Electronic Supplementary Information

Enzymatic Kinetic Resolution of Internal Propargylic Diols. Part I: A New Approach for the Synthesis of *(S)*-Pent-2-yn-1,4-diol, a Natural Product from *Clitocybe catinus.*

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General

All the solvents used in the reactions were purified by distillation prior to use. In the case of dry THF (used to generate bis-lithium salts in the organometallic step), the solvent was dried under reflux in the presence of pieces of metallic sodium using 1,10-phenantroline as indicator. The commercially available Lipase CALB (Novozym 435®; immobilized lipase-B from *Candida antarctica*; 10,000 PLU/g), aldehydes and propylene oxide were obtained from Sigma-Aldrich company and used without any further purification. The 70-230 mesh ASTM silica gel of MACHEREY-NAGEL® was used as the stationary phase in chromatography column purifications. The TLC analyses were performed using aluminium TLC plates 20x20 cm on silica gel 60 of MACHEREY-NAGEL®.

The ^{1}H at 300 MHz and ^{13}C at 75 MHz NMR analysis were performed on a VARIAN® Unity Plus-300 (300 MHz) spectrometer, using deuterated chloroform ($CDCl_3$) as solvent and Me_4Si as internal standard. The chemical shifts were expressed in ppm and coupling constants (J) are in Hz. High-Resolution mass spectral (ESI) analyses were performed on a SHIMADZU® LCMS-IT-TOF HRMS spectrometer. Optical rotations were measured using a JASCO® P-2000 polarimeter. The chiral-GC analysis were performed by using two chromatographs both coupled to a flame ionization detector (FID) and using N_2 as the carrier gas, AGILENT® 7890A equipped with AGILENT HP-CHIRAL-20B (β-cyclodextrin in 35%-phenyl-methylpolysiloxane) capillary column (30m x 0.32 mm x 0.25 μm), and SHIMADZU® 2010 Plus, with Supelco BetaDex™ 120 (b-cyclodextrin packing) capillary column (30 m x 0.25 mm x 0.25 μm). The resolutions were carried out on a TECNAL® orbital shaker stirrer TE-424 with temperature control. The determination of E was based on the equation E = ln[(1 c)(1 eeS)]/ln[(1 c)(1 + eeS)] were the eeS is the enantiomeric excess of mono-acylated product (first round resolution) at conversion c. E values on the use of linear regression (E as the slope of the line ln[(1 c)(1 eeS)] versus ln[(1 c)(1 + eeS)].[22]

General procedure to prepare the diols 1a-h

To a round bottomed flask containing the propargylic alcohol (1 mmol) in THF (5 mL) at -78 ^{0}C using dry N_2 atmosphere under stirring, *n*-butyl lithium (2.2 mmol from 2.4 mL of 0.92 mol/L solution in hexane) was drop wise added. After stirring the solution at the same temperature for 20 min it was transferred to the appropriate electrophile (0.9 mmol, 1M) in THF solution. The reaction was warmed to 0 ^{0}C quenched with a saturated solution of NH_4Cl (2 mL) and the phases separated. The aqueous phase was extracted with ethyl acetate (2 x 5 mL) washed with brine, dried with magnesium sulphate, filtered off and the solvents removed in a rotary evaporator under vacuum. The crude was purified by chromatography on silica gel using a mix of *n*-hexane/ethyl acetate (1:1) as eluent.

The diols **1a-c**, **1e-f** and **1h** were prepared transferring via cannula the 1,4-bis-lithium salt generated in situ, as described above to the aldehydes solution containing catalytic amount (10mol%) of dry $CeCl_3$ salt.

The diols **1d** and **1g** were prepared in a similar procedure, adding propylene oxide in one portion to the bis-lithium salt.

(*R*,*S*)-pent-2-yne-1,4-diol (1a). Obtained as a colourless oil, yield (0.57g) 67%. ^{1}HNMR (300 MHz; $CDCl_3$, ppm): δ 1.44 (3H, d, J^3 = 6.3 Hz), 3.60 (2H, s), 4.28 (2H, d, J^4 = 1.8 Hz), 4.57 (1H, qt, J^3 = 6.3 Hz, J^4 = 1.8 Hz); ^{13}CNMR(75 MHz; $CDCl_3$, ppm): δ 24.0, 50.6, 58.1, 82.1, 87.5; CAS number 927-57-1

(*R*,*S*)-hex-2-yne-1,4-diol (1b). Obtained as a colourless oil, yield (2.76g) 77%. ^{1}HNMR (300 MHz; $CDCl_3$, ppm): δ 0.99 (3H, t, J^3 = 7.5 Hz), 1.65-1.80 (2H, m), 3.99 (2H, s), 4.30 (2H, d, J^4 = 1.5 Hz), 4.35 (1H, tt, J^3 = 6.6 Hz, J^4 = 1.5 Hz); ^{13}CNMR (75 MHz; $CDCl_3$, ppm): δ 9.4, 30.5, 50.4, 63.3, 82.9, 86.3; CAS number 14092-35-4

(*R*,*S*)-5-methyl-hex-2-yne-1,4-diol. (1c): Obtained as a colourless oil, yield (0.9g) 81%. ^{1}HNMR (300 MHz; $CDCl_3$, ppm): δ 1.0 (6H, dd, J^3 = 6 Hz), 1.88 (1H, oct, J^3 = 6 Hz), 3.13 (2H, s), 4.21 (1H, dt, J^3 = 6 Hz, J^4 = 1.5 Hz), 4.32 (2H, d, J^4 = 1.5 Hz); ^{13}CNMR (75 MHz; $CDCl_3$, ppm): δ 17.5, 18.0, 34.3, 50.7, 67.7, 83.7, 85.3; CAS number 35336-44-8

(*R*,*S*)-hex-2-yne-1,5-diol. (1d). Obtained as a colourless oil, yield (0.61g) 64%. ^{1}HNMR (300 MHz; $CDCl_3$, ppm): δ 1.25 (3H, d, J^3 = 6.3 Hz), 2.31 (1H, ddt, J^2 = 16.3 Hz, J^3 = 6.6 Hz, J^4 = 2.1 Hz), 2.44 (1H, ddt, J^2 = 16.3 Hz, J^3 = 6.6 Hz, J^4 = 2.1 Hz), 2.94 (2H, s), 3.97 (1H, sext, J^3 = 6.6 Hz), 4.26 (2H, t, J^4 = 2.1 Hz); ^{13}CNMR (75 MHz; $CDCl_3$, ppm): δ 22.2, 29.1, 51.0, 66.3, 80.7, 82.6; CAS number 343268-16-6

(*R*,*S*)-hex-3-yne-1,5-diol (1e). Obtained as a colourless oil, yield (0.6g) 63%. ^{1}HNMR (300 MHz; $CDCl_3$, ppm): δ 1.40 (3H, d, J^3 = 6.6 Hz), 2.44 (2H, td, J^3 = 6.6 Hz, J^4 = 2.1 Hz), 2.73 (2H, s), 3.69 (2H, t, J^3 = 6.3 Hz), 4.49 (1H, qt, J^3 = 6.3 Hz, J^4 = 2.1 Hz); ^{13}CNMR (75 MHz; $CDCl_3$, ppm): δ 22.9, 24.4, 58.2, 60.8, 81.1, 84.1; CAS number 488099-02-1

(*R*,*S*)-hept-3-yne-1,5-diol (1f). Obtained as a colourless oil, yield (0.78g) 71%. ^{1}HNMR (300 MHz; $CDCl_3$, ppm): δ 1.0 (3H, d, J^3 = 7.5 Hz), 1.6-1.8 (2H, m), 2.48 (2H, td, J^3 = 6 Hz, J^4 = 2.1 Hz), 3.18 (2H, s), 3.72 (2H, t, J^3 = 6 Hz), 4.31 (1H, tt, J^3 = 6.6 Hz, J^4 = 2.1 Hz); ^{13}CNMR (75 MHz; $CDCl_3$, ppm): δ 9.4, 22.9, 30.9, 60.8, 63.6, 82.1, 82.9; IR (film) *v*: 3344, 2964, 2931, 2881, 2245, 1647, 1456, 1424, 1334, 1147, 1044, 963, 845, 646 cm^{-1}; HRMS (ESI) m/z calculated for $C_7H_{12}NaO_2$ $[M+Na]^+$:151.0735, found: 151.0398.

(*R*,*S*)-hept-3-yne-1,6-diol (1g). Obtained as a colourless oil, yield (0.66g) 62%. ^{1}HNMR (300 MHz; $CDCl_3$, ppm): δ 1.22 (3H, d, J^3 = 6.3 Hz), 2.26 (1H, ddt, J^2 = 16.5 Hz, J^3 = 6.9 Hz, J^4 = 1.8 Hz), 2.33-2.38 (1H, m), 2.39-2.47 (2H, m), 2.74 (2H, s), 3.68 (2H, t, J^3 = 6.3 Hz), 3.91 (1H, sext, J^3 = 6.3 Hz); ^{13}CNMR (75 MHz; $CDCl_3$, ppm): δ 22.2, 23.0, 29.1, 61.0, 66.4, 78.5, 79.5; CAS number 1005776-67-9

(*R*,*S*)-2,6-dimethyl-hept-3-yne-2,5-diol (1h). Obtained as a colourless oil, yield (1.28g) 92%. ^{1}HNMR (300 MHz; $CDCl_3$, ppm): δ 0.98 (6H, dd, J^3 = 6.6 Hz), 1.51 (6H, s), 1.85 (1H, oct, J^3 = 6.6 Hz), 3.18 (2H, s), 4.16 (1H, d, J^3 = 6.6 Hz); ^{13}CNMR (75 MHz; $CDCl_3$, ppm): δ 17.4, 18.1, 31.2, 31.3, 34.3, 65.0, 67.5, 81.7, 90.2; CAS number 5486-58-8

General procedure for the enzymatic kinetic resolution of racemic propargylic diols

All the enzymatic resolution were carried out using a 100 mM solution of substrate in an appropriate Erlenmeyer flask capped with red rubber septa and stirred on an orbital shaker under controlled temperature. Concomitant to the resolution, a control reaction with no enzymatic catalyst was made taking aliquots at different times. In each time an aliquot of the crude reaction (100 □l) was taken, filtered off and injected on a GC equipped with chiral column (split 1/100) for analysis.

Kinetic resolution on preparative scale

To an Erlenmeyer flask containing the propargylic diol (2 mmol), were added the appropriated solvent (20 mL), vinyl acetate (10 mmol, 0.92 mL) and CAL-B (100 mg). The100 mM solution, in relation of substrate, was stirred at 35^0C for 0.5 to 48 hours (Table 1). After 100% consumption of racemic diol, the conversion of enantioenriched mono acetate was accomplished until ca. 50%. After the second round resolution had been achieved, the supported enzyme was filtered off and the supernatant concentrated in a rotary evaporator. The crude containing both mono- and bis-enantioenriched acetates were purified by chromatography in silica gel using a mix of n-hexane/ethyl acetate (10:1) as eluent.

(*S*)-1-(acetoxy)-2-pentyn-4-ol (*S*)-(-)-8a: Obtained as a colourless oil, yield (0.12g) 44%.^{1}HNMR (300 MHz; $CDCl_3$, ppm): δ 1.43 (3H, d, *J* = 9 Hz), 2.09 (3H, s), 2.74 (1H, s), 4.55 (1H, qt, *J* = 9 Hz), 4.68 (2H, d, *J* = 1,6 Hz); ^{13}CNMR (75 MHz; $CDCl_3$, ppm): δ 20.6, 23.8, 52.2, 57.9, 77.6, 88.6, 170.4; IR (film) *v*: 3407, 2984, 2936, 2877, 1746, 1437, 1379, 1332, 1231, 1157, 1084, 1028, 965, 890, 608 cm^{-1}; HRMS (ESI) *m/z*; calcd for $C_7H_{10}NaO_3$

$[M+Na]^+$: 165.0528, found: 165.0401; $^{Exp}[\alpha]_D^{20}$ = -21.2 (*c* 1.0, $CHCl_3$), *e.e.*>99%.$^{Lit}[\alpha]_D^{20}$ = +8.1 (*c 0.71*, $CHCl_3$), *e.e.* 90% for (*R*)-(+)-**8a**.[14]

(*R*)-1,4-(bis-acetoxy)-2-pentyne (*R*)-(+)-(9a). Obtained as a colourless oil, yield (0.17g) 47%%. ^{1}HNMR (300 MHz; $CDCl_3$, ppm): δ 1.46 (3H, d, *J* = 6 Hz), 2.05 (3H, s), 2.07 (3H, s), 4.67 (2H, d, *J* = 1.8 Hz), 4.45 (1H, qt, *J* = 6 Hz); ^{13}CNMR (75 MHz; $CDCl_3$, ppm): δ 20.6, 20.9, 21.0, 52.0, 60.0, 78.6, 84.9, 169.7, 170.1; IR (film) *v*: 2991, 2941, 1744, 1438, 1370, 1226, 1169, 1060, 1023, 939, 844, 607 cm^{-1}; HRMS (ESI) *m/z*; calcd for $C_7H_{10}NaO_3$ $[M+Na]^+$: 207.0633, found: 207.0462; $[\alpha]_D^{20}$ = +110.7 (*c* 1.0, $CHCl_3$), 99% *e.e.*

The resolution procedure was scaled up to 2.76 g (24.2 mmol) of diol **1b** resulting to the formation of chiral mono- and bis acetate in 48% and 45% respectively.

(*S*)-1-(acetoxy)-2-hexyn-4-ol (*S*)-(-)-8b: Obtained as a colourless oil, yield (1.82g) 48%.^{1}HNMR (300 MHz; $CDCl_3$, ppm): δ 0.97 (3H, t, *J* = 6 Hz), 1.69 (2H, quint, *J* = 6 Hz), 2.07 (3H, s), 2.51. (1H, s), 4.32 (1H, tt, *J* = 6 Hz), 4.68 (2H, d, *J* = 3 Hz); ^{13}CNMR (75 MHz; $CDCl_3$, ppm): δ 9.3, 20.6, 30.4, 52.2, 63.4, 78.5, 87.6, 170.3; IR (filme) cm^{-1}: 3410, 2967, 2932, 2875, 1740, 1443, 1375, 1231, 1151, 1093, 1032, 966; CAS number 221128-14-9 $[\alpha]_D^{20}$ = -3.3 (*c* 1.0, $CHCl_3$), 95% *e.e.*

(*R*)-1,4-(bis-acetoxy)-2-hexyne (*R*)-(+)-9b. Obtained as a colourless oil, yield (2.15g) 45%. ^{1}HNMR (300 MHz; $CDCl_3$) δ. 0.96 (3H, t, *J* = 6 Hz), 1.75 (2H, quint, *J* = 6 Hz), 2.04 (3H, s), 2.05 (3H, s), 4.67 (2H, d, *J* = 3 Hz), 5.31 (1H, tt, *J* = 3 Hz). ^{13}CNMR (75 MHz; $CDCl_3$) δ 9.1, 20.5, 20.8, 27.7, 52.0, 64.8, 79.3, 83.9, 169.8, 170.0; IR (film)*v*: 2972, 2938, 1745, 1440, 1372, 1228, 1166, 1028, 966 cm^{-1}; HRMS (ESI) *m/z*; calcd for $C_{10}H_{14}NaO_4$ $[M+Na]^+$: 221.0790, found: 221.0292; $[\alpha]_D^{20}$ = +79.6 (*c* 1.0, $CHCl_3$), 99% *e.e.*

(*S*)-1-(acetoxy)-5-methyl-hexyn-4-ol (*S*)-(-)-8c. Obtained as a colourless oil, yield (0.14g) 41%. ^{1}HNMR (300 MHz; $CDCl_3$) δ 0.98 (6H, dd, *J* = 6 Hz), 1.88 (1H, sext, *J* = 6 Hz), 2.1 (3H, s), 2.36 (1H, d, *J* = 6 Hz), 4.15-4.25 (1H, m), 4.71 (2H, d, *J* = 1.6 Hz); ^{13}CNMR (75 MHz; $CDCl_3$, ppm): δ 17.7, 18.2, 21.0, 34.5, 52.6, 67.9, 79.5, 86.8, 170.6; IR (film) *v*: 3430, 2964, 2880, 1742, 1439, 1374, 1231, 1151, 1111, 1030, 970, 928, 835, 609 cm^{-1}; HRMS (ESI) *m/z*; calcd for $C_9H_{14}NaO_3$ $[M+Na]^+$: 193.0841, found: 193.0391.$^{Exp}[\alpha]_D^{20}$ = -0.45 (*c* 1.3, $CHCl_3$); 96% *e.e.*,$^{Lit}[\alpha]_D^{26}$ = - 1.1 (c=4.0, $CHCl_3$).[16]

(*R*)-1,4-(bis-acetoxy)-5-methyl-hexyne (*R*)-(+)-9c. Obtained as a colorless oil, yield (0.17g) 40%. ^{1}HNMR (300 MHz; $CDCl_3$) δ 0.99 (6H, dd, *J* = 6 Hz), 1.4 (1H, d, *J* = 6 Hz), 2.08 (6H, s), 4,7 (2H, d, *J* = 3 Hz), 4.24 (1H, dt, *J* = 6 Hz).^{13}C NMR (75 MHz; $CDCl_3$) δ 17.4, 18.0, 20.6, 20.8, 32.1, 52.0, 52.1, 68.6, 79.8, 82.8, 169.8; IR (film) *v*: 2968, 2936, 2877, 1746, 1435, 1373, 1227, 1159, 1080, 1023, 986, 937, 606 cm^{-1};HRMS (ESI) *m/z*; calcd for $C_{11}H_{16}NaO_4$ $[M+Na]^+$: 235.0946, found: 235.0509.$[\alpha]_D^{20}$ = +83.2 (*c* 1.0, $CHCl_3$); 94% *e.e.*

(*S*)-1-(acetoxy)-2-hexyn-5-ol (*S*)-(+)-8d.Obtained as a colorless oil, yield (0.13g) 43%.^{1}HNMR (300 MHz; $CDCl_3$, ppm): δ 1.25 (3H, d, *J* = 6 Hz), 1.84 (1H, s), 2.09 (3H, s), 2.3-2.55 (2H, m), 3.97 (1H, sext, *J* = 6 Hz), 4.67 (1H, t, *J* = 3 Hz); ^{13}C NMR (75 MHz; $CDCl_3$) δ 20.7, 22.3, 29.2, 52.6, 66.2, 77.2, 83.8, 170.4; IR (film) *v*: 3406, 2956, 2924, 2854, 2238, 1744, 1456, 1378, 1362, 1230, 1150, 1115, 1086, 1026, 966, 833, 606 cm^{-1}; HRMS (ESI) *m/z*; calcd for $C_7H_{10}NaO_3$ $[M+Na]^+$: 179.0684, found: 179.0553. $[\alpha]_D^{20}$ = +10.9 (*c* 1.0, $CHCl_3$), 99% *e.e.*

(*R*)-1,5-(bis-acetoxy)-2-hexyne (*R*)-(+)-9d. Obtained as a colourless oil, yield (0.18g) 46%. ^{1}HNMR (300 MHz; $CDCl_3$) δ 1.31 (3H, d, *J* = 6 Hz), 2.04 (3H, s), 2.09 (3H, s), 2.44-2.54 (2H, m), 4.65 (2H, t, *J* = 3 Hz), 4.98 (1H, sext, *J* = 6 Hz); ^{13}C NMR (75 MHz; $CDCl_3$) δ 19.1, 20.7, 21.2, 25.8, 52.5, 68.5, 76.1, 82.7, 170.3, 170.4; IR (film) *v*: 2955, 2924, 2854, 1744, 1458, 1376, 1224, 1154, 1131, 1061, 1023, 958, 831, 606 cm^{-1}; HRMS (ESI) *m/z*; calcd for $C_7H_{10}NaO_3$ $[M+Na]^+$: 221.0790, found: 221.0618; $[\alpha]_D^{20}$ = +31.0 (*c* 1.0, $CHCl_3$), 96% *e.e.*

