Supplementary Material

Enantioselective synthesis of (-)-(5*R*,6*S*)-6-acetoxyhexadecan-5-olide *via* tandem α-aminooxylation-Henry reaction

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Experimental

General

All reactions were carried out under argon or nitrogen in oven-dried glassware using standard glass syringes and septa. The solvents and chemicals were purchased from Merck and Sigma Aldrich chemical company. Solvents and reagents were purified and dried by standard methods prior to use. Progress of the reactions was monitored by TLC using precoated aluminium plates of Merck kieselgel 60 F254. Column chromatography was performed on silica gel (60-120 and 100-200 mesh) using a mixture of *n*-hexane and ethyl acetate. Optical rotations were measured on automatic polarimeter AA-65. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ (unless otherwise mentioned) on JEOL ECS operating at 400 and 100 MHz, respectively. Chemical shifts are reported in δ (ppm), referenced to TMS. HRMS were recorded on Agilent 6530 Accurate-Mass Q-TOF using Electron Spray Ionization. IR spectra were recorded on Agilent resolution Pro 600 FT-IR spectrometer, fitted with a beam-condensing ATR accessory.

(*R*)-2-((*S*)-1-(Benzyloxy)undecyl)oxirane, 7

To a solution of **6** (100 mg, 0.47 mmol) in anhydrous DMF (4 mL) at 0 ^{o}C under N_2 atmosphere was added NaH (15 mg, 0.56 mmol) portion wise and stirred for 10 min. Then a solution of benzyl bromide (72 μL, 0.61 mmol) in DMF (1 mL) was added to the reaction mixture at the same temperature. After an additional 1 h, it was warmed to room temperature and stirred for another 3 h. The reaction mixture was then quenched with ice cooled water and extracted with EtOAc (3 x 20 mL). The combined organic phase was washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The residual product was subjected to silica gel column chromatography to furnish epoxide derivative **7** (131 mg, 92%). [R_f = 0.4, EtOAc/hexane 1:9 v/v]; $[\alpha]_D^{25}$ -16.88 (*c* 1.0, $CHCl_3$); IR (CH_2Cl_2) *v*: 2921, 2850, 1465, 1053, cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.39-7.27 (m, 5H), 4.65 (d, *J* = 12.08 Hz, 1H), 4.50 (d, *J* = 11.4 Hz, 1H), 3.28-3.23 (m, 1H), 2.95-2.92 (m, 1H), 2.80-2.77 (m, 1H), 2.73-2.70 (m, 1H), 1.68-1.62 (m, 2H), 1.40-1.20 (m, 16H), 0.88 (t, *J* = 7.08 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 138.5, 128.3, 127.8,

127.6, 78.0, 72.2, 53.6, 45.6, 32.8, 31.9, 29.6, 29.5, 29.3, 25.2, 22.7, 14.1; HRMS (ESI)$^+$ m/z calcd for $C_{20}H_{33}O_2^+$ [M+H$^+$] 305.2425; found 305.2427.

Benzyl (5*R*,6*S*)-6-(benzyloxy)-5-hydroxyhexadec-2-ynoate, 8

n-BuLi (2.5 M in hexanes, 0.13 mL, 0.66 mmol) was added dropwise *via* syringe to a flame-dried round-bottomed flask charged with ethyl propiolate (66 mg, 0.66 mmol) in THF (4 mL) at -78 °C. After 1 h, epoxide derivative **7** (100 mg, 0.33 mmol) was added dropwise, followed by $BF_3{\cdot}OEt_2$ (40 μL, 0.66 mmol) at -78 °C and the mixture was stirred for an additional 2 h. Then the reaction was quenched with saturated solution of $NaHCO_3$ and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic layer was dried with anhydrous Na_2SO_4 and concentrated under reduced pressure. Purification by silica gel column chromatography (EtOAc/hexane, 1:3) provided alcohol derivative **8** (107 mg, 81%) as a colourless oil. [R_f = 0.5, EtOAc/hexane 1:1 v/v]; $[\alpha]^D_{25}$ +24.1 (*c* 1.0, $CHCl_3$), {lit.[25] $[\alpha]^D_{25}$ +23 (*c* 1.21, CH_2C1_2)}; IR (CH_2Cl_2) *v*: 3460, 2914, 2235, 1720, 1460, 1368, 1250, cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.38-7.27 (m, 5H), 4.58 (q, *J* = 17.88, 11.48 Hz, 2H), 4.22 (q, *J* = 14.2, 7.32 Hz, 2H), 3.99-3.93 (m, 1H), 3.53-3.47 (m, 1H), 2.62-2.58 (m, 2H), 2.32 (brd, 1H), 1.70-1.60 (m, 2H), 1.56-1.20 (m, 19H), 0.88 (t, *J* = 6.88 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 153.5, 138.0, 128.5, 128.4, 127.8, 85.9, 80.7, 74.7, 72.4, 70.4, 61.9, 31.8, 29.7, 29.6, 29.5, 29.3, 25.1, 24.1, 22.7, 22.6,14.1, 14.0; HRMS (ESI)$^+$ m/z calcd for $C_{25}H_{39}O_4^+$ [M+H$^+$] 403.2848; found 403.2825.

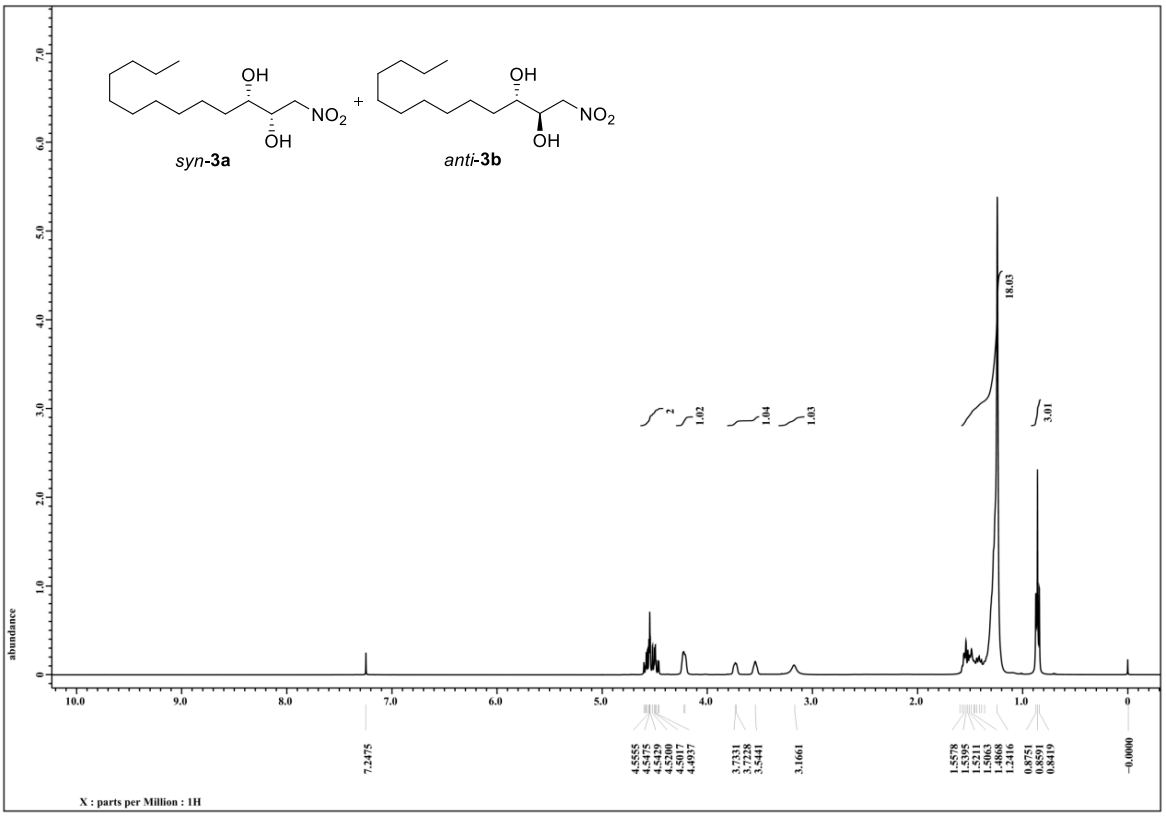
(*R*)-6-((*S*)-1-Hydroxyundecyl)tetrahydro-2*H*-pyran-2-one, 9

Palladium on activated carbon (Pd/C, 10%) was added to a methanolic solution of **8** (50 mg, 0.12 mmol) and the resulting mixture was stirred under an atmosphere of hydrogen for 12 h at rt. Then, Pd catalyst was filtered off through a pad of Celite and the filtrate was concentrated *in vacuo* to provide crude alcohol as a white solid which was used for next step directly.

