ELECTRONIC SUPPLEMENTARY INFORMATION

Synthesis of optically active bifunctional building blocks through enantioselective copper catalyzed allylic alkylation using Grignard reagents

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General Remarks:

^{1}H-NMR spectra were recorded at 300 or 400 MHz with $CDCl_3$ as solvent. ^{13}C-NMR spectra were obtained at 75.4 or 100.59 MHz in $CDCl_3$. Chemical shifts were determined relative to the residual solvent peaks ($CHCl_3$, δ = 7.26 ppm for hydrogen atoms, δ = 77.0 for carbon atoms). The following abbreviations are used to indicate signal multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; bs, broad singlet. Enantiomeric excess determination was performed by capillary GC analysis or HPLC analysis using flame ionization detector or UV-detection, respectively (all in comparison with racemic products, column and conditions further specified in relevant experimentals). Optical rotations were measured in $CHCl_3$ on a polarimeter with a 10 cm cell (*c* given in g/100 mL). Absolute configuration of the products was determined by comparison of optical rotations with those of compounds previously published. Thin-layer chromatography (TLC) was performed using commercial Kieselgel 60, F_{254} silica gel plates, and components were visualized with $KMnO_4$ or phosphomolybdic acid reagent. Flash chromatography was performed on silica gel. Drying of solutions was performed with $MgSO_4$ and concentrations were conducted with a rotary evaporator.

Taniaphos ligand **L1** was prepared according to literature procedures[1] or obtained through a donation. The substrates **1a**,[2] **1b**,[3] and **1c**[4] were prepared according to literature procedures. Grignard reagents were purchased as solutions in Et_2O (EtMgBr, MeMgBr, *n*-PentMgBr) or prepared from the corresponding alkyl bromides and magnesium turnings in Et_2O following standard procedures. Grignard reagents were titrated using *s*-BuOH and catalytic amounts of 1,10-phenanthroline. Et_2O (for preparation of Grignard reagents) and THF were distilled from Na/benzophenone and CH_2Cl_2 was

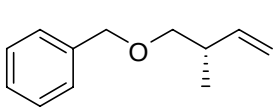
[1] Ireland, T.; Grossheimann, G.; Wieser-Jeunesse, C.; Knochel, P. *Angew. Chem. Int. Ed.* **1999**, *38,* 3212.
[2] Kottirsch, G.; Koch, G.; Feifel, R.; Neumann, U. *J. Med. Chem*. **2002**, *45*, 2289.
[3] a.) Cerezo, S.; Cortès, J.; Galvan, D.; Lago, E.; Marchi, C.; Molins, E.; Moreno-Mañas, M.; Pleixats, R.; Torrejón, J.; Vallribera, A. *Eur. J. Org. Chem.* **2001**, 329; b.) Neustadt, B. R. *Tetrahedron Lett.* **1994**, *35*, 379.
[4] a.) Lemieux, R. M.; Devine, P. N.; Mechelke, M. F.; Meyers, A. I. *J. Org. Chem.* **1999**, *64,* 3585; b.) Thurner, A.; Faigl, F.; Tőke, L.; Mordini, A.; Valacchi, M.; Reginato, G.; Czira, G. *Tetrahedon* **2001**, *57*, 8173; c.) McDonald, W. S.; Verbicky, C. A.; Zercher, C. K. *J. Org. Chem.* **1997**, *62*, 1215.

distilled from CaH_2. All other solvents were used as purchased. Allylic alkylations were conducted under argon atmosphere using standard Schlenk techniques.

Racemic allylic alkylation products were obtained by reaction of the bromides with the corresponding Grignard reagent (5.0 equiv) at -25^{o}C in CH_2Cl_2 in the presence of CuCN (100 mol %). Other racemic products were obtained through the transformations described, *vide infra*, on the racemic allylic alkylation products. The products **2a**, **2c**, **2f**, **3**, **4a**, **5a**, **5c**, **6a**, and **10** have been previously described (see appropriate references in the following pages).

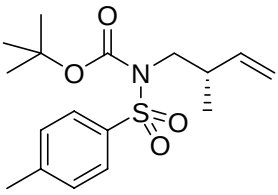
General Procedure for the Preparative Enantioselective Cu-catalysed Allylic Alkylation with Methyl Grignard:

In a Schlenk tube equipped with septum and stirring bar, $CuBr{\cdot}SMe_2$ (75 μmol, 15.4 mg) and ligand **L1** (90 μmol, 61.9 mg) were dissolved in CH_2Cl_2 (15 mL) and stirred under an argon atmosphere at room temperature for 10 min. The mixture was cooled to – 75 ^{o}C and the methyl Grignard reagent (9.0 mmol, 3M solution in Et_2O, 3.0 mL) was added dropwise. Allylic bromide **1a** or **1b** (7.5 mmol) was added dropwise as a solution in 2.5 mL CH_2Cl_2 at that temperature over 60 min *via* a syringe pump. Once the addition was complete the resulting mixture was further stirred at – 75 ^{o}C for 24h. The reaction was quenched by addition of MeOH (2.5 mL) and the mixture was allowed to reach rt. Subsequently, aqueous NH_4Cl solution (1M, 30 mL) and 50 mL Et_2O were added, the organic phase was separated and the resulting aqueous layer was extracted with Et_2O (2x 25 mL). The combined organic phases were dried and concentrated to yield a yellow oil which was purified by flash chromatography.



(–)-(*S*)-((2-Methylbut-3-enyloxy)methyl)benzene (2a):[5]

Purification by column chromatography (SiO_2, 1:99 Et_2O/pentane, $R_f = 0.35$) afforded **2a** (1.24 g) as a colorless oil. [94% yield, 92% ee, $[\alpha]_D = -5.4$ (*c* 1.3, $CHCl_3$); lit.[5] $[\alpha]_D = -6$ (*c* 1.1, $CHCl_3$)]; ^{1}H-NMR δ 7.32-7.21 (m, 5H), 5.81 (ddd, *J* = 6.9, 10.4 and 17.3 Hz, 1H), 5.11-5.00 (m, 2H), 4.53 (s, 2H), 3.35 (ddd, *J* = 6.7, 9.1 and 23.9 Hz, 2H), 2.54-2.49 (m, 1H), 1.05 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR δ 141.3, 138.6, 128.3, 127.5, 127.4, 114.0, 75.0, 72.9, 37.8, 16.6; MS (EI) *m/z* 176 (M^+, 16), 175 (6), 92 (11), 91 (100), 65 (6); HRMS Calcd. for $C_{12}H_{16}O$ 176.1201, found 176.1207. Enantiomeric excess determined of derivatized product **3**.



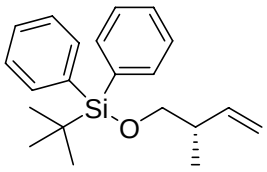
(–)-(*S*)-(*N*-2-Methylbut-3-enyl)(*N*-*t*-butoxycarbonyl) *p*-toluenesulfonamide (2b):

Purification by column chromatography (SiO_2, 10:90 Et_2O/pentane, $R_f = 0.30$) afforded **2b** (2.45 g) as a colorless oil. [96% yield, 95% ee, $[\alpha]_D = -7.7$ (c 1.4, $CHCl_3$)]; ^{1}H-NMR δ 7.78 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 5.73 (ddd, *J* = 8.1, 10.2 and 17.3 Hz, 1H), 5.10-5.00 (m, 2H), 3.82-3.72 (m, 2H), 2.78-2.66 (m, 1H), 2.43 (s, 3H), 1.32 (s, 9H), 1.07 (d, J = 6.8 Hz, 3H); ^{13}C-NMR δ 151.0, 144.0, 140.7, 137.5, 129.1, 127.9, 115.3, 84.0, 51.9, 38.7, 27.8, 21.5, 17.3; MS (EI) *m/z* 283 (9), 216 (20), 185 (6), 184 (64), 155 (42), 91 (39), 68 (7), 65 (11), 57 (100), 56 (5), 55 (13); MS (CI) *m/z* 359 (8), 358 (20), 357 ($[M+NH_4]^+$,100), 302 (7), 301 (40), 284 (6). HRMS Calcd. for $[M-Me_2C{=}CH_2]^+$ $C_{13}H_{17}NO_4S$ 283.0878, found 283.0887. Enantiomeric excess determined of derivatized product **7**. The absolute configuration was assigned by comparison of the sign of the optical rotation of derivatized product **10** with the literature value.

[5] López, F.; van Zijl, A. W.; Minnaard, A. J.; Feringa. B. L. *Chem. Commun.* **2006**, 409.

General Procedure for the Enantioselective Cu-catalysed Allylic Alkylations:

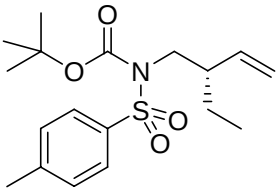
In a Schlenk tube equipped with septum and stirring bar, $CuBr{\cdot}SMe_2$ (15 μmol, 3.1 mg) and ligand **L1** (18 μmol, 12.4 mg) were dissolved in CH_2Cl_2 (2.5 mL) and stirred under argon at room temperature for 10 min. The mixture was cooled to – 75 °C and the Grignard reagent (0.45 mmol, solution in Et_2O) was added dropwise. The allylic bromide (0.3 mmol) was then added dropwise as a solution in 0.5 mL CH_2Cl_2 at – 75 °C over 15 min. Once the addition was complete the resulting mixture was further stirred at – 75 °C. After full conversion was established by TLC the reaction was quenched by addition of MeOH (0.5 mL) and the mixture was allowed to reach rt. Then, sat. aqueous NH_4Cl solution (1.5 mL) was added, the organic phase was separated and the aqueous phase was extracted with Et_2O (2x 2.5 mL). The combined organic phases were dried and concentrated to yield a yellow oil which was purified by flash chromatography.



(–)-(*S*)-4-[(*tert*-Butyldiphenylsilyl)oxy]-3-methylbut-1-ene (2c):[6]

Purification by column chromatography (SiO_2, 0.2:99.8 Et_2O/pentane, R_f = 0.25) afforded **2c** (70.3 mg) as a colorless oil. [72% yield, 94% ee, $[\alpha]_D$ = – 2.7 (c 1.3, $CHCl_3$); lit.[6] $[\alpha]_D$ = – 3.18 (94% ee, c 0.71, $CHCl_3$)]; ^{1}H-NMR δ 7.68 (dd, *J* = 7.7 and 1.6 Hz, 4H), 7.45-7.36 (m, 6H), 5.81 (ddd, *J* = 6.9, 10.4 and 17.4Hz, 1H), 5.06-4.98 (m, 2H), 3.58 (dd, *J* = 9.7 and 6.2 Hz, 1H), 3.50 (dd, *J* = 9.7 and 6.7 Hz, 1H), 2.44-2.37 (m, 1H), 1.06 (s, 9H), 1.04 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR δ 141.3, 135.6, 133.9, 129.5, 127.6, 114.0, 68.5, 40.2, 26.9, 19.3, 16.2; MS (EI) *m/z* 268 (24), 267 ([M-*t*Bu]$^+$, 100), 240 (17), 239 (80), 237 (12), 211(9), 199 (15), 197 (14), 190 (7), 189 (36), 183 (23), 182 (7), 181 (19), 159 (19), 135 (18), 121 (10), 105 (11), 77 (7); MS (CI) *m/z* 344 (8), 343 (28), 342 ([M+NH_4]$^+$, 100), 325 ([M+H]$^+$, 14). HRMS Calcd. for [M-*t*Bu]$^+$ $C_{17}H_{19}OSi$ 267.1205, found 267.1197. Enantiomeric excess determined of derivatized product **5a** (Scheme S1, page S16).

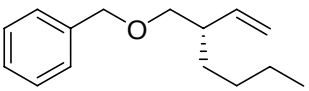
[6] H. Lebel, V. Paquet *J. Am. Chem. Soc.* **2004**, *126*, 320.



(–)-(*N*-2-Ethylbut-3-enyl)(*N*-*tert*-butoxycarbonyl)

***p*-toluenesulfonamide (2e)**:

Purification by column chromatography (SiO_2, 5:95 Et_2O/pentane, R_f = 0.25) afforded **2e** (87.5 mg) as a colorless oil. [83% yield, 91% ee, $[\alpha]_D$ = – 0.4 (c 8.5, $CHCl_3$)]; ^{1}H-NMR δ 7.75 (d, *J* = 8.1Hz, 2H), 7.26 (d, *J* = 8.1Hz, 2H), 5.59-5.49 (m, 1H), 5.06-5.00 (m, 2H), 3.78 (d, *J* = 7.7Hz, 2H), 2.49-2.40 (m, 1H), 2.39 (s, 3H), 1.55-1.44 (m, 1H), 1.29 (s, 9H) ppm 1.26-1.18 (m, 1H), 0.88 (t, *J* = 7.4Hz, 3H); ^{13}C-NMR δ 151.0, 143.9, 139.3, 137.5, 129.0, 127.8, 117.2, 83.9, 50.8, 46.7, 27.7, 24.8, 21.5, 11.5; MS (EI) *m/z* 353 (M^+, 0.1), 297 (15), 216 (10), 185 (9), 184 (88), 155 (49), 92 (5), 91 (39), 82 (39), 69 (7), 65 (9), 57 (100); MS (CI) *m/z* 373 (9), 372 (20), 371 ($[M+NH_4]^+$, 100), 317 (6), 316 (12), 315 (75), 298 (8), 271 (8). HRMS Calcd. for $[M\text{-}Me_2C{=}CH_2]^+$ $C_{14}H_{19}NO_4S$ 297.1035, found 297.1027. Enantiomeric excess determined of derivatized product **5e**. In accordance with the results obtained in the other allylic alkylations, the absolute configuration of this compound is assumed to be (*S*), analogous to the other products.

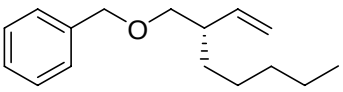


(+)-(*S*)-((2-*n*-Butylbut-3-enyloxy)methyl)benzene (2f):[7]

Purification by column chromatography (SiO_2, 1:99 Et_2O/pentane, R_f = 0.50) afforded **2f** (60.5 mg) as a colorless oil. [93% yield, 94% ee, $[\alpha]_D$ = + 18.5 (c 2.2, $CHCl_3$)]; ^{1}H-NMR δ 7.38-7.27 (m, 5H), 5.70 (ddd, *J* = 8.4, 10.6 and 17.0Hz, 1H), 5.13-5.07 (m, 2H), 4.54 (s, 2H), 3.42 (d, *J* = 6.4Hz, 2H), 2.42-2.32 (m, 1H), 1.60-1.48 (m, 1H), 1.40-1.20 (m, 5H), 0.92 (t, *J* = 7.0Hz, 3H); ^{13}C-NMR δ 140.4, 138.6, 128.3, 127.5, 127.4, 115.4, 73.8, 72.9, 44.1, 30.9, 29.1, 22.8, 14.0; MS (EI) *m/z* 218 (M^+, 11), 107 (13), 105 (6), 104 (7), 97 (8), 96 (6), 92 (15), 91 (100), 85 (11), 83 (16), 69 (6), 65 (8), 57 (8), 55 (21); HRMS Calcd. for $C_{15}H_{22}O$ 218.1671, found 218.1665. Enantiomeric excess determined by chiral HPLC analysis, Chiralcel OD-H (100% heptane), 40ºC, retention times (min):

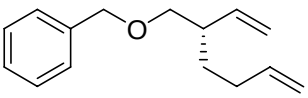
[7] Yadav, J. S.; Reddy, P. S. *Synth. Commun.* **1986**, *16*, 1119.

11.6 (minor) and 13.6 (major). The absolute configuration was assigned by comparison of the sign of optical rotation of the hydrogenated product 2-ethylhexan-1-ol (Pd/C, H_2 in MeOH) with the literature value.[8]



(+)-(*S*)-((2-*n*-Pentylbut-3-enyloxy)methyl)benzene (2g):

Purification by column chromatography (SiO_2, 1:99 Et_2O/pentane, R_f = 0.50) afforded **2g** (60.4 mg) as a colorless oil. [87% yield, 94% ee, $[\alpha]_D$ = + 14.4 (c 2.4, $CHCl_3$)]; ^{1}H-NMR δ 7.38-7.28 (m, 5H), 5.70 (ddd, *J* = 8.4, 10.6 and 17.0Hz, 1H), 5.14-5.07 (m, 2H), 4.55 (s, 2H), 3.42 (d, *J* = 6.5Hz, 2H), 2.42-2.32 (m, 1H), 1.59-1.46 (m, 1H), 1.40-1.21 (m, 7H), 0.91 (t, *J* = 6.9Hz, 3H); ^{13}C-NMR δ 140.4, 138.6, 128.2, 127.5, 127.4, 115.4, 73.8, 72.9, 44.1, 31.9, 31.2, 26.6, 22.6, 14.1; LRMS (EI) *m/z* 232 (M^+, 24), 231 (6), 161 (7), 107 (8), 105 (5), 104 (11), 92 (14), 91 (100), 69 (14), 65 (5), 55 (8); HRMS Calcd. for $C_{16}H_{24}O$ 232.1827, found 232.1835. Enantiomeric excess determined by chiral HPLC analysis, Chiralcel OD-H (100% heptane), 40ºC, retention times (min): 11.5 (minor) and 13.3 (major). The absolute configuration was assigned by comparison of the sign of optical rotation of the hydrogenated product 2-ethylheptan-1-ol (Pd/C, H_2 in MeOH) with the literature value.[9]

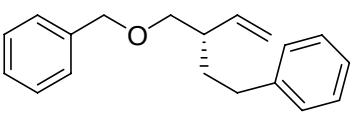


(+)-(*S*)-(2-Vinyl-hex-5-enyloxymethyl)-benzene (2h):

Purification by column chromatography (SiO_2, 1:99 Et_2O/pentane, R_f = 0.50) afforded **2h** as a colorless oil. [89% yield, 90% ee, $[\alpha]_D$ = + 10.0 (c 2.5, $CHCl_3$)]; ^{1}H-NMR δ 7.40-7.27 (m, 5H), 5.82 (tdd, *J* = 6.6, 10.2 and 16.9 Hz, 1H), 5.74-5.64 (m, 1H), 5.14-4.94 (m, 4H), 4.53 (s, 2H), 3.46-3.38 (m, 2H), 2.45-2.36 (m, 1H), 2.18-1.97 (m, 2H), 1.70-1.60 (m, 1H), 1.44-1.34 (m, 1H); ^{13}C-NMR δ 139.9, 138.7, 138.5, 128.3, 127.5, 127.4, 115.8, 114.5, 73.7, 72.9, 43.5, 31.1, 30.4; MS (EI) *m/z* 216 (M^+, 0.4), 173 (6), 95 (6), 92 (11), 91 (100), 79 (6), 67 (8), 65 (11), 55 (5); HRMS Calcd. For

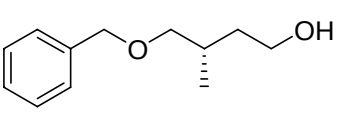
[8] Larpent, C.; Chasseray, X. *Tetrahedron* **1992**, *48*, 3903.
[9] Garcia-Ruiz, V.; Woodward, S. *Tetrahedron: Asymm.* **2002**, *13*, 2177.

$C_{15}H_{20}O$ 216.1514, found 216.1513. Enantiomeric excess determined by chiral HPLC analysis, Chiralcel OD (100% heptane), 40ºC, retention times (min): 7.5 (minor) and 8.5 (major). The absolute configuration was assigned by comparison of the sign of optical rotation of the hydrogenated product 2-ethylhexan-1-ol (Pd/C, H_2 in MeOH) with the literature value.[8]



(+)-(2-Vinyl-4-phenyl-butyloxymethyl)-benzene (2i):

Purification by column chromatography (SiO_2, 1:99 Et_2O/pentane, R_f = 0.50) afforded **2i** (69.0 mg) as a colorless oil. [86% yield, 92% ee, $[\alpha]_D$ = + 3.8 (c 2.2, $CHCl_3$)]; ^{1}H-NMR δ 7.42-7.35 (m, 4H), 7.35-7.29 (m, 3H), 7.25-7.20 (m, 3H), 5.78 (ddd, *J* = 8.5, 11.0 and 16.5Hz, 1H), 5.21-5.15 (m, 2H), 4.55 (s, 2H), 3.51-3.43 (m, 2H), 2.78-2.69 (m, 1H), 2.59 (ddd, *J* = 6.6, 10.2 and 13.8Hz, 1H), 2.51-2.41 (m, 1H), 1.93 (dddd, J = 4.6, 6.6, 11.1 and 13.4Hz, 1H), 1.70-1.60 (m, 1H); ^{13}C-NMR δ 142.4, 139.8, 138.5, 128.4, 128.3, 128.2, 127.5, 127.4, 125.6, 116.1, 73.7, 72.9, 43.7, 33.2, 33.0; MS (EI) *m/z* 266 (M^+, 3), 162 (5), 157 (10), 129 (6), 104 (5), 92 (10), 91 (100), 65 (10); HRMS Calcd. for $C_{19}H_{22}O$ 266.1671, found 266.1682. Enantiomeric excess determined by chiral HPLC analysis, Chiralcel OD (99.5% heptane/*i*-PrOH), 40ºC, retention times (min): 8.1 (minor) and 10.0 (major). In accordance with the results obtained in the other allylic alkylations, the absolute configuration of this compound is assumed to be (*S*), analogous to the other products.

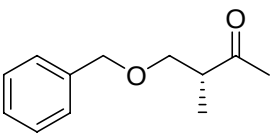


(+)-(*S*)-4-Benzyloxy-3-methylbutan-1-ol (3):[10]

To a cooled solution (0°C) of **2a** (0.5 mmol, 88 mg) in THF (3.5 mL) a solution of 9-BBN (0.75 mmol, 0.5M in THF, 1.5 mL) was added. The reaction mixture was stirred for 3h, then it was allowed to reach rt, after which sequentially EtOH (2.5 mL), aq. NaOH (1M, 2.5 mL) and aq. H_2O_2 (30%, 2.0 mL) were added. The resulting mixture was stirred vigorously overnight at rt,

[10] Smith, A. B., III; Adams, C. M.; Kozmin, S. A.; Paone, D. V. *J. Am. Chem. Soc.* **2001**, *123*, 5925.

then quenched with aq. $Na_2S_2O_3$ (10%, 10 mL). CH_2Cl_2 (20 mL) was added, the organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (20 mL). The combined organic layers were dried and concentrated *in vacuo*. Purification by column chromatography (SiO_2, 40:60 Et_2O/pentane, R_f = 0.25) afforded **3** (77.3 mg) as a colorless oil. [80% yield, 92% ee, $[\alpha]_D$ = + 1.8 (c 2.9, EtOH), – 5.5 (c 2.7, $CHCl_3$), lit.[11] $[\alpha]_D$ = + 2.2 (*c* 1.1, EtOH), + 6.26 (c 5.5, $CHCl_3$)[11c]]; ^{1}H-NMR δ 7.39-7.26 (m, 5H), 4.52 (s, 2H), 3.75-3.61 (m, 2H), 3.35 (ddd, *J* = 6.2, 9.1 and 16.5Hz, 2H), 2.42 (bs, 1H), 1.95 (tq, J = 6.9 and 13.8Hz, 1H), 1.69-1.51 (m, 2H), 0.95 (d, *J* = 6.9Hz, 3H); ^{13}C-NMR δ 138.0, 128.4, 127.7, 76.1, 73.2, 61.2, 38.1, 31.4, 17.7; MS (EI) *m/z* 194 (M^+, 7), 108 (11), 107 (37), 105 (6), 92 (28), 91 (100), 85 (12), 79 (7), 77 (8), 65 (15), 55 (8); HRMS Calcd. for $C_{12}H_{18}O_2$ 194.1307, found 194.1309. Enantiomeric excess determined by chiral HPLC analysis, Chiralcel OD-H (99% heptane/*i*-PrOH), 40ºC, retention times (min): 57.7 (major) and 64.9 (minor).



