SUPPORTING INFORMATION

Expedient Stereoselective Synthesis of Coronafacic Acid Through Intramolecular Diels-Alder Cyclization

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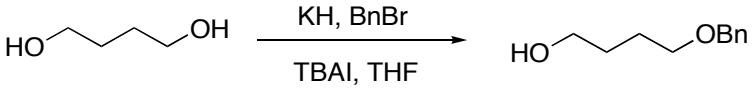
General: All non-aqueous reactions were run under an inert atmosphere (argon) with rigid exclusion of moisture from reagents and glassware using standard techniques for manipulating air-sensitive compounds.[1] All glassware was stored in the oven and/or was flame-dried prior to use under an inert atmosphere of gas. Anhydrous solvents were obtained either by filtration through drying columns (THF, ether, CH_2Cl_2, benzene, DMF, CH_3CN, toluene, hexane, methanol) or by distillation over sodium (chlorobenzene, *o*-xylene). Analytical thin-layer chromatography (TLC) was performed on precoated, glass-backed silica gel. Visualization of the developed chromatogram was performed by UV absorbance, aqueous cerium molybdate, ethanolic phosphomolybdic acid, iodine, or aqueous potassium permanganate. Flash column chromatography was performed using 230-400 mesh silica of the indicated solvent system according to standard technique.[2] Melting points were obtained and are uncorrected. Infrared spectra are reported in reciprocal centimeters (cm^{-1}). Reaction for cycloaddition adduct **31** was conducted in a Biotage Initiator Sixty EXP Microwave system. Nuclear magnetic resonance spectra (^1H, ^{13}C, DEPT 135, COSY, HMQC, NOESY) were recorded either on a 300 MHz, 400 MHz, or 600 MHz spectrometer. Chemical shifts for ^1H NMR spectra are recorded in parts per million from tetramethylsilane with the solvent resonance as the internal standard (chloroform, δ = 7.27 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, m = multiplet and br = broad), coupling constant in Hz, integration, and assignment. Chemical shifts for ^{13}C NMR spectra are recorded in parts per million from tetramethylsilane using the central peak of deuterochloroform (δ 77.00 ppm) as the internal standard. All spectra were obtained with complete proton decoupling. When ambiguous, proton and carbon assignments were established using COSY, HMQC and DEPT experiments. Optical rotations were determined with a polarimeter at 589 or 546 nm. Data are reported as follows: $[\alpha]_{temp}$, concentration (c in g/100 mL), and solvent.

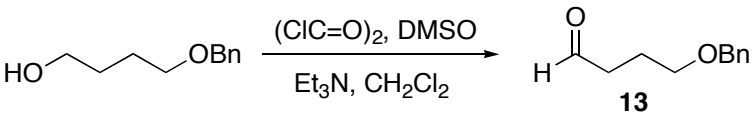
Reagents: Unless otherwise stated, commercial reagents were used without purification. Trifluoromethanesulfonic (triflic) acid was distilled prior to use. Triethylamine and diisopropylethylamine were distilled over calcium hydride. Ethyl (3*E*)-hex-3-enoate is commercially available.

1. Preparation of aldehyde 13

1 Shriver, D.F.; Drezdzon, M. A. the manipulation of air-sensitive compounds; 2nd ed.;Wiley: New York, 1986.
2 Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923-2925.



4-(Benzyloxy)butan-1-ol. Butane-1,4-diol (9 g, 100 mmol) was dissolved in THF (150 mL) then KH (4 g, 100 mmol) was added by portions. BnBr (18.8 g, 110 mmol) and TBAI (3.7 g, 10 mmol) were then added and solution was stirred at room temperature for 5 h. Work up: NH_4Cl (sat. aq. sln) was added and the organic layer was extracted with EtOAc. The organic layer was washed with brine, dried on $MgSO_4$, filtered then evaporated under reduced pressure. The residue was directly distilled to afford product as a colorless oil (15.8 g, 88%). R_f = 0.30 (30% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.32 (m, 4H, Ar-*H*), 7.31-7.27 (m, 1H, Ar-*H*), 4.53 (s, 2H, PhC*H*$_2$OCH$_2$), 3.66-3.63 (t, *J* = 5.8 Hz, 2H, PhCH$_2$OC*H*$_2$), 3.54-3.51 (t, *J* = 5.9 Hz, 2H, C*H*$_2$OH), 1.76-1.64 (m, 4H, HOCH$_2$C*H*$_2$C*H*$_2$CH$_2$OR). Product is identical to that previously reported in the literature.[3]



13

4-(Benzyloxy)butanal (13). Oxalyl chloride (660 mg, 5.2 mmol) was dissolved in CH_2Cl_2 (10 mL), and the solution was cooled to -78 °C. DMSO (750 mg, 9.6 mmol) was then added. 4-(Benzyloxy)butan-1-ol (720 mg, 4 mmol) was dissolved in CH_2Cl_2 (6 mL) and added to the solution 15 min later. The solution was stirred for 25 min, then Et_3N (2.02 g, 20 mmol) was added and the solution was allowed to stir at room temperature. Work up: NH_4Cl (sat. aq. sln) was added and the aqueous layer was extracted with CH_2Cl_2, then washed with $NaHCO_3$ (sat. aq. sln) and brine. The organic layer was dried on Na_2SO_4, filtered and evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (20% EtOAc/hexanes) to afford product **13** as a colorless oil (620 mg, 87%). R_f = 0.35 (20% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79-9.78 (t, *J* = 1.6 Hz, 1H, CH$_2$C(O)*H*), 7.37-7.28 (m, 5H, Ar-*H*), 4.49 (s, 2H, PhC*H*$_2$OCH$_2$), 3.53-3.50 (t, *J* = 6 Hz, 2H, PhCH$_2$OC*H*$_2$), 2.58-2.54 (dt, *J* = 7.2, 1.6 Hz, 2H, C*H*$_2$C(O)), 1.99-1.92 (m, 2H, C*H*$_2$CH$_2$C(O)H). Product is identical to that previously reported in the literature.[4]

2. Preparation of aldehyde 14

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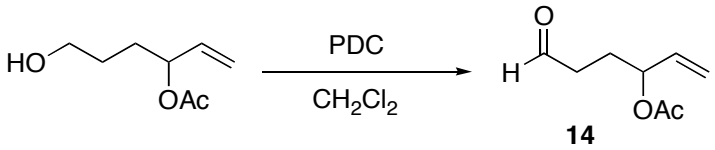
3 Garcia, C.; Martin, T.; Martin, V. S. *J. Org. Chem.* **2001**, *66*, 1420-1428.

4 Mulzer, J.; Kaselow, V.; Graske, K.-D.; Kuehne, H.; Sieg, A.; Martin, H. J. *Tetrahedron* **2004**, *60*, 9599-9614.



14

1-(3-Oxopropyl)prop-2-enyl acetate (14). 1-(3-Hydroxypropyl)prop-2-enyl acetate[5] (1.0 g, 6.3 mmol) was dissolved in CH_2Cl_2 (20 mL) then pyridinium dichromate (PDC) (3.57 g, 9.5 mmol) was added and the solution was stirred at room temperature for 3 h. Work up: a 20% EtOAc/hexane solution (100 mL) was added and the solution was filtered on silica gel. The solvent was evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (20% EtOAc/hexanes) to afford product **14** as a colorless oil (810 mg, 83%). R_f = 0.35 (20% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77-9.76 (t, *J* = 1.4 Hz, 1H, $CH_2C(O)H$), 5.8-5.71 (ddd, *J* = 17.1, 10.6, 6.3 Hz, 1H, CH_2=C*H*CHOAc), 5.30-5.19 (m, 3H, CH_2=CHC*H*OAc), 2.52-2.48 (m, 2H, CH_2C(O)H), 2.06 (s, 3H, O_2CCH_3), 2.01-1.93 (m, 2H, CH_2CH_2C(O)H); NMR ^{13}C: (100 MHz, $CDCl_3$) δ 200.7, 169.7, 135.2, 116.8, 73.1, 39.0, 25.9, 20.7; IR (neat) 3067, 2922, 2811, 2722, 1739 (C=O), 1378, 1240, 899, 736, 630 cm^{-1}; HRMS (ESI, Pos) Calcd for $C_{16}H_{24}O_6Na$ $(M+Na)^+$: 335.1465. Found 335.1474.

3. Diastereoselective aldol reaction

Procedure for preparation of dibutylboron triflate.[6] Tributylborane (4.0 g, 22 mmol) was charged in a Schlenk flask purged under argon. Triflic acid (3.3 g, 22 mmol) was added and the solution was warmed at 50 °C and stirred for 1 h. After this period of time, the solution was kept under argon and used readily.

General procedure for aldol reactions of ethyl (3*E*)-hex-3-enoate with aldehydes. Ethyl (3*E*)-hex-3-enoate (5.2 mmol, 1.3 equiv) was dissolved in CH_2Cl_2 (16 mL) then freshly distilled

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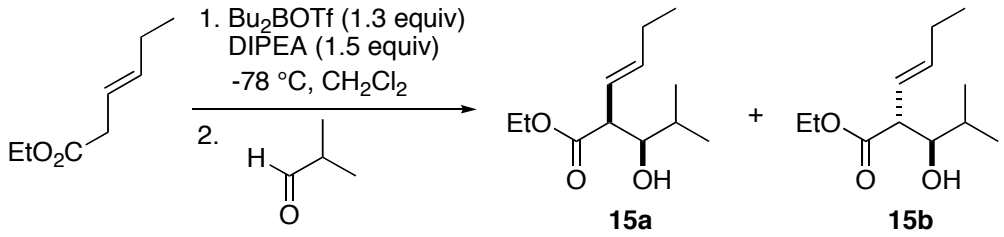
5 Crevisy, C.; Couturier, M.; Dugave, C.; Dory, Y. L. Deslongchamps, P. *Bull. Soc. Chim. Fr.* **1995**, *132*, 360-370.

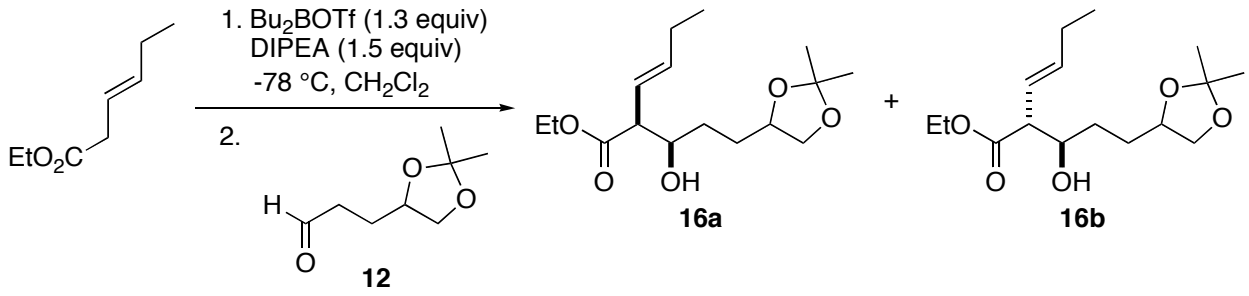
6 Evans, D. A.; Nelson, J. V.; Vogel, E.; Taber, T. R. *J. Am. Chem. Soc.* **1981**, *103*, 3099.

diisopropylethylamine (6 mmol, 1.5 equiv) was added and the solution was cooled to -78 °C. Freshly prepared dibutylboron triflate (5.2 mmol, 1.3 equiv) was slowly added to the solution, which was then stirred for 2 h at -78 °C. The aldehyde (4 mmol, 1 equiv) was dissolved in CH_2Cl_2 (8 mL) and added to the solution, which was stirred at -78 °C for 1 h, then at 0 °C for an additional 1 h. Work up: a phosphate buffer solution at pH = 7 (8 mL) was added along with methanol (12 mL) and hydrogen peroxide (30% aq., 4 mL) and the solution was stirred at room temperature for 12 h. After this period of time, water was added and the organic layer was extracted with CH_2Cl_2. The organic layer was washed with brine, dried on Na_2SO_4, filtered and evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel to afford separately the diastereomers of the aldol product.



Ethyl (1,2-*syn*, *3E*)-2-[1-hydroxy-2-methylpropyl]hex-3-enoate (15a); ethyl (1,2-*anti*, *3E*)-2-[1-hydroxy-2-methylpropyl]hex-3-enoate (15b). Following the general procedure for aldol reactions using isobutyraldehyde (4.7 mmol) and purification by flash chromatography on silica gel (30% EtOAc/hexanes) afforded separately the diastereomers of product **15** as colorless oils (872 mg, 87%, 98:2 *syn:anti*). **15a**: R_f = 0.61 (25% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.75-5.68 (dt, *J* = 15.7, 6.1 Hz, 1H, CH=C*H*CH_2), 5.58-5.51 (dd, *J* = 15.7, 9.2 Hz, 1H, CH=C*H*$CHCO_2Et$), 4.19-4.13 (q, *J* = 7.1 Hz, 2H, $CO_2CH_2CH_3$), 3.58-3.54 (ddd, *J* = 6.9, 5, 2.5 Hz, 1H, C*H*OH), 3.16-3.12 (dd, *J* = 9.2, 5 Hz, 1H, $CHCO_2Et$), 2.66-2.65 (d, *J* = 2.5 Hz, 1H, O*H*), 2.12-2.05 (dq, *J* = 7.1, 6.1 Hz, 2H, $CH=CHCH_2CH_3$), 1.70-1.62 (dh, *J* = 6.9, 6.6 Hz, 1H, $CH(CH_3)_2$), 1.29-1.25 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.02-0.97 (m, 6H, $CH(CH_3)_2$, $CH=CHCH_2CH_3$), 0.91-0.89 (d, *J* = 6.6 Hz, 3H, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 138.3, 122.2, 76.2, 60.7, 52.4, 30.6, 25.7, 19.1, 17.6, 14.1, 13.5; IR (neat) 3506 (O-H), 2962, 2874, 1713 (C=O), 1463, 1370, 1178 cm^{-1}. **15b**: R_f = 0.52 (25% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.71-5.64 (dt, *J* = 15.4, 6.3 Hz, 1H, CH=C*H*CH_2), 5.44-5.37 (ddt, *J* = 15.4, 9, 1.4 Hz, 1H, CH=C*H*$CHCO_2Et$), 4.19-4.13 (dq, *J* = 7.1, 2.2 Hz, 2H, $CO_2CH_2CH_3$), 3.61-3.56 (m, 1H, C*H*OH), 3.17-3.12 (dd, *J* = 8.4, 8.3 Hz, 1H, $CHCO_2Et$), 2.46-2.42 (d, *J* = 6.6 Hz, 1H, O*H*), 2.07-1.99 (m, 2H, $CH=CHCH_2CH_3$), 1.77-1.68 (m, 1H,

C*H*$(CH_3)_2$), 1.28-1.24 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 0.98-0.95 (m, 6H, $CH(CH_3)_2$, $CH{=}CHCH_2CH_3$), 0.89-0.86 (d, *J* = 6.9 Hz, 3H, $CH(CH_3)_2$); NMR ^{13}C: (100 MHz, $CDCl_3$) δ 174.1, 136.7, 123.7, 77.1, 60.7, 53.2, 30.4, 25.5, 19.9, 15.4, 14.1, 13.3; IR (neat) 3480 (O-H), 2962, 2934, 2874, 1716 (C=O), 1464, 1177 cm^{-1}; HRMS for a mixture of **15a** and **15b** (APCI, Pos) Calcd for $C_{12}H_{23}O_3$ $(M+H)^+$: 215.1641. Found 215.1634.



Ethyl (2,3-*syn*)-2-[(*1E*)-but-1-enyl]-2,4,5-trideoxy-6,7-*O*-(1-methylethylidene)-heptonate (16a); ethyl (2,3-*anti*)-2-[(*1E*)-but-1-enyl]-2,4,5-trideoxy-6,7-*O*-(1-methylethylidene)-heptonate (16b). Following the general procedure for aldol reactions using aldehyde **12**[7] (1.4 mmol) and purification by flash chromatography on silica gel (30% EtOAc/hexanes) afforded separately the diastereomers of product **16** as colorless oils (345 mg, 82%, 22:78 *syn:anti*). **16a**: R_f = 0.24 (25% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 5.68-5.60 (dt, *J* = 15.4, 6.4 Hz, 1H), 5.52-5.44 (ddt, *J* = 15.4, 9.1, 1.1 Hz, 1H), 4.15-3.96 (m, 4H), 3.87-3.81 (m, 1H), 3.48-3.44 (dd, *J* = 7.4, 7.1 Hz, 1H), 3.03-2.99 (m, 0.5H), 2.96-2.92 (dd, *J* = 9.1, 4.9 Hz, 1H), 2.91-2.88 (m, 0.5H), 2.08-1.99 (h, *J* = 6.9 Hz, 2H), 1.76-1.66 (m, 1H), 1.61-1.37 (m, 4H), 1.35 (s, 3H), 1.29 (s, 3H), 1.23-1.20 (t, *J* = 6.9 Hz, 3H), 0.97-0.93 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 138.6, 138.5, 122.1, 121.9, 108.8, 76, 71.3, 69.4, 69.3, 60.9, 60.8, 54.9, 54.8, 30.4, 30.3, 29.9, 29.8, 26.9, 26.8, 25.7, 25.6, 14.1, 13.5, 13.4; IR (neat) 3462 (O-H), 2983, 2935, 2873, 1731 (C=O), 1455, 1369, 1215, 1157, 1056 cm^{-1}. **16b**: R_f = 0.16 (25% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 5.7-5.6 (dt, *J* = 15.4, 6.4 Hz, 1H), 5.42-5.31 (dd, *J* = 15.4, 9.2 Hz, 1H), 4.17-3.98 (m, 4H), 3.84-3.75 (dd, *J* = 7.3, 6.8 Hz, 1H), 3.51-3.45 (m, 1H), 3.10-3.08 (d, *J* = 5.6 Hz, 0.5H), 3.03-2.95 (ddd, *J* = 8.6, 8.6, 3 Hz, 1H), 2.89-2.86 (d, *J* = 6.4 Hz, 0.5H), 2.06-1.96 (m, 2H), 1.76-1.58 (m, 4H), 1.37 (s, 3H), 1.31 (s, 3H), 1.26-1.21 (t, *J* = 7.3 Hz, 3H), 0.97-0.92 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 137.2, 137.1, 123.2, 123.1, 108.8, 108.7, 75.9, 75.8, 72.2, 72.1, 69.3, 69.2, 60.5, 55.9, 55.7, 30.7, 30.5, 29.6, 29.3, 26.7, 25.5, 25.4, 14.0, 13.2; IR (neat) 3453 (O-H), 2982, 2934, 2873, 1730

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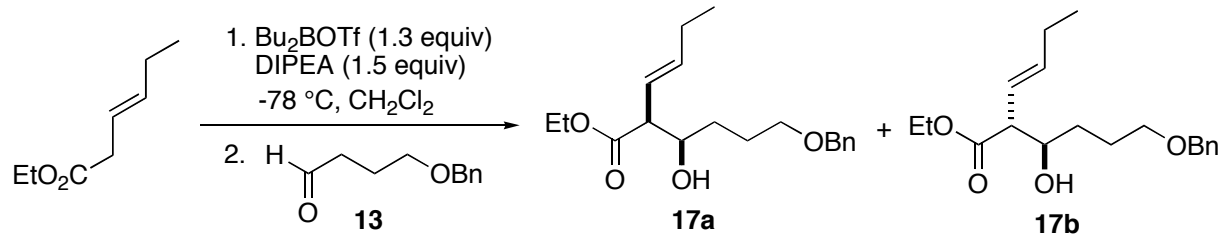
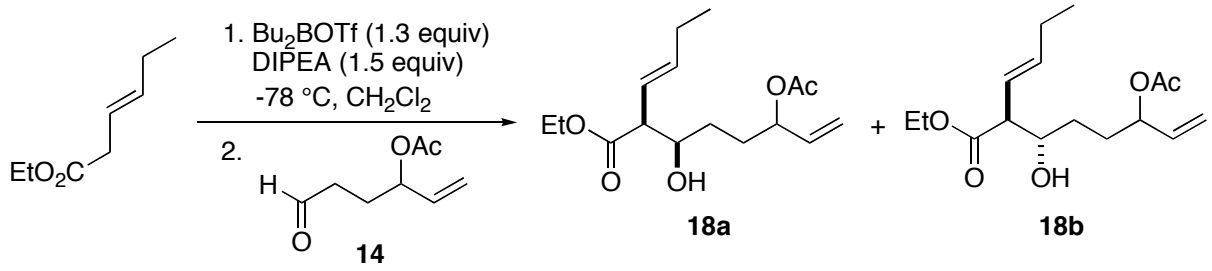
[7] Mulzer, J.; Berger, M. *J. Org. Chem.* **2004**, *69*, 891.

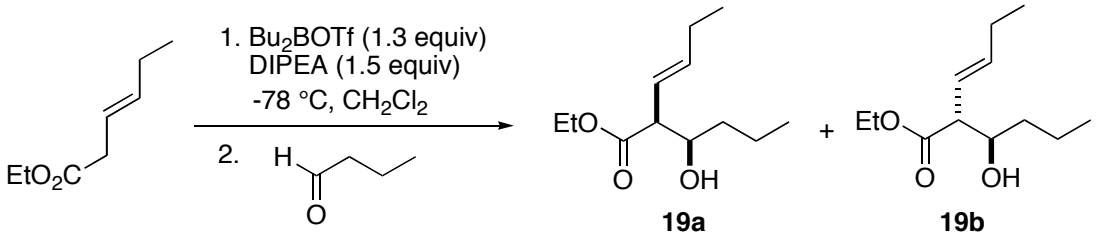
(C=O), 1456, 1369, 1248, 1217, 1156, 1054 cm^{-1}; HRMS for a mixture of **16a** and **16b** (ESI, Pos) Calcd for $C_{16}H_{28}O_5Na$ $(M+Na)^+$: 323.1828. Found 323.1838.



Ethyl (1,2-*syn*, *3E*)-2-[4-(benzyloxy)-1-hydroxybutyl]hex-3-enoate (17a); ethyl (1,2-*anti*, *3E*)-2-[4-(benzyloxy)-1-hydroxybutyl]hex-3-enoate (17b). Following the general procedure for aldol reactions using aldehyde **13** (1.68 mmol) and purification by flash chromatography on silica gel (30% EtOAc/hexanes) afforded separately the diastereomers of product **17** as colorless oils (358 mg, 66%, 18:82 syn:anti). **17a**: R_f = 0.41 (25% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.28 (m, 5H), 5.72-5.65 (dt, *J* = 15.4, 6.2 Hz, 1H, CH=C*H*CH_2), 5.56-5.50 (dd, *J* = 15.4, 9.1 Hz, 1H, CHC*H*=$CHCH_2$), 4.51 (s, 2H, PhCH_2O), 4.19-4.14 (q, *J* = 7.1 Hz, 2H, $CO_2CH_2CH_3$), 3.90-3.86 (m, 1H, C*H*OH), 3.53-3.46 (m, 2H, CH_2OBn), 3.0-2.92 (m, 2H, C*H*CO_2Et, O*H*), 2.11-2.05 (dq, *J* = 7.3, 7.3 Hz, 2H, CH=CHC$H_2$$CH_3$), 1.85-1.64 (m, 2H, BnO-$CH_2CH_2$$CH_2$$CH_2$CH-OH), 1.58-1.49 (m, 2H, BnO-$CH_2CH_2CH_2$CH-OH), 1.28-1.24 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.02-0.98 (t, *J* = 7.3 Hz, 3H, $CH=CHCH_2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 138.3, 128.3 (2C), 127.6, 127.5 (2C), 122.2, 72.8, 71.3, 70.1, 60.8, 54.9, 31.1, 26, 25.7, 14.1, 13.5; IR (neat) 3445 (O-H), 2922, 2852, 1727 (C=O), 1454, 1369, 1247, 1175, 1097, 1028 cm^{-1}. **17b**: R_f = 0.33 (25% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.28 (m, 5H, Ar-*H*), 5.71-5.64 (dt, *J* = 15.4, 6.1 Hz, 1H, CH=C*H*CH_2), 5.44-5.37 (ddt, *J* = 15.4, 9.1, 1.6 Hz, 1H, CH=C*H*CHCO_2Et), 4.51 (s, 2H, PhCH_2O), 4.20-4.14 (dq, *J* = 7.2, 1.6 Hz, 2H, $CO_2CH_2CH_3$), 3.85-3.80 (ddd, *J* = 8.3, 8.2, 2.4 Hz, 1H, C*H*OH), 3.52-3.49 (dd, *J* = 5.7, 6.2 Hz, 2H, CH_2OBn), 3.04-3.00 (dd *J* = 9.1, 8.2 Hz, 1H, C*H*CO_2Et), 2.09-2.01 (ddq, *J* = 7.4, 6.1, 1.6 Hz, 2H, CH=CHC$H_2$$CH_3$), 1.84-1.68 (m, 3H, Bn-O$CH_2CH_2CH_2$CH-OH), 1.44-1.37 (m, 1H, Bn-O$CH_2CH_2CH_2$CH-OH), 1.28-1.25 (t, *J* = 7.2 Hz, 3H, $CO_2CH_2CH_3$), 1.00-0.96 (t, *J* = 7.4 Hz, 3H, $CH=CHCH_2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 138.2, 137.2, 128.3, 127.6, 123.5, 72.9, 72.4, 70.2, 60.7, 56.1, 31.6, 25.9, 25.6, 14.1, 13.3; IR (neat) 3445 (O-H), 2960, 2925, 2853, 1717 (C=O), 1454, 1369, 1307, 1263, 1174, 1096, 1028, 971 cm^{-1}; HRMS for a mixture of **17a** and **17b** (ESI, Pos) Calcd for $C_{19}H_{28}O_4Na$ $(M+Na)^+$: 343.1879. Found 343.1884.

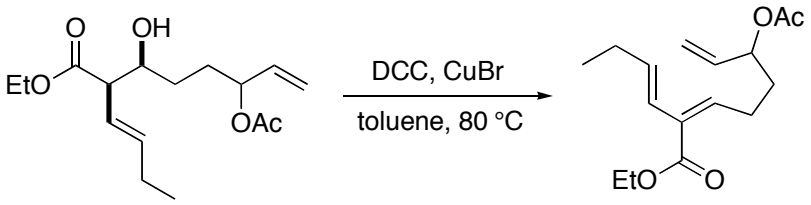


Ethyl (2,3-*syn*)-6-(acetyloxy)-2-[(1*E*)-but-1-enyl]-3-hydroxyoct-7-enoate (18a); ethyl (2,3-*anti*)-6-(acetyloxy)-2-[(1*E*)-but-1-enyl]-3-hydroxyoct-7-enoate (18b). Following the general procedure for aldol reactions using aldehyde **14** (4 mmol) and purification by flash chromatography on silica gel (20% EtOAc/hexanes) afforded separately the diastereomers of product **18** as colorless oils (1.01 g, 85%, 13:87 *syn:anti*); HRMS (ESI, Pos) Calcd for $C_{16}H_{26}O_5Na$ $(M+Na)^+$: 321.1673. Found 321.1660. **18a**: R_f = 0.23 (20% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81-5.67 (m, 2H, CH_2=C*H*CHOAc, CH_2C*H*=CHCH), 5.54-5.47 (ddd, *J* = 15.4, 9.4, 1.4 Hz, 1H, CH_2CH=C*H*CH), 5.30-5.15 (m, 3H, C*H*$_2$=CHC*H*OAc), 4.19-4.13 (dq, *J* = 7.1, 1.9 Hz, 2H, $CO_2CH_2CH_3$), 3.88-3.82 (m, 1H, C*H*OH), 2.98-2.95 (dd, *J* = 9.1, 4.7 Hz, 1H, C*H*CO_2Et), 2.78-2.67 (b, 1H, O*H*), 2.11-2.01 (m, 5H, CH=CHC*H*$_2$$CH_3$, O_2CCH_3), 1.89-1.79 (m, 1H, AcOCHC*H*$_2$$CH_2$CHOH), 1.71-1.61 (m, 1H, AcOCHC*H*$_2$$CH_2$CHOH), 1.55-1.35 (m, 2H. AcOCHCH_2C*H*$_2$CHOH), 1.29-1.24 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.02-0.98 (t, *J* = 7.4 Hz, 3H, CH=CHCH_2C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 170.3, 138.9, 136.3, 136.2, 121.9, 116.9, 116.8, 74.7, 74.3, 71.1, 70.9, 60.9, 54.8, 54.7, 30.3, 30.1, 29.5, 29.3, 25.7, 21.2, 14.1, 13.5; IR (neat) 3456, 2961, 2934, 1731 (C=O), 1371, 1236, 1021 cm^{-1}; **18b**: R_f = 0.18 (20% EtOAc/hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.78-5.65 (m, 2H, CH_2=C*H*CHOAc, CH_2C*H*=CHCH), 5.42-5.33 (ddd, *J* = 15.3, 9.1, 1.6 Hz, 1H, CH_2CH=C*H*CH), 5.25-5.15 (m, 3H, C*H*$_2$=CHC*H*OAc), 4.21-4.13 (dq, *J* = 7.1, 1.9 Hz, 2H, $CO_2CH_2CH_3$), 3.80-3.77 (m, 1H, C*H*OH), 3.03-2.98 (t, *J* = 7.7 Hz, 1H, C*H*CO_2Et), 2.7-2.5 (b, 1H, O*H*), 2.07-2.00 (m, 5H, CH_3C*H*$_2$CH=CH, O_2CCH_3), 1.86-1.82 (m, 1H, AcOCHC*H*$_2$$CH_2$CHOH), 1.72-1.53 (m, 2H, AcO-CHC*H*$_2$$CH_2$CH-OH, AcO-CHC$H_2$C*H*$_2$CH-OH), 1.39-1.34 (m, 1H, AcO-CHCH_2C*H*$_2$CH-OH), 1.29-1.24 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.00-0.95 (t, *J* = 7.4 Hz, 3H, CH=CHCH_2C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.0, 136.7, 136.6, 123.5, 117.4, 117.2, 75.2, 74.7, 72.7, 72.5, 61.3, 56.3, 56.1, 30.6, 30.4, 30.3, 26.0, 21.6, 14.6, 13.8; IR (neat) 3487 (O-H), 2963, 1738 (C=O), 1241 cm^{-1}.



