A New Method for the Synthesis of Stannyl Ethers by Acid-Catalyzed Reaction of Alcohols with Allyltributylstannane

Shigeru Yamago,* Takeshi Yamada, Ryuji Nishimura, Hiroki Ito, Yosuke Mino, and Jun-ichi Yoshida*
Department of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering, Kyoto University, Kyoto 606-8501

(Received October 29, 2001; CL-011071)

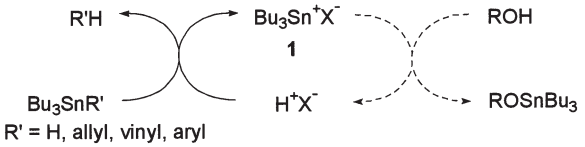
Stannyl ethers are prepared by triflic acid-catalyzed reaction of alcohols with tributylstannane or allyltributylstannane at room temperature. The stannyl ethers thus prepared can be successfully used for the β-bromogycoside-mediated glycosylation reactions.

Stannyl ethers are important intermediates in organic synthesis.[1] The nucleophilicity of stannyl ethers is much higher than that of free hydroxyl groups. Consequently, stannyl groups are used as activating groups for alcohols whereas silyl groups are used as protecting groups.[2] Several methods for the synthesis of stannyl ethers from alcohols have been developed, but more efficient methods are still needed. Conventional synthetic procedures, which are based on the dehydration or the alcohol exchange reaction of the alcohols with dibutyltin oxide, hexabutylditin oxide, or tributyltin methoxide, are carried out under basic conditions.[1] Therefore, base-labile functional groups, such as ester functions, cannot tolerate these reaction conditions. Although diols, especially 1,2-diols, are good substrates, monoalcohols are often problematic.[3,4] An alternative method involving transmetallation of highly basic and nucleophilic metal alkoxide with trialkyltin halides[1b] also lacks functional group compatibility. An elegant method utilizing 1,1′-dimethylstannocene has been reported,[5] but the bulky ligands decrease the reactivity of the ether oxygen.

During the course of the development of new glycosylation reactions for oligosaccharide synthesis,[6] we needed to carry out the selective conversion of alcohols to stannyl ethers in the presence of some base-labile functional groups. Although several attempts to synthesize stannyl ethers by conventional methods were unsuccessful, we found that stannyl ethers could be easily prepared by the reaction of alcohols with tributylstannane (R′ = H) or allyltributylstannane (R′ = allyl) under mild acidic conditions, which are compatible with a variety of base and acid labile functional groups. We report here the preliminary results of this study (eq 1).

$$\mathrm{ROH} + \mathrm{R'SnBu_3} \xrightarrow[-\ \mathrm{R'H}]{\text{cat. } \mathrm{H^+X^-}} \mathrm{ROSnBu_3} \qquad (1)$$

By analogy to the silylation of alcohols, we anticipated that the Lewis acidic tin species (**1**) could serve as stannylating agents of alcohols (Scheme 1). Since the reaction of **1** with an alcohol generates a protic acid which is known to react with appropriate organostannanes (Bu_3SnR' : R′ = H,[7] vinyl,[8] and aryl[9]) to give



Scheme 1.

1, stannyl ethers could be synthesized from alcohols and Bu_3SnR' by the use of a catalytic amount of protic acid. The stannylation step may be in equilibrium, but the formation of the stable R'H would drive the reaction. The concept works.

The hypothesis was verified initially by the reaction of methanol (R = Me, 1.2 equiv) as an alcohol and tributylstannane (R′ = H, 1.2 equiv) in the presence of trifluoromethanesulfonic acid (X = CF_3SO_3, 0.2 equiv) in dichloromethane.[7b] After the reaction mixture was stirred for 16 h at room temperature, the resulting stannyl ether was quenched by addition of benzoyl chloride to give methyl benzoate in almost quantitative yield (Table 1, entry 1). The formation of the stannyl ether was also confirmed by ^{119}Sn NMR spectra (Eq. 2). Thus, an equimolar mixture of methanol and tributylstannane in CD_2Cl_2 was mixed with trifluoromethanesulfonic acid (0.2 equiv), and the progress of the reaction was monitored by ^{119}Sn NMR. The characteristic signal of tributylstannane (−83 ppm, $\delta\nu_{1/2} = 3$ Hz) slowly disappeared, and a new broad signal corresponding to tributylstannyl methyl ether (112 ppm, $\delta\nu_{1/2} = 1950$ Hz) appeared.[10]

$$\underset{\substack{-86\ \mathrm{ppm}\\ \delta\nu_{1/2}=3\ \mathrm{Hz}\\ (1.0\ \mathrm{equiv})}}{\mathrm{MeOH} + \mathrm{Bu_3SnH}} \xrightarrow[\substack{\mathrm{CD_2Cl_2}\\ \text{r.t., 21 h}}]{\substack{\mathrm{CF_3SO_3H}\\ (0.2\ \text{equiv})}} \underset{\substack{112\ \mathrm{ppm}\\ \delta\nu_{1/2}=1950\ \mathrm{Hz}}}{\mathrm{MeOSnBu_3}} \qquad (2)$$

