

Diastereodivergent Total Synthesis of Racemic Mosquito Oviposition Pheromone

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Electronic Supporting Information

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1.0 Supporting Experimental Procedures

1.1 Synthesis of (Z)-5-hexadecenoic acid (7) using *t*-BuOK base (Table 1, entry 1 in text):

Phosphonium bromide (1.12 g, 2.53 mmol) and *t*-BuOK (750 mg, 6.33 mmol) were combined in a flame dried two neck flask equipped with an oval stir bar, a rubber septum on one neck and a vacuum adaptor connected to a two-line Schlenk tube on the side arm. The flask was evacuated then filled with N₂ three times then cooled to 0 °C in an ice bath, and charged with freshly distilled THF (4 ml), under N₂ and with stirring. The resulting deep orange slurry was stirred for 30 minutes then freshly distilled undecanal (464 mg, 2.72 mmol) was added dropwise over 30 minutes with vigorous stirring. The resulting pale yellow suspension was slowly allowed to warm to room temperature overnight. The cream coloured suspension was then concentrated and placed under 0.1 mmHg at 40 °C for 3 h. To the amorphous residue was added water (10 ml) and the flask was left overnight allowing triphenylphosphine oxide to precipitate. The resulting solution was filtered and brought to pH ~2 by slow addition of 2 % H₂SO₄ then extracted with Et₂O (4 x 4 ml), dried (MgSO₄), filtered and concentrated to afford a yellow oil (648 mg). The crude fatty acid residue (106 mg) was purified by flash chromatography (hexane then hexane/EtOAc 1:1) to afford the title compound as a clear colourless oil (47 mg, yield = 45 %, *Z:E* = 9:1). ¹H NMR (600 MHz, CDCl₃): 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 (600 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} .

The remaining crude extract (542 mg) was purified using the urea inclusion method as described in the main text to afford the title compound as a clear colourless oil (172 mg, yield = 32 %, $Z:E = 9:1$). ^1H 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 (600 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} .

1.3 Preparation of sodium *t*-amylate solution and determination of base:

1.3.1 Generation of amylate solution in toluene-THF

t-AmOH (100 ml) was heated under reflux with sodium (2.01 g) until sodium was dissolved. The resulting solution was distilled into dry toluene (100 ml) and sodium. The distillate was heated under reflux for 8 h then transferred hot *via* cannula into an oven dried glass bottle, fitted with a septum and containing dry THF (100 ml). The solution was stored under nitrogen and at -7°C .

1.3.2 Determination of Base concentration

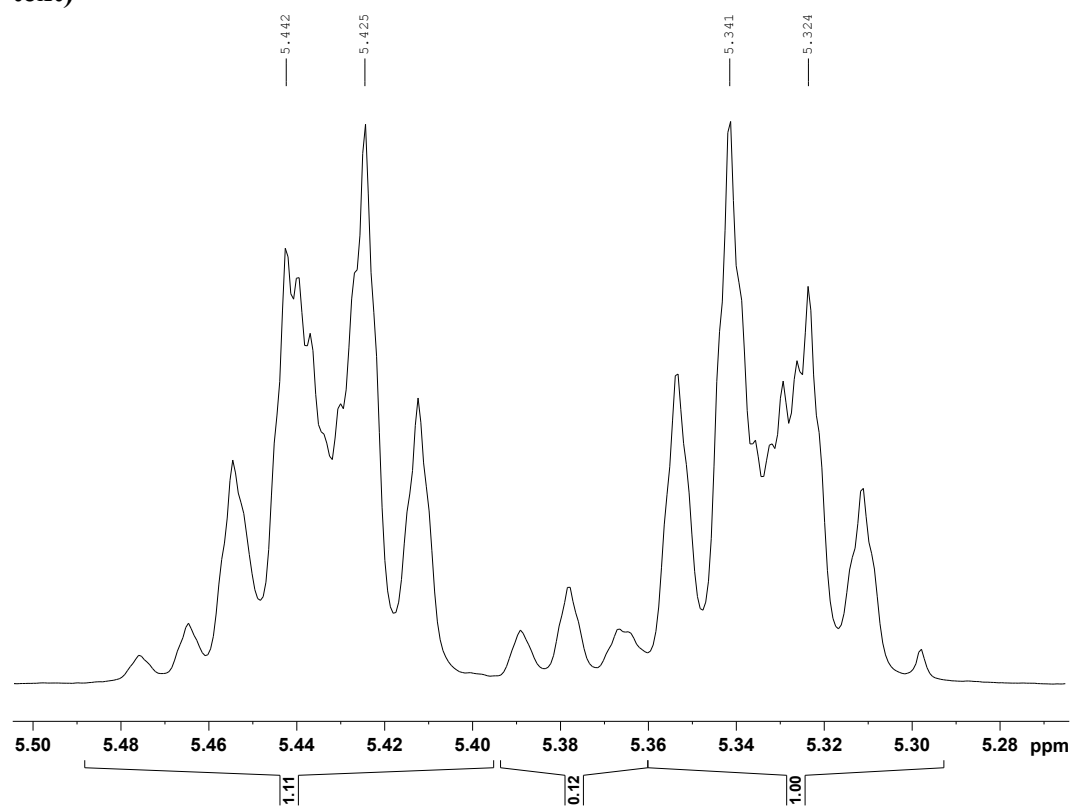
The above solution was warmed to room temperature then transferred (1.0 ml) to distilled water (10 ml) with phenolphthalein indicator. The mixture was titrated with HCl (1.0 M, 0.82 ml) until a colour change was observed.

