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A General and Efficient Method for the Preparation of γ-Alkoxyallylstannanes via an Acetal Cleavage

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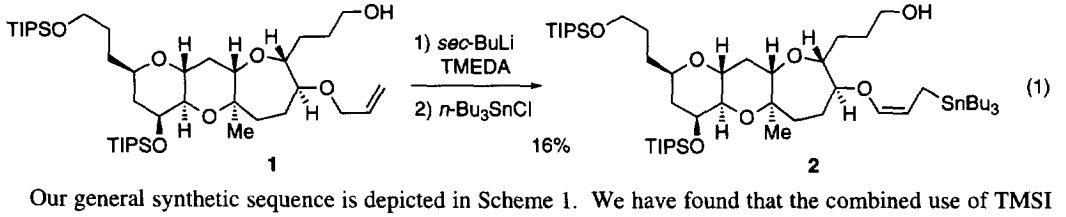
Abstract: The reaction of various alcohols and γ-methoxyallylstannane **3** in the presence of a catalytic amount of CSA afforded mixed acetals in high yields. The treatment of the acetals with TMSI and HMDS produced γ-alkoxyallylstannanes in high yields *via* elimination of methanol.

The synthetic reaction using functionalized allylstannanes is widely appreciated as one of the most useful methods for the stereocontrolled C-C bond formation.[1] Several methods have been reported for the diastereo- and enantioselective synthesis of 1,2-diol derivatives *via* the intermolecular reaction of γ-alkoxyallylstannane with aldehyde.[2,3] Moreover, we recently described an intramolecular version as a powerful method for the construction of medium sized cyclic ethers.[4] The usefulness of this methodology has been demonstrated by the total synthesis of hemibrevetoxin B[5] and related polycyclic ethers.[6] The key compounds, γ-alkoxyallylstannanes, are usually prepared by allylic anion formation followed by trapping with tributyltin chloride.[2,4-6] However, application of such a classical method to the synthesis of marine natural products has proven to be difficult due to the steric bulkiness and the high functionalization of the substrate. For example, the treatment of allylic ether **1** with *sec*-BuLi/TMEDA followed by reaction with *n*-Bu_3SnCl gave desired allystannane **2** in only 16% yield (eq 1).[5] This problem prompted us to develop a new synthetic route. Here, we wish to report a general and efficient method for the preparation of γ-alkoxyallylstannanes *via* an acetal cleavage.



1 **2** (1)

Our general synthetic sequence is depicted in Scheme 1. We have found that the combined use of TMSI and HMDS is the best choice for the cleavage of mixed acetals[7,8] having tributylstannyl group, and the acetals are easily prepared by acid catalyzed reaction of the corresponding alcohols and γ-methoxyallylstannane **3**.[2c] The results of the acetalization of various alcohols are summarized in Table 1. In general, desired mixed acetals were obtained in high yields. Protective groups such as *tert*-butyldimethylsilyl, triisopropylsilyl, and pivaloyl are stable under these reaction conditions. It should be noted that the use of an excess amount of **3** is required to obtain the mixed acetals in high yield, otherwise a significant amount of symmetric acetal would be formed as a by-product.[9]

