Stereoselective Synthesis of C- and N-Ketosides by Lewis Acid-Catalyzed C- and N-Glycosidation of Alkynyl, Phenyl, and Methyl Ketoses

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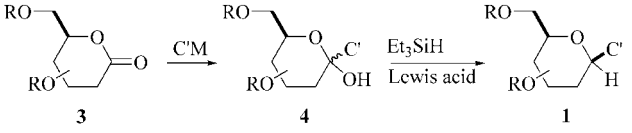
C-Ketosides can be prepared conveniently, in a stereoselective manner, from alkynyl, phenyl and methyl glucopyranose hemiketals by reaction with carbon nucleophiles in the presence of Lewis acids. The reaction of the hemiketals with trimethylsilyl azide provides an efficient route to the corresponding N-ketopyranosides.

Introduction

Carbohydrate analogs in which the glycosidic oxygen atom is replaced by a carbon atom are termed C-glycosides (**1**, Scheme 1).[1] Recently, C-glycosides have become attractive compounds from biological and synthetic standpoints. They are stable analogs of the glycans involved in important intra- and intercellular processes and have potential activity as inhibitors of sugar-processing enzymes,[2] and they have been recognized as important building blocks in the synthesis of biologically important molecules.[3] Additionally, several C-glycosides are potent antitumor, antiviral, or antibiotic agents.[4] On the other hand, C-ketosides[5] or bis-C,C-glycosides[6] (**2**) have not found similar favor,[7] although methods for the preparation of spirocyclic bis-C,C-glycosides[6,8,9] and C-glycosides of ulosonic acids[10,11] have been reported by several groups.

Scheme 1. C-Glycosides and C-ketosides

One of the more extended methods for the stereoselective synthesis of C-glycosides is based in the pioneering work of Kishi and collaborators,[3] and is outlined in Scheme 2. It involves the addition of an organometallic reagent (C′M) to a sugar lactone (**3**), which usually gives a mixture of hemiketals (**4**), followed subsequently by reduction upon treatment with a Lewis acid in the presence of a silicon hydride. Since the hydride is generally delivered to the axial position, because of the anomeric effect, these reactions constitute a very reliable and stereoselective method to produce β-C-glycosides (at least with *gluco* and *galacto* pyranosides; the *manno* isomers, however, are formed with poor diastereoselectivity after reduction, presumably because of a product-like steric destabilization of the transition state that leads to the 1,2-*cis* stereochemistry[3]) and have found widespread use over the years.[12,13]



Scheme 2. Synthesis of C-glycosides from sugar lactones

As a continuation of our interest on the synthesis of C-glycosides,[14] we turned our attention to the synthesis of C-ketosides as a class of C-glycoside analogs having potential for biological activity. We hypothesized that a Lewis acid-catalyzed C-glycosidation of hemiketals **4** would lead efficiently to C-ketopyranosides **2** or, by extension, to the preparation of N-ketopyranosides **5** (Scheme 3).

In fact, although Lewis acid-catalyzed C-glycosidations of glycosyl halides, glycosyl acetates, glycosides, and aldoses have been thoroughly exploited for the synthesis of C-glycosides, at the outset of this study we were unaware of any reports describing the transformation of sugar pyranolactones (**3**) into bis-C,C-glycopyranosides (**2**) via the corre-

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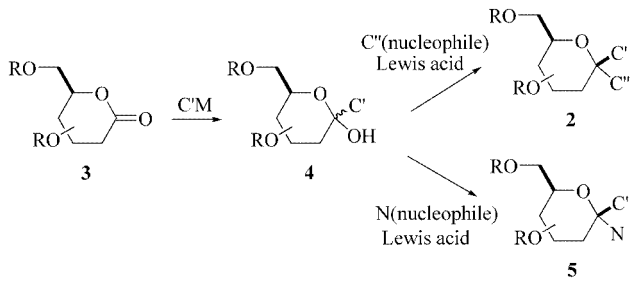
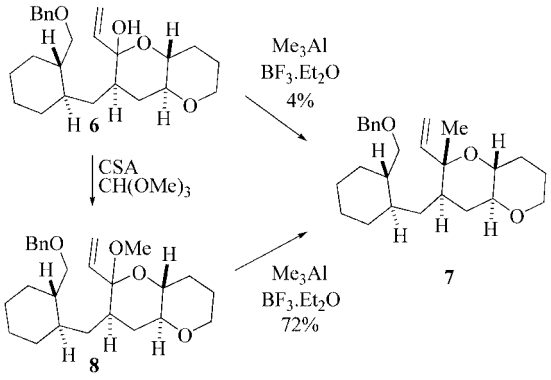


Scheme 3. Synthesis of C- and N-ketosides from sugar lactones

sponding hemiketals **4** (Scheme 3).[11o,12,13,15,16] To the best of our knowledge, only one example of Lewis acid-catalyzed C-glycosidation of pyranosydic lactols **4** has been reported,[13] in which methylation of hemiketal **6** gave C-ketoside **7**, albeit in low yield (4 %), whereas methylation of the corresponding methyl acetal **8** under the same reaction conditions furnished **7** in good yield (Scheme 4).

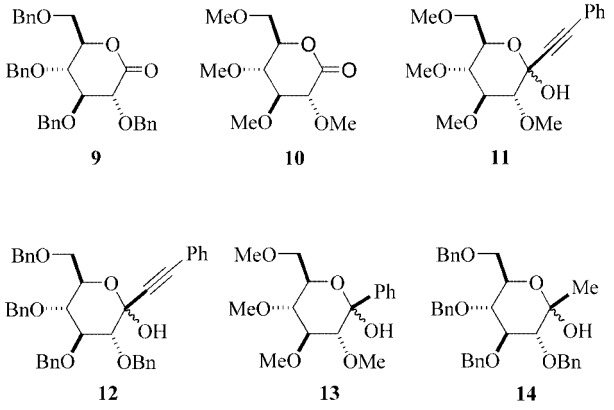


Scheme 4. Synthesis of complex C-ketoside **7**

Ketose-hemiketals (**4**) have been used by Schmidt's group in the preparation of C-ketosides, via the reaction of open-chain intermediates.[7e,17] More recently, after our present study was almost complete, two manuscripts were published that report the synthesis of C-ketosides. Hindsgaul and co-workers described the C-glycosidation of 2-deoxy-3-ulopyranosonates (i.e., **4** having C′ = CH_2CO_2R) with trimethylsilyl cyanide catalyzed by trimethylsilyl trifluoromethanesulfonate (TMS-OTf),[18] and Yamamoi and Oda reported[19] the C-allylation of alkyl hemiketals (i.e., **4** having C′ = alkyl) by reaction with allyltrimethylsilane in the presence of TMS-OTf. Hindsgaul and co-workers have also described the intramolecular Ritter reaction of ketoses for the preparation of N-ketosides.[20] In this paper, we report our results on the reaction of alkynyl, phenyl, and methyl hemiketals (**4**, C′ = alkyne, C′ = phenyl, C′ = alkyl) with allylsilanes, propargylsilanes, silyl enol ethers, silyl cyanides, silyl azides, and electron-rich aromatic compounds in the presence of boron trifluoride–diethyl ether ($BF_3{\cdot}Et_2O$).[21]

Results and Discussion

As starting materials in our study we used the glucose-derived lactols **11**, **12**,[12q] **13**, and **14**,[22] which are readily available from the aldonolactones **9**[12f,23] and **10**[23a,24] (Scheme 5). For the nucleophilic partners we tested allyltrimethylsilane (**15**), 1-phenyl-1-(trimethylsilyloxy)ethylene (**16**), trimethylsilyl cyanide (**17**), trimethylsilyl azide (**18**), 1,3,5-trimethoxybenzene (**19**), 1,4-dimethoxybenzene (**20**), and (trimethylsilyl)acetylene (**21**).

