

An Organocatalytic Approach to 2-Hydroxyalkyl- and 2-Aminoalkyl Furanes

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Supporting Information

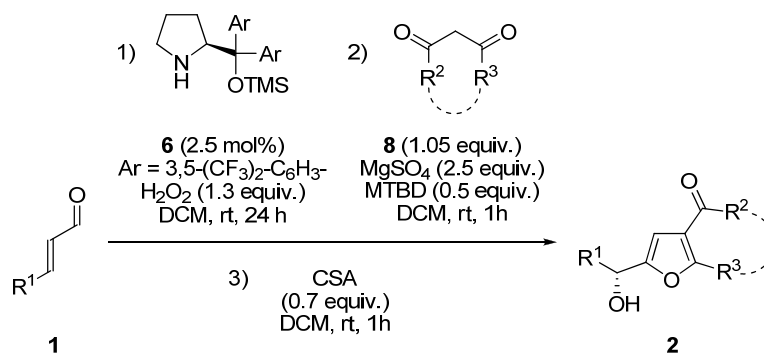
1.	General methods	S-2
2.	Enantioselective synthesis of 2-hydroxyalkyl furanes via epoxidation/Feist-Bénary reaction sequence	S-3
3.	Optimization of the enantioselective aziridination/Feist-Bénary reaction sequence using <i>trans</i> -2-hexenal 1a and methyl acetoacetate 8a as model substrates	S-9
4.	Enantioselective synthesis of 2-aminoalkyl furanes via aziridination/Feist-Bénary reaction sequence	S-10
5.	Optimization of the enantioselective epoxidation/interrupted Feist-Bénary reaction sequence using <i>trans</i> -2-hexenal 1a and methyl or <i>tert</i> -butyl acetoacetates 8a,c as model substrates	S-14
6.	Enantioselective synthesis of hydroxy dihydrofuranes via epoxidation/interrupted Feist-Bénary reaction sequence	S-15
7.	Optimization of the enantioselective aziridination/interrupted Feist-Bénary reaction sequence using <i>trans</i> -2-hexenal 1a and methyl or <i>tert</i> -butyl acetoacetates 8a,c as model substrates	S-20
8.	Enantioselective synthesis of (5 <i>R</i>)-methyl 4-hydroxy-2-methyl-5-((<i>R</i>)-1-(4-methylphenylsulfonamido)butyl)-4,5-dihydrofuran-3-carboxylate via aziridination/interrupted Feist-Bénary reaction sequence	S-21
9.	Direct chemical correlation to (<i>R</i>)-ethyl 5-(1-hydroxyethyl)-2-methylfuran-3-carboxylate 2q	S-24

1. General Methods.

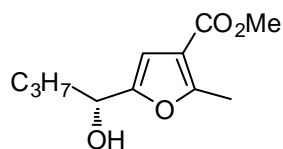
NMR spectra were acquired on a Varian AS 400 spectrometer, running at 400 MHz for ^1H and 100 MHz for ^{13}C , respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals (CHCl_3 , 7.26 ppm for ^1H NMR, CDCl_3 , 77.0 ppm for ^{13}C NMR). The following abbreviations are used to indicate the multiplicity in NMR spectra: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; sext, sextet; oct, octet; m, multiplet; bs, broad signal. ^{13}C NMR spectra were acquired on a broad band decoupled mode. For characterization of diastereomeric mixtures, *denotes major diastereoisomer, +denotes overlap of signals from both diastereoisomers. Mass spectra were recorded on a micromass LCT spectrometer using electrospray (ES^+) ionization techniques. Analytical thin layer chromatography (TLC) was performed using pre-coated aluminum-backed plates (Merck Kieselgel 60 F254) and visualized by ultraviolet irradiation or KMnO_4 dip. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. The enantiomeric excess (ee) of the products was determined by chiral stationary phase HPLC (Daicel Chiralpak AS/AD and Daicel Chiralcel OD/OJ/OB columns) or by GC using a chiral Chrompack CP Chiralsil-Dex C β column. Unless otherwise noted, analytical grade solvents and commercially available reagents were used without further purification. For flash chromatography (FC) silica gel (Silica gel 60, 230-400 mesh, Fluka) was used. Aldehyde **1g,h** and TsNHOTs were synthesized according to literature.¹

¹ Aldehyde **1g** was synthesized by PCC oxidation of the commercially available (Z)-4-(benzyloxy)but-2-en-1-ol, see: (a) Avi, M.; Gaisberger, R.; Feichtenhofer, S.; Griengl, H. *Tetrahedron* **2009**, 65, 5418. Aldehyde **1h** was synthesized from crotonaldehyde and 4-phenyl-1-butene by cross-methatesis using the 2nd generation Grubbs-Hoveyda catalyst, see: (b) Michrowska, A.; List, B. *Nature Chemistry* **2009**, 1, 225. For synthesis of TsNHOTs, see: (c) Albrecht, Ł.; Jiang, H.; Dickmeiss, G.; Gschwend, B.; Hansen, S. G.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2010**, 132, 9188.

2. Enantioselective synthesis of 2-hydroxyalkyl furanes via epoxidation/Feist-Bénary reaction sequence

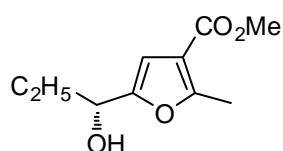


General procedure: A glass vial equipped with a magnetic stirring bar was charged with the aldehyde **1** (0.2 mmol, 1 equiv.), the aminocatalyst **6** (0.005 mmol, 0.025 equiv.) and CH_2Cl_2 (0.4 mL). After short stirring at rt, H_2O_2 (35 wt% in water, 0.26 mmol, 1.3 equiv.) was added. The stirring was maintained at ambient temperature for 24 h to achieve full conversion of the aldehyde **1**. Upon completion of the reaction, MgSO_4 (0.5 mmol, 2.5 equiv.) was added, the reaction mixture was cooled to 0 °C and the corresponding 1,3-dicarbonyl compound **8** (0.21 mmol, 1.05 equiv.) was added followed by MTBD (0.1 mmol, 0.5 equiv.). After stirring for 1 h at ambient temperature the CSA (0.14 mmol, 0.7 equiv.) was added. The resulting mixture was stirred for additional 1 h at ambient temperature and then directly subjected to FC on silica gel to afford the furane **2**.



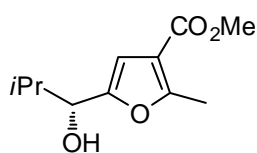
2a (*R*)-Methyl 5-(1-hydroxybutyl)-2-methylfuran-3-carboxylate (Entry 1, Table 2)

Following the general procedure **2a** was isolated by FC (gradient: $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ 100:0 to $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ 90:10) in 72% yield as a pale yellow oil. ^1H NMR (400 MHz, CDCl_3) δ ppm 6.47 (s, 1H), 4.61 (dt, $J = 6.8, 4.9$ Hz, 1H), 3.81 (s, 3H), 2.56 (s, 3H), 1.82 (d, $J = 4.9$ Hz, 1H), 1.81 (q, $J = 7.6$ Hz, 2H), 1.54-1.28 (m, 2H), 0.95 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ ppm 164.5, 158.8, 154.7, 113.6, 106.6, 67.1, 51.3, 37.3, 18.7, 13.8, 13.8. HR-MS: calculated for $(\text{M}+\text{Na})^+$: 235.0946; measured: 235.0948. The ee was determined by HPLC using a Chiralpak AD column (hexane/*i*PrOH 95:5, 1 mL min $^{-1}$); $\tau_{\text{major}} = 19.7$ min, $\tau_{\text{minor}} = 21.3$ min (92% ee). $[\alpha]_{\text{D}}^{25}$: +9.2 ($c = 0.98$, CHCl_3).



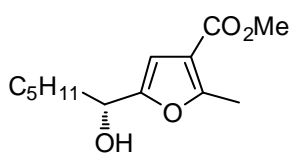
2b (*R*)-methyl 5-(1-hydroxypropyl)-2-methylfuran-3-carboxylate (Entry 2, Table 2)

Following the general procedure **2b** was isolated by FC (gradient: $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ 100:0 to $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ 90:10) in 72% yield as a pale yellow oil. ^1H NMR (400 MHz, CDCl_3) δ ppm 6.46 (s, 1H), 4.52 (t, $J = 6.8$ Hz, 1H), 3.80 (s, 3H), 2.55 (s, 3H), 2.02 (bs, 1H), 1.93-1.76 (m, 2H), 0.95 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ ppm 164.5, 158.8, 154.5, 113.6, 106.8, 68.8, 51.3, 28.3, 13.7, 9.9. HR-MS: calculated for $(\text{M}+\text{Na})^+$: 221.0790; measured: 221.0787. The ee was determined by HPLC using a Chiralpak AD column (hexane/*i*PrOH 95:5, 1 mL min $^{-1}$); $\tau_{\text{major}} = 16.2$ min, $\tau_{\text{minor}} = 17.8$ min (91% ee). $[\alpha]_{\text{D}}^{25}$: +7.0 ($c = 1.0$, CHCl_3).



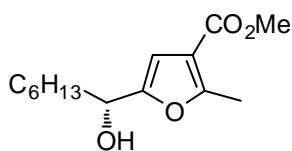
2c (R)-Methyl 5-(1-hydroxy-2-methylpropyl)-2-methylfuran-3-carboxylate (Entry 3, Table 2)

Following the general procedure **2c** was isolated by FC (gradient: CH₂Cl₂/Et₂O 100:0 to CH₂Cl₂/Et₂O 90:10) in 62% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 6.45 (s, 1H), 4.28 (d, *J* = 6.9 Hz, 1H), 3.80 (s, 3H), 2.55 (s, 3H), 2.07 (oct, *J* = 6.8 Hz, 1H), 1.96 (s, 1H), 1.01 (d, *J* = 6.7 Hz, 3H), 0.86 (d, *J* = 6.8 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 164.5, 158.6, 153.9, 113.5, 107.3, 73.1, 51.2, 32.9, 18.7, 18.0, 13.7. HR-MS: calculated for (M+Na)⁺: 235.0946; measured: 235.0946. The ee was determined by HPLC using a Chiralpak AD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); τ_{major} = 14.3 min, τ_{minor} = 16.9 min (94% ee). [α]_D^{rt}: +12.8 (c = 1.0, CHCl₃).



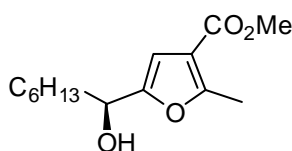
2d (R)-Methyl 5-(1-hydroxyhexyl)-2-methylfuran-3-carboxylate (Entry 4, Table 2)

Following the general procedure **2d** was isolated by FC (gradient: CH₂Cl₂/Et₂O 100:0 to CH₂Cl₂/Et₂O 90:10) in 70% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 6.45 (s, 1H), 4.58 (t, *J* = 6.9 Hz, 1H), 3.80 (s, 3H), 2.55 (s, 3H), 2.01 (s, 1H), 1.84-1.77 (m, 2H), 1.47-1.37 (m, 2H), 1.34-1.27 (m, 4H), 0.87 (t, *J* = 6.7 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 164.4, 158.7, 154.7, 113.6, 106.6, 67.4, 51.2, 35.2, 31.5, 25.1, 22.4, 13.9, 13.7. HR-MS: calculated for (M+Na)⁺: 263.1259; measured: 263.1260. The ee was determined by HPLC using a Chiralpak AD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); τ_{major} = 14.5 min, τ_{minor} = 16.0 min (88% ee). [α]_D^{rt}: +11.0 (c = 1.0, CHCl₃).



