Electronic Supplementary Material (ESI) for Chemical Communications

Trichlorosilyl triflate-mediated enantioselective directed cross-aldol reaction between ketones using chiral phosphine oxide as an organocatalyst

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Electronic Supplementary Information

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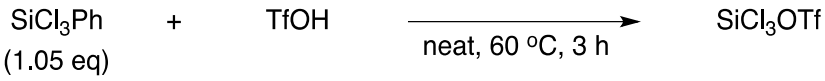
General Methods

Melting points (mp) are uncorrected. ^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$ with JEOL JNM-ECX400 spectrometer. Tetramethylsilane (TMS) (δ = 0 ppm) and $CDCl_3$ (δ = 77.0 ppm) served as an internal standard for ^{1}H and ^{13}C NMR, respectively. Infrared spectra were recorded on JEOL JIR-6500W. Mass spectra were measured with JEOL JMS-DX303HF mass spectrometer and JEOL JMS-T100GCv. Optical rotations were recorded on JASCO P-1010 polarimeter. High-pressure liquid chromatography (HPLC) was performed on JASCO P-980 and UV-1575. Thin-layer chromatography (TLC) analysis was carried out using Merck silica gel plates. Visualization was accomplished with UV light, phosphomolybdic acid and/or anisaldehyde. Column chromatography was performed using Kanto Chemical Silica Gel 60N (spherical, acidic, 63-210 μm).

Reagents were purified by standard procedures or used as received otherwise noted. Propionitrile (the highest grade) was purchased from Wako Pure Chemical Industries and stored over 4Å MS prior to use. Isobutyronitrile (the highest grade) was purchased from Tokyo Chemical Industries and stored over 4Å MS prior to use. Dehydrated stabilizer-free dichloromethane was purchased from Kanto Chemical Co. Inc. (*S*)-BINAP dioxide (BINAPO) and the other chiral phosphine oxides were prepared by oxidation of the corresponding phosphines with hydrogen peroxide in acetone.[1]

Preparation of trichlorosilyl triflate[2]



Trifluoromethanesulfonic acid (2.66 mL, 30.0 mmol, 1.0 equiv.) was added to phenyltrichlorosilane (5.05 mL, 31.5 mmol, 1.05 equiv.) in a screw-top test tube at room temperature under argon atmosphere. The mixture was stirred for 3 h at 60 °C and then diluted with dry dichloromethane. The solution (2.0 M) was stocked in the screw-top test tube with a Teflon packing.

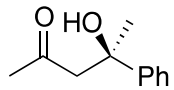
Typical Procedure for Aldol Reaction Catalyzed by (S)-BINAPO (Procedure for ketone 1a, 1b and 1d as an aldol donor)

A solution of trichlorosilyl triflate in dichloromethane (2.0 M, 0.5 mL, 1.0 mmol, 2.0 equiv.) was added dropwise to a solution of aldol donor **1** (0.5 mmol) and (*S*)-BINAPO (0.05 mmol, 10 mol %) in isobutyronitrile (5 mL). Then diisopropylethylamine (0.44 mL, 2.5 mmol, 5.0 equiv.) and aldol acceptor **1'** (1.0 mmol, 2.0 equiv.) was successively added to the mixture. The mixture was stirred for the indicated time. The reaction was quenched with aqueous 1.5 M KF/HCOOH (5.0 mL) and then the slurry was stirred for 10 min at room temperature. The mixture was filtered through cotton pad and the aqueous layer was extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with 10% HCl (10 mL), sat. $NaHCO_3$ (10 mL) and brine (10 mL), and dried over Na_2SO_4. After filtration and concentration, the obtained crude product was purified by column chromatography (SiO_2, acidic) to give an aldol product.

Typical Procedure for Aldol Reaction Catalyzed by (S)-BINAPO (Procedure for ketone 1c, 1e and 1f as an aldol donor)

A solution of trichlorosilyl triflate in dichloromethane (2.0 M, 0.5 mL, 1.0 mmol, 2.0 equiv.) was added dropwise to a solution of aldol donor **1** (0.5 mmol) in isobutyronitrile (5 mL). After the addition of diisopropylethylamine (0.44 mL, 2.5 mmol, 5.0 equiv.), the solution was stirred for 1 hour. Then (*S*)-BINAPO (0.05 mmol, 10 mol %) and aldol acceptor **1'** (1.0 mmol, 2.0 equiv.) was successively added to the reaction mixture. The mixture was stirred for the indicated time. The reaction was quenched with aqueous 1.5 M KF/HCOOH (5.0 mL) and then the slurry was stirred for 10 min at room temperature. The mixture was filtered through cotton pad and the aqueous layer was extracted with EtOAc (3 x 30 mL). The combined organic layers were washed with 10% HCl (10 mL), sat. $NaHCO_3$ (10 mL) and brine (10 mL), and dried over Na_2SO_4. After filtration and concentration, the obtained crude product was purified by column chromatography (SiO_2, acidic) to give an aldol product.

(*R*)-4-Hydroxy-4-phenylpentan-2-one (3ab)[3]



Colorless oil.

TLC: R_f 0.19 (hex/EtOAc = 4/1, stained red with anisaldehyde).

$[\alpha]_D^{17}$ –4.9 (*c* 0.64, $CHCl_3$, 83% ee), [lit.[3]: $[\alpha]_D^{25}$ –5.6 (*c* 0.75, $CHCl_3$, 91% ee, *R*)].

IR (film on NaCl): 1701, 2931, 2978, 3028, 3061, 3088, 3475 cm^{-1}.

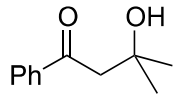
^1H NMR ($CDCl_3$): δ 1.52 (s, 3H), 2.08 (s, 3H), 2.85 (d, 1H, *J* = 16.8 Hz), 3.19 (d, 1H, *J* = 16.8 Hz), 4.50 (brs, 1H), 7.19-7.27 (m, 1H), 7.29-7.37 (m, 2H), 7.41-7.45 (m, 2H).

^{13}C NMR ($CDCl_3$): δ 30.6, 31.8, 53.9, 73.2, 124.3, 126.7, 128.3, 147.2, 210.6.

LRMS (EI): 178 (M^+), 121, 105, 77.

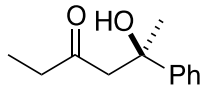
HRMS (EI): Calcd for $C_{11}H_{14}O_2$ 178.0994, found 178.0989.
The enantiomeric excess was determined to be 83% ee by chiral HPLC with Daicel Chiralcel OD-H column [eluent: 100/1 = hex/IPA; flow rate: 1.0 mL/min; detection: 254 nm; t_R: 19.9 min (major, *R*), 22.9 min (minor, *S*)].

3-Hydroxy-3-methyl-1-phenylbutan-1-one (3ba)[4]



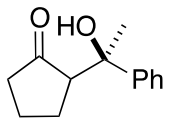
Colorless oil.
TLC: R_f 0.19 (hex/EtOAc = 4/1, stained purple with anisaldehyde).
^{1}H NMR ($CDCl_3$): δ 1.36 (s, 3H), 3.16 (s, 2H), 4.15 (brs, 1H), 7.45-7.51 (m, 2H), 7.57-7.62 (m, 1H), 7.93-7.97 (m, 2H).
^{13}C NMR ($CDCl_3$): δ 29.5, 48.5, 69.9, 128.0, 128.6, 133.6, 137.2, 201.8.

5-Hydroxy-5-phenylhexan-3-one (3cb)



Colorless oil.
TLC: R_f 0.25 (hex/EtOAc = 4/1, stained purple with anisaldehyde).
$[\alpha]_D^{18}$ +8.3 (*c* 0.68, $CHCl_3$, 74% ee).
IR (film on NaCl): 1699, 2937, 2978, 3028, 3061, 3475 cm^{-1}.
^{1}H NMR ($CDCl_3$): δ 0.94 (t, 3H, *J* = 6.8 Hz), 1.52 (s, 3H), 2.22-2.34 (m, 1H), 2.35-2.46 (m, 1H), 2.81 (d, 1H, *J* = 16.8 Hz), 3.15 (d, 1H, *J* = 16.8 Hz), 4.66 (brs, 1H), 7.20-7.28 (m, 1H), 7.30-7.37 (m, 2H), 7.41-7.45 (m, 2H).
^{13}C NMR ($CDCl_3$): δ 7.2, 30.7, 37.8, 52.8, 73.3, 124.3, 126.7, 128.2, 147.2, 213.4.
LRMS (EI): 192 (M^+), 177, 121, 105, 77.
HRMS (EI): Calcd for $C_{12}H_{16}O_2$ 192.1150, found 192.1155.
The enantiomeric excess was determined to be 74% ee by chiral HPLC with Daicel Chiralpak AS-H column [eluent: 200/1 = hex/IPA; flow rate: 1.0 mL/min; detection: 254 nm; t_R: 34.3 min (major), 38.7 min (minor)].

2-(1-Hydroxy-1-phenylethyl)cyclopentanone (3db)[5]

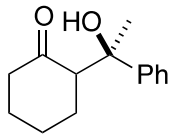


Data for *major*-isomer
Colorless oil.

TLC: R_f 0.26 (hex/EtOAc = 4/1, stained purple with anisaldehyde).
$[\alpha]_D^{18}$ –66.3 (*c* 0.92, $CHCl_3$, 68% ee).
IR (film on NaCl): 1718, 2879, 2972, 3032, 3062, 3086, 3481 cm^{-1}.
^1H NMR ($CDCl_3$): δ 1.58 (s, 3H), 1.60-1.74 (m, 2H), 1.76-1.87 (m, 1H), 1.89-1.98 (m, 1H), 2.10-2.22 (m, 1H), 2.36-2.52 (m, 2H), 4.58 (brs, 1H), 7.22-7.28 (m, 1H), 7.31-7.36 (m, 2H), 7.44-7.49 (m, 2H).
^{13}C NMR ($CDCl_3$): δ 20.0, 23.5, 27.1, 39.9, 59.9, 75.0, 125.2, 127.0, 128.1, 145.9, 222.5.
LRMS (EI): 204 (M^+), 121.
HRMS (EI): Calcd for $C_{13}H_{16}O_2$ 204.1150, found 204.1149.
The enantiomeric excess was determined to be 68% ee by chiral HPLC with Daicel Chiralcel OD-H column [eluent: 100/1 = hex/IPA; flow rate: 1.0 mL/min; detection: 254 nm; t_R: 22.5 min (minor), 26.6 min (major)].

Data for *minor*-isomer
Colorless oil.
TLC: R_f 0.26 (hex/EtOAc = 4/1, stained purple with anisaldehyde).
$[\alpha]_D^{21}$ –64.3 (*c* 0.38, $CHCl_3$, 37% ee).
IR (film on NaCl): 1730, 2877, 2935, 2970, 3024, 3057, 3088, 3446 cm^{-1}.
^1H NMR ($CDCl_3$): δ 1.55-2.00 (m, 5H), 1.73 (s, 3H), 2.21-2.30 (m, 1H), 2.53-2.59 (m, 1H), 4.19 (brs, 1H), 7.21-7.26 (m, 1H), 7.30-7.38 (m, 4H).
^{13}C NMR ($CDCl_3$): δ 20.0, 26.4, 29.0, 39.8, 58.4, 75.4, 125.5, 126.8, 128.0, 145.4, 222.0.
LRMS (FAB): 227 ($M+Na^+$), 187.
HRMS (FAB): Calcd for $C_{13}H_{16}O_2Na$ 227.1048, found 227.1060.
The enantiomeric excess was determined to be 37% ee by chiral HPLC with Daicel Chiralcel OB-H column [eluent: 24/1 = hex/IPA; flow rate: 1.0 mL/min; detection: 254 nm; t_R: 12.4 min (major), 18.9 min (minor)].

2-(1-Hydroxy-1-phenylethyl)cyclohexanone (3eb)

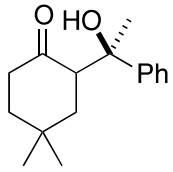


Data for *major*-isomer
Colorless oil.
TLC: R_f 0.31 (hex/EtOAc = 4/1, stained purple with anisaldehyde).
$[\alpha]_D^{18}$ –54.1 (*c* 1.18, $CHCl_3$, 84% ee).
IR (film on NaCl): 1695, 2864, 2939, 3502 cm^{-1}.
^1H NMR ($CDCl_3$): δ 1.49 (s, 3H), 1.58-1.73 (m, 3H), 1.87-1.94 (m, 1H), 2.06-2.13 (m, 2H), 2.29-2.37 (m, 2H), 2.88 (dd, *J* = 4.4, 12.4 Hz, 1H), 4.40 (brs, 1H), 7.20-7.27 (m, 1H), 7.28-7.35 (m,

2H), 7.41-7.49 (m, 2H).
^{13}C NMR ($CDCl_3$): δ 25.3, 25.5, 28.2, 29.6, 43.5, 59.6, 74.8, 124.8, 126.6, 128.0, 147.7, 215.8.
LRMS (EI): 218 (M^+), 121, 98.
HRMS (EI): Calcd for $C_{14}H_{18}O_2$ 218.1307, found 218.1302.
The enantiomeric excess was determined to be 84% ee by chiral HPLC with Daicel Chiralcel OB-H column [eluent: 500/1 = hex/IPA; flow rate: 0.7 mL/min; detection: 254 nm; t_R: 25.1 min (major), 29.9 min (minor)].

Data for *minor*-isomer
Colorless oil.
TLC: R_f 0.45 (hex/EtOAc = 4/1, stained purple with anisaldehyde).
$[\alpha]_D^{16}$ +12.5 (*c* 0.20, $CHCl_3$, 24% ee).
IR (film on NaCl): 1695, 2862, 2935, 3510 cm^{-1}.
^{1}H NMR ($CDCl_3$): δ 1.47-1.62 (m, 3H), 1.66 (s, 3H), 1.67-1.78 (m, 2H), 2.05-2.14 (m, 1H), 2.37-2.49 (m, 2H), 2.73-2.80 (m, 1H), 4.22 (brs, 1H), 7.20-7.26 (m, 1H), 7.31-7.40 (m, 4H).
^{13}C NMR ($CDCl_3$): δ 25.5, 29.4, 30.0, 30.9, 44.3, 59.8, 74.7, 124.6, 126.3, 128.1, 146.0, 217.1.
LRMS (FAB): 241 ($M+Na^+$).
HRMS (FAB): Calcd for $C_{14}H_{18}O_2Na$ 241.1204, found 241.1200.
The enantiomeric excess was determined to be 24% ee by chiral HPLC with Daicel Chiralcel OB-H column [eluent: 500/1 = hex/IPA; flow rate: 0.5 mL/min; detection: 254 nm; t_R: 25.7 min (minor), 28.4 min (major)].

2-(1-Hydroxy-1-phenylethyl)-4,4-dimethylcyclohexanone (3fb)

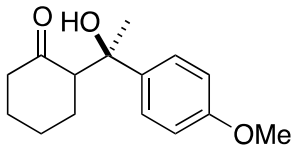


Data for *major*-isomer
Colorless solid.
mp: 57.0-58.0 ˚C.
TLC: R_f 0.37 (hex/EtOAc = 4/1, stained purple with anisaldehyde).
$[\alpha]_D^{22}$ –71.3 (*c* 1.30, $CHCl_3$, 80% ee)
IR (film on NaCl): 1697, 2864, 2933, 2954, 3502 cm^{-1}.
^{1}H NMR ($CDCl_3$): δ 0.86-1.73 (m, 4H), 0.99 (s, 3H), 1.13 (s, 3H), 1.47 (s, 3H), 2.15-2.23 (m, 1H), 2.42-2.52 (m, 1H), 2.98-3.06 (m, 1H), 4.42 (brs, 1H), 7.18-7.27 (m, 1H), 7.28-7.35 (m, 2H), 7.41-7.45 (m, 2H).
^{13}C NMR ($CDCl_3$): δ 24.5, 25.3, 30.8, 31.4, 39.5, 40.0, 41.9, 55.0, 74.8, 124.8, 126.6, 128.0, 147.5, 216.5.

LRMS (FAB): 269 ($M+Na^+$).
HRMS (FAB): Calcd for $C_{16}H_{22}O_2Na$ 269.1517, found 269.1523.
The enantiomeric excess was determined to be 81% ee by chiral HPLC with Daicel Chiralpak AD-H column [eluent: 150/1 = hex/IPA; flow rate: 1.0 mL/min; detection: 254 nm; t_R: 27.8 min (minor), 36.8 min (major)].

Data for *minor*-isomer
Colorless oil.
TLC: R_f 0.45 (hex/EtOAc = 4/1, stained purple with anisaldehyde).
$[\alpha]_D^{18}$ +102.5 (*c* 0.17, $CHCl_3$, 53% ee).
IR (film on NaCl): 1699, 2858, 2931, 2956, 3518 cm^{-1}.
^1H NMR ($CDCl_3$): δ 0.86 (s, 3H), 1.10 (s, 3H), 1.19-1.28 (m, 2H), 1.54-1.78 (m, 5H), 2.24 (ddd, 1H, *J* = 2.8, 4.8, 13.6 Hz), 2.61 (dt, 1H, *J* = 6.4, 13.6 Hz), 2.95 (dd, 1H, *J* =4.8, 13.6 Hz), 4.19 (bds, 1H), 7.19-7.47 (m, 5H).
^{13}C NMR ($CDCl_3$): δ 24.5, 30.4, 30.9, 31.0, 40.2, 41.4, 43.1, 54.7, 74.7, 124.4, 126.3, 128.1, 146.0, 217.8.
LRMS (FAB): 269 ($M+Na^+$), 229.
HRMS (FAB): Calcd for $C_{16}H_{22}O_2Na$ 269.1517, found 269.1509.
The enantiomeric excess was determined to be 53% ee by chiral HPLC with Daicel Chiralpak AD-H column [eluent: 150/1 = hex/IPA; flow rate: 0.7 mL/min; detection: 254 nm; t_R: 14.9 min (major), 19.6 min (minor)].

2-[1-Hydroxy-1-(4-methoxyphenyl)ethyl]cyclohexanone (3eg)

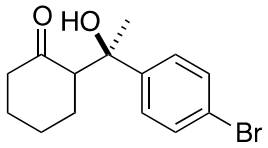


Data for *major*-isomer
Colorless solid.
mp: 77.5-78.0 ˚C.
TLC: R_f 0.19 (hex/EtOAc = 4/1, stained purple with anisaldehyde).
$[\alpha]_D^{18}$ –38.4 (*c* 1.45, $CHCl_3$, 83% ee).
IR (film on NaCl): 1693, 2835, 2864, 2939, 3500 cm^{-1}.
^1H NMR ($CDCl_3$): δ 1.50 (s, 3H), 1.56-1.74 (m, 3H), 1.85-1.92 (m, 1H), 2.01-2.13 (m, 2H), 2.26-2.40 (m, 2H), 2.79-2.85 (m, 1H), 3.79 (s, 3H), 4.42 (brs, 1H), 6.86 (d, 2H, *J* = 8.8 Hz), 7.35 (d, 2H, *J* = 8.8 Hz).
^{13}C NMR ($CDCl_3$): δ 25.2, 25.4, 28.1, 29.7, 43.5, 55.2, 59.9, 74.6, 113.3, 126.1, 139.7, 158.2, 215.9.
LRMS (FAB): 271 ($M+Na^+$), 231, 151.

