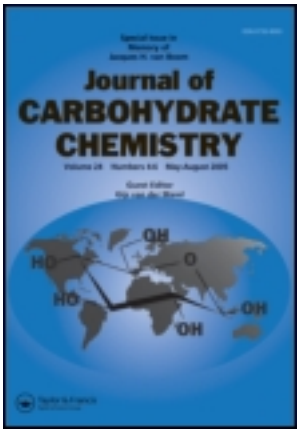

Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lcar20

Rh(II) Carbene-Mediated Synthesis of Methyl α- and β-Ketopyranosides: Preparation of Carbene Precursors, Quaternarization of the Anomeric Position, and Ring Opening of γ-Lactones

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Published online: 14 Dec 2011.

To cite this article: Mélissa Boultadakis-Arapinis , Camille Lescot , Laurent Micouin & Thomas Lecourt (2011): Rh(II) Carbene-Mediated Synthesis of Methyl α- and β-Ketopyranosides: Preparation of Carbene Precursors, Quaternarization of the Anomeric Position, and Ring Opening of γ-Lactones, Journal of Carbohydrate Chemistry, 30:7-9, 587-604

To link to this article: http://dx.doi.org/10.1080/07328303.2011.614983

Journal of Carbohydrate Chemistry, 30:587–604, 2011

ISSN: 0732-8303 print / 1532-2327 online
DOI: 10.1080/07328303.2011.614983

Rh(II) Carbene-Mediated Synthesis of Methyl α- and β-Ketopyranosides: Preparation of Carbene Precursors, Quaternarization of the Anomeric Position, and Ring Opening of γ-Lactones

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Methyl α- and β-ketopyranosides were efficiently prepared by carbene-mediated quaternarization of the anomeric position of corresponding aldopyranosides. Preparation of carbene precursors proved to be tedious and required a two-step procedure involving first bromoacetylation, followed by diazo-transfer with *N*,*N*′-ditosylhydrazine and DBU. Selective functionalization of the anomeric C-H bond was then achieved under $Rh_2(OAc)_4$ or $Rh_2(acam)_4$ catalysis. Finally, ring opening of the resulting γ-lactones delivered α- and β-ketopyranosides with the anomeric position functionalized by an independent chain.

Keywords Keptopyranosides; C-H activation; Carbene; Quaternarization

INTRODUCTION

New synthetic tools in carbohydrate chemistry have attracted tremendous interest over the past decades due to the important role of complex

Received June 1, 2011; accepted August 2, 2011.
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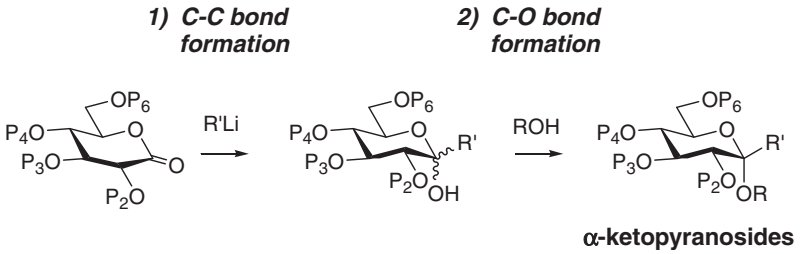
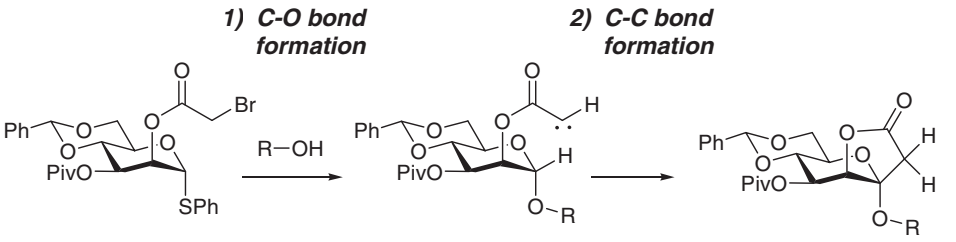
oligosaccharides in many fundamental biological processes.[1] In this context, quaternarization of a specific position represents a highly potent entry toward chemical tools for glycobiology. Thus, quaternary sugars have been critical to determine the conformation of L-iduronic acid in active heparin,[2] and also gave rise to powerful inhibitors of carbohydrate-processing enzymes.[3] However, such a modification of the sugar backbone requires a multistep, time-consuming approach relying on (1) selective protection/deprotection of a given position, (2) oxidation of the resulting alcohol, and (3) addition of an organometallic reagent that creates the new C-C bond. Following this strategy,[4,5] α-ketopyranosides, with the anomeric position quaternarized by an independent equatorial chain, can be prepared from δ-lactones by formation of a new anomeric C-C bond before a glycosylation (Sch. 1).



Scheme 1: Classical approach toward ketopyranosides.

The scope of this approach is, however, strongly limited by the second step. Thus, glycosylation of sterically demanding acceptors with ketopyranoside donors is usually low yielding.[6,7] Moreover, coupling with a donor having an equatorial 2-*O*-acetate delivered the targeted β-ketopyranoside in poor chemical yield.[8] In this context, preparation of both α- and β-ketopyranosides without limitations resulting from the glycosylation step might rely on substitution of the anomeric C-H bond in a late stage of the synthetic process. However, as methods allowing functionalization of anomeric or pseudo-anomeric C-H bonds only deliver polycyclic compounds that cannot be reopened into ketopyranosides without loss of the anomeric configuration (Fig. 1),[9–13] we had to develop a new quaternarization process where a 2-*O*-bromoacetate played a key role.[14] Thus, this protecting group first induced stereoselective glycosylation and, as a carbene precursor, then promoted functionalization of the anomeric C-H bond (Sch. 2). Herein, we would like to report full results concerning carbene-mediated quaternarization of model methyl α-manno- and β-glucopyranosides, with special emphasis on preparation of carbene precursors. We also disclose the influence of various metal catalysts on this quaternarization process, and optimal conditions for ring opening of γ-lactones into ketopyranosides.

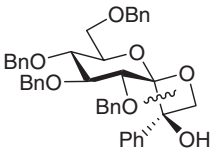


Scheme 2: Carbene-mediated preparation of ketopyranosides.

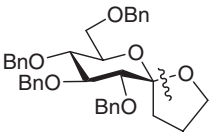
RESULTS AND DISCUSSION

Preparation of Carbene Precursors

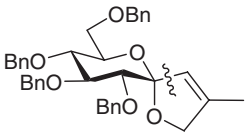
First, orthogonally protected methyl-pyranosides **1–7** were prepared in two steps from commercially available methyl-glycosides. Initial attempts to introduce the required diazoacetate at position 2 were made following Corey and Myers' modification of House's procedure.[15] Unfortunately, acylation of **1** and base-mediated decomposition of the resulting *para*-toluenesulfonylhydrazone delivered the targeted diazosugar in less than 10% yield. We next turned our attention to a two-step procedure involving first bromoacetylation and subsequent diazo-transfer with *N*,*N*'-ditosylhydrazine and DBU (Table 1).[16] However, following reaction conditions reported by Fukuyama for acylation of even unreactive alcohols (bromoacetyl bromide, $NaHCO_3$ in CH_3CN at rt), we did



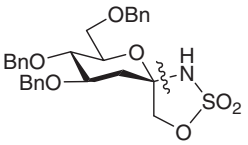
Photochemically-induced
Intramolecular Hydrogen Abstraction
Crich *et al* 1995



