Supporting Information

Zinc and indium-mediated Barbier-type allylation of aldehydes with 3-bromomethyl-5H-furan-2-one: an efficient synthesis of α-methylene-γ-butyrolactone

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1-General details

Unless otherwise noted, all commercial materials were used as received. Et₂O, THF were distilled over sodium under nitrogen, CH₂Cl₂ was distilled over sodium hydride under nitrogen. IR spectra were recorded as thin films or KBr discs, using a MAGNA-560 FTIR spectrophotometer. NMR spectra were recorded on Bruker spectrometer at 400 or 300 (¹H NMR), 100 or 75 (¹³C NMR) MHz with CDCl₃ as solvent. Data are expressed as chemical shifts in parts per million (ppm) relative to residual chloroform (¹H δ 7.27), CDCl₃ (¹³C δ 77.0) as the internal standard on the δ scale. The multiplicity of each signal is designated by the following abbreviations; s, singlet; d, doublet; t, triplet; br, broad. Allylation diastereoselectivity was determined by ¹H NMR integrations of the methylene signals. Melting points were measured on X4 apparatus and uncorrected. High-resolution mass spectra were conducted using an Ionspec 7.0T spectrometer by ESI-FTICR technique.

2-Procedure A: Allylation using indium

to a reaction vessel were added sequentially aldehyde (1 mmol), 3-bromomethyl-5H-furan-2-one (1.5 mmol), water (1.0 ml) and indium powder (2 mmol), the mixture was stirred vigorously at rt. After 12h the reaction mixture was filtered by diatomite, extracted with diethyl ether (20 ml × 3), washed with brine (20 ml), and dried over anhydrous Na₂SO₄. Evaporation under reduced pressure gave a residue which was chromatographed.  

3-Procedure B: Allylation using zinc

to a reaction vessel were added sequentially aldehyde (1 mmol), 3-bromomethyl-5H-furan-2-one (1.5 mmol), THF (1 ml), saturated aqueous NH₄Cl (0.5 ml) and activated zinc powder (1.7 mmol). The mixture was stirred for 15 minutes at rt and filtered by diatomite. Extracted with diethyl ether (20 ml × 3), washed with brine (20 ml) and dried over anhydrous Na₂SO₄. Evaporation under reduced pressure gave a residue which was chromatographed.

4-Characterization data for lactones 2a-2i

4-(4-Chlorophenyl)(hydroxy)methyl)-3-methylenedihydrofuran-2(3H)-one (2a)

Following procedure A, using 4-chlorobenzaldehyde (135mg, 0.96 mmol), afforded the above alcohol 2a (214mg, 93%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

¹H NMR (400 MHz, CDCl₃) δ 7.36 (d, J=1.9 Hz, 1H), 7.35 (t, J=2.3Hz, 1H), 7.29 (d, J=2.0Hz, 1H), 7.27 (d, J=4.2Hz, 1H), 6.32 (d, J=2.3Hz, 1H), 5.69 (d, J=1.8Hz, 1H), 4.73 (d, J=7.1Hz, 1H), 4.21(dd, J=8.2, 9.6Hz, 1H), 4.10(dd, J=4.1, 9.6Hz, 1H), 3.33-3.39(m, 1H), 2.81(br s, 1H).

Discernable data for minor diastereoisomer: 6.20(d, J=2.4Hz, 1H), 5.08(d, J=2.1Hz, 1H), 4.54(dd, J=9.6, 3.9Hz, 1H), 4.35(dd, J=9.6, 7.9Hz, 1H).

¹³C NMR (100 MHz, CDCl₃) δ 170.8, 139.1, 134.5, 134.3, 128.9, 127.9, 125.6, 74.8, 67.6, 45.4.

IR (neat), ν (cm⁻¹) 3457, 1759, 1660, 1272, 1132, 822.


Following procedure B, using 4-chlorobenzaldehyde (141mg, 1.00 mmol), afforded the above alcohol 2a (216mg, 90%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

(2) Synthesis of 4-(3-Chlorophenyl) (hydroxy) methyl)-3-methylenedihydrofuran-2(3H)-one (2b)
Following procedure A, using 3-chlorobenzaldehyde (139mg, 0.99mmol), afforded the above alcohol 2b (212mg, 90%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

\[ \text{H NMR} \ (400 \text{ MHz, CDCl}_3) \delta 7.35\text{(s, 1H), 7.29-7.31(m, 2H), 7.18-7.23(m, 1H), 6.31(d, J=2.2Hz, 1H), 5.67(d, J=1.8, 1H), 4.72(d, J=7.1Hz, 1H), 4.23(t, J=9.5Hz, 1H), 4.12(dd, J=9.6, 4.1Hz, 1H), 3.33-3.40(m, 1H), 2.91(s, 1H).} \]

