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Cross metathesis of allyl alcohols: how to suppress and how to promote double bond isomerization†

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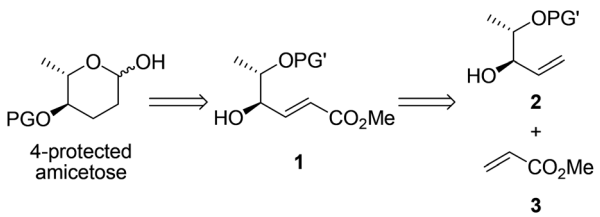
Under standard conditions the cross metathesis of allyl alcohols and methyl acrylate is accompanied by the formation of ketones, resulting from uncontrolled and undesired double bond isomerization. By conducting the CM in the presence of phenol, the catalyst loading and the reaction time required for quantiative conversion can be reduced, and isomerization can be suppressed. On the other hand, consecutive isomerization can be deliberately promoted by evaporating excess methyl acrylate after completing cross metathesis and by adding a base or silane as chemical triggers.

Introduction

De novo synthesis is a useful method to obtain rare carbohydrates from non-carbohydrate precursors.[1–21] Our contributions to the field have focused on the application of the assisted tandem RCM–isomerization sequence[22–24] to the synthesis of deoxy glycals.[25–27] This synthetic method relies on the *in situ* conversion of the Ru-carbene into a Ru-hydride by the addition of a "chemical trigger"[28] after completion of the metathesis step. The Ru-hydride then catalyzes a subsequent double bond isomerization. We and others have proposed several additives to trigger the isomerization reaction, such as a diluted hydrogen atmosphere,[29] inorganic hydrides,[30] NaOH and 2-propanol,[31] vinyl ethers[32,33] or silanes.[32] In particular, with second generation catalysts, uncontrolled isomerization reactions may occur even in the absence of isomerization inducing additives, because the propagating Ru-NHC-methylidene species undergoes a bimolecular decomposition into a Ru-hydride at elevated temperatures.[34,35] In these cases isomerization is often an undesired side reaction and measures to prevent double bond migration by trapping the Ru-hydride, *e.g.* with benzoquinone, have been devised.[36]

We encountered such an undesired isomerization side reaction when investigating a new synthesis of the highly deoxygenated carbohydrate amicetose, based on the cross metathesis[37,38] reaction of allyl alcohols **2** (derived from *S*-ethyl lactate)[26,39] and methyl acrylate (**3**) (Scheme 1).

In spite of a literature precedent describing the successful cross metathesis of various allyl alcohols and methyl acrylate,[40–45] we found that under standard reaction conditions the cross metathesis reaction leading to **1** is accompanied by an isomerization of the double bond to furnish a 1,4-dicarbonyl compound. Although the so-called Ru-catalyzed "redox isomerization" of allyl alcohols is well documented[46–50] and has also been reported as a side reaction of cross metathesis steps involving allyl alcohols,[51,52] we were surprised by the extent of this problem in our case. We expected that the tendency of CM products such as **1** to isomerize to ketones should be comparatively low, because the C–C-double bond to be isomerized is electron deficient. In addition, it has been reported that acrylates inhibit olefin isomerization, presumably by trapping Ru-hydride impurities.[53,54]



Scheme 1 Envisaged synthesis of a protected amicetose.

In this contribution we report conditions that allow the complete suppression of redox isomerization of cross metathesis products of allyl alcohols, and conditions which promote a subsequent double bond isomerization, leading selectively to 1,4-dicarbonyl compounds from allyl alcohols and methyl acrylate.

Results and discussion

Optimization of cross metathesis conditions

Initially, we investigated the cross metathesis of **4a** and methyl acrylate (**3**) using ten equivalents of the CM partner and

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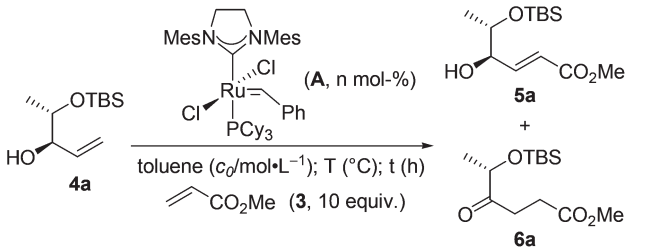
Table 1 Optimization of CM conditions



Entry	Cat. loading	c/mol L^{-1}	Phenol/ equiv.	T/°C	t/h	Yield of **5a**[a]	Yield of **6a**[a,b]
1	5 mol%	1.0	—	110	12	62%	28%
2	5 mol%	0.5	—	110	2.5	80%	12%
3	5 mol%	0.5	—	110	0.5	83%	n.d.
4	5 mol%	0.5	—	80	0.5	73%	n.d.
5	5 mol%	1.0	—	110	0.5	80%	n.d.
6	5 mol%	Neat	—	80	0.5	83%	n.d.
7	2.5 mol%	0.5	—	110	0.5	75%	n.d.
8	2.5 mol%	0.5	0.5	110	0.5	86%	n.d.
9	*2.5 mol%*	*1.0*	*0.5*	*110*	*0.5*	*98%*	*n.d.*
10	2.5 mol%	Neat	0.5	80	0.5	83%	n.d.
11	5 mol%	0.5	0.5	110	2.5	77%	17%
12	2.5 mol%	1.0	0.5	110	12	48%	20%

[a] Yields of isolated and purified products. [b] n.d. = not determined.

second generation catalyst **A**[55] in refluxing toluene for 12 hours. Under these conditions, **5a** and its isomerization product **6a** were obtained in a 2 : 1 ratio (Table 1, entry 1). Reducing the reaction time to 2.5 hours (entry 2) and then to 0.5 hours (entry 3) led to a significant improvement. Upon lowering the temperature to 80 °C (entry 4) the conversion remained incomplete and the yield of **5a** was only 73%. Comparison of entries 2, 5 and 6 suggests that a further improvement by the variation of the initial substrate concentration is not possible. Reducing the catalyst loading to 2.5 mol% (entry 7) results in a lower yield. Based on these results, we thought that the key to an isomerization-free cross metathesis could be a combination of reduced reaction temperatures, short reaction times and lower catalyst loadings, because – as mentioned in the Introduction – the isomerization is caused by a Ru-hydride resulting from a thermally induced bimolecular decomposition of the Ru-NHC-methylidene species.[34] Considering the fact that reducing the reaction temperature to 80 °C resulted in a decrease of the yield by 10% (compare entries 3 and 4) we decided to maintain a reaction temperature of 110 °C and find other means to accelerate the CM reaction while reducing the catalyst loading at the same time. A very simple yet effective method to improve olefin metathesis reactions has been devised by Forman *et al.*, who described a beneficial effect of the added phenol.[56,57] Presumably, phenol coordinates to the catalytically active 14-electron species, leading to a retarded catalyst decomposition. Indeed, the addition of phenol to the reaction mixture led to a significant improvement (86% compared to 75%, entries 7 and 8) under otherwise identical conditions. The yield could be further improved to nearly quantitative by raising the initial substrate concentration to 1.0 M (entry 9), but conducting the reaction without any solvent (entry 10) led to a significantly lower yield, which might, however, be attributed to the lower reaction temperature. In entries 11 and 12 the results for CM reactions in the presence of phenol at longer reaction times are listed. From these experiments it can be concluded that phenol is not an efficient isomerization inhibitor itself, but that the reduced extent of isomerization can be mainly attributed to the short reaction time, which was accomplished by phenol accelerated cross metathesis.

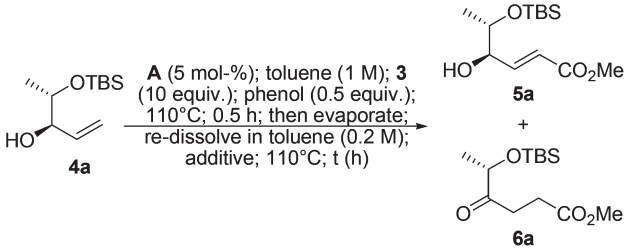
Optimization of cross metathesis–isomerization conditions

Next, we set out to find the conditions that would allow the selective synthesis of the CM–isomerization product **6a**. The results gathered during the optimization of the cross metathesis reaction suggest that the dicarbonyl compound **6a** is not accessible in synthetically useful yields simply by heating the reaction mixture for a prolonged period of time. These experiments are listed in Table 1 as entries 1 and 12, and are repeated for comparison in Table 2 as entries 1 and 3. We suspected that excess methyl acrylate inhibits the isomerization to a certain extent and tested therefore a modification of the CM protocol which involves removal of the unreacted methyl acrylate by evaporation after 0.5 h, re-dissolving the mixture in toluene and heating to induce the isomerization step (Table 2, entries 2 and 4). If phenol is present in the reaction mixture, the product distribution is virtually unaffected by this measure; however, without added phenol the evaporation of excess methyl acrylate prior to inducing the isomerization leads to the formation of a substantial amount of **6a** (entry 4). We then tested various additives to promote the Ru-carbene to Ru-hydride conversion. Surprisingly, ethyl vinyl ether[32,58] proved to be ineffective, as only cross metathesis product **5a** was observed. NaOH did promote the isomerization, but synthetically useful yields could only be obtained in the absence of phenol (entries 7–10), because removal of the phenol turned out to be laborious. We then tested triethyl silane (entries 11 and 12) and the cheaper alternative polymethylhydrosiloxane (PMHS)[59,60] (entry 13) and found incomplete isomerization if phenol was present. However, if the CM reaction was conducted without phenol, the isomerized product **6a** could be isolated in a synthetically useful yield of 76% (entry 14).‡

Trost and Kulawiec proposed a mechanism for Ru-catalyzed redox isomerizations which relies on the initial coordination of the allylic hydroxy group to the Ru centre, followed by β-hydride elimination to furnish an enone bound to a Ru-hydride. This complex reacts further in a migratory insertion to a Ru-enolate, which then undergoes protonation by the allylic alcohol, liberating the ketone and a Ru-alkoxide.[49] In our case, however, a slightly modified scenario might be possible, which is depicted in Scheme 2: after the formation of the Ru-hydride **B** from the reaction of the metathesis catalyst and

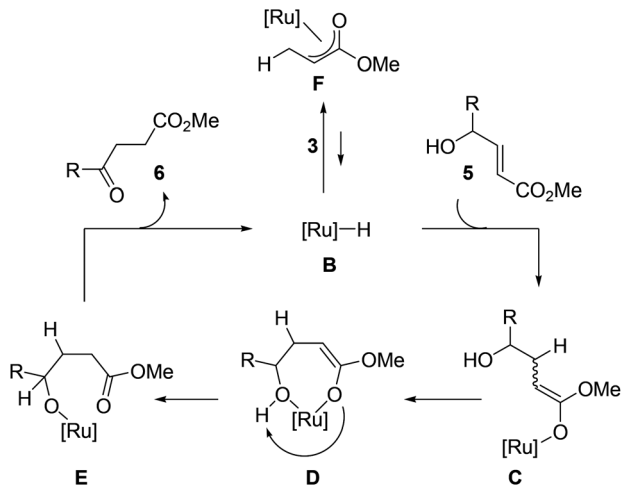
‡When the isolated and purified CM product **5a** was treated with 5 mol% of catalyst **A** and isomerization inducing additives such as ethyl vinyl ether or silanes isomerization product **6a** was obtained in similar yields.

