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Stereoselective synthesis of *C*-ketosides by Lewis acid-catalyzed *C*-glycosylation of alkynyl-ketoses

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Abstract—*C*-Ketosides are conveniently prepared in a stereoselective manner from alkynyl-ketoses by reaction with carbon nucleophiles in the presence of a Lewis acid.

C-glycosides (**1**)[1] (Fig. 1) have become attractive targets for research since they are stable analogs of glycans involved in important intra- and inter-cellular processes with 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 or bis-*C*,*C*-glycosides (**2**),[5] have not found similar favor,[5,6] although methods for the preparation of spirocyclic *C*-ketosides[7] and *C*-glycosides of ulosonic acids[8] have been reported by several groups.[9]

One of the most commonly employed method for the synthesis of *C*-glycosides, based in the pioneering work of Kishi and collaborators,[3] is shown in Scheme 1. It involves the addition of an organometallic reagent to a sugar lactone (**3**) followed by subsequent reduction of the resulting lactol, **4**, by treatment with a Lewis acid in the presence of silicon hydride. Furthermore, as the hydride nucleophile is generally delivered to the axial position, these reactions constitute a very reliable method to produce β-*C*-glycosides (at least with *gluco*- and *galacto*-pyranosides).[10,11]

As a continuation of our interest in the synthesis of *C*-glycosides,[12] we turned our attention to the synthesis of *C*-ketosides as a class of *C*-glycoside analogs with potential biological activity. We hypothesized that a Lewis acid catalyzed *C*-glycosylation of hemiketals, **4**, could efficiently lead to *C*-ketopyranosides, **2** (Scheme 2).

In fact, although Lewis acid catalyzed *C*-glycosylations of glycosyl halides, glycosyl acetates, glycosides and aldoses, have been thoroughly exploited for the synthesis of *C*-glycosides,[1c] we were not aware of any report which would correlate sugar pyrano-lactones (**3**) with bis-*C*,*C*-glycopyranosides (**2**) via the corresponding lactols, **4** which would involve reaction of with a carbon nucleophile in the presence of a Lewis acid (Scheme

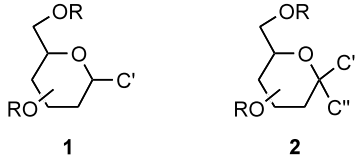
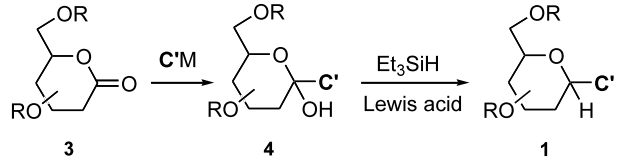
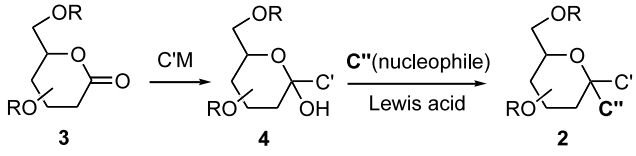


Figure 1. *C*-Glycosides and *C*-ketosides.



Scheme 1. Synthesis of *C*-glycosides from sugar lactones.



Scheme 2. Synthesis of *C*-ketosides from sugar lactones.

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2).[13–15] However, ketose-hemiacetals (e.g. **4**) have been utilized by the Schmidt's group in the preparation of *C*-ketosides, via reaction of open-chain intermediates.[16]

In this letter we disclose our results in the preparation of *C*-ketopyranosides by the Lewis acid mediated *C*-glycosylation of readily available hemiketals of type **4**.

As starting materials in our study we used glucose-derived hemiketals **7** and **8**[10c] (Fig. 2), readily available from aldonolactones **5**[10b,17] and **6**.[17a,18] As nucleophilic partners we tested allylsilanes, propargylsilanes, silylenol ethers, silyl cyanides and azides, and electron rich aromatic compounds.