Discernable data for minor diastereoisomer: 6.22(d, J=2.2Hz, 1H), 5.12(d, J=2.1Hz, 1H), 4.54(dd, J=9.6, 3.9Hz, 1H), 4.34(t, J=8.1Hz, 1H).

\[ \text{C NMR} \ (100 \text{ MHz, CDCl}_3) \delta 170.9, 142.8, 134.8, 134.4, 130.0, 128.6, 125.8, 124.8, 67.7, 45.4. \]

\[ \text{IR (neat), } \nu (\text{cm}^{-1}) \ 3455, 1758, 1659, 1274, 1138, 807. \]

\[ \text{HRMS (ESI): M+Na}^+ \text{ found 261.0289, } \text{C}_{12}\text{H}_{11}\text{ClO}_3\text{Na requires 261.0297.} \]

The reaction of 1b(140mg, 1.00mmol), 3-bromomethyl-5-H-furan-2-one (262mg, 1.49mmol), activated zinc powder (106mg, 166mmol), THF (1 ml), and saturated aqueous NH₄Cl (0.5 ml) at rt for 15 min afforded 2b (219mg, 92%).

\[ \text{mp: 94-108 }^\circ \text{C} \]

\[ \text{H NMR} \ (400 \text{ MHz, CDCl}_3) \delta 7.50(dd, J=7.5, 1.9Hz, 1H), 7.40(dd, J=7.5, 1.7Hz, 1H), 7.27-7.34(m, 2H), 6.27(d, J=2.2Hz, 1H), 5.28(d, J=3.6Hz, 1H), 5.27(s, 1H), 4.37(t, J=9.3Hz, 1H), 4.32(dd, J=9.4, 3.9Hz, 1H), 3.46-3.52(m, 1H), 2.67(br s, 1H). \]

Discernable data for minor diastereoisomer: 7.62(dd, J=7.7, 1.7Hz, 1H), 7.14-7.19(m, 3H), 6.31(d, J=2.5Hz, 1H), 5.59(s, 1H), 5.46(d, J=4.0Hz, 1H), 4.55(dd, J=9.5, 4.1Hz, 1H), 4.21(t, J=8.3Hz, 1H).

\[ \text{C NMR} \ (100 \text{ MHz, CDCl}_3) \delta 171.1, 138.0, 133.8, 131.9, 129.6, 129.4, 128.5, 127.1, 125.6, 71.9, 68.6, 43.6. \]

\[ \text{IR (neat), } \nu (\text{cm}^{-1}) \ 3453, 1742, 1659, 1274, 1141, 768. \]

\[ \text{HRMS (ESI): M+Na}^+ \text{ found 260.0289, } \text{C}_{12}\text{H}_{11}\text{ClO}_3\text{Na requires 261.0297.} \]

Following procedure B, using 2-chlorobenzaldehyde (135mg, 0.96mmol), afforded the above alcohol 2c (212mg, 92%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

\[ \text{mp: 94-108 }^\circ \text{C} \]

\[ \text{H NMR} \ (400 \text{ MHz, CDCl}_3) \delta 7.26(d, J=8.2Hz, 2H), 6.91(d, J=8.7Hz, 2H), 6.36(d, J=2.2Hz, 1H), 5.85(d, J=1.6Hz, 1H), 4.65(d, J=7.9Hz, 1H), 4.16(dd, J=8.4, 9.5Hz, 1H), 4.02(dd, J=4.5, 9.6Hz, 1H), 3.81(s, 3H), 3.36-3.42(m, 1H), 2.40(br s, 1H). \]

Discernable data for minor diastereoisomer: 7.84(d, J=8.8Hz, 2H), 7.02(d, J=8.7Hz, 2H), 6.17(d, J=2.4Hz, 1H), 5.11(d, J=2.1Hz, 1H).
Following procedure B, using 4-methoxybenzaldehyde (134mg, 0.98mmol), afforded the above alcohol 2d (215mg, 93%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

Following procedure A, using 4-(4-Trifluoromethylphenyl)(hydroxy)methyl)-3-methylenedihydrofuran-2(3H)-one (2e)

Following procedure B, using 4-(4-Trifluoromethylphenyl)(hydroxy)methyl) -3-methylenedihydrofuran-2(3H)-one (2f)

Following procedure A, using 4-(4-Tert-butylphenyl)(hydroxy)methyl)-3-methylenedihydrofuran-2(3H)-one (2f)

Following procedure A, using 4-tetrafluoromethylbenzaldehyde (170mg, 0.98mmol), afforded the above alcohol 2e (242mg, 91%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

mp: 76 - 90 °C.

