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# Metathesis-Based De Novo Synthesis of Noviose

**Bernd Schmidt*[a] and Sylvia Hauke[a]**

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The rare carbohydrate L-(+)-noviose was synthesized from enantiomerically pure L-lactate. The configuration at C-4 was established by diastereoselective nucleophilic addition to an in-situ-generated lactaldehyde. The resulting homoallylic alcohol was further transformed into a set of ring-closing metathesis (RCM) precursors. These compounds were converted into noviose in few steps using RCM and RCM–allylic-oxidation sequences.

## Introduction

Noviose is a rare eight-carbon sugar that is present in glycoconjugates, e.g., the natural product novobiocin,[1] a clinically used coumarin antibiotic that acts through DNA-gyrase inhibition.[2] A few years ago, it was discovered that novobiocin also binds to the C-terminal binding site of heat-shock protein 90 (Hsp90), which is involved in protein folding.[3] Inhibition of the action of this protein or of chaperones in general has been identified as a new approach to the chemotherapy of cancer.[4] However, the insufficient activity of novobiocin itself, and the necessity to establish structure–activity relationships,[5] have triggered the synthesis and evaluation of several analogues,[6] of which the indole derivative shown in Figure 1 was found to be particularly active.[7]

Due to its scarcity, noviose is often obtained by chemical synthesis rather than by cleavage of the glycoconjugates. This offers the additional advantage that structural modifications of the glycosidic part of natural or unnatural glycoconjugates can be accomplished more conveniently. The first synthesis of noviose was described by Spiegelberg et al., who started from a D-glucofuranose derivative.[8,9] Alternative routes rely on the modification of other common carbohydrates[10–16] or are de novo syntheses.[17–23] Noviose analogues have been obtained, for instance, from L-arabinose by incorporation of alkyl substituents other than methyl at the C-5 position,[24] or in de novo approaches by the introduction of amino groups at C-3.[25,26] Although ring-closing metathesis (RCM) was recognized early as a method that could be used for the modification and synthesis of carbohydrates,[27] we are aware of only two noviose syntheses that use RCM as a key step. Reddy et al. used

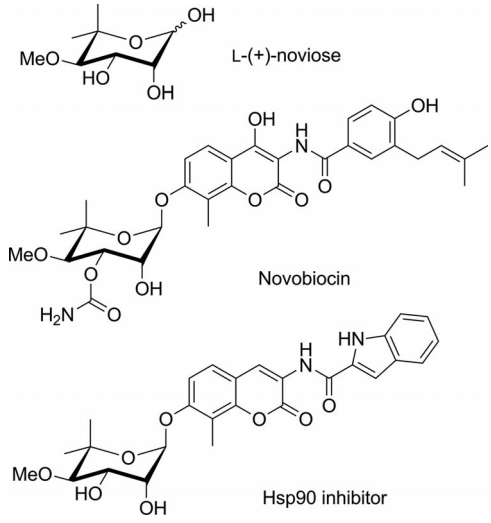


Figure 1. Structures of noviose, novobiocin, and a noviose-containing Hsp-90 inhibitor.

RCM to convert (–)-pantolactone into a cyclopentenone, which was then dihydroxylated and further elaborated by Baeyer–Villiger oxidation to give a protected noviose.[21] In contrast, Hanessian and Auzzas used a RCM step for the synthesis of a dihydropyran, which subsequently underwent allylic oxidation with PCC, reduction of the resulting lactone to the corresponding lactol, and diastereoselective Os-catalysed dihydroxylation to give L-(+)-noviose.[22] In this synthesis, the source of chirality was an enantioselective allylation of a glyoxylate with a chiral allylborane.

In continuation of previous studies from our group on the metathesis-based synthesis of deoxy sugars and their derivatives,[28–34] in this paper, we report a synthesis of L-(+)-noviose using *S*-ethyl lactate as a conveniently available enantiomerically pure starting material. To the best of our knowledge, lactic acid or its derivatives have not been used as enantiopure starting materials for the synthesis of noviose or its derivatives before.

[a] Institut für Chemie, Professur für Organische Synthesechemie, Universität Potsdam,
Karl-Liebknecht-Straße 24-25, 14476 Golm, Germany
E-mail: bernd.schmidt@uni-potsdam.de
http://www.chem.uni-potsdam.de/groups/schmidt/

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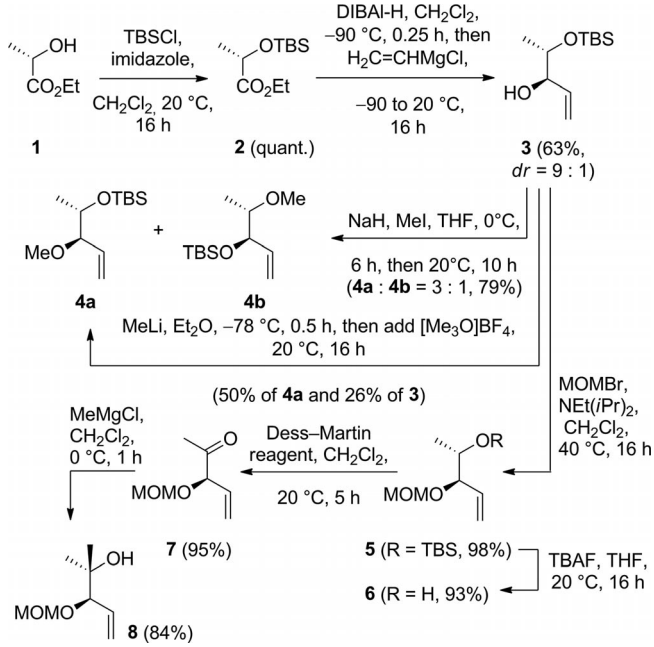
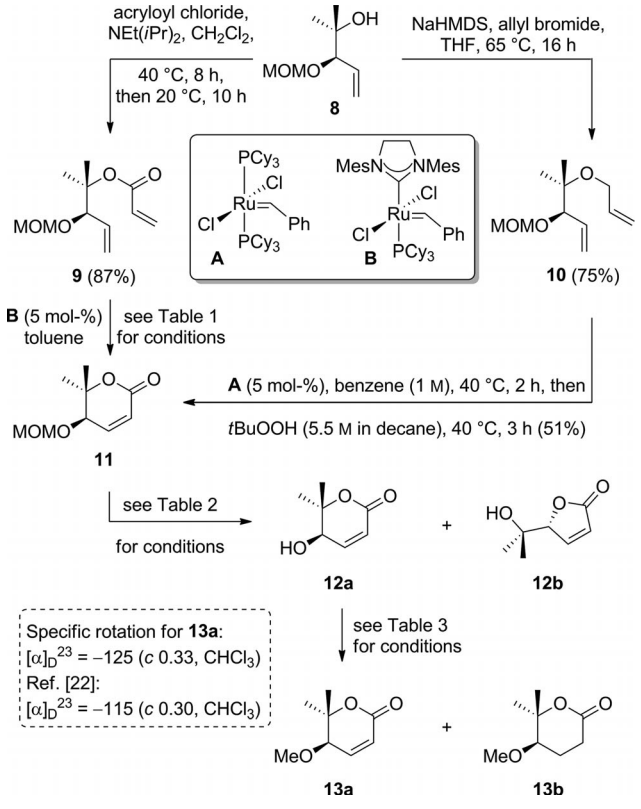
## Results and Discussion

The key idea behind our approach to L-(+)-noviose was to transfer the chirality from the stereocentre of lactaldehyde to the adjacent carbonyl group, and subsequently to destroy the chiral information at the original stereocentre by oxidation and addition of a methyl Grignard reagent. This approach resembles a chirality transfer in so far as a new stereocentre is generated with the loss of an adjacent stereocentre. In true chirality-transfer reactions, the generation of the new stereocentre and the loss of the inducing stereocentre occur simultaneously, which is, of course, not the case here. In the first step, ethyl *S*-lactate (**1**) was protected as a TBS (*tert*-butyldimethylsilyl) ether **2**.[35] This was reduced to the lactaldehyde, which was treated in situ with vinylmagnesium chloride. Under these conditions, Felkin–Anh-product **3** was obtained with a diastereomeric ratio of 9:1.[32,36] In the next step, we wanted to methylate the secondary alcohol in **3** to introduce the methoxy group at C-4 of noviose. With NaH as the base and methyl iodide as the alkylating agent, scrambling of the TBS group occurred to a considerable extent, even at 0 °C, and a 3:1 mixture of isomers **4a** and **4b** was formed. Migration of silyl protecting groups is sometimes observed if a Na alkoxide is in close proximity to a silyl ether, and it most probably proceeds via a cyclic transition state.[37] We reasoned that this side-reaction might be suppressed with a less nucleophilic Li alkoxide, which would, however, require a significantly stronger methylating agent. Therefore, alcohol **3** was deprotonated with MeLi at –78 °C, and the resulting alkoxide was treated with $[Me_3O]BF_4$ (Meerwein's reagent).[38] Scrambling of the TBS group was indeed suppressed under these conditions, but the conversion remained incomplete, even after prolonged reaction times, and the desired methyl ether (i.e., **4a**) was isolated in 50% yield, together with 26% of unreacted starting material **3**. These unsatisfactory results prompted us to protect the alcohol in **3** as a MOM (methoxymethyl) ether to give **5**, which was then desilylated to give **6**. Subsequent oxidation to the ketone gave **7**. Addition of MeMgCl gave carbinol **8**, which served as a key intermediate for further transformations (Scheme 1).




Scheme 1. Synthesis of homoallylic alcohol **8** from ethyl *S*-lactate; TBAF = tetrabutylammonium fluoride.

