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Carbene-Mediated Functionalization of the Anomeric C–H Bond of Carbohydrates: Scope and Limitations

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Abstract: Herein we investigate the scope and limitations of a new synthetic approach towards α- and β-ketopyranosides relying on the functionalization of the anomeric C–H bond of carbohydrates by insertion of a metal carbene. A key bromoacetate grafted at the 2-position is the cornerstone of a stereoselective glycosylation/diazotransfer/quaternarization sequence that makes possible the construction of a quaternary center with complete control of the stereochemistry. This sequence shows a good tolerance toward protecting groups commonly used in carbohydrate chemistry and gives rise to quaternary disaccharides with good efficiency. In the case of a disaccharide with a more restricted conformation, this functionalization process can be hampered by the steric demand next to the targeted anomeric position. In addition, the formation of transient orthoesters during the glycosylation step may also reduce the overall efficiency of the synthetic sequence.

Keywords: carbenes · carbohydrates · C–H functionalization · C-glycosides · insertion · rhodium

Introduction

The prominent role played by complex carbohydrate structures in numerous physiological and pathological processes strongly appeals for the development of new chemical tools for glycobiology.[1] The modification of carbohydrate scaffolds, as well as the assembly of oligosaccharides and glycoconjugates, have attracted tremendous interest over the past decades to investigate the complex nature of carbohydrate-mediated molecular recognition processes.[2] In this context, the design of locked-sugars proved essential to study the biologically-active conformations of carbohydrates[3] and the mechanism of carbohydrate-active enzymes.[4] However, the preparation of such compounds is a long process during which time-consuming modification of the sugar backbone is required to selectively introduce quaternary centers.[5] The transformation of pre-existing functional groups has also been used to prepare sugars displaying a quaternary anomeric position.[6,7] Following this approach, the new anomeric carbon–carbon bond is readily obtained by addition of an organometallic reagent to a δ-lactone, yet the access to the desired ketopyranosides is then strongly limited by the subsequent glycosylation step (Scheme 1a). Whereas α-anomers were most often obtained in moderate yields,[8,9] β-ketopyranosides exhibiting an equatorial aglycone were not accessible by this method, because 2-*O*-acyl protecting groups did not provide the required anchimeric assistance.[10]

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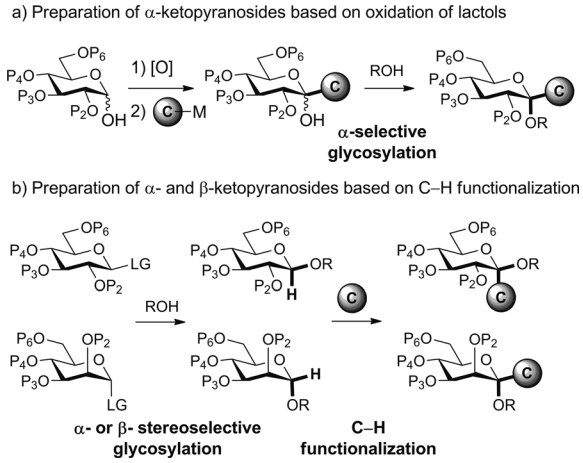
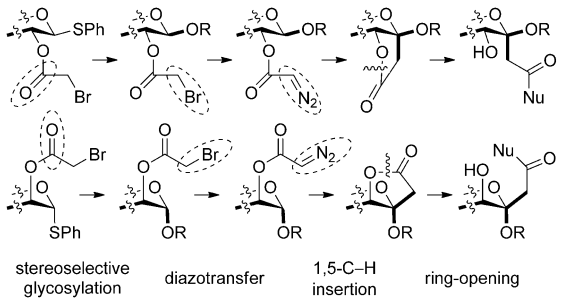


Scheme 1. Synthetic approaches toward ketopyranosides.

We reasoned that formation of the glycosidic linkage before quaternarization might circumvent the limitations inherent to the classical approaches. If successful, this shift in the retrosynthetic paradigm would lead to the functionalization of the anomeric C–H bond of readily available aldopyranosides in a late stage of the synthetic route (Scheme 1b).[11] However, methods already available for the functionalization of anomeric or pseudo-anomeric C–H bonds can only give rise to spiroketals,[12] and, as a consequence, ring-opening of these compounds in a late stage of the synthetic process would result in the loss of the anomeric configuration.

In this context, in which no existing methods could give rise to both anomers of ketopyranosides, we recently reported an alternative strategy in which functionalization of the anomeric position of carbohydrates was relying on the temporary anchoring of a highly reactive carbene at the 2-position of the sugar backbone.[13]

Thus, a bromoacetate anchored at the 2-position first induces a stereoselective glycosylation by anchimeric assistance, and, after conversion into a carbene precursor, promotes functionalization of the anomeric position through a 1,5-C–H insertion process (Scheme 2). Ring-opening of the



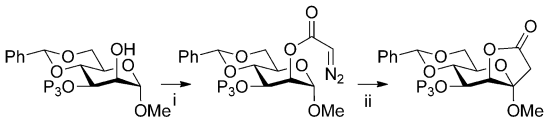
Scheme 2. Dual role of a 2-*O*-bromoacetate for the stereoselective preparation of ketopyranosides.

resulting fused γ-lactone finally delivers both α- and β-ketopyranosides quaternarized at the anomeric position by a pending chain.

Herein, we describe the scope and limitations of this new method with a particular focus on the tolerance toward various protecting groups and glycosidic linkages.

Results and Discussion

Quaternarization of model compounds: We first investigated the quaternarization of model methyl-glycosides to identify the reaction conditions suitable for the functionalization of the anomeric C–H bond[14] without dimerization[15] or other side reactions arising from the formation of transient oxonium ylides.[16,17] Methyl-2-*O*-diazoacetyl-α-mannopyranosides **4–6** having O4 and O6 engaged in a cyclic benzylidene were prepared from the orthogonally protected precursors **1–3** by



P_3 = Piv **1** P_3 = Piv **4** P_3 = Piv **7**
P_3 = TBS **2** P_3 = TBS **5** P_3 = TBS **8**
P_3 = Bn **3** P_3 = Bn **6** P_3 = Bn **9**

Scheme 3. i) a) $BrCOCH_2Br$, pyridine, CH_2Cl_2, 0 °C; b) TsNHNHTs, DBU, THF, 0 °C; 73% for **4**, 64% for **5** and 75% for **6** over the two steps; ii) catalyst (Table 1), 1,2-dichloroethane, 4 Å MS, heat at reflux.

Table 1. Catalytic decomposition of model diazomannosides.

Entry	Diazosugar	Cat. ([mol%])	γ-Lactone	Yield [%]
1	**4**	$[Rh_2(OAc)_4]$ (2)	**7**	77[a]
2	**4**	$[Rh_2(oct)_4]$ (2)	**7**	49[b]
3	**4**	$[Rh_2(tfa)_4]$ (2)	**7**	13[b]
4	**4**	$[Rh_2(cap)_4]$ (2)	**7**	9[b]
5	**4**	$[Rh_2(acam)_4]$ (2)	**7**	35[b]
6	**4**	$[Cu(acac)_2]$ (2)	**7**	20[b]
7	**4**	$[Cu(hfacac)_2]$ (2)	**7**	15[b]
8	**4**	$[\{RuCl_2(p\text{-cym})\}_2]$ (2)	**7**	n.d.[c]
9	**5**	$[Rh_2(OAc)_4]$ (1)	**8**	94[a]
10	**5**	$[Rh_2(acam)_4]$ (1)	**8**	30[b]
11	**5**	$[Cu(acac)_2]$ (2)	**8**	5[b]
12	**5**	$[Cu(hfacac)_2]$ (2)	**8**	15[b]
13	**5**	$[\{RuCl_2(p\text{-cym})\}_2]$ (2)	**8**	n.d.[c]
14	**6**	$[Rh_2(OAc)_4]$ (1)	**9**	20[a,d]
15	**6**	$[Rh_2(acam)_4]$ (1)	**9**	10[b]

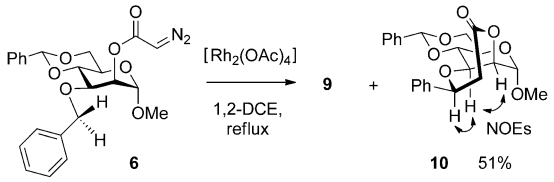
[a] Yield of the isolated product after purification by chromatography. [b] Estimated by ^{1}H NMR spectroscopic analysis of the crude material. [c] Not detectable. [d] Additional 51% of the 1,7-C–H insertion product **10**.

adapting a bromoacetylation/diazotransfer sequence recently reported by Fukuyama and co-workers (Scheme 3).[18,19]

We studied the decomposition of diazosugars **4–6** under dirhodium(II),[20,21] copper(II)[22] or ruthenium(II)[23] catalysis (Table 1). Dimerization of the reactive carbenoid or insertion of adventitious water were prevented by slow addition of the substrate to a refluxed suspension of the catalyst in 1,2-dichloroethane, and by the use of freshly activated molecular sieves (4 Å MS) as an additive, respectively. Decomposition of diazosugars **4** and **5** revealed that $[Rh_2(OAc)_4]$, and, to a lesser extent, $[Rh_2(oct)_4]$, were appropriate for the selective quaternarization of 3-*O*-silylated or 3-*O*-pivaloylated substrates (Table 1, entries 1, 2, and 9). However, dirhodium catalysts with electron-withdrawing or electron-donating ligands, as well as $[Cu(acac)_2]$, $[Cu(hfacac)_2]$, and $[\{RuCl_2(p\text{-cymene})\}_2]$, gave the desired γ-lactones **7** and **8** in moderate to low yields (Table 1, entries 3–8 and 10–13).

With a benzyl group at the 3-position (Table 1, entries 14 and 15), γ-lactone **9** could only be obtained in 20% yield, because of the competitive formation of **10** in 51% yield (Scheme 4).

NMR spectroscopy revealed that **10** resulted from 1,7-insertion of the metal carbene into the benzyl protecting group. NOESY experiments showed that this side reaction occurred selectively in one of the two diasteoreotopic ben-



Scheme 4. Reaction of 3-*O*-benzylated diazomannoside **6**.

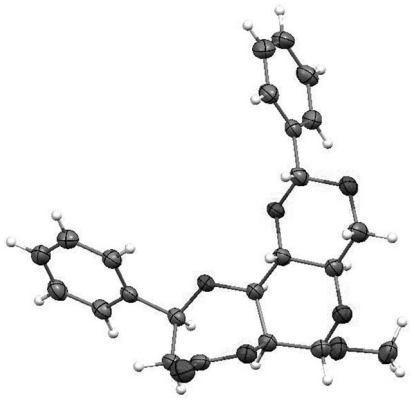
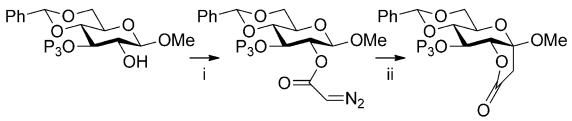


Figure 1. ORTEP diagram of **10** with thermal ellipsoid at 50% probability level.

zylic C–H bonds, a remarkable feature that was further confirmed by X-ray structure analysis of **10** after recrystallization from hexane/ethyl acetate (Figure 1).

Having investigated the functionalization of model methyl-α-mannopyranosides, we next turned our attention to the decomposition of methyl-2-*O*-diazoacetyl-β-glucopyranosides **14**–**16**, prepared from the orthogonally protected precursors **11**–**13**, by rhodium(II), copper(II) or ruthenium(II) catalysts (Scheme 5).



Scheme 5. i) a) $BrCOCH_2Br$, pyridine, CH_2Cl_2, 0 °C; b) TsNHNHTs, DBU, THF, 0 °C, 74% for **14**, 50% for **15** and 74% for **16** over the two steps; ii) catalyst (Table 2), 1,2-dichloroethane, 4 Å MS, heat at reflux.

The use of these model β-glucosides revealed that $[Rh_2(OAc)_4]$, $[Rh_2(acam)_4]$, and, to a lesser extent $[Rh_2(oct)_4]$, were suitable catalysts with a pivalate or a *tert*-butyldimethylsilyl ether at the 3-position (Table 2, entries 1–3, 7, and 8). On the other hand, $[Rh_2(tfa)_4]$, $[Cu(acac)_2]$, $[Cu(hfacac)_2]$, and $[\{RuCl_2(p\text{-cymene})\}_2]$, furnished γ-lactones **17** and **18** in poor yields (Table 2, entries 4–6 and 9–11). With $[Rh_2(OAc)_4]$, decomposition of diazosugar **16** displaying a 3-*O*-benzyl protecting group led to an inseparable mixture of

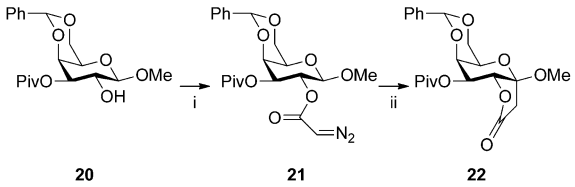
Table 2. Catalytic decomposition of model diazoglucosides.

Entry	Diazosugar	Cat. ([mol%])	γ-Lactone	Yield [%]
1	**14**	$[Rh_2(OAc)_4]$ (2)	**17**	90[a]
2	**14**	$[Rh_2(oct)_4]$ (2)	**17**	60[a]
3	**14**	$[Rh_2(acam)_4]$ (2)	**17**	85[a]
4	**14**	$[Rh_2(tfa)_4]$ (2)	**17**	10[b]
5	**14**	$[Cu(acac)_2]$ (2)	**17**	20[b]
6	**14**	$[Cu(hfacac)_2]$ (2)	**17**	15[b]
7	**15**	$[Rh_2(OAc)_4]$ (1)	**18**	92[a]
8	**15**	$[Rh_2(acam)_4]$ (1)	**18**	70[a]
9	**15**	$[Cu(acac)_2]$ (2)	**18**	10[b]
10	**15**	$[Cu(hfacac)_2]$ (2)	**18**	22[b]
11	**15**	$[\{RuCl_2(p\text{-cym})\}_2]$ (2)	**18**	6[b]
12	**16**	$[Rh_2(OAc)_4]$ (1)	**19**	35[b,c]
13	**16**	$[Rh_2(acam)_4]$ (1)	**19**	35[a]

[a] Yield of the isolated product after purification by chromatography. [b] Estimated by ^1H NMR spectroscopic analysis of the crude material. [c] Additional 35% of the 1,7-C–H insertion product.

products resulting from 1,5- and 1,7-C–H insertions in a 70% combined yield after purification by chromatography (Table 2, entry 12). In contrast, the use of $[Rh_2(acam)_4]$ led to the formation of a less electrophilic metal-carbene, which gave rise to pure γ-lactone **19** by preventing insertion into the benzyl C–H bond (Table 2, entry 13). However, the yield of the isolated product remained modest.

Thus, as shown above, carbene-mediated functionalization of the anomeric position of carbohydrates is efficient with highly rigid scaffolds. We next focused on a methyl β-galactopyranoside in which protection of O4 and O6 as a benzylidene gives the product in the *cis* configuration, instead of the *trans*-fused bicyclic motif, thus making the substrate flexible (Scheme 6).[24] For that purpose, the orthogonally pro-



Scheme 6. i) (a) $BrCOCH_2Br$, pyridine, CH_2Cl_2, 0 °C; b) TsNHNHTs, DBU, THF, 0 °C, 89% over the two steps; ii) catalyst (Table 3), 1,2-dichloroethane, 4 Å MS, heat at reflux.

tected methyl β-galactoside **20** was converted into the carbene precursor **21**. Again, catalytic decomposition worked best with $[Rh_2(OAc)_4]$, with the γ-lactone **22** being obtained in good yield (Table 3). Even if the latter was isolated in slightly lower yields than **17** or **18** (Table 2), similar trends of reactivity in the β-*gluco* and β-*galacto* series show that the insertion of Rh^{II}-carbenes into axially orientated anomeric C–H bonds does not depend on the flexibility of the substrate.

Ring-opening of γ-lactones: Having performed the quaternarization of the anomeric C–H bond in α-*manno*, β-*gluco*,

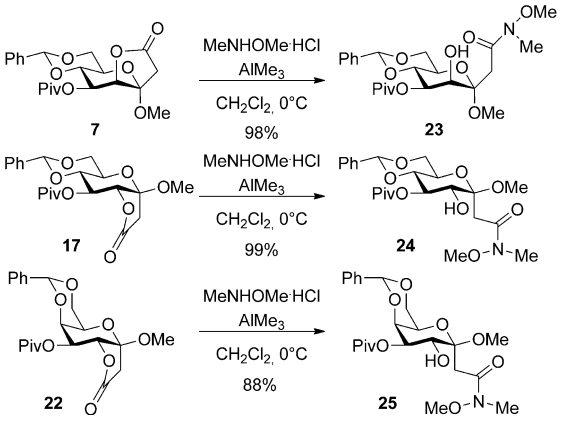
Table 3. Catalytic decomposition of model diazoglucosides.

