Solvent Controlled Asymmetric Strecker Reaction: Stereoselective Synthesis of α -trifluoromethylated α -amino acids

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1. Supplementary Data. All chemicals were reagent grade and used as purchased. All reactions were performed under an inert atmosphere of dry argon or nitrogen using distilled dry solvents. Reactions were monitored by TLC analysis. Flash column chromatography was carried out on silica gel (300-400 mesh). Optical rotations were measured using sodium light (D line 589.3nm)

2. General Procedure and Chemical data of 2-4

1. General Procedure for preparing compounds **2a-2h**.

(S)-1,1,1-Trifluoro-2-(N-(R)-tert-butanesulfinyl)-amino-2-cyano-propane (2a). To a well stirred solution of 0.560 g (5 mmol) of 1,1,1-trifluoroacetone and 1.210 g (10 mmol) of (R)-tert-butanesulfonamide in 10 mL of hexane was added 2.130 g (7.5 mmol) of Ti(Oi-Pr)₄. The reaction mixture was stirred at room temperature for 6 hours, and then quenched with 5 mL of water at 0 °C. After 5 min, the mixture was filtered through celite. Removing solvent of filtrate and purification by chromatography on silica gel (EtOAc/PE = 1/20) gave 0.495 g of **1a** in 46% yield.

0.149 g (1.5 mmol) of TMSCN was added to a solution of 0.215 g (1 mmol) **1a** in 2 mL of hexane at room temperature. After stirred for 48 hours, the mixture was quenched with sat. NH₄Cl. The mixture was extracted with EtOAc for 3 times and the extraction was dried over Na₂SO₄. Removing solvent *in vacuo* and purifying by chromatography on silica gel (EtOAc/PE = 1/6) gave 0.162g of (S)-1,1,1-trifluoro-2-(N-(R)-tert-butanesulfinyl) -amino-2-cyano-propane (**2a**) in 69 % yield as a white solid. m.p. 94-95 °C; [α]_D²⁰ = -78.4 (c = 0.9 in CHCl₃); ¹H NMR (300MHz, CDCl₃, 25 °C, TMS): δ = 1.28 (s, 9H; *t*Bu), 1.87 (s, 3H; Me), 4.07 (s, 1H; NH); ¹³C NMR (75MHz, CDCl₃, 25 °C): δ = 19.5 (s), 22.2 (s), 56.5 (q, *J* (F, C)=33.1Hz), 57.6 (s), 115.2 (s) 121.6 (q, *J* (F, C) = 287.3Hz); ¹⁹F NMR (282MHz, CDCl₃, 25 °C): δ = -79.6 (s); MS (ESI): *m/z* 260.1 [*M*+NH₄⁺]; HRMS [*M*+Na⁺] Anal's Calc'd for C₈H₁₃F₃N₂OSNa: 265.0598, Found: 265.0577; *t*_r (*R*_s, *S*) = 9.18min, *t*_r (*R*_s, *R*) = 12.60min, (Chiralpak AS, column No. AS00CE-JG019, λ =214nm, Hex: *i*-PrOH = 90:10, 0.7mL/min).

(S)-1,1,1-Trifluoro-2-(N-(R)-tert-butanesulfinyl)-amino-2-cyano-butane (2b). m.p. 98-100 °C; $[\alpha]_D^{20} = -33.8$ (c = 0.65 in CHCl₃); ¹H NMR (300MHz, CDCl₃, 25 °C, TMS): δ = 1.27-1.30 (m, 12H; *t*-Bu, Me), 2.15 (m, 2H; CH₂), 3.87 (br, 1H; NH); ¹³C NMR (75MHz, CDCl₃, 25 °C): δ = 8.4 (s), 22.3 (s), 27.2 (s), 58.2 (s), 62.3 (q, *J* = 32.1Hz), 113.7 (s) 122.8 (q, *J* = 289.6Hz); ¹⁹F NMR (282MHz, CDCl₃, 25 °C): δ = -76.7 (s); MS (ESI): *m/z* 274.2 [*M*+NH₄⁺]; HRMS [*M*+Na⁺] Anal's Calc'd for C₉H₁₅F₃N₂OSNa: 279.0755, Found: 279.0748; *t_r* (*R_s*, *S*) = 18.63 min, *t_r* (*R_s*, *R*) = 6.87 min, (Chiralpak AS, column No. AS00CE-JG019+ Chiralpak AS, column No. AS00CC-IL019, λ = 214nm, Hex: *i*-PrOH = 90:10, 0.7mL/min).

