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Ring-rearrangement metathesis of substituted dihydropyrans and dihydrofurans

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ABSTRACT

The rearrangement of dihydropyrans and dihydrofurans featuring appending olefins has been studied. The rearranged products bear resemblance with polyunsaturated di- and trisaccharides. Examples of functionalization prior to, or following, rearrangement are provided suggesting that the method should be useful for the synthesis of nonclassical saccharides. This work also illustrates the power of cascade methatetic processes for increasing molecular complexity starting from relatively simple heterocycles.

1. Introduction

For some time, we have been interested in the Ring-Rearrangement Metathesis (RRM)[1] of oxygen heterocycles as a method for accessing complex, polycyclic, oxygenated molecules. The principle of our approach, which is summarized in Fig. 1, A, consists in subjecting a substrate **A**, containing one or two unsaturated oxygen heterocycles bearing olefinic appendages to metathesis conditions using Grubbs second generation catalyst ([**Ru**]-2, Fig. 1). During the reaction, there is extensive reorganization of bonds and rings and the product **B** bears little resemblance to the substrate. Therefore, the method is expected to be useful for synthesizing otherwise difficult to prepare molecules from relatively simple precursors. One may conceive many possible variations of this general principle: in particular the method should be applicable to the preparation of di- or trisaccharides. Although several efficient methods exist for the preparation of classical oligosaccharides, they are almost invariably based on the coupling of activated monosaccharide units. While this is convenient when using readily available sugars, problems may arise when dealing with uncommon natural or synthetic saccharides and in this case, nontraditional methods may compete.[2]

2. Results and discussion

In recent, exploratory work, we reported the metathesis-based preparation of simple unsaturated disaccharides e.g., **2** from the dihydropyran derivatives **1** (see Fig. 1, B) and the conversion of **2** to a simple polydeoxydisaccharide.[3] The method was subsequently extended to the preparation of polyunsaturated trisaccharides, e.g., **4** from the bis-dihydropyran derivative **3**, using an extended Ring-Closing Metathesis–Ring-Opening Metathesis (RCM–ROM) sequence (Fig. 1, C).[3b]

During these studies we observed that the success of the reaction depended on a number of steric/electronic factors and that the dihydropyrans we used as RRM substrates behaved differently from their carbocyclic (cyclohexenes) counterpart.[4] Our initial studies and the conclusions that could be drawn regarding disaccharide synthesis are summarized in Fig. 1, B.[3a,5] (Experimental and analytical data corresponding to the synthesis of compounds in Fig. 1B are described in the Supplementary data). Briefly:

1. Initiation at the anomeric olefin does not appear to be productive with respect to the expected RRM. The success of the rearrangement requires the initiation step to take place on the 4-*O*-allyl or homoallyl side chain. As a consequence, electron-poor acrylates, 3-butenoyl esters (likely chelate formation)[6] and more surprisingly acrolein ketals, being unsuitable for initiation, no reaction is observed).
2. A cis relationship between the C-4 and C-5 substituents is required see (Fig. 2B).
3. The configuration at the anomeric carbon (α or β) is not important with regard to RRM (see Fig. 2B).

We have attempted to understand the reasons behind the above limitations. It is well established that in some RCM substrates,

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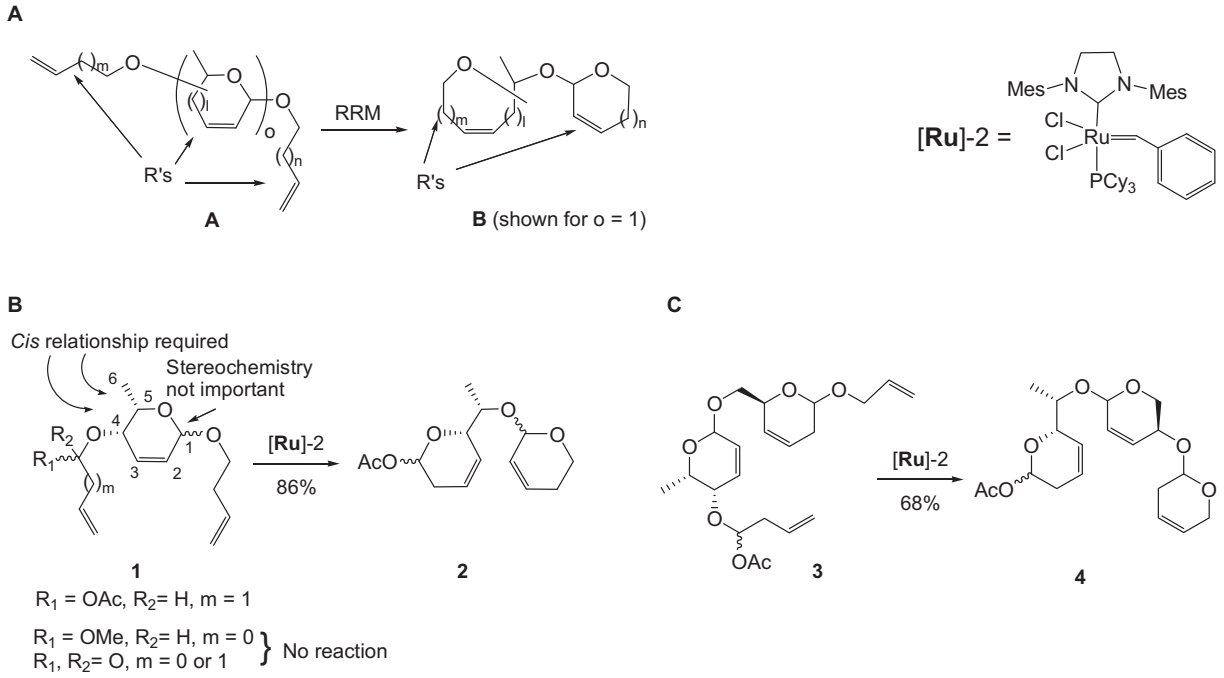


Fig. 1. Examples of RRMs leading to unsaturated saccharides.

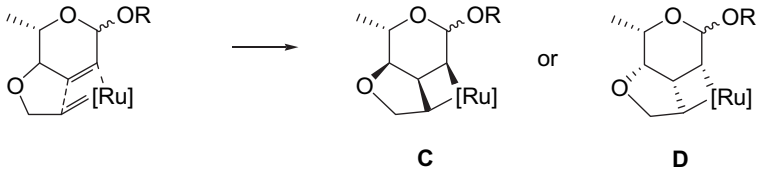


Fig. 2. Transition states for the RRM of trans and cis substrates.

stable 5, 6, or to a lesser extent 7, membered chelates may be formed by complexation of the initial ruthenium carbene by neighboring oxygen-containing functions and that this complexation may inhibit metathesis.[7] In our case it is conceivable that the carbene formed by putative initiation at the anomeric olefin site is sequestered in a way that prevents the ROM to proceed. That α,β-ethylene ketals seem not to be suitable as initiation sites for the RRM is surprising but it is worth noting that although there are numerous literature examples of ethylene ketals participating in RCM, cases in which their involvement at the initiation step has been demonstrated are very rare.[7]

Finally, that a cis relationship between the C-4 and C-5 substituents is required for the RRM to succeed is not unexpected as many examples of RCM successes or failures have been linked to the relative configurations of substituents proximal to the olefinic double bonds of the substrates. It is well established that following initiation, success requires adequate prepositioning of the carbenoid and olefinic double bond so that the strained fused ruthenacyclobutane intermediate can be formed. Generally, failure can be explained by considering steric factors that would hinder access to such fairly rigid bicyclic systems. In our case, the tricyclic intermediates **C** and **D** arise from trans and cis substrates, respectively (Fig. 2).[4] In such completely locked systems, steric/electronic factors are expected to play a crucial role. At the present time however, inspection of molecular models of the possible transition states **C** and **D** do not reveal obvious strain differences that could account for the observed large reactivity difference between trans and cis substrates.

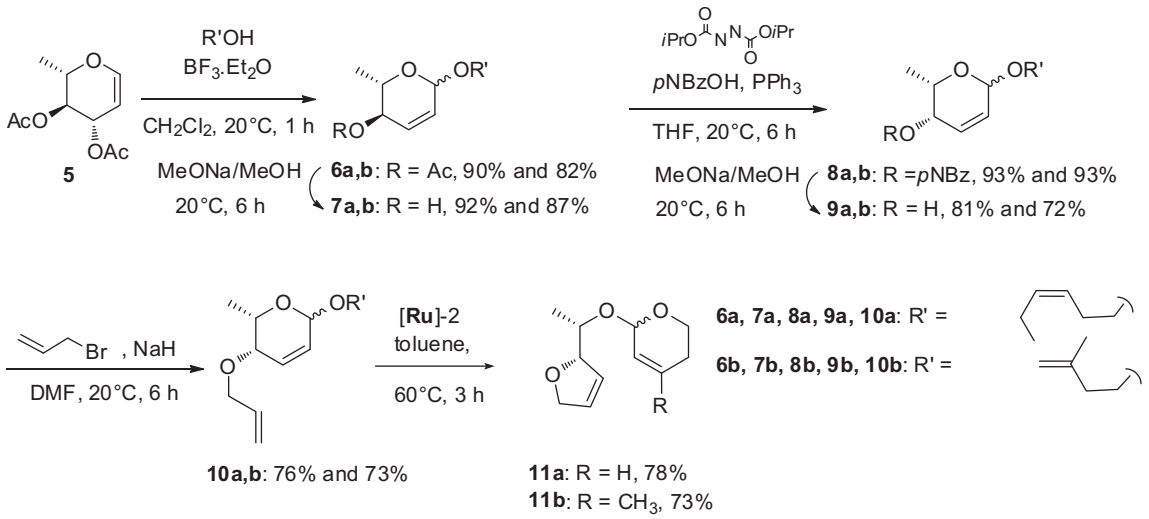
2.1. Dihydropyran-based substrates

Following these initial results, the next step of our program focused on broadening the scope of the method by: (a) increasing the complexity of the RRM substrate and/or chemical modification of the RRM products and (b) using alternative heterocyclic relays.

We first checked that the anomeric olefin could be modified. According to our earlier observations the anomeric olefin intervenes only at the last step of the metathesis cascade therefore we were confident that extensive structural variation should be possible. For the sake of simplicity, we selected for this study the 4-*O*-allyl group as initiation site since it led to good results in our previous exploratory work. Two RRM substrates (**10a** and **10b**) were then prepared by a short sequence starting with Ferrier rearrangement of glycal **5** (commercially available), using hex-3-en-1-ol and 3-methylbut-3-en-1-ol, respectively, as alcohols. As expected, when submitted to RCM conditions a good yield of rearranged products **11a** and **11b** was obtained, suggesting (**11b**) that branched disaccharides could be prepared by this method (Scheme 1).

We then examined another family of RRM substrates derived from 2-allyloxy-6-(hydroxymethyl)-3,6-dihydro-2*H*-pyran **17** (Scheme 2). In these substrates, the endocyclic double bond has been shifted from the 3,4 (as used previously) to the 4,5 position (pyran numbering) and the appending olefins are simple allyloxy groups. Rearrangement should give rise to a new type of disaccharide-like molecules. These substrates were prepared as shown in Scheme 3.

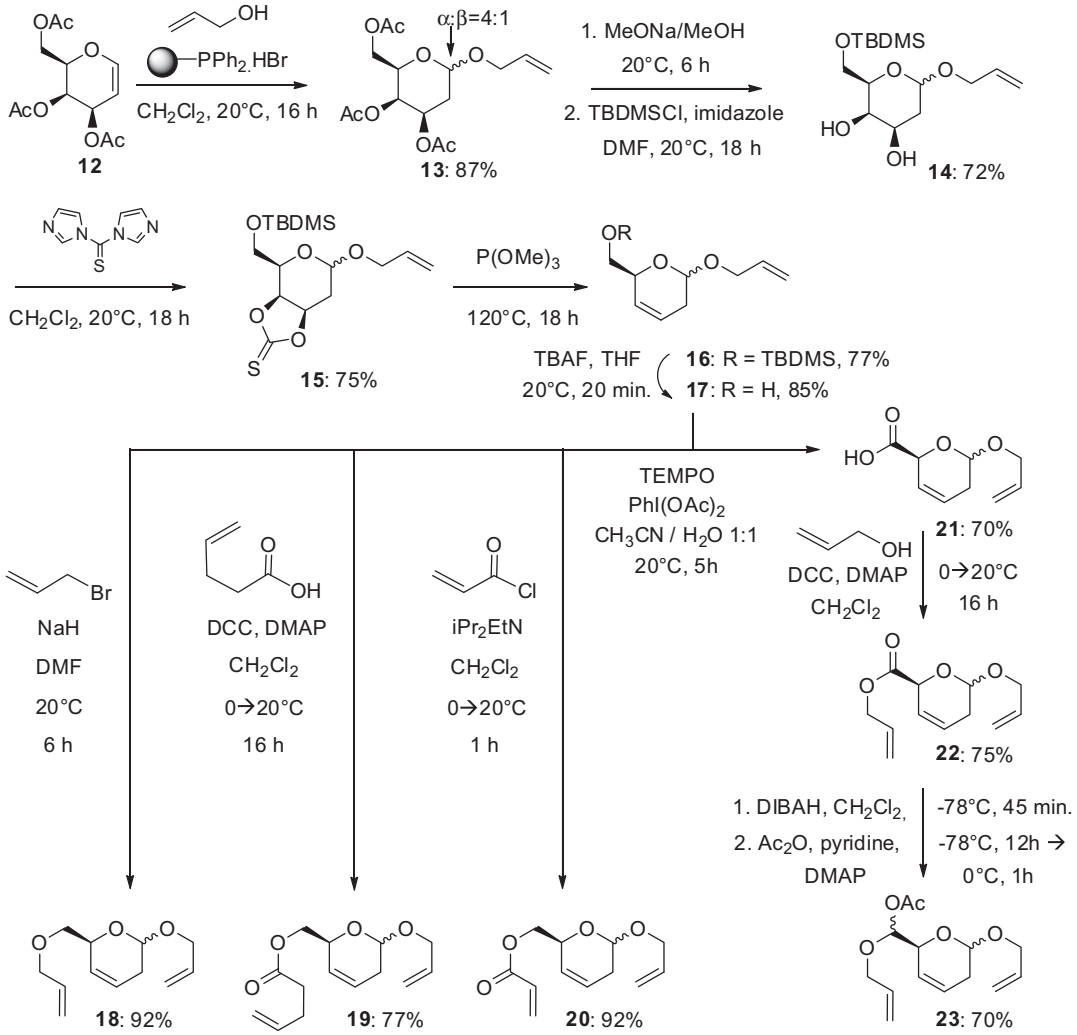
Treatment of tri-*O*-acetyl-D-galactal **12** with allylic alcohol and polymer-supported triphenylphosphine. HBr complex afforded



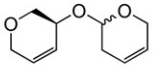
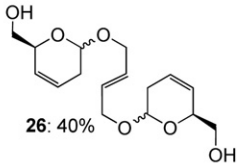
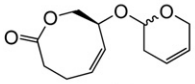
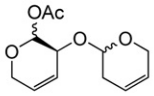
Scheme 1. RRM of 2,5-disubstituted dihydropyrans.

allyl 2-deoxy-3,4-di-*O*-acetyl-D-galactopyranoside **13** as a 4:1 α/β mixture.[8] Standard deacetylation and selective primary alcohol silylation provided diol **14**, which was converted to diene **17** by Corey–Winter olefination.[9] Compound **17** was converted to the RCM substrates **18**, **19**, and **20** by O-alkylation (**18**) and O-acylation (**19** and **20**).

For the preparation of substrates **22** and **23**, we needed to convert **17** to the carboxylic acid **21**. After failing to effect a classical two-step oxidation using several methods (1. TPAP[10]/NMO or IBX[11] or TEMPO, $PhI(OAc)_2$[12] and 2. $NaClO_2$) we found out that direct oxidation using TEMPO, $PhI(OAc)_2$[13] proceeded well to afford the sensitive acid **21** in good yield, which was converted to the corresponding allyl ester **22**.



Scheme 2. RRM of 2,6-disubstituted dihydropyran: preparation of the substrates.

RRM substrate	Conditions	RRM product / yield	RRM substrate	Conditions	RRM product / yield
				a	NR
18	a	 **24**: 84%	**17**	b	 **26**: 40%
19	a	 **25**: 66%	**22**	a	NR
20	a	NR	**23**	a	 **27**: 74%

a) Substrate 0.002 M in toluene, [**Ru**]-2, 5 mol%, 70°C, 3h. b) Substrate 0.1M in toluene, [**Ru**]-2, 5 mol%, 70°C, 3h

Scheme 3. RRM of 2,6-disubstituted dihydropyrans.

Low temperature reduction/acetylation according to Rychnovsky et al.[14] afforded the unsaturated ketal **23**.

The RRM results are reported in Scheme 3. Using standard metathesis conditions (substrate concentration 0.002 M in toluene, [**Ru**]-2, 5 mol %, 70 °C, 3 h), precursors **18** and **19** reacted smoothly to afford the corresponding ring-rearranged products **24** and **25** in good yield. In contrast the acrylic ester **20** remained unchanged. As expected, allyl ester **22** did not cyclize (there is probably formation of a stable ruthenium complex as proposed by Fürstner)[6] but the mixed ketal **23** afforded in good yield the simple unsaturated disaccharide **27**.

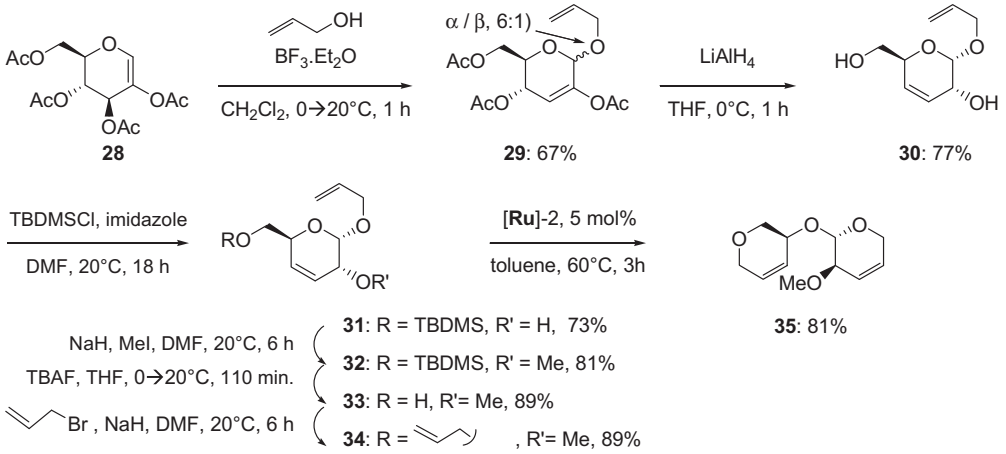
These results are very similar to those obtained in our earlier studies:[3] for the RRM to proceed, initiation of the metathetic process should take place at the olefin distal from the anomeric position. Should this not be possible either for electronic reasons (**20**) or because a stable complex may be formed following initiation (**22**), no reaction is observed. That initial formation of a metalcarbene at the anomeric position does not lead to RRM is further confirmed when using alcohol **17** as substrate. One would expect a mixture of two pyran derivatives to be observed: **17** and the rearranged product **17′** (Fig. 3). In fact, at low substrate concentration (0.003 M) no reaction takes place and in more concentrated solutions (0.1 M) only formation of dimer **26** (Scheme 3) is observed.

Fig. 3. Expected products during rearrangement of **17**.

The method also works with more functionalized substrates as shown in Scheme 4. The triene **34** was prepared in a few steps from tri-*O*-acetyl-2-acetoxy-D-glucal **28**. Ferrier reaction of the latter with allyl alcohol[15a,b] afforded the 2-acetoxy-2,3-unsaturated glycoside **29**, which upon treatment with $LiAlH_4$ collapsed to the rearranged glycoside **30** in good yield. A short protection/deprotection sequence of the primary hydroxyl group allowed the sequential methylation of 2-OH (carbohydrate numbering) and allylation of 6-OH providing the RRM substrate **34**, which smoothly rearranged to **35** upon exposure to [**Ru**]-2.

2.2. Dihydrofuran-based substrates

Another way of increasing the versatility of the method would be to switch to other types of RRM substrates leading to different olefin patterns in the rearranged product. An obvious development of this



Scheme 4. RRM of 2,6-disubstituted dihydropyrans.

work is the use of dihydrofurans instead of dihydropyrans as relay moieties (Fig. 4).