Entry	Cat. ([mol%])	Yield [%]
1	$[Rh_2(OAc)_4]$ (2)	80[b]
2	$[Rh_2(acam)_4]$ (2)	64[b]
3	$[Rh_2(tfa)_4]$ (2)	15[a]

[a] Estimated by ^{1}H NMR spectroscopic analysis of the crude material. [b] Yield of the isolated product after purification by chromatography.

and β-*galacto* series, we then investigated the ring-opening of the resulting γ-lactones to obtain "true" ketopyranosides with an anomeric position substituted by a pending chain.

To this end, lactones **7**, **17**, and **22** were converted in excellent yields into Weinreb amides (**23**–**25**), which are well-known versatile intermediates in organic synthesis (Scheme 7).[25]

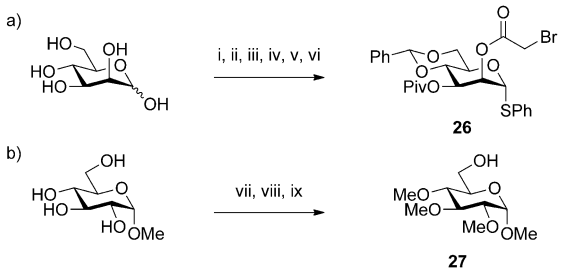


Scheme 7. Ring-opening of γ-lactones **7**, **17**, and **22**.

Preparation and quaternarization of disaccharides: Since 1,5-C–H-insertion of a metal carbene temporary tethered at the 2-position is suitable for inducing efficient functionalization of axial or equatorial anomeric C–H bonds, at least on model compounds, we next attempted the preparation of quaternary disaccharides. On the basis of reports from Kováčs and co-workers,[26] we anticipated that a 2-*O*-bromoacetate would induce the stereoselective formation of a glycosidic linkage by anchimeric assistance. As a participating group and precursor of diazoacetate, it would become the cornerstone of a glycosylation/diazotransfer/carbene-mediated-C–H functionalization sequence, thus providing a stereospecific entry to α- or β-ketopyranosides.

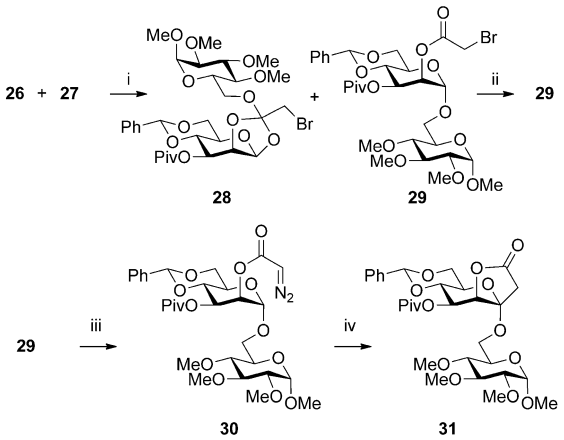
The 2-*O*-bromoacetylated phenyl-thio-α-mannopyranoside donor **26**, with a set of protecting groups that should be compatible with the carbene-mediated functionalization step, was prepared in six steps from D-mannose in an overall yield of 31% (Scheme 8a). As a proof of concept, we first set up a sequence involving the permethylated primary acceptor **27**, which was prepared in 3 steps from methyl-α-D-glucopyranoside in 50% overall yield (Scheme 8b).

The coupling between donor **26** and acceptor **27** using *N*-iodosuccinimide (NIS)/ trifluoromethanesulfonic acid



Scheme 8. i) Ac_2O, I_2, RT; ii) PhSH, $SnCl_4$, CH_2Cl_2, 0°C to RT; iii) MeO-Na, MeOH, RT; iv) $PhCH(OMe)_2$, cat. CSA, DMF, 50°C, 0.1 atm., 42% over 4 steps; v) PivCl, pyridine, 0°C to RT, 85%; vi) $BrCOCH_2Br$, pyridine, CH_2Cl_2, 0°C; 87%; vii) TrCl, pyridine, DMF, RT; viii) MeI, NaH, DMF, 0°C to RT; ix) $AcOH/H_2O$ (4:1), 40°C, 50% over 3 steps.

(TfOH) gave rise to a 1:1 mixture of orthoester **28**, a sample of which could be isolated in pure form for complete characterization, and disaccharide **29**, in a combined yield of 87%. After filtration through a small pad of silica gel, smooth equilibration to the thermodynamic compound **29** was induced under Lewis acidic conditions (Scheme 9). Conversion of the 2-*O*-bromoacetate under TsNHNHTs/1,8-



Scheme 9. i) *N*-Iodosuccinimide (NIS), cat. trifluoromethanesulfonic acid (TfOH), CH_2Cl_2, 4 Å MS, –20°C, 87%; ii) cat. TMSOTf, CH_2Cl_2, 4 Å MS, 0°C, 74%; iii) TsNHNHTs, DBU, THF, 0°C; 84%; iv) $[Rh_2(OAc)_4]$ (2 mol%), 1,2-dichloroethane, heat at reflux, 65%.

diazabicyclo[5.4.0]undec-7-ene (DBU) conditions then delivered the carbene precursor **30** in 84% yield.

Decomposition under $[Rh_2(OAc)_4]$ catalysis finally gave the γ-lactone **31** in 65% yield, showing that carbene-promoted quaternarization of the anomeric C–H bond could also be promoted onto disaccharides.

To evaluate the influence of a more restricted conformational freedom close to the anomeric C–H bond, we next turned our attention to the functionalization of disaccharides displaying secondary aglycones. Thus, we undertook the glycosylation of acceptors **32** and **33**, which only differ by their configuration at the 2-*O*-branching point (Figure 2).[19]

In this case, coupling of **32** and **33** with the thio-glycosyl donor **26** using NIS/TfOH followed by diazotransfer under TsNHNHTs/DBU conditions delivered diazosugars **34** and

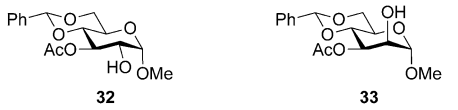
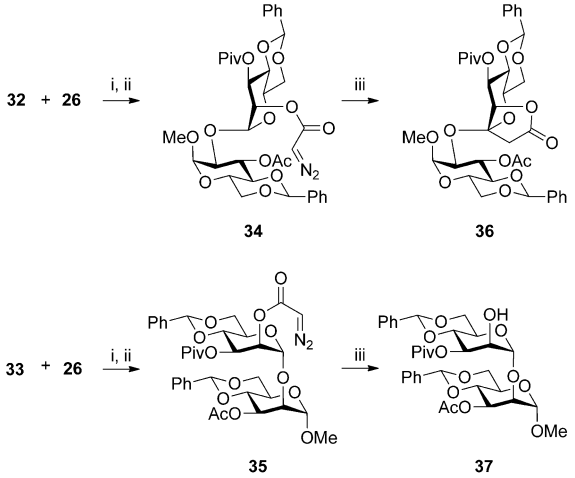


Figure 2. Secondary acceptors considered for the glycosylation/diazotransfer/C–H-functionalization sequence.



Scheme 10. i) NIS, cat. TfOH, CH_2Cl_2, 4 Å MS, −20 °C; ii) TsNHNHTs, DBU, THF, 0 °C; 70% for **34**, 54% for **35** over two steps; iii) [Rh_2-($OAc)_4$] (2 mol%), 1,2-dichloroethane, 4 Å MS, heat at reflux, 60% for **36**, 36% for **37**.

35 in 70 and 54% yields respectively over the two steps (Scheme 10). With the carbene precursors in hand, we then carried out their decomposition by [$Rh_2(OAc)_4$]. In the case of the *manno*-(α-1,2)-*gluco* glycosidic linkage, γ-lactone **36** was obtained in 60% yield from **34** by clean insertion of the metal carbene into the anomeric C–H bond. However, catalytic decomposition of **35** with a *manno*-(α-1,2)-*manno* linkage resulted in the formation of compound **37** having a free alcohol moiety at C2 in 36% yield. To get a better understanding of the divergent behavior of metallocarbenes generated upon decomposition of diazosugars **34** and **35** by [$Rh_2(OAc)_4$], we undertook structural analyses by NMR spectroscopy and molecular modeling of these carbene precusors.

The NOESY experiment carried out with **35** showed correlations between H1 of the acceptor and H5 of the donor on the one hand, and between H2 of the acceptor and H1 of the donor on the other hand (Figure 3a). Molecular modeling [27] confirmed the close proximity between these positions (distance of 3.233 and 2.328 Å, respectively) and revealed a conformation in which the acetate at C3 of the reducing end is pointing toward the targeted anomeric C–H bond (Figure 3a). This steric clash might have prevented the 1,5 insertion, and favored the complexation of the metal carbene with the endocyclic oxygen atom. Decomposition of this oxonium ylide by loss of the reactive moiety[28] might then have delivered alcohol **37**. A similar structural study performed with diazo sugar **34** revealed that the targeted anomeric C–H bond was free from any steric bulk resulting from the reducing end of the molecule (Figure 3b). This study on secondary dimannosides revealed that a conformational restrain can induce a steric bulk close to the targeted position, preventing the functionalization process. As a consequence, insertion of carbenes into the anomeric C–H bond of substrates having a restricted conformational freedom will have to be considered with care in the future.

We next evaluated the tolerance of this reaction toward other protecting groups commonly used in carbohydrate chemistry. Thus, coupling of the 3-*O*-silylated donor **38** (see the Supporting Information) with diacetone galactose **39** under NIS/TfOH conditions, followed by diazotransfer, delivered the carbene precursor **40** in 38% yield over the two steps (Scheme 11). Decomposition of diazosugar **40** by using [$Rh_2(OAc)_4$] gave the expected γ-lactone **41** in 56% yield. Thus, carbene-mediated functionalization of the anomeric position of disaccharides is also compatible with isopropylidene protecting groups on the reducing end of the molecule. However, the bulky 3-*O*-*tert*-butyl silyl (TBS) protecting group markedly reduced the efficiency of the diazotransfer as already observed with compounds **5** and **15**.

Since the glycosylation/diazotransfer/quaternarization sequence proved expedient to obtain quaternary α-dimannosides, we next turned our attention to the functionalization of β-diglucosides following a similar approach (Scheme 12). Thus, we prepared the 2-*O*-bromoacetylated phenyl-thio-β-glucopyranoside donor **42** in 6 steps from D-glucose (see the Supporting Information) and undertook its coupling with acceptor **27**. However, using NIS/TfOH, only traces of impure disaccharide **43** could be collected because of massive degra-

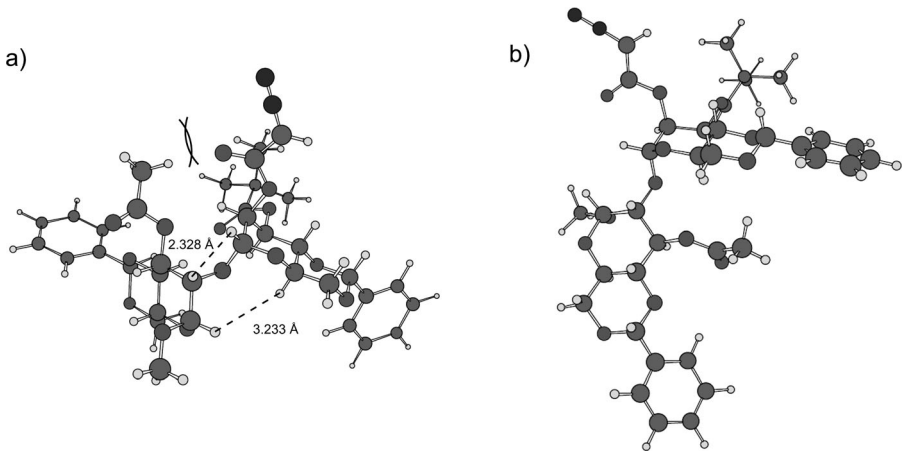
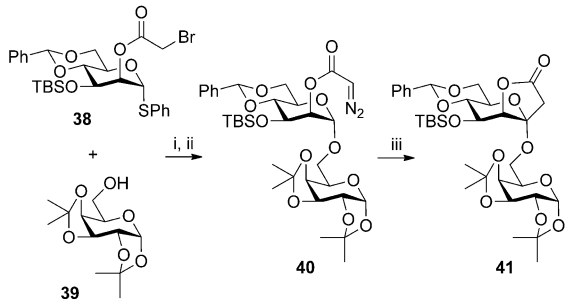
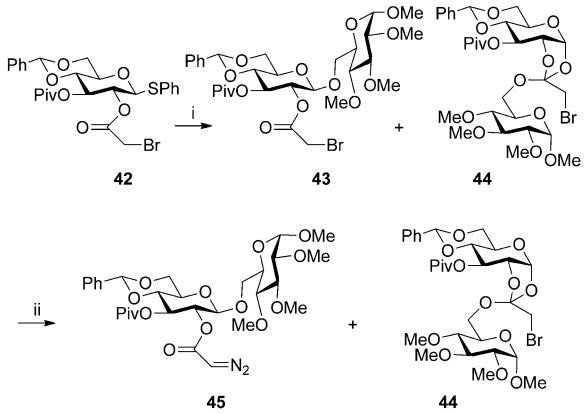


Figure 3. Structural analysis of diazo sugars **34** and **35**.



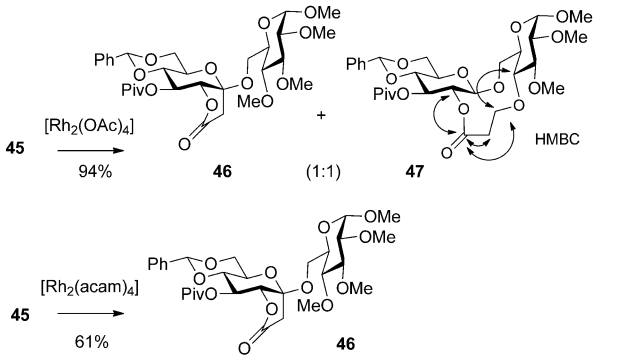
Scheme 11. i) NIS, cat. TfOH, CH_2Cl_2, 4 Å MS, −20 °C; ii) TsNHNHTs, DBU, THF, 0 °C; 38 % over the two steps; iii) $[Rh_2(OAc)_4]$ (2 mol %), 1,2-dichloroethane, 4 Å MS, reflux, 56 %.



Scheme 12. i) Ph_2SO, Tf_2O, TTBP, CH_2Cl_2, 4 Å MS, −70 to −20 °C, then **27**, −70 °C, 1:1 mixture of **43**+**44**, 94 %; ii) TsNHNHTs, DBU, THF, 0 °C; 43 % for **45**, 38 % for **44**.

dation. Furthermore, the use of dimethylthiosulfonium triflate or tetrafluoroborate[29] as glycosylation promoters also resulted in degradation. Finally, a 1:1 inseparable mixture of β-diglucoside **43** and orthoester **44** could be obtained in 84 % yield under neutral conditions involving a reverse activation protocol (Ph_2SO, Tf_2O, TTBP).[30]

However, attempted rearrangement to the thermodynamic disaccharide **43** under Lewis acidic conditions resulted in decomposition. Thus, we directly carried out diazotransfer on the **43**/**44** mixture, believing that the neopentyl position of **44** would not undergo nucleophilic displacement. Treatment of the mixture with TsNHNHTs and DBU eventually gave rise to the carbene precursor **45** admixed with **44**. Since diazosugars are usually slightly more polar than the corresponding bromoacetates, isolation of **45** was then possible by careful chromatography. With the pure material in hand, we investigated the rearrangement of orthoester **44** under Lewis or Brønsted acid catalysis (TMSOTf, TESOTf, TBSOTf, TfOH, $[Yb(OTf)_3]$) at temperature ranging from −50 to 0 °C, in neat methylene chloride or with additional diethylether. Unfortunately, under any of these conditions, only degradation took place.[31] Additionally, decomposition of orthoester **44** in the presence of NIS and catalytic TfOH in methylene chloride at −20 °C revealed that degradation of the substrates under normal glycosylation conditions might have arisen from the formation of this intermediate.

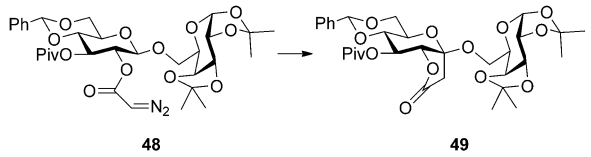


Scheme 13. $[Rh_2L_4]$ (2 mol %), 1,2-dichloroethane, 4 Å MS, heat at reflux.

Lastly, catalytic decomposition of carbene precursor **45** was attempted to obtain the quaternary β-disaccharide **46** (Scheme 13). Under $[Rh_2(OAc)_4]$ catalysis, γ-lactone **46** was obtained admixed with product **47** in a 94 % combined yield. Mass spectrometry analysis of this 1:1 mixture showed a single peak corresponding to an insertion of the metal carbene into the disaccharidic scaffold. Characterization of the side product was then achieved by careful NMR analysis of the mixture of the two compounds. DEPT, HSQC, and HMBC experiments revealed the conversion of the methyl protecting group at the 4-position into a methylene that correlates with the carbonyl of the starting diazoacetate.[32] Macrolactone **47** then resulted from 1,11-C–H insertion of the metal carbene into the reducing end of the disaccharide.