Our results from the reaction of **7** with carbon nucleophiles in the presence of boron trifluoride etherate are shown in Table 1. Reaction with allyltrimethylsilane (**9**) (entry 1) led to *C*-ketoglucoside **10** (70%) (entry 1). The stereochemistry at C-1, in compound **10**; was expected to be the one shown in Table 1, assuming an axial approach of the nucleophile to the anomeric carbenium ion, in keeping with literature precedents,[3] and further proved by the existence of a NOE between the allylic protons and the axially disposed H-3 as shown in Table 1. The reaction of **7** with phenyl-1-(trimethylsilyloxy)ethylene (**11**) afforded *C*-ketoside **12** (entry 2). Trimethyl silyl cyanide and azide reacted smoothly with **7** to yield *C*- and *N*-ketosides **13** and **14**, respectively, in good yields. 1,3,5-Trimethoxybenzene (**15**) reacted with **7** to furnish open chain bis-arylated compound **16**, as the major product. However, 1,4-dimethoxybenzene (**17**) and (trimethylsilyl)acetylene failed to yield any *C*-ketoside upon reaction with **7**. In the latter reactions (entries 6, 7) methylketoside **18**[19] was isolated as the major reaction product.

Table 2 summarizes the reactions carried out with hemiketal **8**, in which more synthetically useful, benzyl protecting groups had been installed, with *C*-nucleophiles. Compound **8** showed similar behavior to that displayed by **7**. Reaction of **8** with allylsilane (**9**) and 1-phenyl-1-(trimethylsilyloxy)ethylene (**11**) yielded the corresponding *C*-ketosides **19** and **20** in moderate yields. Reaction of **8**, with 1,3,5-trimethoxybenzene (**15**) (entry 3) afforded bis-arylated open-chain compound **21** as the major product. Treatment of **8** with 1,4-dimethoxybenzene (**17**) was again unsuccessful to yield any *C*-ketosylated product (entry 4) and only benzyl glucoside **23** could be isolated from the reaction mixture.

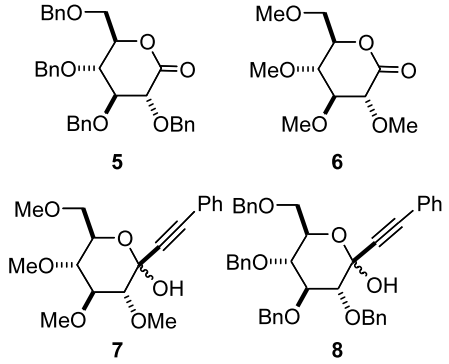


Figure 2.

Table 1. Preparation of bis-*C*,*C*-glucopyranosides from hemiketal **7** catalyzed by $BF_3{\cdot}Et_2O$

Entry	Reagent	Temp. °C (reaction time)	Product	Yield (%)
1	$SiMe_3$ **9**	-30(1h)	**10**	70
2	Ph, $OSiMe_3$ **11**	-15(1h)	**12**	47 (61)[b]
3	$NC\text{-}SiMe_3$	-40 (2h)	**13**	64
4	$N_3\text{-}SiMe_3$	-40 (3h)	**14**	70
5	MeO, OMe, OMe **15**	-30 (3h)	**16**	49
6	OMe, OMe **17**	-30[a]	**18**	48
7	$SiMe_3$	-30[a]	**18**	38

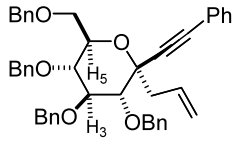
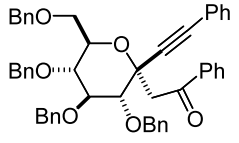
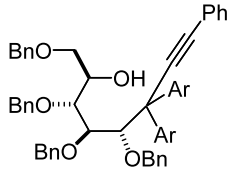
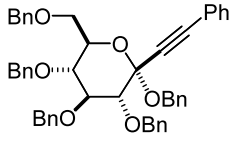
[a]Several other reaction temperatures and Lewis acids ($SnCl_4$, BF_4H) were also used although with no significant variations in terms of yields were observed.

[b]Based on 23% recovered starting material.

