Supporting Information

Diastereoselective Palladium-Catalyzed Formate Reduction of Allylic Carbonates as a New Entry into Propionate Units.

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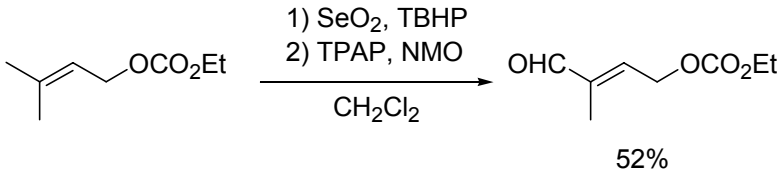
The following includes experimental procedures for the synthesis of the allylic carbonates, general experimental procedures for the formate reduction, isolation and spectroscopic information as well as ^{1}H and ^{13}C spectra for the new compounds prepared. All ^{1}H and ^{13}C NMR spectra were recorded in deuterated chloroform using tetramethylsilane or residual chloroform as internal standard at ambient temperature. High resolution mass spectra were obtained either by electron impact (EI) or electrospray (ES) ionisation. The dr (ratio *syn*/*anti*) of all the reactions was estimated by ^{1}H NMR or ^{13}C spectroscopy. For the purpose of this study, >15:1 dr indicates that the other diastereomer was present in less than 6% (typically 4-6%) whereas >20:1 dr specify that the other diastereomer was not detectable.

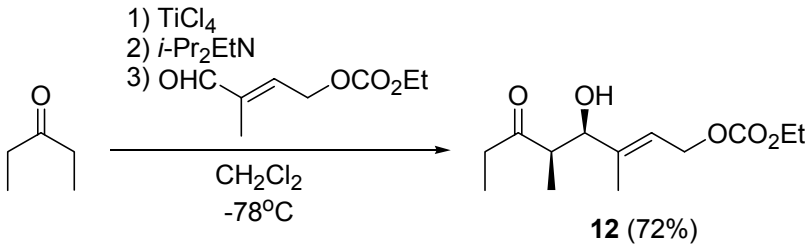
Synthesis of the precursor aldehyde



(2*E*)-4-ethoxycarbonyloxy-2-methylbut-2-enal To a solution of 4-ethoxycarbonyloxy-2-methyl-2-butene[1] (2.0 g, 12.6 mmol) in CH_2Cl_2 (20 mL) was added SeO_2 (2.93 g, 26.5 mmol) and *tert*-butylhydroperoxide (4.46 mL, 31.5 mmol, 70% soln in H_2O) and the resulting mixture was stirred for 72 h (necessary for good conversion). Satd $NaHCO_3$ was carefully added and the aqueous layer was extracted with CH_2Cl_2 (2×). The combined organic layers were washed with brine, dried over $MgSO_4$ to give a mixture of alcohol and aldehyde (~1:1) as a solution in CH_2Cl_2 (~40 mL) that was used without further purification. TPAP (221 mg, 0.63 mmol) and NMO (1.48 g, 12.6 mmol) were added to the above solution and stirred until the reaction was completed as judged by TLC (~3 hrs). The solvent was evaporated and the residue was purified by flash chromatography using 25% Et_2O/hexane to give the desired product as a slightly volatile colorless liquid (1.12 g, 52%). IR (film) ν = 2985, 2937, 1754, 1692, 1271, 1005 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.47 (s, 1H), 6.54 (dt, 1H, *J* = 6.0, 1.5 Hz), 4.97 (dd, 2H, *J* = 6.0, 1.5 Hz), 4.25 (q, 2H, *J* = 7.2 Hz), 1.81 (d, 3H, *J* = 1.5 Hz), 1.33 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 193.7, 154.7, 144.8, 140.4, 64.3, 63.6, 14.0, 9.3; MS-EI (*m*/*z*) 99 $[M - CO_2Et]^+$, 83 $[M - OCO_2Et]^+$.

[1] Matsuhashi, H.; Asai, S.; Hirabayashi, K.; Hatanaka, Y.; Mori, A.; Hiyama, T. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 1943.

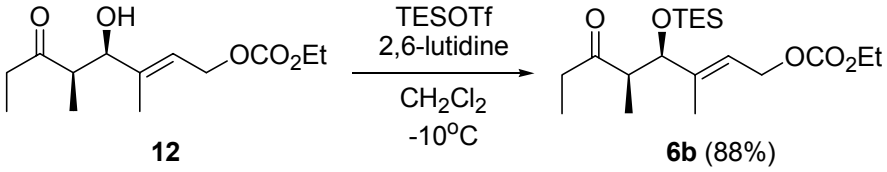
Synthesis of 12



(2*E*)-(4*R,5*R**)-1-ethoxycarbonyloxy-3,5-dimethyl-4-hydroxy-2-octen-6-one (12)** To a -78°C solution of 3-pentanone (656 μL, 6.20 mmol) in CH_2Cl_2 (15 mL) was added dropwise $TiCl_4$ (6.72 mL, 6.72 mmol, 1M/CH_2Cl_2) to give a yellow slurry. After 5 min, *i*-Pr_2EtN (1.26 mL, 7.24 mmol) was added dropwise to give a red solution that was stirred 45 min at -78°C. A solution of (2*E*)-4-ethoxycarbonyloxy-2-methylbut-2-enal (890 mg, 5.17 mmol) in CH_2Cl_2 (5 mL) was added slowly and the resulting mixture was stirred 90 min. The reaction was quenched by the addition of satd $NaHCO_3$ at -78°C and warmed to rt. The aqueous layer was extracted with CH_2Cl_2 (4×). The organic layers were combined, washed with brine, dried over $MgSO_4$, and the solvent was evaporated to yield a yellow liquid that was purified by flash chromatography using 40→50% Et_2O/hexane to give the desired aldol product (958 mg, 72%) as a slightly yellow liquid. IR (neat) ν = 3492, 2982, 2937, 1745, 1727, 1711, 1255, 1009 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.73 (t, 1H, *J* = 6.9 Hz), 4.70 (d, 2H, *J* = 6.9 Hz), 4.38 (br s, 1H), 4.19 (q, 2H, *J* = 7.2 Hz), 3.08 (d, 1H, *J* = 2.7 Hz), 2.74 (m, 1H), 2.54 (m, 2H), 1.69 (s, 3H), 1.30 (t, 3H, *J* = 7.2 Hz), 1.06 (m, 6H); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 215.7, 155.1, 140.3, 119.4, 74.3,

63.8 (2C), 47.6, 34.8, 14.1, 13.6, 9.8, 7.4; HRMS-EI calcd for $C_{13}H_{20}O_4$ [M - H_2O]$^+$ 240.1362, found 240.1366.

Synthesis of 6b

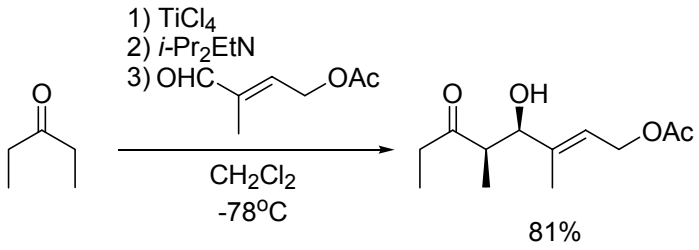


12 **6b** (88%)

(2*E*)-(4*R,5*R**)-1-ethoxycarbonyloxy-3,5-dimethyl-4-triethylsiloxy-2-octen-6-one**

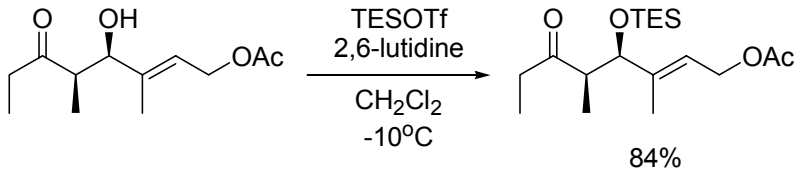
(6b) To a -10°C solution of **12** (512 mg, 1.98 mmol) in CH_2Cl_2 (10 mL) was added successively 2,6-lutidine (254 μL, 2.18 mmol) and TESOTf (471 μL, 2.08 mmol) and the resulting mixture was stirred until the reaction was completed as judged by TLC (~ 45 min). Satd $NaHCO_3$ was added and the aqueous layer was extracted with CH_2Cl_2 (3×). The combined organic layers were washed with brine, dried over $MgSO_4$, and the solvent was evaporated to yield the crude product that was purified by flash chromatography using 20% Et_2O/hexane to afford the desired product (648 mg, 88%) as a colorless liquid. IR (neat) ν = 2958, 2880, 1745, 1715, 1255, 1006 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.53 (t, 1H, *J* = 6.9 Hz), 4.63 (d, 2H, *J* = 6.9 Hz), 4.19 (m, 3H), 2.70 (m, 1H), 2.41 (q, 2H, *J* = 7.2 Hz), 1.70 (s, 3H), 1.30 (t, 3H, *J* = 7.2 Hz), 1.09 (d, 3H, *J* = 6.6 Hz), 0.95 (m, 12H), 0.56 (q, 6H, *J* = 7.5 Hz); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 213.2, 155.0, 142.2, 120.4, 78.3, 63.7, 63.6, 50.5, 35.6, 14.1, 12.3, 12.1, 7.2, 6.6, 4.6; HRMS-EI calcd for $C_{17}H_{31}SiO_5$ [M - Et]$^+$ 343.1941, found 343.1942.

Synthesis of 9

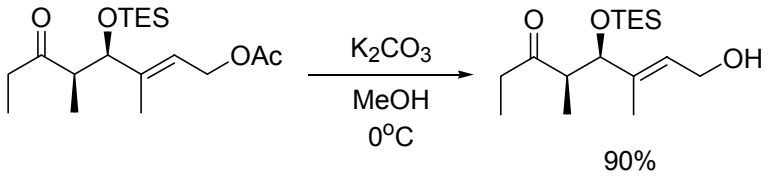


(2*E*)-(4*R,5*R**)-1-acetoxy-3,5-dimethyl-4-hydroxy-2-octen-6-one** Using the same protocol as for **12** using (2*E*)-4-acetoxy-2-methyl-2-butenal[2] (394 mg, 2.77 mmol) gave, after purification by flash chromatography using 50% Et_2O/hexane, the aldol product (511 mg, 81%) as a colorless liquid. IR (neat) ν = 3471, 2978, 2944, 1743, 1725, 1380, 1236, 1025 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.64 (tt, 1H, *J* = 6.9, 1.5 Hz), 4.62 (d, 2H, *J* = 6.9 Hz), 4.34 (br m, 1H), 3.44 (d, 1H, *J* = 3.3 Hz), 2.77 (m, 1H), 2.54 (m, 2H), 2.04 (s, 3H), 1.68 (s, 3H), 1.05 (m, 6H); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 214.9, 170.7, 139.7, 119.7, 74.7, 60.5, 47.9, 34.6, 20.5, 13.0, 10.0, 7.1; HRMS-ES cald for $C_{12}H_{20}O_4Na$ $[M + Na]^+$ 251.1253, found 251.1244.

[2] Tietze, L. F.; Eicher, T. Syntheses and Transformations of Functional Groups. In *Reactions and Syntheses*; University Science Books; Mill Valley, CA, 1989; Chapter G, p. 102.

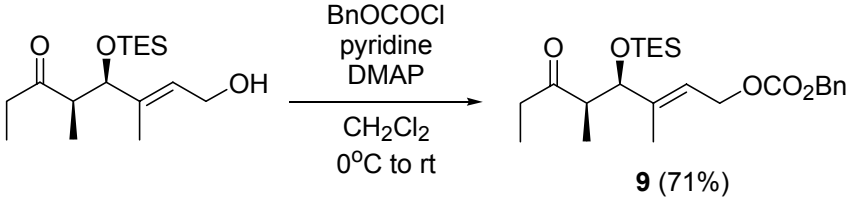


(2*E*)-(4*R,5*R**)-1-acetoxy-3,5-dimethyl-4-triethylsiloxy-2-octen-6-one** Using the same protocol as for **6b** on a 2.12 mmol scale, the desired product (607 mg, 84%) was obtained as a colorless liquid after purification by flash chromatography using 20% Et_2O/hexane. IR (neat) ν = 2957, 2887, 1744, 1708, 1232, 1020 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.47 (t, 1H, *J* = 6.9 Hz), 4.57 (d, 2H, *J* = 6.9 Hz), 4.19 (d, 1H, *J* = 7.5 Hz), 2.72 (m, 1H), 2.40 (m, 2H), 2.03 (s, 3H), 1.68 (s, 3H), 1.09 (d, 3H, *J* = 6.9 Hz), 1.00-0.90 (m, 12H), 0.56 (m, 6H); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 213.3, 170.7, 141.6, 120.9, 78.6, 60.4, 50.6, 35.8, 20.7, 12.6, 11.9, 7.2, 6.6, 4.6; HRMS-EI calcd for $C_{16}H_{29}SiO_4$ $[M - Et]^+$ 313.1835, found 313.1841.



(2*E*)-(4*R,5*R**)-3,5-dimethyl-6-oxo-4-triethylsiloxy-2-octen-1-ol** To a 0°C solution of the acetate (595 mg, 1.74 mmol) in MeOH (10 mL) was added K_2CO_3 (264 m, 1.91 mmol) and the resulting mixture was stirred for 1 h at 0°C. The solvent was evaporated, water was added and the mixture was extracted with Et_2O (3×). The organic layers were combined, washed with brine, dried over $MgSO_4$, and the solvent was evaporated to give the desired product (472 mg, 90%) as a colorless liquid that was used without further

purification. IR (neat) ν = 3428, 2958, 2878, 1710, 1462, 1240, 1007 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.52 (t, 1H, *J* = 6.6 Hz), 4.16 (m, 3H), 2.75 (m, 1H), 2.43 (m, 3H), 1.62 (s, 3H), 1.11 (d, 3H, *J* = 7.2 Hz), 0.96 (m, 12H), 0.58 (q, 6H, *J* = 7.5 Hz); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 214.0, 138.2, 126.4, 78.9, 58.7, 51.0, 35.6, 12.8, 11.6, 7.2, 6.6, 4.6; HRMS-EI calcd for $C_{16}H_{31}SiO_2$ $[M - OH]^+$ 283.2093, found 283.2090.

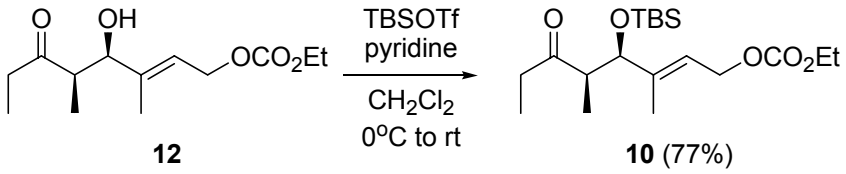


9 (71%)

(2*E*)-(4*R,5*R**)-1-benzyloxycarbonyloxy-3,5-dimethyl-4-triethylsiloxy-2-octen-6-one (9)** To a 0°C solution of the alcohol (438 mg, 1.46 mmol) in CH_2Cl_2 (10 mL) was added pyridine (177 μL, 2.19 mmol) and benzylchloroformate (250 μL, 1.75 mmol) and the reaction mixture was warmed to rt. Additional benzylchloroformate (2 × 250 μL), pyridine (2 × 177 μL), and DMAP (~10 mg) were added in order to drive the reaction to completion. Satd $NaHCO_3$ was added and the aqueous layer was extracted with CH_2Cl_2 (3×). The combined organic layers were washed with brine, dried over $MgSO_4$, and the solvent was evaporated to yield the crude product that was purified by flash chromatography using 10% Et_2O/hexane to afford the desired product (449 mg, 71%) as a colorless liquid. IR (neat) ν = 3038, 2957, 2881, 1746, 1711, 1460, 1247 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35 (m, 5H), 5.53 (t, 1H, *J* = 7.2 Hz), 5.13 (s, 2H), 4.65 (d, 2H, *J* = 7.2 Hz), 4.22 (d, 1H, *J* = 7.2 Hz), 2.68 (m, 1H), 2.39 (q, 2H, *J* = 7.2 Hz), 1.68 (s, 3H), 1.08 (d, 3H, *J* = 7.2 Hz), 0.94 (m, 12H), 0.55 (q, 6H, *J* = 7.8 Hz); ^{13}C NMR (74.5 MHz,

$CDCl_3$) δ 213.2, 155.0, 142.4, 135.1, 128.4, 128.3, 128.1, 120.2, 78.2, 69.3, 63.9, 50.5, 35.6, 12.3, 12.2, 7.2, 6.6, 4.6; HRMS-EI calcd for $C_{22}H_{33}SiO_5$ $[M - Et]^+$ 405.2097, found 405.2105.

Synthesis of 10

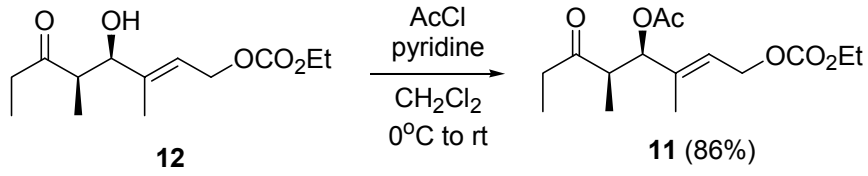


12 **10** (77%)

(2*E*)-(4*R,5*R**)-4-*tert*-butyldimethylsiloxy-1-ethoxycarbonyloxy-3,5-dimethyl-2-octen-6-one (10)** To a 0°C solution of **12** (205 mg, 0.794 mmol) in CH_2Cl_2 (5 mL) was added 2,6-lutidine (139 μL, 1.19 mmol) and TBSOTf (219 μL, 0.953 mmol) and the resulting mixture was stirred at 0°C for 30 min and warmed to rt overnight. Water was added and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3×) and the combined organic layers were washed with brine, dried over $MgSO_4$, and the solvent was evaporated to give the crude product that was purified by flash chromatography using 20% Et_2O/hexane to afford the desired product (228 mg, 77%) as a colorless liquid. IR (neat) ν = 3085, 2933, 2859, 1712, 1462, 1255, 1099 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.48 (t, 1H, *J* = 7.5 Hz), 4.59 (d, 2H, *J* = 7.5 Hz), 4.14 (m, 3H), 2.68 (m, 1H), 2.38 (m, 2H), 1.66 (s, 3H), 1.27 (t, 3H, *J* = 7.2 Hz), 1.05 (d, 3H, *J* = 6.9 Hz), 0.95 (t, 3H, *J* = 7.2 Hz), 0.85 (s, 9H), -0.01 (s, 3H), -0.07 (s, 3H); ^{13}C NMR (74.5 MHz,

$CDCl_3$) δ 213.3, 155.1, 142.2, 120.6, 78.5, 63.8, 63.6, 50.6, 35.8, 25.7, 18.0, 14.2, 12.5, 12.2, 7.3, -4.7, -5.3; HRMS-EI calcd for $C_{19}H_{36}SiO_5$ $[M]^+$ 372.2332, found 372.2326.

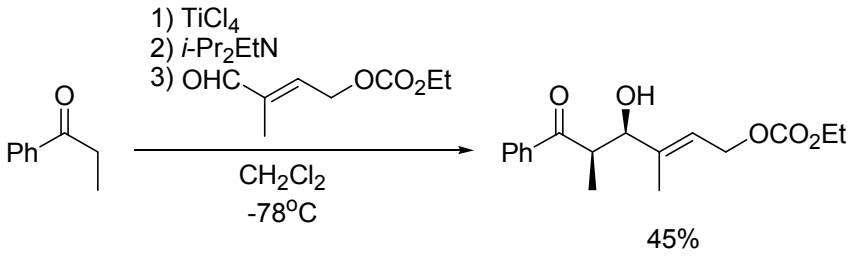
Synthesis of 11



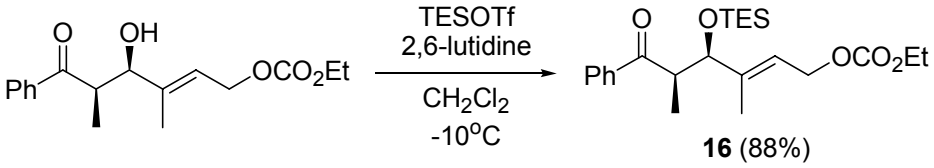
12 **11** (86%)

(2*E*)-(4*R,5*R**)-4-acetoxy-1-ethoxycarbonyloxy-3,5-dimethyl-2-octen-6-one (11)** To a 0°C solution of **12** (141 mg, 0.546 mmol) in CH_2Cl_2 (5 mL) was added pyridine (53 μL, 0.655 mmol) and acetyl chloride (43 μL, 0.600 mmol) and the reaction was warmed to rt. After 4 h, additional pyridine (53 μL) and acetyl chloride (43 μL) were added and the reaction was stirred for 2 h. Water was added, the layers were separated, and the organic layer was washed with 10% HCl, satd $NaHCO_3$, brine, dried over $MgSO_4$, and the solvent was evaporated to give the crude product that was purified by flash chromatography using 25% Et_2O/hexane to afford the desired product (141 mg, 86%) as a colorless liquid. IR (neat) ν = 2982, 2939, 1744, 1371, 1255 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.52 (t, 1H, *J* = 6.6 Hz), 5.41 (d, 1H, *J* = 6.6 Hz), 4.60 (d, 2H, *J* = 6.6 Hz), 4.14 (q, 2H, *J* = 7.2 Hz), 2.83 (m, 1H), 2.43 (m, 2H), 2.01 (s, 3H), 1.69 (s, 3H), 1.25 (t, 3H, *J* = 7.2 Hz), 1.03 (d, 2H, *J* = 6.9 Hz), 0.97 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 211.0, 169.6, 154.9, 137.7, 121.1, 76.6, 63.9, 63.5, 47.8, 34.7, 20.8, 14.1, 13.6, 11.2, 7.4; HRMS-EI calcd for $C_{13}H_{21}O_4$ $[M - OAc]^+$ 241.1440, found 241.1441.

Synthesis of 16



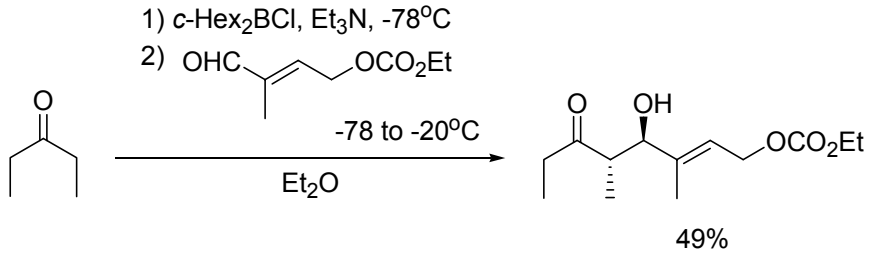
(2*E*)-(4*R,5*R**)-3,5-dimethyl-1-ethoxycarbonyloxy-4-hydroxy-6-phenyl-2-hexan-6-one** Using the same protocol as for **12** using propiophenone (354 μL, 2.66 mmol) gave, after purification by flash chromatography using 50% Et_2O/hexane, the aldol product (303 mg, 40%) as a pale yellow liquid. IR (neat) ν = 3500, 2983, 2939, 1745, 1680, 1449, 1253, 971 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.95 (m, 2H), 7.61 (tt, 1H, *J* = 7.5, 2.1 Hz), 7.50 (m, 2H), 5.84 (tt, 1H, *J* = 7.2, 1.2 Hz), 4.72 (dd, 2H, *J* = 7.2, 2.7 Hz), 4.49 (br s, 1H), 4.19 (q, 2H, *J* = 7.2 Hz), 3.64 (m, 1H), 3.41 (d, 1H, *J* = 2.1 Hz), 1.74 (s, 3H), 1.31 (t, 3H, *J* = 7.2 Hz), 1.19 (d, 3H, *J* = 7.5 Hz); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 204.9, 155.0, 140.0, 135.6, 133.4, 128.6, 128.2, 119.7, 74.5, 63.8, 63.7, 42.3, 14.1, 13.8, 10.9; HRMS-ES calcd for $C_{17}H_{22}O_5Na$ $[M + Na]^+$ 329.1370, found 329.1380.



(2*E*)-(4*R,5*R**)-3,5-dimethyl-1-ethoxycarbonyloxy-6-phenyl-4-triethylsiloxy-2-hexan-6-one (16)** Following the same protocol as for **6b** on a 0.519 mmol scale using

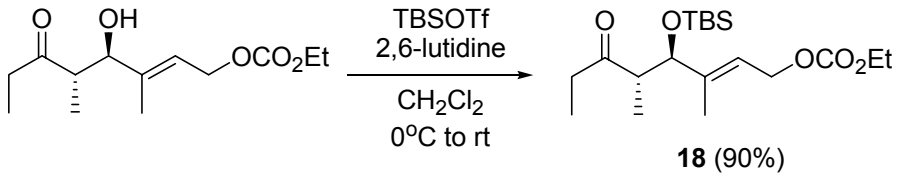
TESOTf (1.1 eq.) and 2,6-lutidine (1.5 eq), the desired product (193 mg, 88%) was obtained as a colorless liquid after purification by flash chromatography using 10% Et_2O/hexane. IR (neat) ν = 2957, 2877, 1746, 1682, 1256, 967 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.87 (m, 2H), 7.55 (tt, 1H, *J* = 7.2, 1.2 Hz), 7.44 (m, 2H), 5.55 (t, 1H, *J* = 7.5 Hz), 4.55 (dd, 1H, *J* = 12.9, 7.8 Hz), 4.42 (dd, 1H, *J* = 12.9, 6.6 Hz), 4.35 (d, 1H, *J* = 7.8 Hz), 4.13 (q, 2H, *J* = 7.2 Hz), 3.69 (m, 1H), 1.62 (s, 3H), 1.27 (m, 6H), 0.91 (t, 9H, *J* = 8.4 Hz), 0.54 (q, 6H, *J* = 8.4 Hz); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 202.7, 155.0, 141.8, 137.0, 132.8, 128.5, 128.1, 121.1, 78.9, 63.8, 63.7, 45.6, 14.2, 13.9, 12.1, 6.7, 4.7; HRMS-ES calcd for $C_{23}H_{36}SiO_5Na$ $[M + Na]^+$ 443.2224, found 443.2235.

Synthesis of 18



(2*E*)-(4*R,5*S**)-1-ethoxycarbonyloxy-3,5-dimethyl-4-hydroxy-2-octen-6-one** To a -78°C solution of *c*-Hex_2BCl (530 μL, 2.42 mmol) in Et_2O (6 mL) was added Et_3N (363 μL, 2.60 mmol) followed by a solution of 3-pentanone (236 μL, 2.23 mmol). After stirring at -78°C for 1 h a solution of (2*E*)-4-ethoxycarbonyloxy-2-methylbut-2-enal (320 mg, 1.86 mmol) in Et_2O (2 mL) was added. The mixture was stirred for 30 min at -78°C and placed in the freezer for 16 h. The reaction mixture was then partitioned

between Et_2O and a 1M pH 7 buffer, the organic extract was concentrated to give an oil which was taken up in MeOH (7.5 mL) and 1M pH 7 buffer (7.5 mL) and stirred at 0°C. H_2O_2 (2.5 mL, 30% soln in H_2O) was added dropwise. After stirring at rt for 2 h, the mixture was diluted with H_2O and extracted with CH_2Cl_2 (2×). The combined organic layers were washed with satd Na_2CO_3, brine, dried over $MgSO_4$, and the solvent and cyclohexanol were evaporated under reduce pressure and heating (~80°C) to give the crude product that was purified by flash chromatography using 40% Et_2O/hexane to yield the desired *anti* aldol product (259 mg, 49%) as a colorless liquid. IR (neat) ν = 3491, 2979, 2935, 1745, 1722, 1711, 1460, 1378, 1255, 1006 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.61 (t, 1H, *J* = 6.9 Hz), 4.68 (d, 2H, *J* = 6.9 Hz), 4.18 (m, 3H), 2.78 (m, 1H), 2.53 (m, 2H), 2.41 (d, 1H, *J* = 4.5 Hz), 1.72 (s, 3H), 1.31 (t, 3H, *J* = 6.9 Hz), 1.06 (t, 3H, *J* = 6.9 Hz), 0.97 (d, 3H, *J* = 7.2 Hz); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 215.4, 155.0, 141.1, 121.9, 79.2, 63.9, 63.7, 48.2, 36.3, 14.1, 14.0, 11.3, 7.3; HRMS-ES calcd for $C_{13}H_{22}O_5Na$ $[M + Na]^+$ 281.1359, found 281.1349.

