Supporting Information

Chemoselective Reduction of Aldehyde via a Combination of $NaBH_4$ and Acetylacetone

Guoqing Sui, [a] Qingyun Lv, [a] Xiaoqing Song, [a] Huihui Guo, [a] Jiatong Dai, [a] Li Ren, [a] Chi-Sing Lee, [d] Wenming Zhou*[a] and Hong-Dong Hao*[abc]

[a]Shaanxi Key Laboratory of Natural Products & Chemical Biology, College of Chemistry & Pharmacy, Northwest A&F University, Yangling, Shaanxi 712100, China

[b]State Key Laboratory of Bioorganic & Natural Products Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China

[c]Key Laboratory of Chemical Genomics, School of Chemical Biology and Biotechnology, Peking University, Shenzhen Graduate School, Shenzhen 518055, China

[d]Department of Chemistry, Hong Kong Baptist University, Kowloon Tong, Hong Kong SAR, China

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1. General Experimental Details

Unless otherwise stated, all reactions were performed with magnetic stirring under a positive pressure of nitrogen or argon gas. Over-dried glassware (over temperature of 70 ^{o}C) was further dried with a heat-gun at 650 ^{o}C under vacuum, followed by back-filling with inert gas, three times and fitted with rubber septa prior to use. Solids were added under inert gas counter flow or were dissolved and transferred in the appropriate solvent. Solutions and liquids reagents were transferred to reaction vessels by oven-dried stainless-steel cannulas or nitrogen flushed syringes. Low temperature reactions were carried out in a Dewar vessel filled with acetone/dry ice ($-$78 ^{o}C) or distilled water/ice (0 ^{o}C). High temperature reactions were conducted using a heated silicon oil bath in reaction vessels equipped with a reflux condenser.

1.1 Materials

Dry Tetrahydrofuran (THF), diethyl ether (Et_2O) Dicholormethane (CH_2Cl_2), triethylamine (Et_3N) and N,N-dimethylformamide (DMF), toluene (PhMe), dioxane and methanol (MeOH) were purchased from Tansoole company as extra dry regents under inert gas atmosphere and stored over molecular sieves. Ethyl acetate (EtOAc), pentane, Et_2O, CH_2Cl_2 and MeOH used specifically for extraction and flash column chromatography were purchased at technical grade from commercial sources and distilled under reduced pressure. All other solvents and regents were used as received from commercial sources (Sigma Aldrich, Energy chemical, 3A, Innochem, and Adamas).

Reactions were monitored by thin-layer chromatography (TLC) using silica gel F254 pre-coated glass plates (*Merck*) and visualized by exposure to ultraviolet light ($\lambda = 254$ nm) or by staining with aqueous potassium permanganate ($KMnO_4$) solution (7.5 g $KMnO_4$, 50 g K_2CO_3, 6.25 mL aqueous 10% NaOH, 1000 mL distilled H_2O), aqueous acid ceric ammonium molybdate (IV) (CAM) solution (2.0 g $Ce(NH_4)_4(SO_4)_4{\cdot}2H_2O$, 48 g $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$, 60 mL concentrated sulfuric acid, 940 mL distilled H_2O) followed by heating with a heat gun (150-600 ºC). Flash column chromatography was performed using silica gel (60 Å, 40-63 µm, *Merck*) and a forced flow of eluent.

1.2 Instrumentation

Proton (^{1}H) and carbon (^{13}C) nuclear magnetic resonance spectra were recorded on a

Brucker Avance III HD 500 MHz spectrometer equipped with a CroProbeTM. Proton chemical shifts are expressed in parts per million (ppm, δ scale) and referenced to residual undeuterated solvent signals ($CDCl_3$: 7.26 ppm; C_6D_6: 7.16 ppm). Carbon chemical shifts are expressed in parts per million (ppm, δ scale) and referenced to the central carbon resonance of the solvent ($CDCl_3$: 77.16 ppm; C_6D_6: 128.06 ppm). The reported data is represented as follows: chemical shift in parts per million (ppm, δ scale) (multiplicity, coupling constants *J* in Hz, integration intensity, proton assignment). Abbreviations used for analysis of multiplets are as follows: s (singlet), br s (broad singlet), d (doublet), t (triplet), q (quartet), quin (quintet), h (hextet), and m (multiplet). Variable temperature NMR spectroscopy was performed at the *Northwest A&F University* NMR facility.

Mass spectroscopy (MS) experiments were performed in high resolution with an AB SCIEX Triple TOF 5600^+ spectrometer (AB SCIEX, Boston, MA, USA) at the *Northwest A&F University* mass spectrometry facility.

2. Experimental Procedures

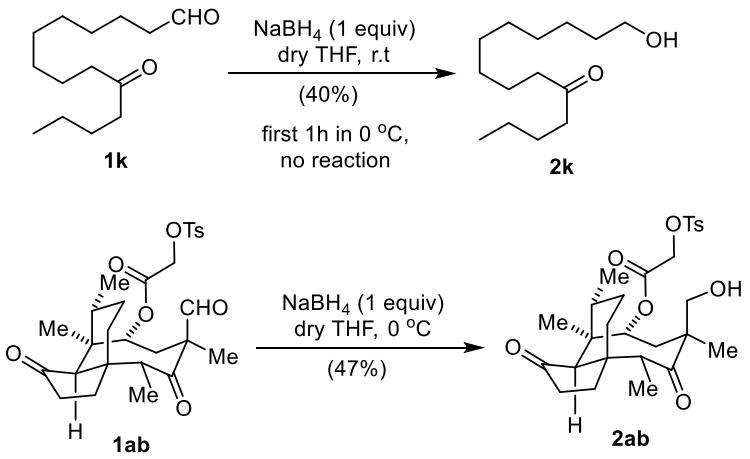
2.1 Preparation of the combination:

To a stirred solution of $NaBH_4$ (1.89 g, 50.0 mmol) in dry THF (80 mL) at 0 °C was added acetylacetone (4.1 mL, 40.0 mmol) dropwise. After stirred at 0 °C for 10 min, the reaction mixture was warm to room temperature slowly and stirred for further 2 h. Then the solvent was concentration in vacuo to afford the combination (5.20 g, 88% yield) as a white power. FT-IR (KBr) 3403, 2968, 2928, 2661, 2368, 2289, 2225, 1625, 1510, 1456, 1412, 1378, 1234, 1156, 1126, 1055, 977, 915, 761, 657, 643 cm^{-1}. Anal. calcd for $C_5H_{13}B_{1.25}Na_{1.25}O_3$ (or alternatively written in a more informative manner, $C_5H_7O_2{\cdot}NaBH_3{\cdot}H_2O{\cdot}0.25NaBH_4$): C 36.75, H 8.02, B 8.27, Na 17.59, O 29.37; found C 36.26, H 8.21, B 8.04, Na 16.03.

Figure S1. Prepared combination for reduction

The combination of $NaBH_4$ (1.25 equiv) with acac (1 mmol) is important for the selective reduction, when $NaBH_4$: acac = 1:1, a sticking solid was obtained, not easy to weigh, while when $NaBH_4$: acac = 1.5:1, a white power was obtained, but the combination is too reactive for the selective reduction.

Control experiment was also carried out use only $NaBH_4$ in THF without acac, which shows inferior yield.



2.2 General Procedure for selective reduction:

To a stirred solution of ketoaldehyde **1** (1.0 mmol) in dry THF (5 mL) at 0 °C was added the $NaBH_4$•acac solid (138 mg, 1.0 mmol), After the reaction was completed according to the TLC, the reaction mixture was quenched by addition of sat.aq.NH_4Cl (2 mL) and followed by extraction with EtOAc (2×10 mL), the combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. After filtration and concentration in vacuo, the crude product was purified by flash column chromatography on silica to afford the desired target compounds.

Representative procedure taking 1a as the example:

To a stirred solution of **1a** (148 mg, 1.0 mmol) in dry THF (5 mL) at 0 °C was added the $NaBH_4$•acac solid (138 mg, 1.0 mmol), after stirred for 12 min, the reaction mixture was quenched by addition of sat.aq.NH_4Cl (2 mL) followed by extraction with EtOAc (2×10 mL), the combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. After filtration and concentration in vacuo, the crude product was purified by flash column

chromatography (Hexanes : EtOAc = 3 : 1) on silica to afforded the desired target compound **2a** (142 mg, 0.95 mmol, 95%) as yellow oil.

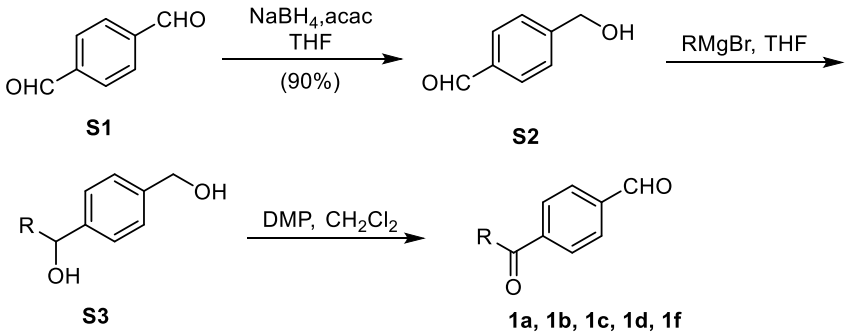
Small scale taking 1i as the example:

To a stirred solution of **1i** (130 mg, 0.70 mmol) in dry THF (5 mL) at 0 ^{o}C was added the $NaBH_4$·acac solid (97 mg, 0.70 mmol). After the reaction was completed in 15 min according to the TLC detection, the reaction mixture was quenched by addition of sat.aq.NH_4Cl (1 mL) and followed by extraction with EtOAc (2×7 mL), the combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. After filtration and concentration in vacuo, the crude product was purified by flash column chromatography (Hexanes : EtOAc = 4 : 1) on silica to afforded the desired target compound **2i** (113 mg, 0.61 mmol, 87%) as white soli

Gram Scale:

To a stirred solution of **1i** (1.10 g, 6.0 mmol) in dry THF (25 mL) at 0 ^{o}C was added the $NaBH_4$·acac solid (830 mg, 6.0 mmol), and. After the reaction was completed according to the TLC detection, the reaction mixture was quenched by addition of sat.aq.NH_4Cl (3 mL) and followed by extraction with EtOAc (2×25 mL), the combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. After filtration and concentration in vacuo, the crude product was purified by flash column chromatography (Hexanes : EtOAc = 4 : 1) on silica to afforded the desired target compound **2i** (0.92 g, 4.95 mmol, 83%) as white solid.

2.3 Experimental procedure for preparing substrates:
Procedure 1 (1a to 1f):

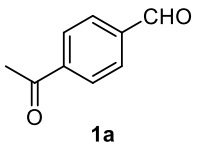


Representative procedure for P1, taking **1a** as the example

- To a stirred solution of terephthalaldehyde (134 mg, 1.0 mmol) in dry THF (5 mL) at 0 ^{o}C was added the $NaBH_4$•acac solid (138 mg, 1.0 mmol), after stirred for 5 min, the reaction mixture was quenched by addition of sat.aq.NH_4Cl (3 mL) and followed by extraction with EtOAc (2×10 mL), the combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. After filtration and concentration in vacuo, the crude product was purified by flash column chromatography (hexanes: EtOAc = 3:1) on silica to afforded **S2** (122 mg, 0.90 mmol, 90%) as a light yellow oil.

To a stirred solution of **S2** (68 mg, 0.5 mmol) in dry THF (5 mL) at − 5 ^{o}C (ice/acetone bath) was added MeMgBr (0.5 mL, 1.5 mmol, 3 mmol/mL solution in Et_2O), and stirred for 2 h. Then the reaction mixture was quench by addition of sat.aq.NH_4Cl (3 mL) and followed by extraction with EtOAc (2×10 mL), the combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. After filtration and concentration in vacuo, the crude product was purified by flash column chromatography (hexanes: EtOAc = 2:1) on silica to afforded **S3a** (53 mg, 0.35 mmol, 69%) as a colorless oil.

To a stirred solution of diol **S3a** (76 mg, 0.5 mmol) in CH_2Cl_2 (10 mL) at 0 ^{o}C was added Dess-Martin periodinane (850 mg, 2 mmol) and stirred for 2 h, then the reaction mixture was quench by addition of sat.aq.NaCl (3 mL) and followed by extraction with EtOAc (2×10 mL), the combined organic layers were washed with 1 N NaOH solution (10 mL) and brine (5 mL) dried over anhydrous Na_2SO_4. After filtration and concentration in vacuo, the crude product was purified by flash column chromatography (hexanes: EtOAc = 4:1) on silica to afforded **1a** (59 mg, 0.40 mmol, 80%) as a pale yellow oil.



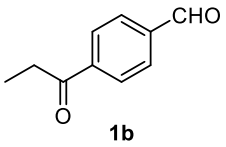
1a

Compound 1a. CAS No. 3457-45-2. Pale yellow oil.

The analytical data of **1a** was in accordance to the reported. [1]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.10 (s, 1H), 8.09 (d, *J* = 8.1 Hz, 2H), 7.97 (d, *J* = 8.1 Hz, 2H), 2.65 (s, 3H) ppm

Compound 1b, 1c, 1d, 1e, 1f were synthesized according to the Procedure 1.

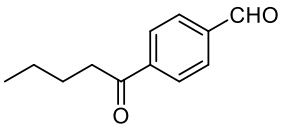


1b

Compound 1b. CAS No. 208453-24-1. White needle crystal.

The analytical data of **1b** was in accordance to the reported.[1]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.11 (s, 1H), 8.11 (d, *J* = 8.2 Hz, 2H), 7.98 (d, *J* = 8.2 Hz, 2H), 3.05 (q, *J* = 7.2 Hz, 2H), 1.26 (t, *J* = 7.2 Hz, 3H) ppm

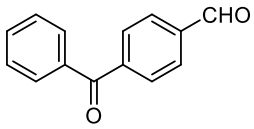


1c

Compound 1c. CAS No. 61363-43-7. White needle crystal.

The analytical data of **1c** was in accordance to the reported. [2]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.11 (s, 1H), 8.10 (d, *J* = 8.2 Hz, 2H), 7.98 (d, *J* = 8.4 Hz, 2H), 3.01 (t, *J* = 7.2 Hz, 2H), 1.77 – 1.71 (m, 2H), 1.46 – 1.39 (m, 2H), 0.97 (t, *J* = 7.4 Hz, 3H) ppm

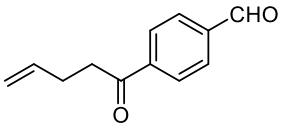


1d

Compound 1d. CAS No. 20912-50-9. White needle crystal.

The analytical data of **1d** was in accordance to the reported one. [1]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.14 (s, 1H), 8.01 (d, *J* = 8.0 Hz, 2H), 7.93 (d, *J* = 7.7 Hz, 2H), 7.81 (d, *J* = 7.7 Hz, 2H), 7.64 (t, *J* = 7.3 Hz, 1H), 7.52 (t, *J* = 7.3 Hz, 2H) ppm



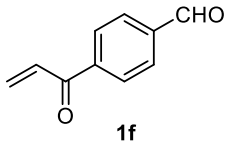
1e

Compound 1e was synthesized as yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.01 (s, 1H), 8.00 (d, *J* = 8.1 Hz, 2H), 7.88 (d, *J* = 8.2 Hz, 2H), 5.84 – 5.76 (m, 1H), 5.00 (d, *J* = 17.2 Hz, 1H), 4.93 (d, *J* = 10.2 Hz, 1H), 3.02 (t, *J* = 7.4 Hz, 2H), 2.44 – 2.40 (m, 2H) ppm

^{13}C NMR (125 MHz, $CDCl_3$): δ = 198.8, 191.6, 141.2, 139.0, 136.9, 129.9, 128.6, 115.7, 38.3, 27.9 ppm

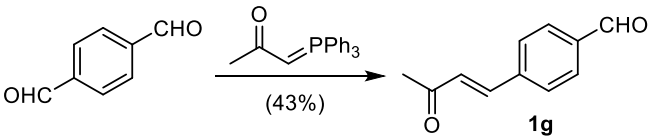
HRMS (APCI) for $C_{12}H_{11}O_2$, $[M-H]^-$: calcd.187.0764, found: 187.0760.



1f

Compound 1f was synthesized as pale yellow flaky solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.12 (s, 1H), 8.07 (d, *J* = 8.7 Hz, 2H), 8.00 (d, *J* = 8.3 Hz, 2H), 7.17-7.11 (m, 1H), 6.47 (d, *J* = 17.3 Hz, 1H), 6.03 (d, *J* = 10.9 Hz, 1H) ppm

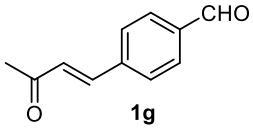


1g

To a stirred solution of terephthalaldehyde (268 mg, 2.0 mmol) in dry THF (8 mL) was added (acetylmethylene)triphenylphosphorane (700 mg, 2.2 mmol), then the reaction mixture heated to 60 ^{o}C and stirred for 10 h. Directly concentrated and purified by preparative TLC plates (hexanes: EtOAc = 5:1) to afford **1g** (150 mg, 0.86 mmol, 43% yield) as a white crystal.

The product **1g** is a mixture of the E/Z isomer, the ratio is E:Z = 6:1.

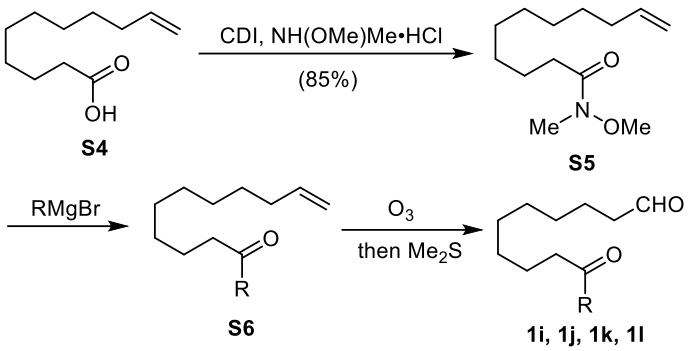
The analytical data of **1g** was in accordance to the reported one. [3]



1g

^{1}H NMR (500 MHz, $CDCl_3$) δ = 10.04 (s, 1H), 7.92 (d, *J* = 8.2 Hz, 2H), 7.70 (d, *J* = 8.2 Hz, 2H), 7.54 (d, *J* = 16.3 Hz, 1H), 6.82(d, *J* = 16.3 Hz, 1H), 2.42 (s, 3H) ppm

Procedure 2 (1i to 1l):

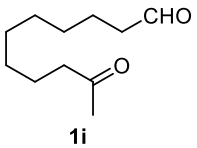


Representative procedure for P2, taking **1i** as the example.

To a stirred solution of 10-undecenoid acid (2.76 g, 15 mmol) in dry CH_2Cl_2 (50 mL) at 0 ^oC was added CDI (3.16 g, 19.5 mmol), after stirred for 30 min, HN(OMe)Me•HCl (3.66 g, 37.5 mmol) was added, stirred at r.t for 24 h. The reaction mixture was filtered and washed with CH_2Cl_2 (3×20 mL), then the combined organic layers washed with 1N HCl (10 mL), brine and dried over anhydrous Na_2SO_4. Concentrated and flash chromatography (hexanes : EtOAc = 5 : 1) to afford product **S5** (2.90 g, 12.75 mmol, 85%) as a colorless oil.

To a stirred solution of above Weinreb amide **S5** (245 mg, 1.08 mmol) in dry THF (8 mL) at 0 ^oC was added MeMgBr (0.72 mL, 2.16 mmol, 3 mmol/mL solution in Et_2O), after stirred for 3 h, the reaction mixture quench with NH_4Cl (5 mL), extract with EtOAc (3×20 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. Concentrated and flash chromatography (hexanes: EtOAc = 25: 1) to afford product **S6** (104 mg, 0.71 mmol, 66%) as a colorless oil.

O_3 was bubbled through a stirred solution of the above product **S6** (182 mg, 1.0 mmol) in CH_2Cl_2 (10 mL) at – 78 ^oC until the reaction mixture color change into blue, an Ar balloon was bubbled to the solution followed by Me_2S (0.44 mL, 6.0 mmol) was added, then stirred at r.t for 12 h. The reaction mixture was directly concentrated and flash chromatography (hexanes: EtOAc = 10: 1) to afford product **1i** (129 mg, 0.70 mmol, 70%) as a white powder.

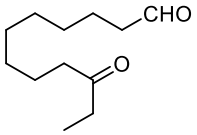


1i

The analytical data of **1i** was in accordance to the reported one. [4]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.76 (s, 1H), 2.43 – 2.39 (m, 4H), 2.13 (s, 3H), 1.66 – 1.52 (m, 4H), 1.34 – 1.23 (m, 8H) ppm

Compound 1j, 1k, 1l were synthesized according to the Procedure 2.

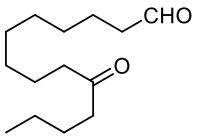


1j

Compound 1j was synthesized as white flaky crystal.

The analytical data of **1j** was in accordance to the reported one. [4]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.76 (s, 1H), 2.42 – 2.38 (m, 6H), 1.62 – 1.56 (m, 4H), 1.34 – 1.22 (m, 8H), 1.05 (t, J = 7.6 Hz, 3H) ppm

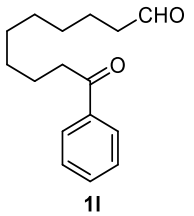


1k

Compound 1k was synthesized as white flaky crystal.

The analytical data of **1k** was in accordance to the reported one. [4]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.76 (s, 1H), 2.43 – 2.37 (m, 6H), 1.65 – 1.58 (m, 2H), 1.58 – 1.51 (m, 4H), 1.33 – 1.24 (m, 10H), 0.90 (t, J = 7.5 Hz, 3H) ppm



1l

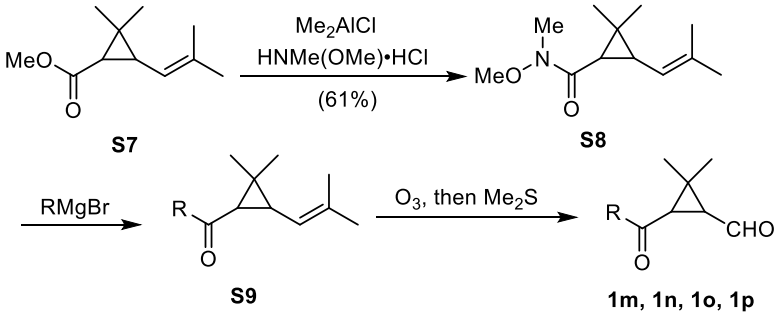
Compound 1l was synthesized as white flaky crystal.

The analytical data of **1l** was in accordance to the reported one. [4]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.76 (s, 1H), 7.96 (d, J = 7.4 Hz, 2H), 7.57 – 7.54 (m, 1H), 7.46

(t, *J* = 7.4 Hz, 2H), 2.96 (t, *J* = 7.4 Hz, 2H), 2.42 (t, *J* = 7.3 Hz, 2H), 1.78 – 1.69 (m, 2H), 1.67 – 1.59 (m, 2H), 1.41 – 1.29 (m, 8H) ppm

Procedure 3 (1m to 1p):



Representative procedure for P3, taking **1m** as the example

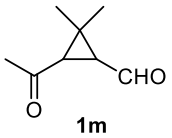
To a stirred solution of NH(OMe)•HCl (1.46 g, 15 mmol) in dry CH_2Cl_2 (50 mL) at 0 ^oC was added Me_2AlCl (15 mL, 1.0 mmol/mL solution in heptane, 15 mmol), then the reaction mixture stirred at r.t for 1 h. A solution of ethyl chrysanthemumate (1.62 mL, 7.5 mmol) in dry CH_2Cl_2 (5 mL) was added to the reaction mixture dropwise and stirred overnight (12 h). Quench the reaction with buffer (pH = 8, 5 mL) and then saturated Rochelle salt solution (50 mL) was added. Stirred for 1 h at r.t until the layers were clear and then extract with EtOAc (3×20 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. Concentrated and flash chromatography (hexanes: EtOAc = 25:1) to afford product **S8** (970 mg, 4.58 mmol, 61%) as a colorless oil.

To a stirred solution of the above weinreb amide (200 mg, 0.95 mmol) in dry THF (8 mL) at 0 ^oC was added MeMgBr (0.63 mL, 3.0 mmol/mL solution in Et_2O, 1.90 mmol), the reaction mixture stirred at 0 ^oC for 3 h and then quench with aq NH_4Cl (5 mL), extract with EtOAc (3×20 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. Concentrated and flash chromatography (hexanes: EtOAc = 100: 1) to afford product **S9** (104 mg, 0.63 mmol, 66%) as a colorless oil.

O_3 was bubbled through a stirred solution of the above product (166 mg, 1.0 mmol) in CH_2Cl_2 (10 mL) at – 78 ^oC until the reaction mixture color change into blue, an Ar balloon was bubbled to the solution followed by Me_2S (0.44 mL, 6.0 mmol) was added, then stirred at r.t for 12 h. The reaction mixture was directly concentrated and flash chromatography (hexanes:

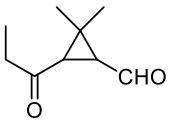
EtOAc = 20: 1) to afford product **1m** (82 mg, 0.58 mmol, 58%) as a pale yellow oil.

Due to the starting material ethyl chrysanthemumate is a 1:1 mixture of cis: trans, Compound **1m,1o,1p and 1q** were obtained as a 1:1 mixture of cis: trans.



1m

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.62 (d, *J* = 2.3 Hz, 1H), 2.76 (d, *J* = 5.3 Hz, 1H), 2.64 (s, 1H), 2.28 (s, 3H), 1.33 (s, 3H), 1.23 (s, 3H) ppm



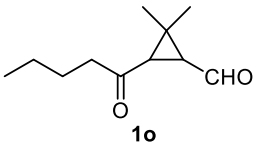
1l

Compound 1l was synthesized as colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.63 (d, *J* = 3.1 Hz, 1H), 2.75 (d, *J* = 5.5 Hz, 1H), 2.66 – 2.64 (m, 1H), 2.60–2.55 (m, 2H), 1.34 (s, 3H), 1.22 (s, 3H), 1.08 (t, *J* = 7.3 Hz, 3H) ppm

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.9, 198.8, 42.3, 41.4, 38.0, 35.4, 21.0, 20.0, 7.8 ppm

HRMS (APCI) for $C_9H_{15}O_2$, $[M+H]^+$: calcd. 155.1067, found: 155.1064.



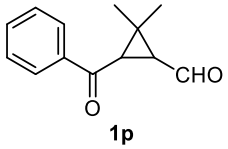
1o

Compound 1o was synthesized as pale yellow oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.60 (d, *J* = 3.2 Hz, 1H), 2.72 (d, *J* = 5.8 Hz, 1H), 2.63 – 2.61 (m, 1H), 2.51 (t, *J* = 7.6 Hz, 2H), 1.58 – 1.51 (m, 2H), 1.34 – 1.27 (m, 5H), 1.18 (s, 3H), 0.89 (t, *J* = 7.6 Hz, 3H) ppm

^{13}C NMR (125 MHz, $CDCl_3$): δ: 205.6, 198.8, 44.6, 42.3, 41.6, 35.6, 25.9, 22.3, 21.0, 20.0, 13.8 ppm

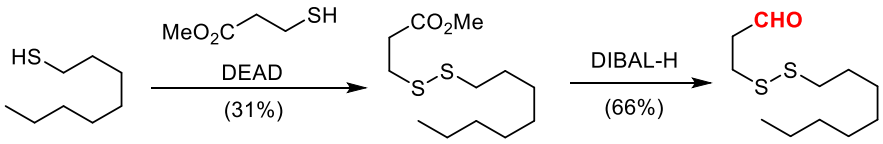
HRMS (APCI) for $C_{10}H_{17}O$, $[M\text{-}CHO]^-$: calcd. 153.1285, found: 153.1287.



1p

Compound 1p was synthesized as colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.76 (d, *J* = 3.0 Hz, 1H), 7.95 (d, *J* = 7.5 Hz, 2H), 7.59 (t, *J* = 7.6 Hz, 1H), 7.49 (t, *J* = 8.0 Hz, 2H), 3.38 (d, *J* = 5.6 Hz, 1H), 2.91 – 2.89 (m, 1H), 1.47 (s, 3H), 1.22 (s, 3H) ppm



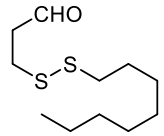
S10 **S11** **1q**

The procedure for prepare **1q** was take from the reported procedure.[5]

To a stirred solution of methyl 3-mercaptopropionate (0.3 mL, 2.71 mmol) in dry CH_2Cl_2 (10 mL) at 0 °C was added DEAD (0.86 mL, 5.42 mmol), after stirred for 1.5 h, 1-mercaptooctane (0.56 mL, 3.26 mmol) was added to the reaction mixture and stirred for 12 h at r.t. Quench the reaction with sat.aq. $NaHCO_3$ (10 mL) and then extract with EtOAc (2 × 20 mL). The combined organic layers were washed with brine (15 mL) and dried over anhydrous Na_2SO_4. Concentrated and flash chromatography (hexanes: EtOAc = 100: 1) to afford product (220 mg, 0.84 mmol, 31%) as a colorless oil.

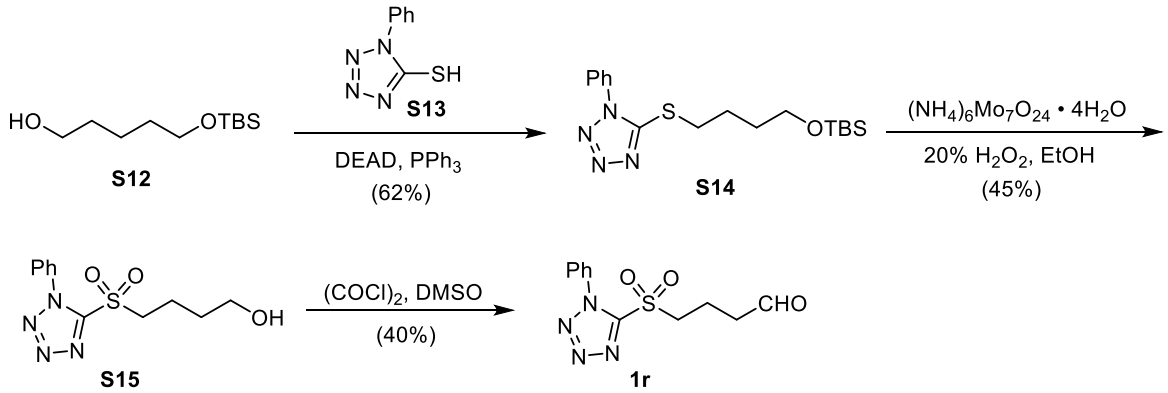
To a solution of above **S11** (120 mg, 0.45 mmol) in dry *t*-BuOMe (8 mL) at – 78 °C was added DIBAL-H (0.90 mL, 0.90 mmol, 1.0 mmol/mL solution in Hexane). After stirred at – 78 °C for 2 h, the reaction mixture was quenched by MeOH (3 mL), then Et_2O (20 mL) and saturated solution of Rochelle salt (15 mL) was added, stirred until the two layers are clear (30 min). Then extract with EtOAc (2 × 20 mL), the combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. Flash chromatography (hexanes: EtOAc = 60: 1)

to afford product **1q** (70 mg, 0.30 mmol, 66%) as a yellowish oil. Compound **1q** was used intermediately after characterized by proton NMR.



