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Supporting Information

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A New Strategy for the Stereoselective Synthesis of Isoxazolidines via Pd-Catalyzed Carboetherification of *N*-Butenylhydroxylamines[**]

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Experimental Section

General: All reactions were carried out under a nitrogen atmosphere in oven- or flame-dried glassware. Tris(dibenzylideneacetone)dipalladium(0), palladium acetate, and bis(2-diphenylphosphinophenyl)ether (DPE-Phos) were purchased from Strem Chemical Co. and used without further purification. All aryl bromides were obtained from commercial sources (Aldrich Chemical Co. or Acros Chemical Co.) and were used as obtained. Toluene, THF, and CH_2Cl_2 were purified using a GlassContour solvent purification system. Structural assignments were based on 2-D NMR experiments (COSY, HSQC); stereochemistry was assigned on the basis of ^{1}H NMR nOe experiments. Ratios of diastereomers were determined by ^{1}H NMR analysis of crude reaction mixtures. Yields refer to isolated yields of compounds estimated to be ≥95% pure as determined by ^{1}H NMR, and either capillary GC (known compounds) or combustion analysis (new compounds). The yields reported in the supporting information describe the result of a single experiment, whereas the yields reported in Tables 1–2 are average yields of two or more experiments. Therefore, the yields reported in the supporting information may differ from those shown in Tables 1–2.

Synthesis of *N*-Butenylhydroxylamines

General Procedure 1: Oxidation of *N*-Butenylamines.[1] An oven- or flame-dried flask was cooled under a stream of nitrogen and charged with Na_2HPO_4 (5 equiv) and a solution of the butenylamine in THF (0.33 M, 1 equiv). The flask was equipped with a reflux condenser and charged with a solution of benzoyl peroxide in THF (1 M, 1.1 equiv). The reaction was heated to 65 ºC until the butenylamine substrate was consumed as judged by TLC or GC analysis. The resulting suspension was cooled to rt, filtered through a pad of celite, and the filtrate was concentrated *in vacuo*. The crude material was purified by flash chromatography on silica gel to afford an *O*-benzoylhydroxylamine product.

General Procedure 2: Deprotection of *O*-Benzoylhydroxylamines.[1] An oven- or flame-dried flask was cooled under a stream of nitrogen and charged with an *O*-benzoylhydroxylamine (1.0 equiv) and MeOH (9 mL MeOH/mmol substrate). A solution of sodium methoxide in methanol (25 %w/w, 1.4 equiv) was added slowly, and the resulting mixture was stirred at rt until the substrate was consumed as judged by TLC or capillary GC analysis. The reaction was concentrated *in vacuo*, and the residue was diluted with saturated aqueous NH_4Cl (10 mL/mmol substrate) and CH_2Cl_2 (10 mL/mmol substrate). The layers were separated and the aqueous layer extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The crude material was purified by column chromatography on silica gel.

***N*-Benzyl-*N*-but-3-enylhydroxylamine (3).** *N*-Benzyl-*N*-but-3-enylamine[2] (1.00 g, 6.2 mmol) was oxidized according to general procedure 1 to afford 0.89 g (51%) of *O*-benzoyl-*N*-benzyl-*N*-but-3-enylhydroxylamine as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.0 Hz, 2 H), 7.64 (d, *J* = 8.0 Hz, 1 H), 7.55–7.51 (m, 2 H), 7.42–7.39 (m, 2 H), 7.27–7.09 (m, 2 H), 7.09 (t, *J* = 7.5 Hz, 1 H), 5.91–5.82 (m, 1 H), 5.09–4.99 (m, 2 H), 4.35 (s, 2 H), 3.20–3.17 (m, 2 H), 2.42 (q, *J* = 8.0 Hz, 2 H).

O-Benzoyl-*N*-benzyl-*N*-but-3-enylhydroxylamine (0.89 g, 3.19 mmol) was treated with sodium methoxide following general procedure 2 to afford 0.34 g (60%) of the title compound as a colorless oil**.** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (s, br, 1 H), 7.27–7.19 (m, 5 H), 5.73–5.68 (m, 1 H), 5.00–4.94 (m, 2 H), 3.67 (s, 2 H), 2.63 (t, *J* = 6.5 Hz, 2 H), 2.24 (q, *J* = 6.5 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.7, 136.0, 129.9, 128.2, 127.4, 115.7, 64.6, 58.5, 31.2; IR (film) 3232, 1453 cm^{-1}. Anal calcd for $C_{11}H_{15}NO$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.37; H, 8.61; N, 7.96.

***N*-Benzyl-*N*-(2-methylbut-3-enyl)hydroxylamine (5).** An oven- or flame-dried flask was cooled under a stream of nitrogen and charged with 2-(2-methylbut-3-enyl)isoindole-1,3-dione[3] (5.83 g, 27.1 mmol) and EtOH (700 mL). Hydrazine hydrate (1.35 g, 1.3 mL, 27.1 mmol) was added and the solution was heated to reflux for 2.5 h. The reaction was cooled to rt and the solution was acidified to pH 2 with conc. HCl. The resulting suspension was filtered, the filtrate was concentrated to approximately one-half volume, and then was diluted with H_2O (250 mL). The resulting suspension was filtered and the filtrate was diluted with Et_2O (500 mL). The mixture was transferred to a separatory funnel, the layers were separated, and the aqueous layer was extracted with Et_2O (2 X 100 mL). The combined organic layers were dried over anhydrous sodium sulfate, decanted into a flask, and treated with benzoyl chloride (4.18 g, 4.2 mL, 29.81 mmol) and triethylamine (3.01 g, 4.2 mL, 29.81 mmol). The resulting solution was stirred at rt for 2.5 h and concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 (200 mL) and aqueous NaOH (100 mL, 1 M). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2 X 100 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated *in vacuo* to afford 4.55 g (88%) of *N*-(2-methylbut-3-enyl)benzamide as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.0 Hz, 2 H), 7.53 (t, *J* = 8.5 Hz, 1 H), 7.46–7.41 (m, 2 H), 6.13 (s, br, 1 H), 5.78–5.71 (m, 1 H), 5.15–5.10 (m, 2 H), 3.24–3.18 (m, 1 H), 3.12–3.07 (m, 1 H), 2.47 (sept, *J* = 7.0 Hz, 1 H), 1.09 (d, *J* = 7.0 Hz, 3 H).

An oven- or flame-dried flask was purged with nitrogen and charged with a solution of $LiAlH_4$ in THF (60 mL, 60 mmol, 1.0 M) and THF (60 mL). The solution was cooled to 0 °C, *N*-(2-methylbut-3-enyl)benzamide (4.55 g, 24.1 mmol) was added dropwise via syringe, and the resulting solution was heated to 65 ºC for 1 h until the starting material was found to be completely consumed as judged by TLC analysis. The reaction was cooled to rt and diluted twofold with THF and quenched according to the Fieser[4] procedure by successively adding water (2.4 mL), aqueous NaOH (2.4 mL, 10 M), and water (7.2 mL) in a dropwise manner. The resulting suspension was decanted and the organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo* to afford 4.11 g (97%) of benzyl-(2-methylbut-3-enyl)amine as a clear liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.36 (m, 1 H), 7.33–7.24 (m, 4 H), 5.70–5.62 (m, 1 H), 5.09–4.99 (m, 2 H), 3.82–3.79 (m, 1 H), 3.77–3.74 (m, 1 H), 2.58–2.46 (m, 2 H), 2.41–2.37 (m, 1 H), 1.60 (s, br, 1 H), 1.00 (d, *J* = 6.4 Hz, 3 H).

Benzyl-(2-methylbut-3-enyl)amine (419 mg, 2.39 mmol) was oxidized according to general procedure 1 to afford 545 mg (77%) of *O*-benzoyl-*N*-benzyl-*N*-(2-methylbut-3-enyl)hydroxylamine as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96–7.92 (m, 2 H), 7.69–7.64 (m, 1 H), 7.56–7.49 (m, 2 H), 7.45–7.38 (m, 2 H), 7.35–7.23 (m, 3 H), 5.82 (qd, 8.8, 11.5 Hz, 1 H), 5.01–4.90 (m, 2 H), 4.24–4.20 (m, 1 H), 4.18–4.13 (m, 1 H), 2.94 (dd, *J* = 8.8, 17.2 Hz, 1 H), 2.81 (dd, *J* = 9.6, 17.2 Hz, 1 H), 2.46 (sept, *J* = 8.8 Hz, 1 H), 1.07 (d, *J* = 9.2 Hz, 3 H).

O-Benzoyl-*N*-benzyl-*N*-(2-methylbut-3-enyl)hydroxylamine (545 mg, 1.85 mmol) was treated with sodium methoxide following general procedure 2 to afford 143 mg (40%) of the title compound as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.31 (m, 3 H), 7.29–7.25 (m, 2 H), 5.86–5.77 (m, 1 H), 5.06–4.97 (m, 2 H), 4.89 (s, br, 1 H), 3.85–3.81 (m, 1 H), 3.81–3.78 (m, 1 H), 2.70–2.65 (m, 1 H), 2.62–2.53 (m, 2 H), 1.03 (d, *J* = 8.0 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.8, 137.5, 129.5, 128.2, 127.3, 113.3, 65.5, 64.8, 35.6, 18.1; IR (film) 3189, 1452 cm^{-1}. Anal calcd for $C_{12}H_{17}NO$: C, 75.35; H, 8.96; N, 7.32. Found: C, 75.41; H, 8.93; N, 7.21.

***N*-Benzyl-*N*-(1-phenylbut-3-enyl)hydroxylamine (6).** An oven- or flame-dried flask was cooled under a stream of nitrogen and charged with *N*-benzylhydroxylamine (3.00 g, 24.0 mmol), benzaldehyde (3.56 g, 3.4 mL, 33.6 mmol), anhydrous sodium sulfate (4.09 g, 28.8 mmol), and CH_2Cl_2 (29 mL). The reaction was stirred at rt until the starting material was consumed as judged by capillary GC analysis. The suspension was filtered and concentrated *in vacuo*. The crude material was purified by flash chromatography on silica gel to afford 3.71 g (73%) of *N*-(benzylidene)benzylamine-*N*-oxide. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26–8.20 (m, 2 H), 7.53–7.47 (m, 2 H), 7.42–7.38 (m, 7 H), 5.05 (s, 2 H).

An oven- or flame-dried flask was purged with nitrogen and charged with *N*-(benzylidene)benzylamine-*N*-oxide (3.71 g, 17.6 mmol), THF (187 mL), and cooled to 0 ºC. A solution of allylmagnesium bromide in THF (52.8 mL, 52.8 mmol, 1.0 M) was added slowly, and the resulting mixture was stirred at 0 ºC for 1 h. The reaction mixture was then quenched with aqueous NH_4Cl (160 mL), warmed to rt, and diluted with ethyl acetate (200 mL). The layers were separated and aqueous layer was extracted with ethyl acetate (2 x 100 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was then purified by flash chromatography on silica gel to afford 1.73 g (39%) of the title compound as a white solid, m.p. 53–54 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39–4.33 (m, 4 H), 7.31–7.28 (m, 5 H), 7.27–7.23 (m, 1 H), 5.71–5.60 (m, 1 H), 5.13 (s, br, 1 H), 5.01–4.93 (m, 2 H), 3.76–3.68 (m, 2 H), 3.57–3.54 (m, 1 H), 2.93–2.87 (m, 1 H), 2.62–2.55 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.9, 138.2, 135.5, 129.3, 128.8, 128.3, 128.2, 127.5, 127.1, 116.5, 71.7, 61.4, 38.2; IR (film) 3030, 1495 cm^{-1}. Anal calcd for $C_{17}H_{19}NO$: C, 80.60; H, 7.56; N, 5.53. Found: C, 80.71; H, 7.66; N, 5.38.

***N*-*tert*-Butyl-*N*-(1-phenylbut-3-enyl)hydroxylamine (7).** An oven- or flame-dried flask was purged with nitrogen and charged with *N*-(benzylidene)-*tert*-butylamine-*N*-oxide (750 mg, 4.23 mmol), THF (6.3 mL), and cooled to 0 ºC. A solution of allylmagnesium bromide in THF (6.3 mL, 6.3 mmol, 1.0 M) was added slowly, and the resulting mixture was stirred at 0 ºC for 1 h. The reaction mixture was quenched with aqueous NH_4Cl (10 mL), warmed to rt, and diluted with ethyl acetate (20 mL). The layers were separated and aqueous layer was extracted with ethyl acetate (2 X 50 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was then purified by flash chromatography on silica gel to afford 694 mg (75%) of the title compound as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50–7.22 (m, 5 H), 5.79–5.64 (m, 1 H), 5.09–4.86 (m, 2 H), 4.34 (br s, 1 H), 4.00–3.89 (m, 1 H), 2.82–2.71 (m, 1 H), 2.64–2.51 (m, 1 H), 0.95 (s, 9 H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.5, 134.8, 127.0, 125.8, 124.7, 113.5, 62.6, 57.4, 37.7, 24.7; IR (film) 3535, 1639 cm^{-1}. MS (CI) 220.1707 (220.1701 calcd for $C_{14}H_{22}NO$, M + H^+).

2-Allylpyrrolidin-1-ol (8). 2-Allylpyrrolidine[5,6] (2.62 g, 23.6 mmol) was oxidized according to general procedure 1 to afford 2.92 g (53%) of *O*-benzoyl-2-allylpyrrolidin-1-ol as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02–7.98 (m, 2H), 7.64–7.26 (m, 3 H), 5.88–5.77 (m, 1 H), 5.10–4.97 (m, 2 H), 3.64–3.56 (m, 1 H), 3.30–3.23 (m, 1 H), 3.10–3.00 (m, 1 H), 2.56–2.50 (m, 1 H), 2.30–2.20 (m, 1 H), 2.09–1.90 (m, 3 H), 1.70–1.58 (m, 1 H).

O-Benzoyl-2-allylpyrrolidin-1-ol (2.92 g, 12.6 mmol) was treated with sodium methoxide following general procedure 2 to afford 583 mg (36%) of the title compound as a pale yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (s, br, 1 H), 5.84–5.74 (m, 1 H), 5.08–4.98 (m, 2 H), 3.27–3.21 (m, 1 H), 2.85–2.75 (m, 2 H), 2.59–2.52 (m, 1 H), 2.18–2.09 (m, 1 H), 1.98–1.87 (m, 1 H), 1.81–1.61 (m, 2 H), 1.42–1.36 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.6, 116.3, 67.6, 57.5, 37.7, 26.7, 19.4; IR (film) 3188, 1458 cm^{-1}. Anal calcd for $C_7H_{13}NO$: C, 66.10; H, 10.30; N, 11.01. Found: C, 65.85; H, 10.26; N, 10.62.

2-Allylpiperidin-1-ol (9). 2-Allylpiperidine[7] (1.94 g, 15.52 mmol) was oxidized according to general procedure 1 to afford 3.66 g (96%) of *O*-benzoyl-2-allylpiperidin-1-ol as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, *J* = 7.5 Hz, 2 H),

7.58–7.52 (m, 1 H), 7.50–7.43 (m, 2 H), 5.89–5.77 (m, 1 H), 5.01–4.98 (m, 2 H), 3.59–3.57 (m, 1 H), 2.85–2.80 (m, 1 H), 2.75–2.71 (m, 1 H), 2.48–2.44 (m, 1 H), 2.28–2.25 (m, 1 H), 1.91–1.83 (m, 2 H), 1.78–1.69 (m, 2 H), 1.59–1.52 (m, 1 H), 1.31–1.26 (m, 1 H).

O-Benzoyl-2-allylpiperidin-1-ol (3.66 g, 14.9 mmol) was treated with sodium methoxide according to general procedure 2 to afford 400 mg (19%) of the title compound as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (s, br, 1 H), 5.84–5.73 (m, 1 H), 5.07–5.00 (m, 2 H), 3.30–3.28 (m, 1 H), 2.82–2.78 (m, 1 H), 2.53–2.47 (m, 1 H), 2.35–2.30 (m, 1 H), 2.09–2.02 (m, 1 H), 1.85–1.80 (m, 1 H), 1.71–1.67 (m, 1 H), 1.60–1.58 (m, 1 H), 1.54–1.47 (m, 1 H), 1.21–1.08 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.7, 116.7, 66.9, 59.7, 37.9, 30.8, 25.8, 23.6; IR (film) 3187, 1441 cm^{-1}. MS (EI) 140.1074 (140.1075 calcd for $C_8H_{14}NO$).

***N*-Cyclopent-2-enylmethyl-*N*-methylhydroxylamine (10).** An oven- or flame-dried flask was purged with nitrogen and charged with a solution of $LiAlH_4$ in THF (37.5 mL, 37.5 mmol, 1.0 M) and THF (38 mL) and cooled to 0 ºC. Cyclopent-2-enylmethylcarbamic acid methyl ester[8] (2.33 g, 15.0 mmol) was added dropwise via syringe and the resulting solution was heated to 65 ºC for 30 min. The reaction was cooled to rt, diluted with THF (40 mL), and quenched according to the Fieser[4] procedure by successively adding water (1.5 mL), NaOH (1.5 mL, 10 M), and water (4.5 mL) in a dropwise manner. The resulting suspension was decanted and the organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo* to afford 1.66 g (99%) of cyclopent-2-enylmethylmethylamine as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.79–5.76 (m, 1 H), 5.68–5.66 (m, 1 H), 2.86–2.83 (m, 1 H), 2.58 (dd, *J* = 6.0, 11.5 Hz, 1 H), 2.48 (dd, *J* = 7.0, 11.0 Hz, 1 H), 2.43 (s, 3 H), 2.37–2.27 (m, 2 H), 2.07–2.00 (m, 1 H), 1.72 (s, br, 1 H), 1.53–1.46 (m, 1 H).

Cyclopent-2-enylmethylmethylamine (1.66 g, 15.0 mmol) was oxidized according to general procedure 1 to afford 2.41 g (70%) of *O*-benzoyl-*N*-cyclopent-2-enylmethyl-*N*-methylhydroxylamine as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07–8.01 (m, 2 H), 7.58–7.50 (m, 1 H), 7.46–7.42 (m, 2 H), 5.77–5.74 (m, 2 H), 3.10–3.07 (m, 2 H), 2.90–2.82 (m, 4 H), 2.39–2.33 (m, 1 H), 2.30–2.23 (m, 1 H), 2.11–2.04 (m, 1 H), 1.67–1.60 (m, 1 H).

O-Benzoyl-*N*-cyclopent-2-enylmethyl-*N*-methylhydroxylamine (2.41 g, 10.4 mmol) was treated with sodium methoxide according to general procedure 2 to afford 0.90 g (68%) of the title compound as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (s, br, 1 H), 5.74–7.72 (m, 2 H), 2.98–2.95 (m, 1 H), 2.66–2.60 (m, 4 H), 2.34–2.23 (m, 3 H), 2.07–2.02 (m, 1 H), 1.50–1.46 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.1, 131.3, 67.3, 48.8, 43.5, 31.6, 28.4; IR (film) 3221, 1436 cm^{-1}. MS (EI) 127.0996 (127.0997 calcd for $C_7H_{13}NO$).

Synthesis of Substituted Isoxazolidines

General procedure for the palladium-catalyzed synthesis of isoxazolidines. An oven- or flame-dried Schlenk tube was cooled under a stream of nitrogen and charged with $Pd(OAc)_2$ (2 mol %), DPE-Phos (2 mol %), NaO*t*Bu (1.2 equiv), and the aryl bromide (1.2 equiv). The tube was purged with nitrogen and the hydroxylamine substrate (1.0 equiv) and THF (8 mL/mmol hydroxylamine) were added. The mixture was heated to 65 °C with stirring until the starting material had been consumed as judged by GC or ^{1}H NMR analysis. The reaction mixture was cooled to room temperature, quenched with saturated aqueous NH_4Cl (2 mL) and diluted with ethyl acetate (10 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (2 X 10 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography on silica gel.

(±)-*N*-Benzyl-5-biphenyl-4-ylmethylisoxazolidine (4). Reaction of 54 mg (0.30 mmol) of **3** with 4-bromobiphenyl (84 mg, 0.36 mmol) following the general procedure afforded 79 mg (80%) of the title compound as a pale yellow oil. ^{1}H NMR (400

MHz, C_6D_6, 75 °C) δ 7.39 (d, *J* = 7.2 Hz, 2 H), 7.34–7.29 (m, 4 H), 7.16–7.00 (m, 8 H), 4.19–4.16 (m, 1 H), 3.80 (s, 2 H), 2.87 (dd, *J* = 6.4, 13.6 Hz, 1 H), 2.59–2.54 (m, 3 H), 1.90–1.85 (m, 1 H), 1.61–1.57 (m, 1 H); ^{13}C NMR (100 MHz, C_6D_6, 75 °C) δ 141.2, 139.2, 137.9, 137.6, 129.6, 128.8, 128.4, 127.7, 127.2, 126.8, 126.7, 77.4, 62.2, 54.2, 40.8, 33.7 (two aromatic signals are incidentally equivalent); IR (film) 3028, 1487 cm^{-1}. MS (ESI) 330.1844 (33.1858 calcd for $C_{23}H_{24}NO$, M + H$^+$).

(±)-*N*-Benzyl-5-(4-trifluoromethylbenzyl)isoxazolidine (11). The reaction of 44 mg (0.25 mmol) of **3** with 4-bromobenzotrifluoride (67 mg, 0.30 mmol) following the general procedure afforded 73 mg (91%) of the title compound as a pale yellow oil. ^{1}H NMR (400 MHz, C_6D_6, 75 °C) δ 7.29–7.27 (m, 4 H), 7.14–7.10 (m, 2 H), 7.05 (t, *J* = 7.2 Hz, 1 H), 6.89 (d, *J* = 8.0 Hz, 2 H), 4.01 (p, *J* = 6.0 Hz, 1 H), 3.76 (s, 2 H), 2.70 (dd, *J* = 7.2, 14.0 Hz, 1 H), 2.51 (s, br, 2 H), 2.40 (dd, *J* = 5.6, 14.0 Hz, 1 H), 1.87–1.79 (m, 1 H), 1.50–1.44 (m, 1 H); ^{13}C NMR (100 MHz, C_6D_6, 75 °C) δ 142.7, 137.7, 129.5, 128.8, 127.9, 126.9, 124.8 (m), 76.7, 62.1, 54.1, 40.8, 33.7 (two aromatic signals are incidentally equivalent); IR (film) 2952, 1325 cm^{-1}. Anal calcd for $C_{18}H_{18}NO$: C, 67.28; H, 5.65; N, 4.36. Found: C, 67.05; H, 5.62; N, 4.32.

(±)-(4*R*,5*S*)-[4-(*N*-Benzyl-4-methylisoxazolidin-5-ylmethyl)phenyl]phenylmethanone (12). The reaction of 48 mg (0.25 mmol) of **5** with 4-bromobenzophenone (78 mg, 0.30 mmol) following the general procedure afforded 58 mg (63%) of the title compound as a pale yellow oil. This compound was isolated as a single diastereomer as judged by ^{1}H NMR analysis (the crude reaction mixture contained a 5:1 mixture of diastereomers). Data are for the major diastereomer. ^{1}H NMR (400 MHz, C_6D_6, 75 °C) δ 7.67 (d, *J* = 6.8 Hz, 2 H), 7.66 (d, *J* = 8.0 Hz, 2 H), 7.31 (d, *J* = 7.6 Hz, 2 H), 7.15–7.11 (m, 4 H), 7.07–7.04 (m, 4 H), 3.89–3.79 (m, 2 H), 3.72–3.67 (m, 1 H), 2.81 (dd, *J* = 7.2, 14.0 Hz, 1 H), 2.79–2.71 (m, 1 H), 2.61 (dd, *J* = 5.2, 14.0 Hz, 1 H), 2.30–2.26 (m, 1 H), 2.07–2.00 (m, 1 H), 0.73 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, C_6D_6, 75 °C) δ 194.8, 143.1, 138.4, 137.7, 136.0, 131.3, 129.7, 129.5, 129.1, 128.8, 127.9, 126.8, 84.5, 62.8, 62.6, 42.1, 40.0, 16.8 (two aromatic signals are incidentally equivalent); IR (film) 2960, 1652, 1278 cm^{-1}. Anal calcd for $C_{25}H_{25}NO_2$: C, 80.83; H, 6.78; N, 3.77. Found: C, 80.64; H, 6.77; N, 3.71.

(±)-(4*R*,5*S*)-8-(*N*-Benzyl-4-methylisoxazolidin-5-ylmethyl)isoquinoline (13). Reaction of 48 mg (0.25 mmol) of **5** with 4-bromoisoquinoline (62 mg, 0.30 mmol) following the general procedure afforded 56 mg (70%) of the title compound as a pale yellow oil. This compound was isolated as a 3:1 mixture of diastereomers as judged by ^{1}H NMR analysis (the crude reaction mixture contained a 3:1 mixture of diastereomers). Data are for the major diastereomer. ^{1}H NMR (400 MHz, C_6D_6, 75 °C) δ 9.13–9.01 (m, 1 H), 8.62–8.50 (m, 1 H), 7.82 (d, *J* = 8.4 Hz, 1 H), 7.48 (d, *J* = 7.2 Hz, 1 H), 7.29–7.23 (m, 2 H), 7.17–7.03 (m, 5 H), 3.86–3.81 (m, 1 H), 3.81–3.78 (m, 2 H), 3.19 (dd, *J* = 6.8, 14.2 Hz, 1 H), 2.92 (dd, *J* = 5.6, 14.2 Hz, 1 H), 2.80–2.70 (m, 1 H), 2.22–2.17 (m, 1 H), 2.16–2.09 (m, 1 H), 0.62 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (100 MHz, C_6D_6, 75 °C) δ 152.4, 145.2, 138.6, 135.8, 130.1, 130.0, 129.8, 128.8, 128.5, 127.7, 126.9, 124.1, 85.2, 63.7, 63.6, 43.2, 35.2, 17.6 (two aromatic signals are incidentally equivalent); IR (film) 2960, 1455 cm^{-1}. Anal calcd for $C_{20}H_{21}N_2O$: C, 79.20; H, 6.96; N, 8.80. Found: C, 78.80; H, 7.00; N, 8.65.

(±)-(4*R*,5*S*)-*N*-Benzyl-5-benzyl-4-methylisoxazolidine (14). The reaction of 48 mg (0.25 mmol) of **5** with bromobenzene (47 mg, 0.30 mmol) following the general procedure afforded 38 mg (57%) of the title compound as a pale yellow oil. This compound was isolated as a single diastereomer as judged by ^{1}H NMR analysis (the crude reaction mixture contained a 3:1 mixture of diastereomers). Data are for the major diastereomer. ^{1}H NMR (400 MHz, C_6D_6, 75 °C) δ 7.32 (d, *J* = 7.6 Hz, 2 H), 7.15–7.05 (m, 7 H), 7.03–6.99 (m, 1 H), 3.91–3.87 (m, 1 H), 3.82–3.79 (m, 1 H), 3.73 (q, *J* = 6.0 Hz, 1 H), 2.88 (dd, *J* = 6.4, 13.8 Hz, 1 H), 2.79–2.70 (m, 1 H), 2.64 (dd, *J* = 6.0, 13.8 Hz, 1 H), 2.34–2.26 (m, 1 H), 2.10–2.03 (m, 1 H), 0.69 (d, *J* = 6.8

Hz, 3 H); ^{13}C NMR (100 MHz, C_6D_6, 75 °C) δ 139.0, 138.4, 129.7, 129.3, 128.4, 128.3, 127.2, 126.4, 85.5, 63.3, 63.2, 42.4, 40.7, 17.3; IR (film) 2957, 1452 cm^{-1}. Anal calcd for $C_{18}H_{21}NO$: C, 80.86; H, 7.92; N, 5.24. Found: C, 80.66; H, 7.85; N, 5.26.

(±)-(3*R*,5*R*)-3-(*N*-Benzyl-3-phenylisoxazolidin-5-ylmethyl)-pyridine (15). Reaction of 61 mg (0.25 mmol) of **6** with 3-bromopyridine (47 mg, 0.30 mmol) following the general procedure afforded 63 mg (80%) of the title compound as a pale yellow oil. This compound was isolated as a 3:1 mixture of diastereomers as judged by ^{1}H NMR analysis (the crude reaction mixture contained a 3:1 mixture of diastereomers). Data are for the major diastereomer. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.42–8.41 (m, 2 H), 7.44–7.42 (m, 2 H), 7.39–7.26 (m, 9 H), 7.07–7.04 (m, 1 H), 4.35–4.32 (m, 1 H), 3.97 (d, *J* = 14.0 Hz, 1 H), 3.86 (t, *J* = 8.0 Hz, 1 H), 3.72 (d, *J* = 14.0 Hz, 1 H), 3.14 (dd, *J* = 8.5, 13.75 Hz, 1 H), 2.86–2.80 (m, 1 H), 2.75 (dd, *J* = 4.5, 13.75 Hz, 1 H), 2.12–2.07 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 147.6, 139.7, 137.8, 137.2, 134.1, 128.8, 128.6, 128.0, 127.7, 127.6, 127.4, 123.1, 77.1, 70.6, 59.8, 45.1, 39.0; IR (film) 3028, 1423 cm^{-1}. MS (ESI) 331.1810 (331.1810 calcd for $C_{22}H_{23}N_2O$, M + H$^+$).

(±)-(3*R*,5*R*)-*N*-Benzyl-5-(*N*-benzyl-3-phenylisoxazolidin-5-ylmethyl)-1-*H*-indole (16). Reaction of 61 mg (0.25 mmol) of **6** with *N*-benzyl-5-bromo-1-*H*-indole (86 mg, 0.30 mmol) following the general procedure afforded 81 mg (82%) of the title compound as a pale yellow oil. This compound was isolated as a 3:1 mixture of diastereomers as judged by ^{1}H NMR analysis (the crude reaction mixture contained a 3:1 mixture of diastereomers). Data are for the major diastereomer. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.5 Hz, 2 H), 7.43 (d, *J* = 7.0 Hz, 4 H), 7.39–7.37 (m, 2 H), 7.36–7.26 (m, 5 H), 7.18–7.10 (m, 5 H), 7.00–6.98 (m, 1 H), 6.47 (d, *J* = 4.0 Hz, 1 H), 5.30 (s, 2 H), 4.49 (p, *J* = 6.5 Hz, 1 H), 4.02 (d, *J* = 14.5 Hz, 1 H), 3.93 (t, *J* = 8.5 Hz, 1 H), 3.86 (d, *J* = 14.0 Hz, 1 H), 3.31 (dd, *J* = 6.0, 13.75 Hz, 1 H), 2.90 (dd, *J* = 7.0, 13.75 Hz, 1 H), 2.74 (dt, 7.0, 12.5 Hz, 1 H), 2.23–2.17 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.5, 138.0, 137.5, 135.1, 129.5, 128.8, 128.6, 128.5, 128.4, 128.3, 128.0, 127.5, 127.48, 127.41, 126.8, 126.7, 123.4, 121.2, 109.3, 101.3, 78.5, 70.5, 60.1, 50.0, 45.1, 41.8; IR (film) 3028, 1453 cm^{-1}. Anal calcd for $C_{31}H_{30}N_2O$: C, 83.81; H, 6.59; N, 6.11. Found: C, 84.08; H, 6.61; N, 6.10.

(±)-(3*R*,5*R*)-5-Biphenyl-4-ylmethyl-2-*tert*-butyl-3-phenylisoxazolidine (17). Reaction of 55 mg (0.25 mmol) of **7** with 4-bromobiphenyl (70 mg, 0.30 mmol) following the general procedure afforded 62 mg (67%) of the title compound as a pale yellow oil. This compound was isolated as a 3:1 mixture of diastereomers as judged by ^{1}H NMR analysis (the crude reaction mixture contained a 3:1 mixture of diastereomers). Data are for the major diastereomer. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.5 Hz, 2 H), 7.54–7.43 (m, 6 H), 7.36–7.31 (m, 5 H), 7.28–7.20 (m, 1 H), 4.37–4.31 (m, 2 H), 3.19 (dd, *J* = 6.5, 13.5 Hz, 1 H), 2.80 (dd, *J* = 6.5, 13.5 Hz, 1 H), 2.67–2.63 (m, 1 H), 2.14–2.10 (m, 1 H), 1.10 (s, 9 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.0, 140.9, 139.1, 137.6, 129.7, 129.5, 128.6, 128.3, 128.2, 127.0, 126.9, 126.7, 79.5, 63.6, 60.1, 48.7, 40.0, 26.1; IR (film) 2971, 1487 cm^{-1}. MS (ESI) 372.2322 (372.2327 calcd for $C_{26}H_{29}NONa$, M + Na$^+$).

(±)-(2*R*,3a*S*)-2-(2-Methylbenzyl)hexahydropyrrolo[1,2-*b*]isoxazole (18). Reaction of 32 mg (0.25 mmol) of **8** with 2-bromotoluene (51 mg, 0.30 mmol) following the general procedure afforded 45 mg (83%) of the title compound as a pale yellow oil. This compound was isolated as a single diastereomer as judged by ^{1}H NMR analysis (the crude mixture contained a 10:1 mixture of diastereomers). Data are for the major diastereomer. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19–7.17 (m, 1 H), 7.13–7.11 (m, 3 H), 4.28 (p, *J* = 6.0 Hz, 1 H), 3.80–3.75 (m, 1 H), 3.14 (t, *J* = 6.5 Hz, 2 H), 3.04 (dd, *J* = 6.0, 14.0 Hz, 1 H), 2.76 (dd, *J* = 6.5, 14.0 Hz, 1 H), 2.33 (s, 3 H), 2.22 (dt, *J* = 8.0, 12.0 Hz, 1 H), 2.02–1.98 (m, 1 H), 1.97–1.95 (m, 1 H), 1.92–1.85 (m, 1 H), 1.72–1.65 (m, 1 H), 1.53–1.47 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.7, 136.3, 130.1, 129.7, 126.3, 125.9, 76.5, 64.9, 57.1, 42.2, 37.4, 31.6, 24.3, 19.6; IR (film) 2959, 1457 cm^{-1}. Anal calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45. Found:

C, 77.08; H, 8.71; N, 6.29.

(±)-(2*R*,3a*S*)-2-Pyridin-3-ylmethylhexahydropyrrolo[1,2-*b*]isoxazole (19). Reaction of 32 mg (0.25 mmol) of **8** with 3-bromopyridine (47 mg, 0.30 mmol) following the general procedure afforded 45 mg (88%) of the title compound as a pale yellow oil. This compound was isolated as a single diastereomer as judged by ^{1}H NMR analysis of the crude reaction mixture (the crude mixture contained a 10:1 mixture of diastereomers). Data are for the major diastereomer. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.46–8.44 (m, 2 H), 7.58–7.56 (m, 1 H), 7.21–7.18 (m, 1 H), 4.23 (p, *J* = 7.0 Hz, 1 H), 3.73–3.69 (m, 1 H), 3.11 (t, *J* = 6.5 Hz, 2 H), 2.94 (dd, *J* = 7.0, 14.0 Hz, 1 H), 2.76 (dd, *J* = 5.5, 14.0 Hz, 1 H), 2.16 (dt, *J* = 7.5, 12.5 Hz, 1 H), 2.04–2.00 (m, 1 H), 1.98–1.93 (m, 1 H), 1.88–1.80 (m, 1 H), 1.69–1.62 (m, 1 H), 1.52–1.47 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) 150.3, 147.8, 136.8, 133.9, 123.2, 76.8, 64.9, 57.1, 42.1, 37.4, 31.5, 24.2; IR (film) 2945, 1423 cm^{-1}. MS (ESI) 205.1334 (205.1341 calcd for $C_{12}H_{16}N_2ONa$, M + Na^+).

(±)-(2*R*,3a*S*)-2-(3-Methoxybenzyl)hexahydroisoxazolo[2,3-*a*]pyridine (20). Reaction of 35 mg (0.25 mmol) of **9** with 3-bromoanisole (56 mg, 0.30 mmol) following the general procedure afforded 57 mg (92%) of the title compound as a pale yellow oil. This compound was isolated as a 19:1 mixture of diastereomers as judged by ^{1}H NMR analysis (the crude mixture contained a 9:1 mixture of diastereomers). Data are for the major diastereomer. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (t, *J* = 7.5 Hz, 1 H), 6.81 (d, *J* = 8.0 Hz, 1 H), 6.78 (s, 1 H), 6.75–6.73 (m, 1 H), 4.25 (p, *J* = 7.0 Hz, 1 H), 3.78 (s, 3 H), 3.44–3.42 (m, 1 H), 3.09 (dd, *J* = 7.5, 13.5 Hz, 1 H), 2.71 (dd, *J* = 7.0, 13.5 Hz, 1 H), 2.45–2.40 (m, 1 H), 2.31–2.26 (m, 1 H), 2.24–2.18 (m, 1 H), 1.93–1.90 (m, 1 H), 1.80–1.77 (m, 1 H), 1.74–1.65 (m, 3 H), 1.43–1.35 (m, 1 H), 1.24–1.17 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.4, 140.3, 129.2, 121.4, 114.9, 111.3, 76.7, 67.3, 55.2, 55.0, 43.0, 41.0, 29.1, 24.7, 23.6; IR (film) 2937, 1489 cm^{-1}. Anal calcd for $C_{15}H_{21}NO_2$: C, 72.84; H, 8.56; N, 5.66. Found: C, 72.46; H, 8.65; N, 5.66.

(±)-(2*R*,3a*S*)-2-(4-Chlorobenzyl)hexahydroisoxazolo[2,3-*a*]pyridine (21). Reaction of 35 mg (0.25 mmol) of **9** with 4-bromochlorobenzene (57 mg, 0.30 mmol) following the general procedure afforded 57 mg (91%) of the title compound as a pale yellow oil. This compound was isolated as a single diastereomer as judged by ^{1}H NMR analysis (the crude mixture contained a 9:1 mixture of diastereomers). Data are for the major diastereomer. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.0 Hz, 2 H), 7.15 (d, *J* = 8.5 Hz, 2 H), 4.20 (p, *J* = 6.5 Hz, 1 H), 3.43–3.41 (m, 1 H), 3.05 (dd, *J* = 7.5, 13.5 Hz, 1 H), 2.68 (dd, *J* = 6.0, 13.5 Hz, 1 H), 2.44–2.39 (m, 1 H), 2.33–2.28 (m, 1 H), 2.21–2.18 (m, 1 H), 1.93–1.90 (m, 1 H), 1.80–1.77 (m, 1 H), 1.73–1.63 (3 H), 1.39–1.36 (m, 1 H), 1.22–1.18 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.4, 131.9, 130.4, 128.3, 76.5, 67.3, 55.2, 42.2, 41.0, 29.1, 24.7, 23.6; IR (film) 2937, 1489 cm^{-1}. Anal calcd for $C_{14}H_{18}NOCl$: C, 66.79; H, 7.21; N, 5.56. Found: C, 66.70; H, 7.36; N, 5.37.

(±)-(3a*R*,6*S*,6a*R*)-6-Biphenyl-4-yl-*N*-methylhexahydrocyclopenta[*d*]isoxazole (22). Reaction of 32 mg (0.25 mmol) of **10** with 4-bromobiphenyl (70 mg, 0.30 mmol) following the general procedure using $Pd_2(dba)_3$ (1 mol %, 2 mol % Pd) in toluene at 110 ºC, afforded 54 mg (77%) of the title compound as a pale yellow oil. This compound was isolated as a single diastereomer as judged by ^{1}H NMR analysis (the product was determined to have formed with >20:1 dr based on ^{1}H NMR analysis of the crude reaction mixture). The NMR spectra acquired at room temperature showed a 1:1 mixture of conformational isomers, but the signals for the two isomers coalesced when the NMR spectra were acquired at 75 °C. ^{1}H NMR (500 MHz, $CDCl_3$, 22ºC) δ 7.60 (d, *J* = 8.5 Hz, 2 H), 7.54 (d, *J* = 8.5 Hz, 2 H), 7.45–7.42 (m, 4 H), 7.33 (t, *J* = 7.0 Hz, 1 H), 4.78–4.75 (m, 0.5 H), 4.63–4.61 (m, 0.5 H), 3.62–3.58 (m, 0.5 H), 3.28–3.19 (m, 1 H), 3.03–2.92 (m, 2 H), 2.68 (s, 1.5 H), 2.61 (s, 1.5 H), 2.22–2.16 (m, 1 H), 2.06–2.03 (m, 0.5 H), 1.96–1.91 (m, 1 H), 1.85–1.81 (m, 0.5 H), 1.76–1.71 (m, 1.5 H); ^{1}H

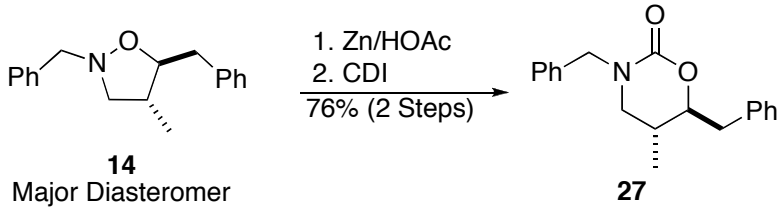
NMR (400 MHz, C_6D_6, 75ºC) δ 7.44–7.41 (m, 4 H), 7.35 (d, *J* = 8.0 Hz, 2 H), 7.12 (t, *J* = 7.6 Hz, 2 H), 7.04 (t, *J* = 7.2 Hz, 1 H), 4.42 (t, *J* = 5.2 Hz, 1 H), 2.73–2.64 (m, 1 H), 2.57 (dt, *J* = 5.2, 13.2 Hz, 1 H), 2.36 (s, 3 H), 2.15–2.10 (m, 2 H), 1.70–1.64 (m, 1 H), 1.38–1.36 (m, 3 H);^{13}C NMR (125 MHz, $CDCl_3$, 22ºC) δ 141.2, 139.1, 139.0, 138.6, 129.2, 128.9, 128.6, 127.0, 126.9, 126.8, 126.7, 84.8, 83.8, 65.8, 64.6, 50.9, 49.7, 47.5, 46.4, 44.7, 44.5, 31.0, 29.7, 28.3; IR (film) 2951, 1487 cm^{-1}. Anal calcd for $C_{19}H_{21}NO$: C, 81.68; H, 7.58; N, 5.01. Found: C, 81.62; H, 7.60; N, 5.02.

(±)-(3a*R*,6*S*,6a*R*)-*N*-Methyl-6-(3-trifluoromethylphenyl)hexahydrocyclopenta[*d*]isoxazole (23). Reaction of 32 mg (0.25 mmol) of **10** with 3-bromobenzotrifluoride (68 mg, 0.30 mmol) following the general procedure using $Pd_2(dba)_3$ (1 mol %, 2 mol % Pd) in toluene at 110 ºC, afforded 48 mg (71%) of the title compound as a pale yellow oil. This compound was isolated as a single diastereomer as judged by ^{1}H NMR analysis (the product was determined to have formed with >20:1 dr based on ^{1}H NMR analysis of the crude reaction mixture). The NMR spectra acquired at room temperature showed a 1:1 mixture of conformational isomers, but the signals for the two isomers coalesced when the NMR spectra were acquired at 75 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61–7.58 (m, 1 H), 7.53 (d, *J* = 7.5 Hz, 1 H), 7.46 (d, *J* = 8.0 Hz, 1 H), 7.39 (t, *J* = 8.0 Hz, 1 H), 4.68–4.66 (m, 0.5 H), 4.58–4.55 (m, 0.5 H), 3.60–3.56 (m, 0.5 H), 3.25–3.18 (m, 1 H), 2.97–2.89 (m, 2 H), 2.63 (s, 1.5 H), 2.58 (s, 1.5 H), 2.19–2.10 (m, 1 H), 2.02–1.94 (m, 0.5 H), 1.94–1.90 (m, 1 H), 1.89–1.77 (m, 0.5 H), 1.77–1.71 (m, 1.5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.0, 140.5, 132.4, 132.0, 128.3, 128.2, 125.9, 125.4, 123.1, 84.4, 83.7, 65.7, 65.0, 51.3, 49.7, 47.6, 46.8, 44.7, 44.4, 31.3, 30.5, 29.6, 28.3; IR (film) 2956, 1449 cm^{-1}. Anal calcd for $C_{14}H_{16}NOF_3$: C, 61.98; H, 5.94; N, 5.16. Found: C, 62.01; H, 6.08; N, 5.14.

Assignment of Stereochemistry

3,4-Disubstituted Isoxazolidines **12**–**14**

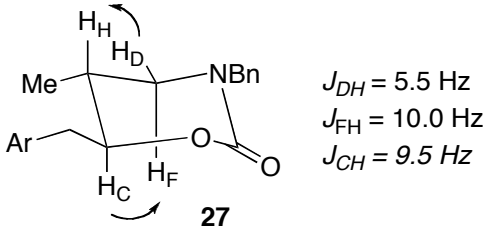
Isoxazolidine **14** was converted to cyclic carbamate **27** using the sequence shown below.



14
Major Diasteromer

27

The relative stereochemistry of **27** was assigned based on the nOe signals and coupling constants depicted below:



27

The relative stereochemistry of isoxazolidines **12** and **13** were assigned based on analogy to **14.**

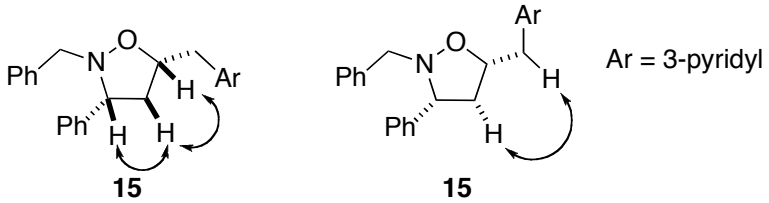
(±)-(5*R*,6*S*)-3,6-Dibenzyl-5-methyl-[1,3]-oxazinan-2-one (27). A flame-dried Schlenk tube was cooled under a stream of argon and charged with **14** (71 mg, 0.26 mmol), zinc dust (169 mg, 2.6 mmol), and acetic acid (1.2 mL). The resulting suspension was stirred at rt for 8 h. The reaction mixture was diluted with CH_2Cl_2 (10 mL) and basified by the addition of aqueous Na_2CO_3 (10 mL). The aqueous layer was removed and extracted with CH_2Cl_2 (2 X 10 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated *in vacuo* to afford 51 mg (73%) of (±)-(2*S*,3*R*)-4-

benzylamino-3-methyl-1-phenylbutan-2-ol. The crude material was used without further purification. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.26 (m, 9 H), 7.25–7.19 (m, 1 H), 4.20 (s, br, 2 H), 3.79–3.75 (m, 1 H), 3.77–3.75 (m, 1 H), 3.74–3.71 (m, 1 H), 2.92 (td, *J* = 3.5, 13.5 Hz, 2 H), 2.69–2.63 (m, 2 H), 1.67–1.62 (m, 1 H), 0.95 (d, *J* = 7.0 Hz, 3 H).

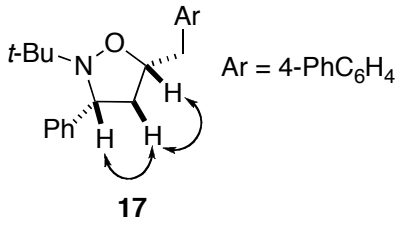
A flame-dried Schlenk tube was cooled under a stream of argon and charged with (±)-(2*S*,3*R*)-4-benzylamino-3-methyl-1-phenylbutan-2-ol (51 mg, 0.18 mmol), carbonyldiimidazole (44 mg, 0.27 mmol), and toluene (1.8 mL). The resulting solution was stirred at rt for 8 h. The mixture was concentrated *in vacuo* and purified by flash chromatography on silica gel to afford 42 mg (79%) of the title compound as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.25 (m, 10 H), 4.58–4.55 (m, 1 H), 4.53–4.50 (m, 1 H), 4.20–4.16 (m, 1 H), 3.12–3.07 (m, 2 H), 2.92–2.84 (m, 2 H), 1.93–1.86 (m, 1 H), 0.97 (d, *J* = 6.5 Hz, 3 H); ^{1}H NMR (500 MHz, $D_3CC(O)CD_3$) (Selected Peaks) δ 4.23 (ddd, *J* = 3.5, 7.5, 9.5 Hz, 1 H), 3.21 (dd, *J* = 5.5, 11.5 Hz, 1 H), 3.07 (dd, *J* = 3.5, 14.25 Hz, 1 H), 2.96 (dd, *J* = 10.0, 11.5 Hz, 1 H), 2.81 (dd, *J* = 7.5, 14.25 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) 153.7, 136.6, 136.3, 129.7, 128.6, 128.3, 128.0, 127.6, 126.6, 82.4, 52.3, 50.2, 38.5, 30.0, 14.4; IR (film) 2921, 1694, 1488 cm^{-1}. MS (ESI) 318.1458 (318.1470 calcd for $C_{19}H_{21}NONa$, M + Na^+).

3,5-Disubstituted Isoxazolidines **15**–**17**

The relative stereochemistry of isoxazolidine **15** was determined based on the nOe signals depicted below. The relative stereochemistry of compounds **16** was assigned based on analogy to **15**.

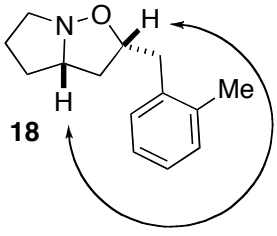


The relative stereochemistry of compound **17** was assigned based on the nOe signals shown below.



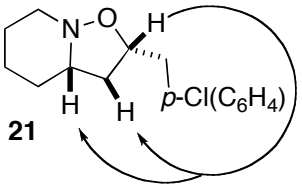
Hexahydropyrrolo[1,2-*b*]isoxazoles (**18** and **19**)

The relative stereochemistry of compound **18** was assigned based on the nOe signals depicted below. The relative stereochemistry of compound **19** was assigned based on analogy to compound **18**.



Hexahydroisoxazolo[2,3-*a*]pyridines (**20** and **21**)

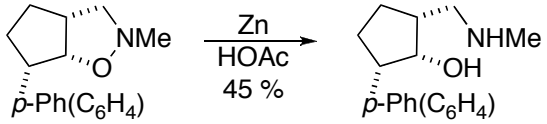
The relative stereochemistry of compound **21** was assigned based on the nOe signals depicted below. The relative stereochemistry of compound **20** was assigned based on analogy to compound **21**.



21

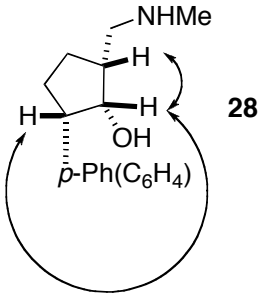
N-Methylhexahydrocyclopenta[*d*]isoxazoles (**22**and **23**)

Isoxazolidine **22** was converted to 1,3-amino alcohol **28** upon treatment with Zn and HOAc as shown below.



22 **28**

The relative stereochemistry of **28** was assigned based on the nOe signals depicted below.



28

The relative stereochemistry of compound **23** was assigned based on analogy to **22**.

(±)-(1*R*,2*S*,5*R*)-2-Biphenyl-4-yl-5-methylaminomethylcyclopentanol (28). A flame-dried Schlenk tube was cooled under a stream of argon and charged with **22** (55 mg, 0.19 mmol), zinc dust (123 mg, 1.9 mmol), and acetic acid (1.0 mL). The resulting suspension was stirred at rt for 8 h. The reaction mixture was diluted with CH_2Cl_2 (10 mL) and basified by the addition of aqueous Na_2CO_3 (10 mL). The aqueous layer was removed and extracted with CH_2Cl_2 (2 X 10 mL). The combined organic layers were dried over anhydrous sodium sulfate and concentrated *in vacuo* to afford 24 mg (45%) of the title compound. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59–7.52 (m, 4 H), 7.44–7.41 (m, 4 H), 7.34–7.32 (m, 1 H), 4.35 (t, *J* = 5.0 Hz, 1 H), 3.72 (s, br, 2 H), 3.15–3.09 (m, 1 H), 2.95 (dd, *J* = 9.5, 15.0 Hz, 1 H), 2.83–2.75 (m, 1 H), 2.42 (s, 3 H), 2.35–2.28 (m, 1 H), 2.26–2.17 (m, 1 H), 2.07–1.98 (m, 1 H), 1.92–1.85 (m, 1 H), 1.72–1.63 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.1, 139.7, 139.0, 128.9, 128.6, 127.0, 126.9, 126.8, 76.8, 52.1, 51.3, 43.4, 36.1, 27.5, 26.3; IR (film) 2934, 2361, 1457 cm^{-1}. MS (ESI) 282.1848 (282.1858 calcd for $C_{19}H_{24}NO$, M + H$^+$).

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