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Preparation of 1-(Tri-n-Butylstannyl) Furanoid Glycals and Their Use in Palladium-Mediated Coupling Reactions

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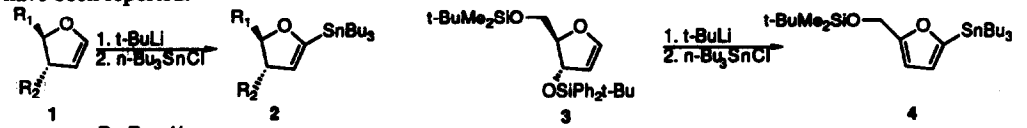
Abstract: 1-(Tri-n-butylstannyl)furanoid glycals have been prepared for the first time by lithiation of the corresponding 3-O-unsubstituted glycals followed by reaction with tri-n-butylstannyl chloride. Furanoid glycals bearing an alkoxy (silyloxy) group at C-3 undergo elimination and furan formation. A 3-O-benzyl-1-(tri-n-butylstannyl)furanoid glycal was prepared from the 1-phenylsulfonyl furanoid glycal using tri-n-butylstannylhydride and AIBN. Stannylated furanoid glycals and iodoglycon derivatives underwent palladium-mediated coupling to yield the corresponding 1-substituted furanoid glycals in good to excellent yields.

We report the first preparation of 1-(tri-n-butylstannyl)furanoid glycals and illustrate their synthetic utility by palladium-mediated coupling reactions with aryl, nitrogen heterocyclic and anthracyclic iodides for C-glycoside syntheses.[1] Similar palladium-mediated coupling reactions of 1-(tri-n-butylstannyl)pyranoid glycals[2,3] have been reported.[4-9]

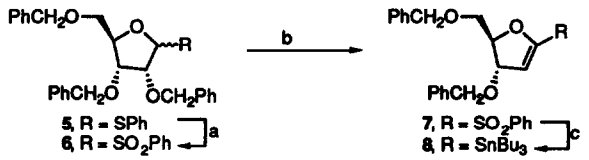


1 2 3 4

a, R_1, R_2 = H
b, R_1 = CH_2OCPh_3, R_2 = H
c, R_1 = CH_2OH, R_2 = OH
d, R_1 = CH_2OSiMe_2t-Bu, R_2 = OH

Tri-n-butyl derivative **2a**, formed by lithiation of 2,3-dihydrofuran (**1a**) and reaction with tri-n-butylstannyl chloride is known.[10] Using this procedure, the 2,3-dideoxyfuranoid glycal (**1b**), prepared in two steps from S(+)-γ-trityloxymethyl-γ-butyrolactone,[11] was converted to the synthetically versatile, chiral 1-stannyl-3-deoxy glycal **2b**. Use of this procedure for tri-n-butylstannylation of 3-substituted hydroxy glycals, e. g. 3[12] failed. Unlike pyranoid glycals[2,3] furanoid glycals, in the presence of t-butyllithium, suffer elimination of the 3-oxy substituent to yield the corresponding furan or, if tri-n-butylstannyl chloride is added, the stannylated furan, e. g. 4. However, by use of the 3-O-unprotected glycals **1c**[13] and **1d**[13] in which formation of a lithium alkoxide inhibits the elimination reaction, we succeeded in preparing stannylated furanoid glycals **2c** and **2d** bearing 3-hydroxy substituents. The resistance of **1c** to base-catalyzed elimination was established when introduction of deutero methanol following treatment with t-butyllithium produced only the 1-deuteroglycal. Following formation of the trilithio derivative of **1c**, addition of tri-n-butylstannyl chloride produced the stannylated glycal **2c** together with the corresponding stannylated furan in ratios varying with the rate of addition. Slow addition led to a 3:1 ratio of **2c** and the stannylated furan; presumably the furan arises from a 3-O-(tri-n-butylstannyl) intermediate. **1d** yielded **2d** (63%) together with a bis-tri-n-butylstannylated product formed by lithiation of a silyl methyl group;[3] in this case, no furan was observed.