Similar long range C–H activation processes have already been reported by Suarez and co-workers from oxygen-centered radicals.[33] In their case, a 1,8-hydrogen shift supplants the kinetically favored 1,5-hydrogen-transfer process because of a conformational bias that brings the two reactive moieties close to each other.[34] In our case, the 1,11-C–H insertion of the metal carbene into the methoxy group should be less favored than insertion into the anomeric C–H bond from an electronic point of view.[35] The long range C–H activation is then probably the consequence of a conformational bias resulting from the strong *exo*-anomeric effect. If so, a less electrophilic carbene might favor the reaction at the electronically most-activated anomeric C–H bond. To verify this hypothesis, we used $[Rh_2(acam)_4]$ to promote the decomposition of **45**. Gratifyingly, a fully selective functionalization process took place, resulting in isolation of the pure γ-lactone **46** in 61 % yield.

Similarly to the α-*manno* series, we also investigated the tolerance of the functionalization process toward temporary protecting groups. Thus, the carbene precursor **48** was prepared by coupling diacetone galactose **39** with donor **42** under reverse activation conditions (see the Supporting Information), followed by diazotransfer. Finally, decomposition of **48** under $[Rh_2(OAc)_4]$ catalysis nicely delivered the targeted γ-lactone **49** in 60 % yield with complete selectivity (Scheme 14).



Scheme 14. $[Rh_2(OAc)_4]$ (2 mol%), 1,2-dichloroethane, 4 Å MS, heat at reflux.

Conclusion

This study reveals that 1,5 insertion of metal carbenes into the anomeric C–H bond of carbohydrates is highly efficient for obtaining ketopyranosides in α-*manno*, β-*gluco*, and β-*galacto* series. Thus, decomposition of carbene precursors grafted at the 2-position of the sugar by $[Rh_2(OAc)_4]$ or $[Rh_2(acam)_4]$ efficiently induces quaternarization of the carbohydrate scaffold, whereas Cu^{II} or Ru^{II} salts gives the targeted γ-lactones in poor yields. This C–H functionalization process, which is compatible with a wide range of protecting groups commonly used in carbohydrate chemistry, also efficiently delivers quaternary disaccharides following a stereoselective glycosylation/diazotranfer/quaternarization sequence. However, even if functionalization of disaccharides is high yielding in the case of primary anomeric substituents, steric bulk resulting from secondary aglycones sometimes fully prevents the quaternarization process. Moreover, the use of a bromoacetate at the 2-position to control the stereoselectivity of the glycosylation step by anchimeric assistance reduces the efficiency of the overall sequence in the β-*gluco* series by giving rise to transient orthoesters that decompose under acidic conditions. Having established the scope and limitations of the functionalization of the anomeric C–H bond of carbohydrates by 1,5 insertion of metal carbenes, we will next turn our attention to the mechanism of this transformation and to the development of new chemical tools for glycobiology based on quaternary carbohydrate scaffolds.

Experimental Section

General: Optical rotations were measured at 20 °C with a Perkin–Elmer Model 341 polarimeter, in a 10 cm, 1 mL cell. Concentrations are given in g 100 mL^{-1}. Infrared spectra were recorded with a Nicolet 510 FT-IR spectrometer. Mass spectrometry spectra were recorded on a Waters ZQ 2000 spectrometer. High Resolution mass spectra were recorded on a Bruker MicrO-Tof-Q 2 spectrometer at CRMPO (Rennes, France). ^{1}H NMR spectra were recorded at 400 MHz with a Bruker Avance 400 or at 300 MHz with a Bruker Avance 300 spectrometer. ^{13}C NMR spectra were recorded at 75 MHz with a Bruker AC 300 spectrometer with adoption of 77.00 ppm for the central line of $CDCl_3$. The relaxation delay (D1) was increased to 60 seconds for ^{13}C NMR spectra of diazo compounds. Assignments were aided by DEPT, COSY, HSQC, and HMQC experiments. In the ^{1}H and ^{13}C NMR spectra, signals for benzylidene and lactone are numbered 7 and 8, respectively, whereas letters A and B refer to the reducing and non-reducing end of disaccharides, respectively. Reactions were monitored by thin-layer chromatography (TLC) on a precoated silica gel 60 F_{254} plate (layer thickness 0.2 mm; E. Merck, Darmstadt, Germany) and detection by charring phosphomolybdic acid. Flash column chromatography was performed on silica gel 60 (230–400 mesh, E. Merck). For reactions, solvents were purchased anhydrous from Sigma–Aldrich (dichloromethane, 1,2-dichloroethane, and pyridine) or distilled (tetrahydrofuran over sodium/benzophenone for diazotransfer, dichloromethane over phosphorous pentoxide for glycosylations). All reactions were conducted under an argon atmosphere. Glycosylations and carbene-insertion reactions were performed in flame-dried glassware. $[Rh_2(OAc)_4]$, $[Rh_2(tfa)_4]$, $[Rh_2(cap)_4]$, and $[Rh_2(oct)_4]$ were purchased from Sigma–Aldrich. $[Rh_2(acam)_4]$ was prepared following Doyle's procedure.[36] *N*,*N*′-ditosylhydrazine was prepared following Fukuyama's procedure.[18]

Methyl 4,6-*O*-benzylidene-2-*O*-diazoacetyl-3-*O*-pivaloyl-α-D-mannopyranoside 4: A Bromoacetyl bromide (717 μL, 8.237 mmol) was added dropwise over 10 min to a solution of **1** (1.503 g, 4.102 mmol) in anhydrous dichloromethane (20 mL) and anhydrous pyridine (830 μL, 10.262 mmol) at 0 °C. After being stirred for 15 min at 0 °C, the reaction mixture was quenched with methanol (0.5 mL) and TLC (cyclohexane/ethyl acetate 2:1) showed complete consumption of the starting material. The organic layer was washed with a saturated aqueous solution of ammonium chloride (10 mL), dried (anhydrous magnesium sulfate), filtered, and concentrated under vacuum. 1,8-diazabicyclo[5.4.0]undec-7-ene (3.067 mL, 16.241 mmol) was added to a solution of the residue and *N*,*N*′-ditosylhydrazine (2.793 g, 8.204 mmol) in distilled tetrahydrofuran (40 mL) at 0 °C. After TLC analysis showed complete consumption of the starting material (cyclohexane/ethyl acetate 2:1), a saturated aqueous solution of sodium hydrogen carbonate (40 mL) and dichloromethane (40 mL) were added, and the organic layer was dried (anhydrous magnesium sulfate), filtered and concentrated under vacuum. The residue was purified by silica gel chromatography (cyclohexane/ethyl acetate 5:1) to give **4** as a bright yellow oil (1.294 g, 73%). $R_f = 0.62$ (silica, cyclohexane/ethyl acetate 2:1). $[\alpha]_D^{20} = -36$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta =$ 7.48–7.30 (m, 5H, Harom.), 5.61 (s, 1H, H7), 5.50–5.35 (m, 2H, H2, H3), 4.91 (brs, 1H, H8), 4.73 (s, 1H, H1), 4.33 (dd, $J = 9.6$, 3.6 Hz, 1H, $H6_{equiv}$), 4.07–3.79 (m, 3H, H4, H5, $H6_{ax.}$), 3.42 (s, 3H, OMe), 1.20 ppm (s, 9H, $(CH_3)_3C$); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 177.0$ (C=O), 165.7 (C=O), 137.2 (Cquat. arom.), 128.9 (CHarom.), 128.2 (CHarom.), 125.9 (CHarom.), 101.4 (C7), 99.7 (C1), 76.5 (C4), 70.4 (C2), 68.8 (C6), 68.1 (C3), 63.6 (C5), 55.3 (OMe), 46.4 (C8), 38.9 ($(CH_3)_3C$), 27.0 ppm ($(CH_3)_3C$); IR (film): $\tilde{\nu} = 2974$, 2115, 1733, 1698, 1457, 1384, 1283, 1177, 1134, 1097, 1031 cm^{-1}; HRMS: *m/z* calcd for $C_{21}H_{26}N_2O_8Na$: 457.1581; found: 457.1581.

Methyl 4,6-*O*-benzylidene-2-*O*-diazoacetyl-3-*O*-*tert*-butyldimethylsilyl-α-D-mannopyranoside 5: Yield 64%. $R_f = 0.52$ (silica, cyclohexane/ethyl acetate 3:1); $[\alpha]_D^{20} = -3$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta =$ 7.60–7.30 (m, 5H, Harom.), 5.60 (s, 1H, H7), 5.26 (dd, $J = 3.7$, 1.1 Hz, 1H, H2), 4.89 (br s, 1H, H8), 4.71 (d, $J = 1.1$ Hz, 1H, H1), 4.29 (d, $J =$ 5.7 Hz, 1H, H6), 4.22 (dd, $J = 9.0$, 3.7 Hz, 1H, H3), 3.92–3.70 (m, 3H, H4, H5, H6), 3.41 (s, 3H, OMe), 0.88 (s, 9H, $C(CH_3)_3$), 0.10 (s, 3H, CH_3Si), 0.07 ppm (s, 3H, CH_3Si); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 166.2$ (C=O), 137.5 (Cquat. arom.), 128.9 (CHarom.), 128.1 (CHarom.), 126.1 (CHarom.), 101.8 (C7), 100.0 (C1), 79.4 (C4), 72.9 (C2), 68.8 (C6), 68.1 (C3), 63.6 (C5), 55.2 (OMe), 46.5 (C8), 25.6 ($C(CH_3)_3$), 18.2 ($SiC(CH_3)_3$), −4.7 ($SiCH_3$), −5.1 ($SiCH_3$); IR (film): $\tilde{\nu} = 2930$, 2113, 1698, 1471, 1384, 1282, 1249, 1216, 1173, 1133, 1079, 1033, 1008 cm^{-1}; HRMS: *m/z* calcd for $C_{22}H_{32}N_2O_7SiNa$: 487.18765; found: 487.1872.

Methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-diazoacetyl-α-D-mannopyranoside 6: Yield 75%. $R_f = 0.40$ (silica, cyclohexane/ethyl acetate 3:1); $[\alpha]_D^{20} = -21$ ($c = 1.0$, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.56$–7.28 (m, 10H, Harom.), 5.65 (s, 1H, H7), 5.52–5.48 (m, 1H, H2), 4.94 (brs, 1H, H8), 4.77 (d, $J = 12.2$ Hz, 1H, *CH*Ph), 4.76 (d, $J = 1.5$ Hz, 1H, H1) 4.69 (d, $J = 12.2$ Hz, 1H, *CH*Ph), 4.29 (dd, $J = 13.3$, 2.8 Hz, 1H, H6), 4.10–3.96 (m, 2H, H3, H5), 3.93–3.78 (m, 2H, H4, H6), 3.40 ppm (s, 3H, OMe); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 166.2$ (C=O), 138.0 (Cquat. arom.), 137.9 (Cquat. arom.), 129.0 (CHarom.), 128.4 (CHarom.), 128.2 (CHarom.), 127.8 (CHarom.), 127.7 (CHarom.), 126.2 (CHarom.), 101.7 (C7), 99.9 (C1), 78.4 (C4), 73.8 (C3), 72.1 (CH_2Ph), 69.9 (C2), 68.8 (C6), 63.7 (C5), 55.2 (OMe), 46.8 ppm (C8); IR (film): $\tilde{\nu} = 3091$, 2912, 2114,

1691, 1497, 1454, 1383, 1282, 1240, 1174, 1133, 1077, 1029, 1005 cm^{-1}; HRMS: *m/z* calcd for $C_{23}H_{24}N_2O_7Na$: 463.1481; found: 463.1478.

Methyl 4,6-*O*-benzylidene-2-*O*-diazoacetyl-3-*O*-pivaloyl-β-D-glucopyranoside 14: Yield 74%. R_f=0.62 (silica, cyclohexane/ethyl acetate 2:1); $[\alpha]_D^{20}$=−66 (*c*=1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.50–7.30 (m, 5H, Harom.), 5.54 (s, 1H, H7), 5.34 (t, *J*=8.0 Hz, 1H, H3), 5.11 (t, *J*=8.0 Hz, 1H, H2), 4.80 (br s, 1H, H8), 4.52 (d, *J*=8.0 Hz, 1H, H1), 4.41 (dd, *J*=10.5, 4.9 Hz, 1H, $H6_{equiv}$), 3.83 (t, *J*=10.5 Hz, 1H, $H6_{ax.}$), 3.73 (t, *J*=8.0 Hz, 1H, H4), 3.62–3.46 (m, 4H, OMe, H5), 1.18 ppm (s, 9H, $(CH_3)_3C$); ^{13}C NMR (75 MHz, $CDCl_3$): δ=177.5 (C=O), 165.4 (C=O), 136.9 (Cquat. arom.), 129.0 (CHarom.), 128.2 (CHarom.), 125.9 (CHarom.), 102.4 (C1), 101.1 (C7), 78.7 (C4), 72.1 (C2), 71.3 (C3), 68.6 (C6), 66.4 (C5), 57.3 (OMe), 46.3 (C8), 38.9 ($(CH_3)_3C$), 26.8 ppm ($(CH_3)_3C$); IR (film): $\tilde{\nu}$=2971, 2114, 1736, 1704, 1380, 1148, 1099 cm^{-1}; HRMS: *m/z* calcd for $C_{21}H_{26}N_2O_8Na$: 457.1581; found: 457.1587.

Methyl 4,6-*O*-benzylidene-2-*O*-diazoacetyl-3-*O*-*tert*-butyldimethylsilyl-β-D-glucopyranoside 15: Yield 50%. R_f=0.46 (silica, cyclohexane/ethyl acetate 3:1); $[\alpha]_D^{20}$=−37 (*c*=1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.60–7.31 (m, 5H, Harom.), 5.54 (s, 1H, H7), 5.02 (t, *J*=8.8 Hz, 1H, H2), 4.81 (br s, 1H, H8), 4.47–4.30 (m, 2H, H1, $H6_{equiv}$), 3.89 (t, *J*=8.8 Hz, 1H, H3), 3.81 (t, *J*=10.2 Hz, 1H, $H6_{ax.}$), 3.57 (m, 1H, H4), 3.53 (s, 3H, OMe), 3.44 (dt, *J*=10.2, 4.8 Hz, 1H, H5), 0.85 (s, 9H, $C(CH_3)_3$), 0.05 (s, 3H, $SiCH_3$), 0.01 ppm (s, 3H, $SiCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ=165.3 (C=O), 137.1 (Cquat. arom.), 129.1 (CHarom.), 128.2 (CHarom.), 126.3 (CHarom.), 102.5 (C1), 101.8 (C7), 81.4 (C4), 74.5 (C2), 72.8 (C3), 68.7 (C6), 66.4 (C5), 57.1 (OMe), 46.5 (C8), 25.6 ($C(CH_3)_3$), 18.1 ($SiC(CH_3)_3$), −4.2 ($SiCH_3$), −5.1 ppm ($SiCH_3$); IR (film): $\tilde{\nu}$=2929, 2112, 1709, 1471, 1380, 1237, 1134, 1098, 1029, 1009 cm^{-1}; HRMS: *m/z* calcd for $C_{22}H_{32}N_2O_7SiNa$: 487.18765; found: 487.1874.

Methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-diazoacetyl-β-D-glucopyranoside 16: Yield 74%. R_f=0.33 (silica, cyclohexane/ethyl acetate 3:1); $[\alpha]_D^{20}$=14 (*c*=1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.62–7.22 (m, 10H, Harom.), 5.61 (s, 1H, H7), 5.10 (t, *J*=8.3 Hz, 1H, H2), 4.91 (d, *J*=12.0 Hz, 1H, *CH*Ph), 4.81–4.68 (m, 2H, H8, *CH*Ph), 4.48–4.33 (m, 2H, H1, $H6_{equiv}$), 3.94–3.67 (m, 3H, H3, H4, $H6_{ax.}$), 3.47 ppm (m, 4H, H5; OMe); ^{13}C NMR (75 MHz, $CDCl_3$): δ=165.4 (C=O), 138.1 (Cquat. arom.), 137.2 (Cquat. arom.), 129.1 (CHarom.), 128.3 (CHarom.), 128.0 (CHarom.), 127.7 (CHarom.), 126.1 (CHarom.), 102.4 (C1), 101.3 (C7), 81.6 (C4), 78.2 (C3), 74.1 (CH_2Ph), 73.1 (C2), 68.7 (C6), 66.2 (C5), 57.1 (OMe), 46.4 ppm (C8); IR (film): $\tilde{\nu}$=2927, 2113, 1705, 1454, 1381, 1237, 1195, 1096, 1058, 1030, 1011 cm^{-1}; HRMS: *m/z* calcd for $C_{23}H_{24}N_2O_7Na$: 463.1481; found: 463.1483.

