Directed Reduction of β–Amino Ketones to *Syn* or *Anti* 1,3- Amino Alcohol Derivatives

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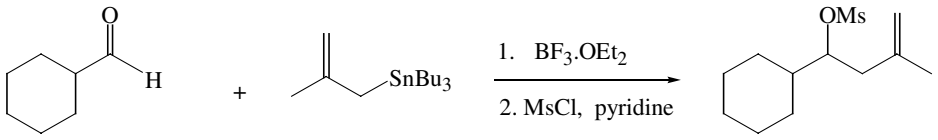
Supplemental Information

General Experimental

Solvents were purified according to the guidelines in Purification of Common Laboratory Chemicals (Perrin, Armarego, and Perrin, Pergamon: Oxford, 1966). Reagent grade methanol was purchased and used without further purification. Samarium metal chips (99.9% REO) were purchased from Strem Chemical Company; all other reagents were purchased from Aldrich and used without further purification. Samarium diiodide was freshly prepared using the method of Kagan[1]. Yields were calculated for material judged homogeneous by thin layer chromatography and NMR. Thin layer chromatography was performed on Merck Kiesegel 60 F_{254} plates eluting with the solvents indicated, visualized by a 254 nm UV lamp, and stained with either a ethanolic solution of 12-molybdophosphoric acid, p-anisaldehyde, or a solution of ammonium molybdate/ceric ammonium sulfate. Flash column chromatography was performed with Davisil 62 silica gel, slurry packed with 2% EtOAc/ hexanes in glass columns, and flushed with hexanes prior to use. Nuclear magnetic resonance spectra were acquired at 300 MHz for ^{1}H and 75 MHz for ^{13}C. Chemical shifts for carbon nuclear magnetic

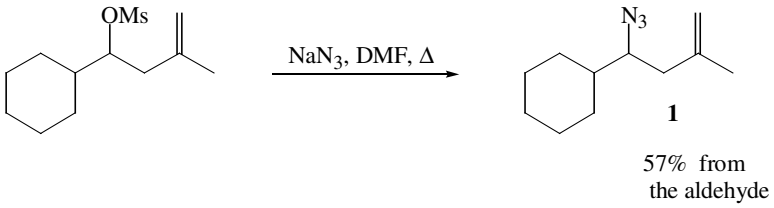
resonance (^{13}C NMR) spectra are reported in parts per million downfield relative to the center line of the $CDCl_3$ triplet at 77.23 ppm. The abbreviations s, d, t, br s, br d, m, and dd, stand for the resonance multiplicities singlet, doublet, triplet, broad single, broad doublet, doublet of doublets, respectively. Melting points were obtained on an Electro thermal melting point apparatus and are uncorrected. Analytical C & H combustion analyses were performed by Atlantic Microlab, Inc., Norcross, Georgia. Glassware for all reactions was oven dried at 125 ^{o}C and cooled in a desiccator prior to use. All samarium reduction reactions were carried out with pretreated flasks and stir bars under an argon atmosphere.



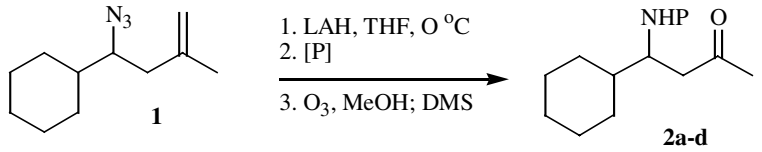
Preparation of 1-cyclohexyl-3-methylbut-3-enyl methylsulfonate. To a solution of cyclohexancarboxaldehyde (4.74 g, 42.30 mmol) in 85 mL of CH_2Cl_2 at -78 ^{o}C, under a nitrogen atmosphere was added methylallyl-tri-*n*-butylstannane (17.53 g, 50.8 mmol). The resulting mixture was stirred at -78 ^{o}C for 15 min, then BF_3 OEt_2 (5.9 mL, 46.6 mmol) was added. The mixture was stirred for 1 h, then 100 mL of saturated aqueous $NaHCO_3$ solution was added dropwise. The suspension was warmed to room temperature, diluted with 100 mL each of saturated aqueous KF solution and CH_2Cl_2, and allowed to stir overnight. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 100 mL). The combined organic layers were then dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude material was taken on directly on the next step without further purification.

To a stirring solution of the crude alcohol prepared above in pyridine (0.5 M in alcohol) was added methansulfonyl chloride (8.08 g, 70.5 mmol) at room temperature. The resulting mixture was stirred overnight, then diluted with water. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 100 mL). The combined organic layers were dried over $MgSO_4$, then concentrated under reduced pressure. The resulting mixture was then purified chromatography over a 5.2 x 30 cm column, eluting

with 10% of EtOAc/hexane, collecting 27 mL fractions. The product containing fractions were collected and concentrated to yield 1-cyclohexyl-3-methylbut-3-enyl methylsulfonate (8.9 g, 85%): R_f 0.41 (20% EtOAc/hexane); 300 MHz ^{1}H NMR ($CDCl_3$) δ 4.86-4.82 (m, 1H), 4.80-4.77 (m, 1H), 4.65 (ddd, *J* = 8.1, 4.9, 4.6 Hz, 1H), 2.93 (s, 3H), 2.40 (dd, *J* = 14.4, 8.1, 1H), 2.31 (dd, *J* = 14.4, 5.1, 1H), 1.80-1.54 (m, 6H), 1.75 (s, 3H), 1.28- 0.96 (m, 5H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 141.2, 114.6, 86.1, 41.6, 40.2, 38.8, 29.0, 27.6, 26.3, 26.1, 26.0, 22.4; IR (neat) 2930, 2856, 1450, 1341 cm^{-1}. Anal. Calcd for $C_{12}H_{22}O_3S$: C, 58.50; H, 9.00. Found C, 58.20; H, 9.01.



Preparation of 1-aza-2-cyclohexyl-1-diazo-4-methylpenta-1,4- diene (1). A solution of 1-cyclohexyl-3-methylbut-3-enyl methylsulfonate was stirred in DMF (0.1 M in mesylate) with sodium azide (13.0 eq) overnight at 90-100 ^{o}C, then cooled to rt. Water was added and the crude mixture was extracted with 20% EtOAc/hex. The organic layers were dried over $MgSO_4$ and concentrated *via vacuo* to give a viscous mixture which was purified by chromatography over a 5.2 x 30 cm column, eluting with a gradient of 2 x 200 mL each of 3, 5, and 10% EtOAc/hex, collecting 27 mL fractions. The product containing fractions were collected and concentrated to yield 1-aza-2-cyclohexyl-1-diazo-4-methylpenta-1,4- diene (4.11 g, 59%): R_f 0.76 (30% EtOAc/hex); 300 MHz NMR ($CDCl_3$) δ 4.89 (br s, 1H), 4.85 (br s, 1H) 3.27 (ddd, *J* = 9.0, 5.4, 4.9 Hz, 1H), 2.28 (dd, *J* = 14.4, 5.4 Hz, 1H), 2.22 (dd, *J* = 14.4, 9.0 Hz, 1H), 1.84-1.64 (m, 6H), 1.79 (s, 3H), 1.53-1.42 (m, 1H), 1.33-1.01 (m, 4H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 142.1, 113.6, 66.2, 42.6, 40.0, 30.3, 28.4, 26.5, 26.4, 26.3, 22.5; IR (neat) 2929, 2854, 2098, 1449 cm^{-1}. Anal. Calcd for $C_{11}H_{19}N_3$ C; 68.35; H, 9.91; N, 21.74. Found C, 67.83; H, 9.90; N, 21.56.



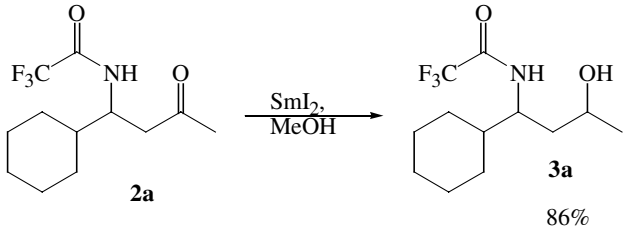
2a P = TFA 59%
2b P = Ac 83%
2c P = Boc 70%
2d P = CBz 54%

Representative Procedure for the Syntheses of the β-Amino Ketones from the Corresponding Alkene Azide (1). Preparation of N-(1-cyclohexyl-3-oxobutyl)-2,2,2-trifloroacetamide (2a). To a stirring solution of 1-aza-2-cyclohexyl-1-diazo-4-methylpenta-1,4-diene (108 mg, 0.516 mmol) in THF (0.35 M in azide) at 0 °C was added $LiAlH_4$ (41 mg, 1.08 mmol) in small portions over 5 min. The mixture was stirred for 30 min and then slowly quenched by the slow addition of $Na_2SO_4 \cdot 10H_20$, followed by the addition of water. The layers were separated and the aqueous layer was extracted with 5% MeOH/$CHCl_3$ (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, then concentrated under reduced pressure. The crude material was taken on directly on the next step without further purification.

To a stirring solution of the total sample of unpurified amine in CH_2Cl_2 (0.5 M in amine) was added TFAA (165 mg, 0.787 mmol) and pyridine (93.8 mg. 1.18 mmol). After 20 min the solution was diluted with CH_2Cl_2 (10 mL) and then washed with saturated aqueous $NaHCO_3$ solution (10 mL). The layers were separated and the organic layer was dried over $MgSO_4$, and then filtered under reduced pressure. The crude material was taken directly to the next step with further purification.

The crude protected amine prepared above was dissolved in methanol/CH_2Cl_2, (1 to 4, 1 mL/4 mL) and cooled to–78 °C with stirring. Ozone was bubbled into the solution until a blue color was achieved (~5 min) then O_2 was bubbled through the solution until the blue color faded and the solution returned to colorless. Dimethyl sulfide (5 mL) was then added and the solution was allowed to warm to rt overnight. The resulting solution was then diluted with saturated aqueous $NaHCO_3$ solution (5 mL) and allowed to stir for 10 min, then the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and

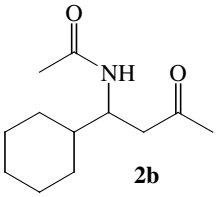
concentrated under reduced pressure. Purification of this material was accomplished by flash chromatography using a 2.0 x 2.7 cm column, eluting with a gradient of 200 mL each of 10%, 20%, and 30% EtOAc/hex, collecting 8 mL fractions. The product containing fractions were collected and concentrated to yield N-(1-cyclohexyl-3-oxobutyl)-2,2,2-trifloroacetamide (82 mg, 59% yield from **2**) as a white solid: mp 110-112 ^{o}C; R_f 0.24 (25% EtOAc/hex); 300 MHz ^{1}H NMR ($CDCl_3$) δ 7.22 (br s, 1H), 4.01-3.91 (m, 1H), 2.92 (dd, *J* = 18.1, 4.6 Hz, 1H), 2.65 (dd, *J* = 18.1, 4.6 Hz, 1H), 2.20 (s, 3H), 1.80-1.60 (m, 6H), 1.30-0.84 (m, 5H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 208.4, 157.0 (q, $J_{C\text{-}F}$ = 37 Hz), 116.1 (q, $J_{C\text{-}F}$ = 288 Hz), 51.9, 43.4, 40.2, 30.8, 30.2, 29.7, 26.1, 26.0, 25.8; IR (KBr) 3289 (br), 2921, 1695 cm^{-1}. Anal. Calcd. for $C_{12}H_{18}F_3NO_2$: C, 54.33; H, 6.84; N, 5.28. Found C, 54.11; H 6.77; N 5.15.



2a **3a** 86%

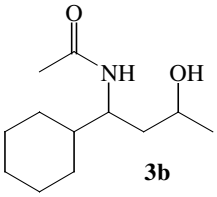
Analytical Data for N-(1-cyclohexyl-3-hydroxybutyl)-2,2,2-trifluoroacetamide. Preparation of N-(1-cyclohexyl-3-hydroxybutyl)-2,2,2-trifluoroacetamide (3a). To a stirring suspension of samarium metal (274 mg, 1.82 mmol) in THF (1.83 mL) was added diiodomethane (73.6 μL, 0.91 mmol) dropwise *via* syringe. The resulting mixture was stirred for 2 h before being cooled to 0 ^{o}C and then a solution of N-(1R)-1-cyclohexyl-3-oxobutyl-trifloroacetamide (**2a**) (80.8 mg, 0.3 mmol) and methanol (240 μL, 6.0 mmol) in THF (1 mL) was added *via* cannula, and the flask was washed with THF (2 x 500 μL). The resulting mixture was stirred for 4.75 h, then quenched by the addition of with a saturated aqueous $Na_2S_2O_3$ solution (5 mL). The resulting mixture was stirred at room temperature for 30 min. The color changed from blue to yellow at which time additional saturated aqueous $Na_2S_2O_3$ solution (25 mL) was added along with EtOAc (25 mL). The layers were separated and the aqueous layer was extracted with EtOAc (2 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification of this material was accomplished by flash chromatography on a 2.0 x 2.7 cm column, eluting with a gradient of 2 x 100 mL of 20%, 30% and 40% EtOAc/hex, collecting 8 mL fractions. The product containing fractions were collected and

concentrated under reduced pressure to give N-(1-cyclohexyl-3-hydroxybutyl)-2,2,2-trifluoroacetamide (68 mg, 84% yield) as a white solid. The ratio of diastereomers was determined to be 90:10 (with $NaBH_4$, 42:58) by HPLC analysis using a mobile phase of 5% *i*PrOH/hexanes and a flow rate of 0.5 mL/min, which gave retention times for the major and minor diastereomers of 10.9 and 13.9 min, respectively. Analytical Data for the major isomer : mp 89.5-90.5 ^{o}C; R_f 0.35 (2 x 30% EtOAc/hex); 300 MHz ^{1}H NMR ($CDCl_3$) δ 6.66 (br d, *J* = 7.35 Hz, 1H), 3.96-3.81 (m, 2H), 1.89 (br s, 1H), 1.82-1.64 (m, 6H), 1.63-1.50 (m, 2H), 1.31-0.90 (m, 5H), 1.24 (d, J= 6.4 Hz, 3H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 157.4 (q, J_{C-F} = 36 Hz), 116.2 (q, J_{C-F} = 286 Hz), 66.9, 54.0, 42.0, 40.0, 29.2, 28.5, 26.4, 26.3, 26.2, 24.6; IR (KBr) 3290 (br), 2921, 2854, 1694, 1563 cm^{-1}. Anal. Calcd. for $C_{12}H_{20}NO_2$: C, 53.92; H, 7.54; N, 5.24. Found: C, 53.87; H, 7.49; N, 5.22.



2b

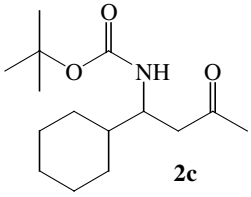
Analytical Data for N-(1-cyclohexyl-3-oxobutyl)acetamide (2b). Isolated as a white solid in 83% yield: mp 98-99 ^{o}C; R*f* 0.76 (5% MeOH/$CHCl_3$); 300 MHz ^{1}H NMR($CDCl_3$) δ 6.06 (br d, *J* = 9.3 Hz, 1H), 4.08-3.98 (m,1H), 2.69 (dd, *J* = 16.6, 6.1 Hz, 1H), 2.62 (dd, *J* = 16.6, 5.1 Hz, 1H), 2.17 (s, 3H), 1.95 (s, 3H), 1.83-1.47 (m, 6H), 1.28-0.84 (m, 5H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 208.9, 169.8, 51.0, 45.1, 41.0, 30.4, 30.2, 29.7, 26.3, 26.2, 26.1, 23.6; IR (KBr) 3288, 2930, 2852, 1714, 1651, 1554 cm^{-1}. Anal. Calcd for $C_{12}H_{21}NO_2$: C, 68.21; H, 10.02; N, 6.63. Found: C, 67.88; H, 10.00; N, 6.54.



3b

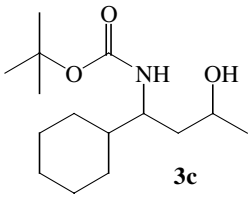
Analytical Data for N-(1-cyclohexyl-3-hydroxybutyl)acetamide (3b). Isolated in 96% yield as a mixture of diastereomers. The major diastereomer was obtained as a white solid: mp 114-115 ^{o}C; R_f 0.57 (5% MeOH/$CHCl_3$); 300 MHz ^{1}H NMR ($CDCl_3$) δ 5.96 (br d, *J* = 8.8 Hz, 1H), 3.90-3.74 (m, 2H), 3.30 (br s, 1H), 2.00 (s, 3H), 1.80-1.62 (m, 6H), 1.54-1.34 (m, 2H), 1.30-0.60 (m, 5H), 1.20 (d, *J*= 6.4 Hz, 3H);

75 MHz ^{13}C NMR ($CDCl_3$) δ 170.7, 66.9, 52.6, 42.6, 42.3, 29.5, 28.6, 26.5, 26.3, 23.8, 23.6; IR (KBr) 3290 (br), 2920, 2851, 1620, 1549 cm^{-1}; HR/EI Spectrum at 70 eV HT Probe $C_{12}H_{23}NO_2$ Calculated Mass (theoretical) = 213.17287. Measured Mass (mass spectrometry) = 213.17192. Difference = 0.00095. amu (Approx. 0.95 mmu). The ratio of diastereomers was determined to be 89:11 (with $NaBH_4$, 42:58) by HPLC analysis using a Microsorb Si 80-125-C5 silica column, using a mobile phase of 15% *i*PrOH/hexanes and a flow rate of 0.5 mL/min, which gave retention times for the major and minor diastereomers of 26.3 and 34.4 min, respectively.



2c

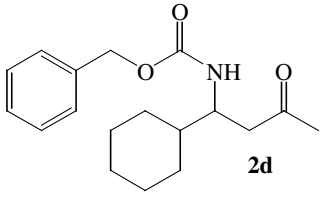
Analytical Data of (tert-butoxy)-N-(1-cyclohexyl-3-oxobutyl) carboxamide (2c). Isolated as a white solid in 70% yield: mp 72-74 ^oC; R_f 0.39 (20% EtOAc/hex); 300 MHz ^1H NMR ($CDCl_3$) δ 4.82 (br d, *J* = 9.5 Hz, 1H), 3.68 (dddd, *J* = 9.8, 6.4, 6.4, 6.4 Hz, 1H), 2.64-2.49 (m, 2H), 2.11 (s, 3H), 1.78-1.50 (m, 6H), 1.36 (s, 9H), 1.24-0.78 (m, 5H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 208.5, 155.8, 79.2, 52.3, 46.0, 41.60, 30.3, 30.1, 29.2, 28.5, 26.4, 26.2, 26.1; IR (KBr) 3375, 2990, 2980, 2855, 1708, 1686, 1527 cm^{-1}. Anal. Calcd. for $C_{15}H_{27}NO_3$: C, 66.88; H, 10.10; N, 5.20. Found: C, 66.64; H, 10.10; N, 5.16.



3c

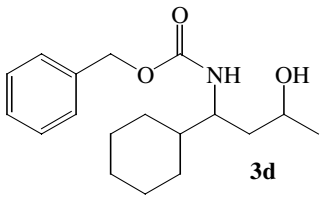
Analytical Data for (tert-butoxy)-N-(1-cyclohexyl-3-hydroxybutyl)carboxamide (3c). Obtained as a white solid in a quantitative yield from the corresponding (tert-butoxy)-N-(1-cyclohexyl-3-oxobutyl) carboxamide (2c).: mp 75.5-76.5 ^oC; R_f 0.33 (2 x 30% EtOAc/hex); 300 MHz ^1H NMR ($CDCl_3$) δ 4.57 (br d, *J* = 9.3 Hz, 1H), 3.95-3.82 (m, 1H), 3.55-3.44 (m,1H), 2.71 (br s, 1H), 1.80-1.57 (m, 6H), 1.52-1.40 (m, 2H), 1.44 (s, 9H),1.30-0.86 (m, 5H), 1.21 (d, *J* = 6.1 Hz, 3H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 156.5, 79.6, 67.1, 53.8, 43.1, 42.7, 29.6, 28.6, 28.3, 26.6, 26.4, 23.7; IR (KBr) 3379, 2925, 2854, 1708, 1679, 1542 cm^{-1}. Anal. Calcd. for $C_{15}H_{29}NO_3$: C, 66.38;

H, 10.77; N, 5.16. Found: C, 66.51; H, 10.83; N, 5.12. The ratio of diastereomers was determined to be 81:19 (with $NaBH_4$, 42:58) by HPLC analysis using a mobile phase of 5% *i*PrOH/hexanes and a flow rate of 0.5 mL/min, which gave retention times for the major and minor diastereomers of 13.1 and 11.4 min, respectively.



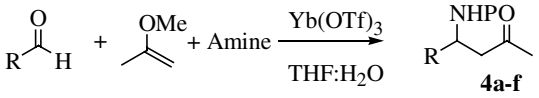
2d

Analytical Data for N-(1-cyclohexyl-3-oxobutyl)phenylmethoxy)carboxamide (2d). Obtained as a white solid in 54% yield: mp 74-75 °C; R_f 0.51 (2 x 30% EtOAc/hex); 300 MHz ^{1}H NMR ($CDCl_3$) δ 7.37-7.26 (m, 5H), 5.25 (br d, *J* = 9.6 Hz, 1H), 5.1 (s, 2H), 3.84-3.75 (m, 1H), 2.67 (dd, *J* = 16.9, 6.4 Hz, 1H), 2.60 (dd, *J* = 16.9, 5.1 Hz, 1H), 2.14 (s, 3H), 1.80 -1.47 (m, 6H), 1.26-0.86 (m, 5H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 208.2, 156.2, 136.7, 128.6, 128.14, 128.09, 66.7, 52.8, 45.5, 41.3, 30.4, 30.1, 29.2, 26.3, 26.1, 26.0; IR (KBr) 3320, 2921, 2851, 1712, 1692, 1542, 1259 cm^{-1}. Anal. Calcd. for $C_{18}H_{25}NO_3$: C, 71.26; H, 8.31; N, 4.62. Found: C, 70.98; H, 8.33; N, 4.67.



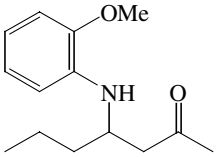
3d

Analytical Data for N-(1-cyclohexyl-3-hydroxybutyl)phenylmethoxy)carboxamide (3d). Isolated in 84% yield as a white solid from the corresponding β-amino ketone (**2d**): mp 75.5-76.5 °C; R_f 0.31 (2 x 30% EtOAc/hex); 300 MHz ^{1}H NMR ($CDCl_3$) δ 7.36-7.31 (m, 5H), 5.09 (s, 2H), 4.87 (br d, *J* = 9.6 Hz, 1H), 3.87 (m, 1H), 3.56 (m, 1H), 2.43 (br s, 1H), 1.76-1.39 (m, 7H), 1.28-0.87 (m, 9H); HR/EI Spectrum at 70 eV HT Probe $C_{18}H_{27}NO_3$ Calculated Mass (theoretical) = 305.2000. Measured Mass (mass spectrometry) = 305.1988 Difference = 0.0012.amu (Approx. 1.2 mmu.). The ratio of diastereomers was determined to be 84:16 (with $NaBH_4$, 53:47) by HPLC analysis using a mobile phase of 5% *i*PrOH/hexanes and a flow rate of 0.5 mL/min, which gave retention times for the major and minor diastereomers of 17.9 and 16.6 min, respectively.



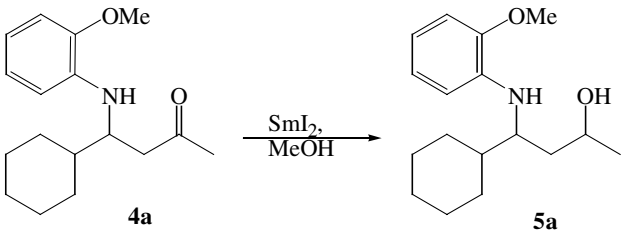
4a-f

4a R = C_3H_7, P = *o*-MeOPh
4b R = C_6H_{11}, P = *o*-MeOPh
4c R = C_8H_7, P = *o*-MeOPh
4d R = C_3H_7, P = *p*-MeOPh
4e R = C_6H_{11}, P = *p*-MeOPh
4f R = C_3H_7, P = Ph



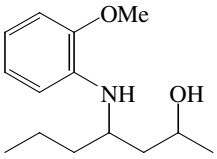
4a

Representative Procedure for the Syntheses of β-Amino Ketones *via* Mannich Reaction (Substrates in Scheme 2).[2] Preparation of 4-[(2-methoxyphenyl)amino]heptan-2-one (4a). To a solution of butanal (0.270 mL, 3 mmol) in 2.5 mL of THF/H_2O (9:1 THF/H_2O) was added *o*-anisdine (0.339 mL, 3 mmol) at 0 °C. To the above mixture was added $Yb(OTf)_3$ (0.3 mmol) followed by a solution of 2-methoxypropene (1.44 mL, 15 mmol) in THF/H_2O (9:1 THF/H_2O, 0.5 mL) at 0 °C. After the solution was stirred for 4 h at 0 °C, saturated aqueous $NaHCO_3$ solution (10 mL) was added and the layers were separated. The aqueous layer was extracted with ether (2 x 25 mL) and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude material was purified by silica flash column chromatography to afford 4-[(2-methoxyphenyl)amino]heptan-2-one (402 mg, 57% yield) as a yellow oil: R_f 0.82 (50% EtOAc/hex); 300 MHz ^{1}H NMR ($CDCl_3$) δ 6.90-6.62 (m, 4H), 4.20 (br s, 1H), 3.94-3.85 (m, 1H), 3.84 (s, 3H), 2.73 (dd, *J* = 16.2, 5.1 Hz, 1H), 2.59 (dd, *J* = 16.2, 7.0 Hz, 1H), 2.15 (s, 3H), 1.62-1.25 (m, 4H), 0.93 (t, *J* = 7.1 Hz, 3H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 208.3, 147.0, 137.2, 121.5, 116.4, 110.2, 109.8, 55.5, 49.1, 48.6, 37.7, 31.0, 19.5, 14.2; IR (neat) 3404, 2958, 1712, 1601, 1514 cm^{-1}. Anal. Calcd. for $C_{14}H_{21}NO_2$: C, 71.46; H, 8.99; N, 5.95. Found: C, 71.74; H, 8.96; N, 5.85.



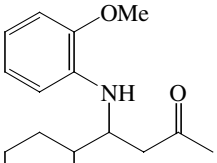
4a **5a**

95%



5a

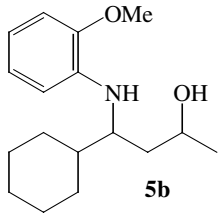
Analytical Data for 4-[(2-methoxyphenyl)amino]heptan-2-ol (5a). Obtained as a colorless oil in 95% yield from the corresponding β-amino ketone (**4a**): R_f 0.77 (50% EtOAc/hex); 300 MHz ^{1}H NMR ($CDCl_3$) δ 6.90-6.64 (m, 4H), 4.1-4.01 (m, 1H), 3.85 (s, 3H), 3.72-3.60 (m, 1H), 1.82-1.70 (m, 1H), 1.65-1.29 (m, 5H), 1.23 (d, *J* = 6.4 Hz, 3H), 0.92 (t, *J* = 7.3 Hz, 3H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 147.1, 137.9, 121.5, 116.6, 110.9, 109.8, 65.3, 55.6, 50.3, 43.8, 38.0, 24.2, 19.4, 14.3; IR (neat) 3410 (br), 3064, 2959, 1600, 1512 cm^{-1}. Anal. Calcd. for $C_{14}H_{23}NO_2$: C, 70.85, H, 9.77; N, 5.90. Found: C, 71.03; H, 9.79; N, 5.78. The ratio of diastereomers was determined to be 93:7 (with $NaBH_4$, 45:55) by HPLC analysis using a mobile phase of 3% *i*PrOH/hexanes and a flow rate of 0.5 mL/min, which gave retention times for the major and minor diastereomers of 13.2 and 14.5 min, respectively.



4b

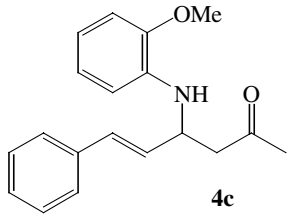
Analytical Data for 4-cyclohexyl-4[(2-methoxyphenyl)amino] butan-2-one (4b). Obtained as a yellow solid: mp 54-55 ^{o}C; R_f 0.82 (50% EtOAc/hex); 300 MHz ^{1}H NMR ($CDCl_3$) δ 6.89-6.60 (m, 4H), 4.30 (br s, 1H), 3.86-3.78 (m, 4H), 2.68 (dd, *J* = 16.1, 5.6 Hz, 1H), 2.60 (dd, *J* = 16.1, 6.6 Hz, 1H), 2.17 (s, 3H), 1.91-1.52 (m, 6H), 1.48-0.90 (m, 5H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 208.3, 146.8, 137.5, 121.4, 116.1, 110.2, 109.7, 55.5, 54.0, 46.1, 42.1, 30.7, 29.4, 29.3, 26.6, 26.4; IR (neat) 3401, 2958,

1712 cm^{-1}. Anal. Calcd. for $C_{17}H_{27}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 73.88; H, 9.15; N, 4.86.



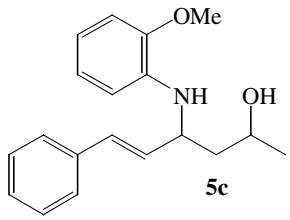
5b

Analytical Data for 4-cyclohexyl-4[(2-methoxyphenyl)amino] butan-2-ol (5b). Obtained as a light yellow oil in 91% yield from the corresponding β-amino ketone (**4b**): R_f 0.77 (50%EtOAc/hex); 300 MHz ^{1}H NMR ($CDCl_3$) δ 6.87-6.59 (m, 4H), 4.03-3.92 (m, 1H), 3.83 (s, 3H), 3.59-3.50 (m, 1H), 1.80-1.62 (m, 6H),1.60-1.48 (m, 2H), 1.32-0.96 (m, 5H), 1.22 (d, *J* = 6.1 Hz, 3H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 146.9, 138.4, 121.5, 116.1, 110.6, 109.8, 65.4, 55.7, 54.5, 42.3, 41.0, 29.5, 29.0, 26.8, 26.6, 26.5, 24.2; IR (neat) 3424 (br), 2925, 2851, 1600, 1517. Anal. Calcd. for $C_{17}H_{27}NO_2$: C, 73.61; H, 9.81; N, 5.05. Found: C, 73.88; H, 9.96; N, 4.95. The ratio of diastereomers was determined to be 98:2 (with $NaBH_4$, 49:51) by HPLC analysis using a mobile phase of 3% *i*PrOH/hexanes and a flow rate of 0.5 mL/min, which gave retention times for the major and minor diastereomers of 12.0 and 13.9 min, respectively.



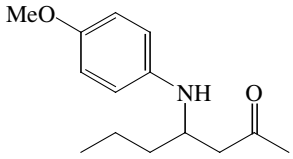
4c

Analytical Data for (5E)-4[(2-methoxyphenyl)amino]-6-phenylhex-5-en-2-one (4c). Obtained as a yellow oil in 79% yield: R_f 0.64 (50% EtOAc/hex); 300 MHz ^{1}H NMR ($CDCl_3$) δ 7.50-7.22 (m, 5H), 7.00-6.64 (m, 5H), 6.40-6.24 (m, 1H), 4.67-4.57 (m, 2H), 3.94 (s, 3H), 2.96 (dd, *J* = 16.4, 6.1 Hz, 1H), 2.89 (dd, *J* = 16.4, 6.8 Hz, 1H), 2.26 (s, 3H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 206.8, 147.1, 136.7, 130.6, 130.4, 128.6, 127.6, 126.5, 121.3, 117.1, 111.2, 109.6, 55.5, 51.5, 49.3, 30.8; IR (neat) 3407 (br), 2956, 1712, 1599 cm^{-1}. Anal. Calcd. for $C_{19}H_{21}NO_2$: C, 77.26; H, 7.17; N, 4.74. Found: C, 77.40; H, 7.26; N, 4.48.



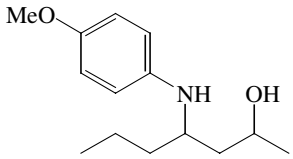
5c

Analytical Data for (5E)-4[(2-methoxyphenyl)amino]-6-phenylhex-5-en-2-ol (5c). Obtained as a light yellow oil in 90% yield from the corresponding β-amino ketone (**4c**): R_f 0.56 (50% EtOAc/hex); 300 MHz ^{1}H NMR ($CDCl_3$) δ 7.40 - 7.16 (m, 5H), 6.90-6.64 (m, 4H), 6.57 (d, *J* = 16.0, 1H), 6.19(dd, *J* = 16.0, 6.1, 1H, 4.32-4.24 (m, 1H), 4.16-4.06 (m, 1H), 3.86 (s, 3H), 1.94-1.75 (m, 2H), 1.30 (br s, 1H), 1.25 (d, *J* = 6.1 Hz, 3H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 147.0, 137.3, 137.0, 132.0, 129.9, 128.6, 127.5, 126.4, 121.4, 116.8, 111.3, 109.6, 65.1, 55.5, 52.8, 44.8, 24.0; IR (neat) 3404 (br), 3059, 2963, 1599, 1513, 1455, 1222 cm^{-1}. Anal. Calcd. for $C_{19}H_{23}NO_2$: C, 76.73; H, 7.80; N, 4.71. Found: C, 76.71; H, 7.96; N, 4.95. The ratio of diastereomers was determined to be 97:3 (with $NaBH_4$, 55:45) by HPLC analysis using a mobile phase of 3% *i*PrOH/hexanes and a flow rate of 0.5 mL/min, which gave retention times for the major and minor diastereomers of 30.6 and 31.2 min, respectively.



4d

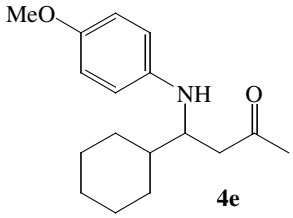
Analytical Data for 4-[(4-methoxyphenyl)amino]heptan-2-one (4d). Isolated as a yellow oil. R_f 0.69 (50% EtOAc/hex); 300 MHz ^{1}H NMR ($CDCl_3$) δ 6.82 - 6.73 (m, 2H), 6.61-6.55(m, 2H), 3.82-3.70 (m, 1H), 3.74 (s, 3H), 3.22 (br s, 1H), 2.66 (dd, *J* = 16.4, 5.6 Hz, 1H), 2.56 (dd, *J* = 16.4, 6.4 Hz, 1H), 2.13 (s, 3H), 1.56-1.26 (m, 4H), 0.91 (t, *J* = 7.1, 3H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 208.6, 152.3, 141.5, 115.1, 115.0, 55.8, 50.9, 48.1, 37.5, 31.0, 19.6, 14.2. IR (neat) 3362, 2959, 1701, 1511 cm^{-1}. Anal. Calcd. C, 71.46; H, 8.99; N, 5.95. Found: C, 71.25; H, 8.97; N, 5.89.



5d

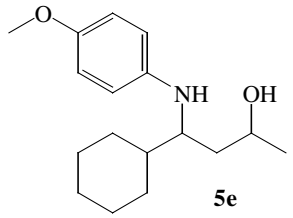
Analytical Data for 4-[(4-methoxyphenyl)amino]heptan-2-ol (5d). Obtained as a brown oil in 95% yield from the corresponding β-amino ketone

(**12**): R_f 0.59 (50% EtOAc/hex); 300 MHz ^{1}H NMR ($CDCl_3$) δ 6.80-6.75 (m, 2H), 6.66-6.62 (m, 2H), 4.13-4.00 (m, 1H), 3.74 (s, 3H), 3.59-3.48 (m, 1H), 3.05 (br s, 1H), 1.74 (ddd, *J* = 14.4, 8.3, 3.4, 1H), 1.60-1.26 (m, 5H), 1.22 (d, *J* = 6.1 Hz, 3H), 0.90 (t, *J* = 7.1 Hz, 3H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 152.7, 142.0, 115.8, 115.1, 65.5, 56.0, 52.2, 42.8, 37.7, 24.1, 19.5, 14.3; IR (Neat) 3458, 3376, 2961, 1524 cm^{-1}. Anal. Calcd. for $C_{14}H_{23}NO_2$: C, 70.85; H, 9.77; N, 5.90. Found: C, 70.65; H, 9.75; N, 5.76. The ratio of diastereomers was determined to be 94:6 (with $NaBH_4$, 52:48) by HPLC analysis using a mobile phase of 3% *i*PrOH/hexanes and a flow rate of 0.5 mL/min, which gave retention times for the major and minor diastereomers of 23.3 and 22.2 min, respectively.



4e

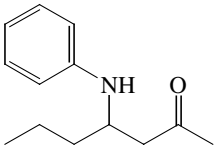
Analytical Data for 4-cyclohexyl-4[(4-methoxyphenyl)amino] butan-2-one (4e). Obtained as a yellow oil: R_f 0.64 (50% EtOAc/hex); 300 MHz ^{1}H NMR ($CDCl_3$) δ 6.78-6.72 (m, 2H), 6.60-6.54 (m, 2H), 3.74 (s, 3H), 3.67-3.60 (m, 1H), 3.4 (br s, 1H), 2.64 (dd, *J* = 16.1, 5.6 Hz, 1H), 2.54 (dd, *J*= 16.1, 6.6 Hz, 1H), 2.13 (s, 3H), 1.90-1.49 (m, 6H), 1.31-0.96 (m, 5H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 208.7, 152.1, 142.0, 115.1, 114.9, 55.9, 45.7, 41.9, 30.8, 29.7, 29.5, 26.6, 26.4; IR (neat) 3386, 2925, 2851, 1710, 1511 cm^{-1}. Anal. Calcd. for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 73.93; H, 9.09; N, 5.12.



5e

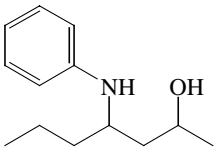
Analytical Data for 4-cyclohexyl-4[(4-methoxyphenyl)amino] butan-2-ol (5e). Isolated in 98% yield as a white solid: mp: 84-84.5 ^{o}C; R*f* = 0.46 (50% EtOAc/hex); 300 MHz ^{1}H NMR ($CDCl_3$) δ 6.82-6.74 (m, 2H),6.68-6.66 (m, 2H), 4.10-3.97 (m, 1H), 3.75 (s, 3H), 3.50-3.38 (m, 1H), 2.97 (br s, 2H), 1.80-1.60 (m, 6H), 1.54-1.44(m, 2H), 1.32-0.94(m, 5H), 1.22(d, *J* = 6.4 Hz, 3H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 152.2, 142.5, 115.3, 115.1, 65.6, 56.4, 55.9, 41.9, 40.2, 29.8, 28.7, 26.8, 26.6, 26.5, 24.1; Anal. Calcd. for $C_{17}H_{27}NO_2$: C, 73.61; H, 9.81; N, 5.05.

Found: C, 73.52; H, 9.76; N, 5.04; IR (neat) 3382, 2927, 1510 cm^{-1}. The ratio of diastereomers was determined to be >99:1 (with $NaBH_4$, 49:51) by HPLC analysis using a mobile phase of 0.5% *i*PrOH/hexanes and a flow rate of 0.5 mL/min, which gave retention times for the major and minor diastereomers of 122 and 133 min, respectively.



4f

Analytical Data for 4-(phenylamino)heptan-2-one (4f). Isolated as a light yellow oil: R_f 0.70 (50% EtOAc/hex); 300 MHz ^{1}H NMR ($CDCl_3$) δ 7.22-7.14 (m, 2H), 6.74-6.68 (m, 1H),6.66-6.60(m, 2H), 3.92-3.83 (m, 1H), 3.66 (br s, 1H), 2.71 (dd, *J* = 16.4, 5.1Hz, 1H), 2.60 (dd, *J* = 16.4, 6.6 Hz, 1H), 2.16 (s, 3H), 1.63-1.33 (m, 4H), 0.95 (t, *J* = 7.3 Hz, 3H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 208.5, 147.5, 129.6, 117.6, 113.5, 49.6, 48.1, 37.6, 31.1, 19.7, 14.2; IR (neat) 3384 (br), 2958, 1709, 1602, 1504 cm^{-1}. Anal. Calcd. for $C_{13}H_{19}NO$: C, 76.06; H, 9.33; N, 6.82. Found: C, 76.05; H, 9.33; N, 6.86.



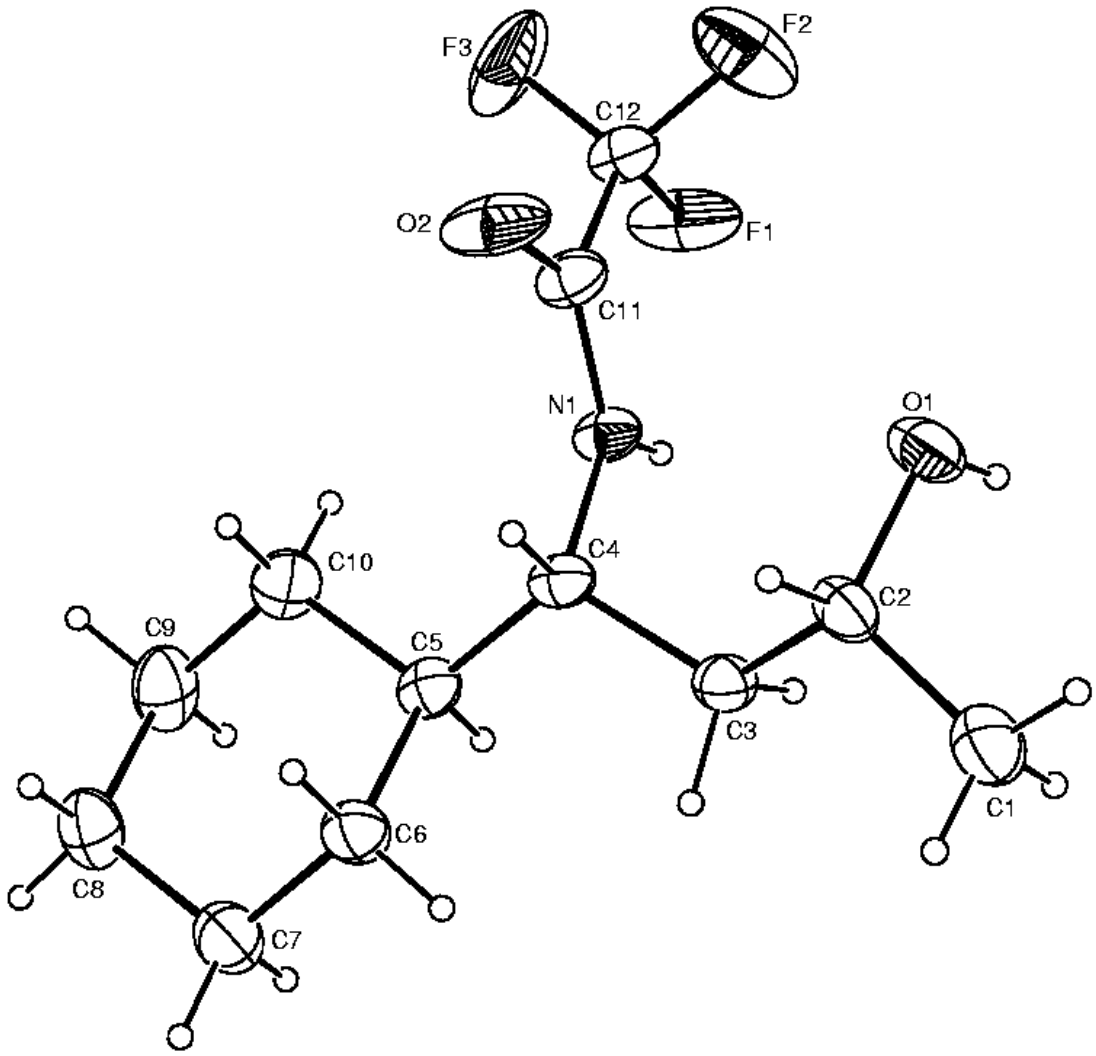
5f

Analytical Data for 4-(phenylamino)heptan-2-ol (5f). Obtained as a light yellow oil in 96% yield from the corresponding β-amino ketone (**4f**): R_f 0.67 (50% EtOAc/hex); 300 MHz ^{1}H NMR ($CDCl_3$) δ 7.24-7.13 (m, 2H), 6.76-6.62 (m, 3H), 4.16-4.02 (m, 1H), 3.74-3.62 (m, 1H), 2.88 (br s, 2H), 1.75 (ddd, *J* = 14.4, 9.0, 3.7, 1H), 1.60-1.30 (m, 5H), 1.22 (d, *J* = 6.4 Hz, 3H), 0.93 (t, *J* = 7.1 Hz, 3H); 75 MHz ^{13}C NMR ($CDCl_3$) δ 148.2, 129.5, 117.5, 113.7, 65.2, 50.6, 43.6, 37.9, 24.2, 19.4, 14.3; IR (neat) 3387 (br), 2960, 2870, 1601, 1503, 1320 cm^{-1}. Anal. Calcd. for $C_{13}H_{19}NO$: C, 75.32; H, 10.21; N, 6.76. Found: C, 75.44; H, 10.27; N, 6.52. The ratio of diastereomers was determined to be 85:15 (with $NaBH_4$, 49:51) by HPLC analysis using a mobile phase of 2% *i*PrOH/hexanes and a flow rate of 0.5 mL/min, which gave retention times for the major and minor diastereomers of 21.8 and 22.6 min, respectively.

References:

1. Girard, P.; Namy, J. L.; Kagan, H. B. *J. Am. Chem. Soc*. **1980**, *102*, 2693.

2. Kobayashi, S.; Ueno, M.; Suzuki, R.; Ishitani, H.; Kim, S. H.; Wataya, Y. *J. Org. Chem*. **1999**, *64*, 6833.


F3
F2
C12
O2
F1
C11
N1
O1
C10
C4
C9
C5
C2
C3
C1
C6
C8
C7

Crystal Structure Report

Experimental:

A colorless prism shaped crystal 0.3 x 0.18 x 0.08 mm in size was mounted on a glass fiber with traces of viscous oil and then transferred to a Nonius KappaCCD diffractometer equipped with Mo Kα radiation (λ = 0.71073 Å). Ten frames of data were collected at 200(1)K with an oscillation range of *1* deg/frame and an exposure time of *20* sec/frame. [REF1] Indexing and unit cell refinement based on all observed reflection from those ten frames, indicated a monoclinic *P* lattice. A total of 4281 reflections (Θ_{max} = 24.96 °) were indexed, integrated and corrected for Lorentz, polarization and absorption effects using DENZO-SMN and SCALEPACK. [REF 2] Post refinement of the unit cell gave *a* = 14.7543(9) Å , b = 4.9869(2) Å, c = 18.3763(11) Å, β =94.690(2), and V = 1347.54(13) Å^3. Axial photographs and systematic absences were consistent with the compound having crystallized in the monoclinic space group $P\,2_1/n$.

The structure was solved by a combination of direct methods and heavy atom using SIR 97. [REF 3]
All of the non-hydrogen atoms were refined with anisotropic displacement coefficients. Hydrogen atoms were located and refined isotropically except H1 which was assigned isotropic displacement coefficients U 1.2U(Ohydroxy), and it's coordinates were allowed to ride on the oxygen atom using SHELXL97. [REF 4] The weighting scheme employed was $w = 1/[\sigma^2(F_o^2) + (0.0232P)^2 + 0.9461P]$ where $P = (F_o^2 + 2F_c^2)/3$. The refinement converged to R1 = 0.0546, wR2 = 0.1135, and S = 1.097 for 1751 reflections with $1 > 2\sigma(I)$, and R1 = 0.0786, wR2 = 0.1228, and S = 1.097 for 2339 unique reflections and 268 parameters. [REF 5] The maximum Δ/σ in the final cycle of the least-squares was 0, and the residual peaks on the final difference-Fourier map ranged from -0.156 to 0.204 e/Å^3. Scattering factors were taken from the International Tables for Crystallography, Volume C. [REF 6, REF 7]

REF 1 COLLECT Data Collection Software. Nonius B.V. 1998.

REF 2 Otwinowski, Z.; Minor, W., "Processing of X-ray Diffraction Data Collected in Oscillation Mode", Methods Enzymol. 1997, 276, 307-326.

REF 3 SIR97 (Release 1.02) - A program for automatic solution and refinement of crystal structure. A. Altomare, M.C. Burla, M. Camalli, G. Cascarano, C. Giacovazzo, A. Guagliardi, A.G. G. Moliteni, G. Polidori, and R. Spagna.

REF 4 SHELX97 [Includes SHELXS97, SHELXL97, CIFTAB] - Sheldrick, G. M. (1997). Programs for Crystal Structure Analysis (Release 97-2). University of Göttingen, Germany.

REF 5 $R1 = \Sigma(\| F_o | - |F_c \|) / \Sigma |F_o|$, $wR2 = [\Sigma(w(F_o^2 - F_c^2)2) / \Sigma(F_o^2)^2]^{1/2}$, and S = Goodness-of-fit on $F^2 = [\Sigma(w(F_o^2 - F_c^2)^2 / (n-p)]^{1/2}$, where n is the number of reflections and p is the number of parameters refined.

REF 6 Maslen, E. N.; Fox, A. G.; O'Keefe, M. A., International Tables for Crystallography: Mathemetical, Physical and Chemical Tables, Vol. C, Chapter 6, Wilson, A. J. C., Ed.; Kluwer, Dordrecht, The Netherlands, 1992; pp. 476-516.

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Table 1. Crystal data and structure refinement for gek002.

Identification code	gek002	
Empirical formula	C12 H20 F3 N O2	
Formula weight	267.29	
Temperature	200(1) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P\,2_1/n$	
Unit cell dimensions	a = 14.7543(9) Å	α= 90°.
	b = 4.9869(2) Å	β= 94.690(2)°.
	c = 18.3763(11) Å	γ = 90°.
Volume	1347.54(13) $Å^3$	
Z	4	
Density (calculated)	1.317 Mg/m^3	
Absorption coefficient	0.116 mm^{-1}	
F(000)	568	
Crystal size	0.30 x 0.18 x 0.08 mm^3	
Theta range for data collection	3.69 to 24.96°.	
Index ranges	-17<=h<=17, -5<=k<=5, -21<=l<=21	
Reflections collected	4281	
Independent reflections	2339 [R(int) = 0.0410]	
Completeness to theta = 24.96°	99.0 %	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9908 and 0.9661	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2339 / 0 / 268	
Goodness-of-fit on F^2	1.097	
Final R indices [I>2sigma(I)]	R1 = 0.0546, wR2 = 0.1135	
R indices (all data)	R1 = 0.0786, wR2 = 0.1228	
Extinction coefficient	0.019(3)	
Largest diff. peak and hole	0.204 and -0.156 e.$Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for gek002. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
F(1)	7311(5)	947(9)	3478(3)	87(2)
F(2)	8130(4)	4227(16)	3293(2)	97(1)
F(3)	6714(5)	4672(18)	3299(2)	116(2)
F(1A)	7829(11)	1550(30)	3459(6)	121(6)
F(2A)	7520(12)	5490(16)	3240(3)	90(3)
F(3A)	6514(6)	2840(30)	3472(5)	110(4)
O(1)	9627(1)	2552(4)	5161(1)	59(1)
O(2)	7527(2)	6520(3)	4621(1)	76(1)
N(1)	7575(1)	2103(4)	4885(1)	41(1)
C(1)	10213(2)	1298(8)	6379(2)	64(1)
C(2)	9430(2)	2487(5)	5912(1)	44(1)
C(3)	8551(2)	1003(5)	5993(1)	41(1)
C(4)	7672(2)	2371(5)	5683(1)	38(1)
C(5)	6819(2)	1338(5)	6020(1)	41(1)
C(6)	6849(2)	1983(6)	6831(1)	50(1)
C(7)	6016(2)	962(7)	7185(2)	58(1)
C(8)	5148(2)	2057(7)	6802(2)	60(1)
C(9)	5101(2)	1455(8)	5990(2)	66(1)
C(10)	5940(2)	2481(6)	5646(2)	54(1)
C(11)	7512(2)	4160(5)	4441(1)	45(1)
C(12)	7390(2)	3484(5)	3627(1)	48(1)

Table 3. Bond lengths [Å] and angles [°] for gek002.

F(1)-C(12)	1.298(5)
F(2)-C(12)	1.347(4)
F(3)-C(12)	1.270(4)
F(1A)-C(12)	1.216(8)
F(2A)-C(12)	1.251(6)
F(3A)-C(12)	1.340(8)
O(1)-C(2)	1.434(3)
O(1)-H(1)	0.8400
O(2)-C(11)	1.222(3)
N(1)-C(11)	1.309(3)
N(1)-C(4)	1.468(3)
N(1)-H(3)	0.86(3)
C(1)-C(2)	1.503(4)
C(1)-H(1A)	0.94(4)
C(1)-H(1B)	0.94(3)
C(1)-H(1C)	1.06(3)
C(2)-C(3)	1.511(3)
C(2)-H(2)	0.98(2)
C(3)-C(4)	1.534(3)
C(3)-H(3A)	0.99(2)
C(3)-H(3B)	0.95(3)
C(4)-C(5)	1.536(3)
C(4)-H(4)	1.00(2)
C(5)-C(6)	1.523(3)
C(5)-C(10)	1.528(4)
C(5)-H(5)	0.97(2)
C(6)-C(7)	1.523(4)
C(6)-H(6A)	1.04(3)
C(6)-H(6B)	0.94(3)
C(7)-C(8)	1.512(4)
C(7)-H(7A)	1.03(3)
C(7)-H(7B)	0.96(3)
C(8)-C(9)	1.517(4)
C(8)-H(8A)	0.95(3)

C(8)-H(8B)	0.97(3)
C(9)-C(10)	1.524(4)
C(9)-H(9A)	0.98(3)
C(9)-H(9B)	1.00(3)
C(10)-H(10A)	0.98(3)
C(10)-H(10B)	0.96(3)
C(11)-C(12)	1.530(3)

C(2)-O(1)-H(1)	109.5
C(11)-N(1)-C(4)	123.2(2)
C(11)-N(1)-H(3)	118.2(16)
C(4)-N(1)-H(3)	118.5(16)
C(2)-C(1)-H(1A)	110(2)
C(2)-C(1)-H(1B)	110.7(18)
H(1A)-C(1)-H(1B)	111(3)
C(2)-C(1)-H(1C)	108.3(16)
H(1A)-C(1)-H(1C)	108(3)
H(1B)-C(1)-H(1C)	108(2)
O(1)-C(2)-C(1)	110.6(2)
O(1)-C(2)-C(3)	110.4(2)
C(1)-C(2)-C(3)	112.1(2)
O(1)-C(2)-H(2)	108.3(13)
C(1)-C(2)-H(2)	108.3(14)
C(3)-C(2)-H(2)	107.0(14)
C(2)-C(3)-C(4)	116.9(2)
C(2)-C(3)-H(3A)	107.6(13)
C(4)-C(3)-H(3A)	108.4(13)
C(2)-C(3)-H(3B)	105.9(14)
C(4)-C(3)-H(3B)	109.9(15)
H(3A)-C(3)-H(3B)	107.9(19)
N(1)-C(4)-C(3)	110.0(2)
N(1)-C(4)-C(5)	110.90(19)
C(3)-C(4)-C(5)	113.34(19)
N(1)-C(4)-H(4)	106.2(12)
C(3)-C(4)-H(4)	106.2(13)
C(5)-C(4)-H(4)	109.8(12)

C(6)-C(5)-C(10)	108.5(2)
C(6)-C(5)-C(4)	111.5(2)
C(10)-C(5)-C(4)	112.7(2)
C(6)-C(5)-H(5)	106.9(13)
C(10)-C(5)-H(5)	108.0(13)
C(4)-C(5)-H(5)	109.0(13)
C(5)-C(6)-C(7)	112.8(2)
C(5)-C(6)-H(6A)	105.2(16)
C(7)-C(6)-H(6A)	109.5(16)
C(5)-C(6)-H(6B)	112.3(17)
C(7)-C(6)-H(6B)	107.7(17)
H(6A)-C(6)-H(6B)	109(2)
C(8)-C(7)-C(6)	111.3(3)
C(8)-C(7)-H(7A)	111.8(15)
C(6)-C(7)-H(7A)	108.5(15)
C(8)-C(7)-H(7B)	105.5(17)
C(6)-C(7)-H(7B)	108.3(17)
H(7A)-C(7)-H(7B)	111(2)
C(7)-C(8)-C(9)	110.8(3)
C(7)-C(8)-H(8A)	104.2(19)
C(9)-C(8)-H(8A)	109.7(19)
C(7)-C(8)-H(8B)	108.9(17)
C(9)-C(8)-H(8B)	112.4(17)
H(8A)-C(8)-H(8B)	111(3)
C(8)-C(9)-C(10)	111.6(3)
C(8)-C(9)-H(9A)	108.7(16)
C(10)-C(9)-H(9A)	107.8(17)
C(8)-C(9)-H(9B)	108.6(16)
C(10)-C(9)-H(9B)	108.0(16)
H(9A)-C(9)-H(9B)	112(2)
C(9)-C(10)-C(5)	112.1(2)
C(9)-C(10)-H(10A)	109.5(16)
C(5)-C(10)-H(10A)	108.2(16)
C(9)-C(10)-H(10B)	109.4(15)
C(5)-C(10)-H(10B)	109.5(15)
H(10A)-C(10)-H(10B)	108(2)

O(2)-C(11)-N(1)	125.9(2)
O(2)-C(11)-C(12)	118.4(2)
N(1)-C(11)-C(12)	115.7(2)
F(1A)-C(12)-F(2A)	112.5(8)
F(1A)-C(12)-F(3)	131.6(6)
F(2A)-C(12)-F(3)	60.5(5)
F(1A)-C(12)-F(1)	38.1(7)
F(2A)-C(12)-F(1)	132.5(5)
F(3)-C(12)-F(1)	107.5(5)
F(1A)-C(12)-F(3A)	106.3(8)
F(2A)-C(12)-F(3A)	105.1(7)
F(3)-C(12)-F(3A)	45.8(4)
F(1)-C(12)-F(3A)	69.7(6)
F(1A)-C(12)-F(2)	68.6(7)
F(2A)-C(12)-F(2)	49.8(6)
F(3)-C(12)-F(2)	106.9(4)
F(1)-C(12)-F(2)	103.6(4)
F(3A)-C(12)-F(2)	140.6(4)
F(1A)-C(12)-C(11)	113.6(5)
F(2A)-C(12)-C(11)	111.6(4)
F(3)-C(12)-C(11)	112.7(3)
F(1)-C(12)-C(11)	115.0(3)
F(3A)-C(12)-C(11)	107.1(4)
F(2)-C(12)-C(11)	110.5(3)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for gek002. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
F(1)	174(7)	44(2)	40(2)	-5(1)	-5(3)	-17(4)
F(2)	101(3)	139(5)	55(2)	-12(3)	22(2)	-40(3)
F(3)	128(5)	153(5)	59(3)	-17(3)	-36(3)	96(4)
F(1A)	164(11)	154(14)	43(4)	-19(7)	-7(7)	132(10)
F(2A)	164(9)	70(4)	34(3)	21(3)	-14(5)	-37(6)
F(3A)	79(5)	188(12)	60(5)	-20(6)	-11(4)	-48(8)
O(1)	82(1)	47(1)	52(1)	6(1)	34(1)	6(1)
O(2)	153(2)	27(1)	47(1)	2(1)	-4(1)	2(1)
N(1)	64(1)	24(1)	33(1)	-1(1)	2(1)	4(1)
C(1)	48(2)	83(2)	61(2)	6(2)	12(2)	-2(2)
C(2)	53(2)	40(1)	43(1)	-1(1)	20(1)	1(1)
C(3)	50(2)	36(1)	39(2)	4(1)	7(1)	2(1)
C(4)	55(2)	29(1)	31(1)	-1(1)	1(1)	2(1)
C(5)	50(2)	30(1)	41(1)	-3(1)	1(1)	1(1)
C(6)	46(2)	66(2)	37(1)	2(1)	0(1)	2(1)
C(7)	54(2)	70(2)	50(2)	-2(2)	9(1)	1(2)
C(8)	45(2)	75(2)	59(2)	-14(2)	6(1)	1(2)
C(9)	44(2)	88(3)	64(2)	-19(2)	-5(1)	5(2)
C(10)	55(2)	65(2)	39(2)	-9(1)	-9(1)	5(1)
C(11)	62(2)	31(1)	41(1)	2(1)	-2(1)	3(1)
C(12)	63(2)	39(2)	42(2)	5(1)	-2(1)	4(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for gek002.

	x	y	z	U(eq)
H(1)	9768	1006	5028	88
H(1A)	10760(20)	2140(70)	6283(18)	91(11)
H(1B)	10110(19)	1420(60)	6877(17)	68(9)
H(1C)	10260(19)	-770(60)	6247(15)	68(9)
H(2)	9340(15)	4340(50)	6075(12)	45(7)
H(3)	7576(16)	510(50)	4697(13)	45(7)
H(3A)	8507(14)	680(40)	6521(13)	39(6)
H(3B)	8614(16)	-680(50)	5765(13)	46(7)
H(4)	7753(14)	4330(50)	5787(11)	36(6)
H(5)	6795(15)	-600(50)	5975(12)	41(6)
H(6A)	6871(19)	4060(70)	6862(15)	76(9)
H(6B)	7365(19)	1270(60)	7093(15)	65(8)
H(7A)	6081(17)	1470(60)	7728(16)	66(8)
H(7B)	5982(18)	-950(60)	7119(15)	66(9)
H(8A)	5190(20)	3940(70)	6878(17)	82(10)
H(8B)	4640(20)	1330(60)	7032(15)	66(8)
H(9A)	4570(20)	2370(60)	5750(15)	68(9)
H(9B)	5072(18)	-530(60)	5922(15)	64(9)
H(10A)	5967(18)	4450(60)	5683(14)	59(8)
H(10B)	5897(16)	2010(50)	5135(15)	53(7)

Table 6. Torsion angles [°] for gek002.

O(1)-C(2)-C(3)-C(4)	-69.4(3)
C(1)-C(2)-C(3)-C(4)	166.8(2)
C(11)-N(1)-C(4)-C(3)	-121.3(2)
C(11)-N(1)-C(4)-C(5)	112.6(3)
C(2)-C(3)-C(4)-N(1)	76.6(3)
C(2)-C(3)-C(4)-C(5)	-158.6(2)
N(1)-C(4)-C(5)-C(6)	-171.5(2)
C(3)-C(4)-C(5)-C(6)	64.3(3)
N(1)-C(4)-C(5)-C(10)	-49.2(3)
C(3)-C(4)-C(5)-C(10)	-173.4(2)
C(10)-C(5)-C(6)-C(7)	55.8(3)
C(4)-C(5)-C(6)-C(7)	-179.5(2)
C(5)-C(6)-C(7)-C(8)	-56.4(4)
C(6)-C(7)-C(8)-C(9)	54.4(4)
C(7)-C(8)-C(9)-C(10)	-54.8(4)
C(8)-C(9)-C(10)-C(5)	56.4(4)
C(6)-C(5)-C(10)-C(9)	-55.6(3)
C(4)-C(5)-C(10)-C(9)	-179.5(2)
C(4)-N(1)-C(11)-O(2)	0.2(4)
C(4)-N(1)-C(11)-C(12)	-178.5(2)
O(2)-C(11)-C(12)-F(1A)	143.1(11)
N(1)-C(11)-C(12)-F(1A)	-38.1(11)
O(2)-C(11)-C(12)-F(2A)	14.7(10)
N(1)-C(11)-C(12)-F(2A)	-166.5(9)
O(2)-C(11)-C(12)-F(3)	-51.2(7)
N(1)-C(11)-C(12)-F(3)	127.6(6)
O(2)-C(11)-C(12)-F(1)	-174.9(5)
N(1)-C(11)-C(12)-F(1)	3.9(5)
O(2)-C(11)-C(12)-F(3A)	-99.8(8)
N(1)-C(11)-C(12)-F(3A)	79.0(8)
O(2)-C(11)-C(12)-F(2)	68.3(5)
N(1)-C(11)-C(12)-F(2)	-112.9(5)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for gek002 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1)...O(1)#1	0.84	2.03	2.855(3)	167.3
N(1)-H(3)...O(2)#2	0.86(3)	2.00(3)	2.826(3)	160(2)

Symmetry transformations used to generate equivalent atoms:

#1 -x+2,-y,-z+1 #2 x,y-1,z