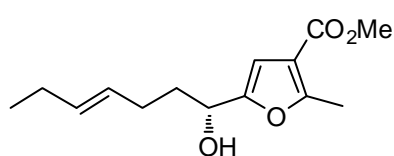
2e (R)-Methyl 5-(1-hydroxyheptyl)-2-methylfuran-3-carboxylate (Entry 5, Table 2)

Following the general procedure **2e** was isolated by FC (gradient: CH₂Cl₂/Et₂O 100:0 to CH₂Cl₂/Et₂O 90:10) in 60% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 6.44 (s, 1H), 4.57 (t, *J* = 6.9 Hz, 1H), 3.79 (s, 3H), 2.54 (s, 3H), 1.94 (s, 1H), 1.85-1.74 (m, 2H), 1.45-1.22 (m, 8H), 0.86 (t, *J* = 6.7 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 164.7, 159.0, 154.9, 113.8, 106.8, 67.7, 51.5, 35.5, 31.9, 29.2, 25.6, 22.7, 14.2, 13.9. HR-MS: calculated for (M+Na)⁺: 277.1416; measured: 277.1418. The ee was determined by HPLC using a Chiralpak AD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); τ_{major} = 15.5 min, τ_{minor} = 17.0 min (91% ee). [α]_D^{rt}: +8.0 (c = 1.0, CHCl₃), +6.0 (c = 0.8, CH₃OH).



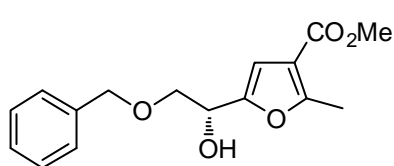
ent-2e (S)-Methyl 5-(1-hydroxyheptyl)-2-methylfuran-3-carboxylate (Entry 6, Table 2)

Pale yellow oil. Yield: 60%. Spectral data were identical to compound **2e**. The ee was determined by HPLC using a Chiralpak AD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); τ_{major} = 17.0 min, τ_{minor} = 15.5 min (90% ee). [α]_D^{rt}: -6.0 (c = 0.8, CH₃OH).



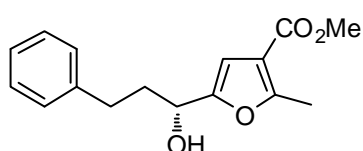
2f (R,E)-Methyl 5-(1-hydroxyhept-4-en-1-yl)-2-methylfuran-3-carboxylate (Entry 7, Table 2)

Following the general procedure **2f** was isolated by FC (gradient: CH₂Cl₂/Et₂O 100:0 to CH₂Cl₂/Et₂O 90:10) in 68% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 6.39 (s, 1H), 5.48-5.28 (m, 2H), 4.54 (t, *J* = 6.8 Hz, 1H), 3.74 (s, 3H), 2.48 (s, 3H), 2.12-1.88 (m, 5H), 1.81 (q, *J* = 7.3 Hz, 2H), 0.89 (t, *J* = 7.5 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 164.5, 158.8, 154.6, 133.2, 127.8, 113.6, 106.7, 66.9, 51.3, 35.0, 28.5, 25.5, 13.8, 13.7. HR-MS: calculated for (M+Na)⁺: 275.1259; measured: 275.1257. The ee was determined by HPLC using a Chiralpak AD column (hexane/*i*PrOH 98:2, 1 mL min⁻¹); τ_{major} = 30.1 min, τ_{minor} = 32.1 min (94% ee). [α]_D^{rt}: -7.0 (c = 0.98, CHCl₃).



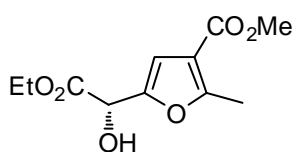
2g (R)-Methyl 5-(2-(benzyloxy)-1-hydroxyethyl)-2-methylfuran-3-carboxylate (Entry 8, Table 2)

Following the general procedure **2g** was isolated by FC (gradient: CH₂Cl₂/Et₂O 100:0 to CH₂Cl₂/Et₂O 90:10) in 73% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.39-7.27 (m, 5H), 6.54 (s, 1H), 4.83 (t, *J* = 5.6 Hz, 1H), 4.62 (d, *J* = 12.0 Hz, 1H), 4.58 (d, *J* = 12.0 Hz, 1H), 3.80 (s, 3H), 3.72 (d, *J* = 5.8 Hz, 2H), 2.86 (bs, 1H), 2.54 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 164.3, 159.1, 151.2, 137.5, 128.8 (2C), 127.9, 127.8 (2C), 113.8, 108.0, 73.5, 72.1, 66.5, 51.3, 13.7. HR-MS: calculated for (M+Na)⁺: 313.1052; measured: 313.1052. The ee was determined by HPLC using a Chiralcel OD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); τ_{major} = 30.2 min, τ_{minor} = 34.6 min (92% ee). [α]_D^{rt}: +4.6 (c = 1.05, CHCl₃).



2h (R)-Methyl 5-(1-hydroxy-3-phenylpropyl)-2-methylfuran-3-carboxylate (Entry 9, Table 2)

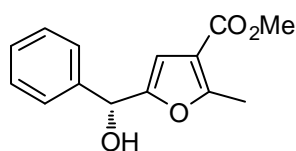
Following the general procedure **2h** was isolated by FC (gradient: CH₂Cl₂/Et₂O 100:0 to CH₂Cl₂/Et₂O 90:10) in 74% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.33-7.16 (m, 5H), 6.49 (s, 1H), 4.61 (t, *J* = 6.7 Hz, 1H), 3.82 (s, 3H), 2.83-2.65 (m, 2H), 2.56 (s, 3H), 2.21-2.11 (m, 2H), 2.03 (s br, 1H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 164.4, 158.8, 154.5, 141.2, 128.3, 128.3, 125.9, 106.8, 66.4, 51.2, 36.6, 31.6, 13.6. HR-MS: calculated for (M+Na)⁺: 297.1103, measured: 297.1100. The ee was determined by HPLC using a Chiralpak OD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); τ_{major} = 32.8 min, τ_{minor} = 20.9 min (90% ee). [α]_D^{rt}: -7.0 (c = 0.54, CHCl₃).



2i (S)-Methyl 5-(2-ethoxy-1-hydroxy-2-oxoethyl)-2-methylfuran-3-carboxylate (Entry 10, Table 2)

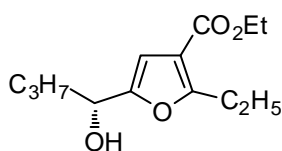
Following the general procedure **2i** was isolated by FC (gradient: CH₂Cl₂/Et₂O 100:0 to CH₂Cl₂/Et₂O 94:6) in 53% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 6.61 (s, 1H), 5.10 (d, *J* = 6.3 Hz, 1H), 4.36-4.21 (m, 2H), 3.81 (s, 3H), 3.39 (d, *J* = 6.4 Hz, 1H), 2.56 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 171.1, 164.1, 159.8, 148.8, 114.1, 109.6, 66.6, 62.7, 51.4, 14.0, 13.7.

HR-MS: calculated for $(M+Na)^+$: 265.0688; measured: 265.0678. The ee was determined by HPLC using a Chiralcel OJ column (hexane/*i*PrOH 90:10, 1 mL min⁻¹); τ_{major} = 19.0 min, τ_{minor} = 25.7 min (88% ee). $[\alpha]_{\text{D}}^{\text{rt}}$: +56.1 (*c* = 0.98, CHCl₃).



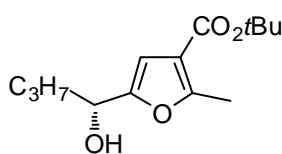
2j (R)-Methyl 5-(hydroxy(phenyl)methyl)-2-methylfuran-3-carboxylate (Entry 11, Table 2)

Following the modified general procedure (using DBU 0.2 mmol, 1 equiv. instead of MTBD as a base) **2j** was isolated by FC (gradient: CH₂Cl₂/Et₂O 100:0 to CH₂Cl₂/Et₂O 90:10) in 56% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.49-7.29 (m, 5H), 6.31 (s, 1H), 5.75 (s, 1H), 3.77 (s, 3H), 2.55 (s, 3H), 2.48 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 164.3, 159.4, 153.8, 140.1, 128.5 (2C), 128.2, 126.5 (2C), 108.4, 69.8, 51.2, 13.7. HR-MS: calculated for $(M+Na)^+$: 269.0790; measured: 269.0796. The ee was determined by HPLC using a Chiralpak AD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); τ_{major} = 22.9 min, τ_{minor} = 25.3 min (88% ee). $[\alpha]_{\text{D}}^{\text{rt}}$: -6.0 (*c* = 1.0, CHCl₃).



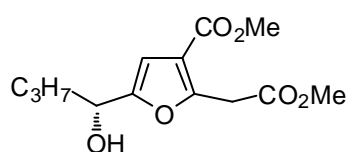
2k (R)-Methyl 5-(1-hydroxybutyl)-2-methylfuran-3-carboxylate (Entry 1, Table 3)

Following the general procedure **2k** was isolated by FC (gradient: CH₂Cl₂/Et₂O 100:0 to CH₂Cl₂/Et₂O 90:10) in 58% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 6.47 (s, 1H), 4.62 (t, *J* = 6.9 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 2.99 (q, *J* = 7.6 Hz, 2H), 1.88 (bs, 1H), 1.81 (sext, *J* = 7.0 Hz, 2H), 1.51-1.36 (m, 2H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.24 (t, *J* = 7.6 Hz, 3H), 0.95 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 163.9, 163.5, 154.6, 113.0, 106.6, 67.2, 60.0, 37.3, 21.2, 18.7, 14.3, 13.8, 12.2. HR-MS: calculated for $(M+Na)^+$: 263.1259; measured: 263.1255. The ee was determined by HPLC using a Chiralpak AD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); τ_{major} = 12.4 min, τ_{minor} = 13.6 min (86% ee). $[\alpha]_{\text{D}}^{\text{rt}}$: +8.0 (*c* = 1.0, CHCl₃).



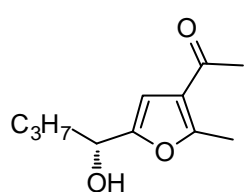
2l (R)-tert-Butyl 5-(1-hydroxybutyl)-2-methylfuran-3-carboxylate (Entry 2, Table 3)

Following the general procedure **2l** was isolated by FC (gradient: CH₂Cl₂/Et₂O 100:0 to CH₂Cl₂/Et₂O 90:10) in 70% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 6.41 (s, 1H), 4.59 (t, *J* = 6.9 Hz, 1H), 2.52 (s, 3H), 1.94 (bs, 1H), 1.79 (q, *J* = 7.0 Hz, 2H), 1.53 (s, 9H), 1.52-1.26 (m, 4H), 0.94 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 163.5, 157.9, 154.4, 115.3, 107.0, 80.5, 67.2, 37.4, 28.3 (3C), 18.7, 13.8, 13.8. HR-MS: calculated for $(M+Na)^+$: 277.1416; measured: 277.1414. The ee was determined by HPLC using two Chiralpak AD columns (hexane/*i*PrOH 97:3, 0.5 mL min⁻¹); τ_{major} = 63.7 min, τ_{minor} = 67.9 min (88% ee). $[\alpha]_{\text{D}}^{\text{rt}}$: +8.1 (*c* = 1.0, CHCl₃).



