Stereoselective Synthesis of Tetrahydropyran-4-ones from Dioxinones Catalyzed by Scandium(III) Triflate

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Supporting Information

General Information. All reactions were carried out under a nitrogen atmosphere in flame-dried glassware with magnetic stirring. THF, Et₂O, CH₂Cl₂, DMF and toluene were purified by passage through a bed of activated alumina.¹ CHCl₃ was purified by passage through a pad of alumina prior to use. Reagents were purified prior to use unless otherwise stated following the guidelines of Perrin and Armarego.² Purification of reaction products was carried out by flash chromatography using EM Reagent silica gel 60 (230-400 mesh). Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light and anisaldehyde, ceric ammonium nitrate stain, potassium permanganate, or phosphomolybic acid followed by heating. Melting points were obtained on a Thomas Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on a Bio-Rad Win FT-IR Pro spectrometer. ¹H-NMR spectra were recorded on a Varian Inova 500 (500 MHz) or Mercury 400 (400 MHz) spectrometer and are reported in ppm using solvent as an internal standard (CDCl₃ at 7.26 ppm). Data are reported as (ap = apparent, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad; coupling constant(s) in Hz; integration. Proton-decoupled ¹³C-NMR spectra were recorded on a Varian Inova 500 (125 MHz) or Mercury 400 (100 MHz) spectrometer and are reported in ppm using solvent as an internal standard (CDCl₃ at 77.0 ppm). Electrospray mass spectra (ESI-MS) were obtained using Micromass Quattro II Triple Quadrupole Mass Spectrometer.

General Procedure for Sc(OTf)₃-catalyzed cyclizations:

A 10 mL round bottom flask was charged with powdered CaSO₄ (3 mmol, 15 equiv) and flame-dried prior to use. Sc(OTf)₃ (0.02 mmol, 0.1 equiv) was added to the flask followed by CH₂Cl₂ (1 mL). The aldehyde (0.21 mmol, 1.05 equiv) was added and the mixture was cooled to -10 °C. To this solution was added β-hydroxy-dioxinone (0.2 mmol, 1 equiv) in CH₂Cl₂ (0.5 mL). The reaction was allowed to stir for 4-24 hours before being quenched by the addition of brine (5 mL) and filtered through a short pad of Celite eluting with CH₂Cl₂. The layers were separated and aqueous layer was extracted with EtOAc (3 x 2 mL). The combined organic layers were

1. Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometal.* **1996**, *15*, 1518-1520.
2. Perrin, D. D. and Armarego, W. L. *Purification of Laboratory Chemicals*; 3rd Ed., Pergamon Press, Oxford. 1988.

dried over Na₂SO₄, filtered, concentrated in vacuo, and purified by flash chromatography to afford cyclized products **3a**, **5-14**.

General Procedure for One-pot cyclization/Ring Opening:

A 10 mL round bottom flask was charged with powdered CaSO₄ (3 mmol, 15 equiv) and flame-dried prior to use. Sc(OTf)₃ (0.04 mmol, 0.2 equiv) was added to the flask followed by CH₂Cl₂ (1 mL). The aldehyde (0.21 mmol, 1.05 equiv) was added and the mixture was brought to -10 °C. To this solution was added β-hydroxy-dioxinone (0.2 mmol, 1 equiv) in CH₂Cl₂ (0.5 mL). The reaction was allowed to stir until the β-hydroxy-dioxinone was consumed as visualized by TLC (1-5 hours) at which time the reaction was warmed to 0 °C and KOEt (0.8 mmol, 4 equiv) was added in one portion. The resulting solution stirred at 0 °C for 30 minutes and room temperature for 4 hours before being quenched by the addition of brine (5 mL) and filtered through a pad of Celite. The aqueous layer was extracted with EtOAc (3 x 3 mL) and the combined organic layers were dried over Na₂SO₄, filtered and concentrated in vacuo. The residue was purified by flash chromatography to afford tetrahydropyran-4-ones **15-20**.