(S)-1,1,1-Trifluoro-2-(N-(R)-tert-butanesulfinyl)-amino-2-cyano-octane (2c). m.p. 65-66 °C; $[\alpha]_D^{20} = -23.0$ (c = 0.2 in CHCl₃); ¹H NMR (300MHz, CDCl₃, 25 °C, TMS): δ = 0.87-0.89 (m, 3H), 1.26-1.42 (m, 15H), 1.59-1.72 (m, 2H), 1.99-2.10 (m, 2H), 4.08-4.11 (br, 1H; NH); ¹³C NMR (75MHz, CDCl₃, 25 °C): δ = 13.9 (s), 22.3 (s), 22.4 (s), 23.9 (s), 28.9 (s), 31.3 (s), 33.3 (s), 58.1 (s), 61.7 (q, *J*(F, C) = 30.6Hz), 114.0 (s) 122.7 (q, *J*(F, C) = 285.7Hz); ¹⁹F NMR (282MHz, CDCl₃ 25 °C): δ = -76.5 (s); MS (ESI): *m/z* 330.2 [*M*+NH₄⁺]; HRMS [*M*+Na⁺] Anal's Calc'd for C₁₃H₂₃F₃N₂OSNa: 335.1381, Found: 335.1377; *t_r* (*R_s*, *S*) = 5.17 min, *t_r* (*R_s*, *R*) = 5.66 min, (Chiralpak AD-H, column No. ADH0CE-DB235, λ = 214nm, Hex: *i*-PrOH = 90:10, 0.7mL/min).

(S)-1,1,1-Trifluoro-2-(N-(R)-tert-butanesulfinyl)-amino-2-cyano-4-phenyl-butane (2d). m.p. 99.5- 100.5 °C. $[\alpha]_D^{20} = -45.0$ (c = 1.0 in CHCl₃); ¹H NMR (300MHz, CDCl₃, 25 °C, TMS): δ = 1.30 (s, 9H; *t*-Bu), 2.42 (t, 2H, ³*J*(H, H) = 9Hz; CH₂), 2.91-3.15 (m, 2H; CH₂), 4.15 (s, 1H; NH), 7.25-7.39 (m, 5H; Ph); ¹³C NMR (75MHz, CDCl₃, 25 °C): δ = 22.3 (s), 30.2 (s), 35.2 (s), 58.2 (s), 61.5 (q, *J*(F,C) =

31.2Hz), 113.8 (s), 122.7 (q, $J(\text{F}, \text{C}) = 287.3\text{Hz}$), 127.0 (s), 128.4 (s), 129.0 (s), 138.7 (s); ^{19}F NMR (282MHz, CDCl_3 , 25°C): $\delta = -76.3$ (s); MS (ESI): m/z 333.1 [$M+H^+$]; HRMS [$M+Na^+$] Anal's Calc'd for $\text{C}_{15}\text{H}_{19}\text{F}_3\text{N}_2\text{OSNa}$: 355.1068, Found: 355.1060; tr (R_s, S) = 8.45 min tr (R_s, R) = 10.43 min, (Chiralpak AD, column No. AD00CE-HI084, $\lambda = 214\text{nm}$, Hex: $i\text{-PrOH} = 95:5$, 0.7mL/min).