Following procedure A, using 4-tetrafluoromethylbenzaldehyde (161mg, 0.99mmol), afforded the above alcohol 2f (233mg, 90%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

Following procedure B, using 4-tetrafluoromethylbenzaldehyde (176mg, 1.01mmol), afforded the above alcohol 2f (234mg, 88%) via column chromatography (petroleum ether/ethyl acetate, 1:1).
4-(4-cyanophenyl) (hydroxy) methyl)-3-methylenedihydrofuran-2(3H)-one (2g)

Following procedure A, using 4-cyanobenzaldehyde (134mg, 1.02mmol), afforded the above alcohol 2g (204mg, 87%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

\[\text{H NMR (400 MHz, CDCl}_3\text{) } \delta 7.71(d, J=8.0Hz, 2H), 7.51(d, J=8.1Hz, 2H), 6.37(s, 1H), 5.61(s, 1H), 4.88(d, J=6.6Hz, 1H), 4.29(t, J=9.4Hz, 1H), 4.19(dd, J=3.6, 9.6Hz, 1H), 3.4(s, 1H), 2.48(br s, 1H).\]

\[\text{C NMR (100 MHz, CDCl}_3\text{) } \delta 170.0, 145.5, 134.0, 132.5, 127.6, 127.2, 125.7, 118.2, 112.4, 74.8, 67.2, 45.3.\]

Following procedure B, using 4-cyanobenzaldehyde (129mg, 0.98mmol), afforded the above alcohol 2f (221mg, 98%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

4-(Hydroxy(naphthalen-3-yl)methyl)-3-methylenedihydrofuran-2(3H)-one (2h)

Following procedure A, using β-naphthaldehyde (160mg, 1.03mmol), afforded the above alcohol 2h (232mg, 89%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

\[\text{H NMR (400 MHz, CDCl}_3\text{) } \delta 7.81-7.86(m, 3H), 7.75(s, 1H), 7.50-7.52(m, 2H), 7.44(d, J=8.4Hz, 1H), 6.34(s, 1H), 5.75(s, 1H), 4.82(d, J=7.5Hz, 1H), 4.15(t, J=9.1Hz, 1H), 4.08(dd, J=9.3, 4.1Hz, 1H), 3.47(s, 1H), 2.66(br s, 1H).\]

Discernable data for minor diastereoisomer: 7.20(d, J=8.9Hz, 1H), 6.17(d, J=2.4Hz, 1H), 4.97(d, J=2.1Hz, 1H), 4.64(dd, J=9.7, 4.1Hz, 1H), 4.39(dd, J=9.4, 7.8Hz, 1H).

\[\text{C NMR (100 MHz, CDCl}_3\text{) } \delta 169.8, 137.0, 133.9, 132.3, 132.0, 127.9, 127.0, 126.7, 125.6, 125.5, 124.9, 124.5, 122.9, 74.7, 66.7, 44.3.\]

\[\text{IR (neat), } \nu (\text{cm}^{-1}) 3443, 1759, 1658, 1273, 1123.\]

\[\text{HRMS (ESI): } M+Na^+ \text{ found 277.0828, C}_{16}H_{14}O_3Na \text{ required 277.0841.}\]

Following procedure B, using β-naphthaldehyde (153mg, 0.98mmol), afforded the above alcohol 2h (212mg, 85%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

4-(Hydroxy(furan-3-yl)methyl)-3-methylenedihydrofuran-2(3H)-one (2i)

Following procedure A, using 2-furaldehyde (101mg, 1.05mmol), afforded the above alcohol 2i (149mg, 73%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

\[\text{H NMR (400 MHz, CDCl}_3\text{) } \delta 7.43(d, J=1.0Hz, 1H), 6.40(d, J=3.7Hz, 2H), 6.36(d, J=3.3Hz, 1H), 5.78(d, J=2.0Hz, 1H), 4.80(d, J=7.4Hz, 1H), 4.39(t, J=9.5Hz, 1H), 4.21(dd, J=9.6, 4.3Hz, 1H), 3.59-3.65(m, 1H), 2.67(br s, 1H).

