First Stereoselective Total Synthesis of Naturally Occurring (6*R*)-6-(4-Oxopentyl)-5,6-dihydro-2*H*-pyran-2-one and Its (6*S*)-Enantiomer[1]

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Abstract: (6*R*)-6-(4-Oxopentyl)-5,6-dihydro-2*H*-pyran-2-one, a naturally occurring α,β-unsaturated δ-lactone, and its (6*S*)-enantiomer have been synthesized stereoselectively starting from pentane-1,5-diol. The synthesis involves Maruoka asymmetric allylation and ring-closing metathesis as the key steps.

Key words: lactones, (6*R*)-6-(4-oxopent-2-enyl)-5,6-dihydro-2*H*-pyran-2-one, (6*S*)-6-(4-oxopent-2-enyl)-5,6-dihydro-2*H*-pyran-2-one, ring-closing metathesis, stereoselective synthesis

6-Substituted 5,6-dihydro-2*H*-pyran-2-ones exhibit various important biological properties including cytotoxic, antifungal, and antibacterial activity;[2] the synthesis of these compounds is an attractive target to organic chemists.[3] (6*R*)-6-(4-Oxopentyl)-5,6-dihydro-2*H*-pyran-2-one [(*R*)-**1**] (Figure 1), a member of this class of compounds, was isolated from *Piper reticulatum* (Piperaceae).[4] The total synthesis of this compound has not yet been reported though several related compounds have recently been synthesized.[5] In continuation of our work[6] on the stereoselective construction of bioactive natural products, we report here the first synthesis of this compound (*R*)-**1** and its (6*S*)-isomer (*S*)-**1**.

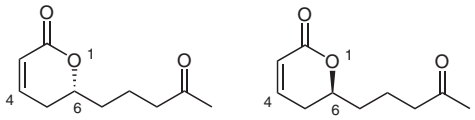
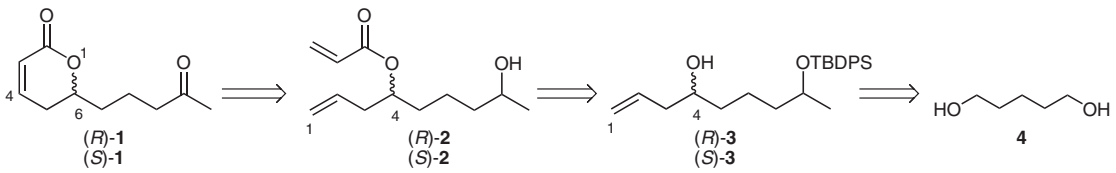


Figure 1

The retrosynthetic analysis (Scheme 1) suggested that (*R*)-**1** and (*S*)-**1** can be prepared from the olefinic esters (*R*)-**2** and (*S*)-**2**, respectively, which can be obtained from pentane-1,5-diol (**4**) via the allylic alcohols (*R*)-**3** [for (*R*)-**1**] and (*S*)-**3** [for(*S*)-**1**].

The synthesis of (6*R*)-6-(4-oxopentyl)-5,6-dihydro-2*H*-pyran-2-one [(*R*)-**1**] was initiated by converting pentane-1,5-diol (**4**) into monobenzyl ether **5** by treatment with benzyl bromide and potassium hydroxide (Scheme 2). The primary hydroxy group of **5** was oxidized with pyridinium chlorochromate to the corresponding aldehyde **6**, which was immediately treated with methylmagnesium iodide to form the racemic alcohol **7**. The hydroxy group of **7** was protected as its TBDPS ether by treatment with *tert*-butyldiphenylsilyl chloride in the presence of imidazole and a catalytic amount of 4-(dimethylamino)pyridine to afford **8**; the benzyl group **8** was deprotected by hydrogenation in the presence of palladium on carbon to furnish the alcohol **9**. This alcohol **9** was oxidized with pyridinium chlorochromate to give the aldehyde **10**, which subsequently underwent Maruoka asymmetric allylation,[7] using the titanium complex (*S*,*S*)-**I** (Figure 2) and allyltributyltin to generate the homoallylic alcohol (*R*)-**3**. Compound (*R*)-**3** was esterified with acryloyl chloride in the presence of triethylamine and a catalytic amount of 4-(dimethylamino)pyridine to produce the acrylate ester (*R*)-**11**. Deprotection of the TBDPS ether group of (*R*)-**11** by treatment with tetrabutylammonium fluoride generated the alcohol (*R*)-**2**, which was oxidized with pyridinium chlorochromate to the corresponding ketone (*R*)-**12**. The ^{13}C NMR spectrum of (*R*)-**3** showed that some of the signals were split, indicating that the compound is a diastereomeric mixture; the diastereomers were not separated because at a later stage one of the chiral center is destroyed. Compounds (*R*)-**11** and (*R*)-**2** were also diastereomeric mixtures (as indicated by their ^{13}C NMR spectra), but compound (*R*)-**12** was a single isomer. The ring-closing metathesis[8] of (*R*)-**12** was efficiently accomplished by using Grubbs' first-generation (Grubbs I) catalyst to afford the α,β-unsaturated δ-lactone (*R*)-**1**, whose optical and spectral properties were found to be identical