Hypoiodite-mediated
Intramolecular Hydrogen Abstraction
Suarez *et al* 1995



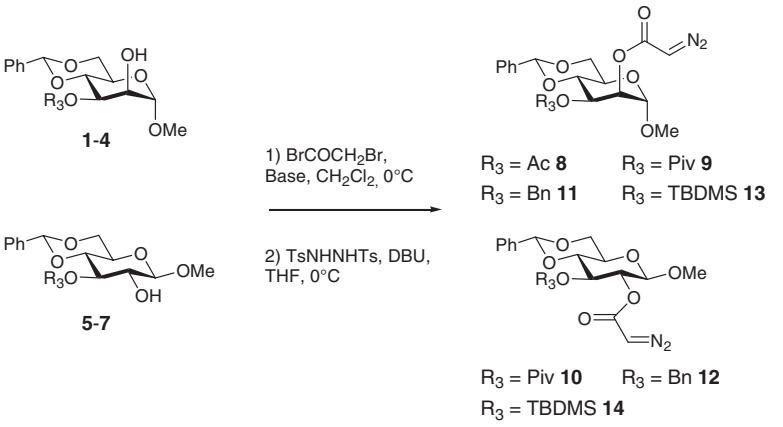
Alkylidene-mediated C-H activation
Wardrop *et al* 2002



Nitrene-mediated C-H activation
Compain *et al* 2005

Figure 1: Spirobicyclic compounds resulting from anomeric C-H functionalization.

Table 1: Preparation of carbene precursors



Entry	Substrate	R_3 =	Base (eq.)	Yield
1	**1**	Ac	$NaHCO_3$[a]	—
2	**1**	Ac	Et_3N (1.2)/DMAP (0.05)	73
3	**1**	Ac	Pyridine (3.5)	73
4	**2**	Piv	Pyridine (2.5)	73
5	**5**	Piv	DMAP (1.5)	74
6	**3**	Bn	DMAP (1.5)	75
7	**6**	Bn	DMAP (1.5)	74
8	**4**	TBDMS	DMAP (4.5)	30
9	**7**	TBDMS	DMAP (7.5)	25
10	**4**	TBDMS	Pyridine (3)	64
11	**7**	TBDMS	Pyridine (4)	50

[a]CH_3CN used as solvent.

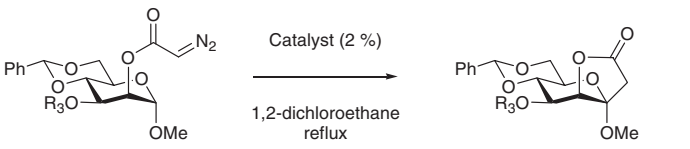
not observe any conversion into the corresponding bromoacetate. Bromoacetylation could finally be promoted in dichloromethane at 0°C with Et_3N as a base and a catalytic amount of *N*-dimethylaminopyridine (DMAP). Treatment of the crude product with *N*,*N*'-ditosylhydrazine and DBU in THF at 0°C delivered the targeted diazoacetate **8** in 73% yield over two steps after purification by silica gel flash chromatography (entry 2). Efficient bromoacetylation could also be performed with stoechiometric pyridine without any detrimental effect on the diazotransfer (entry 3). Similarly, 3-*O*-pivaloylated and 3-*O*-benzylated compounds **2**–**5** were converted into the corresponding diazoacetates **9**–**12** in 73% to 75% yield over two steps after using either pyridine or DMAP as a base in the acylation step (entries 4–7). However, bromoacetylation of more hindered 3-*O*-*tert*-butyldimethylsilyl (TBDMS) substrates **6** and **7** with DMAP as a base required repeated addition of reagents. The sluggish crude compounds

containing pyridinium salts could then only be converted into the corresponding diazosugars in low yields (entries 8 and 9). Clean bromoacetylation was finally achieved with pyridine as a less nucleophilic base, thus delivering diazoacetates **13** and **14** in 64% and 50% yield, respectively, over two steps (entries 10 and 11).

Metal-Mediated Decomposition of Diazosugars

Having in hand carbene precursors **9**–**14**, we next studied their decomposition by transition metals in refluxing 1,2-dichloroethane. Screening catalysts that generate metal carbenes with different steric and electronic properties[17] revealed that $Rh_2(OAc)_4$ was suitable to obtain the targeted γ-lactone **15** from diazosugar **9** (Table 2, entry 1). However, $Rh_2(oct)_4$ and $Rh_2(cap)_4$ with bulky ligands, $Rh_2(tfa)_4$ and $Rh_2(acam)_4$ with strongly and weakly electron withdrawing ligands, respectively, and $Cu(acac)_2$ and $Cu(hfac)_2$ were detrimental to the 1,5-C-H insertion process (entries 2–7). Moreover, quaternarization of the anomeric position occurred in 94% yield with a TBDMS at position 3 (entry 8). However, when a potentially more reactive benzyl-protecting group was

Table 2: Metal-catalyzed insertion into the anomeric C-H bond of methyl-α-mannosides



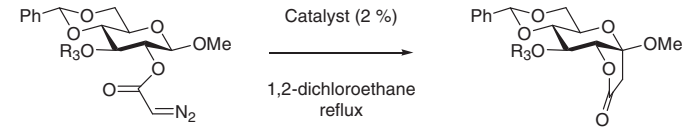
R_3 = Piv **9** R_3 = Bn **11**
R_3 = TBDMS **13**

R_3 = Piv **15** R_3 = Bn **16**
R_3 = TBDMS **17**

Entry	Substrate	R_3 =	Catalyst	Yield (%)
1	**9**	Piv	$Rh_2(OAc)_4$	77[a]
2	**9**	Piv	$Rh_2(oct)_4$	49[b]
3	**9**	Piv	$Rh_2(tfa)_4$	13[b]
4	**9**	Piv	$Rh_2(cap)_4$	9[b]
5	**9**	Piv	$Rh_2(acam)_4$	35[b]
6	**9**	Piv	$Cu(acac)_2$	20[b]
7	**9**	Piv	$Cu(hfac)_2$	15[b]
8	**11**	Bn	$Rh_2(OAc)_4$	20[a,c]
9	**13**	TBDMS	$Rh_2(OAc)_4$	94[a]

[a]Isolated after purification by chromatography.
[b]Estimated by ^1H NMR of the crude product.
[c]Isolation of 51% of 1,7 insertion into the benzilic C-H bond.

Table 3: Metal-catalyzed insertion into the anomeric C-H bond of methyl-β-glucosides



R_3 = Piv **10** R_3 = Bn **12**
R_3 = TBDMS **14**

R_3 = Piv **18** R_3 = Bn **19**
R_3 = TBDMS **20**

Entry	Substrate	R_3 =	Catalyst	Yield (%)
1	**10**	Piv	$Rh_2(OAc)_4$	90[a]
2	**10**	Piv	$Rh_2(tfa)_4$	10[b]
3	**10**	Piv	$Rh_2(acam)_4$	85[a]
4	**10**	Piv	$Cu(acac)_2$	—[b]
5	**10**	Piv	$Cu(hfac)_2$	7[b]
6	**12**	Bn	$Rh_2(OAc)_4$	35[a,c]
7	**12**	Bn	$Rh_2(acam)_4$	35[a]
8	**14**	TBDMS	$Rh_2(OAc)_4$	92[a]

[a]Isolated after purification by chromatography.
[b]Estimated by ^{1}H NMR of the crude product.
[c]In mixture with 35% of 1,7 insertion into the benzylic C-H bond.