Ar =

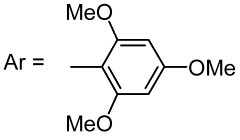
Lewis acid-catalyzed *C*-glycosylation of hemiketals **7** and **8** takes place via an stabilized anomeric oxonium ion (e.g. **A**, Scheme 3) which react efficiently with allyltrimethylsilane, 1-phenyl-1-(trimethylsilyloxy)-ethylene, and silyl cyanide. Electron rich aromatic

Table 2. Preparation of bis-*C*,*C*-glucopyranosides from hemiketal **8** catalyzed by $BF_3{\cdot}Et_2O$

Entry	Reagent	Temp. °C (reaction time)	Product	Yield (%)
1	**9**	-30	 **19**	67
2	**11**	-40 to 0 (2h)	 **20**	33 (42[a])
3	**15** (3 equiv)	-30 (2h)	 **21**	51
4	**17**	-30[b]	 **22**	26

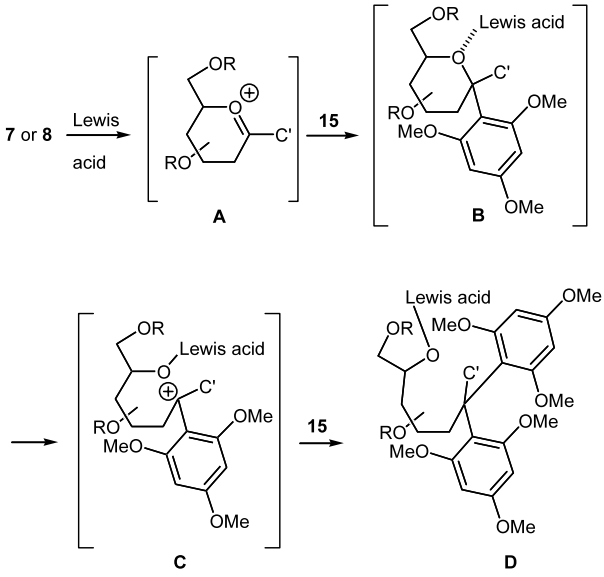
[a]Based on 23% recovered starting material

[b]Several other reaction temperatures and Lewis acids ($SnCl_4$, BF_4H) were also used although with no significant variations in terms of yields were observed.



compounds, e.g. **15**, also behaved as *C*-nucleophiles although the main observed reaction course was the formation of bis-arylated open chain derivatives (**16** and **21**). The formation of bis-arylated compounds (Type **D**, Scheme 3) can be easily rationalized since the intermediate *C*-ketoside (**B**) would be prone to undergo *C*1–*O* cleavage to form a propargyl, benzyl cation (e.g. **C**) which could react further with **12** to generate structures type **D**.

The difference in behavior between 1,3,5-trimethoxybenzene (**15**), which was able to react with the oxonium ion (**A**), and 1,4-dimethoxybenzene (**17**) which did not yield any *C*-glycosylated product (compare entry 6 with entry 5 in Table 1 entry 3 with entry 4 in Table 2) is also of interest. The formation of methyl- and benzyl-glycosides was observed when methyl or benzyl protected hemiketals were treated with not reactive enough



Scheme 3. Reaction of hemiketals **7** and **8** with **15**.

C-nucleophiles (entries 6, 7, Table 1; entry 4 Table 2). Neither of the hemiketals gave any coupled product with trimethylsilylacetylene.

The configurational assignment at *C*-1 for the *C*-ketosides prepared in this study, was inferred from the fact that only one isomeric *C*-ketoglucopyranoside was obtained in each case, and that literature precedents were consistent with an axial attack of the nucleophile onto oxocarbenium ions in derivatives with *gluco*-configuration. The stereochemistry at *C*-1 in compound **10**, vide supra, was also in support of this assumption. Furthermore, NOEs were also observed in compounds **12** and **19** between H-5 and H-3 with the corresponding axially disposed anomeric methylene groups.

In summary we have disclosed herein a novel and concise strategy for the stereocontrolled preparation of *C*-ketosides by Lewis acid-catalyzed *C*-glycosylation of alkynyl-glucopyranose hemiketals. As nucleophilic partners, two silanes and one silyl enol–ether has been successfully employed. One electron rich aromatic compound yielded a open chain bis-arylated compound. Trimethyl silyl azide led efficiently to the corresponding *N*-ketopyranoside. This approach represents an extension of the method by Kishi and co-workers,[3] in which the nucleophile utilized was a hydride, for the stereocontrolled synthesis of β-*C*-glycosides, and permits a rapid correlation between ketones and *C*-ketosides.[20–22]

