Supporting Information

Enantioselective Synthesis of Fluorinated α-Amino Acids and Derivatives in Combination with Ring-Closing Metathesis: Intra-molecular π-Stacking Interactions as a Source of Stereocontrol

General Methods. For general details concerning the treatment of solvents and reagents, and the analytical methods, see reference 4a.

General Procedure for C=N bond Reduction in Sulfinyl *N*-Arylimines 3. To a stirred solution of β-iminosulfoxide **3** in the appropriate solvent (conc. *ca.* 1M) and temperature, an excess of reducing agent (Bu_4NBH_4) was added portion-wise (Table 1). The mixture was then stirred until total disappearance of the starting material **3** (TLC analysis). After quenching of the reaction with saturated aqueous NH_4Cl, the organic layer was separated and the aqueous phases extracted with dichloromethane. The combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo* to furnish a crude mixture of diastereomers **4**. Medium Pressure Liquid Chromatography (MPLC) or Flash Chromatography (FC) [*n*-hexanes/ethyl acetate (3:1), unless otherwise stated] provided the diastereomerically pure sulfinyl *N*-aryl amines **4**.

(-)-(2*S*,*S*$_S$)-3,3,3-Trifluoro-*N*-(*p*-methoxyphenyl)-2-aminopropyl-*p*-tolylsulfoxide (*syn*-4a). Crude mixture of *syn-anti* (88:12) diastereomers was obtained (>98%). MPLC gave the major *syn* diastereomer (*syn*-**4a**) as a white solid: mp 183-185 °C; $[\alpha]^{25}_D$ - 129.8 (*c* 0.65, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) 2.41 (s, 3H), 3.15 (dd, J_1 = 13.9 and J_2 = 9.0, 1H), 3.19 (d, J = 13.9 and J_2 = 5.4, 1H), 3.68 (d, J = 9.0, 1H), 3.77 (s, 3H), 4.19 (m, 1H), 6.59 (d, J = 8.2, 2H), 6.78 (d, J = 8.2, 2H), 7.28 (d, J = 8.0, 2H), 7.45 (d, J = 8.0, 2H); ^{13}C NMR (62.8 MHz, $CDCl_3$) 21.4, 54.1 (q, $^2J_{CF}$ = 30.1), 55.6, 57.9, 115.2, 116.5, 123.9, 125.5 (q, $^1J_{CF}$ = 280.1), 129.8, 139.4, 140.4, 143.2, 153.8; ^{19}F NMR (235 MHz, $CDCl_3$) –75.7 (J_{HF} = 6.9; 3F). Anal. Calcd. for $C_{17}H_{18}NO_2SF_3$: C, 57.14; H, 5.04; N, 3.92; S, 8.96. Found; C, 57.23; H, 4.87; N, 3.98; S, 9.02.

(-)-(2*S*,S_S)-3,3,3-Trifluoro-*N*-(*p*-methoxyphenyl)-2-aminopropyl-1-(1-naphtyl) sulfoxide (*syn*-4b). Crude mixture of *syn-anti* (99:1) diastereomers was obtained (>98%). MPLC gave the major *syn* diastereomer as a white solid: mp 149-150 °C; $[\alpha]^{25}_D$ - 399.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) 3.05 (dd, J_1 = 13.9 and J_2 = 8.2, 1H), 3.39 (dd, J_1 = 13.9 and J_2 = 4.8, 1H), 3.52 (d, J = 9.0, 1H), 3.65 (s, 3H), 4.37 (m, 1H), 6.38 (d, J = 8.8, 2H), 6.63 (d, J = 8.8, 2H), 7.34-7.91 (m, 7H); ^{13}C NMR (62.8 MHz, $CDCl_3$) 51.8 (q, $^2J_{CF}$ = 30.3), 54.7, 55.6, 114.6, 114.9, 120.9, 123.0, 123.2, 125.6, 125.9 (q, $^1J_{CF}$ = 281.4), 126.7, 127.5, 128.3, 129.1, 131.5, 133.3, 137.9, 138.6, 153.2; ^{19}F NMR (235 MHz, $CDCl_3$) –75.7 (d, J = 6.2, 3F). HRMS calc. for $C_{20}H_{18}NO_2SF_3$, 393.1010, found 393.0993. Anal. Calcd. for $C_{20}H_{18}NO_2SF_3$: C, 61.06; H, 4.58; N, 3.56; S, 8.15. Found; C, 60.98; H, 4.52; N, 3.48; S, 8.19.

(-)-(2*S*,S_S)-3,3,3-Trifluoro-*N*-(*p*-methoxyphenyl)-2-aminopropyl-1-(2-naphtyl) sulfoxide (*syn*-4c). Crude mixture of *syn-anti* (93:7) diastereomers was obtained (>98%). *Flash* chromatography on silica gel (R_f=0.45) gave *syn*-**4c** as a white solid: mp 159-160 °C; $[\alpha]^{25}_D$ – 95.3 (*c* 1.05, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) 2.90 (dd, J_1 = 13.2 and J_2 = 11.1, 1H), 3.15 (dd, J_1 = 13.2 and J_2 = 3, 1H), 3.69 (s, 3H), 4.37 (s, 1H), 6.73-8.11 (m, 11H); ^{13}C NMR (75 MHz, $CDCl_3$) 50.0 (q, $^3J_{CF}$ = 30.0), 55.6, 57.3, 114.8, 114.8, 116.4, 116.5, 119.4, 124.8, 127.5, 128.1, 128.1, 128.5, 129.9, 132.9, 134.6, 139.4, 140.1, 153.8; ^{19}F NMR (235 MHz, $CDCl_3$) –76.03 (d, J_{FH} = 5.8, 3F). HRMS calc. for $C_{20}H_{18}NO_2SF_3$ 393.1010, found 393.1019. Anal. Calcd. for $C_{20}H_{18}NO_2SF_3$: C, 61.06; H, 4.58; N, 3.56. Found; C, 61.28; H, 4.78; N, 3.65.