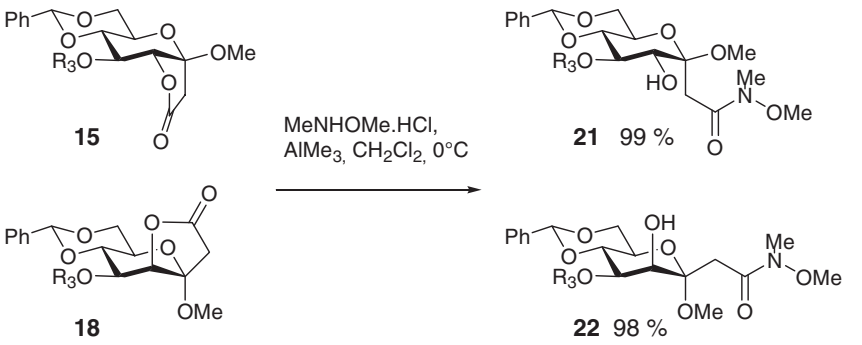
close to the carbene intermediate, γ-lactone **17** was only obtained in 20% yield because of competitive 1,7 insertion into the benzylic position (entry 9).

In the *β-gluco* series, extensive screening of catalysts revealed that $Rh_2(OAc)_4$ and $Rh_2(acam)_4$ were suitable to promote quaternarization of the anomeric position (Table 3, entries 1 and 3), whereas Rh(II) salts with strongly electron-withdrawing ligands (entry 2), as well as copper(II) catalysts (entries 4 and 5), failed to deliver γ-lactone **18**. Moreover, the quaternarization process was also compatible with a TBDMS at position 3 (entry 6). However, with a benzyl-protecting group, results were highly dependent on the catalyst. Thus, $Rh_2(OAc)_4$ gave an inseparable mixture of γ-lactone **19** and 1,7-C-H insertion into the benzylic position (entry 7), whereas a fully selective insertion process was restored by generating a less electrophilic carbene under $Rh_2(acam)_4$ catalysis (entry 8).

Ring Opening of γ-Lactones

Having identified the catalysts of choice to promote clean quaternarization of the anomeric position in both series, we next turned our attention to ring opening of γ-lactones in order to obtain the targeted α- and β-ketopyranosides with the anomeric position substituted by an independent chain. We first

treated γ-lactone **15** under William's conditions (MeNHOMe.HCl, *i*PrMgCl, THF 0°C) in order to convert it into a Weinreb amide.[18] However, because of strongly basic conditions, we only obtained a compound resulting from β-elimination that quickly decomposed during NMR analysis. We next submitted **15** to conditions initially reported by Weinreb (MeNHOMe.HCl, $AlMe_3$, THF 0°C)[19] and obtained the targeted α-ketopyranoside **21** in quantitative yield without purification (Sch. 3). Under similar reaction conditions, γ-lactone **18** was also cleanly converted into the corresponding β-ketopyranoside **22** ready for further modifications. We were very pleased to see that conversion of γ-lactones into Weinreb amides proceeds cleanly under harsh Lewis acid conditions in the presence of 4,6-*O*-benzylidene-protecting groups.



Scheme 3: Ring opening of γ-lactones.

CONCLUSION

In conclusion, we showed that 2-*O*-diazoacetyl β-gluco- and α-mannopyranosides can be efficiently prepared following a two-step procedure involving bromoacetylation and subsequent treatment of the crude product by *N*,*N*′-ditosylhydrazine and DBU in THF at 0°C. Presumably because of strong electronic deactivation of the hydroxyl group at position 2, the acylation step required modification of conditions reported by Fukuyama on nonfunctional substrates. Thus, efficient bromoacetylation was only achieved when using a stoichiometric amount of nucleophilic base that generates a highly reactive acylpyridium intermediate. We also showed that $Rh_2(OAc)_4$ nicely induced quaternarization of the anomeric position in both *α-manno* and *β-gluco* series, whereas a less electrophilic carbene generated under $Rh_2(acam)_4$ catalysis only promoted clean functionalization of axial anomeric C-H bonds. However, other Rh(II) salts with bulky or strongly electron-withdrawing ligands, as well as Cu(II) catalysts, only delivered γ-lactones in low yields. This quaternarization process proved to be compatible with pivaloyl- and *tert*-butyldimethylsilyl-protecting groups at position 3, while 3-*O*-benzylated

compounds gave rise to competitive 1,7-insertion into the benzylic C-H bond. Finally, ring opening of γ-lactones was achieved under Lewis acid conditions to deliver α- and β-ketopyranosides ready for further functionalization.

EXPERIMENTAL

General Methods

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. 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 sec for ^{13}C NMR spectra of diazosugars. Assignments were aided by DEPT, COSY, and HSQC experiments. 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). All reactions were conducted under an argon atmosphere. 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.[20] *N*,*N*′-ditosylhydrazine was prepared following Fukuyama's procedure.[16]

Preparation of 3-O-TBDMS Protected Precursors 4 and 7

*Methyl 4,6-*O*-benzylidene-3-*O*-tert-butyldimethylsilyl-α-D-mannopyranoside* ***4***

Methyl-4,6-*O*-benzylidene-α-D-mannopyranoside (1.00 g, 3.542 mmol) was dissolved in anhydrous dichloromethane and dimethylformamide (7 mL, 11:1 v/v) and cooled to –20°C. Anhydrous triethylamine (543 μL, 3.896 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (894 μL, 3.896 μmol) were subsequently added and the mixture was stirred for 1.5 h, after which it was quenched with a saturated aqueous solution of sodium hydrogen carbonate. The layers were separated and the aqueous layer was extracted twice with

dichloromethane. The combined organic layers were washed with brine, dried (anhydrous magnesium sulfate), filtered, and concentrated under vacuum. The residue was purified by silica gel chromatography (cyclohexane/ethyl acetate 4:1) to give **4** as a colorless oil (927 mg, 66%). TLC analysis: $R_f = 0.47$ (silica, cyclohexane/ethyl acetate 3:1). ^{1}H NMR (300 MHz, *CDCl$_3$*): δ (ppm) 7.53–7.37 (m, 5H, $H_{arom.}$), 5.57 (s, 1H, H-7), 4.82 (s, 1H, H-1), 4.36–4.25 (m, 1H, H-6), 4.10 (dd, $J = 9.0$, 3.5 Hz, 1H, H-3), 3.97–3.75 (m, 4H, H-2, H-4, H-5, H-6), 3.43 (s, 3H, OMe), 2.90 (br s, 1H, OH), 0.93 (s, 9H, C($\underline{CH_3}$)$_3$), 0.13 (s, 3H, $\underline{CH_3}$Si), 0.09 (s, 3H, $\underline{CH_3}$Si). ^{13}C NMR (75 MHz, *CDCl$_3$*): 137.6 ($C_{quat.\ arom.}$), 128.9 ($CH_{arom.}$), 128.1 ($CH_{arom.}$), 126.2 ($CH_{arom.}$), 101.9 (C-7), 100.9 (C-1), 79.1 (C-4), 72.0 (C-3), 69.8 (C-2), 68.9 (C-6), 63.0 (C-5), 55.0 (OMe), 25.8 (C($\underline{CH_3}$)$_3$), 18.2 (Si$\underline{C}$(CH$_3$)$_3$), –4.3 (Si$\underline{CH_3}$), –5.0 (Si$\underline{CH_3}$). IR (film): 3566; 2928; 1472; 1386; 1253; 1215; 1125; 1100; 1076; 1050; 1006; 978; 918; 862; 837; 777; 746; 697; 669. HRMS calculated for $C_{20}H_{32}O_6SiNa$: 419.1866, found: 419.1863. $[\alpha]_D^{20} = +39$ (c = 1.0, $CHCl_3$).

