Diastereoselective Mukaiyama Aldol Reaction of 2-(Trimethylsilyloxy)furan Catalyzed by Bismuth Triflate

Thierry Ollevier,* Jean-Emmanuel Bouchard, and Valerie Desyroy

Département de chimie, Université Laval, Québec (Québec), Canada G1K 7P4
thierry.ollevier@chm.ulaval.ca

Supporting Information

Contents:

Experimental Section S-2 to S-8
Copies of $^1$H NMR and $^{13}$C NMR spectra for compounds 3a-n, 3n’ S-9 to S-38
Experimental section

General: Infrared spectra were recorded on a FT infrared spectrometer and are reported in reciprocal centimeters (cm\(^{-1}\)). \(^1\)H, \(^{13}\)C, and \(^{19}\)F spectra were recorded on a 400 MHz magnetic resonance spectrometer in CDCl\(_3\). For \(^1\)H NMR, tetramethylsilane (TMS) served as internal standard (\(\delta = 0\)) and data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublet, dt = doublet of triplet, t = triplet, m = multiplet, and br = broad), coupling constant in Hz, integration, and assignment. For \(^{13}\)C NMR, CDCl\(_3\) was used as internal standard (\(\delta = 77.0\)) and spectra were obtained with complete proton decoupling. For \(^{19}\)F NMR, CFCl\(_3\) was used as internal standard (\(\delta = 0\)). Column chromatography was performed on silica gel (230–400 mesh) and analytical thin-layer chromatography was carried out using 250 \(\mu\)m commercial silica gel plates. Visualization of the developed chromatogram was performed by UV absorbance or aqueous potassium permanganate.

Typical Procedure for the Bismuth Triflate-Catalyzed Mukaiyama Aldol Reaction with Aromatic Aldehydes: To a solution of the aldehyde (0.71 mmol) in diethyl ether (0.5 mL), was added Bi(OTf)\(_3\)•4H\(_2\)O (0.007 mmol). The mixture was brought to \(-78^\circ\)C, stirred at this temperature for 0.25 h, and a solution of \(2-(\)trimethylsilyloxy)furan \(2a\) (0.85 mmol) in diethyl ether (0.5 mL) was added dropwise. The mixture was stirred at \(-78^\circ\)C until the reaction was completed as indicated by TLC. The reaction was diluted with tetrahydrofuran (1.0 mL) and quenched with 10% aqueous HCl (1.0 mL). The mixture was stirred for 0.25 h at room temperature, neutralized by addition of a saturated aqueous NaHCO\(_3\) solution, and extracted with ethyl acetate. The organic phases were combined, dried over Na\(_2\)SO\(_4\) and concentrated under reduced pressure (rotary evaporator). The \(\text{syn/anti}\) ratio of the product was determined by \(^1\)H NMR analysis of the crude reaction mixture. The relative configurations of the product was assigned according to the literature.\(^1\) The crude product was purified by silica gel chromatography (ethyl acetate/hexane). \(3a, 3d, 3e, 3h, \text{and } 3j\) accord exactly with those that have been previously reported in the literature.\(^1,2,3\)

![OH](https://example.com/image.png)

