Hetero-Diels–Alder Reaction with Thiazolyl Oxabutadienes—Model Studies Toward the Synthesis of Directly Linked *C*-Disaccharides**

Alessandro Dondoni,* Ladislav Kniezo, Miroslava Martinkova, and Jan Imrich

Abstract: A method for the construction of substituted pyranoses by means of the hetero-Diels–Alder (HDA) reaction of ethyl vinyl ether with 1-oxabuta-1,3-dienes bearing a thiazolyl ring at C-2 is described. The cycloaddition with 1-(thiazol-2-yl)-2-penten-1-one (**2**) occurred with good *endo*/*exo* selectivity to give *cis*- and *trans*-3,4-dihydro-2*H*-pyrans **3a** and **3b** in a ca. 9:1 ratio and 91% overall yield. The elaboration of **3a** through the conversion of the thiazole ring into the formyl group and reduction of the latter to alcohol, followed by hydroxylation of the double bond through hydroboration–oxidation led to the ethyl 2,3-dideoxypyranoside **8**. The asymmetric version of this synthetic sequence started from the HDA cycloaddition of the same alkene with the chiral oxabutadiene **10** bearing the D-*galacto*-pentopyranosid-5-yl moiety at C-3. This reaction afforded a mixture of the four diastereomeric cycloadducts—3,4-dihydro-2*H*-pyrans **11a,b** and **12a,b**—in 97% overall yield. The reaction was moderately *endo* and face selective. A high level of *endo* selectivity (96%) was obtained by the use of catalytic $Eu(fod)_3$. The elaboration of the *endo* cycloadducts **11a** and **12a** by the same synthetic sequence as that developed for **3a** (i.e. thiazolyl-to-formyl conversion and hydroxylation of the double bond) gave the uncommon *C*-disaccharides **15** and **16** featuring two directly linked pyranose rings.

Keywords
asymmetric synthesis · butyrolactones · carbonylations · catalyst system · palladium

Introduction

Of the numerous types of the hetero-Diels–Alder (HDA) reactions generated through structural and heteroatom variations in the cycloaddition partners,[1] that involving substituted 1-oxa-1,3-butadienes and electron-rich alkenes appears to be one of the more useful combinations for the de novo synthesis of carbohydrates.[2] The *endo*/*exo* selectivity of the concerted cycloaddition and the asymmetric induction associated with the use of chiral substrates or catalysts determine the relative and absolute configuration at the newly formed stereocenters in the resulting 3,4-dihydro-2*H*-pyrans. This synthetic approach to pyranoid systems has been studied under various conditions by Boger,[3] Tietze,[4] and Schmidt,[5] and their co-workers. Particular attention has been focused on the *endo*/*exo* selective control by Lewis acids and, quite recently, on the internal asymmetric induction.[4c, d]

We report here our results on the HDA-based approach to pyranoses using 1-oxa-1,3-butadienes bearing the thiazolyl ring at C-2 and on the application of this method to the synthesis of modified disaccharides with the two pyranose units directly joined by a carbon–carbon bond. The development of a synthetic route to this uncommon class of *C*-disaccharides[6] by the stereocontrolled construction of a second sugar moiety on an existing one is in fact the main objective of this research. The inhibitory activity that modified disaccharides might exert on carbohydrate-based metabolic processes has provided a strong impetus in recent years for the synthesis of various types of *C*-disaccharides[7] with different tethers between the two sugar moieties.[8]

Results and Discussion

Various 1-oxa-1,3-butadienes activated by electron-withdrawing groups at C-2 or C-3 have been described as convenient partners in HDA-based routes to pyranoses.[3, 4, 5] Our approach relies on the use of derivatives bearing the thiazole ring at C-2. This heteroaromatic system not only serves as a masked formyl group equivalent that tolerates harsh reaction conditions and can be further elaborated at a later stage in the reaction,[9] it is also expected to activate the heterodiene, owing to its elec-

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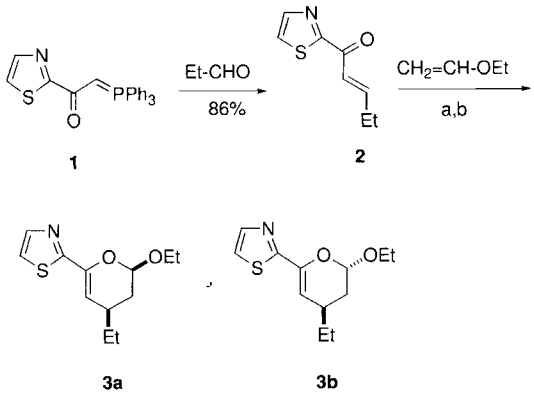
tron-withdrawing character.[10] The access to various oxadienes with C-4 substitution appeared to be secured through the Wittig olefination of suitable aldehydes with the thiazole-substituted phosphorous carbonyl ylide **1**, a readily available reagent, which can be prepared in multigram scale and stored for long periods at room temperature without appreciable decomposition.[11]

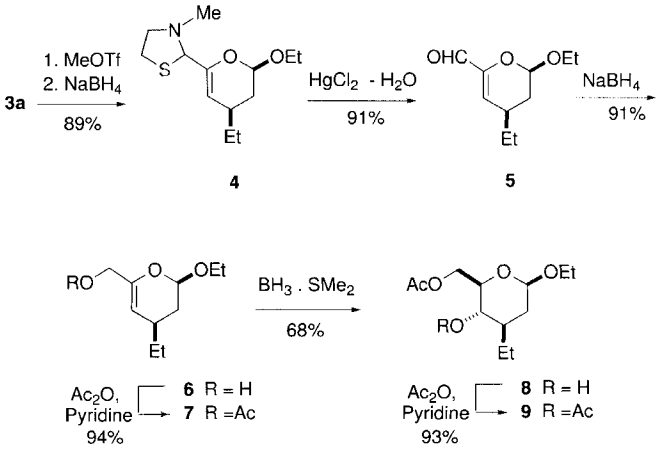
The initial HDA reactions were carried out with the thiazolyl pentenone **2**, which was prepared in 86% yield from propanal and the ylide **1** (Scheme 1). The (*E*) selectivity of this olefination



Scheme 1. a) No catalyst, 8 d, 70 °C: **3a** + **3b** (9:1), 91%. b) $LiClO_4$, 18 h, RT: **3a** + **3b** (2.3:1).

reaction matches earlier reactions of **1** with other aldehydes.[11, 12] The cycloaddition of **2** with neat ethyl vinyl ether in sealed tube at 70 °C occurred with good *endo*/*exo* selectivity to give, after 8 days, the *cis* and *trans* 2,4-disubstituted 3,4-dihydro-2*H*-pyrans **3a** and **3b** in 9:1 ratio (analysis by ^{1}H NMR spectroscopy). The cycloadduct **3a** was isolated by chromatography in 70% yield, while **3b** could not be obtained as pure material. The cycloaddition appeared to be considerably accelerated by the presence of 1 equiv of lithium perchlorate[13, 14] to give, after 18 hours at room temperature, a mixture of **3a** and **3b** in a ratio of 2.3:1, as shown by ^{1}H NMR analysis.[15] The structural assignment of these cycloadducts by ^{1}H NMR spectroscopy relied mainly on the analysis of the H-2 and H-4 signals. In the *cis* cycloadduct **3a**, the H-2 signal exhibits a rather large coupling constant with the H-3_{ax} (J = 8.2 Hz) and a small one with the H-3_{eq} (J = 2.1 Hz). Similarly, the H-4 signal shows a large (J = 9.3 Hz) and a small coupling constant (J = 6.6 Hz) with H-3_{ax} and H-3_{eq}, respectively. These data indicate a preference for the half-chair conformation with equatorial ethoxy and ethyl groups. On the other hand, the H-2 signal of the *trans* isomer **3b** exhibits coupling constants J = 2.6 and 5.4 Hz with H-3_{eq} and H-3_{ax}, respectively; the values for the coupling of H-4 with the same protons are J = 4.5 and 7.7 Hz. A distortion from the half-chair conformation appears to be very likely for this isomer.

