A Silicon Tether Approach for Diastereocontrol in Radical Addition to Chiral Hydrazones

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Supporting Information

Materials and Methods. Reactions employed oven- or flame-dried glassware under nitrogen unless otherwise noted. Benzene, triethylamine and CH_2Cl_2 were distilled from CaH_2 under argon or nitrogen. Nitrogen was passed successively through columns of anhydrous $CaSO_4$ and R3-11 catalyst (Schweizer-Hall, South Plainfield, NJ) for removal of water and oxygen, respectively. All other materials were used as received from Aldrich. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates with UV indicator. Flash chromatography columns were packed with 230-400 mesh silica gel as slurry in the initial elution solvent. Gradient flash chromatography was conducted by adsorption of the crude mixture on silica gel, packing over a short pad of clean silica gel as a slurry in hexane, and eluting with a continuous gradient from hexane to the indicated solvent. Radial chromatography refers to centrifugally accelerated thin-layer chromatography performed using a Chromatotron (Harrison Research, Palo Alto CA) with precast rotors supplied by Analtech (Newark, DE). Melting points were determined on a Meltemp apparatus and are uncorrected. Proton and carbon NMR data were obtained with a Bruker ARX 500 spectrometer. Infrared spectra were recorded with a Perkin-Elmer 2000 FT-IR spectrophotometer. Optical rotations were determined using a Rudolph Research Autopol IV polarimeter. Low resolution mass spectra were obtained with a Finnegan 4610 quadrupole spectrometer. Combustion analyses were performed by Atlantic Microlab (Norcross, GA) or Robertson Laboratories (Madison, NJ).

General Procedure: α-Silyloxy Hydrazones 2. A solution of the ester in dry hexane (ca. 1 M) was cooled to –78 °C and a solution of diisobutylaluminum hydride (1.5 M in toluene, 1.2 equiv) was added dropwise over 30 min. After 1 h at –78 °C, saturated aqueous potassium sodium tartrate (ca. 2 mL/mmol ester) was added. Following dilution with ether/CH_2Cl_2 (1:1, ca. 4 mL/mmol ester) and vigorous stirring, the aqueous phase was extracted with ether (2 x 10 mL). The organic phase was dried (Na_2SO_4) and concentrated. The resulting solution of aldehyde in toluene was diluted with pyridine (ca. 1 mL/mmol ester) and *N*,*N*-diphenylhydrazine hydrochloride (1 mmol/mmol ester) was added at room temperature. The mixture was concentrated and partitioned between CH_2Cl_2 and saturated aqueous $NaHCO_3$. The organic phase was washed with 1 N aqueous HCl, dried (Na_2SO_4) and concentrated. Gradient flash chromatography (**2b-d**, hexane → 10:1 hexane/ethyl acetate) or recrystallization from 90% EtOH (**2a**) afforded α-silyloxy hydrazones. Analytical samples of **2b-d** were obtained by radial chromatography (10:1 hexane/ethyl acetate).

(*S*)-(–)-2-(*tert*-Butyldimethylsilyloxy)propanal Diphenylhydrazone (2a, R = Me). From ester **1a** (0.79 g, 3.6 mmol) was obtained **2a** (0.755 g, 59% yield) as colorless needles; mp 70–71 °C; $[\alpha]_D^{25}$ –1.7° (*c* 1.45, $CHCl_3$); IR (film) 2955, 2929, 2856, 1593, 1496, 1086, 1058 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40-7.36 (m, 4H), 7.16-7.12 (m, 2H), 7.11-7.08 (m, 4H), 6.39 (d, *J* = 5.9 Hz, 1H), 4.54 (m, apparent quintet, *J* = 6.2 Hz, 1H), 1.28 (d, *J* = 6.4 Hz, 3H), 0.87 (s, 9H), 0.09 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ

143.9, 141.6, 129.7, 124.1, 122.4, 69.5, 25.9, 22.6, 18.2, -4.4, -4.6; MS *m/z* (relative intensity) 355 ([M+H]$^+$, 30%), 354 (M$^+$, 50%), 223 (100%), 168 (55%); Anal. Calcd for $C_{21}H_{30}N_2OSi$: C, 71.14; H, 8.53; N, 7.90. Found: C, 71.22; H, 8.54; N, 7.95.

2-(*tert*-Butyldimethylsilyloxy)-4-methylpentanal Diphenylhydrazone (2b, R = ^{i}Bu). From ester **1b** (0.52 g, 2.0 mmol) was obtained **2b** (0.636 g, 80% yield) as a colorless oil; $[\alpha]^{27}_{\mathrm{D}}$ +3.4° (*c* 0.83, $CHCl_3$); IR (film) 2956, 2928, 1595, 1498, 1213, 1077, 1053 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.36 (m, 4H), 7.16-7.08 (m, 6H), 6.34 (d, *J* = 6.4 Hz, 1H), 3.96-3.92 (m, 1H), 1.75-1.68 (m, 1H), 1.48 (ddd, *J* = 13.7, 8.1, 6.1 Hz, 1H), 1.31 (ddd, *J* = 13.7, 7.8, 5.9 Hz, 1H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.86 (s, 9H), 0.11 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.9, 141.3, 129.7, 124.1, 122.4, 71.8, 45.6, 25.9, 24.1, 23.2, 22.3, 18.2, -4.0, -4.7; MS *m/z* (relative intensity) 397 ([M+H]$^+$, 65%), 396 (M$^+$, 85%), 339 (30%), 265 (100%), 168 (35%). Anal. Calcd for $C_{24}H_{36}N_2OSi$: C, 72.68; H, 9.15; N, 7.06. Found: C, 72.86; H, 9.11; N, 7.05.

2-(*tert*-Butyldimethylsilyloxy)-3-methylbutanal Diphenylhydrazone (2c, R = ^{i}Pr). From ester **1c** (0.626 g, 2.39 mmol) was obtained **2c** (0.756 g, 83% yield) as a colorless oil; $[\alpha]^{27}_{\mathrm{D}}$ +26° (*c* 1.74, $CHCl_3$); IR (film) 2957, 2930, 2857, 1592, 1496, 1213, 1072, 1049 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41-7.38 (m, 4H), 7.17-7.13 (m, 2H), 7.12-7.09 (m, 4H), 6.35 (d, *J* = 6.9 Hz, 1H), 4.06 (t, 6.8 Hz, 1H), 1.73 (m, apparent octet, *J* = 6.7 Hz, 1H), 0.93 (d, *J* = 6.7 Hz, 3H), 0.88 (s, 9H), 0.85 (d, *J* = 6.9 Hz, 3H), 0.11 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.0, 140.8, 129.7, 124.1, 122.4, 78.4, 34.0, 25.9, 18.5, 18.2 (2C), -4.0, -4.8; MS *m/z* (relative intensity) 383 ([M+H]$^+$, 50%), 382 (M$^+$, 40%), 325 (30%), 251 (100%), 168 (25%). Anal. Calcd for $C_{23}H_{34}N_2OSi$: C, 72.20; H, 8.96; N, 7.32. Found: C, 72.23; H, 8.93; N, 7.11.

2-(*tert*-Butyldimethylsilyloxy)-2-phenylacetaldehyde Diphenylhydrazone (2d, R = Ph). From racemic ester **1d** (2.61 g, 9.31 mmol) was obtained, using half of the aldehyde intermediate in the second step, **2d** (1.63 g, 84% yield) as a colorless oil; IR (film) 2956, 2929, 2856, 1592, 1496, 1299, 1256, 1214, 1089, 1057 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.35 (m, 6H), 7.33-7.29 (m, 2H), 7.24-7.21 (m, 1H), 7.15-7.11 (m, 2H), 7.10-7.08 (m, 4H), 6.38 (d, *J* = 6.8 Hz, 1H), 5.51 (d, *J* = 6.8 Hz, 1H), 0.92 (s, 9H), 0.13 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8, 142.2, 140.1, 129.7, 128.2, 127.0, 125.8, 124.3, 122.4, 75.1, 25.9, 18.3, -4.2, -4.7; MS *m/z* (relative intensity) 417 ([M+H]+, 40%), 285 (100%), 273 (40%), 221 (30%, 168 (45%). From scalemic ester **1d** (98% ee, 2.68 g, 9.57 mmol) was obtained, using one-fifth of the aldehyde intermediate in the second step, **2d** (0.636 g, 76% yield) as a colorless oil, spectroscopically identical to racemic **2d**; $[\alpha]^{26}_{\mathrm{D}}$ –93° (*c* 0.34, $CHCl_3$); Anal. Calcd for $C_{26}H_{32}N_2OSi$: C, 74.95; H, 7.74; N, 6.72. Found: C, 75.05; H, 7.76; N, 6.70.

General Procedure: α-Hydroxy Hydrazones 3. To a solution of silyloxy hydrazone **2** in tetrahydrofuran (ca. 0.1 M) was added tetrabutylammonium fluoride (1 M in tetrahydrofuran, 1.1 equiv) at room temperature. After 0.5–3 h (TLC monitoring), the mixture was concentrated and filtered through silica gel (step gradient elution, 10:1 → 1:1 hexane/ethyl acetate) to afford α-hydroxy hydrazones **3**.

2-Hydroxypropanal Diphenylhydrazone (3a, R = Me). From α-silyloxy hydrazone **2a** (323 mg, 0.909 mmol) was obtained **3a** (220 mg, 100% yield) as a colorless viscous oil; $[\alpha]_D^{25}$ +38° (*c* 2.1, $CHCl_3$); IR (film) 3380 (br), 1591, 1496, 1214 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.42-7.37 (m, 4H), 7.20-7.15 (m, 2H), 7.14-7.09 (m, 4H), 6.54 (d, *J* = 3.4 Hz, 1H), 4.50-4.44 (m, 1H), 3.05-3.02 (br s, 1H), 1.30 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.7, 139.8, 129.8, 124.4, 122.3, 67.4, 21.6; MS *m*/*z* (relative intensity) 241 ($[M+H]^+$, 100%), 223 ($[M-OH]^+$, 65%), 168 (25%); Anal. Calcd for $C_{15}H_{16}N_2O$: C, 74.97; H, 6.71; N, 11.66. Found: C, 74.68; H, 6.80; N, 11.54.

2-Hydroxy-4-methylpentanal Diphenylhydrazone (3b, R = ^{i}Bu). From α-silyloxy hydrazone **2b** (156 mg, 0.393 mmol) was obtained **3b** (92 mg, 83% yield) as a colorless viscous oil; $[\alpha]_D^{28}$ +27° (*c* 4.6, $CHCl_3$); IR (film) 3400 (br, s), 2955, 1596, 1496, 1213 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41-7.38 (m, 4H), 7.19-7.15 (m, 2H), 7.12-7.09 (m, 4H), 6.52 (d, *J* = 3.7 Hz, 1H), 4.39 (dddd, *J* = 8.4, 4.9, 3.7, 3.7 Hz, 1H), 2.90 (d, *J* = 3.7 Hz, 1H), 1.88-1.78 (m, 1H), 1.46 (ddd, *J* =13.9, 8.6, 5.8 Hz, 1H), 1.35 (ddd, *J* = 13.6, 8.1, 4.9 Hz, 1H), 0.943 (d, *J* = 6.7 Hz, 3H), 0.939 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.7, 139.7, 129.8, 124.4, 122.3, 69.7, 44.9, 24.4, 23.3, 22.2; MS *m*/*z* (relative intensity) 283 ($[M+H]^+$, 100%), 282 (M^+, 45%), 265 ($[M-OH]^+$, 40%), 168 (15%). Anal. Calcd for $C_{18}H_{22}N_2O$: C, 76.56; H, 7.85; N, 9.92. Found: C, 76.56; H, 7.94; N, 9.76.

2-Hydroxy-3-methylbutanal Diphenylhydrazone (3c, R = ^{i}Pr). From α-silyloxy hydrazone **2c** (0. 285 g, 0.745 mmol) was obtained **3c** (0.176 g, 88% yield) as a colorless viscous oil; $[\alpha]_D^{27}$ +34° (*c* 3.8, $CHCl_3$); IR (film) 3435 (br, s), 2960, 1591, 1496, 1299, 1214, 1020 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.43-7.39 (m, 4H), 7.20-7.16 (m, 2H), 7.15-7.12 (m, 4H), 6.59 (d, *J* = 3.4 Hz, 1H), 4.17-4.13 (m, 1H), 3.27 (br s, 1H), 1.87-1.78 (m, 1H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8, 138.7, 129.7, 124.4, 122.2, 75.5, 33.2, 18.2, 17.2; MS *m*/*z* (relative intensity) 269 ([M+H]+, 90%), 268 (M+, 70%), 251 ($[M-OH]^+$, 100%), 168 (90%). Anal. Calcd for $C_{17}H_{20}N_2O$: C, 76.09; H, 7.51; N, 10.44. Found: C, 76.16; H, 7.56; N, 10.34.

2-Hydroxy-2-phenylacetaldehyde Diphenylhydrazone (3d, R = Ph). From α-silyloxy hydrazone **2d** (0.264 g, 0.634 mmol) was obtained **3d** (0.165 g, 86% yield) as a pale tan viscous oil; $[\alpha]_D^{24}$ +97° (*c* 0.50, $CHCl_3$); IR (film) 3406 (br), 1591, 1495, 1214 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41-7.34 (m, 8H), 7.32-7.26 (m, 1H), 7.18-7.15 (m, 2H), 7.14-7.10 (m, 4H), 6.63 (d, *J* = 3.4 Hz, 1H), 5.37 (t, *J* = 3.6 Hz, 1H), 3.81 (d, *J* = 3.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.6, 141.0, 137.8, 129.8, 128.6, 127.8, 126.6, 124.6, 122.3, 73.7;

MS *m/z* (relative intensity) 303 ([M+H]$^+$, 80%), 285 ([M-OH]$^+$, 45%), 170 (80%), 133 (100%), 107 (80%). Anal. Calcd for $C_{20}H_{18}N_2O$: C, 79.44; H, 6.00; N, 9.26. Found: C, 79.38; H, 6.06; N, 9.18.

General Procedure: 2-Hydrazino-1,3-diols 6. A solution of α-hydroxy hydrazone **3** in dry CH_2Cl_2 (ca. 1 M) at 0 °C was treated sequentially with triethylamine (1.3 equiv) and bromomethyldimethylsilyl chloride (1.3 equiv). Copious white precipitate formed immediately. After warming to room temperature over 0.5 h, the mixture was diluted with ether (ca. 4 mL/mmol triethylamine) and filtered through a short plug of silica gel (elution with ether). Rapid flash chromatography (20:1 then 10:1 hexane/ethyl acetate) gave bromomethylsilyl ether **4** as a colorless oil which was used immediately in the next step (prolonged storage or prolonged exposure to silica gel led to decomposition). A solution of the bromomethylsilyl ether **4** and tributyltin hydride (1.4 equiv) in benzene (ca. 0.02 M) was deoxygenated (N_2 via needle) for ca. 10 min. Azobisisobutyronitrile (AIBN, 10 mol %) was added, and the mixture was deoxygenated for 5 min, then heated at reflux for 0.5 h. If TLC indicated incomplete reaction at this point, additional AIBN was added and heating was continued for another 0.5 h. Concentration of the reaction mixture afforded the colorless crude intermediate cyclic silane, which was analyzed by ^{1}H NMR to determine the diastereomer ratio (integral ratios for $SiMe_2$ and $CHNHNPh_2$ resonances). A solution of the cyclic silane in tetrahydrofuran/methanol (1:1, ca. 0.1 M) was treated at room temperature with KF (3.5 equiv), $KHCO_3$ (2 equiv) and H_2O_2 (30% aqueous solution, 10 equiv). After 0.5–2 d, the mixture was diluted with an equal volume of ether, and 50% aqueous $Na_2S_2O_3$ (ca. 0.2 mL/mmol H_2O_2) was added. The mixture was filtered through Celite with the aid of additional ether, concentrated, partitioned between CH_2Cl_2 and brine, and dried (Na_2SO_4). Concentration and gradient flash chromatography provided 2-hydrazino-1,3-diol **6**.

(2R,3S)-2-(*N*,*N*-Diphenylhydrazino)butane-1,3-diol (6a, R = Me). From **3a** (361 mg, 1.02 mmol) was obtained **4a** (215 mg, 60% yield) as a colorless viscous oil. From **4a** (59 mg, 0.15 mmol) was obtained **6a** (30.9 mg, 76% yield, 79:21 diastereomeric ratio). These isomers were not readily separated, but upon hydrolysis of diastereomerically enriched acetonide **7a** (PPTS, methanol), an analytical sample of the major diol *anti*-**6a** (*anti*/*syn* = 90:10) was obtained as a colorless viscous oil; $[\alpha]_D^{27}$ +25° (*c* 0.71, $CHCl_3$); IR (film) 3390 (br, s), 1589, 1495, 1271 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34-7.28 (m, 4H), 7.19-7.15 (m, 4H), 7.05-7.01 (m, 2H), 4.53 (br s, 1H), 4.16-4.10 (m, 1H), 3.92-3.81 (m, 2H), 3.01 (ddd, *J* = 6.8, 3.7, 3.4 Hz, 1H), 2.60 (br s, 1H), 2.11 (br s, 1H), 1.22 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.4, 129.3, 122.9, 120.6, 67.0, 62.5, 60.6, 18.6; MS *m/z* (relative intensity) 273 ([M+H]$^+$, 100%), 168 (90%) (diastereomeric mixture). Anal. Calcd for $C_{16}H_{20}N_2O_2$: C, 70.56; H, 7.40; N, 10.29. Found: C, 70.27; H, 7.38; N, 10.08.

(2R,3S)-2-(*N*,*N*-Diphenylhydrazino)-5-methylhexane-1,3-diol (6b, R =

^{i}Bu). From **3b** (70 mg, 0.25 mmol) was obtained **4b** (103 mg, 83% yield) as a colorless viscous oil. From **4b** (103 mg, 0.238 mmol) was obtained **6b** (51 mg, 68% yield, 85:15 diastereomeric ratio by ^{1}H NMR, major isomer >96% ee by Mosher ester analysis). These isomers were not readily separated, but upon hydrolysis of the diastereomerically pure acetonide **7b** (PPTS, methanol), an analytical sample of the major diol *anti*-**6b** was obtained as a colorless viscous oil; $[\alpha]^{27}_{\mathrm{D}}$ +21° (*c* 0.83, $CHCl_3$); IR (film) 3400 (br, s), 2956, 2929, 1589, 1496, 1272 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34-7.29 (m, 4H), 7.20-7.17 (m, 4H), 7.05-7.01 (m, 2H), 4.65 (br s, 1H), 4.05-4.00 (m, 1H), 3.88-3.80 (m, 2H), 2.99 (ddd, *J* = 6.2, 3.7, 3.2 Hz, 1H), 2.57 (br s, 1H), 2.19 (br s, 1H), 1.70-1.60 (m, 1H), 1.50 (ddd, *J* = 13.9, 9.6, 5.5 Hz, 1H), 1.17 (ddd, *J* = 13.5, 8.6, 3.7, 1H), 0.92 (d, *J* = 6.7 Hz, 3H), 0.88 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.4, 129.3, 122.8, 120.5, 68.9, 62.0, 60.7, 41.9, 24.9, 23.4, 22.0; MS *m*/*z* (relative intensity) 315 ($[M+H]^+$, 80%), 168 (100%). Anal. Calcd for $C_{19}H_{26}N_2O_2$: C, 72.57; H, 8.33; N, 8.91. Found: C, 72.75; H, 8.32; N, 8.87.

(2R,3S)-2-(*N*,*N*-Diphenylhydrazino)-5-methylhexane-1,3-diol (6c, R = ^{i}Pr). From **3c** (93 mg, 0.347 mmol) was obtained **4c** (124 mg, 85% yield) as a colorless viscous oil. From **4c** (123 mg, 0.293 mmol) was obtained **6c**, which was further purified by radial chromatography to afford *syn*-**6c** (3 mg) and *anti*-**6c** (68 mg, 80% combined yield, 96:4 diastereomeric ratio, *anti* isomer >96% ee by Mosher ester analysis). Minor diastereomer *syn*-**6c**: Colorless viscous oil; IR (film) 3401 (br, s), 2962, 2928, 1589, 1496 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32-7.28 (m, 4H), 7.20-7.18 (m, 4H), 7.05-7.00 (m, 2H), 4.65 (br s, 1H), 3.91 (dd, *J* = 11.5, 2.4 Hz, 1H), 3.67-3.60 (m, 1H), 3.52 (dd, *J* = 5.6, 5.3 Hz, 1H), 3.12 (ddd, *J* = 6.4, 3.3, 3.3 Hz, 1H), 2.26 (br s, 1H), 2.10 (br s, 1H), 1.96-1.87 (m, 1H), 0.90 (d, *J* = 6.5 Hz, 3H), 0.88 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.5, 129.3, 122.9, 120.7, 76.5, 61.8, 59.4, 29.9, 19.7, 16.5; MS *m*/*z* (relative intensity) 301 ($[M+H]^+$, 85%), 300 (M^+, 30%), 170 (95%), 168 (100%). Major diastereomer *anti*-**6c**: Colorless viscous oil; $[\alpha]^{20}_{\mathrm{D}}$ +33° (*c* 1.3, $CHCl_3$); IR (film) 3410 (br, s), 2960, 1589, 1496 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34-7.30 (m, 4H), 7.19-7.16 (m, 4H), 7.06-7.02 (m, 2H), 4.47 (br s, 1H), 3.88-3.80 (ABX, J_{AB} = 11.4 Hz, J_{AX} = 3.7 Hz, J_{BX} = 6.1 Hz, $\Delta\nu_{AB}$ = 15.9 Hz, 2H), 3.54 (dd, *J* = 8.7, 3.0 Hz, 1H), 3.17 (ddd, *J* = 6.2, 3.6, 3.5 Hz, 1H), 2.86 (br s, 1H), 2.40 (br s, 1H), 1.77-1.68 (m, 1H), 0.99 (d, *J* = 6.5 Hz, 3H), 0.82 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.4, 129.3, 122.8, 120.6, 76.1, 60.4, 59.3, 30.3, 19.5, 18.8; MS *m*/*z* (relative intensity) 301 ($[M+H]^+$, 100%), 300 (M^+, 45%), 170 (98%), 168 (65%). Anal. Calcd for $C_{18}H_{24}N_2O_2$: C, 71.97; H, 8.05; N, 9.33. Found: C, 71.73; H, 8.24; N, 9.16.

(2R,3S)-2-(*N*,*N*-Diphenylhydrazino)-3-phenylpropane-1,3-diol (6d, R = Ph). From **3d** (104 mg, 0.344 mmol) was obtained **4d** (129 mg, 85% yield) as a colorless viscous oil. From **4d** (129 mg, 0.285 mmol) was obtained **6d** (54 mg, 57% yield, single diastereomer by ^{1}H NMR, 33% ee by Mosher ester analysis) as a colorless viscous oil. $[\alpha]^{25}_{\mathrm{D}}$ –5.4° (*c* 0.14, $CHCl_3$, 33% ee); IR (film) 3390 (br), 1588, 1495 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.27 (m, 9H), 7.12-7.08 (m, 4H), 7.05-7.00 (m, 2H), 5.00 (dd, *J* = 5.2, 2.1 Hz, 1H), 4.34 (br s, 1H), 3.84 (ddd, *J* = 11.5, 5.7, 5.7 Hz, 1H), 3.76 (br d, *J* = 11.5 Hz, 1H), 3.22 (ddd, *J* = 5.3, 5.3, 4.1 Hz, 1H), 2.92 (br s, 1H), 2.00 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.0, 140.5, 129.3, 128.6, 127.9, 126.2, 122.8, 120.5, 73.0, 63.4, 60.6; MS *m*/*z* (relative intensity) 335 ([M+H]+, 40%), 170 (30%), 168 (30%), 107 (100%). Anal. Calcd for $C_{21}H_{22}N_2O_2$: C, 75.42; H, 6.63; N, 8.38. Found: C, 75.56; H, 6.75; N, 8.25.

General Procedure: Acetonides 7. A solution of the hydrazino-1,3-diol **6** in $CHCl_3$ (ca. 0.2 M) was treated with 2,2-dimethoxypropane (ca. 1 mL/mmol diol) and pyridinium *p*-toluenesulfonate (1 equiv). After 1 d at room temperature, the reaction mixture was partitioned between $CHCl_3$ and saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated. Radial chromatography (hexane/ethyl acetate) furnished diastereomerically pure *anti* acetonide **7**.

Acetonide 7a (R = Me). From **6a** (29 mg, 0.107 mmol) was obtained **7a** (21 mg, 63% yield) as a colorless viscous oil; $[\alpha]_D^{27}$ –28° (*c* 0.43, $CHCl_3$); IR (film) 3289 (br, w), 3179 (br, w), 1589, 1497, 1269, 1200, 1180 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.27 (m, 4H), 7.14-7.11 (m, 4H), 7.04-7.00 (m, 2H), 3.94-3.88 (m, 1H), 3.92 (dd, *J* = 11.5, 5.0 Hz, 1H), 3.85 (br s, 1H), 3.73 (dd, *J* = 11.5, 9.5 Hz, 1H), 2.90 (ddd, apparent td, *J* = 9.3, 9.2, 5.0 Hz, 1H), 1.49 (s, 3H), 1.37 (s, 3H), 1.22 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.1, 129.2, 122.7, 120.4, 98.4, 68.2, 62.8, 57.3, 28.9, 19.6, 19.2; MS *m*/*z* (relative intensity) 313 ([M+H]$^+$, 30%), 312 (M$^+$, 25%), 184 (35%), 170 (40%), 168 (100%). Anal. Calcd for $C_{19}H_{24}N_2O_2$: C, 73.05; H, 7.74; N, 8.97. Found: C, 73.33; H, 7.90; N, 8.97.

Acetonide 7b (R = ^{i}Bu). From **6b** (47 mg, 0.15 mmol) was obtained **7b** (38 mg, 72% yield) as a colorless viscous oil which crystallized on standing; mp 59–61 °C; $[\alpha]_D^{27}$ –69° (*c* 1.3, $CHCl_3$); IR (film) 3289 (br), 3183 (br, w), 2956, 1589, 1499, 1273, 1200 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32-7.28 (m, 4H), 7.15-7.12 (m, 4H), 7.04-7.00 (m, 2H), 3.94 (dd, *J* = 11.6, 4.9 Hz, 1H), 3.87 (br s, 1H), 3.81 (ddd, apparent td, *J* = 9.2, 9.2, 2.4 Hz, 1H), 3.75 (dd, *J* = 11.6, 8.5 Hz, 1H), 2.93 (ddd, apparent td, *J* = 8.7, 8.7, 4.9 Hz, 1H), 1.88-1.80 (m, 1H), 1.50 (s, 3H), 1.42-1.30 (m, 2H), 1.36 (s, 3H), 0.91 (d, *J* = 6.8 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.1, 129.2, 122.6, 120.4, 98.5, 69.7, 62.8, 56.4, 41.8, 28.4, 23.8, 23.7, 21.4, 19.9; MS *m*/*z* (relative intensity) 355 ([M+H]$^+$, 97%), 354 (M$^+$, 100%), 297 (25%), 209 (20%), 168 (25%). Anal. Calcd for $C_{22}H_{30}N_2O_2$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.45; H, 8.46; N, 7.81.

Acetonide 7c (R = ^{i}Pr). From *anti*-**6c** (35 mg, 0.117 mmol) was obtained **7c** (23 mg, 58% yield) as a colorless viscous oil; $[\alpha]_D^{20}$ –44° (*c* 1.15, $CHCl_3$); IR (film) 3289 (br, w), 3179 (br, w), 2963, 2876, 1590, 1498, 1265, 1228, 1201, 1076 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33-7.29 (m, 4H), 7.26-7.23 (m, 4H), 7.04-7.00 (m, 2H), 3.90 (dd, *J* = 11.5, 4.7 Hz, 1H), 3.87 (br s, 1H), 3.75 (dd, *J* = 11.5, 7.3 Hz, 1H), 3.56 (ddd, *J* = 8.7, 7.3, 4.7 Hz, 1H), 3.06 (ddd, *J* = 8.7, 7.3, 4.7 Hz, 1H), 1.82 (m, apparent septet of d, *J* = 6 x 6.8, 3.2 Hz, 1H), 1.47 (s, 3H), 1.35 (s, 3H), 0.92 (d, *J* = 6.9 Hz, 3H), 0.78 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.2, 129.2, 122.7, 120.5, 98.7, 75.1, 62.3, 53.5, 29.0, 27.9, 20.4, 19.2, 15.4; MS *m/z* (relative intensity) 341 ($[M+H]^+$, 20%), 340 (M^+, 20%), 174 (35%), 170 (100%), 168 (55%). Anal. Calcd for $C_{21}H_{28}N_2O_2$: C, 74.08; H, 8.29; N, 8.23. Found: C, 74.20; H, 8.27; N, 8.11.

Acetonide 7d (R = Ph). From **6d** (15 mg, 0.045 mmol) was obtained **7d** (12 mg, 71% yield) as a colorless viscous oil; IR (film) 3281 (br, w), 3176 (br, w), 1590, 1498, 1265, 1223, 1198, 1164, 1086 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.38 (m, 5H), 7.20-7.16 (m, 4H), 6.97-6.93 (m, 2H), 6.85-6.82 (m, 4H), 4.69 (d, *J* = 9.7 Hz, 1H), 4.15 (dd, *J* = 11.4, 4.9 Hz, 1H), 4.02 (dd, *J* = 11.3, 10.1 Hz, 1H), 3.90 (br s, 1H), 3.15 (ddd, *J* = 9.8, 9.8, 4.9 Hz, 1H), 1.64 (s, 3H), 1.48 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.2, 129.0, 128.8, 127.6, 122.4, 120.4, 99.3, 74.8, 64.0, 56.0, 29.3, 19.3; MS *m/z* (relative intensity) 375 ([M+H]+, 45%), 374 (M+, 40%), 209 (35%), 183 (90%), 168 (100%). Anal. Calcd for $C_{24}H_{26}N_2O_2$: C, 76.98; H, 7.00; N, 7.48. Found: C, 75.78; H, 6.88; N, 7.13.