2.0 Determination of *Z:E* Ratios

Z:E ratio was calculated as the ratio of *E*- and *Z*- olefinic proton multiplets by ^1H NMR. The corresponding spectra are provided below:

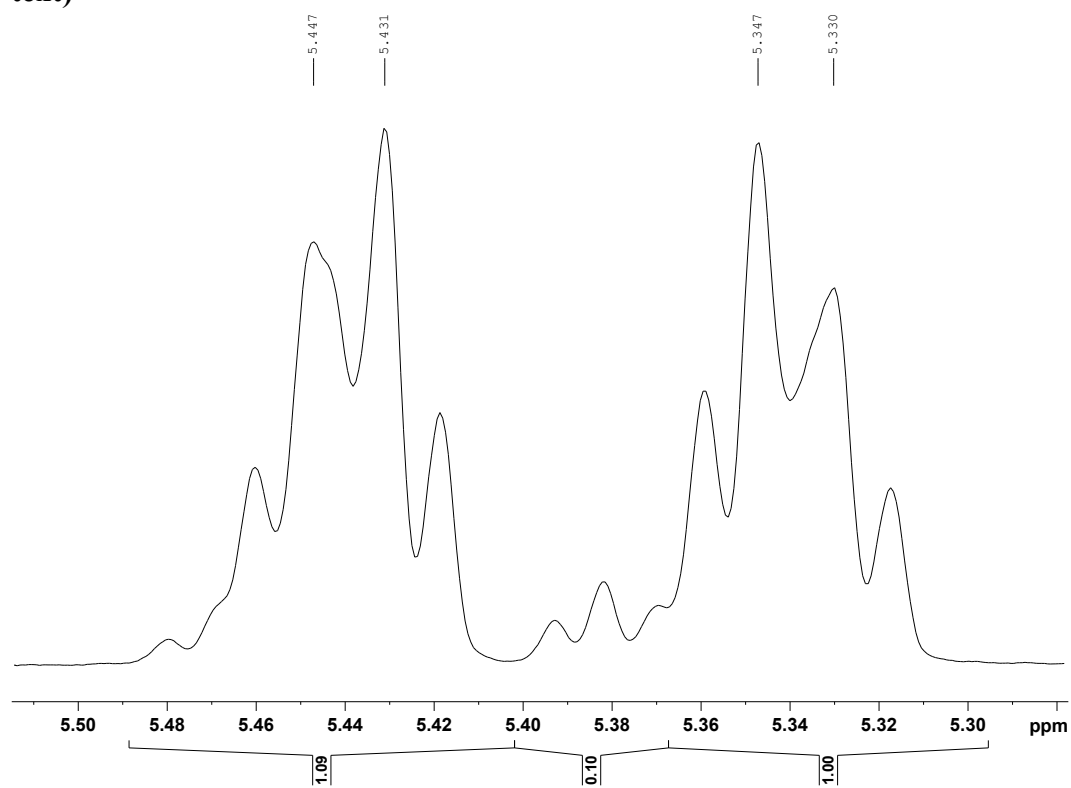
2.1 ^1H NMR Multiplet analyses:

2.1.1 Fatty acid 7 synthesized using *t*-BuOK and isolated from column (Table 1, Entry 1 in text)



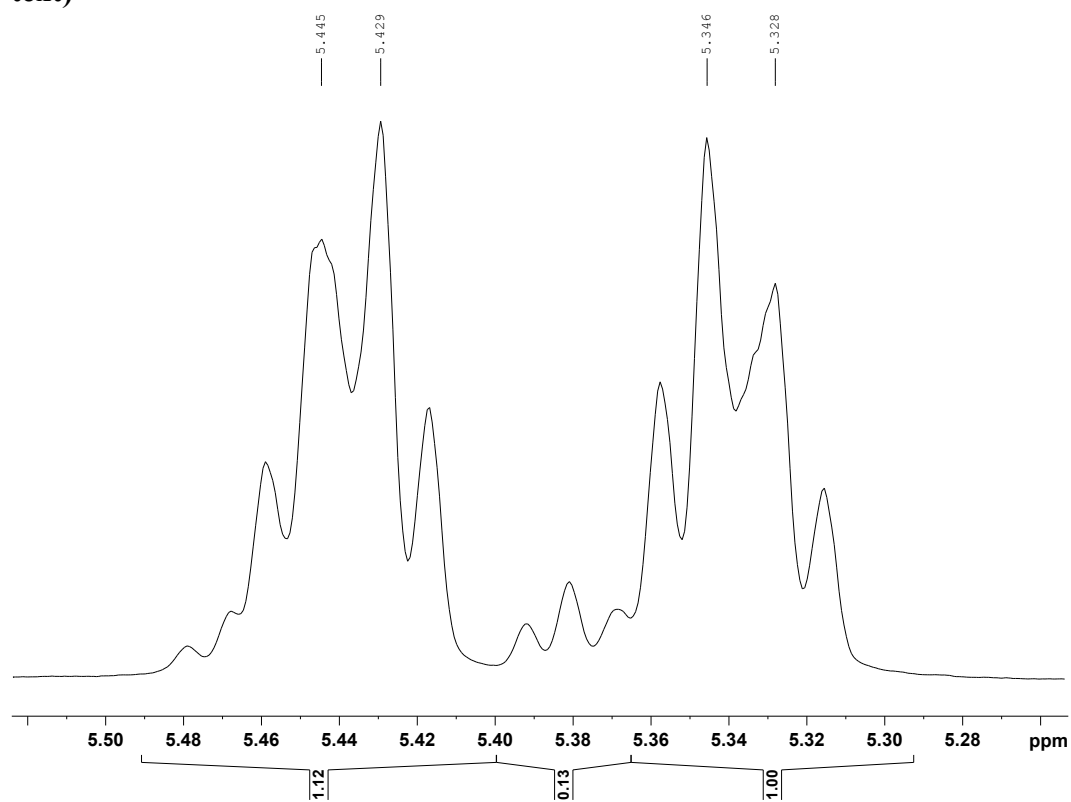
$J = 10.2$ Hz Major, $Z:E = 8:2$

2.1.2 Fatty acid 7 synthesized using *t*-BuOK and isolated from urea (Table 1, Entry 1 in text)



$J = 9.9$ Hz Major, $Z:E = 8:2$