Table 2 Optimization of CM–isomerization conditions



Entry	Cat. loading	Phenol added?	*t*/h	Excess **3** evaporated?	Additive[c] (equiv.)	Yield of **5a**[a,b]	Yield of **6a**[a,b]
1	2.5 mol%	Yes	12	No	—	48%	20%
2	2.5 mol%	Yes	12	Yes	—	55%	21%
3	5 mol%	No	12	No	—	62%	28%
4	5 mol%	No	12	Yes	—	26%	56%
5	5 mol%	Yes	12	Yes	EVE (5)	n.d.	<5%
6	5 mol%	No	12	Yes	EVE (5)	n.d.	<5%
7	5 mol%	Yes	3	Yes	NaOH (0.5)	n.d.	29%
8	5 mol%	No	3	Yes	NaOH (0.5)	n.d.	65%
9	5 mol%	Yes	3	Yes	NaOH (1.5)	n.d.	70%
10	*5 mol%*	*No*	*3*	*Yes*	*NaOH (1.5)*	*n.d.*	*70%*
11	5 mol%	Yes	12	Yes	TESH (0.5)	23%	45%
12	5 mol%	No	12	Yes	TESH (0.5)	n.d.	67%
13	5 mol%	Yes	12	Yes	PMHS (0.2)[d]	29%	39%
14	*5 mol%*	*No*	*12*	*Yes*	*PMHS (0.2)*[d]	*n.d.*	*76%*

[a] Yields of isolated and purified products. [b] n.d. = not determined. [c] Abbreviations for additives: EVE = ethyl vinyl ether; TESH = triethylsilane; PMHS = polymethylhydrosiloxane. [d] Equivalents of PMHS were calculated based on an effective mass of 60 g mol^{-1} per hydride.[59]



Scheme 2 Mechanistic rationale for the isomerization step.

the isomerization inducing additive, a conjugate addition to the cross metathesis product **5** occurs, yielding a Ru-enolate **C**. Precedence for the formation of such Ru-enolates[61] and their intermediacy in catalytic cycles[62,63] exists. In this particular case, the enolate may undergo cyclization to **D**, which reacts in an inter- or intramolecular proton transfer to furnish Ru-alkoxide **E**. From this intermediate, the Ru-hydride can be regenerated *via* β-hydride elimination and formation of the isomerized product **6**. In this scenario, the inhibitory effect of excess methyl acrylate[53,54] can be explained by a conjugate addition of the Ru-hydride to methyl acrylate (**3**), giving the Ru-enolate **F**. Due to the large excess of acrylate, the equilibrium is shifted to the enolate, thereby removing major amounts of the isomerization catalyst from the reaction mixture.

Application of isomerization-free CM and CM–isomerization conditions to other allyl alcohols

The optimization studies revealed that the best conditions for a cross metathesis–isomerization sequence of allyl alcohols appear to be the use of a higher catalyst loading of 5 mol%, absence of phenol, removal of excess acrylate after the completion of the CM step, and addition of either 1.5 equiv. of NaOH or 0.2 equiv. of PMHS to trigger the formation of the isomerization catalyst. On the other hand, for isomerization-free cross metathesis, a reduced catalyst loading of 2.5 mol%, addition of phenol as a rate accelerating agent and short reaction times of 0.5 h at 110 °C appear to be beneficial. Having established the optimum conditions for isomerization-free cross metathesis and for the CM–isomerization sequence of allyl alcohol **4a**, we applied these protocols to several other allyl alcohols **4b–4p** (Table 3). In general, the CM products **5** were obtained in high yields of *ca.* 90%. For the 1,4-dicarbonyl compounds **6**, yields of approximately 70% could be obtained. Although the yields obtained with NaOH are somewhat lower for most examples, reaction times for the isomerization step are significantly shorter (*ca.* 3 h) compared to those with PMHS as an additive (*ca.* 12 h). Notably, isomerization induced by PMHS as a chemical trigger appears to be significantly faster than reduction of the C–C-double bond, which

Table 3 Scope of isomerization-free CM and CM–isomerization sequence

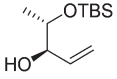
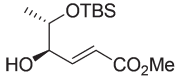
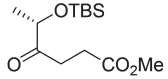
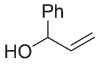
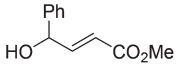
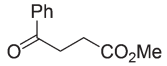
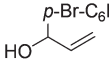
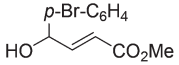
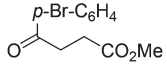
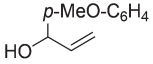
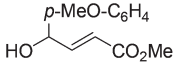
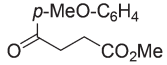
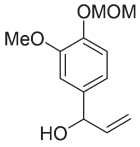
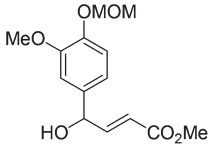
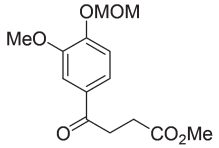
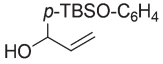
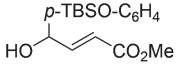
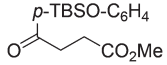
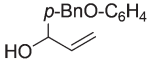
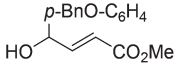
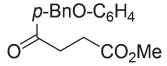
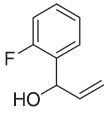
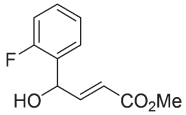
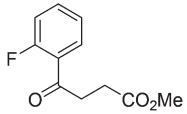
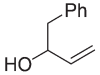
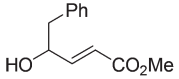
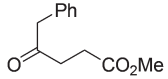
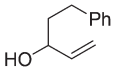
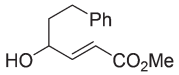
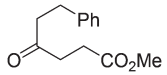
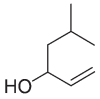
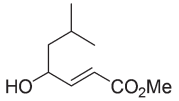
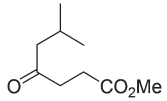
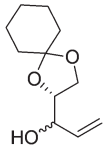
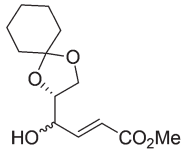
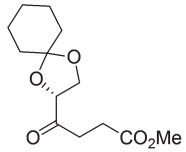
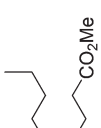
Entry	4	Allyl alcohol	5	CM product	Yield[a]	6	CM–isomerization product	Yield[b]	Yield[c]
1	**4a**		**5a**		98%	**6a**		70%	76%
2	**4b**		**5b**		91%	**6b**		83%	71%
3	**4c**		**5c**		94%	**6c**		63%	67%
4	**4d**		**5d**		91%	**6d**		45%	72%
5	**4e**		**5e**		85%	**6e**		65%	68%
6	**4f**		**5f**		92%	**6f**		27%	70%
7	**4g**		**5g**		88%	**6g**		—[d]	71%
8	**4h**		**5h**		94%	**6h**		68%	76%
9	**4i**		**5i**		88%	**6i**		66%	64%
10	**4j**		**5j**		90%	**6j**		80%	73%
11	**4k**		**5k**		94%	**6k**		44%	61%
12	**4l**		**5l**		91%	**6l**		41%	67%

Table 3 *(Contd.)*

Entry	4	Allyl alcohol	5	CM product	Yield[a]	6	CM-isomerization product	Yield[b]	Yield[c]
13	**4m**		**5m**		93%	**6m**		42%	65%
14	**4n**		**5n**		87%	**6n**		56%	70%
15	**4o**		**5o**		83%[e]	**6o**		55%[e]	37%[e]
16	**4p**		**5p**		82%[e]	**6p**		—[d,e]	43%[e]

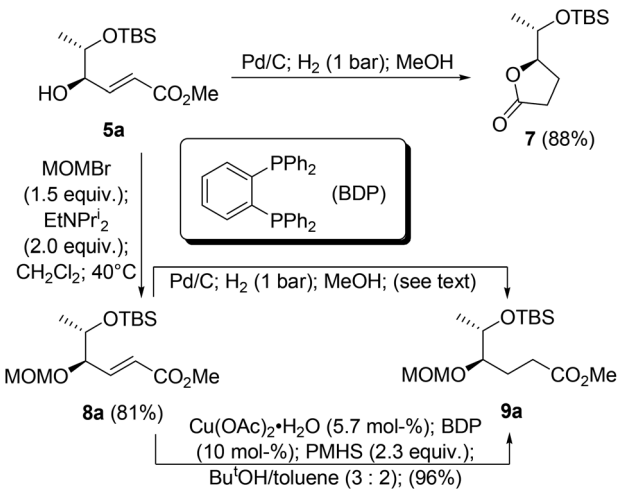
[a] **A** (2.5 mol%); toluene (1.0 M); methyl acrylate (10 equiv.); phenol (0.5 equiv.); 110 °C; 0.5 h. [b] **A** (5 mol%); toluene (1.0 M); methyl acrylate (10 equiv.); 110 °C; 0.5 h; then evaporate and re-dissolve in toluene (0.2 M); add NaOH (s, 1.5 equiv.); 110 °C, 3 h. [c] **A** (5 mol%); toluene (1.0 M); methyl acrylate (10 equiv.); 110 °C; 0.5 h; then evaporate and re-dissolve in toluene (0.2 M); add PMHS (0.2 equiv.); 110 °C, 12 h. [d] A complex mixture of products. [e] 10 mol% of **A** and 20 equiv. of methyl acrylate were used.

has also been observed with silanes in the presence of Ru-carbene complexes.[64,65]