*Methyl 4,6-*O*-benzylidene-3-*O*-tert-butyldimethylsilyl-β-D-glucopyranoside* **7**

To a solution of methyl-4,6-*O*-benzylidene-β-D-glucopyranoside (300 mg, 1.063 mmol) and imidazole (433 mg, 6.360 mmol) in anhydrous dimethylformamide (6 mL) was added dropwise a solution of *tert*-bultyldimethylsilyl chloride (241 mg, 1.599 mmol) in dimethylformamide (1.5 mL). The reaction mixture was stirred at rt for 2 h and quenched with methanol (2 mL). The organic layer was washed with a saturated aqueous solution of ammonium chloride (6 mL), dried (anhydrous magnesium sulfate), filtered, and concentrated under vacuum. The residue was purified by silica gel chromatography (cyclohexane/ethyl acetate 5:1) to give **7** as a white solid (265 mg, 63%). TLC analysis: $R_f = 0.39$ (silica, cyclohexane/ethyl acetate 3:1). ^{1}H NMR (300 MHz, *CDCl$_3$*): δ (ppm) 7.59–7.32 (m, 5H, $H_{arom.}$), 5.54 (s, 1H, H-7), 4.37 (dd, $J = 11.1$, 5.3 Hz 1H, H-6$_{eq.}$), 4.33 (d, $J = 7.9$ Hz, 1H, H-1), 3.86–3.74 (m, 2H, H-3, H-6$_{ax.}$), 3.60 (s, 3H, OMe), 3.56–3.38 (m, 3H, H-2, H-4, H-5), 2.64 (d, $J = 2.7$ Hz, 1H, OH), 0.91 (s, 9H, C($\underline{CH_3}$)$_3$), 0.14 (s, 3H, Si$\underline{CH_3}$), 0.08 (s, 3H, Si$\underline{CH_3}$). ^{13}C NMR (75 MHz, *CDCl$_3$*): δ (ppm) 137.2 ($C_{quat.\ arom.}$), 129.0 ($CH_{arom.}$), 128.2 ($CH_{arom.}$), 126.2 ($CH_{arom.}$), 104.4 (C-1), 101.7 (C-7), 81.3 (C-4), 75.5 (C-2), 74.5 (C-3), 68.8 (C-6), 66.5 (C-5), 57.6 (OMe), 25.9 (C($\underline{CH_3}$)$_3$), 18.4 (Si$\underline{C}$(CH$_3$)$_3$), –4.3 (Si$\underline{CH_3}$), –4.7 (Si$\underline{CH_3}$). IR (film): 3506; 2854; 1471; 1428; 1388; 1249; 1215; 1195; 1169; 1112; 1069; 1019; 998; 837; 779; 697; 668. HRMS calculated for $C_{20}H_{32}O_6SiNa$: 419.1866, found: 419.1862. $[\alpha]_D^{20} = -58$ (c = 1.0, $CHCl_3$).

Preparation of Diazosugars

General procedure

To a solution of orthogonally protected precursors **1**–**7** (4.102 mmol) in anhydrous dichloromethane (20 mL) and anhydrous pyridine (10.262 mmol) at

0°C was added dropwise over 10 min bromoacetyl bromide (8.237 mmol). After being stirred for 15 min at 0°C, the reaction mixture was quenched with methanol (0.5 mL) while TLC (cyclohexane/ethyl acetate 2:1) showed complete consumption of the starting material. After addition of a solution of hydrochloric acid (1N, 10 mL), the organic layer was separated, the aqueous layer was extracted with dichloromethane (3 × 10 mL), and the combined organic layers were dried (anhydrous magnesium sulfate), filtered, and concentrated under vacuum. To a solution of the residue and *N*,*N*′-ditosylhydrazine (8.204 mmol) in distilled tetrahydrofuran (40 mL) at 0°C was added 1,8-diazabicyclo[5.4.0]undec-7-ene (16.241 mmol). 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) to give diazosugars **8**–**14** as bright yellow oils.

Methyl 4,6-O-*benzylidene-2*-O-*diazoacetyl-3*-O-*acetyl-α-D-mannopyranoside* ***8***

Yield: 73%. TLC analysis: R_f = 0.15 (silica, cyclohexane/ethyl acetate 2.5:1). ^{1}H NMR (300 MHz, *CDCl*$_3$): δ (ppm) 7.48–7.28 (m, 5H, $H_{arom.}$), 5.58 (s, 1H, H-7), 5.46–5.31 (m, 2H, H-2, H-3), 4.91 (br s, 1H, H-8), 4.72 (s, 1H, H-1), 4.30 (dd, J = 10.0, 4.0 Hz, 1H, H-6_{eq}), 4.06–3.91 (m, 2H, H-4, H-5), 3.90–3.79 (m, 1H, H-6_{ax}), 3.42 (s, 3H, OMe), 2.05 (s, 3H, ($\underline{CH_3}$)C=O). ^{13}C NMR (75 MHz, *CDCl*$_3$): δ (ppm) 169.9 (C=O), 165.9 (C=O), 137.0 ($C_{quat.\ arom.}$), 129.1 ($CH_{arom.}$), 128.2 ($CH_{arom.}$), 126.1 ($CH_{arom.}$), 101.9 (C-7), 99.5 (C-1), 76.0 (C-4), 70.2(C-2), 68.7 (C-6), 68.3 (C-3), 63.6 (C-5), 55.2 (OMe), 46.5 (C-8), 20.8 (($\underline{CH_3}$)C=O). IR (film): 3110, 2935, 2116, 1746, 1698, 1457, 1384, 1370, 1283, 1229, 1175, 1133, 1097, 1077, 1029, 997, 897, 758, 736, 700MS: m/z = 415 (MNa^+). HRMS calculated for $C_{18}H_{20}N_2O_8Na$: 415.1117, found: 415.1115. $[\alpha]_D^{20}$ = –25 (c = 1.0, $CHCl_3$).

Methyl 4,6-O-*benzylidene-2*-O-*diazoacetyl-3*-O-*pivaloyl-α-D-mannopyranoside* ***9***

Yield: 73%. TLC analysis: R_f = 0.62 (silica, cyclohexane/ethyl acetate 2:1). ^{1}H NMR (300 MHz, *CDCl*$_3$): δ (ppm) 7.48–7.30 (m, 5H, $H_{arom.}$), 5.61 (s, 1H, H-7), 5.50–5.35 (m, 2H, H-2, H-3), 4.91 (br s, 1H, H-8), 4.73 (s, 1H, H-1), 4.33 (dd, J = 9.6, 3.6 Hz, 1H, H-6_{eq}), 4.07–3.79 (m, 3H, H-4, H-5, H-6_{ax}), 3.42 (s, 3H, OMe), 1.20 (s, 9H, ($\underline{CH_3}$)$_3$C). ^{13}C NMR (75 MHz, *CDCl*$_3$): δ (ppm) 177.0 (C=O), 165.7 (C=O), 137.2 ($C_{quat.\ arom.}$), 128.9 ($CH_{arom.}$), 128.2 ($CH_{arom.}$), 125.9 ($CH_{arom.}$), 101.4 (C-7), 99.7 (C-1), 76.5 (C-4), 70.4 (C-2), 68.8 (C-6), 68.1 (C-3), 63.6 (C-5), 55.3 (OMe), 46.4 (C-8), 38.9 ((CH$_3$)$_3\underline{C}$), 27.0 (($\underline{CH_3}$)$_3$C). IR (film): 2974; 2115; 1733; 1698; 1457; 1384; 1283; 1177; 1134; 1097; 1031; 699. MS:

m/z = 457 (MNa^+). HRMS calculated for $C_{21}H_{26}N_2O_8Na$: 457.1581, found: 457.1581. $[\alpha]_D^{20} = -36$ (c = 1.0, $CHCl_3$).

