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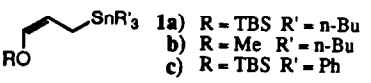
# *NEW ALLYLSTANNANES FOR THE CONNECTIVE CONSTRUCTION OF MONOPROTECTED VICINAL DIOLS*

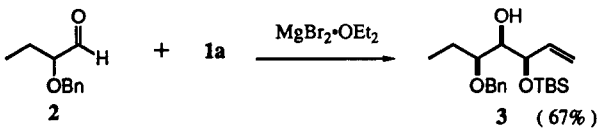
GARY E. KECK,* DUAIN E. ABBOTT, AND MICHAEL R. WILEY
DEPARTMENT OF CHEMISTRY
UNIVERSITY OF UTAH, SALT LAKE CITY, UTAH 84112

SUMMARY: The preparation of allylstannanes 1a-c, all of which bear an oxygen substituent at the allylic terminus, is described. These reagents react with alpha- and beta-alkoxyaldehydes in the presence of $MgBr_2$ as Lewis acid to give $S_{E'}$ products with diastereofacial selectivity consistent with "chelation control"; a syn disposition of substituents about the newly formed bond is highly favored in all cases.

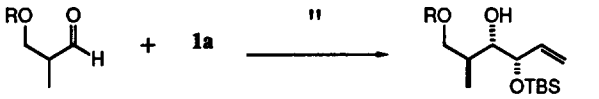
In connection with several ongoing projects in our laboratories involving the total synthesis of highly oxygenated natural products, we have had occasion to examine the viability of constructing such systems via the process described in equations 1-3 below.[1] We record herein the preparation of such reagents, their use in Lewis acid mediated additions to representative α- and β-alkoxy aldehydes, and rigorous proofs of structure for the major products produced.



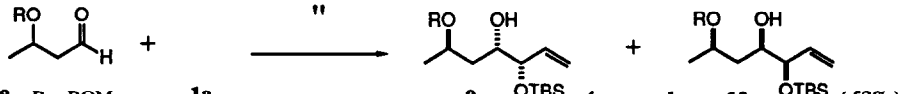

**1a)** R = TBS R' = n-Bu
**b)** R = Me R' = n-Bu
**c)** R = TBS R' = Ph




**2** **3** (67%) Eq. 1



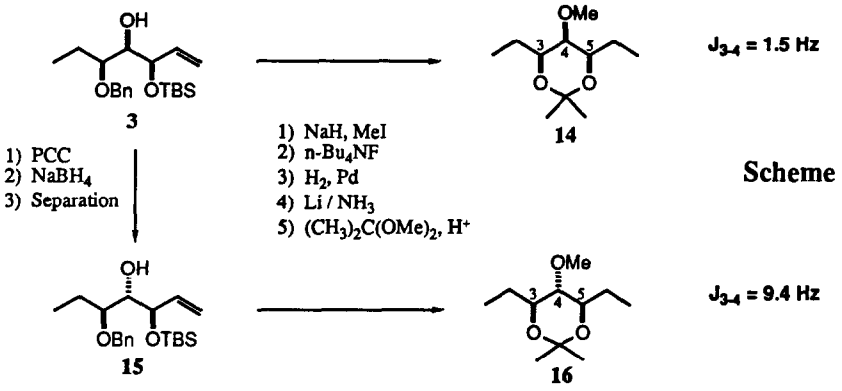

**4** R = BOM **5** (50%) Eq. 2
**6** R = Bn **7** (65%)




| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **8** | R = BOM | **1a** | **9** | 4 | : | 1 | **10** | (52%) Eq. 3 |
| **11** | R = Bn | **1a** | **12** | 4 | : | 1 | **13** | (75%) |
| | R = BOM | **1c** | | 10 | : | 1 | | (49%) |
| | R = Bn | **1c** | | 12 | : | 1 | | (72%) |

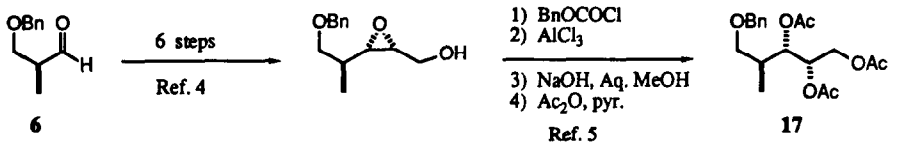
Three such reagents (structure 1a-c above) have been examined in this context. The preparation of all three is very similar: the appropriate allylether (e.g. methyl or tert-butyldimethylsilyl) is metallated by reaction[2] with sec-butyllithium, and the resulting allylic anion is quenched by addition of either tri-n-butyltin chloride or triphenyltin chloride.[3] The products in all cases are exclusively cis.