1q

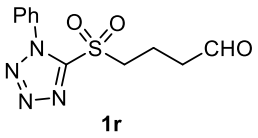
^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.82 (s, 1H), 2.95 – 2.92 (m, 2H), 2.91 – 2.88 (m, 2H), 2.69 – 2.65 (m, 2H), 1.69 – 1.63 (m, 2H), 1.39 – 1.36 (m, 2H), 1.31 – 1.25 (m, 8H), 0.88 (t, *J* = 7.3 Hz, 3H) ppm



To a stirred solution of PPh_3 (660 mg, 2.5 mmol), DEAD (0.47 mL, 3.0 mmol) and **S12** (450 mg, 2.5 mmol) in dry THF (20 mL) at 0 ^oC was added a solution of **S13** (410 mg, 2.0 mmol) in dry THF (5 mL), then the reaction mixture stirred at r.t for 8 h. Quench the reaction with sat.aq.NH_4Cl (5 mL) and H_2O (5 mL), then extracted with EtOAc (2 $\times$ 15 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. Concentrated and flash chromatography (hexanes: EtOAc = 30: 1) to afford product **S14** (450 mg, 1.24 mmol, 62%) as a yellow oil.

To a stirred solution of the above product **S14** (220 mg, 0.55 mmol) in EtOH (10 mL) at 0 ^oC was added Ammonium molybdate tetrahydrate (0.12 g, 0.10 mmol) and H_2O_2 (1.75 mL, 11.0 mmol, 20% W/W solution in H_2O), then after stirred for 10 min at 0 ^oC, the reaction mixture stirred at r.t for 24 h. Quench the reaction with aq. sat. $NaHCO_3$ (5 mL), then extracted with EtOAc (2 $\times$ 15 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. Concentrated and flash chromatography (hexanes: EtOAc = 2:1) to afford product **S15** (70 mg, 0.25 mmol, 45%) as a collorless oil.

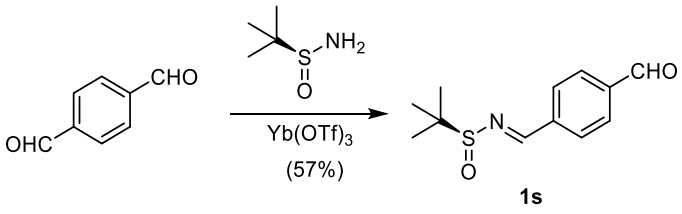
To a stirred solution of $(COCl)_2$ (0.53 mL, 1.06 mmol, 2.0 M solution in CH_2Cl_2) in dry CH_2Cl_2 (5 mL) at – 78 ^oC was added DMSO (0.15 mL, 2.12 mmol). Then the resulting solution stirred at – 78 ^oC for 30 min. A solution of **S15** (150 mg, 0.53 mmol) in CH_2Cl_2 (3 mL) was added to the reaction mixture at – 78 ^oC and stirred for 1 h. Then NEt_3 (0.59 mL, 4.24 mmol) was added to the reaction mixture and stirred at r.t for 1 h. Then reaction was quenched by addition of H_2O (3 mL) and followed by extraction with Et_2O (2×10 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. After filtration and concentration in vacuo, the crude product was purified by flash column chromatography (hexanes: EtOAc = 3:1) on silica to afforded **1r** (60 mg, 0.21 mmol, 40%) as a colorless oil.



1r

The analytical data of **1r** was in accordance to the reported one. [6]

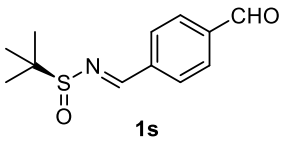
^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.79 (s, 1H), 7.70 – 7.68 (m, 2H), 7.64 – 7.59 (m, 3H), 3.83 – 3.80 (m, 2H), 2.78 (t, J = 6.9 Hz, 2H), 2.32 – 2.26 (m, 2H) ppm



1s

Compound **1s** was prepared through the reported procedure.[7]

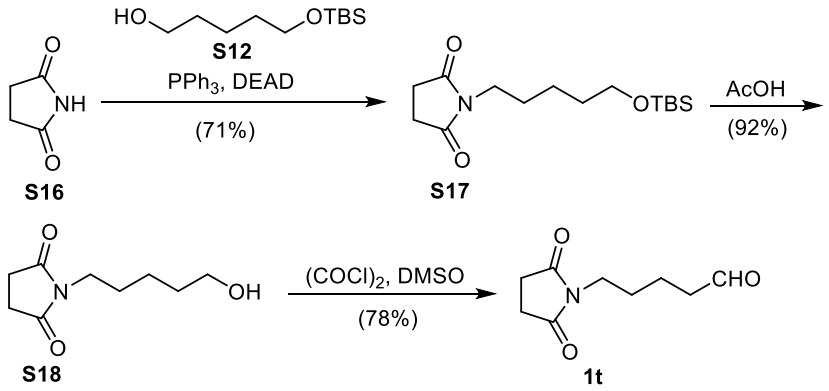
To a stirred solution of terephthalaldehyde (295 mg, 2.2 mmol), R-(+)-*tert*-butylsulfinamide (242 mg, 2.0 mmol) in dry THF (10 mL) at r.t was added $Yb(OTf)_3$ (186 mg, 0.3 mmol), then the reaction mixture stirred at r.t for 24 h. Quench the reaction with H_2O (3 mL) and with EtOAc (2 × 15 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. Concentrated and flash chromatography (hexanes: EtOAc = 12 : 1) to afford product **1s** (270 mg, 1.14 mmol, 57%) as a yellow needle solid.



1s

The analytical data of **1s** was in accordance to the reported one. [7]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.07 (s, 1H), 8.64 (s, 1H), 8.01 – 7.96 (m, 4H), 1.27 (s, 9H) ppm

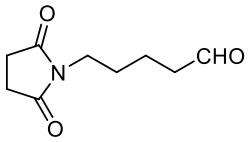


To a stirred solution of PPh_3 (2.1 g, 8.0 mmol), DEAD (1.57 mL, 10 mmol) in dry THF (10 mL) at 0 ^oC was added Succinimide **S16** (0.87 g, 4.0 mmol), after stirred for 10 min, **S12**[8] (0.79 g, 8.0 mmol) was added in one potion and stirred for 7 h. Quench the reaction with sat.aq. NH_4Cl (10 mL) and H_2O (20 mL) and then extract with EtOAc (2 $\times$ 20 mL). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. Concentrated and flash chromatography (hexanes: EtOAc = 8: 1) to afford product **S17** (0.85 g, 2.84 mmol, 71%) as a yellow oil.

A solution of the above product **S17** (400 mg, 1.34 mmol) in AcOH/THF/H_2O (6 mL: 2 mL:2 mL) was stirred at r.t for 8 h. Then the reaction mixture was concentrated and flash chromatography (CH_2Cl_2: MeOH = 70: 1) to afford product **S18** (228 mg, 1.23 mmol, 92%) as a colorless oil.

To a stirred solution of $(COCl)_2$ (1.10 mL, 2.2 mmol, 2.0 M solution in CH_2Cl_2) in dry CH_2Cl_2 (10 mL) at – 78 ^oC was added DMSO (0.32 mL, 4.4 mmol). Then the resulting solution stirred at – 78 ^oC for 30 min. A solution of **S18** (200 mg, 1.1 mmol) in CH_2Cl_2 (3 mL) was added to the reaction mixture at – 78 ^oC and stirred for 1 h. Then NEt_3 (1.23 mL, 8.8 mmol) was added to the reaction mixture and stirred for 30 min at r.t. The reaction was quenched by addition of sat. aq. NH_4Cl (10 mL) and followed by extraction with Et_2O (2×10 mL). The combined organic

layers were washed with brine and dried over anhydrous Na_2SO_4. After filtration and concentration in vacuo, the crude product was purified by flash column chromatography (hexanes: EtOAc = 2: 1) on silica to afforded **1t** (157 mg, 0.86 mmol, 78%) as a yellow oil.

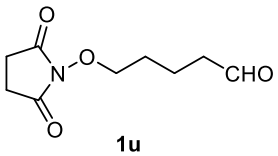


1t

The analytical data of **1s** was in accordance to the reported one. [9]

^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.75 (s, 1H), 3.55 – 3.49 (m, 2H), 2.70 (s, 4H), 2.50 – 2.44 (m, 2H), 1.64 – 1.58 (m, 4H) ppm

Compound 1u was synthesized following in the procedure of **1t** and was obtained as a pale yellow oil.

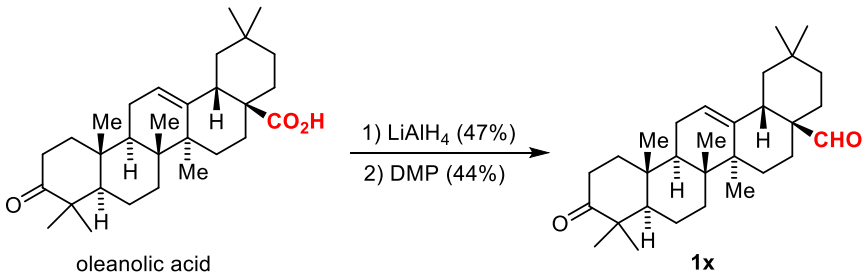


1u

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.76 (t, *J* = 1.5 Hz, 1H), 4.08 (t, *J* = 6.3 Hz, 2H), 2.69 (s, 4H), 2.52 (td, *J* = 7.4, 1.8 Hz, 2H), 1.85 – 1.79 (m, 2H), 1.77 – 1.72 (m, 2H) ppm

^{13}C NMR (125 MHz, $CDCl_3$): δ = 202.1, 171.3, 76.7, 43.2, 27.4, 25.5, 18.3 ppm

HRMS (ESI) for $C_9H_{14}NO_4$, $[M+H]^+$: calcd. 200.0917, found: 200.0918.

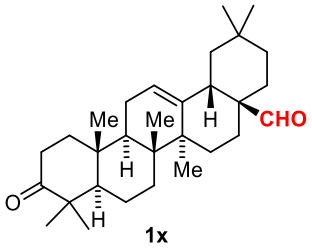


oleanolic acid **1x**

To a stirred solution of oleanolic acid (457 mg, 1.0 mmol) in dry THF (15 mL) at 0 °C was added $LiAlH_4$ (2.0 mL, 2.0 mmol, 1.0 mmol/mL solution in THF), then the reaction mixture heated to reflux and stirred for 12 h. Quench the reaction with MeOH (2 mL) and then Et_2O

(20 mL) and saturated solution of Rochelle salt (30 mL) was added, stirred until the two layers are clear (30 min). Then extract with EtOAc (2 × 30 mL), the combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. Concentrated and flash chromatography (hextanes: EtOAc = 15: 1) to afford diol (210 mg, 0.47 mmol, 47%) as a white powder.

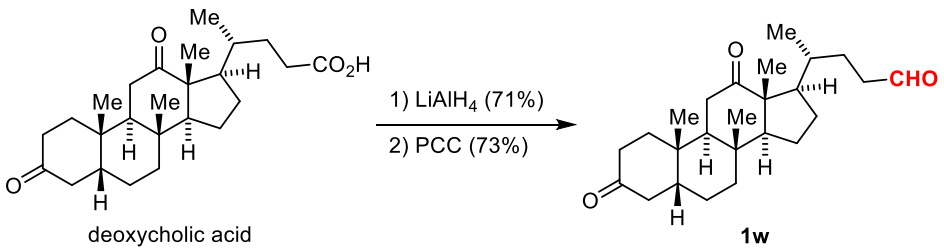
To a stirred solution of the above diol (150 mg, 0.34 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added Dess-Martin periodinane (433 mg, 1.02 mmol), after stirred for 2 h, the reaction was quench with brine (5 mL), then extracted with (2 × 10 mL), the combined organic layers were washed with 1N NaOH solution (10 mL) and dried over anhydrous Na_2SO_4. Concentrated and flash chromatography (hexanes: EtOAc = 30: 1) to afford **1x** (65 mg, 0.15 mmol, 44%) as a white powder.



1x

The analytical data of **1x** was in accordance to the reported one. [10]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.40 (s, 1H), 5.37 (t, *J* = 3.5 Hz, 1H), 2.65 (dd, *J* = 14.0, 4.5 Hz, 1H), 2.58 – 2.51 (m, 1H), 2.39 – 2.34 (m, 1H), 2.02 – 1.94 (m, 2H), 1.92 – 1.86 (m, 2H), 1.69 (t, *J* = 13.5 Hz, 2H), 1.50 – 1.46 (m, 4H), 1.44 – 1.37 (m, 2H), 1.35 – 1.34 (m, 1H), 1.31 – 1.25 (m, 5H), 1.22 – 1.21 (m, 1H), 1.20 – 1.18 (m, 1H), 1.15 (s, 3H), 1.09 (s, 3H), 1.04 (s, 6H), 0.92 (d, *J* = 2.7 Hz, 6H), 0.79 (s, 3H) ppm



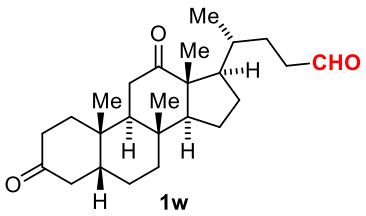
deoxycholic acid **1w**

The procedure for prepare **1w** was take from the reported procedure.[11]

To a stirred solution of deoxycholic acid (393 mg, 1.0 mmol) in dry THF (15 mL) at 0 °C

was added $LiAlH_4$ (2.0 mL, 2.0 mmol, 1.0 mmol/mL solution in THF), then remove the ice bath and the reaction mixture heated to reflux and stirred for 12 h. Quench the reaction with MeOH (0.5 mL), saturated Rochell's salt solution (20 mL) and Et_2O (20 mL) were added and stirred until the two layers are clear. Then extract with EtOAc (2×20 mL). The combined organic layers were washed with brine and then dried over anhydrous Na_2SO_4. Concentrated and flash chromatography (hexanes: EtOAc = 3:1) to afford the triol (270 mg, 0.71 mmol, 71%) as a white power.

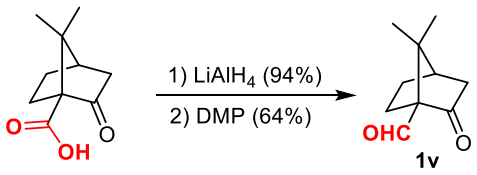
The above triol (200 mg, 0.53 mmol) was dissolved in dry CH_2Cl_2 (10 mL), then PCC (571 mg, 2.65 mmol) and NaOAc (217 mg, 2.65 mmol) was added to the solution and stirred for 1 h. Dilute the reaction mixture with Et_2O (10 mL) and filtered through a plug of silica gel. directly concentrated and flash chromatography (hexanes: EtOAc = 40 : 1) to afford **1w** (300 mg, 0.46 mmol, 86%) as a white powder.



1w

The analytical data of **1w** was in accordance to the reported one. [11]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.75 (s, 1H), 2.61 – 2.53 (m, 2H), 2.51 – 2.45 (m, 1H), 2.40 – 2.34 (m, 1H), 2.30 (dd, *J* = 14.6, 5.1 Hz, 1H), 2.15 (d, *J* = 14.4 Hz, 1H), 2.07 (dd, *J* = 13.0, 4.3 Hz, 1H), 2.03 – 1.98 (m, 2H), 1.95 – 1.86 (m, 6H), 1.82 – 1.78 (m, 1H), 1.76 – 1.73 (m, 1H), 1.58 (d, *J* = 13.9 Hz, 1H), 1.45 – 1.28 (m, 8H), 1.08 (s, 3H), 1.03 (s, 3H), 0.83 (d, *J* = 6.5 Hz, 3H) ppm

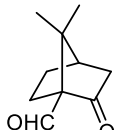


1v

To a stirred solution of ketopinic acid (182 mg, 1 mmol) in dry THF (10 mL) at 0 °C was added $LiAlH_4$ (2.0 mL, 2.0 mmol, 1.0 mmol/mL solution in THF), then the reaction mixture heated to reflux and stirred for 12 h. Quench the reaction with MeOH (2 mL) and then Et_2O

(20 mL) and saturated solution of Rochelle salt (30 mL) was added, stirred until the two layers are clear (30 min). Then extract with EtOAc (2 × 30 mL), the combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. Concentrated to afford diol (160 mg, 0.94 mmol, 94%) as a white powder without further purification.

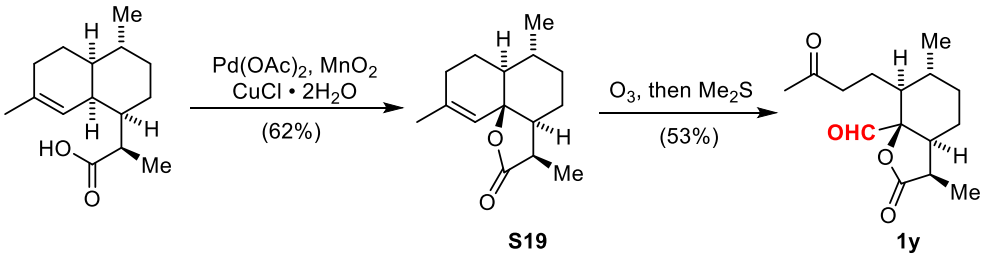
To a stirred solution of the above diol (160 mg, 0.94 mmol) in CH_2Cl_2 at 0 °C was added Dess-Martin periodinane (1.20 g, 2.82 mmol), after stirred for 2 h, the reaction was quench with brine (5 mL), then extracted with (2 × 10 mL), the combined organic layers were washed with 1N NaOH solution and dried over anhydrous Na_2SO_4. Concentrated and flash chromatography (hextanes: EtOAc = 6:1) to afford **1v** (100 mg, 0.60 mmol, 64%) as a white powder.



1v

The analytical data of **1v** was in accordance to the reported one. [12]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.94 (s, 1H), 2.59 (d, *J* = 18.0 Hz, 1H), 2.31 (t, *J* = 12.6 Hz, 1H), 2.16 (s, 1H), 2.08 (t, *J* = 12.7 Hz, 1H), 1.97 (d, *J* = 18.9 Hz, 1H), 1.69 – 1.64 (m, 1H), 1.46 (t, *J* = 10.6 Hz, 1H), 1.22 (s, 3H), 1.09 (s, 3H) ppm

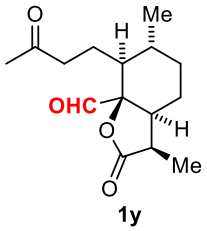


S19 **1y**

Compound **1y** was prepared through the reported procedure.[13]

Dihydroartemisinic acid (473 mg, 2.0 mmol) was dissolved in dry CH_2Cl_2 (20 mL), then $CuCl_2$•$2H_2O$ (426 mg, 2.5 mmol), $Pd(OAc)_2$ (112 mg, 0.5 mmol) and activated MnO_2 (261 mg, 3.0 mmol) were added to the solution and the reaction mixture heated to reflux and stirred for 30 h. Filtered through a plug of silica gel and washed the reaction residue with EtOAc (2×10 mL). Concentrated and flash chromatography (hexanes: EtOAc = 30: 1) to afford product **S19** (290 mg, 1.24 mmol, 62%) as a white solid.

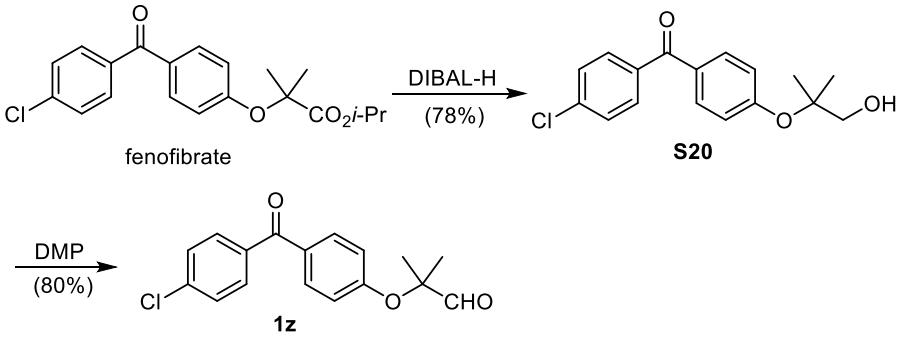
O_3 was bubbled through a stirred solution of the above product **s19** (200 mg, 0.85 mmol) in CH_2Cl_2 (10 mL) at – 78 °C until the reaction mixture color change into blue, an Ar balloon was bubbled to the solution followed by Me_2S (0.31 mL, 4.25 mmol) was added, then stirred at r.t for 12 h. The reaction mixture was directly concentrated and flash chromatography (hexanes: EtOAc = 4: 1) to afford product **1y** (120 mg, 0.45 mmol, 53%) as a colorless oil.



1y

The analytical data of **1y** was in accordance to the reported one. [13]

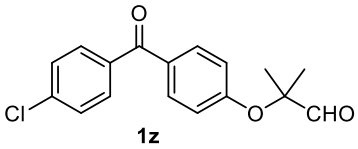
^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.74 (s, 1H), 2.64 – 2.56 (m, 2H), 2.46 – 2.37 (m, 2H), 2.12 (s, 3H), 1.89 – 1.77 (m, 2H), 1.73 – 1.69 (m, 3H), 1.45 (s, 1H), 1.11 (d, *J* = 6.9 Hz, 5H), 0.99 (d, *J* = 6.4 Hz, 3H) ppm



To a stirred solution of fenofibrate (360 mg, 1.0 mmol) in dry CH_2Cl_2 (10 mL) at – 20 °C was added DIBAL-H (4.0 mL, 4.0 mmol, 1.0 M solution in hextane). Then after stirred at – 20 °C for 2 h, the reaction mixture was quenched by MeOH (3 mL), then Et_2O (30 mL) and saturated solution of Rochelle salt (20 mL) was added, stirred until the two layers are clear (30 min). Then extract with EtOAc (2 × 20 mL), the combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. Concentrated afford crude product **S20** which directly used for the next step.

To a stirred solution of the above crude diol **S20** in CH_2Cl_2 (10 mL) at 0 °C was added

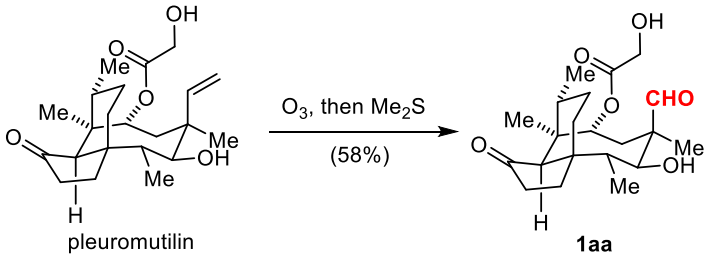
Dess-Martin periodinane (0.99 g, 2.34 mmol), after stirred for 2 h, the reaction was quench with brine (5 mL), then extracted with (2 × 10 mL), the combined organic layers were washed with 1N NaOH solution and dried over anhydrous Na_2SO_4. Concentrated and flash chromatography (hexanes: EtOAc = 20: 1) to afford **1z** (190 mg, 0.63 mmol, 63% over two steps) as a white solid.



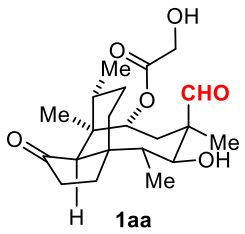
1z

The analytical data of **1z** was in accordance to the reported one. [14]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.82 (s, 1H), 7.75 – 7.70 (m, 4H), 7.45 (d, J = 8.4 Hz, 2H), 6.89 (d, J = 8.5 Hz, 2H), 1.53 (s, 6H) ppm



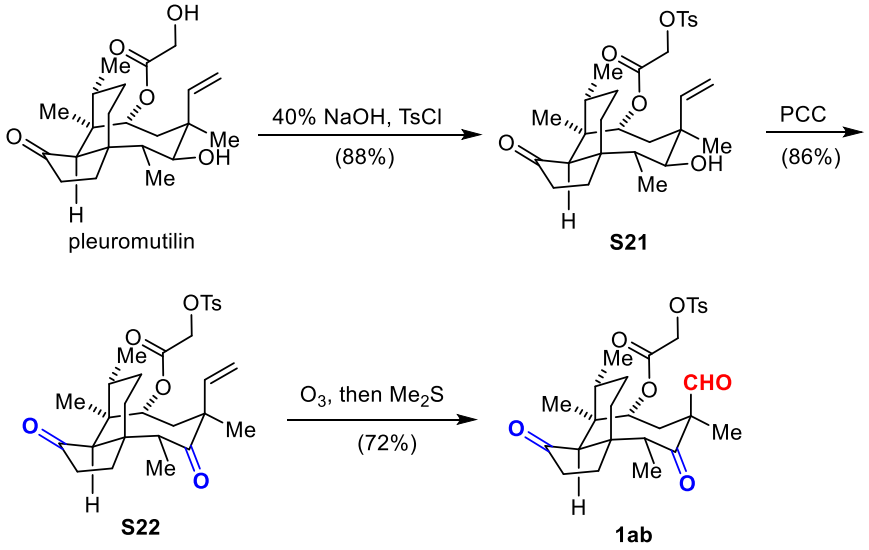
O_3 was bubbled through a stirred solution of pleuromutilin (378.4 mg, 1.0 mmol) in CH_2Cl_2 (10 mL) at – 78 ^{o}C until the reaction mixture color change into blue, an Ar balloon was bubbled to the solution followed by Me_2S (0.37 mL, 5.0 mmol) was added, then the reaction mixture stirred at r.t for 12 h. The reaction mixture was directly concentrated and flash chromatography (hexanes: EtOAc = 1: 1) to afford product **1aa** (220 mg, 0.58 mmol, 58%) as a white powder.



The analytical data of **1aa** was in accordance to the reported one. [15]

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 9.54 (d, J = 3.1 Hz, 1H), 5.34 (d, J = 8.6 Hz, 1H), 4.14 – 4.03 (m, 2H), 3.37 (dd, J = 6.6, 2.6 Hz, 1H), 2.55 (s, 2H), 2.37 – 2.31 (m, 1H), 2.26 – 2.15 (m, 2H), 2.09 –

2.03 (m, 1H), 1.95 (d, *J* = 2.2 Hz, 1H), 1.80–1.72 (m, 2H), 1.68 – 1.61 (m, 2H), 1.51 – 1.46 (m, 1H), 1.44 (s, 3H), 1.39 – 1.34 (m, 2H), 1.27 (s, 3H), 1.16 – 1.11 (m, 1H), 1.09 (d, *J* = 7.2 Hz, 3H), 0.68 (d, *J* = 7.4 Hz, 3H) ppm

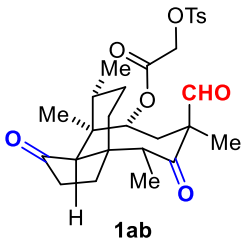


Compound **S21** was prepared through the reported procedure.[16]

40% sodium hydroxide solution (0.5 mL, 5.0 mmol) was added dropwise to a mixture of pleuromutilin (757.0 mg, 2.0 mmol) and *p*-toluenesulfonyl chloride (*p*-TsCl) (457.6 mg, 2.4 mmol) in THF (15 mL) and water (3 mL). The mixture was stirred vigorously under reflux for 1 h, then diluted with water (20 mL) and stirred under an ice bath for 15 min, followed by washing with water (20 mL) and cold THF (20 mL). Filtration afforded **S21** as white solid (937.5 mg, 1.76 mmol, 88%). It was used in the next step without further purification.

The above product **S21** (350 mg, 0.66 mmol) was dissolved in dry CH_2Cl_2 (10 mL), then PCC (356 mg, 1.65 mmol) and NaOAc (217 mg, 2.65 mmol) was added to the solution and stirred for 1 h. Dilute the reaction mixture with Et_2O (10 mL) and filtered through a plug of silica gel. Then concentrated and flash chromatography (hexanes: EtOAc = 10:1) to afford product **s22** (300 mg, 0.57 mmol, 86%) as a white powder.

O_3 was bubbled through a stirred solution of the above product **s22** (200 mg, 0.38 mmol) in CH_2Cl_2 (10 mL) at – 78 ^oC until the reaction mixture color change into blue, an Ar balloon was bubbled to the solution followed by Me_2S (0.14 mL, 1.9 mmol) was added, then stirred at r.t for 12 h. The reaction mixture was directly concentrated and flash chromatography (hexanes : EtOAc = 5:1) to afford product **1ab** (145 mg, 0.27 mmol, 72%) as a white powder.



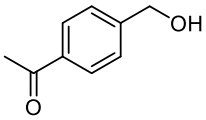
1ab

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.54 (s, 1H), 7.80 (d, *J* = 7.3 Hz, 2H), 7.35 (d, *J* = 7.3 Hz, 2H), 5.64 (d, *J* = 7.4 Hz, 1H), 4.53 (s, 2H), 3.10 (s, 1H), 2.43 (s, 3H), 2.19 – 2.10 (m, 3H), 2.05 – 2.00 (m, 1H), 1.86 (d, *J* = 16.0 Hz, 1H), 1.63 – 1.55 (m, 3H), 1.47 – 1.40 (m, 4H), 1.39 – 1.30 (m, 2H), 1.14 (s, 3H), 1.11 – 1.04 (m, 4H), 0.65 (d, *J* = 4.2 Hz, 3H) ppm

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 215.8, 212.2, 202.6, 165.7, 145.6, 132.5, 130.0, 128.1, 71.8, 64.9, 63.3, 58.7, 47.8, 45.3, 41.9, 38.4, 36.9, 34.5, 29.7, 26.7, 24.6, 21.7, 18.8, 17.2, 14.8, 12.4 ppm

HRMS(ESI) for $C_{28}H_{36}O_8SNa$ $[M+Na]^+$: calcd. 555.2028, found: 555.2016.

3. Data for reduction product:



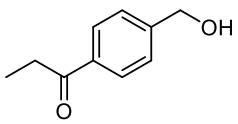
2a

Compound 2a, pale yellow oil.

Yield: 95%. Reaction time: 5 min.