2.1.3 Fatty acid 7 synthesized using *t*-AmONa and isolated from urea (Table 1, Entry 2 in text)

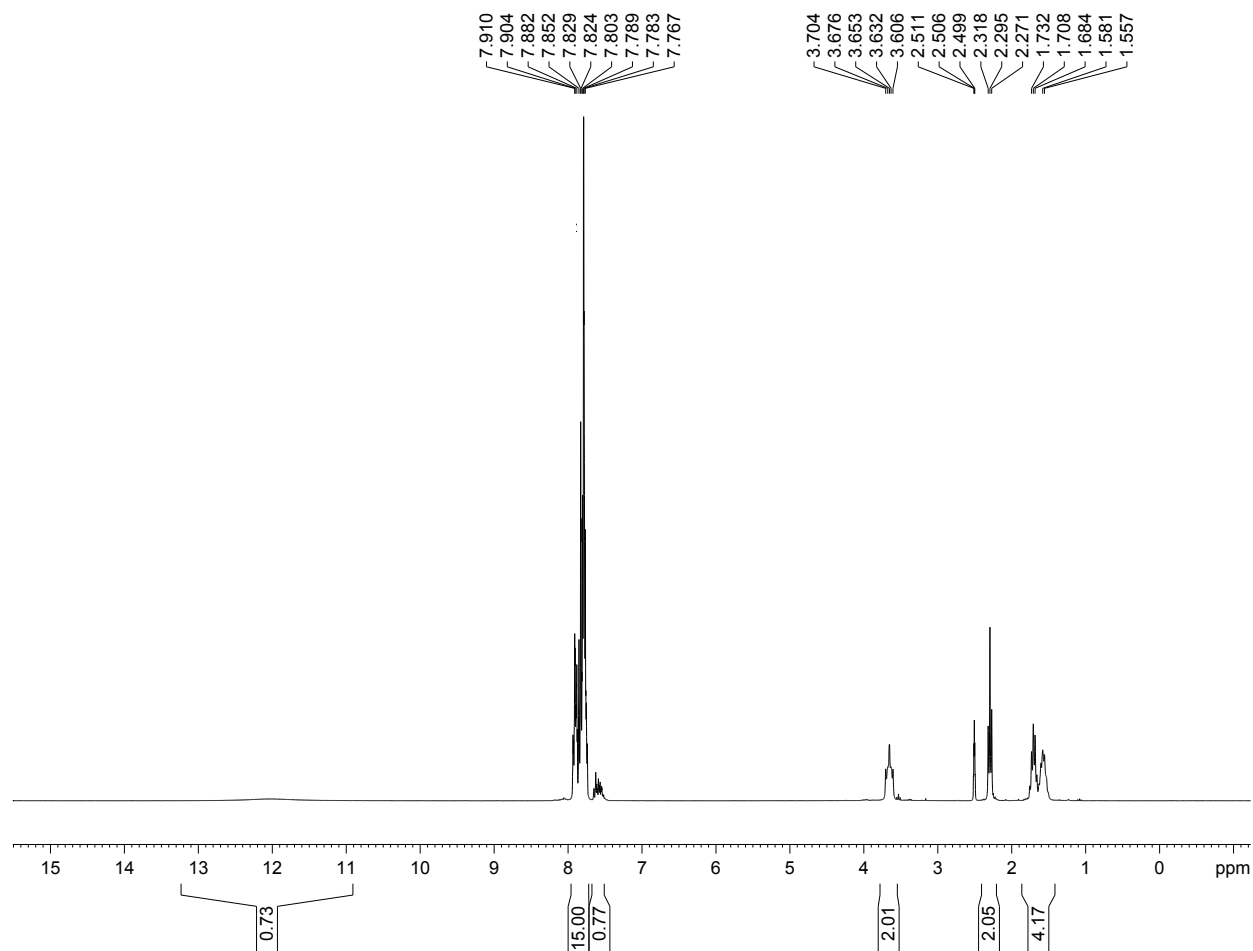


$J = 10.2$ Hz Major, $Z:E = 8:2$

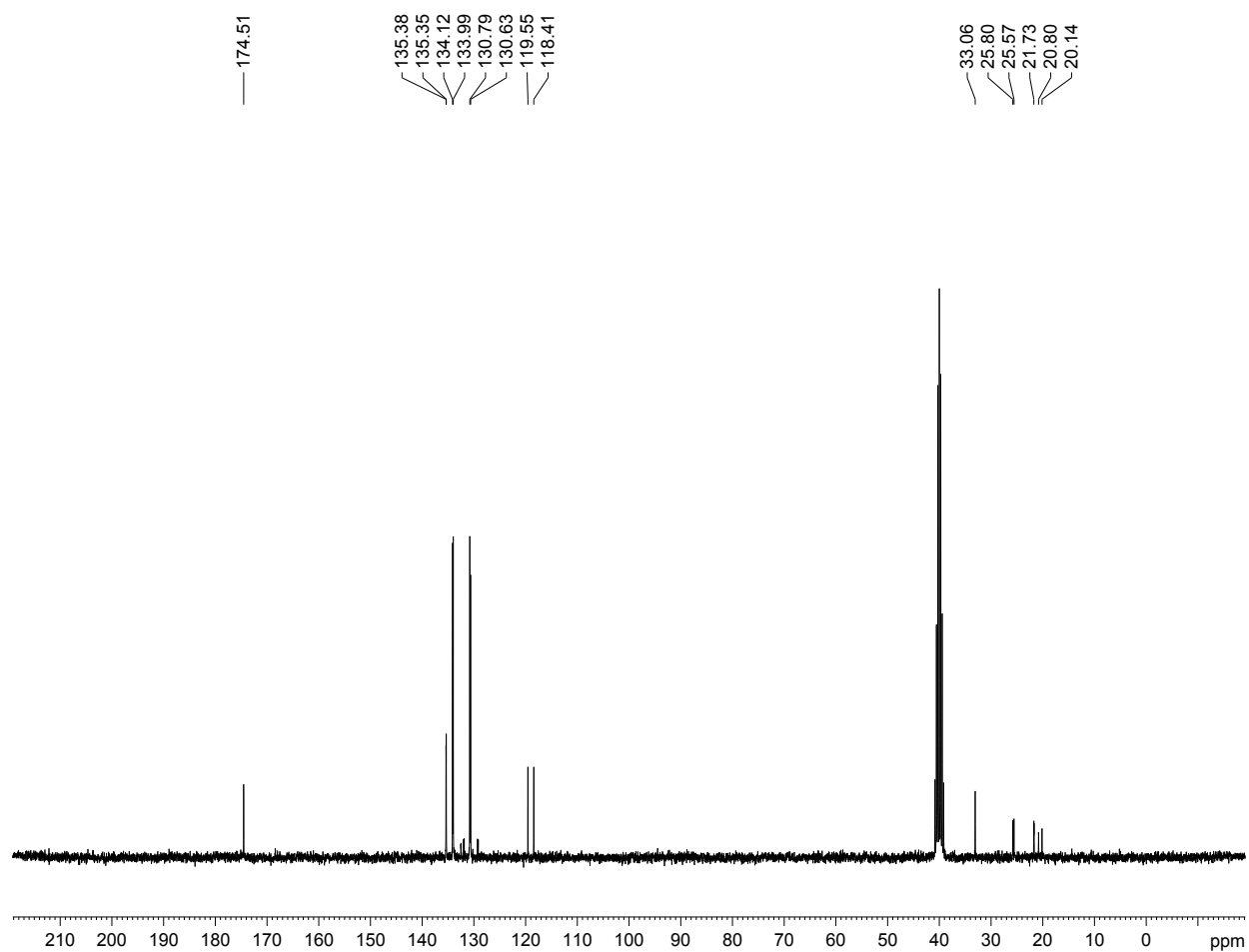
3.0 NMR Spectra of Isolated Products and Synthetic Intermediates

