Asymmetric Synthesis of α,α -Difluoro- β -Amino Acid Derivatives from Enantiomerically Pure *N*-*tert*-Butylsulfinimines

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Supporting Material

X-ray crystal structure of the amide derivative **12**

Crystallographic data for structure **12** have been deposited with the Cambridge Crystallographic Data Centre (CCDC 178107). Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK. (Fax: 44-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

Experimental Section

General Methods: All starting materials were obtained from commercial sources and were used without further purification. Anhydrous solvents were obtained from Aldrich in Sure-seal containers. Commercial diethyl ether was used without further distillation or drying. FTIR spectra were recorded on a Perkin Elmer infrared spectrometer using 3M polyethylene film. Normal phase chromatography was carried out using silica gel 60F (230-400 mesh). Reverse phase chromatography was carried out using a YMC-Pack Pro C18 column (dimensions 150x20 mm, 5 μ m particle size). NMR spectra were recorded in either CDCl_3 or CD_3OD solution on Varian spectrometers as noted below: ^1H NMR spectra were recorded at 300 MHz or 400 MHz as noted below; ^{13}C NMR spectra were recorded at 75 MHz or 100 MHz as noted below. Chemical shifts are expressed in ppm and the ^1H coupling constants (J) are quoted in Hertz (Hz). Multiplicities are abbreviated as follows: singlet, s; broad singlet, br s; doublet, d; triplet, t; quartet, q; doublet of doublets, dd; multiplet, m; broad multiplet, br m; apparent quartet, app q; apparent triplet, app t. High resolution accurate mass measurement data were obtained on two mass spectrometers: Fast atom bombardment (FAB) ionization mass spectral data were acquired on a VG instruments ZAB-HF mass spectrometer. Internal calibration was accomplished from cluster ion signals observed from the glycerol matrix. Electrospray (ES) and atmospheric pressure chemical ionization (APCI) mass spectral data were acquired on a Bruker Daltonics 3T Fourier transform ion cyclotron resonance mass spectrometer (FT/ICR/MS). External/internal calibration was accomplished with polypropylene glycol.

Compounds **4a-c** and **4e** were prepared from the corresponding aldehydes **3a-c** and **3e** according to the procedure described for the preparation of **4d** (see Experimental Section of manuscript) with modifications as noted below:

2-Methyl-N-[(1)-3-methylbutylidene]propane-2-sulfinamide (4a): The crude product was isolated as a light yellow oil and used without further purification (4.88 g, 89%): ^1H NMR (CDCl_3 , 400 MHz): δ 8.06 (t, $J = 5.2$ Hz, 1 H), 2.43-2.40 (m, 2 H), 2.10-2.04 (m, 1 H), 1.21 (s, 9 H), 0.98 (d, $J = 5.6$ Hz, 6 H); ^{13}C NMR (CDCl_3 , 75 MHz): δ 169.60, 56.71, 45.14, 26.37, 22.58; FTIR (cm^{-1}): 2916 (C-H), 1621 (C=N), 1086 (S=O), 677 (C-S); HRMS (FAB) $\text{M}+\text{H}$: calculated for $(\text{C}_9\text{H}_{20}\text{NOS})^+$ 190.1260, found 190.1238.

N-[(1)-butylidene]-2-methylpropane-2-sulfinamide (4b): After filtration of the reaction mixture, the filtrate was washed with brine, dried over sodium sulfate, and concentrated *in vacuo* to afford **4b** as a pale yellow oil in quantitative yield: ^1H NMR (CDCl_3 , 400 MHz): δ 8.05 (t, $J = 4.4$ Hz, 1 H), 2.51-2.46 (m, 2 H), 1.64 (m, 2 H), 1.20 (s, 9 H), 0.97

(t, $J = 7.4$ Hz, 3 H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 169.76, 56.57, 38.14, 22.41, 19.01, 13.88; FTIR (cm^{-1}): 2958 (C-H), 1621 (C=N), 1085 (S=O), 678 (C-S); HRMS (FAB) $\text{M}+\text{H}$: calculated for $(\text{C}_8\text{H}_{18}\text{NOS})^+$ 176.1104, found 176.1086.

4c

2-Methyl-N-[(1-phenylmethylidene)propane-2-sulfinamide (4c): The crude product was purified by silica gel chromatography (isocratic elution with 1:9 ethyl acetate/hexane) to give **4c** as a clear oil (30% yield): ^1H NMR (CDCl_3 , 400 MHz): δ 8.60 (s, 1 H), 7.87-7.85 (m, 2 H), 7.50-7.48 (m, 3 H), 1.27 (s, 9 H); ^{13}C NMR (CDCl_3 , 75 MHz): δ 162.98, 134.29, 132.64, 129.59, 129.15, 57.97, 22.82; FTIR (cm^{-1}): 2976 and 2968 (aromatic C-H), 1605 (C=N), 1086 (S=O), 691 (C-S); HRMS (FAB) $\text{M}+\text{H}$: calculated for $(\text{C}_{11}\text{H}_{16}\text{NOS})^+$ 210.0947, found 210.0943.

4e

2-Methyl-N-[(1-1,3-thiazole-2-ylmethylidene)propane-2-sulfinamide (4e): The crude product was purified by silica gel chromatography (isocratic elution with 1:5 ethyl acetate/hexane) to afford **4e** as a yellow solid (79% yield): ^1H NMR (CDCl_3 , 400 MHz): δ 8.80 (s, 1 H), 8.06 (d, $J = 3.2$ Hz, 1 H), 7.61 (d, $J = 3.2$ Hz, 1 H), 1.29 (s, 9 H); ^{13}C NMR (CDCl_3 , 75 MHz): δ 164.46, 156.59, 145.49, 124.31, 58.83, 22.89; FTIR (cm^{-1}):

2960 (aromatic C-H), 1592 (C=N), 1086 (S=O), 628 (C-S); HRMS (FAB) M+H: calculated for (C₈H₁₃N₂OS₂)⁺ 217.0464, found 217.0463.

Sulfinamides **5a-c** and **5e** were prepared from sulfinimines (**4a-c,e**) according to the procedure described for the preparation of **5d** (see Experimental Section of manuscript) with modifications as noted below:¹

5a

Ethyl 3-[(*tert*-butylsulfinyl)amino]-2,2-difluoro-5-methylhexanoate (5a): 1.4 equivalents of Reformatsky reagent (**1**) were used for the reaction. Silica gel chromatography (gradient elution with 1:3.33 ethyl acetate/hexane to 1:1 ethyl acetate/hexane) afforded the diastereomeric mixture **5a** as a clear oil (51% yield). The minor and major diastereomers eluted at 4.38 and 5.29 min respectively by analytical chiral HPLC [Chiralpak AD column eluting with 95:5 A/B, where A = hexane and B = ethanol (+0.1%DEA)]; diastereomeric ratio 19:81. Data for the diastereomeric mixture **5a**: ¹H NMR (CDCl₃, 400 MHz): δ 4.38 (-COOCH₂CH₃ of major diastereomer, app q, *J* = 7.2 Hz, 2 H), 4.32 (-COOCH₂CH₃ of minor diastereomer, m, 2 H), 3.82 (br m, 1 H), 3.56 (-NH- of major diastereomer, d, *J* = 9.6 Hz, 1 H), 3.09 (-NH- of minor diastereomer, d, *J* = 9.7 Hz), 1.84 (m, 1 H), 1.72-1.71 (m, 1 H), 1.57-1.53 (m, 1 H), 1.26 (t, *J* = 7.2 Hz, 3 H), 1.22 (s, 9 H), 0.97 (d, *J* = 6.4 Hz, 3 H), 0.91 (d, *J* = 6.4 Hz, 3 H); ¹³C NMR (CDCl₃, 75 MHz): δ 63.55, 57.78, 38.00, 23.99, 23.76, 22.89, 20.96, 14.39; FTIR (cm⁻¹): 2916 (C-

H), 1773 (C=O), 1064 (C-O, S=O); HRMS (FAB) M+H: calculated for (C₁₃H₂₆F₂NO₃S)⁺ 314.1598, found 314.1597.

5b

Ethyl 3-[(*tert*-butylsulfinyl)amino]-2,2-difluorohexanoate (5b**):** After the initial 18 hour reaction period, an additional 1.4 equivalents of freshly prepared Reformatsky reagent (**1**) was added and the mixture was stirred for another 18 hours at room temperature to drive the reaction to completion. Silica gel chromatography (gradient elution with 1:3.33 ethyl acetate/hexane to 1:1 ethyl acetate/hexane) afforded the diastereomeric mixture **5b** as a yellow oil (55% yield). The minor and major diastereomers eluted at 5.66 and 6.97 min respectively by analytical chiral HPLC [Chiralpak AD column eluting with 95:5 A/B, where A = hexane and B = ethanol (+0.1% DEA)]; diastereomeric ratio 20:80. Data for the diastereomeric mixture **5b**: ¹H NMR (CDCl₃, 400 MHz): δ 4.38 (-COOCH₂CH₃ of major diastereomer, app q, *J* = 7.2 Hz, 2 H), 4.35 (-COOCH₂CH₃ of minor diastereomer, m, 2 H), 3.82-3.79 (br m, 1 H), 3.57 (-NH- of major diastereomer, d, *J* = 9.6 Hz, 1 H), 3.13 (-NH- of minor diastereomer, d, *J* = 9.8 Hz, 1 H), 1.69-1.53 (m, 4 H), 1.38 (t, *J* = 7.2 Hz, 3 H), 1.23 [(CH₃)₃CSO- of major diastereomer, s, 9 H], 1.20 [(CH₃)₃CSO- of minor diastereomer, s, 9 H], 0.95 (t, *J* = 7.0 Hz, 3 H); ¹³C NMR (CDCl₃, 75 MHz): δ 63.54, 60.55, 58.83, 57.08, 31.13, 22.66, 18.90,

14.35, 14.03; FTIR (cm⁻¹): 2961 (C-H), 1769 (C=O), 1056 (C-O, S=O); HRMS (FAB) M+H: calculated for (C₁₂H₂₄F₂NO₃S)⁺ 300.1440, found 300.1424.

5c

Ethyl-3-[(*tert*-butylsulfinyl)amino]-2,2-difluoro-3-phenylpropanoate (5c): 1.4 equivalents of the Reformatsky reagent (**1**) were used initially in the reaction. After 18 h, an additional 3.0 equivalents of freshly prepared Reformatsky reagent (**1**) was added and the mixture stirred for another 18 h at room temperature to drive the reaction to completion. Silica gel chromatography (isocratic elution with 1:3.33 ethyl acetate/hexane) afforded the diastereomeric mixture **5c** as a pale yellow oil (82% yield). The minor and major diastereomers eluted at 8.53 and 10.0 min respectively by analytical chiral HPLC (Chiralpak AD column eluting with 95:5 A/B, where A = hexane and B = ethanol); diastereomeric ratio 10:90. Data for the diastereomeric mixture **5c**: ¹H NMR (CDCl₃, 400 MHz): δ 7.36 (br m, 5 H), 5.34 (C-3 proton of minor diastereomer, m, 1 H), 4.98 (C-3 proton of major diastereomer, td, *J* = 4.8, 12.4 Hz, 1 H), 4.42 (-COOCH₂CH₃ of minor diastereomer, app q, *J* = 6.7 Hz, 2 H), 4.26 (-COOCH₂CH₃ of major diastereomer, app q, *J* = 7.2 Hz, 2 H), 4.15 (-NH- of major diastereomer, d, *J* = 10 Hz), 3.85 (-NH- of minor diastereomer, d, *J* = 10 Hz), 1.39-1.23 (m, 3 H), 1.22 (s, 9 H); ¹³C NMR (CDCl₃, 75 MHz): δ 129.42, 128.80, 63.63, 61.48, 56.60, 22.62, 14.40, 13.96; FTIR (cm⁻¹): 2978 (aromatic C-H), 1771 (C=O), 1096 (S=O), 1067 (C-O); HRMS (FAB) M+H: calculated for (C₁₅H₂₂F₂NO₃S)⁺ 334.1275, found 334.1275.

5e

Ethyl 3-[(*tert*-butylsulfinyl)amino]-2,2-difluoro-3-(1,3-thiazol-2-yl)propanoate (5e):

Silica gel chromatography (gradient elution with 1:5 ethyl acetate/hexane to 1:1 ethyl acetate/hexane to 7:10 ethyl acetate/hexane) afforded the product as a pale yellow oil (58% yield). The minor and major diastereomers eluted at 7.39 and 9.08 min respectively by analytical chiral HPLC (Chiralpak AD column eluting with 90:10 A/B, where A = hexane and B = 2-propanol); diastereomeric ratio 5:95. Data for the diastereomeric mixture **5e**: ^1H NMR (CDCl_3 , 300 MHz): δ 7.82 (d, J = 3.3 Hz, 1 H), 7.43 (d, J = 3.0 Hz, 1 H), 5.37-5.30 (m, 1 H), 5.01 (d, J = 8.4 Hz, 1 H), 4.32 (app q, J = 7.2 Hz, 2 H), 1.34 (t, J = 7.2 Hz, 3 H), 1.27 (s, 9 H); ^{13}C NMR (CDCl_3 , 75 MHz): δ 162.42, 161.54, 142.82, 121.52, 116.61, 113.22, 109.79, 63.52, 60.03, 57.22, 22.68, 14.06; FTIR (cm^{-1}): 2980 (aromatic C-H), 1774 (C=O), 1067 (S=O, C-O); HRMS (FAB) $\text{M}+\text{H}$: calculated for $(\text{C}_{12}\text{H}_{19}\text{F}_2\text{N}_2\text{O}_3\text{S}_2)^+$ 341.0800, found 341.0800.

12

(3R)-3-[(tert-butylsulfinyl)amino]-3-cyclohexyl-2,2-difluoropropanamide (12):

Ammonia gas was bubbled into a solution of ethyl (3R)-3-[(tert-butylsulfinyl)amino]-3-cyclohexyl-2,2-difluoropropanoate [(R, R)-5d, 557 mg, 1.64 mmol] in diethyl ether (2.5 mL) for 20 min. The mixture was stirred at room temperature for 18 h, during which time the product precipitated out of solution. The solvent was removed *in vacuo* to afford **12** as a white, powdery solid (382 mg, 75%): ^1H NMR (CDCl_3 , 400 MHz): δ 7.00 (br s, 1 H), 6.08 (br s, 1 H), 3.81 (d, $J = 10.8$ Hz, 1 H), 3.69-3.68 (m, 1 H), 1.89-1.63 (br m, 7 H), 1.26 (s, 9 H), 1.29-0.98 (m, 4 H); ^{13}C NMR (CDCl_3 , 75 MHz): δ 165.91, 164.84, 60.07, 57.65, 38.84, 31.61, 27.46, 26.16, 23.89, 22.32; FTIR (cm^{-1}): 3204 (N-H), 2932 and 2921 (C-H), 1714 (C=O), 1633 (N-H), 1212 (C-N), 1046 (S=O); HRMS (ES) $\text{M}+\text{H}^+$: calculated for $(\text{C}_{13}\text{H}_{25}\text{F}_2\text{N}_2\text{O}_2\text{S})^+$ 311.1600, found 311.1603.

N-[(1R)-3-amino-1-cyclohexyl-2,2-difluoropropyl]-2-methylpropane-2-sulfinamide

(13): To a solution of (3R)-3-[(tert-butylsulfinyl)amino]-3-cyclohexyl-2,2-difluoropropanamide (**12**, 352 mg, 1.13 mmol) in THF (9 mL) was added dropwise borane-methyl sulfide complex (591 μL , 6.23 mmol). The mixture was heated to 80 $^{\circ}\text{C}$ under inert atmosphere for 5 hours, then stirred at room temperature for 12 hours. Methanol (3 mL) was added to the mixture which was then concentrated *in vacuo*. The residue was treated with additional methanol (3 mL) and the solvent removed *in vacuo*. Silica gel chromatography (gradient elution with ethyl acetate to 1:49

methanol/chloroform to 1:19 methanol/chloroform to 1:9 methanol/chloroform) afforded amine **13** as a clear oil (199 mg, 59%): ^1H NMR (CDCl_3 , 300 MHz): δ 3.86 (d, $J = 9.3$ Hz, 1 H), 3.64-3.49 (m, 1 H), 3.35-3.03 (m, 2 H), 1.82-1.46 (m, 11 H), 1.25 (s, 9 H), 1.12-0.98 (m, 2 H); ^{13}C NMR (CDCl_3 , 75 MHz): δ 127.07, 123.78, 120.52, 62.97, 61.41, 57.28, 44.69, 38.86, 37.33, 31.22, 27.12, 26.11, 23.97, 23.31, 22.42; FTIR (cm^{-1}) 3388 (N-H), 2916 and 2848 (C-H), 1055 (S=O), 794 (N-H); HRMS (APCI) $\text{M}+\text{H}^+$: calculated for $(\text{C}_{13}\text{H}_{27}\text{F}_2\text{N}_2\text{OS})^+$ 297.1807, found 297.1806.

***N*-{(3*R*)-3-[(*tert*-butylsulfinyl)amino]-3-cyclohexyl-2,2-difluoropropyl}-1-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-*L*-prolinamide (**14**):** To a mixture of *N*-[(1*R*)-3-amino-1-cyclohexyl-2,2-difluoropropyl]-2-methylpropane-2-sulfinamide (**13**, 199 mg, 0.67 mmol), Fmoc-proline (227 mg, 0.67 mmol), and 1-hydroxy-7-azabenzotriazole (45.7 mg, 0.34 mmol) in anhydrous DMF (2 mL) was added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (193 mg, 1.01 mmol). The mixture was stirred at room temperature for 18 hours and was then diluted with water (10 mL), resulting in precipitation of the product which was collected by filtration as a pale yellow powder (381 mg, 92%): ^1H NMR (CDCl_3 , 400 MHz): δ 7.90 (br s, 1 H), 7.77 (d, $J = 6.8$ Hz, 2 H), 7.65-7.55 (m, 2 H), 7.40 (m, 2 H), 7.32 (m, 2 H), 4.43-4.40 (m, 1 H), 4.30-4.20 (m, 3 H), 3.82-3.71 (m, 3 H), 3.59-3.48 (m, 3 H), 2.18-1.58 (m, 10 H), 1.35-1.19 (m, 14 H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 172.56, 155.53, 144.42, 141.53, 127.94, 125.48, 120.21,

67.96, 61.43, 57.49, 47.52, 37.87, 31.29, 29.87, 27.49, 26.38, 24.89, 23.30; FTIR (cm^{-1}) 3278 (N-H), 2932 and 2847 (aliphatic C-H), 1694 (C=O), 1451 (cyclohexane C-H), 1114 (S=O), 739 (N-H); HRMS (ES) $M+H$: calculated for $(\text{C}_{33}\text{H}_{44}\text{F}_2\text{N}_3\text{O}_4\text{S})^+$ 616.3015, found 616.3019.

***N*-[(3R)-3-amino-3-cyclohexyl-2,2-difluoropropyl]-1-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-L-prolinamide (15):** A solution of *N*-[(3R)-3-[(tert-butylsulfinyl)amino]-3-cyclohexyl-2,2-difluoropropyl]-1-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-L-prolinamide (**14**, 476 mg, 0.77 mmol) in 4.0M HCl/diethyl ether (3 mL) was stirred for 30 min at room temperature. The solvent was removed *in vacuo* and the residual oil was purified by reverse phase chromatography [30 min gradient elution with 95:5 water (+0.1% TFA)/acetonitrile (+0.1% TFA) to 5:95 water (+0.1% TFA)/acetonitrile (+0.1% TFA)]. The desired product **15** was obtained as a yellow oil (285 mg, 72%): ^1H NMR (CDCl_3 , 400 MHz): δ 8.83-8.80 (m, 1 H), 7.95 (br m, 2 H), 7.75 (d, $J = 7.6$ Hz, 2 H), 7.56-7.51 (m, 2 H), 7.41-7.37 (m, 2 H), 7.32-7.26 (m, 2 H), 4.56-4.41 (m, 1 H), 4.32-4.14 (m, 3 H), 3.67-3.46 (m, 3 H), 3.34-3.28 (m, 1 H), 3.21-3.17 (m, 1 H), 2.22-1.95 (m, 3 H), 1.88-1.82 (m, 3 H), 1.77-1.67 (m, 2 H), 1.57-1.53 (m, 2 H), 1.26-1.23 (m, 1 H), 1.05-1.03 (m, 4 H); ^{13}C NMR (CDCl_3 , 100 MHz): δ 173.63, 155.47, 143.92, 141.49, 128.07, 127.41, 125.28, 120.20, 68.20, 60.45, 47.41, 36.19, 29.43, 25.43; FTIR (cm^{-1}) 3270 (N-H), 2952 and 2846 (aliphatic C-H), 1644 (C=O), 1454

(cyclohexane C-H), 741 (N-H); HRMS (ES) M+H: calculated for (C₂₉H₃₆F₂N₃O₃)⁺ 512.2719, found 512.2698.

***N*-[**(3R)**-3-cyclohexyl-3-({*N*-[**(9H**-fluoren-9-ylmethoxy)carbonyl]-**D**-phenylalanyl}amino)-2,2-difluoropropyl]-[**(9H**-fluoren-9-ylmethoxy)carbonyl]-**L**-prolinamide (**16**):** To a mixture of *N*-[**(3R)**-3-amino-3-cyclohexyl-2,2-difluoropropyl]-1-[**(9H**-fluoren-9-ylmethoxy)carbonyl]-**L**-prolinamide (**15**, 120 mg, 0.23 mmol), Fmoc-**D**-phenylalanine (91 mg, 0.23 mmol), and 1-hydroxy-7-azabenzotriazole (16 mg, 0.12 mmol) in anhydrous DMF (1 mL) was added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (68 mg, 0.35 mmol). The mixture was stirred for 18 h at room temperature, diluted with water (8 mL), and extracted twice into ethyl acetate. The organic layers were combined, dried over sodium sulfate, and concentrated *in vacuo*. Silica gel chromatography (gradient elution with 3:7 ethyl acetate/hexanes to 1:1 ethyl acetate/hexanes to 7:3 ethyl acetate/hexanes) afforded **16** as a white powder (64 mg, 31%): ¹H NMR (CDCl₃, 400 MHz): δ 7.76-6.94 (m, 21 H), 6.50 (d, *J* = 9.6 Hz, 1 H), 4.97 (br m, 1 H), 4.62 (br m, 1 H), 4.47-4.39 (m, 2 H), 4.26-4.15 (m, 3 H), 4.03 (br s, 1 H), 3.77-3.55 (m, 3 H), 3.07-2.93 (m, 4 H), 2.19-1.96 (m, 4 H), 1.72-1.50 (m, 6 H), 1.32-0.78 (m, 5 H); ¹³C NMR (CDCl₃, 100 MHz): δ 171.71, 155.79, 143.52, 141.31, 136.50, 129.45, 128.74, 127.73, 124.97, 121.01, 120.01, 119.74, 67.81, 67.24, 61.11, 56.30,

47.07, 37.81, 35.83, 30.56, 29.70, 27.55, 25.85; FTIR (cm^{-1}) 3294 (N-H), 3065 (aliphatic C-H), 1693 and 1660 (C=O), 1538 (amide N-H), 738 (aromatic C-H); HRMS (ES) $\text{M}+\text{H}^+$: calculated for $(\text{C}_{53}\text{H}_{55}\text{F}_2\text{N}_4\text{O}_6)^+$ 881.4084, found 881.4083.

***N*-[(3*R*)-3-cyclohexyl-2,2-difluoro-3-(*D*-phenylalanyl)amino]propyl-*L*-prolinamide**

bis(trifluoroacetate) (17): *N*-[(3*R*)-3-cyclohexyl-3-({*N*-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-*D*-phenylalanyl}amino)-2,2-difluoropropyl]-[(9*H*-fluoren-9-ylmethoxy)carbonyl]-*L*-prolinamide (**16**, 41.2 mg, 0.05 mmol) was dissolved in a solution of 10% piperidine/DMF (1 mL). The mixture was stirred for 18 hours at room temperature followed by removal of solvent *in vacuo*. The residue was purified by reverse phase chromatography [gradient elution with 95:5 water (+0.1% TFA)/acetonitrile (+0.1% TFA) to 5:95 water (+0.1% TFA)/acetonitrile (+0.1% TFA)] to give the TFA salt of **17** as a white powder (18 mg, 54%): ^1H NMR (CD_3OD , 400 MHz): δ 7.40-7.29 (m, 5 H), 4.31-4.22 (m, 3 H), 3.72-3.31 (m, 5 H), 3.05-2.99 (m, 1 H), 2.48-2.42 (m, 1 H), 2.10-2.03 (m, 3 H), 2.01-1.69 (m, 6 H), 1.36-1.12 (m, 5 H); ^{13}C NMR (CD_3OD , 100 MHz): δ 169.37, 169.12, 134.43, 129.35, 129.03, 127.76, 121.98, 59.91, 54.41, 46.24, 41.77, 37.62, 37.34, 30.62, 29.96, 27.44, 26.12, 25.91, 25.85, 23.77; FTIR (cm^{-1}) 3336 (N-H), 2935 and 2862 (aliphatic C-H), 1698 and 1657 (C=O), 724 (aromatic C-H); HRMS (ES) $\text{M}+\text{H}^+$: calculated for $(\text{C}_{23}\text{H}_{35}\text{F}_2\text{N}_4\text{O}_2)^+$ 437.2728, found 437.2715.

(3R)-3-[(tert-butylsulfinyl)amino]-3-cyclohexyl-2,2-difluoropropanoic acid (18): To a solution of ethyl (3R)-3-[(tert-butylsulfinyl)amino]-3-cyclohexyl-2,2-difluoropropanoate [(**R,R**)-**5d**, 300 mg, 0.88 mmol] in ethanol (1 mL) was added sodium hydroxide (35 mg, 0.88 mmol). The mixture was stirred at 60 °C for 18 hours. The solvent was removed *in vacuo*, and the remaining residue was suspended in water. The mixture was cooled to 0 °C, acidified with 1N hydrochloric acid to pH 3 and extracted into ethyl acetate. The organic layer was washed with brine. The combined aqueous layers were saturated with sodium chloride and extracted twice into ethyl acetate and once into THF. The combined organic layers were dried over sodium sulfate and concentrated *in vacuo* to afford the acid **18** as a yellow solid (133 mg, 48%). ¹H NMR (CD₃OD, 300 MHz): δ 3.59-3.54 (m, 1 H), 1.89-1.85 (m, 1 H), 1.76-1.59 (m, 4 H), 1.40 (br s, 3 H), 1.28 (s, 9 H), 1.24-1.08 (m, 3 H); ¹³C NMR (CDCl₃, 100 MHz): δ 125.74, 57.82, 37.67, 34.44, 31.32, 30.54, 27.49, 26.68, 23.27, 23.01; FTIR (cm⁻¹): 3404 and 3298 (N-H, O-H), 2920 and 2848 (C-H), 1644 (C=O), 1101 (S=O), 772 (N-H); HRMS (FAB) M+Na: calculated for (C₁₃H₂₄F₂NaNO₃S)⁺ 334.1264, found 334.1254.

19

Methyl N-((3R)-3-((tert-butylsulfinyl)amino)-3-cyclohexyl-2,2-difluoropropanoyl)-L-phenylalaninate (19): To a mixture of (3R)-3-((tert-butylsulfinyl)amino)-3-cyclohexyl-2,2-difluoropropanoic acid (**18**, 100 mg, 0.32 mmol), phenylalanine methyl ester hydrochloride salt (69 mg, 0.32 mmol), and 1-hydroxy-7-azabenzotriazole (22 mg, 0.16 mmol) in anhydrous DMF (1 mL) was added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (92 mg, 0.48 mmol). The pH of the mixture was adjusted to 8 by the dropwise addition of Hünig's base. The mixture was stirred at room temperature for 18 hours and was then diluted with water and extracted into ethyl acetate (x3). The organic layers were combined, dried over sodium sulfate, and concentrated *in vacuo*. Purification by silica gel chromatography (gradient elution with 1:4 ethyl acetate/hexanes to 1:1 ethyl acetate/hexanes) afforded **19** as a yellow oil (94 mg, 62%): ^1H NMR (CDCl_3 , 300 MHz): δ 8.41 (d, $J = 7.5$ Hz, 1 H), 7.32-7.20 (m, 5 H), 4.83 (d, $J = 11.4$ Hz, 1 H), 4.65-4.58 (m, 1 H), 3.73 (s, 3 H), 3.46-3.36 (m, 1 H), 3.22 (dd, $J = 4.5$, 13.8 Hz, 1 H), 2.98 (dd, $J = 10.2$, 13.8 Hz, 1 H), 1.91-1.60 (m, 7 H), 1.27 (s, 9 H), 1.24-1.05 (m, 3 H), 0.96-0.88 (m, 1H); ^{13}C NMR (CDCl_3 , 75 MHz): δ 172.99, 163.73, 136.28, 130.10, 129.65, 128.51, 128.05, 57.77, 56.29, 54.68, 37.14, 27.46, 26.09, 23.91, 22.32; FTIR (cm^{-1}): 3258 (N-H), 2935 (aliphatic C-H), 1738 and 1704 (C=O), 1453 (cyclohexane C-H), 1097 (S=O), 1045 (C-O), 734 (N-H), 701 (aromatic C-H); HRMS (ES) $\text{M}+\text{H}^+$: calculated for $(\text{C}_{23}\text{H}_{35}\text{F}_2\text{N}_2\text{O}_4\text{S})^+$ 437.2280, found 437.2298.

20

Methyl *N*-[(3R)-3-amino-3-cyclohexyl-2,2-difluoropropanoyl]-L-phenylalaninate hydrochloride (20): A solution of methyl *N*-{[(3R)-3-[(tert-butylsulfinyl)amino]-3-cyclohexyl-2,2-difluoropropanoyl]-L-phenylalaninate (**19**, 94 mg, 0.20 mmol) in 4.0M HCl/diethyl ether was stirred at room temperature for 18 hours. The product precipitated over the course of the reaction. The solvent was removed *in vacuo* to afford the HCl salt of **20** as a white solid (62 mg, 77%): ^1H NMR (CD_3OD , 400 MHz): δ 7.39-7.22 (m, 5 H), 4.84-4.80 (m, 1 H), 3.80-3.68 (m, 4 H), 3.41-3.30 (m, 1 H), 3.12-3.06 (m, 1 H), 1.84-1.63 (m, 6 H), 1.38-1.09 (m, 5 H); ^{13}C NMR (CD_3OD , 100 MHz): δ 171.06, 136.90, 128.89, 128.43, 126.85, 57.65, 54.05, 51.89, 36.20, 29.67, 25.91, 25.36; FTIR (cm^{-1}): 3328 (N-H), 2916 (aliphatic C-H), 1746 and 1682 (C=O), 1454 (cyclohexane C-H), 1067 (C-O), 702 (aromatic C-H); HRMS (ES) $\text{M}+\text{H}$: calculated for $(\text{C}_{19}\text{H}_{27}\text{F}_2\text{N}_2\text{O}_3)^+$ 369.1984, found 369.1949.

21

Methyl *N*-((3R)-3-[[1-*tert*-butoxycarbonyl]-L-prolyl]amino}-3-cyclohexyl-2,2-difluoropropanoyl)-L-phenylalaninate (21): To a mixture of methyl *N*-[(3R)-3-amino-3-cyclohexyl-2,2-difluoropropanoyl]-L-phenylalaninate hydrochloride (**20**, 39.4 mg, 0.10 mmol), *tert*-butoxycarbonyl-L-proline (20.9 mg, 0.10 mmol), and 1-hydroxy-7-azabenzotriazole (6.6 mg, 0.05 mmol) in anhydrous DMF (1 mL) was added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (28 mg, 0.15 mmol). The pH of the mixture was adjusted to 8 by the dropwise addition of Hünig's base. The mixture was stirred at room temperature for 18 hours and was then diluted with water and extracted into ethyl acetate (x3). The organic layers were combined, dried over sodium sulfate, and concentrated to afford **21** as a yellow solid (54mg, 96%): ¹H NMR (CD₃OD, 300 MHz): δ 7.32-7.19 (m, 5 H), 4.80-4.71 (m, 1 H), 4.30 (br m, 1 H), 3.74 (s, 3 H), 3.53-3.38 (m, 2 H), 3.27-2.96 (m, 3 H), 2.30-2.05 (m, 1 H), 1.93-1.88 (m, 3 H), 1.65-1.51 (m, 3 H), 1.42 (s, 10 H), 1.29-1.05 (m, 4 H), 0.97-0.92 (m, 3 H); ¹³C NMR (CD₃OD, 100 MHz): δ 164.32, 136.98, 128.94, 128.42, 126.84, 60.54, 55.63, 54.00, 51.82, 42.31, 37.56, 36.41, 30.44, 27.43, 27.19, 25.88, 25.78, 25.69; FTIR (cm⁻¹): 3304 (N-H), 2932 and 2848 (aliphatic C-H), 1748 and 1694 (C=O), 1451 (cyclohexane C-H), 1164 (C-O), 772 (amide N-H); HRMS (APCI) M+H: calculated for (C₂₉H₄₂F₂N₃O₆)⁺ 566.3036, found 566.3032.

22

Methyl *N*-[(3R)-3-cyclohexyl-2,2-difluoro-3-(D-prolylamino)propanoyl]-L-phenylalaninate chloride (**22**): Methanol was added dropwise to a suspension of methyl *N*-((3R)-3-{[1-*tert*-butoxycarbonyl]-L-prolyl}amino)-3-cyclohexyl-2,2-difluoropropanoyl)-L-phenylalaninate (**21**, 50.3 mg, 0.09 mmol) in 4.0M HCl/diethyl ether (1 mL) until all solids dissolved. The mixture was stirred at room temperature for 18 hours. Hydrogen chloride gas was bubbled through the solution for 1 min and the mixture was then stirred at room temperature for 1 hour. All solvents were removed *in vacuo* to yield the HCl salt of **22** as a yellow solid in quantitative yield (45 mg): ¹H NMR (CD₃OD, 400 MHz): δ 8.58 (d, *J* = 10 Hz, 1 H), 7.31-7.20 (m, 5 H), 4.70-4.66 (m, 1 H), 4.53-4.48 (m, 1 H), 4.34-4.31 (m, 1 H), 3.74 (s, 3 H), 3.44-3.37 (m, 2 H), 3.32-3.25 (m, 2 H), 3.09-2.98 (m, 1 H), 2.09-1.97 (m, 3 H), 1.82-1.56 (m, 5 H), 1.36-0.92 (m, 6 H); ¹³C NMR (CD₃OD, 100 MHz): δ 171.5, 169.3, 137.1, 128.9, 128.4, 126.7, 61.2, 54.3, 51.9, 37.5, 36.1, 31.9, 31.5, 27.3, 26.0, 25.9, 23.9; FTIR (cm⁻¹): 3328 (N-H), 2923 and 2848 (aliphatic C-H), 1692 (C=O), 1452 (cyclohexane C-H), 1203 (C-O), 741 (aromatic C-H); HRMS (APCI) M+H: calculated for (C₂₄H₃₄F₂N₃O₄)⁺ 466.2512, found 466.2494.

¹¹ Peaks of the major and minor diastereomers overlap unless otherwise noted.

DC1574-30674A

exp1 stdlh

SAMPLE		DEC. & VT	
date	Aug 9 2000	dfrq	399.291
solvent	CDCl3	dn	H1
file	exp	dpwr	6
operator	savageke	dof	0
storfile		ds	nnn
ACQUISITION		PROCESSING	
sfrq	399.252	dsf	200
in	H1	dsq	
at	2.568	dres	1.0
np	32000	hoso	n
sw	6000.0	teap	25.0
fb	3000		
ds	4	lb	0.25
tpwr	53	wtfile	
pw	4.0	proc	ft
d1	0.500	fn	65536
tof	800.0	math	f
nt	16		
ct	16	WARR	
elock	n	wexp	wft cdc aph t-
gain	not used	msref	ds
FLAGS		vbs	
il	n	int	
in	y		
dp	y		
hs	nn		
DISPLAY			
sp	-392.1		
wg	4392.2		
vs	200		
sc	0		
wc	250		
h2mm	17.57		
ls	346.86		
rfl	392.1		
rffp	0		
th	2		
ins	19.569		
na	ph

4a

0C1574-30684A

exptl stdih

SAMPLE		DEC. & VT	
date	Aug 17 2000	dfrq	399.281
solvent	CDCl3	dn	RI
file	exp	dpwr	6
operator	savageke	dof	0
storfile	da	mn	nn
ACQUISITION			
sfrq	399.282	dsw	c
tn	RI	dseq	200
at	2.566	dres	1.0
np	32000	homo	n
sw	6000.6	temp	25.0
fb	3000	PROCESSING	
bs	4	tb	0.25
tpwr	53	wtfile	
pw	4.0	proc	ft
d1	0.500	fn	\$5536
tof	600.0	math	f
nt	16		
ct	16	werr	
atlock	n	wexp	wft cdc aph t-
gain	not used	wsref	ds
il	FLAGS	wbs	
in	n	wmt	
dp	y		
hs	nn		
DISPLAY			
sp	-391.3		
wp	4392.2		
vs	280		
sc	0		
wc	250		
hzmm	17.57		
ls	355.56		
rft	391.3		
rfd	0		
th	2		
ins	22.254		
nm	cdc ph

4b

0C1574-306348

expl stdih

SAMPLE DEC. & VT
 date Aug 29 2000 dfrq 399.931
 solvent CDCl3 dn H1
 file exp dpr 6
 operator savageke dof 0
 storfile dm nnn
 ACQUISITION dm c
 sfrq 399.932 def 200
 tn H1 dseq
 at 3.744 dres 1.0
 np 44932 hmo n
 sw 6000.6 temp 25.0
 fu 3988
 PROCESSING
 bs 16 lb 0.25
 tpwr 57 wtfile
 pw 7.1 proc ft
 d1 0 fn 131072
 tof 480.6 math f
 nt 16
 ct 18 werr
 alock n wexp wft cdc aph t-
 gain not used msref ds
 FLAGS n
 in y
 dp y
 hs nn
 DISPLAY
 sp -399.9
 wp 4399.2
 vs 200
 sc 0
 wc 250
 hzmm 17.60
 is 500.00
 rft 596.1
 rfp 0
 th 10
 ins 18.668
 nm ph

0C1574-331058

exp1 stdih

SAMPLE		DEC. & VT	
date	Sep 8 2000	dfrq	399.291
solvent	CDCl3	sm	H1
file	exp	dpwr	6
operator	savageke	dof	0
storfile		da	nnn
ACQUISITION		dam	c
sfrq	399.292	daf	200
ta	H1	dseq	
at	2.000	dres	1.8
np	32000	homo	n
sw	6000.0	temp	25.0
fb	3600	PROCESSING	
bs	4	lb	0.25
tpwr	53	wtfile	
pw	4.0	proc	ft
el	0.500	fn	05536
tof	800.0	meth	r
nt	10		
ct	16	werr	
alock	n	wexp	wft cdc aph tw
gain	not used	wref	ds
FLAGS		vbs	wnt
it	n		
in	y		
dp	y		
hs	nn		
DISPLAY			
sp	-390.4		
wp	4302.2		
vs	167		
sc	0		
uc	250		
h2nm	17.57		
ls	315.37		
rf1	390.4		
rfp	0		
th	2		
ins	22.624		
na	ph

0c1374-3313

expl stidh

SAMPLE DEC. & VT
 date Oct 4 2000 dfrq 399.281
 solvent CDCl3 dn H1
 file exp dpr 8
 operator savageko dof 8
 storfile da nnn
 ACQUISITION
 sfrq 399.282 def 288
 in H1 dres 1.8
 at 2.884 dres 1.8
 np 32000 homo n
 sw 6000.6 temp 25.0
 fb 3000
 PROCESSING
 ls 4 lb 0.25
 spwr 53 wfile
 pw 4.0 proc ft
 dl 0.500 fn 65536
 tof 600.0 math f
 nt 16
 ct 16 warr
 alock n wexp wft cdc aph t-
 gain not used msref ds
 FLAGS vbs
 il n wnt
 in y
 dp y
 he nm
 DISPLAY
 sp -367.8
 wp 4392.2
 va 200
 sc 0
 wc 250
 hzma 17.57
 ls 351.44
 rfl 387.0
 rfp 0
 th 11
 lns 13.514
 nm ph

DC1574-309788

expl st01b

SAMPLE DEC. & VT
 date Aug 11 2009 dfrq 399.281
 solvent CDCl3 dn H1
 file exp dpr S
 operator savagere dof S
 st01b1a dn em
 ACQUISITION den C
 zfrq 399.281 dof 109
 in 01 dseq
 at 0.056 dres 1.9
 np 31080 homo n
 cv 6500.6 temp 25.9
 fb 3080 PROCESSING
 ss 4 lb 0.25
 tpr 53 wfile
 pw 4.8 proc ft
 d1 0.586 fu 85530
 tof 650.6 math r
 nt 15
 cl 16 werr
 a lock n werr wft cdc dph 1-
 gain not used mref do
 l1 FLAGS n
 in x
 dp x
 ds 00
 DISPLAY
 sp -391.5
 up 4292.1
 vs 153
 uc 2
 uc 259
 hzmm 17.57
 la 287.49
 rft 391.5
 rfa 0
 lb 2
 ins 24.882
 na ph

001574-360958

4991 11/11/11

SAMPLE SEC. & VT
 date Aug 21 2010 dfrq 389.281
 solvent CDCl3 dt NL
 file exp dpr 6
 operator savagosa dot 9
 storfile de am
 ACQUISITION dm c
 dfrq 389.281 det 200
 ts H1 eve 1.0
 st 2.888 pres 1.0
 rs 2000 homo n
 sv 8090.8 temp 25.0
 fs 3000 PROCESSING 0.25
 ts 4 tb
 spwr 53 wfile fs
 pr 4.8 proc fs
 ds 0.500 pa 85536
 sof 890.8 math t
 nt 15
 ct 18 werr
 alock not used wexp wft cdc aph 1-
 gain FLAGS n wnt mref ds
 t1 n
 tn y
 ep y
 bs no
 DISPLAY
 sp -389.9
 vp 4382.2
 va 1.26
 ec 8
 wt 200
 hnm 17.37
 ts 217.31
 rft 389.6
 rfd 6
 ts 2
 tms 30.302
 nm gh

063574-30817A

expt st01h

SAMPLE SEC. & VT
 data Ang 51 2880 dffs 389.281
 solvent CDCl3 ds H1
 file exp dpr 8
 operator savapke dof 9
 starfile dm mm
 ACQUISITION dm c
 sfrs 355.232 daf 260
 tn B1 dtag
 at 5.868 dres 1.0
 ap 32000 hwno n
 sv 8980.6 temp 25.0
 fb 3050 PROCESSING
 bc 6 th 6.25
 tpwr 53 wfile ft
 av 6.5 proc
 di 6.500 fn 65534
 tot 680.8 math f
 vt 15
 ct 15 werr
 stock not used
 gals FLAG5 mto
 l1 a vnt
 la y
 dp y
 ts no
 DISPLAY
 sp -384.8
 vs 4392.2
 vs 154
 vc 0
 vc 250
 s2m 17.37
 is 385.31
 rfp 384.6
 th 6
 lms 2
 me ph 20.810

QC1574-231878

exp1 st41h

SAMPLE SEC. & VT
 date Sep 7 2000 dfrq 289.281
 solvent CDCl3 ds H1
 file exp dpr 4
 operator sawagene dof 8
 storfile dm mm
 ACQUISITION
 afreq 399.282 dmf 200
 tn H1 dmeg
 at 2.466 draz 1.4
 ru 32696 homo n
 sw 8030.8 temp 25.8
 fd 3030 PROCESSING
 bs 4 lb 0.25
 tpwr 52 wfile
 pw 4.2 proc
 sl 0.590 fn 65520
 tof 690.8 meth f
 nl 18
 ct 18
 alock n verr vexp wft cac aph 1-
 gain not used vbs mref ds
 FLAG n vit
 li n
 dp y
 bs m
 DISPLAY
 sp -307.3
 wd 4392.2
 vs 152
 xc 0
 wc 350
 gnm 17.57
 fs 353.46
 rft 367.5
 rfp 0
 ts 2
 lms 39.216
 em ph

OC1574-331066

exp1 stdsh

SAMPLE DEC. & VT
 date Oct 1 2008 effq 036.532
 solvent DMSO d5 en 81
 file exp spwr 10
 operator sawagake sof 8
 sterfile dm ann c
 ACQUISITION
 sfrq 300.832 cat 260
 tn H1 zcas 1.0
 at 2.600 dres n
 rp 16384 hmo n
 sw 4096.0 temp 25.0
 rs 2208 PROCESSING
 bs 18 tb 0.25
 spwr 50 wfile ft
 pw 8.0 proc 32768
 at 8 fn f
 tof 508.0 meth f
 nt 32
 ct 32 verr
 atoch n vexp wft cac aph t-
 gain not used mired 65
 FLAG vbs
 ii n vnt
 ni y
 ap y
 hc ni
 DISPLAY
 xp -300.0
 wp 3300.0
 vs 280
 sc 0
 wc 250
 bcam 13.35
 rs 819.22
 rft 417.0
 rfp 0
 sh 2
 lms 20.090
 rm gh

DC1574-34979A

exp1 stdih

SAMPLE		DEC. & VT	
date	May 23 2001	dfrq	399.931
solvent	CDCl3	dn	H1
file	exp	dpwr	8
operator	savageke	dof	0
storfile		dm	nmn
ACQUISITION		dsm	c
sfrq	399.932	def	200
tn	H1	dseq	
at	3.744	dres	1.0
np	44532	homo	n
sw	8000.8	temp	25.0
rb	3000	PROCESSING	
bs	18	lb	0.25
tpwr	57	wtfile	
pw	7.1	proc	ft
d1	0	fn	131072
tof	400.0	mdlh	f
nt	18		
ct	16	verr	
alock		wexp	wft cdc aph t-
gain	not used	msref	ds
FLAGS			
ii	n	vbs	
in	y	wnt	
dp	y		
hs	nm		
DISPLAY			
sp	-399.9		
wp	4399.2		
vs	154		
sc	0		
wc	250		
hzam	17.80		
is	239.08		
rfl	597.2		
rfp	0		
th	2		
ins	28.345		
nm	cdc ph

12

0C1674-362100

expt stidh

SAMPLE DEC. A VT
 date Jul 19 2001 dfrq 300.632
 solvent CDCl3 dn H1
 file exp dpwr 15
 operator savageke dof 0
 storfile da mn
 ACQUISITION
 sfrq 300.632 daf 280
 sn H1 dseq
 at 2.048 dres 1.0
 np 16384 hmo n
 sw 4000.0 temp 25.0
 fl 2200
 lb 15 PROCESSING 9.25
 tpwr 58 wtfile
 pw 6.0 proc ft
 dl 0 fn 32768
 tof 500.0 math f
 nt 32
 ct 32 werr
 alock n wexp wft cdc sph t~
 gain not used msref ds
 FLAGS vbe wnt
 il n
 in y
 dp y
 hs nn
 DISPLAY
 ap -300.8
 vp 3306.0
 vs 200
 sc 0
 wc 250
 hzma 13.23
 ls 441.54
 rfl 421.1
 rfp 0
 th 1
 rms 66.667
 nm ph

13

0C1574-36211A

expl stdih

SAMPLE		DEC. & VT	
date	Nov 15 2001	effq	399.291
solvent	CDC13	dn	H1
file	exp	dpwr	0
operator	savageke	dof	0
storfile		dm	nm
ACQUISITION			
sfreq	399.292	dof	200
tn	H1	dseq	
at	2.666	dres	1.0
np	32900	homo	n
sw	6000.6	temp	25.0
fu	3900	PROCESSING	
bs	4	lb	0.25
lgwr	53	wtfile	
gw	4.0	proc	ft
al	0.500	fn	55536
tof	000.0	math	f
nt	18		
ct	18	werr	
clock	n	wexp	wft cdc aph t-
gain	not used	whs	msref ds
FLAOS		wni	
l1	n		
l2	y		
dp	y		
hs	nn		
DISPLAY			
ep	-385.2		
wp	4392.2		
vs	153		
sc	0		
wc	259		
h2am	17.57		
ls	171.09		
rfl	395.2		
rfp	0		
th	5		
ins	40.000		
nm	ph

14

exp1 stdih

SAMPLE		DEC. A		VT
date	Jul 25 2001	afreq	399.932	931
solvent	CDC13	dn		M1
file	exp	dpr		0
operator	savageke	dof		0
storfile		dm		ann
ACQUISITION		dm		100
afreq	399.932	def		
tn	M1	dseq		
at	3.744	dres		1.0
np	44332	homo		n
fw	6088.6	temp		25.0
su	3000	PROCESSING		
lb	16	lb		0.25
dpr	57	wfile		
pw	7.1	proc		ft
d1	0	fn		131672
tof	400.0	math		f
nt	16			
ct	16	werr		
block		wexp	wft	exp
gain	not used		wref	ds
FLAGS		wbe		
il		wnt		
in	y			
dp	y			
hs	y			
DISPLAY				
sp	-399.9			
vp	4399.2			
vc	153			
sc	0			
wc	250			
hzmm	17.00			
ls	276.39			
rfl	606.6			
rff	0			
th	6			
ins	41.667			
nm	ph

0C1574-36267A

expl std1h

SAMPLE DEC. & VT
 date Nov 18 2001 dfrq 399.283
 solvent CD300 dn H1
 file exp dpwr 6
 operator savageke dof 0
 storfile dm nm
 ACQUISITION dm c
 sfrq 399.283 daf 200
 tn H1 dseq
 at 2.466 dres 1.0
 np 32000 hmo n
 sw 6000.6 temp 25.0
 rs 3800 PROCESSING 0.25
 bs 4 lb
 tpwr 53 wfile
 pw 4.0 proc ft
 dl 0.500 fn 5536
 tof 600.0 math f
 nl 15
 ct 16 werr
 alock n wexp wft cdc aph t-
 gain not used mref ds
 FLAGS n
 in y wnt
 dp y
 hs nm
 DISPLAY
 sp -395.7
 up 4392.2
 vs 735
 sc 0
 wc 250
 hznm 17.57
 fs 266.94
 rfl 395.7
 rfp 6
 th 3
 lns 30.303
 nm ph

0C1574-362618

expt stdih

SAMPLE DEC. & VT
 date Nov 84 dfrq 300.633
 solvent CD3OD dn 15
 file exp dpr 0
 operator savageke dof 0
 storfile da nnn
 ACQUISITION dam c
 rfrq 300.634 dmf 200
 tn H1 dseq
 at 2.048 dres 1.0
 ng 16384 hrow n
 sw 4000.0 temp 25.0
 fd 2200 PROCESSING
 bs 16 lb 8.25
 tgr 58 wtfile
 pw 6.0 proc ft
 dl 0 fm 32768
 tof 500.0 math f
 nt 32
 ct 32 werr
 alock n wexp wft cdc aph t-
 gain not used wref ds
 FLAGS n
 in y
 dp y
 hs nn
 DISPLAY
 ep -300.8
 wp 3306.8
 vs 108
 sc 0
 wc 250
 h2am 13.23
 is 350.63
 rft 410.7
 rfp 0
 th 2
 rms 99.090
 nm ph

0C1574-382628

expt stdih

SAMPLE		DEC. & VT	
date	Nov 8 2001	dfrq	386.632
solvent	CDCl3	dn	H1
file	exp	dpwr	15
operator	savageks	dof	0
storfile	ds	nnn	
ACQUISITION			
sfrq	386.632	dsf	200
tn	H1	dseq	
at	2.046	dres	1.0
np	16384	homo	n
sw	4800.0	temp	25.0
fb	2200	PROCESSING	
bs	16	lb	0.25
tpwr	58	wtfile	
pw	6.0	proc	ft
d1	0	fn	32788
tof	500.0	meth	f
nt	32		
ct	32	werr	
alock	n	wexp	wft cdc aph t-
gain	not used	msref	ds
FLAGS		ws	wnt
ii	n		
in	y		
dp	y		
hs	nm		
DISPLAY			
sp	-300.8		
wp	3306.8		
vs	161		
sc	0		
vc	250		
hznm	13.23		
is	305.04		
rfl	421.1		
rfp	0		
lh	1		
lms	38.760		
nm	ph

0C1574-36265A

exp1 std1h

SAMPLE DEC. & VT

date Nov 9 2001 dfrq 399.933

solvent CD300 dn H1

file exp dpwr 6

operator savageke dof 0

storfile dm nmh

ACQUISITION dm c

sfrq 399.933 def 200

tn H1 dseg 1.0

at 3.744 dres 1.0

np 44932 homo n

sw 6000.6 temp 25.0

fb 3000 PROCESSING

bs 16 lb 0.25

tpwr 57 wtfile

pw 7.1 proc ft

dl 8 fn 131072

lof 400.8 math f

nt 16

ct 16 verr

alock n wep wft cdc aph t-

gain not used msref ds

ll flags n vbs

in y vnt

dp y

hs nn

DISPLAY

sp -399.8

vp 4999.2

vs 160

sc 0

wc 250

h2mm 17.00

ts 399.90

rfl 577.7

rtp 0

th 2

ins 25.000

nm ph

DC1574-36266A

expl stdlh

SAMPLE DEC. A VT
 date Nov 16 2001 dfrq 300.633
 solvent CD300 dn H1
 file exp dgar 15
 operator savageke dof 8
 storfile de nnn
 ACQUISITION dnm C
 sfrq 300.634 def 200
 tn H1 ds4q
 at 2.848 drec 1.8
 np 18384 homo n
 sw 4000.0 temp 25.0
 fb 2200
 ps 16 PROCESSING lb 8.25
 tpwr 58 wtfile
 pw 8.0 proc ft
 d1 0 fn 32768
 tof 500.0 math f
 nt 32
 ct 32 werr
 alock n wexp wft cdc aph t-
 gain not used wref ds
 FLAGS n
 in y wnt
 dp y
 ha nn
 DISPLAY
 ap -300.8
 wp 3300.8
 vs 200
 sc 0
 wc 250
 hzmm 13.23
 ls 274.24
 rft 420.4
 rfp 0
 lh 2
 lns 50.000
 nm ph

21

DC1574-36288A

expl stdih

SAMPLE		DEC. & VT	
date	Nov 21 2001	dfrq	399.233
solvent	CD300	dn	H1
file	exp	dpr	6
operator	savagss	dof	0
storfile		ds	nnn
ACQUISITION			
sfrq	399.233	daf	200
in	H1	dseq	1.0
at	2.600	drea	n
np	32000	homo	25.0
sw	6000.0	temp	0.25
fb	3000	PROCESSING	
bs	4	lb	0.25
tpwr	53	vrfile	
pw	4.0	proc	ft
dl	0.500	fn	65536
tof	600.0	meth	f
nt	16		
ct	10	verr	
alock	n	wexp wft cdc aph t=	
gain	not used	msref ds	
flags	n	vbs	
il	n	wnt	
in	y		
dp	y		
hs	nn		
DISPLAY			
sp	-394.5		
wp	4332.2		
vs	200		
sc	0		
wc	250		
hzmm	17.57		
ls	265.83		
rfl	394.5		
rfg	0		
th	2		
ins	38.462		
nm	ph

22