**3asyn**

5-(Hydroxy(phenyl)methyl)furan-2(5H)-one (3a):\(^1\) Reagents: benzaldehyde (75 mg, 0.71 mmol), \(2-(\)trimethylsilyloxy)furan \(2a\) (133 mg, 0.85 mmol), and Bi(OTf)\(_3\)•4H\(_2\)O (5.0 mg, 0.007 mmol). The reaction was stirred for 0.5 h at \(-78^\circ\)C and quenched according to the typical procedure. The \(\text{syn/anti}\) ratio (94:6) was determined by \(^1\)H NMR analysis of the crude product (\(\delta\) major: 4.71 ppm, \(\delta\) minor: 5.10 ppm). The crude product was then purified on silica gel (25% ethyl acetate/hexane) to afford 122 mg (91%) of 3a as two separated diastereoisomers: Syn diastereoisomer: mp 57 \(^\circ\)C (white solid); \(R_f = 0.26\) (30% ethyl acetate/hexane); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.36–7.42\) (m, 5H), 7.18 (dd, \(J = 5.8, 1.6\) Hz, 1H) 6.13 (dd, \(J = 5.8, 2.0\) Hz, 1H), 5.17 (dt, \(J = 7.1, 1.6\) Hz, 1H), 4.71 (d, \(J = 7.1\) Hz, 1H), 2.73 (br s, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 172.6, 153.2, 137.9, 129.2, 129.1, 126.9, 123.3, 87.1, 76.0\); IR (film): 3438, 3098, 2958, 2867, 1720, 1604, 1511, 1450, 1362, 1294, 1155, 1032, 947, 843, 780 cm\(^{-1}\).
Anti diastereoisomer: $R_f = 0.28$ (30% ethyl acetate/hexane); $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.34$–7.42 (m, 6H), 6.20 (dd, $J = 5.8$, 2.0 Hz, 1H), 5.19 (dt, $J = 3.6$, 1.8 Hz, 1H), 5.10 (t, $J = 4.2$ Hz, 1H), 2.45 (br s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 173.2$, 152.9, 139.1, 129.0, 128.8, 126.3, 123.5, 86.7, 73.4. IR (film): 3438, 1764 cm$^{-1}$.

5-(Hydroxy(4-toly)methyl)furan-2(5H)-one (3b): Reagents: $p$-tolualdehyde (85 mg, 0.71 mmol), 2-(trimethylsilyloxy)furan 2a (133 mg, 0.85 mmol), and Bi(OTf)$_3$•4H$_2$O (5.0 mg, 0.007 mmol). The reaction was stirred for 1 h at –78 $^\circ$C and quenched according to the typical procedure. The syn/anti ratio (94:6) was determined by $^1$H NMR analysis of the crude product ($\delta$ major: 4.66 ppm, $\delta$ minor: 5.03 ppm). The residue was purified by silica gel chromatography (25% ethyl acetate/hexane) to afford 130 mg (90%) of 3b as a mixture of unseparable diastereoisomers: $R_f = 0.20$ (30% ethyl acetate/hexane); $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.37$ (dd, $J = 5.9$, 1.6 Hz, 1H (anti)), 7.25 (d, $J = 7.6$ Hz, 2H), 7.21 (d, $J = 7.6$ Hz, 2H), 7.13 (dd, $J = 5.9$, 2.0 Hz, 1H (anti)), 6.17 (dd, $J = 5.9$, 2.0 Hz, 1H (syn)), 6.12 (dd, $J = 5.9$, 2.0 Hz, 1H (syn)), 5.13–5.16 (m, 2H), 5.03 (m, 1H (anti)), 4.66 (d, $J = 7.2$ Hz, 1H (syn)), 2.77 (br s, 1H), 2.36 (s, 3H); $^{13}$C (100 MHz, CDCl$_3$): $\delta = 172.6$, 153.4, 139.1, 134.9, 129.7, 126.9, 123.2, 87.2, 75.8, 21.5; IR (KBr): 3411, 1742 cm$^{-1}$; HRMS: Calcd for C$_{12}$H$_{12}$O$_3$ (M$^+$) 204.0786, found 204.0782.

