Supporting Information

Asymmetric 1,3-Dipolar Cycloaddition Reaction of Nitrones and Acrolein with a Bis-Titanium Catalyst as Chiral Lewis Acid

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General Information. Infrared (IR) spectra were recorded on a Shimadzu IRPrestige-21 spectrometer. ^1H NMR spectra were measured on a JEOL JNM-FX400 (400 MHz) spectrometer. Data were reported as follows: chemical shifts in ppm from tetramethylsilane as an internal standard, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = double-doublet, m = multiplet, br = broad), coupling constants (Hz), and assignment. ^{13}C NMR spectra were measured on a JEOL JNM-FX400 (100 MHz) spectrometer with complete proton decoupling. Chemical shifts were reported in ppm from the residual solvent as an internal standard. High performance liquid chromatography (HPLC) was performed on Shimadzu 10A instruments at 220 nm using 4.6 mm x 25 cm Daicel Chiralcel OD-H. High-resolution mass spectra (HRMS) were performed on Applied Biosystems Mariner 8295 API-TOF workstation. Optical rotations were measured on a JASCO DIP-1000 digital polarimeter. For thin layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF₂₅₄, 0.25 mm) were used. The products were purified by flash column chromatography on silica gel 60 (Merck 1.09386.9025, 230-400 mesh). CH_2Cl_2 was freshly distilled over CaH_2 and degassed before use. (Z)-N-benzylidenebenzylamine N-oxide, benzylhydroxylamine¹ and 2-methyl-1,3-dithian-2-carboxaldehyde² were prepared according to the literature procedures. Acrolein was freshly distilled before use. Other simple chemicals were purchased and used as such.

Preparation of Chiral Bis-Ti() Oxide (S,S)-1. To a stirred mixture of Ag_2O (0.10 mmol, 23.2 mg) in CH_2Cl_2 (1.0 mL) was added 1.0 M hexanes solution of $\text{ClTi}(\text{OPr}^i)_3$ (0.20 mmol, 200 mL) at room temperature. After stirring for 5 h at room temperature, a solution of (S)-BINOL (0.20 mmol, 57.2 mg) in CH_2Cl_2 (2.0 mL) was added to the mixture, which was then stirred for 2 h at room temperature to afford the dark orange colored solution of chiral bis-Ti() oxide (S,S)-1.

General Procedure. To the catalyst solution prepared as described above were added freshly distilled acrolein (1.5 mmol, 100 μ L) and a solution of nitron (1.0 mmol) in CH_2Cl_2 (1.0 mL) dropwise at $-40\text{ }^\circ\text{C}$. The reaction mixture was stirred at the same temperature until the completion of the reaction. The mixture was then treated with ethanol solution of NaBH_4 (2.0 mmol) and allowed to warm to $0\text{ }^\circ\text{C}$. After stirring for 30 min, the resulting mixture was treated with aqueous NH_4Cl , filtered to remove insoluble materials and extracted with CH_2Cl_2 . The combined organic layers were washed with 1N NaOH to remove (*S*)-BINOL, then dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate) to give the cycloadduct.

(3*S*,4*S*)-2-Benzyl-4-hydroxymethyl-3-phenylisoxazoline (Table 2, entry 1). The title compound was prepared according to the general procedure with (*Z*)-*N*-benzylidenebenzylamine *N*-oxide (211 mg, 1.0 mmol) over the course of 24 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 2:1) to give the cycloadduct as a colorless oil [94% yield (253 mg), *endo:exo* = >97:3, 93% ee (*endo*)].

The enantiomeric purity was determined by HPLC analysis (Daicel Chiralcel OD-H, hexane/2-propanol = 20:1, flow rate = 1.0 mL/min, retention time; 17.3 min (minor) and 20.0 min (major)).