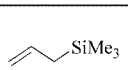
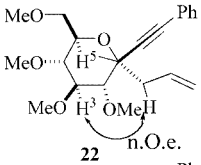
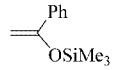
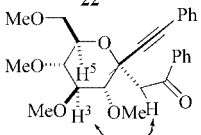
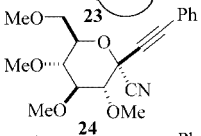
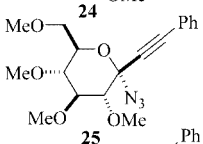
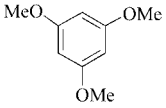
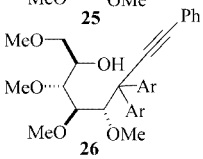
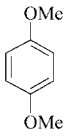
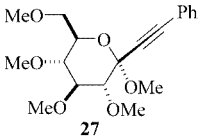
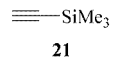


Scheme 5. Sugar lactones and hemiketals

Table 1 presents our results of the reactions of **11** with nucleophiles in the presence of $BF_3{\cdot}Et_2O$. Reaction with allyltrimethylsilane (**15**) led to the bis-C,C-glucoside **22** in 70 % yield (Table 1, Entry 1). We expect that the stereochemistry at the C-1 position is that shown in Table 1 (arising from axial approach of the nucleophile to the anomeric carbenium ion) in keeping with literature precedents.[3] Furthermore, we proved this stereochemistry by the existence of an NOE between the allylic protons and the axially disposed H-3 atom, as shown in Table 1. The reaction of **11** with 1-phenyl-1-(trimethylsilyloxy)ethylene (**16**) afforded the C-ketoside **23** (Entry 2). Trimethylsilyl cyanide (**17**) and trimethylsilyl azide (**18**) reacted smoothly with **11** to yield C- and N-ketosides **24** and **25**, respectively, in good yields (Entries 3, 4). 1,3,5-Trimethoxybenzene (**19**) reacted with **11** to furnish the open-chain bis-arylated compound **26** as the major reaction product. 1,4-Dimethoxybenzene and trimethylsilylacetylene, however, failed to yield any C-ketoside upon their reactions with **11** (Entries 6, 7). In the latter reactions, methyl ketoside **27**[25] was isolated as the major reaction product. The use of other acid catalysts, such as tin(IV) chloride ($SnCl_4$) or tetrafluoroboric acid (HBF_4), did not lead to significant variations in the observed yields.

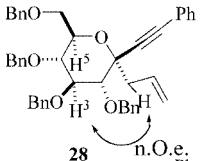
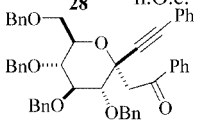
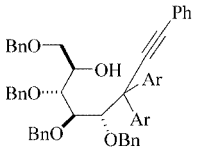
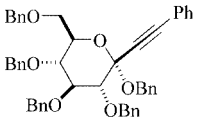
Next, we studied the hemiketal **12**, which differs from **11** by the presence of the more synthetically useful benzyl protecting groups. Table 2 summarizes the results of the reactions of **12** with carbon nucleophiles. According to these results, we deduce that **11** and **12** display similar behavior. Reaction of **12** with allylsilane (**15**) and 1-phenyl-1-(tri-

Table 1. Preparation of bis-C,C-glucopyranosides from hemiketal **11**, catalyzed by $BF_3{\cdot}Et_2O$ [Ar = 2,4,6-$(MeO)_3C_6H_2$]

Entry	Reagent[a]	Temp. °C (reaction time)	Product	Yield (%)
1	 **15**	– 30 (1 h)	 **22**	70
2	 **16**	– 15 (1 h)	 **23**	47 (61[b])
3	$NC\text{-}SiMe_3$ **17**	– 40 (2 h)	 **24**	64
4	$N_3\text{-}SiMe_3$ **18**	– 40 (3 h)	 **25**	70
5	 **19**	– 30 (3 h)	 **26**	49
6	 **20**	– 30	 **27**	48
7	 **21**	– 30	**27**	38

[a] 1.5 equiv. of nucleophile was used. [b]Based on 23 % recovered starting material.

Table 2. Reaction of hemiketal **12** with C-nucleophiles, catalyzed by $BF_3{\cdot}Et_2O$ [Ar = 2,4,6-$(MeO)_3C_6H_2$]

Entry	Reagent[a]	Temp. °C (reaction time)	Product	Yield (%)
1	**15**	– 30	 **28**	67
2	**16**	– 40 to 0 (2 h)	 **29**	42 (52[b])
3	**19** (3 equiv.)	– 30 (2 h)	 **30**	51
4	**20**	– 30	 **31**	26

[a] Unless otherwise noted, 1.5 equiv. of nucleophile was used. [b] Based on 23 % recovered starting material.

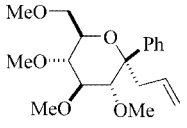
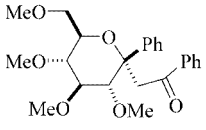
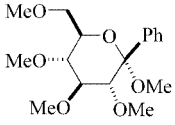
methylsilyloxy)ethylene (**16**) yielded the corresponding C-ketosides **28** and **29** in moderate yields (Table 2, Entries 1, 2). Reaction of **12**, with 1,3,5-trimethoxybenzene (**19**) afforded the bis-arylated open-chain compound **30** as the major product (Table 2, Entry 3). Once again, treatment of **12** with 1,4-dimethoxybenzene (**20**) did not yield any C-ketosylated product (Table 2, Entry 4), and only the benzyl glucoside **31** was isolated from the reaction mixture.

Hemiketal **13** (Table 3) yielded the bis-C,C-glucopyranosides **32** and **33** upon treatment with allylsilane (**15**) and silyl enol ether **16** (Entries 1, 2). Unlike the hemiketals **11** and **12**, however, reaction of **13** with 1,3,5-trimethoxybenzene (**19**) did not afford any bis-arylated product, but resulted instead in the formation of methyl glucoside **34** (Entry 3). Methyl glucoside **34** was also formed upon reaction of **13** with **20** and **21** (Entries 4, 5).

Finally, the methyl ketose **14** was tested in C- and N-glycosidation reactions (Table 4). Reaction of **14** with allyltrimethylsilane (**15**) led to the bis-C,C-glucoside **35** in 86 % yield (Table 4, Entry 1). The reaction of **14** with 1-phenyl-1-(trimethylsilyloxy)ethylene (**16**) afforded the C-ketoside **36** (80 %, Entry 2). Trimethylsilyl cyanide (**17**) and trimethylsilyl azide (**18**) reacted smoothly with **14** to yield the C- and N-ketosides **37** (96 %) and **38** (92 %), respectively, in excellent yields (Entries 3, 4). 1,3,5-Trimethoxybenzene (**19**) failed to react with **14** and onlythe benzyl glycoside **39**[26] was isolated from a complex reaction mixture (Entry 5).

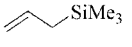
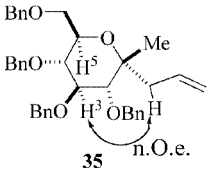
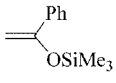
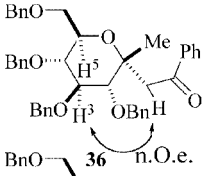
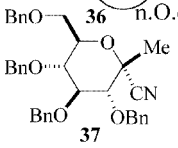
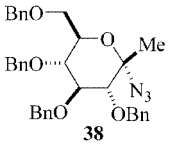
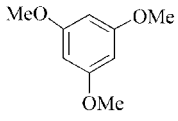
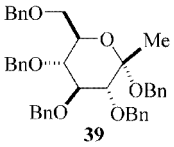
Lewis acid-catalyzed C-glycosidation of hemiketals **11**–**14** takes place via a stabilized anomeric oxonium ion (e.g., **A**, Scheme 6) that reacts efficiently with allyltrimethylsilane, 1-phenyl-1-(trimethylsilyloxy)ethylene, silyl cyanide, and silyl azide. Electron-rich aromatic compounds (e.g., **19**) behave as C-nucleophiles only when faced with alkynyl ketoses (**11**, **12**), although the main reaction course observed was the formation of bis-arylated open-chain derivatives (**26** and **30**). The formation of bis-arylated compounds (Type **D**, Scheme 6) can be rationalized simply by considering that the intermediate C-ketoside (**B**) would be prone to undergo C1–O bond cleavage to form a propargyl-benzyl cation (e.g., **C**) that could react further with **12** to generate structures of type **D**. It is noteworthy, however, that the ketoses **13** and **14** fail to undergo similar reactions with **19**, and we ascribe this behavior to steric and stereoelectronic factors, respectively. It is also interesting to note the difference in behavior between 1,3,5-trimethoxybenzene (**19**), which reacts in certain instances with the oxonium ion (**A**), and 1,4-dimethoxybenzene (**20**), which does not yield any coupled product (cf. Entries 6 and 5 in Table 1, and Entries 3 and 4 in Table 2). We observed the formation of methyl

Table 3. Preparation of bis-C,C-glucopyranosides from hemiketal **13**, catalyzed by $BF_3{\cdot}Et_2O$

Entry	Reagent[a]	Temp. °C (reaction time)	Product	Yield (%)
1	**15**	– 30 (1 h)	 **32**	71
2	**16**	– 15 (1 h)	 **33**	84
3	**19**	– 30[b]	 **34**	33
4	**20**	– 30[b]	**34**	75
5	**21**	– 30[b]	**34**	55

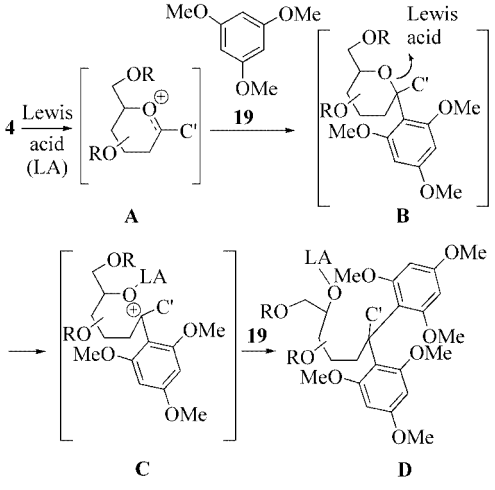
[a] 1.5 equiv of nucleophile was used. [b] Several other reaction temperatures and acids ($SnCl_4$, HBF_4) were used.