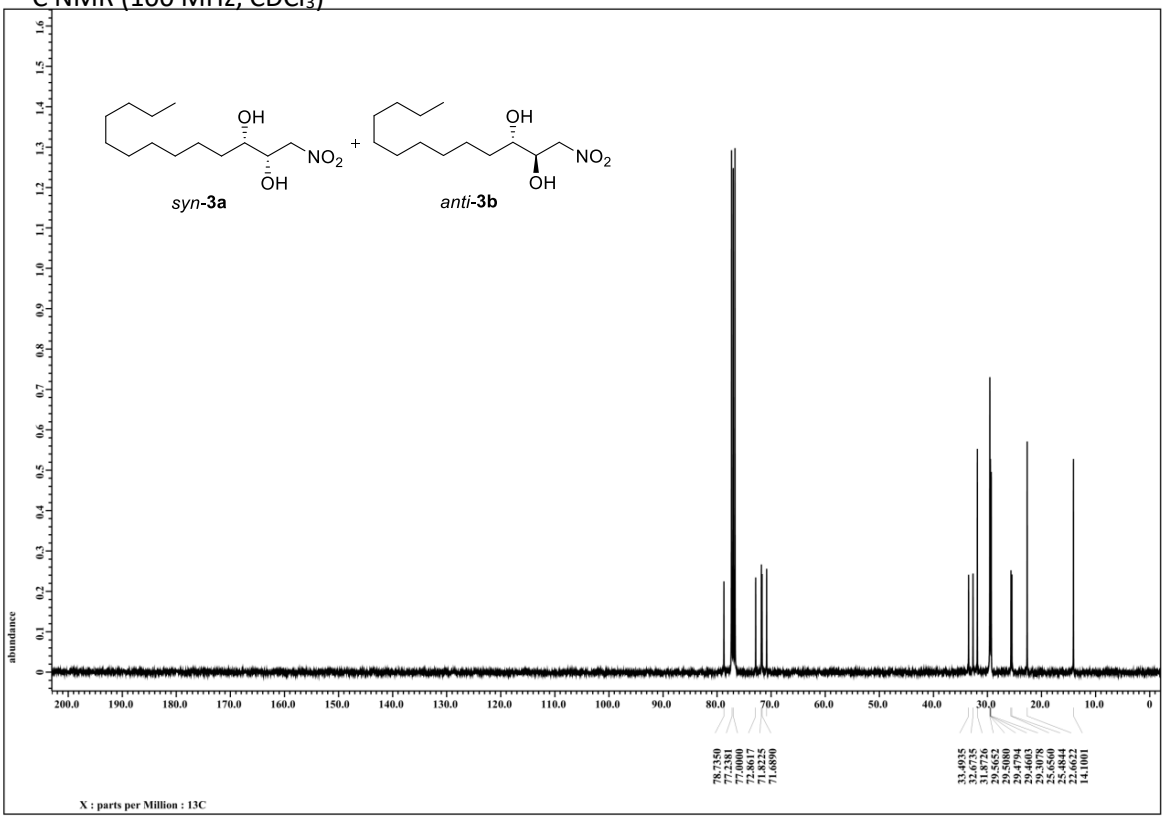
Catalytic amount of *p*-TSA was added to a stirred solution of above crude in benzene and the mixture was allowed to be refluxed for 1 h. Then, the reaction mixture was quenched by saturated aqueous solution of $NaHCO_3$ and extracted with EtOAc (3 x 10 mL). The organic layer was washed with brine solution, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Silica gel column chromatography of the crude afforded **9** (29

mg, 91%) as a white solid. [R_f = 0.5, EtOAc/hexane 1:1 v/v]; $[\alpha]_D^{25}$ -10.86 (*c* 0.8, $CHCl_3$); IR (CH_2Cl_2) *v*: 3280, 2935, 2861, 1710, 1468, 1253 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 4.27-4.23 (m, 1H), 3.85-3.80 (m, 1H), 2.65-2.58 (m, 1H), 2.50-2.41(m, 1H), 2.04-1.71 (m, 4H),1.65-1.40 (m, 4H), 1.38-1.26 (m, 15H), 0.88 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.7, 83.4, 72.4, 31.9, 31.6, 29.8, 29.6, 29.5, 29.3, 25.9, 22.7, 21.2, 18.3, 14.1; HRMS $(ESI)^+$ m/z calcd for $C_{16}H_{31}O_3^+$ $[M+H^+]$ 271.2273; found 271.2269.

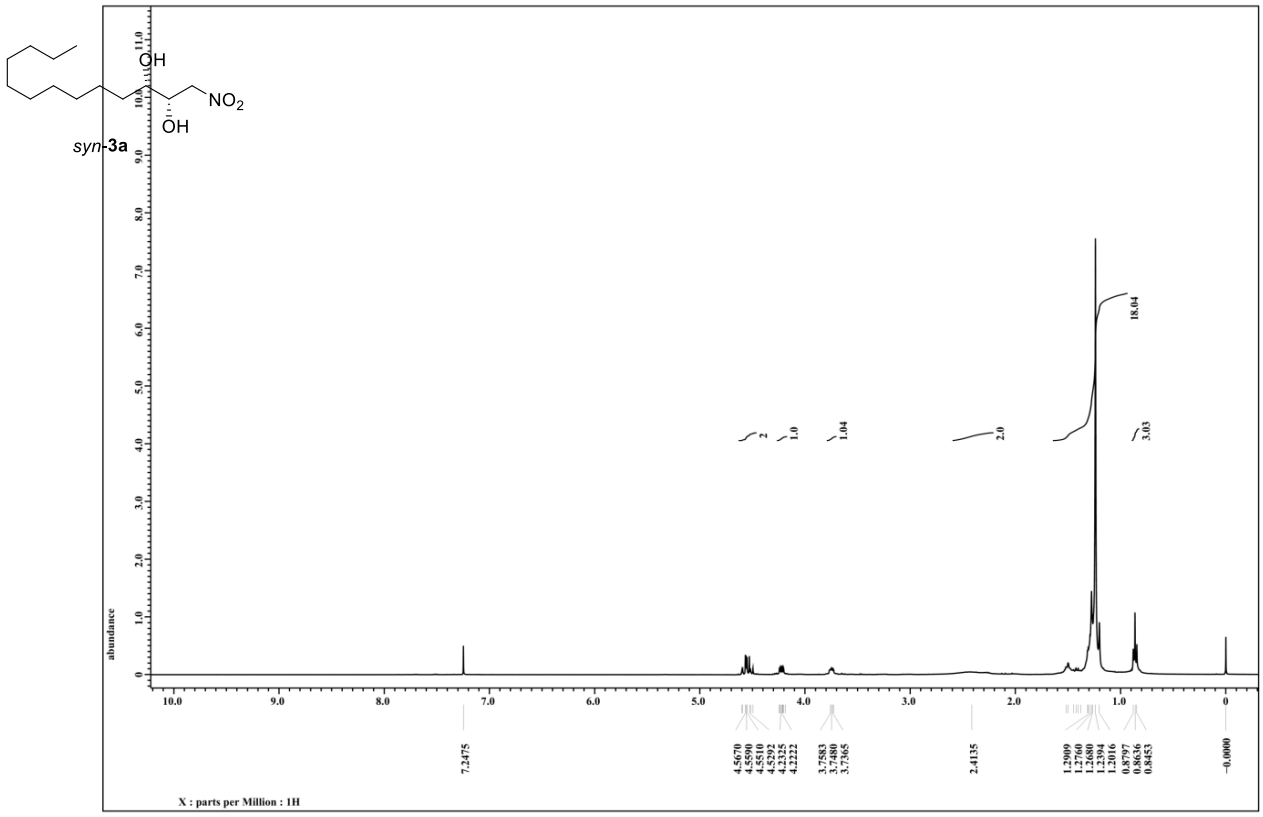
^{1}H NMR (400 MHz, $CDCl_3$/TMS)



^{13}C NMR (100 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, $CDCl_3$/TMS)