(-)-(2*S*,S_S)-3-Chloro-3,3-difluoro-*N*-(*p*-methoxyphenyl)-2-aminopropyl-1-(1-naphtyl)sulfoxide (*syn*-4d). Crude mixture of *syn-anti* (99:1) diastereomers was obtained (>98%). MPLC gave the major *syn* diastereomer as a white solid: mp. 145-147 °C; $[\alpha]^{25}_D$ - 239.7 (*c* 0.2, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) 3.05 (dd, J_1 = 13.9 and J_2 = 8.5, 1H), 3.46 (d, J = 9.3, 1H), 3.52 (dd, J_1 = 13.9 and J_2 = 4.3, 1H), 3.70 (s, 3H), 4.46 (m, 1H), 6.42 (d, J = 8.8, 2H), 6.66 (d, J = 8.8, 2H), 7.37-7.96 (m, 7H); ^{13}C NMR (62.8 MHz, $CDCl_3$) 55.6, 55.8, 56.8 (t, $^2J_{CF}$ = 26.0), 114.5, 115.1, 121.0, 123.3, 125.3, 125.5, 126.7, 127.5, 128.3, 129.1, 130.1 (t, $^1J_{CF}$ = 290.0), 131.5, 133.3, 134.9, 137.8, 138.6, 153.2; ^{19}F NMR (235 MHz, $CDCl_3$) –59.9 (d, J_{FH} = 4.9, 1F), –59.9 (d, J_{FH} = 4.9, 1F). HRMS calc. for $C_{20}H_{18}NO_2SF_2Cl$, 409.0714,

found 409.0718. Anal. Calcd. for $C_{20}H_{18}NO_2SF_2Cl$: C, 58.68; H, 4.40; N, 3.42; S, 7.82. Found; C, 58.91; H, 4.32; N, 3.52; S, 7.93.

(-)-(2*S*,*S*$_S$)-3,3-Difluoro-*N*-(*p*-methoxyphenyl)-2-aminopropyl-1-(1-naphtyl) sulfoxide (*syn*-4e). Crude mixture of *syn-anti* (91:9) diastereomers was obtained (>98%). *Flash* chromatography on silica gel gave the major *syn* diastereomer as a white solid: mp 121-122 °C; $[\alpha]^{23}_D$ –440.0 (*c* 0.99, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) 3.07 (dd, J_1 = 14.0 and J_2 = 5.7, 1H), 3.44 (dd, J_1 = 14.0 and J_2 = 6.1, 1H), 3.73 (m, 3H), 4.20 (m, 1H), 6.10 (t, J = 55.7, 1H), 6.43 (d, J = 7.2, 2H), 6.68 (d, J = 7.2, 2H), 7.59 (m, 3H), 7.84 (d, J = 7.3, 1H), 7.96 (m, 2H), 8.11 (d, J = 6.8, 1H); ^{13}C NMR (62.4 MHz, $CDCl_3$) 52.0 (t, $^2J_{CF}$ = 22.7), 53.0, 55.7, 114.9, 114.9 (t, $^1J_{CF}$ = 246), 115.4, 121.3,123.2, 125.6, 126.8, 127.6, 128.6, 129.1, 131.5, 133.5, 138.4, 138.7, 153.3; ^{19}F NMR (235 MHz, $CDCl_3$) -127.6 (ddd, J_{FF} = 283.0, $^1J_{FH}$ = 55.7, $^2J_{FH}$ = 9.6, 1F), -131.3 (ddd, J_{FF} = 283.0, 55.7 and 15.4, 1F); EI-MS 375 $[M]^+$. Anal. Calcd. for $C_{20}H_{19}NO_2SF_2$: C, 64.00; H, 5.06; N, 3.73. Found; C, 64.23; H, 4.91; N, 3.62.

(-)-(2*S*,*S*$_S$)-3,3,3-Trifluoro-*N*-(*o*-methoxyphenyl)-2-aminopropyl-1-(1-naphtyl) sulfoxide (*syn*-4f). Crude mixture of *syn-anti* (97:3) diastereomers was obtained (>98%). *Flash* chromatography [*n*-hexanes-EtOAc (2:1)] on silica gel (R_f=0.45) gave the major *syn* diastereomer as a white solid: mp 144-146 °C; $[\alpha]^{25}_D$ –385.5 (*c* 1.01, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) 3.15 (dd, J_1 = 13.2 and J_2 = 4.3, 1H), 3.52 (s, 3H), 3.53 (dd, J_1 = 13.3 and J_2 = 9.6, 1H), 3.97 (br d, J = 10.4, 1H), 4.48-4.51 (m, 1H), 6.64 (m, 4H), 7.20-8.87 (m, 7H); ^{13}C NMR (62.8 MHz, $CDCl_3$) 48.5 (q, $^3J_{CF}$ = 29.5), 54.1, 54.8, 109.3, 110.5, 118.2, 120.8, 123.1, 125.5 (q, $^1J_{CF}$ = 284.3), 127.6, 128.2, 128.5, 128.9, 131.1, 133.2, 134.0, 137.1, 146.3; ^{19}F NMR (235 MHz, $CDCl_3$) –75.6 (d, J_{FH} = 6.5, 3F). HRMS calc. for $C_{20}H_{18}NO_2SF_3$ 393.1010, found 393.1019. Anal. Calcd. for $C_{20}H_{18}NO_2SF_3$: C, 61.06; H, 4.58; N, 3.56. Found; C, 60.89; H, 4.53; N, 3.49.

(+)-(2*S*,*S*$_S$)-3,3,3-Trifluoro-*N*-(*p*-fluorophenyl)-2-aminopropyl-1-(1-naphtyl) sulfoxide (*syn*-4g). Crude mixture of *syn-anti* (98:2) diastereomers was obtained (>98%). *Flash* chromatography [*n*-hexanes-EtOAc (4:1)] on silica gel (R_f=0.45) gave the major *syn* diastereomer as a white solid: mp 196-198 °C; $[\alpha]^{25}_D$ +5.74 (*c* 1.18, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) 3.04 (dd, J_1 = 8.5 and J_2 = 7.0, 1H), 3.44 (dd, J_1 = 7.0 and J_2 = 4.3, 1H), 4.42 (m, 1H), 6.33-7.94 (m, 11H); ^{13}C NMR (62.8 MHz, $CDCl_3$) 51.4 (q, $^3J_{CF}$ = 31.1), 54.3, 54.8,

114.7, 114.8, 115.5, 120.8, 123.3, 125.6 (q, $^1J_{CF}$ = 284.3), 126.8, 127.4, 128.2, 128.5, 129.2, 133.4, 137.6, 140.8, 158.7; ^{19}F NMR (235 MHz, $CDCl_3$) –75.8 (d, J_{FH} = 6.1, 3F), -125.8 (m, 1F). HRMS calc. for $C_{19}H_{15}NOSF_4$, 382.0888 found 382.0888.

