Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Investigation of asymmetric alcohol dehydrogenase (ADH) reduction of acetophenone derivatives: Part I - Effect of charge density

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Electronic Supplementary Information

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1.0 Experimental

1.1. General Information

All reactions were performed under an Argon atmosphere, in flame-dried or heat-gun-dried glassware and standard precautions against moisture were taken. An oil bath was used to obtain a temperature of above room temperature. An ice bath was used to obtain 0 °C. Silica gel 60 Å (40-60 μm) from SdS was used for flash column chromatography unless otherwise stated. Reactions were monitored by thin-layer chromatography (TLC) carried out on SigmaAldrich silica gel 60 F254 plates. Visualization of TLC plates was carried out with 254 nm UV light. Sodium sulfate was used as drying agent. Yields refer to chromatographically and spectroscopically pure compounds.

1.2. Instrumentation

^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury Vx spectrometer operating at 400 MHz at 22 ºC unless otherwise stated. Chemical shift data are reported in units of δ (ppm) using as the internal standard residual $CHCl_3$ (δ = 7.26 for ^{1}H NMR spectra and δ = 77.0 for ^{13}C NMR spectra). Multiplicities are given as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad) for 1H spectra. Coupling constants, *J*, are reported in Hz. Infrared spectra were recorded on a Jasco FT-IR-460 Plus spectrometer equipped with a Specac MKII Golden Gate Single Reflection Diamond ATR System and is reported in wave numbers (cm^{-1}).

The GC-MS mass spectra were recorded on a Varian 450-GC gas chromatograph equipped with an autosampler and a Varian 220-MS mass selective detector on a factor four capillary column VF-5ms 25M×0.25MM with Injector and FID temperatures at 300°C, and a gradient oven

temperature programme from 50°C (for 2 min) to 280°C at 10°C/min holding at 280°C for 5 minutes. Chiral GC: Varian 430-GC system with FID and a CP Chiralsil-DEXCB column (25M×0.25MM) with Injector temperature at 210°C and FID temperatures at 250°C, and a gradient oven temperature programme from 50°C (for 5 min) to 195°C at 15°C/min holding at 195°C for 5 minutes. Optical rotation was determined by using a JASCO DIP-370 Digital Polarimeter (590 nm, Na D-line, 25 °C) with a cylindrical glass cell (ϕ 3.5 ID X 50 mm) at a concentration of 10 mg ml^{-1} (ethyl acetate).

1.3. Materials

Commercial reagents were used as received. Solvents for reactions (distilled THF, Et_2O; commercial benzene, toluene and CH_2Cl_2) were filtered over columns of dried alumina under a positive pressure of argon. Solvents for extractions and flash column chromatography were of technical grade and were distilled prior to use. The *p*-vinylacetophenone (**II**) was synthesized as described previously.[26] Acetophenone (**I**), *N*-(4-acetylphenyl)acetamide (**IX**), 4'-ethynylacetophenone (**III**) and 4-hydroxy acetophenone (**VIII**) were purchased from Acros. 4-aminoacetophenone (**X**), 1-(4-methoxyphenyl)ethanone (**XI**), 1-(4-*tert*-butylphenyl)ethanone (**XII**), 1-(biphenyl-4-yl)ethanone (**XIII**), 2-chloroethyl benzene, sodium azide (NaN_3), glycidylmethacrylate (GMA), pMDETA, aluminum oxide (Al_2O_3), copper (I) bromide (Cu(I)Br), cesium carbonate ($CsCO_3$), triethylamine (TEA), hydrochloric acid (HCl) and $NaHCO_3$ were purchased from Aldrich whilst ammonium chloride (NH4Cl), methacryloyl chloride and monochlorodiethyleneglycol were obtained from Fluka and all used as received. *N*-(4-acetylphenyl)methacrylamide (**IV**), 1-(4-(2-(2-hydroethoxy)ethoxy)phenyl)ethanone (**V**), 2-(2-(4-acetylphnoxy)ethoxy)ethyl methacrylate (**VI**), and 5-(4-(4-acetylphenyl)-1*H*-1,2,3-triazol-1-

yl)-4-hydroxy-2-methylpent-1-en-3-one (**VII**), were synthesized in our lab. NADPH and alcohol dehydrogenase from *Lactobacillus brevis* (4100 U/mL) (ADH-LB) and *Thermoanaerobacter sp*. (331 U/mL) (ADH-T) were purchased from Julich Chiral Solutions GmbH, a Codexis company, Germany. All the solvents are obtained from Biosolve.

1.4. Computational details

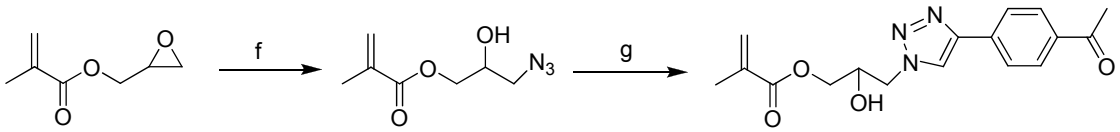
The SPARTAN 06 program[39] running on Workstation Intel® Core™2 Quad CPU Q9550 2.66 GHz processor with 4GB RAM under Windows XP operating system, was used to carry out HF and DFT-B3LYP calculations. The geometries were fully optimized at the DFT B3LYP level of theory with a 6-311G* basis set and using ab-initio HF method with 6-311G* basis set. Electrostatic density potential and local ionization density surfaces were calculated at both HF/6-31G* and DFT/B3LYP/6-31G* levels. The electrostatic density potential surfaces are represented in kJ mol^{-1} at default isovalue 0.002 electron/Bohrs.

1.5. Synthesis of ketones

1.5.1. 3-(4-(4-acetylphenyl)-1H-1,2,3-triazol-1-yl)-2-hydroxypropyl methacrylate (VII) (Scheme 2)

To a solution of NaN_3 (1.37 g, 21.1 mmol), NH_4Cl (1.67 g, 31.2 mmol) and N,N-dimethyl formamide (DMF, 10 ml) at 50°C, glycidyl methacrylate (1g, 7.0 mmol) was added slowly and the mixture was stirred for 8 hours in an argon atmosphere. The precipitated salts were filtered off and a solution of 4-ethynyl acetophenone (1.11 g, 7.67 mmol) in 60 mL of tetrahydrofuran was added followed by Cu(I)Br (0.200 g, 1.4 mmol) and PMDETA(0.318 g, 1.83 mmol) under

an argon flow at room temperature. After 2 hours of reaction, the mixture was passed through a column of alumina (Al_2O_3) to remove Cu(I)Br, concentrated and then treated with a large excess of water. The product was extracted in chloroform, washed with brine, dried over sodium sulfate and concentrated under reduced pressure. The residual yellow oil re-crystallized in a small amount of toluene at 50°C to give white crystalline materials which were dried in a vacuum oven (0.78 g, 2.4 mmol, 34.3 % yield). Formula: $C_{17}H_{19}N_3O_4$; ^{1}H-NMR ($CDCl_3$): δ 1.97 (t, 3H), 2.62 (s, 3H), 3.52 (s, OH), 4.30 (ddd, 2H), 4.45 (m, 2H), 4.65 (dd, 1H), 5.65 (s, 1H), 6.17 (s, 1H), 7.85(dt, 2H), 7.98(m, 3H); ^{13}C-NMR ($CDCl_3$): δ (ppm) 18.5, 27.0, 53.5, 65.8, 68.5, 122.5, 125.7, 127.0, 129.0, 134.5, 135.8, 136.5, 146.2, 167.5, 197.6; FTIR (neat) cm^{-1} : 3354, 1717, 1674, 1637, 1611, 1296, 1164, 958, 814; LC-MS (m/z (%)) : 330.2 (100)



VII

Scheme 2. Synthesis of 3-(4-(4-acetylphenyl)-1H-1,2,3-triazol-1-yl)-2-hydroxypropyl methacrylate (**7**); f) NaN_3, DMF, 60°C, 12h; g) $CH{\equiv}CC_6H_4COCH3$, CuBr, PMDETA, DMF, 25°C.

1.5.2. 2-(2-(4-acetylphenoxy)ethoxy)ethyl methacrylate (VI) (Scheme 3)

A solution of 4-hydroxy acetophenone (20 g, 146.9 mmol), mono-chlorodiethyleneglycol (21 g, 168.6) in 200 mL of N,N-dimethylformamide (DMF) was refluxed with $CsCO_3$ (82 g, 251.7 mmol) in an argon atmosphere for 15 h. The reaction mixture was then treated with excess of water and extracted in ethyl acetate. The organic layer was washed with water, brine, dried over

sodium sulfate and concentrated to obtain **V** (29.52 g = 131.78 mmol = 89.7 % yield), which then was dissolved in anhydrous dichloromethane (200 mL) and treated with triethylamine (158.14 mmol) followed by slow addition of a solution of methacryloyl chloride (131.78 mmol) in 50 mL of anhydrous dichloromethane in an argon atmosphere at 0°C. The reaction mixture was allowed to stir for 1 hour at 0°C and then 12 hours at room temperature before it was quenched by adding 10% NaOH solution at 0°C and extracting with ethyl acetate. The organic layer was washed with 2M HCl, water, and brine, dried over sodium sulfate and concentrated to get a yellowish oil. The crude oil was purified by column chromatography (hexane: ethyl acetate:: 90:10) to get pure **VI** (32.43 g = 111.02 mmol = 84.25 % yield).

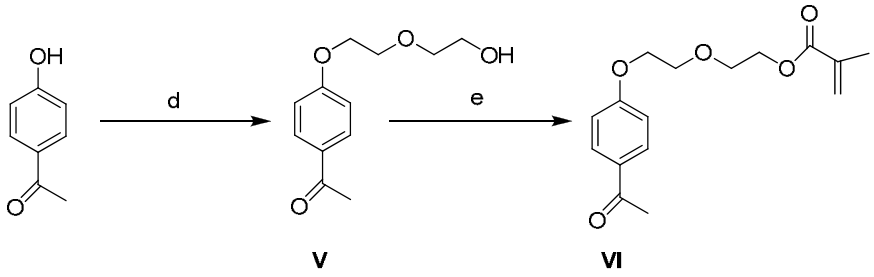
Analysis of 1-(4-(2-(2-hydroxyethoxy)ethoxy)phenyl)ethanone (**V**):

Formula: $C_{12}H_{16}O_4$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 2.53 (s, 3H), 3.65 (t, *J*=4.79, 4.19 Hz, 2H), 3.75 (m, 2H), 3.80 (t, *J*=4.80, 4.51 Hz, 2H), 4.17 (t, *J*=4.57, 4.77 Hz, 2H), 6.92 (d, *J*=8.75 Hz, 2 H), 7.90 (d, *J*=8.71 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ (ppm) 26.24, 61.52, 67.50, 69.28, 72.71, 114.16, 130.51, 162.552, 196.86; FTIR (neat) cm^{-1}: 3430, 2927, 2874, 1671, 1598, 1575, 1508, 1454, 1419, 1358, 1307, 1252, 1172, 1127, 1050, 957, 927, 886, 834, 732; GC-MS (m/z (%)) : 224.2 (6)

Analysis of 2-(2-(4-acetylphenoxy)ethoxy)ethyl methacrylate (**VI**):

Formula: $C_{16}H_{20}O_5$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 2.06 (s, 3H), 2.68 (s, 3H), 3.95 (t, *J* = 4.81, 2H), 4.01 (t, *J*=4.70, 2H), 4.32 (t, *J*=4.71, 2H), 4.46 (t, *J* = 4.81, 2H), 5.69 (d, *J* = 1.33, 1H), 6.25 (d, *J* = 1.33, 1H), 7.07 (d, *J* = 8.73, 2H), 8.05 (d, *J* = 8.72, 2H); ^{13}C NMR ($CDCl_3$): δ (ppm) 18.20, 26.23, 63.65, 67.54, 69.26, 69.37, 114.18, 125.70, 130.37, 130.45, 136.00, 162.58, 167.16,

196.56; FTIR (neat) cm^{-1}: 2926, 2874, 1715, 1673, 1598, 1576, 1509, 1453, 1420, 1358, 1297, 1251, 1155, 1126, 1052, 936, 831, 733; GC-MS (m/z (%)) : 293.3 (13.5)

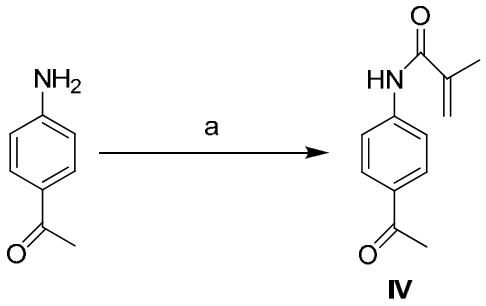


Scheme 3. Synthesis of 2-(2-(4-acetylphenoxy)ethoxy)ethyl methacrylate (**VI**); d) $HOCH_2CH_2OCH_2CH_2Cl$, Cs2CO3, 1,4-dioxan, 80°C, 24h; e) $CH_2=C(CH_3)COCl$, $N(C_2H_5)_3$, dichloromethane.

1.5.3. N-(4-acetylphenyl)methacrylamide (IV) (Scheme 4)

A solution of 4-amino acetophenone (5.0 g = 37 mmol) dissolved in anhydrous THF (75 mL) was treated with triethylamine (4.49 g = 6.22 mL = 44 mmol) followed by drop-wise addition of a solution of methacryloyl chloride (4.25 g = 3.98 mL = 41 mmol) in 25 mL of anhydrous THF in an Argon atmosphere at 0°C. The reaction mixture was allowed to stir for 1 hour at 0°C and then 12 hours at room temperature before it was quenched by adding 20% $NaHCO_3$ solution at 0°C and extracted with ethyl acetate. The organic layer was washed with 2M HCl, water, and brine, dried over sodium sulfate and concentrated to get a yellowish solid. The crude product was re-crystallized in petroleum ether (7.39 g = 36.37 mmol = 98.2 % yield). Formula: $C_{12}H_{13}NO_2$; ^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 2.06 (s, 3H), 2.57 (s, 3H), 5.51 (d, J = 1.48 Hz, 1H), 5.82 (s, 1H), 7.69 (d, J = 8.72, 1H), 7.93 (d, J = 8.70, 2H), 7.89 (s, 2H); ^{13}C NMR

($CDCl_3$): δ (ppm) 18.68, 26.41, 119.36, 120.62, 129.59, 137.72, 140.52, 142.56, 167.10, 197.22; FTIR (neat) cm^{-1} : 3351, 3328, 1671, 1627, 1516, 1273, 832; LC-MS (m/z (%)) : 204.2 (4)



IV

Scheme 4. Modification of the amino group of 4-aminoacetophenone; a) $CH_2=C(CH_3)COCl$, $N(C_2H_5)_3$, dichloromethane, room temperature.

1.6. Enantioselective reductions of ketones using alcohol dehydrogenase

1.6.1. General Procedure A: (In a homogeneous medium)

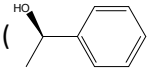
1.6.1.1. Alcohol Dehydrogenase-02 (ADH-LB): 1g of the substrate (ketone) was dissolved/suspended in a reaction mixture of 2-propanol (40mL) and PBS buffer solution (pH 7.4, 160mL) containing 20mM NADPH and 0.5mM $MgCl_2$ and maintained at 37°C with uniform mixing. The enzyme ADH-02 (50µL, 4100U/mL) was then added to the reaction mixture and the mixture was allowed to stir overnight. The progress of the reaction was monitored by TLC and Chiral GC (Varian 430-GC) measurements and the mixture was treated with excess of water and extracted in methyl t-butyl ether. The organic layer was washed with brine, dried over magnesium sulfate and concentrated under reduced pressure.

1.6.1.2. Alcohol Dehydrogenase-05 (ADH-T): Substrates were reduced by ADH-05 using the procedure similar to the one used for ADH-02 enzyme but without $MgCl_2$. In brief, 1g of the

substrate (ketone) was dissolved/suspended in a reaction mixture of 2-propanol (40mL) and PBS buffer solution (pH 7.4, 160mL) containing 20mM NADPH and maintained at 37°C with uniform mixing, followed by the addition of ADH-05 enzyme (285 µL, 331U/mL). The reaction mixture was allowed to stir overnight and the progress of the reaction was monitored by TLC and Chiral GC (Varian 430-GC) measurements. The mixture was treated with excess of water and extracted in methyl t-butyl ether. The organic layer was washed with brine, dried over magnesium sulfate and concentrated under reduced pressure.

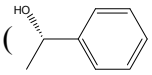
1.6.2. General Procedure B: (In a heterogeneous medium)

In this method, the substrates were reduced by the respective enzymes in a heterogeneous organic/aqueous biphasic medium to improve the solubility of the poorly water-soluble or water insoluble ketones. The reaction conditions were similar to those in procedure A for both the enzymes, except that the medium contained a varying aqueous (PBS buffer pH 7.4/2-propanol) to an organic solvent (dichloromethane, diisopropylether, ethylacetate or ionic liquid (AMMOENG^{TM} 100)) ratio by volume.

