Supporting Information

(*S*,*S*)-(+)-PSEUDOEPHEDRINE AS CHIRAL AUXILIARY IN ASYMMETRIC CONJUGATE ADDITION AND TANDEM CONJUGATE ADDITION/α-ALKYLATION REACTIONS

Efraim Reyes, Jose L. Vicario, Luisa Carrillo, Dolores Badía,* Uxue Uria and Ainara Iza.

1. General methods:

Melting points were determined in unsealed capillary tubes and are uncorrected. IR spectra were obtained on KBr pellets (solids) or $CHCl_3$ solution (oils). NMR spectra were recorded at 20-25ºC, running at 250 MHz for ^1H and 62.8 MHz for ^{13}C in $CDCl_3$ solution and resonances are reported in ppm relative to tetramethylsilane unless otherwise stated. Mass spectra were recorded under electron impact at 70 eV. TLC was carried out with 0.2 mm. thick silica gel plates (Merck Kiesegel GF_{254}) and visualization was accomplished by UV light or by spraying with phosphomolybdic acid. Flash column chromatography on silica gel was performed with Merck Kiesegel 60 (230-400 mesh). All solvents used in reactions were dried and purified according to standard procedures. All air- or moisture-sensitive reactions were performed under argon. The glassware was oven dried (140ºC) overnight and purged with argon prior to use. Organolithium reagents were titrated periodically with diphenylacetic acid. All other reagents were used as purchased. Diastereomeric ratios (dr) were determined by HPLC under conditions specified in each case. The characterization of amides **3a-s**, indanone **7a** and alcohols **9a-s** was reported in our preliminary communication.[1]

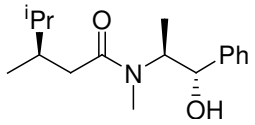
[1] Reyes, E.; Vicario, J. L.; Badia, D.; Carrillo, L.; Iza, A.; Uria, U. *Org. Lett.* **2006**, *8*, 2535.

2.- Diastereoselective conjugate addition.

General procedure:

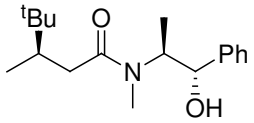
A solution of organolithium reagent (4.10 mmol) was carefully added to a suspension of the corresponding enamide **1a-e** (2.00 mmol) and LiCl (10.0 mmol) in dry THF (60 mL) at –105ºC and the reaction was stirred at this temperature for 10-30 min (TLC monitoring). The mixture was allowed to warm to r.t. and it was quenched with a saturated NH_4Cl solution (30 mL). The mixture was extracted with CH_2Cl_2 (3 x 30ml) and the combined organic fractions were collected, dried over Na_2SO_4, filtered and the solvent removed *in vacuo* affording the wanted amides after flash column chromatography purification.

(+)-(1'*S*,2'*S*,3*R*)-*N*-(2'-hydroxy-1'-methylethyl-2'-phenyl)-*N*,3,4-trimethyl-pentanamide (2b).



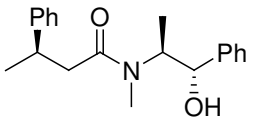
Amide **2b** (0.44g, 1.61mmol) was prepared according to the general procedure starting from enamide **1a** (0.46g, 2.00mmol), LiCl (0.42g, 10.00mmol) and ^{i}PrLi (6.3 mL of a 0.7M solution in hexanes). HPLC analysis of the crude reaction mixture (Chiracel OD column, hexanes/*iso*-propanol 98:2, flow rate 0.85 mL/min) indicated a 89:11 diastereomeric ratio: t_R for the major isomer: 35.77 min. t_R for the minor isomer: 41.74 min. Amide **2b** was isolated as a yellowish oil after flash column chromatography purification (hexanes/AcOEt 1:1). Yield: 80%. $[\alpha]_D^{20}$= +95.4 (*c*=0.23, CH_2Cl_2). ^{1}H-NMR (δ, ppm) (4:1 rotamer ratio; indicates minor rotamer resonances): 0.79 (m, 9H); 0.92* (d, 3H, *J*= 6.7 Hz); 1.03 (d, 3H, *J*= 6.3 Hz); 1.53 (m, 1H); 2.01 (m, 1H); 2.19 (m, 1H); 2.26 (m, 1H); 2.76 (s, 3H); 2.84* (s, 3H); 3.76* (m, 1H), 3.96 (m, 1H); 4.52 (m, 2H); 4.54* (bs, 1H); 7.28 (m, 5H). ^{13}C-NMR (δ, ppm) (4:1 rotamer ratio; indicates minor rotamer resonances): 14.3; 15.4; 15.5*; 17.9; 18.0*; 19.8; 20.0*; 26.8; 31.8; 31.9*; 35.3; 35.5*; 37.8*; 38.4; 58.1*; 58.2; 75.1*; 76.1; 126.2; 126.7*; 127.3; 127.8*; 128.0; 128.4*; 141.7*; 142.3; 173.9*; 175.0. IR ($CHCl_3$): 3380 (OH); 1618 (C=O). MS (EI) *m/z* (Rel. Int.): 259 (M^+-18, 9), 244 (6), 216 (85); 170 (11), 148 (100), 117 (12); 91 (11), 69 (33), 58 (91), 56 (13). Anal. Calcd. for $C_{17}H_{27}NO_2$: C, 73.61; H, 9.81; N, 5.05. Found: C, 73.77; H, 9.90; N, 5.01.

(+)-(1'*S*,2'*S*,3*R*)-*N*-(2'-hydroxy-1'-methylethyl-2'-phenyl)-*N*,3,4,4-tetramethyl-pentanamide (2c).



Amide **2c** (0.30g, 0.16mmol) was prepared according to the general procedure starting from enamide **1a** (0.46g, 2.00mmol), LiCl (0.42g, 10.00mmol) and ^{t}BuLi (2.4mL of a 1.5M solution in hexanes). HPLC analysis of the crude reaction mixture (Chiracel OD column, hexanes/*iso*-propanol 95:5, flow rate 1.00 mL/min) indicated a 90:10 diastereomeric ratio: t_R for the major isomer: 13.99 min. t_R for the minor isomer: 12.21 min. Amide **2c** was isolated as a white solid after flash column chromatography purification (hexanes/AcOEt 1:1). Yield: 52%. M.p. 82-84ºC (hexanes/AcOEt). $[\alpha]_D^{20}$= +106.5 (*c*=0.40, CH_2Cl_2). ^{1}H-NMR (δ, ppm) (3:1 rotamer ratio; indicates minor rotamer resonances): 0.77* (s, 9H); 0.81 (s, 9H); 0.94* (d, 3H, *J*= 6.5 Hz); 1.02 (d, 3H, *J*= 6.7 Hz); 1.70 (m, 1H); 1.85 (m, 1H); 2.33 (m, 1H); 2.75 (s, 3H); 2.79* (s, 3H); 4.00 (m, 1H); 4.47 (m, 1H); 4.75 (bs, 1H); 7.27 (m, 5H). ^{13}C-NMR (δ, ppm) (3:1 rotamer ratio; indicates minor rotamer resonances): 14.2; 14.4; 14.7*; 26.9; 27.0*; 30.5; 30.8*; 31.3*; 31.7; 32.5; 36.3*; 39.3; 39.4*; 57.9*; 58.1; 75.8; 76.4*; 126.1; 126.5*; 127.1; 127.9*; 128.1; 128.3*; 142.2*; 142.3; 174.2*; 175.2. IR (KBr): 3380 (OH); 1617 (C=O). MS (EI) *m/z* (Rel. Int.): 273 (M^+-18, 7), 215 (60), 170 (23), 148 (100), 118 (9); 91 (7), 69 (54), 63 (20); 58 (84), 56 (10). Anal. Calcd. for $C_{18}H_{29}NO_2$: C, 74.18; H, 10.03; N, 4.81. Found: C, 74.03; H, 9.89; N, 4.74.

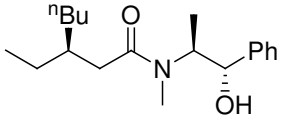
(+)-(1'*S*,2'*S*,3*R*)-*N*-(2'-hydroxy-1'-methylethyl-2'-phenyl)-*N*-methyl-3-phenyl-butanamide (2d).



Amide **2d** (0.63g, 1.72mmol) was prepared according to the general procedure starting from enamide **1a** (0.46g, 2.00mmol), LiCl (0.42g, 10.00mmol) and PhLi (4.4 mL of a 1.0M solution in dibutyl ether). HPLC analysis of the crude reaction mixture (Chiracel OD column, hexanes/*iso*-propanol 95:5, flow rate 1.00 mL/min) indicated a 94:6 diastereomeric ratio: t_R for the major isomer: 34.42 min. t_R for the minor isomer: 30.34 min. Amide **2d** was isolated as a yellowish oil after flash column chromatography purification (hexanes/AcOEt 1:1). Yield: 86%. $[\alpha]_D^{20}$= +66.5 (*c*=0.30, CH_2Cl_2). ^{1}H-NMR (δ, ppm)

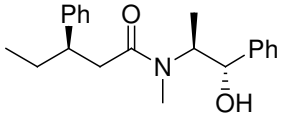
(4:1 rotamer ratio; indicates minor rotamer resonances): 0.97 (d, 3H, *J*=5.5Hz); 1.31 (d, 3H, *J*= 6.7 Hz); 2.54 (m, 2H); 2.71 (s, 3H); 2.89* (s, 3H); 3.34 (m, 1H), 3.40* (m, 1H); 4.53 (m 1H); 4.51-4.58 (bs, 2H); 7.31 (m, 10H). ^{13}C-NMR (δ, ppm) (4:1 rotamer ratio; indicates minor rotamer resonances): 14.1; 15.2*; 21.4; 21.5*; 26.7, 32.0*; 36.1*; 36.3; 41.4*; 42.3; 57.3*; 58.1; 74.9*; 75.9; 125.8*; 126.0; 126.2; 126.6; 126.7; 127.3*; 127.8*; 128.0; 128.2; 128.4*; 141.4*; 142.1; 146.0; 146.6*; 172.4*; 173.6. IR ($CHCl_3$): 3381 (OH); 1617 (C=O). MS (EI) *m/z* (Rel. Int.): 311 (M^+-18, 10), 202 (31), 160 (10), 147 (100), 132 (11); 105 (44); 91 (17), 58 (28). Anal. Calcd. for $C_{20}H_{25}NO_2$: C, 77.14; H, 8.09; N, 4.50. Found: C, 77.19; H, 8.01; N, 4.51.

(+)-(1'*S*,2'*S*,3*S*)-3-ethyl-*N*-(2'-hydroxy-1'-methylethyl-2'-phenyl)-*N*-methyl-heptanamide (2e).



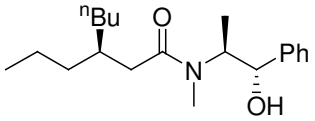
Amide **2e** (0.45g, 1.46mmol) was prepared according to the general procedure starting from enamide **1b** (0.49g, 2.00mmol), LiCl (0.42g, 10.00mmol) and ^{n}BuLi (5.5 mL of a 0.8M solution in hexanes). HPLC analysis of the crude reaction mixture (Chiracel OD column, hexanes/*iso*-propanol 95:5, flow rate 1.00 mL/min) indicated a 98:2 diastereomeric ratio: t_R for the major isomer: 16.42 min. t_R for the minor isomer: 25.16 min. Amide **2e** was isolated as a yellowish oil after flash column chromatography purification (hexanes/AcOEt 1:1). Yield: 73%. $[\alpha]_D^{20}$= +82.7 (*c*=0.53, CH_2Cl_2). ^{1}H-NMR (δ, ppm) (3:1 rotamer ratio; indicates minor rotamer resonances): 0.87 (m, 6H); 0.94* (d, 3H, *J*= 6.7 Hz); 1.03 (d, 3H, *J*= 6.0 Hz); 1.22 (m, 6H); 1.77 (m, 1H); 2.13 (m, 2H); 2.36 (dd, 1H, *J*= 14.7, 6.7 Hz); 2.76 (s, 3H); 2.83* (s, 3H); 3.97* (m, 1H); 4.51 (m, 2H); 4.90 (bs, 1H); 7.29 (m, 5H). ^{13}C-NMR (δ, ppm) (3:1 rotamer ratio; indicates minor rotamer resonances): 10.4; 13.7; 14.0*; 15.2; 22.6; 25.7; 25.9*; 26.7; 28.4; 28.6*; 32.4*; 32.6; 32.7*; 35.6; 35.8*; 37.7*; 38.0; 57.4*; 58.0; 74.8; 75.6; 126.0; 126.5*; 127.0; 127.5*; 127.8; 128.0; 141.8*; 142.2; 173.7*; 174.6. IR ($CHCl_3$): 3380 (OH); 1619 (C=O). MS (EI) *m/z* (Rel. Int.): 287 (M^+-18, 9), 258 (10), 230 (11); 198 (11), 147 (83), 131 (10); 91 (12), 71 (11), 58 (100). Anal. Calcd. for $C_{19}H_{31}NO_2$: C, 74.71; H, 10.23; N, 4.59. Found: C, 74.65; H, 10.28; N, 4.67.