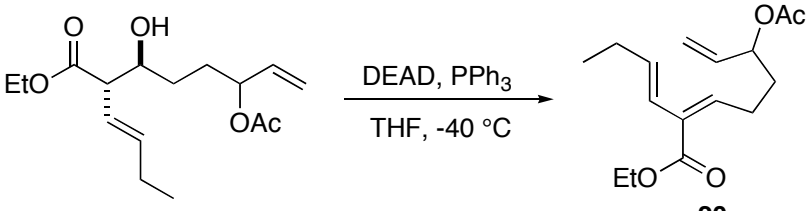
Ethyl (1,2-*syn*, 3*E*)-2-[1-hydroxybutyl]hex-3-enoate (19a); ethyl (1,2-*anti*, 3*E*)-2-[1-hydroxybutyl]hex-3-enoate (19b). Following the general procedure for aldol reactions using butyraldehyde (1 mmol) and purification by flash chromatography on silica gel (30% EtOAc/hexanes) afforded separately the diastereomers of product **18** as colorless oils (144 mg, 67%, 32:68 *syn:anti*). **19a**: R_f = 0.52 (25% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.74-5.65 (dt, *J* = 15.3, 6.1 Hz, 1H, CH=C*H*CH_2), 5.56-5.47 (ddt, *J* = 15.3, 9, 1.4 Hz, 1H, CH=C*H*$CHCO_2Et$), 4.20-4.13 (q, *J* = 7.1 Hz, 2H,$CO_2CH_2CH_3$), 3.89-3.84 (m, 1H, C*H*OH), 2.99-2.95 (dd, *J* = 9, 4.7 Hz, 1H, C*H*CO_2Et), 2.68-2.59 (b, 1H, O*H*), 2.14-2.04 (dq, *J* = 7.5, 6.1 Hz, 2H, CH=CHCH_2CH_3), 1.55-1.30 (m, 4H, $CH_2CH_2CH_3$), 1.29-1.25 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.03-0.97 (t, *J* = 7.5 Hz, 3H, $CH=CHCH_2CH_3$), 0.94-0.89 (t, *J* = 6.9 Hz, 3H, $CH_2CH_2CH_3$); NMR ^{13}C: (100 MHz, $CDCl_3$) δ 174, 138.5, 122, 71.2, 60.8, 54.8, 36.1, 25.7, 18.8, 14.1, 14, 13.5; IR (neat) 3504 (O-H), 2962, 2874, 1714 (C=O), 1464, 1370, 1248, 1178, 1029 cm^{-1}. **19b**: R_f = 0.47 (25% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.72-5.63 (dt, *J* = 15.5, 6.1 Hz, 1H, CH=C*H*CH_2), 5.46-5.37 (ddt, *J* = 15.5, 9.0, 1.4 Hz, 1H, CH=C*H*$CHCO_2Et$), 4.21-4.13 (dq, *J* = 7.1, 1.5 Hz, 2H, $CO_2CH_2CH_3$), 3.82-3.75 (m, 1H, C*H*OH), 3.05-2.99 (dd, *J* = 8.3, 8.2 Hz, 1H, C*H*CO_2Et), 2.48-2.38 (b, 1H, O*H*), 2.10-2.0 (dq, *J* = 7.6, 6.1 Hz, 2H, CH=CHCH_2CH_3), 1.58-1.30 (m, 4H, $CH_2CH_2CH_3$), 1.29-1.24 (t, *J* = 7.1 Hz, 3H, $CO_2CH_2CH_3$), 1.00-0.96 (t, *J* = 7.6 Hz, 3H, $CH=CHCH_2CH_3$), 0.93-0.89 (t, *J* = 6.9 Hz, 3H, $CH_2CH_2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 137.2, 123.4, 72.4, 60.7, 55.8, 36.7, 25.6, 18.6, 14.1, 14.0, 13.4; IR (neat) 3484 (O-H), 2962, 2934, 2875, 1715 (C=O), 1464, 1370, 1279, 1176 cm^{-1}; HRMS for a mixture of **19a** and **19b** (ESI, Pos) Calcd for $C_{12}H_{22}O_3Na$ $(M+Na)^+$: 237.1461. Found 237.1456.

4. Stereoselective elimination of the aldol products 18a and 18b



18a **20**

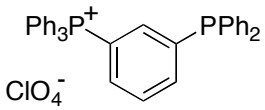
Ethyl (2*Z*)-6-(acetyloxy)-2-[(1*E*)-but-1-enyl]octa-2,7-dienoate (20). Alcohol **18a** (385 mg, 1.29 mmol) was dissolved in toluene (10 mL), DCC (400 mg, 1.94 mmol), CuBr (19 mg, 0.13 mmol) and molecular sieves (about 200 mg) were added at once, and the solution was warmed to 80 °C and stirred at this temperature for 15 h. Work up: the solution was filtered on Celite then washed with brine. The organic layer was extracted with EtOAc, dried on $MgSO_4$, filtered and evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (10% EtOAc/hexanes) to afford product **20** as a colorless oil (311 mg, 86%, *Z* isomer exclusively). R_f = 0.30 (10% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.03-5.97 (d, *J* = 16 Hz, 1H, C*H*CCO$_2$Et), 5.82-5.69 (m, 3H, CH$_2$=C*H*CHOAc, CH$_2$C*H*=C*H*CH), 5.28-5.15 (m, 3H, C*H*$_2$=CHC*H*OAc), 4.31-4.24 (q, *J* = 7.4 Hz, 2H, CO$_2$C*H*$_2$CH$_3$), 2.31-2.23 (m, 2H, C*H*$_2$CH=CCO$_2$Et), 2.16-2.06 (m, 2H, CH$_3$C*H*$_2$CH=CH), 2.06 (s, 3H, O$_2$CC*H*$_3$), 1.81-1.69 (m, 2H, AcO-CHC*H*$_2$), 1.36-1.31 (t, *J* = 7.4 Hz, 3H, CO$_2$CH$_2$C*H*$_3$), 1.03-0.98 (t, *J* = 7.3 Hz, 3H, CH=CHCH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 168.4, 136.4, 134.8, 134.6, 134.2, 127.0, 117.4, 74.6, 61.0, 34.0, 26.3, 25.8, 21.6, 14.7, 13.7; IR (neat) 2964, 2934, 1735 (C=O), 1731 (C=O), 1372, 1233 (C=C), 1154, 1021, 963 cm^{-1}; HRMS (ESI, Pos) Calcd for $C_{16}H_{24}O_4Na$ (M+Na)$^+$: 303.1567. Found 303.1558 (100 %); also $C_{16}H_{25}O_4$ (M+H)$^+$: 281.1747. Found 281.1734 (5 %).



18b **20**

Ethyl (2*Z*)-6-(acetyloxy)-2-[(1*E*)-but-1-enyl]octa-2,7-dienoate (20). Alcohol **18b** (193 mg, 0.65 mmol) was dissolved in THF (3.2 mL), PPh_3 (338 mg, 1.29 mmol) was added and the solution was cooled to -40 °C. DEAD (225 mg, 1.29 mmol) was added dropwise to the solution which was stirred for 3 h. Work up: $NaHCO_3$ (sat. aq. sln) was added and the organic layer was extracted with CH_2Cl_2, then washed with brine. The organic layer was dried on Na_2SO_4, filtered and evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (10%

EtOAc/hexanes) to afford product **20** as a colorless oil (160 mg, 88%, 97:3 *Z*/*E*). R_f = 0.30 (10% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.03-5.97 (d, *J* = 16 Hz, 1H, C*H*CCO$_2$Et), 5.82-5.69 (m, 3H, CH$_2$=C*H*CHOAc, CH$_2$C*H*=C*H*CH), 5.28-5.15 (m, 3H, C*H*$_2$=CHC*H*OAc), 4.31-4.24 (q, *J* = 7.4 Hz, 2H, CO$_2$C*H*$_2$CH$_3$), 2.31-2.23 (m, 2H, C*H*$_2$CH=CCO$_2$Et), 2.16-2.06 (m, 2H, CH$_3$C*H*$_2$CH=CH), 2.06 (s, 3H, O$_2$CC*H*$_3$), 1.81-1.69 (m, 2H, AcO-CHC*H*$_2$), 1.36-1.31 (t, *J* = 7.4 Hz, 3H, CO$_2$CH$_2$C*H*$_3$), 1.03-0.98 (t, *J* = 7.3 Hz, 3H, CH=CHCH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 168.4, 136.4, 134.8, 134.6, 134.2, 127.0, 117.4, 74.6, 61.0, 34.0, 26.3, 25.8, 21.6, 14.7, 13.7; IR (neat) 2964, 2934, 1735 (C=O), 1731 (C=O), 1372, 1233 (C=C), 1154, 1021, 963 cm^{-1}; HRMS (ESI, Pos) Calcd for $C_{16}H_{24}O_4Na$ $(M+Na)^+$: 303.1567. Found 303.1558 (100 %); also $C_{16}H_{25}O_4$ $(M+H)^+$: 281.1747. Found 281.1734 (5 %).



21

[3-(Diphenylphosphino)phenyl](triphenyl)phosphonium perchlorate (21).[8] To [3-(diphenylphosphino)phenyl](triphenyl)phosphonium bromide[8] (15.0 g, 25 mmol, 1.0 equiv) in CH_3CN (30 mL) and CH_2Cl_2 (10 mL) was added $LiClO_4 \cdot 3H_2O$ (4.2 g, 26 mmol, 1.05 equiv). After 15 min, the mixture was concentrated under reduced pressure and diluted with CH_2Cl_2 (200 mL). The resulting mixture was washed with water (100 mL). The aqueous layer was washed with CH_2Cl_2 (100 mL). The organic solution was washed three times with water (50mL), dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was diluted with CH_2Cl_2 (30 mL) and was crunched with Et_2O (150 mL). This operation was repeated twice to afford pure **21** as a white solid (14.7 g, 95%): mp 160-165 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60-6.80 (m, 29H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.1 (dd, *J* = 18.5, 11.1 Hz, 1C), 139.4 (dd, *J* = 22.1, 2.3 Hz, 1C), 137.2 (dd, *J* = 13.2, 11.0 Hz, 1C), 135.4 (d, *J* = 2.6 Hz, 3C), 134.5 (d, *J* = 10.6 Hz, 2C), 133.9 (d, *J* = 10.3 Hz, 6C), 133.8 (dd, *J* = 10.4, 1.1 Hz, 1C), 133.4 (d, *J* = 20.2 Hz, 4C), 130.4 (d, *J* = 12.8 Hz, 6C), 129.7 (dd, *J* = 12.6, 6.4 Hz, 1C), 129.5 (s, 2C), 128.7 (d, *J* = 7.4 Hz, 4C), 118.1 (dd, *J* = 86.9, 3.1 Hz, 1C), 116.7 (d, *J* = 88.7 Hz, 3C); ^{31}P NMR (162 MHZ, $CDCl_3$) δ 23.2, -4.5; IR (film) 1585, 1483, 1435, 1388, 1079 cm^{-1}; HRMS (ESI, Pos) calc. for $C_{36}H_{29}P_2$ $(M)^+$: 523.1739. Found 523.1747; LRMS (ESI, Neg) calc. for $^{35}ClO_4$ $(M)^-$: 99.0, found 99.0; calc. for $^{37}ClO_4$ $(M)^-$: 101.0, found 101.1.

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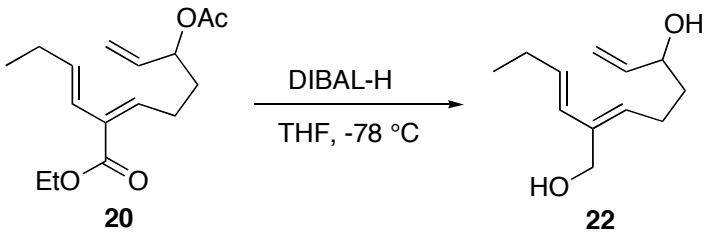
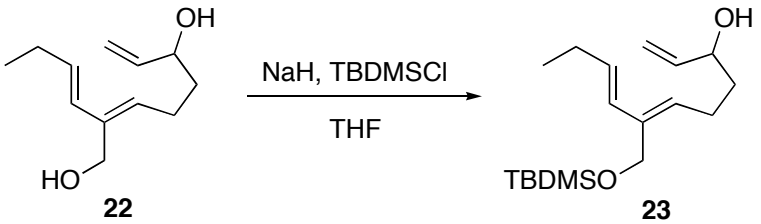
8 Poupon, J.-C.; Boezio, A. A.; Charette, A. B. *Angew. Chem., Int. Ed.* **2006**, *45*, 1415-1420.

5. Synthesis of coronafacic acid via triene 23



20 **22**

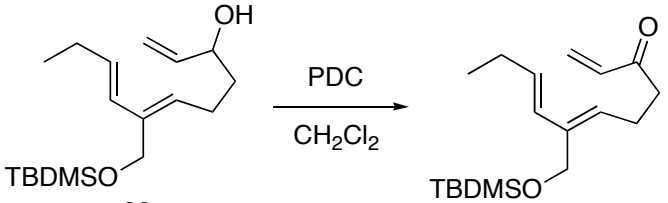
(2*Z*)-2-[(1*E*)-But-1-enyl]octa-2,7-diene-1,6-diol (22). Diester **20** (280 mg, 1.0 mmol) was dissolved in THF (6 mL) then the solution was cooled to -78 °C. DIBAL-H (710 mg, 5.0 mmol) was added, then the solution was stirred at 0 °C for 2 h 30. Work up: HCl (sln. aq. 10%) was added then the organic layer was extracted with EtOAc. The organic layer was washed with brine, dried on Na_2SO_4, filtered and evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (50% EtOAc/hexanes) to afford product **22** as a colorless oil (145 mg, 74%). R_f = 0.35 (50% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.99-5.95 (d, *J* = 15.8 Hz, 1H, C*H*=CHCH$_2$CH$_3$), 5.89-5.78 (m, 2H, CH$_2$=C*H*CH-OH, CH=C*H*CH$_2$CH$_3$), 5.49-5.45 (dd, *J* = 9.5, 6.6 Hz, 1H, CH$_2$CH$_2$C*H*=CCH$_2$OH), 5.24-5.18 (dt, *J* = 17.5, 1.6 Hz, 1H, (*Z*)-C*H*$_2$=CHCH-OH), 5.08-5.05 (dt, *J* = 10.6, 1.4 Hz, 1H, (*E*)-C*H*$_2$=CHCH-OH), 4.36-4.33 (d, *J* = 11.7 Hz, 1H, C*H*$_2$OH), 4.24-4.21 (d, *J* = 11.7 Hz, 1H, C*H*$_2$OH), 4.10-4.05 (m, 1H, C*H*OH), 3.16-2.96 (b, 2H, O-*H*), 2.50-2.40 (m, 1H, C*H*$_2$CHOH), 2.25-2.17 (m, 1H, C*H*$_2$CHOH), 2.15-2.08 (dq, *J* = 7.3, 7.2 Hz, 2H, CH=CHC*H*$_2$CH$_3$), 1.63-1.58 (dt, *J* = 7.7, 6.9 Hz, 2H, C*H*$_2$CH$_2$CHOH), 1.03-0.99 (t, *J* = 7.4 Hz, 3H, CH=CHCH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.0, 137.7, 132.4, 130.7, 130.4, 114.4, 71.0, 56.8, 36.2, 25.8, 23.7, 13.6; IR (neat) 3307 (O-H), 2962, 2929, 1426, 1326, 992, 964, 921 cm^{-1}; HRMS (ESI, Pos) Calcd for $C_{12}H_{20}O_2Na$ $(M+Na)^+$: 219.1355. Found 219.1353.



22 **23**

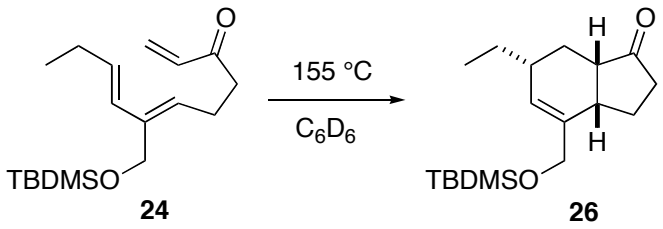
(6*Z*,8*E*)-7-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)undeca-1,6,8-trien-3-ol (23). Diol **22** (98 mg, 0.50 mmol) was dissolved in THF (5 mL), NaH (12 mg, 0.50 mmol) was added followed by TBSCl (75 mg, 0.50 mmol). The solution was stirred at room temperature for 3 h. Work up: NH_4Cl (sat. aq. sln) was added and the organic layer was extracted with CH_2Cl_2, then washed with brine. The

organic layer was dried on Na_2SO_4, filtered and evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (10 to 20% EtOAc/hexanes) to afford product **23** as a clear oil (124 mg, 78%). R_f = 0.45 (20% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.98-5.93 (d, *J* = 15.6 Hz, 1H, C*H*=CHCH$_2$CH$_3$), 5.90-5.76 (m, 2H, CH$_2$=C*H*CH-OH, CH=C*H*CH$_2$CH$_3$), 5.51-5.47 (t, *J* = 7.6 Hz, 1H, CH$_2$CH$_2$C*H*=CCH$_2$OTBS), 5.26-5.21 (dt, *J* = 17.3, 1.5 Hz, 1H, (*Z*)-C*H*$_2$=CHCH-OH), 5.11-5.08 (dt, *J* = 10.4, 1.5 Hz, 1H, (*E*)-C*H*$_2$=CHCH-OH), 4.37-4.29 (m, 2H, CH$_2$OTBS), 4.15-4.08 (m, 1H, CH$_2$=CHC*H*OH), 2.41-2.31 (m, 1H, C*H*$_2$CHOH), 2.29-2.20 (m, 1H, C*H*$_2$CHOH), 2.16-2.07 (m, 2H, CH=CHC*H*$_2$CH$_3$), 1.85-1.73 (b, 1H, CH$_2$=CHCHO*H*), 1.66-1.58 (m, 2H, C*H*$_2$CH$_2$CHOH), 1.03-0.99 (t, *J* = 7.5 Hz, 3H, CH=CHCH$_2$C*H*$_3$), 0.91 (s, 9H, SiC(C*H*$_3$)$_3$), 0.10 (s, 6H, Si(C*H*$_3$)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.0, 137.2, 131.8, 130.8, 130.7, 114.4, 71.8, 58.1, 36.6, 26.0, 25.9, 24.0, 18.4, 13.8 (3C), -5.2 (2C); IR (neat) 3356, 2957, 2928, 2856, 1462, 1251, 1076, 834 (O-Si), 774 cm^{-1}; HRMS (ESI, Pos) Calcd for $C_{18}H_{35}O_2Si$ (M+H)$^+$: 311.2401. Found 311.2400 (100 %); also $C_{18}H_{34}O_2SiNa$ (M+Na)$^+$: 333.2220. Found 333.2220 (95 %).



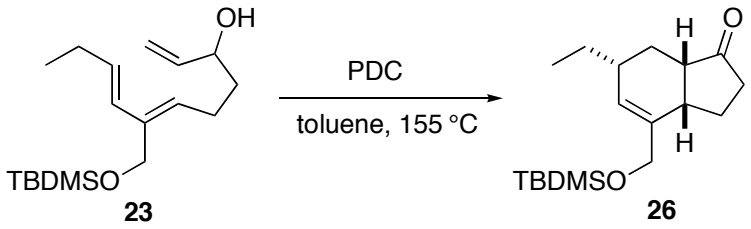
23 **24**

(6*Z*,8*E*)-7-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)undeca-1,6,8-trien-3-one (24). Alcohol **23** (36 mg, 0.116 mmol) was dissolved in CH_2Cl_2 (1 mL), PDC (65 mg, 0.174 mmol) was added and the solution was stirred at room temperature overnight. Work up: a 20% ethyl acetate/hexanes solution was added and solution was filtered on silica gel. The solvent was evaporated and the residue was purified by flash chromatography on silica gel (5 to 10% Et_2O/pentane) to afford product **24** as a colorless oil (15 mg, 42%). R_f = 0.40 (10% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.38-6.31 (dd, *J* = 17.6, 10.5 Hz, 1H), 6.23-6.18 (dd, *J* = 17.8, 1.1 Hz, 1H), 5.95-5.91 (d, *J* = 16.1 Hz, 1H), 5.86-5.79 (m, 2H), 5.48-5.44 (t, *J* = 7.7 Hz, 1H), 4.33 (s, 2H, *CH*$_2$OTBS), 2.71-2.67 (t, *J* = 7.3 Hz, 2H), 2.52-2.46 (dt, *J* = 7.7, 7.3 Hz, 2H), 2.13-2.06 (dq, *J* = 7.3, Hz, 2H), 1.02-0.98 (t, *J* = 7.3 Hz, 3H, CH=CHCH$_2$C*H*$_3$), 0.89 (s, 9H, SiC(C*H*$_3$)$_3$), 0.08 (s, 6H, Si*(CH*$_3$*)*$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.9, 137.9, 136.5, 131.3, 130.5, 130.1, 128.2, 58.1, 39.5, 29.7, 26.1, 25.9, 22.3, 18.3, 13.7, -5.2; IR (neat) 2957, 2927, 2855, 1703, 1684, 1615, 1462, 1400, 1251, 1076, 962, 835 (O-Si), 774 cm^{-1}; HRMS (ESI, Pos) Calcd for $C_{18}H_{33}O_2Si_1$ (M+H)$^+$: 309.2244. Found 309.2248.



24 **26**

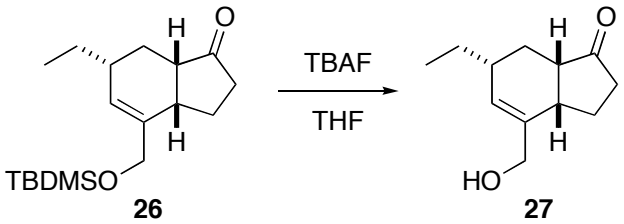
(3a, 6 *trans*; 3a, 7a *cis*)-4-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)-6-ethyl-2,3,3a,6,7,7a-hexahydro-*1H*-inden-1-one (26). Triene **24** (5 mg, 0.016 mmol) was dissolved in C_6D_6 (1 mL) in a sealed tube, then the solution was warmed to 155 °C for 3 h. Work up: the solvent was evaporated under reduced pressure then the residue was purified by flash chromatography on silica gel (5% EtOAc/hexanes) to afford product **26** as a colorless oil (1.2 mg, 24%). R_f = 0.35 (5% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.63-5.59 (b, 1H), 4.24-4.09 (m, 2H), 2.8-2.71 (m, 1H), 2.49-2.17 (m, 3H), 2.09-1.88 (m, 2H) 1.86-1.80 (dt, *J* = 12.4, 4.1 Hz, 1H), 1.66-1.49 (m, 1H), 1.44-1.23 (m, 2H), 1.10-0.99 (m, 1H), 0.92 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 221.5, 138.0, 127.1, 65.7, 47.0, 38.2, 37.1, 36.7, 28.7, 27.5, 27.2, 25.9 (3C), 18.4, 11.1, -5.3, -5.4; IR (neat) 2956, 2927, 2855 1743 (C=O), 1462, 1253, 1137, 1069, 836, 775 cm^{-1}; HRMS (ESI, Pos) Calcd for $C_{18}H_{33}O_2Si_1$ $(M+H)^+$: 309.2244. Found 309.2255 (100%); also $C_{18}H_{32}O_2Si_1Na$ $(M+Na)^+$: 331.2064. Found 331.2075 (60%).



23 **26**

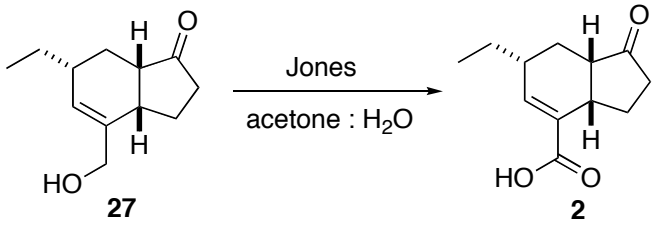
(3a, 6 *trans*; 3a, 7a *cis*)-4-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)-6-ethyl-2,3,3a,6,7,7a-hexahydro-1H-inden-1-one (26). Optimized procedure: tandem oxidation and cyclization. Triene **23** (97 mg, 0.313 mmol) was dissolved in toluene (10 mL) in a Schlenk flask, then PDC (176 mg, 0.469 mmol) was added and the solution was heated to 155 °C for 4 h. Work up: the solvent was evaporated under reduced pressure then the residue was purified by flash chromatography on silica gel (5% EtOAc/hexanes) to afford product **26** as a colorless oil (59 mg, 61%). R_f = 0.35 (5% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.63-5.59 (bs, 1H), 4.24-4.09 (m, 2H), 2.80-2.71 (m, 1H), 2.49-2.17 (m, 3H), 2.09-1.88 (m, 2H) 1.86-1.80 (dt, *J* = 12.4, 4.1 Hz, 1H), 1.66-1.49 (m, 1H),

1.44-1.23 (m, 2H), 1.10-0.99 (m, 1H), 0.92 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 221.5, 138.0, 127.1, 65.7, 47.0, 38.2, 37.1, 36.7, 28.7, 27.5, 27.2, 25.9 (3C), 18.4, 11.1, -5.3, -5.4; IR (neat) 2956, 2927, 2855, 1743 (C=O), 1462, 1253, 1137, 1069, 836, 775 cm^{-1}; ; HRMS (ESI, Pos) Calcd for $C_{18}H_{33}O_2Si_1$ $(M+H)^+$: 309.2244. Found 309.2255 (100%); also $C_{18}H_{32}O_2Si_1Na$ $(M+Na)^+$: 331.2064. Found 331.2075 (60%).



26 **27**

(3a, 6 *trans*; 3a, 7a *cis*)-6-Ethyl-4-(hydroxymethyl)-2,3,3a,6,7,7a-hexahydro-*1H*-inden-1-one (27). Silyl ether **26** (54 mg, 0.175 mmol) was dissolved in THF (500 μL) then a solution of tetrabutylammonium fluoride (1 M in THF, 260 μL, 0.26 mmol) was added, and the solution was stirred for 5 min. The solvent was reduced and the residue was purified by flash chromatography on silica gel (30% EtOAc/hexanes) to afford product **27** as a colorless oil (32 mg, 94%). R_f = 0.30 (40% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.66-5.61 (s, 1H), 5.19-5.11 (m, 2H), 2.85-2.79 (m, 1H), 2.44-2.21 (m, 3H), 2.11-2.01 (b, 1H), 1.87-1.82 (dt, *J* = 12.7, 4.7 Hz, 1H), 1.67-1.56 (1H), 1.54-1.20 (m, 4H), 1.06-0.92 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 215.0, 138.3, 128.7, 65.8, 46.9, 38.3, 37.2, 36.8, 28.6, 27.5, 27.0, 11.1; IR (neat) 3389 (O-H), 2958, 2920, 2853, 1736 (C=O), 1461, 1155, 1135, 1079, 1038, 1011, 912, 850 cm^{-1}; HRMS (APCI, Pos) Calcd for $C_{12}H_{19}O_2$ $(M+H)^+$: 195.1379. Found 195.1374 ; also $C_{12}H_{17}O$ $(M+H-H_2O)^+$: 177.1274. Found 177.1271.

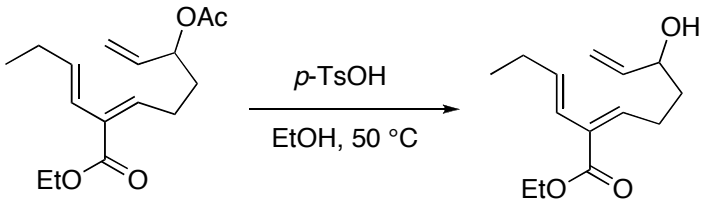


27 **2**

(±)-(3a,6-*trans*; 3a,7a-*cis*)-6-Ethyl-1-oxo-2,3,3a,6,7,7a-hexahydro-1*H*-indene-4-carboxylate (coronafacic acid) (2). Chromium(VI) oxide (267 mg) as well as concentrated sulfuric acid (230 μL) were dissolved in water (1 mL) to obtain a Jones oxidant solution. Alcohol **27** (21 mg, 0.107 mmol) was dissolved in acetone, then a 50 μL of Jones oxidant solution was added. The solution

was stirred at room temperature for 3 h. Work up: the solvent was evaporated, then the residue was purified by flash chromatography on silica gel (30% EtOAc/hexanes) to afford coronafacic acid (**2**) as a white solid (16.5 mg, 74%). R_f = 0.25 (30% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09-7.07 (bs, 1H, H_5), 3.13-3.05 (m, 1H, H_{3a}), 2.66-2.57 (m, 1H, H_3), 2.46-2.17 (m, 4H, H_2 (2H), H_{7a}, H_6), 1.92-1.86 (m, 1H, H_7), 1.66-1.38 (m, 3H, CHC*H*$_2$CH$_3$ (2H), H_3), 1.15-1.06 (m, 1H, H_7), 1.01-0.97 (t, *J* = 7.4 Hz, 3H, CHCH$_2$C*H*$_3$). Product is identical in all respects to authentic material.[9]

7. Synthesis of coronafacic acid via triene 28



20 **28**

Ethyl (2*Z*)-2-[(1*E*)-but-1-enyl]-6-hydroxyocta-2,7-dienoate (28). Triene **20** (311 mg, 1.11 mmol) was dissolved in ethanol (10 mL), *p*-TsOH (211 mg, 1.11 mmol) was added then the solution was warmed to 50 °C and stirred for 18 h. Work up: the solvent was evaporated under reduced pressure, then the residue was purified by flash chromatography on silica gel (40% EtOAc/hexanes) to afford product **28** as a colorless oil (225 mg, 85%). R_f = 0.35 (50% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.01-5.97 (d, *J* = 16 Hz, 1H, C*H*CCO$_2$Et), 5.89-5.81 (ddd, *J* = 17.1, 10.4, 6.1 Hz, 1H, CH$_2$=C*H*CHOH), 5.79-5.69 (m, 2H, CH$_2$C*H*=C*H*CH), 5.25-5.20 (dt, *J* = 17.1, 1.4 Hz, 1H, (*Z*)-C*H*$_2$=CHCHOH), 5.10-5.06 (dt, *J* = 10.4, 1.4 Hz, 1H, (*E*)-C*H*$_2$=CHCH-OH), 4.30-4.25 (q, *J* = 7.2 Hz, 2H, CO$_2$C*H*$_2$CH$_3$), 4.13-4.08 (m, 1H, C*H*OH), 2.48-2.43 (bs, 1H, O*H*), 2.42-2.24 (m, 2H, CH$_2$C*H*$_2$CH=CCO$_2$Et), 2.14-2.06 (dq, *J* = 7.2, 6.4 Hz, 2H, CH$_3$C*H*$_2$CH=CH), 1.67-1.61 (m, 2H, C*H*$_2$CH=CCO$_2$Et), 1.35-1.31 (t, *J* = 7.2 Hz, 3H, CO$_2$CH$_2$C*H*$_3$), 1.02-0.98 (t, *J* = 7.4 Hz, 3H, CH=CHCH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 140.7, 135.3, 134.2, 133.8, 126.5, 114.5, 71.5, 60.9, 36.1, 25.8, 25.6, 14.3, 13.3; IR (neat) 3423 (O-H), 2964, 2932, 1712 (C=O), 1645, 1445, 1378, 1253, 1187, 1151, 1022, 991, 962, 920 cm^{-1}; HRMS (ESI, Pos) Calcd for $C_{14}H_{22}O_3Na$ $(M+Na)^+$: 261.1461. Found 261.1459.