Preparation of β-hydroxy-dioxinone **1a**:

To a -78 °C solution of silyl dienol ether³ (600 mg, 2.34 mmol), and hydrocinnamaldehyde (0.1 mL, 0.76 mmol), in CH₂Cl₂ (4 mL) was added BF₃·OEt₂ (0.3 mL, 2.34 mmol) drop-wise over 2 minutes. Reaction was allowed to stir for 4 hours and was quenched with pH 7.0 phosphate buffer (8 mL). The resulting mixture was extracted with EtOAc (3 x 3 mL) and the combined organic layers were dried over Na₂SO₄, filtered, concentrated, and purified by flash chromatography to afford **1a**. All additional β-hydroxy-dioxinones were prepared in the same manner.

(5,7cis)-7,8-dihydro-2,2-dimethyl-5,7-diphenethylpyrano[4,3-d][1,3]dioxin-4(5H)-one: Purified with 30% ethyl acetate/hexanes, yielding 78 mg (85%) of **3a** as a yellow oil. *R_f* = 0.61 (30% ethyl acetate/hexanes); IR (film) 3079, 3059, 3026, 2999, 2927, 2858, 1724, 1647, 1495, 1452, 1403 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.33-7.21 (m, 10H); 4.43 (m, 1H), 3.51 (m, 1H); 2.88 (m, 2H); 2.79 (m, 2H); 2.50 (m, 1H); 2.22 (m, 1H); 1.98 (m, 2H); 1.85 (m, 2H); 1.70 (s, 3H); 1.69 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 163.7, 159.2, 142.3, 141.6, 128.8, 128.7, 128.6, 128.5, 126.2, 125.9, 105.9, 105.1, 72.6, 71.5, 37.2, 35.9, 33.8, 31.7, 28.4, 27.8, 22.4; LRMS (ESI): Mass calculated for C₂₅H₂₈O₄ [M+Na]⁺, 415.1. Found 415.7.

3. Denmark, S. E.; Beutner, G. L. *J. Am. Chem. Soc.* **2003**, *125*, 7800-7801.

(5,7cis)-5-hexyl-7,8-dihydro-2,2-dimethyl-7-diphenethylpyrano[4,3-d][1,3]dioxin-4(5H)-one: Purified with 30% ethyl acetate/hexanes, yielding 54 mg (80%) of **5** as a yellow oil. R_f = 0.74 (30% ethyl acetate/hexanes); IR (film) 3061, 3026, 2997, 2927, 2857, 1727, 1650, 1495, 1403 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.30-7.18 (m, 5 H); 4.35 (m, 1H); 3.44 (m, 1H); 2.80 (m, 1H); 2.74 (m, 1H); 2.18-2.04 (m, 2H); 1.94 (m, 1H); 1.80 (m, 1H); 1.68 (s, 3H); 1.66 (s, 3H); 1.58 (m, 4H); 1.47 (m, 2H); 1.30 (m, 4H); 0.89 (m, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 163.7, 159.8, 141.7, 128.7, 128.6, 126.2, 105.8, 105.5, 73.3, 71.3, 37.1, 34.2, 33.7, 32.2, 31.6, 29.5, 27.8, 25.5, 25.4, 22.9, 22.4; LRMS (ESI): Mass calculated for $\text{C}_{23}\text{H}_{32}\text{O}_4$ $[\text{M}+\text{Na}]^+$, 395.5 Found 395.1.

(5,7cis)-7,8-dihydro-2,2-dimethyl-7-phenethyl-5-phenylpyrano[4,3-d][1,3]dioxin-4(5H)-one: Purified with 30% ethyl acetate/hexanes, yielding 78 mg (71%) of **6** as a yellow oil. R_f = 0.48 (30% ethyl acetate/hexanes); IR (film) 3030, 2999, 2936, 2858, 1729, 1652, 1403, 1275 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) 7.45-7.11 (m, 10H); 5.36 (s, 1H); 3.69 (m, 1H); 2.76 (m, 2H); 2.44-2.24 (m, 2H); 2.02 (m, 1H); 1.86 (m, 1H); 1.69 (s, 3H); 1.68 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 163.6, 159.2, 142.0, 140.1, 128.8, 128.7, 128.6, 128.5, 128.3, 126.3, 106.2, 76.1, 72.4, 36.8, 33.7, 31.5, 27.8, 22.9; LRMS (ESI): Mass calculated for $\text{C}_{23}\text{H}_{24}\text{O}_4$ $[\text{M}+\text{Na}]^+$, 387.4 Found 387.0.