1.6.3. (1*R*)-1-phenylethanol ()

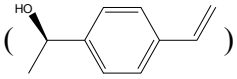
Formula : $C_8H_{10}O$; Yield: 88 %; $[\alpha]_D^{22}$ =+55.12 (c = 0.01 in $CHCl_3$)

^{1}H-NMR ($CDCl_3$): δ (ppm) 1.51 (d, *J* =6.46 Hz, 3H), 1.98 (b, 1H, OH), 4.91 (q, *J* =6.46 Hz, 1H), 7.29 (m, 1H), 7.39 (m,5H); ^{13}C NMR ($CDCl_3$): δ (ppm) 25.16, 70.23, 125.46, 127.37, 128.44, 145.93; FTIR (neat) cm^{-1}: 3336, 2973, 2927, 2874, 1493, 1451, 1368, 1285, 1203, 1097, 1075, 1028, 1010, 996, 897, 758, 690; GC-MS (m/z (%)) : 122.1 (16); Chiral GC : retention time, *t* = 8.41 min; ee (%) = 99.0.

1.6.4. (1*S*)-1-phenylethanol ()

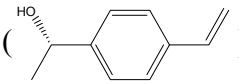
Formula: $C_8H_{10}O$; Yield: 89 %; $[\alpha]_D^{22}$ = -52.83 (c = 0.01 in $CHCl_3$)

^{1}H-NMR ($CDCl_3$): δ (ppm) 1.50 (d, *J*=6.46, 3H,), 1.93 (b, 1H, OH), 4.89 (q, *J*=6.45, 1H), 7.28 (m,1H), 7.37 (m, 4H); ^{13}C NMR ($CDCl_3$): δ (ppm) 25.15, 70.25, 125.45, 127.38, 128.45, 145.92; FTIR (neat) cm^{-1}: 3333, 2973, 2927, 2874, 1493, 1451, 1368, 1286, 1203, 1097, 1075, 1028, 1010, 996, 897, 758, 690; GC-MS (m/z (%)) : 122.1 (16); Chiral GC : retention time, *t* = 8.69 min, ee (%) = 100.

1.6.5. (1*R*)-1-(4-vinylphenyl)ethanol ()

Formula: $C_{10}H_{12}O$; Yield: 98 %; $[\alpha]_D^{22}$ = +26.21 (c = 0.01 in ethylacetate)

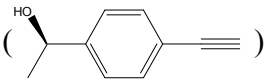
^{1}H NMR (400 MHz,$CDCl_3$): δ ppm 1.49 (d, *J* = 6.45 Hz, 3H), 4.88 (q, *J* = 6.45 Hz, 1H), 5.24 (dd, *J* = 10.88, 0.91 Hz, 1H), 5.75 (dd, *J* = 17.60, 0.92 Hz, 1H), 6.71 (dd, *J* = 17.61, 10.89 Hz, 1H), 7.36 (m, 4H), ^{13}C-NMR ($CDCl_3$): δ (ppm) 25.1, 70.1, 113.7, 125.6, 126.3, 136.5, 136.8, 145.5; FTIR (neat) cm^{-1} : 3353, 2972, 1675, 1630, 1511, 1270, 1088, 1071, 989, 900, 840, 755; GC-MS (m/z (%)) : 147.8 (6); Chiral GC : retention time, *t* = 13.28 min, ee (%) = 99.9.

1.6.6. (1*S*)-1-(4-vinylphenyl)ethanol ()

Formula: $C_{10}H_{12}O$; Yield: 95 %; $[\alpha]_D^{22}$ = -29.13 (c = 0.01 in ethylacetate)

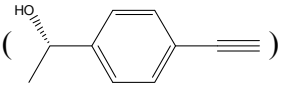
^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 1.49 (dd, *J* = 6.45, 1.18 Hz, 3H), 4.88 (q, *J* = 6.45 Hz, 1H), 5.24 (d, *J* = 10.88 Hz, 1H), 5.75 (d, *J* = 17.61 Hz, 1H), 6.72 (dd, *J* = 17.60, 10.88 Hz, 1H), 7.36 (m, 4H); ^{13}C-NMR ($CDCl_3$): δ (ppm) 25.1, 70.1, 113.7, 125.6, 126.3, 136.5, 136.8, 145.4; FTIR

(neat) cm^{-1} : 3359, 2973, 1675, 1630, 1510, 1272, 1088, 1071, 989, 899, 840; GC-MS (m/z (%)): 147.8 (7); Chiral GC : retention time, *t* = 13.45 min, ee (%) = 99.9.

1.6.7. (R)-1-(4-ethynylphenyl)ethanol ()

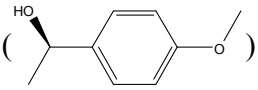
Formula: $C_{10}H_{10}O$; Yield: 99 %; $[\alpha]_D^{22}$ = +50.90 (c = 0.01 in THF)

^{1}H-NMR ($CDCl_3$): δ (ppm) 7.46 (d, *J* = 7.74 Hz, 2H)), 7.30 (d, *J* = 7.78, 2H), 4.86 (q, *J* = 6.46, 6.46, 6.44 Hz, 1H), 3.06 (s, 3H), 1.45 (d, *J* = 6.46 Hz, 3H); ^{13}C-NMR ($CDCl_3$): δ (ppm) 25.0, 69.9, 77.0, 83.2, 121.1, 125.0, 132.2, 146.4; FTIR (neat) cm^{-1} : 3287, 2973, 1670, 1603, 1500, 1402, 1263, 1081, 1070, 1007, 897, 834, 734; GC-MS (m/z (%)): 145.0 (10); Chiral GC : retention time, *t* = 12.95 min, ee (%) = 91.0.

1.6.8. (1*S*)-1-(4-ethynylphenyl)ethanol ()

Formula: $C_{10}H_{10}O$; Yield: 98 %; $[\alpha]_D^{22}$ = -51.04 (c = 0.01 in THF)

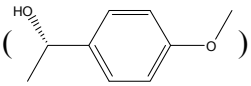
1H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.47 (d, *J* = 8.39 Hz, 1H) , 7.32 (d, *J* = 7.99 Hz, 1H), 4.89 (q, *J* = 6.47 Hz, 1H), 3.06 (s, 1H), 1.47 (d, *J* = 6.47 Hz, 1H); ^{13}C-NMR ($CDCl_3$): δ (ppm) 25.1, 70.0, 83.6, 121.1, 125.5, 132.2, 146.6; FTIR (neat) cm^{-1} : 3287, 2973, 1672, 1603, 1502, 1402, 1265, 1085, 1070, 1008, 896, 796, 737; GC-MS (m/z (%)): 145.0 (11); Chiral GC : retention time, *t* = 12.98 min, ee (%) = 99.9.

1.6.9. (1*R*)-1-(4-methoxyphenyl)ethanol ()

Formula: $C_9H_{12}O2$; Yield: 89 %; $[\alpha]_D^{22}$ = +51.00 (c = 0.01 in $CHCl_3$)

1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.46 (d, *J* = 6.40 Hz, 3H), 1.81 (b, 1H, OH), 3.80 (s, 3H), 4.85 (q, *J*=6.40 Hz, 1H), 6.88 (m, 2H), 7.30 (m, 2H); ^{13}C-NMR ($CDCl_3$): δ (ppm) 25.02, 55.21,

69.64, 113.73, 126.68, 138.18, 158.75; FTIR (neat) cm^{-1} : 3373, 2971, 2933, 2837, 1611, 1586, 1511, 1456, 1369, 1299, 1240, 1205, 1175, 1085, 1032, 1005, 985, 829, 808; GC-MS (m/z (%)): 152 (5); Chiral GC : retention time, *t* = 12.53 min, ee (%) = 99.0.

1.6.10. (1*S*)-1-(4-methoxyphenyl)ethanol ()

Formula: $C_9H_{12}O2$; Yield: 82 %; $[\alpha]_D^{22}$ = -56.61 (c = 0.01 in $CHCl_3$)

1H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.48 (d, *J* = 6.40 Hz, 3H), 1.81 (b, 1H, OH), 3.80 (s, 3H), 4.85 (q, *J*=6.40 Hz, 1H), 6.88 (m, 2H), 7.30 (m, 2H); ^{13}C-NMR ($CDCl_3$): δ (ppm) 25.02, 55.23, 69.74, 113.76, 126.66, 138.13, 158.81; FTIR (neat) cm^{-1} : 3374, 2970, 2982, 2837, 1611, 1586, 1511, 1456, 1368, 1299, 1240, 1174, 1085, 1032, 1005, 895, 829, 807; GC-MS (m/z (%)): 152.0 (5); Chiral GC : retention time, *t* = 12.92 min, ee (%) = 100.

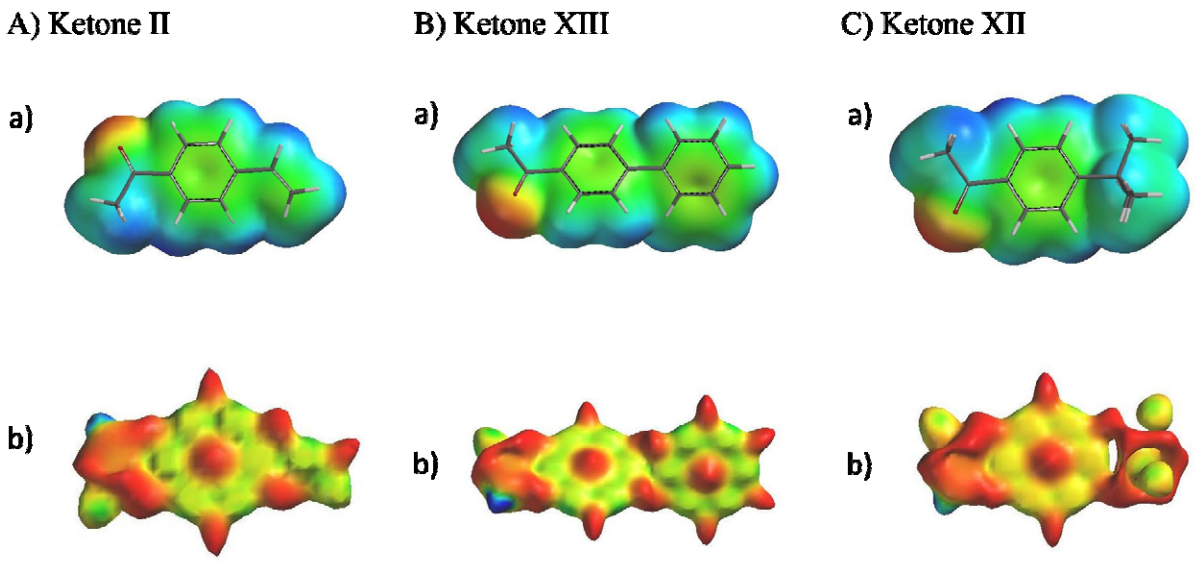


Figure 1. Calculated electrostatic density potential (a) (in kJ mol-1 at the default isovalue 0.002 electron/Bohr^3) and local ionization density (b) (in kJ mol-1 at the default isovalue 20.0 electron/Bohr^3) surfaces showing the electron charge distribution on the molecule for reducible Ketones: (A) Ketone II, (B) Ketone XIII, (C) Ketone XII.

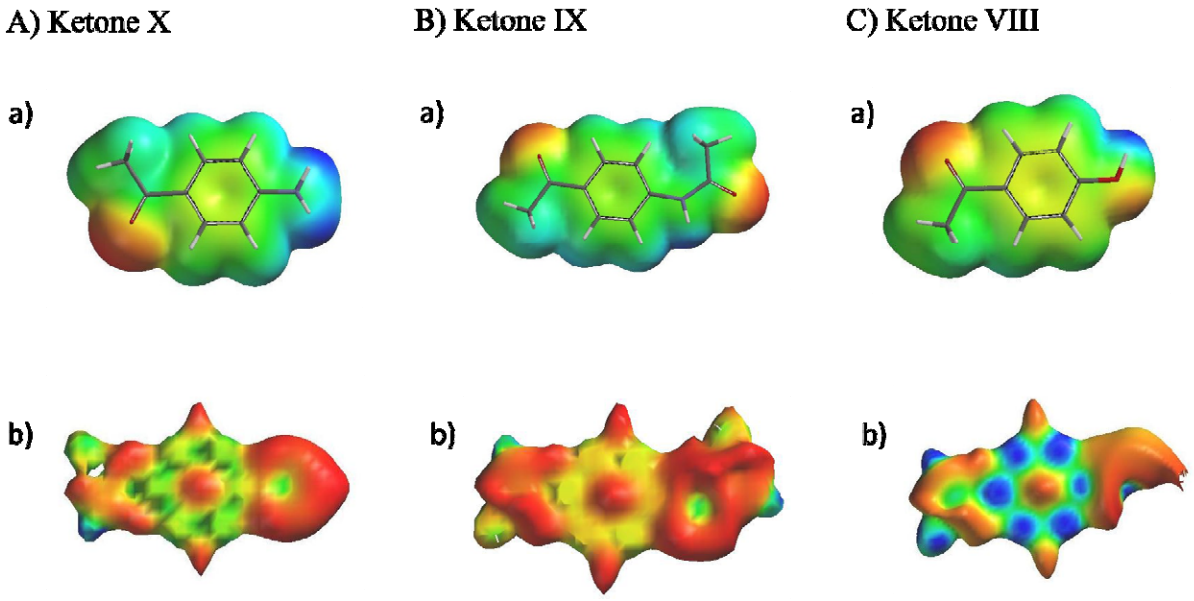


Figure 2. Calculated electrostatic density potential (a) (in kJ mol-1 at the default isovalue 0.002 electron/Bohr^3) and local ionization density (b) (in kJ mol-1 at the default isovalue 20.0 electron/Bohr^3) surfaces showing the electron charge distribution on the molecule for non-reducible Ketones: (A) Ketone X, (B) Ketone IX, (C) Ketone VIII.

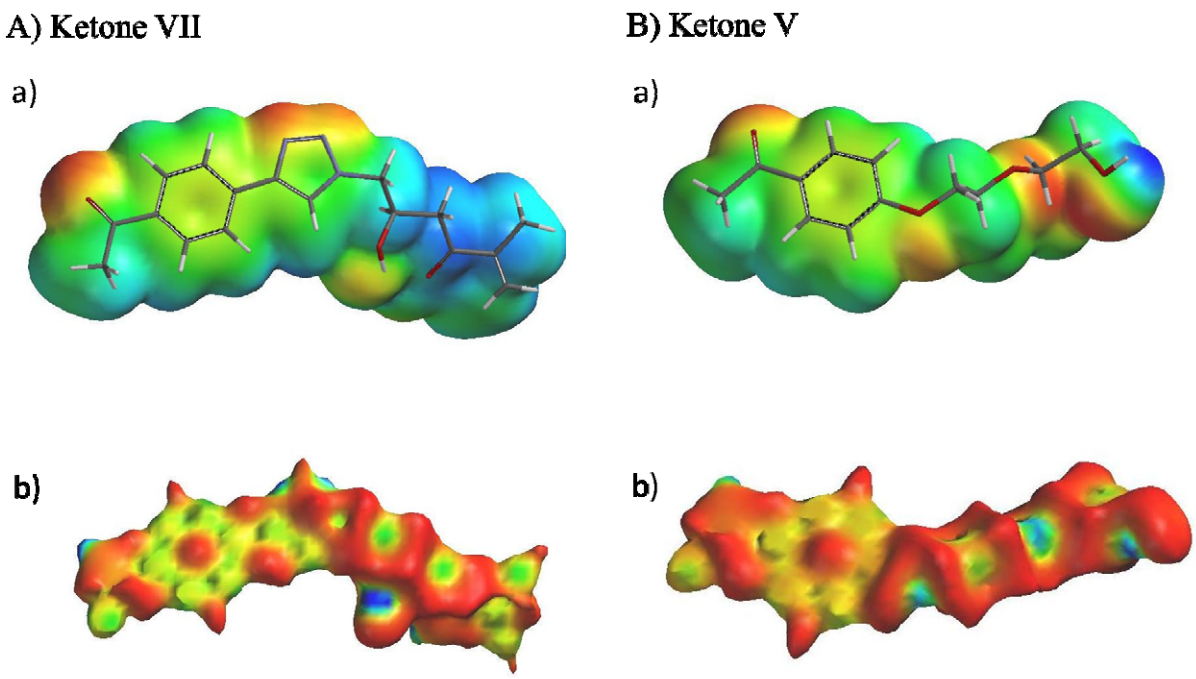


Figure 3. Calculated electrostatic density potential (a) (in kJ mol-1 at the default isovalue 0.002 electron/Bohr^3) and local ionization density (b) (in kJ mol-1 at the default isovalue 20.0 electron/Bohr^3) surfaces showing the electron charge distribution on the molecule for non-reducible Ketones: (A) Ketone VII, (B) Ketone V.