(*S*)-1-(acetoxy)-3-hexyn-5-ol (*S*)-(-)-8e. Obtained as a colourless oil, yield (0.12g) 40%.^{1}HNMR (300 MHz; $CDCl_3$) δ. 1.4 (3H, d, *J* = 6 Hz), 2.05 (3H, s), 2.21 (1H, s), 2.52 (2H, td, *J* = 6 Hz), 4.13 (2H, t, *J* = 6 Hz), 4.43-4.55 (1H, m); ^{13}C NMR (75 MHz; $CDCl_3$) δ 19.1, 20.7, 24.4, 58.2, 62.2, 79.8, 83.8, 170.8; IR (film) *v*: 3409, 2973, 2923, 1735, 1376, 1241, 1154, 1076, 1042 cm^{-1}; HRMS (ESI) *m/z*; calcd for $C_8H_{12}NaO_3$ $[M+Na]^+$: 179.0684, found: 179.0403; CAS number 72132-21-9; $[\alpha]_D^{20}$ = -18.4 (*c* 1.0, $CHCl_3$); *e.e.* > 99%; lit. for (*R*)-enantiomer: $[\alpha]_D^{25}$ = +11.0 (*c 0.69*, $CHCl_3$)[17]

(*R*)-1,5-(bis-acetoxy)-3-hexyne (*R*)-(+)-9e. Obtained as a colourless oil, yield (0.17g) 44%. ^{1}HNMR (300 MHz; $CDCl_3$, ppm): δ 1.42 (3H, d, *J* = 6 Hz), 2.04 (6H, s), 2.52 (2H, td, *J* = 6 Hz), 4.12 (2H, t, *J* = 6 Hz), 5.4 (1H, qt, *J* = 6 Hz). ^{13}C NMR (75 MHz; $CDCl_3$) δ 19.1, 20.7, 21.1, 21.4, 60.4, 61.9, 80.1, 80.7, 169.8, 170.6; IR (film) *v*: 2926, 2860, 2251, 1740, 1445, 1374, 1234, 1169, 1050, 948, 848, 644, 608, 523 cm^{-1}; HRMS (ESI) *m/z*; calcd for $C_{10}H_{14}NaO_4$ $[M+Na]^+$: 221.0790, found: 221.0655; $[\alpha]_D^{20}$ = +95.4 (*c* 1.0, $CHCl_3$), 99% *e.e.*

(*S*)-1-(acetoxy)-3-heptyne-5-ol (*S*)-(-)-8f. Obtained as a colourless oil, yield (0.15g) 45%.^{1}H NMR (300 MHz; $CDCl_3$) δ 0.98 (3H, t, *J* = 6 Hz), 1.6-1.75 (2H, m), 2.2 (1H, m), 2.05 (3H, s), 2.54 (2H, td, *J* = 6 Hz), 4.14 (2H, t, *J* = 6 Hz), 4.28 (1H, m); ^{13}C NMR (75 MHz; $CDCl_3$) δ 9.3, 19.1, 20.8, 30.9, 62.2, 63.7, 80.7, 82.7, 170.8; IR (film) *v*: 3419, 2968, 2931, 2877, 1736, 1453, 1426, 1378, 1241, 1148, 1041, 967, 606 cm^{-1}; HRMS (ESI) *m/z*; calcd for $C_9H_{14}NaO_3$ $[M+Na]^+$: 193.0841, found: 193.0427; $[\alpha]_D^{20}$ = -2.6 (*c* 1.0, $CHCl_3$), 85% e.e.

(*R*)-1,5-(bis-acetoxy)-3-heptyne (*R*)-(+)-9f.Obtained as a colourless oil, yield (0.20g) 48%.^{1}H NMR (300 MHz; $CDCl_3$) δ 0.97 (3H, t, *J* = 7 Hz), 1.73 (2H, quint, *J* = 7 Hz), 2.04 (3H, s), 2.05 (3H, s), 2.54 (2H, td, *J* = 6 Hz), 4.13 (2H, t, *J* = 6 Hz), 5.27 (1H, tt, *J* = 7 Hz); ^{13}C NMR (75 MHz; $CDCl_3$) δ 9.2, 19.1, 20.7, 20.9, 28.0, 62.4, 65.3, 79.0, 81.4, 169.9, 170.6. IR (film) *v*: 2970, 2936, 1741, 1453, 1374, 1233, 1165, 1037, 965, 893, 606 cm^{-1}; HRMS (ESI) *m/z*; calcd for $C_{11}H_{16}NaO_4$ $[M+Na]^+$: 235.0946, found: 235.0628; $[\alpha]_D^{20}$ = +94.0 (*c* 1.0, $CHCl_3$), 99% *e.e.*

(*S*)-1-(acetoxy)-6-methyl-3-hepyne-5-ol (*S*)-(+)-8g. Obtained as a colourless oil, yield (0.14g) 42%.^{1}HNMR (300 MHz; $CDCl_3$) δ 1.22 (3H, d, *J* = 6 Hz), 2.06 (3H, s), 2.19-2.43 (2H, m), 2.5 (2H, tt, *J* = 6 Hz), 3.99 (1H, sext, *J* = 6 Hz), 4.14 (2H, t, *J* = 6 Hz); ^{13}C NMR (75 MHz; $CDCl_3$) δ 19.2, 20.8, 22.1, 29.2, 62.5, 66.3, 78.1, 78.4, 170.9; IR (film) *v*: 3421, 2962, 2921, 2860, 1735, 1454, 1376, 1239, 1114, 1041, 939, 824, 641, 608 cm^{-1}; HRMS (ESI) *m/z*; calcd for $C_9H_{14}NaO_3$ $[M+Na]^+$: 193.0841, found: 193.0443; . $[\alpha]_D^{20}$ = +11.6 (*c* 1.0, $CHCl_3$), > 99% e.e.

(*R*)-1,5-(bis-acetoxy)-6-methyl-3-heptyne (*R*)-(+)-9g. Obtained as a colourless oil, yield (0.2g) 48%.^{1}HNMR (300 MHz; $CDCl_3$) δ 1.28 (3H, d, *J* = 6 Hz), 2.02 (3H, s), 2.04 (3H, s), 2.35-2.42 (2H, m), 2.43-2.51 (2H, m), 4.11 (2H, t, *J* = 6 Hz), 4.93 (1H, sext, *J* = 6 Hz); ^{13}C NMR (75 MHz; $CDCl_3$) δ 19.0, 19.1, 20.7, 21.1, 25.7, 62.5, 68.9, 77.1, 77.8, 170.3, 170.7; IR (film) *v*: 2970, 2926, 2863, 1739, 1443, 1375, 1239, 1136, 1048, 961, 641, 607 cm^{-1}; HRMS (ESI) *m/z*; calcd for $C_{11}H_{16}NaO_4$ $[M+Na]^+$: 235.0946, found: 235.0396. $[\alpha]_D^{20}$ = +19.0 (*c* 1.0, $CHCl_3$), 95% *e.e.*

(*R*)-5-(acetoxy)-2,6-dimethyl-3-heptyn-2-ol (*R*)-(+)-8h. Obtained as a colourless oil, yield (0.17g) 44%.^{1}HNMR (300 MHz; $CDCl_3$) δ 1.0 (6H, d, *J* = 6 Hz), 1.52 (6H, s), 1.99 (1H, oct, *J* = 6 Hz), 2.09 (3H, s), 2.62 (1H, s), 5.24 (1H, d, *J* = 6 Hz). ^{13}C NMR (75 MHz; $CDCl_3$) δ 17.4, 18.1, 31.2, 32.3, 65.4, 68.8, , 78.1, 90.6, 170.1. IR (film) cm^{-1}: 3429,

2976, 2932, 2875, 1740, 1467, 1372, 1229, 1170, 1021, 982, 956, 900, 863, 716, 607. HRMS (ESI) *m/z*; calcd for $C_8H_{14}NaO_2$ $[M+Na]^+$: 221.1154, found: 221.0964. $[\alpha]_D^{20}$ = +99.7 (*c* 1.0, $CHCl_3$), 98% *e.e.*

(*S*)-2,6-dimethyl-hept-3-yne-2,5-diol (*S*)-(+)-1h. Obtained as a colourless oil, yield (0.15g) 48%. Oil; yield: conversão 50% (0,23g); ^{1}H NMR (300 MHz; $CDCl_3$) δ 0.98 (6H, dd, *J* = 6 Hz), 1.51 (6H, s), 1.85 (1H, oct, *J* = 6 Hz), 3.18 (2H, s), 4.16 (1H, d, *J* = 6 Hz). ^{13}C NMR (75 MHz; $CDCl_3$) δ 17.4, 18.1, 31.2, 31.3, 34.3, 64.9, 67.5, 81.7, 90.2. IR (film) cm^{-1}: 3345, 2962, 2930, 2873, 1640, 1461, 1378, 1365, 1328, 1235, 1166, 1021, 952, 861, 827, 802, 717. HRMS (ESI) *m/z*; calcd for $C_8H_{14}NaO_2$ $[M+Na]^+$: 179.1048, found: 179.0638; CAS number 321903-25-7$[\alpha]_D^{20}$ = +1.3 (*c* 1.0, $CHCl_3$), 99% e.e; $^{Lit}[\alpha]_D^{31}$ = +1.83 (*c* 0.77, $CHCl_3$), 98% *e.e.* for (*S*)-(+)-**1h**[18]

General procedure for the hydrogenation/hydrolysis sequence of compounds (*S*)-8d, (*R*)-9d,(*S*)-8f, (*R*)-9f,(*S*)-8h and (*R*)-9h

To a round bottomed flask containing a solution of propargylic acetate (1.0 mmol) in MeOH (5 mL), at room temperature, were added 10 mg of Pd/C catalyst in on portion. To the mix was coupled an atmosphere of H_2 (1 atm) and was allowed to react overnight. The suspension was filtered off on silica and the organic solvent removed by evaporation in a rotary evaporator under vacuum. Then, the crude was subjected to hydrolysis reaction in the presence of K_2CO_3 in MeOH. The residue was purified by chromatography on silica gel using a mix of *n*-hexane/ethyl acetate (2:1) as eluent.

(*R*)-**10d** from (*R*)-**9d**: $^{Exp}[\alpha]_D^{20}$ = -9.7 (c 1.0, MeOH);
(*S*)-**10d** from (*S*)-**8d**: $^{Exp}[\alpha]_D^{20}$ = +7.6 (c 1.3, MeOH);
$^{Lit}[\alpha]_D^{25}$ = -11 (c 0.41, MeOH) for (*R*)-1,5-hexanediol.[19]

(*R*)-**10f** from (*R*)-**9f**: $^{Exp}[\alpha]_D^{20}$ = -5.5 (c 1.3, $CHCl_3$);
(*S*)-**10f** from (*S*)-**8f**: $^{Exp}[\alpha]_D^{20}$ = +2.4 (c 1.0, $CHCl_3$);
$^{Lit}[\alpha]_D^{23}$ = + 11.2 (c 1.02, MeOH) for (*S*)-1,5-heptanediol.[20]

(*R*)-**10g** from (*R*)-**9g**: $^{Exp}[\alpha]_D^{20}$ = -8.1 (c 1.0, MeOH);
(*S*)-**10g** from (*S*)-**8g**: $^{Exp}[\alpha]_D^{20}$ = +9.2 (c 1.0, MeOH);
$^{Lit}[\alpha]_D^{25}$ = -7.6 (c 0.74, MeOH) for (*R*)-1,6-heptanediol.[21]

General procedure to prepare the bis-acetates 9a-h

To a round bottomed flask containing the propargylic diol (1 mmol) in DCM (2 mL) at room temperature using dry N_2 atmosphere under stirring, acetic anhydride (2.5 mmol) and Et_3N (5 mmol) were added. After stirring the solution at same temperature for 30 min the crude reaction was quenched saturated solution of $NaHCO_3$ (1 mL) and the phases separated. The aqueous phase was extracted twice with DCM (2 x 2 mL) washed with brine, dried with magnesium sulphate, filtered off and the solvent removed in a rotary evaporator under vacuum. The crude was purified by chromatography on silica gel using a mix of *n*-hexane/ethyl acetate (10:1) as eluent.
The spectroscopic data found for racemic acetates are in agreement with those found for the biotransformed products.

***(R/S)*-1,4-(Bis-acetoxy)-2-pentyne (9a).** Obtained as a colourless oil, yield (0.17g) 92%.CAS number 50625-86-0

(R/S)-1,4-(bis-acetoxy)-2-hexyne (9b). Obtained as a colourless oil, yield (0.19g) 95%.

***(R/S)*- 1,4-(bis-acetoxy)-5-methyl-hexyne (9c).** Obtained as a colourless oil, yield (0.19g) 91%**.** CAS number 111480-80-9

***(R/S)*-1,5-(bis-acetoxy)-2-hexyne (9d).** Obtained as a colourless oil, yield (0.17g) 88%.

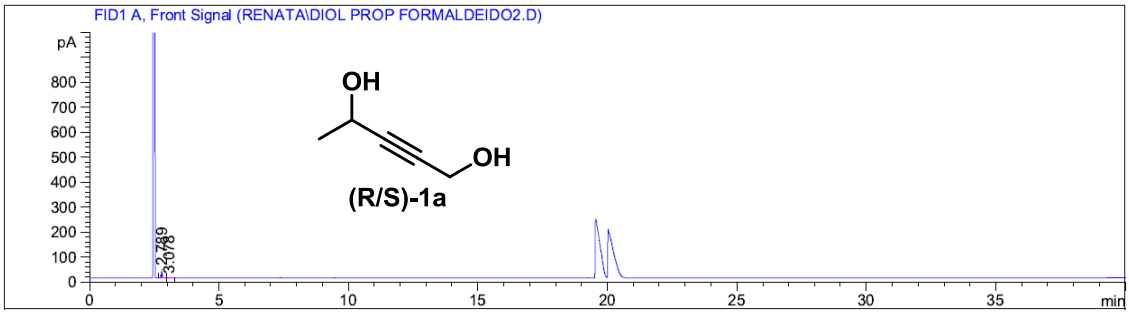
***(R/S)*-1,5-(bis-acetoxy)-3-hexyne (9e).** Obtained as a colourless oil, yield (0.16g) 83%.

***(R/S)*-1,5-(bis-acetoxy)-3-heptyne (9f).**Obtained as a colourless oil, yield (0.21g) 99%.

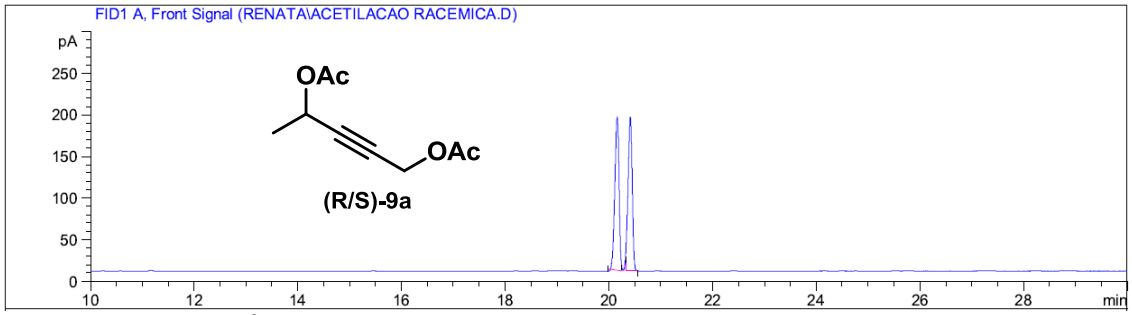
***(R/S)*-1,5-(bis-acetoxy)-6-methyl-3-heptyne (9g).** Obtained as a colourless oil, yield (0.18g) 85%.

GC Analysis on Chiral Column

The enantiomeric excess of bis-acetoxy alkynes were determined by comparing the pre-injected racemic bis-acetoxy standards, prepared previously as described above, with the biotransformed products on a GC/FID equipped with a chiral column. The conditions for chiral GC analyses as well as Chromatograms are shown below:

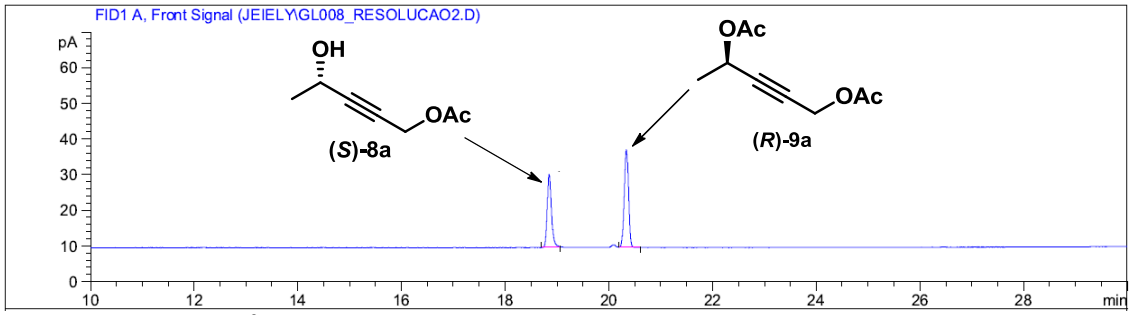


Conditions: Rate 100-180°C at 2ºC/min, 10 psi; t_R1 = 19.8 min, t_R2 = 20.2 min.

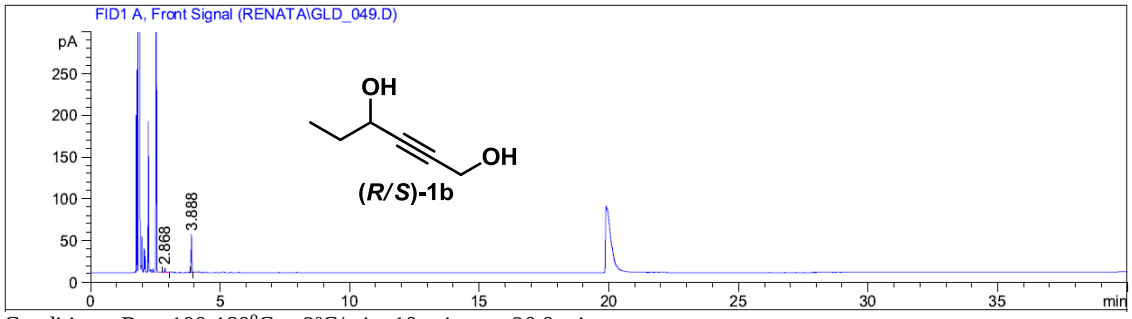


Conditions: Rate 100-180°C at 2ºC/min, 10 psi; t_R1 = 20.1 min, t_R2 = 20.4 min.