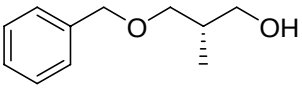
(–)-(*R*)-4-Benzyloxy-3-methylbutan-2-one (4a):[12]

A suspension of $PdCl_2$ (50 µmol, 8.9 mg) and CuCl (1.0 mmol, 99 mg) in DMF/H_2O (6:1, 5 mL) was stirred vigorously under an O_2-stream for 1.5h at rt. After addition of **2a** (0.5 mmol, 88 mg) vigorous stirring was continued for 32h under an O_2-atmosphere at rt. Then, H_2O (20 mL) was added and the mixture was extracted with Et_2O/pentane (1:1, 10 mL, 3x). The combined organic layers were washed with H_2O (10 mL), dried and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 10:90 Et_2O/pentane, R_f = 0.20) afforded **4a** (82.4 mg) as a colorless oil. [86% yield, 92% ee, $[\alpha]_D$ = – 14.0 (c 4.0, $CHCl_3$), lit.[12b] $[\alpha]_D$ = – 16.7 (c 3.91, $CHCl_3$)]; ^{1}H-NMR δ 7.37-7.26 (m, 5H), 4.50 (d, *J* = 1.8Hz, 2H), 3.63 (dd, *J* = 7.5 and 9.2Hz, 1H), 3.49 (dd, *J* = 5.5 and

[11] a.) Fuganti, C.; Grasselli, P. *J. Chem. Soc. Chem. Commun.* **1979**, 995; b.) Schmid, R.; Hansen, H.-J. *Helv. Chim. Acta* **1990**, *73*, 1258; c.) The optical rotation in $CHCl_3$ is reported only once, but appears to be given in the wrong sign: Schmid, R.; Antoulas, S.; Rüttimann, A.; Schmid, M.; Vecchi, M.; Weiser, H. *Helv. Chim. Acta* **1990**, *73*, 1276.

[12] a.) Myers, A. G.; Yang, B. H.; Chen, H.; McKinstry, L.; Kopecky, D. J.; Gleason, J. L. *J. Am. Chem. Soc.* **1997**, *119*, 6496; b.) McGuirk, P. R.; Collum, D. B. *J. Org. Chem.* **1984**, *49*, 843.

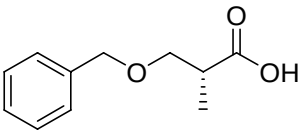
9.2Hz, 1H), 2.91-2.81 (m, 1H), 2.18 (s, 3H), 1.10 (d, *J* = 7.1Hz, 3H); ^{13}C-NMR δ 211.1, 138.0, 128.4, 127.6, 127.6, 73.2, 72.1, 47.2, 29.0, 13.4; MS (EI) *m/z* 192 (M^+, 4), 134 (27), 108 (18), 107 (46), 105 (12), 92 (14), 91 (100), 86 (43), 85 (6), 79 (8), 77 (7), 71 (27), 65 (9); HRMS Calcd. for $C_{12}H_{16}O_2$ 192.1150, found 192.1144. Enantiomeric excess determined by chiral HPLC analysis, Chiralcel AS (99.5% heptane/*i*-PrOH), 40ºC, retention times (min): 11.8 (minor) and 16.4 (major).



(–)-(*S*)-3-Benzyloxy-2-methylpropan-1-ol (5a):[13]

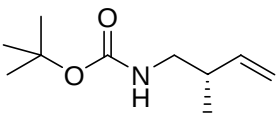
Ozone was bubbled for 10 min through a solution of **2a** (0.5 mmol) in CH_2Cl_2/MeOH (1:1,15mL) cooled to -78°C. $NaBH_4$ (2.5 eq., 2.5 mmol, 95 mg) was added at -78°C after which the cooling bath was removed and the reaction mixture was stirred at rt for 2 h. The reaction was quenched by addition of aq. HCl (1M, 15 mL). The organic layer was separated and the resulting aqueous layer extracted with CH_2Cl_2 (25 mL, 2x) the combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 30:70 Et_2O/pentane, R_f = 0.30) afforded **5a** (47.0 mg) as a colorless oil. [52% yield, 92% ee, $[\alpha]_D$ = – 13.0 (c 2.3, $CHCl_3$), lit.[13] $[\alpha]_D$ = – 15.5 (c 1.8, $CHCl_3$)]; ^{1}H-NMR δ 7.39-7.26 (m, 5H), 4.52 (s, 2H), 3.66-3.53 (m, 3H), 3.43 (dd, *J* = 8.0 and 9.0Hz, 1H), 2.56 (bs, 1H), 2.14-2.02 (m, 1H), 0.89 (d, *J* = 7.0Hz, 3H); ^{13}C-NMR δ 138.0, 128.4, 127.6, 127.5, 75.1, 73.3, 67.5, 35.5, 13.4; LRMS (EI) *m/z* 180 (M^+, 10), 108 (13), 107 (51), 105 (6), 92 (23), 91 (100), 89 (5), 79 (15), 78 (5), 77 (13), 65 (18), 51 (7); HRMS Calcd. for $C_{11}H_{16}O_2$ 180.1150, found 180.1157. Enantiomeric excess determined by chiral HPLC analysis, Chiralcel AS (98.5% heptane/*i*-PrOH), 40ºC, retention times (min): 11.9 (minor) and 14.0 (major).

[13] Paquette, L. A.; Guevel, R.; Sakamoto, S.; Kim, I. H.; Crawford, J. *J. Org. Chem.* **2003**, *68*, 6096.



(–)-(*R*)-3-Benzyloxy-2-methylpropionic acid (6a):

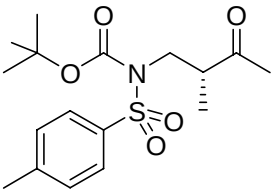
To a biphasic system of **2a** (0.5 mmol) and $NaIO_4$ (2.05 mmol, 438 mg) in CCl_4/MeCN/H_2O (1:1:1.5, 5 mL), $RuCl_3 \cdot xH_2O$ (25 µmol, 5.2 mg) was added and the reaction was stirred vigorously overnight. Afterwards, 10 mL CH_2Cl_2 and 5 mL H_2O were added and the organic layer was separated, the aqueous layer was further extracted with CH_2Cl_2 (3x 5mL) and the combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The residue was dissolved in Et_2O (10 mL) and extracted with sat. aq. $NaHCO_3$ (3x 5 mL), the combined aqueous layers were acidified and extracted with CH_2Cl_2 (3x 10 mL). Drying ($MgSO_4$) and concentrating the combined CH_2Cl_2 layers *in vacuo* afforded **6a** (50.3 mg) as a colorless oil. [52% yield, 92% ee, $[\alpha]_D$ = – 6.7 (c 2.7, $CHCl_3$), lit.[12b] $[\alpha]_D$ = – 8.5 (c 3.7, $CHCl_3$)]; ^{1}H-NMR δ 10.78 (bs, 1H), 7.40-7.27 (m, 5H), 4.56 (s, 2H), 3.66 (dd, *J* = 7.5 and 9.0Hz, 1H), 3.55 (dd, *J* = 5.7 and 9.1Hz, 1H), 2.88-2.78 (m, 1H), 1.22 (d, *J* = 7.1Hz, 3H); ^{13}C-NMR δ 180.8, 137.8, 128.3, 127.6, 127.6, 73.1, 71.5, 40.1, 13.7; MS (EI) *m/z* 194 (M^+, 16), 108 (9), 107 (83), 105 (8), 92 (13), 91 (100), 89 (5), 79 (23), 77 (14), 73 (6), 65 (18), 51 (7); HRMS Calcd. for $C_{11}H_{14}O_3$ 194.0943, found 194.0948. Enantiomeric excess determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m x 0.25 mm), isothermic 150 ºC, retention times (min): 41.5 (minor) and 42.9 (major).



(–)-(*S*)-(*N*-*tert*-Butoxycarbonyl)(2-methylbut-3-enyl)amine (7):

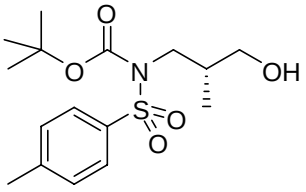
To a solution of **2b** (0.5 mmol, 170 mg) in MeOH (6 mL) Mg-powder (2.5 mmol, 61 mg) was added and the mixture was sonicated for 60 min at rt. The resulting suspension was diluted with CH_2Cl_2 (20 mL) and poured in aq. HCl (0.5M, 20 mL). The organic phase was separated and washed with aq. sat. $NaHCO_3$ (2x 10 mL), dried and concentrated *in vacuo*, affording **7** (83.3 mg) as a colorless oil. [90% yield, 95% ee, $[\alpha]_D$ = – 16.1 (c 2.7, $CHCl_3$)]; ^{1}H-NMR δ 5.67 (ddd, *J* = 7.6, 10.4 and 17.6Hz, 1H), 5.09-5.02 (m, 2H), 4.54 (bs, 1H), 3.20-3.09 (m, 1H), 2.95 (ddd, *J* = 5.4, 8.0 and

13.3Hz, 1H), 2.37-2.26 (m, 1H), 1.44 (s, 9H), 1.01 (d, J = 6.8Hz, 3H); ^{13}C-NMR δ 155.9, 141.3, 114.9, 78.9, 45.6, 38.3, 28.3, 17.3; MS (EI) *m/z* 130 (6), 129 (17), 59 (19), 57 (100), 56 (7), 55 (11); MS (CI) *m/z* 204 (13), 203 ([M+NH_4]$^+$, 100), 202 (5), 187 (7), 186 ([M+H]$^+$, 58), 163 (9), 148 (5), 147 (63), 130 (33), 86 (7). HRMS Calcd. for [M-Me_2C=CH_2]$^+$ $C_6H_{11}NO_2$ 129.0790, found 129.0797. Enantiomeric excess determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m x 0.25 mm), initial temp. 85 ºC, rate 10 °C/min., fin. temp. 120 °C, retention times (min): 61.4 (major) and 64.7 (minor).



(+)-(*R*)-4-((*tert*-Butoxycarbonyl)(*p*-toluenesulfonyl)amino)-3-methylbutan-2-one (4b):

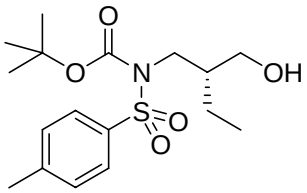
The title compound was prepared in an analogous way to **4a** from **2b**. Purification by flash column chromatography (SiO_2, 10:90 Et_2O/pentane, R_f = 0.05) afforded **4b** (145.3 mg) as a colorless oil. [82% yield, 95% ee, $[\alpha]_D$ = + 2.6 (c 7.1, $CHCl_3$]; ^{1}H-NMR δ 7.77 (d, J = 8.2Hz, 2H), 7.30 (d, J = 8.0Hz, 2H), 4.04 (dd, J = 6.0 and 14.6Hz, 1H), 3.90 (dd, J = 8.0 and 14.6Hz, 1H), 3.16-3.02 (m, 1H), 2.43 (s, 3H), 2.21 (s, 3H), 1.31 (s, 9H), 1.21 (d, J = 7.2Hz, 3H); ^{13}C-NMR δ 210.1, 150.8, 144.2, 136.9, 129.1, 127.7, 84.4, 48.5, 47.1, 28.6, 27.6, 21.4, 14.2; MS (EI) *m/z* 282 ([M-*t*BuO]$^+$, 5), 200 (9), 198 (6), 191 (27), 184 (35), 156 (5), 155 (53), 144 (31), 120 (15), 108 (27), 102 (7), 100 (27), 91 (50), 72 (10), 65 (11), 61 (9), 58 (20), 57 (100), 56 (6); MS (CI) *m/z* 375 (11), 374 (31), 373 ([M+NH_4]$^+$, 100), 317 (5), 219 (6), 69 (5). HRMS Calcd. for [M-*t*BuO]$^+$ $C_{13}H_{16}NO_4S$ 282.0800, found 282.0805. Enantiomeric excess determined by chiral HPLC analysis, Chiralcel AD (98% heptane/*i*-PrOH), 40ºC, retention times (min): 16.8 (major) and 20.9 (minor).



(–)-(*R*)-3-((*tert*-Butoxycarbonyl)(*p*-toluenesulfonyl)amino)-2-methylpropan-1-ol (5b):

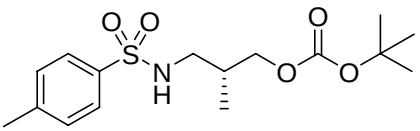
The title compound was prepared in an analogous way to **5a** from **2b**.

Purification by flash column chromatography (SiO_2, 50:50 Et_2O/pentane, R_f = 0.25) afforded **5b** (132.8 mg) as a colorless oil, which crystallized upon standing. [77% yield, 95% ee, $[\alpha]_D$ = – 3.3 (c 8.1, $CHCl_3$), mp = 59.8-60.4 °C]; ^{1}H-NMR δ 7.73 (d, *J* = 8.2Hz, 2H), 7.28 (d, *J* = 8.5Hz, 2H), 3.85 (dd, *J* = 9.1 and 14.6Hz, 1H), 3.72 (dd, *J* = 5.3 and 14.6Hz, 1H), 3.70-3.63 (m, 1H), 3.51-3.43 (m, 1H), 2.63 (bs, 1H), 2.41 (s, 3H), 2.16-2.04 (m, 1H),m 1.29 (s, 9H), 1.00 (d, *J* = 7.0Hz, 3H); ^{13}C-NMR δ 151.9, 144.3, 137.1, 129.2, 127.6, 84.8, 63.6, 49.1, 36.4, 27.7, 21.5, 14.5; MS (EI) *m/z* 270 ([M-*t*BuO]$^+$, 5), 184 (47), 179 (28), 155 (48), 120 (14), 108 (26), 92 (8), 91 (52), 65 (12), 58 (6), 57 (100), 56 (6); MS (CI) *m/z* 363 (8), 362 (22), 361 ([M+NH_4]$^+$, 100), 305 (11). HRMS Calcd. for [M-*t*BuO]$^+$ $C_{12}H_{16}NO_4S$ 270.0800, found 270.0787. Enantiomeric excess determined by chiral HPLC analysis, Chiralcel AD (98% heptane/*i*-PrOH), 40ºC, retention times (min): 38.6 (major) and 51.0 (minor).



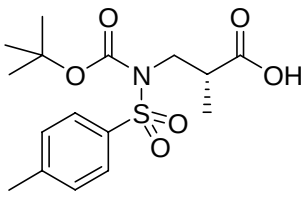
(–)-3-((*tert*-Butoxycarbonyl)(*p*-toluenesulfonyl)amino)-2-ethylpropan-1-ol (5e):

The title compound was prepared in an analogous way to **5a** from **2e**. Purification by flash column chromatography (SiO_2, 50:50 Et_2O/pentane, R_f = 0.25) afforded **5e** (131.0 mg) as a colorless oil. [74% yield, 90% ee, $[\alpha]_D$ = – 6.8 (c 5.8, $CHCl_3$]; ^{1}H-NMR δ 7.73 (d, *J* = 8.4Hz, 2H), 7.29 (d, *J* = 8.6Hz, 2H), 3.87-3.74 (m, 2H), 3.73-3.56 (m, 2H), 2.69 (bs, 1H), 2.42 (s, 3H), 1.86-1.77 (m, 1H), 1.56-1.44 (m, 1H), 1.43-1.32 (m, 1H), 1.30 (s, 9H), 0.99 (t, *J* = 7.5Hz, 3H); ^{13}C-NMR δ 152.0, 144.3, 137.0, 129.2, 127.6, 85.0, 60.3, 48.0, 42.9, 27.7, 21.6, 21.5, 11.5; MS (EI) *m/z* 284 ([M-*t*BuO]$^+$, 2), 216 (5), 193 (15), 184 (25), 155 (29), 120 (5), 108 (14), 92 (9), 91 (49), 65 (14), 57 (100), 56 (8), 55 (7); MS (CI) *m/z* 377 (10), 376 (27), 375 ([M+NH_4]$^+$, 100), 319 (47). HRMS Calcd. for [M-*t*BuO]$^+$ $C_{13}H_{18}NO_4S$ 284.0956, found 284.0973. Enantiomeric excess determined by chiral HPLC analysis, Chiralcel AD (98% heptane/*i*-PrOH), 40ºC, retention times (min): 35.2 (major) and 52.7 (minor).



(+)-(*R*)-3-(*p*-Toluenesulfonylamino)-1-(*tert*-butoxycarbonyloxy)-2-methylpropane (8):

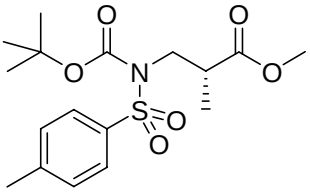
Ozone was bubbled for 10 min through a solution of **2b** (0.5 mmol) in CH_2Cl_2/MeOH (1:1,15mL) cooled to -78°C. $NaBH_4$ (2.5 eq., 2.5 mmol, 95 mg) was added at -78°C after which the cooling bath was removed and the reaction mixture was stirred at rt for 2 h. The solvents were removed from the reaction mixture by rotavap (waterbath at 60 °C), followed by addition of aq. HCl (1M, 15 mL) and Et_2O (25 mL). The organic layer was separated and the resulting aqueous layer extracted with Et_2O (2x 25 mL), the combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 30:70 Et_2O/pentane, R_f = 0.30) afforded **8** (123.8 mg) as a colorless oil. [69% yield, 95% ee, $[\alpha]_D$ = + 0.6 (c 7.9, $CHCl_3$)]; ^{1}H-NMR δ 7.74 (d, *J* = 8.2Hz, 2H), 7.29 (d, *J* = 8.2Hz, 2H), 5.22 (t, *J* = 6.6Hz, 1H), 4.00 (dd, *J* = 4.7 and 11.2Hz, 1H), 3.88 (dd, *J* = 6.7 and 11.2Hz, 1H), 2.95-2.79 (m, 2H), 2.41 (s, 3H), 2.06-1.90 (m, 1H), 1.44 (s, 9H), 0.93 (d, *J* = 6.9Hz, 3H); ^{13}C-NMR δ 153.6, 143.2, 136.9, 129.6, 126.9, 82.2, 68.8, 45.6, 33.2, 27.6, 21.4, 14.4; MS (EI) *m/z* 226 (25), 225 (6), 224 (23), 199 (7), 197 (8), 188 (9), 185 (9), 184 (88), 157 (6), 156 (9), 155 (100), 133 (8), 132 (25), 119 (6), 92 (12), 91 (80), 70 (73), 65 (17), 59 (6), 57 (71), 56 (12); MS (CI) *m/z* 363 (7), 362 (19), 361 ($[M+NH_4]^+$, 100), 333 (14), 305 (6), 289 (14). HRMS Calcd. for $[M-t\text{BuO}]^+$ $C_{12}H_{16}NO_4S$ 270.0800, found 270.0795. Enantiomeric excess determined by chiral HPLC analysis, Chiralcel AS-H (90% heptane/*i*-PrOH), 40ºC, retention times (min): 40.3 (minor) and 43.0 (major).



(−)-(*R*)-3-((*tert*-Butoxycarbonyl)(*p*-toluenesulfonyl)amino)-2-methylpropionic acid (6b):

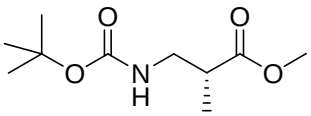
The title compound was prepared in an analogous way to **6a** from **2b**. The product **6b** (140.9 mg) was obtained as a white crystalline solid. [79% yield, 95% ee, $[\alpha]_D$ = – 9.5 (c 3.6, $CHCl_3$), mp = 114.4-116.3 °C]; ^{1}H-NMR δ 10.27 (bs, 1H), 7.80 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* =

8.6 Hz, 2H), 4.14 (dd, *J* = 6.8 and 14.5 Hz, 1H), 3.96 (dd, *J* = 7.7 and 14.5 Hz, 1H), 3.10-3.01 (m, 1H), 2.44 (s, 3H), 1.33 (s, 9H), 1.29 (d, *J* = 7.2 Hz, 3H); ^{13}C-NMR δ 180.5, 150.9, 144.3, 137.0, 129.2, 127.9, 84.7, 48.7, 39.7, 27.7, 21.6, 14.5; MS (EI) *m/z* 284 ([M-*t*BuO]$^+$, 4), 194 (5), 193 (44), 185 (5), 184 (54), 156 (5), 155 (55), 120 (18), 112 (7), 108 (34), 102 (11), 92 (7), 91 (57), 65 (14), 57 (100), 56 (7); MS (CI) *m/z* 377 (8), 376 (19), 375 ([M+NH_4]$^+$, 100), 319 (16), 275 (6), 174 (7). HRMS Calcd. for [M-*t*BuO]$^+$ $C_{12}H_{14}NO_5S$ 284.0592, found 284.0607. Enantiomeric excess determined on derivatized product **9**.