Reaction of 1a with the α-alkoxy aldehyde 2 in methylene chloride, using 1.0 eq of $MgBr_2$-$OEt_2$ as Lewis acid (-23°C to 0°C) gave the expected product 3 with complete diastereofacial selectivity and bond construction stereoselectivity, as only a single compound was detected by 300 MHz $^1H$ NMR, 75 MHz $^{13}C$ NMR, and capillary VPC analysis. Proof of the structure of this material as 14 was readily achieved using symmetry considerations and NMR spectroscopy as outlined in Scheme I.




**Scheme I**

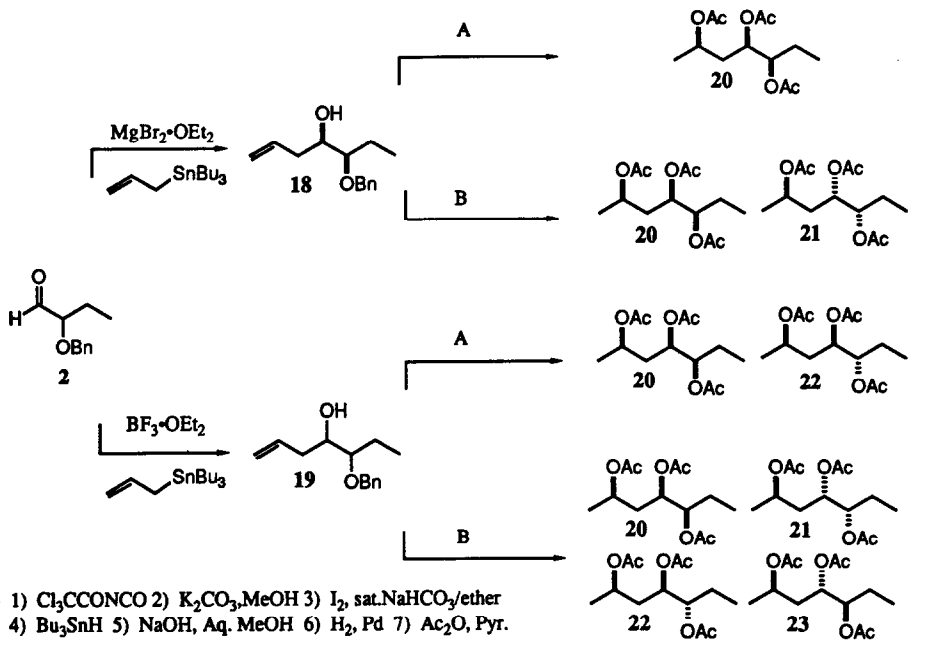
Reaction of the complex derived from $MgBr_2$ and β-alkoxy aldehyde 4 or 6 with 1a ($CH_2Cl_2$; -23°C to 0°C) gave the expected product 5 or 7 with essentially complete diastereofacial selectivity and bond construction selectivity (ca. 50:1). Proof of structure in this case was accomplished by conversion of 6 (ozonolysis; borohydride reduction; desilylation; and acetylation) to a triacetate 17 which was independently prepared using methodology previously described by Kishi,[4,5] as shown in Scheme II below.




**Scheme II**

Finally, with β-alkoxy aldehyde 8 or 11, chiral by virtue of substitution at C-3, the $MgBr_2$ mediated addition of 1a afforded a 4:1 mixture of two products; 12 was shown to be the major isomer via independent synthesis as outlined in Scheme III below. Thus, the aldehyde 2 was converted to 18 via a chelation controlled addition of allyltri-n-butylstannane,[1a] which could then be converted stereoselectively to triacetate 20 via the method of Hirama,[6] or to a mixture of triacetates 20 and 21 via a non-selective oxymercuration-reduction procedure.

Access to a third diastereomer 22 was obtained by employing the Hirama procedure with the mixture of diastereomers 19 obtained from a non-selective addition of allyltri-n-butylstannane to 2.[1a] A mixture of all four possible diastereomers of the triacetates resulted from oxymercuration of this same mixture and thus provided the fourth possible diastereomer 23. Since all four triacetates could be distinguished by capillary VPC and also by $^{13}C$ NMR analysis, structures could be assigned to all products produced in the addition of 1a or 1c to 8 or 11.




**Scheme III**

A- 1) $Cl_3CCONCO$ 2) $K_2CO_3$,MeOH 3) $I_2$, sat.$NaHCO_3$/ether 4) $Bu_3SnH$ 5) NaOH, Aq. MeOH 6) $H_2$, Pd 7) $Ac_2O$, Pyr.

B- 1) $Hg(OAc)_2$, $H_2O$ 2) -OH, $NaBH_4$ 3) $H_2$, Pd 4) $Ac_2O$, Pyr.