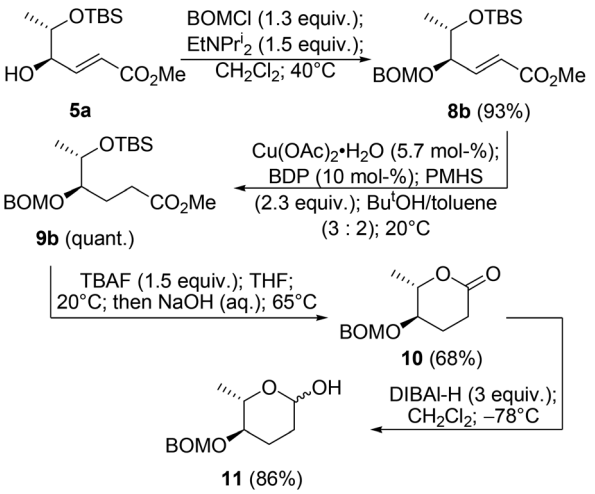
Synthesis of BOM-protected amicetose

Hydrogenation of **5a** using commercial Pd/C as a catalyst resulted in spontaneous cyclization to the γ-butyrolactone **7**. For these reasons we thought it might be advantageous to mask the C4–OH group prior to hydrogenation with a protecting group orthogonal to TBS. Initially, the MOM-group was chosen, and the corresponding MOM-ether **8a** could be isolated in 81% yield. Hydrogenation was again accomplished in quantitative yield using hydrogen and Pd/C. Unfortunately, this method turned out to be very unreliable, because when we changed the sample of Pd/C the reaction failed completely. Reproducibility problems associated with Pd/C have been known for quite some time[66] and the *in situ* preparation of such catalysts from $Pd(OAc)_2$ and activated carbon has been suggested as an alternative.[67,68] Considering that the hydrogenation in question involves a double bond in conjugation with an ester group, we thought that Lipshutz' variant[60] of Stryker's reagent[69] should work well. Indeed, the desired ester **9a** was reliably and reproducibly obtained in nearly quantitative yield with [(BDP)CuH] as a catalyst, which was formed *in situ* from 1,2-bis(diphenyl-phosphino)benzene (BDP), Cu-(II)-acetate and polymethylhydro-siloxane (PMHS) as a reducing agent (Scheme 3).

Unfortunately, it turned out at this point that the MOM-protecting group was rather impractical, because after desilylation it became virtually impossible to control the progress of any reaction steps *via* TLC. For this reason, we replaced the MOM-group by the UV-active benzyloxymethyl-(BOM)-protecting group. The analogous compound **8b** was obtained in somewhat better yield than **8a**, and the subsequent conjugate reduction with the modified Stryker's reagent gave **9b** in quantitative yield. Desilylation and lactonization led to compound **10**, which was finally reduced with DIBAl-H to the desired BOM-protected amicetose **11** (Scheme 4).



Scheme 3 Towards MOM-protected amicetose.



Scheme 4 Synthesis of BOM-protected amicetose.

Conclusions

In summary, we have described a protocol for the rapid, isomerization-free cross metathesis of allyl alcohols and methyl acrylate using phenol as an efficient rate-accelerating reagent. These conditions were applied to an allylic alcohol derived from *S*-ethyl lactate, and the resulting cross metathesis product could be elaborated in a few steps to the 2,3,6-trideoxy sugar amicetose as a BOM-ether. The isomerization-free CM conditions were complemented by the development of a protocol which allows the synthesis of 1,4-dicarbonyl compounds from allyl alcohols through an assisted tandem CM–isomerization sequence, using a single precatalyst and base or a silane as a chemical trigger for inducing the conversion of the Ru-carbene catalyst into a Ru-hydride.

Experimental

General remarks

All experiments were conducted in dry reaction vessels in an atmosphere of dry nitrogen. Solvents were purified by standard procedures. ^{1}H NMR spectra were obtained at 300 MHz or at 600 MHz in $CDCl_3$ with $CHCl_3$ (δ = 7.24 ppm) as an internal standard. Coupling constants (J) are given in Hz. ^{13}C NMR spectra were recorded at 75 MHz or at 150 MHz in $CDCl_3$ with $CDCl_3$ (δ = 77.0 ppm) as an internal standard. The number of coupled protons was analyzed by APT-experiments and is denoted by the number in parentheses following the chemical shift value. IR spectra were recorded neat on NaCl or KBr plates. Wavenumbers (ν) 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.

General procedure for isomerization-free cross metathesis

To a solution of the corresponding allyl alcohol (1.0 mmol), methyl acrylate (0.9 mL, 10.0 mmol) and phenol (47 mg, 0.5 mmol) in dry toluene (1.0 mL) was added Ru-catalyst **A** (21.2 mg, 2.5 mol%). The solution was heated to 110 °C for 0.5 h, all volatiles were removed *in vacuo* and the residue was purified by column chromatography on silica using hexane–MTBE mixtures of increasing polarity.

(4*R*, 5*S*, *E*)-Methyl-5-(*tert*-butyldimethylsilyloxy)-4-hydroxyhex-2-enoate (5a). Following the general procedure, **5a** was obtained from **4a** (200 mg, 0.92 mmol) as a colourless oil (249 mg, 98%). $[\alpha]_D^{27}$ = +21.3 (c = 0.61, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.89 (dd, J = 15.7, 4.7, 1H), 6.10 (dd, J = 15.7, 1.8, 1H), 4.22 (ddd, J = 8.6, 4.0, 1.8, 1H), 3.91 (qd, J = 6.3, 3.9, 1H), 3.73 (s, 3H), 2.57 (d, J = 4.0, 1H), 1.07 (d, J = 6.3, 3H), 0.89 (s, 9H), 0.07 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2 (0), 146.4 (1), 121.7 (1), 75.2 (1), 71.1 (1), 51.9 (3), 26.1 (1), 18.4 (0), 18.2 (1), −4.7 (3), −4.8 (3); IR (neat): ν 3481 (w), 2930 (m), 2857 (m), 1726 (s), 1093 (s), 834 (s), 775 (s); MS (EI): m/z 275 (23), 257 (100), 213 (34), 143 (11), 111 (90); HRMS (ESI) calcd for $C_{13}H_{27}O_4Si$ $[M + H]^+$: 275.1679, found: 275.1694; Anal. calcd for $C_{13}H_{26}O_4Si$: C, 56.9; H, 9.6; found: C, 56.9; H, 9.7.

(*E*)-Methyl-4-hydroxy-4-phenylbut-2-enoate (5b). Following the general procedure, **5b** was obtained from **4b** (134 mg, 1.0 mmol) as a colourless liquid (174 mg, 91%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43–7.22 (5H), 7.02 (d, J = 15.6, 1H), 6.14 (d, J = 15.6, 1H), 5.31 (bs, 1H), 3.70 (s, 3H), 2.62 (bs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.0 (0), 148.9 (1), 140.8 (0), 128.8 (1), 128.3 (1), 126.5 (1), 119.6 (1), 73.4 (1), 51.6 (3); IR (neat): ν 3430 (w), 2952 (w), 1705 (s), 1657 (m), 1436 (m), 1271 (s), 1167 (s), 981 (s), 698 (s); MS (EI): m/z 192 (10, $[M + H]^+$), 174 (30), 163 (100), 131 (100), 115 (41), 105 (74), 87 (60), 77 (85), 55 (33); HRMS (EI): calcd for $C_{11}H_{12}O_3$ $[M]^+$: 192.0786, found: 192.0776; Anal. calcd for $C_{11}H_{12}O_3$: C, 68.7; H, 6.3, found: C, 68.2; H, 6.5.

(*E*)-Methyl-4-(4-bromophenyl)-4-hydroxy-but-2-enoate (5c). Following the general procedure, **5c** was obtained from **4c** (213 mg, 1.0 mmol) as a colourless liquid (254 mg, 94%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (ddd, J = 8.4, 2H), 7.18 (ddd, J = 8.5, 2H), 6.95 (dd, J = 15.6, 4.9, 1H), 6.10 (dd, J = 15.6, 1.6, 1H), 5.26 (dm, J = 4.0, 1H), 3.70 (s, 3H), 3.01 (bs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.8 (0), 148.4 (1), 139.8 (0), 131.8 (1), 128.2 (1), 122.1 (0), 120.1 (1), 72.6 (1), 51.7 (3); IR (neat): ν 3426 (m), 2951 (w), 1703 (s), 1436 (m), 1275 (s), 1167 (s), 1010 (s), 827 (s); MS (EI): m/z 270 (8, $[M + H]^+$), 255 (18), 254 (28), 243 (79), 241 (100), 213 (25), 211 (65), 185 (57), 183 (62), 131 (47), 87 (91), 77 (54), 55 (28); HRMS (ESI): calcd for $C_{11}H_{12}O_3Br$ $[M + H]^+$: 270.9970, found: 270.9994.

(*E*)-Methyl-4-hydroxy-4-(4-methoxyphenyl)-but-2-enoate (5d). Following the general procedure, **5d** was obtained from **4d** (164 mg, 1.0 mmol) as a colourless liquid (203 mg, 91%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24 (dm, J = 8.5, 2H), 7.02 (ddd, J = 15.6, 4.7, 0.5, 1H), 6.87 (dm, J = 8.6, 2H), 6.14 (ddd, J = 15.6, 0.8, 0.7, 1H), 5.28 (d, J = 4.6, 1H), 3.79 (s, 3H), 3.72 (s, 3H), 2.37 (bs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.0 (0), 159.6 (0), 149.1 (1), 133.0 (0), 128.0 (1), 119.5 (1), 114.2 (1), 73.0 (1), 55.3 (3), 51.6 (3); IR (neat): ν 3443 (m), 2953 (w), 1716 (s), 1511 (s), 1247 (s), 1168 (s), 1030 (s), 833 (m); MS (EI): m/z 222 (41, $[M]^+$), 193

(28), 161 (75), 145 (41), 135 (100), 121 (43), 91 (37), 77 (55), 55 (31); HRMS (EI): calcd for $C_{12}H_{14}O_4$ $[M]^+$: 222.0892, found: 222.0874; Anal. calcd for $C_{12}H_{14}O_4$: C, 64.9; H, 6.4, found: C, 64.6; H, 6.5.

(*E*)-Methyl 4-hydroxy-4-(3-methoxy-4-(methoxymethoxy)-phenyl)-but-2-enoate (5e). Following the general procedure, **5e** was obtained from **4e** (224 mg, 1.0 mmol) as a colourless liquid (239 mg, 85%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.09 (d, J = 8.2, 1H), 7.01 (dd, J = 15.6, 4.8, 1H), 6.88 (d, J = 2.0, 1H), 6.82 (dd, J = 8.3, 2.0, 1H), 6.13 (dd, J = 15.6, 1.7, 1H), 5.28 (m, 1H), 5.19 (s, 2H), 3.85 (s, 3H), 3.71 (s, 3H), 3.48 (s, 3H), 2.53 (bs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7 (0), 148.8 (1), 135.3 (0), 119.6 (1), 119.0 (1), 116.5 (1), 110.0 (1), 95.4 (2), 73.2 (1), 56.1 (3), 55.9 (3), 51.6 (3); IR (neat): ν 3454 (w), 2952 (w), 1720 (m), 1508 (m), 1261 (s), 1152 (s), 979 (s); MS (EI): m/z 282 (87, $[M]^+$), 265 (27), 233 (30), 220 (29), 45 (100); HRMS (ESI): calcd for $C_{14}H_{19}O_6$ $[M + H]^+$: 283.1182, found: 283.1198; Anal. calcd for $C_{14}H_{18}O_6$: C, 59.6; H, 6.4; found: C, 59.4; H, 6.6.