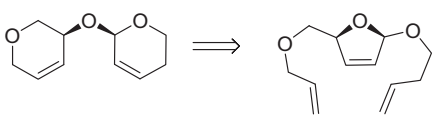


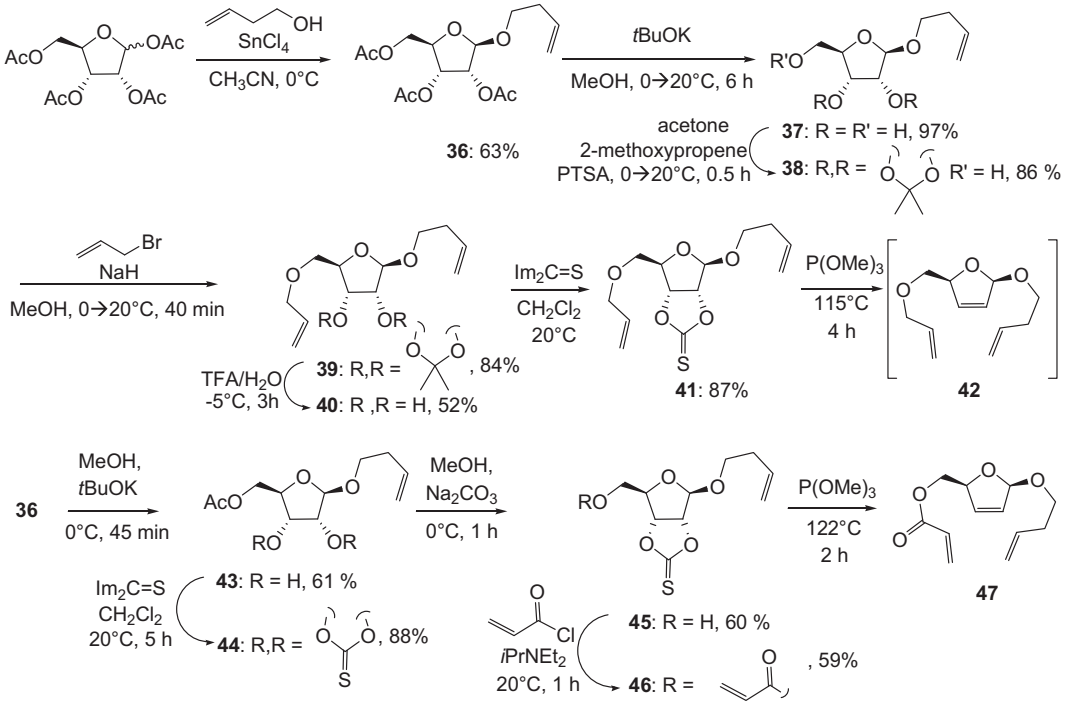
Fig. 4. Example of RRM with dihydrofuran relays.

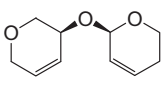
The synthesis of the required substituted dihydrofuran substrates is shown in Scheme 5: tetra-*O*-acetyl-D-ribofuranose (commercially available) was first converted to the β-homoallylribofuranoside **36**. Removal of the acetates, selective protection of 2-OH and 3-OH by acetonide formation and allylation of 5-OH afforded intermediate **39**. After cleavage of the acetonide, treatment by 1,1′-(thiocarbonyl)diimidazole (TCDI) afforded the thiocarbonate **41**, which, upon heating in trimethylphosphite, furnished the sensitive crude triene **41**.[16a] Alternatively, selective removal of the 2- and 3-acetates in **36**[16b] and treatment by TCDI led to thiocarbonate **44**, which was converted in a few steps (acetate removal, acrylate formation, Corey–Winter olefin formation), to the crude RRM substrate **47**. The RRM results are reported in Scheme 5: the triene **42** afforded cleanly the rearranged product **48**. In contrast, the acrylate **47** did not react. As observed earlier, using dihydropyrans as relays (see Scheme 1), successful RRM apparently requires the initiation step to take place on the olefin distal to the anomeric position. This is possible in **42** but not in **47**.

Thus we could show that provided certain structural requirements in the substrates are respected, RRM is a valid approach to simple disaccharides. We could also show that utilization of functionalized RRM substrates (e.g., **23** and **34**) and dihydrofurans (e.g., **42**) as relays is possible, thereby further broadening the scope of the method. The RRM products feature two olefinic double bonds, whose position is determined by the choice of the RRM substrate and which should be easily functionalized by conventional methods, giving rise to various 1-deoxy disaccharide-analogues.

The remaining problem is linked to the unexpected lack of reactivity of acrolein ketals (e.g., **20**), which restricts the variety of substrates that can be used. Indeed, although 1-deoxy-2,3-unsaturated disaccharides such as **11**, **24** or **35** are readily obtained by rearrangement of allyl ether-containing substrates, direct access to 'real' disaccharides would require using the corresponding non-reactive acrolein ketals.

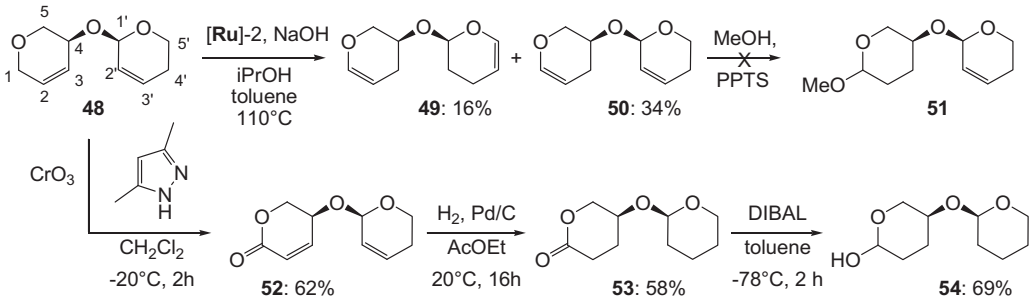
An appealing solution to this problem would be to perform the functionalization after the RRM has taken place and the key question is whether one can perform a selective oxidation at C-1 in 1-deoxy-2,3-unsaturated disaccharides, such as **11**, **24**, **35** or **48**. For these studies **48** was chosen as model compound (Scheme 6). We initially attempted to selectively shift the 2,3-olefinic double bond in **48** to the 1,2 position using [**Ru**]-2, as described by Schmidt,[17] with the aim of converting the resulting glycal **50** to the corresponding 2-deoxy disaccharide. Unfortunately **50** could never be obtained in useful yield without simultaneous formation of the undesired isomer **49** in which both the 2,3 and the 2′,3′ double bonds have migrated. Furthermore, despite numerous attempts, we



RRM substrate	Conditions	RRM product / yield	RRM substrate	Conditions	RRM product / yield
42*	a	 **48**: 58%	**47**	a	NR

a) Substrate 0.002 M in toluene, [**Ru**]-2, 5 mol%, 60°C, 30 min. * Crude Corey-Winter product was used

Scheme 5. RRM of 2,5-disubstituted dihydrofurans.



Scheme 6. Functionalization of RRM products.

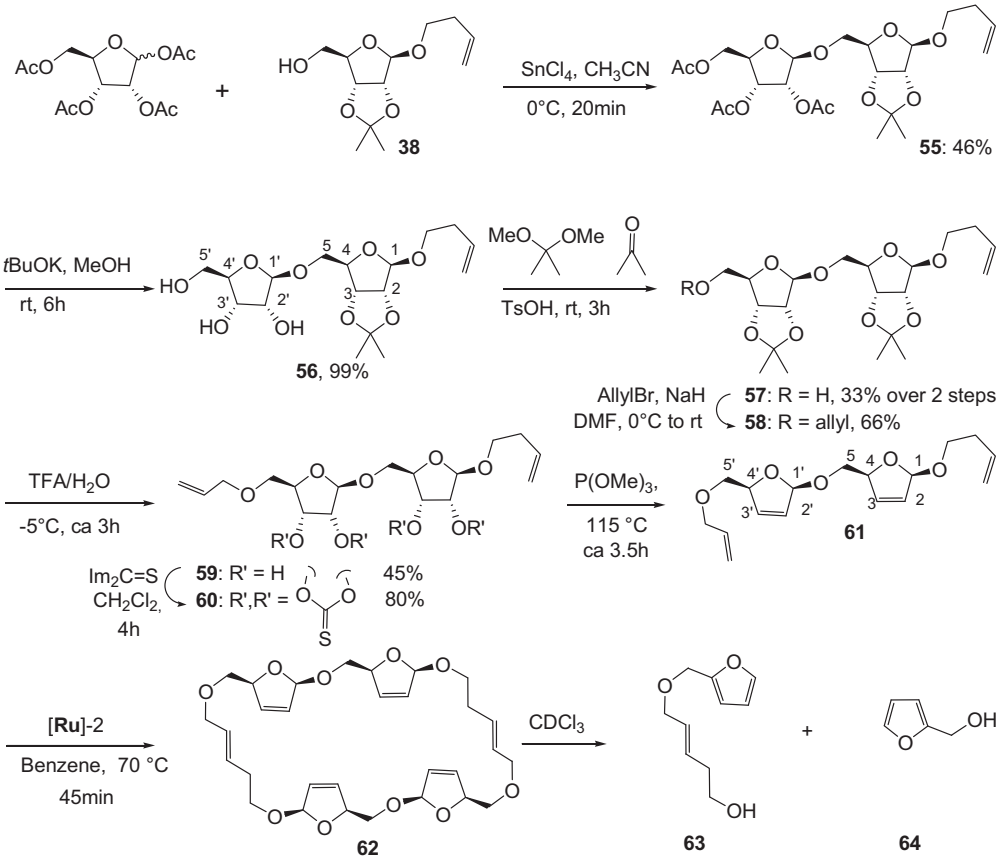
were unable to cleanly convert the vinyl ether moiety in **50** to the desired corresponding *O*-methyl *O*-methyl polydeoxyglycoside **51**. It is likely that the sensitive α,β-unsaturated ketal also present in the molecule does not stand the acidic conditions of the reaction.

We were more successful when performing a direct, regioselective, CrO_3 oxidation at the C-1 allylic position which led cleanly to lactone **52**.[18] Catalytic hydrogenation of both olefinic double bonds in **52** and DIBAL reduction of the lactone **53** afforded the simple polydeoxydisaccharide **54**.

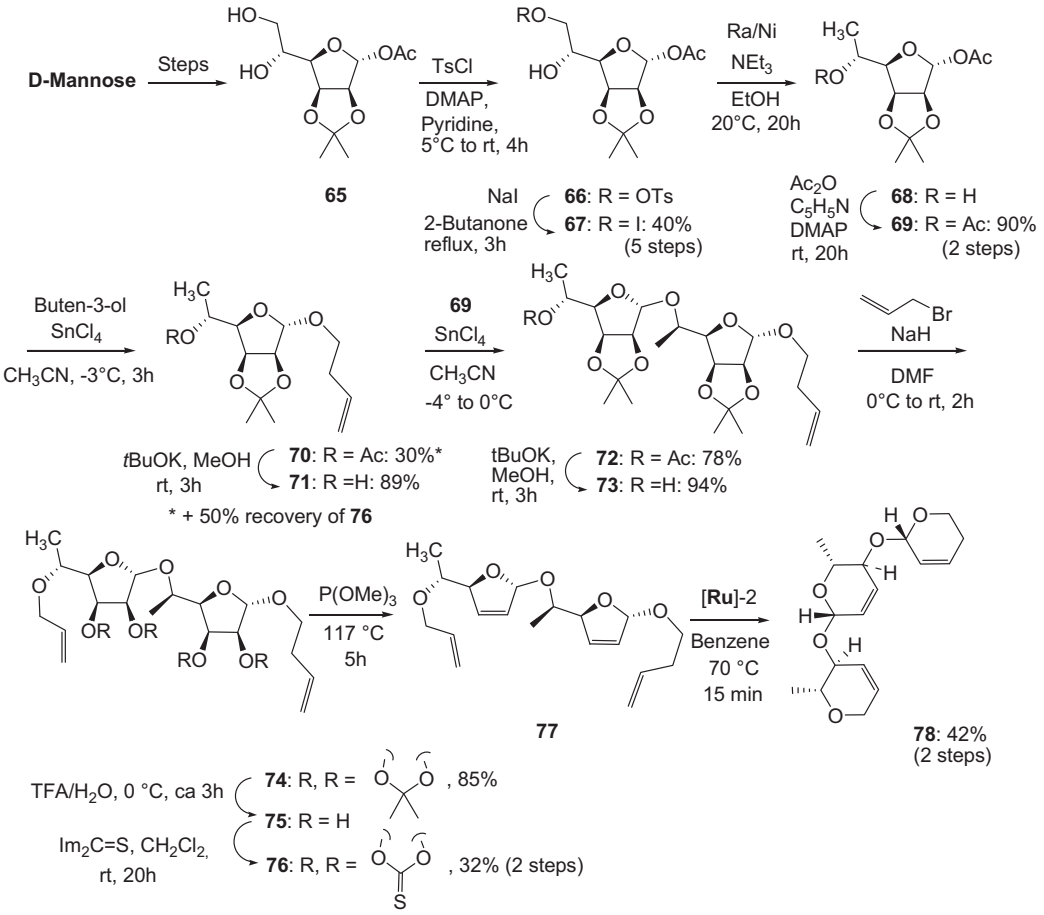
It is worth mentioning that in lactone **52** the two olefinic double bonds have different chemical reactivities and should be easily functionalized independently.

Having explored the scope of the method with regard to disaccharide synthesis, we turned our attention to more elaborated targets involving more complex metathetic rearrangements. We had already shown that trisaccharide analogues could be synthesized by RRM, using dihydropyran relays (see Fig. 1, C) and we deemed it worthwhile to examine whether dihydrofuran relays could be used for the same purpose. Our initial attempts (Scheme 7) used ribose as a readily available starting material and involved the construction of a tetraene applying the methodology developed previously.

Tetra-*O*-acetyl-D-ribofuranose was condensed with ribofuranoside **38** to afford the protected disaccharide **55**. Deacetylation and isopropylidene formation produced **57** in which only the unprotected primary hydroxyl group OH-5′ is available for allylation. The intermediate **58** thus obtained is converted in a few steps to the crude RRM substrate **61**. The RRM results were unexpected and disappointing: in contrast to the facile conversion **42**→**48** (Scheme 5), only dimer **62** was formed. The structure of this dimer was determined by NMR of **62** and of the decomposition products **63** and **64**, which are cleanly and rapidly formed upon standing of **62** in $CDCl_3$ solution. Although we cannot offer a clear explanation to this (in our view) surprising behavior, it is well established that in olefin metathesis apparently minor structural differences may result in important changes in reactivity and we suspected that the cis relationship between the C1, C4 and C1′, C4′ substituents in **61** might be responsible for the RRM failure. To check this possibility we decided to prepare an 'all trans' substrate with respect to C1, C4 and C1′, C4′ and to examine the effects of this modification on the reaction course.



Scheme 7. Failed trisaccharide synthesis by RRM of 2,5-disubstituted dihydrofurans.



Scheme 8. Trisaccharide synthesis by RRM of 2,5-disubstituted dihydrofurans.

This study is summarized in Scheme 8. The synthesis started from the known intermediate **65**, easily prepared in a few steps from mannose.[19] Selective tosylation of the primary hydroxyl in **65** and displacement of the tosyl group by iodine was followed by reduction using Raney nickel to afford the 6-deoxy mannose derivative **68**. The latter was converted to glycoside **71**, which was condensed with **69** to furnish the protected α-disaccharide **72**. Finally, deacetylation, allylation and Corey–Winter olefin formation provided the crude tetraene **77**. We were pleased to observe that in sharp contrast with the 'all cis' substrate **61**, the 'all trans' **77** smoothly rearranged to the expected 1-deoxy unsaturated trisaccharide **78**. The behavior of **61** and **77** with respect to metathesis is puzzling as no obvious structural difference can be identified explaining the considerable reactivity difference between these two substrates (cross-metathesis followed by macrocycle formation for **61** and RRM for **77**). While one can assume that initiation should be similar in **61** and **77**, subtle steric factors must operate during the propagation step, which change dramatically the course of the reaction.

3. Conclusion

In summary, several trienes and tetraenes were synthesized containing built-in dihydropyran or dihydrofuran moieties. They were designed to serve as relays in domino metathesis processes in a new approach to di- or trisaccharides. The method was successfully applied to the preparation of a series of advanced, versatile, intermediates structurally close to di- or trisaccharides. We could show that regioselective functionalization of these intermediates is possible either prior to, or following, the rearrangement, thereby suggesting that unusual di- or trisaccharides as well as otherwise difficult to prepare related analogues such as 1-deoxy saccharides are indeed reachable using our approach.

From the methodological viewpoint, the method illustrates again the power of ring-rearrangement metathesis regarding access to complex molecules from readily available starting materials. Except in simple cases (formation of medium-size rings), the difficulty of predicting the course of a particular metathesis is a known problem and our work is no exception: why certain conversions (e.g., **77**→**78**) work well whereas others (e.g., RRM of **61**) fail despite apparent close similarities is unclear and this lack of predictability constitutes an obvious limitation of the method. Despite this drawback, we are confident that the RRM approach can be used for the preparation of natural, uncommon, saccharides. This work is underway in our laboratory.

4. Experimental section

4.1. (2*S*,3*R*)-6-((*Z*)-Hex-3-enyloxy)-2-methyl-3,6-dihydro-2*H*-pyran-3-yl acetate (6a)

Under argon, to a solution of 3,4-di-*O*-acetyl L-rhamnal (870 mg, 3.25 mmol, 1 equiv) in dichloromethane (5 mL) was added *cis*-3-hexen-1-ol (587 μL, 4.87 mmol, 1.5 equiv). At 0 °C, 4 drops of $BF_3 \cdot Et_2O$ were added and the resulting solution was allowed to warm up slowly to room temperature. After 1 h, the reaction was quenched with $NaHCO_{3(aq)}$ (15 mL) and extracted with ethyl acetate (3×15 mL). The organic layers were combined, washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash column chromatography with silica gel (10% EtOAc in cyclohexane) provided 744 mg (2.92 mmol, 90%) of the title

compound as a clear, pale yellow oil. The compound was obtained as an anomeric mixture (α/β=6:1). ^{1}H NMR ($CDCl_3$, 300 MHz) major isomer: δ 5.83 (m, 2H), 5.47 (m, 1H), 5.35 (m, 1H), 5.05 (m, 1H), 4.97 (s, 1H), 3.98 (m, 1H), 3.76 (m, 1H), 3.51 (m, 1H), 2.36 (q, *J*=7.0 Hz, 2H), 2.07 (s, 3H), 2.03 (m, 2H), 1.22 (d, *J*=6.3 Hz, 3H), 0.97 (t, *J*=7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) major isomer: δ 170.5, 133.8, 129.5, 127.8, 124.6, 94.2, 70.8, 68.2, 64.7, 27.9, 21.1, 20.6, 17.9, 14.2. LRMS calcd for $C_{14}H_{22}NaO_4$ [M+Na] 277.14, found 277.

4.2. (2*S*,3*R*)-2-Methyl-6-(3-methylbut-3-enyloxy)-3,6-dihydro-2*H*-pyran-3-yl acetate (6b)

Under argon, to a solution of 3,4-di-*O*-acetyl L-rhamnal (2 g, 9.34 mmol, 1 equiv) in dichloromethane (15 mL) was added 3-methyl-3-buten-1-ol (1.42 mL, 14 mmol, 1.5 equiv). At 0 °C, 8 drops of $BF_3 \cdot Et_2O$ were added and the resulting solution was allowed to warm up slowly to room temperature. After 1 h, the reaction was quenched with $NaHCO_{3(aq)}$ (45 mL) and extracted with ethyl acetate (3×45 mL). The organic layers were combined, washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash column chromatography (silica gel, 10% EtOAc in cyclohexane) provided **6b** (1.86 g, 7.72 mmol, 82%) as a clear, pale yellow oil. The compound was obtained as an anomeric mixture (α/β=6:1). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.83 (m, 2H), 5.03 (dd, *J*=1.3, 9.1 Hz, 1H), 4.96 (s, 1H), 4.78 (s, 1H), 4.73 (s, 1H), 3.91 (m, 2H), 3.60 (dt, *J*=6.8, 9.7 Hz, 1H), 2.32 (t, *J*=6.9 Hz, 2H), 2.07 (s, 3H), 1.75 (s, 3H), 1.30 β, 1.21 α (d, *J*=6.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) major isomer: δ 170.5, 142.6, 129.5, 127.7, 111.6, 94.3, 70.8, 66.9, 64.8, 37.8, 22.7, 21.0, 17.9. LRMS calcd for $C_{13}H_{20}NaO_4$ [M+Na] 263.13, found 263.

4.3. (2*S*,3*R*)-6-((*Z*)-Hex-3-enyloxy)-2-methyl-3,6-dihydro-2*H*-pyran-3-ol (7a)

Under argon, to a solution of **6a** (677 mg, 2.66 mmol, 1 equiv) in methanol (35 mL), sodium (183 mg, 7.98 mmol) was added portionwise. The resulting mixture was stirred for 6 h at room temperature, quenched with $NH_4Cl_{(aq)}$ (15 mL) and extracted with ethyl acetate (3×35 mL). Organic layers were combined, washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash column chromatography (silica gel, 40% EtOAc in cyclohexane) provided alcohol **7a** (517 mg, 2.44 mmol, 92%) as a clear, colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.91 (d, *J*=10.0 Hz, 1H), 5.73 (m, 1H), 5.46 (m, 1H), 5.33 (m, 1H), 5.10 β, 4.93 α (s, 1H), 3.77 (m, 3H), 3.49 (m, 1H), 2.34 (q, *J*=7.0 Hz, 2H), 2.05 (p, *J*=7.4 Hz, 2H), 1.35 β, 1.31 α (d, *J*=6.1 Hz, 3H), 0.95 (t, *J*=7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) major isomer: δ 133.8, 133.4, 126.6, 124.6, 94.2, 69.6, 68.1, 67.9, 27.9, 20.6, 17.9, 14.2. HRMS calcd for $C_{12}H_{20}NaO_3$ [M+Na] 235.1310, found 235.1314.

