A Simple and General Chiral Silicon Lewis Acid for Asymmetric Synthesis: Highly Enantioselective [3+2] Acylhydrazone-Enol Ether Cycloadditions

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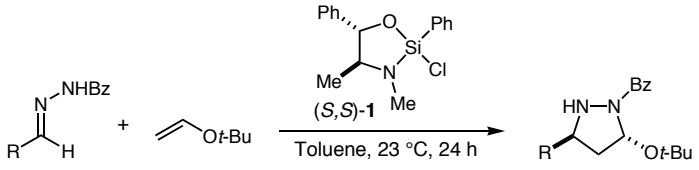
Supporting Information

General Information. All reactions were carried out under an atmosphere of nitrogen in flame- or oven-dried glassware with magnetic stirring unless otherwise indicated. Degassed solvents were purified by passage through an activated alumina column. ^{1}H NMR spectra were recorded on a Bruker DPX-300 (300 MHz) spectrometer and are reported in ppm from $CDCl_3$ internal standard (7.26 ppm). Data are reported as follows: (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sep = septet, m = multiplet, dd = doublet of doublets, td = triplet of doublets, tt = triplet of triplets, dq = doublet of quartets, ddt = doublet of doublet of triplets; coupling constant(s) in Hz; integration; assignment). Proton decoupled ^{13}C NMR spectra were recorded on a Bruker DPX-300 (75 MHz) and are reported in ppm from $CDCl_3$ internal standard (77.0 ppm). Infrared spectra were recorded on a Perkin Elmer Paragon 1000 FT-IR spectrometer. Optical rotations were recorded on a Jasco DIP-1000 digital polarimeter.

Preparation of reagent (*S*,*S*)-1: A detailed procedure for the preparation of (*S*,*S*)-**1** has been previously described.[1] See the supporting information files.



General procedure for the enantioselective [3+2] cycloaddition of benzoylhydrazones with *tert*-butyl vinyl ether promoted by (*S*,*S*)-1: To a solution of the benzoylhydrazone (0.200 mmol) and (*S*,*S*)-**1**

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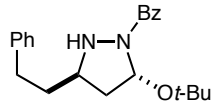
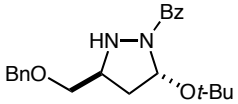
(1) (a) Berger, R.; Duff, K.; Leighton, J. L. *J. Am. Chem. Soc.* **2004**, *126*, 5686-5687. (b) Shirakawa, S.; Berger, R.; Leighton, J. L. *J. Am. Chem. Soc.* **2005**, *127*, 2858-2859.

(91.2 mg, 0.300 mmol) in toluene (2 mL) is added *tert*-butyl vinyl ether (78.9 μl, 0.600 mmol) and the resulting mixture is stirred at 23 °C for 24 h. The reaction is quenched by the addition of H_2O (5 mL) and the resulting mixture is stirred for 15 min, and then diluted with EtOAc (5 mL). The phases are separated, and the aqueous layer is extracted with EtOAc (5 mL x 2). The combined organic layers are dried ($MgSO_4$), filtered and concentrated. Purification by flash chromatography on silica gel affords the products.

Characterization data for the cycloaddition products from Table 1 and Scheme 4:

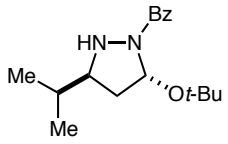


(3*R*,5*R*)-1-(Benzoyl)-5-(*tert*-butoxy)-3-(phenethyl)pyrazolidine: $[\alpha]^{26}_{D}$ = +99.9° (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (dd, 2H, *J* = 1.5, 8.0 Hz, Ar-**H**), 7.33-7.44 (m, 3H, Ar-**H**), 7.10-7.22 (m, 3H, Ar-**H**), 7.00 (d, 2H, *J* = 7.9 Hz, Ar-**H**), 6.18 (br d, 1H, *J* = 4.0 Hz, N**H**), 4.05 (br d, 1H, *J* = 11.6 Hz, C**H**O*t*-Bu), 2.77-2.91 (br m, 1H, NHC**H**), 2.60 (t, 2H, *J* = 7.6 Hz, PhC$\mathbf{H}_2$), 2.48 (ddd, 1H, *J* = 6.8, 7.7, 13.2 Hz, CHC$\mathbf{H}_2$CH), 1.71-1.95 (m, 2H, $PhCH_2C\mathbf{H}_2$), 1.60 (ddd, 1H, *J* = 2.9, 8.5, 13.2 Hz, CHC$\mathbf{H}_2$CH), 1.30 (s, 9H, C(C$\mathbf{H}_3$)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 141.0, 135.1, 130.4, 129.2, 128.34, 128.30, 127.4, 125.9, 81.9, 74.8, 60.0, 42.7, 34.5, 33.0, 28.5; IR (thin film) 3238, 2978, 2937, 1643, 1627, 1389, 1368, 1057, 1026, 699 cm^{-1}; LRMS (FAB+) calcd for $C_{22}H_{29}N_2O_2$: 353 ([M+H]$^+$), found 353 ([M+H]$^+$).

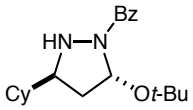


(3*S*,5*R*)-1-(Benzoyl)-3-(benzyloxymethyl)-5-(*tert*-butoxy)pyrazolidine: $[\alpha]^{24}_{D}$ = +63.4° (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66-7.69 (m, 2H, Ar-**H**), 7.24-7.43 (m, 8H, Ar-**H**), 6.20 (br d, 1H, *J* = 4.6 Hz, N**H**), 4.61 (br d, 1H, *J* = 11.1 Hz, C**H**O*t*-Bu), 4.54 (d, 1H, *J* = 12.1 Hz, PhC$\mathbf{H}_2$), 4.49 (d, 1H, *J* = 12.1 Hz, PhC$\mathbf{H}_2$), 3.62 (dd, 1H, *J* = 3.9, 10.0 Hz, OC$\mathbf{H}_2$CH), 3.53 (dd, 1H, *J* = 4.7, 10.0 Hz, OC$\mathbf{H}_2$CH), 3.15-3.27 (br m, 1H, NHC**H**), 2.37 (ddd, 1H, *J* = 6.5, 8.5, 13.1 Hz, CHC$\mathbf{H}_2$CH), 1.69 (ddd, 1H, *J* = 2.6, 8.6, 13.1 Hz, CHC$\mathbf{H}_2$CH), 1.29 (s, 9H, C(C$\mathbf{H}_3$)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 137.9, 135.1, 130.5, 129.1, 128.4, 127.7, 127.4, 81.5, 74.7, 73.0, 68.8, 59.8, 38.6, 28.5; IR (thin film) 3258, 2975, 2932,

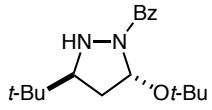
2866, 1643, 1474, 1367, 1100, 1059, 1028, 697 cm^{-1}; LRMS (FAB+) calcd for $C_{22}H_{29}N_2O_3$: 369 ($[M+H]^+$), found 369 ($[M+H]^+$).



