H) δ 1.24 (t, *J* = 7, 3H), δ 0.88 (t, *J* = 7, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 174.12, 60.20, 34.38, 31.33, 24.68, 22.33, 14.22, 13.88.

Stepwise reduction of 6-bromohexanoic acid using binary hydrides DIBAL-H and $HInCl_2$ to produce 1-hexanol (known)[3]

The following procedure was used for the stepwise reduction of ethyl 6-bromohexanoate using binary hydride DIBAL-H and $HInCl_2$ (Table 1, entry 4). An oven-dried RBF (50-mL) fit with a rubber septum and stir bar, was cooled under argon to 25 °C. Ethyl 6-bromohexanoate (0.53 mL, 3 mmol) was added followed by anhydrous THF (10 mL). DIBAL-H (1.2 M in hexanes, 5.0 mL, 6 mmol) was then added dropwise over 10 minutes at 25 °C. The mixture was stirred for 4 hours at 25 °C under argon. TLC analysis indicated complete absence of starting material. The reaction mixture was quenched with 3M NaOH (15 mL) and the mixture was extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated under reduced pressure (25 °C, 1 Torr) to afford crude 6-bromohexanol, the product of the first stage of the tandem reduction. In a separate reaction flask with a rubber septum, cooled under argon and charged with a stir bar, was added anhydrous $InCl_3$ (1.326 g, 6 mmol). Anhydrous THF (20 mL) was added and the mixture stirred vigorously for 5 minutes and 25 °C. The RBF was then submerged in a water bath and DIBAL-H (1.2 M in hexanes, 5.0 mL, 6 mmol) was added dropwise over 10 minutes at 25 °C. The reaction was allowed to stir for 1 hour. Crude 6-bromohexanol (0.39 mL, 3 mmol) was added to the $HInCl_2$-Al(*i*Bu)$_2$Cl mixture (*Caution: Hydrogen evolution!*) and stirred for 4 hours at 25 °C under argon. The reaction mixture was quenched with 3M NaOH (15 mL) (*Caution: Hydrogen evolution!)* and the mixture was extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to afford 1-hexanol (0.281 g, 2.76 mmol, 92%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.60 (t, *J* = 6.5, 2H), δ 1.53 (m, 2H), δ 1.27 (m, 7H), δ 0.87 (t, *J* = 7, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 63.11, 32.98, 31.69, 27.97, 25.47, 22.65, 14.01.

Selective reduction of Ethyl 6-bromohexanoate using binary hydrides $HInCl_2$ and BH_3:THF to produce 6-bromohexanol (known)[1]

Ethyl 6-bromohexanoate underwent a selective reduction using binary hydrides $HInCl_2$ and BH_3:THF to produce 6-bromohexanol by the following method (Table 1, entry 5). An oven-dried RBF (50-mL) was fitted with a rubber septum, stir bar and allowed to cool under argon to 25 °C. Anhydrous $InCl_3$ (0.663 g, 3 mmol) was added and the RBF was re-purged with argon. Anhydrous THF (10 mL) was then added and the mixture stirred vigorously for 5 minutes at 25 °C. Sodium borohydride ($NaBH_4$, 0.340 g, 9 mmol) was added and the reaction flask was reflushed with argon. The reaction mixture stirred at 25 °C for 1 hour and during this time, the reaction mixture became an opaque silver color. Ethyl 6-bromohexanoate (0.53 mL, 3 mmol) was then added and the mixture was stirred for additional 4 hours at 25 °C under argon. Thin layer chromatography analysis indicated completion of the reaction. The reaction was quenched with 3M NaOH (10 mL) (*Caution: Hydrogen evolution!)*. The mixture was filtered using a Büchner funnel, and the solid was discarded. The filtrate was extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated under reduced pressure (25 °C, 1 Torr) to afford the 6-bromohexanol product as a colorless oil (0.386 g, 2.13 mmol, 71%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.60 (t, *J* = 6.5; 2H), δ 3.38 (t, *J* = 6.5; 2H), δ 2.60 (s br, 1H), δ 1.83 (m, 2H), δ 1.54 (m, 2H), δ 1.42 (m, 2H), δ 1.36 (m, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 62.68, 33.95, 32.73, 32.44, 27.96, 24.96 ppm.

Selective carbon-halogen bond reduction of ethyl 6-bromohexanoate using single hydride $HInCl_2$ to generate ethyl hexanoate[4]

Ethyl 6-bromohexanoate underwent a selective carbon-halogen bond reduction using $HInCl_2$ (Table 1, entry 6). An oven dried 50-mL RBF was cooled to 25 °C using argon, and was fit with a rubber septum and stir bar. Anhydrous $InCl_3$ (0.663 g, 3 mmol) was added and the flask was reflushed with argon. To this was added anhydrous MeCN (10 mL) and the mixture stirred vigorously for 5 minutes until the indium trichloride dissolved. Sodium borohydride (0.340 g, 9 mmol) was added and the flask was flushed with argon. The heterogeneous reaction mixture stirred for 1 hour at 25 °C. Over the course of the hour, the reaction turned an opaque silver color. Ethyl 6-bromohexanoate (0.27 mL, 1.5

mmol) was added to the reaction mixture and stirred for 4 hours. TLC analysis indicated complete absence of the starting material. The reaction mixture was quenched with 3M NH_4OH (10 mL) to avoid hydrolysis of the ester functional group (*Caution: Hydrogen evolution!)*. The mixture was filtered using a Büchner funnel, and the solid was discarded. The filtrate was extracted with Et_2O (3 X 10 mL). The combined organic layers were dried using $MgSO_4$, filtered, and evaporated under reduced pressure (25 °C, 1 Torr) to afford the product ethyl hexanoate as a colorless oil (0.141 g, 1.38 mmol, 92%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.12 (q, *J* = 7, 2H), δ 2.27 (t, *J* = 7.5, 2H), δ 1.61 (m, 2H) δ 1.30 (m, 4H) δ 1.24 (t, *J* = 7, 3H), δ 0.88 (t, *J* = 7, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 174.12, 60.20, 34.38, 31.33, 24.68, 22.33, 14.22, 13.88.

General Method for the reduction of Methyl Octanoate to produce 1-octanol (known) [5]

The following is the representative general procedure for the reduction of methyl octoanoate. An oven-dried RBF (50-mL) was cooled under argon and charged with a stir bar and methyl octanoate (0.54 mL, 3 mmol). To this was added anhydrous THF (10 mL) followed by DIBAL-H (1.2 M in hexanes, 5.0 mL, 6 mmol), dropwise over 5 minutes at 25 °C (Table 2, entry 1). The mixture was stirred for 4 hours at 25 °C under argon. Thin layer chromatography analysis indicated completion of the reaction. The reaction mixture was quenched with 3M NaOH (15 mL) (*Caution: Hydrogen evolution!)* and the mixture was extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to afford the 1-octanol product as a colorless oil (0.387g, 2.97 mmol, 99%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.63 (t, *J* = 6.5; 2H), δ 2.54 (s br, 1H), δ 1.55 (m, 2H), δ 1.27 (m, 10H), δ 0.87 (t, *J* = 6.5; 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 63.123 32.72, 31.85, 29.44, 29.31, 25.78, 22.69, 14.10 ppm.

Using binary hydrides DIBAL-H-$HInCl_2$ for the reduction of methyl octanoate (Table 2, entry 3) [5]

Methyl octanoate (0.54 mL, 3 mmol) was added to an oven-dried RBF that was fit with a rubber septum, stir bar, and cooled under argon to 25 °C. Anhydrous THF (10 mL) was then added at 25 °C. DIBAL-H (1.2 M in hexanes, 5.0 mL, 6 mmol) was added, dropwise over 5 minutes at 25 °C and allowed to stir for 4 hours. In a separate oven-dried RBF (50-mL) that was cooled to 25 °C under argon, fit with a rubber septum and stir bar was added anhydrous $InCl_3$ (0.663 g, 3 mmol) and anhydrous THF (10 mL). The mixture was allowed to stir for 5 minutes until all of the $InCl_3$ was dissolved. DIBAL-H (1.2 M in hexanes, 2.5 mL, 3 mmol) was added dropwise over 5 minutes. The reaction stirred for 1 hour at 25 °C to generate $HInCl_2$ and $ClAl(i\text{Bu})_2$. The mixture was then transferred via cannula to the RBF that contained methyl octanoate and DIBAL-H. The mixture was allowed to stir for an additional 4 hours. The reaction was then quenched and worked up according to the general method for the reduction of methyl octanoate (0.387 g, 2.97 mmol, 99%).

Using $HInCl_2$-BH_3:THF for the reduction of methyl octanoate (Table 2, entry 4) [5]

An oven-dried RBF (50-mL) was cooled under argon and charged with a stir bar, anh[5]ydrous $InCl_3$ (0.663 g, 3 mmol) fit with a rubber septum and purged with argon. Anhydrous THF (10 mL) was added via and the mixture stirred vigorously for 5 minutes and 25 °C. Sodium borohydride (0.340 g, 9 mmol) was added and the flask was reflushed with argon. The reaction mixture stirred at 25 °C for 1 hour and during this time the mixture turned an opaque silver color. Methyl octanoate (0.54 mL, 3 mmol) was then added and the reaction mixture was further stirred for 4 hours at 25 °C under argon to complete the reduction. 1-octanol was isolated as explained in the general method for the reduction of methyl octanoate (0.387 g, 2.97 mmol, 99%).

Attempted Reduction of Methyl Octanoate using BH_3:THF

The following procedure is for the reduction of methyl octanoate using BH_3:THF (stabilized with $NaBH_4$) (Table 2, entry 2). An oven-dried RBF (50-mL) was fitted with a rubber septum, cooled under argon and charged with a stir bar. Methyl octanoate (0.54 mL, 3 mmol) was added and then anhydrous THF (10 mL) at 25 °C. BH_3:THF (1.0 M in THF, 3.0 mL, 3 mmol) was added dropwise over 5 minutes at 25 °C. The mixture was stirred for 4 hours at 25 °C under argon. The reaction mixture was quenched with 3M NH_4OH (10 mL) to avoid hydrolyzing the ester group (*Caution: Hydrogen evolution!)* and the mixture was extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated under reduced pressure (25 °C, 1 Torr) to afford a mixture of methyl octanoate (20%) and 1-octanol (80%) products as determined by integration of ^{1}H NMR spectral analysis.

Selective reduction of Methyl 4-(bromomethyl)benzoate using DIBAL-H to produce [4-(bromomethyl)phenyl]methanol (known) [6]

The following procedure was employed for the selective reduction of methyl 4-(bromomethyl)benzoate using DIBAL-H (table 3, entry 1). An oven-dried RBF (50-mL) was cooled under argon and charged with a stir bar, methyl 4-(bromomethyl)benzoate (0.687 g, 3 mmol), and repurged with argon. To this was added anhydrous THF (10 mL) at 25 °C followed by DIBAL-H (1.2 M in hexanes, 5.5 mL, 6.6 mmol) dropwise over 5 minutes at 25 °C. The mixture was stirred for 4 hours at 25 °C under argon. Thin layer chromatography analysis indicated completion of the reaction. The reaction mixture was quenched with 3M NaOH (15 mL) (*Caution: Hydrogen evolution!)* and the mixture was extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated under reduced pressure (25 °C, 1 Torr) to afford 4-(bromomethyl)phenyl]methanol as a white solid (0.542g, 2.70 mmol, 90%). **^{1}H**

NMR (500 MHz, $CDCl_3$) δ 7.35 (d, J = 7.5; 2H), δ 7.27 (d, J = 7.5, 2H), δ 4.57 (s, 2H), δ 4.46 (s, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 141.32, 137.21, 129.37, 127.45, 64.56, 33.45 ppm.

Selective reduction of carbon-bromide bond in methyl 4-(bromomethyl)benzoate using $HInCl_2$ to synthesize methyl *para*-toluate (known) [7]

The following procedure was used for the selective reduction of the carbon-bromide bond of methyl 4-(bromomethyl)benzoate using $HInCl_2$ (Table 3, entry 4). An oven-dried RBF (100-mL) was fitted with a rubber septum, stir bar, and was cooled under argon to 25 °C. Anhydrous $InCl_3$ (0.796 g, 3.6 mmol) was added and the flask was re-purged with argon. Anhydrous THF (12 mL) was added to the mixture and stirred vigorously for 5 minutes and 25 °C. The RBF was then submerged in a water bath and DIBAL-H (1.2 M in hexanes, 3 mL, 3.6 mmol) was added dropwise over 5 minutes at 25 °C. The reaction stirred for 1 hour. Methyl 4-(bromomethyl)benzoate (0.687 g, 3 mmol) was quickly added and the flask and re-purged with argon. The mixture stirred for 4 hours at 25 °C. TLC analysis indicated completion of the reaction. The reaction mixture was quenched with 3M NH_4OH (15 mL) (*Caution: Hydrogen evolution!)* and the mixture was extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to afford the product, methyl *para*-toluate, a colorless oil (0.351 g, 2.34 mmol, 78%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.94 (d, J = 7.5; 2H), δ 7.24 (d, J = 7.5, 2H), δ 3.9 (s, 3H), δ 2.41 (s, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.36, 143.68, 129.73, 129.31, 129.20, 51.97, 21.64 ppm.

Tandem reduction of methyl 4-(bromomethyl)benzoate using binary hydrides methyl-LAB and $HInCl_2$ to produce *para*-tolylmethanol (known) [6]

Tandem reduction of methyl-(bromomethyl)benzoate using binary hydride system methyl-LAB and $HInCl_2$ was carried out as follows (Table 3, entry 4). An oven-dried RBF (100-mL) was cooled under argon to 25 °C and was fitted with a stir bar and rubber septum. Anhydrous $InCl_3$ (0.796 g, 3.6 mmol) was added and the flask was flushed using argon. Anhydrous THF (12 mL) was then added, and the mixture and stirred vigorously for 5 minutes and 25 °C until the $InCl_3$ was fully dissolved. The RBF was then immersed in a water bath and DIBAL-H (1.2 M in hexanes, 3 mL, 3.6 mmol) was added dropwise over 5 minutes at 25 °C and the reaction stirred for 1 hour. Methyl-(bromomethyl)benzoate (0.687 g, 3 mmol) was added to the flask and was re-flushed with argon. The mixture was stirred for 4 additional hours at 25 °C under argon. For the reduction of the ester group, methyl-LAB (1.0 M in THF, 9 mL, 9 mmol) was added and a precipitate crashed out and aggregated which formed a metal nugget consisting of In(0) (the metal nugget was determined to be pure indium by PXRD analysis) and reaction stirred for 1 hour at 25 °C. TLC indicated completion of the reaction. The reaction mixture was quenched with 3M NaOH (10 mL) (*Caution: Hydrogen evolution!)* and the mixture was extracted with Et_2O (3 X 10 mL). The organic layer was then washed with 3M HCl (10 mL) and the acidic solution was extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to afford the *para*-tolylmethanol product as a white solid (0.330, 2.70 mmol, 90%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.26 (d, J = 7.5; 2H), δ 7.18 (d, J = 7.5, 2H), δ 4.64 (s, 3H), δ 2.25 (s, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 137.52, 129.37, 127.27, 65.32, 28.01, 21.18 ppm.

