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Tandem Enzyme/Gold-Catalysis: From Racemic α-Allenic Acetates to Enantiomerically Enriched 2,5-Dihydrofurans in One Pot

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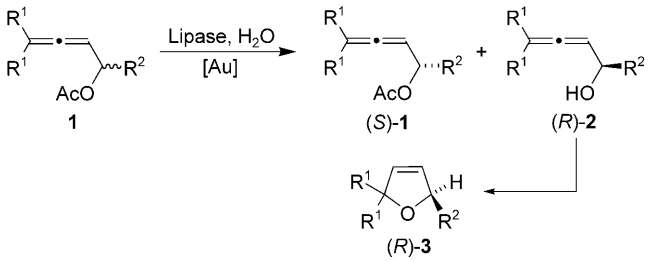
Abstract: We report the first example of a tandem kinetic resolution/cycloisomerization of racemic allenic acetates in the presence of *Burkholderia cepacia* lipase (PS Amano SD) and catalytic amounts of chloroauric acid ($HAuCl_4$) which affords 2,5-dihydrofurans, as well as unreacted starting material, in one pot with high enantiomeric excess and moderate to good yield.

Keywords: allenes; cycloisomerization; enzyme catalysis; gold catalysis; kinetic resolution; tandem reactions

The combination of two or more catalytic transformations in a tandem or one-pot process[1] is one of the most powerful tools in sustainable chemistry.[2] Among various catalytic methodologies, the combination of enzyme and transition metal catalysis seems to have received little attention so far.[3] For example, the lipase-catalyzed kinetic resolution of secondary alcohols, which is a widely used method for the generation of enantiomerically enriched or pure compounds,[4,5] has so far only been combined with transition metal catalysts which were designed to racemize the substrate.[3,6] There seems to be no precedent for tandem enzyme/transition metal-catalyzed transformations that involves C–C or C–heteroatom bond formation, resulting in products with increased molecular complexity. A possible reason might be the propensity of enzymes and transition metals to deactivate each other. Based on our interest in homogeneous gold catalysis,[7] we now report a novel approach to tandem enzyme/transition metal catalysis by combining the lipase-catalyzed kinetic resolution of racemic α-allenic acetates **1** with the gold-catalyzed cycloisomerization of the resulting enantiomerically enriched α-hydroxyallenes **2** to the corresponding 2,5-dihydrofurans **3**[7,8] in one pot (Scheme 1).

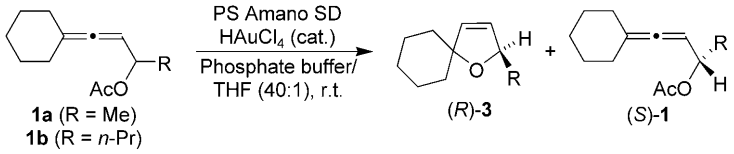
We started our investigation with substrates of the type **1** which bear a stereogenic center in the α-position, but no axis of chirality. Screening of various enzymes in aqueous phosphate buffer showed a high hydrolytic activity of lipases from *Pseudomonas fluorescens*, *Pseudomonas cepacia* and *Burkholderia cepacia* towards substrate **1a** whereas bulkier allenic acetates (e.g., **1b**) were effectively resolved only with lipase from *Burkholderia cepacia* (PS Amano SD). In contrast to this, all attempts for a lipase-catalyzed alcoholysis of the racemic acetate **1a** failed due to extremely slow conversions. Consequently, the gold-catalyzed cycloisomerization of the allenic alcohol **2** had to be carried out in aqueous medium in order to establish the desired tandem process. Recently, we have shown that chloroauric acid ($HAuCl_4$) is an efficient precatalyst for the cyclization of various functionalized allenes in water.[9] Thus, we optimized the conditions for the tandem hydrolysis/cycloisomerization of model substrate **1a** using the lipase from *Burkholderia cepacia* and $HAuCl_4$ (Table 1).

Since reactions in pure aqueous buffer resulted in very low conversions, we performed the optimization in the presence of 2.5 vol% of THF as cosolvent which improves the solubility of the substrate in the phosphate buffer.[9] In the presence of 10 mg of the lipase and 1 mol% of $HAuCl_4$, substrate **1a** (10 mg) afforded 2,5-dihydrofuran **3a**[10] with high enantiomeric excess (>90%), but the conversion reached only 25–30% after 48 h at room temperature (Table 1,



Scheme 1. Tandem lipase-catalyzed kinetic resolution/gold-catalyzed cycloisomerization of racemic allenic acetates **1**.