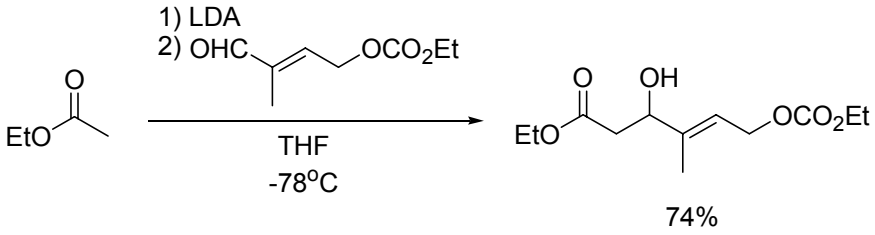


18 (90%)

(2*E*)-(4*R,5*S**)-4-*tert*-butyldimethylsiloxy-1-ethoxycarbonyloxy-3,5-dimethyl-2-octen-6-one (18)** Following the same protocol as for **10** on a 0.588 mmol scale, the desired product (198 mg, 90%) was obtained as a colorless liquid after purification by flash chromatography using 20% Et_2O/hexane. IR (neat) ν = 2956, 2934, 2853, 1747,

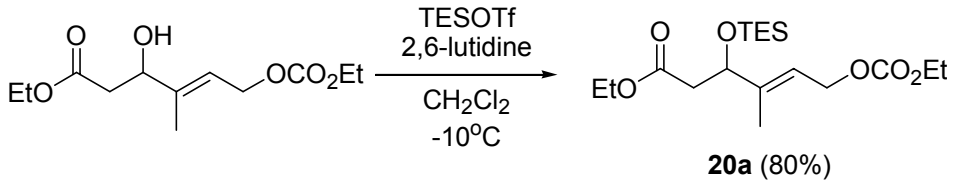
1720, 1256, 1064 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.54 (td, 1H, *J* = 6.9, 0.9 Hz), 4.67 (dd, 2H, *J* = 6.9, 2.4 Hz), 4.17 (m, 3H), 2.78 (m, 1H), 2.54 (q, 2H, *J* = 7.2 Hz), 1.68 (s, 3H), 1.31 (t, 3H, *J* = 6.9 Hz), 1.03 (t, 3H, *J* = 7.2 Hz), 0.81 (s, 9H), -0.04 (s, 3H), -0.06 (s, 3H); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 214.3, 155.1, 141.5, 122.0, 81.2, 64.0, 63.7, 48.9, 37.9, 25.6, 17.9, 14.2, 13.8, 10.8, 7.2, -4.8, -5.6; HRMS-EI calcd for $C_{15}H_{27}SiO_5$ $[M - t\text{-Bu}]^+$ 315.1628, found 315.1623.

Synthesis of 20a



Ethyl (4*E*)-6-ethoxycarbonyloxy-3-hydroxy-4-methyl-4-hexenoate To a 0°C solution of diisopropylamine (518 μL, 3.70 mmol) in THF (10 mL) was added dropwise *n*-BuLi (2.3 mL, 3.70 mmol, 1.6M/hexane). The mixture was warmed to rt for 15 min and cooled to -78°C. Ethyl acetate (389 μL, 4.00 mmol) was added dropwise and the resulting mixture was stirred for 1 h at -78°C. A solution of (2*E*)-4-ethoxycarbonyloxy-2-methylbut-2-enal (530 mg, 3.08 mmol) in THF (2 mL) was added dropwise and stirred for 1 h at -78°C. The reaction was quenched by the addition of satd $NaHCO_3$. The aqueous layer was extracted with Et_2O (3×) and the combined organic layers were washed with brine, dried over $MgSO_4$, and the solvent was evaporated to give the crude

product (590 mg, 74%) that can be used without further purification. Analytically pure sample can be obtained by flash chromatography using 40% Et_2O/hexane. IR (neat) ν = 3497, 2985, 1744, 1371, 1268, 1010 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.72 (tt, 1H, *J* = 6.9, 1.2 Hz), 4.69 (d, 2H, *J* = 6.9 Hz), 4.47 (m, 1H), 4.19 (m, 4H), 2.96 (d, 1H, *J* = 3.6 Hz), 2.56 (s, 1H), 2.54 (d, 1H, *J* = 2.1 Hz), 1.74 (s, 3H), 1.29 (m, 6H); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 172.2, 155.0, 141.8, 119.3, 72.2, 63.9, 63.7, 60.7, 39.8, 14.1, 14.0, 12.4; HRMS-EI calcd for $C_{12}H_{19}O_5$ $[M - OH]^+$ 243.1232, found 243.1234.

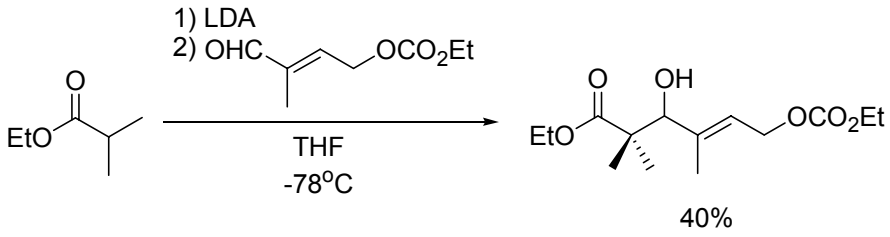


20a (80%)

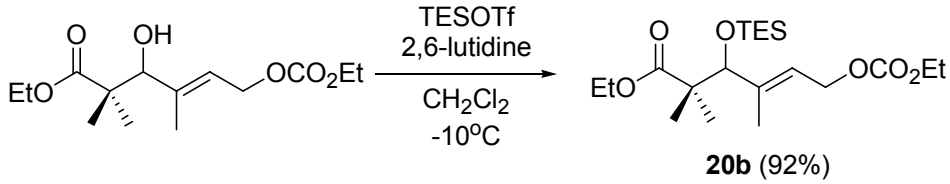
Ethyl (4*E*)-6-ethoxycarbonyloxy-4-methyl-3-triethylsiloxy-4-hexenoate (20a)

Following the same protocol as for **6b** on a 0.423 mmol scale using TESOTf (3 eq.) and 2,6-lutidine (3.3 eq), the desired product (127 mg, 80%) was obtained as a colorless liquid after purification by flash chromatography using 15% Et_2O/hexane. IR (neat) ν = 2956, 2912, 2877, 1745, 1254, 1006 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.64 (tt, 1H, *J* = 6.9, 0.9 Hz), 4.66 (dd, 2H, *J* = 6.9, 3.0 Hz), 4.54 (dd, 1H, *J* = 8.7, 4.2 Hz), 4.15 (m, 4H), 2.47 (m, 2H), 1.71 (d, 3H, *J* = 0.9 Hz), 1.28 (m, 6H), 0.91 (t, 9H, *J* = 8.1 Hz), 0.56 (q, 6H, *J* = 8.1 Hz); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 171.1, 155.1, 143.1, 119.3, 74.3, 63.9, 63.8, 60.4, 42.3, 14.2, 14.1, 11.6, 6.6, 4.6; HRMS-EI calcd for $C_{16}H_{29}SiO_6$ $[M - Et]^+$ 345.1733, found 345.1740.

Synthesis of 20b



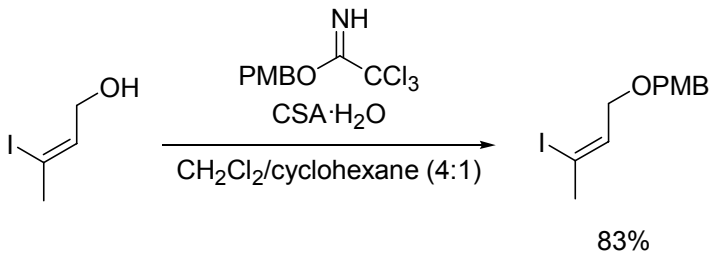
Ethyl (4*E*)-6-ethoxycarbonyloxy-3-hydroxy-2,2,4-trimethyl-4-hexenoate Following the same protocol as for **20a** using ethyl isobutyrate (561 μL, 4.20 mmol), the desired product was obtained as a colorless liquid (372 mg, 40%) after purification by flash chromatography using 30% Et_2O/pentane. IR (neat) ν = 3514, 2984, 2935, 1745, 1725, 1468, 1254, 1007 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.58 (tt, 1H, *J* = 6.6, 0.9 Hz), 4.69 (d, 2H, *J* = 6.6 Hz), 4.18 (m, 5H), 3.32 (d, 1H, *J* = 5.7 Hz), 1.69 (s, 3H), 1.29 (m, 6H), 1.21 (s, 3H), 1.15 (s, 3H); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 177.6, 155.0, 140.5, 122.6, 81.5, 63.9, 63.8, 60.9, 46.2, 23.6, 20.7, 14.2, 13.9, 13.4; HRMS-ES calcd for $C_{14}H_{24}O_6Na$ $[M + Na]^+$ 311.1465, found 311.1478.



Ethyl (4*E*)-6-ethoxycarbonyloxy-2,2,4-trimethyl-3-triethylsilyloxy-4-hexenoate (20b) Following the same protocol as for **6b** on a 0.503 mmol scale using TESOTf (1.1 eq.) and 2,6-lutidine (1.5 eq), the desired product (185 mg, 92%) was obtained as a colorless

liquid after purification by flash chromatography using 10% Et_2O/pentane. IR (neat) ν = 2957, 2874, 1746, 1467, 1255, 1007 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.56 (t, 1H, *J* = 6.8 Hz), 4.67 (m, 2H), 4.36 (s, 1H), 4.19 (q, 2H, *J* = 7.2 Hz), 4.09 (m, 2H), 1.70 (s, 3H), 1.31 (t, 3H, *J* = 7.2 Hz), 1.25 (t, 3H, *J* = 7.2 Hz), 1.17 (s, 3H), 1.05 (s, 3H), 0.92 (t, 9H, *J* = 8.0 Hz), 0.55 (q, 6H, *J* = 7.2 Hz) ; ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 176.6, 155.1, 141.4, 122.3, 81.1, 63.9, 63.8, 60.4, 48.6, 21.4, 21.2, 14.2, 14.0, 13.9, 6.8, 4.6; HRMS-ES calcd for $C_{20}H_{38}SiO_6Na$ $[M + Na]^+$ 425.2329, found 425.2333.

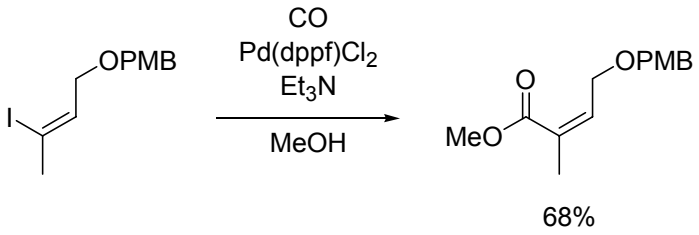
Synthesis of 22



(2*Z*)-2-iodo-4-(4-methoxybenzyloxy)-2-butene To a solution of (2*Z*)-3-iodo-2-buten-1-ol[3] (1.66 g, 8.39 mmol) and p-methoxybenzyl trichloroacetamidate (3.56 g, 12.59 mmol) in CH_2Cl_2 (40 mL) and cyclohexane (10 mL) was added camphorsulfonic acid monohydrate (210 mg, 0.84 mmol). The resulting mixture was stirred 16 h. Satd $NaHCO_3$ was added and the aqueous layer was extracted with CH_2Cl_2 (2×). The organic layers were combined, washed with brine, dried over $MgSO_4$, the solvent was evaporated, and the crude product that was purified by flash chromatography using 10% Et_2O/hexane

[3] Dakoji, S.; Li, D.; Agnihotri, G.; Zhou, H.-Q.; Liu, H.-W. *J. Am. Chem. Soc.* **2001**, *123*, 9749.

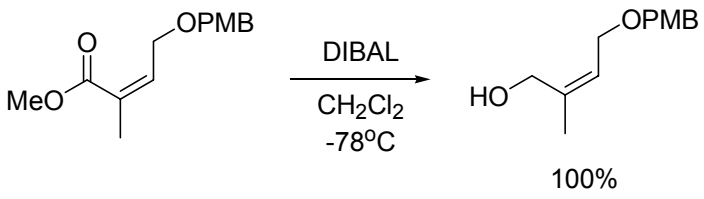
to give the protected alcohol (2.21 g, 83%) as an orange liquid. IR (neat) ν = 3006, 2959, 2912, 2836, 1612, 1513, 1248, 1095 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, 2H, *J* = 8.4 Hz), 6.87 (d, 2H, *J* = 8.4 Hz), 5.74 (m, 1H), 4.44 (s, 2H), 4.03 (dd, 2H, *J* = 6.0, 1.5 Hz), 3.78 (s, 3H), 2.52 (d, 3H, *J* = 1.5 Hz); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 159.1, 132.2, 130.0, 129.4, 113.7, 102.3, 74.2, 72.0, 55.2, 33.6; HRMS-EI calcd for $C_{12}H_{15}O_2I$ $[M]^+$ 318.0117, found 318.0116.



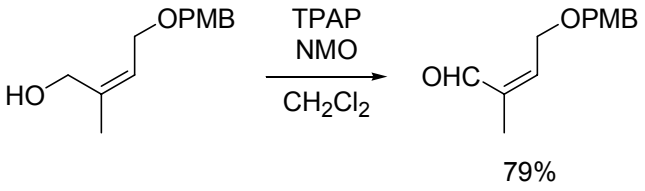
68%

Methyl (2*Z*)-4-(4-methoxybenzyloxy)-2-methyl-2-butenoate To a stirred solution of the protected alcohol (623 mg, 1.96 mmol) and triethylamine (820 μL, 5.88 mmol) in MeOH (50 mL) was added $Pd(dppf)Cl_2$ (146 mg, 0.20 mmol). CO was bubbled through the reaction mixture for 6 h. The dark mixture was diluted with Et_2O and washed with 10% HCl, brine, dried over $MgSO_4$, and the solvent was evaporated to give the crude product that was purified by flash chromatography using 20% Et_2O/hexane to give the desired ester (335 mg, 68%) as a colorless liquid. IR (neat) ν = 3004, 2952, 2839, 1712, 1613, 1514, 1247 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, 2H, *J* = 8.4 Hz), 6.88 (d, 2H, *J* = 8.4 Hz), 6.17 (m, 1H), 4.46 (m, 4H), 3.80 (s, 3H), 3.72 (s, 3H), 1.92 (q, 3H, *J* = 1.5 Hz); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 167.8, 159.3, 142.3, 130.2, 129.5, 127.2, 113.9,

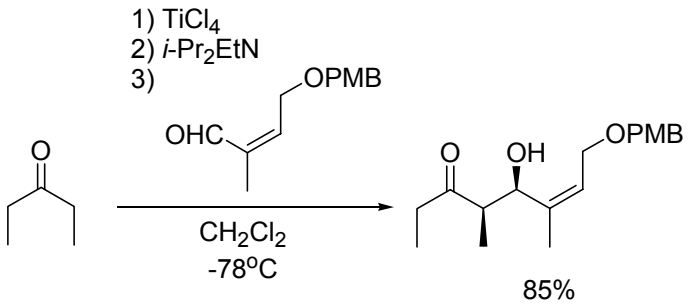
72.5, 68.7, 55.3, 51.6, 19.9; HRMS-EI calcd for $C_{14}H_{18}O_4$ $[M]^+$ 250.1205, found 250.1210.



(2*Z*)-2-methyl-4-(4-methoxybenzyloxy)-2-buten-1-ol To a -78°C solution of the ester (335 mg, 1.34 mmol) in CH_2Cl_2 was added slowly DIBAL (2.94 ml, 2.94 mmol, 1M/heptane). The reaction mixture was stirred 45 min at -78°C and poured into a 0°C solution of 10% HCl (5 mL) and stirred 30 min. The organic layer was washed with H_2O, dried over $MgSO_4$, and the solvent was evaporated to yield the crude alcohol (300 mg, 100%) that was used without further purification. IR (neat) ν = 3411, 2942, 2915, 2858, 1612, 1514, 1249 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, 2H, *J* = 9.0 Hz), 6.87 (d, 2H, *J* = 9.0 Hz), 5.54 (t, 1H, *J* = 6.9 Hz), 4.43 (s, 2H), 4.06 (d, 2H, *J* = 5.4 Hz), 4.00 (d, 2H, *J* = 6.9 Hz), 3.79 (s, 3H), 1.82 (d, 3H, *J* = 0.6 Hz); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 159.3, 140.9, 130.1, 129.6, 123.7, 113.9, 72.1, 65.4, 61.9, 55.3, 21.7; HRMS-EI calcd for $C_{13}H_{18}O_3$ $[M]^+$ 222.1256, found 222.1261.



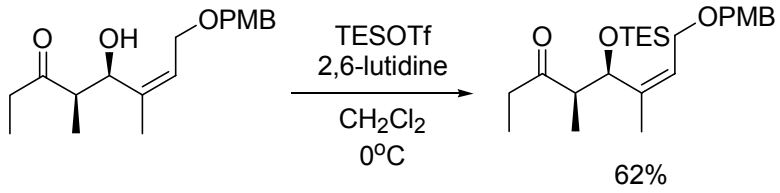
(2*Z*)-4-(4-methoxybenzyloxy)-2-methyl-2-butenal To a solution of the alcohol (300 mg, 1.35 mmol) in CH_2Cl_2 (10 mL) was added TPAP (47 mg, 0.135 mmol) followed by NMO (239 mg, 2.03 mmol), and the resulting mixture was stirred for 4 h. The solvent was evaporated and the crude product was purified by flash chromatography using 40% Et_2O/hexane to yield the desired aldehyde (234 mg, 79%) as a colorless liquid. IR (neat) ν = 3007, 2930, 2839, 1679, 1514, 1249 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 10.07 (s, 1H), 7.27 (d, 2H, *J* = 8.4 Hz), 6.89 (d, 2H, *J* = 8.4 Hz), 6.58 (tq, 1H, *J* = 6.3, 1.2 Hz), 4.51 (s, 2H), 4.46 (dd, 2H, *J* = 6.3, 1.5 Hz), 3.81 (s, 3H), 1.83 (q, 3H, *J* = 1.5 Hz); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 191.2, 159.4, 149.6, 143.6, 137.6, 129.5, 113.9, 72.5, 64.2, 55.2, 16.3; HRMS-EI calcd for $C_{13}H_{16}O_3$ $[M]^+$ 220.1099, found 220.1100.



(2*Z*)-(4*R,5*R**)-3,5-dimethyl-4-hydroxy-1-(4-methoxybenzyloxy)-2-octen-6-one**

Following the same protocol describe earlier for **12**, using (2*Z*)-4-(4-methoxybenzyloxy)-2-methyl-2-butenal (234 mg, 1.06 mmol), the desired product (275 mg, 85%) was

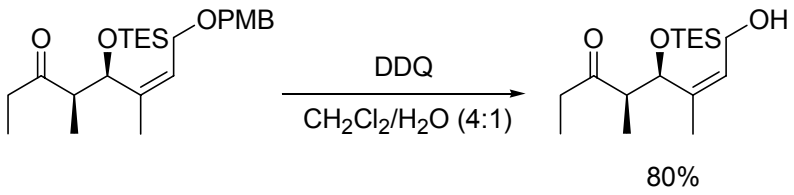
obtained as a colorless liquid after purification by flash chromatography using 40→50% Et_2O/hexane. IR (neat) ν = 3436, 2972, 2937, 1710, 1613, 1514, 1249, 1034 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, 2H, *J* = 8.7 Hz), 6.86 (d, 2H, *J* = 8.7 Hz), 5.46 (t, 1H, *J* = 6.6 Hz), 4.54 (dd, 1H, *J* = 7.2, 3.0 Hz), 4.41 (s, 2H), 4.09 (m, 1H), 3.87 (m, 1H), 3.78 (s, 3H), 3.05 (br m, 1H), 2.77 (m, 1H), 2.39 (m, 2H), 1.73 (s, 3H), 1.16 (d, 3H, *J* = 6.9 Hz), 0.97 (t, 3H, *J* = 7.2 Hz); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 214.2, 195.1, 139.7, 130.0, 129.4, 124.5, 113.6, 72.0, 70.9, 65.4, 55.1, 49.5, 35.5, 18.9, 12.8, 7.3; MS-EI (*m*/*z*) 289 $[M - OH]^+$.



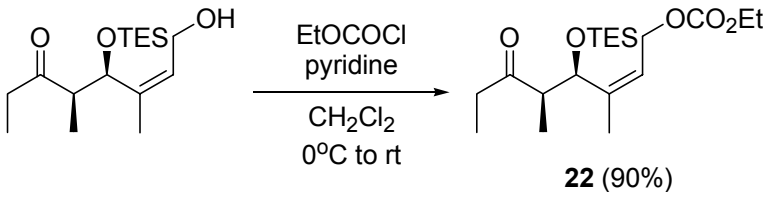
(2*Z*)-(4*R,5*R**)-3,5-dimethyl-1-(4-methoxybenzyloxy)-4-triethylsiloxy-2-octen-6-one**

Following the same protocol describe earlier for **6b** but using a 4-fold excess of both TESOTf and 2,6-lutidine on a 0.894 mmol scale, the desired product (233 mg, 62%) was obtained as a colorless liquid after purification by flash chromatography using 15% Et_2O/hexane. IR (neat) ν = 2956, 2874, 1712, 1613, 1514, 1461, 1248, 1075 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.27 (d, 2H, *J* = 8.7 Hz), 6.87 (d, 2H, *J* = 8.7 Hz), 5.37 (br m, 1H), 4.43 (m, 1H), 4.12 (m, 1H), 3.79 (m, 4H), 2.84 (m, 1H), 2.36 (m, 2H), 1.73 (d, 3H, *J* = 0.9 Hz), 1.11 (d, 3H, *J* = 6.9 Hz), 0.93 (m, 12H), 0.56 (q, 6H, *J* = 7.2 Hz); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 213.3, 159.1, 138.7, 130.5, 129.3, 124.7, 113.6, 72.3, 71.8, 66.1,

55.1, 50.4, 36.8, 18.0, 14.4, 7.2, 6.7, 4.6; HRMS-EI calcd for $C_{22}H_{35}SiO_4$ [M - Et]$^+$ 391.2305, found 391.2303.



(2*Z*)-(4*R,5*R**)-3,5-dimethyl-6-oxo-4-triethylsiloxy-2-octen-1-ol** To a solution of the protected diol (150 mg, 0.357 mmol) in a mixture of CH_2Cl_2 (2.8 mL) and H_2O (0.7 mL) was added DDQ (122 mg, 0.535 mmol). After 15 min, satd $NaHCO_3$ was added, and the aqueous layer was extracted with CH_2Cl_2 (3×). The organic layers were combined, washed with satd $NaHCO_3$, brine, dried over $MgSO_4$, and the solvent was evaporated to give the crude product that was purified by flash chromatography using 30→35% Et_2O/hexane to afford the desired product (86 mg, 80 %) as a colorless liquid. IR (neat) ν = 3447, 2957, 2881, 1710, 1461, 1075, 1008 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.45 (m, 1H), 4.62 (d, 1H, *J* = 9.6 Hz), 4.21 (m, 1H), 3.94 (m, 1H), 2.95 (m, 1H), 2.51 (m, 1H), 2.34 (m, 2H), 1.72 (br s, 3H), 1.18 (d, 3H, *J* = 6.9 Hz), 0.95 (m, 12H), 0.58 (q, 6H, *J* = 8.1 Hz); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 215.8, 139.1, 126.6, 71.3, 58.2, 51.0, 37.0, 17.9, 15.0, 7.2, 6.7, 4.7; HRMS-EI calcd for $C_{14}H_{27}SiO_3$ [M - OH]$^+$ 271.1729, found 271.1738.

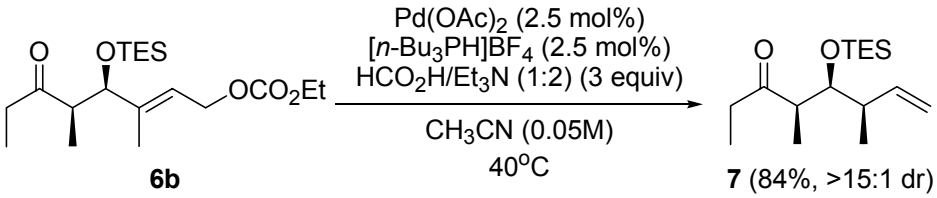


22 (90%)

(2*Z*)-(4*R,5*R**)-1-ethoxycarbonyloxy-3,5-dimethyl-4-triethylsiloxy-2-octen-6-one**

(22) To 0°C solution of the alcohol (80.8 mg, 0.269 mmol) in CH_2Cl_2 (2 mL) was added pyridine (52 μL, 0.645 mmol) and ethyl chloroformate (31 μL, 0.323 mmol). The mixture was allowed to warm to rt overnight. The reaction was quenched by the addition of satd $NaHCO_3$ and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3×). The organic layers were combined, washed with brine, dried over $MgSO_4$, and the solvent was evaporated to give the crude product that was purified by flash chromatography using 20% Et_2O/hexane to afford the desired product (90.4 mg, 90%) as a colorless liquid. IR (neat) ν = 2958, 2881, 1746, 1715, 1460, 1382, 1257, 1080 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.34 (br m, 1H), 4.77 (dd, 1H, *J* = 12.9, 8.4 Hz), 4.49 (m, 2H), 4.20 (q, 2H, *J* = 7.2 Hz), 2.86 (dq, 1H, *J* = 8.4, 6.9 Hz), 2.39 (m, 2H), 1.74 (s, 3H), 1.31 (t, 3H, *J* = 7.2 Hz), 1.14 (d, 3H, *J* = 6.9 Hz), 0.95 (m, 12H), 0.60 (q, 6H, *J* = 7.8 Hz); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 213.2, 155.0, 141.5, 121.3, 71.9, 63.8, 63.7, 50.7, 36.8, 18.5, 14.4, 14.2, 7.2, 6.7, 4.6; HRMS-EI calcd for $C_{17}H_{31}SiO_5$ $[M - Et]^+$ 343.1941, found 343.1930.

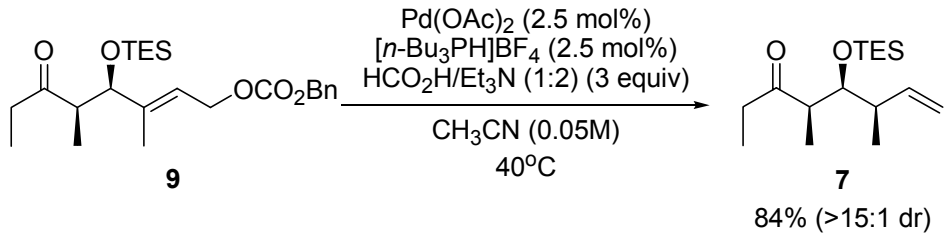
Diastereoselective palladium-catalyzed formate reduction



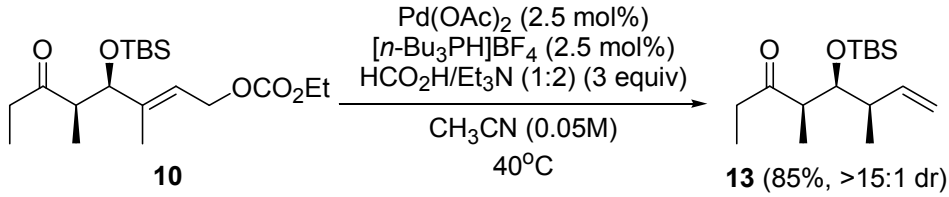
6b **7** (84%, >15:1 dr)

(4*R,5*S**,6*R**)-4,6-dimethyl-5-triethylsiloxy-7-octen-3-one (7) General protocol:** To a solution of $Pd(OAc)_2$/[*n*-$Bu_3PH]BF_4$ (1:1) (83 μL, 0.06M/CH_3CN) under nitrogen was added a solution of **6b** (75.2 mg, 0.202 mmol) and HCO_2H/Et_3N (1:2) (606 μL, 1M /CH_3CN) in CH_3CN (3.35 mL) via canula. The resulting mixture was heated to 40°C until the reaction turned dark (~ 1 h). Water was added and the aqueous layer was extracted with Et_2O (3×). The combined organic layers were washed with H_2O, brine, dried over $MgSO_4$, and the solvent was evaporated to yield the crude product (>15:1 dr by ^1H NMR spectroscopy) that is pure enough to be used without further purification. An analytical pure sample (48.3 mg, 84% yield, >15:1 dr by ^1H NMR spectroscopy) can be obtained by flash chromatography using 2% Et_2O/hexane. The spectral data were identical to those reported before.[4]

[4] Hughes, G.; Lautens, M.; Wen, C. *Org. Lett.* **2000**, *2*, 107.

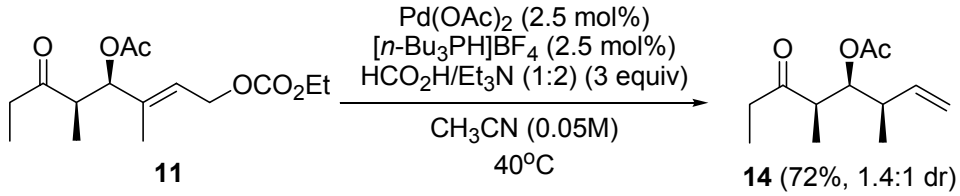


(4*R,5*S**,6*R**)-4,6-dimethyl-5-triethylsiloxy-7-octen-3-one (7)** Following the general procedure on a 0.201 mmol scale using **9**, the desired product (48.0 mg, 84%, >15:1 dr by ^{1}H NMR spectroscopy) was isolated as a colorless liquid after purification by flash chromatography using 2% Et_2O/hexane. The spectral data were identical to those reported before.[4]



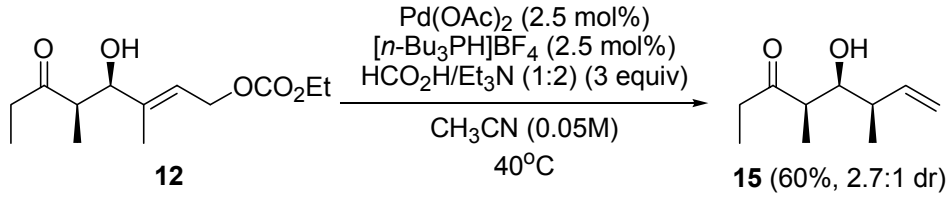
(4*R,5*S**,6*R**)-5-*tert*-butyldimethylsiloxy-4,6-dimethyl-7-octen-3-one (15)** Following the general procedure on a 0.200 mmol scale using **10**, the desired product (48.4 mg, 84%, >15:1 dr by ^{1}H NMR spectroscopy) was isolated as a colorless liquid after purification by flash chromatography using 2% Et_2O/hexane. The spectral data were identical with those previously reported.[5]

[5] White, J. D.; Hanselmann, R.; Jackson, R. W.; Porter, W. J.; Ohba, Y.; Tiller, T.; Wang, S. *J. Org. Chem.* **2001**, *66*, 5217.