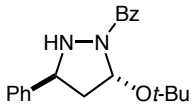
(3*S*,5*R*)-1-(Benzoyl)-5-(*tert*-butoxy)-3-(isopropyl)pyrazolidine: $[\alpha]^{24}_D = +100.9°$ (*c* 0.65, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.74 (dd, 2H, *J* = 1.4, 8.1 Hz, Ar-**H**), 7.33-7.44 (m, 3H, Ar-**H**), 6.18 (br s, 1H, N**H**), 4.10 (br d, 1H, *J* = 11.0 Hz, C**H**O*t*-Bu), 2.65 (br quin, *J* = 8.5 Hz, 1H, NHC**H**), 2.44 (ddd, 1H, *J* = 6.8, 7.9, 13.2 Hz, CHC$\mathbf{H}_2$CH), 1.58-1.71 (m, 1H + 1H, CHC$\mathbf{H}_2$CH + $(CH_3)_2$C**H**), 1.30 (s, 9H, C(C$\mathbf{H}_3$)$_3$), 0.92 (d, 3H, *J* = 6.7 Hz, (C$\mathbf{H}_3$)$_2$CH)**,** 0.90 (d, 3H, *J* = 6.7 Hz, (C$\mathbf{H}_3$)$_2$CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 135.0, 130.3, 129.2, 127.3, 82.0, 74.7, 67.1, 40.9, 31.1, 28.5, 20.5, 19.2; IR (thin film) 3227, 2968, 2947, 2875, 1618, 1509, 1389, 1363, 1052, 694 cm^{-1}; LRMS (FAB+) calcd for $C_{17}H_{27}N_2O_2$: 291 ($[M+H]^+$), found 291 ($[M+H]^+$).



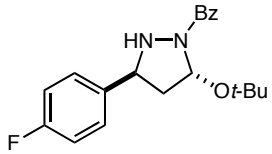
(3*S*,5*R*)-1-(Benzoyl)-5-(*tert*-butoxy)-3-(cyclohexyl)pyrazolidine: $[\alpha]^{25}_D = +82.7°$ (*c* 1.2, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.71 (dd, 2H, *J* = 1.4, 8.0 Hz, Ar-**H**), 7.30-7.41 (m, 3H, Ar-**H**), 6.16 (br s, 1H, N**H**), 4.06 (br d, 1H, *J* = 11.0 Hz, C**H**O*t*-Bu), 2.59-2.71 (br m, 1H, NHC**H**), 2.43 (ddd, 1H, *J* = 6.8, 7.6, 13.2 Hz, CHC$\mathbf{H}_2$CH), 1.58-1.79 (m, 4H + 1H + 1H, C$\mathbf{H}_2$C$\mathbf{H}_2$ + CHC$\mathbf{H}_2$CH + CH_2C**H**CH_2), 1.29 (s, 9H, C(C$\mathbf{H}_3$)$_3$), 1.08-1.41 (m, 4H, C$\mathbf{H}_2$C$\mathbf{H}_2$), 0.85-1.02 (m, 2H, C$\mathbf{H}_2$C$\mathbf{H}_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 135.0, 130.3, 129.2, 127.3, 81.8, 74.7, 66.1, 41.0, 40.9, 31.0, 29.6, 28.5, 26.3, 25.8, 25.7; IR (thin film) 3238, 2974, 2923, 2856, 1646, 1473, 1447, 1392, 1363, 1054, 1029, 695 cm^{-1}; LRMS (FAB+) calcd for $C_{20}H_{31}N_2O_2$: 331 ($[M+H]^+$), found 331 ($[M+H]^+$).



(3*S*,5*R*)-1-(Benzoyl)-5-(*tert*-butoxy)-3-(*tert*-butyl)pyrazolidine: $[\alpha]^{25}_{D} = +108.8°$ (*c* 0.73, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.73 (dd, 2H, *J* = 1.5, 8.0 Hz, Ar-**H**), 7.30-7.42 (m, 3H, Ar-**H**), 6.15 (br s, 1H, N**H**), 4.16 (br d, 1H, *J* = 11.0 Hz, C**H**O*t*-Bu), 2.68-2.79 (br m, 1H, NHC**H**), 2.28 (ddd, 1H, *J* = 6.6, 8.3, 13.2 Hz, CHC**H**$_2$CH), 1.69 (ddd, 1H, *J* = 2.6, 9.0, 13.2 Hz, CHC**H**$_2$CH), 1.28 (s, 9H, OC(C**H**$_3$)$_3$), 0.91 (s, 9H, CHC(C**H**$_3$)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 135.1, 130.3, 129.3, 127.3, 81.8, 74.6, 69.8, 38.2, 31.3, 28.5, 26.5; IR (thin film) 3248, 2968, 2875, 1618, 1374, 1057, 793, 715, 694 cm^{-1}; LRMS (FAB+) calcd for $C_{18}H_{29}N_2O_2$: 305 ($[M+H]^+$), found 305 ($[M+H]^+$).

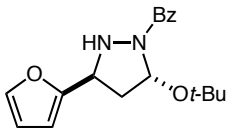


(3*S*,5*R*)-1-(Benzoyl)-5-(*tert*-butoxy)-3-(phenyl)pyrazolidine: $[\alpha]^{24}_{D} = +40.3°$ (*c* 0.80, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.73 (dd, 2H, *J* = 1.3, 8.0 Hz, Ar-**H**), 7.23-7.43 (m, 8H, Ar-**H**), 6.38 (br d, 1H, *J* = 5.0 Hz, N**H**), 4.40 (d, 1H, *J* = 11.4 Hz, C**H**O*t*-Bu), 4.01-4.10 (m, 1H, NHC**H**), 2.75 (ddd, 1H, *J* = 6.4, 9.1, 13.5 Hz, CHC**H**$_2$CH), 2.12 (ddd, 1H, *J* = 2.1, 7.4, 13.5 Hz, CHC**H**$_2$CH), 1.36 (s, 9H, C(C**H**$_3$)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 139.0, 134.8, 130.6, 129.3, 128.7, 128.1, 127.7, 127.4, 81.6, 75.1, 64.1, 43.4, 28.6; IR (thin film) 3248, 2978, 2926, 1643, 1472, 1368, 1052, 1026, 761, 699 cm^{-1}; LRMS (FAB+) calcd for $C_{20}H_{25}N_2O_2$: 325 ($[M+H]^+$), found 325 ($[M+H]^+$).