Methyl 4,6-*O*-benzylidene-2-*O*-diazoacetyl-3-*O*-pivaloyl-β-D-galactopyranoside 21: Yield 89%. R_f=0.51 (silica, cyclohexane/ethyl acetate 1:1); $[\alpha]_D^{20}$=74 (*c*=1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.54–7.42 (m, 2H, Harom.), 7.40–7.29 (m, 3H, Harom.), 5.52 (s, 1H, H7), 5.47 (dd, *J*=10.3, 8.1 Hz, 1H, H2), 4.91 (dd, *J*=10.3, 3.7 Hz, 1H, H3), 4.77 (br s, 1H, H8), 4.44 (d, *J*=8.1 Hz, 1H, H1), 4.40 (d, *J*=3.7 Hz, 1H, H4), 4.36 (dd, *J*=12.5, 1.3 Hz, 1H, H6), 4.08 (dd, *J*=12.3, 1.3 Hz, 1H, H6′), 3.58–3.44 (m, 1H, H5), 3.52 (s, 3H, OMe), 1.19 ppm (s, 9H, $(CH_3)_3C$); ^{13}C NMR (75 MHz, $CDCl_3$): δ=178.1 (C=O), 165.2 (C=O), 137.4 (Cquat. arom.), 128.7 (CHarom.), 128.0 (CHarom.), 125.9 (CHarom.), 101.5 (C1), 100.4 (C7), 73.2 (C4), 71.8 (C3), 68.8 (C6), 68.7 (C2), 66.3 (C5), 56.4 (OMe), 46.1 (C8), 38.8 ($C(CH_3)_3$), 26.8 ppm ($(CH_3)_3C$). IR (film): $\tilde{\nu}$=2974, 2113, 1731, 1702, 1480, 1453, 1370, 1279, 1181, 1146, 1102, 1057, 1027, 1003 cm^{-1}; HRMS: *m/z* calcd for $C_{21}H_{26}N_2O_8Na$: 457.15869; found: 457.1589.

γ-Lactone 7: A solution of **4** (216 mg, 0.5 mmol) in anhydrous 1,2-dichloroethane (2 mL) was added dropwise through a syringe pump (20 μmol h^{-1}) to a suspension of $[Rh_2(OAc)_4]$ (1.1 mg, 2.5 μmol) in anhydrous 1,2-dichloroethane (80 mL) heated at reflux. After the end of the addition, the reaction mixture was cooled to room temperature and concentrated under vacuum. The residue was purified by silica gel chromatography (cyclohexane/ethyl acetate 5:2) to give **7** as a colorless solid (159 mg, 77%). Recrystalization from dichloromethane gave single crystals suitable for characterization by X-ray crystallography. R_f=0.57 (silica, cyclohexane/ethyl acetate 2:1); $[\alpha]_D^{20}$=−82 (*c*=1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.53–7.30 (m, 5H, Harom.), 5.59 (s, 1H, H7), 5.34 (dd, *J*=10.3, 4.0 Hz, 1H, H3), 4.75 (d, *J*=4.0 Hz, 1H, H2), 4.32 (dd, *J*=9.5, 3.9 Hz, 1H, $H6_{equiv}$), 4.06 (t, *J*=10.3 Hz, 1H, H4), 3.95–3.75 (m, 2H, H5, $H6_{ax.}$), 3.39 (s, 3H, OMe), 2.83 (d, *J*=16.4 Hz, 1H, H8), 2.70 (d, *J*=16.4 Hz, 1H, H8′), 1.26 ppm (s, 9H, $(CH_3)_3C$); ^{13}C NMR (75 MHz, $CDCl_3$): δ=177.8 (C=O), 171.5 (C=O), 136.9 (Cquat. arom.), 129.0 (CHarom.), 128.2 (CHarom.), 125.9 (CHarom.), 103.7 (C1), 101.3 (C7), 79.0 (C2), 74.8 (C4), 68.21 (C6), 68.20 (C3), 64.5 (C5), 51.9 (OMe), 40.3 (C8), 39.0 ($(CH_3)_3C$), 27.0 ppm ($(CH_3)_3C$); IR (film): $\tilde{\nu}$=2971, 1806, 1734, 1704, 1279, 1154, 1098, 1073, 1004 cm^{-1}; HRMS: *m/z* calcd for $C_{21}H_{26}O_8Na$: 429.1520; found: 429.1524.

γ-Lactone 8: Yield 94%. R_f=0.41 (silica, cyclohexane/ethyl acetate 3:1); $[\alpha]_D^{20}$=−75 (*c*=1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.56–7.33 (m, 5H, Harom.), 5.57 (s, 1H, H7), 4.47 (d, *J*=4.0 Hz, 1H, H2), 4.33–4.24 (m, 1H, H6), 4.19 (dd, *J*=9.5, 4.0 Hz, 1H, H3), 3.93–3.69 (m, 3H, H4, H5, H6), 3.38 (s, 3H, OMe), 2.82 (d, *J*=16.3 Hz, 1H, H8), 2.70 (d, *J*=16.3 Hz, 1H, H8′), 0.90 (s, 9H, $C(CH_3)_3$), 0.12 (s, 3H, $SiCH_3$), 0.07 ppm (s, 3H, $SiCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ=172.0 (C=O), 137.2 (Cquat. arom.), 129.0 (CHarom.), 128.2 (CHarom.), 126.1 (CHarom.), 103.7 (C1), 101.7 (C7), 82.4 (C2), 77.6 (C4), 68.5 (C3), 68.2 (C6), 64.7 (C5), 51.8 (OMe), 40.6 (C8), 25.7 ($(CH_3)_3C$), 18.3 ($(CH_3)_3CSi$), −4.4 ($SiCH_3$), −5.1 ppm ($SiCH_3$); IR (film): $\tilde{\nu}$=2930, 1795, 1457, 1386, 1250, 1213, 1174, 1118, 1099, 1027 cm^{-1}; HRMS: *m/z* calcd for $C_{22}H_{32}O_7SiNa$: 459.1815; found: 459.1811.

γ-Lactone 9: Yield 20%. R_f=0.24 (silica, cyclohexane/ethyl acetate 3:1); $[\alpha]_D^{20}$=40 (*c*=1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.41–7.27 (m, 10H, Harom.), 5.61 (s, 1H, H7), 4.89 (d, *J*=12.2 Hz, 1H, *CH*Ph), 4.78 (d, *J*=12.2 Hz, 1H, *CH*Ph), 4.58 (d, *J*=3.7 Hz, 1H, H2), 4.28 (dd, *J*=9.3, 3.8 Hz, 1H, $H6_{equiv}$), 4.12–3.95 (m, 2H, H3, H4), 3.86–3.70 (m, 2H, H5, $H6_{ax.}$), 3.34 (s, 3H, OMe), 2.81 (d, *J*=16.3 Hz, 1H, H8), 2.67 ppm (d, *J*=16.3 Hz, 1H, H8′); ^{13}C NMR (75 MHz, $CDCl_3$): δ=171.5 (C=O), 137.8 (Cquat. arom.), 137.2 (Cquat. arom.), 129.1 (CHarom.), 128.5 (CHarom.), 128.3 (CHarom.), 127.9 (CHarom.), 126.1 (CHarom.), 103.7 (C1), 101.6 (C7), 80.1 (C2), 77.6 (C4), 73.1 (C3), 73.0 (CH_2Ph), 68.3 (C6), 64.6 (C5), 51.8 (OMe), 40.3 ppm (C8); IR (film): $\tilde{\nu}$=2933, 2871, 1797, 1493, 1454, 1377, 1302, 1282, 1217, 1177, 1155, 1096, 1077, 1004 cm^{-1}; HRMS: *m/z* calculated for $C_{23}H_{24}O_7Na$: 435.1420; found: 435.1418.

ε-Lactone 10: Recrystallization from ethyl acetate/hexane. Yield 51%. R_f=0.16 (silica, cyclohexane/ethyl acetate 3:1); $[\alpha]_D^{20}$=−69 (*c*=1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.52–7.28 (m, 10H, Harom.), 5.62 (s, 1H, H7), 5.01 (s, 1H, H1), 4.89 (d, *J*=3.8 Hz, 1H, H2), 4.81 (dd, *J*=9.2, 5.2 Hz, 1H, H9), 4.33 (dd, *J*=9.0, 3.3 Hz, 1H, $H6_{equiv}$), 4.26 (dd, *J*=9.2, 3.8 Hz, 1H, H3), 4.05 (t, *J*=9.2 Hz, 1H, H4), 3.99–3.82 (m, 2H, H5, $H6_{ax.}$), 3.63 (dd, *J*=15.6, 9.2 Hz, 1H, H8), 3.47 (s, 3H, OMe), 3.15 ppm (dd, *J*=15.6, 5.2 Hz, 1H, H8′); ^{13}C NMR (75 MHz, $CDCl_3$): δ=169.1 (C=O), 142.0 (Cquat. arom.), 137.2 (Cquat. arom.), 129.1 (CHarom.), 128.7 (CHarom.), 128.3 (CHarom.), 128.1 (CHarom.), 126.2 (CHarom.), 125.7 (CHarom.), 101.9 (C7), 99.1 (C1), 77.4 (C4), 74.4 (C2), 74.3 (C3), 71.2 (C9), 68.7 (C6), 62.3 (C5), 50.7 (OMe), 44.3 ppm (C8); IR (film): $\tilde{\nu}$=2920, 1449, 1496, 1455, 1367, 1301, 1246, 1218, 1134, 1093, 1040 cm^{-1}; HRMS: *m/z* calcd for $C_{23}H_{24}O_7Na$: 435.1420; found: 435.1412.

γ-Lactone 17: Yield 90%. R_f=0.60 (silica, cyclohexane/ethyl acetate 2:1); $[\alpha]_D^{20}$=1 (*c*=1.0, $CHCl_3$); ^{1}H NMR (300 MHz, 50°C, $CDCl_3$): δ=7.51–7.31 (m, 5H, Harom.), 5.57 (s, 1H, H7), 5.31 (dd, *J*=10.3, 6.1 Hz, 1H, H3), 4.47 (d, *J*=6.1 Hz,1H, H2), 4.42–4.33 (m, 1H, H6), 4.03–3.91 (m, 1H, H4), 3.85–3.71 (m, 2H, H5, H6), 3.42 (s, 3H, OMe), 2.92 (d, *J*=17.1 Hz, 1H, H8), 2.69 (d, *J*=17.1 Hz, 1H, H8′), 1.24 (s, 9H ppm $(CH_3)_3C$); ^{13}C NMR (75 MHz, $CDCl_3$): δ=177.0 (C=O), 171.0 (C=O), 136.6 (Cquat. arom.), 129.1 (CHarom.), 128.3 (CHarom.), 125.9 (CHarom.), 103.9 (C1), 101.4 (C7), 82.0 (C2), 76.1 (C4), 71.9 (C3), 68.9 (C6), 66.4 (C5), 50.7 (OMe), 38.8 ($(CH_3)_3C$), 36.5 (C8), 27.0 ppm ($(CH_3)_3C$); IR (film): $\tilde{\nu}$=2971, 1798, 1740, 1457, 1375, 1277, 1135, 1078, 1031 cm^{-1}; HRMS: *m/z* calcd for $C_{21}H_{26}O_8Na$: 429.1520; found: 429.1521.

γ-Lactone 18: Yield 92%. R_f=0.49 (silica, cyclohexane/ethyl acetate 3:1); $[\alpha]_D^{20}$=−8 (*c*=1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.57–7.32 (m, 5H; Harom.), 5.58 (s, 1H, H7), 4.47–4.29 (m, 2H, H2, H6), 3.89 (dd, *J*=9.6, 5.8 Hz, 1H, H3), 3.83–3.71 (m, 2H, H4, H6), 3.69–3.55 (m, 1H, H5), 3.41 (s, 3H, OMe), 2.86 (d, *J*=17.2 Hz, 1H, H8), 2.68 (d, *J*=17.2 Hz, 1H, H8′), 0.90 (s, 9H, $C(CH_3)_3$), 0.13 (s, 3H, $SiCH_3$), 0.06 ppm

(s, 3H, SiCH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.8 (C=O), 136.9 (Cquat. arom.), 129.2 (CHarom.), 128.2 (CHarom.), 126.1 (CHarom.), 103.8 (C1), 101.8 (C7), 85.4 (C2), 78.6 (C4), 74.1 (C3), 68.8 (C6), 66.5 (C5), 50.5 (OMe), 36.5 (C8), 25.7 ($(CH_3)_3$C), 18.2 ($(CH_3)_3C$Si), −4.5 (SiCH_3), −4.9 ppm (SiCH_3); IR (film): $\tilde{\nu}$ = 2930, 1800, 1462, 1386, 1282, 1254, 1095, 1063, 1004 cm^{-1}; HRMS: *m/z* calcd for $C_{22}H_{32}O_7SiNa$: 459.1815; found: 459.1812.

γ-Lactone 19: Yield 35%. R_f = 0.34 (silica, cyclohexane/ethyl acetate 3:1); $[\alpha]_D^{20}$ = 5 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52–7.31 (m, 10H, Harom.), 5.63 (s, 1H, H7), 4.85 (s, 2H, CH_2Ph), 4.56 (d, *J* = 5.6 Hz, 1H, H2), 4.37 (dd, *J* = 10.3, 4.8 Hz, 1H, H6$_{equiv}$), 3.99 (t, *J* = 9.7 Hz, 1H, H4), 3.87–3.74 (m, 2H, H3, H6$_{ax}$), 3.67 (dt, *J* = 9.7, 4.8 Hz, 1H, H5), 3.40 (s, 3H, OMe), 2.86 (d, *J* = 17.2 Hz, 1H, H8), 2.69 ppm (d, *J* = 17.2 Hz, 1H, H8′); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.6 (C=O), 137.4 (Cquat. arom.), 136.9 (Cquat. arom.), 129.2 (CHarom.), 128.5 (CHarom.), 128.4 (CHarom.), 128.0 (CHarom.), 126.1 (CHarom.), 103.9 (C1), 101.6 (C7), 83.9 (C2), 78.8 (C3), 78.2 (C4), 73.7 (CH_2Ph), 68.9 (C6), 66.4 (C5), 50.7 (OMe), 36.8 ppm (C8); IR (film): $\tilde{\nu}$ = 2933, 1793, 1605, 1497, 1454, 1372, 1331, 1268, 1245, 1213, 1170, 1091, 1028 cm^{-1}; HRMS: *m/z* calcd for $C_{23}H_{24}O_7Na$: 435.1420; found: 435.1415.

γ-Lactone 22: Yield 80%. R_f = 0.61 (silica, cyclohexane/ethyl acetate 1:1); $[\alpha]_D^{20}$ = 76 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, 50°C, $CDCl_3$): δ = 7.51–7.34 (m, 5H, Harom.), 5.53 (s, 1H, H7), 4.93–4.81 (m, 2H, H2, H3), 4.42 (dd, *J* = 2.3, 1.6 Hz,1H, H4), 4.35 (dd, *J* = 12.6, 1.5 Hz, 1H, H6), 4.09 (dd, *J* = 12.6, 1.6 Hz, 1H, H6), 3.77 (d, *J* = 1.5 Hz, 1H, H5), 3.47 (s, 3H, OMe), 2.85 (d, *J* = 17.5 Hz, 1H, H8), 2.70 (d, *J* = 17.5 Hz, 1H, H8′), 1.24 ppm (s, 9H, $(CH_3)_3$C); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.1 (C=O), 172.0 (C=O), 137.4 (Cquat. arom.), 129.1 (CHarom.), 128.3 (CHarom.), 125.9 (CHarom.), 103.4 (C1), 100.9 (C7), 76.3 (C2), 73.2 (C3), 72.0 (C4), 69.6 (C6), 66.2 (C5), 50.3 (OMe), 38.9 ($(CH_3)_3C$), 37.4 (C8), 26.9 ppm ($(CH_3)_3$C); IR (film): $\tilde{\nu}$ = 2976, 2934, 2873, 1794, 1732, 1479, 1457, 1404, 1370, 1324, 1276, 1261, 1176, 1147, 1101, 1077, 1040, 1005 cm^{-1}; HRMS: *m/z* calcd for $C_{21}H_{26}O_8Na$: 429.1525; found: 429.1523.