*Methyl 4,6-*O*-benzylidene-2-*O*-diazoacetyl-3-*O*-pivaloyl-β-D-glucopyranoside* ***10***

Yield: 74%. TLC analysis: $R_f = 0.62$ (silica, cyclohexane/ethyl acetate 2:1). ^{1}H NMR (300 MHz, *CDCl$_3$*): δ (ppm) 7.50–7.30 (m, 5H, $H_{arom.}$), 5.54 (s, 1H, H-7), 5.34 (t, J = 8.0 Hz, 1H, H-3), 5.11 (t, J = 8.0 Hz, 1H, H-2), 4.80 (br s, 1H, H-8), 4.52 (d, J = 8.0 Hz, 1H, H-1), 4.41 (dd, J = 10.5, 4.9 Hz, 1H, H-6_{eq}), 3.83 (t, J = 10.5 Hz, 1H, H-6_{ax}), 3.73 (t, J = 8.0 Hz, 1H, H-4), 3.62–3.46 (m, 4H, OMe, H-5), 1.18 (s, 9H, $(\underline{CH_3})_3C$). ^{13}C NMR (75 MHz, *CDCl$_3$*): δ (ppm) 177.5 (C=O), 165.4 (C=O), 136.9 ($C_{quat.\ arom.}$), 129.0 ($CH_{arom.}$), 128.2 ($CH_{arom.}$), 125.9 ($CH_{arom.}$), 102.4 (C-1), 101.1 (C-7), 78.7 (C-4), 72.1 (C-2), 71.3 (C-3), 68.6 (C-6), 66.4 (C-5), 57.3 (OMe), 46.3 (C-8), 38.9 ($(CH_3)_3\underline{C}$), 26.8 ($(\underline{CH_3})_3C$). IR (film): 2971; 2114; 1736; 1704; 1380; 1148; 1099. MS: m/z = 457 (MNa^+). HRMS calculated for $C_{21}H_{26}N_2O_8Na$: 457.1581, found: 457.1587. $[\alpha]_D^{20}$ = - 66 (c = 1.0, $CHCl_3$).

*Methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-diazoacetyl-α-D-mannopyranoside* ***11***

Yield: 75%. TLC analysis: $R_f = 0.40$ (silica, cyclohexane/ethyl acetate 3:1). ^{1}H NMR (300 MHz, *CDCl$_3$*): δ (ppm) 7.56–7.28 (m, 10H, $H_{arom.}$), 5.65 (s, 1H, H-7), 5.52–5.48 (m, 1H, H-2), 4.94 (br s, 1H, H-8), 4.77 (d, J = 12.2 Hz, 1H, $\underline{CH}$Ph), 4.76 (d, J = 1.5 Hz, 1H, H-1) 4.69 (d, J = 12.2 Hz, 1H, $\underline{CH}$Ph), 4.29 (dd, J = 13.3, 2.8 Hz, 1H, H-6), 4.10–3.96 (m, 2H, H-3, H-5), 3.93–3.78 (m, 2H, H-4, H-6), 3.40 (s, 3H, OMe). ^{13}C NMR (75 MHz, *CDCl$_3$*): δ (ppm) 166.2 (C=O), 138.0 ($C_{quat.\ arom.}$), 137.9 ($C_{quat.\ arom.}$), 129.0 ($CH_{arom.}$), 128.4 ($CH_{arom.}$), 128.2 ($CH_{arom.}$), 127.8 ($CH_{arom.}$), 127.7 ($CH_{arom.}$), 126.2 ($CH_{arom.}$), 101.7 (C-7), 99.9 (C-1), 78.4 (C-4), 73.8 (C-3), 72.1 ($\underline{CH_2}$Ph), 69.9 (C-2), 68.8 (C6), 63.7 (C-5), 55.2 (OMe), 46.8 (C-8). IR (film): 3091; 2912; 2114; 1691; 1497; 1454; 1383; 1282; 1240; 1174; 1133; 1077; 1029; 1005; 977; 913; 886; 734; 698; 666. HRMS calculated for $C_{23}H_{24}N_2O_7Na$: 463.1481, found: 463.1478. $[\alpha]_D^{20} = -21$ (c = 1.0, $CHCl_3$).

*Methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-diazoacetyl-β-D-glucopyranoside* ***12***

Yield: 74%. TLC analysis: $R_f = 0.33$ (silica, cyclohexane/ethyl acetate 3:1). ^{1}H NMR (300 MHz, *CDCl$_3$*): δ (ppm) 7.62–7.22 (m, 10H, $H_{arom.}$), 5.61 (s, 1H, H-7), 5.10 (t, J = 8.3 Hz, 1H, H-2), 4.91 (d, J = 12.0 Hz, 1H, $\underline{CH}$Ph), 4.81–4.68 (m, 2H, H-8, $\underline{CH}$Ph), 4.48–4.33 (m, 2H, H-1, H-$6_{eq.}$), 3.94–3.67 (m, 3H, H-3, H-4, H-$6_{ax.}$), 3.47 (m, 4H, H-5; OMe). ^{13}C NMR (75 MHz, *CDCl$_3$*): δ (ppm) 165.4 (C=O), 138.1 ($C_{quat.\ arom.}$), 137.2 ($C_{quat.\ arom.}$), 129.1 ($CH_{arom.}$), 128.3 ($CH_{arom.}$), 128.0 ($CH_{arom.}$), 127.7 ($CH_{arom.}$), 126.1 ($CH_{arom.}$), 102.4 (C-1), 101.3 (C-7), 81.6 (C-4), 78.2 (C-3), 74.1 ($\underline{CH_2}$Ph), 73.1 (C-2), 68.7 (C-6), 66.2 (C-5), 57.1 (OMe),

46.4 (C-8). IR (film): 2927; 2113; 1705; 1454; 1381; 1237; 1195; 1096; 1058; 1030; 1011; 751; 698; 696. HRMS calculated for $C_{23}H_{24}N_2O_7Na$: 463.1481, found: 463.1483. $[\alpha]_D^{20} = +14$ (c = 1.0, $CHCl_3$).

Methyl 4,6-O-*benzylidene-2*-O-*diazoacetyl-3*-O-tert-*butyldimethylsilyl-α-D-mannopyranoside* ***13***

Yield: 64%. TLC analysis: $R_f = 0.52$ (silica, cyclohexane/ethyl acetate 3:1). ^{1}H NMR (300 MHz, *CDCl$_3$*): δ (ppm) 7.60–7.30 (m, 5H, $H_{arom.}$), 5.60 (s, 1H, H-7), 5.26 (dd, $J = 3.7$, 1.1 Hz, 1H, H-2), 4.89 (br s, 1H, H-8), 4.71 (d, $J = 1.1$ Hz, 1H, H-1), 4.29 (d, $J = 5.7$ Hz, 1H, H-6), 4.22 (dd, $J = 9.0$, 3.7 Hz, 1H, H-3), 3.92–3.70 (m, 3H, H-4, H-5, H-6), 3.41 (s, 3H, OMe), 0.88 (s, 9H, C($\underline{CH_3}$)$_3$), 0.10 (s, 3H, $\underline{CH_3}$Si), 0.07 (s, 3H, $\underline{CH_3}$Si). ^{13}C NMR (75 MHz, *CDCl$_3$*): δ (ppm) 166.2 (C=O), 137.5 ($C_{quat.\ arom.}$), 128.9 ($CH_{arom.}$), 128.1 ($CH_{arom.}$), 126.1 ($CH_{arom.}$), 101.8 (C-7), 100.0 (C-1), 79.4 (C-4), 72.9 (C-2), 68.8 (C-6), 68.1 (C-3), 63.6 (C-5), 55.2 (OMe), 46.5 (C-8), 25.6 (C($\underline{CH_3}$)$_3$), 18.2 (Si$\underline{C}$(CH$_3$)$_3$), –4.7 (Si$\underline{CH_3}$), –5.1 (Si$\underline{CH_3}$). IR (film): 2930; 2113; 1698; 1471; 1384; 1282; 1249; 1216; 1173; 1133; 1079; 1033; 1008; 978; 914; 888; 863; 838; 779; 758; 734; 698; 668. HRMS calculated for $C_{22}H_{32}N_2O_7SiNa$: 487.18765, found: 487.1872. $[\alpha]_D^{20} = -3$ (c = 1.0, $CHCl_3$).

