

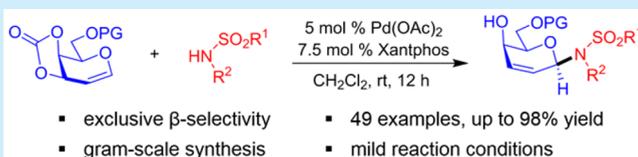
General Strategy for Stereoselective Synthesis of β -*N*-Glycosyl Sulfonamides via Palladium-Catalyzed Glycosylation

Yuanwei Dai, Jianfeng Zheng, and Qiang Zhang*¹

Department of Chemistry, University at Albany, State University of New York, 1400 Washington Avenue, Albany, New York 12222, United States

S Supporting Information

ABSTRACT: A highly efficient and mild glycosylation reaction between 3,4-*O*-carbonate glycal and *N*-tosyl functionalized aliphatic and aromatic amines via palladium-catalyzed decarboxylative allylation is disclosed. A wide range of highly functionalized 2,3-unsaturated β -*N*-glycosides are furnished in good to excellent yields and complete regioselectivity and stereoselectivity. In addition, applications of the glycosyl sulfonamides as the precursor to assemble functional derivatives have also been explored, including glycosylation, dihydroxylation, and nucleophilic addition to the *N*-glycosides.



Investigations into the stereoselective construction of *N*-glycosides have drawn significant attention, because of the ubiquity of their scaffolds in glycoproteins and medically relevant compounds.¹ Synthetic studies toward *N*-glycosidic bond formation in sulfonamidoglycosides² have garnered great interest, because of the promising antitumor,³ antiviral,⁴ and other biological activities of such compounds.⁵ Among all the synthetic strategies, research on the Ferrier glycosylation has proven practical for efficient sulfonamidoglycoside preparation.⁶ (see Figure 1) However, most of the reported methods

ular, the palladium-catalyzed Tsuji–Trost reaction¹¹ has enabled expansion of the classic Ferrier rearrangement in *N*-glycosylation. Trost,^{12b} O’Doherty,^{12c} Nguyen,^{12d,e} and Liu^{12g,h} have delicately demonstrated the production of *N*-glycosides facilitated by palladium complexes, and they are believed to proceed via π -allyl intermediates. However, methodologies for the efficient and stereoselective preparation of sulfonamidoglycosides remain limited. Herein, we describe a mild and highly efficient Pd-catalyzed glycosylation strategy for the β -stereoselective synthesis of 2,3-unsaturated *N*-glycosyl sulfonamides from readily available 3,4-*O*-carbonate glycals.

Our initial studies began with the screening of a series of commercially available palladium catalysts for their ability to promote the Ferrier-type stereoselective *N*-glycosylation of the 3,4-*O*-carbonate galactal **1a** with benzenesulfonamide **1b** as the acceptor in the presence of 5 mol % catalyst loading, with 15 mol % Ph₃P as the ligand in dichloromethane at ambient temperature. As summarized in Table 1, among the palladium catalysts that we examined, Pd(TFA)₂, Pd(Ph₃P)₂Cl₂, and Pd(PhCN)₂Cl₂ failed to catalyze the reaction (entries 1, 2, and 4 in Table 1). Pd(Ph₃P)₄ and Pd₂(dba)₃ successfully furnished the desired sulfonamidoglycoside in 40% and 36% yields, respectively, with incomplete conversion of **1a** (entries 5 and 6 in Table 1). Pd(OAc)₂ was found to be the best catalyst and afforded **1c** in 48% yield. It is worth noting that both Pd(II) and Pd(0) catalysts were found to produce β -selective adducts exclusively (>30:1). Because the ligands play a critical role in stabilizing and activating the central metal atom and fine-tuning the selectivity of the transformation, in our attempts to optimize the yield, a series of commercially available monodentate and bidentate phosphine ligands were surveyed. Among the ligands that we examined, *t*-Bu₃P, DPPE, DPPP,