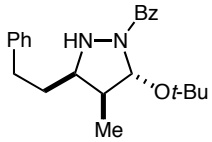


(3*S*,5*R*)-1-(Benzoyl)-5-(*tert*-butoxy)-3-(4-fluoro-phenyl)pyrazolidine: $[\alpha]^{26}_{D} = +41.0°$ (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.70-7.74 (m, 2H, Ar-**H**), 7.32-7.44 (m, 5H, Ar-**H**), 6.99-7.04 (m, 2H, Ar-**H**), 6.37 (br d, 1H, *J* = 4.9 Hz, N**H**), 4.33 (d, 1H, *J* = 11.3 Hz, C**H**O*t*-Bu), 4.00-4.09 (m, 1H, NHC**H**), 2.74 (ddd, 1H, *J* = 6.3, 9.2, 13.5 Hz, CHC**H**$_2$CH), 2.07 (ddd, 1H, *J* = 2.0, 7.2, 13.5 Hz, CHC**H**$_2$CH), 1.36 (s, 9H, C(C**H**$_3$)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 164.1, 160.8, 134.91, 134.87,

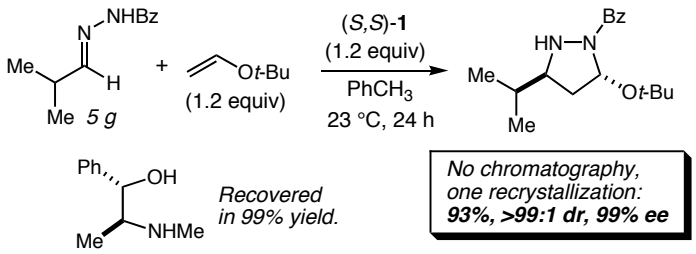
134.7, 130.6, 129.6, 129.5, 129.3, 127.5, 115.7, 115.4, 81.5, 75.2, 63.3, 43.3, 28.5; IR (thin film) 3244, 2976, 1645, 1514, 1472, 1368, 1227, 1052, 836, 697 cm^{-1}; LRMS (FAB+) calcd for $C_{20}H_{24}FN_2O_2$: 343 ($[M+H]^+$), found 343 ($[M+H]^+$).



(3*S*,5*R*)-1-(Benzoyl)-5-(*tert*-butoxy)-3-(furan-2-yl)pyrazolidine: $[\alpha]^{23}_D$ = +42.3° (*c* 1.3, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.70 (dd, 2H, *J* = 1.5, 8.2 Hz, Ar-**H**), 7.31-7.44 (m, 4H, Ar-**H**), 6.27-6.35 (m, 1H + 2H, N**H** + Ar-**H**), 4.53 (d, 1H, *J* = 11.6 Hz, C**H**O*t*-Bu), 4.02-4.11 (m, 1H, NHC**H**), 2.69 (ddd, 1H, *J* = 6.6, 8.6, 13.4 Hz, CHC**H**$_2$CH), 2.21 (ddd, 1H, *J* = 2.7, 8.5, 13.4 Hz, CHC**H**$_2$CH), 1.33 (s, 9H, C(C**H**$_3$)$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 151.3, 142.4, 134.8, 130.7, 129.3, 127.5, 110.4, 108.1, 81.6, 75.0, 57.6, 41.7, 28.5; IR (thin film) 3239, 2974, 2933, 1646, 1473, 1366, 1188, 1050, 1025, 696 cm^{-1}; LRMS (FAB+) calcd for $C_{18}H_{23}N_2O_3$: 315 ($[M+H]^+$), found 315 ($[M+H]^+$).

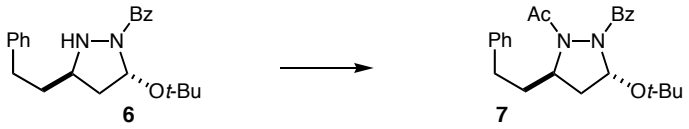


(3*R*,4*S*,5*R*)-1-(Benzoyl)-5-(*tert*-butoxy)-4-(methyl)-3-(phenethyl)pyrazolidine: $[\alpha]^{26}_D$ = +115.6° (*c* 1.1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.68 (d, 2H, *J* = 6.6 Hz, Ar-**H**), 7.34-7.45 (m, 3H, Ar-**H**), 7.12-7.23 (m, 3H, Ar-**H**), 7.04 (d, 2H, *J* = 6.7 Hz, Ar-**H**), 5.99 (d, 1H, *J* = 5.6 Hz, N**H**), 4.11 (br d, 1H, *J* = 9.5 Hz, C**H**O*t*-Bu), 2.98-3.09 (br m, 1H, NHC**H**), 2.50-2.70 (m, 2H, PhC**H**$_2$), 2.38 (m, 1H, *J* = 7.3 Hz, C**H**CH$_3$), 1.62-1.83 (m, 2H, PhCH$_2$C**H**$_2$), 1.29 (s, 9H, C(C**H**$_3$)$_3$), 0.96 (d, 3H, *J* = 7.3 Hz, CHC**H**$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 141.3, 135.1, 130.4, 129.2, 128.5, 128.3, 127.4, 125.9, 82.5, 74.7, 60.9, 40.6, 33.3, 31.9, 28.3, 8.9; IR (thin film) 3237, 2971, 2936, 1630, 1497, 1388, 1368, 1195, 1104 cm^{-1}; LRMS (FAB+) calcd for $C_{23}H_{31}N_2O_2$: 367 ($[M+H]^+$), found 367 ($[M+H]^+$).



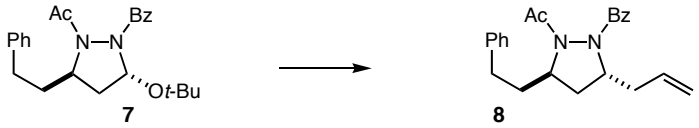
Procedure for the diastereo- and enantioselective [3+2] cycoaddition of benzoic acid isobutylidene-hydrazide with *tert*-butyl vinyl ether on a 5.0 g scale: To a solution of (*S*,*S*)-**1** (9.60 g, 31.6 mmol) in toluene (200 mL) was added benzoic acid isobutylidene-hydrazide (5.00 g, 26.3 mmol). After 10 min, *tert*-butyl vinyl ether (4.15 mL, 31.6 mmol) was added. After 24 h, the reaction was quenched by the addition of H_2O (150 mL). The resulting mixture was stirred for 30 min, and the phases were then separated. The aqueous layer was extracted with EtOAc (100 mL x 2). The combined organic layers were washed with H_2O (100 mL), and then dried ($MgSO_4$) and filtered. The filtrate was concentrated to a volume of ~50 mL, and then hexane (50 mL) was gradually added. The resulting solution was placed in a refrigerator for 3 h and the resulting crystalline solid was filtered and dried to yield 1-(benzoyl)-5-(*tert*-butoxy)-3-(isopropyl)pyrazolidine as a white crystalline solid (7.08 g, 24.4 mmol, 93% yield). $[\alpha]^{22}_{D}$ = +108.0° (*c* 1.0, $CHCl_3$). The enantiomeric excess of this material was determined to be 99% by chiral HPLC analysis (see below for the details of the assay).

The pseudoephedrine was recovered by the following procedure: the combined aqueous extracts from the above workup were basified with 1*N* aqueous NaOH (150 ml) and the cloudy suspension was extracted with EtOAc (100 mL x 3). The combined organic layers were washed with H_2O (50 ml) and brine (100 mL), and then dried ($MgSO_4$), filtered and concentrated to yield pure (*S*,*S*)-pseudoephedrine as a white solid (5.22 g, 31.6 mmol, >99% recovery).



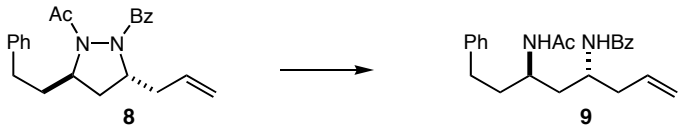
(3*R*,5*R*)-2-(Acetyl)-1-(benzoyl)-5-(*tert*-butoxy)-3-(phenethyl)pyrazolidine: To a cooled (0 °C) solution of 1-(benzoyl)-5-(*tert*-butoxy)-3-(phenethyl)pyrazolidine (1.06 g, 3.00 mmol), 4-(dimethylamino)pyridine (73.3 mg, 0.600 mmol), and pyridine (2.43 mL, 30.0 mmol) in CH_2Cl_2 (25 mL)

was added acetyl chloride (2.13 mL, 30.0 mmol). The reaction mixture was allowed to warm to ambient temperature and stirred for 2 h. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (20 mL) and the phases were separated. The aqueous layer was extracted with CH_2Cl_2 (10 mL x 2), and the combined organic layers were dried ($MgSO_4$), filtered, concentrated. The residue was purified by flash chromatography on silica gel (hexane/EtOAc gradient 2/1 to 1/1) to yield 2-(acetyl)-1-(benzoyl)-5-(*tert*-butoxy)-3-(phenethyl)pyrazolidine as a slightly yellow oil (1.17 g, 2.96 mmol, 99% yield). $[\alpha]^{27}_D = -25.7°$ (*c* 1.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65-7.68 (br m, 2H, Ar-**H**), 7.38-7.48 (m, 3H, Ar-**H**), 7.15-7.26 (m, 5H, Ar-**H**), 5.54 (br d, 1H, *J* = 4.2 Hz, C**H**O*t*-Bu), 4.25 and 4.73 (br, 1H, NAcC**H**), 2.62-3.03 (m, 2H, PhC$\mathbf{H}_2$), 1.76-2.39 (m, 2H + 2H + 3H, $PhCH_2C\mathbf{H}_2$, $CHC\mathbf{H}_2CH$, $C{=}OC\mathbf{H}_3$), 0.73 and 1.24 (br, 9H, $C(C\mathbf{H}_3)_3$); IR (thin film) 3062, 3027, 2975, 2936, 2864, 1679, 1664, 1449, 1393, 1379, 1319, 1102, 1056, 911, 732, 700 cm^{-1}; LRMS (FAB+) calcd for $C_{24}H_{30}N_2O_3$: 394 (M^+), found 394 (M^+).



(3*R*,5*R*)-2-(Acetyl)-5-(allyl)-1-(benzoyl)-3-(phenethyl)pyrazolidine: To a cooled (-15 °C) solution of 2-(acetyl)-1-(benzoyl)-5-(*tert*-butoxy)-3-(phenethyl)pyrazolidine (0.370 g, 0.938 mmol) and allyltrimethylsilane (0.745 mL, 4.69 mmol) in CH_2Cl_2 (10 mL) was added trimethylsilyl trifluoromethanesulfonate (204 μL, 1.13 mmol). After 24 h, the reaction was quenched by the addition of H_2O (15 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (15 mL x 2). The combined organic layers were dried ($MgSO_4$), filtered, concentrated. The residue was purified by flash chromatography on silica gel (CH_2Cl_2/EtOAc gradient 20/1 to 15/1) to yield 2-(acetyl)-5-(allyl)-1-(benzoyl)-3-(phenethyl)pyrazolidine as a white solid (222 mg, 0.612 mmol, 65% yield). $[\alpha]^{27}_D = -44.6°$ (*c* 0.75, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, 2H, *J* = 7.2 Hz, Ar-**H**), 7.50 (t, 1H, *J* = 7.2 Hz, Ar-**H**), 7.42 (t, 2H, *J* = 7.2 Hz, Ar-**H**), 7.13-7.28 (m, 5H, Ar-**H**), 5.65-5.78 (m, 1H, C**H**=CH_2), 5.09-5.17 (m, 2H, CH=C$\mathbf{H}_2$), 4.41-4.58 (br m, 1H, NAcC**H**), 4.12-4.31 (br m, 1H, NBzC**H**), 2.61-2.80 (m, 2H, PhC$\mathbf{H}_2$), 2.39-2.49 (m, 1H, C$\mathbf{H}_2$CH=CH_2), 2.16-2.28 (m, 1H + 2H + 3H, C$\mathbf{H}_2$CH=CH_2 + $CHC\mathbf{H}_2CH$, $COC\mathbf{H}_3$), 1.65-1.78 (m, 2H, $PhCH_2C\mathbf{H}_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.9, 172.7, 141.5, 134.0, 133.1, 131.6,

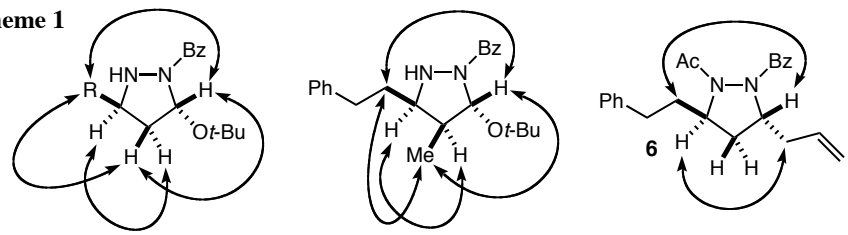
128.6, 128.4, 128.3, 127.9, 125.8, 119.0, 61.0, 55.8, 37.8, 37.3, 36.3, 32.6, 21.3; IR (thin film) 3083, 3025, 2980, 2929, 2852, 1671, 1447, 1402, 1351, 1319, 921, 703 cm^{-1}; LRMS (FAB+) calcd for $C_{23}H_{27}N_2O_2$: 363 ($[M+H]^+$), found 363 ($[M+H]^+$).



(4*R*,6*R*)-6-(Acetylamino)-4-(benzoylamino)-8-phenyl-1-octene: To a degassed solution of 2-(acetyl)-5-(allyl)-1-(benzoyl)-3-(phenethyl)pyrazolidine (72.5 mg, 0.200 mmol) in MeOH (2 mL) was added SmI_2 (6.00 mL, 0.600 mmol, 0.1 M in THF). After 30 min, the reaction mixture was concentrated. The residue was purified by flash chromatography on silica gel (CH_2Cl_2/Acetone gradient 5/1 to 1/1) to give 6-(acetylamino)-4-(benzoylamino)-8-phenyl-1-octene as a slightly yellow solid (63.4 mg, 0.174 mmol, 87% yield). $[\alpha]^{26}_D$ = -3.2° (*c* 0.37, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, 2H, *J* = 7.2 Hz, Ar-**H**), 7.47 (t, 1H, *J* = 7.2 Hz, Ar-**H**), 7.40 (t, 2H, *J* = 7.2 Hz, Ar-**H**), 7.20-7.25 (m, 2H, Ar-**H**), 7.11-7.15 (m, 3H, Ar-**H**), 6.41 (d, 1H, *J* = 8.3, N**H**), 5.71-5.85 (m, 1H + 1H, N**H** + C**H**=CH_2), 5.08-5.15 (m, 2H, CH=C**H**$_2$), 4.04-4.16 (m, 1H, NC**H**), 3.88-4.00 (m, 1H, NC**H**), 2.57-2.73 (m, 2H, PhC**H**$_2$), 2.33-2.54 (m, 2H, C**H**$_2$CH=CH_2), 1.75-2.03 (m, 2H + 2H + 3H, $PhCH_2CH_2$, $CHCH_2CH$, C=OC**H**$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 167.3, 141.4, 134.4, 134.3, 131.5, 128.6, 128.4, 128.3, 126.8, 126.0, 118.3, 46.9, 46.8, 39.2, 38.8, 36.4, 32.6, 23.5; IR (thin film) 3287, 3064, 3028, 2953, 2925, 2856, 1636, 1539, 1491, 1440, 1373, 1313, 1265, 1093, 1029, 916, 802, 752, 699 cm^{-1}; LRMS (FAB+) calcd for $C_{23}H_{29}N_2O_2$: 365 ($[M+H]^+$), found 365 ($[M+H]^+$).

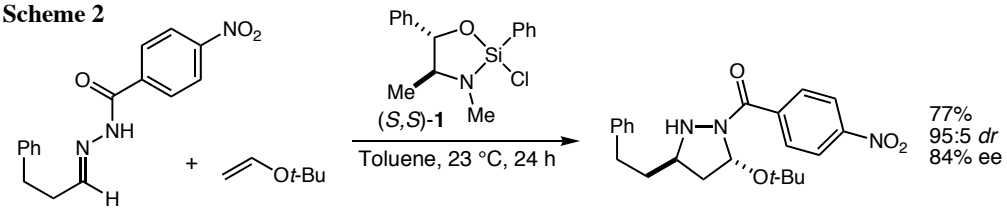
Proof of relative stereochemistry of the cycloaddition products and 6: The relative stereochemistry of the cycloaddition products and compound **6** was determined by selective 1D NOESY experiments as illustrated in Scheme 1:

Scheme 1



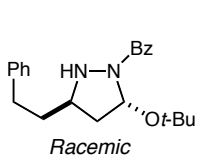
Proof of absolute configuration of the cycloaddition products: The *p*-nitrobenzoylhydrazone of dihydrocinnamaldehyde was prepared and subjected to the cycloaddition reaction with *tert*-butyl vinyl ether (Scheme 2). The product is a known compound previously prepared by Kobayashi and coworkers.[2] Comparison of the chiral HPLC traces (DAICEL Chiralpak AD-H, hexane/*i*-PrOH = 97.5/2.5, 0.8 mL/min, retention time = 25.6 (minor) and 33.5 (major) min) allowed the assignment of absolute stereochemistry for this cycloaddition product. The absolute configurations of all other cycloaddition products were assigned by analogy.

Scheme 2

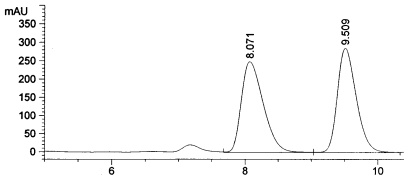


Determination of ee of the cycloaddition products by chiral HPLC analysis:

Table 1, entry 1: DAICEL Chiralpak AD-H, hexane/EtOH = 97/3, 1.0 mL/min.



Racemic



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.071	VV	0.3555	5736.98242	249.63403	50.2526
2	9.509	VV	0.3072	5679.29639	286.27591	49.7474
Totals :				1.14163e4	535.90994	

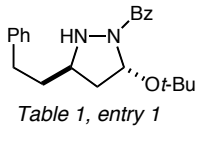
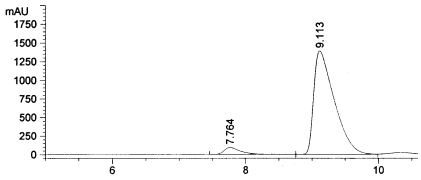


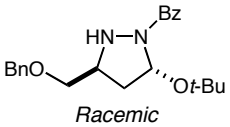
Table 1, entry 1



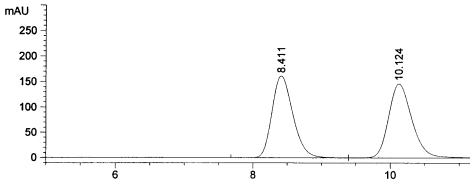
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.764	VP	0.2581	1606.79919	93.79798	5.1292
2	9.113	VV	0.3201	2.97195e4	1385.77893	94.8708
Totals :				3.13263e4	1479.57691	

(2)Yamashita, Y.; Kobayashi, S. *J. Am. Chem. Soc*. **2004**, *126*, 11279-11282.

Table 1, entry 2: DAICEL Chiralpak AD-H, hexane/EtOH = 95/5, 1.0 mL/min.



Racemic



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.411	VV	0.3353	3415.20703	160.72360	49.7601
2	10.124	VV	0.3634	3448.14355	145.72412	50.2399
Totals :				6863.35059	306.44772	

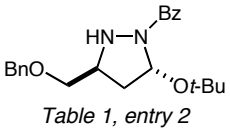
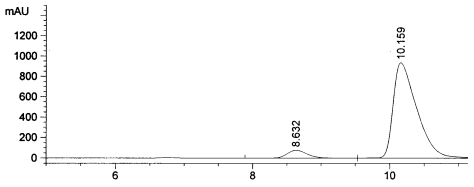
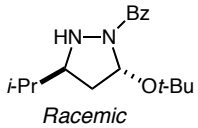


Table 1, entry 2

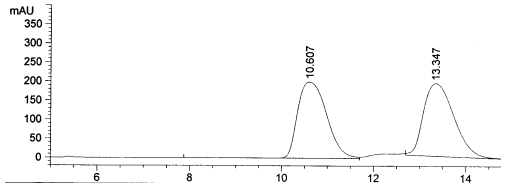


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.632	MM	0.2899	1168.33459	67.15922	4.9915
2	10.159	VV	0.3598	2.22383e4	932.40851	95.0085
Totals :				2.34066e4	999.56773	

Table 1, entry 3: DAICEL Chiralcel OD, hexane/*i*-PrOH = 99/1, 0.7 mL/min.



Racemic



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.607	VV	0.7225	8783.30859	199.81802	50.1013
2	13.347	MM	0.7648	8747.79395	190.62334	49.8987
Totals :				1.75311e4	390.44136	

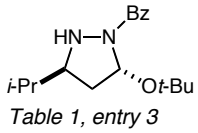
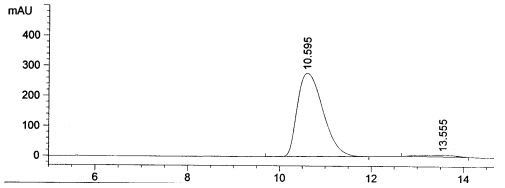
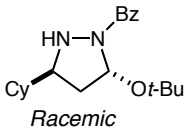


Table 1, entry 3

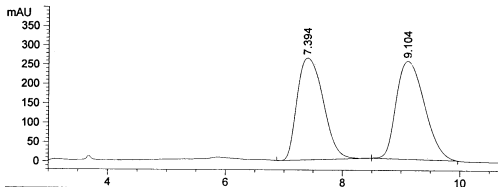


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.595	MM	0.6524	1.08525e4	277.22952	96.7907
2	13.555	MM	0.9852	359.84131	6.08729	3.2093
Totals :				1.12123e4	283.31681	

Table 1, entry 4: DAICEL Chiralcel OD, hexane/*i*-PrOH = 99/1, 1.0 mL/min.



Racemic



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.394	MM	0.5183	8201.55273	263.75348	49.2189
2	9.104	MM	0.5561	8461.88477	253.59879	50.7811
Totals :				1.66634e4	517.35226	

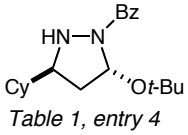
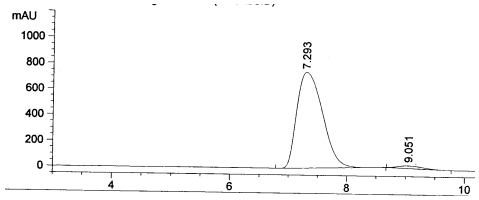
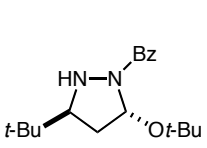


Table 1, entry 4

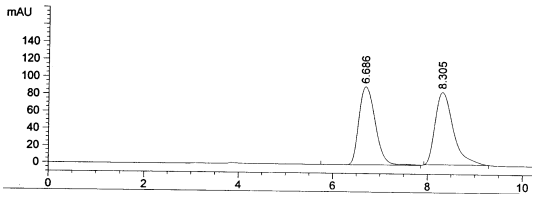


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.293	MM	0.5067	2.26018e4	743.36499	97.3260
2	9.051	MM	0.4869	620.96942	21.25661	2.6740
Totals :				2.32228e4	764.62160	

Table 1, entry 5: DAICEL Chiralcel OD, hexane/*i*-PrOH = 99/1, 1.0 mL/min.



Racemic



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.686	MM	0.4054	2211.64038	90.93437	49.5230
2	8.305	MM	0.4464	2254.24658	84.15672	50.4770
Totals :				4465.88696	175.09109	

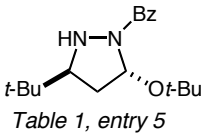
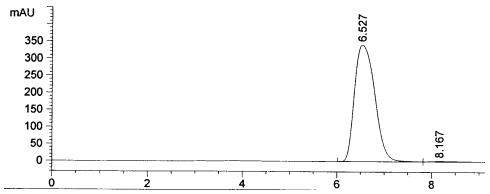
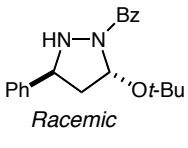


Table 1, entry 5

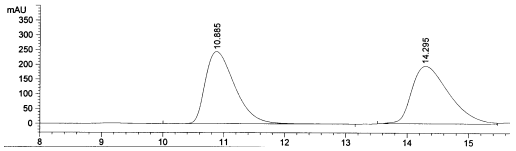


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.527	BV	0.4878	1.01677e4	340.87558	98.9377
2	8.167	VV	0.7008	109.16932	2.11644	1.0623
Totals :				1.02769e4	342.99202	

Table 1, entry 6: DAICEL Chiralcel OD, hexane/*i*-PrOH = 99/1, 1.0 mL/min.



Racemic



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.885	VV	0.5220	8222.91113	243.53552	49.9612
2	14.295	MM	0.7021	8235.67285	195.49411	50.0388
Totals :				1.64586e4	439.02963	

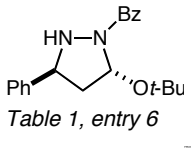
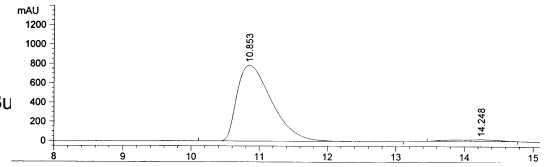
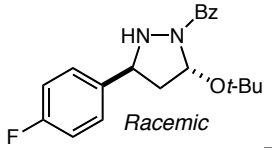


Table 1, entry 6

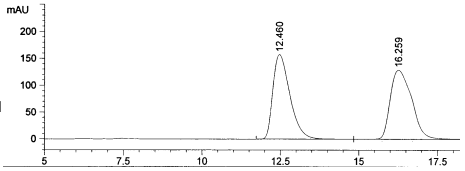


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.853	VV	0.5535	2.78632e4	785.66418	96.8627
2	14.248	MM	0.8239	902.47742	18.25592	3.1373
Totals :				2.87657e4	803.92010	

Table 1, entry 7: DAICEL Chiralcel OD, hexane/*i*-PrOH = 99/1, 1.0 mL/min



Racemic



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.460	BV	0.5932	5957.21143	157.32727	49.5268
2	16.259	VB	0.7839	6071.05078	128.55563	50.4732
Totals :				1.20283e4	285.88290	

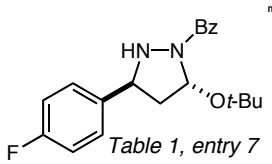
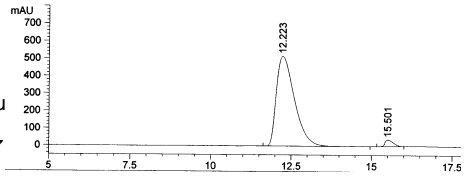
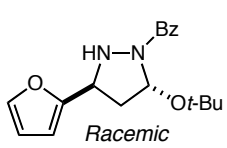


Table 1, entry 7

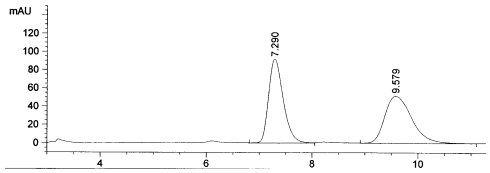


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.223	VV	0.6093	2.02317e4	515.51691	96.7397
2	15.501	MM	0.3036	681.84149	37.42780	3.2603
Totals :				2.09136e4	552.94471	

Table 1, entry 8: DAICEL Chiralcel OD, hexane/*i*-PrOH = 97/3, 1.0 mL/min



Racemic



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.290	VV	0.3021	1775.09863	91.49013	49.4433
2	9.579	VV	0.5515	1815.06909	51.42993	50.5567
Totals :				3590.16772	142.92006	

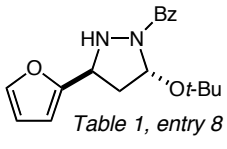
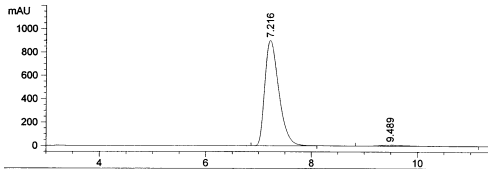
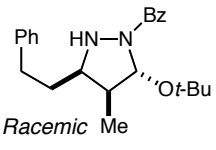


Table 1, entry 8

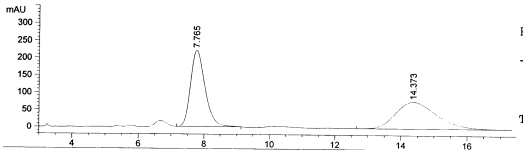


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.216	VV	0.2851	1.66425e4	902.22797	97.5665
2	9.489	VV	0.5717	415.09116	10.63718	2.4335
Totals :				1.70576e4	912.86515	

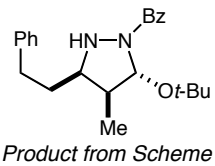
Product from Scheme 4: DAICEL Chiralcel OJ-H, hexane/EtOH = 93/7, 1.0 mL/min.



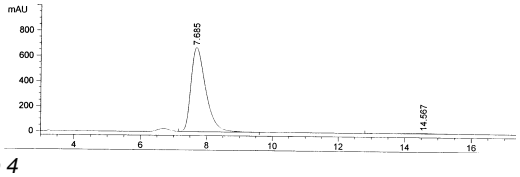
Racemic Me



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.765	MM	0.5115	6773.84570	220.71989	49.7866
2	14.373	VBA	1.3487	6831.92822	77.94564	50.2134
Totals :				1.36058e4	298.66553	



Product from Scheme 4



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.685	VV	0.4831	2.10107e4	668.61035	98.3274
2	14.567	VBA	1.5676	357.40546	3.63131	1.6726
Totals :				2.13682e4	672.24166	

^{1}H NMR Spectra of the cycloaddition products and compounds 6 and 7 from Scheme 6:

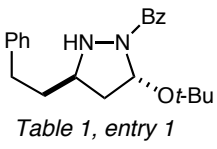
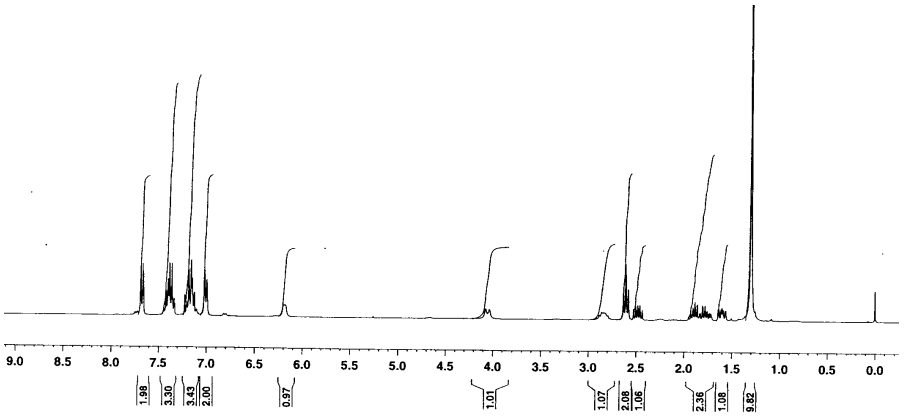


Table 1, entry 1



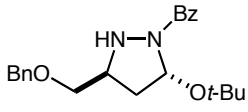
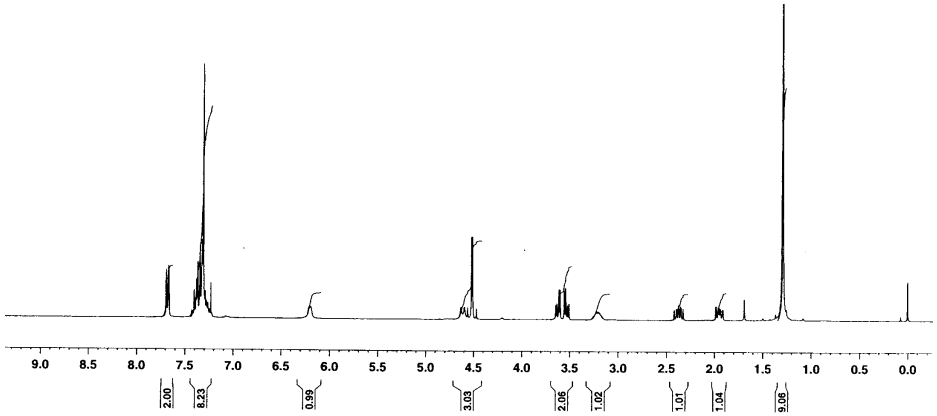


Table 1, entry 2



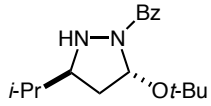
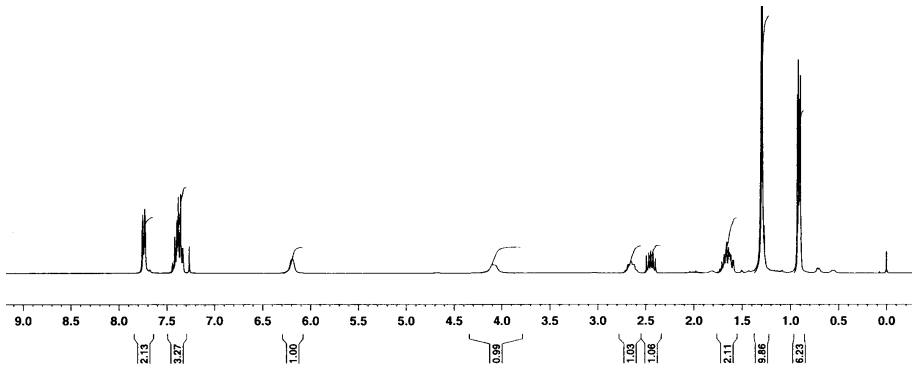


Table 1, entry 3



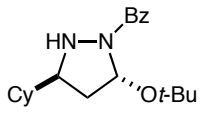
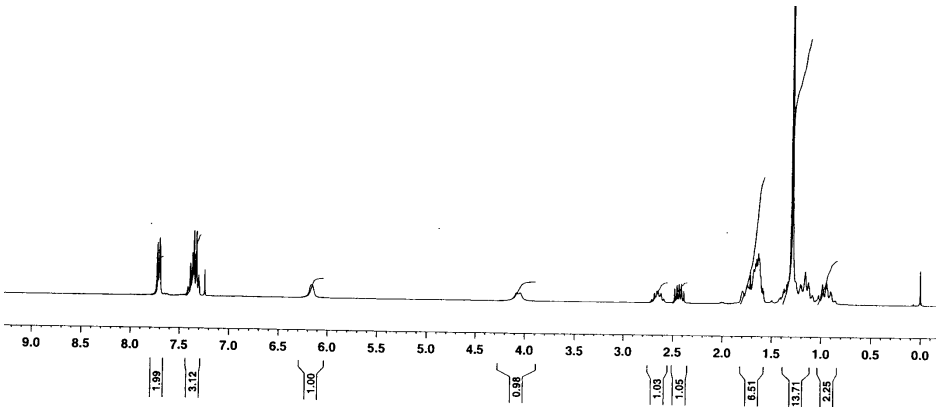
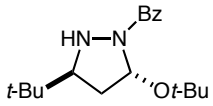


Table 1, entry 4





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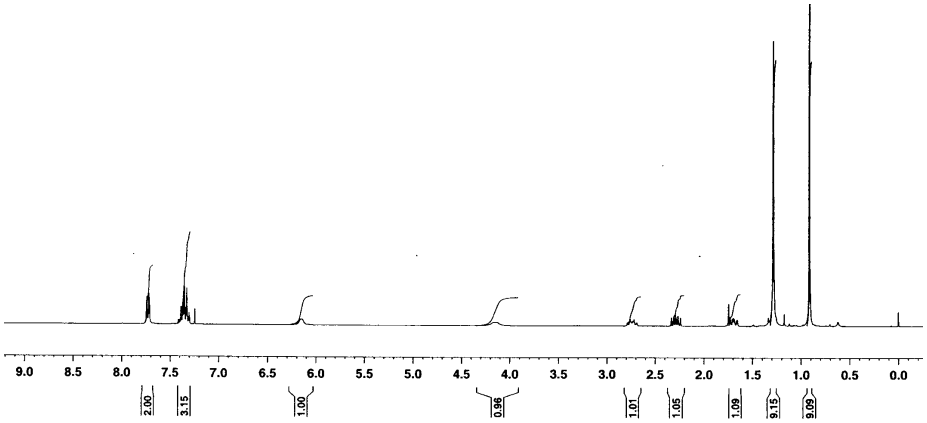


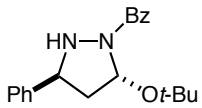
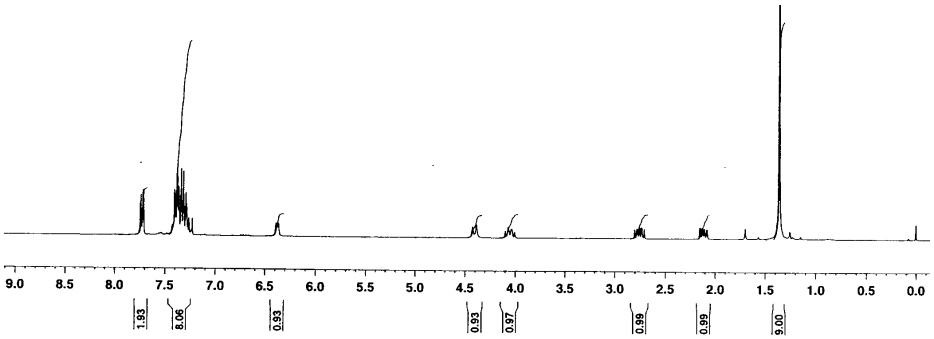


Table 1, entry 6



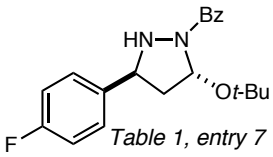
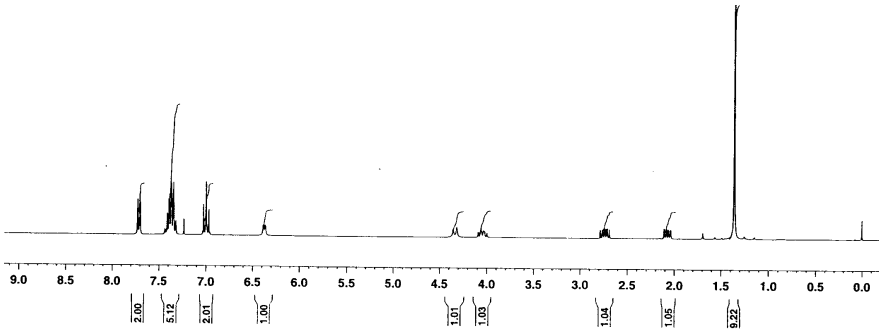


Table 1, entry 7



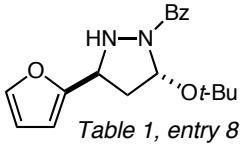
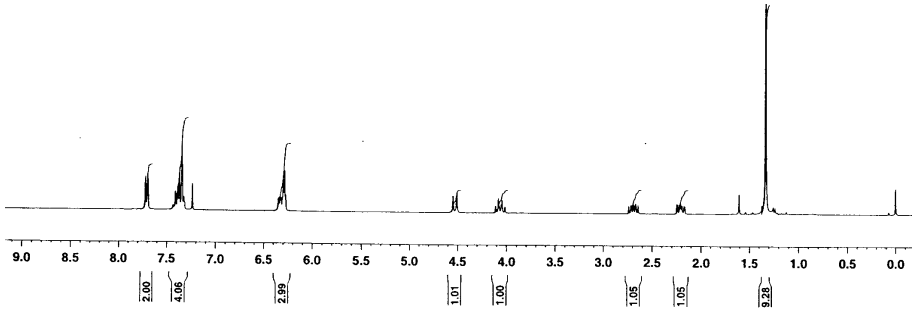
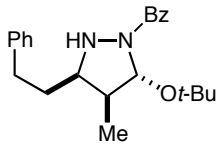
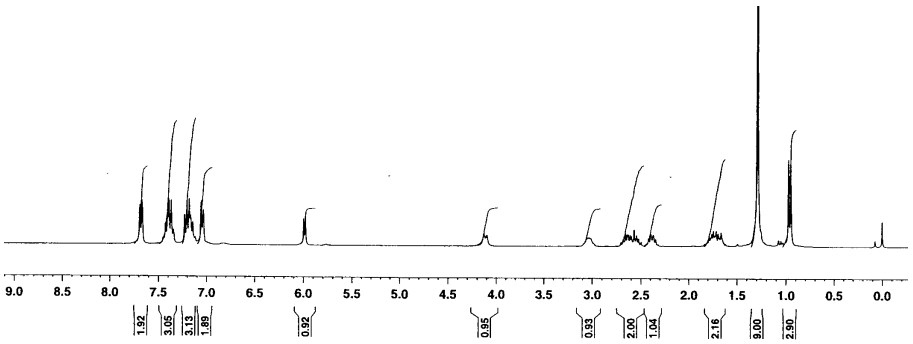


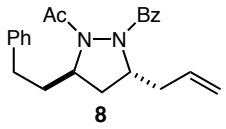
Table 1, entry 8



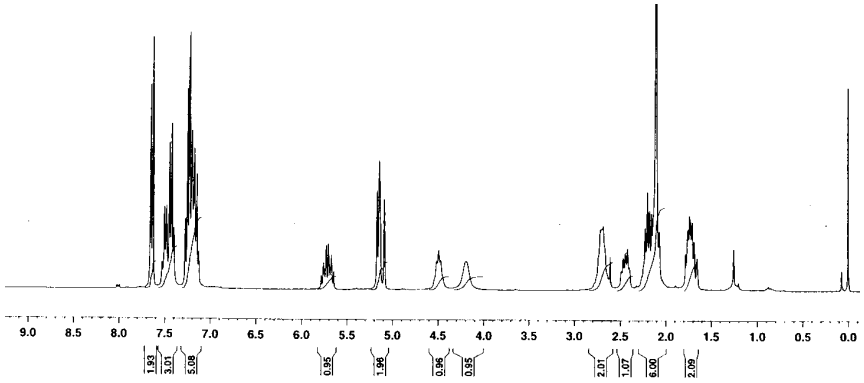


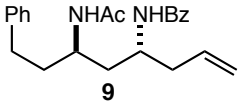
Product from Scheme 4





8





9