

Zinc or indium-mediated Barbier-type allylation of aldehydes with 3-bromomethyl-5*H*-furan-2-one in aqueous media: an efficient synthesis method for α -methylene- γ -butyrolactone†

YuZhe Gao, Xue Wang, LiDong Sun, LongGuan Xie and XiaoHua Xu*

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A zinc or indium-mediated Barbier-type allylation of aldehydes with 3-bromomethyl-5*H*-furan-2-one in aqueous solvents was developed to provide an efficient route to α -methylene- γ -butyrolactone, which is synthetically very useful. The desired products were obtained in moderate to high yields in aqueous solvents. Excellent drs were achieved, among which the best diastereomeric ratios of products were found when water was used in the indium-mediated reaction, and THF-NH₄Cl (sat, aq) (2:1) mixture in the zinc-mediated reaction. Furthermore, the allylation can be induced by chiral centers, especially those in the α -position, as a substrate-controlled reaction to obtain the enantioselective homoallylation alcohols.

Introduction

There are about 10% natural products containing the γ -butyrolactone construction that display a broad biological profile which attracts much attention. In many cases, the α -methylene groups in the lactone ring lead to their biological activities,¹ which is not easy to build² (Fig. 1).

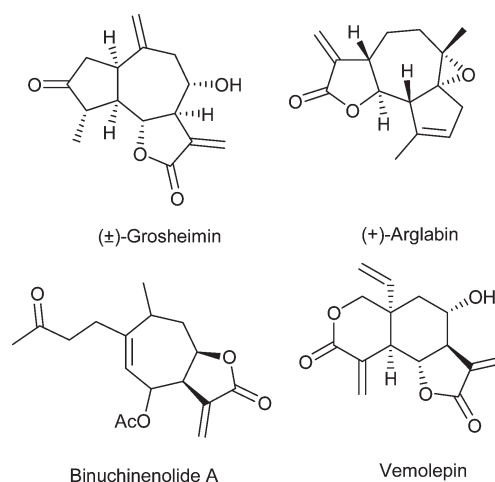
On the other hand, carbon-carbon bond formation constitutes one of the fundamental processes in organic synthesis and a wide variety of synthetic protocols have been developed to date for effecting this, amongst which organometallic reactions have played a major role. It was noticed in the early 1980s that allylic halides in particular can be used to react with aldehydes in the presence of metal powder to afford homoallylic alcohols in aqueous media. This type of allylic carbonyl addition has been called the Barbier-type allylation. Then there was a surge of great interest in the Barbier-type allylation. The use of water as solvent could reduce or eliminate environmental damage by

organic wastes. The development of such reactions offers the possibility of obtaining environmentally benign reaction conditions. The metals employed therein include magnesium,³ tin,⁴ indium,⁵ zinc,⁶ cadmium,⁷ manganese,⁸ antimony⁹ and bismuth.¹⁰

In our earlier work, it was found that the construction of α -methylene- γ -butyrolactone can be easily carried out though Barbier-type reaction of 3-bromomethyl-5*H*-furan-2-one, and two natural products were successfully synthesized and reported,^{11,12} which proved that this bromolactone is quite a useful synthon for α -methylene- γ -butyrolactone.

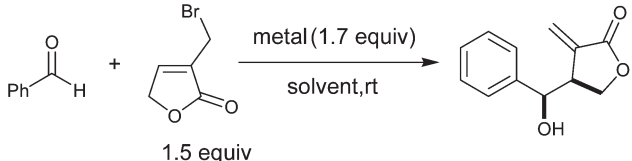
The first reported compound using 3-bromomethyl-5*H*-furan-2-one as a synthon was (\pm)-cedarmycin B,¹¹ which was accomplished in a yield of 8%. Then 8-epigrosheimin was successfully synthesized¹² and a final yield of 45% obtained after the route was improved.¹³ (\pm)-Hydroxymatairesinol and (\pm)-methylenolactocin were the latest compounds reported.¹⁴

Although it has been used in synthesis for some years, the study and application of allylation reactions with 3-bromo-5*H*-furan-2-one is still in its infancy and only a little research has been reported,¹⁴ in which the allylation takes place in organic solvents or is complicated to manipulate, and so the

**Fig. 1** Representative α -methylene γ -butyrolactones.

State Key Laboratory of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, China. E-mail: xiaohuaxu@nankai.edu.cn; Fax: +88 22 23504284

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Table 1 Effect of metal and solvent on the allylation of benzaldehyde


Entry	Metal	Solvent	Time (h)	Yield ^a (%)	dr ^b
1	In	H ₂ O	12	87	99 : 1
2	In ^c	H ₂ O	12	76	99 : 1
3	In ^d	H ₂ O	12	96	99 : 1
4	In	NH ₄ Cl (sat, aq)	12	88	98 : 2
5	In	THF–H ₂ O = 2 : 1	6	91	98 : 2
6	In	THF–NH ₄ Cl (sat, aq) = 2 : 1	6	89	98 : 2
7	Zn	H ₂ O	12	82	85 : 15
8	Zn	THF–H ₂ O = 2 : 1	6	90	95 : 5
9	Zn	THF–NH ₄ Cl (sat, aq) = 2 : 1	0.25	92	96 : 4

^a Isolated yield. ^b Determined by ¹H NMR. ^c 1.5 Equiv of indium were used. ^d 2.0 Equiv of indium were used.

full synthetic potential of such reactions is still waiting to be explored.

Of the metals that have been used in the Barbier-type reaction, indium and zinc are widely represented. The use of indium metal as a mediator in the addition of allyl bromides to carbonyl compounds under Barbier-type conditions was first reported in 1988.¹⁵ Compared to other metals, indium offers a number of advantages: indium has the lowest first ionization potential relative to zinc, tin and magnesium which makes high reactivity in the absence of external activators and proton sources.¹⁶ Meanwhile, it is not sensitive to boiling water or alkali and does not form oxides in air, which makes indium a promising metal for Barbier-type allylation. Zinc was first employed in Barbier-type allylations by Wolinsky and co-workers in 1977, and has likewise proved to be a highly useful mediator for the allylation of various substrates. Zinc offers the greatest potential for industrial application because of its relatively low cost and ready availability. In contrast to In-mediated allylations, which commonly are carried out in water–THF mixtures without additives, the use of Zn generally requires the application of saturated aqueous NH₄Cl as a proton source together with the organic solvent.

Herein we wish to report our recent studies on Barbier-type reactions of aldehydes with 3-bromomethyl-5H-furan-2-one using zinc or indium under aqueous conditions, which is more convenient and environmentally friendly.