HRMS (FAB): Calcd for $C_{15}H_{20}O_3Na$ 271.1310, found 271.1325.
The enantiomeric excess was determined to be 83% ee by chiral HPLC with Daicel Chiralpak AD-H column [eluent: 49/1 = hex/IPA; flow rate: 1.0 mL/min; detection: 254 nm; t_R: 36.1 min (minor), 49.7 min (major)].

Data for *minor*-isomer
Colorless oil.
TLC: R_f 0.31 (hex/EtOAc = 4/1, stained purple with anisaldehyde).
$[\alpha]_D^{20}$ –18.9 (*c* 0.16, $CHCl_3$, 27% ee).
IR (film on NaCl): 1693, 2856, 2931, 3514 cm^{-1}.
^1H NMR ($CDCl_3$): δ 1.47-1.79 (m, 5H), 1.64 (s, 3H), 2.04-2.13 (m, 1H), 2.36-2.47 (m, 2H), 2.71 (dd, 1H, *J* = 5.6, 11.6 Hz), 3.81 (s, 3H), 4.19 (brs, 1H), 6.87 (d, 2H, *J* = 8.8 Hz), 7.29 (d, 2H, *J* = 8.8 Hz).
^{13}C NMR ($CDCl_3$): δ 25.5, 29.4, 30.0, 30.9, 44.2, 55.2, 60.0, 74.5, 113.4, 125.8, 138.3, 158.0, 217.2.
LRMS (FAB): 271 ($M+Na^+$), 231, 151.
HRMS (FAB): Calcd for $C_{15}H_{20}O_3Na$ 271.1310, found 271.1310.
The enantiomeric excess was determined to be 27% ee by chiral HPLC with Daicel Chiralpak AD-H column [eluent: 200/1 = hex/IPA; flow rate: 1.0 mL/min; detection: 254 nm; t_R: 33.3 min (minor), 44.3 min (major)].

2-[1-Hydroxy-1-(4-bromophenyl)ethyl]cyclohexanone (3eh)

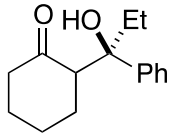


Data for *major*-isomer
Colorless oil.
TLC: R_f 0.26 (hex/EtOAc = 4/1, stained purple with anisaldehyde).
$[\alpha]_D^{16}$ –46.8 (*c* 0.93, $CHCl_3$, 84% ee).
IR (film on NaCl): 1695, 2864, 2939, 2980, 3498 cm^{-1}.
^1H NMR ($CDCl_3$): δ 1.46 (s, 3H), 1.59-1.75 (m, 3H), 1.89-1.96 (m, 1H), 2.06-2.15 (m, 2H), 2.25-2.38 (m, 2H), 2.79-2.86 (m, 1H), 4.38 (brs, 1H), 7.31 (d, 2H, *J* = 8.8 Hz), 7.44 (d, 2H, *J* = 8.8 Hz).
^{13}C NMR ($CDCl_3$): δ 25.3, 25.5, 28.2, 29.6, 43.5, 59.5, 74.6, 120.5, 126.8, 131.1, 147.0, 215.7.
LRMS (FAB): 321, 319 ($M+Na^+$).
HRMS (FAB): Calcd for $C_{14}H_{17}BrO_2Na$ 319.0310, found 319.0307.
The enantiomeric excess was determined to be 84% ee by chiral HPLC with Daicel Chiralpak AD-H column [eluent: 39/1 = hex/IPA; flow rate: 1.0 mL/min; detection: 254 nm; t_R: 23.7 min

(minor), 37.6 min (major)].

Data for *minor*-isomer
Colorless oil.
TLC: R_f 0.39 (hex/EtOAc = 4/1, stained purple with anisaldehyde).
$[\alpha]_D^{16}$ +14.6 (*c* 0.13, $CHCl_3$, 21% ee).
IR (film on NaCl): 1695, 2864, 2939, 3506 cm^{-1}.
^1H NMR ($CDCl_3$): δ 1.49-1.56 (m, 3H), 1.63 (s, 3H), 1.64-1.79 (m, 2H), 2.06-2.15 (m, 1H), 2.38-2.49 (m, 2H), 2.69-2.75 (m, 1H), 4.23 (brs, 1H), 7.26 (d, 2H, *J* = 8.4 Hz), 7.45 (d, 2H, *J* = 8.4 Hz).
^{13}C NMR ($CDCl_3$): δ 25.5, 29.4, 29.8, 30.8, 44.2, 59.6, 74.6, 120.3, 126.6, 131.2, 145.2, 216.8.
LRMS (FAB): 321, 319 ($M+Na^+$), 281, 279.
HRMS (FAB): Calcd for $C_{14}H_{17}BrO_2Na$ 319.0310, found 319.0299.
The enantiomeric excess was determined to be 21% ee by chiral HPLC with Daicel Chiralpak AD-H column [eluent: 49/1 = hex/IPA; flow rate: 1.0 mL/min; detection: 254 nm; t_R: 9.7 min (major), 15.0 min (minor)].

2-(1-Hydroxy-1-phenylpropyl)cyclohexanone (3ei)

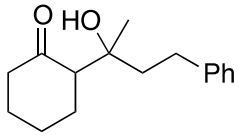


Data for *major*-isomer
Colorless oil.
TLC: R_f 0.23 (hex/EtOAc = 4/1, stained purple with anisaldehyde).
$[\alpha]_D^{17}$ –91.4 (*c* 0.78, $CHCl_3$, 80% ee).
IR (film on NaCl): 1697, 2866, 2939, 2964, 3500 cm^{-1}.
^1H NMR ($CDCl_3$): δ 0.64 (t, 3H, *J* = 7.6 Hz), 1.60-1.89 (m, 5H), 1.90-1.99 (m, 1H), 2.06-2.17 (m, 1H), 2.22-2.38 (m, 3H), 3.01 (dd, 1H, *J* = 4.8, 12.4 Hz), 4.21 (brs, 1H), 7.17-7.23 (m, 1H), 7.28-7.34 (m, 2H), 7.35-7.41 (m, 2H).
^{13}C NMR ($CDCl_3$): δ 7.5, 25.6, 28.8, 29.3, 30.5, 43.9, 58.6, 77.5, 125.4, 126.3, 127.8, 145.9, 216.1.
LRMS (FAB): 255 ($M+Na^+$), 215, 105.
HRMS (FAB): Calcd for $C_{15}H_{20}O_2Na$ 255.1361, found 255.1359.
The enantiomeric excess was determined to be 80% ee by chiral HPLC with Daicel Chiralcel OD-H column [eluent: 200/1 = hex/IPA; flow rate: 0.5 mL/min; detection: 254 nm; t_R: 23.6 min (major), 26.4 min (minor)].

Data for *minor*-isomer
Colorless oil.

TLC: R_f 0.31 (hex/EtOAc = 4/1, stained purple with anisaldehyde).
$[\alpha]_D^{17}$ +50.9 (*c* 0.63, $CHCl_3$, 36% ee).
IR (film on NaCl): 1693, 2866, 2937, 2966, 3504 cm^{-1}.
^1H NMR ($CDCl_3$): δ 0.64 (t, 3H, *J* = 7.2 Hz), 1.47-1.58 (m, 3H), 1.60-1.81 (m, 3H), 2.04-2.13 (m, 1H), 2.17-2.29 (m, 1H), 2.35-2.52 (m, 2H), 2.78 (dd, 1H, *J* = 6.8, 10.0 Hz), 4.00 (brs, 1H), 7.19-7.24 (m, 1H), 7.30-7.35 (m, 4H).
^{13}C NMR ($CDCl_3$): δ 7.7, 25.6, 29.6, 31.0, 33.7, 44.4, 59.7, 77.7, 125.2, 126.1, 128.0, 143.5, 217.7.
LRMS (FAB): 255 ($M+Na^+$).
HRMS (FAB): Calcd for $C_{15}H_{20}O_2Na$ 255.1361, found 255.1339.
The enantiomeric excess was determined to be 36% ee by chiral HPLC with Daicel Chiralpak AD-H column [eluent: 200/1 = hex/IPA; flow rate: 1.0 mL/min; detection: 254 nm; t_R: 10.6 min (major), 18.4 min (minor)].

2-(1-Hydroxy-1-methyl-3-phenylpropyl)cyclohexanone (3ej)



Data for *major*-isomer
Colorless oil.
TLC: R_f 0.32 (hex/EtOAc = 4/1, stained purple with anisaldehyde).
$[\alpha]_D^{17}$ +8.0 (*c* 1.37, $CHCl_3$, 68% ee).
IR (film on NaCl): 1693, 2864, 2939, 3514 cm^{-1}.
^1H NMR ($CDCl_3$): δ 1.26 (s, 3H), 1.47-1.74 (m, 3H), 1.75-1.82 (m, 2H), 1.89-1.96 (m, 1H), 2.04-2.18 (m, 2H), 2.23-2.33 (m, 1H), 2.36-2.43 (m, 1H), 2.47-2.54 (m, 1H), 2.68-2.74 (m, 1H), 4.14 (brs, 1H), 7.14-7.22 (m, 2H), 7.26-7.30 (m, 3H).
^{13}C NMR ($CDCl_3$): δ 23.6, 25.2, 27.4, 29.4, 29.6, 42.4, 43.3, 57.7, 73.1, 125.7, 128.4, 142.7, 216.1.
LRMS (FAB): 269 ($M+Na^+$).
HRMS (FAB): Calcd for $C_{16}H_{22}O_2Na$ 269.1517, found 269.1521.
The enantiomeric excess was determined to be 68% ee by chiral HPLC with Daicel Chiralcel OD-H column [eluent: 19/1 = hex/IPA; flow rate: 1.0 mL/min; detection: 254 nm; t_R: 9.0 min (major), 13.2 min (minor)].

Data for *minor*-isomer
Colorless oil.
TLC: R_f 0.21 (hex/EtOAc = 4/1, stained blue with anisaldehyde).
$[\alpha]_D^{16}$ –10.7 (*c* 0.66, EtOH, 51% ee).
IR (film on NaCl): 1695, 2864, 2937, 3504 cm^{-1}.
^1H NMR ($CDCl_3$): δ 1.29 (s, 3H), 1.51-1.72 (m, 4H), 1.90-2.00 (m, 2H), 2.02-2.11 (m, 1H),

2.14-2.21 (m, 1H), 2.25-2.42 (m, 2H), 2.45-2.52 (m, 1H), 2.55-2.66 (m, 1H), 2.76-2.89 (m, 1H), 3.93 (brs, 1H), 7.14-7.31 (m, 5H).

^{13}C NMR ($CDCl_3$): δ 25.2, 25.4, 27.7, 29.3, 29.8, 39.8, 43.4, 59.7, 73.1, 125.7, 128.35, 128.37, 142.7, 215.8.

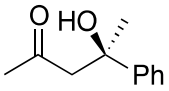
LRMS (FAB): 269 ($M+Na^+$).

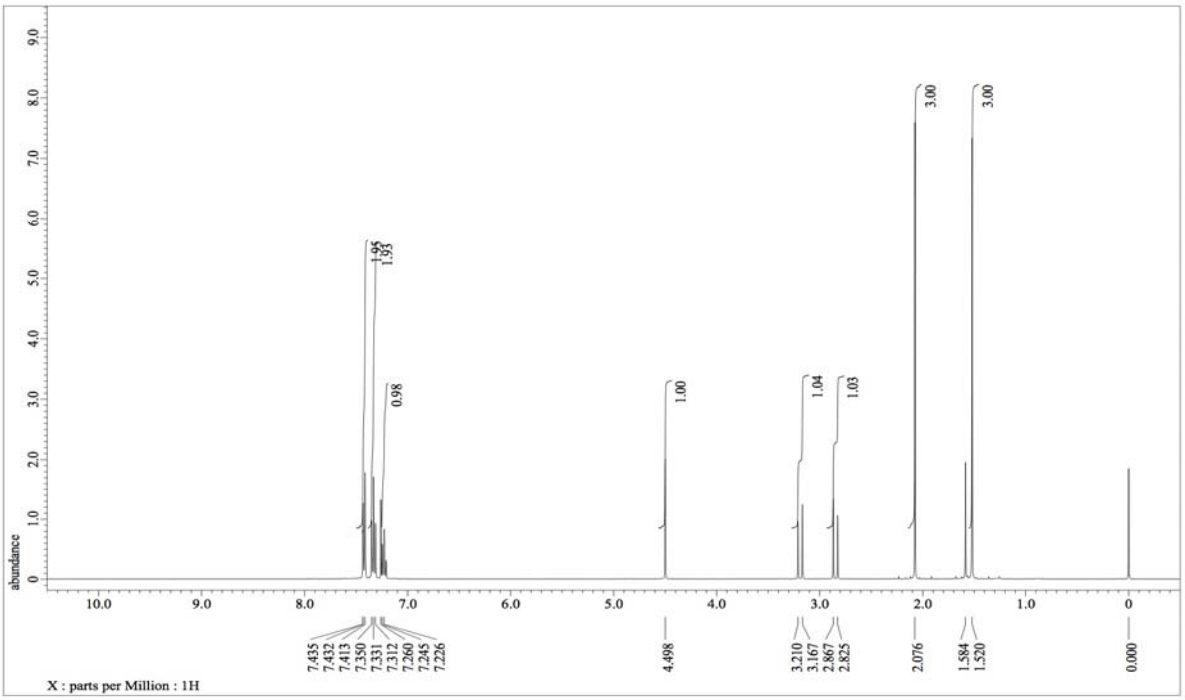
HRMS (FAB): Calcd for $C_{16}H_{22}O_2Na$ 269.1517, found 269.1506.

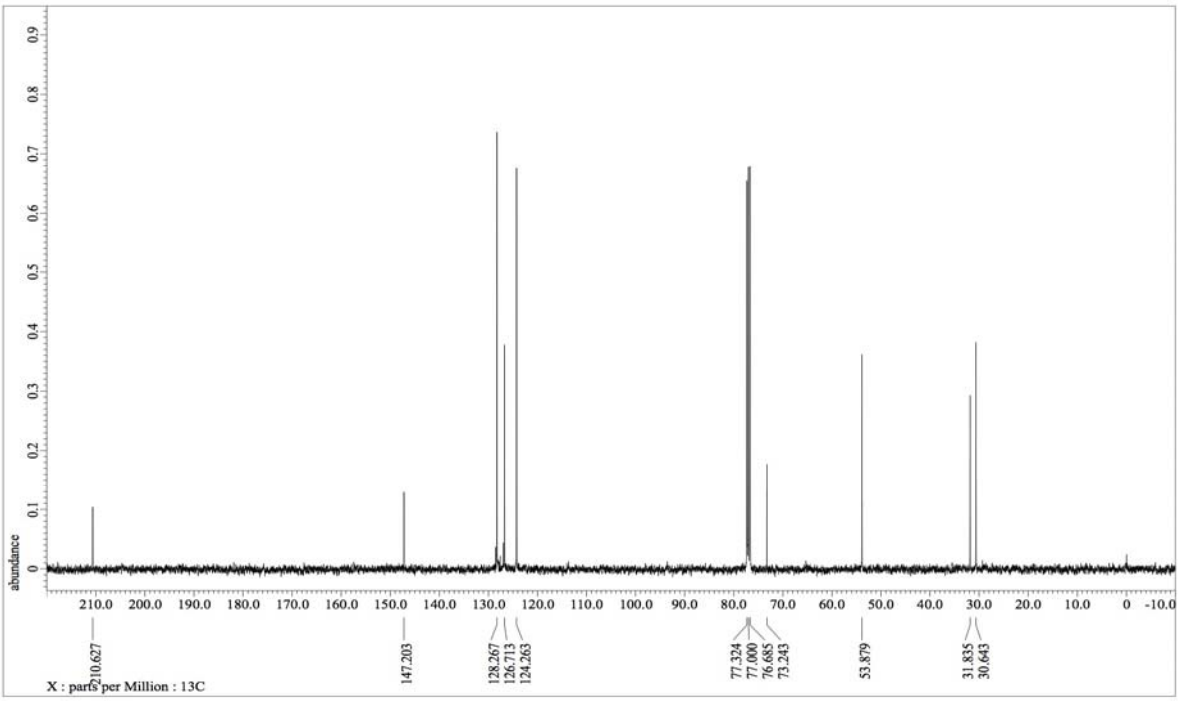
The enantiomeric excess was determined to be 51% ee by chiral HPLC with Daicel Chiralcel OD-H column [eluent: 19/1 = hex/IPA; flow rate: 1.0 mL/min; detection: 254 nm; t_R: 10.0 min (minor), 13.1 min (major)].