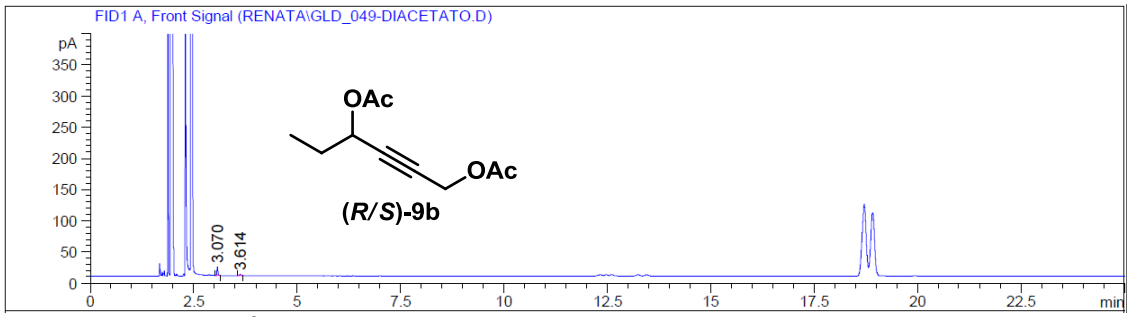
EKR of racemic 1a



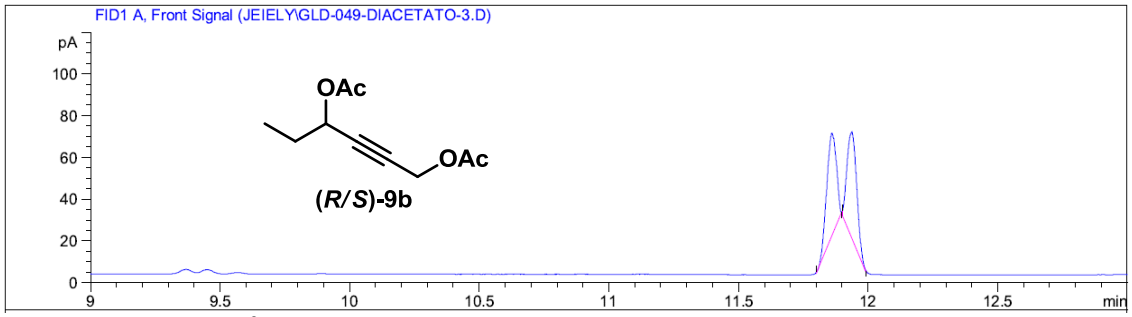
Conditions: Rate 100-180°C at 2ºC/min, 10 psi; t_R1 = 18.9 min, t_R2 = 20.4 min.



Conditions: Rate 100-180°C at 2ºC/min, 10 psi; t_R = 20.0 min.

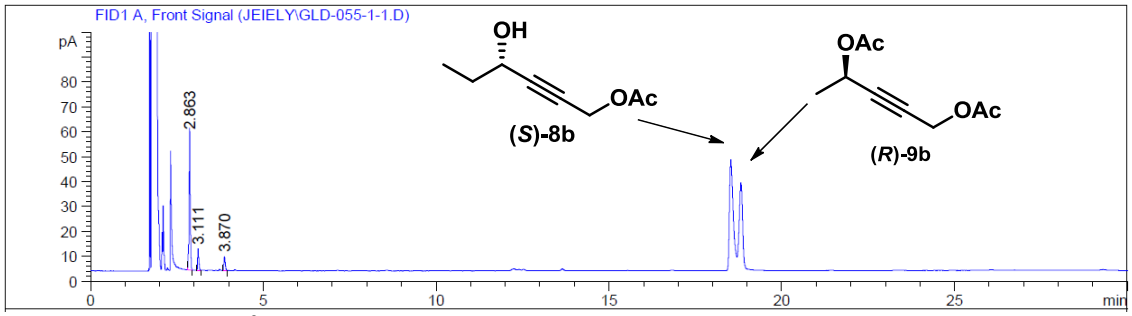


Conditions: Rate 100-180°C at 2ºC/min, 10 psi; t_R1 = 18.6 min, t_R2 = 18.9 min.

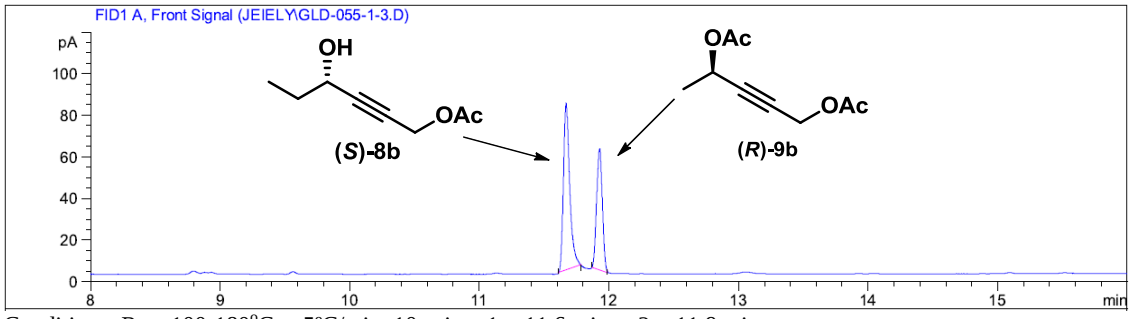


Conditions: Rate 100-180°C at 5ºC/min, 10 psi; t_R1 = 11.8 min, t_R2 = 11.9 min.

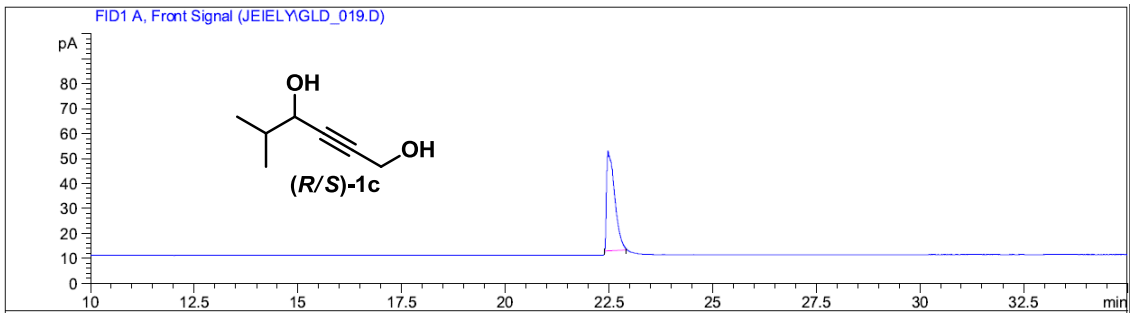
EKR of racemic 1b



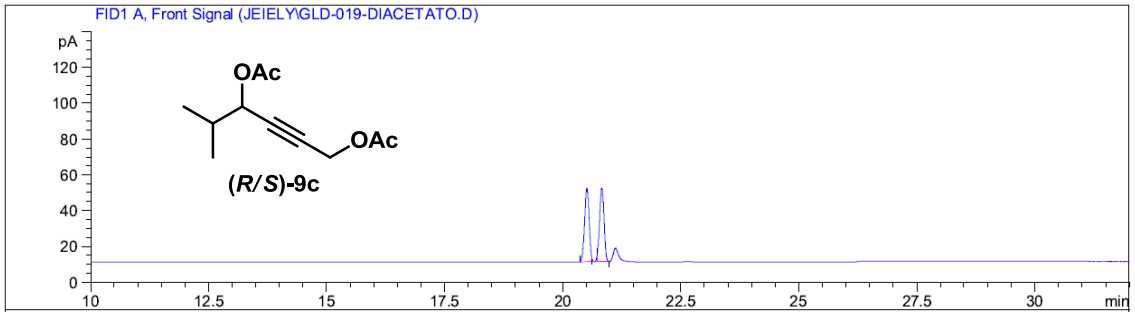
Conditions: Rate 100-180°C at 2ºC/min, 10 psi; t_R1 = 18.5 min, t_R2 = 18.9 min.



Conditions: Rate 100-180°C at 5ºC/min, 10 psi; t_R1 = 11.6 min, t_R2 = 11.9 min.

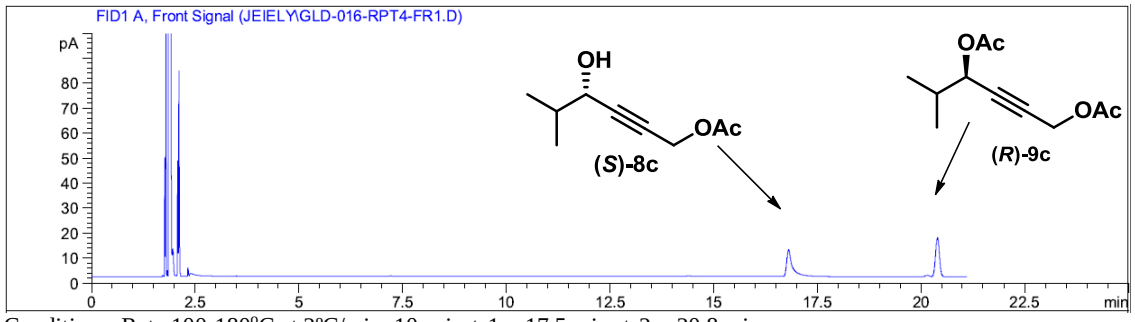


Conditions: Rate 100-180°C at 2°C/min, 10 psi; t_R = 22.4 min.

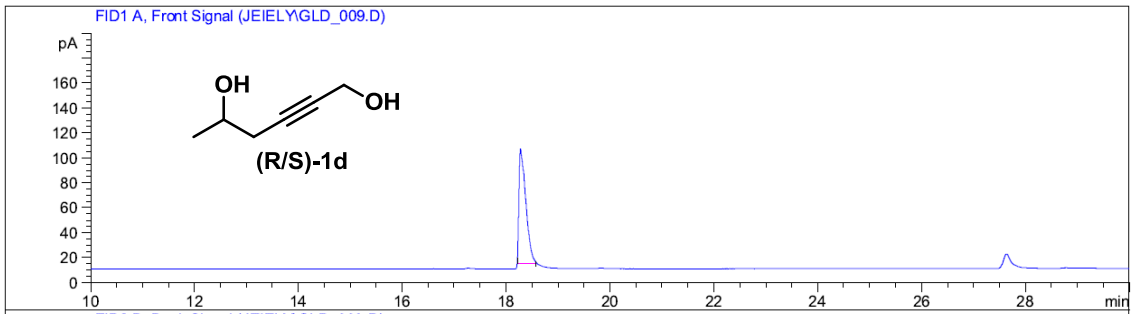


Conditions: Rate 100-180°C at 2°C/min, 10 psi; t_R1 = 20.5 min, t_R2 = 20.8 min.

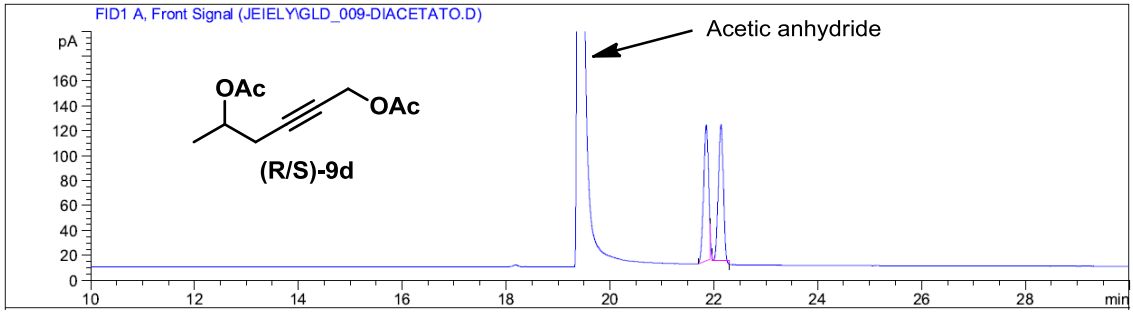
EKR of racemic 1c



Conditions: Rate 100-180°C at 2°C/min, 10 psi; t_R1 = 17.5 min, t_R2 = 20.8 min.

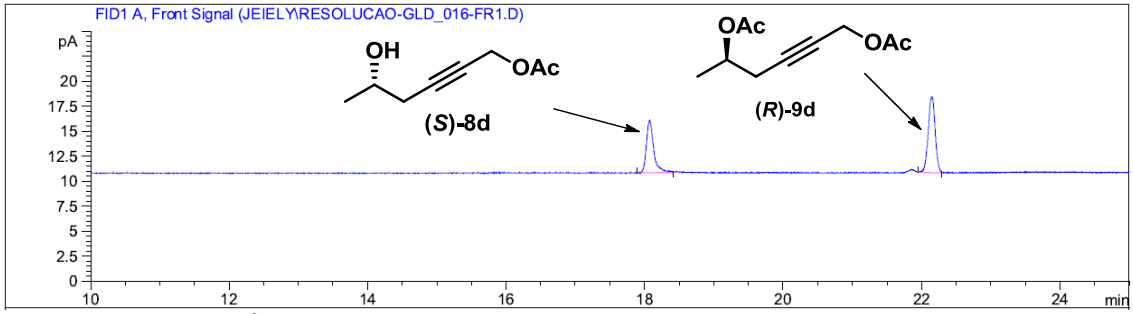


Conditions: Rate 100-180°C at 2ºC/min, 10 psi; t_R = 18.2 min.

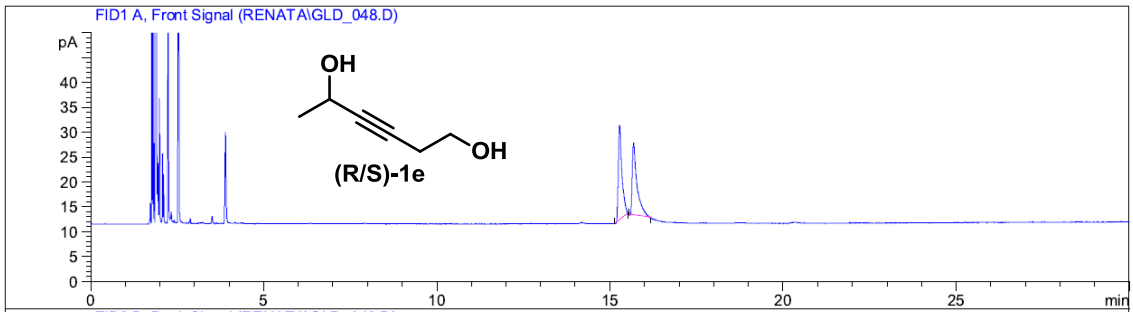


Conditions: Rate 100-180°C at 2ºC/min, 10 psi; t_R1 = 21.8 min, t_R2 = 22.1 min.

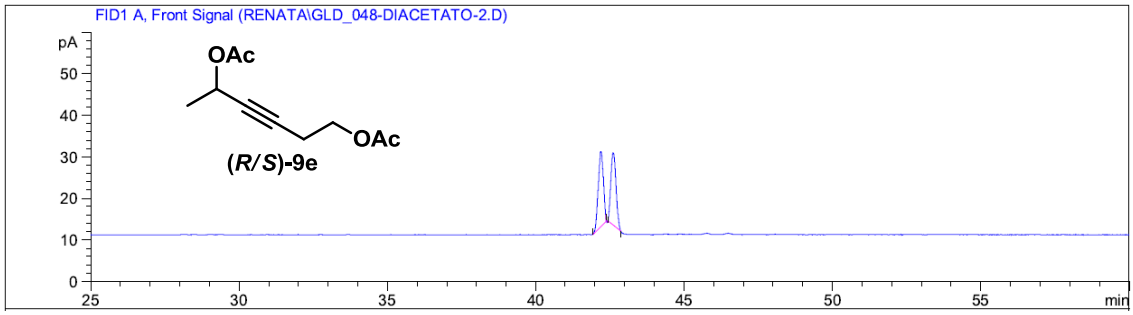
EKR of racemic 1d



Conditions: Rate 100-180°C at 2ºC/min, 10 psi; t_R1 = 18.0 min, t_R2 = 22.1 min.

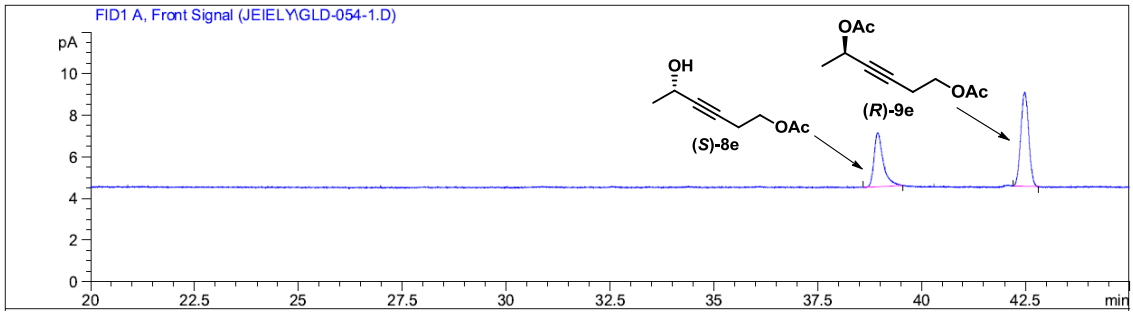


Conditions: Rate 100-180°C at 2ºC/min, 10 psi; t_R1 = 15.2 min, t_R2 = 15.7 min.

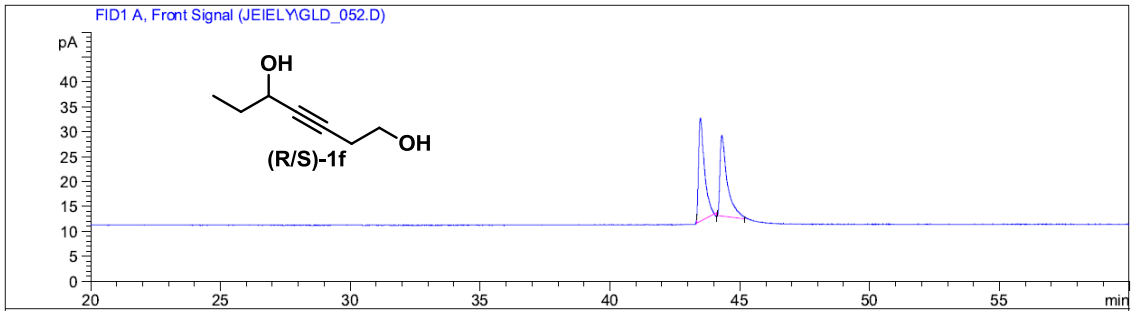


Conditions: Rate 100-180°C at 2ºC/min, 10 psi; t_R1 = 42.2 min, t_R2 = 42.6 min.

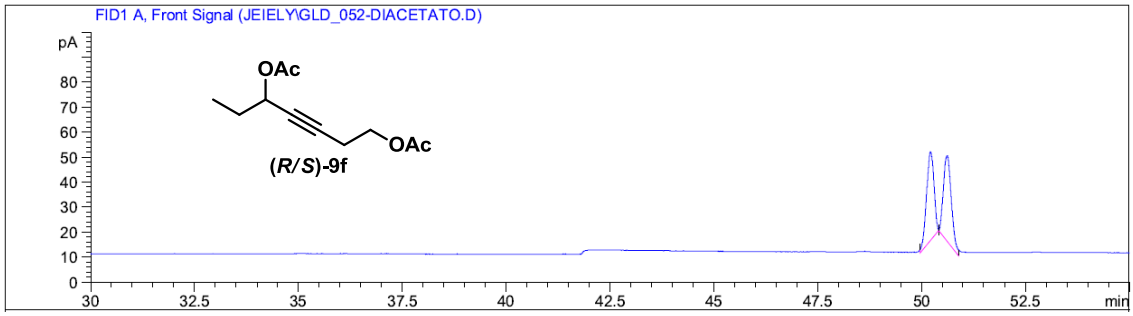
EKR of racemic 1e



Conditions: Rate 100-180°C at 2ºC/min, 10 psi; t_R1 = 38.9 min, t_R2 = 42.6 min.

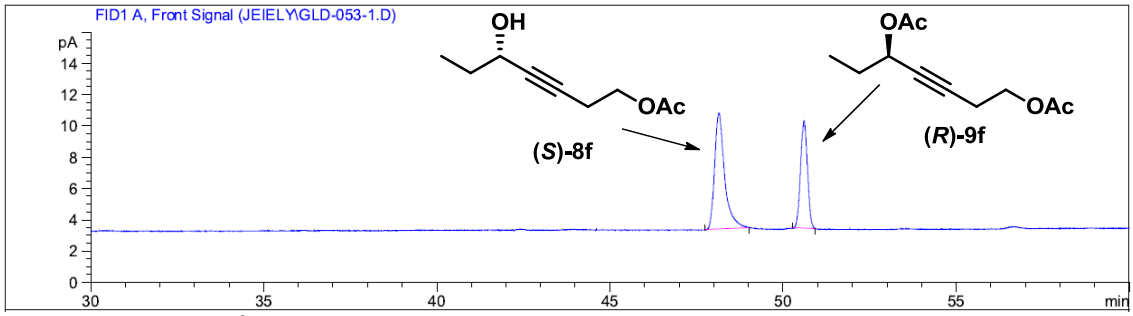


Conditions: Rate 80-160°C at 1°C/min, 10 psi; t_R1 = 43.4 min, t_R2 = 44.3 min.