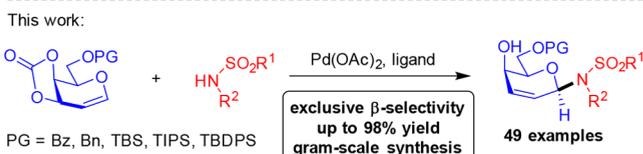
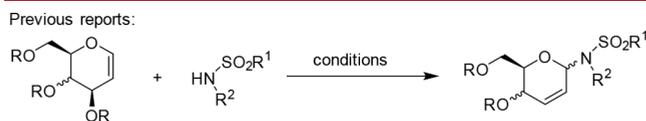
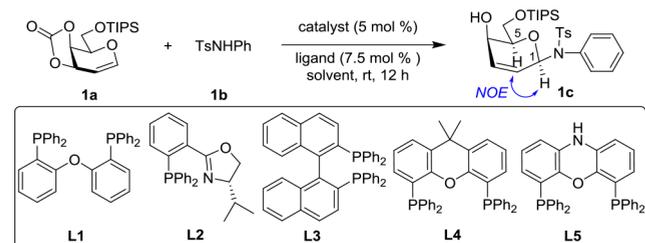


Figure 1. Pd-catalyzed β -selective *N*-glycosylation of 3,4-*O*-carbonate glycals.

require reagents such as BF₃·OEt₂,^{7b,e} RuCl₃,^{7f} iodine,^{7g} Zn(OTf)₂,^{7h} and Er(OTf)₃⁷ⁱ to facilitate the transformations. These conditions generally provide modest stereoselectivities, except for the report from the Colinas group,⁸ where they elegantly realized the synthesis of 2-deoxy- β -glycosyl sulfonamides from benzylated glycals using triphenylphosphine hydrobromide. Recently, palladium-catalyzed stereoselective glycosylation has been developed and applied in the synthesis of complex oligosaccharides and glycoconjugates.^{9,10} In partic-

Received: May 12, 2018

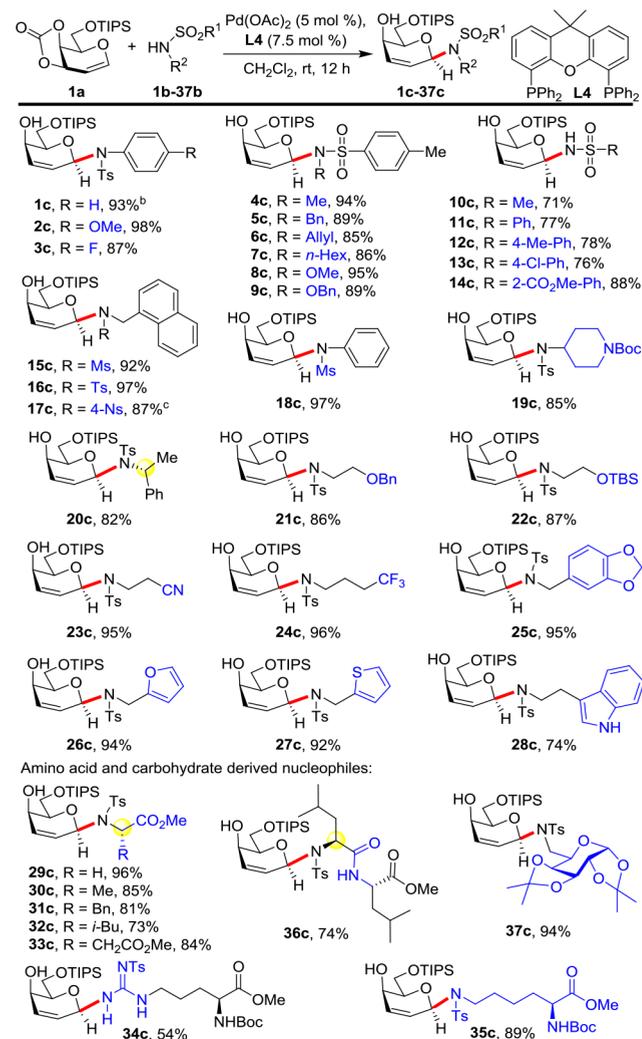
Table 1. Reaction Optimization for the *N*-Glycosylation^a