Methyl 4,6-O-*benzylidene-2*-O-*diazoacetyl-3*-O-tert-*butyldimethylsilyl-β-D-glucopyranoside* ***14***

Yield: 50%. TLC analysis: $R_f = 0.46$ (silica, cyclohexane/ethyl acetate 3:1). ^{1}H NMR (300 MHz, *CDCl$_3$*): δ (ppm) 7.60–7.31 (m, 5H, $H_{arom.}$), 5.54 (s, 1H, H-7), 5.02 (t, $J = 8.8$ Hz, 1H, H-2), 4.81 (br s, 1H, H-8), 4.47–4.30 (m, 2H, H-1, $H\text{-}6_{eq.}$), 3.89 (t, $J = 8.8$ Hz, 1H, H-3), 3.81 (t, $J = 10.2$ Hz, 1H, $H\text{-}6_{ax.}$), 3.57 (m, 1H, H-4), 3.53 (s, 3H, OMe), 3.44 (dt, $J = 10.2$, 4.8 Hz, 1H, H-5), 0.85 (s, 9H, C($\underline{CH_3}$)$_3$), 0.05 (s, 3H, Si$\underline{CH_3}$), 0.01 (s, 3H, Si$\underline{CH_3}$). ^{13}C NMR (75 MHz, *CDCl$_3$*): δ (ppm) 165.3 (C=O), 137.1 ($C_{quat.\ arom.}$), 129.1 ($CH_{arom.}$), 128.2 ($CH_{arom.}$), 126.3 ($CH_{arom.}$), 102.5 (C-1), 101.8 (C-7), 81.4 (C-4), 74.5 (C-2), 72.8 (C-3), 68.7 (C-6), 66.4 (C-5), 57.1 (OMe), 46.5 (C-8), 25.6 (C($\underline{CH_3}$)$_3$), 18.1 (Si$\underline{C}$(CH$_3$)$_3$), –4.2 (Si$\underline{CH_3}$), –5.1 (Si$\underline{CH_3}$). IR (film): 2929; 2112; 1709; 1471; 1380; 1237; 1134; 1098; 1029; 1009; 838; 777; 731; 698; 668. HRMS calculated for $C_{22}H_{32}N_2O_7SiNa$: 487.18765, found: 487.1874. $[\alpha]_D^{20} = -37$ (c = 1.0, $CHCl_3$).

Metal-Catalyzed Decomposition of Diazosugars (General Procedure)

To a suspension of $Rh_2(OAc)_4$ (2.5 μmol) in refluxing anhydrous 1,2-dichloroethane (80 mL) was added dropwise via syringe pump (20 μmol/h) a solution of diazosugars **9**–**14** (0.5 mmol) in anhydrous 1,2-dichloroethane (2 mL). After the end of the addition, the reaction mixture was cooled to rt

and concentrated under vacuum. The residue was purified by silica gel chromatography (cyclohexane/ethyl acetate) to give γ-lactones **15**–**20**.

15: Yield: 77%. TLC analysis: $R_f = 0.57$ (silica, cyclohexane/ethyl acetate 2:1). ^{1}H NMR (300 MHz, *CDCl$_3$*): δ (ppm) 7.53–7.30 (m, 5H, $H_{arom.}$), 5.59 (s, 1H, H-7), 5.34 (dd, $J = 10.3$, 4.0 Hz, 1H, H-3), 4.75 (d, $J = 4.0$ Hz, 1H, H-2), 4.32 (dd, $J = 9.5$, 3.9 Hz, 1H, H-$6_{eq.}$), 4.06 (t, $J = 10.3$ Hz, 1H, H-4), 3.95–3.75 (m, 2H, H-5, H-$6_{ax.}$), 3.39 (s, 3H, OMe), 2.83 (d, $J = 16.4$ Hz, 1H, H-8), 2.70 (d, $J = 16.4$ Hz, 1H, H-8'), 1.26 (s, 9H, $(\underline{CH_3})_3C$). ^{13}C NMR (75 MHz, *CDCl$_3$*): δ (ppm) 177.8 (C=O), 171.5 (C=O), 136.9 ($C_{quat.\ arom.}$), 129.0 ($CH_{arom.}$), 128.2 ($CH_{arom.}$), 125.9 ($CH_{arom.}$), 103.7 (C-1), 101.3 (C-7), 79.0 (C-2), 74.8 (C-4), 68.21 (C-6), 68.20 (C-3), 64.5 (C-5), 51.9 (OMe), 40.3 (C-8), 39.0 ($(CH_3)_3\underline{C}$), 27.0 ($(\underline{CH_3})_3C$). IR (film): 2971; 1806; 1734; 1704; 1279; 1154; 1098; 1073; 1004; 964. MS: $m/z = 429$ (MNa^+). HRMS calculated for $C_{21}H_{26}O_8Na$: 429.1520, found: 429.1524. $[\alpha]_D^{20} = -82$ (c = 1.0, $CHCl_3$).

16: Yield: 20%. TLC analysis: $R_f = 0.24$ (silica, cyclohexane/ethyl acetate 3:1). ^{1}H NMR (300 MHz, *CDCl$_3$*): δ (ppm) 7.41–7.27 (m, 10H, $H_{arom.}$), 5.61 (s, 1H,H-7), 4.89 (d, $J = 12.2$ Hz, 1H, $\underline{CH}$Ph), 4.78 (d, $J = 12.2$ Hz, 1H, $\underline{CH}$Ph), 4.58 (d, $J = 3.7$ Hz, 1H, H-2), 4.28 (dd, $J = 9.3$, 3.8 Hz, 1H, H-$6_{eq.}$), 4.12–3.95 (m, 2H, H-3, H-4), 3.86–3.70 (m, 2H, H-5, H-$6_{ax.}$), 3.34 (s, 3H, OMe), 2.81 (d, $J = 16.3$ Hz, 1H, H-8), 2.67 (d, $J = 16.3$ Hz, 1H, H-8'). ^{13}C NMR (75 MHz, *CDCl$_3$*): δ (ppm) 171.5 (C=O), 137.8 ($C_{quat.\ arom.}$), 137.2 ($C_{quat.\ arom.}$), 129.1 ($CH_{arom.}$), 128.5 ($CH_{arom.}$), 128.3 ($CH_{arom.}$), 127.9 ($CH_{arom.}$), 126.1 ($CH_{arom.}$), 103.7 (C1), 101.6 (C-7), 80.1 (C-2), 77.6 (C-4), 73.1 (C-3), 73.0 ($\underline{CH_2}$Ph), 68.3 (C-6), 64.6 (C-5), 51.8 (OMe), 40.3 (C-8). IR (film): 2933; 2871; 1797; 1493; 1454; 1377; 1302; 1282; 1217; 1177; 1155; 1096; 1077; 1004; 962; 750; 698. HRMS calculated for $C_{23}H_{24}O_7Na$: 435.1420, found: 435.1418. $[\alpha]_D^{20} = -40$ (c = 1.0, $CHCl_3$).