Scheme 1 Retrosynthetic analysis of 6-(4-oxopentyl)-5,6-dihydropyran-2-one

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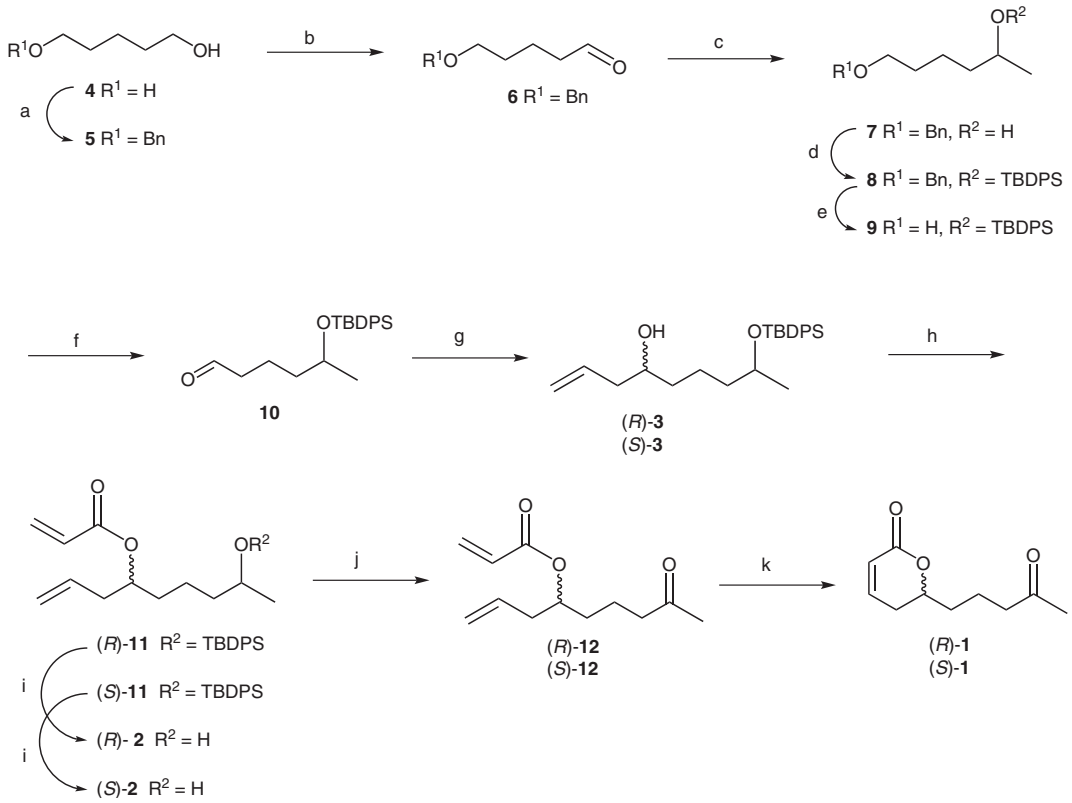