(+)-(1'*S*,2'*S*,3*R*)-*N*-(2'-hydroxy-1'-methylethyl-2'-phenyl)-*N*-methyl-3-phenyl-pentanamide (2f).



Amide **2f** (0.53g, 1.64mmol) was prepared according to the general procedure starting from enamide **1b** (0.49g, 2.00mmol), LiCl (0.42g, 10.00mmol) and PhLi (4.4mL of a 1.0M solution in hexanes). HPLC analysis of the crude reaction mixture (Chiracel OD column, hexanes/*iso*-propanol 95:5, flow rate 1.00 mL/min) indicated a 91:9 diastereomeric ratio: t_R for the major isomer: 24.64 min. t_R for the minor isomer: 30.34 min. Amide **2f** was isolated as a white solid after flash column chromatography purification (hexanes/AcOEt 1:1). Yield: 82%. M.p. 85-87ºC (hexanes/AcOEt). $[\alpha]_D^{20}$= +72.4 (*c*=0.41, CH_2Cl_2). ^{1}H-NMR (δ, ppm) (4:1 rotamer ratio; indicates minor rotamer resonances): 0.85 (t, 3H, *J*= 7.3 Hz); 0.97 (d, 3H, *J*= 6.5 Hz); 1.01* (d, 3H, *J*= 6.9 Hz); 1.66 (m, 2H); 1.72 (m, 2H); 2.71 (s, 3H); 2.88* (s, 3H); 3.08 (m, 1H); 4.07* (m, 1H); 4.55 (m, 3H); 7.32 (m, 10H). ^{13}C-NMR (δ, ppm) (4:1 rotamer ratio; indicates minor rotamer resonances): 11.9; 14.1; 15.1*; 26.7; 28.7; 32.3*; 40.0*; 40.9; 43.6*; 43.9; 57.6*; 58.2; 74.9; 75.7*; 125.9*; 126.1; 126.2; 126.7*; 127.3; 127.4; 127.6*; 128.0*; 128.2; 128.3; 141.3*; 142.1; 144.1; 144.7*; 172.6*; 173.9. IR (KBr): 3381 (OH); 1619 (C=O). MS (EI) *m/z* (Rel. Int.): 307 (M^+-18, 5), 218 (10), 147 (38), 131 (9); 119 (12); 91 (42), 58 (100). Anal. Calcd. for $C_{21}H_{27}NO_2$: C, 77.50; H, 8.36; N, 4.30. Found: C, 77.42; H, 8.44; N, 4.21.

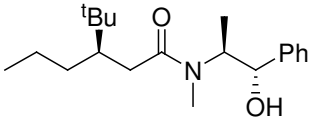
(+)-(1'*S*,2'*S*,3*S*)-*N*-(2'-hydroxy-1'-methylethyl-2'-phenyl)-*N*-methyl-3-propyl-heptanamide (2g).



Amide **2g** (0.46g, 1.46mmol) was prepared according to the general procedure starting from enamide **1c** (0.52g, 2.00mmol), LiCl (0.42g, 10.00mmol) and ^{n}BuLi (5.5mL of a 0.8M solution in hexanes). HPLC analysis of the crude reaction mixture (Chiracel OD column, hexanes/*iso*-propanol 95:5, flow rate 1.00 mL/min) indicated a 98:2 diastereomeric ratio: t_R for the major isomer: 13.54 min. t_R for the minor isomer: 18.10 min. Amide **2g** was isolated as a yellowish oil after flash column chromatography purification (hexanes/AcOEt 1:1). Yield: 73%. $[\alpha]_D^{20}$= +76.4 (*c*=1.0, CH_2Cl_2). ^{1}H-NMR

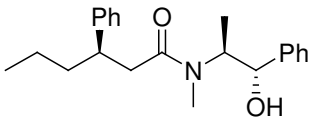
(δ, ppm) (3:2 rotamer ratio; indicates minor rotamer resonances): 0.85 (t, 3H, *J*= 8.2 Hz); 0.93* (d, 3H, *J*= 5.7 Hz); 1.03 (d, 3H, *J*= 6.0 Hz); 1.22 (m, 10H); 1.83 (m, 1H); 2.12 (d, 2H, *J*=6.3Hz); 2.75 (s, 3H); 2.83* (s, 3H); 3.93 (m, 1H); 4.21* (m, 1H); 4.51 (m, 2H); 4.51* (bs, 1H); 7.28 (m, 5H). ^{13}C-NMR (δ, ppm) (3:2 rotamer ratio; indicates minor rotamer resonances): 13.8; 14.0; 14.1; 15.2*; 19.4; 22.7; 26.7; 28.4; 28.6*; 32.6*; 33.2; 33.3*; 34.1; 34.4*; 35.8; 36.1*; 38.2*; 38.6; 57.8*; 58.1; 74.9*; 75.8; 126.1; 126.6*; 127.1; 127.6*; 127.9; 128.1*; 141.8*; 142.3; 173.8*; 174.8. IR ($CHCl_3$): 3380 (OH); 1620 (C=O). MS (EI) *m/z* (Rel. Int.): 301 (M^+-18, 7), 258 (11), 244 (10), 212 (10), 147 (100), 132 (9); 118 (10); 91 (12), 71 (14), 58 (76). Anal. Calcd. for $C_{20}H_{33}NO_2$: C, 75.19; H, 10.41; N, 4.38. Found: C, 75.03; H, 10.47; N, 4.44.

(+)-(1'*S*,2'*S*,3*R*)-3-*tert*-butyl-*N*-(2'-hydroxy-1'-methylethyl-2'-phenyl)-*N*-methyl-hexanamide (2h).



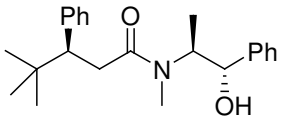
Amide **2h** (0.59g, 1.88mmol) was prepared according to the general procedure starting from enamide **1c** (0.52g, 2.00mmol), LiCl (0.42g, 10.00mmol) and ^{t}BuLi (4.4 mL of a 1.0M solution in hexanes). HPLC analysis of the crude reaction mixture (Chiracel OD column, hexanes/*iso*-propanol 99:1, flow rate 0.75 mL/min) indicated a 90:10 diastereomeric ratio: t_R for the major isomer: 21.46 min. t_R for the minor isomer: 24.42 min. Amide **2h** was isolated as a white solid after flash column chromatography purification (hexanes/AcOEt 1:1). Yield: 94%. Mp. 69-71ºC (hexanes/AcOEt). $[\alpha]_D^{20}$= +73.6 (*c*=0.02, CH_2Cl_2). ^{1}H-NMR (δ, ppm) (5:1 rotamer ratio; indicates minor rotamer resonances): 0.85 (s, 9H,); 0.90* (s, 9H); 0.99* (d, 3H, *J*= 6.9 Hz); 1.05 (d, 3H, *J*= 6.7 Hz); 1.26 (m, 2H); 1.43 (m, 2H); 1.92 (m, 1H); 2.02 (dd, 1H, *J*=15.7, 6.5Hz); 2.31 (dd, 1H, *J*=15.7, 4.6Hz); 2.85 (s, 3H); 2.90* (s, 3H); 4.07* (m, 1H); 4.46 (m, 1H); 4.56 (m, 1H); 7.33 (m, 5H). ^{13}C-NMR (δ, ppm) (5:1 rotamer ratio; indicates minor rotamer resonances): 14.4; 14.6; 15.3*; 21.9; 27.1*; 27.4; 32.7; 33.4; 33.6; 33.9*; 35.0*; 35.6; 43.6; 58.0; 58.6*; 76.5; 76.7*; 126.3*; 126.4; 126.8*; 127.5; 128.3; 128.6*; 141.3*; 142.5; 176.0*; 176.2. IR (KBr): 3371 (OH); 1655 (C=O). MS (EI) *m/z* (Rel. Int.): 301 (M^+-18, 4), 244 (100), 212 (8), 148 (82), 118 (12); 105 (14); 97 (48); 91 (12), 71 (13), 58 (100). Anal. Calcd. for $C_{20}H_{33}NO_2$: C, 75.19; H, 10.41; N, 4.38. Found: C, 75.22; H, 10.37; N, 4.46.

(+)-(1'*S*,2'*S*,3*R*)-*N*-(2'-hydroxy-1'-methylethyl-2'-phenyl)-*N*-methyl-3-phenyl-hexanamide (2i).



Amide **2i** (0.55g, 1.64mmol) was prepared according to the general procedure starting from enamide **1c** (0.52g, 2.00mmol), LiCl (0.42g, 10.00mmol) and PhLi (4.4 mL of a 1.0M solution in hexanes). HPLC analysis of the crude reaction mixture (Chiracel OD column, hexanes/*iso*-propanol 95:5, flow rate 1.00 mL/min) indicated a 93:7 diastereomeric ratio: t_R for the major isomer: 21.85 min. t_R for the minor isomer: 30.08 min. Amide **2i** was isolated as a yellowish oil after flash column chromatography purification (hexanes/AcOEt 1:1). Yield: 82%. $[\alpha]_D^{20}$= +62.5 (*c*=0.18, CH_2Cl_2). ^{1}H-NMR (δ, ppm) (5:1 rotamer ratio; indicates minor rotamer resonances): 0.87 (m, 6H); 1.18 (m, 2H); 1.62 (m, 2H); 2.55 (d, 1H, *J*=4.9Hz); 2.63 (s, 3H); 2.84* (s, 3H); 3.12 (m, 1H); 4.02* (m, 1H); 4.42 (m, 2H); 7.45 (m, 10H). ^{13}C-NMR (δ, ppm) (5:1 rotamer ratio; indicates minor rotamer resonances): 14.2; 14.7; 15.2*; 21.5; 26.3*; 32.5; 35.4*; 35.8; 40.2*; 41.4; 43.6; 58.7*; 59.2; 74.3*; 76.5; 126.3; 126.4; 126.7*; 127.2; 127.5; 128.1; 128.3*; 128.7; 141.2*; 142.0; 143.4; 144.0; 172.5*; 175.4. IR ($CHCl_3$): 3380 (OH); 1620 (C=O). MS (EI) *m/z* (Rel. Int.): 321 (M^+-18, 10), 230 (28), 173 (28), 147 (45), 131 (9); 117 (10); 91 (46); 58 (100). Anal. Calcd. for $C_{22}H_{29}NO_2$: C, 77.84; H, 8.61; N, 4.13. Found: C, 77.98; H, 8.65; N, 4.21.

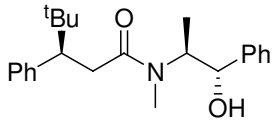
(+)-(1'*S*,2'*S*,3*S*)-*N*-(2'-hydroxy-1'-methylethyl-2'-phenyl)-*N*,4,4-trimethyl-3-phenylpentanamide (2j).