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

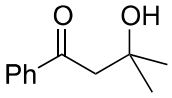
(*R*)-4-Hydroxy-4-phenylpentan-2-one (3ab)

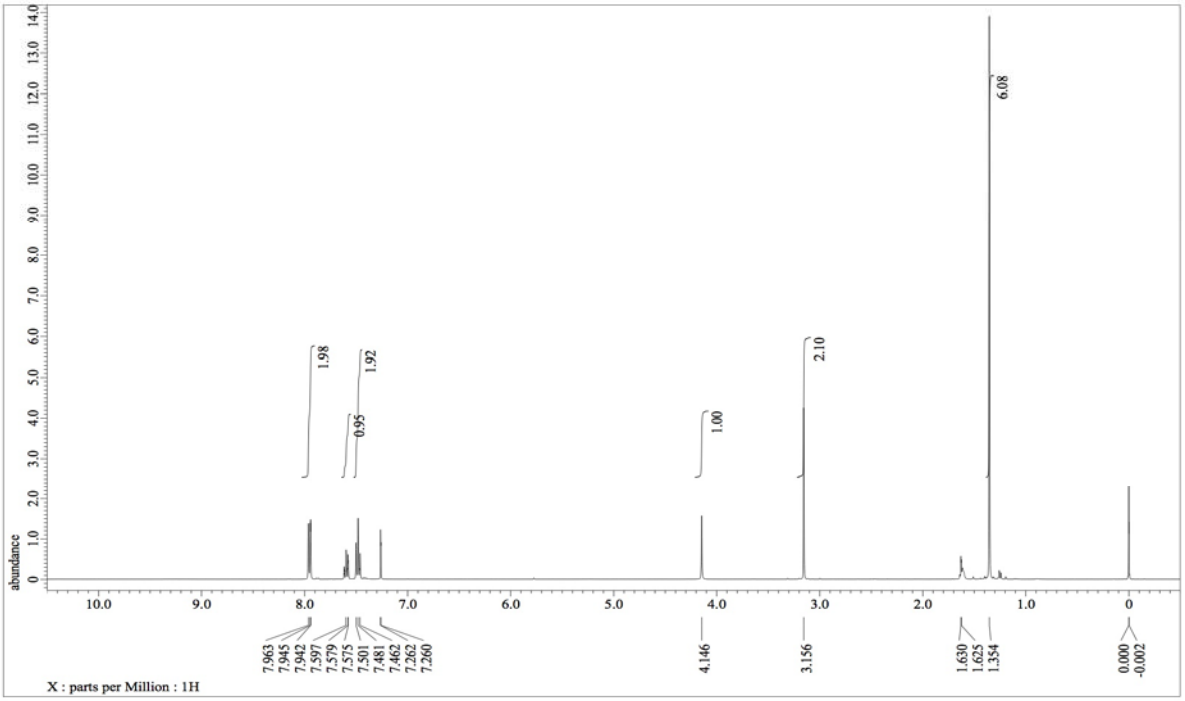


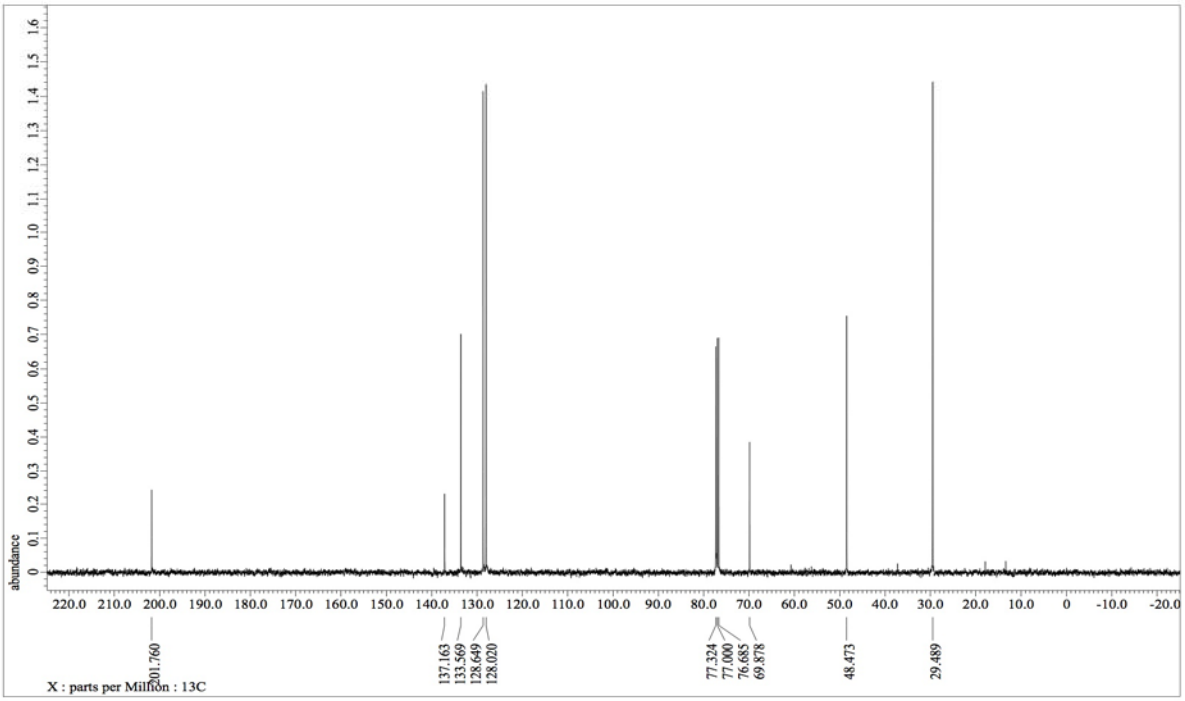




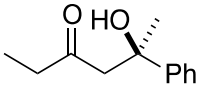
3-Hydroxy-3-methyl-1-phenylbutan-1-one (3ba)

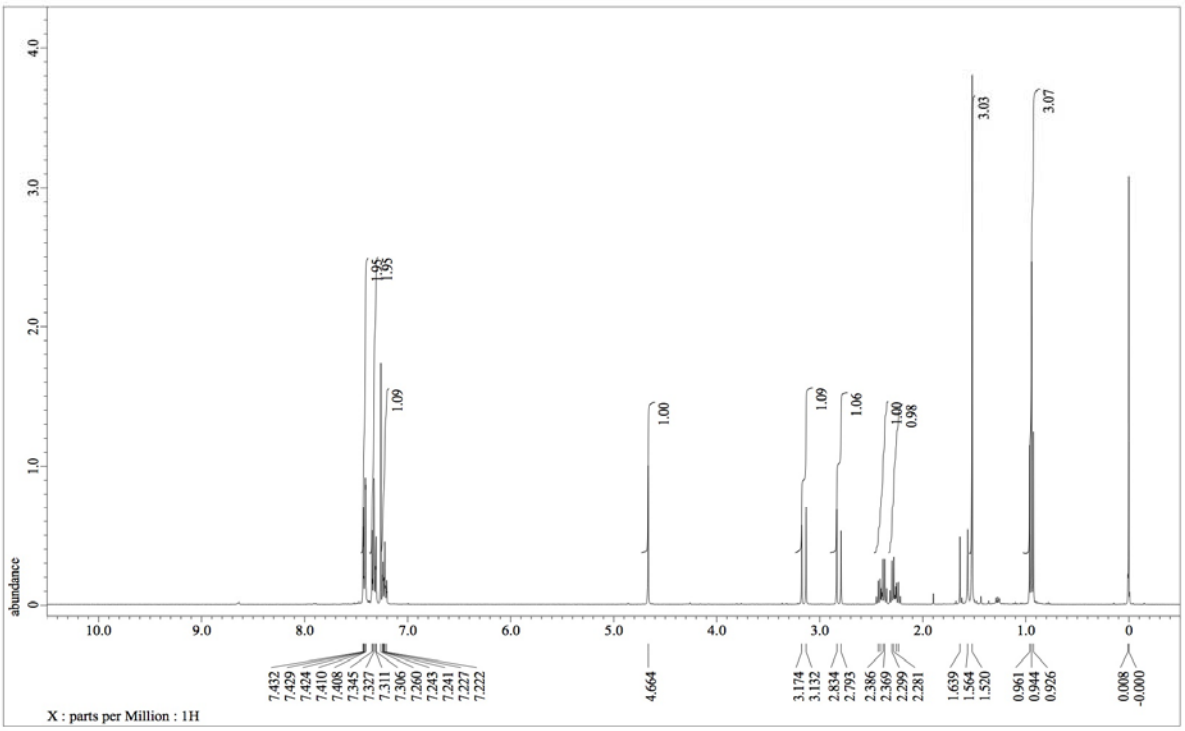


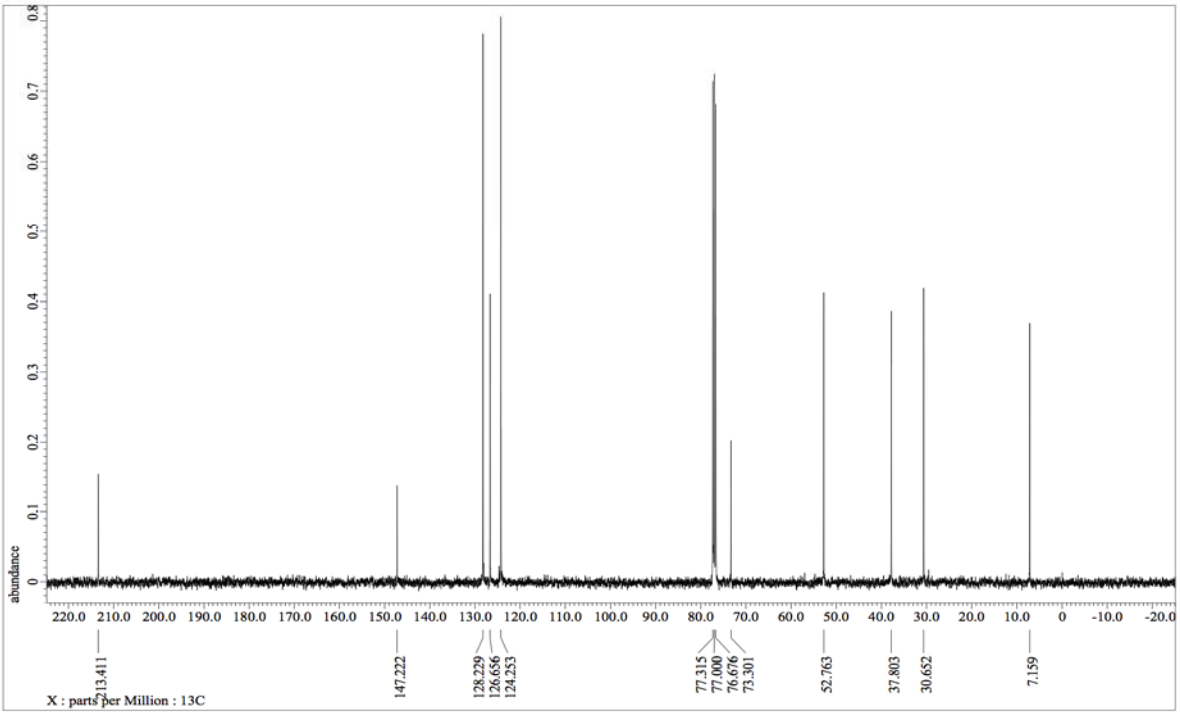




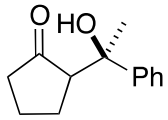
5-Hydroxy-5-phenylhexan-3-one (3cb)



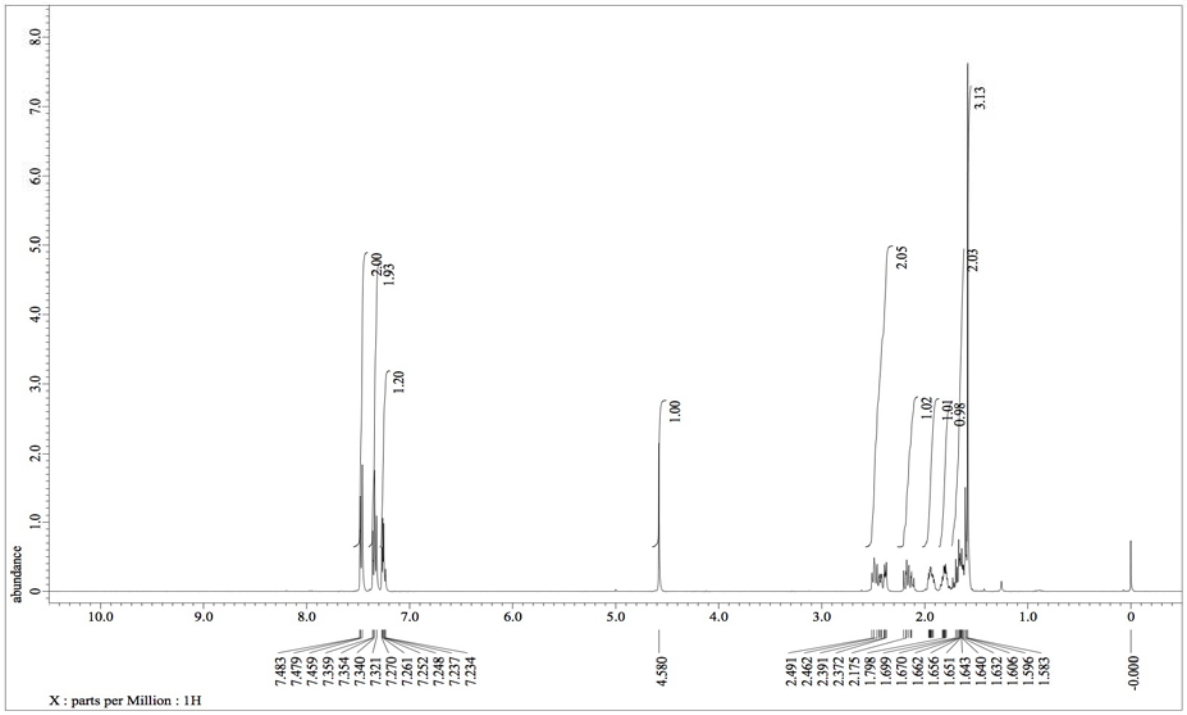


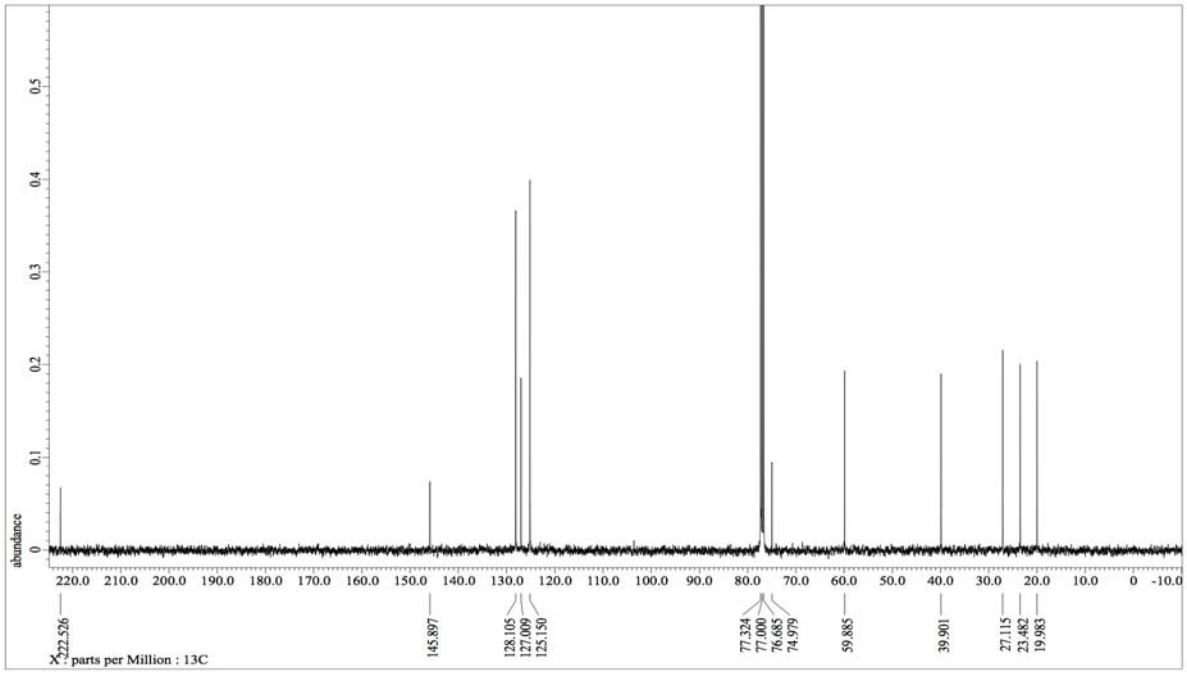


2-(1-Hydroxy-1-phenylethyl)cyclopentanone (3db)



Data for *major*-isomer





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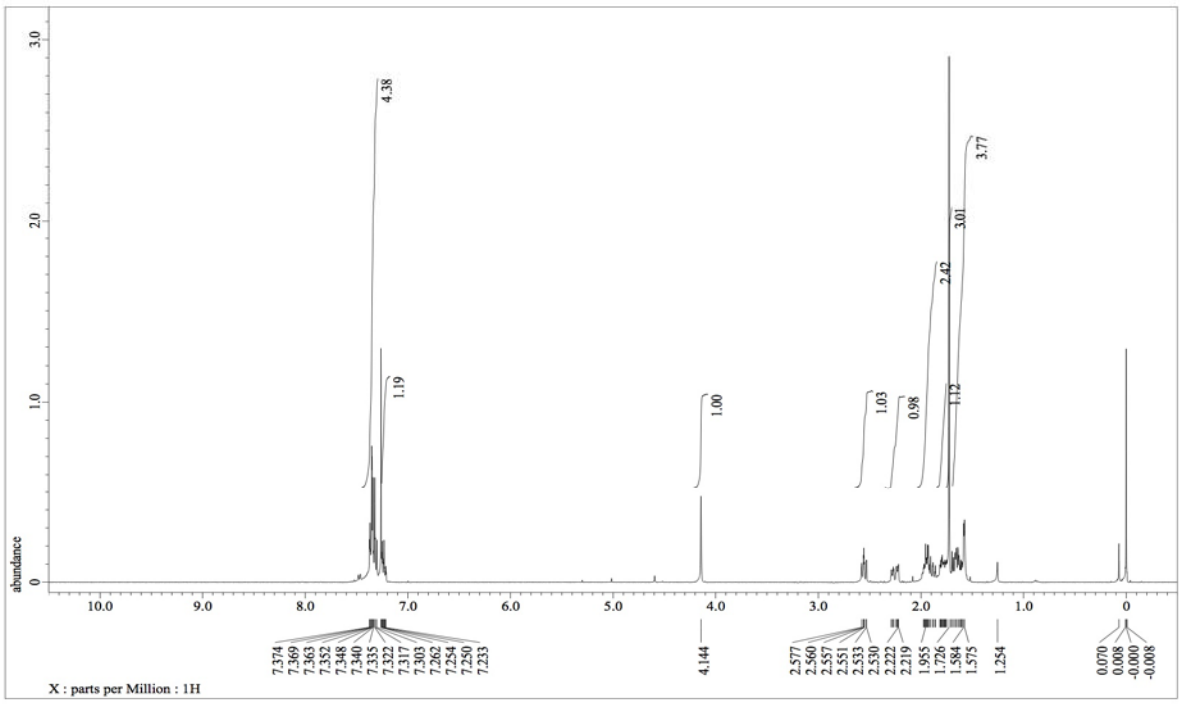
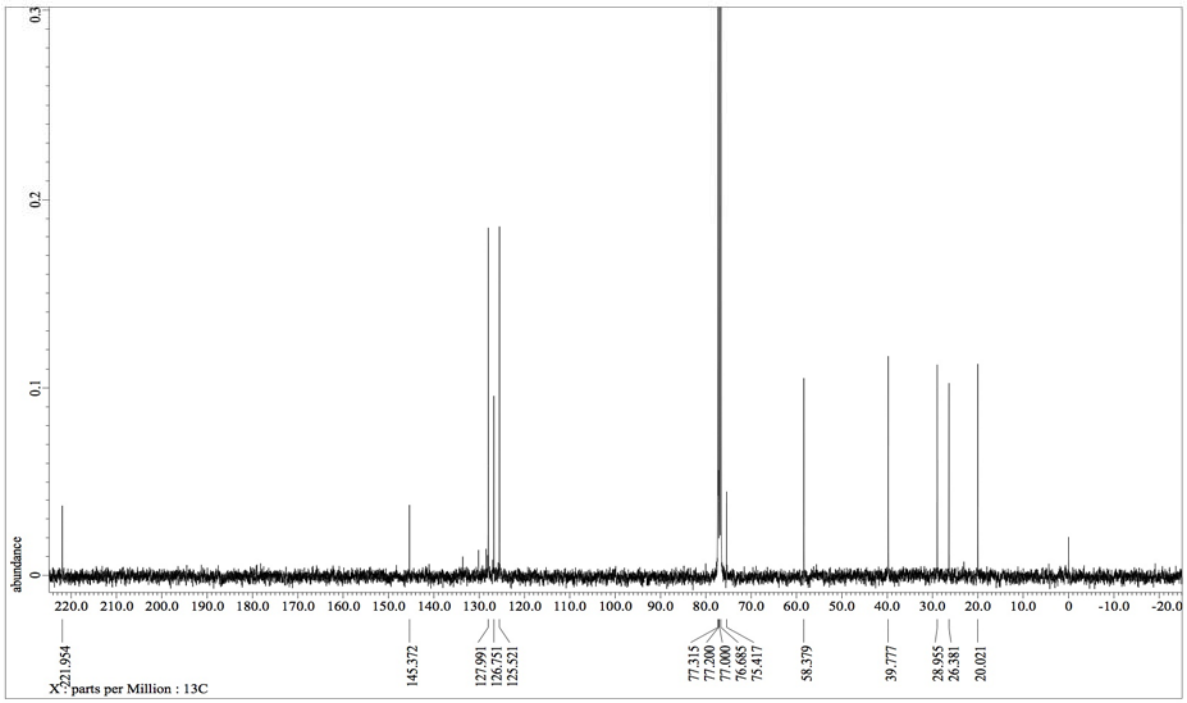
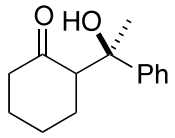




