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STEREOSELECTIVE ACYCLIC SYNTHESIS VIA ALLYLMETALS: STRUCTURAL DEPENDENCE IN A LEWIS-ACID CATALYZED ADDITION OF ALLYLTINS TO ALDEHYDES

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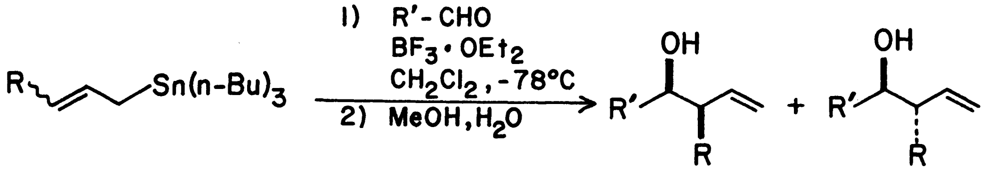
Lewis-acid catalyzed reaction of allyltins with aldehydes at -78°C provide homoallyl alcohols with high stereoselectivity; 2-alkenyltins in general provide erythro adducts preferentially with an erythro/threo ratio greater than 12/1, whereas only threo adducts can be obtained from E-cinnamyltins.

The stereocontrolled synthesis of α-alkyl-β-hydroxycarbonyl chains and their equivalents have presented a formidable challenge in the synthesis of natural products. One successful strategy to this end involves stereoselective reaction of Z- and E-2-alkenyl- or allylmetals with aldehydes.[1] This approach, however, suffers a serious drawback in that the starting organometallics with the Z-configuration are often not synthetically readily accessible. Recently, Yamamoto, et al.[2] have described an efficient and highly erythro selective reaction of either Z- or E-crotyltrialkyltin (1: R = Me) with aldehydes (eq 1).[3] Further, they have attributed this unique stereoselectivity to the non-cyclic transition state of the reaction. Herein we wish to report that our studies using various allyltins in their reactions with aldehydes have led to some useful and intriguing results providing high erythro or threo selectivity depending upon the allyltins employed.

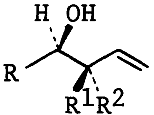
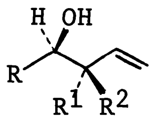
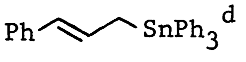
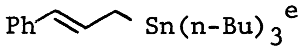
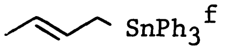
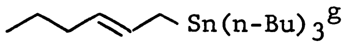
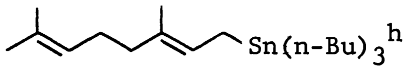
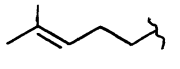
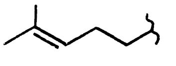
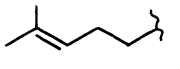
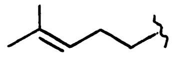


(1)

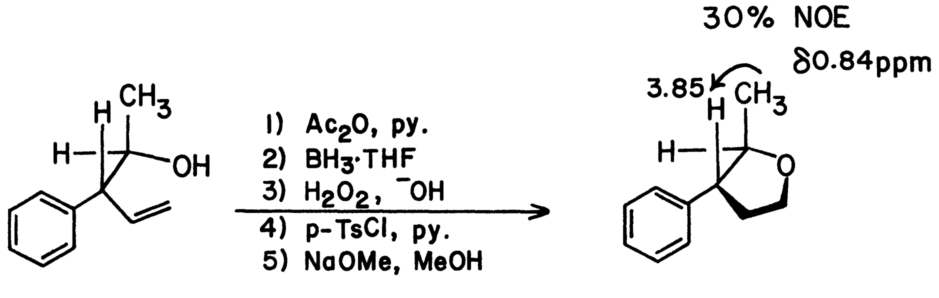
1 2 erythro 3 threo

Both Z- and E-crotyltri-n-butyltins provided predominantly the erythro adducts 2 (2/3 ~19) upon their $BF_3 \cdot OEt_2$-catalyzed[4] reaction with a wide variety of aldehydes (e.g., CH_3CHO, $PhCH_2CH_2CHO$, c-$C_6H_{11}CHO$, and PhCHO; in 90 - 95% isolated yield) in accordance with the reported results.[2] In contrast, however, E-cinnamyltriphenyltin[5] gave only threo isomers (entries 1 - 4 in Table I), indicating a chair-like cyclic transition state for this reaction. The threo stereochemistry of these adducts were ascertained by nuclear Overhauser effect (NOE) measurements. Thus, the adduct was converted into the tetrahydrofuran derivative [e.g., 5 from 4 (eq 2); see entry 4 in Table I] which showed a strongly positive NOE on the benzylic proton upon irradiation of the methyl protons (see 5).

