Electronic Supplementary Material (ESI) for RSC Advances.

Enantioselective Synthesis of Mosquito Oviposition Pheromone and its Epimer from a Naturally Occurring Fatty Acid

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Electronic Supplementary Information

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Contents

Supporting Experimental Procedures:

***cis*-5-hexadecenoic acid (4):**
Fatty acid **4** was isolated as a colourless liquid, synthesized using a previously established Conia-Dauben modified Wittig method and isolated using urea inclusion crystallization.[12]

(2.56 g, 74 %, *Z*:*E* = 8:2) ^{1}H NMR (600 MHz, $CDCl_3$): δ 11.5 (s, 1H), 5.46-5.32 (m, 2H), 2.36 (t, *J* = 6.7 Hz, 2H), 2.14-2.01 (m, 4H), 1.74-1.70 (m, 2H), 1.35-1.10 (m, 18 H), 0.92-0.87 (t, *J* = 6.7 Hz, 3H) ; ^{13}C NMR (150.9 MHz, $CDCl_3$): δ 180.5, 131.3, 128.1, 33.4, 31.9, 29.8-29.2, 27.3, 26.5, 24.5, 22.6, 14.1; IR (KBr pellet): ν 3500-2500, 2920, 2856, 1710, 1460, 1410, 935 cm^{-1}; HRMS (FAB): m/z calcd for $C_{16}H_{30}O_2$ $[M + H]^+$, 255.2324; found, 255.2304. Characterization data were in good agreement with literature.[12]

(±)-*threo*-6-hydroxy-5-hexadecanolide [(±)-2]:
Racemic hydroxylactone **(±)-2** was obtained as a white powder using a previously reported procedure starting from **4**.[12]

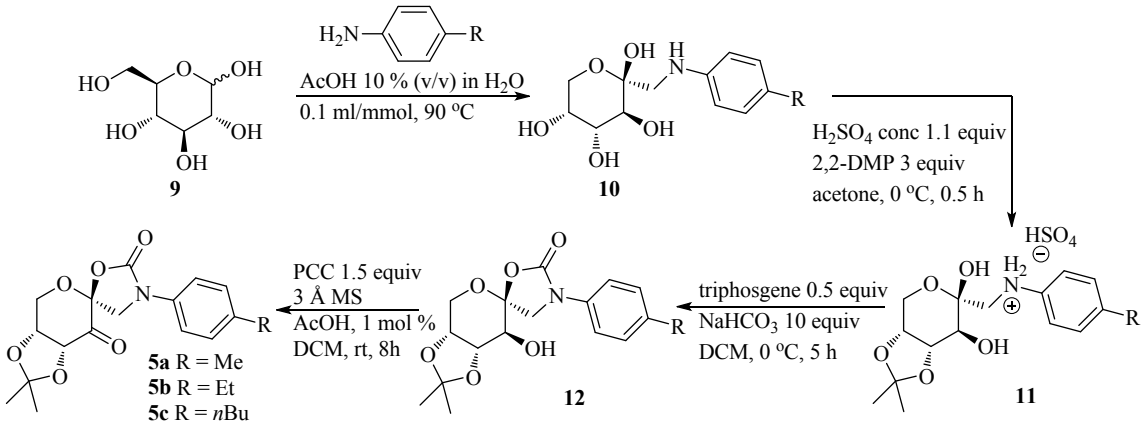
(275 mg, 69 %) m.p.: 65-67 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.2 (m, 1H), 3.6 (m, 1 H), 2.6-2.5 (m, 2H), 2.0-1.2 (m, 22H), 0.9 (t, *J* = 6.7 Hz, 3H); ^{13}C NMR (75.50 MHz, $CDCl_3$): δ 171.6, 83.2, 73.3, 32.6, 31.9, 29.5, 25.4, 24.2, 22.7, 18.4, 14.1; IR (KBr pellet): ν 3554(br), 2955, 1706 cm^{-1}; HRMS (FAB): m/z calcd for $C_{16}H_{30}O_3$ $[M + H]^+$ 271.2273, found 271.2258. Characterization data were in good agreement with literature.[12]

***p*-chlorophenyl acetate:**
In a 10 ml microwave vial, was added Ac_2O (1.0 ml) and silica gel (1.0 g) and stirred until a uniform silica paste was formed. To the above mixture was added 4-chlorophenol (521 mg, 4.06 mmol) and heated at 135 ^{o}C for 2.5 min using microwave radiation. The mixture was extracted with hexane (3 x 4 ml), dried ($MgSO_4$), filtered and residual solvent and acetic acid was removed under reduced pressure (0.1 mmHg, 30 ^{o}C, 3 h) to yield the title compound as a brown liquid (548 mg, 79 %). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35 (d, 2H), 7.05 (d, 2H), 2.30 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 169.1, 149.2, 131.1, 129.5, 123.0, 21.0. Characterization data were in good agreement with literature.[21]

Shvo's catalyst (6):
To a flame-dried two-neck flask equipped with an oval magnetic stir bar, septum, and flame dried condenser connected to a two line Schlenk manifold was added triruthenium dodecacarbonyl (100 mg, 0.157 mmol) and tetraphenylcyclopentadienone (181 mg, 0.470 mmol) under a rapid flow of N_2. The flask was charged with anhydrous methanol (17 ml) and heated under reflux for 24 h. The reaction was cooled to room temperature and the yellow precipitate was collected by vacuum filtration and washing with hexanes (3 x 1 ml). Drying under reduced pressure afforded catalyst **6** as a bright yellow powder (174 mg, 39 %) ^{1}H NMR (300 MHz, benzene-d_6): δ 13.8 (s, 1H), 7.46 (m, 8H), 7.09 (m, 8H), 6.91 (m,

12 H), 6.72 (m, 12H), -17.75 (s, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 201.6, 155.0, 132.2, 131.1-130.8, 128.1-126.9, 104.0, 87.8. Characterization data were in good agreement with literature.[19b]

Shi catalyst synthesis:



Scheme 1. **Representative Synthesis of Shi Epoxidation Catalysts**

Catalysts **5a-c** were synthesized according to previously outlined representative synthetic procedures (Scheme 1).[14a, b] Shi epoxidation conditions were based on published representative epoxidation procedures.[14c] Characterization data for catalysts were in good agreement with literature.[14a]

Catalyst (5a):
White granular crystals; m.p.: 162-163 °C (hexanes-EtOAc); lit[14a] 162.0-163.5 °C (hexanes-EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 4.89 (d, *J* = 5.4 Hz, 1H), 4.76 (d, *J* = 10.5 Hz, 1H), 4.67-4.64 (m, 2H), 4.29 (d, *J* = 14.1 Hz, 1H), 3.76 (d, *J* = 10.2 Hz, 1H), 2.36 (s, 3H), 1.50 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 195.1, 151.2, 134.8, 134.5, 129.8, 118.8, 111.1, 99.1, 77.5, 75.5, 60.9, 49.8, 27.1, 26.0, 20.8.

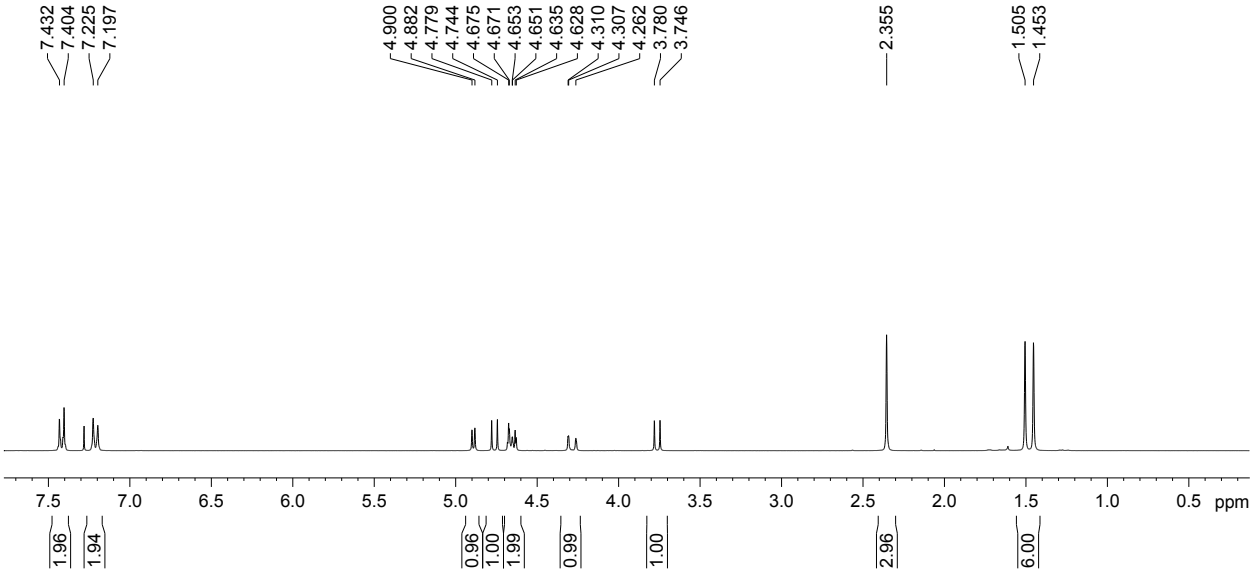
Catalyst (5b):
Clear plate-like crystals; m.p.: 135-136°C (hexanes-EtOAc); lit[14a] 135-136 °C (hexanes-EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44 (d, *J* = 9.3 Hz, 2H), 7.23 (d, *J* = 9.3 Hz, 2H), 4.89 (d, *J* = 5.4 Hz, 1H), 4.75 (d, *J* = 10.5 Hz, 1H), 4.67-4.64 (m, 2H), 4.29 (d, *J* = 13.8 Hz, 1H), 3.76 (d, *J* = 10.5 Hz, 1H), 2.65 (m, 2H), 1.50 (s, 3H), 1.45 (s, 3H), 1.23 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 195.1, 151.2, 141.2, 134.6, 128.6, 118.9, 111.1, 99.1, 75.5, 60.9, 49.8, 28.2, 27.1, 26.0, 15.6.

Catalyst (5c):
Clear plate-like crystals. m.p.: 165-166°C (hexanes-EtOAc); lit[14a] 164-166 °C (hexanes-EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45 (d, *J* = 8.7 Hz, 2H), 7.21 (d, *J* = 8.7 Hz, 2H), 4.89 (d, *J* = 5.4 Hz, 1H), 4.76 (d, *J* = 10.5 Hz, 1H), 4.67-4.62 (m, 2H), 4.29 (d, *J* = 13.2 Hz, 1H), 3.76 (d, *J* = 10.5 Hz, 1H), 2.61 (m, 2H), 1.59 (m, 2H), 1.50 (s, 3H), 1.45 (s, 3H), 1.33 (m, 2H), 0.93 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 195.1, 151.2, 139.9, 134.6, 129.2, 118.8, 111.1, 99.1, 75.5, 60.9, 49.8, 34.9, 33.6, 27.1, 26.0, 22.2, 13.9.