4.4. (2*S*,3*R*)-2-Methyl-6-(3-methylbut-3-enyloxy)-3,6-dihydro-2*H*-pyran-3-ol (7b)

Under argon, to a solution of **6b** (1.75 g, 7.30 mmol, 1 equiv) in methanol (60 mL), sodium (503 mg, 21.90 mmol) was added portionwise. The resulting mixture was stirred for 6 h at room temperature, quenched with $NH_4Cl_{(aq)}$ (30 mL) and extracted with ethyl acetate (3×60 mL). The organic layers were combined, washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash column chromatography (silica gel, 40% EtOAc in cyclohexane) provided 1.26 g (6.34 mmol, 87%) of **7b** as a clear, colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.90 (d, *J*=10.0 Hz, 1H), 5.73 (m, 1H), 5.11 β, 4.93 α (s, 1H), 4.77 (s, 1H), 4.73 (s, 1H), 3.86 (m, 2H), 3.65 (m, 2H), 2.31 (t, *J*=7.0 Hz, 2H), 1.74 (s, 3H), 1.35 *β*, 1.31 α (d, *J*=6.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) major isomer: δ 142.5, 133.4, 126.6, 111.4, 94.3, 69.6, 68.0, 66.8, 37.8, 22.8, 18.0. HRMS calcd for $C_{11}H_{18}NaO_3$ [M+Na] 221.1154, found 221.1158.

4.5. (2*S*,3*S*)-6-((*Z*)-Hex-3-enyloxy)-2-methyl-3,6-dihydro-2*H*-pyran-3-yl 4-nitrobenzoate (8a)

Under argon, to a solution of DIAD (1.42 mL, 7.07 mmol, 1.2 equiv) in THF (15 mL) were added sequentially triphenylphosphine (1.85 g, 7.07 mmol, 1.2 equiv), *p*-nitro-benzoic acid (1.07 g, 7.07 mmol, 1.2 equiv), and finally a solution of alcohol **7a** (1.25 g, 5.88 mmol, 1 equiv) in THF (3 mL). The resulting mixture was stirred for 6 h at room temperature, then concentrated in vacuo, and purified by flash column chromatography with silica gel (20% EtOAc in cyclohexane) to provide *p*-nitro-benzoate **16a** (1.98 g, 5.47 mmol, 93%) as a yellow solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.26 (m, 4H), 6.19 (dd, *J*=5.2, 10.0 Hz, 1H), 6.09 (dd, *J*=3.0, 10.0 Hz, 1H), 5.49 (m, 1H), 5.35 (m, 1H), 5.16 (dd, *J*=2.4, 5.3 Hz, 1H), 5.09 (d, *J*=2.9 Hz, 1H), 4.37 (dq, *J*=2.3, 6.6 Hz, 1H), 3.78 (m, 1H), 3.56 (m, 1H), 2.40 (q, *J*=7.1 Hz, 2H), 2.07 (p, *J*=7.2 Hz, 2H), 1.42 β, 1.29 α (d, *J*=6.6 Hz, 3H), 0.97 (t, *J*=7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) major isomer: δ 164.25, 150.55, 133.90, 131.24, 130.84, 130.60, 125.12, 124.49, 123.44, 94.09, 68.13, 66.64, 64.52, 27.82, 20.61, 16.21, 14.22. LRMS calcd for $C_{19}H_{23}NNaO_6$ [M+Na] 384.14, found 384.

4.6. (2*S*,3*S*)-2-Methyl-6-(3-methylbut-3-enyloxy)-3,6-dihydro-2*H*-pyran-3-yl 4-nitrobenzoate (8b)

Under argon, to a solution of DIAD (1.43 mL, 7.21 mmol, 1.2 equiv) in THF (15 mL) were added sequentially triphenylphosphine (1.85 g, 7.07 mmol, 1.2 equiv), *p*-nitro-benzoic acid (1.09 g, 7.21 mmol, 1.2 equiv), and finally a solution of alcohol **7b** (1.19 g, 6.02 mmol, 1 equiv) in THF (3 mL). The resulting mixture was stirred for 6 h at room temperature, then concentrated in vacuo, and purified by flash column chromatography (silica gel, 20% EtOAc in cyclohexane) to provide 2.07 g (5.91 mmol, 93%) of the title compound as a yellow solid. ^{1}H NMR ($CDCl_3$, 300 MHz) major isomer: δ 8.26 (m, 4H), 6.19 (dd, *J*=5.2, 10.0 Hz, 1H), 6.09 (dd, *J*=3.0, 10.0 Hz, 1H), 5.16 (dd, *J*=2.4, 5.3 Hz, 1H), 5.10 (d, *J*=2.9 Hz, 1H), 4.80 (s, 1H), 4.76 (s, 1H), 4.37 (dq, *J*=2.4, 6.5 Hz, 1H), 3.93 (m, 1H), 3.68 (m, 1H), 2.35 (t, *J*=6.9 Hz, 2H), 1.78 (s, 3H), 1.31 (d, *J*=6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) major isomer: δ 164.2, 150.6, 142.5, 135.2, 131.2, 130.8, 125.2, 123.5, 111.5, 94.2, 66.8, 66.6, 64.6, 37.7, 22.7, 22.0, 21.9, 16.2. LRMS calcd for $C_{18}H_{21}NNaO_6$ [M+Na] 370.13, found 370.

4.7. (2*S*,3*S*)-6-((*Z*)-Hex-3-enyloxy)-2-methyl-3,6-dihydro-2*H*-pyran-3-ol (9a)

Under argon, to a solution of **8a** (1.91 g, 5.47 mg, 1 equiv) in methanol (50 mL), sodium (377 mg, 16.41 mmol) was added portionwise. The resulting mixture was stirred for 6 h at room temperature, quenched with $NH_4Cl_{(aq)}$ (40 mL) and extracted with ethyl acetate (3×50 mL). Organic layers were combined, washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash column chromatography (silica gel, 40% EtOAc in cyclohexane) provided alcohol **9a** (945 mg, 4.45 mmol, 81%) as a clear, yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) major isomer: δ 6.15 (dd, *J*=5.5, 9.9 Hz, 1H), 5.86 (dd, *J*=3, 9.9 Hz, 1H), 5.46 (m, 1H), 5.32 (m, 1H), 4.94 (d, *J*=3.0 Hz, 1H), 4.13 (dq, *J*=2.1, 6.6 Hz, 1H), 3.72 (m, 1H), 3.56 (m, 1H), 3.48 (m, 1H), 2.33 (q, *J*=7.0 Hz, 2H), 2.04 (p, *J*=7.3 Hz, 2H), 1.84 (br s, 1H), 1.28 (d, *J*=6.6 Hz, 3H), 0.95 (t, *J*=7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) major isomer: δ 133.8, 130.3, 128.1, 124.6, 94.3, 67.9, 66.3, 63.9, 27.8, 20.6, 16.1, 14.2. HRMS calcd for $C_{12}H_{20}NaO_3$ [M+Na] 235.1310, found 235.1312.

4.8. (2*S*,3*S*)-2-Methyl-6-(3-methylbut-3-enyloxy)-3,6-dihydro-2*H*-pyran-3-ol (9b)

Under argon, to a solution of **8b** (2.0 g, 5.72 mg, 1 equiv) in methanol (60 mL), sodium (394 mg, 17.2 mmol) was added portionwise. The

resulting mixture was stirred for 6 h at room temperature, quenched with $NH_4Cl_{(aq)}$ (50 mL) and extracted with ethyl acetate (3×60 mL). Organic layers were combined, washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash column chromatography (silica gel, 40% EtOAc in cyclohexane) provided alcohol **9b** (823 mg, 4.17 mmol, 72%) as a clear, yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) major isomer: δ 6.15 (dd, J=5.5, 9.9 Hz, 1H), 5.86 (dd, J=3.1, 9.9 Hz, 1H), 4.95 (d, J=3.1 Hz, 1H), 4.77 (s, 1H), 4.73 (s, 1H), 4.12 (dq, J=2.1, 6.6 Hz, 1H), 3.87 (dt, J=7.1, 9.8 Hz, 1H), 3.59 (dt, J=6.9, 9.7 Hz, 1H), 3.54 (m, 1H), 2.30 (t, J=6.9 Hz, 2H), 1.83 (br s, 1H), 1.74 (s, 3H), 1.28 (d, J=6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) major isomer: δ 142.5, 130.3, 128.0, 111.4, 94.4, 66.6, 66.4, 63.9, 37.7, 22.7, 16.1. HRMS calcd for $C_{11}H_{18}NaO_3$ [M+Na] 221.1154, found 221.1156.

4.9. (2*S*,3*S*)-3-(Allyloxy)-6-((*Z*)-hex-3-enyloxy)-2-methyl-3,6-dihydro-2*H*-pyran (10a)

Under argon, at 0 °C, to a solution of alcohol **9a** (80 mg, 0.38 mmol, 1 equiv) in DMF (1 mL) were added sequentially NaH (14 mg, 0.53 mmol, 1.5 equiv) and allyl bromide (52 μL, 0.61 mmol, 1.3 equiv). The resulting mixture was stirred for 6 h at room temperature, quenched with $NH_4Cl_{(aq)}$ (3 mL) and extracted with ethyl acetate (3×3 mL). The organic layers were combined, washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash column chromatography with silica gel (10% EtOAc in cyclohexane) provided 74 mg (0.29 mmol, 76%) of the title compound as a clear, colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) major isomer: δ 6.13 (dd, J=5.0, 10.2 Hz, 1H), 5.91 (m, 2H), 5.45 (m, 1H), 5.34 (m, 1H), 5.26 (dq, J=1.6, 17.2 Hz, 1H), 5.16 (dq, J=1.3, 10.4 Hz, 1H), 5.00 (d, J=2.9 Hz, 1H), 4.12 (m, 2H), 4.02 (ddt, J=1.3, 5.7, 12.8 Hz, 1H), 3.72 (dt, J=7.2, 9.6 Hz, 1H), 3.49 (dt, J=7.1, 9.6 Hz, 1H), 3.44 (dd, J=2.6, 5.3 Hz, 1H), 2.33 (q, J=7.0 Hz, 2H), 2.04 (p, J=7.4 Hz, 2H), 1.30 (d, J=6.7 Hz, 3H), 0.95 (t, J=7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) major isomer: δ 135.1, 133.7, 129.3, 127.5, 124.6, 116.8, 94.2, 70.0, 69.3, 67.8, 66.2, 27.9, 20.6, 16.2, 14.2. HRMS calcd for $C_{15}H_{24}NaO_3$ [M+Na] 275.1623, found 275.1631.

4.10. (2*S*,3*S*)-3-(Allyloxy)-2-methyl-6-(3-methylbut-3-enyloxy)-3,6-dihydro-2*H*-pyran (10b)

Under argon, at 0 °C, to a solution of alcohol **9b** (80 mg, 0.40 mmol, 1 equiv) in DMF (1 mL) were added sequentially NaH (14 mg, 0.53 mmol, 1.5 equiv) and allyl bromide (52 μL, 0.61 mmol, 1.3 equiv). The resulting mixture was stirred for 6 h at room temperature, quenched with $NH_4Cl_{(aq)}$ (3 mL) and extracted with ethyl acetate (3×3 mL). The organic layers were combined, washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash column chromatography with silica gel (10% EtOAc in cyclohexane) provided 70 mg (0.30 mmol, 73%) of the title compound as a clear, colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) major isomer: δ 6.13 (dd, J=5.2 et 10.1, 1H), 5.96 (dd, J=3.4, 9.9 Hz, 1H), 5.88 (m, 1H), 5.26 (dq, J=1.6, 17.2 Hz, 1H), 5.15 (dq, J=1.2, 10.3 Hz, 1H), 5.00 (d, J=2.9 Hz, 1H), 4.76 (s, 1H), 4.72 (s, 1H), 4.13 (m, 2H), 4.02 (ddt, J=1.3, 5.7, 12.8 Hz, 1H), 3.87 (dt, J=7.1, 9.8 Hz, 1H), 3.60 (dt, J=6.8, 9.8 Hz, 1H), 3.44 (dd, J=2.7, 5.2 Hz, 1H), 2.31 (t, J=6.9 Hz, 2H), 1.74 (s, 3H), 1.31 (d, J=6.7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) major isomer: δ 142.6, 135.1, 129.3, 127.5, 116.8, 111.4, 94.3, 70.0, 69.3, 66.4, 66.3, 37.8, 22.7, 16.2. HRMS calcd for $C_{14}H_{22}NaO_3$ [M+Na]261.1467, found 261.1470.

4.11. 6-((*S*)-1-((*S*)-2,5-Dihydrofuran-2-yl)ethoxy)-3,6-dihydro-2*H*-pyran (11a)

Under argon, at 40 °C, to a solution of **10a** (220 mg, 0.98 mmol, 1 equiv) in degassed toluene (200 mL, c=2.10^{-3} M), was added [**Ru**]-2 (42 mg, 49 μmol, 5 mol %). The resulting mixture was stirred at this temperature for 2 h, concentrated in vacuo, and purified by flash column chromatography (silica gel, 10% EtOAc in cyclohexane) to provide the ring-rearranged product **11a** (160 mg, 0.81 mmol, 83%) of the title compound as a clear oil. ^{1}H NMR ($CDCl_3$, 300 MHz) major isomer: δ 6.02 (m, 2H), 5.86 (dq, J=2.3, 8.6 Hz, 1H), 5.72 (dtd, J=1.3, 2.8, 10.1 Hz, 1H), 5.03 (t, J=1 Hz, 1H), 4.96 (m, 1H), 4.67 (m, 2H), 3.98 (m, 2H), 3.71 (ddt, J=1, 6.2, 11.1 Hz, 1H), 2.31 (m, 1H), 1.90 (dddt, J=1, 4.1, 5.1, 17.8 Hz, 1H), 1.11 (d, J=6.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) major isomer: δ 129.1, 128.1, 126.7, 126.1, 92.0, 88.5, 75.6, 74.1, 57.2, 24.7, 14.7. HRMS calcd for $C_{11}H_{16}NaO_3$ [M+Na] 219.0992, found 219.0976.

4.12. 6-((*S*)-1-((*S*)-2,5-Dihydrofuran-2-yl)ethoxy)-4-methyl-3,6-dihydro-2*H*-pyran (11b)

Under argon, at 40 °C, to a solution of **10b** (40 mg, 0.17 mmol, 1 equiv) in degassed toluene (90 mL, c=2.10^{-3} M), was added [**Ru**]-2 (7 mg, 8 μmol, 5 mol %). The resulting mixture was stirred at 40 °C for 2 h, concentrated in vacuo, and purified by flash column chromatography (silica gel, 10% EtOAc in cyclohexane) to provide 26 mg (0.12 mmol, 73%) of ring-rearranged product **11b** as a clear oil. ^{1}H NMR ($CDCl_3$, 300 MHz) major isomer: δ 5.97 (dq, J=1.7, 6.3 Hz, 1H), 5.82 (m, 1H), 5.42 (s, 1H), 5.01 (s, 1H), 4.94 (m, 1H), 4.64 (m, 2H), 3.94 (m, 2H), 3.69 (dd, J=6.2, 11.4 Hz, 1H), 2.24 (m, 1H), 1.73 (m, 4H), 1.08 (d, J=6.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) major isomer: δ 137.5, 128.0, 126.6, 120.1, 92.7, 88.5, 75.5, 74.2, 57.3, 29.5, 23.0, 14.7. HRMS calcd for $C_{12}H_{18}NaO_3$ [M+Na] 233.1154, found 233.1165.

4.13. Allyl 2-deoxy-3,4,6-tri-*O*-acetyl-D-galactopyranoside (13)

Under argon, to a solution of 3,4,6-tri-*O*-acetyl D-galactal (1.0 g, 3.7 mmol, 1 equiv) **12** and allyl alcohol (816 μL, 12 mmol, 3.2 equiv) in anhydrous dichloromethane (20 mL) was added polymer-supported TPHB ($PPh_3 \cdot HBr$)[20] (240 mg, 0.74 mmol, 0.2 equiv). The mixture was stirred overnight, filtered, and concentrated in vacuo to provide the title compound (1.06g, 87%, pale yellow oil) as an α/β (4:1) mixture of anomers, in agreement with the litterature.[21]

It is also possible to perform the reaction using nonsupported TPHB following the procedure described by Falk, Mioskowski et al.[8] followed by purification by flash column chromatography (silica gel, 20% EtOAc in cyclohexane). ^{1}H NMR ($CDCl_3$, 300 MHz) (major isomer α) δ 5.97–5.84 (m, 1H), 5.37–5.17 (m, 4H), 5.06 (br d, J=2.9 Hz, 1H), 4.19–4.08 (m, 4H), 3.99 (ddt, J=12.9, 6.0, 1.3 Hz, 1H), 2.14 (s, 3H), 2.11 (m, 1H), 2.06 (s, 3H), 1.98 (s, 3H), 1.91 (m, 1H). ^{13}C NMR (major isomer α) ($CDCl_3$, 75 MHz) δ 170.5, 170.3, 170.0, 133.7, 117.5, 96.6, 68.2, 66.7, 66.6, 66.2, 62.4, 30.1, 20.8, 20.8 (2C). LRMS calcd for $C_{15}H_{22}NaO_8$ [M+Na] 353.12, found 353.0.

4.14. Allyl 6-O-*tert*-butyl-dimethylsilyl-2-deoxy-3,4,6-tri-*O*-acetyl-D-galactopyranoside (14)

A cold (0 °C) solution of **13** (8.27 g, 25 mmol, 1 equiv) in methanol (20 mL) was placed under Ar atmosphere. Sodium methanolate (135 mg, 2.5 mmol) was added and the mixture was allowed to warm to room temperature and stirred for 2 h. The methanol was removed in vacuo and the residue was co-evaporated with toluene and dried under vacuum for 3 h. The diol was dissolved in DMF (30 mL), the solution was placed under argon atmosphere and imidazole (2.50 g, 36.7 mmol, 1.5 equiv) and *tert*-butyldimethylsilyl chloride (4.11 g, 27.5 mmol, 1.1 equiv) were added. The mixture was allowed to warm to room temperature and stirred for 18 h, then it was diluted with ether (100 mL). The mixture was washed with brine (2×80 mL). The aqueous layers were extracted with ether (3×100 mL), the combined organic layers were washed with brine (200 mL), dried over anhydrous $MgSO_4$, filtrated, and concentrated in vacuo. Purification by flash column

chromatography (silica gel, 40% EtOAc in cyclohexane) provided the title compound (5.73 g, 72%, colorless oil) as an α/β (4:1) mixture of anomers. ^{1}H NMR ($CDCl_3$, 300 MHz) (major isomer α) δ 5.97–5.84 (m, 1H), 5.28 (ddt, *J*=17.2, 3.4, 1.7 Hz, 1H), 5.18 (ddt, *J*=10.5, 3.1, 1.5 Hz, 1H), 4.99–4.97 (m, 1H), 4.17–4.09 (m, 1H), 4.13 (ddt, *J*=13.1, 5.2, 1.6 Hz, 1H), 4.02–3.87 (m, 4H), 3.79–3.72 (m, 1H), 1.89 (m, 2H), 0.89 (s, 9H), 0.08 (s, 6H). ^{13}C NMR (major isomer α) δ 134.1, 116.9, 96.9, 69.5, 69.0, 67.7, 65.8, 64.0, 33.0, 25.8 (3C), 18.2, −5.4 (2C). LRMS calcd for $C_{15}H_{30}NaO_5Si$ [M+Na] 341.18, found 341.1.

4.15. Allyl 6-*O*-*tert*-butyl-dimethylsilyl-2-deoxy-D-galactopyranoside 3,4-thionocarbonate (15)

Under argon, at room temperature, to a solution of diol **14** (5.40 g, 17 mmol, 1 equiv) in anhydrous dichloromethane (25 mL) was added 1,1′-(thiocarbonyl)diimidazole (4.50 g, 25 mmol, 1.5 equiv). The mixture was stirred for 18 h, diluted with ether (50 mL), and quenched with water (30 mL). The aqueous layer was extracted with ether (3×50 mL), the combined organic layers were washed with brine (80 mL), dried over anhydrous $MgSO_4$, filtrated, and concentrated in vacuo. Purification by flash column chromatography (silica gel, 15% EtOAc in cyclohexane) provided the title compound (4.60 g, 75%, yellow oil) as an α/β (4:1) mixture of anomers. ^{1}H NMR ($CDCl_3$, 300 MHz) (major isomer α) δ 5.99–5.76 (m, 1H), 5.27 (ddt, *J*=17.2, 3.2, 1.5 Hz, 1H), 5.22–5.17 (m, 2H), 5.08–4.92 (m, 2H), 4.22 (ddt, *J*=12.9, 5.2, 1.4 Hz, 1H), 4.02 (dt, *J*=6.2, 1.1 Hz, 2H), 3.96 (td, *J*=6.8, 1.4 Hz, 1H), 3.85–3.73 (m, 1H), 2.48 (ddd, *J*=15.8, 5.6, 4.2 Hz, 1H), 1.91 (ddd, *J*=15.8, 6.4, 3.6 Hz, 1H), 0.89 (s, 9H), 0.09 (2s, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz) (major isomer α) δ 191.8, 133.7, 117.6, 94.3, 78.3, 76.9, 68.4, 67.7, 60.7, 29.0, 25.8 (3C), 18.17, 0.99 (2C). HRMS calcd for $C_{16}H_{28}NaO_5SSi$ [M+Na] 383.1324, found 383.1311.