Selective reduction of methyl 4-(bromomethyl)benzoate using binary hydrides $HInCl_2$ and BH_3:THF to produce methyl *para*-toluate (known) [7]

Selective reduction of methyl-(bromomethyl)benzoate using binary hydrides $HInCl_2$ and BH_3:THF (Table 3, entry 5) was carried out as follows. An oven-dried RBF (50-mL) was cooled under argon and charged with a stir bar, anhydrous $InCl_3$ (0.663 g, 3 mmol) fitted with a rubber septum and purged with argon. Anhydrous THF (10 mL) was added and the mixture stirred vigorously for 5 minutes at 25 °C. Sodium borohydride ($NaBH_4$, 0.340 g, 9 mmol) was added and the flask was reflushed with argon. The reaction mixture stirred at 25 °C for 1 hour; during this time the mixture turned an opaque silver color. To the reaction flask was added methyl-(bromomethyl)benzoate (0.687 g, 3 mmol) and again re-purged with argon. The mixture was stirred for 4 hours at 25 °C under argon. After TLC analysis indicated the reaction was complete, the mixture was quenched with 3M NH_4OH (10 mL) (*Caution: Hydrogen evolution!)* and the solid precipitate was filtered and discarded. The filtrate was extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to afford the methyl *para*-toluate product as a white solid (0.446 g, 2.97 mmol, 99%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.94 (d, J = 7.5; 2H), δ 7.24 (d, J = 7.5, 2H), δ 3.9 (s, 3H), δ 2.41 (s, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.36, 143.68, 129.73, 129.31, 129.20, 51.97, 21.64 ppm.

Selective reduction of Methyl 4-(bromomethyl)benzoate using $HInCl_2$ to produce methyl *para*-toluate (known) [7]

The same procedure using $InCl_3$ and $NaBH_4$ in THF was followed for the selective reduction of the carbon-bromide bond of methyl-(bromomethyl)benzoate using $InCl_3$ and $NaBH_4$ (Table 4, entry 6), however the solvent was changed from THF to MeCN. Methyl *para*-toluate was also obtained (0.378 g, 2.52 mmol, 84%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.94 (d, J = 7.5; 2H), δ 7.24 (d, J = 7.5, 2H), δ 3.9 (s, 3H), δ 2.41 (s, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.36, 143.68, 129.73, 129.31, 129.20, 51.97, 21.64 ppm.

Selective reduction of 4-(bromomethyl)phenylacetic acid using DIBAL-H to produce 2-(4-(bromomethyl)phenyl)ethanol (known) [8]

The following procedure was used for the selective reduction of 4-(bromomethyl)phenyl acetic acid using DIBAL-H (scheme 2, b). An oven-dried RBF (50-mL) was cooled under argon, charged with a stir bar and methyl 4-(bromomethyl)phenyl acetic acid (0.687 g, 3 mmol). To this was added anhydrous THF (10 mL) followed by DIBAL-H (1.2 M in hexanes, 7.5 mL, 9 mmol), dropwise over 10 minutes at 25 °C (*Caution: Hydrogen evolution!)*. The mixture was stirred for 4 hours at 25 °C under argon. Thin layer chromatography analysis indicated completion of the reaction. The reaction mixture was quenched with 3M NaOH (15 mL) (*Caution: Hydrogen evolution!)* the mixture was extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to afford the 2-(4-(bromomethyl)phenyl)ethanol product as a white solid (0.548 g, 2.55 mmol, 85%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.34 (d, *J* = 7.5; 2H), δ 7.21 (d, *J* = 7.5, 2H), δ 4.49 (s, 2H), δ 3.85 (t, *J* = 6.5, 2H), δ 2.89 (t, *J* = 6.5, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 139.22, 136.11, 129.64, 129.40, 63.38, 38.86, 33.54 ppm.

Selective reduction of 4-(bromomethyl)phenyl acetic acid using BH_3:THF to produce 2-(4-(bromomethyl)phenyl)ethanol (known) [8]

Selective reduction of 4-(bromomethyl)phenyl acetic acid using BH_3:THF (scheme 2, c) was carried out the following way. An oven-dried RBF (50-mL) was fit with a rubber septum and charged with a stir bar. The flask was cooled to 25 °C with argon. Methyl 4-(bromomethyl)phenyl acetic acid (0.687 g, 3 mmol) was added and followed by anhydrous THF (10 mL). BH_3:THF (1.0 M in THF, 3.0 mL, 3 mmol) was added dropwise over 10 minutes at 25 °C (*Caution: Hydrogen evolution!)*. After 4 hrs, reaction mixture was quenched with 3M NaOH (10 mL) (*Caution: Hydrogen evolution!)*, and extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to afford the 2-(4-(bromomethyl)phenyl)ethanol product as a white solid (0.606 g, 2.82 mmol, 94%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.34 (d, *J* = 7.5; 2H), δ 7.21 (d, *J* = 7.5, 2H), δ 4.49 (s, 2H), δ 3.85 (t, *J* = 6.5, 2H), δ 2.89 (t, *J* = 6.5, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 139.22, 136.11, 129.64, 129.40, 63.38, 38.86, 33.54 ppm.

Selective reduction of 4-(bromomethyl)phenyl acetic acid using $HInCl_2$ forming *para*-tolylacetic acid (known) [10]

The following is for the selective reduction of 4-(bromomethyl)phenyl acetic acid using $HInCl_2$ (scheme 2, d). An oven-dried RBF (100-mL) was cooled under argon and charged with a stir bar and fit with a rubber septum. Anhydrous $InCl_3$ (1.326 g, 6 mmol) was then added and the flask was re-purged with argon. Anhydrous THF (20 mL) was added and the mixture stirred vigorously for 5 minutes at 25 °C. The RBF was then immersed in a water bath and DIBAL-H (1.2 M in hexanes, 5.0 mL, 6 mmol) was added dropwise over 10 minutes at 25 °C. The reaction was allowed to stir for 1 hour at 25 °C. Methyl 4-(bromomethyl)phenyl acetic acid (0.687 g, 3 mmol) was added and the stirring continued for an additional 4 hours at 25 °C under argon. Thin layer chromatography analysis indicated completion of the reaction. The reaction mixture was quenched with 3M NaOH (15 mL) (*Caution: Hydrogen evolution!)* and acidified using acetic acid to pH 4. The mixture was extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to afford *para*-tolylacetic acid as a white solid (0.405 g, 2.70 mmol, 90%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.21 (d, *J* = 8, 2H), δ 7.18 (d, *J* = 8, 2H), δ 3.80 (s, 2H), δ 2.36(s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.25, 137.29, 129.61, 129.44, 70.28, 54.29, 41.23, 28.83 ppm.

Tandem reduction of 4-(bromomethyl)phenyl acetic acid using binary hydrides DIBAL-H and $HInCl_2$ to produce 4-Methylphenethyl alcohol (known) [9]

The following method was used for the tandem reduction of 4-(bromomethyl)phenyl acetic acid using binary hydride system DIBAL-H and $HInCl_2$ (scheme 2, e). An oven-dried RBF (100-mL) was cooled under argon and charged with a stir bar, 4-(bromomethyl)phenyl acetic acid (0.687 g, 3 mmol) and reflushed with argon. Anhydrous THF (10 mL) was added at 25 °C followed by DIBAL-H (1.2 M in hexanes, 7.5 mL, 9 mmol), dropwise over 5 minutes at 25 °C (*Caution: Hydrogen evolution!)*. The mixture stirred for 4 hours at 25 °C under argon. In a separate reaction flask (100-mL), cooled under argon, fit with a septum and charged with a stir bar, was added anhydrous $InCl_3$ (0.663 g, 3 mmol). Anhydrous THF (10 mL) was added, and the mixture stirred vigorously for 5 minutes at 25 °C. The RBF was then submerged in a water bath and DIBAL-H (1.2 M in hexanes, 2.5 mL, 3 mmol) was added dropwise over 5 minutes at 25 °C. The reaction was allowed to stir for 1 hour at 25 °C. To the reaction flask containing 4-(bromomethyl)phenyl acetic acid and DIBAL-H was added $HInCl_2$, transferred via cannula, and the mixture was stirred for 4 more hours at 25 °C under argon. Thin layer chromatography analysis indicated completion of the reaction. The reaction mixture was quenched with 3M NaOH (15 mL) (*Caution: Hydrogen evolution!)* and the mixture was extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to afford the 4-methylphenethyl alcohol l product as a white solid (0.286 g, 2.1 mmol, 70%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.23 (d, *J* = 7.5, 2H), δ 7.21 (d, *J* = 7.5, 2H), δ 3.85 (t, *J* = 6.5, 2H), δ 2.94(s br, 1H), δ 2.89 (t, *J* = 6.5, 2H), δ 2.42 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 136.03, 135.78, 129.43, 129.16, 63.78, 38.89, 21.16 ppm.

Tandem reduction of 4-(bromomethyl)phenyl acetic acid using binary hydrides BH_3:THF and $HInCl_2$ to produce 4-Methylphenethyl alcohol (known)[9]

The following method was used for the tandem reduction of 4-(bromomethyl)phenyl acetic acid using binary hydrides $HInCl_2$ and BH_3:THF (scheme 2, f). An oven-dried RBF (50-mL) was cooled under argon and charged with a stir bar, anhydrous $InCl_3$ (0.663 g, 3 mmol) and purged with argon. Anhydrous THF (10 mL) was added and the mixture stirred vigorously for 5 minutes at 25 °C. Sodium borohydride ($NaBH_4$, 0.340 g, 9 mmol) was added and the flask was reflushed with argon. The reaction mixture stirred at 25 °C for 1 hour and the mixture turned an opaque silver color. 4-(bromomethyl)phenyl acetic acid (0.687 g, 3 mmol) was added quickly and the flask was reflushed with argon. The mixture was stirred for 4 hours at 25 °C under argon. Thin layer chromatography analysis indicated completion of the reaction. The reaction mixture was quenched with 3M NaOH (10 mL) (*Caution: Hydrogen evolution!)*. The solid precipitate was filtered and discarded. The filtrate was extracted with Et_2O (3 X 10 mL). The combined organic layers were dried with $MgSO_4$, filtered, and evaporated in vacuo (25 °C, 1 Torr) to afford the 4-methylphenethyl alcohol product as a white solid (0.384 g, 2.82 mmol, 94%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.23 (d, *J* = 7.5, 2H), δ 7.21 (d, *J* = 7.5, 2H), δ 3.85 (t, *J* = 6.5, 2H), δ 2.94(s br, 1H), δ 2.89 (t, *J* = 6.5, 2H), δ 2.42 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 136.03, 135.78, 129.43, 129.16, 63.78, 38.89, 21.16 ppm.

Tandem reduction of 4-(bromomethyl)phenyl acetic acid using $HInCl_2$ to produce 4-Methylphenethyl alcohol (known)[9]

The same procedure as $InCl_3$ and $NaBH_4$ in THF was used for the selective reduction of the carbon-bromide bond of 4-(bromomethyl)phenyl acetic acid using $InCl_3$ and $NaBH_4$ (scheme 2, g), however the solvent was changed from THF to MeCN. 4-Methylphenethyl alcohol was also obtained as a white solid (0.241 g, 1.77 mmol, 59%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.23 (d, *J* = 7.5, 2H), δ 7.21 (d, *J* = 7.5, 2H), δ 3.85 (t, *J* = 6.5, 2H), δ 2.94 (s br, 1H), δ 2.89 (t, *J* = 6.5, 2H), δ 2.42 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 136.03, 135.78, 129.43, 129.16, 63.78, 38.89, 21.16 ppm.

Partial reduction of 4-(halomethyl)benzonitrile using DIBAL-H to produce *para*-(halomethyl)benzaldehyde (known)[10]

The following procedure for the partial reduction of 4-(halomethyl)benzonitrile is as follows (Table 4, entry 1). An oven dried round bottom flask (25-mL) fitted with a rubber septum was cooled under argon and charged with a stir bar. Anhydrous THF (5 mL) and 4-(halomethyl)benzonitrile (0.455 g, 3 mmol) were added at 25 °C. DIBAL-H (1 M in hexanes, 3 mL, 3 mmol) was added to the reaction mixture dropwise via syringe over 5 min. and the reaction stirred at 25 °C for 4 h. Thin layer chromatography analysis indicated the completion of the reaction. The reaction was quenched with 1.5 M hydrochloric acid (10 mL), methanol (5 mL) and the mixture stirred for 30 min (*Caution: Hydrogen evolution!)*. The reaction mixture was then, filtered and extracted with Et_2O/THF (3 x 10 mL) and the combined organic layers were dried with anhydrous $MgSO_4$, filtered and evaporated in vacuo (25 °C, 1 Torr) to afford the tandem reduction 4-(halomethyl)benzaldehyde product as a white solid (Cl = 0.371 g, 2.40 mmol, 80%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.05 (s, 1H), δ 7.89 (d, *J* = 8, 2H), δ 7.52 (d, *J* = 8, 2H), δ 4.61 (s, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 191.7, 143.8, 132.7, 130.2, 129.2, 45.3 ppm. (Br = 0.507 g, 2.55 mmol, 85%) **^{1}H NMR** (500 MHz, $CDCl_3$) δ 10.07 (s, 1H), δ 7.91 (d, *J* = 8, 2H), δ 7.59 (d, *J* = 8, 2H), δ 4.56 (s, 1H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 191.9, 144.6, 136.4, 130.2, 129.8, 33.1 ppm.