3.1 (4-carboxybutyl)triphenylphosphonium bromide (11):

^1H NMR, 300 MHz, $\text{DMSO}-d_6$

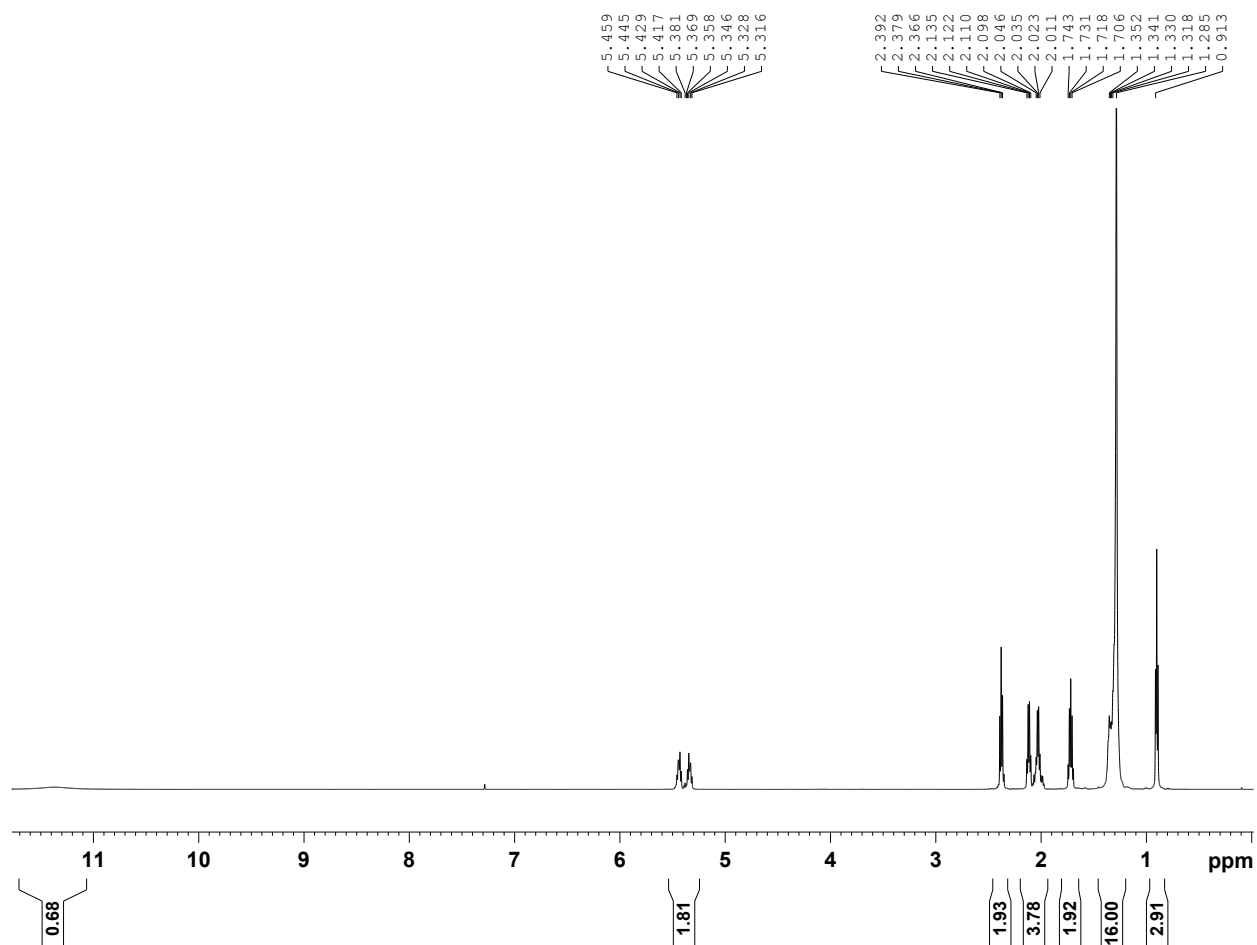


^{13}C NMR, 300 MHz, $\text{DMSO-}d_6$

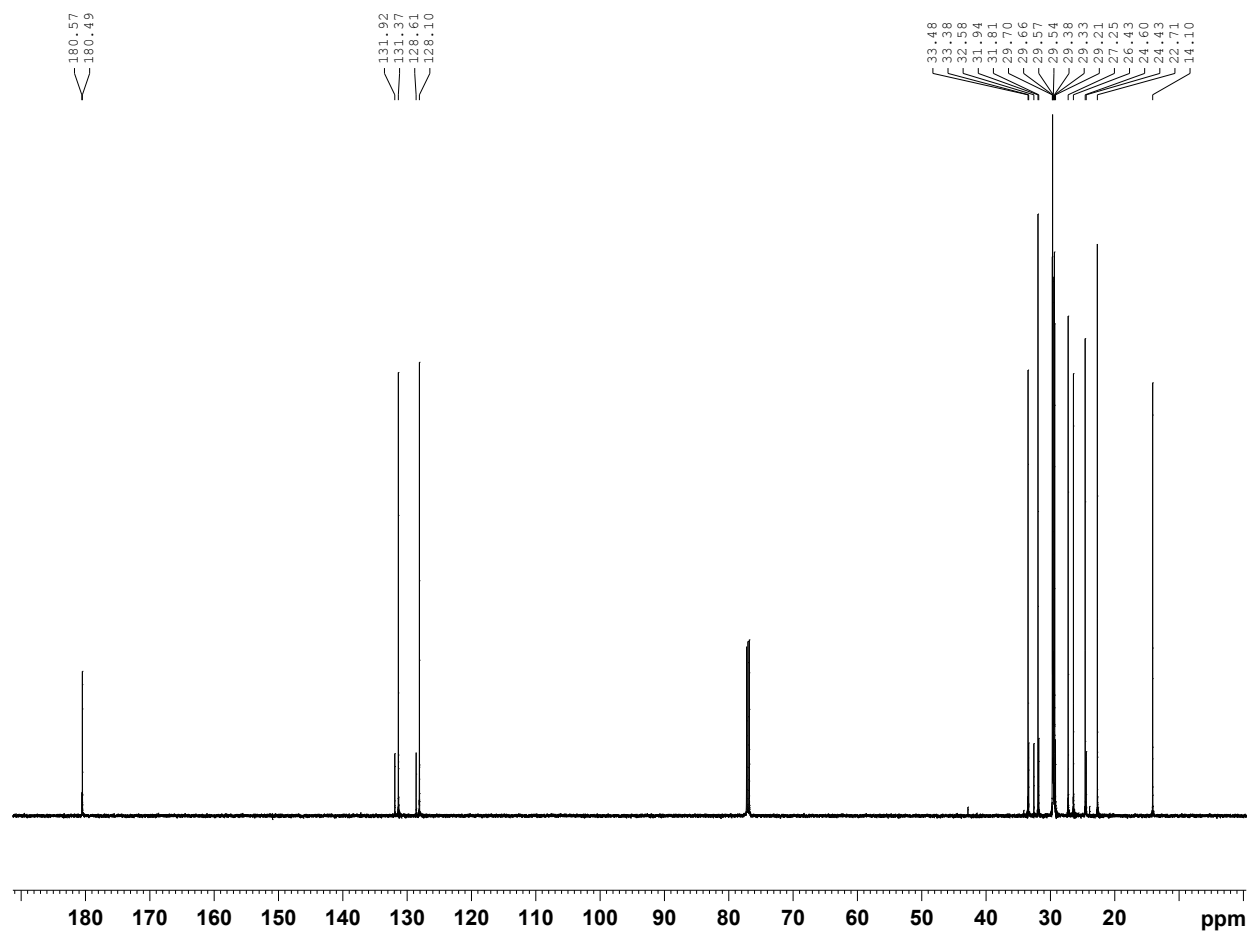


3.2 (*Z*)-5-hexadecenoic acid (7):