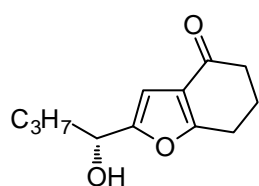
2m (R)-Methyl 5-(1-hydroxybutyl)-2-(2-methoxy-2-oxoethyl)furan-3-carboxylate (Entry 3, Table 3)

Following the general procedure **2m** was isolated by FC (gradient: CH₂Cl₂/Et₂O 100:0 to CH₂Cl₂/Et₂O 90:10) in 40% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 6.51 (s, 1H), 4.62 (t, *J* = 6.8 Hz, 1H), 4.04 (s, 2H), 3.79 (s, 3H), 3.70 (s, 3H), 2.36 (bs, 1H), 1.79 (q, *J* = 7.5 Hz, 2H), 1.52-1.28 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 169.1, 163.8, 156.5, 153.3, 115.8, 106.6, 67.0, 52.3, 51.5, 37.3, 33.4, 18.6, 13.7. HR-MS: calculated for (M+Na)⁺: 293.1001; measured: 293.0999. The ee was determined by HPLC using a Chiralcel OJ column (hexane/*i*PrOH 98:2, 1 mL min⁻¹); τ_{major} = 51.9 min, τ_{minor} = 58.1 min (94% ee). [α]_D^{rt}: +8.0 (c = 0.68, CHCl₃).



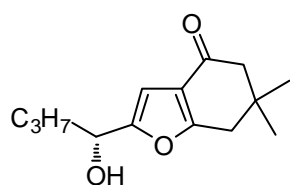
2n (R)-1-(5-(1-Hydroxybutyl)-2-methylfuran-3-yl)ethanone (Entry 4, Table 3)

Following the general procedure **2n** was isolated by FC (gradient: CH₂Cl₂/Et₂O 100:0 to CH₂Cl₂/Et₂O 85:15) in 75% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 6.43 (s, 1H), 4.61 (t, *J* = 6.8 Hz, 1H), 2.55 (s, 3H), 2.36 (s, 3H), 2.27 (bs, 1H), 1.80 (q, *J* = 7.5 Hz, 2H), 1.53-1.27 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 194.3, 157.9, 154.8, 121.8, 106.3, 67.1, 37.4, 29.0, 18.7, 14.4, 13.8. HR-MS: calculated for (M+Na)⁺: 219.0997; measured: 219.0997. The ee was determined by HPLC using a Chiralcel OD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); τ_{major} = 14.8 min, τ_{minor} = 13.6 min (89% ee). [α]_D^{rt}: +11.7 (c = 0.98, CHCl₃).



2o (R)-2-(1-Hydroxybutyl)-6,7-dihydrobenzofuran-4(5H)-one (Entry 5, Table 3)

Following the general procedure **2o** was isolated by FC (gradient: CH₂Cl₂/Et₂O 100:0 to CH₂Cl₂/Et₂O 90:10) in 52% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 6.48 (s, 1H), 4.65 (t, *J* = 6.9 Hz, 1H), 2.86 (t, *J* = 6.3 Hz, 2H), 2.47 (t, *J* = 6.6 Hz, 2H), 2.16 (quint, *J* = 6.4 Hz, 2H), 2.15 (bs, 1H), 1.82 (sext, *J* = 7.2 Hz, 2H), 1.53-1.28 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 194.5, 166.8, 157.2, 121.5, 102.4, 67.2, 37.5, 37.3, 23.3, 22.5, 18.7, 13.7. HR-MS: calculated for (M+Na)⁺: 231.0997; measured: 231.0991. The ee was determined by HPLC using a Chiralpak AD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); τ_{major} = 46.4 min, τ_{minor} = 49.1 min (92% ee). [α]_D^{rt}: +13.3 (c = 1.0, CHCl₃).

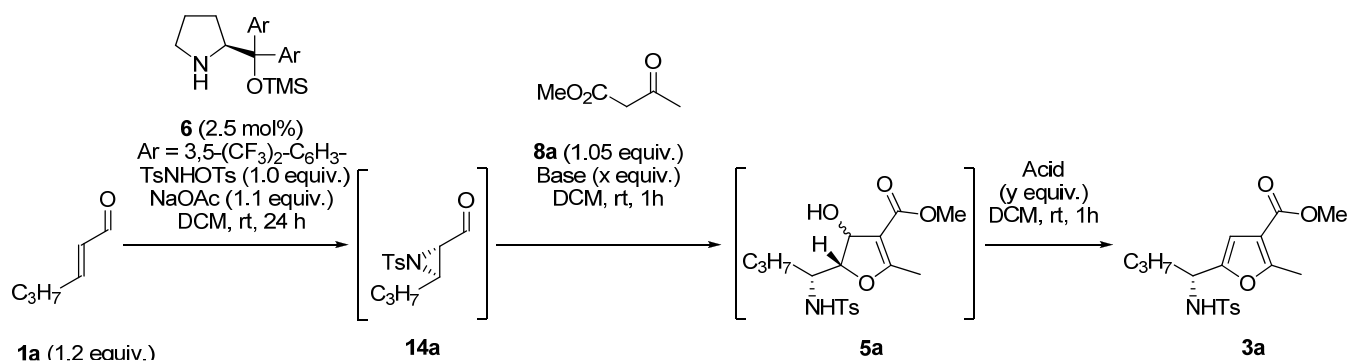


2p (R)-2-(1-Hydroxybutyl)-6,6-dimethyl-6,7-dihydrobenzofuran-4(5H)-one (Entry 6, Table 3)

Following the general procedure **2p** was isolated by FC (gradient: CH₂Cl₂/Et₂O 100:0 to CH₂Cl₂/Et₂O 85:15) in 62% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 6.48 (s, 1H), 4.65 (t, *J* = 6.7 Hz, 1H), 2.72 (s, 3H), 2.34 (s, 3H), 2.14 (bs, 1H), 1.81 (q, *J* = 7.4 Hz, 1H), 1.55-1.29 (m, 2H), 1.12 (s, 6H), 0.94 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 194.0, 166.0, 157.6, 120.4, 102.3, 67.3, 51.9, 37.4, 37.3, 35.2, 28.6, 28.6, 18.7, 13.8. HR-MS: calculated for (M+Na)⁺: 259.1310; measured: 259.1311. The

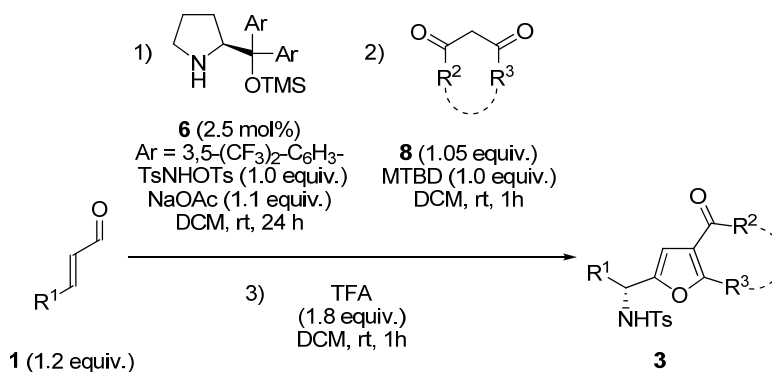
ee was determined by HPLC using a Chiralpak AD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); $\tau_{\text{major}} = 22.8$ min, $\tau_{\text{minor}} = 26.0$ min (94% ee). $[\alpha]_{\text{D}}^{\text{rt}}: +5.6$ (c 1.3, CHCl₃).

3. Optimization of the enantioselective aziridination/Feist-Bénary reaction sequence using *trans*-2-hexenal **1a and methyl acetoacetate **8a** as model substrates**

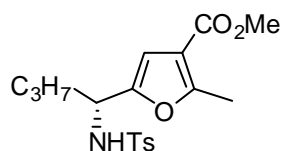


entry	Base (equiv.)	Acid (equiv.)	yield [%]	ee [%]
1	-	CSA (1.3)	-	-
2	MTBD (1)	CSA (1.3)	57	95
3	MTBD (1)	CSA (1.8)	63	95
4	MTBD (1)	CSA (2.3)	59	95
5	MTBD (1)	TFA (1.8)	68	95
6	DBU (1)	CSA (1.8)	58	94
7	MTBD (1.5)	TFA (2.3)	61	95
8	DBU (1.5)	TFA (2.3)	53	94

4. Enantioselective synthesis of 2-aminoalkyl furanes via aziridination/Feist-Bénary reaction sequence

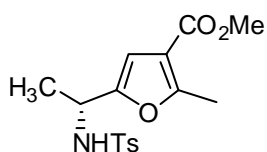


General procedure: A glass vial equipped with a magnetic stirring bar was charged with the aldehyde **1** (0.12 mmol, 1.2 equiv), the catalyst **6** (0.0025 mmol, 0.025 equiv) and CH_2Cl_2 (0.5 mL). After short stirring at rt, TsNHOTs (0.1 mmol, 1 equiv) was added followed by NaOAc (0.11 mmol, 1.1 equiv.). The stirring was maintained at ambient temperature for 18 h to achieve full conversion of the nucleophile. Upon completion of the reaction, the reaction mixture was cooled to 0 °C and the corresponding 1,3-dicarbonyl compound **8** (0.105 mmol, 1.05 equiv.) was added followed by MTBD (0.1 mmol, 1 equiv.). After stirring for 1 h at ambient temperature the TFA (0.18 mmol, 1.8 equiv.) was added. The resulting mixture was stirred for additional 1 h at ambient temperature and then directly subjected to FC on silica gel to afford the furane **3**.



3a (*R*)-Methyl 2-methyl-5-(1-(4-methylphenylsulfonamido)butyl)furan-3-carboxylate (Entry 1, Table 4)

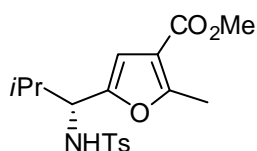
Following the general procedure **3a** was isolated by FC (gradient: EtOAc/pentane 5:95 to EtOAc/pentane 20:80) in 68% yield as a pale yellow oil. ^1H NMR (400 MHz, CDCl_3) δ ppm 7.59 (d, $J = 8.1$ Hz, 2H), 7.16 (d, $J = 8.0$ Hz, 2H), 6.12 (s, 1H), 5.02 (d, $J = 8.6$ Hz, 1H), 4.31 (q, $J = 7.6$ Hz, 1H), 3.76 (s, 3H), 2.35 (s, 3H), 2.29 (s, 3H), 1.78-1.65 (m, 2H), 1.39-1.17 (m, 2H), 0.85 (t, $J = 7.3$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ ppm 164.1, 158.5, 150.8, 143.0, 137.6, 129.1 (2C), 127.0 (2C), 113.3, 107.8, 51.2, 51.2, 36.5, 21.3, 18.8, 13.4, 13.4. HR-MS: calculated for $(\text{M}+\text{Na})^+$: 388.1195; measured: 388.1189. The ee was determined by HPLC using a Chiralcel OJ column (hexane/*i*PrOH 95:5, 1 mL min $^{-1}$); $\tau_{\text{major}} = 25.9$ min, $\tau_{\text{minor}} = 23.7$ min (95% ee). $[\alpha]_{\text{D}}^{25}$: +47.9 ($c = 1.0$, CHCl_3).