Discernable data for minor diastereoisomer: 7.45(s, 1H), 6.28(d, J=2.5Hz, 1H), 5.24(d, J=2.2Hz, 1H), 4.77(d, J=7.6Hz, 1H), 4.58(dd, J=9.6, 4.3Hz, 1H), 4.49(t, J=8.1Hz, 1H).}
\( ^{13}\text{C} \text{ NMR} \) (100 MHz, CDCl\(_3\)) \( \delta \) 169.6, 152.2, 141.8, 133.2, 124.7, 109.5, 107.2, 68.2, 66.4, 42.3.

\( \text{IR} \) (neat), \( \nu \) (cm\(^{-1}\)) 3418, 1755, 1660, 1274, 1123.

\( \text{HRMS} \) (ESI): M+Na\(^+\) found 217.0470, \( \text{C}_{10}\text{H}_{10}\text{O}_4\text{Na} \) required 2170.477.

Following procedure B, using 2-furaldehyde (98mg, 1.02mmol), afforded the above alcohol 2\( i \) (187mg, 94%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

\( \text{IR} \) (neat), \( \nu \) (cm\(^{-1}\)) 3443, 1759, 1659, 1276, 1129.

\( \text{HRMS} \) (ESI): M+Na\(^+\) found 233.0240, \( \text{C}_{10}\text{H}_{18}\text{O}_3\text{Na} \) required 233.0248.

Following procedure B, using 2-thiophenaldehyde (113mg, 1.01mmol), afforded the above alcohol 2\( j \) (197mg, 93%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

\( ^1\text{H} \text{ NMR} \) (400 MHz, CDCl\(_3\)) \( \delta \) 7.25(d, \( J=5.1\text{Hz} \), 1H), 6.91(dd, \( J=4.9, 3.6\text{Hz} \), 1H), 6.81(d, \( J=2.7\text{Hz} \), 1H), 6.26(d, \( J=2.5\text{Hz} \), 1H), 5.20(d, \( J=2.1\text{Hz} \), 1H), 4.56(dd, \( J=9.8, 4.2\text{Hz} \), 1H), 4.45(t, \( J=8.1\text{Hz} \), 1H).

Discernable data for minor diastereoisomer: 7.25(d, \( J=5.1\text{Hz} \), 1H), 6.91(dd, \( J=4.9, 3.6\text{Hz} \), 1H), 6.81(d, \( J=2.7\text{Hz} \), 1H), 6.26(d, \( J=2.5\text{Hz} \), 1H), 5.20(d, \( J=2.1\text{Hz} \), 1H), 4.56(dd, \( J=9.8, 4.2\text{Hz} \), 1H), 4.45(t, \( J=8.1\text{Hz} \), 1H).

\( ^{13}\text{C} \text{ NMR} \) (100 MHz, CDCl\(_3\)) \( \delta \) 169.6, 143.3, 133.6, 126.0, 124.9, 124.3, 70.6, 66.4, 44.9.

Following procedure A, using 2-thiophenaldehyde (115mg, 1.03mmol), afforded the above alcohol 2\( j \) (184mg, 85%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

\( ^{13}\text{C} \text{ NMR} \) (100 MHz, CDCl\(_3\)) \( \delta \) 169.6, 143.3, 133.6, 126.0, 124.9, 124.3, 70.6, 66.4, 44.9.

Following procedure B, using 2-thiophenaldehyde (100mg, 1mmol), afforded the above alcohol 4a (193mg, 97%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

\( ^{13}\text{C} \text{ NMR} \) (100 MHz, CDCl\(_3\)) \( \delta \) 169.6, 143.3, 133.6, 126.0, 124.9, 124.3, 70.6, 66.4, 44.9.

IR (neat), \( \nu \) (cm\(^{-1}\)) 3445, 1765, 1661, 1276, 1129.

HRMS (ESI): M+Na\(^+\) found 221.1146, \( \text{C}_{10}\text{H}_{18}\text{O}_3\text{Na} \) required 221.1154.

Following procedure B, using n-hexaldehyde (100mg, 1mmol), afforded the above alcohol 4a (193mg, 97%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

4-(1-Hydroxybutyl)-3-methylenedihydrofuran-2(3H)-one (4b)
Following procedure A, using butyraldehyde (80mg, 1.11mmol), afforded the above alcohol 4b (176mg, 93%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

\[ ^1H \text{NMR (400 MHz, CDCl}_3) \delta 6.37(d, J=2.1Hz, 1H), 5.82(d, J=1.8Hz, 1H), 4.42(t, J=9.2Hz, 1H), 4.30(dd, J=9.4, 3.7Hz, 1H), 3.68-3.72(m, 1H), 3.13-3.15(m, 1H), 2.08(br s, 1H), 1.34-1.60(m, 4H), 0.97(t, J=7.2Hz, 3H) \]

Discernable data for minor diastereoisomer: 6.17(d, J=2.2Hz, 1H), 5.61(d, J=2.0Hz, 1H), 4.61(t, J=9.1Hz, 1H).

\[ ^13C \text{NMR (100 MHz, CDCl}_3) \delta 170.9, 135.1, 124.6, 72.9, 68.1, 44.6, 35.6, 18.9, 13.9. \]

IR (neat), \( \nu (\text{cm}^{-1}) \) 3453, 1761, 1660, 1274, 1123.