Table 1. Optimization of the tandem hydrolysis/cycloisomerization of allenic acetates **1a/b**.[a]



Entry	**1**	Lipase [mg]	$HAuCl_4$ [mol%]	t [h]	(*R*)-**3** % Conversion.	% *ee*
1	**1a**	10	1	48	25–30	90–95
2[b]	**1a**	10	1	24	25–30	90–95
3	**1a**	100	1	24	45–50	55–60
4	**1a**	10	10	24	0	
5	**1a**	10	0.5	24	27	96
6	**1a**	50	0.5	24	35	87
7	**1a**	100	0.5	24	46	63
8	**1b**	100	0.5	48	45	94

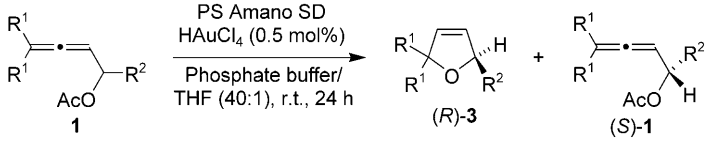
[a] *Reaction conditions:* **1** (10 mg) of in 2 mL of phosphate buffer (pH 7) and 50 μL of THF was treated with PS Amano SD (30000 U) and aqueous $HAuCl_4$ solution at room temperature.
[b] Reaction temperature: 50 °C.

entry 1). Increasing the temperature to 50 °C gave the same result after 24 h, albeit with formation of unidentified by-products (entry 2). Increasing the amount of the lipase to 100 mg resulted in improved conversion, but lower stereoselectivity (entry 3), whereas no reaction took place with 10 mol% of $HAuCl_4$ (entry 4). Thus, not only the conversion but also the ratio of enzyme to gold precatalyst strongly affects the tandem transformation. This observation was confirmed in subsequent reactions of **1a** with different amounts of the lipase and 0.5 mol% of $HAuCl_4$: we could obtain a satisfactory *ee* of 96% for (*R*)-**3a** only at rather low conversion of 27% (entry 5), whereas higher conversions resulted in lower *ee*s (entries 6 and 7). However, this normal behaviour for a kinetic resolution[11] was not observed for the somewhat bulkier propyl-substituted allenic acetate **1b** which gave a high enantioselectivity of 94% *ee* for cyclization product (*R*)-**3b** at a high conversion of 45% (entry 8).

Having established that the activities of the lipase and the gold catalyst do not compromise each other as long as low amounts of the gold precatalyst are used, we examined the tandem lipase/gold-catalyzed hydrolysis/cycloisomerization of various allenic acetates **1** (Table 2).

Whereas the tandem reaction works very well for substrates with a straight alkyl chain at the acetate

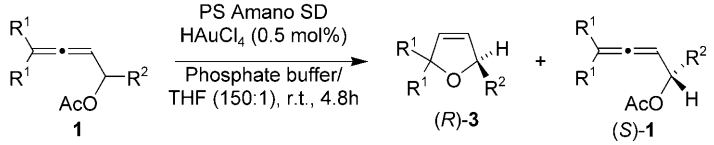
Table 2. Tandem hydrolysis/cycloisomerization of allenic acetates **1**.[a]



Entry	**1**	R^1	R^2	Lipase [mg]	(*R*)-**3** % Conversion	% *ee*
1	**1a**	$(CH_2)_5$	Me	50	35	87
2[b]	**1b**	$(CH_2)_5$	*n*-Pr	100	45	94
3	**1c**	$(CH_2)_5$	*c*-Hex	100	0	
4	**1d**	$(CH_2)_5$	*i*-Bu	100	0	
5[c]	**1e**	$(CH_2)_5$	$(CH_2)_2Ph$	100	4	nd
6	**1f**	$(CH_2)_4$	*n*-Pr	50	30	94
7	**1g**	Me	*n*-Pr	50	46	99
8	**1h**	Me	*n*-Oct	50	44	86

[a] *Reaction conditions:* **1** (10 mg) of in 2 mL of phosphate buffer (pH 7) and 50 μL of THF was treated with PS Amano SD (30000 U) and aqueous $HAuCl_4$ solution (0.5 mol%) at room temperature for 24 h.
[b] Reaction time: 48 h.
[c] Reaction time: 40 h.