(S)-1,1,1-Trifluoro-2-(N-(R)-tert-butanesulfinyl)-amino-2-cyano-2-phenyl-ethane (2e). m.p. 125-126 $^\circ\text{C}$; $[\alpha]_D^{20} = -124.6$ (c = 0.6 in CHCl_3); ^1H NMR (300MHz, CDCl_3 , 25°C , TMS): $\delta = 1.29$ (s, 9H; $t\text{-Bu}$), 4.30 (s, 1H; NH), 7.48-7.59 (m, 3H; Ph), 7.71-7.76 (m, 2H; Ph); ^{13}C NMR (75MHz, CDCl_3 , 25°C): $\delta = 22.4$ (s), 58.0 (s), 64.2 (q, $J(\text{F}, \text{C}) = 23.78\text{Hz}$), 114.4 (s), 122.2 (q, $J(\text{F}, \text{C}) = 284.6\text{Hz}$), 124.1 (s), 128.7 (s), 129.1 (s), 131.4 (s); ^{19}F NMR (282MHz, CDCl_3 , 25°C): $\delta = -76.0$ (s); MS (ESI): m/z 322.1 [$M+NH_4^+$]; HRMS [$M+Na^+$] Anal's Calc'd for $\text{C}_{13}\text{H}_{15}\text{F}_3\text{N}_2\text{OSNa}$: 327.0755, Found: 327.0737; tr (R_s, S) = 6.58 min, tr (R_s, R) = 5.73 min, (Chiralpak AD-H, column No. ADH0CE-DB235, $\lambda = 254\text{nm}$, Hex: $i\text{-PrOH} = 80:20$, 0.7 mL/min).

(S)-1,1,1-Trifluoro-2-(N-(R)-tert-butanesulfinyl)-amino-2-cyano-2-(4-methyl-phenyl)-ethane (2f). m.p. 92-94 $^\circ\text{C}$; $[\alpha]_D^{20} = -49.2$ (c = 0.65 in CHCl_3); ^1H NMR (300MHz, CDCl_3 , 25°C , TMS): $\delta = 1.29$ (s, 9H; $t\text{-Bu}$), 2.43 (s, 3H; Me), 4.27 (s, 1H; NH), 7.32 (d, 2H, $^3J(\text{H}, \text{H}) = 8.1\text{Hz}$; Ph), 7.60 (d, 2H, $^3J(\text{H}, \text{H}) = 8.1\text{Hz}$; Ph); ^{13}C NMR (75MHz, CDCl_3 , 25°C): $\delta = 21.2$ (s), 22.4 (s), 57.8 (s), 64.0 (q, $J(\text{F}, \text{C}) = 31.7\text{Hz}$), 114.5 (s), 122.2 (q, $J(\text{F}, \text{C}) = 284.5\text{Hz}$), 124.5 (s), 127.9 (s), 129.9 (s), 141.8 (s); ^{19}F NMR (282MHz, CDCl_3 , 25°C): $\delta = -76.2$ (s); MS (ESI): m/z 336.1 [$M+NH_4^+$]; HRMS [$M+Na^+$] Anal's Calc'd for $\text{C}_{14}\text{H}_{17}\text{F}_3\text{N}_2\text{OSNa}$: 341.0911, Found: 341.0907; tr (R_s, S) = 18.45 min, tr (R_s, R) = 7.20 min, Chiralpak AD-H, column No. ADH0CE-DB235, $\lambda = 230\text{ nm}$, Hex: $i\text{-PrOH} = 90:10$, 0.7 mL/min).

