Pergamon

Tetrahedron Letters, Vol. 38, No. 4, pp. 543-546, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(96)02367-2

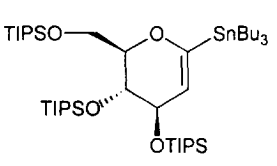
C-Glycosides and C-Disaccharide Precursors Through Carbonylative Stille Coupling Reactions

Vincent Jeanneret, Lieven Meerpoel[1] and Pierre Vogel*

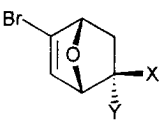
Section de chimie de l'Université de Lausanne, BCH, CH-1015-Lausanne-Dorigny, Switzerland.
e-mail: vincent@icosun5.unil.ch; fax: 41-21-6923975

Abstract: Under CO atmosphere and in the presence of $Pd_2(dba)_3$ and Ph_3As a suitably protected 1-stannylglucal derivative could be carbonylated and coupled to 5-bromo-7-oxabicyclo[2.2.1]hept-5-en-2-yl derivatives. The carbonylative Stille coupling was also successful between 1-iodoglucals and tributyl(vinyl)stannane or tributyl(fur-2-yl)stannane. A cross-conjugated dienone was also obtained through coupling of a 1-stannylglucal with a 1-iodoglucal derivative.

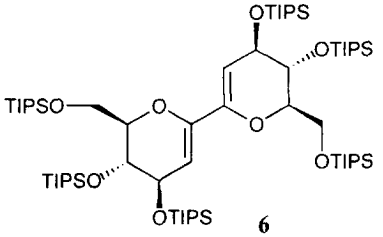
Oligosaccharides play vital roles in intercellular communication and all cell mediated processes.[2,3] Mimics of oligosaccharides such as the C-disaccharides[4] may or may not imitate the physical and biological properties of the corresponding O-glycosides[5]; they present the advantage to resist acidic and enzymatic hydrolysis. This constitutes for these C-glycosides a potential as glycosidase inhibitors and as non-hydrolysable epitopes. Since the first synthesis of a β-(1→6)-C-disaccharide by Rouzaud and Sinaÿ[6] several approaches to the C-disaccharides have been proposed.[4,7] They usually imply multiple step transformations of two sugars, one of them being implemented by a carbon function, subsequent coupling through C-C bond formation and further transformations. We disclose here our preliminary results on a new approach that generates the C-link between two hexose precursors in a single step. The method relies on the carbonylative Stille coupling reaction[8] between 1-stannylglycals and 5-bromo-7-oxabicyclo[2.2.1]hept-5-en-2-yl derivatives obtained readily from the Diels-Alder adducts of furan to 1-cyano-vinyl esters.[9,10] Earlier attempts to carry out anomeric alkylcarbonylations of glycosyl bromides involved the reactions of the corresponding (pentacarbonyl)glycosylmanganese with Michael acceptors under very high pressure.[11,12]



1 TIPS=(*i*-Pr)$_3$Si



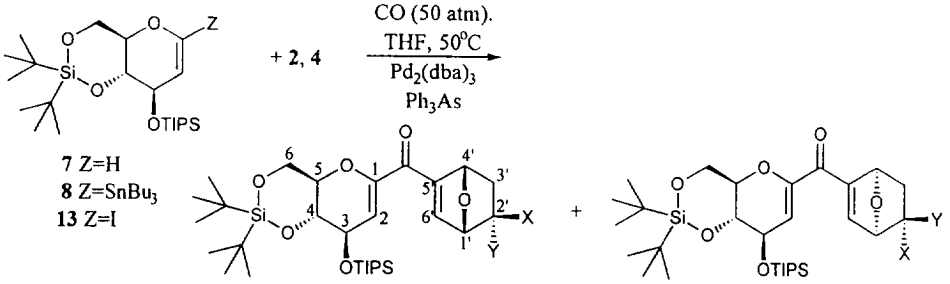
2 X=CN, Y=OAc
3 X, Y=O
4 X, Y=OCH_2CH_2O
5 X=H, Y=OBn
11 X=CN, Y=(1*R*)-camphanoyl