3b (*R*)-Methyl 2-methyl-5-(1-(4-methylphenylsulfonamido)ethyl)furan-3-carboxylate (Entry 2, Table 4)

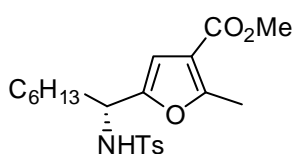
Following the general procedure **3b** was isolated by FC (gradient: $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ 100:0 to $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ 95:5) in 68% yield as a pale yellow oil. ^1H NMR (400 MHz, CDCl_3) δ ppm 7.65 (d, $J = 8.4$ Hz, 2H), 7.21 (d, $J = 8.4$ Hz, 2H), 6.20 (s, 1H), 5.05 (d, $J = 8.2$ Hz, 1H), 4.51-4.43 (m, 1H), 3.76 (s, 3H), 2.38 (s, 3H), 2.32 (s, 3H), 1.42 (d, $J = 7.0$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ ppm 173.8, 164.1, 158.7, 151.7,

143.2, 129.3 (2C), 127.0 (2C), 113.4, 107.2, 51.3, 47.0, 21.4, 20.5, 13.4. HR-MS: calculated for (M+Na)⁺: 360.0882; measured: 360.0879. The ee was determined by HPLC using a Chiralpak OJ column (hexane/*i*PrOH 90:10, 1 mL min⁻¹); $\tau_{\text{major}} = 44.4$ min, $\tau_{\text{minor}} = 39.3$ min (89% ee). $[\alpha]_{\text{D}}^{25} +66.9$ (c = 1.2, CHCl₃).



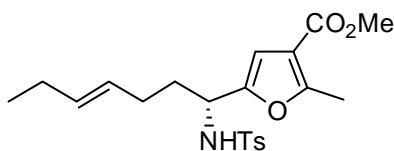
3c (R)-Methyl 2-methyl-5-(2-methyl-1-(4-methylphenylsulfonamido)propyl)furan-3-carboxylate (Entry 3, Table 4)

Following the general procedure **3c** was isolated by FC (gradient: EtOAc/pentane 5:95 to EtOAc/pentane 20:80) in 38% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.56 (d, *J* = 8.27 Hz, 2H), 7.15 (d, *J* = 8.51 Hz, 2H), 6.03 (s, 1H), 4.76 (d, *J* = 9.56 Hz, 1H), 4.05 (dd, *J* = 9.54 Hz, 7.24 Hz, 1H), 3.77 (s, 3H), 2.34 (s, 3H), 2.32 (s, 3H), 1.99 (oct, *J* = 6.7 Hz, 1H), 0.97 (d, *J* = 6.74 Hz, 3H), 0.81 (d, *J* = 6.73 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 164.0, 158.3, 150.0, 143.1, 137.4, 129.1 (2C), 127.0 (2C), 113.3, 108.4, 57.3, 51.2, 32.4, 21.3, 18.9, 18.7, 13.4. HR-MS: calculated for (M+Na)⁺: 388.1195; measured: 388.1202. The ee was determined by HPLC using a Chiralcel OD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); $\tau_{\text{major}} = 17.8$ min, $\tau_{\text{minor}} = 21.8$ min (95% ee). $[\alpha]_{\text{D}}^{25} +31.9$ (c = 1.0, CHCl₃).



3d (R)-Methyl 2-methyl-5-(1-(4-methylphenylsulfonamido)heptyl)furan-3-carboxylate (Entry 4, Table 4)

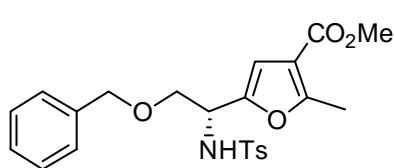
Following the general procedure **3d** was isolated by FC (gradient: CH₂Cl₂/Et₂O 100:0 to CH₂Cl₂/Et₂O 96:4) in 66% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.59 (d, *J* = 8.3 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 2H), 6.13 (s, 1H), 4.87 (d, *J* = 8.9 Hz, 1H), 4.29 (q, *J* = 7.7 Hz, 1H), 3.77 (s, 3H), 2.36 (s, 3H), 2.31 (s, 3H), 1.72 (q, *J* = 7.2 Hz, 2H), 1.34-1.10 (m, 8H), 0.84 (t, *J* = 6.8 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 164.1, 158.5, 150.9, 143.1, 137.7, 129.2 (2C), 127.0 (2C), 113.4, 107.9, 107.8, 51.5, 51.2, 34.5, 31.5, 28.6, 25.5, 22.5, 21.3, 14.0, 13.4. HR-MS: calculated for (M+Na)⁺: 430.1664; measured: 430.1671. The ee was determined by HPLC using a Chiralcel OD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); $\tau_{\text{major}} = 13.3$ min, $\tau_{\text{minor}} = 18.1$ min (93% ee). $[\alpha]_{\text{D}}^{25} +42.4$ (c = 1.2, CHCl₃).



3e (R,E)-Methyl 2-methyl-5-(1-(4-methylphenylsulfonamido)hept-4-enyl)furan-3-carboxylate (Entry 5, Table 4)

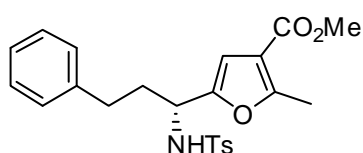
Following the general procedure **3e** was isolated by FC (gradient: EtOAc/pentane 5:95 to EtOAc/pentane 20:80) in 61% yield as an amorphous off-white solid, mp: 63-68 °C. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.59 (d, *J* = 8.3 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 2H), 6.13 (s, 1H), 5.47-5.36 (m, 1H), 5.32-5.22 (m, 1H), 4.86 (d, *J* = 8.7 Hz, 1H), 4.32 (q, *J* = 7.7 Hz, 1H), 3.77 (s, 3H), 2.36 (s, 3H), 2.31 (s, 3H), 2.02-1.91 (m, 4H), 1.83-1.75 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 164.1, 158.6, 150.5, 143.1, 137.6, 133.7, 129.2 (2C), 127.1 (2C), 126.9, 113.4, 108.1, 51.3, 50.9, 34.3, 28.5, 25.5, 21.4, 13.8, 13.4. HR-MS: calculated for (M+Na)⁺: 428.1508; measured: 428.1511. The ee was determined by HPLC

using a Chiralcel OD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); $\tau_{\text{major}} = 19.3$ min, $\tau_{\text{minor}} = 27.4$ min (90% ee). $[\alpha]_{\text{D}}^{25}$: +33.1 (*c* = 0.94, CHCl₃).



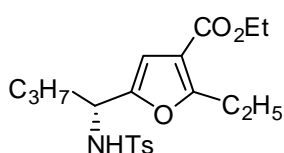
3f (R)-Methyl 5-(2-(benzyloxy)-1-(4-methylphenylsulfonamido)ethyl)-2-methylfuran-3-carboxylate (Entry 6, Table 4)

Following the general procedure **3f** was isolated by FC (gradient: CH₂Cl₂/Et₂O 100:0 to CH₂Cl₂/Et₂O 95:5) in 65% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.63 (d, *J* = 8.2 Hz, 2H), 7.38-7.14 (m, 7H), 6.34 (s, 1H), 5.28 (d, *J* = 7.5 Hz, 1H), 4.58-4.50 (m, 1H), 4.44 (s, 2H), 3.78 (s, 3H), 3.67 (dd, *J* = 9.6 Hz, 5.3 Hz, 1H), 3.58 (dd, *J* = 9.6 Hz, 4.9 Hz, 1H), 2.37 (s, 3H), 2.35 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 164.0, 158.7, 148.9, 143.2, 137.4, 137.2, 129.3 (2C), 128.4 (2C), 127.9, 127.7 (2C), 127.1 (2C), 113.7, 109.0, 73.2, 70.4, 51.2, 51.0, 21.4, 13.4. HR-MS: calculated for (M+Na)⁺: 466.1300, measured: 466.1302. The ee was determined by HPLC using a Chiralcel OD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); $\tau_{\text{major}} = 35.5$ min, $\tau_{\text{minor}} = 42.0$ min (93% ee). $[\alpha]_{\text{D}}^{25}$: +49.4 (*c* = 1.0, CHCl₃).



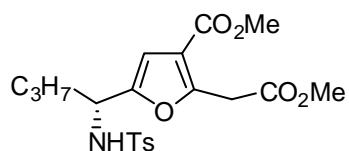
3g (R)-Methyl 2-methyl-5-(1-(4-methylphenylsulfonamido)-3-phenylpropyl)furan-3-carboxylate (Entry 7, Table 4)

Following the general procedure **3g** was isolated by FC (gradient: CH₂Cl₂/Et₂O 100:0 to CH₂Cl₂/Et₂O 96:4) in 68% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.58 (d, *J* = 8.1 Hz, 2H), 7.30-7.06 (m, 7H), 6.14 (s, 1H), 5.08 (d, *J* = 8.6 Hz, 1H), 4.38-4.26 (m, 1H), 3.77 (s, 3H), 2.70-2.50 (m, 2H), 2.36 (s, 3H), 2.31 (s, 3H), 2.16-2.00 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 164.0, 158.6, 150.4, 143.2, 140.5, 137.5, 129.2 (2C), 128.4 (2C), 128.4 (2C), 127.0 (2C), 126.1, 113.4, 108.2, 51.3, 51.0, 36.0, 31.8, 21.4, 13.4. HR-MS: calculated for (M+Na)⁺: 450.1351, measured: 450.1345. The ee was determined by HPLC using a Chiralpak OD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); $\tau_{\text{major}} = 15.8$ min, $\tau_{\text{minor}} = 27.5$ min (91% ee). $[\alpha]_{\text{D}}^{25}$: +18.0 (*c* = 1.0, CHCl₃).



3h (R)-Ethyl 2-ethyl-5-(1-(4-methylphenylsulfonamido)butyl)furan-3-carboxylate (Entry 8, Table 4)

Following the general procedure **3h** was isolated by FC (gradient: EtOAc/pentane 5:95 to EtOAc/pentane 20:80) in 55% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.60 (d, *J* = 8.28 Hz, 2H), 7.17 (d, *J* = 8.04 Hz, 2H), 6.12 (s, 1H), 4.77 (d, *J* = 8.85 Hz, 1H), 4.33 (q, *J* = 7.46 Hz, 1H), 4.23 (q, *J* = 7.13 Hz, 2H), 2.76 (q, *J* = 7.58 Hz, 2H), 2.35 (s, 3H), 1.77-1.69 (m, 2H), 1.21-1.39 (m, 2H), 1.32 (t, *J* = 7.13 Hz, 3H), 1.07 (t, *J* = 7.57 Hz, 3H), 0.87 (t, *J* = 7.36 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 163.5, 163.2, 150.5, 143.0, 137.6, 129.2 (2C), 126.9 (2C), 112.7, 107.9, 60.0, 51.2, 36.6, 21.3, 20.9, 18.8, 14.3, 13.4, 12.0. HR-MS: calculated for (M+Na)⁺: 416.1508; measured: 416.1510. The ee was determined by HPLC using a Chiralcel OD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); $\tau_{\text{major}} = 12.8$ min, $\tau_{\text{minor}} = 17.1$ min (93% ee). $[\alpha]_{\text{D}}^{25}$: +50.9 (*c* = 1.0, CHCl₃).