Acknowledgements

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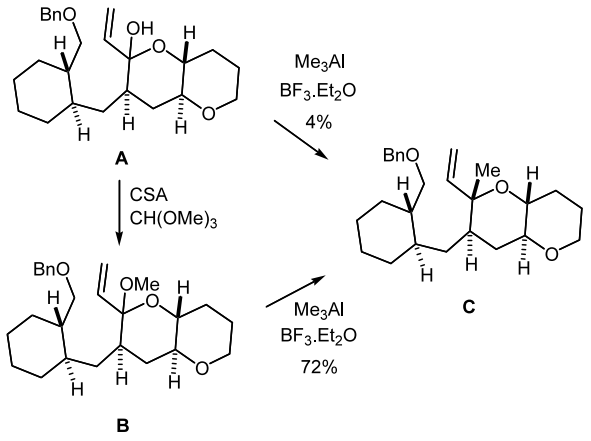
References

1. Reviews: (a) Du, Y.; Linhardt, R. J.; Vlahov, I. R. *Tetrahedron* **1998**, *54*, 9913; (b) Beau, J.-M.; Gallagher, T. *Topics Curr. Chem.* **1997**, *187*, 1; (c) Nicotra, F. *Topics Curr. Chem.* **1997**, *187*, 55; (d) Sinaÿ, P. *Pure Appl. Chem.* **1997**, *69*, 459; (e) Postema, M. H. D. In *C-Glycoside Synthesis*; CRC press: Boca Raton, 1995; Levy, D. E.; Tang, C. *The Chemistry of* C-*Glycosides*; Pergamon: Oxford, 1995; (f) Jaramillo, C.; Knapp, S. *Synthesis*, **1994**, 1; (g) Postema, M. H. D. *Tetrahedron* **1992**, *48*, 8545; (h) Buchanan, J. G. *Prog. Chem. Org. Nat. Prod.* **1983**, *9*, 415; (i) Hanessian, S.; Pernet, A. G. *Adv. Carbohydr. Chem. Biochem.* **1976**, *33*, 111. Bonner, W. A. *Adv. Carbohydr. Chem. Biochem.* **1951**, *6*, 251.
2. (a) Kihlberg, J.; Elofsson, M. *Curr. Med. Chem.* **1997**, *4*, 85; (b) Weatherman, R. V.; Kiessling, L. L. *J. Org. Chem.* **1996**, *61*, 534; (c) Weatherman, R. V.; Mortell, K. H.; Chervenak, M.; Kiessling, L. L.; Toone, E. J. *Biochemistry* **1996**, *35*, 3619.
3. Lewis, M. D.; Cha, J. K.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 4976.
4. (a) Hacksell, U.; Daves, G. D. *Prog. Med. Chem.* **1985**, *22*, 1; (b) Suzuki, K. *Pure Appl. Chem.* **1994**, *66*, 2175.
5. These are the *C*-glycosides of keto sugars: Tam, T. F.; Fraser-Reid, B. *J. Org. Chem.* **1980**, *45*, 1344.
6. (a) Dupuis, J.; Giese, B.; Hartung, J.; Leising, M.; Korth, H. G.; Sustmann, R. *J. Am. Chem. Soc.* **1985**, *107*, 4332; (b) RajanBabu, T. V.; Reddy, G. S. *J. Org. Chem.* **1986**, *51*, 5458; (c) Lay, L.; Nicotra, F.; Panza, L.; Russo, G.; Cavena, E. *J. Org. Chem.* **1992**, *57*, 1304; (d) Tomooka, K.; Yamamoto, H.; Nakai, T. *J. Am. Chem. Soc.* **1996**, *118*, 3317; (e) Streicher, H.; Geyer, A.; Schmidt, R. R. *Chem. Eur. J.* **1996**, *2*, 502; (f) Turner, D.; Vogel, P. *Synlett* **1998**, 304; (g) Carrel, F.; Vogel, P. *Tetrahedron: Asymmetry* **2000**, *11*, 4661; (h) Matsuo, G.; Hiroko, M.; Hori, N.; Nakata, T. *Tetrahedron Lett.* **2000**, *41*, 7673.
7. (a) Praly, J.-P.; El-Kharraf, Z.; Descotes, G. *J. Chem. Soc., Chem. Commun.* **1990**, 431; (b) Praly, J.-P.; El-Kharraf, Z.; Descotes, G. *Tetrahedron Lett.* **1990**, *31*, 4441; (c) Paquette, L. A.; Kinney, M. J.; Dullweber, U. *J. Org. Chem.* **1997**, *62*, 1713; (d) Waldraff, C.; Bernet, B.; Vasella, A. *Helv. Chim. Acta* **1997**, *80*, 1882 and references cited therein.
8. 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*).
9. (a) Norbeck, D. W.; Kramer, J. B.; Lartey, P. A. *J. Org. Chem.* **1987**, *52*, 2174; (b) Luthman, K.; Orbe, M.; Waglund, T.; Claesson, A. *J. Org. Chem.* **1987**, *52*, 3777; (c) Crich, D.; Lim, L. B. L. *Tetrahedron Lett.* **1990**, *31*, 1897; (d) Paulsen, H.; Matschulat, P. *Liebigs Ann. Chem.* **1991**, 487; (e) Wallimann, K.; Vasella, A. *Helv. Chim. Acta* **1991**, *74*, 1520; (f) Nagy, J. O.; Bernadsky, M. D. *Tetrahedron Lett.* **1991**, *32*, 3953; (g) Bazin, H. G.; Du, Y.; Polat, T.; Linhardt, R. J. *J. Org. Chem.* **1999**, *64*, 7254; (h) Kuribayashi, T.; Mizuno, Y.; Gohya, S.; Satoh, S. *J. Carbohydr. Chem.* **1999**, *18*, 371; (i) Bazin, H. G.; Du, Y.; Polat, T.; Linhardt, R. J. *J. Org. Chem.* **1999**, *64*, 7254; (j) Poveda, A.; Asensio, J. L.; Polat, T.; Bazin, H.; Linhardt, R. J.; Jiménez-Barbero, J. *Eur. J. Org. Chem.* **2000**, 1805; (k) Wang, Q.; Wolff, M.; Polat, T.; Du, Y.; Linhardt, R. J. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 941; (l) Koketsu, M.; Kuberan, B.; Linhardt, R. J. *Org. Lett.* **2000**, *2*, 3361; (m) Notz, W.; Hartel, C.; Waldscheck, B.; Schmidt, R. R. *J. Org. Chem.* **2001**, *66*, 4250.