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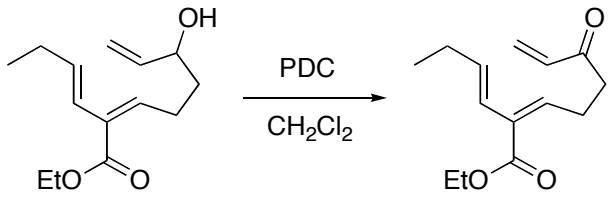
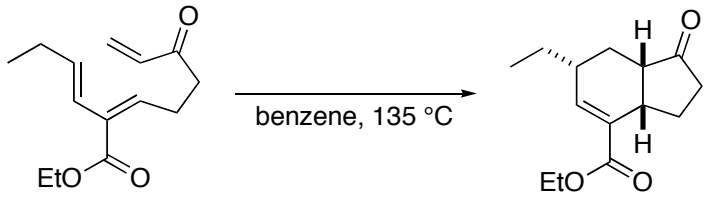
9 Nara, S.; Toshima, H.; Ichihara, A. *Tetrahedron* **1997**, *53*, 9509-9524.



28 **29**

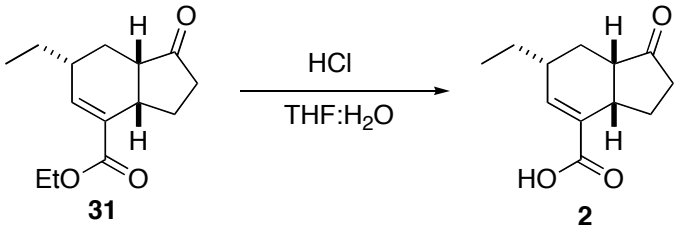
Ethyl (*2Z*)-2-[(*1E*)-but-1-enyl]-6-oxoocta-2,7-dienoate (29). Alcohol **28** (100 mg, 0.42 mmol) was dissolved in CH_2Cl_2 (2 mL), PDC (236 mg, 0.64 mmol) was added and the solution was stirred at room temperature for 4 h. Work up: a EtOAc/hexanes (20%) solution was added and the solution was filtered on silica gel. The solvent was evaporated and the residue was purified by flash chromatography on silica gel (10% EtOAc/hexanes) to afford product **29** as a colorless oil (77 mg, 77%). R_f = 0.35 (10% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.38-6.31 (dd, *J* = 17.1, 10.4 Hz, 1H, CH_2=C*H*C=O), 6.25-6.20 (dd, *J* = 17.1, 1.1 Hz, 1H, (*E*)-C*H*$_2$=CHC=O), 6.01-5.97 (d, *J* = 15.6 Hz, 1H, C*H*CCO$_2$Et), 5.86-5.72 (m, 3H, (*Z*)-C*H*$_2$=CHC=O, C*H*=C*H*CH$_2$CH$_3$), 4.31-4.26 (q, *J* = 7.1 Hz, 2H, CO$_2$C*H*$_2$CH$_3$), 2.76-2.72 (t, *J* = 7.6 Hz, 2H, O=CC*H*$_2$CH$_2$), 2.56-2.50 (dt, *J* = 9, 7.6 Hz, 2H, O=CCH$_2$C*H*$_2$), 2.15-2.07 (dq, *J* = 7.6, 6.4 Hz, 2H, CH=CHC*H*$_2$CH$_3$), 1.35-1.31 (t, *J* = 7.1 Hz, 3H, CO$_2$CH$_2$C*H*$_3$), 1.03-0.99 (t, *J* = 7.6 Hz, 3H, CH=CHCH$_2$C*H*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.5, 167.9, 136.3, 134.4, 134.0, 133.9, 128.4, 126.5, 60.7, 38.9, 25.8, 23.9, 14.3, 13.3; IR (neat) 2964, 2932, 1715 (C=O), 1682 (C=O), 1615, 1445, 1399, 1378, 1217, 1181, 1143, 1096, 1023, 962 cm^{-1}; HRMS (ESI, Pos) Calcd for $C_{14}H_{20}O_3Na$ (M+Na)$^+$: 259.1304. Found 259.1302.



29 **31**

Ethyl (3a,6-*trans*; 3a,7a-*cis*)-6-ethyl-1-oxo-2,3,3a,6,7,7a-hexahydro-1*H*-indene-4-carboxylate (31). Triene **29** (30 mg, 0.127 mmol) was dissolved in benzene (1 mL) and DMSO (1 mL) in a sealed tube, then the solution was heated to 180 °C for 5 min in a microwave apparatus. NMR monitoring of the reaction indicated that **30** was initially formed by complete epimerization to **31** upon purification. Work up: the solvent was evaporated under reduced pressure then the residue was purified by flash chromatography on silica gel (10% EtOAc/hexanes) to afford product **31** as a colorless oil (23.4 mg, 78%). R_f = 0.25 (10% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.93-

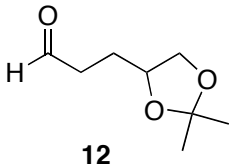
6.91 (bs, 1H, H_5), 4.30-4.16 (m, 2H, $CO_2CH_2CH_3$), 3.13-3.05 (m, 1H, H_{3a}), 2.61-2.53 (m, 1H, H_3), 2.44-2.25 (m, 3H, H_2 (2H), H_{7a}), 2.23-2.14 (m, 1H, H_6), 1.89-1.84 (dt, J = 12.7, 5 Hz, 1H, H_7), 1.64-1.47 (m, 2H, $CHCH_2CH_3$, H_3), 1.45-1.37 (m, 1H, $CHCH_2CH_3$), 1.34-1.30 (t, J = 7 Hz, 3H, $CO_2CH_2CH_3$), 1.12-1.02 (m, 1H, H_7), 1.00-0.96 (t, J = 7.5 Hz, 3H, $CHCH_2CH_3$). Product was identical in all respects to authentic material.[9]



31 **2**

(±)-(3a,6-*trans*; 3a,7a-*cis*)-6-Ethyl-1-oxo-2,3,3a,6,7,7a-hexahydro-1*H*-indene-4-carboxylate (coronafacic acid) (2). Ester **31** (20 mg, 0.085 mmol) was dissolved in THF (1 mL) then HCl 10% (sln. aq.) (1 mL) was added and the solution was heated to 50 °C for 20 h. Work up: the organic layer was extracted with ether (2x).The organic layer was dried on Na_2SO_4, filtered and evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (30% EtOAc/hexanes) to afford coronafacic acid (**2**) as a white solid (16 mg, 90%) R_f = 0.25 (30% EtOAc/hexanes) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09-7.07 (bs, 1H, H_5), 3.13-3.05 (m, 1H, H_{3a}), 2.66-2.57 (m, 1H, H_3), 2.46-2.17 (m, 4H, H_2 (2H), H_{7a}, H_6), 1.92-1.86 (m, 1H, H_7), 1.66-1.38 (m, 3H, $CHCH_2CH_3$, H_3), 1.15-1.06 (m, 1H, H_7), 1.01-0.97 (t, J = 7.4 Hz, 3H, $CHCH_2CH_3$). Product was identical in all respects to authentic material.[9]

^{1}H and ^{13}C spectra of selected compounds



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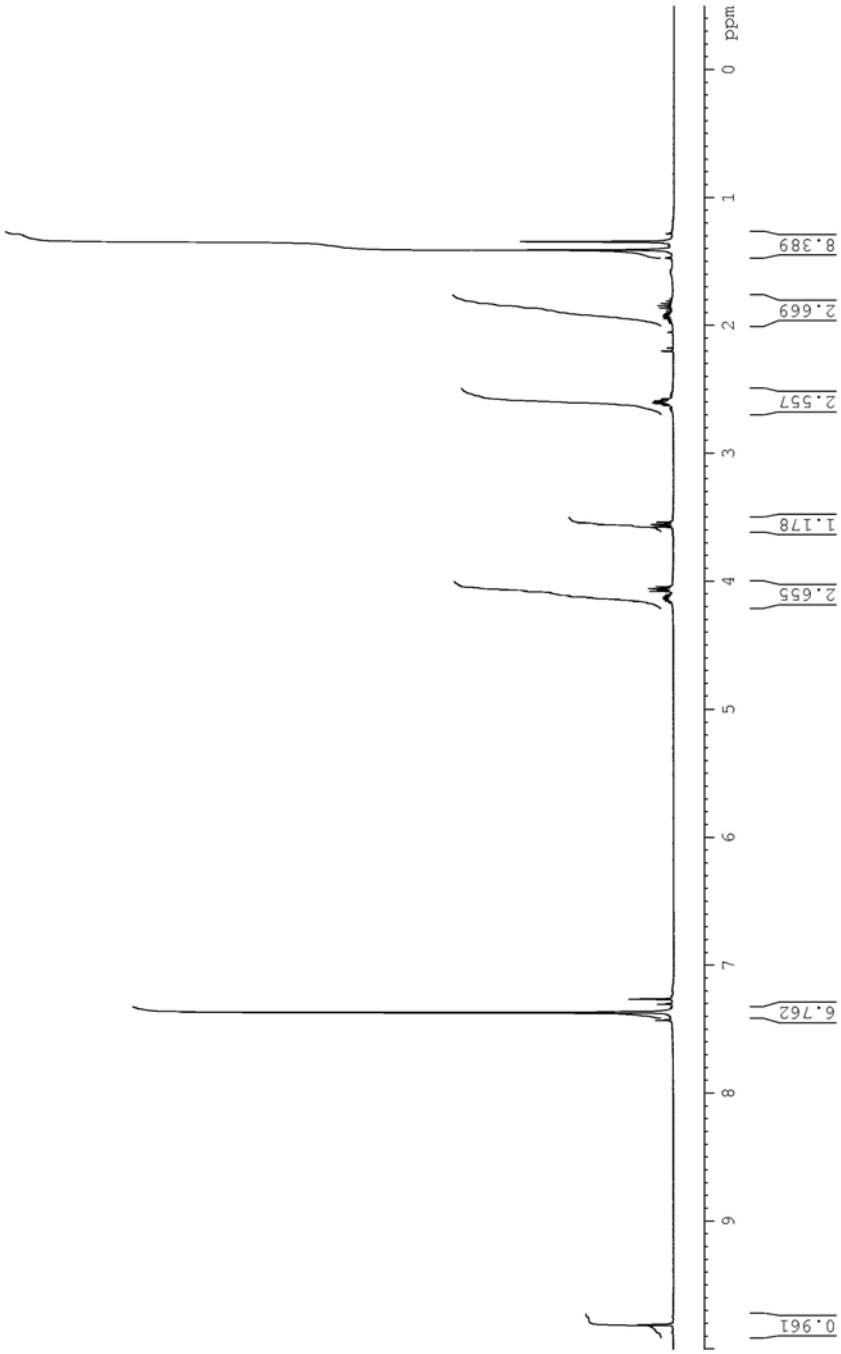

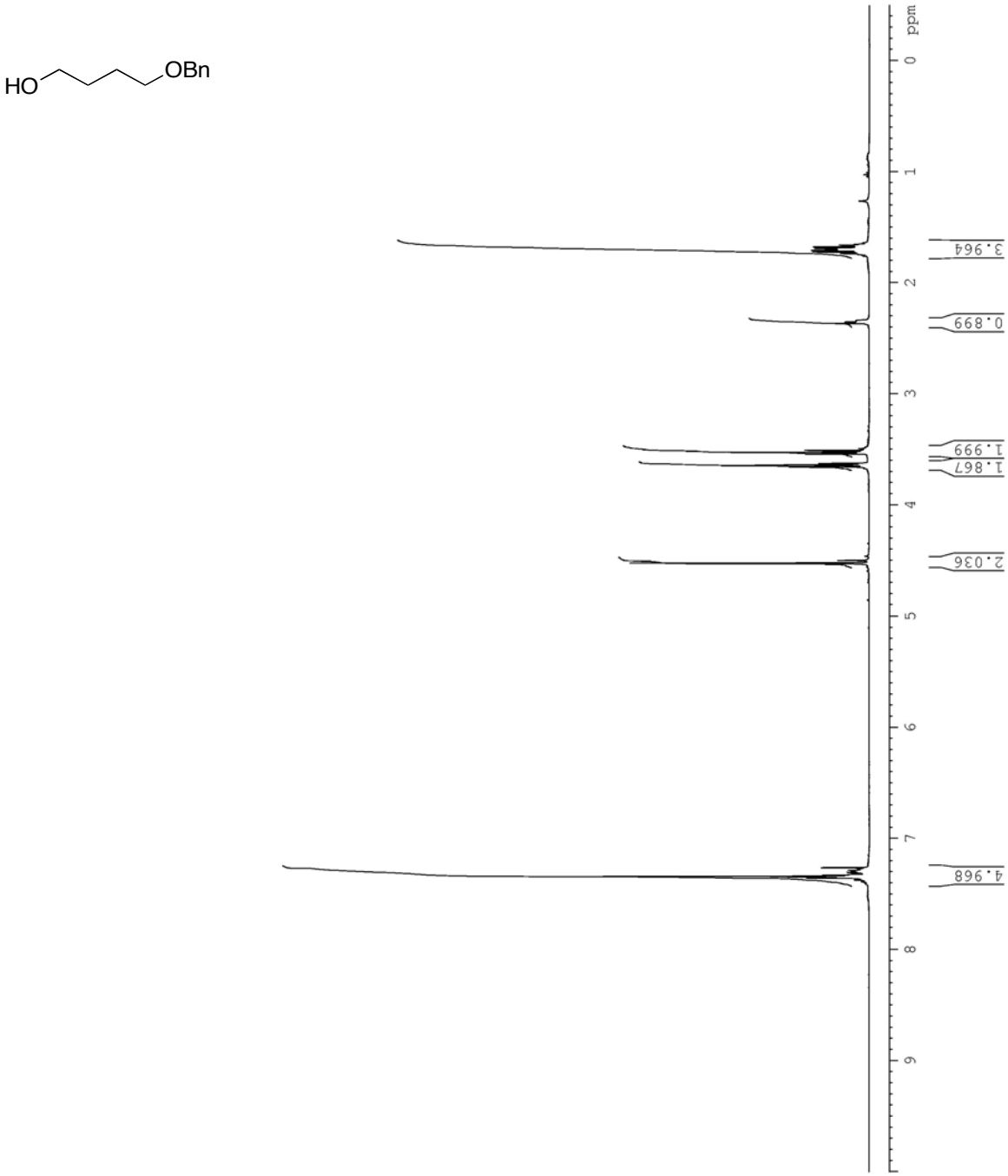
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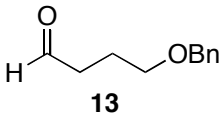
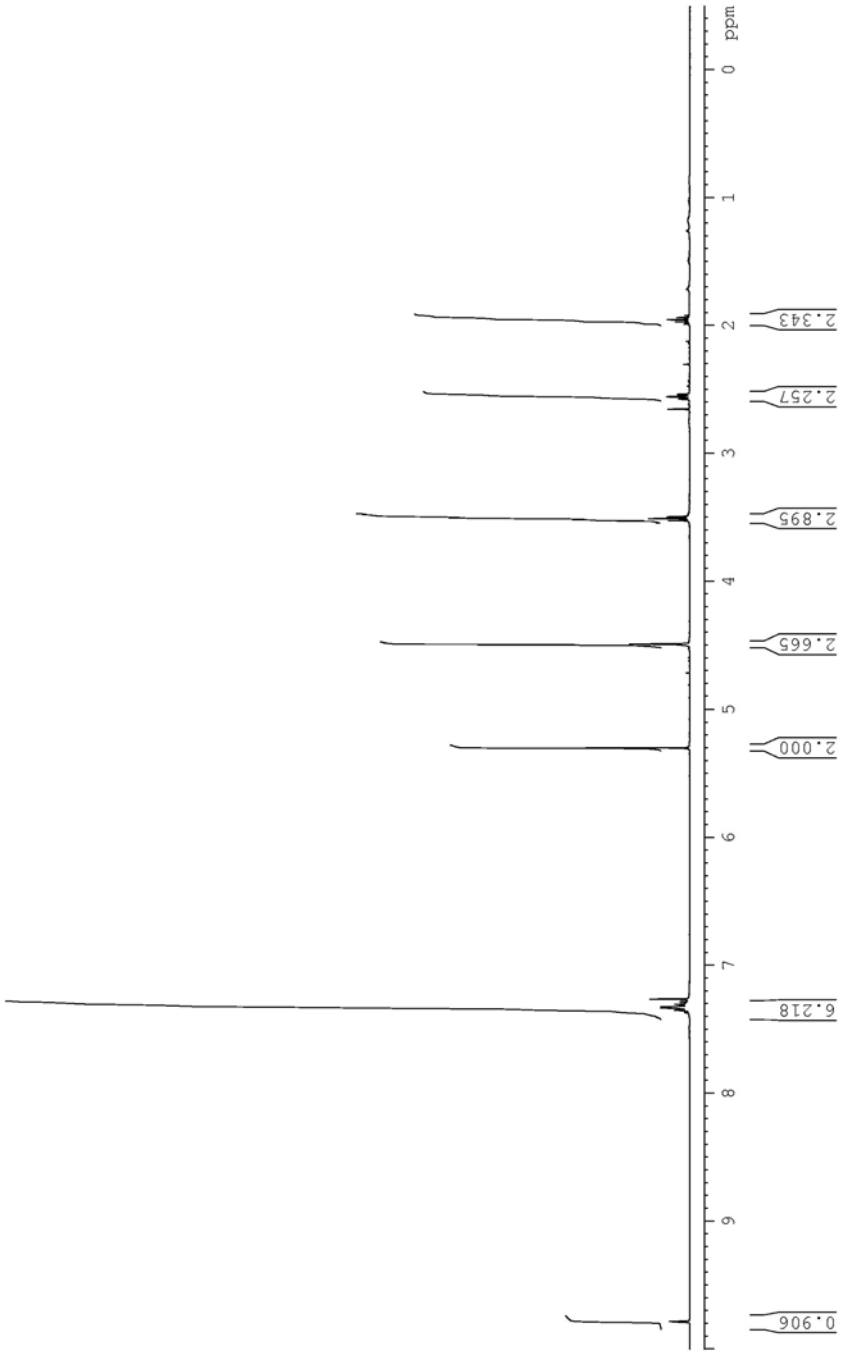
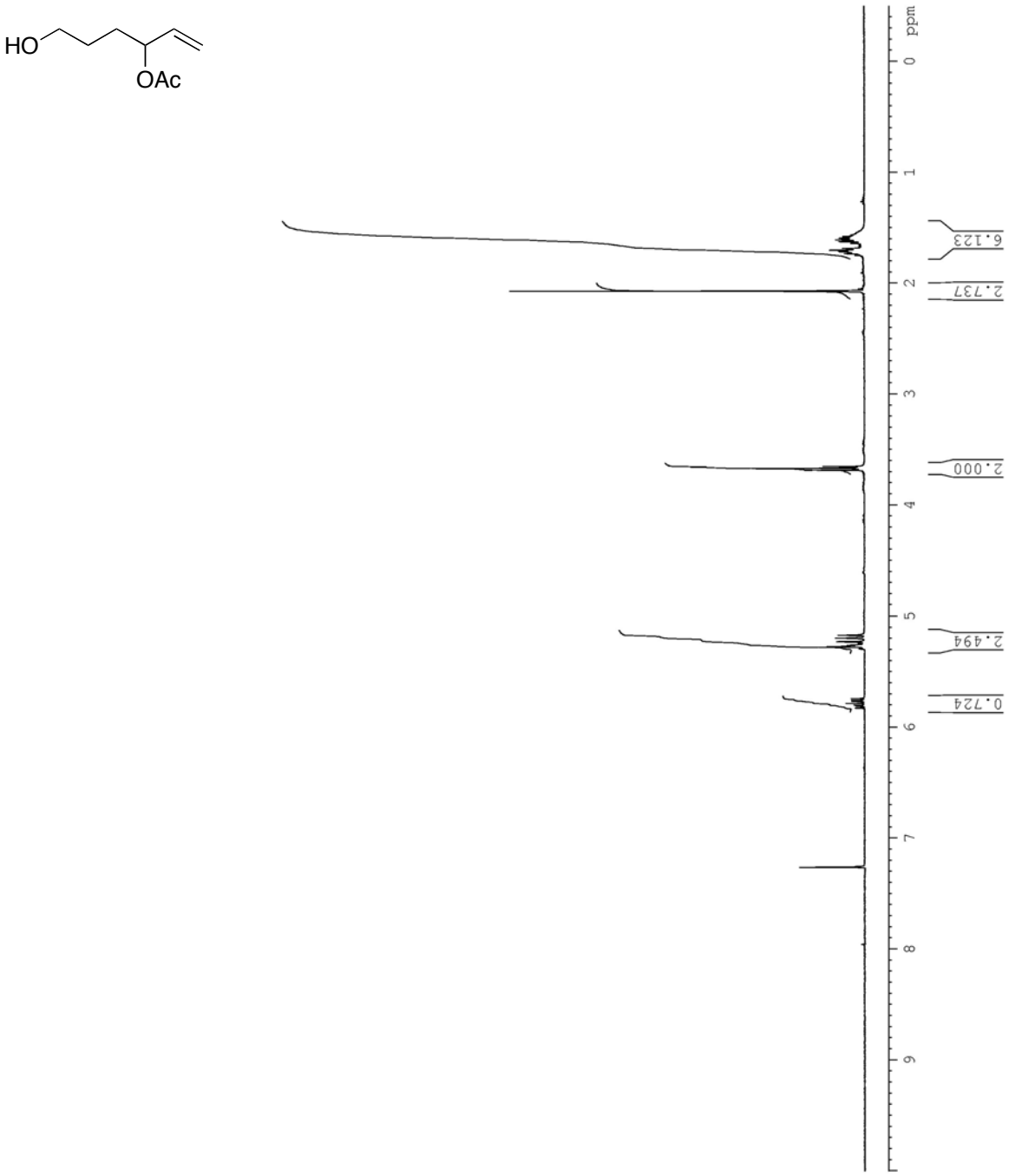


13

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OAc
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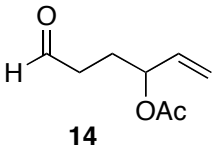
2.494
0.724



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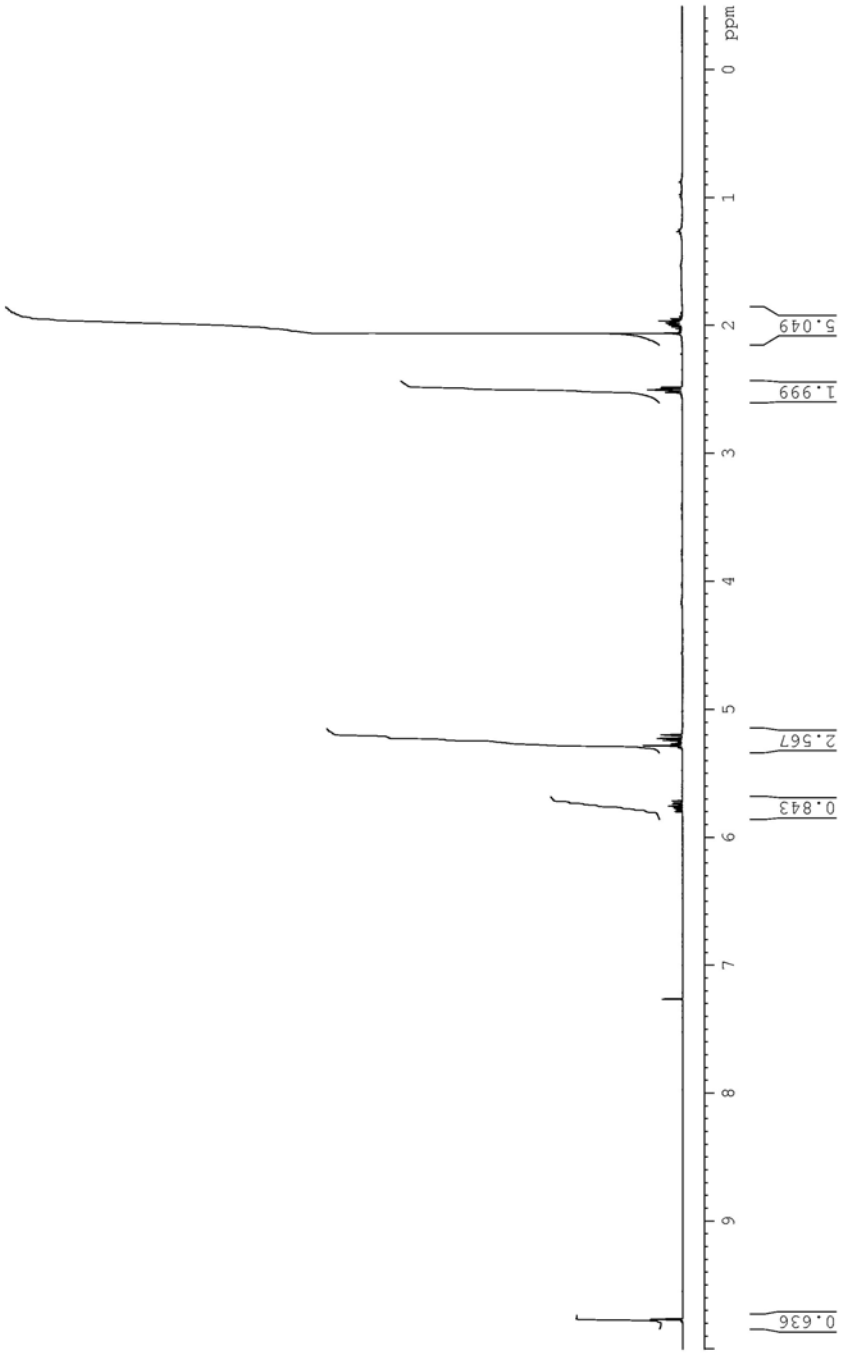
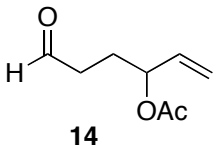
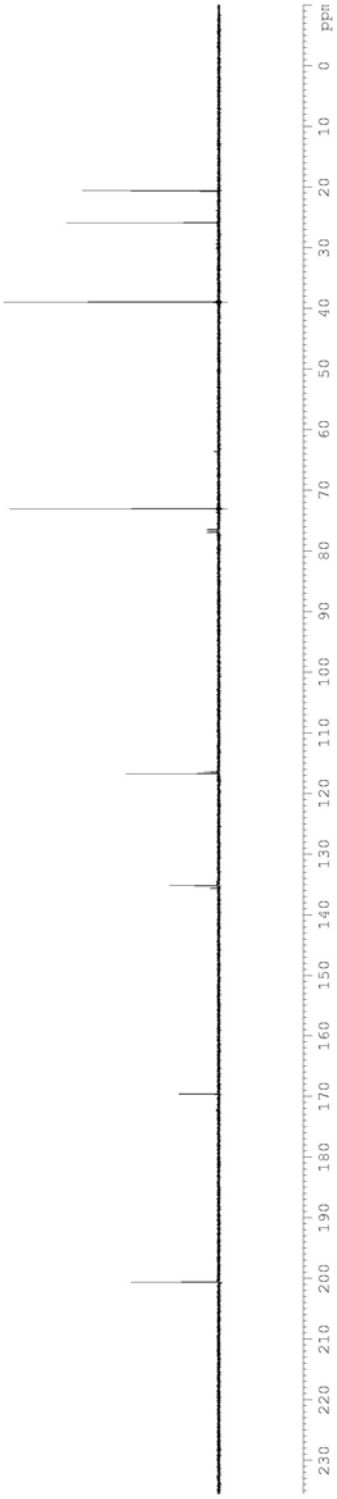