Results and discussion

As a starting point, the Barbier-type addition reaction of benzaldehyde was chosen to establish the protocol. Some representative results are listed in Table 1. From Table 1, it is observed that with 1.7 equiv indium the reaction of 1.5 equiv of 3-bromomethyl-5H-furan-2-one with benzaldehyde in water at room temperature afford homoallylic alcohol in 88% yield with a diastereomeric ratio of 99 : 1 (entry 1, Table 1). By using saturated

aqueous NH₄Cl solution instead of water, the yield of product increased a little, but the dr dropped (entry 4, Table 1). We also observed that in a mixture of THF and water (2 : 1) or THF and saturated aqueous NH₄Cl (2 : 1), the reaction can be finished more quickly but still with a dr of 98 : 2 (entries 5 and 6, Table 1). Then we found that, with 2.0 equiv of indium, the reaction in water can be accomplished in a yield of 96%, while with 1.5 equiv of indium, the yield decreased to 76% (entries 2 and 3, Table 1). Thus, conditions A (1.5 equiv of 3-bromomethyl-5H-furan-2-one, 2 equiv of indium, water, rt) were established as the optimized reaction conditions. When indium was replaced with activated zinc powder, the mixture of THF and saturated aqueous NH₄Cl proved to be the best media (entry 9, Table 1, conditions B), with the best yield and the highest dr. While in water or a mixture of THF and water (2 : 1), the zinc-mediated reaction gave worse yields and lower drs.

Then we investigated the Barbier-type reaction of benzaldehyde with 3-bromomethyl-5H-furan-2-one in organic media. The zinc and indium-mediated reaction afforded 86%, 79% yields with 88 : 12 and 98 : 2 drs in DMF, while the yields dropped to 35%–54% in DCM, THF and ether when indium was used, in contrast to no products being observed with zinc. But the reaction with zinc can take place in THF with BF₃·Et₂O catalysis, affording 42% yield and 92 : 8 dr. However, both yields and drs dropped in the indium-mediated reaction with BF₃·Et₂O catalysis in organic solvents. This proves aqueous media is much better for the reaction.

Also, we tried to use tin in the reaction.⁴ But in water with a catalytic amount of hydrobromic acid or a 1 : 1 mixture of THF and saturated aqueous NH₄Cl, no reaction occurred.

Subsequently, the scope of the allylation of aromatic aldehydes and aliphatic aldehydes was studied, with some typical results listed (Tables 2 and 3).

We found that the Barbier-type allylation of aromatic aldehydes took place smoothly under conditions A or B, giving the expected homoallylic alcohols in moderate to good yields (Table 2). Various differently substituted benzaldehydes were investigated, such as 2-chlorobenzaldehyde (entry 3, Table 2), 3-chlorobenzaldehyde (entry 2, Table 2), 4-chlorobenzaldehyde (entry 1, Table 2), 4-methoxybenzaldehyde (entry 4, Table 2), 4-trifluoromethylbenzaldehyde (entry 5, Table 2), 4-*tert*-butylbenzaldehyde (entry 6, Table 2), 4-cyanobenzaldehyde (entry 7, Table 2), and the other aromatic aldehydes like β-naphthaldehyde (entry 8, Table 2), 2-furaldehyde (entry 9, Table 2), 2-thiophenylaldehyde (entry 10, Table 2). All these reagents afforded the expected products which indicated the wide scope of the reaction. In all cases, the diastereomeric ratios of the homoallylic alcohols formed using indium were higher than those formed using activated zinc, which showed the better stereoselectivity of the reaction when indium is used.

During the reaction of aliphatic aldehydes with 3-bromomethyl-5H-furan-2-one, we investigated regular aldehydes (entries 1 and 2, Table 3) and aldehydes with a conjugated C=C bond (entry 3, Table 3), an unconjugated C=C bond (entry 5, Table 3), a heteroatom (entry 4, Table 3), a group with a large steric effect (entry 6, Table 3) and a phenyl group (entry 7, Table 3). Moderate to good yields were achieved in most cases. Better drs were found with indium compared to the situations with activated zinc. The indium-mediated reactions yielded

Table 2 Allylation of aromatic aldehydes using In or Zn

Entry	Aromatic aldehyde	Conditions	Yield of 2 ^a (%)	dr ^b
1		A	93 (2a)	95 : 5
		B	90 (2a)	90 : 10
2		A	90 (2b)	99 : 1
		B	92 (2b)	94 : 6
3		A	96 (2c)	94 : 6
		B	92 (2c)	87 : 13
4		A	89 (2d)	98 : 2
		B	93 (2d)	95 : 5
5		A	91 (2e)	96 : 4
		B	91 (2e)	93 : 7
6		A	90 (2f)	98 : 2
		B	88 (2f)	97 : 3
7		A	87 (2g)	99 : 1
		B	98 (2g)	99 : 1
8		A	89 (2h)	98 : 2
		B	85 (2h)	95 : 5
9		A	73 (2i)	76 : 24
		B	94 (2i)	73 : 26
10		A	85 (2j)	97 : 3
		B	93 (2j)	83 : 17

^a Isolated yield. ^b Determined by ¹H NMR.

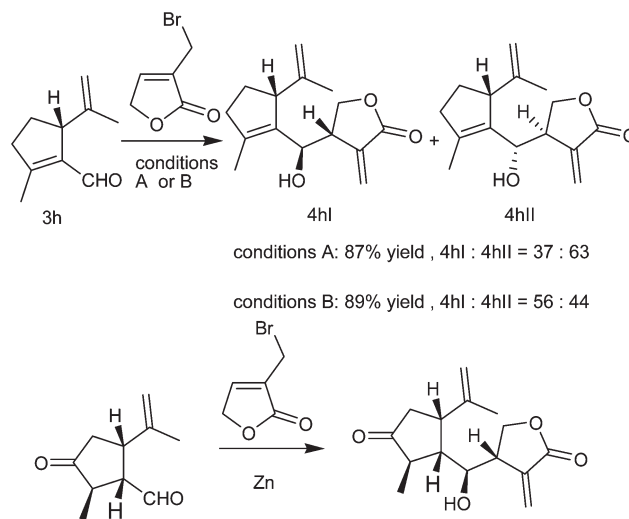
diastereomeric ratios of up to 99 : 1 dr, especially when the aldehydes were hexanal and trans-2-hexenal. When 4-pentenal was used, a better dr was achieved in the reaction with zinc (96 : 4), rather than in the reaction with indium (95 : 5), and we cannot figure out what factor leads to this result. In addition, it should be noted that 1,4-addition to the conjugated C=C bond in the aldehydes was not observed, indicating the excellent chemoselectivity of reaction.