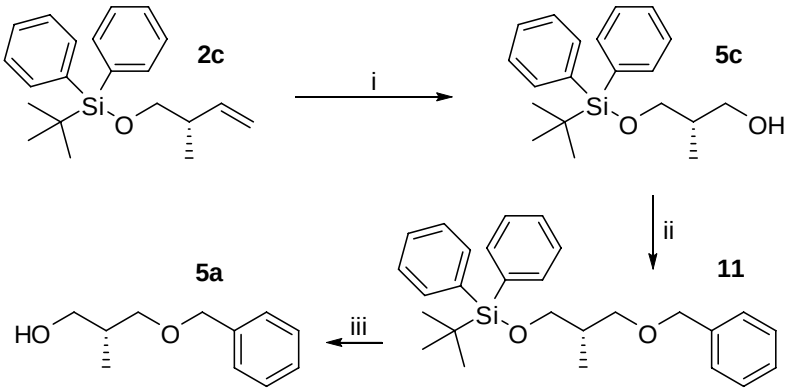
(–)-(*R*)-Methyl 3-((*tert*-butoxycarbonyl)(*p*-toluenesulfonyl)amino)-2-methylpropionate (9):

To a solution of **6b** (0.19 mmol, 65 mg) and MeOH (1mL) in toluene (3mL), $TMSCHN_2$ (1.0 mmol, 1.0M in Et_2O, 0.5 mL) was added. The reaction mixture was stirred at rt for 1h, then MeOH (2mL) was added and the excess $TMSCHN_2$ was destroyed through addition of AcOH (0.5 mL). The mixture was diluted with toluene (5mL) and washed with sat. aq. $NaHCO_3$ (5 mL, 2x). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo* to yield **9** (63.6 mg) as a colorless oil, which crystallised upon standing. [94% yield, 95% ee, $[\alpha]_D$ = – 20.8 (c 2.8, $CHCl_3$), mp = 75.8-78.6 °C]; ^{1}H-NMR δ 7.77 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.3 Hz, 2H), 4.08 (dd, *J* = 7.3 and 14.4 Hz, 1H), 3.89 (dd, *J* = 7.2 and 14.4 Hz, 1H), 3.65 (s, 3H), 3.04-2.94 (m, 1H), 2.41 (s, 3H), 1.30 (s, 9H), 1.22 (d, *J* = 7.1 Hz, 3H); ^{13}C-NMR δ 174.6, 150.9, 144.2, 137.2, 129.2, 127.8, 84.4, 51.8, 49.1, 39.8, 27.7, 21.5, 14.6; MS (EI) *m/z* 298 ([M-*t*BuO]$^+$, 4), 284 (12), 208 (7), 207 (56), 185 (6), 184 (56), 160, (7), 156 (5), 155 (59), 120 (17), 116 (29), 112 (8), 108 (32), 92 (7), 91 (54), 88 (9), 84 (6), 65 (12), 57 (100), 56 (7); MS (CI) m/z 391 (7), 390 (20), 389 ([M+NH_4]$^+$, 100), 333 (13), 289 (6). HRMS Calcd. for [M-*t*BuO]$^+$ $C_{13}H_{16}NO_5S$ 298.0749, found 298.0733. Enantiomeric excess determined by chiral HPLC analysis, Chiralcel AD (99% heptane/*i*-PrOH), 40ºC, retention times (min): 26.9 (major) and 35.2 (minor).



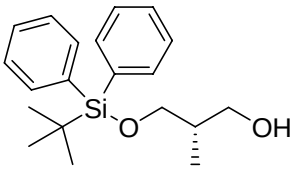
(–)-(*R*)-Methyl 3-*tert*-butoxycarbonylamino-2-methyl-propionate (10):[14] The title compound was prepared in an analogous way to **7** from **9** (0.104 mmol, 38.8 mg). Work-up afforded compound **10** (20.5 mg) as a colorless oil. [90% yield, 95% ee, $[\alpha]_D = -21.8$ (c 1.9, $CHCl_3$); lit.[14] $[\alpha]_D = -17.6$ (c 2.74, $CHCl_3$)]; ^{1}H-NMR 4.94 (bs, 1H), 3.68 (s, 3H), 3.35-3.19 (m, 2H), 2.72-2.61 (m, 1H), 1.41 (s, 9H), 1.15 (d, J = 7.2 Hz, 3H); ^{13}C-NMR δ 175.8, 155.9, 79.3, 51.8, 42.9, 39.9, 28.3, 14.7; MS (EI) *m/z* 217 (M^+, 1), 161 (29), 160 (8), 144 (19), 130 (30), 116 (6), 112 (20), 101 (7), 88 (24), 84 (8), 59 (17), 58 (6), 57 (100), 56 (8); MS (CI) *m/z* 452 ($[2M+NH_4]^+$, 10), 236 (12), 235 ($[M+NH_4]^+$, 100), 219 (6), 218 ($[M+H]^+$, 45), 179 (16), 162 (11), 69 (9); HRMS Calcd. for $C_{10}H_{19}NO_4$ 217.1314, found 217.1327. Enantiomeric excess determined by chiral GC analysis, CP-Chiralsil-Dex-CB (25 m x 0.25 mm), isothermic 130 ºC, retention times (min): 13.3 (major) and 14.6 (minor).

Scheme S1: Derivatizations to establish ee of product **2c**



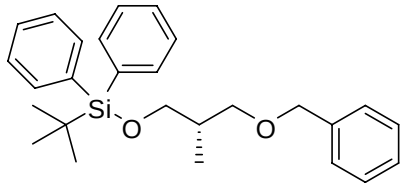
Reagents and conditions: i) 1. O_3, DCM/MeOH, -78°C, 2. $NaBH_4$ (5 eq.), rt, 77%; ii) $BnOC(NH)CCl_3$, TfOH, cyclohexane, CCl_4, rt, 25%; iii) TBAF, THF, rt.

[14] Ghosh, A. K.; Bischoff, A. *Eur. J. Org. Chem.* **2004**, 2131.



(–)-(*S*)-3-(*tert*-Butyl-diphenyl-silanyloxy)-2-methylpropan-1-ol (5c):[15]

The title compound was prepared in an analogous way to **5a** from **2c** (0.29 mmol, 93.1 mg). Purification by flash column chromatography (SiO_2, 15:85 Et_2O/pentane, R_f = 0.20) afforded **5c** (73.0 mg) as a colorless oil. [77% yield, 94% ee, $[\alpha]_D$ = – 6.0 (c 1.5, $CHCl_3$); lit.[15] $[\alpha]_D$ = – 5.3 (c 3.3, $CHCl_3$)]; ^{1}H-NMR δ 7.71 (dd, J = 1.6 and 7.8Hz, 4H), 7.49-7.39 (m, 6H), 3.77-3.59 (m, 4H), 2.68 (bs, 1H), 2.07-1.96 (m, 1H), 1.09 (s, 9H), 0.86 (d, *J* = 6.9Hz, 3H); ^{13}C-NMR δ 135.5, 135.5, 133.1, 133.1, 129.7, 127.7, 68.6, 67.5, 37.3, 26.8, 19.1, 13.1; MS (EI) *m/z* 272 (7), 271 ([M-tBu]$^+$, 30), 229 (8), 201 (5), 200 (19), 199 (100), 197 (7), 193 (18), 181 (9), 139 (20), 77 (7); MS (CI) *m/z* 348 (8), 347 (28), 346 ([M+NH_4]$^+$, 100), 330 (13), 329 ([M+H]$^+$, 47), 69 (14). HRMS Calcd. for [M-*t*Bu]$^+$ $C_{16}H_{19}O_2Si$ 271.1154, found 271.1149. Enantiomeric excess determined on derivatized product **5a**.



(*S*)-1-Benzyloxy-3-(*tert*-butyl-diphenyl-silanyloxy)-2-methylpropane (11):

To a solution of **5c** (0.15 mmol, 49.8 mg), benzyltrichloroacetimidate (0.3 mmol, 56 µL) and cyclohexane (0.3 mmol, 33 µL) in CCl_4 (1 mL) a catalytic amount of TfOH (2 µL) was added. The mixture was stirred at rt for 2.5h and quenched with 1 mL sat. aq. $NaHCO_3$, after which 10 mL Et_2O was added and the resulting solution washed with 10 mL H_2O and 10 mL sat. aq. NaCl. The organic layer was dried with $MgSO_4$ and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, 1:99 Et_2O/pentane, R_f = 0.20) afforded an inseparable mixture of **11** and the byproduct dibenzylether[16] (32.4 mg) as a colorless oil. [**11**:Bn_2O = 4:3, 25% calc. yield of **11**, 94% ee]; ^{1}H-NMR δ 7.69-7.64 (m, 4H), 7.45-7.26 (m, 11H + Bn_2O, 10H), 4.58 (Bn_2O, s, 4H), 4.50 (s,

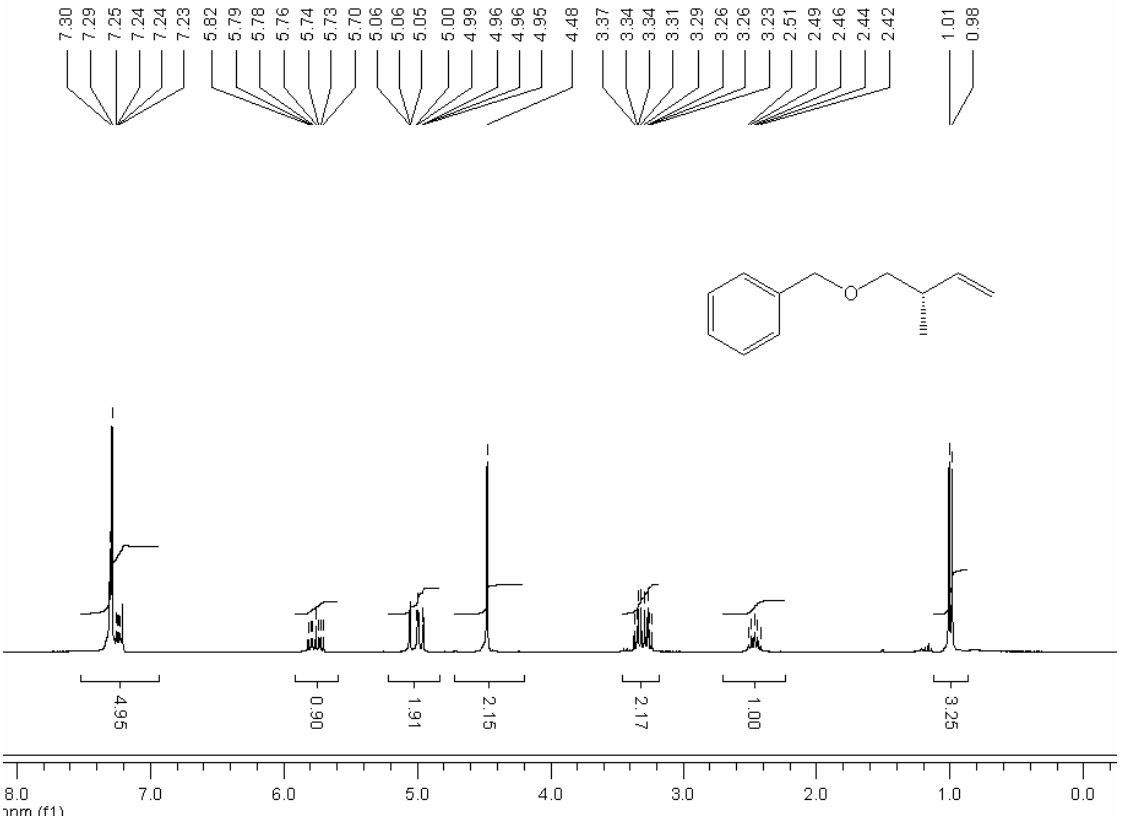
[15] P. R. Blakemore, C. C. Browder, J. Hong, C. M. Lincoln, P. A. Nagornyy, L. A. Robarge, D. J. Wardrop, J. D. White *J. Org. Chem.* **2005**, *70*, 5449.

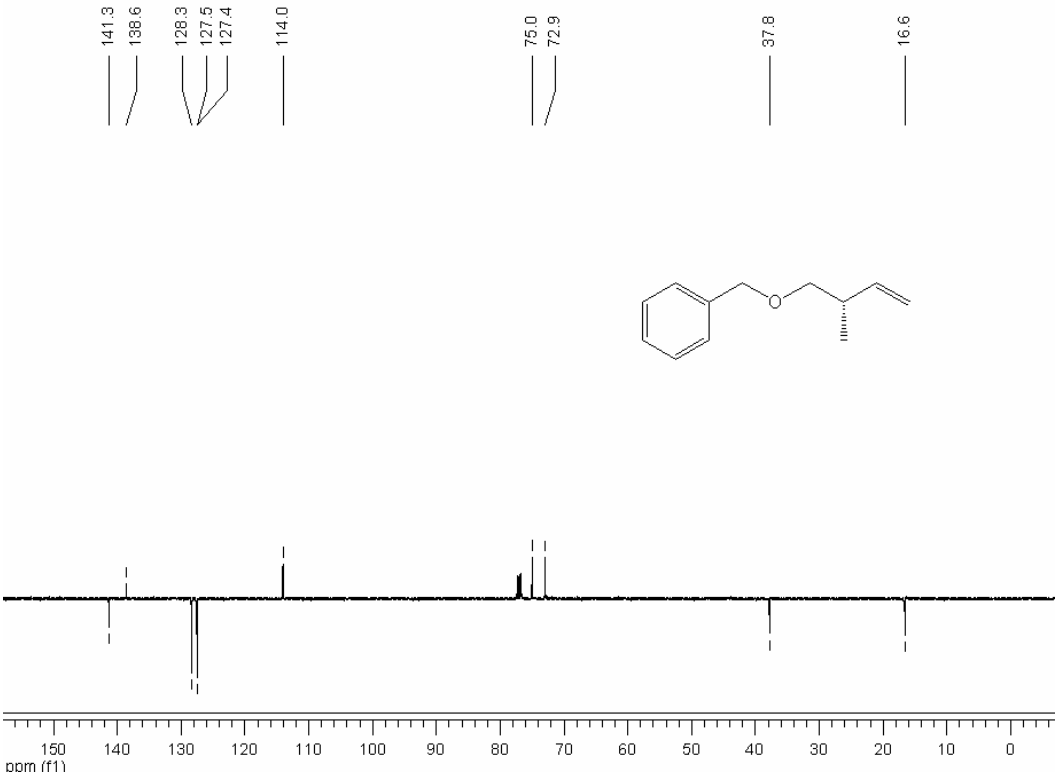
[16] The identity of the byproduct was established through comparison of ^{1}H-NMR, ^{13}C-NMR and GCMS-data with a commercial sample. The characterisation of **10** was performed with the mixture of compounds.

2H), 3.68-3.61 (m, 2H), 3.56 (dd, J = 6.4 and 9.0 Hz, 1H), 3.40 (dd, J = 6.1 and 9.0 Hz, 1H), 2.09-1.97 (m, 1H), 1.06 (s, 9H), 0.99 (d, J = 6.9 Hz, 3H);^{13}C-NMR δ 138.8, 138.3 (Bn_2O), 135.6, 133.9, 129.5, 128.4 (Bn_2O), 128.3, 127.8 (Bn_2O), 127.6 (Bn_2O), 127.6, 127.5, 127.3, 73.0, 72.5, 72.1 (Bn_2O), 65.7, 36.3, 26.9, 19.3, 14.1; MS (EI) *m/z* 199 (8), 195 (7), 194 (18), 193 ([M - Ph, *t*Bu, Bn]$^+$, 100), 181 (6), 91 (50); MS (CI) *m/z* 438 (13), 437 (35), 436 ([M+NH_4]$^+$, 100), 419 ([M+H]$^+$, 14). HRMS Calcd. for [M - Ph, *t*Bu, Bn]$^+$ $C_{10}H_{13}O_2Si$ 193.0685, found 193.0676. Enantiomeric excess determined of derivatized product **5a**. To the mixture of **11** and dibenzylether (approx. 37 μmol **11**, 21mg) 4 equivalents of TBAF (0.15 mmol, 1.0M in THF, 0.15mL) were added at room temperature. After stirring for 2.5h, the reaction mixture was diluted with Et_2O/pentane (1:1, 1mL) and the resulting mixture was flushed over a $MgSO_4$ and SiO_2 plug. The solution was concentrated providing the mixture of **5a** and Bn_2O as an oil. The enantiomeric excess of **5a** was determined to be 94% by chiral HPLC analysis, Chiralcel AS (98.5% heptane/*i*-PrOH), 40ºC, retention times (min): 4.7 (Bn_2O), 11.8 (major) and 14.1 (minor).

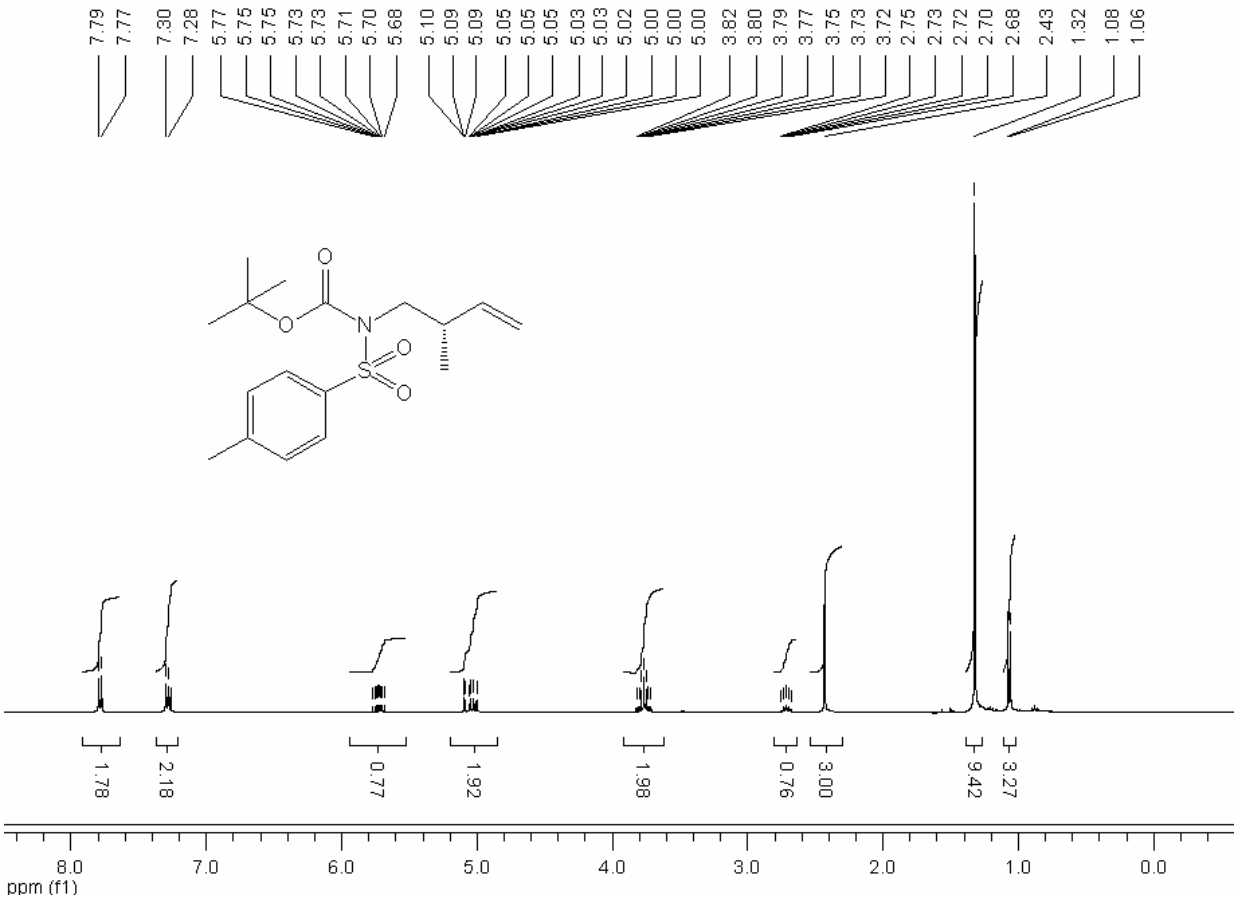
^{1}H NMR and ^{13}C-NMR:

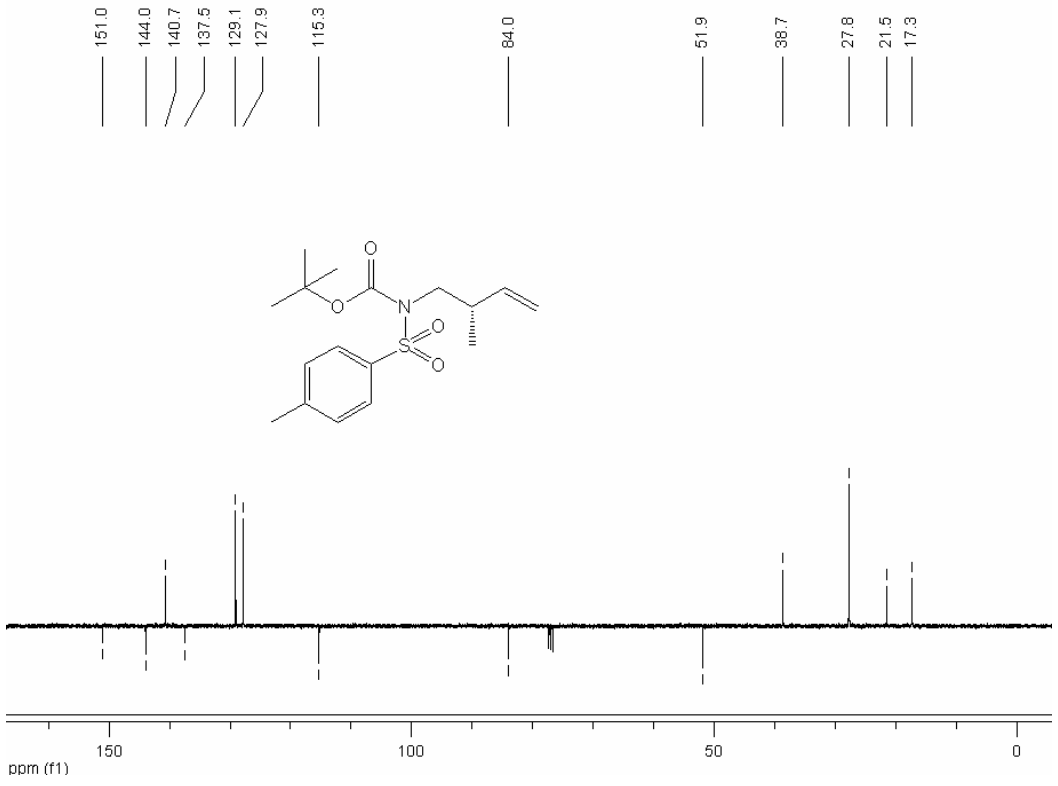
(–)-(*S*)-((2-Methylbut-3-enyloxy)methyl)benzene (2a):