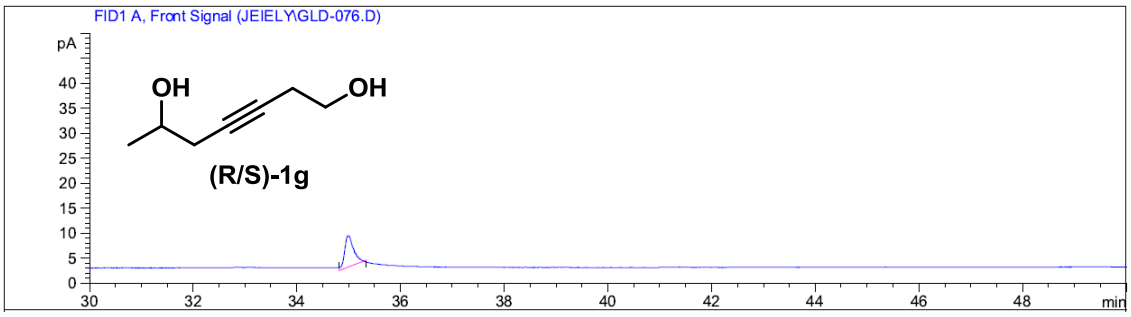


Conditions: Rate 80-160°C at 1°C/min, 10 psi; t_R1 = 50.2 min, t_R2 = 50.6 min.

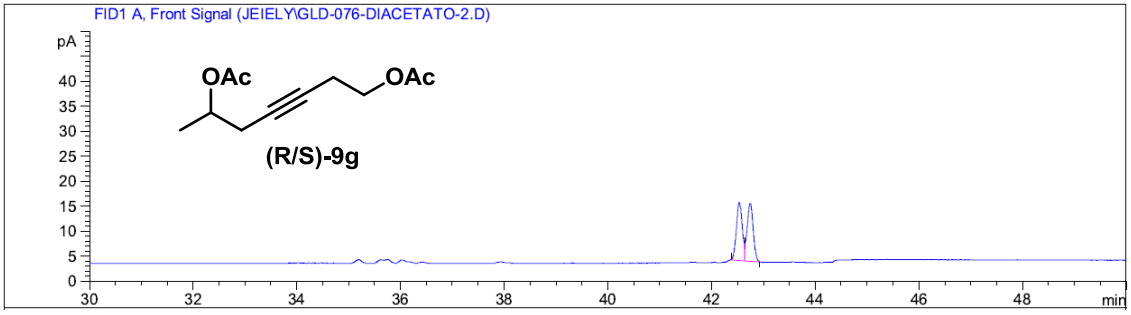
EKR of racemic 1f



Conditions: Rate 80-160°C at 1°C/min, 10 psi; t_R1 = 48.1 min, t_R2 = 50.6 min.

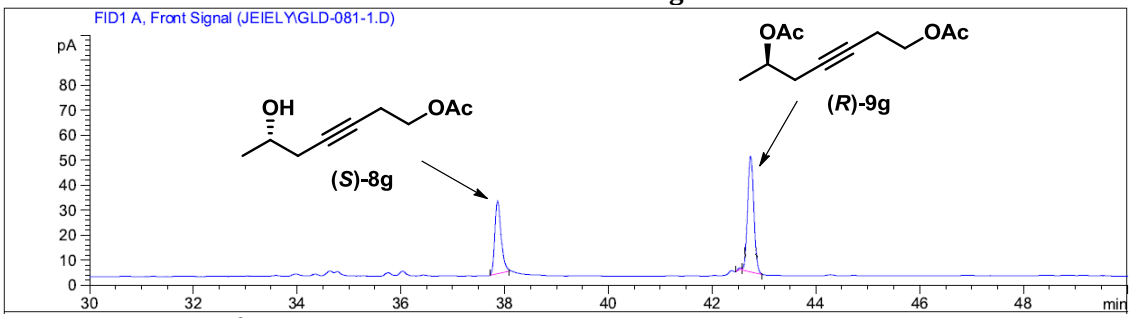


Conditions: Rate 80-180°C at 1ºC/min, 10 psi; t_R = 34.9 min.

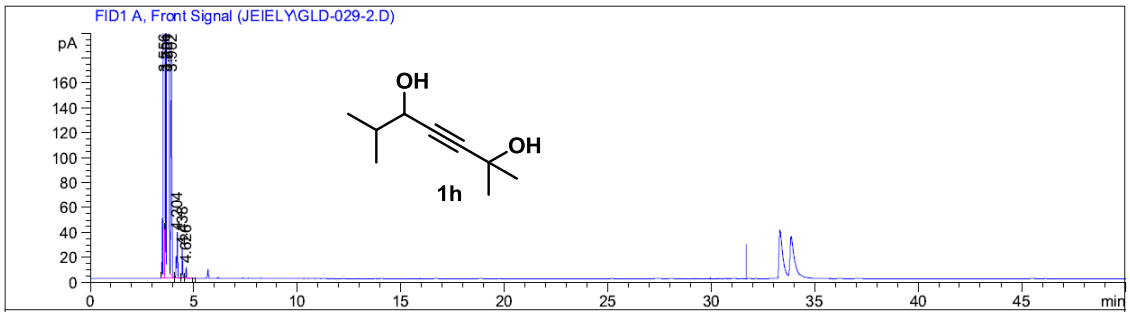


Conditions: Rate 80-180°C at 1ºC/min, 10 psi; t_R1 = 42.5 min, t_R2 = 42.7 min.

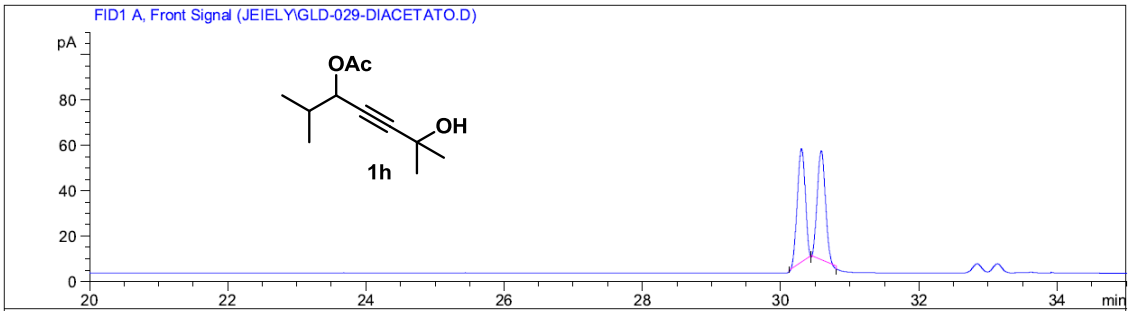
EKR of racemic 1g



Conditions: Rate 80-180°C at 1ºC/min, 10 psi; t_R1 = 37.8 min, t_R2 = 42.7 min.

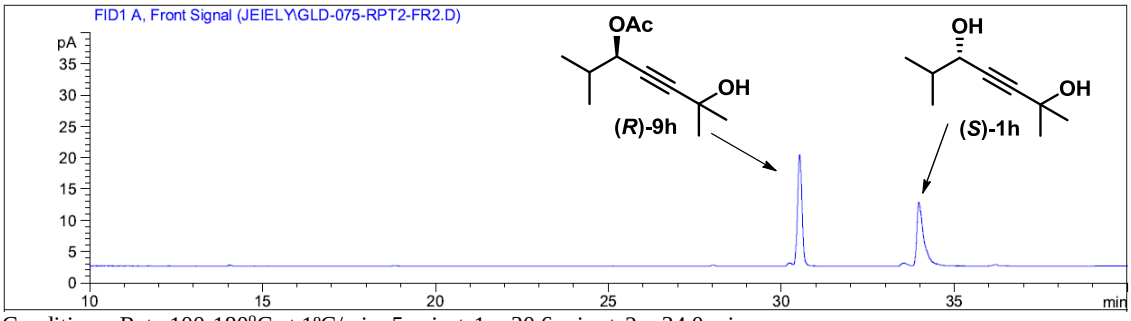


Conditions: Rate 100-180°C at 1°C/min, 5 psi; t_R1 = 33.5 min, t_R2 = 34.0 min.



Conditions: Rate 100-180°C at 1°C/min, 5 psi; t_R1 = 30.2 min, t_R2 = 30.6 min.

EKR of racemic 1h



Conditions: Rate 100-180°C at 1°C/min, 5 psi; t_R1 = 30.6 min, t_R2 = 34.0 min.

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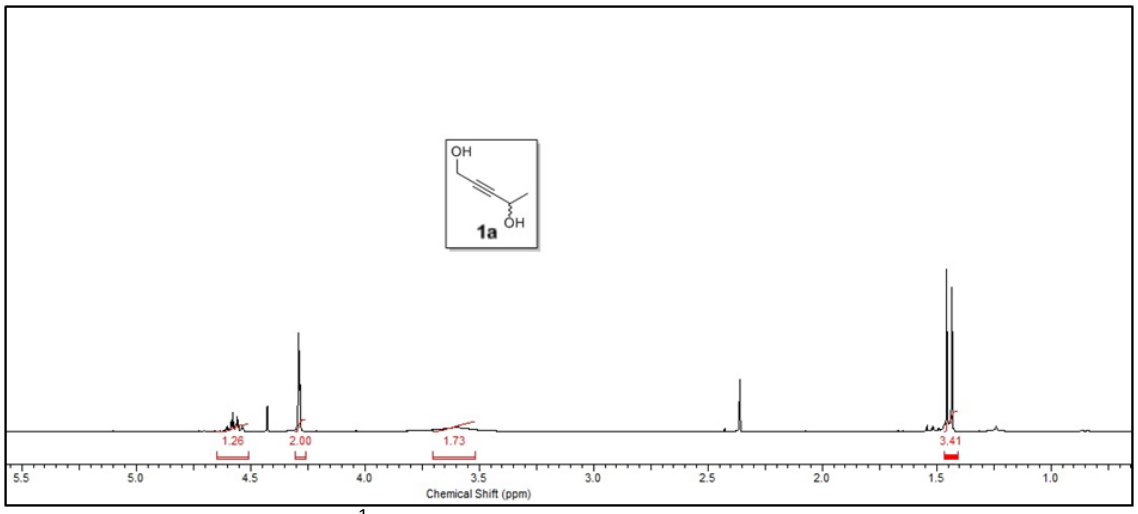
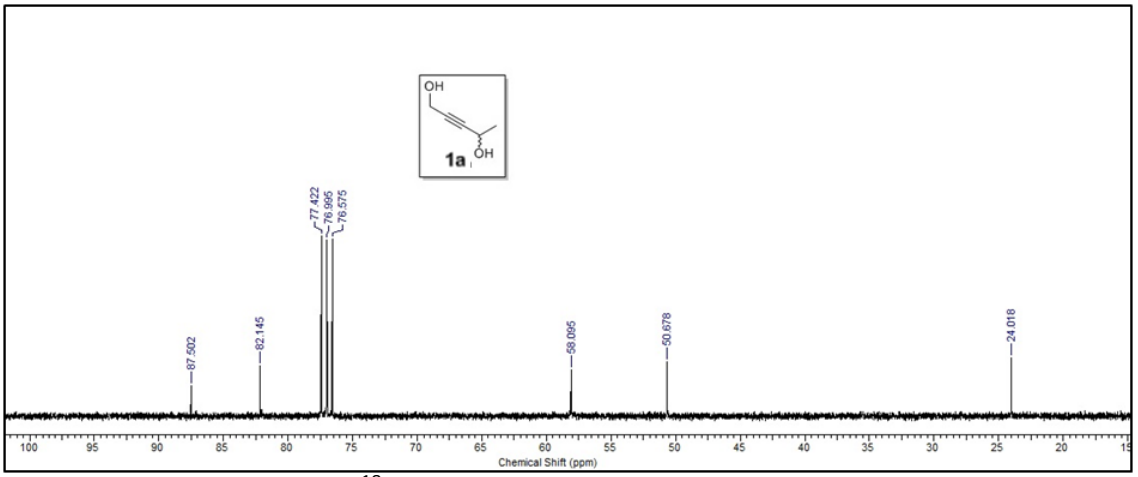
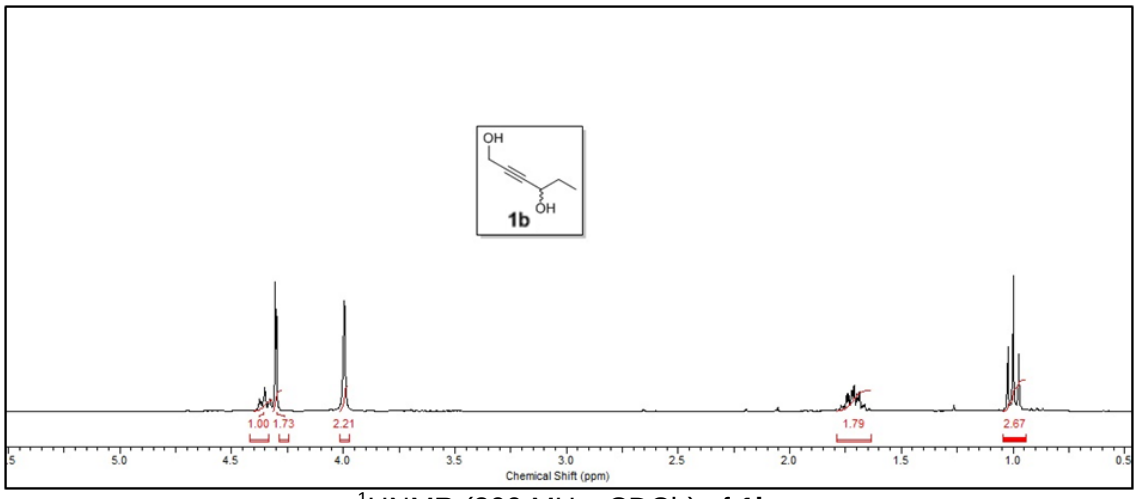


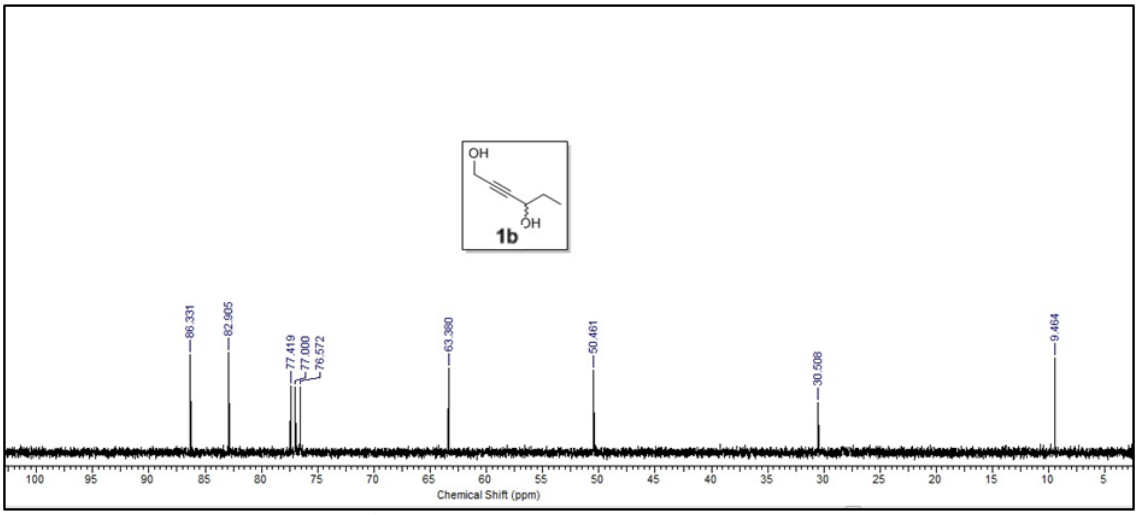
^{1}HNMR (300 MHz, $CDCl_3$) of **1a**.



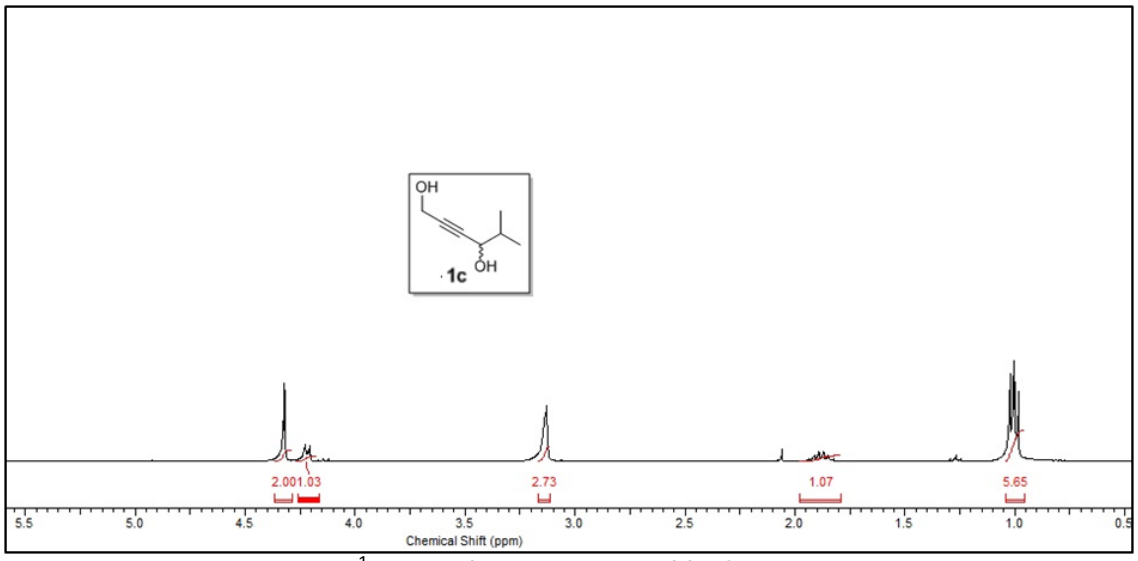
^{13}CNMR (75 MHz, $CDCl_3$) of **1a**.



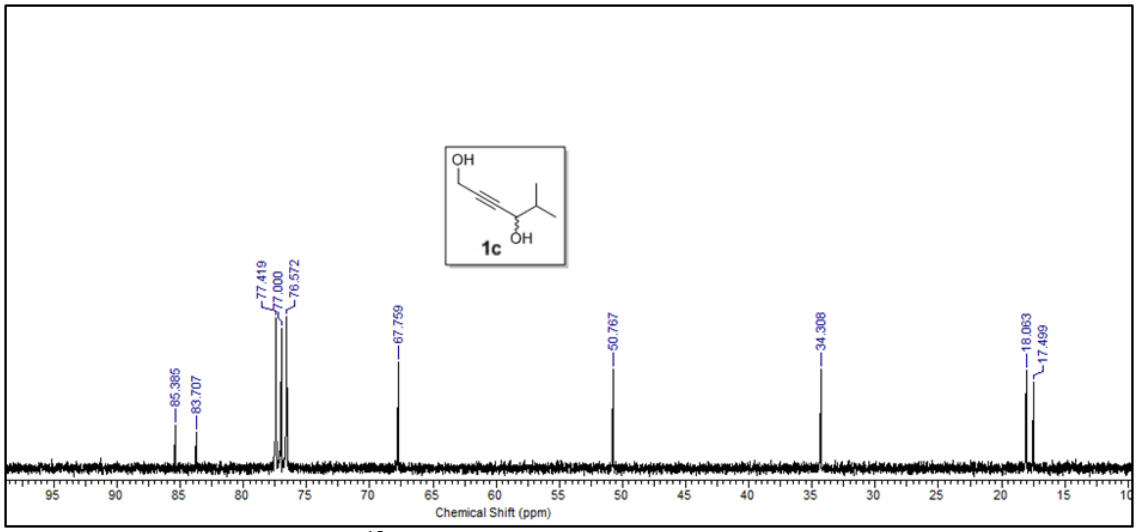
^{1}HNMR (300 MHz, $CDCl_3$) of **1b**.