(-)-(2*S*,*S*$_S$)-3,3,3-Trifluoro-*N*-(1-naphtyl)-2-aminopropyl-1-(1-naphtyl)sulfoxide (*syn*-4h). Crude mixture of *syn-anti* (99:1) diastereomers was obtained (>98%). *Flash* chromatography on silica gel (R_f=0.45) gave the major *syn* diastereomer as a white solid: mp 195-196 °C; $[\alpha]^{25}_D$ –283.3 (*c* 0.99, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) 3.26 (dd, J_1 = 8.0 and J_2 = 7.0, 1H), 3.68 (dd, J_1 = 7.0 and J_2 = 4.4, 1H), 4.17 (d, J = 8.0, 1H) 4.79 (m, 1H), 6.68-7.83 (m, 14H); ^{13}C NMR (62.8 MHz, $CDCl_3$) 49.8 (q, $^3J_{CF}$ = 31.1), 54.3 ,105.9, 119.2, 119.3, 120.6, 123.2, 124.9, 125.1, 125.7, 126.0 126.6, 127.5, 127.6, 128.0, 129.3, 131.1, 133.3, 134.1, 134.1, 136.8, 139.6; ^{19}F NMR (235 MHz, $CDCl_3$) –75.2 (d, J_{FH} = 6.3, 3F). HRMS calc. for $C_{23}H_{18}NOSF_3$ 413.1061, found 413.1061.

(-)-(2*S*,*S*$_S$)-3,3-Difluoro-*N*-(*p*-methoxyphenyl)-2-amino-5-hexenyl-1-(1-naphtyl) sulfoxide (*syn*-4j). Crude mixture of *syn-anti* (99:1) diastereomers was obtained (>98%). *Flash* chromatography [*n*-hexane-EtOAc (2:1)] on silica gel (R_f=0.50) gave the major *syn* diastereomer as a white solid: m.p. 150-151 °C; $[\alpha]^{25}_D$: -491.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) 2.78-2.89 (m, 2H), 2.96 (dd, J_1 = 14.0, J_2 = 4.0, 1H), 3.50 (dd, J_1 = 14.0, J_2 = 7.0, 2H), 3.76 (s, 3H), 4.34-4.40 (m, 1H), 5.17-5.28 (m, 2H), 5.82-5.89 (m, 1H), 6.61 (d, J = 9.0, 2H), 6.78 (d, J = 9.0, 2H), 7.53-8.10 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) 39.2 (t, $^2J_{CF}$ = 24.0), 52.8 (dd, $^2J_{1CF}$ = 30.1, $^2J_{2CF}$ = 24.3), 56.1, 115.3, 115.6, 121.8, 123.1, 124.4 (t, $^1J_{CF}$ = 246.0), 126.1, 127.1, 127.8, 128.9, 129.4, 131.6, 133.8, 139.1, 140.1, 153.4; ^{19}F NMR (235 MHz, $CDCl_3$) -103.7 (m, J_{FF} = 250.1, 1F), -111.4 (m, J_{FF} = 250.1, 1F). HRMS calc. for $C_{23}H_{23}F_2NO_2S$ 415.1418, found 415.1428.

General Procedure for the Synthesis of *N*-Cbz protected β-aminosulfoxides 5. *First step:* To a solution of *N*-PMP β-aminosulfoxide **4** (0.5 mmol) in acetonitrile (11 mL) at 0 ºC was added dropwise a solution of CAN (2.5 mmol) in water (8 mL). The mixture was stirred for 30 minutes at the same temperature, then aqueous 5% $NaHCO_3$ was added until pH 6 was reached. Na_2SO_3 was added portion-wise until a brown slurry was formed. The mixture was extracted with ethyl acetate (5 x 30 mL) and the organics were dried (Na_2SO_4). After filtration

and evaporation of the solvents a solid residue was obtained. FC [Et_3N 1% in ethyl acetate/*n*-hexanes (3:2)] gave the *N*-unsubstituted β-aminosulfoxides *syn*-**4** (R^1=H).

Second step: To a solution of a *N*-unsubstituted β-aminosulfoxide (6.0 mmol) in dioxane (7.5 mL) at room temperature were added 1.5 mL of a 50% K_2CO_3 aqueous solution, followed by benzyl chloroformate (7.1 mmol). The mixture was stirred for 2 hours at the same temperature and a white solid was formed. Then, the organic solvent was evaporated and the residue was diluted with water (20 mL) and extracted with CH_2Cl_2 (3 x 20 mL). Finally, the organics were washed with brine and after drying ($MgSO_4$), filtration and evaporation of the solvents a solid residue was obtained. FC [*n*-hexanes/ethyl acetate (7:3)] afforded compounds **5**.

(–)-(2*S*,*S*$_S$)-2-(*N*-Benzyloxycarbonyl)amino-3,3,3-trifluoropropyl-1-(1-naphthyl) sulfoxide (*syn*-5b). FC gave a white solid (95%): mp 150-152 ºC; $[\alpha]^{25}_D$ –234.9 (*c* 1.0, CH_3COCH_3); ^{1}H NMR (250 MHz, $CDCl_3$) 2.99 (dd, J_1 = 14.2, J_2 = 9.9; 1H), 3.38 (d, J_1 = 14.2 and J_2 = 3.7, 1H), 4.97 (s, 2H), 4.81-5.0 (m, 1H), 5.14 (br d, J = 9.7, 1H), 7.20-8.03 (m, 12H); ^{13}C NMR (62.8 MHz, $CDCl_3$) 48.2 (q, $^2J_{CF}$ = 32.1), 53.2, 67.5, 120.9, 123.6, 124.2 (q, $^1J_{CF}$ = 280.7), 125.6, 126.9, 127.8, 128.1, 128.2, 128.3, 128.5, 129.3, 130.9, 133.4, 135.5, 137.4, 155.0; ^{19}F NMR (235 MHz, $CDCl_3$) –76.5 (d, J_{HF} = 7.4, 3F). HRMS calc. (M^++1) $C_{21}H_{19}NO_3SF_3$, 422.1038, found 422.1052. Anal. Calcd. for $C_{21}H_{18}NO_3SF_3$: C, 59.85; H, 4.27; N, 3.32. Found; C, 59.67; H, 4.34; N, 3.16.