The analytical data of **2a** was in accordance to the reported one. [17]

^{1}H NMR (500 MHz, $CDCl_3$) : δ = 7.96 (d, *J* = 8.2 Hz, 2H), 7.46 (d, *J* = 8.0 Hz, 2H), 4.78 (s, 2H), 2.61 (s, 3H), 1.82 (s, 1H) ppm



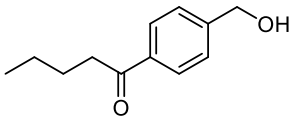
2b

Compound 2b, white powder solid.

Yield: 76%. Reaction time: 12 min at 0 °C.

The analytical data of **2b** was in accordance to the reported one. [18]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.96 (d, *J* = 8.2 Hz, 2H), 7.45 (d, *J* = 8.2 Hz, 2H), 4.78 (s, 2H), 3.01 (q, *J* = 7.2 Hz, 2H), 1.79 (s, 1H), 1.23 (t, *J* = 7.0 Hz, 3H) ppm



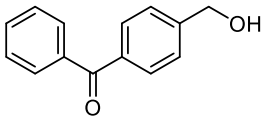
2c

Compound 2c, white powder solid.

Yield: 92%. Reaction time: 15 min at 0 °C.

The analytical data of **2c** was in accordance to the reported one. [19]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 8.2 Hz, 2H), 7.45 (d, *J* = 8.1 Hz, 2H), 4.77 (s, 2H), 2.96 (t, *J* = 7.5 Hz, 2H), 1.98 (s, 1H), 1.75–1.68 (m, 2H), 1.45–1.37 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H) ppm



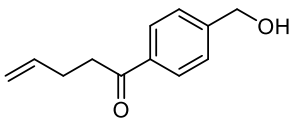
2d

Compound 2d, white needle crystal.

Yield: 86%. Reaction time: 3 min at 0 °C.

The analytical data of **2d** was in accordance to the reported one. [20]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.83 – 7.77 (m, 4H), 7.62 – 7.56 (m, 1H), 7.51 – 7.45 (m, 4H), 4.81 (s, 2H), 1.82 (s, 1H) ppm



2e

Compound 2e, yellow oil.

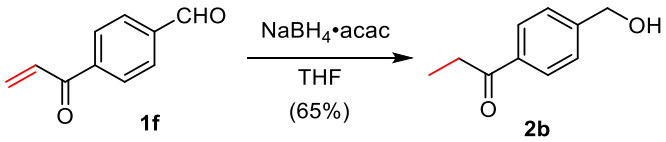
Yield: 94%. Reaction time: 25 min at 0 °C.

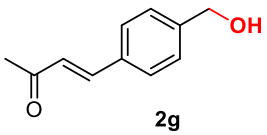
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 8.1 Hz, 2H), 7.43 (d, *J* = 8.3 Hz, 2H), 5.93 – 5.85 (m, 1H), 5.07 (d, *J* = 17.1 Hz, 1H), 5.00 (d, *J* = 10.2 Hz, 1H), 4.75 (s, 2H), 3.05 (t, *J* = 7.6 Hz, 2H), 2.50–2.45 (m, 2H), 2.27 (s, 1H) ppm

^{13}C NMR (125 MHz, $CDCl_3$): δ = 199.4, 146.3, 137.3, 136.1, 128.3, 126.7, 115.4, 64.6, 37.8, 28.2 ppm

HRMS (APCI) for $C_{12}H_{13}O_2$ $[M-H]^-$ calcd. 189.0921, found: 189.0921.

When **1f** was submit to the reaction condition, only **2b** was obtained.



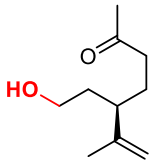


Compound 2g, white powder solid.

Yield: 85%. Reaction time: 20 min at 0 °C.

The analytical data of **2g** was in accordance to the reported one. [21]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.55 – 7.49 (m, 3H), 7.41(d, *J* = 8.2 Hz, 2H), 6.71(d, *J* = 16.3 Hz, 1H), 4.74 (s, 2H), 2.39 (s, 3H) ppm



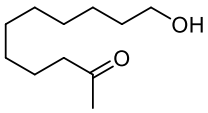
2h

Compound 2h, colorless oil.

Yield: 73%. Reaction time: 15 min at 0 °C.

The analytical data of **2h** was in accordance to the reported one. [22]

^{1}H NMR (500 MHz, $CDCl_3$) δ = 4.80 – 4.78 (m, 1H), 4.73 – 4.72 (m, 1H), 3.64 – 3.55 (m, 2H), 2.36 (t, *J* = 7.5 Hz, 2H), 2.22 – 2.15 (m, 1H), 2.11 (s, 3H), 1.71 – 1.63 (m, 2H), 1.62 – 1.61 (m, 1H), 1.60 (s, 3H), 1.57 – 1.52 (m, 1H) ppm



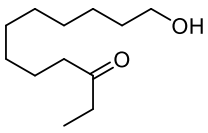
2i

Compound 2i, white flaky crystal.

Yield: 87%. Reaction time: 15 min at 0 °C.

The analytical data of **2i** was in accordance to the reported one. [23]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.65 – 3.62 (m, 2H), 2.42 – 2.40 (m, 2H), 2.13 (s, 3H), 1.60 – 1.51 (m, 4H), 1.47 (s, 1H), 1.33 – 1.24 (m, 10H) ppm



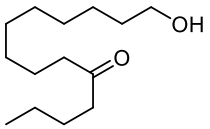
2j

Compound 2j, white flaky crystal.

Yield: 80%. Reaction time: 20 min at 0 °C.

The analytical data of **2j** was in accordance to the reported one. [24]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.64 – 3.62 (m, 2H), 2.44 – 2.37 (m, 4H), 1.59 – 1.51 (m, 4H), 1.33 – 1.22 (m, 10H), 1.05 (t, *J* = 7.2 Hz, 3H) ppm

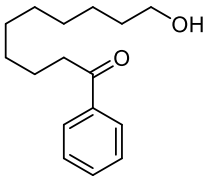


2k

Compound 2k, white flaky crystal.

Yield: 81%. Reaction time: 30 min at 0 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.65 – 3.63 (m, 2H), 2.40 – 2.37 (m, 4H), 1.60 – 1.50 (m, 6H), 1.33 – 1.24 (m, 12H), 0.90 (t, *J* = 7.6 Hz, 3H) ppm

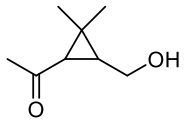


2l

Compound 2l, white flaky crystal.

Yield: 83%. Reaction time: 20 min at 0 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.96 (d, *J* = 7.4 Hz, 2H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 3.64 (t, *J* = 6.6 Hz, 2H), 2.96 (t, *J* = 7.4 Hz, 2H), 1.76 – 1.71 (m, 2H), 1.59 – 1.54 (m, 2H), 1.40 – 1.28 (m, 10H) ppm



2m

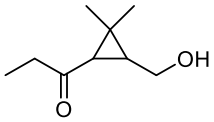
Compound 2m, colorless oil.

Yield: 67%. Reaction time: 20 min at 0 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.73 – 3.69 (m, 1H), 3.64 – 3.60 (m, 1H), 2.23 (s, 3H), 1.86 (q, *J* = 6.8 Hz, 1H), 1.77 (d, *J* = 5.4 Hz, 1H), 1.27 (s, 3H), 1.14 (s, 3H) ppm

^{13}C NMR (125 MHz, $CDCl_3$): δ = 205.7, 62.0, 40.2, 35.6, 3 2.2, 24.3, 21.4, 20.1 ppm

HRMS (APCI) for $C_8H_{13}O_2$ $[M-H]^-$: calcd. 141.0921, found: 141.0923.



2n

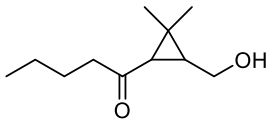
Compound 2n. colorless oil.

Yield: 75%. Reaction time: 15 min at 0 ^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.72 – 3.68 (m, 1H), 3.64 – 3.60 (m, 1H), 2.57 – 2.45 (m, 2H), 1.86 (q, *J* = 6.9 Hz, 1H), 1.74 (d, *J* = 5.4 Hz, 1H), 1.26 (s, 3H), 1.12 (s, 3H), 1.06 (t, *J* = 7.4 Hz, 3H) ppm

^{13}C NMR (125 MHz, $CDCl_3$): δ = 208.5, 62.0, 39.3, 38.1, 35.1, 30.3, 21.4, 20.2, 8.0 ppm

HRMS (APCI) for $C_9H_{17}O_2$ $[M+H]^+$: calcd. 157.1223, found: 157.1221.



2o

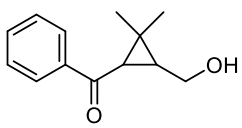
Compound 2o. colorless oil.

Yield: 74%. Reaction time: 70 min at r.t.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.70 – 3.66 (m, 1H), 3.62 – 3.58 (m, 1H), 2.47 (t, *J* = 7.6 Hz, 2H), 1.86 – 1.82 (m, 1H), 1.73 (d, *J* = 4.8 Hz, 2H), 1.60 – 1.49 (m, 2H), 1.34 – 1.28 (m, 2H), 1.25 (s, 3H), 1.10 (s, 3H), 0.89 (t, *J* = 7.0 Hz, 3H) ppm

^{13}C NMR (125 MHz, $CDCl_3$): δ = 208.4, 61.9, 44.8, 39.6, 35.2, 30.6, 26.2, 22.4, 21.4, 20.2, 13.9 ppm

HRMS (APCI) for $C_{11}H_{19}O_2$ $[M-H]^-$: calcd. 183.1390, found: 183.1393.



2p

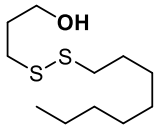
Compound 2p. colorless oil.

Yield: 95%. Reaction time: 80 min at 0 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.91 (d, *J* = 7.4 Hz, 2H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 3.82 – 3.78 (m, 1H), 3.73 – 3.69 (m, 1H), 2.38 (d, *J* = 5.6 Hz, 1H), 2.12 (q, *J* = 6.8 Hz, 1H), 1.79 (s, 1H), 1.42 (s, 3H), 1.13 (s, 3H) ppm

^{13}C NMR (125 MHz, $CDCl_3$): δ = 197.9, 138.7, 132.7, 128.5, 128.0, 62.0, 37.4, 34.3, 31.0, 21.2, 20.4 ppm

HRMS (APCI) for $C_{13}H_{15}O_2$ $[M-H]^-$: calcd. 203.1078, found: 203.1074.



2q

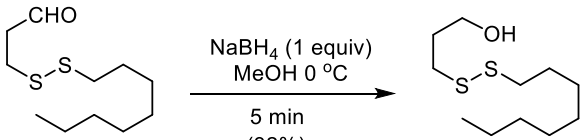
Compound 2q. Colorless oil.

Yield: 81%. Reaction time: 8 min at 0 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.76 (td, *J* = 6.2, 2.2 Hz, 2H), 2.83 – 2.78 (m, 2H), 2.68 (q, *J* = 7.2 Hz, 2H), 1.98 – 1.92 (m, 2H), 1.72 (s, 1H), 1.69 – 1.63 (m, 2H), 1.40 – 1.34 (m, 2H), 1.31 – 1.24 (m, 8H), 0.87 (t, *J* = 7.1 Hz, 3H) ppm

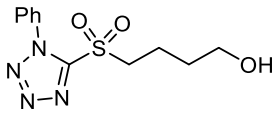
^{13}C NMR (125 MHz, $CDCl_3$): δ = 61.1, 61.0, 39.2, 39.1, 35.2, 35.1, 31.8, 29.2, 28.6, 22.7, 14.1 ppm

HRMS (ESI) for $C_{11}H_{25}OS_2$ $[M+H]^+$: calcd . 237.1341, found: 237.1346.



1q **2q**

When compound **1q** was submitted to the control condition ($NaBH_4$ (1 equiv) in MeOH at 0°C), the product **2q** was obtained with 32% yield.



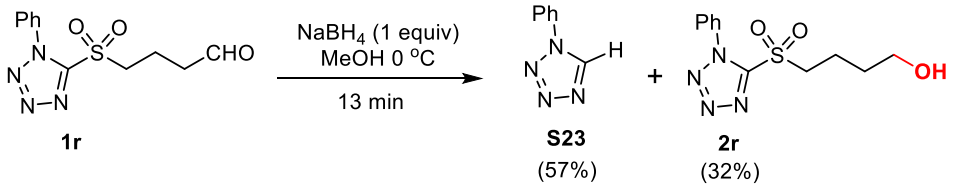
2r

Compound 2r. Pale yellow oil.

Yield: 84%. Reaction time: 10 min at 0 °C.

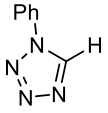
The analytical data of **2r** was in accordance to the reported one. [25]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.69 – 7.67 (m, 2H), 7.64 – 7.57 (m, 3H), 3.81 (t, J = 8.2 Hz, 2H), 3.71 (t, J = 6.3 Hz, 2H), 2.11 – 2.05 (m, 2H), 1.82 (s, 1H), 1.78 – 1.73 (m, 2H) ppm



1r **S23** (57%) **2r** (32%)

When compound **1r** was submitted to the control condition ($NaBH_4$ (1 equiv) in MeOH at 0°C), the product **2r** was obtained with 32% yield, compound **S23** was also obtained with 57% yield.

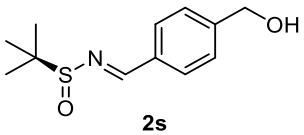


S23

Compound S23. Colorless oil

The analytical data of **S23** was in accordance to the reported one. [26]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.99 (s, 1H), 7.72 (d, J = 7.8 Hz, 2H), 7.60 (t, J = 7.9 Hz, 2H), 7.55 (t, J = 7.5 Hz, 1H) ppm



2s

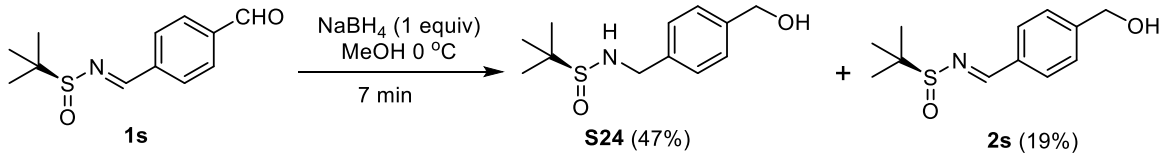
Compound 2s. White needle solid.

Yield: 97%. Reaction time: 25 min at 0 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.43 (s, 1H), 7.77 (d, J = 8.2 Hz, 2H), 7.45 (d, J = 8.1 Hz, 2H), 4.74 (s, 2H), 2.80 (s, 1H), 1.23 (s, 9H) ppm

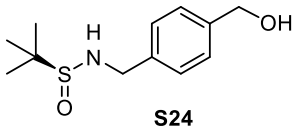
^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.4, 146.0, 133.2, 129.6, 127.1, 64.6, 57.9, 22.6 ppm

HRMS (ESI) for $C_{12}H_{17}NO_2SNa$ $[M+Na]^+$: calcd. 262.0877, found: 262.0889.



1s **S24** (47%) **2s** (19%)

When compound **1s** was submitted to the control condition ($NaBH_4$ (1 equiv) in MeOH at 0°C), the product **2s** was obtained with 19% yield, the fully reduced compound **S24** was obtained with 47% yield.



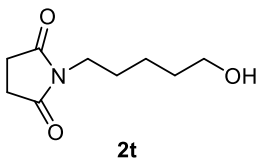
S24

Compound S24. Colorless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34 – 7.29 (m, 4H), 4.66 (s, 2H), 4.29 (dd, *J* = 13.9, 4.1 Hz, 1H), 4.20 (dd, *J* = 13.8, 7.5 Hz, 1H), 3.50 – 3.47 (m, 1H), 2.40 (s, 1H), 1.22 (s, 9H) ppm

^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.7, 137.7, 128.3, 127.3, 64.8, 56.0, 49.2, 22.7 ppm

HRMS (ESI) for $C_{12}H_{19}NO_2SNa$ $[M+Na]^+$: calcd. 264.1034, found: 264.1031.



2t

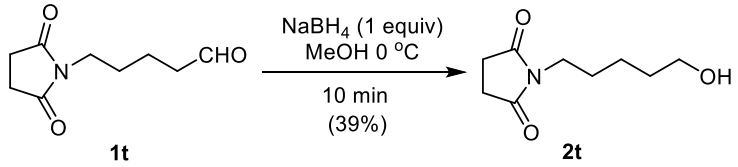
Compound 2t. Colorless oil.

Yield: 83%. Reaction time: 25 min at 0 °C.

The analytical data of **2t** was in accordance to the reported one. [27]

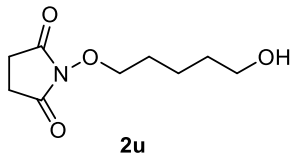
^{1}H NMR (500 MHz, $CDCl_3$) δ = 3.61 (t, *J* = 6.6 Hz, 2H), 3.50 (t, *J* = 7.4 Hz, 2H), 2.68 (s, 4H), 1.77

(s, 1H), 1.60 – 1.56 (m, 4H), 1.38 – 1.32 (m, 2H) ppm



1t **2t**

When compound **1t** was submitted to the control condition ($NaBH_4$ (1 equiv) in MeOH at 0°C), the product **2t** was obtained only with 39% yield.



2u

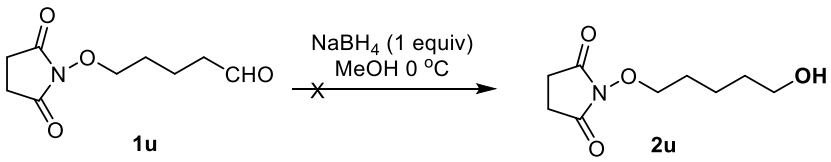
Compound 2u. Pale yellow oil.

Yield: 91%. Reaction time: 13 min at 0 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 4.08 (t, *J* = 6.3 Hz, 2H), 3.64 (t, *J* = 6.2 Hz, 2H), 2.69 (s, 4H), 1.87 (s, 1H), 1.77 – 1.71 (m, 2H), 1.62–1.53 (m, 4H) ppm

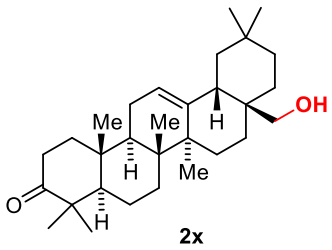
^{13}C NMR (125 MHz, $CDCl_3$) δ = 171.4, 77.3, 62.5, 32.2, 27.8, 25.5, 21.8 ppm

HRMS(ESI) for $C_9H_{15}NO_4Na$ $[M+Na]^+$: calcd 224.0899, found: 224.0894.



1u **2u**

When compound **1u** was submitted to the control condition ($NaBH_4$ (1 equiv) in MeOH at 0°C), the product **2u** was not obtained.



2x

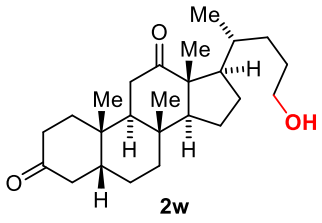
Compound 2x. White flaky crystal.

Yield: 83%. Reaction time: 90 min at 0 °C.

The analytical data of **2x** was in accordance to the reported one. [28]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.22 (t, *J* = 3.5 Hz, 1H), 3.56 (d, *J* = 11.0 Hz, 1H), 3.23 (d, *J* = 11.2 Hz, 1H), 2.58 – 2.51 (m, 1H), 2.40 – 2.34 (m, 1H), 2.02 – 1.98 (m, 1H), 1.97 – 1.93 (m, 1H), 1.90 – 1.85 (m, 3H), 1.76 – 1.71 (m, 2H), 1.66 – 1.63 (m, 1H), 1.57 – 1.49 (m, 4H), 1.44 – 1.36 (m, 3H), 1.34 – 1.30 (m, 3H), 1.28 – 1.20 (m, 3H), 1.18 (s, 3H), 1.10 (s, 3H), 1.06 (d, *J* = 6.2 Hz, 6H), 1.00 (s, 3H), 0.88 (d, *J* = 6.0 Hz, 6H) ppm

^{13}C NMR (125 MHz, $CDCl_3$): δ = 217.8, 144.3, 122.2, 69.7, 55.3, 47.5, 46.8, 46.5, 42.4, 41.9, 39.8, 39.3, 37.0, 36.7, 34.2, 34.1, 33.2, 32.1, 31.0, 30.9, 26.5, 25.8, 25.5, 23.7, 23.6, 22.0, 21.5, 19.7, 16.7, 15.3 ppm



2w

Compound 2w. Colorless oil.

Yield: 83%. Reaction time: 25 min at 0 °C.

The analytical data of **2w** was in accordance to the reported one. [29]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.62 (s, 2H), 2.64 – 2.55 (m, 2H), 2.34 (t, *J* = 14.8 Hz, 1H), 2.18 (d, *J* = 14.6 Hz, 1H), 2.10 (d, *J* = 12.6 Hz, 1H), 2.06 – 2.01 (m, 2H), 1.91 (d, *J* = 11.8 Hz, 6H), 1.75 – 1.74 (m, 1H), 1.67 – 1.59 (m, 3H), 1.49 – 1.39 (m, 4H), 1.34 – 1.30 (m, 4H), 1.25 (s, 1H),

1.11 (s, 3H), 1.06 (s, 3H), 1.01 (s, 1H), 0.87(d, *J* = 6.5 Hz, 3H) ppm

^{13}C NMR (125 MHz, $CDCl_3$): δ = 214.3, 212.2, 63.5, 58.6, 57.6, 46.7, 44.3, 43.8, 42.2, 38.4, 37.0, 36.8, 36.0, 35.6, 35.5, 31.4, 29.9, 27.7, 26.6, 25.5, 24.4, 22.2, 19.0, 11.8 ppm

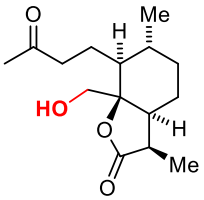
2v

Compound 2v. white powder.

Yield: 89%. Reaction time: 5 min at 0 °C.

The analytical data of **2v** was in accordance to the reported one. [30]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.89 (d, *J* = 11.9 Hz, 1H), 3.67 – 3.63 (m, 1H), 2.50 (s, 1H), 2.42 (d, *J* = 18.8 Hz, 1H), 2.08 (s, 1H), 2.01 (t, *J* = 10.7 Hz, 1H), 1.89 – 1.82 (m, 2H), 1.61 (s, 1H), 1.40 (t, *J* = 11.4 Hz, 1H), 1.00 (d, *J* = 11.9 Hz, 6H) ppm



2y

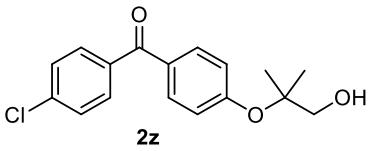
Compound 2y. Colorless oil.

Yield: 76%. Reaction time: 10 min at 0 °C.

The analytical data of **2y** was in accordance to the reported one. [13]

^{1}H NMR (500 MHz, $CDCl_3$) δ = 3.91 (d, *J* = 11.7 Hz, 1H), 3.59 (d, *J* = 11.3 Hz, 1H), 3.14 (t, *J* = 6.7 Hz, 2H), 2.79 – 2.75 (m, 1H), 2.62 – 2.51 (m, 2H), 2.17 (s, 3H), 2.07 – 2.04 (m, 1H), 1.70 (s, 1H), 1.60 – 1.53 (m, 2H), 1.44 (s, 2H), 1.25 (s, 1H), 1.12 (d, *J* = 6.8 Hz, 3H), 0.98 (d, *J* = 5.1 Hz, 3H) ppm

^{13}C NMR (125 MHz, $CDCl_3$) δ = 211.0, 179.6, 87.1, 61.8, 42.7, 42.4, 39.5, 38.8, 33.2, 32.2, 30.4, 24.3, 21.9, 21.1, 9.5 ppm



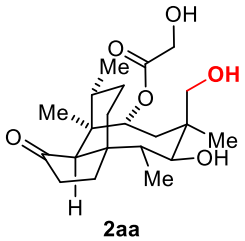
2z

Compound 2z. white flaky crystal.

Yield: 77%. Reaction time: 20 min at 0 °C.

The analytical data of **2z** was in accordance to the reported one. [14]

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.75 – 7.71 (m, 4H), 7.45 (d, *J* = 8.6 Hz, 2H), 7.07 (d, *J* = 8.7 Hz, 2H), 3.63 (s, 2H), 2.31 (s, 1H), 1.37 (s, 6H) ppm



2aa

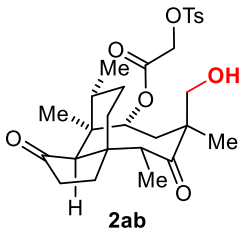
Compound 2aa. White powder solid.

Yield: 82%. Reaction time: 10 min at 0 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.52 (d, *J* = 7.5 Hz, 1H), 4.36 (d, *J* = 10.9 Hz, 1H), 4.05 (q, *J* = 17.2 Hz, 2H), 3.58 (d, *J* = 10.4 Hz, 1H), 3.47 (s, 1H), 3.29 (s, 2H), 2.44 (s, 1H), 2.28 – 2.14 (m, 2H), 2.07(s, 1H), 1.91 – 1.86 (m, 1H), 1.77 (d, *J* = 13.8 Hz, 1H), 1.68 – 1.60 (m, 2H), 1.47 (d, *J* = 11.9 Hz, 2H), 1.39 (s, 3H), 1.23 (s, 1H), 1.18 (s, 3H), 1.13 (d, *J* = 15.7 Hz, 2H), 0.97 (d, *J* = 3.8 Hz, 3H), 0.67 (d, *J* = 4.6 Hz, 3H) ppm

^{13}C NMR (125 MHz, $CDCl_3$): δ = 217.2, 173.1, 76.0, 70.6, 67.3, 61.3, 57.8, 45.5, 41.8, 41.7, 36.5, 35.3, 34.5, 30.3, 29.7, 27.1, 26.0, 24.7, 17.0, 14.6, 11.2 ppm

HRMS (ESI) for $C_{21}H_{34}O_6Na$ $[M+Na]^+$: calcd . 405.2253, found: 405.2250.



2ab

Compound 2ab. White powder solid.

Yield: 80%. Reaction time: 13 min at 0 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.82 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 5.89 (d, *J* = 9.2 Hz, 1H), 4.54 (s, 2H), 4.03 (d, *J* = 11.6 Hz, 1H), 3.81 (d, *J* = 11.7 Hz, 1H), 3.47 (q, *J* = 6.7 Hz, 1H), 2.46 (s, 3H), 2.30 – 2.21 (m, 1H), 2.18 – 2.10 (m, 2H), 1.88 (dd, *J* = 15.9, 9.3 Hz, 1H), 1.67 – 1.58 (m, 3H), 1.57 – 1.48 (m, 1H), 1.46 – 1.37 (m, 6H), 1.18 – 1.11 (m, 1H), 1.06 (d, *J* = 6.6 Hz, 3H), 1.03 (s, 3H), 0.70 (d, *J* = 7.0 Hz, 3H) ppm

^{13}C NMR (125 MHz, $CDCl_3$): δ = 216.3, 216.2, 166.7, 145.6, 132.5, 130.0, 128.1, 72.0, 67.9, 64.9, 58.6, 53.6, 45.2, 43.6, 41.9, 39.1, 37.0, 34.6, 29.9, 26.9, 24.2, 21.7, 21.3, 17.3, 14.7, 12.3 ppm

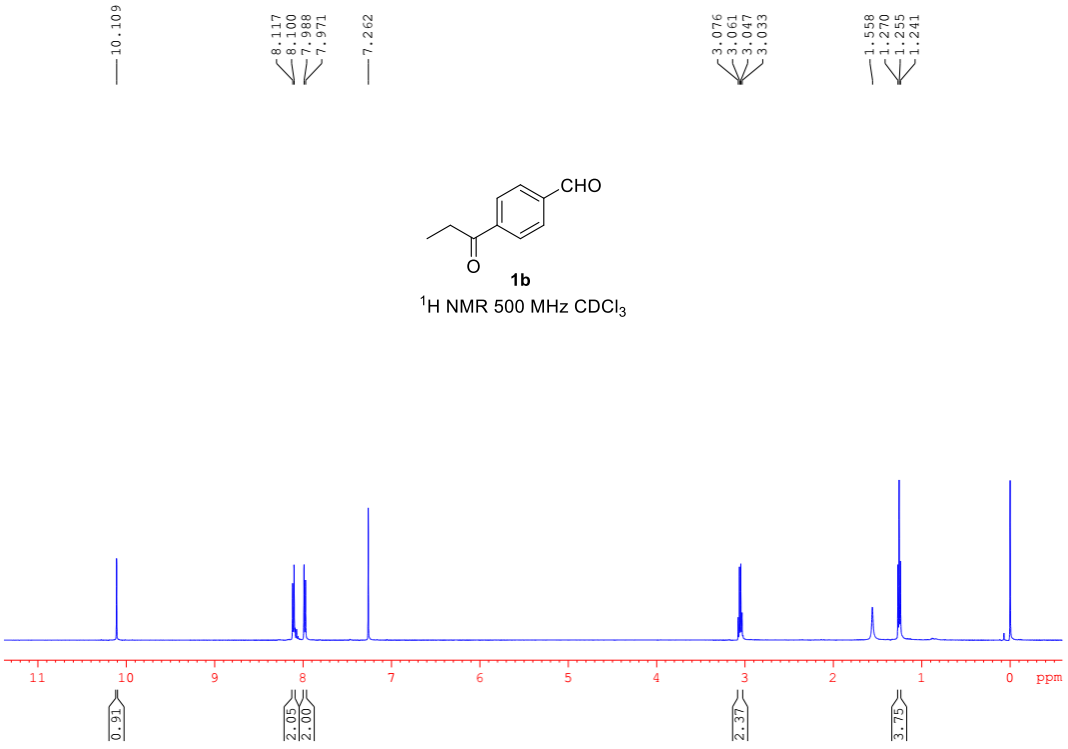
HRMS (ESI) for $C_{28}H_{38}O_8SNa$ $[M+Na]^+$: calcd. 557.2185, found: 557.2176.