Scheme 2 Synthesis of 6-(4-oxopentyl)-5,6-dihydro-2*H*-pyran-2-ones (*R*)-**1** and (*S*)-**1**. *Reagents and conditions*: (a) BnBr, KOH, r.t., 1 h, 80%; (b) PCC, Celite, CH_2Cl_2, r.t., 1 h, 95%; (c) Mg, MeI, anhyd Et_2O, 0 °C to r.t., 2 h, 92%; (d) TBDPSCl, Et_3N, DMAP, CH_2Cl_2, 0 °C to r.t., 2 h, 95%; (e) H_2, Pd/C, EtOAc, 10 h, 97%; (f) PCC, Celite, CH_2Cl_2, r.t., 1 h, 94%, (g) [(*S*,*S*)-**I**, 10 mol%, for (*R*)-**3**], [(*R*,*R*)-**I**, 10 mol%, for (*S*)-**3**], $Bu_3SnCH_2CH{=}CH_2$, CH_2Cl_2, –15 °C to 0 °C, 15 h, 84%; (h) acryloyl chloride, Et_3N, DMAP, CH_2Cl_2, 0 °C to r.t., 3 h, 88%; (i) TBAF, anhyd THF, 0 °C to r.t., 3 h, 80%; (j) PCC, Celite, CH_2Cl_2, r.t., 1 h, 90%; (k) Grubbs I catalyst (10 mol%), CH_2Cl_2, 50 °C, 24 h, 86%.

to those reported for naturally occurring (6*R*)-6-(4-oxopentyl)-5,6-dihydro-2*H*-pyran-2-one.[4]

The (6*S*)-enantiomer (*S*)-**1** of the natural lactone (*R*)-**1** was also synthesized from **9**, which was prepared from pentane 1,5-diol (**4**) (Scheme 2). Compound **9** was oxidized with pyridinium chlorochromate to the corresponding aldehyde **10**, which was then subjected to Maruoka asymmetric allylation[7] using titanium complex (*R*,*R*)-**I** (Figure 2) and allyltributyltin to form the homoallylic alcohol (*S*)-**3**. The subsequent conversion of this homoallylic alcohol (*S*)-**3** into (*S*)-**1** was completed by following a similar sequence of reactions to that used for conversion of the enantiomeric homoallylic alcohol (*R*)-**3** into the natural lactone (*R*)-**1** [i.e., acrylation with acryloyl chloride to form (*S*)-**11** and deprotection of the TBDPS ether to the alcohol (*S*)-**2**, followed by oxidation to ketone (*S*)-**12** and finally ring-closing metathesis[8] to generate (*S*)-**1**].

In conclusion, we have developed the first stereoselective total synthesis of the naturally occurring lactone, (6*R*)-(4-oxopentyl)-5,6-dihydro-2*H*-pyran-2-one and its (6*S*)-enantiomer involving some simple steps including Maruoka asymmetric allylation and ring-closing metathesis.

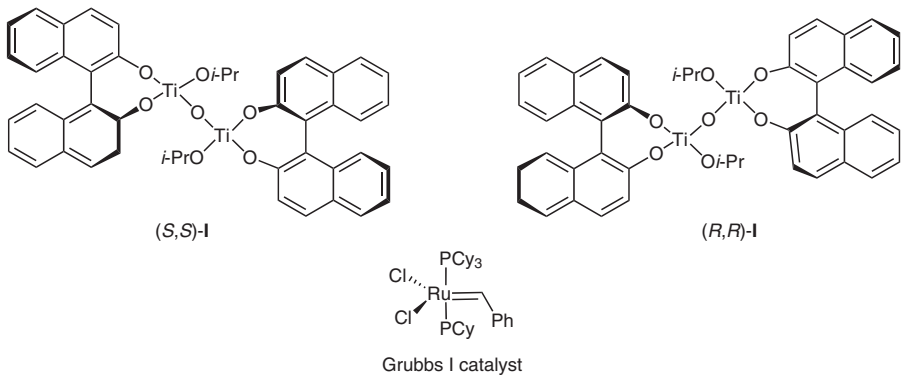

Figure 2

TLC used silica gel F_{254} plates and the spots were examined under UV light and then developed by an iodine vapor. Column chromatography was performed with silica gel (BDH 100–200 mesh). Solvents were purified according to standard procedures. The spectra were recorded with the following instruments; IR: Perkin-Elmer RX FT-IR spectrophotometer; NMR: Varian Gemini 200 MHz (^{1}H) and 50 MHz (^{13}C) spectrometer; ESIMS: VG-Autospec micromass. Organic extracts were dried over anhyd Na_2SO_4. Optical rotations were measured with Jasco DIP 300 digital polarimeter at 25 °C.