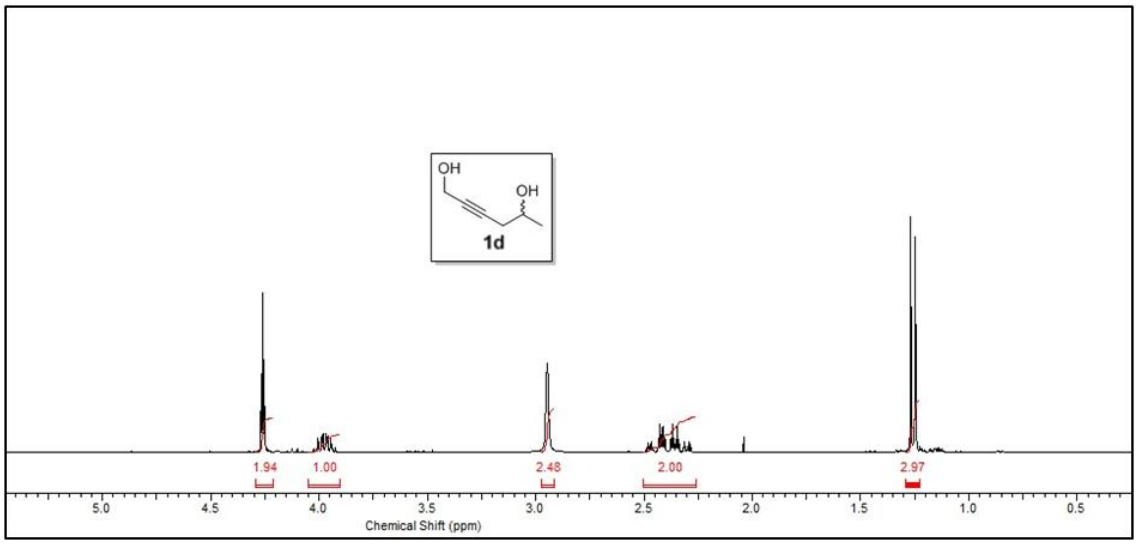
^{13}CNMR (75 MHz, $CDCl_3$) of **1b**.



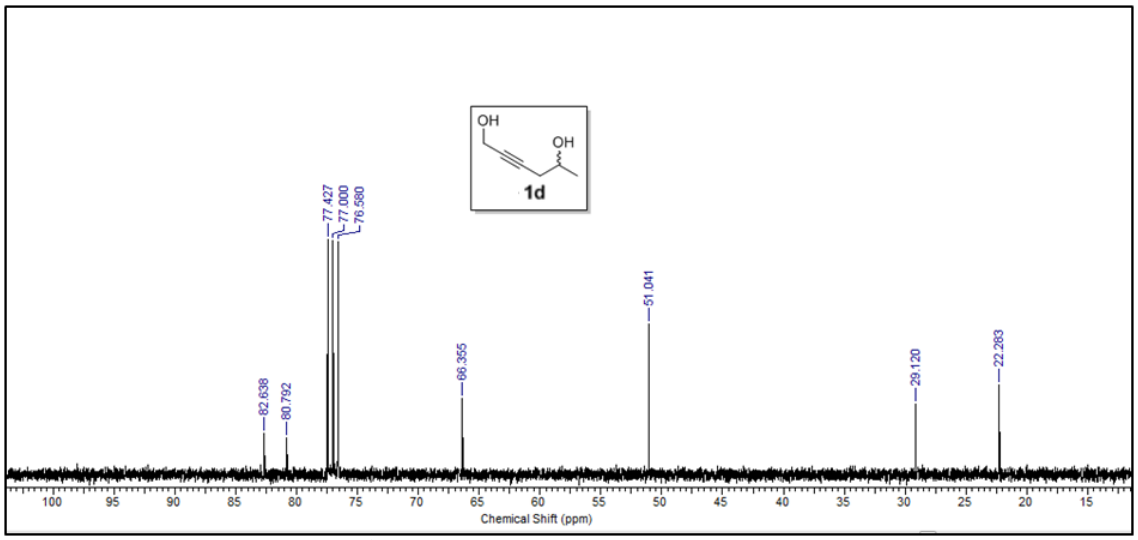
^{1}HNMR (300 MHz, $CDCl_3$) of **1c**.



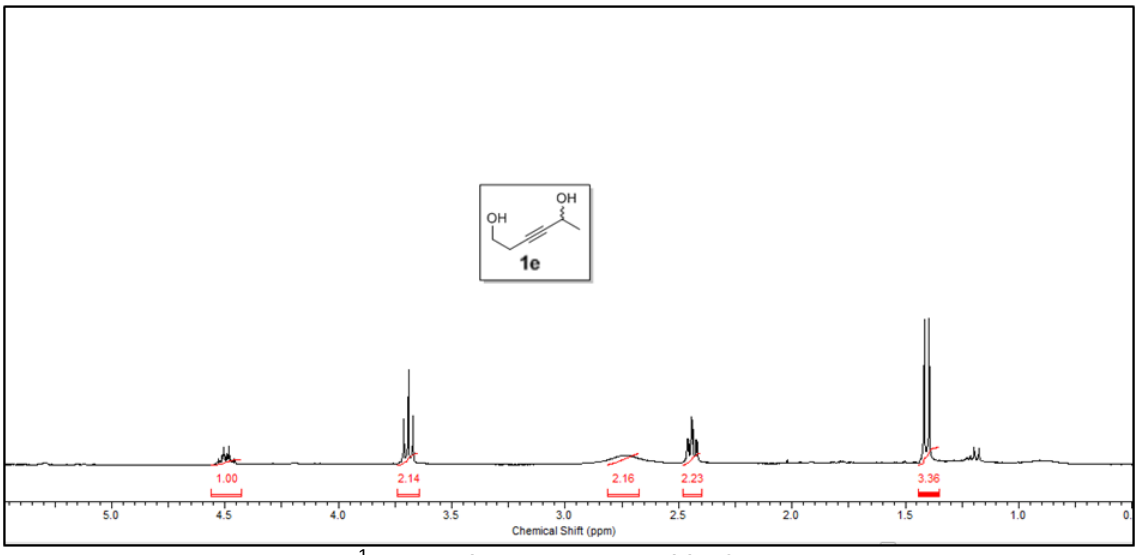
^{13}CNMR (75 MHz, $CDCl_3$)of **1c**.



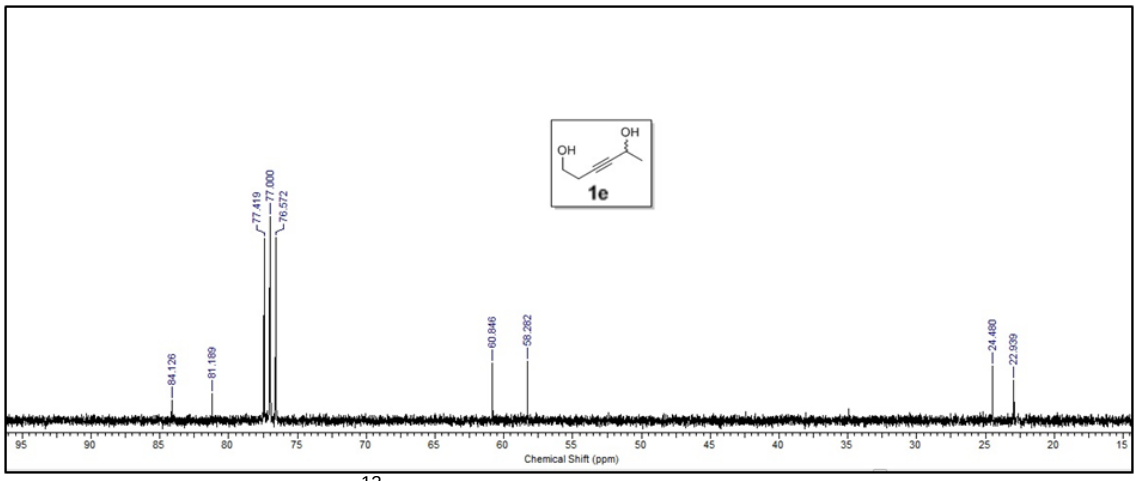
^{1}HNMR (300 MHz, $CDCl_3$) of **1d**.



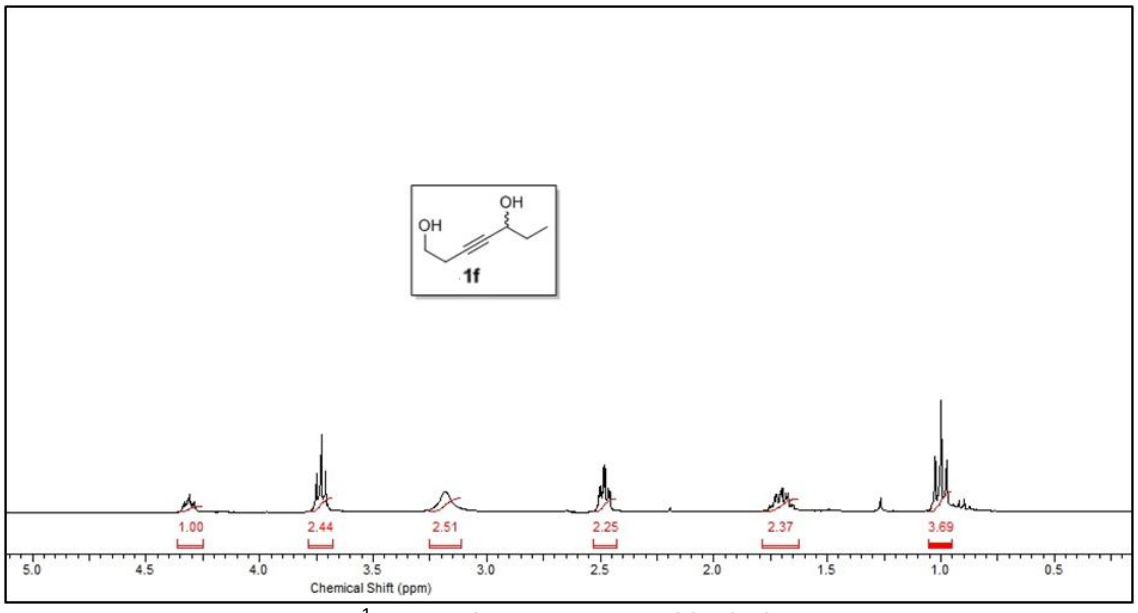
^{13}CNMR (75 MHz, $CDCl_3$) of **1d**.



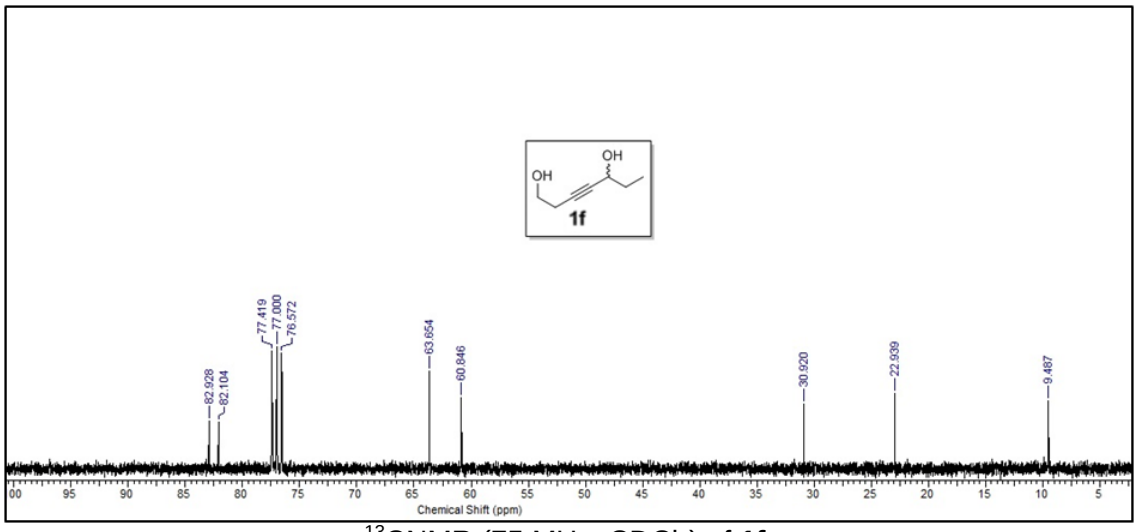
^{1}HNMR (300 MHz, $CDCl_3$) of **1e**.



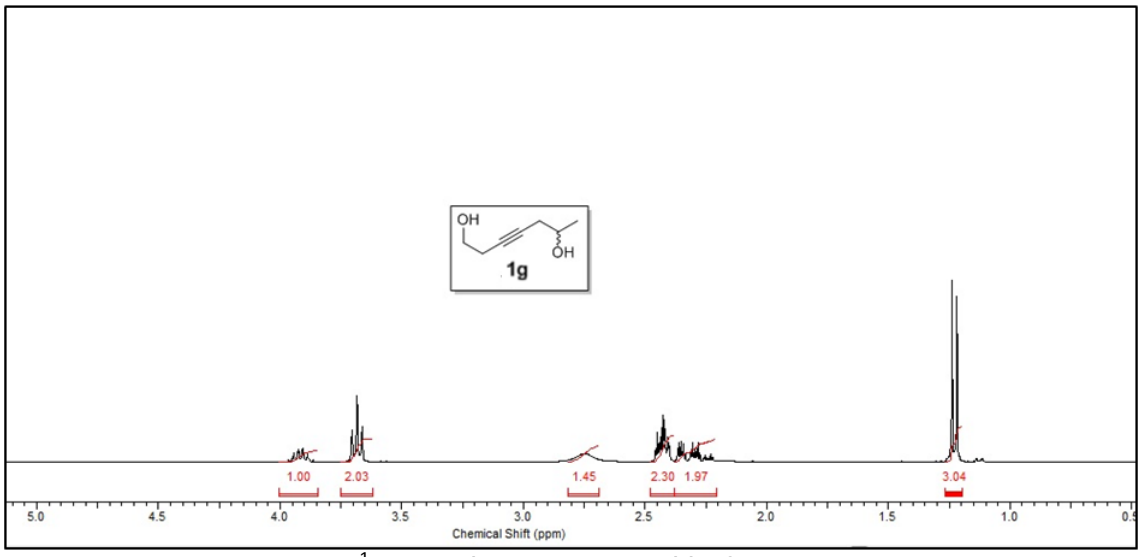
^{13}CNMR (75 MHz, $CDCl_3$) of **1e**.



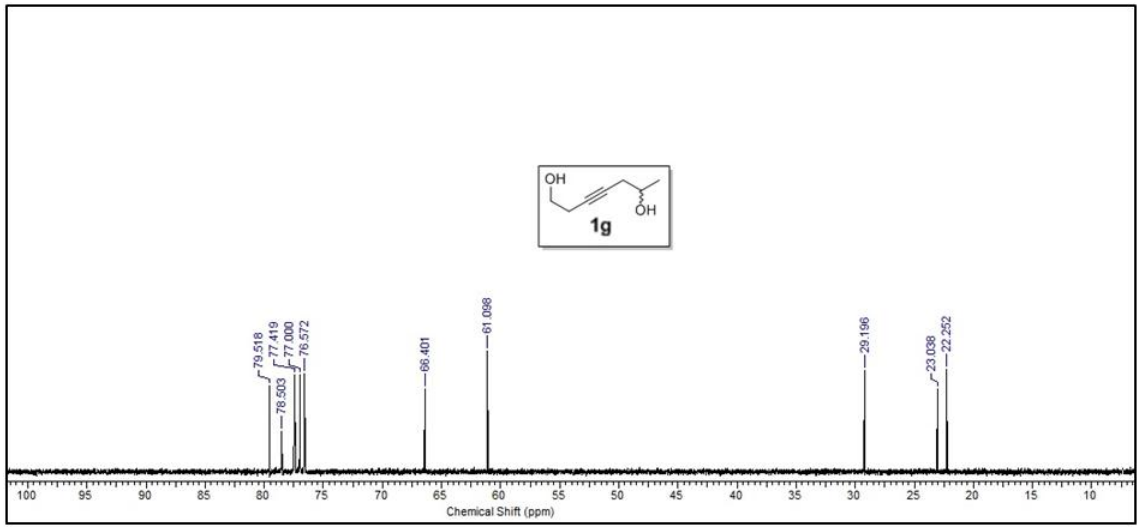
^{1}HNMR (300 MHz, $CDCl_3$) of **1f**.



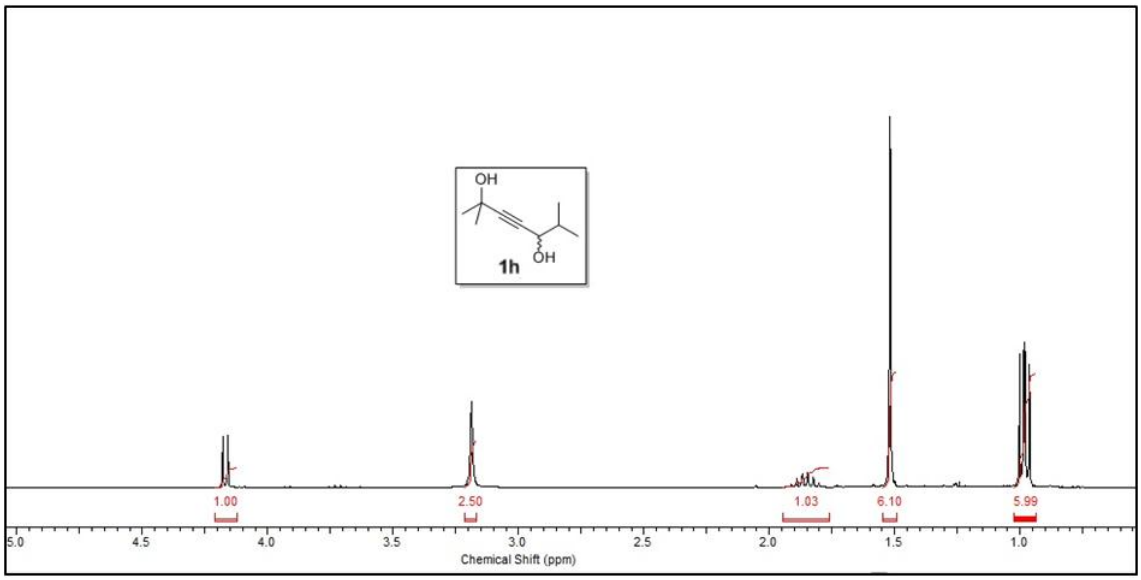
^{13}CNMR (75 MHz, $CDCl_3$) of **1f**.