Selective reduction of 4-(halomethyl)benzonitrile using $HInCl_2$ to produce *para*-tolunitrile (known)[11]

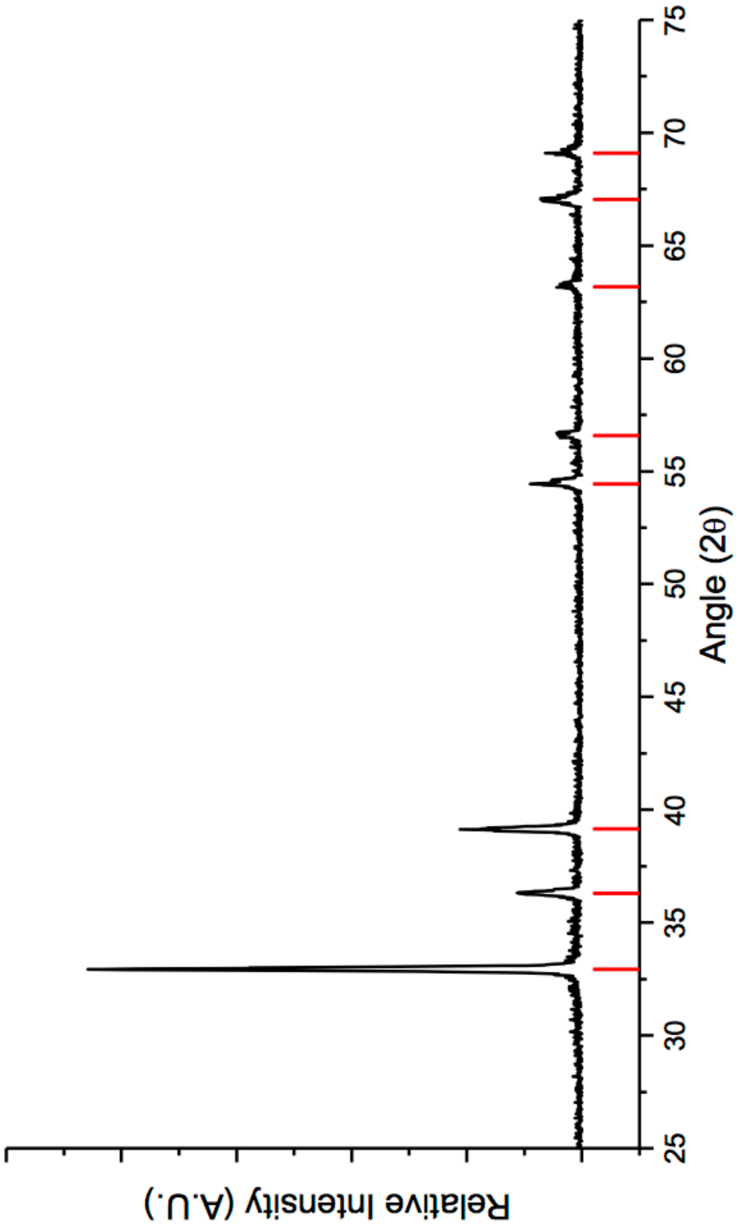
For the selective reduction of 4-(halomethyl)benzonitrile using $HInCl_2$ the following procedure was used (Table 2, entry 3). An oven dried round bottom flask (50-mL) fitted with a rubber septum was cooled under argon and charged with a stir bar, anhydrous $InCl_3$ (0.663 g, 3 mmol), anhydrous THF (10 mL) and DIBAL-H (1 M in hexanes, 3.1 mL, 3.1 mmol). The reaction was then stirred at 25 °C for 1 h. 4-(halomethyl)benzonitrile (0.588 g, 3 mmol) was added to the RBF and the reaction mixture was stirred at 25 °C. After 4 h, TLC analysis indicated completion of the reaction. The reaction was quenched with deionized water (10 mL) (*Caution: Hydrogen evolution!)* and the mixture extracted with Et_2O (3 x 10 mL). The combined organic layers were dried with anhydrous $MgSO_4$, filtered and evaporated in vacuo (25 °C, 1 Torr) to afford the selectively reduced *para*-tolunitrile product as a colorless oil (Cl = 0.260 g, 2.22 mmol, 74%. Br = 0.299 g, 2.55 mmol, 85% yield). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.52 (d, 2H), δ 7.28 (d, 2H), δ 2.41 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 143.9, 132.2, 130.0, 119.3, 109.4, 21.9 ppm.

Tandem reduction of 4-(halomethyl)benzonitrile using binary hydrides DIBAL-H and $HInCl_2$ to produce *para*-methylbenzaldehyde (known)[12]

The following procedure is for the tandem reduction of 4-(halomethyl)benzonitrile (Table 4, entry 4). An oven dried round bottom flask (50-mL), fitted with a rubber septum and stir bar, was cooled under argon to 25 °C. Anhydrous THF (5 mL) and 4-(halomethyl)benzonitrile (0.588 g, 3 mmol) were added to the RBF. DIBAL-H (1M in hexanes, 3 mL, 3 mmol) was then added to the reaction mixture dropwise over 5 min. and the reaction stirred at 25 °C for 4 h. A second equivalent of DIBAL-H (1 M in hexanes, 3.3 mL, 3.3 mmol) followed by anhydrous $InCl_3$ (0.663 g, 3 mmol) was then added and the reaction stirred at 25 °C for 4 h. TLC analysis and infrared spectroscopy indicated the completion of the reaction. The reaction was quenched with 1.5 M hydrochloric acid (10 mL), methanol (5 mL) and the mixture stirred for 30 min (*Caution: Hydrogen evolution!)*. The reaction mixture was then, filtered and the remaining acidic solution was extracted with Et_2O/THF (3 x 10 mL). The combined organic layers were dried with anhydrous $MgSO_4$, filtered and evaporated in vacuo (25 °C, 1 Torr) to afford the tandem reduction 4-(methyl)benzaldehyde product as a colorless oil (Cl = 0.227 g, 1.89 mmol, 63%. Br = 0.242 g, 2.01 mmol, 67%). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.96 (s, 1H), δ 7.81 (d, *J* = 8.5, 2H), δ 7.28 (d, *J* = 8.5, 2H), δ 2.43 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 191.7, 145.6, 134.3, 129.5 (4 C), 21.8 ppm.

References:

1. H. Mattes, C. Benezra. *J. Org, Chem.* 1988, *53*, 2732.
2. B. R. Travis, M. Sivakumar, G. O. Hollist, B. Borhan. *Org. Lett*., 2003, **5**, 1031.
3. Y. J. Zhang, W. Dayoub, G. R. Chen, M. Lemaire. *Tetrahedron*, 2012, **68**, 7400.
4. S. F. Wnuk, M. Robins. *J. Amer. Chem. Soc.* 1996*,* **118**, 2519.
5. G. Zhang, B. L. Scott, S. K. Hanson. *Angew Chem Int. Ed.* 2012, **51**, 12102.
6. S. Vassiliou, M. Xeilari, A. Yiotakis, J. Grembecka, M. Pawelczak, P. Kararski, A. Mucha. *Bioorg. Med. Chem.* 2007*,* **15**, 3187.
7. J. B. Henderickson, Md. S. Hussoin. *J. Org. Chem*, 1989, **54**, 1144.
8. J, Zheng, S. Chevance, C. Darcel, J. B. Sortais. *Chem. Commun*, 2013, **49**, 10010.
9. S. Kumar, S. K. Dixit, S. K. Awasthi *Tetrahedron Lett.* 2014, **55**, 3802.
10. P. Nateus, R. Delgado, P. Groves, S. R. R. Campos, A. M. Baptista, P. Brandão, V. Félix. *J. Org. Chem.* 2012, **77**, 6816.
11. D. Cantillo, O. de Frutos, J. A. Rincon, C. Mateos, C. O. Kappe. *J. Org. Chem.* 2014, **79**, 223.
12. C. Chen, B. Liu, W. Chen *SYNTHESIS*, 2013*,* **45**, 3387.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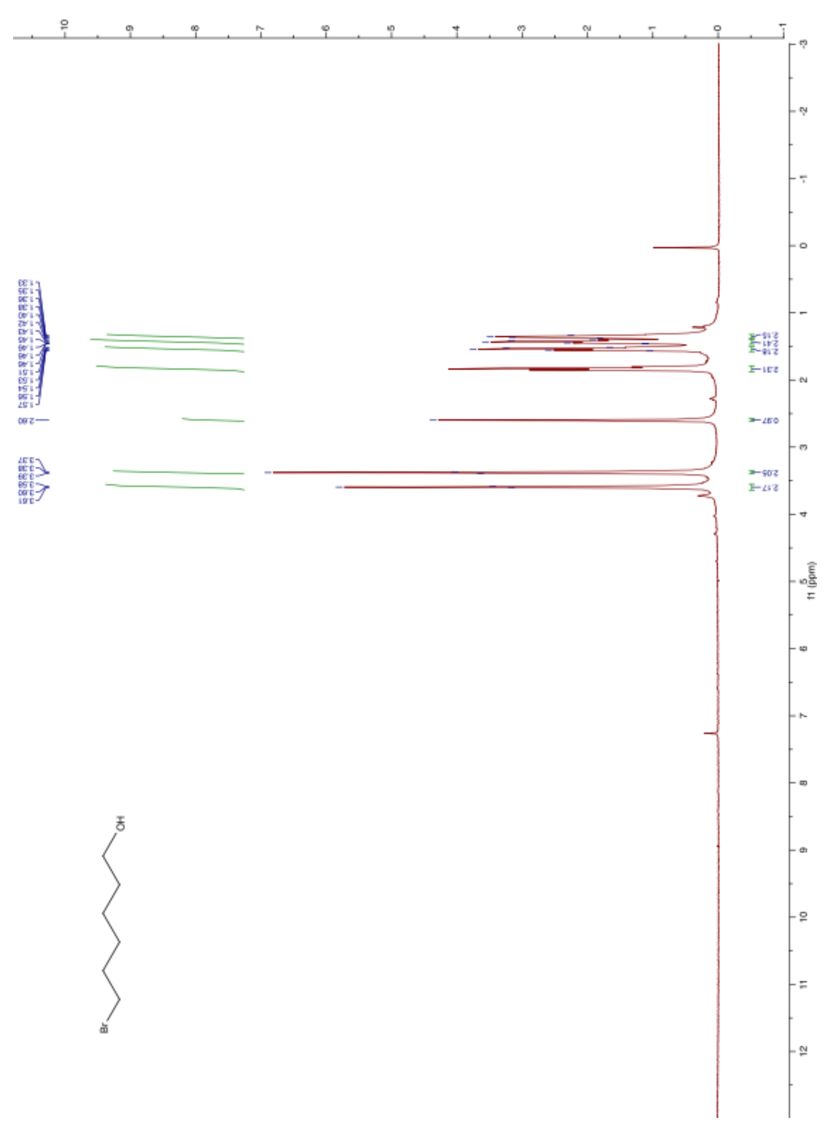

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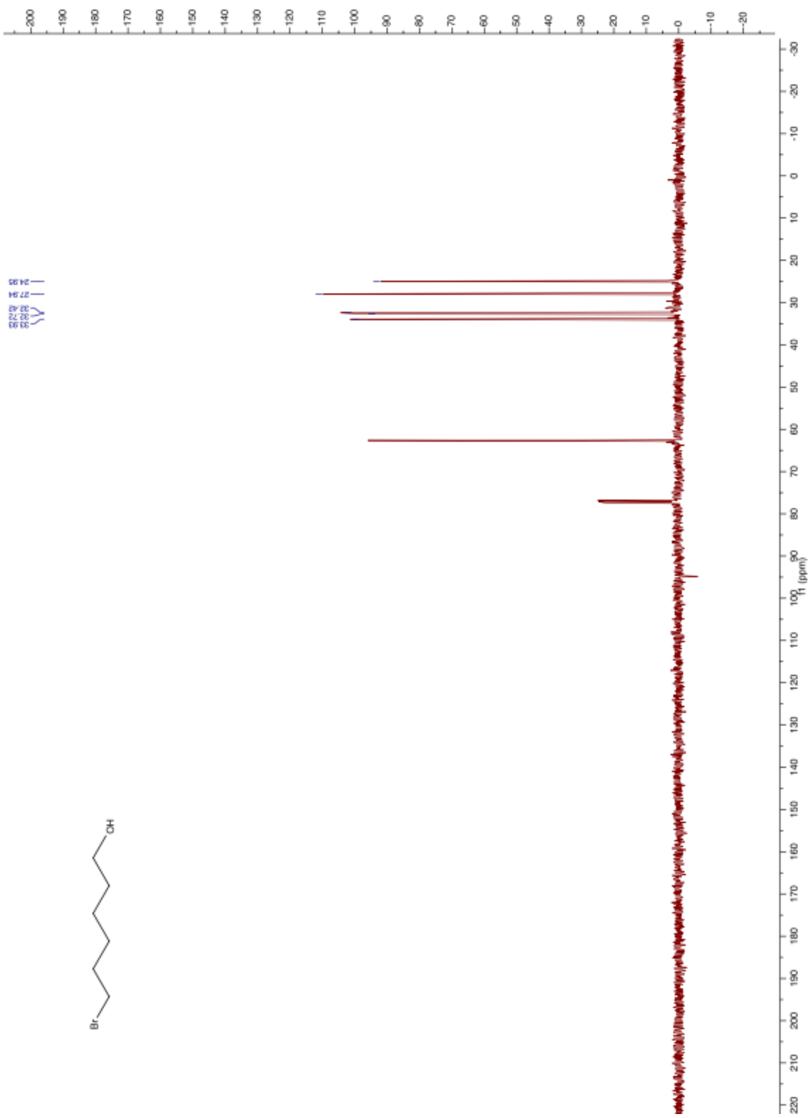
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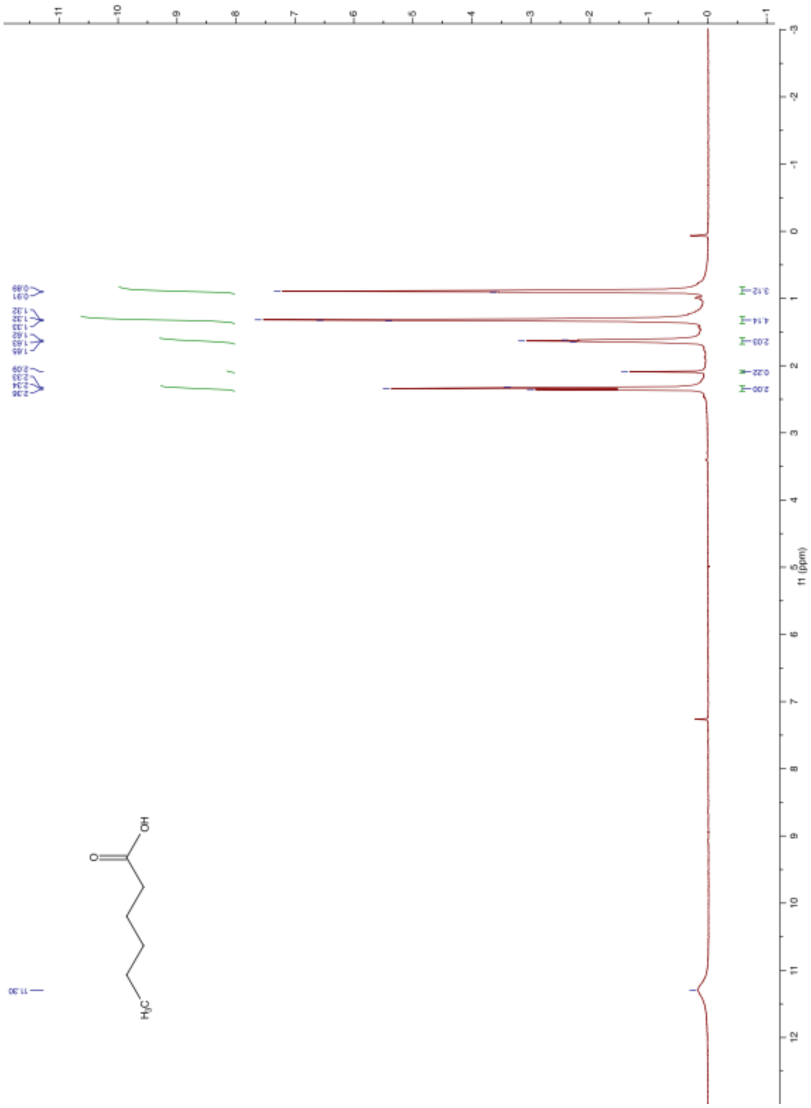
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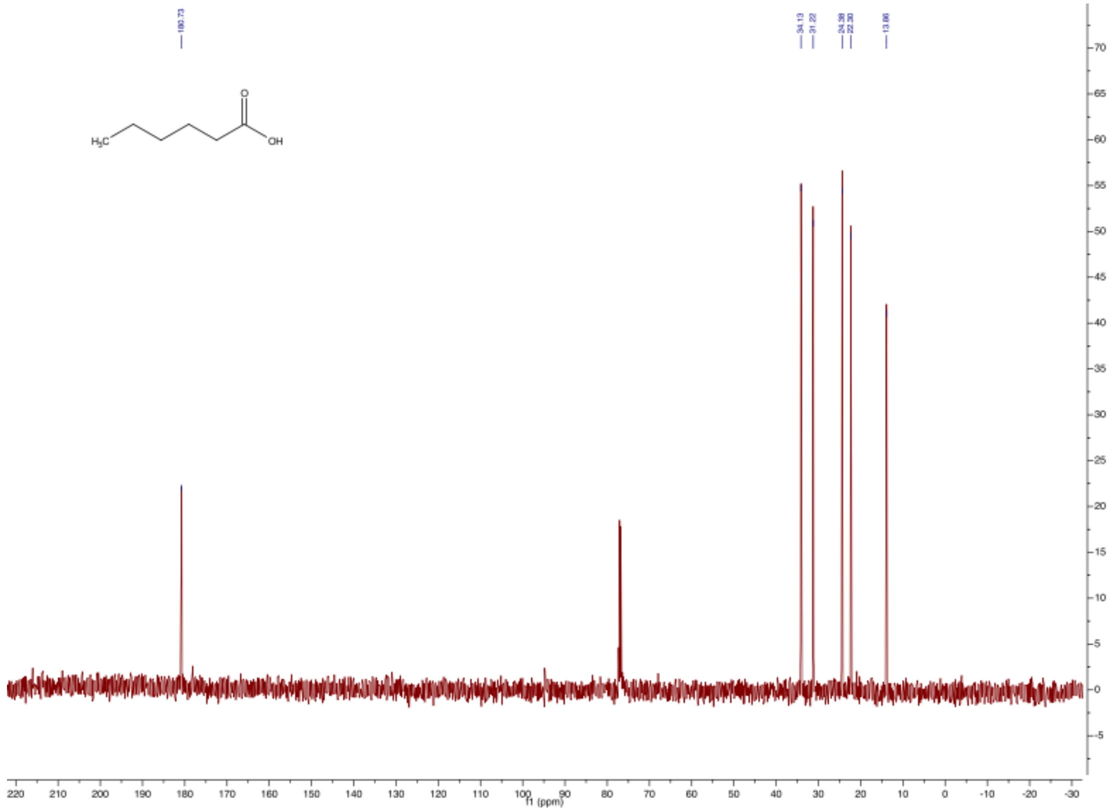