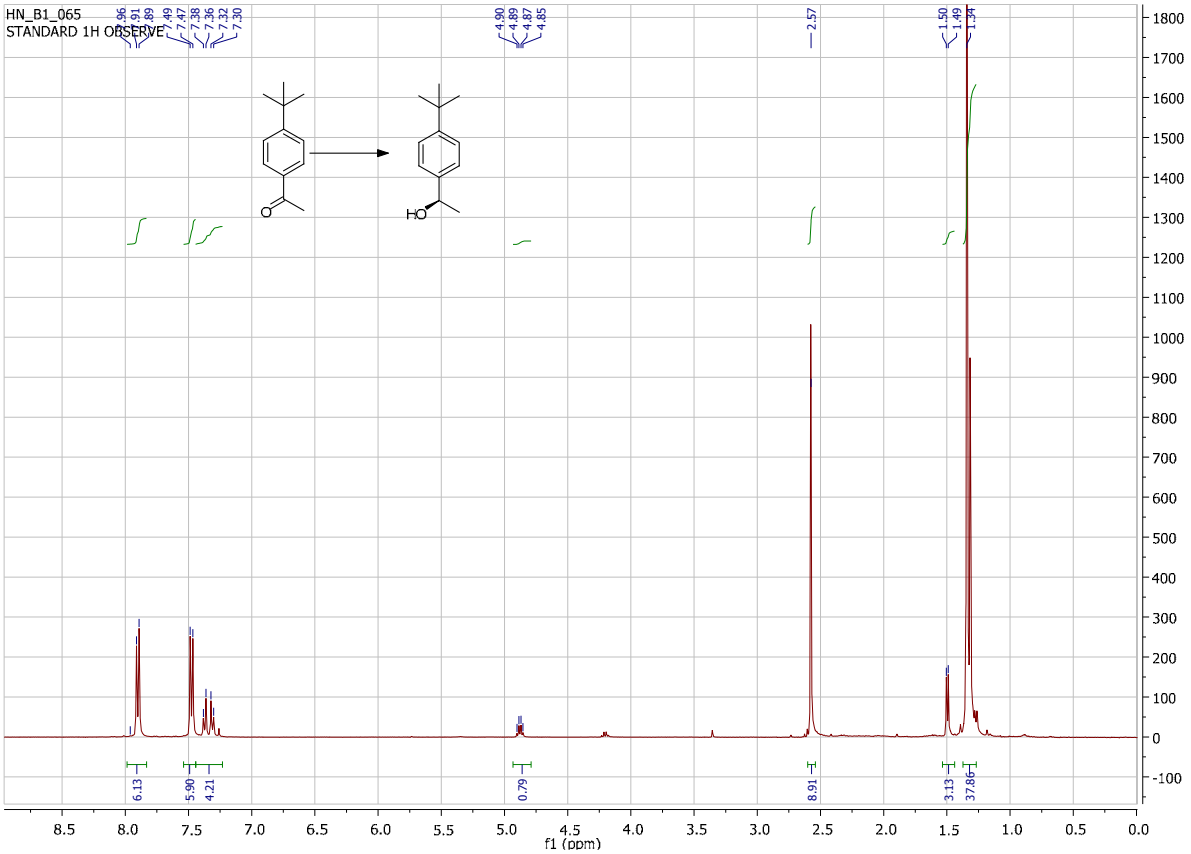


Figure 4. NMR spectra of 4-*tert*-butyl acetophenone reduced by ADH-LB (not isolated).

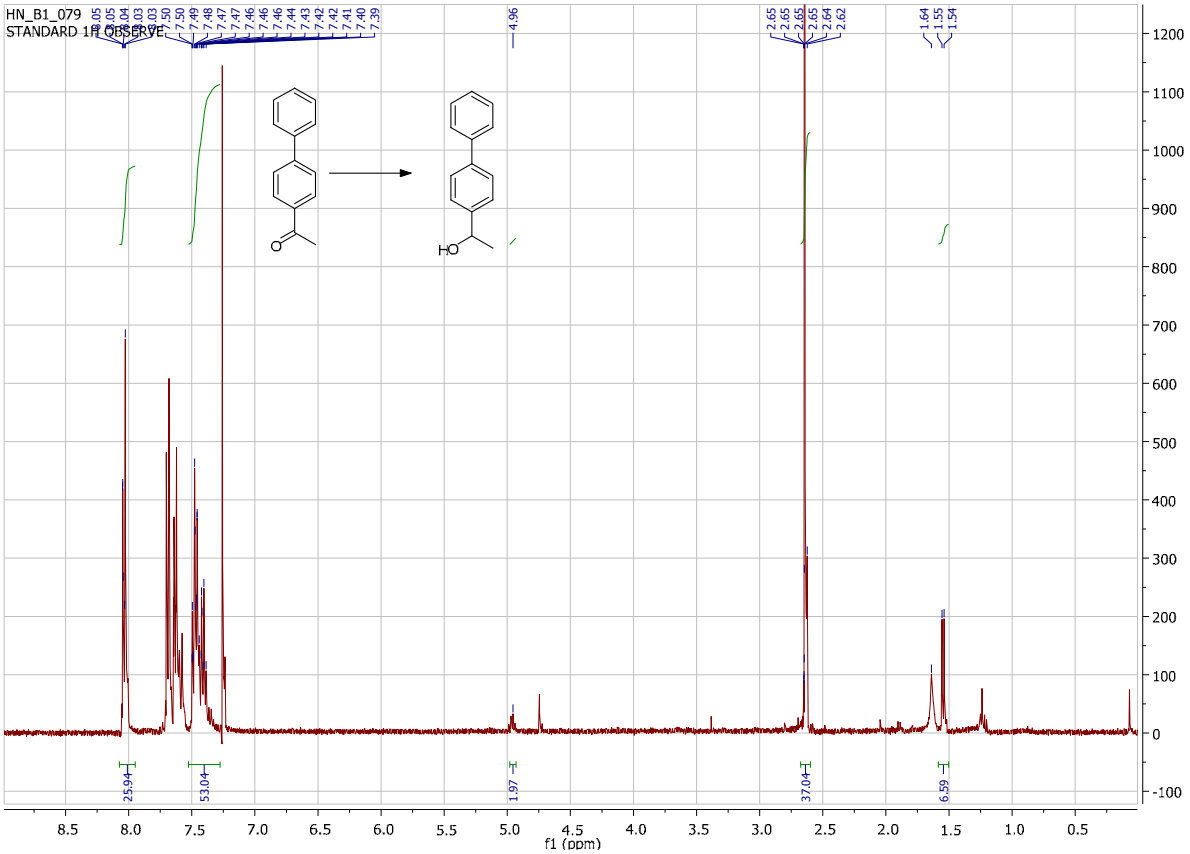
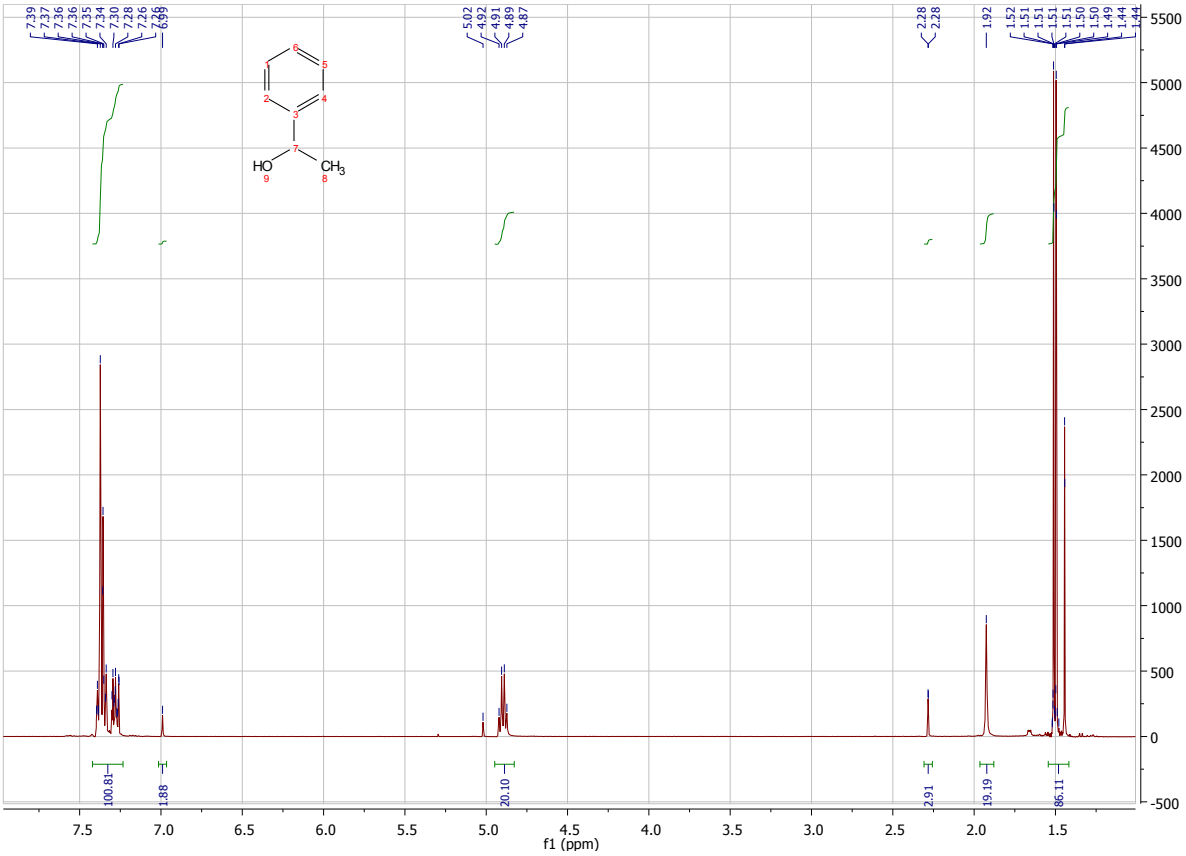


Figure 5. NMR spectra of 1-(biphenyl-4-yl)ethanone reduced by ADH-LB (not isolated) using Method B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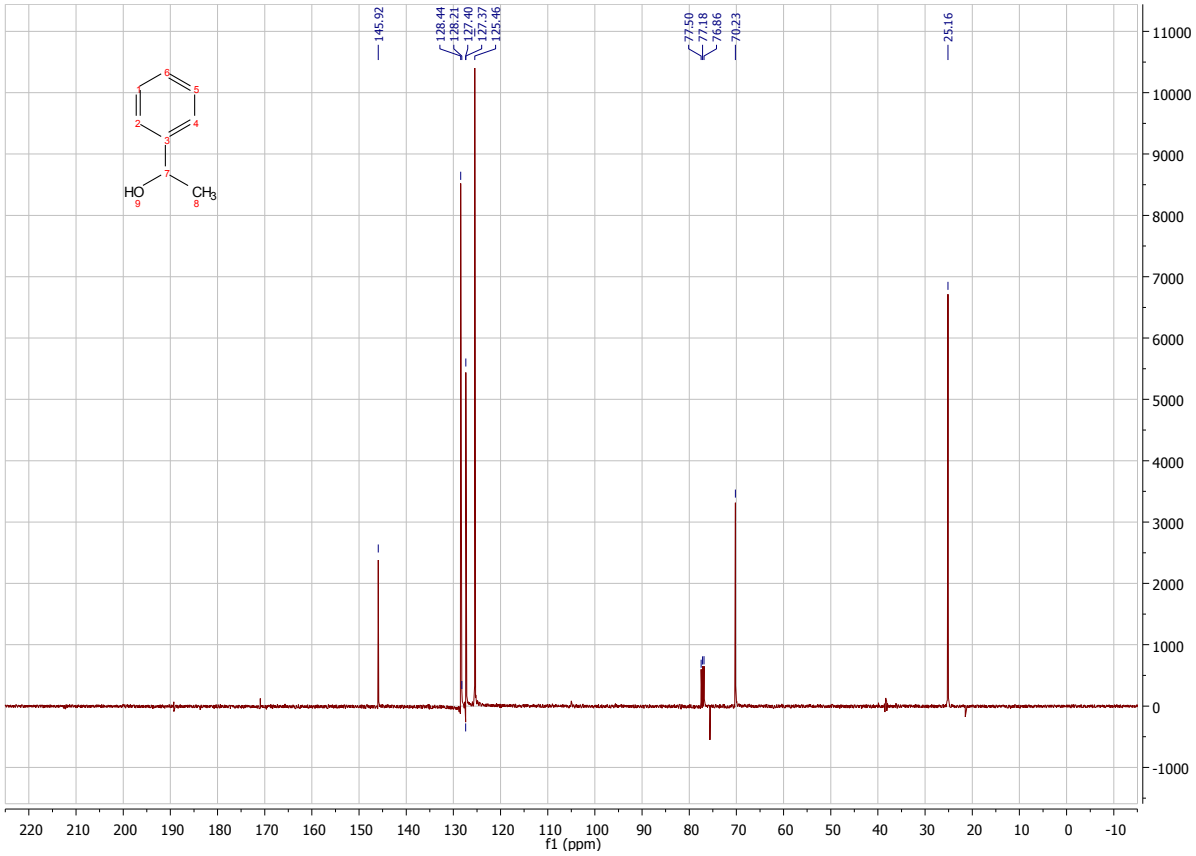
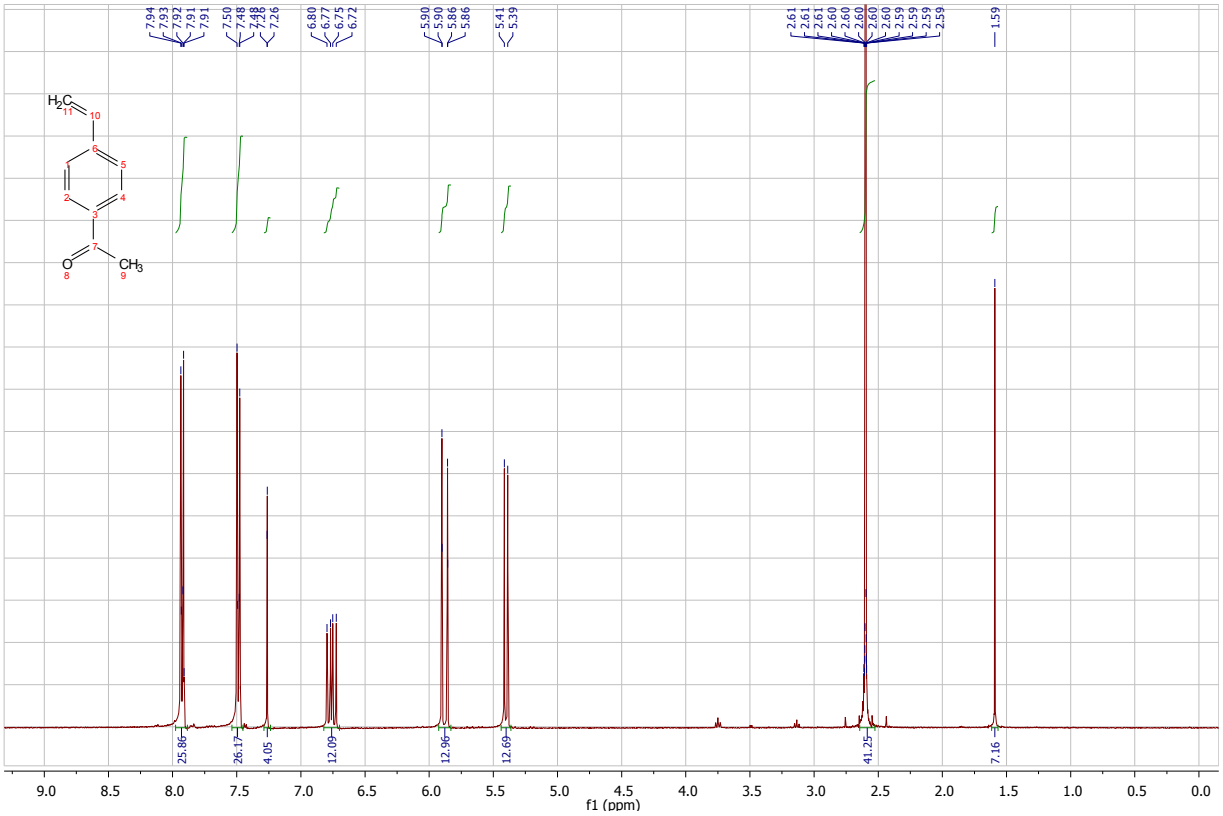
7.37
7.36
7.36
7.35
7.34
7.30
7.28
7.26
7.08
7.06
6.99
5.02
4.92
4.91
4.89
4.87
2.28
2.28
1.92
1.52
1.51
1.51
1.51
1.51
1.50
1.50
1.49
1.44
1.44
HO
CH3
100.81
1.88
20.10
2.91
19.19
86.11
f1 (ppm)