entry	ligand	catalyst	solvent	yield ^b (%)	β/α ^c
1	Ph ₃ P	Pd(TFA) ₂	CH ₂ Cl ₂	0	ND ^d
2	Ph ₃ P	Pd(PhCN) ₂ Cl ₂	CH ₂ Cl ₂	0	ND ^d
3	Ph ₃ P	Pd(OAc) ₂	CH ₂ Cl ₂	48	>30:1
4	Ph ₃ P	Pd(Ph ₃ P) ₂ Cl ₂	CH ₂ Cl ₂	0	ND ^d
5 ^e	Ph ₃ P	Pd ₂ (dba) ₃	CH ₂ Cl ₂	36	>30:1
6	Ph ₃ P	Pd(Ph ₃ P) ₄	CH ₂ Cl ₂	40	>30:1
7	<i>t</i> -Bu ₃ P	Pd(OAc) ₂	CH ₂ Cl ₂	0	ND ^d
8	dppf	Pd(OAc) ₂	CH ₂ Cl ₂	0	ND ^d
9	dppp	Pd(OAc) ₂	CH ₂ Cl ₂	0	ND ^d
10	dppf	Pd(OAc) ₂	CH ₂ Cl ₂	14	>30:1
11	L1	Pd(OAc) ₂	CH ₂ Cl ₂	29	>30:1
12	L2	Pd(OAc) ₂	CH ₂ Cl ₂	0	ND ^d
13	L3	Pd(OAc) ₂	CH ₂ Cl ₂	0	ND ^d
14	L4	Pd(OAc) ₂	CH ₂ Cl ₂	98 (93 ^f)	>30:1
15	L5	Pd(OAc) ₂	CH ₂ Cl ₂	87	>30:1
16		Pd(OAc) ₂	CH ₂ Cl ₂	0	ND ^d
17	L4	Pd(OAc) ₂	THF	46	>30:1
18	L4	Pd(OAc) ₂	ClCH ₂ CH ₂ Cl	57	>30:1
19	L4	Pd(OAc) ₂	toluene	35	>30:1
20 ^g	L4	Pd(OAc) ₂	CH ₂ Cl ₂	88 (84 ^f)	>30:1

^aUnless otherwise specified, all reactions were carried out with 0.1 mmol of glycal **1a**, 0.15 mmol of benzenesulfonamide **1b** in 2 mL solvent, 5 mol % Pd catalyst, 15 mol % monodentate phosphine ligands or 7.5 mol % bidentate phosphine ligands were used. ^bYield determined by crude ¹H NMR using CH₂Br₂ as an internal standard. ^c β/α ratio determined by crude ¹H NMR. ^dNot determined. ^e2.5 mol % Pd₂(dba)₃ was used. ^fIsolated yield. ^g2 mol % Pd(OAc)₂ and 3 mol % of L4 were used.

L2, and L3 failed to promote the reaction, and with more than 95% of starting materials being recovered (entries 7–9, 12, and 13 in Table 1). Bidentate ligands, DPPPE, L1, and L5 were able to activate the glycal, and **1c** was obtained in low to good yields (14%–87%). The optimized conditions were achieved by using Xantphos L4 as the ligand, which produced **1c** in 93% yield and exclusive β -selectivity (entry 14 in Table 1).¹³ A strong NOESY correlation between H-1 (δ_{H} 6.27) and H-5 (δ_{H} 3.76) of **1c** was observed in CDCl₃, confirming the β configuration of the glycosidic bond.¹⁴ Next, we explored solvent effects and catalyst loadings. The use of tetrahydrofuran, dichloroethane, or toluene proved to be detrimental to the reaction (entries 17–19 in Table 1). We believe that the high yield of dichloromethane contributes to its moderately polar and noncoordinating solvent properties.¹⁵ Furthermore, lowering the loading of Pd(OAc)₂ to 2 mol % and L4 to 3 mol % maintained a decent yield and β -stereocontrol (entry 20 in Table 1). However, no product was detected without using ligand (entry 16 in Table 1).