Some limitations were noted in the use of such reagents. With the β-benzyloxymethyl protected substrates 4 and 8 side products resulting from cleavage of the benzyloxymethyl group were observed. Such side reactions are presumably a result of the relatively low nucleophilicity of silyloxyallylstannanes, which requires that somewhat higher reaction temperatures be employed with these reagents than with, e.g., allyl- or crotyltri-n-butylstannane. Thus, Lewis acid mediated cleavage of certain acid sensitive protecting groups can begin to compete with the desired addition process.[7,8] Finally, although the level of stereoselectivity realized for reaction of 1a with 11 was rather low, the stereoselectivity could be increased dramatically, to 12:1, through use of the triphenyl reagent 1c under optimal conditions.[9] The minor isomer produced could be shown to result from facial as opposed to simple diastereoselectivity; thus bond construction selectivity (in a syn sense) is complete in this case.[10,11,12] ACKNOWLEDGMENT: Support of this research by the National Institutes of Health (through grant GM-28961) is gratefully acknowledged.

References and Notes:


1. For our other studies in this area: (a) Keck, G. E.; Boden, E. P. Tetrahedron Lett. **1984**, 25, 265. (b) Keck, G. E.; Boden, E. P. Tetrahedron Lett. **1984**, 25, 265. (b) Keck, G. E.; Abbott, D. A. Tetrahedron Lett. **1984**, 25, 1883.

2. (a) Evans, D. A.; Andrews, G. C.; Buckwalter, B. J. Am. Chem. Soc. **1974**, 967, 5560. (b) Still, W. C.; Macdonald, T. L. J. Am. Chem. Soc. **1974**, 96, 5561.

3. An experimental procedure for the preparation of reagent 1a is summarized here. To a solution of tert-butyldimethylsilylallyl ether (3.21 g, 0.02 mol) in THF (50 mL) at -78°C was added sec-butyllithium (1.2 eq) followed by 5 mL of HMPA. After 15 min, tri-n-butyltin chloride (5.45 mL, 0.022 mol) was added. After an additional 15 min, the mixture was allowed to warm to room temperature and then poured into 100 mL of hexane. The resulting solution was washed with saturated aqueous $NH_4Cl$ solution (50 mL), with water (50 mL), then dried over $MgSO_4$ and concentrated in vacuo. Kugelrohr distillation gave 7.12 g (77%) of 1a as a colorless liquid: bp 195°C - 200°C (0.01 mm, oven temperature); $^1H$ NMR ($CDCl_3$) $\delta$ 6.03 (d, 1 H, J = 6), 4.59 (dt, 1 H, J = 6, 9), 1.68 (d, 2 H, J = 9), 1.36 (m, 18 H), 0.90 (m, 18 H), 0.11 (s, 6 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 134.9, 109.1, 29.1, 27.3, 25.5, 18.0, 13.4, 9.1, 5.4, -5.6.

4. Kishi, Y.; Nagoaka, H. Tetrahedron **1981**, 37, 3873.

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6. Hirama, M.; Vei, M. Tetrahedron Lett. **1982**, 23, 5307.

7. Such considerations also place limits on the Lewis acids which can be utilized with such allylstannanes. For example, $TiCl_4$[1a] rapidly destroys the oxygen substituted reagents 1a-1c.

8. For other examples of complications which can arise with very strong Lewis acids and/or elevated temperatures, note: (a) Kiyooka, S.; Heathcock, C. Tetrahedron Lett. **1983**, 24, 4765. (b) Reetz, M.; Kesseler, K.; Jung, A. Tetrahedron Lett. **1984**, 25, 729.

9. (a) We are currently investigating the source of this increase in stereoselectivity. (b) The results of an NMR investigation suggest that allyltriphenylstannane should be less nucleophilic than allyltri-n-butylstannane: Matarasso-Tchiroukine, E.; Cadiot, P. Can. J. Chem. **1983**, 61, 2476.

10. For other studies on such "1-3 asymmetric induction", note (a) Reetz, M.; Jung, A. J. Am. Chem. Soc. **1983**, 105, 4833. (b) Reetz, M. Angew. Chem. Int. Ed. Engl. **1984**, 23, 556. (c) Keck, G. E.; Castellino, S. J. Am. Chem. Soc. **1986**, 108, 3847. (d) Keck, G. E.; Castellino, S.; Wiley, M. R. J. Org. Chem. in press.

11. The methoxy substituted reagent 1b shows lower stereoselectivity in such reactions than either 1a or 1c. For example, a 93:7 mixture of diastereomers was obtained upon reaction with substrate 6.

12. For related allylboron reagents note: (a) Hoffmann, R. W.; Kemper, B. Tetrahedron Lett. **1982**, 23, 845. (b) Wuts, P. G. M.; Bigelow, S. S. J. Org. Chem. **1982**, 47, 2498.


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