(S)-1,1,1-Trifluoro-2-(N-(R)-tert-butanesulfinyl)-amino-2-cyano-2-(4-methoxy-phenyl)-ethane (2g). m.p. 73-74 °C; $[\alpha]_D^{20} = -76.8$ (c = 0.75 in CHCl₃); ¹H NMR (300MHz, CDCl₃, 25 °C, TMS): δ = 1.28 (s, 9H; *t*-Bu), 3.86 (s, 3H; Me), 4.26 (s, 1H; NH), 7.03 (d, 2H, ³*J*(H, H) = 9.0Hz; Ph), 7.62 (d, 2H, ³*J*(H, H) = 8.7Hz; Ph); ¹³C NMR (75MHz, CDCl₃, 25 °C): δ = 22.4 (s), 55.5 (s), 57.8 (s), 64.8 (q, *J*(F, C) = 32.0Hz), 114.6 (s), 114.6 (s), 119.0 (s), 122.3 (q, *J*(F, C) = 284.5Hz), 130.3 (s), 161.8 (s); ¹⁹F NMR (282MHz, CDCl₃, 25 °C): δ = -76.7 (s); MS (ESI): *m/z* 352.1 [*M*+NH₄⁺]; HRMS [*M*+Na⁺] Anal's Calc'd for C₁₄H₁₇F₃N₂O₂SNa: 357.0861, Found: 357.0854; tr (*R*_S, *S*) = 13.14 min, tr (*R*_S, *R*) = 6.50 min, (Chiralpak AD-H, column No. ADH0CE-DB235, λ = 254nm, Hex: *i*-PrOH = 80:20, 0.7 mL/min).

(S)-1,1,1-Trifluoro-2-(N-(R)-tert-butanesulfinyl)-amino-2-cyano-2-(4-chlor-phenyl)-ethane (2h). Oil. $[\alpha]_D^{20} = -88.8$ (c = 0.6 in CHCl₃); ¹H NMR (300MHz, CDCl₃, 25 °C, TMS): δ = 1.27 (s, 9H; *t*-Bu), 4.29 (s, 1H; NH), 7.50 (d, 2H, ³*J*(H, H) = 6.9Hz; Ph), 7.65 (d, 2H, ³*J*(H, H) = 6.9Hz; Ph); ¹³C NMR (75MHz, CDCl₃, 25 °C): δ = 22.2 (s), 58.5 (s), 64.5 (q, *J*(F, C) = 32.5Hz), 113.8 (s), 121.9 (q, *J*(F, C) = 284.3Hz), 128.4 (s), 129.1 (s), 129.7 (s), 137.9 (s); ¹⁹F NMR (282MHz, CDCl₃, 25 °C): δ = -76.4 (s); MS (ESI): *m/z* 356.2 [*M*+NH₄⁺]; HRMS [*M*+Na⁺] Anal's Calc'd for C₁₃H₁₄ClF₃N₂O₂SNa: 361.0365, Found: 361.0363; tr (*R*_S, *S*) = 6.11 min, tr (*R*_S, *R*) = 7.02 min, (Chiralpak AD, column No. AD00CE-HI084, λ = 214 nm, Hex: *i*-PrOH = 90:10, 0.7 mL/min).