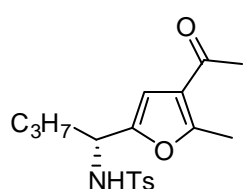
3i

(R)-Methyl

2-(2-methoxy-2-oxoethyl)-5-(1-(4-

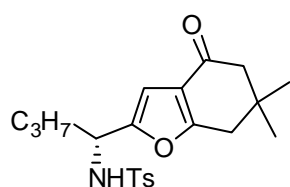
methylphenylsulfonamido)butyl)furan-3-carboxylate (Entry 9, Table 4)

Following the general procedure **3i** was isolated by FC (gradient: CH₂Cl₂/Et₂O 100:0 to CH₂Cl₂/Et₂O 95:5) in 64% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.60 (d, *J* = 8.3 Hz, 2H), 7.19 (d, *J* = 7.9 Hz, 2H), 6.13 (s, 1H), 4.65 (d, *J* = 8.5 Hz, 1H), 4.34 (q, *J* = 7.4 Hz, 1H), 3.87 (d, *J* = 17.1 Hz, 1H), 3.80 (d, *J* = 17.1 Hz, 1H), 3.78 (s, 3H), 3.72 (s, 3H), 2.37 (s, 3H), 1.74 (q, *J* = 7.3 Hz, 2H), 1.39-1.20 (m, 2H), 0.87 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 168.7, 163.4, 153.2, 152.5, 143.1, 137.6, 129.3 (2C), 127.0 (2C), 115.6, 107.7, 52.3, 51.5, 51.1, 36.4, 33.1, 21.4, 18.7, 13.4. HR-MS: calculated for (M+Na)⁺: 446.1249; measured: 446.1241. The ee was determined by HPLC using a Chiralcel OD column (hexane/*i*PrOH 90:10, 1 mL min⁻¹); τ_{major} = 19.7 min, τ_{minor} = 24.3 min (95% ee). [α]_D^{rt}: +52.2 (*c* = 1.3, CHCl₃).



3j (R)-N-(1-(4-acetyl-5-methylfuran-2-yl)butyl)-4-methylbenzenesulfonamide (Entry 10, Table 4)

Following the general procedure **3j** was isolated by FC (gradient: CH₂Cl₂/Et₂O 100:0 to CH₂Cl₂/Et₂O 95:5) in 83% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.59 (d, *J* = 8.2 Hz, 2H), 7.15 (d, *J* = 8.2 Hz, 2H), 6.08 (s, 1H), 5.18 (d, *J* = 8.5 Hz, 1H), 4.37-4.28 (m, 1H), 2.35 (s, 3H), 2.31 (s, 3H), 2.23 (s, 3H), 1.76-1.68 (m, 2H), 1.40-1.18 (m, 2H), 0.86 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 193.7, 157.6, 150.7, 143.1, 137.7, 129.1 (2C), 127.0 (2C), 121.3, 107.6, 51.2, 36.4, 28.8, 21.3, 18.8, 14.0, 13.4. HR-MS: calculated for (M+Na)⁺: 372.1245, measured: 372.1240. The ee was determined by HPLC using a Chiralcel OD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); τ_{major} = 19.7 min, τ_{minor} = 25.4 min (95% ee). [α]_D^{rt}: +65.4 (*c* = 1.0, CHCl₃).

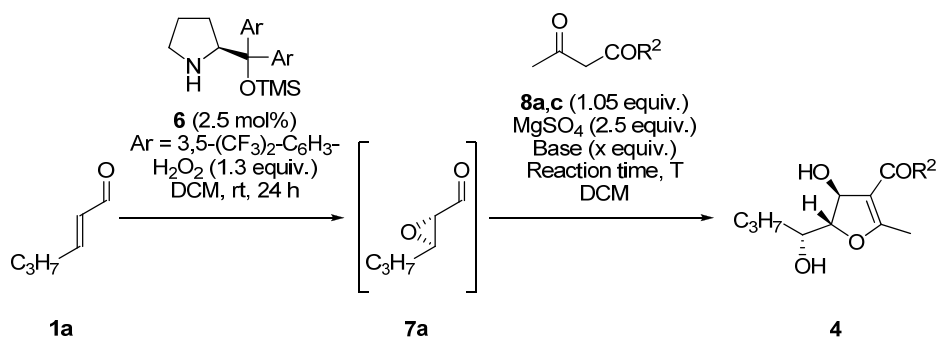


3k

(R)-N-(1-(6,6-dimethyl-4-oxo-4,5,6,7-tetrahydrobenzofuran-2-yl)butyl)-4-methylbenzenesulfonamide (Entry 11, Table 4)

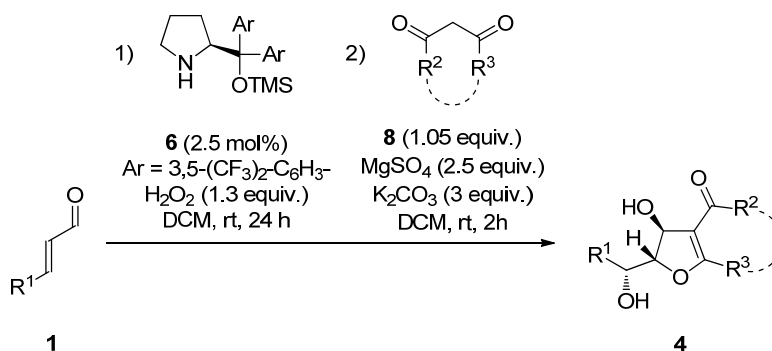
Following the general procedure **3k** was isolated by FC (gradient: CH₂Cl₂/Et₂O 100:0 to CH₂Cl₂/Et₂O 93:7) in 66% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 7.61 (d, *J* = 8.3 Hz, 2H), 7.16 (d, *J* = 8.1 Hz, 2H), 6.15 (s, 1H), 5.04 (d, *J* = 8.7 Hz, 1H), 4.37 (q, *J* = 7.6 Hz, 1H), 2.51 (d, *J* = 17.3 Hz, 1H), 2.42 (d, *J* = 17.2 Hz, 1H), 2.35 (s, 3H), 2.27 (d, *J* = 16.1 Hz, 1H), 2.21 (d, *J* = 16.1 Hz, 1H), 1.79-1.66 (m, 2H), 1.40-1.17 (m, 2H), 1.06 (s, 3H), 1.04 (s, 3H), 0.86 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 193.4, 165.5, 153.8, 143.1, 137.7, 129.3 (2C), 127.1 (2C), 120.1, 103.3, 51.8, 51.3, 37.1, 36.6, 35.0, 28.6, 28.4, 21.4, 18.8, 13.4. HR-MS: calculated for (M+Na)⁺: 412.1559; measured: 412.1562. The ee was determined by HPLC using a Chiralcel OJ column (hexane/*i*PrOH 90:10, 1 mL min⁻¹); τ_{major} = 22.2 min, τ_{minor} = 17.5 min (91% ee). [α]_D^{rt}: +40.7 (*c* 0.95, CHCl₃).

5. Optimization of the enantioselective epoxidation/interrupted Feist-Bénary reaction sequence using *trans*-2-hexenal **1a** and methyl or *tert*-butyl acetoacetates **8a,c** as model substrates

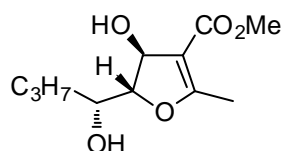


Entry	8 (R^2)	Base (equiv.)	T	Reaction time	Conv. (yield [%])	dr	ee [%]
1	8a (OMe)	DBU	RT	1h	>95%	1:1	nd
2	8a (OMe)	MTBD	RT	1h	>95%	1:1	nd
3	8a (OMe)	NaOAc (3)	RT	3h	72%	3:1	nd
4	8a (OMe)	<i>t</i> BuOK (1.2)	RT	3h	>95%	3:1	nd
5	8a (OMe)	DIPEA (1.2)	RT	3h	87%	2:1	nd
	8a (OMe)	K_2CO_3 (3)	-20 °C	overnight	>95%	3:1	nd
7	8a (OMe)	K_2CO_3 (3)	RT	2h	>95% (74%)	3:1	97/98
8	8c (OtBu)	K_2CO_3 (3)	-20 °C	overnight	>95%	4:1	nd
9	8c (OtBu)	K_2CO_3 (3)	RT	2h	>95% (75%)	4:1	98/98

6. Enantioselective synthesis of hydroxy dihydrofuranes via epoxidation/interrupted Feist-Bénary reaction sequence



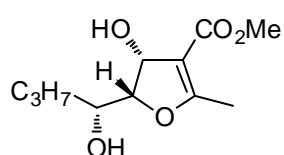
General procedure: A glass vial equipped with a magnetic stirring bar was charged with the aldehyde **1** (0.5 mmol, 1 equiv.), the aminocatalyst **6** (0.0125 mmol, 0.025 equiv.) and CH₂Cl₂ (1.0 mL). After short stirring at rt, H₂O₂ (35 wt% in water, 0.65 mmol, 1.3 equiv.) was added. The stirring was maintained at ambient temperature for 24 h to achieve full conversion of the aldehyde **1**. Upon completion of the reaction, MgSO₄ (1.25 mmol, 2.5 equiv.) was added, the reaction mixture was cooled to 0 °C and the corresponding 1,3-dicarbonyl compound **8** (0.525 mmol, 1.05 equiv.) was added followed by K₂CO₃ (1.5 mmol, 3 equiv.). After stirring for 2 h at ambient temperature the reaction mixture was directly subjected to FC on silica gel to afford the dihydrofuran **4**. Interrupted Feist-Bénary products should be handled with care due to the possibility of the dehydration to form furane derivatives.



4a (4S,5R)-Methyl 4-hydroxy-5-((R)-1-hydroxybutyl)-2-methyl-4,5-dihydrofuran-3-carboxylate (Entry 1, Table 5)

Following the general procedure **4a** was isolated by FC (gradient: CH₂Cl₂/Et₂O 5:1 to CH₂Cl₂/Et₂O 1:4) in 74% yield (3:1 dr). Diastereoisomers were separated by FC.

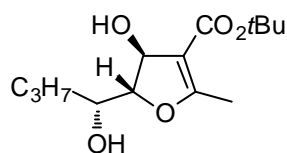
Major diastereoisomer (pale-yellow oil): ¹H NMR (400 MHz, CDCl₃) δ ppm 5.15 (s, 1H), 4.28-4.24 (m, 1H), 3.72-3.65 (m, 1H), 3.71 (s, 3H), 3.35 (d, *J* = 2.3 Hz, 1H), 2.69 (d, *J* = 4.7 Hz, 1H), 2.21 (s, 3H), 1.60-1.30 (m, 4H), 0.92 (t, *J* = 6.7 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 171.5, 166.2, 106.3, 92.0, 73.7, 70.5, 51.0, 34.1, 18.5, 14.5, 13.9. HR-MS: calculated for (M+Na)⁺: 253.1052; measured: 253.1046. The ee was determined by HPLC using a Chiralcel AD column (hexane/*i*PrOH 88:12, 1 mL min⁻¹); τ_{major} = 11.7 min, τ_{minor} = 11.0 min (97% ee). [α]_D^{rt}: +124.7 (c = 0.9, CHCl₃).