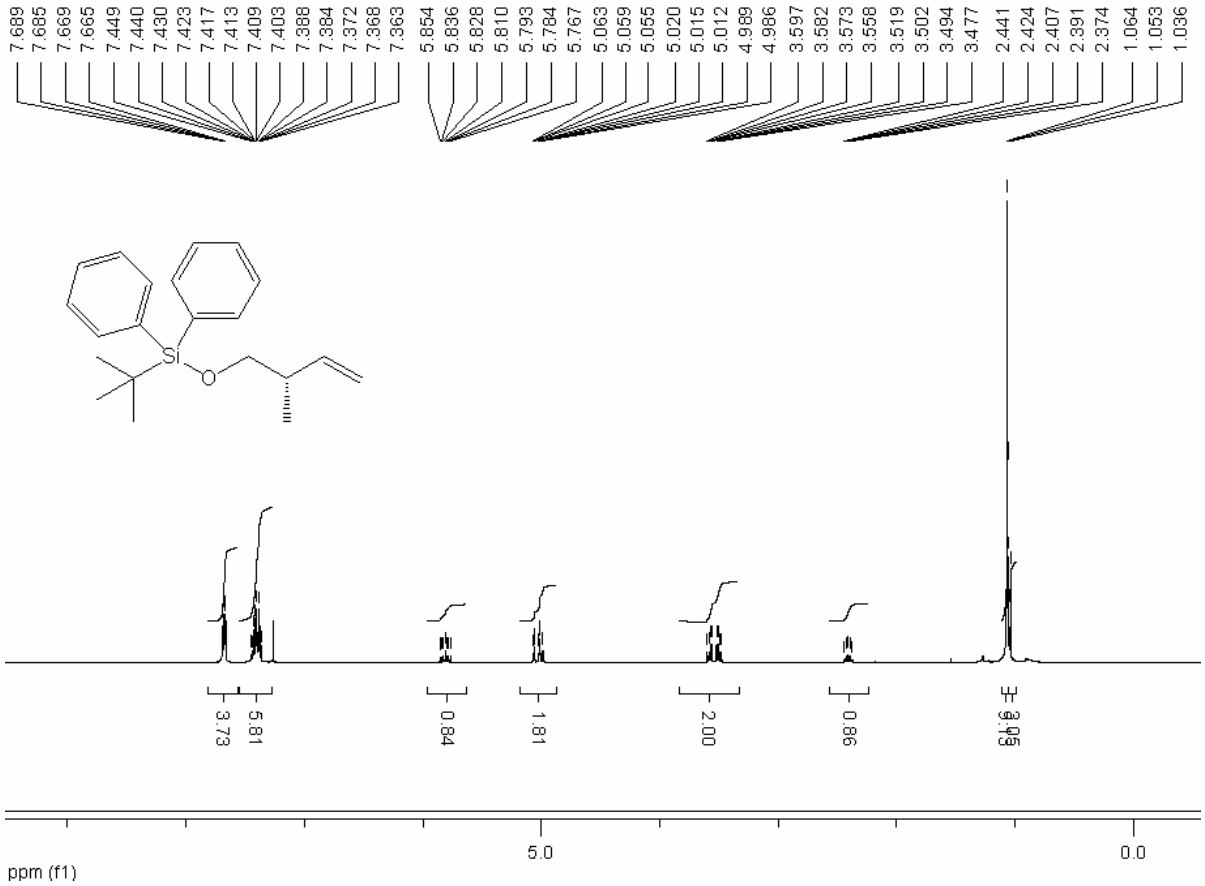


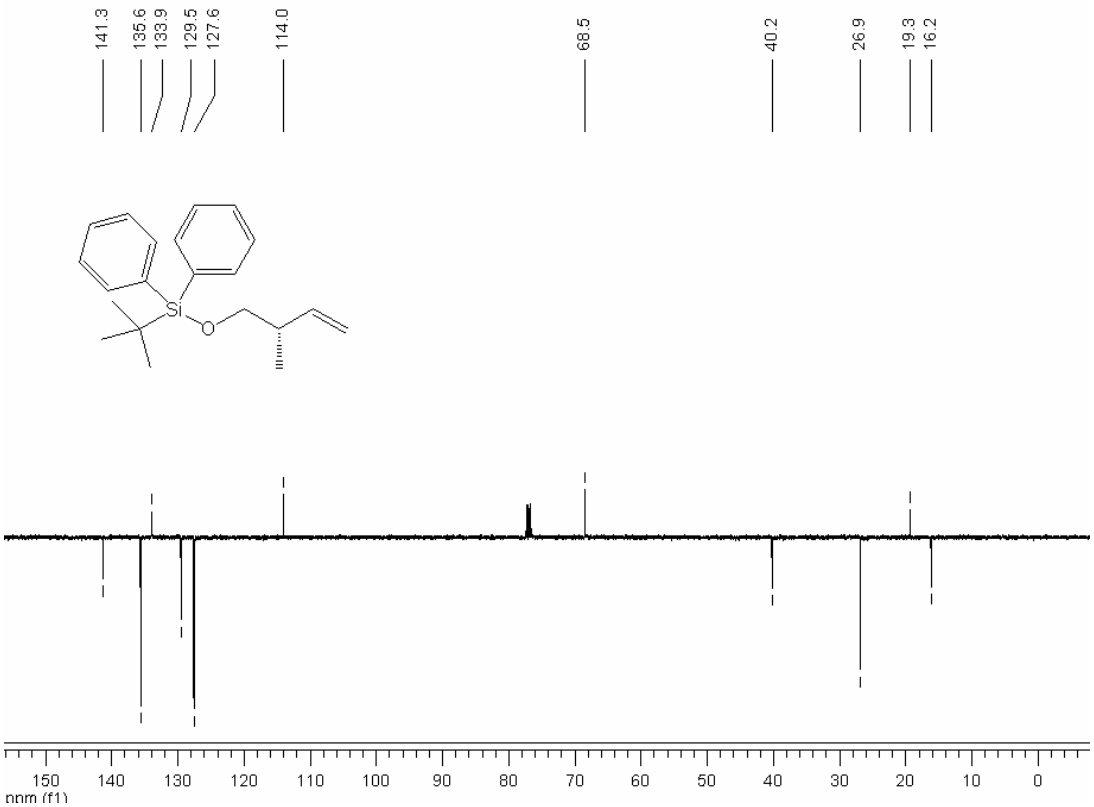
(–)-(*S*)-(*N*-2-Methylbut-3-enyl)(*N*-*t*-butoxycarbonyl)-*p*-toluenesulfonamide (2b):



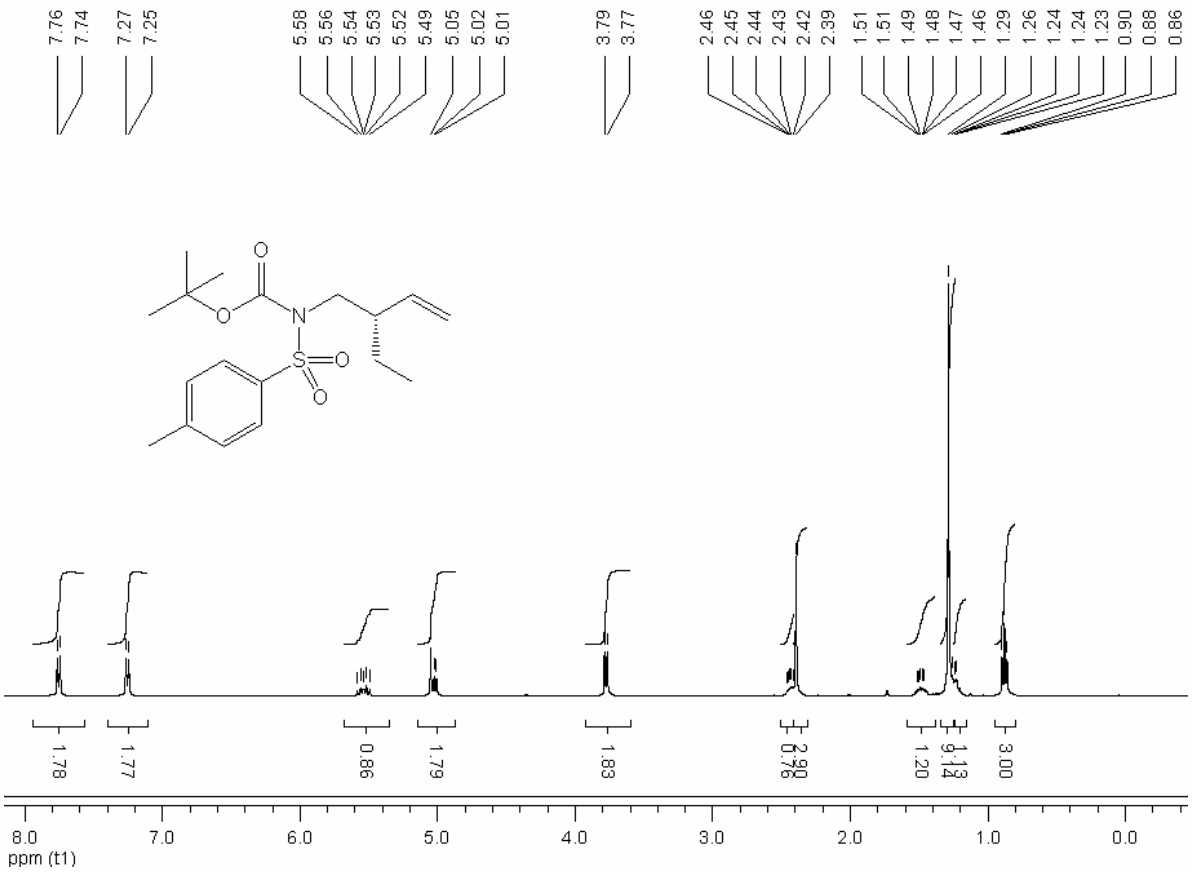


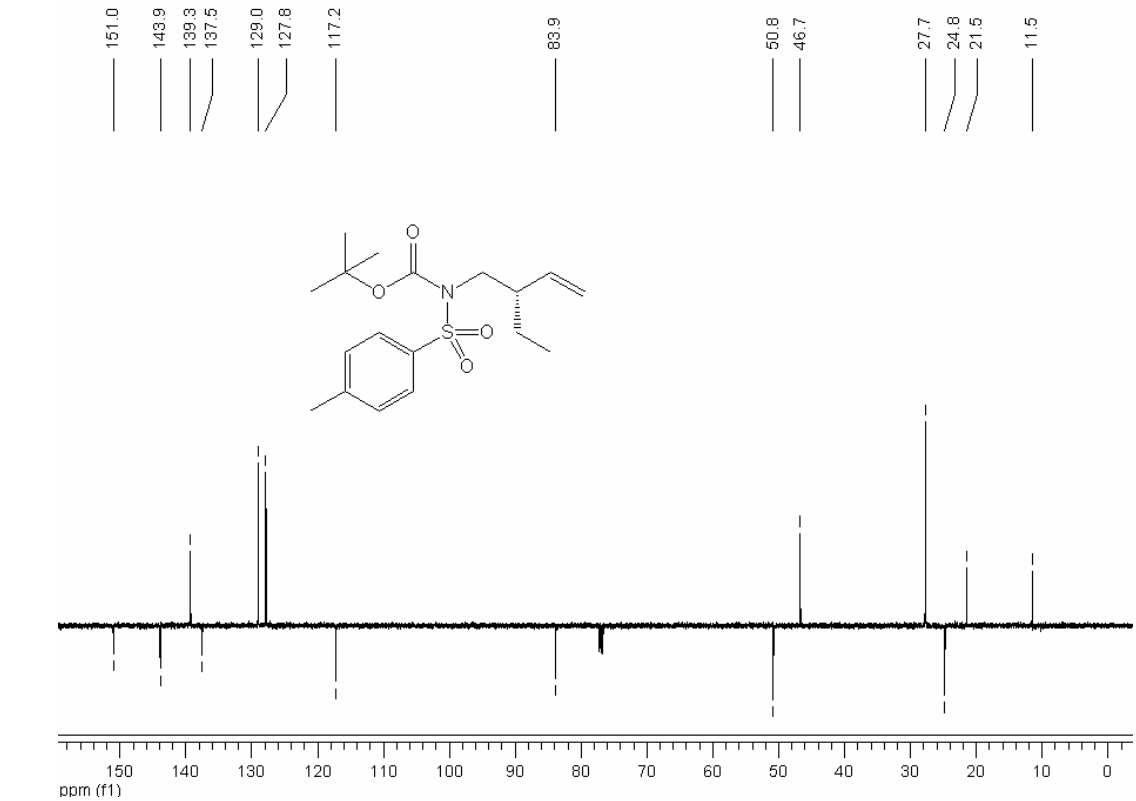
(–)-(*S*)-4-[(*tert*-Butyldiphenylsilyl)oxy]-3-methylbut-1-ene (2c):



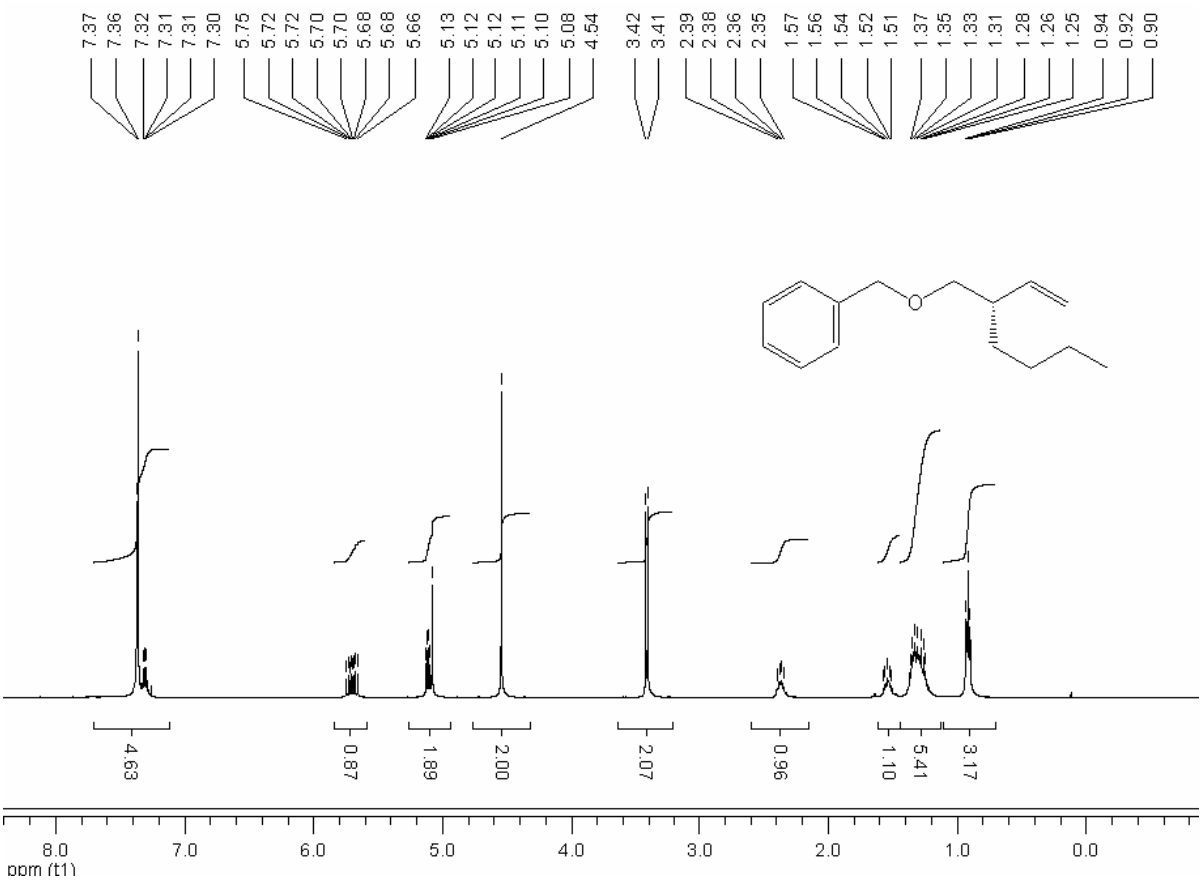


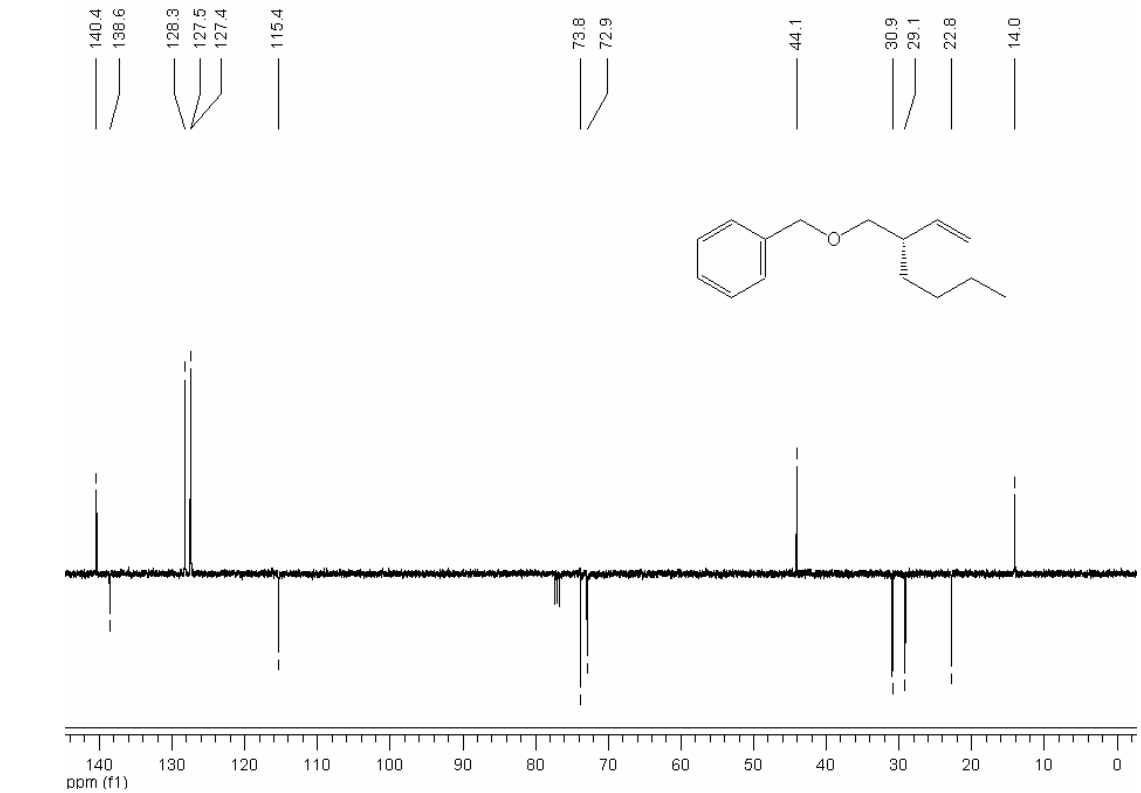
(–)-(*N*-2-Ethylbut-3-enyl)(*N*-*tert*-butoxycarbonyl)-*p*-toluenesulfonamide (2e):



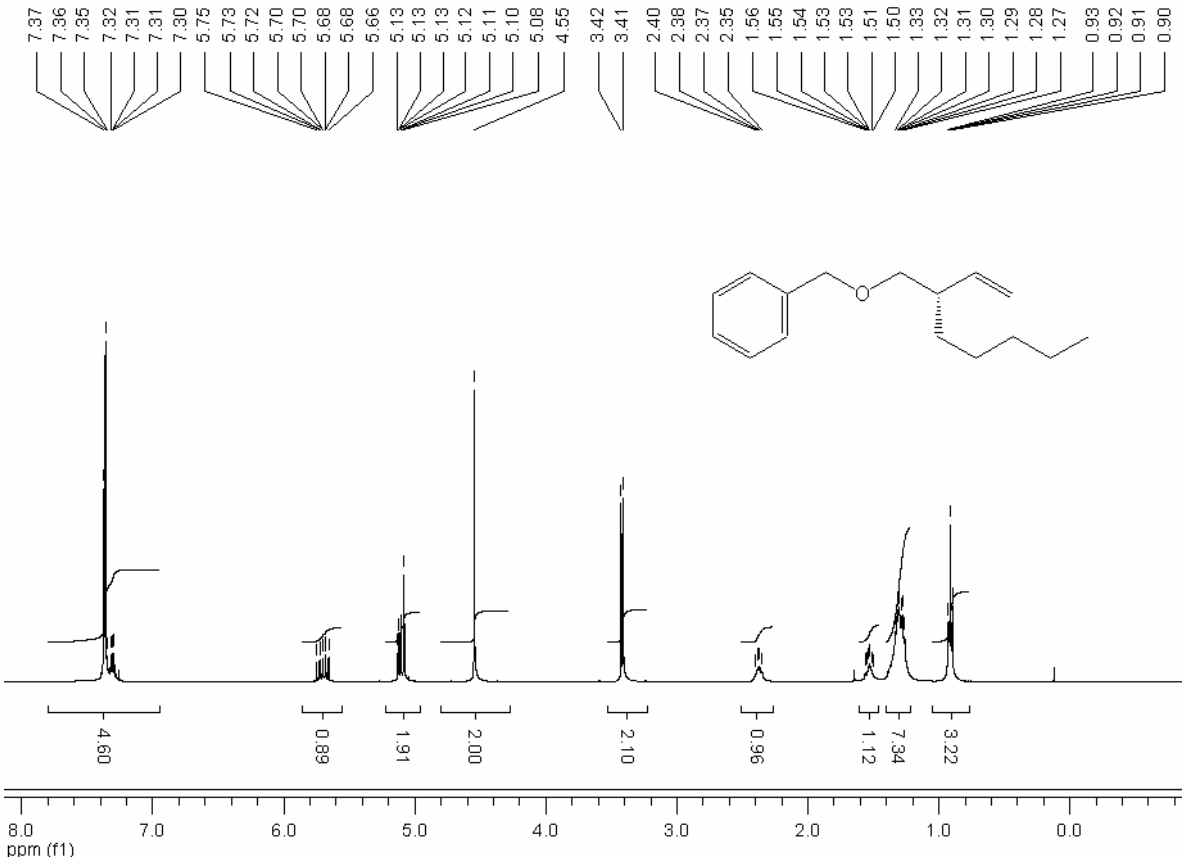


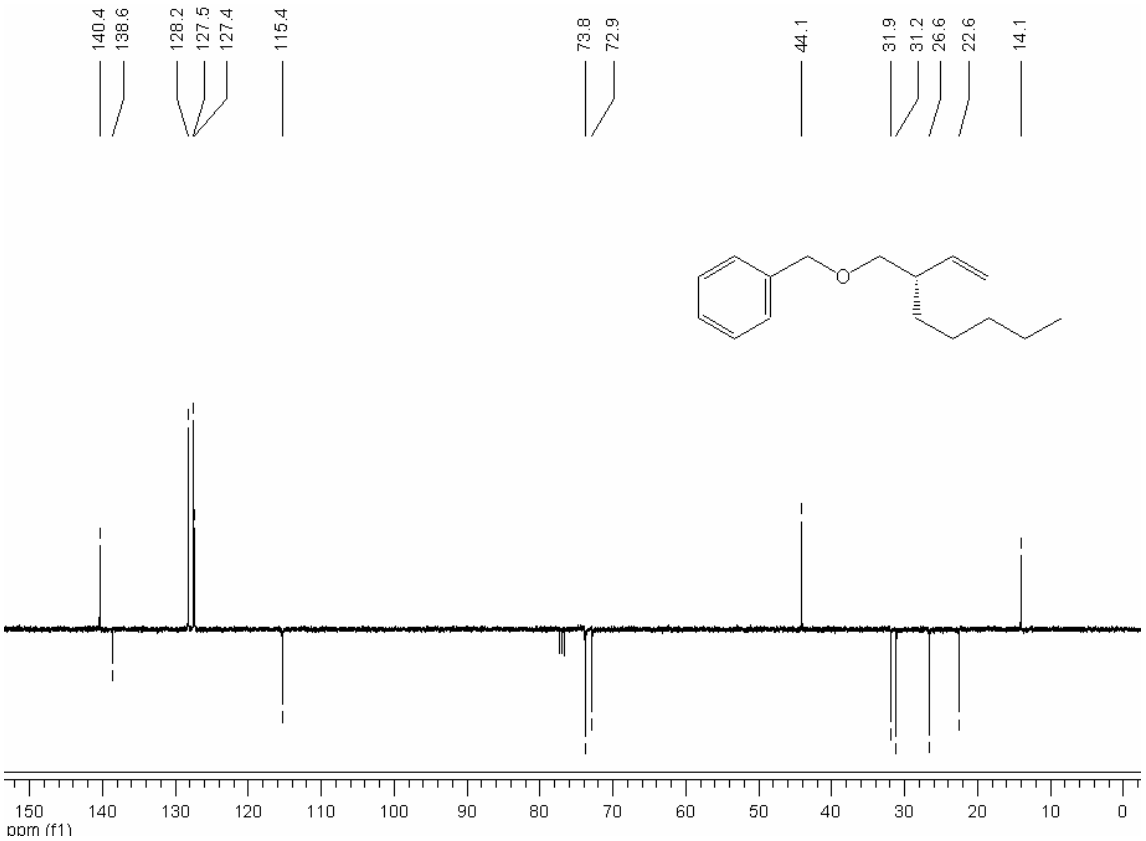
(+)-(*S*)-((2-*n*-Butylbut-3-enyloxy)methyl)benzene (2f):