Starting from homoallylic alcohol **8**, two alternative routes to the envisaged noviose precursor **11** were investigated (Scheme 2). Upon treatment with acryloyl chloride, acrylate **9** was obtained in good yield, and this compound underwent ring-closing metathesis to give α,β-unsaturated δ-lactone **11**. Although a few examples of successful RCM reactions involving electron-deficient double bonds catalysed by first-generation catalyst **A**[39] have been described in the literature,[40] such transformations usually require more active second-generation catalysts, e.g., **B**.[41,42] The initial substrate concentration is particularly important; in most cases it should not exceed 0.01 M if synthetically useful yields of RCM product are to be obtained.[43] Finally, a beneficial effect of added phenol, originally described by Forman et al.[44] for cross-metathesis reactions, has also been documented for other less facile metathesis reactions.[34,45,46]




Scheme 2. Synthesis of lactone intermediate **11** and OH-deprotection; NaHMDS = sodium hexamethyldisilazide.

We investigated the RCM of acrylate **9** (Table 1), and identified **B** (5 mol-%) in toluene at 110 °C, pseudo high dilution, and phenol (0.5 equiv.) as the optimum conditions. The beneficial effect of the phenol additive (Table 1, entry 4

vs. entry 5) is clearly shown by an increased isolated yield. An alternative synthesis of **11** starts from allyl ether **10**, which is available from **8** by a Williamson ether synthesis. Precursor **10** was subjected to the conditions of a tandem RCM–allylic-oxidation sequence, which was recently described by us[47] and shortly afterwards by Arisawa et al.[48] In this transformation, the metathesis catalyst is converted into an allylic oxidation catalyst in situ by the addition of *tert*-butyl hydroperoxide, which also serves as an oxidant. Although the yield for the reaction of **10** to **11** is considerably lower than the direct conversion of **9** to **11** by RCM, it proceeds with the cheaper first-generation catalyst **A**, and does not require high- or pseudo high-dilution conditions.

Table 1. Optimization of conditions for RCM of acrylate **9**.

| Entry | Phenol [equiv.] | $c_0$ [M][a] | $T$ [°C] | Yield of **11** [%][b] |
|---|---|---|---|---|
| 1 | 0.5 | 0.01 | 80 | 65 |
| 2 | 0.5 | 0.01 | 110 | 79 |
| 3 | 0.5 | 0.005 | 110 | 74 |
| 4 | none | –[c] | 110 | 67 |
| 5 | 0.5 | –[c] | 110 | 89 |

[a] Initial substrate concentration. [b] Yield of isolated product. [c] Pseudo high-dilution conditions were used.

The next steps involved cleavage of the MOM group and methylation of the OH group at C-4. When a substoichiometric amount of $CeCl_3 \cdot 7H_2O$ was used in a methanol/acetonitrile solvent mixture,[49] the deprotection remained incomplete, and only 42% of **12a** was isolated, along with 41% of **11** (Table 2, entry 1). In contrast, when MOM ether **11** was dissolved in a 1:1 mixture of HCl (2 M aq.) and THF, the complete consumption of the starting material was observed, but this also led to a partial rearrangement of **12a** into butenolide **12b** (Table 2, entry 2). Under less acidic conditions, using trifluoroacetic acid (2 equiv.) in dichloromethane (Table 2, entry 3), this ring contraction was suppressed, but the conversion of the starting material was again incomplete, and the isolated yield of **12a** remained unsatisfactory. A quantitative yield of **12a** was eventually achieved by using $CF_3CO_2H$ as a cosolvent at ambient temperature.[50] Under these conditions, neither unreacted starting material nor ring-contracted lactone **12b** was detected (Table 2, entry 4). Inspired by Mitchell and Bode's report on the synthesis of dialkyl ethers from MOM ethers[51] we considered a synthesis of methyl ether **13a** directly from **11** (Table 2, entry 5). We thought that a combination of the strong Lewis acid $BF_3 \cdot OEt_2$ and triethylsilane as a hydride source might result in the substitution of the methoxy part of the MOM group by hydride, which would eventually yield the desired methyl ether (i.e., **13a**). Unfortunately, we could only isolate the deprotected product (i.e., **12a**) and its ring-contracted isomer (i.e., **12b**) in a ratio of 2:1 and a combined yield of 95%.

The apparently straightforward methylation of **12a** was also associated with some unexpected difficulties. Under the standard conditions of Williamson etherification (Table 3, entry 1), alkylated product **13a** was not observed. In DMF at 0 °C (Table 3, entry 2), only trace amounts of the methyl ether were obtained, whereas increasing the temperature to

Table 2. Optimization of conditions for the deprotection of MOM ether **11**.

| Entry | Reaction conditions | Yield of **12a** | Yield of **12b** |
|---|---|---|---|
| 1[a] | $CeCl_3 \cdot 7H_2O$ (0.5 equiv.), methanol/$CH_3CN$ (1:1), 65 °C, 48 h | 42% | n.d. |
| 2 | HCl (2 M)/THF (1:1), 20 °C, 16 h, then 40 °C, 5 h | 82% | 14% |
| 3[b] | $CF_3CO_2H$ (1.0 equiv.), $CH_2Cl_2$, 20 °C, 24 h, then $CF_3CO_2H$ (1.0 equiv.), 40 °C, 6 h | 54% | n.d. |
| 4 | $CF_3CO_2H/CH_2Cl_2$ (1:4), 20 °C, 16 h | >98% | n.d. |
| 5 | $BF_3 \cdot OEt_2$ (1.6 equiv.), $Et_3SiH$ (1.6 equiv.), $CH_3CN$, –45 °C, 0.5 h, 20 °C, 16 h | 95% combined yield (**12a**/**12b** = 2:1) | |

[a] Starting material **11** was partially recovered (41%). [b] Starting material **11** was partially recovered (10%); n.d.: not determined.

80 °C resulted in the formation of hydrogenated product **13b** (Table 3, entry 3). Most probably, a contamination of the starting material (i.e., **12a**) with trace amounts of Ru originating from the metathesis reaction is responsible for the concomitant hydrogenation. The Ru residues are presumably converted into Ru hydrides, which then catalyse the addition of hydrogen to the double bond. We have previously made similar observations for other metathesis reactions.[52] A successful methylation of the C-4 hydroxy group was eventually accomplished by replacing the strongly basic reagent NaH by silver oxide. This method has previously been used for the alkylation of base-sensitive substrates[29,53,54] or sterically encumbered alcohols.[22,55] Differing from literature precedent, we carried out the methylation in the absence of any solvent, and we isolated methyl ether **13a** as the sole product in quantitative yield (Table 3, entry 4).

Table 3. Optimization of conditions for the methylation of **12a**.

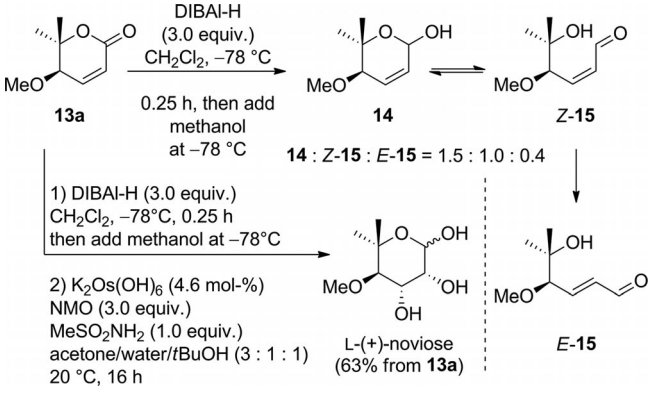
| Entry | Conditions | Time [h] | Product[a] | Yield [%] |
|---|---|---|---|---|
| 1 | NaH (1.2 equiv.), MeI (2.0 equiv.), THF, 65 °C | 16 | n.r. | – |
| 2 | NaH (1.2 equiv.), MeI (2.0 equiv.), DMF, 0 °C | 16 | **13a** | traces |
| 3 | NaH (1.2 equiv.), MeI (2.0 equiv.), DMF, 80 °C | 16 | **13b** | 20 |
| 4[b] | $Ag_2O$ (1.1 equiv.), MeI (1.5 equiv.), 40 °C | 48 | **13a** | >98 |

[a] n.r.: no reaction. [b] Reaction was run in the dark.

Compound **13a** was a key intermediate in the synthesis of noviose by Hanessian and Auzzas,[22] but they obtained it by a different route. All the spectroscopic data we observed for this compound match those reported in the literature perfectly, apart from the value for the specific rotation, for which our observed value was slightly higher. The

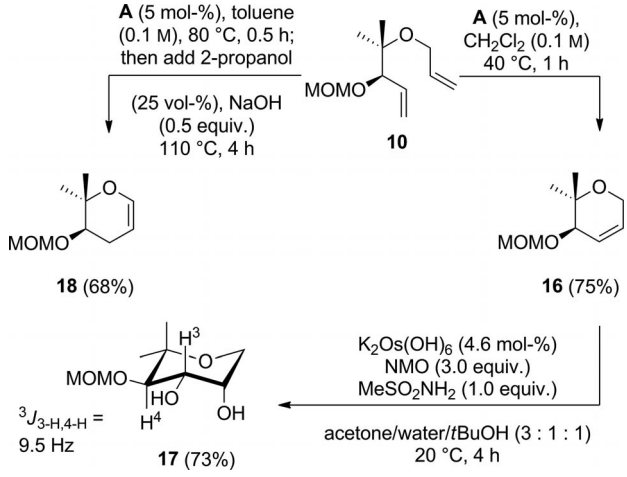
final steps to noviose were a *cis*-dihydroxylation of the double bond and a reduction of the lactone to the lactol. Hanessian and Auzzas mentioned that the Os-catalysed dihydroxylation of lactone **13a** was not feasible because the isolated yields of the diol were low under various conditions. We checked this statement, and we can confirm the observation. This prompted us to revert to the order of steps proposed by Hanessian and Auzzas, i.e., reduction to the lactol prior to dihydroxylation. Thus, lactone **13a** was treated with DIBAl-H (diisobutylaluminium hydride) at –78 °C, and the reaction was quenched at this temperature by the addition of methanol (Scheme 3). The $^1$H NMR spectrum of the crude reaction mixture showed that four products were formed. Notably, two doublets at $\delta >$ 9.5 ppm indicate the presence of two aldehydes, and a multiplet at $\delta$ = 5.33 can be attributed to a lactol. Our interpretation of the NMR spectrum is that the crude reduction product consists of both anomers of lactol **14**, which are in equilibrium with δ-hydroxy aldehyde *Z*-**15**. The third product was identified as *E*-configured enal *E*-**15**, based on a large $^3J_{2\text{-H},3\text{-H}}$ value of 15.8 Hz; a $^3J_{2\text{-H},3\text{-H}}$ value of 11.6 Hz was observed for the *Z* isomer. After the NMR sample of the crude reduction mixture had been stored for two weeks, only the signals of *E*-**15** were detected in the NMR spectrum, which indicates a slow and irreversible *Z*/*E* isomerization. In contrast to our observations, Hanessian and Auzzas report the presence of two epimeric lactols **14**, but they do not mention the presence of any δ-hydroxy aldehydes. A comparison of the NMR spectra obtained by us with those provided in the Supporting Information of the previous report[22] shows that they are identical, apart from the presence of a certain amount of *E*-enal *E*-**15** in our spectra.