O
H
OAc

14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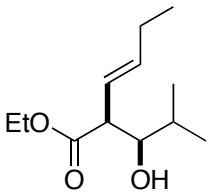
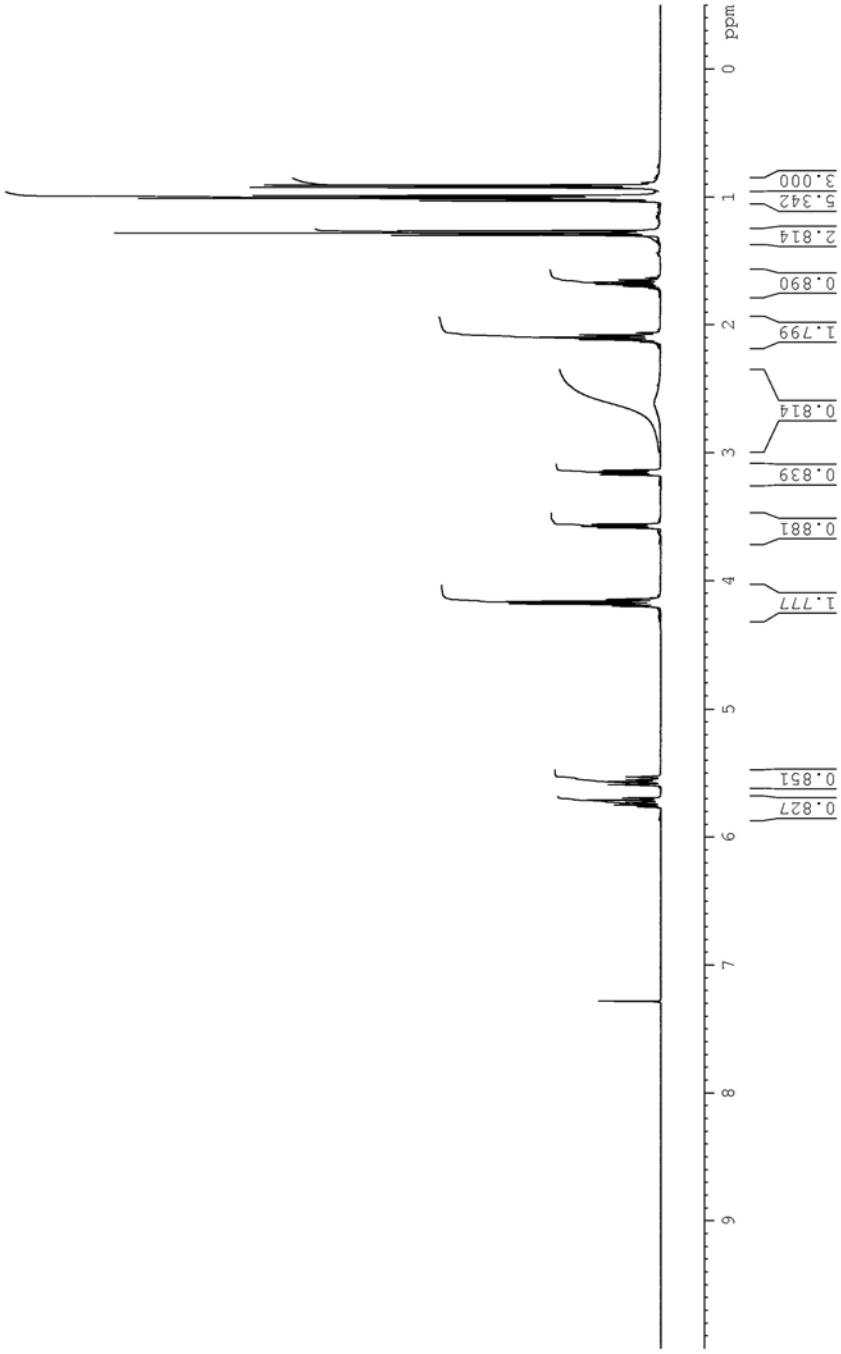

EtO
O
OH

15a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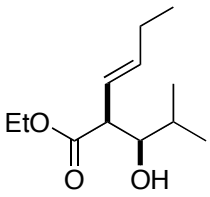
0.851
0.827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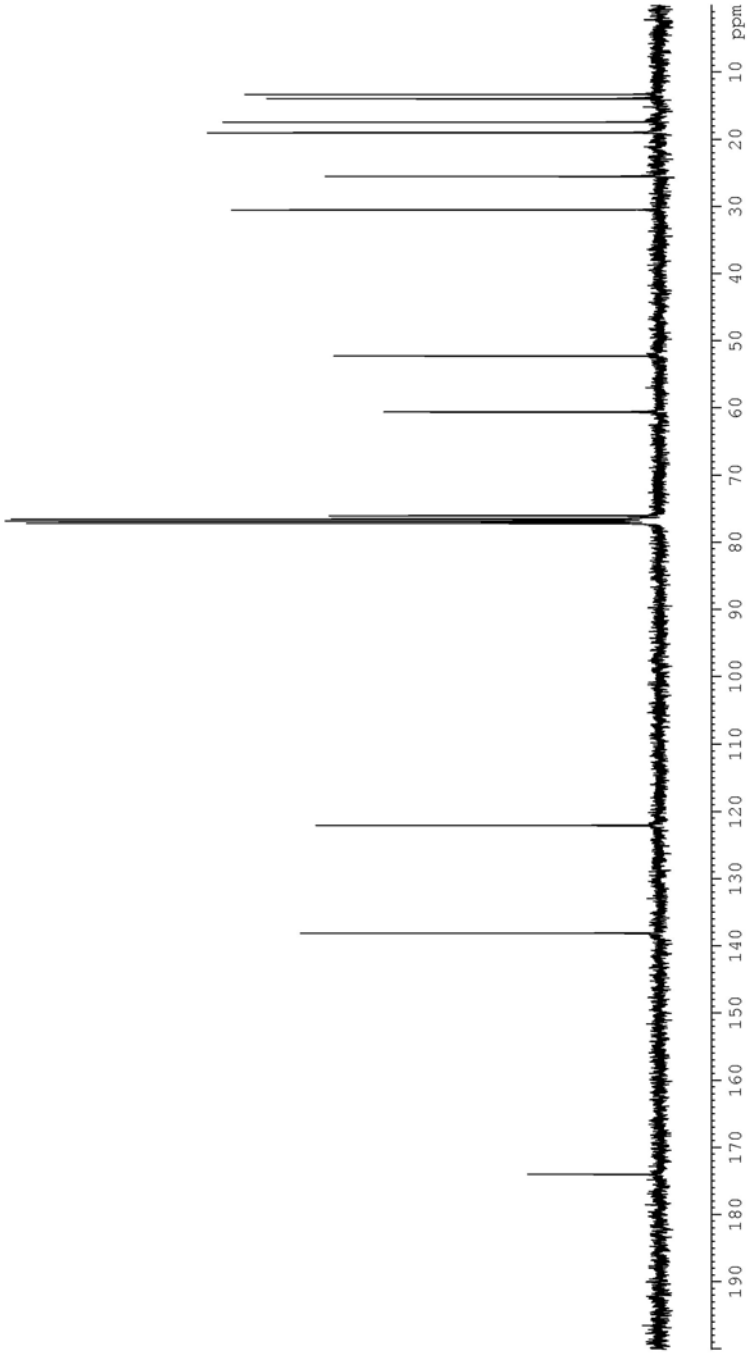
OH

15a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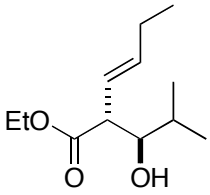
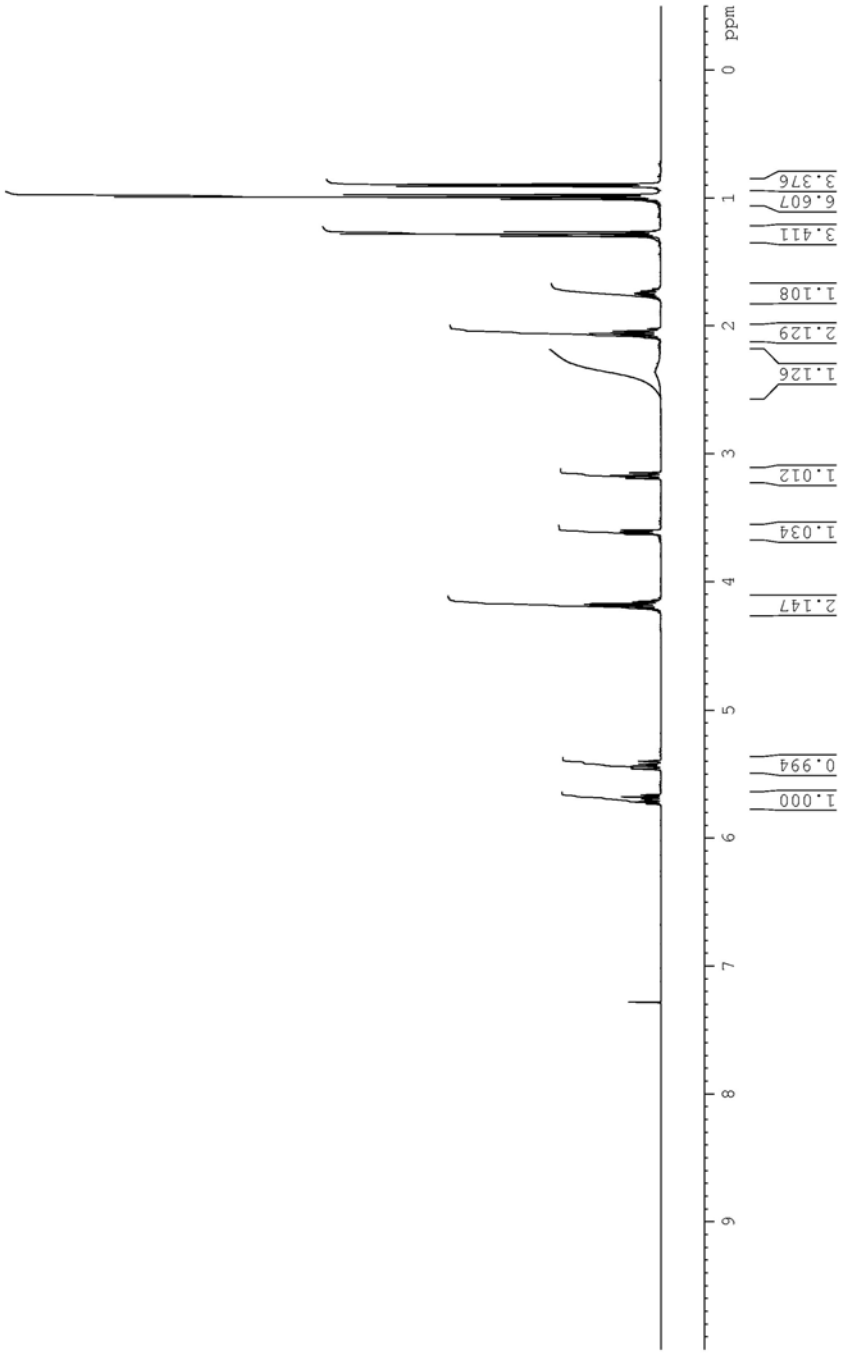

EtO
O
OH

15b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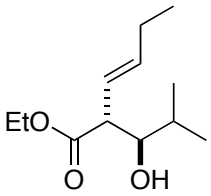
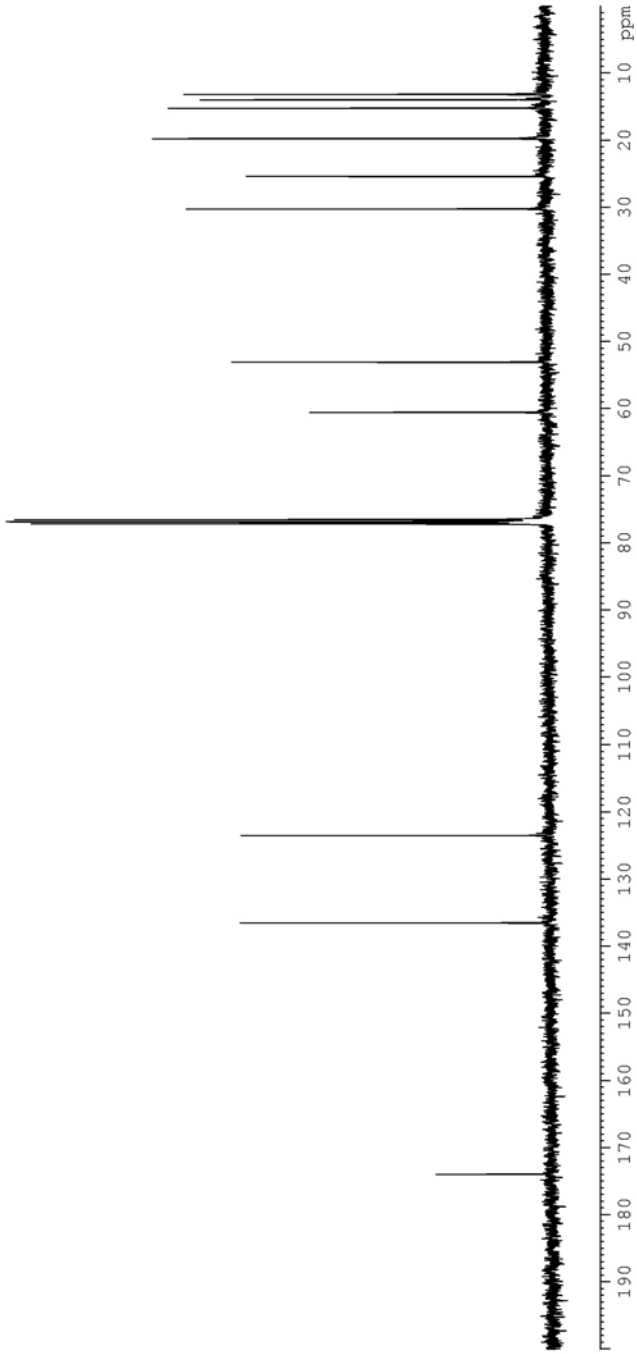
1.126
1.012
1.034
2.147
0.994
1.000


EtO
O
OH

15b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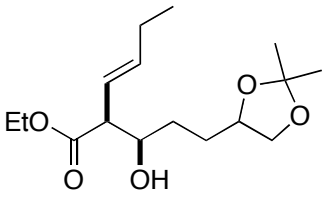
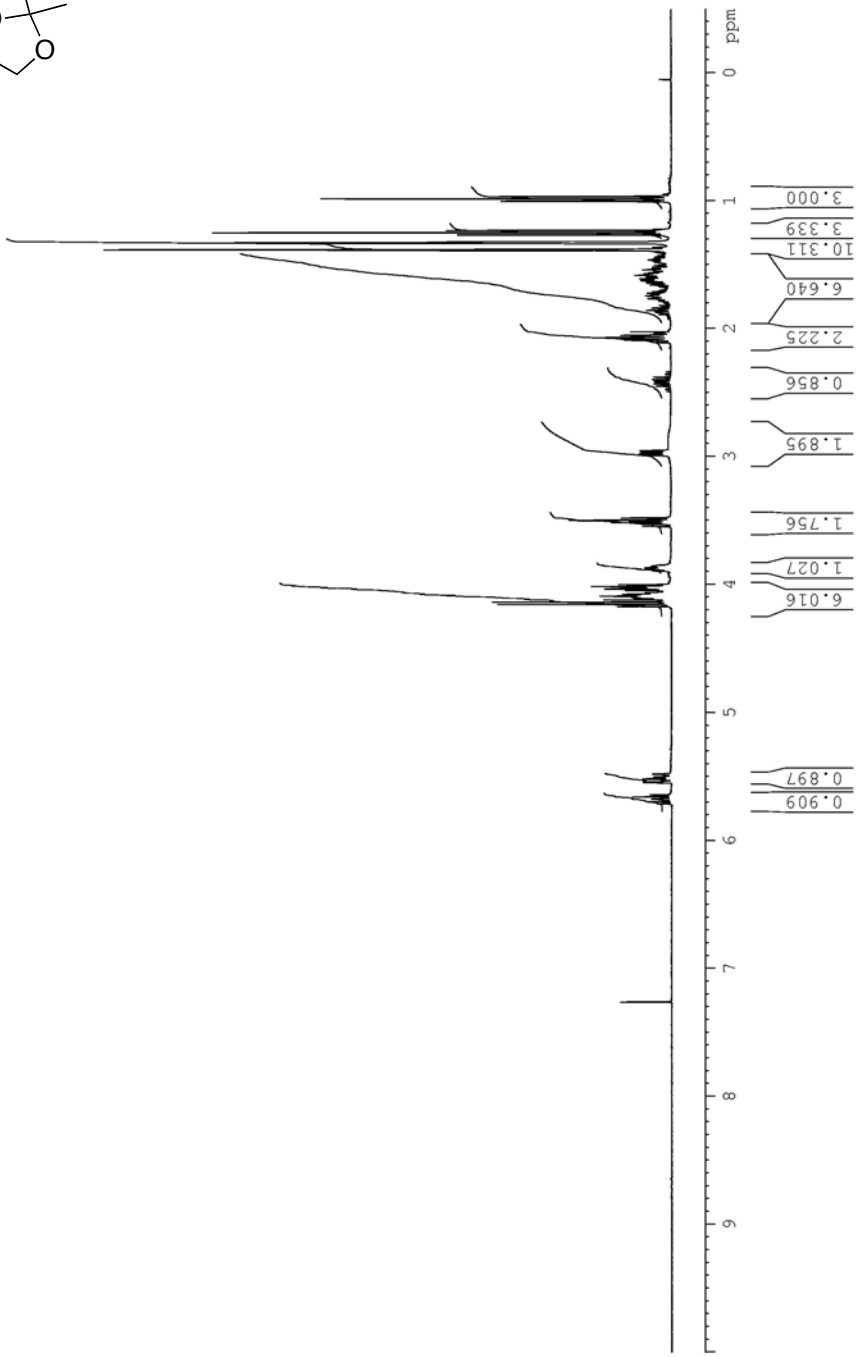

EtO
O
OH
O
O

16a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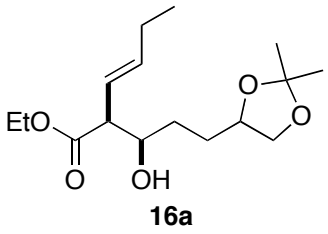
1.756
1.027
6.016
0.897
0.909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OH
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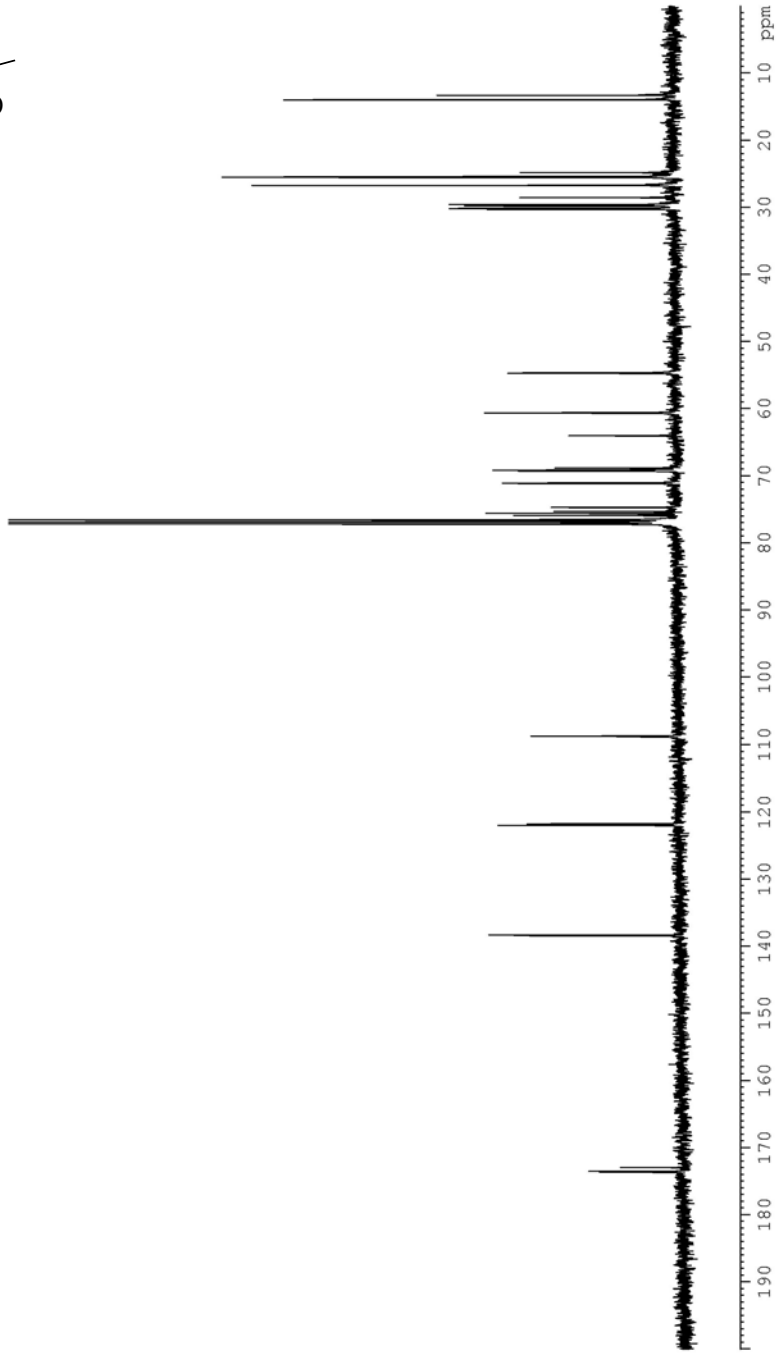
O

16a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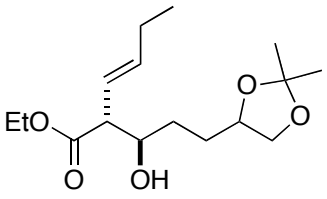
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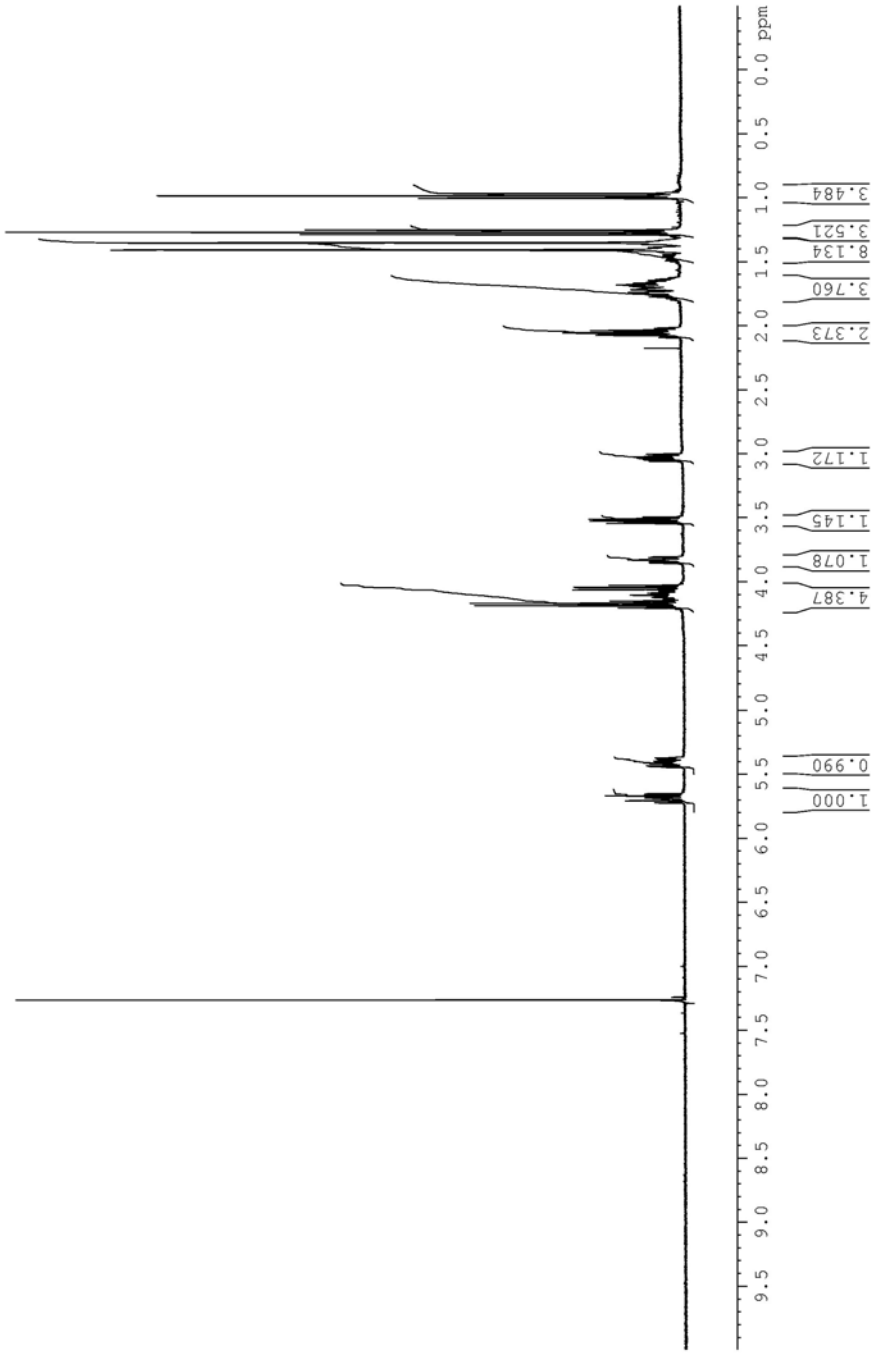
OH
O
O

16b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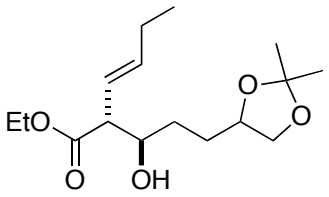
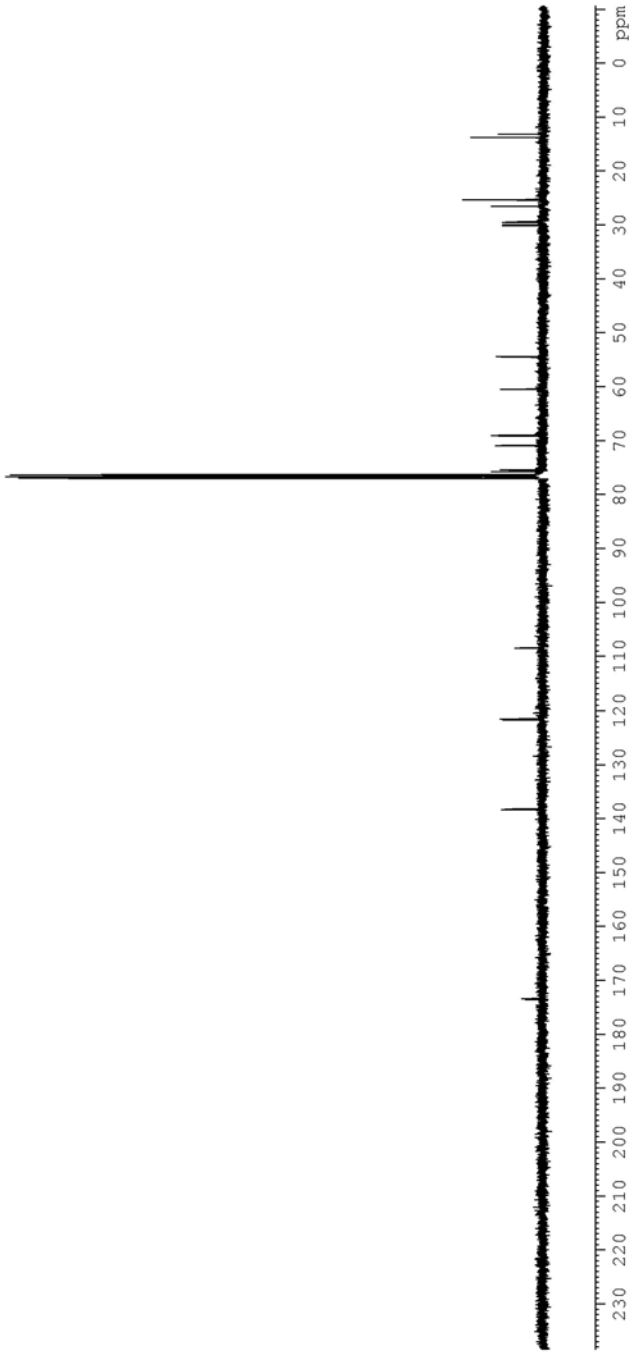
0.990
1.000
ppm