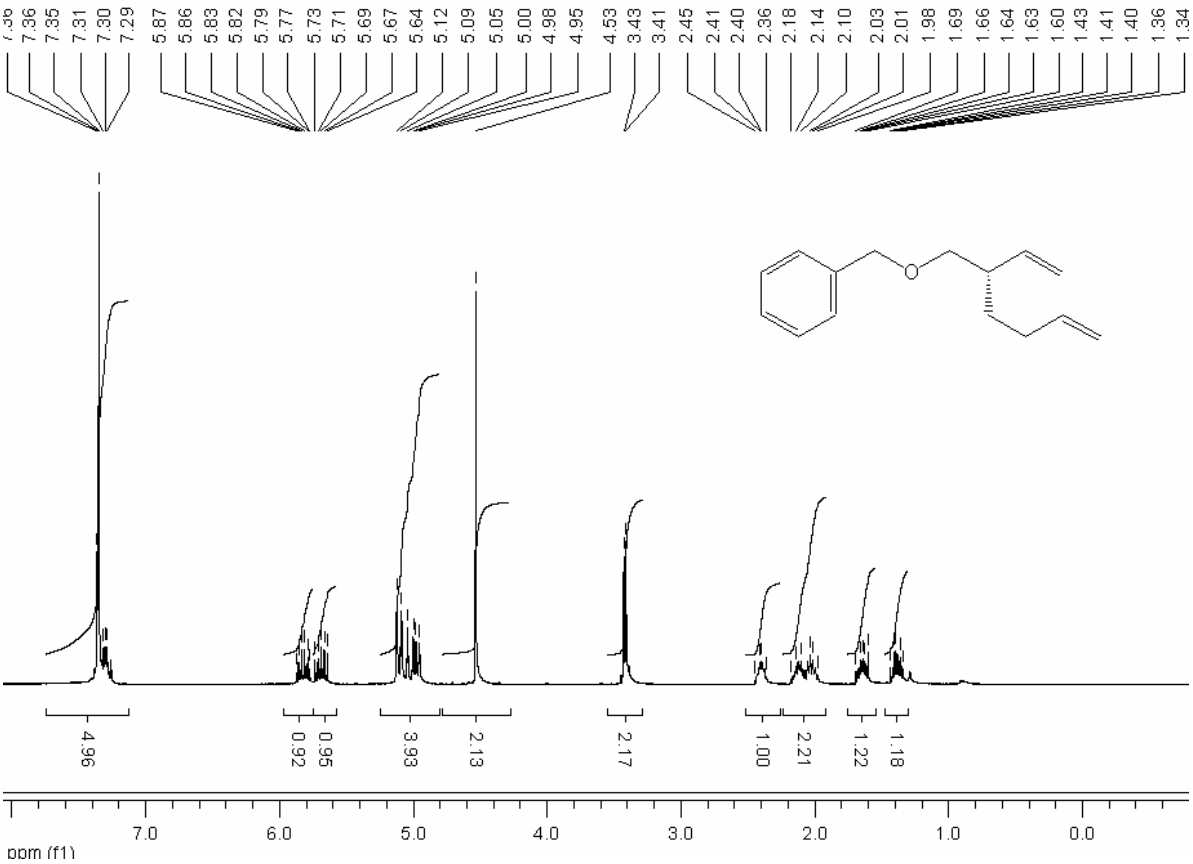


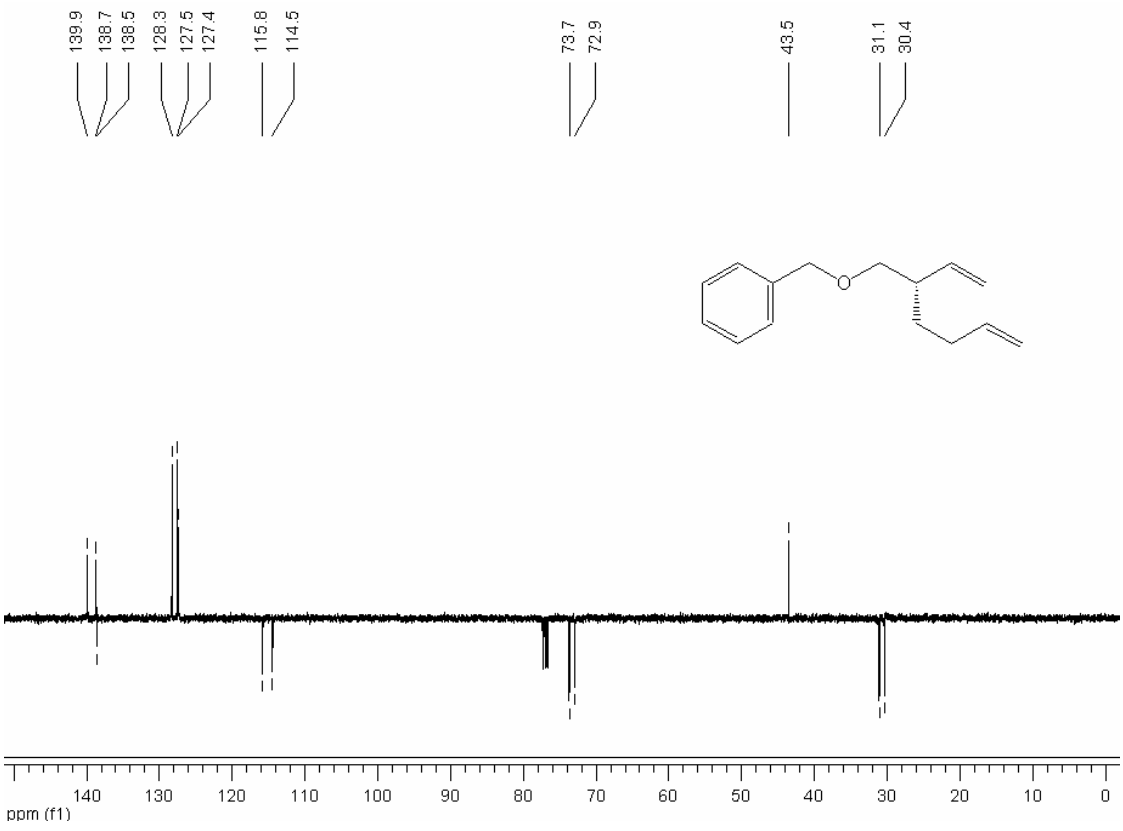
(+)-(*S*)-((2-*n*-Pentylbut-3-enyloxy)methyl)benzene (2g):



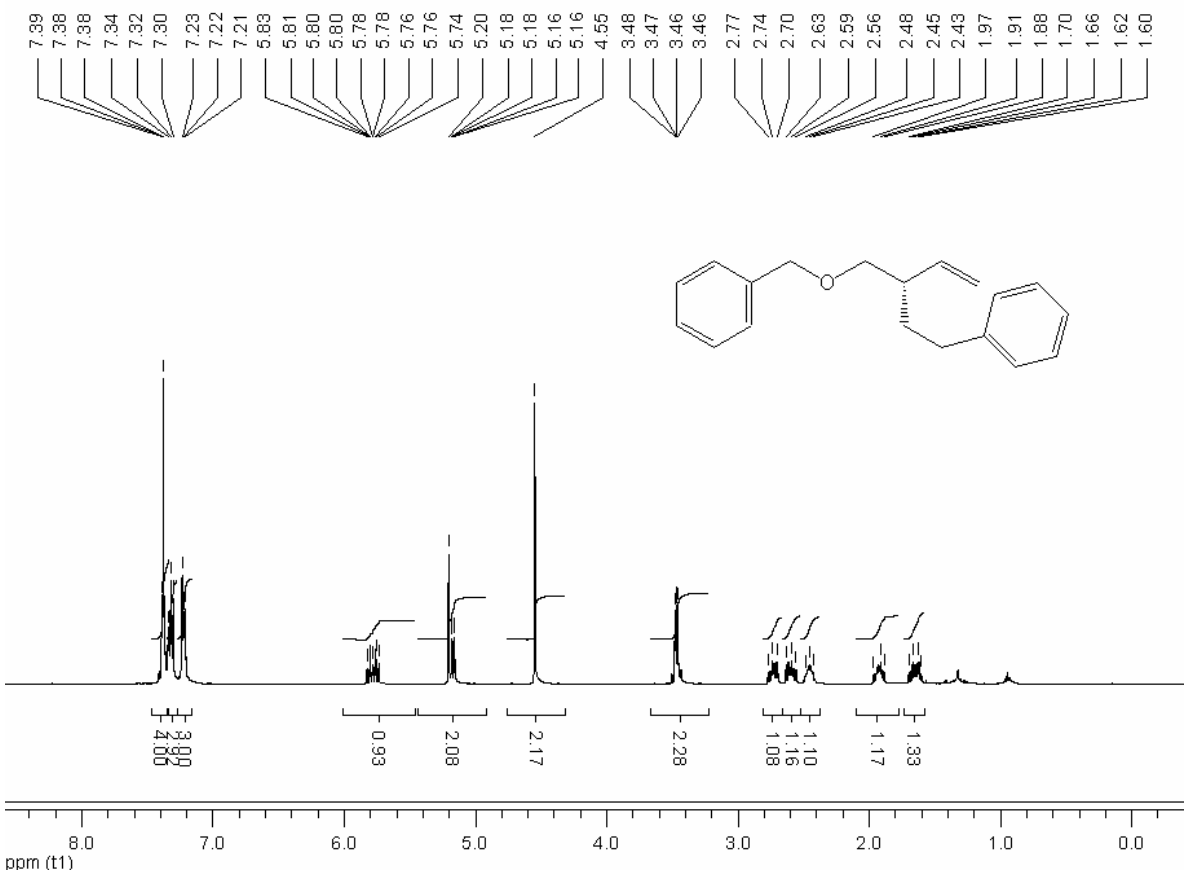


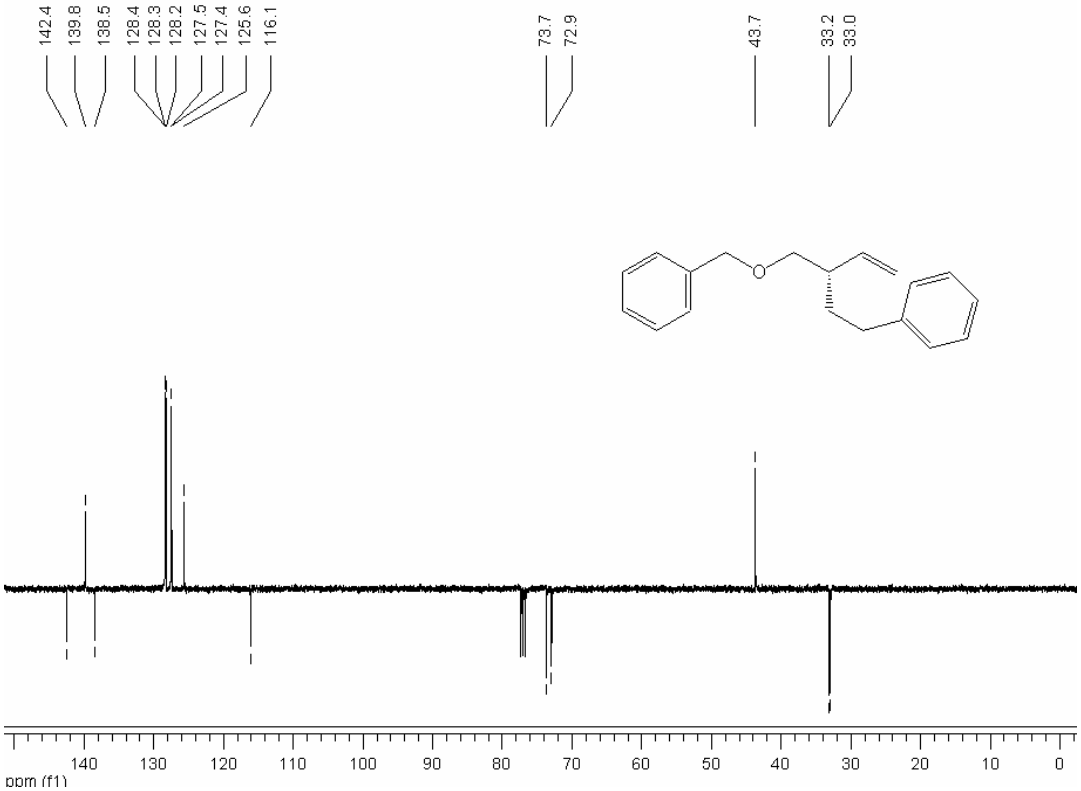
(+)-(*S*)-(2-Vinyl-hex-5-enyloxymethyl)-benzene (2h):



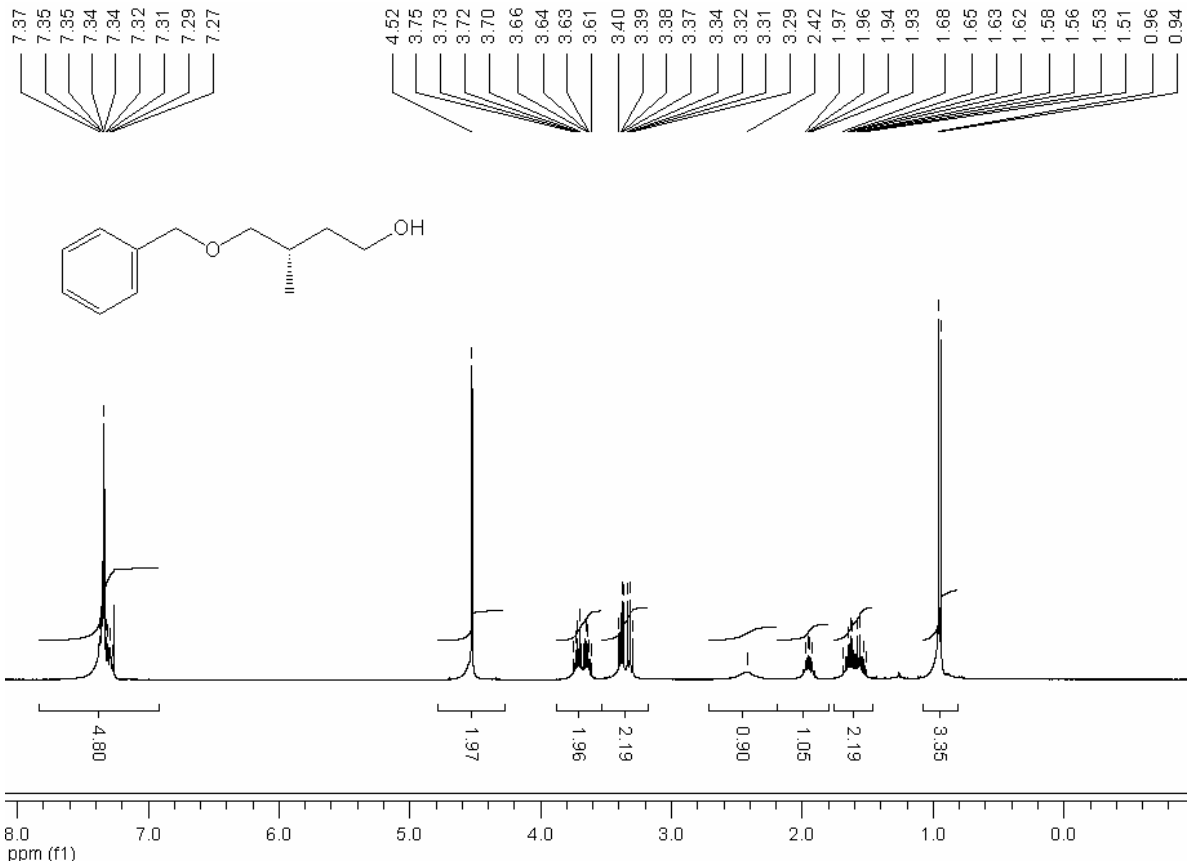


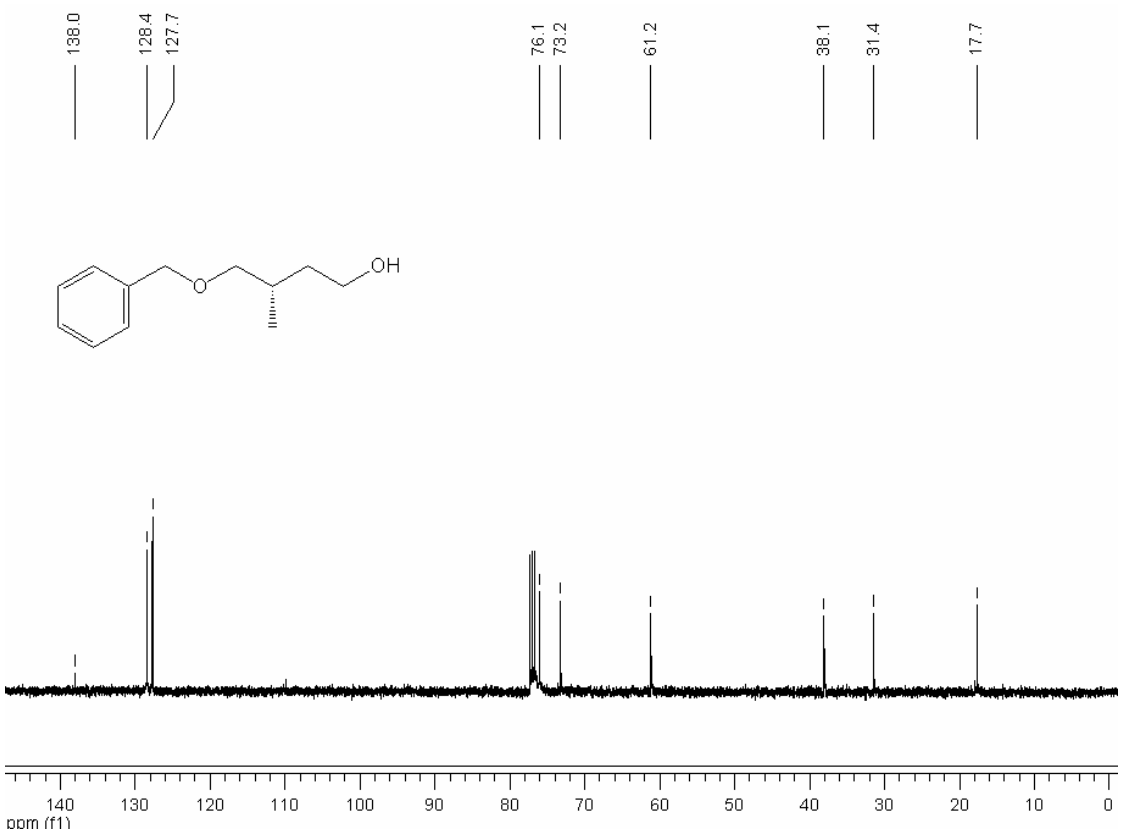
(+)-(2-Vinyl-4-phenyl-butyloxymethyl)-benzene (2i):