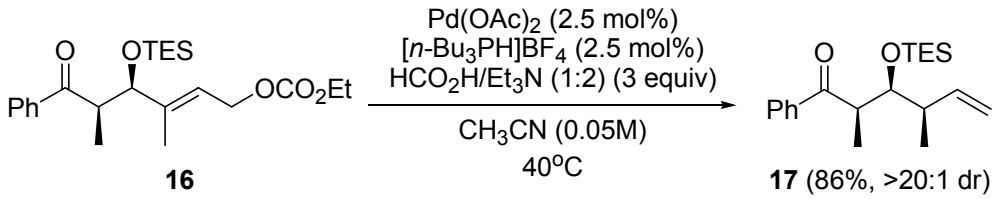


11 **14** (72%, 1.4:1 dr)

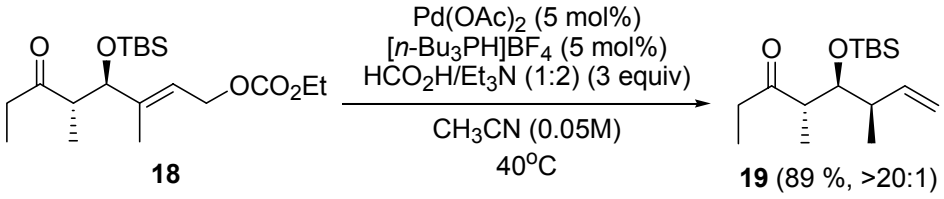
(4R*,5S*,6R*)-5-acetoxy-4,6-dimethyl-7-octen-3-one and (4R*,5S*,6S*)-5-acetoxy-4,6-dimethyl-7-octen-3-one (14) Following the general procedure on a 0.201 mmol scale using **11**, the inseparable mixture of diastereomers (30.7 mg, 72%, 1.4:1 dr by ^{13}C NMR spectroscopy) was isolated as a colorless liquid after purification by flash chromatography using 10% Et_2O/hexane. IR (neat) ν = 3077, 2978, 2937, 2887, 1743, 1712, 1462, 1373, 1235, 1022 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.69 (m, 1H), 5.23-4.97 (m, 3H), 2.82 (m, 1H), 2.61 (m, 1H), 2.54-2.35 (m, 2H), 2.03 (s, 3H), 1.03 (m, 9H); ^{13}C NMR (s = syn; a = anti) δ 212.2^a, 211.9^s, 173.6^a, 170.5^s, 139.5^s, 139.3^a, 116.1^s, 116.0^a, 76.1^a, 75.6^s, 47.7^a, 47.6^s, 40.7^{s,a}, 34.9^a, 34.5^s, 20.7^{s,a}, 17.3^a, 16.4^s, 12.0^a, 9.9^s, 7.7^s, 7.6^a; MS-ES (*m/z*) 235 $[M + Na]^+$, 251 $[M + K]^+$, 213 $[M + H]^+$; HRMS-EI calcd for $C_8H_{13}O_3$ $[M - C_4H_7]^+$ 157.0865, found 157.0857. The spectral data were identical to an authentic sample (*syn* isomer only) prepared from the acetylation (AcCl, py, CH_2Cl_2, 0°C to rt) of alcohol **15** obtained from deprotection of **7** (PTSA, THF/H_2O).



(4*R,5*S**,6*R**)-4,6-dimethyl-5-hydroxy-7-octen-3-one and (4*R**,5*S**,6*S**)-4,6-dimethyl-5-hydroxy-7-octen-3-one (15)** Following the general procedure on a 0.202 mmol scale using **12**, the desired product (20.4 mg, 60%, 2.7:1 dr by ^{1}H NMR spectroscopy) was isolated as a colorless liquid after purification by flash chromatography using 40% Et_2O/hexane. Careful flash chromatography using 40% Et_2O/hexane allows for isolation of a clean sample of *syn*-**15** (10.1 mg, 30%). IR (neat) ν = 3488, 3078, 2977, 2935, 1707, 1460, 977 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.60 (m, 1H), 5.06 (m, 2H), 3.68 (dt, 1H, *J* = 9.0, 2.7 Hz), 2.94 (d, 1H, *J* = 2.7 Hz), 2.73 (dq, 1H, *J* = 7.2, 2.7 Hz), 2.51 (m, 2H), 2.26 (m, 1H), 1.13 (d, 3H, *J* = 3.0 Hz), 1.11 (d, 3H, *J* = 2.7 Hz), 1.05 (t, 3H, *J* = 7.5 Hz); ^{13}C NMR (74.5 MHz, $CDCl_3$) δ 217.1, 140.5, 115.2, 73.9, 47.3, 41.5, 34.7, 17.0, 9.3, 7.6; HRMS-EI calcd for $C_{10}H_{19}O_2$ $[M + H]^+$ 171.1385, found 171.1392. The spectral data were identical to an authentic sample prepared from the deprotection of **7** (PTSA, H_2O/THF).

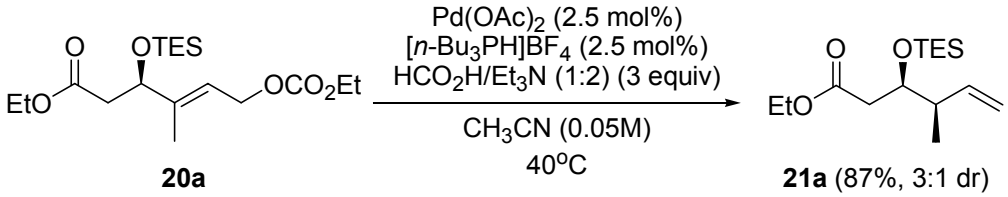


(2*R,3*S**,4*R**)-2,4-dimethyl-1-phenyl-3-triethylsiloxy-5-hexen-1-one (17)** Following the general procedure on a 0.200 mmol scale using **16**, the crude product (>15:1 dr by ^{1}H NMR spectroscopy) was purified by flash chromatography using 10% Et_2O/hexane to give **17** (56.9 mg, 86%, >20:1 dr by ^{1}H NMR spectroscopy) as a slightly yellow liquid. IR (neat) ν = 3065, 2957, 2877, 1681, 1459, 1117, 1003, 969 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (m, 2H), 7.55 (tt, 1H, *J* = 7.6, 1.2 Hz), 7.46 (m, 2H), 5.88 (m, 1H), 5.06 (d, 1H, *J* = 1.6 Hz), 5.02 (dt, 1H, *J* = 6.8, 1.6 Hz), 4.09 (t, 1H, *J* = 5.6 Hz), 3.65 (m, 1H), 2.33 (m, 1H), 1.20 (d, 3H, *J* = 6.8 Hz), 0.93 (m, 12H), 0.57 (q, 6H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.1, 141.4, 136.6, 132.8, 128.6, 128.4, 114.9, 77.1, 44.5, 43.2, 15.3, 13.3, 7.0, 5.4; HRMS-EI calcd for $C_{19}H_{29}SiO_2$ $[M - CH_3]^+$ 317.1937, found 317.1930. The stereochemistry was established based on a comparison of spectral data and the selectivity observed with similar compounds.



(4*S,5*S**,6*R**)-5-*tert*-butyldimethylsilyl-4,6-dimethyl-7-octen-3-one (19)** Following the general procedure on a 0.188 mmol scale using **18** and 5 mol% the catalyst system,

the crude product (>15:1 dr by ^{1}H NMR spectroscopy) was purified by flash chromatography using 10% Et_2O/pentane to give the desired product (47.8 mg, 89%, >20:1 dr by ^{1}H NMR spectroscopy) as a colorless liquid. IR (neat) ν = 2953, 2935, 2853, 1720, 1462, 1255, 1037, 838 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 (m, 1H), 5.02 (m, 2H), 3.93 (dd, 1H, *J* = 7.2, 3.6 Hz), 2.74 (m, 1H), 2.49 (m, 2H), 2.34 (m, 1H), 1.01 (m, 9H), 0.86 (s, 9H), 0.05 (s, 3H), -0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.7, 141.5, 114.5, 77.5, 50.3, 41.2, 36.7, 26.0, 18.2, 13.8, 13.4, 7.3, -4.2, -4.4; HRMS-EI calcd for $C_{16}H_{32}SiO_2$ $[M]^+$ 285.2244, found 285.2255. Compound **19** was submitted to ozonolysis ((i) O_3, CH_2Cl_2, -78°C (ii) Ph_3P, -78°C to rt). The spectral data were different from the previously reported *anti-anti* triad.[6] Some epimerized (10-15%) material was also present and matches the spectral data reported further supporting the assignment as *anti-syn*.

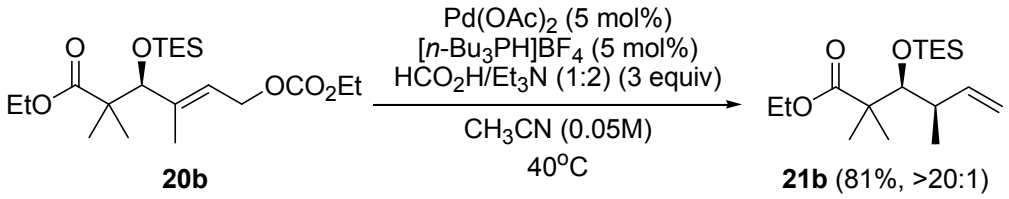


20a **21a** (87%, 3:1 dr)

Ethyl (3*R,4*R**)-4-methyl-3-triethylsiloxy-5-hexenoate and ethyl (3*R**,4*S**)-4-methyl-3-triethylsiloxy-5-hexenoate (21)** Following the general procedure on a 0.201 mmol scale using **20**, the inseparable mixture of diastereomers (50.1 mg, 87%, 3:1 dr ^{13}C NMR spectroscopy) was isolated as a colorless liquid after purification by flash chromatography using 3% Et_2O/hexane. IR (neat) ν = 3077, 2858, 2880, 1739, 1462,

[6] Hoffmann, R. W.; Dahmann, G.; Andersen, M. W. *Synthesis* **1994**, 629.

1377, 1180, 1085, 1012 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.81 (m, 1H), 5.04 (m, 2H), 4.13 (m, 3H), 2.38 (m, 3H), 1.26 (t, 3H, *J* = 7.2 Hz), 0.98 (m, 12H), 0.60 (q, 6H, *J* = 7.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 140.2, 139.8, 115.3, 114.9, 72.9, 72.4, 60.3, 43.8, 43.7, 40.0, 39.4, 14.9, 14.1, 6.8, 5.0, 4.9; HRMS calcd for $C_{13}H_{25}SiO_3$ $[M - Et]^+$ 257.1573, found 257.1572. Compound **21a** was reduced ((i) DIBAL, CH_2Cl_2, -78°C (ii) 10% HCl) to give the diol. The spectral data of the minor isomer (*anti*) were identical to the previously reported compound.[7]

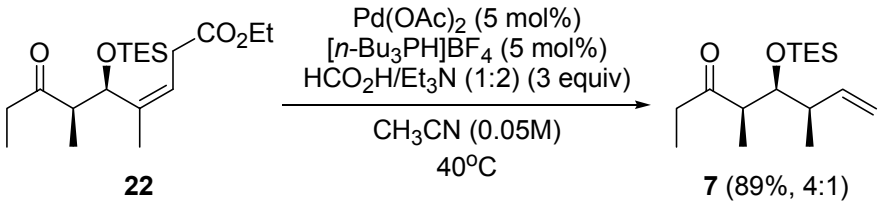


20b **21b** (81%, >20:1)

Ethyl (3*S,4*R**)-2,2,4-trimethyl-3-triethylsilyloxy-5-hexenoate (21b)** Following the general procedure on a 0.200 mmol scale using **20b** and 5 mol% of the catalyst system, the desired product (50.7 mg, 81%, >20:1 dr by ^1H NMR spectroscopy) was isolated as a colorless liquid after purification by flash chromatography using 10% Et_2O/pentane. IR (neat) ν = 2958, 2878, 1735, 1463, 1264, 1113, 1085, 1006 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.73 (ddd, 1H, *J* = 17.2, 10.4, 8.0 Hz), 4.95 (dt, 1H, *J* = 17.2, 1.6 Hz), 4.90 (ddd, 1H, *J* = 10.4, 1.6, 0.8 Hz), 4.07 (q, 2H, *J* = 7.2 Hz), 3.95 (d, 1H, *J* = 4.4 Hz), 2.28 (m, 1H), 1.24 (t, 3H, *J* = 7.2 Hz), 1.17 (s, 3H), 1.12 (s, 3H), 0.98 (m, 12H), 0.63 (q, 6H, *J* = 7.6 Hz); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 177.2, 143.0, 113.4, 79.7, 60.2, 48.4, 41.4, 24.7, 29.0, 16.2, 14.0, 7.1, 5.5; HRMS-ES calcd for $C_{17}H_{34}SiO_3Na$ $[M + Na]^+$ 337.2169,

[7] Drouet, K.E.; Theodorakis, E.A. *Chem. Eur. J.* **2000**, *6*, 1987.

found 337.2174. The spectral data were identical to an authentic sample prepared from ethyl 2,2-dimethyl-3-oxopropanoate[8] by crotylation ((*Z*)-crotyltrifluroborate, Bu_4NI (10 mol%), CH_2Cl_2/H_2O (1:1))[9] followed by protection (TESOTf, 2,6-lutidine, CH_2Cl_2, 0°C to rt).

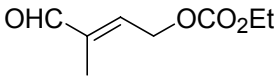


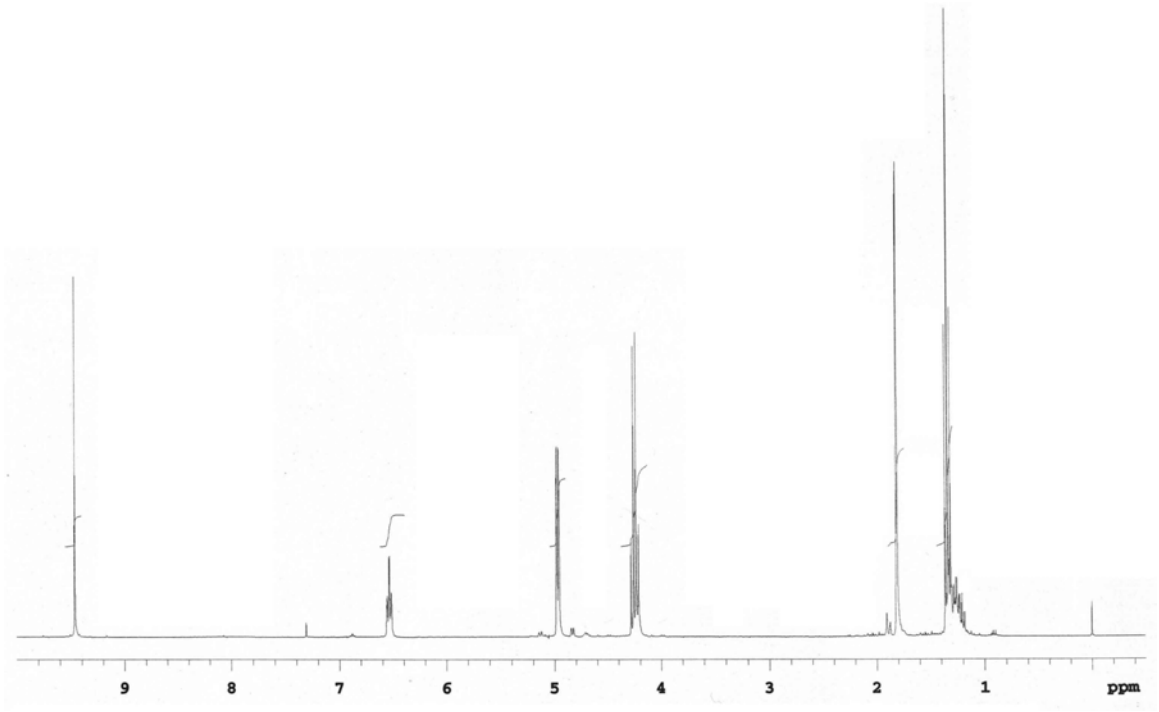
22 **7** (89%, 4:1)

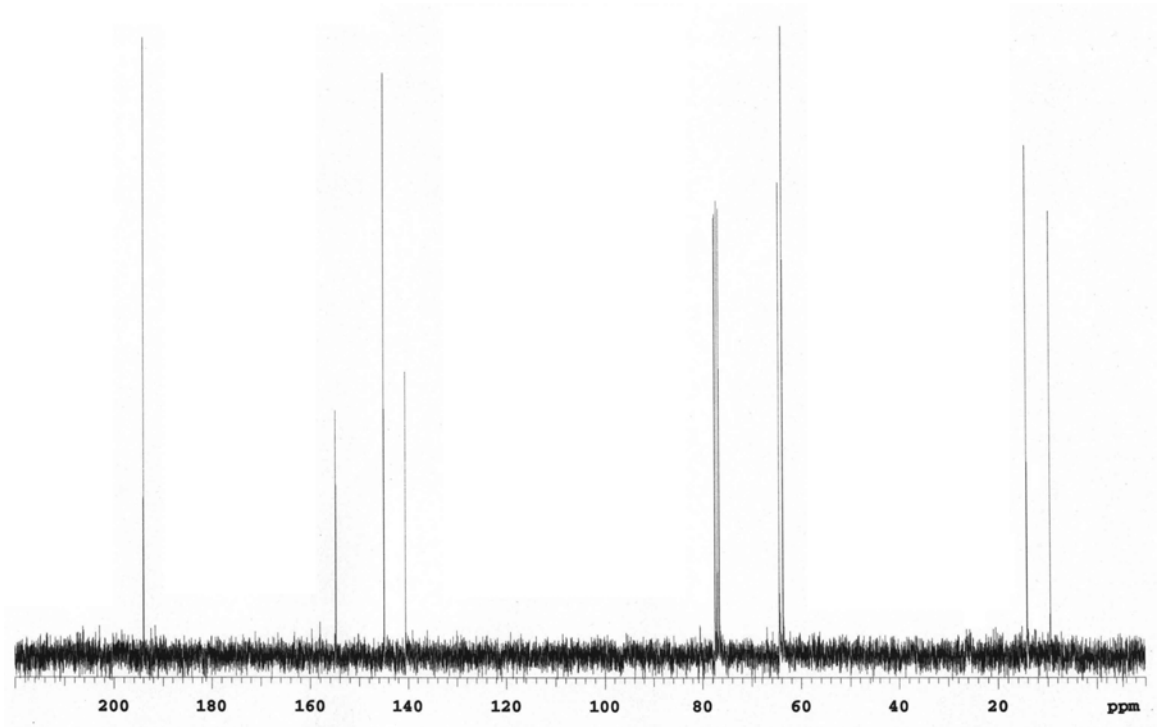
(4*R,5*S**,6*R**)-4,6-dimethyl-5-triethylsiloxy-7-octen-3-one (7)** Following the general procedure on a 0.200 mmol scale using **22** and 5 mol% of the catalyst system, the desired product (50.4 mg, 89%, 4:1 dr by ^{1}H NMR spectroscopy) was isolated as a colorless liquid after purification by flash chromatography using 10% Et_2O/pentane. The spectral data are identical to those previously reported.[4]

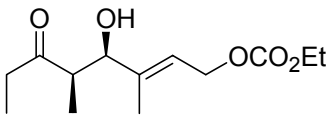
[8] Chaganti P, R.; Tanimoto, S. *Synthesis* **1987**, 575.
[9] Thadani, A. N.; Batey, R. A. *Org. Lett.* **2002**, *4*, 3827.