Scheme 3. Reduction and reduction/dihydroxylation of lactone **13a**.

As the configurational integrity of the lactol (or δ-hydroxy aldehyde) is essential for the correct relative configuration of the C-2,C-3 diol moiety, we conducted the dihydroxylation immediately after quenching the reduction of the lactone. Thus, the crude reaction mixture obtained after aqueous work-up of the reduction of lactone **13a** was redissolved in the solvent mixture required for the Sharpless dihydroxylation without delay. Then the precatalyst $K_2Os(OH)_6$, the oxidant *N*-methylmorpholine *N*-oxide (NMO), and methanesulfonamide (a rate-accelerating reagent for the hydrolysis of the intermediate osmate)[56] were added immediately. L-(+)-Noviose was isolated in 63% yield over the two steps as a mixture of α and β anomers in a ratio of 1:2. The α and β configurations were assigned based on a comparison of $^1$H and $^{13}$C NMR spectroscopic data with the values previously reported by Pankau and Kreiser.[18] For this anomeric mixture, we observed a specific rotation of $[a]_D^{25}$ = +29.7 [*c* = 0.30, ethanol/water (1:1)], which matches previously reported values well. For example, Hanessian and Auzzas obtained two slightly different values for L-(+)-noviose, depending on the starting material they used: $[a]_D^{25}$ = +33.6 [*c* = 0.2, ethanol/water (1:1)], and $[a]_D^{25}$ = +27.4 [*c* = 0.2, ethanol/water (1:1)].[22] Pankau and Kreiser synthesized D-(–)-noviose, and they reported a specific rotation of $[a]_D^{25}$ = –29.2 [*c* = 1.0, ethanol/water (1:1)].[18]

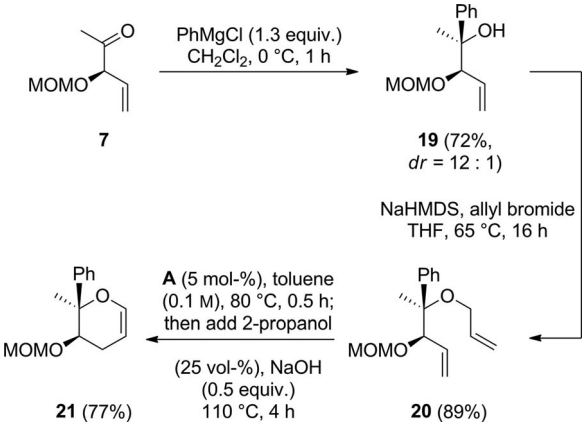
Two intermediates en route to noviose, i.e., ketone **7** and RCM precursor **10**, offer additional opportunities for the synthesis of noviose derivatives. Ring-closing metathesis of **10** gave MOM-protected dihydropyran **16**, which was subsequently dihydroxylated under the same conditions as for the dihydroxylation of lactol **14**. Dihydroxylation proceeded *trans* to the MOM group, as expected, to give tetrahydropyran **17** as the only product. Subjecting diene **10** to RCM–isomerization conditions[57–59] gave glycal **18** (Scheme 4).




Scheme 4. Synthesis of noviose derivatives from metathesis precursor **10**.

Some 5,5-dialkylnoviose derivatives have been reported to show improved antibiotic activity when conjugated to the coumarin aglycon part,[24,60] which prompted us to investigate the possibility of synthesizing such derivatives by a modification of our sequence. For this purpose, ketone **7** (Scheme 1) was identified as a suitable intermediate, as outlined for one example in Scheme 5. Treatment of **7** with phenylmagnesium chloride gave tertiary alcohol **19** with a diastereomeric ratio of 12:1 in favour of the Cram-type chelate product. The RCM precursor, allyl ether **20**, was synthesized from **19** in high yield, and was subjected to the same RCM–isomerization conditions previously used for glycal **18**. This gave the expected 5-methyl-5-phenyl-substituted glycal (i.e., **21**) as a single diastereoisomer in synthetically useful yield (Scheme 5).




Scheme 5. Synthesis of noviose derivative **21** from ketone **7**.

## Conclusions

In summary, we report the synthesis of L-(+)-noviose from L-lactate as a chiral pool starting material. The sequence involves the transfer of chirality from the enantiopure starting compound to an adjacent prochiral centre, a ring-closing metathesis or a ring-closing metathesis/allylic oxidation sequence for the construction of the six-membered ring, and a reduction of the lactone followed by dihydroxylation to establish the *cis*-C-2,C-3 diol motif. A modification of the sequence to make unnatural noviose derivatives available has been exemplified for the synthesis of a polyhydroxylated tetrahydropyran and two 3-deoxy glycals. Further syntheses of unnatural noviose derivatives and their conjugation to novobiocin aglycons are currently under investigation in our laboratory.

## Experimental Section

**General Remarks:** All experiments were carried out in dry reaction vessels under an atmosphere of dry nitrogen. Solvents were purified by standard procedures. $^1$H NMR spectra were obtained at 300 MHz in $CDCl_3$ with $CHCl_3$ ($\delta$ = 7.26 ppm) as an internal standard, or in $CD_3OD$ with $CHD_2OD$ ($\delta$ = 3.31 ppm) as an internal standard. Coupling constants (*J*) are given in Hz. $^{13}$C NMR spectra were recorded at 75 MHz in $CDCl_3$ with $CDCl_3$ ($\delta$ = 77.0 ppm) as an internal standard, or in $CD_3OD$ with $CD_3OD$ ($\delta$ = 49.2 ppm) as an internal standard. The number of coupled protons was analysed by DEPT or APT experiments, and is denoted by a number in parantheses after the chemical shift value. IR spectra were recorded neat. Wavenumbers ($\tilde{\nu}$) are given in cm$^{-1}$. The peak intensities are defined as strong (s), medium (m), or weak (w). Mass spectra were obtained at 70 eV.

**Ethyl (*S*)-2-(*tert*-butyldimethylsilyloxy)propanoate (2):**[32,35] Imidazole (4.32 g, 63.5 mmol) and TBSCl (7.65 g, 51.0 mmol) were added to a solution of L-ethyl lactate (5.00 g, 42.3 mmol) in dry $CH_2Cl_2$ (100 mL) at 0 °C. The mixture was warmed to ambient temperature and stirred for 12 h. The reaction was quenched by the addition of water, and the aqueous layer extracted with diethyl ether. The combined organic extracts were washed with HCl (1 M aq.) and brine, dried with $MgSO_4$ and filtered, and the solvents were evaporated. The residue was distilled (b.p. 90–92 °C at 14 mbar) to give **2** (9.83 g, 42.3 mmol, quant.) as a colourless liquid. $[\alpha]_D^{24}$ = –26.4 (*c* = 0.24, $CH_2Cl_2$). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 4.30 (q, *J* = 6.7 Hz, 1 H), 4.33–4.11 (m, 2 H), 1.38 (d, *J* = 6.7 Hz, 3 H), 1.27 (t, *J* = 7.1 Hz, 3 H), 0.90 (s, 9 H), 0.09 (s, 3 H), 0.06 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 174.1 (0), 68.5 (1), 60.7 (2), 25.8 (3), 21.3 (3), 18.3 (0), 14.2 (3), –5.0 (3), –5.3 (3) ppm. IR (neat): $\tilde{\nu}$ = 2930 (w), 2858 (w), 1753 (m), 1473 (w), 1252 (m), 1141 (s), 830 (s), 776 (s) cm$^{-1}$. MS (EI): *m*/*z* (%) = 255 (8) $[M + Na]^+$, 251 (26), 217 (100), 197 (20), 189 (100), 161 (32), 155 (18), 119 (12), 105 (11). HRMS (ESI): calcd. for $C_{11}H_{24}O_3NaSi$ $[M + Na]^+$ 255.1392; found 255.1379. $C_{11}H_{24}O_3Si$ (232.39): calcd. C 56.9, H 10.4; found C 56.5, H 10.9.