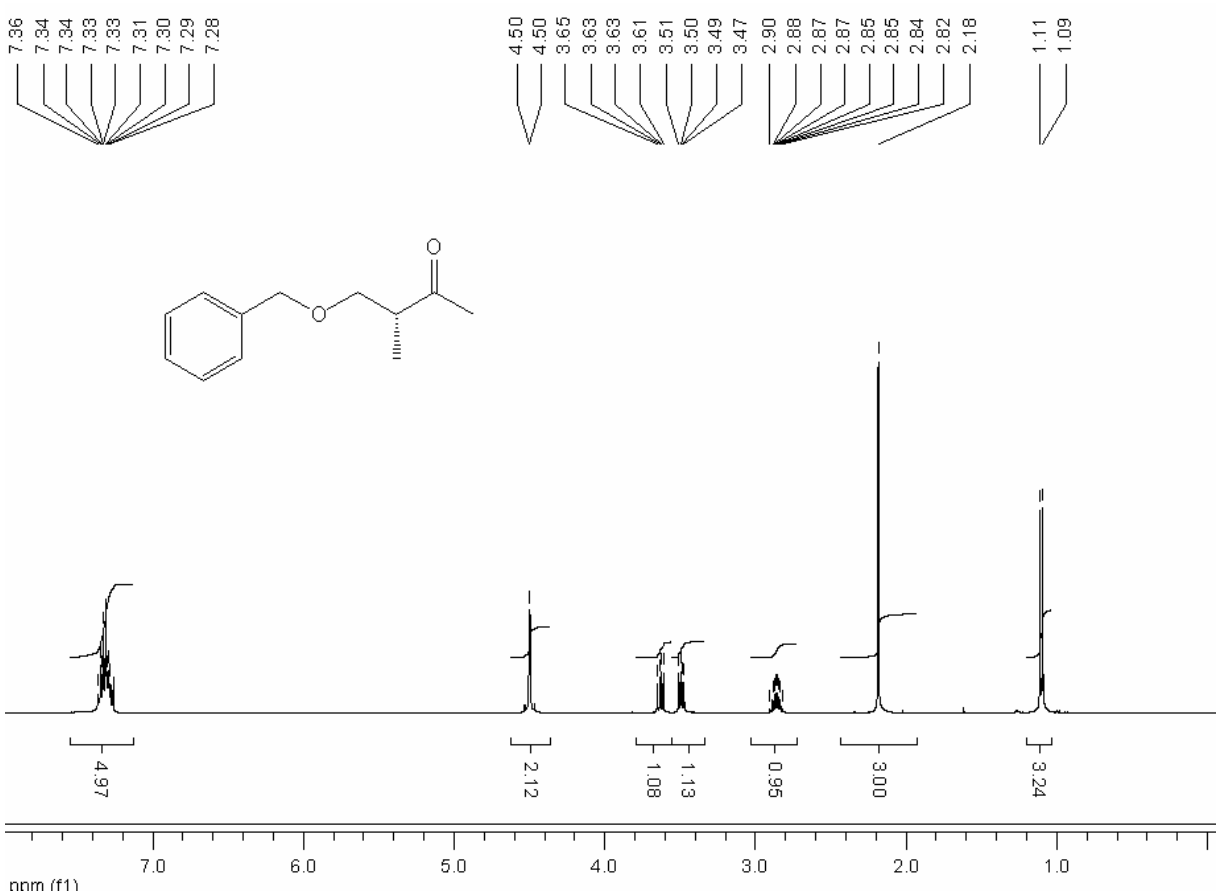


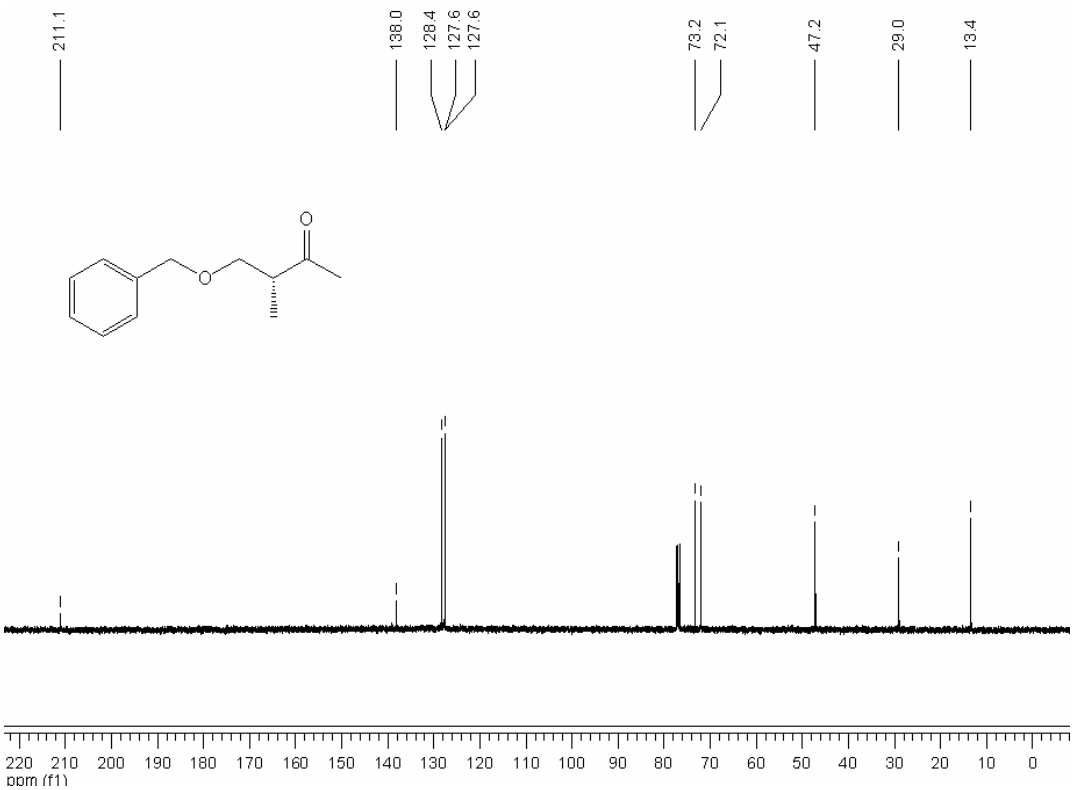
(+)-(*S*)-4-Benzyloxy-3-methylbutan-1-ol (3):



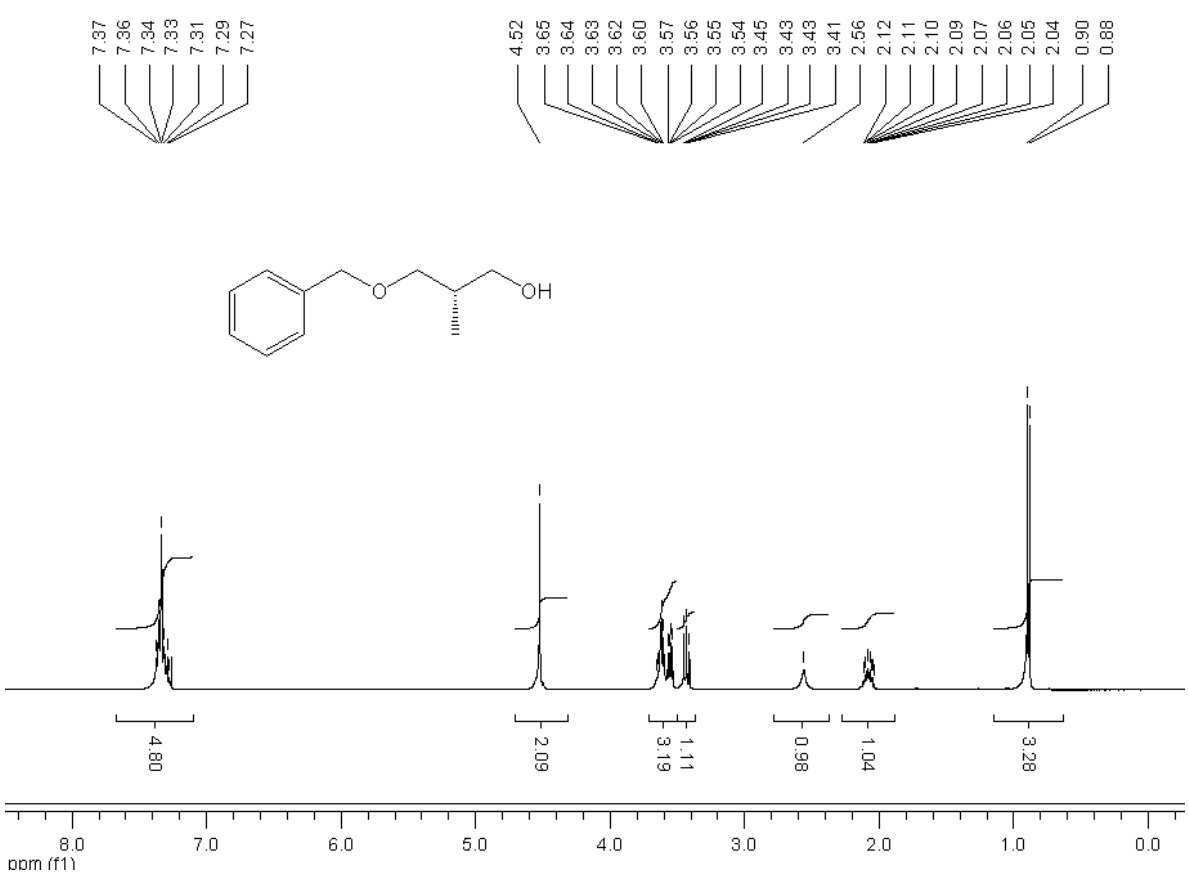


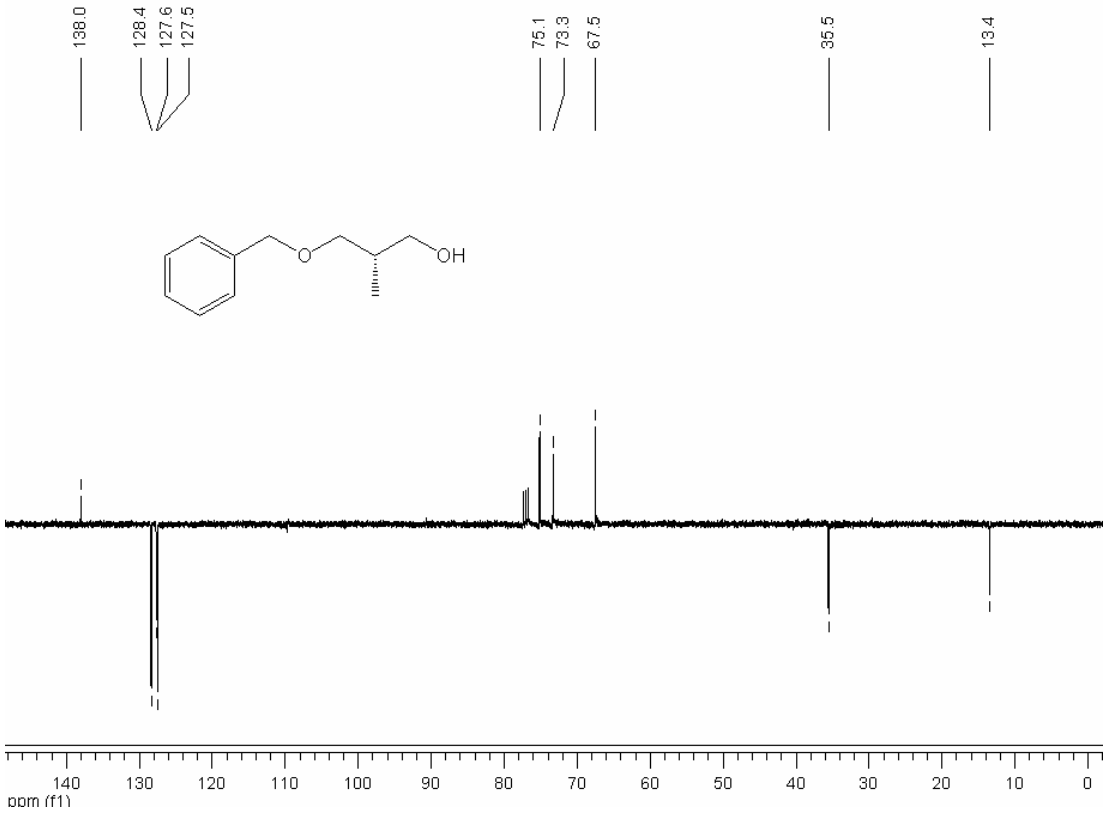
(–)-(*R*)-4-Benzyloxy-3-methylbutan-2-one (4a):



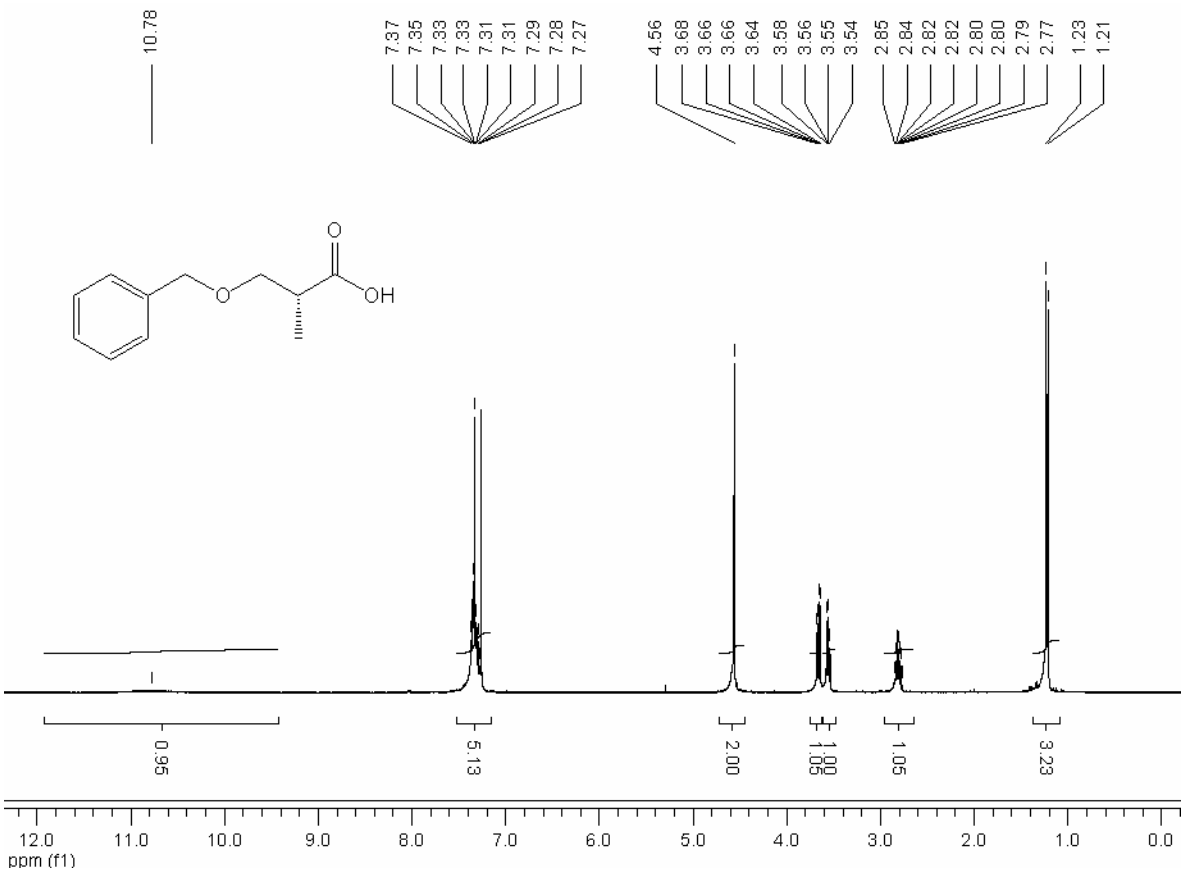


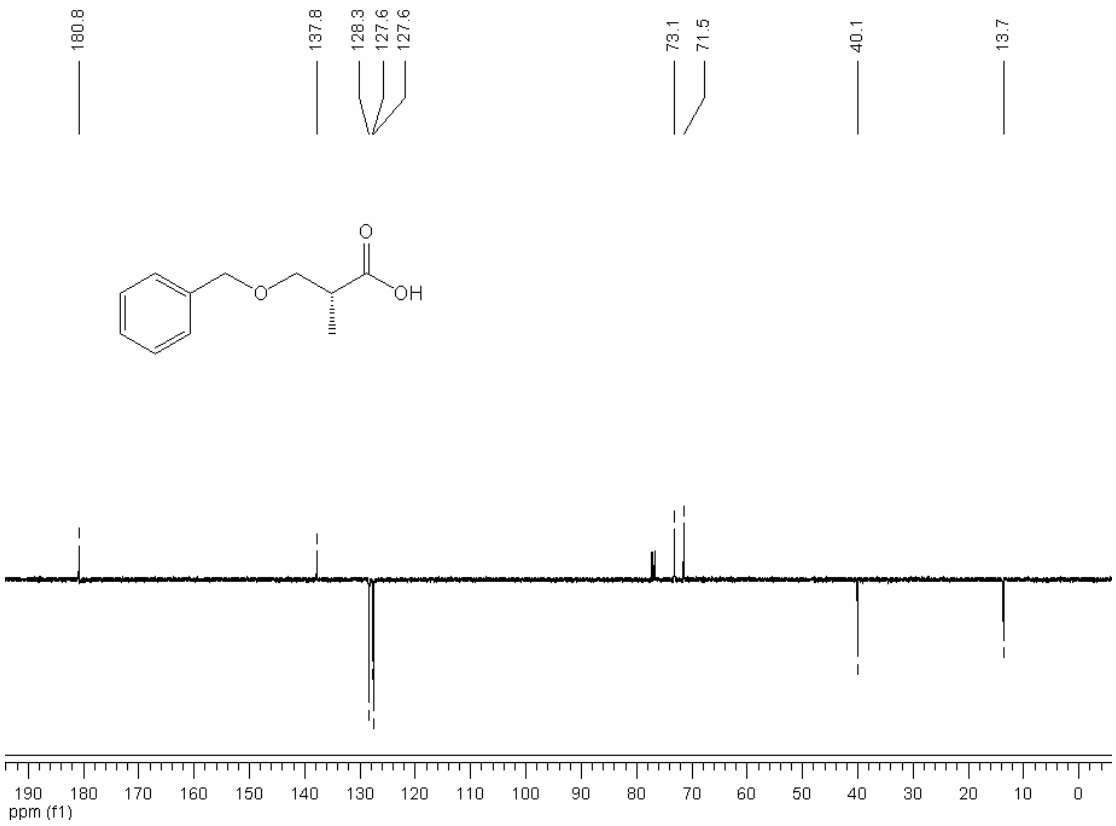
(–)-(*S*)-3-Benzyloxy-2-methylpropan-1-ol (5a):



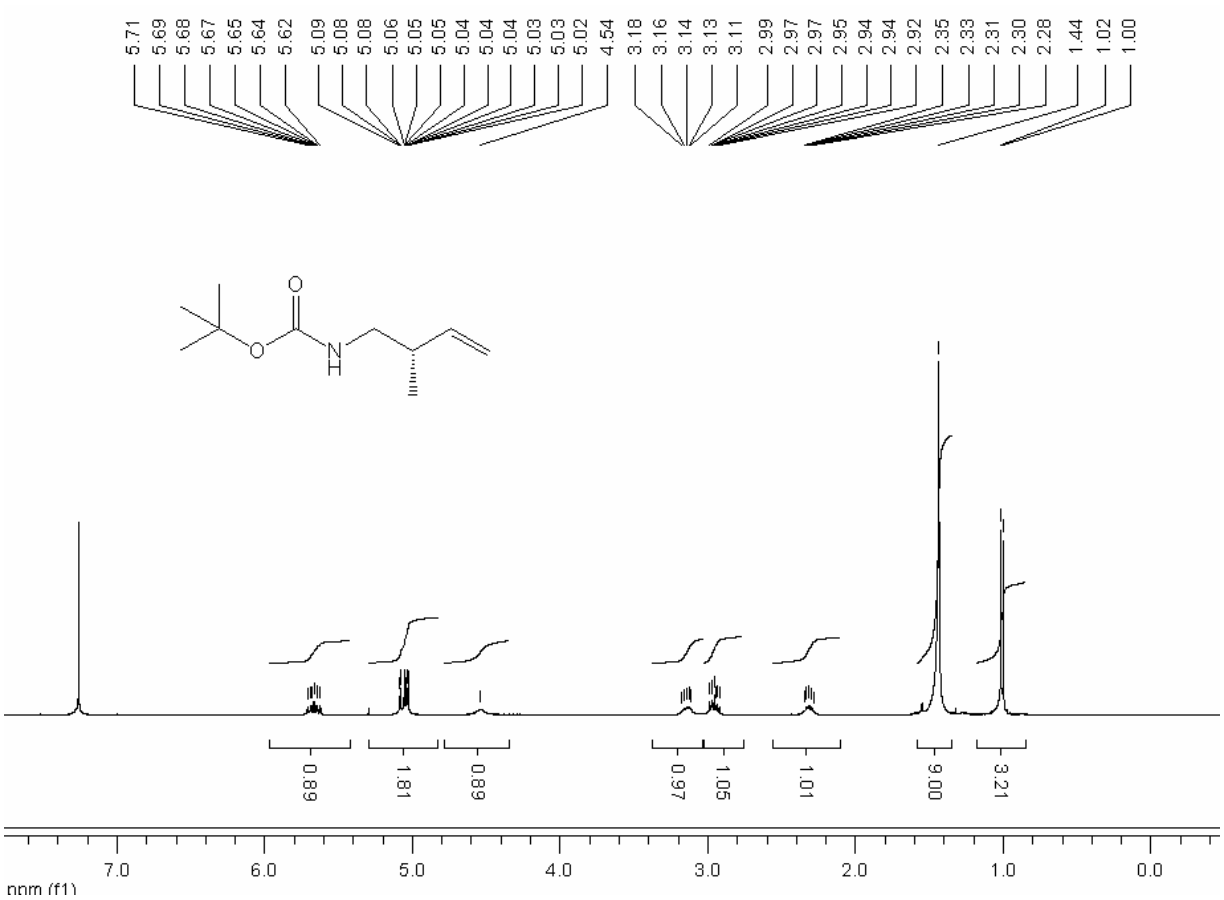


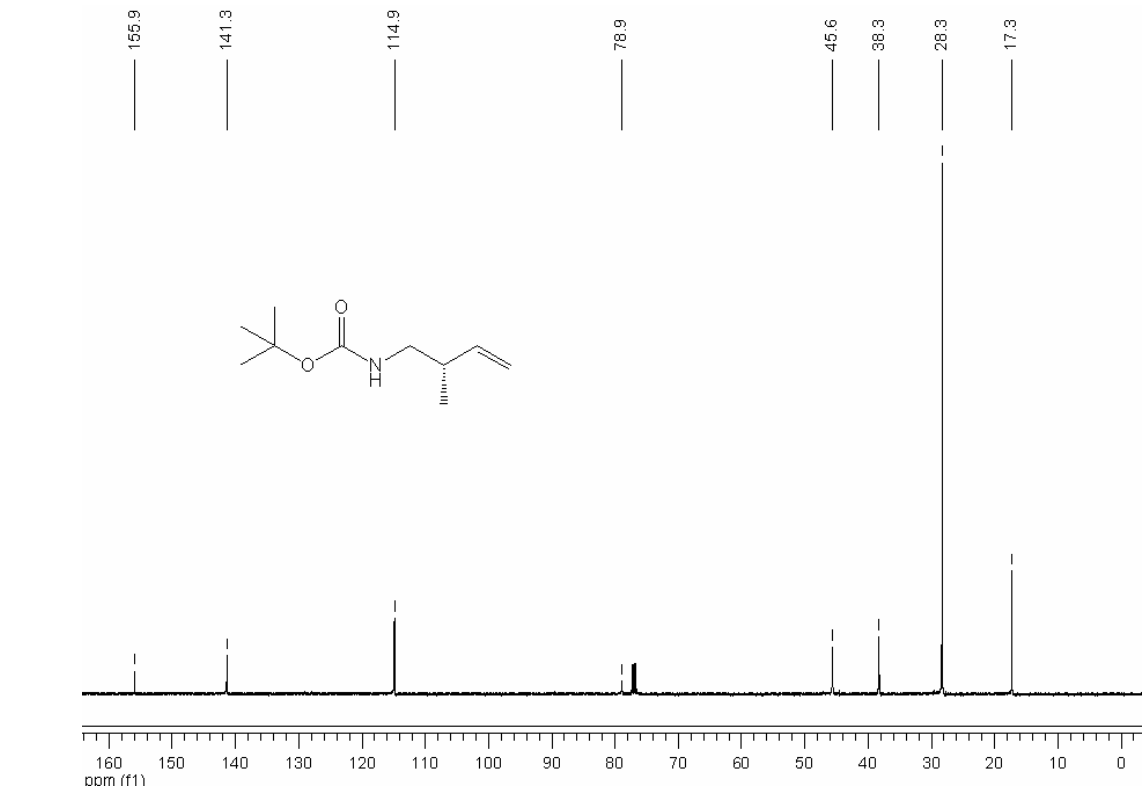
(–)-(*R*)-3-Benzyloxy-2-methylpropionic acid (6a):