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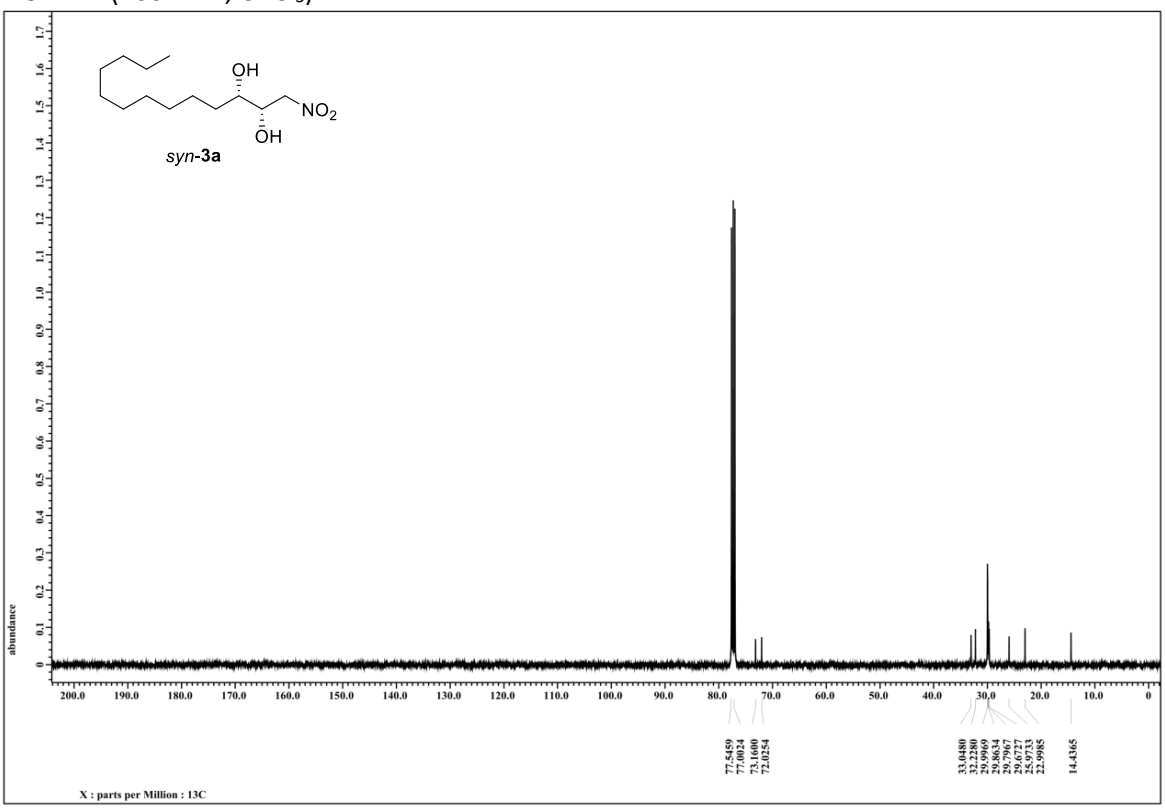

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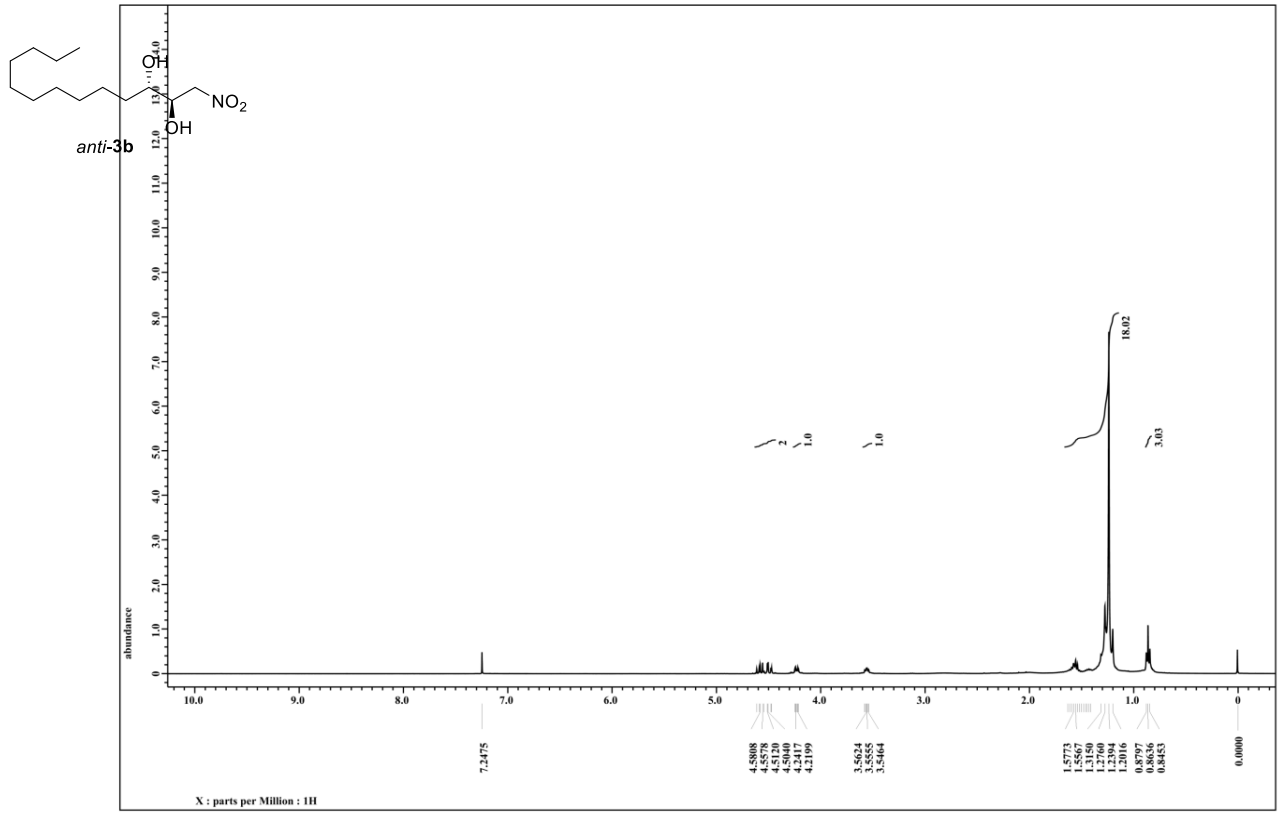
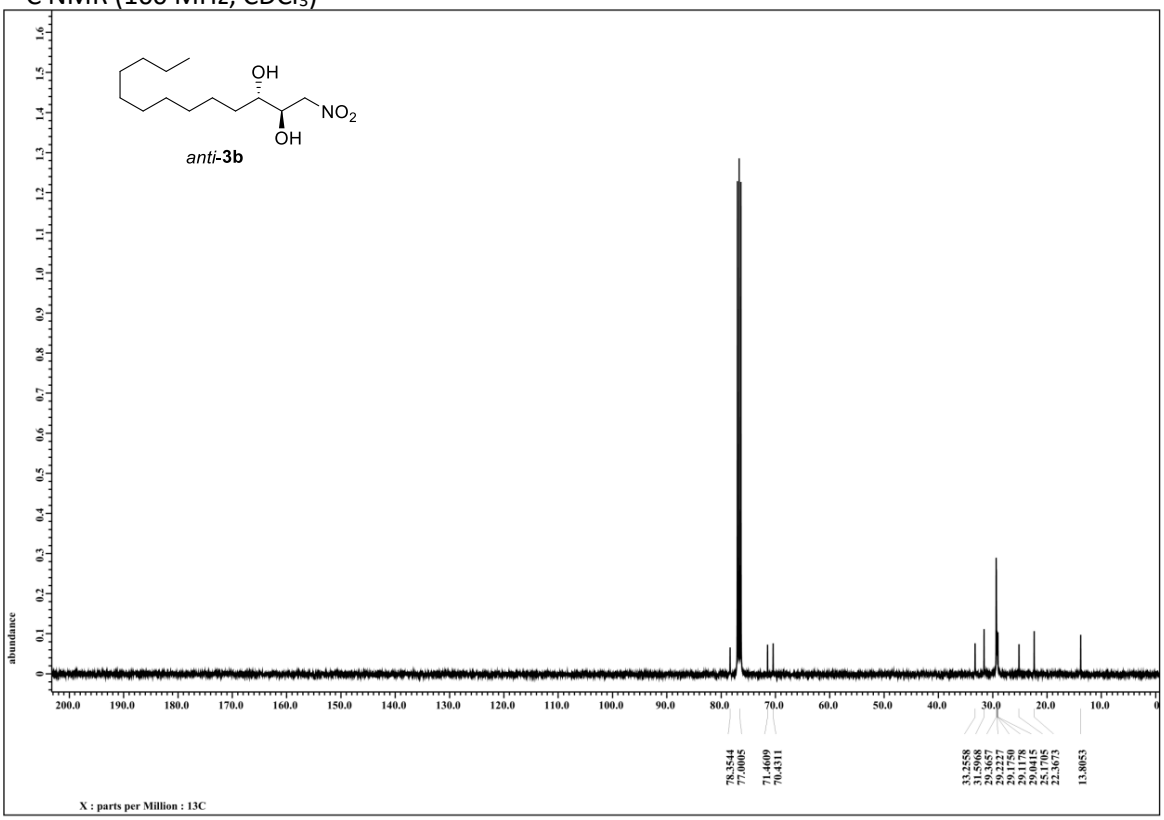
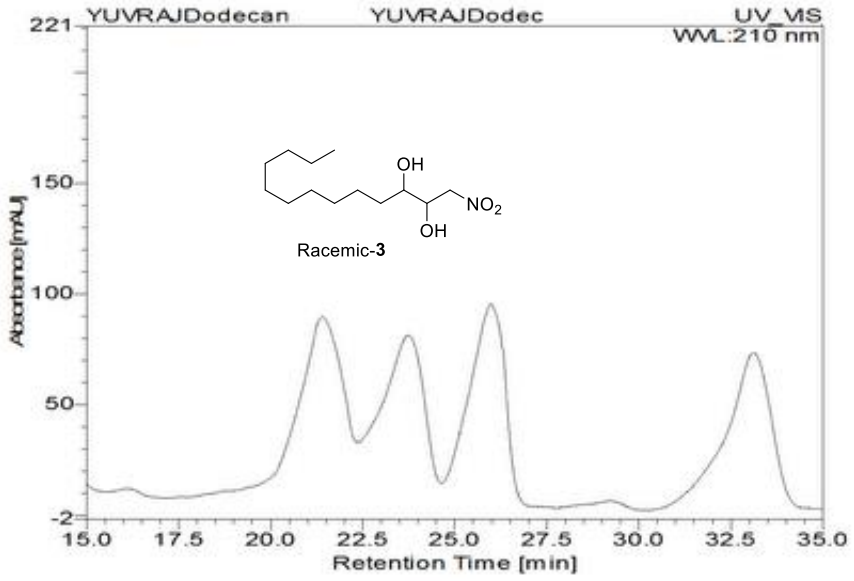


