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STEREOSELECTIVE ACYCLIC SYNTHESIS VIA ALLYLMETALS: THREO VICINAL DIOLS FROM BOTH E- AND Z-γ-ALKOXYALLYLTINS AND ALDEHYDES

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Abstract: Both E- and Z-γ-alkoxyallyltins stereoselectively add to aldehydes in the presence of $BF_3 \cdot OEt_2$ at -78°C in CH_2Cl_2 to produce the threo (or syn) vicinal diol monoalkyl ether unit.

Interest in the stereocontrolled synthesis of polyhydroxylated natural products has stimulated considerable efforts in both enantio- and diastereoselective syntheses of acyclic 1,2- and 1,3-diol units.[1] One strategy for the diastereoselective synthesis of acyclic vicinal or 1,2-diols employs the reaction of γ-alkoxyallylmetals with aldehydes.[2] In the following, we delineate a highly threo (or syn) diastereoselective vicinal diol synthesis using E- or Z-γ-alkoxyallyltins and its application to the synthesis of exo-brevicomin.

Yamamoto, et al.[3] have described an efficient and highly erythro selective reaction of either E- or Z-crotyltin (1: R = Me) with aldehydes (eq. 1) in the presence of a Lewis acid. The unique stereoselectivity was attributed to the non-cyclic transition state of the reaction. We have observed that the stereoselectivity is dependent upon the nature of the R group in 1.[4] Thus, all γ-alkylallyltins seem to produce erythro adducts 2a via a non-cyclic transition state In contrast, E-cinnamyltrialkyl- or -triaryltins provided exclusively threo adducts 2b through a cyclic transition state. We further speculated that this difference in the transition state may be accounted for in terms of the ionic property of the allylic C-Sn bond. An allyltin with a greater ionic contribution from the C-Sn bond appears to increase the propensity for the cyclic transition state in its reaction with aldehydes.[4] In this respect, we felt that γ-alkoxyallyltins 3 would provide stereoselectively threo vicinal diol derivatives 4a via non-cyclic transition states, regardless the geometry of the double bond of the allyltins (eq. 2).

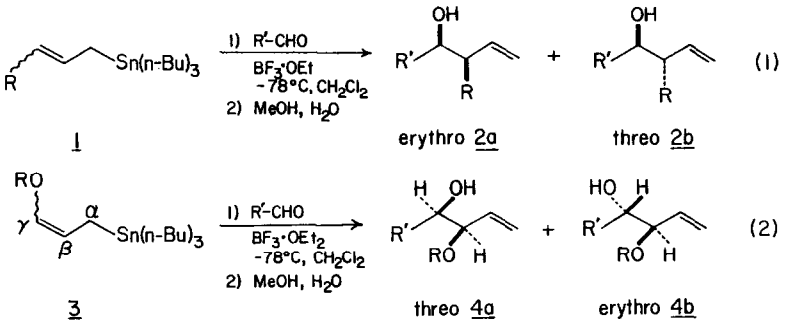
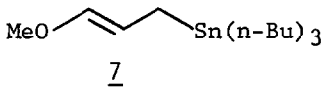
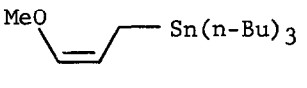
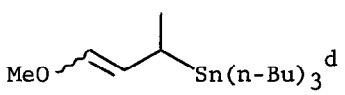
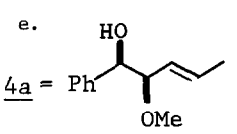
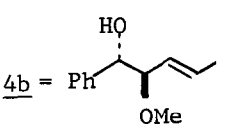
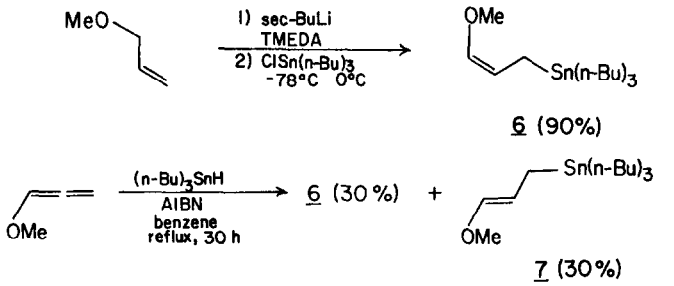


Table I. Stereoselective Synthesis of Vicinal Diol Derivatives[a]