^{1}H and ^{13}C NMR spectra





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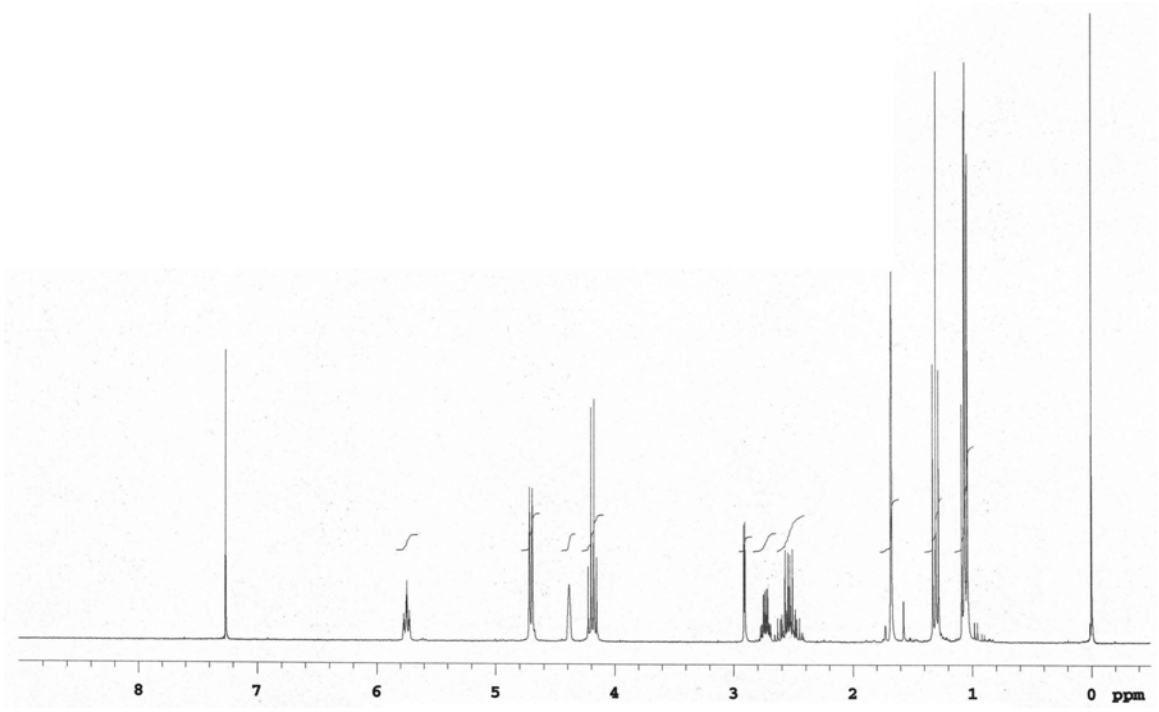
12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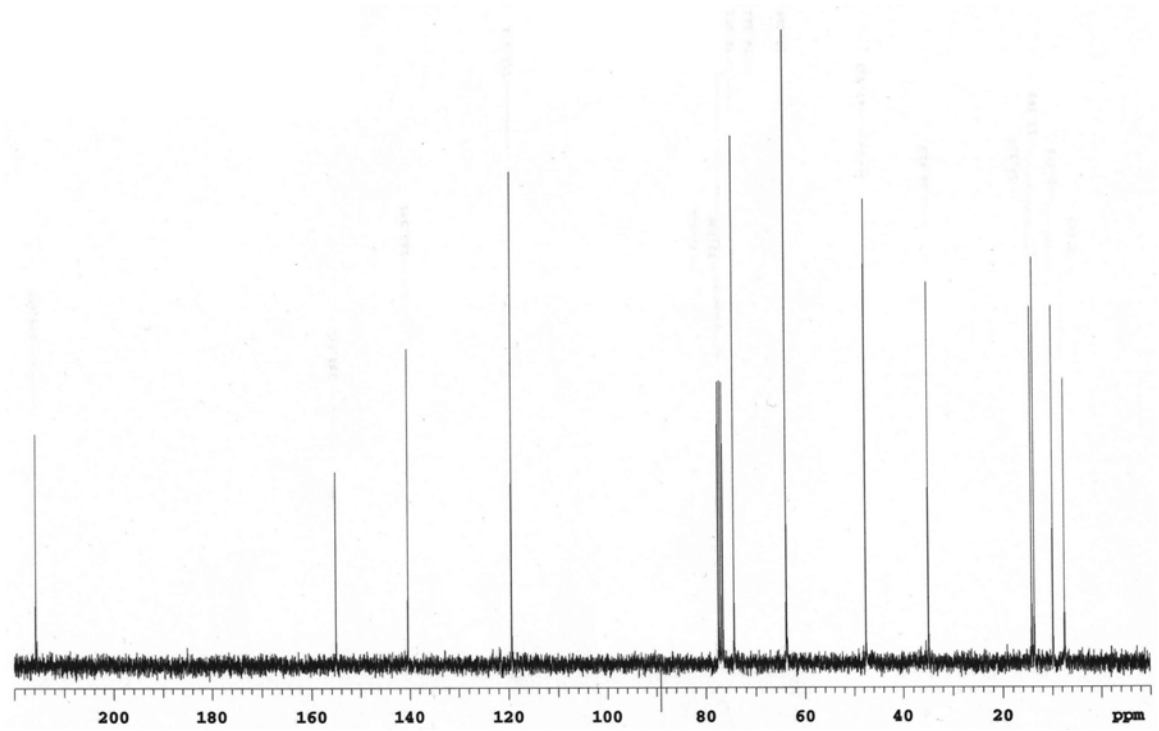
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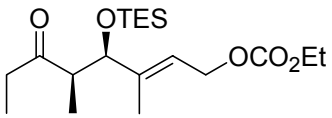
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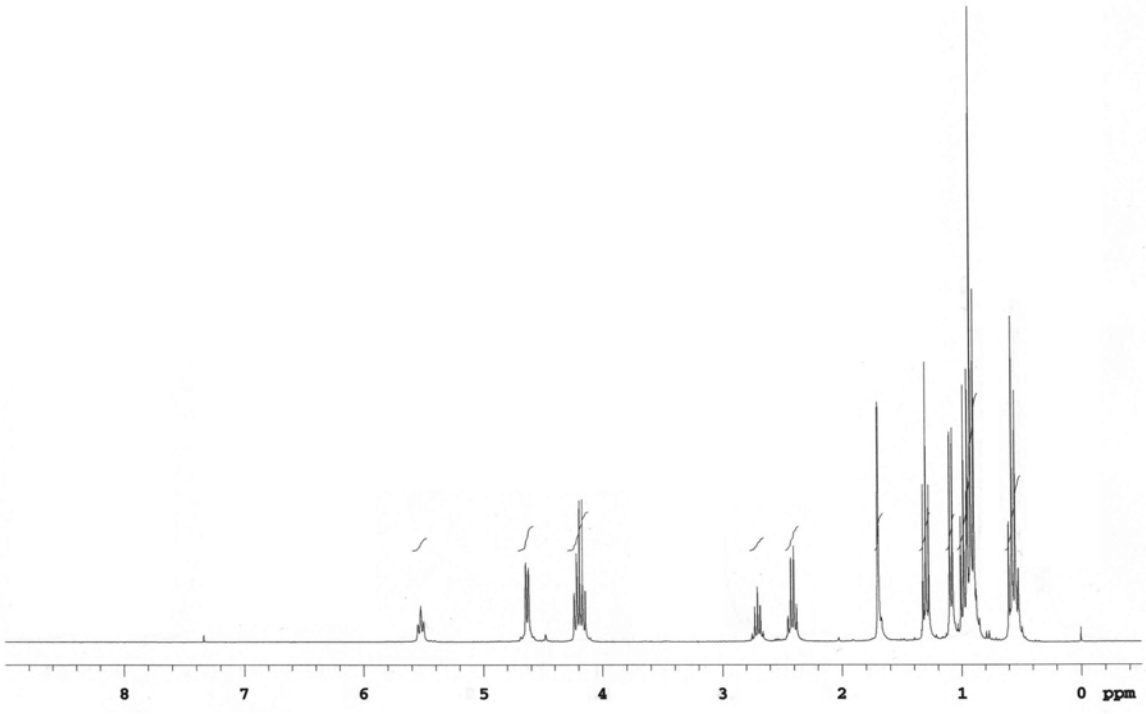
6b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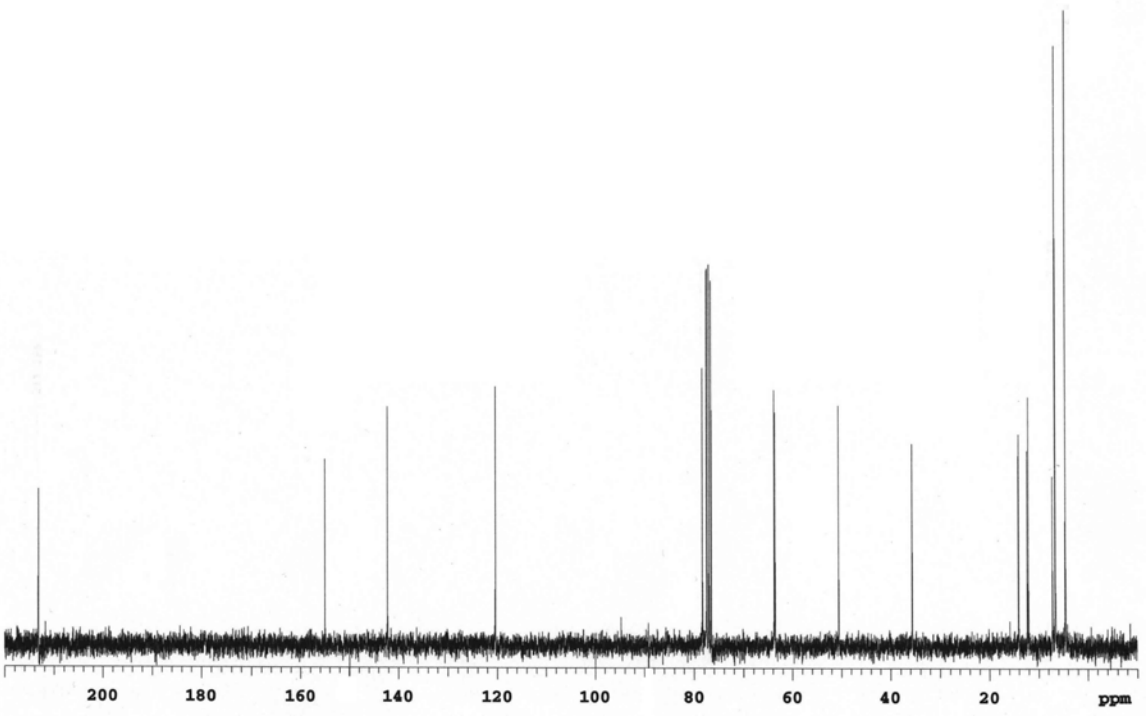
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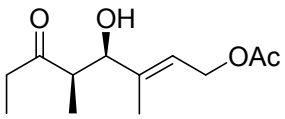
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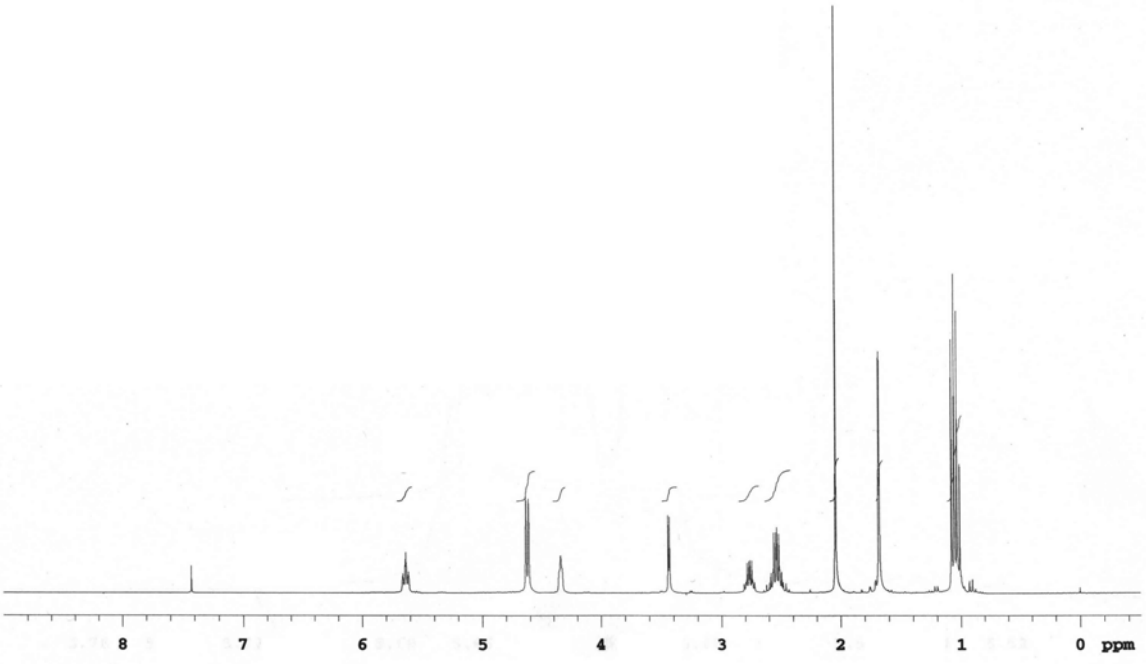
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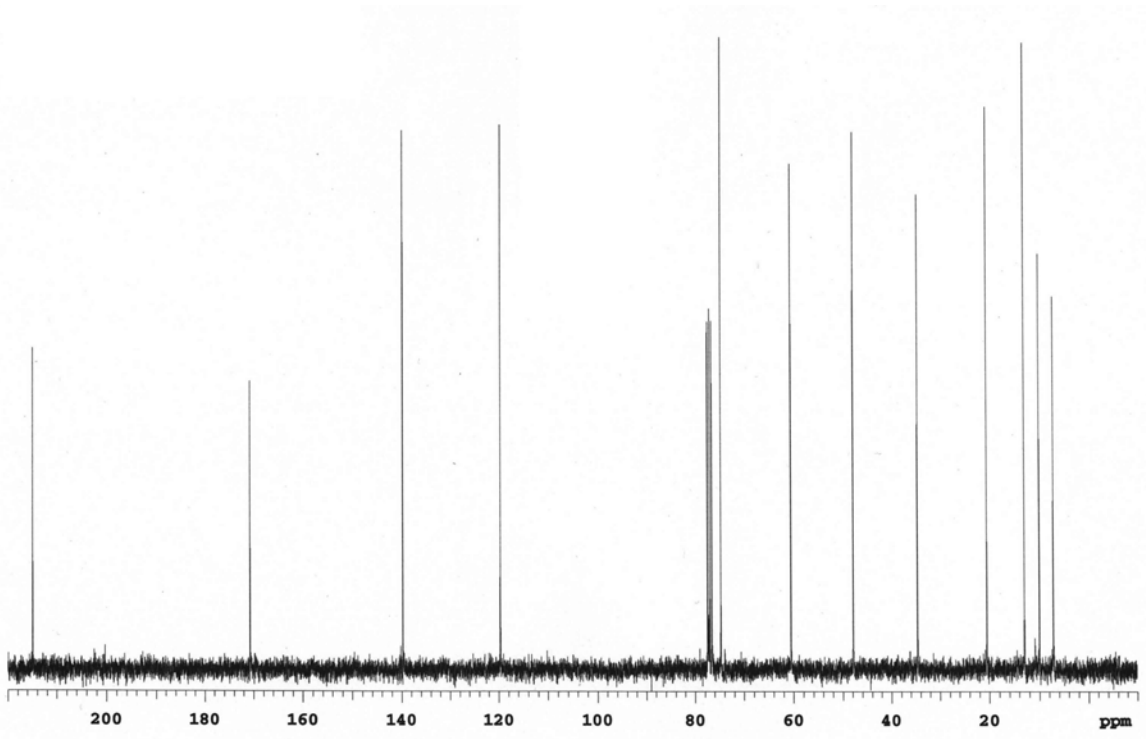
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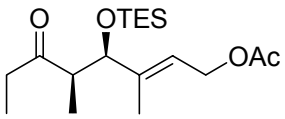
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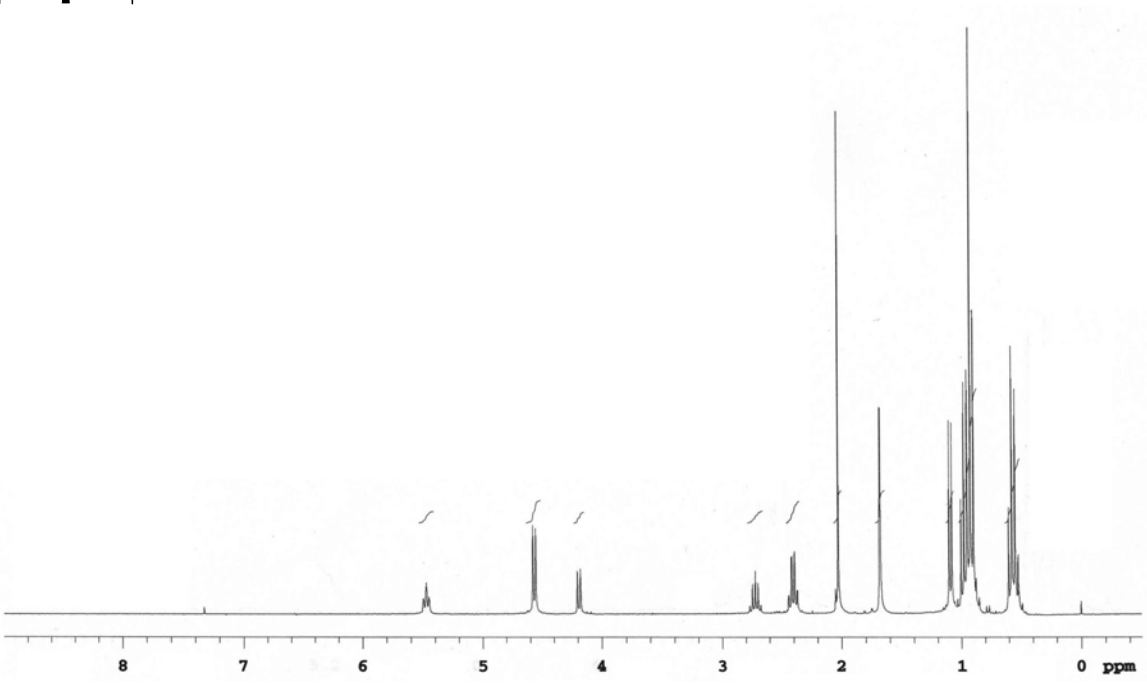
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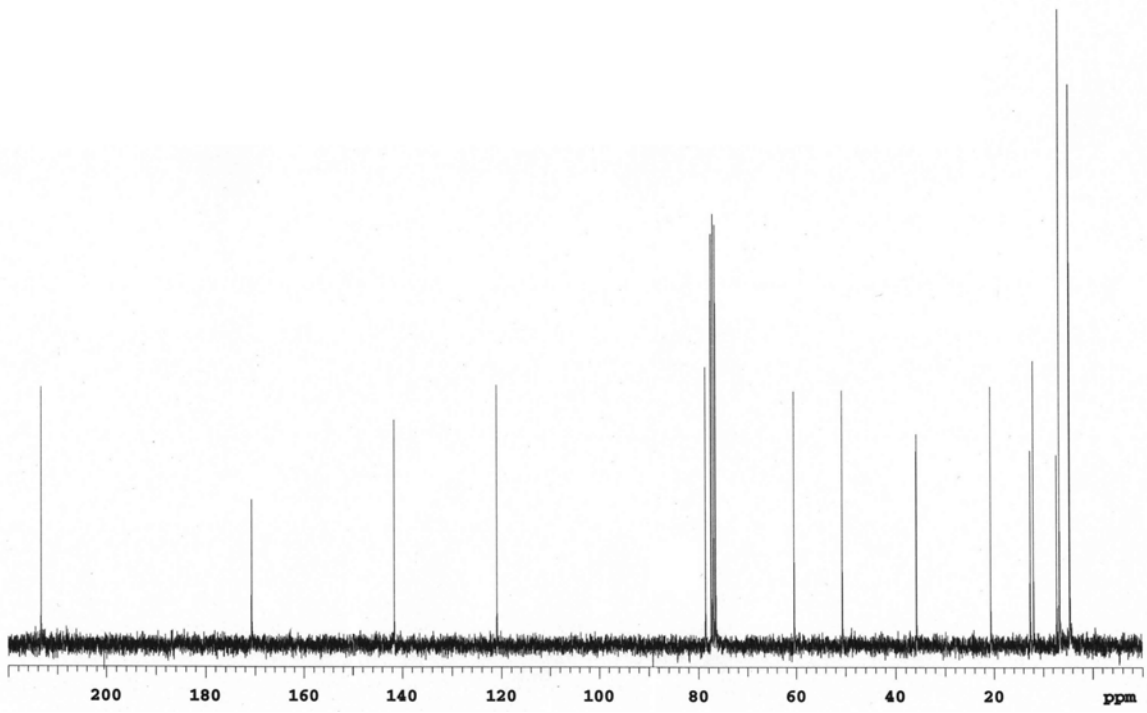
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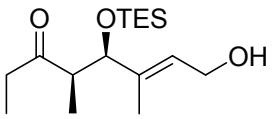
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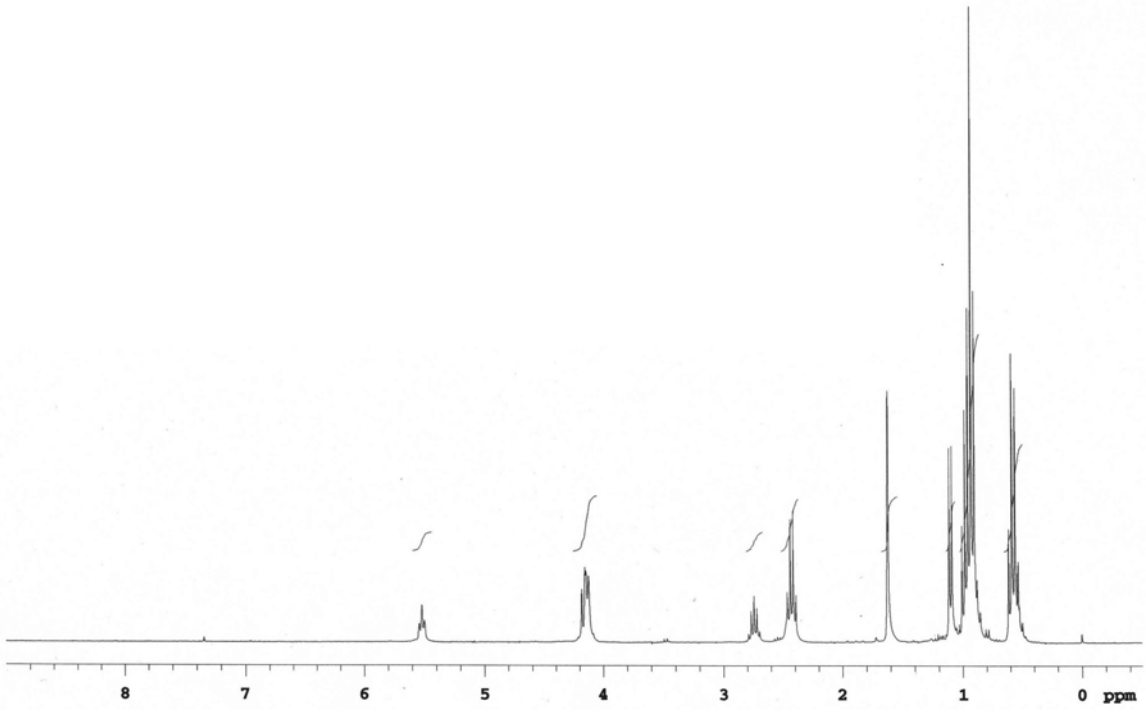
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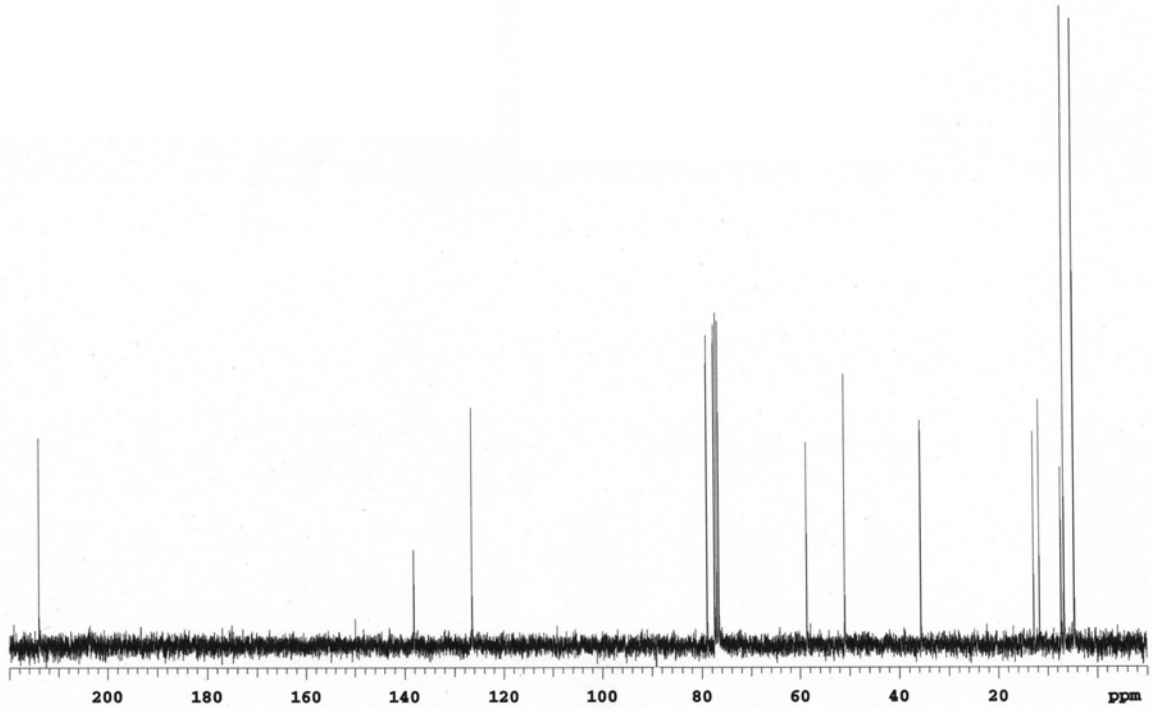
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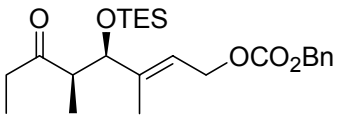
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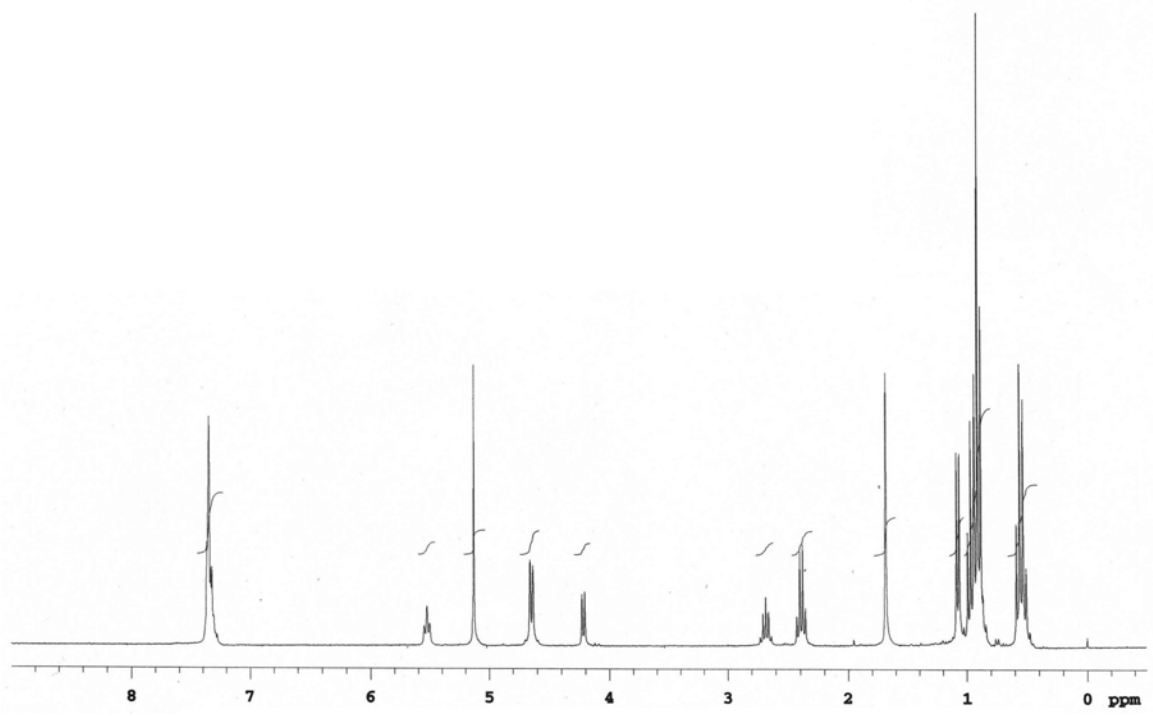
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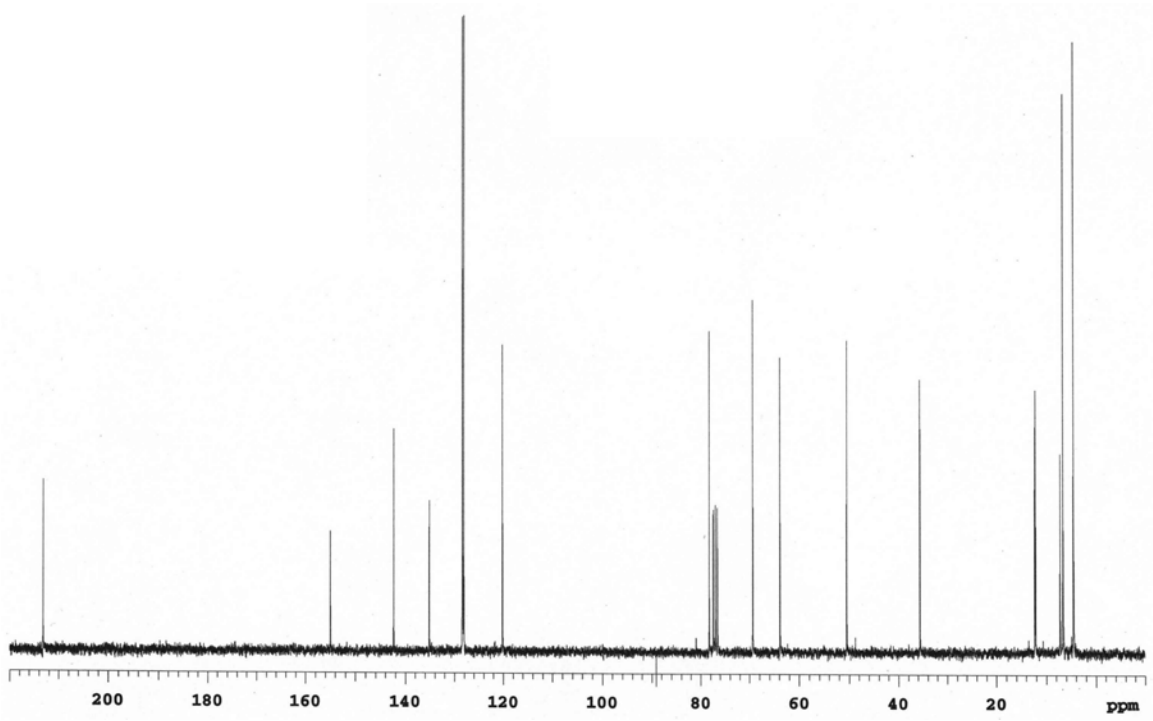
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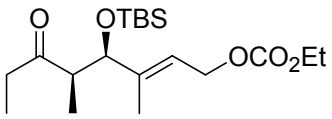
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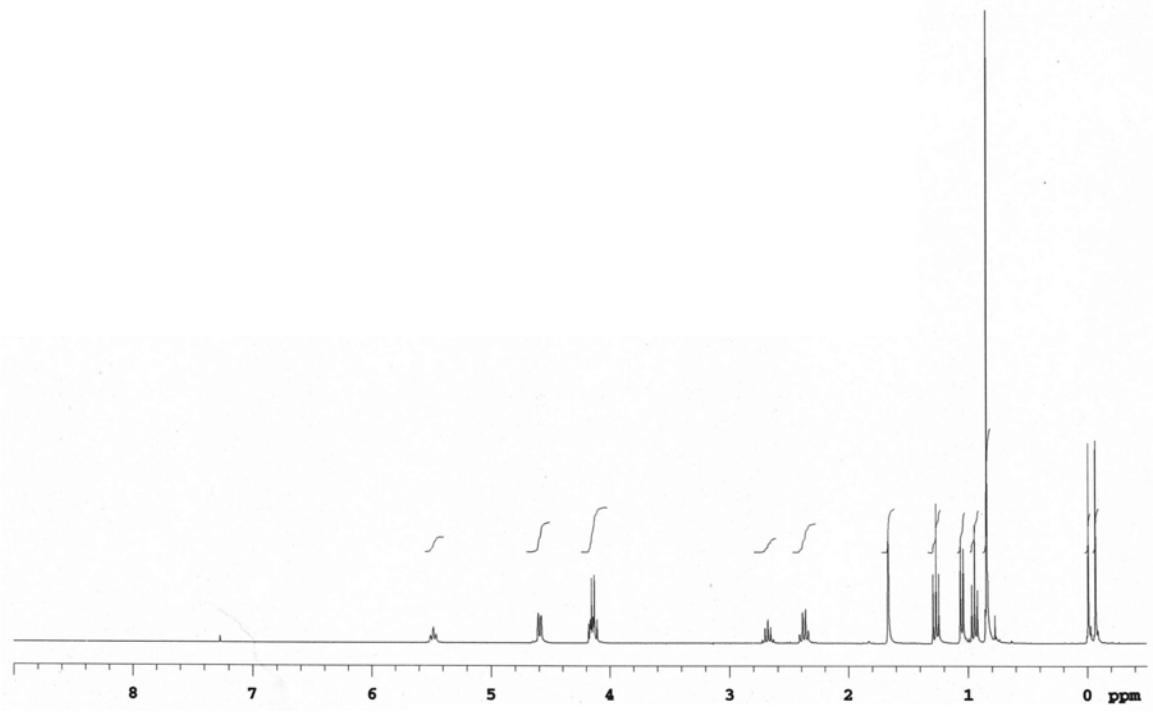
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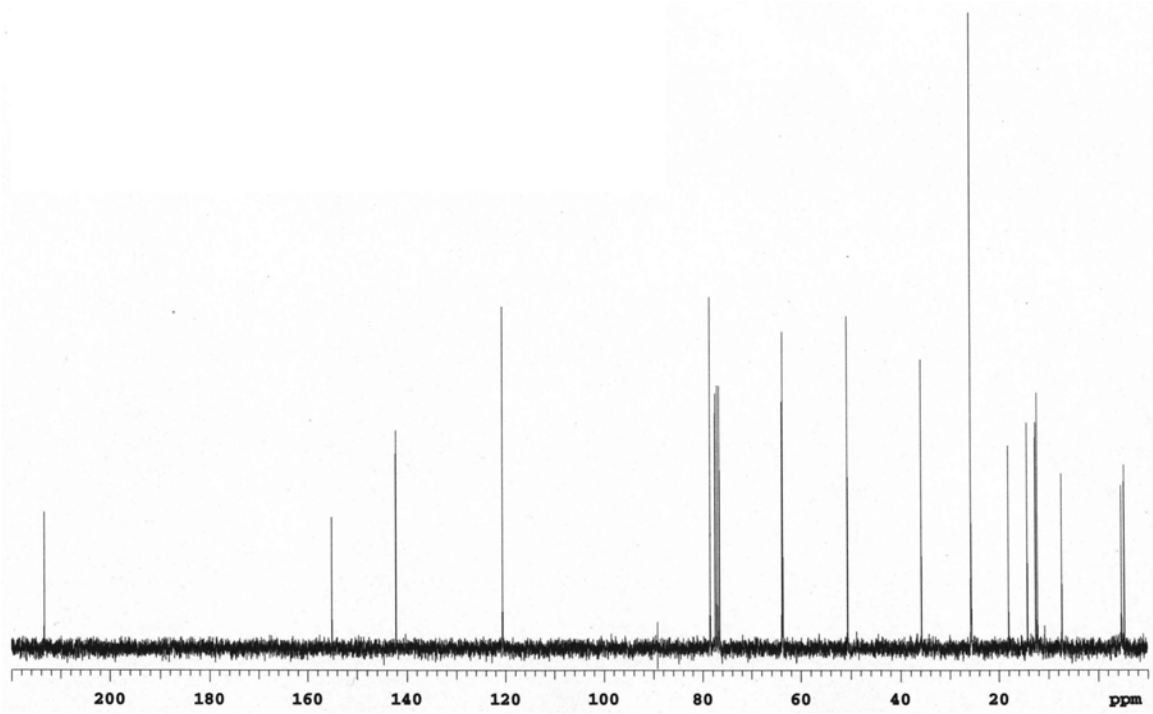
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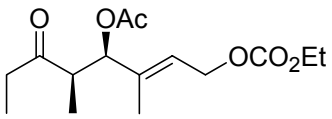
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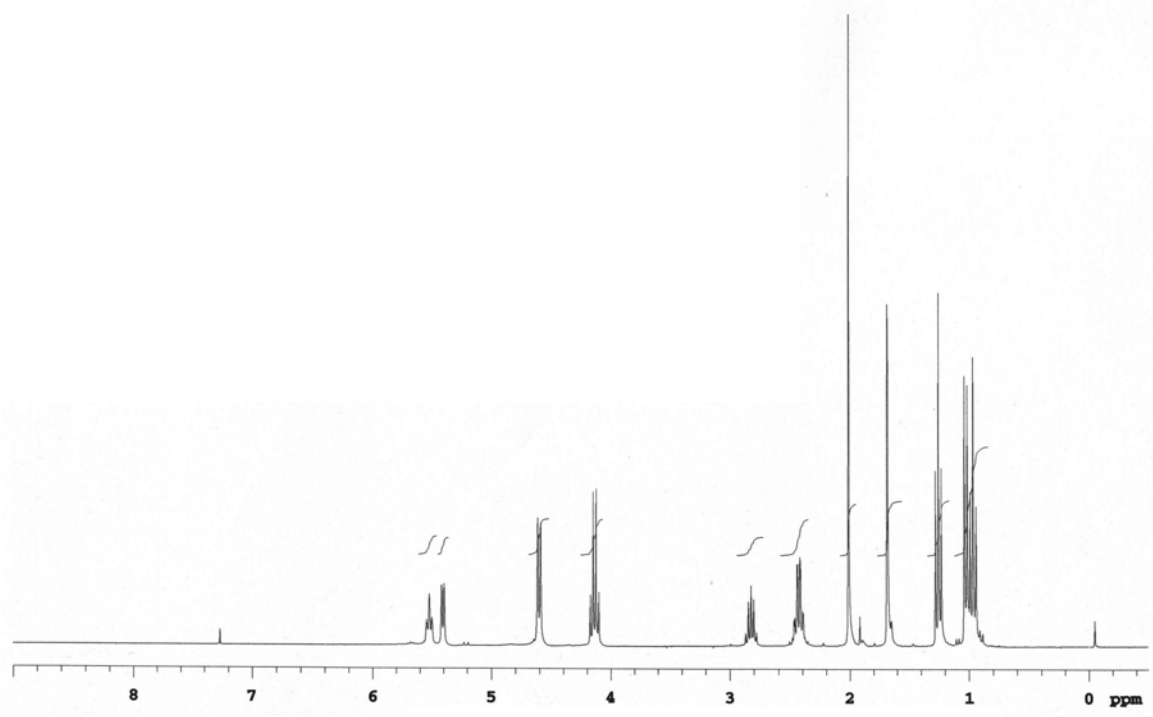
11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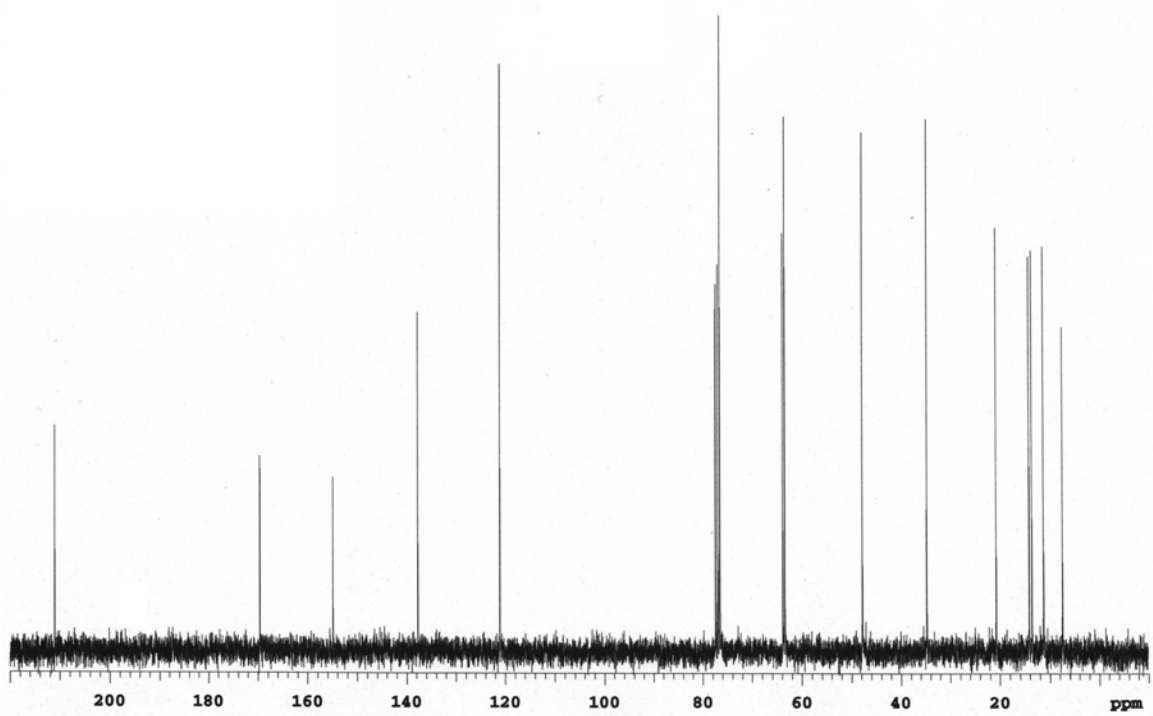
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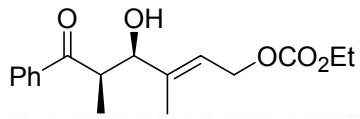
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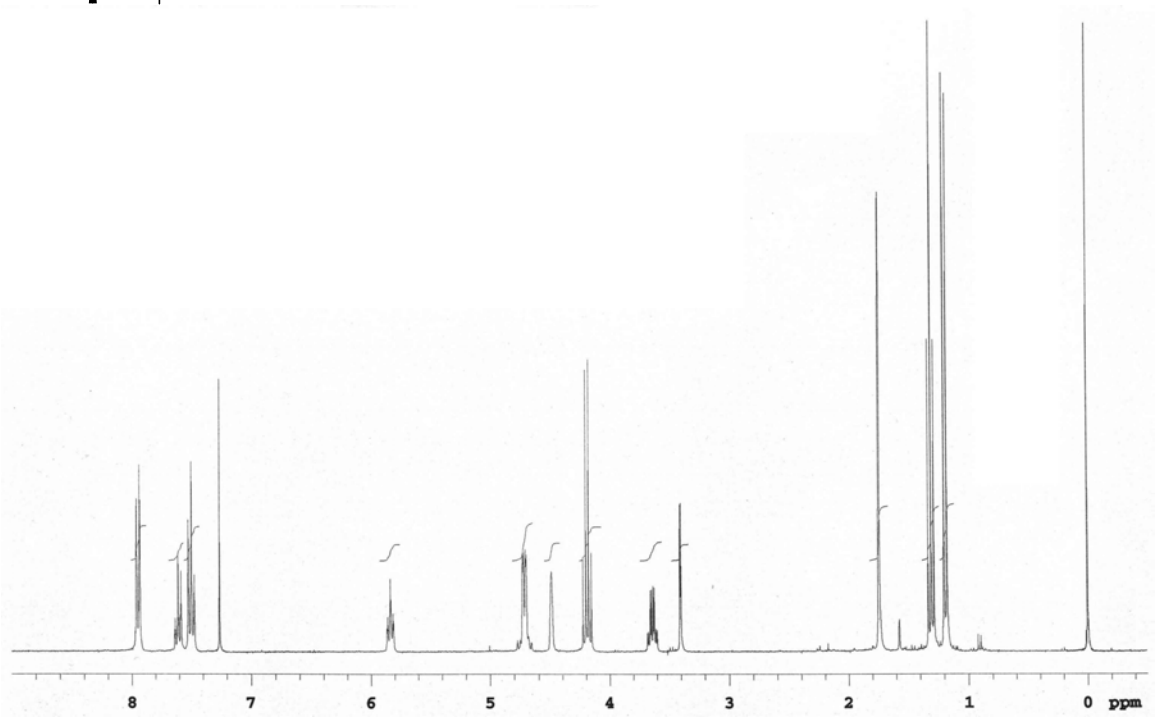
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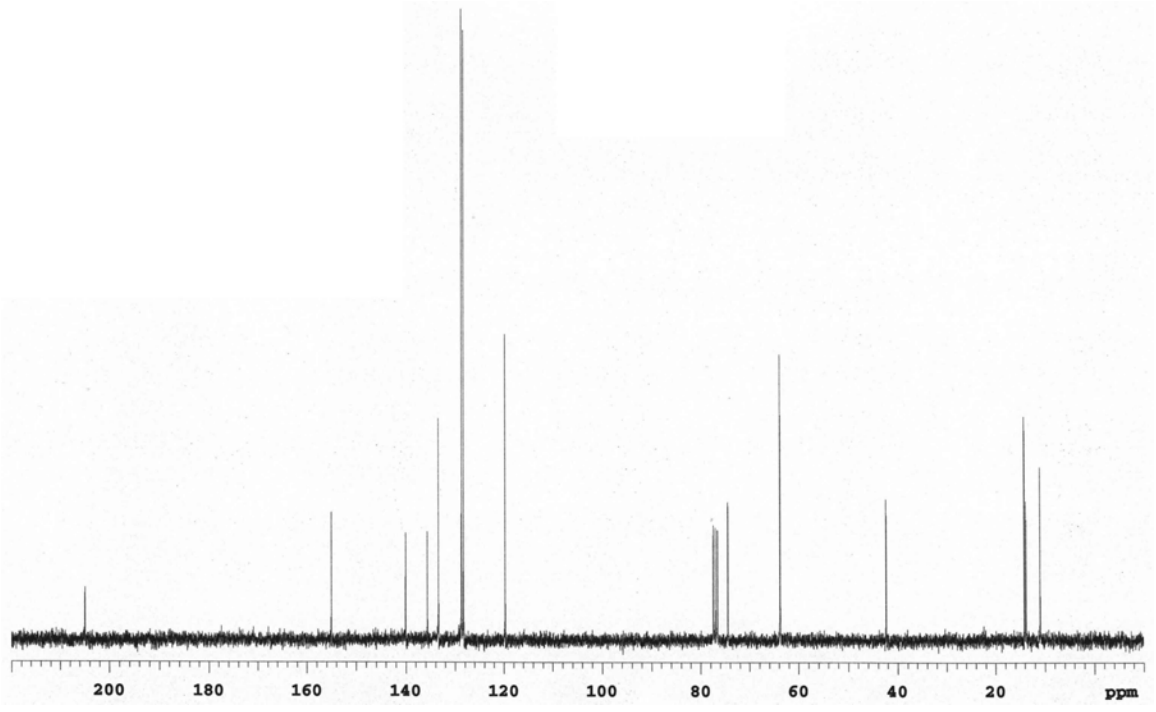
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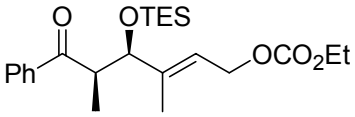
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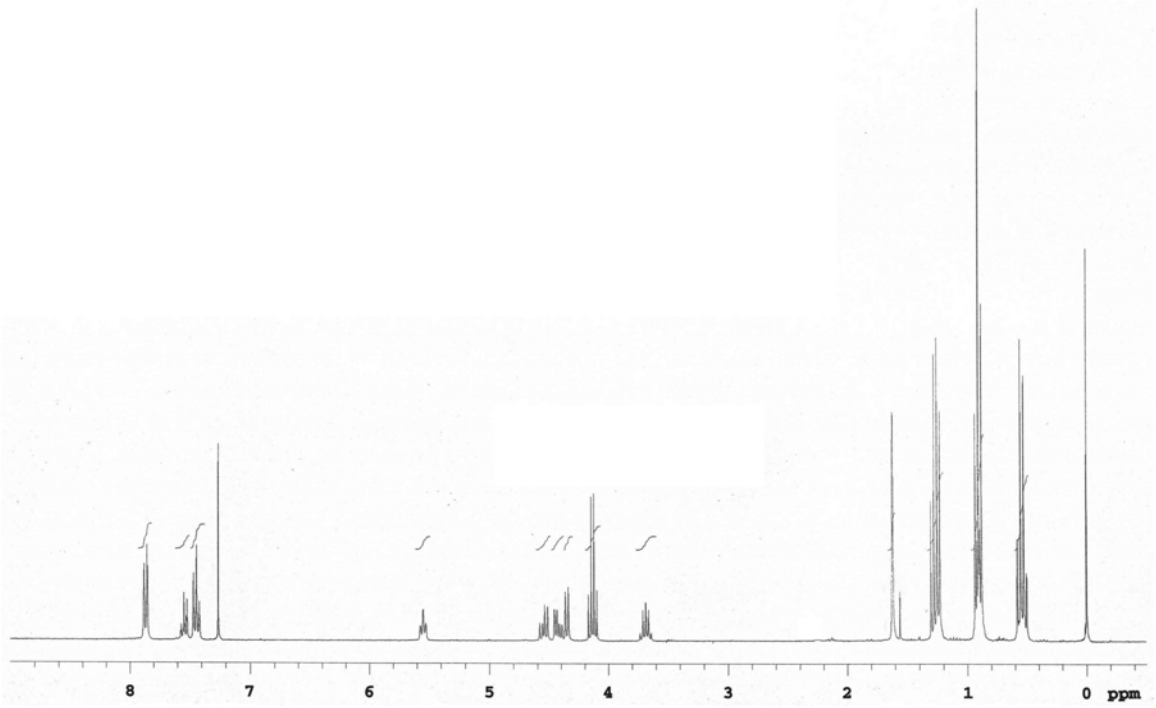
OTES
Ph
OCO2Et