We succeeded in preparing stannylated 3-O-benzyl furanoid glycal **8** by a route previously employed for preparation of stannylated pyranoid glycals.[14] Phenylthioglycoside **5**[15] was oxidized to the corresponding sulfone (**6**) using *m*-chloro perbenzoic acid (MCPBA). Treatment of **6** with n-butyllithium resulted in elimination of the 2-benzyloxy substituent and formation of the unsaturated sulfone **7**; replacement of the sulfonyl group with tri-n-butylstannyl was accomplished using tri-n-butylstannylhydride in the presence of 2,2'-azobis(2-methylpropionitrile) (AIBN). We were unable to accomplish this latter step in yields better than 40%; invariably the corresponding stannylated furan and 1,4-anhydro-2-deoxy-3,5-bis-*O*-benzyl-D-*erythro*-pent-1-enitol, the glycal formed by replacement of the sulfonyl group by hydrogen, were also formed.



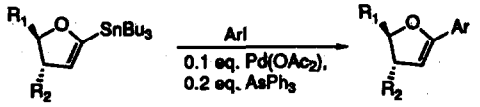
a, MCPBA (2.2 eq.), $NaHCO_3$, CH_2Cl_2, 0 °C, 84%; b, n-BuLi, THF, -78 °C, 90%; c, $n\text{-}Bu_3SnH$ (2.5 eq.), AIBN, toluene, reflux, 40%

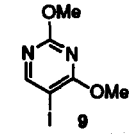
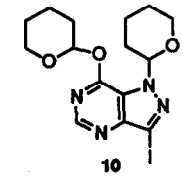
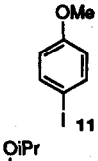
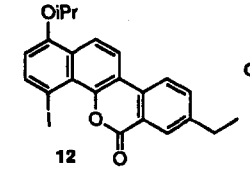
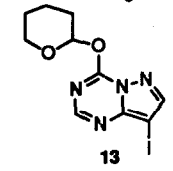
served to characterize the 1-(tri-n-butylstannyl)furanoid glycals formed. Since the stannylated glycals are labile and often difficult to purify,[16] we found it generally convenient to utilize them without purification for palladium-mediated coupling reactions with iodoaglycon derivatives **9**,[17] **10**,[18] **11**, **12**[19] and **13**.[20] Results obtained for these coupling reactions, which demonstrate impressive generality, are summarized in Table 1.

In a typical procedure glycal **1d** in tetrahydrofuran (THF) at -78 °C was treated with 3.5 equivalents of t-butyllithium followed by warming to 0 °C for 15 minutes. Then the reaction mixture was recooled to -78 °C and 3 equivalents of tri-n-butylstannyl chloride was added slowly. The reaction mixture was monitored by tlc; when the reaction was complete, water was added and the stannylated glycal was extracted into ether and dried over Na_2SO_4. The solvent was removed and the stannylated furanoid glycal **2d** was separated by flash chromatography using ether-hexane-triethylamine (1 : 3 : 0.06). A mixture of **2d** (1.3 eq.), iodaglycon **13** (1.0 eq.), triethylamine (2.0 eq.), triphenylarsine[21] (0.2 eq.) and palladium(II) acetate (0.1 eq.) in dried CH_3CN-THF (2:1) was stirred under nitrogen at 40 °C for 16 hours. The coupled product (Table 1, entry 8) was separated by flash chromatography using ethyl acetate-hexane-triethylamine (3 : 1 : 0.1).

Palladium-mediated coupling reactions of stannylated dihydrofuran derivative **2a**[10] with vinyl and aryl halides have been reported.[22] We found this stannylated derivative to undergo facile palladium-mediated coupling with even complex nitrogen heterocyclic iodo derivatives[18] under mild conditions (Table 1, entries 1, 2). Stannylated furanoid glycals **2b** (entries 3-6), **2c** (entries 7), **2d** (entry 8) and **8** (entry 9) were coupled equally effectively. Typically, tlc of the coupling reaction mixture indicated the formation of a single product; The somewhat modest yields isolated in some instance (e. g. entries 3, 7) are a result of difficulties experienced in purifying these arylated enol ethers which undergo elimination to furans and facile double bond hydration, particularly when the aryl group is relatively electron rich.