Weinreb amide 23: A solution of Cl(Me)AlN(Me)OMe (400 µL, 0.4 mmol) (prepared by stirring *N*,*O*-dimethylhydroxylamine hydrochloride (390 mg, 4 mmol) and trimethylaluminum (2 mL of a 2M solution in toluene) in anhydrous dichloromethane (2 mL) for 30 min at 0°C) was added to a solution of lactone **7** (61 mg, 0.150 mmol) in anhydrous dichloromethane (1.5 mL) at 0°C. After being stirred for 20 min, TLC (cyclohexane/ethylacetate 1:1) showed complete consumption of the starting material. The reaction mixture was quenched with a 1M solution of Rochelle's salt (5 mL), diluted with dichloromethane (10 mL) and stirred for 1 hour at room temperature. The organic layer was separated, dried (anhydrous magnesium sulfate), filtered and concentrated under vacuum to give **23** (73 mg, 99%). R_f = 0.26 (silica, cyclohexane/ethyl acetate 2:1); $[\alpha]_D^{20}$ = 12 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45–7.34 (m, 5H, Harom.), 5.59 (s, 1H, H7), 5.40 (dd, *J* = 10.4, 3.4 Hz, 1H, H3), 4.36–4.06 (m, 4H, H2, H4, H6, OH), 3.87 (t, *J* = 10.2 Hz, 1H, H6′), 3.79–3.61 (m, 4H OMe, H5), 3.46–3.11 (m, 7H, OMe, NMe, H8), 2.81 (d, *J* = 14.6 Hz, 1H, H8′), 1.26 ppm (s, 9H, $(CH_3)_3$C); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.6 (C=O), 169.5 (C=O), 137.4 (Cquat. arom.), 128.8 (CHarom.), 128.2 (CHarom.), 125.9 (CHarom.), 103.0 (C1), 101.2 (C7), 75.5 (C4), 70.6 (C2), 70.0 (C3), 68.7 (C6), 65.1 (C5), 61.6 (OMe), 48.4 (OMe), 39.0 ($(CH_3)_3C$), 33.2 (C8), 32.0 (NMe), 27.2 ppm ($(CH_3)_3$C); IR (film): $\tilde{\nu}$ = 3441, 2970, 1731, 1645, 1457, 1385, 1284, 1163, 1097, 1030 cm^{-1}; HRMS: calcd for $C_{23}H_{33}NO_9Na$: 490.2047; found: 490.2048.

Weinreb amide 24: Yield 98%. R_f = 0.27 (silica, cyclohexane/ethyl acetate 2:1); $[\alpha]_D^{20}$ = −8 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.50–7.30 (m, 5H, Harom.), 5.54 (s, 1H, H7), 5.23 (dd, *J* = 8.2, 6.9 Hz, 1H, H3), 5.09 (d, *J* = 4.3 Hz, 1H, OH), 4.38 (dd, *J* = 9.9, 3.6 Hz, 1H, H6), 3.97 (t, *J* = 6.9 Hz, 1H, H4), 3.93–3.80 (m, 2H, H2, H5), 3.79–3.67 (m, 4H, H6′, OMe), 3.42 (s, 3H, OMe), 3.33–3.04 (m, 5H, NMe, 2×H8), 1.23 ppm (s, 9H, $(CH_3)_3$C); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.2 (C=O), 170.1 (C=O), 137.1 (Cquat. arom.), 129.0 (CHarom.), 128.2 (CHarom.), 126.0 (CHarom.), 102.1 (C1), 101.3 (C7), 78.9 (C4), 74.3 (C3), 73.0 (C2), 69.3 (C6), 65.3 (C5), 61.6 (OMe), 49.1 (OMe), 38.9 ($(CH_3)_3C$), 35.2 (C8), 32.2 (NMe), 27.2 ppm ($(CH_3)_3$C); IR (film): $\tilde{\nu}$ = 3437, 2970, 1734, 1634, 1457, 1378, 1282, 1091, 1031 cm^{-1}; HRMS: *m/z* calcd for $C_{30}H_{42}O_{13}Na$: 490.2047; found: 490.2046.

Weinreb amide 25: Yield 89%. R_f = 0.13 (silica, cyclohexane/ethyl acetate 1:1); $[\alpha]_D^{20}$ = 113 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.53–7.31 (m, 5H, Harom.), 5.50 (s, 1H, H7), 4.98 (dd, *J* = 10.5, 3.4 Hz, 1H, H3), 4.62 (br s, 1H, OH), 4.58–4.47 (m, 1H, H2), 4.43–4.29 (m, 2H, H4, H6), 4.04 (dd, *J* = 12.5, 1.4 Hz, 1H, H6), 3.82–3.71 (m, 4H, H5, NOMe), 3.50 (s, 3H, OMe), 3.30–3.12 (m, 4H, H8, NCH_3), 3.02 (d, *J* = 14.0 Hz, 1H, H8′), 1.23 ppm (s, 9H, $(CH_3)_3$C); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.6 (C=O), 170.4 (C=O), 138.0 (Cquat. arom.), 128.8 (CHarom.), 128.1 (CHarom.), 125.9 (CHarom.), 101.7 (C1), 100.4 (C7), 73.4 (C4), 73.3 (C3), 69.3 (C6), 65.4 (C2), 65.3 (C5), 61.5 (NOMe), 49.3 (OMe), 39.0 ($(CH_3)_3C$), 35.1 (C8), 32.1 (NCH_3), 27.0 ppm ($(CH_3)_3$C); IR (film): $\tilde{\nu}$ = 3415, 2972, 2939, 1726, 1634, 1480, 1457, 1397, 1368, 1288, 1173, 1100, 1042, 1003 cm^{-1}; MS: *m/z* = 468 [$M+H^+$].

Phenyl 4,6-*O*-benzylidene-2-*O*-bromoacetyl-3-*O*-pivaloyl-1-thio-α-D-mannopyranoside 26: Pivaloyl chloride (1.228 mL, 10.445 mmol) was added to a stirred solution of phenyl-4,6-*O*-benzylidene-1-thio-α-D-mannopyranoside[37] (1.506 g, 4.178 mmol) in anhydrous pyridine (30 mL) at 0°C. The reaction mixture was stirred overnight (0°C to room temperature) and quenched with methanol (2 mL) and TLC (cyclohexane/ethyl acetate 2:1) showed complete consumption of the starting material. After being concentrated under vacuum, the residue was dissolved in dichloromethane (30 mL) and washed with a saturated aqueous solution of ammonium chloride (15 mL). The organic layer was dried (anhydrous magnesium sulfate), filtered, and concentrated under vacuum. The residue was purified by silica gel chromatography (cyclohexane/ethyl acetate 3:1) to give phenyl-4,6-*O*-benzylidene-3-*O*-pivaloyl-1-thio-α-D-mannopyranoside as a white solid (1.578 g, 85%). R_f = 0.66 (silica, cyclohexane/ethyl acetate 2:1); $[\alpha]_D^{20}$ = 76 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.57–7.29 (m, 10H, Harom.), 5.61 (s, 1H, H7), 5.58 (d, *J* = 1.2 Hz, 1H, H1), 5.39 (dd, *J* = 10.2, 3.3 Hz, 1H, H3), 4.43–4.51 (m, 2H, H2, H5), 4.31–4.18 (m, 2H, H4, H6$_{equiv}$), 3.90 (t, *J* = 10.3 Hz, 1H, H6$_{ax}$), 2.38 (br s, 1H, OH), 1.26 ppm (s, 9H, $(CH_3)_3$C); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.3 (C=O), 137.2 (Cquat. arom.), 133.3 (Cquat. arom.), 131.9 (CHarom.), 129.2 (CHarom.), 128.9 (CHarom.), 128.2 (CHarom.), 127.8 (CHarom.), 125.9 (CHarom.), 101.5 (C7), 88.4 (C1), 76.3 (C4), 71.4 (C2), 70.6 (C3), 68.5 (C6), 65.1 (C5), 39.1 ($(CH_3)_3C$), 27.2 ppm ($(CH_3)_3$C); IR (film): $\tilde{\nu}$ = 3365, 2970, 1738, 1476, 1268, 1099, 1083; HRMS: *m/z* calcd for $C_{24}H_{28}O_6NaS$: 467.1499; found: 467.1502.

Pyridine (513 µL, 6.343 mmol) and bromoacetyl bromide (444 µL, 5.078 mmol) were added to a stirred solution of phenyl-4,6-*O*-benzylidene-3-*O*-pivaloyl-1-thio-α-D-mannopyranoside (1.129 g, 2.539 mmol) in anhydrous dichloromethane (20 mL) at 0°C. After the mixture had been stirred for 20 min at 0°C, TLC (cyclohexane/ethyl acetate 5:1) showed complete consumption of the starting material, and methanol (1 mL) was added. The reaction mixture was diluted with dichloromethane (20 mL) and washed with a saturated aqueous solution of ammonium chloride (20 mL). The organic layer was dried (anhydrous magnesium sulfate), filtered, and concentrated under vacuum. The residue was purified by silica gel chromatography (cyclohexane/ethyl acetate 7:1) to give **26** as a white foam (1.249 g, 87%). R_f = 0.67 (silica, cyclohexane/ethyl acetate 5:1); $[\alpha]_D^{20}$ = 84 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.54–7.34 (m, 10H, Harom.), 5.74 (dd, *J* = 3.4, 1.4 Hz, 1H, H2), 5.68 (s, 1H, H7), 5.53 (dd, *J* = 10.2, 3.4 Hz, 1H, H3), 5.51 (d, *J* = 1.4 Hz, 1H, H1), 4.53 (td, *J* = 10.2, 4.8 Hz, 1H, H5), 4.32 (dd, *J* = 10.3, 4.8 Hz, 1H, H6$_{equiv}$), 4.23 (t, *J* = 10.2 Hz, 1H, H4), 3.97–3.20 (m, 3H, H8, H8′, H6$_{ax}$), 1.25 ppm (s, 9H, $(CH_3)_3$C); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.2 (C=O), 166.1 (C=O), 137.1 (Cquat. arom.), 132.7 (Cquat. arom.), 132.4 (CHarom.), 129.4 (CHarom.), 129.1 (CHarom.), 128.4 (CHarom.), 128.3 (CHarom.), 126.0 (CHarom.), 101.5 (C7), 86.7 (C1), 76.4 (C4), 73.4 (C2), 68.4 (C3 and C6), 65.4 (C5) 39.0 ($(CH_3)_3C$), 27.1 ($(CH_3)_3$C), 25.2 ppm (C8); IR (film): $\tilde{\nu}$ = 2972, 1736, 1478, 1264, 1139, 1100, 1084 cm^{-1}; HRMS: *m/z* calcd for $C_{26}H_{29}O_7{}^{79}BrNaS$: 587.0710; found: 587.0708.

Methyl 2,3,4-tri-*O*-methyl-α-D-glucopyranoside 27: Anhydrous pyridine (6.1 mL, 74.948 mmol) and triphenylmethylchloride (18.282 g, 65.579 mmol) was added to a stirred suspension of methyl-α-D-glucopyranoside (12.128 g, 62.457 mmol) in DMF (60 mL) at room temperature.

After being stirred for 18 h, methanol (2 mL) was added and the reaction mixture was concentrated under vacuum. Methyl iodide (17.5 mL, 281.104 mmol) and sodium hydride (60% in mineral oil, 6.745 g, 281.104 mmol) were then added portion wise at 0°C to a solution of the residue in DMF (250 mL). After the mixture had been stirred for 18 h at room temperature, methanol was added (20 mL) and the reaction mixture was concentrated under vacuum. The residue was dissolved in dichloromethane (400 mL) and washed with a saturated aqueous solution of ammonium chloride (200 mL). The organic layer was dried (anhydrous magnesium sulfate), filtered, and concentrated under vacuum. The residue was dissolved in a 4:1 mixture of acetic acid and water (200 mL) and heated for 4 h at 40°C. The reaction mixture was filtered to remove the precipitate, and concentrated under vacuum. The residue was dissolved in dichloromethane (400 mL) and washed with a saturated aqueous solution of sodium hydrogen carbonate (20 mL). The organic layer was dried (anhydrous magnesium sulfate), filtered, and concentrated under vacuum. The residue was purified by silica gel chromatography (ethyl acetate) to give **27** as a pale yellow viscous liquid (7.3 g, 50%). $R_f = 0.28$ (silica, cyclohexane/ethyl acetate 1:1); $[\alpha]_D^{20} = 158$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 4.82$ (d, $J = 3.6$ Hz, 1H, H1), 3.85 (dd, $J = 11.8$, 2.9 Hz, 1H, H6), 3.74 (dd, $J = 11.8$, 2.9 Hz, 1H, H6′), 3.65 (s, 3H, OMe), 3.61–3.48 (m, 8H, H3, H5, 2×OMe), 3.42 (s, 3H, OMe), 3.14–3.21 (m, 2H, H2, H4), 2.58 ppm (m, 1H, OH). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 97.5$ (C1), 83.4 (C3), 81.8 (C2), 79.5 (C4), 70.6 (C5), 61.8 (C6), 60.9 (OMe), 60.6 (OMe), 59.0 (OMe), 55.1 ppm (OMe); IR (film): $\tilde{\nu} = 3471$, 2932, 2833, 1190, 1159, 1098, 1051, 1002 cm^{-1}; HRMS: *m/z* calcd for $C_{10}H_{20}O_6Na$: 259.1152; found: 252.1154.

Methyl (4,6-*O*-benzylidene-2-*O*-bromoacetyl-3-*O*-pivaloyl-α-D-mannopyranoside)-(1→6)-2,3,4-*O*-methyl-α-D-glucopyranoside 29: A solution of **26** (264 mg, 1.117 mmol) and **27** (486 mg, 0.859 mmol) in distilled dichloromethane (8 mL) were stirred for 1 hour at room temperature over activated 4 Å MS (700 mg). *N*-iodosuccinimide (NIS, 387 mg, 1.720 mmol) was added, and after cooling to −20°C, trifluoromethanesulfonic acid (23 μL, 0.258 mmol) was added dropwise. After being stirred for 30 min at −20°C, the reaction mixture became dark brown. A saturated aqueous solution of sodium hydrogen carbonate (8 mL) was added, followed by a saturated aqueous solution of sodium thiosulfate (8 mL). The colorless reaction mixture was then diluted with dichloromethane (20 mL) and filtered through a Celite pad. The organic layer was dried (anhydrous magnesium sulfate), filtered, and concentrated under vacuum. The residue was purified by silica gel chromatography (cyclohexane/ethyl acetate 1.5:1) to give a 1:1 mixture of disaccharide **29** and orthoester **28** (a sample of which was collected in a pure form for complete characterization) as a white foam (514 mg, 87%). Orthoester **28**: $R_f = 0.48$ (silica, cyclohexane/ethyl acetate 1:1); $[\alpha]_D^{20} = 12$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.50$–7.31 (m, 5H, Harom.), 5.63 (s, 1H, H7B), 5.57 (d, $J = 2.2$ Hz, 1H, H1B), 5.13 (dd, $J = 9.9$, 4.1 Hz, 1H, H3B), 4.84 (d, $J = 3.4$ Hz, 1H, H1A), 4.78 (dd, $J = 4.1$, 2.2 Hz, 1H, H2B), 4.37 (dd, $J = 10.7$, 5.2 Hz, 1H, H6B), 4.05 (t, $J = 9.9$ Hz, 1H, H4B), 3.56 (m, 21H, H3A, H4A, H5A, H5B, 2×H6A, H6B, 2×H8A, 4×OMe), 3.23 (dd, $J =$ 9.6, 3.4 Hz, 1H, H2A), 1.26 ppm (s, 9H, $(CH_3)_3$C); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 178.0$ (C=O), 136.9 (Cquat. arom.), 129.1 (CHarom.), 128.3 (CHarom.), 125.9 (CHarom.), 121.6 (C9B), 101.2 (C7B), 97.61 (C1), 97.59 (C1), 83.7 (C3A), 81.6 (C4A), 78.7 (C2A), 77.9 (C2B), 74.9 (C4B), 70.0 (C3B), 69.0 (C5), 68.4 (C6B), 65.2 (C5), 61.0 (OMe), 60.7 (OMe), 60.5 (C6A), 59.1 (OMe), 55.2 (OMe), 39.0 ($(CH_3)_3C$), 34.1 (C8B), 27.0 ppm ($(CH_3)_3$C); IR (film): $\tilde{\nu} = 2930$, 1734, 1280, 1160, 1102, 1061 cm^{-1}; HRMS: *m/z* calcd for $C_{30}H_{43}O_{13}{}^{79}$BrNa: 713.1779; found: 713.1781.