5-(Benzyloxy)pentan-1-ol (5)

To pentane-1,5-diol (**4**, 2.00 g, 19.23 mmol) was added KOH pellets (1.08 g, 19.23 mmol) and the mixture was stirred for 5 min. BnBr (1.64 g, 14.43 mmol) was added in one portion and the mixture was stirred for 1 h at r.t. When the reaction was complete (TLC), it was quenched with cold H_2O, and the mixture was extracted with EtOAc (3 × 50 mL). The organic layer was dried (anhyd Na_2SO_4). Evaporation of the solvents and purification of the residue by column chromatography (EtOAc–hexane, 3:7) gave pure **5** (2.98 g, 80%) as a colorless liquid.

IR: 3417, 1635, 1453, 1362, 1209, 1098 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.33–7.25 (m, 5 H), 4.46 (s, 2 H), 3.58 (t, *J* = 7.0 Hz, 2 H), 3.44 (t, *J* = 7.0 Hz, 2 H), 1.66–1.39 (m, 6 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 138.5, 128.4, 127.6, 127.5, 72.9, 70.3, 62.8, 32.5, 29.5, 22.2.

MS (ESI): *m*/*z* = 195 [M + H]$^+$, 222 [M + Na]$^+$.

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.18; H, 9.35. Found: C, 74.22; H, 9.40.

6-(Benzyloxy)hexan-2-ol (7)

To a stirred suspension of Celite (5.00 g) in CH_2Cl_2 (20 mL) was added a soln of **5** (2.80 g, 14.44 mmol) in CH_2Cl_2 (30 mL) at r.t. To this suspension PCC (4.65 g, 21.65 mmol) was added at r.t. After 1 h, the mixture was filtered off through a Celite pad. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography (EtOAc–hexane, 1:9). The purified aldehyde **6** (2.63 g, 95%) was directly subjected to Grignard reaction.

The Grignard reagent was made by slow addition of MeI (4.81 g, 33.85 mmol) to small pieces of Mg metal (0.82 g, 33.85 mmol) in a 2-necked round-bottom flask containing anhyd Et_2O (30 mL). The flask was fitted with a reflux condenser. The mixture was stirred until the soln became ash color. The soln of aldehyde **6** (2.60 g, 13.54 mmol) in anhyd Et_2O (20 mL) was added dropwise to the freshly prepared Grignard reagent at 0 °C. The mixture was stirred for 2 h at 0 °C to r.t. and the reaction was quenched with aq sat. NH_4Cl soln (25 mL). The aqueous layer was extracted with Et_2O (3 × 25 mL) and the combined organic layers were washed with brine soln (20 mL), dried (anhyd Na_2SO_4), and concentrated in vacuo. The residue was purified by column chromatography (EtOAc–hexane, 2:8) to afford **7** (2.56 g, 92%) as a colorless liquid.

IR: 3367, 1642, 1453, 1360, 1215, 1091 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.35–7.25 (m, 5 H), 4.46 (s, 2 H), 3.75 (m, 1 H), 3.46 (t, *J* = 7.0 Hz, 2 H), 1.68–1.41 (m, 6 H), 1.16 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 138.5, 128.3, 127.6, 127.5, 72.9, 70.2, 67.9, 39.1, 29.7, 23.6, 22.5.

MS (ESI): *m*/*z* = 209 [M + H]$^+$, 231 [M + Na]$^+$.

Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.94; H, 9.65. Found: C, 74.99; H, 9.74.