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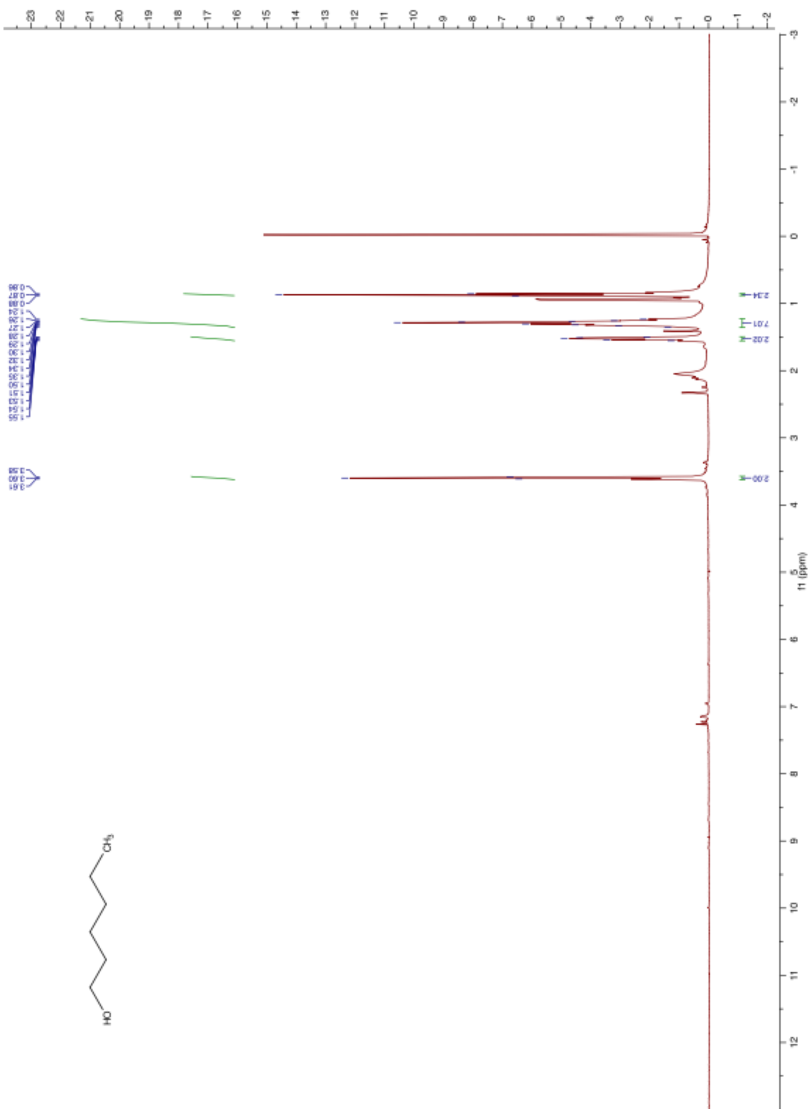
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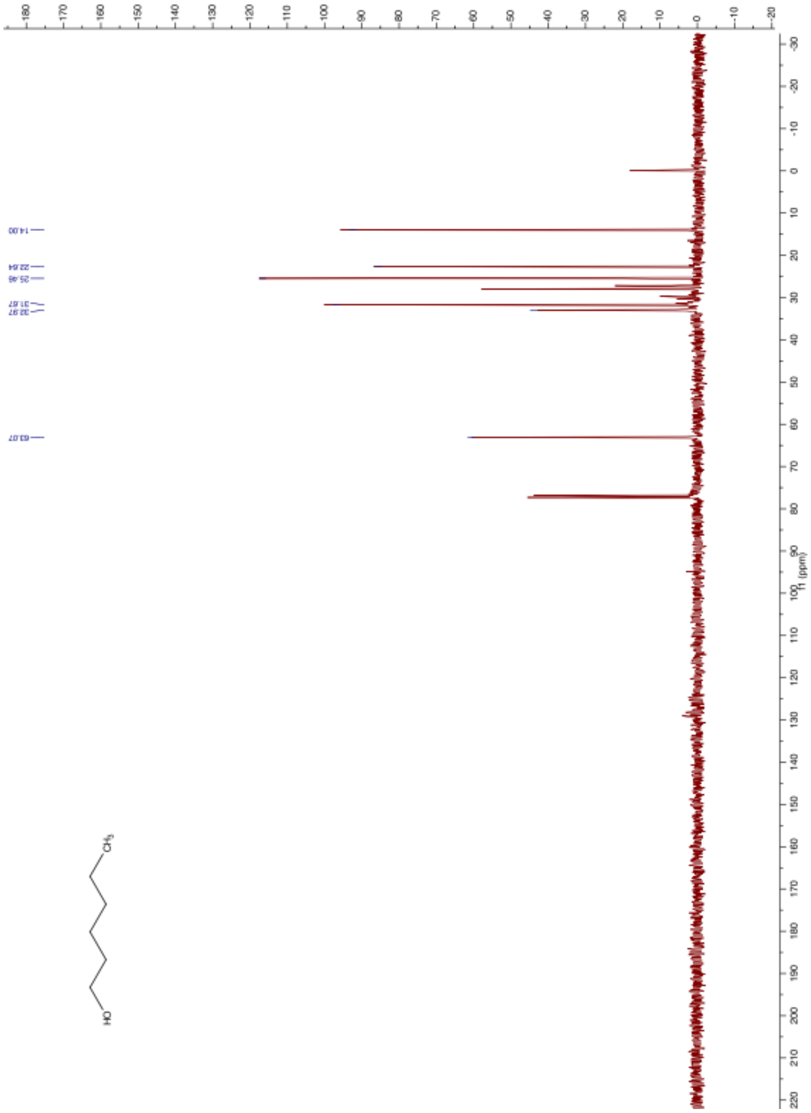
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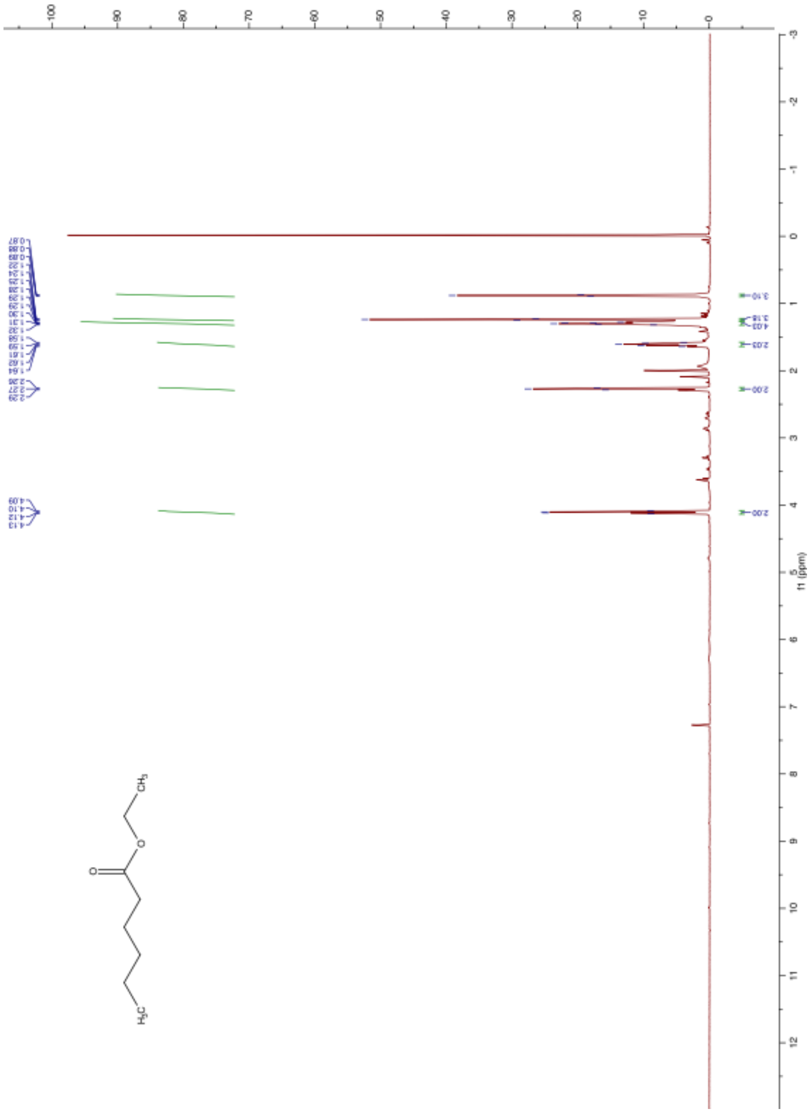
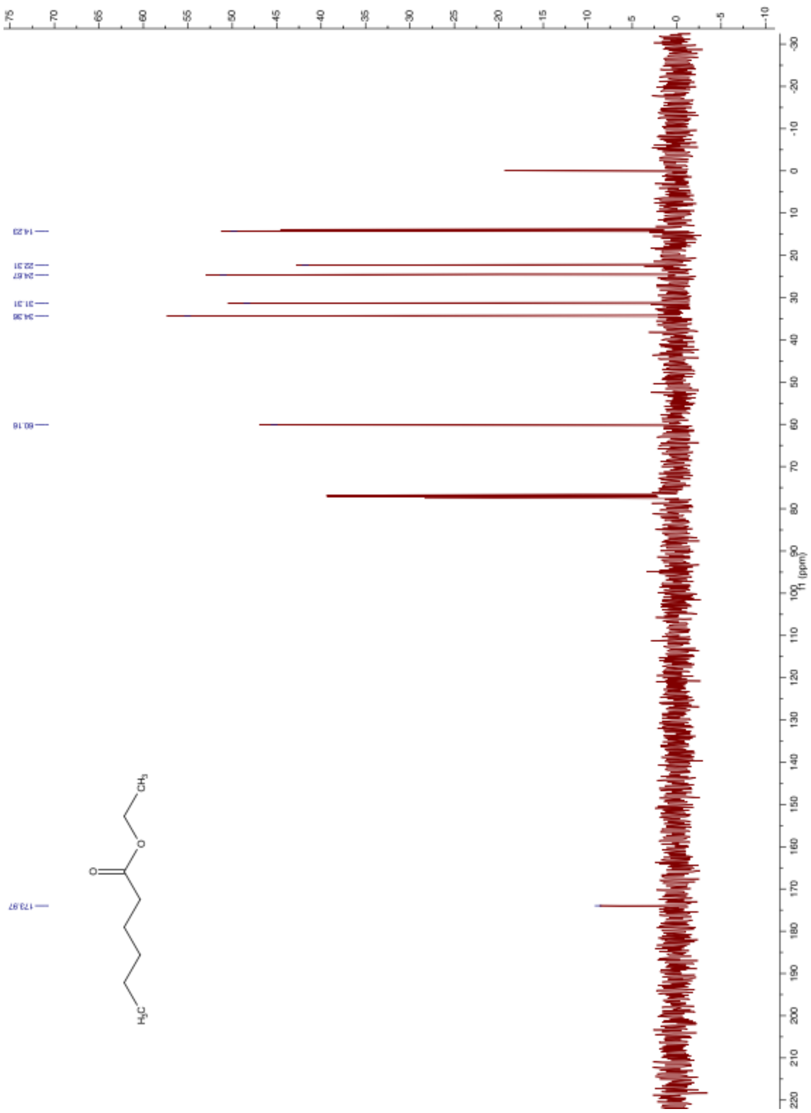
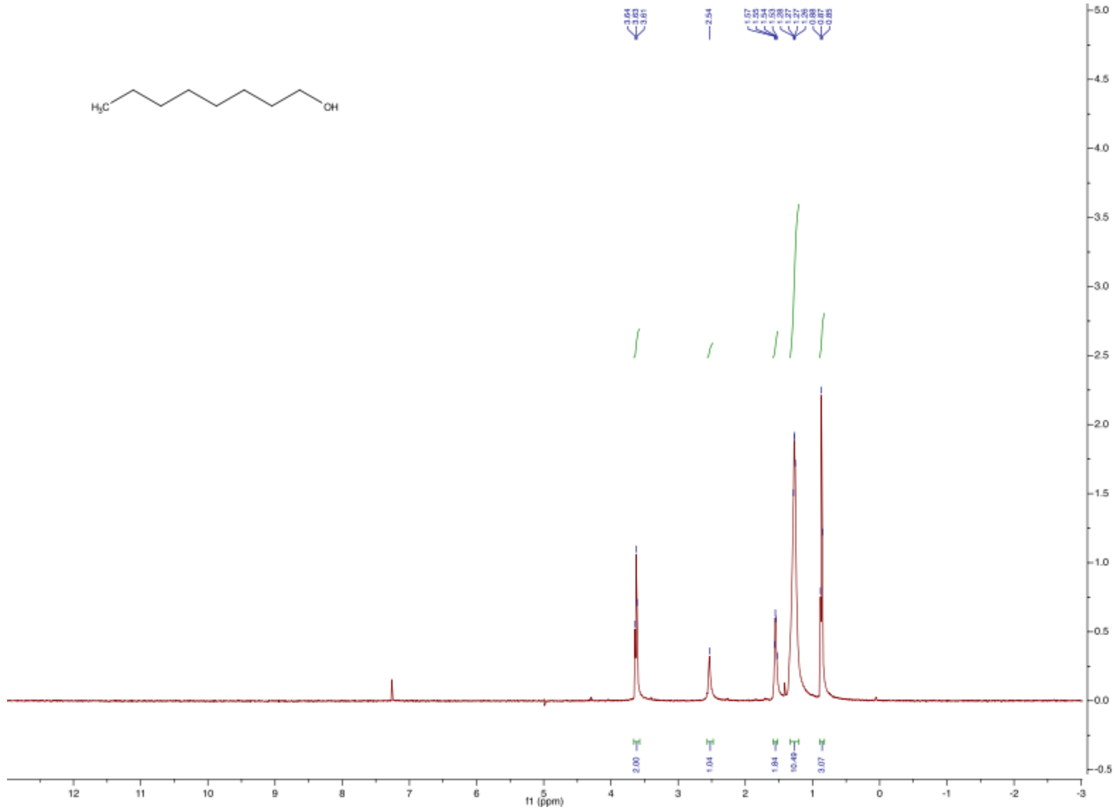
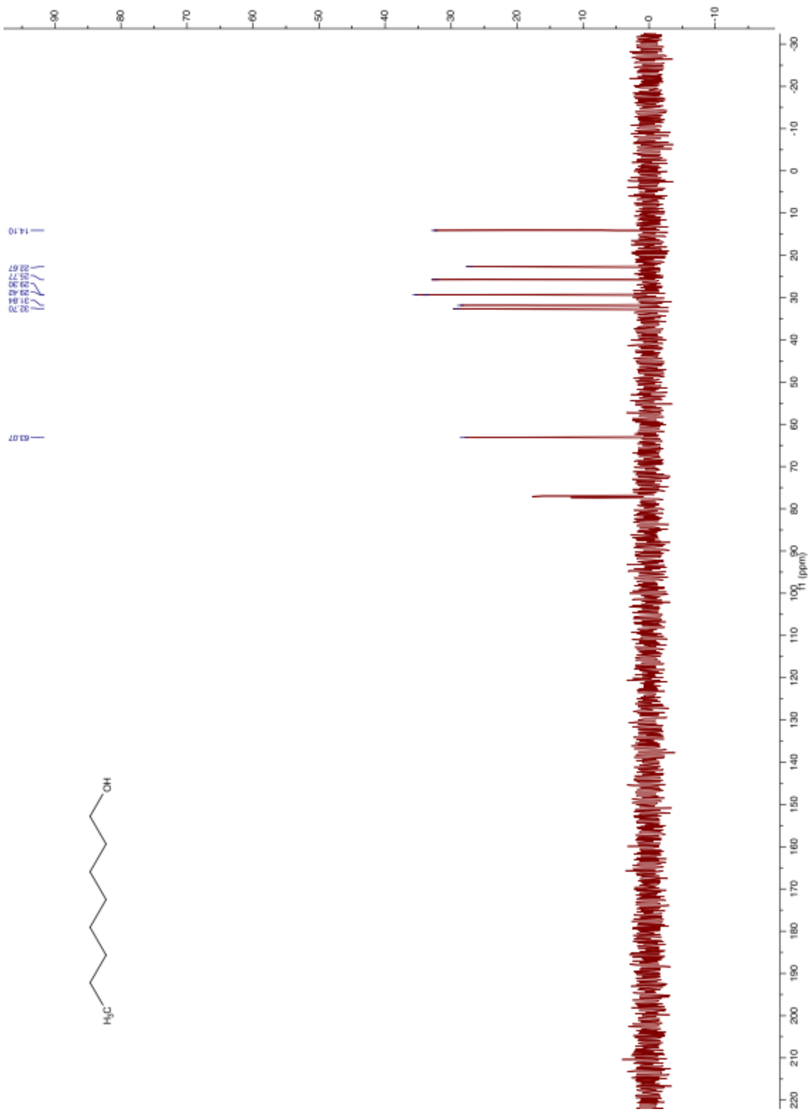
f1 (ppm)