Entry	γ-Alkoxyallyltins	Aldehydes (R'-CHO) R'	Products (R = Me)[b] 4a : 4b	Total Yields (%)[c]
1	 7	Ph	14 : 1	87
2	 6	Ph	10 : 1	86
3		o-Me-Ph	1.4: 1	77
4		i-Pr	>25 : 1	60
5		c-C_6H_{11}	5 : 1	44
6	 (E/Z = 1/2)	Ph	19 : 1[e]	86

a. All reactions were carried out at - 78°C in methylene chloride under argon using 1.4 - 2.0 equivalents of $BF_3 \cdot OEt_2$ for 2 - 4 hours. b. The diastereoisomeric ratio was determined by 360 MHz ^1H and 90.56 MHz ^{13}C NMR analyses of the crude reaction products. c. Yields are of the chromatographically pure products and based on the carbonyl compounds. d. bp 165 - 170°C (3 mmHg, kugelrohr); prepared as a stereoisomeric mixture in 87% yield from crotyl alcohol methyl ether via deprotonation with s-BuLi/TMEDA in THF at -78°C followed by treatment with $(n\text{-Bu})_3SnCl$ at -78°C. E-isomer: ^1H NMR (360 MHz, $CDCl_3$): δ 1.26 (d, 3H, J = 7.3 Hz), 2.41 (ddq, 1H, J = 1.2 (d), 7.3 (q), and 10.7 Hz (d)), 3.54 (s, 3H), 4.41 (dd, 1H, J = 6.1 and 10.7 Hz), and 5.67 ppm (dd, 1H, J = 1.2 and 6.1 Hz) and $Sn(n\text{-Bu})_3$ protons Z-isomer: ^1H NMR (360 MHz, $CDCl_3$): δ 1.28 (d, 3H, J = 7.6 Hz), 2.01 (ddq, 1H, J = 0.98 (d), 7.6 (q), and 8.8 Hz (d)), 3.48 (s, 3H), 5.03 (dd, 1H, J = 9.0 and 12.5 Hz), and 6.10 ppm (dd, 1H, J = 0.98 and 12.5 Hz) and $Sn(n\text{-Bu})_3$ protons. e.  4a =  4b

Scheme I

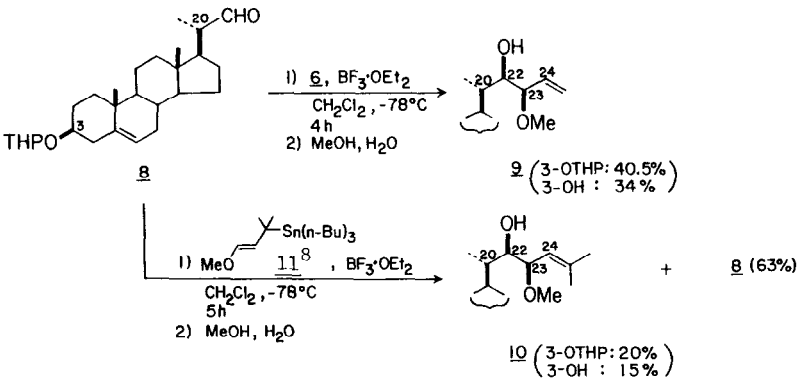


Requisite Z- and E-γ-methoxyallyltins 6 and 7 were prepared as shown in Scheme I. The presence of N,N,N',N'-tetramethylethylenediamine (TMEDA) during the deprotonation of allyl methyl ether[5] was essential to effect exclusive formation of 6.[6] The E-isomer 7[6] was separated via flash column chromatography from the mixture of 6 and 7 generated by a radical addition of tributyltin to methoxyallene. As is evident from Table I, both Z- and E-γ-methoxyallyl(tri-n-butyl)tins reacted with aldehydes exclusively at the γ-position with high threo (or syn) diastereoselectivity. The stereochemistry of the major products was unequivocally assigned by transforming the adducts into their dihydro dimethyl ethers. These were in turn synthesized from the corresponding E-olefins via OsO_4-cis-dihydroxylation followed by dimethylation with NaH/MeI.

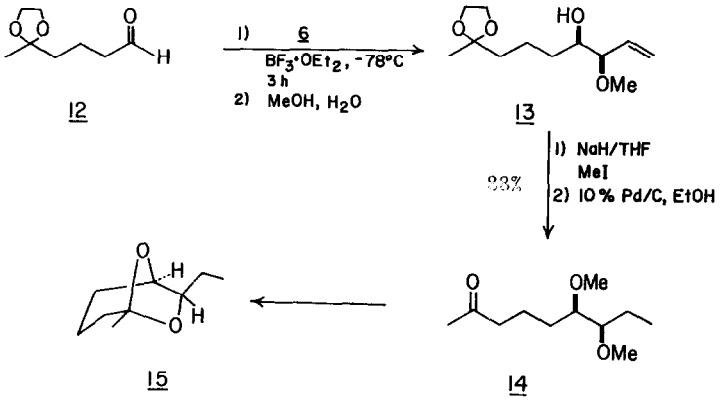
The examples shown in Schemes II and III demonstrate the versatility of this new threo selective vicinal diol synthesis. Adducts 9 and 10 were the only stereoisomers isolated. The stereochemistry of the hydroxyls in the steroid side chains is based on the vicinal proton-proton coupling constants.[7] The key synthetic intermediate 14 to exo-brevicomin 15[9] was conveniently synthesized in three steps from aldehyde 12[10] (Scheme III). The diol monomethyl ether 13 was obtained in 80% yield from 12 with stereoselectivity greater than 20/1. The minor erythro adduct was removed during purification via flash column chromatography. The dimethyl ether 14 has been converted in three steps to exo-brevicomin (15) by Mori.[11]