(5,7cis)-5-(4-chlorophenyl)-7,8-dihydro-2,2-dimethyl-7-phenethylpyrano[4,3-d][1,3]dioxin-4(5H)-one: Purified with 30% ethyl acetate/hexanes, yielding 56 mg (73%) of **7** as a yellow oil. R_f = 0.54 (30% ethyl acetate/hexanes); IR (film) 3059, 3027, 2997, 2938, 2858, 1728, 1649, 1403, 1275, 1202 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) 7.38-7.16 (m, 9H); 5.32 (s, 1H); 3.68 (m, 1H); 2.77 (m, 2H); 2.38-2.24 (m, 2H); 2.03 (m, 1H); 1.86 (m, 1H); 1.66 (s, 3H); 1.65 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 163.8, 159.1, 141.3, 139.1, 134.2, 129.6, 128.8, 128.7, 128.6, 126.3, 106.4, 105.1, 75.4, 72.5, 36.8, 33.6, 31.6, 27.8, 22.9; LRMS (ESI): Mass calculated for $\text{C}_{23}\text{H}_{23}\text{ClO}_4$ $[\text{M}+\text{Na}]^+$, 422.3 Found 422.1.

(5,7cis)-5-(4-fluorophenyl)-7,8-dihydro-2,2-dimethyl-7-phenethylpyrano[4,3-d][1,3]dioxin-4(5H)-one: Purified with 30% ethyl acetate/hexanes, yielding 59 mg (83%) of **8** as a yellow oil. R_f = 0.56 (30% ethyl acetate/hexanes); IR (film) 3060, 2999, 2935, 2858, 1728, 1649, 1510, 1400, 1275, 1219 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) 7.40-7.03 (m, 9H); 5.34 (s, 1H); 3.69 (m, 1H); 2.80-2.72 (m, 2H); 2.38-2.25 (m, 2H); 2.01-1.98 (m, 1H); 1.86-1.85 (m, 1H); 1.67

(s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 163.8, 159.1, 141.9, 136.5, 130.0, 129.9, 128.8, 128.7, 126.3, 115.6, 115.5, 106.3, 105.3, 75.4, 72.3, 36.9, 33.6, 31.5, 27.6, 22.9; LRMS (ESI): Mass calculated for $\text{C}_{23}\text{H}_{23}\text{FO}_4$ $[\text{M}+\text{Na}]^+$, 405.3 Found 405.2

(5,7cis)-7,8-dihydro-5-(4-methoxyphenyl)-2,2-dimethyl-7-phenethylpyrano[4,3-d][1,3]dioxin-4(5H)-one: Purified with 30% ethyl acetate/hexanes, yielding 44 mg (54%) of **9** as a yellow oil. R_f = 0.35 (30% ethyl acetate/hexanes); IR (film) 2931, 2859, 1728, 1652, 1512, 1403, 1273, 1248 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) 7.36-7.26 (m, 3H); 7.23-7.18 (m, 4H); 6.92-6.89 (m, 2H); 5.32 (s, 1H); 3.80 (s, 3H); 3.67 (m, 1H); 2.80 (m, 2H); 2.40 (m, 1H); 2.27 (m, 1H); 1.99 (m, 1H); 1.77 (m, 1H); 1.69 (s, 3H); 1.67 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 163.5, 159.7, 158.9, 141.6, 132.8, 129.3, 128.7, 128.6, 128.5, 126.2, 114.1, 106.2, 75.6, 72.3, 55.5, 36.8, 33.7, 31.5, 27.8, 22.8; LRMS (ESI): Mass calculated for $\text{C}_{24}\text{H}_{26}\text{O}_5$ $[\text{M}+\text{Na}]^+$, 417.4 Found 417.0