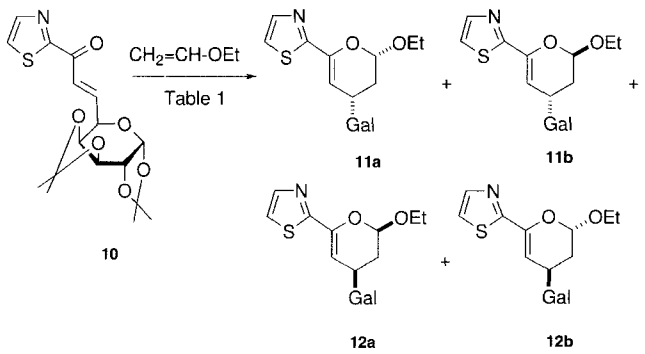
We next examined the hydroboration of the double bond of **3a** with the aim of achieving the stereoselective hydroxylation at C-5. Attempts hydroboration with $BH_3 \cdot SMe_2$ or $BH_3 \cdot THF$ complexes were unsuccessful. We therefore proceeded with the unmasking of the formyl group from the thiazole ring, although we wondered whether this operation might be accompanied by the reduction of the double bond of the dihydropyran ring.[16] Fortunately, the captodative double bond remained intact. Thus, the methylation of **3a** with methyl triflate and reduction with sodium borohydride[17] gave the 3,4-dihydro-2*H*-pyran derivative **4** bearing the *N*-methylthiazolidine ring at C-6 in very good yield (Scheme 2). This compound was then transformed



Scheme 2. Hydroxylation at C-5.

into the aldehyde **5** by mercuric chloride assisted hydrolysis of the thiazolidine ring.[9a] The reduction of the formyl group of **5** afforded the alcohol **6**, which was acetylated to give the acetate **7** (69% isolated yield from **3a**). The *cis*-selective hydroboration of this compound with $BH_3 \cdot SMe_2$ followed by introduction of a hydroxyl group by addition of hydrogen peroxide smoothly gave the ethyl pyranoside **8**, which was fully characterized in the form of the acetate **9**. The *trans*–*trans* relationship of the substituents at C-3, C-4, and C-5 in the pyranose ring (carbohydrate numbering) was established by the coupling constants of the following signals: H-1/H-2_{ax}, J = 9.6 Hz; H-2_{ax}/H-3, J = 13.0 Hz; H-3/H-4, J = 10.2 Hz; and H-4/H-5, J = 9.8 Hz. The predictably stereoselective hydroboration of the 3,4-dihydro-2*H*-pyran derivative **7** is in agreement with previous observations[3, 5] and is consistent with the attack of the borane reagent at the less hindered side of the double bond, *anti* to the C-4 ethyl substituent.

Having set up the Diels–Alder route toward the tetrasubstituted pyranoid system, we next considered its application to the planned *C*-disaccharide synthesis. The readily available[18] chiral thiazolyl propenone **10**, bearing a D-*galacto*-pyranosidyl ring at C-4, was chosen as starting material. This compound, although quite sluggish, reacted with neat ethyl vinyl ether in sealed tube at 70 °C to give, after 5 days, a mixture of four diastereomeric 3,4-dihydro-2*H*-pyrans **11a,b** and **12a,b** in 97% overall yield (Scheme 3). The HPLC analysis of the mixture allowed an accurate evaluation of its composition (Table 1). As judged from the ratio between the major products *cis* **11a** and **12a** and the *trans* isomers **11b** and **12b** (ca. 5:1), the cycloaddition appeared to be moderately *endo* selective. The diastereofacial selectivity was even lower as the ratio between **11a,b** and **12a,b** was ca. 3.5:1. The reaction was dramatically accelerated by catalytic $ZnCl_2$ and $Eu(fod)_3$ (fod = 1,1,1,2,2,3,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione). Moreover, the europium complex increased the level of *endo* selectivity up to a 96% (24:1

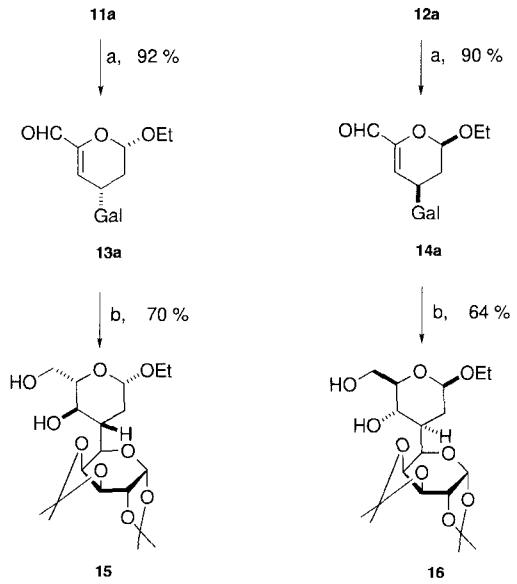


Scheme 3. Gal = galactopyranoside moiety.

Table 1. Stereoselectivity of the cycloaddition [a] of ethyl vinyl ether to the galactopyranosidyl oxabutadiene **10**.

10, mmol	Solvent	Cat. (mmol)	*t*/h	*T*/°C	Yield [b]	**11a**:**11b**:**12a**:**12b** [c]
16.9	–	–	120	70	97	64:14:20:2
1.36	CH_2Cl_2	$ZnCl_2$ (0.18)	0.5	25	–	30:5:58:7
0.27	CH_2Cl_2	$Eu(fod)_3$ (0.027)	8	25	90	43:4:53:–

[a] Reactions in CH_2Cl_2 were carried out with a 4 molar excess of ethyl vinyl ether. [b] Isolated products (%). [c] HPLC of crude mixtures.



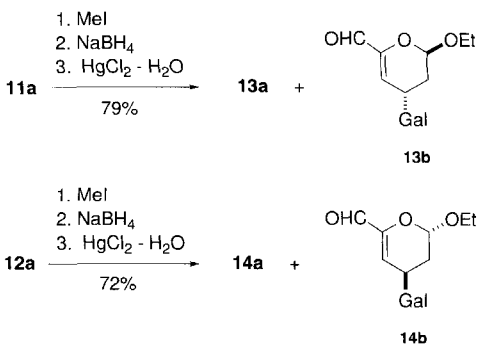
Scheme 4. a) 1. CF_3SO_3Me, 2. $NaBH_4$; $HgCl_2$, $MeCN-H_2O$ (4:1). b) 1. BH_3·THF, 2. H_2O_2 (Gal = galactopyranoside moiety)

cis:*trans* isomers). These catalysts also produced a reversal of the diastereofacial selectivity, slightly in favor of the isomer **12a**. In all cases, the ratio of the cycloadducts determined at the end of the reaction (monitored by means of the oxadiene **10**) coincided with the values obtained during the course of the reaction. This supports the assumption that kinetic mixtures of products were observed. When the mixture from the $ZnCl_2$-catalyzed reaction was left to stand for 24 h at room temperature, the *trans* isomers **11b** and **12b** increased substantially,[19] and these products could be isolated by preparative HPLC (see Experimental Section). The *cis* products **11a** and **12a** were separated by flash chromatography from the uncatalyzed reaction mixture and even more easily from the $Eu(fod)_3$-catalyzed reaction. The *cis* and *trans* isomers were characterized on the basis of the coupling constant values of H-2 and H-4 with the diastereotopic axial and equatorial H-3 protons.[20] The absolute configuration at C-2 and C-4 in **12a** was established directly by means of its crystal structure,[21] while that of **11a** was deduced from the structure of a derivative (see below). The formation of **11a** as a major product of the cycloaddition in the absence of catalysts indicates that the dienophile mainly attacks the oxadiene in **10** at the stereoface opposed to the plane of the pyranose ring. The reactive conformation of **10** shown in Scheme 3 has already been postulated to accommodate the results of 1,4-conjugate addition reactions.[18] The change in the diastereofacial selectivity for the reactions carried out in the presence of catalysts may be ascribed to other reactive conformations induced by chelation, as already described in many instances.[4c]

The cycloadducts **11a** and **12a** were converted into the diastereomeric *C*-disaccharides **15** and **16** through implementation of the same reaction sequence established for the 2*H*-pyran **3a**. First, **11a** and **12a** were subjected to the improved thiazolyl-to-formyl conversion protocol[17] to give the corresponding aldehydes **13a** and **14a** (Scheme 4). The hydroxylation of these compounds by stereoselective hydroboration–oxidation proceeded with the concomitant reduction of the formyl group, giving rise to the *C*-dipyranosides **15** and **16** in one-pot reaction sequence. In both cases the stereoselectivity of the hydroboration was that expected on the basis of the prior observation with 3,4-dihydro-2*H*-pyran derivative **7**, that is, a *cis* addition to the face of the double bond *anti* to the C-4 galactopyranosidyl moiety. Compounds **15** and **16** were isolated and purified[22] by careful chromatography on silica gel, although this led to a partial epimerization at C-2 of the newly formed pyran ring.[23] The anomer of **15** (10–15%) was occasionally isolated during this operation.