Amide **2j** (0.63g, 1.82mmol) was prepared according to the general procedure starting from enamide **1d** (0.55g, 2.00mmol), LiCl (0.42g, 10.00mmol) and PhLi (4.4 mL of a 1.0M solution in hexanes). HPLC analysis of the crude reaction mixture (Chiracel OD column, hexanes/*iso*-propanol 95:5, flow rate 1.00 mL/min) indicated a 97:3 diastereomeric ratio: t_R for the major isomer: 22.31 min. t_R for the minor isomer: 18.23min. Amide **2j** was isolated as a white solid after flash column chromatography purification (hexanes/AcOEt 1:1). Yield: 84%. Mp. 115-116ºC (hexanes/AcOEt). $[\alpha]_D^{20}$= +71.3 (*c*=0.14, CH_2Cl_2). ^{1}H-NMR (δ, ppm) (3:1 rotamer ratio; indicates minor

rotamer resonances): 0.82 (d, 3H, *J*=6.9Hz); 0.91 (s, 9H); 0.97 (d, 3H, *J*=6.7Hz); 2.63 (dd, 1H, *J*=15.1, 3.7Hz); 2.70* (s, 3H); 2.75 (s, 3H); 2.81 (dd, 1H, *J*=15.1, 4.7Hz); 3.08 (dd, 1H, *J*=10.3, 3.7Hz); 4.05* (m, 1H); 4.19 (m, 1H); 4.42 (m, 1H); 7.21 (m, 10H). ^{13}C-NMR (δ, ppm) (3:1 rotamer ratio; indicates minor rotamer resonances): 14.1; 15.2*; 26.7*; 28.0; 32.8*; 33.5; 34.0; 34.6; 51.7*; 52.0; 58.1; 58.5*; 74.9*; 76.2; 125.8*; 126.0; 126.2; 126.7*; 127.2; 127.4*; 127.5*; 127.6; 127.9*; 128.1; 128.4*; 129.1; 141.1*; 142.0; 142.2; 172.9*; 174.6. IR (KBr): 3381 (OH); 1621 (C=O). MS (EI) *m/z* (Rel. Int.): 353 (M^+-18, 8), 278 (10); 246 (10); 188 (42), 147 (82), 131 (100); 104 (21); 91 (33); 77 (11); 58 (68). Anal. Calcd. for $C_{23}H_{31}NO_2$: C, 78.15; H, 8.84; N, 3.96. Found: C, 78.22; H, 8.96; N, 4.07.

(+)-(1'*S*,2'*S*,3*R*)-*N*-(2'-hydroxy-1'-methylethyl-2'-phenyl-)-*N*,4,4-trimethyl-3-phenylpentanamide (2k).



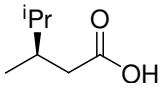
Amide **2k** (0.43g, 1.22mmol) was prepared according to the general procedure starting from enamide **1e** (0.58g, 2.00mmol), LiCl (0.42g, 10.00mmol) and ^{t}BuLi (4.4 mL of a 1.0M solution in hexanes). HPLC analysis of the crude reaction mixture (Chiracel OD column, hexanes/*iso*-propanol 95:5, flow rate 1.00 mL/min) indicated a 91:9 diastereomeric ratio: t_R for the major isomer: 18.23 min. t_R for the minor isomer: 22.31 min. Amide **2k** was isolated as a white solid after flash column chromatography purification (hexanes/AcOEt 1:1). Yield: 61%. Mp. 134-137ºC (hexanes/AcOEt). $[\alpha]_D^{20}$= +70.0 (*c*=0.6, CH_2Cl_2). ^{1}H-NMR (δ, ppm) (4:1 rotamer ratio; indicates minor rotamer resonances): 0.69 (d, 3H, *J*=6.9Hz); 0.83 (d, 3H, *J*=6.8Hz); 0.91 (s, 9H); 2.59 (dd, 1H, *J*=14.9, 4.0Hz); 2.72 (s, 3H); 2.74* (s, 3H); 2.79 (dd, 1H, *J*=15.0, 10.5Hz); 3.10 (m, 1H); 3.96* (m, 1H); 4.16 (m, 1H); 4.40 (m, 1H); 7.23 (m, 10H). ^{13}C-NMR (δ, ppm) (4:1 rotamer ratio; indicates minor rotamer resonances): 13.9; 15.2*; 26.9*; 28.0; 33.4; 33.7*; 33.8*; 33.9; 34.5*; 34.7; 52.1*; 52.7; 58.4; 59.0*; 75.4*; 75.9; 126.0*; 126.3; 126.4; 126.7*; 127.4; 127.5*; 127.6; 127.8*; 128.1; 128.3*; 128.6*; 129.3; 141.3*; 141.9; 142.0*; 142.8; 173.8*; 174.7. IR (KBr): 3377 (OH); 1618 (C=O). MS (EI) *m/z* (Rel. Int.): 353 (M^+-18, 6), 278 (42); 246 (9); 188 (30), 147 (90), 131 (100); 117 (9); 104 (36); 91 (38); 77 (14); 58 (60). Anal. Calcd. for $C_{23}H_{31}NO_2$: C, 78.15; H, 8.84; N, 3.96. Found: C, 78.08; H, 8.75; N, 4.03.

3.- Hydrolysis. Synthesis of carboxylic acids 4b-k, 5a, 5e, 5i, 5m, 5r and 5s

General procedure:

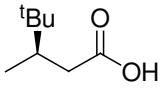
4M H_2SO_4 (10 mL) was slowly added over a cooled (0ºC) solution of the corresponding amide **2a-k**, **3a**, **3e**, **3i**, **3m**, **3r** or **3s** (1 mmol) in 1,4-dioxane (10 mL). The reaction was refluxed for 6h after which it was cooled down to r.t. Water (20 mL) was added and the mixture was carefully basified to pH=12 and washed with EtOAc (3x20mL). The aqueous layer was carefully driven to pH=3 and extracted with CH_2Cl_2 (3x20mL). After drying (Na_2SO_4), filtering and removing the solvent from the basic organic extracts it was possible to recover, after crystallization (hexanes/EtOAc) pure (+)-(*S*,*S*)-pseudoephedrine in c.a. 83% yield. The collected organic acidic fractions were dried over Na_2SO_4, filtered and the solvent was removed *in vacuo* yielding the wanted acids **4a-k, 5a, 5e, 5i, 5m, 5r** and **5s** as pure compounds as their ^{1}H- and ^{13}C-NMR spectra indicated.

(+)-(*R*)-3,4-Dimethylpentanoic acid (4b).



Carboxylic acid **4b** (87mg, 0.67mmol) was obtained as a yellowish oil starting from amide **2b** (0.21g, 0.75mmol) according to the general procedure. Yield: 89%. $[\alpha]_D^{20}$= +7.6 (*c*=1.00, C_6H_6) (Lit.[2] $[\alpha]_D^{20}$= –6.95, *c*=1.18, C_6H_6 for the *S* isomer). ^{1}H-NMR (δ, ppm): 0.89 (m, 9H); 1.61 (m, 1H); 1.88 (m, 1H); 2.06 (dd, 1H, *J*=15.0, 9.1Hz,); 2.38 (m, 1H, *J*=14.6, 5.2Hz); 10.2-11.0 (bs, 1H). ^{13}C-NMR (δ, ppm): 15.7; 18.2; 19.7; 31.9; 35.7; 39.0; 180.6. IR ($CHCl_3$): 3035 (OH); 1711 (C=O). MS (EI) *m/z* (Rel. Int.): 130 (M^+, 12), 96 (33), 81 (100), 79 (73), 68 (20), 65 (11), 51 (75).

(+)-(*R*)-3,4,4-Trimethylpentanoic acid (4c).

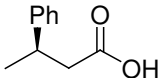


Carboxylic acid **4c** (0.12g, 0.85mmol) was obtained as a yellowish oil starting from amide **2c** (0.25g, 0.85mmol) according to the general procedure. Yield: 99%. $[\alpha]_D^{20}$= +19.6 (*c*=0.9, EtOH) (Lit.[3] $[\alpha]_D^{20}$= +21.7, *c*=0.9, EtOH). ^{1}H-NMR (δ, ppm): 0.82 (s, 9H); 1.02 (d, 3H, *J*= 6.5 Hz); 1.82 (m, 1H); 2.01 (m, 1H); 2.43 (m, 1H); 10.5-11.0 (bs, 1H). ^{13}C-

[2] Enders, D.; Rendebach, B. E. M. *Tetrahedron* **1986**, *42*, 2235.
[3] Zhang, W.-Y.; Jakiela, D. J.; Maul, A.; Knors, C.; Lauher, J. W.; Helquist, P.; Enders, D. *J. Am. Chem. Soc.* **1988**, *110*, 4652.

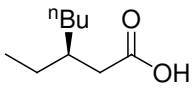
NMR (δ, ppm): 14.7; 15.4; 22.7; 25.3; 36.6; 180.7. IR ($CHCl_3$): 3027 (OH); 1711 (C=O). MS (EI) *m/z* (Rel. Int.): 144 (M^+, 9), 118 (20), 97 (15), 91 (24), 77 (26), 65 (100), 51 (16).

(-)-(*R*)-3-Phenylbutanoic acid (4d).



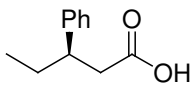
Carboxylic acid **4d** (0.17g, 0.96mmol) was obtained as a yellowish oil starting from amide **2d** (0.35g, 1.12mmol) according to the general procedure. Yield: 91%. $[\alpha]_D^{20}$= –42.3 (*c*=0.70, C_6H_6) (Lit.[4] $[\alpha]_D^{20}$= –45.8, *c*=0.77, C_6H_6). ^{1}H-NMR (δ, ppm): 1.36 (t, 3H, *J*=7.2Hz); 2.68 (m, 2H); 3.35 (m, 1H); 7.33 (m, 5H); 11.2-11.9 (bs, 1H). ^{13}C-NMR (δ, ppm): 21.8; 36.0; 42.5; 126.4; 126.6; 128.5; 145.3; 179.1. IR ($CHCl_3$): 3028 (OH); 1707 (C=O). MS (EI) *m/z* (Rel. Int.): 164 (M^+, 17), 118 (16), 105 (100), 85 (23), 79 (16), 77 (17), 57 (15).

(-)-(*S*)-3-Ethylheptanoic acid (4e).



Carboxylic acid **4e** (46mg, 0.31mmol) was obtained as a yellowish oil starting from amide **2e** (0.12g, 0.39mmol) according to the general procedure. Yield: 75%. $[\alpha]_D^{20}$= –3.4 (*c*=0.02, $CHCl_3$) (Lit.[5] $[\alpha]_D^{20}$= –1.15, *c*=0.02). ^{1}H-NMR (δ, ppm): 0.88 (m, 6H); 1.27 (m, 8H); 1.79 (m, 1H); 2.26 (d, 2H, *J*=6.9Hz); 9.2-9.8 (bs, 1H). ^{13}C-NMR (δ, ppm): 10.7; 14.0; 22.8; 26.2; 28.7; 32.9; 36.2; 38.6; 180.4. IR ($CHCl_3$): 3030 (OH); 1705 (C=O). MS (EI) *m/z* (Rel. Int.): 158 (M^+, 8), 111 (13), 97 (29), 85 (47), 83 (32), 73 (15), 71 (64), 60 (20), 57 (100).

(-)-(*R*)-3-Phenylpentanoic acid (4f).

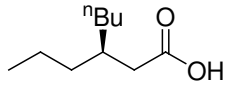


Carboxylic acid **4f** (84mg, 0.45mmol) was obtained as a yellowish oil starting from amide **2f** (0.15g, 0.46mmol) according to the general procedure. Yield: 99%. $[\alpha]_D^{20}$= –41.7 (*c*=0.30, $CHCl_3$) (Lit.[6] $[\alpha]_D^{20}$= –43.64, *c*=0.35, $CHCl_3$). ^{1}H-NMR (δ, ppm): 0.83 (t, 3H, *J*=7.5Hz); 1.66 (m, 2H); 2.66 (m, 2H); 3.01 (m, 1H); 7.30 (m, 5H); 10.8-11.6 (bs,

[4] Suzuki, I.; Kin, H.; Yamamoto, Y. *J. Am. Chem. Soc.* **1993**, *115*, 10139.
[5] Norsikian, S.; Marek, I.; Klein, S., Poisson, J. F.; Normant, J. F. *Chem. Eur. J.* **1999**, 2055.
[6] Chiacchio, U.; Corsaro, A.; Gambera, G., Rescifina, A.; Piperno, A.; Romeo, R.; Romeo, G. *Tetrahedron: Asymmetry* **2002**, *13*, 1915

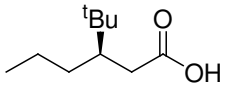
1H). ^{13}C-NMR (δ, ppm): 11.8; 29.0; 41.1; 43.4; 126.4; 127.4; 128.4; 143.5; 179.1. IR ($CHCl_3$): 2962 (OH); 1707 (C=O). MS (EI) *m/z* (Rel. Int.): 178 (M^+, 15), 118 (37), 107 (76), 97 (10), 91 (77), 83 (100), 79 (35); 77 (29); 71 (28), 57 (49).

(+)-(*S*)-3-Propylheptanoic acid (4g).