145.92
128.44
128.21
127.40
127.37
125.46
77.50
77.18
76.86
70.23
25.16
HO
CH3
f1 (ppm)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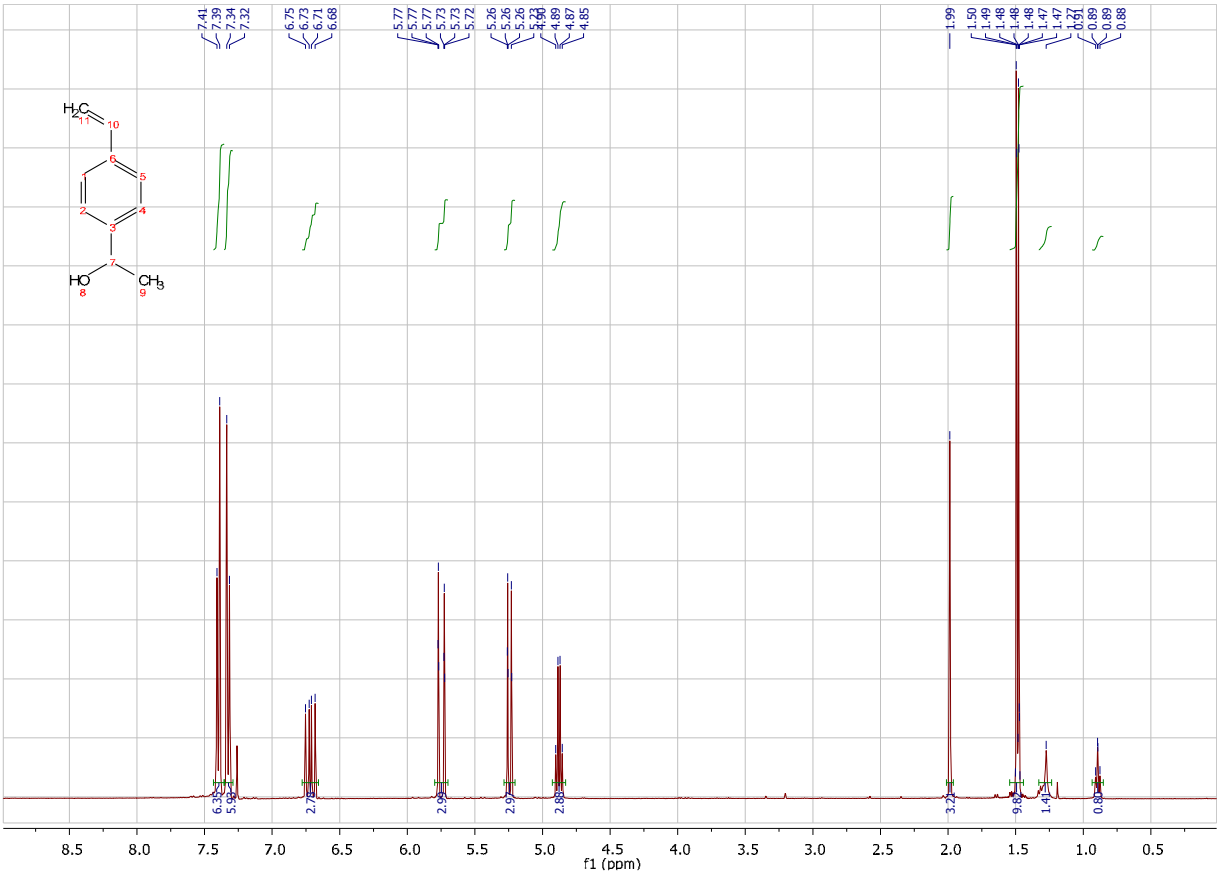
7.93
7.92
7.91
7.91
7.50
7.48
7.48
7.26
7.26
6.80
6.77
6.75
6.72
5.90
5.90
5.86
5.86
5.41
5.39
2.61
2.61
2.61
2.60
2.60
2.60
2.60
2.60
2.59
2.59
2.59
2.59
1.59
H2C
11
10
9
1
5
2
4
3
7
O
8
CH3
9
25.86
26.17
4.05
12.09
12.96
12.69
41.25
7.16
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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7.39
7.34
7.32
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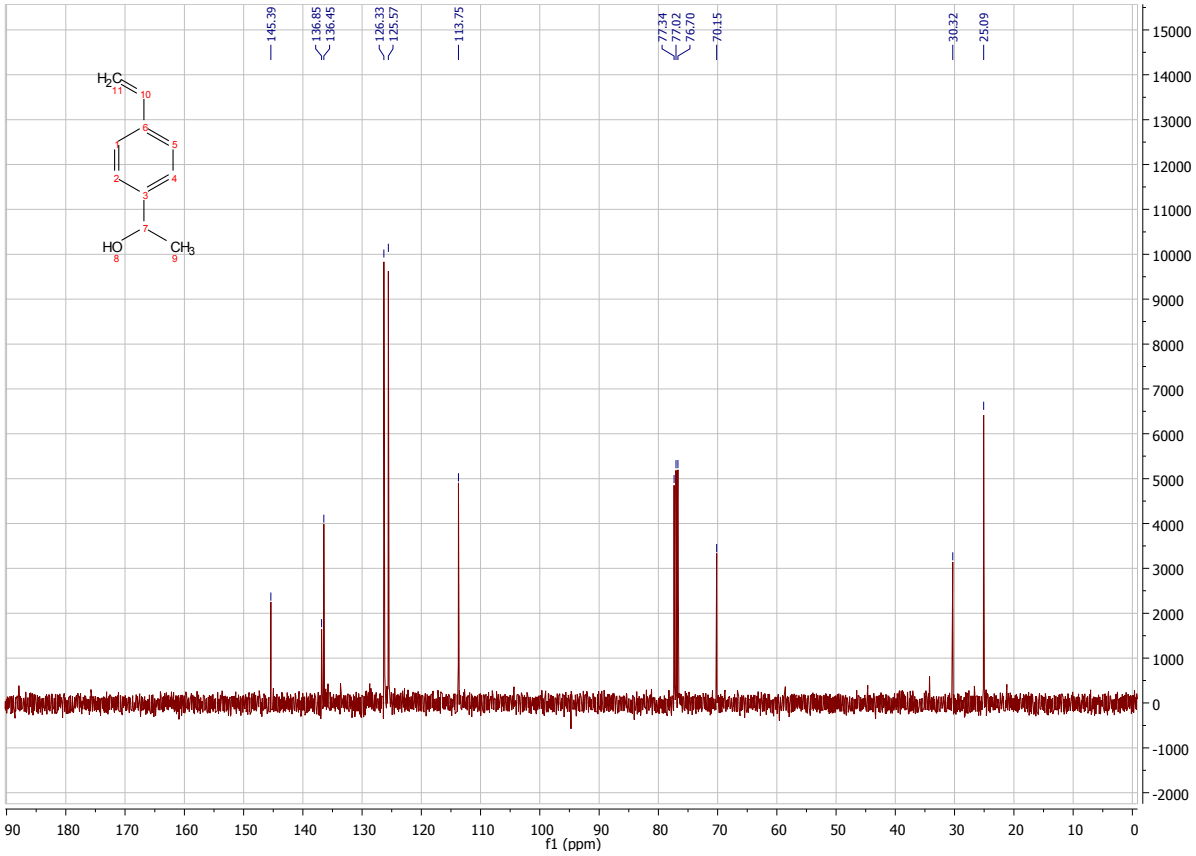
6.73
6.71
6.68
5.77
5.77
5.77
5.73
5.73
5.72
5.26
5.26
5.26
4.89
4.87
4.85
1.99
1.50
1.49
1.48
1.48
1.48
1.47
1.47
0.91
0.89
0.89
0.89
0.88
H2C
11
10
9
1
5
2
4
3
7
HO
8
CH3
9
6.32
5.93
2.77
2.99
2.97
2.80
3.22
9.82
1.41
0.82
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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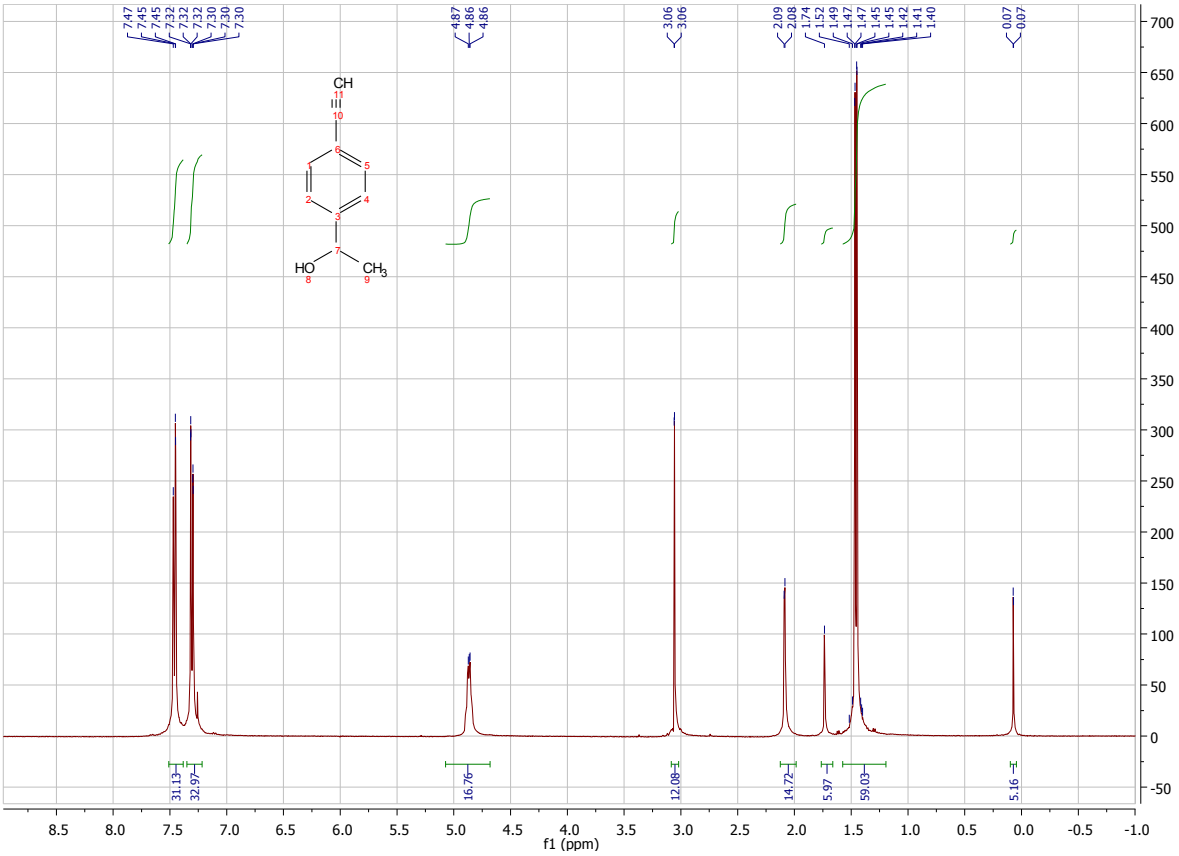
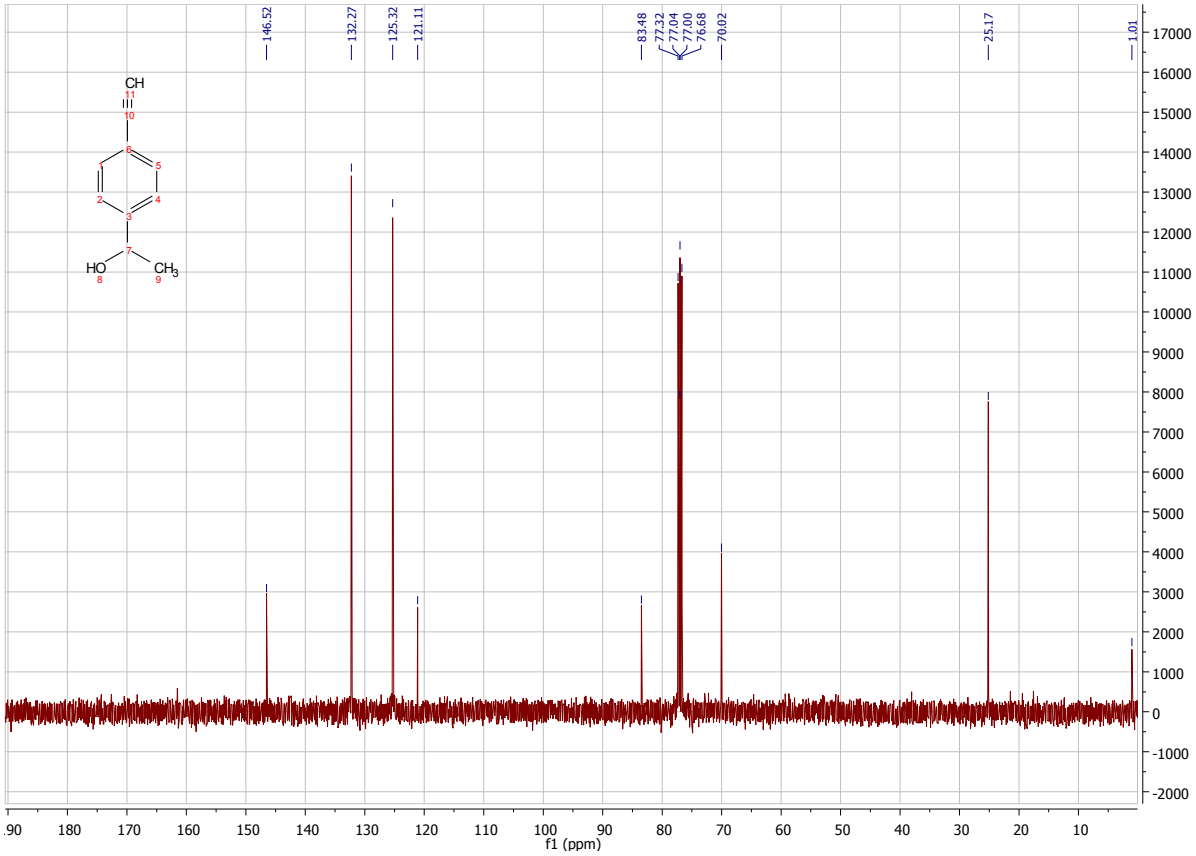
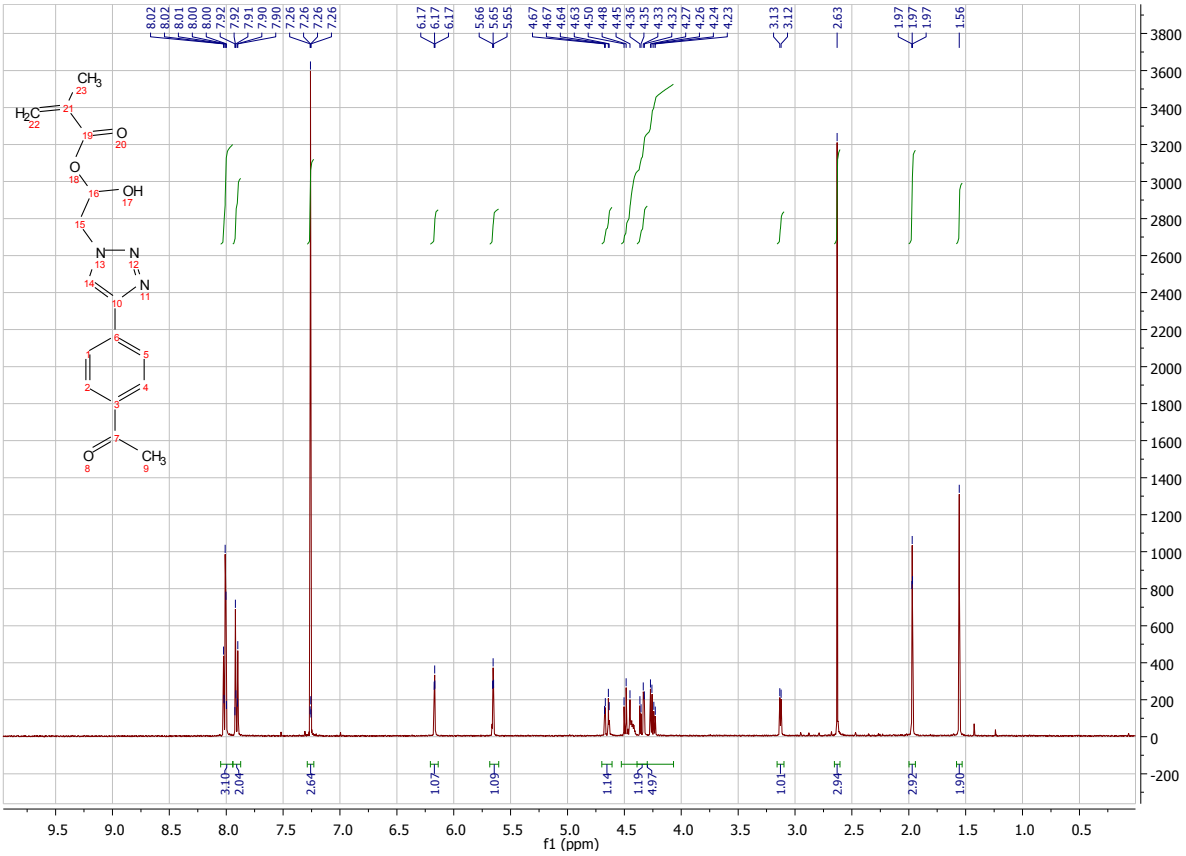
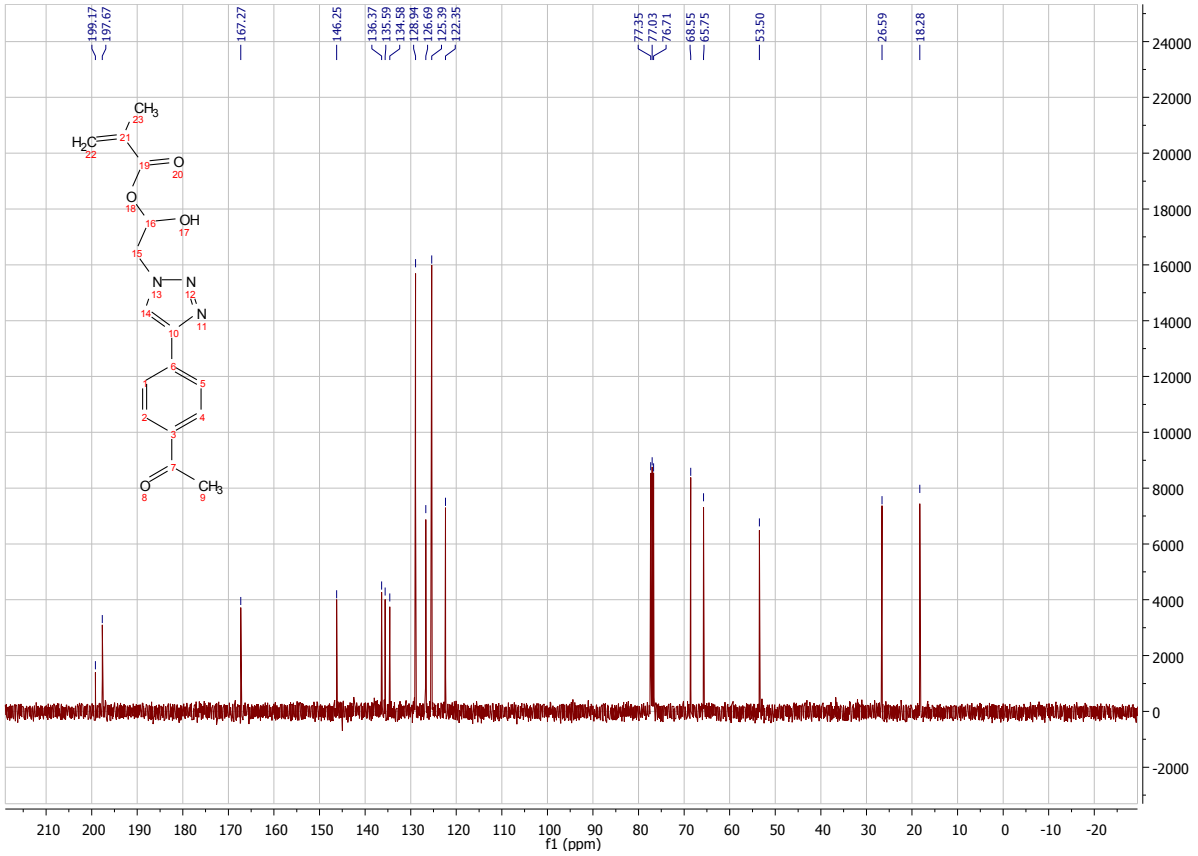
136.85
136.45
126.33
125.57
113.75
77.34
77.02
76.70
70.15
30.32
25.09
H2C
HO
CH3
f1 (ppm)