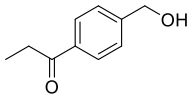
4. References:

1. Y. Lin, L. Zhu, Y. Lan and Y. Rao, *Chem. Eur. J*., 2015, **21**, 14937.
2. C. U. Pittman and R. M. Hanes, *J. Org. Chem*., 1977, **42**, 1194.
3. M. Z. Zhu, E. Ruijter and L. A. Wessjohann, *Org. Lett*., 2004, **6**, 3921.
4. M. M. Wang, X. S. Ning, J. P. Qu and Y. B. Kang, *ACS catal*., 2017, **7**, 4000.
5. Y. Q. Mu, M. Nodwell, J. L. Pace, J. Shaw and J. K. Judice, *Bioorg. Med. Chem. Lett*., 2004, **14**, 735.
6. J. R. Vakiti and S. Ghosh, *Tetrahedron Lett*., 2014, **55**, 6438.
7. Z. Y. Jiang, W. H. Chan and A. W. M. Lee, *J. Org. Chem*., 2005, **70**, 1081.
8. A. Throup, L. H. Patterson and H. M. Sheldrake, *Org. Biomol. Chem*., 2016, **14**, 9554.
9. G. Ding, C. J. Li, Y. F. Shen, B. Lu, Z. G. Zhang and X. M. Xie, *Adv. Synth, Catal*., 2016, **358**, 1241.
10. L. Chen, J. B. Wu, F. Lei, S. Qian and Y. Wu, *J. Asian. Nat. Prod. Res*., 2012, **14**, 355.
11. V. C. Edelsztein, P. H. D. Chenna and G. Burton, *Tetrahedron*, 2009, **65**, 3615.
12. T. Polonski, *J. Chem. Soc. Perkin Trans.*, 1983, 305.
13. H. J. Chen, H. D. Hao and Y. K. Wu, *Eur. J. Org. Chem*., 2015, 4423.
14. M. Craighead, R. Palin, N. Murray and D. Lindsay, WO 2012063085.
15. M. F. Richter, B. S. Drown, A. P. Riley, A. Garcia, T. Shirai, R. L. Svec and P. J. Hergenrother, *Nature,* 2017,

545, 299.
16. B. B. Liu, F. L. Jin, T. J. Wang, X. R. Yuan and W. Han, *Angew. Chem. Int. Ed*., 2017, **56**, 12712.
17. T. Osako, K. Torii, S. Hirata and Y. Uozumi, *ACS Catal*., 2017, **7**, 7371.
18. J. Bálint, I. Markovits, G. Egri, Z. Tuza, L. Párkányi and E. Fogassy, *Tetrahedron Asy*., 2001, **12**, 719.
19. (*a*) P. C. Meltzer, D. Butler, J. R. Deschamps and B. K. Madras, *J. Med. Chem*., 2006, **49**, 1420. (*b*) W. Michaelis, J. H. Russel and O. Schindler, *J. Med. Chem*., 1970, **13**, 497.
20. S. S. Husain, S. Nirthanan, D. Ruesch, K. Solt, Q. Cheng, G. D. Li, E. Arevalo, R. W. Olsen, D. E. Raines, S. A. Forman, J. B. Cohen and K. W. Miller, *J. Med. Chem*., 2006, **49**, 4818.
21. K. Yahata, M. Minami, K. Watanabe and H. Fujioka, *Org. Lett*., 2014, **16**, 3680.
22. C. F. Nutaitis and G. W. Gribble, *Tetrahedron Lett*., 1983, **24**, 4287.
23. T. Kusakabe, Y. Ito, M. Kamimura, T. Shirai, K. Takahashi, T. Mochida and K. Kato, *Chem. Asian. J*., 2017, **6**, 1086.
24. M. Linuma, K. Moriyama and H. Togo, *Eur. J. Org. Chem*., 2014, 772.
25. D. Crépin, J. Dawick and C. Aissa, *Angew. Chem. Int. Ed*., 2010, **49**, 620.
26. K. Vega-Hernández, R. Senatore, M. Miele, E. Urban, W. Holzer and V. Pace, *Org. Biomol. Chem*., 2019, **17**, 1970.
27. I. M. Pinilla, M. B. Martínez and J. A. Galbis, *Macromolecules*, 2002, **35**, 2985.
28. S. Qian, H. J. Li, Y. Chen, W. Y. Zhang, S. Y. Yang and Y. Wu, *J. Nat. Prod*., 2010, **73**, 1743.
29. H. P. Hsieh, J. G. Muller and C. J. Burrows, *Bioorg. Med. Chem*., 1995, **3**, 823.
30. B. Föhlisch, D. A. Bakr and P. Fischer, *J. Org. Chem*., 2002, **67**, 3682.

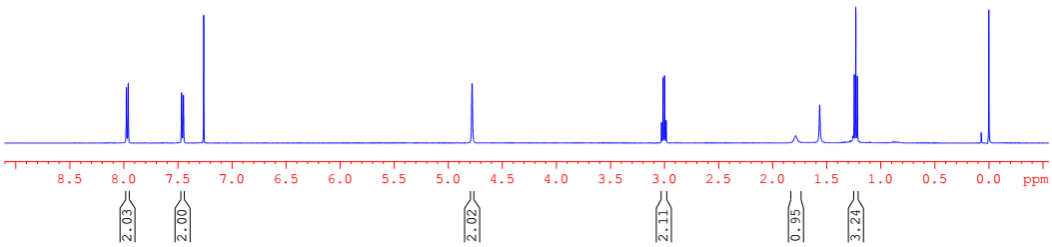
5. ^{1}H and ^{13}C NMR Spectra

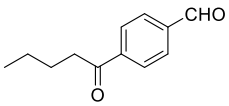




2b

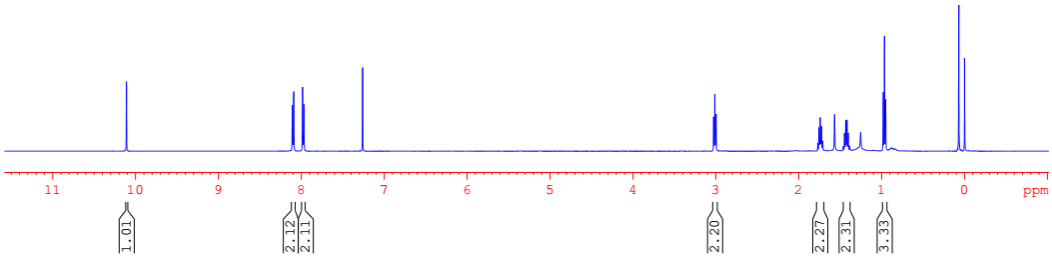
^{1}H NMR 500 MHz $CDCl_3$

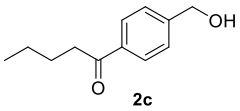




1c

^{1}H NMR 500 MHz $CDCl_3$





2c

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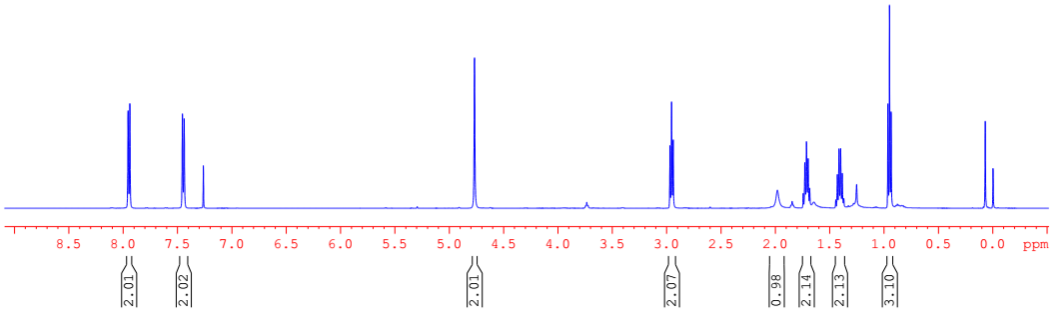
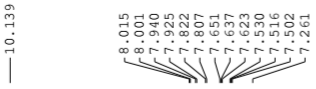
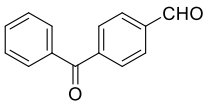
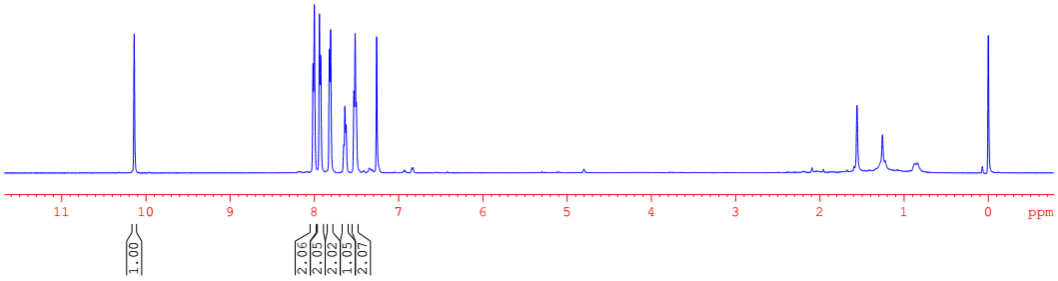


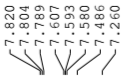


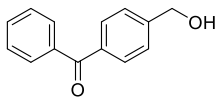


1d

^{1}H NMR 500 MHz $CDCl_3$

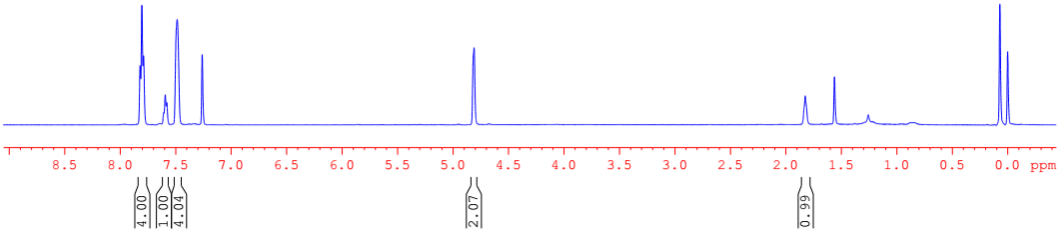


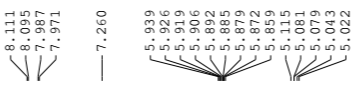


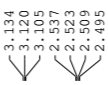


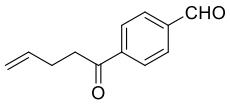
2d

^{1}H NMR 500 MHz $CDCl_3$



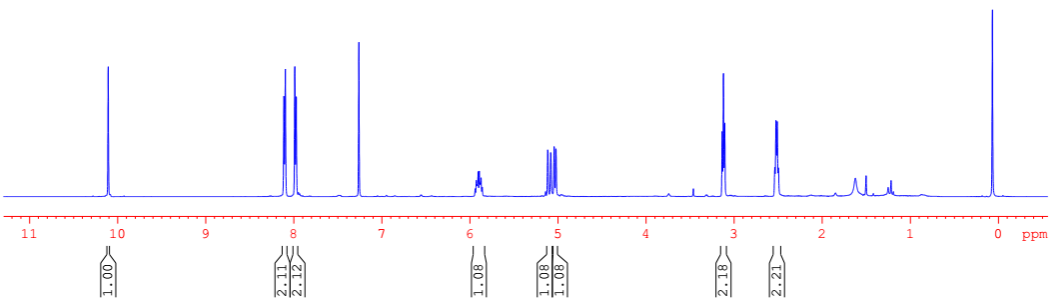


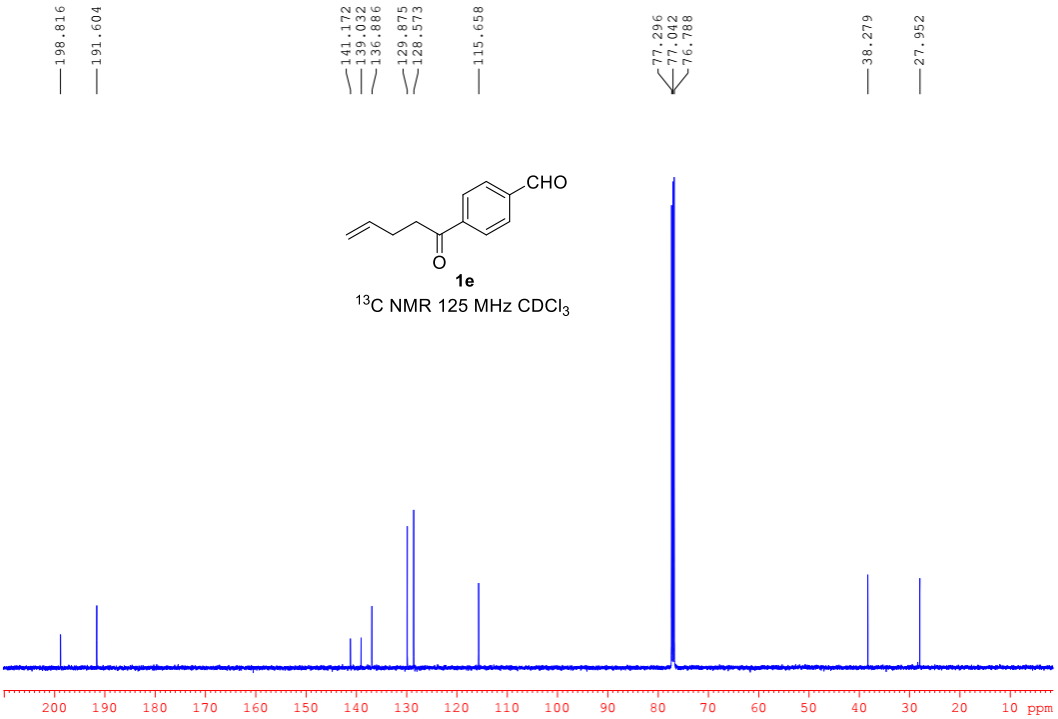




1e

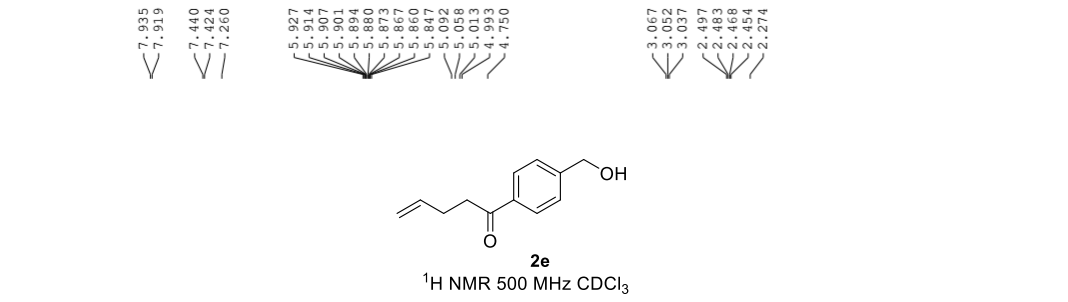
^{1}H NMR 500 MHz $CDCl_3$





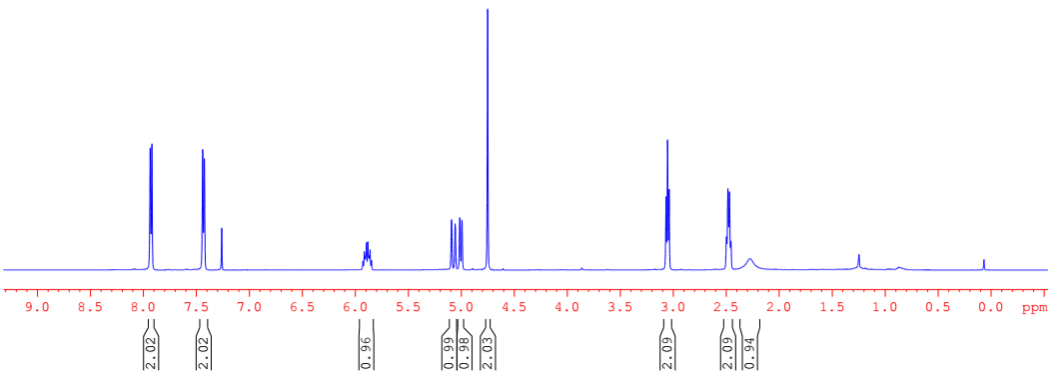
1e

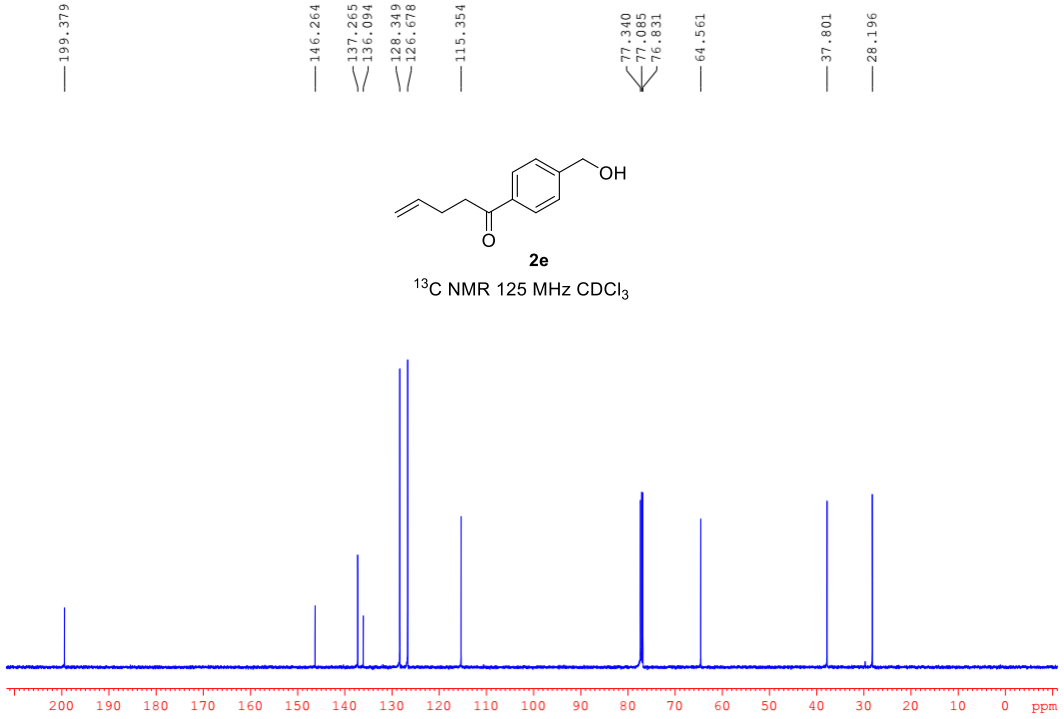
^{13}C NMR 125 MHz $CDCl_3$



2e

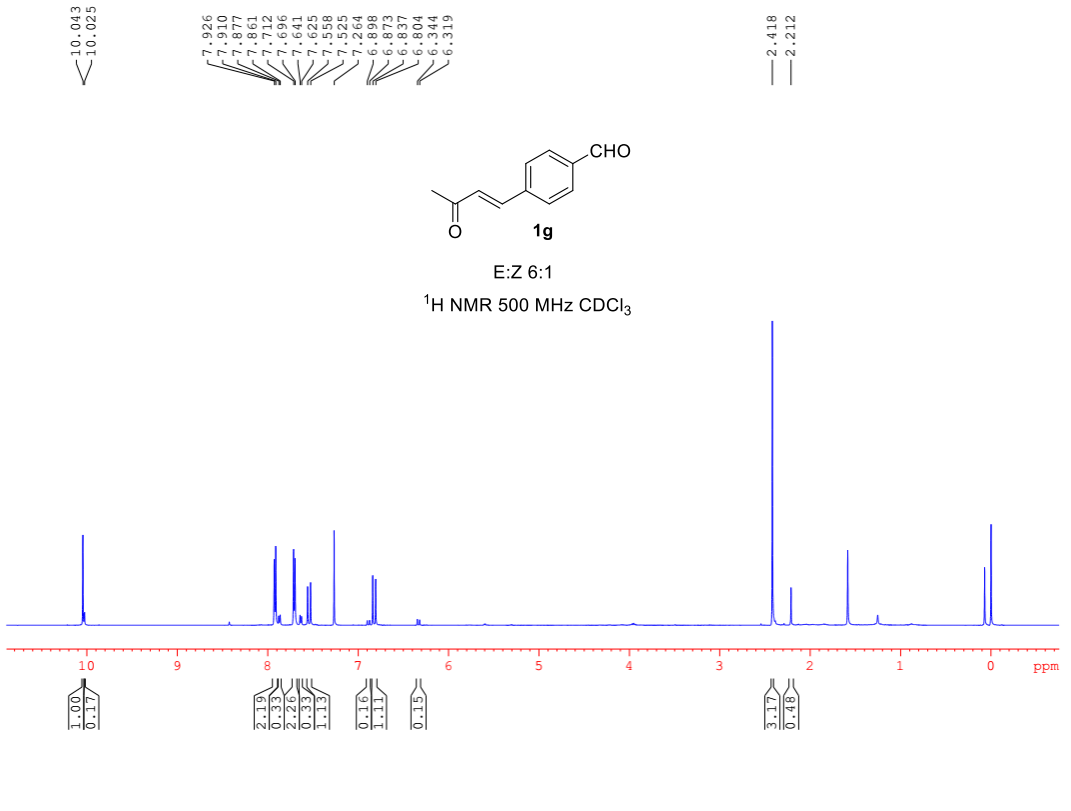
^{1}H NMR 500 MHz $CDCl_3$





2e

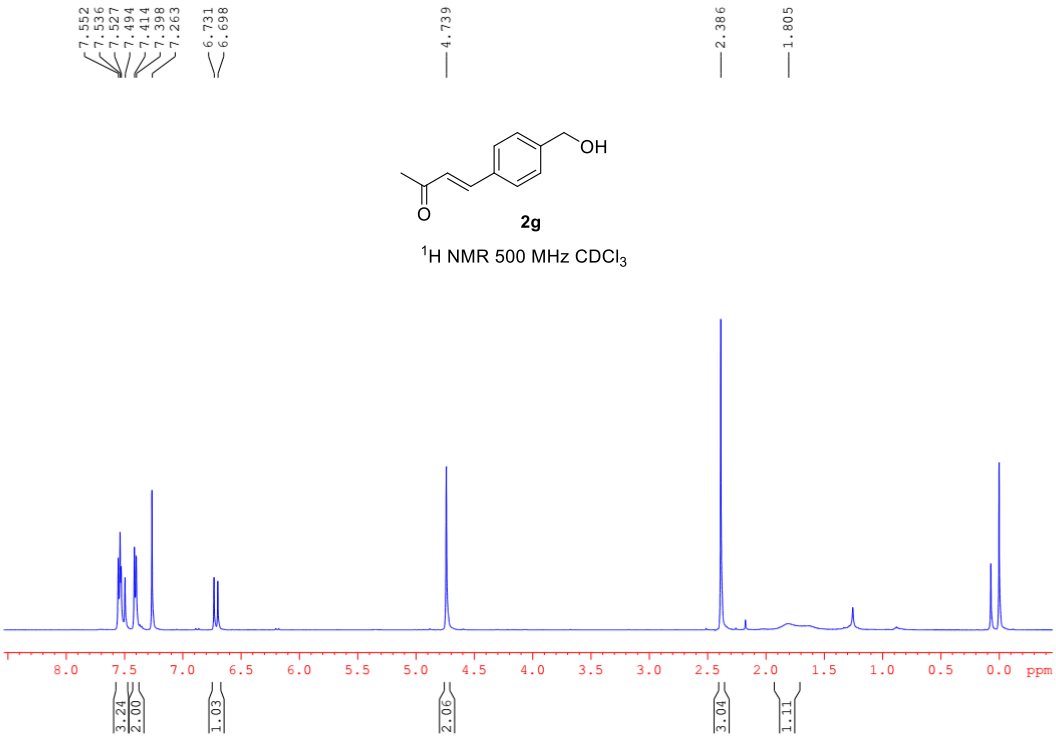
^{13}C NMR 125 MHz $CDCl_3$



1g

E:Z 6:1

^{1}H NMR 500 MHz $CDCl_3$



2g

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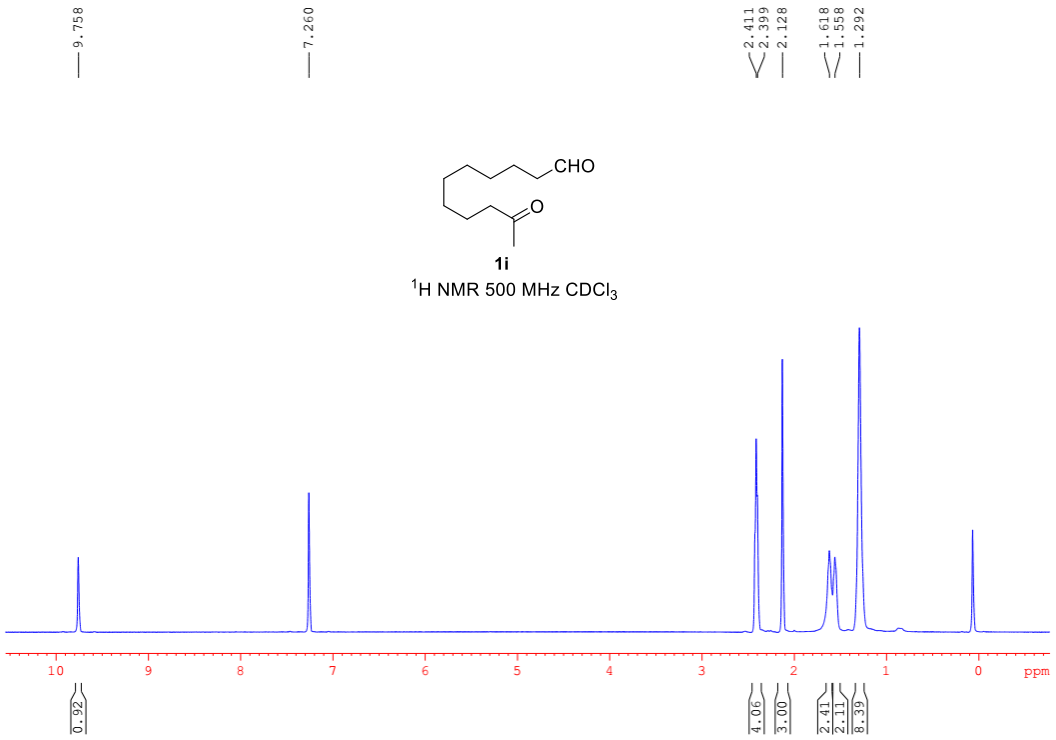
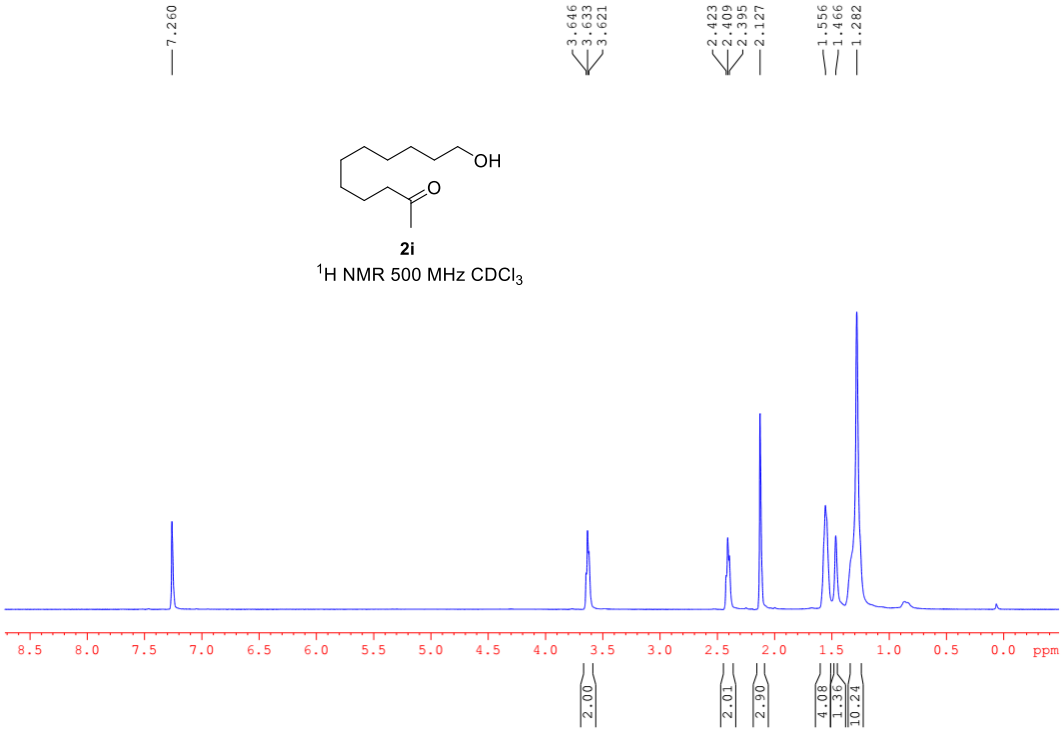