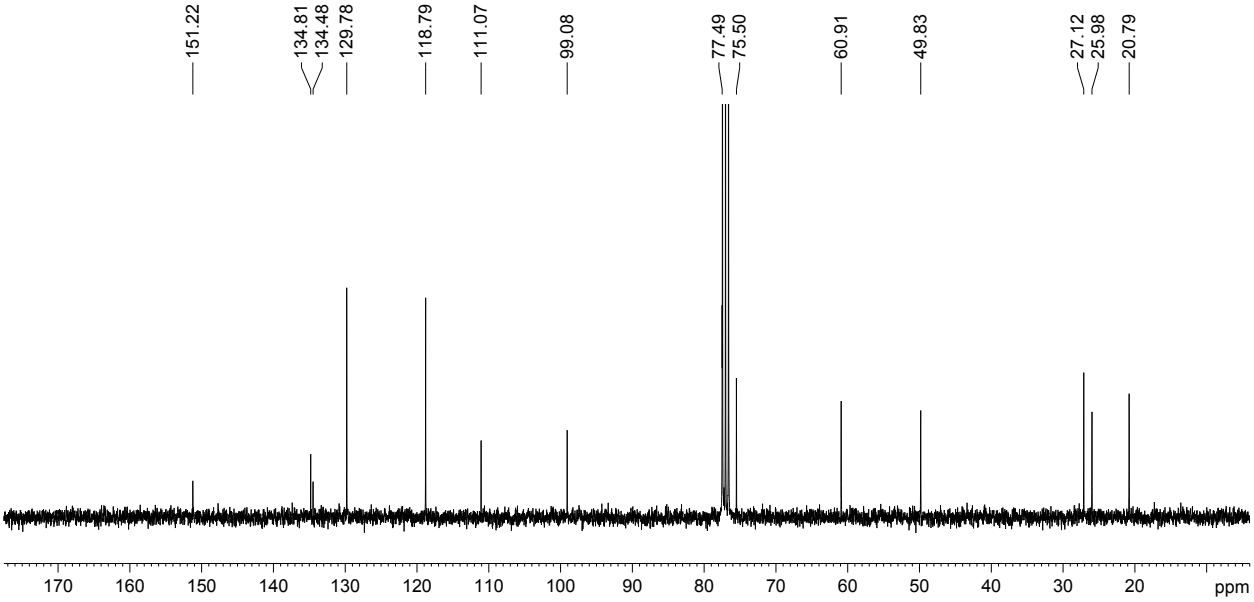
NMR Spectra

Shi Catalyst 5a:

^{1}H NMR, 300 MHz, $CDCl_3$

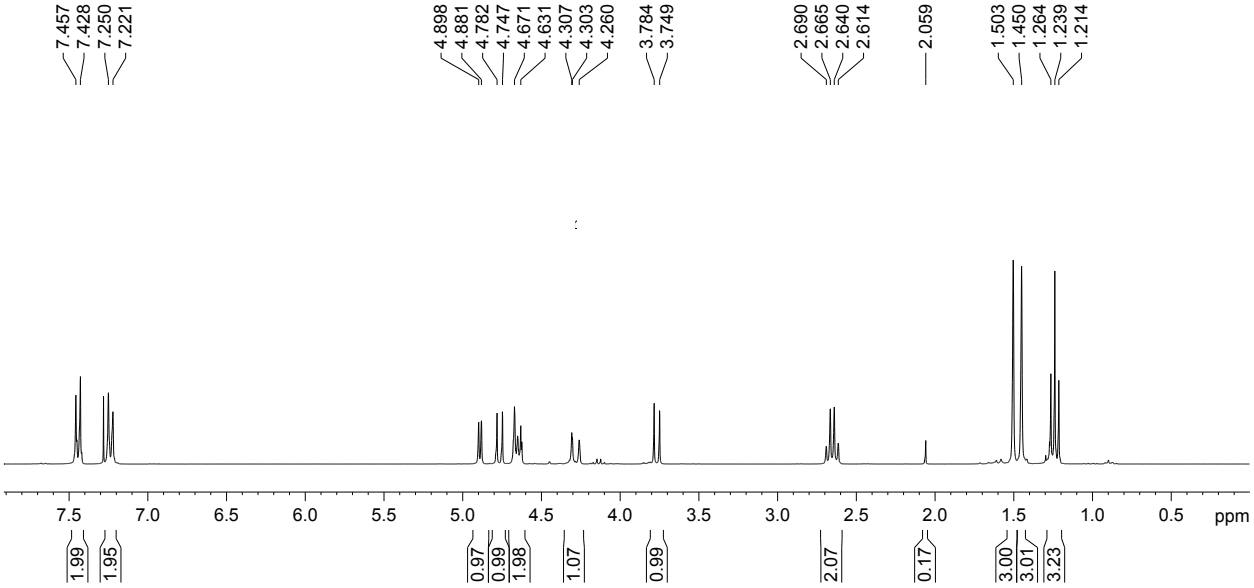


^{13}C NMR, 75.5 MHz, $CDCl_3$

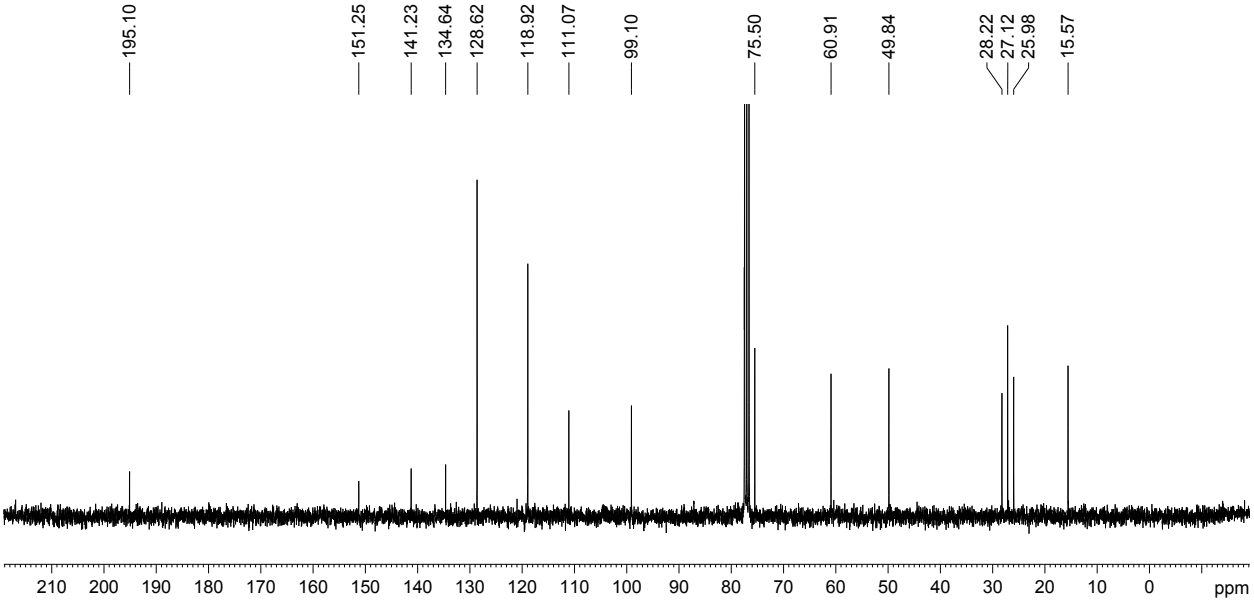


Shi Catalyst 5b:

^{1}H NMR, 300 MHz, $CDCl_3$

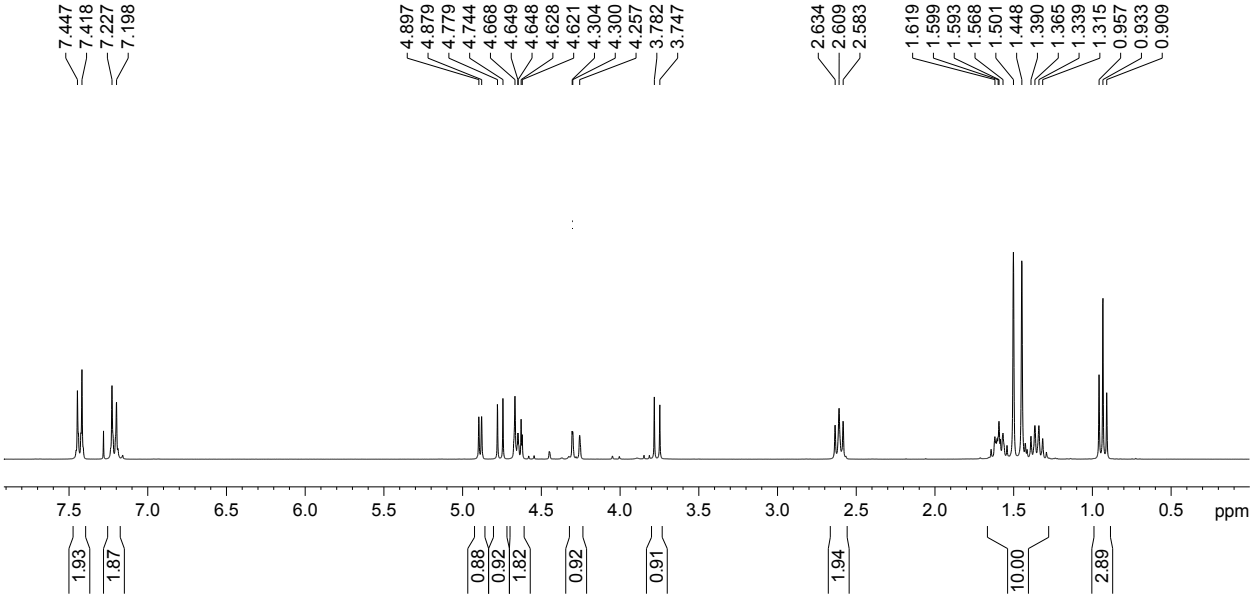


^{13}C NMR, 75.5 MHz, $CDCl_3$

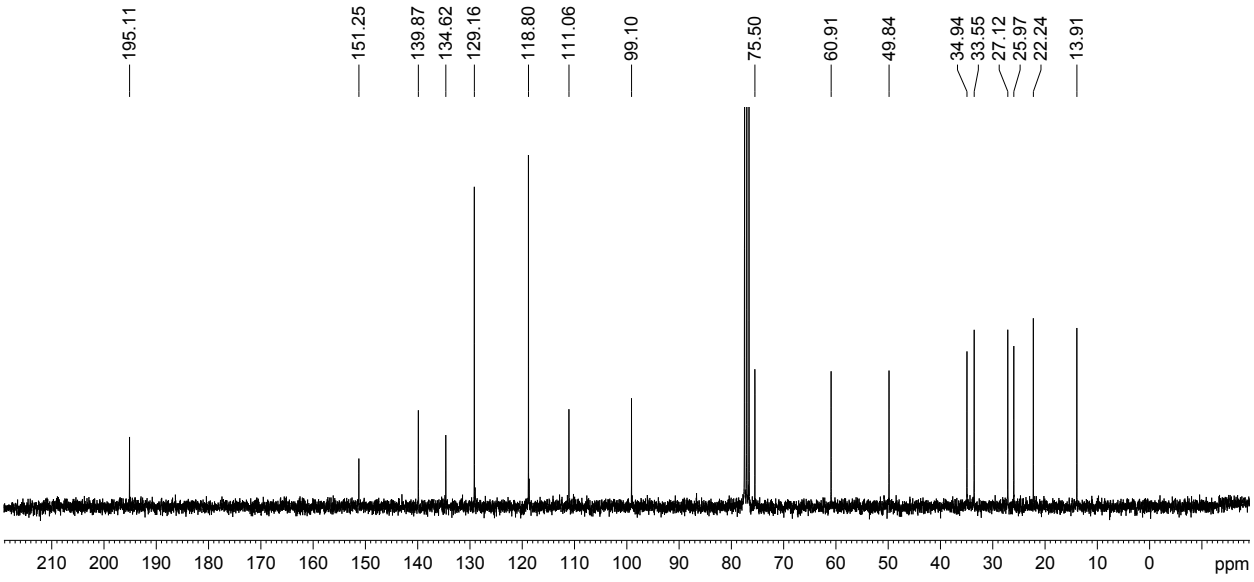


Shi Catalyst 5c:

^{1}H NMR, 300 MHz, $CDCl_3$

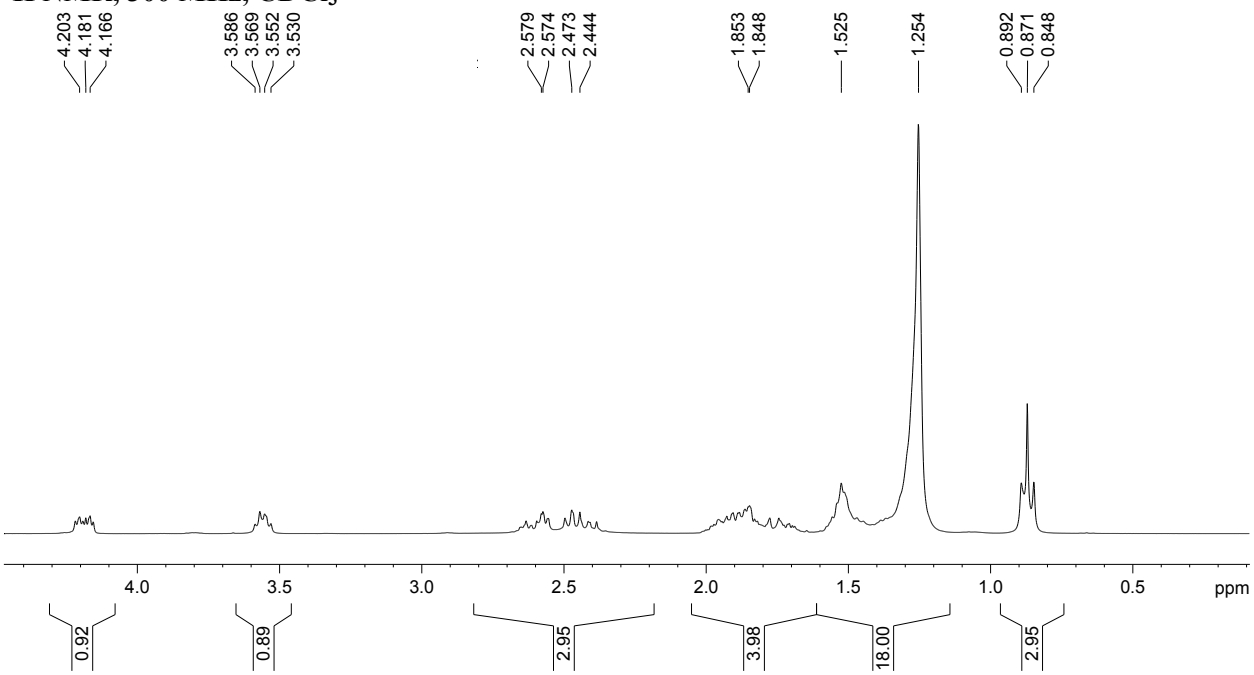


^{13}C NMR, 75.5 MHz, $CDCl_3$

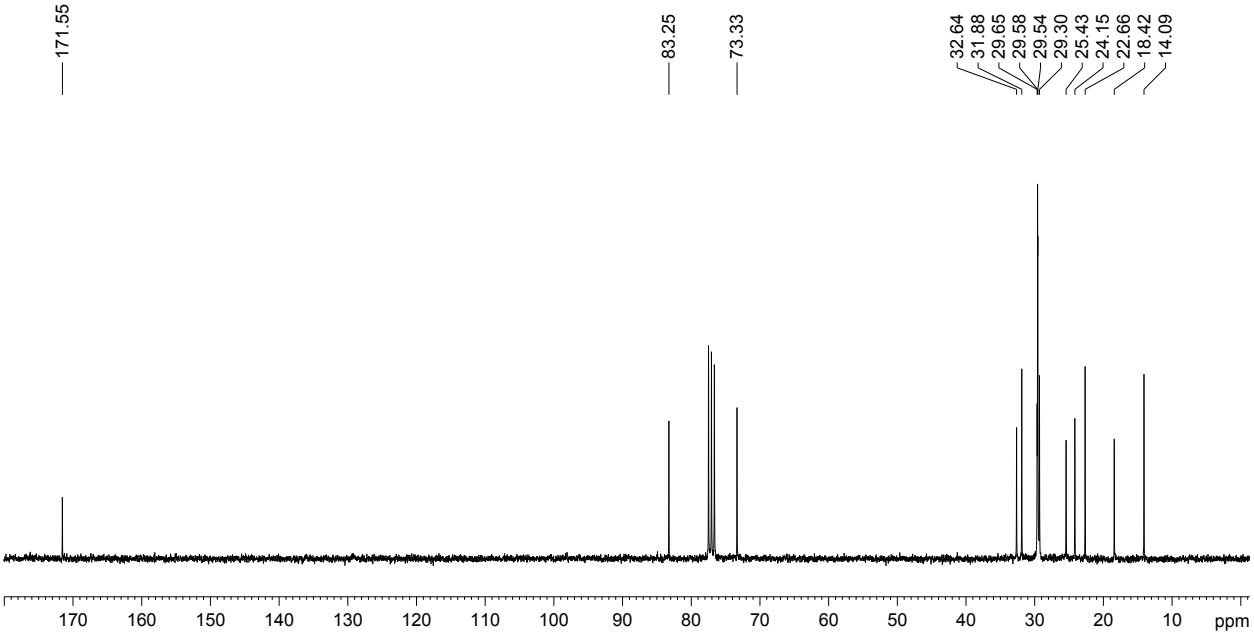


Hydroxylactone (-)-2 using catalyst 5a:

^{1}H NMR, 300 MHz, $CDCl_3$

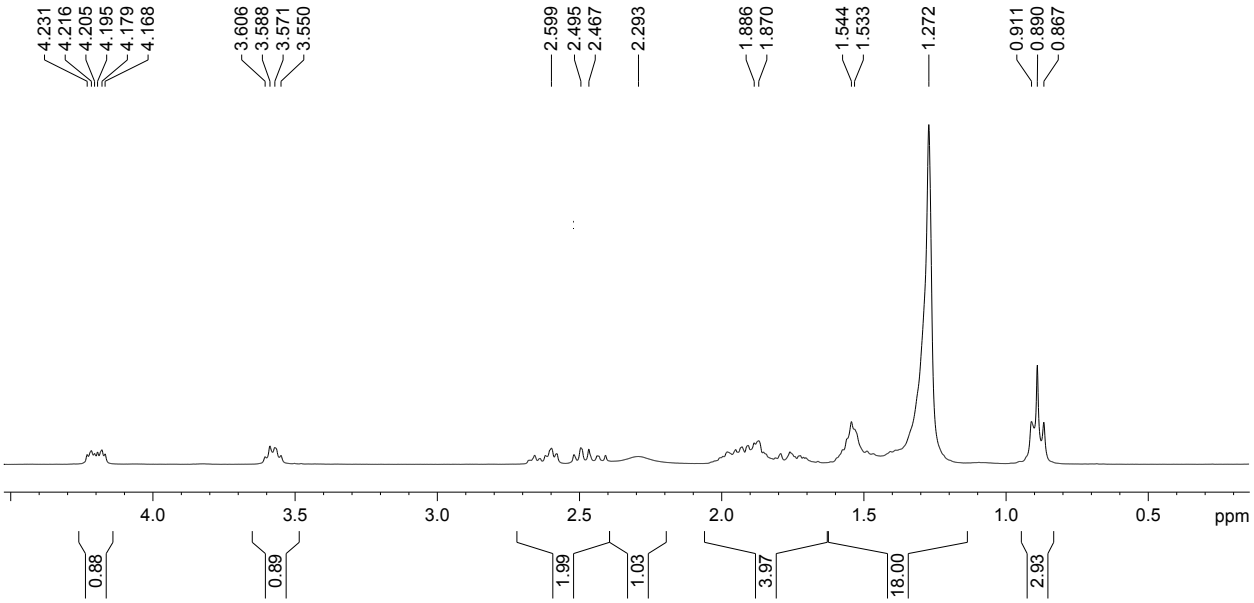


^{13}C NMR, 75.5 MHz, $CDCl_3$

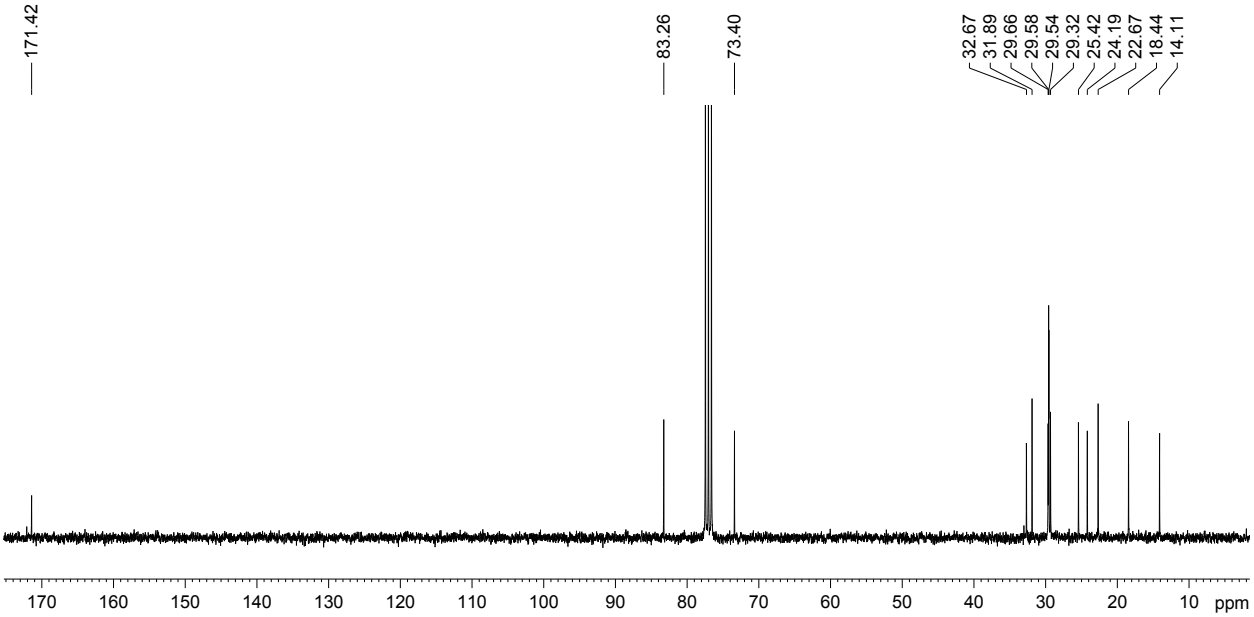


Hydroxylactone (-)-2 using catalyst 5b:

^{1}H NMR, 300 MHz, $CDCl_3$

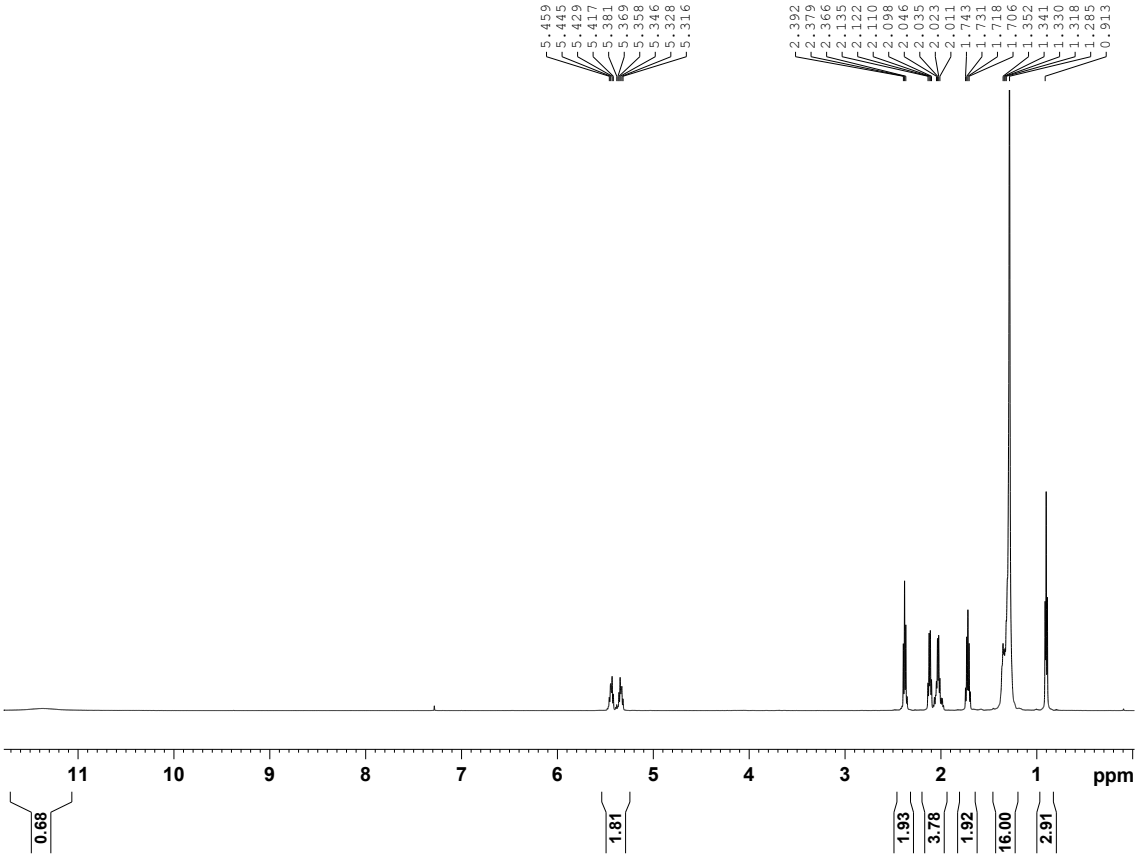


^{13}C NMR, 75.5 MHz, $CDCl_3$

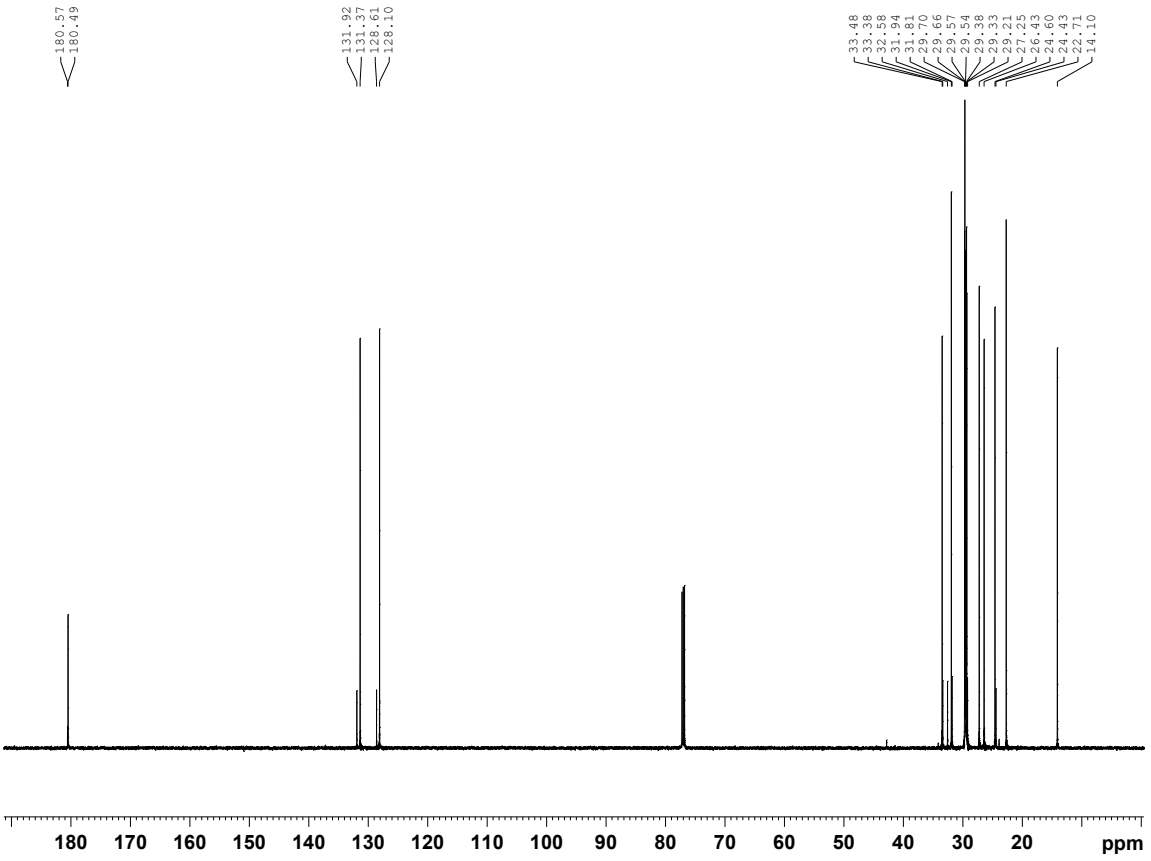


Fatty acid 4 :

^{1}H NMR, 600 MHz, $CDCl_3$

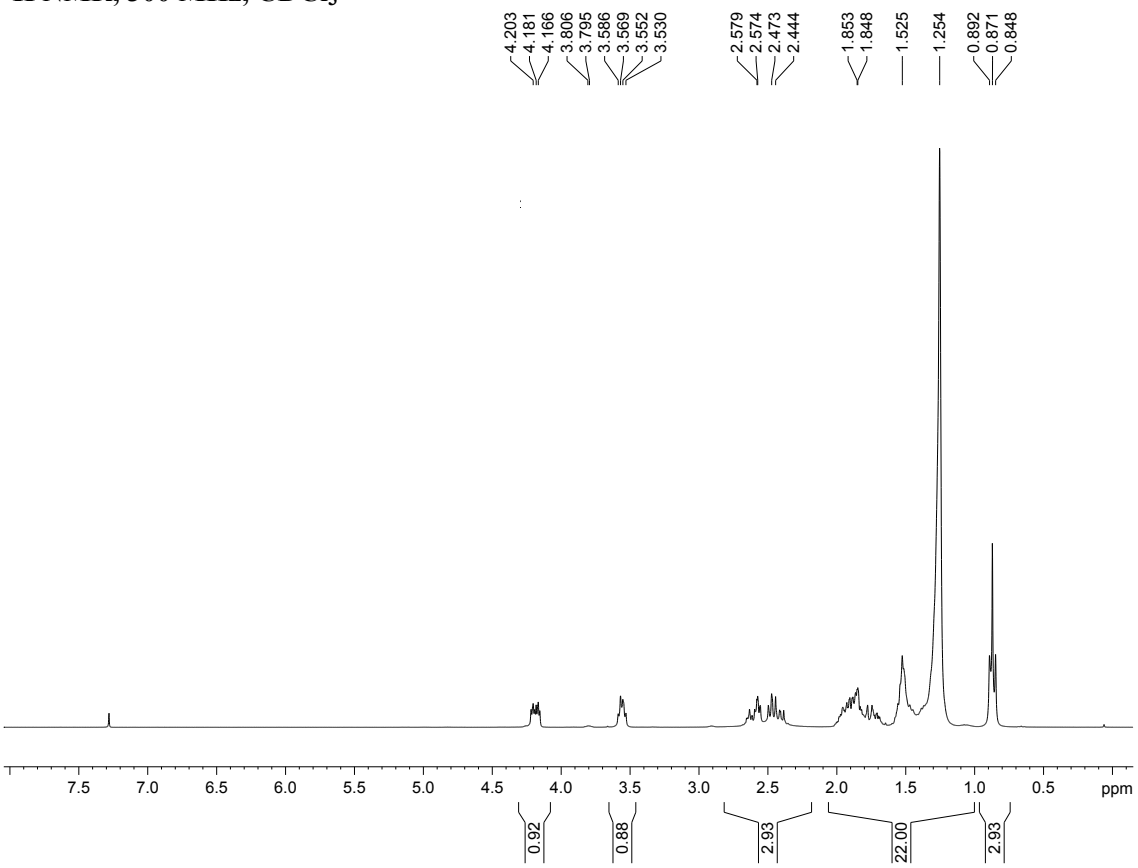


^{13}C NMR, 150.9 MHz, $CDCl_3$

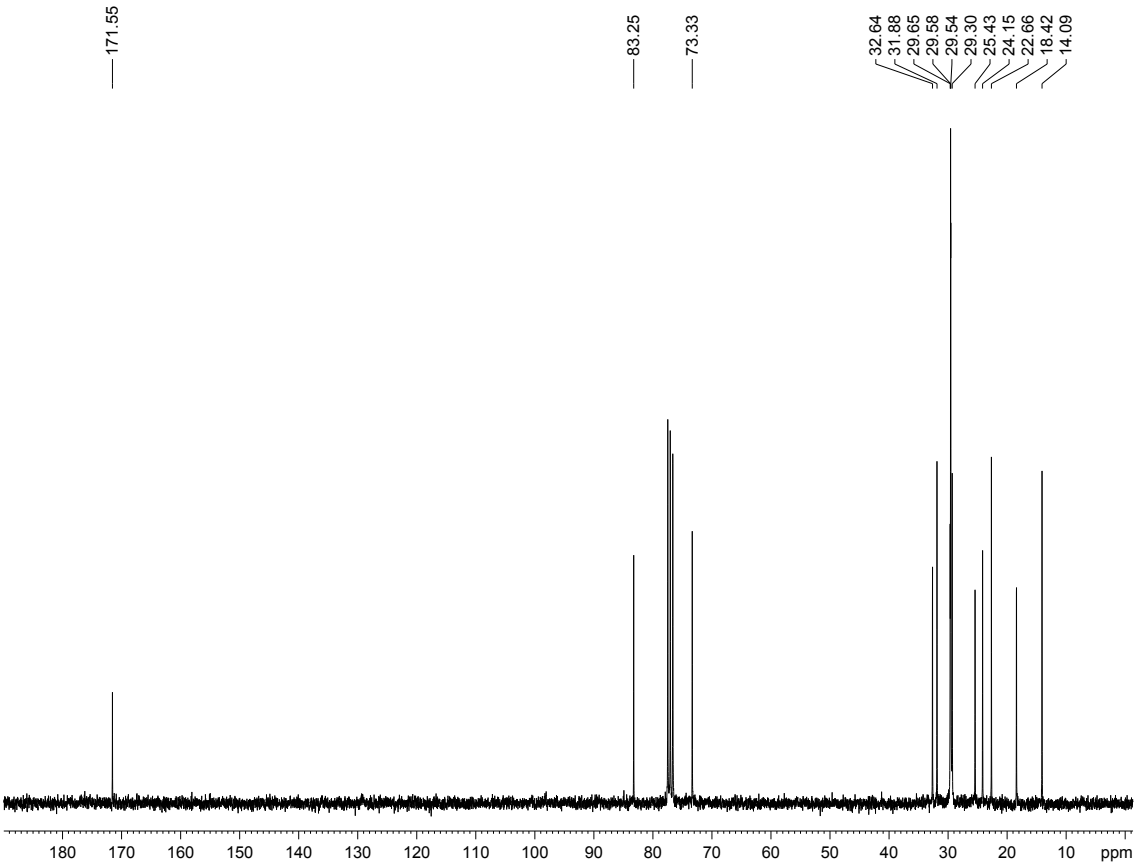


Hydroxylactone (±)-2:

^{1}H NMR, 300 MHz, $CDCl_3$

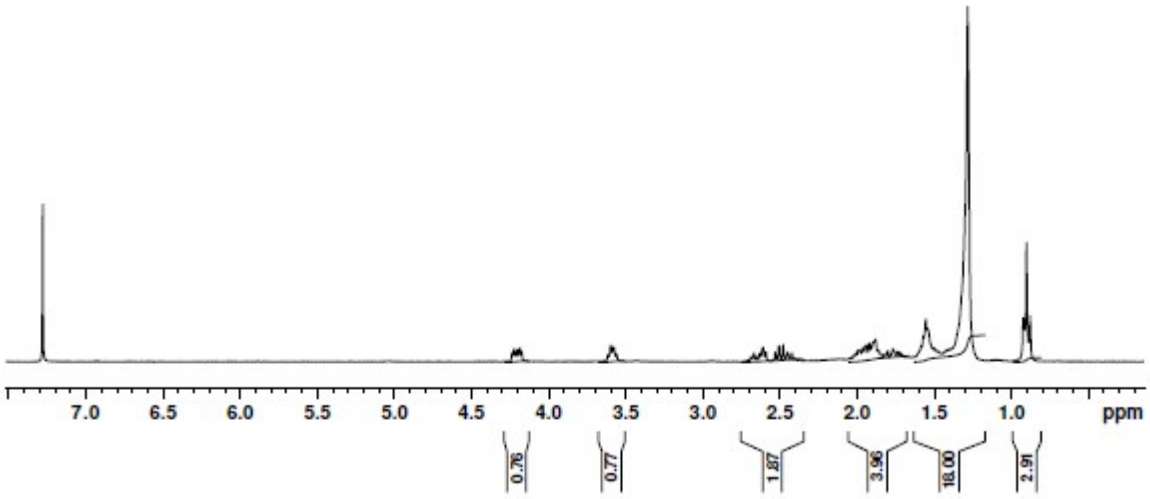


^{13}C NMR, 75.5 MHz, $CDCl_3$

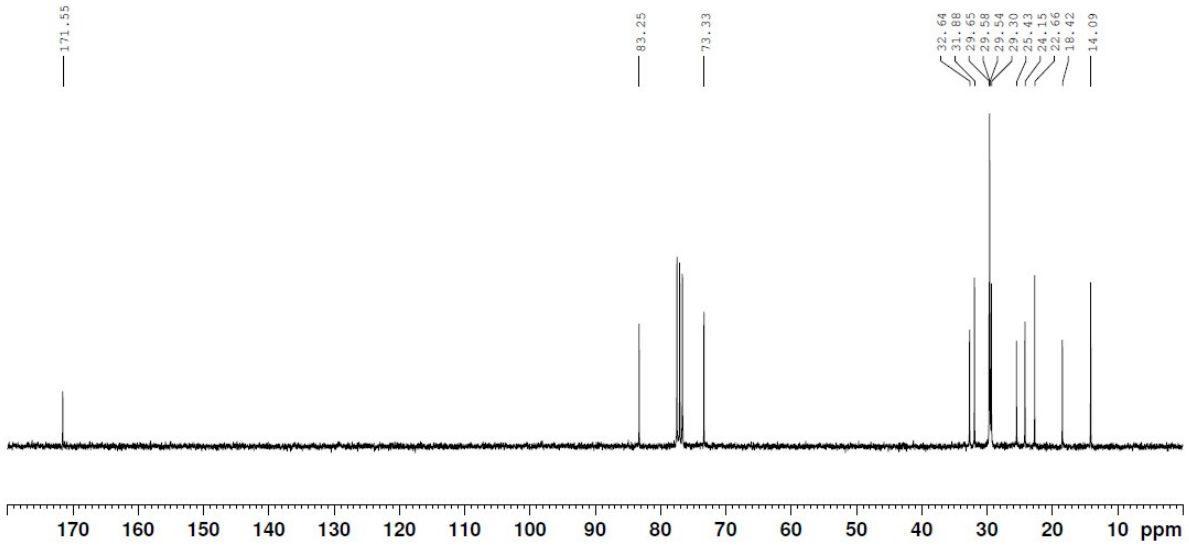


Hydroxylactone (-)-2 using catalyst 5c:

^{1}H NMR, 300 MHz, $CDCl_3$

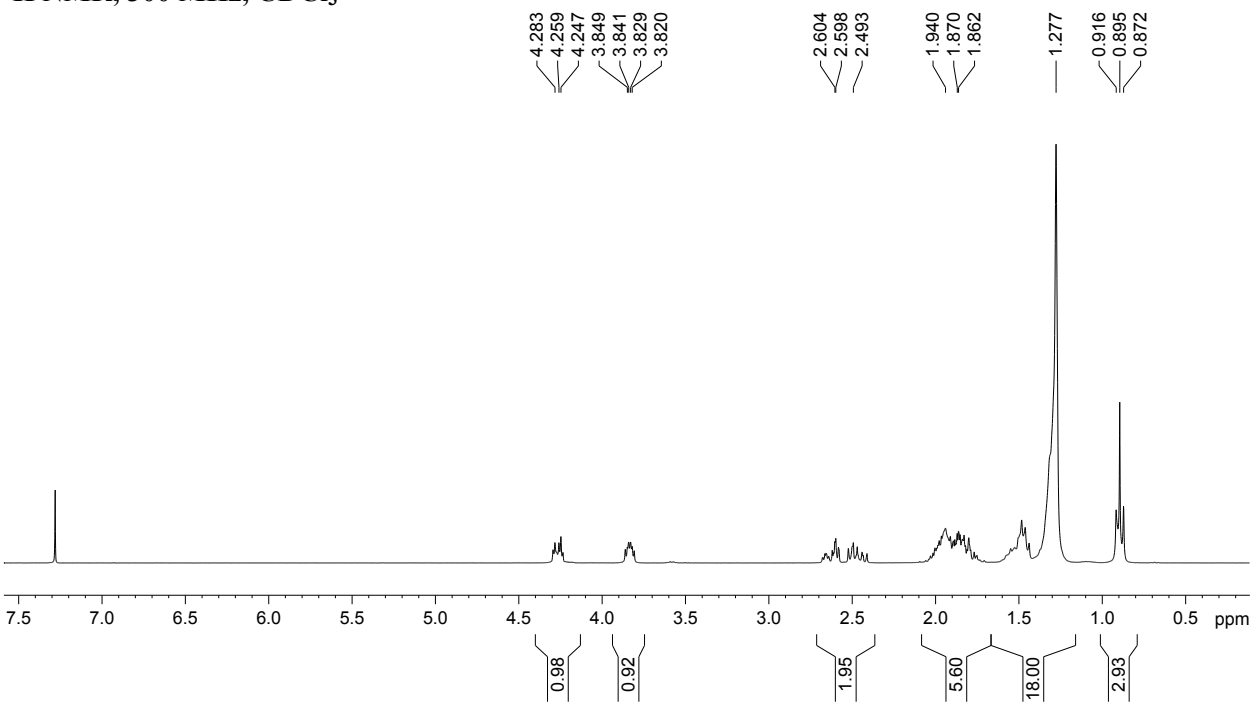


^{13}C NMR, 75.5 MHz, $CDCl_3$

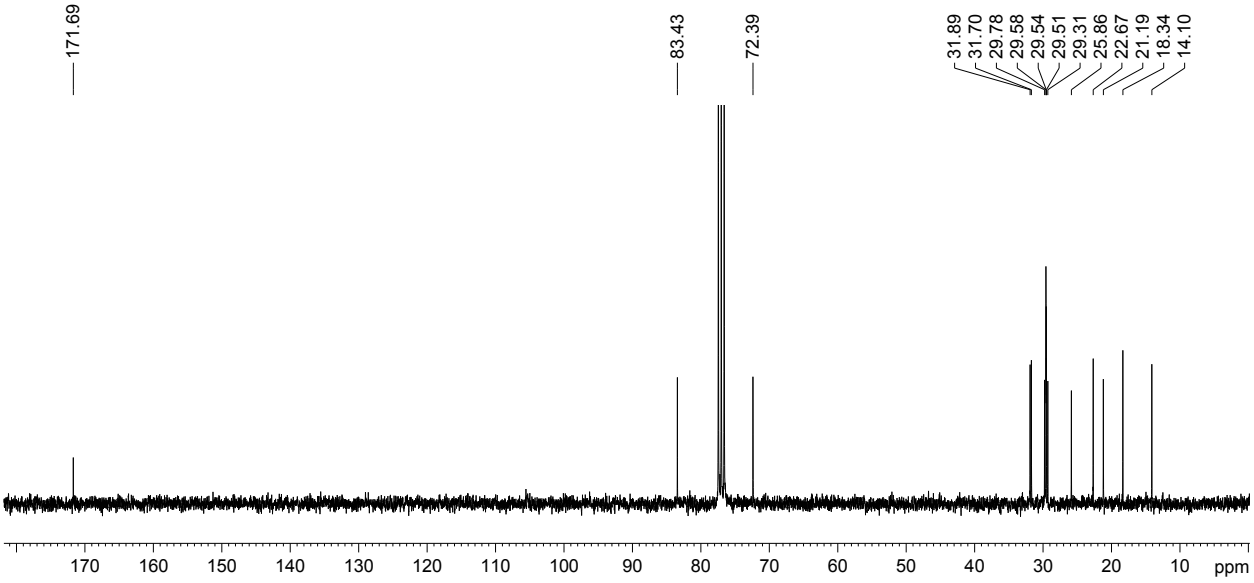


Hydroxylactone (-)-8 using L-proline:

^{1}H NMR, 300 MHz, $CDCl_3$

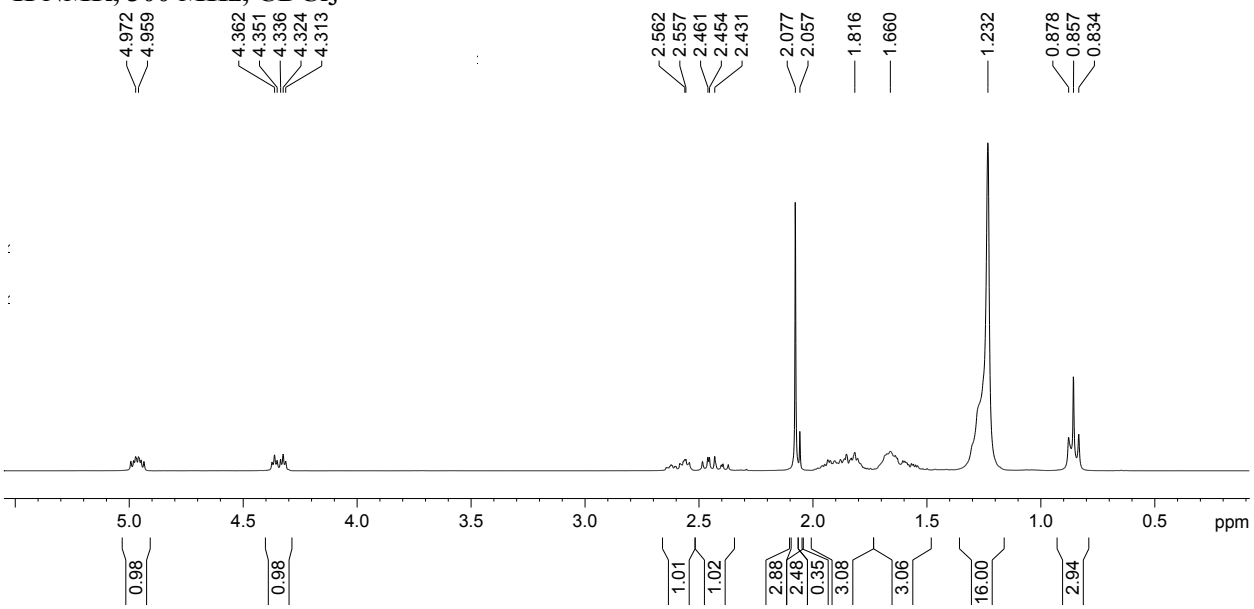


^{13}C NMR, 75.5 MHz, $CDCl_3$

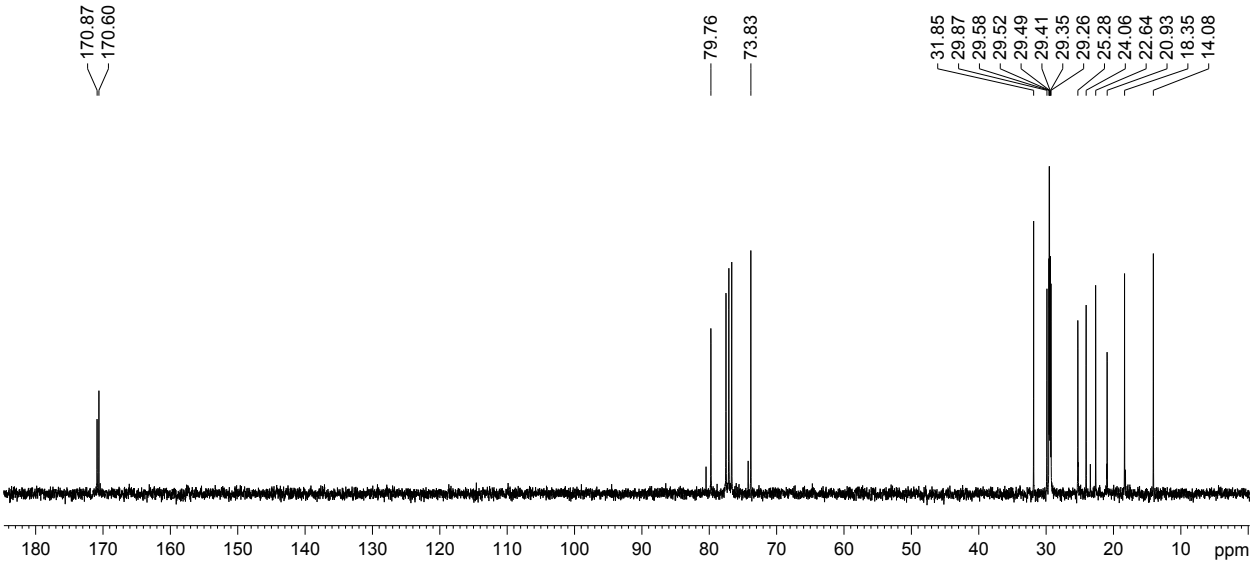


(5*R*, 6*R*)-6-Acetoxy-5-hexadecanolide (-)-9 with chirality from catalyst 5c:

^{1}H NMR, 300 MHz, $CDCl_3$

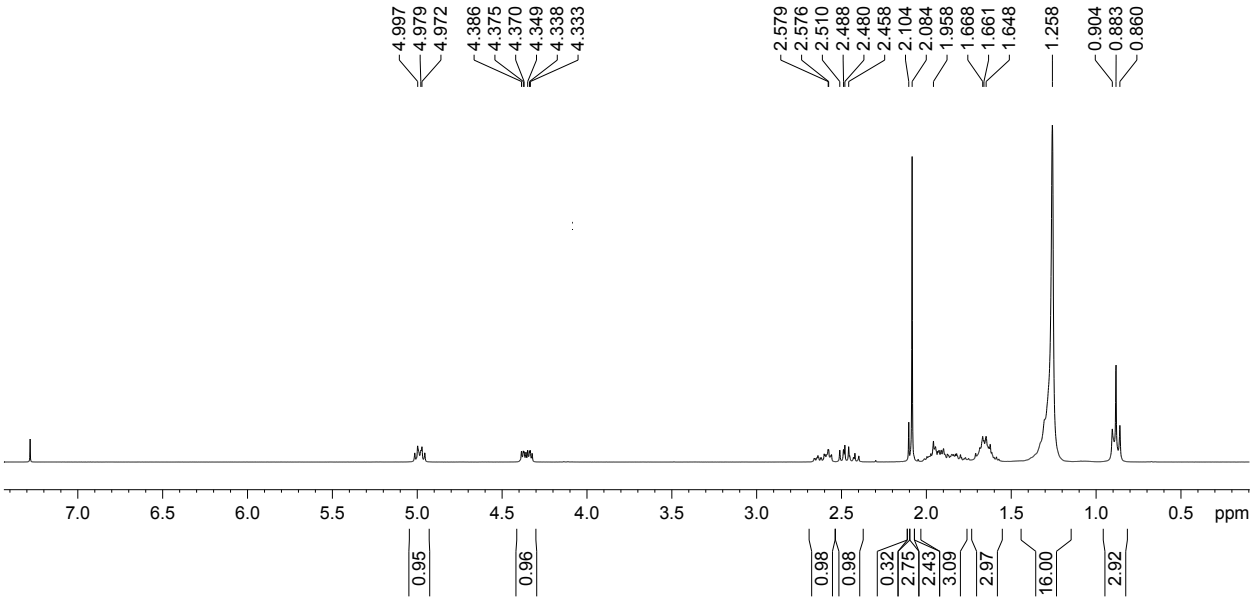


^{13}C NMR, 75.5 MHz, $CDCl_3$

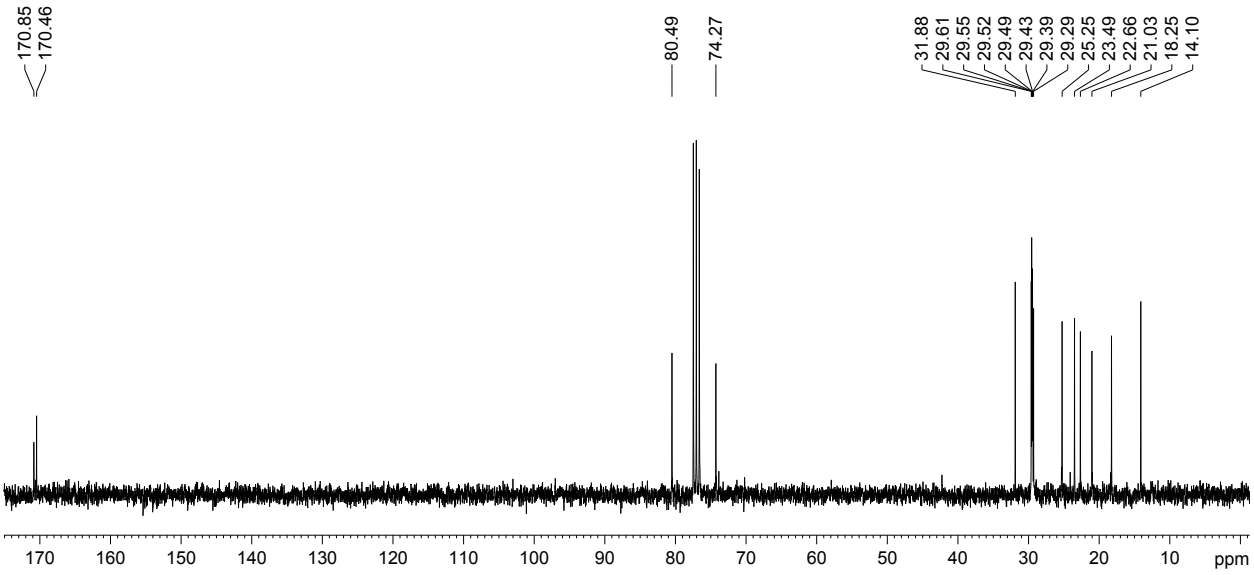


(5*R*, 6*S*)-6-Acetoxy-5-hexadecanolide (-)-1 with chirality from catalyst 5c:

^{1}H NMR, 300 MHz, $CDCl_3$

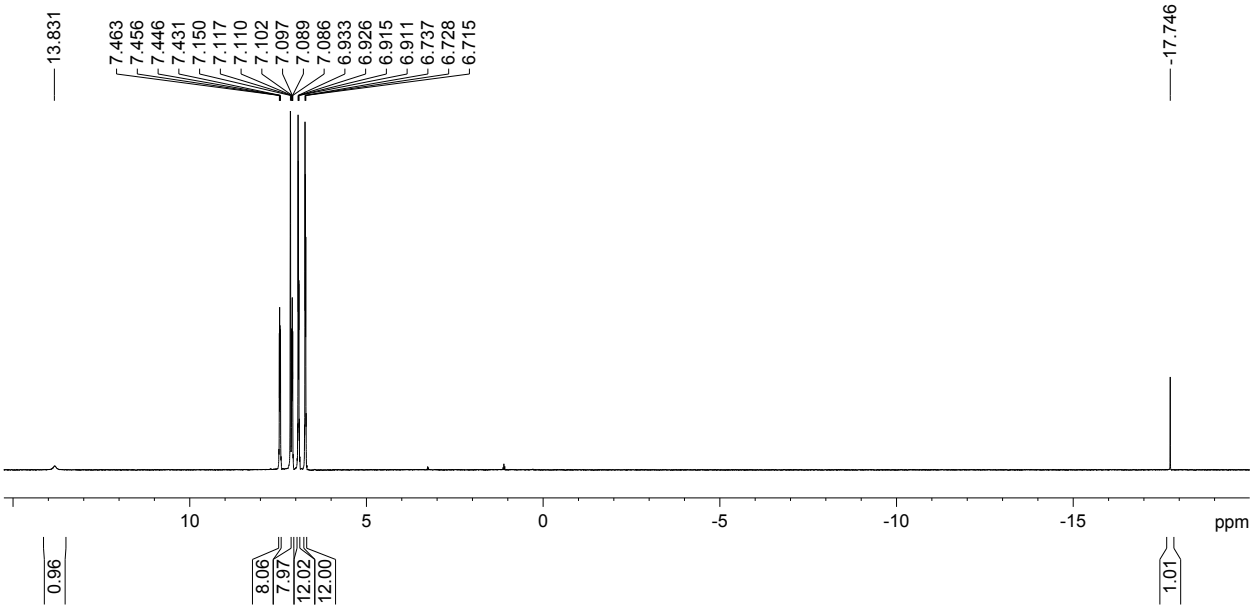


^{13}C NMR, 75.5 MHz, $CDCl_3$

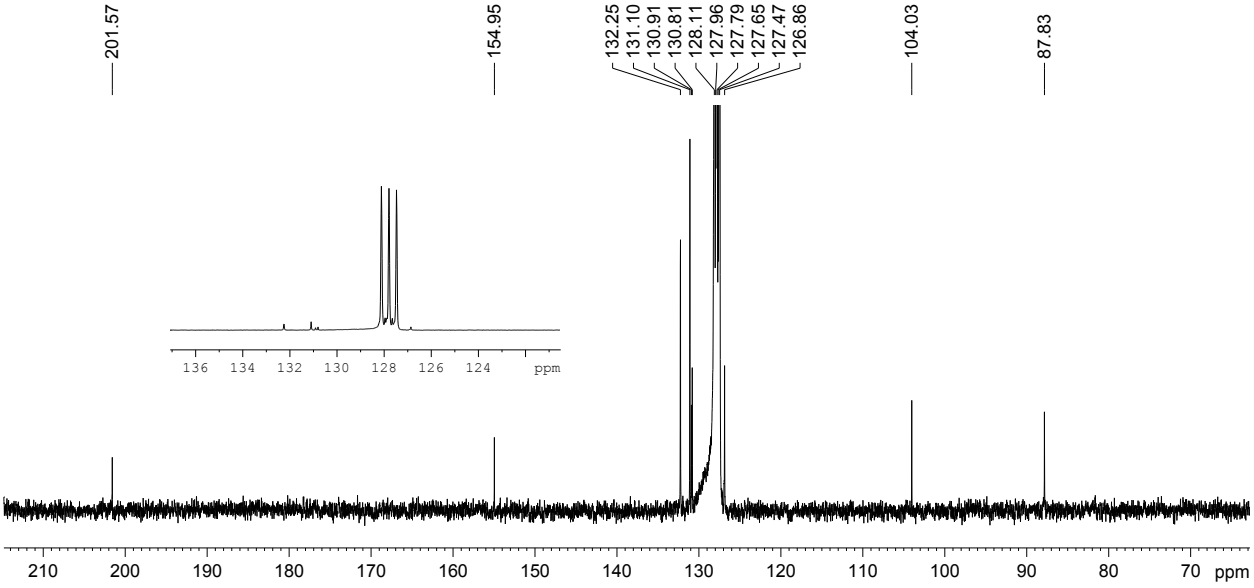


Shvo's Catalyst 6:

^{1}H NMR, 300 MHz, toluene-d_8

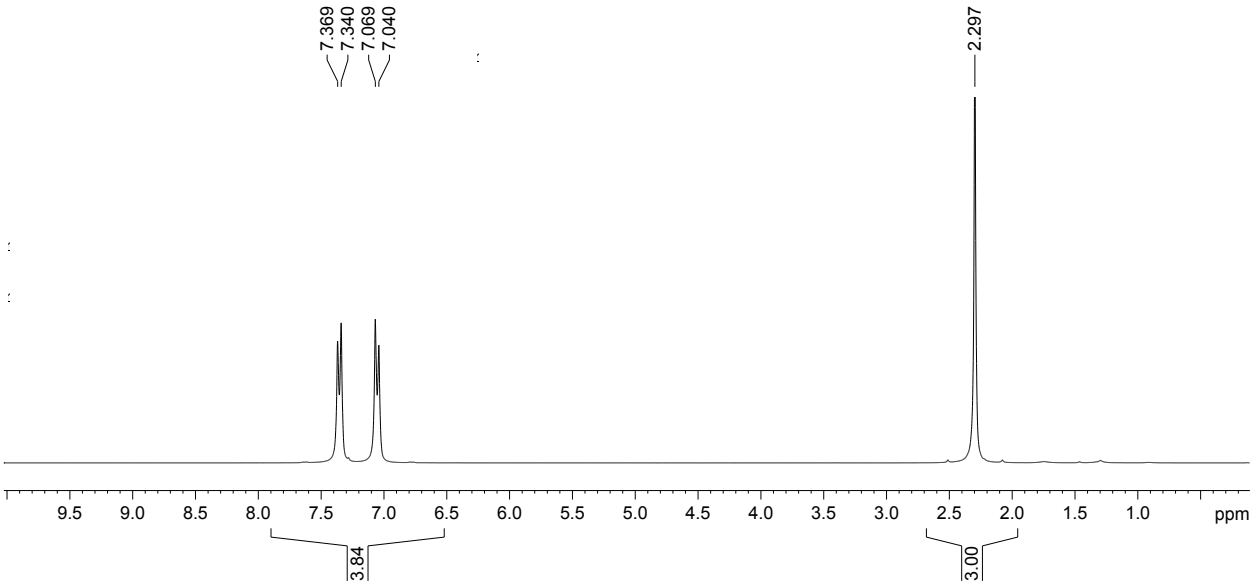


^{13}C NMR, 75.5 MHz, toluene-d_8

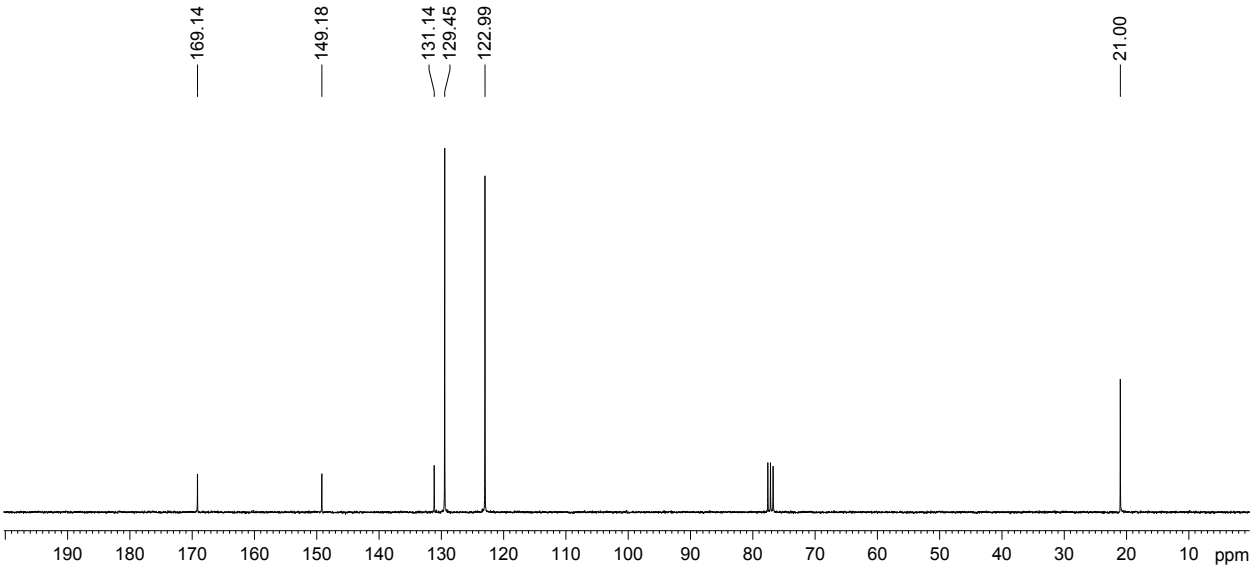


p-chlorophenyl acetate:

^{1}H NMR, 300 MHz, $CDCl_3$

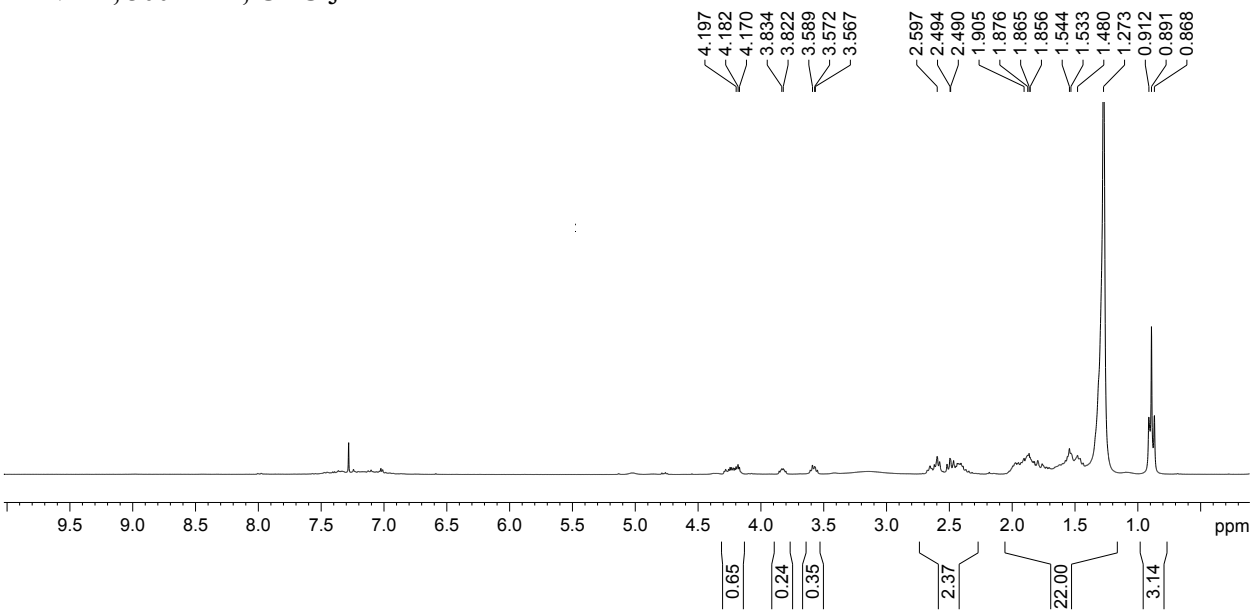


^{13}C NMR, 75.5 MHz, $CDCl_3$



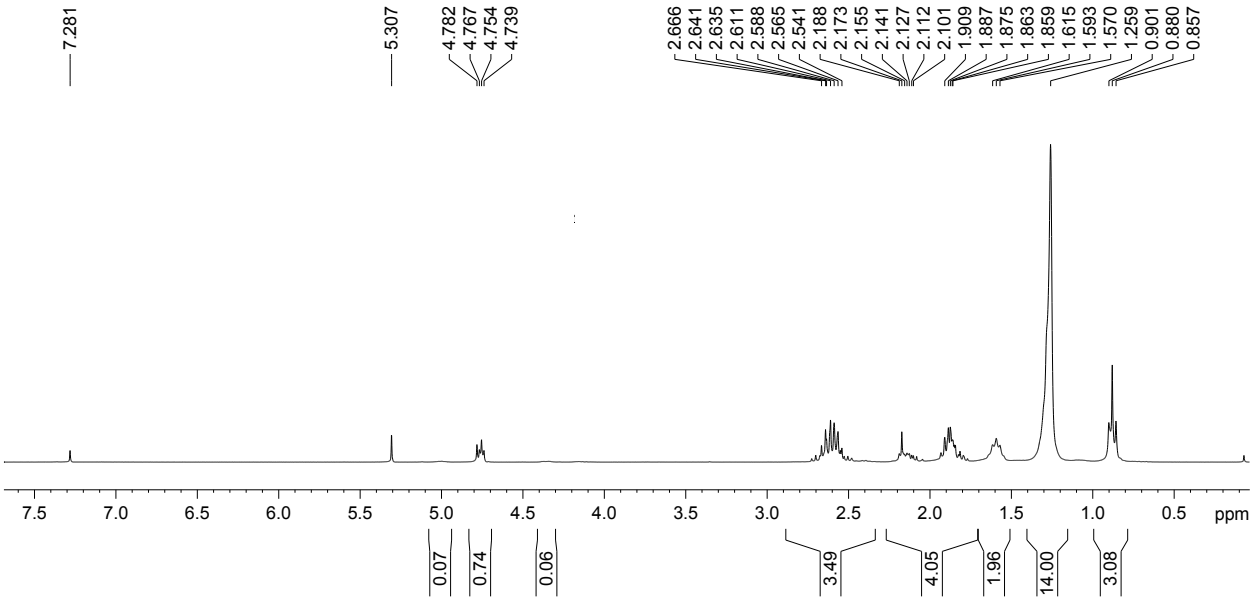
Epimerization between (±)-2 and (±)-8 using Shvo`s Catalyst 6:

^{1}H NMR, 300 MHz, $CDCl_3$

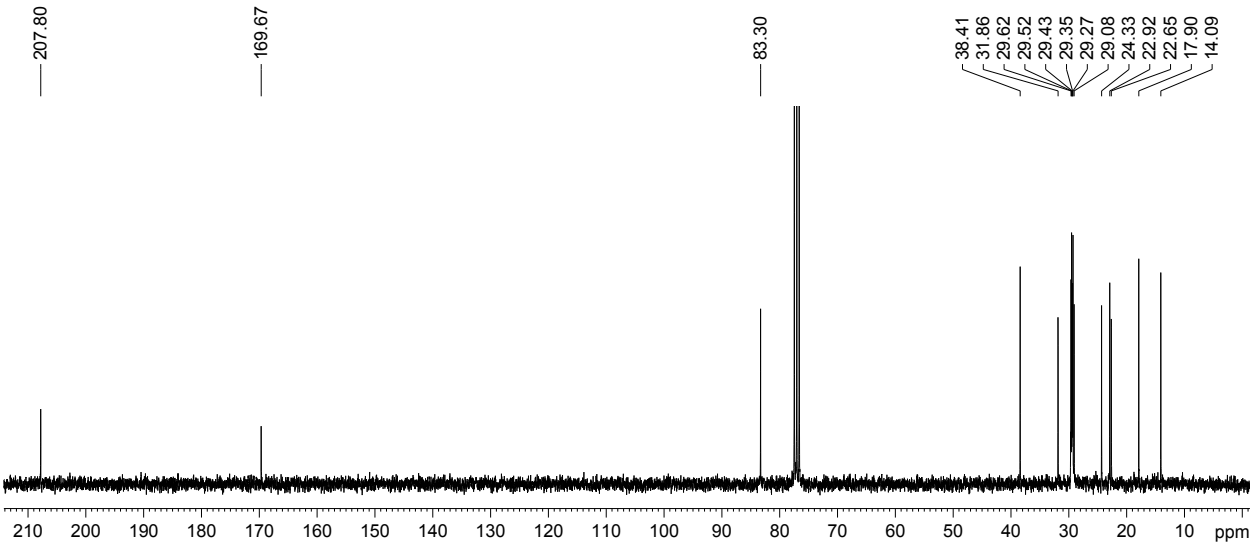


Product from Attempted DYKAT of (±)-2 using VA donor:

^{1}H NMR, 300 MHz, $CDCl_3$

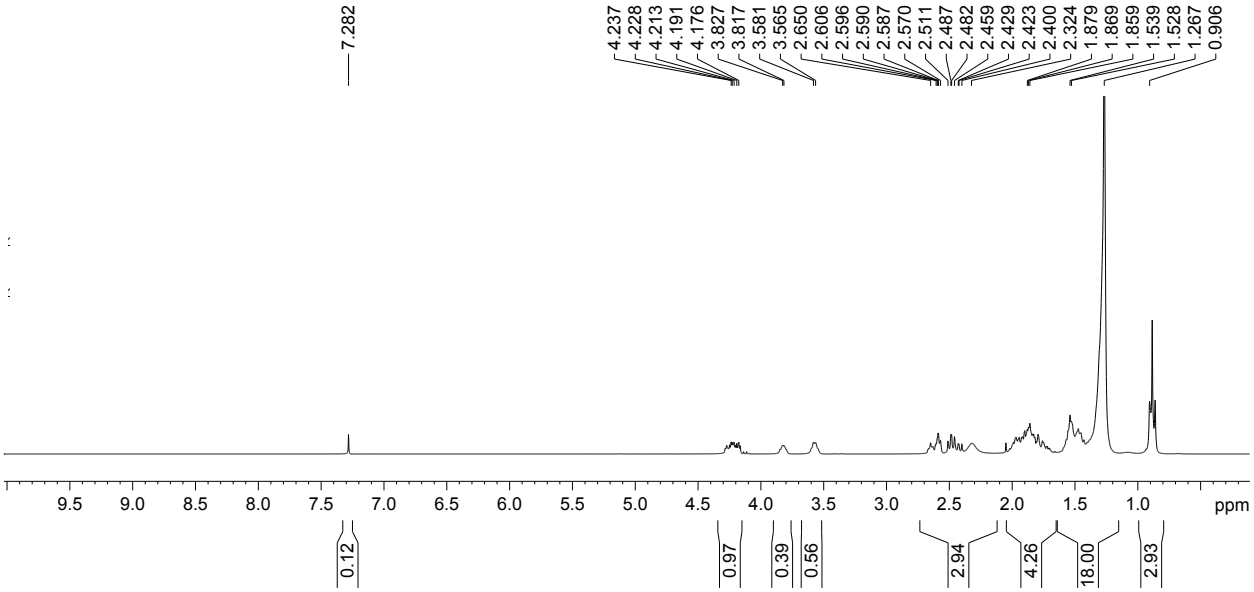


^{13}C NMR, 75.5 MHz, $CDCl_3$

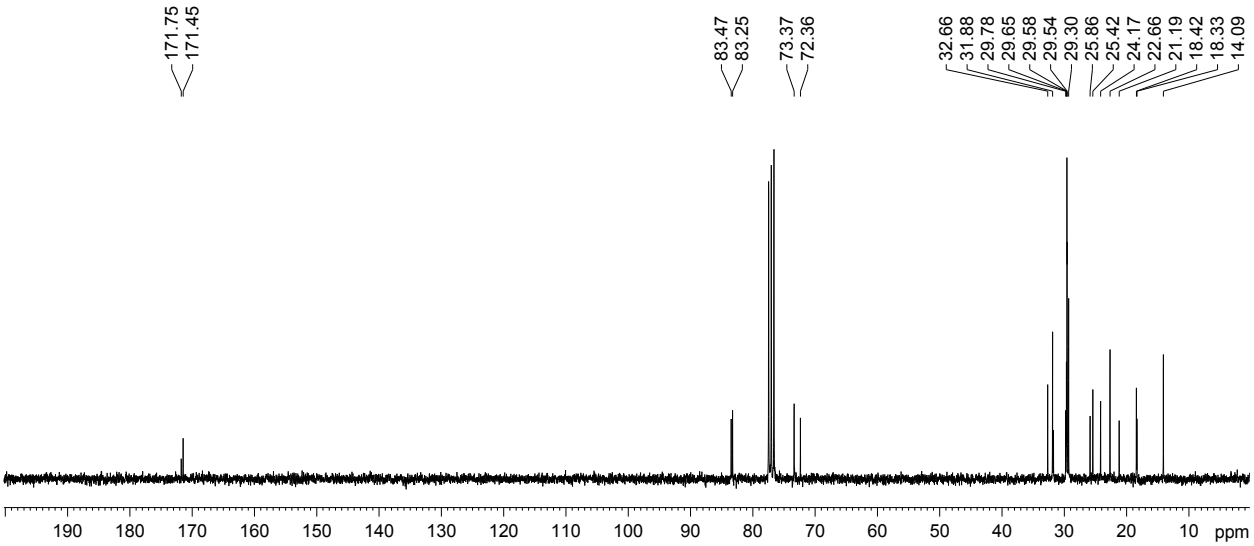


Starting Material from Attempted DYKAT of (±)-2 using VA donor:

^{1}H NMR, 300 MHz, $CDCl_3$

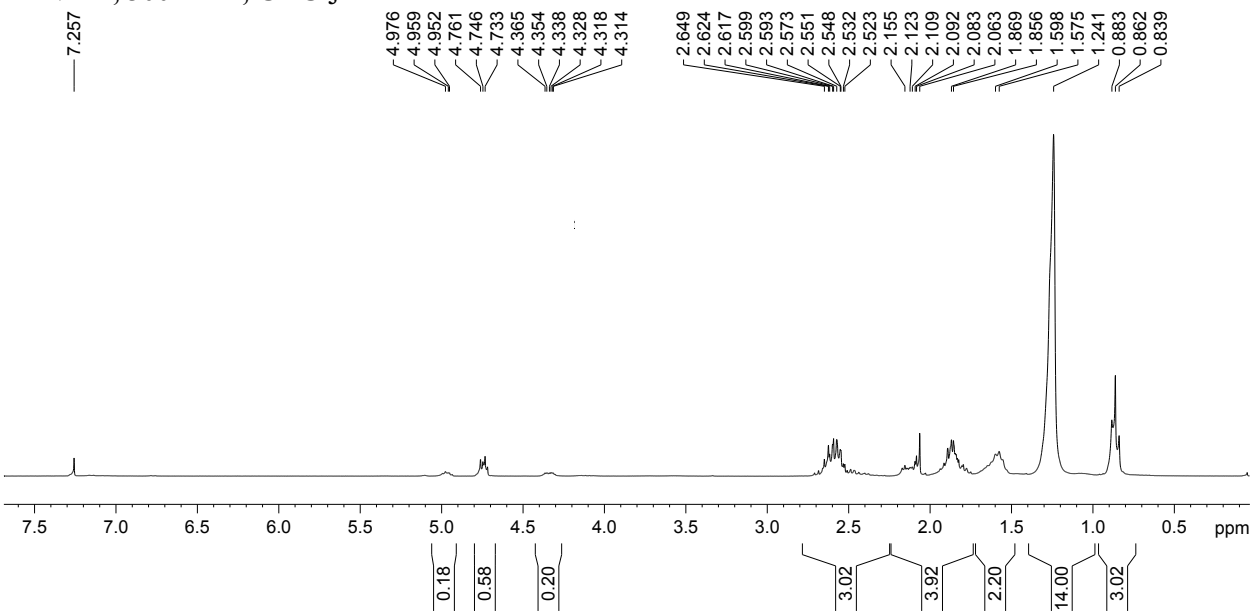


^{13}C NMR, 75.5 MHz, $CDCl_3$

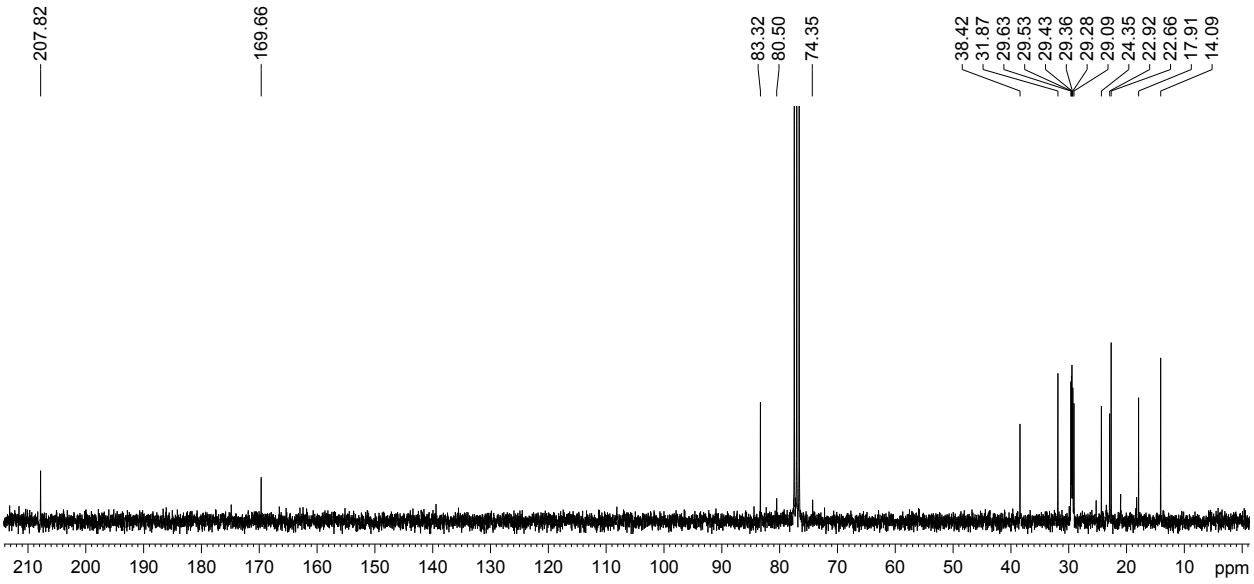


Representative DYKAT of chiral hydroxylactone (-)-2 using PCPA:

^{1}H NMR, 300 MHz, $CDCl_3$

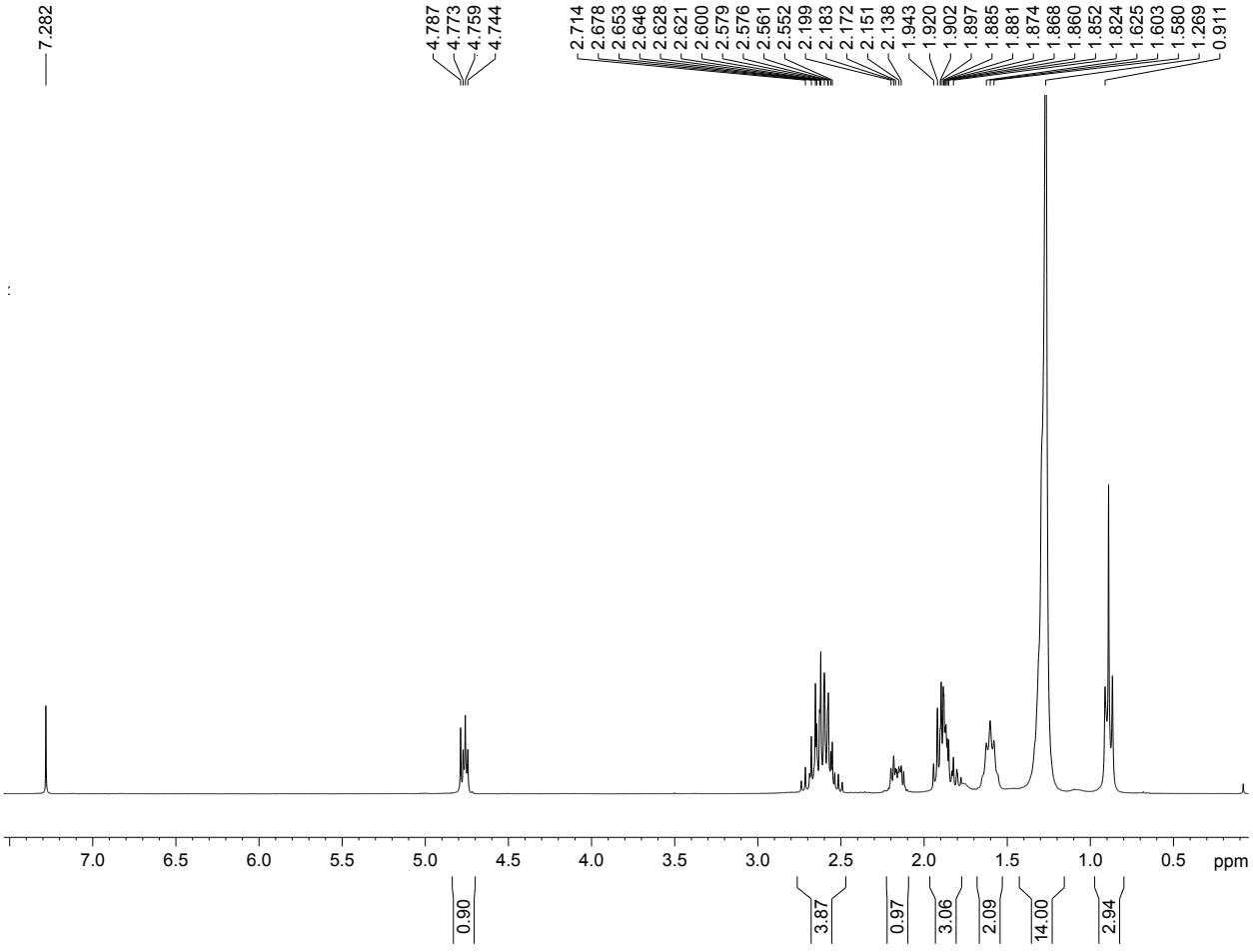


^{13}C NMR, 75.5 MHz, $CDCl_3$



(±)-6-oxy-5-hexadecanolide (±)-7:

^{1}H NMR, 300 MHz, $CDCl_3$



^{13}C NMR, 75.5 MHz, $CDCl_3$