A more substantial epimerization[23] occurred when the aldehyde unmasking from **11a** and **12a** was carried out by the original procedure[9a] employing MeI in refluxing acetonitrile for the *N*-methylation of the thiazole ring. This method produced mixtures of diastereomeric aldehydes **13a**,**b** and **14a**,**b** in variable ratios depending on the refluxing time (Scheme 5).

The assignment of the *cis* and *trans* relationship of the substituents at C-2 and C-4 of these 3,4-dihydro-2*H*-pyran derivatives was based on the coupling constants of the H-2 and H-4 signals.[24] Fortunately, compound **13b** was a crystalline material whose structure was determined by X-ray crystallographic analysis.[21] This provided indirect evidence for the stereochemical relationship between the ethoxy group and the galactopyra-



Scheme 5. Gal = galactopyranoside moiety.

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nosidyl moiety in the epimer **13a** and consequently in the original cycloadduct **11a**. It is worth noting that the two pyranose rings which have been constructed are antipodes having the L-*arabino* (in **15**) and D-*arabino* (in **16**) configuration. Evidently, the same structures can be obtained by the elaboration of **13b** and **14b**.

Conclusion

An asymmetric hetero-Diels–Alder route for the synthesis of *C*-disaccharides directly linked by a carbon–carbon bond has been described. The construction of a new pyranose ring on an existing one through cycloaddition occurs with some degree of asymmetric induction, which controls the configuration of the two new stereocenters. This successful model study suggests that this strategy can be extended to other 1-oxabuta-1,3-dienes bearing different pyranosyl and furanosyl fragments as well as to other electron-rich dienophiles.

Experimental Section

Melting points are uncorrected. Unless otherwise stated the ^{1}H and ^{13}C NMR spectra were recorded on a 300 MHz Gemini 300 Varian spectrometer and the chemical shifts are given in ppm downfield from TMS as internal standard. HPLC analyses were carried out on a Kontron Instrument using a C-18 reversed-phase column (Spherisorb S 5 ODS 2, 125 × 4.6 mm) with a UV detector operating at 254 nm, and elution with a methanol/water mixture (60:40) at 0.55 mL min^{-1}. The new compounds were purified by flash chromatography on Merck silicagel grade 60, 230 - 400 mesh. All reactions were carried out under nitrogen atmosphere with freshly distilled and dried solvents.

1-Oxa-2-(thiazol-2-yl)-1,3-(*E*)-hexadiene (2): A mixture of propanal (0.5 g, 8.6 mmol) and triphenyl(thiazol-2-ylcarbonylmethylene)phosphorane[11] (**1**) (3.4 g, 8.66 mmol) in 20 mL of chloroform was stirred at room temperature for 28 h. After evaporation of the solvent under reduced pressure, the chromatography of the residue (1:5 diethyl ether–hexane) gave 1.25 g (87%) of compound **2** as a colorless oil. ^{1}H NMR ($CDCl_3$): δ = 1.16 (t, 3H, J = 7.2 Hz), 2.39 (ddq, 2H, J = 7.2, 6.5, 1.5 Hz), 7.29 (dt, 1H, J = 15.8, 1.5 Hz), 7.42 (dt, 1H, J = 15.8, 6.5 Hz), 7.68 (d, 1H, J = 3.1 Hz), 8.03 (d, 1H, J = 3.1 Hz). ^{13}C NMR ($CDCl_3$): δ = 12.2, 26.1, 123.8, 126.1, 144.7, 152.9, 168.6, 181.8. Anal. calcd for C_8H_9NOS: C, 57.46; H, 5.42; N, 8.38. Found: C, 57.71; H, 5.69; N, 8.53 .

***cis*-2-Ethoxy-4-ethyl-6-(thiazol-2-yl)-3,4-dihydro-2*H*-pyran (3a)**: A solution of the 1-oxadiene **2** (0.23 g, 1.38 mmol) in 15 mL of ethyl vinyl ether was heated in a sealed tube at 70 °C for 8 d. After evaporation of the excess of ethyl vinyl ether at reduced pressure, the ^{1}H NMR analysis of the residue showed a 9:1 mixture of the cycloadducts **3a** and **3b** (H-2 of **3a**: δ = 5.16 (dd, 1H, J = 8.1, 2.1 Hz); H-2 of **3b**: δ = 5.28 (dd, 1H, J = 5.4, 2.6 Hz)). Chromatography of the mixture (1:3 diethyl ether–cyclohexane) afforded 0.23 g (70%) of the *cis* diastereoisomer **3a** as a colorless oil: ^{1}H NMR ($CDCl_3$): δ = 0.99 (t, 3H, J = 7.4 Hz), 1.31 (t, 3H, J = 7.1 Hz), 1.49 (ddq, 1H, J = 13.4, 7.4, 7.4 Hz), 1.58 (ddq, 1H, J = 13.4, 7.4, 6.7 Hz), 1.65 (ddd, 1H, J = 13.3, 9.3, 8.2 Hz), 2.14 (dddd, 1H, J = 13.3, 6.6, 2.1, 1.1 Hz), 2.42 (ddddd, 1H, J = 9.3, 7.4, 6.7, 6.6, 3.0 Hz), 3.69 (dq, 1H, J = 9.6, 7.1 Hz), 4.07 (dq, 1H, J = 9.6, 7.1 Hz), 5.16 (dd, 1H, J = 8.2, 2.1 Hz), 5.95 (dd, 1H, J = 3.0, 1.1 Hz), 7.28 (d, 1H, J = 3.2 Hz), 7.78 (d, 1H, J = 3.2 Hz). ^{13}C NMR ($CDCl_3$): δ = 11.4, 15.3, 28.5, 33.4, 34.0, 64.8, 100.6, 105.1, 118.4, 143.2, 144.0, 164.8. Anal. calcd for $C_{12}H_{17}NO_2S$: C, 60.22; H, 7.16; N, 5.85. Found: C, 60.42; H, 7.39; N, 6.03.

^{1}H NMR ($CDCl_3$) data of the *trans* stereoisomer **3b** obtained from the spectrum of the mixture with **3a**: δ = 0.82 (t, 3H, J = 7.4 Hz), 1.25 (t, 3H, J = 7.1 Hz), 1.4–1.7 (m, 2H), 1.97 (ddd, 1H, J = 13.1, 4.5, 2.6 Hz), 2.24 (ddd, 1H, J = 13.1, 7.7, 5.4 Hz), 2.75 (ddddd, 1H, J = 15.7 (this is the sum of two coupling constants of H4 with CH_2 of ethyl group), 7.7, 7.5, 4.5 Hz), 3.53 (dq, 1H, J = 9.5, 7.1 Hz), 4.00 (dq, 1H, J = 9.5, 7.1 Hz), 5.28 (dd, 1H, J = 5.4, 2.6 Hz), 5.76 (d, 1H, J = 7.5 Hz), 7.70 (d, 1H, J = 3.0 Hz), 8.01 (d, 1H, J = 3.0 Hz).