4.16. (((2*S*)-6-(Allyloxy)-5,6-dihydro-2*H*-pyran-2-yl)methoxy)(*tert*-butyl)dimethylsilane (16)

Under argon, a solution of thiocarbonate **15** (2.60g, 7.2 mmol, 1 equiv) in trimethylphosphite (25 mL) was refluxed overnight before the mixture was concentrated in vacuo. Purification by flash column chromatography (silica gel, 10% EtOAc in cyclohexane) provided the title compound (1.58 g, 77%, clear, colorless oil) as an α/β (4:1) mixture of anomers. ^{1}H NMR ($CDCl_3$, 300 MHz) (major isomer α) δ 6.01–5.89 (m, 1H), 5.77 (br s, 2H), 5.29 (dq, *J*=17.1, 1.5 Hz, 1H), 5.20–5.16 (m, 1H), 5.04 (d, *J*=4.8 Hz, 1H), 4.31–4.18 (m, 2H), 4.06 (ddt, *J*=12.9, 6.3, 1.2 Hz, 1H), 3.75 (dd, *J*=10.2, 6.0 Hz, 1H), 3.63 (dd, *J*=10.2, 6.0 Hz, 1H), 2.47–2.39 (m, 1H), 2.13–2.05 (m, 1H), 0.90 (s, 9H), 0.07 (s, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz) (major isomer α) δ 134.3, 126.0, 122.1, 117.0, 94.7, 68.5, 67.8, 65.5, 29.8, 25.7 (3C), 18.1, −5.7 (2C). LRMS calcd for $C_{15}H_{28}NaO_3Si$ [M+Na] 307.17, found 307.2.

4.17. ((2*S*)-6-(Allyloxy)-5,6-dihydro-2*H*-pyran-2-yl)-methanol (17)

A solution of **16** (1.68 g, 5.9 mmol, 1 equiv) in anhydrous THF (30 mL), under argon, at 0 °C, was treated dropwise with 1 M TBAF in THF (5.9 mL, 5.9 mmol, 1 equiv). The mixture was stirred for 20 min at 0 °C and then was allowed to warm to room temperature within 90 min. The reaction was quenched by addition of water (20 mL) and extracted with ether (2×50 mL). The organic layers were washed with brine (40 mL), dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash column chromatography (silica gel, 30% EtOAc in cyclohexane) provided the title compound (851 mg, 85%, pale yellow oil) as an α/β (4:1) mixture of anomers. ^{1}H NMR ($CDCl_3$, 300 MHz) (major isomer α) δ 6.00–5.81 (m, 2H), 5.67–5.63 (m, 1H), 5.30 (ddt, *J*=17.2, 3.9, 1.5 Hz, 1H), 5.20 (ddt, *J*=10.3, 2.8, 1.3 Hz, 1H), 5.08 (br d, *J*=4.7 Hz, 1H), 4.35–4.22 (m, 2H), 4.08 (ddt, *J*=12.9, 6.1, 1.3 Hz, 1H), 3.74 (ddd, *J*=11.4, 7.0, 3.3 Hz, 1H), 3.63 (ddd, *J*=11.4, 5.8, 5.8 Hz, 1H), 2.54–2.40 (m, 1H), 2.16–2.07 (m, 1H), 1.90 (br s,1H). ^{13}C NMR ($CDCl_3$, 75 MHz) (major isomer α) δ 134.3, 125.0, 123.8, 117.3, 95.0, 68.4, 68.2, 65.1, 29.9. HRMS calcd for $C_9H_{14}NaO_3$ [M+Na] 193.0841, found 193.0838.

4.18. (*S*)-2-(Allyloxy)-6-(allyloxymethyl)-3,6-dihydro-2*H*-pyran (18)

Under argon at 0 °C, to a solution of alcohol **17** (80 mg, 0.47 mmol, 1 equiv) in DMF (1 mL) were added, respectively, dry NaH (19 mg, 0.70 mmol, 1.5 equiv) and allyl bromide (52 μL, 0.61 mmol, 1.3 equiv). Then the reaction was stirred at room temperature for 6 h, quenched with $NH_4Cl_{(aq)}$ (3 mL) and extracted with ethyl acetate (3×3 mL). The organic layers were combined, dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash column chromatography (silica gel, 10% EtOAc in cyclohexane) provided the title compound (91 mg, 92%, colorless oil) as an α/β (4:1) mixture of anomers. ^{1}H NMR ($CDCl_3$, 300 MHz) (major isomer α) δ 6.02–5.88 (m, 2H), 5.81 (ddt, *J*=2.2, 4.0, 9.6 Hz, 2H), 5.73–5.69 (m, 1H), 5.30 (ddq, *J*=1.6, 3.3, 17.0 Hz, 2H), 5.20 (ddq, *J*=1.6, 2.9, 10.4 Hz, 2H), 5.09 (br d, *J*=4.8 Hz, 1H), 4.42–4.36 (m, 1H), 4.29 (ddt, *J*=1.4, 5.2, 12.9 Hz, 1H), 4.12–4.05 (m, 3H), 3.59–3.50 (m, 2H), 2.53–2.43 (m, 1H), 2.15–2.06 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) (major isomer α) δ 134.6, 134.4, 125.7, 122.9, 117.2, 117.1, 95.0, 72.4, 72.3, 68.1, 67.1, 29.8. HRMS calcd for $C_{12}H_{18}NaO_3$ [M+Na] 233.1148, found 233.1149.

4.19. (*S*)-(6-(Allyloxy)-5,6-dihydro-2*H*-pyran-2-yl)methyl pent-4-enoate (19)

Under argon, to a solution of pent-4-enoic acid (42 μL, 0.46 mmol, 1.05 equiv) in DCM (3 mL) were added alcohol **17** (75 mg, 0.44 mmol, 1 equiv) and DMAP (2 mg, 0.02 mmol, 4 mol %). Then the reaction mixture was cooled down to 0 °C and DCC (96 mg, 0.46 mmol, 1.05 equiv) was added. Finally the mixture was let to stir at room temperature for a night. The white precipitate was then removed by filtration over Celite. The filtrate was then washed twice with a cold saturated solution of citric acid (2×5 mL), three times with $NaHCO_{3satd}$, and finally once with brine. The organic layers were combined, dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash column chromatography (silica gel, 10% EtOAc in cyclohexane) provided the title compound (86 mg, 0.34 mmol, 77%, colorless oil) as an α/β (4:1) mixture of anomers. ^{1}H NMR ($CDCl_3$, 300 MHz) (major isomer α) δ 6.21–6.12 (m, 1H), 6.03–5.94 (m, 2H), 5.32–5.19 (m, 2H), 5.10 (bd. *J*=4.2 Hz 1H), 5.02–4.91 (m, 2H), 4.45–4.32 (m. 2H), 4.15 (ddt, *J*=13.0, 6.1, 1.5 Hz, 1H), 3.73 (ddd. *J*=11.4, 7.3, 3.0 Hz, 1H), 3.54 (m, 1H), 2.85–2.65 (m, 4H), 2.50–2.38 (m, 1H), 2.20–2.05 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) (major isomer α) δ 175.2, 136.2, 135.1, 125.4, 124.2, 117.5, 116.4, 96.1, 67.1, 66.9, 65.0, 34.7, 30.1, 28.7.

4.20. (*S*)-(6-(Allyloxy)-5,6-dihydro-2*H*-pyran-2-yl)methyl prop-2-enoate (20)

Under argon, to a solution of alcohol **17** (100 mg, 0.59 mmol, 1 equiv) in dichloromethane (5 mL) was added diisopropylethylamine (623 μL, 3.54 mmol, 6 equiv). Then, the resulting mixture was cooled to 0 °C, acryloyl chloride (142 μL, 1.77 mmol, 3 equiv) was added and the solution was stirred for 1 h at room temperature. The reaction was quenched with $NH_4Cl_{(aq)}$ (5 mL) and extracted with ethyl acetate (3×5 mL). The organic layers were combined, washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification of the brown crude residue by flash column chromatography (silica gel, 10% EtOAc in cyclohexane)

provided acrylate **20** 120 mg (0.54 mmol, 92%) as a clear, colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) (major isomer α) δ 6.27–6.23 (m, 1H), 6.00–5.81 (m, 2H), 5.72–5.63 (m, 1H), 5.51–5.43 (m, 2H), 5.35 (ddt, *J*=17.2, 3.9, 1.7 Hz, 1H), 5.22 (ddt, *J*=10.3, 2.8, 1.5 Hz, 1H), 5.08 (br d, *J*=4.7 Hz, 1H), 4.50–4.32 (m, 2H), 4.08 (ddt, *J*=12.9, 6.1, 1.3 Hz, 1H), 3.74 (ddd, *J*=11.4, 7.0, 3.3 Hz, 1H), 3.63 (ddd, *J*=11.4, 5.8, 5.8 Hz, 1H), 2.52–2.40 (m, 1H), 2.20–2.05 (m, 1H). LRMS calcd for $C_{12}H_{17}O_4$ [M+H] 225.11, found 225.2.

4.21. (2*S*)-6-(Allyloxy)-5,6-dihydro-2*H*-pyran-2-carboxylic acid (21)

Under argon, $PhIOAc_2$ (827 mg, 2.57 mmol, 2.2 equiv), TEMPO (36 mg, 0.23 mmol, 0.2 equiv) and the alcohol **17** (200 mg, 1.17 mmol, 1 equiv) were dissolved in a 1:1 aqueous acetonitrile (2 mL, 0.5 M). The reaction mixture was stirred for 5 h, then filtered, and concentrated in vacuo. Purification by flash column chromatography (silica gel, 60% EtOAc in cyclohexane) provided the title compound (151 mg, 70%, pale yellow oil) as an α/β (4:1) mixture of anomers. ^{1}H NMR ($CDCl_3$, 300 MHz) (major isomer α) δ 9.66 (s, 1H), 6.01–5.83 (m, 3H), 5.32 (ddt, *J*=18.9, 3.3, 1.5 Hz, 1H), 5.22 (ddt, *J*=10.2, 2.7, 1.5 Hz, 1H), 5.16 (dd. *J*=2.1, 1.5 Hz, 1H), 4.89–4.86 (m, 1H), 4.33 (ddd, *J*=12.9, 1.5, 1.5 Hz), 4.14 (ddd, *J*=12.9, 1.5, 1.5 Hz, 1H), 2.53–2.43 (m, 1H), 2.23–2.13 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) (major isomer α) δ 171.9, 133.7, 124.1, 122.2, 117.8, 95.4, 78.2, 68.9, 29.4. HRMS calcd for $C_9H_{12}NaO_4$ [M+Na] 207.0628, found 207.0625.

4.22. (2*S*)-Allyl 6-(allyloxy)-5,6-dihydro-2*H*-pyran-2-carboxylate (22)

Under argon, to a solution of acid **21** (150 mg, O.81 mmol, 1 equiv) in CH_2Cl_2 (6 mL) were added allylic alcohol (61 μL, 0.89 mmol, 1 equiv) and DMAP (2 mg, 0.02 mmol, 3 mol %). The mixture was cooled to 0 °C and DCC (177 mg, 0.85 mmol, 1.05 equiv) was added. Then, the reaction was allowed to warm to room temperature and was stirred over the night. After elimination of the white precipitate by filtration on Celite, the mixture was washed twice with a saturated aqueous solution of citric acid, once with $NaHCO_{3(aq)}$, and once with water. The organic layer was dried over anhydrous $MgSO_4$ and concentrated in vacuo. Purification by flash column chromatography (silica gel, 20% EtOAc in cyclohexane) provided the title compound (137 mg, 75%, pale yellow oil) as an α/β (4:1) mixture of anomers. ^{1}H NMR ($CDCl_3$, 300 MHz) (major isomer α) δ 6.02–5.86 (m, 3H), 5.34 (ddt, *J*=17.2, 7.5, 1.5 Hz, 1H), 5.30–5.29 (m, 1H), 5.24 (ddt, *J*=22.3, 10.4, 1.5 Hz, 1H), 5.12 (dd, *J*=4, 4 Hz, 1H), 4.93–4.92 (m, 1H), 4.69 (dt, *J*=5.8, 1.3 Hz, 2H), 4.39 (ddt, *J*=12.9, 5.2, 1.4 Hz, 1H), 4.18 (ddt, *J*=12.9; 6.2, 1.3 Hz, 1H), 2.48–2.38 (m, 1H), 2.24–2.14 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) (major isomer α) δ 170.1, 134.1, 131.7, 124.5, 122.9, 118.9, 117.4, 95.4, 70.2, 68.8, 65.8, 27.7. HRMS calcd for $C_{12}H_{16}NaO_4$ [M+Na] 247.0941, found 247.0941.

4.23. (*S*)-Allyloxy(6-(allyloxy)-5,6-dihydro-2*H*-pyran-2-yl) methyl ethanoate (23)

Under argon, at −78 °C, to a solution of ester **22** (80 mg, 0.35 mmol, 1 equiv) in dichloromethane (3 mL), DIBAH (1.5 M in toluene, 468 μL, 0.70 mmol, 2 equiv) was added slowly over a period of 15 min (*Caution! The internal solution temperature must be kept below* −72 °C). The solution was stirred for an additional 45 min at −78 °C and pyridine (85 μL, 1.05 mmol, 3 equiv) was added dropwise, while maintaining the temperature below −76 °C. Then a solution of DMAP (86 mg, 0.70 mmol, 2 equiv) in dichloromethane (1 mL) was immediately added at a rate such as to maintain the temperature below −72 °C. Finally, acetic anhydride (198 μL, 2.10 mmol, 6 equiv) was added and, again, the internal temperature was not allowed to rise above −72 °C. The resulting light yellow solution was stirred at −78 °C for 12 h, and then the mixture was warmed to 0 °C and stirred for additional 30 min. The reaction was quenched by the sequential addition of $NH_4Cl_{(aq)}$ (3 mL) and saturated aqueous sodium potassium tartrate (3 mL). The resulting emulsion was removed from the ice water bath and stirred vigorously for one night. The obtained biphasic mixture was extracted with dichloromethane (3×4 mL). The organic layers were combined, washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash column chromatography (triethylamine-deactivated silica gel, 10% EtOAc in cyclohexane with 3% Et_3N) provided 66 mg (0.25 mmol, 70%) of the title compound **23** as clear, colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz) (major isomers α) δ 6.02–5.83 (m, 3H), 5.35 (ddt, *J*=16.7, 7.4, 1.5 Hz, 1H), 5.30–5.29 (m, 1H), 5.24 (ddt, *J*=22.3, 10.4, 1.5 Hz, 1H), 5.14 (dd, *J*=3.8, 3.8 Hz, 1H), 4.93–4.91 (m, 1H), 4.69 (dt, *J*=5.8, 1.3 Hz, 2H), 4.38 (ddt, *J*=12.9, 5.2, 1.4 Hz, 1H), 4.29–4.13 (m, 2H), 2.48–2.38 (m, 1H), 2.24–2.14 (m, 1H), 2.12 and 2.14 (2s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) (major isomers α) δ 170.2, 170.1, 134.1, 131.6, 124.5, 123.5, 123.0, 118.9, 117.4, 117.3, 95.4, 95.1, 95.0, 70.3, 68.9, 65.8, 29.9, 29.8, 21.2. LRMS calcd for $C_{14}H_{21}O_5$ [M+H] 269.14, found 269.0.

4.24. (*S*)-5,6′-Oxybis(5,6-dihydro-2*H*-pyran) (24)

Under argon, at 70 °C, to a solution of **18** (50 mg, 0.24 mmol, 1 equiv) in degassed toluene (110 mL, $c=2.10^{-3}$ M), was added [**Ru**]-2 (11 mg, 12 μmol, 5 mol %). The resulting mixture was stirred at 70 °C for 3 h, concentrated in vacuo, and purified by flash column chromatography (silica gel, 10% EtOAc in cyclohexane) to provide 36 mg (0.20 mmol, 84%) of ring-rearranged product **24** as a clear oil. ^{1}H NMR ($CDCl_3$, 300 MHz) (major isomer α) δ 5.97 (br s, 2H), 5.72 (br s, 2H), 4.97 (t, *J*=4.0 Hz, 1H), 4.33–4.25 (m, 1H), 4.24–4.15 (m, 3H), 4.11–4.03 (m, 1H), 3.88 (dd, *J*=3.8, 11.8 Hz, 1H), 3.79 (dd, *J*=3.5, 11.8 Hz, 1H), 2.43–2.35 (m, 1H), 2.23–2.15 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) (major isomer α) δ 130.0, 125.5, 125.1, 121.7, 95.5, 67.5, 67.1, 65.1, 61.3, 30.5. LRMS calcd for $C_{10}H_{14}NaO_3$ [M+Na] 205.08, found 205.1.

4.25. (*S*,5*Z*)-7-(3,6-Dihydro-2*H*-pyran-2-yloxy)-3,4,7,8-tetrahydrooxocin-2-one (25)

Under argon, at 70 °C, to a solution of **19** (20 mg, 0.08 mmol, 1 equiv) in degassed toluene (35 mL, $c=2.10^{-3}$ M), was added [**Ru**]-2 (4 mg, 4 μmol, 5 mol %). The resulting mixture was stirred at 70 °C for 3 h, concentrated in vacuo, and purified by flash column chromatography (silica gel, 10% EtOAc in cyclohexane) to provide 11 mg (0.05 mmol, 66%) of ring-rearranged product **25** as a clear oil. ^{1}H NMR ($CDCl_3$, 300 MHz) (major isomer α) δ 5.80–5.71 (m, 3H), 5.61 (ddt, *J*=10.5, 3.7, 1.8 Hz, 1H), 5.15 (d, *J*=5.5 Hz, 1H), 4.70 (dd, 11.3, 2.13 HZ, 1H), 4.50–4.41 (m, 2H), 3.94–3.86 (m, 1H), 3.74 (dd, *J*=10.9, 10.9 Hz, 1H), 2.56–2.46 (m, 2H), 2.41–2.43 (m, 2H), 2.10–2.01 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) (major isomer α) δ 173.7, 130.7, 130.6, 124.3, 123.6, 99.4, 72.6, 66.5, 64.8, 33.7, 30.4, 30.2. LRMS calcd for $C_{12}H_{17}O_4$ [M+H] 225.11, found 225.2.

4.26. (*S*)-3-(3,6-Dihydro-2*H*-pyran-2-yloxy)-3,6-dihydro-2*H*-pyran-2-yl ethanoate (27)

Under argon, at 70 °C, to a solution of **23** (20 mg, 0.07 mmol, 1 equiv) in degassed toluene (35 mL, $c=2.10^{-3}$ M), was added [**Ru**]-2 (4 mg, 4 μmol, 5 mol %). The resulting mixture was stirred at 70 °C for 3 h, concentrated in vacuo, and purified by flash column chromatography (silica gel, 10% EtOAc in cyclohexane) to provide 12 mg (0.05 mmol, 74%) of ring-rearranged product **27** as a clear oil. ^{1}H NMR ($CDCl_3$, 300 MHz) (major isomers α) δ 6.53–5.46 (m, 5H), 5.00–4.87 (m, 1H), 4.96–4.91 (m, 1H), 4.43–3.59 (m, 4H), 2.64–2.37 (m, 1H), 2.21–2.07 (m, including 2s at δ=2.12 and 2.10,

4H). ^{13}C NMR ($CDCl_3$, 75 MHz) (major isomers α) δ 169.7, 129.0, 125.0, 122.5, 121.6, 96.2, 92.5, 67.7, 61.3, 30.3, 29.7, 21.0.

4.27. (2*R*,3*S*)-6-(Allyloxy)-2-(ethanoyloxymethyl)-3,6-dihydro-2*H*-pyran-3,5-diyl diethanoate (29)

Under argon, to a solution of 2,3,4,6-tetra-*O*-acetyl D-glucal (500 mg, 1.51 mmol, 1 equiv) **28** in dichloromethane (2 mL) was added allylic alcohol (154 μL, 2.26 mmol, 1.5 equiv). The mixture was cooled to 0 °C, 3 drops of $BF_3{\cdot}Et_2O$ were added and the resulting solution was allowed to warm up slowly to room temperature. After 1 h, the reaction was quenched with $NaHCO_{3(aq)}$ (10 mL) and extracted with ethyl acetate (3×10 mL). The organic layers were combined, washed with brine, dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash column chromatography (silica gel, 10% EtOAc in cyclohexane) provided the title compound (332 mg, 1.01 mmol, 67%) as a clear, pale yellow oil. The compound was obtained as an anomeric mixture with a 6:1 (α/β) ratio. ^{1}H NMR ($CDCl_3$, 300 MHz) (major isomer α) δ 5.96–5.82 (m, 1H), 5.73 (d, *J*=2.15 Hz, 1H), 5.47–5.43 (m, 1H), 5.35–5.17 (m, 3H), 5.08 (br s, 1H), 4.38–4.05 (m, 5H), 2.15 (s, 3H), 2.08 (s, 3H), 2.06 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) (major isomer α) δ 170.6, 170.0, 168.1, 148.1, 133.6, 117.7, 115.3, 92.9, 69.3, 67.1, 65.2, 62.4, 20.9 (3C). HRMS calcd for $C_{15}H_{20}NaO_8$ [M+Na] 351.1050, found 351.1053.