Table 4. Preparation of bis-C,C-glucopyranosides from hemiketal **14**, catalyzed by $BF_3{\cdot}Et_2O$

Entry	Reagent	Temp. °C (reaction time)	Product	Yield (%)
1	 **15** (2 equiv.)	– 20 (0.5 h)	 **35**	86
2	 **16** (4 equiv.)	– 20 to – 10 (2 h)	 **36**	80
3	NC-$SiMe_3$ **17** (2 equiv.)	– 20 (0.5 h)	 **37**	96
4	N_3-$SiMe_3$ **18** (2 equiv.)	– 20 (0.5 h)	 **38**	92
5	 **19** (4 equiv.)	– 20 to r.t. (18 h)	 **39**	27

and benzyl glycosides when methyl- or benzyl-protected ketoses were unable to react with their C-nucleophile partners (Entries 6 and 7 in Table 1; Entry 4 in Table 2; Entries 4, and 5 in Table 3; Entry 5 in Table 4). These glycosides are likely to arise from degradation of the starting material, in which intra- or intermolecular glycosidation of the intermediate oxocarbenium ions might be involved. Neither of the hemiketals gave any coupled product when allowed to react with trimethylsilylacetylene.

The configurational assignments at the C-1 positions of the C- and N-ketosides prepared in this study were inferred from the fact that only one isomeric C-ketoglucopyranoside was obtained in each case; literature precedents are consistent with an axial attack of the nucleophile onto oxocarbenium ions having *gluco* configurations. The stereochemistry at the C-1 atom in compound **22** (vide supra) also supports this assumption. Furthermore, NOEs were observed in compounds **23**, **28**, **35**, and **36** between the H-5 and H-3 atoms and the corresponding axially disposed anomeric methylene groups.



Scheme 6. Reaction of hemiketals (**4**) with **19**

Conclusion

We have reported herein a concise strategy for the stereocontrolled preparation of C-ketosides by Lewis acid-catalyzed C-glycosidation of alkynyl, phenyl, and methyl glucopyranose hemiketals. As successful nucleophilic partners, we have identified allyltrimethylsilane, trimethylsilyl cyanide, trimethylsilylazide, and one silyl enol ether. 1,3,5-Trimethoxybenzene behaves as a nucleophile and yielded an open-chain bis-arylated compound upon reaction with alkynyl ketoses (**11**, **12**), whereas the phenyl and methyl ketoses (**13**, **14**) failed to yield any coupled product. The

reaction of ketoses with trimethylsilyl azide permits an efficient entry into the corresponding N-ketopyranosides. This approach, which represents an extension of the method developed by Kishi and co-workers[3] for the stereocontrolled synthesis of β-C-glycosides, permits a rapid correlation between lactones and C-ketosides. When working with D-glucose derivatives, this strategy allows a stereodefined route to C-ketosides with the incoming nucleophile finally occupying the anomeric axial position.

Experimental Section

General Remarks: All reactions were performed in dry flasks fitted with glass stoppers or rubber septa under a positive pressure of Ar, unless otherwise noted. Air- and moisture-sensitive liquids and solutions were transferred by syringe or stainless steel cannula. Flash column chromatography was performed using 230−400-mesh silica gel. Thin-layer chromatography was conducted on Kieselgel 60 F_{254} (Merck). Spots were observed first under UV irradiation (254 nm) then by charring with a solution of 20 % aqueous H_2SO_4 (200 mL) in AcOH (800 mL). Anhydrous $MgSO_4$ or $NaSO_4$ was used to dry organic solutions during workup, and evaporation of the solvents was performed under vacuum using a rotary evaporator. Solvents were dried and purified using standard methods. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 300, 400, or 500 MHz and 75 or 50 MHz, respectively. Chemical shifts are expressed in parts per million (δ scale) downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$: δ = 7.25 ppm).

Ketoside 11: BuLi (51.0 mmol, 32 mL of 1.6 M solution in *n*-hexane) was added to a solution of phenylacetylene (5.6 mL, 51 mmol) in dry THF (30 mL) under Ar at −78 °C and then the mixture was stirred for 10 min. A solution of **10**[23a] (4.0 g, 17 mmol) in dry THF (20 mL) was added dropwise at −78 °C and then the reaction mixture was stirred for 1 h. The reaction mixture was diluted with Et_2O and washed successively with aqueous NH_4Cl, H_2O and brine. The organic layer was dried and concentrated and the residue was purified by flash chromatography (hexane/ EtOAc, 7:3) to give **11** (4.2 g, 73 %). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.13−3.94 (m, 6 H), 3.39 (s, 3 H), 3.53 (s, 3 H), 3.63 (s, 3 H), 3.73 (s, 3 H), 7.25−7.48 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 59.2, 60.5, 61.0, 61.6, 71.3, 71.3, 79.5, 84.2, 86.3, 91.9, 121.8, 128.3, 128.4, 131.9 ppm. API-ES (positive): *m*/*z* = 359.2 $[M + Na]^+$, 375.1 $[M + K]^+$, 695.4 $[2M + Na]^+$.

Ketoside 13: PhLi (12.2 mmol, 6.8 mL of 1.8 M solution in *n*-hexane) was added to a solution of **10** (2.5 g, 11.0 mmol) in dry THF (30 mL) under Ar at −78 °C and then the mixture was stirred for 90 min. The reaction mixture was diluted with Et_2O and washed successively with aqueous NH_4Cl, H_2O, and brine. The organic layer was dried and concentrated and the residue was purified by flash chromatography (hexane/EtOAc, 6:4) to give **13** (2.1 g, 60 %). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.03 (s, 3 H), 3.39 (s, 3 H), 3.56 (s, 3 H), 3.63 (s, 3 H), 3.00−4.02 (m, 6 H), 7.26−7.38 (m, 3 H), 7.55−7.62 (m, 2 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 59.3, 60.2, 60.8, 60.9, 71.6, 79.9, 85.2, 87.2), 97.5, 126.0, 128.0, 128.2, 142.4 ppm. API-ES (positive): *m*/*z* = 335.2 $[M + Na]^+$, 647.5 $[2M + Na]^+$.

General Procedure for the Lewis Acid-Catalyzed C-Glycosidation of Ketosides: $BF_3{\cdot}OEt_2$ (0.5 equiv., unless otherwise noted) and the corresponding nucleophile (1.5 equiv., unless otherwise noted) were added to a solution of the hemiketal in anhydrous CH_2Cl_2 (20 mL/mmol), which was cooled to the appropriate temperature (see Table) under Ar. The resulting solution was stirred until consumption of the starting material (TLC; usually between 30 min and 3 h). The reaction was then quenched with a saturated aqueous solution of $NaHCO_3$ and extracted with CH_2Cl_2. The organic phase was dried with anhydrous $MgSO_4$, filtered, and concentrated. Flash chromatography of the residue gave the corresponding bis-C,C-glycosides.