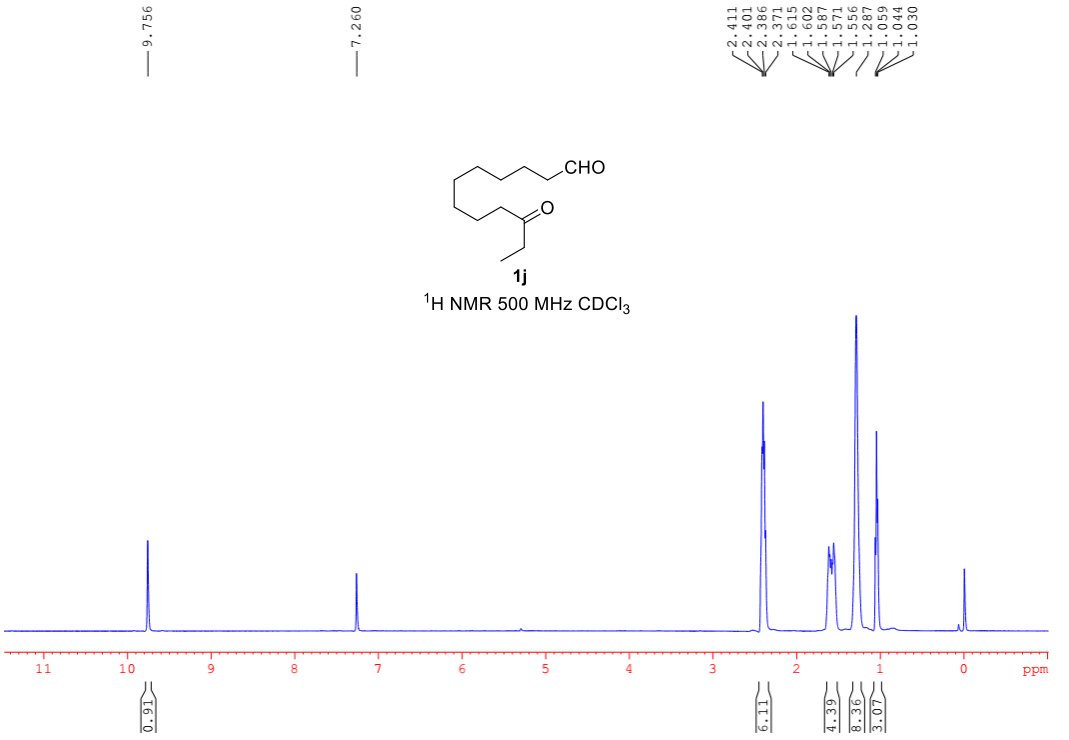
1i

^{1}H NMR 500 MHz $CDCl_3$



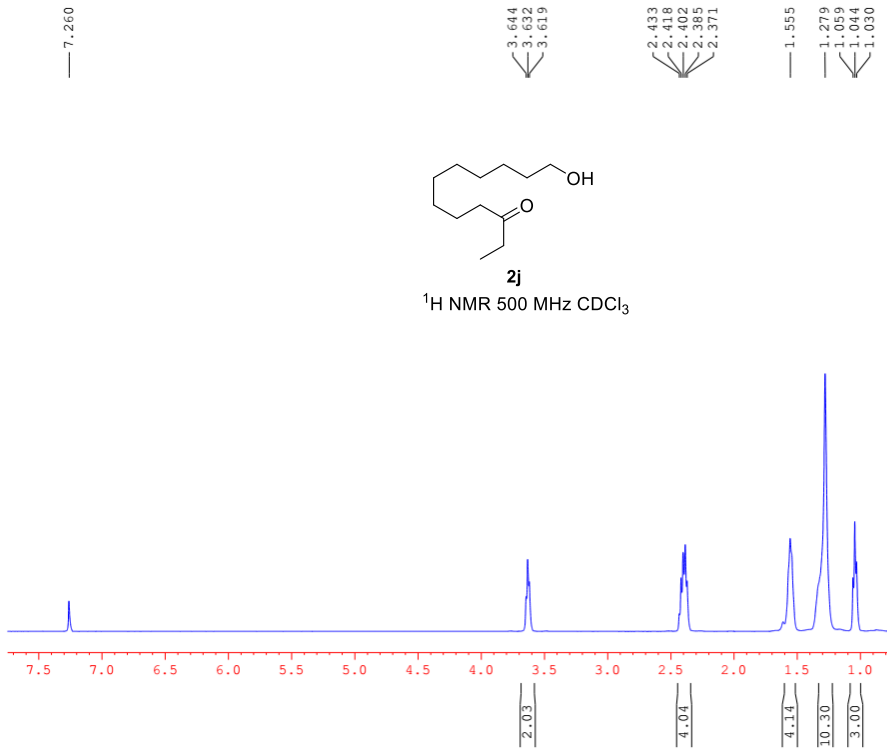
2i

^{1}H NMR 500 MHz $CDCl_3$



1j

^{1}H NMR 500 MHz $CDCl_3$



2j

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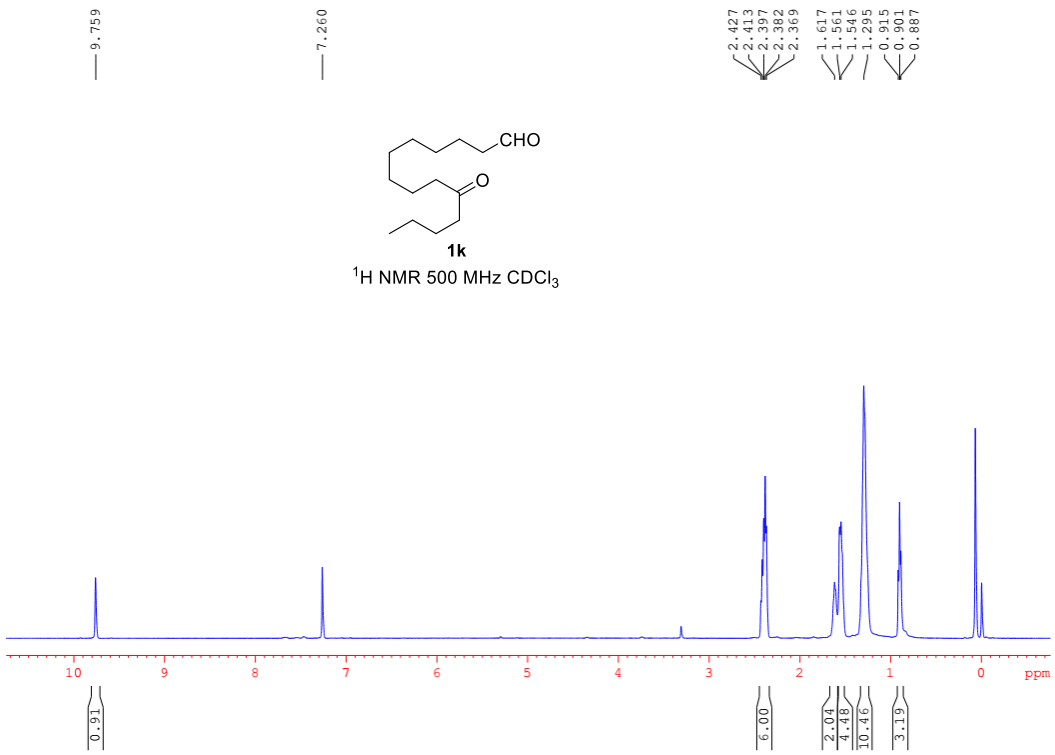
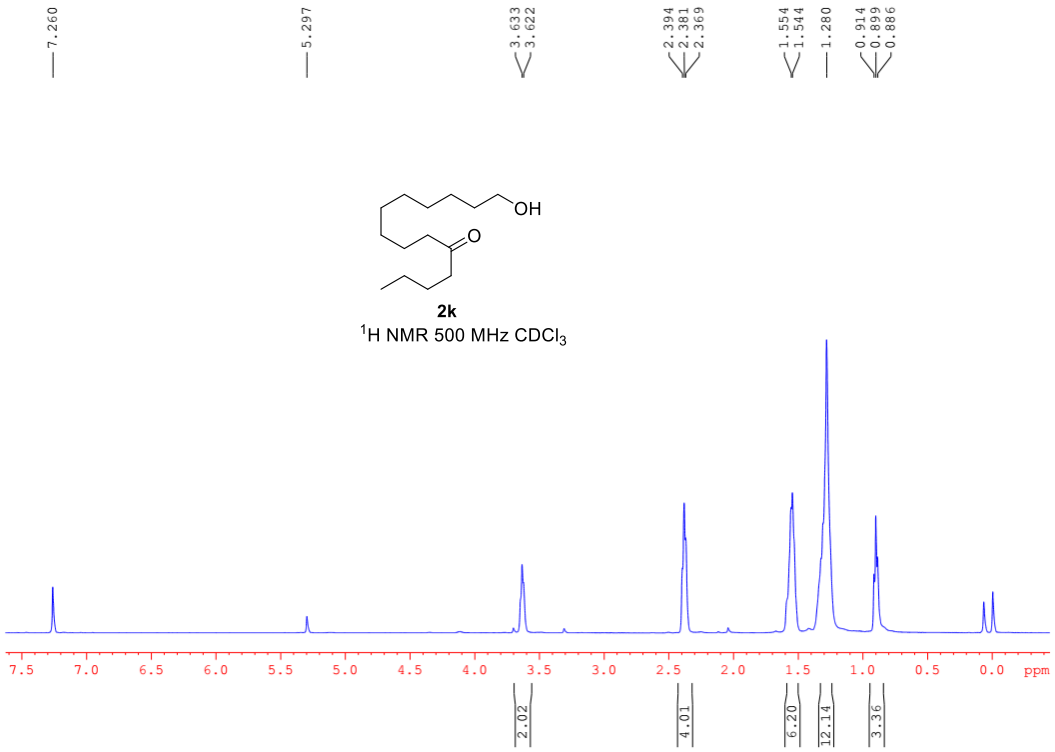


1k

^{1}H NMR 500 MHz $CDCl_3$



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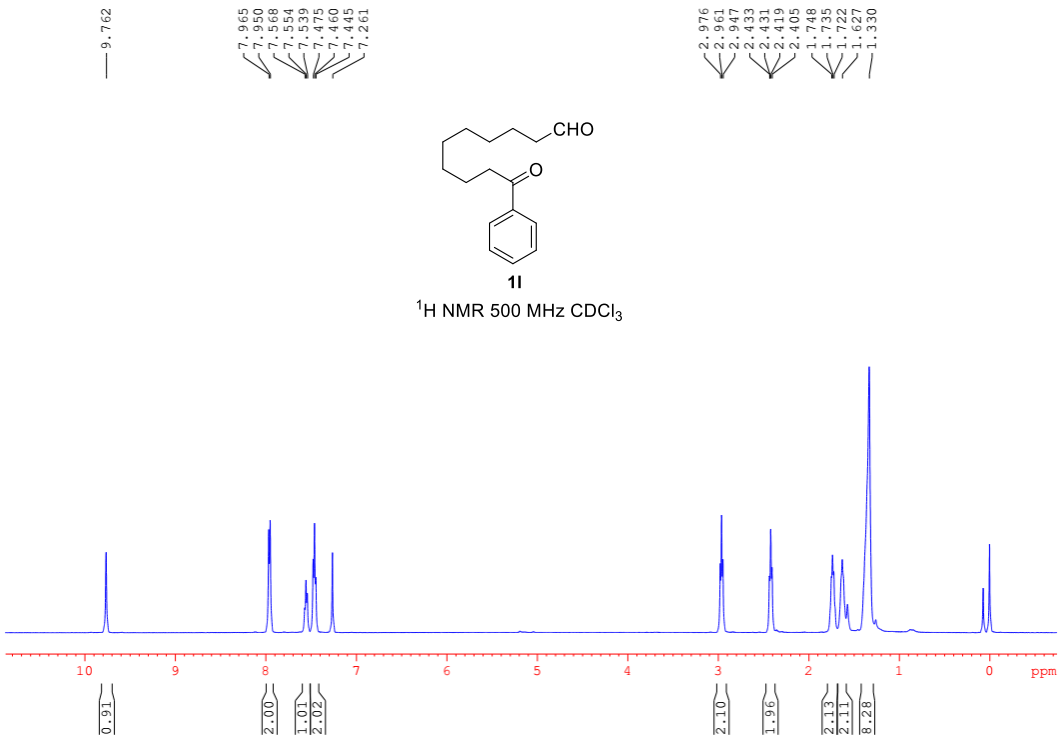
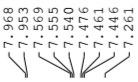
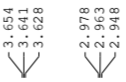
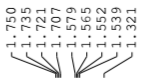


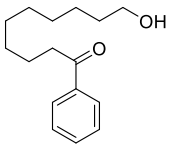
1l

^{1}H NMR 500 MHz $CDCl_3$



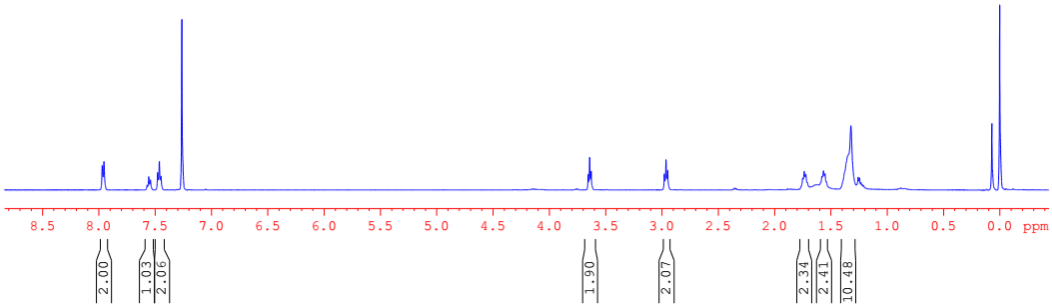


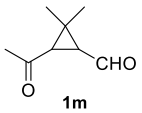




2l

^{1}H NMR 500 MHz $CDCl_3$





1m

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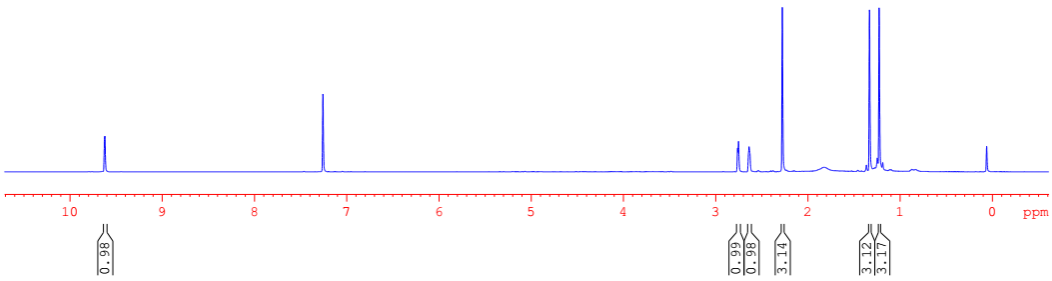
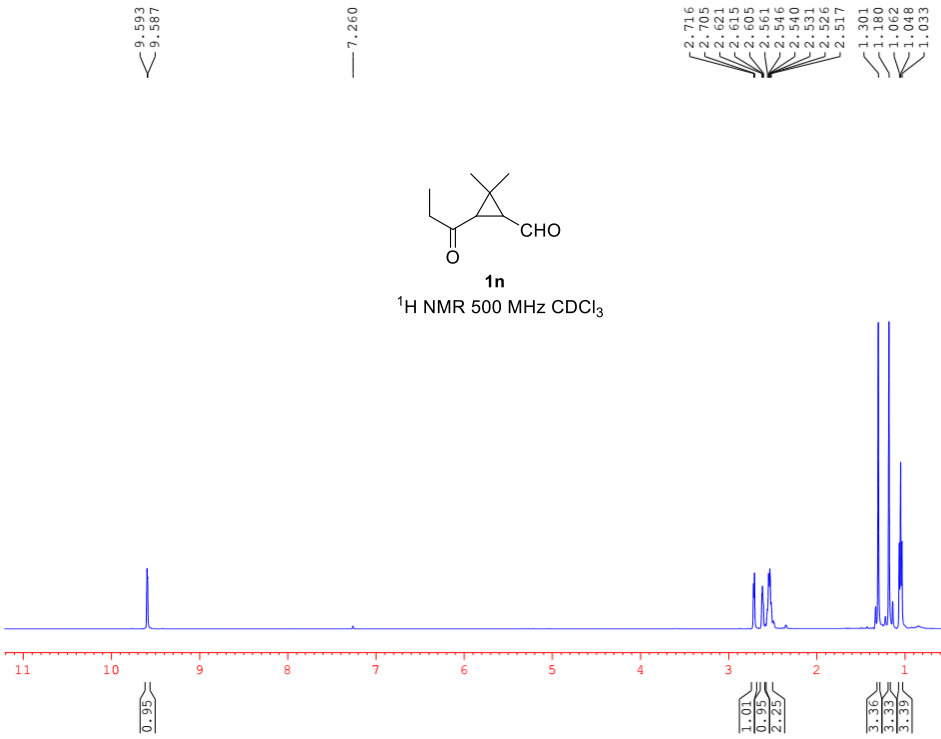
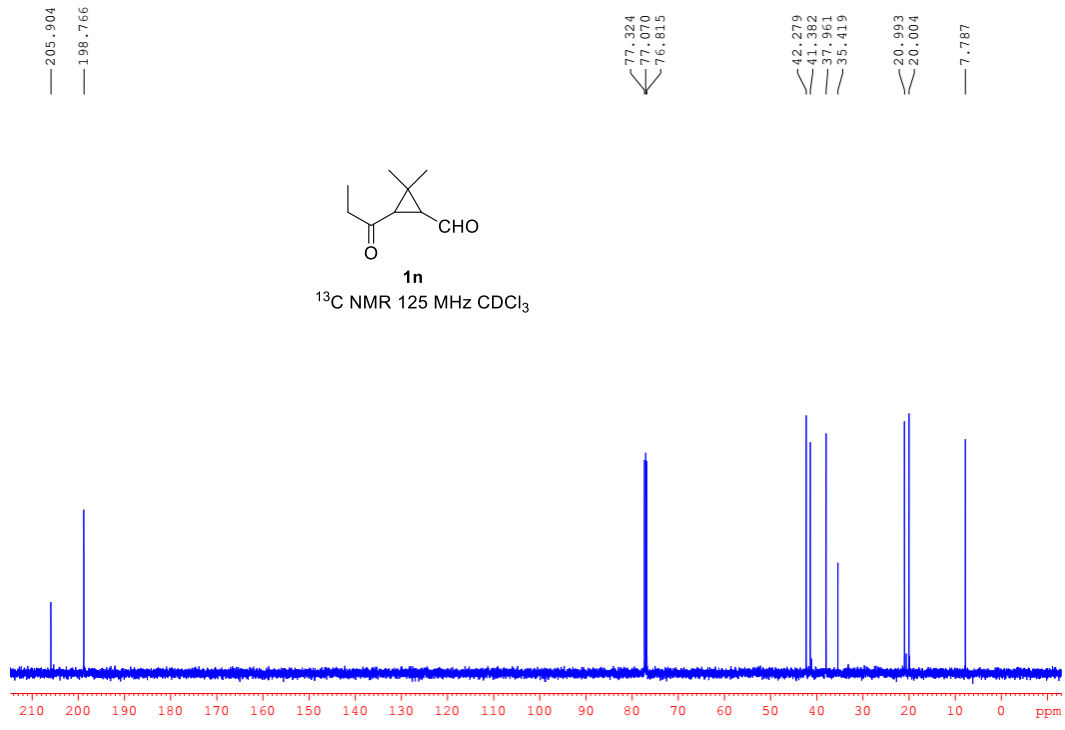




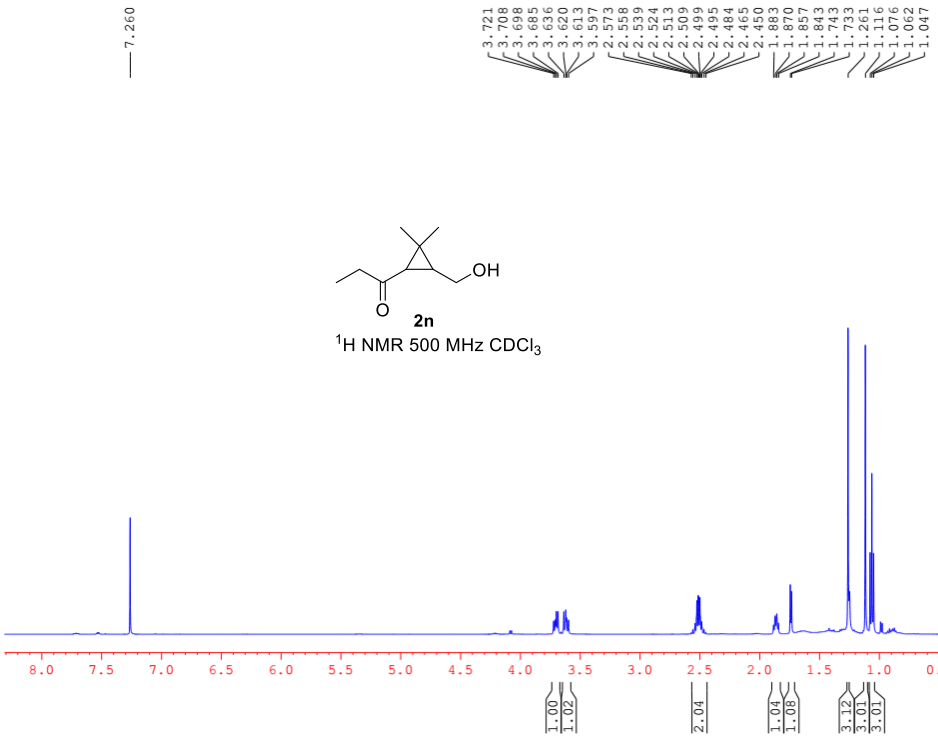
1n

^{1}H NMR 500 MHz $CDCl_3$



1n

^{13}C NMR 125 MHz $CDCl_3$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3.685
3.636
3.620
3.613
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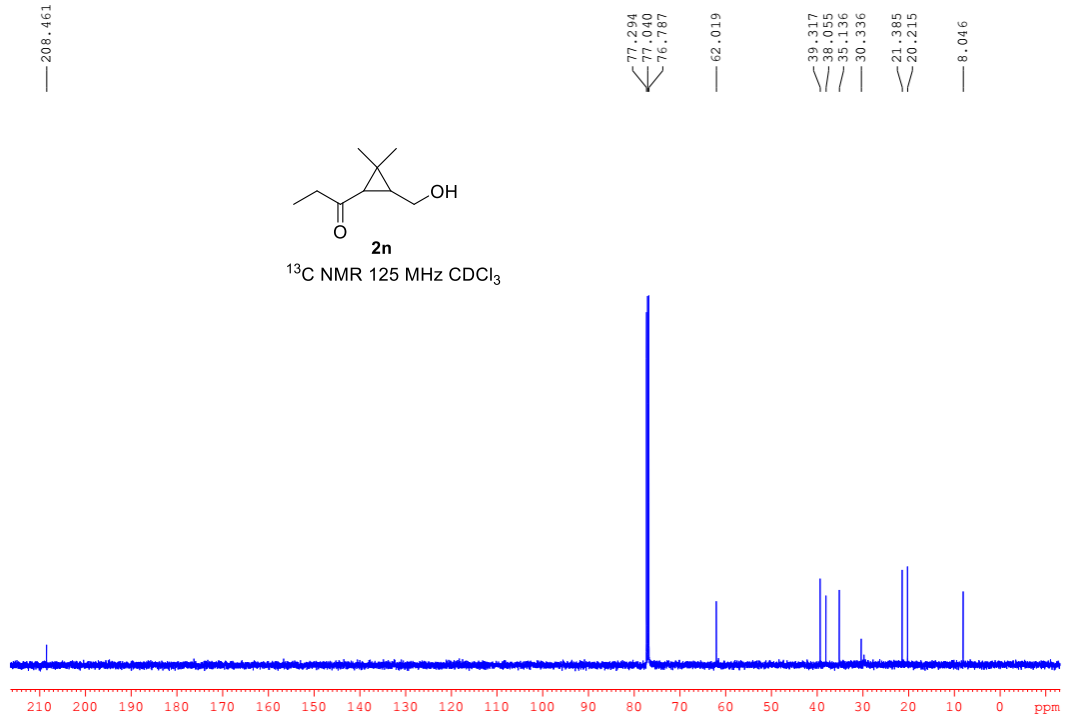
2.573
2.558
2.539
2.524
2.513
2.509
2.499
2.495
2.484
2.465
2.450
1.883
1.870
1.857
1.843
1.743
1.733
1.261
1.116
1.076
1.062
1.047
OH
O
2n
1H NMR 500 MHz CDCl3
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.02
2.04
1.04
1.08
3.12
3.01
3.01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35.136
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21.385
20.215
8.046
OH
O
2n
13C NMR 125 MHz CDCl3
210
200
190
180
170
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150
140
130
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110
100
90
80
70
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50
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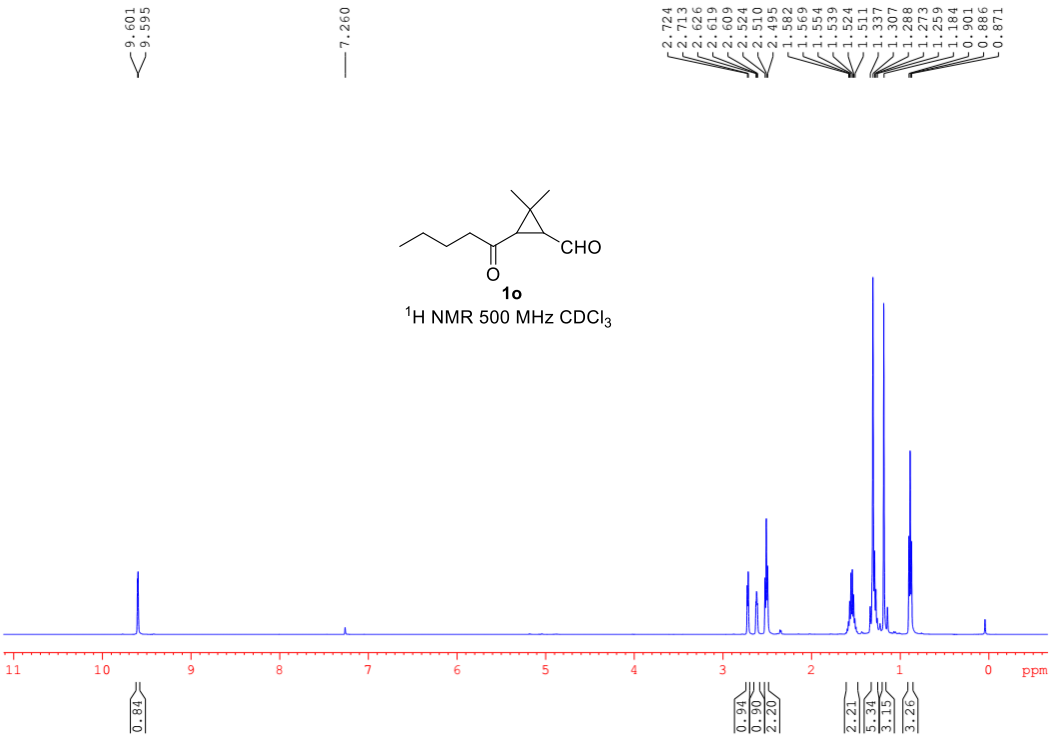
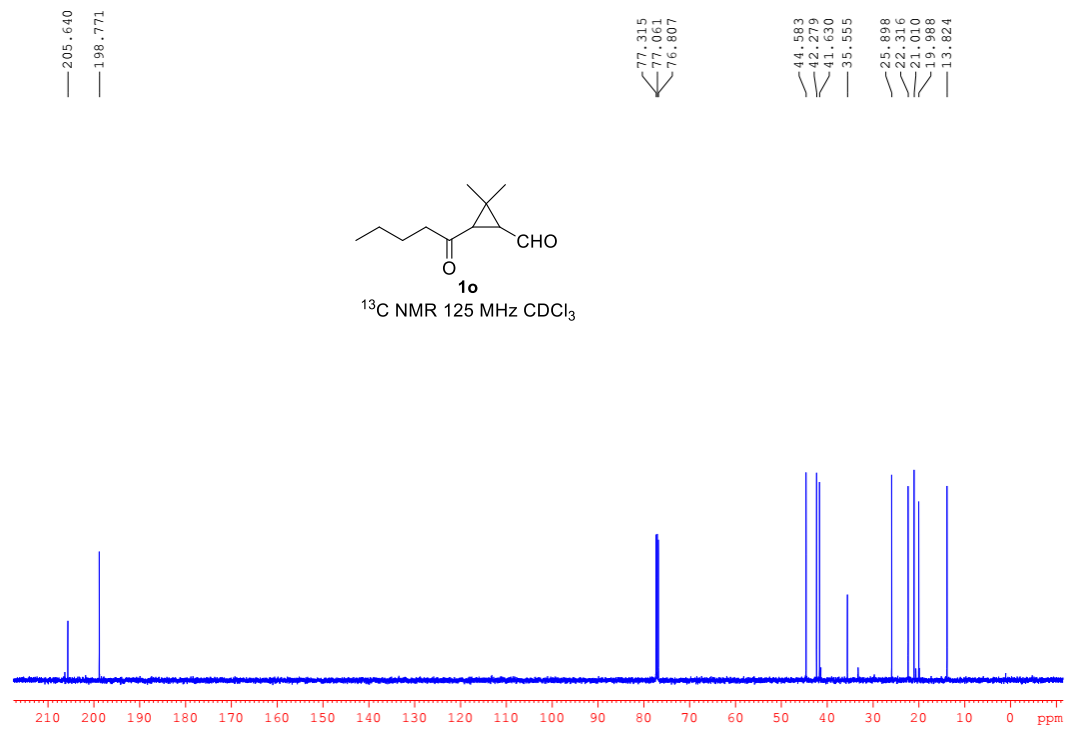
20
10
0
ppm