EtO
O
OH
O
O

16b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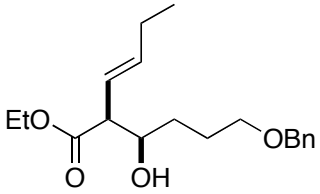
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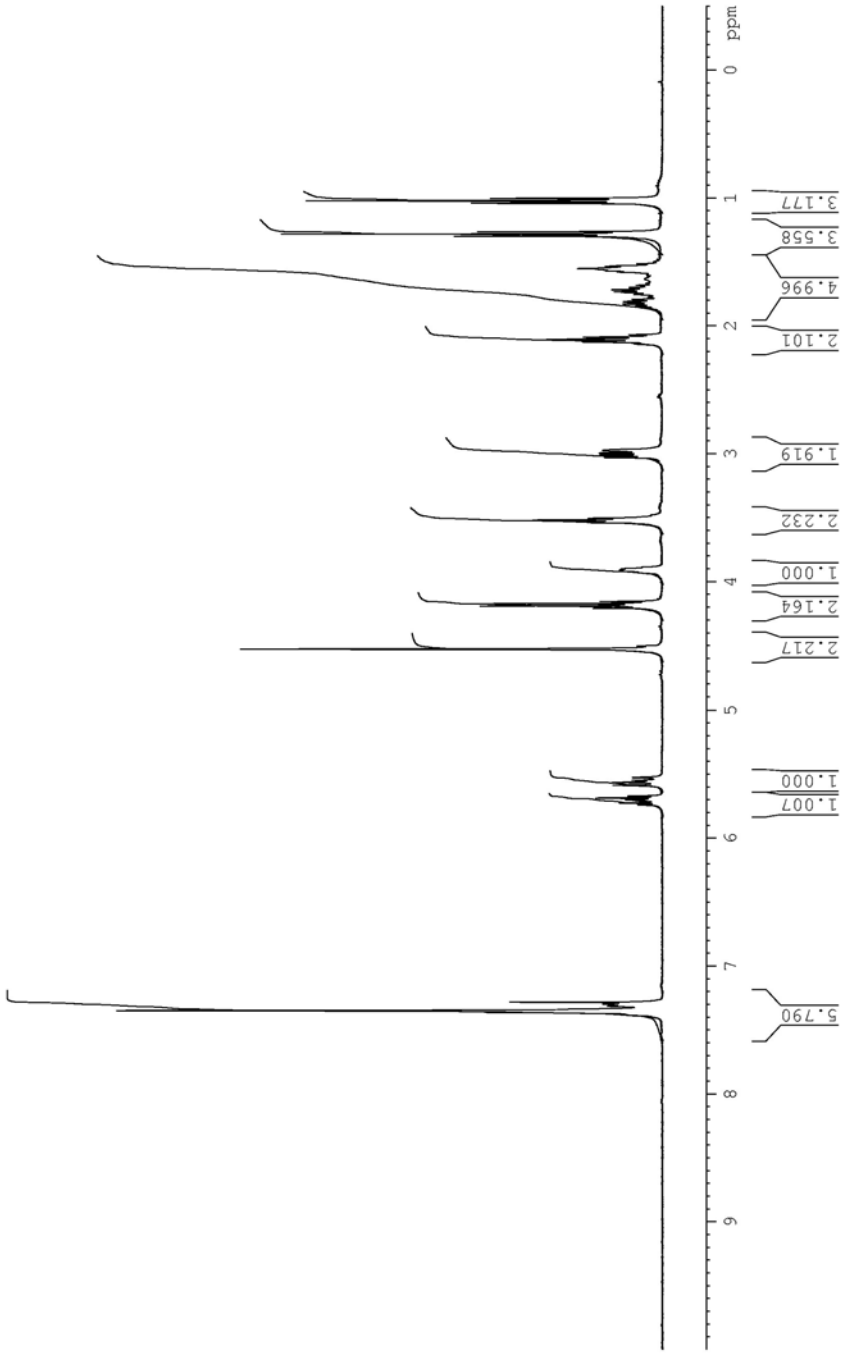
OH
OBn

17a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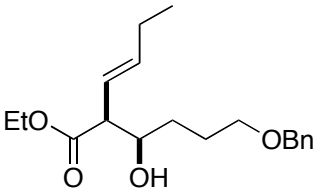
2.164
2.217
1.000
1.007
5.790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OBn

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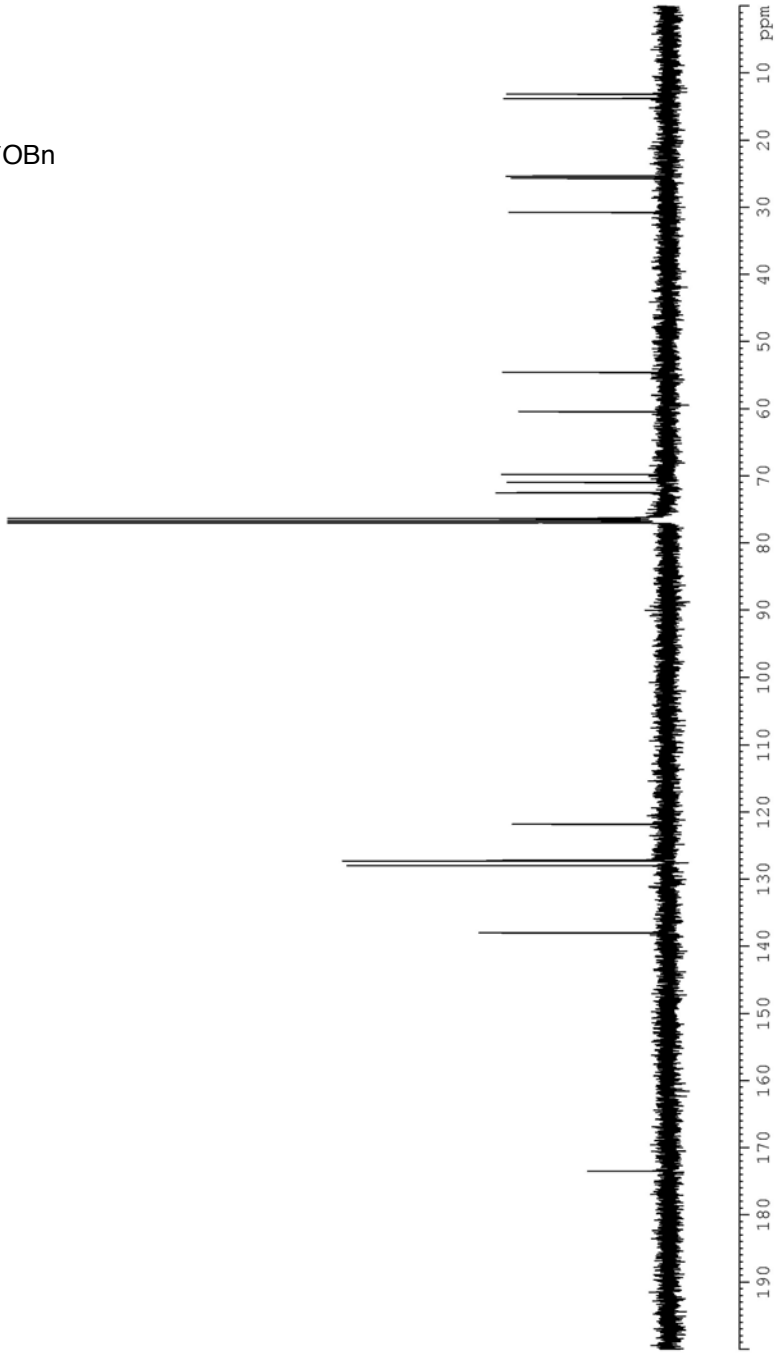
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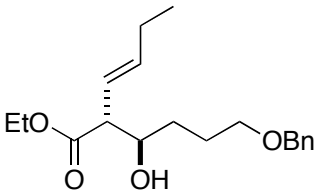
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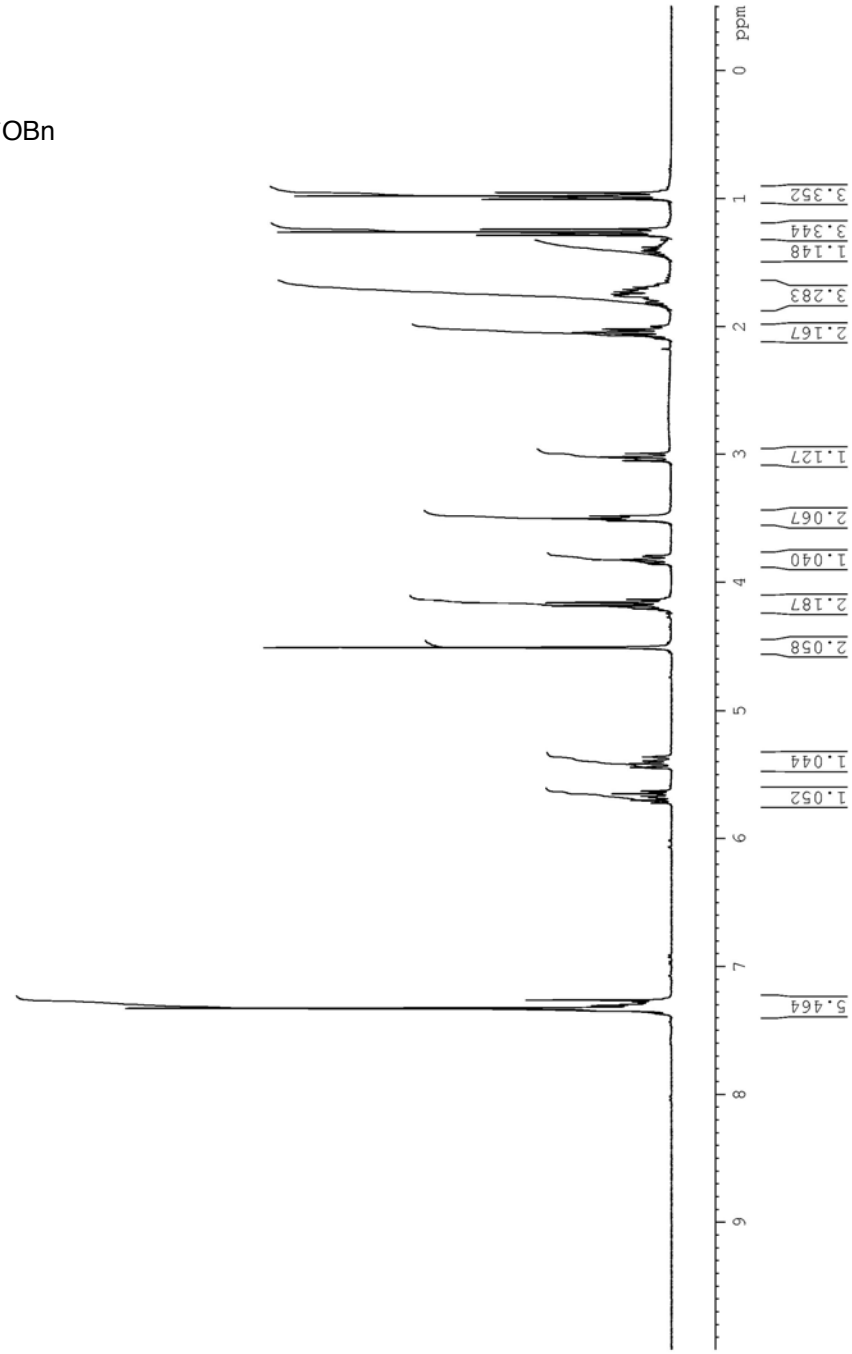
OH
OBn

17b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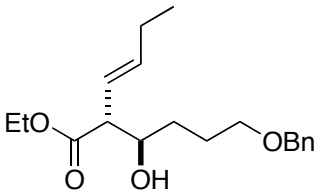
1.052
5.464


EtO
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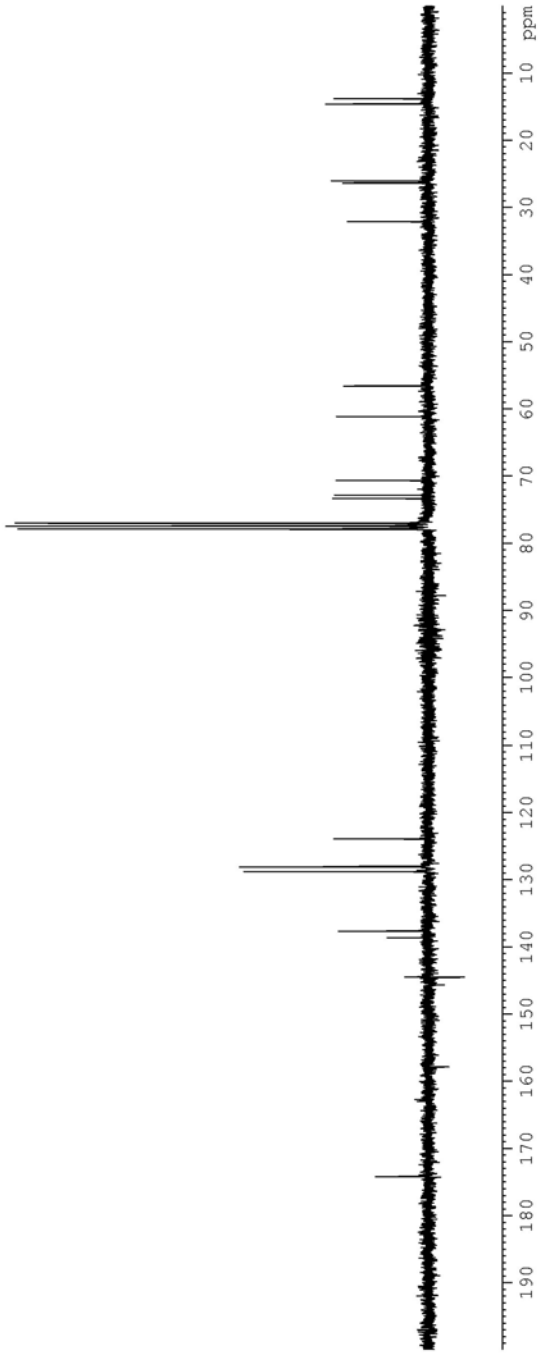
OBn

17b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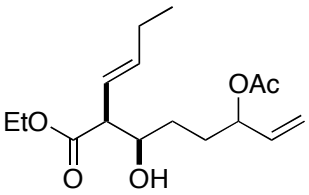
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O
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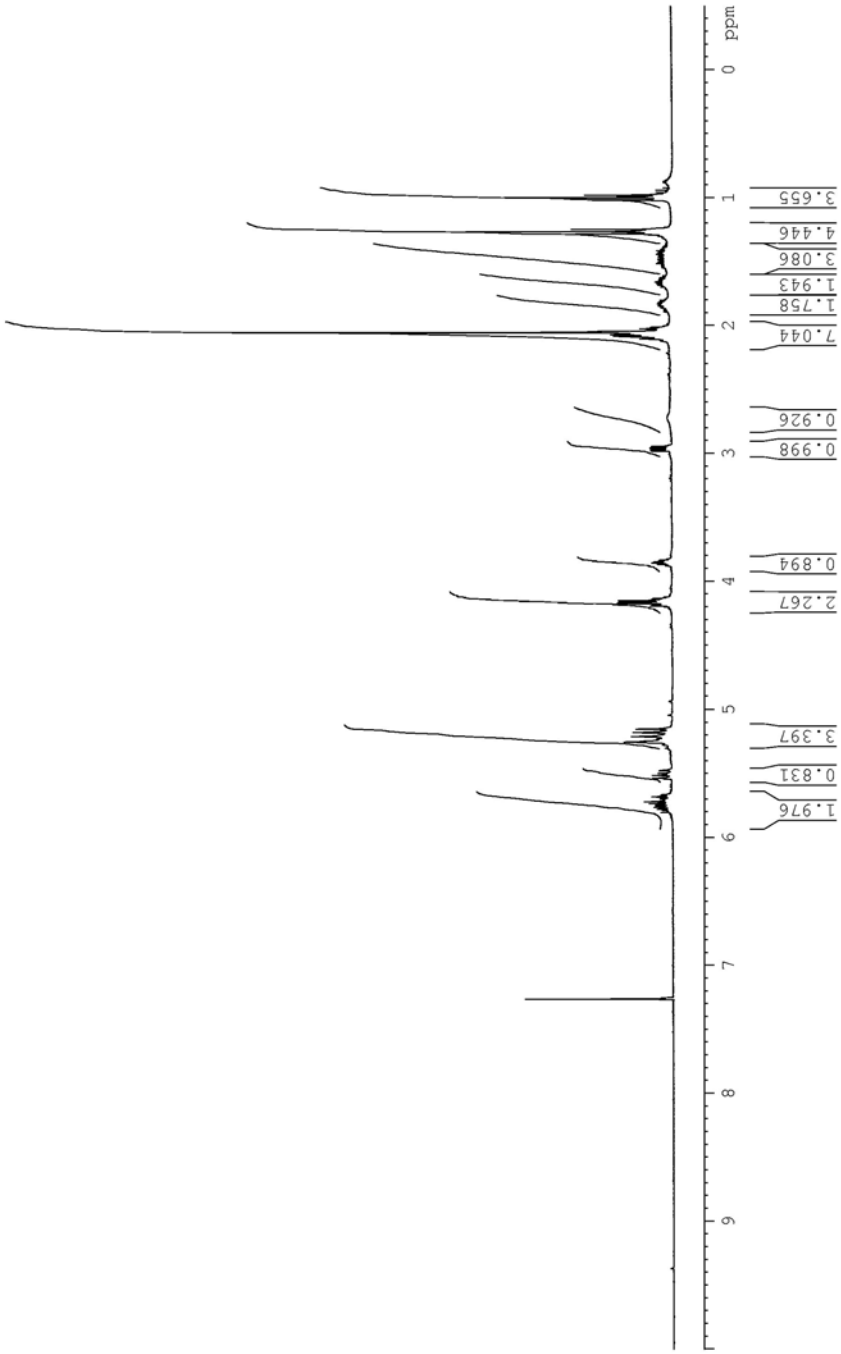
OAc

18a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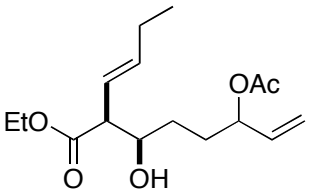
0.831
1.976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OAc

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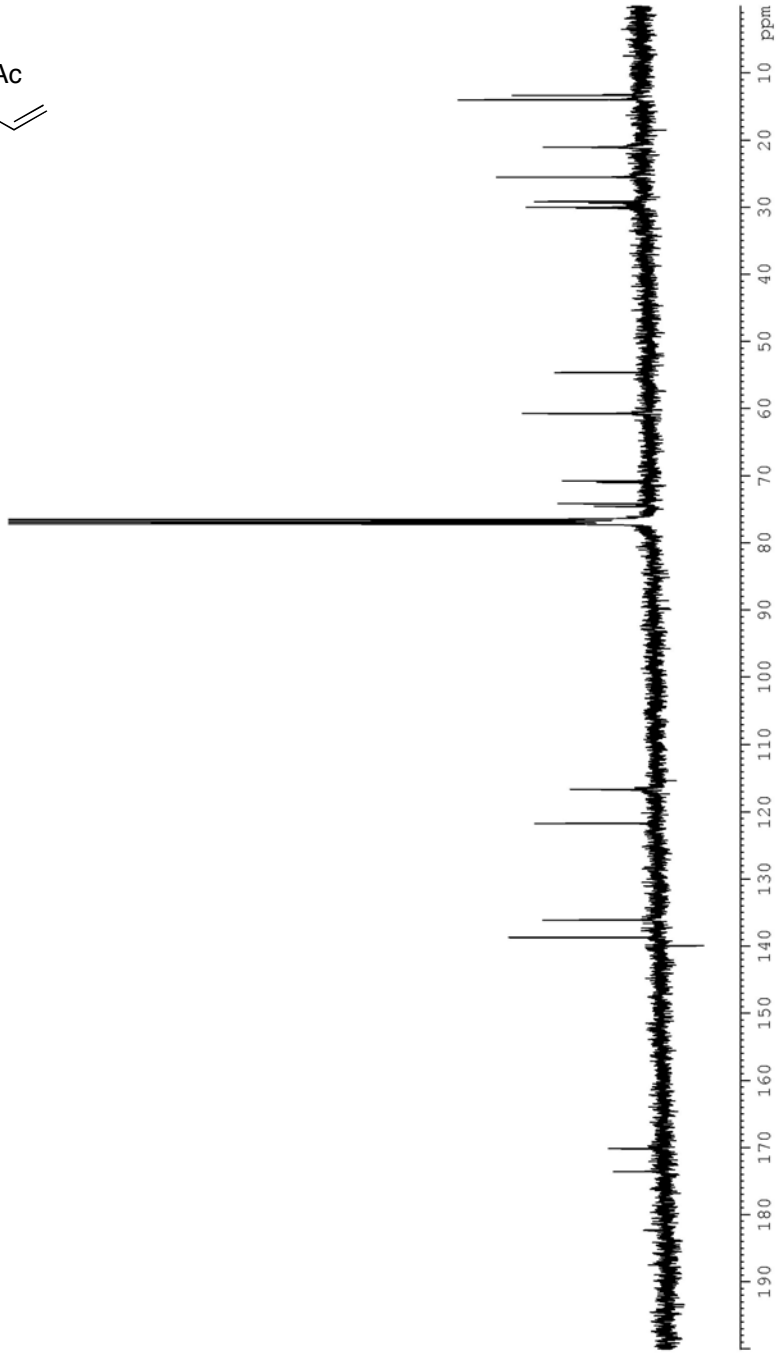
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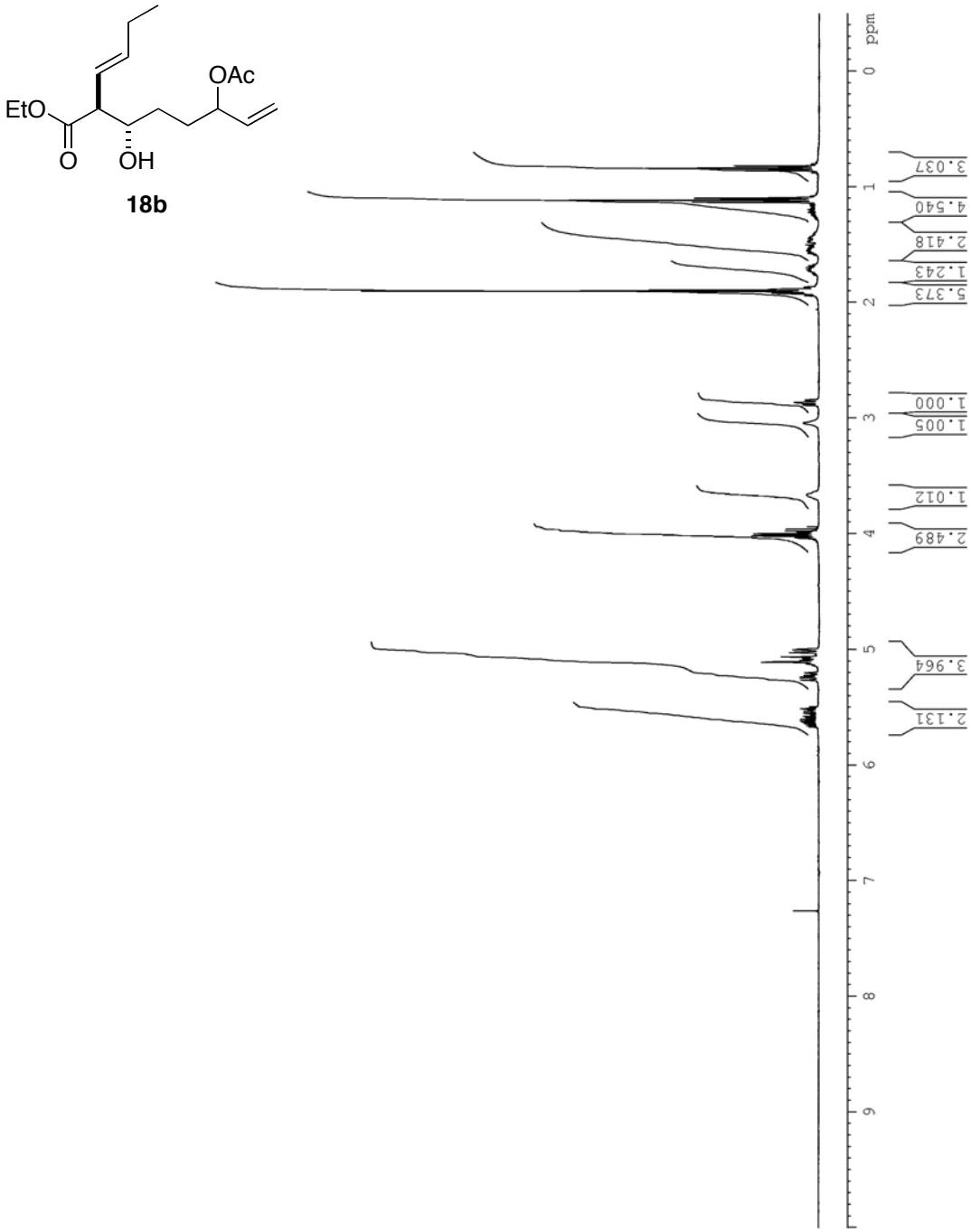
EtO
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OH
OAc
18b
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1.012
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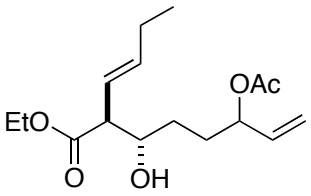
2.131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EtO
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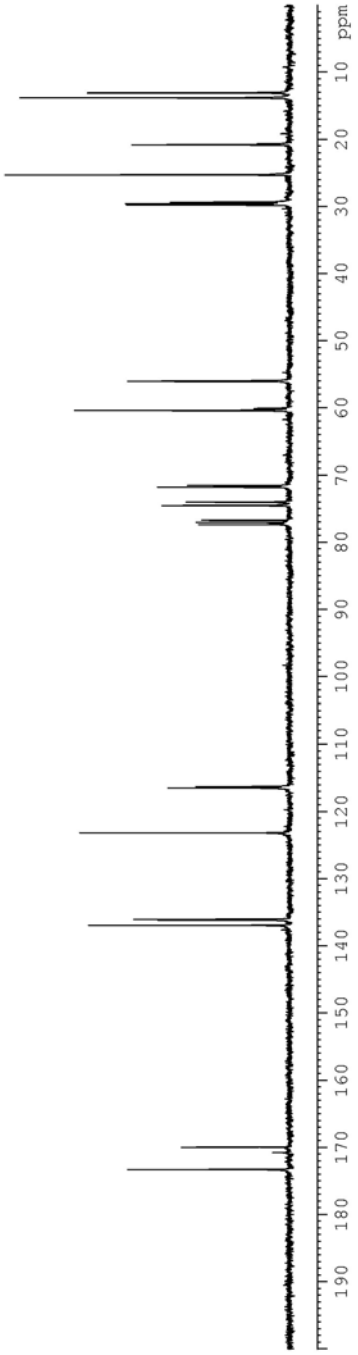
OH

18b


ppm
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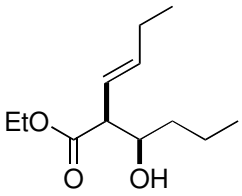
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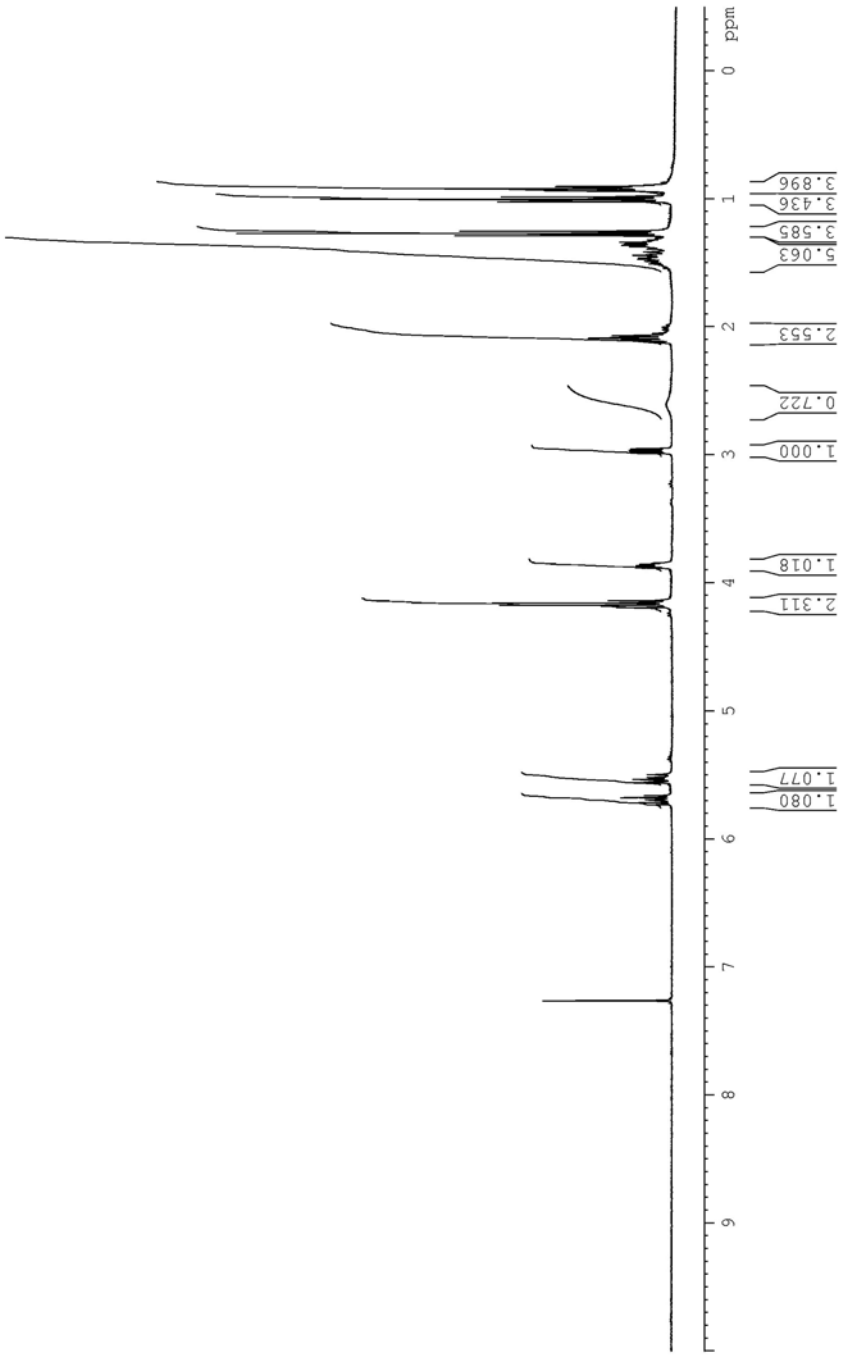
19a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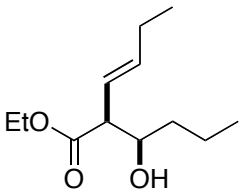
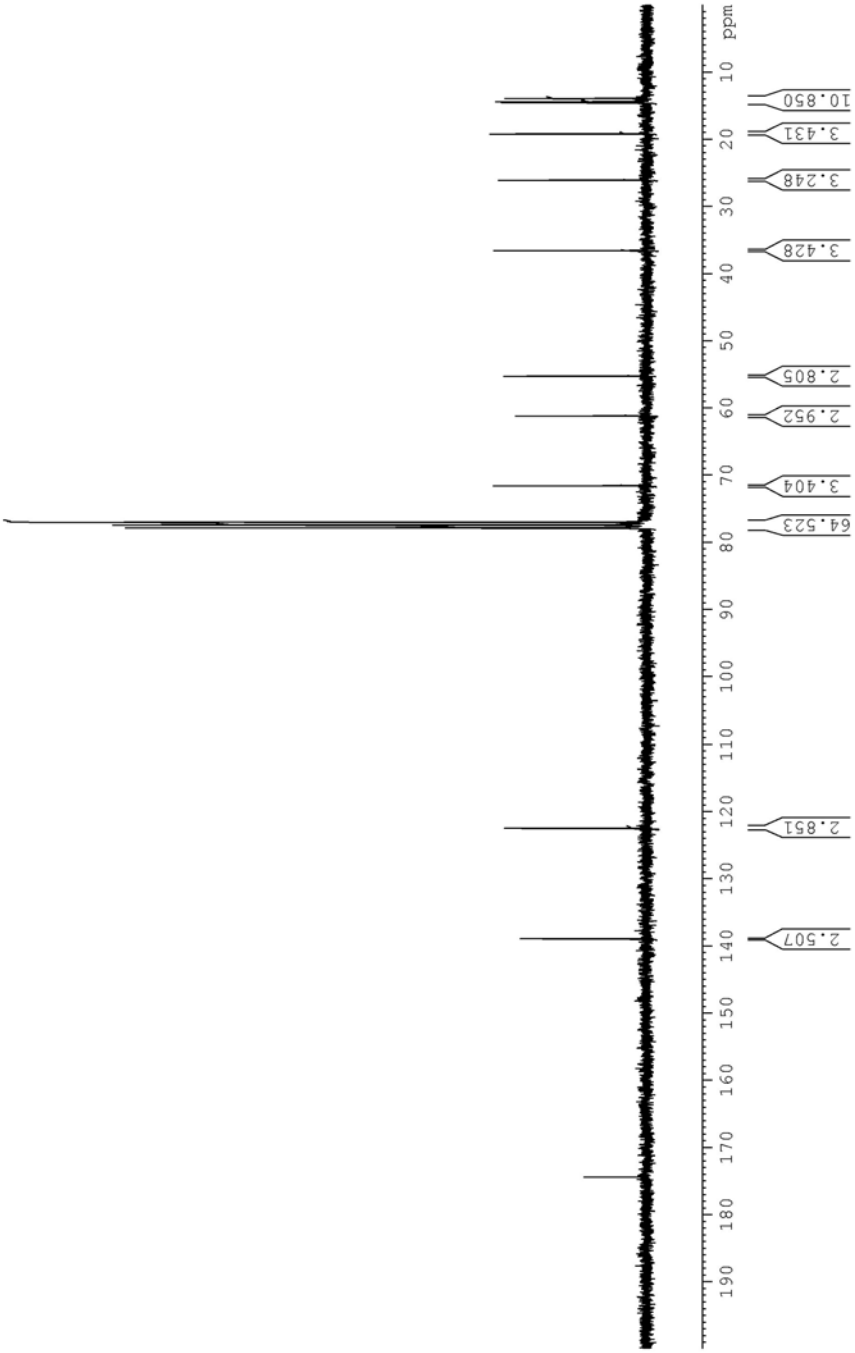
1.077
1.080