6

In a first series of experiments we treated the known stannylated glucal derivative **1**[13] with racemic 5-bromo-7-oxabicyclo[2.2.1]hept-5-en-2-yl derivatives (±)-**2** - (±)-**5** under CO atmosphere (1-150 atm.) in the presence of a variety of palladium complexes, ligands and solvents [8,14] but we failed to detect any product of carbonylative Stille coupling. In some cases, and as expected for reactions in the absence of CO,[15] we

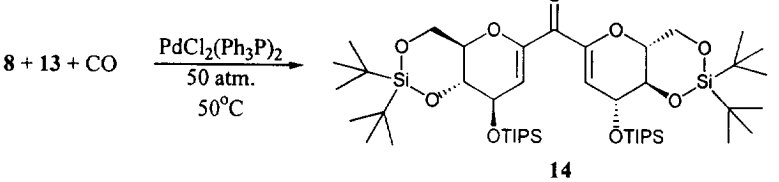
observed the formation of **6** resulting from the Stille homocoupling of **1**. We suspected that the three bulky TIPS protective groups in **1** could impede the carbonylation for steric or/and conformational reasons. We thus converted tri-O-acetyl-D-glucal into **7** via methanolysis (MeONa/MeOH, 25°C, 2 h) of the acetates, followed by silylation first with $(t\text{-Bu})_2Si(OSO_2CF_3)_2$/2,6-lutidine in anhydrous DMF (-50°C, 10 h), then with $(i\text{-Pr})_3SiCl$/imidazole (DMF, 50°C, 24 h). Treatment of **7** with *t*-BuLi,[16] then with Bu_3SnCl furnished **8** (80% based on tri-O-acetyl-D-glucal).



9a X=CN, Y=OAc
10a X, Y=OCH_2CH_2O
12 X=CN, Y=(1*R*)-camphanoyl

9b X=CN, Y=OAc
10b X, Y=OCH_2CH_2O

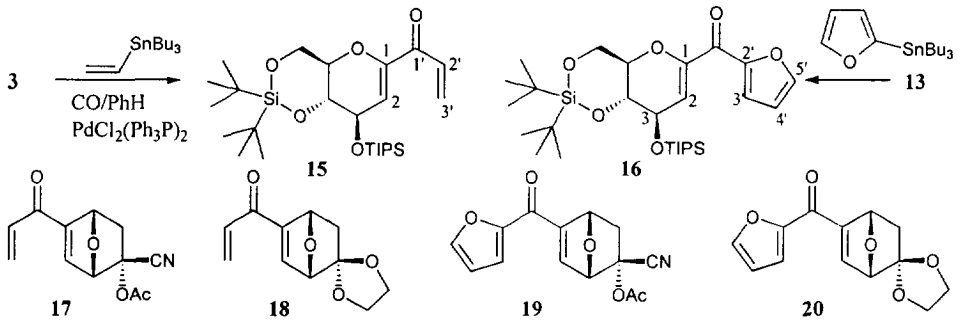
In the presence of 5-10 mol% of $Pd_2(dba)_3$ (dibenzylideneacetone-palladium), 10-20 mol% of Ph_3As in anhydrous THF and under 50 atmospheres of CO at 50°C, 1:1 mixtures of **8** + (±)-**2** and **8** + (±)-**4** led to 1:1 mixtures of **9a/9b** and **10a/10b**, respectively, in 30-55% yield. Applying this process to the enantiomerically pure derivative **11**, dienone **12** was isolated (47%).[17] Replacement of Ph_3As for Ph_3P failed to produce products of carbonylative Stille coupling **9** and **10**. When **8** was treated with 0.5 equiv. of I_2 in CH_2Cl_2 (what generates 0.5 equiv. of 1-iodoglucal **13**) and then pressurized with CO (50 atm.) in the presence of 30% mol of $PdCl_2(Ph_3P)_2$, dienone **14**[18] was obtained in 65% yield.[19]



14

In order to test whether other C-glycosides could be generated through the carbonylative Stille heterocoupling reaction we treated the 1-iodo-D-glucal derivative **13** with commercially available (tributyl)vinylstannane and (tributyl)(fur-2-yl)stannane under CO pressure (50 atm) in benzene, at 60°C and in the presence of $PdCl_2(Ph_3P)_2$. The expected cross-conjugated dienones **15**[20] and **16**[21] were isolated in 71 and 91% yield, respectively. Under similar conditions (THF, 50°C, $Pd(Ph_3P)_4$) 5-bromo-7-oxanorbornenes (±)-**2** and (±)-**4** were coupled with CO and the same stannanes giving the corresponding products of carbonylative heterocoupling **17**, **18**, **19** and **20** in 71, 70, 90 and 90% yield, respectively.