17: Yield: 94%. TLC analysis: $R_f = 0.41$ (silica, cyclohexane/ethyl acetate 3:1). ^{1}H NMR (300 MHz, *CDCl$_3$*): δ (ppm) 7.56–7.33 (m, 5H, $H_{arom.}$), 5.57 (s, 1H, H-7), 4.47 (d, $J = 4.0$ Hz, 1H, H-2), 4.33–4.24 (m, 1H, H-6), 4.19 (dd, $J = 9.5$, 4.0 Hz, 1H, H-3), 3.93–3.69 (m, 3H, H-4, H-5, H-6), 3.38 (s, 3H, OMe), 2.82 (d, $J = 16.3$ Hz, 1H, H-8), 2.70 (d, $J = 16.3$ Hz, 1H, H-8′), 0.90 (s, 9H, $C(\underline{CH_3})_3$), 0.12 (s, 3H, $Si\underline{CH_3}$), 0.07 (s, 3H, $Si\underline{CH_3}$). ^{13}C NMR (75 MHz, *CDCl$_3$*): δ (ppm) 172.0 (C=O), 137.2 ($C_{quat.\ arom.}$), 129.0 ($CH_{arom.}$), 128.2 ($CH_{arom.}$), 126.1 ($CH_{arom.}$), 103.7 (C-1), 101.7 (C-7), 82.4 (C-2), 77.6 (C-4), 68.5 (C-3), 68.2 (C-6), 64.7 (C-5), 51.8 (OMe), 40.6 (C-8), 25.7 ($(\underline{CH_3})_3C$), 18.3 ($(CH_3)_3\underline{C}Si$), –4.4 ($Si\underline{CH_3}$), –5.1 ($Si\underline{CH_3}$). IR (film): 2930; 1795; 1457; 1386; 1250; 1213; 1174; 1118; 1099; 1027; 838; 779; 697; 669. HRMS calculated for $C_{22}H_{32}O_7SiNa$: 459.1815, found: 459.1811. $[\alpha]_D^{20} = -75$ (c = 1.0, $CHCl_3$).

ε-lactone: Yield: 51%. TLC analysis: $R_f = 0.16$ (silica, cyclohexane/ethyl acetate 3:1). ^{1}H NMR (300 MHz, *CDCl$_3$*): δ (ppm) 7.38 (m, 10H, $H_{arom.}$), 5.62 (s, 1H, H-7), 5.01 (s, 1H, H-1), 4.89 (d, $J = 3.8$ Hz, 1H, H-2), 4.81 (dd, $J = 9.2$, 5.2 Hz, 1H, CHPh), 4.33 (dd, $J = 9.0$, 3.3 Hz, 1H, H-$6_{eq.}$), 4.26 (dd, $J = 9.2$, 3.8 Hz, 1H, H-3), 4.05 (t, $J = 9.2$ Hz, 1H, H-4), 3.99–3.82 (m, 2H, H-5, H-$6_{ax.}$), 3.63 (dd, $J = 15.6$, 9.2 Hz, 1H, H-8), 3.47 (s, 3H, OMe), 3.15 (dd, $J = 15.6$, 5.2 Hz, 1H, H-8′). ^{13}C NMR (75 MHz, *CDCl$_3$*): δ (ppm) 169.1 (C=O), 142.0 ($C_{quat.\ arom.}$), 137.2 ($C_{quat.\ arom.}$), 129.1 ($CH_{arom.}$), 128.7 ($CH_{arom.}$), 128.3 ($CH_{arom.}$), 128.1 ($CH_{arom.}$), 126.2 ($CH_{arom.}$), 125.7 ($CH_{arom.}$), 101.9 (C-7), 99.1 (C-1), 77.4 (C-4), 74.4 (C-2), 74.3 (C-3), 71.2 (CHPh), 68.7 (C-6), 62.3 (C-5), 50.7 (OMe), 44.3 (C-8). IR (film): 2920; 1449; 1496; 1455; 1367; 1301; 1246; 1218; 1134; 1093; 1040; 919; 848; 754; 699; 669. HRMS calculated for $C_{23}H_{24}O_7Na$: 435.1420, found: 435.1412, $[\alpha]_D^{20} = -69$ (c = 1.0, $CHCl_3$).

18: Yield: 90%. TLC analysis: $R_f = 0.60$ (silica, cyclohexane/ethyl acetate 2:1). ^{1}H NMR (300 MHz, 50°C, *CDCl$_3$*) δ (ppm): 7.51–7.31 (m, 5H, $H_{arom.}$), 5.57 (s, 1H, H-7), 5.31 (dd, $J = 10.3$, 6.1 Hz, 1H, H-3), 4.47 (d, $J = 6.1$ Hz,1H, H-2), 4.42–4.33 (m, 1H, H-6), 4.03–3.91 (m, 1H, H-4), 3.85–3.71 (m, 2H, H-5, H-6), 3.42 (s, 3H, OMe), 2.92 (d, $J = 17.1$ Hz, 1H, H-8), 2.69 (d, $J = 17.1$ Hz, 1H, H-8′), 1.24 (s, 9H, $(CH_3)_3C$). ^{13}C NMR (75 MHz, *CDCl$_3$*) δ (ppm): 177.0 (C=O), 171.0 (C=O), 136.6 ($C_{quat.\ arom.}$), 129.1 ($CH_{arom.}$), 128.3 ($CH_{arom.}$), 125.9 ($CH_{arom.}$), 103.9 (C-1), 101.4 (C-7), 82.0 (C-2), 76.1 (C-4), 71.9 (C-3), 68.9 (C-6), 66.4 (C-5), 50.7 (OMe), 38.8 ($(CH_3)_3C$), 36.5 (C-8), 27.0 ($(CH_3)_3C$). IR (film): 2971; 1798; 1740; 1457; 1375; 1277; 1135; 1078; 1031; 699. MS: $m/z = 429$ (MNa^+). HRMS calculated for $C_{21}H_{26}O_8Na$: 429.1520, found: 429.1521. $[\alpha]_D^{20} = +1$ (c = 1.0, $CHCl_3$).

19: Yield: 35%. TLC analysis: $R_f = 0.34$ (silica, cyclohexane/ethyl acetate 3:1). ^{1}H NMR (300 MHz, *CDCl$_3$*): δ (ppm) 7.52–7.31 (m, 10H, $H_{arom.}$), 5.63 (s, 1H, H-7), 4.85 (s, 2H, CH_2Ph), 4.56 (d, $J = 5.6$ Hz, 1H, H-2), 4.37 (dd, $J = 10.3$, 4.8 Hz, 1H, H-$6_{eq.}$), 3.99 (t, $J = 9.7$ Hz, 1H, H-4), 3.87–3.74 (m, 2H, H-3, H-$6_{ax.}$), 3.67 (dt, $J = 9.7$, 4.8 Hz, 1H, H-5), 3.40 (s, 3H, OMe), 2.86 (d, $J = 17.2$ Hz, 1H, H-8), 2.69 (d, $J = 17.2$ Hz, 1H, H-8′). ^{13}C NMR (75 MHz, *CDCl$_3$*): δ (ppm) 171.6 (C=O), 137.4 ($C_{quat.\ arom.}$), 136.9 ($C_{quat.\ arom.}$), 129.2 ($CH_{arom.}$), 128.5 ($CH_{arom.}$), 128.4 ($CH_{arom.}$), 128.0 ($CH_{arom.}$), 126.1 ($CH_{arom.}$), 103.9 (C-1), 101.6 (C-7), 83.9 (C-2), 78.8 (C-3), 78.2 (C-4), 73.7 (CH_2Ph), 68.9 (C-6), 66.4 (C-5), 50.7 (OMe), 36.8 (C-8). IR (film): 2933; 1793; 1605; 1497; 1454; 1372; 1331; 1268; 1245; 1213; 1170; 1091; 1028; 916; 890; 752; 698; 601. HRMS calculated for $C_{23}H_{24}O_7Na$: 435.1420, found: 435.1415. $[\alpha]_D^{20} = +5$ (c = 1.0, $CHCl_3$).