The results described herein clearly demonstrate that both Z- and E-γ-alkoxyallyltins undergo threo selective addition reactions to aldehydes via a non-cyclic transition states as in the case of crotyltins.[3] This highly stereoselective vicinal diol synthesis should find useful applications in the synthesis of various polyhydroxy natural products.[12]

Scheme II.



Scheme III.



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References and Footnotes:

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2. Reviews: (a) Yamamoto, Y.; Maruyama, K. Heterocycles 1982, 18, 357. (b) Hoffmann, R. W. Angew. Chem. Int. Ed. Engl. 1982, 21, 555. See also: (c) Yamamoto, Y.; Saito, Y.; Maruyama, K. Tetrahedron Lett. 1982, 23, 4959. (d) Keck, G. E.; Abbott, D. E.; Boden, E. P.; Enholm, E. J. ibid. 1984, 25, 3927. (e) Trost, B. M.; Bonk, P. J. J. Am. Chem. Soc. 1985, 107, 1778 and references cited therein.
3. Yamamoto, Y.; Yatagai, H.; Naruta, Y.; Maruyama, K. J. Am. Chem. Soc. 1980, 102, 7107.
4. Koreeda, M.; Tanaka, Y. Chem. Lett. 1982, 1297 and 1299.
5. (a) Evans, D. A.; Andrews, G. C.; Buckwalter, B. J. Am. Chem. Soc. 1974, 96, 5560. (b) Still, W. C.; Macdonald, T. L. ibid. 1974, 96, 5561.
6. 6: bp 163 - 165°C (3 mmHg); ^{1}H NMR (90 MHz, $CDCl_3$): δ 1.65 (d, 2H, J = 8.8 Hz), 3.55 (s, 3H), 4.53 (dt, 1H, J = 6.1 (d) and 8.8 Hz (t)) and 5.72 ppm (d, 1H, J = 6.1 Hz) and Sn(n-Bu)$_3$ protons; 7: ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.55 (d, 2H, J = 8.5 Hz), 3.47 (s, 3H), 4.95 (dt, 1H, J = 12.7 (d) and 8.5 Hz (t)) and 6.19 ppm (d, 1H, J = 12.7 Hz) and Sn(n-Bu)$_3$ protons.
7. 9: ^{1}H NMR (360 MHz, $CDCl_3$): $J_{20,22}$ = 1.2 Hz, $J_{22,23}$ = 8.8 Hz, and $J_{23,24}$ = 8.6 Hz; 10: ^{1}H NMR (360 MHz, $CDCl_3$): $J_{20,22}$ = 0.98 Hz, $J_{22,23}$ = 8.8 Hz, and $J_{23,24}$ = 9.8 Hz. cf.: Takatsuto, S.; Ikekawa, N. J. Chem. Soc. Perkin Trans. I 1983, 2133.
8. Prepared in 50% yield from γ,γ-dimethylallyl methyl ether via deprotonation with s-BuLi/TMEDA in THF at -78°C (1 h) followed by treatment with $(n\text{-Bu})_3SnCl$ at - 78°C - 0°C (1.5 h). ^{1}H NMR (360 MHz, $CDCl_3$): δ 1.19 (s, 6H), 3.46 (s, 3H), 5.05 (d, 1H, J = 12.6 Hz), and 5.93 ppm (d, 1H, J = 12.6 Hz) and Sn(n-Bu)$_3$ protons; ^{13}C NMR (22.5 MHz, $CDCl_3$): δ 8.43 (t), 13.57 (q), 27.11 (q), 27.55 (t), 28.79 (s), 29.28 (t), 56.17 (q), 116.12 (d), and 142.29 ppm (d).
9. (a) Brand, J. M.; Young, J. C.; Silverstein, R. M. Prog. Org. Nat. Prod. 1979, 37, 1. (b) Koreeda, M.; Tanaka, Y. J. Chem. Soc., Chem. Commun. 1982, 845 and references cited therein.
10. bp 82 - 85°C (5mmHg, kugelrohr bath temp). Synthesized from hex-5-en-2-one in four steps (see ref. 9b).
11. Mori, K. Tetrahedron 1974, 30, 4223.
12. After completion of this work, we learned from Professor G. E. Keck (University of Utah) that he has recently prepared a similar Z-γ-silyloxyallyltin reagent for his studies on stereocontrolled syntheses of acyclic polyols.

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