**(3*R*,4*S*)-4-(*tert*-Butyldimethylsilyloxy)pent-1-ene-3-ol (3):**[32,36] A solution of **2** (4.30 g, 18.5 mmol) in dry $CH_2Cl_2$ (100 mL) was cooled to –90 °C. DIBAl-H (1.1 M in cyclohexane; 25.2 mL, 27.8 mmol) was slowly added at this temperature. Conversion of ester **2** was monitored by TLC, and after it had been completely consumed, vinylmagnesium chloride (1.7 M in THF; 21.8 mL, 37.0 mmol) was added slowly. The reaction mixture was warmed to ambient temperature over 12 h, and then it was poured into a mixture of water and diethyl ether. A saturated solution of tartaric acid was added to solubilize the inorganic precipitates, the organic phase was separated, and the aqueous phase was extracted with diethyl ether. The combined organic phases were dried with $MgSO_4$ and filtered, and the solvents were evaporated. The residue was purified by column chromatography on silica to give **3** (2.52 g, 11.6 mmol, 63%) as a colourless liquid. $[\alpha]_D^{25}$ = +13.9 (*c* = 0.26, $CH_2Cl_2$). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 5.81 (ddd, *J* = 17.1, 10.5, 6.2 Hz, 1 H), 5.28 (ddd, *J* = 17.3, 1.6, 1.5 Hz, 1 H), 5.17 (ddd, *J* = 10.6, 1.5, 1.5 Hz, 1 H), 4.02 (m, 1 H), 3.85 (qd, *J* = 6.3, 3.6 Hz, 1 H), 2.29 (br. d, *J* = 3.4 Hz, 1 H), 1.08 (d, *J* = 6.3 Hz, 3 H), 0.90 (s, 9 H), 0.08 (s, 3 H), 0.02 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 136.6 (1), 116.5 (2), 76.7 (1), 71.3 (1), 25.8 (3), 18.1 (0), 17.6 (3), –4.5 (3), –4.8 (3) ppm. IR (neat): $\tilde{\nu}$ = 2930 (w), 2857 (w), 1472 (w), 1253 (m), 1087 (m), 832 (s), 774 (m) cm$^{-1}$. MS (EI): *m*/*z* (%) = 239 (17) $[M + Na]^+$, 213 (100), 199 (60), 197 (34), 155 (34), 133 (12), 115 (26). HRMS (ESI): calcd. for $C_{11}H_{24}O_2NaSi$ $[M + Na]^+$ 239.1443; found 239.1452.

***tert*-Butyl-[(2*S*,3*R*)-3-methoxypent-4-ene-2-yloxy]dimethylsilane (4a) and *tert*-Butyl-[(3*R*,4*S*)-4-methoxypent-1-ene-3-yloxy]dimethylsilane (4b)**

**Attempted Synthesis of 4a by Methylation of the Na Alkoxide of 3:** NaH (60 wt.-% dispersion in mineral oil; 222 mg, 5.6 mmol) and $CH_3I$ (0.27 mL, 4.3 mmol) were added to a solution of **3** (400 mg, 1.9 mmol) in dry, degassed THF (20 mL) at 0 °C. The mixture was warmed to ambient temperature and stirred for 12 h. The reaction was quenched by the careful addition of water and MTBE (methyl *tert*-butyl ether). The organic layer was separated, and the aqueous layer was extracted with MTBE. The combined organic extracts were dried with $MgSO_4$ and filtered, and the solvents were evaporated. NMR spectroscopy of the crude reaction mixture revealed the presence of two isomeric products **4a** and **4b** in a ratio of 2.7:1, which could be partially separated by column chromatography to give **4a**,**b** (345 mg, 1.5 mmol, 79% combined yield).

**Attempted Synthesis of 4a by Methylation of the Li Alkoxide of 3:** A solution of **3** (150 mg, 0.69 mmol) in dry, degassed diethyl ether (3.5 mL) was cooled to –78 °C. MeLi (1.6 M in diethyl ether; 0.40 mL, 0.69 mmol) was added, and the mixture was stirred for 0.5 h. Then Meerwein's reagent $[Et_3O]BF_4$ (154 mg, 1.04 mmol) was added. Stirring was continued for 2 h at –78 °C, and then the mixture was warmed to ambient temperature over 12 h. A saturated aqueous solution of $NH_4Cl$ was added, the aqueous layer was separated and extracted with diethyl ether. The combined organic layers

were dried with $MgSO_4$ and filtered, and the solvents were evaporated. The residue was purified by chromatography on silica to give **4a** (80 mg, 0.35 mmol, 50%) as a colourless liquid, along with unreacted starting material **3** (40 mg, 0.18 mmol, 26%).

Analytical data for **4a**: $[\alpha]_D^{24}$ = –12.2 (*c* = 0.63, $CH_2Cl_2$). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 5.71 (ddd, *J* = 17.3, 10.5, 7.6 Hz, 1 H), 5.28–5.18 (m, 2 H), 3.77 (qd, *J* = 6.2, 5.0 Hz, 1 H), 3.34 (ddm, *J* = 7.5, 5.0 Hz, 1 H), 3.30 (s, 3 H), 1.14 (d, *J* = 6.2 Hz, 3 H), 0.85 (s, 9 H), 0.04 (s, 3 H), 0.03 (s, 3 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 136.2, 118.3, 87.8, 70.8, 56.8, 25.9, 19.9, 18.1, –4.5, –4.6 ppm. IR (neat): $\tilde{\nu}$ = 2929 (m), 2856 (m), 1252 (m), 1116 (s), 924 (s), 830 (s), 777 (s) $cm^{-1}$. MS (EI): *m*/*z* (%) = 231 (37) $[M + H]^+$, 227 (57), 213 (93), 199 (100), 99 (8). HRMS (ESI): calcd. for $C_{12}H_{27}O_2Si$ $[M + H]^+$ 231.1780; found 231.1784. $C_{12}H_{26}O_2Si$ (230.42): calcd. C 62.6, H 11.4; found C 62.5, H 11.8.

Analytical data for **4b**: $[\alpha]_D^{22}$ = –1.5 (*c* = 0.68, $CH_2Cl_2$). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 5.86 (ddd, *J* = 17.2, 10.5, 5.8 Hz, 1 H), 5.24 (ddd, *J* = 17.2, 1.7, 1.7 Hz, 1 H), 5.14 (ddd, *J* = 10.4, 1.9, 1.4 Hz, 1 H), 4.07 (dddd, *J* = 5.7, 4.2, 1.4, 1.4 Hz, 1 H), 3.36 (s, 3 H), 3.22 (qd, *J* = 6.3, 4.2 Hz, 1 H), 1.09 (d, *J* = 6.3 Hz, 3 H), 0.91 (s, 9 H), 0.07 (s, 3 H), 0.03 (s, 3 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 138.6, 115.4, 80.9, 76.2, 57.1, 25.9, 18.2, 14.9, –4.5, –4.7 ppm. IR (neat): $\tilde{\nu}$ = 2929 (m), 2857 (m), 1252 (m), 1102 (s), 1031 (m), 834 (s), 775 (s) $cm^{-1}$. MS (EI): *m*/*z* (%) = 231 (26) $[M + H]^+$, 227 (33), 213 (100), 199 (17), 113 (20), 99 (35). HRMS (ESI): calcd. for $C_{12}H_{28}O_2Si$ $[M + H]^+$ 231.1780; found 231.1799. $C_{12}H_{27}O_2Si$ (230.42): calcd. C 62.6, H 11.4; found C 62.7, H 11.1.

**(2*S*,3*R*)-2-(*tert*-Butyldimethylsilyloxy)-3-(methoxymethoxy)pent-4-ene (5):** A solution of **3** (2.00 g, 9.2 mmol) in dry, degassed $CH_2Cl_2$ (100 mL) was cooled to 0 °C. MOM bromide (90 wt.-%; 1.7 mL, 18.7 mmol) and $NEt(iPr)_2$ (4.7 mL, 33.8 mmol) were added, and the reaction mixture was heated to reflux for 12 h. The reaction was quenched by the addition of water, then the aqueous layer was separated and extracted with MTBE. The combined organic extracts were dried with $MgSO_4$ and filtered, and the solvents were evaporated. The residue was purified by column chromatography on silica to give **5** (2.35 g, 9.0 mmol, 98%) as a colourless liquid. $[\alpha]_D^{22}$ = –56.0 (*c* = 0.53, $CH_2Cl_2$). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 5.73 (ddd, *J* = 16.9, 10.8, 7.4 Hz, 1 H), 5.29–5.19 (m, 2 H), 4.70 (d, *J* = 6.6 Hz, 1 H), 4.58 (d, *J* = 6.6 Hz, 1 H), 3.87–3.77 (m, 2 H), 3.37 (s, 3 H), 1.15 (d, *J* = 6.1 Hz, 3 H), 0.88 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 135.6 (1), 118.6 (2), 94.0 (2), 81.7 (1), 70.8 (1), 55.4 (3), 25.8 (3), 19.6 (3), 18.1 (0), –4.6 (3), –4.7 (3) ppm. IR (neat): $\tilde{\nu}$ = 2929 (w), 2857 (w), 1252 (m), 1100 (m), 1034 (s), 830 (s), 774 (s) $cm^{-1}$. MS (EI): *m*/*z* (%) = 283 (4) $[M + Na]^+$, 265 (19), 227 (100), 213 (82), 199 (33), 159 (33), 147 (21), 133 (28), 115 (49). HRMS (ESI): calcd. for $C_{13}H_{28}O_3NaSi$ $[M + Na]^+$ 283.1705; found 283.1719. $C_{13}H_{28}O_3Si$ (260.45): calcd. C 60.0, H 10.8; found C 60.0, H 11.0.