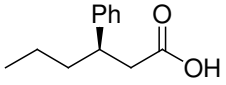
Carboxylic acid **4g** (81mg, 0.47mmol) was obtained as a yellowish oil starting from amide **2g** (0.19g, 0.59mmol) according to the general procedure. Yield: 79%. $[\alpha]_D^{20}$= +48.7 (*c*=0.25, $CHCl_3$). ^{1}H-NMR (δ, ppm): 0.88 (m, 6H); 1.28 (m, 10H); 1.86 (m, 1H); 2.26 (d, 2H, *J*=6.8Hz); 10.8-11.4 (bs, 1H). ^{13}C-NMR (δ, ppm): 14.0; 14.2; 19.6; 22.8; 28.6; 33.4; 36.1; 39.1; 180.6. IR ($CHCl_3$): 3380 (OH); 1620 (C=O). MS (EI) *m/z* (Rel. Int.): 172 (M^+, 6), 145 (12), 117 (10); 91 (30); 77 (100), 51 (12). Anal. Calcd. for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.85; H, 11.86

(-)-(*R*)-3-*tert*-Butylhexanoic acid (4h).



Carboxylic acid **4h** (29mg, 0.16mmol) was obtained as a yellowish oil starting from amide **2h** (62mg, 0.19mmol) according to the general procedure. Yield: 87%. $[\alpha]_D^{20}$= –14.7 (*c*=1.2, $CHCl_3$). ^{1}H-NMR (δ, ppm): 0.86 (s, 9H); 0.92 (t, 3H, *J*=7.3Hz); 0.96 (d, 3H, *J*= 6.5 Hz); 1.43 (m, 4H); 1.54 (m, 1H); 2.11 (dd, 1H, *J*=15.2, 6.3Hz); 2.45 (dd, 1H, *J*=15.2, 5.3Hz). ^{13}C-NMR (δ, ppm): 14.4; 21.7; 27.3; 33.4; 33.5; 35.9; 44.6; 181.5. IR ($CHCl_3$): 3375 (OH); 1710 (C=O). MS (EI) *m/z* (Rel. Int.): 172 (M^+, 4), 117 (17), 97 (14), 85 (54), 83 (73); 71 (18); 57 (100). Anal. Calcd. for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.62; H, 11.94.

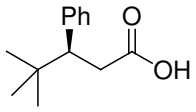
(-)-(*R*)-3-Phenylhexanoic acid (4i).



Carboxylic acid **4i** (0.25g, 1.45mmol) was obtained as a yellowish oil starting from amide **2i** (0.52g, 1.53mmol) according to the general procedure. Yield: 97%. $[\alpha]_D^{20}$= –48.3 (*c*=01.1, $CHCl_3$). ^{1}H-NMR (δ, ppm): 0.92 (t, 3H, *J*=7.3Hz); 1.23 (m, 2H); 1.66 (m, 2H); 2.70 (d, 1H, *J*=6.9Hz); 3.16 (m, 1H); 11.4-12.0 (bs, 1H). ^{13}C-NMR (δ, ppm): 13.8; 20.3; 38.3; 41.5; 126.4; 127.3; 128.4; 143.8; 179.0. IR ($CHCl_3$): 3350 (OH); 1703 (C=O). MS (EI) *m/z* (Rel. Int.): 192 (M^+, 6), 132 (30), 117 (11), 107 (78), 104 (15); 91

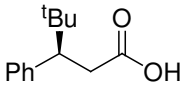
(100); 85 (16), 83 (26), 79 (27), 77 (27), 51 (10). Anal. Calcd. for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.08; H, 8.43.

(+)-(*R*)-5,5-Dimethyl-3-phenylhexanoic acid (4j).



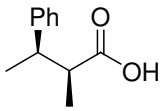
Carboxylic acid **4j** (33mg, 0.16mmol) was obtained as a yellowish oil starting from amide **2j** (87mg, 0.24mmol) according to the general procedure. Yield: 64%. $[\alpha]_D^{20}$= +19.7 (*c*=2.2, $CHCl_3$) (Lit.[7] $[\alpha]_D^{20}$= –20.4, *c*=2.2, $CHCl_3$ for the *S* isomer). ^{1}H-NMR (δ, ppm): 0.88 (s, 9H); 2.71 (m, 2H); 2.95 (dd, 1H, *J*=10.4, 4.5Hz); 9.5-10.5 (bs, 1H). ^{13}C-NMR (δ, ppm): 27.8; 33.6; 35.4; 51.7; 126.4; 127.6; 129.2; 141.3; 179.3. IR ($CHCl_3$): 3340 (OH); 1708 (C=O). MS (EI) *m/z* (Rel. Int.): 206 (M^+, 4), 150 (23), 104 (20), 91 (15), 85 (69), 83 (100), 71 (16), 57 (67), 55 (12).

(-)-(*S*)-5,5-Dimethyl-3-phenylhexanoic acid (4k).



Carboxylic acid **4k** (0.23g, 1.08mmol) was obtained as a yellowish oil starting from amide **2k** (0.39g, 1.09mmol) according to the general procedure. Yield: 99%. $[\alpha]_D^{20}$= –19.8 (*c*=2.2, $CHCl_3$) (Lit.[7] $[\alpha]_D^{20}$= –20.4, *c*=2.2, $CHCl_3$). The rest of spectroscopic properties recorded were identical to those of its enantiomer **4j**.

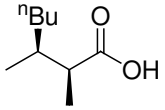
(+)-(2*S*,3*R*)-2-methyl-3-phenylbutanoic acid (5a).



Carboxylic acid **5a** (166mg, 0.93mmol) was obtained as a yellowish oil starting from amide **3a** (0.31g, 0.95mmol) according to the general procedure. Yield: 98%. $[\alpha]_D^{20}$= +11.3 (*c*=0.30, $CHCl_3$). ^{1}H-NMR (δ, ppm): 1.02 (d, 3H, *J*=7.2Hz); 1.38 (d, 3H, *J*=7.2Hz); 2.61 (m, 1H); 2.98 (m, 1H); 7.33 (m, 5H); 9.2-10.4 (bs, 1H). ^{13}C-NMR (δ, ppm): 16.2; 20.8; 43.1; 46.8; 126.6; 127.6; 128.5; 143.9; 183.1. IR ($CHCl_3$): 1964 (OH); 1889 (C=O). MS (EI) *m/z* (Rel. Int.): 178 (M^+, 5), 117 (4), 105 (73), 85 (69), 83 (100), 87 (15). Anal. Calcd. for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.01; H, 8.11.

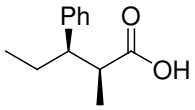
[7] Tanaka, K.; Fu, G. C. *J. Org. Chem.* **2001**, *66*, 8177.

(+)-(2*S*,3*S*)-2,3-dimethylpentanoic acid (5e).



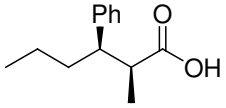
Carboxylic acid **5e** (131mg, 0.82mmol) was obtained as a yellowish oil starting from amide **3e** (0.27g, 0.88mmol) according to the general procedure. Yield: 93%. $[\alpha]_D^{20}$= +38.7 (c = 0.4, $CHCl_3$). ^{1}H-NMR (δ, ppm): 0.90 (m, 6H), 1.31 (m, 9H), 1.69 (m, 1H), 2.38 (m, 1H). ^{13}C-NMR (δ, ppm): 13.0; 13.2; 17.3; 22.6; 28.7; 32.2; 35.1; 44.2; 182.6. IR ($CHCl_3$): 1706 (C=O), 3010 (OH). MS (EI) *m/z* (Rel. Int.): 159 (M^+, 7), 144 (3), 115 (12), 105 (73), 85 (100). Anal. Calcd. for $C_9H_{18}O_2$: C, 68.31; H, 11.47. Found: C, 68.44; H, 11.56.

(+)-(2*S*,3*R*)-2-methyl-3-phenylpentanoic acid (5i).



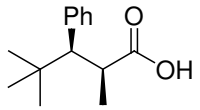
Carboxylic acid **5i** (127mg, 0.66mmol) was obtained as a yellowish oil starting from amide **3i** (0.28g, 0.83mmol) according to the general procedure. Yield: 80%. $[\alpha]_D^{20}$= +5.1 (*c*=0.3, $CHCl_3$). ^{1}H-NMR (δ, ppm): 0.81 (t, 3H, *J* = 7.2 Hz), 0.97 (d, 3H, *J* = 7.4 Hz), 1.35 (m, 1H); 1.42 (m, 1H); 2.58 (m, 1H), 2.65 (m, 1H), 7.42 (m, 5H), 9.50 (bs, 1H).^{13}C-NMR (δ, ppm): 13.6; 15.4; 28.4; 43.8; 47.6; 126.7; 127.5; 128.1; 141.7; 181.9. IR ($CHCl_3$): 1970 (OH); 1884 (C=O). MS (EI) *m/z* (Rel. Int.): 192 (M^+, 17), 177 (9), 133 (15), 85 (58), 83 (100). Anal. Calcd. for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.08; H, 8.48.

(+)-(2*S*,3*R*)-2-methyl-3-phenylhexanoic acid (5m).



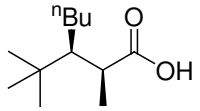
Carboxylic acid **5m** (173mg, 0.84mmol) was obtained as a yellowish oil starting from amide **3m** (0.30g, 0.85mmol) according to the general procedure. Yield: 99%. $[\alpha]_D^{20}$= +7.8 (c = 0.5, $CHCl_3$). ^{1}H-NMR (δ, ppm): 0.81 (t, 3H, *J* = 7.1 Hz), 0.94 (d, 3H, *J* = 7.3 Hz), 1.06 (m, 2H), 1.65 (m, 2H), 2.69 (m, 1H), 2.77 (m, 1H), 7.29 (m, 5H), 8.44 (bs, 1H).^{13}C-NMR (δ, ppm): 13.8; 16.0; 20.5; 36.6; 46.0; 48.5; 126.4; 127.4; 128.2; 141.9; 182.4. IR ($CHCl_3$): 1648 (OH); 3439 (C=O). MS (EI) *m/z* (Rel. Int.): 206 (M^+, 12), 191 (7), 105 (54), 85 (17), 83 (100), 58 (8). Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.77; H, 8.86.

(-)-(2*S*,3*S*)-2,4,4-trimethyl-3-phenylpentanoic acid (5r).



Carboxylic acid **5r** (107mg, 0.48mmol) was obtained as a yellowish oil starting from amide **3r** (0.18g, 0.49mmol) according to the general procedure. Yield: 99%. $[\alpha]_D^{20}$= -4.4 (c = 0.8, $CHCl_3$). ^{1}H-NMR (δ, ppm): 0.90 (m, 12H), 2.90 (m, 2H), 7.20 (m, 5H). ^{13}C-NMR (δ, ppm): 18.7; 28.5; 34.7; 39.9; 58.1; 126.0; 127.2; 130.1; 141.2; 184.0. IR ($CHCl_3$): 1705 (C=O), 3225 (OH). MS (EI) *m/z* (Rel. Int.): 220 (M^+, 1), 215 (18), 160 (22), 101 (58), 85 (91), 57 (100). Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.21; H, 9.07.

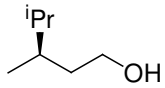
(+)-(2*S*,3*S*)-3-*tert*-Butyl-2-methylheptanoic acid (5s).



Carboxylic acid **5s** (95mg, 0.47mmol) was obtained as a yellowish oil starting from amide **3s** (0.21g, 0.61mmol) according to the general procedure. Yield: 78%. $[\alpha]_D^{20}$= +44.1 (c = 0.07, $CHCl_3$). ^{1}H-NMR (δ, ppm):): 0.87 (m, 12H), 1.13 (d, 3H, *J* = 7.1 Hz), 1.39 (m, 6H), 1.79 (m, 1H), 2.77 (m, 1H). ^{13}C-NMR (δ, ppm): 12.1; 13.9; 23.0; 25.9; 27.3; 28.5; 31.8; 38.5; 49.0; 184.3. IR ($CHCl_3$): 1645 (C=O), 3426 (OH). MS (EI) *m/z* (Rel. Int.): 200 (M^+, 2), 105 (21), 153 (48), 85 (100), 57 (62). Anal. Calcd. for $C_{12}H_{24}O_2$: C, 71.95; H, 12.08. Found: C, 71.89; H, 12.14.

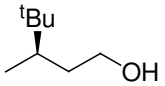
4.- LAB-mediated reduction. Synthesis of alcohols 8b-k

(+)-(*R*)-3,4-Dimethylpentan-1-ol (8b).