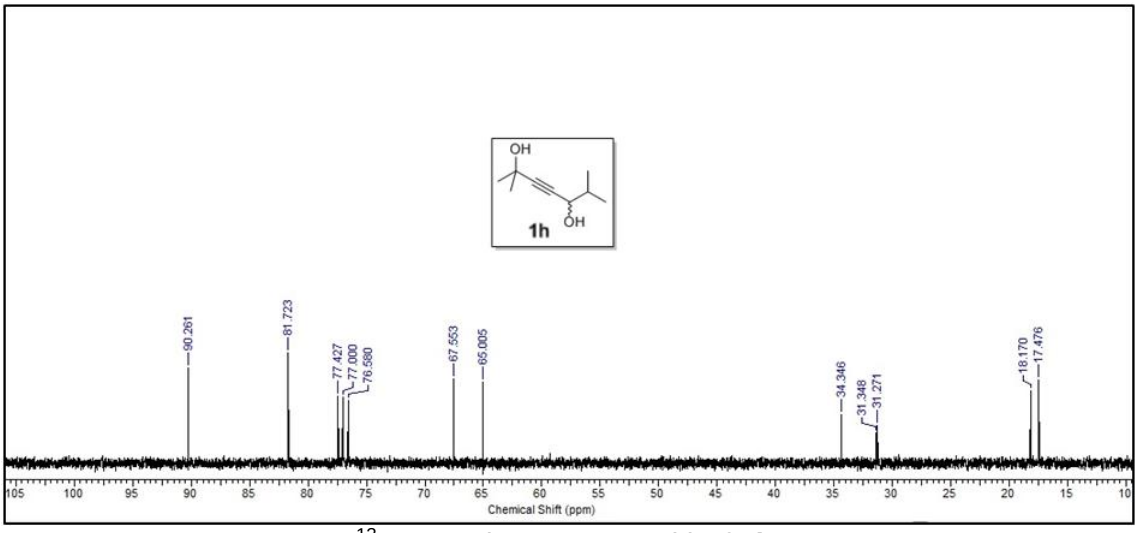
^{1}HNMR (300 MHz, $CDCl_3$) of **1g.**



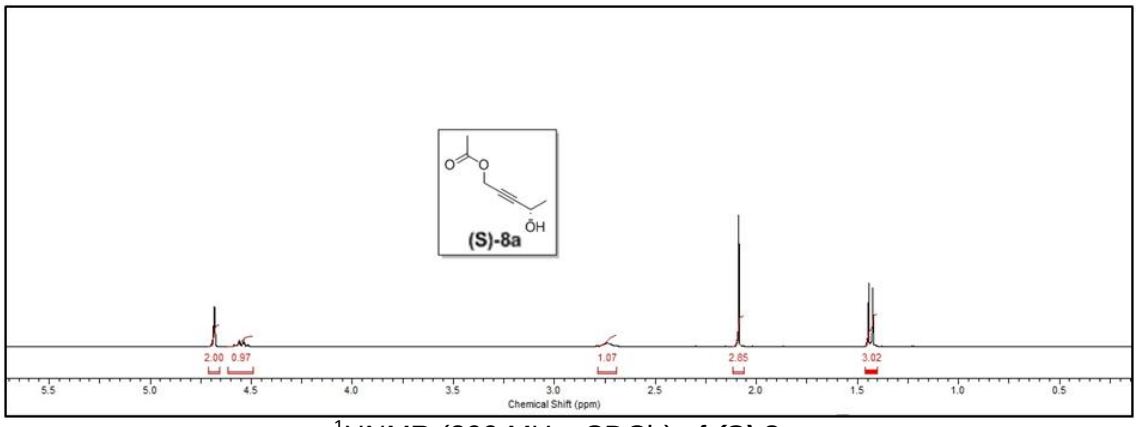
^{13}CNMR (75 MHz, $CDCl_3$) of **1g**.



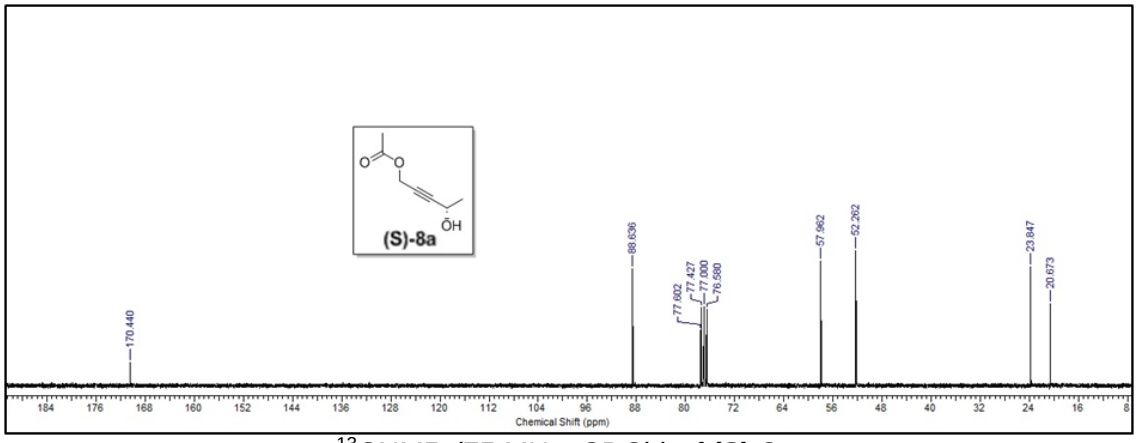
^{1}HNMR (300 MHz, $CDCl_3$) of **1h**.



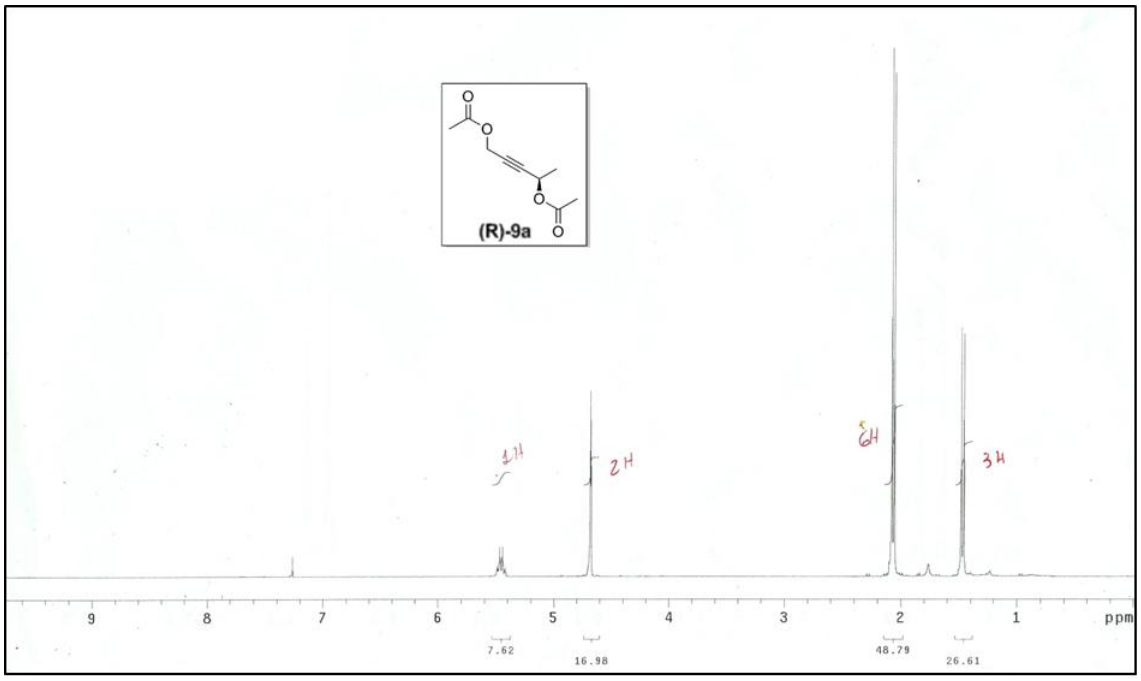
^{13}CNMR (75 MHz, $CDCl_3$) of **1h.**



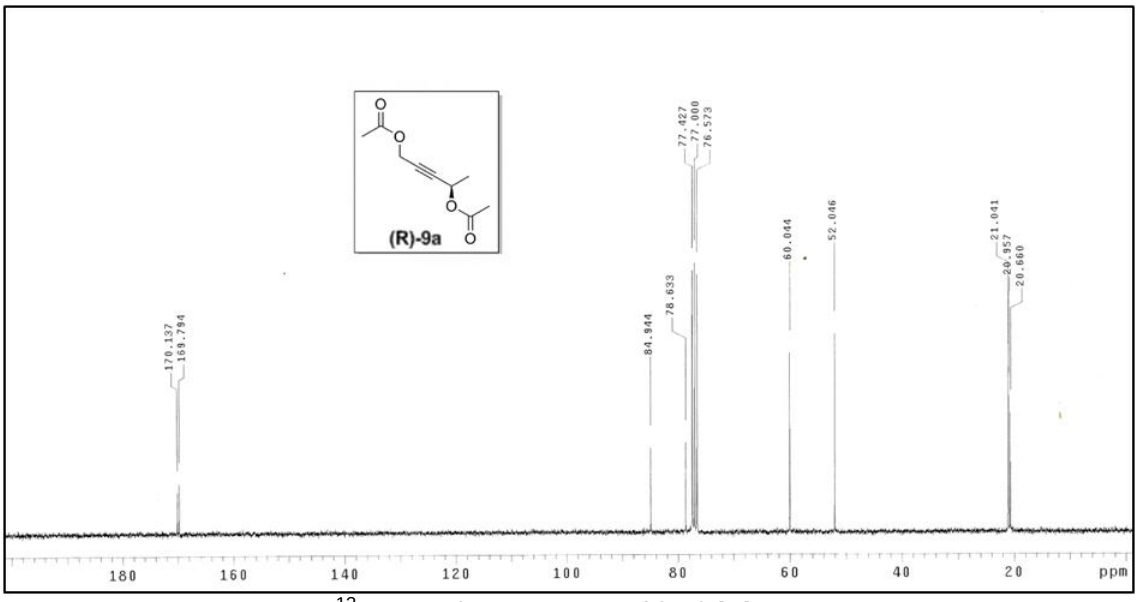
^{1}HNMR (300 MHz, $CDCl_3$) of ***(S)*-8a.**



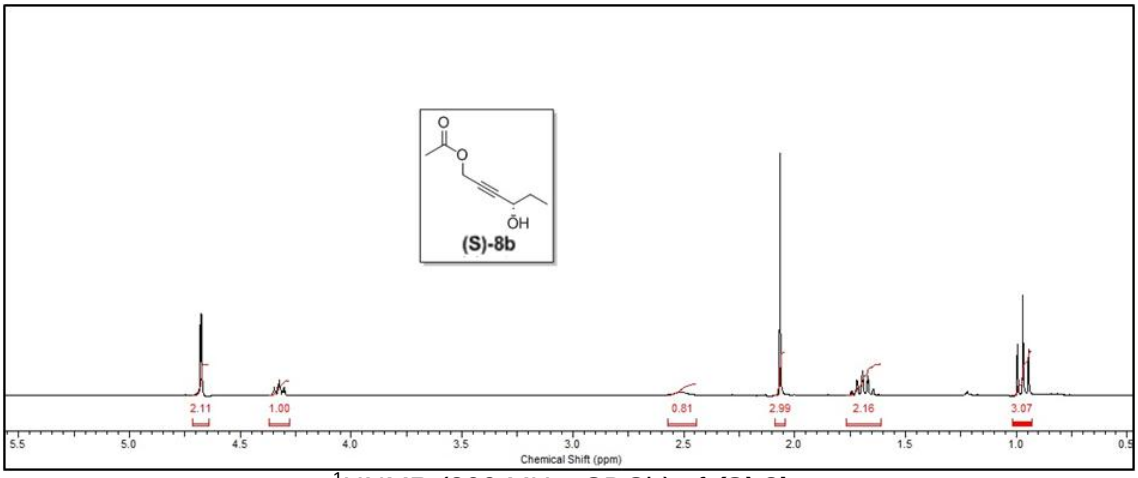
^{13}CNMR (75 MHz, $CDCl_3$) of **(S)-8a.**



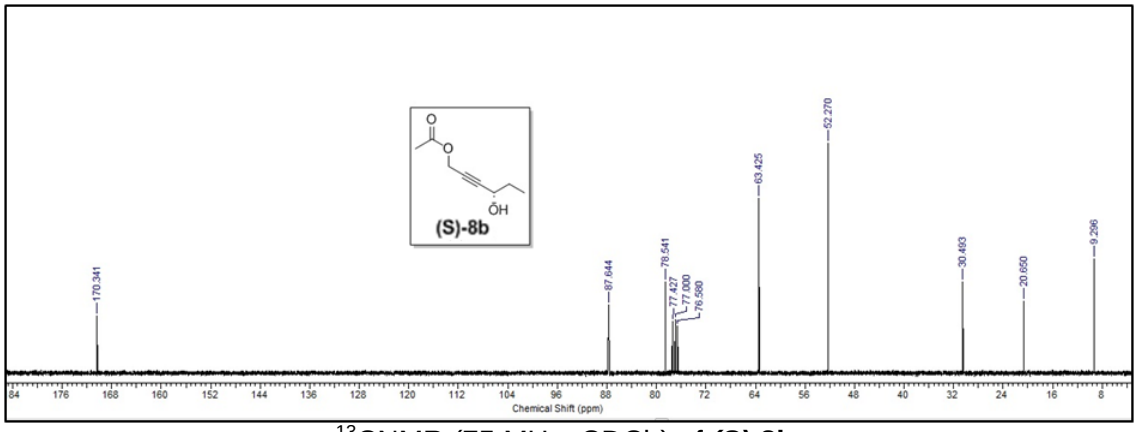
^{1}HNMR (300 MHz, $CDCl_3$) of ***(R)*-9a.**



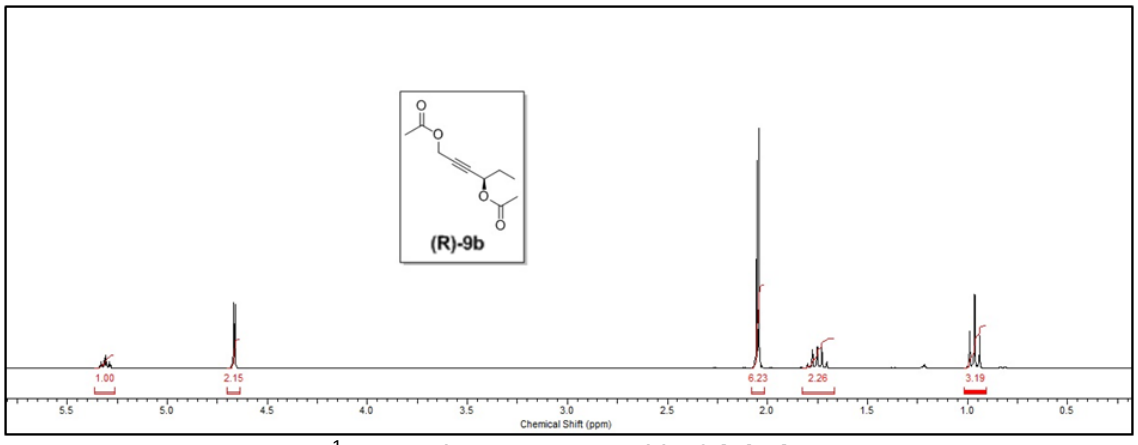
^{13}CNMR (75 MHz, $CDCl_3$) of ***(R)*-9a.**



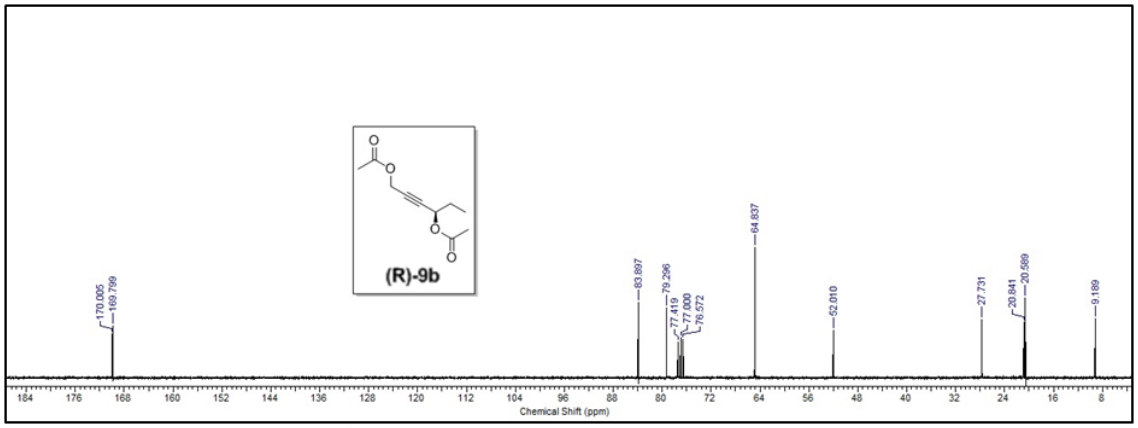
^{1}HNMR (300 MHz, $CDCl_3$) of ***(S)*-8b.**



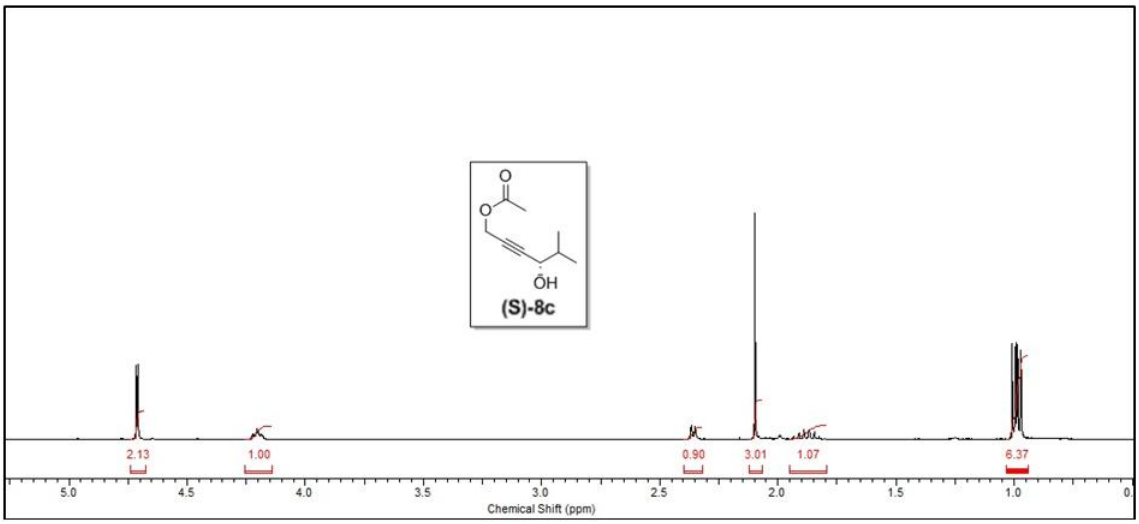
^{13}CNMR (75 MHz, $CDCl_3$) of ***(S)*-8b.**



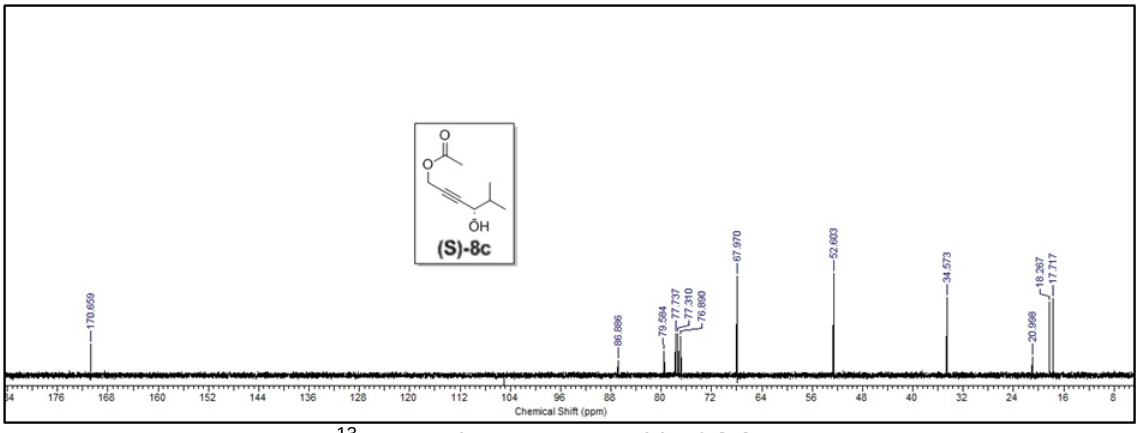
^{1}HNMR (300 MHz, $CDCl_3$) of ***(R)*-9b.**