A solution of the 1:1 mixture of **28** and **29** (468 mg, 0.677 mmol) in distilled dichloromethane (10 mL) was stirred for 1 hour over activated 4 Å MS (500 mg). After cooling to 0°C, trimethylsilyl trifluoromethanesulfonate (25 μL, 0.138 mmol) was added dropwise to give a bright yellow solution. After 20 min, TLC analysis (cyclohexane/ethyl acetate 1:1) showed complete conversion of **28** to **29**. The reaction mixture was quenched with triethylamine (0.5 mL), filtered through a Celite pad, and concentrated under vacuum. The residue was purified by silica gel chromatography (cyclohexane/ethyl acetate 1.5:1) to give **29** as a white foam (346 mg, 74%). TLC analysis: $R_f = 0.52$ (silica, cyclohexane/ethyl acetate 1:1); $[\alpha]_D^{20} = 68$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.45$–7.39 (m, 5H, Harom.), 5.62 (s, 1H, H7), 5.53–5.43 (m, 2H, H2B, H3B), 4.92 (d, $J = 1.2$ Hz, 1H, H1B), 4.79 (d, $J = 3.6$ Hz, 1H, H1A), 4.34 (dd, $J = 10.1$, 4.0 Hz, 1H, H6B), 4.12–4.01 (m, 2H, H4B, H5B), 3.96–3.84 (m, 4H, 2× H6A, 2×H8B), 3.71 (dd, $J = 11.2$, 1.8 Hz, 1H, H6B), 3.67–3.61 (m, 4H, OMe, H5A), 3.58 (s, 3H, OMe), 3.57–3.47 (m, 4H, OMe, H3A) 3.42 (s, 3H, OMe), 3.24 (dd, $J = 9.6$, 3.6 Hz, 1H, H2A), 3.14 (dd, $J = 10.0$, 8.9 Hz, 1H, H4A), 1.19 ppm (s, 9H, $(CH_3)_3$C); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta =$ 177.1 (C=O), 166.1 (C=O), 137.1 (Cquat. arom.), 129.0 (CHarom.), 128.2 (CHarom.), 125.9 (CHarom.), 101.5 (C7B), 98.5 (C1B), 97.4 (C1A), 83.6 (C3A), 81.7 (C2A), 79.4 (C4A), 71.8 (C4B), 69.7 (C5A), 68.7 (C6B), 68.0 (C3B), 66.6 (C6A), 64.0 (C5B), 60.8 (OMe), 60.7 (OMe), 59.1 (OMe), 55.3 (OMe), 38.9 ($(CH_3)_3C$), 27.1 ($(CH_3)_3$C), 25.2 ppm (C8B); IR (film): $\tilde{\nu} = 2932$, 1737, 1375, 1282, 1099 cm^{-1}; HRMS: m/z calcd for $C_{30}H_{43}O_{13}{}^{79}$BrNa: 713.1779; found: 713.1777.

Methyl (4,6-*O*-benzylidene-2-*O*-diazoacetyl-3-*O*-pivaloyl-α-D-mannopyranoside)-(1→6)-2,3,4-*O*-methyl-α-D-glucopyranoside 30: 1,8-Diazabicyclo-[5.4.0]undec-7-ene (374 μL, 2.5 mmol) was added to a solution of **29** (346 mg, 0.5 mmol) and *N*,*N*′-ditosylhydrazine (341 g, 1 mmol) in distilled tetrahydrofuran (4 mL) at 0°C. After TLC analysis showed complete consumption of the starting material (cyclohexane/ethyl acetate 1:1), a saturated aqueous solution of sodium hydrogen carbonate (10 mL) and dichloromethane (20 mL) were added, and the organic layer was dried (anhydrous magnesium sulfate), filtered and concentrated under vacuum. The residue was purified by silica gel chromatography (cyclohexane/ethyl acetate 1.5:1) to give **30** as a bright yellow oil (269 mg, 84%). $R_f = 0.46$ (silica, cyclohexane/ethyl acetate 1:1); $[\alpha]_D^{20} = 58$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.45$–7.33 (m, 5H, Harom.), 5.60 (s, 1H, H7B), 5.49 (dd, $J = 3.6$, 1.2 Hz, 1H, H2B), 5.42 (dd, $J = 9.7$, 3.6 Hz, 1H, H3B), 4.93 (d, 4.90, $J = 1.2$ Hz, 1H, H1B), 4.90 (br s, 1H, H8B), 4.79 (d, $J = 3.6$ Hz, 1H, H1A), 4.32 (dd, $J = 10.1$, 4.3 Hz, 1H, H6B), 4.11–3.94 (m, 2H, H5B, H6A), 3.87 (m, 2H, H4B, H6A), 3.70 (dd, $J = 10.1$, 1.7 Hz, 1H, H6B), 3.68–3.37 (m, 14H, 4×OMe, H3A, H5A), 3.24 (dd, $J = 9.6$, 3.6 Hz, 1H, H2A), 3.14 (t, $J = 9.1$ Hz, 1H, H4A), 1.19 ppm (s, 9H, $(CH_3)_3$C); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 177.1$ (C=O), 165.6 (C=O), 137.2 (Cquat. arom.), 128.9 (CHarom.), 128.2 (CHarom.), 125.9 (CHarom.), 101.4 (C7B), 98.9 (C1B), 97.4 (C1A), 83.6 (C3A), 81.7 (C2A), 79.4 (C4A), 76.7 (C4B), 70.3 (C2B), 69.7 (C5A), 68.8 (C6B), 68.1 (C3B), 66.5 (C6A), 63.8 (C5B), 60.8 (OMe), 60.7 (OMe), 59.1 (OMe), 55.3 (OMe), 46.3 (C8B), 38.9 ($(CH_3)_3C$), 27.0 ppm ($(CH_3)_3$C); IR (film): $\tilde{\nu} = 2933$, 2114, 1736, 1700, 1382, 1282, 1143, 1099 cm^{-1}; HRMS: *m/z* calcd for $C_{30}H_{42}N_2O_{13}Na$: 661.2579; found: 661.2581.

γ-Lactone 31: A solution of **30** (120 mg, 0.190 mmol) in anhydrous 1,2-dichloroethane (2 mL) was added dropwise through a syringe pump (20 μmol h^{-1}) to a suspension of $[Rh_2(OAc)_4]$ (0.85 mg, 2 μmol) in anhydrous 1,2-dichloroethane (25 mL) heated at reflux. After the end of the addition, the reaction mixture was cooled to room temperature and concentrated under vacuum. The residue was purified by silica gel chromatography (cyclohexane/ethylacetate 3:2) to give **31** as a colorless solid (78 mg, 65%). $R_f = 0.51$ (silica, cyclohexane/ethyl acetate 1:1); $[\alpha]_D^{20} = 11$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.53$–7.32 (m, 5H, Harom.), 5.59 (s, 1H, H7B), 5.32 (dd, $J = 9.8$, 4.0 Hz, 1H, H3B), 4.81 (d, $J = 4.0$ Hz, 1H, H2B), 4.80 (d, $J = 3.6$ Hz, 1H, H1A), 4.31 (dd, $J = 10.2$, 4.7 Hz, 1H, H6B), 4.07 (t, $J = 9.8$ Hz, 1H, H4B), 3.97 (dt, $J = 9.8$, 4.7 Hz, 1H, H5B), 3.84 (m, 2H, H6A, H6B), 3.68–3.48 (m, 12H, 3×OMe, H6A, H3A, H5A), 3.43 (s, 3H OMe), 3.20 (dd, $J = 9.6$, 3.6 Hz, 1H, H2A), 3.11 (dd, $J = 10.0$, 8.9 Hz, 1H, H4A), 2.83 (br s, 2H, H8B), 1.25 ppm (s, 9H, $(CH_3)_3$C); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 177.9$ (C=O), 171.6 (C=O), 136.9 (Cquat. arom.), 129.1 (CHarom.), 128.3 (CHarom.), 125.9 (CHarom.), 103.6 (C1B), 101.4 (C7B), 97.5 (C1A), 83.6 (C3A), 81.9 (C2A), 79.2 (C4A), 78.9 (C2B), 74.7 (C4B), 69.1 (C5A), 68.3 (C3B), 68.2 (C6B), 64.7 (C5B), 63.9 (C6A), 60.8 (OMe), 60.6 (OMe), 59.1 (OMe), 55.4 (OMe), 40.9 (C8B), 39.0 ($(CH_3)_3C$), 27.0 ppm ($(CH_3)_3$C); IR (film): $\tilde{\nu} = 2935$, 1804, 1735, 1281, 1155, 1099 cm^{-1}; HRMS: *m/z* calcd for $C_{23}H_{33}NO_9Na$: 633.2518; found: 633.2519.

Methyl (4,6-*O*-benzylidene-2-*O*-diazoacetyl-3-*O*-pivaloyl-α-D-mannopyranoside)-(1→2)-4,6-*O*-benzylidene-3-*O*-acetyl-α-D-glucopyranoside 34: A solution of donor **26** (109 mg, 0.193 mmol) and acceptor **33** (65 mg,

0.251 mmol) in distilled dichloromethane (3.5 mL) was stirred for 1 hour at room temperature over activated 4 Å MS (175 mg). NIS (87 mg, 0.386 mmol) was added, and after cooling to −20 °C, trifluoromethanesulfonic acid (5 μL, 0.058 mmol) was added dropwise. After being stirred for 2 h at −20 °C, the reaction mixture became dark-brown. A saturated aqueous solution of sodium hydrogen carbonate (5 mL) was added, followed by a saturated aqueous solution of sodium thiosulfate (3 mL). The colorless reaction mixture was then diluted with dichloromethane (10 mL) and filtered through a Celite pad. The organic layer was dried (anhydrous magnesium sulfate), filtered, and concentrated under vacuum. The residue was purified for complete characterization by silica gel chromatography (dichloromethane/ethyl acetate 24:1) to give the disaccharide as a white foam (130 mg, 87 %). R_f = 0.64 (silica, cyclohexane/ethyl acetate 1:1); $[\alpha]_D^{20}$ = 46 (c = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.50–7.31 (m, 10H, Harom.), 5.65–5.54 (m, 2H, H3A, H7A or H7B), 5.49 (s, 1H, H7A or H7B), 5.46–5.36 (m, 2H, H2B, H3B), 4.93 (d, J = 1.1 Hz, 1H, H1B), 4.91 (d, J = 3.5 Hz, 1H, H1A), 4.38–4.27 (m, 2H, H6A, H6B), 4.11–4.02 (m, 2H, H6A, H6B), 4.00–3.81 (m, 5H, H2A, H5A, H6B, 2×H8B), 3.75 (t, J = 10.2 Hz, 1H, H6A), 3.59 (t, J = 9.6 Hz, 1H, H4A), 3.47 (s, 3H, OMe), 2.13 (s, 3H, (CH_3)C=O), 1.18 ppm (s, 9H, (CH_3)$_3$C); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.7 (C=O), 169.5 (C=O), 166.1 (C=O), 137.0 (Cquat. arom.), 136.9 (Cquat. arom.), 129.0 (CHarom.), 128.9 (CHarom.), 128.2 (2×CHarom.), 126.1 (CHarom.), 125.8 (CHarom.), 101.5 (C7A and C7B), 97.4 (C1A), 95.9 (C1B), 79.5 (C4A), 76.1 (C5B), 74.5 (C2A), 72.0 (C2B), 69.4 (C3A), 68.9 (C6A), 68.4 (C6B), 67.4 (C3B), 64.3 (C4B), 62.4 (C5A), 55.6 (OMe), 38.8 ((CH$_3$)$_3$$C$), 27.0 (($CH_3$)$_3$C), 25.1 (C8B), 21.0 ppm ((CH_3)C=O); IR (film): $\tilde{\nu}$ = 2976, 2929, 2868, 1740, 1457, 1372, 1276, 1261, 1228, 1125, 1098, 1074, 1038 cm^{-1}; HRMS: m/z calcd for $C_{36}H_{43}N_2O_{14}{}^{79}$BrNa: 801.17284; found: 801.1728.

1,8-Diazabicyclo[5.4.0]undec-7-ene (280 μL, 1.860 mmol) was added to a solution of the disaccharide (290 mg, 0.372 mmol) and *N*,*N*′-ditosylhydrazine (253 mg, 0.744 mmol) in distilled tetrahydrofuran (25 mL) at 0 °C. After TLC analysis showed complete consumption of the starting material (dichloromethane/ethyl acetate 15:1), a saturated aqueous solution of sodium hydrogen carbonate (15 mL) and dichloromethane (20 mL) were added, and the organic layer was dried (anhydrous magnesium sulfate), filtered and concentrated under vacuum. The residue was purified by silica gel chromatography (dichloromethane/ethyl acetate 15:1) to give **34** as a bright yellow oil (200 mg, 74 %). R_f = 0.53 (silica, cyclohexane/ethyl acetate 1:1); $[\alpha]_D^{20}$ = 25 (c = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.49–7.31 (m, 10H, Harom.), 5.66–5.55 (m, 2H, H7A or H7B, H3A), 5.50 (s, 1H, H7A or H7B), 5.45–5.33 (m, 2H, H2B, H3B), 4.97 (br s, 2H, H1B, H8B), 4.92 (d, J = 3.4 Hz, 1H, H1A), 4.38–4.27 (m, 2H, H6A, H6B), 4.11–3.79 (m, 5H, H2A, H5A, H4B, H5B, H6B), 3.75 (t, J = 10.3 Hz, 1H, H6A), 3.59 (t, J = 9.6 Hz, 1H, H4A), 3.47 (s, 3H, OMe), 2.13 (s, 3H, CH_3C=O), 1.19 ppm (s, 9H, (CH_3)$_3$C); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.6 (C=O), 169.5 (C=O), 165.7 (C=O), 137.0 (Cquat. arom.), 136.9 (Cquat. arom.), 128.9 (CHarom.), 128.8 (CHarom.), 128.1 (CHarom.), 126.1 (CHarom.), 125.7 (CHarom.), 101.4 (C7A and C7B), 97.4 (C1A), 96.5 (C1B), 79.4 (C4A), 76.1 (C4B), 74.5 (C2A), 70.4 (C2B), 69.4 (C3A), 68.8 (C6A), 68.4 (C6B), 67.5 (C3B), 64.0 (C5B), 62.3 (C5A), 55.6 (OMe), 46.3 (C8B), 38.7 ((CH$_3$)$_3$$C$), 26.8 (($CH_3$)$_3$C), 20.9 ppm ($CH_3$C=O); IR (film): $\tilde{\nu}$ = 2974, 2932, 2868, 2117, 1753, 1737, 1699, 1457, 1379, 1278, 1229, 1148, 1096, 1073, 1038 cm^{-1}; HRMS: m/z calcd for $C_{36}H_{42}N_2O_{14}$Na: 749.25282; found: 749.2528.

Methyl (4,6-*O*-benzylidene-2-*O*-diazoacetyl-3-*O*-pivaloyl-α-D-mannopyranoside)-(1→2)-4,6-*O*-benzylidene-3-*O*-acetyl-α-D-mannopyranoside 35: A solution of donor **26** (32 mg, 67.20 μmol) and acceptor **32** (28 mg, 87.36 μmol) in distilled dichloromethane (1.5 mL) was stirred for 1 hour at room temperature over activated 4 Å MS (75 mg). NIS (30 mg, 134.4 μmol) was added, and after cooling to −20 °C, trifluoromethanesulfonic acid (1.8 μL, 20.16 μmol) was added dropwise. After being stirred for 45 min at −20 °C, the reaction mixture became dark-brown. A saturated aqueous solution of sodium hydrogen carbonate (2 mL) was added, followed by a saturated aqueous solution of sodium thiosulfate (2 mL). The colorless reaction mixture was then diluted with dichloromethane (5 mL) and filtered through a Celite pad. The organic layer was dried (anhydrous magnesium sulfate), filtered, and concentrated under vacuum. The residue was purified for full characterization by silica gel chromatography (dichloromethane/ethyl acetate 24:1) to give the disaccharide as a white foam (35 mg, 67 %). R_f = 0.24 (silica, cyclohexane/ethyl acetate 3:1); $[\alpha]_D^{20}$ = −19 (c = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52–7.32 (m, 10H, Harom.), 5.64 (s, 1H, H7A or H7B), 5.62 (s, 1H, H7A or H7B), 5.58–5.47 (m, 2H, H2B, H3B), 5.29 (dd, J = 10.3, 3.3 Hz, 1H, H3A), 4.87 (d, J = 1.1 Hz, 1H, H1B), 4.71 (d, J = 1.3 Hz, 1H, H1A), 4.34–4.22 (m, 2H, H6A, H6B), 4.18–4.02 (m, 4H, H2A, H4B, H5A, H5B), 3.99–3.81 (m, 5H, H4A, H6A, H6B, H8B), 3.40 (s, 3H, OMe), 2.10 (s, 3H, (CH_3)C=O), 1.22 ppm (s, 9H, (CH_3)$_3$C); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.4 (C=O), 170.4 (C=O), 166.1 (C=O), 137.2 (Cquat. arom.), 136.9 (Cquat. arom.), 129.0 (2×CHarom.), 128.2 (2×CHarom.), 126.2 (CHarom.), 125.7 (CHarom.), 101.8 (C7A or C7B), 101.3 (C7A or C7B), 100.4 (C1A), 100.3 (C1B), 77.2 (C2A), 76.1 (C5A or C5B), 75.9 (C5A or C5B), 71.6 (C2B), 70.0 (C3A), 68.6 (C6A or C6B), 68.3 (C6A or C6B), 67.7 (C3B), 64.4 (C4B), 63.7 (C4A), 55.0 (OMe), 39.0 ((CH$_3$)$_3$$C$), 27.0 (($CH_3$)$_3$C), 24.9 (C8B), 20.9 ppm ((CH_3)C=O); IR (film): $\tilde{\nu}$ = 2972, 2929, 2868, 1739, 1457, 1372, 1276, 1267, 1232, 1129, 1097, 1064, 1028 cm^{-1}; HRMS: m/z calcd for $C_{36}H_{43}N_2O_{14}{}^{79}$BrNa: 801.17284; found: 801.1726.