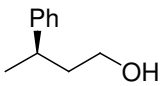
Alcohol **8b** (100mg, 0.86mmol) was prepared according to the general procedure starting from amide **3b** (0.38g, 1.37mmol), ^{n}BuLi (7.6 mL of a 0.7M solution in hexanes, 5.36 mmol), $^{i}Pr_2NH$ (0.7mL, 5.36mmol) and $BH_3{\cdot}NH_3$ (0.19g 5.48mmol) and isolated as a yellowish oil after flash column chromatography purification (hexanes/AcOEt 8:2). Yield: 63%. $[\alpha]_D^{20}$= + 13.2 (*c*=1.0, $CHCl_3$) (Lit.[5] $[\alpha]_D^{20}$= –13.5, neat for the *S* isomer). ^{1}H-NMR (δ, ppm): 0.85 (m, 9H); 1.47 (m, 5H); 3.66 (m, 2H). ^{13}C-NMR (δ, ppm): 15.4; 17.9; 20.2; 31.7; 35.0; 38.2; 61.5. IR ($CHCl_3$): 3204 (OH). MS (EI) *m/z* (Rel. Int.): 130 (M^+, 35), 115 (33), 99 (100), 85 (27), 65 (36), 59 (12), 52 (26). MS (EI) *m/z* (Rel. Int.): 116 (M^+, 5), 101 (33), 91 (100), 79 (15), 65 (30), 55 (32), 52 (23).

(+)-(*R*)-3,4,4-Trimethylpentan-1-ol (8c).



Alcohol **8c** (132mg, 1.00mmol) was prepared according to the general procedure starting from amide **3c** (0.39g, 1.35mmol), ^{n}BuLi (5.4 mL of a 1.0M solution in hexanes, 5.43mmol), $^{i}Pr_2NH$ (0.7mL, 5.43mmol) and $BH_3{\cdot}NH_3$ (0.18 g 5.43 mmol) and isolated as a yellowish oil after flash column chromatography purification (hexanes/AcOEt 8:2). Yield: 75%. $[\alpha]_D^{20}$= +23.7 (*c*=3.32, EtOH) (Lit.[8] $[\alpha]_D^{20}$= +27.5, *c*=3.32, EtOH). ^{1}H-NMR (δ, ppm): 0.76 (t, 3H, *J*=7.2Hz); 0.82 (s, 9H); 1.25 (m, 2H); 1.74 (m, 1H); 2.27 (bs, 1H); 3.55 (m, 1H); 3.67 (m, 1H). ^{13}C-NMR (δ, ppm): 14.3; 32.7; 34.7; 39.2; 62.1. IR ($CHCl_3$): 3440 (OH). MS (EI) *m/z* (Rel. Int.): 130 (M^+, 7), 115 (28), 91 (100), 79 (12), 65 (43), 55 (12), 51 (14).

(+)-(*R*)-3-Phenylbutan-1-ol (8d).

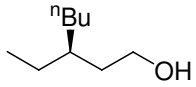


Alcohol **8d** (85mg, 0.57mmol) was prepared according to the general procedure starting from amide **3d** (0.24g, 0.79mmol), ^{n}BuLi (4.4 mL of a 0.7M solution in hexanes, 3.12 mmol), $^{i}Pr_2NH$ (0.4mL, 3.12mmol) and $BH_3{\cdot}NH_3$ (100mg 3.12 mmol) and isolated as a yellowish oil after flash column chromatography purification (hexanes/AcOEt 8:2).

[8] Giacomelli, G.; Lardicci, L.; Caporusso, A. M. *J. Chem. Soc. Perkin Trans. 1* **1975**, 1795.

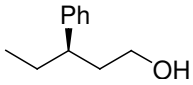
Yield: 72%. $[\alpha]_D^{20}$= +1.3 (*c*=1.02, $CHCl_3$) (Lit.[9] $[\alpha]_D^{20}$= -1.28, *c*=1.02, $CHCl_3$ for the *S* isomer). ^{1}H-NMR (δ, ppm): 1.25 (d, 3H, *J*=6.9Hz); 1.87 (m, 2H); 2.80 (m, 1H); 3.62 (m, 2H); 7.26 (m, 5H). ^{13}C-NMR (δ, ppm): 21.7; 35.4; 40.3; 65.4; 126.2; 126.8; 127.3 145.3; IR ($CHCl_3$): 3355 (OH). MS (EI) m/z (Rel. Int.): 132 (M^+-18, 32), 117 (100), 105 (70), 96 (65); 85 (40), 83 (32), 79 (25), 77 (33), 69 (45), 55 (23).

(-)-(*S*)-3-Ethylheptan-1-ol (8e).



Alcohol **8e** (37mg, 0.26mmol) was prepared according to the general procedure starting from amide **3e** (0.12g, 0.39mmol), ^{n}BuLi (1.56 mL of a 1.0M solution in hexanes, 1.56 mmol), $^i Pr_2NH$ (0.22mL, 1.56mmol) and $BH_3{\cdot}NH_3$ (33mg 1.56mmol) and isolated as a yellowish oil after flash column chromatography purification (hexanes/AcOEt 9:1). Yield: 65%. $[\alpha]_D^{20}$= –2.4 (*c*=1.0, $CHCl_3$) (Lit[5] $[\alpha]_D^{20}$= –0.32, *c*=0.05, $CHCl_3$). ^{1}H-NMR (δ, ppm): 0.83 (m, 6H); 1.26 (m, 8H); 1.54 (m, 2H); 3.63 (d, 2H, *J*=6.1Hz). ^{13}C-NMR (δ, ppm): 10.7; 14.1; 23.0; 25.9; 28.8; 32.8; 35.5; 36.4; 61.3. IR ($CHCl_3$): 3447 (OH). MS (EI) *m/z* (Rel. Int.): 126 (M^+-18, 5), 106 (56), 92 (42), 77 (81), 63 (100), 51 (42).

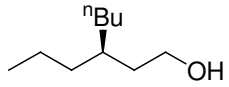
(+)-(*R*)-3-Phenylpentan-1-ol (8f).



Alcohol **8f** (55mg, 0.34mmol) was prepared according to the general procedure starting from amide **3f** (0.14g, 0.43mmol), ^{n}BuLi (2.8 mL of a 0.6M solution in hexanes, 1.74 mmol), $^i Pr_2NH$ (0.2mL, 1.74mmol) and $BH_3{\cdot}NH_3$ (53mg 1.74mmol) and isolated as a yellowish oil after flash column chromatography purification (hexanes/AcOEt 8:2). Yield: 78%. $[\alpha]_D^{20}$= +6.3 (*c*=0.95, $CHCl_3$) (Lit.[10] $[\alpha]_D^{20}$= –7.0, *c*=0.95, $CHCl_3$ for the *S* isomer). ^{1}H-NMR (δ, ppm): 0.78 (t, 3H, *J*=7.1Hz); 1.65 (m, 2H); 1.74 (m, 1H); 1.93 (m, 1H); 2.59 (m, 1H); 3.50 (m, 1H); 7.18 (m, 3H); 7.30 (m, 2H). ^{13}C-NMR (δ, ppm): 12.0; 29.7; 39.2; 44.2; 61.1; 126.1; 127.6; 128.3; 144.9. IR ($CHCl_3$): 3454 (OH). MS (EI) *m/z* (Rel. Int.): 164 (M^+, 26), 125 (61), 113 (73), 99 (100), 85 (12), 73 (6), 59 (7).

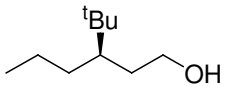
[9] Ito, H.; Nagahara, T.; Ishihara, K.; Saito, S.; Yamamoto, H. *Angew. Chem. Int. Ed.* **2004**, *43*, 994
[10] Pridgen, L. N.; Mokhallalati, M. K.; Wu, M.-J. *J. Org. Chem.* **1992**, *57*, 1237.

(-)-(*S*)-3-Propylheptan-1-ol (8g).



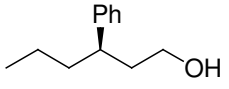
Alcohol **8g** (0.20g, 1.27mmol) was prepared according to the general procedure starting from amide **3g** (0.61g, 1.92mmol), ^{n}BuLi (10.7mL of a 0.7M solution in hexanes, 7.52 mmol), $^{i}Pr_2NH$ (1.1mL, 7.52mmol) and $BH_3{\cdot}NH_3$ (0.26g 7.51mmol) and isolated as a yellowish oil after flash column chromatography purification (hexanes/AcOEt 8:2). Yield: 66%. $[\alpha]_D^{20}$= –1.8 (*c*=1.0, $CHCl_3$). ^{1}H-NMR (δ, ppm): 0.84 (m, 6H); 1.22 (m, 10H); 1.47 (m, 3H); 2.33 (bs, 1H); 3.60 (t, 2H, *J*=7.1Hz). ^{13}C-NMR (δ, ppm): 14.0; 14.3; 19.6; 23.0; 28.7; 33.3; 33.9; 36.0; 36.7; 60.9. IR ($CHCl_3$): 3333 (OH). MS (EI) m/z (Rel. Int.): 158 (M^+, 1), 140 (3), 112 (25), 97 (22), 83 (36); 70 (56); 55 (100). Anal. Calcd. for $C_{10}H_{22}O$: C, 75.88; H, 14.01. Found: C, 75.92; H, 13.93.

(-)-(*R*)-3-*tert*-Butylhexan-1-ol (8h).



Alcohol **8h** (0.18g, 1.15mmol) was prepared according to the general procedure starting from amide **3h** (0.61g, 1.92mmol), ^{n}BuLi (10.8mL of a 0.7M solution in hexanes, 7.71mmol), $^{i}Pr_2NH$ (1.2mL, 7.71mmol) and $BH_3{\cdot}NH_3$ (0.26g 7.71mmol) and isolated as a yellowish oil after flash column chromatography purification (hexanes/AcOEt 8:2). Yield: 84%. $[\alpha]_D^{20}$= –20.7 (*c*=0.06, $CHCl_3$). ^{1}H-NMR (δ, ppm): 0.85 (s, 9H); 0.89 (t, 3H, *J*=7.3Hz); 1.34 (m, 6H); 1.40 (bs, 1H); 1.54 (m, 1H); 3.62 (m, 2H). ^{13}C-NMR (δ, ppm): 14.5; 22.8; 27.6; 33.6; 33.9; 34.8; 44.7; 63.3. IR ($CHCl_3$): 3458 (OH). MS (EI) m/z (Rel. Int.): 140 (M^+-18, 4), 95 (35), 77 (100), 63 (77), 51 (28). Anal. Calcd. for $C_{10}H_{22}O$: C, 75.88; H, 14.01. Found: C, 76.01; H, 13.88.

(-)-(*R*)-3-Phenylhexan-1-ol (8i).

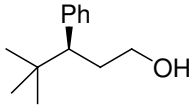


Alcohol **8i** (71mg, 0.40mmol) was prepared according to the general procedure starting from amide **3i** (0.18g, 0.54mmol), ^{n}BuLi (3.5mL of a 0.6M solution in hexanes, 2.1 mmol), $^{i}Pr_2NH$ (0.3mL, 2.1mmol) and $BH_3{\cdot}NH_3$ (70mg 2.1mmol) and isolated as a yellowish oil after flash column chromatography purification (hexanes/AcOEt 9:1). Yield: 74%. $[\alpha]_D^{20}$= –6.7 (*c*=2.0, $CHCl_3$) (Lit.[11] $[\alpha]_D^{20}$= –3.5,

[11] Chang, C.-J.; Fang, J.-M.; Liao, L.-F. *J. Org. Chem.* **1993**, *58*, 1754.

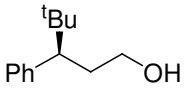
c=0.1, $CHCl_3$). ^{1}H-NMR (δ, ppm): 0.86 (t, 3H, *J*=7.2Hz); 1.18 (m, 2H); 1.59 (m, 2H); 1.89 (m, 2H); 2.70 (m, 1H); 3.50 (m, 2H); 7.18 (m, 3H); 7.33 (m, 2H). ^{13}C-NMR (δ, ppm): 14.0; 20.5; 39.1; 39.5; 42.1; 61.0; 126.0; 127.5; 128.3; 145.2. IR ($CHCl_3$): 3418 (OH). MS (EI) m/z (Rel. Int.): 178 (M^+, 7), 120 (5), 95 (30), 81 (70), 77 (100), 65 (60), 53 (16).

(-)-(*S*)-4,4-Dimethyl-3-phenylpentan-1-ol (8j).