Table I. Stereoselctive Synthesis of Homoallyl Alcohols via Allyltins[a]

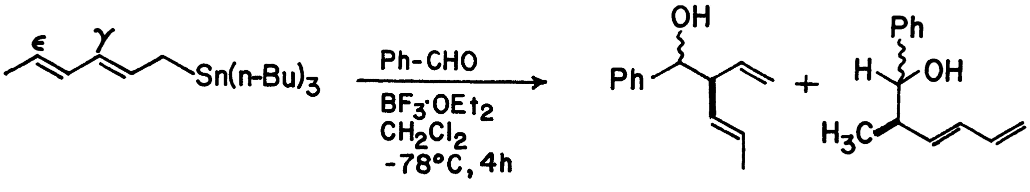
entry	allyltins	aldehydes (R-CHO) R	products  erythro R^1	 threo R^2	erythro[b] / threo	yield[c] (%)
1	 [d]	CH_3	Ph	H	1 : >99	84
2		$PhCH_2CH_2$	Ph	H	1 : >99	69
3		c-C_6H_{11}	Ph	H	1 : >99	65
4		Ph	Ph	H	1 : >99	76
5	 [e]	CH_3	Ph	H	1 : 9	81
6	 [f]	Ph	CH_3	H	5 : 1	92
7	 [g]	Ph	n-Pr	H	12 : 1	93
8	 [h]	CH_3		CH_3	>99 : 1	81
9		$PhCH_2CH_2$		CH_3	>99 : 1	60
10		c-C_6H_{11}		CH_3	>99 : 1	67
11		Ph		CH_3	>99 : 1	98

a. All reactions were carried out at -78°C in CH_2Cl_2 under argon. b. The erythro/threo ratio was determined by 360 MHz ^{1}H nmr analysis of the crude products. c. Isolated yield of the chromatographically pure products (erythro/threo mixture). d. mp 73 - 74°C [lit. mp 73°C; J. L. Wardell and S. J. Ahmed, J. Organometal. Chem., 78, 395 (1974)]. e. bp 196 - 203°C/1 mmHg (Kugelrohr) [lit. bp 163 - 164°C/0.4 mmHg; Y. Naruta, J. Am. Chem. Soc., 102, 3774 (1980)]. f. mp 59°C [lit. mp 59°C; R. M. Roberts, J. Organometal. Chem., 24, 675 (1970)]. g. Prepared from *E*-1-chloro-2-hexene and (n-Bu)$_3$SnLi. See: W. C. Still, J. Am. Chem. Soc., 100, 1481 (1978). h. bp 200 - 205°C/1 mmHg (Kugelrohr). See: K. Maruyama and Y. Naruta, J. Org. Chem., 43, 3796 (1978).



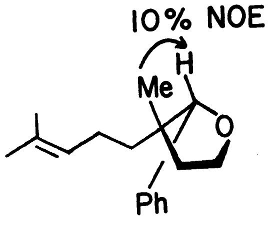
4 40% 5 (nmr in $CDCl_3$) (2)

In order to unravel the origin of this seemingly contradictory stereoselectivity in the $BF_3\cdot OEt_2$-catalyzed reactions of allyltins with aldehydes, first the effect of the non-allyl groups attached to tin was ,examined. As is evident from Table I, while the stereoselectivity diminshed drastically by changing the non-allyl group from phenyl to n-butyl (entry 5) or vice versa (entry 6), the original trend for threo or erythro preference of the cinnamyl or crotyltin remained unchanged. Furthermore, E-2-hexenyltri-n-butyltin (entry 7) exhibited the same erythro selectivity as crotyltri-n-butyltin. Therefore, one may conclude that the structural variation at the γ-carbon of the allyl moiety, i.e., alkyl or aryl, and not the size of the group, is the deciding factor in the erythro or threo preference of the adduct. These observations may be accounted for in terms of the ionic property of the allylic carbon-tin bond. Thus, the allyltin with a greater ionic contribution from the carbon-tin bond increases the propensity for the cyclic transition state in its reactions with aldehydes. Interestingly, in this regard, the conjugated dienyltin, E,E-2,4-hexadienyltri-n-butyltin (6)[6] exhibited intermediate property by providing a 5/3 ratio of the stereoisomers of the γ-adducts 7 (stereochemistry unassigned) in addition to the ε-adducts 8 in a 2/1 stereoisomeric mixture (eq 3).