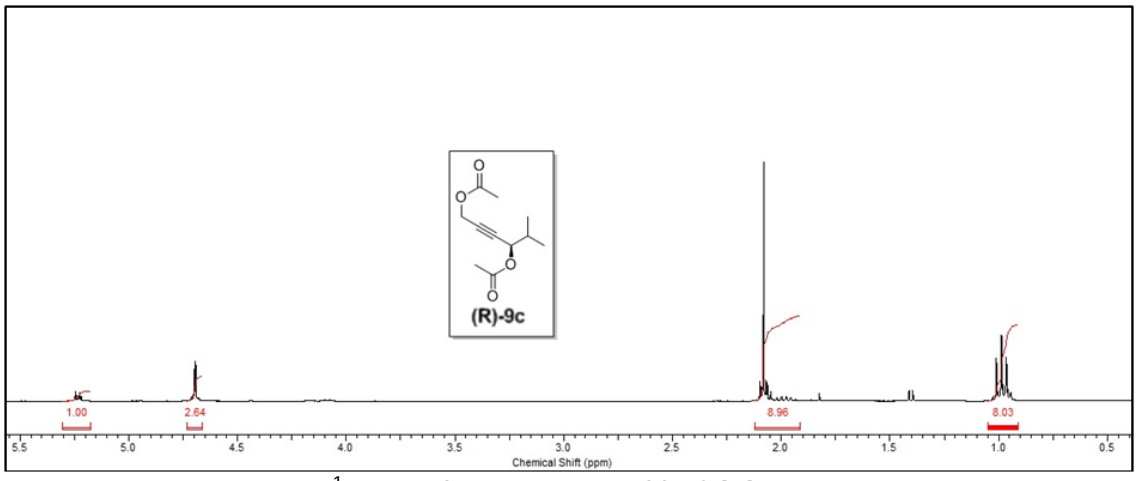
^{13}CNMR (75 MHz, $CDCl_3$) of ***(R)*-9b.**



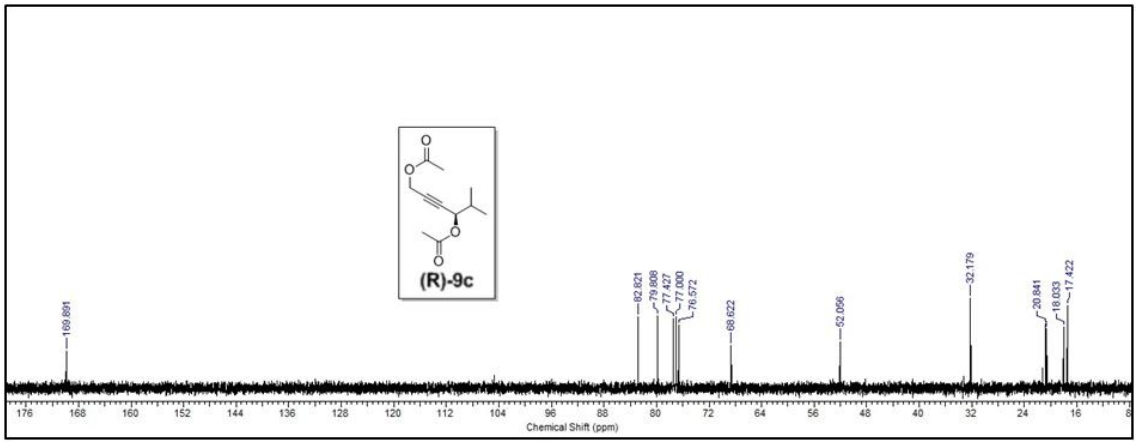
^{1}HNMR (300 MHz, $CDCl_3$) of ***(S)*-8c.**



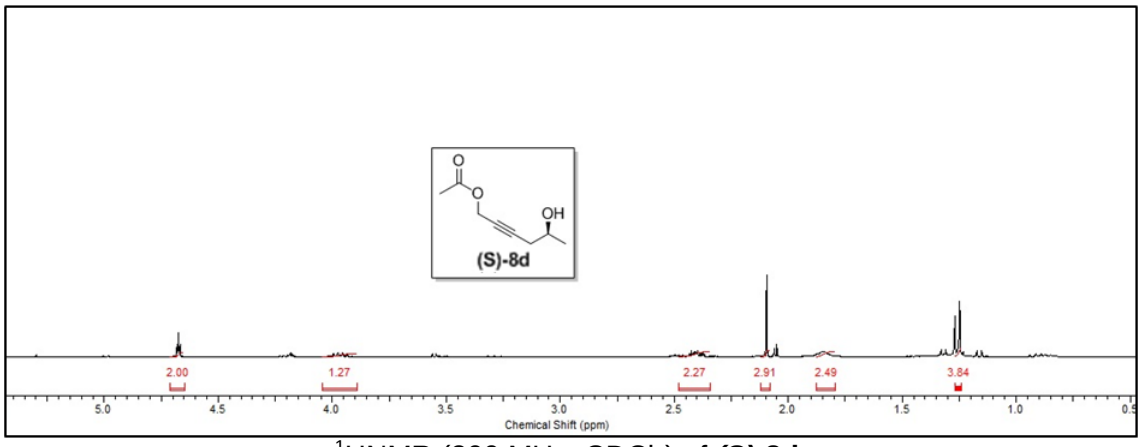
^{13}CNMR (75 MHz, $CDCl_3$) of ***(S)*-8c.**



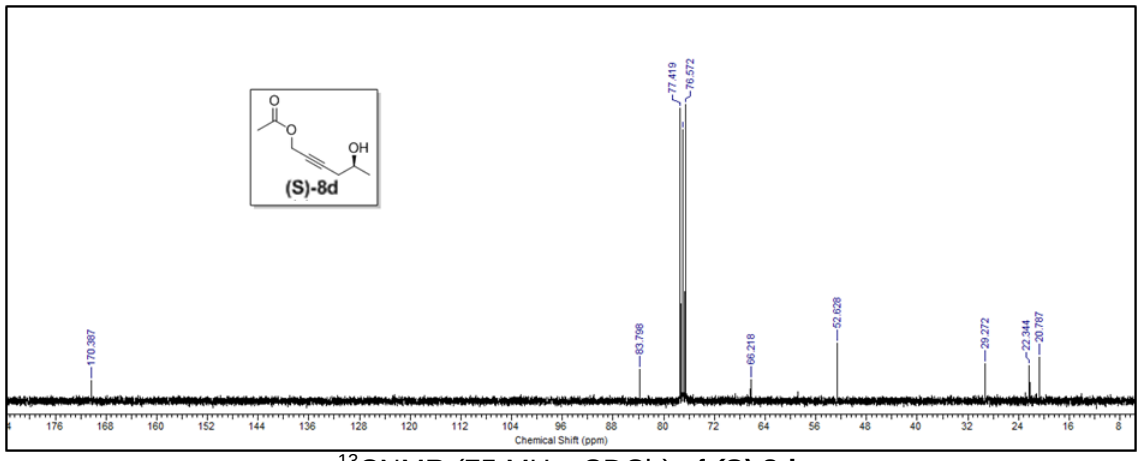
^{1}HNMR (300 MHz, $CDCl_3$) of ***(R)*-9c.**



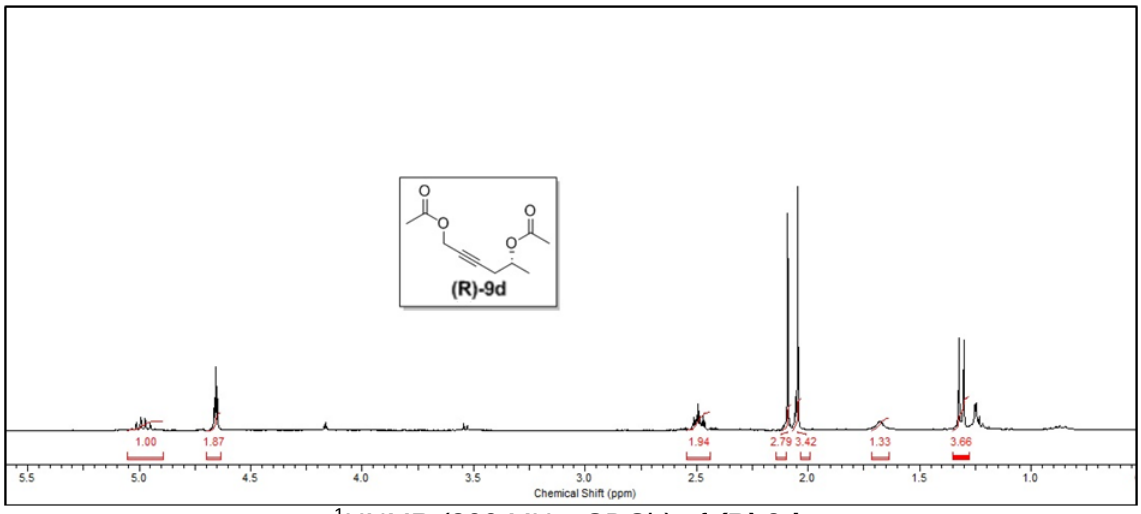
^{13}CNMR (75 MHz, $CDCl_3$) of ***(R)*-9c.**



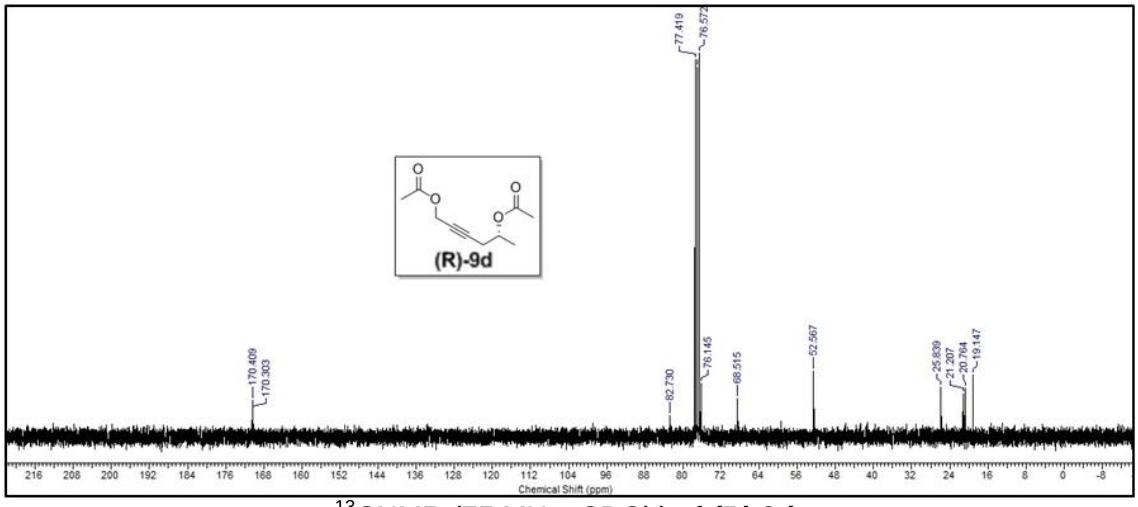
^{1}HNMR (300 MHz, $CDCl_3$) of ***(S)*-8d.**



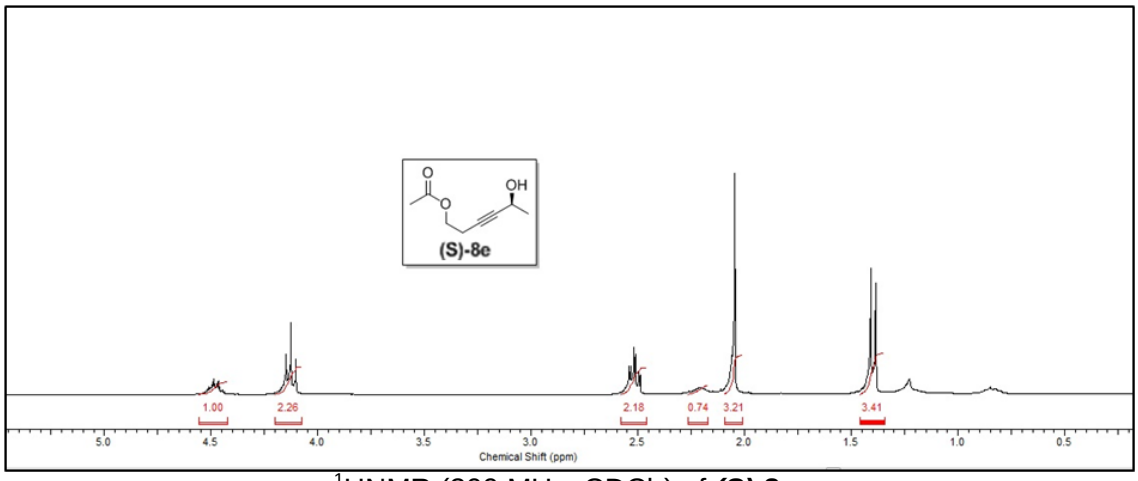
^{13}CNMR (75 MHz, $CDCl_3$) of ***(S)*-8d.**



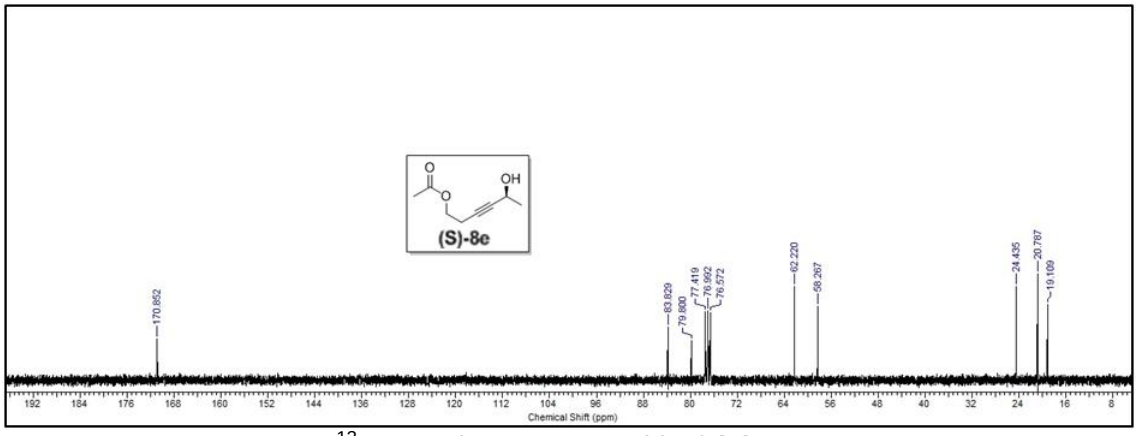
^{1}HNMR (300 MHz, $CDCl_3$) of ***(R)*-9d.**



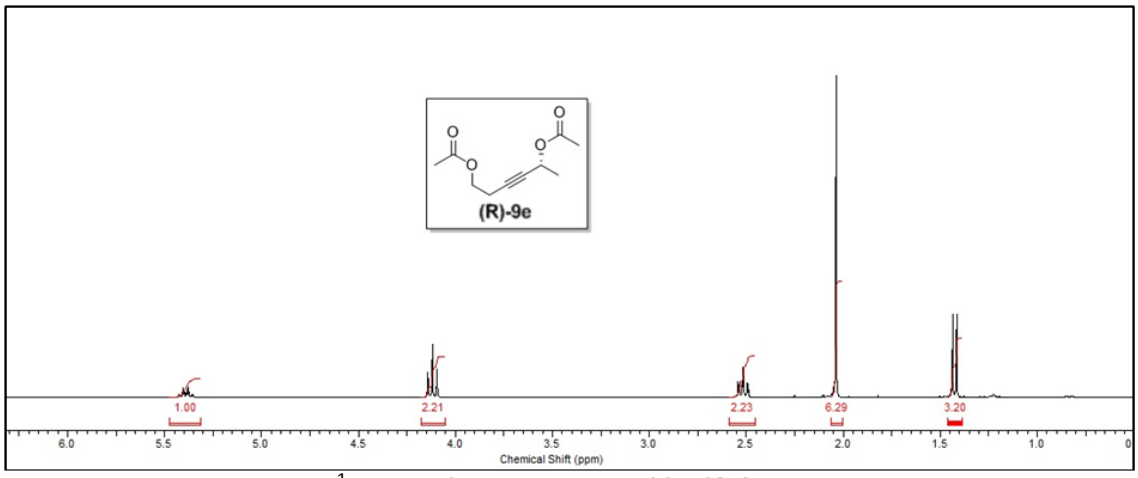
^{13}CNMR (75 MHz, $CDCl_3$) of ***(R)*-9d.**



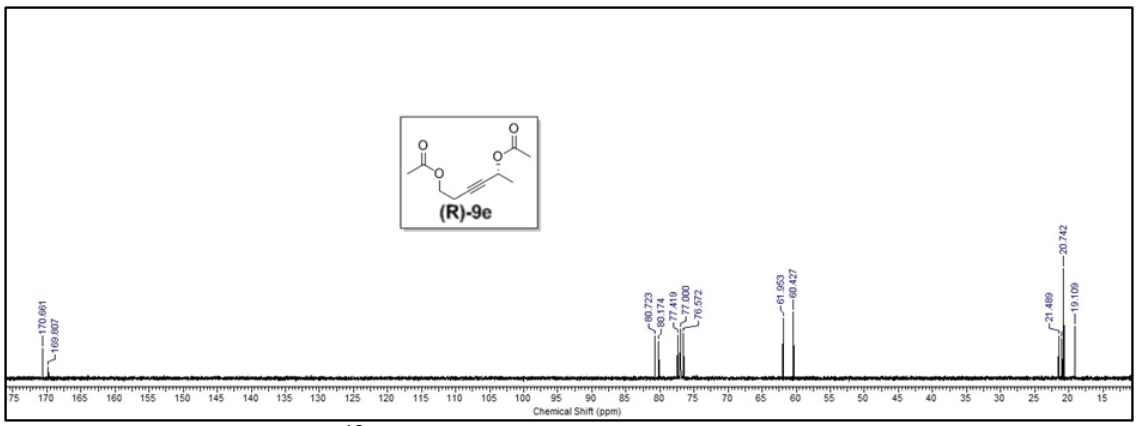
^{1}HNMR (300 MHz, $CDCl_3$) of ***(S)*-8e.**



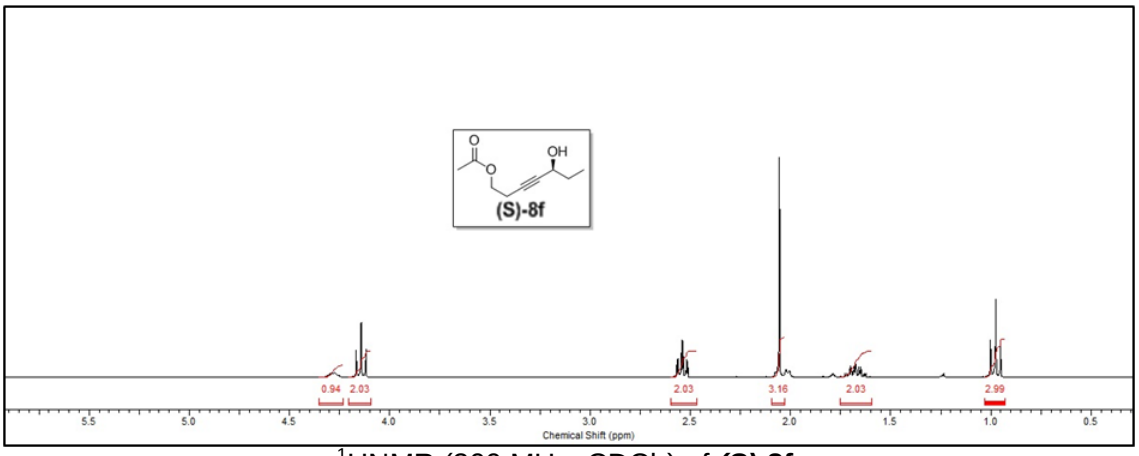
^{13}CNMR (75 MHz, $CDCl_3$) of ***(S)*-8e.**