(*E*)-Methyl-4-(4-(*tert*-butyldimethylsilyloxy)phenyl)-4-hydroxybut-2-enoate (5f). Following the general procedure, **5f** was obtained from **4f** (264 mg, 1.0 mmol) as a colourless liquid (295 mg, 92%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18 (d, J = 7.4, 2H), 7.03 (dm, J = 15.6, 1H), 6.81 (d, J = 7.4, 2H), 6.14 (d, J = 15.6, 1H), 5.28 (bs, 1H), 3.73 (s, 3H), 2.30 (bs, 1H), 0.97 (s, 9H), 0.18 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.0 (0), 155.8 (0), 149.1 (1), 133.6 (0), 127.9 (1), 120.4 (1), 119.5 (1), 73.1 (1), 51.6 (3), 25.7 (3), 18.2 (0), −4.5 (3); IR (neat): ν 3431 (m), 2932 (w), 1723 (m), 1508 (s), 1255 (s), 1165 (s), 910 (s), 837 (s), 780 (s); MS (EI): m/z 322 (38, $[M]^+$), 291 (31), 265 (100), 235 (50), 209 (49), 179 (30), 135 (25), 89 (50), 55 (20); HRMS (EI): calcd for $C_{17}H_{26}O_4Si$ $[M]^+$: 322.1600, found: 322.1628; Anal. calcd for $C_{17}H_{26}O_4Si$: C, 63.3; H, 8.1, found: C, 63.2; H, 8.4.

(*E*)-Methyl-4-(4-benzyloxyphenyl)-4-hydroxybut-2-enoate (5g). Following the general procedure, **5g** was obtained from **4g** (240 mg, 1.0 mmol) as a colourless solid (263 mg, 88%), mp 69–70 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.49–7.30 (5H), 7.26 (d, J = 6.8, 2H), 7.05 (dm, J = 15.7, 1H), 6.97 (d, J = 6.9, 2H), 6.16 (d, J = 15.6, 1H), 5.30 (bs, 1H), 5.07 (s, 2H), 3.74 (s, 3H), 3.72 (s, 3H), 2.36 (bs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.0 (0), 159.6 (0), 149.1 (1), 133.0 (0), 128.0 (1), 119.5 (1), 114.2 (1), 73.0 (1), 55.3 (3), 51.6 (3); IR (neat): ν 3436 (m), 3031 (w), 1707 (s), 1509 (s), 1238 (s), 1168 (s), 1016 (s), 739 (s); MS (EI): m/z 298 (20, $[M]^+$), 281 (7), 91 (100), 65 (7); HRMS (EI): calcd for $C_{18}H_{18}O_4$ $[M]^+$: 298.1205, found: 298.1206; Anal. calcd for $C_{18}H_{18}O_4$: C, 72.5; H, 6.1, found: C, 72.5; H, 6.2.

(*E*)-Methyl-4-(2-fluorophenyl)-4-hydroxybut-2-enoate (5h). Following the general procedure, **5h** was obtained from **4h** (152 mg, 1.0 mmol) as a colourless liquid (198 mg, 94%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (t, J = 7.2, 1H), 7.27 (m, 1H), 7.14 (m, 1H), 7.09–6.95 (2H), 6.15 (d, J = 15.6, 1H), 5.66 (bs, 1H), 3.71 (s, 3H), 3.06 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.0 (0), 159.7 (d, J = 246.9, 0), 147.8 (1), 129.7 (d, J = 8.3, 1), 128.0 (d, J = 13.4, 0), 127.7 (d, J = 3.8, 1), 124.5 (d, J = 3.5, 1), 120.0 (1), 115.5 (d, J = 21.5, 1), 67.0 (d, J = 3.4, 1), 51.7 (3); IR (neat): ν 3436 (m), 2953 (w), 1705 (s), 1274 (s), 1171 (s), 759 (s); MS (EI): m/z 210 (3, $[M]^+$), 181 (100), 149 (77), 123 (56), 87 (56), 55 (31); HRMS (EI): calcd for $C_{11}H_{11}O_3F$ $[M]^+$: 210.0692, found: 210.0685.

(*E*)-Methyl-4-hydroxy-5-phenylpent-2-enoate (5i). Following the general procedure, **5i** was obtained from **4i** (148 mg, 1.0 mmol) as a colourless liquid (182 mg, 88%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42–7.17 (5H), 7.02 (dm, J = 15.7, 1H), 6.06 (d, J = 15.6, 1H), 4.52 (bs, 1H), 3.74 (s, 3H), 3.02–2.72 (2H), 2.09 (bs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.0 (0), 149.2 (1), 136.8 (0), 129.4 (1), 128.6 (1), 126.9 (1), 120.1 (1), 71.7 (1), 51.6 (3), 43.2 (2); IR (neat): ν 3435 (m), 2950 (w), 1707 (s), 1437 (m), 1275 (s), 1168 (s), 702 (s); MS (EI): m/z 206 (1, $[M]^+$), 115 (18), 91 (100), 83 (76); HRMS (EI): calcd for $C_{12}H_{14}O_3$ $[M]^+$: 206.0943, found: 206.0954; Anal. calcd for $C_{12}H_{14}O_3$: C, 69.9; H, 6.8, found: C, 69.4; H, 7.1.

(*E*)-Methyl-4-hydroxy-6-phenylhex-2-enoate (5j). Following the general procedure, **5j** was obtained from **4j** (162 mg, 1.0 mmol) as a colourless solid (197 mg, 90%), mp 29–31 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36–7.16 (5H), 6.97 (dd, J = 15.7, 4.9, 1H), 6.07 (dd, J = 15.6, 1.7, 1H), 4.32 (m, 1H), 3.75 (s, 3H), 2.85–2.66 (2H), 2.41 (bs, 1H), 1.98–1.81 (2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.0 (0), 150.3 (1), 141.2 (0), 128.4 (1), 128.4 (1), 126.0 (1), 119.9 (1), 70.2 (1), 51.6 (3), 37.9 (2), 31.3 (2); IR (neat): ν 3436 (m), 2949 (w), 1705 (s), 1275 (s), 1169 (m), 700 (s); MS (EI): m/z 221 (18, $[M + H]^+$), 220 (7, $[M]^+$), 202 (18), 142 (30), 128 (30), 105 (67), 91 (100), 87 (46); HRMS (EI): calcd for $C_{13}H_{16}O_3$ $[M]^+$: 220.1099, found: 220.1111; Anal. calcd for $C_{13}H_{16}O_3$: C, 70.9; H, 7.3, found: C, 70.4; H, 7.2.

(*E*)-Methyl-4-hydroxy-6-methylhept-2-enoate (5k). Following the general procedure, **5k** was obtained from **4k** (114 mg, 1.0 mmol) as a colourless liquid (162 mg, 94%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.93 (dm, J = 15.7, 1H), 6.02 (d, J = 15.6, 1H), 4.34 (bs, 1H), 3.72 (s, 3H), 2.10 (bs, 1H), 1.78 (m, 1H), 1.57–1.28 (2H), 0.92 (d, J = 5.2, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.1 (0), 151.0 (1), 119.3 (1), 69.3 (1), 51.6 (3), 45.6 (2), 24.4 (1), 23.0 (3), 22.0 (3); IR (neat): ν 3432 (m), 2956 (m), 1706 (s), 1275 (s), 1170 (s), 938 (s); MS (EI): m/z 143 (31), 115 (42), 87 (100), 55 (38), 41 (25); HRMS (ESI): calcd for $C_9H_{17}O_3$ $[M + H]^+$: 173.1178, found: 173.1192; Anal. calcd for $C_9H_{16}O_3$: C, 62.8; H, 9.4, found: C, 62.8; H, 9.6.

(*E*)-Methyl-4-hydroxy-4-((*R*)-1,4-dioxaspiro[4.5]decan-2-yl)-but-2-enoate (5l). Following the general procedure, **5l** was obtained from **4l** (198 mg, 1.0 mmol) as a colourless liquid (233 mg, 91%) as an inseparable mixture of diastereomers. Analytical data were obtained from the mixture. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.90 (dd, J = 15.8, 4.1, 0.5H), 6.85 (dd, J = 15.7, 4.7, 0.5H), 6.16 (dd, J = 15.7, 2.6, 0.5H), 6.14 (dd, J = 15.7, 2.6, 0.5H), 4.46 (m, 0.5H), 4.21 (m, 0.5H), 4.17–3.78 (3H), 3.73 (s, 3H), 2.68 (bs, 0.5H), 2.57 (bs, 0.5H), 1.69–1.47 (8H), 1.47–1.30 (2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.6 (0), 166.5 (0), 145.4 (1), 145.2 (1), 122.3 (1), 121.6 (1), 110.6 (0), 110.3 (0), 77.5 (1), 77.0 (1), 71.8 (1), 70.5 (1), 65.3 (2), 64.3 (2), 51.6 (3), 36.2 (2), 36.1 (2), 34.6 (2), 34.5 (2), 25.0 (2), 25.0 (2), 23.9 (2), 23.9 (2), 23.6 (2); IR (neat): ν 3457 (m), 2936 (w), 1722 (s), 1274 (s), 1165 (s), 1097 (s), 927 (s); MS (EI): m/z 256 (22, $[M]^+$), 227 (23), 213 (83), 141 (100), 109 (35), 81 (31), 55 (42); HRMS (EI): calcd for $C_{13}H_{20}O_5$ $[M]^+$: 256.1311, found: 256.1313;

Anal. calcd for $C_{13}H_{20}O_5$: C, 60.9; H, 7.9, found: C, 60.7; H, 7.9.