2,3,4,6-Tetra-*O*-methyl-1-*C*-allyl-1-*C*-(2-phenylethynyl)-β-D-glucopyranose (22): This compound was prepared by the general procedure from ketal **11** (100 mg, 0.3 mmol) followed by flash chromatography (hexane/EtOAc, 7:3) to give **22** (75 mg, 70 %). $[\alpha]_D$ = −22.5 (*c* = 0.6, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.67 (m, 2 H), 3.21−3.70 (m, 6 H), 3.39 (s, 3 H), 3.56 (s, 3 H), 3.66 (s, 3 H), 3.70 (s, 3 H), 5.18 (m, 2 H), 6.04 (m, 1 H), 7.30 (m, 3 H), 7.43 (m, 2 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 34.6, 59.2, 60.5, 60.9, 61.5, 71.2, 71.9, 79.7, 84.9, 86.5, 84.8, 90.2, 118.2, 122.6, 128.1, 128.3, 131.7, 132.4 ppm. API-ES (positive): *m*/*z* = 383.1 $[M + Na]^+$, 361.3 $[M + H]^+$. $C_{21}H_{28}O_5$ (360.4): calcd. C 69.98, H 7.83; found C 69.77, H 7.98.

2,3,4,6-Tetra-*O*-methyl-1-*C*-(2-oxo-2-phenylethyl)-β-1-*C*-(2-phenylethynyl)-D-glucopyranose (23): This compound was prepared from ketal **11** (100 mg, 0.3 mmol) by a modification of the general procedure using 3 equiv. of $BF_3{\cdot}Et_2O$ and 4 equiv. of 1-phenyl-1-(trimethylsilyloxy)ethylene **16**. Flash chromatography (hexane/EtOAc, 9:1) gave **23** (48 mg, 42 %). $[\alpha]_D$ = −35.1 (*c* = 2.0, $CHCl_3$,). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.26 (d, *J* = 13.5 Hz, 1 H), 3.78−4.06 (m, 7 H), 4.53 (d, *J* = 12.0 Hz, 1 H), 4.59 (d, *J* = 10.8 Hz, 1 H), 4.74 (d, *J* = 12.0 Hz, 1 H), 4.83 (d, *J* = 10.8 Hz, 1 H), 4.87 (d, *J* = 11.0 Hz, 1 H), 4.93 (d, *J* = 10.6 Hz, 1 H), 4.94 (d, *J* = 11.0 Hz, 1 H), 5.08 (d, *J* = 10.6 Hz, 1 H), 6.96−8.06 (m, 30 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 37.0, 68.5, 73.0, 73.5, 74.6, 75.0, 75.5, 76.1, 78.0, 82.8, 84.9, 86.6, 89.7, 121.9, 127.5, 127.6, 127.6, 127.7, 127.8, 127.9, 127.9, 128.1, 128.1, 128.2, 128.3, 128.4, 128.5, 129.0, 131.6, 132.8, 138.1, 138.2, 138.5, 197.0 ppm. API-ES (positive): *m*/*z* = 439.2 $[M + H]^+$. $C_{26}H_{30}O_6$ (438.5): calcd. C 71.21, H 6.90; found C 70.98, H 6.83.

1-*C*-Cyano-β-2,3,4,6-tetra-*O*-methyl-1-*C*-(2-phenylethynyl)-D-glucopyranose (24): This compound was prepared from ketal **11** (100 mg, 0.3 mmol). Flash chromatography (hexane/EtOAc, 8:2) gave **24** (66 mg, 64 %). $[\alpha]_D$ = +45.9 (*c* = 0.65, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.22−3.65 (m, 6 H), 3.39 (s, 3 H), 3.54 (s, 3 H), 3.66 (s, 3 H), 3.74 (s, 3 H), 7.31−7.49 (m, 5 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 70.7, 71.0, 76.8, 78.3, 85.5, 85.7, 82.6, 87.3, 114.6, 121.0, 128.8 (× 2), 130.1, 132.4 (× 2) ppm. API-ES (positive): *m*/*z* = 346.5 $[M + H]^+$. $C_{19}H_{23}NO_5$ (345.4): calcd. C 66.07, H 6.71, N 4.06; found C 65.94, H 6.92, N 3.95.

1-Azido-β-2,3,4,6-tetra-*O*-methyl-1-*C*-(2-phenylethynyl)-D-glucopyranose (25): This compound was prepared from ketal **11** (100 mg, 0.3 mmol). Flash chromatography (hexane/EtOAc, 8:2) gave **25** (76 mg, 70 %). $[\alpha]_D$ = +61.9 (*c* = 1.08, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.19−3.26 (m, 1 H), 3.37 (m, 1 H), 3.39 (s, 3 H), 3.52 (s, 3 H), 3.53−3.64 (m, 3 H), 3.63 (s, 3 H), 3.70 (s, 3 H), 3.74−3.79 (m, 1 H), 7.27−7.52 (m, 5 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 59.5, 60.8, 61.3, 62.0 (4 × OMe), 70.9, 73.4, 78.9, 84.2, 86.2, 82.9, 88.0, 89.4, 121.2, 128.6 (× 2), 129.6, 132.4 (× 2) ppm. API-ES (positive): *m*/*z* = 384.5 $[M + Na]^+$. $C_{18}H_{23}N_3O_5$ (361.4): calcd. C 59.82, H 6.41, N 11.63; found C 59.57, H 6.28, N 11.51.

Open-Chain Bis-Arylated Compound 26: Application of the general procedure to hemiketal **11** (100 mg, 0.3 mmol), followed by flash

chromatography (hexane/EtOAc, 7:3 to 1:1 to 3:7), gave the open-chain bis-arylated compound **26** (95 mg, 49 %). $[\alpha]_D = -96.1$ (c = 0.6, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.05 (s, 3 H), 3.22 (s, 3 H), 3.26 (s, 3 H), 3.57 (s, 3 H), 3.73 (s, 3 H), 3.77 (s, 3 H), 3.45 (s, 3 H), 3.58 (s, 3 H), 3.10−3.78 (m, 6 H), 4.36 (d, J = 5.5 Hz, 1 H), 6.07 (s, 2 H), 6.09 (s, 2 H), 7.02−7.38 (m, 7 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 55.0, 55.1, 55.4 (× 2), 55.5 (× 2), 57.3, 57.8, 58.7, 59.9, 70.6, 73.9, 78.6, 80.3, 81.8, 90.9, 98.6, 101.2, 105.2, 125.6, 126.5 (× 2), 127.4 (× 2), 137.0, 158.7 (× 2), 159.0 (× 2), 160.2, 160.5 ppm. MS (EI): m/z = 677.6 $[M + Na]^+$. $C_{60}H_{62}O_{11}$ (959.1): calcd. C 75.14, H 6.52; found C 75.01, H 6.84.

Methyl 2,3,4,6-Tetra-*O*-methyl-1-*C*-(2-phenylethynyl)-α-D-glucopyranoside (27): This compound was obtained following the general procedure from hemiketal **11** (50 mg, 0.15 mmol) with 0.5 equiv. of BF_3Et_2O and 10 equiv. of MeOH. Flash chromatography (hexane/EtOAc, 6:4) gave **27** (33 mg, 63 %). $[\alpha]_D = +20.8°$(c = 0.3, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ = 3.20−3.66 (m, 6 H), 3.44 (s, 3 H), 3.51 (s, 3 H), 3.58 (s, 3 H), 3.67 (s, 3 H), 3.75 (s, 3 H), 7.31−7.38 (m, 3 H), 7.47−7.53 (m, 2 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 50.9, 59.3, 60.4, 60.9, 61.7, 71.1, 71.5, 79.5, 84.2, 86.4, 96.6, 121.9, 128.3, 128.9, 131.9 ppm. MS (EI): m/z = 373.1 $[M + Na]^+$, 723.3 $[2M + Na]^+$.

1-*C*-Allyl-2,3,4,6-tetra-*O*-benzyl-1-*C*-(2-phenylethynyl)-β-D-glucopyranose (28): This compound was prepared by the general procedure from hemiketal **12** (80 mg, 0.13 mmol), followed by flash chromatography (hexane/EtOAc, 9:1), to give **28** (55 mg, 67 %). $[\alpha]_D = -16.8$ (c = 0.4, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.70 (d, J = 6.9 Hz, 2 H), 3.65−4.00 (m, 6 H), 4.42 (d, J = 12.0 Hz, 1 H), 4.43 (d, J = 10.5 Hz, 1 H), 4.56 (d, J = 12.0 Hz, 1 H), 4.71 (d, J = 10.5 Hz, 1 H), 4.72 (d, J = 11.5 Hz, 1 H), 4.75 (d, J = 9.9 Hz, 1 H), 4.80 (d, J = 10.8 Hz, 1 H), 4.99 (d, J = 11.5 Hz, 1 H), 5.08 (dd, J = 1.2, 13.5 Hz, 2 H), 6.04 (ddt, J = 10.2, 10.5, 13.5 Hz, 1 H), 7.16 (m, 25 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 35.0, 68.8, 72.3, 73.4, 75.2, 75.5, 75.6, 75.9, 78.2, 83.1, 84.8, 85.1, 90.4, 118.3, 122.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 128.6, 131.7, 132.50, 138.0, 138.2, 138.3, 138.6 ppm. MS (EI): m/z = 665.4 $[M + Na]^+$. $C_{45}H_{44}O_5$: calcd. C 81.30, H 6.67; found C 80.98, H 6.44.