5-(Hydroxy(4-methoxyphenyl)methyl)furan-2(5H)-one (3d):$^2$ Reagents: $p$-anisaldehyde (100 mg, 0.73 mmol), 2-(trimethylsilyloxy)furan 2a (138 mg, 0.88 mmol), and Bi(OTf)$_3$•4H$_2$O (5.0 mg, 0.0072 mmol). The reaction was stirred at –78 $^\circ$C for 0.5 h and quenched according to the typical procedure. The syn/anti ratio (90:10) was determined by $^1$H NMR analysis of the crude product ($\delta$ major: 4.65 ppm, $\delta$ minor: 5.00 ppm). The crude product was then purified on silica gel (30% to 50% ethyl acetate/hexane) to afford 136 mg (84%) of 3d as a mixture of unseparable diastereoisomers: $R_f = 0.25$ (40% ethyl acetate/hexane); $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.38$ (dd, $J = 5.9$, 1.6 Hz, 1H (anti)), 7.30 (d, $J = 8.4$ Hz, 2H), 7.16 (dd, $J = 5.9$, 1.6 Hz, 1H (syn)), 6.91 (d, $J = 8.4$ Hz, 2H), 6.18 (dd, $J = 5.9$, 2.0 Hz, 1H (anti)), 6.12 (dd, $J = 5.9$, 2.0 Hz, 1H (syn)), 5.15 (dt, $J = 6.8$, 1.2 Hz, 2H (syn)), 5.00 (dd, $J = 7.1$, 2.7 Hz, 1H (anti)), 4.65 (dd, $J = 7.1$, 2.7 Hz, 1H (syn)), 3.82 (s, 3H), 2.75 (br s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 172.8$, 160.2, 153.4, 153.2, 129.9, 128.3, 127.6, 123.4, 123.2, 114.4, 87.3, 86.8, 75.5, 73.2, 55.6; IR (film): 3404, 1751 cm$^{-1}$.
5-(Hydroxy(3-methoxyphenyl)methyl)furan-2(5H)-one (3e): Reagents: m-anisaldehyde (100 mg, 0.73 mmol), 2-(trimethylsilyloxy)furan 2a (138 mg, 0.88 mmol), and Bi(OTf)_3•4H_2O (5.0 mg, 0.0072 mmol). The reaction was stirred at –78 °C for 2 h, then at –45 °C for 0.5 h, and quenched according to the typical procedure. The syn/anti ratio (93:7) was determined by ^1H NMR analysis of the crude product (δ major: 4.68 ppm, δ minor: 5.09 ppm). The residue was purified by silica gel chromatography (20% to 40% ethyl acetate/hexane) to afford 131 mg (81%) of 3e as the pure syn diastereoisomer (colorless oil): R_f = 0.20 (50% ethyl acetate/hexane); ^1H NMR (400 MHz, CDCl_3): δ = 7.32 (t, J = 8.1 Hz, 1H), 7.18 (dd, J = 5.8, 1.5 Hz, 2H), 6.85–6.96 (m, 3H), 6.13 (dd, J = 5.8, 2.0 Hz, 1H), 5.15–5.19 (m, 2H), 4.68 (d, J = 7.2 Hz, 1H), 3.83 (s, 3H), 3.13 (br s, 1H); ^13C NMR (100 MHz, CDCl_3): δ = 172.9, 160.1, 153.6, 139.7, 130.1, 123.1, 119.2, 114.1, 112.5, 87.2, 75.7, 55.6; IR (film): 3442, 1747 cm\(^{-1}\).