146.52
132.27
125.32
121.11
83.48
77.32
77.04
77.00
76.68
70.02
25.17
1.01
CH
HO
CH3
f1 (ppm)

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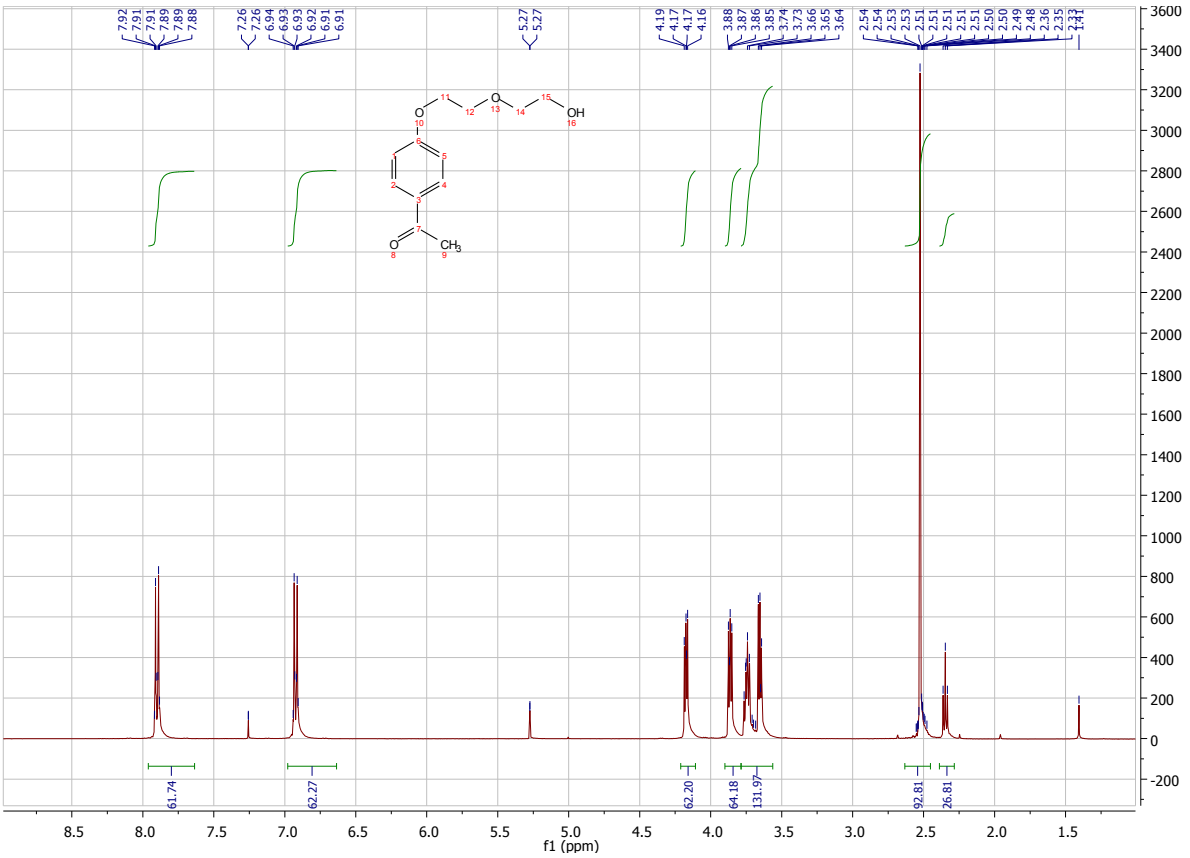
197.67
167.27
146.25
136.37
135.59
134.58
128.94
126.69
125.39
122.35
77.35
77.03
76.71
68.55
65.75
53.50
26.59
18.28
f1 (ppm)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7.91
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7.89
7.88
7.26
7.26
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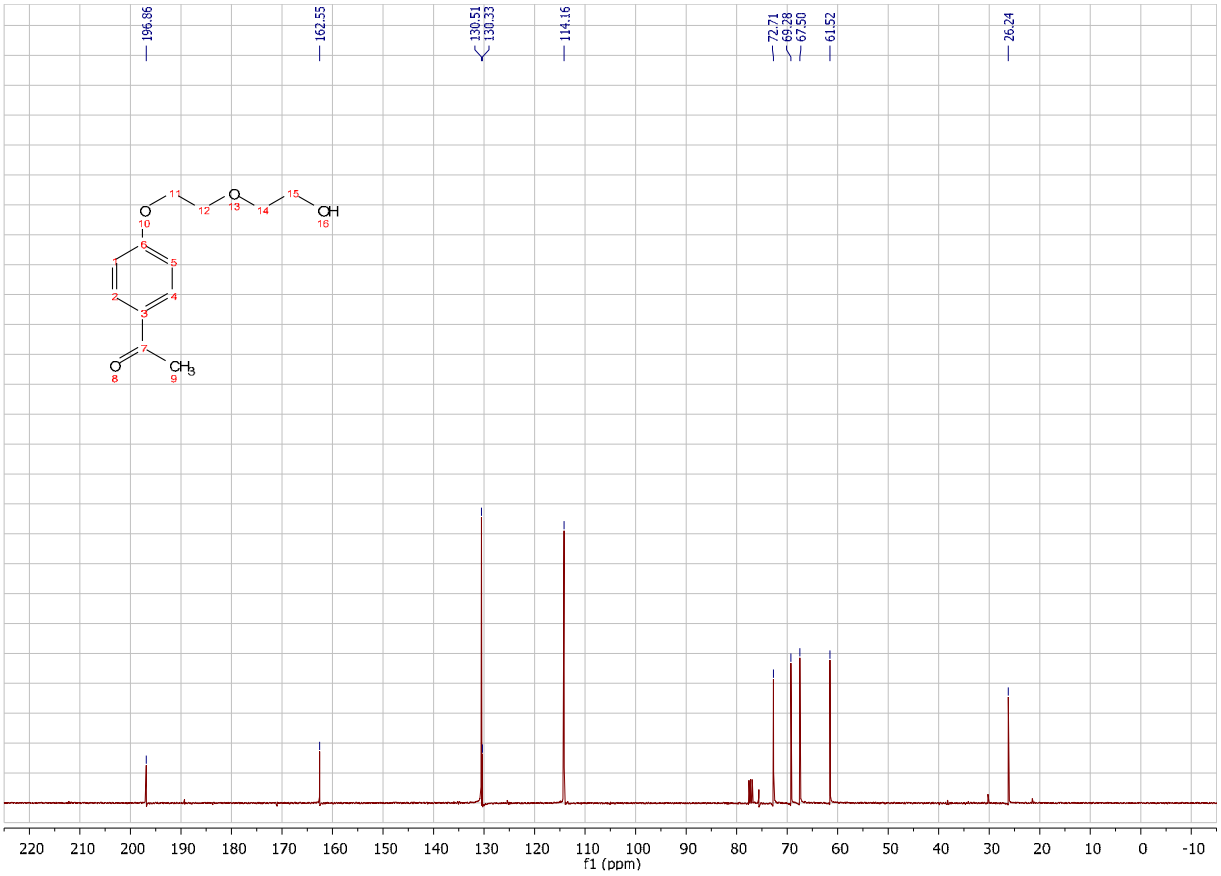
6.93
6.93
6.92
6.91
6.91
5.27
5.27
4.19
4.17
4.17
4.16
3.88
3.87
3.86
3.85
3.74
3.73
3.66
3.65
3.64
2.54
2.54
2.53
2.53
2.51
2.51
2.51
2.51
2.51
2.50
2.50
2.49
2.48
2.36
2.35
2.33
1.41
O
11
12
O
13
14
15
OH
16
10
1
6
5
2
4
3
7
O
8
CH3
9
61.74
62.27
62.20
64.18
131.97
92.81
26.81
f1 (ppm)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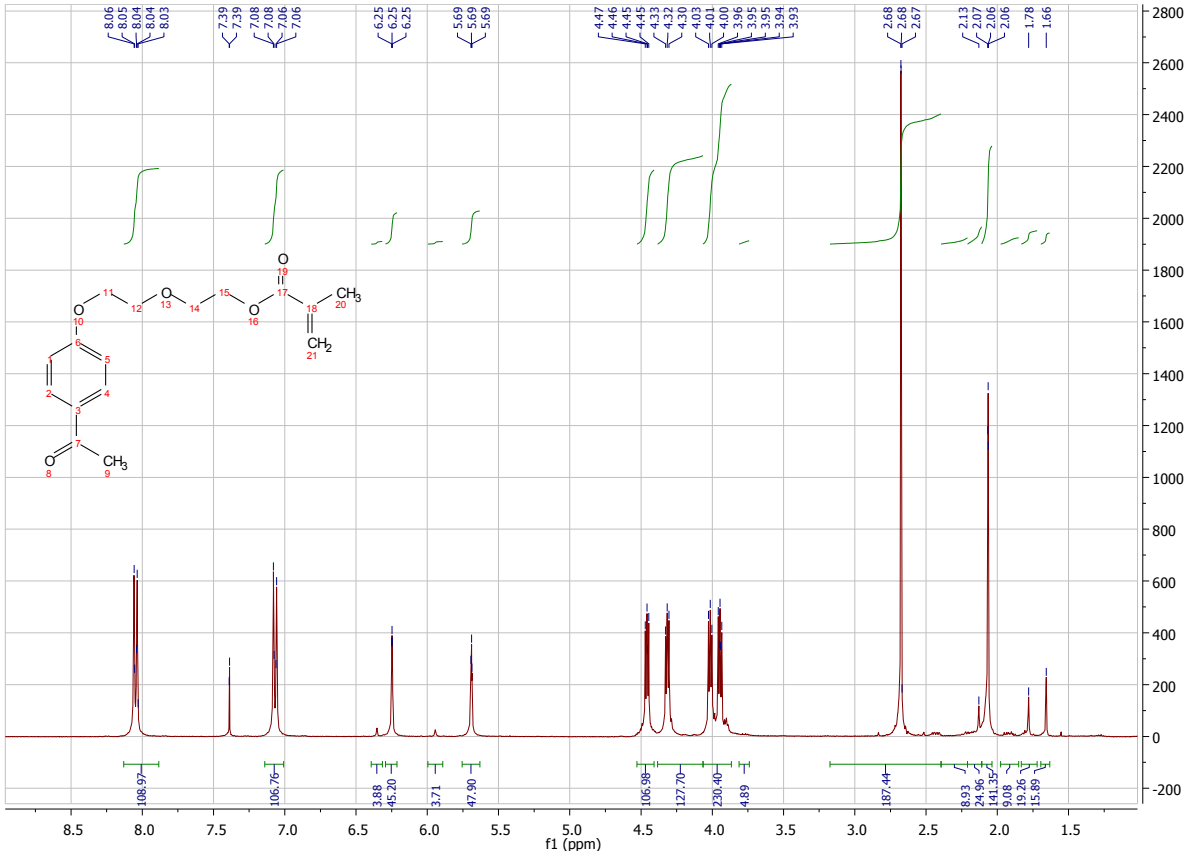
114.16
72.71
69.28
67.50
61.52
26.24
O
OH
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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8.04
8.04
8.03
7.39
7.39
7.08
7.08
7.06
7.06
6.25
6.25
6.25
5.69
5.69
5.69
4.47
4.46
4.45
4.45
4.33
4.32
4.30
4.03
4.01
4.00
3.96
3.95
3.95
3.94
3.93
2.68
2.68
2.67
2.13
2.07
2.06
2.06
1.78
1.66
O
19
O
10
11
12
O
13
14
15
O
16
17
CH3
20
18
CH2
21
1
2
3
4
5
6
7
O
8
CH3
9
108.97
106.76
3.88
45.20
3.71
47.90
106.98
127.70
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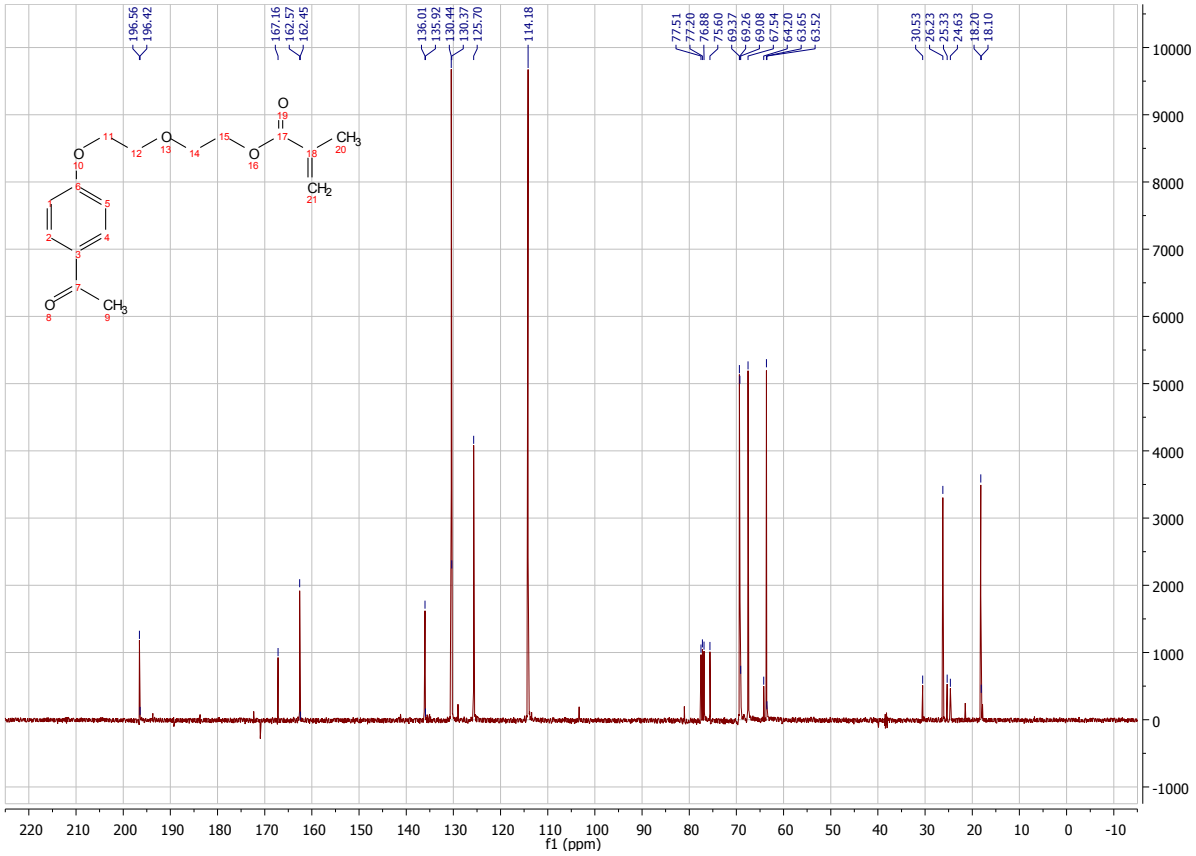
187.44
8.93
24.96
41.35
9.08
19.26
15.89
f1 (ppm)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136.01
135.92
130.44
130.37
125.70
114.18
77.51
77.20
76.88
75.60
69.37
69.26
69.08
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64.20
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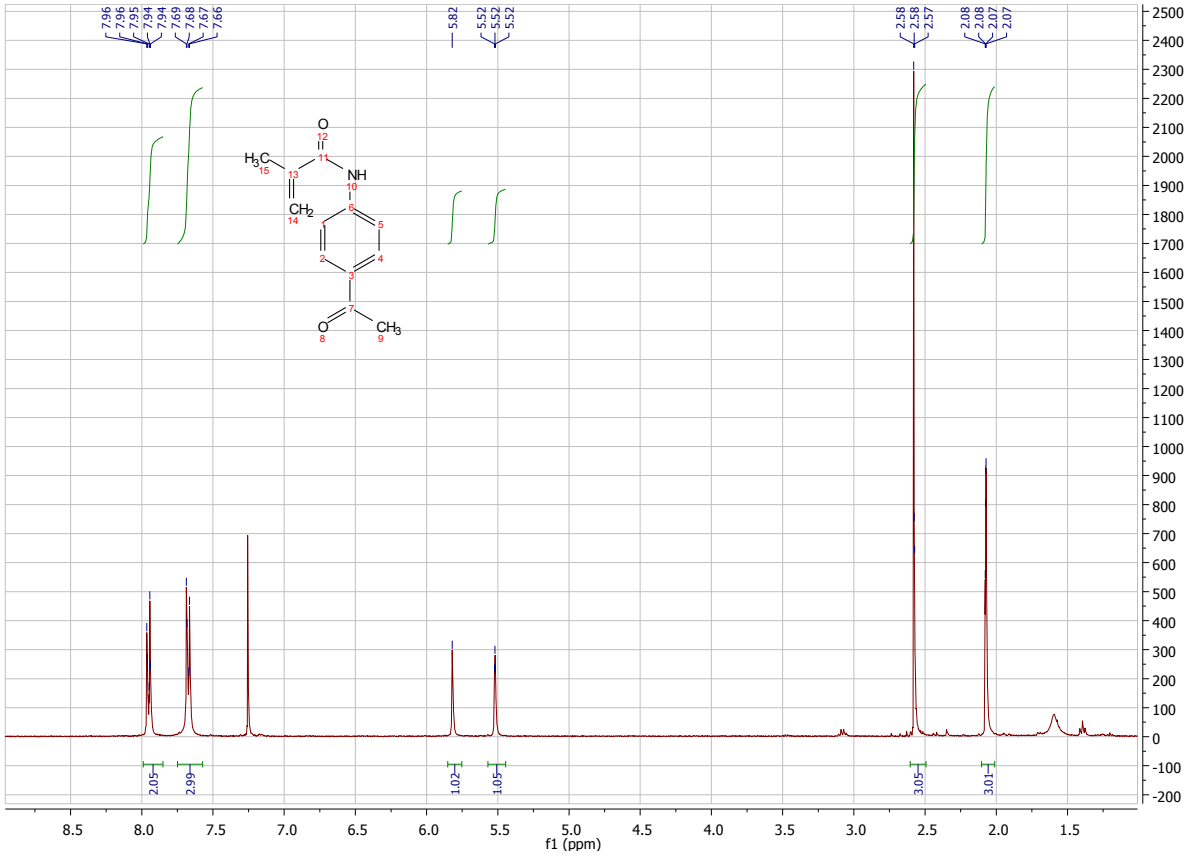
63.52
30.53
26.23
25.33
24.63
18.20
18.10
f1 (ppm)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5.52
5.52
2.58
2.58
2.57
2.08
2.08
2.07
2.07
O
12
H3C
15
11
NH
10
13
CH2
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2.05
2.99
1.02
1.05
3.05
3.01
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)
2500
2400
2300
2200
2100
2000
1900
1800
1700
1600
1500
1400
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1200
1100
1000
900
800
700
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500
400
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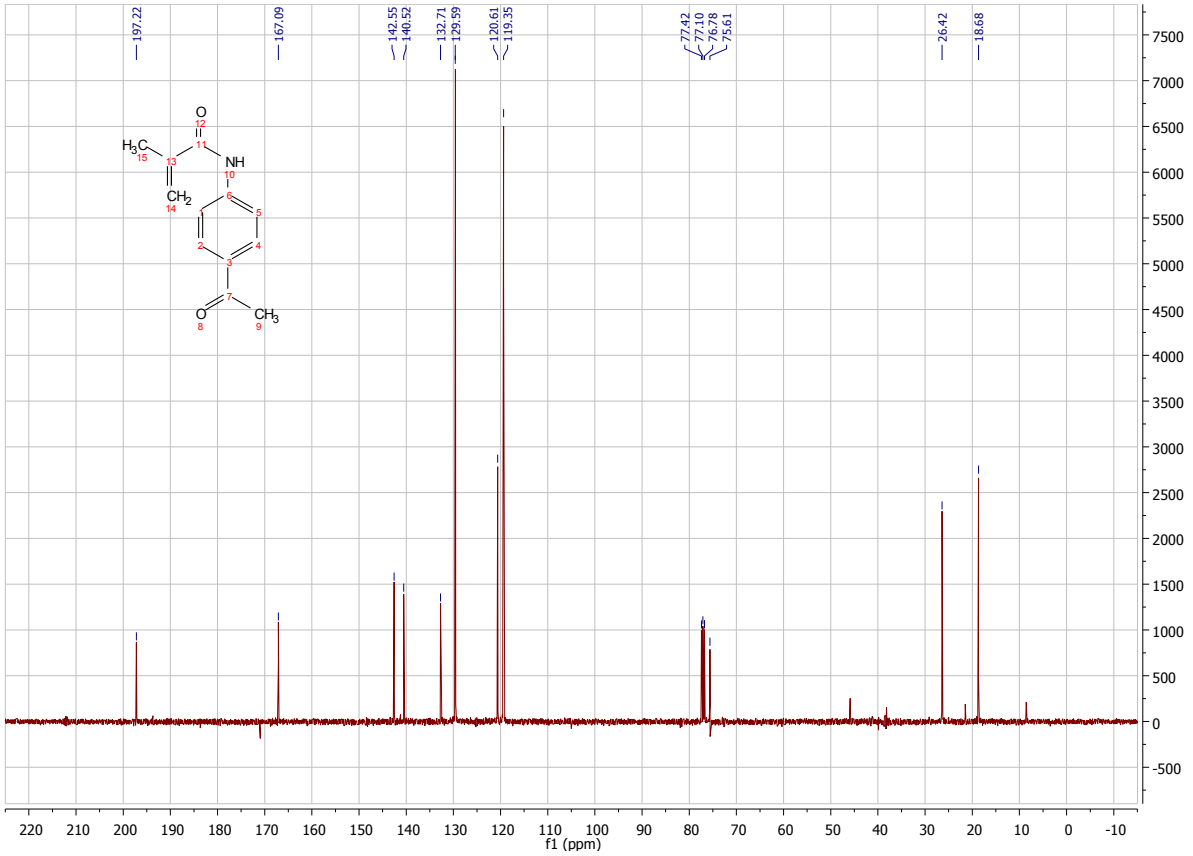
0
-100
-200