(*E*)-Methyl-4-hydroxynon-2-enoate (5m). Following the general procedure, **5m** was obtained from **4m** (128 mg, 1.0 mmol) (172 mg, 93%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.93 (dm, J = 15.7, 1H), 6.00 (d, J = 15.7, 1H), 4.27 (bs, 1H), 3.71 (s, 3H), 2.22 (bs, 1H), 1.63–1.47 (2H), 1.47–1.18 (6H), 0.92–0.78 (3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.1 (0), 150.7 (1), 119.5 (1), 71.0 (1), 51.6 (3), 36.5 (2), 31.6 (2), 22.5 (2), 13.9 (3); IR (neat): ν 3437 (m), 2930 (m), 1723 (s), 1437 (m), 1274 (s), 1169 (s); MS (EI): *m*/*z* 157 (39), 115 (46), 87 (100), 55 (32), 43 (20); HRMS (ESI): calcd for $C_{10}H_{19}O_3$ $[M + H]^+$: 187.1334, found: 187.1327; Anal. calcd for $C_{10}H_{18}O_3$: C, 64.5; H, 9.7, found: C, 64.4; H, 10.1.

(*E*)-Methyl-4-hydroxyhept-2-enoate (5n). Following the general procedure, **5n** was obtained from **4n** (100 mg, 1.0 mmol) as a colourless liquid (138 mg, 87%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.93 (dd, J = 15.7, 4.9, 1H), 6.01 (dd, J = 15.7, 1.7, 1H), 4.29 (ddm, J = 6.2, 1.6, 1H), 3.72 (s, 3H), 2.09 (bs, 1H), 1.60–1.48 (2H), 1.48–1.30 (2H), 0.92 (t, J = 7.3, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.6 (0), 119.6 (1), 70.8 (1), 51.5 (3), 38.7 (2), 18.4 (2), 13.8 (3); IR (neat): ν 3441 (w), 2958 (m), 1724 (s), 1705 (s), 1659 (m), 1436 (m), 1274 (s), 1169 (s), 981 (s); MS (EI): *m*/*z* 129 (44), 115 (50), 87 (100), 83 (37), 71 (25), 55 (35); HRMS (ESI): calcd for $C_8H_{15}O_3$ $[M + H]^+$: 159.1021, found: 159.1015 Anal. calcd for $C_8H_{14}O_3$: C, 60.7; H, 8.9, found: C, 60.8; H, 8.9.

(2*E*, 2′*E*)-Dimethyl-4,4′-(1,4-phenylene)bis(4-hydroxybut-2-enoate) (5o). Following the general procedure, **5o** was obtained from **4o** (190 mg, 1.0 mmol) as a colourless solid (254 mg, 83%), mp 98–99 °C, as a mixture of diastereomers. The general procedure was modified by using increased amounts of catalyst **A** (85 mg, 10 mol%) and methyl acrylate (1.80 mL, 20.0 mmol). Analytical data were obtained from the mixture. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30–7.22 (4H), 6.94 (ddm, J = 15.6, 4.8, 2H), 6.14–6.01 (ddm, J = 15.6, 1.6, 2H), 5.28 (bs, 2H), 3.65 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9 (0), 149.0 (1), 141.1 (0), 126.8 (1), 119.5 (1), 72.7 (1), 51.4 (3); IR (neat): ν 3424 (m), 2953 (w), 1702 (s), 1437 (m), 1274 (s), 1168 (s), 983 (m); MS (EI): *m*/*z* 277 (91), 245 (100), 219 (49), 159 (30), 131 (52), 115 (58), 87 (77), 55 (36); HRMS (ESI): calcd for $C_{16}H_{19}O_6$ $[M + H]^+$: 307.1182, found: 307.1178; Anal. calcd for $C_{16}H_{18}O_6$: C, 62.7; H, 5.9; found: C, 62.7; H, 5.8.

(2*E*, 9*E*)-Dimethyl-4,8-dihydroxyundeca-2,9-dienedioate (5p). Following the general procedure, **5p** was obtained from **4p** (156 mg, 1.0 mmol) as a colourless solid (176 mg, 82%), mp 82–84 °C, as a mixture of diastereomers. The general procedure was modified by using increased amounts of catalyst **A** (85 mg, 10 mol%) and methyl acrylate (1.80 mL, 20.0 mmol). Analytical data were obtained from the mixture. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.92 (dm, J = 15.6, 2H), 6.02 (d, J = 15.6, 2H), 4.30 (2H), 3.72 (s, 6H), 2.81 (bs, 2H), 1.75–1.40 (6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.1 (0), 150.4 (1), 119.7 (1), 70.7 (1), 70.6 (1), 51.7 (3), 36.0 (2), 36.0 (2), 20.9 (2), 20.9 (2); IR (neat): ν 3427 (m), 2950 (w), 1706 (s), 1276 (s), 1171 (s), 982 (s); MS (EI): *m*/*z* 255 (16), 223 (54), 191 (54), 162 (43), 140 (100), 111 (76), 83 (94), 55 (74); HRMS (ESI): calcd for $C_{13}H_{20}O_6Na$ $[M + Na]^+$: 295.1158, found: 295.1164; Anal. calcd for $C_{13}H_{20}O_6$: C, 57.3; H, 7.4, found: C, 57.2; H, 7.4.

General procedure for tandem cross metathesis–isomerization

To a solution of the corresponding allyl alcohol (1.0 mmol) and methyl acrylate (0.9 mL, 10.0 mmol) in dry toluene (1.0 mL) was added Ru-catalyst **A** (42.5 mg, 5 mol%). The solution was heated to 110 °C for 0.5 h, cooled to ambient temperature, and excess methyl acrylate was removed *in vacuo*. The residue was re-dissolved in toluene (5.0 mL), and either NaOH (60 mg, 1.5 mmol) was added and the mixture was heated to reflux (oil bath temperature 130 °C) for 3 h (method A), or PMHS (16 μL, 0.2 mmol) was added and the mixture was heated to reflux (oil bath temperature = 130 °C) for 12 h (method B).

Work-up procedure for method A: The reaction mixture was hydrolyzed, and the aqueous layer was extracted twice with MTBE. The combined organic layers were washed with brine, dried with $MgSO_4$, filtered and all volatiles were removed *in vacuo*. The residue was purified by column chromatography on silica, using hexane–MTBE mixtures of increasing polarity.

Work-up procedure for method B: All volatiles were removed *in vacuo* and the residue was purified by column chromatography, on silica, using hexane–MTBE mixtures of increasing polarity.

(*S*)-Methyl-5-(*tert*-butyldimethylsilyloxy)-4-oxohexanoate (6a). Following the general procedure, **6a** was obtained from **4a** (200 mg, 0.92 mmol) *via* method A (178 mg, 70%) or *via* method B (193 mg, 76%) as a colourless liquid. $[\alpha]_D^{26}$ = −8.2 (*c* = 0.63, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.18 (q, J = 6.8, 1H), 3.66 (s, 3H), 2.97 (ddd, J = 19.1, 6.8, 6.6, 1H), 2.83 (ddd, J = 19.1, 6.8, 5.9, 1H), 2.57 (ddd, J = 6.8, 5.9, 2.5, 1H), 2.56 (ddd, J = 6.7, 6.6, 3.1, 1H), 1.29 (d, J = 6.8, 3H), 0.91 (s, 9H), 0.08 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.8 (0), 173.6 (0), 75.2 (1), 52.1 (3), 32.4 (2), 27.7 (2), 26.1 (3), 21.2 (3), 18.4 (0), −4.3 (3), −4.7 (3); IR (neat): ν 2930 (m), 2857 (m), 1741 (s), 1721 (s), 1116 (s), 832 (s), 776 (s); MS (EI) *m*/*z* 275 (19), 259 (21), 243 (100), 213 (9), 185 (11), 143 (82), 111 (29); HRMS (ESI) calcd for $C_{13}H_{27}O_4Si$ $(M + H^+)$: 275.1679, found: 275.1653; Anal. calcd for $C_{13}H_{26}O_4Si$: C, 56.9; H, 9.6; found: C, 57.1; H: 9.6.

Methyl 4-oxo-4-phenylbutanoate (6b). Following the general procedure, **6b** was obtained from **4b** (134 mg, 1.0 mmol) *via* method A (160 mg, 83%) or *via* method B (136 mg, 71%) as a colourless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.98 (ddd, J = 7.1, 1.5, 1.0, 2H), 7.56 (tt, J = 7.3, 1.3, 1H), 7.45 (ddd, J = 7.6, 7.3, 1.3, 2H), 3.70 (s, 3H), 3.32 (t, J = 6.6, 2H), 2.76 (t, J = 6.6, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.9 (0), 173.2 (0), 136.6 (0), 133.1 (1), 128.6 (1), 128.0 (1), 51.7 (3), 33.4 (2), 28.0 (2); IR (neat): ν 2952 (w), 1734 (s), 1684 (s), 1218 (s), 1162 (s), 751 (s), 690 (s); MS (EI): *m*/*z* 192 (10, $[M + H]^+$), 185 (30), 159 (52), 105 (100), 77 (40), 73 (55), 45 (80); HRMS (EI): calcd for $C_{11}H_{12}O_3$ $[M]^+$: 192.0786, found: 192.0783; Anal. calcd for $C_{11}H_{12}O_3$: C, 68.7; H, 6.3, found: C, 68.4; H, 6.8.

Methyl-4-(4-bromophenyl)-4-oxobutanoate (6c). Following the general procedure, **6c** was obtained from **4c** (213 mg, 1.0 mmol) *via* method A (170 mg, 63%) or *via* method B (182 mg, 67%) as a colourless solid, mp 45–47 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (ddd, J = 8.7, 2H), 7.61 (ddd, J = 8.7, 2H), 3.70 (s, 3H), 3.27 (t, J = 6.5, 2H), 2.76 (t, J = 6.6, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.0 (0), 173.2 (0), 135.3 (0), 131.9 (1), 129.5 (1), 128.4 (0), 51.8 (3), 33.3 (2), 27.9 (2); IR (neat): ν 2952 (w), 1734 (s), 1686 (s), 1585 (s), 1218 (s), 1167 (s), 1070 (s), 816 (s); MS (EI): m/z 272 (13), 270 (15, $[M]^+$), 241 (12), 239 (15), 185 (90), 183 (100), 157 (20), 155 (22), 76 (17), 75 (15); HRMS (EI): calcd for $C_{11}H_{11}O_3Br$ $[M]^+$: 269.9892, found: 269.9884; Anal. calcd for $C_{11}H_{11}O_3Br$: C, 48.7; H, 4.1, found: C, 48.5; H, 4.1.