16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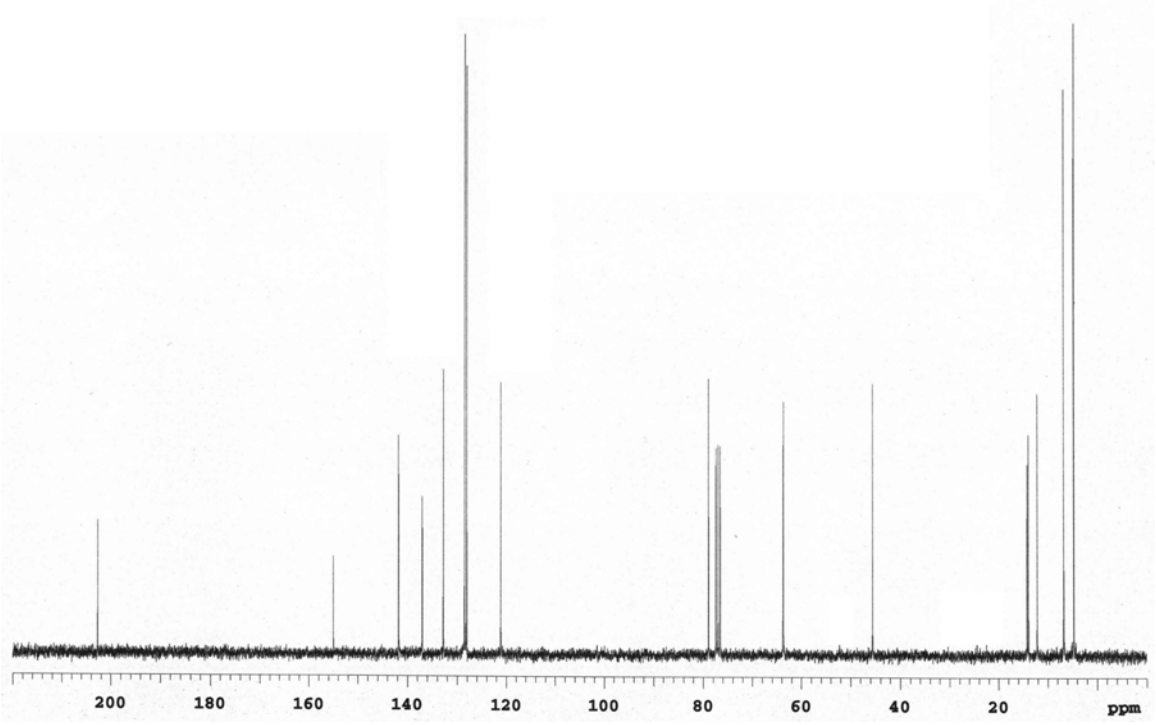
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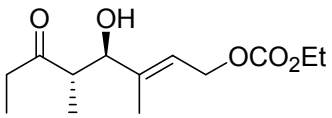
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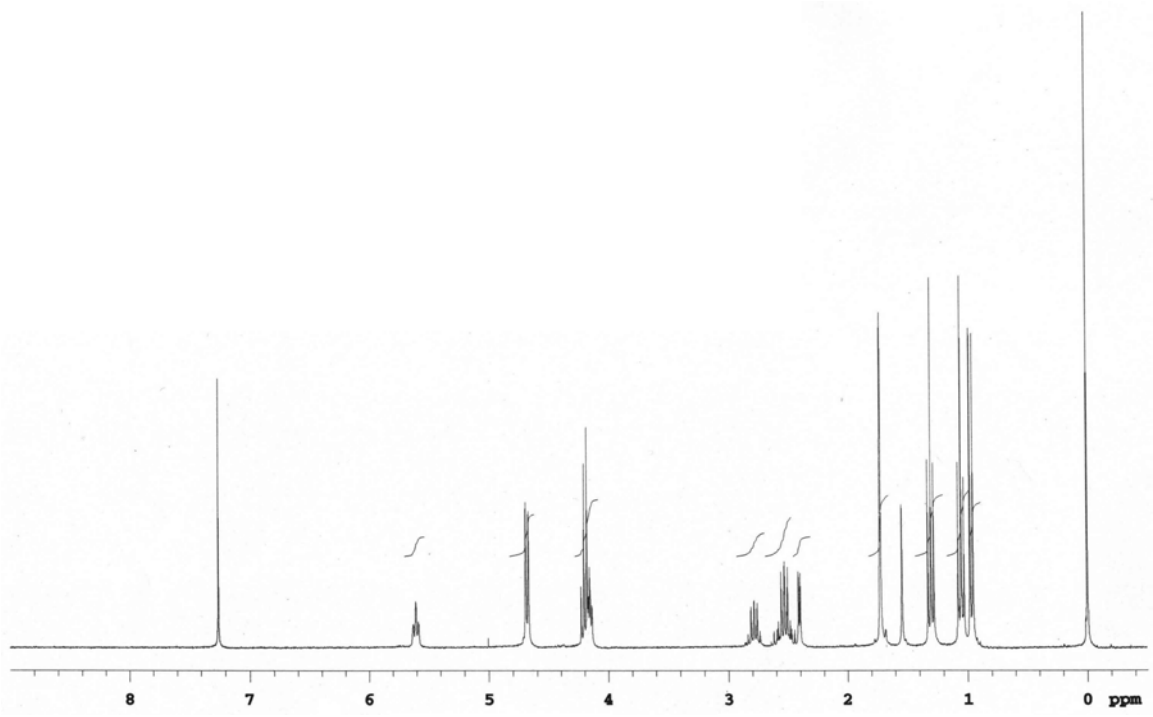
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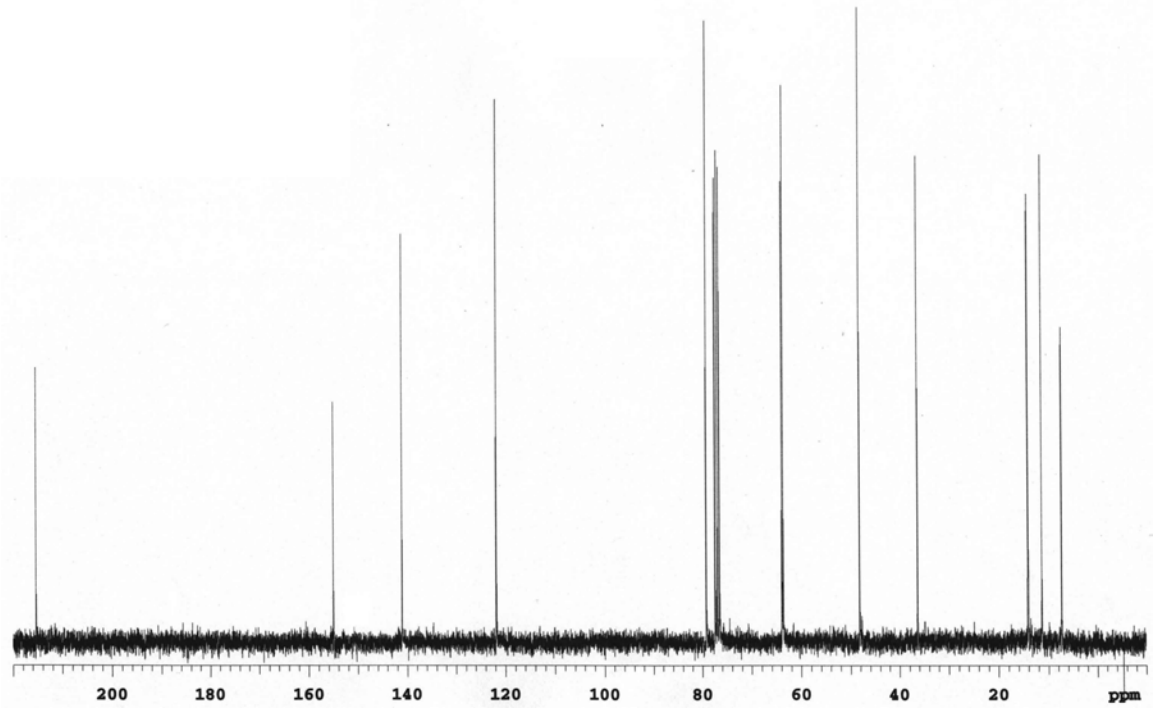
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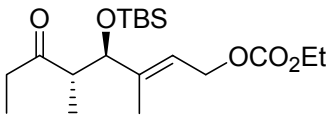
O
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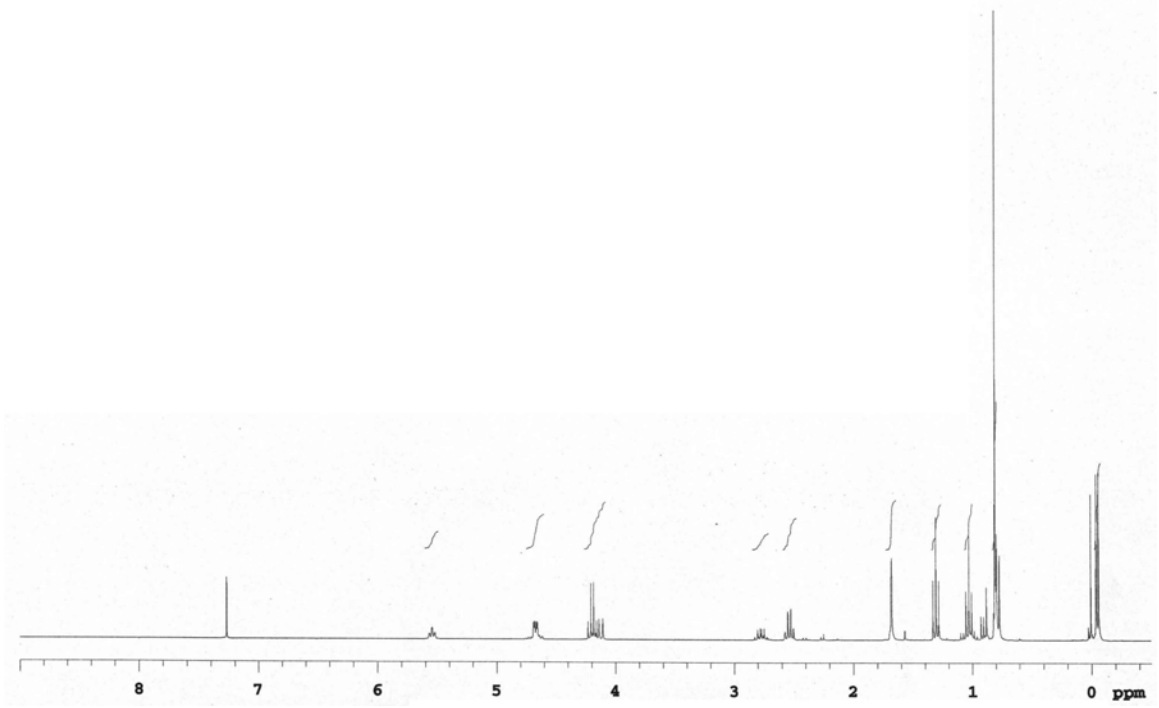
OCO2Et

18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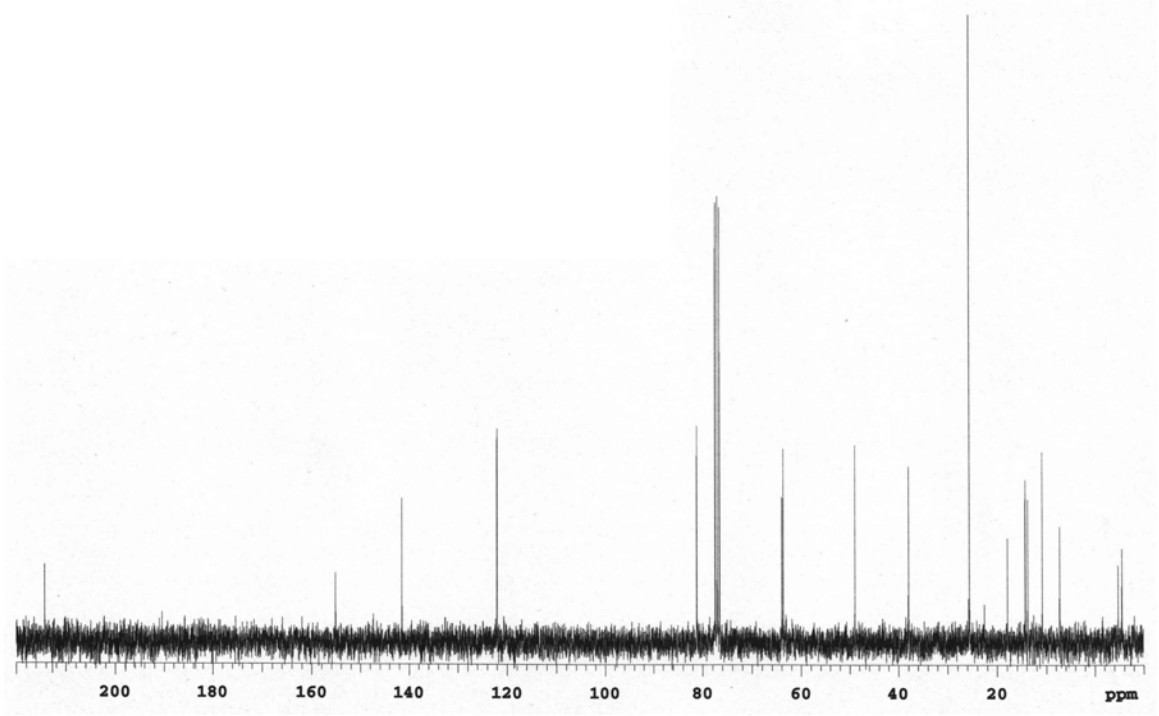
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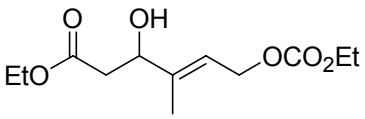
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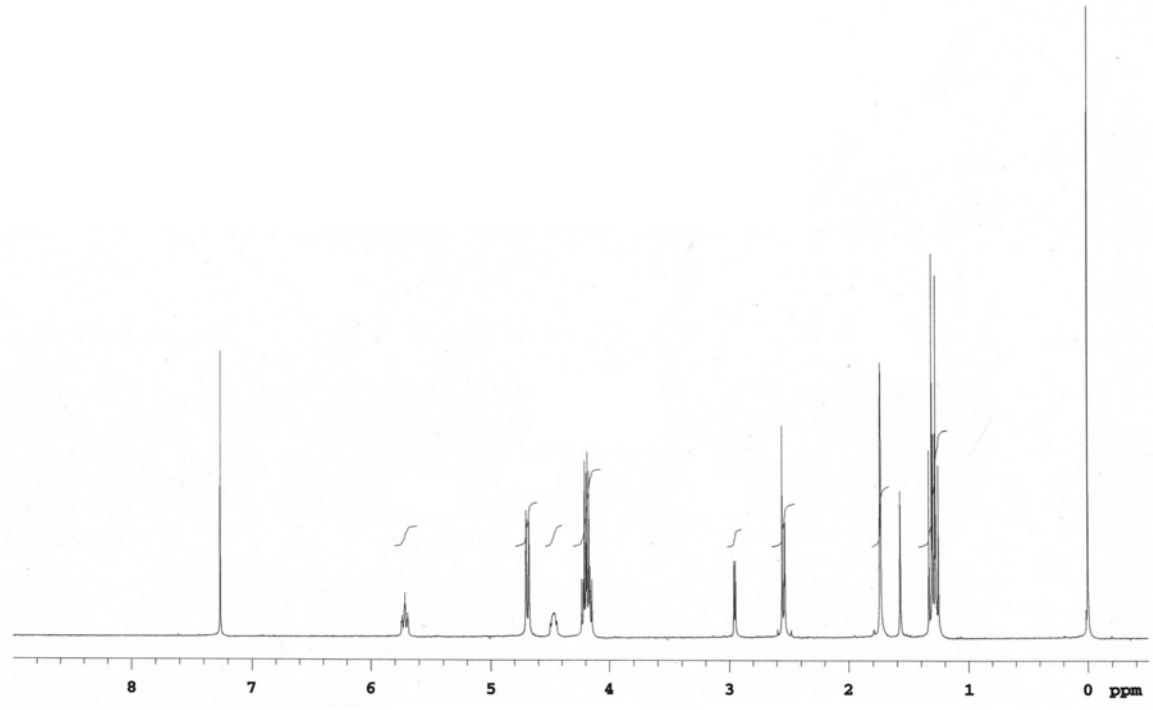
EtO
OCO2Et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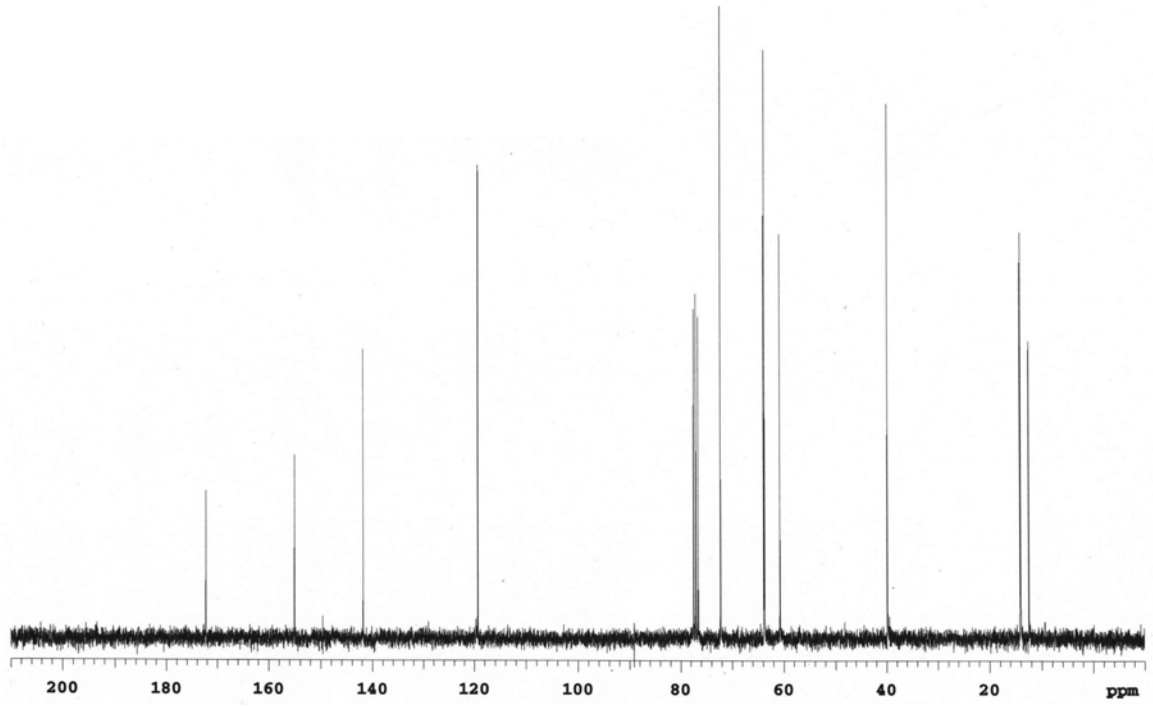
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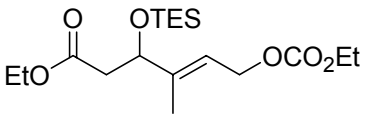
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OTES
EtO
OCO2Et