2. General procedure for preparing 3a-3h

(R)-1,1,1-Trifluoro-2-(N-(R)-*tert*-butanesulfinyl)-amino-2-cyano-propane (3a). 0.149 g (1.5 mmol) of TMSCN was added into a solution of 0.215 g (1 mmol) **1a** in 2 mL DMF at -35°C . After stirred for 8 hours, the reaction mixture was quenched with sat. NH_4Cl . The mixture was extracted by EtOAc for 3 times and the extraction was dried over Na_2SO_4 . Removing solvent *in vacuo* and purifying by chromatography on silica gel (EtOAc/PE = 1/6) gave 0.164g of (R)-1,1,1-trifluoro-2-(N-(R)-*tert*-butanesulfinyl)-amino-2-cyano-propane (**3a**) in 67% yield as a white solid. m.p. $128.5\text{--}129.5^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{20} = -81.6$ ($c = 0.5$ in CHCl_3); ^1H NMR (300MHz, CDCl_3 , 25°C , TMS): $\delta = 1.29$ (s, 9H; *t*-Bu), 1.95 (s, 3H; Me), 3.78 (s, 1H; NH); ^{13}C NMR (75MHz, CDCl_3 , 25°C): $\delta = 21.8$ (s), 22.2 (s), 57.6 (q, $J(\text{F}, \text{C}) = 32.5\text{Hz}$), 114.3 (s) 122.5 (q, $J(\text{F}, \text{C}) = 283.1\text{Hz}$); ^{19}F NMR (282MHz, CDCl_3 , 25°C): $\delta = -79.0$ (s); MS (ESI): m/z 260.0 [$M + \text{NH}_4^+$]; HRMS [$M + \text{Na}^+$] Anal's Calc'd for $\text{C}_8\text{H}_{13}\text{F}_3\text{N}_2\text{OSNa}$: 265.0598, Found: 265.0597; t_{r} (*R*_s, *S*) = 7.59 min, t_{r} (*R*_s, *R*) = 11.50 min, (Chiralpak AS, column No. AS00CE-JG019+ Chiralpak AS, column No. AS00CC-IL019, $\lambda = 214\text{nm}$, Hex: *i*-PrOH = 90:10, 0.7 mL/min).

(R)-1,1,1-Trifluoro-2-(N-(R)-*tert*-butanesulfinyl)-amino-2-cyano-butane (3b). m.p. $140\text{--}142^{\circ}\text{C}$; $[\alpha]_{\text{D}}^{20} = -91.2$ ($c = 0.5$ in CHCl_3); ^1H NMR (300MHz, CDCl_3 , 25°C , TMS): $\delta = 1.20\text{--}1.32$ (m, 12H), 1.99-2.29 (m, 2H; CH_2), 3.59 (s, 1H; NH); ^{13}C NMR (75MHz, CDCl_3 , 25°C): $\delta = 8.0$ (s), 22.3 (s), 27.6 (s), 58.1 (s), 62.8 (q, $J(\text{F}, \text{C}) = 36.1\text{Hz}$), 113.0 (s) 122.7 (q, $J(\text{F}, \text{C}) = 283.5\text{Hz}$); ^{19}F NMR (282MHz, CDCl_3 , 25°C): $\delta = -77.2$ (s); MS (ESI): m/z 274.1 [$M + \text{NH}_4^+$]; HRMS [$M + \text{Na}^+$] Anal's Calc'd for $\text{C}_9\text{H}_{15}\text{F}_3\text{N}_2\text{OSNa}$: 279.0755, Found: 279.0753; t_{r} (*R*_s, *S*) = 6.18 min, t_{r} (*R*_s, *R*) = 8.77 min, (Chiralpak AS, column No. AS00CE-JG019+ Chiralpak AS, column No. AS00CC-IL019, $\lambda = 214\text{nm}$, Hex: *i*-PrOH = 80:20, 0.7 mL/min).

(R)-1,1,1-Trifluoro-2-(N-(R)-*tert*-butanesulfinyl)-amino-2-cyano-octane (3c). m.p. 94-95 °C; $[\alpha]_D^{20} = -76.7$ ($c = 1.0$ in CHCl_3); ^1H NMR (300MHz, CDCl_3 , 25 °C, TMS): $\delta = 0.87$ -0.91 (m, 3H), 1.28 (s, 9H), 1.29-1.42 (m, 6H), 1.60-1.69 (m, 2H), 1.90-2.00 (m, 1H), 2.09-2.16 (m, 1H), 3.57 (s, 1H; NH); ^{13}C NMR (75MHz, CDCl_3 , 25 °C): $\delta = 13.9$ (s), 22.3 (s), 22.42 (s), 23.5 (s), 28.7 (s), 31.2 (s), 33.8 (s), 58.1 (s), 61.9 (q, $J(\text{F}, \text{C}) = 45.9\text{Hz}$), 113.2 (s) 122.6 (q, $J(\text{F}, \text{C}) = 267.8\text{Hz}$); ^{19}F NMR (282MHz, CDCl_3 , 25 °C): $\delta = -77.4$ (s); MS (ESI): m/z 330.1 [$M + \text{NH}_4^+$]; HRMS [$M + \text{Na}^+$] Anal's Calc'd for $\text{C}_{13}\text{H}_{23}\text{F}_3\text{N}_2\text{OSNa}$: 335.1381, Found: 335.1374; tr (R_s, S) = 4.79 min, tr (R_s, R) = 5.09 min, (Chiralpak AD-H, column No. ADH0CE-DB235, $\lambda = 214$ nm, Hex: *i*-PrOH = 90:10, 0.7 mL/min).