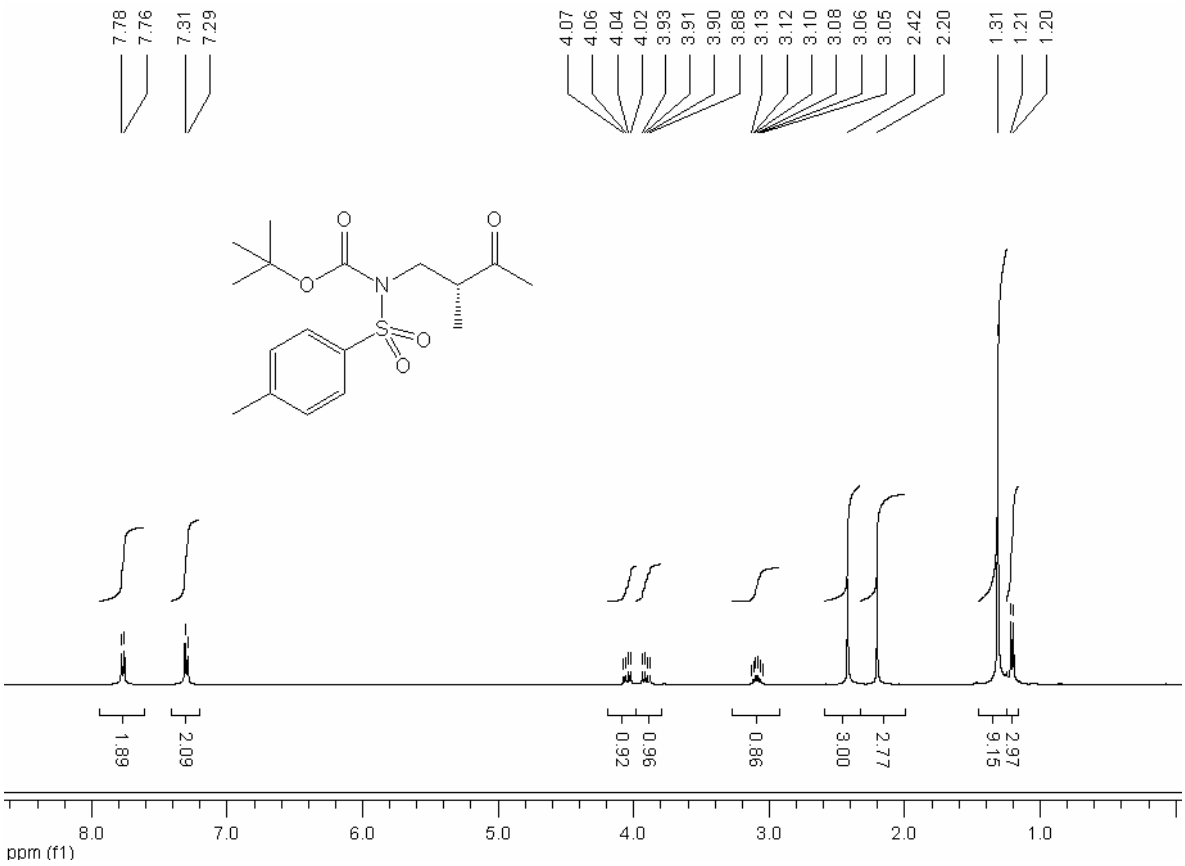


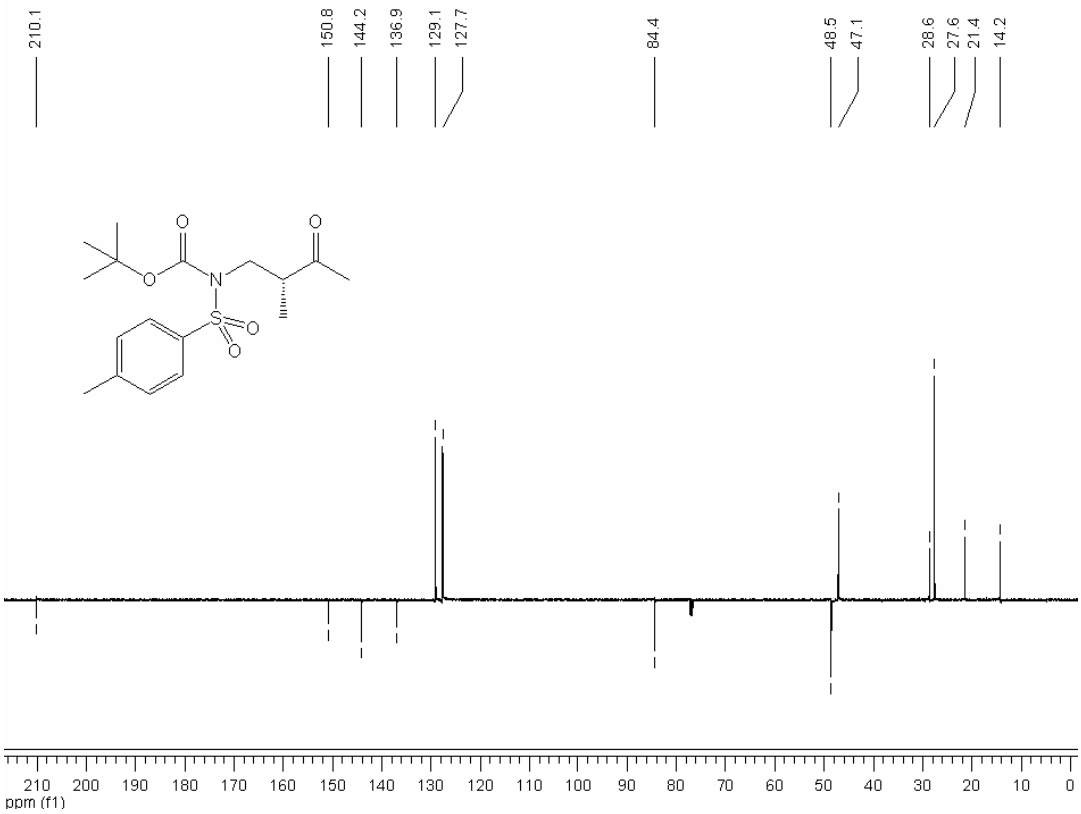
(–)-(*S*)-(*N*-*tert*-Butoxycarbonyl)(2-methylbut-3-enyl)amine (7):



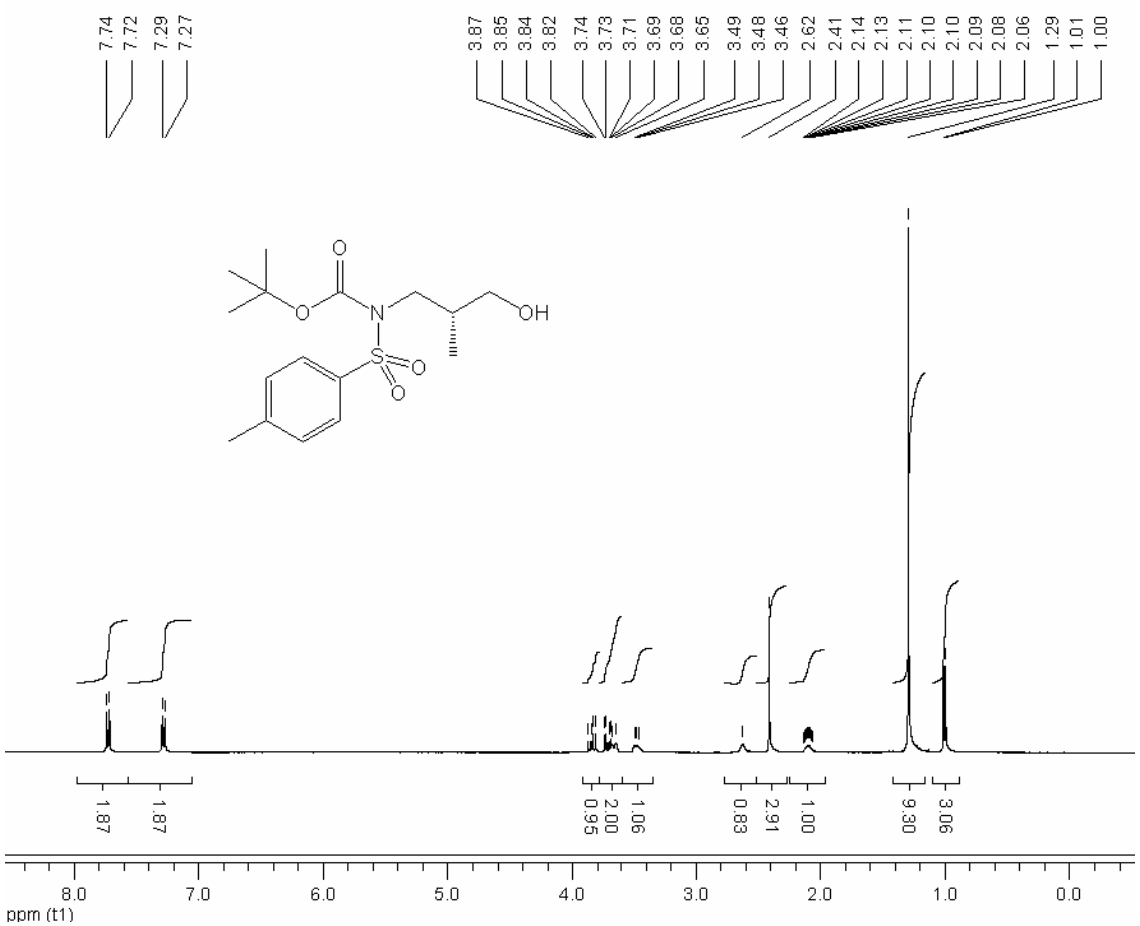


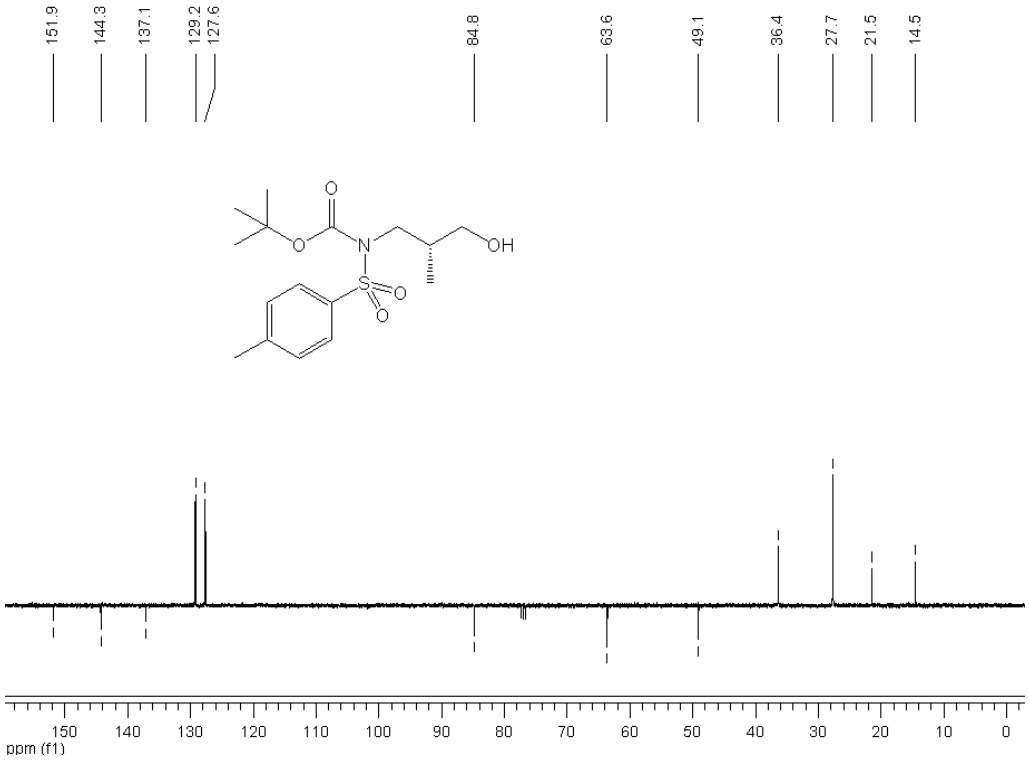
(+)-(*R*)-4-((*tert*-Butoxycarbonyl)(*p*-toluenesulfonyl)amino)-3-methylbutan-2-one (4b):



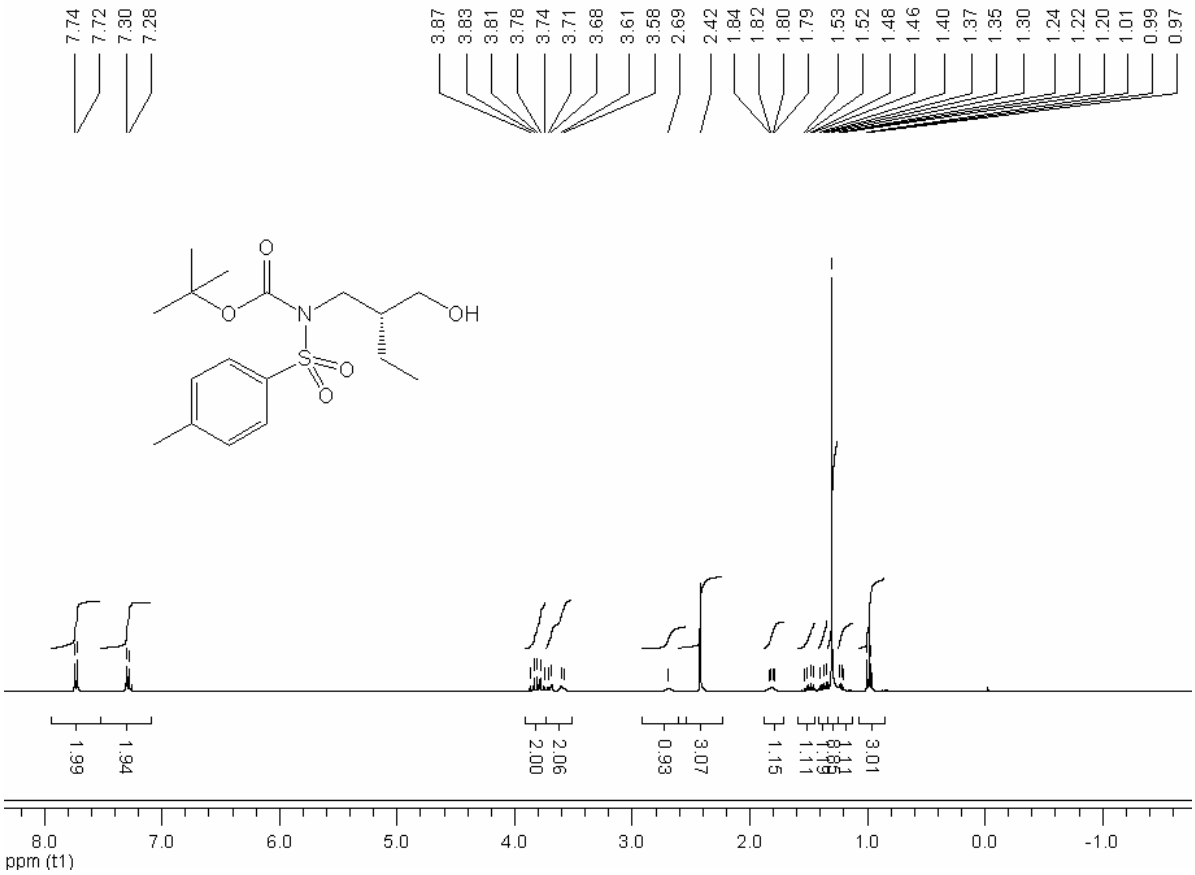


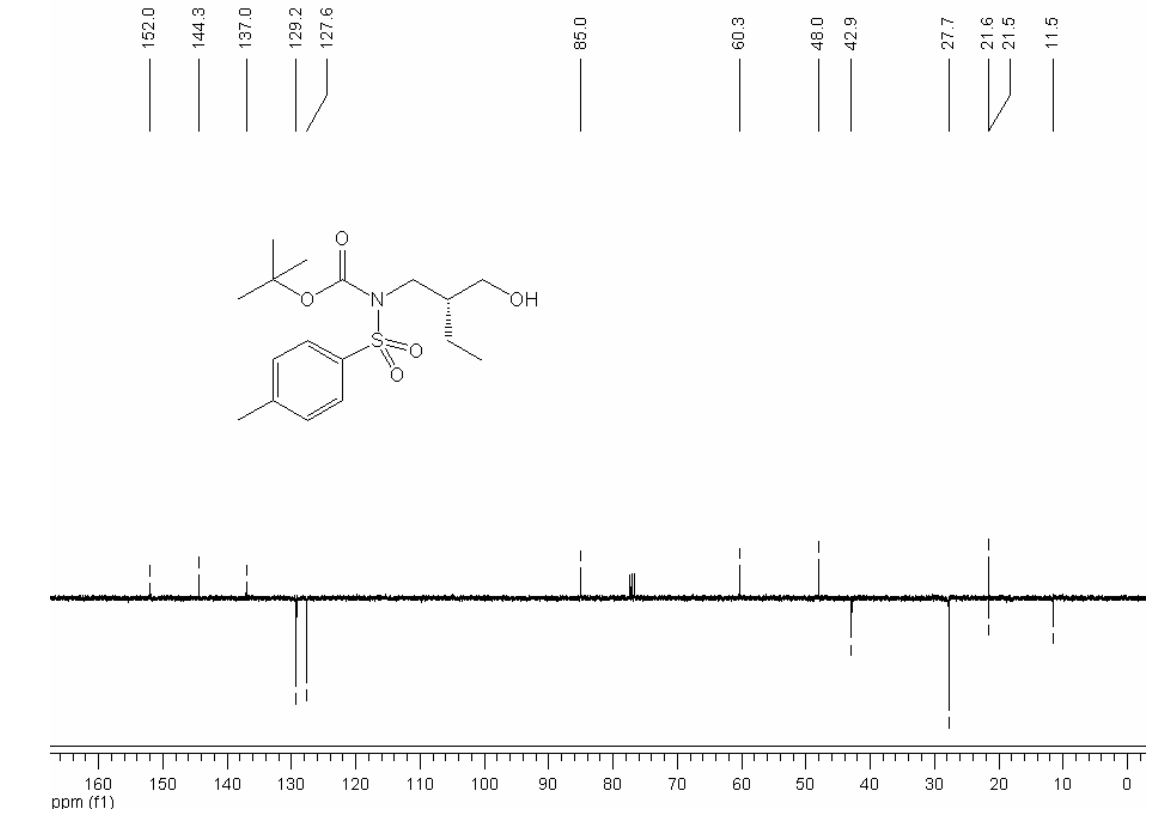
(–)-(*R*)-3-((*tert*-Butoxycarbonyl)(*p*-toluenesulfonyl)amino)-2-methylpropan-1-ol (5b):



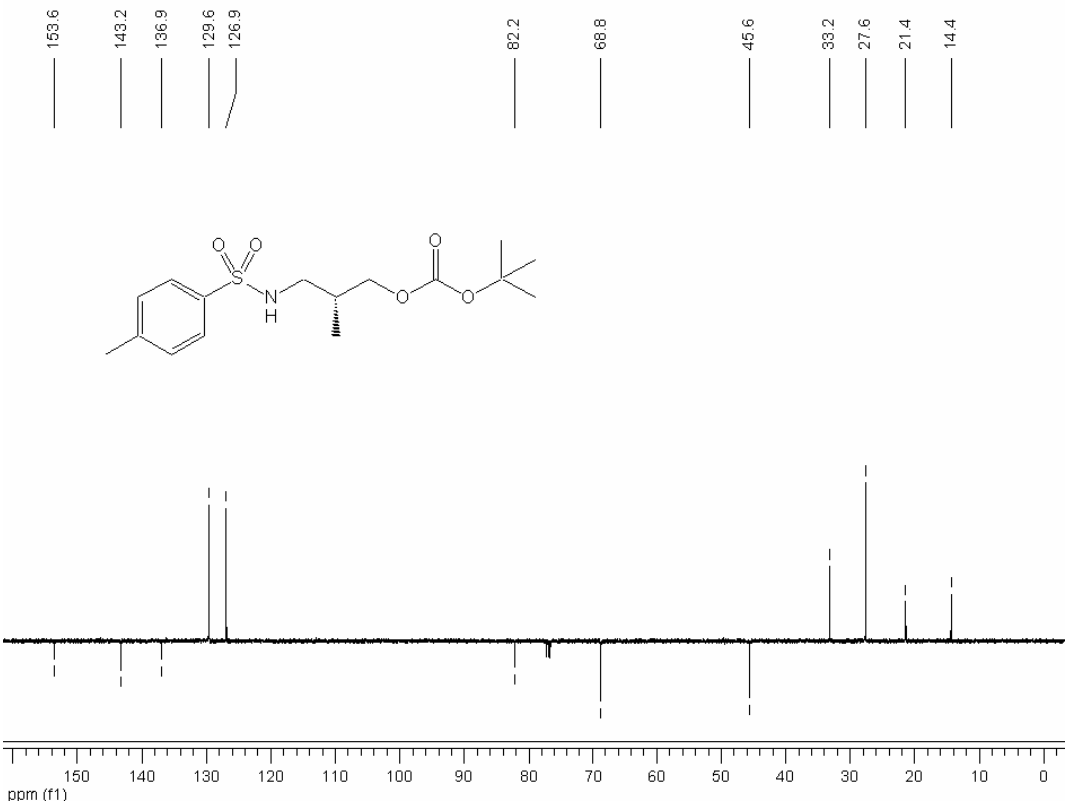


(–)-3-((*tert*-Butoxycarbonyl)(*p*-toluenesulfonyl)amino)-2-ethylpropan-1-ol (5e):