Table 3. Tandem hydrolysis/cycloisomerization of allenic acetates **1** on preparative scale.[a]



Entry	**1**	R^1	R^2	(*R*)-**3**		(*S*)-**1**	
				% Yield	*ee*	% Yield	*ee*
1	**1a**	$(CH_2)_5$	Me	28	86	31	93
2	**1b**	$(CH_2)_5$	*n*-Pr	45	95	40	>95
3	**1f**	$(CH_2)_4$	*n*-Pr	38	88	33	>95
4	**1h**	Me	*n*-Oct	50	98	36	95

[a] *Reaction conditions:* **1** (0.5 mmol) of in 15 mL of phosphate buffer (pH 7) and 0.1 mL of THF was treated with PS Amano SD (30000 U) and aqueous $HAuCl_4$ solution (0.5 mol%) at room temperature for 48 h.

(entries 1, 2, 6–8), bulkier groups R^2 bearing either a phenyl substituent or a branch at the α- or β-carbon atom give low or no conversion (entries 3–5). Thus, the lipase is very sensitive to any steric hindrance at this position. In contrast to this, both five- (entry 6) and six-membered rings at the allene (entries 1 and 2) are tolerated, as well as acyclic allenic acetates **1g** and **h** (entries 7 and 8). The latter substrates show the highest reactivity and afford the corresponding 2,5-dihydrofurans with good to excellent *ee* at high conversion.

After these small-scale experiments, the tandem hydrolysis/cycloisomerization was performed on preparative scale with 0.5 mmol of the allenic acetates **1a**, **1b**, **1f**, and **1h** (Table 3). Both the 2,5-dihydrofurans (*R*)-**3** and the unreacted allenic acetates (*S*)-**1** were obtained with moderate to good isolated yields (28–50%) and good to excellent enantioselectivities (86–98% *ee*). In some cases (e.g., **3a**), the yield was compromised by the high volatility of the product.

In conclusion, we have developed the first example for a tandem lipase/gold-catalyzed transformation by treating racemic allenic acetates **1** with *Burkholderia cepacia* lipase (PS Amano SD) and catalytic amounts of chloroauric acid ($HAuCl_4$). The one-pot kinetic resolution/cycloisomerization affords 2,5-dihydrofurans (*R*)-**3**, as well as unreacted starting material (*S*)-**1**, with 28–50% isolated yield and 86–98% *ee*. Our results indicate a high mutual tolerance of the lipase and gold catalyst which opens intriguing possibilities for further tandem processes involving biocatalysts and transition metals.

Experimental Section

General Remarks

The syntheses of racemic alcohols, acetates and 2,5-dihydrofurans were performed under an inert atmosphere in oven-dried glassware. Tandem reactions were performed in vials under air. Lipase PS Amano SD (30000 U) was obtained from Amano Europe Ltd. and used as received. Aldehydes were distilled prior to use. All other chemicals were purchased from commercial sources and used as received. Column chromatography was carried out with Acros silica gel 60. ^1H and ^{13}C NMR spectra were recorded with Bruker DRX 400 or DRX 500 spectrometers at room temperature in $CDCl_3$ as solvent. Chemical shifts were determined relative to the residual solvent peaks ($CHCl_3$: $\delta = 7.26$ for protons, $\delta = 77.1$ for carbon atoms). GC analysis was carried out with a CE Instruments GC 8000 on a octakis-(2,3-di-*O*-pentyl-6-*O*-methyl)-γ-cyclodextrin capillary column with hydrogen as carrier gas.

General Procedure for the Synthesis of α-Allenic Acetates 1

Racemic α-hydroxyallenes were prepared according to a known procedure[12] using *p*-TsOH (1 mol%) instead of HCl gas. These were converted into the racemic acetates **1** according to a known procedure[12] using DMAP (20 mol%) and Et_3N (2 equiv.) instead of pyridine.

General Procedure for the Tandem Gold/Enzyme-Catalyzed Hydrolysis/Cyclization on an Analytical Scale

Racemic acetate **1** (10 mg) was dissolved in 2 mL of phosphate buffer (pH 7) and 50 μL of THF. Lipase from *Burkholderia cepacia* (PS Amano SD; 10–100 mg) was added, followed by $HAuCl_4$ solution (0.012 M in water, 20 μL, 0.5 mol%). The reaction mixture was stirred at room temperature for 24–48 h, and the conversion and *ee* were determined by GC analysis.