Table 1. Palladium-Mediated Coupling of Stannylated Furanoid Glycals with Iodoaglycon Derivatives



entry	stannyl derivative	ArI	solvent	temp. (°C)	time (h)	% yield[a] of arylglycal
1	2a	 9	CH_3CN	40	8	65
2	2a	 10	CH_3CN	25	8	85
3	2b[b]	 11	CH_3CN -THF 2:1	40	8	59
4	2b[b]	 12	CH_3CN -THF 2:1	40	10	78
5	2b[b]	9	CH_3CN -THF 2:1	40	10	66
6	2b[b]	10	CH_3CN -THF 2:1	25	12	82
7	2c[b]	9	CH_3CN	40	14	54
8	2d	 13	CH_3CN - THF 2:1	40	16	81
9	8	9	CH_3CN	60	0.5	88

[a] Isolated yields following chromatography; based on ArI
[b] Used without purification

It is noteworthy that iodopyrazolo[4,3-d]pyrimidine derivative **10**[18] undergoes palladium-mediated coupling with stannyl derivatives **2a** and **2b** (entries 2 and 6) more facilely than iodopyrimidine derivative **9** (entries 1 and 5). This contrasts with the mechanistically different[1] palladium-mediated coupling reactions of these iododerivatives with glycals in which **9** is more reactive than **10**.[18] Presumably these differences in reactivity are owing to the relative electron densities of the heterocyclic ring systems.

The formation and palladium-mediated coupling of stannylated furanoid glycals with iodo aryl and heterocyclic derivatives provides a route to furanosyl C-glycosides which is complementary to that developed in our laboratory which involves palladium-mediated coupling of glycals with halo, mercurial or stannylated[23] derivatives of aryl and hererocyclic aglycones.[1]

Acknowledgment

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References and Notes

1. Daves, G. D., Jr. *Acc. Chem. Res.* **1990**, *23*, 201; Hacksell, U.; Daves, G. D., Jr. *Prog. Med. Chem.* **1985**, *22*, 1.
2. Hanessian, S.; Martin, M; Desai, R. C. *J. Chem. Soc., Chem. Commun.* **1986**, 926.
3. Friesen, R. W.; Sturino, C. F.; Daljeet, A. K.; Kolaczewska, A. *J. Org. Chem.* **1991**, *56*, 1944.
4. Friesen, R. W.; Sturino, C. F. *J. Org. Chem.* **1990**, *55*, 2572.
5. Friesen, R. W.; Sturino, C. F. *J. Org. Chem.* **1990**, *55*, 5808.
6. Dubois, E.; Beau, J.-M. *J. Chem. Soc., Chem. Commun.* **1990**, 1191.
7. Friesen, R. W.; Daljeet, A. K. *Tetrahedron Lett.* **1990**, *31*, 6133.
8. Tius, M. A.; Gu, X.; Gomez-Galeno, J. *J. Am. Chem. Soc.* **1990**, *112*, 8188.
9. Tius, M. A.; Gomez-Galeno, J.; Gu, X.; Zaidi, J. H. *J. Am. Chem. Soc.* **1991**, *113*, 5775.
10. Boeckman, R. K.; Bruza, K. J. *Tetrahedron* **1981**, *37*, 3997.
11. Takle, A; Kocienski, P. *Tetrahedron* **1990**, *46*, 4503.
12. Farr, R. N.; Daves, G. D., Jr. *J. Carbohydr. Chem.* **1990**, *9*, 653.
13. Cheng, J. C.-Y.; Hacksell, U.; Daves, G. D., Jr. *J. Org. Chem.* **1985**, *50*, 2778.
14. Lesimple, P.; Beau, J.-M.; Jaurand, G.; Sinay, P. *Tetrahedron Lett.* **1986**, *27*, 6201.
15. Kametani, T.; Kawamura, K.; Honda, T. *J. Am. Chem. Soc.* **1987**, *109*, 3010.
16. Farina, V. *J. Org. Chem.* **1991**, *56*, 4985.
17. Prystas, M.; Sorm, F. *Collect. Czech. Chem. Commun.* **1964**, *29*, 121.
18. Zhang, H.-C.; Daves, G. D., Jr. *J. Org. Chem.* **1992**, *57*, 4690.
19. Kwok, D.-I.; Farr, R. N.; Daves, G. D., Jr. *J. Org. Chem.* **1991**, *56*, 3711.
20. Brakta, M; Daves, G. D., Jr., unpublished results.
21. Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585.
22. MacLeod, D.; Moorcroft, D.; Quayle, P.; Dorrity, M. R.; Malone, J. F.; Davies, G. M. *Tetrahedron Lett.* **1990**, *31*, 6077.
23. Outten, R. A.; Daves, G. D., Jr. *J. Org. Chem.* **1989**, *54*, 29.

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