Work in underway in our laboratory to convert the new C-glycosides described in this report to a variety of disaccharide mimics and other compounds of biological interest.[22]



Acknowledgments. We thank the *Swiss National Science Foundation* and *"Les Laboratoires Fournier"* Dijon, France, for generous financial support.

References and Notes

1. Current address: Labo. Organic Synthesis, B 3001 Leuven, Belgium.
2. See e.g.: Feizi, T. *Curr. Opin. Struct. Biol.* **1993**, *3*, 701-710; Varki, A. *Proc. Natl. Acad. Sci. USA.* **1994**, *91*, 7390-7397; Morenem, K. W.; Trimble, R. B.; Hersovics, A. *Glycobiology* **1994**. *4*, 113-125; Glaudemans, C. P. J. *Chem. Rev.* **1991**, *91*, 25-33; Carver, J. P. *Pure & Appl. Chem.* **1993**, *65*, 763-770.
3. Toyokuni, T.; Singhal, A. K. *Chem. Soc. Rev.* **1995**, *24*, 231-242; Rye, P. D.; Bovin, N. V.; Vlasova, E. V.; Walker, R. A. *Glycobiology* **1995**, *5*, 385-389.
4. Levy, D. E.; Tang, C. "The Chemistry of C-Glycosides", Tetrahedron Organic Chemistry Series, Eds.: Baldwin, J. E.; Magnus, P. D. Pergamon-Elsevier, Science Ltd, Oxford, 1995; Postema, M. H. D. *Tetrahedron* **1992**, *48*, 8545-8599; Postema, M. H. D. *C-Glycoside Synthesis*, CRC, Boca Raton, F. L. **1995**.
5. Berthault, P.; Birkirakis, N.; Rubinstenn, G.; Sinaÿ, P.; Desvaux, H. J. *J. Biomolecular NMR.* **1996**, 8, 23-35; Ferritto, R.; Vogel, P. *Tetrahedron Asymmetry* **1994**, *5*, 2077-2092 and ref. cited therein; Wei, A.; Boy, K. M.; Kishi, Y. *J. Am. Chem. Soc.* **1995**, *117*, 9432-9436; Wei A.; Haudrechy A.; Audin C.; Jun H.-S.; Hauderchy-Bretel N.; Kishi Y. *J. Org. Chem.* **1995**, *60*, 2160-2169. Espinosa, J.-F.; Cañada, F. J.; Asencio, J. L.; Martín-Pastor, M.; Dietrich, H.; Martín-Lomas, M.; Schmidt, R. R.; Jiménez-Barbero, J. *J. Am. Chem. Soc.* **1996**, *118*, 10862-10871.
6. Rouzaud, D.; Sinaÿ, P. *J. Chem. Soc., Chem. Commun.* **1983**, 1353-1354.
7. See also: Jarreten, O.; Skrydstrup, T.; Beau, J.-M. *J. Chem. Soc., Chem. Commun.* **1996**, 1661-1662; Fairbanks, A. J.; Perrin, E.; Sinaÿ, P. *Synlett* **1996**, 679-681; Streicher, H.; Geyer, A.; Schmidt, R. R. *Chem. Eur.* **1996**, *2*, 502-510; Kobertz, W. R.; Bertozzi, C. R.; Bednarski, M. D. *J. Org. Chem.* **1996**, *61*, 1894-1897; Sarabia-García, F.; López-Herrera, F. J.; Pino González, M. S. *Tetrahedron* **1995**, *51*, 5491-5500; Herpin, T. F.; Motherwell, W. B.; Tozer, M. J. *Tetrahedron Asymmetry* **1994**, *5*, 2269-2282 and ref. cited in these papers.
8. Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508-524.
9. Vogel, P.; Fattori, D.; Gasparini, F.; Le Drian, C. *Synlett* **1990**, 173-185.
10. Meerpoel, L.; Vrahami, M.-M.; Ancerewicz, J.; Vogel, P. *Tetrahedron Lett.* **1994**, *35*, 111-114.
11. DeShong, P.; Slough, G. A.; Elango, V.; Trainor, G. L. *J. Am. Chem. Soc.* **1985**, *107*, 7788-7790.