Alcohol **8j** (72mg, 0.38mmol) was prepared according to the general procedure starting from amide **3j** (0.15g, 0.43mmol), ^{n}BuLi (2.8 mL of a 0.6M solution in hexanes, 1.74 mmol), $^i Pr_2NH$ (0.2mL, 1.74mmol) and $BH_3 \cdot NH_3$ (53mg 1.74mmol) and isolated as a yellowish oil after flash column chromatography purification (hexanes/AcOEt 8:2). Yield: 80%. $[\alpha]_D^{20}$= –7.4 (*c*=0.1, C_6H_6) (Lit.[12] $[\alpha]_D^{20}$= +7.31, *c*=1.0, C_6H_6 for the *R* isomer). ^{1}H-NMR (δ, ppm): 0.88 (s, 9H); 2.0 (m, 2H); 2.50 (dd, 1H, *J*=11.9, 3.2Hz); 2.31 (m, 1H); 3.47 (m, 1H). ^{13}C-NMR (δ, ppm): 28.1; 32.4; 33.6; 52.8; 62.1; 126.1; 127.7; 129.4; 142.3. IR ($CHCl_3$): 3320 (OH). MS (EI) m/z (Rel. Int.): 192 (M^+, 2), 178 (15), 141 (12), 125 (35), 99 (100), 85 (9), 73 (6), 58 (5).

(+)-(*R*)-4,4-Dimethyl-3-phenylpentan-1-ol (8k).

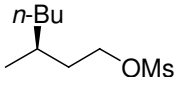


Alcohol **8k** (107mg, 0.30mmol) was prepared according to the general procedure starting from amide **3k** (0.15g, 0.43mmol), ^{n}BuLi (2.8 mL of a 0.6M solution in hexanes, 1.74 mmol), $^i Pr_2NH$ (0.2mL, 1.74mmol) and $BH_3 \cdot NH_3$ (53mg 1.74mmol) and isolated as a yellowish oil after flash column chromatography purification (hexanes/AcOEt 8:2). Yield: 71%. $[\alpha]_D^{20}$= +7.7 (*c*=0.1, $CHCl_3$) (Lit.[12] $[\alpha]_D^{20}$= +7.31, *c*=1.0, C_6H_6). The rest of spectroscopic properties recorded were identical to those of its enantiomer **7j**.

[12] Menicagli, R.; Lardicci, L. *Chem. Ind.* **1974**, 576.

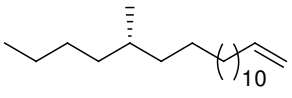
5.- Synthesis of (S)-14-methyloctadec-1-ene

(+)-(*S*)-3-Methylheptyl methanesulfonate (11a).



n-BuLi (3.7 mL of a 1.25 M solution in hexanes, 4.71 mmol) was added over a solution of diisopropylamine (0.71 mL, 5.00 mmol) in dry THF (10 mL) at –78ºC and the mixture was stirred for 15 minutes. The reaction was warmed to 0ºC and $NH_3{\cdot}BH_3$ (0.15 g, 4.8 mmol) was added at once. The mixture was stirred 15 min at 0ºC and another 15 min at room temperature, after which a solution of the amide **2a** (0.35 g, 1.2 mmol) in THF (20 mL) was added via canula at 0ºC and the reaction was stirred for 2 hours at room temperature. Then the reaction was quenched with 1M HCl (15 mL) and extracted with AcOEt (3 x 15 mL). The organic fractions were collected, washed with sat. $NaHCO_3$, dried over Na_2SO_4, filtered and the solvent removed *in vacuo.* Next, the resulting oil was dissolved in dry CH_2Cl_2 (15 mL) and the mixture was cooled down to 0ºC, at which temperature Et_3N (0.51 mL, 3.62 mmol) and MsCl (0.27 mL, 3.62 mmol) were added at once. After stirring for 2h, NH_4Cl (sat.) was added (15 mL) and the resulting mixture was extracted with Et_2O (3 x 15 mL). The organic fractions were collected, dried over Na_2SO_4, filtered and the solvent removed *in vacuo.* affording mesylate **11a** (0.20 g, 0.82 mmol) after flash column chromatography purification (hexanes/AcOEt 8:2). Yield: 89%. $[\alpha]_D^{20}$= +2.13 (*c*=0.1, $CHCl_3$) ^{1}H-NMR (δ, ppm): 0.86 (m, 6H), 1.26 (m, 6H), 1.51 (m, 3H), 1.72 (m, 1H), 2.94 (s, 3H), 4.22 (m, 2H). ^{13}C-NMR (δ, ppm): 13.1; 19.8; 22.6; 24.7; 25.2; 36.6; 37.2; 38.9; 67.5.

(+)-(*S*)-14-Methyloctadec-1-ene (12a).



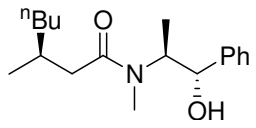
t-BuLi (1.49 mL of a 1.10 M solution in hexanes, 1.64 mmol) was added to a cooled (-78ºC) solution of 11-bromoundec-1-ene (0.17 mL, 0.82 mmol) in dry THF (10mL). After stirring for 15 min. at this temperature, a solution of mesylate **11a** (0.17 g, 0.82 mmol) in dry THF (10 mL) was added at once and the mixture was stirred for 60 min at –78ºC and for further 60 min at rt. The reaction was quenched with sat. NH_4Cl (15 mL) and the resulting mixture was extracted with Et_2O (3 x 15 mL). The organic fractions were collected, dried over Na_2SO_4, filtered and the solvent removed *in vacuo.* affording target compound **12a** (0.11 g, 0.40 mmol) after flash column chromatography purification (hexanes/AcOEt 8:2). Yield:

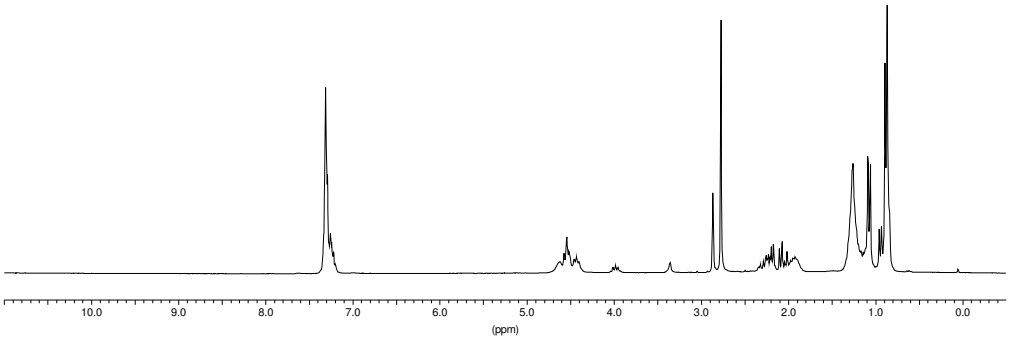
48%. $[\alpha]_D^{20}$= +0.90 (*c*=1, $CHCl_3$). Lit.[13] $[\alpha]_D^{20}$: +1.18, (*c* = 5.1, $CHCl_3$). ^{1}H-NMR (δ, ppm): 0.89 (m, 6H), 1.32 (m, 22H), 1.53 (m, 2H), 1.71 (m, 1H), 2.03 (m, 2H), 4.92 (m, 2H), 5.80 (m, 1H). The other spectroscopic and analytical data matched with those reported in the literature.

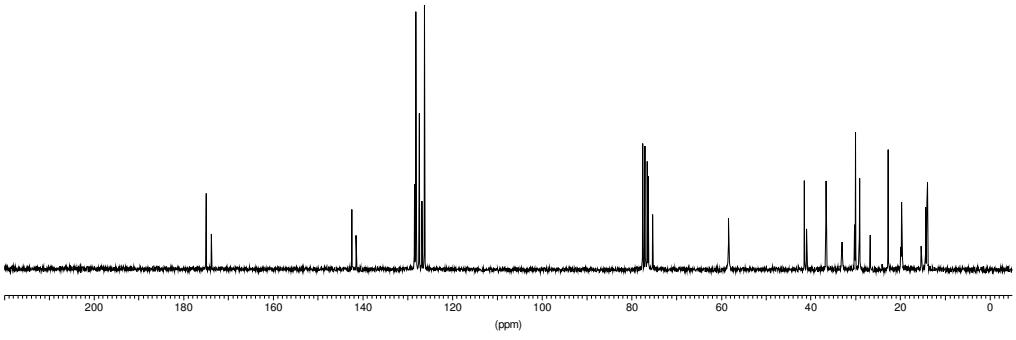
[13] Kharisov, R. Y.; Latypova, E. R.; Talipov, R. F.; Muslukhov, R. R.; Ishmuratov, G. Y.; Tolstikov, G. A. *Russ. Chem. Bull.* **2003**, *52*, 2267.

6.- ^{1}H- and ^{13}C-NMR spectra of amides 2a-k.

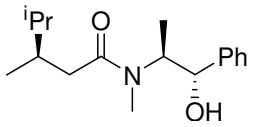
6.1.- ^{1}H- and ^{13}C-NMR espectra of amide **2a**.

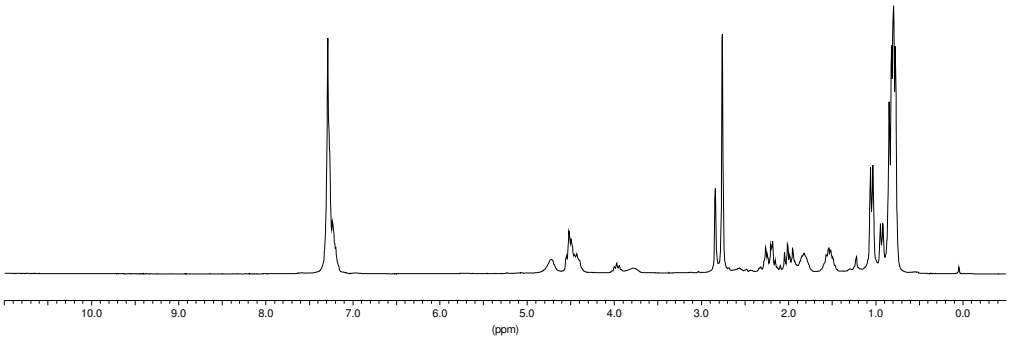


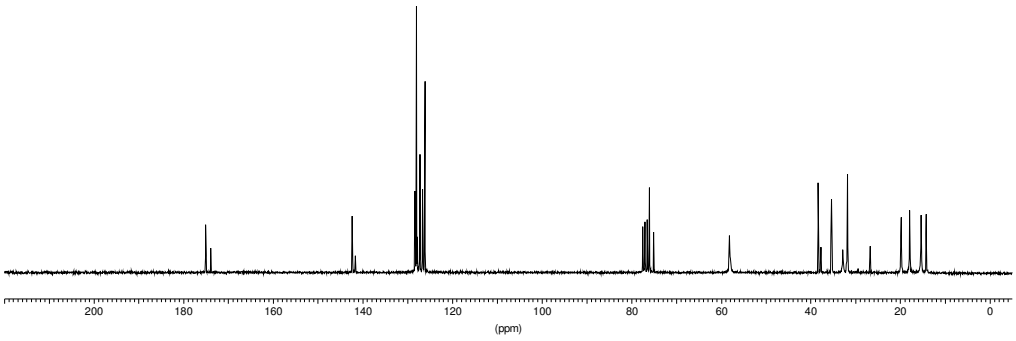




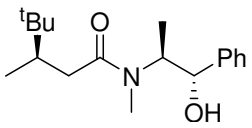
6.2.- ^{1}H- and ^{13}C-NMR espectra of amide **2b.**

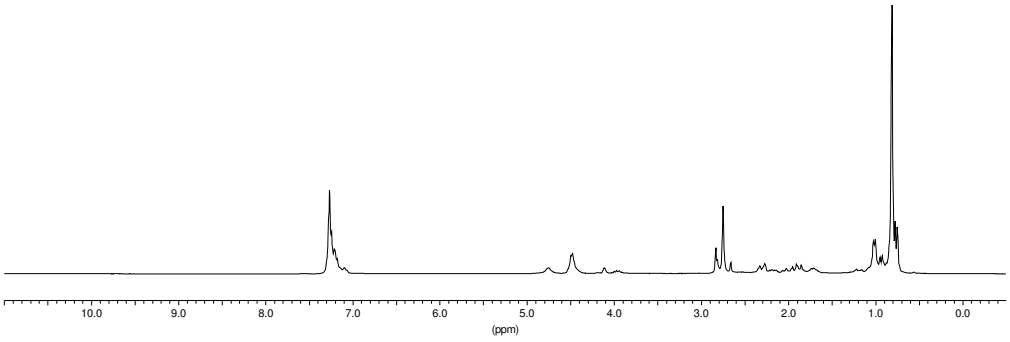


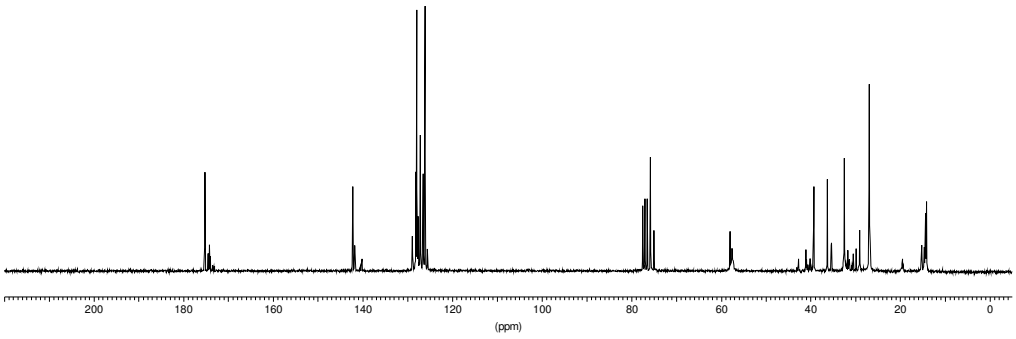




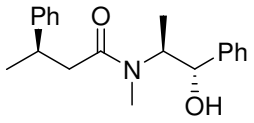
6.3.- ^{1}H- and ^{13}C-NMR espectra of amide **2c.**