2-(1-Hydroxy-1-phenylethyl)cyclohexanone (3eb)



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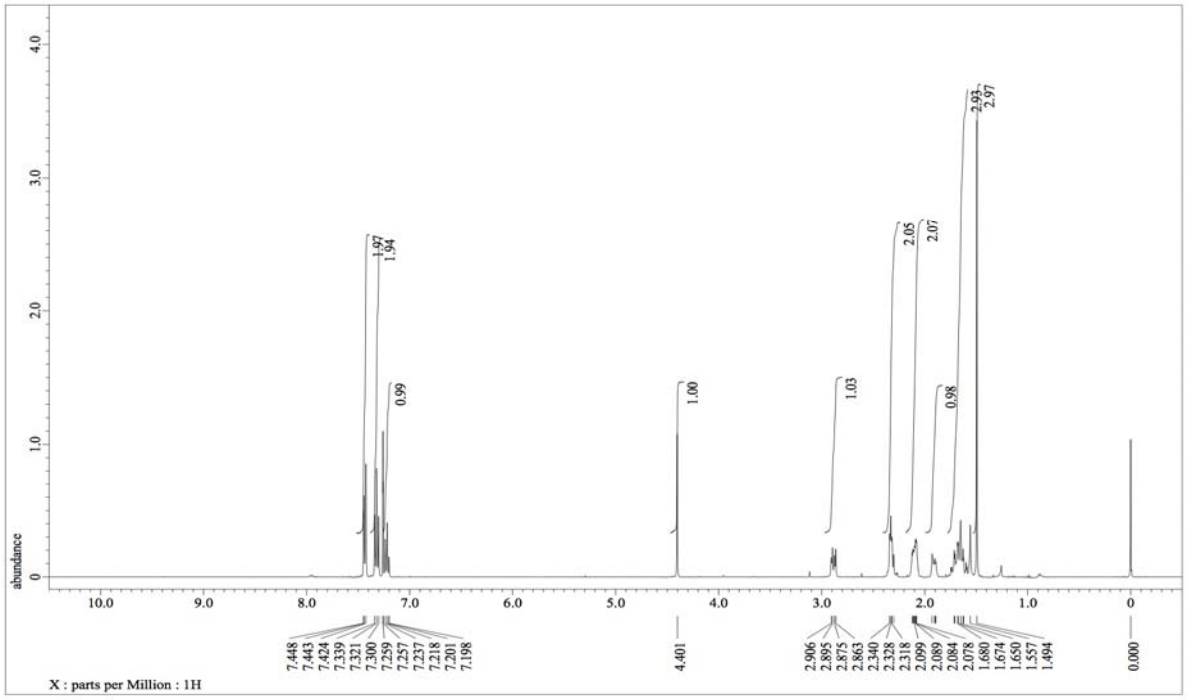

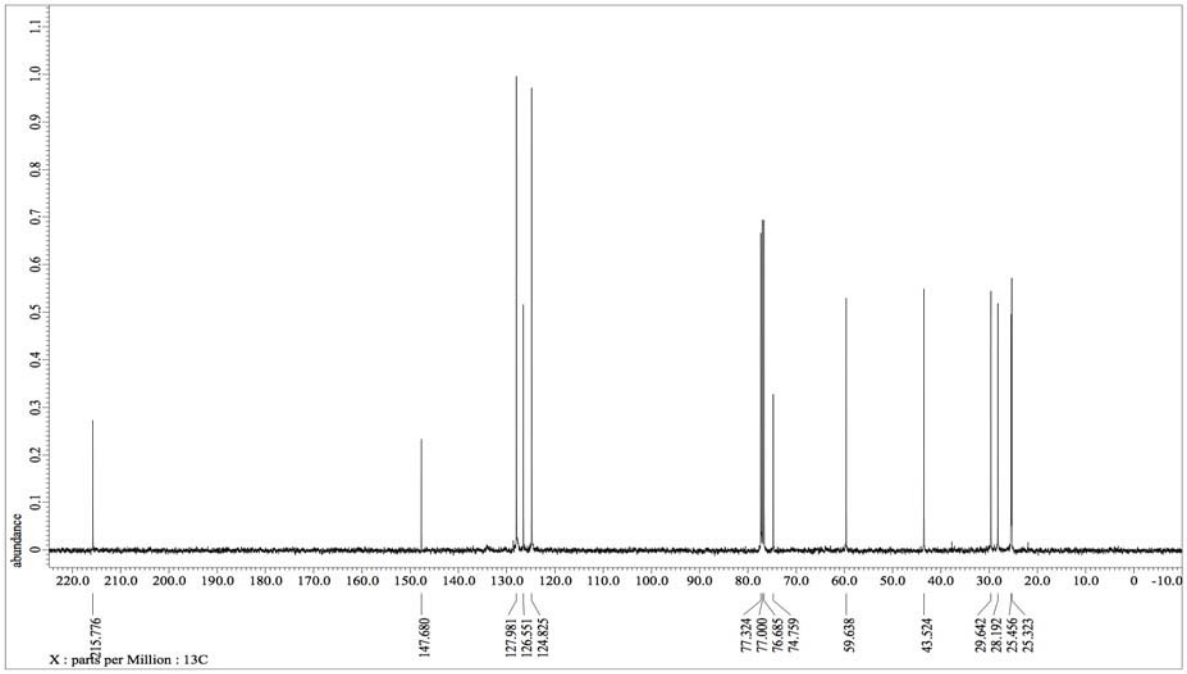

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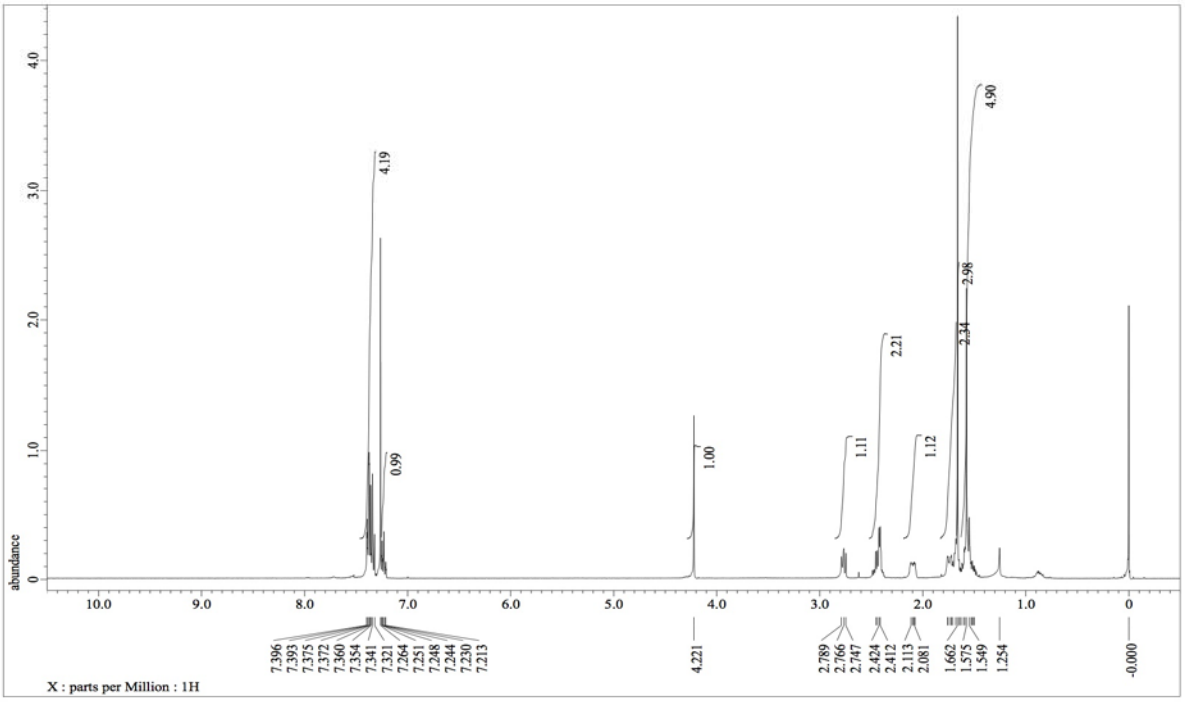
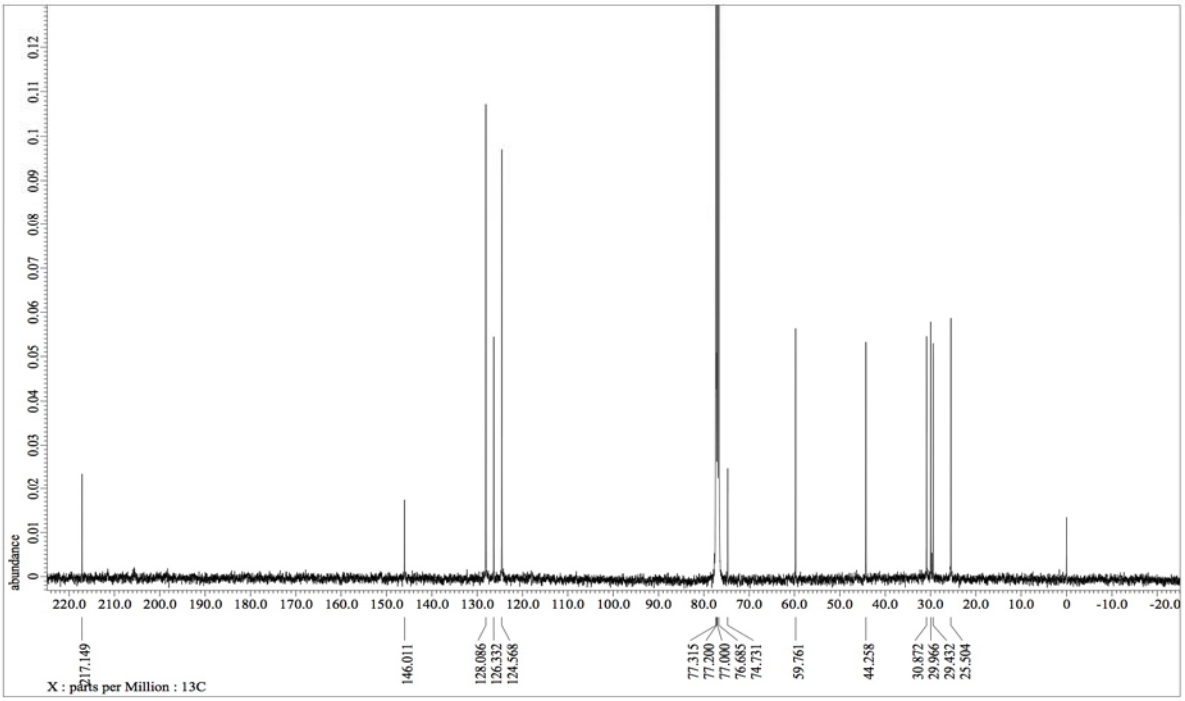
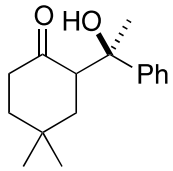




2-(1-Hydroxy-1-phenylethyl)-4,4-dimethylcyclohexanone (3fb)



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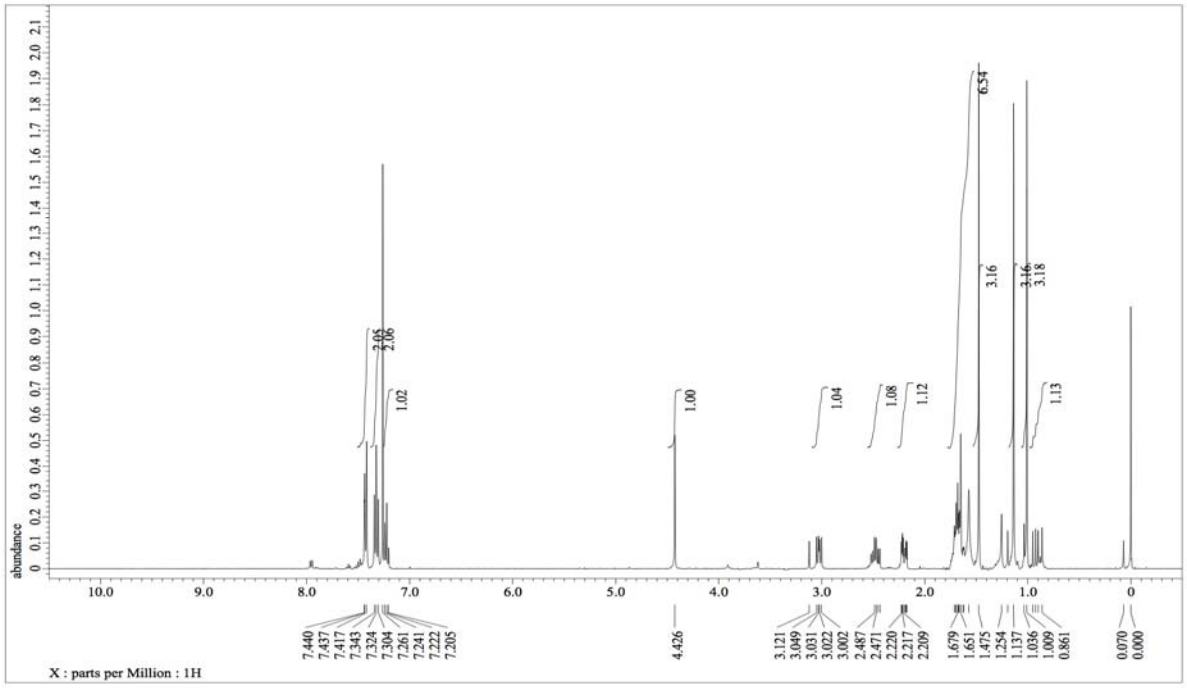