10. Selected references: (a) Rouzaud, D.; Sinaÿ, P. *J. Chem. Soc., Chem. Commun.* **1983**, 1353; (b) Kraus, G. A.; Molina, M. T.; Walling, J. A. *J. Org. Chem.* **1987**, *52*, 1273; (c) Bihovsky, R.; Selick, C.; Giusti, I. *J. Org. Chem.* **1988**, *53*, 4026; (d) Daly, S. M.; Armstrong, R. W. *Tetrahedron Lett.* **1989**, *30*, 5713; (e) Czernecki, S.; Ville, G. *J. Org. Chem.* **1989**, *54*, 610; (f) Tsang, R.; Fraser-Reid, B. *J. Org. Chem.* **1992**, *57*, 1065; (g) Dondoni, A.; Marra, A.; Scherrmann, M.-Ch. *Tetrahedron Lett.* **1993**, *34*, 7323; (h) Nicotra, F.; Panza, L.; Russo, G.; Verani, A. *Tetrahedron: Asymmetry* **1993**, *4*, 1203; (i) Lasterra Sánchez, M. E.; Michelet, V.; Besnier, I.; Genêt, J. P. *Synlett* **1994**, 705; (j) Alzeer, J.; Cai, C.; Vasella, A. *Helv. Chim. Acta* **1995**, *78*, 242; (k) Zheng, W.; DeMattei, J. A.; Wu, J.-P.; Duan, J. J.-W.; Cook, L. R.; Oinuma, H.; Kishi, Y. *J. Am. Chem. Soc.* **1996**, *118*, 7946; (l) Nicolaou, K. C.; Postema, M. H. D.; Yue, E. W.; Nadin, A. *J. Am. Chem. Soc.* **1996**, *118*, 10335; (m) Pulley, S. R.; Carey, J. P. *J. Org. Chem.* **1998**, *63*, 5275; (n) Lowary, T.; Meldal, M.; Helmboldt, A.; Vasella, A.; Bock, K. *J. Org. Chem.* **1998**, *63*, 9657; (o) Barrett, A. G. M.; Bennett, A. J.; Menzer, S.; Smith, M. L.; White, A. J. P.; Williams, D. J. *J. Org. Chem.* **1999**, *64*, 162; (p) Fujiwara, K.; Saka, K.; Takaoka, D.; Murai, A. *Synlett* **1999**, 1037; (q) Paquette, L. A.; Barriault, L.; Pissarnitski, D. *J. Am. Chem. Soc.* **1999**, *121*, 4542; (r) Xin, Y.-C.; Zhang, Y.-M.; Mallet, J.-M.; Glaudemans, C. P. J.; Sinaÿ, P. *Eur. J. Org. Chem.* **1999**, 471; (s) Saleh, T.; Rousseau, G. *Synlett* **1999**, 617; (t) Evans, D. A.; Carter, P. H.; Carreira, E. M.; Charette, A. B.; Prunet, J. A.; Lautens, M. *J. Am. Chem. Soc.* **1999**, *121*, 7540; (u) Debenham, S. D.; Cossrow, J.; Toone, E. J. *J. Org. Chem.* **1999**, *64*, 9153; (v) Fuganti, C.; Serra, S. *Synlett* **1999**, 1241; (w) Paquette, L. A.; Barriault, L.; Pissarnitski, D.; Johnston, J. N. *J. Am. Chem. Soc.* **2000**, *122*, 619; (x) Debenham, S. D.; Toone, E. J. *Tetrahedron: Asymmetry* **2000**, *11*, 385; (y) Matsuo, G.; Hinou, H.; Koshino, H.; Suenaga, T.; Nakata, T. *Tetrahedron Lett.* **2000**, *41*, 903; (z) Liu, T.-Z.; Kirschbaum, B.; Isobe, M. *Synlett* **2000**, 587; (aa) Dondoni, A.; Marra, A.; Pasti, C. *Tetrahedron: Asymmetry* **2000**, *11*, 305; (ab) Dondoni, A.; Mariotti, G.; Marra, A.; Massi, A. *Synthesis* **2001**, 2129.
11. Oishi, T.; Nagumo, Y.; Hirama, M. *Chem. Commun.* **1998**, 1041.
12. (a) López, J. C.; Gómez, A. M.; Fraser-Reid, B. *J. Org. Chem.* **1995**, *60*, 3871; (b) Gómez, A. M.; Casillas, M.; Valverde, S.; López, J. C. *Chem. Commun.* **1996**, 2357.
13. To the best of our knowledge, only one example of Lewis acid-catalyzed *C*-glycosylation of pyranosydic lactols type **4**, has been reported[11] in which, methylation of hemiketal **A**, gave *C*-ketoside, **C**, only in low yield (4%), whereas methylation of the corresponding methyl acetal, **B**, under the same reaction conditions gave **C** in good yield.