197.22
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132.71
129.59
120.61
119.35
77.42
77.10
76.78
75.61
26.42
18.68
O
12
11
H3C
15
13
NH
10
CH2
14
6
5
1
2
4
3
7
O
8
CH3
9
7500
7000
6500
6000
5500
5000
4500
4000
3500
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2500
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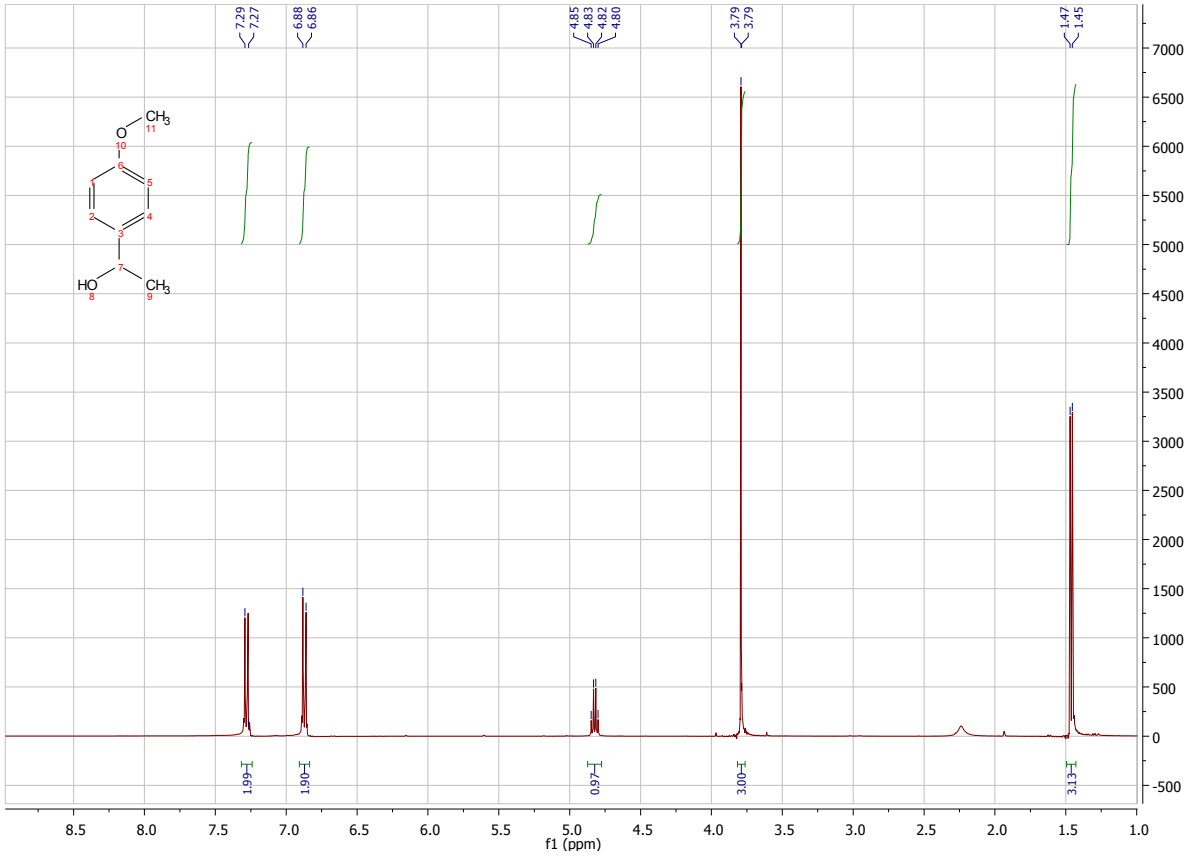
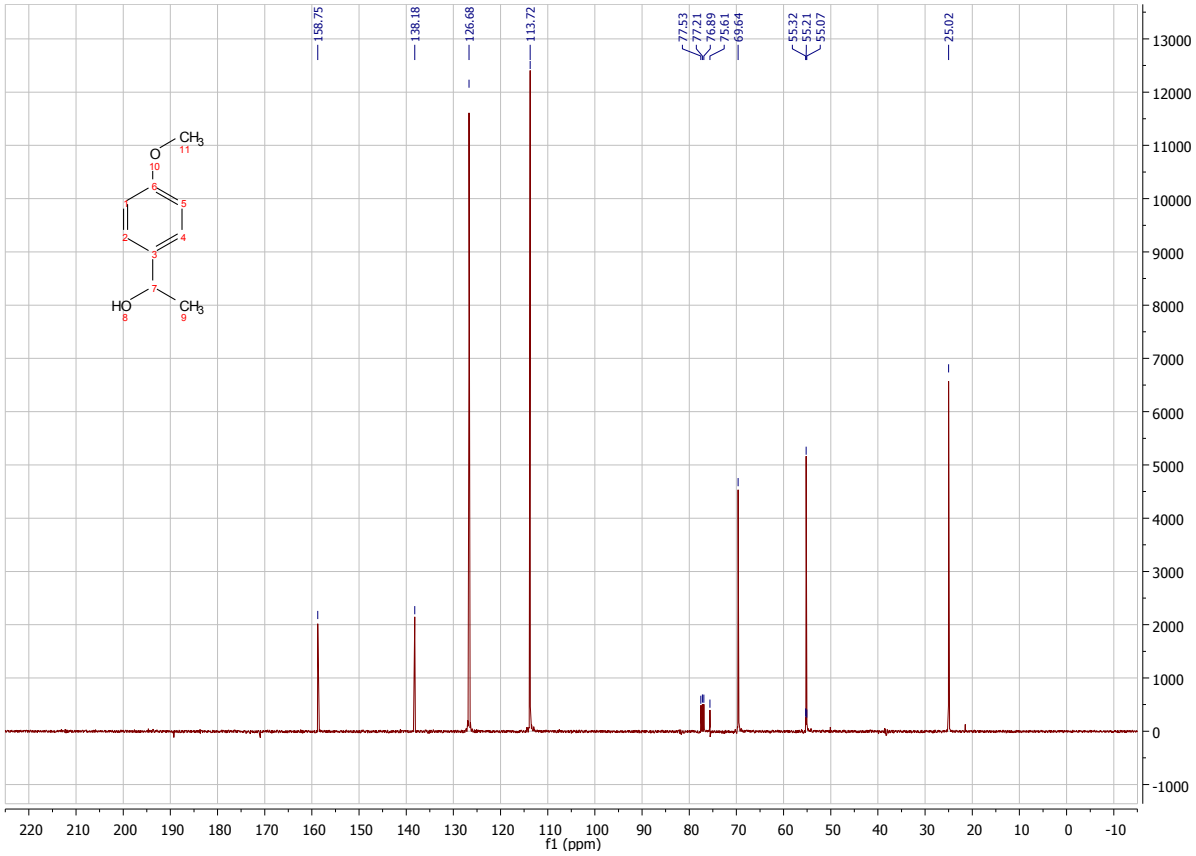
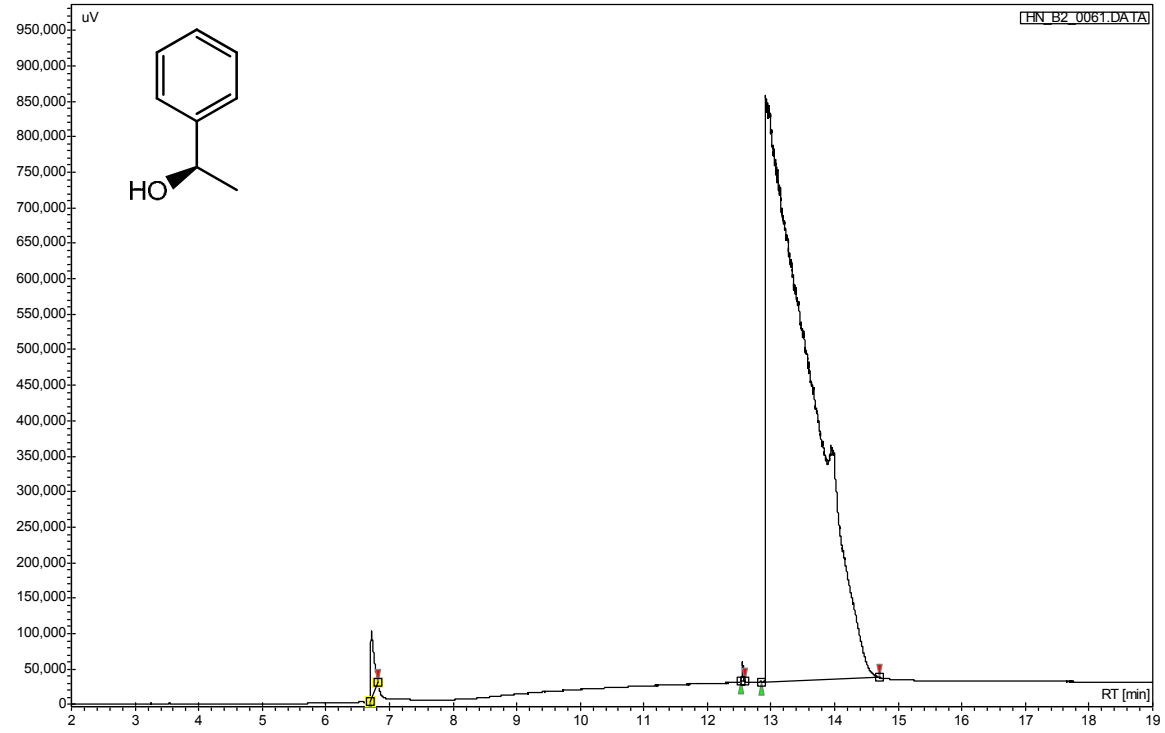
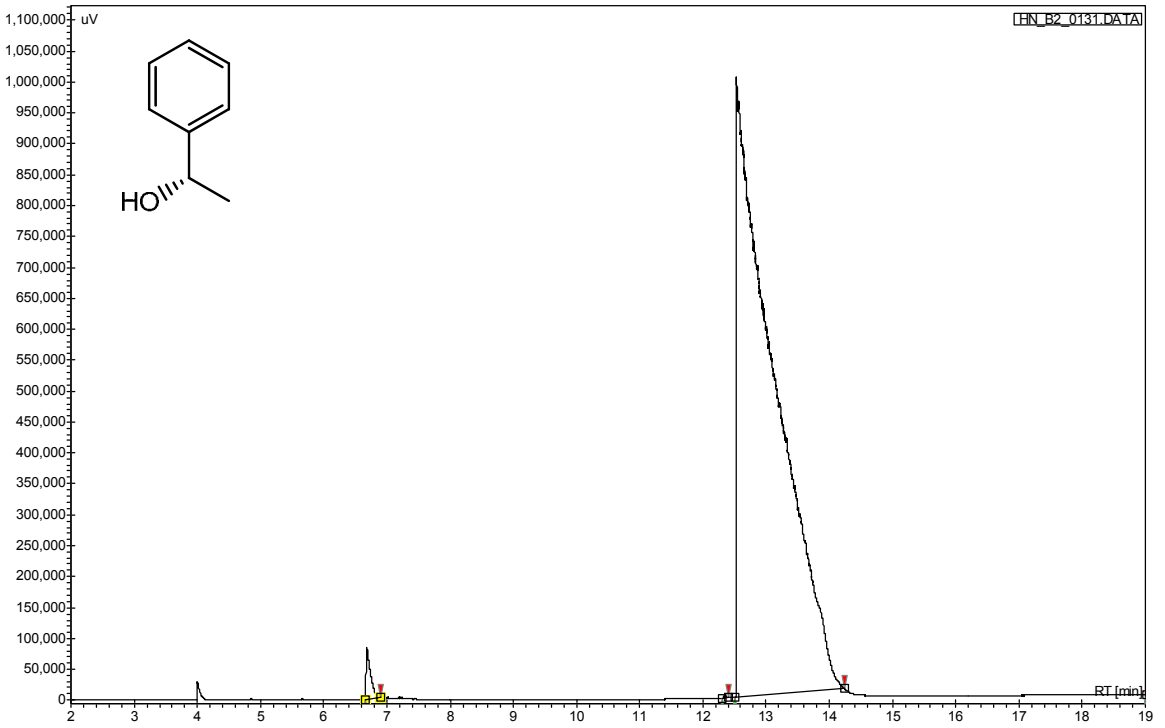
1500
1000
500
0
-500
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