(–)-(2*S*,*S*$_S$)-2-(*N*-Benzyloxycarbonyl)amino-3-chloro-3,3-difluoropropyl-1-(1-naphthyl)sulfoxide (*syn*-5d). FC gave a white solid (99%): mp 140-142 ºC; $[\alpha]^{25}_D$ –234.3 (*c* 0.2, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) 1.63 (s, 1H), 3.00 (dd, J_1 = 14.2 and J_2 = 9.7, 1H), 3.51 (d, J = 14.2 and J_2 = 2.9, 1H), 4.98-5.10 (m, 1H), 5.02 (s, 2H), 7.28-7.92 (m, 12H); ^{13}C NMR (62.8 MHz, $CDCl_3$) 53.3 (t, $^2J_{CF}$ = 27.8), 54.3, 67.5, 121.0, 123.7, 125.6, 126.9, 127.7, 128.1, 128.2, 128.3, 128.5, 129.3, 131.1 (t, $^1J_{CF}$ = 279.0), 131.7, 133.4, 135.6, 137.5, 138.9, 155.0; ^{19}F NMR (235 MHz, $CDCl_3$) –61.2 (dd, J_{FF} = 163.1 and J_{FH} = 7.7, 1F) and –62.3 (dd, J_{FF} = 163.1 and J_{FH} = 7.7, 1F). HRMS calc. (M^+) $C_{21}H_{18}NO_3SF_2Cl$, 437.0634, found 437.0644. Anal. Calcd. for $C_{21}H_{18}NO_3SF_2Cl$: C, 57.66; H, 4.12; N, 3.20; S, 7.32. Found; C, 57.47; H, 4.09; N, 3.11; S, 7.20.

(-)-(2*S*,S_S)-2-(*N*-Benxzyloxycarbonyl)amino-3,3-difluoropropyl-1-(1-naphtyl) sulfoxide (*syn*-5e). FC on silica gel [*n*-hexanes-EtOAc (3:2)] gave a white solid (81%): mp 158-159 °C; $[\alpha]^{23}_{D}$ –304.1 (*c* 0.60, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) 3.07 (dd, J_1 = 14.3 and J_2 = 8.8, 1H), 3.42 (dd, J_1 = 14.3 and J_2 = 4.4, 1H), 4.55 (m, 1H), 5.02 (s, 2H), 5.45 (br s, 1H), 6.00 (t, *J* = 56.1, 1H), 7.33 (m, 4H), 7.58 (m, 3H), 7.89 (m, 3H), 8.10 (d, *J* = 6.8, 1H), ^{13}C NMR (62.4 MHz, $CDCl_3$) 49.4 (t, $^2J_{CF}$ = 23.7), 52.5, 67.3, 113.9, (t, $^1J_{CF}$ = 246.7), 121.2, 123.4, 125.6, 126.9, 127.7, 128.1, 128.3, 128.50, 128.54, 129.2, 131.7, 133.6, 135.9, 138.3, 155.5; ^{19}F NMR (235 MHz, $CDCl_3$) -126.1 (ddd, J_{FF} = 284.1, $^1J_{FH}$ = 56.1 and $^2J_{FH}$ = 8.0 Hz, 1F), -131.3 (ddd, J_{FF} = 284.1, $^1J_{FH}$ = 56.1 and $^2J_{FH}$ = 18.1, 1F); EIMS 404 $[M+1]^+$. Anal. Calcd. for $C_{21}H_{19}NO_3SF_2$: C, 65.50; H, 4.71; N, 3.47; S, 7.94. Found; C, 65.34; H, 4.88; N, 3.60; S, 7.89.

(-)-(2*R*,S_S)-2-(*N*-Benzyloxycarbonyl)amino-3,3-difluoropropyl-1-(1-naphtyl) sulfoxide (*anti*-5e). FC [*n*-hexanes-EtOAc (3:2)] on silica gel (R_f=0.45) gave a white solid (6%): mp 144-146 °C; $[\alpha]^{25}_{D}$ -274.9 (*c* 1.01, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) 1.82 (br s, 1H), 3.00 (dd, J_1 = 13.5 and J_2 = 3.4, 1H), 3.38 (dd, J_1 = 13.5 and J_2 = 9.0, 1H), 4.42 (m, 1H), 5.13 (d, *J* = 12.0, 1H), 5.17 (d, *J*= 12.0, 1H), 6.06 (dt, J_{FF} = 53.1, J_{FH} = 3.0), 7.31-7.99 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) 50.2 (t, $^2J_{CF}$ = 27.0), 52.8, 67.3, 113.9 (t, $^1J_{CF}$ = 244.3), 121.0, 122.9, 125.6, 126.8, 127.6, 128.1, 128.3, 128.3, 129.1, 131.7, 133.4, 135.8, 138.5; ^{19}F NMR (235 MHz, $CDCl_3$) -128.9 (ddd, J_{FF} = 283.4, $^1J_{FH}$ = 73.5 and $^2J_{FH}$ = 17.6), -125.0 (ddd, J_{FF} = 283.4, $^1J_{FH}$ = 54.9 and $^2J_{FH}$ = 8.2). HRMS calc. $C_{21}H_{19}NO_3SF_2$ 403.1053, found 403.1065.

(-)-(2*S*,S_S)-2-(*N*-Benzyloxycarbonyl)amino-3,3-difluoro-5-hexenyl-1-(1-naphtyl) sulfoxide (*syn*-5j). FC [*n*-hexane-EtOAc (3:2)] on silica gel (R_f=0.50) gave a white solid (76%): m.p. 127-129 °C; $[\alpha]^{25}_{D}$: - 191.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) 2.50-2.58 (m, 2H), 2.97 (dd, J_1 = 14.0, J_2 = 9.6, 1H), 3.42 (dd, J_1 = 14.0, J_2 = 3.5, 1H), 4.58-4.63 (m, 1H), 4.92-5.08 (m, 4H), 5.51-5.53 (m, 1H), 5.54-5.72 (m, 1H), 7.21 (s, 5H), 7.44-8.00 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) 38.2 (t, $^2J_{CF}$ = 24.0), 50.2 (dd, $^2J_{1CF}$ = 32.0, $^2J_{2CF}$ = 25.0), 54.6, 67.1, 121.0, 122.2 (t, $^1J_{CF}$ = 246.0), 121.3, 123.5, 125.4, 126.6, 127.4, 127.7, 127.9, 128.1, 128.4, 129.1, 131.4, 133.3, 135.9, 138.4, 155.5; ^{19}F NMR (235 MHz, $CDCl_3$) -105.1

(ddt, J_{FF} = 247.2, J_1 = 20.2, J_2 = 16.5, 1F), -110.2 (dq, J_{FF} = 247.2, J = 19.0, 1F). HRMS calc. for $C_{24}H_{23}F_2NO_3S$ 443.1367, found 443.1366.