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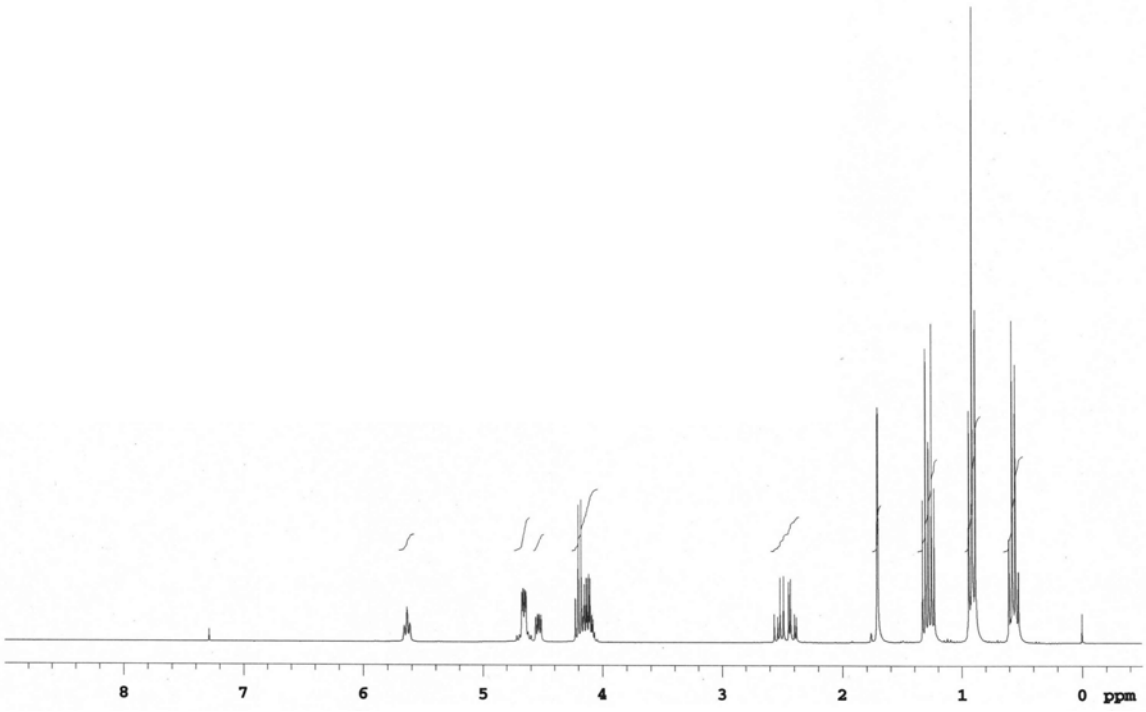
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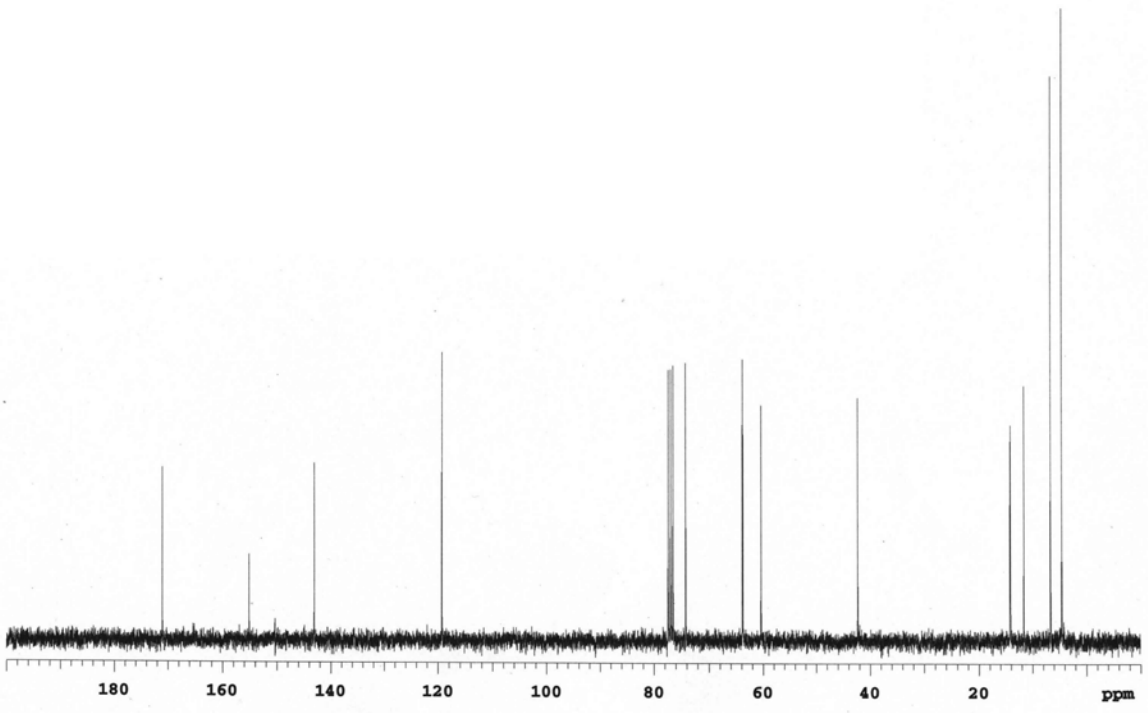
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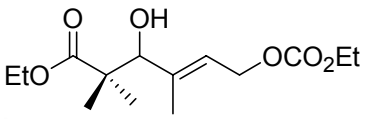
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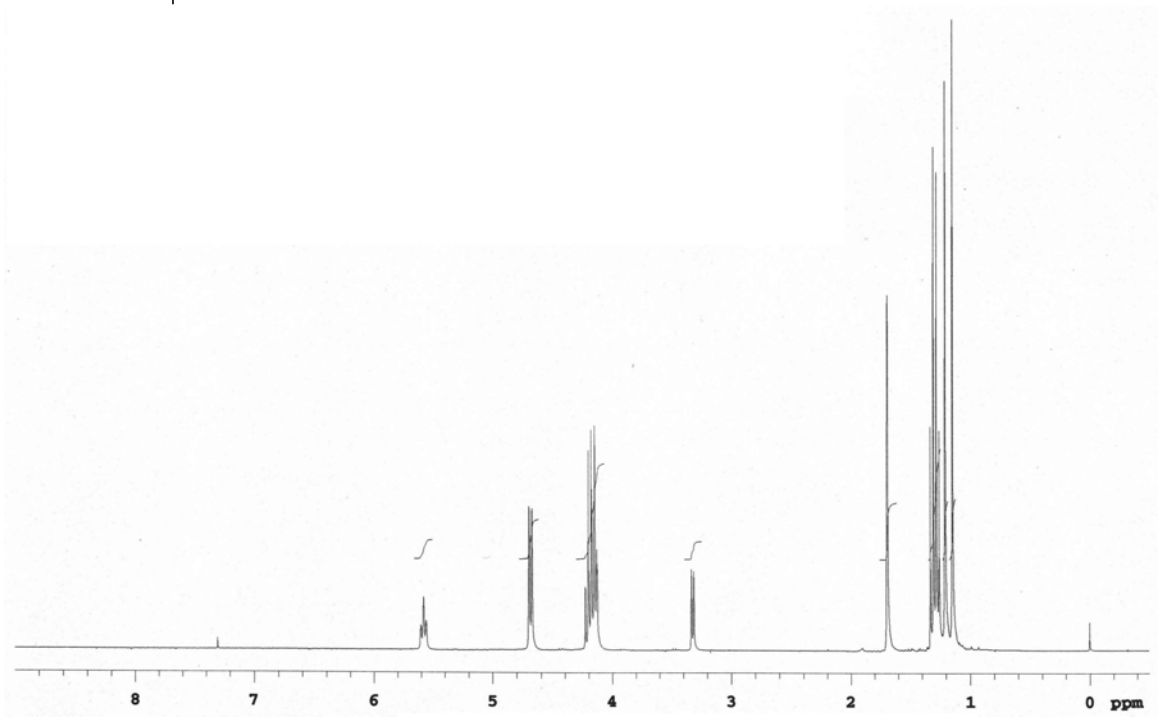
EtO
OCO2Et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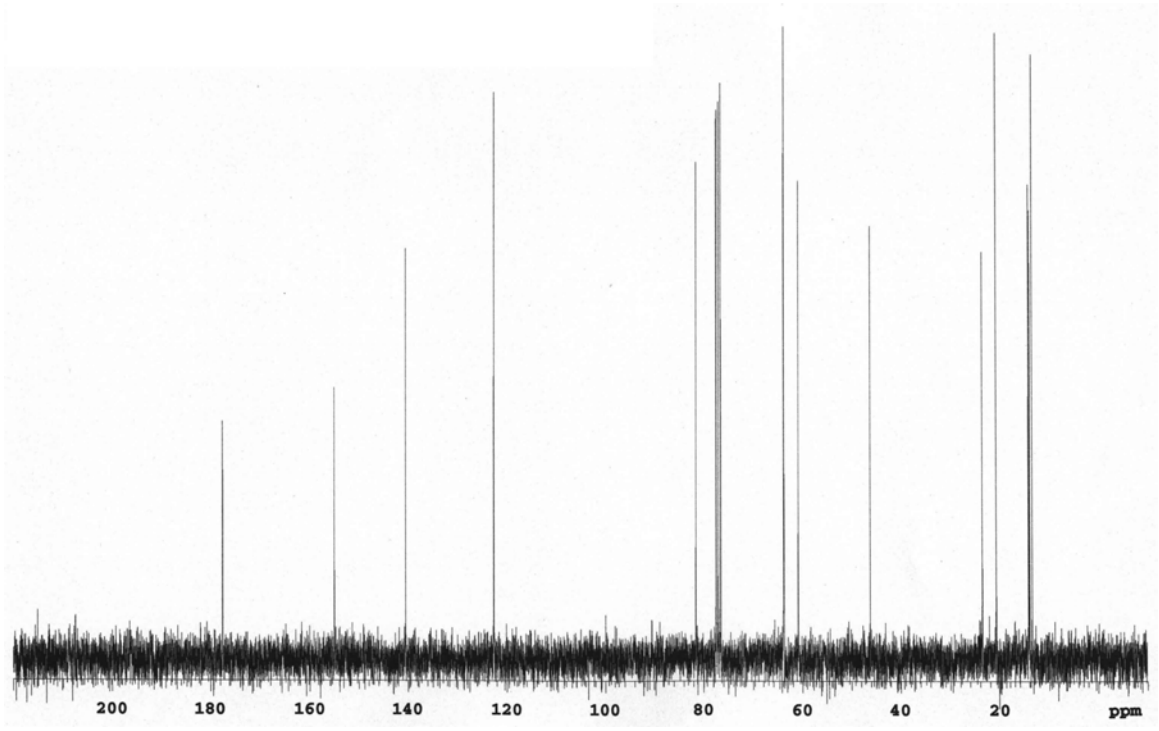
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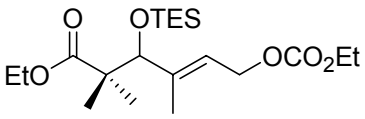
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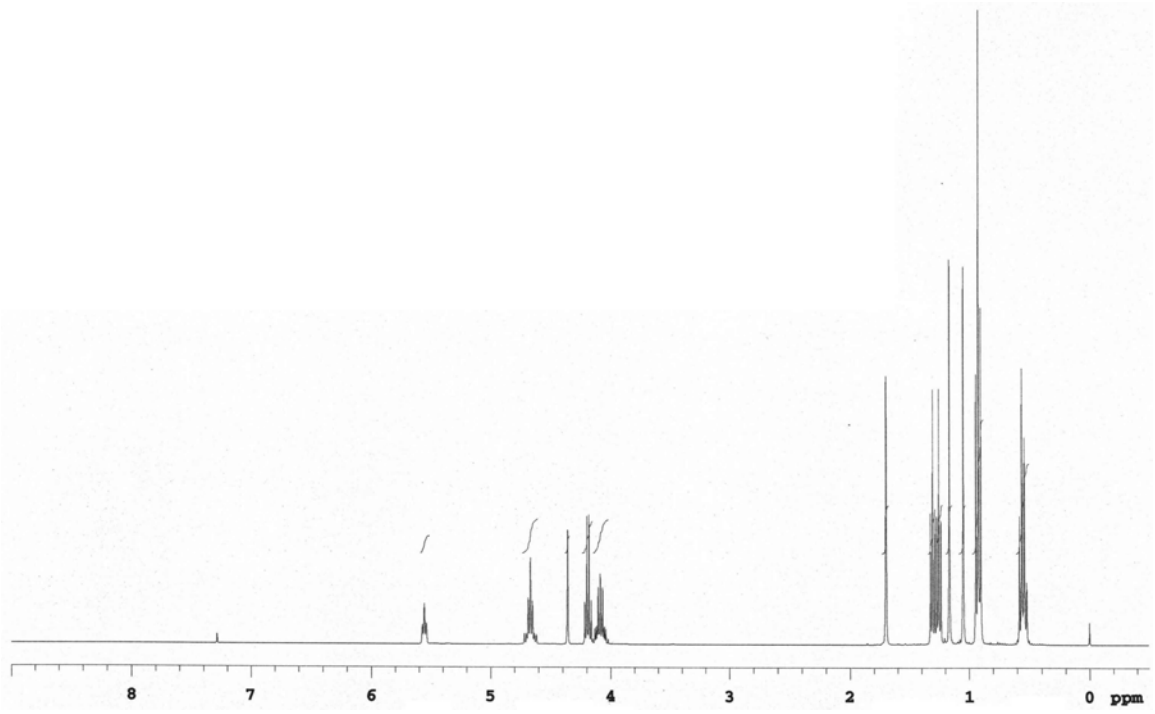
EtO
OCO2Et