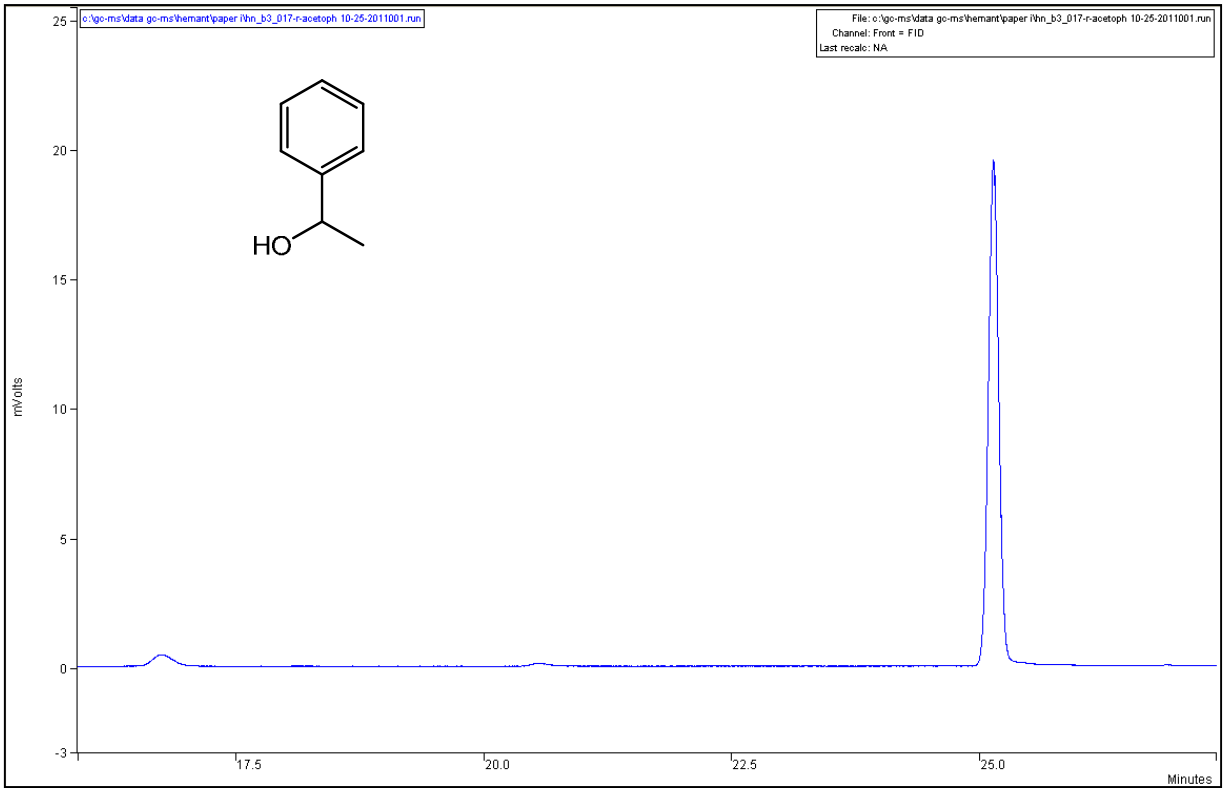



158.75
138.18
126.68
113.72
77.53
77.21
76.89
75.61
69.64
55.32
55.21
55.07
25.02
CH3
O
HO
CH3
f1 (ppm)

GLC Chromatograms of compounds:



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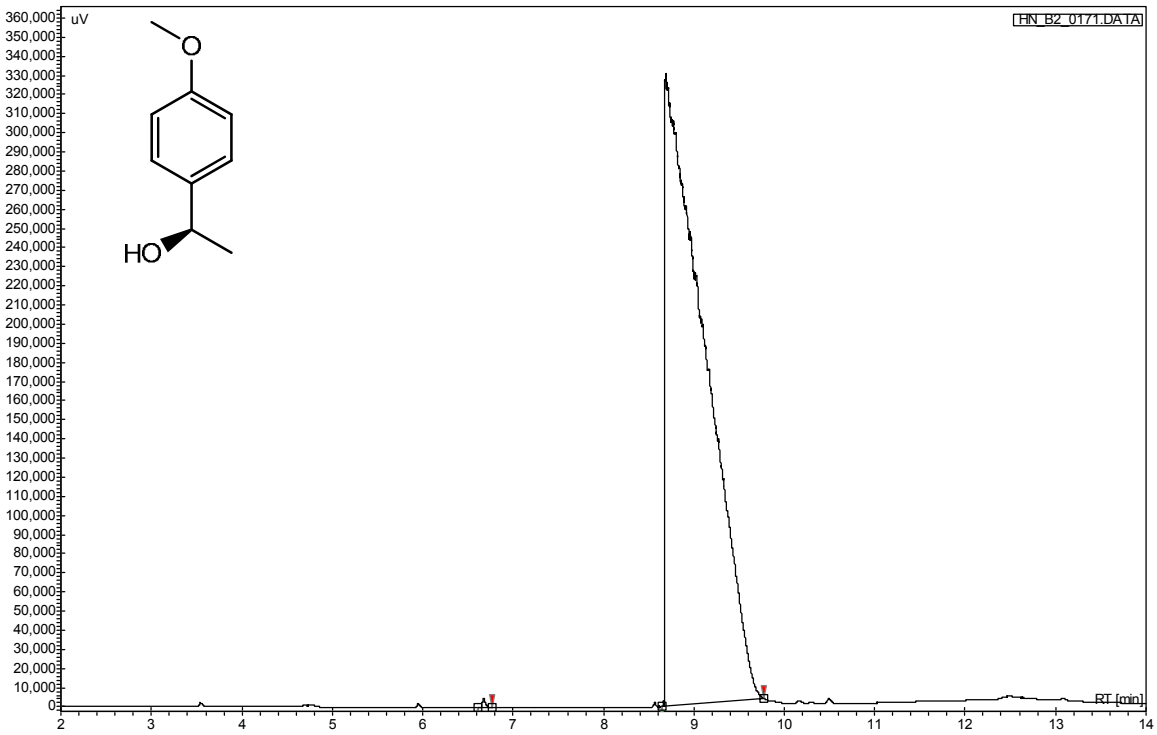
File: c:\gc-ms\data gc-ms\hemant\paper i\hn_b3_017-r-acetoph 10-25-2011001.run
Channel: Front = FID
Last recalc: NA
HO
mVolts
25
20
15
10
5
0
-3
17.5
20.0
22.5
25.0
Minutes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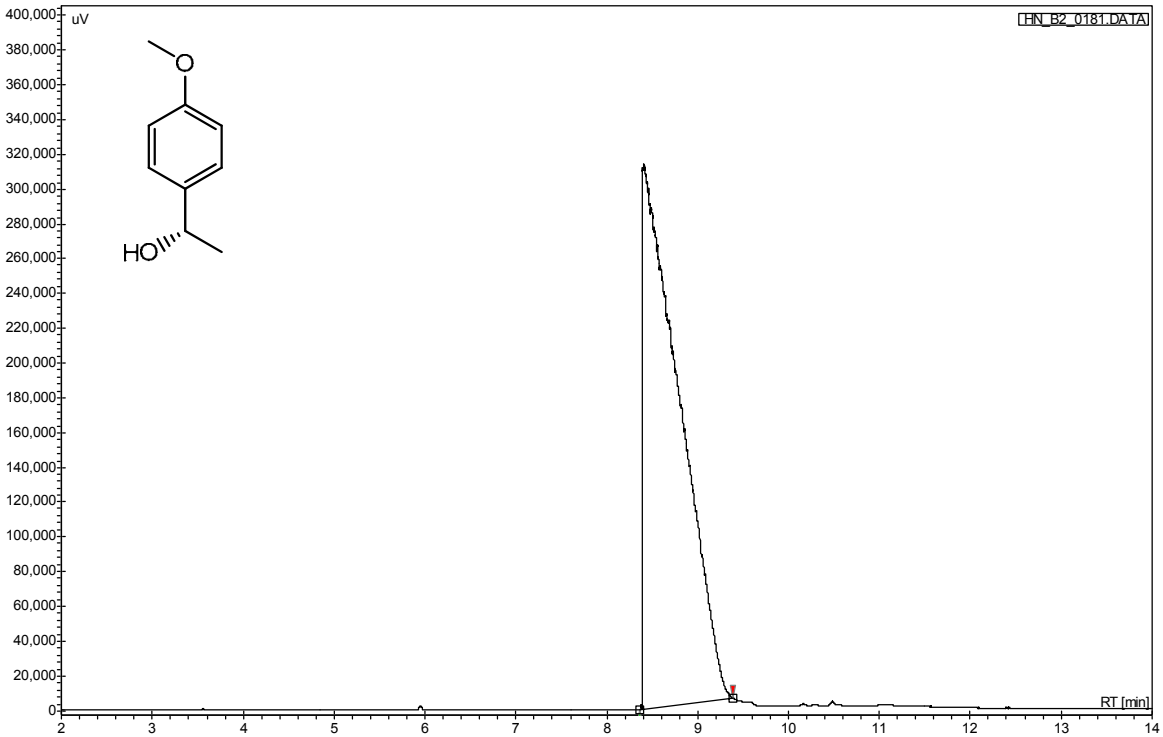
HN_B2_0171.DATA
O
HO
RT [min]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HO
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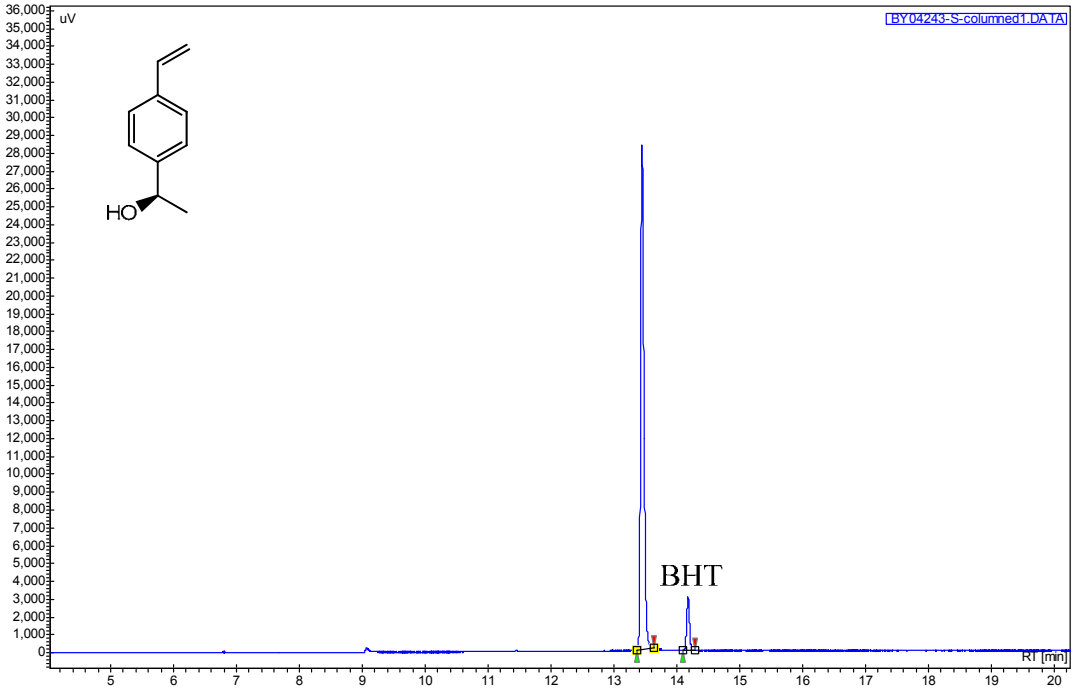
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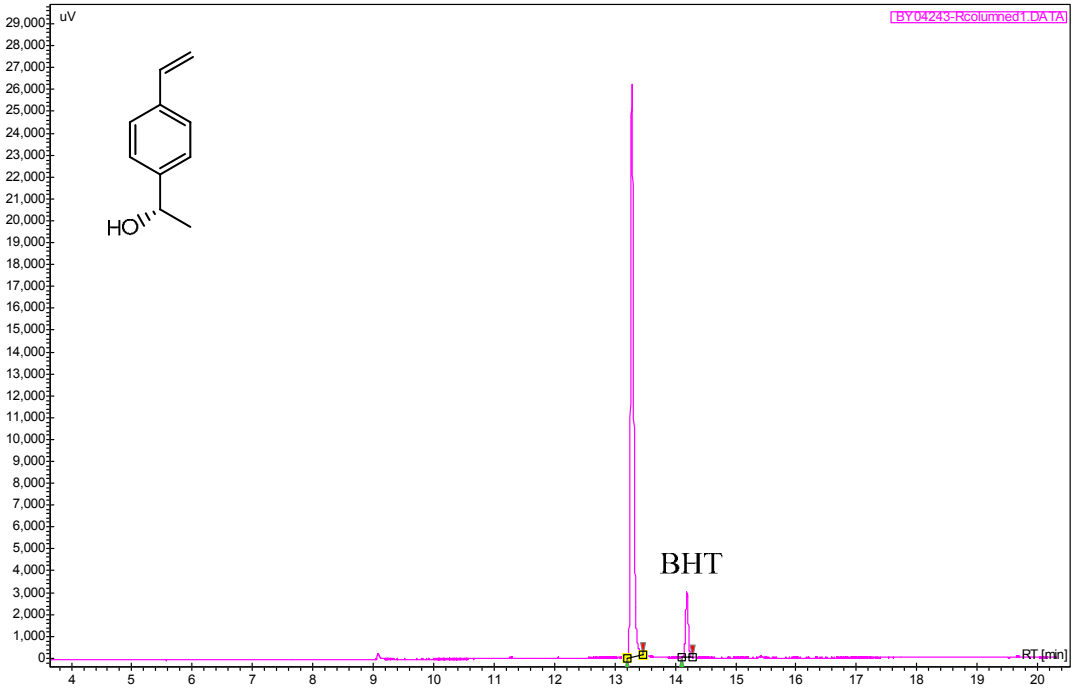
BY04243-S-columned1.DATA
HO
BHT
RT [min]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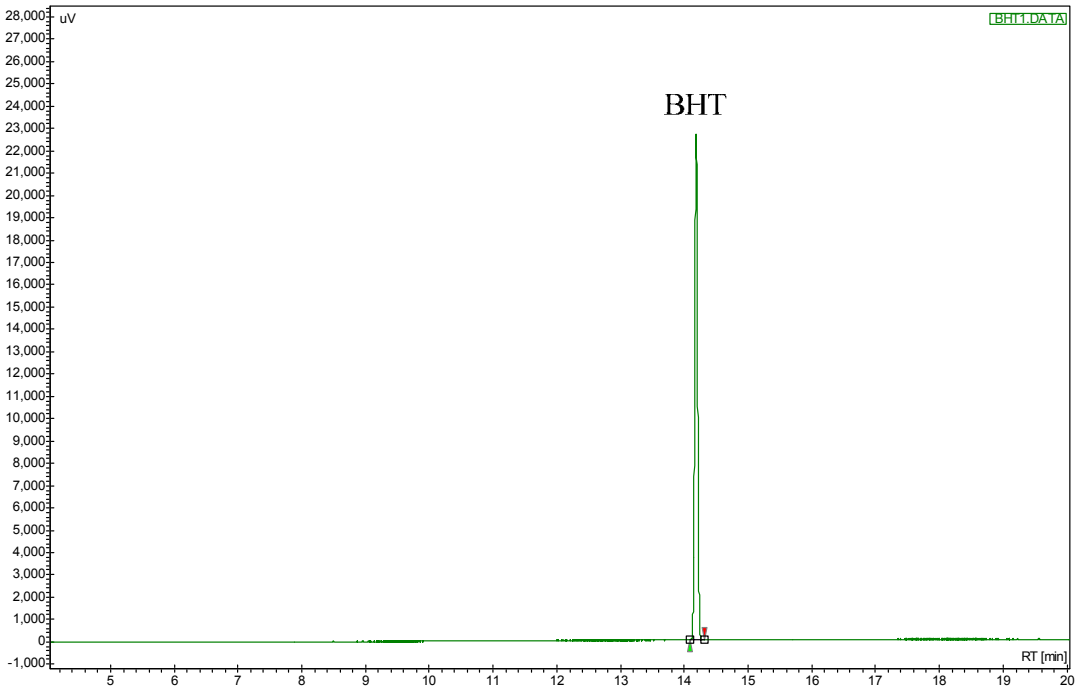
HO
BHT
RT [min]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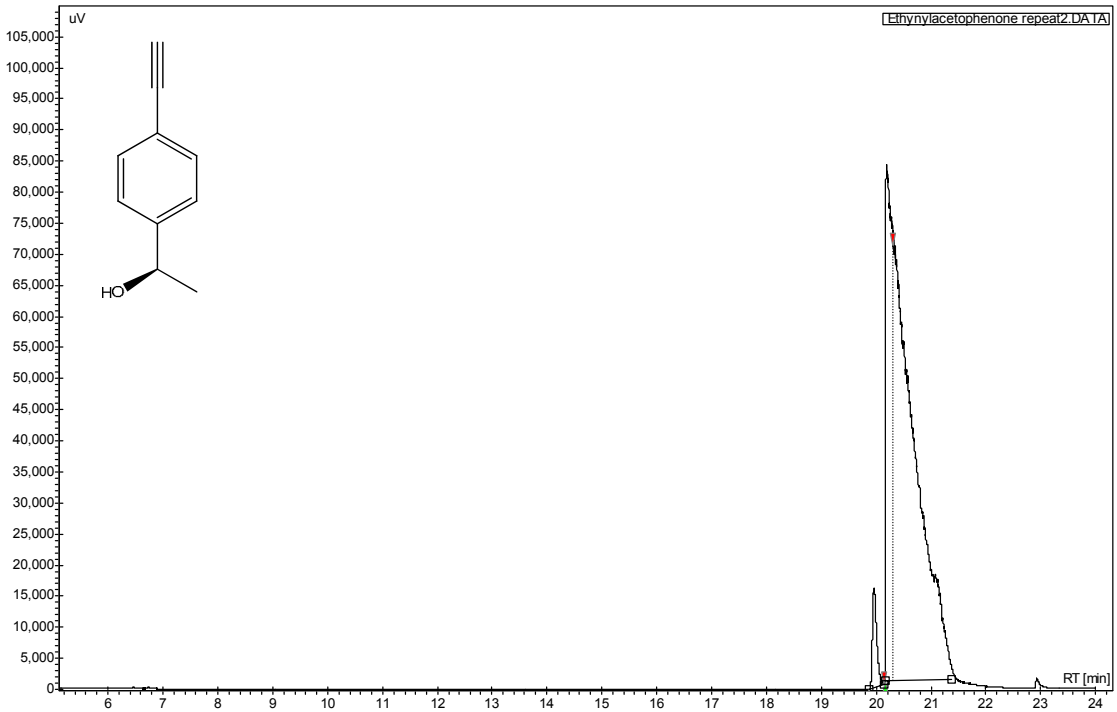
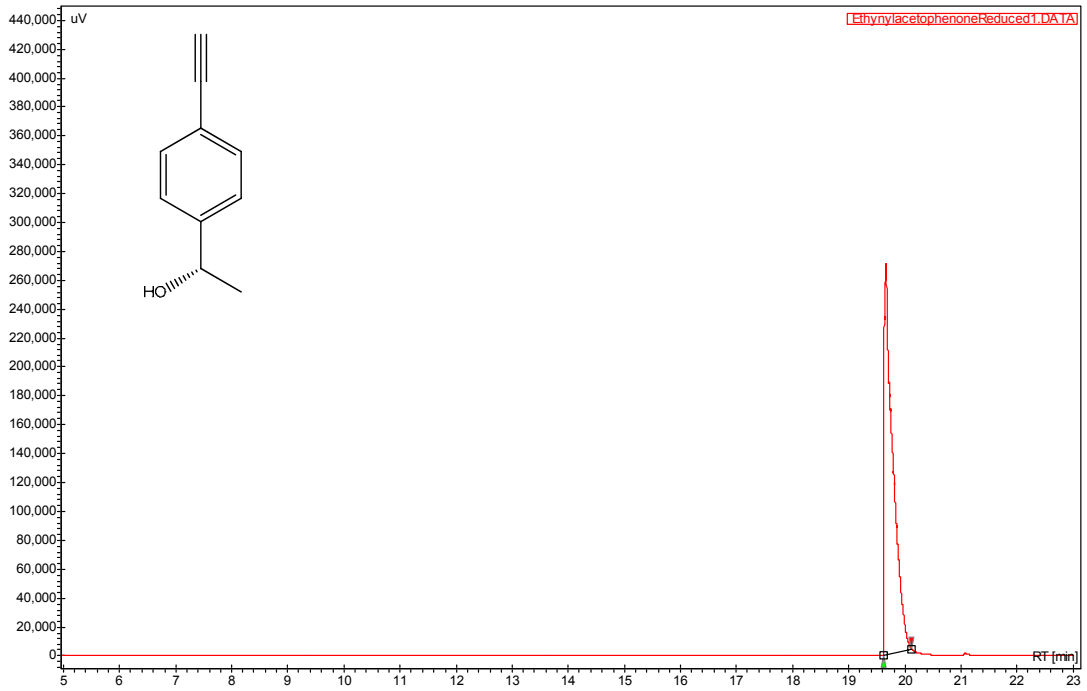
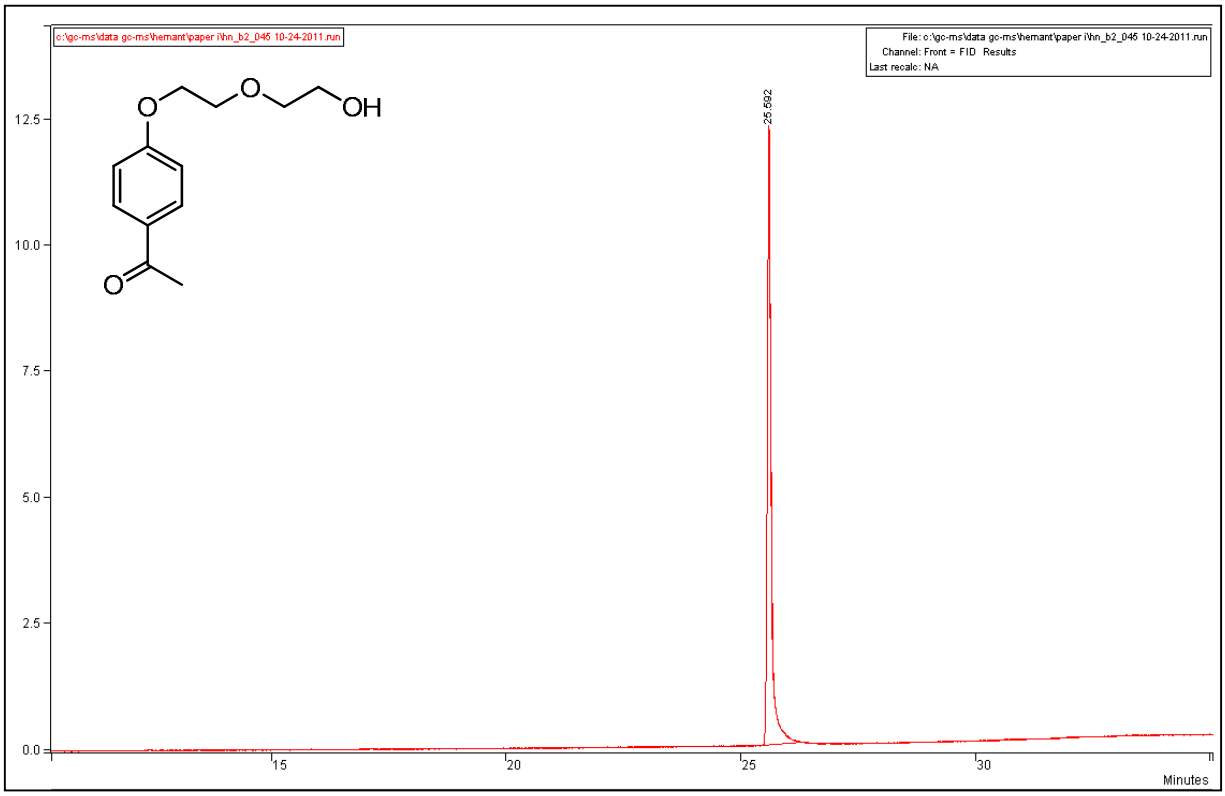
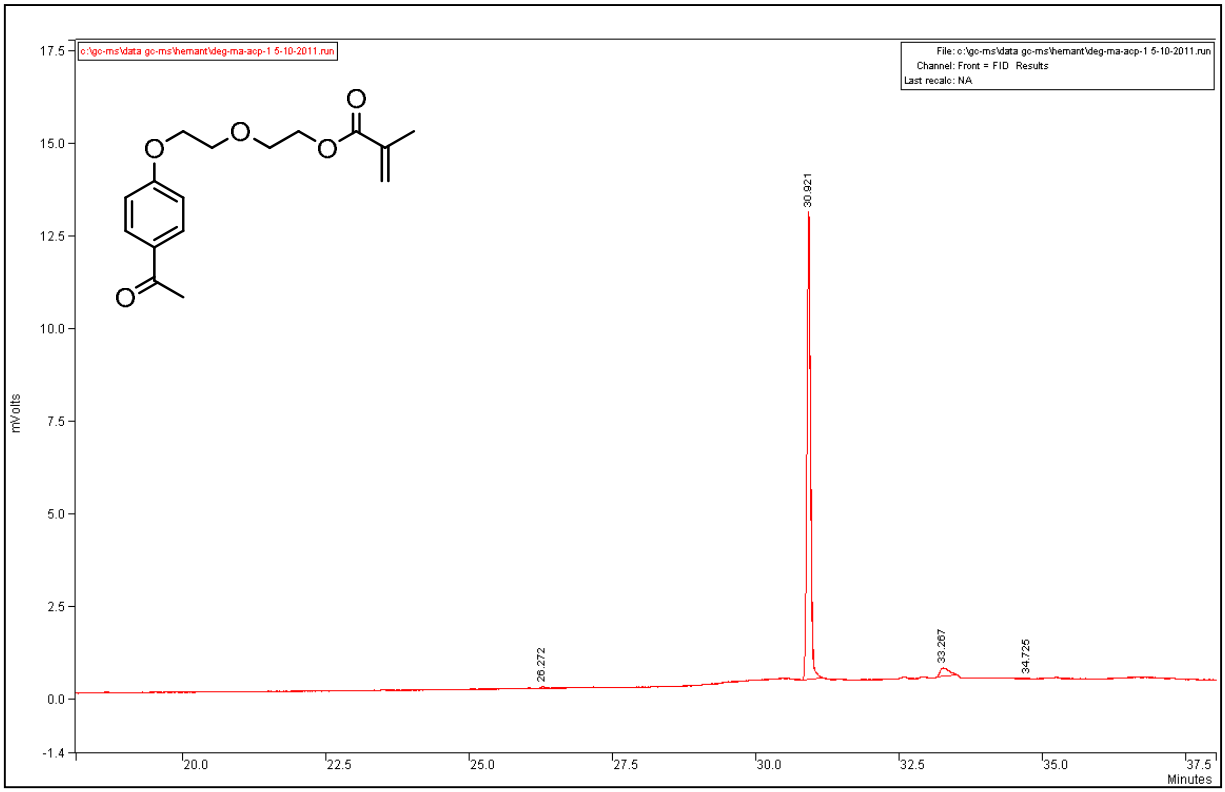
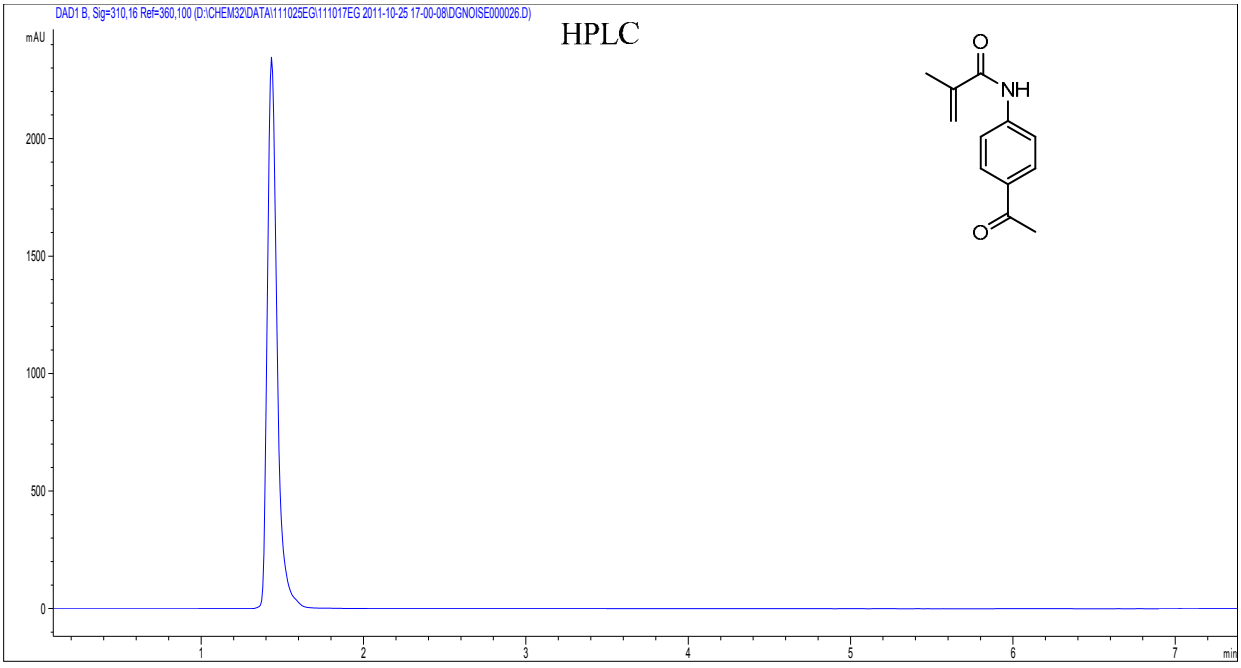
BHT1.DATA
BHT
RT [min]


uV
Ethynylacetophenone repeat2.DATA
HO
RT [min]


uV
EthynylacetophenoneReduced1.DATA
HO
RT [min]


c:\gc-ms\data gc-ms\hemant\paper i\hn_b2_046 10-24-2011.run
File: c:\gc-ms\data gc-ms\hemant\paper i\hn_b2_046 10-24-2011.run
Channel: Front = FID Results
Last recalc: NA
O
O
OH
O
25.592
Minutes


c:\gc-ms\data gc-ms\hemant\deg-ma-acp-1 5-10-2011.run
File: c:\gc-ms\data gc-ms\hemant\deg-ma-acp-1 5-10-2011.run
Channel: Front = FID Results
Last recalc: NA
mVolts
Minutes
30.921
26.272
33.267
34.725


DAD1 B, Sig=310,16 Ref=360,100 (D:\CHEM32\DATA\111025EG\111017EG 2011-10-25 17-00-08\DGNOISE000026.D)
HPLC
mAU
min
NH