5-(Hydroxy(4-chlorophenyl)methyl)furan-2(5H)-one (3f): Reagents: 4-chlorobenzaldehyde (100 mg, 0.71 mmol), 2-(trimethylsilyloxy)furan 2a (133 mg, 0.85 mmol), and Bi(OTf)_3•4H_2O (5.0 mg, 0.0072 mmol). The reaction was stirred for 0.5 h at –78 °C and quenched according to the typical procedure. The syn/anti ratio (93:7) was determined by ^1H NMR analysis of the crude product (δ major: 4.75 ppm, δ minor: 5.06 ppm). The residue was purified by flash chromatography (30% ethyl acetate/hexane) to afford 144 mg (90%) of 3f as a mixture of unseparable diastereoisomers: R_f = 0.17 (30% ethyl acetate/hexane); ^1H NMR (400 MHz, CDCl_3): δ = 7.36 (d, J = 2.0 Hz, 2H), 7.33 (d, J = 2.0 Hz, 2H), 7.20 (dd, J = 5.8, 1.6 Hz, 1H), 6.13 (dd, J = 5.9, 2.1 Hz, 1H), 5.13–5.16 (m, 2H), 4.75 (d, J = 6.7 Hz, 1H); ^13C NMR (100 MHz, CDCl_3): δ = 172.5, 152.9, 136.4, 135.0, 129.2, 128.4, 123.5, 86.6, 74.9; IR (KBr): 3440, 1766 cm\(^{-1}\); HRMS: Calcd for C_{11}H_{9}ClO_3 (M^+) 224.0240, found 224.0236.
5-(Hydroxy(4-trifluoromethylphenyl)methyl)furan-2(5H)-one (3g): Reagents: α,α,α-trifluoro-p-tolualdehyde (125 mg, 0.718 mmol), 2-(trimethylsilyloxy)furan 2a (135 mg, 0.861 mmol), and Bi(OTf)$_3$•4H$_2$O (10.0 mg, 0.014 mmol). The reaction was stirred for 0.5 h at –45 °C and quenched according to the typical procedure. The syn/anti ratio (> 98:2) was determined by $^1$H NMR analysis of the crude product. The residue was purified by flash chromatography (40% ethyl acetate/hexane) to afford 120 mg (65%) of 3g as the pure syn diastereoisomer (colorless oil): $R_f$ = 0.13 (30% ethyl acetate/hexane); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.88 (d, $J$ = 7.8 Hz, 1H), 7.72 (d, $J$ = 7.8 Hz, 1H), 7.67 (t, $J$ = 7.6 Hz, 1H), 7.52 (t, $J$ = 7.6 Hz, 1H), 7.12–7.14 (m, 1H), 6.20 (dd, $J$ = 5.7, 2.0 Hz, 1H), 5.19–5.21 (m, 2H), 5.14 (d, $J$ = 5.9 Hz, 1H), 2.99 (br s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 173.1, 152.9, 132.8, 129.2, 127.5 (q, $J$ = 29.8 Hz), 126.0 (q, $J$ = 6.1 Hz), 124.2 (q, $J$ = 273.8 Hz), 123.3, 86.9, 69.9; $^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ = –57.84; IR (film) 3443, 1751 cm$^{-1}$; HRMS: Calcd for C$_{12}$H$_9$F$_3$O$_3$(M + H)$^+$ 259.0582, found 259.0577.