After establishing the optimized reaction conditions, our substrate scope investigation turned to the coupling between galactal donor **1a** and various sulfonamide nucleophiles (see Scheme 1). We found that anilines could be introduced with

Scheme 1. Substrate Scope^a

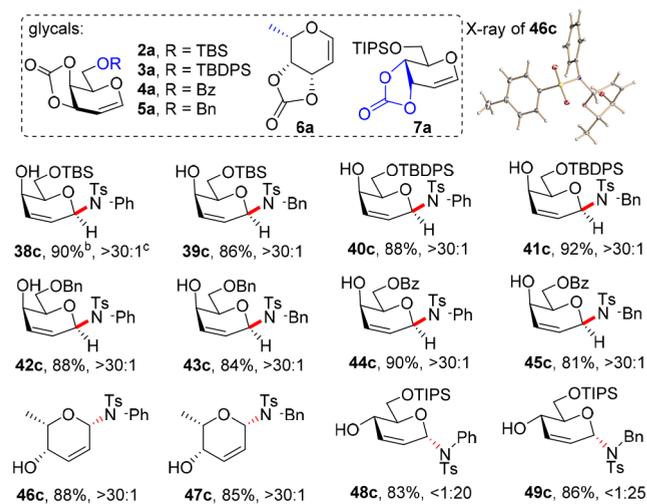
^aReaction conditions: glycal **1a** (0.1 mmol), sulfonamides (0.15 mmol), Pd(OAc)₂ (5 mol %), L4 (7.5 mol %), CH₂Cl₂ (2 mL). All β/α ratios were more than 30:1, which were determined by crude ¹H NMR. ^bIsolated yield. ^cReaction performed at 40 °C.

high yields and excellent β -stereoselectivity (**1c-3c**). Simple aliphatic amines such as methyl, allyl, and hexamine were well-tolerated (**4c-7c**). Hydroxylamine is an important molecule in biology that serves as an intermediate in the nitrogen cycle. Hydroxylamine derivatives provided the *N*-glycosides in high yields (**8c, 9c**). We also found that primary sulfonamides could be introduced in good yields. Aromatic substituents with an electron-donating methyl group and electron-withdrawing chloro and ester groups at different positions were well-tolerated (**10c-14c**). Naphthylmethylamine with different sulfonyl groups, such as Ts, Ms, and 4-Ns, provided the corresponding glycosides in excellent yields (**15c-17c**). In addition, disubstituted amines and chiral amines furnished products in decent yields (**19c, 20c**). Notably, amines with functional groups such as NBoc, OBn, OTBS, CN, CF₃ all generated the desired adducts in high yields (**21c-24c**). Heterocyclic amines and piperonylamine, which are commonly used in drug discovery, proved to be suitable substrates to produce the corresponding products in excellent yields (**25c-28c**). Encouraged by this success, we shifted our focus to the

amino-acid-derived nucleophiles with α -stereocenters. To our delight, those nucleophiles smoothly underwent *N*-glycosylation without epimerization (**29c–33c**). Furthermore, a Leu-Leu dipeptide-derived nucleophile furnished the desired glycopeptide **36c** in satisfactory yield. Notably, glycosylation of amino acid side chains could be efficiently achieved in one step. Arginine¹⁶ and lysine side-chain-derived nucleophiles afforded the desired *N*-glycosides in moderate to good yield (**34c**, **35c**). The structure of **34c** was determined by NOESY and TOCSY spectra.¹⁴ Finally, our galactose-derived substrate **37b** provided the *N*-linked disaccharide **37c** with excellent yield and stereoselectivity.

To explore the scope of the glycal donors, a range of differentially protected *D*-galactal, *L*-fucal, and *D*-allal bearing silyl ether, benzyl, benzoate protecting groups were prepared. Glycal donors (**2a–7a**) were subjected to the optimized reaction conditions with sulfonamides **1b** and **5b** as glycosyl acceptors (Scheme 2). The change of protecting group to TBS