4.28. (3*R*,6*S*)-2-(Allyloxy)-6-(hydroxymethyl)-3,6-dihydro-2*H*-pyran-3-ol (30)

Under argon at 0 °C, to a solution of LAH (70 mg, 1.82 mmol, 3 equiv) in THF (4 mL), a THF (1 mL) solution of compound **29** (200 mg, 0.61 mmol, 1 equiv) was added dropwise over 30 min. After 1 h at the same temperature were added successively EtOAc (0.1 mL), water (0.1 mL), heptane (6 mL), and finally a 15% NaOH aqueous solution (0.1 mL). Then, the mixture is warmed up to room temperature and stirred overnight. After filtration over Celite, the reaction mixture is concentrated in vacuo. Purification by flash column chromatography (silica gel, 40% EtOAc in cyclohexane) provided the title compound (87 mg, 0.47 mmol, 77%) as a clear, pale yellow oil. The compound was obtained as an anomeric mixture with a 6:1 (α/β) ratio. ^{1}H NMR ($CDCl_3$, 300 MHz) (major isomer α) δ 6.03–5.87 (m, 1H), 5.82 (d, *J*=10.6 Hz, 1H), 5.70 (d, *J*=10.6 Hz, 1H), 5.32 (ddt, *J*=17.2, 3.1, 1.5 Hz, 1H), 5.23 (ddt, *J*=10.6, 2.5, 1.5 Hz, 1H), 5.08–5.07 (m, 1H), 4.30 (ddt, *J*=12.8, 5.3, 1.3 Hz, 1H), 4.26–4.21 (m. 2H), 4.12 (ddt, *J*=12.8, 6.2, 1.2 Hz, 1H), 3.73 (dd, *J*=10.6, 3.1 Hz, 1H), 3.60 (dd, *J*=11.5, 5.9 Hz, 1H), 2.09 (br s, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) (major isomer α) δ 133.6, 128.8, 126.3, 117.9, 95.9, 69.1, 69.0, 64.8, 64.1. LRMS calcd for $C_9H_{15}O_4$ [M+H] 187.10, found 187.1.

4.29. (3*R*,6*S*)-2-(Allyloxy)-6-((*tert*-butyldimethylsilyloxy) methyl)-3,6-dihydro-2*H*-pyran-3-ol (31)

To alcohol **30** (80 mg, 0.43 mmol, 1 equiv) in solution in DMF (1 mL) under argon at 0 °C, imidazole (44 mg, 0.65 mmol, 1.5 equiv) and TBDMSCl (72 mg, 0.48 mmol, 1.1 equiv) were added. Then the reaction is allowed to warm up to room temperature and let like this for 18 h. Then the mixture was diluted with ether (2 mL) and washed with brine (2×1 mL). The aqueous phase was then extracted thrice with ether (3×2 mL). The combined organic layers were then washed with brine, dried over $MgSO_4$, filtrated, and concentrated in vacuo. Purification by flash column chromatography (silica gel, 10% EtOAc in cyclohexane) provided the title compound (93 mg, 0.31 mmol, 73%) as a clear, pale yellow oil. The compound was obtained as an anomeric mixture with a 6:1 (α/β) ratio. ^{1}H NMR ($CDCl_3$, 300 MHz) (major isomer α) δ 6.01–5.88 (m, 1H), 5.83 (d, *J*=10.5 Hz, 1H), 5.75 (d, *J*=10.5 Hz, 1H), 5.31 (ddt, *J*=17.2, 3.1, 1.6 Hz, 1H), 5.23 (ddt, *J*=10.5, 2.6, 1.2 Hz, 1H), 5.04 (br d, *J*=4.4 Hz, 1H), 4.31 (ddt, *J*=12.8, 5.2, 1.6 Hz, 1H), 4.21–4.20 (m, 1H), 4.17–4.10 (m, 2H), 3.70 (dd, *J*=10.2, 5.7 Hz, 1H), 3.59 (dd, *J*=10.2, 6.0 Hz, 1H), 1.60 (br s, 1H), 0.90 (s. 9H), 0.07 (s, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz) (major isomer α) δ 133.8, 127.6, 127.3, 117.8, 95.9, 69.2, 68.9, 65.5, 64.3, 25.9 (3C), −5.2, −5.3. LRMS calcd for $C_{15}H_{28}NaO_8Si$ [M+Na] 323.17, found 323.2.

4.30. (((2*S*,5*R*)-6-(Allyloxy)-5-methoxy-5,6-dihydro-2*H*-pyran-2-yl)methoxy)(*tert*-butyl)dimethylsilane (32)

Under argon at 0 °C, to a solution of alcohol **31** (70 mg, 0.23 mmol, 1 equiv) in DMF (1 mL), NaH (9 mg, 0.35 mmol, 1.5 equiv) and MeI (19 μL, 0.30 mmol, 1.3 equiv) were added. Then the reaction was let to stir at room temperature for 6 h, quenched with $NH_4Cl_{(aq)}$ (2 mL), and extracted thrice with EtOAc (3×2 mL). Organic layers were combined, washed with brine, dried over $MgSO_4$, and finally concentrated in vacuo. Purification by flash column chromatography (silica gel, 5% EtOAc in cyclohexane) provided the title compound (60 mg, 0.19 mmol, 81%) as a clear, colorless oil. The compound was obtained as an anomeric mixture with a 6:1 (α/β) ratio. ^{1}H NMR ($CDCl_3$, 300 MHz) (major isomer α) δ 6.05–5.91 (m, 1H), 5.87–5.76 (m, 2H), 5.33 (ddt, *J*=17.2, 3.0, 1.4 Hz, 1H), 5.24–5.19 (m, 1H), 5.15 (br d, *J*=4 Hz, 1H), 3.29 (ddt, *J*=12.9, 5.2, 1.3 Hz, 1H), 4.21–4.12 (m, 2H), 3.97–3.93 (m, 1H), 3.70 (dd, *J*=10.3, 5.8 Hz, 1H), 3.61 (dd, *J*=10.3, 5.9 Hz, 1H), 3.44 (br s, 3H), 0.91 (s, 9H), 0.08 (s, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz) (major isomer α) δ 134.1, 127.8, 124.2, 118.0, 73.2, 69.7, 68.5, 65.5, 56.6, 25.9, −5.2, −5.3. LRMS: [calcd 314.19]; found 314 [337.2=M+Na]. LRMS calcd for $C_{16}H_{30}NaO_4Si$ [M+Na] 337.18, found 337.2.

4.31. ((2*S*,5*R*)-6-(Allyloxy)-5-methoxy-5,6-dihydro-2*H*-pyran-2-yl)methanol (33)

To a solution of **32** (60 mg, 0.19 mmol, 1 equiv) in anhydrous THF (1 mL), under argon at 0 °C, TBAF (1 M in THF, 0.19 mmol, 1 equiv) was added dropwise. After 20 min at 0 °C, the reaction mixture was allowed to warm up to room temperature. After 90 min the reaction was quenched with water (2 mL) and extracted with ether (2×2 mL). Organic layers were combined, washed with brine, dried over $MgSO_4$, filtrated, and concentrated in vacuo. Purification by flash column chromatography (silica gel, 20% EtOAc in cyclohexane) provided the title compound (34 mg, 0.17 mmol, 89%) as a clear, colorless oil. The compound was obtained as an anomeric mixture with a 6:1 (α/β) ratio. ^{1}H NMR ($CDCl_3$, 300 MHz) (major isomer α) δ 6.04–5.91 (m, 1H), 5.86 (ddd, *J*=10.7, 3.6, 1.6 Hz, 1H), 5.73 (dt, 10.7, 1.8 Hz, 1H), 5.34 (ddt, *J*=17.2, 3.0, 1.5 Hz, 1H), 5.25–5.21 (m, 1H), 5.18 (br d, *J*=3.9 Hz, 1H), 4.33–4.27 (m, 2H), 4.17 (ddt, *J*=10.8, 6.6, 1.1 Hz, 1H), 3.99–3.96 (m, 1H), 3.75 (dd, *J*=11.5, 3.3 Hz, 1H), 3.61 (dd, *J*=11.5, 5.9 Hz, 1H), 3.44 (s, 3H), 1.89 (br s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) (major isomer α) δ 133.9, 126.5, 125.7, 118.1, 94.2, 73.1, 69.6, 68.7, 64.8, 56.6. HRMS calcd for $C_{10}H_{16}NaO_4$ [M+Na] 223.0941, found 223.0940.

4.32. (3*R*,6*S*)-2-(Allyloxy)-6-(allyloxymethyl)-3-methoxy-3,6-dihydro-2*H*-pyran (34)

Under argon at 0 °C, to a solution of alcohol **33** (50 mg, 0.25 mmol, 1 equiv) in DMF (1 mL) were added, respectively, dry NaH (10 mg, 0.41 mmol, 1.5 equiv) and allyl bromide (29 μL, 0.33 mmol, 1.3 equiv). Then the reaction was stirred at room temperature for 6 h, quenched with $NH_4Cl_{(aq)}$ (2 mL), and extracted with ethyl acetate (3×2 mL). The organic layers were combined, dried over anhydrous $MgSO_4$, and concentrated in vacuo. Purification by flash column chromatography (silica gel, 10% EtOAc in cyclohexane) provided the title compound (53 mg, 0.22 mmol, 89%, colorless oil) as an α/β (6:1) mixture of anomers. ^{1}H NMR ($CDCl_3$, 300 MHz) (major isomer α) δ 6.04–5.85 (m, 2H), 5.80–5.79 (m, 2H), 5.37–5.32 (m, 2H),

5.26–5.17 (m, 3H), 4.36–4.28 (m, 2H), 4.17 (dd, *J*=12.9, 6.6 Hz, 1H), 4.06 (br d, 5.6 Hz, 2H), 4.00–3.98 (m, 2H), 3.51 (br d, *J*=5.4 Hz, 1H), 3.43 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) (major isomer α) δ 134.5, 134.0, 127.2, 124.8, 118.0, 117.4, 94.2, 73.1, 72.5, 72.0, 68.6, 68.2, 56.6. LRMS calcd for $C_{13}H_{21}O_4$ [M+H] 241.14, found 241.3.

4.33. (*R*)-2-((*S*)-3,6-Dihydro-2*H*-pyran-3-yloxy)-3-methoxy-3,6-dihydro-2*H*-pyran (35)

Under argon, at 60 °C, to a solution of **34** (50 mg, 0.21 mmol, 1 equiv) in degassed toluene (105 mL, c=2.10^{-3} M), was added [**Ru**]-2 (10 mg, 11 μmol, 5 mol %). The resulting mixture was stirred at 60 °C for 3 h, concentrated in vacuo, and purified by flash column chromatography (silica gel, 5→10% EtOAc in cyclohexane) to provide 36 mg (0.17 mmol, 81%) of ring-rearranged product **35** as a clear oil. The compound was obtained as an anomeric mixture with a 6:1 (α/β) ratio. ^{1}H NMR ($CDCl_3$, 300 MHz) (major isomer α) δ 6.01–5.85 (m, 4H), 4.92 (d, *J*=2.4 Hz, 1H), 4.24 (ddt, *J*=16.8, 4.25, 2.1 Hz, 1H), 4.18–4.17 (m, 2H), 4.13–4.04 (m, 2H), 3.91 (dd, *J*=11.8, 3.6 Hz, 1H), 3.81 (dd, *J*=11.8, 3.5 Hz, 1H), 3.63–3.60 (m, 1H), 3.46 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) (major isomer α) δ 130.5, 129.4, 125.0, 122.2, 97.8, 73.2, 67.8, 67.6, 65.1, 60.6, 56.9. HRMS calcd for $C_{11}H_{16}NaO_4$ [M+Na] 235.0941, found 235.0931.

4.34. 3-Butenyl 2,4,6-tri-*O*-acetyl-D-ribofuranoside (36 α anomer and β anomer)

To a solution of 1,2,3,5-tetra-*O*-acetyl-D-ribofuranose (2.500 g, 7.85 mmol) (commercially available) in acetonitrile (40 mL) was added 3-buten-1-ol (1.00 mL, 1.5 equiv). The reaction mixture was cooled at 0 °C and $SnCl_4$ (1.8 mL, 15.4 mmol, 2.0 equiv) was added slowly. After 20 min (TLC, silica gel, AcOEt/cyclohexane 4:6, formation of two less polar compounds), the reaction was quenched with aqueous $NaHCO_3$ (5 mL).

The same reaction was repeated four times and all the mixtures were combined and extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$, filtered, and evaporated to dryness. The residue was chromatographed (AcOEt/cyclohexane 2:8) to afford **36β** (β anomer), (oil, 6.31 g, 63%) and the corresponding α anomer (**36α**, oil, 1.24 g, 12%).

36β: $[\alpha]_D^{20}$ −27 (c 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.79 (ddt, *J*=17.0, 10.2, 6.7 Hz, 1H), 5.33 (dd, *J*=6.8, 4.8 Hz, 1H), 5.24 (db, *J*=4.5 Hz, 1H), 5.09 (dq, *J*=17.1, 1.5 Hz, 1H), 5.05 (dm, *J*=10.3 Hz, 1H), 5.01 (1H, s), 4.35–4.27 (m, 2H), 4.12 (dd, *J*=13.3, 5.3 Hz, 1H), 3.77 (dt, *J*=9.3, 6.8 Hz, 1H), 3.46 (dt, *J*=9.3, 6.8 Hz, 1H), 2.32 (qt, *J*=6.8, 1.3 Hz, 2H), 2.11 (s, 3H), 2.09 (s, 3H), 2.06 (s, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ=170.6, 169.6, 169.6, 134.6, 116.8, 105.1, 78.4, 74.7, 71.6, 67.4, 64.7, 33.8, 20.8, 20.6, 20.5. HRMS calcd for $C_{15}H_{22}NaO_8$ [M+Na]: 353.1207, found 353.1207. Anal. Calcd for $C_{15}H_{22}O_8$: C 54.54; H 6.71, found C 54.67; H 6.74.

36α: $[\alpha]_D^{20}$ +141 (c 1.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.80 (ddt, *J*=17.1, 10.3, 6.8 Hz, 1H), 5.26 (d, *J*=4.5 Hz, 1H), 5.15 (dd, *J*=7.3, 4.3 Hz, 1H), 5.09 (dq, *J*=17.1, 1.6 Hz, 1H), 5.04 (dm, *J*=10.3 Hz, 1H), 4.96 (dd, *J*=7.3, 4.5 Hz, 1H), 4.36 (dd, *J*=11.8, 3.0 Hz, 1H), 4.28 (q, *J*=4.0 Hz, 1H), 4.20 (dd, *J*=11.8, 4.3 Hz, 1H), 3.78 (dt, *J*=10.1, 6.8 Hz, 1H), 3.57 (dt, *J*=10.1, 6.8 Hz, 1H), 2.36 (qt, *J*=6.8, 1.1 Hz, 2H), 2.13 (s, 3H), 2.11 (s, 3H), 2.10 (s, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ=170.6, 170.4, 169.9, 134.9, 116.5, 100.4, 78.8, 70.7, 69.8, 67.7, 63.4, 34.0, 20.8, 20.7, 20.5. Anal. Calcd for $C_{15}H_{22}O_8$: C 54.54; H 6.71, found C 54.32; H 6.88.

4.35. 3-Butenyl β-D-ribofuranoside (37)

A solution of triacetate **36** (6.04 g, 18.3 mmol) in MeOH (120 mL) was divided in two parts. To each one *t*-BuOK (42 mg) was added at 0 °C and stirred under Ar. The reaction was gradually warmed to 20 °C and stirred for 6 h. Ion exchange resin Dowex 50×8 (H^+) was added. The two reaction mixtures were combined, filtered, and evaporated to dryness. The residue was chromatographed (AcOEt/cyclohexane 8:2 then 9:1 then pure AcOEt) to yield the crude triol **37** (3.61 g, 97%). $[\alpha]_D^{20}$ −66 (c 1.0, $CHCl_3$) (compound not clean in NMR). ^{1}H NMR(400 MHz, $CDCl_3$): δ=5.79 (ddd, *J*=17.1, 10.3, 6.8 Hz, 1H), 5.11 (dq, *J*=17.1, 1.5 Hz, 1H), 5.07 (dm, *J*=10.1 Hz, 1H), 4.97 (br s, 1H), 4.38 (t, *J*=5.3 Hz, 1H), 4.08 (dt, *J*=5.5, 3.5 Hz, 1H), 4.07 (d, *J*=5.5 Hz, 1H), 3.81 (dd, *J*=12.1, 3.3 Hz, 1H), 3.78 (dt, *J*=9.6, 6.8 Hz, 1H), 3.67 (dd, *J*=12.1, 3.8 Hz, 1H), 3.54 (dt, *J*=9.6, 6.6 Hz, 1H), 2.34 (qt, *J*=6.8, 1.1 Hz, 2H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ=134.7, 116.9, 107.3, 83.6, 75.3, 71.9, 67.6, 63.9, 33.9. HRMS calcd for $C_9H_{16}NaO_5$ [M+Na] 227.0890, found 227.0886.

4.36. 3-Butenyl 2,3-*O*-isopropylidene-β-D-ribofuranoside (38)

To a stirred solution of crude triol **37** (2.848 g, 13.94 mmol) in acetone (50 mL) and 2-methoxypropene (15 mL) at 0 °C was added a solution of PTSA (26 mg) in acetone (2 mL). After 10 min the reaction was warmed to 20 °C and stirred for 30 min (TLC, silica gel, AcOEt/cyclohexane 3:7). When the starting material had disappeared the reaction was quenched with MeOH (5 mL) and H_2O (2 mL), stirred 2 h at 20 °C and neutralized with solid $NaHCO_3$ (ca. 100 mg). The solvent was evaporated and the residue chromatographed (AcOEt/cyclohexane 1:9) to yield acetonide **38** (2.912 g, 86%). $[\alpha]_D^{20}$ −67 (c 1.2, $CHCl_3$). ^{1}H NMR(400 MHz, $CDCl_3$): δ=5.78 (ddt, *J*=17.1, 10.1, 6.8 Hz, 1H), 5.12 (dq, *J*=17.1, 1.7 Hz, 1H), 5.09 (dm, *J*=10.3 Hz, 1H), 5.07 (s, 1H), 4.85 (d, *J*=5.8 Hz, 1H), 4.61 (d, *J*=6.0 Hz, 1H), 4.42 (t, *J*=2.6 Hz, 1H), 3.81 (dt, *J*=9.6, 6.7 Hz, 1H), 3.70 (dd, *J*=12.6, 2.0 Hz, 1H), 3.61 (ddb, *J*=12.8, 2.8 Hz, 1H), 3.57 (dt, *J*=9.6, 6.6 Hz, 1H), 3.25 (br s, 1H, O*H*), 2.36 (qt, *J*=6.6, 1.3 Hz, 2H), 1.49 (, s, 3H), 1.32 (s, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ=134.3, 117.3, 112.0, 109.0, 88.0, 86.0, 81.5, 67.8, 64.0, 33.8, 26.3, 24.6. HRMS calcd for $C_{12}H_{20}NaO_5$ [M+Na] 267.1203, found 267.1209.

4.37. 3-Butenyl 5-*O*-allyl-2,3-*O*-isopropylidene-β-D-ribofuranoside (39)

A solution of acetonide **38** (3.005 g, 12.30 mmol) in DMF (30 mL) was divided in three parts. To each one was added at 0 °C NaH/oil (55%) (400 mg, ca. 2 equiv). After 5 min the reaction was warmed to 20 °C, allyl bromide (710 μL, 2 equiv) was added slowly and the reaction was stirred for 40 min (TLC, silica gel, AcOEt/cyclohexane 3:7). The reaction was cooled to 0 °C and hydrolysed with MeOH. The three reaction mixtures were combined and poured in water, extracted with CH_2Cl_2, dried over $MgSO_4$, filtered, and evaporated to dryness. The residue was chromatographed (AcOEt/cyclohexane 0.5:9.5) to yield the allyl ether **39** (2.949 g, 84%). $[\alpha]_D^{20}$ −69 (c 1.0, $CHCl_3$). ^{1}H NMR(400 MHz, $CDCl_3$): δ=5.90 (ddt, *J*=17.1, 10.3, 5.5 Hz, 1H), 5.80 (ddt, *J*=17.1, 10.3, 6.8 Hz, 1H), 5.28 (dq, *J*=17.1, 1.6 Hz, 1H), 5.19 (dq, *J*=10.6, 1.3 Hz, 1H), 5.08 (dq, *J*=17.1, 1.5 Hz, 1H), 5.06 (s, 1H), 5.04 (dm, *J*=10.3 Hz, 1H), 4.68 (d, *J*=5.8 Hz, 1H), 4.60 (d, *J*=6.0 Hz, 1H), 4.32 (dd, *J*=8.3, 6.8 Hz, 1H), 4.06–3.96 (m, 2H), 3.70 (dt, *J*=9.6, 7.1 Hz, 1H), 3.50–3.40 (m, 3H), 2.30 (qd, *J*=6.8, 1.3 Hz, 2H), 1.48 (s, 3H), 1.32 (s, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ=135.0, 134.5, 117.2, 116.6, 112.3, 108.0, 85.2, 85.0, 82.2, 72.2, 71.0, 66.8, 33.8, 26.4, 24.9.