20b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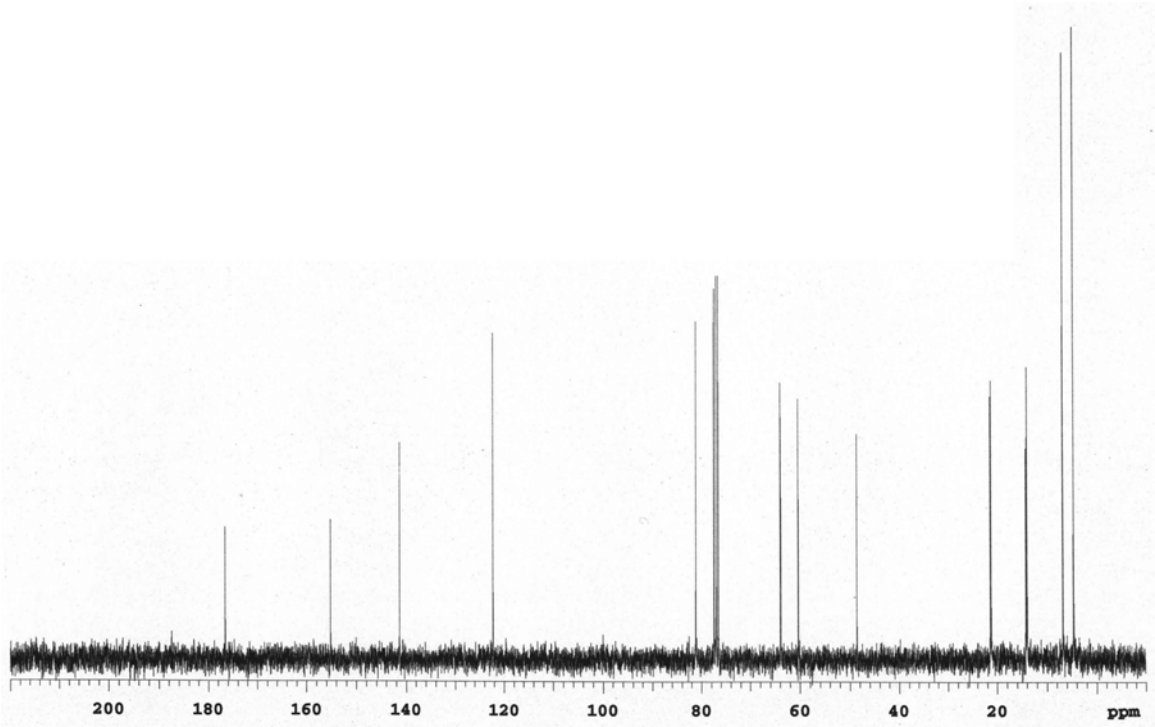
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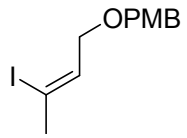
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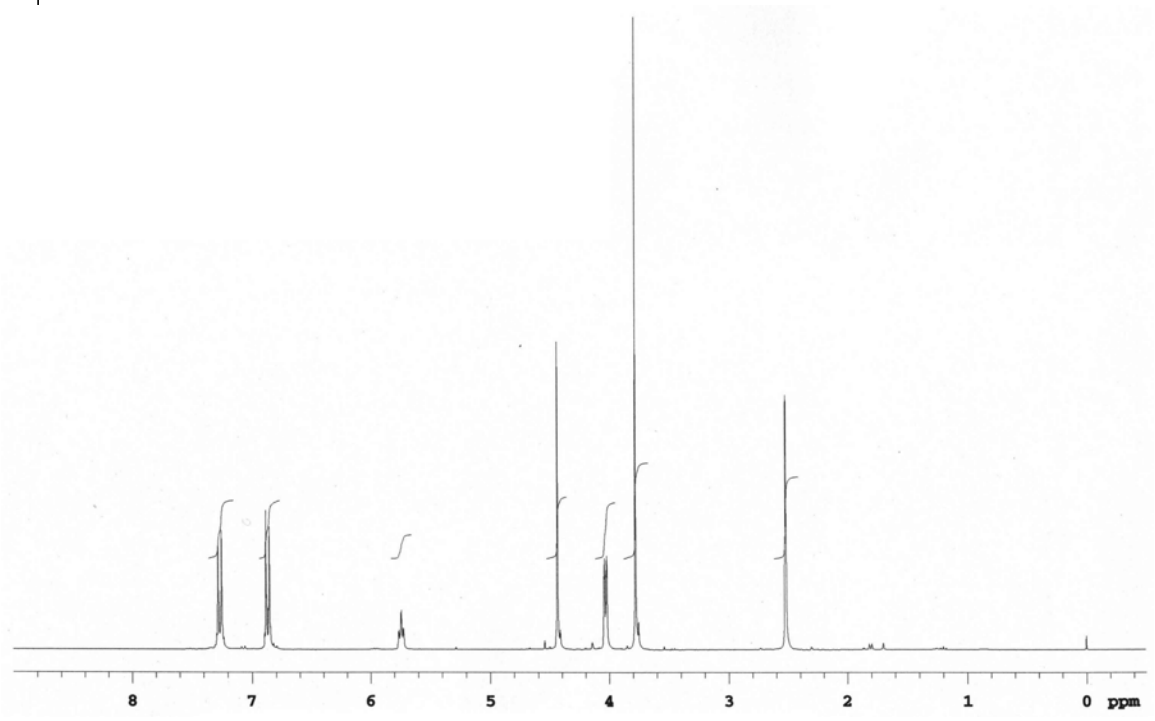
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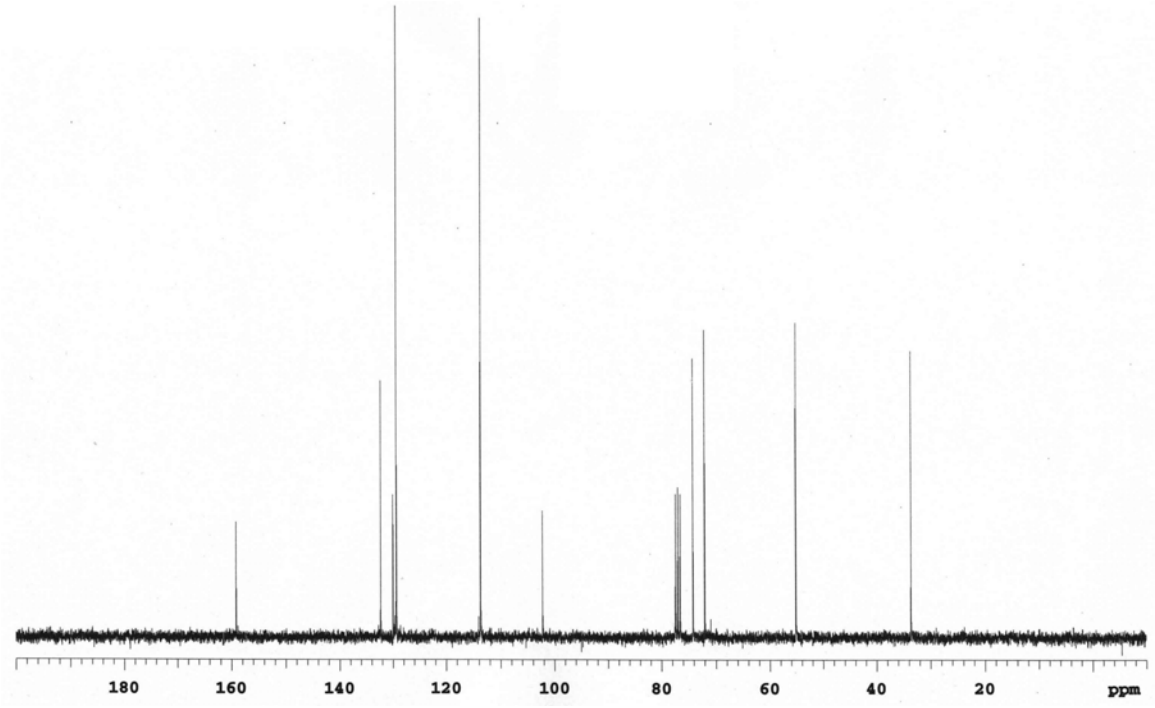
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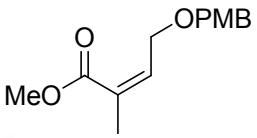
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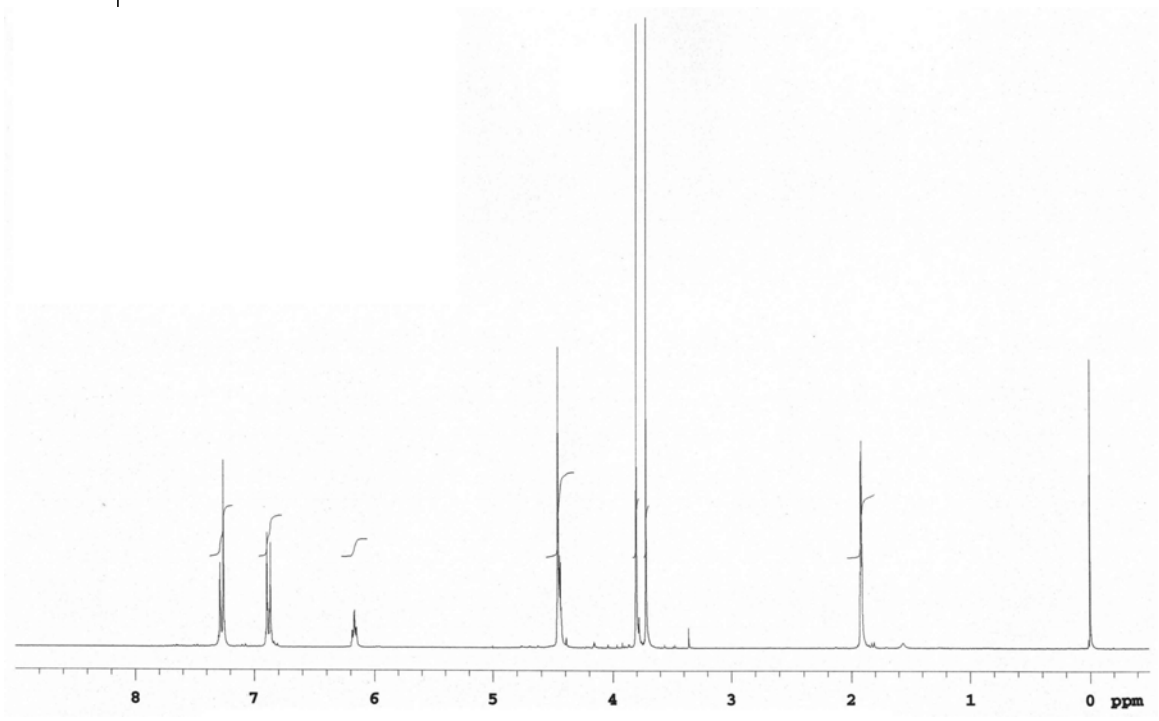
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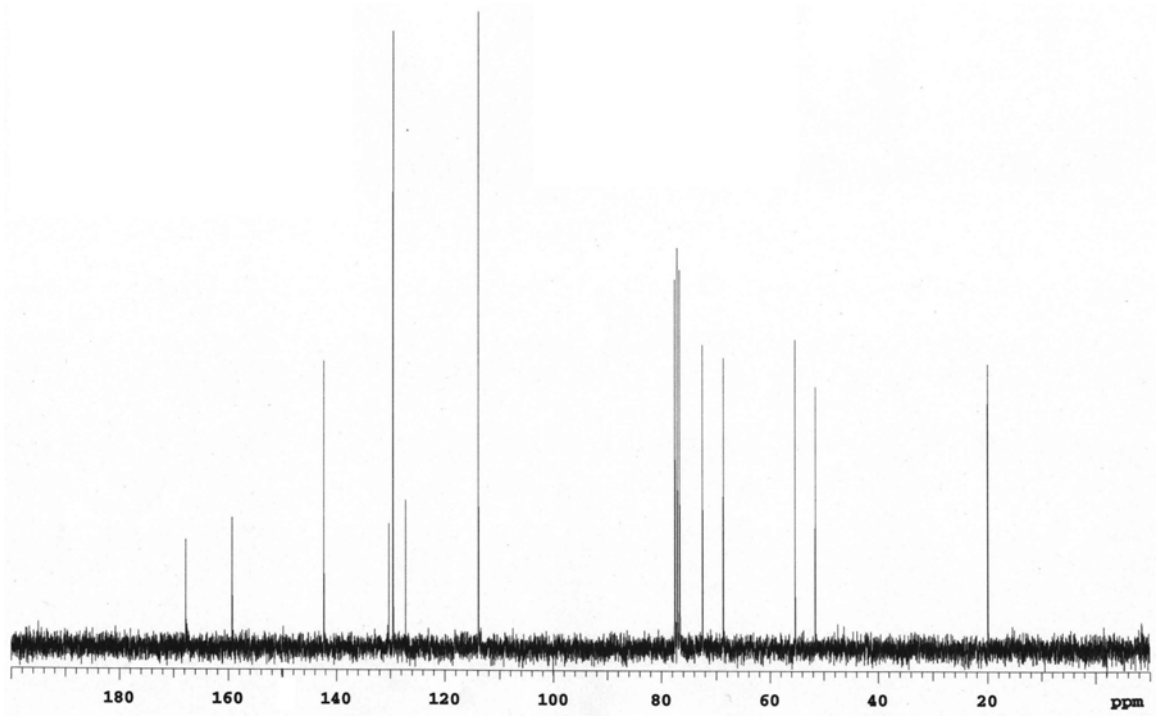
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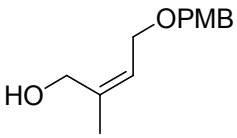
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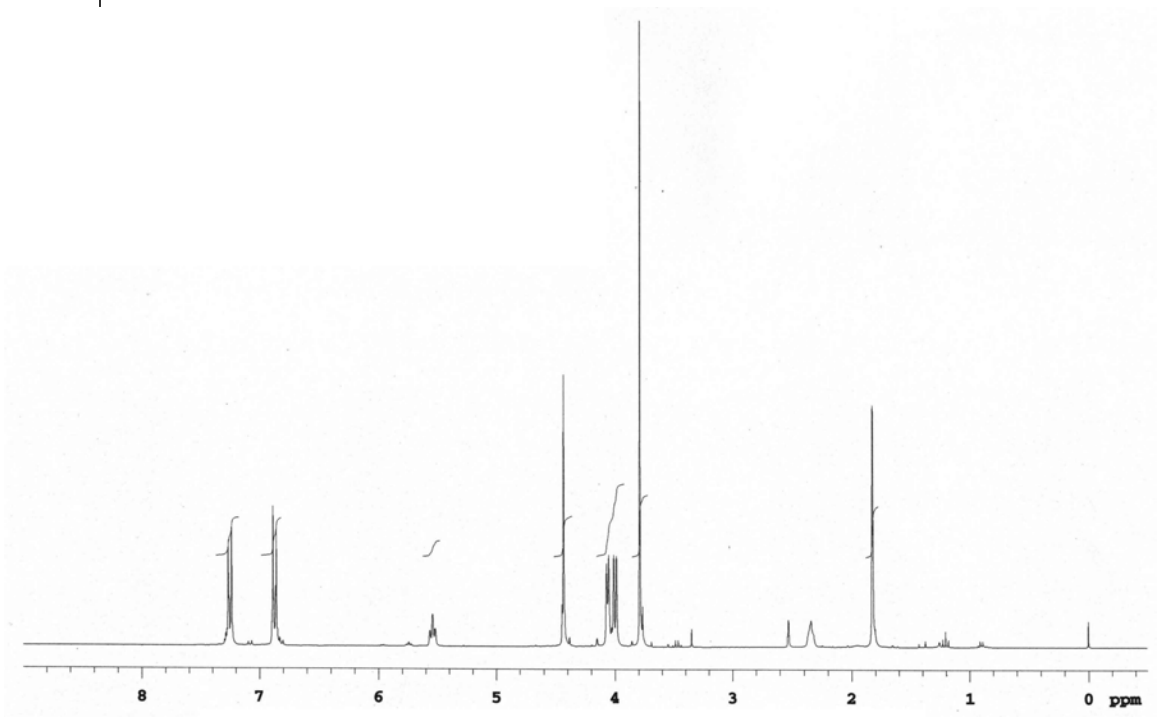
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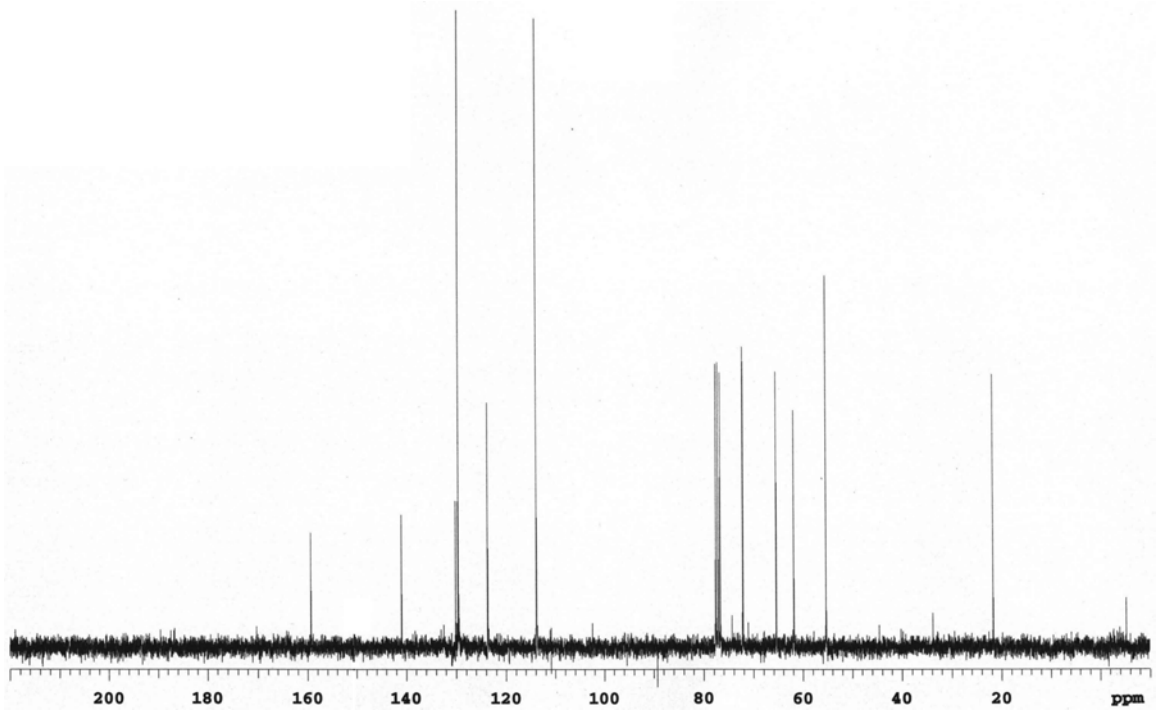
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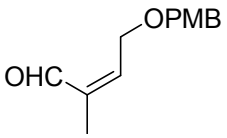
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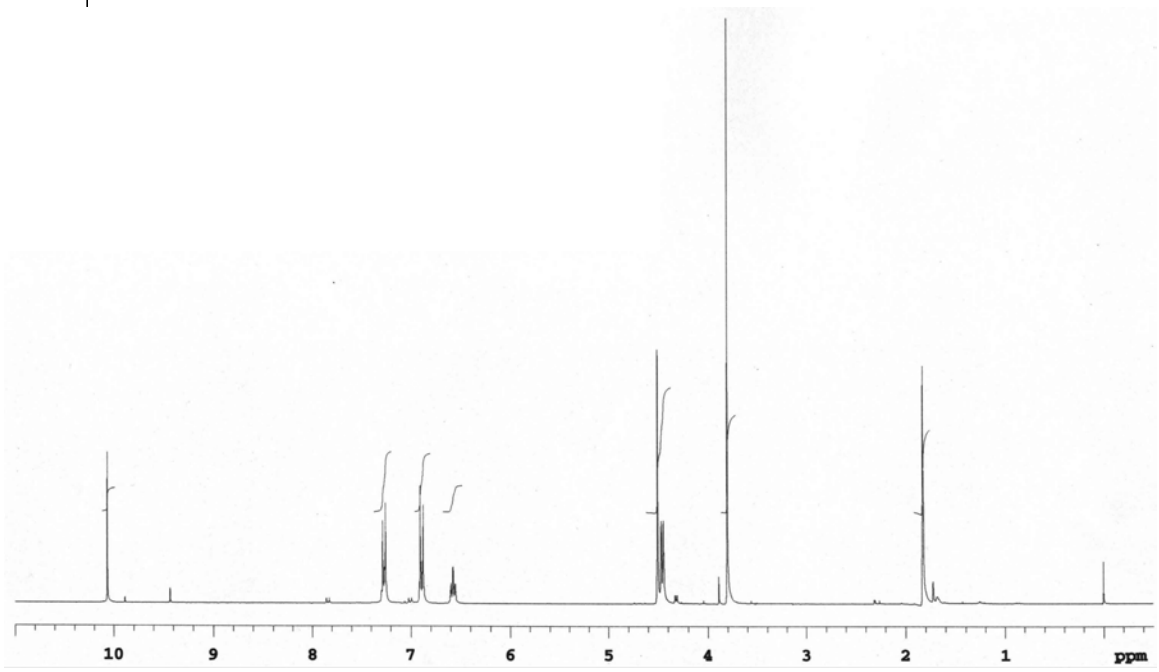
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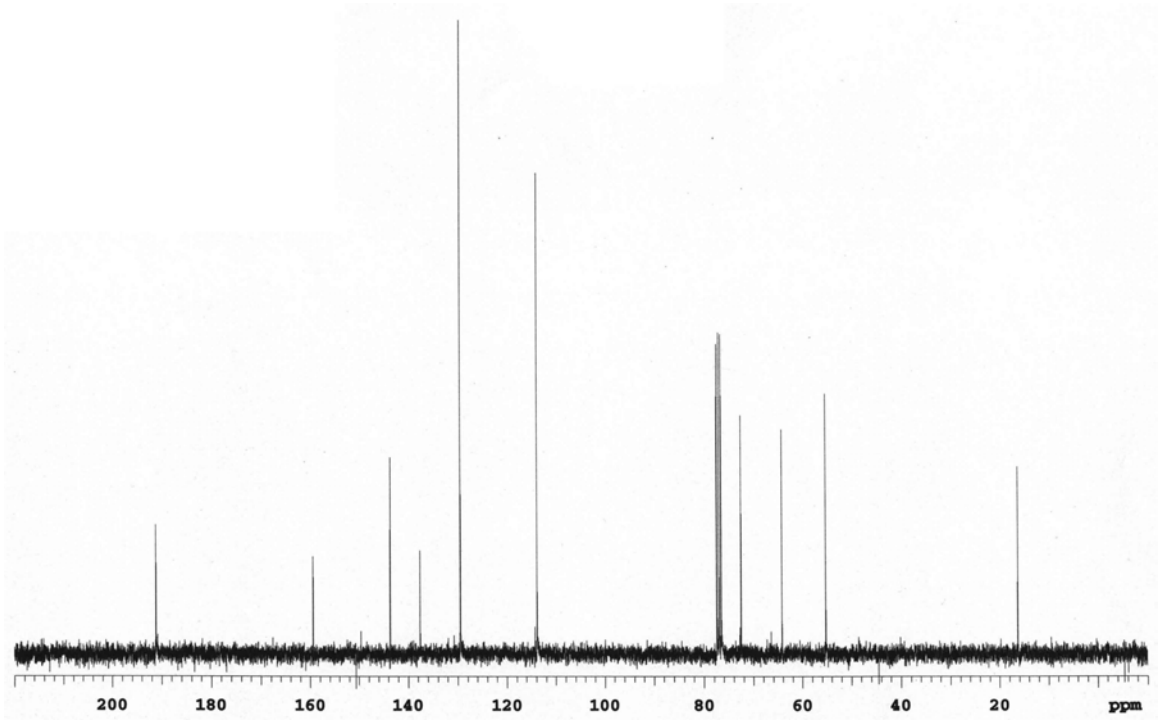
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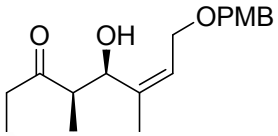
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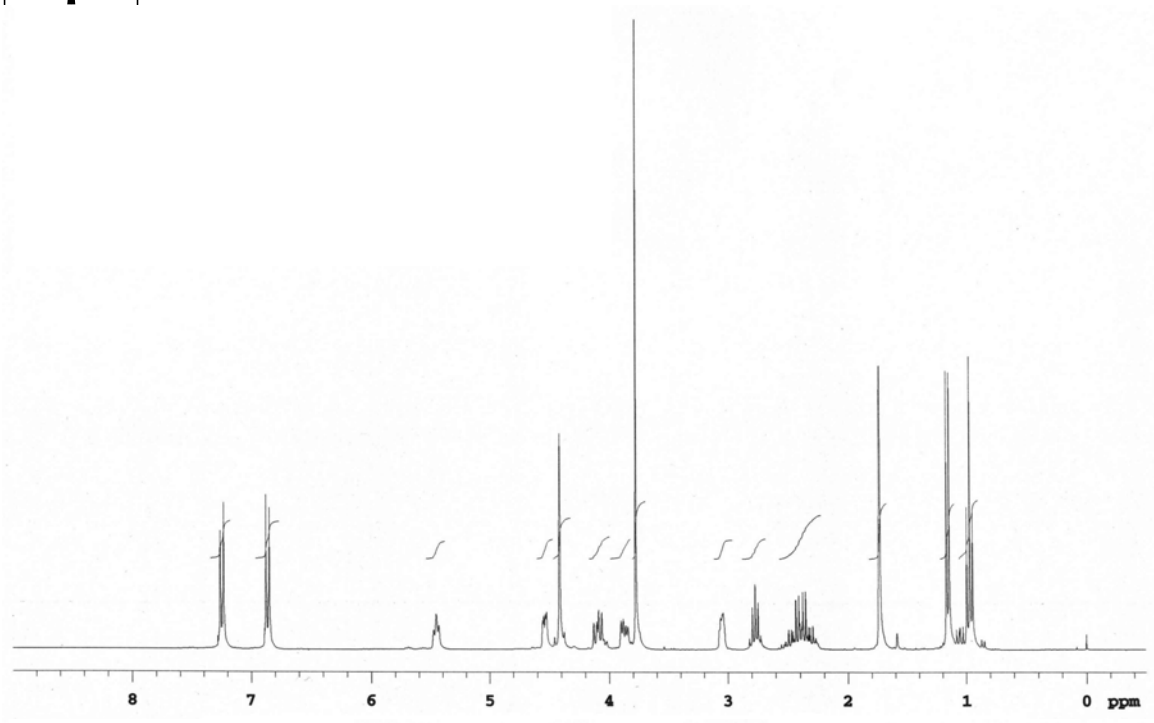
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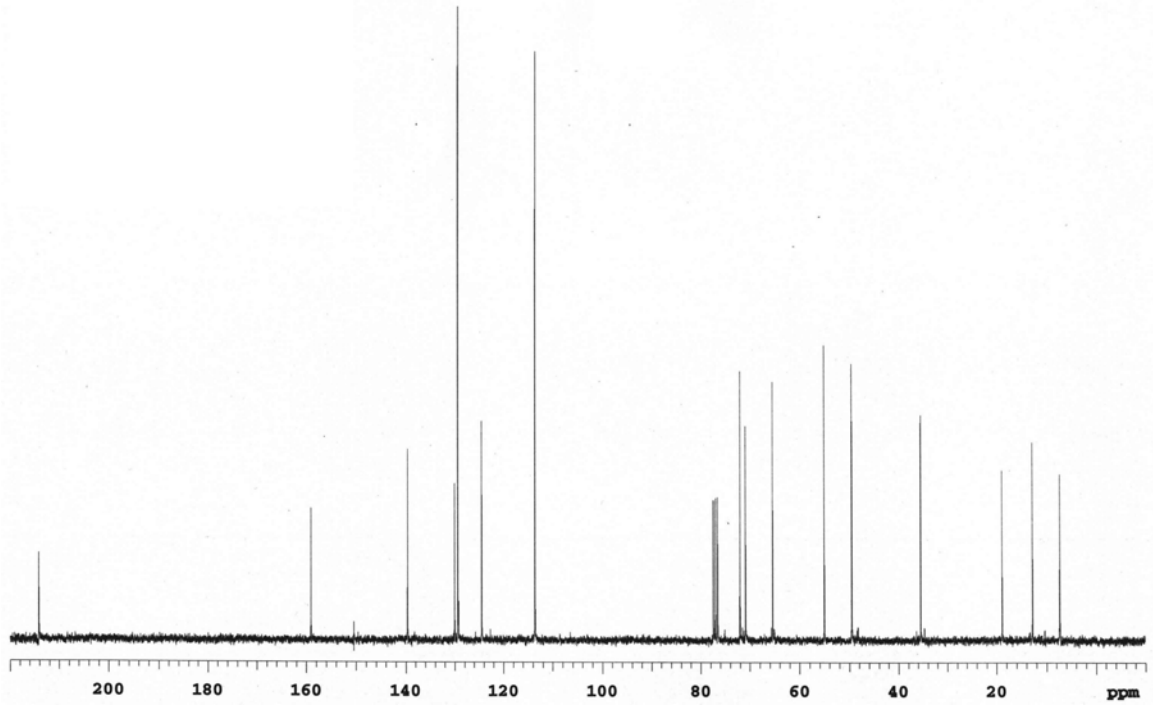
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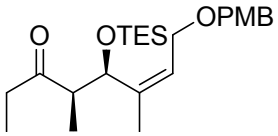
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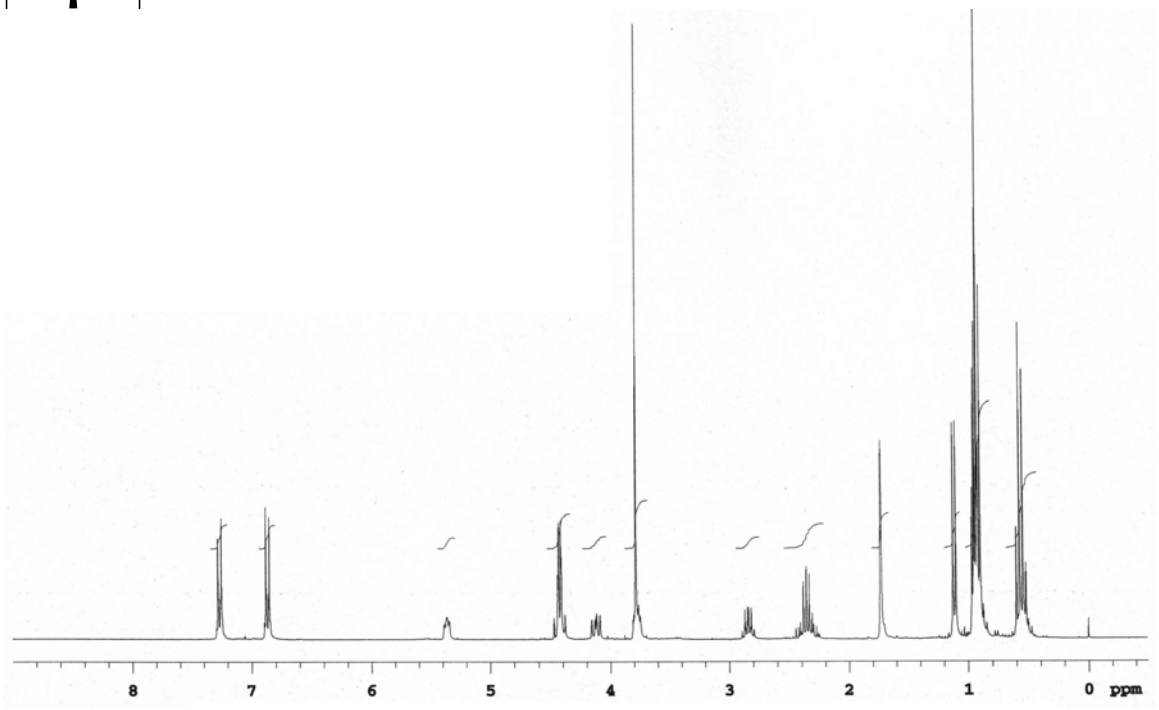
OPMB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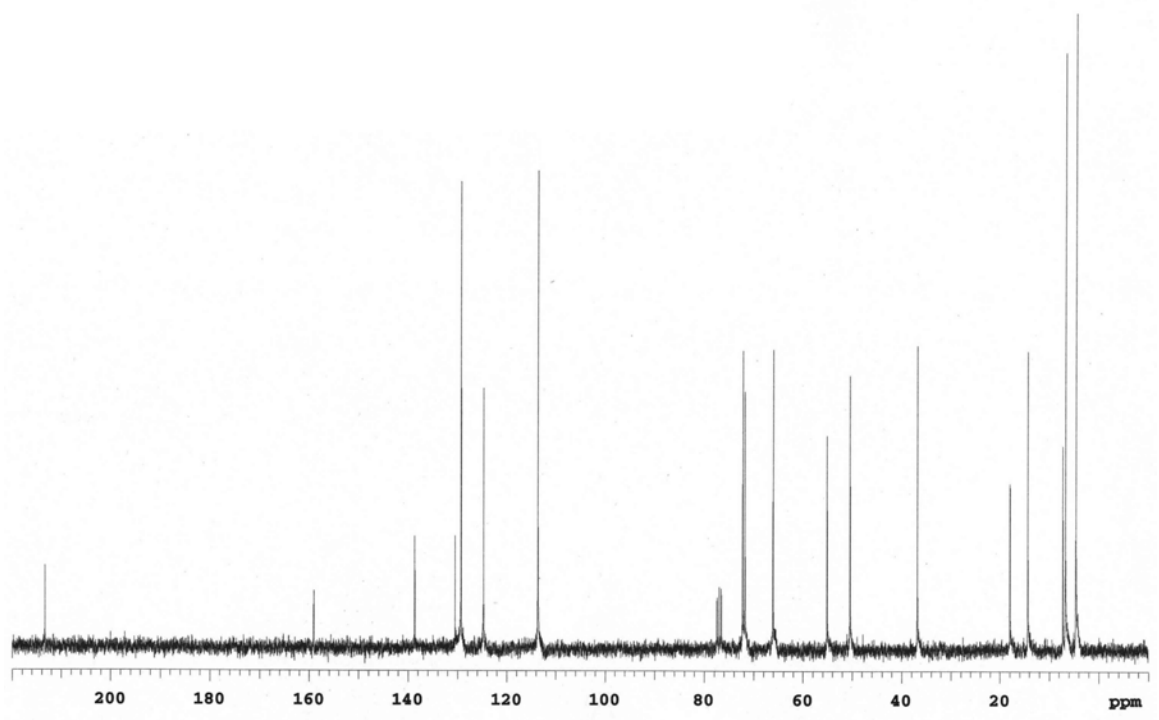
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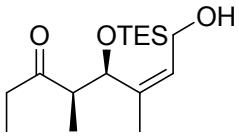
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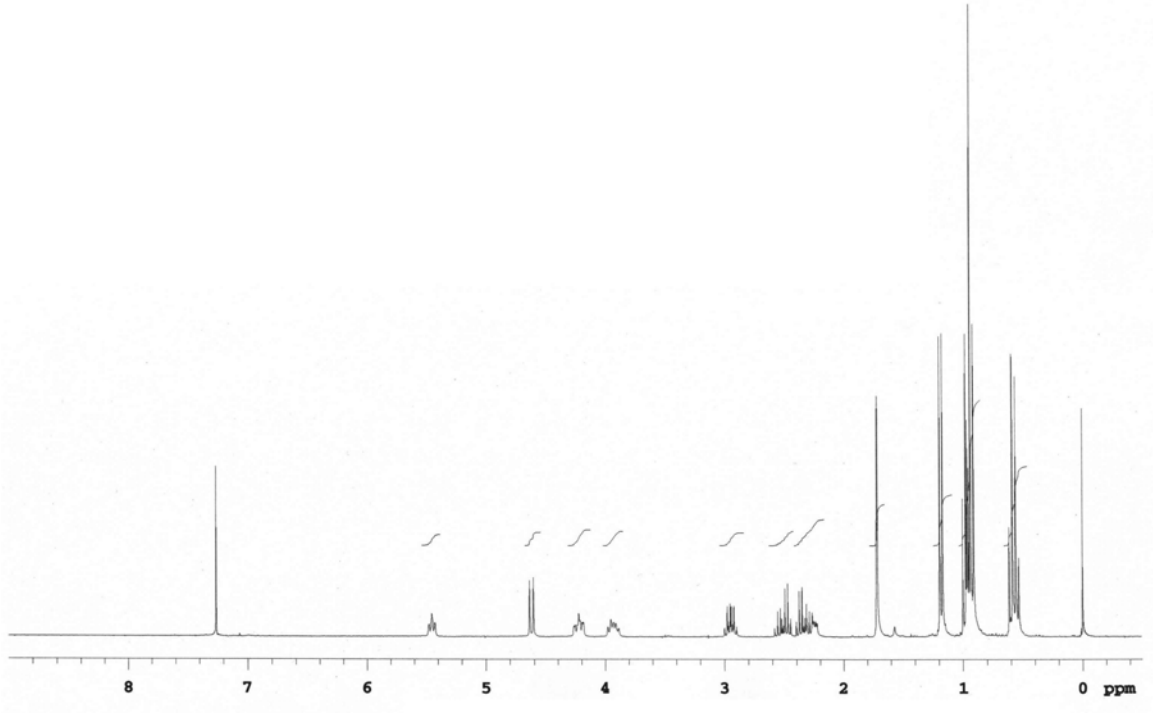
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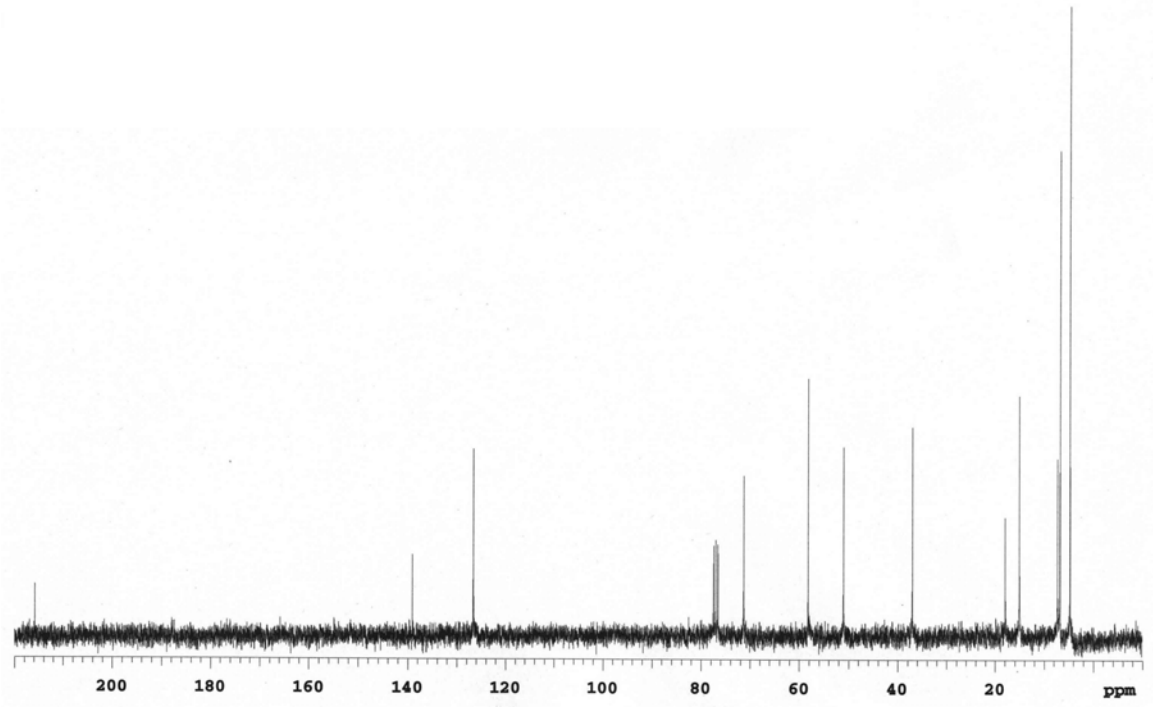
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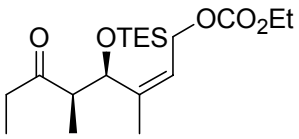
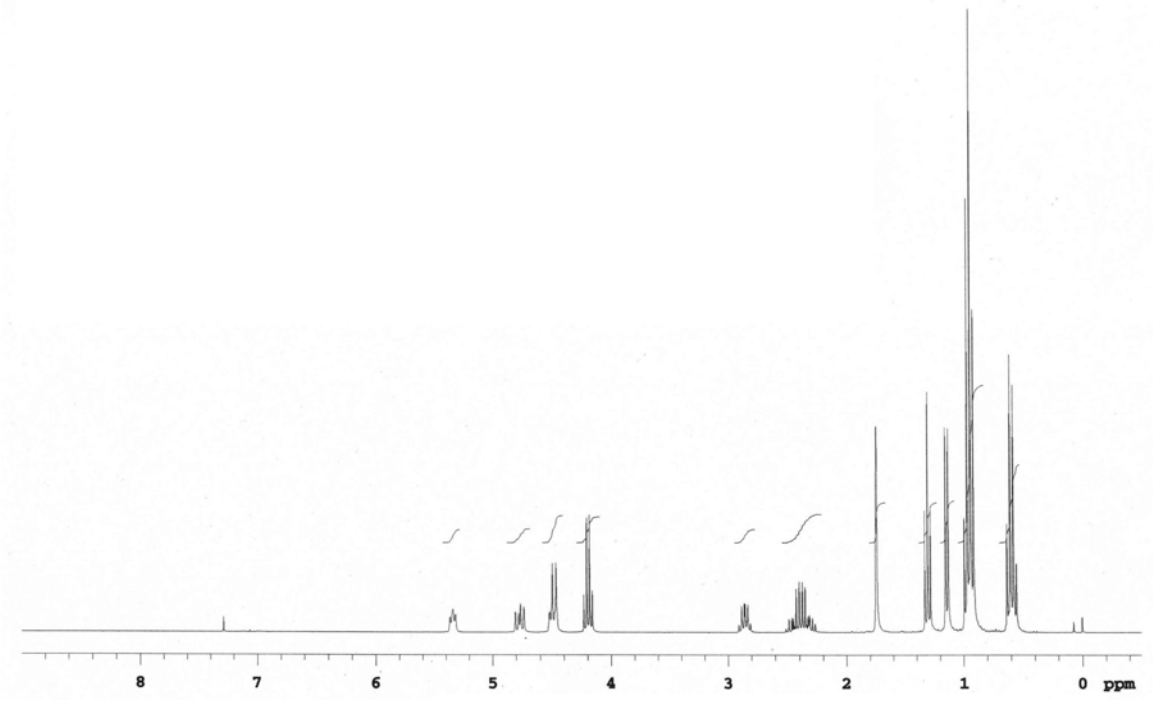