1,8-Diazabicyclo[5.4.0]undec-7-ene (33 μL, 224.47 μmol) was added to a solution of the disaccharide (35 mg, 44.894 μmol) and *N*,*N*′-ditosylhydrazine (31 mg, 89.788 μmol) in distilled tetrahydrofuran (3 mL) at 0 °C. After TLC analysis showed complete consumption of the starting material (cyclohexane/ethyl acetate 5:1), a saturated aqueous solution of sodium hydrogen carbonate (2 mL) and dichloromethane (5 mL) were added, and the organic layer was dried (anhydrous magnesium sulfate), filtered and concentrated under vacuum. The residue was purified by silica gel chromatography (dichloromethane/ethyl acetate 24:1) to give **35** as a bright-yellow oil (26 mg, 81 %). R_f = 0.63 (silica, cyclohexane/ethyl acetate 1:1); $[\alpha]_D^{20}$ = −37 (c = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.54–7.31 (m, 10H, Harom.), 5.63 (s, 2H, H7A, H7B), 5.56–5.46 (m, 2H, H2B, H3B), 5.28 (dd, J = 10.3, 3.4 Hz, 1H, H3A), 4.90 (br s, 2H, H1B, H8B), 4.71 (d, J = 1.5 Hz, 1H, H1A), 4.33–4.24 (m, 2H, H6A, H6B), 4.18–3.99 (m, 4H, H2A, H4A, H4B, H5B), 3.92–3.79 (m, 3H, H5A, H6A, H4B, H6B), 3.40 (s, 3H, OMe), 2.12 (s, 3H, CH_3C=O), 1.23 ppm (s, 9H, (CH_3)$_3$C); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.3 (C=O), 170.5 (C=O), 137.3 (Cquat. arom.), 137.0 (Cquat. arom.), 129.0 (CHarom.), 128.2 (2×CHarom.), 126.2 (CHarom.), 126.0 (CHarom.), 125.8 (CHarom.), 101.8 (C7A or C7B), 101.3 (C7A or C7B), 100.9 (C1B), 100.5 (C1A), 77.2 (C2A), 76.3 (C4B), 75.9 (C4A), 70.2 (C2B), 70.0 (C3A), 68.7 (C6A or C6B), 68.4 (C6A or C6B), 67.8 (C3B), 64.2 (C5B), 63.7 (C5A), 55.0 (OMe), 46.2 (C8B), 38.9 ((CH$_3$)$_3$$C$), 26.9 (($CH_3$)$_3$C), 20.9 ppm ($CH_3$C=O); IR (film): $\tilde{\nu}$ = 2974, 2933, 2868, 2116, 1738, 1705, 1457, 1380, 1277, 1261, 1236, 1133, 1098, 1064, 1029 cm^{-1}; HRMS: m/z calcd for $C_{36}H_{42}N_2O_{14}$Na: 749.25282; found: 749.2530.

γ-Lactone 36: a solution of **34** (60 mg, 82.563 μmol) in anhydrous 1,2-dichloroethane (5 mL) was added dropwise through a syringe pump (0.01 mmol h^{-1}) to a suspension of $[Rh_2(OAc)_4]$ (0.73 mg, 1.651 μmol) in anhydrous 1,2-dichloroethane (30 mL) heated at reflux. After the end of the addition, the reaction mixture was cooled to room temperature and concentrated under vacuum. The residue was purified by silica gel chromatography (cyclohexane/ethyl acetate 2.5:1) to give **36** as a white foam (34 mg, 60 %). R_f = 0.52 (silica, cyclohexane/ethyl acetate 1:1); $[\alpha]_D^{20}$ = −1 (c = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.49–7.32 (m, 10H, Harom.), 5.63–5.54 (m, 2H, H3A, H7A or H7B), 5.50 (s, 1H, H7A or H7B), 5.25 (dd, J = 9.8, 3.9 Hz, 1H, H3B), 4.79 (d, J = 3.9 Hz, 1H, H2B), 4.76 (d, J = 3.6 Hz, 1H, H1A), 4.39–4.28 (m, 2H, H6A and H6B), 4.06 (t, J = 9.8 Hz, 1H, H4B), 4.02–3.78 (m, 4H, H2A, H5A, H5B, H6B), 3.76 (t, J = 10.2 Hz, 1H, H6A), 3.62 (t, J = 9.6 Hz, 1H, H4A), 3.44 (s, 3H, OMe), 2.78 (d, J = 15.9 Hz, 1H, H8B), 2.70 (d, J = 15.9 Hz, 1H, H8B), 2.18 (s, 3H, CH_3C=O), 1.22 ppm (s, 9H, (CH_3)$_3$C); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.3 (C=O), 171.0 (C=O), 169.4 (C=O), 136.8 (Cquat. arom.), 136.7 (Cquat. arom.), 129.1 (2×CHarom.), 128.2 (2×CHarom.), 126.1 (CHarom.), 125.8 (CHarom.), 102.3 (C1B), 101.6 (C7A and C7B), 98.2 (C1A), 79.3 (C4A), 79.1 (C2B), 74.4 (C4B), 71.5 (C2A), 69.2 (C3A), 68.7 (C6A), 67.8 (C6B), 67.4 (C3B), 65.1 (C5B), 62.3 (C5A), 55.2 (OMe), 42.4 (C8B), 38.9 ((CH$_3$)$_3$$C$), 27.0 (($CH_3$)$_3$C), 20.9 ppm ($CH_3$C=O); IR (film): $\tilde{\nu}$ = 3010, 2974, 2926, 2853, 1788, 1755, 1734, 1450, 1371,

1276, 1261, 1231, 1183, 1130, 1099, 1071, 1043, 1012 cm^{-1}; HRMS: *m/z* calcd for $C_{36}H_{42}O_{14}Na$: 721.24668; found: 721.2467.

Decomposition of diazo-sugar 35: A solution of **35** (25 mg, 34.40 μmol) in anhydrous 1,2-dichloroethane (5 mL) was added dropwise through a syringe pump (5 $\mu mol\,h^{-1}$) to a suspension of $[Rh_2(OAc)_4]$ (0.30 mg, 0.688 μmol) in anhydrous 1,2-dichloroethane (20 mL) heated at reflux. After the end of the addition, the reaction mixture was cooled to room temperature and concentrated under vacuum. The residue was a complex mixture, which was purified by silica gel chromatography (dichloromethane/ethyl acetate 24:1) to give **37** as a white foam (8 mg, 36%). R_f = 0.53 (silica, cyclohexane/ethyl acetate 1:1); $[\alpha]_D^{20} = -6$ (c = 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.51–7.32 (m, 10H, Harom.), 5.60 (2 s, 2H, H7A and H7B), 5.45 (dd, J = 10.1, 3.3 Hz, 1H, H3B), 5.32 (dd, J = 10.2, 3.4 Hz, 1H, H3A), 4.95 (d, J = 1.2 Hz, 1H, H1B), 4.74 (d, J = 1.3 Hz, 1H, H1A), 4.33–4.22 (m, 3H, H2B, H6A, H6B), 4.19–3.98 (m, 4H, H2A, H4A, H4B, H5B), 3.95–3.80 (m, 3H, H5A, H6A, H6B), 3.40 (s, 3H, OMe), 2.09 (s, 3H, CH_3C=O), 1.28 ppm (s, 9H, $(CH_3)_3$C); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.4 (C=O), 170.1 (C=O), 137.2 (Cquat. arom.), 137.1 (Cquat. arom.), 129.0 (CHarom.), 128.9 (CHarom.), 128.2 (2×CHarom.), 126.2 (CHarom.), 125.8 (CHarom.), 102.4 (C1B), 101.8 (C7A or C7B), 101.3 (C7A or C7B), 100.5 (C1A), 77.2 (C2A), 76.1 (C4B), 76.0 (C4A), 70.2 (C3B), 70.2 (C3A), 69.9 (C2B), 68.7 (C6A or C6B), 68.5 (C6A or C6B), 64.3 (C5B), 63.8 (C5A), 55.0 (OMe), 39.1 ($(CH_3)_3C$), 27.2 ($(CH_3)_3$C), 21.0 ppm (CH_3C=O); IR (film): $\tilde{\nu}$ = 3520, 2964, 2917, 1743, 1722, 1458, 1371, 1244, 1130, 1097, 1074, 1056, 1026 cm^{-1}; MS: *m/z* = 681 $[M+Na^+]$.

4,6-*O*-benzylidene-2-*O*-diazoacetyl-3-*O*-*tert*-butyldimethylsilyl-α-D-mannopyranoside-(1→6)-1,2–3,4-diacetone-α-D-galactopyranoside 40: A solution of donor **38** (90 mg, 0.151 mmol) and acceptor **39** (51 mg, 0.196 mmol) in distilled dichloromethane (5 mL) were stirred for 1 hour at room temperature over activated 4 Å MS (150 mg). NIS (68 mg, 0.302 mmol) was added, and after cooling to −20 °C, trifluoromethanesulfonic acid (4 μL, 0.045 mmol) was added dropwise. After being stirred for 2 h at −20 °C, the reaction mixture became dark-brown. A saturated aqueous solution of sodium hydrogen carbonate (5 mL) was added, followed by a saturated aqueous solution of sodium thiosulfate (3 mL). The colorless reaction mixture was then diluted with dichloromethane (10 mL) and filtered through a Celite pad. The organic layer was dried (anhydrous magnesium sulfate), filtered, and concentrated under vacuum. The residue was purified by silica gel chromatography (cyclohexane/ethyl acetate 6:1) to give the disaccharide (73 mg, 65%) as a white foam. R_f = 0.38 (silica, cyclohexane/ethyl acetate 3:1); $[\alpha]_D^{20} = -20$ (c = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.57–7.31 (m, 5H, Harom.), 5.59 (s, 1H, H7), 5.53 (d, J = 4.9 Hz, 1H, H1A), 5.25 (d, J = 2.2 Hz, 1H, H2B), 4.83 (s, 1H, H1B), 4.64 (dd, J = 7.9, 2.3 Hz, 1H, H3A), 4.39–4.19 (m, 4H, H2A, H3B, H4A, H6B), 4.06–3.67 (m, 8H, H4B, H5A, H5B, 2×H6A, H6B, 2×H8B), 1.56 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 0.84 (s, 9H, $(CH_3)_3$C), 0.07 (s, 3H, CH_3Si), 0.04 ppm (s, 3H, CH_3Si); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.3 (C=O), 137.4 (Cquat. arom.), 128.8 (CHarom.), 128.0 (CHarom.), 126.1 (CHarom.), 109.4 (Cquat. isoprop.), 108.6 (Cquat. isoprop.), 101.8 (C7B), 98.6 (C1B), 96.2 (C1A), 79.0 (C5B), 74.2 (C2B), 70.8 (C4A), 70.5 (C2A and C3A), 68.6 (C6B), 68.0 (C3B), 66.8 (C6A), 66.1 (C5A), 63.8 (C4B), 26.1 (2×CH_3), 25.9 (C8B), 25.7 ($(CH_3)_3$C), 24.9 (CH_3), 24.4 (CH_3), 18.1 ($(CH_3)_3C$), −4.7 (CH_3Si), −5.2 ppm (CH_3Si); IR (film): $\tilde{\nu}$ = 2990, 2929, 2857, 1747, 1458, 1382, 1257, 1213, 1167, 1113, 1092, 1071, 1028, 1007 cm^{-1}; HRMS: *m/z* calcd for $C_{33}H_{49}O_{12}{}^{79}BrNaSi$: 767.20689; found: 767.2069.

1,8-Diazabicyclo[5.4.0]undec-7-ene (296 μL, 1.980 mmol) was added to a solution of the disaccharide (295 mg, 396 μmol) and *N*,*N*′-ditosylhydrazine (270 g, 792 μmol) in distilled tetrahydrofuran (15 mL) at 0 °C. After TLC analysis showed complete consumption of the starting material (cyclohexane/ethyl acetate 5:1), a saturated aqueous solution of sodium hydrogen carbonate (10 mL) and dichloromethane (15 mL) were added, and the organic layer was dried (anhydrous magnesium sulfate), filtered and concentrated under vacuum. The residue was purified by silica gel chromatography (dichloromethaneane/ethyl acetate 25:1) to give **40** as a bright-yellow oil (165 mg, 60%). R_f = 0.33 (silica, cyclohexane/ethyl acetate 3:1); $[\alpha]_D^{20} = -30$ (c = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55–7.46 (m, 2H, Harom.), 7.42–7.31 (m, 3H, Harom.), 5.57 (s, 1H, H7B), 5.53 (d, J = 5.0 Hz, 1H, H1A), 5.25 (d, J = 2.6 Hz, 1H, H2B), 4.85 (br s, 2H, H1B, H8B), 4.64 (dd, J = 7.9, 2.4 Hz, 1H, H3A), 4.32 (dd, J = 5.0, 2.4 Hz, 1H, H2A), 4.31–4.16 (m, 3H, H3B, H4A, H6A), 4.00 (t, J = 6.2 Hz, 1H, H5B), 3.89 (dd, J = 9.5, 4.4 Hz, 1H, H5A), 3.84–3.66 (m, 4H, H4B, H6A, 2×H6B), 1.56 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 0.85 (s, 9H, $(CH_3)_3$C), 0.07 (s, 3H, CH_3Si), 0.05 ppm (s, 3H, CH_3Si); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.0 (C=O), 137.4 (Cquat. arom.), 128.8 (CHarom.), 128.0 (CHarom.), 126.1 (CHarom.), 109.4 (Cquat. isoprop.), 108.6 (Cquat. isoprop.), 101.7 (C7B), 99.2 (C1B), 96.2 (C1A), 79.2 (C4B), 72.8 (C2B), 70.9 (C4A), 70.5 (C3A or C2A), 70.6 (C3A or C2A), 68.7 (C6A), 68.0 (C3B), 66.9 (C6B), 66.3 (C5B), 63.7 (C5A), 46.4 (C8B), 26.1 (CH_3), 25.9 (CH_3), 25.6 ($(CH_3)_3$C), 24.9 (CH_3), 24.4 (CH_3), 18.1 ($(CH_3)_3C$), −4.7 (CH_3Si), −5.1 ppm (CH_3Si); IR (film): $\tilde{\nu}$ = 2985, 2929, 2857, 2113, 1701, 1463, 1382, 1276, 1259, 1213, 1174, 1132, 1115, 1092, 1071, 1030, 1007 cm^{-1}; HRMS: *m/z* calcd for $C_{33}H_{48}N_2O_{12}NaSi$: 715.28687; found: 715.2869.

γ-Lactone 41: A solution of **40** (145 mg, 0.209 mmol) in anhydrous 1,2-dichloroethane (5 mL) was added dropwise through a syringe pump (10 $\mu mol\,h^{-1}$) to a suspension of $[Rh_2(OAc)_4]$ (1.85 mg, 4.180 μmol) in refluxing anhydrous 1,2-dichloroethane (65 mL). After the end of the addition, the reaction mixture was cooled to room temperature and concentrated under vacuum. The residue was purified by silica gel chromatography (dichloromethane/ethyl acetate 20:1) to give **41** as a colorless solid (82 mg, 59%). R_f = 0.29 (silica, cyclohexane/ethyl acetate 3:1); $[\alpha]_D^{20} = -68$ (c = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.51–7.42 (m, 2H, Harom.), 7.41–7.29 (m, 3H, Harom.), 5.57–5.48 (m, 2H, H7B, H1A), 4.65 (dd, J = 7.9, 2.4 Hz, 1H, H3A), 4.48 (d, J = 4.1 Hz, 1H, H2B), 4.36 (dd, J = 5.0, 2.4 Hz, 1H, H2A), 4.29–4.21 (m, 2H, H4A, H6A), 4.21–4.15 (m, 1H, H3B), 3.96 (m, 1H, H5B), 3.86–3.69 (m, 4H, H4B, H5A, H6A, H6B), 3.61 (dd, J = 9.8, 7.5 Hz, 1H, H6B), 2.82 (s, 2H, H8B), 1.57 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.36 (s, 6H, 2×CH_3), 0.89 (s, 9H, $(CH_3)_3$C), 0.10 (s, 3H, CH_3Si), 0.05 ppm (s, 3H, CH_3Si); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.1 (C=O), 137.2 (Cquat. arom.), 128.9 (CHarom.), 128.1 (CHarom.), 126.1 (CHarom.), 109.5 (Cquat. isoprop.), 108.7 (Cquat. isoprop.), 103.6 (C1B), 101.6 (C7B), 96.2 (C1A), 82.2 (C2B), 77.5 (C4B), 70.7 (C4A), 70.6 (C3A), 70.5 (C2A), 68.5 (C3B), 68.1 (C6A), 65.9 (C5B), 64.7 (C5A), 63.3 (C6B), 41.0 (C8B), 26.1 (CH_3), 25.9 (CH_3), 25.7 ($(CH_3)_3$C), 24.9 (CH_3), 24.6 (CH_3), 18.2 ($(CH_3)_3C$), −4.4 (CH_3Si), −5.1 ppm (CH_3Si); IR (film): $\tilde{\nu}$ = 2990, 2933, 2898, 2858, 1800, 1472, 1459, 1383, 1276, 1259, 1215, 1174, 1117, 1096, 1070, 1008 cm^{-1}; HRMS: *m/z* calcd for $C_{33}H_{48}O_{12}NaSi$: 687.2807; found: 687.2813.