**(2*S*,3*R*)-3-(Methoxymethoxy)pent-4-ene-2-ol (6):** Compound **5** (2.30 g, 8.8 mmol) and $TBAF{\cdot}3H_2O$ (4.62 g, 17.7 mmol) were dissolved in THF (100 mL), and the mixture was stirred for 16 h at ambient temperature. The mixture was diluted with diethyl ether and washed with brine. The organic layer was separated, dried with $MgSO_4$, and filtered, and the solvents were evaporated. The residue was purified by column chromatography on silica using pentane/diethyl ether (5:1) as eluent, to give **6** (1.19 g, 8.2 mmol, 93%) as a colourless liquid. $[\alpha]_D^{21}$ = –111.6 (*c* = 0.68, $CH_2Cl_2$). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 5.76 (ddd, *J* = 17.4, 10.6, 7.6 Hz, 1 H), 5.37–5.25 (m, 2 H), 4.71 (d, *J* = 6.7 Hz, 1 H), 4.60 (d, *J* = 6.7 Hz, 1 H), 3.93 (dd, *J* = 7.6, 3.8 Hz, 1 H), 3.87 (qd, *J* = 6.3, 3.8 Hz, 1 H), 3.38 (s, 3 H), 2.28 (br. s, 1 H), 1.14 (d, *J* = 6.4 Hz, 3 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 134.0 (1), 119.9 (2), 94.3 (2), 81.9 (1), 69.3 (1), 55.5 (3), 17.8 (3) ppm. IR (neat): $\tilde{\nu}$ = 3445 (w), 2889 (w), 1152 (m), 1096 (s), 1026 (s), 919 (s) $cm^{-1}$. MS (EI): *m*/*z* (%) = 147 (39) $[M + H]^+$, 141 (33), 115 (42), 99 (100). HRMS (ESI): calcd. for $C_7H_{15}O_3$ $[M + H]^+$ 147.1021; found 147.1033. $C_7H_{14}O_3$ (146.18): calcd. C 57.5, H 9.7; found C 57.5, H 9.8.

**(*R*)-3-(Methoxymethoxy)pent-4-en-2-one (7):** Dess–Martin periodinane (3.82 g, 9.0 mmol) was added to a solution of **6** (1.32 g, 9.0 mmol) in dry, degassed $CH_2Cl_2$ (30 mL) at 0 °C. The mixture was warmed to ambient temperature and stirred for 1 h. Then it was diluted with $CH_2Cl_2$ and washed repeatedly with a saturated aqueous solution of $NaHCO_3$ and $Na_2S_2O_3{\cdot}5H_2O$ (250 g/L). The aqueous layer was separated and extracted with $CH_2Cl_2$, the combined organic extracts were dried with $MgSO_4$ and filtered, and the solvents were evaporated. The residue was purified by column chromatography to give ketone **7** (1.23 g, 8.6 mmol, 95%) as a colourless liquid. $[\alpha]_D^{22}$ = –35.6 (*c* = 0.56, $CH_2Cl_2$). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 5.77 (ddd, *J* = 17.0, 10.4, 6.5 Hz, 1 H), 5.46 (ddd, *J* = 17.2, 1.3, 1.3 Hz, 1 H), 5.36 (ddd, *J* = 10.4, 1.3, 1.3 Hz, 1 H), 4.71 (d, *J* = 6.7 Hz, 1 H), 4.62 (d, *J* = 6.7 Hz, 1 H), 4.51 (ddd, *J* = 6.5, 1.3, 1.3 Hz, 1 H), 3.37 (s, 3 H), 2.18 (s, 3 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 206.3 (0), 132.4 (1), 119.9 (2), 94.9 (2), 83.1 (1), 55.9 (3), 25.6 (3) ppm. IR (neat): $\tilde{\nu}$ = 2893 (w), 1719 (s), 1152 (s), 1036 (s), 919 (s) $cm^{-1}$. MS (EI): *m*/*z* (%) = 167 (5) $[M + Na]^+$, 143 (58), 121 (20), 113 (100), 99 (8). HRMS (ESI): calcd. for $C_7H_{12}O_3Na$ $[M + Na]^+$ 167.0684; found 167.0697.

**(*R*)-3-(Methoxymethoxy)-2-methylpent-4-ene-2-ol (8):** A solution of **7** (1.01 g, 7.0 mmol) in dry, degassed $CH_2Cl_2$ (30 mL) was cooled to 0 °C. MeMgCl (3 M in THF; 4.7 mL, 14.0 mmol) was slowly added by syringe, and the reaction mixture was stirred at 0 °C for 1 h. The reaction mixture was poured into a stirred water/diethyl ether mixture, and a saturated aqueous solution of tartaric acid was added. The organic layer was separated, the aqueous layer was extracted with diethyl ether, and the combined organic layers were washed with brine and then dried with $MgSO_4$. The residue was purified by column chromatography on silica to give **8** (937 mg, 5.9 mmol, 84%) as a colourless liquid. $[\alpha]_D^{22}$ = –78.5 (*c* = 0.98, $CH_2Cl_2$). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 5.72 (ddd, *J* = 17.2, 10.5, 8.2 Hz, 1 H), 5.35–5.24 (m, 2 H), 4.72 (d, *J* = 6.7 Hz, 1 H), 4.57 (d, *J* = 6.7 Hz, 1 H), 3.77 (d, *J* = 8.2 Hz, 1 H), 3.39 (s, 3 H), 2.44 (s, 1 H), 1.20 (s, 3 H), 1.16 (s, 3 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 134.5 (1), 120.2 (2), 94.2 (2), 84.8 (1), 71.8 (0), 55.7 (3), 26.1 (3), 24.6 (3) ppm. IR (neat): $\tilde{\nu}$ = 3465 (w), 2976 (w), 1372 (w), 1146 (m), 1030 (s), 919 (s) $cm^{-1}$. MS (EI): *m*/*z* (%) = 161 (55) $[M + H]^+$, 139 (24), 129 (73), 113 (44), 99 (23), 91 (100). HRMS (ESI): calcd. for $C_8H_{17}O_3$ $[M + H]^+$ 161.1178; found 161.1182. $C_8H_{16}O_3$ (160.21): calcd. C 60.0, H 10.1; found C 60.2, H 9.9.

**(*R*)-3-[(Methoxymethoxy)-2-methylpent-4-en-2-yl]acrylate (9):** $NEt(iPr)_2$ (1.00 mL, 12.6 mmol) and acryloyl chloride (2.7 mL, 15.7 mmol) were added to a solution of **8** (1.00 g, 6.3 mmol) in dry, degassed $CH_2Cl_2$ (20 mL). The mixture was heated to reflux for 8 h, and then it was stirred at ambient temperature for 10 h. The reaction was quenched by the addition of aqueous $NaHCO_3$ solution, and the mixture was extracted with MTBE. The organic layer was separated, dried with $MgSO_4$ and filtered, and the solvents were evaporated. The residue was purified by column chromatography on silica to give **9** (1.20 g, 5.5 mmol, 87%) as a colourless liquid. $[\alpha]_D^{25}$ = –64.0 (*c* = 0.84, $CH_2Cl_2$). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 6.31 (dd, *J* = 17.3, 1.4 Hz, 1 H), 6.05 (dd, *J* = 17.3, 10.3 Hz, 1 H), 5.82–5.68 (m, 2 H), 5.36–5.28 (m, 2 H), 4.70 (d, *J* = 6.7 Hz, 1 H), 4.56 (d, *J* = 6.7 Hz, 1 H), 4.36 (d, *J* = 7.8 Hz, 1 H), 3.37 (s, 3 H), 1.51 (s, 3 H), 1.53 (s, 3 H) ppm. $^{13}C$ NMR

(75 MHz, $CDCl_3$): $\delta$ = 165.5 (0), 133.8 (1), 130.1 (1), 129.7 (2), 120.3 (2), 94.3 (2), 83.5 (0), 81.5 (1), 55.8 (3), 22.4 (3), 22.3 (3) ppm. IR (neat): $\tilde{\nu}$ = 2986 (w), 1721 (s), 1403 (m), 1206 (s), 1032 (s), 919 (m) $cm^{-1}$. MS (EI): *m*/*z* (%) = 215 (3) $[M + H]^+$, 115 (16), 75 (23), 73 (46), 55 (62), 45 (62), 41 (100). HRMS (ESI): calcd. for $C_{11}H_{18}O_4Na$ $[M + Na]^+$ 237.1103; found 237.1113. $C_{11}H_{18}O_4$ (214.26): calcd. C 61.7, H 8.5; found C 61.5, H 8.5.

**(*R*)-4-(Allyloxy)-3-(methoxymethoxy)-4-methylpent-1-ene (10):** NaHMDS (1.5 M in THF; 3.4 mL, 5.0 mmol) was added to a solution of **8** (400 mg, 2.5 mmol) in dry, degassed THF (20 mL). The solution was stirred at ambient temperature for 1 h, and then allyl bromide (0.9 mL, 10.0 mmol) was added. The reaction mixture was heated to reflux for 16 h. After cooling to ambient temperature, the reaction was quenched by the addition of water. The aqueous layer was extracted with MTBE. The combined organic layers were washed with brine, dried with $MgSO_4$ and filtered, and the solvents were evaporated. The residue was purified by column chromatography to give **10** (377 mg, 1.9 mmol, 75%) as a colourless liquid. $[\alpha]_D^{22}$ = –77.3 (*c* = 0.77, $CH_2Cl_2$). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 5.91 (ddd, *J* = 17.2, 10.4, 5.2 Hz, 1 H), 5.81 (ddd, *J* = 17.2, 10.5, 7.7 Hz, 1 H), 5.32–5.19 (m, 3 H), 5.08 (ddd, *J* = 10.4, 3.4, 1.5 Hz, 1 H), 4.70 (d, *J* = 6.7 Hz, 1 H), 4.66 (d, *J* = 6.7 Hz, 1 H), 4.00 (dddd, *J* = 5.2, 4.2, 1.6, 1.6 Hz, 2 H), 3.94 (dm, *J* = 7.6 Hz, 1 H), 3.38 (s, 3 H), 1.22 (s, 3 H), 1.20 (s, 3 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 136.1 (1), 134.8 (1), 119.1 (2), 115.3 (2), 94.2 (2), 82.6 (1), 65.8 (0), 63.2 (2), 55.7 (3), 22.8 (3), 21.9 (3) ppm. IR (neat): $\tilde{\nu}$ = 2980 (w), 1381 (w), 1146 (m), 1033 (s), 917 (s) $cm^{-1}$. MS (EI): *m*/*z* (%) = 223 (100) $[M + Na]^+$, 214 (51), 197 (30), 169 (36), 139 (7). HRMS (ESI): calcd. for $C_{11}H_{20}O_3Na$ $[M + Na]^+$ 223.1310; found 223.1325. $C_{11}H_{20}O_3$ (200.27): calcd. C 66.0, H 10.1; found C 65.9, H 10.0.