^{13}C NMR (100 MHz, $CDCl_3$)



Thermofisher HPLC System Report

Application: HPLC
Column: Chiralpak IA (4.6 mm x 250 mm)
Sample Name: YUVRAJDodec (racemic)
Wavelength: 210 nm
Mobile Phase: hexane/*i*-PrOH (95:5)
Flow Rate: 1 mL/min
Injection Volume: 20 μL
Sample Conc: 1 mg/mL



No.	RT (min)	Height mAU	Area mAU*min	Area %
1	21.414	89.971	30.61	41.15
2	23.733	80.408	12.84	17.26
3	25.982	95.825	16.79	22.57
4	33.111	73.744	14.14	19.02
		339.948	74.38	100

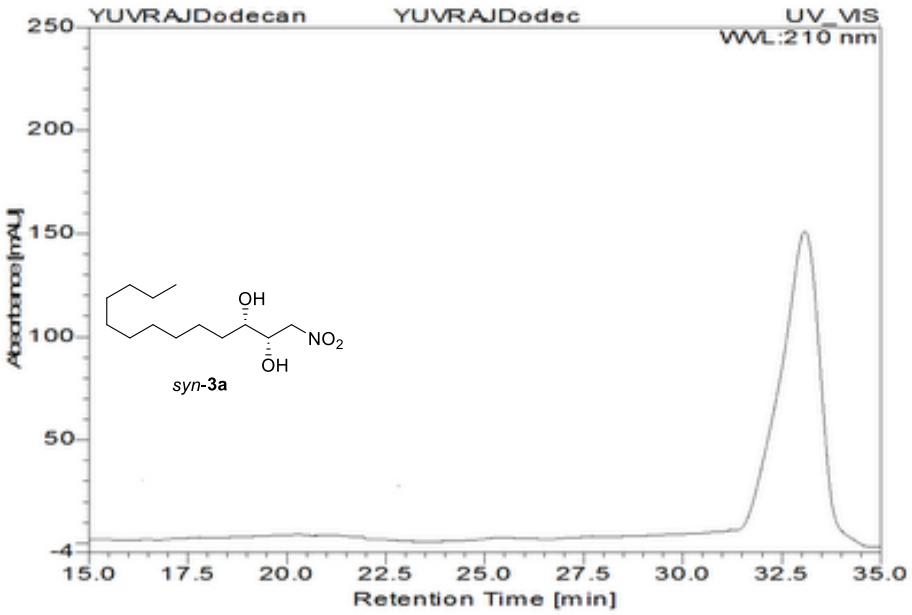
Thermofisher HPLC System Report

Application: HPLC Column: Chiralpak IA (4.6 mm x 250 mm)

Sample Name: YUVRAJDodec2 (chiral) Wavelength: 210 nm

Mobile Phase: hexane/*i*-PrOH (95:5) Flow Rate: 1 mL/min

Injection Volume: 20 μL Sample Conc: 1 mg/mL



syn-**3a**

No.	RT (min)	Height mAU	Area mAU*min	Area %
1	25.847	3.112	0.02	0.025
2	33.045	152.844	81.13	99.975
		155.956	81.15	100

Thermofisher HPLC System Report

Application: HPLC

Column: Chiralpak IA (4.6 mm x 250 mm)

Sample Name: YUVRAJDodec1 (chiral)

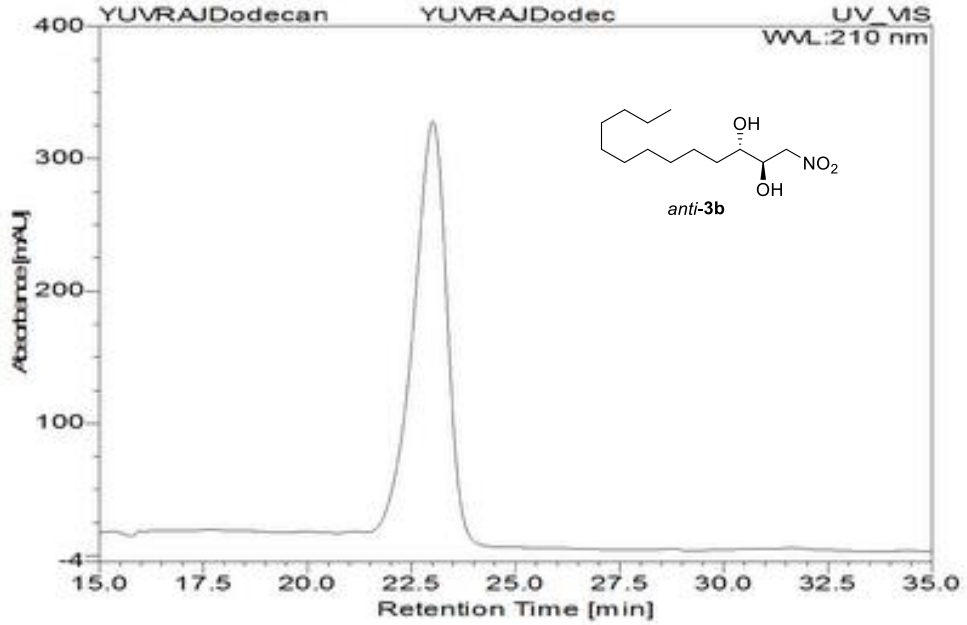
Wavelength: 210 nm

Mobile Phase: hexane/*i*-PrOH (95:5)

Flow Rate: 1 mL/min

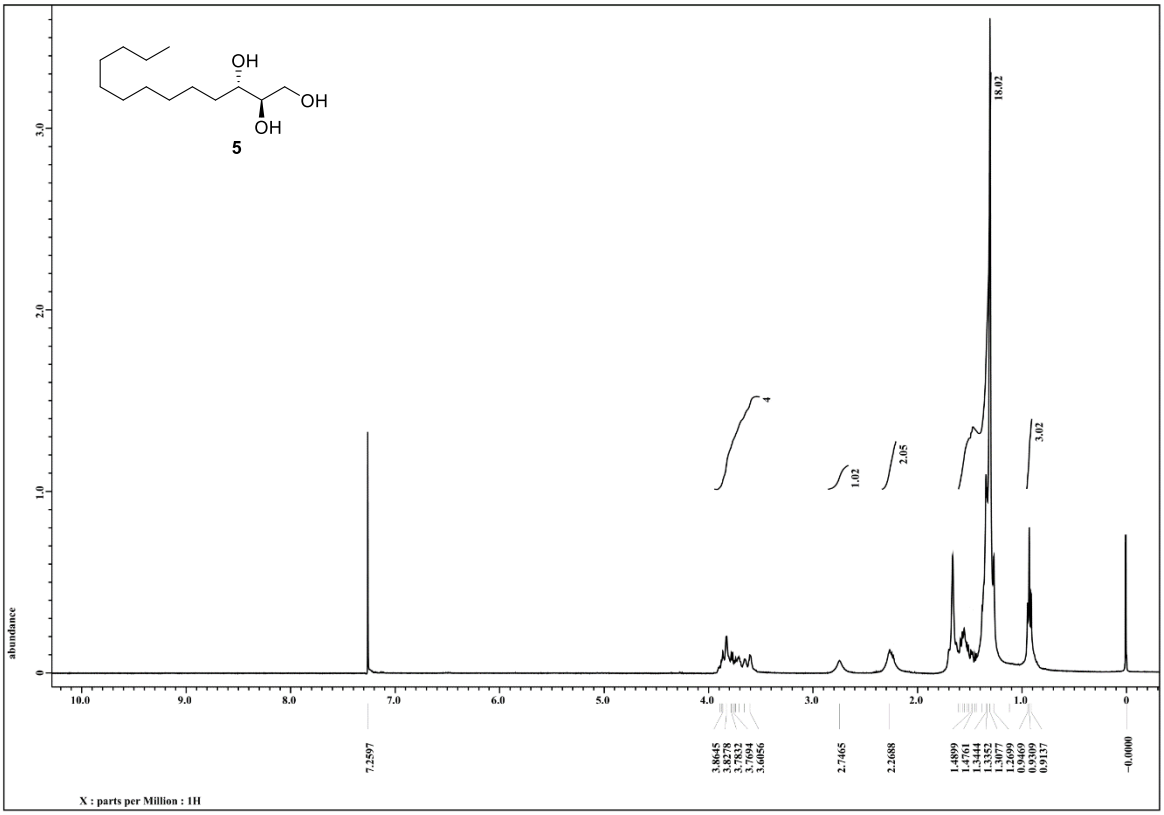
Injection Volume: 20 μL

Sample Conc: 1 mg/mL



No.	RT (min)	Height mAU	Area mAU*min	Area %
1	20.995	2.224	0.09	0.11
2	23.045	312.058	78.94	99.89
		314.282	79.03	100