^1H NMR, 600 MHz, CDCl_3

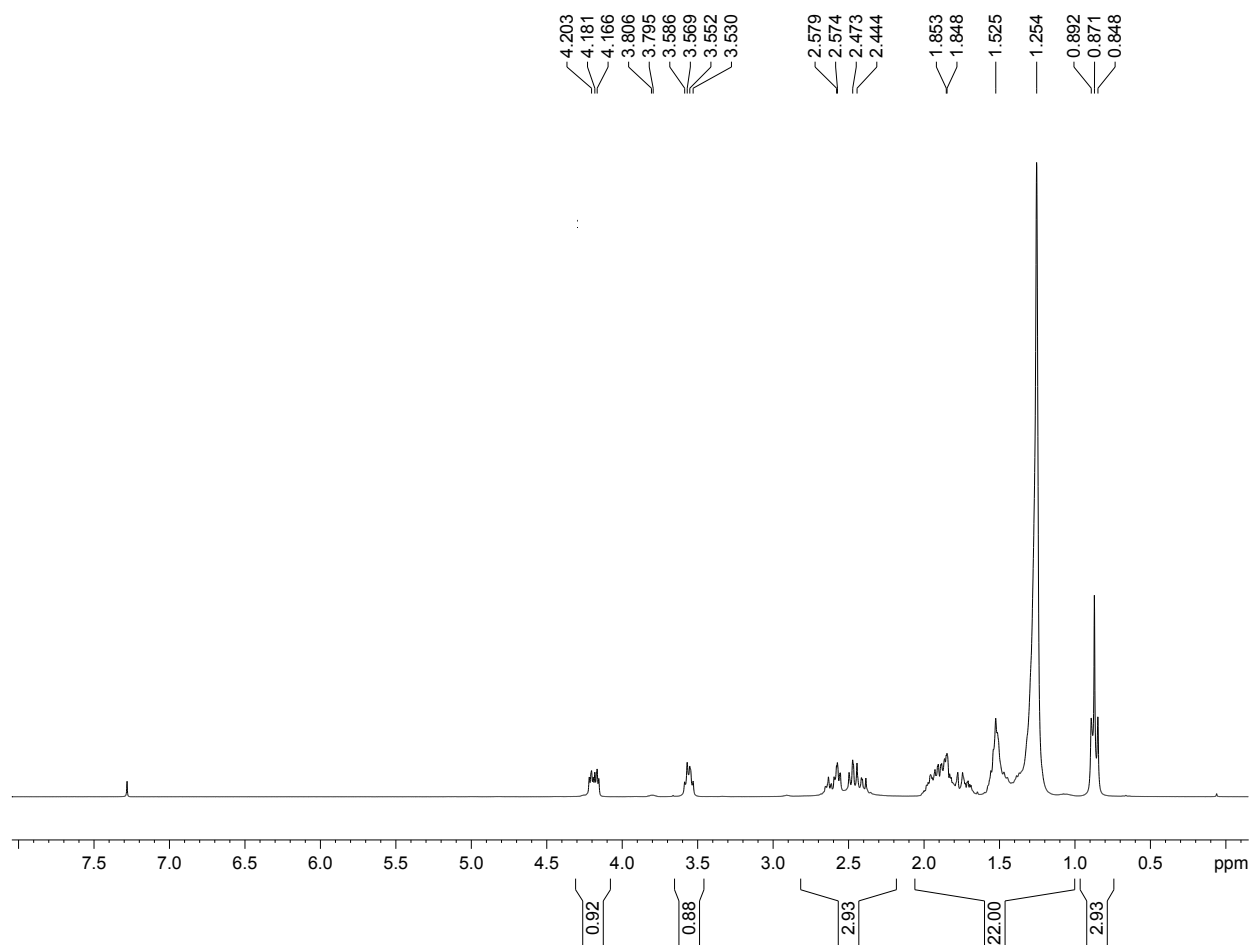


^{13}C NMR, 600 MHz, CDCl_3

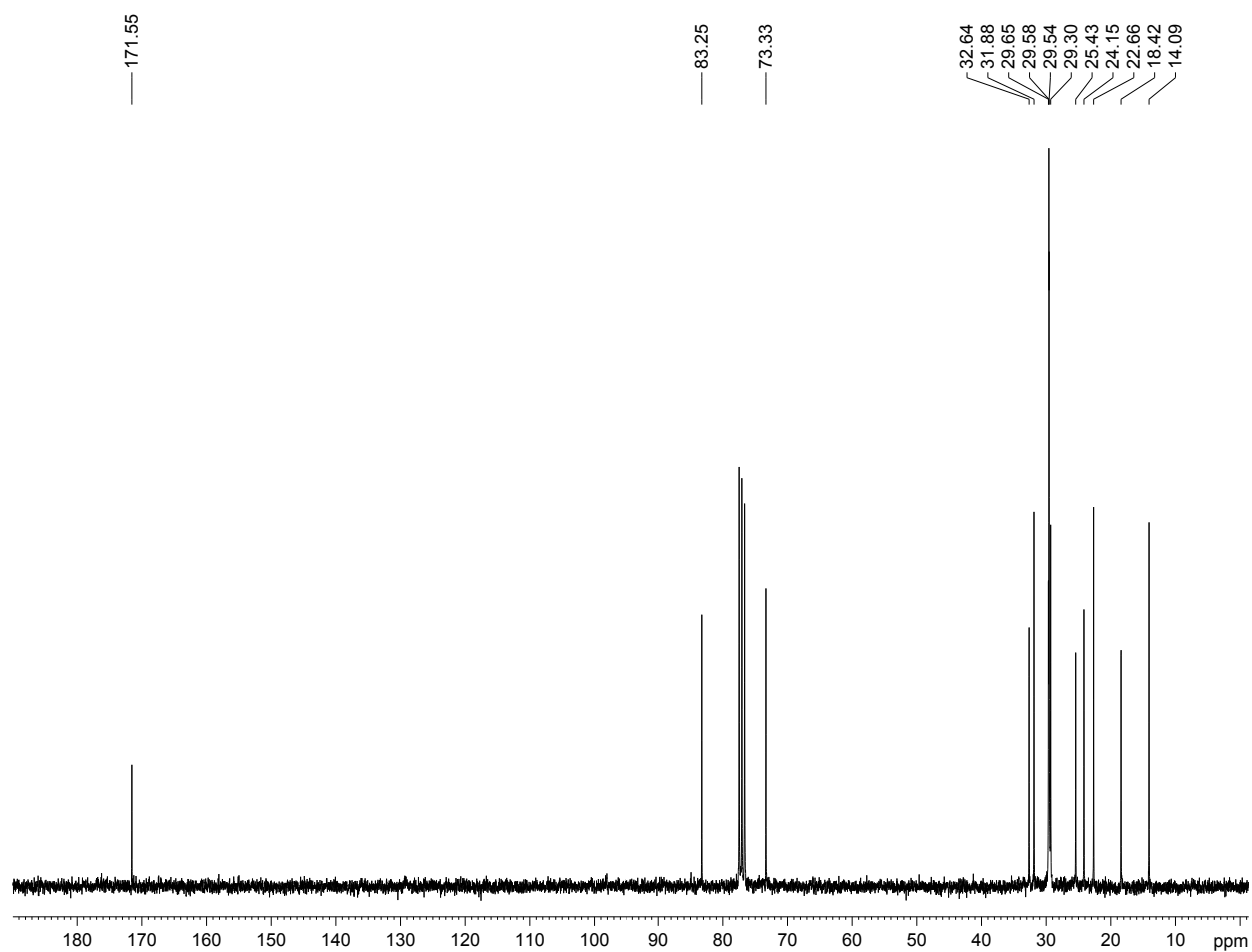


3.3 *threo*-6-hydroxy-5-hexadecanolide (8):