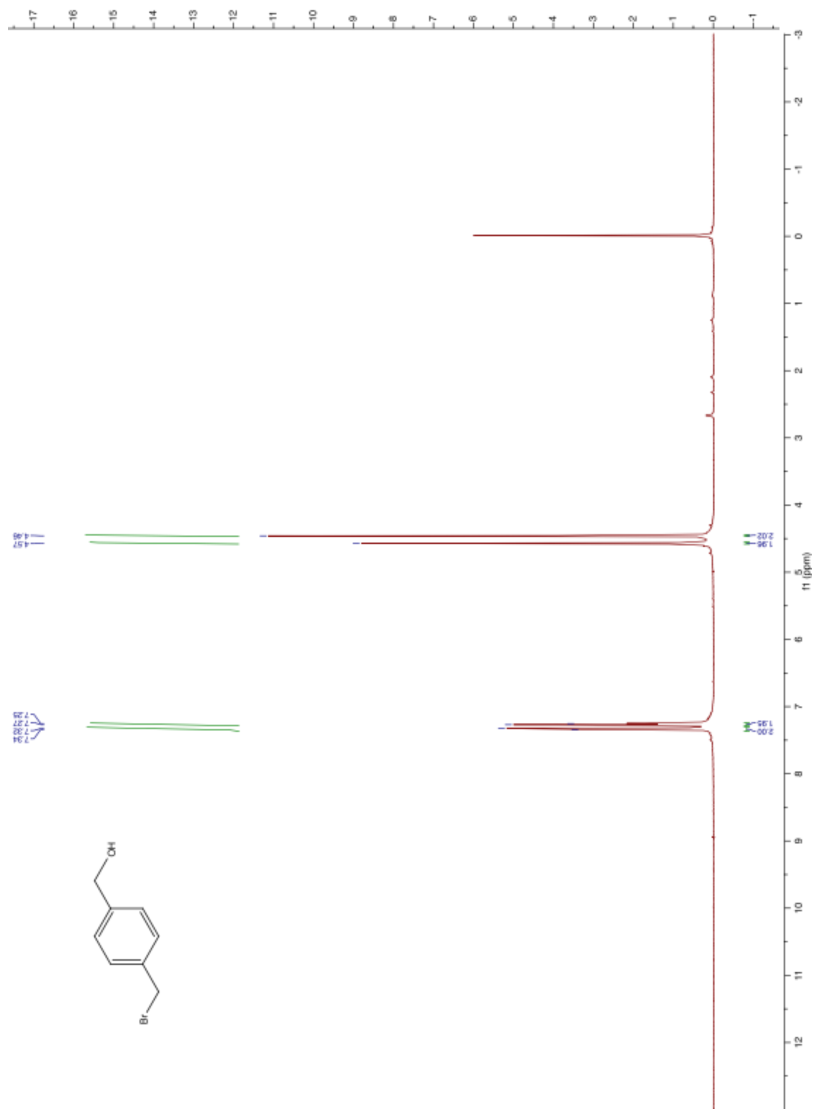

0.87
0.88
0.89
1.23
1.24
1.25
1.28
1.29
1.29
1.30
1.31
1.32
1.58
1.59
1.61
1.62
1.64
2.26
2.27
2.29
4.09
4.10
4.12
4.13
3.10
3.18
4.03
2.03
2.00
2.00
f1 (ppm)
H3C
O
O
CH3
-3
-2
-1
0
1
2
3
4
5
6
7
8
9
10
11
12
100
90
80
70
60
50
40
30
20
10
0



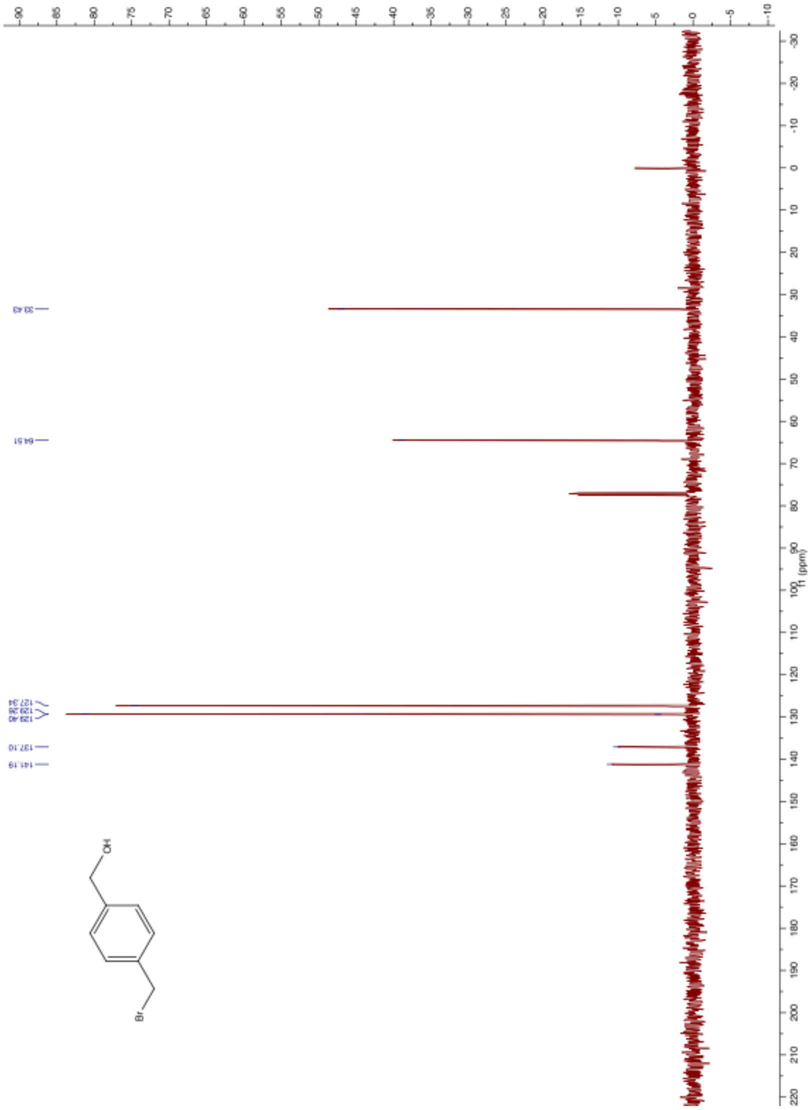
14.23
22.31
24.67
31.31
34.36
60.16
173.97
O
H3C
CH3
f1 (ppm)

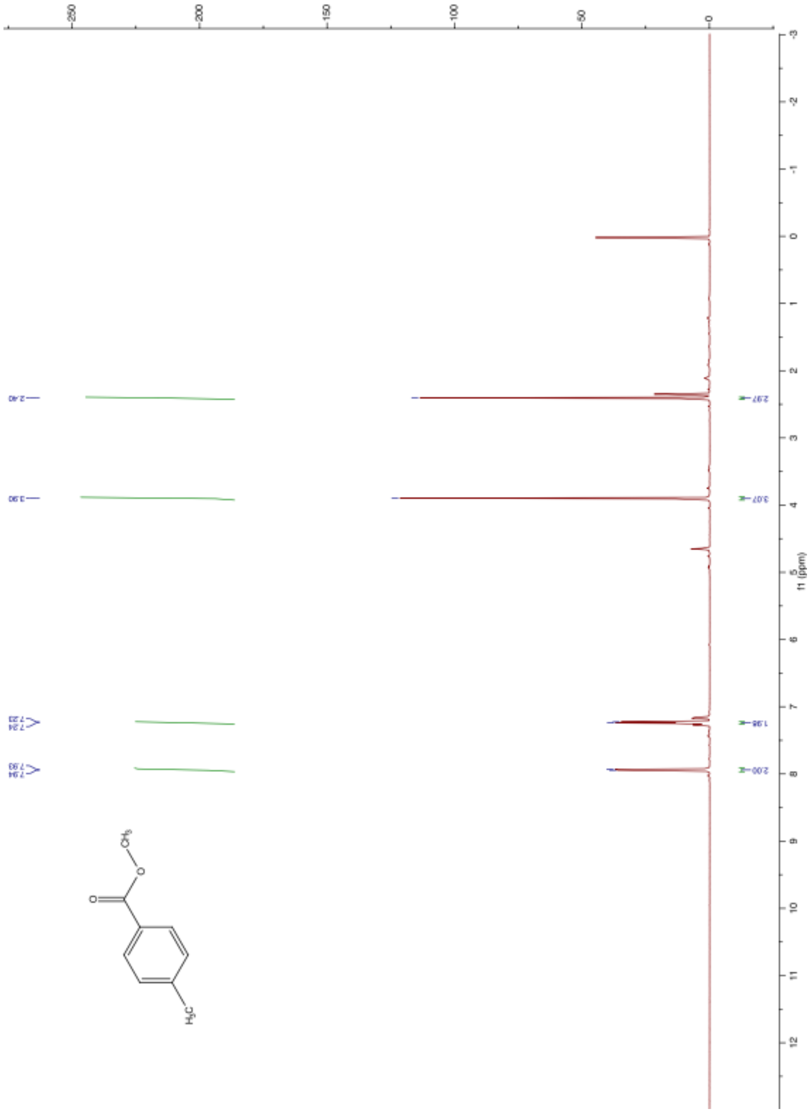

3.64
3.63
3.61
2.54
1.57
1.55
1.54
1.53
1.28
1.27
1.27
1.26
0.88
0.87
0.85
H3C
OH
2.00
1.04
1.84
10.49
3.07
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
f1 (ppm)
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