[6-(Benzyloxy)hexan-2-yloxy)*tert*-butyldiphenylsilane (8)

To a stirred soln of **7** (2.40 g, 11.54 mmol) in anhyd CH_2Cl_2 (25 mL) were added imidazole (1.57 g, 23.08 mmol), cat. DMAP (0.14 g, 1.15 mmol), and TBDPSCl (3.81 g, 13.85 mmol) at 0 °C to r.t. The mixture was stirred for 2 h and then diluted with CH_2Cl_2 (25 mL). The organic layer was washed with brine (35 mL), and dried (anhyd Na_2SO_4). Evaporation of the solvent under reduced pressure followed by column chromatography (EtOAc–hexane, 1:9) afforded **8** (4.89 g, 95%) as a yellowish liquid.

IR: 1461, 1428, 1368, 1108 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.70–7.61 (m, 4 H), 7.39–7.19 (m, 11 H), 4.43 (s, 2 H), 3.82 (m, 1 H), 3.35 (t, *J* = 7.0 Hz, 2 H), 1.53–1.22 (m, 6 H), 1.02 (s, 12 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 138.7, 135.9, 134.9, 134.4, 129.5, 129.4, 128.3, 127.6, 127.5, 127.4, 72.8, 70.3, 69.5, 39.3, 29.8, 27.2, 23.3, 21.9, 19.4.

MS (ESI): *m*/*z* = 469 [M + Na]$^+$.

Anal. Calcd for $C_{29}H_{38}O_2Si$: C, 77.98; H, 8.57; Si, 6.29. Found: C, 78.01; H, 8.62; Si, 6.23%.

5-(*tert*-Butyldiphenylsiloxy)hexan-1-ol (9)

A soln of **8** (4.60 g, 10.31 mmol) in EtOAc (45 mL) was mixed with Pd/C (10% mol) and stirred for 10 h under a H_2 atmosphere (3.8 bars). The catalyst was removed by filtration and the solvent was evaporated to give a residue that was purified by column chromatography (EtOAc–hexane, 4:6) to afford pure **9** (3.56 g, 97%) as pale-yellow liquid.

IR: 3450, 1460, 1427, 1366, 1107 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.72–7.62 (m, 4 H), 7.44–7.32 (m, 6 H), 3.83 (m, 1 H), 3.51 (t, *J* = 7.0 Hz, 2 H), 1.56–1.24 (m, 6 H), 1.08 (s, 12 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 136.1, 136.0, 134.9, 134.5, 129.5, 129.4, 127.8, 127.7, 69.5, 39.0, 32.8, 27.0, 23.1, 21.2, 19.3.

MS (ESI): *m*/*z* = 379 [M + Na]$^+$.

Anal. Calcd for $C_{22}H_{32}O_2Si$: C, 74.10; H, 9.05; Si, 7.88. Found: C, 74.14; H, 9.08; Si, 7.93.

5-(*tert*-Butyldiphenylsiloxy)hexanal (10)

To a stirred suspension of Celite (2.00 g) in CH_2Cl_2 (20 mL) was added a soln of **9** (1.50 g, 4.21 mmol) in CH_2Cl_2 (20 mL) at r.t. To this suspension PCC (1.36 g, 6.32 mmol) was added r.t. After 1 h, the mixture was filtered off through a Celite pad. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography (EtOAc–hexane, 1:9) to give purified **10** (1.40 g, 94%) as a pale-yellow liquid.

IR: 3450, 1460, 1427, 1366, 1107 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 9.61 (s, 1 H), 7.68–7.60 (m, 4 H), 7.44–7.30 (m, 6 H), 3.84 (m, 1 H), 2.25 (t, *J* = 7.0 Hz, 2 H), 1.67–1.55 (m, 2 H), 1.50–1.38 (m, 2 H), 1.08 (s, 12 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 202.2, 136.0, 135.9, 134.9, 134.7, 130.1, 130.0, 128.2, 128.1, 69.4, 44.6, 39.2, 27.1, 23.2, 19.9, 18.4.