5-((Furan-2-yl)(hydroxy)methyl)furan-2(5H)-one (3h):$^2$ Reagents: 2-furaldehyde (70 mg, 0.73 mmol), 2-(trimethylsilyloxy)furan 2a (137 mg, 0.87 mmol), and Bi(OTf)$_3$•4H$_2$O (5.0 mg, 0.0072 mmol). The reaction was stirred at –78 °C for 0.15 h, then at –45 °C for 0.5 h, and quenched with sat. aqueous NH$_4$Cl (1 mL). The mixture was then treated according to the typical procedure. The syn/anti ratio (72:28) was determined by $^1$H NMR analysis of the crude product (δ major: 4.80 ppm, δ minor: 5.03 ppm). The residue was purified by silica gel chromatography (20% ethyl acetate/hexane) to afford 113 mg (86%) of 3h as a mixture of unseparable diastereoisomers: $R_f$ = 0.22 (25% ethyl acetate/hexane); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.57 (dd, $J$ = 5.7, 1.6 Hz, 1H (anti)), 7.42 (s, 1H), 7.35 (dd, $J$ = 5.8, 1.5 Hz, 1H (syn)), 6.44 (dd, $J$ = 5.8, 1.6 Hz, 1H), 6.38–6.42 (m, 1H), 6.22 (dd, $J$ = 5.9, 2.0 Hz, 1H (anti)) 6.18 (dd, $J$ = 5.9, 2.0 Hz, 1H (syn)), 5.32–5.35 (m, 2H), 5.03 (d, $J$ = 4.7 Hz, 1H (anti)), 4.80 (d, $J$ = 6.1 Hz, 1H (syn)), 2.74 (br s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 172.9, 153.5, 153.3, 151.6, 151.3, 143.1, 123.2, 110.9, 108.9, 108.7, 85.2, 84.7, 69.1, 67.9; IR (film): 3382, 1755 cm$^{-1}$.
5-(Hydroxy(3-thiophenyl)methyl)furan-2(5H)-one (3i): Reagents: 3-thiophene-carboxaldehyde (80 mg, 0.71 mmol), 2-(trimethylsilyloxy)furan 2a (134 mg, 0.85 mmol), and Bi(OTf)$_3$•4H$_2$O (5.0 mg, 0.0071 mmol). The reaction was stirred for 0.25 h at –78 °C and quenched according to the typical procedure. The syn/anti ratio (80:20) was determined by $^1$H NMR analysis of the crude product (δ major: 4.87 ppm, δ minor: 5.16 ppm). The residue was purified by silica gel chromatography (30% to 50% ethyl acetate/hexane) to afford 127 mg (85%) of 3i as a mixture of unseparable diastereoisomers: $R_f$ = 0.15 (30% ethyl acetate/hexane); $^1$H NMR (400 MHz, CDCl$_3$): δ = 7.34–7.37 (m, 2H), 7.26 (m, 1H), 7.12 (dd, $J$ = 6.2, 1.5 Hz, 1H), 6.15 (dd, $J$ = 5.7, 2.0 Hz, 1H), 5.22 (m, 2H), 4.87 (d, $J$ = 6.4 Hz, 1H), 2.42 (br s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ = 172.8, 153.5, 139.5, 127.0, 126.1, 123.4, 123.3, 86.5, 71.6; IR (KBr): 3491, 1780 cm$^{-1}$; HRMS: Calcd for C$_9$H$_8$O$_3$S (M$^+$) 196.0194, found 196.0199.

5-((E)-1-Hydroxy-3-phenylallyl)furan-2(5H)-one (3j):$^2$ Reagents: trans-cinnamaldehyde (95 mg, 0.71 mmol), 2-(trimethylsilyloxy)furan 2a (135 mg, 0.86 mmol), and Bi(OTf)$_3$•4H$_2$O (5.0 mg, 0.0072 mmol). The reaction was stirred at –78 °C for 0.15 h and quenched according to the typical procedure. The syn/anti ratio (70:30) was determined by $^1$H NMR analysis of the crude product (δ major: 4.43 ppm, δ minor: 4.65 ppm). The crude product was then purified on silica gel (20% ethyl acetate/hexane) to afford 119 mg (80%) of 3j as the pure syn diastereoisomer (white solid): mp 128 °C; $R_f$ = 0.32 (40% ethyl acetate/hexane); $^1$H NMR (400 MHz, CDCl$_3$): δ = 7.46 (dd, $J$ = 5.8, 1.5 Hz, 1H); 7.26–7.42 (m, 5H), 6.76 (d, $J$ = 16.0 Hz, 1H), 6.20 (dd, $J$ = 5.5, 1.9 Hz, 2H), 6.15 (d, $J$ = 7.1 Hz, 1H), 5.08 (dt, $J$ = 5.8, 1.7 Hz, 1H), 4.42 (t, $J$ = 7.1 Hz, 1H), 1.92 (br s, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ = 172.8, 153.4, 135.8, 134.8, 128.9, 128.7, 126.9, 125.2, 123.4, 86.1, 73.8; IR (film): 3413, 1751 cm$^{-1}$.