Optimization of the reaction conditions was carried out, and the results are summarized in Table 1. The efficiency of the stannylation was analyzed by benzoylation of the resulting stannyl ethers because it was generally not easy to isolate stannyl ethers.[1c] The following points are worth noting. First, the acidity of the catalyst was found to be an important controlling factor. The activity of the catalyst increases with the acidity;

Table 1. Preparation of stannyl ethers from alcohols

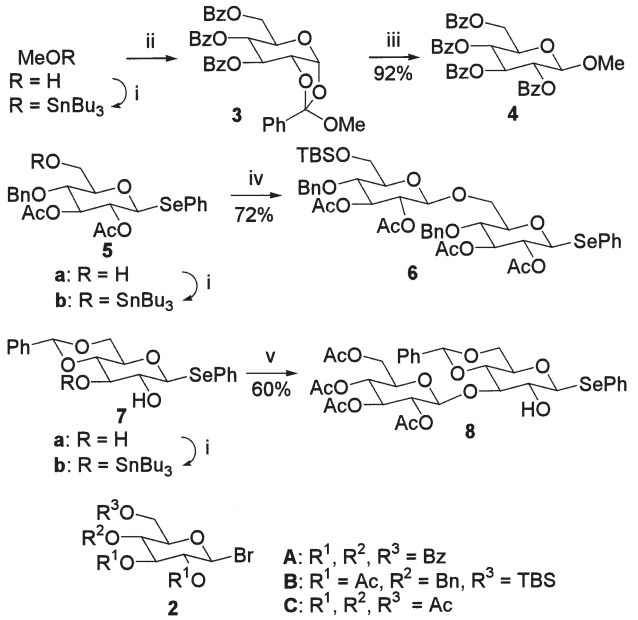
$$\mathrm{ROH} \xrightarrow[\substack{\mathrm{CH_2Cl_2}\\ \text{r.t., 16-25 h}}]{\substack{\mathrm{Bu_3SnR'}\ (1.2\ \text{equiv})\\ \mathrm{HX}\ (0.2\ \text{equiv})}} \boxed{\mathrm{ROSnBu_3}} \xrightarrow[\text{r.t., 1 h}]{\substack{\mathrm{BzCl}\\ (1.2\ \text{equiv})}} \mathrm{ROBz}$$

Run	R	R'	HX	Time/h	Yield/%
1	Me	H	CF_3SO_3H	16	82
2	Me	H	$MeSO_3H$	16	87
3	Me	H	CF_3CO_2H	16	65
4	Me	H	$MeCO_2H$	16	18
5	*i*-Pr	H	CF_3SO_3H	25	75
6	*i*-Pr	H	$MeSO_3H$	25	43
7	*t*-Bu	H	CF_3SO_3H	19	0[a]
8	Me	allyl	CF_3SO_3H	23	98
9	*i*-Pr	allyl	CF_3SO_3H	23	82
10[b]	*i*-Pr	allyl	CF_3SO_3H	1	98

[a] *t*-BuCl formed quantitatively. [b] A slight excess of allyltributylstanane (1.3 equiv) and triflic acid (0.3 equiv) was used.

$CH_3CO_2H \ll CF_3CO_2H \ll CH_3SO_3H < CF_3SO_3H$ (entries 1–6). Second, allyltributylstannane was found to be a more effective precursor than tributylstannane, and the desired stannyl ethers formed in excellent yields (entries 8 and 9). Third, the current method was generally applicable for primary, secondary and tertiary alcohols, though the stannyl ether derived from *t*-butyl alcohol did not give the acylated product but instead gave the *t*-butyl chloride quantitatively (entry 7).[11] Finally, when 0.2 equiv of the acid catalyst was used, very slow conversion sometimes resulted; however the use of 0.3 equiv of the acid catalyst gave rise to satisfactory and reproducible conversion to the desired stannyl ether within 1 h in quantitative yield (entry 10).

As the formation of the stannyl ether takes place under mild conditions, the current method could be successfully applied to glycosylation reactions (Scheme 2). Thus, the coupling of methyl tributylstannyl ether prepared by the present protocol with β-bromoglycoside **2A**[6] proceeded smoothly to give the orthoester **3**. While the acid labile orthoester **3** was not affected by Bu_3SnOTf that was present in the reaction medium,[12] it was converted to the *O*-glycoside **4** by the action of TMSOTf.



Scheme 2. Reaction conditions: i) Allyl tribuytin (1.3 equiv), CF_3SO_3H (0.3 equiv), CH_2Cl_2, rt, 2 h. ii) **2A** (1.0 equiv), 0 °C, 1 h. iii) TMSOTf (0.1 equiv), 0 °C, 0.1 h. iv) **2B** (1.5 equiv), r.t., 0.5 h, then TMSOTf (0.1 equiv), 0 °C, 0.1 h. v) **2C** (1.5 equiv), r.t., 0.5 h, then TMSOTf (0.1 equiv), 0 °C, 0.1 h.