12. See also the $Co_2(CO)_8$-catalyzed silyloxymethylation of glycosides: Chatani, N.; Ikeda, T.; Sano, T.; Sonoda, N.; Kurosawa, H.; Kawasaki, Y.; Murai, S. *J. Org. Chem.* **1988**, *53*, 3387-3389.
13. Friesen, R. W.; Sturino, C. F.; Daljeet, A. K.; Kolaczewska, A. *J. Org. Chem.* **1991**, *56*, 1944-1947.
14. Farina, V.; Kapadia, S.; Krishnan, B.; Wang, C.; Liebeskind, L. S. *J. Org. Chem.* **1994**, *59*, 5905-5911; Falck, J. R.; Bhatt, R. K.; J. Ye, *J. Am. Chem. Soc.* **1995**, *117*, 5973-5982.
15. See e.g.: Dubois, E., Beau, J.-M. *J. Chem. Soc., Chem. Commun.* **1990**. 1191-1192; *idem. Tetrahedron Lett.* **1990**, *31*, 5165-5168; Friesen, R. W.; Sturino, C. F. *J. Org. Chem.* **1990**, *55*, 2572-2574; see also: Nicolaou, K. C.; Sato, M.; Miller, N. D.; Gunzner, J. L.; Renaud, J.; Untersteller, E. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 889-891.
16. Lesimple, P.; Beau, J.-M.; Jaurand, G.; Sinaÿ, P. *Tetrahedron Lett.* **1986**, *27*, 6201-6204.
17. Data for **12**: $[\alpha]_{589}^{25}$ = -66, $[\alpha]_{577}^{25}$ = -69, $[\alpha]_{546}^{25}$ = -79, $[\alpha]_{435}^{25}$ = -123, $[\alpha]_{405}^{25}$ = -115 (*c*=1.44, $CHCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H: 6.87 (d, ^3J = 1.8, HC(6')), 5.85 (d, ^3J=2.5, HC(2)), 5.47 (d, ^3J=1.8, HC(1')), 5.38 (dd, ^3J=4.9, 1.0, HC(4')), 4.56 (dd, ^3J=7.0, 2.5, HC(3)), 4.26 (dd, ^2J=10.2, ^3J=4.9, HC(6)), 4.12-4.00 (m, ^2J=10.2, ^3J=10.2, 7.0, 4.7, HC(4), HC(6)), 3.94 (ddd, ^3J=10.2, 4.9, 4.7, HC(5)), 2.91 (dd, ^2J=13.1, ^3J=4.9, H_{exo}C(3')), 1.88 (dd, ^2J=13.1, ^3J=1.0, H_{endo}C(3')), 2.34, 2.04-1.91, 0.96 (4H camphanate), 1.09, 1.04, 0.96 (3 Me camphanate), 1.38-1.10 (m, OTIPS), 1.08, 1.00 (2s, 2 Si(*t*-Bu)).
18. Data for **14**: IR (film) ν: 2935, 2890, 2865, 2360, 2340, 1470, 1160, 1110, 1070 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H: 5.82 (d, ^3J = 2.4, HC(2)), 4.54 (dd, ^3J=7.1, 2.4, HC(3)), 4.27 (ddd, ^3J=10.3, 5.0, 4.9, HC(5)), 4.08-3.99 (m, ^2J=10.3, ^3J=10.3, 7.1, 5.0, HC(6), HC(4)), 3.89 (dd, ^2J=10.3, ^3J=4.9, HC(6)), 1.12-0.98 (m, OTIPS, 2 Si(*t*-Bu)); ^{13}C-NMR (100.61 MHz, $CDCl_3$) δ_C: 182.4 (s, CO), 148.4 (s, C(1)), 115.5 (d, ^1J(C,H)=169, C(2)), 76.4, 73.2, 71.0 (3d, ^1J(C,H)=150, C(3), C(4), C(5)), 65.7 (t, ^1J(C,H)=147, C(6)), 27.3, 26.8 (3q, ^1J(C,H)=125, $Si(C(\underline{C}H_3)_3)_2$, $SiCH(\underline{C}H_3)_2$), 22.7, 19.8 (2s, $Si(\underline{C}(CH_3)_3)_2$), 12.3 (d, ^1J(C,H)=118, $Si\underline{C}H(CH_3)_2$).