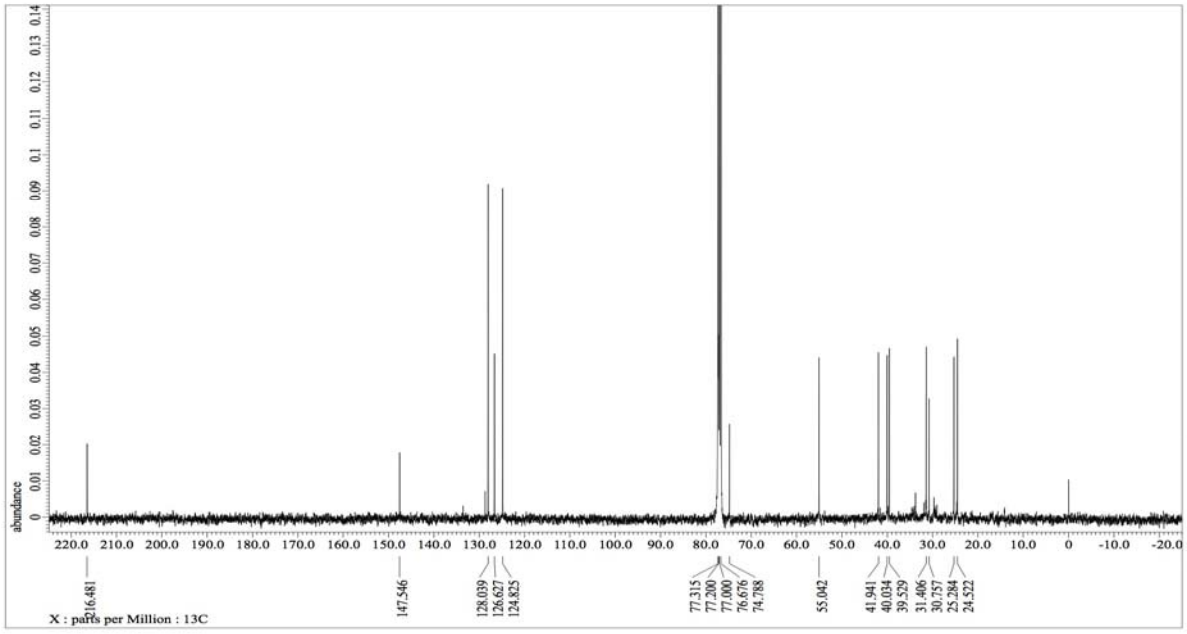

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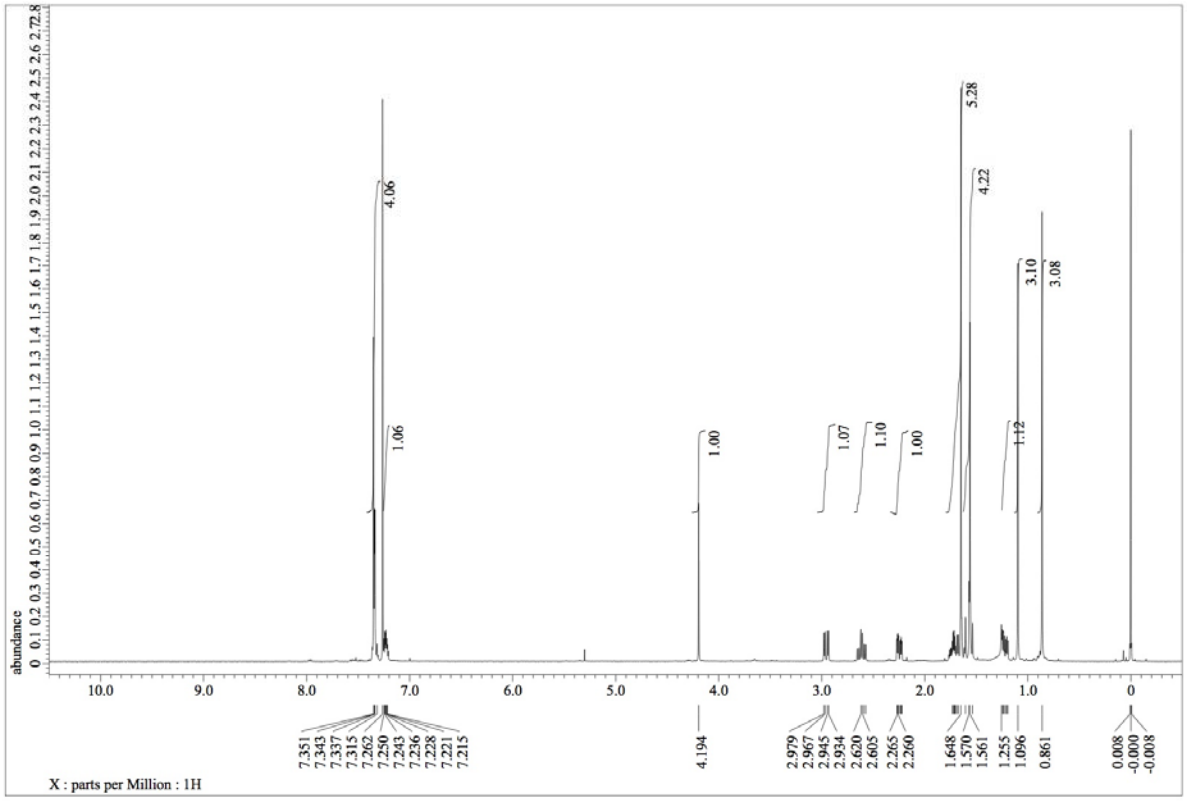
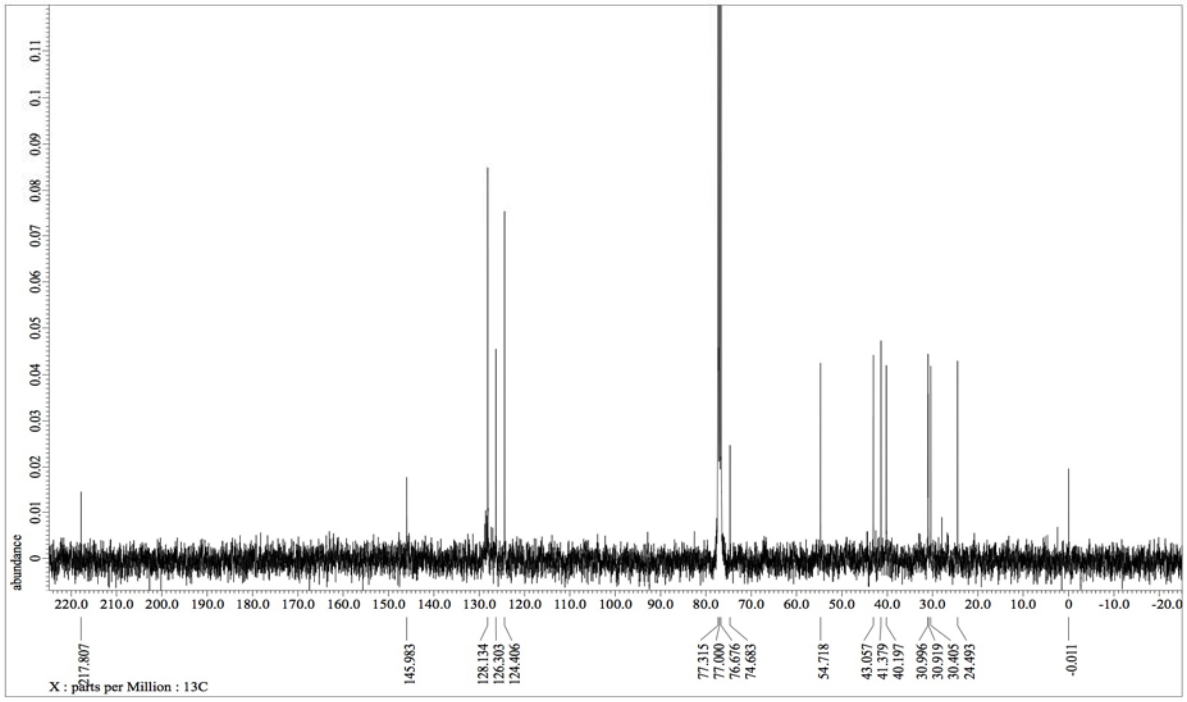
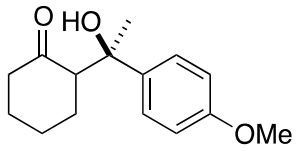




2-[1-Hydroxy-1-(4-methoxyphenyl)ethyl]cyclohexanone (3eg)



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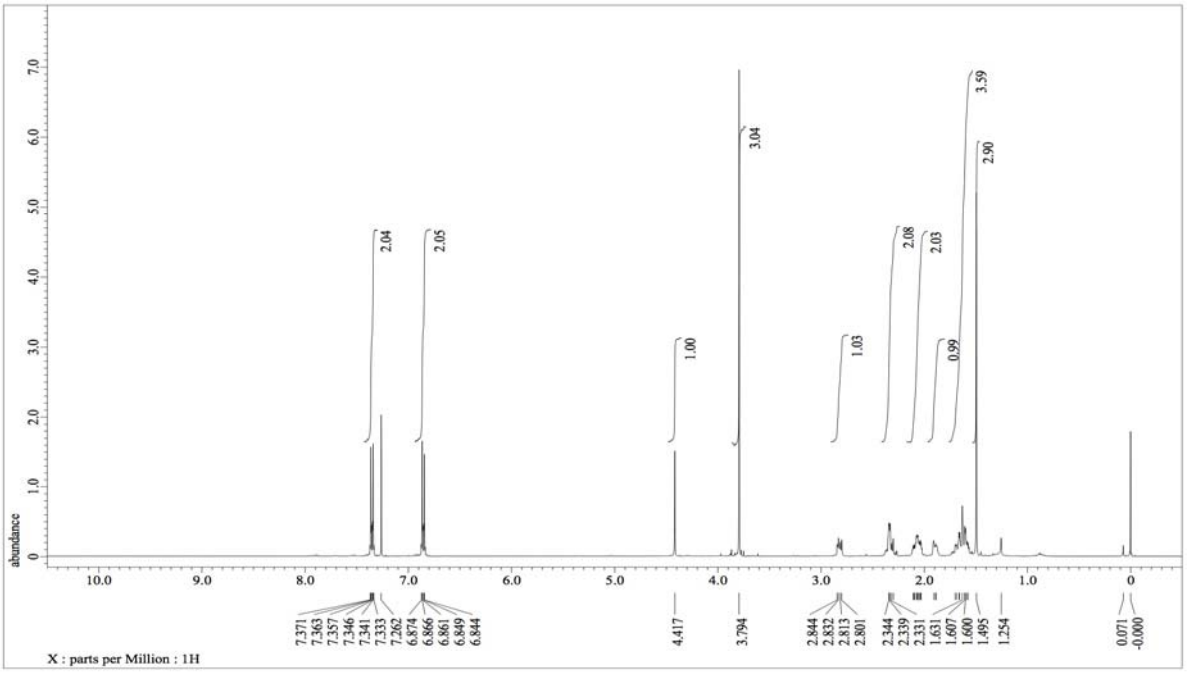

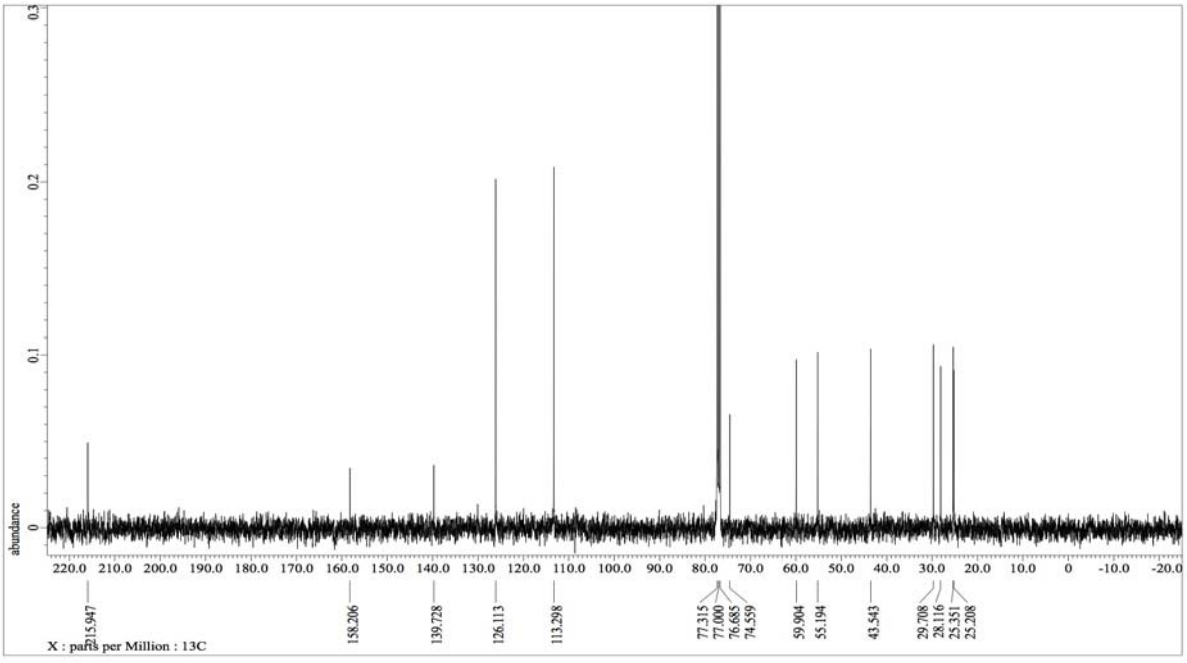

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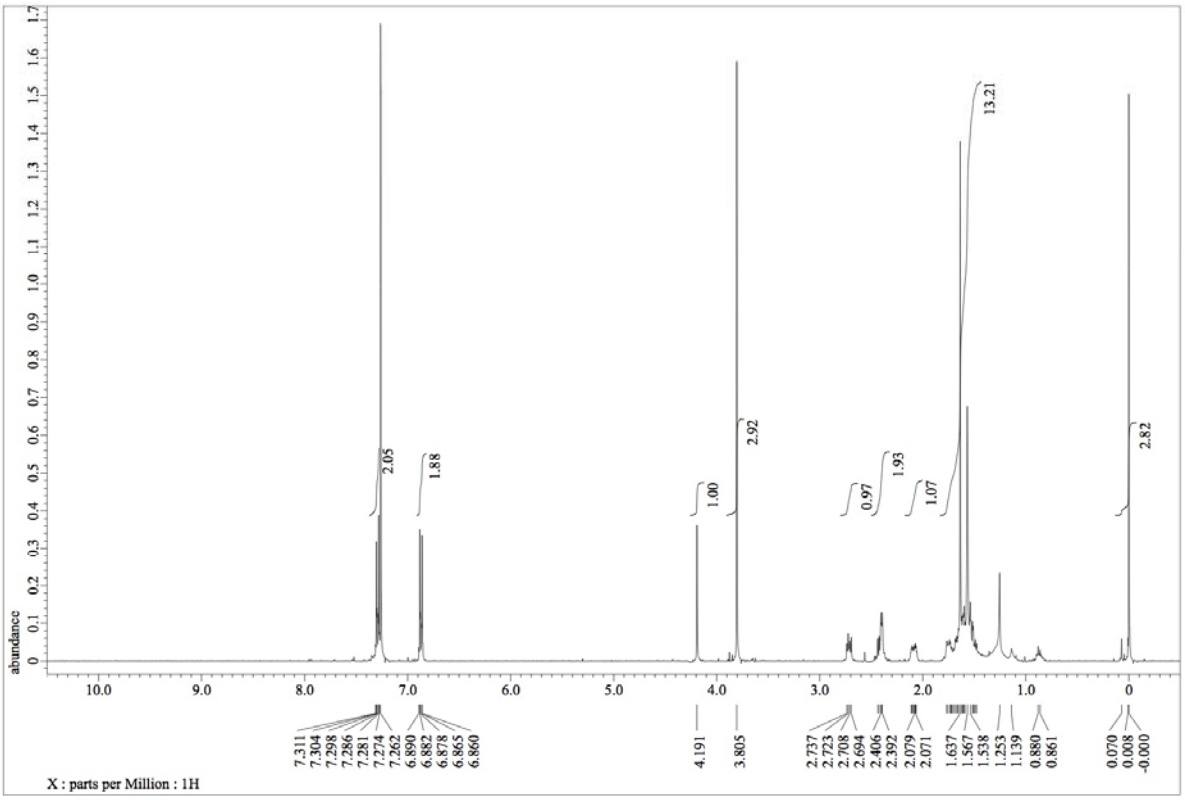
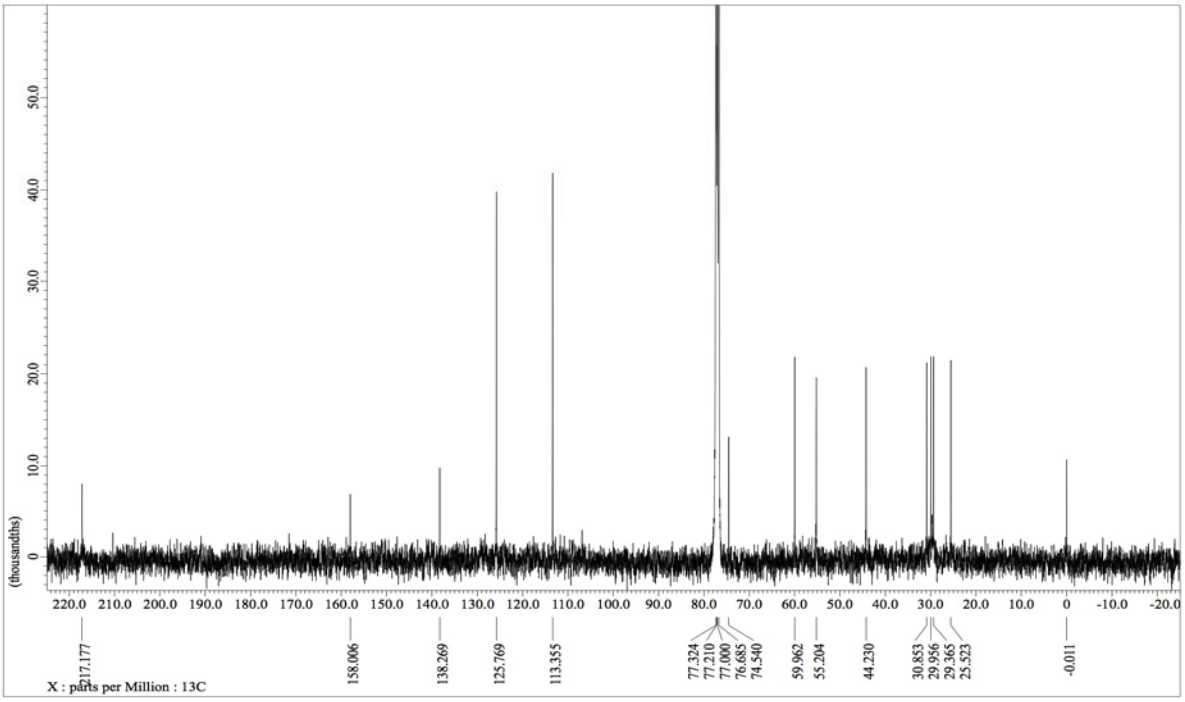
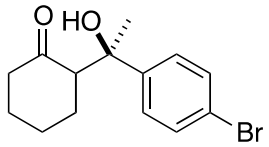




2-[1-Hydroxy-1-(4-bromophenyl)ethyl]cyclohexanone (3eh)



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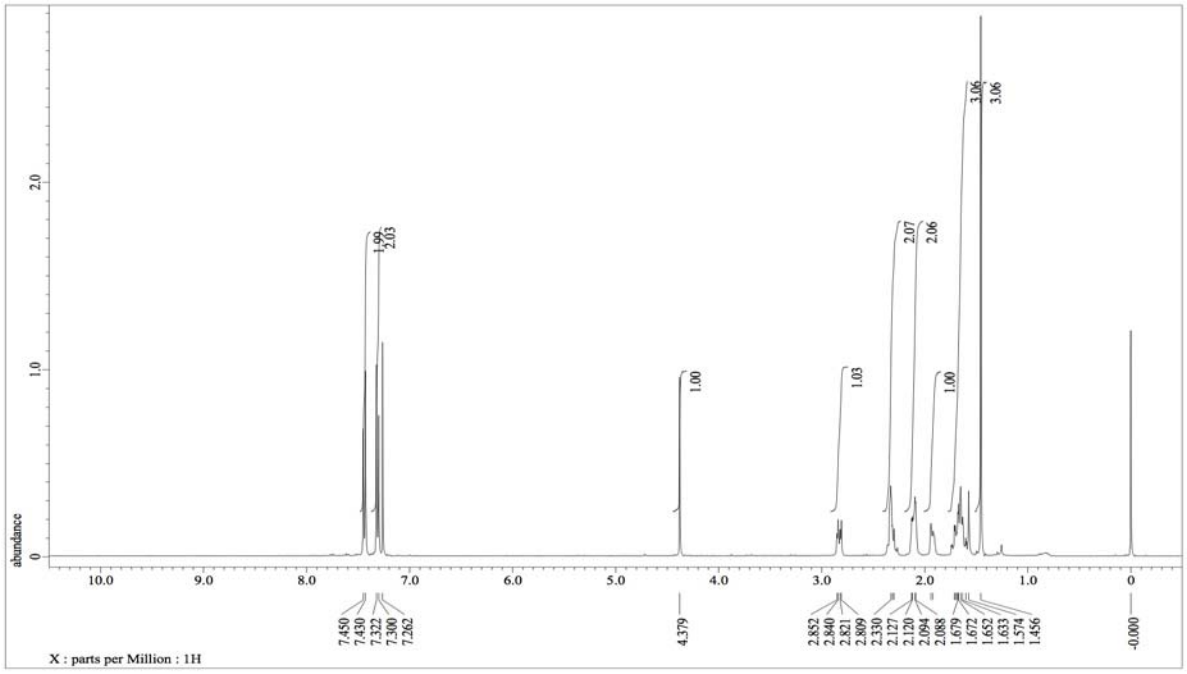