4a' (4R,5R)-Methyl 4-hydroxy-5-((R)-1-hydroxybutyl)-2-methyl-4,5-dihydrofuran-3-carboxylate (Entry 1, Table 5)

Minor diastereoisomer (pale-yellow oil): ¹H NMR (400 MHz, CDCl₃) δ ppm 5.23 (d, *J* = 6.8 Hz, 1H), 4.19 (t, *J* = 7.4 Hz, 1H), 3.74 (s, 3H), 3.25 (d, *J* = 4.4 Hz, 1H), 3.08 (s, 1H), 2.23 (s, 3H), 1.76-1.52 (m, 3H), 1.50-1.36 (m, 1H), 0.95 (t, *J* = 6.9 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 172.2, 166.0,

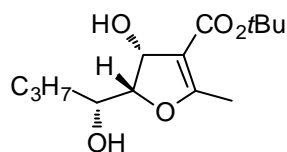
106.6, 86.6, 73.6, 69.4, 51.1, 35.8, 18.6, 14.5, 14.0. HR-MS: calculated for (M+Na)⁺: 253.1052; measured: 253.1060. The ee was determined by HPLC using a Chiralcel AD column (hexane/*i*PrOH 90:10, 1 mL min⁻¹); τ_{major} = 12.9 min, τ_{minor} = 12.2 min (98% ee). $[\alpha]_{\text{D}}^{25}$: +36.8 (c = 1.2, CHCl₃).



4b (4*S*,5*R*)-*tert*-Butyl 4-hydroxy-5-((*R*)-1-hydroxybutyl)-2-methyl-4,5-dihydrofuran-3-carboxylate (Entry 2, Table 5)

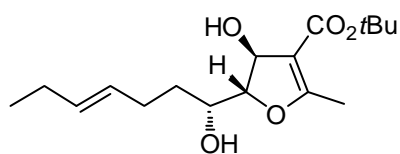
Following the general procedure **4b** was isolated by FC (gradient: CH₂Cl₂ to CH₂Cl₂/Et₂O 1:2) in 75% yield (4:1 dr). Diastereoisomers were separated by FC.

Major diastereoisomer (pale-yellow oil): ¹H NMR (400 MHz, CDCl₃) δ ppm 5.13 (s, 1H), 4.22 (t, *J* = 4.1 Hz, 1H), 3.75-3.65 (m, 1H), 3.33 (s, 1H), 2.68 (d, *J* = 3.7 Hz, 1H), 2.26 (s, 3H), 1.60-1.28 (m, 4H), 1.47 (s, 9H), 0.92 (t, *J* = 6.1 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 169.8, 165.3, 107.7, 91.3, 80.5, 74.0, 70.6, 34.0, 28.3, 18.6, 14.5, 13.9. HR-MS: calculated for (M+Na)⁺: 295.1521; measured: 295.1524. The ee was determined by HPLC using a Chiralcel AD column (hexane/*i*PrOH 97:3, 1 mL min⁻¹); τ_{major} = 40.0 min, τ_{minor} = 48.0 min (98% ee). $[\alpha]_{\text{D}}^{25}$: +116.8 (c = 1.0, CHCl₃).



4b' (4*R*,5*R*)-*tert*-Butyl 4-hydroxy-5-((*R*)-1-hydroxybutyl)-2-methyl-4,5-dihydrofuran-3-carboxylate (Entry 2, Table 5)

Minor diastereoisomer (pale-yellow oil): ¹H NMR (400 MHz, CDCl₃) δ ppm 5.22 (d, *J* = 7.3 Hz, 1H), 4.17 (t, *J* = 7.6 Hz, 1H), 4.05-3.95 (m, 1H), 3.27 (d, *J* = 4.8 Hz, 1H), 3.05 (s, 1H), 2.19 (s, 3H), 1.75-1.35 (m, 4H), 1.50 (s, 9H), 0.95 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 170.6, 165.3, 107.8, 86.1, 80.6, 74.0, 69.5, 35.8, 28.4, 18.6, 14.4, 14.0. HR-MS: calculated for (M+Na)⁺: 295.1521; measured: 295.1525. The ee was determined by HPLC using a Chiralcel OD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); τ_{major} = 7.1 min, τ_{minor} = 8.2 min (98% ee). $[\alpha]_{\text{D}}^{25}$: +29.5 (c = 1.0, CHCl₃).

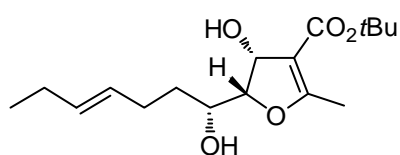


4c (4*S*,5*R*)-*tert*-Butyl 4-hydroxy-5-((*R*,*E*)-1-hydroxyhept-4-en-1-yl)-2-methyl-4,5-dihydrofuran-3-carboxylate (Entry 3, Table 5)

Following the general procedure **4c** was isolated by FC (gradient: EtOAc/pentane 5:95 to EtOAc/pentane 20:80) in 86% yield (3:1 dr).

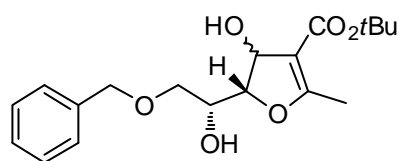
Diastereoisomers were separated by FC.

Major diastereoisomer (pale-yellow oil): ¹H NMR (400 MHz, CDCl₃) δ ppm 5.57-5.34 (m, 2H), 5.14 (d, *J* = 4.0 Hz, 1H), 4.24 (t, *J* = 4.4 Hz, 1H), 3.78-3.69 (m, 1H), 3.19 (bs, 1H), 2.43 (bs, 1H), 2.27-2.18 (m, 1H), 2.17 (s, 3H), 2.15-2.04 (m, 1H), 2.03-1.93 (m, 2H), 1.67-1.50 (m, 2H), 1.48 (s, 9H), 0.94 (t, *J* = 7.5 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 169.8, 165.2, 133.1, 128.1, 107.8, 91.2, 80.5, 74.0, 70.5, 31.7, 28.4, 28.4, 25.5, 14.5, 13.8. HR-MS: calculated for (M+Na)⁺: 335.1834; measured: 335.1828. The ee was determined by HPLC using a Chiralpak AD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); τ_{major} = 16.8 min, τ_{minor} = 19.4 min (95% ee). $[\alpha]_{\text{D}}^{25}$: +77.3 (c = 1.0, CHCl₃).



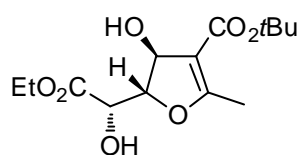
4c' (4R,5R)-tert-Butyl 4-hydroxy-5-((R,E)-1-hydroxyhept-4-en-1-yl)-2-methyl-4,5-dihydrofuran-3-carboxylate (Entry 3, Table 5)

Minor diastereoisomer (waxy white solid): ^1H NMR (400 MHz, CDCl_3) δ ppm 5.58-5.39 (m, 2H), 5.24 (d, $J = 7.3$ Hz, 1H), 4.19 (t, $J = 7.6$ Hz, 1H), 4.05-3.98 (m, 1H), 3.18 (d, $J = 4.8$ Hz, 1H), 2.84 (bs, 1H), 2.36-2.23 (m, 1H), 2.20 (s, 3H), 2.18-2.08 (m, 1H), 2.06-1.96 (m, 2H), 1.86-1.74 (m, 1H), 1.71-1.62 (m, 1H), 1.51 (s, 9H), 0.97 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ ppm 170.6, 165.2, 132.6, 128.5, 107.8, 86.0, 80.7, 74.1, 69.3, 33.6, 28.4, 28.4, 25.6, 14.4, 13.9. HR-MS: calculated for $(\text{M}+\text{Na})^+$: 335.1834; measured: 335.1826. The ee was determined by HPLC using a Chiralcel OD column (hexane/*i*PrOH 95:5, 1 mL min $^{-1}$); $\tau_{\text{major}} = 8.4$ min, $\tau_{\text{minor}} = 7.3$ min (98% ee). $[\alpha]_{\text{D}}^{25}$: +11.4 ($c = 0.38$, CHCl_3).



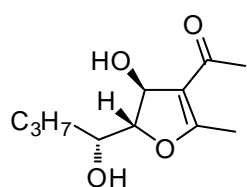
4d (5S)-tert-Butyl 5-((R)-2-(benzyloxy)-1-hydroxyethyl)-4-hydroxy-2-methyl-4,5-dihydrofuran-3-carboxylate (Entry 4, Table 5)

Following the general procedure **4d** was isolated by FC (gradient: DCM/EtOAc 10:1 to DCM/EtOAc 7:3) in 60% yield as a pale yellow oil (2:1 dr). ^1H NMR (400 MHz, CDCl_3) δ ppm 7.29-7.19 $^+$ (m, 5H), 5.15* (d, $J = 2.5$ Hz, 1H), 5.12 (d, $J = 7.0$ Hz, 1H), 4.56 (d, $J = 12.1$ Hz, 1H), 4.52 (d, $J = 8.5$ Hz, 1H), 4.49* (s, 2H), 4.35-4.29 $^+$ (m, 1H), 3.74-3.47 $^+$ (m, 3H), 3.35 (bs, 2H), 3.21* (bs, 2H), 2.11 (s, 3H), 2.10* (s, 3H), 1.43 (s, 9H), 1.43* (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ ppm 170.4, 169.6*, 165.1*, 165.1, 137.9, 137.6*, 128.3* (2C), 128.2 (2C), 127.7 (2C), 127.6* (2C), 127.6*, 127.6, 108.2, 107.6*, 88.0*, 83.0, 80.4, 80.4*, 74.8*, 73.4, 73.4 $^+$, 71.1, 70.4*, 69.5*, 68.7, 28.3 $^+$, 14.4 $^+$. HR-MS: calculated for $(\text{M}+\text{Na})^+$: 373.1627; measured: 373.1626. The ee for major diastereoisomer was determined by HPLC using a Chiralpak AD column (hexane/*i*PrOH 95:5, 0.5 mL min $^{-1}$) $\tau_{\text{major}} = 95.1$ min, $\tau_{\text{minor}} = 106.1$ min (96% ee). $[\alpha]_{\text{D}}^{25}$: +45.8 ($c = 1.5$, CHCl_3).



4e (4S,5S)-tert-Butyl 5-((S)-2-ethoxy-1-hydroxy-2-oxoethyl)-4-hydroxy-2-methyl-4,5-dihydrofuran-3-carboxylate (Entry 5, Table 5)

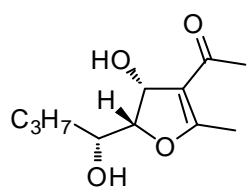
Following the general procedure **4e** was isolated by FC (gradient: EtOAc/ CH_2Cl_2 1:5 to EtOAc/ CH_2Cl_2 1:2) in 46% yield as a pale yellow oil (7:1 dr). Major diastereoisomer: ^1H NMR (400 MHz, CDCl_3) δ ppm 5.14 (dd, $J = 3.7, 1.0$ Hz, 1H), 4.59 (t, $J = 3.6$ Hz, 1H), 4.40-4.12 (m, 3H), 3.43 (d, $J = 6.2$ Hz, 1H), 3.07 (d, $J = 2.3$ Hz, 1H), 2.51 (s, 3H), 1.46 (s, 9H), 1.25 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ ppm 171.2, 169.8, 164.8, 108.1, 88.9, 80.5, 73.9, 70.9, 62.2, 28.3, 14.3, 14.0. HR-MS: calculated for $(\text{M}+\text{Na})^+$: 325.1263; measured: 325.1261. The ee was determined by HPLC using a Chiralcel AS column (hexane/*i*PrOH 95:5, 1 mL min $^{-1}$); $\tau_{\text{major}} = 23.4$ min, $\tau_{\text{minor}} = 18.1$ min (97% ee). $[\alpha]_{\text{D}}^{25}$: +95.4 ($c = 1.0$, CHCl_3).