Typical Procedure for the Bismuth-Catalyzed Mukaiyama Aldol Reaction with Aliphatic Aldehydes and Ketones: To a solution of Bi(OTf)$_3$•4H$_2$O (0.036 mmol) and the aldehyde or ketone (0.71 mmol) in diethyl ether (0.5 mL) at –45 °C, was added dropwise a solution of 2-(trimethylsilyloxy)furan 2a (1.1 mmol) in diethyl ether (0.5 mL). The mixture was stirred at –45 °C for 3 h. The reaction was diluted with tetrahydrofuran (1.0 mL) and quenched with 10% aqueous HCl (1.0 mL). The biphasic sytem was stirred for 0.25 h at room temperature, neutralized by addition of NaHCO$_3$ saturated solution, and extracted with ethyl acetate. The organic phases were combined, dried over Na$_2$SO$_4$, and concentrated under reduced pressure.
(rotary evaporator). Syn/anti ratios of the products were determined by $^1$H NMR analysis of the crude reaction mixtures. The relative configurations of the products were assigned according to the literature.$^{1,5}$ The crude products were purified by silica gel chromatography (ethyl acetate/hexane). 3k, 3l, 3n, and 3n’ accord exactly with those that have been previously reported in the literature.$^{1,4,5}$

5-(1-Hydroxybutyl)furan-2(5H)one (3k):$^4$ Reagents: butyraldehyde (52 mg, 0.72 mmol), 2-(trimethylsilyloxy)furan 2a (135 mg, 0.87 mmol), and Bi(OTf)$_3$•4H$_2$O (25 mg, 0.036 mmol). The reaction was stirred for 3 h at $-45$ °C and quenched according to the typical procedure. The syn/anti ratio (70:30) was determined by $^1$H NMR analysis of the crude product ($\delta$ major: 3.90 ppm, $\delta$ minor: 4.97 ppm). The crude product was then purified on silica gel (40% ethyl acetate/hexane) to afford 34 mg (30%) of 3k as a mixture of unseparable diastereoisomers: $R_f = 0.23$ (40% ethyl acetate/hexane); $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.55$ (dd, $J = 5.8$, 1.6 Hz, 1H (anti)), 7.48 (dd, $J = 5.8$, 1.6 Hz, 1H (syn)), 6.20 (dd, $J = 5.6$, 2.0 Hz, 1H (anti)), 6.17 (dd, $J = 5.6$, 2.0 Hz, 1H (syn)), 4.99 (ddd, $J = 4.5$, 2.0, 1.5 Hz, 1H (anti)), 4.97 (ddd, $J = 4.5$, 2.0, 1.5 Hz, 1H (syn)), 3.90 (m, 1H (anti)), 3.78 (m, 1H (syn)), 2.00 (br s, 1H), 1.30–1.80 (m, 4H), 0.95 (m, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 173.2$, 153.9, 153.7, 153.6, 123.1, 122.9, 86.4, 86.3, 71.8, 71.5, 35.5, 35.3, 19.0, 18.9, 14.1; IR (KBr): 3404, 1752 cm$^{-1}$.