***cis*-2-Ethoxy-4-ethyl-6-[(*N*-methyl)thiazolidin-2-yl]-3,4-dihydro-2*H*-pyran (4)**: A solution of **3a** (1 g, 4.2 mmol) in 27 mL of CH_3CN containing activated 4 Å powdered molecular sieve (4.1 g) was stirred at room temperature for 10 min. After addition of methyl triflate (0.61 mL, 5.4 mmol), the mixture was stirred at room temperature for another 15 min. The solvent was evaporated under reduced pressure, and the residue suspended in methanol (27 mL), cooled to 0 °C, and treated with $NaBH_4$ (0.35 g, 9.25 mmol). The mixture was stirred for 10 min at room temperature and then diluted with acetone (27 mL), filtered through Celite and concentrated. The crude product was partitioned between diethyl ether and saturated aqueous $NaHCO_3$, the organic layer was dried (Na_2SO_4), and the solvent evaporated under reduced pressure. Chromatography of the residue (1:2 diethyl ether–cyclohexane) afforded 0.95 g (90%) of compound **4** as a colorless oil: ^{1}H NMR ($CDCl_3$): δ = 0.90 (t, 3H, J = 7.4 Hz), 1.24 (t, 3H, J = 7.2 Hz), 1.35 (m, 1H), 1.40 (m, 1H), 1.50 (ddd, 1H, J = 13.1, 9.2, 8.2 Hz), 1.99 (m, 1H), 2.20 (m, 1H), 2.38 (s, 3H), 3.00 (m, 3H), 3.29 (m, 1H), 3.58 (dq, 1H, J = 9.6, 7.2 Hz), 3.98 (dq, 1H, J = 9.6, 7.2 Hz), 4.47 (s, 1H), 4.87 (m, 1H), 4.95 (ddd, 1H, J = 8.2, 7.3, 2.2 Hz). ^{13}C NMR ($CDCl_3$): δ = 11.3, 15.2, 28.7, 30.0, 30.8, 33.0, 33.9, 41.4, 59.2, 64.3, 100.1, 102.1, 149.6 . Anal. calcd for $C_{13}H_{23}NO_2S$: C, 60.66; H, 9.01; N, 5.44. Found: C, 60.89; H, 9.39; N, 5.72.

***cis*-2-Ethoxy-4-ethyl-6-formyl-3,4-dihydro-2*H*-pyran (5)**: A solution of **4** (0.9 g, 3.5 mmol) in CH_3CN (18 mL) was added dropwise to a stirred solution of $HgCl_2$ (1.13 g, 4.16 mmol) in 20% H_2O–CH_3CN (5 mL). After having been stirred for 15 min at room temperature, the mixture was partitioned between diethyl ether and brine. The organic layer was separated, washed with 20% aqueous KI, and dried (Na_2SO_4). The solvent was evaporated under reduced pressure. Purification by chromatography (1:5 diethyl ether–hexane) afforded 0.58 g (91%) of **5** as a colorless oil: ^{1}H NMR ($CDCl_3$): δ = 0.99 (t, 3H, J = 7.4 Hz), 1.22 (dd, 3H, J = 7.2, 7.1 Hz), 1.45–1.80 (m, 2H), 1.63 (ddd, 1H, J = 13.5, 7.0, 6.8 Hz), 2.08 (ddd, 1H, J = 13.5, 6.4, 2.6 Hz), 2.43 (dddt, 1H, J = 7.2, 7.0, 6.4, 3.3 Hz), 3.63 (dq, 1H, J = 9.6, 7.1 Hz), 3.99 (dq, 1H, J = 9.6, 7.2 Hz), 5.12 (dd, 1H, J = 6.8, 2.6 Hz), 5.83 (d, 1H, J = 3.3 Hz), 9.17 (s, 1H). ^{13}C NMR ($CDCl_3$): δ = 11.5, 15.1, 27.8, 32.8, 33.5, 64.7, 99.6, 126.7, 149.9, 186.9. Anal. calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.34; H, 8.98.

***cis*-2-Ethoxy-4-ethyl-6-hydroxymethyl-3,4-dihydro-2*H*-pyran (6)**: A solution of the aldehyde **5** (0.55 g, 3 mmol) in MeOH (10 mL) was treated at 0 °C with $NaBH_4$ (0.23 g, 6 mmol). After having been stirred for 20 min at room temperature, the solvent was evaporated, and the residue partitioned between diethyl ether and saturated aqueous $NaHCO_3$. The organic layer was dried (Na_2SO_4), and the solvent evaporated under reduced pressure. Purification by chromatography (1:2 diethyl ether–cyclohexane) afforded 0.51 g (91%) of the alcohol **6** as a colorless oil: ^{1}H NMR (80 MHz, $CDCl_3$): δ = 0.91 (t, 3H, J = 7.3 Hz), 1.23 (t, 3H, J = 7.1 Hz), 1.44 (m, 1H), 1.46 (m, 1H), 1.56 (m, 1H), 1.98 (m, 1H), 2.21 (m, 1H), 3.37 (m, 2H), 3.64 (dq, 1H, J = 9.6, 7.1 Hz), 3.93 (dq, 1H, J = 9.6, 7.1 Hz), 4.73 (dd, 1H, J = 3.0, 0.9 Hz), 4.98 (dd, 1H, J = 9.0, 2.6 Hz). ^{13}C NMR ($CDCl_3$): δ = 11.3, 15.3, 28.7, 33.0, 34.3, 62.9, 64.4, 100.9, 102.2, 150.3. Anal. calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.76; H, 9.92.

***cis*-6-Acetoxymethyl-2-ethoxy-4-ethyl-3,4-dihydro-2*H*-pyran (7)**: The alcohol **6** (0.5 g, 2,7 mmol), 5.2 mL of pyridine, and 3.2 mL of acetic anhydride were stirred for 15 h. at room temperature. The reaction mixture was poured into ice water (20 mL) and extracted with diethyl ether (4 × 20 mL). The combined organic layers were washed successively with 10% aqueous HCl (20 mL), water (20 mL), and saturated aqueous $NaHCO_3$ (25 mL). The solution was dried (Na_2SO_4), and the solvent evaporated under reduced pressure. Purification by chromatography (1:3 diethyl ether–cyclohexane) afforded 0.58 g (94%) of compound **7** as a colorless oil: ^{1}H NMR ($CDCl_3$): δ = 0.91 (t, 3H, J = 7.4 Hz), 1.24 (t, 3H, J = 7.1 Hz), 1.37 (ddq, 1H, J = 13.4, 7.4, 7.2 Hz), 1.44 (ddq, 1H, J = 13.4, 7.4, 7.0 Hz), 1.50 (ddd, 1H, J = 13.1, 9.5, 8.3 Hz), 2.02 (dddd, 1H, J = 13.1, 6.5, 2.3, 1.2 Hz), 2.09 (s, 3H), 2.23 (ddddd, 1H, J = 9.5, 7.2, 7.0, 6.5, 2.4 Hz), 3.58 (dq, 1H, J = 9.5, 7.1 Hz), 3.94 (dq, 1H, J = 9.5, 7.1 Hz), 4.44 (d, 1H, J = 12.9 Hz), 4.47 (d, 1H, J = 12.9 Hz), 4.81 (dd, 1H, J = 2.4, 1.2 Hz), 4.98 (dd, 1H, J = 8.3, 2.3 Hz). ^{13}C NMR

($CDCl_3$): δ = 11.3, 15.2, 20.9, 28.5, 32.9, 33.8, 64.2, 64.3, 100.0, 105.5, 146.2, 170.6. Anal. calcd for $C_{12}H_{20}O_4$: C, 63.14; H, 8.83. Found: C, 63.33; H, 9.05.