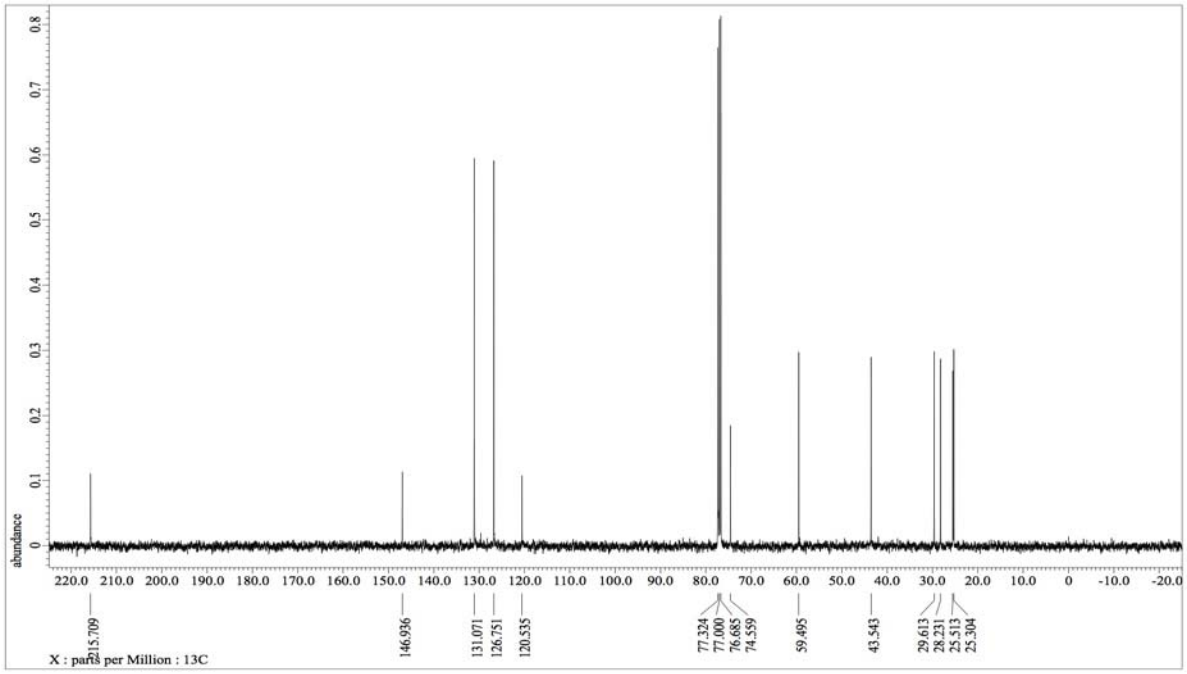

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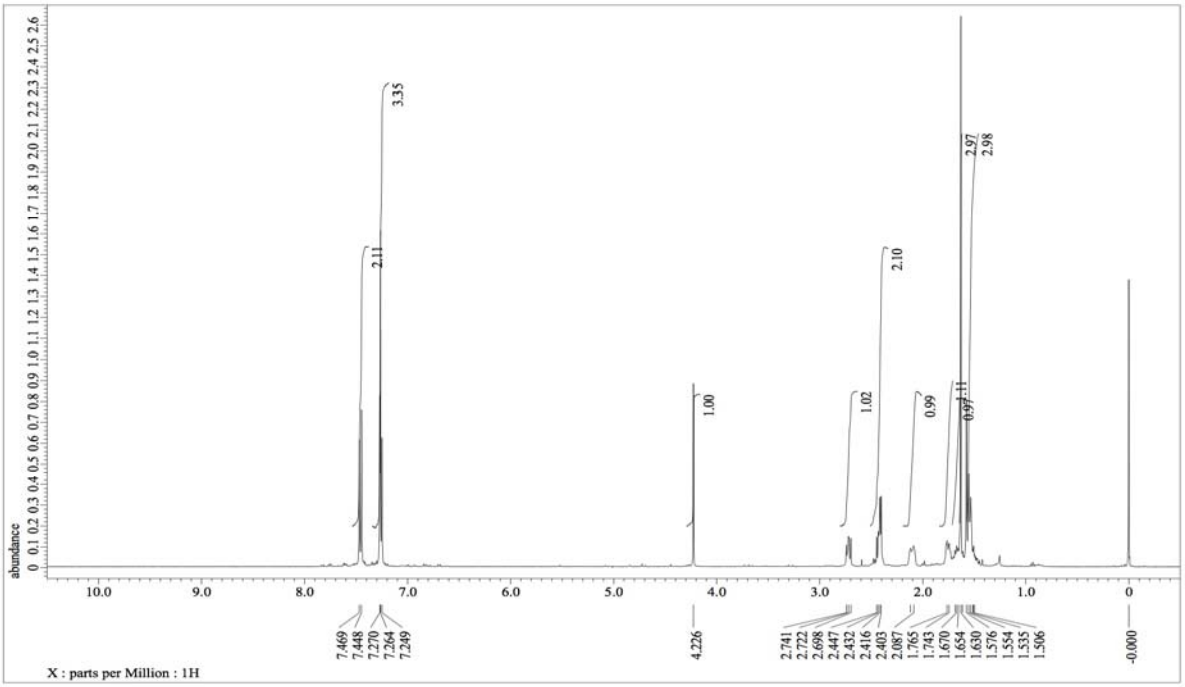
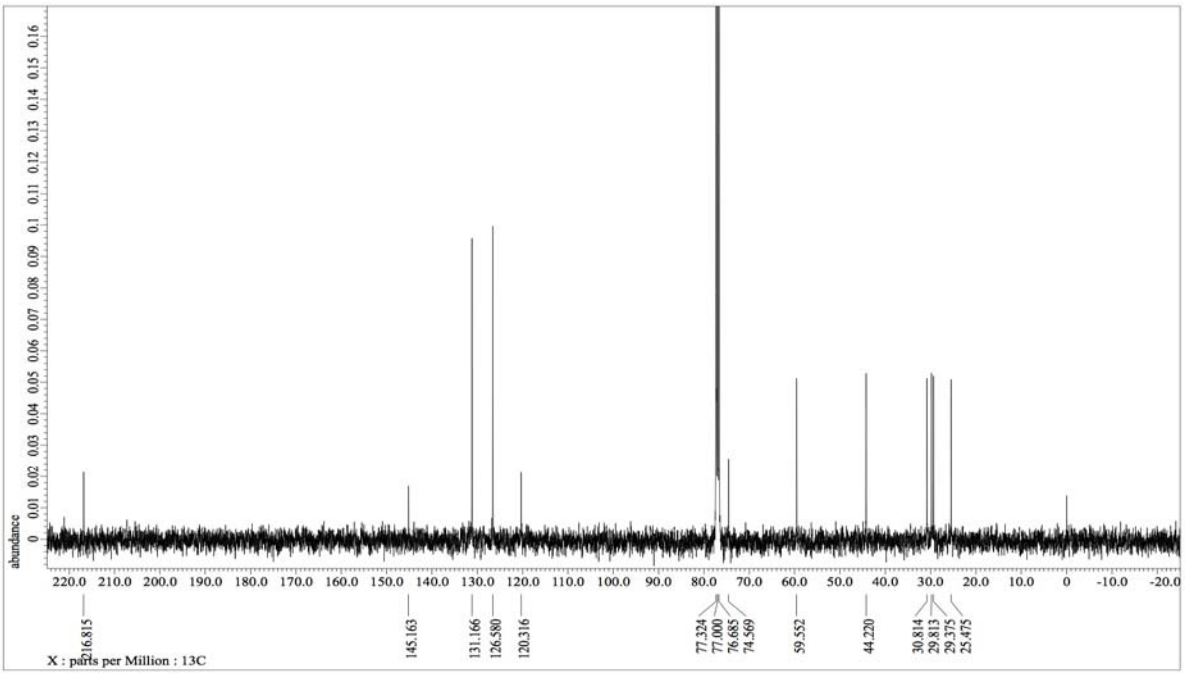
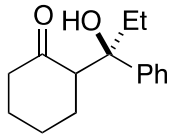




2-(1-Hydroxy-1-phenylpropyl)cyclohexanone (3ei)



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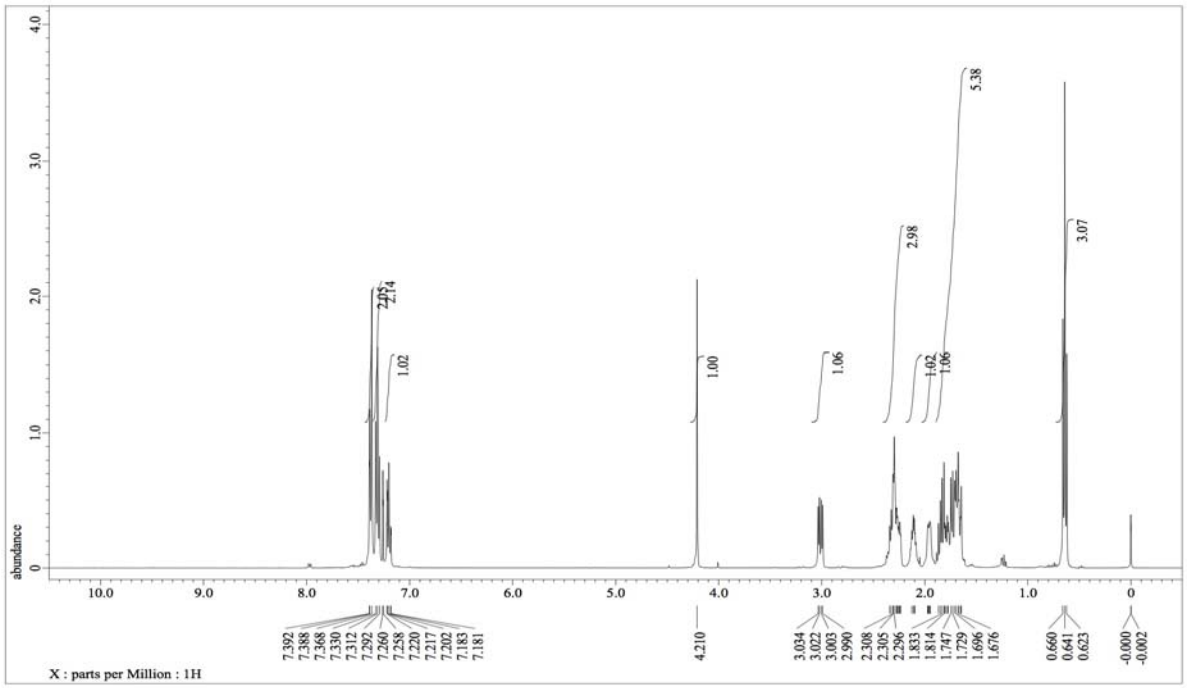
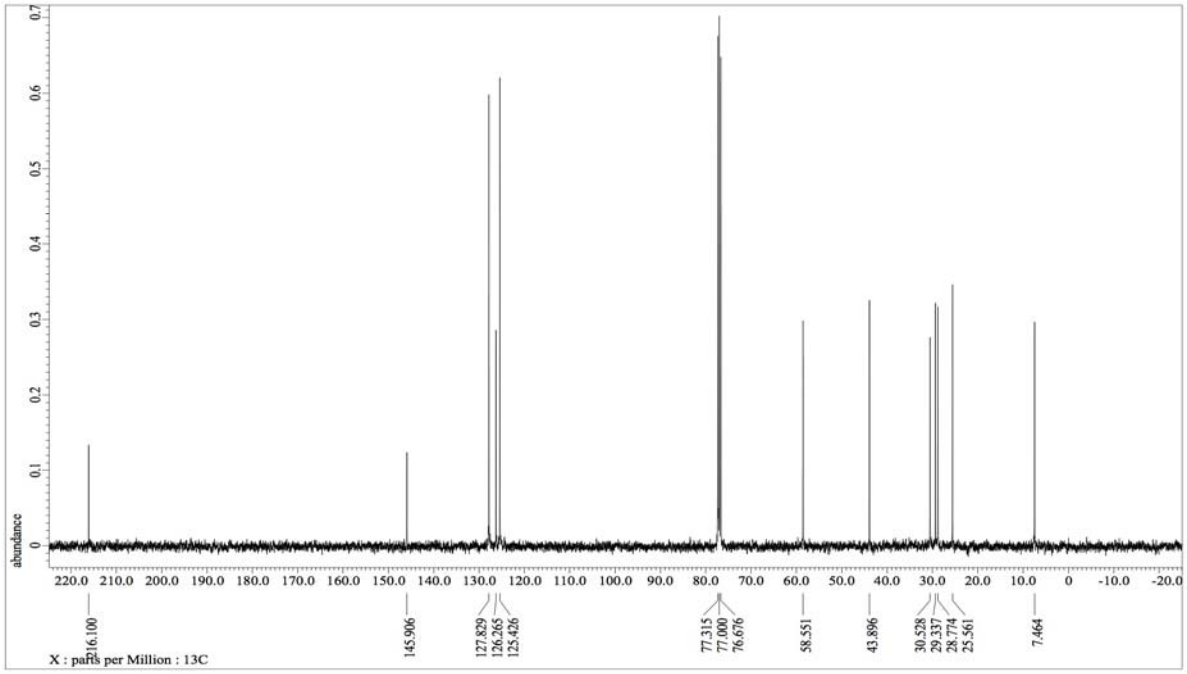
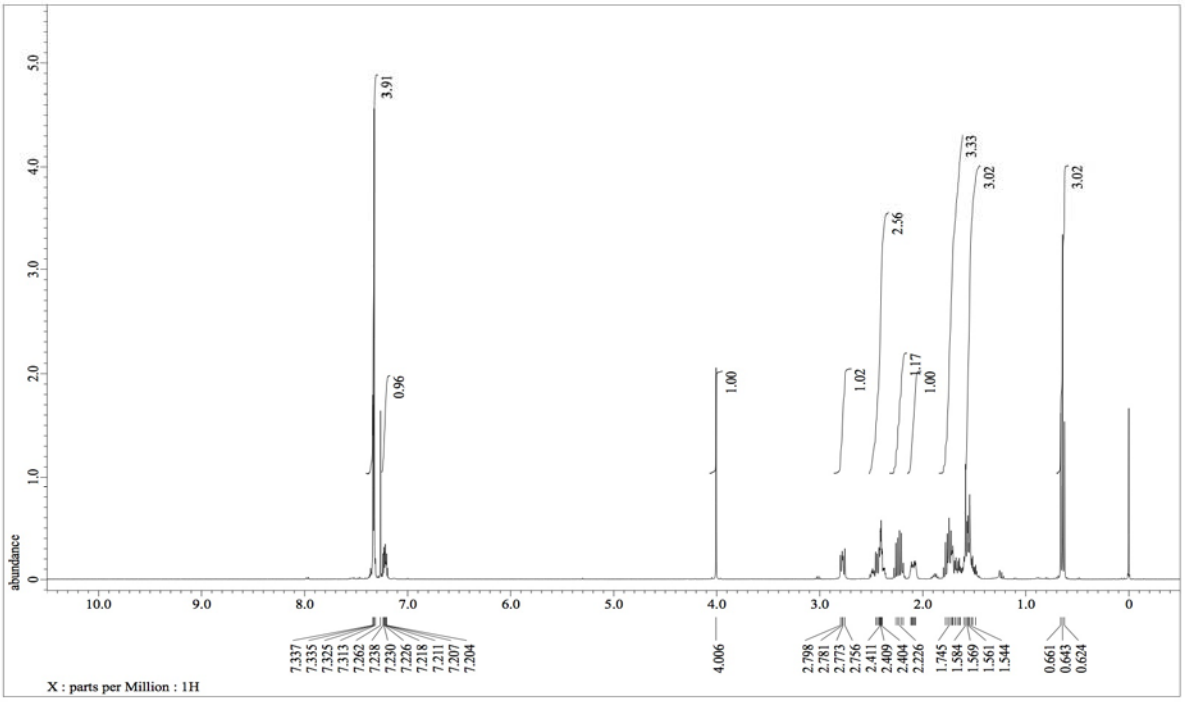
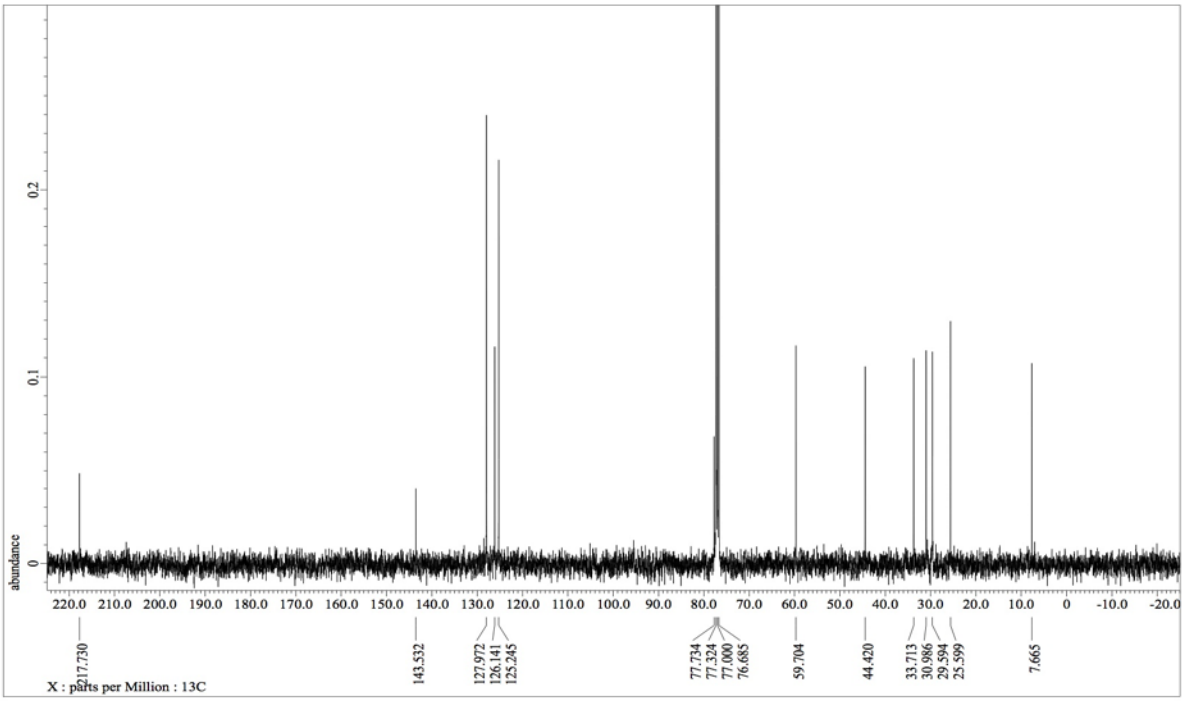