^{1}H NMR (400 MHz, $CDCl_3$/TMS)



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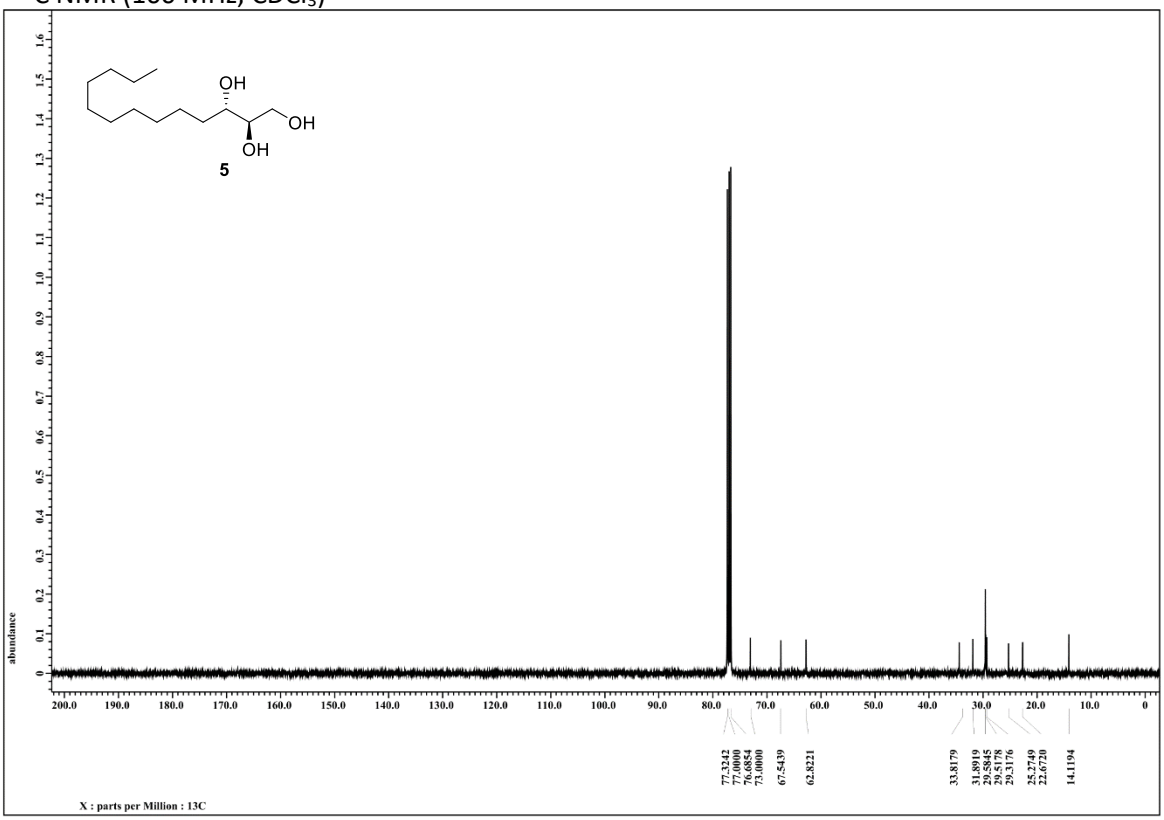
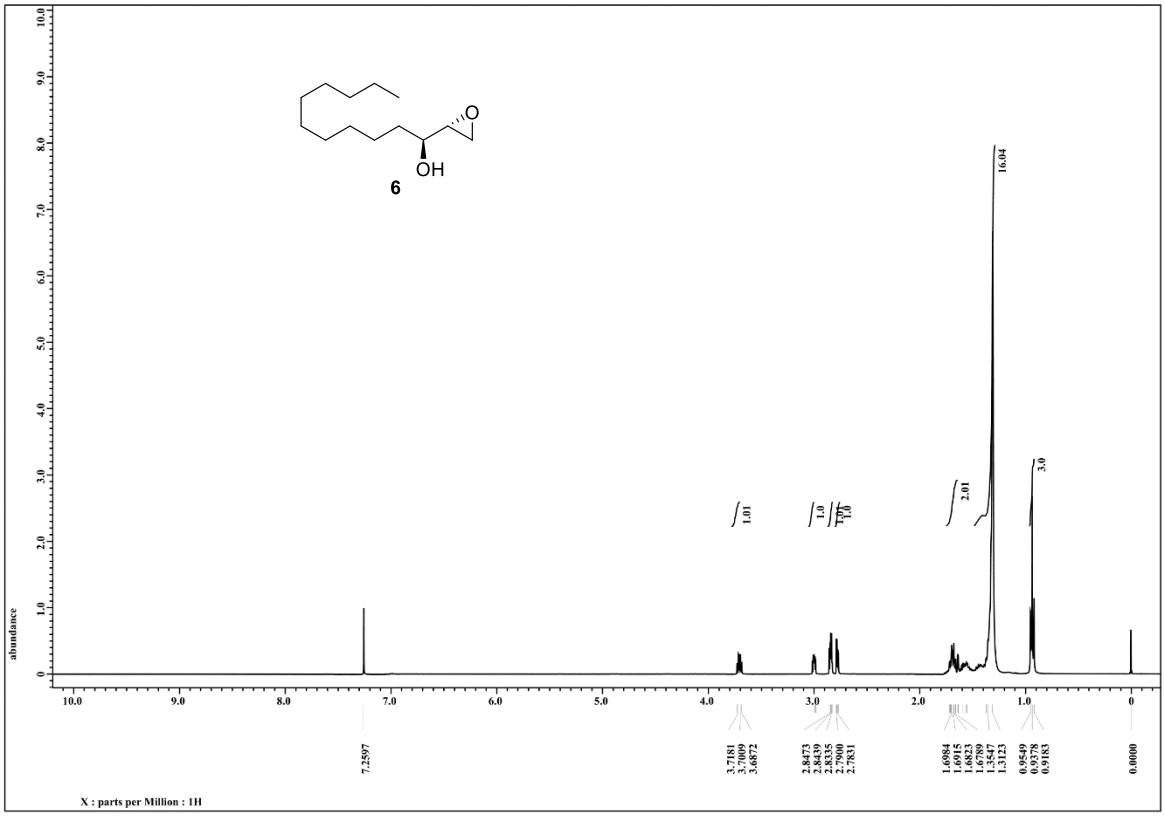
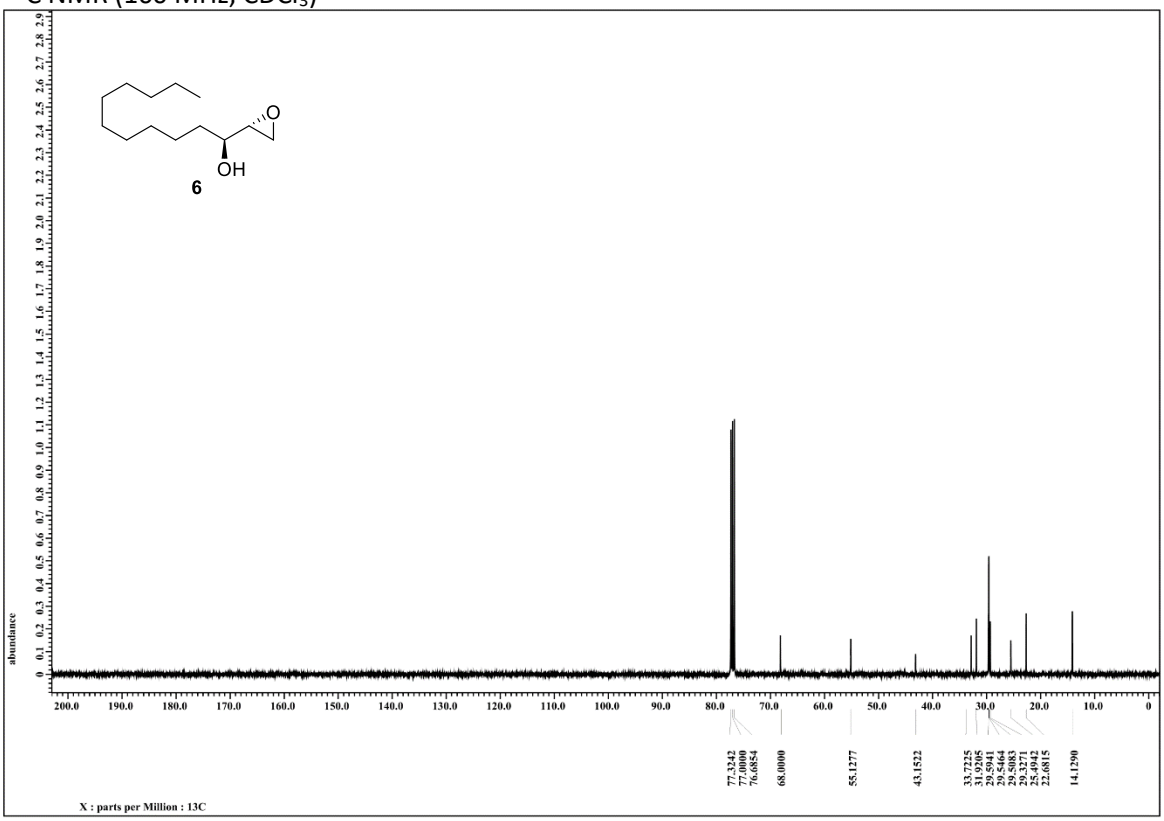