EtO
O
OH

19a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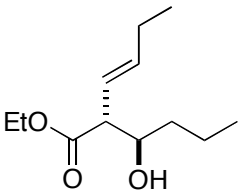
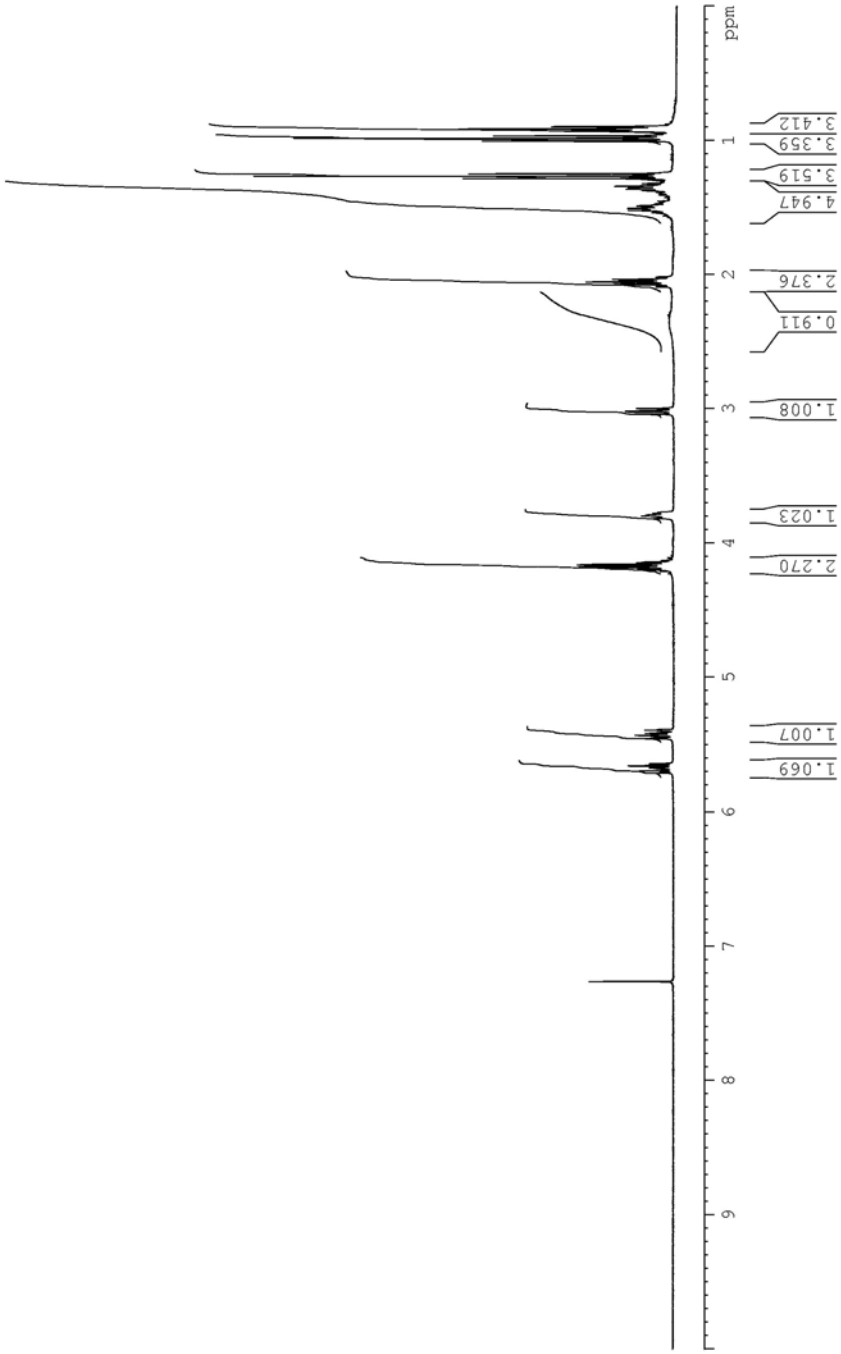
2.507


EtO
O
OH

19b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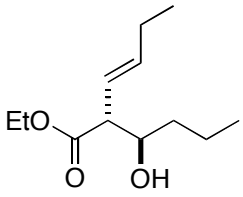
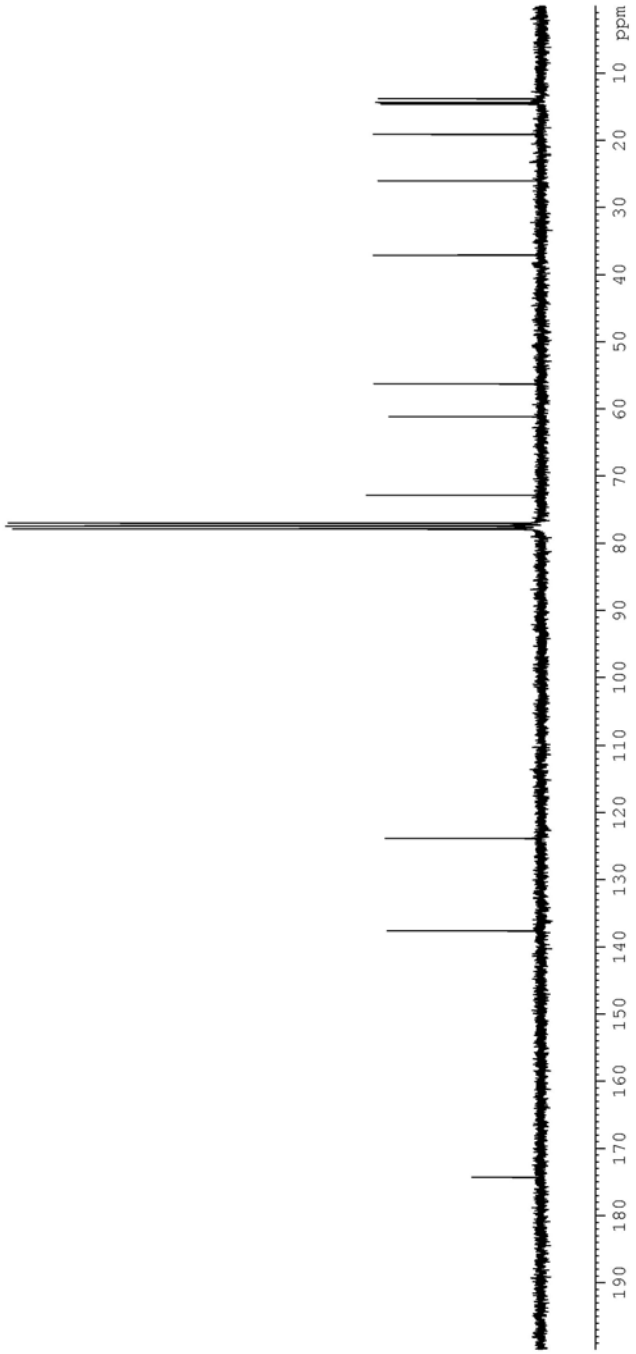
1.069


EtO
O
OH

19b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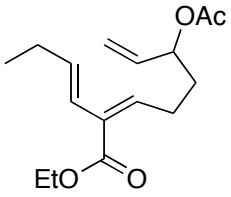
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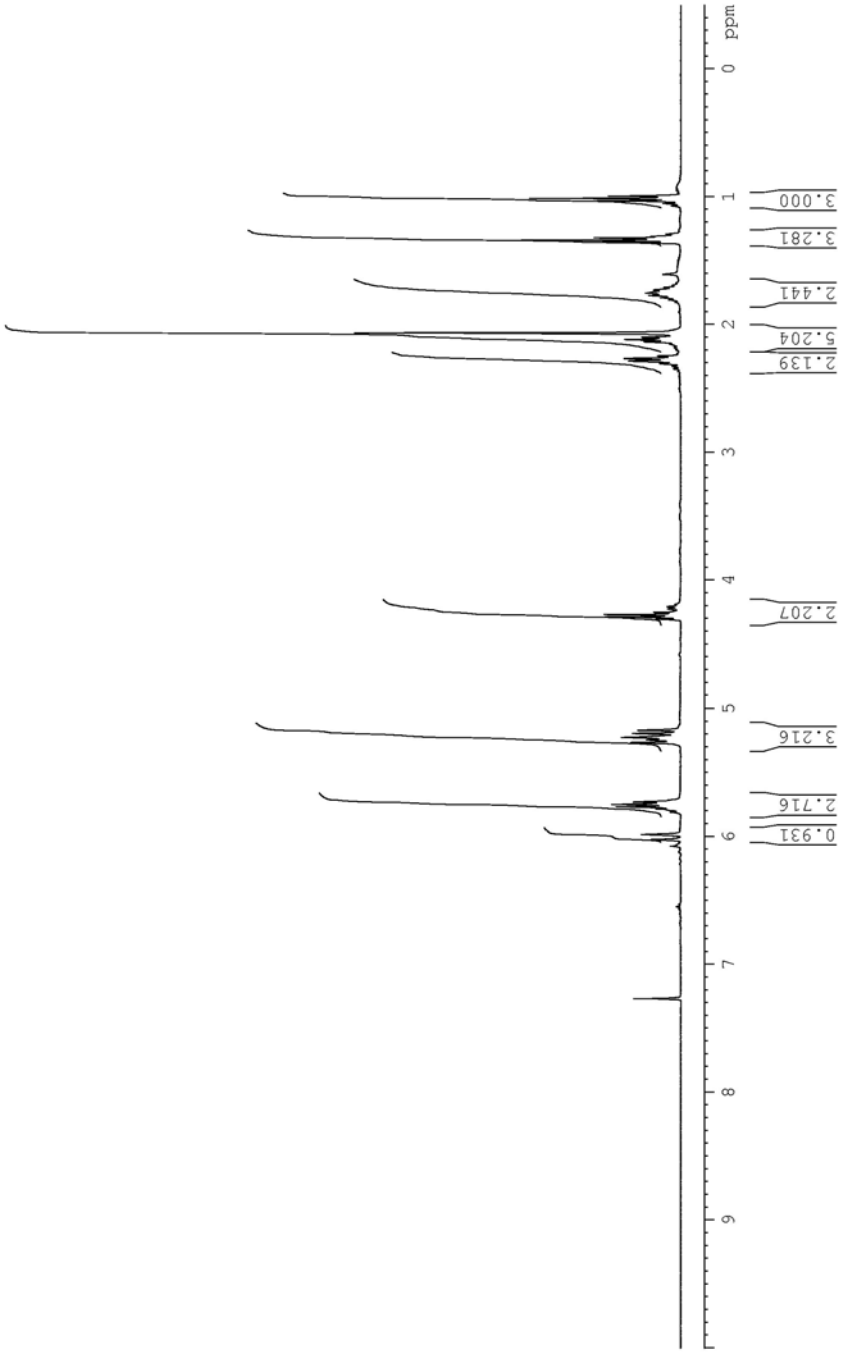
EtO
O

20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2
3
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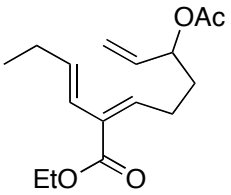
5.204
2.139
2.207
3.216
2.716
0.931


OAc
EtO
O

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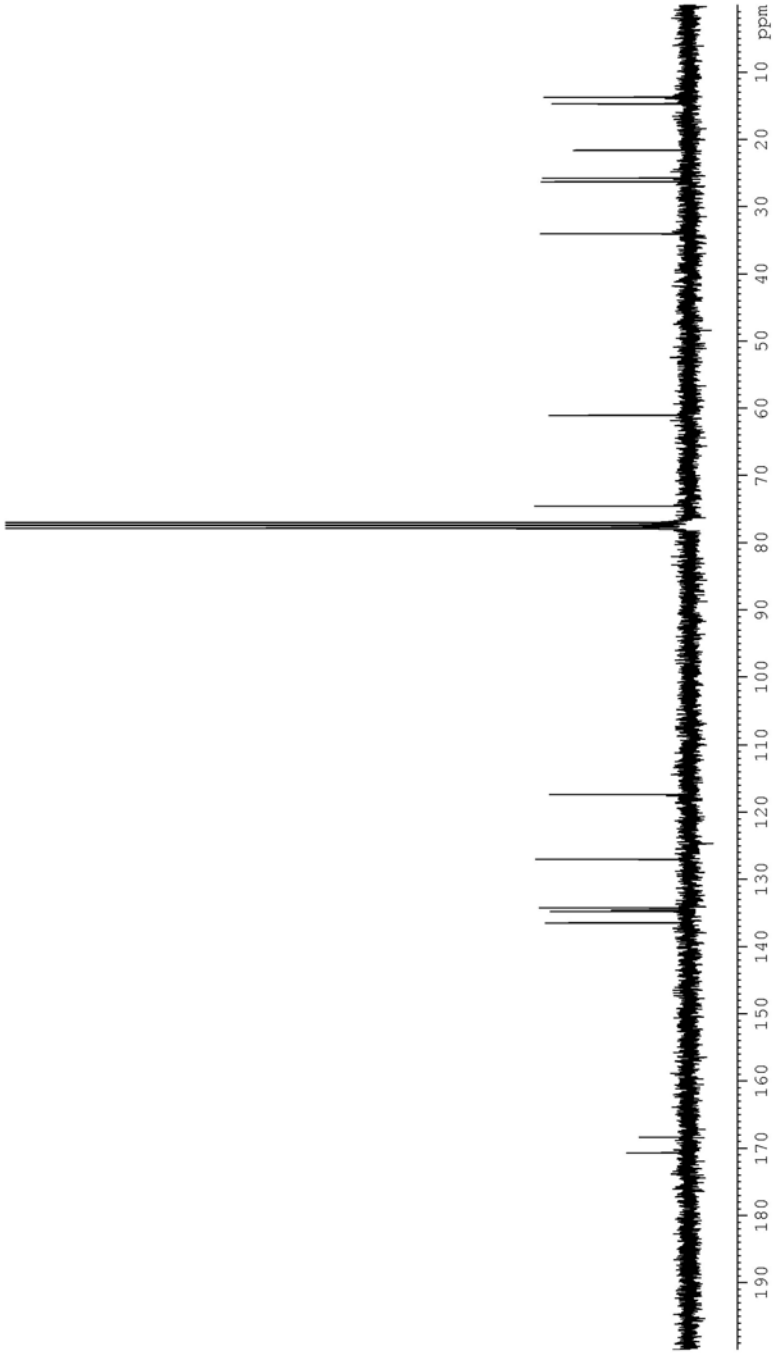
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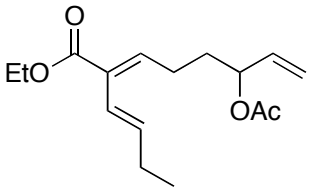
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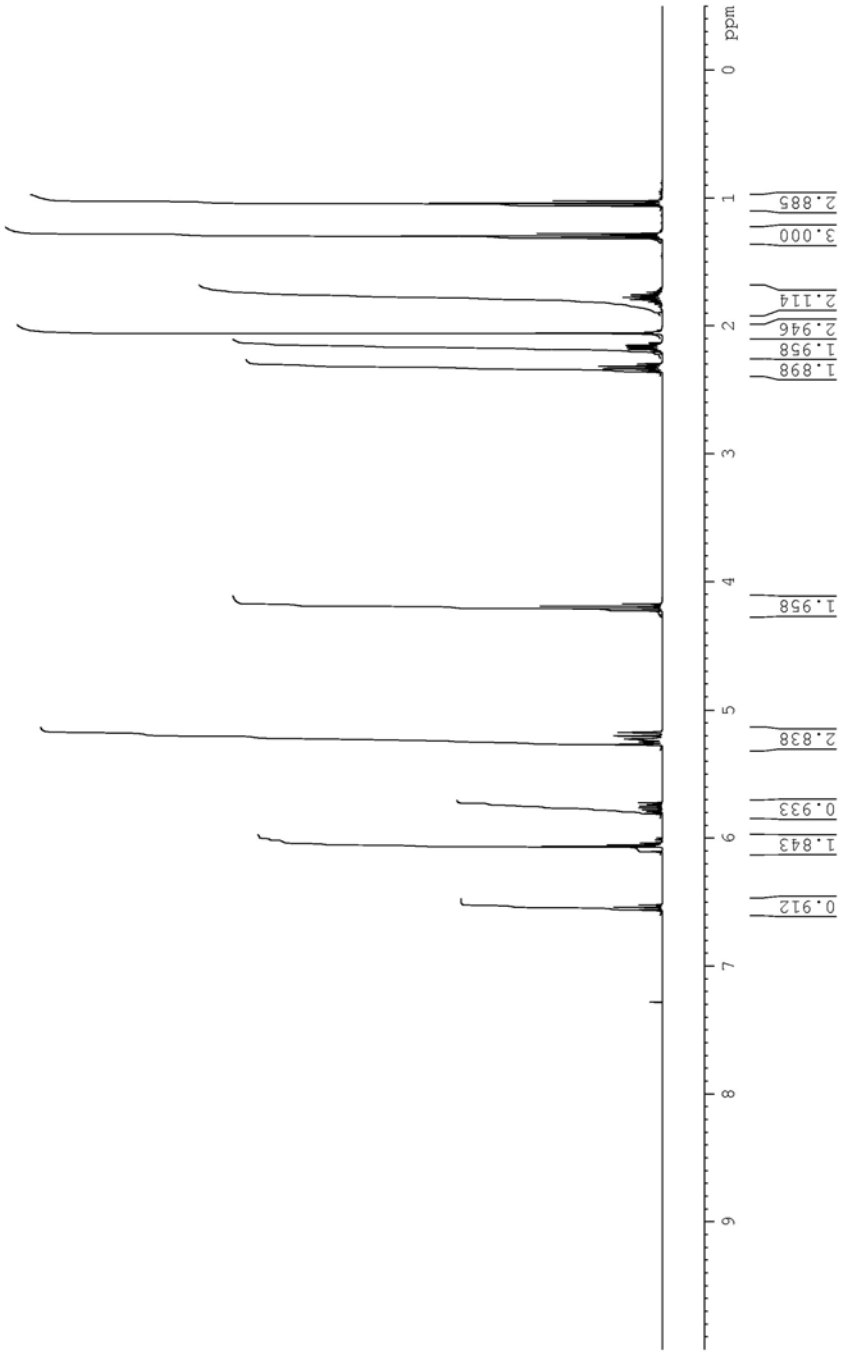
EtO
OAc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1.958
2.838
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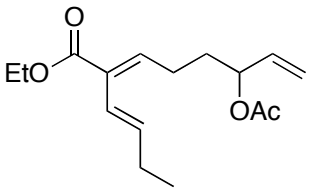
0.912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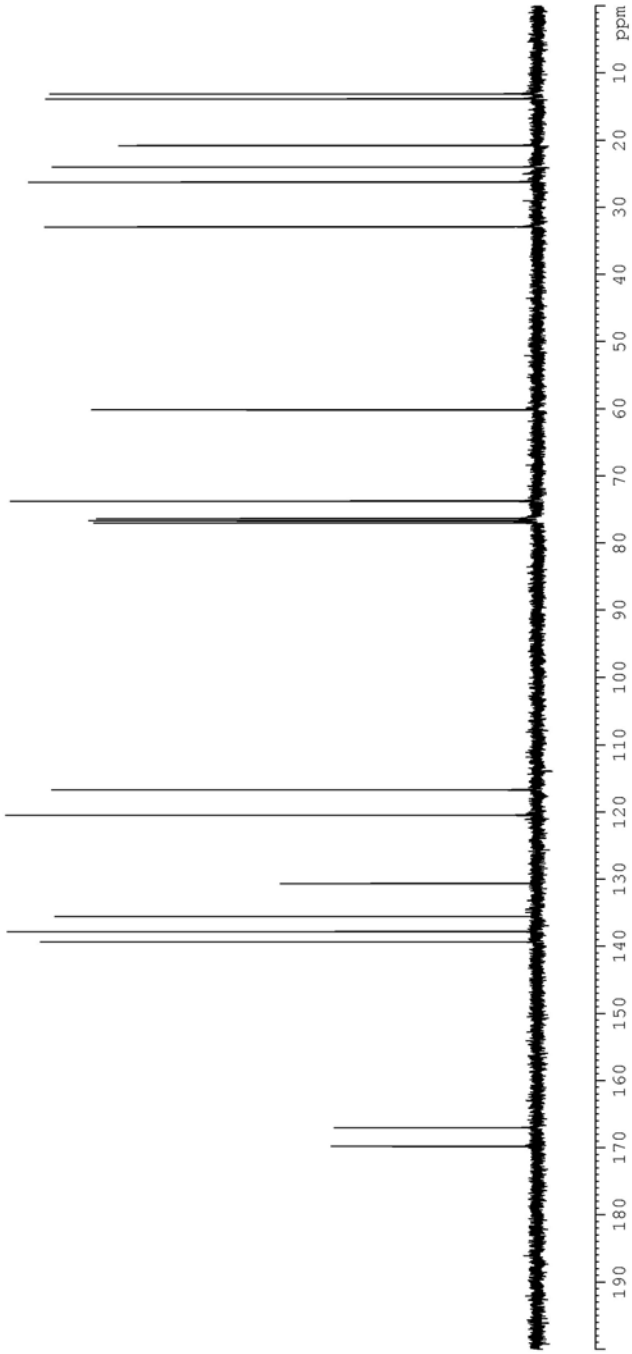
EtO
OAc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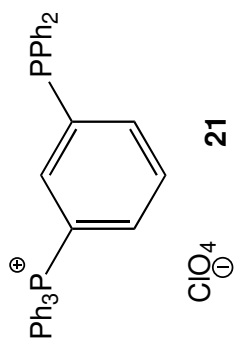
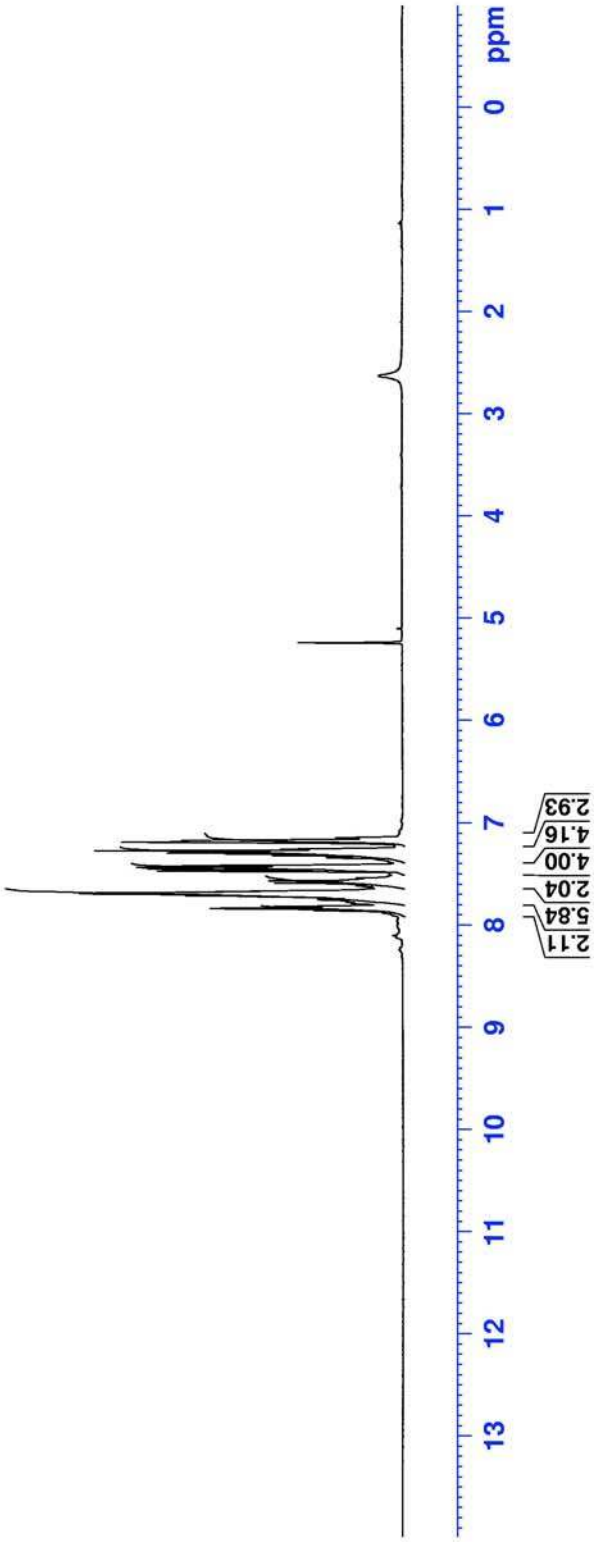