19. Product of carbonylative homocoupling of glycal derivatives have been obtained by treatment of 1-lithiated tri-O-benzyl-D-glucal with dimethyl carbonate.[16]
20. Data for **15**: ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H: 6.86 (dd, ^3J=17.2, 10.5, HC(2')), 6.40 (dd, ^2J=1.8, ^3J=17.2, H_{trans}C(3')), 5.84 (d, ^3J=2.5, HC(2)), 5.79 (dd, ^2J=1.8, ^3J=10.5, H_{cis}C(3')), 4.56 (dd, ^3J=7.0, 2.5, HC(3)), 4.31 (dd, ^2J=10.3, ^3J=5.0, HC(6)), 4.10-4.03 (m, ^2J=10.3, ^3J=10.3, 7.0, 4.9, HC(6), HC(4)), 3.92 (ddd, ^3J=10.3, 5.0, 4.9, HC(5)), 1.13-0.91 (m, OTIPS, 2 Si(*t*-Bu)).
21. Data for **16**: $[\alpha]_{589}^{25}$ = -40, $[\alpha]_{577}^{25}$ = -41, $[\alpha]_{546}^{25}$ = -48, $[\alpha]_{435}^{25}$ = -92, $[\alpha]_{405}^{25}$ = -121 (*c*=1.48, $CHCl_3$); IR (film) ν: 2940, 2890, 2865, 2360, 2340, 1465, 1060 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ_H: 7.64 (dd, ^3J=1.7, ^4J=0.7, HC(5')), 7.33 (dd, ^3J=3.6, ^4J=0.7, HC(3')), 6.52 (dd, ^3J=3.6, 1.7, HC(4')), 5.99 (d, ^3J=2.5, HC(2)), 4.57 (dd, ^3J=7.1, 2.5, HC(3)), 4.33 (dd, ^2J=10.2, ^3J=4.9, HC(6)), 4.15-4.07 (m, ^2J=10.2, ^3J=10.3, 7.1, 5.0, HC(4), HC(6)), 3.99 (ddd, ^3J=10.3, 5.0, 4.9, HC(5)). 1.25-0.90 (m, 2 (*t*-BuSi), OTIPS); ^{13}C-NMR (100.61 MHz, $CDCl_3$) δ_C: 174.3 (s, CO), 150.6 (s, C(1)), 148.8 (s, C(2')), 147.4 (d, ^1J(C,H)=200, C(5')), 121.4 (d, ^1J(C,H)=180, C(2)), 113.6 (d, ^1J(C,H)=164, C(3')), 112.1 (d, ^1J(C,H)=178, C(4')), 76.6, 73.6, 71.1 (3d, ^1J(C,H)= 150, C(3), C(4), C(5)), 65.7 (t, ^1J(C,H)= 147, C(6)), 27.3, 26.8, 18.0 (3q, ^1J(C,H)= 125, $Si(C(\underline{C}H_3)_3)_2$, $SiCH(\underline{C}H_3)_2$), 22.7, 20.9 (2s, $Si(\underline{C}(CH_3)_3)_2$), 13.8 (d, ^1J(C,H)= 117, $SiCH(CH_3)_2$).
22. Part of this work has been disclosed at the 2nd ECCM, Lago di Garda, Italy, July 16-19, 1996.

(*Received in France* 14 *October* 1996; *accepted* 28 *November* 1996)