HRMS (ESI): M+Na\(^+\) found 193.0830, C\(_9\)H\(_{14}\)O\(_3\)Na required 193.0841.

Following procedure B, using butyraldehyde (75mg, 1.04mmol), afforded the above alcohol 4b (170mg, 96%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

(E)-4-(1-Hydroxyhex-2-en-1-yl)-3-methylenedihydrofuran-2(3H)-one (4c)

Following procedure A, using (E)-2-hexenal (97mg, 0.99mmol), afforded the above alcohol 4c (162mg, 83%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

\[ ^1H \text{NMR (400 MHz, CDCl}_3) \delta 6.38(d, J=2.2Hz, 1H), 5.88(d, J=1.8Hz, 1H), 5.74-5.82(m, 1H), 5.48(dd, J=15.4,7.3Hz, 1H), 4.37(t, J=9.4Hz, 1H), 4.26(dd, J=8.5, 4.1Hz, 1H), 4.20(t, J=7.0Hz, 1H), 3.21-3.25(m, 1H), 2.00-2.10(m, 2H), 1.99(br s, 1H), 1.37-1.47(m, 2H), 0.94(t, J=7.3Hz, 3H) \]

Discernable data for minor diastereoisomer: 6.17(d, J=2.3Hz, 1H), 5.93(d, J=1.8Hz, 1H).

\[ ^13C \text{NMR (100 MHz, CDCl}_3) \delta 170.7, 135.9, 135.2, 128.2, 124.6, 74.6, 67.3, 44.1, 34.3, 22.2, 13.6. \]

IR (neat), \( \nu (\text{cm}^{-1}) \) 3454, 1760, 1662, 1274, 1124.

HRMS (ESI): M+Na\(^+\) found 219.0990, C\(_{11}\)H\(_{16}\)O\(_3\)Na 219.0997.

Following procedure B, using (E)-2-hexenal (101mg, 1.03mmol), afforded the above alcohol 4c (192mg, 95%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

4-(3-Methylthio-1-hydroxypropyl)-3-methylenedihydrofuran-2(3H)-one (4d)

Following procedure A, using 3-(Methylthio)propionaldehyde (104mg, 1mmol), afforded the above alcohol 4d (162mg, 80%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

\[ ^1H \text{NMR (400 MHz, CDCl}_3) \delta 6.38(d, J=2.1Hz, 1H), 5.83(d, J=1.7Hz, 1H), 4.44(t, J=9.4Hz, 1H), 4.31(dd, J=9.4, 3.6Hz, 1H), 3.87-3.93(m, 1H), 3.17-3.22(m, 1H), 2.71(t, J=6.7Hz, 2H), 2.52(br s, 1H), 2.12(s, 3H), 1.68-1.83(m, 2H) \]

Discernable data for minor diastereoisomer: 5.76(d, J=2.1Hz, 1H), 3.81-3.43(m, 1H), 2.35(br s, 1H).

\[ ^13C \text{NMR (100 MHz, CDCl}_3) \delta 169.7, 134.0, 123.8, 71.4, 66.8, 43.6, 30.6, 29.9, 14.4. \]
**IR** (neat), v (cm⁻¹) 3453, 1762, 1660, 1414, 1279, 1122.

**HRMS** (ESI): M+Na⁺ found 225.0562, C₉H₁₄O₃Na required 225.0561.

Following procedure B, using 3-(Methylthio)propionaldehyde (107mg, 1.03mmol), afforded the above alcohol 4d (198mg, 95%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

4-(1-Hydroxypent-4-en-1-yl)-3-methylenedihydrofuran-2(3H)-one (4e)

Following procedure A, using 4-pentenal (90mg, 1.07mmol), afforded the above alcohol 4e (177mg, 91%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

**¹H NMR** (400 MHz, CDCl₃) δ 6.37(d, J=1.5Hz, 1H), 5.76-5.86(m, 2H), 5.09(d, J=17.1Hz, 1H), 5.02(d, J=10.1Hz, 1H), 4.41(t, J=9.2Hz, 1H), 4.27(dd, J=9.4, 3.6Hz, 1H), 3.69-3.74(m, 1H), 3.14(s, 1H), 2.25-2.31(m, 2H), 2.12-2.21(m, 1H), 1.54-1.60(m, 2H).