PPh2
Ph3P
ClO4

21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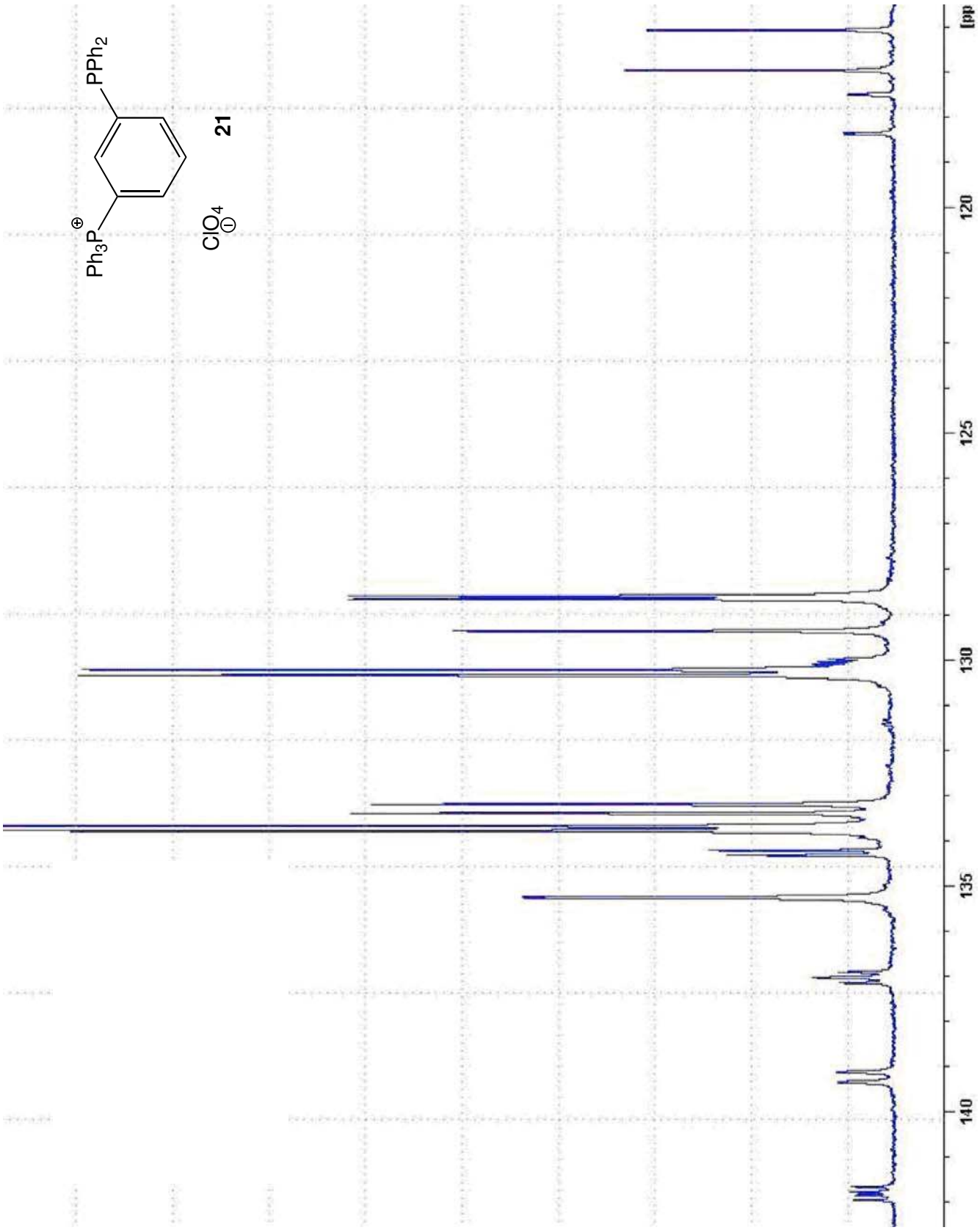
2.93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Ph3P
ClO4
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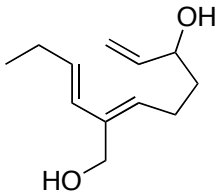
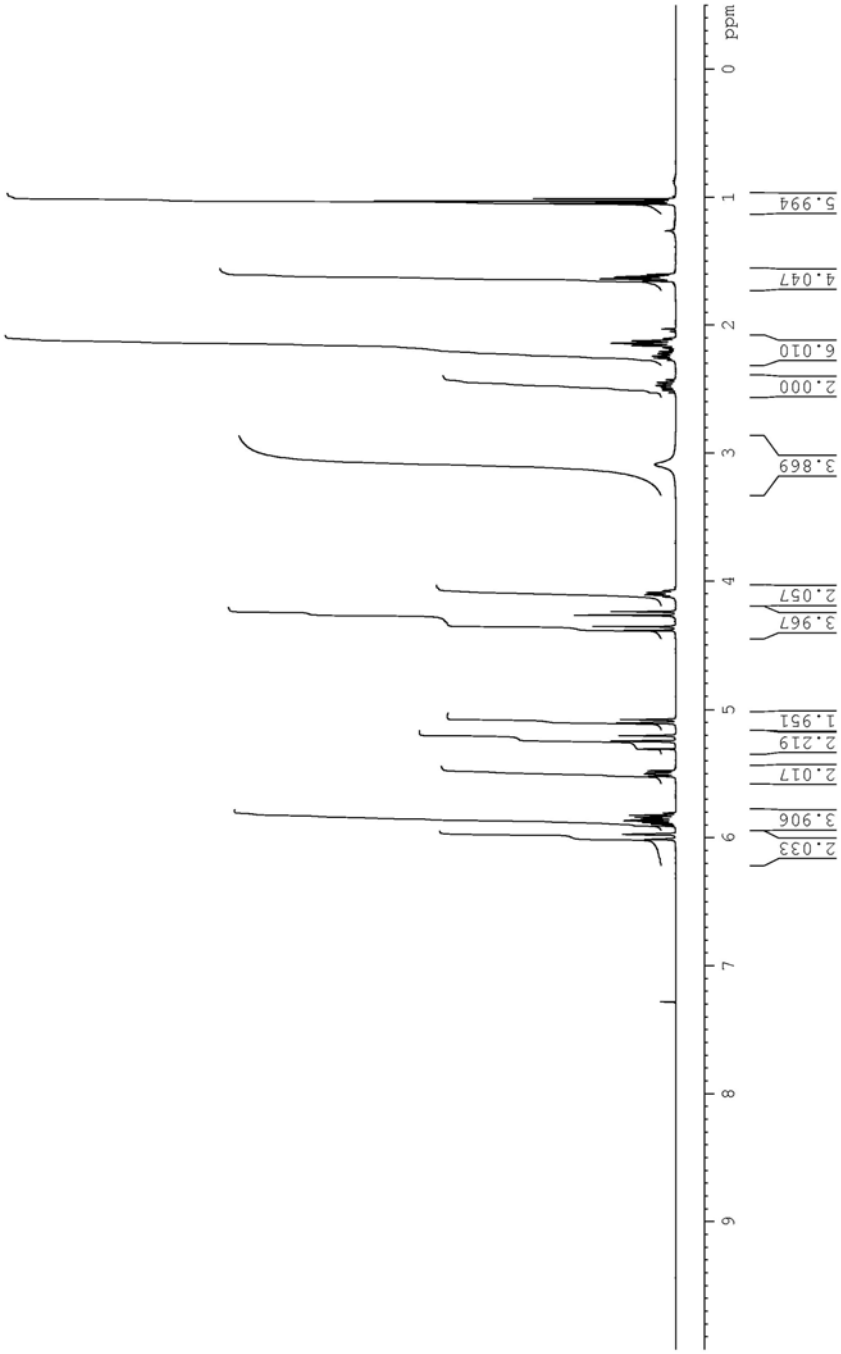
120
125
130
135
140


OH
HO

22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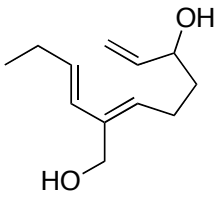
2.017
3.906
2.033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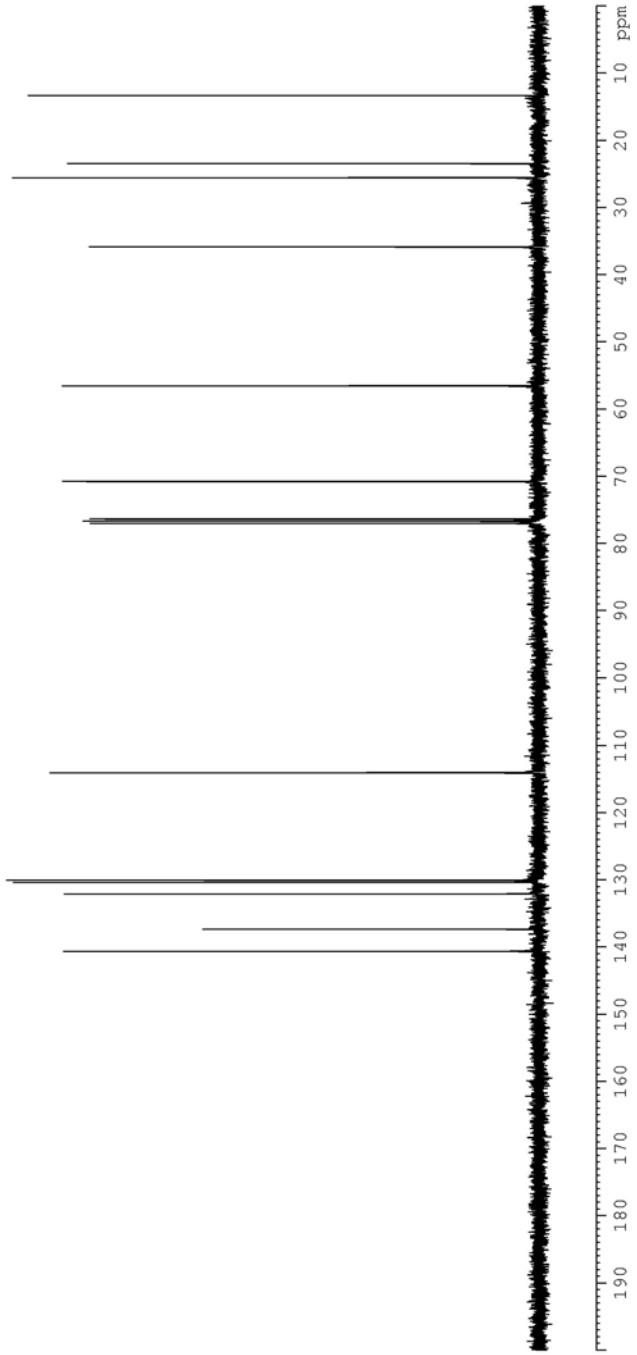
HO

22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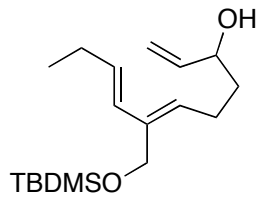
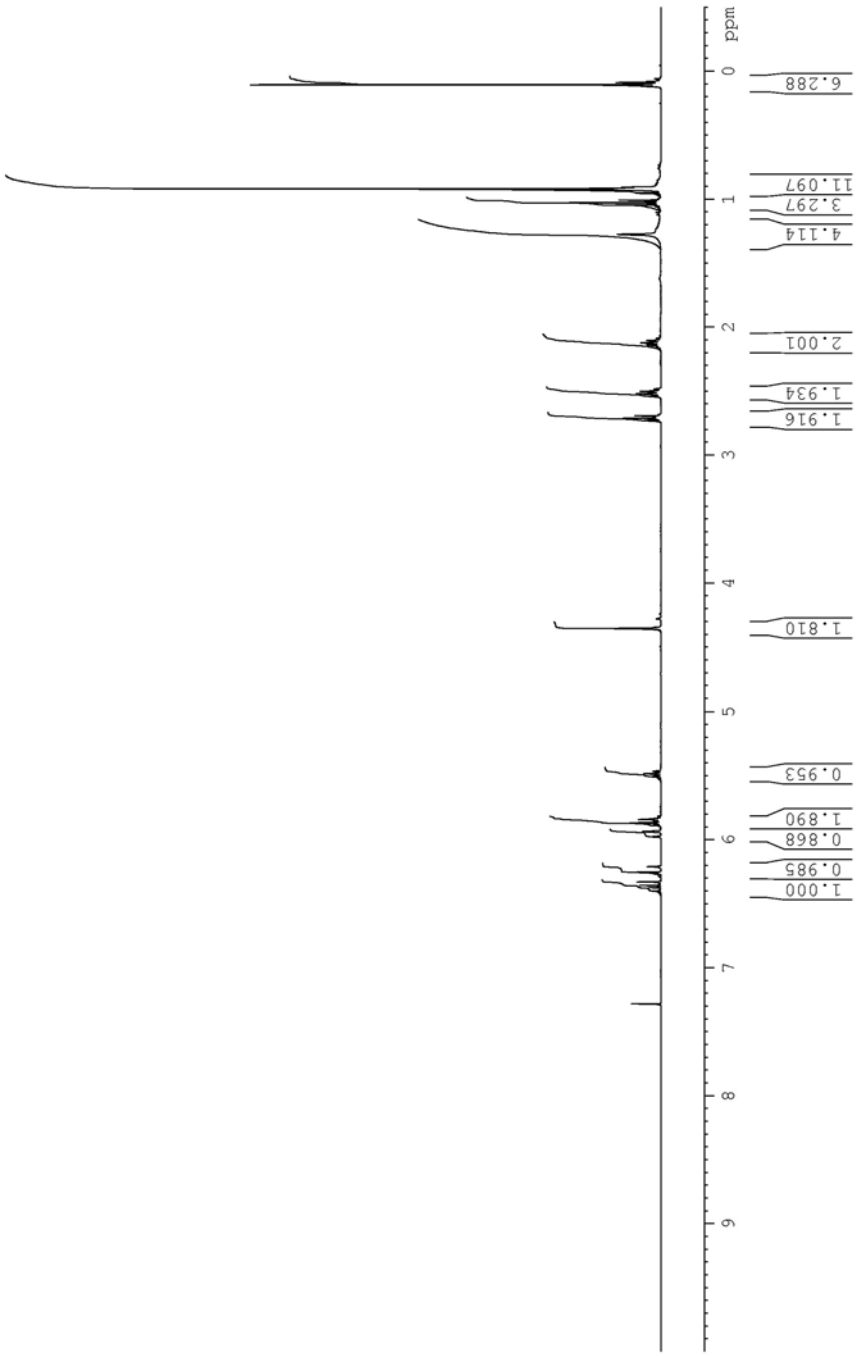

OH
TBDMSO

23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0.953
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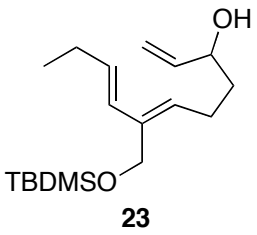
0.985
1.000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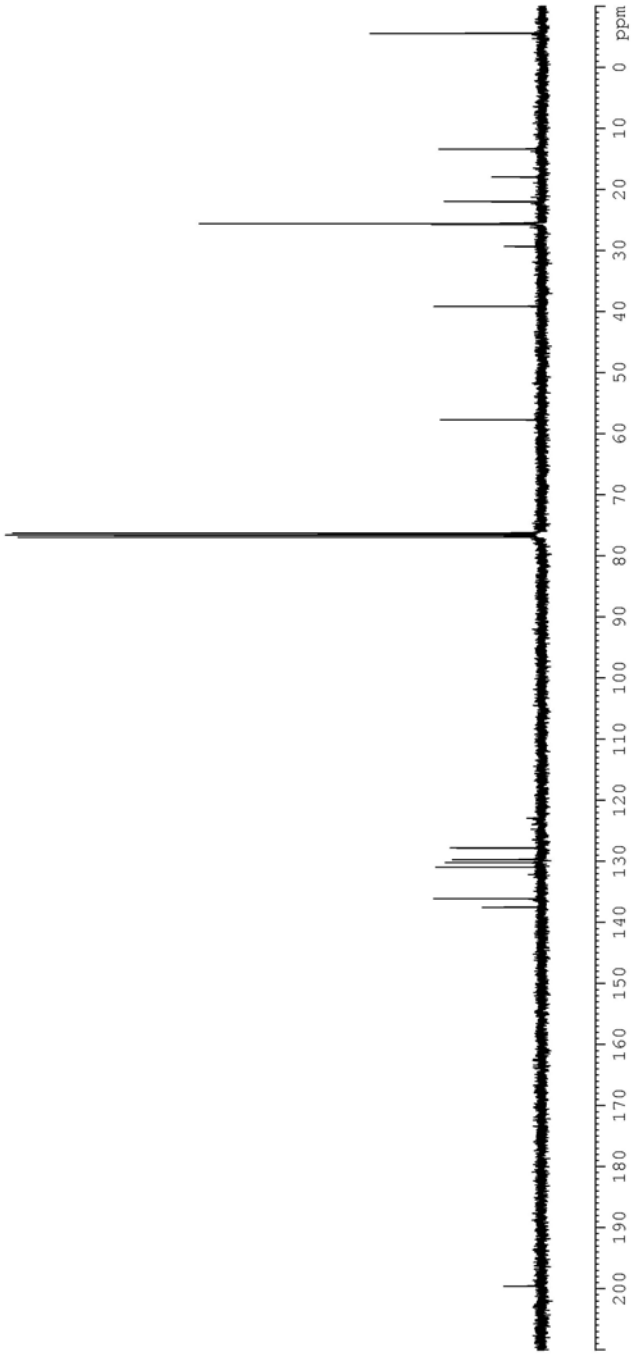
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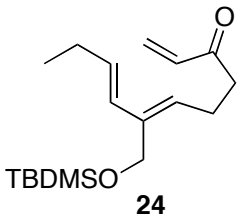
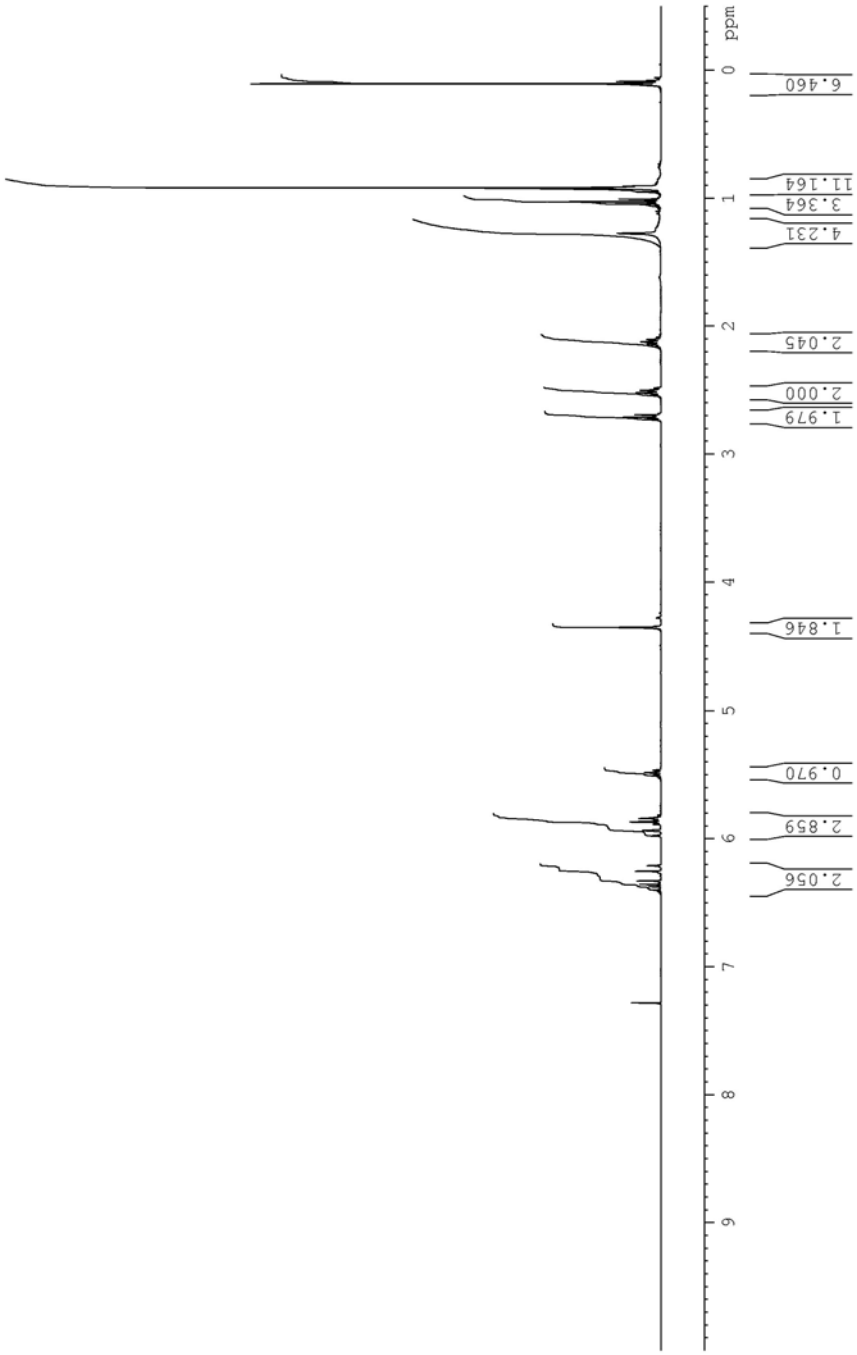
200


O
TBDMSO

24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0.970
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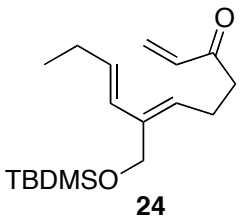
2.056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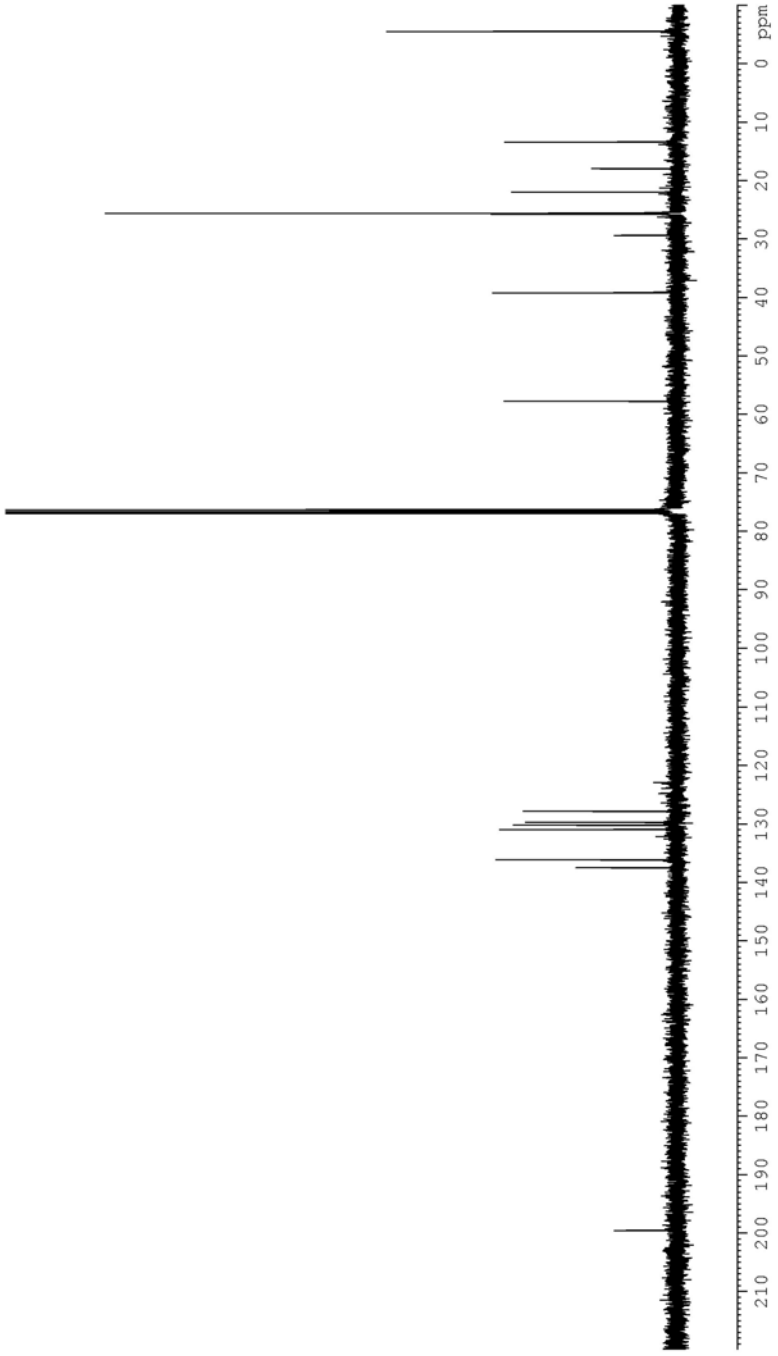
24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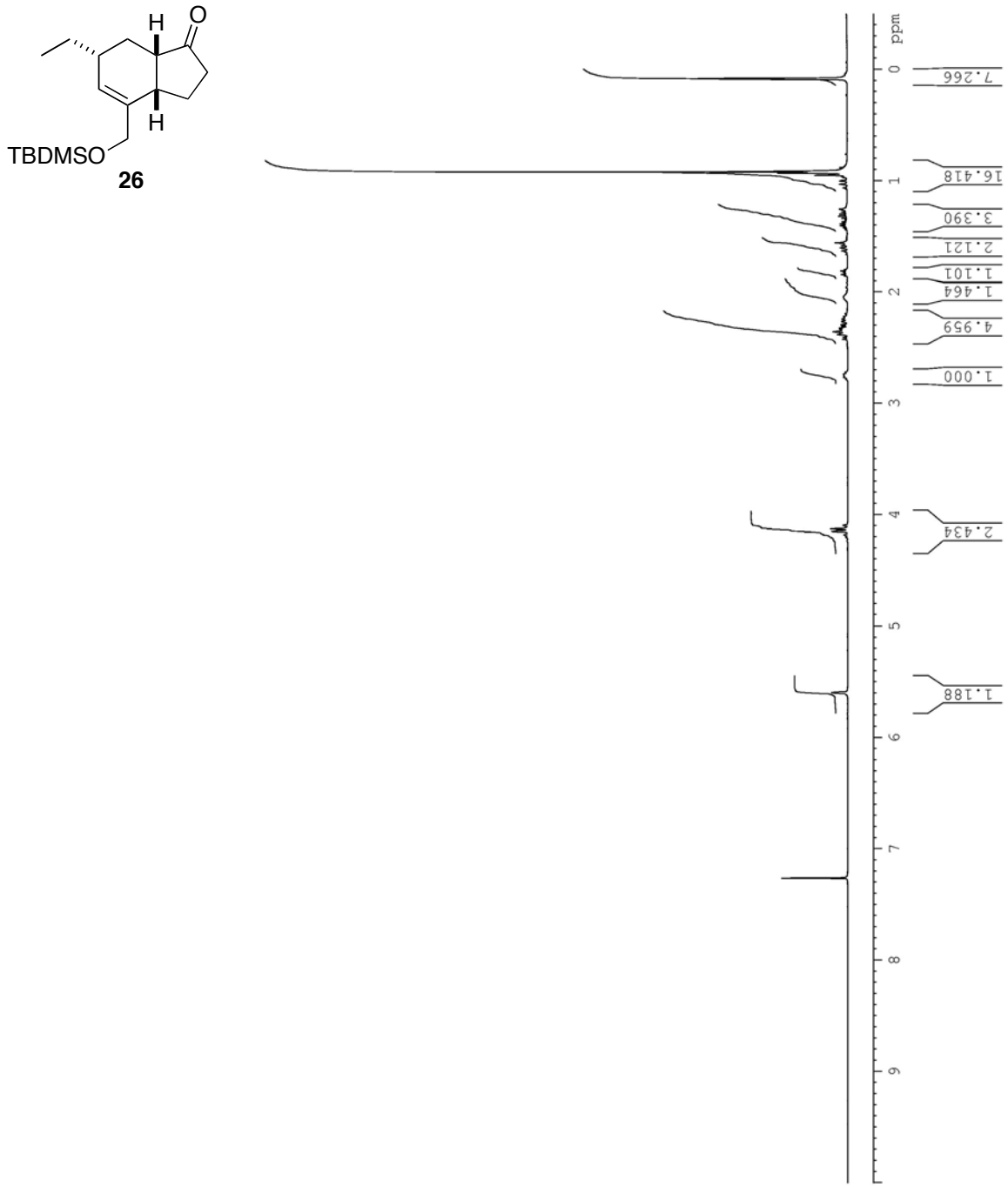
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O
H
TBDMSO
26
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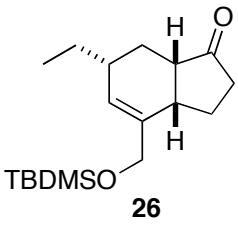
2.434
1.188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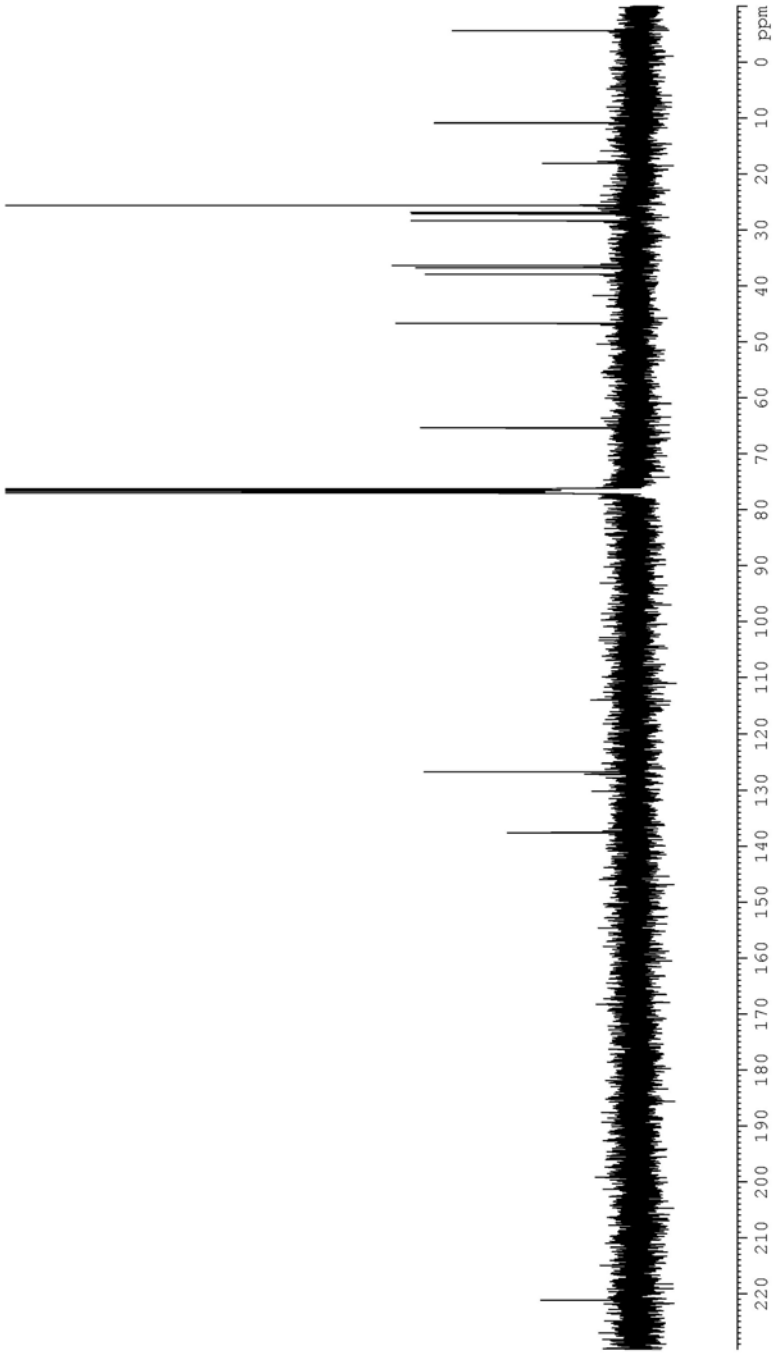
H
TBDMSO