**(*R*)-5-(Methoxymethoxy)-6,6-dimethyl-3,4-dihydropyran-2-one (11)**

**By RCM of Acrylate 9:** Phenol (44 mg, 0.47 mmol) was dissolved in toluene (30 mL) in a three-necked round-bottomed flask equipped with two dropping funnels and a reflux condenser, and the solution was heated to reflux. Solutions of acrylate **9** (200 mg, 0.94 mmol) in toluene (30 mL) and precatalyst **B** (40 mg, 5 mol-%) in toluene (30 mL) were simultaneously added dropwise using the two dropping funnels at 110 °C. After the addition of both solutions was complete, the heating to reflux was continued for a further 2 h. Then the mixture was cooled to ambient temperature and evaporated, and the residue was purified by column chromatography on silica to give **11** (156 mg, 0.84 mmol, 89%) as a colourless oil.

**By RCM/Allylic Oxidation:** A solution of **10** (300 mg, 1.51 mmol) in dry, degassed benzene (15 mL) was heated to 40 °C. First generation Grubbs' catalyst **A** (62 mg, 5 mol-%) was added, and the mixture was stirred at 40 °C until the starting material had been fully consumed, as indicated by TLC (approx. 2 h). *t*BuOOH (5.5 M in decane; 1.10 mL, 6.04 mmol) was added over a period of 20 min using a syringe pump, and the stirring at 40 °C was continued for 3 h. The mixture was cooled to ambient temperature, then it was diluted with MTBE and filtered through a short pad of silica. All the volatiles were evaporated, and the residue was purified by chromatography on silica to give **11** (145 mg, 0.77 mmol, 51%) as a colourless oil. $[\alpha]_D^{24}$ = –91.7 (*c* = 0.60, $CH_2Cl_2$). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 6.80 (dd, *J* = 9.9, 3.4 Hz, 1 H), 6.04 (dd, *J* = 9.9, 1.4 Hz, 1 H), 4.76 (d, *J* = 7.0 Hz, 1 H), 4.69 (d, *J* = 7.0 Hz, 1 H), 4.13 (dd, *J* = 3.4, 1.4 Hz, 1 H), 3.40 (s, 3 H), 1.46 (s, 3 H), 1.42 (s, 3 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 162.6 (0), 144.7 (1), 121.4 (1), 96.6 (2), 82.6 (0), 74.2 (1), 55.9 (3), 26.6 (3), 21.9 (3) ppm. IR (neat): $\tilde{\nu}$ = 2940 (w), 1715 (s), 1292 (m), 1108 (s), 1034 (s), 969 (m) $cm^{-1}$. MS (EI): *m*/*z* (%) = 128 (38), 99 (4), 83 (4), 55 (7), 45 (100), 43 (22). HRMS (EI): calcd. for $C_9H_{14}O_4$ $[M]^+$ 186.0892; found 186.0909. $C_9H_{14}O_4$ (186.21): calcd. C 58.1, H 7.6; found C 57.8, H 7.4.

**(*R*)-5-Hydroxy-6,6-dimethyl-3,4-dihydropyran-2-one (12a) and (*R*)-5-(2-Hydroxypropan-2-yl)furan-2(5*H*)-one (12b)**

**Method 1:** MOM-protected lactone **11** (433 mg, 2.34 mmol) was dissolved in a mixture of $CH_2Cl_2$ (8 mL) and $CF_3CO_2H$ (2 mL). The solution was stirred at ambient temperature for 16 h. All the volatiles were evaporated under reduced pressure. The residue was dissolved in MTBE, and the solution was washed with $Na_2CO_3$ (aq.). The aqueous layer was separated and extracted with MTBE. The organic extracts were dried with $MgSO_4$ and filtered, and the solvents were evaporated. The residue was purified by chromatography on silica to give **12a** (324 mg, 2.31 mmol, quant.) as a colourless oil.

**Method 2:** Compound **11** (193 mg, 1.00 mmol) was dissolved in THF (5 mL), and HCl (2 M aq.; 5 mL) was added. The mixture was stirred for 16 h at ambient temperature, and then for 5 h at 40 °C. A saturated aqueous solution of $Na_2CO_3$ was carefully added, and the aqueous layer was separated and extracted with MTBE. The combined organic extracts were dried with $MgSO_4$ and filtered, and the solvents were evaporated. The residue was purified by chromatography on silica to give **12a** (120 mg, 0.80 mmol, 82%) and **12b** (27 mg, 0.10 mmol, 14%) as colourless oils.

Analytical data for **12a**: $[\alpha]_D^{21}$ = –62.4, (*c* = 0.53, $CH_2Cl_2$). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 6.81, (dd, *J* = 9.8, 4.0 Hz, 1 H), 6.00, (dd, *J* = 9.9, 1.4 Hz, 1 H), 4.18, (d, *J* = 3.0 Hz, 1 H), 3.34, (br. s, 1 H), 1.44, (s, 3 H), 1.43, (s, 3 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 163.4, (0), 146.1, (1), 121.1, (1), 83.6, (0), 68.3, (1), 26.3, (3), 21.7, (3) ppm. MS (EI): *m*/*z* = 84, (100), 55, (47), 43, (25), 39, (12). HRMS (EI): calcd. for $C_7H_{10}O_3$ $[M]^+$ 142.0630; found 142.0633.

Analytical data for **12b**: $[\alpha]_D^{21}$ = +1.9 (*c* = 0.58, $CH_2Cl_2$). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 7.51 (dd, *J* = 5.8, 1.5 Hz, 1 H), 6.18 (dd, *J* = 5.8, 2.0 Hz, 1 H), 4.87 (d, *J* = 2.0, 1.5 Hz, 1 H), 2.55 (s, 3 H), 1.27 (s, 3 H), 1.26 (s, 3 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 173.3 (0), 153.9 (1), 122.7 (1), 89.5 (1), 71.6 (0), 28.6 (3), 25.3 (3) ppm. IR (neat): $\tilde{\nu}$ = 3416 (s), 2980 (m), 1740 (s), 1172 (m), 1096 (m), 827 (m) $cm^{-1}$. HRMS (EI): $C_7H_{10}O_3Na$ $[M + Na]^+$ 165.0528; found 165.0531.

**(*R*)-5-Methoxy-6,6-dimethyltetrahydro-2*H*-pyran-2-one (13b):** NaH (60 wt.-% dispersion in mineral oil; 31 mg, 0.77 mmol) and MeI (0.08 mL, 1.28 mmol) were added to a solution of **12a** (90 mg, 0.64 mmol) in DMF (5 mL), and the mixture was heated at 80 °C for 16 h. The mixture was cooled to ambient temperature, then the reaction was quenched by the careful addition of water, and the mixture was extracted twice with MTBE. The combined organic extracts were dried with $MgSO_4$ and filtered, and the solvents were evaporated. The residue was purified by chromatography on silica to give hydrogenated product **13b** (20 mg, 0.13 mmol, 20%) as a colourless oil. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 3.67 (s, 3 H), 3.60 (m, 1 H), 2.89–2.85 (m, 2 H), 2.68–2.63 (m, 2 H), 1.40 (s, 3 H), 1.40 (s, 3 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 173.0 (0), 76.3 (0), 51.8 (3), 30.5 (2), 27.8 (2), 26.6 (3), 26.6 (3) ppm.

**(*R*)-5-Methoxy-6,6-dimethyl-5,6-dihydropyran-2-one (13a):** $Ag_2O$ (105 mg, 0.45 mmol) was added to a solution of **12a** (58 mg, 0.41 mmol) in MeI (0.6 mL). The reaction mixture was stirred in the dark for 2 d at reflux temperature. After cooling to ambient temperature, the mixture was diluted with $CH_2Cl_2$, and filtered through a short pad of Celite, which was subsequently washed with MTBE. All the volatiles were evaporated, and the residue was puri-

fied by chromatography on silica to give **13a** (64 mg, 0.41 mmol, quant.) as a colourless oil. $[\alpha]_D^{23}$ = –124.7 (*c* = 0.33, $CHCl_3$). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 6.80 (dd, *J* = 10.0, 3.0 Hz, 1 H), 6.03 (dd, *J* = 10.0, 1.5 Hz, 1 H), 3.82 (dd, *J* = 2.9, 1.6 Hz, 1 H), 3.45 (s, 3 H), 1.45 (s, 3 H), 1.36 (s, 3 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 162.7 (0), 143.6 (1), 121.4 (1), 82.9 (0), 77.9 (1), 57.9 (3), 26.9 (3), 21.3 (3) ppm. IR (neat): $\tilde{\nu}$ = 2986 (w), 2939 (w), 2830 (w), 1715 (s), 1275 (m), 1110 (s), 973 (m) $cm^{-1}$. MS (EI): *m*/*z* (%) = 125 (11), 98 (71), 43 (100), 41 (27). HRMS (ESI): calcd. for $C_8H_{12}O_3Na$ $[M + Na]^+$ 179.0684; found 179.0691. $C_8H_{12}O_3$ (156.18): calcd. C 61.5, H 7.7; found C 61.4, H 8.1.