Discernable data for minor diastereoisomer: 5.72(d, J=1.9Hz, 1H), 3.83-3.88(m, 1H).

**¹³C NMR** (100 MHz, CDCl₃) δ 171.4, 138.2, 135.6, 125.3, 116.3, 73.2, 68.6, 45.1, 33.1, 30.6.

**IR** (neat), ν (cm⁻¹) 3444, 1760, 1660, 1271, 1123.

**HRMS** (ESI): M+Na⁺ found 182.0940, C₁₀H₁₄O₃Na required 182.0943.

Following procedure B, using 4-pentenal (86mg, 1.02mmol), afforded the above alcohol 4e (166mg, 89%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

4-(Hydroxy(cyclohex-2-yl)methyl)-3-methylenedihydrofuran-2(3H)-one (4f)

Following procedure A, using cyclohexanal (114mg, 1.02mmol), afforded the above alcohol 4f (205mg, 96%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

**¹H NMR** (400 MHz, CDCl₃) δ 6.32(d, J=2.1Hz, 1H), 5.77(d, J=1.6Hz, 1H), 4.37(t, J=8.8Hz, 1H), 4.14(dd, J=9.1, 4.2Hz, 1H), 3.35(t, J=6.1Hz, 1H), 1.63-1.76(m, 6H), 1.35-1.37(m, 1H), 1.02-1.18(m, 5H);

Discernable data for minor diastereoisomer: 6.10(d, J=1.8Hz, 1H), 5.56(d, J=1.2Hz, 1H), 4.54(t, J=8.9Hz, 1H).

**¹³C NMR** (100 MHz, CDCl₃) δ 170.0, 134.2, 123.7, 75.7, 67.6, 40.0, 39.4, 29.0, 26.2, 25.2, 25.1, 24.9.

**IR** (neat), v (cm⁻¹) 3490, 1741, 1659, 1265, 1134.


Following procedure B, using cyclohexanal (116mg, 1.04mmol), afforded the above alcohol 4f (201mg, 92%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

4-(3-phenyl-1-hydroxypropyl)-3-methylenedihydrofuran-2(3H)-one (4g)

Following procedure A, using 3-phenylpropanal (142mg, 1.06mmol), afforded the above alcohol 4g (162mg, 80%)
via column chromatography (petroleum ether/ethyl acetate, 1:1).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.33(t, $J$=7.3Hz, 2H), 7.24(dd, $J$=7.2, 11.8Hz, 3H), 6.37(d, $J$=1.6Hz, 1H), 5.79(d, $J$=1.0Hz, 1H), 4.40(t, $J$=8.9Hz, 1H), 4.24(dd, $J$=3.4, 9.4Hz, 1H), 3.71(t, $J$=9.2Hz, 1H), 3.13(s, 1H), 2.93(m, 1H), 2.75(m, 1H), 2.05(br s, 1H), 1.18(s, 1H);

Discernable data for minor diastereoisomer: 5.70(d, $J$=1.7Hz, 1H), 4.40(t, $J$=8.9Hz, 1H), 4.24(dd, $J$=3.4, 9.4Hz, 1H), 3.71(t, $J$=9.2Hz, 1H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 170.7, 141.1, 135.0, 128.6, 128.4, 126.3, 124.8, 72.4, 68.0, 44.7, 35.2, 32.0.

Following procedure A, using isopropenyl (130mg, 0.97mmol), afforded the above alcohol 4g (189mg, 84%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

4-(Hydroxy-(5-isopropenyl-2-methyl-1-en-cyclopentyl) methyl) -3-methylenedihydrofuran-2(3H)-one (4h)

Following procedure A, using isopropenyl-2-methyl-1-en-cyclopentane-carboxaldehyde (153mg, 1.02mmol), afforded the above alcohol 4h (220mg, 87%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.34(s, 1H), 5.93(s,1H), 4.78(s, 1H), 4.72(s, 1H), 4.30(d, $J$=9.4Hz, 1H), 4.22(t, $J$=8.8Hz, 1H), 3.97(dd, $J$=9.4, 3.4Hz, 1H), 3.53(d, $J$=8.6Hz, 1H), 3.32(s, 1H), 2.44-2.52(m, 1H), 2.22-2.28(t, $J$=9.6Hz, 1H), 2.00-2.10(m, 1H), 1.93(s, 1H), 1.81(s, 3H), 1.66-1.72(m, 1H), 1.64(s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 170.8, 148.5, 141.0, 135.8, 134.7, 125.2, 112.5, 70.3, 67.8, 53.7, 43.4, 38.3, 29.0, 19.1, 14.7.