When we used 5-isopropenyl-2-methyl-1-en-cyclopentane-carboxaldehyde in the Barbier reaction, two isomer products were observed, compared to the single 5-isopropenyl-2-methyl-3-oxo-cyclopentanecarboxaldehyde allylation product¹² (Scheme 1). If there is no chiral center in the starting aldehyde, potentially four isomers can be produced in the reaction. The reaction of **3h** in both the In-H₂O or Zn-THF-NH₄Cl reaction systems indicated that when there is one chiral center in the

Table 3 Allylation of aldehyde using In or Zn

Entry	Aldehyde	Conditions	Yield of 4 ^a (%)	dr ^b
1		A	94 (4a)	99 : 1
		B	97 (4a)	74 : 26
2		A	93 (4b)	99 : 1
		B	96 (4b)	91 : 9
3		A	83 (4c)	97 : 3
		B	95 (4c)	45 : 55
4		A	80 (4d)	99 : 1
		B	95 (4d)	90 : 10
5		A	91 (4e)	95 : 5
		B	89 (4e)	96 : 4
6		A	96 (4f)	99 : 1
		B	92 (4f)	98 : 2
7		A	79 (4g)	99 : 1
		B	84 (4g)	96 : 4

^a Isolated yield. ^b Determined by ¹H NMR.



Scheme 1 Allylation of 5-isopropenyl-2-methyl-1-en-cyclopentane-carboxaldehyde and 5-isopropenyl-2-methyl-3-oxo-cyclopentanecarboxaldehyde.

aldehyde at the β-position, two isomer products are obtained. Both of these isomers have anti-configuration as a result of the stereoselectivity derived from the chiral center. When the aldehyde contains two or more chiral centers, especially when the α-carbon is chiral, it might lead to a unique homoallylic alcohol, which would provide a quite valuable method for chiral organic synthesis according to the Barbier-type reaction with 3-bromo-methyl-5H-furan-2-one.

The ratio was 63:37 (**4hII**:**4hI**) using conditions A and dropped to 44:56 using conditions B. After the two isomers were separated and both treated with two further steps,¹² we obtained the related compounds which confirmed the absolute configuration by X-ray crystallographic analysis, proving the configuration of the two isomers of **4h**.¹⁷

Conclusions

In summary, we have developed a convenient allylation reaction of aldehydes with 3-bromomethyl-5*H*-furan-2-one by using indium or zinc in aqueous media, providing an efficient, environmentally friendly route to α -methylene- γ -butyrolactone. Due to the synthetic potential of the products and mild reaction conditions, this method may be very useful in organic synthesis. Further studies on the scope and applications of this reaction with 3-bromomethyl-5*H*-furan-2-one are being carried out in our laboratory.

Experimental section

(1) Synthesis of 4-((4-chlorophenyl)(hydroxy)methyl)-3-methylenedihydrofuran-2(3*H*)-one (**2a**)

Typical procedure for the reaction with indium. To a reaction vessel were added sequentially **1a** (135 mg, 0.96 mmol), 3-bromomethyl-5*H*-furan-2-one (254 mg, 1.44 mmol), water (1.0 ml) and indium powder (225 mg, 1.97 mmol). The mixture was stirred vigorously at rt. After 12 h the reaction mixture was filtered by diatomite, extracted with diethyl ether (20 ml \times 3), washed with brine (20 mL), and dried over anhydrous Na₂SO₄. Evaporation and column chromatography on silica gel (petroleum ether–ethyl acetate = 1:1) afforded **2a** (214 mg, 93%): oil, ¹H NMR (400 MHz, CDCl₃) δ 7.36 (d, *J* = 1.9 Hz, 1H), 7.35 (t, *J* = 2.3 Hz, 1H), 7.29 (d, *J* = 2.0 Hz, 1H), 7.27 (d, *J* = 4.2 Hz, 1H), 6.32 (d, *J* = 2.3 Hz, 1H), 5.69 (d, *J* = 1.8 Hz, 1H), 4.73 (d, *J* = 7.1 Hz, 1H), 4.21 (dd, *J* = 8.2, 9.6 Hz, 1H), 4.10 (dd, *J* = 4.1, 9.6 Hz, 1H), 3.33–3.39 (m, 1H), 2.81 (br s, 1H).

Discernable data for minor diastereoisomer: 6.20 (d, *J* = 2.4 Hz, 1H), 5.08 (d, *J* = 2.1 Hz, 1H), 4.54 (dd, *J* = 9.6, 3.9 Hz, 1H), 4.35 (dd, *J* = 9.6, 7.9 Hz, 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; HRMS (ESI): M + Na⁺ found 260.0291, C₁₂H₁₁ClO₃Na requires 261.0297.

Typical procedure for the reaction with zinc. To a reaction vessel were added sequentially **1a** (141 mg, 1.00 mmol), 3-bromomethyl-5*H*-furan-2-one (260 mg, 1.47 mmol), THF (1 ml), saturated aqueous NH₄Cl (0.5 ml) and activated zinc powder (110 mg, 1.72 mmol). The mixture was stirred for 15 min at rt and filtered by diatomite, extracted with diethyl ether (20 ml \times 3), washed with brine (20 ml) and dried over anhydrous Na₂SO₄. Evaporation and column chromatography on silica gel (petroleum ether–ethyl acetate = 1:1) afforded **2a** (216 mg, 90%).

The following Barbier-type products were prepared according to this procedure.

(2) Synthesis of 4-((3-chlorophenyl)(hydroxy)methyl)-3-methylenedihydrofuran-2(3*H*)-one (**2b**)

The reaction of **1b** (139 mg, 0.99 mmol), 3-bromomethyl-5*H*-furan-2-one (263 mg, 1.49 mmol), indium powder (225 mg, 1.96 mmol) and water (1.0 ml) at rt for 12 h afforded **2b** (212 mg, 90%): oil. ¹H NMR (400 MHz, CDCl₃) δ 7.35 (s, 1H), 7.29–7.31 (m, 2H), 7.18–7.23 (m, 1H), 6.31 (d, *J* = 2.2 Hz, 1H), 5.67 (d, *J* = 1.8, 1H), 4.72 (d, *J* = 7.1 Hz, 1H), 4.23 (t, *J* = 9.5 Hz, 1H), 4.12 (dd, *J* = 9.6, 4.1 Hz, 1H), 3.33–3.40 (m, 1H), 2.91 (s, 1H).