Scheme 2. Scope of the Glycal Donors^a

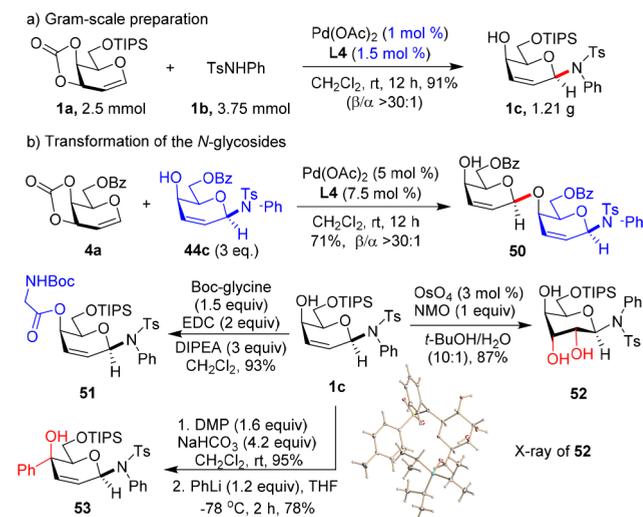


^aReaction conditions: glycal (0.1 mmol), sulfonamides (0.15 mmol), Pd(OAc)₂ (5 mol %), **L4** (7.5 mol %), CH₂Cl₂ (2 mL). ^bIsolated yield. ^c β/α ratio was determined by crude ¹H NMR.

or TBDPS at C6 did not alter the stereoselectivity outcome of the adducts. When the 6-*O*-protecting group was replaced by a much smaller Bn or Bz, good to excellent yields (81%–90%) and exclusive selectivity were obtained for the formation of β -linked glycosides ($\beta/\alpha > 30:1$) (**42c–45c**). Both armed benzyl groups and disarmed benzoate groups were well-tolerated. When *L*-fucal **6a** was applied as the donor, β -*N*-glycoside could be obtained as the only product (**46c**, **47c**). The stereochemistry of the anomeric center was confirmed by X-ray diffraction (XRD) crystallographic analysis. These results indicate that stereoselectivity of the glycosylation is not determined by the C6 steric effect. *D*-Allal (**7a**) was also evaluated, and the coupling of **7a** with sulfonamide acceptors afforded the corresponding glycosides in good yields with high α -stereocontrol (**48c**, **49c**).

To demonstrate the synthetic value of this work, we first attempted the transformation of **1a** with **1b** on a 2.5 mmol scale with 1 mol % catalyst loading, which afforded the *N*-glycoside **1c** in 91% yield and good β -stereocontrol (see Scheme 3a). Furthermore, application of 2,3-unsaturated *N*-glycosyl sulfonamides as the precursor to assemble potentially

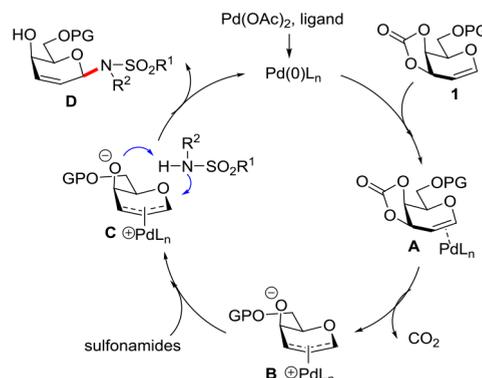
Scheme 3. Synthetic Applications of the Glycosyl Sulfonamides



bioactive derivatives was also explored. Glycosylation on 4-OH of the *N*-glycoside **44c** with galactal donor **4a** under the established reaction conditions afforded the desired disaccharide **50** in 71% yield with excellent β -stereoselectivity (see Scheme 3b). EDC-mediated esterification of *N*-glycoside **1c** was performed with Boc-glycine to provide **51** in 93% yield. Moreover, treatment of **1c** with OsO₄ and *N*-methylmorpholine-*N*-oxide afforded the corresponding triol **52** in 87% yield as a single diastereomer, which gave access to a chiral scaffold that could be further developed as a medically active compound. The structure of **52** was confirmed by X-ray analysis. The result indicates that dihydroxylation occurred at the less-hindered α -face of **1c**. In addition, **1c** was subjected to a Dess–Martin oxidation to yield an enone sugar in excellent yield. Subsequent nucleophilic addition of the ketone using phenyllithium furnished **53** in 78% yield as a single diastereomer.