(R)-1,1,1-Trifluoro-2-(N-(R)-*tert*-butanesulfinyl)-amino-2-cyano-4-phenyl-butane (3d). m.p. 94-95 °C; $[\alpha]_D^{20} = -48.8$ ($c = 1.0$ in CHCl_3); ^1H NMR (300MHz, CDCl_3 , 25 °C, TMS): $\delta = 1.24$ (s, 9H; *t*-Bu), 2.30-2.54 (m, 2H; CH_2), 3.04 (t, 2H, $^3J(\text{H}, \text{H}) = 8.4\text{Hz}$), 3.84 (s, 1H; NH), 7.23-7.38 (m, 5H; Ph); ^{13}C NMR (75MHz, CDCl_3 , 25 °C): $\delta = 22.4$ (s), 29.85 (s), 35.3 (s), 58.1 (s), 62.0 (q, $J(\text{F}, \text{C}) = 30.7\text{Hz}$), 113.2 (s), 122.6 (q, $J(\text{F}, \text{C}) = 284.0\text{Hz}$), 127.0 (s), 128.6 (s), 129.0 (s), 138.5 (s); ^{19}F NMR (282MHz, CDCl_3 , 25 °C): $\delta = -77.1$ (s); MS (ESI): m/z 333.1 [$M + \text{H}^+$]; HRMS [$M + \text{Na}^+$] Anal's Calc'd for $\text{C}_{15}\text{H}_{19}\text{F}_3\text{N}_2\text{OSNa}$: 355.1068, Found: 355.1061; tr (R_s, S) = 8.41 min, tr (R_s, R) = 11.76 min, (Chiralpak AD-H, column No. ADH0CE-DB235, $\lambda = 254\text{nm}$, Hex: *i*-PrOH = 90:10, 0.7 mL/min).

(R)-1,1,1-Trifluoro-2-(N-(R)-tert-butanesulfinyl)-amino-2-cyano-2-phenyl-ethane (3e). m.p.

117-120 °C; $[\alpha]_D^{20} = -41.6$ (c = 1.0 in CHCl₃); ¹H NMR (300MHz, CDCl₃, 25 °C, TMS): δ = 1.25 (s, 9H; *t*-Bu), 4.50 (s, 1H; NH), 7.48-7.53 (m, 3H; Ph), 7.71-7.75 (m, 2H; Ph); ¹³C NMR (75MHz, CDCl₃, 25 °C): δ = 22.2 (s), 58.4 (s), 64.3 (q, *J*(F, C) = 31.3Hz), 114.0 (s), 122.1 (q, *J*(F, C) = 279.3Hz), 127.6 (s), 129.4 (s), 130.1 (s), 131.2 (s); ¹⁹F NMR (282MHz, CDCl₃, 25 °C): δ = -75.2 (s); MS (ESI): *m/z* 305.0 [*M*+*H*⁺]; HRMS [*M*+*Na*⁺] Anal's Calc'd for C₁₃H₁₅F₃N₂OSNa: 327.0755, Found: 327.0747; tr (*R*_s, *S*) = 6.05 min, tr (*R*_s, *R*) = 5.49 min, (Chiralpak AD-H, column No. ADH0CE-DB235, λ = 254nm, Hex: *i*-PrOH = 80:20, 0.7mL/min).