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

¹³C NMR (100 MHz, CDCl₃) δ 170.9, 142.8, 134.8, 134.4, 130.0, 128.6, 125.8, 124.8, 67.7, 45.4; IR (neat), ν (cm⁻¹) 3455, 1758, 1659, 1274, 1138, 807; HRMS (ESI): M + Na⁺ found 261.0289, C₁₂H₁₁ClO₃Na requires 261.0297.

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

(3) Synthesis of 4-((2-chlorophenyl)(hydroxyl)methyl)-3-methylenedihydrofuran-2(3*H*)-one (**2c**)

The reaction of **1c** (138 mg, 0.99 mmol), 3-bromomethyl-5*H*-furan-2-one (265 mg, 1.51 mmol), indium powder (227 mg, 1.99 mmol) and water (1.0 ml) at rt for 12 h afforded **2c** (226 mg, 96%): white solid, mp: 94–108 °C. ¹H NMR (400 MHz, CDCl₃) δ 7.50 (dd, *J* = 7.5, 1.9 Hz, 1H), 7.40 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.26–7.34 (m, 2H), 6.27 (d, *J* = 2.2 Hz, 1H), 5.28 (d, *J* = 3.6 Hz, 1H), 5.27 (s, 1H), 4.37 (t, *J* = 9.3 Hz, 1H), 4.32 (dd, *J* = 9.4, 3.9 Hz, 1H), 3.46–3.52 (m, 1H), 2.67 (br s, 1H).

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

¹³C NMR (100 MHz, CDCl₃) δ 171.1, 138.0, 133.8, 131.9, 129.6, 129.4, 128.5, 127.1, 125.6, 71.9, 68.6, 43.6; IR (neat), ν (cm⁻¹) 3453, 1742, 1659, 1274, 1141, 768; HRMS (ESI): M + Na⁺ found 260.0289, C₁₂H₁₁ClO₃Na requires 261.0297.

The reaction of **1c** (135 mg, 0.96 mmol), 3-bromomethyl-5*H*-furan-2-one (263 mg, 1.49 mmol), activated zinc powder (107 mg, 1.67 mmol), THF (1 ml), and saturated aqueous NH₄Cl (0.5 ml) at rt for 15 min afforded **2c** (212 mg, 92%).

(4) Synthesis of 4-((4-methoxyphenyl)(hydroxy)methyl)-3-methylenedihydrofuran-2(3*H*)-one (**2d**)

The reaction of **1d** (140 mg, 1.03 mmol), 3-bromomethyl-5*H*-furan-2-one (264 mg, 1.5 mmol), indium powder (225 mg, 1.97 mmol) and water (1.0 ml) at rt for 12 h afforded **2d** (215 mg, 89%): oil, ¹H NMR (400 MHz, CDCl₃) δ 7.26 (d, *J* = 8.2 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 6.36 (d, *J* = 2.2 Hz, 1H), 5.85 (d, *J* = 1.6 Hz, 1H), 4.65 (d, *J* = 7.9 Hz, 1H), 4.16 (dd, *J* = 8.4, 9.5 Hz, 1H), 4.02 (dd, *J* = 4.5, 9.6 Hz, 1H), 3.81 (s, 3H), 3.36–3.42 (m, 1H), 2.40 (br s, 1H).

Discernable data for minor diastereoisomer: 7.84 (d, $J = 8.8$ Hz, 2H), 7.02 (d, $J = 8.7$ Hz, 2H), 6.17 (d, $J = 2.4$ Hz, 1H), 4.97 (d, $J = 2.0$ Hz, 1H), 4.40 (dd, $J = 9.4, 7.9$ Hz, 1H), 4.31 (t, $J = 6.7$ Hz, 1H), 3.89 (s, 3H).

^{13}C NMR (100 MHz, CDCl_3) δ 170.8, 159.8, 135.2, 132.8, 127.8, 125.4, 114.2, 75.3, 67.5, 55.3, 45.5; IR (neat), ν (cm^{-1}) 3454, 1759, 1658, 1465, 1250, 1120, 819; HRMS (ESI): $\text{M} + \text{Na}^+$ found 257.0787, $\text{C}_{13}\text{H}_{14}\text{O}_4\text{Na}$ required 257.0792.

The reaction of **1d** (134 mg, 0.98 mmol), 3-bromomethyl-5H-furan-2-one (258 mg, 1.47 mmol), activated zinc powder (106 mg, 1.66 mmol), THF (1 ml), and saturated aqueous NH_4Cl (0.5 ml) at rt for 15 min afforded **2d** (215 mg, 93%).

(5) Synthesis of 4-((4-trifluoromethylphenyl)(hydroxy)methyl)-3-methylenedihydrofuran-2(3H)-one (**2e**)

The reaction of **1e** (170 mg, 0.98 mmol), 3-bromomethyl-5H-furan-2-one (264 mg, 1.5 mmol), indium powder (228 mg, 2 mmol) and water (1.0 ml) at rt for 12 h afforded **2e** (242 mg, 91%): solid, mp: 76–90 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.67 (d, $J = 8.1$ Hz, 2H), 7.50 (d, $J = 8.1$ Hz, 2H), 6.36 (d, $J = 2.1$ Hz, 1H), 5.67 (d, $J = 1.7$ Hz, 1H), 4.85 (d, $J = 7.0$ Hz, 1H), 4.26 (t, $J = 9.6$ Hz, 1H), 4.16 (dd, $J = 9.6, 3.9$ Hz, 1H), 3.39–3.43 (m, 1H), 2.59 (br s, 1H).

Discernable data for minor diastereoisomer: 8.12 (d, $J = 7.9$ Hz, 2H), 7.77 (d, $J = 8.1$ Hz, 2H), 6.27 (d, $J = 2.4$ Hz, 1H), 5.96 (s, 1H), 5.15 (d, $J = 2.0$ Hz, 1H).

^{13}C NMR (100 MHz, CDCl_3) δ 170.1, 144.5, 134.4, 127.0, 125.8, 125.77, 125.73, 75.0, 67.5, 45.5; IR (neat), ν (cm^{-1}) 3466, 1735, 1662, 1276, 1124, 828; HRMS (ESI): $\text{M} + \text{Na}^+$ found 295.0546, $\text{C}_{13}\text{H}_{11}\text{O}_3\text{F}_3\text{Na}$ required 295.1560.

The reaction of **1e** (176 mg, 1.01 mmol), 3-bromomethyl-5H-furan-2-one (265 mg, 1.51 mmol), activated zinc powder (111 mg, 1.73 mmol), THF (1 ml), and saturated aqueous NH_4Cl (0.5 ml) at rt for 15 min afforded **2e** (251 mg, 91%).