14. Lewis acid-catalyzed *C*-glycosylation of furanosydic methyl ketals has been reported: Wilcox, C. S.; Long, G. W.; Suh, H. *Tetrahedron Lett*. **1984**, *25*, 395; Nicotra, F.; Panza, L.; Russo, G. *J. Org. Chem*. **1987**, *52*, 5627; Suh, H.; Wilcox, C. S. *J. Am. Chem. Soc*. **1988**, *110*, 470; Hosokawa, T.; Nakajima, F.; Iwasa, S.; Murahashi, S.-I. *Chem. Lett*. **1990**, 1387; O'Leary, D. J.; Kishi, Y. *J. Org. Chem*. **1994**, *59*, 6629.
15. Lewis acid-catalyzed allylation of furanosydic hemiketals has been reported: (a) Brückner, C.; Lorey, H.; Reissig, H.-U. *Angew. Chem., Int. Ed. Engl*. **1986**, *25*, 556; (b) Barluenga, J.; Llavona, L.; Yus, M.; Concellón, J. M. *Tetrahedron*, **1991**, *47*, 7875. However, their reaction with silyl enol ethers was reported to be unsuccessful.[16a]
16. (a) Streicher, H.; Geyer, A.; Schmidt, R. R. *Chem. Eur. J*. **1996**, *2*, 502; (b) Waldscheck, B.; Streiff, M.; Notz, W.; Kinzy, W.; Schmidt, R. R. *Angew. Chem., Int. Ed. Engl*. **2001**, *40*, 4007.
17. Aldono lactone **5**: (a) Borbás, A.; Szabovik, G.; Antal, Z.; Fehér, K.; Csávás, M.; Szilágyi, L.; Herczegh, P.; Lipták, A. *Tetrahedron: Asymmetry* **2000**, *11*; 549; (b) Benhaddou, R.; Czernecki, S.; Farid, W.; Ville, G.; Xie, J.; Zegar, A. *Carbohydr. Res*. **1994**, *260*, 243; (c) Kuzuhara, H.; Fletcher, H. G. *J. Org. Chem*. **1967**, *32*, 2531.
18. Aldonolactone **6**: (a) Moeller, P. *Justus Liebigs Ann. Chem*. **1972**, *755*, 191; (b) Purdie, T.; Irvine, J. C. *J. Chem. Soc*. **1903**, *83*, 1033.
19. An authentic sample of methyl ketoside, **17**, was prepared from **7** by treatment with methanol (10 equiv.) in CH_2Cl_2 in the presence of boron trifluoride etherate.
20. After this work was underway two closely related papers appeared: Schweizer, F.; Otter, A.; Hindsgaul, O. *Synlett* **2001**, 1743; Gasch, C.; Pradera, M. A.; Salameh, B. A. B.; Molina, J. L.; Fuentes, J. *Tetrahedron: Asymmetry* **2001**, *12*, 1267.
21. *General procedure for the Lewis acid-catalyzed C-glycosylation of ketoses*: To a solution of the hemiketal in anhydrous CH_2Cl_2 (20 ml/mmol), cooled to the appropriate temperature (see Tables 1 and 2) and under argon, BF_3OEt_2 (0.5 equiv. unless otherwise noted) and the corresponding nucleophile (1.5 equiv. unless otherwise noted) were added. The resulting solution was stirred until consumption of the starting material was observed (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 over anhydrous $MgSO_4$, filtrated and concentrated. Flash chromatography of the residue gave the corresponding *C*-ketoside.