"Non-Oxidative" Pummerer Rearrangement. Synthesis of *N*-Cbz amino alcohols (*R*)-6. To a solution of *N*-Cbz derivative **5** (2.8 mmol) and *sym*-collidine (8.5 mmol) in acetonitrile (56 mL) at 0 ºC and under argon atmosphere was added dropwise trifluoroacetic anhydride (14.0 mmol), and the mixture was stirred for 5 minutes at the same temperature. After complete consumption of the starting material (TLC) a 10% K_2CO_3 aqueous solution was added until neutral pH was reached. Then an excess of $NaBH_4$ (ca. 14.0 mmol) was added portion-wise and the reaction was allowed to reach room temperature. After 15 minutes (TLC analysis) the reaction was quenched with saturated solution of NH_4Cl and extracted with ethyl acetate (3 x 25 mL). The organics were washed successively with HCl 1*N* (2 x 15 mL) and then aqueous 5% $NaHCO_3$ (2 x 15 mL). After drying (Na_2SO_4), filtration and removal of solvents *in vacuo*, FC [*n*-hexanes-EtOAc (3:1)] gave the pure amino alcohol **6**.

(–)-(2*R*)-2-(*N*-Benzyloxycarbonyl)amino-3,3,3-trifluoropropanol [(*R*)-6a]. FC gave a white solid (75%): mp 84-86 ºC; $[\alpha]^{25}_D$ –12.0 (*c* 1.0, $CHCl_3$); for spectroscopical ^1H and ^{19}F NMR data, see reference 10b. ^{13}C NMR (62.8 MHz, $CDCl_3$) 53.7 (q, $^2J_{CF}$ = 29.3), 59.4, 67.6, 121.4 (q, $^1J_{CF}$ = 280.6), 128.2, 128.4, 128.6, 135.6; 156.2. HRMS calc. for (M^+) $C_{11}H_{12}NO_3F_3$, 263.0769, found 263.0764.

(–)-(2*R*)-2-(*N*-Benzyloxycarbonyl)amino-3-chloro-3,3-difluoropropanol [(*R*)-6b]. FC gave a white solid (70%): mp 65-67 ºC; $[\alpha]^{25}_D$ –8.7 (*c* 0.4; $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$) 2.09 (s, 1H), 3.77 (d, *J* = 4.8, 2H), 4.34 (m, 1H), 5.03 (s, 2H), 5.67 (d, *J* = 9.7, 1H), 7.22-7.29 (s, 5H); ^{13}C NMR (62.8 MHz, $CDCl_3$) 59.0 (t, $^2J_{CF}$ = 25.0), 59.9, 67.6, 128.1, 128.3 (t, $^1J_{CF}$ = 295.5), 128.4, 128.6, 135.6, 156.3; ^{19}F NMR (235 MHz, $CDCl_3$) –59.7 (dd, J_{FF} = 167.3 and J_{FH} = 9.1, 1F); –60.3 (dd, J_{FF} = 167.3 and J_{FH} = 9.3, 1F). Anal. Calcd. for $C_{11}H_{12}NO_3F_2Cl$: C, 47.31; H, 4.30; N, 5.01. Found; C, 47.51; H, 4.32; N, 5.12.

(-)-(2*R*)-2-(*N*-Benzyloxycarbonyl)amino-3,3-difluoropropanol [(*R*)-6c]. FC on silica gel [*n*-hexanes-EtOAc (3:2)] gave a white solid (90%): mp 54-56 ºC; $[\alpha]^{23}_D$ –6.1 (*c* 0.80, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$) 2.23 (s, 1H), 3.70 (dd, J_1 = 10.7 and J_2 = 4.8, 1H), 3.90 (dd, J_1 = 10.7 and J_2 = 3.6, 1H), 4.03 (m, 1H), 5.12 (s, 2H), 5.38 (d, *J* = 8.0, 1H), 5.93 (dt, J_{FH}

= 55.5 and J_{FH} =2.9, 1H), 7.34 (m, 5H), ^{13}C NMR (62.4 MHz, $CDCl_3$) 54.1 (t, $^2J_{CF}$ = 22.1), 59.7, 67.5, 114.6 (t, $^1J_{CF}$ = 244.5), 128.2, 128.4, 128.6, 136.0, 156.4; ^{19}F NMR (235 MHz, $CDCl_3$) -128.8 (dd, J_1 = 55.5 and J_2 = 13.7, 2F); EI-MS 245 $[M]^+$. Anal. Calcd. for $C_{11}H_{13}NO_3F_2$: C, 53.88; H, 5.30; N, 5.71. Found; C, 54.02; H, 5.25; N, 5.83.

(-)-(2*R*)-2-(*N*-Benzyloxycarbonyl)amino-3,3-difluoro-5-hexen-1-ol [(*R*)-6d]. FC [*n*-hexane-EtOAc (3:2)] on silica gel (R_f=0.50) gave a white solid (88%): m.p. 75-77 ^oC; $[\alpha]^{25}{}_D$: -4.66 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) 2.10 (br s, 1H), 2.53-2.70 (m, 2H), 3.74 (dd, J_1 = 11.9, J_2 = 3.5, 1H), 3.84 (dd, J_1 = 11.9, J_2 = 4.6, 1H), 3.97-4.06 (m, 1H), 5.11-5.18 (m, 2H), 5.05 (s, 2H), 5.37 (d, J = 9.5, 1H), 5.69-5.75 (m, 1H), 7.28 (s, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) 38.8 (t, $^2J_{CF}$ = 24.0), 55.2 (dd, $^2J_{1CF}$ = 29.0, $^2J_{2CF}$ = 23.0), 59.7 (t, $^3J_{CF}$ = 3.9), 67.2, 120.8, 122.9 (t, $^1J_{CF}$ = 245.0), 128.0, 128.2, 128.4, 135.9, 156.5; ^{19}F NMR (235 MHz, $CDCl_3$) -105.8 (ddt, J_{FF} = 249.0, J_1 = 18.0, J_2 = 8.2, 1F), -107.5 (dq, J_{FF} = 249.0, J = 16.7, 1F). HRMS calc. for $C_{14}H_{17}F_2NO_3$ 285.1177, found 285.1176.

Oxidation of amino alcohols 6. To a solution of *N*-Cbz amino alcohol **6** (1.05 mmol) in 5 mL of a mixture of acetone and water (3:2) at room temperature was added solid $NaIO_4$ (340 mg; 1.60 mmol) followed by $RuO_2.xH_2O$ (30 mg; 0.22 mmol). The mixture was stirred for 1 hour and then 5 mL of *i*-PrOH were added. The solid was filtered through a *Celite* column and washed with acetone. After evaporation of the solvents *in vacuo* the residue was dissolved in 5 mL of ethyl acetate and extracted with a 5% aqueous solution of $NaHCO_3$ (3 x 5 mL). The aqueous phases were acidified with HCl 1*N*. The white slurry was then extracted with ethyl acetate (3 x 10 mL). The organics were dried ($MgSO_4$), filtered and concentrated *in vacuo* to furnish an orange solid. FC (MeOH 100%) in silica gel gave the *N*-Cbz-α-amino acid (*R*)-**7**.