MS (ESI): *m*/*z* = 377 [M + Na]$^+$

(*R*)-8-(*tert*-Butyldiphenylsiloxy)non-1-en-4-ol [(*R*)-3]; Typical Procedure

To a stirred soln of $TiCl_4$ (0.10 g, 0.34 mmol) in CH_2Cl_2 (10 mL) was added dried Ti(O*i*-Pr)$_4$ (0.03 g, 0.19 mmol) at 0 °C under a N_2 atmosphere and the mixture was allowed to warm to r.t. After 1.5 h, Ag_2O (0.08 g, 0.34 mmol) was added and the reaction was continued for 6 h under exclusion of direct light. The mixture was diluted with CH_2Cl_2 (20 mL), treated with (*S*)-BINOL (0.19 g, 0.68 mmol) at r.t. for 2.5 h to furnish the chiral bis-Ti(IV) oxide (*S*,*S*)-**I**. This

complex was cooled to –15 °C and treated sequentially with **10** (1.20 g, 3.40 mmol) and allyltributyltin (1.46 g, 4.42 mmol) at the same temperature. The mixture was allowed to warm to 0 °C and stirred for 15 h. The mixture was quenched with sat. aq $NaHCO_3$ (50 mL) and extracted with EtOAc (3 × 20 mL). The combined organic extracts were dried (anhyd Na_2SO_4). Evaporation of the solvents and purification of the residue by column chromatography (EtOAc–hexane, 2:8) gave pure (*R*)-**3** (1.12 g, 84%) as a colorless liquid; $[\alpha]_D^{32}$ +3.36 (*c* 0.6, $CHCl_3$).

IR: 3382, 1466, 1428, 1108, cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.71–7.59 (m, 4 H), 7.41–7.28 (m, 6 H), 5.72 (m, 1 H), 5.14–5.03 (m, 2 H), 3.82 (m, 1 H), 3.50 (m, 1 H), 2.25–1.98 (m, 2 H), 1.52–1.22 (m, 6 H), 1.04 (m, 12 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 136.0, 135.9, 134.9, 134.8, 134.5, 129.4, 127.5, 127.4, 118.9, 70.4, 69.5, 69.4*, 42.0, 41.9*, 39.4, 39.3*, 36.8, 36.7*, 27.2, 23.5, 23.4*, 21.4, 21.3*, 19.4; * signal for the diastereomer.

MS (ESI): *m*/*z* = 397 $[M + H]^+$, 419 $[M + Na]^+$.

Anal. Calcd for $C_{25}H_{36}O_2Si$: C, 75.70; H, 9.15. Found: C, 75.74; H, 9.17.

(*S*)-8-(*tert*-Butyldiphenylsiloxy)non-1-en-4-ol [(*S*)-3]

Following the typical procedure for (*R*)-**3** using $TiCl_4$ (0.10 g, 0.34 mmol) in CH_2Cl_2 (10 mL), dried Ti(O*i*-Pr)$_4$ (0.03 g, 0.19 mmol), Ag_2O (0.08 g, 0.34 mmol), CH_2Cl_2 (20 mL), and (*R*)-BINOL (0.19 g, 0.68 mmol) to give chiral bis-Ti(IV) oxide (*R*,*R*)-**I**, which was reacted with **10** (1.20 g, 3.40 mmol) and allyltributyltin (1.46 g, 4.42 mmol) and purified in the same manner to give (*S*)-**3** (1.12 g, 84%) as a colorless liquid; $[\alpha]_D^{32}$ –3.17 (*c* 0.6, $CHCl_3$). Spectral data (^1H, ^{13}C NMR and MS) were identical to those of (*R*)-**3**.

(*R*)-8-(*tert*-Butyldiphenylsiloxy)non-1-en-4-yl Acrylate [(*R*)-11]; Typical Procedure

To a stirred soln of (*R*)-**3** (1.00 g, 2.53 mmol) in anhyd CH_2Cl_2 (15 mL) were added, at 0 °C, Et_3N (0.64 g, 6.33 mmol) and cat. DMAP (0.03 g, 0.25 mmol). After 10 min, acryloyl chloride (0.27 g, 3.03 mmol) was added. The mixture was allowed to warm to r.t. and stirred for 3 h. The mixture was diluted with H_2O (20 mL) and extracted into CH_2Cl_2 (3 × 20 mL). The combined organic extracts were washed with brine (10 mL), dried (anhyd Na_2SO_4), and concentrated in vacuo. The gummy mass was purified by column chromatography (EtOAc–hexane, 1:9) to afford pure (*R*)-**11** (0.99 g, 88%) as a yellow liquid; $[\alpha]_D^{32}$ +7.87 (*c* 1.5, $CHCl_3$).