22. *Data for selected compounds*: *(2,3,4,6-tetra-O-methyl-1-C-allyl-1-C-(2-phenyl-ethynyl)-β-D-glucopyranose* (**10**). (75 mg, 70%): $\alpha_D = -22.5°$ ($CHCl_3$, *c* 0.6); ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.67 (m, 2H), 3.21–3.70 (m, 6H), 3.39 (s, 3H), 3.56 (s, 3H), 3.66 (s, 3H), 3.70 (s, 3H), 5.18 (m, 2H), 6.04 (m, 1H), 7.30 (m, 3H), 7.43 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 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; API-ES positive: 383.1 $(M+Na)^+$, 361.3 $(M+H)^+$. Anal. calcd for $C_{21}H_{28}O_5$: C, 69,98; H, 7.83. Found: C, 69.73; H, 7.94. *(2,3,4,6-Tetra-O-methyl-1-C-(2-phenyl-ethynyl)-1-C-(2-oxo-2-phenyl-ethyl)-β-D-glucopyranose* (**12**). $\alpha_D = +12.3°$ ($CHCl_3$, *c* 1.2); ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 3.01 (d, 1H, $J = 15.0$ Hz), 3.34–3.88 (m, 6H), 3.41 (s, 3H), 3.57 (s, 3H), 3.68 (s, 3H), 3.74 (s, 3H), 3.91 (d, 1H, $J = 15$ Hz), 6.97–8.07 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 37.0, 59.1, 60.3, 60.7, 61.6, 70.9, 72.7, 74.3, 79.5, 84.7, 86.2, 86.7, 89.7, 122.1, 127.9, 128.0, 128.3, 128.4, 128.9, 131.6, 132.7, 138.2, 197.1; MS (EI) *m/z*: 439.2 $(M+H)^+$. Anal. calcd for $C_{26}H_{30}O_6$: C, 71.21; H, 6.90. Found: C, 71.53; H, 6.74. *Bis-arylated compound* **16**: $\alpha_D = -96.1°$ ($CHCl_3$, *c* 0.6); ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 3.05 (s, 3H), 3.22 (s, 3H), 3.26 (s, 3H), 3.57 (s, 3H), 3.73 (s, 3H), 3.77 (s, 3H), 3.45 (s, 3H), 3.58 (s, 3H), 3.10–3.78 (m, 6H), 4.36 (d, 1H, $J = 5.5$ Hz), 6.07 (s, 2H), 6.09 (s, 2H), 7.02–7.38 (m, 7H); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 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; API-ES positive: 677.6 $(M+Na)^+$. Anal. calcd for $C_{60}H_{62}O_{11}$: C, 75.14; H, 6.52. Found: C, 75.01; H, 6.84. *(2,3,4,6-Tetra-O-benzyl-1-C-allyl-1-C-(2-phenyl-ethynyl)-β-D-glucopyranose* (**19**). $\alpha_D = -16.8°$ ($CHCl_3$, *c* 0.4); ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.70 (d, 2H, $J = 6.9$ Hz), 3.65–4.00 (m, 6H), 4.42 (d, 1H, $J = 12.0$ Hz), 4.43 (d, 1H, $J = 10.5$ Hz), 4.56 (d, 1H, $J = 12.0$ Hz), 4.71 (d, 1H, $J = 10.5$ Hz), 4.72 (d, 1H, $J = 10.8$ Hz), 4.75 (d, 1H, $J = 9.9$ Hz), 4.80 (d, 1H, $J = 10.8$ Hz), 4.99 (d, 1H, $J = 10.8$ Hz), 5.08 (dd, 2H, $J = 1.2$, 13.5 Hz), 6.04 (ddt, 1H, $J = 10.2$, 10.5 and 14.5 Hz), 7.16 (m, 25H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 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, 127.9, 128.0, 128.2, 128.3, 128.3, 128.4, 128.4, 131.7, 132.50, 138.0, 138.2, 138.3, 138.6; API-ES positive: 665.4 $(M+Na)^+$. Anal. calcd for $C_{45}H_{44}O_5$: C, 81.30; H, 6.67. Found: C, 80.98; H, 6.44. *(2,3,4,6-Tetra-O-benzyl-1-C-(2-phenyl-ethynyl)-1-C-(2-oxo-2-phenylethyl)-β-D-glucopyranose* (**20**). $\alpha_D = -35.1°$ ($CHCl_3$, *c* 2.0); ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 3.26 (d, 1H, $J = 13.5$ Hz), 3.78–4.06 (m, 7H), 4.53 (d, 1H, $J = 11.9$ Hz), 4.59 (d, 1H, $J = 10.7$ Hz,), 4.74 (d, 1H, $J = 12.1$ Hz), 4.83 (d, 1H, $J = 10.9$ Hz), 4.87 (d, 1H, $J = 11.2$ Hz), 4.93 (d, 1H, $J = 10.6$ Hz), 4.94 (d, 1H, $J = 10.9$ Hz), 5.08 (d, 1H, $J = 10.6$ Hz), 6.96–8.06 (m, 30H, Ar); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm): 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, 128.3,