(–)-(2*R*)-*N*-Benzyloxycarbonyl-3,3,3-trifluoroalanine [(*R*)-7a]. FC gave a white solid (70%): mp 100-102 ºC; $[\alpha]^{25}{}_D$ –6.0 (*c* 0.5, MeOH); for spectroscopical ^{1}H and ^{19}F NMR data, see reference 10b. ^{13}C NMR (62.8 MHz, CD_3OD) 57.1 (q, $^2J_{CF}$ = 31.4), 68.2, 124.6 (q, $^1J_{CF}$ = 279.3), 128.9, 129.1, 129.5, 137.8, 158.3, 167.2. HRMS calc. for (M^+) $C_{11}H_{10}NO_4F_3$, 277.0562, found 277.0562.

(-)-(2*R*)-*N*-Benzyloxycarbonyl-3-chloro-3,3-difluoroalanine [(*R*)-7b]. FC gave a white solid (65%): mp 90-92 ºC; $[\alpha]^{25}{}_D$ -1.1 (*c* 0.6, MeOH); ^{1}H NMR (250 MHz, CD_3OD)

4.89 (s, 2H), 4.98 (t, J_{HF} = 8.2, 1H), 5.07 (br s, 1H), 7.12-7.23 (m, 5H); ^{13}C NMR (62.8 MHz, CD_3OD) 62.3 (t, $^2J_{CF}$ = 27.2), 68.3, 128.2 (t, $^1J_{CF}$ = 295.4), 128.9, 129.2, 129.5, 137.8, 158.2, 167.4; ^{19}F NMR (235 MHz, CD_3OD) –58.9 (dd, J_{FF} = 160.6 and J_{FH} = 6.0, 1F), –59.7 (dd, J_{FF} = 160.6 and $J_{F\text{-}H}$ = 10.0, 1F). Anal. Calcd. for $C_{11}H_{10}NO_4F_2Cl$: C, 45.05; H, 3.41; N, 4.78. Found; C, 44.92; H, 3.25; N, 4.89.

(-)-(2*R*)-*N*-Benzyloxycarbonyl-3,3-difluoroalanine [(*R*)-7c]. FC on silica gel ($CHCl_3$-CH_3OH 9:1) gave a white solid (70%): mp 89-90 ºC; $[\alpha]^{23}_D$ –2.8 (*c* 0.9, CH_3OH); ^{1}H NMR (250 MHz, CD_3OD) 4.59 (dd, J_1 = 23.5 and J_2 = 8.3, 1H), 5.11 (s, 2H), 5.21 (br s, 1H), 6.25 (t, J = 54.7, 1H), 7.33 (m, 5H); ^{13}C NMR (62.4 MHz, CD_3OD) 58.3 (br t), 68.0, 115.8 (t, $^1J_{CF}$ = 244.1), 128.9, 129.0, 129.5, 138.0, 158.7, 172.2; ^{19}F NMR (235 MHz, CD_3OD) -123.3 (ddd, J_{FF} = 281.6, $^1J_{FH}$ = 54.7 and $^2J_{FH}$ = 8.3, 1F), -127.6 (ddd, J_{FF} = 281.6, $^1J_{FH}$ = 54.7 and $^2J_{FH}$ = 23.5 Hz, 1F); EI-MS 259 $[M]^+$.

(-)-(1*R*)-2,2-Difluoro-1-methyl-*O*-benzoyl-4-pentenyl(benzyloxycarbonyl)amine (*R*)-8. To a solution of *N*-Cbz amino alcohol (*R*)-**6d** (0.53 mmol) in CH_2Cl_2 (2 mL) at room temperature and under argon atmosphere was added dicyclohexylcarbodiimide (1.0 mmol), benzoic acid (0.8 mmol) and a catalytic amount of DMAP. The mixture was stirred for 7 hours and the formation of urea, as a precipitate, is observed. After quenching of the reaction with saturated aqueous NH_4Cl, the organic layer was separated and the aqueous phase extracted with dichloromethane. The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo*. Flash chromatography (FC) [*n*-hexanes/ethyl acetate (3:1)] provided *O*-benzoyl amino alcohol (*R*)-**8** as a white solid. *Flash* chromatography [*n*-hexane-EtOAc (3:1)] on silica gel (R_f=0.50) gave a white solid (95%): m.p. 38-40 ºC; $[\alpha]^{25}_D$: -0.7 (*c* 1.1, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) 2.57-2.74 (m, 2H), 4.36-4.47 (m, 3H), 5.01 (s, 2H), 5.13-5.20 (m, 3H), 5.67-5.81 (m, 1H), 7.20 (s, 5H), 7.30-7.93 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) 38.9 (t, $^2J_{CF}$ = 25.0), 53.2 (dd, $^2J_{1CF}$ = 29.7, $^2J_{2CF}$ = 23.6), 61.7 (t, ^3J = 4.0), 67.3, 121.4, 122.2 (t, $^1J_{CF}$ = 246.0), 128.0, 128.2, 128.4, 128.5, 129.4, 129.7, 133.2, 135.9, 155.9, 166.2;^{19} F NMR (235 MHz, $CDCl_3$) -106.1 (ddt, J_{FF} = 106.0, J_1 = 7.7, J_2 = 2.8, 1F), -107.9 (dq, J_{FF} = 106.0, J = 14.4, 1F). HRMS calc. for $C_{21}H_{21}F_2NO_4$ 389.1439, found 389.1438.

N*1*-(4-Methoxyphenyl)-1-chloro-2,2-difluoro-4-penten-1-imine (2j). This compound has been prepared, starting from the corresponding acid, following the protocol described by

Uneyama (see reference 14b). Yellow oil (70 %), B.p. 80 °C (10^{-2} Torr). ^{1}H NMR (400 MHz, $CDCl_3$) 3.05-3.87 (m, 2H), 3.72 (s, 3H), 5.19-5.26 (m, 2H), 5.71-5.78 (m, 1H), 6.83 (d, J = 9.0, 2H), 7.04 (d, J = 9.0, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) 39.5 (t, $^2J_{CF}$ = 25.0), 55.4 (q), 114.1 (d), 117.1 (t, $^1J_{CF}$ = 245.0), 121.4 (t), 123.1 (d), 127.9 (t, $^3J_{CF}$ = 5.0), 136.9 (t, $^2J_{CF}$ = 33.0), 158.6 (s); ^{19} F NMR (235 MHz, $CDCl_3$) –98.6 (t, J_{FH} = 16.0, 2F). HRMS calc. for $C_{12}H_{12}ClF_2NO$ 259.0575, found 259.0580.