2,3,4,6-Tetra-*O*-benzyl-1-*C*-(2-oxo-2-phenylethyl)-1-*C*-(2-phenylethynyl)-β-D-glucopyranose (29): This compound was prepared from hemiketal **12** (100 mg, 0.156 mmol), using the general procedure. Flash chromatography (hexane/EtOAc, 9:1) gave **29** (48 mg, 42 %). $[\alpha]_D = -35.1$ (c = 2.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.26 (d, J = 13.5 Hz, 1 H), 3.78−4.06 (m, 7 H), 4.53 (d, J = 12.0 Hz, 1 H), 4.59 (d, J = 10.7 Hz, 1 H), 4.74 (d, J = 12.0 Hz, 1 H), 4.83 (d, J = 10.9 Hz, 1 H), 4.87 (d, J = 11.0 Hz, 1 H), 4.93 (d, J = 10.6 Hz, 1 H), 4.94 (d, J = 11.0 Hz, 1 H), 5.08 (d, J = 10.6 Hz, 1 H), 6.96−8.06 (m, 30 H, Ar) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 37.0, 68.5, 73.0, 73.5, 74.6, 75.0, 75.5, 76.1, 78.0, 82.8, 84.9, 86.6, 89.7, 121.9, 127.4, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.1, 128.2, 128.3, 128.4, 128.5, 129.0, 131.6, 132.8, 138.1, 138.2, 138.5, 197.0 ppm. MS (EI): m/z = 743.2 $[M + H]^+$, 765.3 $[M + Na]^+$. $C_{50}H_{46}O_6$ (742.9): calcd. C 80.84, H 6.24; found C 80.67, H 6.41.

Open-Chain Bis-Arylated Compound 30: Application of the general procedure to hemiketal **12** (100 mg, 0.16 mmol) with 3 equiv. of 1,3,5-trimethoxybenzene, followed by flash chromatography (hexane/EtOAc, 7:3 to 1:1 to 2:8), gave the open-chain bis-arylated compound **30** (72 mg, 51 %). $[\alpha]_D = +57.2$ (c = 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.36 (s, 6 H), 3.49 (s, 6 H) 3.80 (s, 3 H), 3.85 (s, 3 H), 3.40−3.88 (m, 4 H), 3.94 (d, J = 11.4 Hz, 1 H), 4.07 (dd, J = 2.6, 6.0 Hz, 1 H), 4.24 (d, J = 11.4 Hz, 1 H), 4.43 (d, J = 12.2 Hz, 1 H), 4.50 (d, J = 11.4 Hz, 1 H), 4.72 (d, J = 12.0 Hz, 1 H), 4.80 (d, J = 11.4 Hz, 1 H), 4.86 (d, J = 6.0 Hz, 1 H), 4.97 (d, J = 11.4 Hz, 1 H), 6.07 (s, 2 H), 6.12 (s, 2 H), 6.97−7.47 (m, 25 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.2, 55.3, 55.4, 55.5, 71.0, 71.4, 71.7, 72.5, 73.2, 74.1, 78.0, 79.0, 80.8, 91.0, 91.1, 99.6, 102.0, 107.1, 125.8, 126.7, 126.8, 127.0, 127.2, 127.3, 127.4, 127.6, 127.7, 127.8, 127.9, 128.1, 128.2, 128.4, 137.1, 138.6, 139.0, 139.6, 158.8, 159.1, 160.4, 160.7 ppm. MS (CI): m/z = 982.4 $[M + Na]^+$. $C_{60}H_{62}O_{11}$ (959.1): calcd. C 75.14, H 6.52; found C 74.86, H 6.74.

Benzyl 2,3,4,6-Tetra-*O*-benzyl-1-*C*-(2-phenylethynyl)-α-D-glucopyranoside (31): $[\alpha]_D = -19.9$ (c = 0.4, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 3.64−4.11 (m, 6 H), 4.54 (d, J = 10.6 Hz, 1 H), 4.56 (d, J = 12.1 Hz, 1 H), 4.66 (d, J = 12.3 Hz, 1 H), 4.78 (d, J = 12.3 Hz, 1 H), 4.82 (d, J = 10.9 Hz, 1 H), 4.85 (d, J = 10.6 Hz, 1 H), 4.94 (d, J = 11.1 Hz, 1 H), 4.95 (d, J = 10.9 Hz, 1 H), 5.06 (d, J = 12.1 Hz, 1 H), 5.12 (d, J = 11.1 Hz, 1 H), 7.12−7.48 (m, 25 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 66.1, 68.4, 73.4, 75.1, 75.7, 77.8, 77.9, 82.4, 84.6, 96.8, 121.5, 127.3, 127.4, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 128.9, 131.9, 132.1, 137.9, 138.1, 138.2, 138.4, 138.7 ppm. MS (EI): m/z = 731.7 $[M + H]^+$. $C_{49}H_{46}O_6$ (730.9): calcd. C 80.52, H 6.34; found C 80.08, H 6.05.

1-*C*-Allyl-2,3,4,6-tetra-*O*-methyl-1-*C*-phenyl-β-D-glucopyranose (32): This compound was prepared by the general procedure from hemiketal **13** (100 mg, 0.32 mmol), followed by flash chromatography (hexane/EtOAc, 7:3), to give **32** (76 mg, 71 %). $[\alpha]_D = +34.1$ (c = 2.3, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.78 (dd, J = 7.6, 15.9 Hz, 1 H), 2.91 (d, J = 9.4 Hz, 1 H) 3.02 (dd, J = 5.9, 15.9 Hz, 1 H), 3.16 (s, 3 H), 3.46 (s, 3 H), 3.58 (s, 3 H), 3.65 (s, 3 H), 3.21−3.71 (m, 4 H), 4.93−5.07 (m, 2 H), 5.38−5.51 (m, 1 H), 7.24−7.60 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.5, 59.8, 60.7, 61.0, 61.7, 72.2, 79.6, 80.3, 80.7, 86.5, 88.6, 117.9, 126.3, 127.0, 128.1, 132.8, 143.6 ppm. MS (EI): m/z = 354.2 $[M + NH_4]^+$, 359.2 $[M + Na]^+$. $C_{19}H_{28}O_5$ (336.4): calcd. C 67.83, H 8.39; found C 67.53, H 8.11.

2,3,4,6-Tetra-*O*-methyl-1-*C*-(2-oxo-2-phenylethyl)-1-*C*-phenyl-β-D-glucopyranose (33): This compound was prepared from hemiketal **13** (100 mg, 0.32 mmol) by using the general procedure. Flash chromatography (hexane/EtOAc, 8:2) gave **33** (111 mg, 84 %). $[\alpha]_D = -54.8$ (c = 1.1, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ = 3.01 (d, J = 10.5 Hz, 1 H), 3.28 (s, 3 H), 3.48 (s, 3 H), 3.60 (s, 3 H), 3.71 (s, 3 H), 3.31−3.76 (m, 6 H), 4.08 (d, J = 16.0 Hz, 1 H), 7.13−7.81 (m, 10 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 36.5, 59.4, 61.2, 71.6, 72.8, 79.1, 80.1, 86.4, 88.3, 124.1, 124.9, 125.5, 126.7, 127.7, 127.9, 128.1, 132.2, 138.5, 143.6, 196.8 ppm. MS (EI): m/z = 415.2 $[M + H]^+$, 437.3 $[M + Na]^+$, 851.2 $[2M + Na]^+$. $C_{24}H_{30}O_6$: calcd. C 69.54, H 7.30; found C 69.19, H 6.98.

Methyl 2,3,4,6-Tetra-*O*-methyl-1-*C*-phenyl-α-D-glucopyranoside (34): $[\alpha]_D = +43.7$ (c = 1.7, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ = 3.08 (s, 3 H), 3.10 (s, 3 H), 3.48 (s, 3 H), 3.59 (s, 3 H), 3.65 (s, 3 H), 3.28−3.77 (m, 6 H), 7.28−7.41 (m, 3 H), 7.52−7.60 (m, 2 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 49.3, 59.7, 60.6, 61.0, 61.6, 71.7, 71.8, 79.9, 85.3, 87.8, 100.9, 127.4, 128.0, 128.1, 128.2 ppm. MS (EI): m/z = 349.1 $[M + Na]^+$. $C_{17}H_{26}O_6$: calcd. C 62.56, H 8.03; found C 62.53, H 7.91.