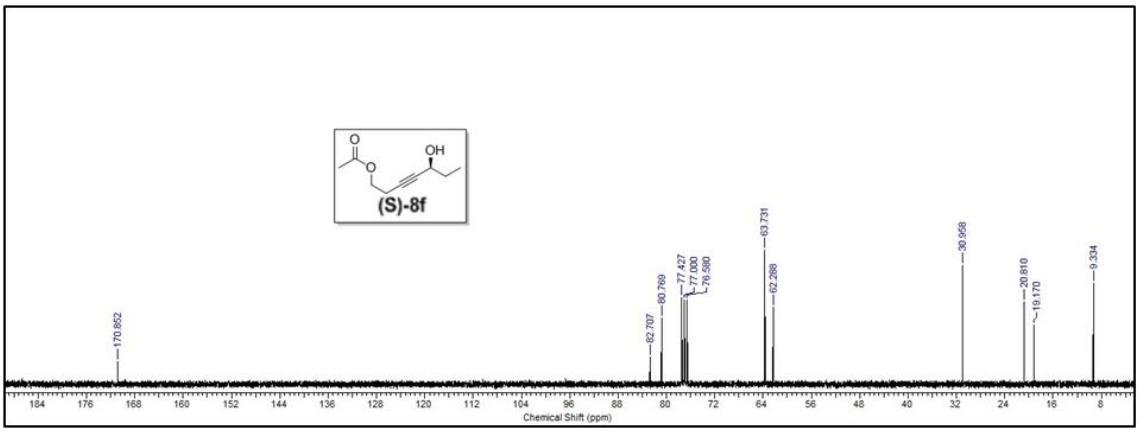
^{1}HNMR (300 MHz, $CDCl_3$) of***(R)*-9e.**



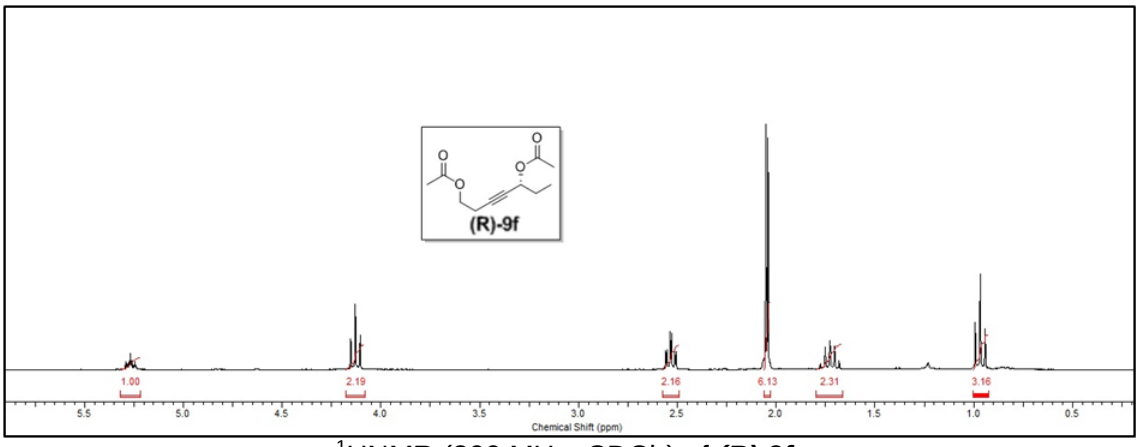
^{13}CNMR (75 MHz, $CDCl_3$)of***(R)*-9e.**



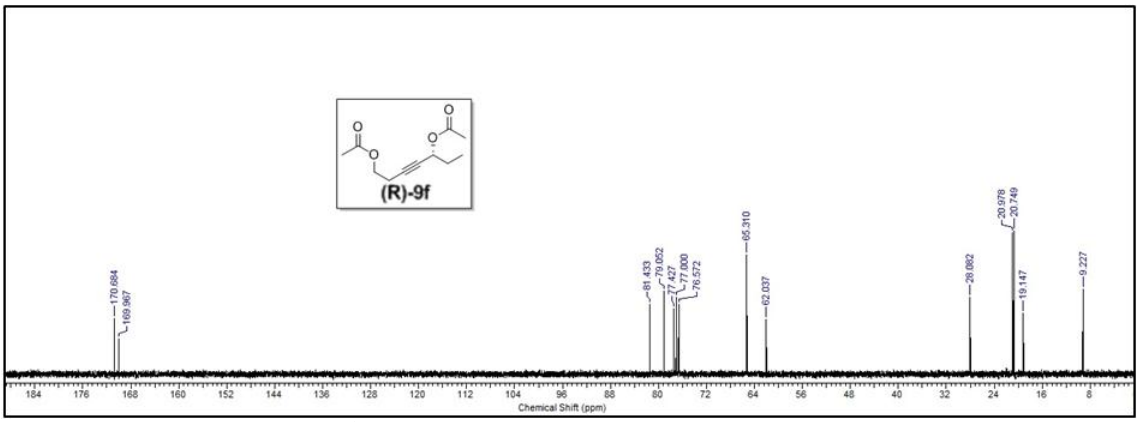
^{1}HNMR (300 MHz, $CDCl_3$) of ***(S)*-8f.**



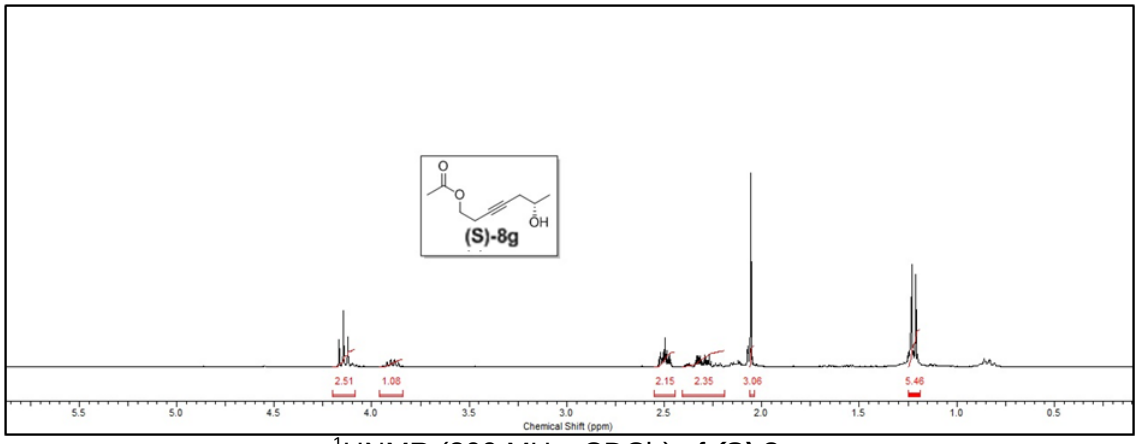
^{13}CNMR (75 MHz, $CDCl_3$) of ***(S)*-8f.**



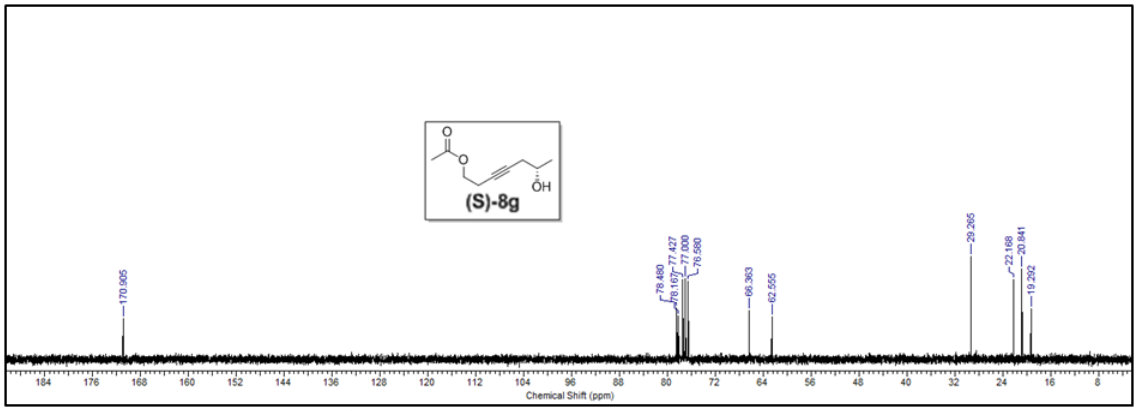
^{1}HNMR (300 MHz, $CDCl_3$) of ***(R)*-9f.**



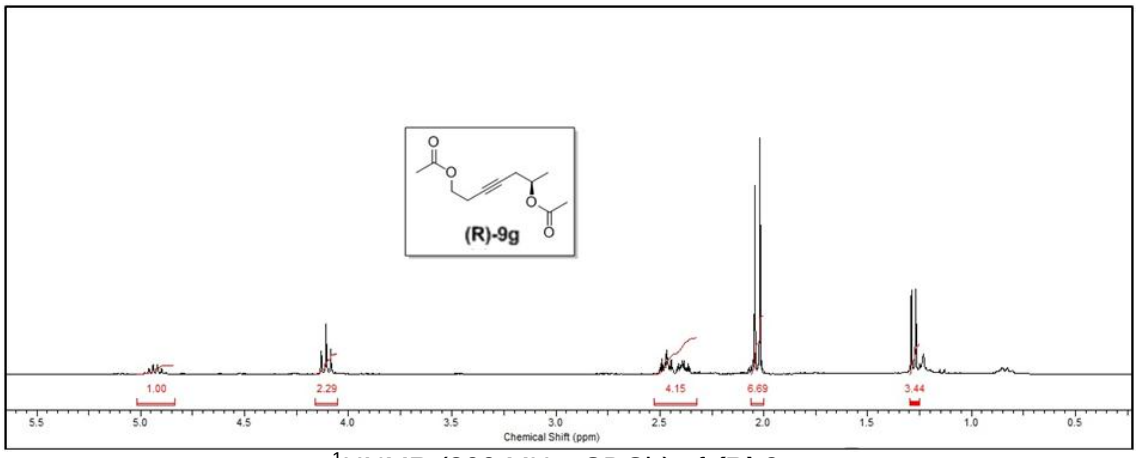
^{13}CNMR (75 MHz, $CDCl_3$) of ***(R)*-9f.**



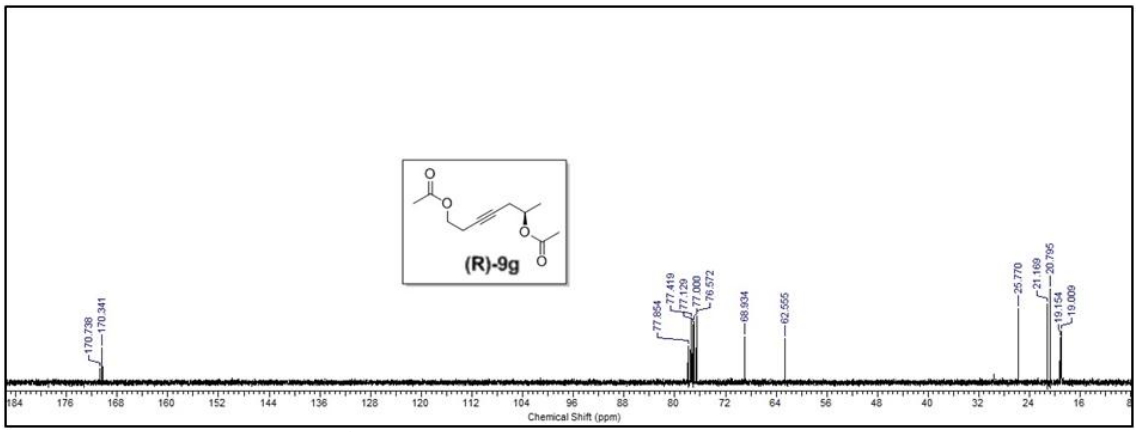
^{1}HNMR (300 MHz, $CDCl_3$) of ***(S)*-8g.**



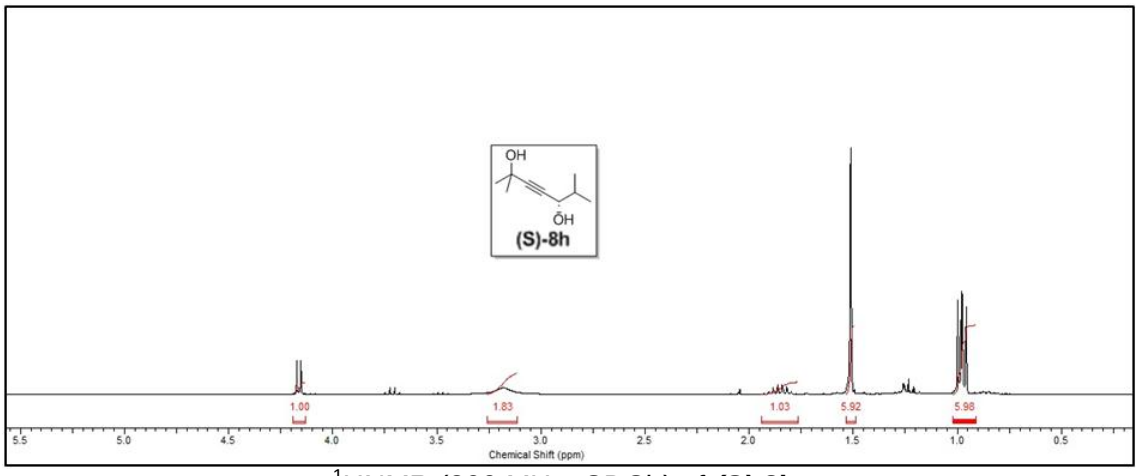
^{13}CNMR (75 MHz, $CDCl_3$) of ***(S)*-8g.**



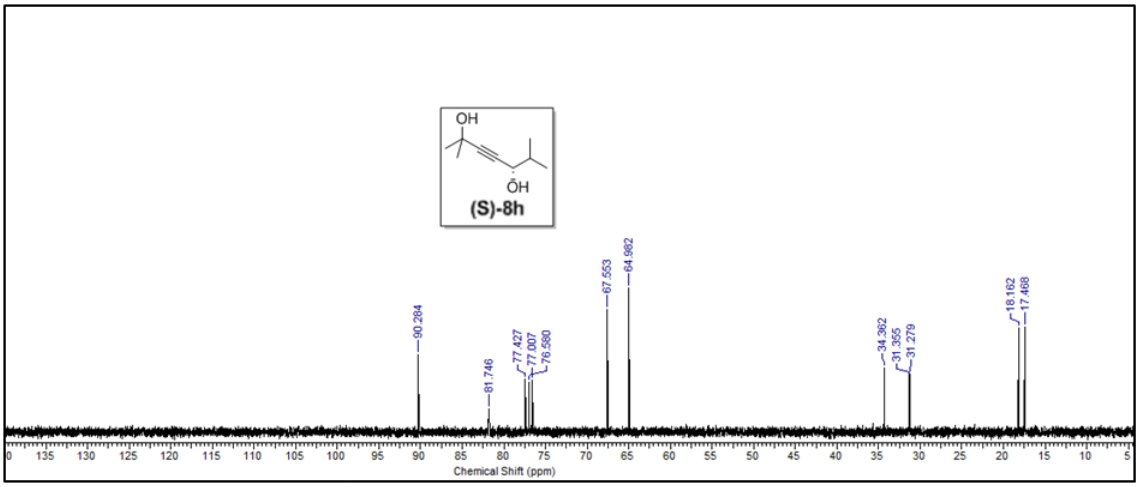
^{1}HNMR (300 MHz, $CDCl_3$) of ***(R)*-9g.**



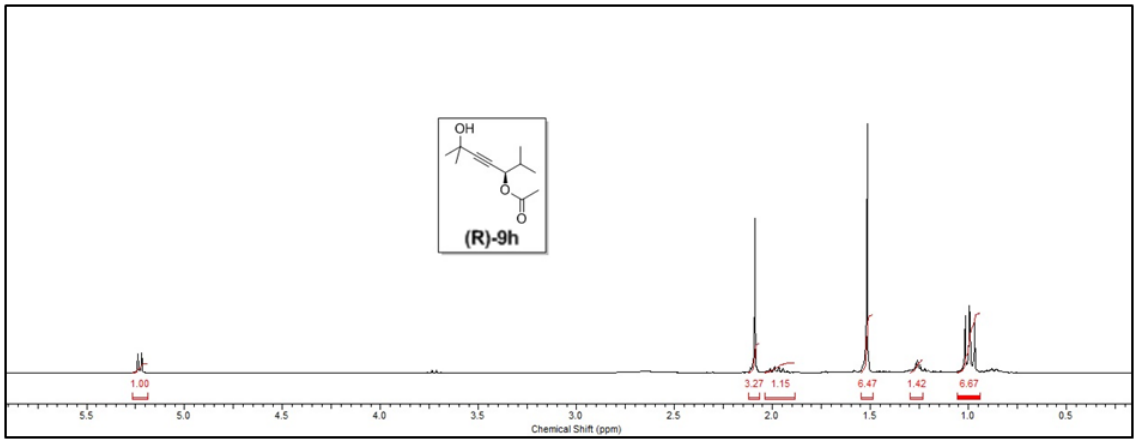
^{13}CNMR (75 MHz, $CDCl_3$) of ***(R)*-9g.**



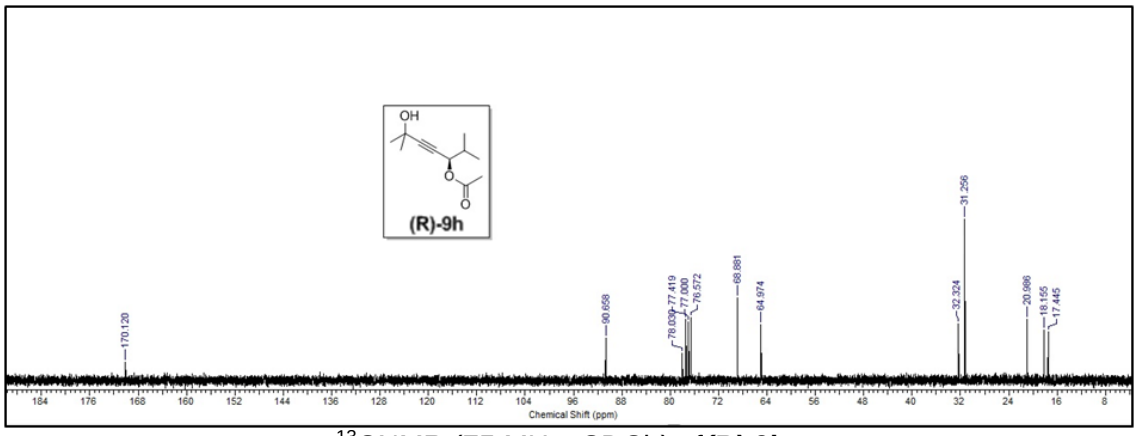
^{1}HNMR (300 MHz, $CDCl_3$) of ***(S)*-8h.**



^{13}CNMR (75 MHz, $CDCl_3$) of ***(S)*-8h.**



^{1}HNMR (300 MHz, $CDCl_3$) of***(R)*-9h.**



^{13}CNMR (75 MHz, $CDCl_3$) of***(R)*-9h.**