4.38. 3-Butenyl 5-*O*-allyl-β-D-ribofuranoside (40)

To acetonide **39** (1.049 g, 3.69 mmol) cooled at −5 °C was added a cold (−5 °C) mixture of TFA/H_2O (7:3) (5 mL). The reaction was stirred at −5/−3 °C for ca. 3 h. The reaction was monitored by TLC (silica gel, AcOEt/cyclohexane 6:4) and stopped by addition of cold ethyl acetate when the spot at R_f=0.25 corresponding to the desired diol **40** became the major one. Other products present in the reaction mixture were 4-*O*-allyl-D-ribofuranose (R_f=0.05) and the starting material **39** (R_f=0.70). The volatile components were evaporated at

0 °C under reduced pressure at 0 °C. The residue was diluted again with AcOEt and the mixture was concentrated almost to dryness at 0 °C. Finally, the residue was diluted with toluene and the solvent was removed under reduced pressure at 20 °C. Chromatography (AcOEt/cyclohexane 6:4) gave the starting acetonide **39** (591 mg, 20%), the desired diol **40** (469 mg, 52%) and 4-*O*-allyl-D-ribofuranose (156 mg, 22%). **40**: ^{1}H NMR(400 MHz, $CDCl_3$): δ=5.91 (ddt, *J*=17.1, 10.3, 5.8 Hz, 1H), 5.79 (ddt, *J*=17.0, 10.3, 6.7 Hz, 1H), 5.29 (dq, *J*=17.1, 1.5 Hz, 1H), 5.20 (dq, *J*=10.3, 1.5 Hz, 1H), 5.08 (dq, *J*=17.1, 1.8 Hz, 1H), 5.04 (dm, *J*=10.3 Hz, 1H), 4.96 (s, 1H), 4.24 (dd, *J*=6.4, 4.9 Hz, 1H), 4.09–4.04 (m, 4H), 3.75 (dt, *J*=9.6, 6.9 Hz, 1H), 3.62 (dd, *J*=9.8, 5.9 Hz, 1H), 3.56 (dd, *J*=9.8, 5.8 Hz, 1H), 3.45 (dt, *J*=9.6, 6.7 Hz, 1H), 2.31 (qt, *J*=6.8, 1.3 Hz, 2H). ^{13}C NMR(100.6 MHz, $CDCl_3$): δ=134.9, 134.4, 117.5, 116.5, 107.1, 81.6, 75.0, 72.8, 72.4, 72.1, 67.1, 33.9. HRMS calcd for $C_{12}H_{20}NaO_5$ [M+Na] 267.1203, found 267.1203.

4.39. 3-Butenyl 5-*O*-allyl-2,3-*O*-thiocarbonyl-β-D-ribofuranoside (41)

To a solution of diol **40** (1.318 g, 5.39 mmol) in CH_2Cl_2 (40 mL) was added 1,1′-thiocarbonyldiimidazole (1.442 g, 8.09 mmol, 1.5 equiv). After stirring at 20 °C for 24 h, the solvent was removed under vacuum and the residue was chromatographed (AcOEt/cyclohexane 2:8) to yield the thiocarbonyl derivative **41** (1.342 g, 87%). $[\alpha]_D^{20}$ −82 (*c* 1.1, $CHCl_3$). IR (neat, cm^{-1}) ν 2945, 2866, 1363, 1348, 1304, 1277, 1252, 1158, 1102, 1063. ^{1}H NMR(400 MHz, $CDCl_3$): δ=5.88 (ddt, *J*=17.2, 10.4, 5.6 Hz, 1H), 5.75 (ddt, *J*=17.0, 10.2, 6.8 Hz, 1H), 5.38 (d, *J*=6.8 Hz, 1H), 5.29 (s, 1H), 5.28 (dq, *J*=17.1, 1.5 Hz, 1H), 5.22 (dq, *J*=10.3, 1.3 Hz, 1H), 5.21 (d, *J*=6.8 Hz, 1H), 5.10 (dq, *J*=17.1, 1.5 Hz, 1H), 5.07 (dm, *J*=10.3 Hz, 1H), 4.59 (dd, *J*=9.3, 5.8 Hz, 1H), 4.03 (ddt, *J*=12.8, 5.8, 1.5 Hz, 1H), 3.99 (ddt, *J*=12.8, 5.8, 1.5 Hz, 1H), 3.72 (dt, *J*=9.6, 6.8 Hz, 1H), 3.54 (dd, *J*=10.1, 5.8 Hz, 1H), 3.50 (dt, *J*=9.6, 6.6 Hz, 1H), 3.46 (t, *J*=9.7 Hz, 1H), 2.31 (qt, *J*=6.7, 1.4 Hz, 2H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ=189.9, 134.3, 133.9, 117.7, 117.1, 106.3, 88.4, 86.5, 83.8, 72.2, 69.2, 67.6, 33.6. HRMS calcd for $C_{13}H_{19}O_5S$ [M+H] 287.0948, found 287.0964.

4.40. 3-Butenyl 5-*O*-acetyl-β-D-ribofuranoside (43)

To a solution of triacetate **36** (β anomer, 454 mg, 1.37 mmol) in MeOH (17 mL) at 0 °C was added potassium *tert*-butoxide (10 mg). The reaction was stirred under Ar for ca. 45 min and carefully monitored by TLC (silica gel, AcOEt/cyclohexane 6:4). Four spots gradually appeared. By order of increasing polarity: the starting material, a monodeacylated compound, the desired diol **43** and the fully deacylated sugar **37**. When the spot corresponding to the diol became the major one, the reaction was stopped by addition of Dowex H^+. The resin was filtered-off and the solvent was evaporated. The residue was chromatographed (AcOEt/cyclohexane 6:4) to afford successively **36** (14 mg, 3%), a diacetate (5 mg, 1%), **43** (208 mg, 61%), and the triol **37** (72 mg, 26%).

Compound **43**: ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.79, (ddt, *J*=17.0, 10.3, 6.7 Hz, 1H), 5.09 (dq, *J*=17.2, 1.7 Hz, 1H), 5.05 (dm, *J*=10.3 Hz, 1H), 4.96 (s, 1H), 4.35–4.05 (m, 5H), 3.76 (dt, *J*=9.5, 6.7 Hz, 1H), 3.45 (dt, *J*=9.5, 6.9 Hz, 1H), 2.58 (dd, *J*=3.8, 1.7 Hz, 1H), 2.52 (dd, *J*=7.2, 1.9 Hz, 1H), 2.31 (qt, *J*=6.7, 1.2 Hz, 2H), 2.11 (s, 3H).

4.41. 3-Butenyl 5-*O*-acetyl-2,3-*O*-thiocarbonyl-β-D-ribofuranoside (44)

To a solution of diol **43** (201 mg, 0.82 mmol) in CH_2Cl_2 (15 mL) was added thiocarbonyldiimidazole (150 mg, 0.84 mmol) and the reaction was stirred under Ar at 20 °C and monitored by TLC (silica gel, AcOEt/cyclohexane 5:5). After 3 h, more thiocarbonyldiimidazole (150 mg) was added and stirring was continued for 2 h. The solvent was evaporated and the residue chromatographed (AcOEt/cyclohexane 2:8) to afford the thiocarbonyl derivate **44** (208 mg, 88%). ^{1}H NMR(300 MHz, $CDCl_3$): δ=5.75 (ddt, *J*=10.6, 6.8 Hz, H), 5.37 (d, *J*=6.8 Hz, 1H), 5.32 (s, 1H), 5.24 (d, *J*=6.8 Hz, 1H), 5.10 (dq, *J*=17.2, 1.7 Hz, 1H), 5.07 (dm, *J*=10.4 Hz, 1H), 4.63 (dd, *J*=8.0, 6.4 Hz, 1H), 4.19 (dd, *J*=11.5, 8.0 Hz, H), 4.14 (dd, *J*=11.6, 6.5 Hz, 1H), 3.75 (dt, *J*=9.5, 6.8 Hz, 1H), 3.52 (dt, *J*=9.5, 6.2 Hz, 1H), 2.32 (qt, *J*=6.7, 1.4 Hz, 2H), 2.11 (s, 3H). HRMS calcd for $C_{12}H_{16}NaO_6S$ [M+Na] 311.0560, found 311.0564.

4.42. 3-Butenyl 2,3-*O*-thiocarbonyl-β-D-ribofuranoside (45)

To a solution of **44** (315 mg, 1.09 mmol) in MeOH was added solid Na_2CO_3 (25 mg) and the heterogeneous mixture was stirred at 20 °C for 1 h (monitoring by TLC, silica gel, AcOEt/cyclohexane 2:8). The reaction was poured in a concentrated solution of NH_4Cl in water and extracted with CH_2Cl_2. The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed (AcOEt/cyclohexane 2:8) to yield **45** (181 mg, 60%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.77 (ddt, *J*=17.2, 10.3, 6.9 Hz, 1H), 5.50 (d, *J*=6.7 Hz, 1H), 5.32 (s, 1H), 5.22 (d, *J*=6.7 Hz, 1H), 5.15 (dq, *J*=17.2, 1.7 Hz, 1H), 5.13 (dm, *J*=10.3 Hz, 1H), 4.70 (t, *J*=2.9 Hz, 1H), 3.87 (dt, *J*=9.5, 6.7 Hz, 1H), 3.80–3.71 (m, 2H), 3.67 (dt, *J*=9.5, 6.2 Hz, 1H), 3.08 (dd, *J*=10.0, 4.1 Hz, 1H), 2.39 (qt, *J*=6.4, 1.2 Hz, 2H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=189.7, 133.7, 117.9, 106.8, 89.0, 87.1, 86.5, 68.6, 63.0, 33.6.

4.43. 3-Butenyl 5-*O*-acryloyl-2,3-*O*-thiocarbonyl-β-D-ribofuranoside (46)

To a solution of alcohol **45** (140 mg, 0.57 mmol) in CH_2Cl_2 (5 mL) was added acryloyl chloride (55 μL, 1.2 equiv) and *N*,*N*-diisopropylethylamine (300 μL) and the reaction was stirred at 20 °C for 1 h under Ar (TLC, silica gel, AcOEt/cyclohexane 2:8). The mixture was poured in a diluted aqueous solution of NH_4Cl, extracted with CH_2Cl_2, the organic layer was dried over $MgSO_4$, filtered and the solvent was removed. The residue was chromatographed (AcOEt/cyclohexane 2:8) to yield **46** (100 mg, 59%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.47 (dd, *J*=17.2, 1.2 Hz, H), 6.14 (dd, *J*=17.2, 10.5 Hz, 1H), 5.93 (dd, *J*=10.5, 1.2 Hz, 1H), 5.75 (ddt, *J*=17.2, 10.5, 6.9 Hz, 1H), 5.39 (d, *J*=6.7 Hz, 1H), 5.33 (s, 1H), 5.25 (d, *J*=6.7 Hz, 1H), 5.09 (dq, *J*=17.2, 1.7 Hz, 1H), 5.08 (dm, *J*=10.3 Hz, 1H), 4.68 (t, *J*=7.2 Hz, 1H), 4.28 (dd, *J*=11.7, 8.1 Hz, 1H), 4.23 (dd, *J*=11.7, 6.7 Hz, 1H), 3.76 (dt, *J*=9.5, 6.9 Hz, 1H), 3.52 (dt, *J*=9.5, 6.7 Hz, 1H), 2.32 (qt, *J*=6.7, 1.2 Hz, 2H).

4.44. (5-But-3-enoxy-2,5-dihydrofuran-2-yl)methyl prop-2-enoate (47)

A solution of thiocarbonate **46** (100 mg, 0.33 mmol) in $P(OMe)_3$ was stirred in an oil bath at 122 °C for 2 h. Progress of the reaction was controlled by ^{1}H NMR of aliquots. The solvent was thoroughly removed under vacuum at 60 °C to afford crude **47**. ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.46 (dd, *J*=17.4, 1.5 Hz, 1H), 6.16 (dd, *J*=17.2 Hz, 1H), 6.15 (dt, *J*=6.0, 1.2 Hz, 1H), 5.93 (ddd, *J*=6.0, 2.2, 1.0 Hz, 1H), 5.86 (dd, *J*=10.3, 1.4 Hz, 1H), 5.81 (ddt, *J*=17.2, 10.3, 6.7 Hz, 1H), 5.31 (s, 1H), 5.10 (dq, *J*=17.2, 1.4 Hz, 1H), 5.03 (dm, *J*=10.3 Hz, 1H), 4.93 (m, 1H), 4.32 (dd, *J*=11.4, 3.8 Hz, H), 4.17 (dd, *J*=11.7, 6.2 Hz, 1H), 3.79 (dt, *J*=9.5, 6.9 Hz, 1H), 3.58 (dt, *J*=9.3, 6.7 Hz, 1H), 2.35 (qt, *J*=5.5, 1.2 Hz, 2H).

4.45. (*S*)-3-[[(6*R*)-3,6-Dihydro-2*H*-pyran-6-yl]oxy]-3,6-dihydro-2*H*-pyran (48)

A solution of thiocarbonyl derivative **41** (715 mg, 2.50 mmol) in trimethylphosphite was heated under Ar at 115 °C for ca. 4 h. Progress of the reaction was controlled by ^{1}H NMR of aliquots after evaporation of the solvent. The reaction mixture was concentrated

under vacuum and the crude **42** (470 mg) was diluted in benzene (200 mL) and divided in two parts. To each part, [**Ru**]-2 catalyst (45 mg) was added and the solution was heated to 60 °C and stirred for 30 min at which time formation of a more polar compound was observed (TLC, silica gel, AcOEt/cyclohexane 2:8). After evaporation of the solvents, the two residues were combined and chromatographed to yield the bis-dihydropyran **48** (266 mg, 58% over two steps).

Compound **42**: ^{1}H NMR(300 MHz, C_6D_6): δ=5.88–5.73 (m, 3H), 5.70 (q, *J*=1.1 Hz, 1H), 5.58 (ddd, *J*=6.0, 2.3, 1.1 Hz, 1H), 5.20 (dq, *J*=17.3, 1.7 Hz, 1H), 5.05 (dm, *J*=12.2 Hz, 1H), 5.02–4.97 (m, 2H), 4.84 (tm, *J*=6.2 Hz, 1H), 3.84–3.77 (m, 3H), 3.53 (dd, *J*=9.6, 6.2 Hz, 1H), 3.48–3.31 (m, 2H), 2.30 (qt, *J*=6.6, 1.5 Hz, 2H). HRMS calcd for $C_{12}H_{18}NaO_3$ [M+Na] 233.1148, found 233.1147.

Compound **48**: $[\alpha]_D^{20}$ +75 (*c* 1.0, $CHCl_3$). ^{1}H NMR(400 MHz, C_6D_6): δ=5.85 (dq, *J*=10.3, 2.5 Hz, 1H), 5.68 (d, AB, *J*=10.1 Hz, 1H), 5.65 (d, AB, *J*=10.1 Hz, 1H), 5.47 (dtd, *J*=10.6, 2.6, 1.5 Hz, 1H), 5.02 (br s, 1H), 4.15 (m, 1H), 4.07 (dd, *J*=11.3, 4.5 Hz, 1H), 3.88 (dq, *J*=16.6, 2.3 Hz, 1H), 3.87–3.78 (m, 2H), 3.79 (dq, *J*=16.9, 2.5 Hz, 1H), 3.43 (dd, *J*=10.8, 6.1 Hz, 1H), 1.96 (ddd, *J*=17.6, 11.6, 5.8 Hz, 1H), 1.34 (dt, *J*=17.9, 3.3 Hz, 1H). ^{13}C NMR (100.6 MHz, C_6D_6): δ=129.6, 128.6, 126.9, 126.1, 93.9, 69.5, 69.2, 65.1, 57.2, 24.9. HRMS calcd for $C_{10}H_{14}NaO_3$ [M+Na] 205.035, found 205.0832.

4.46. (3*S*)-3-[[(2*R*)-3,4-Dihydro-2*H*-pyran-2-yl]oxy]-3,4-dihydro-2*H*-pyran (49) and (3*S*)-3-[[(6*R*)-3,6-dihydro-2*H*-pyran-6-yl]oxy]-3,4-dihydro-2*H*-pyran (50)

To a solution of bis-dihydropyran **48** (64 mg, 0.35 mmol) in toluene (2 mL) was added isopropanol (0.25 mL), solid NaOH (~9 mg), and [**Ru**]-2 catalyst (~1.5 mg). The reaction was heated at 110 °C for 0.5–1 h. The progress of the reaction was monitored by TLC (silica gel, AcOEt/cyclohexane 2:8, **50**: R_f ~0.50, **48**: R_f ~0.62): when the spot corresponding to **50** became the major one the reaction was cooled to 20 °C and ethyl acetate was added. Prolonged reaction times lead to increased formation of the apparently thermodynamically favored **49** at the expense of **50** while **48** is still present in the mixture. After washing with water, the organic layer was dried over $MgSO_4$, filtered, and evaporated. The residue was chromatographed (AcOEt/cyclohexane 0.5:9.5 then 1:9) to yield **49** (10 mg, 16%), a mixture of **49** and **50** (8 mg, 12%), pure **50** (21.5 mg, 34%), and remaining **48** (6.5 mg, 10%).

Compound **49**: ^{1}H NMR(400 MHz, C_6D_6): δ=6.33 (dt, *J*=6.0, 2.0 Hz, 1H), 6.14 (ddd, *J*=6.0, 1.8, 1.3 Hz, 1H), 4.86 (t, *J*=3.0 Hz, 1H), 4.60 (m, 1H), 4.43 (ddd, *J*=6.0, 4.8, 3.0 Hz, 1H), 4.21 (ddd, *J*=10.3, 3.5, 2.0 Hz, 1H), 3.97 (m, 1H′), 3.72 (dd, *J*=10.0, 9.0 Hz, 1H), 2.10–2.00 (m, 2H), 1.94 (ddt, *J*=16.6, 7.7, 2.5 Hz, 1H), 1.67–1.49 (m, 3H). ^{13}C NMR (100.6 MHz, C_6D_6): δ=144.2, 140.7, 101.7, 97.3, 95.8, 69.4, 68.5, 27.2, 26.9, 16.3. HRMS calcd for $C_{10}H_{14}NaO_3$ [M+Na] 205.0835, found 205.0831.

Compound **50**: ^{1}H NMR(400 MHz, C_6D_6): δ=6.36 (dt, *J*=6.0, 2.0 Hz, 1H), 5.67 (dd, *J*=10.0, 5.3 Hz, 1H), 5.61 (dt, *J*=10.5, 2.5 Hz, 1H), 4.97 (s, 1H), 4.45 (ddd, *J*=6.0, 4.5, 3.0 Hz, 1H), 4.23 (ddd, *J*=10.3, 3.3, 1.8 Hz, 1H), 3.97–3.90 (m, 1H), 3.81 (t, *J*=9.5 Hz, 1H), 3.77 (td, *J*=11.3, 3.5 Hz, 1H), 3.42 (dd, *J*=10.9, 6.2 Hz, 1H), 2.12–2.04 (m, 1H), 2.01–1.90 (m, 2H), 1.34 (ddd, *J*=17.6, 4.8, 4.0 Hz, 1H). ^{13}C NMR (100.6 MHz, C_6D_6): δ=144.2, 128.6, 126.8, 97.6, 93.5, 69.6, 68.8, 57.2, 27.2, 24.9. HRMS calcd for $C_{10}H_{14}NaO_3$ [M+Na] 205.0835, found 205.0830.

4.47. (3*S*)-3-[[(6*R*)-3,6-Dihydro-2*H*-pyran-6-yl]oxy]-2,3-dihydropyran-6-one (52)

Powdered CrO_3 (824 mg, 8.24 mmol) previously dried under vacuum over P_2O_5 was suspended in dry CH_2Cl_2 (7 mL) under Ar. The mixture was cooled at −20 °C and 3,5-dimethylpyrazole (795 mg, 8.27 mmol) was added rapidly under stirring. After 15 min a solution of bis-dihydropyran **48** (124 mg, 0.68 mmol) in CH_2Cl_2 (2 mL) was added. After stirring at −20 °C for 2 h, the reaction mixture was quickly filtered over silica gel (eluent: AcOEt). The filtrate was evaporated and the residue immediately chromatographed (AcOEt/cyclohexane 4:6) to yield lactone **52** (83 mg, 62%). ^{1}H NMR (400 MHz, C_6D_6): δ=6.05 (dd, *J*=10.1, 3.8 Hz, 1H), 5.69 (dd, *J*=10.1, 1.1 Hz, 1H), 5.63 (ddm, *J*=10.2, 5.8 Hz, 1H), 5.46 (dtd, *J*=10.1, 2.8, 1.3 Hz, 1H), 4.69 (s, 1H), 4.06 (ddd, *J*=11.6, 6.0, 0.5 Hz, 1H), 3.97 (ddd, *J*=11.6, 4.5, 0.5 Hz, 1H), 3.63 (m, 1H), 3.53 (td, *J*=11.6, 3.6 Hz, 1H), 3.28 (dd, *J*=11.1, 6.1 Hz, 1H), 1.88 (m, 1H), 1.27 (dm, *J*=17.9 Hz, 1H). ^{13}C NMR (100.6 MHz, C_6D_6): δ=162.1, 144.3, 129.4, 125.7, 122.4, 94.2, 70.5, 66.6, 57.3, 24.6.

4.48. (5*S*)-5-[(2*R*)-Tetrahydropyran-2-yl]oxytetrahydropyran-2-one (53)

A solution of lactone **52** (233 mg, 1.19 mmol) in AcOEt (14 mL) was hydrogenated for 16 h at atmospheric pressure (1 atm) in presence of Pd/C 10% (80 mg). The reaction mixture was filtered over Celite and the solvent was evaporated. Chromatography (silica gel, AcOEt/cyclohexane 4:6) afforded **53** (138 mg, 58%). IR (neat, cm^{-1}) ν 3407, 2942, 2868, 1710, 1134, 1072, 1021, 988. ^{1}H NMR (400 MHz, C_6D_6): δ=4.33 (t, *J*=3.5 Hz, 1H), 4.09 (ddd, *J*=11.8, 4.0, 1.8 Hz, 1H), 3.75 (dd, *J*=11.8, 3.5 Hz, 1H), 3.59 (ddd, *J*=11.3, 9.1, 2.8 Hz, 1H), 3.37 (quint., *J*=4.3 Hz, 1H), 3.24 (dtd, *J*=11.1, 4.4, 1.3 Hz, 1H), 2.29 (ddd, *J*=17.1, 9.6, 7.0 Hz, 1H), 1.96 (ddd, *J*=17.1, 6.8, 5.5 Hz, 1H), 1.62–1.53 and 1.43–1.10 (m, 8H). ^{13}C NMR (100.6 MHz, C_6D_6) δ=169.3, 97.3, 72.0, 67.7, 62.0, 31.0, 26.7, 25.6, 24.5, 19.4. HRMS calcd for $C_{10}H_{16}NaO_4$ [M+Na] 223.0941, found 223.0938.