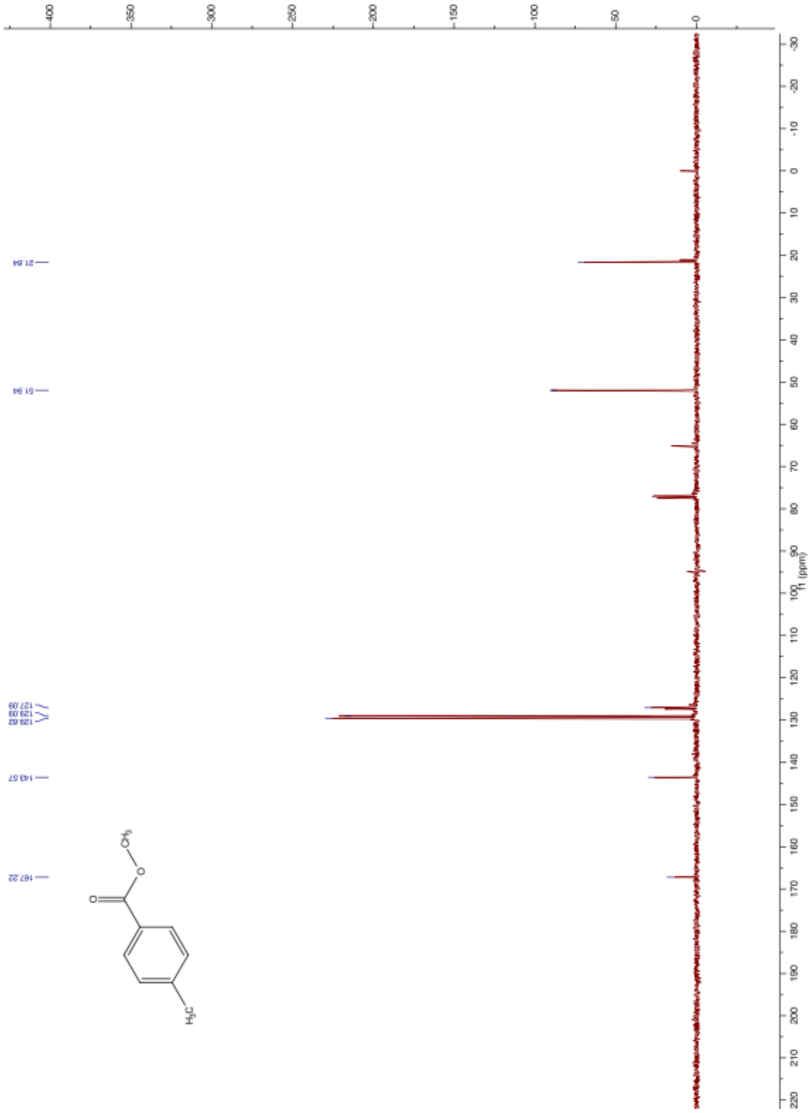

14.10
22.67
25.77
29.30
29.42
31.84
32.70
63.07
H3C
OH
f1 (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
90
80
70
60
50
40
30
20
10
0
-10

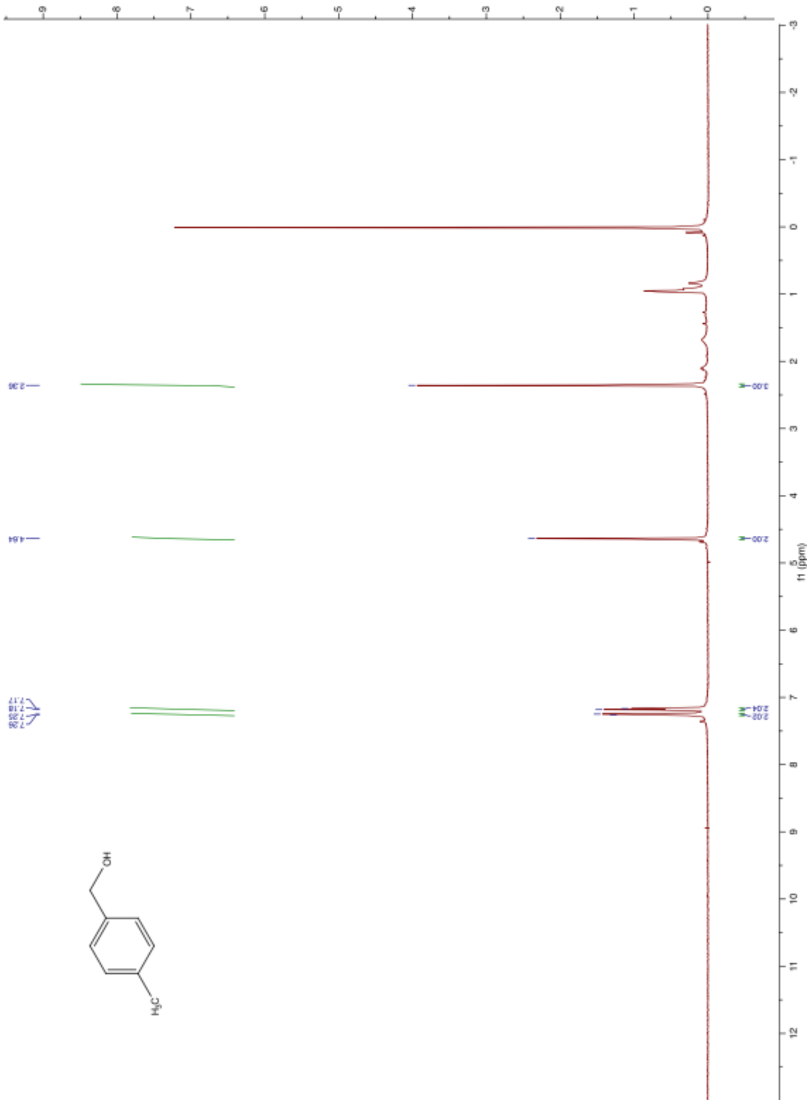


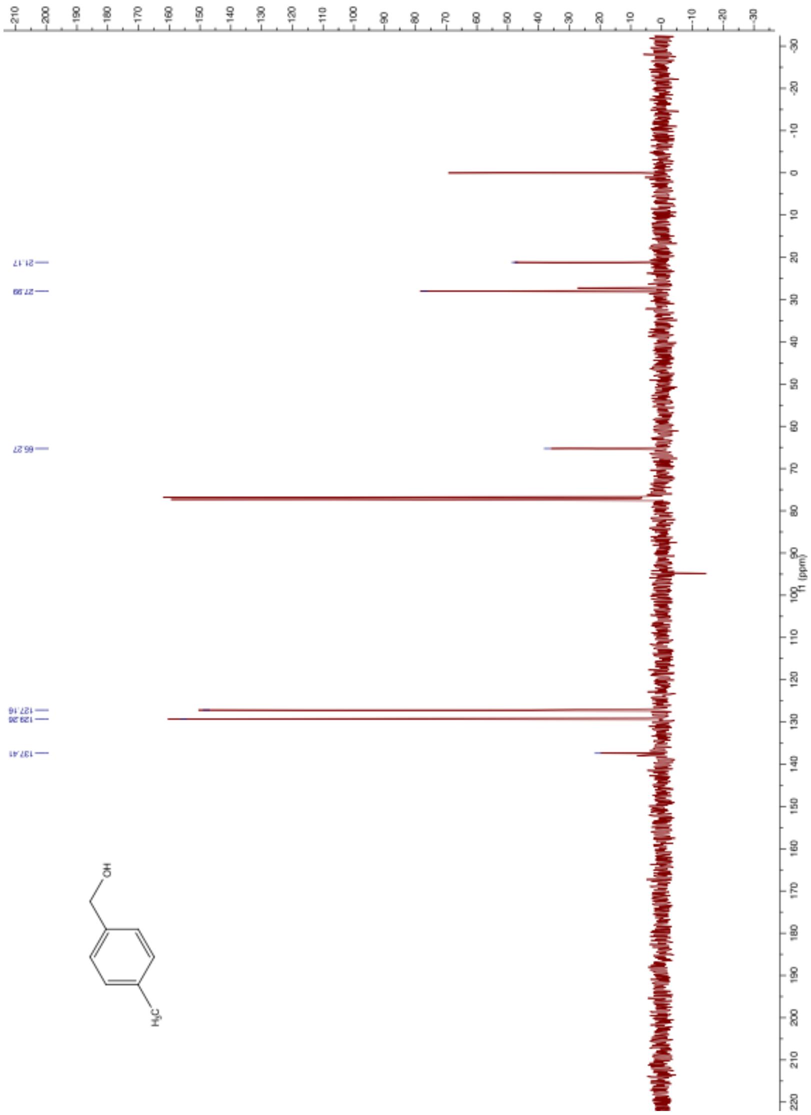
4.46
4.57
7.25
7.27
7.32
7.34
OH
Br
2.02
1.96
1.95
2.00
f1 (ppm)

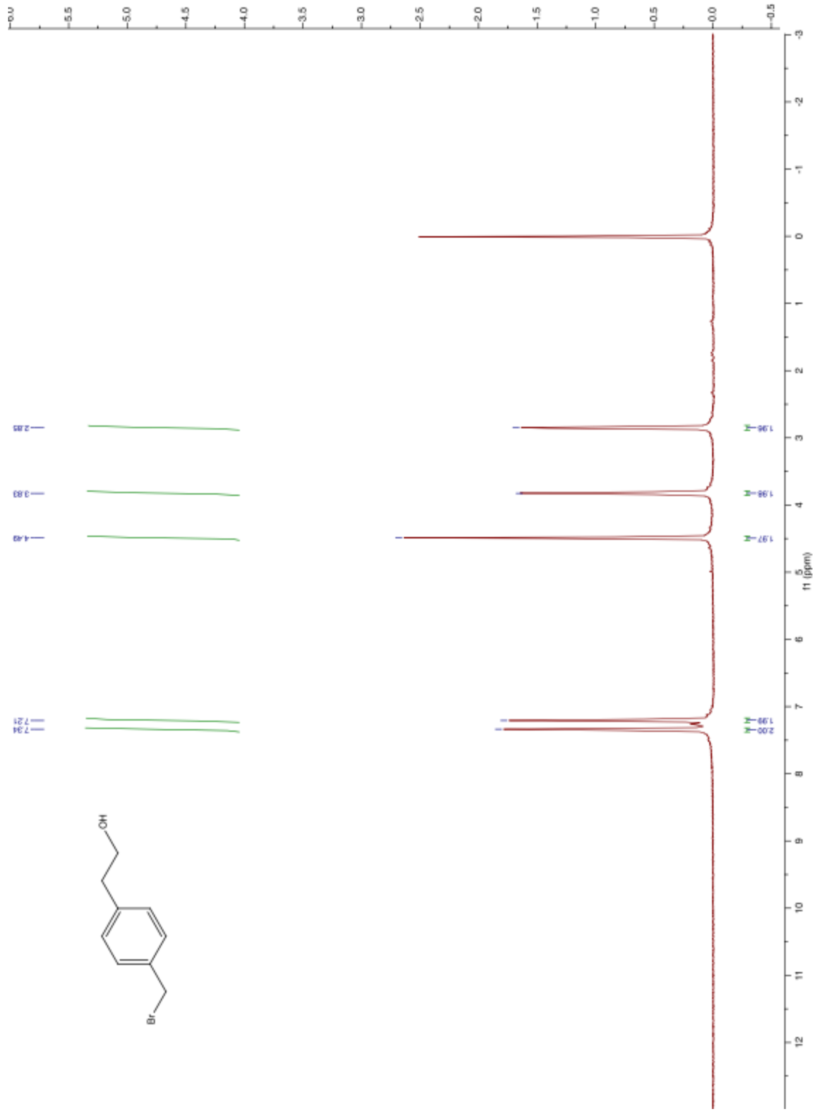

33.43
64.51
127.34
129.38
129.40
137.10
141.19
Br
OH
f1 (ppm)
-30
-20
-10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
-10


7.94
7.93
7.24
7.23
3.90
2.40
2.00
1.98
3.07
2.97
f1 (ppm)
O
O
CH3
H3C

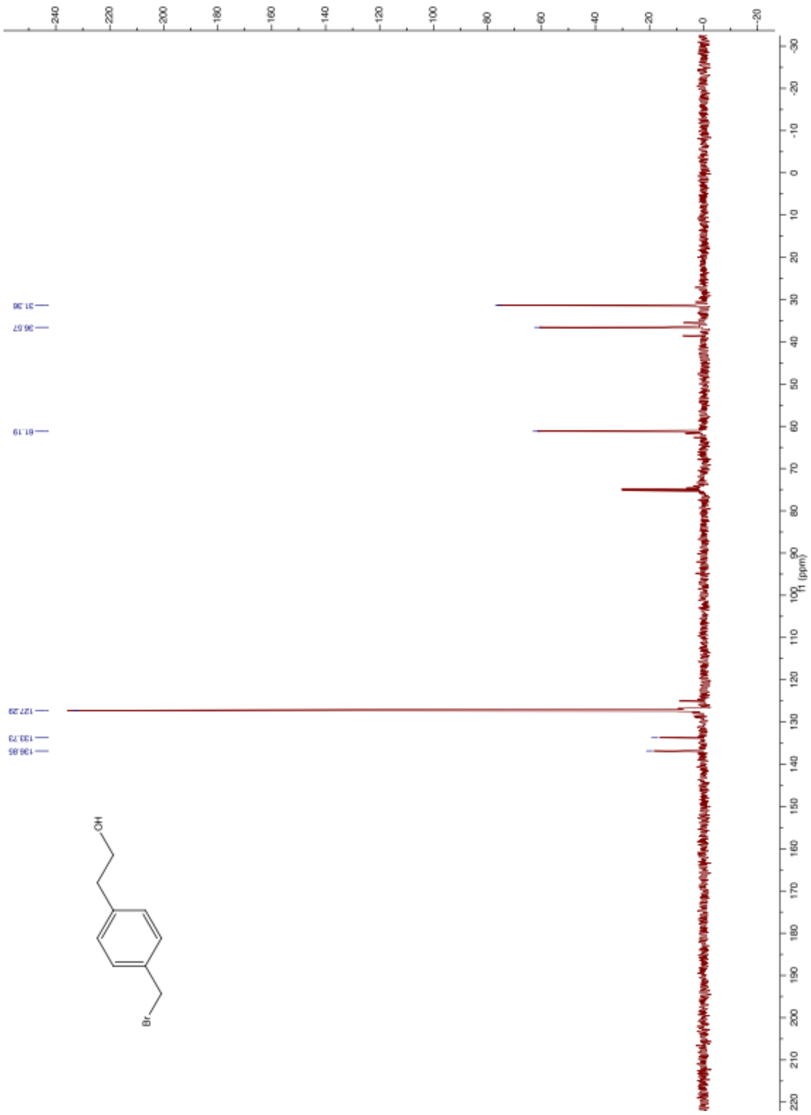

21.64
51.94
127.09
129.09
129.62
143.57
167.22
H3C
O
O
CH3
f1 (ppm)
-30
-20
-10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
400
350
300
250
200
150
100
50
0