General procedure for regioselective *N*-alkylation of (*R*)-8. To a solution of *O*-benzoyl amino alcohol (0.26 mmol) in dry DMF (1.5 mL) at 0 °C was added oil-free NaH (0.52 mmol). After 5 min the suspension was treated with the corresponding alkenyl bromide (5.0 equiv.). The mixture was stirred until total disappearance of the starting material was observed (TLC) and then the solvent was evaporated under reduced pressure. The residue was treated with water, followed by a routine work-up.

(-)-(4*R*)-3-Allyl-4-(1,1-difluoro-3-butenyl)-1,3-oxazolan-2-one (*R*)-9a. After the addition of allyl bromide the mixture was stirred at room temperature for 90 min. *Flash* chromatography [*n*-hexane-EtOAc (10:1)] on silica gel (R_f=0.20) gave a light yellow oil (84%): $[\alpha]^{25}_D$: -27.9 (*c* 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) 2.53-2.65 (m, 2H), 3.60 (dd, J_1 = 15.0, J_2 = 7.5, 1H), 3.97-4.03 (m, 1H), 4.18-4.31 (m, 3H), 5.18-5.24 (m, 4H), 5.68-5.77 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) 37.0 (t, ^2J = 24.3), 46.2 (t, ^4J = 2.0), 57.4 (dd, $^2J_{1CF}$ = 32.0, $^2J_{2CF}$ = 27.0), 62.5 (dd, $^3J_{1CF}$ = 5.8, $^3J_{2CF}$ = 4.0), 119.9, 121.6, 122.5 (t, $^1J_{CF}$ = 246.0), 127.0 (t, $^3J_{CF}$ = 5.8), 130.9, 157.7; ^{19}F NMR (235 MHz, $CDCl_3$) -102.7 (m, J_{FF} = 259.7, 1F), -105.3 (m, J_{FF} = 259.7, 1F). HRMS calc. for $C_{10}H_{13}F_2NO_2$ 217.0914, found 217.0914.

(-)-(4*R*)-3-(3-Butenyl)-4-(1,1-difluoro-3-butenyl)-1,3-oxazolan-2-one (*R*)-9b. After the addition of 1-butenyl bromide the mixture was stirred at room temperature for 7 hours. *Flash* chromatography [*n*-hexane-EtOAc (5:1)] on silica gel (R_f=0.40) gave a yellow oil (45%): $[\alpha]^{25}_D$: -7.14 (*c* 0.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) 2.24-2.38 (m, 2H), 2.52-2.64 (m, 2H), 3.12-3.19 (m, 1H), 3.60-3.67 (m, 1H), 3.96-4.04 (m, 1H), 4.17 (dd, J_1 = 10.0, J_2 = 4.0, 1H), 4.23-4.27 (m, 1H), 5.01-5.09 (m, 2H), 5.18-5.24 (m, 2H), 5.65-5.77 (m, 2H);^{13}C NMR (75.5 MHz, $CDCl_3$) 31.4, 36.8 (t, ^2J = 24.0), 42.7, 58.0 (dd, $^2J_{1CF}$ = 33.0, $^2J_{2CF}$ = 28.0), 62.4 (dd, $^3J_{1CF}$ = 6.3, $^3J_{2CF}$ = 3.5), 117.7, 121.6, 126.9 (t, $^3J_{CF}$ = 5.8), 134.4, 157.9; ^{19}F NMR (282.4

MHz, $CDCl_3$) -102.7 (m, J_{FF} = 260.3, 1F), -105.4 (m, J_{FF} = 260.3, 1F). HRMS calc. for $C_{11}H_{15}F_2NO_2$ 231.1071, found 231.1075.

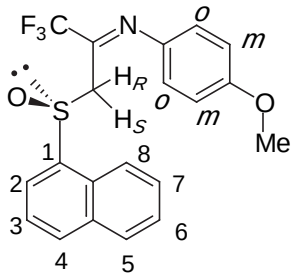
(-)-(4*R*)-4-(1,1-Difluoro-3-butenyl)-3-(4-pentenyl)-1,3-oxazolan-2-one (*R*)-9c. After the addition of 1-pentenyl bromide the mixture was stirred at room temperature for 7 hours. *Flash* chromatography [*n*-hexane-EtOAc (7:1)] on silica gel (R_f=0.20) gave a yellow oil (90%): $[\alpha]^{25}{}_D$: -2.14 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) 1.58-1.70 (m, 2H), 2.01 (dd, J_1 = 14.0, J_2 = 7.5, 2H), 2.52-2.63 (m, 2H), 3.07-3.14 (m, 1H), 3.47-3.55 (m, 1H), 4.00-4.02 (m, 1H), 4.15-4.19 (m, 1H), 4.25-4.30 (m, 1H), 4.92-5.00 (m, 2H), 5.18-5.24 (m, 2H), 5.68-5.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) 25.9, 30.6, 36.8 (t, $^2J_{CF}$ = 24), 43.3, 58.1 (dd, $^2J_{1CF}$ = 32.8, $^2J_{2CF}$ = 27.0), 62.4 (dd, $^3J_{1CF}$ = 6.8, $^3J_{2CF}$ = 4.8), 115.4, 120.0, 122.5 (t, $^1J_{CF}$ = 245.0), 126.9 (t, $^3J_{CF}$ = 5.8), 137.1, 157.8; ^{19} F NMR (282.4 MHz, $CDCl_3$) -102.8 (m, J_{FF} = 261.0, 1F), -105.4 (m, J_{FF} = 261.0, 1F). HRMS calc. for $C_{12}H_{17}F_2NO_2$ 245.1227, found 245.1220.

Representative procedure for ring closing metathesis of (*R*)-9. The amount of catalyst [$(PCy_3)_2Cl_2Ru{=}CHPh$] necessary in each case was weighed under argon atmosphere and added via cannula to a solution of the corresponding diene (*R*)-**9** in dry CH_2Cl_2 (final concentration of diene was 5 x 10^{-3} M). When addition finished, the vessel was sealed, and the reaction mixture was stirred at room temperature. When reaction finished (TLC), solvent was removed *in vacuo*, and the residue was purified by flash chromatography, affording the expected unsaturated heterocycle (*R*)-**10**.