1-*C*-Allyl-2,3,4,6-tetra-*O*-benzyl-1-*C*-methyl-β-D-glucopyranose (35): This compound was prepared by the general procedure from hemiketal **14** (83 mg, 0.15 mmol), followed by flash chromatography (hexane/EtOAc, 9:1), to give **35** (83 mg, 86 %). $[\alpha]_D = +37.5$

(c = 1.6, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ = 1.28 (s, 3 H,), 2.34 (dd, J = 7.6, 15.1 Hz, 1 H), 2.67 (dd, J = 6.3, 15.1 Hz, 1 H), 3.37 (d, J = 9.5 Hz, 1 H), 3.63−6.73 (m, 4 H), 3.88 (m, 1 H), 4.54 (d, J = 12.3 Hz, 1 H), 4.55 (d, J = 9.5 Hz, 1 H), 4.66 (d, J = 12.2 Hz, 1 H), 4.69 (d, J = 11.2 Hz, 1 H), 4.82 (d, J = 10.7 Hz, 1 H), 4.88 (m, 2 H), 4.92 (d, J = 11.2 Hz, 1 H), 5.10 (m, 2 H), 5.84 (m, 1 H), 7.14−7.35 (m, 20 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 24.9, 34.0, 69.2, 72.2, 73.3, 75.0, 75.4, 75.7, 79.1, 84.0, 86.1, 117.8, 127.4, 127.5, 127.6, 127.7, 127.9, 128.2, 128.3, 128.4, 132.6, 138.1, 138.3, 138.5, 138.6 (× 4) ppm. API-ES (positive): m/z = 579.2 $[M + H]^+$. $C_{38}H_{42}O_5$ (578.7): calcd. C 78.86, H 7.31; found C 78.93, H 7.43.

2,3,4,6-Tetra-*O*-benzyl-1-*C*-methyl-1-*C*-(2-oxo-2-phenylethyl)-β-D-glucopyranose (36): This compound was prepared from hemiketal **14** (83 mg, 0.15 mmol) by using the general procedure. Flash chromatography (hexane/EtOAc, 9:1) gave **36** (78 mg, 80 %). $[\alpha]_D$ = +24.1 (c = 0.8, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ = 1.40 (s, 3 H), 3.18 (d, J = 14.2 Hz, 1 H), 3.41 (d, J = 9.5 Hz, 1 H), 3.54 (d, J = 14.2 Hz, 1 H), 3.64 (m, 1 H), 3.73−3.80 (m, 2 H), 3.84−3.90 (m, 2 H), 4.51 (d, J = 12.2 Hz, 1 H), 4.58 (d, J = 10.5 Hz, 1 H), 4.68 (d, J = 12.1 Hz, 1 H), 4.70 (d, J = 11.1 Hz, 1 H), 4.82 (d, J = 10.5 Hz, 1 H), 4.86 (d, J = 10.5 Hz, 1 H), 4.92 (d, J = 12.1 Hz, 1 H), 4.93 (d, J = 11.1 Hz, 1 H), 7.16−7.54 (m, 23 H), 7.88−7.91 (m, 2 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 26.1, 37.0, 68.8, 72.7, 73.3, 74.9, 75.3, 75.8, 77.8, 78.7, 83.6, 86.2, 127.4, 127.6, 127.6, 127.7, 127.7, 127.8, 127.9, 128.2, 128.2, 128.3, 128.4, 128.4, 132.7, 138.0, 138.2, 138.3, 138.4, 138.7, 198.6 ppm. API-ES (positive): m/z = 657.3 $[M + H]^+$. $C_{43}H_{44}O_6$ (656.8): calcd. C 78.63, H 6.75; found C 78.57, H 6.64.

2,3,4,6-Tetra-*O*-benzyl-1-*C*-cyano-1-*C*-methyl-β-D-glucopyranose (37): This compound was prepared by the general procedure from hemiketal **14** (83 mg, 0.15 mmol) using 2 equiv. of **17**, followed by flash chromatography (hexane/EtOAc, 9:1), to give **37** (81 mg, 96 %): $[\alpha]_D$ = +5.1 (c = 0.7, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ = 1.62 (s, 3 H), 3.34 (d, J = 9.3 Hz, 1 H), 3.73 (m, 1 H), 3.75 (dt, J = 9.0, 10.0 Hz, 1 H), 3.82 (dd, J = 11.2, 3.4 Hz, 1 H), 3.91 (m, 1 H, H-5), 3.96 (t, J = 9.3 Hz, 1 H), 4.53 (d, J = 12.1 Hz, 1 H), 4.61 (d, J = 11.5 Hz, 1 H), 4.64 (d, J = 12.1 Hz, 1 H), 4.76 (d, J = 11.5 Hz, 1 H), 4.87 (d, J = 11.2 Hz, 1 H), 4.90 (d, J = 11.5 Hz, 1 H), 4.95 (d, J = 11.2 Hz, 1 H), 4.99 (d, J = 11.5 Hz, 1 H), 7.22−7.38 (m, 20 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 24.2, 68.0, 73.4, 75.0, 75.5, 75.8 (x, 4), 76.6, 77.0, 82.3, 84.5, 117.9, 127.7, 127.7, 127.8, 127.8, 127.9, 128.4, 128.4, 128.4, 137.3, 137.7, 137.9, 138.1 ppm. API-ES (positive): m/z = 581.1 $[M + NH_4]^+$. $C_{36}H_{37}NO_5$ (563.7): calcd. C 76.61, H 6.62, N 2.48; found C 78.57, H 6.64, N 2.36.

1-Azido-2,3,4,6-tetra-*O*-benzyl-1-*C*-methyl-β-D-glucopyranose (38): This compound was prepared by the general procedure from hemiketal **14** (83 mg, 0.15 mmol) using 2 equiv. of **18**, followed by flash chromatography (hexane/EtOAc, 9:1), to give **38** (80 mg, 92 %): $[\alpha]_D$ = +62.9 (c = 0.8, $CHCl_3$). ^1H NMR (200 MHz, $CDCl_3$): δ = 1.55 (s, 3 H), 3.38 (d, J = 9.3 Hz, 1 H), 3.69 (m, 1 H), 3.68 (t, J = 9.3 Hz, 10.0 Hz,1 H), 3.75 (dd, J = 3.4, 11.0 Hz, 1 H), 3.88 (ddd, J = 1.95, 3.4, 10.0 Hz, 1 H, H-5), 3.94 (t, J = 9.3 Hz, 1 H, H-3), 4.51 (d, J = 12.45 Hz, 1 H), 4.58 (d, J = 11.0 Hz, 1 H), 4.62 (d, J = 11.0 Hz, 1 H), 4.69 (d, J = 11.2 Hz, 1 H), 4.83 (d, J = 10.5 Hz, 1 H), 4.86 (d, J = 11.2 Hz, 1 H), 4.89 (d, J = 10.5 Hz, 1 H), 4.93 (d, J = 11.2 Hz, 1 H), 7.14−7.36 (m, 20 H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$): δ = 22.5 (Me), 68.3, 73.4 (× 2), 74.9, 75.6, 75.7, 77.7, 83.2, 83.3, 93.0, 127.6, 127.6, 127.7, 127.8, 127.9, 128.1, 128.2, 128.3, 128.4, 137.6, 137.9, 138.0, 138.3 ppm. API-ES (positive): m/z = 602.0 $[M + Na]^+$. $C_{35}H_{37}N_3O_5$ (579.7): calcd. C 72.52, H 6.43, N 7.25; found C 72.27, H 6.34, N 7.17.

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[1] Reviews: [1a] Y. Du, R. J. Linhardt, I. R. Vlahov, *Tetrahedron* **1998**, *54*, 9913−9959. [1b] J.-M. Beau, T. Gallagher, *Top. Curr. Chem.* **1997**, *187*, 1−54. [1c] F. Nicotra, *Top. Curr. Chem.* **1997**, *187*, 55−83. [1d] P. Sinaÿ, *Pure Appl. Chem.* **1997**, *69*, 459−464. [1e] M. H. D. Postema, *C-Glycoside Synthesis*, CRC Press: Boca Raton, **1995**. [1f] D. E. Levy, C. Tang, *The Chemistry of C-Glycosides*, Pergamon: Oxford, **1995**. [1g] C. Jaramillo, S. Knapp, *Synthesis* **1994**, 1−20. [1h] M. H. D. Postema, *Tetrahedron* **1992**, *48*, 8545−8599. [1i] S. Hanessian, A. G. Pernet, *Adv. Carbohydr. Chem. Biochem.* **1976**, *33*, 111−188. [1j] W. A. Bonner, *Adv. Carbohydr. Chem. Biochem.* **1951**, *6*, 251−289.