IR: 3446, 2932, 2858, 1723, 1638, 1466, 1194, 1108, 1054 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.67–7.62 (m, 4 H), 7.40–7.30 (m, 6 H), 6.37 (dd, *J* = 8.0, 3.0 Hz, 1 H), 6.06 (m, 1 H), 5.79–5.66 (m, 2 H), 5.09–5.02 (m, 2 H), 4.92 (m, 1 H), 3.81 (m, 1 H), 2.28 (t, *J* = 7.0 Hz, 2 H), 1.52–1.26 (m, 6 H), 1.04 (s, 12 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 165.8, 135.8, 135.7, 134.8, 134.4, 133.6, 130.3, 129.5, 129.4, 128.8, 127.5, 127.4, 117.6, 73.4, 69.3, 69.2*, 39.2, 39.1*, 38.5, 38.4*, 33.5, 27.0, 23.2, 23.1*, 21.1, 20.8*, 19.2; * signal for the diastereomer.

MS (ESI): *m*/*z* = 473 $[M + Na]^+$.

Anal. Calcd for $C_{28}H_{38}O_3Si$: C, 74.63; H, 8.51; Si, 6.23. Found: C, 74.66; H, 8.54; Si, 6.26.

(*S*)-8-(*tert*-Butyldiphenylsiloxy)non-1-en-4-yl Acrylate [(*S*)-11]

Following the typical procedure for (*R*)-**11** using (*S*)-**3** (1.00 g, 2.53 mmol), CH_2Cl_2 (15 mL), Et_3N (0.64 g, 6.33 mmol), cat. DMAP (0.03g, 0.25 mmol), and acryloyl chloride (0.27 g, 3.03 mmol) gave pure (*S*)-**11** (0.99 g, 88%) as a yellow liquid; $[\alpha]_D^{32}$ –7.66 (*c* 1.5, $CHCl_3$). Spectral data (^1H, ^{13}C NMR and MS) were identical to those of (*R*)-**11**.

(*R*)-8-Hydroxynon-1-en-4-yl Acrylate [(*R*)-2]; Typical Procedure

To a soln of (*R*)-**11** (0.80 g, 1.77 mmol) in anhyd THF (10 mL) was added 1 M TBAF in THF (3.55 mL, 3.55 mmol) dropwise at 0 °C and the mixture was stirred for 3 h. H_2O (20 mL) was added and the mixture was extracted with EtOAc (3 × 20 mL). The organic extracts were washed with brine (30 mL), dried (anhyd Na_2SO_4), and concentrated in vacuo. Evaporation of the solvents and purification of the residue by column chromatography (EtOAc–hexane, 3:7) gave pure (*R*)-**2** (1.12 g, 80%) as a colorless liquid; $[\alpha]_D^{32}$ +21.75 (*c* 0.4, $CHCl_3$).

IR: 3448, 1713, 1632, 1412, 1201 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 6.39 (dd, *J* = 14.0, 2.0 Hz, 1 H), 6.06 (m, 1 H), 5.85–5.66 (m, 2 H), 5.10–4.93 (m, 3 H), 3.70 (m, 1 H), 2.33 (t, *J* = 7.0 Hz, 2 H), 1.64–1.24 (m, 6 H), 1.14 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 166.2, 133.3, 130.6, 128.5, 117.9, 73.5, 68.1, 68.0*, 39.1, 39.0, 38.9* , 33.8, 23.5, 23.4*, 21.9; * signal for the diastereomer.

MS (ESI): *m*/*z* = 235 $[M + Na]^+$.

Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.93; H, 9.54.

(*S*)-8-Hydroxynon-1-en-4-yl Acrylate [(*S*)-2]

Following the typical procedure for (*R*)-**2** using (*S*)-**11** (0.80 g, 1.77 mmol), THF (10 mL), and 1 M TBAF in THF (3.55 mL, 3.55 mmol) gave pure (*S*)-**2** (1.12 g, 80%) as a colorless liquid; $[\alpha]_D^{32}$ –21.58 (*c* 0.4, $CHCl_3$). Spectral data (^1H, ^{13}C NMR and MS) were identical to those of (*R*)-**2**.