Phenyl 4,6-*O*-benzylidene-2-*O*-bromoacetyl-3-*O*-pivaloyl-1-thio-β-D-glucopyranoside 42: Bromoacetyl bromide (179 μL, 2.051 mmol) was added to a stirred solution of 4,6-*O*-benzylidene-3-*O*-pivaloyl-1-thio-β-D-glucopyranoside (600 mg, 1.350 mmol) and 4-dimethylaminopyridine (255 mg, 2.000 mmol) in anhydrous dichloromethane (18 mL) at 0 °C. After the mixture had been stirred for 30 min at 0 °C, TLC (cyclohexane/ethyl acetate 1.5:1) showed complete consumption of the starting material, and methanol (1 mL) was added. The reaction mixture was diluted with dichloromethane (20 mL) and washed with a saturated aqueous solution of ammonium chloride (15 mL). The organic layer was dried (anhydrous magnesium sulfate), filtered, and concentrated under vacuum. The residue was purified by silica gel chromatography (dichloromethane/cyclohexane 4:1) to give **42** as a white solid (672 mg, 88%). R_f = 0.49 (silica, cyclohexane/ethyl acetate 5:1); $[\alpha]_D^{20} = -40$ (c = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.58–7.31 (m, 10H, Harom.), 5.54 (s, 1H, H7), 5.40 (dd, J = 9.4, 9.2 Hz, 1H, H3), 5.09 (dd, J = 10.0, 9.2 Hz, 1H, H2), 4.86 (d, J = 10.0 Hz, 1H, H1), 4.44 (dd, J = 10.5, 4.9 Hz, 1H, $H6_{ax}$), 3.94–3.74 (m, 3H, $H6_{equiv}$, H8, H8′), 3.72 (t, J = 9.4 Hz, 1H, H4), 3.61 (m, 1H, H5), 1.19 ppm (s, 9H, $(CH_3)_3$C); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.4 (C=O), 165.8 (C=O), 136.7 (Cquat. arom.), 133.2 (CHarom.), 131.4 (Cquat. arom.), 129.2 (CHarom.), 129.1 (CHarom.), 128.6 (CHarom.), 128.3 (CHarom.), 125.9 (CHarom.), 101.1 (C7), 86.3 (C1), 78.3 (C4), 72.3 (C3), 72.0 (C2), 70.7 (C5), 68.4 (C6), 38.9 ($(CH_3)_3C$), 27.1 ($(CH_3)_3$C), 25.3 ppm (C8); IR (film): $\tilde{\nu}$ = 2971, 1742, 1480, 1373, 1278, 1180, 1137, 1100, 1013 cm^{-1}; HRMS: *m/z* calcd for $C_{26}H_{29}O_7{}^{79}BrNaS$: 587.0710; found: 587.0709.

Methyl (4,6-*O*-benzylidene-2-*O*-diazoacetyl-3-*O*-pivaloyl-β-D-glucopyranoside)-(1→6)-2,3,4-*O*-methyl-α-D-glucopyranoside 45: A solution of **42** (281 mg, 497 μmol), diphenylsulfoxide (151 mg, 747 μmol), and 2,4,6-tri-*tert*-butylpyridine (369 mg, 1.49 mmol) in distilled dichloromethane (15 mL) was stirred for 1 hour at room temperature over activated 4 Å MS (350 mg) and cooled to −70 °C under argon. Trifluoromethanesulfonic acid (142 μL, 845 μmol) was then added and the mixture was stirred at −20 °C for 10 min. The reaction mixture was then cooled to −70 °C, and a solution of **27** (235 mg, 995 μmol) in distilled dichloromethane (3 mL) was added dropwise. After 2 h of stirring at −70 °C, a saturated aqueous solution of sodium hydrogen carbonate (6 mL) was added. The reaction mixture was then diluted with dichloromethane (10 mL) and filtered through a Celite pad. The organic layer was dried (anhydrous magnesium sulfate), filtered, and concentrated under vacuum. The residue was purified by silica gel chromatography (cyclohexane/ethyl acetate 1.5:1) to give an inseparable mixture (1:1) of disaccharide **43** and orthoester **44** as a bright yellow foam (297 mg, 86 %). 1,8-diazabicyclo[5.4.0]undec-7-ene (160 μL, 1.07 mmol) was added to a solution of the 1:1 mixture of **43** and **44** (297 mg, 429 μmol) and *N*,*N*′-ditosylhydrazine (146 mg, 429 μmol) in distilled tetrahydrofuran (6 mL) at 0 °C. After the mixture had been stirred for 40 min at 0 °C, a saturated aqueous solution of sodium hydrogen carbonate (8 mL) and dichloromethane (15 mL) were added. The organic layer was then dried (anhydrous magnesium sulfate), filtered and concentrated under vacuum. The residue was purified by silica gel chromatography (cyclohexane/ethyl acetate 1.5:1) to give orthoester **44** as a colorless oil (113 mg, 38 %) and diazoacetate **45** as a bright yellow oil (118 mg, 43 %). Orthoester **44**: R_f = 0.44 (silica, cyclohexane/ethyl acetate 1:1); $[\alpha]_D^{20}$ = 22 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52–7.34 (m, 5H, Harom.), 5.90 (d, *J* = 5.5 Hz, 1H, H1B), 5.54 (s, 1H, H7B), 5.38 (dd, *J* = 9.3, 4.3 Hz, 1H, H3B), 4.81 (d, *J* = 3.5 Hz, 1H, H1A), 4.49–4.38 (m, 2H, H2B, H6B), 4.09 (dt, *J* = 10.4 Hz, 5.3 Hz, 1H, H5B), 3.81–3.67 (m, 6H, H6B, 2×H6A, H4B, 2×H8B), 3.65–3.55 (m, 7H, H5A, 2×OMe), 3.55–3.45 (m, 4H, H3A, OMe), 3.40 (s, 3H, OMe), 3.23–3.15 (m, 2H, H2A, H4A), 1.24 ppm (s, 9H, *(CH$_3$)$_3$*C); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.3 (C=O), 136.8 (Cquat. arom.), 129.1 (CHarom.), 128.3 (CHarom.), 125.9 (CHarom.), 118.1 (C9B), 101.2 (C7B), 98.9 (C1B), 97.5 (C1A), 83.5 (C3A), 81.7 (C4A), 79.0 (C2A), 77.6 (C2B), 76.9 (C4B), 73.1 (C3B), 69.2 (C5A), 68.6 (C6B), 63.1 (C5B), 61.9 (C6A), 60.9 (OMe), 60.6 (OMe), 59.1 (OMe), 55.2 (OMe), 38.8 ((CH$_3$)$_3$*C*), 31.8 (C8B), 27.1 ppm (*(CH$_3$)$_3$*C); IR (film): $\tilde{\nu}$ = 2934, 1739, 1457, 1375, 1276, 1140, 1100, 1028 cm^{-1}. HRMS: calculated for $C_{30}H_{43}O_{13}{}^{79}BrNa$: 713.1779, found: 713.1778. **45**: R_f = 0.33 (silica, cyclohexane/ethyl acetate 1:1); $[\alpha]_D^{20}$ = 86 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52–7.34 (m, 5H, Harom.), 5.53 (s, 1H, H7B), 5.34 (t, *J* = 9.5 Hz, 1H, H3B), 5.18 (dd, *J* = 9.5, 7.9 Hz, 1H, H2B), 4.83 (d, *J* = 3.6 Hz, 1H, H1A), 4.75 (br s, 1H, H8B), 4.69 (d, *J* = 7.9 Hz, 1H, H1B), 4.40 (dd, *J* = 10.4, 4.9 Hz, 1H, H6B), 4.10 (dd, *J* = 10.7, 1.6 Hz, 1H, H6A), 3.85 (t, *J* = 10.4 Hz, 1H, H6B), 3.79–3.67 (m, 2H, H6A, H4B), 3.66–3.44 (m, 12H, 3×OMe, H5A, H5B, H3A), 3.40 (s, 1H, OMe), 3.20 (dd, *J* = 9.5, 3.6 Hz, 1H, H2A), 3.13 (t, *J* = 9.3 Hz, 1H, H4A), 1.19 (s, 9H ppm *(CH$_3$)$_3$*C); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.6 (C=O), 164.9 (C=O), 136.8 (Cquat. arom.), 129.0 (CHarom.), 128.2 (CHarom.), 125.9 (CHarom.), 101.5 (C1B), 101.1 (C7B), 97.4 (C1A), 83.5 (C3A), 81.6 (C2A), 79.0 (C4A), 78.5 (C4B), 72.2 (C2B), 71.4 (C3B), 69.5 (C5A), 68.6 (C6A and C6B), 66.6 (C5B), 60.9 (OMe), 60.3 (OMe), 59.0 (OMe), 55.2 (OMe), 46.1 (C8B), 38.9 ((CH$_3$)$_3$*C*), 27.0 ppm (*(CH$_3$)$_3$*C); IR (film): $\tilde{\nu}$ = 2925, 2113, 1739, 1706, 1380, 1277, 1154, 1100 cm^{-1}; MS: *m/z* = 661 [*M* + Na$^+$].

γ-Lactone 46: A solution of **45** (50 mg, 79 μmol) in anhydrous 1,2-dichloroethane (1.5 mL) was added dropwise through a syringe pump (10 μmol h^{-1}) to a suspension of $[Rh_2(acam)_4]$ (0.70 mg, 1.58 μmol) in anhydrous 1,2-dichloroethane (20 mL) heated at reflux. After the end of the addition, the reaction mixture was cooled to room temperature and concentrated under vacuum. The residue was purified by silica gel chromatography (diethyloxide/petroleum ether 3.5:1) to give **46** as a colorless oil (29 mg, 61 %). R_f = 0.39 (silica, cyclohexane/ethyl acetate 1:1); $[\alpha]_D^{20}$ = 23 (*c* = 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.47–7.33 (m, 5H, Harom.), 5.55 (s, 1H, H7B), 5.30 (dd, *J* = 10.2, 6.4 Hz, 1H, H3B), 4.83 (d, *J* = 3.7 Hz, 1H, H1A), 4.53 (d, *J* = 6.4 Hz, 1H, H2B), 4.39 (dd, *J* = 9.9, 4.5 Hz, 1H, H6B), 3.98–3.84 (m, 2H, H6A, H4B), 3.83–3.68 (m, 3H, H6B, H5B, H6A), 3.68–3.60 (m, 4H, H5A, OMe), 3.59–3.23 (m, 7H, H3A, 2×OMe), 3.41 (s, 3H, OMe), 3.20 (dd, *J* = 9.8, 3.7 Hz, 1H, H2A), 3.08 (dd, *J* = 9.8, 8.9 Hz, 1H, H4A), 2.93 (d, *J* = 17.6 Hz, 1H, H8B), 2.83 (d, *J* = 17.6 Hz, 1H, H8B′), 1.23 ppm (s, 9H, *(CH$_3$)$_3$*C); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.9 (C=O), 171.0 (C=O), 136.5 (Cquat. arom.), 129.2 (CHarom.), 128.3 (CHarom.), 125.9 (CHarom.), 104.0 (C1B), 101.4 (C7B), 97.4 (C1A), 83.6 (C3A), 82.6 (C2B), 81.8 (C2A), 79.3 (C4A), 76.1 (C4B), 72.0 (C3B), 69.2 (C5A), 68.7 (C6B), 66.3 (C5B), 62.7 (C6A), 60.9 (OMe), 60.6 (OMe), 59.1 (OMe), 55.2 (OMe), 38.8 ((CH$_3$)$_3$*C*), 36.1 (C8B), 27.1 ppm (*(CH$_3$)$_3$*C); IR (film): $\tilde{\nu}$ = 2932, 1801, 1743, 1458, 1276, 1219, 1101 cm^{-1}; MS: *m/z* = 633 [*M* + Na$^+$].

Macrolactone 47: A solution of **45** (19 mg, 30 μmol) in anhydrous 1,2-dichloroethane (1.5 mL) was added dropwise through a syringe pump (0.02 mmol h^{-1}) to a suspension of $[Rh_2(OAc)_4]$ (0.27 mg, 0.600 μmol) in anhydrous 1,2-dichloroethane (20 mL) heated at reflux. After the end of the addition, the reaction mixture was cooled to room temperature and concentrated under vacuum. The residue was purified by silica gel chromatography (cyclohexane/ethyl acetate 1:1) to give a 1:1 **46/47** mixture as a white foam (17 mg, 94 %). Macrolactone **47**: R_f = 0.39 (silica, cyclohexane/ethyl acetate 1:1); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.46–7.31 (m, 5H, Harom.), 5.52 (s, 1H, H7B′), 5.44 (t, *J* = 9.8 Hz, 1H, H3B′), 5.1 (dd, *J* = 9.8, 8.0 Hz, 1H, H2B′), 4.81 (m, 1H, H1A′), 4.62 (d, *J* = 8.0 Hz, 1H, H1B′), 4.56–4.47 (m, 1H, H7A′), 4.40 (m, 1H, H6B′), 4.15–4.07 (m, 2H, H6A′, H7A′), 4.02–3.98 (m, 1H, H6A′), 3.82 (t, *J* = 10.4 Hz, 1H, H6B′), 3.78–3.67 (m, 1H, H4B′), 3.66–3.47 (m, 13H, H3A′, H4A′, H5A′, H5B′, 3×OMe), 3.38 (s, 3H, OMe), 3.21 (m, 1H, H2A′), 2.57 (td, *J* = 13.7, 3.3 Hz, 1H, H8B′), 2.30 (m, 1H, H8B′), 1.17 ppm (s, 9H, *(CH$_3$)$_3$*C); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.9 (C=O), 171.0 (C=O), 136.5 (Cquat. arom.), 129.2 (CHarom.), 128.3 (CHarom.), 125.9 (CHarom.), 104.0 (C1B), 101.4 (C7B), 97.4 (C1A), 83.6 (C3A), 82.6 (C2B), 81.8 (C2A), 79.3 (C4A), 76.1 (C4B), 72.0 (C3B), 69.2 (C5A), 68.7 (C6B), 66.3 (C5B), 62.7 (C6A), 60.9 (OMe), 60.6 (OMe), 59.1 (OMe), 55.2 (OMe), 38.8 ((CH$_3$)$_3$*C*), 36.1 (C8B), 27.1 ppm (*(CH$_3$)$_3$*C); IR (film): $\tilde{\nu}$ = 3479, 2934, 1741, 1450, 1367, 1281, 1187, 1157, 1098, 1047, 1002 cm^{-1}; MS: *m/z* = 633 [*M* + Na$^+$].

γ-Lactone 49: A solution of **48** (52 mg, 78.470 μmol) in anhydrous 1,2-dichloroethane (4 mL) was added dropwise through a syringe pump (10 μmol h^{-1}) to a suspension of $[Rh_2(OAc)_4]$ (0.70 mg, 1.570 μmol) in anhydrous 1,2-dichloroethane (25 mL) heated at reflux. After the end of the addition, the reaction mixture was cooled to room temperature and concentrated under vacuum. The residue was purified by silica gel chromatography (dichloromethane/ethylacetate 30:1) to give **49** as a colorless oil (33 mg, 60 %). R_f = 0.21 (silica, cyclohexane/ethyl acetate 3:1); $[\alpha]_D^{20}$ = −44 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.46–7.31 (m, 5H, Harom.), 5.58–5.50 (m, 2H, H7B, H1A), 5.28 (dd, *J* = 10.2, 6.1 Hz, 1H, H3B), 4.71–4.60 (m, 2H, H2B, H3A), 4.41–4.30 (m, 2H, H2A, H6B), 4.26 (dd, *J* = 7.9, 1.7 Hz, 1H, H4A), 4.02–3.90 (m, 2H, H4B, H5A), 3.88–3.64 (m, 4H, H5B, H6B, 2×H6A), 2.93 (d, *J* = 17.2 Hz, 1H, H8B), 2.73 (d, *J* = 17.2 Hz, 1H, H8B′), 1.55 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.22 ppm (s, 9H, *(CH$_3$)$_3$*C); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.8 (C=O), 171.1 (C=O), 136.5 (Cquat. arom.), 129.1 (CHarom.), 128.2 (CHarom.), 125.8 (CHarom.), 109.2 (Cquat. isoprop.), 108.7 (Cquat. isoprop.), 104.0 (C1B), 101.3 (C7B), 96.2 (C1A), 81.5 (C2B), 76.0 (C4B), 71.9 (C3B), 70.6 (C2A), 70.4 (C3A), 70.3 (C4A), 68.6 (C6B), 66.3 (C5B), 66.0 (C5A), 62.2 (C6A), 38.7 ((CH$_3$)$_3$*C*), 37.4 (C8B), 27.0 (*(CH$_3$)$_3$*C), 26.1 (CH_3), 26.0 (CH_3), 24.8 (CH_3), 24.3 ppm (CH_3); IR (film): $\tilde{\nu}$ = 2981, 2939, 1801, 1744, 1479, 1457, 1382, 1256, 1212, 1136, 1114, 1070, 1002 cm^{-1}.

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