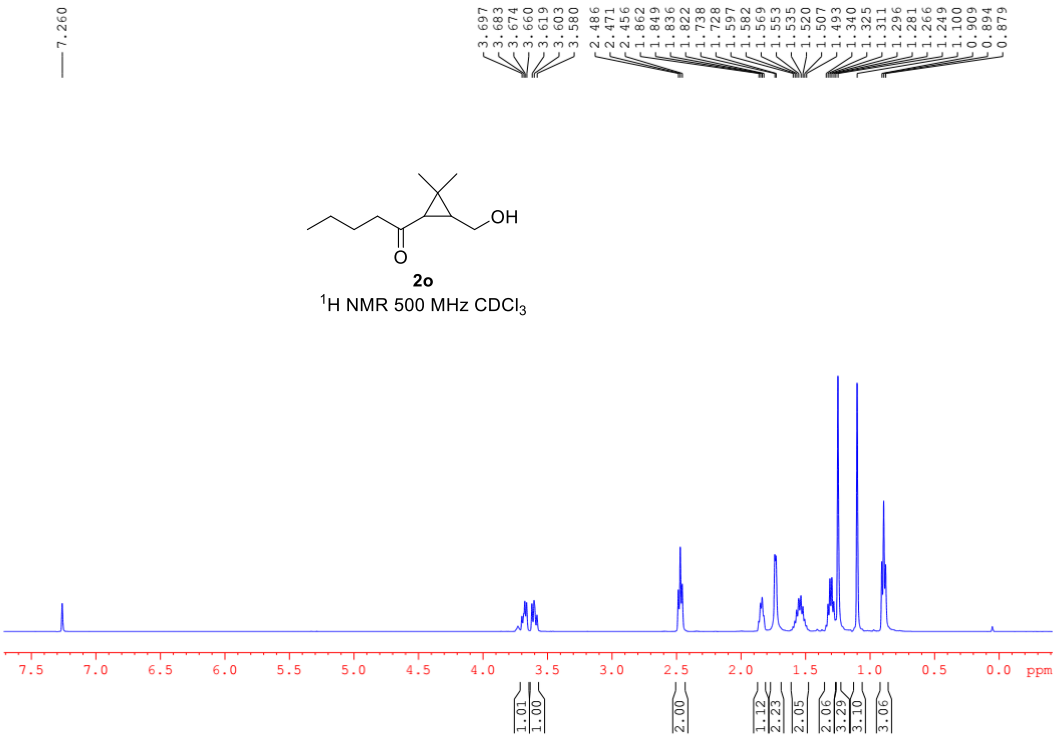
1o

^{1}H NMR 500 MHz $CDCl_3$



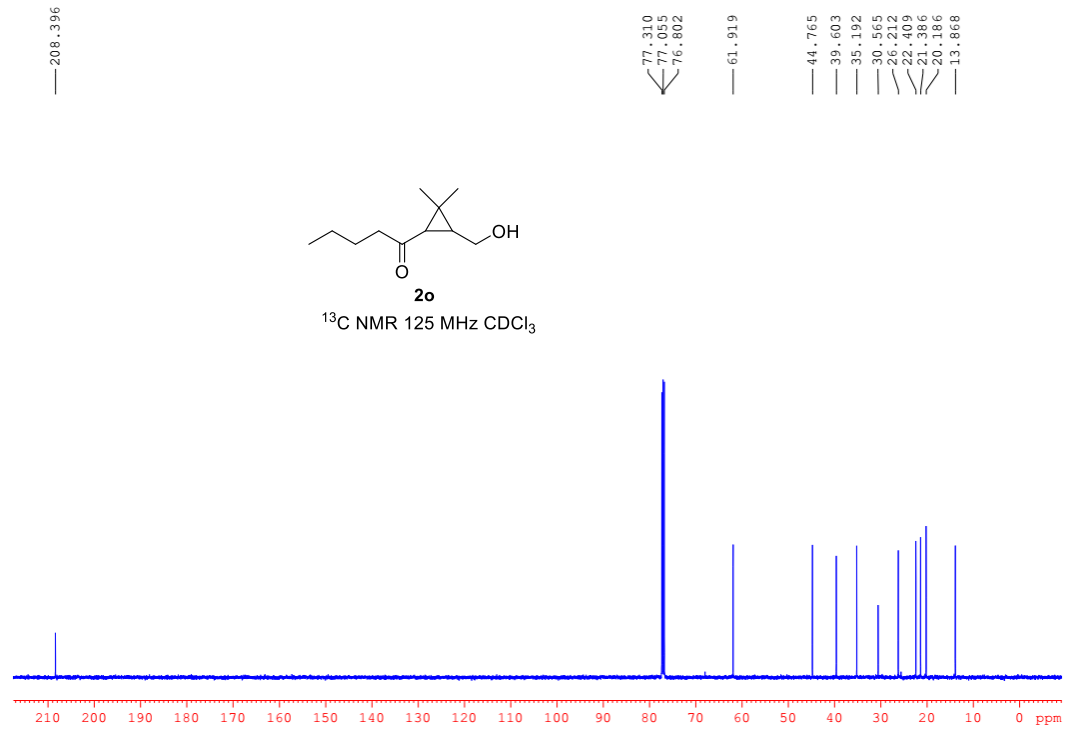
1o

^{13}C NMR 125 MHz $CDCl_3$



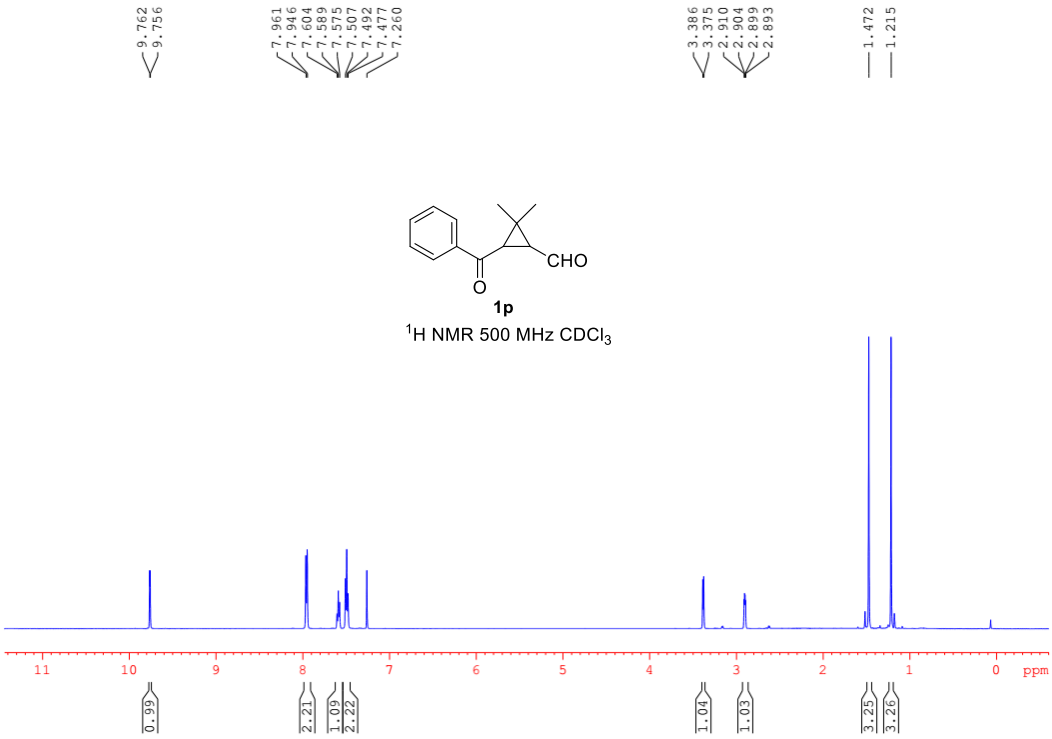
2o

^{1}H NMR 500 MHz $CDCl_3$



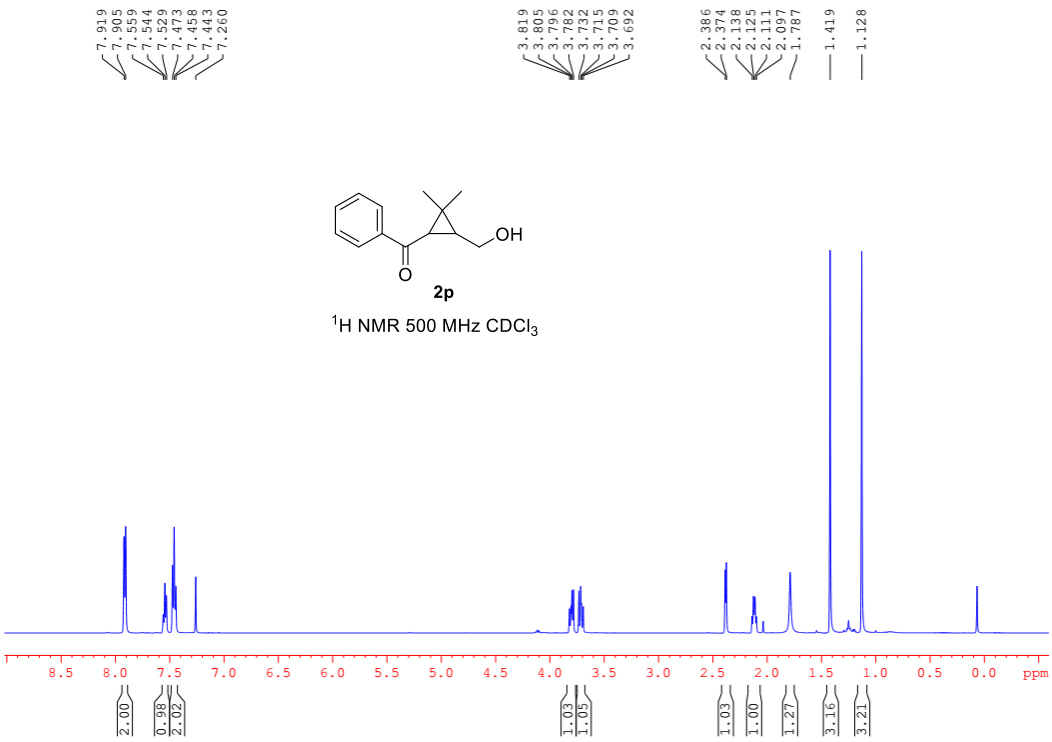
2o

^{13}C NMR 125 MHz $CDCl_3$



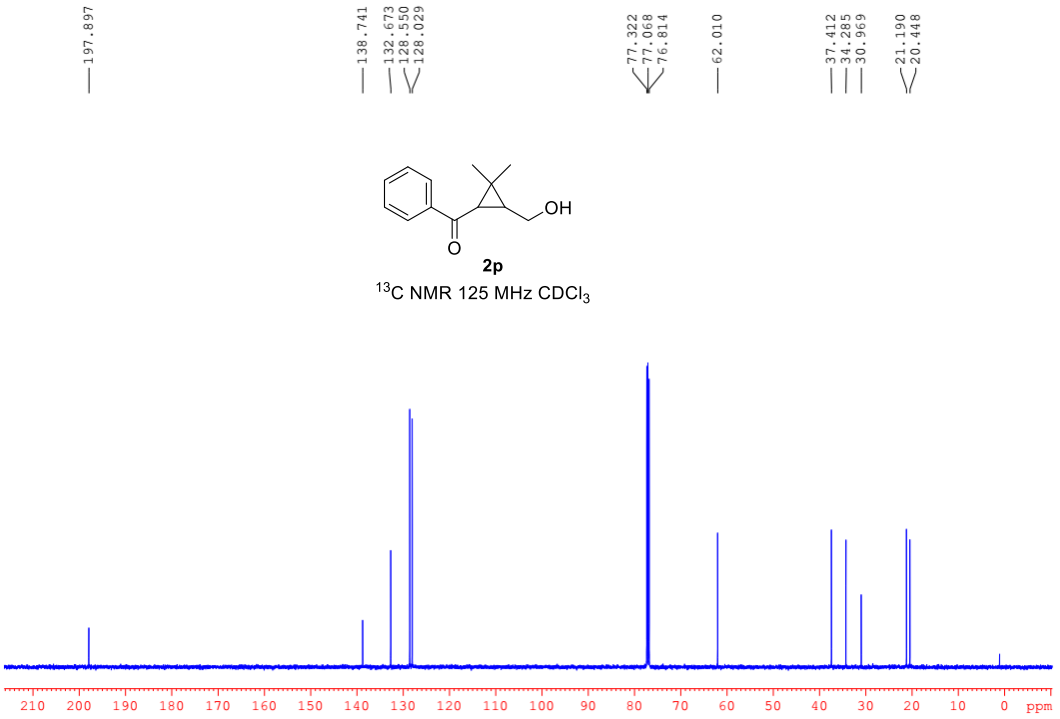
1p

^{1}H NMR 500 MHz $CDCl_3$



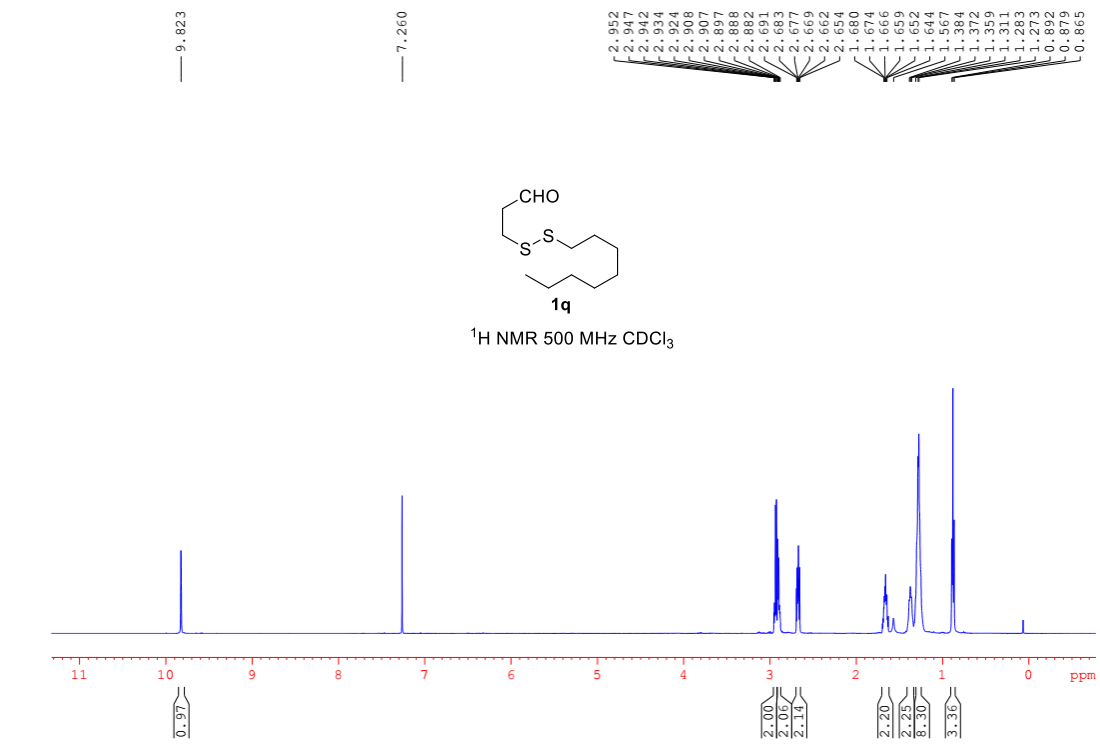
2p

^{1}H NMR 500 MHz $CDCl_3$



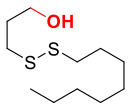
2p

^{13}C NMR 125 MHz $CDCl_3$



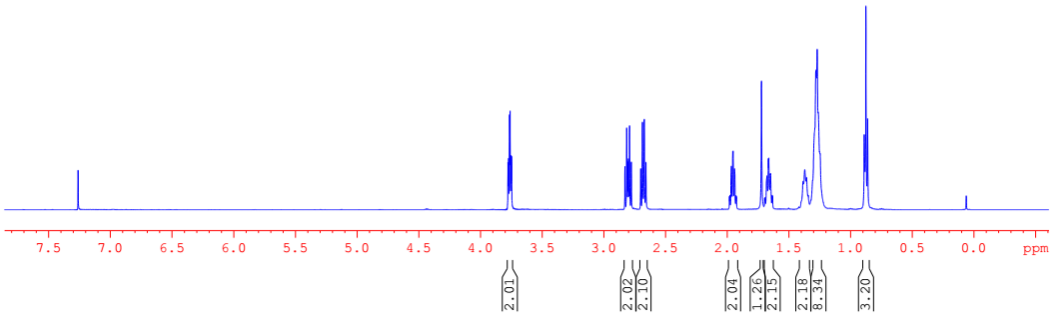
1q

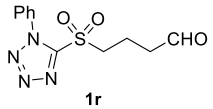
^{1}H NMR 500 MHz $CDCl_3$



2q

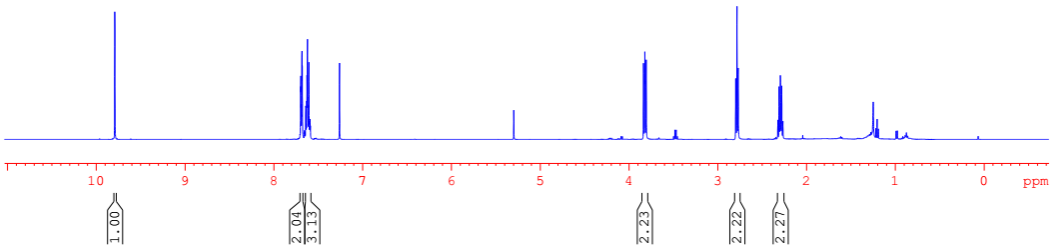
^{1}H NMR 500 MHz $CDCl_3$

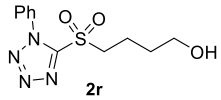




1r

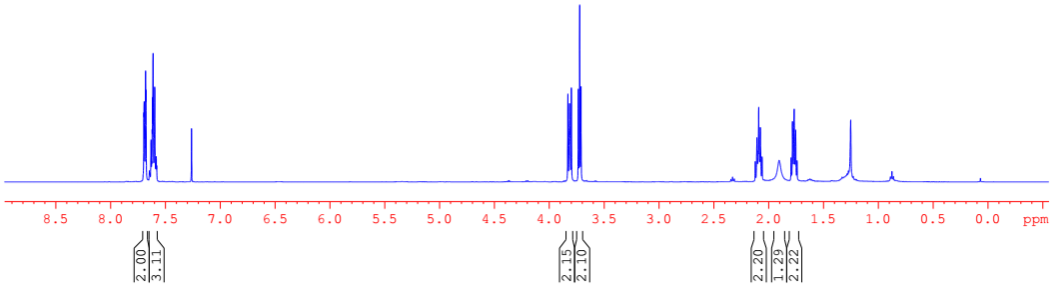
^{1}H NMR 500 MHz $CDCl_3$





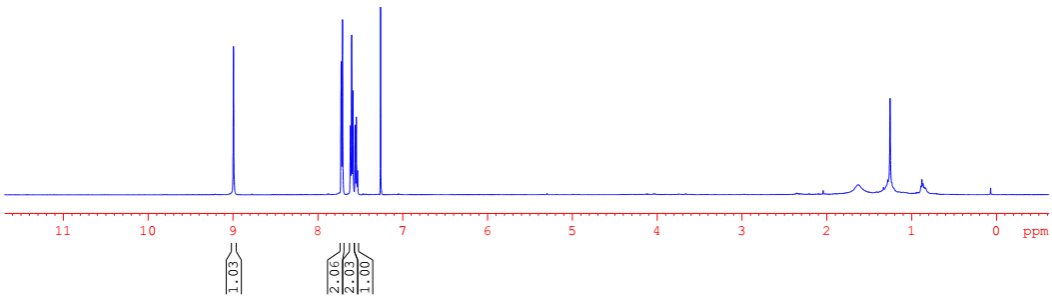
2r

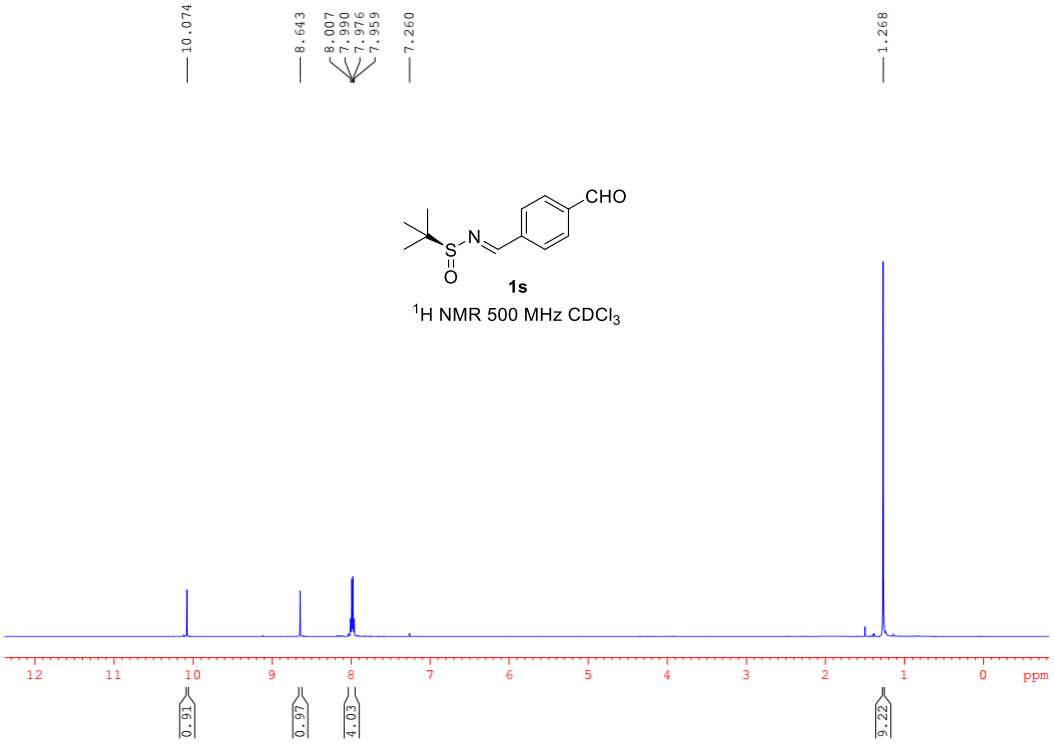
^{1}H NMR 500 MHz $CDCl_3$



S23

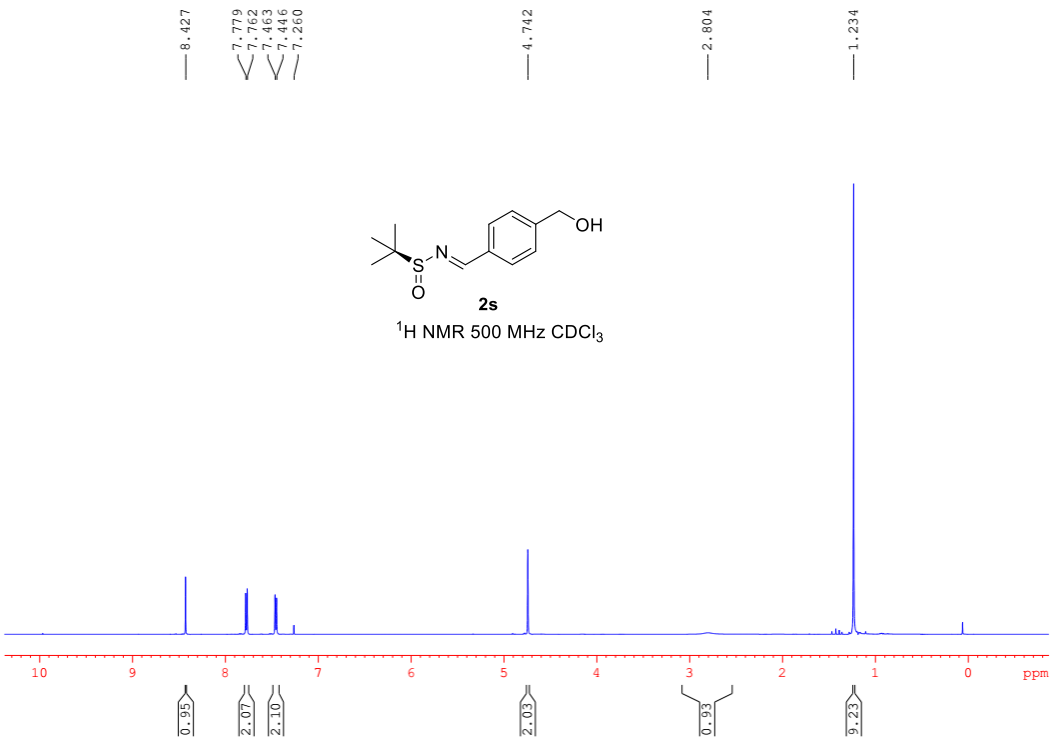
^{1}H NMR 500 MHz $CDCl_3$





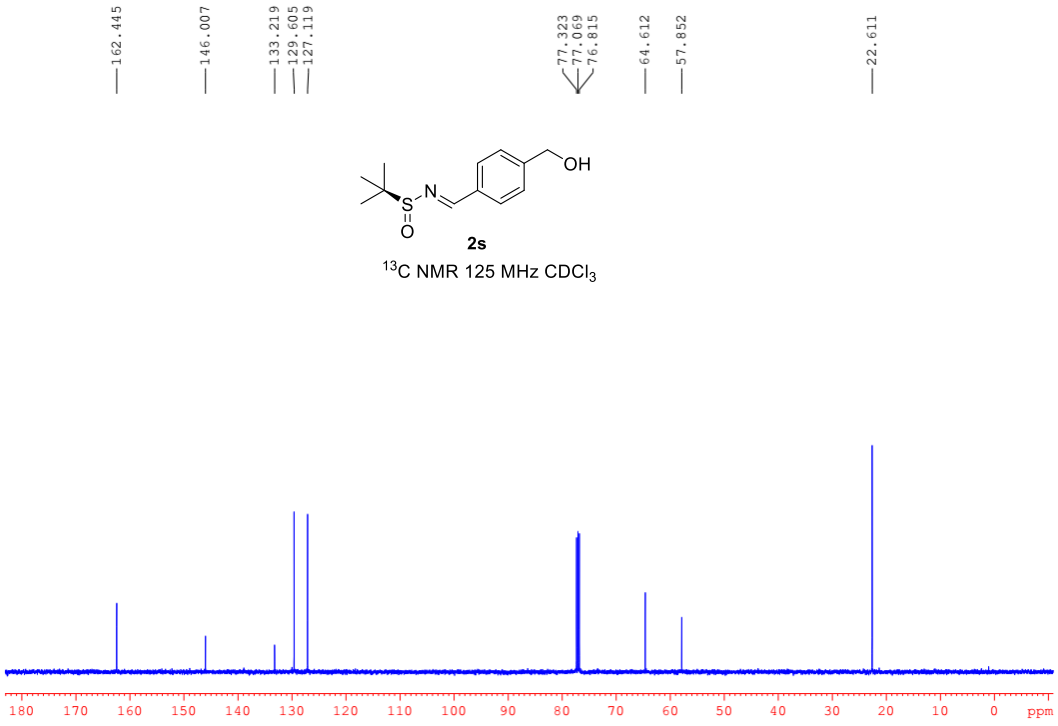
1s

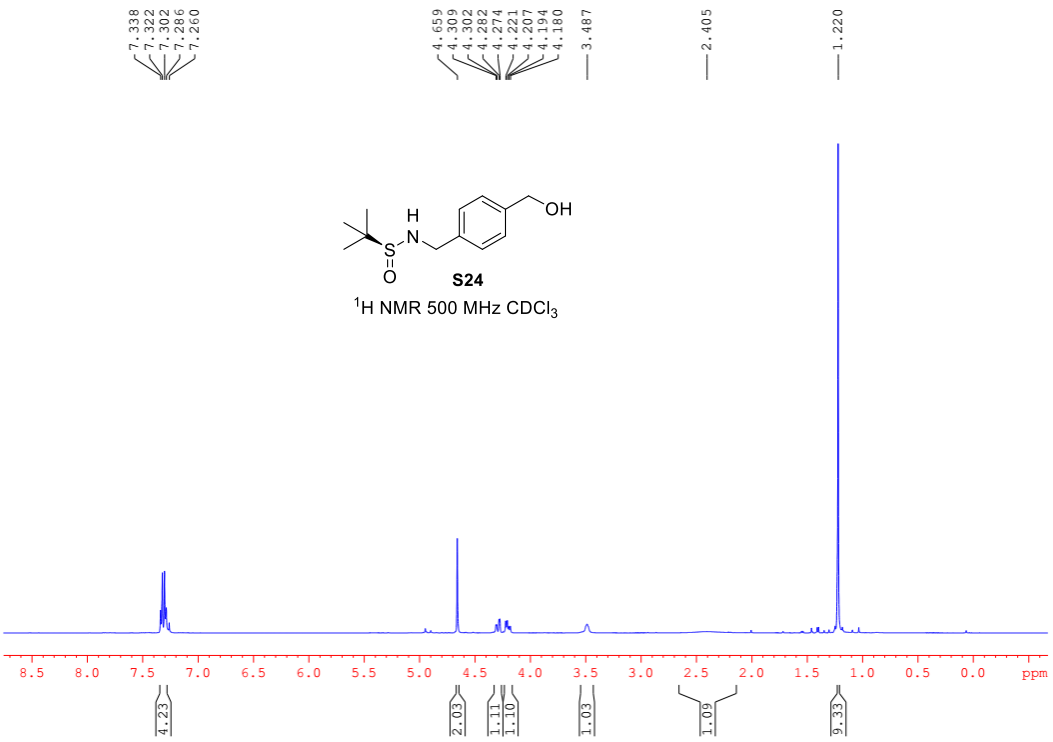
^{1}H NMR 500 MHz $CDCl_3$

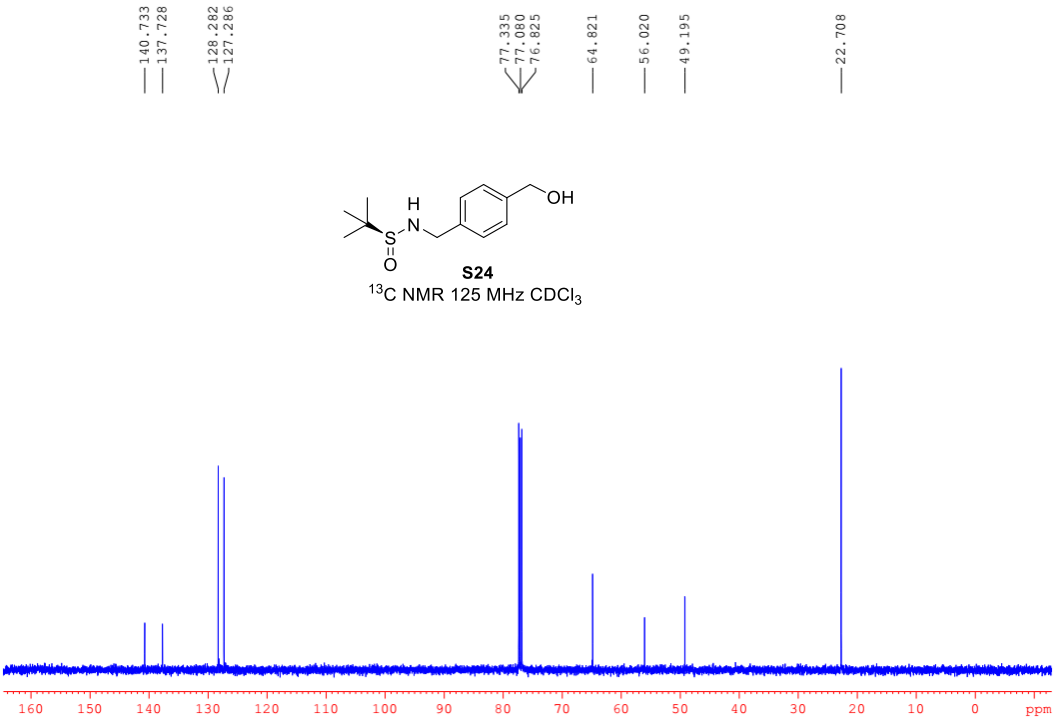


2s

^{1}H NMR 500 MHz $CDCl_3$

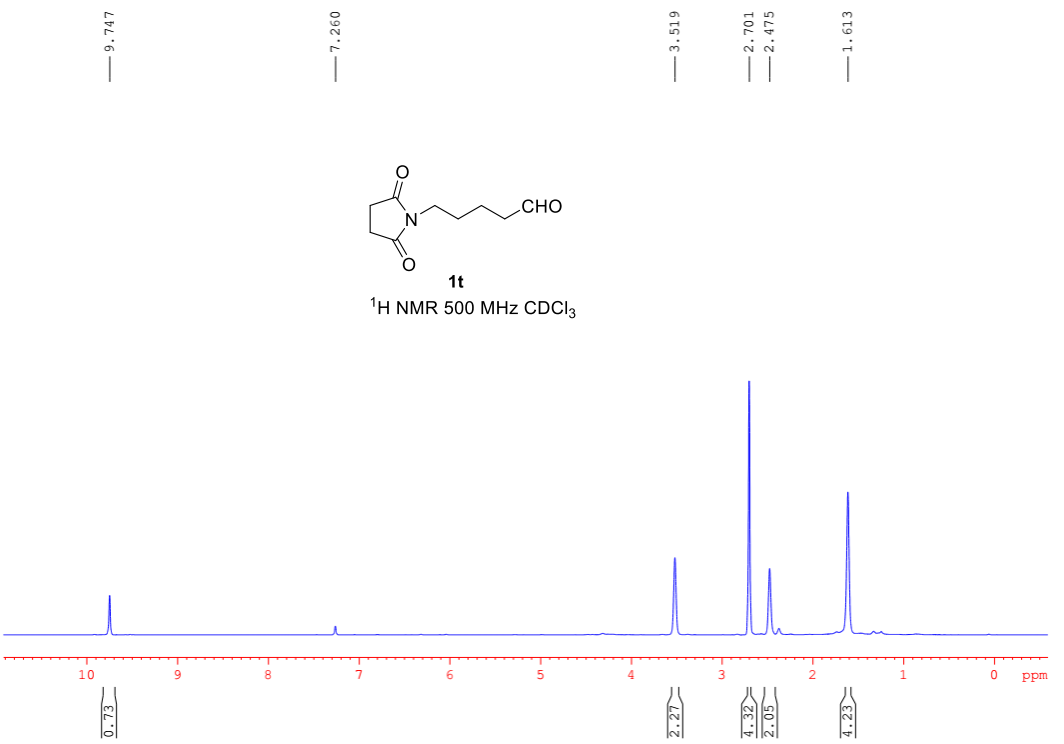

162.445
146.007
133.219
129.605
127.119
77.323
77.069
76.815
64.612
57.852
22.611
OH
N
S
O
2s
13C NMR 125 MHz CDCl3
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