**(4*R*,*E*)-5-Hydroxy-4-methoxy-5-methylhex-2-enal (*E*-15):** A solution of **13a** (100 mg, 0.64 mmol) in $CH_2Cl_2$ (6.4 mL) was cooled to –78 °C, and DIBAl-H (1.1 M in cyclohexane; 1.75 mL, 1.92 mmol) was added. The mixture was stirred at this temperature until the starting material had been fully consumed (TLC, approx. 0.25 h). Then the reaction was quenched by the addition of methanol (2.2 mL). The reaction mixture was warmed to ambient temperature, a saturated aqueous solution of sodium potassium tartrate was added, and the resulting mixture was stirred for 1 h. The aqueous layer was separated and extracted with diethyl ether, the combined organic extracts were dried with $MgSO_4$ and filtered, and the solvents were evaporated. NMR spectroscopy of the crude reaction mixture revealed the presence of *Z*-**15**, a minor amount of *E*-**15**, and anomeric lactols **14**.

Selected spectroscopic data of *Z*-**15** obtained from the mixture: $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 10.08 (d, *J* = 7.5 Hz, 1 H), 6.44 (dd, *J* = 11.6, 9.4 Hz, 1 H), 6.23 (dd, *J* = 11.6, 7.5 Hz, 1 H), 4.29 (d, *J* = 9.4 Hz, 1 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 190.9 (1), 147.5 (1), 133.8 (1), 83.1 (1) ppm.

Selected spectroscopic data of the anomers of **14**: $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 6.05–5.93 (m, 1 H), 5.87–5.80 (m, 1 H), 5.38–5.30 (br. m, 1 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 128.5 (1, major anomer), 128.3 (1, minor anomer), 127.8 (1, major anomer), 127.7 (1, minor anomer), 89.0 (1, major anomer), 88.8 (1, minor anomer) 79.2 (1, minor anomer), 78.4 (1, major anomer) ppm.

The crude mixture was purified by column chromatography on silica to give aldehyde *E*-**15** (102 mg, 0.64 mmol, quant.) as a colourless oil. $[\alpha]_D^{24}$ = –66.3 (*c* = 0.40, $CHCl_3$). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 9.61 (d, *J* = 7.8 Hz, 1 H), 6.74 (dd, *J* = 15.9, 6.7 Hz, 1 H), 6.29 (ddd, *J* = 15.9, 7.8, 0.8 Hz, 1 H), 3.63 (d, *J* = 6.2 Hz, 1 H), 3.36 (s, 3 H), 2.51 (br. s, 1 H), 1.21 (s, 3 H), 1.15 (s, 3 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 192.9 (1), 152.7 (1), 134.8 (1), 87.8 (1), 72.4 (0), 58.1 (3), 25.8 (3), 24.8 (3) ppm. IR (neat): $\tilde{\nu}$ = 3442 (m), 2935 (m), 1688 (s), 1100 (s), 981 (m) $cm^{-1}$. MS (EI): *m*/*z* (%) = 149 (73), 141 (77), 100 (86), 71 (100), 59 (72), 45 (74). HRMS (ESI): calcd. for $C_8H_{13}O_3$ $[M + H]^+$ 157.0865; found 157.0854.

**L-(+)-Noviose:** A solution of **13a** (75 mg, 0.48 mmol) in dry, degassed $CH_2Cl_2$ was cooled to –78 °C. DIBAl-H (1.1 M in cyclohexane; 1.31 mL, 1.44 mmol) was added, and the resulting solution was stirred until the starting material had been fully consumed, as indicated by TLC (approx. 0.25 h). The reaction was quenched by the addition of methanol (2 mL), then the mixture was warmed to ambient temperature, a saturated aqueous solution of sodium potassium tartrate was added, and the mixture was stirred for 1 h. The aqueous layer was separated and extracted with diethyl ether, the combined organic extracts were dried with $MgSO_4$ and filtered, and the solvents were evaporated. The crude product was redissolved without delay in a mixture of acetone (1.5 mL), water (0.5 mL), and *tert*-butanol (0.5 mL). *N*-Methylmorpholine *N*-oxide (167 mg, 1.42 mmol), methane sulfonamide (46 mg, 0.48 mmol), and $K_2Os(OH)_6$ (8.1 mg, 0.022 mmol, 4.6 mol-%) were added to the solution, and the resulting mixture was stirred at ambient temperature for 16 h. $MgSO_4$ was added to the mixture, which was then filtered, and the filter cake was thoroughly washed with ethyl acetate. All the volatiles were evaporated from the filtrate, and the residue was purified by column chromatography on silica (ethyl acetate and then ethyl acetate/methanol, 9:1) to give L-(+)-noviose (58 mg, 0.30 mmol, 63%) as a mixture of α and β anomers (1:2 ratio). $[\alpha]_D^{25}$ = +29.7 (*c* = 0.30, EtOH/$H_2O$, 1:1). $^1H$ NMR (500 MHz, [$D_4$]methanol): $\delta$ = 5.00 (d, *J* = 3.4 Hz, 1 H, α, minor), 4.86 (d, *J* = 0.8 Hz, 1 H, β, major), 3.99 (dd, *J* = 8.3, 3.4 Hz, 1 H, minor), 3.77 (dd, *J* = 3.2, 1.1 Hz, 1 H, major), 3.70 (dd, *J* = 3.4, 3.4 Hz, 1 H, minor), 3.66 (dd, *J* = 10.0, 3.4 Hz, 1 H, major), 3.57 (s, 3 H, major), 3.53 (s, 3 H, minor), 3.21 (d, *J* = 8.3 Hz, 1 H, minor), 3.17 (d, *J* = 10.0 Hz, 1 H, major), 1.31 (s, 3 H, minor), 1.28 (s, 3 H, major), 1.27 (s, 3 H, minor), 1.14 (s, 3 H, major) ppm. $^{13}C$ NMR (125 MHz, [$D_4$]methanol): $\delta$ = 95.6, 91.0, 85.8, 85.2, 78.1, 75.1, 73.8, 73.3, 72.5, 69.7, 62.2, 61.5, 29.0, 28.5, 25.1, 18.6 ppm. IR (neat): $\tilde{\nu}$ = 3392 (s), 2933 (w), 1595 (w), 1329 (m), 1102 (s), 1023 (s), 774 (s) $cm^{-1}$. HRMS (ESI): calcd. for $C_8H_{16}O_5Na$ $[M + Na]^+$ 215.0895; found 215.0892.

**(*R*)-3-(Methoxymethoxy)-2,2-dimethyl-3,6-dihydro-2*H*-pyran (16):** First generation Grubbs' catalyst **A** (52 mg, 5 mol-%) was added to a solution of **10** (250 mg, 1.3 mmol) in dry, degassed $CH_2Cl_2$ (12.5 mL), and the solution was heated to reflux for 1 h. After cooling to ambient temperature, the solvent was evaporated, and the residue was purified by chromatography on silica to give **16** (163 mg, 1.0 mmol, 75%) as a colourless oil. $[\alpha]_D^{21}$ = –72.1 (*c* = 0.86, $CH_2Cl_2$). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 5.86–5.77 (m, 2 H), 4.77 (d, *J* = 6.8 Hz, 1 H), 4.65 (d, *J* = 6.9 Hz, 1 H), 4.20–4.03 (m, 2 H), 3.77 (m, 1 H), 3.39 (s, 3 H), 1.26 (s, 3 H), 1.21 (s, 3 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 127.9 (1), 125.1 (1), 96.1 (2), 75.4 (1), 72.7 (0), 61.1 (2), 55.6 (3), 25.3 (3), 20.5 (3) ppm. IR (neat): $\tilde{\nu}$ = 2933 (w), 1727 (w), 1144 (m), 1035 (s), 917 (m) $cm^{-1}$. HRMS (ESI): calcd. for $C_9H_{17}O_3$ $[M + H]^+$ 173.1178; found 173.1190.

**(3*S*,4*S*,5*R*)-5-(Methoxymethoxy)-6,6-dimethyltetrahydro-2*H*-pyran-3,4-diol (17):** Dihydropyran **16** (172 mg, 1.0 mmol) was dissolved in a mixture of acetone (3 mL), water (1 mL), and *tert*-butanol (1 mL). *N*-Methylmorpholine *N*-oxide (352 mg, 3.0 mmol), methane sulfonamide (95 mg, 1.0 mmol), and $K_2Os(OH)_6$ (17.0 mg, 0.046 mmol, 4.6 mol-%) were added to this solution, and the resulting mixture was stirred at ambient temperature for 4 h. A saturated aqueous solution of $Na_2S_2O_3$ was added, and the mixture was stirred for 1 h. The aqueous layer was separated and extracted with ethyl acetate, the combined organic layers were dried with $MgSO_4$ and filtered, and the solvents were evaporated. The residue was purified by chromatography on silica (hexane/ethyl acetate, 1:7) to give diol **17** (151 mg, 0.73 mmol, 73%) as a colourless solid, m.p. 63–64 °C. $[\alpha]_D^{25}$ = +53.1 (*c* = 0.30, $CH_3CN$). $^1H$ NMR (300 MHz, [$D_4$]methanol): $\delta$ = 4.87 (d, *J* = 6.6 Hz, 1 H), 4.85 (br. s, 2 H), 4.68 (d, *J* = 6.6 Hz, 1 H), 3.82 (m, 1 H), 3.72 (dd, *J* = 12.8, 1.5 Hz, 1 H), 3.67 (dd, *J* = 9.4, 3.5 Hz, 1 H), 3.63 (dd, *J* = 12.8, 2.3 Hz, 1 H), 3.47 (d, *J* = 9.5 Hz, 3 H), 3.41 (s, 3 H), 1.29 (s, 3 H), 1.16 (s, 3 H) ppm. $^{13}C$ NMR (75 MHz, [$D_4$]methanol): $\delta$ = 99.8, 83.6, 77.1, 71.8, 71.0, 65.3, 56.3, 28.4, 18.0 ppm. IR (neat): $\tilde{\nu}$ = 3412 (s), 2935 (m), 1097 (s), 1036 (s), 767 (m) $cm^{-1}$. MS (EI): *m*/*z* (%) = 180 (20), 117 (23), 85 (62), 82 (97), 45 (61). HRMS (ESI): calcd. for $C_9H_{19}O_5$ $[M + H]^+$ 207.1232; found 207.1239. $C_9H_{18}O_5$ (206.24): calcd. C 52.4, H 8.8; found C 52.3, H 8.8.