***rel*-(2*R*,4*R*,5*S*,6*R*)-2-Ethoxy-4-ethyl-5-hydroxy-6-hydroxymethyltetrahydro-2*H*-pyran (8)**: A solution of **7** (0.55 g, 2.4 mmol) in anhydrous THF (24 mL) was cooled to 0 °C and then treated with a 2.0 M solution of $BH_3 \cdot SMe_2$ in THF (3 mL, 6 mmol). The reaction mixture was stirred for 1 h at 0 °C and then for 18 h at room temperature. This mixture was treated with 30% aqueous NaOH (1.2 mL) and 30% aqueous H_2O_2 (1.2 mL) at the same temperature and then heated at 60 °C for 1 h. The solution was diluted with water (15 mL), then saturated with NaCl, and extracted with ethyl acetate (5 × 15 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to give an oily product, which was purified by chromatography (ethyl acetate) to give product **8** (0,33 g, 68%). M.p. 75–76 °C (from diethyl ether–hexane); ^1H NMR ($CDCl_3$): δ = 0.91 (t, 3H, J = 7.7 Hz), 1.18 (m, 1H), 1.23 (dd, 3H, J = 7.1, 7.2 Hz), 1.26 (m, 1H,), 1.49 (m, 1H,), 1.83 (m, 1H), 1.96 (ddd, 1H, J = 13.1, 4.1, 2.0 Hz), 2.58 (t, 1H), 2.77 (brs, 1H), 3.27 (m, 1H,), 3.28 (m, 1H,), 3.55 (dq, 1H, J = 9.6, 7.2 Hz), 3.84 (m, 2H), 3.91 (dq, 1H, J = 9.6, 7.1 Hz), 4.54 (dd, 1H, J = 9.6, 2.0 Hz). ^{13}C NMR ($CDCl_3$): δ = 10.4, 15.2, 24.3, 35.3, 42.1, 63.2, 64.6, 70.6, 78.2, 101.6 . Anal. calcd for $C_{10}H_{20}O_4$: C,58.80; H,9.87. Found: C, 59.08; H, 10.11.

***rel*-(2*R*,4*R*,5*S*,6*R*)-5-Acetoxy-6-acetoxymethyl-2-ethoxy-4-ethyltetrahydro-2*H*-pyran (9)**: The same procedure as for the preparation of **7** starting from compound **8** (0.1 g, 0.49 mmol), 2 mL pyridine, and 1.3 mL of acetic anhydride. The purification of the product by chromatography (1:3 diethyl ether–cyclohexane) gave 0.13 g (93%) of diacetate **9** as a colorless oil: ^1H NMR ($CDCl_3$): δ = 0.87 (t, 3H, J = 7.6 Hz), 1.15 (ddq, 1H, J = 13.6, 8.3, 7.6 Hz), 1.24 (t, 3H, J = 7.0 Hz), 1.36 (ddd, 1H, J = 13.0, 13.0, 9.6 Hz), 1.50 (ddq, 1H, J = 13.6, 7.6, 3.6 Hz), 1.67 (ddddd, 1H, J = 13.0, 10.2, 8.3, 4.2, 3.6 Hz), 2.03 (ddd, 1H, J = 13.0, 4.2, 2.1 Hz), 2.06 (s, 3H), 2.07 (s, 3H), 3.54 (dq, 1H, J = 9.5, 7.0 Hz), 3.55 (ddd, 1H, J = 9.8, 5.3, 2.6 Hz), 3.95 (dq, 1H, J = 9.5, 7.0 Hz), 4.05 (dd, 1H, J = 12.1, 2.6 Hz), 4.23 (dd, 1H, J = 12.1, 5.3 Hz), 4.53 (dd, 1H, J = 9.6, 2.1 Hz), 4.68 (dd, 1H, J = 10.2, 9.8 Hz). ^{13}C NMR ($CDCl_3$): δ = 10.1, 15.0, 20.7, 24.0, 34.9, 40.2, 63.2, 64.5, 70.7, 74.6, 101.4, 170.1, 170.8. Anal. calcd for $C_{14}H_{24}O_6$: C, 58.32; H, 8.39. Found: C, 58.42; H, 8.12.

(2*S*)-Ethoxy-(4*S*)-(1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-1,5-pyranose-5-yl)-6-(thiazol-2-yl)-3,4-dihydro-2*H*-pyran (11a), (2*R*)-Ethoxy-(4*S*)-(1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-1,5-pyranose-5-yl)-6-(thiazol-2-yl)-3,4-dihydro-2*H*-pyran (11b), (2*R*)-ethoxy-(4*R*)-(1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-1,5-pyranose-5-yl)-6-(thiazol-2-yl)-3,4-dihydro-2*H*-pyran (12a), and **(2*S*)-ethoxy-(4*R*)-(1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-1,5-pyranose-5-yl)-6-(thiazol-2-yl)-3,4-dihydro-2*H*-pyran (12b)**:

a) Uncatalyzed reaction: A solution of the 1-oxadiene **10**[18] (6.2 g, 16.9 mmol) in 35 mL of ethyl vinyl ether (0.36 mol) was heated in sealed tube at 70 °C for 5 d. The HPLC analysis of the reaction mixture showed very little (ca. 2%) unreacted **10** and four diastereomeric cycloadducts **11a**, **11b**, **12a**, and **12b** in 64.2:13.7:20.4:1.7 ratio. The ethyl vinyl ether was evaporated under reduced pressure and the residue was chromatographed (1:4 diethyl ether–hexane) to give two fractions: the first one (5.77 g, 78%) contained the cycloadducts **11a,b**, and the second (1.49 g, 20%) **12a,b**. Subsequent chromatography (1:6 diethyl ether–hexane) of the first fraction afforded 4.07 g (55%) of **11a** (oil): $[\alpha]_D^{20} = -82.0$ (c = 2.72, $CHCl_3$); ^1H NMR ($CDCl_3$): δ = 1.21 (dd, 3H, J = 7.1, 6.5 Hz), 1.31 (s, 3H), 1.37 (s, 3H), 1.46 (s, 3H), 1.51 (s, 3H), 2.13–2.17 (m, 2H), 2.76 (dddd, 1H, J = 9.9, 6.3, 5.5, 4.2 Hz), 3.69 (dq, 1H, J = 10.2, 6.5 Hz), 3.89 (dq, 1H, J = 10.2, 7.1 Hz), 3.90 (dd, 1H, J = 9.9, 1.9 Hz), 4.29 (dd, 1H, J = 5.1, 2.4 Hz), 4.43 (dd, 1H, J = 8.2, 1.9 Hz), 4.59 (dd, 1H, J = 8.2, 2.4 Hz), 5.29 (t, 1H, J = 3.5 Hz), 5.54 (d, 1H, J = 5.1 Hz), 6.12 (d, 1H, J = 4.2 Hz), 7.30 (d, 1H, J = 3.2 Hz), 7.80 (d, 1H, J = 3.2 Hz). ^{13}C NMR ($CDCl_3$): δ = 15.0, 24.2, 24.7, 25.7, 25.8, 28.9, 30.5, 64.6, 69.9, 70.6, 70.9, 71.1, 96.7, 98.9, 100.3, 108.8, 109.3, 118.9, 143.7, 145.0, 165.3. Anal. calcd for $C_{21}H_{29}NO_7S$: C, 57.39; H, 6.65; N, 3.19. Found: C, 57.26; H, 6.54; N, 3.23.

Crystallization of the second fraction from diethyl ether afforded 1.1 g (15%) of the cycloadduct **12a**, m.p. 158–160 °C (diethyl ether). $[\alpha]_D^{20} = -77.4$ (c = 0.51, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 1.25 (dd, 3H, J = 6.9, 6.8 Hz), 1.29 (s, 3H), 1.33 (s, 3H), 1.43 (s, 3H), 1.46 (s, 3H), 1.83 (ddd, 1H, J = 13.5, 7.1, 6.4 Hz), 2.18 (ddd, 1H, J = 13.5, 6.7, 2.3 Hz), 2.77 (dddd, 1H, J = 10.1, 7.1, 6.7, 3.6 Hz), 3.67 (dq, 1H, J = 9.5, 6.9 Hz), 3.73 (dd, 1H, J = 10.0, 2.0 Hz), 4.0 (dq, 1H, J = 9.5, 6.8 Hz), 4.28 (dd, 1H, J = 7.9, 2.0 Hz), 4.29 (dd, 1H, J = 5.1, 2.6 Hz), 4.60 (dd, 1H, J = 7.9, 2.6 Hz), 5.21 (dd, 1H, J = 6.4, 2.3 Hz) 5.54 (d, 1H, J = 5.0 Hz), 6.23 (d, 1H, J = 3.6 Hz), 7.25 (d, 1H, J = 3.2 Hz), 7.78 (d, 1H, J = 3.2 Hz). ^{13}C NMR ($CDCl_3$): δ = 14.9, 24.2, 24.8, 25.6, 25.7, 29.1, 31.3, 64.6, 70.5, 70.6, 71.0 71.1, 96.1, 99.1, 103.3, 108.7, 109.4, 118.5, 143.8, 144.3, 164.9. Anal. calcd for $C_{21}H_{29}NO_7S$: C, 57.39; H, 6.65; N, 3.19. Found: C, 57.21; H, 6.58; N, 3.26.