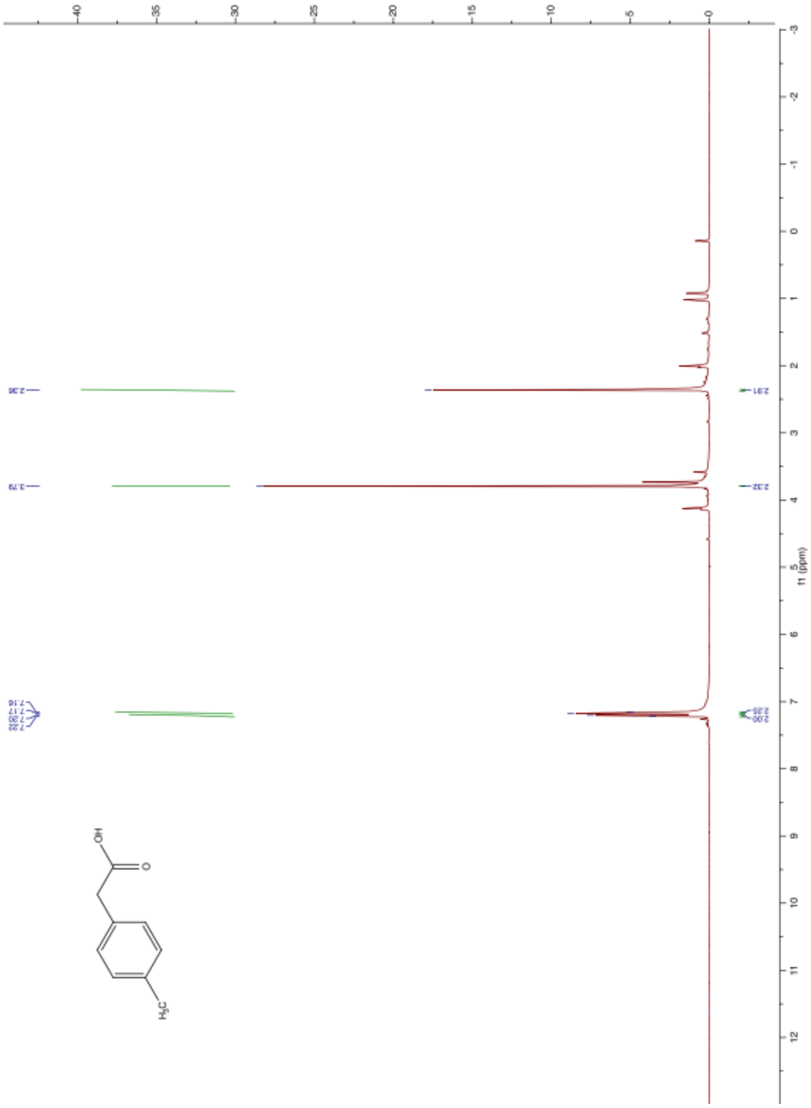

7.26
7.25
7.18
7.17
4.64
2.36
2.02
2.04
2.00
3.00
OH
H3C
f1 (ppm)
-3
-2
-1
0
1
2
3
4
5
6
7
8
9
10
11
12

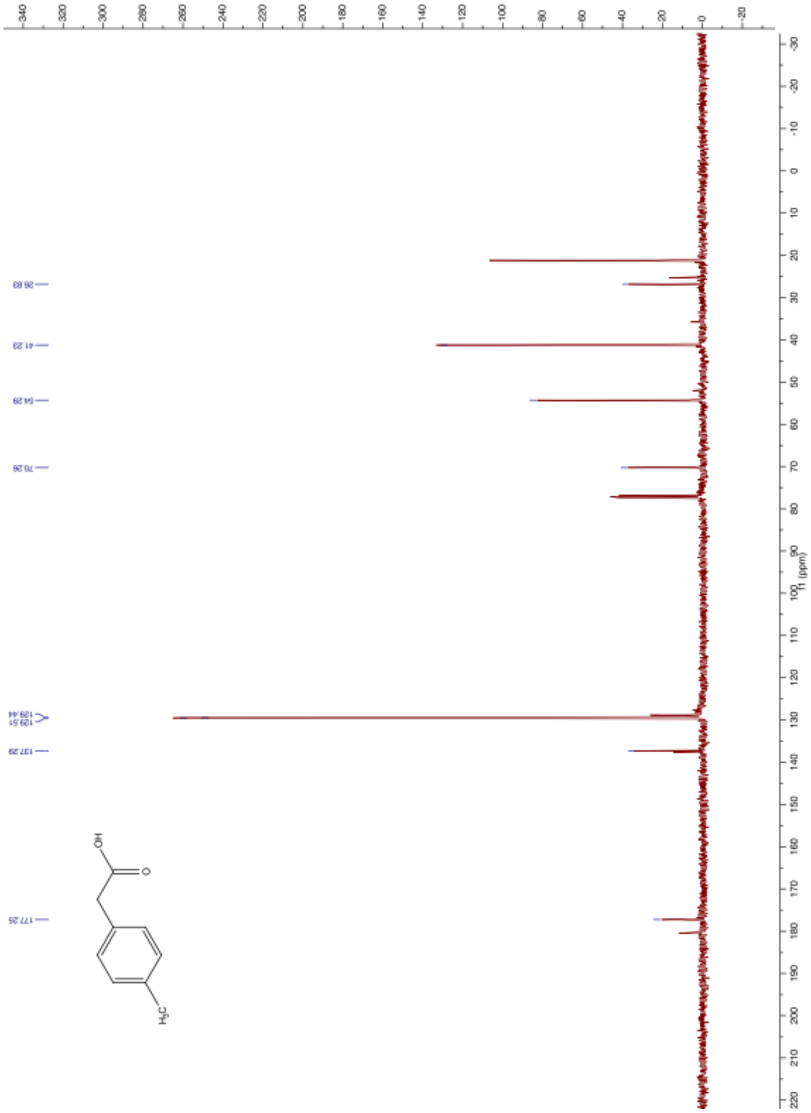

21.17
27.99
65.27
127.16
129.26
137.41
OH
H3C
f1 (ppm)

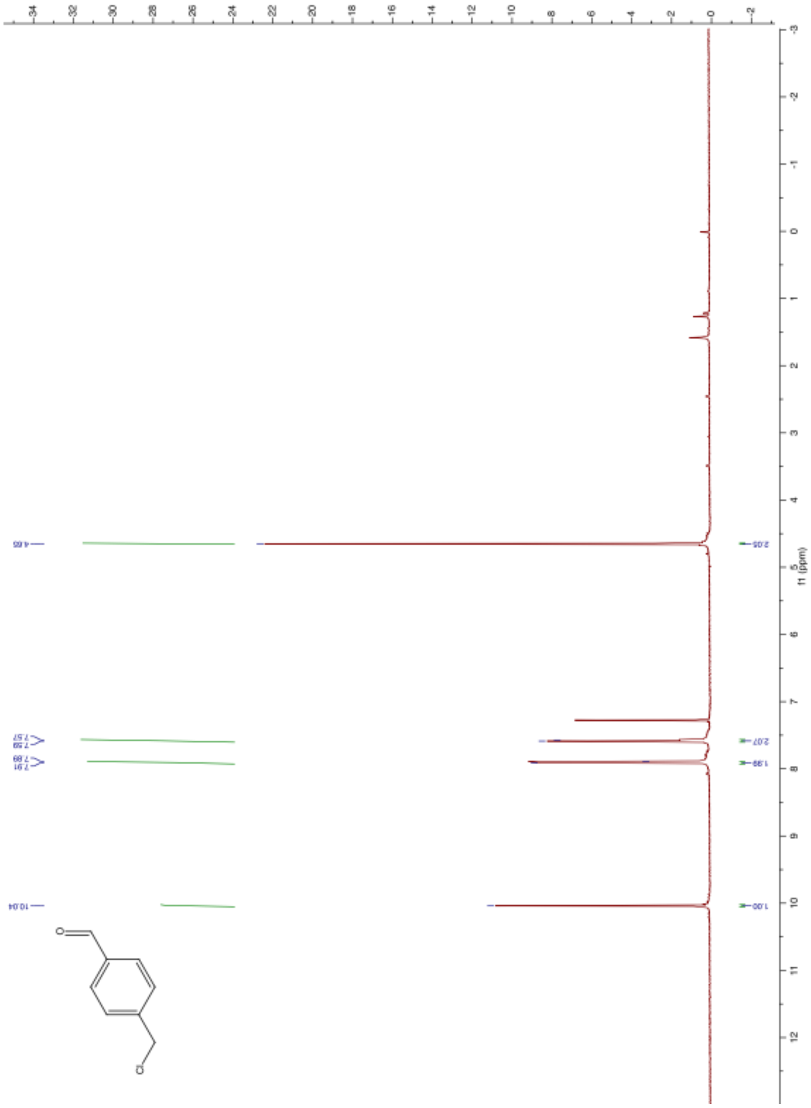


7.34
7.21
4.49
3.83
2.85
2.00
1.99
1.97
1.98
1.96
Br
OH
f1 (ppm)

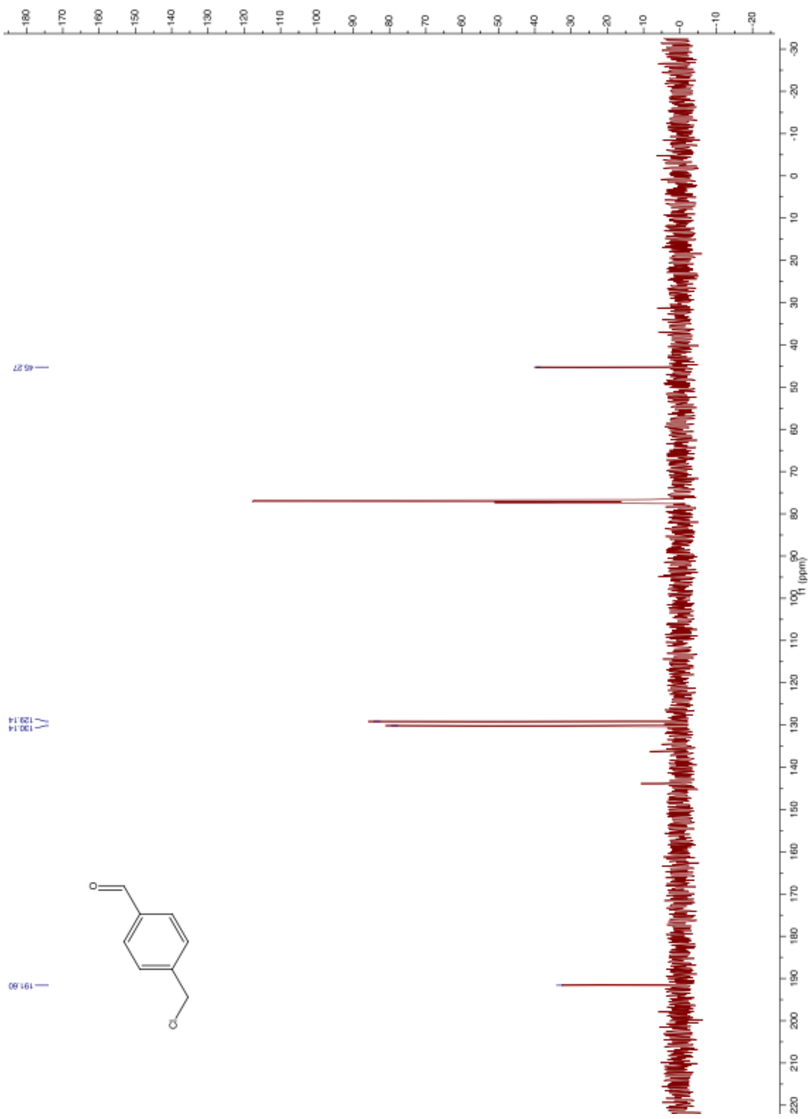

31.38
36.57
61.19
127.29
133.73
136.85
f1 (ppm)
Br
OH


7.22
7.20
7.17
7.16
3.79
2.36
2.00
2.05
2.02
2.91
f1 (ppm)
OH
O
H_3C

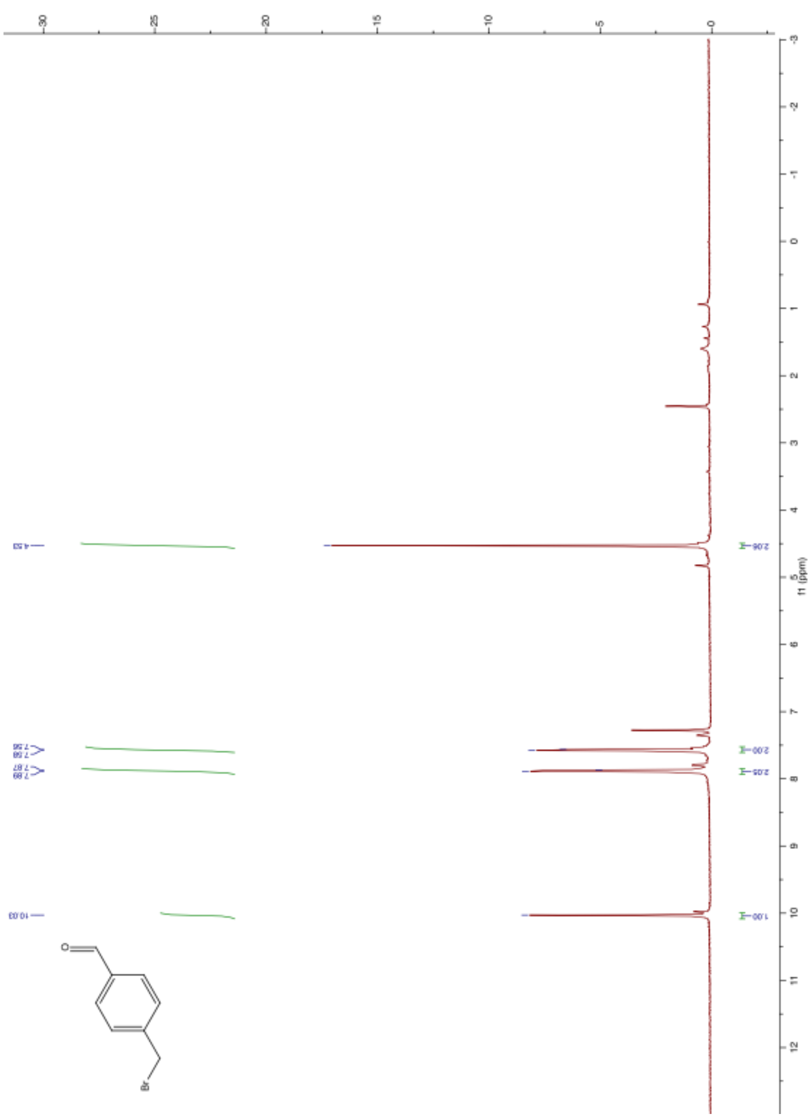

177.25
137.28
129.51
129.44
70.26
54.29
41.23
26.83
HO
O
H3C
f1 (ppm)