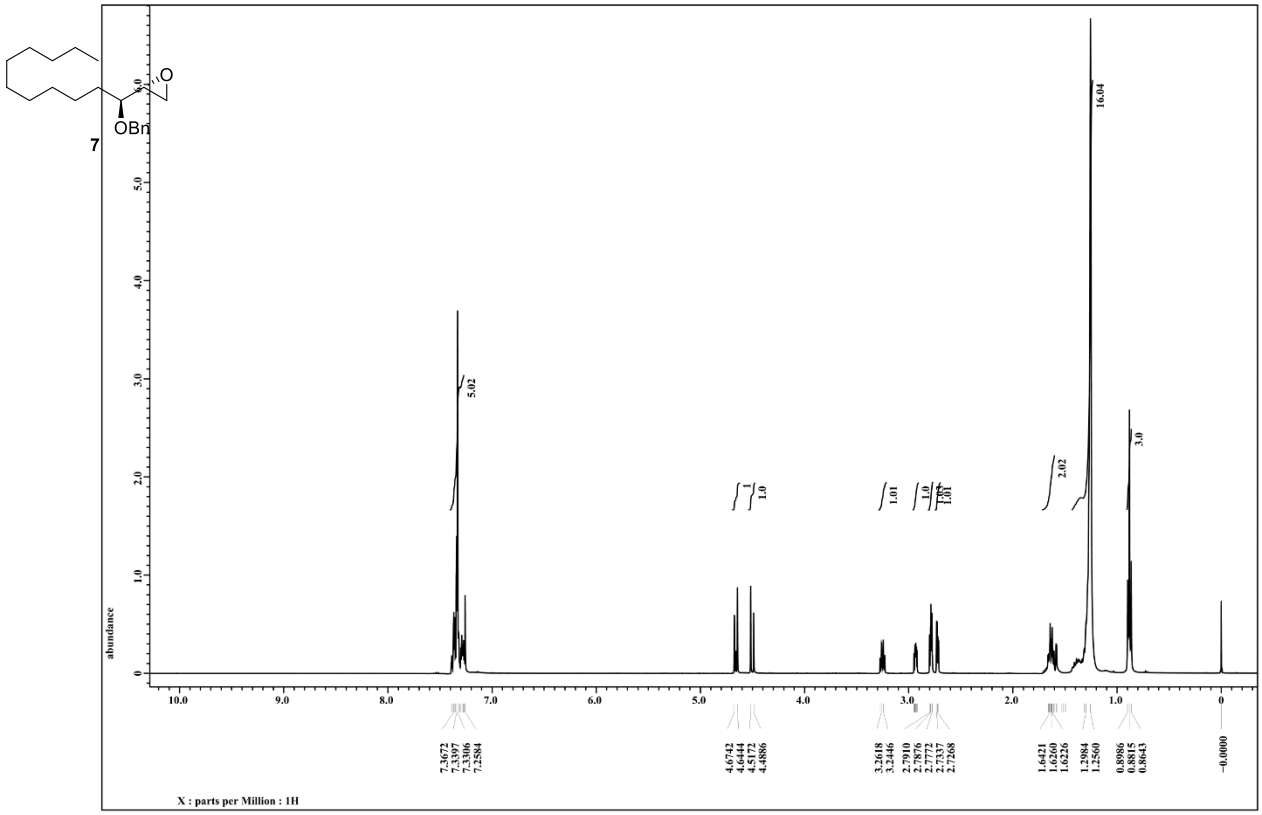
^{1}H NMR (400 MHz, $CDCl_3$/TMS)



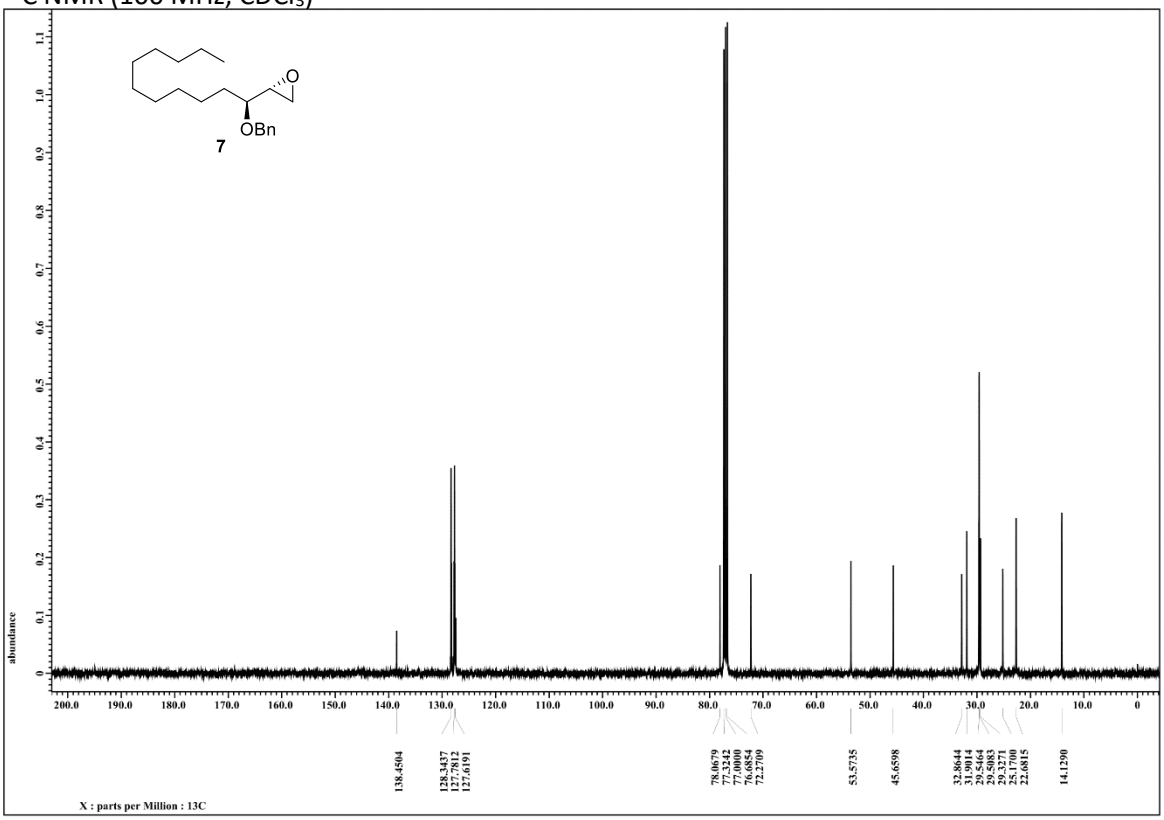
^{13}C NMR (100 MHz, $CDCl_3$)