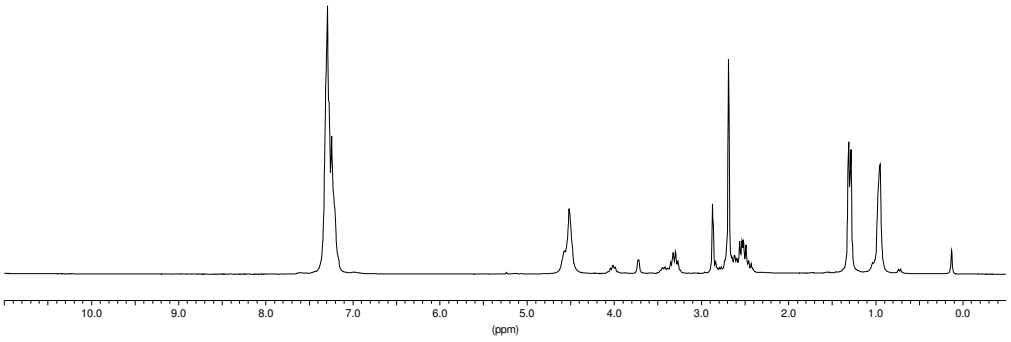


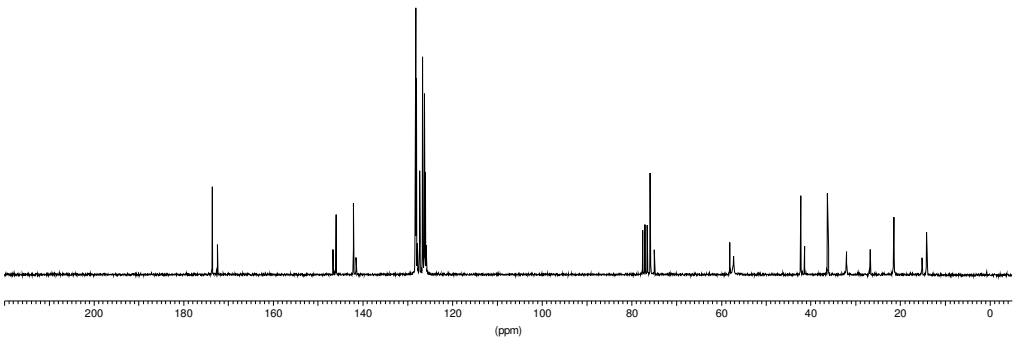




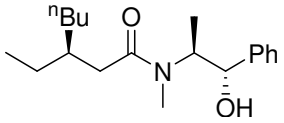
6.4.- ^{1}H- and ^{13}C-NMR espectra of amide **2d.**

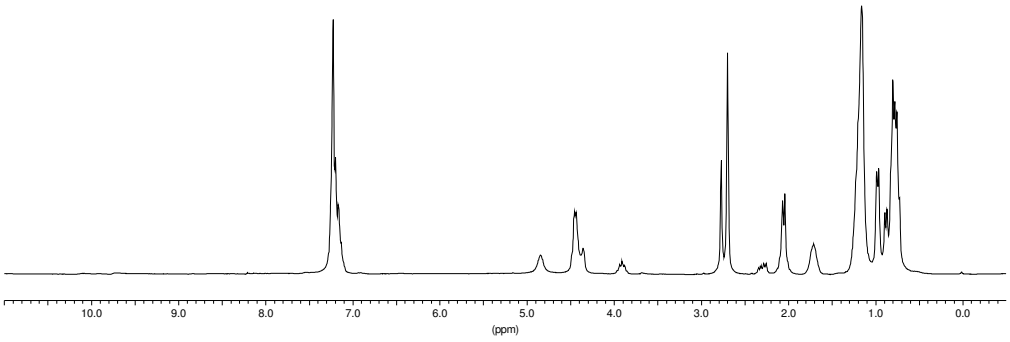


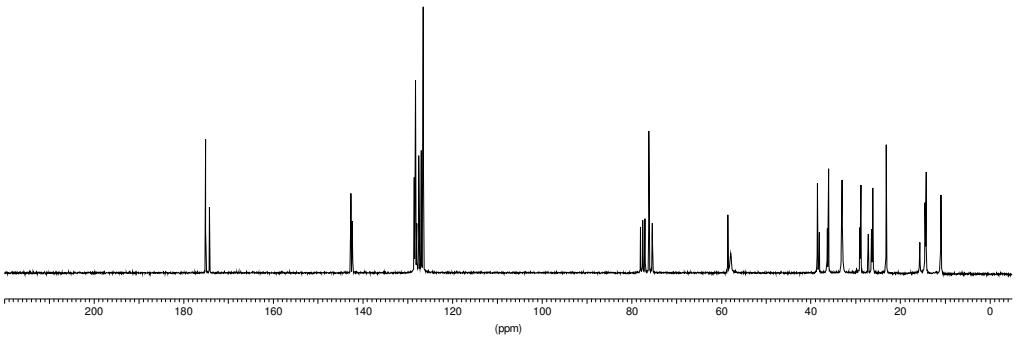




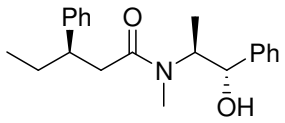
6.5.- ^{1}H- and ^{13}C-NMR espectra of amide **2e.**

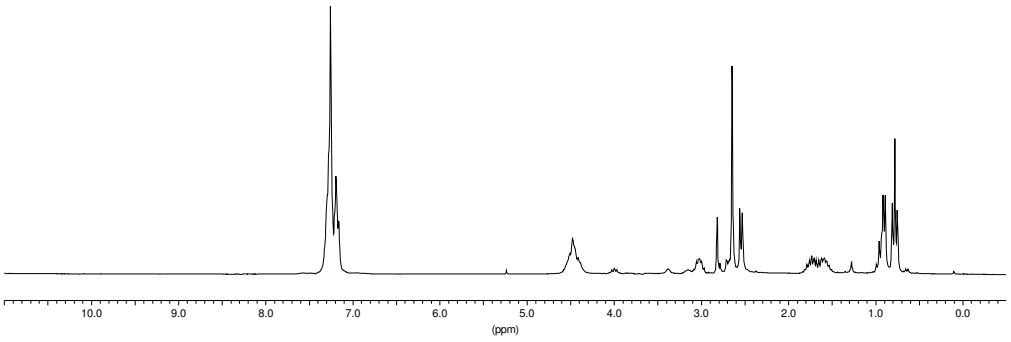


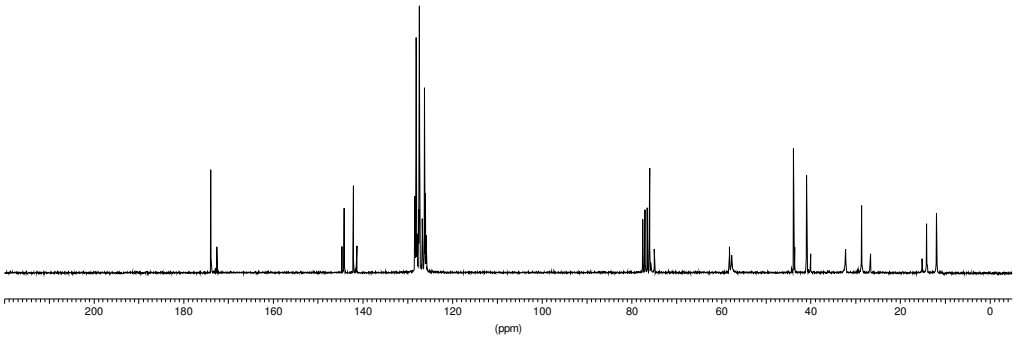




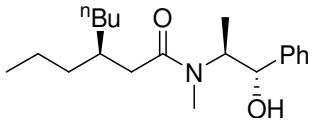
6.6.- ^{1}H- and ^{13}C-NMR espectra of amide **2f.**

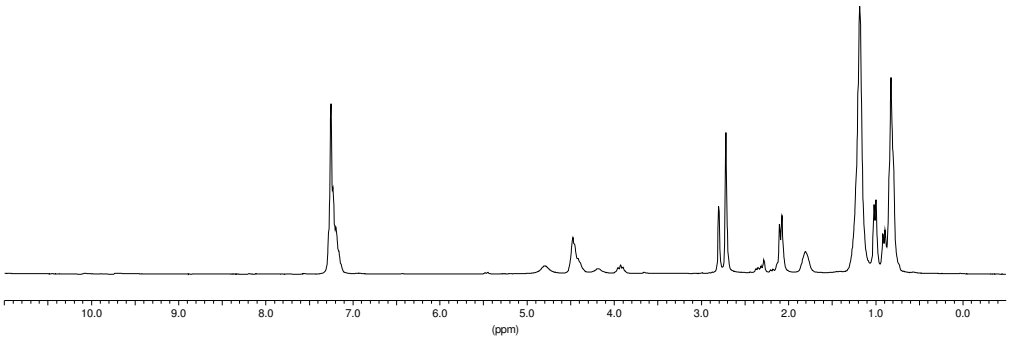


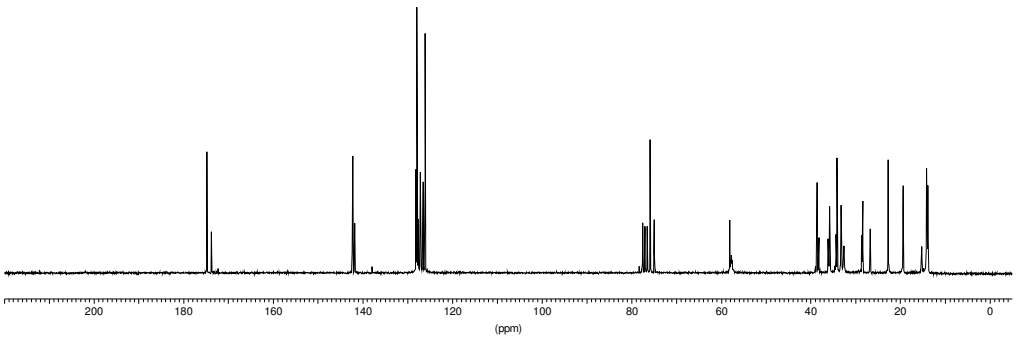




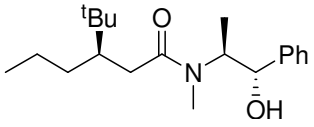
6.7.- ^{1}H- and ^{13}C-NMR espectra of amide **2g.**