Scheme 1

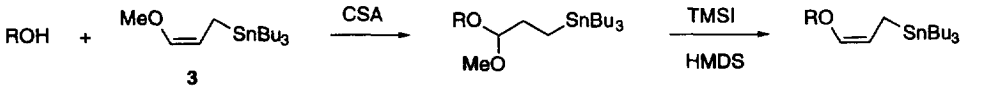
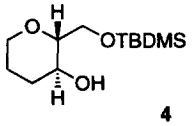
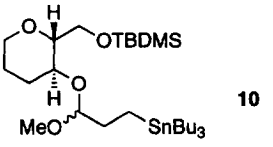
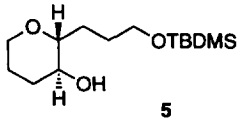
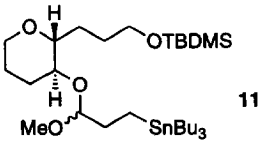
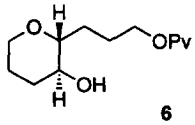
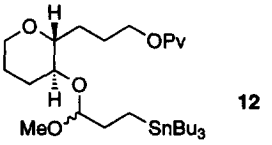
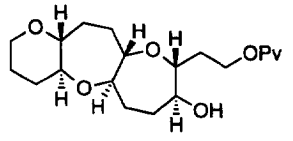
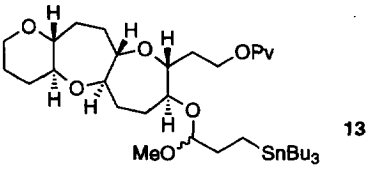
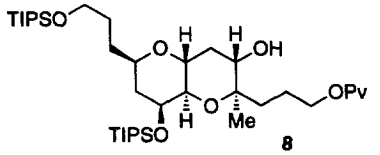
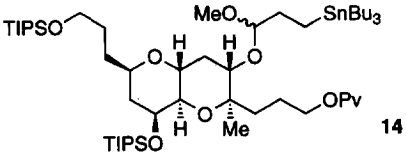
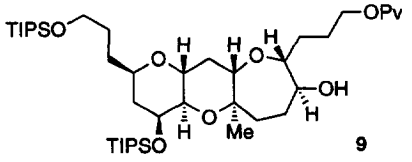
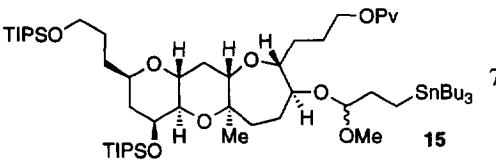


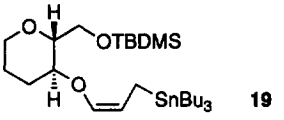
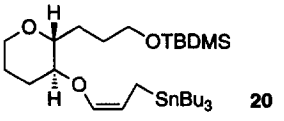
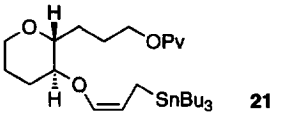
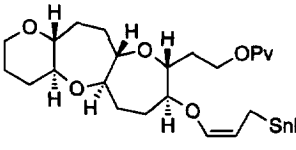
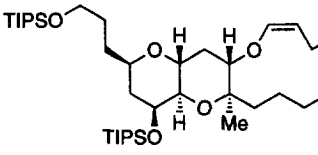
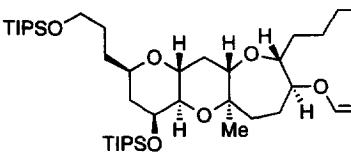
Table 1. Preparation of Mixed Acetals[a]

alcohol	time (h)	product	yield, %[b]
 **4**	3.0	 **10**	80(17)[c]
 **5**	2.5	 **11**	84
 **6**	0.5	 **12**	83
 **7**	0.5	 **13**	96
 **8**	1.0	 **14**	85
 **9**	2.0	 **15**	79(15)[c]

[a]*Typical procedure*: To a solution of alcohol **4** (60 mg, 0.24 mmol) and **3** (250μL, 0.73 mmol) in dry CH_2Cl_2 (1 mL) was added CSA (11 mg, 0.049 mmol), and the resulting solution was stirred at room temperature for 3 h. The reaction was quenched with Et_3N (0.1 mL), and the mixture was filtered through alumina pad. Following solvent removal, the residue was purified by silica gel column chromatography (hexane/AcOEt/Et_3N = 100:1:1) to give mixed acetal **10** (116 mg, 80%) and recovered **4** (8 mg, 17%). [b]Isolated yield. [c]Values in parentheses are recovery yields of ROH.

The results of transformation of the acetals to allylic stannanes are summarized in Table 2. In all cases, elimination of methanol from the mixed acetals proceeded smoothly in the presence of TMSI and HMDS to give desired γ-alkoxyallylstannanes in good yields. Interestingly, only *Z*-allylic stannanes were produced, perhaps, due to the coordination of ether oxygen to a tin atom. It is notable that both of the acetal formation and cleavage were not affected by steric bulkiness of the substrates. Thus, highly functionalized allylstannane **24** was obtained in 85% yield.