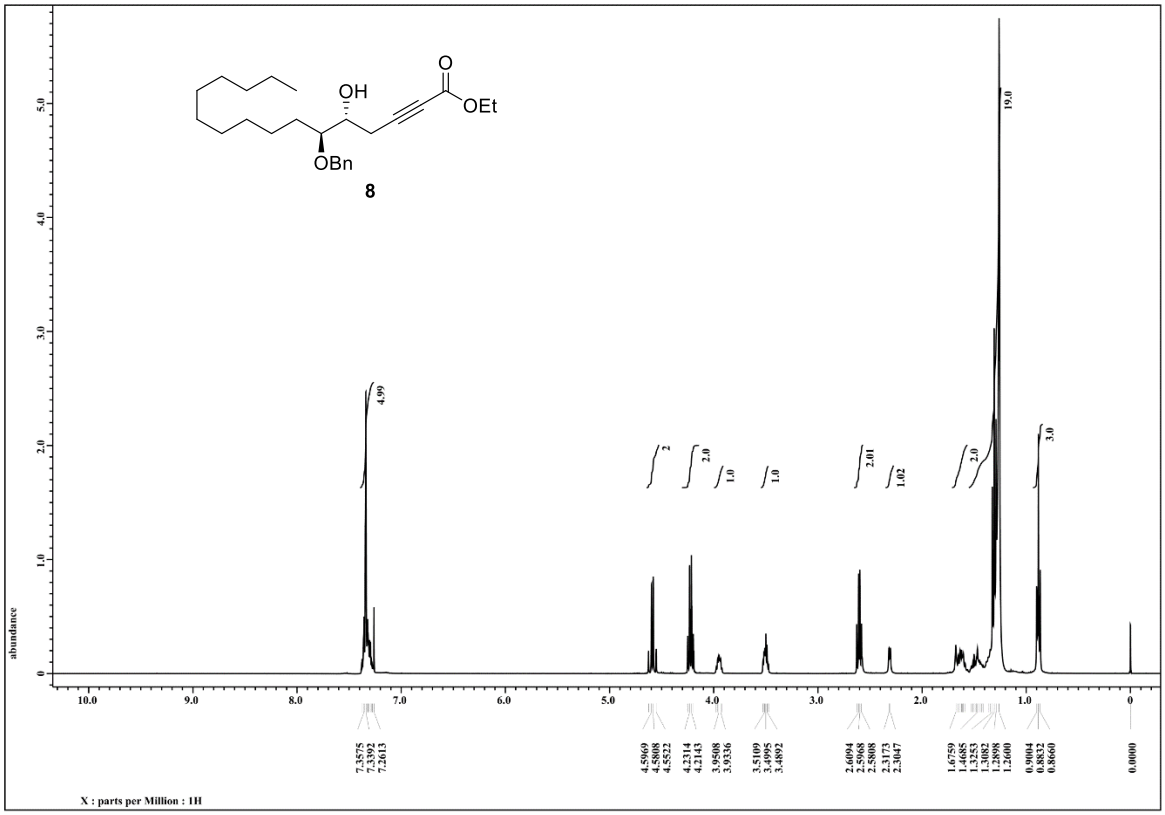
^{1}H NMR (400 MHz, $CDCl_3$/TMS)



^{13}C NMR (100 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, $CDCl_3$/TMS)



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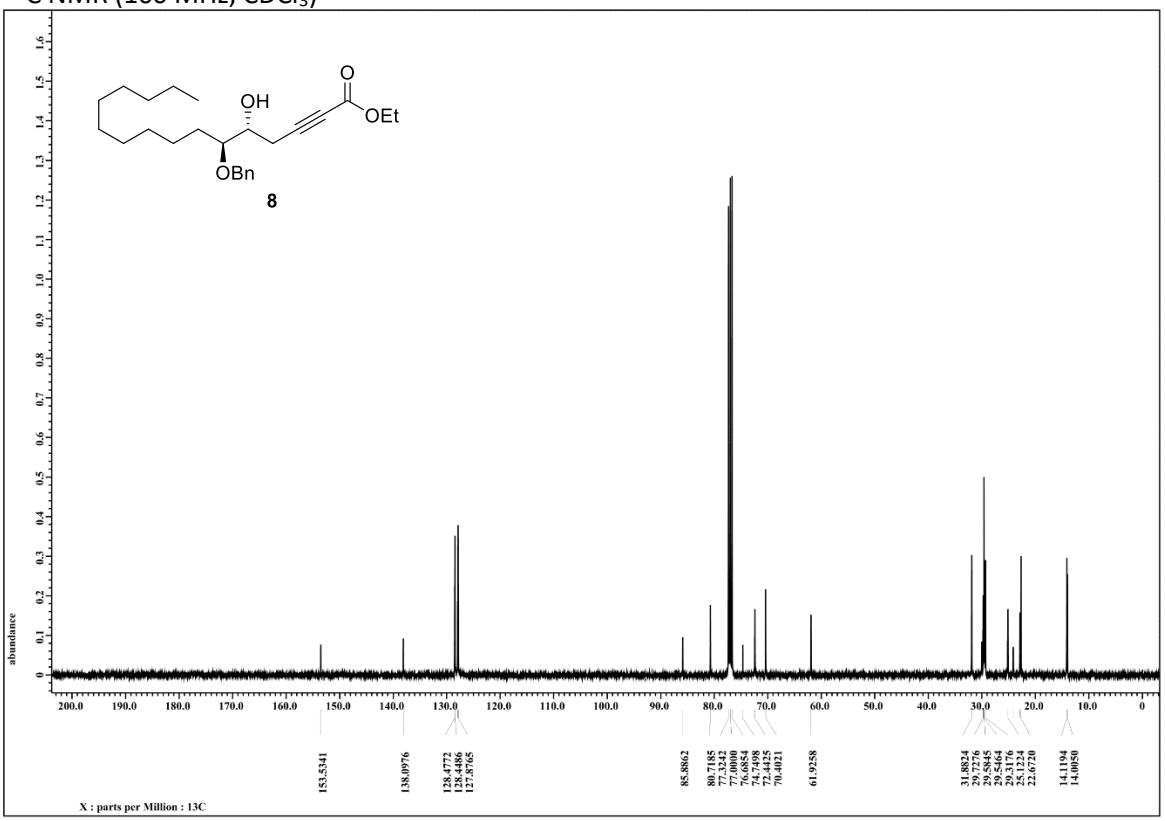

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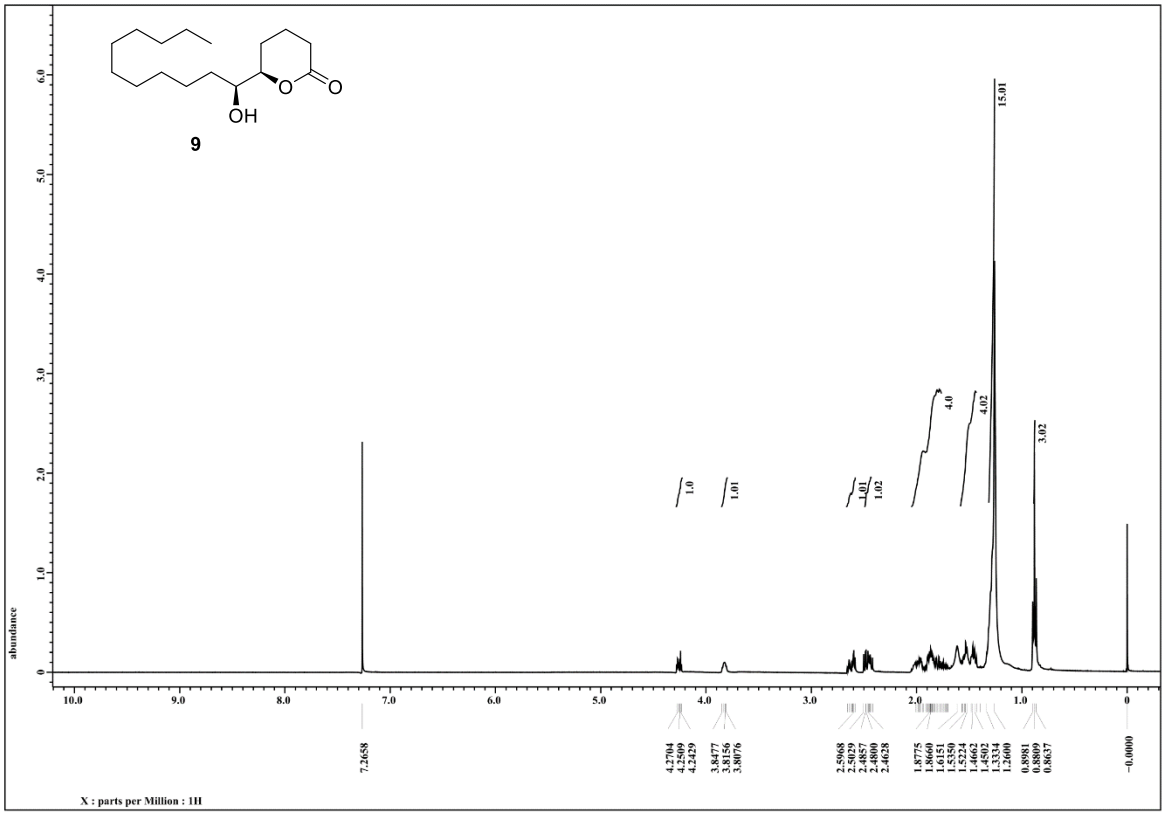
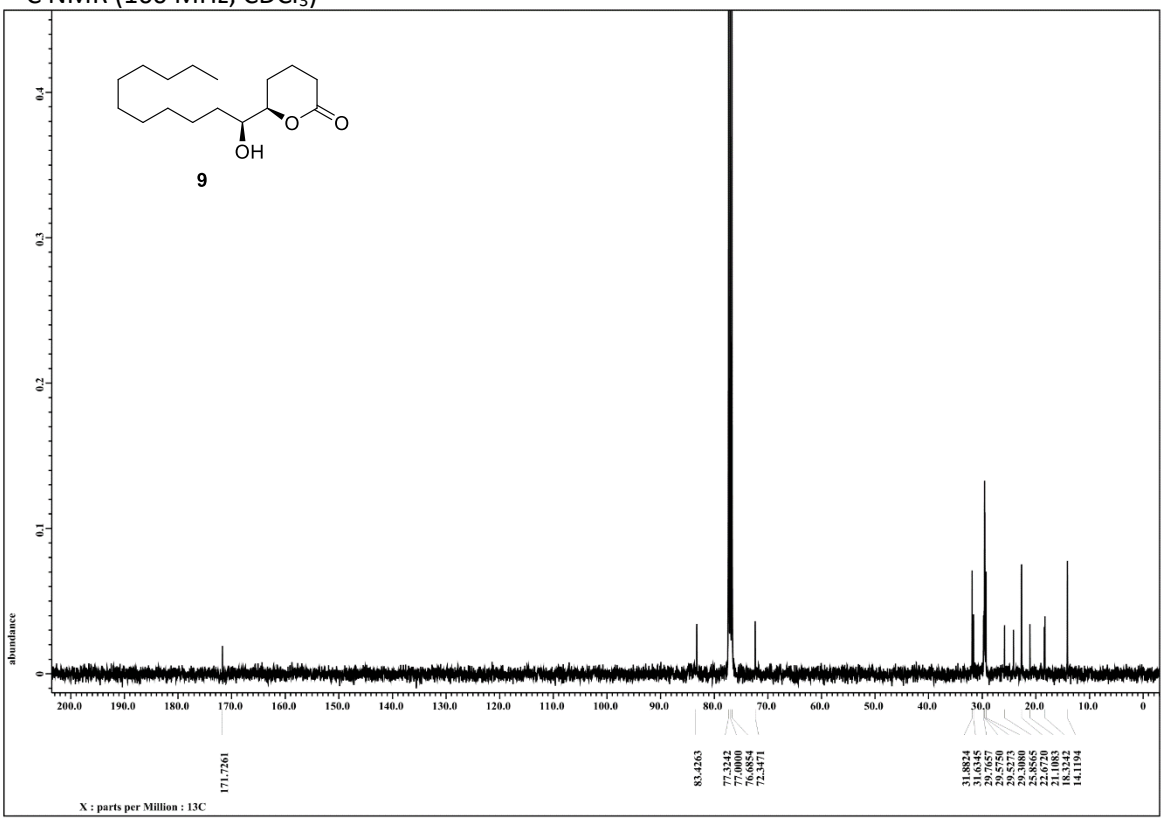