^1H NMR, 300 MHz, CDCl_3

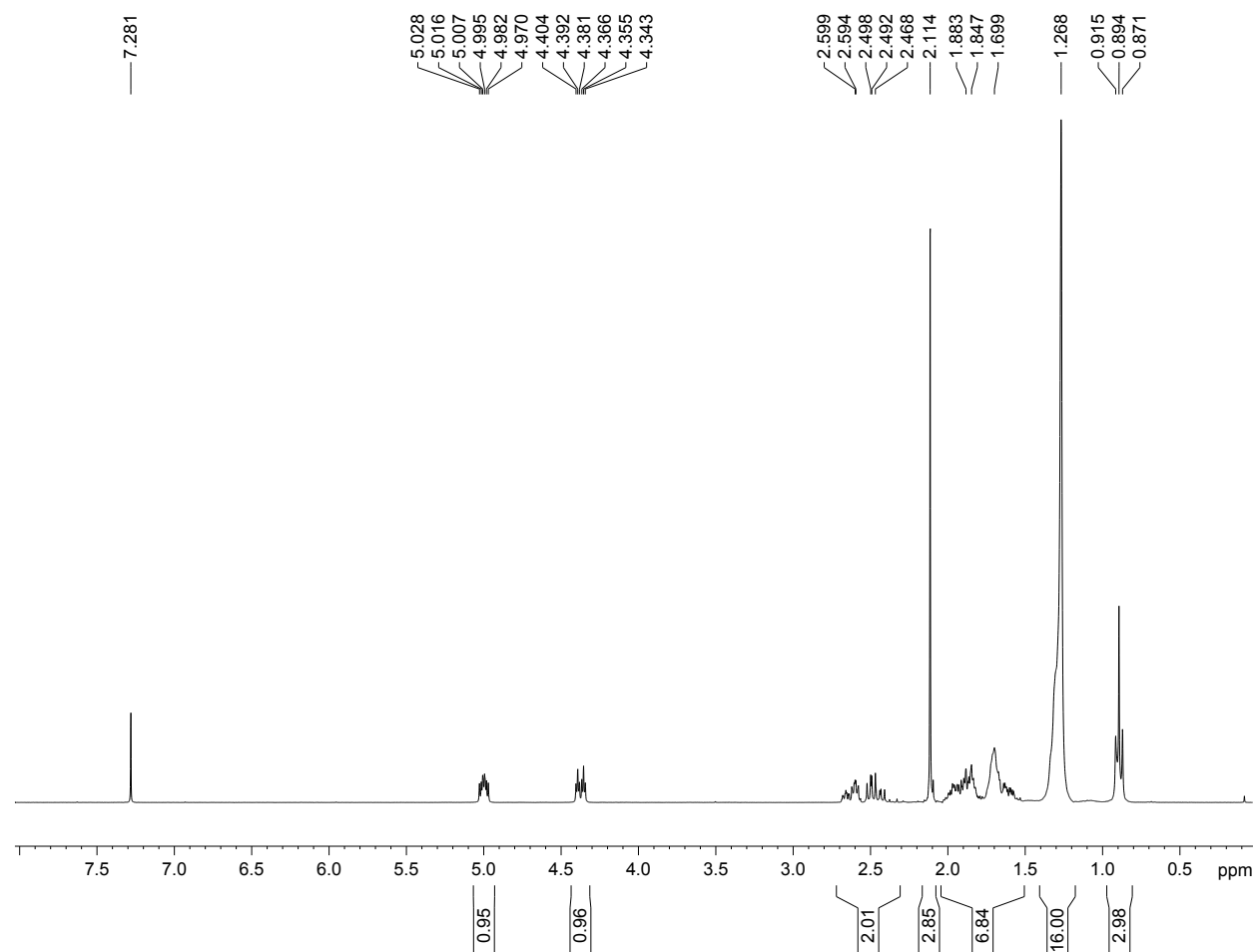


^{13}C NMR, 300 MHz, CDCl_3

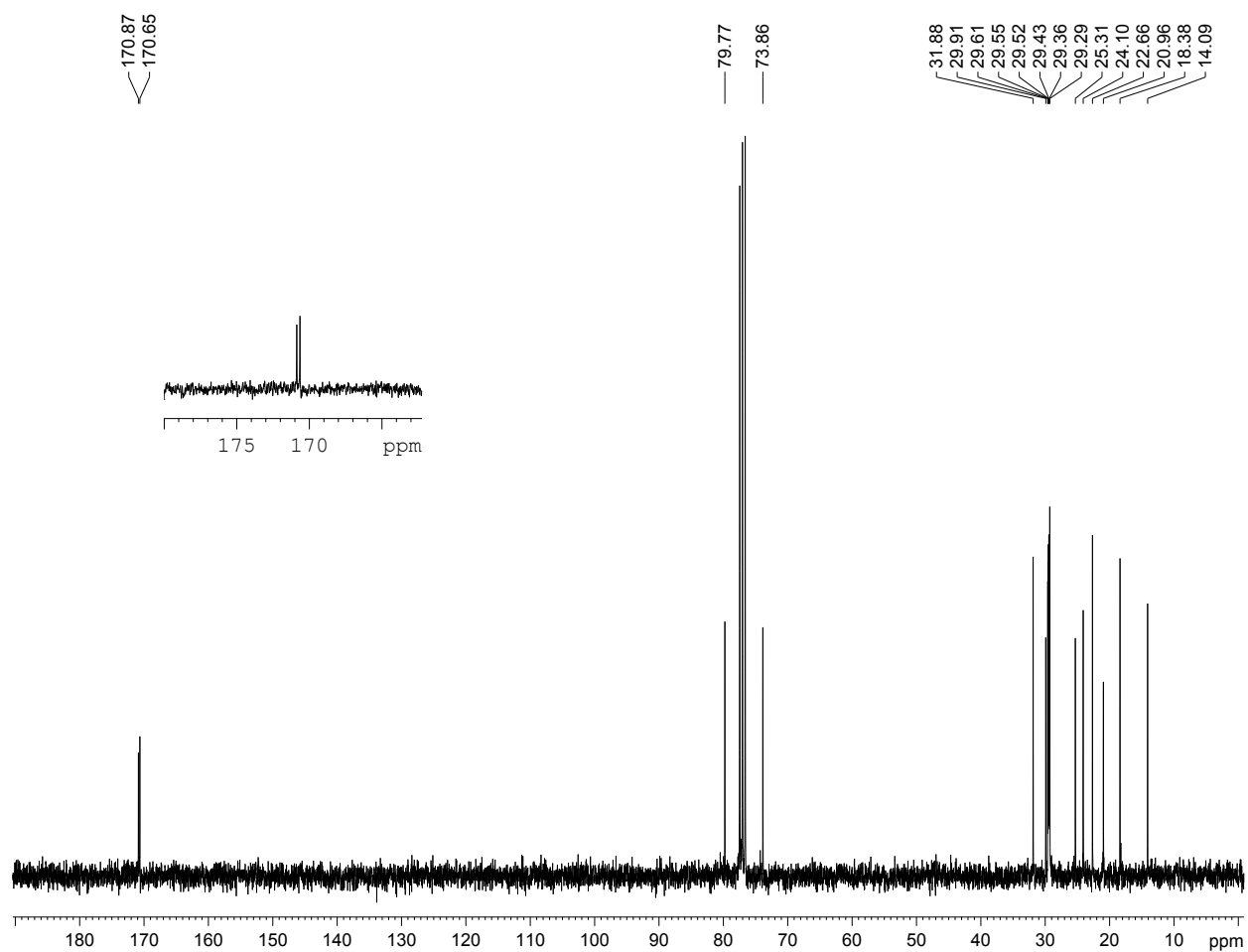


3.4 *threo*-6-acetoxy-5-hexadecanolide ((±)-2):