(5,7cis)-7,8-dihydro-2,2-dimethyl-5-(naphthalene-3-yl)-7-phenethylpyrano[4,3-d][1,3]dioxin-4(5H)-one: Purified with 30% ethyl acetate/hexanes, yielding 62 mg (81%) of **10** as a yellow oil. R_f = 0.43 (30% ethyl acetate/hexanes); IR (film) 3057, 2998, 2930, 2858, 1727, 1651, 1403, 1267, 1403, 1267, 1203 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) 7.95-7.20 (m, 12H); 5.55 (s, 1H); 3.77-3.74 (m, 1H); 2.83-2.75 (m, 2H); 2.41-2.29 (m, 2H); 2.06-2.02 (m, 2H); 1.71 (s, 3H); 1.68 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 163.6, 141.5, 137.8, 133.6, 133.5, 128.8, 128.7, 128.5, 128.4, 128.3, 128.0, 127.8, 126.3, 126.2, 126.1, 125.5, 106.2, 76.2, 72.4, 36.9, 33.7, 31.5, 27.8, 22.8; LRMS (APCI): Mass calculated for $\text{C}_{27}\text{H}_{26}\text{O}_4$ $[\text{M}]^+$, 414.5 Found 415.1

(5,7s)-5-(3-(benzyloxy)propyl)-7,8-dihydro-2,2-dimethyl-5-phenethyl-7-phenethylpyrano[4,3-d][1,3]dioxin-4(5H)-one: Purified with 30% ethyl acetate/hexanes, yielding 64 mg (80%) of **13** as a yellow oil. R_f = 0.50 (30% ethyl acetate/hexanes); IR (film) 2929, 2856, 1724, 1647, 1403, 1267, 1204, 1101 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) 7.36-7.17 (m, 10H); 4.53 (s, 2H); 4.41-4.40 (d, 1H); 3.55-3.44 (m, 3H); 2.81-2.78 (m, 1H); 2.75-2.71 (m, 1H); 2.18-2.10 (m, 3H); 1.93-1.73 (m, 5H); 1.68 (s, 3H); 1.66 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 163.9, 159.7, 141.6, 138.8, 128.7, 128.6, 128.5, 127.9, 127.7, 126.2, 105.9, 105.0, 73.1, 72.9, 71.3, 70.7, 37.0, 33.7, 31.1, 30.7, 27.7, 25.7, 22.4; LRMS (APCI): Mass calculated for $\text{C}_{27}\text{H}_{32}\text{O}_5$ $[\text{M}+\text{H}]^+$, 436.5 Found 437.0

(5,7*cis*)-7,8-dihydro-2,2-dimethyl-5-phenethyl-7-phenylpyrano[4,3-*d*][1,3]dioxin-4(5*H*)-one: Purified with 30% ethyl acetate/hexanes, yielding 48 mg (64%) of **13** as a yellow oil. R_f = 0.57 (30% ethyl acetate/hexanes); IR (film) 3061, 3028, 2998, 2926, 2855, 1725, 1650, 1402, 1271, 1204 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) 7.44-7.16 (m, 10H); 4.67 (m, 2H); 2.86 (m, 2H); 2.50 (m, 3H); 2.10 (m, 1H); 1.73 (s, 3H); 1.72 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 163.6, 159.6, 142.4, 140.9, 128.9, 128.8, 128.5, 128.2, 125.9, 125.8, 106.3, 104.9, 74.2, 73.1, 35.9, 35.5, 31.5, 27.6, 22.5; LRMS (ESI): Mass calculated for $\text{C}_{23}\text{H}_{24}\text{O}_4$ $[\text{M}+\text{Na}]^+$, 387.2 Found 387.4