b) Reactions catalyzed with $ZnCl_2$: A solution of **10** (0.5 g, 1.36 mmol), catalyst (25 mg, 0.18 mmol), and ethyl vinyl ether (0.52 mL, 5.4 mmol) in 55 mL of CH_2Cl_2 was stirred at room temperature. The HPLC analysis of the reaction mixture showed that the reaction went to completion after 30 min to give the cycloadducts **11a**, **11b**, **12a**, and **12b** in 30.1:5.9:57.6:6.4 ratio. After 24 h at room temperature the ratio changed to 18.3:18.3:47.9:15.5. Samples of the *trans* isomers **11b** and **12b** were isolated from the latter mixture by preparative HPLC.

Compound **11b**: ^1H NMR ($CDCl_3$): δ = 1.23 (dd, 3H, J = 7.1, 7.1 Hz), 1.32 (s, 3H), 1.37 (s, 3H), 1.47 (s, 3H), 1.49 (s, 3H), 1.82 (ddd, 1H, J = 13.7, 9.1, 2.6 Hz), 2.26 (ddd, 1H, J = 13.7, 6.7, 3.8 Hz), 2.95 (dddd, 1H, J = 10.1, 9.1, 6.7, 2.8 Hz), 3.51 (dd, 1H, J = 10.1, 1.6 Hz), 3.68 (dq, 1H, J = 9.6, 7.1 Hz), 3.93 (dq, 1H, J = 9.6, 7.1 Hz), 4.32 (dd, 1H, J = 5.1, 2.3 Hz), 4.49 (dd, 1H, J = 8.0, 1.6 Hz), 4.61 (dd, 1H, J = 8.0, 2.3 Hz), 5.26 (dd, 1H, J = 3.8, 2.6 Hz), 5.55 (d, 1H, J = 5.1 Hz), 6.04 (d, 1H, J = 2.8 Hz), 7.30 (d, 1H, J = 3.2 Hz), 7.80 (d, 1H, J = 3.2 Hz). ^{13}C NMR ($CDCl_3$): δ = 15.9, 25.2, 25.6, 26.7, 26.8, 30.0, 31.3, 65.1, 71.3, 71.5, 71.6, 71.8, 97.3, 98.7, 100.7, 109.1, 110.0, 119.3, 144.0, 145.4, 165.4.

Compound **12b**: ^1H NMR ($CDCl_3$): δ = 1.21 (dd, 3H, J = 7.1, 7.0 Hz); 1.32 (s, 3H); 1.35 (s, 3H); 1.48 (s, 3H); 1.50 (s, 3H); 1.73 (ddd, 1H, J = 13.1, 11.8, 2.6 Hz); 2.15 (dddd, 1H, J = 13.1, 6.0, 2.6, 1.4 Hz), 2.95 (dddd, 1H, J = 11.8, 8.6, 6.0, 2.4 Hz), 3.54 (dd, 1H, J = 8.6, 1.5 Hz), 3.67 (dq, 1H, J = 9.7, 7.0 Hz), 3.89 (dq, 1H, J = 9.7, 7.1 Hz), 4.25 (dd, 1H, J = 7.9, 1.5 Hz), 4.32 (dd, 1H, J = 5.0, 2.3 Hz), 4.61 (dd, 1H, J = 7.9, 2.3 Hz), 5.35 (t, 1H, J = 2.6 Hz) 5.59 (d, 1H, J = 5.0 Hz), 6.30 (dd, 1H, J = 2.4,1.4 Hz), 7.24 (d, 1H, J = 3.2 Hz), 7.78 (d, 1H, J = 3.2 Hz). ^{13}C NMR ($CDCl_3$): δ = 15.8, 25.2, 25.6, 26.7, 26.8, 29.6, 29.7, 64.5, 64.6, 70.8, 71.3 71.7, 72.3, 97.3, 97.6, 104.6, 109.1, 110.1, 118.7, 143.8, 144.0, 165.4.

c) Reactions catalyzed with $Eu(fod)_3$: A solution of **10** (0.1 g, 0.27 mmol), catalyst (28 mg, 0.027 mmol), and ethyl vinyl ether (0.1 mL, 1.1 mmol) in 11 mL of CH_2Cl_2 was stirred for 8 h at room temperature. The HPLC analysis showed the presence of 0.8% unreacted oxadiene **10** and the cycloadducts **11a**, **11b**, **12a**, **12b** in a 42.6:3.9:53.4:0.1 ratio. The chromatography of this material (1:5 diethyl ether–hexane) afforded 0.045 g (39%) of **11a** and 0.059 g (51%) of **12a**.

(2*S*)-Ethoxy-(4*S*)-(1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-1,5-pyranose-5-yl)-6-formyl-3,4-dihydro-2*H*-pyran (13a):

Method A: A mixture of **11a** (2.0 g, 4.55 mmol) in 30 mL of CH_3CN and activated 4 Å powdered molecular sieve (4.2 g) was stirred at room temperature for 10 min. After the addition of methyl triflate (0.7 mL, 6.2 mmol), the mixture was stirred at room temperature for another 15 min. The solvent was evaporated under reduced pressure, and the residue suspended in methanol (30 mL), cooled to 0 °C, and treated with $NaBH_4$ (0.4 g, 10.6 mmol). The mixture was stirred for 15 min at room temperature and then diluted with acetone (30 mL), filtered through Celite and concentrated. The crude product was partitioned between diethyl ether and saturated aqueous $NaHCO_3$, the organic layer was dried (Na_2SO_4), and the solvent evaporated under reduced pressure. A solution of the residue in CH_3CN (25 mL) was added dropwise to a stirred solution of $HgCl_2$ (1.5 g, 5.5 mmol) in 20% H_2O–CH_3CN (6.5 mL). After it had been stirred for 15 min at room temperature, the reaction mixture was partitioned between diethyl ether and brine. The organic layer was separated, washed with 20% aqueous KI, and dried (Na_2SO_4). The solvent was evaporated under reduced pressure. The chromatography of the residue (1:4 diethyl ether–hexane) afforded 1.61 g (92%) of the aldehyde **13a** as a colorless oil: $[\alpha]_D^{20} = -64.4$ (c = 0.63 in $CHCl_3$); ^1H NMR ($CDCl_3$): δ = 1.13 (t, 3H, J = 7.2 Hz); 1.31 (s, 3H); 1.38 (s, 3H); 1.46 (s, 3H); 1.50 (s, 3H); 1.95 (ddd, 1H, J = 14.6, 7.8, 3.0 Hz), 2.23 (dddd, 1H, J = 14.6, 3.0, 2.5, 1.0 Hz); 2.72 (dddd, 1H, J = 9.7, 7.8, 4.6, 2.5 Hz), 3.60 (dq, 1H, J = 10.3, 7.2 Hz), 3.74 (dq, 1H, J = 10.3, 7.2 Hz), 3.99 (dd, 1H, J = 9.7, 1.9 Hz), 4.29 (dd, 1H, J = 5.1, 2.4 Hz), 4.30 (dd, 1H, J = 8.0, 1.9 Hz), 4.60 (dd, 1H, J = 8.0, 2.4 Hz), 5.26 (t, 1H, J = 3.0 Hz), 5.51 (d, 1H, J = 5.1 Hz); 6.02 (dd, 1H, J = 4.6, 1.0 Hz), 9.19 (s, 1H). ^{13}C NMR ($CDCl_3$): δ = 14.8, 24.2, 24.6,

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25.6, 25.7, 27.3, 30.9, 64.4, 68.8, 70.3, 70.7, 71.1, 96.5, 97.5, 108.9, 109.4, 123.0, 150.5, 187.9. Anal. calcd for $C_{19}H_{28}O_8$: C, 59.36; H, 7.34. Found: C, 59.18; H, 7.27.