(6) Synthesis of 4-((4-*tert*-butylphenyl)(hydroxy)methyl)-3-methylenedihydrofuran-2(3H)-one (**2f**)

The reaction of **1f** (161 mg, 0.99 mmol), 3-bromomethyl-5H-furan-2-one (267 mg, 1.52 mmol), indium powder (231 mg, 2.03 mmol) and water (1.0 ml) at rt for 12 h afforded **2f** (233 mg, 90%): oil, ^1H NMR (400 MHz, CDCl_3) δ 7.43 (d, $J = 8.3$ Hz, 2H), 7.29 (d, $J = 8.8$ Hz, 2H), 6.39 (d, $J = 2.0$ Hz, 1H), 5.89 (d, $J = 1.4$ Hz, 1H), 4.68 (d, $J = 8.1$ Hz, 1H), 4.18 (t, $J = 9.5$ Hz, 1H), 4.04 (dd, $J = 9.6, 4.5$ Hz, 1H), 3.41–3.46 (m, 1H), 2.17 (br s, 1H), 1.33 (s, 3H).

Discernable data for minor diastereoisomer: 7.73–7.71 (m, 2H), 7.55 (dd, $J = 6.1, 2.9$ Hz, 2H), 6.22 (d, $J = 2.4$ Hz, 1H), 5.84 (d, $J = 1.8$ Hz, 1H), 5.04 (d, $J = 2.0$ Hz, 1H), 4.42 (dd, $J = 9.4, 8.1$ Hz, 1H), 4.33 (t, $J = 6.8$ Hz, 1H).

^{13}C NMR (100 MHz, CDCl_3) δ 170.7, 151.9, 137.7, 135.3, 126.4, 125.8, 125.4, 75.5, 67.6, 45.4, 34.7, 31.3; IR (neat), ν (cm^{-1}) 3305, 1764, 1656, 1286, 1124, 837; HRMS (ESI): $\text{M} + \text{Na}^+$ found 283.1309, $\text{C}_{16}\text{H}_{20}\text{O}_3\text{Na}$ required 283.1310.

The reaction of **1f** (176 mg, 1.09 mmol), 3-bromomethyl-5H-furan-2-one (265 mg, 1.51 mmol), activated zinc powder

(106 mg, 1.66 mmol), THF (1 ml), and saturated aqueous NH_4Cl (0.5 ml) at rt for 15 min afforded **2f** (234 mg, 88%).

(7) Synthesis of 4-((4-cyanophenyl)(hydroxy)methyl)-3-methylenedihydrofuran-2(3H)-one (**2g**)¹⁸

The reaction of **1g** (134 mg, 1.02 mmol), 3-bromomethyl-5H-furan-2-one (264 mg, 1.5 mmol), indium powder (225 mg, 1.97 mmol) and water (1.0 ml) at rt for 12 h afforded **2g** (204 mg, 87%): white solid, mp: 151–155 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.71 (d, $J = 8.0$ Hz, 2H), 7.51 (d, $J = 8.1$ Hz, 2H), 6.37 (s, 1H), 5.61 (s, 1H), 4.88 (d, $J = 6.6$ Hz, 1H), 4.29 (t, $J = 9.4$ Hz, 1H), 4.19 (dd, $J = 3.6, 9.6$ Hz, 1H), 3.4 (s, 1H), 2.48 (br s, 1H).

^{13}C NMR (100 MHz, CDCl_3) δ 170.0, 145.5, 134.0, 132.5, 127.6, 127.2, 125.7, 118.2, 112.4, 74.8, 67.2, 45.3.

The reaction of **1g** (129 mg, 0.98 mmol), 3-bromomethyl-5H-furan-2-one (267 mg, 1.52 mmol), activated zinc powder (113 mg, 1.77 mmol), THF (1 ml), and saturated aqueous NH_4Cl (0.5 ml) at rt for 15 min afforded **2g** (221 mg, 98%).

(8) Synthesis of 4-(hydroxy(naphthalen-3-yl)methyl)-3-methylenedihydrofuran-2(3H)-one (**2h**)

The reaction of **1h** (160 mg, 1.03 mmol), 3-bromomethyl-5H-furan-2-one (263 mg, 1.49 mmol), indium powder (228 mg, 2 mmol) and water (1.0 ml) at rt for 12 h afforded **2h** (232 mg, 89%): oil, ^1H NMR (400 MHz, CDCl_3) δ 7.83–7.88 (m, 3H), 7.77 (s, 1H), 7.52–7.54 (m, 2H), 7.46 (d, $J = 8.4$ Hz, 1H), 6.36 (s, 1H), 5.77 (s, 1H), 4.84 (d, $J = 7.5$ Hz, 1H), 4.17 (t, $J = 9.1$ Hz, 1H), 4.10 (dd, $J = 9.3, 4.1$ Hz, 1H), 3.49 (s, 1H), 2.67 (br s, 1H).

Discernable data for minor diastereoisomer: 7.22 (d, $J = 8.9$ Hz, 1H), 6.16 (d, $J = 2.4$ Hz, 1H), 4.99 (d, $J = 2.1$ Hz, 1H), 4.65 (dd, $J = 9.7, 4.1$ Hz, 1H), 4.41 (dd, $J = 9.4, 7.8$ Hz, 1H).

^{13}C NMR (100 MHz, CDCl_3) δ 170.8, 138.0, 134.9, 133.3, 133.0, 128.9, 128.0, 127.7, 126.5, 125.5, 123.9, 75.7, 67.7, 45.3; IR (neat), ν (cm^{-1}) 3443, 1759, 1658, 1273, 1123; HRMS (ESI): $\text{M} + \text{Na}^+$ found 277.0828, $\text{C}_{16}\text{H}_{14}\text{O}_3\text{Na}$ required 277.0841.

The reaction of **1h** (153 mg, 0.98 mmol), 3-bromomethyl-5H-furan-2-one (264 mg, 1.5 mmol), activated zinc powder (113 mg, 1.77 mmol), THF (1 ml), and saturated aqueous NH_4Cl (0.5 ml) at rt for 15 min afforded **2h** (212 mg, 85%).

(9) Synthesis of 4-(hydroxy(furan-3-yl)methyl)-3-methylenedihydrofuran-2(3H)-one (**2i**)

The reaction of **1i** (101 mg, 1.05 mmol), 3-bromomethyl-5H-furan-2-one (261 mg, 1.48 mmol), indium powder (225 mg, 1.97 mmol) and water (1.0 ml) at rt for 12 h afforded **2i** (149 mg, 73%): oil, ^1H NMR (400 MHz, CDCl_3) δ 7.41 (d, $J = 1.0$ Hz, 1H), 6.36 (d, $J = 3.7$ Hz, 2H), 6.33 (d, $J = 3.3$ Hz, 1H), 5.76 (d, $J = 2.0$ Hz, 1H), 4.77 (d, $J = 7.4$ Hz, 1H), 4.32 (t, $J = 9.5$ Hz, 1H), 4.18 (dd, $J = 9.6, 4.3$ Hz, 1H), 3.56–3.63 (m, 1H), 2.65 (br s, 1H).