(5,7*cis*)-7-cyclohexyl-7,8-dihydro-2,2-dimethyl-5-phenethylpyrano[4,3-*d*][1,3]dioxin-4(5*H*)-one: Purified with 30% ethyl acetate/hexanes, yielding 52 mg (70%) of **14** as a yellow oil. R_f = 0.67 (30% ethyl acetate/hexanes); IR (film) 3060, 3026, 2998, 2926, 2853, 1727, 1649, 1402, 1267, 1203 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) 7.28-7.16 (m, 5H); 4.36 (m, 1H); 3.25 (m, 1H); 2.82 (m, 1H); 2.78 (m, 1H); 2.43 (m, 1H); 2.21-2.05 (m, 2H); 1.88-1.71 (m, 2H); 1.68 (s, 6H); 1.58-1.02 (m, 10H); ^{13}C NMR (125 MHz, CDCl_3) δ 164.4, 159.1, 142.4, 128.8, 128.5, 125.9, 105.9, 105.2, 72.6, 42.6, 35.8, 31.6, 31.4, 29.0, 28.1, 27.6, 26.7, 26.2, 26.0, 22.4; LRMS (ESI): Mass calculated for $\text{C}_{23}\text{H}_{30}\text{O}_4$ $[\text{M}+\text{Na}]^+$, 393.2 Found 393.4

Note: For tetrahydropyran-4-ones **15-20** the reported ^{13}C NMR reflects a mixture of keto:enol tautomers. For ^1H spectra, the major constituent (keto tautomer) is reported.

Tetrahydropyran-4-one 15: Purified with 15% EtOAc/hexanes, yielding 88 mg (78%) of **15** as a yellow oil. R_f = 0.55 (25% ethyl acetate/hexanes); IR (film) 3026, 2926, 2861, 1741, 1716, 1651, 1603, 1494, 1452, 1126 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) major:keto tautomer δ 7.32-7.21 (m, 10 H); 4.20 (m, 2H); 3.87 (m, 1H); 3.60 (m, 1H); 3.26 (d, J = 10.7 Hz, 1H); 2.99 (m, 1H); 2.89 (m, 1H); 2.79 (m, 2H); 2.42-2.20 (m, 2H); 2.06-1.81 (m, 4H); 1.26 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 202.3, 170.9, 168.3, 141.5, 141.4, 128.9, 128.7, 128.6, 128.4, 126.4, 125.4, 77.7, 75.9, 72.2, 70.9, 63.4, 61.4, 60.6, 47.6, 38.1, 36.9, 35.9, 31.9, 32.0, 31.7, 31.3, 14.3; LRMS (APCI): Mass calculated for $\text{C}_{24}\text{H}_{28}\text{O}_4$ $[\text{M}]^+$, 380.2. Found 380.9.

Tetrahydropyran-4-one 16: Purified with 15% diethyl ether/hexanes, yielding 72 mg (72%) of **16** as a yellow oil. R_f = 0.60 (25% ethyl acetate/hexanes); IR (film) 3061, 3026, 2926, 2853, 1741, 1716, 1653, 1604, 1450 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) major:keto tautomer δ 7.30-7.18(m, 5H); 4.16 (m, 2H); 3.80 (m 1H); 3.38 (m, 1H); 3.23 (d, J = 10.6 Hz, 1H); 2.94 (m, 1H); 2.77 (m, 1H); 2.52 (m, 2H); 2.05 (m, 1H); 1.9-1.4 (m, 12H); 1.26 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 203.3, 171.4, 168.3, 142.9, 141.6, 128.8, 128.7, 128.4, 126.2, 125.7, 81.3, 76.5, 72.2, 63.7, 63.7,

61.3, 60.5, 45.0, 43.4, 42.6, 36.9, 33.1, 31.8, 31.2, 29.2, 29.0, 28.7, 26.7, 26.6, 26.1, 22.9, 14.3; LRMS (ESI): Mass calculated for $C_{22}H_{30}O_4$ $[M+Na]^+$, 381.1. Found 381.1