4f 1-((4*S*,5*R*)-4-hydroxy-5-((*R*)-1-hydroxybutyl)-2-methyl-4,5-dihydrofuran-3-yl)ethanone (Entry 6, Table 5)

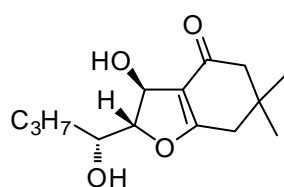
Following the general procedure **4f** was isolated by FC (EtOAc/CH₂Cl₂ 1:1) in 87% yield (1.6:1 dr). Diastereoisomers were separated by FC.

Major diastereoisomer (pale-yellow oil): ¹H NMR (400 MHz, CDCl₃) δ ppm 5.26 (d, *J* = 2.9 Hz, 1H), 4.28 (t, *J* = 4.3 Hz, 1H), 3.85-3.78 (m, 1H), 2.93 (bs, 1H), 2.32 (s, 3H), 2.28 (s, 3H), 1.65-1.48 (m, 3H), 1.49-1.35 (m, 1H), 0.96 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 195.6, 170.9, 116.9, 92.2, 74.3, 70.6, 34.3, 29.0, 18.6, 15.6, 13.9. HR-MS: calculated for (M+Na)⁺: 237.1103; measured: 237.1100. The ee was determined by HPLC using a Chiralcel OJ column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); τ_{major} = 25.3 min, τ_{minor} = 21.9 min (98% ee). [α]_D^{rt}: +69.8 (c = 1.01, CHCl₃).



4f' 1-((4*R*,5*R*)-4-hydroxy-5-((*R*)-1-hydroxybutyl)-2-methyl-4,5-dihydrofuran-3-yl)ethanone (Entry 6, Table 5)

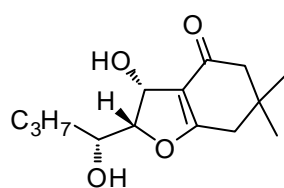
Minor diastereoisomer (pale-yellow oil): ¹H NMR (400 MHz, CDCl₃) δ ppm 5.31 (d, *J* = 6.8 Hz, 1H), 4.19 (t, *J* = 7.5 Hz, 1H), 4.08-3.99 (m, 1H), 3.15 (d, *J* = 3.2 Hz, 1H), 3.08 (d, *J* = 4.6 Hz, 1H), 2.32 (s, 3H), 2.28 (s, 3H), 1.80-1.53 (m, 3H), 1.53-1.35 (m, 1H), 0.97 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 195.4, 171.2, 117.3, 86.4, 74.281, 69.6, 35.8, 28.9, 18.6, 15.7, 14.0. HR-MS: calculated for (M+Na)⁺: 237.1103; measured: 237.1112. The ee was determined by HPLC using a Chiralcel OB column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); τ_{major} = 7.3 min, τ_{minor} = 12.1 min (98% ee). [α]_D^{rt}: +48.2 (c = 0.86, CHCl₃).



4g (2*R*,3*S*)-3-hydroxy-2-((*R*)-1-hydroxybutyl)-6,6-dimethyl-2,3,6,7-tetrahydrobenzofuran-4(5*H*)-one (Entry 7, Table 5)

Following the general procedure **4g** was isolated by FC (gradient: CH₂Cl₂/MeOH 100:1 to CH₂Cl₂/MeOH 100:5) in 80% yield (2.5:1 dr). Diastereoisomers were separated by FC.

Major diastereoisomer (white solid, mp: 115-119 °C): ¹H NMR (400 MHz, CDCl₃) δ ppm 5.22 (d, *J* = 3.1 Hz, 1H), 4.44 (t, *J* = 4.1 Hz, 1H), 4.34 (bs, 1H), 3.80-3.64 (m, 2H), 2.36 (d, *J* = 17.7 Hz, 1H), 2.30 (d, *J* = 17.8 Hz, 1H), 2.23 (d, *J* = 16.3 Hz, 1H), 2.14 (d, *J* = 16.3 Hz, 1H), 1.61-1.47 (m, 3H), 1.45-1.31 (m, 1H), 1.10 (s, 3H), 1.03 (s, 3H), 0.92 (t, *J* = 6.9 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 195.9, 179.9, 115.4, 95.8, 70.5, 69.9, 50.9, 37.8, 34.2, 34.1, 28.6, 28.5, 18.6, 13.9. HR-MS: calculated for (M+Na)⁺: 277.1416; measured: 277.1411. The ee was determined by HPLC using two Chiralcel OD columns (hexane/*i*PrOH 90:10, 0.5 mL min⁻¹); τ_{major} = 52.8 min, τ_{minor} = 47.6 min (98% ee). [α]_D^{rt}: +66.0 (c = 0.99, CHCl₃).

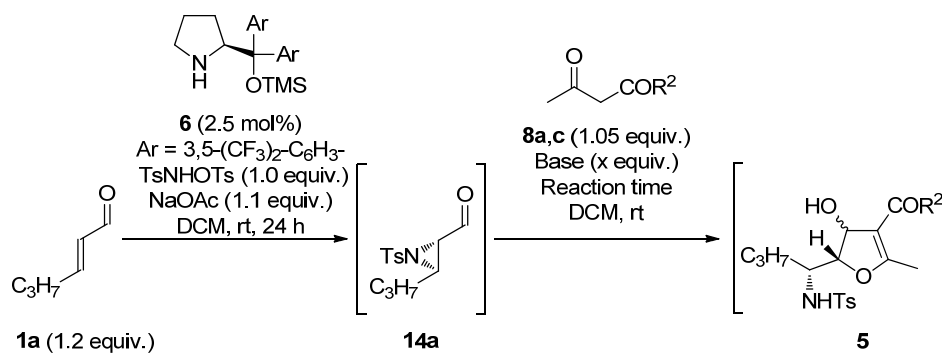


4g' (2*R*,3*R*)-3-hydroxy-2-((*R*)-1-hydroxybutyl)-6,6-dimethyl-2,3,6,7-tetrahydrobenzofuran-4(5*H*)-one (Entry 7, Table 5)

Minor diastereoisomer (white solid, mp: 107-111 °C): ¹H NMR (400 MHz, CDCl₃) δ ppm 5.34 (d, *J* = 6.8 Hz, 1H), 4.32 (t, *J* = 7.4 Hz, 1H), 4.14-3.97 (m, 2H), 3.57 (bs, 1H), 2.39 (d, *J* = 17.7 Hz, 1H), 2.29 (d, *J* = 18.1 Hz, 1H), 2.25 (d, *J* = 16.7 Hz, 1H), 2.21 (d, *J* = 16.4 Hz, 1H), 1.79-1.55 (m, 3H), 1.53-

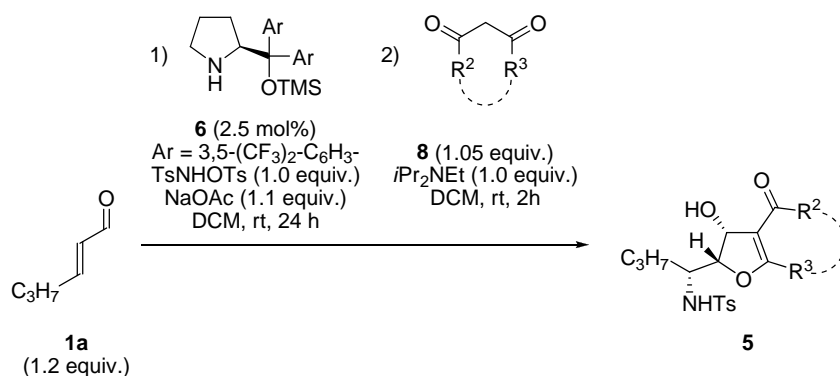
1.38 (m, 1H), 1.11 (s, 3H), 1.09 (s, 3H), 0.96 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ ppm 195.6, 179.7, 115.6, 90.0, 69.7, 69.0, 50.9, 37.8, 35.8, 34.1, 28.8, 28.4, 18.6, 14.0. HR-MS: calculated for $(\text{M}+\text{Na})^+$: 277.1416; measured: 277.1425. $[\alpha]_{\text{D}}^{25}$: +36.7 ($c = 1.02$, CHCl_3).

7. Optimization of the enantioselective aziridination/interrupted Feist-Bénary reaction sequence using *trans*-2-hexenal **1a and methyl or *tert*-butyl acetoacetates **8a,c** as model substrates**

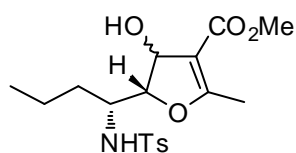


Entry	6 (R ²)	Base (equiv.)	Reaction time	Conv. (yield [%])	dr	ee [%]
1	8a (OMe)	MTBD (1)	1h	>95%	2:1	nd
2	8a (OMe)	K ₂ CO ₃ (1)	1h	>95%	1:1	nd
3	8a (OMe)	DIPEA (1)	3h	>95% (70)	2:1	98/96
4	8a (OMe)	Imidazole (3)	1h	>95%	2:1	nd
5	8a (OMe)	NEt ₃ (1)	1.5h	>95%	2:1	nd
6	8c (OtBu)	MTBD (1)	1h	>95%	1:1	nd
7	8c (OtBu)	DIPEA (1)	3h	>95%	1.5:1	nd
8	8c (OtBu)	Cs ₂ CO ₃ (1)	1h	>95%	1.5:1	nd

8. Enantioselective synthesis of hydroxy dihydrofuranes **5** via aziridination/interrupted Feist-Bénary reaction sequence



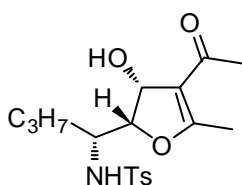
A glass vial equipped with a magnetic stirring bar was charged with the aldehyde **1a** (0.24 mmol, 1.2 equiv), the catalyst **6** (0.005 mmol, 0.025 equiv) and CH₂Cl₂ (1.0 mL). After short stirring at rt, TsNHOTs (0.2 mmol, 1 equiv) was added followed by NaOAc (0.22 mmol, 1.1 equiv.). The stirring was maintained at ambient temperature for 18 h to achieve full conversion of the nucleophile. Upon completion of the reaction, the reaction mixture was cooled to 0 °C and the corresponding 1,3-dicarbonyl compound **8** (0.21 mmol, 1.05 equiv.) was added followed by *i*Pr₂NEt (0.2 mmol, 1.0 equiv.). After stirring for 2 h at ambient temperature the reaction mixture was directly subjected to FC on silica gel to afford the dihydrofuran **5**. Interrupted Feist-Bénary products should be handled with care due to the possibility of the dehydration to form furane derivatives.



5a (5*R*)-Methyl 4-hydroxy-2-methyl-5-((*R*)-1-(4-methylphenylsulfonamido)butyl)-4,5-dihydrofuran-3-carboxylate (Entry 8, Table 5)

Following the general procedure **5a** was isolated by FC (EtOAc/pentane 20:80 to EtOAc/pentane 40:60) in 70% yield as a pale yellow oil (2:1 dr).