O
OTES
OCO2Et

22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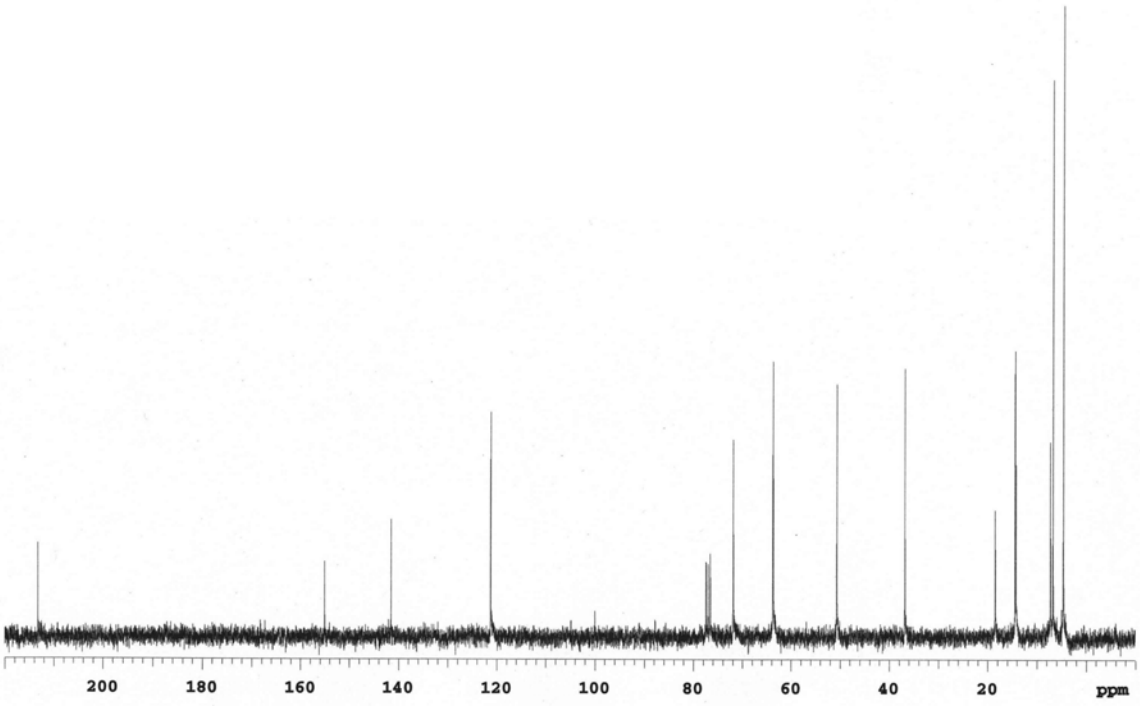
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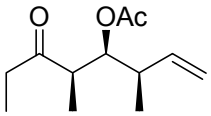
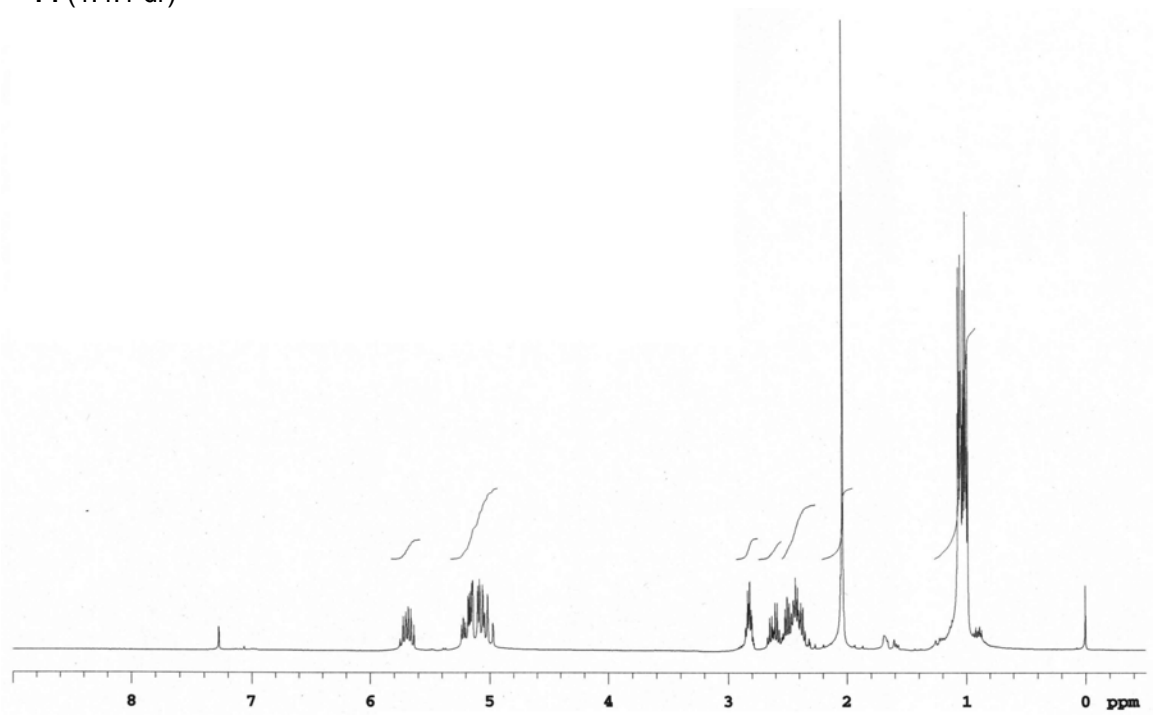
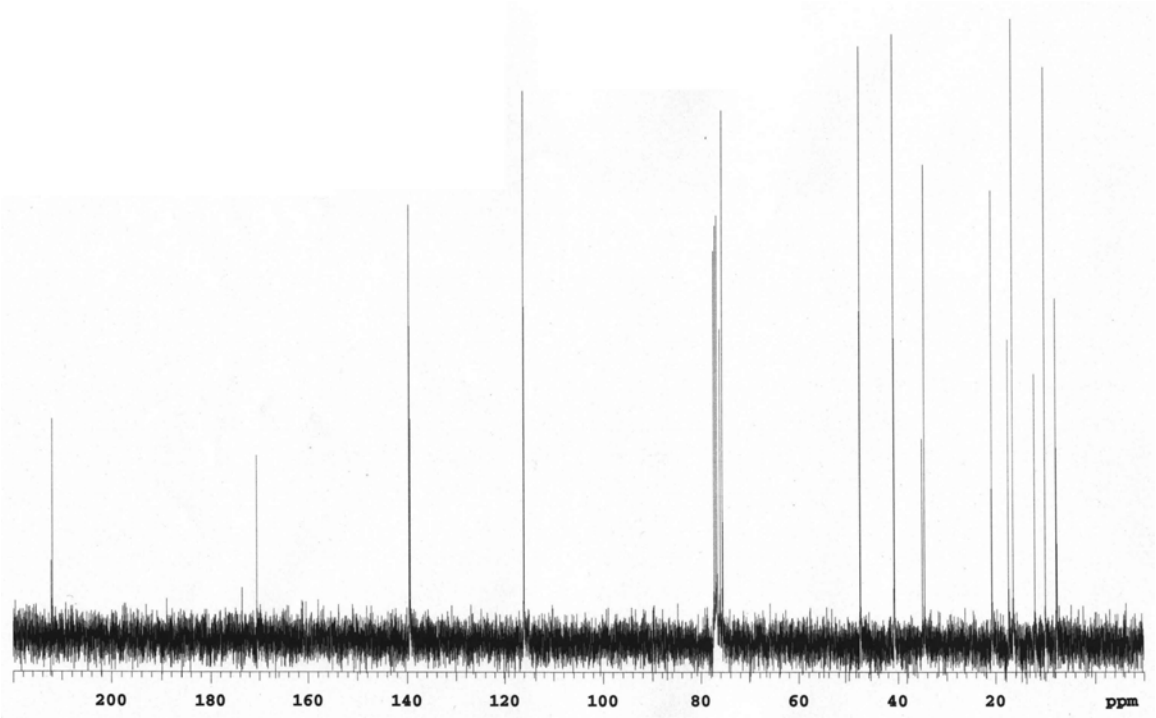
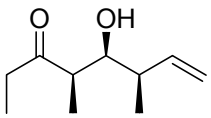


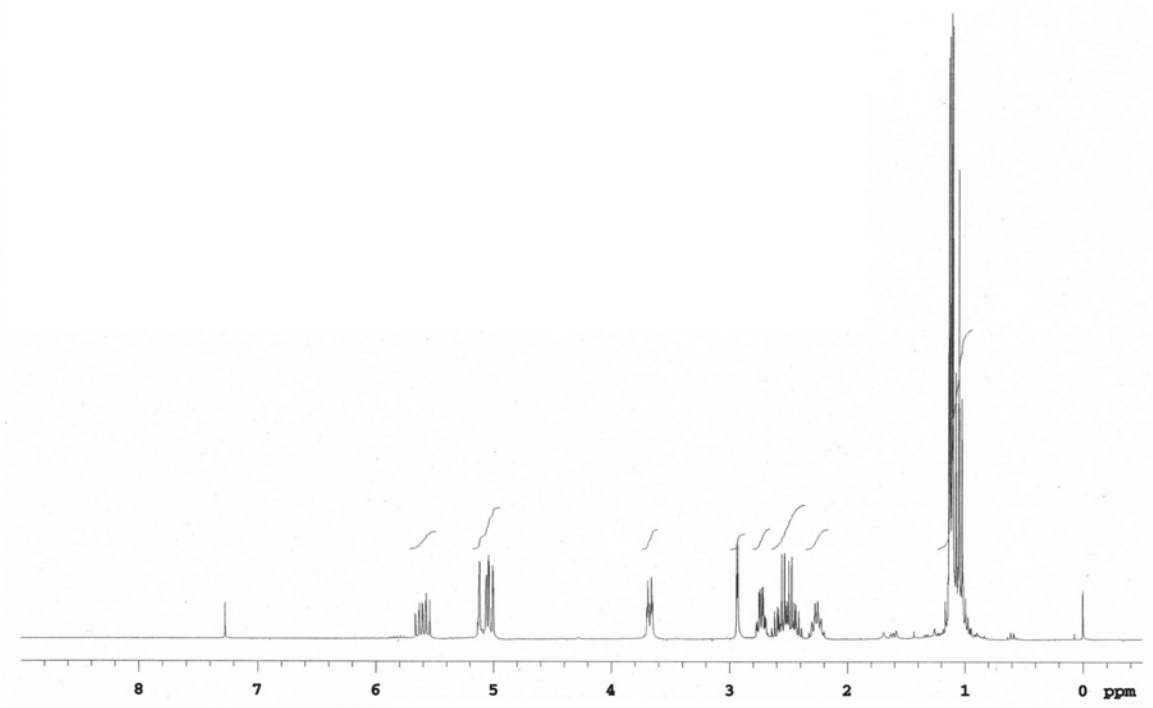
14 (1.4:1 dr)

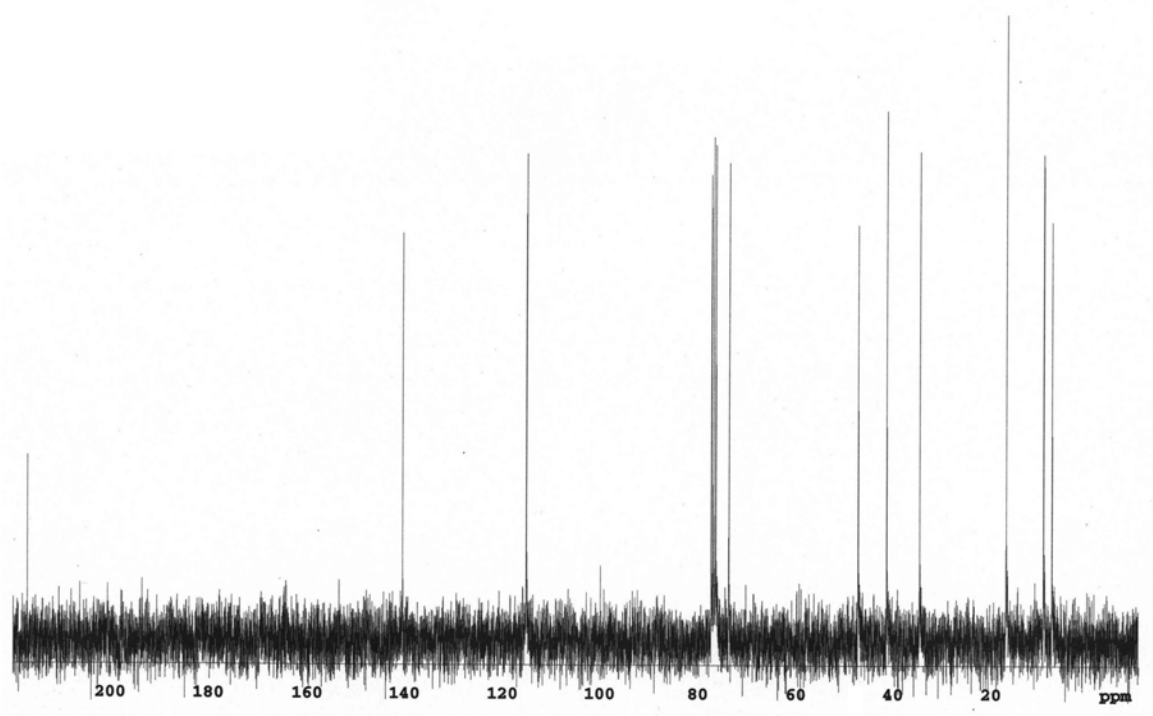


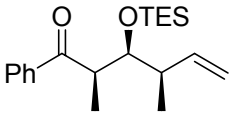




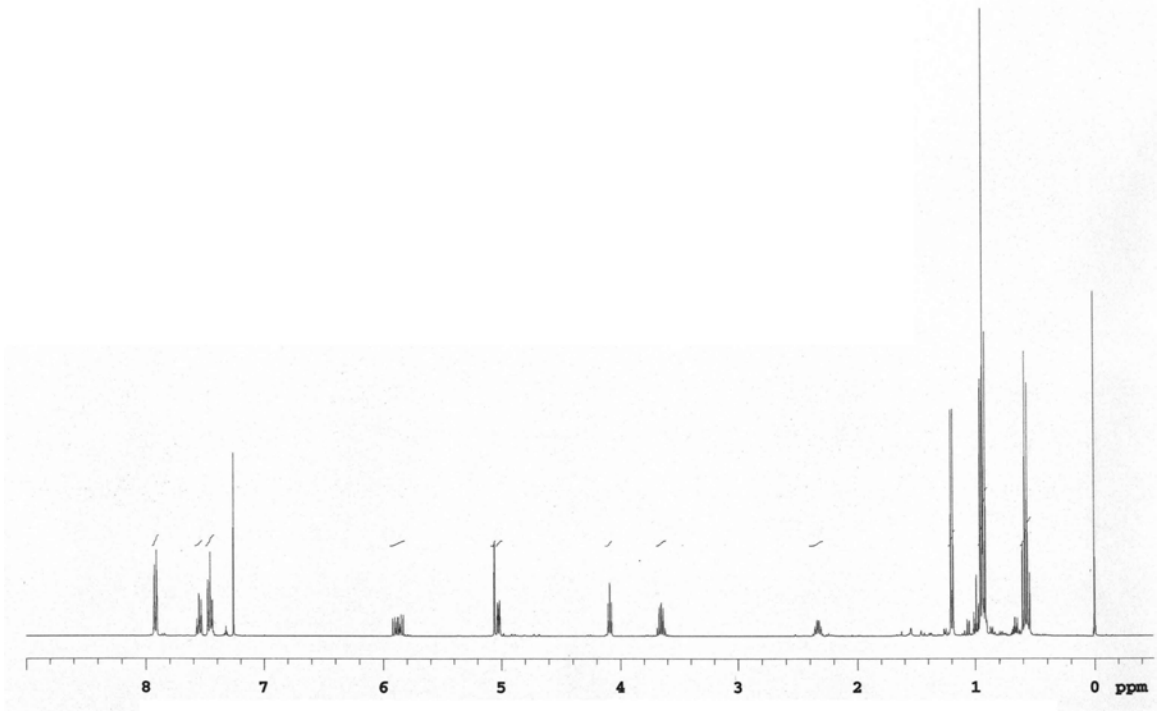
syn-**15**

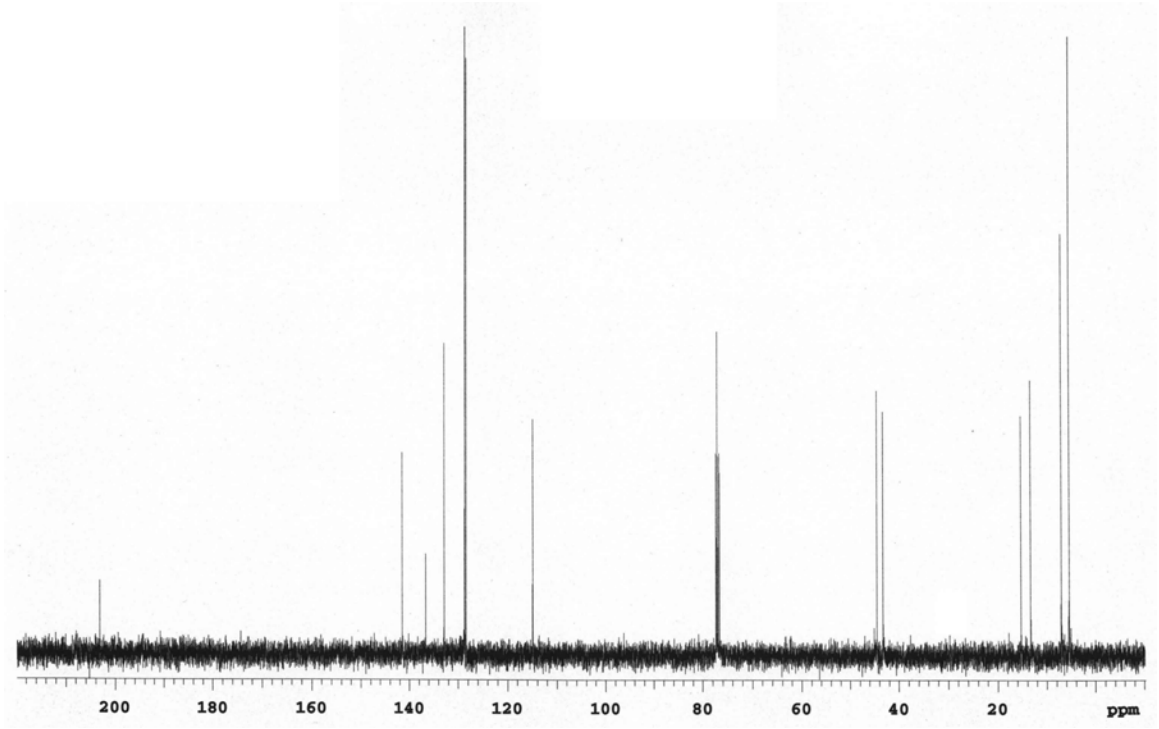


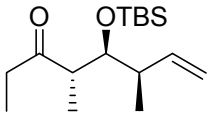




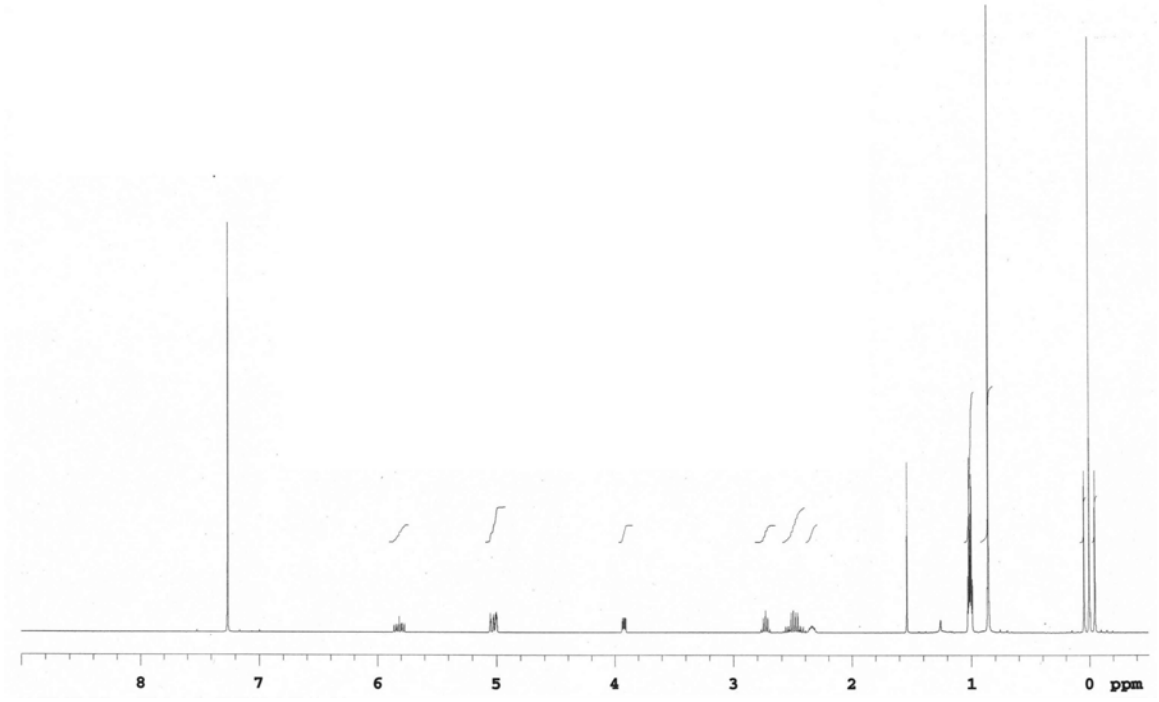
17 (>20:1 dr)

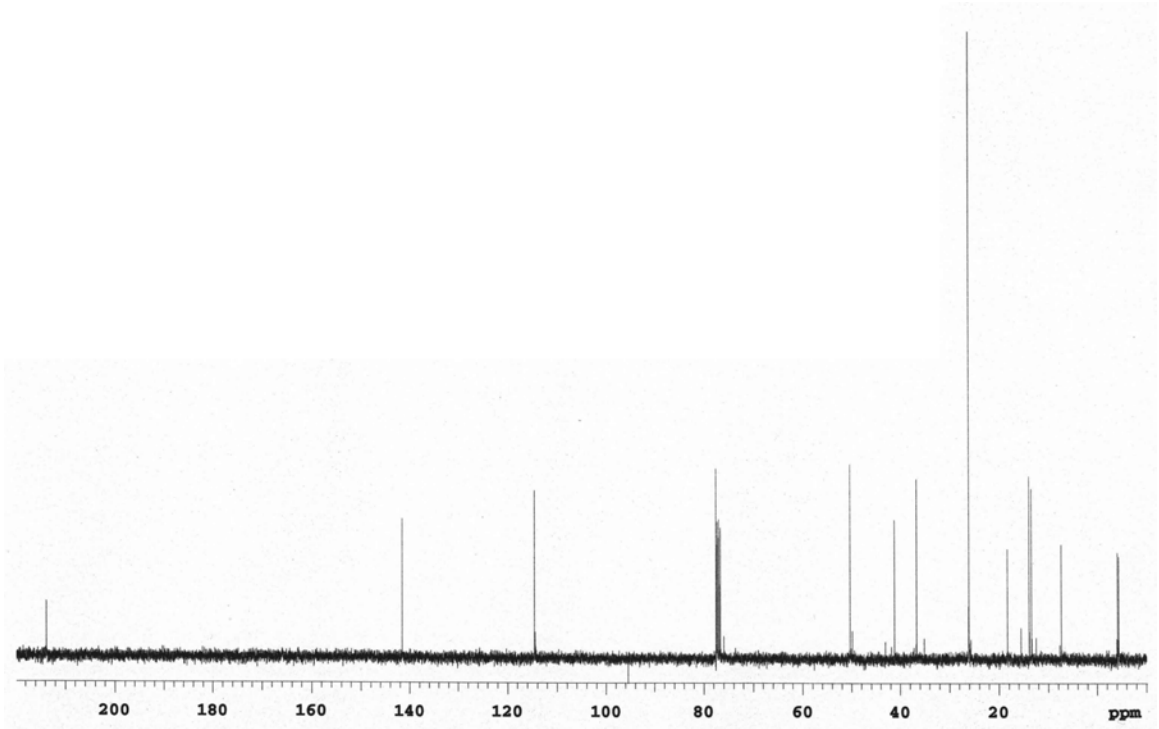


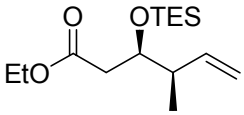




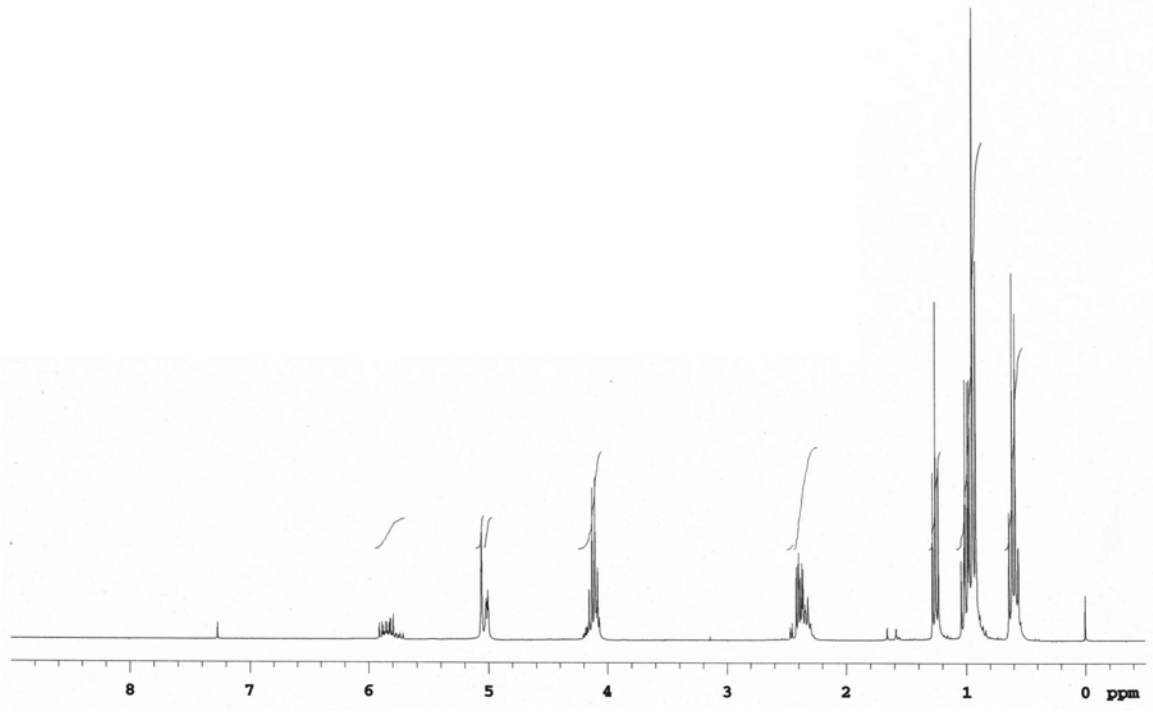
19 (>20:1 dr)

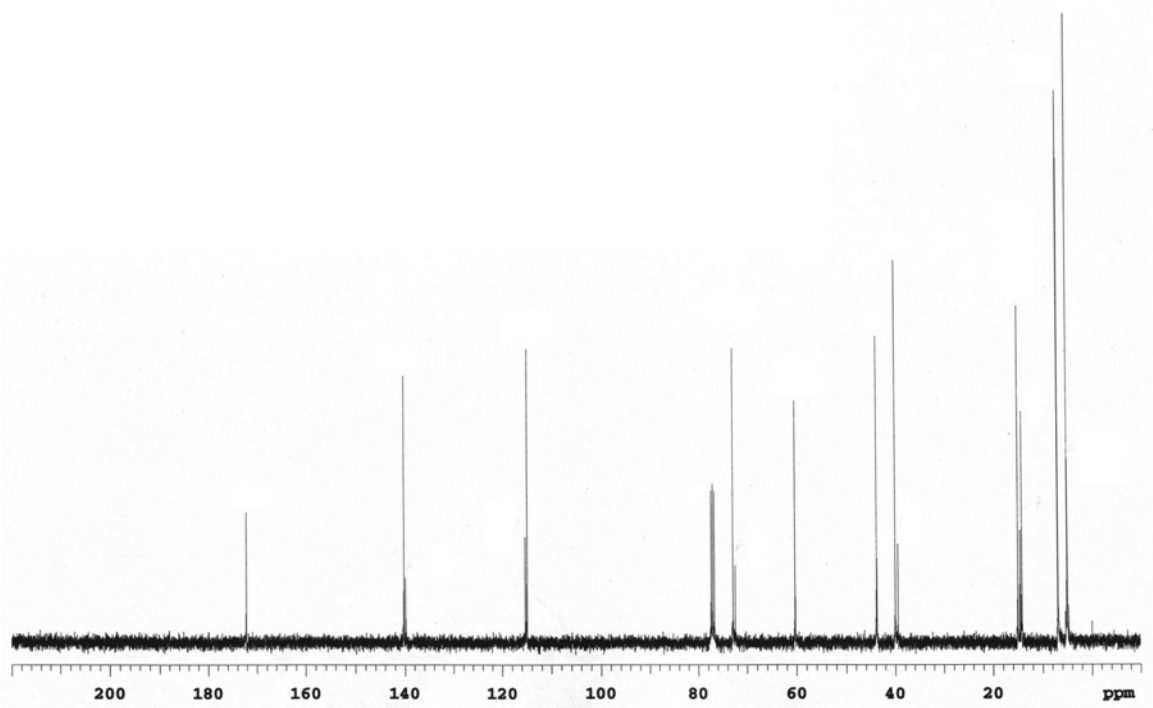


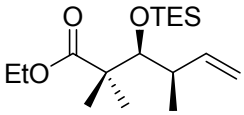




21a (3:1 dr)







21b (>20:1 dr)