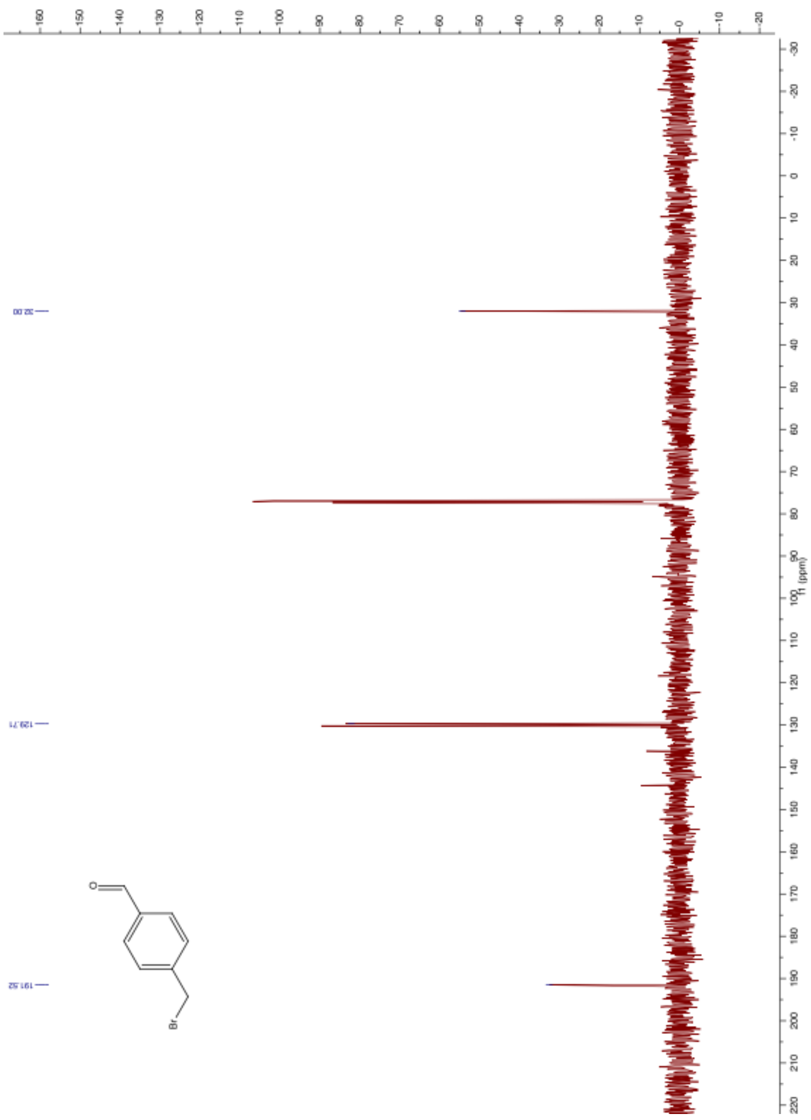
10.04
7.91
7.89
7.59
7.57
4.65
1.00
1.99
2.07
2.05
O
Cl
f1 (ppm)

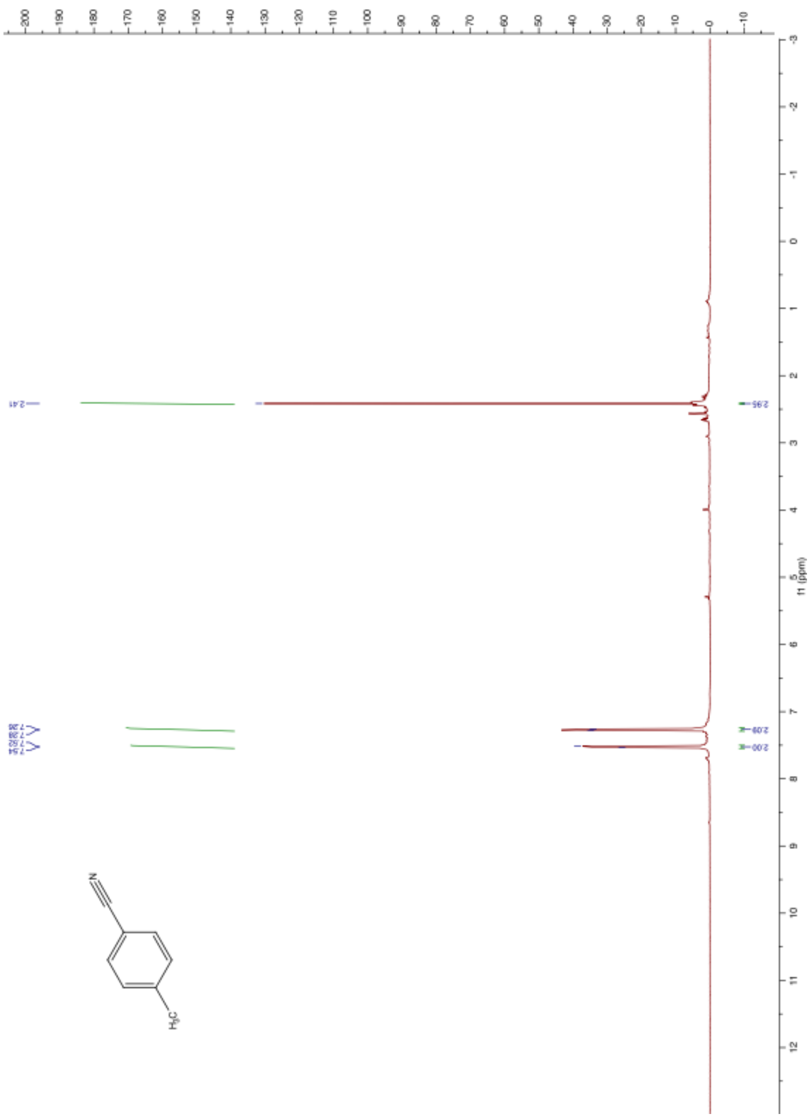


191.60
130.14
129.14
45.27
O
Cl
f1 (ppm)

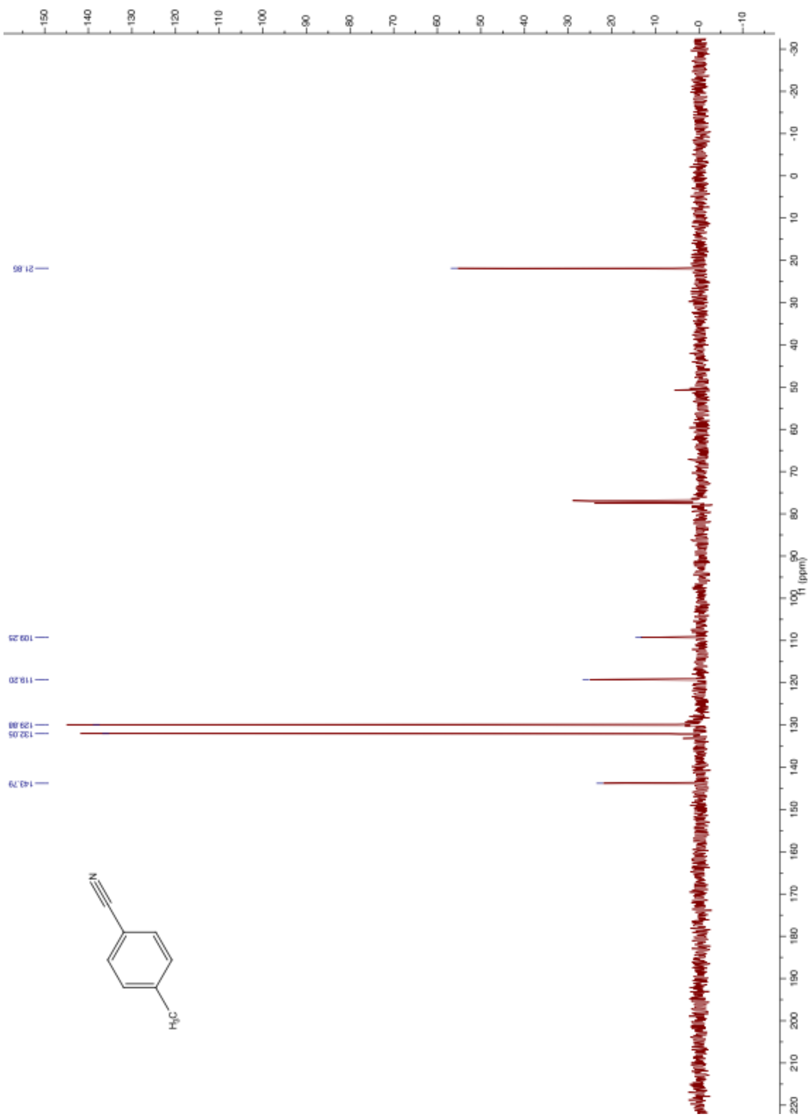


10.03
7.89
7.87
7.58
7.56
4.53
1.00
2.05
2.00
2.06
Br
O
f1 (ppm)

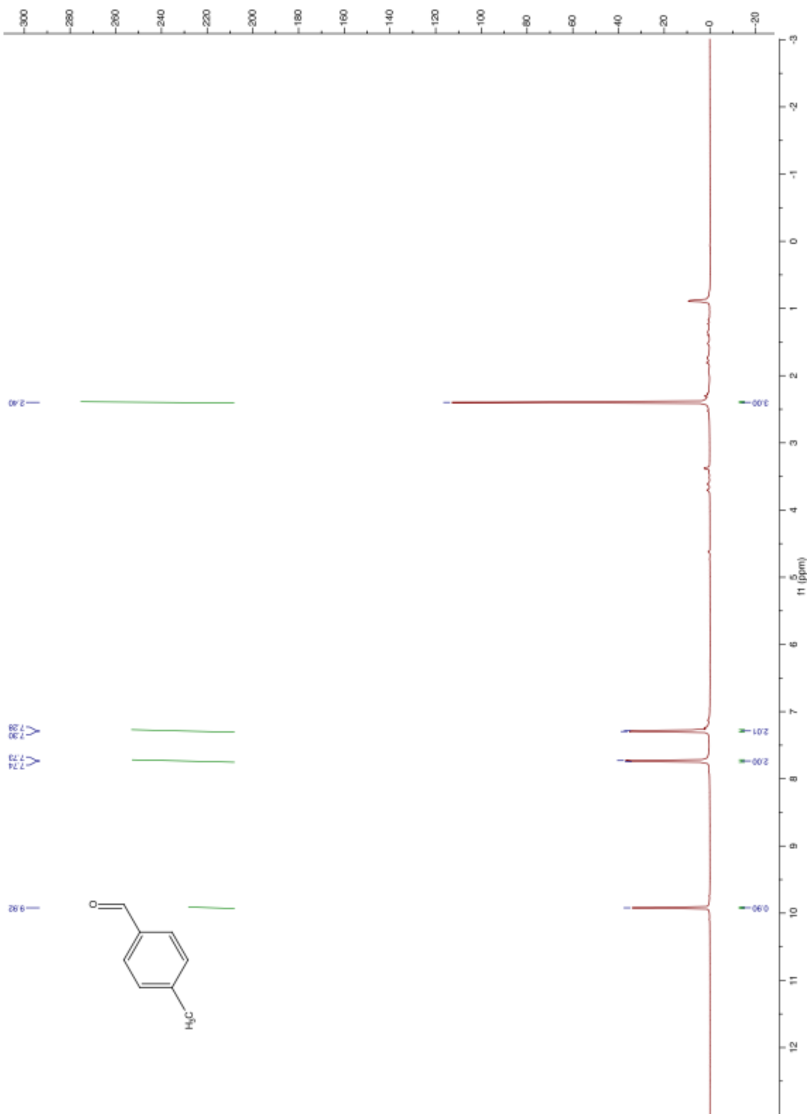

191.52
129.71
32.00
Br
O
f1 (ppm)
-30
-20
-10
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220

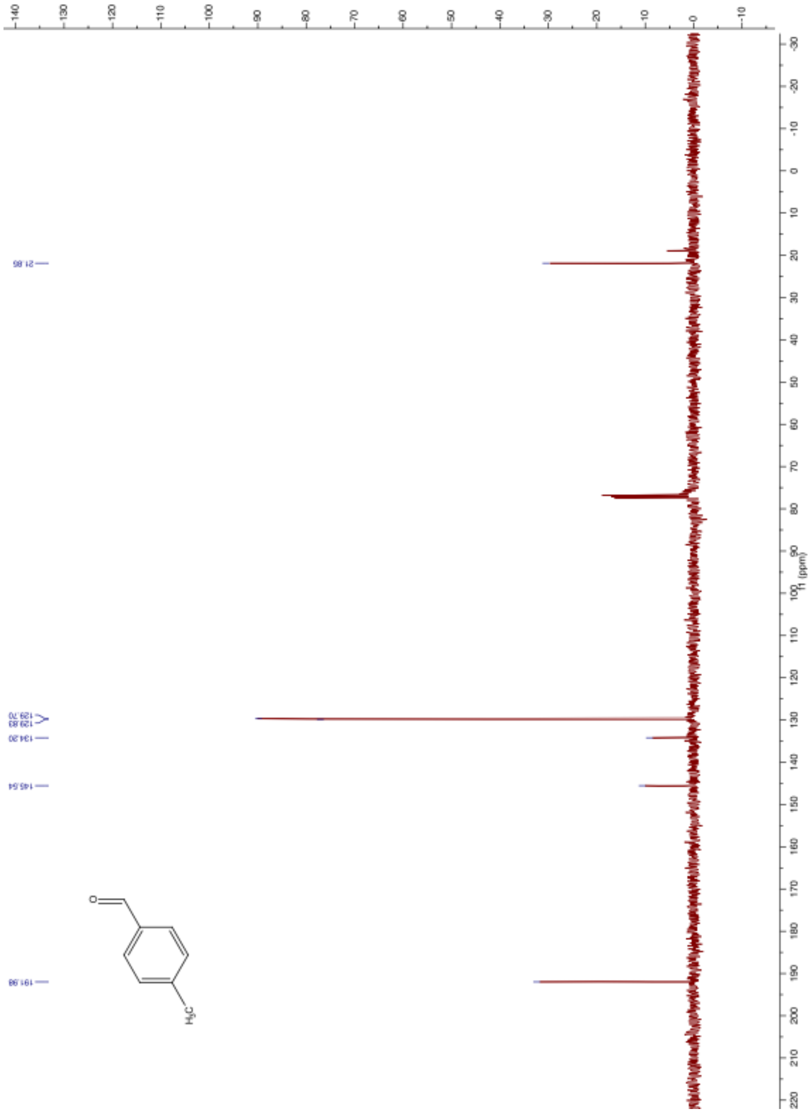


2.41
7.26
7.28
7.52
7.54
2.95
2.09
2.00
H3C
N
f1 (ppm)
-3
-2
-1
0
1
2
3
4
5
6
7
8
9
10
11
12
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10



21.86
109.25
119.20
129.88
132.05
143.79
H3C
N
f1 (ppm)


9.92
7.74
7.73
7.30
7.28
2.40
0.90
2.00
2.01
3.00
H$_3$C
O
f1 (ppm)
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20


191.98
145.54
134.20
129.83
129.70
21.86
H3C
O
f1 (ppm)