General Procedure for the Tandem Gold/Enzyme-Catalyzed Hydrolysis/Cyclization on a Preparative Scale

Racemic acetate **1** (0.5 mmol) was dissolved in 15 mL of phosphate buffer (pH 7) and 0.1 mL of THF. Lipase from *Burkholdia cepacia* (PS Amano SD; 160–800 mg) and $HAuCl_4$ solution (0.012 M in water, 0.2 mL, 0.5 mol%) were

added. The reaction mixture was stirred at room temperature for 48 h, and the conversion was controlled by GC analysis. The reaction mixture was then extracted 5 times with Et_2O, and the combined organic extracts were washed with satd. NaCl solution and dried with Na_2SO_4. After removal of the solvent under vacuum, the crude product was purified by flash column chromatography (pentane/Et_2O, 30:1).

4-Cyclohexylidenebut-3-en-2-yl acetate (1a): Colorless oil. R_f=0.65 (cyclohexane/EtOAc, 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.35–5.29 (m, 1H), 5.11–5.09 (m, 1H), 2.15–2.09 (m, 4H), 2.04 (s, 3H), 1.62–1.52 (m, 6H), 1.31 (d, J=6.5 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$): δ=198.3, 170.6, 105.7, 90.6, 69.4, 31.4, 27.5, 26.2, 21.6, 19.9; IR: ν=3055, 2983, 2932, 2891, 2855, 1731, 1447, 1370, 1265, 1245, 1038, 738 cm^{-1}; HR-MS: m/z=194.1301, calcd. for $C_{12}H_{18}O_2$ [M$^+$]: 194.1307. (*S*)-**1a** (93% *ee*); $[\alpha]_D$: −117.4 (*c* 0.45, CH_2Cl_2).

1-Cyclohexylidenehex-1-en-3-yl acetate (1b): Colorless oil. R_f=0.66 (cyclohexane/EtOAc, 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.21–5.16 (m, 1H), 5.02–5.00 (m, 1H), 2.14–2.11 (m, 4H), 2.04 (s, 3H), 1.65–1.33 (m, 10H), 0.92 (t, J=8.0 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$): δ=198.6, 89.3, 73.0, 36.3, 31.4, 27.5, 26.2, 21.6, 18.8, 14.0; IR: ν=2957, 2932, 2855, 1968, 1732, 1371, 1239, 1017, 738 cm^{-1}; HR-MS: m/z=222.1614, calcd. for $C_{14}H_{22}O_2$ [M$^+$]: 222.1620. (*S*)-**1b** (>95% *ee*); $[\alpha]_D$: −99.6 (*c* 1.40, CH_2Cl_2).

1-Cyclohexyl-3-cyclohexylideneallyl acetate (1c): Colorless viscous oil. R_f=0.57 (cyclohexane/EtOAc, 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.00–4.92 (m, 2H), 2.14–2.08 (m, 4H), 2.05 (s, 3H), 1.78–1.72 (m, 4H), 1.64–1.49 (m, 8H), 1.26–0.99 (m, 5H); ^{13}C NMR (400 MHz, $CDCl_3$): δ=199.0, 170.6, 104.5, 87.6, 41.8, 31.4, 31.3, 28.9, 28.6, 27.4, 26.6, 26.2, 26.1, 26.1; IR: ν=2930, 2854, 2253, 1725, 1248, 909, 733 cm^{-1}; HR-MS: m/z=262.1927, calcd. for $C_{17}H_{26}O_2$ [M$^+$]: 262.1933.

1-Cyclohexylidene-5-methylhex-1-en-3-yl acetate (1d): Yellow oil. R_f=0.64 (cyclohexane/EtOAc, 10:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.28–5.23 (m, 1H), 5.02–4.99 (m, 1H), 2.14–2.06 (m, 4H), 2.04 (s, 3H), 1.69–1.42 (m, 9H), 0.91 (dd, J=6.5/3.0 Hz, 6H); ^{13}C NMR (400 MHz, $CDCl_3$): δ=198.6, 170.6, 105.1, 89.4, 71.8, 43.2, 31.4, 31.3, 27.5, 27.4, 26.2, 24.9, 22.8, 22.7, 21.6. IR: ν=3054, 2934, 2305, 1726, 1421, 1265, 896, 739, 705 cm^{-1}; HR-MS: m/z= 236.1772, calcd. for $C_{15}H_{24}O_2$ [M$^+$]: 236.1776.