Method B: CH_3I (7.1 mL, 114 mmol) was added to a solution of compound **11a** (5.13 g, 11.7 mmol) in 40 mL of CH_3CN. The mixture was stirred at 80 °C for 15 h. The solvent and the excess CH_3I were evaporated under reduced pressure, and the residue was dissolved in 40 mL of MeOH. The solution was cooled to 0 °C, and then $NaBH_4$ (0.82 g, 21.7 mmol) was added in portions. The reaction mixture was stirred for 15 min at room temperature and then concentrated under reduced pressure. The residue was partitioned between CH_2Cl_2 and saturated aqueous $NaHCO_3$. The organic layer was dried (Na_2SO_4), the solvent evaporated at reduced pressure, and the residue dissolved in CH_3CN (10 mL). This solution was added dropwise to a solution of $HgCl_2$ (3.56 g, 13.1 mmol) in 25 mL of 20% H_2O–CH_3CN. After 15 min of stirring at room temperature, the reaction mixture was partitioned between diethyl ether and brine. The organic layer was washed with 20% aqueous KI and dried (Na_2SO_4). The solvent was evaporated at reduced pressure. Chromatography of the residue (1:4 diethyl ether–hexane) gave 2.51 g (56%) of the aldehyde **13a** and 1.05 g (23%) of the (2*R*) epimer **13b**. **13b**: m.p. 163–164 °C (diethyl ether–hexane); $[\alpha]_D^{20} = -253.5$ ($c = 0.51$ in $CHCl_3$). ^1H NMR ($CDCl_3$): $\delta = 1.18$ (t, 3H, $J = 7.0$ Hz), 1.33 (s, 3H), 1.38 (s, 3H), 1.47 (s, 3H), 1.49 (s, 3H), 1.68 (ddd, 1H, $J = 13.6$, 10.0, 2.7 Hz), 2.27 (dddd, 1H, $J = 13.6$, 6.4, 2.7, 1.1 Hz); 3.02 (dddd, 1H, $J = 10.0$, 9.5, 6.4, 2.9 Hz), 3.55 (dd, 1H, $J = 9.5$, 1.8 Hz), 3.62 (dq, 1H, $J = 9.6$, 7.0 Hz), 3.85 (dq, 1H, $J = 9.6$, 7.0 Hz), 4.34 (dd, 1H, $J = 5.1$, 2.5 Hz); 4.36 (dd, 1H, $J = 7.6$, 1.8 Hz), 4.64 (dd, 1H, $J = 7.6$, 2.5 Hz); 5.26 (t, 1H, $J = 2.7$ Hz), 5.55 (d, 1H, $J = 5.1$ Hz), 5.94 (dd, 1H, $J = 2.9$, 1.1 Hz), 9.18 (s, 1H). ^{13}C NMR ($CDCl_3$): $\delta = 14.7$, 24.1, 24.5, 25.6, 25.7, 29.6, 29.7, 64.2, 70.1, 70.2, 70.7, 70.8, 96.6, 97.4, 108.7, 109.7, 123.2, 150.5, 187.7. Anal. calcd for $C_{19}H_{28}O_8$: C, 59.36; H, 7.34. Found: C, 59.23; H, 7.39.

(2*R*)-Ethoxy-(4*R*)-(1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-1,5-pyranose-5-yl)-6-formyl-3,4-dihydro-2*H*-pyran (14a):
Method A: According to Method A described above, the aldehyde **14a** (0.79 g, 90%) was obtained as a colorless oil from **12a** (1.0 g, 2.27 mmol): $[\alpha]_D^{20} = -39.0$ ($c = 1.10$ in $CDCl_3$); ^1H NMR ($CDCl_3$): $\delta = 1.18$ (t, 3H, $J = 6.9$ Hz), 1.32 (s, 3H), 1.36 (s, 3H), 1.44 (s, 3H), 1.46 (s, 3H), 1.91 (ddd, 1H, $J = 14.2$, 5.1, 5.1 Hz), 2.09 (ddd, 1H, $J = 14.2$, 7.3, 2.5 Hz); 2.79 (m, 1H,), 3.61 (dq, 1H, $J = 9.9$, 6.9 Hz), 3.85 (dd, 1H, $J = 10.2$, 1.9 Hz), 3.92 (dq, 1H, $J = 9.9$, 6.9 Hz), 4.30 (dd, 1H, $J = 8.0$, 1.9 Hz), 4.32 (dd, 1H, $J = 5.0$, 2.4 Hz), 4.63 (dd, 1H, $J = 8.0$, 2.4 Hz), 5.19 (dd, 1H, $J = 5.1$, 2.5 Hz); 5.55 (d, 1H, $J = 5.1$ Hz), 6.20 (d, 1H, $J = 4.1$ Hz), 9.19 (s, 1H). ^{13}C NMR ($CDCl_3$): $\delta = 14.8$, 24.1, 24.7, 25.6, 25.7, 28.0, 31.2, 64.6, 70.0, 70.3, 70.7, 70.8, 96.6, 97.9, 108.9, 109.4, 125.9, 149.9, 187.9. Anal. calcd for $C_{19}H_{28}O_8$: C, 59.36; H, 7.34. Found: C, 59.28; H, 7.27.

Method B: According to Method B described above, 0.65 g (50%) of the aldehyde **14a** and 0.27 g (22%) of the (2*S*) epimer **14b** were obtained as colorless oils from 1.49 g (3.4 mmol) of **12a**. **14b**: $[\alpha]_D^{20} = +14.4$ ($c = 0.64$ in $CHCl_3$); ^1H NMR ($CDCl_3$): $\delta = 1.16$ (t, 3H, $J = 7.3$ Hz), 1.32 (s, 3H), 1.35 (s, 3H), 1.46 (s, 3H), 1.47 (s, 3H), 1.57 (ddd, 1H, $J = 13.0$, 12.1, 2.7 Hz), 2.11 (dddd, 1H, $J = 13.0$, 6.3, 2.2, 1.4 Hz); 3.00 (dddd, 1H, $J = 12.1$, 9.2, 6.3, 2.1 Hz), 3.47 (dd, 1H, $J = 9.2$, 1.8 Hz), 3.62 (dq, 1H, $J = 9.6$, 7.3 Hz), 3.81 (dq, 1H, $J = 9.6$, 7.3 Hz), 4.21 (dd, 1H, $J = 8.0$, 1.7 Hz), 4.33 (dd, 1H, $J = 5.1$, 2.4 Hz), 4.62 (dd, 1H, $J = 8.0$, 2.4 Hz), 5.31 (dd, 1H, $J = 2.7$, 2.2 Hz), 5.57 (d, 1H, $J = 5.1$ Hz), 6.28 (dd, 1H, $J = 2.1$, 1.4 Hz), 9.17 (s, 1H). ^{13}C NMR ($CDCl_3$): $\delta = 14.7$, 24.1, 24.6, 25.6, 25.7, 28.2, 29.1, 63.9, 69.4, 70.3, 70.8, 71.2, 96.4, 96.7, 108.8, 109.7, 126.5, 149.5, 188.0. Anal. calcd for $C_{19}H_{28}O_8$: C, 59.36; H, 7.34. Found: C, 59.12; H, 7.38.