Methyl-4-(4-methoxyphenyl)-4-oxobutanoate (6d). Following the general procedure, **6d** was obtained from **4d** (164 mg, 1.0 mmol) *via* method A (99 mg, 45%) or *via* method B (160 mg, 72%) as a colourless solid, mp 43–45 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (ddd, J = 8.9, 2H), 6.90 (ddd, J = 8.9, 2H), 3.82 (s, 3H), 3.66 (s, 3H), 3.23 (t, J = 6.7, 2H), 2.71 (t, J = 6.7, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.4 (0), 173.3 (0), 163.5 (0), 131.9 (1), 130.1 (1), 129.6 (0), 113.6 (1), 55.3 (3), 51.6 (3), 32.8 (2), 28.0 (2); IR (neat): ν 2984 (m), 1738 (s), 1678 (s), 1602 (s), 1257 (s), 1167 (s), 1030 (s), 833 (m); MS (EI): m/z 223 (5, $[M + H]^+$), 222 (17, $[M]^+$), 191 (15), 177 (7), 136 (10), 135 (100), 107 (8), 92 (8), 77 (10); HRMS (EI): calcd for $C_{12}H_{14}O_4$ $[M]^+$: 222.0892, found: 222.0894; Anal. calcd for $C_{12}H_{14}O_4$: C, 64.9; H, 6.4, found: C, 65.0; H, 6.5.

Methyl-4-(3-methoxy-4-(methoxymethoxy)-phenyl)-4-oxobutanoate (6e). Following the general procedure, **6e** was obtained from **4e** (224 mg, 1.0 mmol) *via* method A (183 mg, 65%) or *via* method B (193 mg, 68%) as a colourless solid, mp 74–75 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 (dd, J = 8.4, 2.0, 1H), 7.53 (d, J = 2.0, 1H), 7.16 (d, J = 8.4, 1H), 5.28 (s, 2H), 3.91 (s, 3H), 3.68 (s, 3H), 3.49 (s, 3H), 3.27 (t, J = 6.6, 2H), 2.73 (t, J = 6.6, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.7, 173.4, 150.8, 149.4, 130.8, 122.3, 114.3, 110.5, 94.9, 56.4, 55.9, 51.8, 32.9, 28.1; IR (neat): ν 2953 (w), 1735 (m), 1676 (m), 1511 (m), 1417 (m), 1262 (s), 1155 (s), 1138 (s), 1080 (s), 980 (s); MS (EI): m/z 283 (32, $[M + H]^+$), 282 (57, $[M]^+$), 251 (45), 181 (38), 165 (30), 151 (10), 137 (18), 115 (23), 45 (100); HRMS (EI): calcd for $C_{14}H_{18}O_6$ $[M]^+$: 282.1103, found: 282.1103; Anal. calcd for $C_{14}H_{18}O_6$: C, 59.6; H, 6.4, found: C, 59.5; H, 6.7.

Methyl-4-(4-(*tert*-butyldimethylsilyloxy)phenyl)-4-oxobutanoate (6f). Following the general procedure, **6f** was obtained from **4f** (264 mg, 1.0 mmol) *via* method A (84 mg, 27%) or *via* method B (225 mg, 70%) as a colourless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (ddd, J = 8.7, 2H), 6.87 (ddd, J = 8.7, 2H), 3.69 (s, 3H), 3.26 (t, J = 6.7, 2H), 2.74 (t, J = 6.7, 2H), 0.97 (s, 9H), 0.22 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.6 (0), 173.4 (0), 160.4 (0), 130.2 (1), 119.9 (1), 51.7 (3), 33.0 (2), 28.1 (2), 25.5 (3), 18.2 (0), −4.4 (3); IR (neat): ν 2932 (w), 1739 (s), 1680 (s), 1597 (s), 1255 (s), 1161 (s), 906 (s), 832 (s), 781 (s); MS (EI): m/z 322 (38, $[M]^+$), 291 (31), 265 (100), 235 (50), 209 (49), 179 (30), 135 (25), 89 (50), 55 (20); HRMS (EI): calcd for $C_{17}H_{26}O_4Si$ $[M]^+$: 322.1600, found: 322.1600; Anal. calcd for $C_{17}H_{26}O_4Si$: C, 63.3; H, 8.1, found: C, 63.3; H, 8.0.

Methyl-4-(4-benzyloxyphenyl)-4-oxobutanoate (6g). Following the general procedure, **6g** was obtained from **4g** (240 mg, 1.0 mmol) *via* method B (212 mg, 71%) as a colourless solid, mp 70–71 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (dm, J = 8.9, 2H), 7.46–7.30 (5H), 7.01 (dm, J = 8.9, 2H), 5.13 (s, 2H), 3.70 (s, 3H), 3.27 (t, J = 6.7, 2H), 2.75 (t, J = 6.7, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.4 (0), 173.4 (0), 162.7 (0), 136.2 (0), 130.3 (1), 129.9 (0), 128.6 (1), 128.2 (1), 127.4 (1), 114.6 (1), 70.1 (2), 51.7 (3), 33.0 (2), 28.1 (2); IR (neat): ν 3021 (w), 1734 (m), 1676 (m), 1599 (m), 1218 (s), 1165 (s), 746 (s); MS (EI): m/z 299 (13, $[M + H]^+$), 298 (18, $[M]^+$), 267 (6), 211 (5), 115 (15), 91 (100); HRMS (EI): calcd for $C_{18}H_{18}O_4$ $[M]^+$: 298.1205, found: 298.1205; Anal. calcd for $C_{18}H_{18}O_4$: C, 72.5; H, 6.1, found: C, 72.0; H, 6.2.

Methyl-4-(2-fluorophenyl)-4-oxobutanoate (6h). Following the general procedure, **6h** was obtained from **4h** (152 mg, 1.0 mmol) *via* method A (143 mg, 68%) or *via* method B (159 mg, 76%) as a colourless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (td, J = 7.7, 1.9, 1H), 7.50 (m, 1H), 7.21 (ddd, J = 8.4, 7.9, 1.1, 1H), 7.12 (ddd, J = 11.3, 8.3, 0.9, 1H), 3.69 (s, 3H), 3.30 (td, J = 6.6, 3.3, 2H), 2.73 (t, J = 6.5, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.2 (d, J = 4.1, 0), 173.2 (0), 162.1 (d, J = 254.8, 0), 134.7 (d, J = 8.8, 1), 130.6 (d, J = 2.5, 1), 125.1 (d, J = 3.2, 0), 124.4 (d, J = 3.4, 1), 116.6 (d, J = 23.8, 1), 51.7 (3), 38.2 (d, J = 8.4, 2), 28.0 (d, J = 2.3, 2); IR (neat): ν 2953 (w), 1734 (s), 1686 (s), 1609 (s), 1452 (s), 1212 (s), 1166 (s), 1152 (s), 762 (s); MS (EI): m/z 210 (8, $[M]^+$), 179 (8), 135 (30), 123 (100), 95 (15), 75 (11); HRMS (EI): calcd for $C_{11}H_{11}O_3F$ $[M]^+$: 210.0692, found: 210.0700.

Methyl-4-oxo-5-phenylpentanoate (6i). Following the general procedure, **6i** was obtained from **4i** (148 mg, 1.0 mmol) *via* method A (136 mg, 66%) or *via* method B (132 mg, 64%) as a colourless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37–7.17 (5H), 3.74 (s, 2H), 3.65 (s, 3H), 2.76 (t, J = 6.6, 2H), 2.56 (t, J = 6.6, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.2 (0), 173.0 (0), 134.0 (0), 129.4 (1), 128.7 (1), 127.0 (1), 51.6 (3), 50.0 (2), 36.4 (2), 27.8 (2); IR (neat): ν 2952 (w), 1716 (s), 1357 (m), 1200 (s), 1174 (s), 700 (s); MS (EI): m/z 206 (15, $[M]^+$), 175 (20), 115 (100), 91 (63), 55 (26); HRMS (EI): calcd for $C_{12}H_{14}O_3$ $[M]^+$: 206.0943, found: 206.0930; Anal. calcd for $C_{12}H_{14}O_3$: C, 69.9; H, 6.8, found: C, 69.4; H, 7.0.

Methyl-4-oxo-6-phenylhexanoate (6j). Following the general procedure, **6j** was obtained from **4j** (162 mg, 1.0 mmol) *via* method A (175 mg, 80%) or *via* method B (160 mg, 73%) as a colourless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.15 (5H), 3.67 (s, 3H), 2.92 (td, J = 6.9, 2.4, 2H), 2.79 (td, J = 7.1, 2.3, 2H), 2.71 (t, J = 6.6, 2H), 2.59 (t, J = 6.6, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.8 (0), 173.1 (0), 140.9 (0), 128.4 (1), 128.2 (1), 126.1 (1), 51.7 (3), 44.2 (2), 37.2 (2), 29.6 (2), 27.6 (2); IR (neat): ν 2951 (w), 1735 (s), 1713 (s), 1362 (m), 1204 (s), 1174 (s), 699 (s); MS (EI): m/z 221 (18, $[M + H]^+$), 220 (55, $[M]^+$), 188 (60), 105 (75), 91 (100), 55 (18); HRMS (EI): calcd for $C_{13}H_{16}O_3$ $[M]^+$: 220.1099, found: 220.1100; Anal. calcd for $C_{13}H_{16}O_3$: C, 70.9; H, 7.3, found: C, 70.6; H, 7.6.

Methyl-6-methyl-4-oxoheptanoate (6k). Following the general procedure, **6k** was obtained from **4k** (114 mg, 1.0 mmol) *via* method A (76 mg, 44%) or *via* method B (105 mg, 61%) as a colourless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.62 (s, 3H), 2.66 (t, J = 6.5, 2H), 2.53 (t, J = 6.5, 2H), 2.28 (d, J = 6.8, 2H), 2.12 (tq, J = 6.6, 1.2, 1H), 0.88 (d, J = 1.2, 3H), 0.86 (d, J = 1.2, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.5 (0), 173.1 (0), 51.6 (3), 51.6 (2), 37.5 (2), 27.6 (2), 24.6 (1), 22.4 (3); IR (neat): ν 2956 (m), 1738 (s), 1712 (s), 1363 (s), 1206 (s), 1167 (s); MS (EI): m/z 134 (24), 115 (26), 98 (38), 85 (42), 71 (43), 57 (100), 43 (63); HRMS (ESI): calcd for $C_9H_{17}O_3$ $[M + H]^+$: 173.1178, found: 173.1194; Anal. calcd for $C_9H_{16}O_3$: C, 62.8; H, 9.4, found: C, 62.6; H, 9.6.