1-Cyclohexylidene-5-phenylpent-1-en-3-yl acetate (1e): Colorless oil. R_f=0.59 (cyclohexane/EtOAc, 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.31–7.18 (m, 5H), 5.23 (q, J=6.2 Hz, 1H,), 5.09–5.07 (m, 1H), 2.73–2.65 (m, 2H), 2.21–2.10 (m, 4H), 2.06 (s, 3H), 1.68–1.49 (m, 8H); ^{13}C NMR (400 MHz, $CDCl_3$): δ=198.7, 170.5, 141.6, 128.5, 128.5, 126.0, 105.3, 89.1, 72.5, 35.8, 31.8, 31.4, 31.3, 27.4, 27.0, 26.1, 21.4; IR: ν=3027, 2928, 2852, 2253, 1967, 1735, 1448, 1371, 1245, 1020, 911, 738, 650 cm^{-1}; HR-MS: m/z=284.1776, calcd. for $C_{19}H_{24}O_2$ [M$^+$]: 284.1776.

1-Cyclopentylidenehex-1-en-3-yl acetate (1f): Colorless oil. R_f=0.58 (cyclohexane/EtOAc, 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.19 (q, J=6.5 Hz, 1H), 5.10–5.05 (m, 1H), 2.38–2.31 (m, 4H), 2.03 (s, 3H), 1.70–1.64 (m, 4H), 1.62–1.51 (m, 2H), 1.38–1.29 (m, 2H), 0.90 (t, J=7.5 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$): δ=197.4, 170.6, 106.3, 91.8, 73.0, 36.3, 31.33, 31.25, 27.2, 27.0, 21.5, 18.8, 14.0; IR: ν=2960, 2253, 1727, 1372, 1248, 911, 741, 650 cm^{-1}; HR-MS: m/z=209.1448, calcd. for $C_{13}H_{20}O_2$ [M$^+$]: 208.1463. (*S*)-**1f** (>95% *ee*); $[\alpha]_D$: −113.2 (*c* 0.70, CH_2Cl_2).

7-Methylocta-5,6-dien-4-yl acetate (1g): Colorless oil. R_f=0.55 (cyclohexane/EtOAc, 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.17 (q, J=6.5 Hz, 1H,), 5.00–4–97 (m, 1H), 2.03 (s, 3H), 1.70–1.68 (m, 6H), 1.64–1.53 (m, 2H), 1.42–1.30 (m, 2H), 0.91 (t, J=7.5 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$): δ=202.0, 170.6, 97.8, 89.4, 72.9, 36.4, 21.5, 20.4, 18.8, 14.0; IR: ν=3054, 2962, 2912, 2874, 1728, 1371, 1265, 1248, 738, 704 cm^{-1}; HR-MS: m/z=182.1301, calcd. for $C_{11}H_{18}O_2$ [M$^+$]: 182.1307.

2-Methyltrideca-2, 3-dien-5-yl acetate (1h): Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.18–5.13 (q, J=6.5 Hz, 1H), 5.00–4.97 (m, 1H), 2.04 (s, 3H), 1.70–1.68 (m, 6H), 1.64–1.50 (m, 2H), 1.33–1.26 (m, 12H), 0.89–0.86 (m, 3H); ^{13}C NMR (400 MHz, $CDCl_3$): δ=202.0, 170.6, 97.8, 89.5, 77.5, 73.2, 34.3, 32.0, 29.7, 29.5, 25.5, 22.8, 20.4, 14.3; IR: ν=3154, 2928, 2856, 2253, 1971, 1726, 1250, 912, 735, 650 cm^{-1}; HR-MS: m/z=252.2084, calcd. for $C_{16}H_{28}O_2$ [M$^+$]: 252.2089. (*S*)-**1h** (95% *ee*); $[\alpha]_D$: −76.0 (*c* 0.65, CH_2Cl_2).