(2*S*)-Ethoxy-(4*S*)-(1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-1,5-pyranose-5-yl)-(5*R*)-hydroxy-(6*S*)-hydroxymethyltetrahydropyran (15): A solution of the aldehyde **13a** (0.3 g, 0.78 mmol) in 8 mL of THF was cooled to 0 °C and then treated with a 1 M solution of BH_3 in THF (3.9 mL, 3.9 mmol). The reaction mixture was stirred for 1 h at 0 °C and for 18 h at room temperature. Then, 0.35 mL of 30% NaOH and 0.35 mL of 30% H_2O_2 were added, and the solution was heated at 60 °C for 1 h. After dilution with H_2O (10 mL), the solution was extracted with diethyl ether (6 × 10 mL), and the combined organic layers were dried (Na_2SO_4). The evaporation of the solvent at reduced pressure and chromatography of the residue (1:5 diethyl ether–cyclohexane) afforded 0.22 g (70%) of the diol **15** as a colorless oil: $[\alpha]_D^{20} = -29.1$ ($c = 0.70$ in $CHCl_3$) ^1H NMR ($CDCl_3$): $\delta = 1.21$ (t, 3H, $J = 7.0$ Hz), 1.31 (s, 3H), 1.33(s, 3H), 1.39–1.45 (m, 1H), 1.45 (s, 3H), 1.49 (s, 3H), 1.99 (dddd, 1H, $J = 12.4$, 10.5, 6.6, 4.1 Hz), 2.26 (ddd, 1H, $J = 13.2$, 4.4, 2.0 Hz), 2.42 (brt, 1H, $J = 5.5$ Hz), 3.26(d, 1H, $J = 4.4$ Hz), 3.31 (ddd, 1H, $J = 9.2$, 4.9, 4.0 Hz), 3.34 (dq, 1H, $J = 9.3$, 7.0 Hz), 3.56 (ddd, 1H, $J = 10.5$, 9.2, 4.4 Hz), 3.76 (dd, 1H, $J = 7.0$, 1.9 Hz), 3.78 (m, 1H), 3.90 (m, 1H), 3.91 (dq, 1H, $J = 9.3$, 7.0 Hz), 4.28 (dd, 1H, $J = 5.2$, 2.2 Hz), 4.39 (dd, 1H, $J = 7.9$, 1.9 Hz), 4.56 (dd, 1H, $J = 9.0$, 2.0 Hz), 4.59 (dd, 1H, $J = 7.9$, 2.2 Hz), 5.52 (d, 1H, $J = 5.2$ Hz). ^{13}C NMR ($CDCl_3$): $\delta = 15.6$, 24.6, 25.3, 26.3, 26.4, 33.8, 42.5, 63.9, 65.0, 68.7, 69.3, 71.0, 71.4, 73.2, 78.8, 97.1, 101.7, 109.1, 109.8. Anal. calcd for $C_{19}H_{32}O_9$: C, 56.42; H, 7.97. Found: C, 56.52; H, 8.02.

C-2 epimer of **15** (oil): $[\alpha]_D^{20}$: −26.7 ($c = 0.75$ in $CHCl_3$); ^1H NMR ($CDCl_3$): $\delta = 1.22$ (t, 3H, $J = 7.2$ Hz) 1.32 (s, 3H), 1.34 (s, 3H), 1.44 (s, 3H), 1.52 (s, 3H), 1.65 (brs, 1H), 1.67 (ddd, 1H, $J = 14.0$, 10.6, 5.4 Hz), 2.04 (dddd, 1H, $J = 10.6$, 9.7, 8.3, 5.4 Hz), 2.23 (ddd, 1H, $J = 14.0$, 5.4, 5.4 Hz), 2.83 (dd, 1H, $J = 7.2$, 0.8 Hz), 3.53 (dq, 1H, $J = 9.8$, 7.2 Hz), 3.73 (m, 1H), 3.74 (ddd, 1H, $J = 8.3$, 7.5, 2.3 Hz), 3.80 (dq, 1H, $J = 9.8$, 7.2 Hz), 3.83 (dd, 1H, 7.5, 4.5 Hz), 3.84 (m, 1H), 3.91 (dd, 1H, $J = 9.7$, 1.8 Hz), 4.30 (dd, 1H, $J = 5.0$, 2.5 Hz), 4.43 (dd, 1H, $J = 7.9$, 1.8 Hz), 4.60 (dd, 1H, $J = 7.9$, 2.5 Hz), 4.89 (dd, 1H, $J = 5.4$, 5.4 Hz), 5.52 (d, 1H, $J = 5.0$ Hz); ^{13}C NMR ($CDCl_3$): $\delta = 15.2$, 24.2, 24.9, 25.9, 26.0, 30.6, 42.1, 60.6, 64.6, 68.4, 69.2, 70.5, 70.9, 72.5, 78.4, 96.5, 101.1, 108.6, 109.3.

(2*R*)-Ethoxy-(4*R*)-(1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-1,5-pyranose-5-yl)-(5*S*)-hydroxy-(6*R*)-hydroxymethyltetrahydropyran (16): The same procedure was used as for the hydroboration of **13a**. From the aldehyde **14a** (0.3 g, 0.78 mmol) and 3.9 mL of a 1 M solution of BH_3 in THF, 0.2 g (64%) of compound **16** was obtained: m.p. 114–116 °C (diethyl ether–hexane); $[\alpha]_D^{20} = -82.8$ ($c = 0.62$ in $CHCl_3$) .^1H NMR ($CDCl_3$): $\delta = 1.23$ (t, 3H, $J = 7.1$ Hz), 1.33 (s, 6H), 1.50 (s, 3H), 1.53(s, 3H), 1.23–1.30 (m, 1H,), 2.02 (ddd, 1H, $J = 12.7$, 4.5, 2.1 Hz), 2.14 (dddd, 1H, $J = 12.7$, 9.2, 9.1, 4.5 Hz), 2.32 (dd, 1H, $J = 6.9$, 6.2 Hz), 3.38 (ddd, 1H, $J = 9.4$, 5.4, 4.2 Hz), 3.50 (dd, 1H, $J = 9.4$, 9.1 Hz), 3.56 (dq, 1H, $J = 9.4$, 7.1 Hz), 3.76 (dd, 1H, $J = 9.2$, 1.7 Hz), 3.77(ddd, 1H, $J = 11.5$, 6.9, 5.4 Hz), 3.93 (ddd, 1H, $J = 11.5$, 6.2, 4.2 Hz), 3.96 (dq, 1H, $J = 9.4$, 7.1 Hz), 4.15 (s,1H), 4.20 (dd, 1H, $J = 8.0$, 1.7 Hz), 4.33 (dd, 1H, $J = 5.0$, 2.5 Hz), 4.60 (dd, 1H, $J = 8.0$, 2.5 Hz), 4.63 (dd, 1H, $J = 9.7$, 2.1 Hz), 5.52 (d, 1H, $J = 5.0$ Hz); ^{13}C NMR ($CDCl_3$): $\delta = 15.1$, 24.2, 24.8, 25.8, 26.0, 32.1, 39.5, 63.5, 64.6, 70.3, 72.7, 73.7, 77.5, 96.2, 100.7, 109.3, 109.6 Anal. calcd for $C_{19}H_{32}O_9$: C, 56.42; H, 7.97. Found: C, 56.35; H, 7.90.

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[20] Selected NMR data: **11a**, H-2/H-3_{ax} J = 3.5 Hz, H-2/H-3_{eq} J = 3.5 Hz, H-4/H-3_{ax} J = 6.3 Hz, and H-4/H-3_{eq} J = 5.5 Hz; **12a**, H-2/H-3_{ax} J = 6.4 Hz, H-2/H-3_{eq} J = 2.3 Hz, H-4/H-3_{ax} J = 7.1 Hz, and H-4/H-3_{eq} J = 6.7 Hz; **11b**, H-2/H-3_{ax} J = 2.6 Hz, H-2/H-3_{eq} J = 3.8 Hz, H-4/H-3_{ax} J = 9.1 Hz, and H-4/H-3_{eq} J = 6.7 Hz; **12b**, H-2/H-3_{ax} J = 2.6 Hz, H-2/H-3_{eq} J = 2.6 Hz, H-4/H-3_{ax} J = 11.8 Hz, and H-4/H-3_{eq} J = 6.0 Hz.

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[23] The facile anomerization of **15** as well as of **11a** and **12a**, or their products, is very likely due to acid catalysis by silica gel or traces of acetic acid contained in acetonitrile. This enhanced reactivity at the anomeric center is typical of 2-deoxy sugars. See: P. M. Collins, R. J. Ferrier, *Monosaccharides*, Wiley, New York, **1995**, pp. 73 and 217.

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