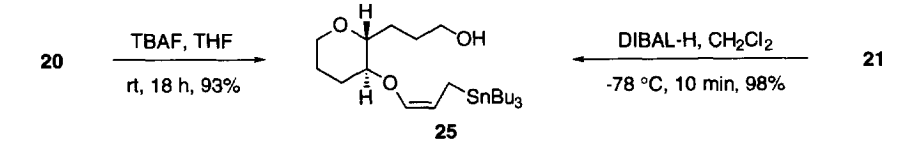
Table 2. Cleavage of Acetals[a]

acetal	time (h)	product	yield, %[b]
10	3.0	 **19**	71
11	0.5	 **20**	80
12	0.5	 **21**	78
13	0.5	 **22**	76
14	1.5	 **23**	83
15	1.0	 **24**	85

[a]*Typical procedure*: To a solution of **10** (55 mg, 0.091 mmol) in dry CH_2Cl_2 (1 mL) at -15 °C were added HMDS (130 μL, 0.62 mmol) and TMSI (65 μL, 0.46 mmol), and the resulting mixture was stirred for 3 h. The reaction was then quenched with saturated aqueous $NaHCO_3$ (1 mL), and mixture was extracted with ether. The organic layer was washed with brine and dried over $MgSO_4$. Following solvent removal, the residue was purified by silica gel column chromatography (hexane/AcOEt/Et_3N = 100:5:1) to give allylstannane **19** (37 mg, 71%). [b]Isolated yields.

To enhance synthetic utility and generality of this method, we next examined deprotection of the obtained products (Scheme 2). The treatment of silyl ether **20** with TBAF afforded an alcohol **25** in 93% yield. The pivaloyl group of **21** was removed reductively by using DIBAL-H to give **25** in 98% yield. The allylic stannane moiety is stable under these reaction conditions.

Scheme 2



In conclusion, we are in a position to synthesize highly functionalized and sterically crowded γ-alkoxyallylstannanes such as **24** in high yields. The newly developed acetal formation-cleavage procedure is widely applicable to the synthesis of γ-alkoxyallylstannanes which are not easily obtainable *via* previous method. The application of this methodology to the total synthesis of hemibrevetoxin B is in progress.

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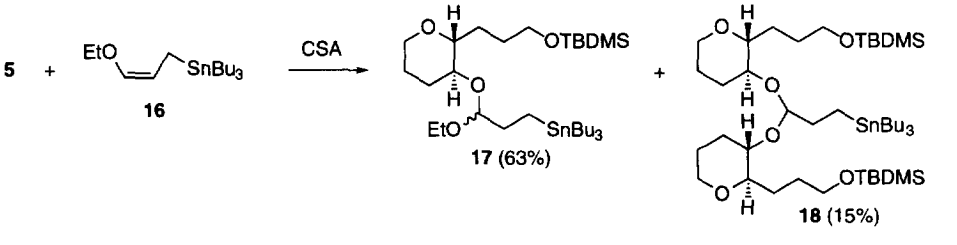
8. For other examples of this type of transformation, see: (a) $HC(OMe)_3$/TsOH: Wohl, R. A. *Synthesis* **1974**, 38-40. (b) $AlCl_3/Et_3N$: Barbot, F.; Miginiac, P. *Helv. Chim. Acta* **1979**, 1451-1457. (c) $(CO)_5MnSiMe_3$: Marsi, M.; Gladysz, J. A. *Organometallics* **1982**, *1*, 1467-1473. (d) $TiCl_4$/DBU: Fleet, G. W. J.; James, K.; Lunn, R. J. *Tetrahedron Lett.* **1986**, *27*, 3053-3056. (e) $^iBu_3Al$: Naruse, Y.; Yamamoto, H. *Tetrahedron Lett.* **1986**, *27*, 1363-1366.
9. For example, the reaction of **5** and 1.2 equiv of **16** gave a mixture of **17** and **18**.



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