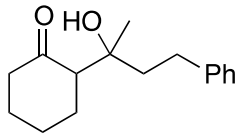


Data for *minor*-isomer

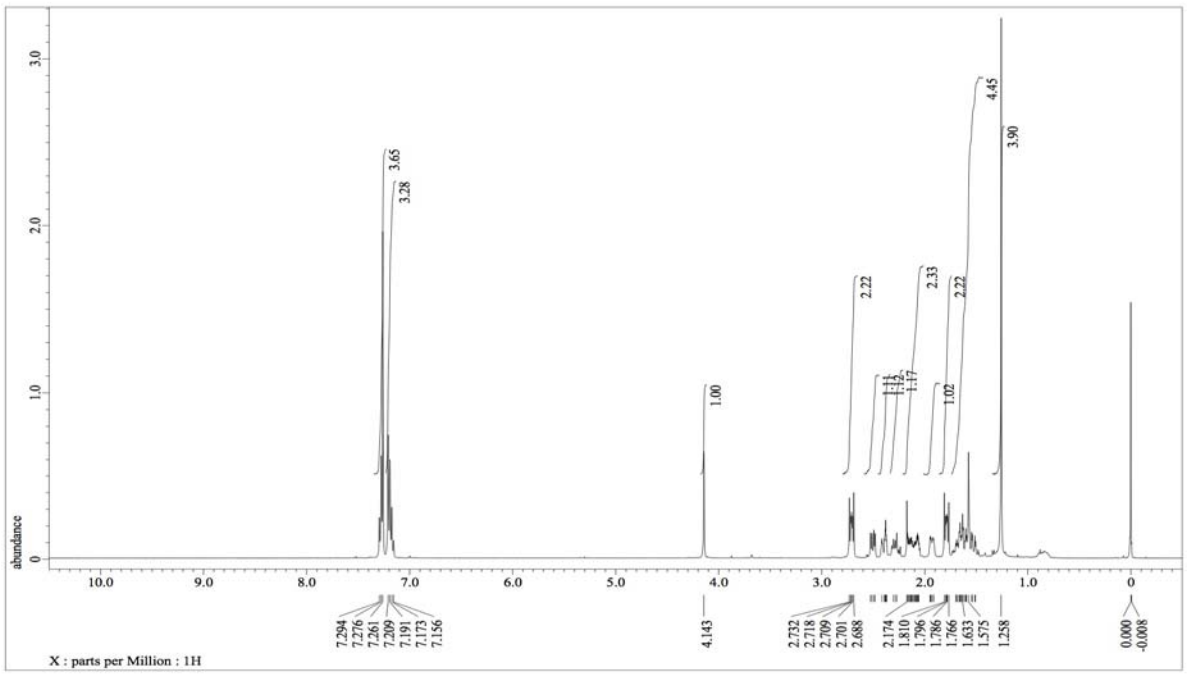


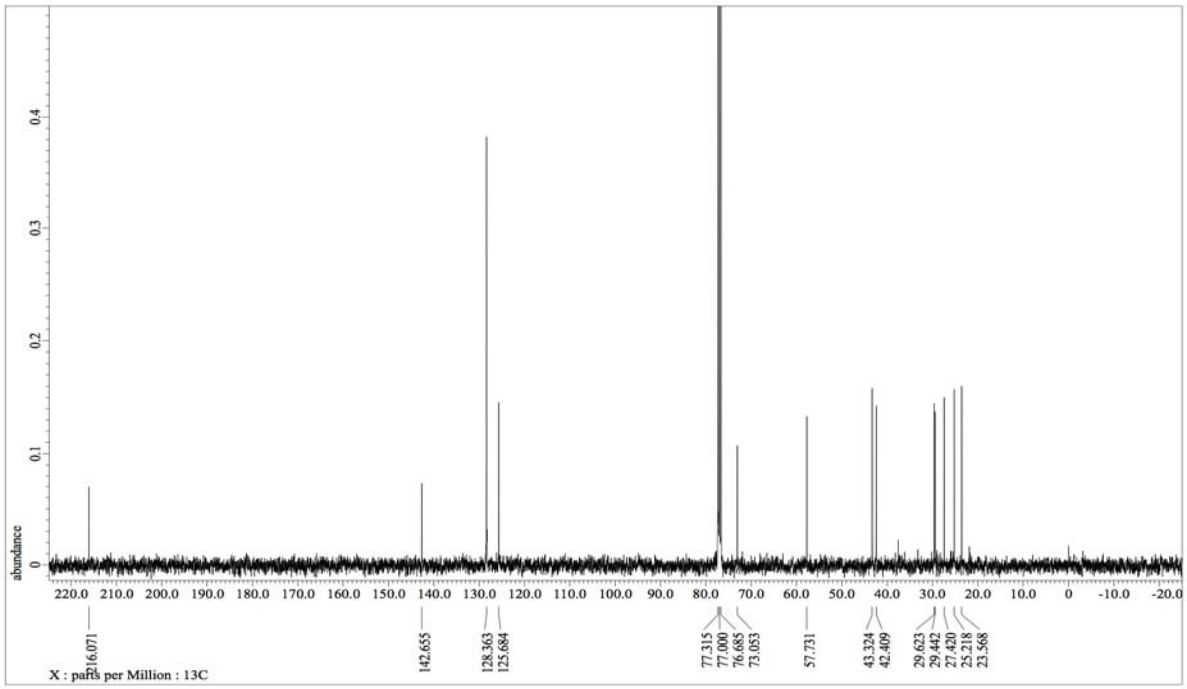


2-(1-Hydroxy-1-methyl-3-phenylpropyl)cyclohexanone (3ej)

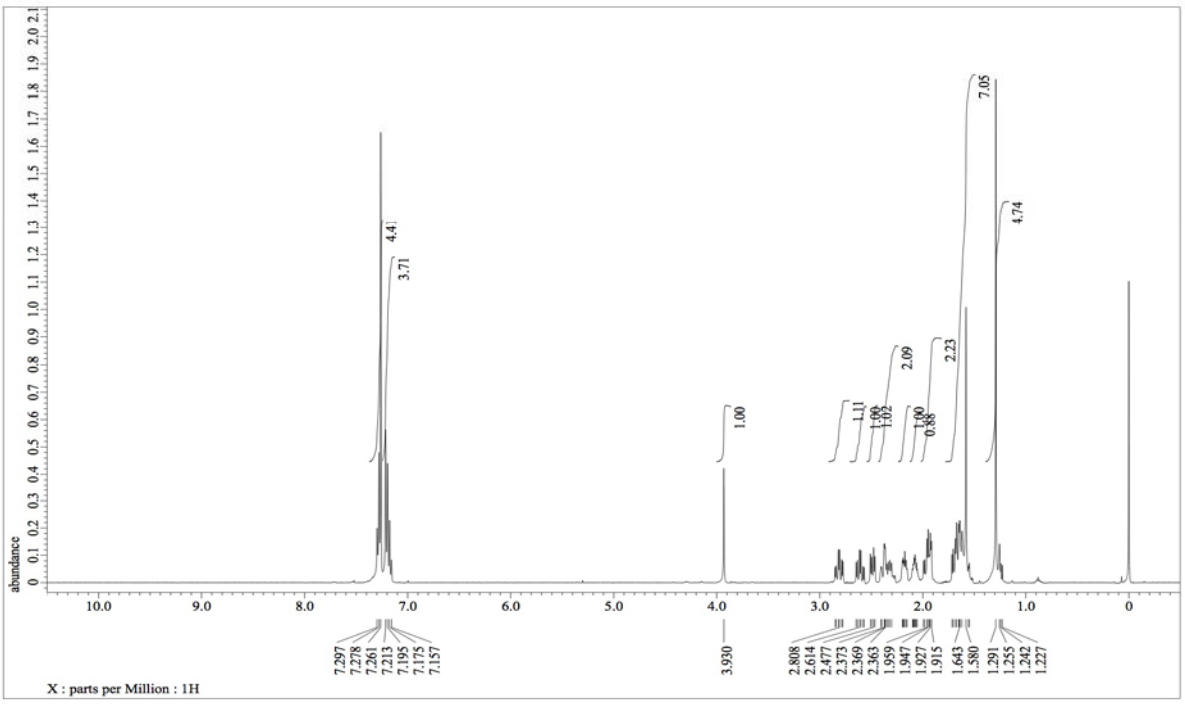


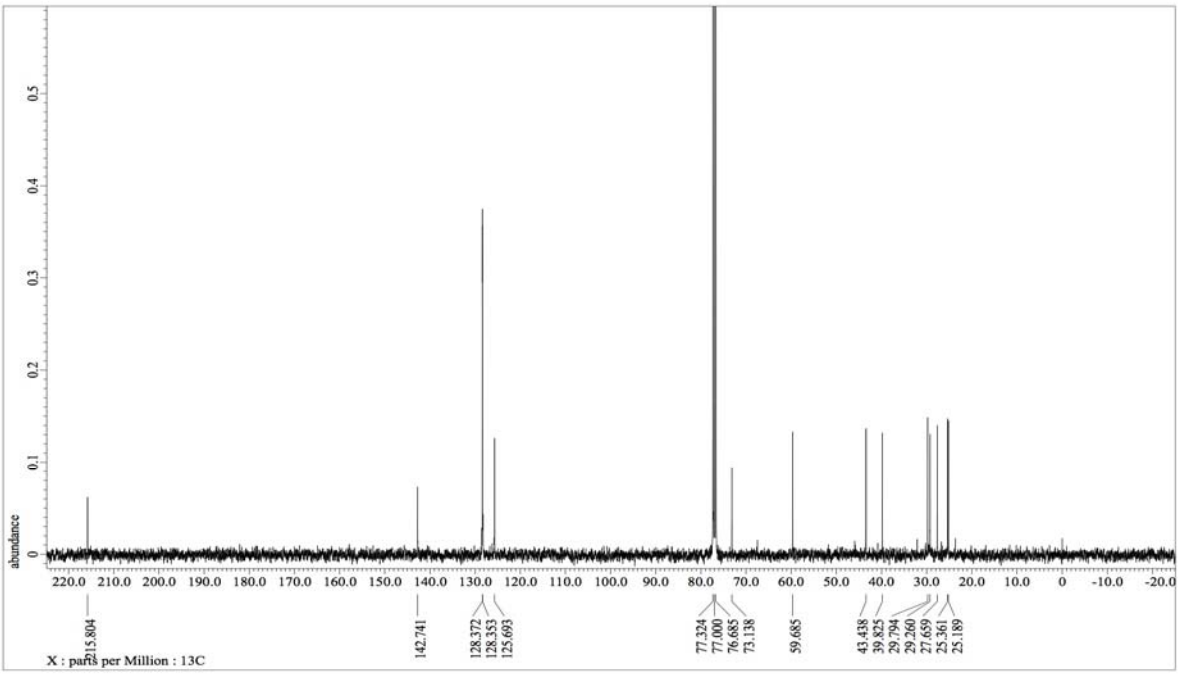
Data for *major*-isomer





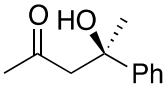
Data for *minor*-isomer

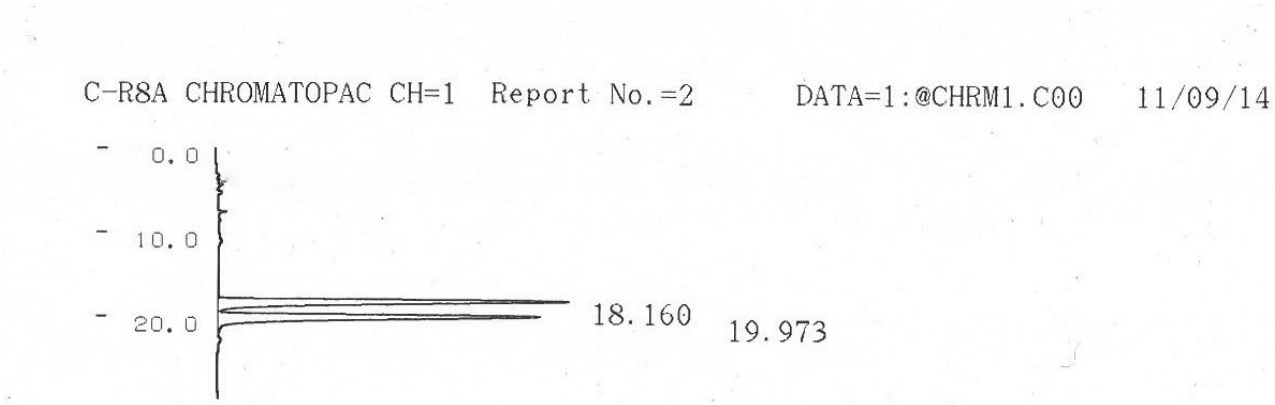




HPLC Traces of Optically Active Compounds

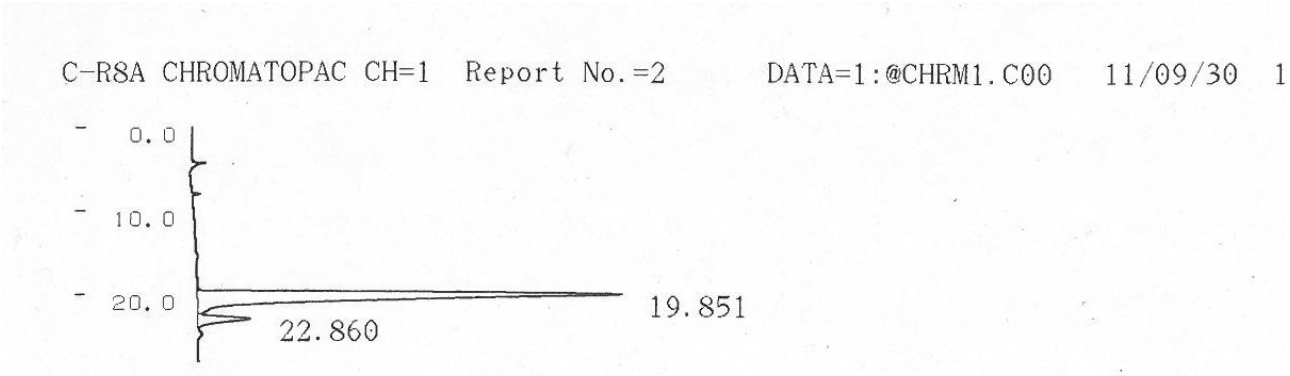
(*R*)-4-Hydroxy-4-phenylpentan-2-one (3ab)





** CALCULATION REPORT **

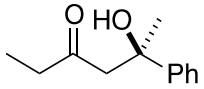
CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC
1	11	18.16	5565633	151360	V		50.1707
	12	19.973	5527764	138961	V		49.8293
		TOTAL	11093396	290322			100

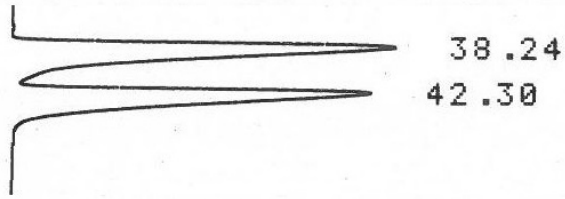


** CALCULATION REPORT **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC
1	7	19.851	2689902	46130			91.3856
	8	22.86	253560	5650	V		8.6143
		TOTAL	2943462	51780			100

5-Hydroxy-5-phenylhexan-3-one (3cb)





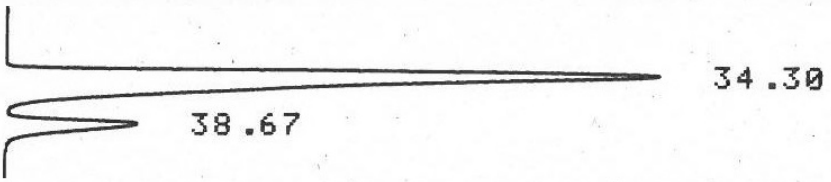
D-2500

METHOD: TAG: 2 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	38.24	5905465	50.434	BV
2	42.30	5803925	49.566	VB
TOTAL		11709390	100.000	

PEAK REJ : 100000



D-2500

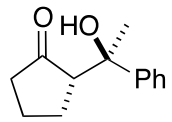
METHOD: TAG: 1 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

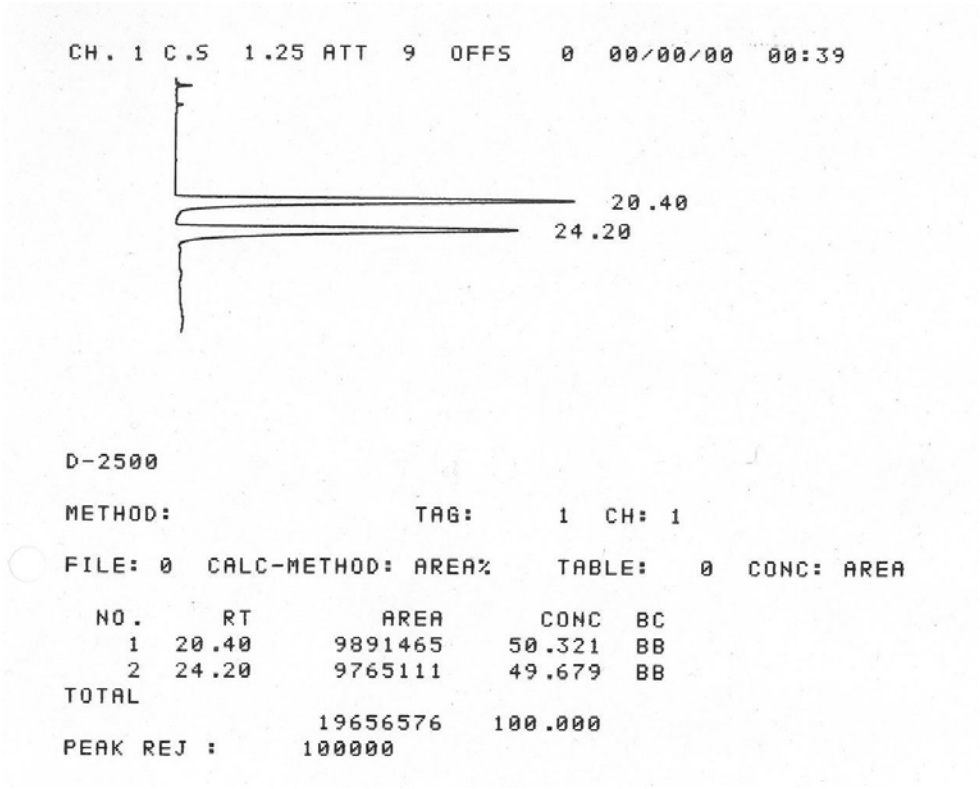
NO.	RT	AREA	CONC	BC
1	34.30	10292325	86.772	BV
2	38.67	1569020	13.228	VB
TOTAL		11861345	100.000	

PEAK REJ : 100000

2-(1-Hydroxy-1-phenylethyl)cyclopentanone (3db)



Data for *major*-isomer



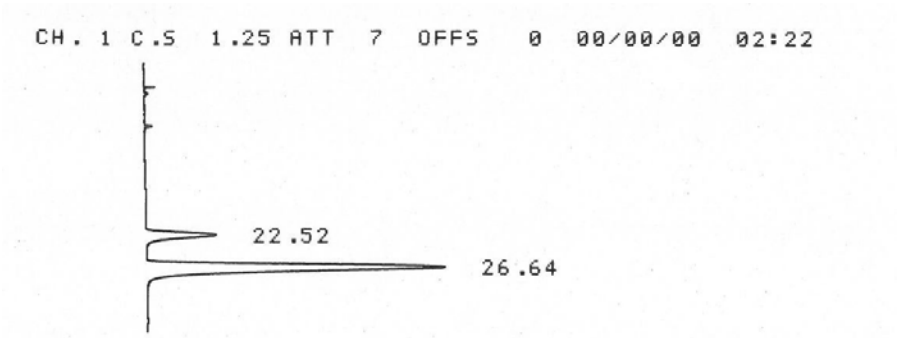
D-2500

METHOD: TAG: 1 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	20.40	9891465	50.321	BB
2	24.20	9765111	49.679	BB
TOTAL		19656576	100.000	

PEAK REJ : 100000



D-2500

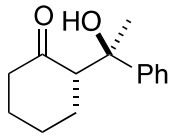
METHOD: TAG: 2 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