4.49. (5*S*)-5-[(2*R*)-Tetrahydropyran-2-yl]oxytetrahydropyran-2-ol (54)

To a cold (−78 °C) solution of lactone **53** (99 mg, 0.494 mmol) in dry toluene (9 mL), DIBAL-H (1 M in toluene, 0.66 mL) was added under stirring. Stirring at −78 °C was continued for 45 min after which time more DIBAL-H (0.33 mL) was added. After an additional 1.5 h the reaction was quenched with Rochelle salt (3 mL), allowed to warm to 20 °C, neutralized with saturated $NaHCO_3$ (6 mL), and extracted with Et_2O (three times). The organic layer was dried over $MgSO_4$, filtered, and evaporated. The residue was chromatographed (silica gel, AcOEt/cyclohexane 4:6) to yield the polydeoxydisaccharide **54** (69 mg, 69%, as a mixture of two anomers (M+m) in the ratio of 0.55: 0.45) (M=Major product, m=minor product). ^{1}H NMR (400 MHz, C_6D_6): δ=4.80 (t, *J*=3.1 Hz, 1H,), 4.71 (m,1H), 4.63 (t, *J*=3.6 Hz, 1H), 4.56 (t, *J*=3.5 Hz, 1H), 4.20 (m,1H), 4.05 (dd, *J*=11.1, 8.5 Hz, 1H), 3.85 (ddd, *J*=10.8, 4.1, 1.6 Hz, 1H), 3.78 (dt, *J*=8.8, 3.1 Hz, 1H), 3.76 (dt, *J*=8.8, 3.1 Hz, 1H), 3.67–3.56 (m, 3H), 3.35–3.28 (m, 2H), 1.9–1.2 (m). ^{13}C NMR (100.6 MHz, C_6D_6): δ=97.4 (m), 97.1 (M), 94.2 (m), 92.2 (M), 70.6 (M), 70.5 (M), 66.6 (m), 65.1 (M), 62.01 (m), 61.98 (M), 31.3 (m), 31.2 (M), 29.5 (M), 29.0 (m), 25.8 (2C) (M+m), 25.3 (m), 24.9 (M), 19.7 (m), 19.6 (M). HRMS calcd for $C_{10}H_{17}O_3$ [(M+H)−H_2O] 185.1172, found 185.1163.

4.50. 3-Butenyl 2,3-*O*-isopropylidene-5-*O*-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-β-D-ribofuranoside (55)

A solution of acetonide **38** (0.963 g, 3.94 mmol) and commercial 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose (1.50 g, 4.73 mmol, 1.20 equiv) in acetonitrile (25 mL) was stirred at 0 °C, under Ar. $SnCl_4$ (276 μL) was slowly dripped along the wall of the flask during which formation of a white solid was observed. The reaction was monitored by TLC (silica gel, AcOEt/cyclohexane 4:6, the spot corresponding to **55** appears between those of the starting materials) and was complete after 15–20 min. The reaction was quenched

with aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The organic layer was washed with water, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Chromatography of the residue (AcOEt/cyclohexane 2:8) afforded the protected disaccharide **55** (0.963 g, 46%). $[\alpha]_D^{20}$ −63 ($CHCl_3$, *c* 1.0). IR (neat, cm^{-1}) ν 2982, 2939, 1745, 1371, 1214, 1085, 1043. ^1H NMR (400 MHz, $CDCl_3$): δ=5.77 (ddt, *J*=17.1, 10.3, 6.7 Hz, 1H), 5.34 (dd, *J*=6.7, 4.8 Hz, 1H), 5.26 (dd, *J*=4.8, 1.0 Hz, 1H), 5.07 (dq, *J*=17.4, 1.7 Hz, 1H), 5.06 (s, 1H), 5.04 (br s, 1H), 5.04 (dm, *J*=10.3 Hz, 1H), 4.64 (br d, *J*=6.0 Hz, 1H), 4.60 (d, *J*=6.0 Hz, 1H), 4.34–4.27 (m, 3H), 4.17–4.11 (m, 1H), 3.70 (dd, *J*=10.1, 8.1 Hz, 1H), 3.69 (dt, *J*=9.6, 6.8 Hz, 1H), 3.50 (dd, *J*=10.1, 6.6 Hz, 1H), 3.42 (dt, *J*=9.6, 6.6 Hz, 1H), 2.29 (qt, *J*=6.8, 1.3 Hz, 2H), 2.11 (s, 3H), 2.10 (s, 3H), 2.06 (s, 3H), 1.48 (s, 3H), 1.32 (s, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ=170.6, 169.6, 169.5, 134.9, 116.6, 112.4, 108.1, 105.3, 85.1, 84.8, 81.9, 78.6, 74.7, 71.3, 69.2, 66.9, 64.4, 33.8, 26.3, 24.9, 20.7, 20.5, 20.5. HRMS calcd for $C_{23}H_{34}NaO_{12}$ [M+Na] 525.1943, found 525.1949.

4.51. 3-Butenyl 2,3-*O*-isopropylidene-5-*O*-(-β-D-ribofuranosyl)-β-D-ribofuranoside (56)

A solution of **55** (1.271 g, 2.53 mmol) in MeOH (35 mL) was placed under argon atmosphere and maintained at 20 °C. *t*-BuOK (12 mg) was added and the reaction was stirred for 6 h (monitoring: TLC, silica gel, AcOEt/cyclohexane 5:5). Quenching (Dowex H^+) followed by evaporation of the solvent afforded the crude **56** (0.947 g, 99%). ^1H NMR (300 MHz, $CDCl_3$) δ=5.77 (ddt, *J*=17.2, 10.3, 6.7 Hz, 1H), 5.09 (s, 1H), 5.09 (dq, *J*=17.2, 1.8 Hz, 1H), 5.04 (dm, *J*=10.0 Hz, 1H), 4.98 (s, 1H), 4.63–4.59 (m, 2H), 4.47–4.39 (m, 2H), 4.08–4.02 (m, 2H), 3.87 (dd, *J*=12.4, 2.9 Hz, 1H), 3.73 (dt, *J*=9.5, 6.7 Hz, 1H), 3.70–3.59 (m, 3H), 3.43 (dt, *J*=9.5, 6.7 Hz, 1H), 2.30 (qt, *J*=6.7, 1.2 Hz, 2H), 1.48 (s, 3H), 1.32 (s, 3H).

4.52. 3-Butenyl 2,3-*O*-isopropylidene-5-*O*-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)-β-D-ribofuranoside (57)

A solution of crude **56** (1.895 g, 5.034 mmol) and *p*-toluenesulfonic acid (50 mg) in acetone (26 mL) and 2-methoxypropene (13 mL) was stirred for 3 h at 20 °C (monitoring: TLC, silica gel, AcOEt/cyclohexane 8:2 and 3:7). Methanol (5 mL) and water (1 mL) were added and the reaction was stirred for 2 h. Solid $NaHCO_3$ (ca. 100 mg), was added. After filtration, the solvent was evaporated and the residue was chromatographed (silica gel: AcOEt/cyclohexane 2:8) to yield **57** (702 mg, 33% over two steps). ^1H NMR (300 MHz, $CDCl_3$): δ=5.78 (ddt, *J*=17.2, 10.3, 6.7 Hz, 1H), 5.12 (s, 1H), 5.10 (s, 1H), 5.09 (dm, *J*=17.2 Hz, 1H), 5.04 (dm, *J*=10.1 Hz, 1H), 4.79 (d, *J*=6.0 Hz, 1H), 4.65 (d, *J*=7.2 Hz, 1H), 4.61 (d, *J*=6.0 Hz, 1H), 4.56 (dl, *J*=6.2 Hz, 1H), 4.45–4.39 (m, 2H), 3.77–3.60 (m, 5H), 3.45 (dt, *J*=9.5, 6.4 Hz, 1H), 1.49 (s, 3H), 1.48 (s, 3H), 1.32 (s, 3H), 1.31 (s, 3H).

4.53. 3-Butenyl 2,3-*O*-isopropylidene-5-*O*-(5-*O*-allyl-2,3-*O*-isopropylidene-β-D-ribofuranosyl)-β-D-ribofuranoside (58)

To a stirred solution of **57** (700 mg, 1.68 mmol) in DMF (8 mL) at 0 °C was added NaH (55% in oil) (200 mg). After 5 min the reaction mixture was allowed to warm to 20 °C. Allyl bromide (350 μL, >2 equiv) was added and the reaction was stirred for 1h (TLC, silica gel, AcOEt/cyclohexane 3:7). MeOH was added slowly at 0 °C, the solvents were evaporated and the residue dissolved in CH_2Cl_2 and water. After extraction with water, the organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was chromatographed (AcOEt/cyclohexane 1:9) to afford **58** (509 mg, 66%). $[\alpha]_D^{20}$ −88 ($CHCl_3$, *c* 1.1). IR (neat, cm^{-1}) ν 2984, 2932, 2911, 1370, 1272, 1245, 1207, 1161, 1111, 1082, 1045. ^1H NMR (300 MHz, $CDCl_3$): δ=5.90 (ddt, *J*=17.1, 10.3, 5.5 Hz, 1H), 5.77 (ddt, *J*=17.1, 10.3, 6.8 Hz, 1H), 5.29 (dq, *J*=17.1, 1.5 Hz, 1H), 5.20 (dq, *J*=10.3, 1.5 Hz, 1H), 5.09 (dq, *J*=17.1, 1.5 Hz, 1H), 5.05 (dm, *J*=10.3 Hz, 1H), 4.68 (dd, *J*=6.0, 0.8 Hz, 1H), 4.65 (d, *J*=6.0 Hz, 1H), 4.59 (s, 2H), 4.35 (ddd, *J*=7.8, 6.8, 0.8 Hz, 1H), 4.26 (t, *J*=7.3 Hz, 1H), 4.01 (dq, *J*=5.5, 1.3 Hz, 2H), 3.70 (dt, *J*=9.6, 6.8 Hz, 1H), 3.65 (dd, *J*=10.1, 7.8 Hz, 1H), 3.48 (dd, *J*=9.6, 6.6 Hz, 1H), 3.46–3.39 (m, 3H), 2.29 (qt, *J*=6.6, 1.3 Hz, 2H), 1.48 (s, 3H), 1.32 (s, 3H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ=134.9, 134.5, 117.4, 116.7, 112.4 (2C), 108.5, 108.0, 85.2, 85.2 (2C), 85.1, 82.1, 82.0, 72.2, 70.9, 68.8, 66.9, 33.8, 26.4 (2C), 25.0, 24.9. HRMS calcd for $C_{23}H_{36}NaO_9$ [M+Na] 479.2252, found 479.2258.

4.54. 3-Butenyl 5-*O*-(5-*O*-allyl-β-D-ribofuranosyl)-β-D-ribofuranoside (59)

The protected disaccharide **58** (466 mg, 0.102 mmol) was placed in a round-bottomed flask and cooled to −5 °C. A cold (−5 °C) mixture of TFA/H_2O (7:3, 6 mL) was added and the reaction mixture was stirred. Monitoring of the reaction (TLC, silica gel, AcOEt/cyclohexane 6:4) revealed transient formation of a compound (R_f=0.28; AcOEt, R_f=0.54), presumably a diol, then of the more polar **59** (AcOEt, R_f=0.15). When **59** became the main product according to TLC, cold AcOEt (6 mL) was added and the solvent was evaporated at 0 °C (high vacuum necessary). This operation was repeated twice and the residue was dissolved in toluene and evaporated at 20 °C. Chromatography (AcOEt) afforded crude **59** (172 mg, 45%). ^1H NMR (300 MHz, $CDCl_3$): δ=5.91 (ddt, *J*=17.2, 10.6, 5.8 Hz, 1H), 5.78 (ddt, *J*=17.1, 10.2, 6.8 Hz, 1H), 5.30 (dq, *J*=17.2, 1.1 Hz, 1H), 5.22 (dq, *J*=10.3, 1.1 Hz, 1H), 5.09 (dq, *J*=17.1, 1.4 Hz, 1H), 5.04 (dm, *J*=10.3 Hz, 1H), 5.02 (1H, s), 4.93 (s, 1H), 4.22 (t, *J*=5.4 Hz, 1H), 4.16–4.01 (m), 3.81–3.39 (m), 2.30 (br q, *J*=6.7 Hz, 2H).

4.55. 3-Butenyl 5-*O*-(5-*O*-allyl-2,3-*O*-thiocarbonyl-β-D-ribofuranosyl)-2,3-*O*-thiocarbonyl β-D-ribofuranoside (60)

Under argon atmosphere, a solution of **59** (172 mg, 0.457 mmol) and thiocarbonyldiimidazole (300 mg, 3.7 equiv) in dry (dist. over CaH_2) CH_2Cl_2 (5 mL) was stirred for 4 h. The solvent was removed and the residue chromatographed (AcOEt/cyclohexane 2:8) to give pure **60** (169 mg, 0.367 mmol, 80%). Mp: 119–124 °C. $[\alpha]_b^{20}$ −90 ($CHCl_3$, *c* 1.0). IR (neat, cm^{-1}) ν 2950, 2879, 1357, 1320, 1300, 1279, 1244, 1158, 1101, 1051, 1002. ^1H NMR (400 MHz, $CDCl_3$): δ=5.88 (ddt, *J*=17.1, 10.3, 5.5 Hz, 1H), 5.75 (ddt, *J*=17.1, 10.3, 6.8 Hz, 1H), 5.39 (d, *J*=6.8 Hz, 1H), 5.33–5.23 (m, 4H), 5.32 (s, 1H), 5.30 (s, 1H), 5.18 (d, *J*=6.8 Hz, 1H), 5.11 (dq, *J*=17.1, 1.5 Hz, 1H), 5.10 (dm, *J*=10.3 Hz, 1H), 4.67 (t, *J*=6.6 Hz, 1H), 4.53 (dd, *J*=8.3, 6.8 Hz, 1H), 4.03 (dt, *J*=5.5, 1.1 Hz, 1H), 3.76–3.69 (m, 2H), 3.63 (dd, *J*=10.3, 6.6 Hz, 1H), 3.57 (dd, *J*=10.3, 6.0 Hz, 1H), 3.53 (dt, *J*=9.6, 6.3 Hz, 1H), 3.48 (dd, *J*=10.3, 7.5 Hz, 1H), 2.32 (qt, *J*=6.6, 1.2 Hz, 2H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ=189.5, 189.5, 134.1, 133.7, 118.1, 117.5, 107.1, 106.3, 88.4, 88.2, 86.2, 85.9, 84.4, 83.7, 72.3, 69.2, 68.2, 67.9, 33.6. HRMS calcd for $C_{19}H_{24}NaO_9S_2$ [M+Na] 483.0754, found 483.0758.

4.56. Attempted RRM of 60

A solution of **60** (53 mg, 0.11 mmol) in $P(OMe)_3$ (3 mL) was placed under Ar atmosphere and heated at 115 °C for 3.25 h. The solvent was evaporated under vacuum and the resulting crude tetraene **61** was dissolved in dry benzene (12 mL). [**Ru**]-2 (6 mg) was added and the temperature of the mixture was raised from 20 °C to 70 °C. After 45 min at 70 °C, the solvent was evaporated and the residue was chromatographed (silica gel, AcOEt/cyclohexane 1:9 then 2:8) to provide the unstable pseudo dimer **62** (14 mg) and recovered crude **61** (3 mg).

Compound **61** (crude): ^1H NMR (300 MHz, C_6D_6): δ=5.88–5.75 (m), 5.71 (q, *J*=1.1 Hz, 1H), 5.59 (ddd, *J*=6.1, 2.2, 1.1 Hz, 2H), 5.21 (dq, *J*=17.3, 1.8 Hz, 1H), 5.07–4.97 (m, 3H), 4.93 (tm, *J*=5.8 Hz, 1H), 4.81

(tm, J=5.9 Hz, 1H), 3.84–3.76 (m, 4H?), 3.51 (dd, J=9.7, 6.2 Hz, 1H), 3.47–3.31 (m, 4H), 2.29 (qt, J=6.7, 1.4 Hz, 2H).

Compound **62**: ^{1}H NMR (400 MHz, C_6D_6): δ=6.11 (br s, 1H), 6.05 (, dt, J=6.0, 1.3 Hz, 1H), 5.94 (dtt, J=15.6, 6.8, 1.6 Hz, 1H), 5.72 (dt, J=6.0, 1.3 Hz, 1H), 5.62 (dt, J=5.8, 1.5 Hz, 1H), 5.59 (s, 1H), 5.44 (dtt, J=15.6, 4.8, 1.3 Hz, 1H), 5.34 (ddd, J=5.8, 2.0, 0.7 Hz, 1H), 4.93 (m,1H), 4.63 (m, 1H), 3.93 (dd, J=9.6, 4.8 Hz, 1H), 3.81–3.69 (m, 3H), 3.57 (dd, J=9.6, 7.6 Hz, 1H), 3.49 (dd, J=10.3, 3.3 Hz, 1H), 3.44 (dt, J=8.8, 3.8 Hz, 1H), 3.30 (dd, J=10.3, 4.3 Hz, 1H), 2.31–2.21 (m, 1H), 2.03–1.95 (m, 1H). ^{13}C NMR (100.6 MHz, C_6D_6): δ=134.3, 133.9, 131.0, 127.4, 127.4, 127.0, 108.1, 108.0, 85.1, 84.3, 71.3, 70.5, 67.8.

4.57. 1-*O*-Acetyl-2,3-*O*-isopropylidene-6-*O*-tosyl-α-D-mannofuranose (66)

The monoacetonide **65** (16.39 g, 62.5 mmol) was dissolved at 0 °C in pyridine (320 mL) and DMAP (7.60 g, 62.2 mmol) was added in four portions. The mixture was stirred until clear and tosyl chloride (23.8 g, 124.8 mmol) was added portionwise. Stirring was continued at 5–6 °C for 45 min and for 4 h at 20 °C. Then the reaction was cooled in an ice bath and water (10 mL) was added. The solvents were co-evaporated with toluene and the residue was partitioned between ethyl acetate and water. The organic layer was extracted with ethyl acetate, the combined organic layers were dried ($MgSO_4$) and the solvent was removed under reduced pressure to afford **66** (20.50 g), which was used directly for the next step. For analytical purposes, a pure sample was prepared by chromatography (silica gel, AcOEt/cyclohexane 4:6). $[\alpha]_D^{20}$ +38 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.80 (d, J=8.3 Hz, 2H), 7.36 (d, J=8.1 Hz, 2H), 6.12 (s, 1H), 4.90 (dd, J=5.8, 3.8 Hz, 1H), 4.69 (d, J=5.8 Hz, 1H), 4.28 (m, 1H), 4.19–4.09 (m, 2H), 4.05 (dd, J=8.1, 3.8 Hz, 1H), 2.72 (d, J=5.1 Hz, 1H, OH), 2.46 (s, 3H), 2.07 (s, 3H), 1.45 (s, 3H), 1.33 (s, 3H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=169.3, 145.1, 132.5, 129.9 (2C), 128.0 (2C), 113.4, 100.3, 84.6, 80.3, 79.4, 71.6, 67.8, 25.9, 24.6, 21.6, 21.0. HRMS calcd for $C_{18}H_{24}NaO_9S$ [M+Na] 439.1033, found 439.1034.

4.58. 1-*O*-Acetyl-6-iodo-2,3-*O*-isopropylidene-α-D-mannofuranose (67)

A solution of **66** (20.50 g) in butanone (400 mL) was refluxed with NaI, $2H_2O$ (21.2 g, 113.98 mmol) for 3 h (monitoring: TLC, silica gel, AcOEt/cyclohexane 5:5). The solvent was evaporated and the residue partitioned between diethyl ether and aqueous sodium hydrogenosulfite. The organic layer was extracted with H_2O, dried over $MgSO_4$, and the solvents were evaporated. Chromatography of the residue (silica gel, AcOEt/cyclohexane 4:6) yielded **67** (10.02 g, yield from mannose over five steps: 40%). ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.15 (s, 1H), 4.92 (dd, J=5.8, 4.0 Hz, 1H), 4.71 (d, J=5.8 Hz, 1H), 4.01 (dd, J=8.2, 3.8 Hz, 1H), 3.79 (m, 1H), 3.57 (dd, J=10.4, 3.3 Hz, 1H), 3.38 (dd, J=10.5, 6.8 Hz, 1H), 2.60 (d, J=5.8 Hz, 1H, OH), 2.08 (s, 3H), 1.50 (s, 3H), 1.35 (s, 3H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=169.4, 113.4, 100.4, 84.8, 83.5, 79.4, 68.8, 26.0, 24.7, 21.1, 12.4. HRMS calcd for $C_{11}H_{17}INaO_6$ [M+Na] 394.9962, found 394.9960.