(R)-1,1,1-Trifluoro-2-(N-(R)-tert-butanesulfinyl)-amino-2-cyano-2-(4-methyl-phenyl)-ethane

(3f). m.p. 156-158 °C; $[\alpha]_D^{20} = -36.1$ (c = 1.0 in CHCl₃); ¹H NMR (300MHz, CDCl₃, 25 °C, TMS): δ = 1.27 (s, 9H; *t*-Bu), 2.40 (s, 3H; Me), 4.31 (s, 1H; NH), 7.30 (d, 2H, ³*J*(H, H) = 8.1Hz; CH₂), 7.60 (d, 2H, ³*J*(H, H) = 8.1Hz; CH₂); ¹³C NMR (75MHz, CDCl₃, 25 °C): δ = 21.2 (s), 22.2 (s), 58.3 (s), 64.6 (q, *J*(F, C) = 35.8Hz), 114.1 (s), 122.1 (q, *J*(F, C) = 277.1Hz), 127.1 (s), 127.1 (s), 130.0 (s), 141.7 (s); ¹⁹F NMR (282MHz, CDCl₃, 25 °C): δ = -76.2 (s); MS (ESI): *m/z* 336.1 [*M*+*NH*₄⁺]; HRMS [*M*+*Na*⁺] Anal's Calc'd for C₁₄H₁₇F₃N₂OSNa: 341.0911, Found: 341.0904; tr (*R*_s, *S*) = 9.83 min, tr (*R*_s, *R*) = 8.84 min, (Chiralpak AD-H, column No. ADH0CE-DB235, λ = 254nm, Hex: *i*-PrOH = 80:20, 0.7 mL/min).

(R)-1,1,1-Trifluoro-2-(N-(R)-tert-butanesulfinyl)-amino-2-cyano-2-(4-methoxy-phenyl)-ethane

(3g). m.p. 148-149 °C; $[\alpha]_D^{20} = -30.1$ (c = 1.0 in CHCl₃); ¹H NMR (300MHz, CDCl₃, 25 °C, TMS): δ

= 1.29 (s, 9H; *t*-Bu), 3.85 (s, 3H; Me), 4.06 (s, 1H; NH), 6.98-7.02 (m, 2H; Ph), 7.61-7.65 (m, 2H, Ph); ^{13}C NMR (75MHz, CDCl_3 , 25 °C): δ = 22.2 (s), 55.5 (s), 58.2 (s), 64.3 (q, $J(\text{F}, \text{C}) = 31.6\text{Hz}$), 114.2 (s), 114.7 (s), 121.7 (s), 122.1 (q, $J(\text{F}, \text{C}) = 284.3\text{Hz}$), 129.0 (s), 161.7 (s); ^{19}F NMR (282MHz, CDCl_3 , 25 °C): δ = -75.5 (s); MS (ESI): m/z 335.0 [$M+H^+$]; HRMS [$M+Na^+$] Anal's Calc'd for $\text{C}_{14}\text{H}_{17}\text{F}_3\text{N}_2\text{O}_2\text{SNa}$: 357.0861, Found: 357.0855; tr (*R*_s, *S*) = 8.53 min, tr (*R*_s, *R*) = 7.04 min, (Chiralpak AD-H, column No. ADH0CE-DB235, λ = 254nm, Hex: *i*-PrOH = 80:20, 0.7 mL/min).