Based on the experimental results and the classic Tsuji–Trost reaction mechanism,¹¹ a plausible reaction mechanism is outlined in Scheme 4. Initially, reduction of Pd(II) acetate provided Pd(0), which is subsequently complexed with the ligand.¹⁷ The Pd(0) complex coordinates to the double bond of glycal **1** from less sterically demanding α -face to form a η^2 - π -allyl Pd(0) species **A**. Next, an oxidative addition, during which the carbonate group is expelled, produces a η^3 - π -allyl-Pd(II)

Scheme 4. Proposed Mechanism



moiety **B**. Subsequently, nucleophilic addition by soft nucleophile sulfonamides^{11d,18} generates the β -*N*-glycoside **D** with a net retention of stereochemistry.

In summary, we have successfully developed a highly efficient approach for the catalytic β -stereoselective synthesis of 2,3-unsaturated glycosyl sulfonamides from readily available 3,4-*O*-carbonate glycals and sulfonamides. This reaction was based on a palladium-catalyzed decarboxylative allylation. Various *N*-nucleophiles were examined during the study and afforded the corresponding 2,3-unsaturated β -*N*-glycosides in excellent yields and exclusive regioselectivity and stereoselectivity ($\beta/\alpha > 30:1$). In addition, this method employs mild reaction conditions, is amenable to gram-scale synthesis, and shows excellent functional group compatibility. Moreover, further functionalization of sulfonamidoglycosides by glycosylation, dihydroxylation, and nucleophilic addition has been successfully applied. Overall, our reported Pd-catalyzed, stereoselective *N*-glycosylation protocol provides a powerful tool for the access of glycosyl sulfonamides in practical quality and quantities that could enable biological evaluations of this class of substrates. Studies toward the synthesis of complex *N*-glycosides using our approach will be reported in due course.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.8b01506.

Experimental procedures and analysis data for all new compounds (PDF)

■ Accession Codes

CCDC 1826601 and CCDC 1833027 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.; fax: +44 1223 336033.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: qzhang5@albany.edu.

ORCID

Qiang Zhang: 0000-0003-2787-1781

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Support for this work was provided by the National Science Foundation (Nos. CHE 1710174 and MRI 1337594), and the University at Albany–SUNY to Q.Z. Thanks are extended to Prof. Alexander Shekhtman (University at Albany–SUNY) for NMR structure elucidation. We thank Dr. Zheng Wei (University at Albany–SUNY) for single-crystal structure determination and analysis. We thank Prof. David Crich (Wayne State University) for helpful suggestions.

■ REFERENCES

(1) (a) Gamblin, D. P.; Scanlan, E. M.; Davis, B. G. *Chem. Rev.* **2009**, *109*, 131. (b) Unverzagt, C.; Kajihara, Y. *Chem. Soc. Rev.* **2013**,

42, 4408. (c) Wilson, R. M.; Dong, S.; Wang, P.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2013**, *52*, 7646.

(2) (a) Srivastava, A.; Varghese, B.; Loganathan, D. *Chem. - Eur. J.* **2013**, *19*, 17720. (b) Suthagar, K.; Polson, M. J.; Fairbanks, A. J. *Org. Biomol. Chem.* **2015**, *13*, 6573.

(3) (a) Colinas, P. A.; Bravo, R. D.; Vullo, D.; Scozzafava, A.; Supuran, C. T. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 5086. (b) Wilkinson, B. L.; Bornaghi, L. F.; Houston, T. A.; Innocenti, A.; Vullo, D.; Supuran, C. T.; Poulsen, S. A. *J. Med. Chem.* **2007**, *50*, 1651. (c) Winum, J.-Y.; Thiry, A.; El Cheikh, K.; Dogne, J. M.; Montero, J. L.; Vullo, D.; Scozzafava, A.; Masereel, B.; Supuran, C. T. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 2685.

(4) Mitsuya, H.; Yarchoan, R.; Broder, S. *Science* **1990**, *249*, 1533.

(5) (a) Winum, J. Y.; Montero, J. L.; Scozzafava, A.; Supuran, C. T. *Mini-Rev. Med. Chem.* **2006**, *6*, 921. (b) Winum, J. Y.; Poulsen, S.-A.; Supuran, C. T. *Med. Res. Rev.* **2009**, *29*, 419.