[2] [2a] J. Kihlberg, M. Elofsson, *Curr. Med. Chem.* **1997**, *4*, 85−116. [2b] R. V. Weatherman, L. L. Kiessling, *J. Org. Chem.* **1996**, *61*, 534−538. [2c] R. V. Weatherman, K. H. Mortell, M. Chervenak, L. L. Kiessling, E. J. Toone, *Biochemistry* **1996**, *35*, 3619−3624.

[3] M. D. Lewis, J. K. Cha, Y. Kishi, *J. Am. Chem. Soc.* **1982**, *104*, 4976−4978.

[4] [4a] U. Hacksell, G. D. Daves, *Prog. Med. Chem.* **1985**, *22*, 1−65. [4b] K. Suzuki, *Pure Appl. Chem.* **1994**, *66*, 2175−2178.

[5] These compounds are the *C*-glycosides of keto sugars. See: T. F. Tam, B. Fraser-Reid, *J. Org. Chem.* **1980**, *45*, 1344−1346.

[6] L. A. Paquette, M. J. Kinney, U. Dullweber, *J. Org. Chem.* **1997**, *62*, 1713−1722.

[7] [7a] C. S. Wilcox, G. W. Long, H. Suh, *Tetrahedron Lett.* **1984**, *25*, 395−398. [7b] J. Dupuis, B. Giese, J. Hartung, M. Leising, H.-G. Korth, R. Sustmann, *J. Am. Chem. Soc.* **1985**, *107*, 4332−4333. [7c] T. V. RajanBabu, G. S. Reddy, *J. Org. Chem.* **1986**, *51*, 5458−5461. L. Lay, F. Nicotra, L. Panza, G. Russo, E. Cavena, *J. Org. Chem.* **1992**, *57*, 1304−1306. [7d] K. Tomooka, H. Yamamoto, T. Nakai, *J. Am. Chem. Soc.* **1996**, *118*, 3317−3318. [7e] H. Streicher, A. Geyer, R. R. Schmidt, *Chem. Eur. J.* **1996**, *2*, 502−510. [7f] D. Turner, P. Vogel, *Synlett* **1998**, 304−306. [7g] F. Carrel, P. Vogel, *Tetrahedron: Asymmetry* **2000**, *11*, 4661−4680. [7h] G. Matsuo, M. Hiroko, N. Hori, T. Nakata, *Tetrahedron Lett.* **2000**, *41*, 7673−7676.

[8] [8a] J.-P. Praly, Z. El-Kharraf, G. Descotes, *J. Chem. Soc., Chem. Commun.* **1990**, 431−432. [8b] J.-P. Praly, Z. El-Kharraf, G. Descotes, *Tetrahedron Lett.* **1990**, *31*, 4441−4442.

[9] [9a] R. Meuwly, A. Vasella, *Helv. Chim. Acta* **1989**, *69*, 751−760. [9b] K. Briner, A. Vasella, *Helv. Chim. Acta* **1989**, *72*, 1371−1382. [9c] A. Vasella, C. A. A. Waldraff, *Helv. Chim. Acta* **1991**, *74*, 585−593. [9d] C. Waldraff, B. Bernet, A. Vasella, *Helv. Chim. Acta* **1997**, *80*, 1882−1900.

[10] The most common ulosonic acids are *N*-acetylneuraminic acid (NANA), 3-deoxy-D-glycero-D-*galacto*-2-nonulosonic acid (KDN), and 3-deoxy-D-*manno*-2-octulosonic acid (KDO).

[11] [11a] D. W. Norbeck, J. B. Kramer, P. A. Lartey, *J. Org. Chem.* **1987**, *52*, 2174−2179. [11b] K. Luthman, M. Orbe, T. Waglund, A. Claesson, *J. Org. Chem.* **1987**, *52*, 3777−3784. [11c] D. Crich, L. B. L. Lim, *Tetrahedron Lett.* **1990**, *31*, 1897−1900. [11d] H. Paulsen, P. Matschulat, *Liebigs Ann. Chem.* **1991**, 487−495. [11e] K. Wallimann, A. Vasella, *Helv. Chim. Acta* **1991**, *74*, 1520−1532. [11f] J. O. Nagy, M. D. Bernadsky, *Tetrahedron Lett.* **1991**, *32*, 3953−3956. [11g] A. Poveda, J. L. Asensio, T. Polat, H. Bazin, R. J. Linhardt, J. Jiménez-Barbero, *Eur. J. Org.*

Chem. **2000**, 1805−1814. [11h] Q. Wang, M. Wolff, T. Polat, Y. Du, R. J. Linhardt, *Bioorg. Med. Chem. Lett.* **2000**, *10*, 941−944. [11i] M. Koketsu, B. Kuberan, R. J. Linhardt, *Org. Lett.* **2000**, *2*, 3361−3363. [11j] H. G. Bazin, Y. Du, T. Polat, R. J. Linhardt, *J. Org. Chem.* **1999**, *64*, 7254−7259. [11k] Y. Du, T. Polat, R. J. Linhardt, *Tetrahedron Lett.* **1998**, *39*, 5007−5010. [11l] T. Polat, Y. Du, R. J. Linhardt, *Synlett* **1998**, 1195−1196. [11m] I. R. Vlahov, P. I. Vlahova, R. J. Linhardt, *J. Am. Chem. Soc.* **1997**, *119*, 1480−1481. [11n] T. Kuribayashi, Y. Mizuno, S. Gohya, S. Satoh, *J. Carbohydr. Chem.* **1999**, *18*, 371−382. [11o] W. Notz, C. Hartel, B. Waldscheck, R. R. Schmidt, *J. Org. Chem.* **2001**, *66*, 4250−4260.