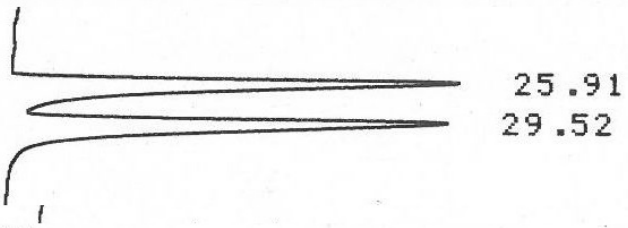
NO.	RT	AREA	CONC	BC
1	22.52	434226	16.189	BB
2	26.64	2248027	83.811	BB
TOTAL		2682253	100.000	

PEAK REJ : 100000

2-(1-Hydroxy-1-phenylethyl)cyclohexanone (3eb)



Data for *major*-isomer



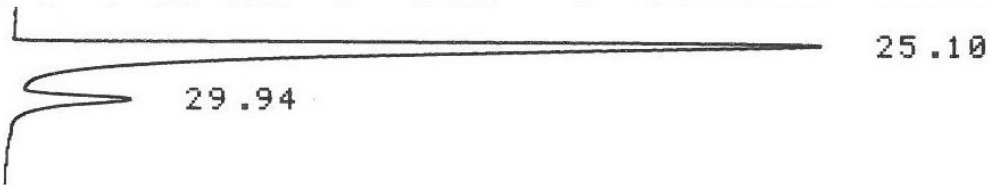
D-2500

METHOD: TAG: 2 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	25.91	2760904	49.538	BV
2	29.52	2812423	50.462	VB
TOTAL		5573327	100.000	

PEAK REJ : 100000



D-2500

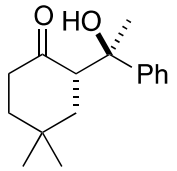
METHOD: TAG: 9 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

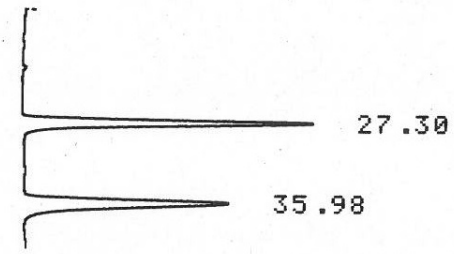
NO.	RT	AREA	CONC	BC
2	25.10	11748022	91.845	BV
3	29.94	1043077	8.155	TBB
TOTAL		12791099	100.000	

PEAK REJ : 100000

2-(1-Hydroxy-1-phenylethyl)-4,4-dimethylcyclohexanone (3fb)



Data for *major*-isomer



D-2500 00/00/00

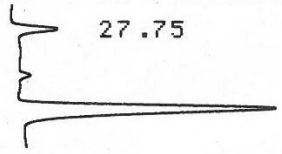
METHOD: TAG: 15 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	27.30	1254985	49.949	BB
2	35.98	1257561	50.051	BB
TOTAL		2512546	100.000	

PEAK REJ : 400000

CH. 1 C.S 1.25 ATT 7 OFFS 0 00/00/00 15:40



D-2500 00/00/00 15:40

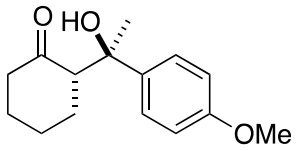
METHOD: TAG: 16 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

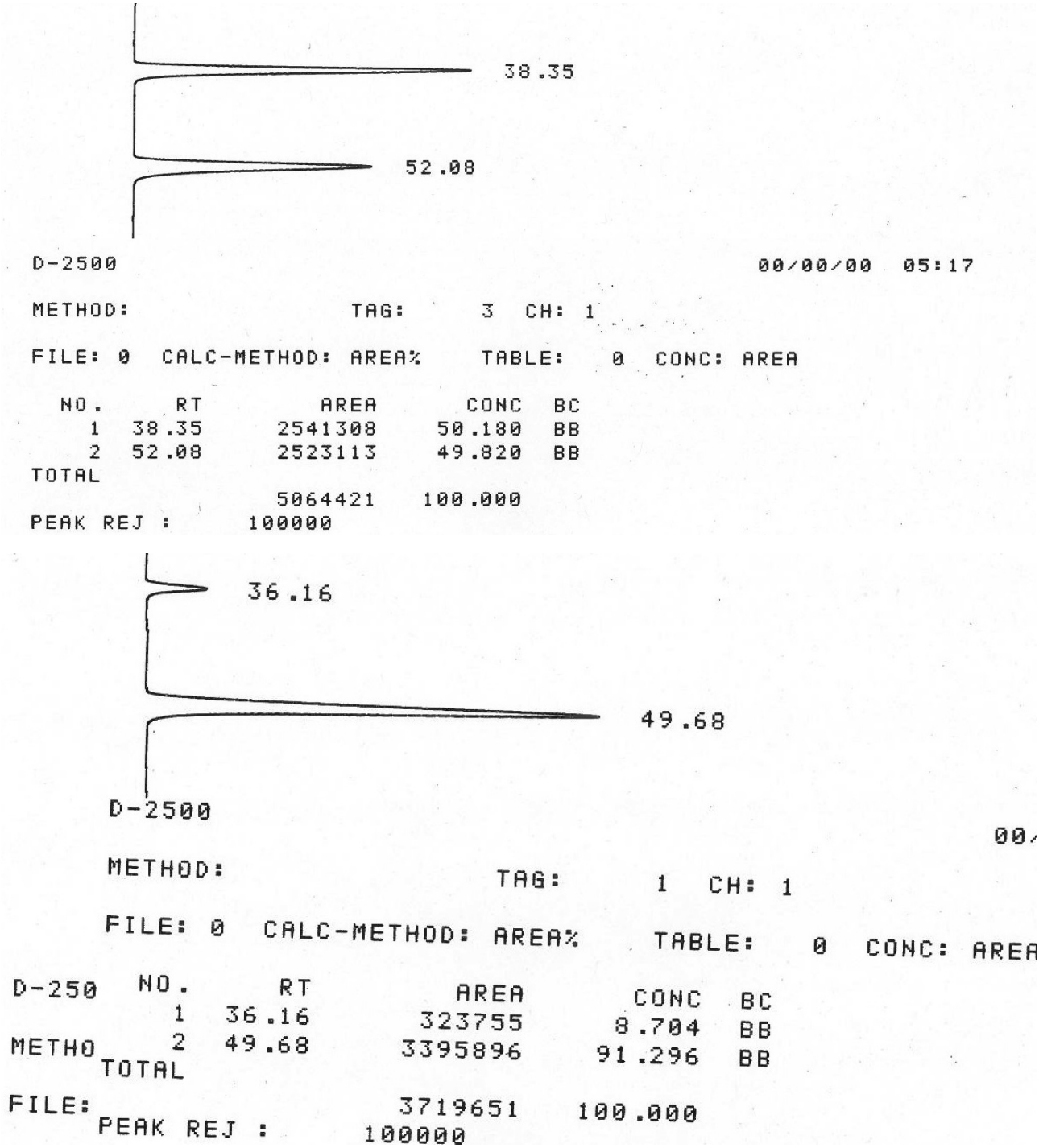
NO.	RT	AREA	CONC	BC
1	27.75	200836	9.869	BB
2	36.83	1834208	90.131	BB
TOTAL		2035044	100.000	

PEAK REJ : 10000

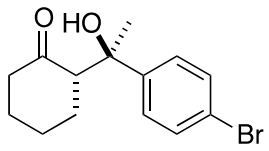
2-[1-Hydroxy-1-(4-methoxyphenyl)ethyl]cyclohexanone (3eg)



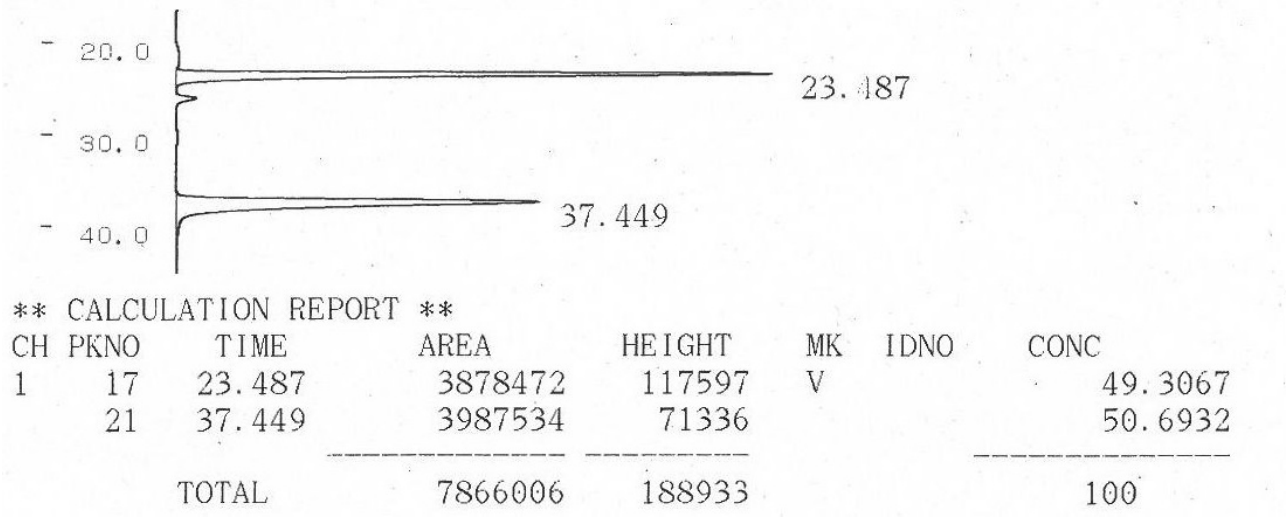
Data for *major*-isomer



2-[1-Hydroxy-1-(4-bromophenyl)ethyl]cyclohexanone (3eh)

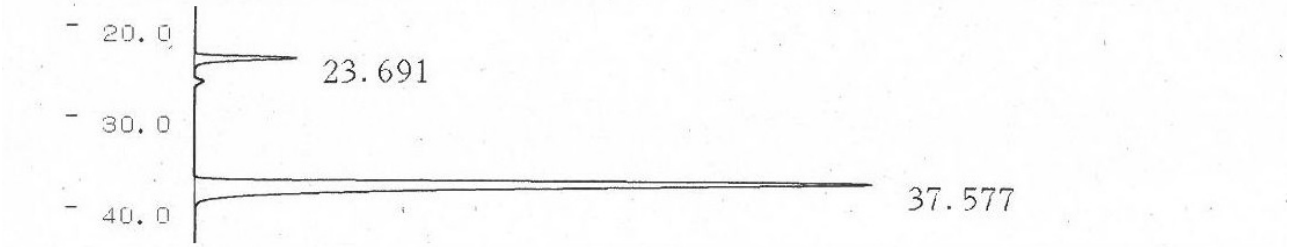


Data for *major*-isomer



** CALCULATION REPORT **

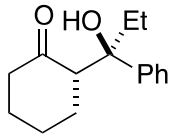
CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC
1	17	23.487	3878472	117597	V		49.3067
	21	37.449	3987534	71336			50.6932
		TOTAL	7866006	188933			100



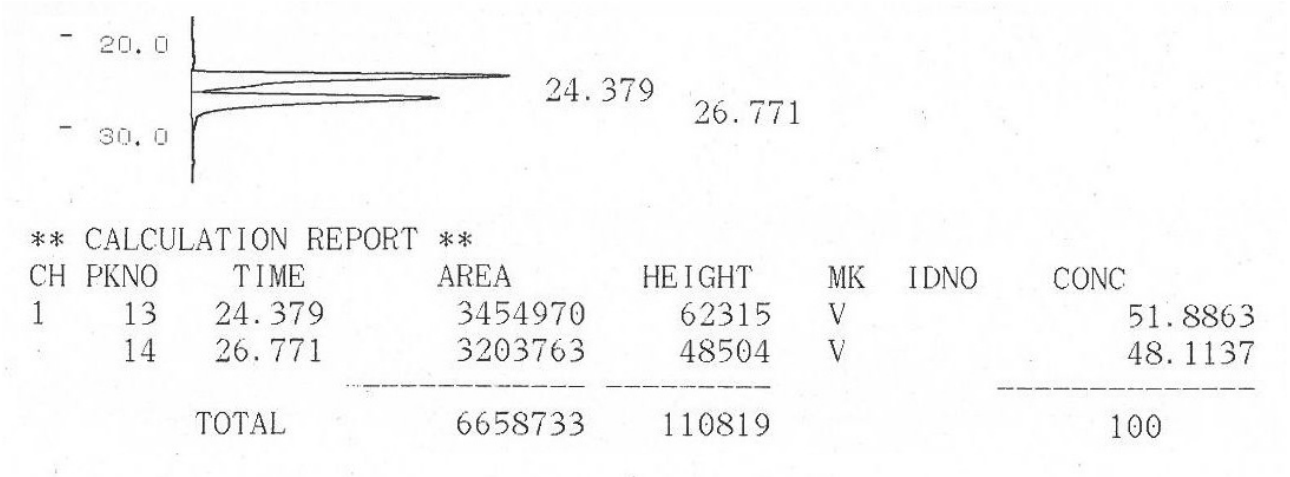
** CALCULATION REPORT **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC
1	9	23.691	679416	20304			8.1663
	11	37.577	7640307	135226			91.8337
		TOTAL	8319723	155530			100

2-(1-Hydroxy-1-phenylpropyl)cyclohexanone (3ei)

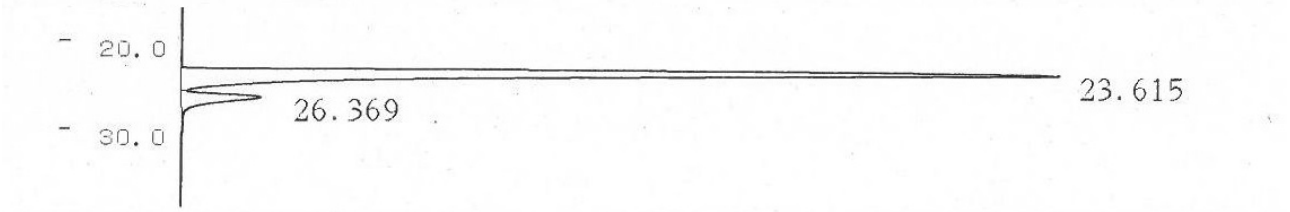


Data for *major*-isomer



** CALCULATION REPORT **

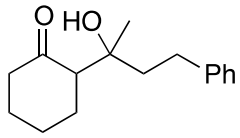
CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC
1	13	24.379	3454970	62315	V		51.8863
	14	26.771	3203763	48504	V		48.1137
		TOTAL	6658733	110819			100



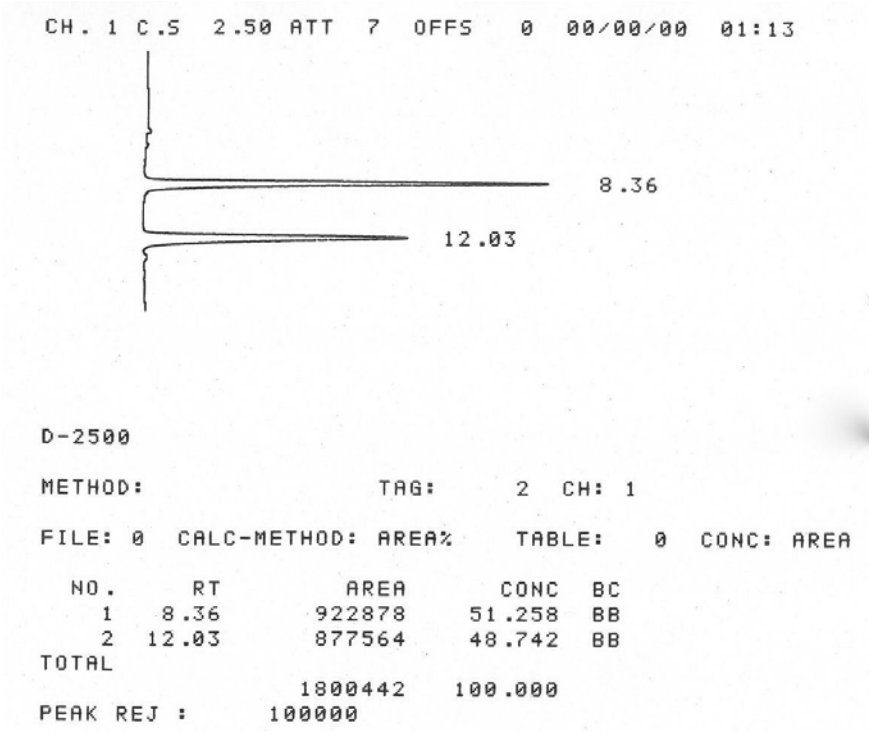
** CALCULATION REPORT **

CH	PKNO	TIME	AREA	HEIGHT	MK	IDNO	CONC
1	11	23.615	9452274	180359			90.1502
	12	26.369	1032757	16397	V		9.8498
		TOTAL	10485031	196757			100

2-(1-Hydroxy-1-methyl-3-phenylpropyl)cyclohexanone (3ej)



Data for *major*-isomer

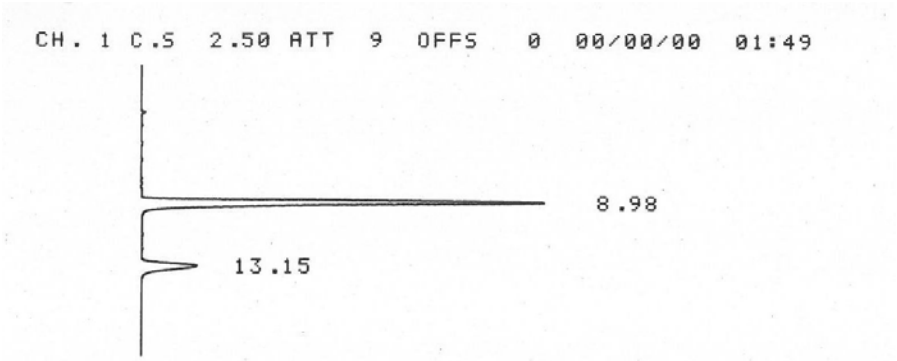


D-2500

METHOD: TAG: 2 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	8.36	922878	51.258	BB
2	12.03	877564	48.742	BB
TOTAL		1800442	100.000	
PEAK REJ :		100000		



D-2500

METHOD: TAG: 3 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	8.98	3935649	83.832	BB
2	13.15	759024	16.168	BB
TOTAL		4694673	100.000	
PEAK REJ :		100000		

References

1) S. Kotani, S. Hashimoto and M. Nakajima, *Tetrahedron,* 2007, **63**, 3122-3132.
2) A. R. Bassindale and T. Stout, *J. Organomet. Chem.,* 1984, **271**, C1-C3.
3) (a) I. Stahl and J. Gosselck, *Synthesis,* 1980, 561-563, (b) I-H. Chen, M. Kanai and M. Shibasaki, *Org. Lett*., 2010, **12**, 4098-4101.
4) C. Schneider, M. Hansch and T. Weide, *Chem. Eur. J*., 2005, **11**, 3010-3021.
5) Y. Tanabe, N. Matsumoto, T. Higashi, T. Misaki, T. Itho, M. Yamamoto, K. Mitarai and Y. Nishii, *Tetrahedron,* 2002, **58**, 8269-8280.