5-(cyclohexyl(hydroxy)methyl)furan-2(5H)one (3l):$^1$ Reagents: cyclohexanecarboxyaldehyde (80 mg, 0.71 mmol), 2-(trimethylsilyloxy)furan 2a (167 mg, 1.1 mmol), and Bi(OTf)$_3$•4H$_2$O (10 mg, 0.014 mmol). The reaction was stirred at $-45$ °C for 0.5 h and quenched according to the typical procedure. The syn/anti ratio (75:25) was determined by $^1$H NMR analysis of the crude product ($\delta$ major: 3.47 ppm, $\delta$ minor: 3.60 ppm). The crude product was then purified on silica gel (20% ethyl acetate/hexane) to afford 35 mg (25%) of 3l as the pure syn diastereoisomer (white solid): mp 103 °C; $R_f = 0.23$ (30% ethyl acetate/hexane); $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.45$ (dd, $J = 5.8$, 1.6 Hz, 1H), 6.17 (dd, $J = 5.6$, 2.0 Hz, 1H), 5.18 (ddd, $J = 1.8$, 3.7, 1.8 Hz, 1H), 5.00 (br s, 1H), 3.47 (dd, $J = 6.7$, 3.7 Hz, 1H), 1.95 (m, 1H), 1.79 (m, 2H), 1.70 (m, 1H), 1.60 (m, 2H), 1.09–1.34 (m, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 173.3$, 154.7, 122.5, 84.1, 75.6, 41.1, 29.4, 28.4, 26.0; IR (film): 3491, 1760 cm$^{-1}$.
5-(1-Hydroxy-2-methylcyclohexyl)furan-2(5H)-one (3n): 5 Reagents: 2-methylcyclohexanone (80 mg, 0.71 mmol), 2-(trimethylsilyloxy)furan 2a (167 mg, 1.1 mmol), and Bi(OTf)$_3$·4H$_2$O (25 mg, 0.036 mmol). The mixture was stirred at –45 °C for 3 h, then quenched according to the typical procedure. The diastereoisomeric ratio (82:7:7:4) was determined by $^1$H NMR analysis of the crude product. The crude product was then purified on silica gel (20% ethyl acetate/hexane) to afford 91 mg (65%) of 3n as a single diastereoisomer (white solid): mp 110 °C; $R_f$ = 0.19 (30% ethyl acetate/hexane); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.44 (dd, $J$ = 5.8, 1.6 Hz, 1H), 6.14 (dd, $J$ = 5.9, 2.0 Hz, 1H), 5.20 (t, $J$ = 1.4 Hz, 1H), 1.89 (br s, 1H), 1.39–1.70 (m, 7H), 1.13–1.27 (m, 1H), 1.04 (d, $J$ = 6.3 Hz, 3H), 0.98–1.03 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 173.2, 153.0, 122.9, 88.9, 74.8, 31.4, 30.5, 25.6, 20.8, 15.7; IR (KBr): 3469, 1771 cm$^{-1}$; HRMS: Calcd for C$_{11}$H$_{16}$O$_3$(M + H)$^+$ 197.1178, found 197.1172.

5-(1-Hydroxy-2-methylcyclohexyl)-3-methylfuran-2(5H)-one (3n‘): 5 Reagents: 2-methylcyclohexanone (56 mg, 0.5 mmol), 3-methyl-2-(trimethylsilyloxy)furan 2b (128 mg, 0.75 mmol), and Bi(OTf)$_3$·4H$_2$O (18 mg, 0.025 mmol). The reaction mixture was stirred at –45 °C for 3 h, then at 0 °C for 1 extra h. The mixture was brought back to room temperature and quenched according to the typical procedure. The syn/anti ratios were determined by $^1$H NMR analysis of the crude mixture: anti(R)-5-(1R,2S)/syn(S)-5-(1R,2S) = 73:10:9 + 8. The crude product was purified on silica gel (2 % ethyl acetate/hexane) to afford 81 mg (78%) of 3n as a single diastereoisomer (colorless solid): mp 80–84 °C; $R_f$ = 0.21 (20% ethyl acetate/hexane); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.02 (dq, $J$ = 1.7, 1.7 Hz, 1H), 5.10 (dq, $J$ = 1.7, 1.7 Hz, 1H), 1.95 (dd, $J$ = 1.7, 1.7 Hz, 3H), 1.77 (br s, 1H), 1.67 (m, 1H), 1.36–1.56 (m, 7H), 1.16 (m, 1H), 1.09 (d, $J$ = 6.4 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 174.9, 145.2, 131.5, 86.5, 74.7, 37.7, 31.3, 30.5, 25.7, 20.8, 15.7, 11.0; IR (KBr): 3469, 1771 cm$^{-1}$.

References

(1) Szlosek, M; Figadère, B. Angew. Chem., Int. Ed. 2000, 39, 1799–1801.