(6) For reviews of Ferrier glycosylation, see: (a) Ferrier, R. J. *Top. Curr. Chem.* **2001**, *215*, 153. (b) Gómez, A. M.; Lobo, F.; Uriel, C.; López, J. C. *Eur. J. Org. Chem.* **2013**, *2013*, 7221.

(7) (a) Chandrasekhar, S.; Reddy, C. R.; Chandrashekar, G. *Tetrahedron Lett.* **2004**, *45*, 6481. (b) Colinas, P. A.; Bravo, R. D. *Carbohydr. Res.* **2007**, *342*, 2297. (c) Témpera, C. A.; Colinas, P. A.; Bravo, R. D. *Tetrahedron Lett.* **2010**, *51*, 5372. (d) Ding, F.; William, R.; Gorityala, B. K.; Ma, J.; Wang, S.; Liu, X.-W. *Tetrahedron Lett.* **2010**, *51*, 3146. (e) Ding, J.-X.; William, R.; Liu, X.-W. *J. Org. Chem.* **2013**, *78*, 1293. (f) Reddy, T. R.; Chittela, S.; Kashyap, S. *Tetrahedron* **2014**, *70*, 9224. (g) Begum, Z.; Kishore, V.; Veerabhadra Reddy, V.; Subba Reddy, B. V. *Tetrahedron Lett.* **2014**, *55*, 6048. (h) Reddy, T. R.; Battina, S. K.; Kashyap, S. *J. Carbohydr. Chem.* **2015**, *34*, 133. (i) Nardi, M.; Cano, N. H.; De Nino, A.; Di Gioia, M. L.; Maiuolo, L.; Oliverio, M.; Santiago, A.; Sorrentino, D.; Procopio, A. *Tetrahedron Lett.* **2017**, *58*, 1721.

(8) Colinas, P. A.; Bravo, R. D. *Org. Lett.* **2003**, *5*, 4509.

(9) For selected examples of palladium-catalyzed O-glycosylation, see: (a) Babu, R. S.; O'Doherty, G. A. *J. Am. Chem. Soc.* **2003**, *125*, 12406. (b) Babu, R. S.; Zhou, M.; O'Doherty, G. A. *J. Am. Chem. Soc.* **2004**, *126*, 3428. (c) Comely, A. C.; Eelkema, R.; Minnaard, A. J.; Feringa, B. L. *J. Am. Chem. Soc.* **2003**, *125*, 8714. (d) Sherry, B. D.; Loy, R. N.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 4510. (e) Kim, H.; Men, H.; Lee, C. *J. Am. Chem. Soc.* **2004**, *126*, 1336. (f) Schuff, B. P.; Mercer, G. J.; Nguyen, H. M. *Org. Lett.* **2007**, *9*, 3173. (g) Zeng, J.; Ma, J.; Xiang, S.; Cai, S.; Liu, X.-W. *Angew. Chem., Int. Ed.* **2013**, *52*, 5134. (h) Xiang, S.; Hoang, K. L. M.; He, J.; Tan, Y.-J.; Liu, X.-W. *Angew. Chem., Int. Ed.* **2015**, *54*, 604. (i) Yao, H.; Zhang, S.-S.; Leng, W.-L.; Leow, M.-L.; Xiang, S.-H.; He, J.-X.; Liao, H.-Z.; Hoang, K. L. M.; Liu, X.-W. *ACS Catal.* **2017**, *7*, 5456. (j) Sau, A.; Williams, R.; Palo-Nieto, C.; Franconetti, A.; Medina, S.; Galan, M. C. *Angew. Chem., Int. Ed.* **2017**, *56*, 3640. (k) Sau, A.; Galan, M. C. *Org. Lett.* **2017**, *19*, 2857.

(10) For recent reviews, see: (a) Ress, D. K.; Linhardt, R. *Curr. Org. Synth.* **2004**, *1*, 31. (b) Crich, D. *Acc. Chem. Res.* **2010**, *43*, 1144. (c) McKay, M. J.; Nguyen, H. M. *ACS Catal.* **2012**, *2*, 1563. (d) Yu, B.; Sun, J.; Yang, X. *Acc. Chem. Res.* **2012**, *45*, 1227. (e) Li, X. H.; Zhu, J. L. *J. Carbohydr. Chem.* **2012**, *31*, 284. (f) Li, X. H.; Zhu, J. L. *Eur. J. Org. Chem.* **2016**, *2016*, 4724. (g) Yu, B. *Acc. Chem. Res.* **2018**, *51*, 507. (h) Leng, W.-L.; Yao, H.; He, J.-X.; Liu, X.-W. *Acc. Chem. Res.* **2018**, *51*, 628.