128.3, 128.4, 128.5, 129.0, 131.6, 132.8, 138.1, 138.2, 138.5, 197.0; MS (EI) m/z: 743.2 $(M+H)^+$, 765.3 $(M+Na)^+$. Anal. calcd for $C_{50}H_{46}O_6$: C, 80.84; H, 6.24. Found: C, 80.67; H, 6.41. *Bis-arylated compound* **21**: $\alpha_D = +57.19°$ ($CHCl_3$, *c* 1.0); ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 3.49 (s, 6H) 3.80 (s, 3H), 3.85 (s, 3H), 3.40–3.88 (m, 4H), 3.94 (d, 1H, $J = 11.4$ Hz), 4.07 (dd, 1H, $J = 2.6$, 6.0 Hz), 4.24 (d, 1H, $J = 11.4$ Hz), 4.43 (d, 1H, $J = 12.2$ Hz), 4.50 (d, 1H, $J = 11.4$ Hz), 4.72 (d, 1H, $J = 12.0$ Hz), 4.80 (d, 1H, $J = 11.4$ Hz), 4.86 (d, 1H, $J = 6.0$ Hz), 4.97 (d, 1H, $J = 11.4$ Hz), 6.07 (s, 2H), 6.12 (s, 2H), 6.97–7.47 (m, 25H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 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, 127.4, 127.4, 127.6, 127.8, 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;); MS (CI) m/z: 982.4 $(M+Na)^+$. Anal. calcd for $C_{60}H_{62}O_{11}$: C, 75.14; H, 6.52. Found: C, 74.86; H, 6.74.