**(*R*)-3-(Methoxymethoxy)-2,2-dimethyl-3,4-dihydro-2*H*-pyran (18):** First generation Grubbs' catalyst **A** (47.5 mg, 5 mol-%) was added to a solution of **10** (230 mg, 1.2 mmol) in dry, degassed toluene

(12 mL), and the mixture was heated to 80 °C until the starting material had been fully consumed (approx. 0.5 h). 2-Propanol (3 mL) and NaOH (solid, 23 mg, 0.06 mmol) were added, and the mixture was heated to reflux until the intermediate RCM product had been fully converted (TLC, approx. 4 h). The mixture was cooled to ambient temperature, and water and MTBE were added. The aqueous layer was separated and extracted with MTBE, the combined organic extracts were dried with $MgSO_4$ and filtered, and the solvents were evaporated. The residue was purified by chromatography on silica to give **18** (125 mg, 0.8 mmol, 68%) as a colourless oil. $[\alpha]_D^{22}$ = –24.0 (*c* = 0.58, $CH_2Cl_2$). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 6.24 (ddd, *J* = 6.1, 1.9, 1.9 Hz, 1 H), 4.75 (d, *J* = 6.9 Hz, 1 H), 4.64 (d, *J* = 6.9 Hz, 1 H), 4.59 (ddd, *J* = 6.1, 4.0, 4.0 Hz, 1 H), 3.56 (dd, *J* = 6.9, 5.4 Hz, 1 H), 3.39 (s, 3 H), 2.29 (dddd, *J* = 17.1, 5.5, 4.2, 1.8 Hz, 1 H), 2.02 (dddd, *J* = 17.1, 6.9, 3.3, 2.1 Hz, 1 H), 1.29 (s, 3 H), 1.23 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 141.7 (1), 96.8 (1), 95.6 (2), 75.6 (0), 75.3 (1), 55.6 (3), 25.4 (3), 24.3 (2), 20.6 (3) ppm. IR (neat): $\tilde{\nu}$ = 3063 (m), 2934 (m), 1652 (s), 1247 (s), 1041 (s) cm$^{-1}$. MS (EI): *m*/*z* (%) = 172, (2) $[M]^+$, 116 (5), 110 (33), 95 (32), 85 (11), 71 (18), 57 (23), 45 (100), 43 (40). HRMS (EI): calcd. for $C_9H_{16}O_3$ $[M]^+$ 172.1099; found 172.1084. $C_9H_{16}O_3$ (172.22): calcd. C 62.8, H 9.4; found C 62.4, H 9.0.

**(2*R*,3*R*)-3-(Methoxymethoxy)-2-phenylpent-4-ene-2-ol (19):** A solution of ketone **7** (300 mg, 2.1 mmol) in dry, degassed $CH_2Cl_2$ (20 mL) was cooled to 0 °C. Phenylmagnesium chloride (25 wt.-% solution in THF; 1.5 mL, 2.7 mmol) was added slowly, and the reaction mixture was stirred for 1 h at 0 °C. It was then poured into water/diethyl ether (1:1), and a saturated aqueous solution of tartaric acid was added. The aqueous layer was separated and extracted with diethyl ether, the combined organic layers were washed with brine, dried with $MgSO_4$, and filtered, and the solvents were evaporated. The residue was purified by column chromatography on silica to give alcohol **19** (334 mg, 1.5 mmol, 72%) as a colourless liquid. $[\alpha]_D^{23}$ = –42.1 (*c* = 0.44, $CHCl_3$). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.58–7.19 (m, 5 H), 5.78 (ddd, *J* = 17.3, 10.4, 8.0 Hz, 1 H), 5.36 (ddd, *J* = 10.4, 1.8, 0.6 Hz, 1 H), 5.26 (ddd, *J* = 17.3, 1.7, 0.8 Hz, 1 H), 4.64 (d, *J* = 6.8 Hz, 1 H), 4.39 (d, *J* = 6.8 Hz, 1 H), 4.19 (d, *J* = 8.1 Hz, 1 H), 2.94 (s, 3 H), 1.46 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 133.8 (1), 131.4 (0), 127.9 (1), 126.7 (1), 125.5 (1), 120.5 (2), 93.9 (2), 84.1 (1), 75.8 (0), 55.4 (3), 25.4 (3) ppm. IR (neat): $\tilde{\nu}$ = 3464 (w), 2935 (w), 1446 (w), 1147 (m), 1022 (s), 917 (m), 699 (m) cm$^{-1}$. MS (EI): *m*/*z* (%) = 221 (32), 121 (100), 105 (65), 91 (46), 78 (53), 45 (68). HRMS (ESI): calcd. for $C_{13}H_{18}O_3Na$ $[M + Na]^+$ 245.1154; found 245.1160. $C_{13}H_{18}O_3$ (222.28): calcd. C 70.2, H 8.2; found C 70.0, H 8.5.

**[(2*R*,3*R*)-2-(Allyloxy)-3-(methoxymethoxy)pent-4-ene-2-yl]benzene (20):** Alcohol **19** (110 mg, 0.50 mmol) was dissolved in dry, degassed THF (5 mL), and NaHMDS (1.5 M in THF; 1.0 mL, 1.5 mmol), allyl bromide, (0.09 mL, 1.0 mmol), and $[NBu_4]I$ (18 mg, 0.05 mmol) were added. The mixture was heated to reflux for 3 h. The reaction was quenched by the addition of HCl (1 M aq.; 2 mL), and the aqueous layer was separated and extracted with MTBE. The combined organic extracts were dried with $MgSO_4$ and filtered, and the solvents were evaporated. The residue was purified by chromatography on silica to give ether **20** (116 mg, 0.44 mmol, 89%) as a colourless oil. $[\alpha]_D^{24}$ = –36.0 (*c* = 0.23, $CH_2Cl_2$). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.43–7.21 (m, 5 H), 5.93 (dddm, *J* = 17.2, 10.4, 4.9 Hz, 1 H), 5.55 (ddd, *J* = 16.9, 10.9, 7.0 Hz, 1 H), 5.31 (ddd, *J* = 17.2, 3.6, 1.8 Hz, 1 H), 5.19–5.07 (m, 3 H), 4.67 (d, *J* = 6.7 Hz, 1 H), 4.61 (d, *J* = 6.7 Hz, 1 H), 4.13 (dm, *J* = 7.0 Hz, 1 H), 3.89 (dddd, *J* = 13.0, 5.0, 1.7, 1.5 Hz, 1 H), 3.72 (dddd, *J* = 13.0, 4.8, 1.8, 1.7 Hz, 1 H), 3.17 (s, 3 H), 1.61 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 142.4 (0), 135.7 (1), 134.4 (1), 127.8 (1), 127.3 (1), 127.1 (1), 118.6 (2), 115.0 (2), 94.7 (2), 83.8 (1), 81.6 (0), 63.8 (2), 55.4 (3), 18.8 (3) ppm. IR (neat): $\tilde{\nu}$ = 2984 (m), 2888 (m), 1446 (m), 1027 (s), 918 (s), 701 (s) cm$^{-1}$. HRMS (ESI): calcd. for $C_{16}H_{23}O_3$ $[M + H]^+$ 263.1647; found 263.1660.

**(2*R*,3*R*)-3-(Methoxymethoxy)-2-methyl-2-phenyl-3,4-dihydro-2*H*-pyran (21):** First generation Grubbs' catalyst **A** (9.1 mg, 5 mol-%) was added to a solution of ether **20** (58 mg, 0.22 mmol) in dry, degassed toluene (2.2 mL). The solution was heated to 80 °C until the starting material had been fully converted (TLC, approx. 2 h). 2-Propanol (0.46 mL) and NaOH (solid, 4.4 mg, 0.11 mmol) were added, and the mixture was heated to reflux until the intermediate RCM product had been fully converted (TLC, approx. 3 h). The mixture was cooled to ambient temperature, and water and MTBE were added. The aqueous layer was separated and extracted with MTBE, the combined organic extracts were dried with $MgSO_4$ and filtered, and the solvents were evaporated. The residue was purified by chromatography on silica to give **21** (40 mg, 0.17 mmol, 77%) as a colourless oil. $[\alpha]_D^{22}$ = –34.1 (*c* = 0.20, $CH_2Cl_2$). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.53 (dm, *J* = 7.3 Hz, 2 H), 7.33 (ddm, *J* = 7.8, 7.1 Hz, 2 H), 7.24 (m, 1 H), 6.50 (ddd, *J* = 6.2, 1.8, 1.7 Hz, 1 H), 4.67 (m, 1 H), 4.59 (d, *J* = 7.1 Hz, 1 H), 4.32 (d, *J* = 7.1 Hz, 1 H), 3.97 (dd, *J* = 4.6, 4.6 Hz, 1 H), 2.97 (s, 3 H) 2.35 (dddd, *J* = 17.4, 4.7, 3.2, 2.3 Hz, 1 H), 2.02 (dddd, *J* = 17.3, 4.6, 4.3, 1.6 Hz, 1 H), 1.56 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 143.8, 142.0, 127.9, 126.7, 125.5, 97.3, 95.2, 79.0, 75.4, 55.3, 25.4, 24.2 ppm. IR (neat): $\tilde{\nu}$ = 2931 (m), 1653 (m), 1244 (m), 1150 (m), 1038 (s), 764 (m), 700 (m) cm$^{-1}$. HRMS (ESI): calcd. for $C_{14}H_{19}O_3$ $[M + H]^+$ 235.1334; found 235.1332.

**Supporting Information** (see footnote on the first page of this article): Copies of $^1$H and $^{13}$C NMR spectra for all products.

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