¹H NMR, 300 MHz, CDCl₃

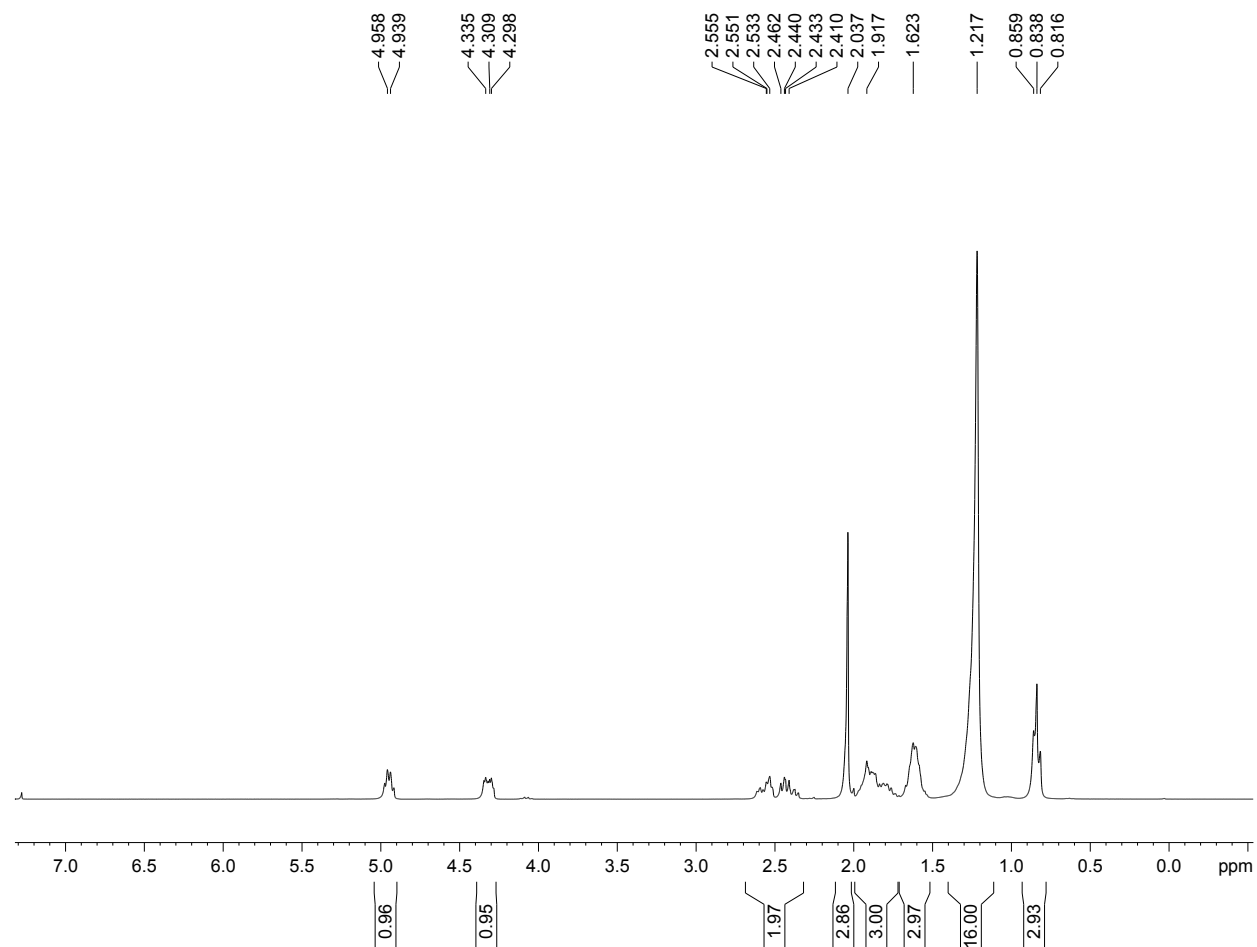


^{13}C NMR, 300 MHz, CDCl_3



3.5 *erythro*-6-acetoxy-5-hexadecanolide ((±)-1):

¹H NMR, 300 MHz, CDCl₃



^{13}C NMR, 300 MHz, CDCl_3