We next examined the glycosidation reactions of the glycosides **5** and **7** in order to examine the functional group compatibility of the present method. We were very pleased to find that the base labile acetyl group and the acid labile acetal and arylselenyl groups in **5** and **7** were completely inert under the reaction conditions, and that the coupling reaction of tributylstannyl ethers **5b** and **7b** with **2B** or **2C** gave the corresponding disaccharides **6** and **8**, respectively, in good yields. Several attempts to prepare **5b** by conventional methods from **5a** with $(Bu_3Sn)_2O$ or Bu_3SnOMe in benzene under reflux were unsuccessful due to the instability of the acetyl groups under the reaction conditions.

In summary, we have developed a new method for the synthesis of stannyl ethers from alcohols under very mild conditions, which are compatible with a variety of acid- and base-labile functional groups. Further synthetic investigation is underway and will be reported in due course.

This work was partly supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports, and Culture, Japan.

This paper is dedicated to Professor Teruaki Mukaiyama on the occasion of his 75th birthday.

References and Notes

1 a) S. David, in "Preparative Carbohydrate Chemistry," ed. by S. Hanessian, Marcel Dekker, Inc., New York (1997), Chap. 4. b) A. G. Davis, in "Organotin Chemistry," VCH, Weinheim (1997), Chap. 12. c) M. Pereyre, J.-P. Quintard, and A. Rahm, in "Tin in Organic Synthesis," Butterworths, London (1987), Chap. 4. d) Y. Tsuda, *J. Syn. Org. Chem. Jpn.*, **55**, 907 (1997). e) S. David and S. Hanessian, *Tetrahedron*, **41**, 643 (1985). f) C. Cruzado, M. Bernabé, and M. M.-Lomas, *J. Org. Chem.*, **54**, 465 (1989).
2 T. W. Greene and G. M. Wuts, in "Protective Groups in Organic Synthesis," John Wiley & Sons, Inc., New York (1999), Chap. 2.
3 B. Herradón, A. Morcuende, and S. Valverde, *Synlett*, **1995**, 455 and references therein.
4 While elegant applications of stannyl ethers in organic synthesis have recently appeared, all have dealt with 1,2-diol systems. See recent examples: F. Iwasaki, T. Maki, O. Osamura, W. Nakashima, and Y. Matsumura, *J. Org. Chem.*, **65**, 996 (2000); E. Kaji, and N. Harita, *Tetrahedron Lett.*, **41**, 53 (2000); R. Martinez-Bernhardt, P. P. Castro, G. Godjoian, and C. G. Gutiérrez, *Tetrahedron*, **54**, 8919 (1998); G. Hodosi and P. Kovác, *Carbohyd. Res.*, **308**, 63 (1998); G. Hodosi and P. Kovác, *J. Am. Chem. Soc.*, **119**, 2335 (1997); K. C. Nicolaou, F. L. van Delft, S. R. Conley, H. J. Mitchell, Z. Jin, and R. M. Rodriguez, *J. Am. Chem. Soc.*, **119**, 9057 (1997); S. J. Danishefsky, J. Gervay, J. M. Peterson, F. E. McDonald, K. Koseki, D. A. Griffith, T. Oriyama, and S. P. Marsden, *J. Am. Chem. Soc.* **117**, 1940 (1995).
5 T. Mukaiyama, J. Ichikawa, and M. Asami, *Chem. Lett.*, **1983**, 293; J. Ichikawa, M. Asami, and T. Mukaiyama, *Chem. Lett.*, **1984**, 949.
6 S. Yamago, T. Yamada, O. Hara, H. Ito, Y. Mino, and J. Yoshida, *Org. Lett.*, **3**, 3867 (2001).
7 a) A. K. Sawyer and H. G. Kuivila, *J. Org. Chem.*, **41**, 610 (1962); b) Y. T. Xian, P. Four, F. Guibé, and G. Balavoine, *Nouv. J. Chim.*, **8**, 611 (1984).
8 A. Saitow, E. G. Rochow, and D. Seyferth, *J. Org. Chem.*, **23**, 116 (1958).
9 X. Kong, T. B. Grindley, P. K. Bakshi, and T. S. Cameron, *Organometallics*, **12**, 4881 (1993).
10 While pure tributylstannyl methyl ether gives a sharp signal at 108 ppm ($\delta\nu_{1/2} = 15$ Hz), addition of 0.2 equiv of trifluoromethanesulfonic acid resulted in a lower field shift with considerable line broadening (112 ppm, $\delta\nu_{1/2} = 149$ Hz).
11 *t*-Butyl alcohol and benzoyl chloride did not give *t*-butyl chloride under similar conditions. Therefore, the *t*-butyl chloride must be formed by way of the corresponding stannyl ether.
12 The result clearly revealed that the reactivity of tributyltin methoxide prepared by the current method, which contains tributyltin triflate, and that of commercially available one without such contaminant was identical.