Discernable data for minor diastereoisomer: 7.43 (d, $J = 1.0$ Hz, 1H), 6.26 (d, $J = 2.5$ Hz, 1H), 5.21 (d, $J = 2.2$ Hz, 1H), 4.75

(d, $J = 7.6$ Hz, 1H), 4.56 (dd, $J = 9.6, 4.3$ Hz, 1H), 4.47 (t, $J = 8.1$ Hz, 1H).

^{13}C NMR (100 MHz, CDCl_3) δ 170.6, 153.2, 142.8, 134.2, 125.7, 110.5, 108.2, 69.2, 67.4, 43.3; IR (neat), ν (cm^{-1}) 3418, 1755, 1660, 1274, 1123; HRMS (ESI): $\text{M} + \text{Na}^+$ found 217.0470, $\text{C}_{10}\text{H}_{10}\text{O}_4\text{Na}$ required 217.0477.

The reaction of **1i** (98 mg, 1.02 mmol), 3-bromomethyl-5H-furan-2-one (264 mg, 1.5 mmol), activated zinc powder (110 mg, 1.72 mmol), THF (1 ml), and saturated aqueous NH_4Cl (0.5 ml) at rt for 15 min afforded **2i** (187 mg, 94%).

(10) Synthesis of 4-(hydroxy(thiophene-3-yl)methyl)-3-methylenedihydrofuran-2(3H)-one (**2j**)

The reaction of **1j** (115 mg, 1.03 mmol), 3-bromomethyl-5H-furan-2-one (264 mg, 1.5 mmol), indium powder (230 mg, 2.02 mmol) and water (1.0 ml) at rt for 12 h afforded **2j** (184 mg, 85%): oil, ^1H NMR (400 MHz, CDCl_3) δ 7.32 (dd, $J = 4.9, 1.1$ Hz, 1H), 6.98–7.02 (m, 2H), 6.39 (d, $J = 2.3$ Hz, 1H), 5.90 (d, $J = 1.8$ Hz, 1H), 4.98 (d, $J = 7.7$ Hz, 1H), 4.28 (t, $J = 9.7$ Hz, 1H), 4.13 (dd, $J = 9.7, 4.4$ Hz, 1H), 3.44–3.50 (m, 1H), 2.75 (br s, 1H).

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

^{13}C NMR (100 MHz, CDCl_3) δ 170.5, 144.3, 134.6, 127.0, 125.9, 125.3, 71.6, 67.4, 45.9; IR (neat), ν (cm^{-1}) 3443, 1759, 1659, 1276, 1125; HRMS (ESI): $\text{M} + \text{Na}^+$ found 233.0240, $\text{C}_{10}\text{H}_{10}\text{O}_3\text{SNa}$ required 233.0248.

The reaction of **1j** (113 mg, 1.01 mmol), 3-bromomethyl-5H-furan-2-one (260 mg, 1.47 mmol), activated zinc powder (107 mg, 1.67 mmol), THF (1 ml), and saturated aqueous NH_4Cl (0.5 ml) at rt for 15 min afforded **2j** (197 mg, 93%).

(11) Synthesis of 4-(1-hydroxyhexyl)-3-methylenedihydrofuran-2(3H)-one (**4a**)¹⁸

The reaction of **3a** (103 mg, 1.03 mmol), 3-bromomethyl-5H-furan-2-one (261 mg, 1.48 mmol), indium powder (227 mg, 1.99 mmol) and water (1.0 ml) at rt for 12 h afforded **4a** (192 mg, 94%): oil, ^1H NMR (400 MHz, CDCl_3) δ 6.38 (d, $J = 2.0$ Hz, 1H), 5.82 (d, $J = 1.6$ Hz, 1H), 4.43 (t, $J = 9.3$ Hz, 1H), 4.27 (dd, $J = 9.4, 3.7$ Hz, 1H), 3.71 (dd, $J = 11.6, 5.9$ Hz, 1H), 3.13–3.16 (m, 1H), 1.90 (br s, 1H), 1.44–1.50 (m, 3H), 1.31 (s, 5H), 0.92 (t, $J = 6.5$ Hz, 3H).

Discernable data for minor diastereoisomer: 5.72 (d, $J = 0.8$ Hz, 1H), 3.81–3.87 (m, 1H).

^{13}C NMR (100 MHz, CDCl_3) δ 170.9, 135.2, 124.6, 73.2, 68.1, 44.5, 33.5, 31.6, 25.4, 22.6, 14.0; IR (neat), ν (cm^{-1}) 3445, 1765, 1661, 1270, 1129; HRMS (ESI): $\text{M} + \text{Na}^+$ found 221.1146, $\text{C}_{10}\text{H}_{18}\text{O}_3\text{Na}$ required 221.1154.

The reaction of **3a** (100 mg, 1 mmol), 3-bromomethyl-5H-furan-2-one (263 mg, 1.49 mmol), activated zinc powder (106 mg, 1.66 mmol), THF (1 ml), and saturated aqueous NH_4Cl (0.5 ml) at rt for 15 min afforded **4a** (193 mg, 97%).

(12) Synthesis of 4-(1-hydroxybutyl)-3-methylenedihydrofuran-2(3H)-one (**4b**)

The reaction of **3b** (80 mg, 1.11 mmol), 3-bromomethyl-5H-furan-2-one (258 mg, 1.47 mmol), indium powder (230 mg, 2.02 mmol) and water (1.0 ml) at rt for 12 h afforded **4b** (176 mg, 93%): oil, ^1H NMR (400 MHz, CDCl_3) δ 6.37 (d, $J = 2.1$ Hz, 1H), 5.81 (d, $J = 1.8$ Hz, 1H), 4.41 (t, $J = 9.2$ Hz, 1H), 4.27 (dd, $J = 9.4, 3.7$ Hz, 1H), 3.67–3.71 (m, 1H), 3.12–3.15 (m, 1H), 2.07 (br s, 1H), 1.33–1.59 (m, 4H), 0.96 (t, $J = 7.2$ Hz, 3H).

Discernable data for minor diastereoisomer: 5.71 (d, $J = 2.0$ Hz, 1H), 4.76 (t, $J = 9.1$ Hz, 1H), 3.85 (dd, $J = 10.3, 5.5$ Hz, 1H).