7.338
7.322
7.302
7.286
7.260
4.659
4.309
4.302
4.282
4.274
4.221
4.207
4.194
4.180
3.487
2.405
1.220
OH
H
N
S
O
S24
1H NMR 500 MHz CDCl3
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
4.23
2.03
1.11
1.10
1.03
1.09
9.33



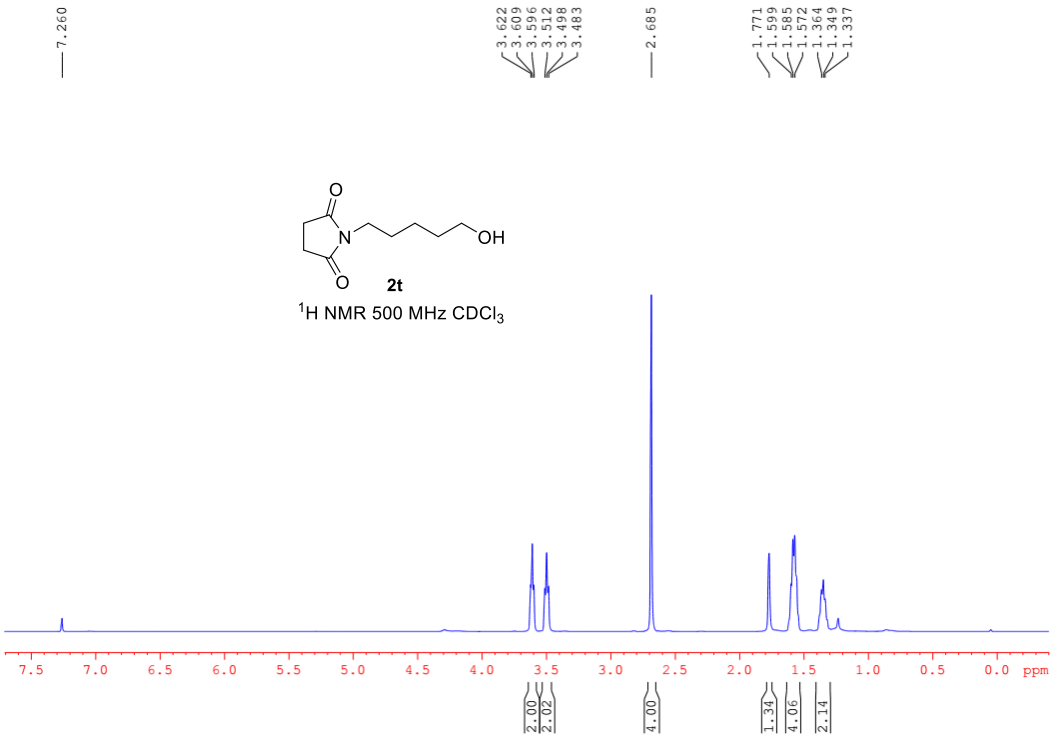
S24

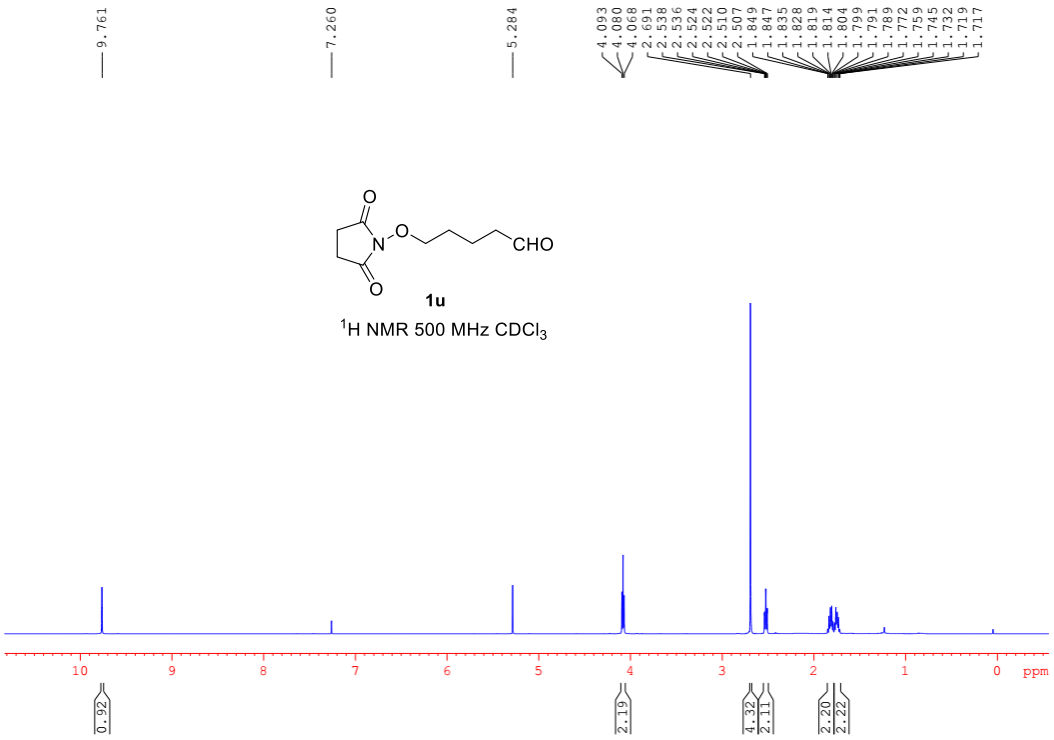
^{13}C NMR 125 MHz $CDCl_3$

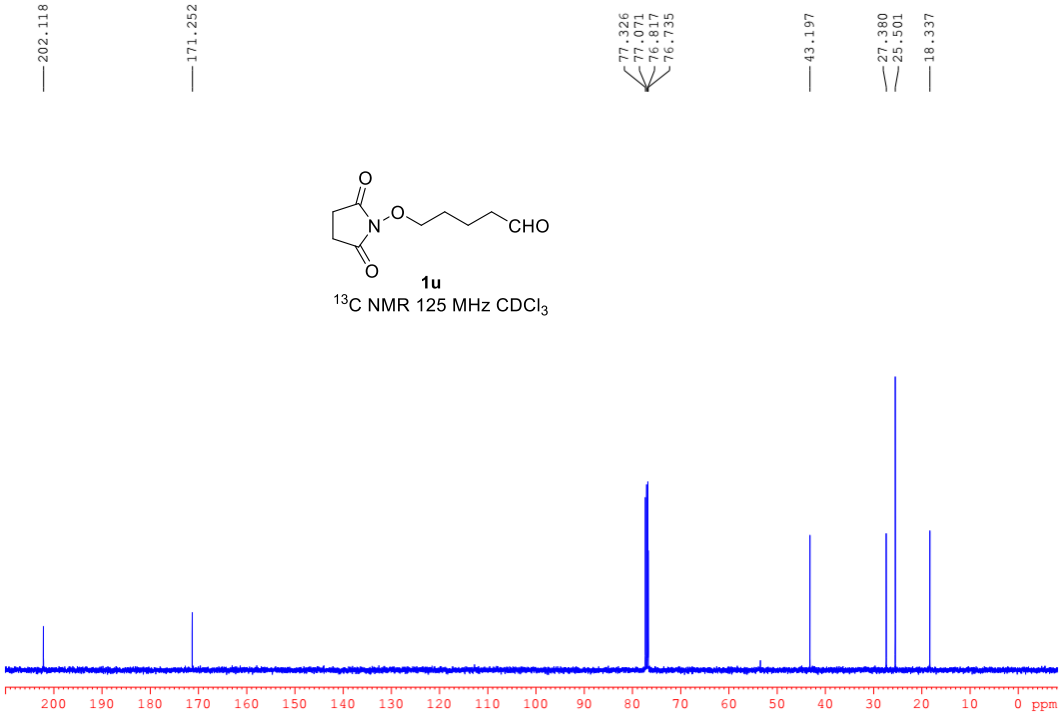


1t

^{1}H NMR 500 MHz $CDCl_3$

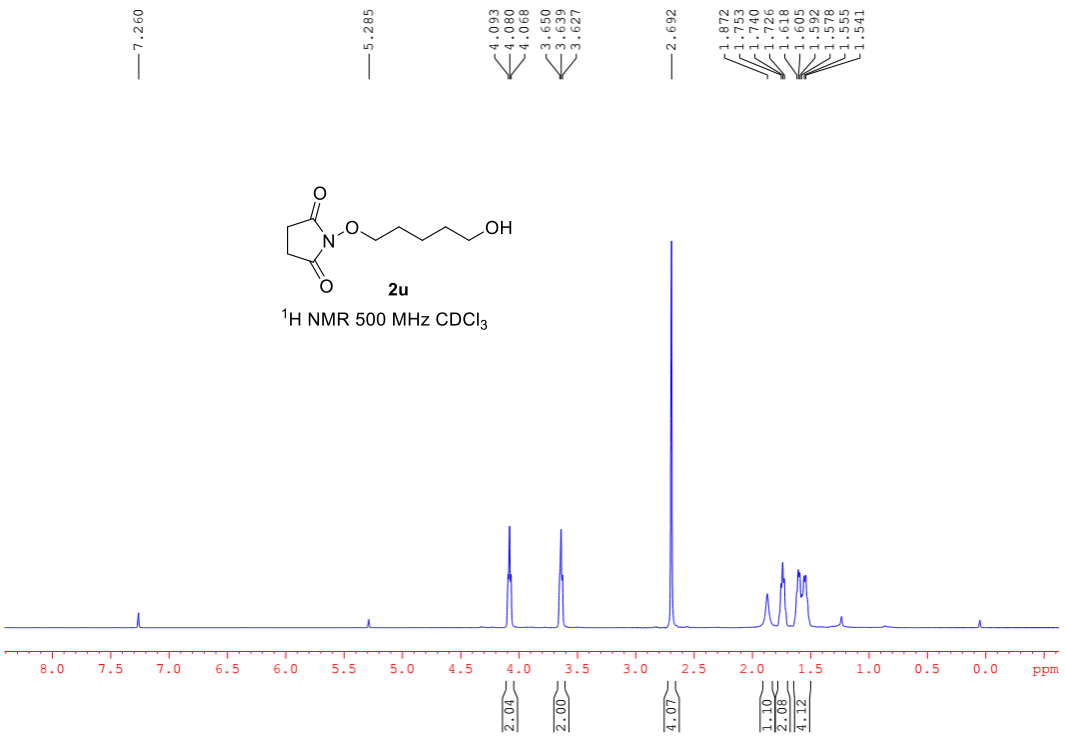

7.260
3.622
3.609
3.596
3.512
3.498
3.483
2.685
1.771
1.599
1.585
1.572
1.364
1.349
1.337
OH
2t
1H NMR 500 MHz CDCl3
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
2.00
2.02
4.00
1.34
4.06
2.14


9.761
7.260
5.284
4.093
4.080
4.068
2.691
2.538
2.536
2.524
2.522
2.510
2.507
1.849
1.847
1.835
1.828
1.819
1.814
1.804
1.799
1.791
1.789
1.772
1.759
1.745
1.732
1.719
1.717
CHO
1u
1H NMR 500 MHz CDCl3
10 9 8 7 6 5 4 3 2 1 0 ppm
0.92
2.19
4.32
2.11
2.20
2.22



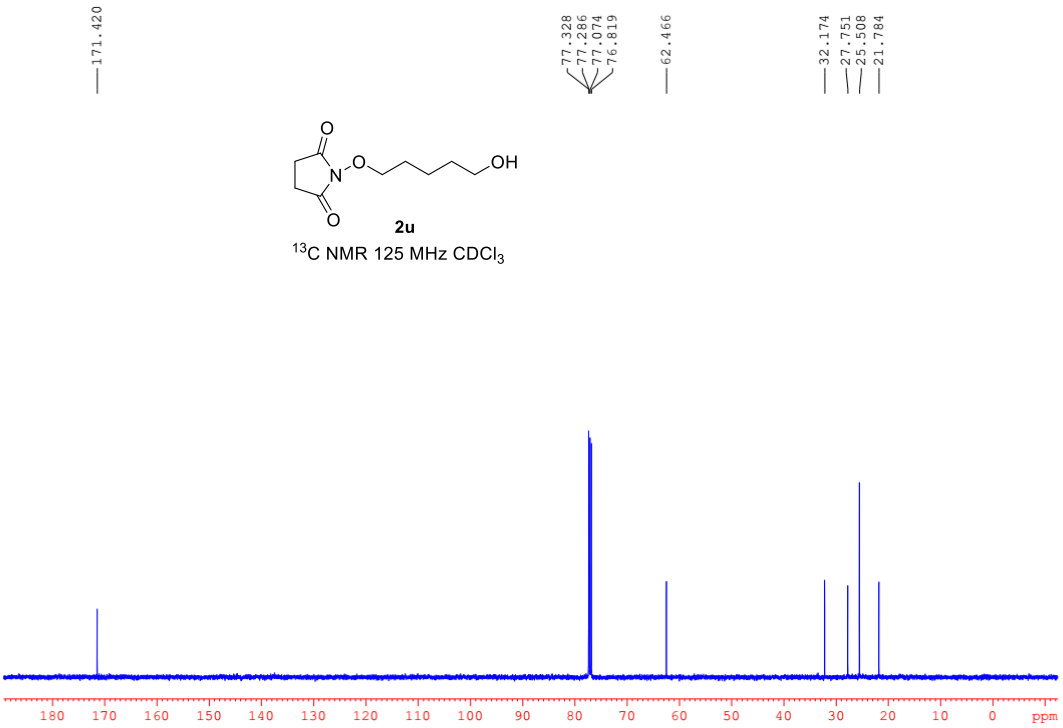
1u

^{13}C NMR 125 MHz $CDCl_3$

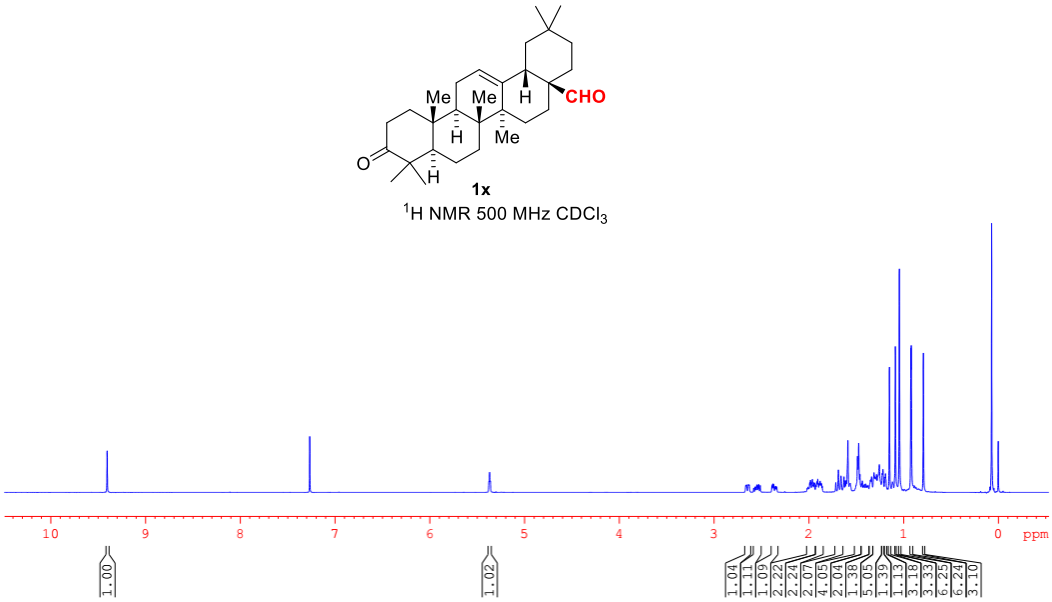


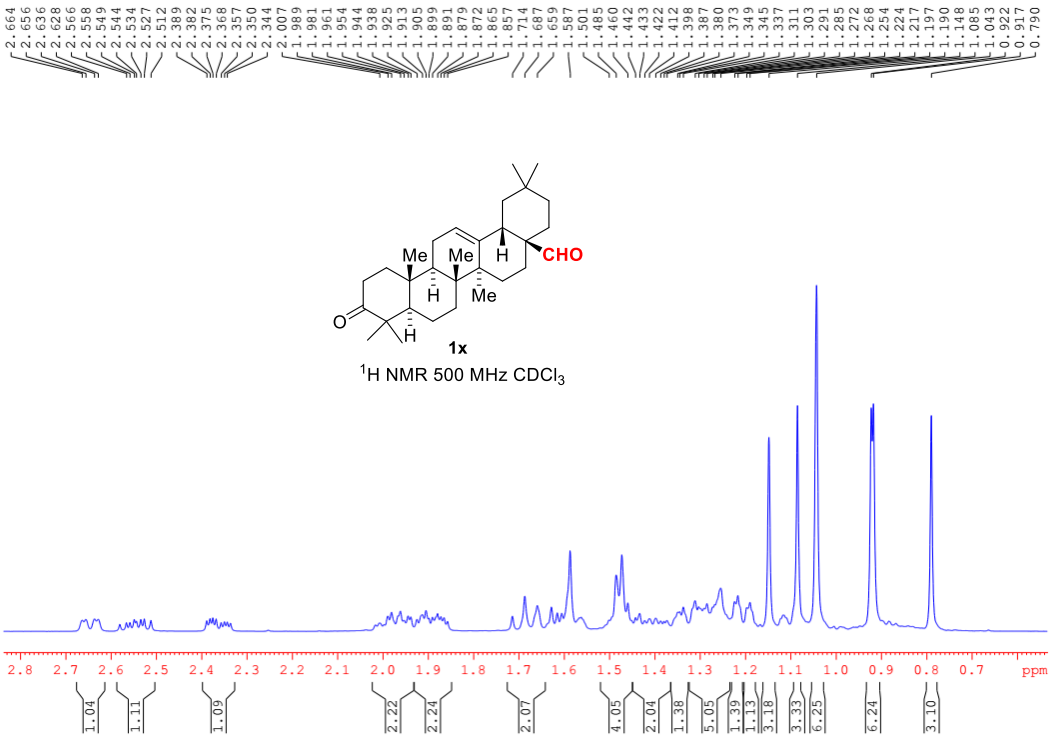
2u

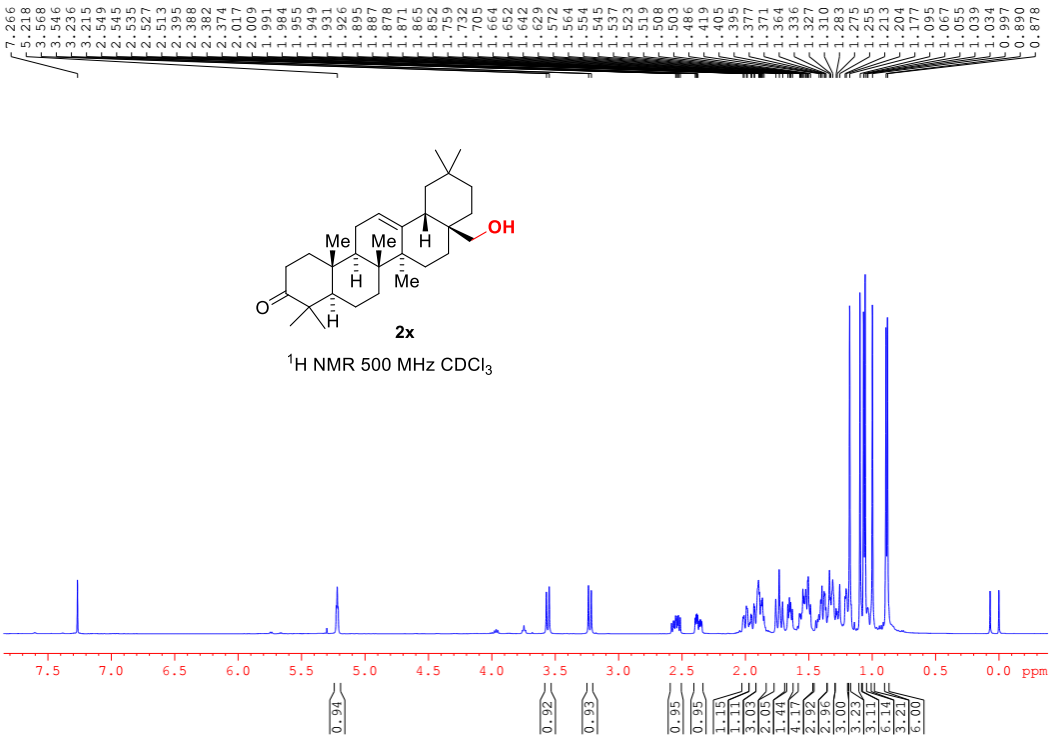
^{1}H NMR 500 MHz $CDCl_3$

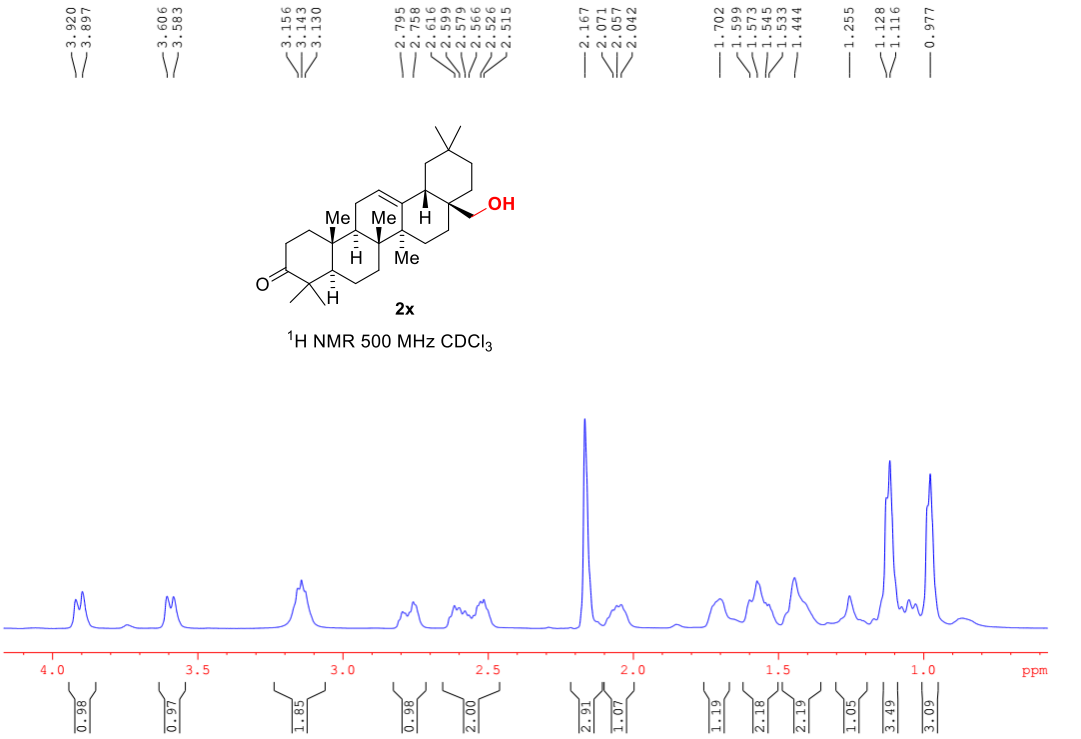

171.420
77.328
77.286
77.074
76.819
62.466
32.174
27.751
25.508
21.784
O
N
O
OH
O
2u
13C NMR 125 MHz CDCl3
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


9.402
7.264
5.375
5.368
5.361
2.664
2.656
2.636
2.628
2.549
2.544
2.534
2.527
2.512
2.389
2.382
2.375
2.368
2.350
1.989
1.981
1.961
1.954
1.944
1.938
1.925
1.913
1.905
1.899
1.891
1.879
1.872
1.865
1.857
1.714
1.687
1.659
1.587
1.501
1.485
1.460
1.442
1.433
1.422
1.412
1.398
1.387
1.380
1.373
1.349
1.345
1.337
1.311
1.303
1.291
1.285
1.272
1.268
1.254
1.224
1.217
1.197
1.190
1.148
1.085
1.043
0.922
0.917
0.790

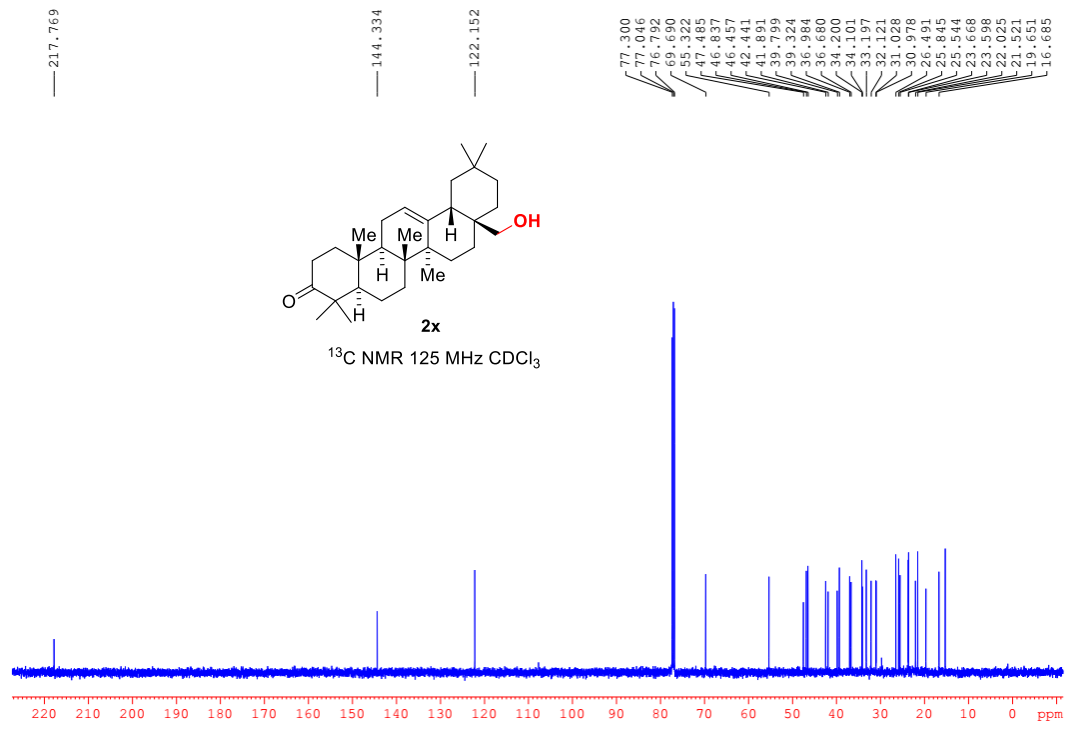

Me
Me
H
CHO
H
Me
O
H
1x
1H NMR 500 MHz CDCl3
10 9 8 7 6 5 4 3 2 1 0 ppm
1.00
1.02
1.04
1.11
1.09
2.22
2.24
2.07
4.05
2.04
1.38
5.05
1.39
1.13
3.18
3.33
6.25
6.24
3.10