Tetrahydropyran-4-one 17: Purified with 15% diethyl ether/hexanes, yielding 63 mg (60%) of **17** as a yellow oil. R_f = 0.50 (25% ethyl acetate/hexanes); IR (film) 3027, 2980, 2928, 2865, 1742, 1716, 1653, 1494, 1452, 1263 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) major:keto tautomer δ 7.49-7.15 (m, 10H); 4.74 (dd, J = 2.4, 11.5 Hz, 1H); 4.20 (m, 2H); 4.09 (m 1H); 3.41 (d, J = 10.7 Hz, 1H); 2.97 (m, 1H); 2.81 (m, 2H); 2.60 (m, 1H); 2.04 (m, 2H); 1.25 (t, J = 7.0, Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.0, 168.2, 141.5, 140.5, 128.9, 128.7, 128.4, 126.3, 125.9, 125.7, 78.5, 78.0, 63.2, 61.5, 48.9, 36.8, 31.7, 14.4; LRMS (ESI): Mass calculated for $C_{22}H_{24}O_4$ $[M+Na]^+$, 375.2. Found 375.1.

Tetrahydropyran-4-one 18: Purified with 20% diethyl ether/hexanes, yielding 42 mg (67%) of **18** as a yellow oil. R_f = 0.45 (25% ethyl acetate/hexanes); IR (film) 3028, 2980, 2931, 2864, 1744, 1716, 1653, 1494, 1452 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) major:keto tautomer δ 7.44-7.12 (m 10H); 4.89 (d, J = 10.4 Hz, 1H); 4.10 (m, 2H); 3.84 (m, 1H); 3.60 (d, J = 10.4 Hz, 1H); 2.79 (m, 2H); 2.55-2.32 (m, 2H); 1.97-1.80 (m, 2H); 1.26 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz) δ 202.0, 185.2, 170.6, 167.6, 141.3, 139.0, 128.9, 128.8, 128.7, 128.6, 128.4, 128.3, 128.0, 127.1, 126.3, 126.0, 81.0, 76.8, 76.4, 72.3, 64.7, 61.3, 60.3, 47.9, 47.2, 37.8, 36.9, 35.3, 31.4, 14.2; LRMS (ESI): Mass calculated for $C_{22}H_{24}O_4$ $[M+Na]^+$, 375.2. Found 375.0.

Tetrahydropyran-4-one 19 Purified with 20% diethyl ether/hexanes, yielding 80 mg (82%) of **19** as an oil. R_f = 0.48 (25% ethyl acetate/hexanes); IR (film) 3061, 3027, 2924, 2862, 1743, 1716, 1653, 1603, 1494, 1452, 1336, 1257, 1124 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) major:keto tautomer δ 7.39-7.06 (m, 15H); 5.25 (d, A of AB system, J = 12.2 Hz, 1H); 5.14 (d, B of AB system, J = 12.2 Hz, 1H); 3.88 (m, 1H); 3.62 (m 1H); 3.32 (d, J = 10.7 Hz, 1H); 2.92 (m 2H); 2.74 (m, 2H); 2.47-2.20 (m, 2H); 2.00-1.80 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.1, 168.1, 141.4, 141.3, 135.6, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 126.7, 126.2, 77.8, 76.0, 67.2, 63.5, 47.4, 38.1, 36.8, 31.9, 31.7; LRMS (APCI): Mass calculated for $C_{29}H_{30}O_4$ $[M-H]^+$, 441.5. Found 441.1.

Tetrahydropyran-4-one 20 Purified with 10% diethyl ether/hexanes, yielding 88 mg (72%) of **20** as an oil. R_f = 0.53 (25% ethyl acetate/hexanes); IR (film) 3061, 3026, 2952, 2923, 2862, 1739, 1715, 1651, 1604 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) major:keto tautomer δ 7.33-7.18 (m, 10 H); 4.24 (m, 2H); 3.88 (m, 1H); 3.64 (m, 1H); 3.25 (d, J = 10.4 Hz, 1H); 3.02-2.75 (m, 4H); 2.47-2.28 (m, 2H); 2.06-1.81 (m, 4H); 0.89 (t, 2H); 0.05 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.1, 171.3, 170.7, 168.4, 142.8, 142.0, 141.5,