^{13}C NMR (100 MHz, CDCl_3) δ 170.9, 135.1, 124.6, 72.9, 68.1, 44.6, 35.6, 18.9, 13.9; IR (neat), ν (cm^{-1}) 3453, 1761, 1660, 1274, 1123; HRMS (ESI): $\text{M} + \text{Na}^+$ found 193.0830, $\text{C}_9\text{H}_{14}\text{O}_3\text{Na}$ required 193.0841.

The reaction of **3b** (75 mg, 1.04 mmol), 3-bromomethyl-5H-furan-2-one (261 mg, 1.48 mmol), activated zinc powder (109 mg, 1.70 mmol), THF (1 ml), and saturated aqueous NH_4Cl (0.5 ml) at rt for 15 min afforded **4b** (170 mg, 96%).

(13) Synthesis of (E)-4-(1-hydroxyhex-2-en-1-yl)-3-methylenedihydrofuran-2(3H)-one (**4c**)

The reaction of **3c** (97 mg, 0.99 mmol), 3-bromomethyl-5H-furan-2-one (265 mg, 1.51 mmol), indium powder (230 mg, 2.02 mmol) and water (1.0 ml) at rt for 12 h afforded **4c** (162 mg, 83%): oil, ^1H NMR (400 MHz, CDCl_3) δ 6.35 (d, $J = 2.2$ Hz, 1H), 5.85 (d, $J = 1.8$ Hz, 1H), 5.72–5.79 (m, 1H), 5.46 (dd, $J = 15.4, 7.3$ Hz, 1H), 4.35 (t, $J = 9.4$ Hz, 1H), 4.24 (dd, $J = 8.5, 4.1$ Hz, 1H), 4.17 (t, $J = 7.0$ Hz, 1H), 3.19–3.23 (m, 1H), 1.98–2.06 (m, 2H), 1.96 (br s, 1H), 1.35–1.43 (m, 2H), 0.91 (t, $J = 7.3$ Hz, 3H).

Discernable data for minor diastereoisomer: 6.38 (d, $J = 2.2$ Hz, 1H), 5.74 (s, 1H).

^{13}C NMR (100 MHz, CDCl_3) δ 170.7, 135.9, 135.2, 128.2, 124.6, 74.6, 67.3, 44.1, 34.3, 22.2, 13.6; IR (neat), ν (cm^{-1}) 3454, 1760, 1662, 1274, 1124; HRMS (ESI): $\text{M} + \text{Na}^+$ found 219.0990, $\text{C}_{11}\text{H}_{16}\text{O}_3\text{Na}$ 219.0997.

The reaction of **3c** (101 mg, 1.03 mmol), 3-bromomethyl-5H-furan-2-one (267 mg, 1.52 mmol), activated zinc powder (105 mg, 1.64 mmol), THF (1 ml), and saturated aqueous NH_4Cl (0.5 ml) at rt for 15 min afforded **4c** (192 mg, 95%).

(14) Synthesis of 4-(3-methylthio-1-hydroxypropyl)-3-methylenedihydrofuran-2(3H)-one (**4d**)

The reaction of **3d** (104 mg, 1 mmol), 3-bromomethyl-5H-furan-2-one (263 mg, 1.49 mmol), indium powder (227 mg, 1.99 mmol) and water (1.0 ml) at rt for 12 h afforded **4d** (162 mg, 80%): oil, ^1H NMR (400 MHz, CDCl_3) δ 6.38 (d, $J = 2.1$ Hz, 1H), 5.82 (d, $J = 1.7$ Hz, 1H), 4.43 (t, $J = 9.4$ Hz, 1H), 4.30 (dd, $J = 9.4, 3.6$ Hz, 1H), 3.86–3.92 (m, 1H), 3.16–3.20 (m, 1H), 2.70 (t, $J = 6.7$ Hz, 2H), 2.51 (br s, 1H), 2.11 (s, 3H), 1.69–1.82 (m, 2H).

Discernable data for minor diastereoisomer: 5.75 (d, $J = 2.1$ Hz, 1H), 3.96–4.01 (m, 1H), 2.33 (br s, 1H).

^{13}C NMR (100 MHz, CDCl_3) δ 170.7, 135.0, 124.8, 72.4, 67.8, 44.6, 31.6, 30.9, 15.4; IR (neat), ν (cm^{-1}) 3453, 1762, 1660, 1414, 1279, 1122; HRMS (ESI): $\text{M} + \text{Na}^+$ found 225.0562, $\text{C}_9\text{H}_{14}\text{O}_3\text{SNa}$ required 225.0561.

The reaction of **3d** (107 mg, 1.03 mmol), 3-bromomethyl-5H-furan-2-one (262 mg, 1.49 mmol), activated zinc powder (107 mg, 1.67 mmol), THF (1 ml), and saturated aqueous NH_4Cl (0.5 ml) at rt for 15 min afforded **4d** (198 mg, 95%).

(15) Synthesis of 4-(1-hydroxypent-4-en-1-yl)-3-methylenedi-hydrofuran-2(3H)-one (**4e**)

The reaction of **3e** (90 mg, 1.07 mmol), 3-bromomethyl-5H-furan-2-one (264 mg, 2 mmol), indium powder (226 mg, 1.98 mmol) and water (1.0 ml) at rt for 12 h afforded **4e** (177 mg, 91%): oil, ^1H NMR (400 MHz, CDCl_3) δ : 6.37 (d, $J = 1.5$ Hz, 1H), 5.76–5.86 (m, 2H), 5.09 (d, $J = 17.1$ Hz, 1H), 5.02 (d, $J = 10.1$ Hz, 1H), 4.41 (t, $J = 9.2$ Hz, 1H), 4.27 (dd, $J = 9.4$, 3.6 Hz, 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, $J = 1.9$ Hz, 1H), 3.83–3.88 (m, 1H).

^{13}C NMR (100 MHz, CDCl_3) 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): $\text{M} + \text{Na}^+$ found 182.0940, $\text{C}_{10}\text{H}_{14}\text{O}_3\text{Na}$ required 182.0943.

The reaction of **3e** (86 mg, 1.02 mmol), 3-bromomethyl-5H-furan-2-one (267 mg, 1.52 mmol), activated zinc powder (108 mg, 1.69 mmol), THF (1 ml), and saturated aqueous NH_4Cl (0.5 ml) at rt for 15 min afforded **4e** (166 mg, 89%).