(*R*)-8-Oxonon-1-en-4-yl Acrylate [(*R*)-12]; Typical Procedure

To a stirred suspension of Celite (1.00 g) in CH_2Cl_2 (5 mL) was added a soln of (*R*)-**2** (0.25 g, 1.18 mmol) in CH_2Cl_2 (10 mL) at r.t. To this suspension PCC (0.51 g, 2.36 mmol) was added at 0 °C and the mixture was warmed to r.t. After 1 h, the mixture was filtered off through a Celite pad. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography (EtOAc–hexane, 2:8) to give (*R*)-**12** (0.22 g, 90%) as a colorless liquid; $[\alpha]_D^{32}$ +15.12 (*c* 1.25, $CHCl_3$).

IR: 1719, 1639, 1407, 1196 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 6.39 (dd, *J* = 14.0, 2.0 Hz, 1 H), 6.07 (m, 1 H), 5.84–5.62 (m, 2 H), 5.11–5.01 (m, 2 H), 4.92 (m, 1 H), 2–48–2.36 (m, 2 H), 2.32 (t, *J* = 7.0 Hz, 2 H), 2.09 (s, 3 H), 1.62–1.52 (m, 4 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 208.7, 165.4, 134.9, 130.2, 127.8, 117.5, 73.1, 43.2, 38.4, 32.0, 26.6, 18.3.

MS (ESI): *m*/*z* = 233 $[M + Na]^+$.

Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 6.63. Found: C, 68.58; H, 6.66.

(*S*)-8-Oxonon-1-en-4-yl Acrylate [(*S*)-12]

Following the typical procedure for (*R*)-**12** using Celite (1.00 g) in CH_2Cl_2 (5 mL), (*S*)-**2** (0.25 g, 1.18 mmol) in CH_2Cl_2 (10 mL), and PCC (0.51 g, 2.36 mmol) gave (*S*)-**12** (0.22 g, 90%) as a colorless liquid; $[\alpha]_D^{32}$ –15.03 (*c* 1.25, $CHCl_3$). Spectral data (^1H, ^{13}C NMR and MS) were identical to those of (*R*)-**12**.

(6*R*)-6-(4-Oxopentyl)-5,6-dihydropyran-2-one [(*R*)-1]; Typical Procedure

To a stirred soln of Grubbs I catalyst (10 mol%) in anhyd CH_2Cl_2 (100 mL) at 55 °C was added (*R*)-**12** (100 mg, 0.48 mmol) dissolved in CH_2Cl_2 (50 mL). The resulting mixture was heated for 14 h. After completion of the reaction, the contents were cooled and the solvent

was removed under reduced pressure to yield a crude product, which was purified by column chromatography (silica gel, EtOAc–hexane, 2:8) to afford pure (*R*)-**1** (75 mg, 86%) as a colorless liquid; $[\alpha]_D^{32}$ –89.05 (*c* 0.1, $CHCl_3$).

IR: 1713, 1691, 1628, 1380, 1251 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 6.94, (m, 1 H), 5.99 (d, *J* = 10.0, 2.0 Hz, 1 H), 4.40 (m, 1 H), 2.49 (t, *J* = 7.0 Hz, 2 H), 2.38–2.25 (m, 2 H), 2.13 (s, 3 H), 1.81–160 (m, 4 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 208.4, 164.6, 144.9, 120.4, 76.8, 42.5, 33.8, 29.7, 28.8, 19.2.

MS (ESI): *m*/*z* = 183 $[M + H]^+$.

Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.90; H, 7.75. Found: C, 65.93; H, 7.79.

(6*S*)-6-(4-Oxopentyl)-5,6-dihydropyran-2-one [(*S*)-1]

Following the typical procedure for (*R*)-**1** using Grubbs I catalyst (10 mol%) in anhyd CH_2Cl_2 (100 mL) and (*S*)-**12** (100 mg, 0.48 mmol) in CH_2Cl_2 (50 mL) gave pure (*S*)-**1** (75 mg, 86%) as a colorless liquid; $[\alpha]_D^{32}$ +88.25 (*c* 0.1, $CHCl_3$). Spectral data (^1H, ^{13}C NMR and MS) were identical to those of (*R*)-**1**.

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