26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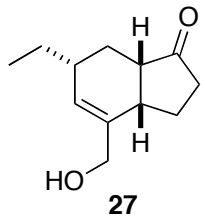
220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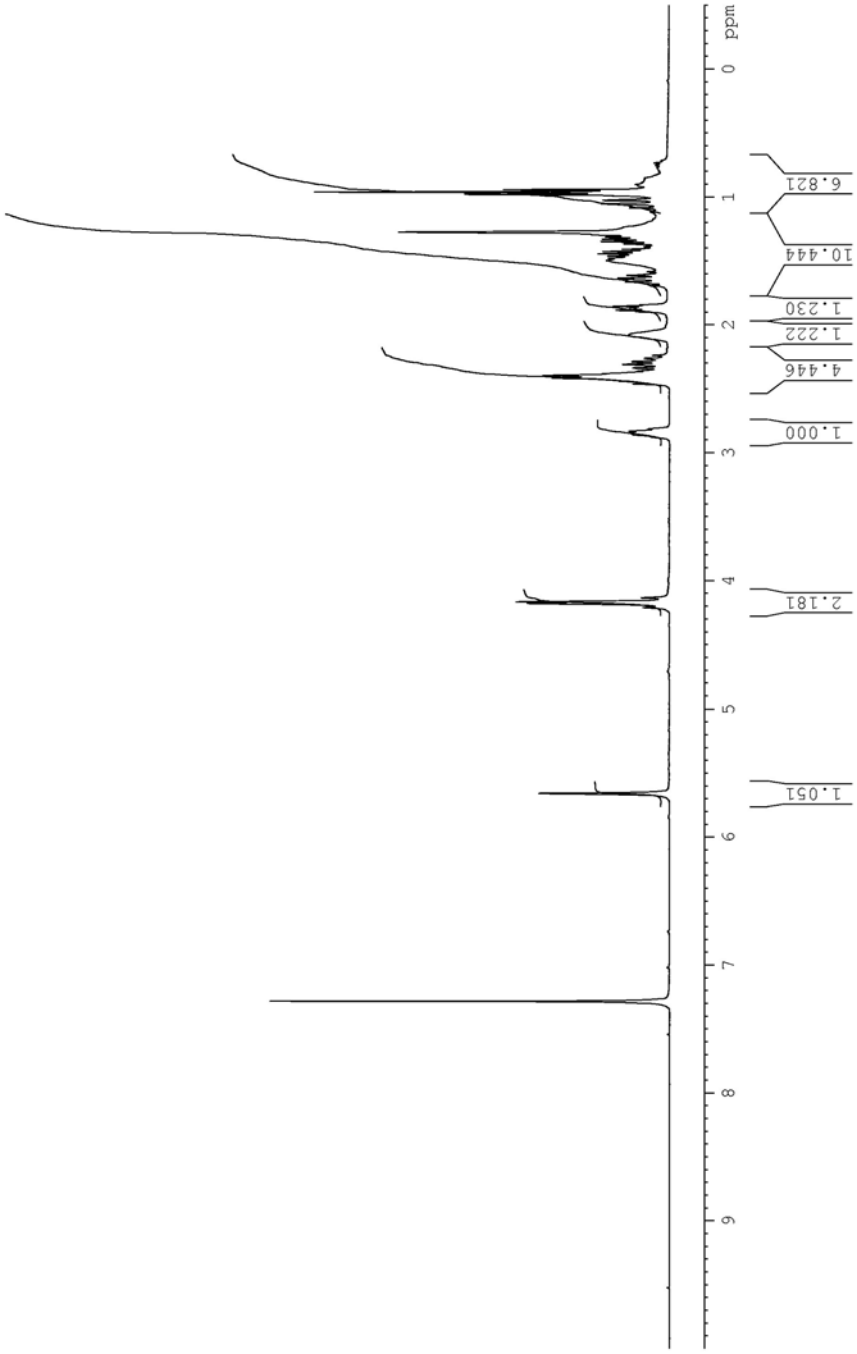
O
H
HO

27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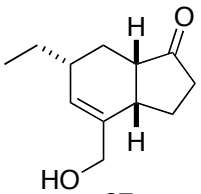
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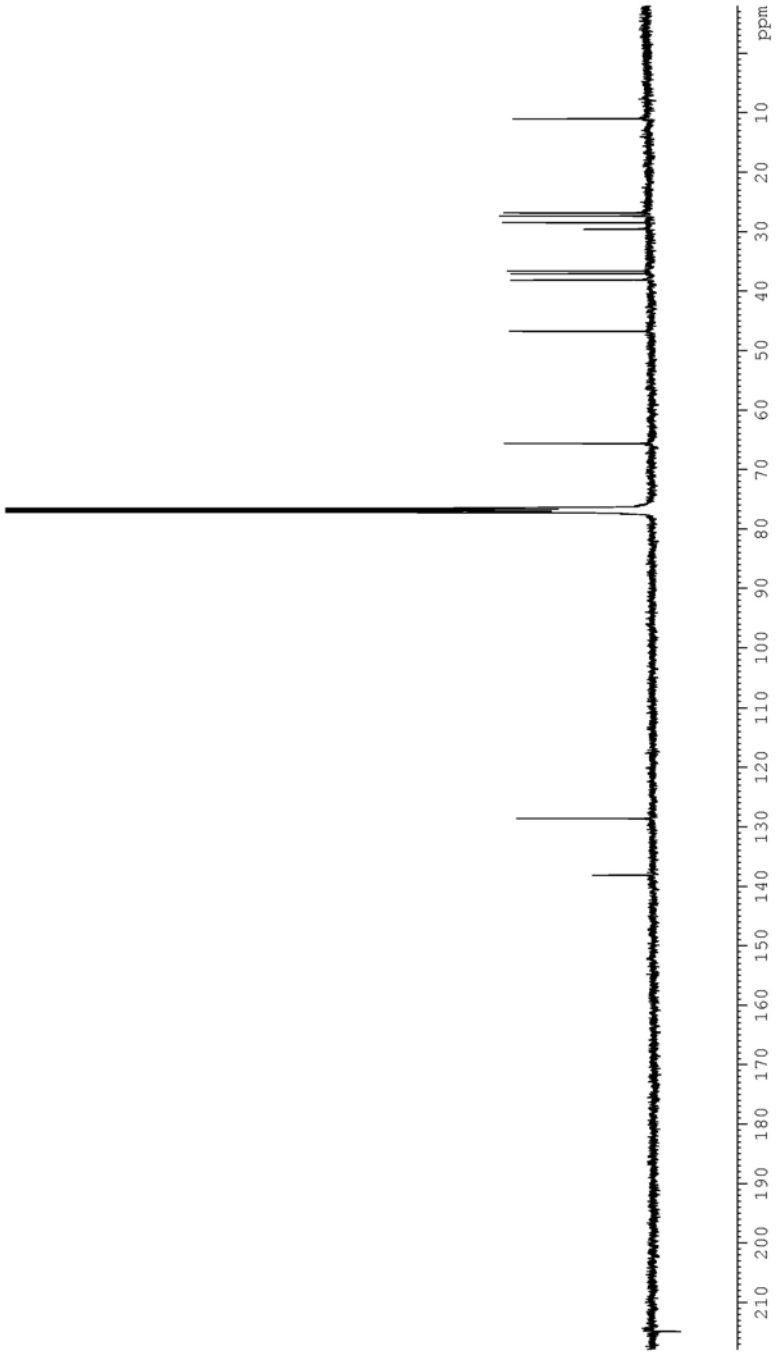
O
H
HO

27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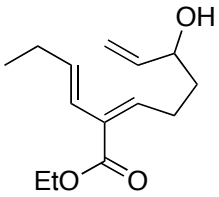
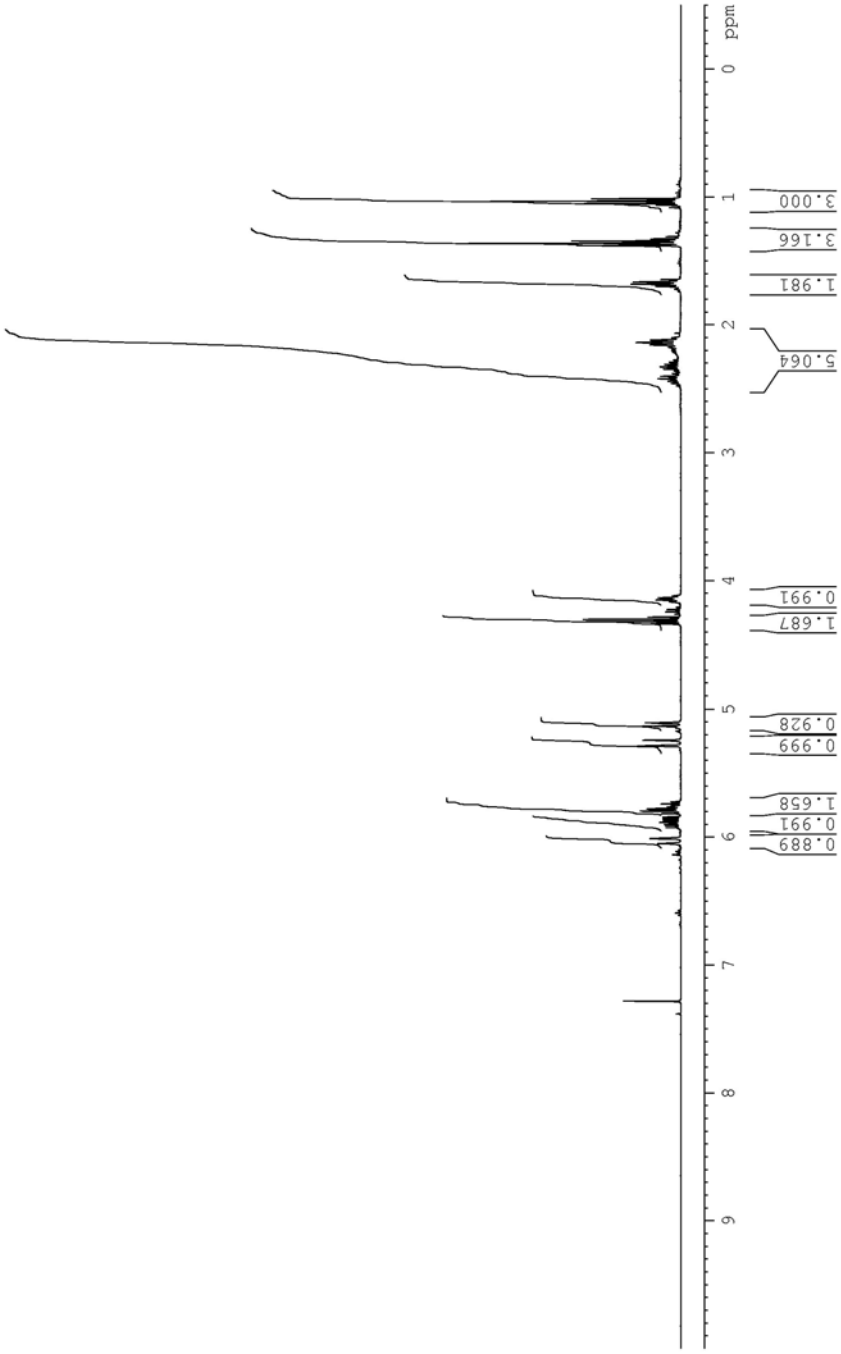

OH
EtO
O

28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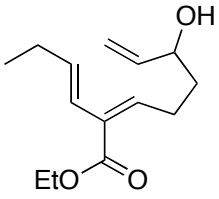
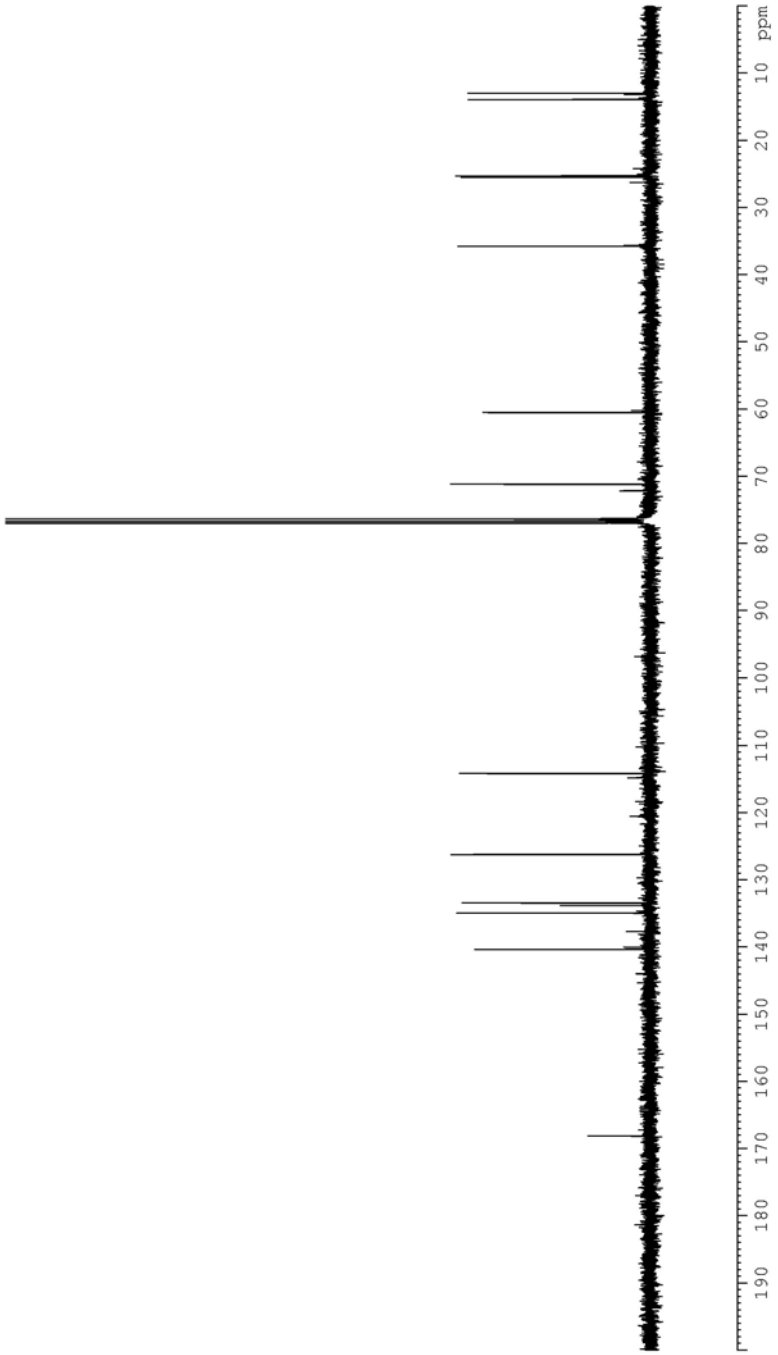

OH
EtO
O

28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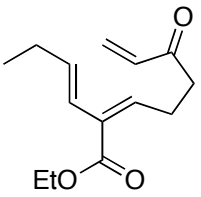
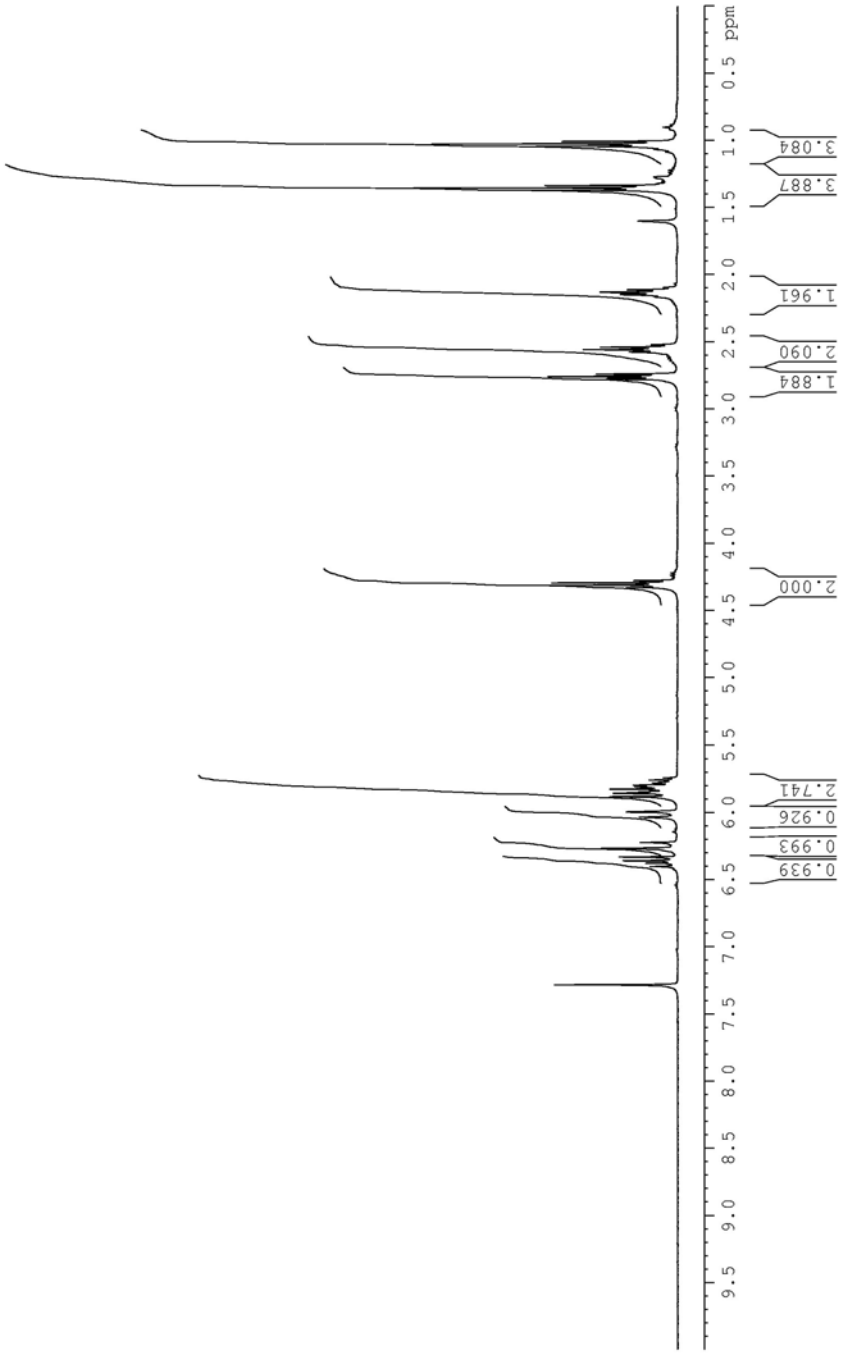

O
EtO
O

29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2.0
1.5
1.0
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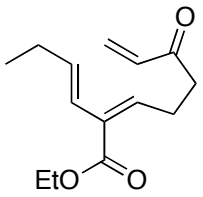
3.084


O
EtO
O

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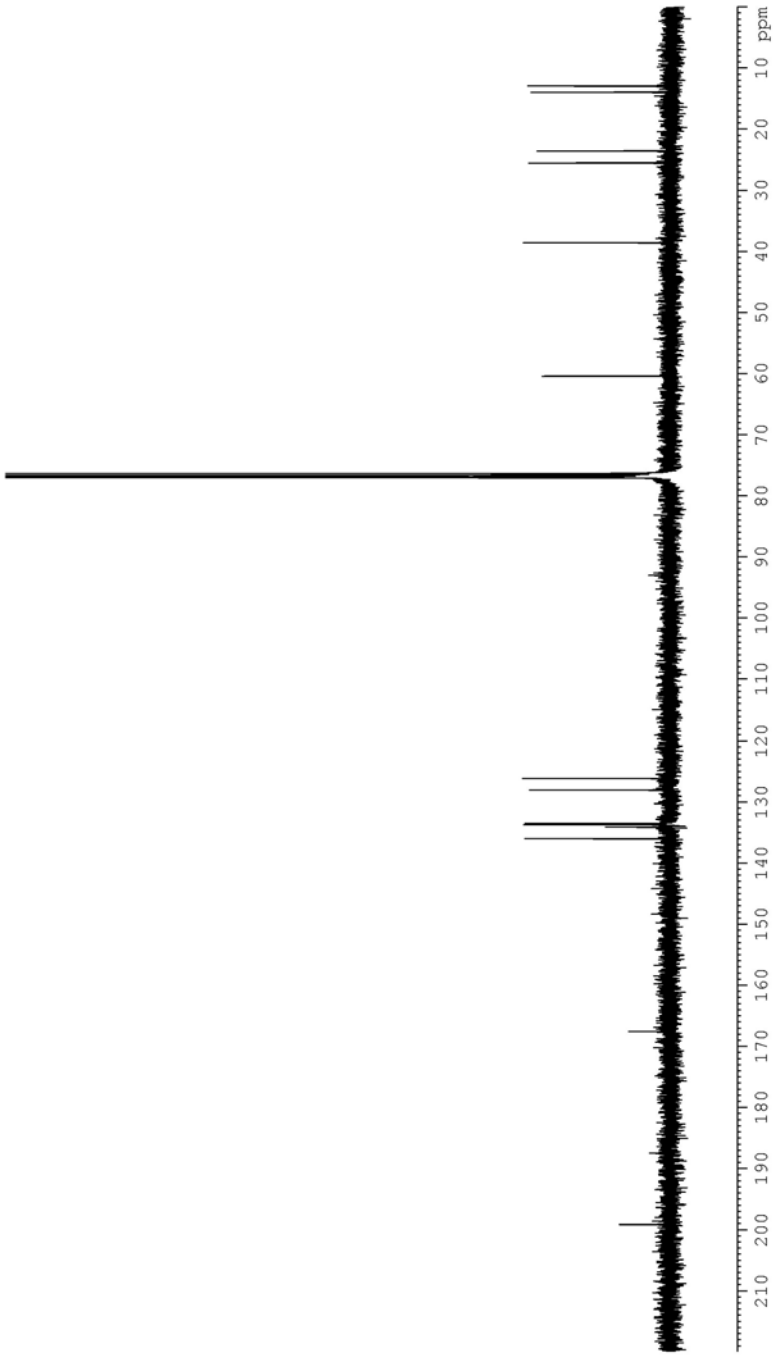
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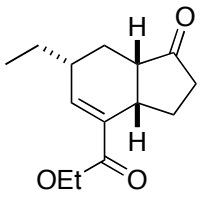
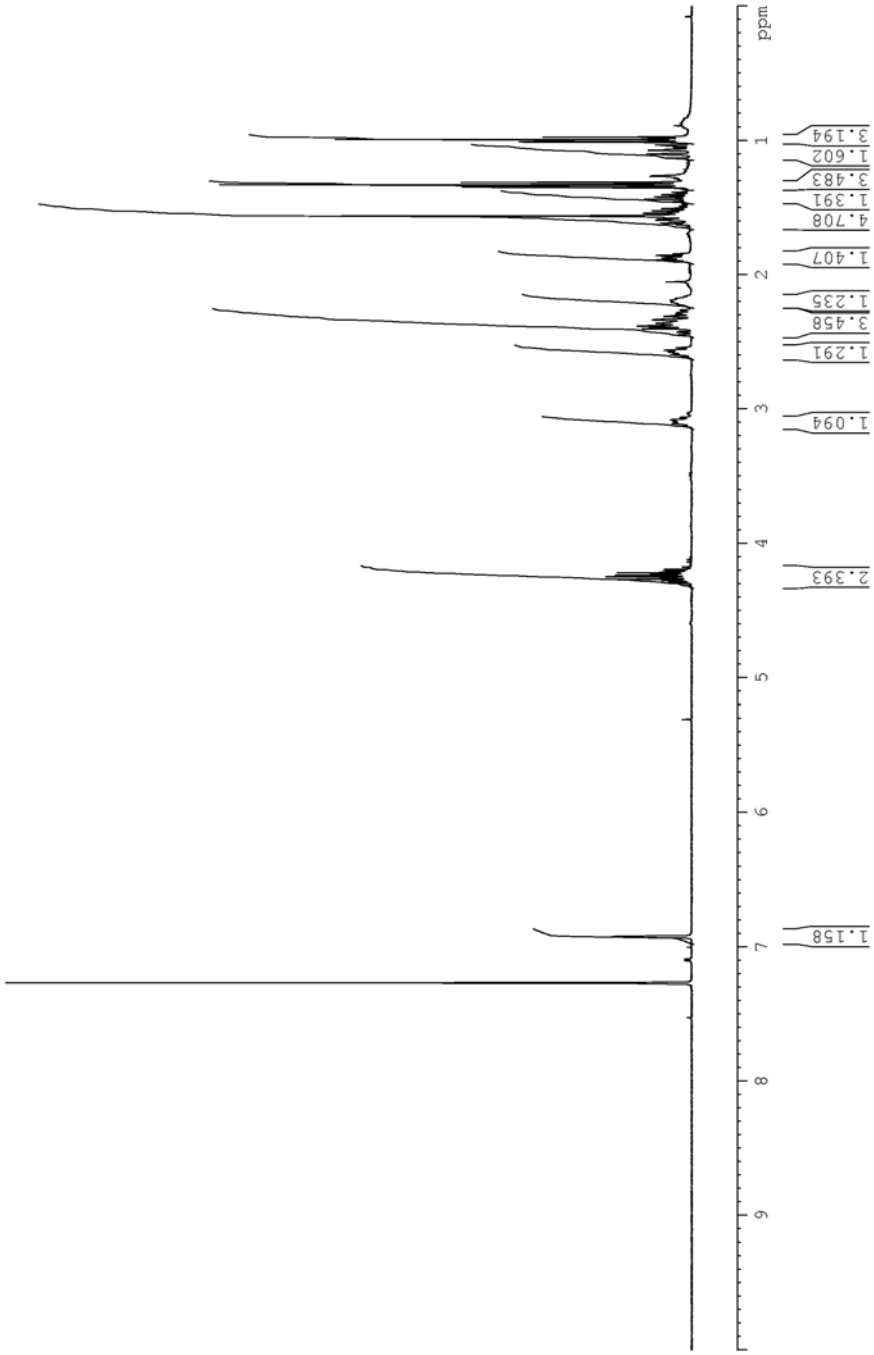

H
O
H
OEt
O

31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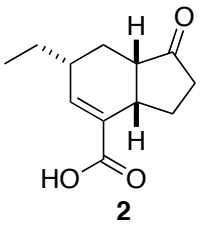
1.158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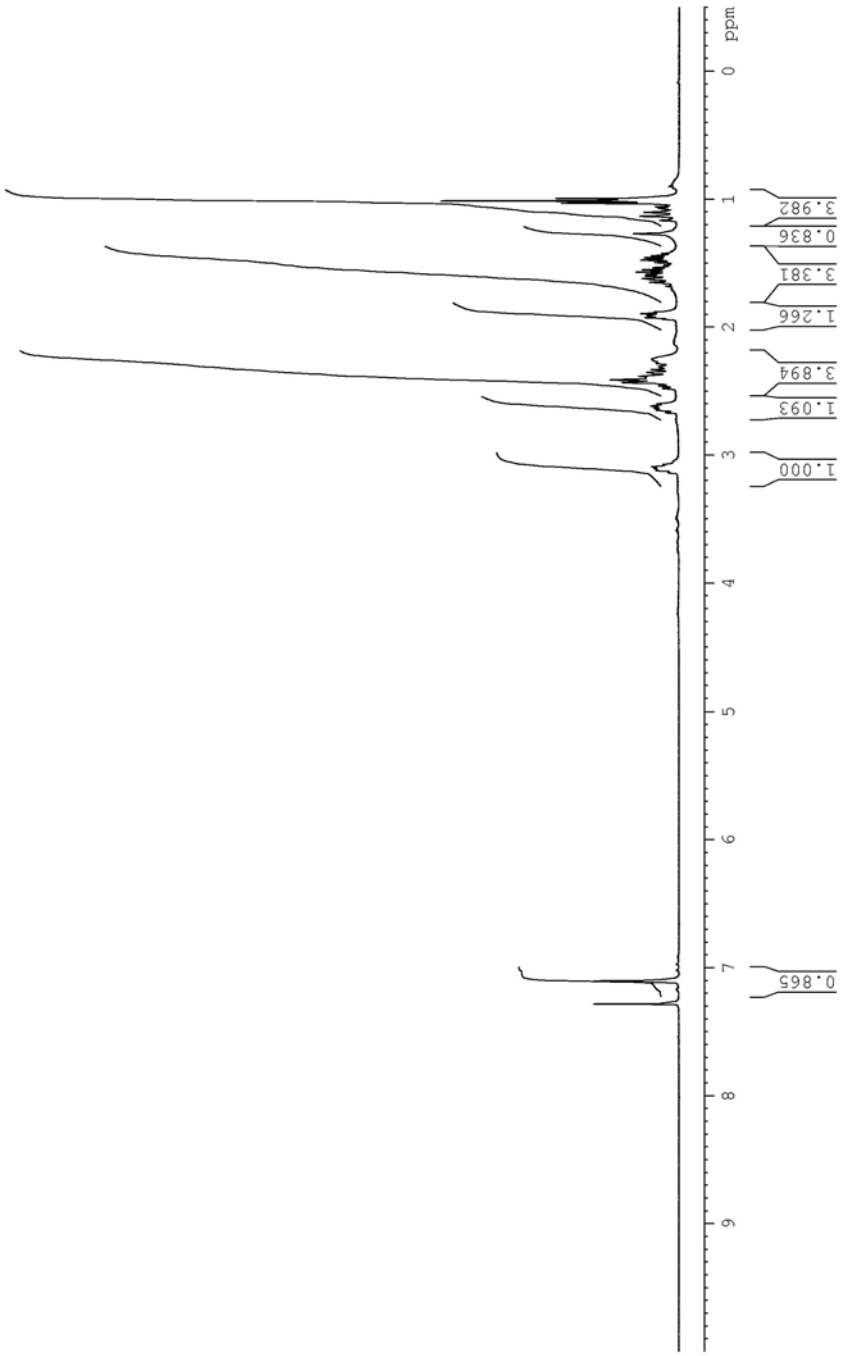
O
H
HO
O

2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3.381
1.266
3.894
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