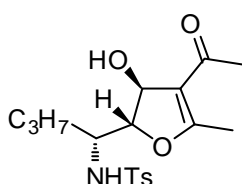
¹H NMR (400 MHz, CDCl₃) δ ppm 7.73* (d, *J* = 8.3 Hz, 2H), 7.70 (d, *J* = 8.3 Hz, 2H), 7.25⁺ (d, *J* = 8.3 Hz, 2H), 5.88* (d, *J* = 9.5 Hz, 1H), 5.78 (d, *J* = 9.0 Hz, 1H), 5.42 (s, 1H), 5.14* (d, *J* = 7.0 Hz, 1H), 4.22* (dd, *J* = 6.8, 4.7 Hz, 1H), 4.07-4.01 (m, 1H), 3.97-3.89* (m, 1H), 3.71* (s, 3H), 3.68 (s, 3H), 3.54-3.46 (m, 1H), 3.01* (d, *J* = 2.0 Hz, 1H), 2.80 (d, *J* = 1.5 Hz, 1H), 2.40* (s, 3H), 2.39 (s, 3H), 2.12 (s, 3H), 1.84* (s, 3H), 1.73-1.15⁺ (m, 4H), 0.88* (t, *J* = 7.2 Hz, 3H), 0.81 (t, *J* = 6.9 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 171.9*, 168.2, 166.5, 165.8*, 143.0, 142.6*, 139.3*, 138.2, 129.5 (2C), 129.3* (2C), 127.0 (2C), 126.9* (2C), 102.3, 102.0*, 84.8⁺, 73.5⁺, 54.3, 53.9*, 51.2, 51.1*, 34.6*, 34.4, 21.5, 21.4*, 19.3*, 19.0, 14.8, 13.9*, 13.8*, 13.6. HR-MS: calculated for (M+Na)⁺: 406.1300; measured: 406.1310. The ee was determined by HPLC using a Chiralpak AD column (hexane/*i*PrOH 90:10, 1 mL min⁻¹). Major diastereoisomer: τ_{major} = 26.7 min, τ_{minor} = 23.4 min (98% ee). Minor diastereoisomer: τ_{major} = 109.1 min, τ_{minor} = 62.9 min (96% ee). [α]_D^{rt}: +45.9 (c = 1.5, CHCl₃).



5b *N-((R)-1-((2R,3R)-4-acetyl-3-hydroxy-5-methyl-2,3-dihydrofuran-2-yl)butyl)-4-methylbenzenesulfonamide (Entry 9, Table 5)*

Following the general procedure **5b** was isolated by FC (gradient: EtOAc/CH₂Cl₂ 4:6 to EtOAc/CH₂Cl₂ 7:3) in 91% yield (2.5:1 dr). Diastereoisomers were separated by FC.

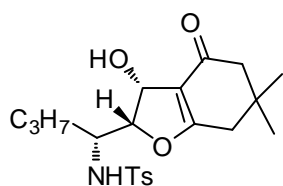
Major diastereoisomer (white solid, mp: 118-124 °C): ¹H NMR (400 MHz, CDCl₃) δ ppm 7.74 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 5.73 (d, *J* = 9.3 Hz, 1H), 5.20 (dd, *J* = 6.5, 2.0 Hz, 1H), 4.17 (t, *J* = 6.0 Hz, 1H), 3.95-3.87 (m, 1H), 3.48 (s, 1H), 2.41 (s, 3H), 2.27 (s, 3H), 1.97 (s, 3H), 1.65-1.49 (m, 2H), 1.28-1.16 (m, 2H), 0.83 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 195.2, 170.8, 143.0, 138.9, 129.4, 127.0, 117.5, 85.0, 73.8, 53.3, 34.4, 28.8, 21.4, 19.0, 15.0, 13.7. HR-MS: calculated for (M+Na)⁺: 390.1351; measured: 390.1355. The ee was determined by HPLC using a Chiralpak AD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); τ_{major} = 79.5 min, τ_{minor} = 64.5 min (98% ee). [α]_D^{rt}: +82.7 (c = 1.01, CHCl₃).



5b' *N-((R)-1-((2R,3S)-4-acetyl-3-hydroxy-5-methyl-2,3-dihydrofuran-2-yl)butyl)-4-methylbenzenesulfonamide (Entry 9, Table 5)*

Minor diastereoisomer (pale-yellow oil): ¹H NMR (400 MHz, CDCl₃) δ ppm 7.74 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 5.10 (d, *J* = 8.7 Hz, 1H), 5.06 (d, *J* = 3.2 Hz, 1H), 4.25 (dd, *J* =

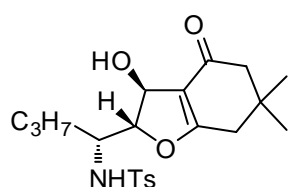
5.4, 3.6 Hz, 1H), 3.53-3.41 (m, 1H), 3.16 (bs, 1H), 2.42 (s, 3H), 2.26 (s, 3H), 2.14 (s, 3H), 1.44-1.26 (m, 4H), 0.76 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 195.3, 170.9, 143.5, 138.2, 129.7, 127.0, 116.7, 90.2, 75.0, 54.8, 32.6, 29.0, 21.5, 18.2, 15.3, 13.7. HR-MS: calculated for (M+Na)⁺: 390.1351 measured: 390.1350. The ee was determined by HPLC using a Chiralpak AD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); τ_{major} = 93.6 min, τ_{minor} = 83.3 min (92% ee). [α]_D^{rt}: +92.9 (c = 1.02, CHCl₃).



5c *N-((R)-1-((2R,3R)-3-hydroxy-6,6-dimethyl-4-oxo-2,3,4,5,6,7-hexahydrobenzofuran-2-yl)butyl)-4-methylbenzenesulfonamide (Entry 10, Table 5)*

Following the general procedure **5c** was isolated by FC (gradient: EtOAc/CH₂Cl₂ 4:6 to EtOAc/CH₂Cl₂ 7:3) in 80% yield (1:1 dr). Diastereoisomers were separated by FC.

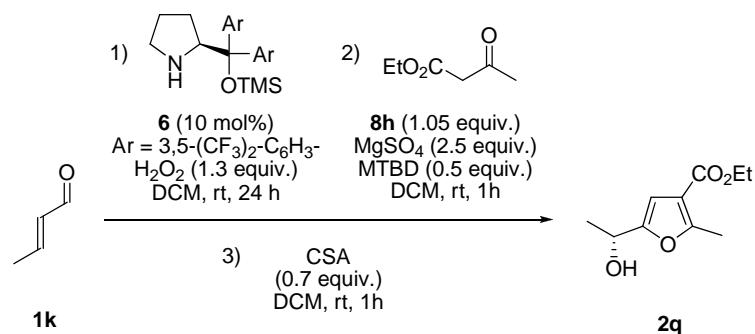
First diastereoisomer (pale-yellow oil): ¹H NMR (400 MHz, CDCl₃) δ ppm 7.74 (d, *J* = 8.3 Hz, 2H), 7.26 (d, *J* = 7.9 Hz, 2H), 5.92 (d, *J* = 9.5 Hz, 1H), 5.27 (d, *J* = 6.8 Hz, 1H), 4.40 (dd, *J* = 6.9, 4.3 Hz, 1H), 4.07-3.98 (m, 1H), 3.67 (bs, 1H), 2.42 (s, 3H), 2.21-1.99 (m, 4H), 1.76-1.43 (m, 4H), 1.02 (s, 3H), 0.99 (s, 3H), 0.90 (t, *J* = 7.2 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 195.2, 179.1, 142.4, 139.7, 129.3, 127.0, 115.6, 87.9, 70.0, 54.3, 50.8, 37.1, 34.5, 33.9, 28.9, 28.1, 21.4, 19.4, 13.7. HR-MS: calculated for (M+Na)⁺: 430.1664; measured: 430.1672. The ee was determined by HPLC using a Chiralcel OJ column (hexane/*i*PrOH 90:10, 1 mL min⁻¹); τ_{major} = 30.1 min, τ_{minor} = 18.5 min (94% ee). [α]_D^{rt}: +50.6 (c = 1.02, CHCl₃).



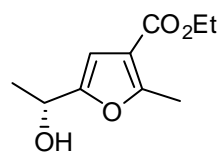
5c' *N*-((*R*)-1-((2*R*,3*S*)-3-hydroxy-6,6-dimethyl-4-oxo-2,3,4,5,6,7-hexahydrobenzofuran-2-yl)butyl)-4-methylbenzenesulfonamide (Entry 10, Table 5)

Second diastereoisomer (white foam): ^1H NMR (400 MHz, CDCl_3) δ ppm 7.71 (d, $J = 8.2$ Hz, 2H), 7.27 (d, $J = 7.4$ Hz, 2H), 5.61 (d, $J = 9.0$ Hz, 1H), 5.20 (d, $J = 2.2$ Hz, 1H), 4.49 (t, $J = 3.7$ Hz, 1H), 3.99 (bs, 1H), 3.65-3.56 (m, 1H), 2.41 (s, 3H), 2.32-2.09 (m, 4H), 1.47-1.28 (m, 2H), 1.28-1.18 (m, 2H), 1.09 (s, 3H), 1.06 (s, 3H), 0.74 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ ppm 196.0, 180.4, 143.4, 138.8, 129.8, 127.1, 115.4, 94.2, 70.7, 55.2, 51.1, 37.8, 34.3, 32.6, 28.8, 28.8, 21.7, 18.8, 13.9. HR-MS: calculated for $(\text{M}+\text{Na})^+$: 430.1664; measured: 430.1664. The ee was determined by HPLC using a Chiralcel OD column (hexane/*i*PrOH 90:10, 1 mL min $^{-1}$); $\tau_{\text{major}} = 31.2$ min, $\tau_{\text{minor}} = 18.3$ min (97% ee). $[\alpha]_{\text{D}}^{25}$: +68.2 ($c = 0.99$, CHCl_3).

9. Direct chemical correlation to (*R*)-ethyl 5-(1-hydroxyethyl)-2-methylfuran-3-carboxylate **2q**



2q (*R*)-Ethyl 5-(1-hydroxyethyl)-2-methylfuran-3-carboxylate (Scheme 5)



Following the modified general procedure for enantioselective synthesis of 2-hydroxy alkylfuranes via epoxidation/Feist-Bénary reaction sequence (using 10 mol% of catalyst **6** and crotonaldehyde **1k** and ethyl acetoacetate **8h** as starting materials) **2q** was isolated by FC

(gradient: pentane/EtOAc 90:10 to pentane/EtOAc 80:20) in 70% yield as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ ppm 6.47 (s, 1H), 4.80 (q, *J* = 6.5 Hz, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 2.55 (s, 3H), 2.06 (bs, 1H), 1.52 (d, *J* = 6.6 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ ppm 164.1, 158.7, 155.3, 113.9, 106.1, 63.3, 60.1, 21.1, 14.3, 13.8. HR-MS: calculated for (M+Na)⁺: 221.0790; measured: 221.0800. The ee was determined by HPLC using a Chiralpak AD column (hexane/*i*PrOH 95:5, 1 mL min⁻¹); τ_{major} = 17.9 min, τ_{minor} = 20.8 min (89% ee). [α]_D^{rt}: +5.9 (c = 1.0, CHCl₃) (lit.² [α]_D^{rt}: +8.8 (c = 1.0, CHCl₃), 89% ee).

² (a) Adam, W.; Korb, M. N. *Tetrahedron: Asymmetry* **1997**, *8*, 1131. (b) Adam, W.; Humpf, H. U.; Korb, M. N.; Schreier, P. *Tetrahedron: Asymmetry* **1997**, *8*, 3555.