(*R*)-Methyl-4-oxo-4-(1,4-dioxaspiro[4.5]decan-2-yl)-butanoate (6l). Following the general procedure, **6l** was obtained from **4l** (198 mg, 1.0 mmol) *via* method A (105 mg, 41%) or *via* method B (171 mg, 67%) as a colourless liquid. $[\alpha]_{24}^{D}$ = +13.9 (c 0.37, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.45 (dd, J = 7.7, 5.7, 1H), 4.18 (dd, J = 8.7, 7.7, 1H), 4.01 (dd, J = 8.7, 5.7, 1H), 3.66 (s, 3H), 3.04–2.81 (2H), 2.64–2.55 (2H), 1.76–1.50 (8H), 1.50–1.34 (2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.3 (0), 173.0 (0), 111.7 (0), 79.9 (1), 66.1 (2), 51.7 (3), 35.6 (2), 34.5 (2), 33.4 (2), 27.1 (2), 25.0 (2), 23.9 (2), 23.7 (2); IR (neat): ν 2931 (w), 1253 (m), 1090 (m), 832 (s), 775 (s); MS (EI): m/z 256 (15, $[M]^+$), 213 (55), 141 (100), 115 (15), 83 (17), 55 (32); HRMS (EI): calcd for $C_{13}H_{20}O_5$ $[M]^+$: 256.1311, found: 256.1309; Anal. calcd for $C_{13}H_{20}O_5$: C, 60.9; H, 7.9, found: C, 60.9; H, 8.0.

Methyl-4-oxononanoate (6m). Following the general procedure, **6m** was obtained from **4m** (128 mg, 1.0 mmol) *via* method A (79 mg, 42%) or *via* method B (122 mg, 65%) as a colourless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.63 (s, 3H), 2.68 (t, J = 6.3, 2H), 2.54 (t, J = 6.3, 2H), 2.40 (t, J = 7.5, 2H), 1.62–1.47 (2H), 1.35–1.15 (4H), 0.85 (t, J = 6.9, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.9 (0), 173.2 (0), 51.6 (3), 42.6 (2), 31.3 (2), 27.6 (2), 23.4 (2), 22.3 (2), 13.8 (3); IR (neat): ν 2930 (m), 1738 (s), 1715 (s), 1361 (m), 1198 (m), 1166 (m); MS (EI): m/z 155 (23), 130 (39), 115 (42), 98 (95), 71 (70), 57 (89), 43 (100); HRMS (ESI): calcd for $C_{10}H_{19}O_3$ $[M + H]^+$: 187.1334, found: 187.1334; Anal. calcd for $C_{10}H_{18}O_3$: C, 64.5; H, 9.7, found: C, 64.2; H, 9.8.

Methyl-4-oxoheptanoate (6n). Following the general procedure, **6n** was obtained from **4n** (100 mg, 1.0 mmol) *via* method A (89 mg, 56%) or *via* method B (110 mg, 70%) as a colourless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.63 (s, 3H), 2.68 (t, J = 6.3, 2H), 2.54 (t, J = 6.3, 2H), 2.40 (t, J = 7.4, 2H), 1.58 (tq, J = 7.4, 7.4, 2H), 0.88 (t, J = 7.4, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.8 (0), 173.2 (0), 51.6 (3), 44.6 (2), 36.9 (2), 27.6 (2), 17.2 (2), 13.6 (3); IR (neat): ν 2960 (w), 1737 (s), 1713 (s), 1362 (m), 1205 (s), 1165 (s); MS (EI): m/z 148 (23), 134 (33), 115 (55), 98 (48), 71 (88), 57 (77), 43 (100); HRMS (ESI): calcd for $C_8H_{15}O_3$ $[M + H]^+$: 159.1021, found: 159.1029; Anal. calcd for $C_8H_{14}O_3$: C, 60.7; H, 8.9, found: C, 60.5; H, 9.2.

Dimethyl-4,4′-(1,4-phenylen)bis(4-oxobutanoate) (6o). Following the general procedure, **6o** was obtained from **4o** (190 mg, 1.0 mmol) *via* method A (167 mg, 55%) or *via* method B (114 mg, 37%) as a colourless solid, mp 116–117 °C. The general procedure was modified by using increased amounts of catalyst **A** (85 mg, 10 mol%) and methyl acrylate (1.80 mL, 20.0 mmol). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (s, 4H), 3.71 (s, 6H), 3.33 (t, J = 6.5, 4H), 2.78 (t, J = 6.5, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.5 (0), 173.1 (0), 139.8 (0), 128.3 (1), 51.9 (3), 33.8 (2), 27.9 (2); IR (neat): ν 2952 (w), 1722 (s), 1682 (s), 1213 (s), 1162 (s), 754 (s); MS (EI): m/z 306 (7, $[M]^+$), 275 (20), 219 (100), 159 (17), 104 (15), 55 (6); HRMS (EI): calcd for $C_{16}H_{18}O_6$ $[M]^+$: 306.1103, found: 306.1098; Anal. calcd for $C_{16}H_{18}O_6$: C, 62.7; H, 5.9, found: C, 62.7; H, 5.9.

Dimethyl-4,8-dioxoundecandioate (6p). Following the general procedure, **6p** was obtained from **4p** (156 mg, 1.0 mmol) *via* method B (116 mg, 43%) as a colourless liquid. The general procedure was modified by using increased amounts of catalyst **A** (85 mg, 10 mol%) and methyl acrylate (1.80 mL, 20.0 mmol). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.65 (s, 6H), 2.68 (t, J = 6.8, 4H), 2.56 (t, J = 6.6, 4H), 2.48 (t, J = 7.1, 4H), 1.86 (quint, J = 7.0, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.3 (0), 173.1 (0), 51.7 (3), 41.4 (2), 37.0 (2), 27.7 (2), 17.1 (2); IR (neat): ν 2953 (w), 1733 (s), 1712 (s), 1362 (m), 1198 (s), 1171 (s); MS (EI): m/z 273 (10, $[M + H]^+$), 255 (41), 223 (41), 167 (42), 153 (72), 125 (54), 115 (100), 97 (46), 55 (67); HRMS (ESI): calcd for $C_{13}H_{20}O_6Na$ $[M + Na]^+$: 295.1158, found: 295.1153; Anal. calcd for $C_{13}H_{20}O_6$: C, 57.3; H, 7.4, found: C, 56.8; H, 7.7.

Synthesis of protected L-amicetose

(*R*)-5-((*S*)-1-(*tert*-Butyldimethylsilyloxy)ethyl)-dihydro-furan-2(3H)-one (7). To a solution of **5a** (300 mg, 1.1 mmol) in dry and degassed methanol (20 mL) was added Pd/C (30 mg, 10 wt%). The suspension was stirred for 12 h in an atmosphere of hydrogen (1 bar). The mixture was filtered through a pad of Celite®, and the pad was washed three times with MTBE. Evaporation of the solvents furnished **7** (235 mg, 88%) as a colourless liquid. $[\alpha]_D^{26}$ = +13.3 (c 0.55, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.33 (ddd, J = 8.1, 5.5, 3.2, 1H), 4.06 (qd, J = 6.4, 3.2, 1H), 2.55 (ddd, J = 17.7, 10.2, 7.0, 1H), 2.44 (ddd, J = 17.7, 10.0, 6.6, 1H), 2.27 (dddd, J = 12.6, 10.1, 6.7, 5.6, 1H), 2.22 (m, 1H), 1.13 (d, J = 6.5, 3H), 0.87 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.4 (0), 83.5 (1), 68.8 (1), 28.5 (2), 25.8 (3), 23.6 (0), 20.9 (2), 19.5 (3), −4.8 (3), −4.9 (3); IR (neat): ν 2930 (m), 2857 (m), 1776 (s), 1082 (m), 834 (s), 776 (s); MS (EI): m/z 245 (35, $[M + H]^+$), 242 (69), 227 (37), 185 (17), 113 (100); HRMS (ESI): calcd for $C_{12}H_{25}O_3Si$ $[M + H]^+$: 245.1573, found: 245.1593; Anal. calcd for $C_{12}H_{24}O_3Si$: C, 59.0; H, 9.9, found: C, 58.9; H, 10.2.

(4*R*, 5*S*, *E*)-Methyl-5-(*tert*-butyldimethylsilyloxy)-4-(methoxy-methoxy)-hex-2-enoate (8a). To a solution of **5a** (300 mg, 1.1 mmol) in dry dichloromethane (20 mL) were added ^{i}Pr$_2$EtN (0.8 mL, 4.4 mmol) and MOM-bromide (0.3 mL, 3.2 mmol, 90%). The solution was heated to reflux for 12 h, cooled to ambient temperature and hydrolyzed. The aqueous layer was separated and extracted twice with MTBE. The combined organic layers were dried with $MgSO_4$, filtered and all volatiles were removed *in vacuo*. After purification by column chromatography on silica, using hexane–MTBE mixtures as the eluent,

8a was obtained as a colourless liquid (280 mg, 81%). $[\alpha]_{22}^{D}$ −38.0 (*c* 0.50, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.86 (dd, *J* = 15.8, 6.3, 1H), 6.01 (dd, *J* = 15.9, 1.3, 1H), 4.63 (s, 2H), 4.04 (ddd, *J* = 6.3, 5.0, 1.3, 1H), 3.83 (qd, *J* = 6.2, 5.1, 1H), 3.74 (s, 3H), 3.37 (s, 3H), 1.17 (d, *J* = 6.2, 3H), 0.87 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.8 (0), 146.3 (1), 123.3 (1), 95.5 (2), 80.3 (1), 71.1 (1), 56.1 (3), 51.8 (3), 26.1 (3), 18.4 (0), −4.3 (3), −4.5 (3); IR (neat): ν 2953 (w), 2932 (w), 1728 (s), 1102 (s), 1032 (s), 832 (s), 775 (s); MS (EI): *m*/*z* 159 (34), 89 (29), 73 (74), 45 (100); HRMS (ESI): calcd for $C_{15}H_{31}O_5Si$ $[M + H]^+$: 319.1941, found: 319.1938; Anal. calcd for $C_{15}H_{30}O_5Si$: C, 56.6; H, 9.5, found: C, 56.3; H, 9.6.

(4*R*, 5*S*)-Methyl-5-(*tert*-butyldimethylsilyloxy)-4-(methoxymethoxy)-hex-2-enoate (9a)

Hydrogenation catalyzed by Pd/C. To a solution of **8a** (150 mg, 0.47 mmol) in dry and degassed methanol (10 mL) was added Pd/C (15 mg, 10 wt%). The suspension was stirred for 12 h in an atmosphere of hydrogen (1 bar). The mixture was filtered through a pad of Celite®, and the pad was washed three times with MTBE. Evaporation of the solvents gave **9a** (151 mg, quantitative) as a colourless liquid.