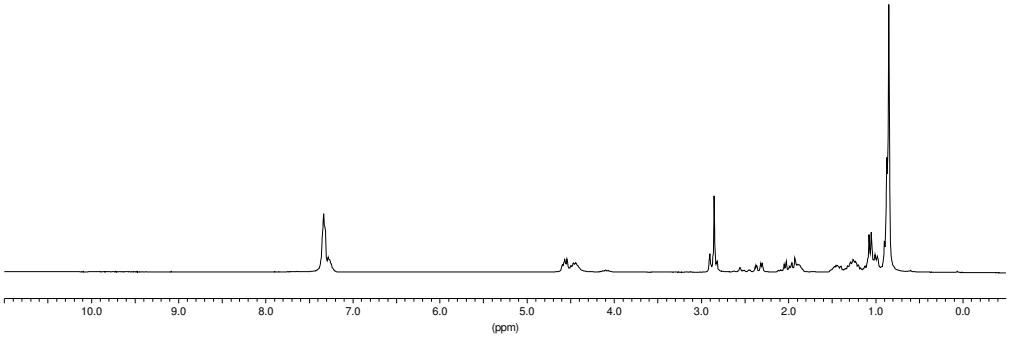


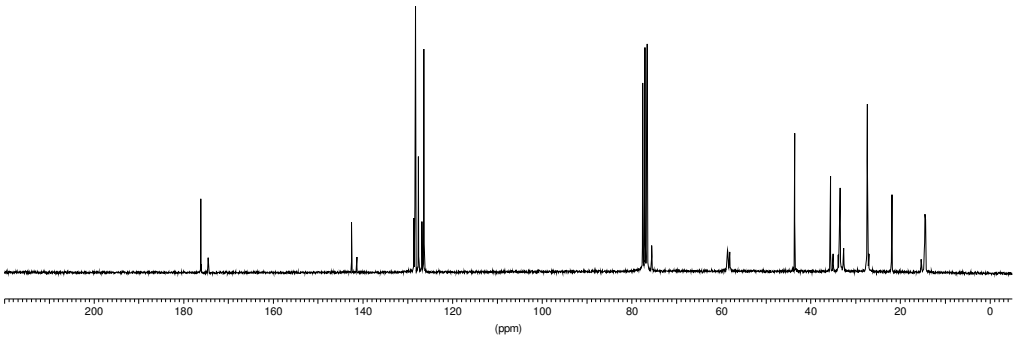




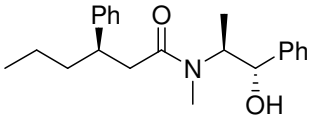
6.8.- ^{1}H- and ^{13}C-NMR espectra of amide **2h.**

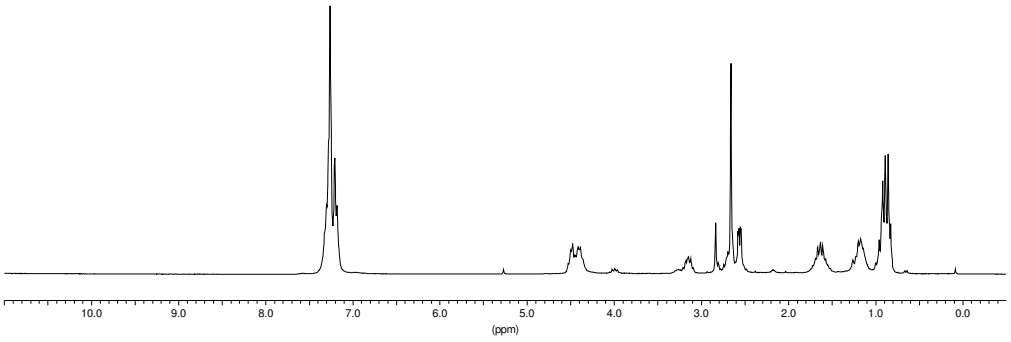


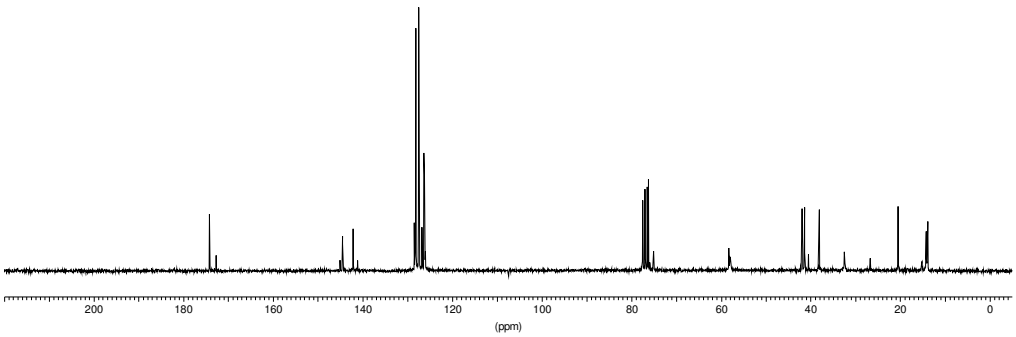




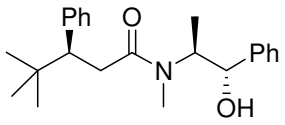
6.9.- ^{1}H- and ^{13}C-NMR espectra of amide **2i.**

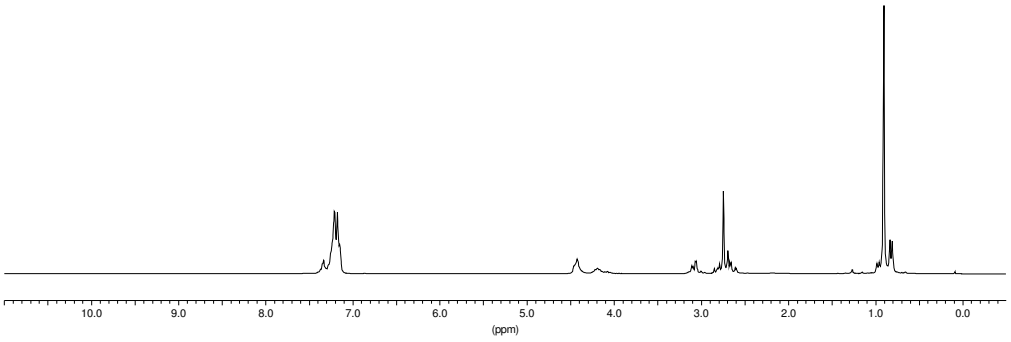


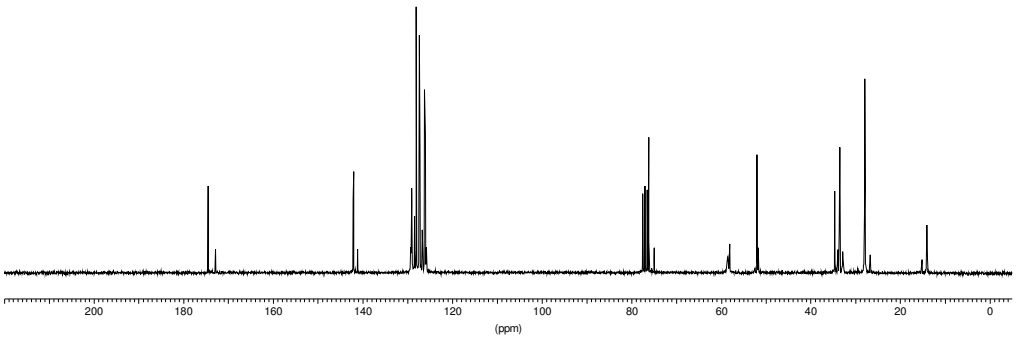




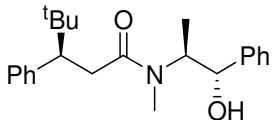
6.10.- ^{1}H- and ^{13}C-NMR espectra of amide **2j.**

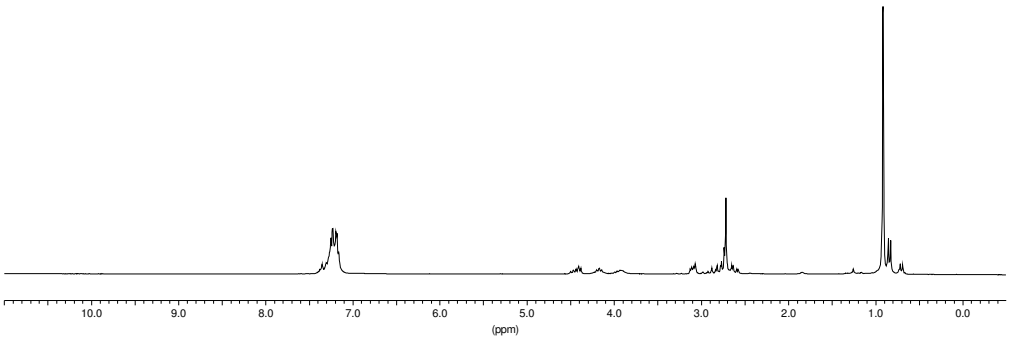


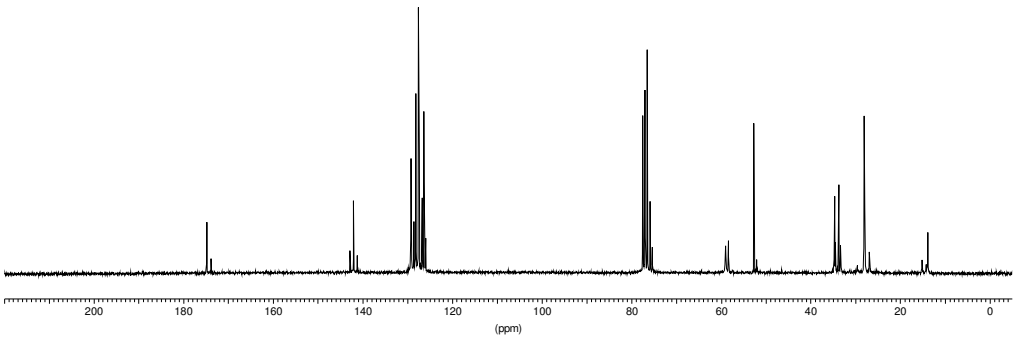




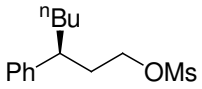
6.11.- ^{1}H- and ^{13}C-NMR espectra of amide **2k.**

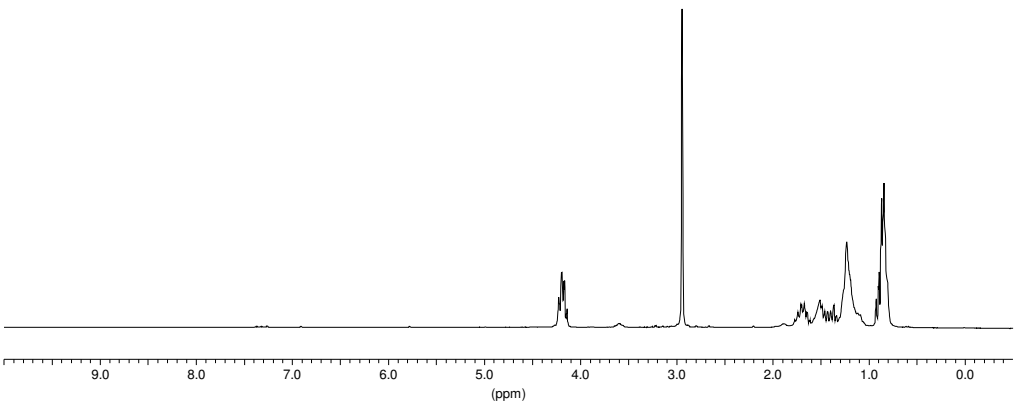


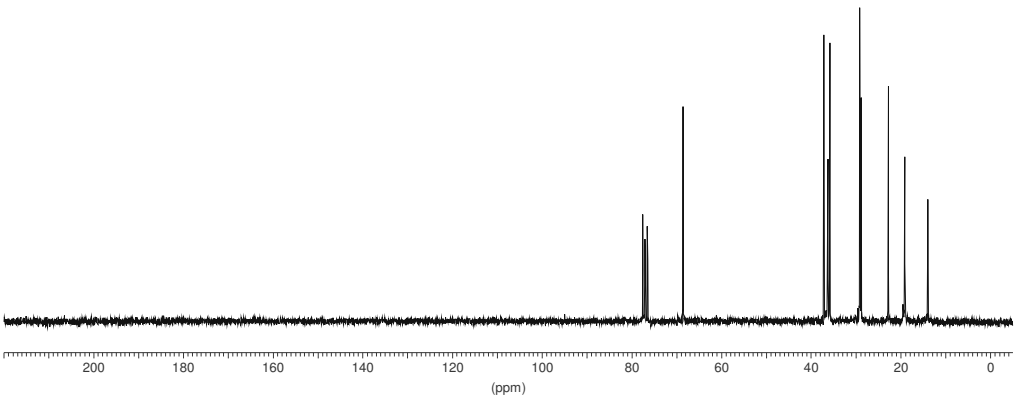




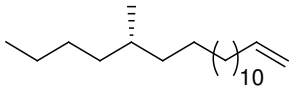
7.- ^{1}H- and ^{13}C-NMR espectra of mesylate **11a.**







8.- ^{1}H-NMR espectra of (+)-(*S*)-14-Methyloctadec-1-ene (**12a**)



(S)-14-methyloctadec-1-ene