20: Yield: 92%. TLC analysis: $R_f = 0.49$ (silica, cyclohexane/ethyl acetate 3:1). ^{1}H NMR (300 MHz, *CDCl$_3$*): δ (ppm) 7.57–7.32 (m, 5H; $H_{arom.}$), 5.58 (s, 1H, H-7), 4.47–4.29 (m, 2H, H-2, H-6), 3.89 (dd, $J = 9.6$, 5.8 Hz, 1H, H-3),

3.83–3.71 (m, 2H, H-4, H-6), 3.69–3.55 (m, 1H, H-5), 3.41 (s, 3H, OMe), 2.86 (d, J = 17.2 Hz, 1H, H-8), 2.68 (d, J = 17.2 Hz, 1H, H-8′), 0.90 (s, 9H, C($\underline{CH_3}$)$_3$), 0.13 (s, 3H, Si$\underline{CH_3}$), 0.06 (s, 3H, Si$\underline{CH_3}$). ^{13}C NMR (75 MHz, *CDCl$_3$*): δ (ppm) 171.8 (C=O), 136.9 ($C_{quat.\ arom.}$), 129.2 ($CH_{arom.}$), 128.2 ($CH_{arom.}$), 126.1 ($CH_{arom.}$), 103.8 (C-1), 101.8 (C-7), 85.4 (C-2), 78.6 (C-4), 74.1 (C-3), 68.8 (C-6), 66.5 (C-5), 50.5 (OMe), 36.5 (C-8), 25.7 (($\underline{CH_3}$)$_3$C), 18.2 ((CH$_3$)$_3\underline{C}$Si), –4.5 (Si$\underline{CH_3}$), –4.9 (Si$\underline{CH_3}$). IR (film): 2930; 1800; 1462; 1386; 1282; 1254; 1095; 1063; 1004; 964; 867; 837; 778; 752; 698; 669. HRMS calculated for $C_{22}H_{32}O_7SiNa$: 459.1815, found: 459.1812. $[\alpha]_D^{20} = -8$ (c = 1.0, $CHCl_3$).

Ring Opening of γ-Lactones (General Procedure)

To a solution of lactone **15** or **18** (0.150 mmol) in anhydrous dichloromethane (1.5 mL) at 0°C was added 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 2 M solution in toluene) in anhydrous dichloromethane (2 mL) for 30 min 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 1 M solution of Rochelle's salt (5 mL), diluted with dichloromethane (10 mL), and stirred for 1 h at rt. The organic layer was separated, dried (anhydrous magnesium sulfate), filtered, and concentrated under vacuum to give **21** or **22**.

21: Yield: 99%. TLC analysis: R_f = 0.26 (silica, cyclohexane/ethyl acetate 2:1). ^{1}H NMR (300 MHz, *CDCl$_3$*): δ (ppm) 7.45–7.34 (m, 5H, $H_{arom.}$), 5.59 (s, 1H, H-7), 5.40 (dd, J = 10.4, 3.4 Hz, 1H, H-3), 4.36–4.06 (m, 4H, H-2, H-4, H-6, OH), 3.87 (t, J = 10.2 Hz, 1H, H-6'), 3.79–3.61 (m, 4H OMe, H-5), 3.46–3.11 (m, 7H, OMe, NMe, H-8), 2.81 (d, J = 14.6 Hz, 1H, H-8′), 1.26 (s, 9H, ($\underline{CH_3}$)$_3$C). ^{13}C NMR (75 MHz, *CDCl$_3$*): δ (ppm) 177.6 (C=O), 169.5 (C=O), 137.4 ($C_{quat.\ arom.}$), 128.8 ($CH_{arom.}$), 128.2 ($CH_{arom.}$), 125.9 ($CH_{arom.}$), 103.0 (C-1), 101.2 (C-7), 75.5 (C-4), 70.6 (C-2), 70.0 (C-3), 68.7 (C-6), 65.1 (C-5), 61.6 (OMe), 48.4 (OMe), 39.0 ((CH$_3$)$_3\underline{C}$), 33.2 (C-8), 32.0 (NMe), 27.2 (($\underline{CH_3}$)$_3$C). IR (film): 3441; 2970; 1731; 1645; 1457; 1385; 1284; 1163; 1097; 1030; 754; 699. MS: m/z = 490 (MNa^+). HRMS calculated for $C_{23}H_{33}NO_9Na$: 490.2047, found: 490.2048. $[\alpha]_D^{20} = +12$ (c = 1.0, $CHCl_3$).

22: Yield: 98%. TLC analysis: R_f = 0.27 (silica, cyclohexane/ethyl acetate 2:1). ^{1}H NMR (300 MHz, *CDCl$_3$*) δ (ppm): 7.50–7.30 (m, 5H, $H_{arom.}$), 5.54 (s, 1H, H-7), 5.23 (dd, J = 8.2, 6.9 Hz, 1H, H-3), 5.09 (d, J = 4.3 Hz, 1H, OH), 4.38 (dd, J = 9.9, 3.6 Hz, 1H, H-6), 3.97 (t, J = 6.9 Hz, 1H, H-4), 3.93–3.80 (m, 2H, H-2, H-5), 3.79–3.67 (m, 4H, H-6', OMe), 3.42 (s, 3H, OMe), 3.33–3.04 (m, 5H, NMe, 2 × H-8), 1.23 (s, 9H, ($\underline{CH_3}$)$_3$C). ^{13}C NMR (75 MHz, *CDCl$_3$*) δ (ppm): 178.2 (C=O), 170.1 (C=O), 137.1 ($C_{quat.\ arom.}$), 129.0 ($CH_{arom.}$), 128.2

($CH_{arom.}$), 126.0 ($CH_{arom.}$), 102.1 (C-1), 101.3 (C-7), 78.9 (C-4), 74.3 (C-3), 73.0 (C-2), 69.3 (C-6), 65.3 (C-5), 61.6 (OMe), 49.1 (OMe), 38.9 ((CH_3)$_3$C), 35.2 (C-8), 32.2 (NMe), 27.2 ((CH_3)$_3$C). IR (film): 3437; 2970; 1734; 1634; 1457; 1378; 1282; 1091; 1031. MS: $m/z = 490$ (MNa^+). HRMS calculated for $C_{23}H_{33}NO_9Na$: 490.2047, found: 490.2046. $[\alpha]_D^{20} = -8$ (c = 1.0, $CHCl_3$).

ACKNOWLEDGEMENTS

Financial support of this work by CNRS (Research Fellowship to T.L.) and Université Paris Descartes (MESR grant to M.B.A.) is gratefully acknowledged.

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