141.4, 140.2, 128.8, 128.7, 128.6, 128.5, 126.2, 126.1, 125.8, 100.8, 81.3, 77.8, 75.9, 72.3, 70.9, 63.8, 63.5, 62.9, 47.5, 38.1, 37.2, 36.9, 35.6, 31.9, 31.8, 31.7, 22.9, 17.7, 14.3, -1.2; LRMS (ESI): Mass calculated for $C_{27}H_{36}O_4Si$ $[M+Na]^+$, 475.3. Found 475.1.

Preparation of tetrahydropyran-4-one **21**:

A solution of **3a** (120 mg, 0.30 mmol) in DMSO (4 mL) and H_2O (0.5 mL) was heated to 130 °C (bath temperature) for 14 hours. The mixture was then cooled to room temperature and diluted with brine (10 mL) and extracted with EtOAc (3 x 3mL). The combined organic layers were filtered, concentrated and purified by flash chromatography (15% ethyl acetate/hexanes) to yield 67 mg (71%) of **21** as a clear oil. R_f = 0.40 (25% ethyl acetate/hexanes); IR (film) 3061, 3028, 2924, 2856, 1717, 1494, 1452 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 7.32-7.19 (m, 10H); 3.54 (m, 2H); 2.91 (m, 2H); 2.78 (m, 2H); 2.37-2.25 (m, 4H); 2.05 (m, 2H); 1.82 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.5, 141.7, 128.7, 128.6, 126.3, 76.0, 48.2, 38.3, 31.9; LRMS (EI): Mass calculated for $C_{21}H_{24}O_2$ $[M]^+$, 308.2. Found 308.0.

Preparation of Amide **22**:

A solution of **3a** (75 mg, 0.20 mmol) and benzyl amine (0.4 mL, 3.68 mmol) in xylenes was vented and submerged into an oil bath that had been preheated to 150 °C. The reaction stirred for 1 hour before being concentrated *in vacuo*. The crude oil was purified by flash chromatography (30% ethyl acetate/hexanes) to yield 53 mg (63%) of **22** as an oil. R_f = 0.36 (25% ethyl acetate/hexanes); IR (film) 3062, 3026, 2923, 2862, 1718, 1643, 1554, 1496, 1452, 1349 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) major:keto tautomer δ 7.40-7.15 (m, 15H); 6.17 (s, 1H); 4.51 (dd, A of AB system, J = 5.7, 14.9 Hz, 1H); 4.40 (dd, B of AB system, J = 5.7, 14.9 Hz, 1H); 3.97 (m, 1H); 3.65 (m, 1H); 3.00 (d, J = 10.1 Hz, 1H); 2.99 (m, 1H); 2.88 (m, 1H); 2.78 (m, 2H); 2.43 (m, 1H); 2.26 (m, 1H); 2.00 (m, 2H); 1.90 (m, 1H); 1.80 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.1, 167.2, 141.7, 141.5, 138.1, 128.9, 128.8, 128.7, 128.6, 127.9, 127.7, 126.3, 126.2, 78.3,

75.6, 63.7, 47.5, 43.8, 38.1, 36.9, 32.0, 31.8; LRMS (ESI): Mass calculated for $C_{29}H_{31}NO_3 [M]^+$, 442.3 Found 442.1.

Preparation of enantioenriched 1a:

Enantioenriched β -hydroxy dioxinone **1a** was prepared by the procedure previously reported by Denmark.³ Enantiomeric excess was determined by analytic HPLC analysis (Chiralcel OD-H, 70:30 Hexanes/ i -PrOH, 1 mL/min, 254 nm): (*5R*) enantiomer t_r = 8.7 min (major), (*5S*) enantiomer t_r = 6.4 min (minor).

³ Denmark, S. E.; Beutner, G. L. *J. Am. Chem. Soc.* **2003**, *125*, 7800-7801.