^1H NMR (400 MHz, CDCl_3) δ 7.19-7.46 (10H, m, ArH), 4.17 (1H, dd, J = 8.4, 8.4 Hz, NOCHH), 3.93 (1H, d, J = 14.4 Hz, PhCHH), 3.88 (1H, dd, J = 4.4, 8.4 Hz, NOCHH), 3.69 (1H, d, 14.4 Hz, PhCHH), 3.65-3.74 (2H, m, CH_2OH), 3.46 (1H, d, J = 7.2 Hz, ONCH), 2.74 (1H, m, CHCH_2OH) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 139.2, 137.5, 128.6, 128.0, 127.9, 127.8, 127.0, 73.5, 69.1, 63.3, 60.0, 54.9 ppm; IR (neat) 3397, 3061, 3030, 2941, 2872, 1495, 1454, 1373, 1344, 1307, 1105, 1070, 1042, 1030, 1007, 972 cm^{-1} ; HRMS (ESI) exact mass calcd for $\text{C}_{17}\text{H}_{20}\text{NO}_2$: m/z 270.1489 ($[\text{M} + \text{H}]^+$), found: m/z 270.1492 ($[\text{M} + \text{H}]^+$); $[\alpha]_D^{31} = -84.9^\circ$ (c = 1.0, CHCl_3 ; 93% ee).

(3S,4S)-2-Benzyl-4-hydroxymethyl-3-(4-methylphenyl)isoxazoline (Table 2, entry 2). The title compound was prepared according to the general procedure with (*Z*)-*N*-(4-methylbenzylidene) benzylamine *N*-oxide (225 mg, 1.0 mmol) over the course of 24 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 2:1) to give the cycloadduct as a colorless oil [81% yield (230 mg), *endo:exo* = >97:3, 94% ee (*endo*)].

The enantiomeric purity was determined by HPLC analysis (Daicel Chiralcel OD-H, hexane/2-propanol = 20:1, flow rate = 1.0 mL/min, retention time; 14.4 min (minor) and 18.9 min (major)).

^1H NMR (400 MHz, CDCl_3) δ 7.16-7.36 (9H, m, ArH), 4.17 (1H, dd, J = 8.4, 8.4 Hz, NOCHH), 3.93 (1H, d, J = 14.4 Hz, PhCHH), 3.87 (1H, dd, J = 4.4, 8.4 Hz, NOCHH), 3.67 (1H, d, 14.0 Hz, PhCHH), 3.67-3.75 (2H, m, CH_2OH), 3.43 (1H, d, J = 7.6 Hz, ONCH), 2.74 (1H, m, CHCH_2OH), 2.35 (3H, s, $\text{C}_6\text{H}_4\text{CH}_3$) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 137.6, 137.5, 129.3, 128.6, 128.0, 127.8, 127.0, 73.3, 69.1, 63.4, 59.9, 54.8, 21.2 ppm; IR (neat) 3385, 3028, 2941, 2870, 1514, 1497, 1454, 1342, 1040, 1001, 802 cm^{-1} ; HRMS (ESI) exact mass calcd for $\text{C}_{18}\text{H}_{22}\text{NO}_2$: m/z 284.1645 ($[\text{M} + \text{H}]^+$), found: m/z 284.1646 ($[\text{M} + \text{H}]^+$); $[\alpha]_D^{30} = -82.0^\circ$ (c = 1.0, CHCl_3 ; 93% ee).

(3S,4S)-2-Benzyl-4-hydroxymethyl-3-(4-methoxyphenyl)isoxazoline (Table 2, entry 3).

The title compound was prepared according to the general procedure with (*Z*)-*N*-(4-methoxybenzylidene) benzylamine *N*-oxide (241 mg, 1.0 mmol) over the course of 40 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 2:1) to give the cycloadduct as a colorless oil [85% yield (255 mg), *endo:exo* = >97:3, 88% ee (*endo*)].

The enantiomeric purity was determined by HPLC analysis (Daicel Chiralcel OD-H, hexane/2-propanol = 20:1, flow rate = 1.0 mL/min, retention time; 23.5 min (minor) and 29.7

min (major)).

^1H NMR (400 MHz, CDCl_3) δ 6.88-7.37 (9H, m, ArH), 4.16 (1H, dd, $J = 8.4, 8.4$ Hz, NOCHH), 3.92 (1H, d, $J = 14.4$ Hz, PhCHH), 3.86 (1H, dd, $J = 4.8, 8.8$ Hz, NOCHH), 3.80 (3H, s, OCH₃), 3.65 (1H, d, $J = 14.4$ Hz, PhCHH), 3.62-3.73 (2H, m, CH₂OH), 3.41 (1H, d, $J = 7.6$ Hz, ONCH), 2.72 (1H, m, CHCH₂OH) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 159.2, 137.6, 130.9, 129.0, 128.6, 128.0, 127.0, 114.0, 73.0, 69.1, 63.3, 59.8, 55.3, 54.6 ppm; IR (neat) 3385, 3030, 2938, 2872, 2835, 1610, 1512, 1454, 1302, 1175, 1031, 829 cm^{-1} ; HRMS (ESI) exact mass calcd for $\text{C}_{18}\text{H}_{22}\text{NO}_3$: m/z 300.1594 ($[\text{M} + \text{H}]^+$), found: m/z 300.1954 ($[\text{M} + \text{H}]^+$); $[\alpha]_{\text{D}}^{31} = -76.2^\circ$ ($c = 1.0$, CHCl_3 ; 88% ee).

(3*S*,4*S*)-2-Benzyl-3-(4-chlorophenyl)-4-hydroxymethylisoxazoline (Table 2, entry 4). The title compound was prepared according to the general procedure with (*Z*)-*N*-(4-chlorobenzylidene) benzylamine *N*-oxide (246 mg, 1.0 mmol) over the course of 39 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 2:1) to give the cycloadduct as a colorless oil [76% yield (232 mg), *endo:exo* = >97:3, 88% ee (*endo*)].

The enantiomeric purity was determined by HPLC analysis (Daicel Chiralcel OD-H, hexane/2-propanol = 20:1, flow rate = 1.0 mL/min, retention time; 17.4 min (minor) and 19.7 min (major)).

^1H NMR (400 MHz, CDCl_3) δ 7.20-7.40 (9H, m, ArH), 4.16 (1H, dd, $J = 8.0, 8.4$ Hz, NOCHH), 3.90 (1H, d, $J = 14.0$ Hz, PhCHH), 3.87 (1H, dd, $J = 4.4, 8.8$ Hz, NOCHH), 3.72 (1H, d, 14.4 Hz, PhCHH), 3.68-3.78 (2H, m, CH₂OH), 3.49 (1H, d, $J = 7.6$ Hz, ONCH), 2.70 (1H, m, CHCH₂OH) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 138.1, 137.3, 133.5, 129.2, 128.8, 128.6, 128.1, 127.1, 72.8, 69.0, 63.2, 60.0, 55.0 ppm; IR (neat) 3391, 3030, 2926, 2872, 1493, 1454, 1410, 1371, 1090, 1041, 1015, 856, 823 cm^{-1} ; HRMS (ESI) exact mass calcd for $\text{C}_{17}\text{H}_{19}\text{ClNO}_2$: m/z 304.1099 ($[\text{M} + \text{H}]^+$), found: m/z 304.1099 ($[\text{M} + \text{H}]^+$); $[\alpha]_{\text{D}}^{30} = -70.5^\circ$ ($c = 1.0$, CHCl_3 ; 88% ee).

(3S,4S)-2-Benzyl-4-hydroxymethyl-3-(2-naphthyl)isoxazoline (Table 2, entry 5). The title compound was prepared according to the general procedure with (Z)-N-(2-naphthyl)methylidene benzylamine N-oxide (261 mg, 1.0 mmol) over the course of 24 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 2:1) to give the cycloadduct as a colorless oil [92% yield (292 mg), *endo:exo* = >97:3, 93% ee (*endo*)].

The enantiomeric purity was determined by HPLC analysis (Daicel Chiralcel OD-H, hexane/2-propanol = 20:1, flow rate = 1.0 mL/min, retention time; 27.0 min (minor) and 52.7 min (major)).

^1H NMR (400 MHz, CDCl_3) δ 7.17-7.85 (12H, m, ArH), 4.21 (1H, dd, J = 8.4, 8.0 Hz, NOCHH), 3.96 (1H, d, J = 14.0 Hz, PhCHH), 3.91 (1H, dd, J = 4.8, 8.8 Hz, NOCHH), 3.73 (1H, d, 14.8 Hz, PhCHH), 3.66-3.74 (2H, m, CH_2OH), 3.63 (1H, d, J = 7.6 Hz, ONCH), 2.82 (1H, m, CHCH_2OH) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 137.5, 136.7, 133.2, 133.0, 128.7, 128.5, 128.0, 127.7, 127.6, 127.2, 127.0, 126.1, 125.9, 125.4, 73.6, 69.2, 63.2, 60.1, 54.8 ppm; IR (neat) 3383, 3057, 3030, 2939, 2872, 1506, 1497, 1454, 1373, 1313, 1030, 1005, 856, 820 cm^{-1} ; HRMS (ESI) exact mass calcd for $\text{C}_{21}\text{H}_{22}\text{NO}_2$: m/z 320.1645 ($[\text{M} + \text{H}]^+$), found: m/z 320.1644 ($[\text{M} + \text{H}]^+$); $[\alpha]_D^{29} = -53.7^\circ$ (c = 1.0, CHCl_3 ; 93% ee).

(3S,4S)-2-Benzyl-3-(tert-butyl)-4-hydroxymethylisoxazoline (Table 2, entry 6). The title compound was prepared according to the general procedure with (Z)-N-tert-butylmethylidenebenzylamine N-oxide (191 mg, 1.0 mmol) over the course of 14 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 2:1) to give the cycloadduct as a white solid [90% yield (224 mg), *endo:exo* = >97:3, 97% ee (*endo*)].

The enantiomeric purity was determined by HPLC analysis (Daicel Chiralcel OD-H, hexane/2-propanol = 20:1, flow rate = 1.0 mL/min, retention time; 10.0 min (minor) and 13.5

min (major)).

^1H NMR (400 MHz, CDCl_3) δ 7.22-7.41 (5H, m, ArH), 4.05 (1H, d, $J = 13.6$ Hz, PhCHH), 3.98 (2H, d, $J = 6.4$ Hz, CH_2OH), 3.91 (1H, d, $J = 13.6$ Hz, PhCHH), 3.80 (1H, m, NOCHH), 3.70 (1H, m, NOCHH), 2.65 (1H, m, CHCH $_2$ OH), 2.45 (1H, d, $J = 4.4$ Hz, ONCH), 0.90 (9H, s, *t*-Bu) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 137.9, 129.0, 128.1, 127.0, 75.6, 69.1, 64.8, 62.3, 48.0, 34.3, 26.6 ppm; IR (neat) 3420, 2953, 2868, 1476, 1454, 1395, 1362, 1074, 1045, 999 cm^{-1} ; HRMS (ESI) exact mass calcd for $\text{C}_{15}\text{H}_{24}\text{NO}_2$: m/z 250.1802 ($[\text{M} + \text{H}]^+$), found: m/z 250.1802 ($[\text{M} + \text{H}]^+$); $[\alpha]_{\text{D}}^{30} = -63.5^\circ$ ($c = 1.0$, CHCl_3 ; 97% ee).

(3R,4S)-2-Benzyl-3-cyclohexyl-4-hydroxymethylisoxazoline (Table 2, entry 7). The title compound was prepared according to the general procedure with (*Z*)-*N*-cyclohexylmethylidenebenzylamine *N*-oxide (217 mg, 1.0 mmol) over the course of 24 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 2:1) to give the cycloadduct as a white solid [52% yield (142 mg), *endo:exo* = >97:3, 70% ee (*endo*)].

The enantiomeric excess was determined by HPLC analysis (Daicel Chiralcel OD-H, hexane/2-propanol = 20:1, flow rate = 0.5 mL/min, retention time; 22.5 min (minor) and 31.8 min (major)).

^1H NMR (400 MHz, CDCl_3) δ 7.22-7.39 (5H, m, ArH), 3.94 (2H, s, PhCH $_2$), 3.90 (2H, d, $J = 6.0$ Hz, CH_2OH), 3.70 (1H, dd, $J = 5.2, 10.4$ Hz, NOCHH), 3.62 (1H, dd, $J = 8.4, 10.4$ Hz, NOCHH), 2.57 (1H, m, CHCH $_2$ OH), 2.40 (1H, dd, $J = 4.4, 6.4$ Hz, ONCH), 0.90-1.83 (11H, m, *c*-Hex) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 137.8, 128.9, 128.1, 127.1, 72.4, 68.8, 64.7, 61.8, 49.1, 41.7, 30.6, 29.3, 26.7, 26.4, 26.3 ppm; IR (neat) 3385, 2922, 2851, 1497, 1450, 1339, 1055, 1030, 993, 966, 750, 729, 696 cm^{-1} ; HRMS (ESI) exact mass calcd for $\text{C}_{17}\text{H}_{26}\text{NO}_2$: m/z 276.1958 ($[\text{M} + \text{H}]^+$), found: m/z 276.1957 ($[\text{M} + \text{H}]^+$); $[\alpha]_{\text{D}}^{29} = -46.4^\circ$ ($c = 1.0$, CHCl_3 ; 70% ee).

(3*S*,4*S*)-2-Benzyl-4-hydroxymethyl-3-(2-methyl-1,3-dithian-2-yl)isoxazoline (Table 2, entry 8). The title compound was prepared according to the general procedure with (*Z*)-*N*-(2-methyl-1,3-dithian-2-yl)methylidenebenzylamine *N*-oxide (267 mg, 1.0 mmol) over the course of 24 h. The crude material was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 2:1) to give the cycloadduct as a colorless oil [86% yield (280 mg), *endo:exo* = >97:3, 97% ee (*endo*)].

The enantiomeric purity was determined by HPLC analysis (Daicel Chiralcel OD-H, hexane/2-propanol = 20:1, flow rate = 1.0 mL/min, retention time; 21.8 min (minor) and 29.7 min (major)).

¹H NMR (400 MHz, CDCl₃) δ 7.22-7.44 (5H, m, ArH), 4.13 (2H, s, C₆H₅CH₂), 4.04 (2H, m, CH₂OH), 3.83 (1H, dd, *J* = 10.4, 5.6 Hz, NOCHH), 3.77 (1H, dd, *J* = 10.4, 6.8 Hz, NOCHH), 3.41 (1H, d, *J* = 4.0 Hz, ONCH), 2.59-3.00 (5H, m, SCH₂CHCH₂S, CHCH₂OH), 1.90 (2H, m, SCH₂CH₂CH₂S), 1.58 (3H, s, CH₃) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 137.3, 129.2, 128.0, 127.1, 71.8, 69.0, 63.7, 61.7, 52.2, 48.9, 26.3, 26.0, 24.7, 24.1 ppm; IR (neat) 3419, 2926, 2870, 1748, 1454, 1418, 1373, 1061, 1028, 908, 730, 696 cm⁻¹; HRMS (ESI) exact mass calcd for C₁₆H₂₄NO₂S₂: *m/z* 326.1243 ([M + H]⁺), found: *m/z* 326.1244 ([M + H]⁺); [α]_D²⁹ = -29.4° (*c* = 1.0, CHCl₃; 97% ee).

General Procedure for the Syntheses of (*Z*)-*N*-Alkylidenebenzylamine *N*-Oxide and (*Z*)-*N*-Arylidenebenzylamine *N*-Oxide. To a solution of benzyldhydroxylamine was added 1.5 equiv of aldehyde at room temperature. After stirring for 3 h, the mixture was concentrated *in vacuo* and the residue was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate/CH₂Cl₂ = 5:5:2) to give the corresponding nitron.

(*Z*)-*N*-(4-Methylbenzylidene)benzylamine *N*-Oxide. ¹H NMR (400 MHz, CDCl₃) δ 8.10 (2H, d, *J* = 8.4 Hz, ArH), 7.38-7.49 (5H, m, ArH), 7.34 (1H, s, N=CH), 7.20 (2H, d, *J* = 8.0 Hz, ArH), 5.04 (2H, s, PhCH₂), 2.36 (3H, s, ArCH₃) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 140.8, 134.2, 133.2, 129.1, 128.8, 128.5, 127.7, 71.0, 21.7 ppm; IR (neat) 3066, 3032, 1609,

1497, 1458, 1431, 1180, 1146, 939, 849, 829 cm^{-1} ; HRMS (ESI) exact mass calcd for $\text{C}_{15}\text{H}_{16}\text{NO}$: m/z 226.1226 ($[\text{M} + \text{H}]^+$), found: m/z 226.1224 ($[\text{M} + \text{H}]^+$).

(Z)-N-(4-Methoxybenzylidene)benzylamine N-Oxide. ^1H NMR (400 MHz, CDCl_3) δ 8.20 (2H, d, $J = 8.8$ Hz, ArH), 7.37-7.48 (5H, m, ArH), 7.31 (1H, s, N=CH), 5.02 (2H, s, PhCH₂), 3.83 (3H, s, OCH₃) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 160.9, 133.7, 133.3, 130.4, 129.1, 128.8, 128.7, 123.3, 113.7, 70.7, 55.3 ppm; IR (neat) 3065, 2979, 2939, 1603, 1566, 1506, 1458, 1321, 1252, 1200, 1173, 1146, 1023, 937, 841, 829 cm^{-1} ; HRMS (ESI) exact mass calcd for $\text{C}_{15}\text{H}_{16}\text{NO}_2$: m/z 242.1176 ($[\text{M} + \text{H}]^+$), found: m/z 242.1175 ($[\text{M} + \text{H}]^+$).

(Z)-N-(4-Chlorobenzylidene)benzylamine N-Oxide. ^1H NMR (400 MHz, CDCl_3) δ 8.16 (2H, d, $J = 8.8$ Hz, ArH), 7.25-7.48 (8H, m, ArH, N=CH), 5.05 (2H, s, PhCH₂) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 135.7, 132.9, 129.6, 129.2, 129.0, 128.8, 128.6, 71.4 ppm; IR (neat) 3068, 3032, 1584, 1557, 1487, 1458, 1431, 1194, 1148, 1088, 1015, 907, 854, 831 cm^{-1} ; HRMS (ESI) exact mass calcd for $\text{C}_{14}\text{H}_{13}\text{ClNO}$: m/z 246.0680 ($[\text{M} + \text{H}]^+$), found: m/z 246.0678 ($[\text{M} + \text{H}]^+$).

(Z)-N-(2-Naphthyl)methylidenebenzylamine N-Oxide. ^1H NMR (400 MHz, CDCl_3) δ 9.23 (1H, s, N=CH), 7.78-7.90 (4H, m, ArH), 7.40-7.54 (8H, m, ArH), 5.11 (2H, s, PhCH₂) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 134.2, 134.0, 133.1, 133.0, 129.2, 129.1, 128.9, 128.5, 127.8, 127.5, 127.4, 127.2, 126.4, 125.7, 71.3 ppm; IR (neat) 3397, 3057, 3032, 1566, 1497, 1456, 1423, 1354, 1179, 1150, 1140, 945, 907, 864, 827 cm^{-1} ; HRMS (ESI) exact mass calcd for $\text{C}_{18}\text{H}_{16}\text{NO}$: m/z 262.1226 ($[\text{M} + \text{H}]^+$), found: m/z 262.1225 ($[\text{M} + \text{H}]^+$).

(Z)-N-tert-Butylmethylidenbenzylamine N-Oxide. ^1H NMR (400 MHz, CDCl_3) δ 7.38 (5H, br, ArH), 6.49 (1H, s, N=CH), 4.84 (2H, s, PhCH_2), 1.26 (1H, s, *t*-Bu) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 144.8, 133.4, 128.7, 128.6, 128.5, 70.6, 32.9, 26.1 ppm; IR (neat) 2959, 2914, 1583, 1497, 1483, 1456, 1423, 1360, 1227, 1204, 1144, 937 cm^{-1} ; HRMS (ESI) exact mass calcd for $\text{C}_{12}\text{H}_{18}\text{NO}$: m/z 192.1383 ($[\text{M} + \text{H}]^+$), found: m/z 192.1382 ($[\text{M} + \text{H}]^+$).

(Z)-N-Cyclohexylmethylidenbenzylamine N-Oxide. ^1H NMR (400 MHz, CDCl_3) δ 7.38 (5H, br, ArH), 6.46 (1H, d, $J = 7.6$, N=CH), 4.86 (2H, s, PhCH_2), 2.99 (1H, m, N=CHCH), 1.08-1.87 (10H, m, CyH) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 142.9, 133.1, 128.9, 128.7, 128.6, 69.4, 35.1, 28.9, 26.0, 25.3 ppm; IR (neat) 2920, 2849, 1591, 1497, 1447, 1427, 1188, 1173, 1121, 937 cm^{-1} ; HRMS (ESI) exact mass calcd for $\text{C}_{14}\text{H}_{20}\text{NO}$: m/z 218.1539 ($[\text{M} + \text{H}]^+$), found: m/z 218.1540 ($[\text{M} + \text{H}]^+$).

(Z)-N-(2-Methyl-1,3-dithian-2-yl)methylidenbenzylamine N-Oxide. A mixture of benzylhydroxylamine and 2-methyl-1,3-dithian-2-carboxaldehyde in benzene was azeotroped for 12 h. Benzene was then removed *in vacuo* and the residue was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate/ $\text{CH}_2\text{Cl}_2 = 5:5:2$). ^1H NMR (400 MHz, CDCl_3) δ 7.39-7.43 (5H, m, ArH), 7.03 (1H, s, N=CH), 4.93 (2H, s, PhCH_2), 2.78-2.85 (2H, m, SCH_2), 2.65-2.70 (2H, m, SCH_2), 2.03-2.09 (m, 1H, $\text{SCH}_2\text{CHHCH}_2\text{S}$), 1.63-1.93 (1H, m, $\text{SCH}_2\text{CHHCH}_2\text{S}$), 1.88 (3H, s, CH_3) ppm; ^{13}C NMR (100 MHz, CDCl_3) δ 138.3, 133.1, 128.9, 70.9, 45.9, 28.2, 24.7, 23.4 ppm; IR (neat) 3063, 2930, 2901, 1564, 1456, 1420, 1194, 1141, 1069, 905, 729, 702 cm^{-1} ; HRMS (ESI) exact mass calcd for $\text{C}_{13}\text{H}_{18}\text{NOS}_2$: m/z 268.0824 ($[\text{M} + \text{H}]^+$), found: m/z 268.0823 ($[\text{M} + \text{H}]^+$).

(3S,4S)-3-Acetyl-2-benzyl-4-hydroxymethylisoxazoline 4 (Scheme 2). To a solution of

(3*S*,4*S*)-2-benzyl-4-hydroxymethyl-3-(2-methyl-1,3-dithian-2-yl)isoxazoline (65.1 mg, 0.20 mmol) in CH₃CN (1.6 mL) and H₂O (0.4 mL) were added HgO (47.6 mg, 0.22 mmol) and HgCl₂ (120 mg, 0.44 mmol) at room temperature. The suspension was then stirred for 1 h, filtered through Celite and extracted with ethyl acetate. The organic layers were washed with brine, dried over Na₂SO₄ and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 1:1) to afford the isoxazoline **4** as a colorless oil [63% (29.8 mg), *endo:exo* = >97:3, *endo* 97% ee].

The enantiomeric purity of **4** was determined by HPLC analysis (Daicel Chiralcel OD-H, hexane/2-propanol = 20:1, flow rate = 1.0 mL/min, retention time; 23.0 min (minor) and 24.6 min (major)).

¹H NMR (400 MHz, CDCl₃) δ 7.26-7.39 (5H, m, ArH), 4.18 (1H, d, *J* = 12.8 Hz, PhCHH), 4.07 (1H, dd, *J* = 8.0, 8.8 Hz, NOCHH), 3.94 (1H, d, *J* = 12.8 Hz, PhCHH), 3.92 (1H, dd, *J* = 6.8, 8.8 Hz, NOCHH), 3.78 (2H, m, CH₂OH), 3.31 (1H, d, *J* = 6.0 Hz, ONCH), 2.90 (1H, m, CHCH₂OH), 2.15 (1H, s, COCH₃) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 209.0, 136.0, 129.3, 128.4, 127.7, 76.3, 68.3, 62.7, 61.6, 50.1, 26.6 ppm; IR (neat) 3391, 2918, 2849, 1709, 1354, 1236, 1030, 800, 700 cm⁻¹; HRMS (ESI) exact mass calcd for C₁₃H₁₈NO₃: *m/z* 236.1281 ([M + H]⁺), found: *m/z* 236.1293 ([M + H]⁺); [α]_D³⁰ = -55.1° (*c* = 1.0, CHCl₃; 97% ee).

(2*R*,3*R*)-*N*-(*tert*-Butoxycarbonyl)-3-amino-2-(*tert*-butyldiphenylsiloxy)methyl-1-pentanol **5 (Scheme 2).** To a solution of (3*S*,4*S*)-2-benzyl-4-hydroxymethyl-3-(2-methyl-1,3-dithian-2-yl)isoxazoline (54.0 mg, 0.166 mmol) in CH₂Cl₂ (2 mL) were added triethylamine (32.3 μL, 0.232 mmol), *tert*-butylchlorodiphenylsilane (59.4 μL, 0.232 mmol) and a catalytic amount of *N,N*-dimethylaminopyridine (2.0 mg, 0.017 mmol) at room temperature. After stirring for 15 h, the reaction mixture was treated with aqueous NaHCO₃ and extracted with CH₂Cl₂. The combined organic layers were dried over Na₂SO₄, filtered and concentrated. The residue was passed through a short plug of silica gel (eluting with hexane/ethyl acetate = 10:1) to remove highly polar impurities, and used for the next step without further purification.

To the residue in 2-propanol (4 mL) were added Boc₂O (191 μL, 0.830 mmol) and Raney-Ni (1.7 g) at room temperature. Hydrogen gas (balloon) was then charged to the reaction flask. After stirring for 1 h at 80 °C, Raney-Ni was filtered off and the solvent was evaporated *in vacuo*. The residue was purified by column chromatography on silica gel (eluting with

hexane/ethyl acetate = 4:1) to afford (2*R*,3*R*)-*N*-(*tert*-butoxycarbonyl)-3-amino-2-(*tert*-butyldiphenylsiloxymethyl)-1-butanol **5** as a colorless oil [43% yield (33.7 mg), 97% ee].

The enantiomeric purity of **5** was determined by HPLC analysis (Daicel Chiralcel OD-H, hexane/2-propanol = 50:1, flow rate = 0.5 mL/min, retention time; 16.0 min (major) and 18.0 min (minor)).

¹H NMR (400 MHz, CDCl₃) δ 7.58-7.65 (4H, m, ArH), 7.36-7.45 (6H, m, ArH), 4.80 (1H, d, *J* = 9.2 Hz, NH), 3.71-3.86 (4H, m, CH₂OH and CH₂OSi), 3.52 (1H, m, NCH), 2.55 (1H, m, CHCH₂OH), 1.30-1.57 (2H, m, CH₃CH₂), 1.41 (9H, s, *t*-Bu) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 156.3, 135.5, 135.4, 133.2, 133.1, 129.6, 127.6, 79.2, 63.6, 61.1, 51.5, 46.6, 28.5, 27.0, 25.8, 19.2, 10.5 ppm; IR (neat) 3408, 2962, 2930, 2878, 2859, 1686, 1506, 1366, 1244, 1173, 1111, 1076, 824, 741, 702, 613 cm⁻¹; HRMS (ESI) exact mass calcd for C₂₇H₄₁NNaO₄Si: *m/z* 494.2697 ([M + Na]⁺), found: *m/z* 494.2697 ([M + Na]⁺); [α]_D²⁵ = +12.4° (*c* = 1.0, CHCl₃; 97% ee).

Determination of the Absolute Configuration of (3*S*,4*S*)-2-Benzyl-4-hydroxymethyl-3-phenylisoxazoline. To a solution of (3*S*,4*S*)-2-benzyl-4-hydroxymethyl-3-phenylisoxazoline (53.9 mg, 0.20 mmol) in CH₂Cl₂ was added Dess-Martin periodinane (110 mg, 0.26 mmol) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 1 h. The resulting mixture was then treated with aqueous Na₂SO₃, washed with aqueous NaHCO₃ and extracted with CH₂Cl₂. The combined organic layers were dried over Na₂SO₄ and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 3:1) to give (3*S*,4*R*)-2-benzyl-4-formyl-3-phenylisoxazoline as a colorless oil in 82% yield (43.8 mg, 0.16 mmol); [α]_D²² = -59.6° (*c* = 1.0, CHCl₃; 93% ee).

The absolute configuration was assigned by the comparison with the data in the literature.³

References

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