2-Methyl-1-oxaspiro[4.5]dec-3-ene (3a): R_f=0.74 (cyclohexane/EtOAc, 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.87 (dd, J=6.0/2.5 Hz, 1H), 5.70 (d, J=6.0 Hz, 1H), 4.90 (dd, J=6.5/2.0 Hz, 1H), 1.63–1.73 (m, 2H), 1.53–1.61 (m, 4H), 1.37–1.50 (m, 4H), 1.25 (d, J=6.5 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$): δ=133.4, 130.4, 89.6, 80.5, 39.6, 37.6, 25.6, 23.5; IR: ν=2972, 2934, 2858, 2253, 1087 (cyclic ether), 907, 734, 650 cm^{-1}; HR-MS: m/z=152.1196, calcd. for $C_{10}H_{16}O$ [M$^+$]: 152.1201. (*R*)-**3a** (86% *ee*); $[\alpha]_D$: −90.4 (*c* 0.38, CH_2Cl_2).

2-Propyl-1-oxaspiro[4.5]dec-3-ene (3b): R_f=0.67 (cyclohexane/EtOAc, 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.09 (dd, J=6.0/2.0 Hz, 1H), 5.72 (dd, J=5.5/1.0 Hz, 1H), 4.81–4.78 (m, 1H), 1.76–1.64 (m, 4H), 1.60–1.49 (m, 9H), 1.48–1.37 (m, 1H), 0.93 (t, J=7.3 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$): δ=129.0, 89.2, 84.5, 39.6, 39.1, 37.7, 25.7, 23.8, 18.8, 14.4; IR: ν=3053, 2933, 1448, 1265, 1109, 705 cm^{-1}; HR-MS: m/z=180.1509, calcd. for $C_{12}H_{20}O$ [M$^+$]: 180.1514. (*R*)-**3b** (95% *ee*); $[\alpha]_D$: −100.6 (*c* 0.74, CH_2Cl_2).

2-Propyl-1-oxaspiro[4.4]non-3-ene (3f): R_f=0.60 (cyclohexane/EtOAc, 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.70 (s, 2H), 4.77 (t, J=5.8 Hz, 1H), 1.80–1.70 (m, 4H), 1.62–1.59 (m, 4H), 1.52–1.49 (m, 2H), 1.41–1.33 (m, 2H), 0.92 (t, J=7.3 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$): δ=133.4, 128.8, 84.8, 40.2, 39.2, 38.8, 27.1, 24.8, 24.7, 18.6, 14.5; IR: ν=2959, 2253, 1466, 1383, 912, 742, 650 cm^{-1}; HR-MS: m/z=166.1354, calcd. for $C_{11}H_{18}O$ [M$^+$]: 166.1358. (*R*)-**3f** (88% *ee*); $[\alpha]_D$: −94.4 (*c* 0.64, CH_2Cl_2).

2,2-Dimethyl-5-propyl-2,5-dihydrofuran (3g): R_f=0.59 (cyclohexane/EtOAc, 4:1). Due to solvent residues in this very volatile product, not all NMR peaks could be resolved. ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.68 (dd, J=6.0/2.0 Hz, 1H), 5.64 (dd, J=6.0/1.0 Hz, 1H), 1.49 (s, 6H), 1.40–0.95 (m, 4H), 0.92 (t, J=7.6 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$): δ=135.4, 128.4, 87.1, 85.0, 39.4, 29.3, 28.0, 27.1, 26.0, 18.8; IR: ν=2977, 2873, 2253, 1110, 907, 732, 650 cm^{-1}; HRMS: m/z=140.1195, calcd. for $C_9H_{16}O$ [M$^+$]: 140.1201.

2,2-Dimethyl-5-octyl-2,5-dihydrofuran (3h): R_f=0.62 (cyclohexane/EtOAc, 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.70 (dd, J=6.0/2.5 Hz, 1H), 5.65 (dd, J=6.0/1.5 Hz, 1H), 4.81–4.78 (m, 1H), 1.55–1.49 (m, 2H), 1.32 (s, 6H), 1.29–1.25 (m, 12H), 0.87 (t, J=8.0 Hz, 3H); ^{13}C NMR (400 MHz,

$CDCl_3$): $\delta = 135.4$, 128.4, 87.1, 85.2, 37.1, 32.0, 30.00, 29.4, 28.1, 22.8, 14.3; IR: $\nu = 2927$, 2855, 2253, 1097, 911, 734 cm^{-1}; HR-MS: $m/z = 210.1978$, calcd. for $C_{14}H_{26}O$ $[M^+]$: 210.1984. (*R*)-**3h** (98% *ee*); $[\alpha]_D$: −78.2 (*c* 1.37, CH_2Cl_2).

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