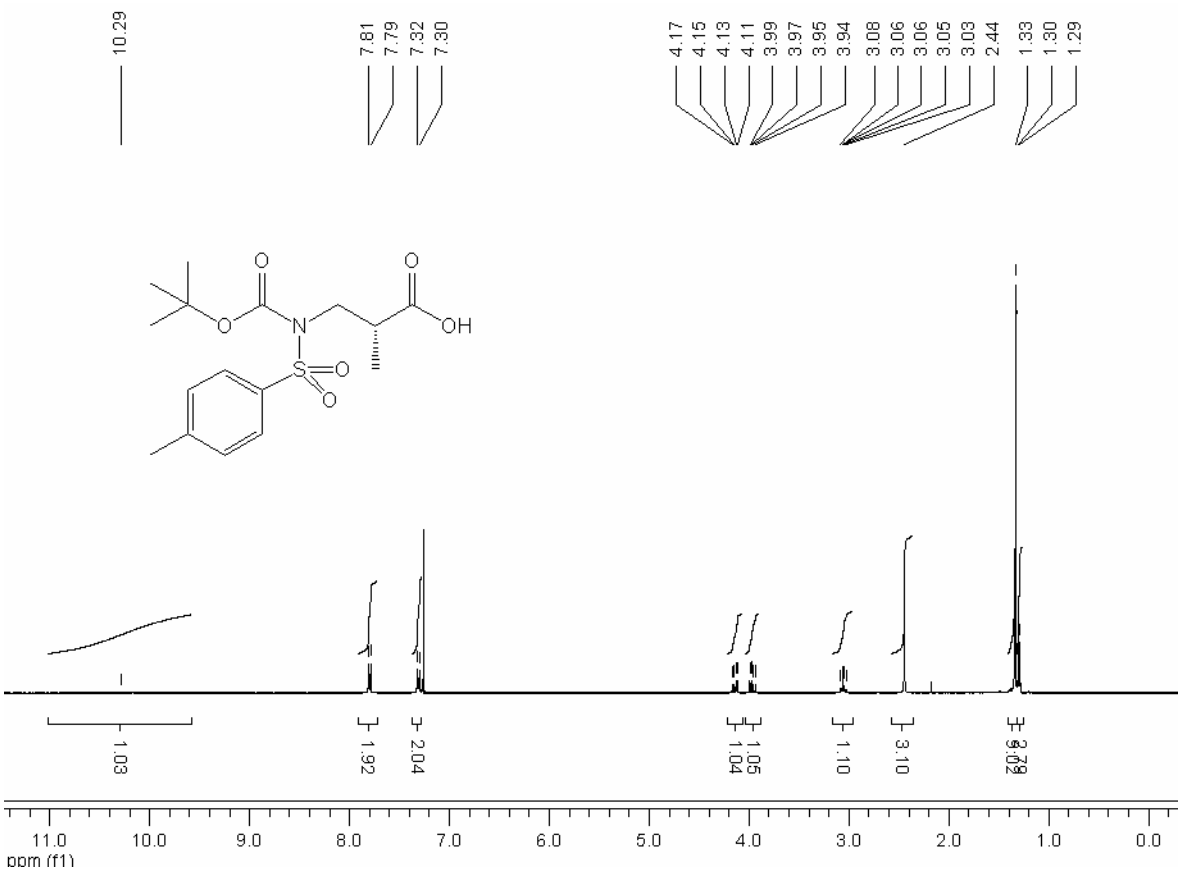


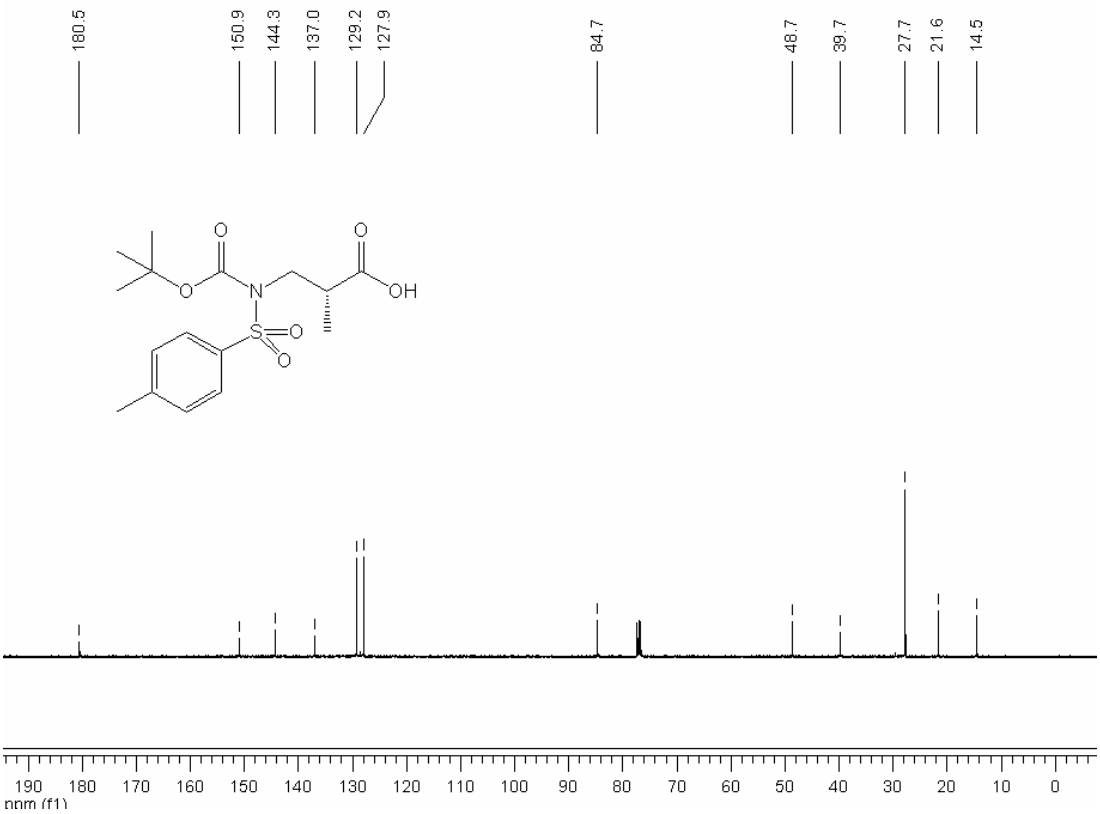


(+)-(*R*)-3-(*p*-Toluenesulfonylamino)-1-(*tert*-butoxycarbonyloxy)-2-methylpropane (8):

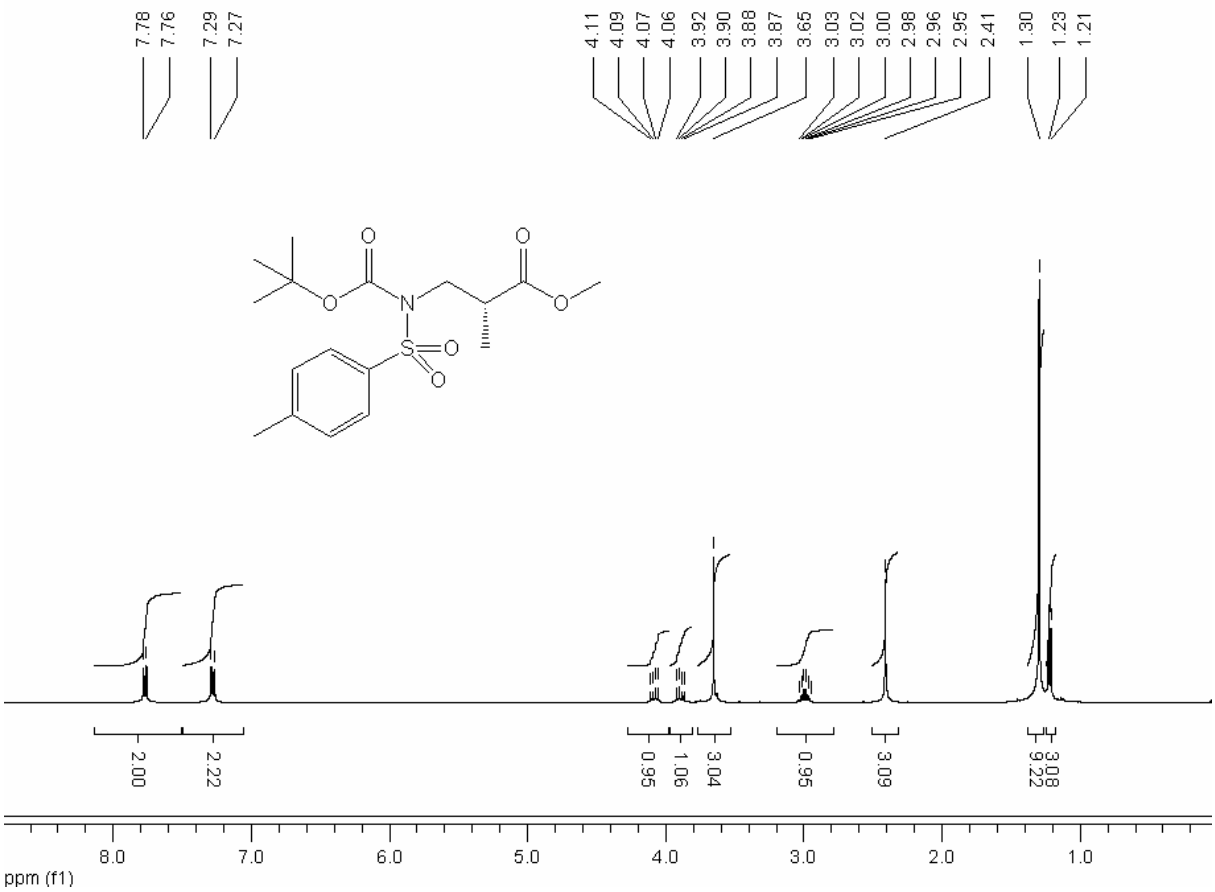


(–)-(*R*)-3-((*tert*-Butoxycarbonyl)(*p*-toluenesulfonyl)amino)-2-methylpropionic acid (6b):

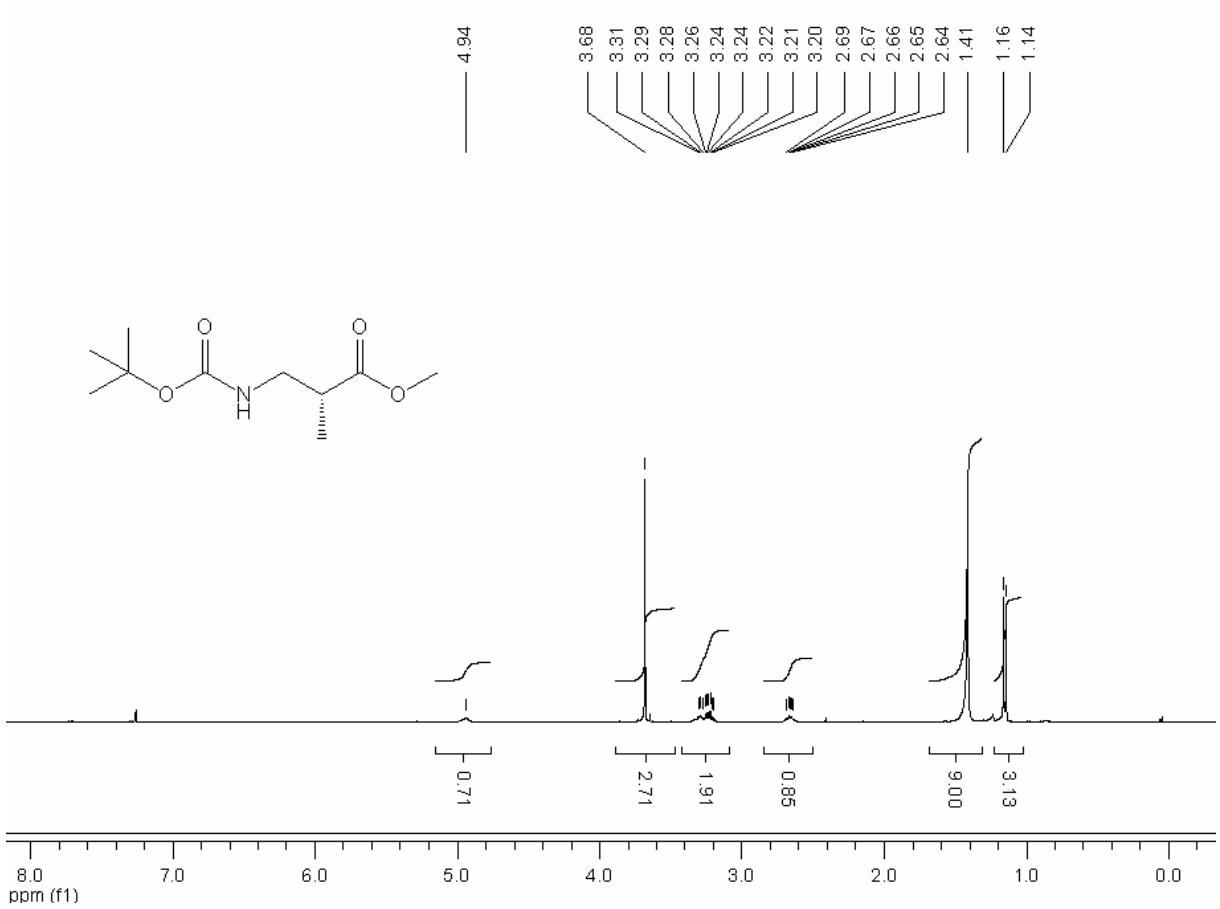


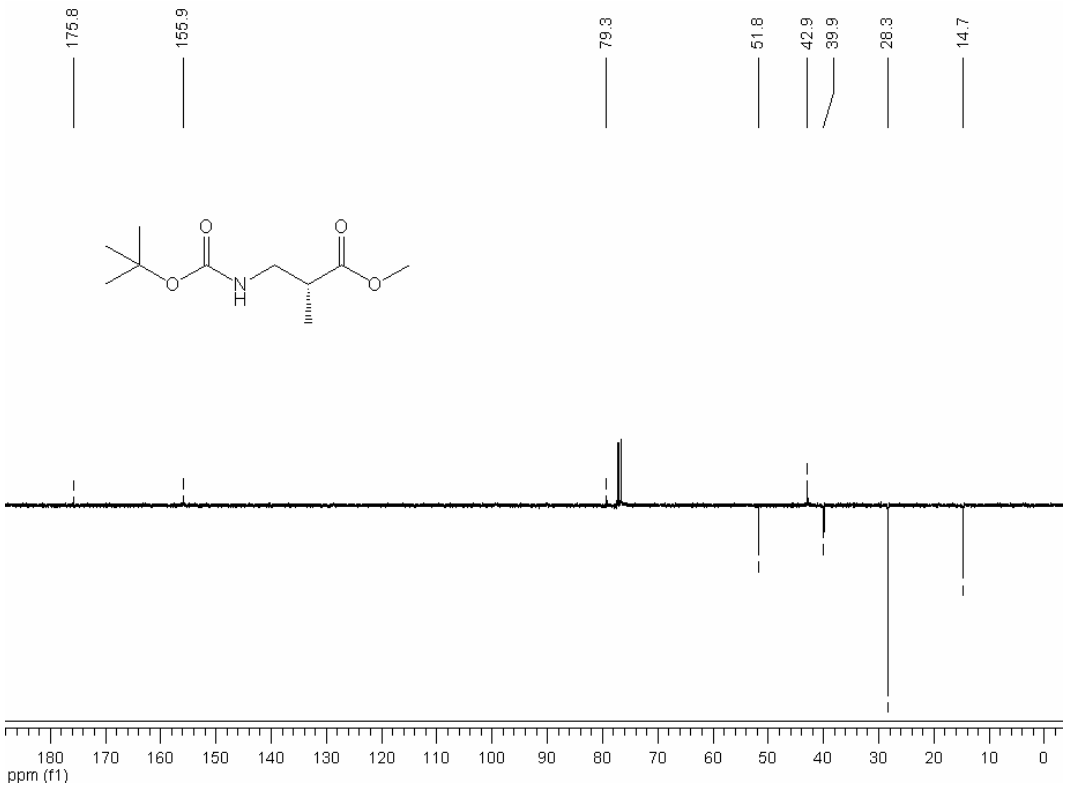


(–)-(*R*)-Methyl 3-((*tert*-butoxycarbonyl)(*p*-toluenesulfonyl)amino)-2-methylpropionate (9):

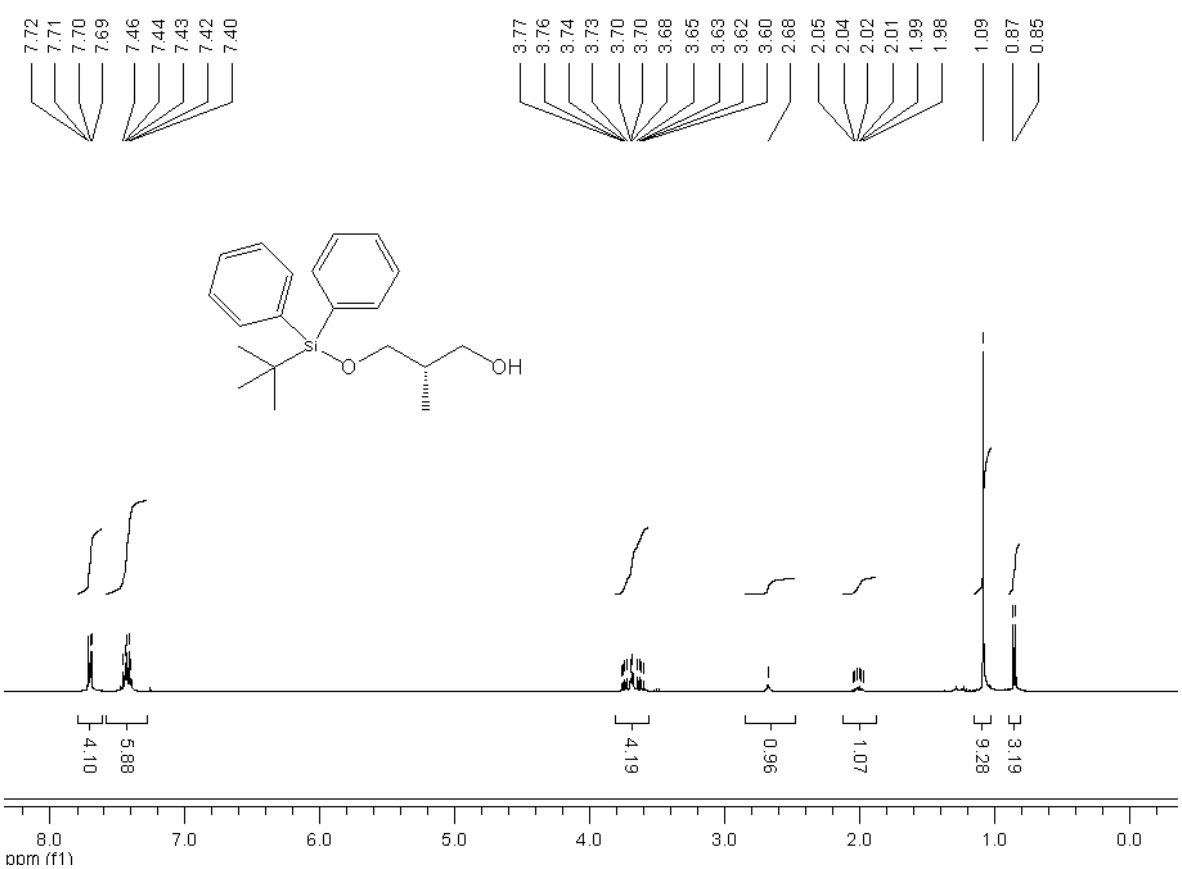


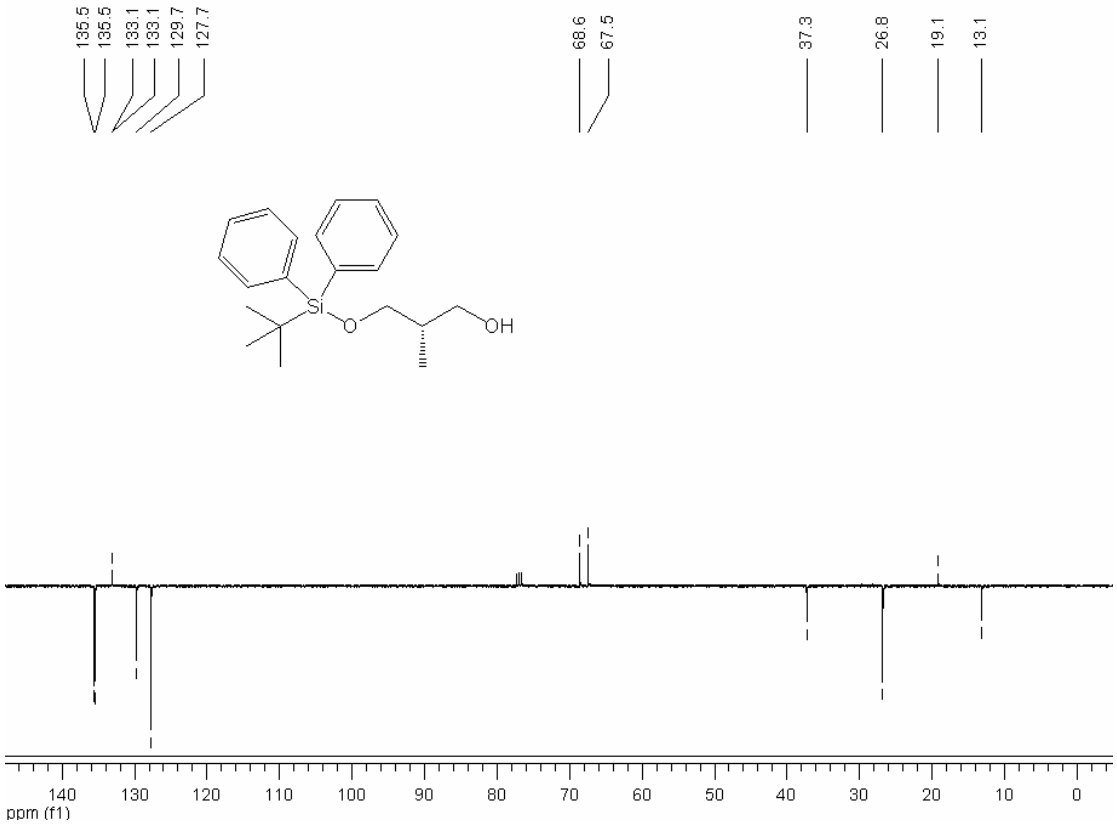
(–)-(*R*)-Methyl 3-*tert*-butoxycarbonylamino-2-methyl-propionate (10):





(−)-(*S*)-3-(*tert*-Butyl-diphenyl-silanyloxy)-2-methylpropan-1-ol (5c):





(*S*)-1-Benzyloxy-3-(*tert*-butyl-diphenyl-silanyloxy)-2-methylpropane (11):