6 7(30%) 8(30%) (3)

We have examined further the γ,γ-dialkylallyltin systems using E-geranyltri-n-butyltin (entries 8 - 11 in Table I) in order to evaluate the contribution of the two different alkyl groups at the γ-carbon to the stereoselectivity of the reaction. Results clearly indicate that the bulkier alkyl group dictates the mode of addition reaction with aldehydes by generating the stereoisomer with the bulkier alkyl moiety erythro to the hydroxy group. The erythro stereochemistry was verified by the NOE experiment using the tetrahydrofuran derivative of the



9

product as described earlier (e.g., 9 prepared in overall 30% yield from the reaction product of entry 11 in Table I).

In conclusion, therefore, the $BF_3\cdot OEt_2$-catalyzed reactions of all 2-alkenyltins with aldehydes appear to proceed through non-cyclic transition state as proposed for crotyltins,[2] whereas those with E-cinnamyltins prefer the conventional chair-like cyclic transition state. These stereocontrolled reactions described herein should find useful applications in the synthesis of the acyclic fragments of a number of natural products.[7]

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References

1. See the following for the stereoselective synthesis of homoallyl alcohols using allylmetals: boron: (a) R. W. Hoffmann and H. J. Zeiss, Angew. Chem. Int. Ed. Engl., 18, 306 (1979); (b) Idem, J. Org. Chem., 46, 1309 (1981); (c) M. Yamaguchi and T. Mukaiyama, Chem. Lett., 993 (1980); aluminium: (d) D. B. Collum, J. H. McDonald, and W. C. Still, J. Am. Chem. Soc., 102, 2118, (1980); chromium: (e) Y. Okude, S. Hirano, T. Hiyama, and H. Nozaki, J. Am. Chem. Soc., 99, 3179 (1977); (f) C. T. Buse and C. H. Heathcock, Tetrahedron Lett., 1685 (1978); (g) T. Hiyama, K. Kimura, and H. Nozaki, Tetrahedron Lett., 22, 1037 (1981); tin: (h) H. Yatagai, Y. Yamamoto, and K. Maruyama, J. Am. Chem. Soc., 102, 4548 (1980); titanium: (i) F. Sato, K. Iida, S. Iijima, H. Moriya, and M. Sato, J. Chem. Soc., Chem. Commun., 1140 (1981); zirconium: (j) Y. Yamamoto and K. Maruyama, Tetrahedron Lett., 22, 2895 (1981). See also a recent excellent review on the subject by: (k) Y. Yamamoto and K. Maruyama, Heterocycles, 18, 357 (1982).

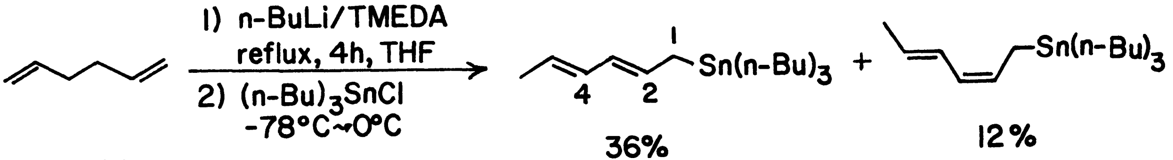
2. Y. Yamamoto, H. Yatagai, Y. Naruta, and K. Maruyama, J. Am. Chem. Soc., 102, 7107 (1980).

3. The terms erythro and threo are used as indicated in eq 1 following the convention described by Heathcock, et al. [J. Org. Chem., 45, 1066 (1980)]. While this is commonly adopted by many chemists involved in the field of stereoselective acyclic synthesis, it shoud be noted that this definition contradicts the original rule [see Chem. Abst., Index Guide, 76, 941 (1972)].

4. Other Lewis acids such as $AlCl_3$ and $TiCl_4$ also catalyze the reaction. However, $BF_3\cdot OEt_2$ was superior to others in terms of yield and cleanness of the reaction.

5. At the present time, due to its ready isomerization, attempts to prepare pure Z-cinnamyltrialkyl- or triphenyltin have not been successful. However, this Z-isomer is not considered essential in the mechanistic investigation of the present reaction, since the erythro adducts are expected through either a non-cyclic or cyclic transition state.

6. Obtained by the separation of the stereoisomeric mixture of 2,4-hexadienyltri-n-butyltins by flash silica gel chromatography. The diene mixture was prepared as follows:



7. See ref. 1 (k) and accompanying communication.

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