[12] [12a] D. Rouzaud, P. Sinaÿ, *J. Chem. Soc., Chem. Commun.* **1983**, 1353−1354. [12b] J.-M. Lancelin, P. H. A. Zollo, P. Sinaÿ, *Tetrahedron Lett.* **1983**, *24*, 4833−4836. [12c] G. A. Kraus, M. T. Molina, J. A. Walling, *J. Chem. Soc., Chem. Commun.* **1986**, 1568−1569. [12d] G. A. Kraus, M. T. Molina, J. A. Walling, *J. Org. Chem.* **1987**, *52*, 1273−1276. [12e] S. A. Babirad, Y. Wang, Y. Kishi, *J. Org. Chem.* **1987**, *52*, 1370−1372. [12f] R. Bihovsky, C. Selick, I. Giusti, *J. Org. Chem.* **1988**, *53*, 4026−4031. [12g] S. M. Daly, R. W. Armstrong, *Tetrahedron Lett.* **1989**, *30*, 5713−5716. [12h] S. Czernecki, G. Ville, *J. Org. Chem.* **1989**, *54*, 610−612. [12i] Kopka, I. E, *Tetrahedron Lett.* **1990**, *31*, 4711−4714. [12j] K. Tatsuta, H. Ozeki, M. Yamaguchi, M. Tanaka, T. Okui, *Tetrahedron Lett.* **1990**, *31*, 5495−5498. [12k] J.-I. Sakaki, Y. Sugita, M. Sato, C. Kaneoko, *Tetrahedron* **1991**, *47*, 6197−6214. [12l] R. Tsang, B. Fraser-Reid, *J. Org. Chem.* **1992**, *57*, 1065−1067. [12m] A. Dondoni, A. Marra, M.-C. Scherrmann, *Tetrahedron Lett.* **1993**, *34*, 7323−7326. [12n] F. Nicotra, L. Panza, G. Russo, A. Verani, *Tetrahedron: Asymmetry* **1993**, *4*, 1203−1204. [12o] V. A. Boyd, B. E. Drake, G. A. Sulikowski, *J. Org. Chem.* **1993**, *58*, 3191−3193. [12p] D. P. Sutherlin, R. W. Armstrong, *Tetrahedron Lett.* **1993**, *34*, 4897−4900. [12q] M. E. Lasterra Sánchez, V. Michelet, I. Besnier, J. P. Genêt, *Synlett* **1994**, 705−708. [12r] J. Alzeer, C. Cai, A. Vasella, *Helv. Chim. Acta* **1995**, *78*, 242−264. [12s] J. Alzeer, A. Vasella, *Helv. Chim. Acta* **1995**, *78*, 177−193. [12t] E. Ayadi, S. Czernecki, J. Xie, *Chem. Commun.* **1996**, 347−348. [12u] E. Alvarez, R. Pérez, M. Rico, R. M. Rodríguez, J. D. Martin, *J. Org. Chem.* **1996**, *61*, 3003−3016. [12v] C. Toedter, H. Lackner, *Liebigs Ann. Org. Bioorg. Chem.* **1996**, 1385−1394. [12w] W. Zheng, J. A. DeMattei, J.-P. Wu, J. J.-W. Duan, L. R. Cook, H. Oinuma, Y. Kishi, *J. Am. Chem. Soc.* **1996**, *118*, 7946−7968. [12x] K. C. Nicolaou, M. H. D. Postema, E. W. Yue, A. Nadin, *J. Am. Chem. Soc.* **1996**, *118*, 10335−10336. [12y] M. Kiffe, D. Schummer, G. Hoefle, *Liebigs Ann. Org. Bioorg. Chem.* **1997**, 245−252. [12z] L. Cipolla, F. Nicotra, E. Vismara, M. Guerrini, *Tetrahedron* **1997**, *53*, 6163−6170.[12aa] Z. J. Witczak, R. Chhabra, J. Chojnacki, *Tetrahedron Lett.* **1997**, *38*, 2215−2218. [12ab] W. M. Best, V. Ferro, J. Harle, R. V. Stick, D. Tilbrook, G. Matthew, *Aust. J. Chem.* **1997**, *50*, 463−472. [12ac] T. Yoshimitsu, J. J. Song, G.-Q. Wang, S. Masamune, *J. Org. Chem.* **1997**, *62*, 8978−8979. [12ad] T. Takahashi, S. Ebata, H. Yamada, *Synlett* **1998**, 381−382. [12ae] S. R. Pulley, J. P. Carey, *J. Org. Chem.* **1998**, *63*, 5275−5279. [12af] M. Sasaki, H. Fuwa, M. Inoue, K. Tachibana, *Tetrahedron Lett.* **1998**, *39*, 9027−9030. [12ag] L. A. Paquette, D. Pissarnitski, L. Barriault, *J. Org. Chem.* **1998**, *63*, 7389−7398. [12ah] T. Lowary, M. Meldal, A. Helmboldt, A. Vasella, K. Bock, *J. Org. Chem.* **1998**, *63*, 9657−9668. [12ai] A. G. M. Barrett, A. J. Bennett, S. Menzer, M. L. Smith, A. J. P. White, D. J. Williams, *J. Org. Chem.* **1999**, *64*, 162−171. [12aj] K. Fujiwara, K. Saka, D. Takaoka, A. Murai, *Synlett* **1999**, 1037−1040. [12ak] L. A. Paquette, L. Barriault, D. Pissarnitski, *J. Am. Chem. Soc.* **1999**, *121*, 4542−4543. [12al] Y.-C. Xin, Y.-M. Zhang, J.-M. Mallet, C. P. J. Glaudemans, P. Sinaÿ, *Eur. J. Org. Chem.* **1999**, 471−476. [12am] T. Saleh, G. Rousseau, *Synlett* **1999**, 617−619. [12an] D. A. Evans, P. H. Carter, E. M. Carreira, A. B. Charette, J. A. Prunet, M. Lautens, *J. Am. Chem. Soc.* **1999**, *121*, 7540−7552. [12ao] S. D. Debenham, J. Cossrow, E. J. Toone, *J. Org. Chem.* **1999**, *64*, 9153−9163. [12ap] C. Fuganti, S. Serra, *Synlett* **1999**, 1241−1242. [12aq] L. A. Paquette, L. Barriault, D. Pissarnitski, J. N. Johnston, *J. Am. Chem. Soc.* **2000**, *122*, 619−631. [12ar] S. D. Debenham, E. J. Toone, *Tetrahedron: Asymmetry* **2000**, *11*, 385−388. [12as] G. Matsuo, H. Hinou, H. Koshino, T. Suenaga, T. Nakata, *Tetrahedron Lett.* **2000**, *41*, 903−906. [12at] T.-Z. Liu, B. Kirschbaum, M. Isobe, *Synlett* **2000**, 587−590. [12au] A. Dondoni, A. Marra, C. Pasti, *Tetrahedron: Asymmetry* **2000**, *11*, 305−318. [12av] R. Saeeng, M. Isobe, *Heterocycles* **2001**, *54*, 789−798. [12av] K. V. S. N. Murty, A. Vasella, *Helv. Chim. Acta* **2001**, *84*, 939−963. [12aw] A. Dondoni, P. P. Giovannini, A. Marra, *J. Chem. Soc., Perkin Trans. 1* **2001**, 2380−2388. [12ax] H. H. A. M. Hassan, A. H. F. El-Husseiny, *Pol. J. Chem.* **2001**, *75*, 803−812. [12ay] S. Takahashi, T. Nakata, *J. Org. Chem.* **2002**, *67*, 5739−5752.

[13] T. Oishi, Y. Nagumo, M. Hirama, *Chem. Commun.* **1998**, 1041−1042.

[14] [14a] J. C. López, A. M. Gómez, B. Fraser-Reid, *J. Org. Chem.* **1995**, *60*, 3871−3878. [14b] A. M. Gómez, M. Casillas, S. Valverde, J. C. López, *Chem. Commun.* **1996**, 2357−2358.

[15] Lewis acid-catalyzed C-glycosidation of furanosydic methyl ketals has been reported. See: [15a] C. S. Wilcox, G. W. Long, H. Suh, *Tetrahedron Lett.* **1984**, *25*, 395−398. [15b] F. Nicotra, L. Panza, G. Russo, *J. Org. Chem.* **1987**, *52*, 5627−5630. [15c] H. Suh, C. S. Wilcox, *J. Am. Chem. Soc.* **1988**, *110*, 470−481. [15d] T. Hosokawa, F. Nakajima, S. Iwasa, S.-I. Murahashi, *Chem. Lett.* **1990**, 1387−1390. [15e] D. J. O'Leary, Y. Kishi, *J. Org. Chem.* **1994**, *59*, 6629−6636.

[16] Lewis acid-catalyzed allylation of furanosydic hemiketals has been reported. See: [16a] C. Brueckner, H. Lorey, H.-U. Reissig, *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 556−557. [16b] J. Barluenga, L. Llavona, M. Yus, J. M. Concellón, *Tetrahedron* **1991**, *47*, 7875−7886. In this paper, the reaction with silyl enol ethers was reported to be unsuccessful.

[17] B. Waldscheck, M. Streiff, W. Notz, W. Kinzy, R. R. Schmidt, *Angew. Chem. Int. Ed.* **2001**, *40*, 4007−4011.

[18] F. Schweizer, A. Otter, O. Hindsgaul, *Synlett* **2001**, 1743−1746.

[19] T. Yamamoi, Y. Oda, *Heterocycles* **2002**, 57, 229−234.

[20] F. Scheizer, A. Lohse, A. Otter, O. Hindsgaul, *Synlett* **2001**, 1434−1436.

[21] A preliminary communication of this work has already appeared. See: A. M. Gómez, C. Uriel, S. Valverde, S. Jarosz, J. C. López, *Tetrahedron Lett.* **2002**, *43*, 8935−8940.

[22] X. Li, H. Ohtake, H. Takahashi, S. Ikegami, *Tetrahedron* **2001**, *57*, 4297−4309.

[23] [23a] A. Borbás, G. Szabovik, Z. Antal, K. Fehér, M. Csávás, L. Szilágyi, P. Herczegh, A. Lipták, *Tetrahedron: Asymmetry* **2000**, *11*; 549−566. [23b] R. Benhaddou, S. Czernecki, W. Farid, G. Ville, J. Xie, A. Zegar, *Carbohydr. Res.* **1994**, *260*, 243−250. [23c] H. Kuzuhara, H. G. Fletcher, *J. Org. Chem.* **1967**, *32*, 2531−2534.

[24] P. Moeller, *Justus Liebigs Ann. Chem.* **1972**, *755*, 191−193.

[25] An authentic sample of methyl ketoside **27** was prepared from **11** by treatment with MeOH (10 equiv.) in CH_2Cl_2 in the presence of boron trifluoride−diethyl ether.

[26] X. Li, H. Ohtake, H. Takahashi, S. Ikegami, *Tetrahedron* **2001**, *57*, 4283−4295.

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