(16) Synthesis of 4-(hydroxy(cyclohex-2-yl)methyl)-3-methylenedi-hydrofuran-2(3H)-one (**4f**)

The reaction of **3f** (114 mg, 1.02 mmol), 3-bromomethyl-5H-furan-2-one (258 mg, 1.47 mmol), indium powder (231 mg, 2.03 mmol) and water (1.0 ml) at rt for 12 h afforded **4f** (205 mg, 96%): oil, ^1H NMR (400 MHz, CDCl_3) δ 6.39 (d, $J = 2.1$ Hz, 1H), 5.84 (d, $J = 1.6$ Hz, 1H), 4.44 (t, $J = 8.8$ Hz, 1H), 4.22 (dd, $J = 9.1$, 4.2 Hz, 1H), 3.42 (t, $J = 6.1$ Hz, 1H), 3.24–3.30 (m, 1H), 1.70–1.83 (m, 6H), 1.42–1.44 (m, 1H), 1.09–1.26 (m, 5H).

Discernable data for minor diastereoisomer: 6.66 (d, $J = 2.1$ Hz, 1H), 5.57 (d, $J = 1.2$ Hz, 1H), 4.54 (t, $J = 8.9$ Hz, 1H).

^{13}C NMR (100 MHz, CDCl_3) δ 170.7, 134.8, 124.4, 76.4, 68.3, 40.7, 40.0, 29.7, 26.8, 25.9, 25.8, 25.5; IR (neat), ν (cm^{-1}) 3490, 1741, 1659, 1265, 1134; HRMS (ESI): $\text{M} + \text{Na}^+$ found 233.1146, $\text{C}_{12}\text{H}_{18}\text{O}_3\text{Na}$ required 233.1154.

The reaction of **3f** (116 mg, 1.04 mmol), 3-bromomethyl-5H-furan-2-one (261 mg, 1.48 mmol), activated zinc powder (113 mg, 1.77 mmol), THF (1 ml), and saturated aqueous NH_4Cl (0.5 ml) at rt for 15 min afforded **4f** (194 mg, 79%).

(17) Synthesis of 4-(3-phenyl-1-hydroxypropyl)-3-methylenedi-hydrofuran-2(3H)-one (**4g**)¹⁸

The reaction of **3g** (142 mg, 1.06 mmol), 3-bromomethyl-5H-furan-2-one (270 mg, 1.53 mmol), indium powder (235 mg,

2.04 mmol) and water (1.0 ml) at rt for 12 h afforded **4g** (162 mg, 80%): oil, ^1H NMR (400 MHz, CDCl_3) δ 7.33 (t, $J = 7.3$ Hz, 2H), 7.24 (dd, $J = 7.2$, 11.8 Hz, 3H), 6.37 (d, $J = 1.6$ Hz, 1H), 5.79 (d, $J = 1.0$ Hz, 1H), 4.40 (t, $J = 8.9$ Hz, 1H), 4.24 (dd, $J = 3.4$, 9.4 Hz, 1H), 3.71 (t, $J = 9.2$ Hz, 1H), 3.13 (s, 1H), 2.93 (m, 1H), 2.75 (m, 1H), 2.05 (br s, 1H), 1.84 (m, 2H).

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

^{13}C NMR (100 MHz, CDCl_3) δ 170.7, 141.1, 135.0, 128.6, 128.4, 126.3, 124.8, 72.4, 68.0, 44.7, 35.2, 32.0.

The reaction of **3g** (130 mg, 0.97 mmol), 3-bromomethyl-5H-furan-2-one (261 mg, 1.48 mmol), activated zinc powder (113 mg, 1.77 mmol), THF (1 ml), and saturated aqueous NH_4Cl (0.5 ml) at rt for 15 min afforded **4g** (189 mg, 84%).

(18) Synthesis of 4-(hydroxy-(5-isopropenyl-2-methyl-1-en-cyclopentyl)methyl)-3-methylenedi-hydrofuran-2(3H)-one (**4g**)

The reaction of **3g** (153 mg, 1.02 mmol), 3-bromomethyl-5H-furan-2-one (261 mg, 1.48 mmol), indium powder (228 mg, 2 mmol) and water (1.0 ml) at rt for 12 h afford **4g** (220 mg, 87%): oil.

4gI (81 mg, 32%): $[\alpha]_{\text{D}}^{20} = -150.7$ ($c = 0.01$, EtOH); ^1H NMR (400 MHz, CDCl_3) δ 6.34 (s, 1H), 5.93 (s, 1H), 4.78 (s, 1H), 4.72 (s, 1H), 4.30 (d, $J = 9.4$ Hz, 1H), 4.22 (t, $J = 8.8$ Hz, 1H), 3.97 (dd, $J = 9.4$, 3.4 Hz, 1H), 3.53 (d, $J = 8.6$ Hz, 1H), 3.32 (s, 1H), 2.44–2.52 (m, 1H), 2.22–2.28 (t, $J = 9.6$ Hz, 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) δ 170.8, 148.5, 141.0, 135.8, 134.7, 125.2, 111.5, 70.3, 67.8, 53.7, 43.4, 38.3, 29.0, 19.1, 14.7; IR (neat) ν (cm^{-1}) 3481, 1766, 1659, 1275, 1119; HRMS (ESI) $\text{M} + \text{Na}^+$ found 271.1313, $\text{C}_{15}\text{H}_{20}\text{O}_3\text{Na}$ required 271.1305.

4gII (139 mg, 55%): $[\alpha]_{\text{D}}^{20} = +2.8$ ($c = 0.01$, EtOH); ^1H NMR (400 MHz, CDCl_3) δ 6.33 (dd, $J = 2.4$, 0.8 Hz, 1H), 6.04 (dd, $J = 2.2$, 0.9 Hz, 1H), 4.85 (s, 1H), 4.78 (t, $J = 1.5$ Hz, 1H), 4.48 (dd, $J = 9.2$, 5.9 Hz, 1H), 4.26 (dd, $J = 9.4$, 8.5 Hz, 1H), 3.86 (dd, $J = 9.5$, 5.0 Hz, 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) δ 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) ν (cm^{-1}) 3481, 1766, 1658, 1276, 1121; HRMS (ESI) $\text{M} + \text{Na}^+$ found 271.1311, $\text{C}_{15}\text{H}_{20}\text{O}_3\text{Na}$ required 271.1305.

The reaction of **3g** (150 mg, 1.0 mmol), 3-bromomethyl-5H-furan-2-one (264 mg, 1.5 mmol), activated zinc powder (107 mg, 1.67 mmol), THF (1 ml), and saturated aqueous NH_4Cl (0.5 ml) at rt for 15 min afforded **4g** (221 mg, 89%).

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