(11) (a) Tsuji, J. *Pure Appl. Chem.* **1982**, *54*, 197. (b) Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395. (c) Trost, B. M.; Crawley, M. L. *Chem. Rev.* **2003**, *103*, 2921. (d) Trost, B. M.; Thaisrivongs, D. A. *J. Am. Chem. Soc.* **2008**, *130*, 14092. (e) Trost, B. M. *Tetrahedron* **2015**, *71*, 5708.

(12) For palladium-catalyzed *N*-glycosylation, see: (a) Bolitt, V.; Chaguir, B.; Sinou, D. *Tetrahedron Lett.* **1992**, *33*, 2481. (b) Trost, B. M.; Krusche, M. J.; Berl, V.; Grenzer, E. M. *Org. Lett.* **2002**, *4*, 2005. (c) Guppi, S. R.; Zhou, M.-Q.; O'Doherty, G. A. *Org. Lett.* **2006**, *8*, 293. (d) Yang, J.; Mercer, G. J.; Nguyen, H. M. *Org. Lett.* **2007**, *9*, 4231. (e) Mercer, G. J.; Yang, J.; McKay, M. J.; Nguyen, H. M. *J. Am. Chem. Soc.* **2008**, *130*, 11210. (f) Zhang, Q.; Sun, J.; Zhu, Y.; Zhang,

F.; Yu, B. *Angew. Chem., Int. Ed.* **2011**, *50*, 4933. (g) Xiang, S.-H.; He, J.-X.; Ma, J.-M.; Liu, X.-W. *Chem. Commun.* **2014**, *50*, 4222. (h) Ji, L.; Xiang, S.-H.; Leng, W.-L.; Hoang, K. L. M.; Liu, X.-W. *Org. Lett.* **2015**, *17*, 1357.

(13) We do not fully understand why the Xantphos attains superior reactivities, compared with other bidentate phosphine ligands. However, according to the literature, it has been suggested that a wide metal–ligand cone angle between **L4** and Pd enhances oxidative addition and product dissociation, thus accelerating the reaction rate. Please see the related references: (a) van Haaren, R.; Goubitz, K.; Fraanje, J.; van Strijdonck, G.; Oevering, H.; Coussens, B.; Reek, J.; Kamer, P.; van Leeuwen, P. *Inorg. Chem.* **2001**, *40*, 3363. (b) Martinelli, J.; Watson, D.; Freckmann, D.; Barder, T.; Buchwald, S. J. *Org. Chem.* **2008**, *73*, 7102.

(14) See [Supporting Information](#) for structure determination details.

(15) Mong, K.; Nokami, T.; Trana, N.; Be Nhi, P. In *Selective Glycosylations: Synthetic Methods and Catalysts*; Bennett, C. S., Ed.; Wiley–VCH: Weinheim, Germany, 2017; Chapter 3.

(16) (a) Pan, M.; Li, S.; Li, X.; Shao, F.; Liu, L.; Hu, H.-G. *Angew. Chem., Int. Ed.* **2014**, *53*, 14517. (b) Wang, S. Y.; Corcilius, L.; Sharp, P. P.; Rajkovic, A.; Ibba, M.; Parker, B. L.; Payne, R. J. *Chem. Sci.* **2017**, *8*, 2296.

(17) Amatore, C.; Jutand, A.; Thuilliez, A. *Organometallics* **2001**, *20*, 3241.

(18) For pK_a value of sulfonamides, see: (a) Bordwell, F. G.; Algrim, D. J. *Org. Chem.* **1976**, *41*, 2507. (b) Bordwell, F. G.; Harrelson, J. A.; Lynch, T. Y. *J. Org. Chem.* **1990**, *55*, 3337.