IR (neat) $\nu$ (cm$^{-1}$) 3481, 1766, 1659, 1275, 1119.

HRMS (ESI) M+Na$^+$ found 271.1313, C$_7$H$_8$O$_2$Na required 271.1305.

4hII (139, 55%) : [a]$_D^{20}$ = +2.8 (c = 0.01, EtOH).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.33(dd, $J$=2.4, 0.8Hz, 1H), 6.04(dd, $J$=2.2, 0.9Hz, 1H), 4.85(s, 1H), 4.78(t, $J$=1.5Hz, 1H), 4.48(dd, $J$=9.2, 5.9Hz, 1H), 4.26(dd, $J$=9.4, 8.5Hz, 1H), 3.86(dd, $J$=9.5, 5.0Hz, 1H), 3.27-3.33(m, 1H), 2.41-2.50(m, 1H), 2.23-2.29(m, 2H), 1.95-2.06(m, 1H), 1.76(s, 3H), 1.64-1.71(m, 1H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 170.8, 151.3, 141.4, 135.9, 133.7, 125.0, 110.7, 71.0, 67.3, 53.1, 43.6, 37.5, 28.9, 19.7, 14.3.

IR (neat) $\nu$ (cm$^{-1}$) 3481, 1766, 1658, 1276, 1121.

HRMS (ESI) M+Na$^+$ found 271.1311, C$_7$H$_8$O$_2$Na required 271.1305.

Following procedure B, using isopropenyl-2-methyl-1-en-cyclopentane-carboxaldehyde (150mg, 1.0mmol), afforded the above alcohol 4h (221mg, 89%) via column chromatography (petroleum ether/ethyl acetate, 1:1).

6-Procedure for 4h into 8
Synthesis of 4-Hydroxymethyl-5-(5-isopropenyl-2-methyl-1-en-cyclopentyl)-3-methylenedihydrofuran-2(3H)-one (5,7)

A mixture of lactone 4hl (296mg, 1.19mmol), NaOH (220mg, 5.5mmol) were combined in 6 ml of a 1:1 mixture of THF and water for 2 h. The mixture was carefully acidified to pH 1 and extracted with CH$_2$Cl$_2$. The combined extracts were dried, concentrated and chromatographed to give 5 (178mg, 60%): oil.

$[\alpha]_{D}^{20} = -150.0$ (c = 0.01, EtOH).

$^{1}$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.29(d, J = 2.6Hz, 1H), 5.65(d, J = 1.8Hz, 1H), 5.16(d, J = 5.6Hz, 1H), 4.72(d, J = 1.8Hz, 1H), 4.63(t, J = 1.4Hz, 1H), 3.81(d, J = 10.9, 5.8Hz, 1H), 3.73(dd, J = 10.9, 5.4Hz, 1H), 3.47(d, J = 9.4Hz, 1H), 3.08-3.12(m, 1H), 2.43-2.52(m, 1H), 2.22-2.26(m, 1H), 2.01-2.11(m, 2H), 1.79(s, 3H), 1.64-1.69(m, 1H), 1.63(s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 170.5, 148.0, 141.7, 136.7, 132.5, 122.5, 111.7, 77.7, 63.2, 53.2, 45.7, 38.3, 28.8, 18.9, 14.3.

IR (neat) $\nu$ (cm$^{-1}$) 3457, 1732, 1659, 1269, 1141.

HRMS (ESI) M+Na$^+$ found 271.1301, C$_{15}$H$_{20}$O$_{3}$Na required 271.1305.

Compound 7 was prepared according to the same procedure. The reaction of 4hl (251mg, 0.93mmol), NaOH (193mg, 4.8mmol) and 1:1 mixture of THF and water (6 ml) afforded 7 (190mg, 70%): oil.

$[\alpha]_{D}^{20} = -70.7$ (c = 0.01, EtOH).