4.59. 1-*O*-Acetyl-2,3-*O*-isopropylidene-α-D-rhamnofuranose (68) and 1,5-Di-*O*-acetyl-2,3-*O*-isopropylidene-α-D-rhamnofuranose (69)

To a solution of **67** (4.47 g, 12 mmol) in ethanol (100 mL) were added 2.5 g of a Ra/Ni slurry and triethylamine (2.5 mL). The reaction was stirred under H_2 atmosphere at 20 °C for 20 h. The mixture was filtered over Celite, the Celite was carefully washed with EtOH and the filtrate was concentrated to afford the crude **75**, which was directly treated with pyridine (25 mL), Ac_2O (15 mL), and DMAP (one crystal) and stirred at 20 °C overnight (monitoring: TLC, silica gel, AcOEt/cyclohexane 3:7). The solvent was co-evaporated with toluene under reduced pressure and the residue was purified by chromatography (silica gel, AcOEt/cyclohexane 2:8 then 3:7) to yield **69** (3.107 g, 90%).

Compound **68**: ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.17 (s, 1H), 4.91 (dd, J=5.8, 3.8 Hz, 1H), 4.70 (d, J=6.0 Hz, 1H), 4.08 (dq, J=7.4, 6.3 Hz, 1H), 3.96 (ddd, J=7.7, 4.0, 0.5 Hz, 1H), 2.08 (s, 3H), 1.50 (s, 3H), 1.35 (s, 3H), 1.34 (d, J=6.2 Hz, 3H).

Compound **69**: mp 54–55 °C (AcOEt/pentane). $[\alpha]_D^{20}$ +53 (c 1.1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.16 (s, 1H), 5.15 (dq, J=7.3, 6.4 Hz, 1H), 4.79 (dd, J=5.8, 3.6 Hz, 1H), 4.66 (d, J=6.0 Hz, 1H), 4.03 (dd, J=7.5, 3.8 Hz, 1H), 2.08 (3H, s, Ac), 2.06 (3H, s, Ac), 1.45 (3H, s, CH_3), 1.35 (3H, d, J=6.2 Hz, CH_3), 1.30 (3H, s, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=169.8, 169.4, 113.2, 100.6, 84.8, 83.7, 79.2, 68.2, 26.0, 24.9, 21.2, 21.1, 17.2. HRMS calcd for $C_{13}H_{20}NaO_7$ [M+Na] 311.1101, found 311.1105. Anal. Calcd for $C_{13}H_{20}O_7$: C 54.16, H 6.99, O 38.85. Found: C 54.25, H 7.05.

4.60. 3-Butenyl 5-*O*-acetyl-2,3-*O*-isopropylidene-α-D-rhamnofuranoside (70)

To a cold (−3 °C) solution of **69** (0.483 g, 1.67 mmol) in acetonitrile (15 mL) and under argon atmosphere were sequentially added 3-buten-1-ol (90 μL) and $SnCl_4$ (24 μL). After stirring for 3 h the reaction was quenched with aqueous $NaHCO_3$. The mixture was extracted with CH_2Cl_2, the organic layer was washed with water, dried over $MgSO_4$ and, after filtration, the solvent was removed under reduced pressure. The residue was chromatographed (silica gel, AcOEt/cyclohexane 2:8) to yield **70** (151 mg 30%) and along with recovered **69** (0.236 g, 50%). $[\alpha]_D^{20}$ +57 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.79 (ddt, J=17.0, 10.2, 6.6 Hz, 1H), 5.13 (dq, J=7.7, 6.2 Hz, 1H), 5.09 (dm, J=17.0 Hz, 1H), 5.05 (ddt, J=10.2, 1.9, 1.2 Hz, 1H), 5.00 (s, 1H), 4.70 (dd, J=5.8, 3.6 Hz, 1H), 4.56 (d, J=5.8 Hz, 1H), 3.89 (ddd, J=7.9, 3.6, 0.4 Hz, 1H), 3.68 (dt, J=9.8, 6.6 Hz, 1H), 3.48 (dt, J=9.8, 6.6 Hz, 1H), 2.32 (qt, J=6.6, 1.3 Hz, 2H), 2.05 (s, 3H), 1.43 (s, 3H), 1.36 (d, J=6.4 Hz, 3H), 1.28 (s, 3H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=169.9, 135.0, 116.6, 112.5, 106.0, 84.8, 81.5, 79.4, 68.4, 66.6, 33.9, 26.0, 24.9, 21.3, 17.5. HRMS calcd for $C_{15}H_{24}NaO_6$ [M+Na] 323.1465, found 323.1466.

4.61. 3-Butenyl 2,3-*O*-isopropylidene-α-D-rhamnofuranoside (71)

To a solution of **70** (599 mg, 1.99 mmol) in methanol (25 mL) was added *t*-BuOK (300 mg) and the reaction was stirred under Ar atmosphere at 20 °C for 3 h. Dowex H^+ was added and after stirring for 5 min the resin was filtered-off and the solvent was evaporated. Pure **71** (458 mg, 1.77 mmol, 89%).was obtained by column chromatography (silica gel, AcOEt/cyclohexane 2:8). $[\alpha]_D^{20}$ +59 (c 1.1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.79 (ddt, J=17.1, 10.3, 6.7 Hz, 1H), 5.09 (dq, J=17.3, 1.5 Hz, 1H), 5.04 (s, 1H), 5.04 (ddt, J=10.2, 2.1, 1.3 Hz, 1H), 4.85 (dd, J=6.0, 3.8 Hz, 1H), 4.59 (d, J=6.0 Hz, 1H), 4.08 (dt, J=7.0, 6.4 Hz, 1H), 3.75 (ddd, J=7.2, 3.8, 0.5 Hz, 1H), 3.69 (dt, J=9.8, 6.8 Hz, 1H), 3.47 (dt, J=9.8, 6.6 Hz, 1H), 2.31 (qt, J=6.8, 1.3 Hz, 2H), 1.49 (s, 3H), 1.35 (d, J=6.4 Hz, 3H), 1.32 (s, 3H). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ=135.0, 116.5, 112.6, 105.8, 84.9, 83.0, 80.0, 66.5 (2C), 33.8, 25.9, 24.5, 20.4. HRMS calcd for $C_{13}H_{22}NaO_5$ [M+Na] 281.1359, found 281.1359.

4.62. 3-Butenyl 2,3-*O*-isopropylidene-5-*O*-(5-*O*-acetyl-2,3-*O*-isopropylidene-α-D-rhamnofuranosyl)-α-D-rhamnofuranoside (72)

A solution of **71** (222 mg, 0.86 mmol) in acetonitrile (10 mL) and **68** (186 mg, 0.64 mmol, 1.5 equiv) was cooled at −4 °C and placed under argon atmosphere. $SnCl_4$ (60 μL) was added and the reaction

mixture was stirred for 1.5 h at 0 °C. Aqueous $NaHCO_3$ was added and the mixture was extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Chromatography (AcOEt/cyclohexane 2:8) yielded **72** (327 mg, 78%), which was used directly for the next step, along with recovered **68** (107 mg).

Compound **72**: ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.79 (ddt, J=17.0, 10.2, 6.6 Hz, 1H), 5.26 (s, 1H), 5.14 (dq, J=7.9, 6.2 Hz, 1H), 5.08 (dm, J=17.1 Hz, 1H), 5.04 (dm, J=9.8 Hz, 1H), 4.96 (s, 1H), 4.70 (d, J=6.0 Hz, 1H), 4.69 (d, J=5.8 Hz, 1H), 4.55 (d, J=5.8 Hz, 1H), 4.54 (d, J=6.0 Hz, 1H), 4.01 (dq, J=9.0, 6.2 Hz, 1H), 3.97 (dd, J=8.1, 3.7 Hz, 1H), 3.69 (dd, J=8.6, 3.4 Hz, 1H), 3.65 (dt, J=9.8, 6.8 Hz, 1H), 3.45 (dt, J=9.8, 6.6 Hz, 1H), 2.30 (qt, J=6.6, 1.4 Hz, 2H), 2.05 (s, 3H), 1.44 (s, 6H), 1.37 (d, J=6.2 Hz, 3H), 1.31 (s, 3H), 1.29 (d, J=6.2 Hz, 3H), 1.29 (s, 3H).

4.63. 3-Butenyl 2,3-*O*-isopropylidene-5-*O*-(2,3-*O*-isopropylidene-α-D-rhamnofuranosyl)-α-D-rhamnofuranoside (73)

To a solution of **72** (654 mg, 1.34 mmol) in methanol (27 mL) was added *t*-BuOK (300 mg) and the reaction was stirred under Ar atmosphere at 20 °C for 3 h. Dowex H^+ was added and after stirring for 5 min the resin was filtered-off and the solvent was evaporated. Compound **73** was purified by column chromatography (silica gel, AcOEt/cyclohexane 2:8) (562 mg, 94%). $[\alpha]_D^{20}$ +72 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.78 (ddt, J=17.1, 10.3, 6.6 Hz, 1H), 5.30 (s, 1H), 5.08 (dq, J=17.3, 1.5 Hz, 1H), 5.03 (dm, J=10.1 Hz, 1H), 4.95 (s, 1H), 4.84 (dd, J=5.8, 3.8 Hz, 1H), 4.70 (dd, J=5.8, 3.3 Hz, 1H), 4.57 (d, J=5.8 Hz, 1H), 4.54 (d, J=5.8 Hz, 1H), 4.07 (quint., J=6.9 Hz, 1H), 4.01 (dq, J=9.1, 6.3 Hz, 1H), 3.81 (dd, J=7.6, 3.8 Hz, 1H), 3.69 (dd, J=9.1, 3.5 Hz, 1H), 3.64 (dt, J=9.8, 6.8 Hz, 1H), 3.45 (dt, J=9.8, 6.6 Hz, 1H), 2.30 (qt, J=6.6, 1.3 Hz, 2H), 1.49 (s, 3H), 1.44 (s, 3H), 1.36 (d, J=6.6 Hz, 3H), 1.33 (s, 3H), 1.30 (s, 3H), 1.28 (d, J=6.3 Hz, 1H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ=135.0, 116., 112., 112., 106.6, 106.1, 85.0 (2C), 83.1, 82.6, 80.0, 79.5, 71.9, 66.6, 66.5, 33.9, 26.1, 25.9, 25.0, 24.5, 20.4, 19.0. HRMS calcd for $C_{22}H_{36}NaO_9$ [M+Na] 467.2252, found 467.2251.

4.64. 3-Butenyl 2,3-*O*-isopropylidene-5-*O*-(5-*O*-allyl-2,3-*O*-isopropylidene-α-D-rhamnofuranosyl)-α-D-rhamnofuranoside (74)

To a cool (0 °C) solution of **73** (502 mg, 1.13 mmol) in DMF (10 mL) was added NaH/oil (55%) (180 mg). After stirring for 10 min under an argon atmosphere at 0 °C, the bath was removed, the reaction was allowed to reach 20 °C and allyl bromide (250 μL) was added. Stirring was continued for 2 h (monitoring: TLC, silica gel, AcOEt/cyclohexane 2:8), the reaction was cooled again to 0 °C and quenched with methanol and H_2O. The reaction mixture was extracted with CH_2Cl_2, the organic layer was dried over $MgSO_4$ and the solvent was evaporated. The residue was chromatographed (column chromatography, silica gel, AcOEt/cyclohexane 0.5:9.5) to furnish **74** as an oil (466 mg, 85%). $[\alpha]_D^{20}$ +70 (*c* 1.0, $CHCl_3$). IR (neat, cm^{-1}) ν 2979, 2945, 2890, 1383, 1373, 1206, 1080, 1017. ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.96 (ddt, J=17.1, 10.3, 5.5 Hz, 1H), 5.78 (ddt, J=17.1, 10.9, 6.8 Hz, 1H), 5.28 (dq, J=17.4, 1.5 Hz, 1H), 5.21 (s, 1H), 5.15 (dm, J=10.3 Hz, 1H), 5.08 (dq, J=17.1, 1.5 Hz, 1H), 5.04 (dm, J=10.3 Hz, 1H), 4.95 (s, 1H), 4.77 (dd, J=5.8, 3.0 Hz, 1H), 4.70 (dd, J=6.0, 3.5 Hz, 1H), 4.54 (2×d, J=6.0 Hz, 2H), 4.54 (2×d, 2× J=6.0 Hz, 2H), 4.12 (ddt, J=12.6, 5.8, 1.5 Hz, 1H), 4.06 (ddt, J=12.6, 5.8, 1.5 Hz, 1H), 4.00 (dq, J=9.1, 6.0 Hz, 1H), 3.85–3.77 (m, 2H), 3.69 (dd, J=9.1, 3.3 Hz, 1H), 3.64 (dt, J=9.6, 6.6 Hz, 1H), 3.45 (dt, J=9.8, 6.6 Hz, 1H), 2.30 (qt, J=6.8, 1.3 Hz, 2H), 1.46 (s, 3H), 1.44 (s, 3H), 1.32 (s, 3H), 1.30 (s, 3H), 1.29 (d, J=5.5 Hz, 3H), 1.28 (d, J=6.5 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ=135.5, 135.0, 116.5 (2C), 112.3, 111.8, 106.7, 106.0, 85.0, 84.9, 82.6, 82.5, 79.5, 79.4, 72.2, 71.8, 70.3, 66.4, 33.9, 26.11, 26.07, 25.0, 24.9, 19.5, 17.7. HRMS calcd for $C_{25}H_{40}NaO_9$ [M+Na] 507.2565, found 507.2560.

4.65. 3-Butenyl 5-*O*-(5-*O*-allyl-α-D-rhamnofuranosyl)-α-D-rhamnofuranoside (75)

Compound **74** (105 mg, 0.22 mmol) was cooled to −8 °C and a cold (−5 °C) mixture of TFA/H_2O (7:3, 4 mL) was slowly added. The reaction mixture was stirred and allowed to warm up to 0 °C. The reaction was monitored by TLC (silica gel, AcOEt, R_f ca. 0.35 for **75**). After 3 h, the starting material was almost completely consumed and a polar impurity (possibly resulting from cleavage of the homoallylic side chain) begins to appear. At that time, cold AcOEt was added and the solvents were evaporated under reduced pressure while maintaining the temperature at 0 °C. The residue was dissolved in AcOEt and the solvent evaporated again at 0 °C. The residue was then taken up in toluene and evaporated at 20–30 °C. Column chromatography (silica gel, AcOEt/cyclohexane 4:6 then 8:2) afforded **75** (56 mg), which was used directly for the next step. ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.99–5.86 (m, 1H), 5.80 (ddt, J=17.0, 10.2, 6.6 Hz, 1H), 4.44 (m, 1H), 5.30 (dq, J=17.1, 1.5 Hz, 1H), 5.22 (dq, J=10.2, 1.5 Hz, 1H), 5.22 (d, J=3.0 Hz, 1H), 5.09 (dm, J=17.1 Hz, 1H), 5.04 (dm, J=10.2 Hz, 1H), 4.97 (dd, J=10.4, 1.5 Hz, 1H), 4.24–4.04 (m), 4.01–3.85 (m), 3.71 (dtd, J=9.4, 6.8, 4.3 Hz, 1H), 3.50 (dtd, J=9.6, 6.8, 0.9 Hz, 1H), 2.33 (br q, J=6.8 Hz, 2H), 1.36 (d, J=6.6 Hz, 3H), 1.33 (d, J=6.6 Hz, 3H).

4.66. 3-Butenyl 5-*O*-(5-*O*-allyl-2,3-*O*-thiocarbonyl-α-D-rhamnofuranosyl)-2,3-*O*-thiocarbonyl-α-D-rhamnofuranoside (76)

To a solution of **75** (169 mg) in CH_2Cl_2 (12 mL) was added 1,1′-thiocarbonyldiimidazole (250 mg) and the reaction was stirred under argon for 3 h (monitoring: TLC, AcOEt/cyclohexane 8:2 then 3:7) at which time more 1,1′-thiocarbonyldiimidazole (136 mg) was added. After stirring overnight, the solvent was evaporated and the residue chromatographed (silica gel, AcOEt/cyclohexane 3:7, R_f ca. 0.37) to give pure **76** (101 mg, 32% over two steps). $[\alpha]_D^{20}$ −4 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.94 (ddt, J=17.1, 10.3, 5.5 Hz, 1H), 5.76 (ddt, J=17.1, 10.3, 6.6 Hz, 1H), 5.49 (s, 1H), 5.45 (dd, J=6.6, 3.3 Hz, 1H), 5.38 (dd, J=6.8, 3.8 Hz, 1H), 5.30 (dq, J=17.1, 1.5 Hz, 1H), 5.26 (s, 1H), 5.20 (dq, J=10.3, 1.5 Hz, 1H), 5.16 (d, J=6.6 Hz, 1H), 5.14 (d, J=6.6 Hz, 1H), 5.10 (dq, J=17.1, 1.8 Hz, 1H), 5.08 (br dq, J=10.3, 1.2 Hz, 1H), 4.16 (ddt, J=12.1, 5.8, 1.3 Hz, 1H), 4.09 (dd, J=7.3, 6.6 Hz, 1H), 4.06 (ddt, J=12.1, 5.5, 1.5 Hz, 1H), 4.02 (dd, J=9.3, 3.5 Hz, 1H), 3.93 (dd, J=7.6, 3.8 Hz, 1H),3.77 (dq, J=8.8, 6.0 Hz, 1H), 3.71 (dt, J=9.6, 6.6 Hz, 1H), 3.56 (dt, J=9.8, 6.6 Hz, 1H), 2.32 (qt, J=6.6, 1.3 Hz, 2H), 1.37 (d, J=6.3 Hz, 3H), 1.32 (d, J=6.0 Hz, 3H). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ=190.2, 189.8, 134.6, 134.3, 117.23, 117.17, 105.4, 104.0, 87.5, 87.4, 84.7, 84.1, 82.8, 81.9, 72.6, 71.6, 70.3, 67.3, 33.6, 18.7, 17.2. HRMS calcd for $C_{21}H_{28}NaO_9S_2$ [M+Na] 511.1067, found 511.1063.

4.67. (2*S*,5*S*)-2-[(1*R*)-1-Allyloxyethyl]-5-[(1*R*)-1-[(2*S*,5*S*)-5-but-3-enoxy-2,5-dihydrofuran-2-yl]ethoxy]-2,5-dihydrofuran (77) and (2*R*,3*S*,6*S*)-3-[[(6*S*)-3,6-dihydro-2*H*-pyran-6-yl]oxy]-2-methyl-6-[[(2*R*,3*S*)-2-methyl-3,6-dihydro-2*H*-pyran-3-yl]oxy]-3,6-dihydro-2*H*-pyran (78)

Compound **76** (30 mg, 0.06 mmol) was dissolved in trimethylphosphite (1 mL) and heated under argon at 117 °C for 5 h. The reaction was monitored by ^{1}H NMR in of aliquots (C_6D_6), after evaporation of most of the trimethylphosphite. $P(OMe)_3$ was removed under reduced pressure to furnish crude **77**, which was

taken up in benzene (4 mL). [**Ru**]-2 (3 mg) was added and the reaction mixture was heated at 70 °C for 15 min. The solvent was evaporated and chromatography afforded pure **78** (AcOEt/cyclohexane 1:9) (8 mg, 42%, two steps from **76**).

Compound **77**: ^{1}H NMR (300 MHz, C_6D_6): δ=6.01–5.96 (m), 5.90–5.73 (m), 5.70–5.57, 5.21 (dq, J=17.1, 1.7 Hz, 1H), 5.09–4.97 (m), 4.84–4.75 (m), 3.92–3.70 (m), 3.49–3.38 (m), 3.25 (quint., J=6.0 Hz, 1H), 2.32 (q, J=6.8 Hz, 2H), 1.32 (d, J=6.4 Hz, 3H), 1.09 (d, J=6.2 Hz, 3H).

Compound **78**: $[\alpha]_D^{20}$ +187 (c 1.1, C_6H_6). IR (neat, cm^{-1}) ν 3450, 2974, 2933, 2880, 2827, 1448, 1400, 1377, 1295, 1186, 1151, 1098, 1033. ^{1}H NMR (400 MHz, C_6D_6): δ=6.22 (dq, J=10.3, 2.0 Hz, 1H), 6.13 (dt, J=10.3, 2.0 Hz, 1H), 5.72 (dt, J=10.3, 1.8 Hz, 1H), 5.68 (ddm, J=10.3, 5.8 Hz, 1H), 5.60 (dtd, J=10.1, 2.5, 1.0 Hz, 1H), 5.45 (dq, J=10.3, 2.5 Hz, 1H), 5.10 (q, J=1.6 Hz, 1H), 4.92 (s, 1H), 4.01 (dm, J=8.3 Hz, 1H), 3.91 (dq, J=8.3, 2.3 Hz, 1H), 3.90–3.86 (m, 2H,), 3.83 (dd, J=11.3, 3.5 Hz, 1H), 3.72 (dq, J=8.0, 6.3 Hz, 1H), 3.60 (dq, J=8.1, 6.2 Hz, 1H), 3.46 (ddt, J=10.8, 6.0, 1.0 Hz, 1H), 1.97 (m, 1H), 1.37 (m, 1H), 1.37 (d, J=6.3 Hz, 3H), 1.27 (d, J=6.0 Hz, 3H). ^{13}C NMR (100.6 MHz, C_6D_6): δ=132.9, 129.3, 129.1, 128.8, 127.6, 126.5, 99.1, 95.9, 77.5, 76.8, 73.6, 72.9, 65.3, 57.3, 24.9, 18.9, 18.6. HRMS calcd for $C_{17}H_{24}NaO_5$ [M+Na] 331.1516, found 331.1507.

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Supplementary data

^{1}H and ^{13}C NMR spectra for all described compounds. Experimental and analytical data corresponding to the synthesis of compounds in Fig. 1B are also described. Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2010.11.036. These data include MOL files and InChIKeys of the most important compounds described in this article.

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