(-)-(9a*R*)-9,9-Difluoro-5,8,9,9a-tetrahydro-1*H*-[1,3]oxazolo [3,4-*a*] azepin-3-one [(*R*)-10a]. The amount of catalyst used was 3 mol %. The mixture of the reaction was stirred for 6 hours at room temperature. *Flash* chromatography [*n*-hexane-EtOAc (2:1)] on silica gel (R_f=0.30) gave a white solid (75%): m.p. 51-53 ^{o}C; $[\alpha]^{25}{}_D$= -14.1 (*c* 0.99 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ= 2.62-2.73 (m, 1H), 2.80-2.90 (m, 1H), 3.54-3.60 (m, 1H), 4.07-4.15 (m, 1H), 4.32-4.38 (m, 3H), 5.54-5.57 (m, 1H), 5.80-5.85 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) ($CDCl_3$): δ= 34.1 (t, $^2J_{CF}$ = 26.0), 41.9, 62.0 (dd, $^2J_{1CF}$ = 33.0, $^2J_{2CF}$ = 31.1), 62.1 (dd, $^3J_{1CF}$ = 5.8, $^3J_{2CF}$ = 4.0), 120.2 (t, $^1J_{CF}$ = 243.0), 122.0 (dd, $^3J_{1CF}$ = 7.8, $^3J_{2CF}$ = 4.9), 129.1, 157.0; ^{19}F NMR (282.4 MHz, $CDCl_3$): δ= -97.8 (dd, J_{FF} = 256.2, J = 21.7, 1F), -109.9 (m double, J_{FF} = 256.2, 1F); HRMS calc. for $C_8H_9F_2NO_2$ 189.0601, found 189.0608; elemental analyses calcd. for $C_8H_9NO_2F_2$: C, 50.79, H, 4.76, N, 7.40; found; C, 50.62, H, 4.65, N, 7.48.

(-)-(10a*R*)-10,10-Difluoro-1,5,6,9,10,10a-hexahydro[1,3]oxazolo[3,4-*a*]azocin-3-one [(*R*)-10b]. The amount of catalyst used was 10 mol %. The mixture of the reaction was stirred for 6 hours at room temperature. *Flash* chromatography [*n*-hexane-EtOAc (2:1)] on silica gel (R_f=0.30) gave a white solid (87%): m.p. 84-86 ºC; $[\alpha]^{25}_{D}$: -40.1 (*c* 0.80, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) 2.24-2.36 (m, 1H), 2.45-2.68 (m, 2H), 2.96-3.05 (m, 2H), 3.80-4.05 (m, 2H), 4.21 (dt, J_1 = 8.8, J_2 = 1.7, 1H), 4.54 (dd, J_1 = 9.2, J_2 = 2.1, 1H), 5.64-5.72 (m, 1H), 5.94 (q, J = 8.6, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$) 27.4, 32.5 (dd, $^2J_{1CF}$ = 27.6, $^2J_{2CF}$ = 24.7), 46.1, 59.1 (dd, $^2J_{1CF}$ = 41.4, $^2J_{2CF}$ = 25.3), 63.1 (d, $^3J_{CF}$ = 6.9), 123.6 (dd, $^3J_{1CF}$ = 10.3, $^3J_{2CF}$ = 1.7), 123.8 (t, $^1J_{CF}$ = 244.0), 133.2, 159.8; ^{19} F NMR (282.4 MHz, $CDCl_3$) -101.9 (m, J_{FF} = 252.1, 1F), -111.2 (m, J_{FF} = 252.1, 1F). HRMS calc. for $C_9H_{11}F_2NO_2$ 203.0758, found 203.0749.

NMR Experiments on (-)-(S_S)-3,3,3-Trifluoro-*N*-(*p*-methoxyphenyl)-2-iminopropyl-1-(1-naphtyl)sulfoxide [(*S*)-*Z*-3b]. We have carried out several NMR experiments on (*S*)-*Z*-**3b** to measure all possible intramolecular Nuclear Overhauser Effects with special attention to those occurring between the aromatic rings.



(*S*)-*Z*-**3b**

The experiments were carried out at 195 °K (*ca.* -80 °C) and in two different solvents [methanol (CD_3OD) and methylene chloride (CD_2Cl_2)]. Rotating frame NOE experiments (ROESY) were performed at low temperature since in these conditions the correlation time of the molecular motion in solution is such that the NOE in the laboratory frame (NOESY or NOE difference experiments) is near the null region.

ROESY in methanol (CD_3OD) at low temperature (195 K).

1) The methylene hydrogens show distinct NOEs with the protons H-2 and H-8 of the naphthalene moiety. The hydrogen resonating at 4.14 ppm (see below) display contacts with the protons H*o* of the *p*-substituted phenyl ring and with the hydrogen H-2 of the naphthalene ring. The hydrogen at 4.41 ppm shows contacts with H*o* and with the naphtyl H-8 proton (a very small NOE is also detected with the H-2 proton). These observations strongly suggest that at low temperature the fragment CH_2-S-C_1 is rather rigid and that no fast rotation around CH_2-S or S-C_1 bonds is allowed. Moreover it is possible to assign in the spectrum the configurations pro-*S* (4.14 ppm) and pro-*R* (4.41 ppm) to the methylene hydrogens.

2) The four hydrogens H*o* and H*m* of the *p*-methoxyphenyl ring show NOEs with all protons of the naphtalene ring clearly showing that the two aromatic moieties are rather close in the space.

3) The *p*-methoxy substituent displays small but definite NOE contacts with the hydrogens 5, 6 and 7 of the naphtalene ring indicating that the methoxyl group is located relatively near the rim of the unsubstituted ring of the naphtyl residue.

All these data point to the fact that the molecule has a U shape with the fragment –N=C-CH_2-S- acting as a spacer and the two aromatic units aligned in a nearly parallel arrangement.

Analysis of the proton spectrum of (*S*)-*Z*-**3b** *in CD_3OD at low temperature (195 °K):*

Proton	δ (ppm)	Proton	δ (ppm)
H-2	8.05	Ho	6.91
H-3	7.73	H*m*	6.88
H-4	8.11		
H-5	8.00	H_R	4.41
H-6	7.60	H_S	4.14
H-7	7.48		
H-8	7.32	OCH_3	3.80

ROESY in methylene chloride at low temperature (195 K).

In this solvent the pro-*R* and pro-*S* hydrogens of the methylene group resonate very near and their NOEs cannot be evaluated separately. Effects are observed between the CH_2 hydrogens and the hydrogens H-2, H-8 and also H-7 (small) of the naphthalene residue. The four hydrogens of the *p*-substituted phenyl ring and the OCH_3 protons show NOEs with the naphthalene protons similar to that observed in methanol. These data allow to conclude that the molecular conformation is not very different in methanol and in methylene chloride at low temperature.