$^{1}$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.27(d, J = 2.5Hz, 1H), 5.69(d, J = 2.5Hz, 1H), 5.22(d, J = 5.0Hz, 1H), 4.61(s, 1H), 4.60(d, J = 1.2Hz, 1H), 3.80(dd, J = 10.8, 6.2Hz, 1H), 3.74(dd, J = 10.8, 5.6Hz, 1H), 3.46(d, J = 8.2Hz, 1H), 3.13-3.17(m, 1H), 2.43-2.51(m, 1H), 2.26-2.34(m, 1H), 1.99-2.06(m, 2H), 1.81(s, 3H), 1.65-1.72(m, 1H), 1.62(s, 3H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 170.8, 148.1, 143.8, 137.0, 132.5, 122.3, 111.4, 76.9, 63.7, 53.9, 44.9, 38.2, 28.1, 17.8, 14.2.

IR (neat) $\nu$ (cm$^{-1}$) 3439, 1747, 1661, 1271, 1153.

HRMS (ESI) M+Na$^+$ found 271.1304, C$_{15}$H$_{20}$O$_{3}$Na required 271.1305.

Synthesis of 4-Hydroxymethyl-5-(5-isopropenyl-2-methyl-1-en-cyclopentyl)-3-phenthiomethyl-dihydrofuran-2(3H)-one (6, 8)
To a solution of the 5 (160 mg, 0.59 mmol) and DMAP (11 mg) in CH₂Cl₂ (4 mL) was added benzenethiol (190 µl, 1.9 mmol) at ice cold temperature. After stirring at room temperature for 3 h, the solution was concentrated directly, and the crude oil was chromatographed to give thioether 6 (180 mg, 85%): white solid. mp = 52-56 °C; [α]D²⁰ = -96.0 (c = 0.01, EtOH).

¹H NMR (400 MHz, CDCl₃) δ 7.40(d, J=7.3Hz, 2H), 7.34(t, J=7.4Hz, 2H), 7.24(t, J=7.1Hz, 1H), 5.05(d, J=9.9Hz, 1H), 4.79(d, J=1.6Hz, 1H), 4.67(s, 1H), 3.85(dd, J=11.3, 3.5Hz, 1H), 3.56-3.65(m, 3H), 2.88-2.97(m, 2H), 2.45-2.58(m, 2H), 2.23-2.29(m, 1H), 2.02-2.12(m, 1H), 1.89(s, 1H), 1.78(s, 3H), 1.65-1.72(m, 1H), 1.63(s, 3H).

¹³C NMR (100 MHz, CDCl₃) δ 176.8, 148.6, 142.6, 134.8, 130.9, 129.5, 139.3, 126.8, 111.8, 76.9, 60.1, 53.2, 48.0, 41.9, 38.4, 33.9, 28.6, 18.6, 14.4.

IR (neat) ν (cm⁻¹) 3388, 1748, 1670, 1277, 1191.

HRMS (ESI) M+Na⁺ found 381.1499, C₂¹H₂₆O₃SNa required 381.1495.

Compound 8 was prepared according to the same procedure. The reaction of 6 (219 mg, 0.81 mmol), DMAP (15 mg), benzenethiol (248 µl, 2.4 mmol) in CH₂Cl₂ (6 ml) afforded 8 (271 mg, 88%): white solid. mp = 115-118 °C; [α]D²⁰ = -20.8 (c = 0.01, EtOH).

¹H NMR (400 MHz, CDCl₃) δ 7.41(d, J=7.8Hz, 2H), 7.35(t, J=7.6Hz, 2H), 7.26(t, J=7.0Hz, 1H), 5.05(d, J=9.5Hz, 1H), 4.73(s, 1H), 4.68(s, 1H), 3.81(d, J=11.2Hz, 1H), 3.69(dd, J=11.3, 4.0Hz, 2H), 3.52(s, 1H), 2.84-2.96(m, 2H), 2.66(s, 1H), 2.45-2.49(m, 1H), 2.30-2.34(m, 1H), 2.04(s, 1H), 1.89(s, 1H), 1.79(s, 1H), 1.69-1.73(m, 1H), 1.65(s, 3H).

¹³C NMR (100 MHz, CDCl₃) δ 176.4, 148.8, 145.8, 134.5, 130.4, 129.6, 129.3, 126.9, 111.1, 76.0, 60.9, 54.1, 46.9, 42.0, 38.2, 34.1, 28.0, 18.0, 14.3.

IR (neat) ν (cm⁻¹) 3422, 1768, 1664, 1315, 1197.

HRMS (ESI) M+Na⁺ found 381.1497, C₂¹H₂₆O₃SNa required 381.1495.
7-References


$^{1}H$ and $^{13}C$ Spectra

![Spectra Image]

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2b

2b
9-Structure of 6, 8 by X-ray

Structure of 6

Structure of 8