Reduction with modified Stryker's reagent. $Cu(OAc)_2{\cdot}H_2O$ (10 mg, 5 mol%) and BDP (4.5 mg, 10 mol%) were dissolved in dry and degassed toluene (2.0 mL) and *tert*-butanol (1.5 mL). The mixture was stirred for 10 min at ambient temperature, and PMHS (134 μL, 2.0 mmol) was added. Stirring was continued for 0.5 h, after which time the colour changed from blue to green. A solution of **8a** (318 mg, 1.0 mmol) in toluene (1.0 mL) was added and the solution was stirred at ambient temperature for 12 h. The reaction mixture was diluted with MTBE, and washed with a saturated aqueous $NaHCO_3$ solution, followed by aqueous HCl (1 M). The aqueous layer was extracted twice with MTBE, and the combined organic layers were dried with $MgSO_4$. Purification by column chromatography on silica, using hexane–MTBE as an eluent, furnished **9a** (266 mg, 96%) as a colourless liquid. $[\alpha]_{22}^{D}$ = +22.1 (*c* 0.66, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.75 (d, *J* = 6.7, 1H), 4.62 (d, *J* = 6.7, 1H), 3.80 (qd, *J* = 6.3, 3.7, 1H), 3.66 (s, 3H), 3.44 (dt, *J* = 3.9, 3.9, 1H), 3.38 (s, 3H), 2.55–2.32 (2H), 1.90–1.67 (2H), 1.12 (d, *J* = 6.3, 3H), 0.87 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.1 (0), 96.5 (2), 80.9 (1), 70.4 (1), 56.1 (3), 55.8 (3), 51.8 (3), 30.3 (2), 25.9 (2), 25.8 (3), 19.1 (3), 18.0 (0), −4.5 (3), −4.9 (3); IR (neat): ν 2953 (w), 2932 (w), 1740 (s), 1253 (s), 1100 (s), 1032 (s), 832 (s); MS (EI): *m*/*z* 289 (7), 233 (40), 201 (100), 187 (19), 159 (84), 113 (27), 89 (32), 73 (53), 45 (41); HRMS (ESI): calcd for $C_{15}H_{33}O_5Si$ $[M + H]^+$: 321.2097, found: 321.2124; Anal. calcd for $C_{15}H_{32}O_5Si$: C, 56.2; H, 10.1, found: C, 56.1; H, 9.9.

(4*R*, 5*S*, *E*)-Methyl-4-(benzyloxymethoxy)-5-(*tert*-butyldimethylsilyloxy)-hex-2-enoate (8b). To a solution of **5a** (1.30 g, 4.70 mmol) in dry dichloromethane (20 mL) were added ^{i}Pr$_2$EtN (1.3 mL, 7.05 mmol) and BOM-chloride (0.8 mL, 6.10 mmol), and the solution was heated to reflux for 12 h. The reaction mixture was hydrolyzed and the aqueous layer was extracted twice with MTBE. The combined organic layers were dried with $MgSO_4$, filtered and all volatiles were removed *in vacuo*. After purification by column chromatography on silica, using hexane–MTBE as an eluent, **8b** was obtained as a colourless liquid (1.72 g, 93%). $[\alpha]_{24}^{D}$ = −39.4 (*c* 0.73, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38–7.27 (5H), 6.90 (dd, *J* = 15.8, 6.5, 1H), 6.04 (dd, *J* = 15.8, 1.3, 1H), 4.79 (d, *J* = 6.9, 1H), 4.75 (d, *J* = 6.9, 1H), 4.67 (d, *J* = 11.8, 1H), 4.58 (d, *J* = 11.8, 1H), 4.12 (ddd, *J* = 6.3, 5.0, 1.2, 1H), 3.85 (qd, *J* = 6.2, 5.1, 1H), 3.75 (s, 3H), 1.19 (d, *J* = 6.2, 3H), 0.88 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4 (0), 145.9 (1), 137.6 (0), 128.4 (1), 127.8 (1), 127.7 (1), 123.0 (1), 93.0 (2), 80.0 (1), 70.6 (1), 69.7 (2), 51.5 (3), 25.7 (3), 19.9 (3), 18.0 (0), −4.6 (3), −4.8 (3); IR (neat): ν 2930 (w), 1724 (m), 1034 (m), 753 (s); MS (EI): *m*/*z* 307 (8), 257 (19), 159 (48), 91 (100), 73 (31); HRMS (ESI): calcd for $C_{21}H_{34}O_5SiNa$ $[M + Na]^+$: 417.2073, found: 417.2083; Anal. calcd for $C_{21}H_{34}O_5Si$: C, 63.9; H, 8.7, found: C, 63.8; H, 8.9.

(4*R*, 5*S*)-Methyl-4-(benzyloxymethoxy)-5-(*tert*-butyldimethylsilyloxy)-hex-2-enoate (9b). Following the procedure stated above for **9a**, the title compound **9b** was obtained from **8b** (395 mg, 1.0 mmol) as a colourless liquid (375 mg, 95%). $[\alpha]_{24}^{D}$ = +36.9 (*c* 0.52, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39–7.27 (5H), 4.88 (d, *J* = 6.8, 1H), 4.80 (d, *J* = 6.8, 1H), 4.70 (d, *J* = 11.9, 1H), 4.59 (d, *J* = 11.9, 1H), 3.85 (qd, *J* = 6.3, 3.7, 1H), 3.65 (s, 3H), 3.54 (dt, *J* = 3.9, 3.9, 1H), 2.59–2.34 (2H), 1.95–1.75 (2H), 1.15 (d, *J* = 6.3, 3H), 0.89 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.1 (0), 137.9 (0), 128.4 (1), 127.7 (1), 127.6 (1), 94.4 (2), 80.9 (1), 70.2 (1), 69.8 (2), 51.4 (3), 30.2 (2), 25.8 (3), 25.7 (2), 19.1 (3), 18.0 (0), −4.5 (3), −4.9 (3); IR (neat): ν 2954 (w), 2858 (w), 1740 (s), 1255 (s), 1104 (s), 1037 (s), 834 (s); MS (EI): *m*/*z* 309 (12), 201 (22), 159 (27), 91 (100), 73 (20); HRMS (ESI): calcd for $C_{21}H_{37}O_5Si$ $[M + H]^+$: 397.2410, found: 397.2415; Anal. calcd for $C_{21}H_{36}O_5Si$: C, 63.6; H, 9.2, found: C, 63.1; H, 9.3.

(5*R*, 6*S*)-5-(Benzyloxymethoxy)-6-methyl-tetrahydropyran-2-one (10). To a solution of **9b** (250 mg, 0.63 mmol) in THF (10 mL) was added TBAF (248 mg, 0.95 mmol). The reaction mixture was stirred at ambient temperature for 12 h. Then aqueous NaOH (5%, 10 mL) was added and the solution was stirred for 2 h at 40 °C. After neutralization with aqueous HCl (1 M, 10 mL) the aqueous layer was extracted several times with ethyl acetate and the organic layer was dried with $MgSO_4$. Purification by column chromatography on silica, using hexane–ethyl acetate as an eluent, furnished **10** (107 mg, 68%) as a colourless liquid. $[\alpha]_{24}^{D}$ = −64.1 (*c* 0.49, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39–7.27 (5H), 4.85 (d, *J* = 7.2, 1H), 4.81 (d, *J* = 7.2, 1H), 4.64 (d, *J* = 11.9, 1H), 4.60 (d, *J* = 11.9, 1H), 4.45 (qd, *J* = 6.3, 6.2, 1H), 3.72 (ddm, *J* = 5.6, 4.4, 1H), 2.70 (ddd, *J* = 17.6, 9.5, 7.2, 1H), 2.48 (ddd, *J* = 17.6, 6.4, 5.3, 1H), 2.10 (dddd, *J* = 13.9, 10.7, 6.5, 4.3, 1H), 2.01–1.87 (1H), 1.38 (d, *J* = 6.5, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5 (0), 137.3 (0), 128.4 (1), 127.8 (1), 127.7 (1), 93.2 (2), 78.3 (1), 72.9 (1), 70.0 (2), 26.4 (2), 23.2 (2), 19.3 (3); IR (neat): ν 2941 (w), 1731 (s), 1030 (s), 741 (m); MS (EI): *m*/*z* 114 (18), 107 (15), 91 (100), 85 (65), 65 (14), 43 (20); HRMS (ESI): calcd for $C_{14}H_{18}O_4Na$ $[M + Na]^+$: 273.1103, found: 273.1100; Anal. calcd for $C_{14}H_{18}O_4$: C, 67.2; H, 7.3, found: C, 67.1; H, 7.2.

(5*R*, 6*S*)-5-(Benzyloxymethoxy)-6-methyl-tetrahydro-2*H*-pyran-2-ol (11). To a solution of **10** (66 mg, 0.26 mmol) in dry CH_2Cl_2 (1.3 mL) was added DIBAL-H (0.77 mL, 1.02 M solution in cyclohexane, 0.78 mmol) dropwise at −78 °C. The solution was stirred for 0.25 h and then quenched at this temperature by the addition of MeOH (1.3 mL). A saturated aqueous solution of Na^+/K^+-tartrate (2 mL) was added at ambient temperature and the mixture was repeatedly extracted with MTBE. The combined organic layers were dried with $MgSO_4$ and concentrated under reduced pressure to furnish **11** (57 mg, 86%, a 1 : 1 mixture of anomeric lactols in $CHCl_3$) as a colourless liquid. $[\alpha]_D^{22}$ = −59.0 (*c* 0.53, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.27 (5H), 4.21 (dm, *J* = 2.6, 0.5H), 4.89 (d, *J* = 7.1, 0.5H), 4.85 (d, *J* = 7.0, 0.5H), 4.82–4.76 (0.5H), 4.77 (d, *J* = 3.3, 0.5H), 4.74 (d, *J* = 3.2, 0.5H), 4.63 (s, 1H), 4.62 (s, 1H), 3.98 (qd, *J* = 6.3, 2.9, 0.5H), 3.48 (qd, *J* = 6.1, 2.9, 0.5H), 3.38–3.23 (1H), 2.25–2.16 (0.5H), 2.03–1.64 (2.5H), 1.60–1.45 (1H), 1.32 (d, *J* = 6.1, 1.5H), 1.26 (d, *J* = 6.2, 1.5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.7 (0), 137.6 (0), 128.4 (1), 128.4 (1), 127.8 (1), 127.8 (1), 127.7 (1), 127.7 (1), 95.7 (1), 93.3 (2), 93.0 (2), 90.7 (1), 77.2 (1), 76.5 (1), 74.7 (1), 69.6 (2), 69.5 (2), 67.9 (1), 31.8 (2), 29.3 (2), 28.1 (2), 23.9 (2), 18.3 (3), 18.2 (3); IR (neat): ν 3405 (m), 2936 (m), 1453 (w), 1032 (s), 989 (s); MS (EI): *m*/*z* 235 (7), 190 (5), 129 (12), 91 (100), 87 (41), 69 (13); HRMS (ESI): calcd for $C_{14}H_{20}O_4Na$ $[M + Na]^+$: 275.1259, found: 275.1269.

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