^{13}C NMR (100 MHz, $CDCl_3$)



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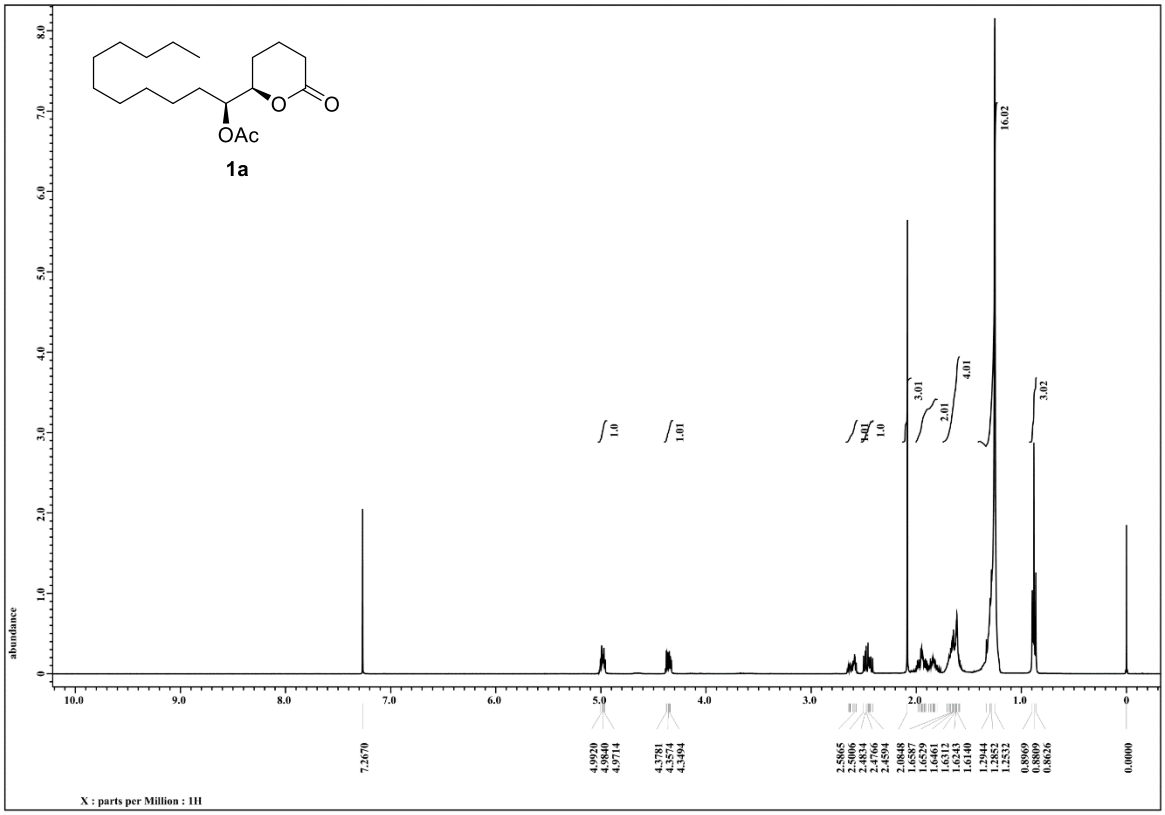

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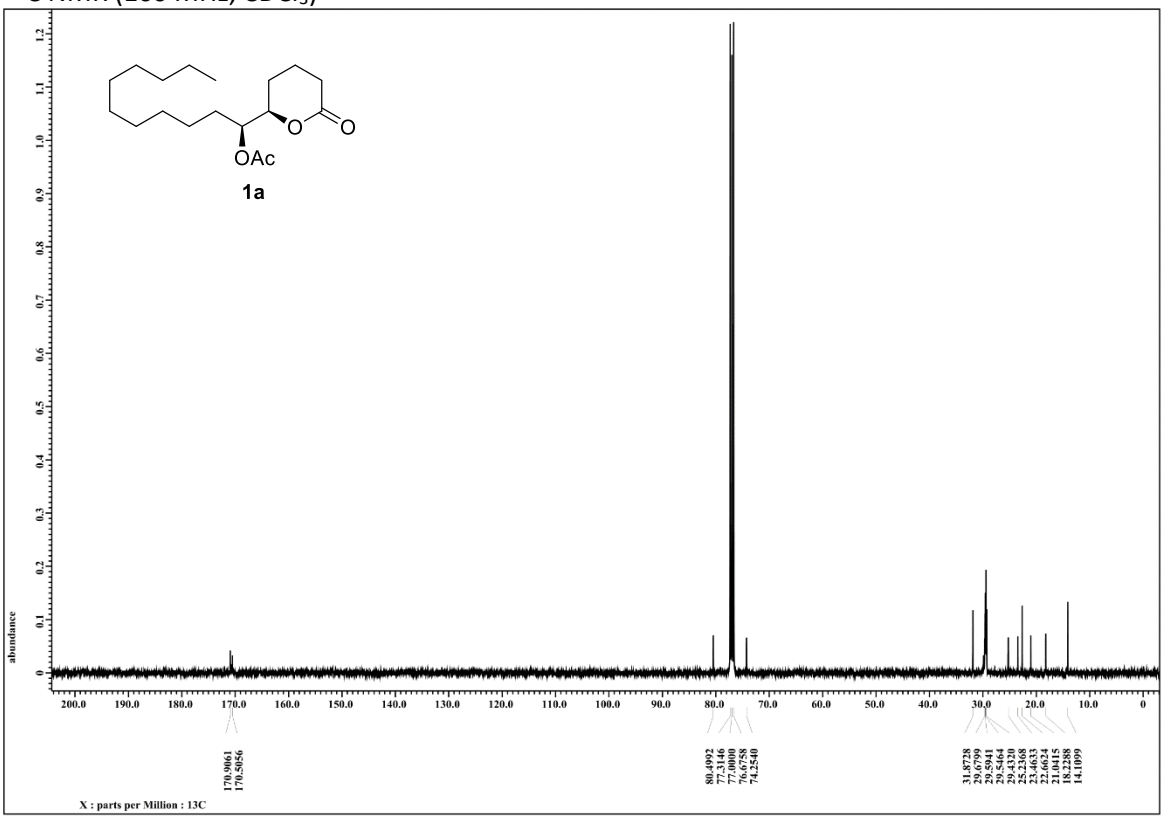

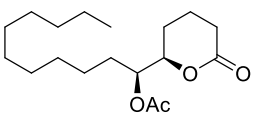

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