Me
Me
H
CHO
H
Me
O
H
1x
1H NMR 500 MHz CDCl3
ppm

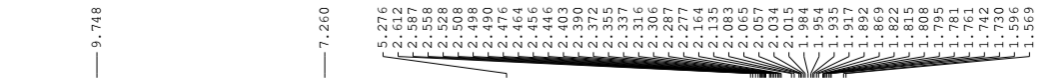

Me
Me
H
OH
H
Me
O
H
2x
1H NMR 500 MHz CDCl3
ppm

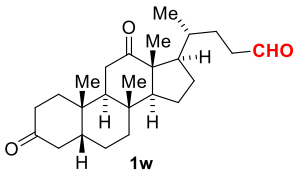


^{1}H NMR 500 MHz $CDCl_3$

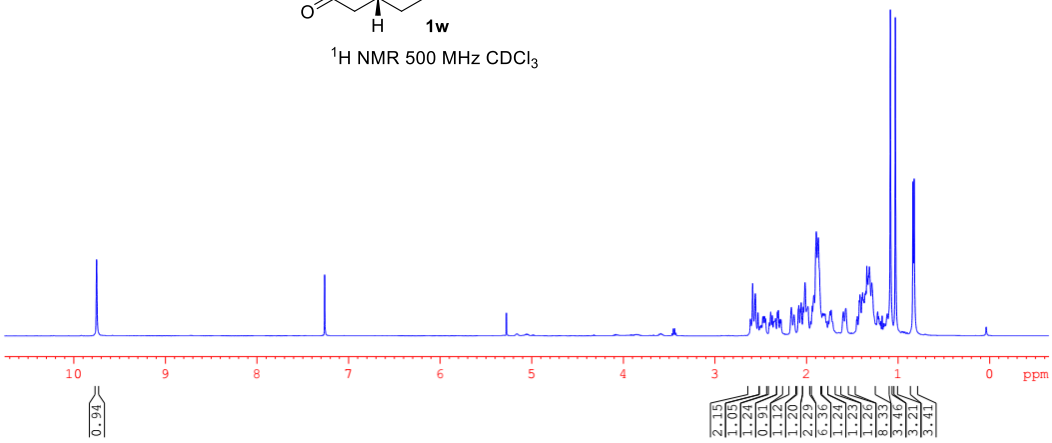


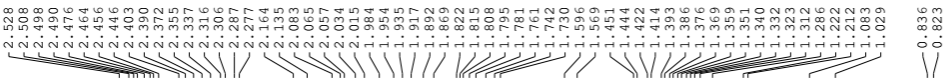
^{13}C NMR 125 MHz $CDCl_3$

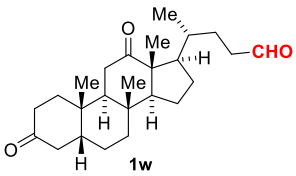




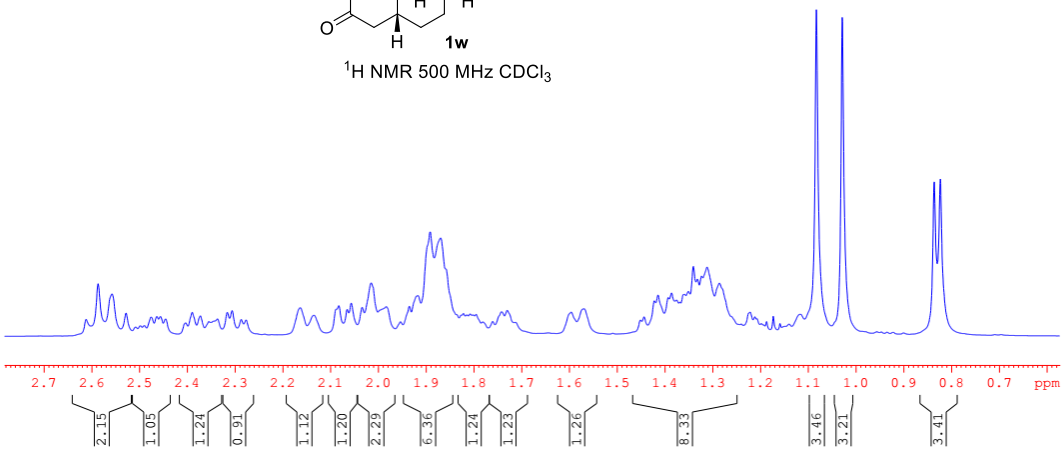
^{1}H NMR 500 MHz $CDCl_3$

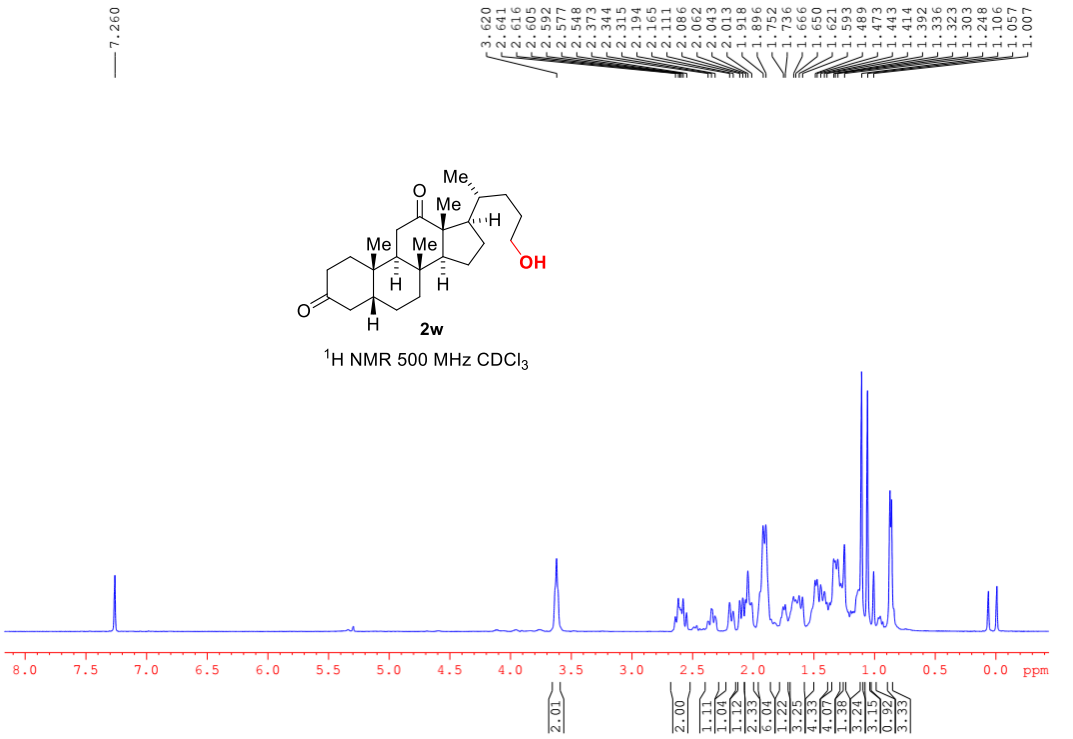




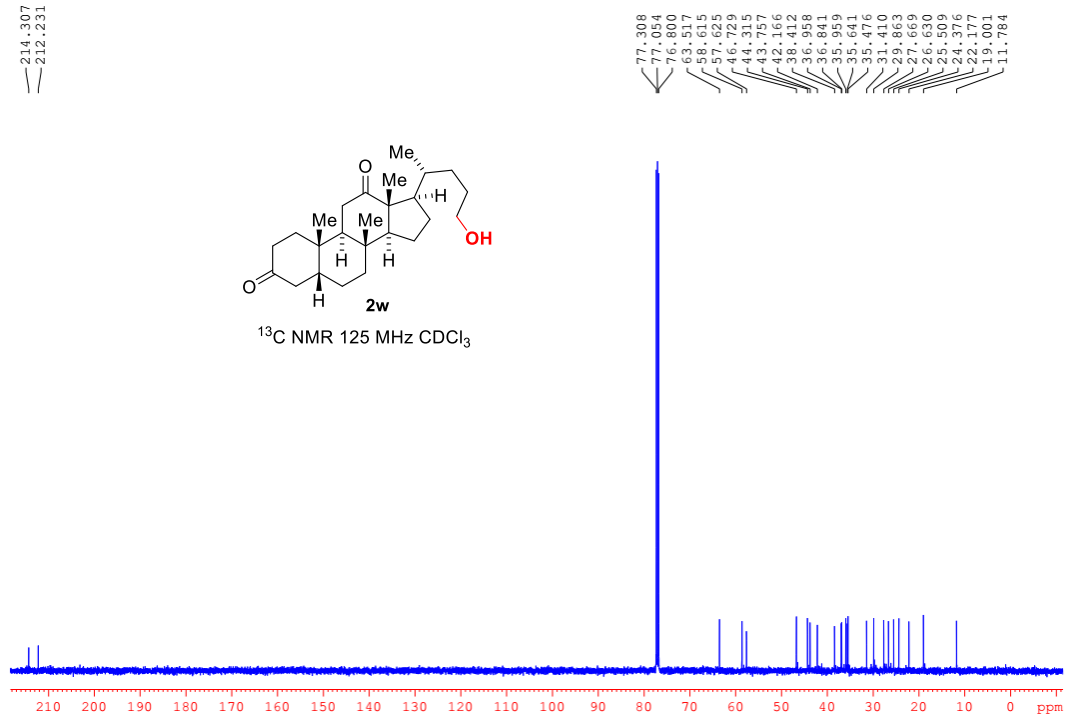


^{1}H NMR 500 MHz $CDCl_3$



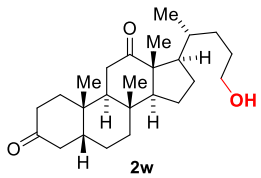


^{1}H NMR 500 MHz $CDCl_3$



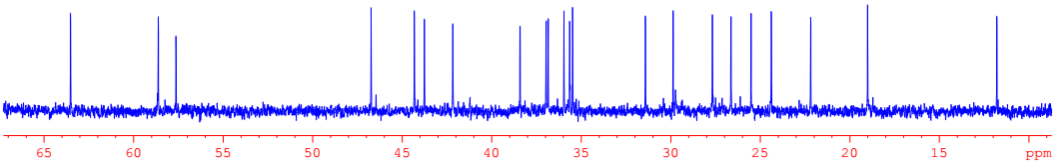
^{13}C NMR 125 MHz $CDCl_3$

63.517
58.615
57.625
46.729
44.315
43.757
42.166
38.412
36.958
36.841
35.959
35.641
35.476
31.410
29.863
27.669
26.630
25.509
24.376
22.177
19.001
11.784

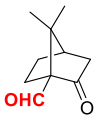


2w

^{13}C NMR 125 MHz $CDCl_3$

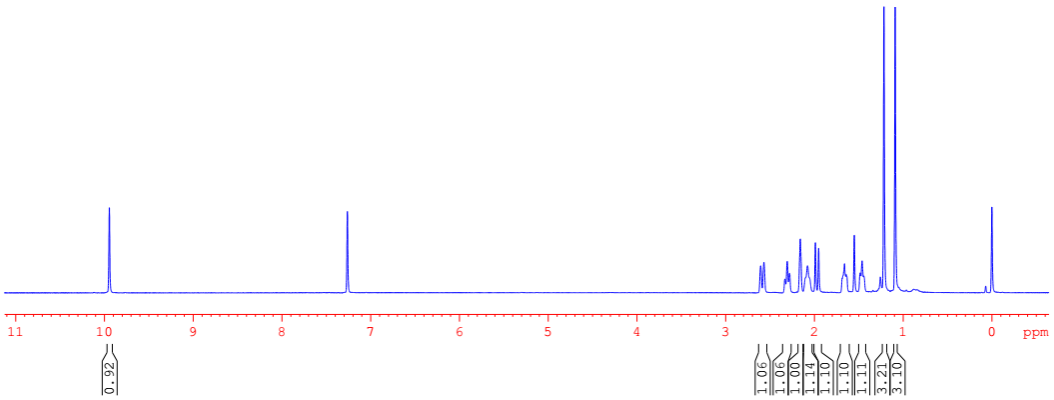


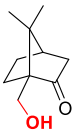
9.942
7.262
2.605
2.568
2.331
2.305
2.281
2.159
2.078
1.988
1.951
1.686
1.661
1.642
1.482
1.462
1.443
1.216
1.089



1v

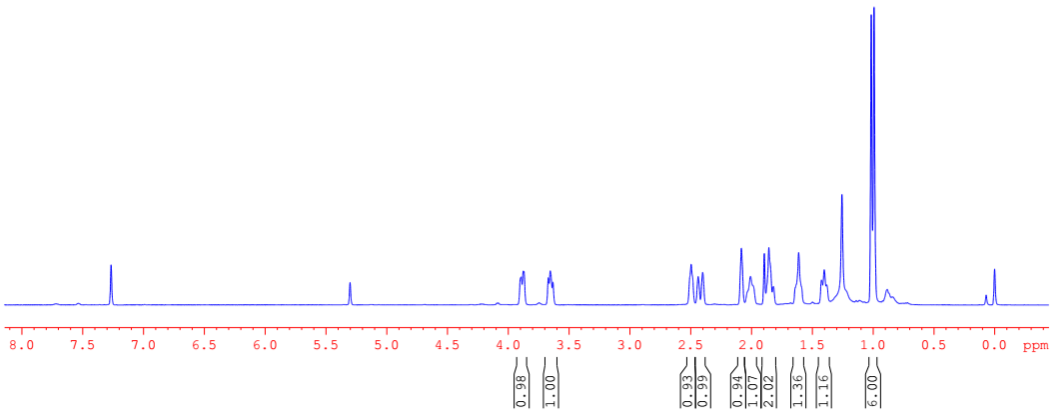
^{1}H NMR 500 MHz $CDCl_3$

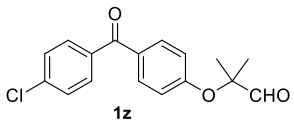




2v

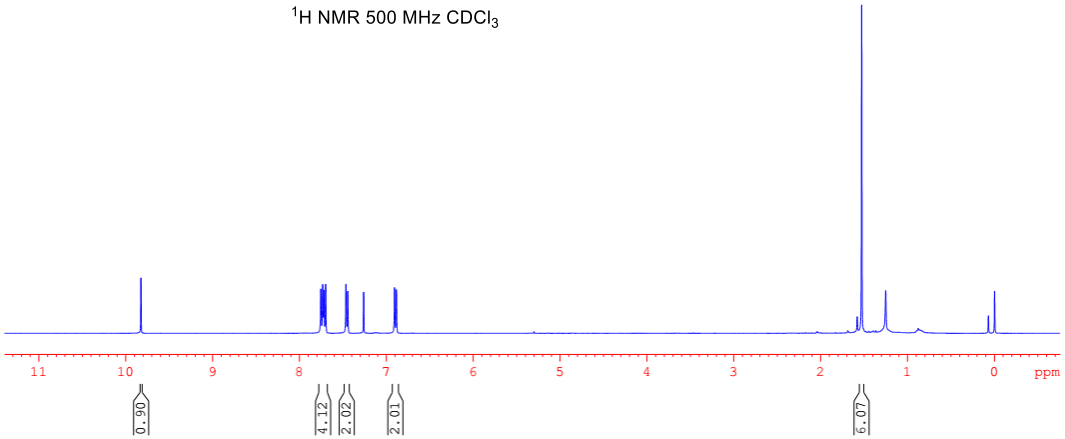
^{1}H NMR 500 MHz $CDCl_3$

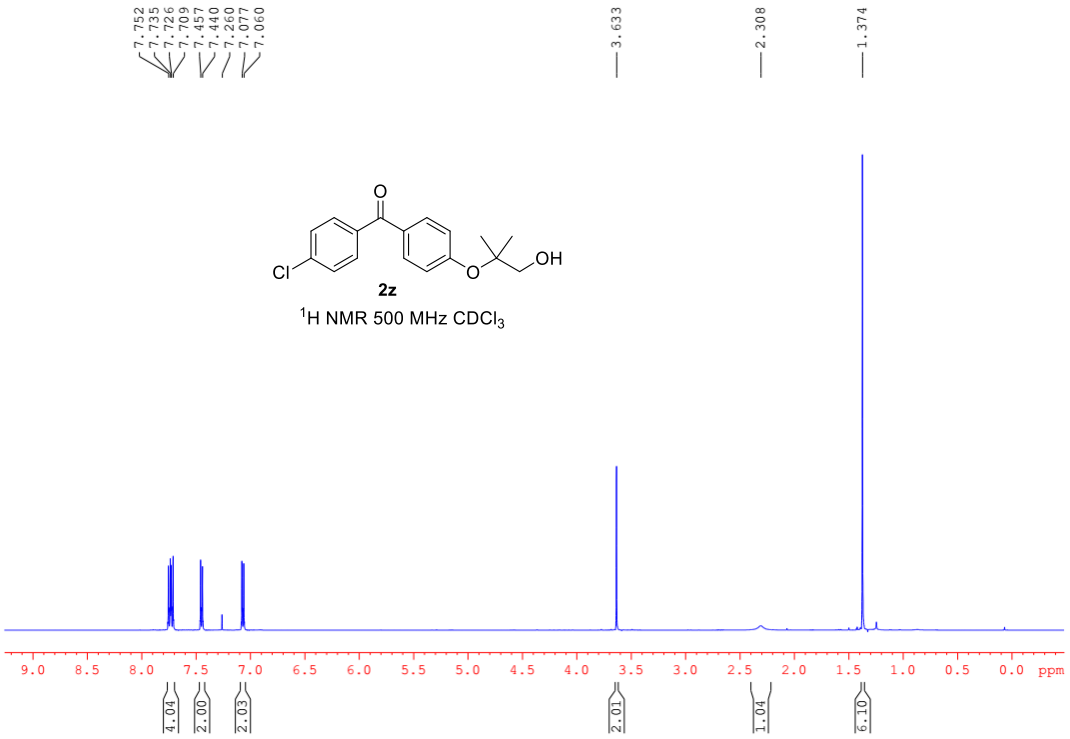


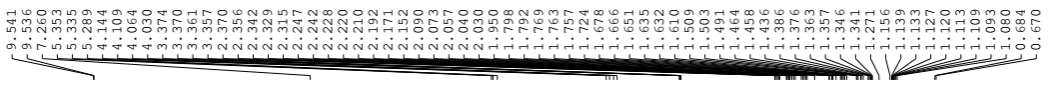


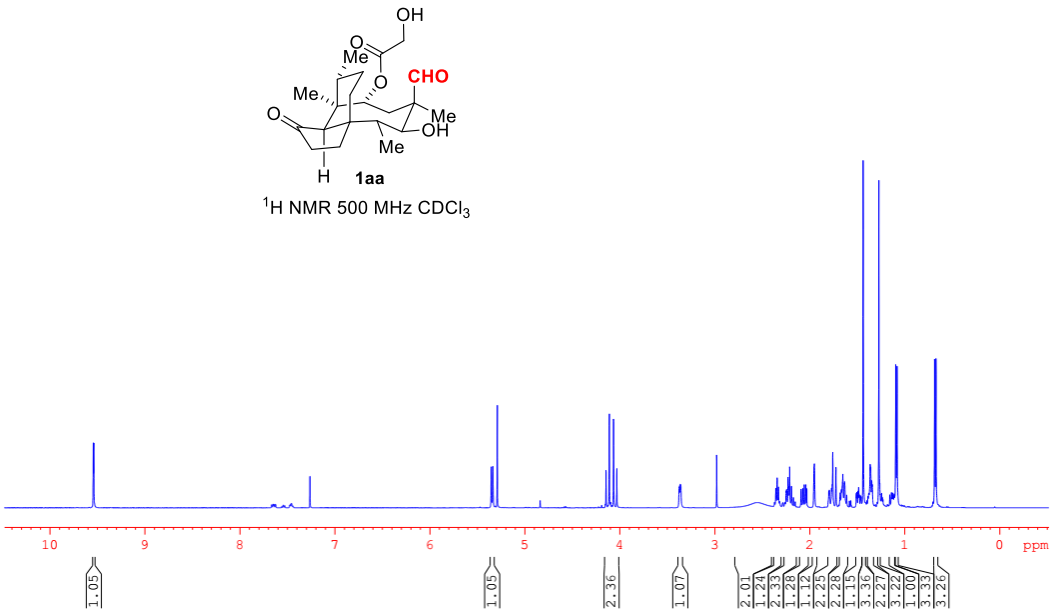
1z

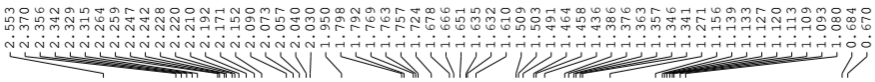
^{1}H NMR 500 MHz $CDCl_3$

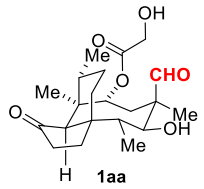



7.752
7.735
7.726
7.709
7.457
7.440
7.260
7.077
7.060
3.633
2.308
1.374
O
Cl
O
OH
2z
1H NMR 500 MHz CDCl3
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
4.04
2.00
2.03
2.01
1.04
6.10


9.541
9.536
7.260
5.353
5.335
5.289
4.144
4.109
4.064
4.030
3.374
3.370
3.361
3.357
2.370
2.356
2.342
2.329
2.315
2.247
2.242
2.228
2.220
2.210
2.192
2.171
2.152
2.090
2.073
2.057
2.040
2.030
1.950
1.798
1.792
1.769
1.763
1.757
1.724
1.678
1.666
1.651
1.635
1.632
1.610
1.509
1.503
1.491
1.464
1.458
1.436
1.386
1.376
1.363
1.357
1.346
1.341
1.271
1.156
1.139
1.133
1.127
1.120
1.113
1.109
1.093
1.080
0.684
0.670

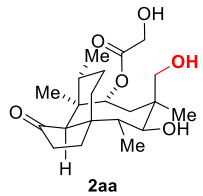

OH
O
Me
O
CHO
Me
O
Me
OH
Me
H
1aa
1H NMR 500 MHz CDCl3
10 9 8 7 6 5 4 3 2 1 0 ppm
1.05
1.05
2.36
1.07
2.01
1.24
2.33
1.28
1.12
2.25
2.28
1.15
3.36
2.27
3.22
1.00
3.33
3.26





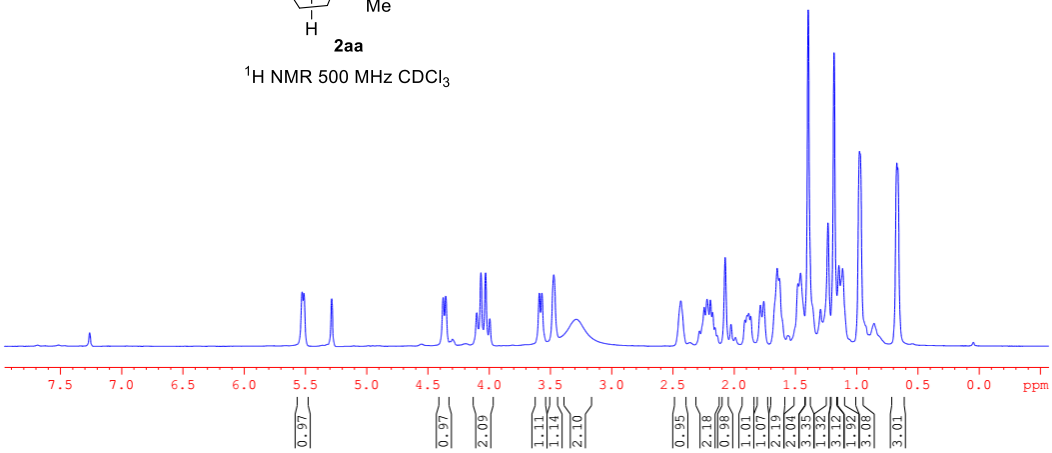
1aa

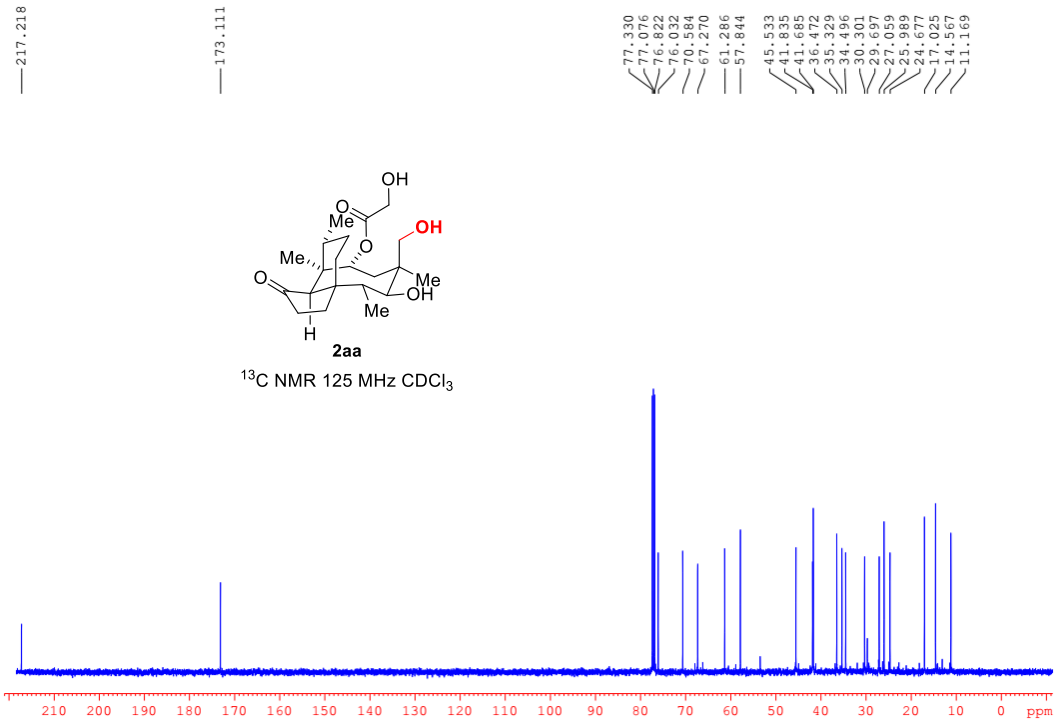
^{1}H NMR 500 MHz $CDCl_3$



2aa

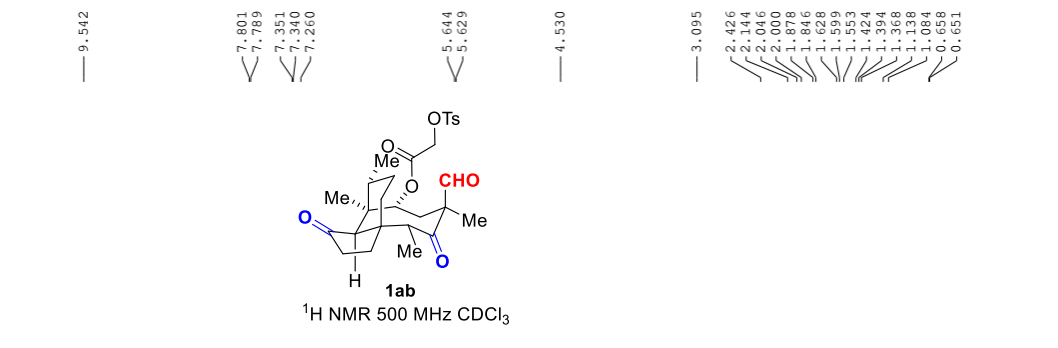
^{1}H NMR 500 MHz $CDCl_3$





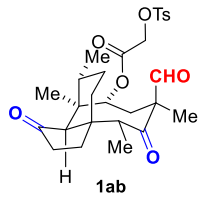
2aa

^{13}C NMR 125 MHz $CDCl_3$



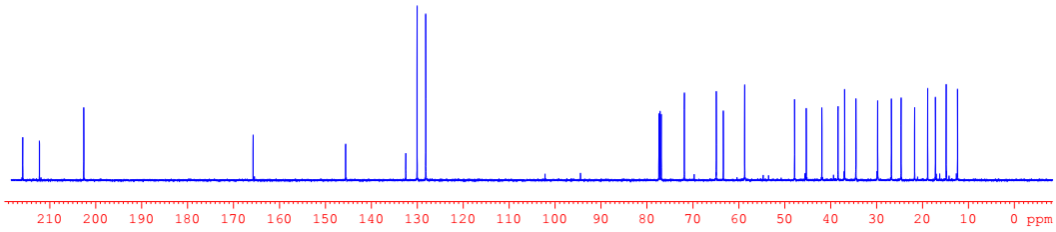
1ab

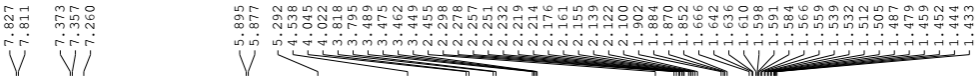
^{1}H NMR 500 MHz $CDCl_3$

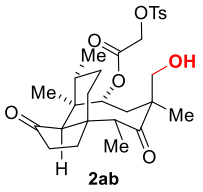


1ab

^{13}C NMR 125 MHz $CDCl_3$

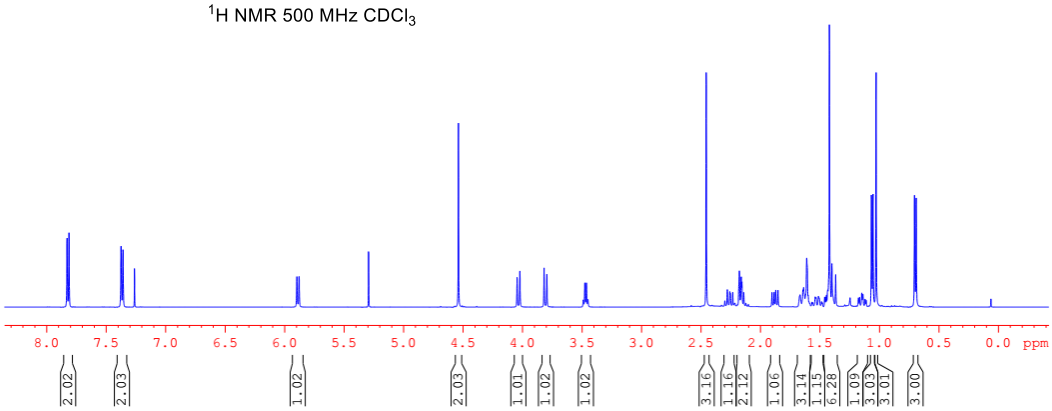


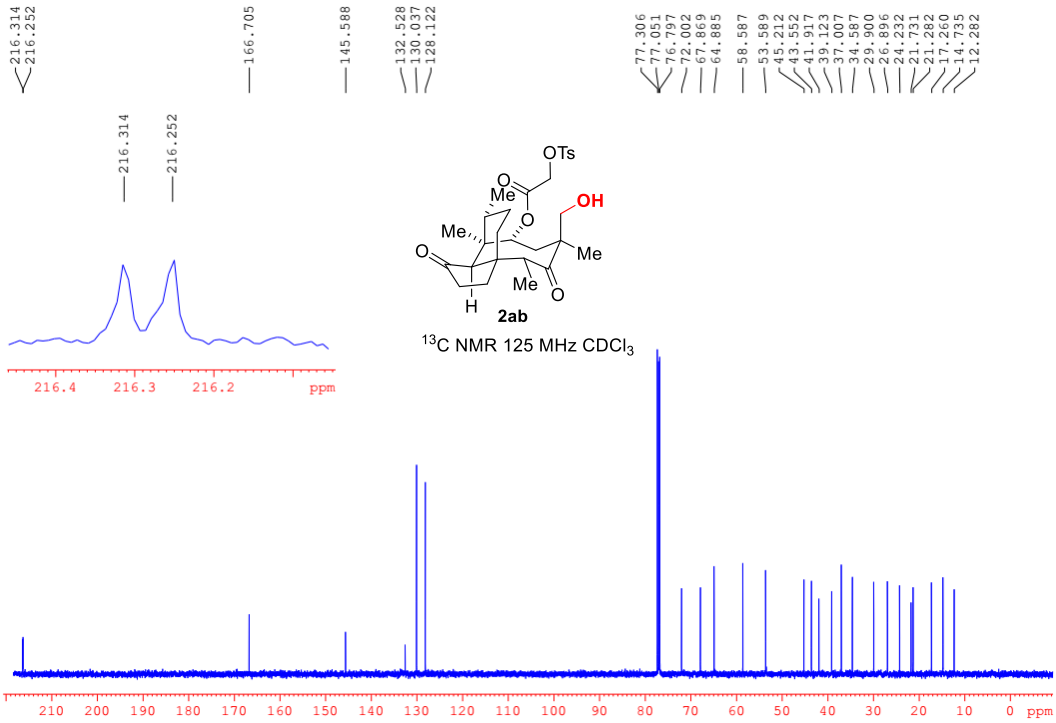




2ab

^{1}H NMR 500 MHz $CDCl_3$

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216.252
166.705
145.588
132.528
130.037
128.122
77.306
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76.797
72.002
67.869
64.885
58.587
53.589
45.212
43.552
41.917
41.123
39.123
37.007
34.587
29.900
26.896
24.232
21.731
21.282
17.260
14.735
12.282
OTs
OH
Me
Me
Me
Me
O
O
O
O
H
2ab
13C NMR 125 MHz CDCl3
216.4
216.3
216.2
ppm
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm