Haloacetal Radical Cyclizations of α - and β -Hydroxyhydrazones

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Supporting Information

Materials and Methods. Reactions employed oven- or flame-dried glassware under nitrogen unless otherwise noted. Tetrahydrofuran (THF) and toluene were distilled from sodium/benzophenone ketyl under argon. 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 or purified by standard procedures. 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 a slurry in the initial elution solvent. Gradient flash chromatography was conducted by adsorption of product mixtures 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 or a Hewlett Packard 5988 GCMS. High resolution mass spectra were provided by the Washington University Mass Spectrometry Resource (St. Louis, MO). Combustion analyses were performed by Atlantic Microlab (Norcross, GA) or Robertson Laboratories (Madison, NJ).

Hydroxyhydrazone 5b. A solution of dry DMSO (3.69 mL, 52.0 mmol) in dry dichloromethane (17 mL) was added dropwise via addition funnel to a stirred solution of oxalyl chloride (2 M in dichloromethane, 13 mL, 26 mmol) at -78°C under an N_2 atmosphere.

After 30 min at -78°C , a solution of 3-(*tert*-butyldimethylsilyloxy)-1-propanol (**6**¹) (3.96 g, 20.1 mmol) in dry dichloromethane (44 mL) was added dropwise via cannula over 15 min. After 45 min at -78°C , a solution of triethylamine (8.7 mL) in dry dichloromethane (4 mL) was added dropwise. The mixture was warmed slowly to ambient temperature and partitioned between dichloromethane (200 mL, 3x50 mL) and water (25 mL). The organic phase was washed with 0.1 N HCl (2x50 mL) and brine (100 mL), dried (Na_2SO_4), and concentrated. The resulting 3-(*tert*-butyldimethylsilyloxy)propanal was used without further purification. To a solution of this aldehyde in pyridine (15 mL) was added *N,N*-diphenylhydrazine hydrochloride (4.59 g, 20.1 mmol). After 3 d, the reaction mixture was partitioned between CH_2Cl_2 and saturated aqueous NaHCO_3 , extracted with CH_2Cl_2 , dried (Na_2SO_4), and concentrated in vacuo. Flash chromatography (10:1 hexane:ethyl acetate) furnished the TBS-protected hydroxyhydrazone as a pale yellow oil (4.36 g, 59%); IR (film, CHCl_3) 2928.0, 1590.7, 1496.0, 1091.0 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.40–7.35 (m, 4H), 7.15–7.05 (m, 6H), 6.59 (t, $J = 5.4$ Hz, 1H), 3.78 (t, $J = 6.5$ Hz, 2H), 2.52 (dt, $J = 6.5, 5.5$ Hz, 2H), 0.85 (s, 9H), 0.0 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 144.18, 137.35, 129.60, 123.86, 122.36, 61.34, 36.09, 25.83, 18.20; MS (CI) m/z (relative intensity) 355 ($[\text{M}+\text{H}]^+$, 100%), 164 (75%); Anal. Calcd for $\text{C}_{21}\text{H}_{31}\text{N}_2\text{O}$: C, 71.14; H, 8.53; N, 7.90. Found: C, 71.46; H, 8.61; N, 7.76.

A solution of the TBS-protected hydroxyhydrazone (0.150 g, 0.42 mmol) obtained as described above in THF (4.2 mL) was treated with TBAF (0.5 mL, 0.5 mmol) at ambient temperature under nitrogen. After 2 h, the mixture was concentrated and purified by flash chromatography (10:1 hexane/ethyl acetate $\rightarrow$ 1:1 hexane/ethyl acetate) to obtain β -hydroxyhydrazone **5b** as a pale pink solid (77 mg, 76%); IR (film, CHCl_3) 3379.0, 2917.0, 1590.0, 1496.0, 1212.0 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.45–7.32 (m, 4H), 7.15–7.05 (m, 6H), 6.63 (t, $J = 4.1$ Hz, 1H), 3.91 (q, $J = 5.9$ Hz, 2H), 2.69 (t, $J = 6.2$ Hz, 1H), 2.50 (q, $J = 5.8$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 143.83, 137.06, 129.75, 124.19, 122.31, 60.10, 34.89; MS (CI) m/z (relative intensity) 240 ($[\text{M}+\text{H}]^+$, 100%), 164 (40%) Anal. Calcd for $\text{C}_{15}\text{H}_{16}\text{N}_2\text{O}$: C, 74.97 ; H, 6.71 ; N, 11.65. Found: C, 74.97; H, 6.79; N, 11.44.

Hydroxyhydrazone 5d. To a solution of TBS-protected ester (*S*)-**7**² (500 mg, 1.55 mmol) in dry hexane (1.5 mL) at -78°C was added DIBAL-H (1.24 mL, 1.85 mmol) dropwise. After 1 h at -78°C , the reaction mixture was partitioned between ether (6 mL)

and saturated aqueous potassium sodium tartrate (6 mL). The aqueous phase was extracted with ether (3x10 mL), dried over Na_2SO_4 , and concentrated. The resulting (*S*)-3-(*tert*-butyldimethylsilyloxy)butanal was used without further purification. To a solution of this aldehyde in pyridine (3.75 mL) was added *N,N*-diphenylhydrazine hydrochloride (3.42 g, 1.55 mmol). After 3 d, the reaction mixture was partitioned between CH_2Cl_2 and saturated aqueous NaHCO_3 . The organic phase was dried with Na_2SO_4 and concentrated in vacuo. Flash chromatography (10:1 hexane/ethyl acetate) furnished the TBS-protected hydroxyhydrazone as a colorless oil (0.440 g, 74%); IR (film, CHCl_3) 2928.0, 1591.0, 1496.0, 1211.0 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.40–7.35 (m, 4H), 7.15–7.10 (m, 6H), 6.59 (dd, $J = 5.7, 5.7$ Hz, 1H), 3.97 (m, apparent sextet, $J = 6.1$ Hz, 1H), 2.42 (dd, $J = 5.9, 5.9$ Hz, 2H), 1.15 (d, $J = 6.1$ Hz, 3H), 0.80 (s, 9H), 0.05 (s, 3H), -0.09 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 144.23, 137.67, 129.60, 123.80, 122.38, 67.57, 42.64, 25.74, 23.93, 17.91; MS (CI) m/z (relative intensity) 369 ($[\text{M}+\text{H}]^+$, 100%) 168 (50%); Anal. Calcd for $\text{C}_{22}\text{H}_{32}\text{N}_2\text{OSi}$: C, 71.69; H, 8.75; N 7.60. Found: C, 71.66; H, 8.63; N, 7.50.

To a solution of the TBS-protected hydroxyhydrazone (1.14 mmol, 450 mg), obtained as described above, in THF (1 mL) was added TBAF (1 M in THF, 1.37 mL, 1.37 mmol) at ambient temperature.

After 2 h, the mixture was concentrated in vacuo and purified by column chromatography (10:1 → 1:1 hexane:ethyl acetate) affording β -hydroxyhydrazone **5d** as a colorless oil (282 mg, 92%); IR (film, CHCl_3) 3429.1, 2965.8, 1589.5, 1495.5, 1213.4, cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.45-7.35 (m, 4H), 7.15-7.05 (m, 6H), 6.63 (dd, $J = 4.5, 4.5$ Hz, 1H), 4.24-4.17 (m, 1H), 3.02 (br s, 1H), 2.42-2.33 (m, 2H), 1.25 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 143.83, 137.14, 129.75, 124.20, 122.31, 65.74, 41.11, 22.69; MS (EI) m/z (relative intensity) 254 ($[\text{M}^+]$, 100%), 168 (98%); Anal. Calcd for $\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}$: C, 75.56; H, 7.13; N, 11.01. Found: C, 75.76; H, 7.13; N, 11.10.

General Procedure A: Formation of Iodo and Bromoacetals

A mixture of *N*-iodosuccinimide (NIS, 1.3 equiv) or *N*-bromosuccinimide (NBS, 4 equiv) and freshly distilled ethyl vinyl ether (EVE, used as solvent, ca. 0.1 M) was stirred at 0°C for 1 h. A solution of alcohol in EVE was added to the mixture and the mixture was allowed to warm slowly to ambient temperature overnight. The mixture was partitioned between saturated aqueous sodium thiosulfate and ether, washed with brine, dried over Na_2SO_4 , and concentrated. Radial chromatography eluting with 10:1 hexane/ethyl acetate afforded the iodo or bromoacetals as pale yellow oils.

Bromoacetal 8a From **5a** (0.54 mmol, 0.121 g), and NBS (2.16 mmol, 0.191 g) by General Procedure A was obtained **8a** (96 mg, 48%) as a pale yellow oil; IR (film, CHCl_3) 2976.0, 1594.0, 1496.0, 1296.0, 1034.0 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.20-7.05 (m, 8H), 6.92-6.88 (m, 2H), 6.62 (t, $J = 5.4$ Hz, 1H), 4.60 (t, $J = 5.5$ Hz, 1H), 4.26-4.17 (m, 2H), 3.45 (dddd, $J = 9.3, 7.1, 7.1, 7.1$ Hz, 1H), 3.20 (dddd, $J = 9.3, 7.1, 7.1, 7.1$ Hz, 1H), 3.19-3.14 (m, 2H), 1.01 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 143.78, 133.57, 129.69, 124.37, 122.44, 101.36, 66.82, 62.26, 31.62, 14.92; MS (CI) m/z (relative intensity) 376 ($[\text{M}-\text{H}]^-$, 15%), 168 (100%). Anal. Calcd for $\text{C}_{18}\text{H}_{21}\text{N}_2\text{O}_2\text{Br}$: C, 57.30; H, 5.61; N, 7.43. Found: C, 57.46; H, 5.62; N, 7.39.

Iodoacetal 9a From **5a** (0.16 mmol, 36 mg) and NIS (0.21 mmol, 72 mg) by General Procedure A was obtained iodoacetal **9a** (32 mg, 47%) as a pale yellow oil; IR (film, CHCl_3) 2975.0, 1594.0, 1496.0, 1097.0 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.20-7.05 (m, 8H), 6.90-6.85 (m, 2H), 6.60 (dd, $J = 5.5, 5.5$ Hz, 1H), 4.50 (dd, $J = 5.5, 5.5$ Hz, 1H), 4.2-4.1 (m, 2H), 3.35 (dddd, $J = 9.3, 7.1, 7.1, 7.1$ Hz, 1H), 3.18 (dddd, $J = 8.9, 6.8, 6.8, 6.8$ Hz, 1H), 2.94 (d, $J = 5.6$ Hz, 2H), 1.0 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 143.79, 133.57, 129.68, 124.36, 122.45, 101.59, 66.54, 61.95, 14.89, 5.07; MS (EI) m/z (relative intensity) 424 (M^+ , 10%), 168 (100%).

Bromoacetal 8b From **5b** (72 mg, 0.30 mmol), and NBS (1.2 mmol, 103 mg) by General Procedure A was obtained the bromoacetal **8b** (40 mg, 36%) as solid white crystals; IR (film, CHCl_3) 2975.0, 1597.0, 1496.0, 1211.0, 1060.0 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.20-7.05 (m, 8H), 6.98-6.93 (m, 2H), 6.53 (dd, $J = 5.2, 5.2$ Hz, 1H), 4.47 (t, $J = 5.5$ Hz, 1H), 3.53 (ddd, $J = 9.3, 6.6, 6.6$ Hz, 1H), 3.40 (ddd, $J = 9.3, 6.6, 6.6$ Hz, 1H), 3.35 (dddd, $J = 9.3, 7.0, 7.0, 7.0$ Hz, 1H), 3.17 (dddd, $J = 9.4, 7.0, 7.0, 7.0$ Hz, 1H), 3.12-3.06 (m, 2H), 2.48 (ddd, $J = 6.6, 6.6, 5.2$ Hz, 2H), 1.0 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 144.40, 135.55, 129.64, 123.96, 122.51, 101.54, 64.26, 61.99, 33.25, 31.52, 14.96; MS (CI) m/z (relative intensity) 390 (M^+ , 10%), 168 (100%).

Iodoacetal 9b. From **5b** (101 mg, 0.42 mmol) and NIS (0.55 mmol, 123 mg) by General Procedure A afforded **9b** as a pale yellow oil (86 mg, 49%); IR (film, CHCl_3) 2974.0, 1590.0, 1496.0, 1211.0, 1058.0 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.2-7.1 (m, 8H), 7.0-6.9 (m, 2H), 6.56 (t, $J = 10.3, 5.1$ Hz, 1H), 4.36 (dd, $J = 5.6, 5.6$ Hz, 1H), 3.5 (ddd, $J = 6.5, 6.5, 6.5$ Hz, 1H), 3.36 (ddd, $J = 9.3, 6.6, 6.6$ Hz, 1H) 3.31 (dddd, $J = 9.3, 7.0, 7.0, 7.0$ Hz, 1H), 3.15 (dddd, $J = 9.2, 7.0, 7.0, 7.0$

Hz, 1H), 2.9 (d, $J = 5.6$ Hz, 2H), 2.44 (ddd, $J = 5.3, 6.6, 6.6$ Hz, 2H), 0.99 (dd, $J = 7.1, 7.1$ Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 144.41, 135.61, 129.64, 123.95, 122.53, 101.74, 63.95, 61.71, 33.22, 14.92, 5.04; MS (CI) m/z (relative intensity) 439 ($[\text{M}+\text{H}]^+$, 40%), 168 (100%).

Bromoacetal 8c. From **5c** (70 mg, 0.292 mmol) and NBS (1.16 mmol, 0.103g) by General Procedure A was obtained bromoacetal **8c** as a pale yellow oil (46 mg, 44%, 1:1 mixture of diastereomers); IR (film, CHCl_3) 2975.9, 1591.6, 1495.6, 1051.9 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.25-7.12 (m, 8H), 6.98-6.93 (m, 2H), 6.59 (d, $J = 6.0$ Hz, 0.5H), 6.54 (d, $J = 6.6$ Hz, 0.5H), 4.82 (dd, $J = 5.9, 4.9$ Hz, 0.5H), 4.70 (dd, $J = 5.5, 5.5$ Hz, 0.5H), 4.59 (m, apparent quintet, $J = 6.5$ Hz, 0.5H), 4.44 (m, apparent quintet, $J = 6.4$ Hz, 0.5H), 3.51 (dddd, $J = 9.3, 7.1, 7.1, 7.1$ Hz, 0.5H), 3.44 (dddd, $J = 9.1, 7.0, 7.0, 7.0$ Hz, 0.5H), 3.36 (dddd, $J = 9.3, 7.1, 7.1, 7.1$ Hz, 0.5H), 3.26-3.16 (m, 2.5H), 1.28 (d, $J = 6.4$ Hz, 1.5H), 1.26 (d, $J = 6.6$ Hz, 1.5H), 1.10 (t, $J = 7.1$ Hz, 1.5H), 1.02 (t, $J = 6.9$ Hz, 1.5H); ^{13}C NMR (125 MHz, C_6D_6) δ 143.87 (2C), 138.72, 138.18, 129.73, 129.68, 124.40, 124.31, 122.44, 122.42, 101.04, 99.97, 73.68, 73.05, 62.03, 61.98, 32.34, 32.33, 19.54, 19.33, 15.15, 14.92; MS (EI) m/z (relative intensity) 390 (M^+ , 10%), 168 (100%).

Iodoacetal 9c. From the hydroxyhydrazone obtained from the TBAF deprotection of **5c** (92 mg, 0.384 mmol), and NIS (112 mg, 0.499 mmol) by General Procedure A was obtained iodoacetal **9c** as a pale yellow oil (59 mg, 38%) (1:1 mixture of diastereomers); IR (film, CHCl_3) 2975.0, 1591.0, 1495.0 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.20-7.08 (m, 8H), 6.95-6.90 (m, 2H), 6.55 (d, $J = 5.9$ Hz, 0.5H), 6.52 (d, $J = 6.7$ Hz, 0.5H), 4.7 (dd, $J = 5.2, 5.2$ Hz, 0.5H), 4.59 (dd, $J = 5.5, 5.2$ Hz, 0.5H), 4.54 (m, apparent quintet, $J = 6.6$ Hz, 0.5H), 4.35 (m, apparent quintet, $J = 6.3$ Hz, 0.5H), 3.45-3.35 (m, 1H), 3.3 (dddd, $J = 8.8, 7.2, 7.2, 7.2$ Hz, 0.5H), 3.17 (dddd, $J = 8.9, 7.1, 7.1, 7.1$ Hz, 0.5H), 3.02-2.95 (m, 2H), 1.24 (d, $J = 6.6$ Hz, 1.5H), 1.21 (d, $J = 6.6$ Hz, 1.5H), 1.06 (t, $J = 7.1$ Hz, 1.5H), 0.98 (t, $J = 7.1$ Hz, 1.5H); ^{13}C NMR (125 MHz, C_6D_6) δ 143.88, 143.87, 138.75, 138.14, 129.74, 129.68, 124.40, 124.30, 122.48, 122.42, 101.23, 100.14, 73.75, 72.81, 61.66, 61.49, 19.53, 19.28, 15.10, 14.89, 6.07, 6.05; MS (CI) m/z (relative intensity) 439 ($[\text{M}+\text{H}]^+$, 15%), 223 (100%).

Bromoacetal 8d. From **5d** (10 mg, 0.039 mmol) and NBS (0.156 mmol, 14 mg) by General Procedure A was obtained bromoacetal **8d** as a pale yellow oil (mixture of diastereomers, 1:1) (7 mg, 44%); IR (film, CHCl_3) 2973.8, 1590.3, 1495.9, 1211.4, 1058.0 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.20-7.10 (m, 6H), 6.95-6.90 (m, 4H), 6.62-6.58 (m, 1H), 4.52-4.48 (m, 1H), 3.67 (m, apparent sextet, $J = 6.1$ Hz, 0.5H), 3.61 (m, apparent sextet, $J = 6.1$ Hz, 0.5H), 3.34-3.12 (m, 2H), 3.10-3.02 (m, 2H), 2.55-2.35 (m, 2H), 1.07 (d, $J = 6.3$ Hz, 1.5H), 1.01 (t, $J = 7.0$ Hz, 1.5H), 0.99 (d, $J = 6.1$ Hz, 1.5H), 0.97 (t, $J = 7.0$ Hz, 1.5H); ^{13}C NMR (125 MHz, C_6D_6) δ 144.47 (2C), 135.69, 135.58, 129.68, 129.62, 124.00, 123.94, 122.51 (2C), 100.99, 99.99, 72.65, 71.56, 61.15, 60.85, 40.30, 39.80, 32.22, 32.04, 20.92, 19.82, 15.06, 15.00; MS (CI) m/z (relative intensity) 405 ($[\text{M}+\text{H}]^+$, 60%), 162 (100%).

Iodoacetal 9d. From **5d** (158 mg, 0.62 mmol) and NIS (0.81 mmol, 182 mg) by General Procedure A was obtained iodoacetal **9d** as a pale yellow oil (127 mg, 44%); IR (film, CHCl_3) 2973.0, 1596.0, 1496.0, 1211.0, 1026.0 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.25-7.15 (m, 8H), 6.95-6.90 (m, 2H), 6.62 (dd, $J = 5.5, 5.5$ Hz, 0.5H), 6.60 (dd, $J = 5.5, 5.5$ Hz, 0.5H), 4.43 (dd, $J = 5.5, 5.5$ Hz, 0.5H), 4.40 (dd, $J = 5.3, 5.3$ Hz, 0.5H), 3.64 (m, apparent sextet, $J = 6.2$ Hz, 0.5H), 3.59 (m, apparent sextet, $J = 6.1$ Hz, 0.5H), 3.31-3.09 (m, 2H), 2.91-2.84 (m, 2H), 2.53-2.33 (m, 2H), 1.07 (d, $J = 6.2$ Hz, 1.5H), 1.01 (t, $J = 7.0$ Hz, 1.5H), 0.99 (d, $J = 6.2$ Hz, 1.5H), 0.98 (t, $J = 7.1$ Hz, 1.5H); ^{13}C NMR (125 MHz, C_6D_6) δ 144.48, 144.47, 135.74 (2C), 129.70, 129.63,

124.00, 123.93, 122.53 (2C), 101.07, 100.08, 72.31, 71.27, 60.81, 60.51, 40.30, 39.72, 20.87, 19.77, 15.01, 14.95, 6.15, 5.76; MS (EI) m/z (relative intensity) 452 (M^+ , 10%) 168 (100%).

General Procedure B: Haloacetal Radical Cyclization to Hydrazones

To a solution of bromoacetal or iodoacetal in benzene (0.02 M, deoxygenated via nitrogen bubbling through a syringe needle for ca. 10 min) was added 2,2'-azobisisobutyronitrile (AIBN, 10 mol%) and Bu_3SnH (1.2 equiv). The reaction mixture was stirred at reflux until all starting material had been consumed (TLC monitoring). If necessary, additional AIBN (10 mol%) was added. The solvent was replaced with ethyl acetate (0.02M) and the mixture was stirred with KF (5 equiv) overnight. The mixture was adsorbed on silica gel, placed on a pad of clean silica gel, and eluted with ethyl acetate. Concentration and radial chromatography (5:1 hexane/ethyl acetate) afforded **10a–10d**.

Furan 10a. From bromoacetal **8a** (29 mg, 0.076 mmol) and Bu_3SnH (25 μ L, 0.091 mmol) by General Procedure B afforded furan **10a** (16 mg, 69% yield, dr 2:1) as a pale yellow oil. From iodoacetal **9a** (102 mg, 0.24 mmol) and Bu_3SnH (80 μ L, 0.29 mmol) by General Procedure B afforded the furan **10a** (48 mg, 68% yield, dr 2:1) as a pale yellow oil; IR (film, $CHCl_3$) 2975.0, 1589.0, 1497.0, 1273.0, cm^{-1} ; 1H NMR (500 MHz, C_6D_6) δ 7.18–7.05 (m, 8H), 6.90–6.85 (m, 2H), 5.29 (dd, $J = 5.5, 2.5$ Hz, 0.7H), 4.96 (dd, $J = 5.5, 1.5$ Hz 0.3H), 3.93 (dd, $J = 8.9, 4.6$ Hz, 0.3H), 3.86–3.69 (m, 3H), 3.53–3.49 (m, 0.7H), 3.43–3.38 (m, 0.3H), 3.37–3.29 (m, 1.7H), 1.84 (ddd, $J = 13.6, 6.8, 2.5$ Hz, 0.7H), 1.78 (ddd, $J = 13.5, 3.3, 1.5$ Hz, 0.3H), 1.73 (ddd, $J = 13.6, 5.4, 3.1$ Hz, 0.7H), 1.66 (ddd, $J = 13.5, 8.0, 5.6$ Hz, 0.3H), 1.16 (t, $J = 2.0$ Hz, 0.9H), 1.09 (t, $J = 7.1$ Hz, 2.1H); ^{13}C NMR (125 MHz, C_6D_6) δ 148.25, 148.00, 129.13, 122.39, 122.32, 120.58, 120.49, 104.20, 103.74, 71.27, 69.73, 62.91, 62.83, 57.08, 56.85, 15.22, 15.18; MS (EI) m/z (relative intensity) 299 ($[M+H]^+$, 100%) 168 (90%).

Pyran 10b. From bromoacetal **8b** (36 mg, 0.096 mmol) and Bu_3SnH (31 μ L, 0.12 mmol) by General Procedure B was obtained pyran **10b** as a colorless solid (13 mg, 44%, dr 2.5:1). From iodoacetal **9b** (213 mg, 0.49 mmol) and Bu_3SnH (0.16 mL, 0.59 mmol) by General Procedure B was obtained pyran **10b** as a colorless solid (101 mg, 70%, dr 2.5:1). Major diastereomer *trans*-**10b**: IR (film, $CHCl_3$) 2928.1, 1588.6, 1496.6, 1123.0 cm^{-1} ; 1H NMR (500 MHz, C_6D_6) δ 7.20–7.10 (m, 8H), 6.88–6.85 (m, 2H), 4.82 (dd, $J = 2.8, 2.8$ Hz, 1H), 3.65–3.55 (m, 2H), 3.52 (ddd, $J = 11.0, 4.2, 4.2$ Hz, 1H), 3.48–3.40 (m, 1H), 3.42 (br s, 1H), 3.25 (dddd, 9.8, 7.1, 7.1, 7.1 Hz, 1H), 1.82 (br d, $J = 12.8$ Hz, 1H), 1.55–1.45 (m, 3H), 1.0 (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 148.70, 129.00, 122.14, 120.47, 96.93, 62.34, 58.26, 49.11, 35.53, 30.86, 14.95; MS (EI) m/z (relative intensity) 312 (M^+ , 35%), 162 (95%) Anal. calcd for $C_{19}H_{24}N_2O_2$: C, 73.05; H, 7.74; N, 8.97. Found: C, 73.02; H, 7.84; N, 8.80. Minor diastereomer *cis*-**10b**: IR (film, $CHCl_3$) 2926.0, 1496.0, 1272.0, 1072.0 cm^{-1} ; 1H NMR (500 MHz,) δ 7.2–7.1 (m, 8H), 6.90–6.85 (m, 2H), 4.1 (dd, $J = 8.4, 2.3$ Hz, 1H), 3.9 (dddd, $J = 9.4, 7.1, 7.1, 7.1$ Hz, 1H), 3.8 (ddd, $J = 11.8, 3.9, 3.7$ Hz, 1H), 3.65–3.60 (br s, 1H), 3.32 (dddd, $J = 9.4, 7.1, 7.1, 7.1$ Hz, 1H), 2.96 (ddd, $J = 11.5, 11.2, 2.7$ Hz, 1H), 2.92–2.85 (m, 1H), 1.87 (br d, $J = 12.5$ Hz, 1H), 1.59 (ddd, $J = 12.4, 10.4, 8.4$ Hz, 1H), 1.46–1.32 (m, 2H), 1.14 (dd, $J = 7.1, 7.1$ Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 148.26, 129.00, 122.16, 120.41, 100.02, 63.59, 61.60, 52.31, 36.51, 30.63, 15.23; MS (EI) m/z (relative intensity) 312 (M^+ , 25%) 192 (100%).

Furan 10c. From bromoacetal **8c** (124 mg, 0.31 mmol) and Bu_3SnH (100 μ L, 0.372 mmol) by General Procedure B was obtained furan **10c** as a pale yellow oil (50 mg, 52%, dr 3:1). From iodoacetal **9c** (92 mg, 0.21 mmol) and Bu_3SnH (68 μ L, 0.252 mmol) by General Procedure B was obtained furan **10c** (42 mg, 64%, dr 3:1); IR (film, $CHCl_3$)

3281.0, 2973.9, 1588.8, 1496.6, 1059.9 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.30-7.05 (m, 8H), 6.95-6.85 (m, 2H), 5.25 (dd, $J = 5.5, 2.7$ Hz, 0.5H), 4.97 (dd, $J = 5.5, 2.0$ Hz, 0.5H), 4.29 (m, apparent quintet, $J = 6.2$ Hz, 0.5H), 4.25 (dddd, $J = 6.5, 6.5, 6.5, 3.4$ Hz, 1H), 3.92 (br s, 0.5H), 3.88-3.80 (m, 1H), 3.50 (br s, 0.5H), 3.43-3.39 (m, 0.5H), 3.38-3.30 (m, 1H), 3.10-3.05 (m, 0.5H), 1.99 (ddd, $J = 13.3, 6.7, 2.7$ Hz, 0.5H), 1.87 (ddd, $J = 13.4, 8.4, 5.5$ Hz, 0.5H), 1.80-1.73 (m, 1H), 1.20 (d, $J = 6.5$ Hz, 1.5H), 1.17 (t, $J = 7.1$ Hz, 1.5H), 1.14 (d, $J = 6.3$ Hz, 0.5H), 1.10 (t, $J = 7.1$ Hz, 0.5H); ^{13}C NMR (125 MHz, C_6D_6) δ 148.30, 148.18, 129.09, 129.04, 122.42, 122.30, 120.52, 120.50, 104.30, 103.02, 79.50, 78.22, 63.60, 63.07, 62.80, 62.68, 38.22 (2C), 21.52, 19.70, 15.21, 15.18; MS (EI) m/z (relative intensity) 312 ($[\text{M}+\text{H}]^+$, 15%), 162 (100%).

Pyran 10d. From bromoacetal **8d** (36 mg, 0.089 mmol) and Bu_3SnH (29 μL , 0.107 mmol) by General Procedure B gave a mixture of diastereomeric pyrans $2\alpha,4\beta\text{-10d}$, $2\beta,4\alpha\text{-10d}$, and $2\beta,4\beta\text{-10d}$ as a pale yellow solid (16 mg, 57%, dr 3:1:1). From iodoacetal **9d** (51 mg, 0.109 mmol) and

Bu_3SnH (35 μL , 0.131 mmol) by General Procedure B was obtained the same mixture of pyrans (15 mg, 41%, dr 3:1:1). Further radial chromatography separated a small amount of $2\beta,4\alpha\text{-10d}$, but the other two were characterized as a mixture. Diastereomeric mixture $2\alpha,4\beta\text{-10d}$ and $2\beta,4\beta\text{-10d}$ (dr 3:1): IR (film, CHCl_3) 3400.0, 2972.5, 1496.7 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.20-7.08 (m, 8H), 6.91-6.85 (m, 2H), 4.82 (d, $J = 3.7$ Hz, 0.75H), 4.09 (dd, $J = 9.6, 2.0$ Hz, 0.25H), 3.96 (dddd, $J = 9.4, 7.1, 7.1, 7.1$ Hz, 0.25H), 3.70 (dddd, $J = 12.3, 6.1, 6.1, 6.1, 2.1$ Hz, 0.75H), 3.58-3.47 (m, 3H), 3.47 (br s, 0.75H), 3.34 (dddd, $J = 9.4, 7.0, 7.0, 7.0$ Hz, 0.25H), 3.23 (dddd, $J = 9.8, 7.0, 7.0, 7.0$ Hz, 0.75H), 3.03 (dddd, $J = 12.4, 6.3, 6.3, 6.3, 2.0$ Hz, 0.25H), 2.95-2.85 (m, 0.25H), 1.91 (dddd, $J = 12.2, 4.0, 2.2, 1.9$ Hz, 0.75H), 1.85 (dddd, $J = 12.8, 3.6, 2.3, 1.7$ Hz, 0.75H), 1.62 (dddd, $J = 12.4, 3.8, 2.1, 1.7$ Hz, 0.75H), 1.57 (ddd, $J = 11.9, 11.9, 9.6$ Hz, 1H), 1.50-1.45 (m, 0.25H), 1.45 (ddd, $J = 12.8, 11.8, 3.7$ Hz, 0.75H), 1.24-1.15 (m, 1H), 1.14 (t, $J = 7.1$ Hz, 0.75H), 1.12 (d, $J = 6.2$ Hz, 0.75H), 1.09 (d, $J = 6.3$ Hz, 2.25H), 1.00 (t, $J = 7.0$ Hz, 2.25H); ^{13}C NMR (125 MHz, C_6D_6) δ 148.76, 129.02, 122.22, 120.48, 97.07, 63.30, 62.13, 38.38, 36.58, 35.22, 21.47, 15.25, (peaks of major diastereomer $2\alpha,4\beta\text{-10d}$ only); MS (EI) m/z (relative intensity) 326 ($[\text{M}+\text{H}]^+$, 20%), 162 (100%). Minor diastereomer $2\beta,4\alpha\text{-10d}$: ^1H NMR (500 MHz, C_6D_6) δ 7.30-7.10 (m, 8H), 6.95-6.90 (m, 2H), 5.08 (dd, $J = 9.4, 2.2$ Hz, 1H), 4.15 (dddd, $J = 12.5, 6.6, 6.6, 6.6, 2.0$ Hz, 1H), 4.10 (dddd, $J = 9.4, 7.1, 7.1, 7.1$ Hz, 1H), 3.55 (dddd, $J = 9.4, 7.1, 7.1, 7.1$ Hz, 1H), 3.23 (br s, 1H), 3.23-3.20 (m, 1H), 1.79 (dddd, $J = 13.7, 2.0, 2.0, 2.0$ Hz, 1H), 1.63 (ddd, $J = 13.7, 9.5, 4.2$ Hz, 1H), 1.39 (dddd, $J = 13.9, 2.0, 2.0, 2.0$ Hz, 1H), 1.22 (d, $J = 6.2$ Hz, 3H), 1.21 (t, $J = 7.0$ Hz, 3H), 1.17 (ddd, $J = 14.3, 11.2, 4.0$ Hz, 1H); MS (EI) m/z (relative intensity) 326 ($[\text{M}+\text{H}]^+$, 6%), 81 (100%).

Furanose 11. To a solution of furan **10c** (68 mg, 0.22 mmol) in THF (3 mL) was added a mixture of aqueous 1N HCl and THF (1:1, 1.8 mL). After 1 h the mixture was extracted with ether, dried over Na_2SO_4 and concentrated. Flash chromatography (10:1 hexane/ethyl acetate $\rightarrow$ 1:1 hexane/EtOAc) afforded **11** (29 mg, 47%) as a yellow oil; IR (film, CHCl_3)

2970.0, 3405.0 (br), 1589.0, 1496.0, 1272.0, 1071.0 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.20-6.85 (m, 10H), 5.47 (ddd, $J = 5.0, 3.3, 3.3$ Hz, 0.4H), 5.41 (dd, $J = 9.5, 4.9$ Hz, 0.6H), 4.46 (dddd, $J = 6.5, 6.5, 6.5, 1.9$ Hz, 0.6H), 4.13 (dddd, $J = 6.4, 6.4, 6.4, 3.7$ Hz, 0.4H), 3.84 (d, $J = 9.6$ Hz, 0.6H), 3.65 (br s, 0.6H), 3.45 (br s, 0.4H), 3.36-3.32 (m, 0.4H), 2.99 (br d, $J = 6.5$ Hz, 0.6H), 2.41 (br d, $J = 3.6$ Hz, 0.4H), 1.82 (ddd, $J = 13.2, 6.5, 3.0$ Hz, 0.4H), 1.7-1.6 (m, 1H), 1.44 (dd, $J = 13.6, 0.7$ Hz, 0.6H), 1.19 (d, $J = 6.5$ Hz, 1.2H), 0.90 (d, $J = 6.4, 1.8$ Hz); ^{13}C NMR (125 MHz, C_6D_6) δ 148.15, 147.78, 129.2, 129.1, 122.77, 122.44, 120.73, 120.49, 99.0, 98.71, 79.49, 78.01, 63.02, 62.43, 38.91, 37.83, 21.67, 20.91; MS

(CI) m/z (relative intensity) 284 ($[M+H]^+$, 100%), 168 (100%); Anal. Calcd for $C_{17}H_{20}N_2O_2$: C, 71.81; H, 7.09; N, 9.85. Found: C, 72.03; H, 7.08; N, 9.85.

Data Used in Assignment of Pyran Configurations

Pyran 10b

Major Diastereomer (trans)

H	δ (ppm)	J (Hz)	ΣJ (Hz)
H_1	4.81	3.5, ca. 2	
H_{2eq}	1.82	12.8, ca. 2, ca. 2	
H_{2ax}	1.52	13.7, 10.6, 3.5	
H_3	3.43		
H_{5eq}	3.53	11.1, 4.2, 3.8	19.1
H_{5ax}	3.59	11.1, 9.2, 4.8	25.1

Minor Diastereomer (cis)

H	δ (ppm)	J (Hz)	ΣJ (Hz)
H_1	4.09	8.4, 2.3	
H_{2eq}	1.87		
H_{2ax}	1.59	12.4, 10.4, 8.4	
H_3	2.88		
H_{5eq}	3.80	11.8, 3.9, 3.7	19.4
H_{5ax}	2.96	11.5, 11.2, 2.7	25.4

Pyran 10d

Major Diastereomer (2 α ,4 β)

H	δ (ppm)	J (Hz)	ΣJ (Hz)
H ₁	4.82	3.7, <2 ^a	
H _{2eq}	1.85	12.8, 3.6, 2.3, 1.7 ^b	20.4
H _{2ax}	1.45	12.8, 11.8, 3.7	28.3
H ₃	3.5 ^a		
H _{4eq}	1.62	12.4, 3.8, 2.1, 1.7 ^b	20.0
H ₅	3.70	12, 6.7, 6.7, 6.7, 1.9	34

^a not resolved ^b four-bond W-coupling

Minor Diastereomer (2 β ,4 β)

H	δ (ppm)	J (Hz)	ΣJ (Hz)
H ₁	4.09	9.6, 2.0	
H _{2eq}	1.91	11.9, 4.5, 2.2, 1.9 ^a	
H _{2ax}	1.57	11.9, 11.9, 9.6	
H ₃	2.90		
H ₅	3.02	12, 6.7, 6.7, 6.7, 1.9	34

^a four-bond W-coupling

Minor Diastereomer (2 β ,4 α)

H	δ (ppm)	J (Hz)	ΣJ (Hz)
H ₁	5.08	9.4, 2.2	
H _{2eq}	1.79	13.7, 2, 2, 2 ^b	
H _{2ax}	1.63	13.7, 9.5, 4.2	
H ₃	3.21		
H _{4eq}	1.39	13.9, 2, 2, 2 ^b	
H ₅	4.15 ^a		34

^a not resolved ^b four-bond W-coupling

References and Notes

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