(R)-1,1,1-Trifluoro-2-(N-(R)-*tert*-butanesulfinyl)-amino-2-cyano-2-(4-chlor-phenyl)-ethane (3h). m.p.99.5-100.5 °C; [α]_D²⁰ = -26.3 (c = 0.96 in CHCl_3); ^1H NMR (300MHz, CDCl_3 , 25 °C, TMS): δ = 1.30 (s, 9H; *t*-Bu), 4.25 (s, 1H; NH), 7.50-7.53 (m, 2H; Ph), 7.69 (d, 2H, $^3J(\text{H}, \text{H}) = 8.4\text{Hz}$); ^{13}C NMR (75MHz, CDCl_3 , 25 °C): δ = 22.4 (s), 58.4 (s), 64.6 (q, $J(\text{F}, \text{C}) = 31.6\text{Hz}$), 113.7 (s), 121.9 (q, $J(\text{F}, \text{C}) = 284.8\text{Hz}$), 128.5 (s), 129.1 (s), 129.7 (s), 137.8 (s); ^{19}F NMR (282MHz, CDCl_3 , 25 °C): δ = -75.3 (s); MS (ESI): m/z 356.0 [$M+NH_4^+$]; HRMS [$M+Na^+$] Anal's Calc'd for $\text{C}_{13}\text{H}_{14}\text{ClF}_3\text{N}_2\text{O}_2\text{SNa}$: 361.0365, Found: 361.0362; tr (*R*_s, *S*) = 6.13 min, tr (*R*_s, *R*) = 7.61min, (Chiralpak AD-H, column No. ADH0CE-DB235, λ = 254nm, Hex: *i*-PrOH = 80:20, 0.7 mL/min).

3. General procedure for preparing α -Trifluoromethylated- α -amino acids.

(S)-2-Amino-2-phenyl-1,1,1-trifluoropropanoic acid (4a). Compound **2e** (152 mg, 0.5 mmol) was refluxed with 12N HCl (10 mL) for 12 hours. The mixture was diluted with 10 mL water, extracted with ethyl ester, and the water layer neutralized at 0 °C with pyridine. The solid that formed was separated, washed with water and recrystallized from ethanol-water to give amino acid **4a** (88mg, 80%)

yield). $[\alpha]_D^{20} = -0.6$ (c = 1.0 in H₂O); ^1H NMR (300MHz, D₂O, 25 °C): $\delta = 7.36\text{--}7.48$ (m, 5H; Ph); ^{19}F NMR(282MHz, D₂O, 25 °C): $\delta = -73.1$ (s). MS (ESI): m/z 220.1 $[M+H^+]$; HRMS $[M+H^+]$ Anal's Calc'd for C₉H₈F₃NO₂H: 220.0585, Found: 220.0579.

(S)-2-Amino-2-methyl-1,1,1-trifluoropropanoic acid (4b). 1 73% yield. $[\alpha]_D^{20} = -13.0$ (c = 1.0 in H₂O); ^1H NMR (300MHz, D₂O, 25 °C): $\delta = 1.7$ (s, 3H; Me); ^{19}F NMR(282MHz, D₂O, 25 °C): $\delta = -75.9$ (s). MS (ESI): m/z 158.1 $[M+H^+]$; HRMS $[M+H^+]$ Anal's Calc'd for C₄H₆F₃NO₂H: 158.0429, Found: 158.0426.

(1) Bravo, P.; Capelli, S.; Meille, S. E.; Viani, F.; Zanda, M.; Kukhar, V. P.; Soloshonok, V. A. *Tetrahedron: Asymmetry* **1994**, 35, 2009-2018.

100%

1296

3.52
2.18

0.90

9.00

7.605
7.579
7.323
7.296
7.275

4.288

2.421

1.286

0.005

7.670
7.641
7.608
7.478

4.292

1.285
1.271
1.257

7.647
7.647
7.645
7.617
7.617
7.263
7.020
7.010
7.002
6.987
6.980
6.969

4.056
3.848

1.294

-0.003

spect, D2O,		SW1: 6173		OF1: 1882.8		PTSIId: 16384	
F1: 300.132		PW: 10.2 usec		PD: 2.0 sec		NA: 8	
EX: zg30						LB: 0.0	

USER: sioc -- DATE: Mon Feb 13 05:12:45 2006

WinNuts - \$-17025H

An ORTEP view of 2a

An ORTEP view of 2e