

THE ALLYLIC ALCOHOL FUNCTION IN ALKYLtin(IV)-MEDIATED CARBOCYCLIZATION.  
REGIOSPECIFIC OCTALIN AND HYDRINDENE SYNTHESIS.

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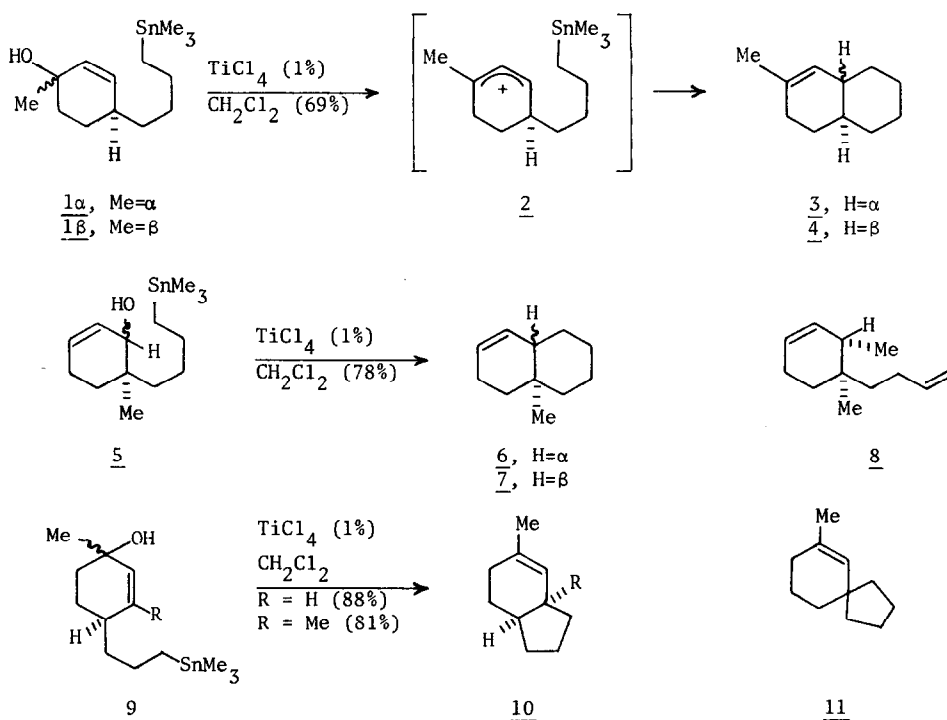
Abstract. The employment of the allylic alcohol function in the initiation of tetraalkylstannane-mediated carbocyclization and the application of this methodology to the regio-specific synthesis of  $\Delta^{1,2}$ -octalins and  $\Delta^{4,5}$ -hydrindene ring systems is described.

We have been examining the employment of the carbon-tin  $\sigma$  bond as a latent carbanionic nucleophile for the formation of carbon-carbon bonds with in situ generated carbon-centered electrophiles.<sup>1,2</sup> Our initial studies utilized allyl carbocationic electrophiles generated from  $\alpha$ -enones for initiation of this carbocyclization process.<sup>1a</sup> Subsequent work has expanded the class of viable electrophilic precursors to include allylic and tertiary alcohols, acetals, epoxides, olefinic cyclization and imminium ions.<sup>1c</sup> We report here of the use of the allylic alcohol function to initiate alkyltin(IV)-mediated carbocyclization and the application of this methodology to the regiospecific synthesis of  $\Delta^{1,2}$ -octalin and  $\Delta^{4,5}$ -hydrindene ring systems.

The cyclization method proceeds via acid catalyzed generation of an allyl carbocation which is sufficiently electron deficient to undergo electrophilic substitution on a stereoproximate carbon-tin  $\sigma$  bond (eg. 1 + 2 + 3 + 4). The allylic alcohol and tetraalkyltin functions are compatible until such electrophilic activation due in part to the weakly polarized nature of the carbon-tin sigma bond ( $C^{\delta-} - Sn^{\delta+}$ ). Thus, when a representative allylic alcohol substrate 1<sup>3</sup> is treated with a Lewis acid catalyst in methylene chloride a mixture of cis- and trans-2-methyl- $\Delta^{1,2}$ -octalins (3 and 4)<sup>3</sup> is obtained. The ratio of  $\Delta^{1,2}$ -octalin products (3/4) was not related to the stereochemistry of the allylic alcohol precursor 1 and was directly related to the reaction temperature. The independence of starting material stereochemistry and cyclization product ratio supports an allyl carbocationic intermediate 2 as the electrophile in the cyclization process. The dependence of cis/trans product ratio upon reaction temperature is a synthetically useful feature of this cyclization and generates product ratios (3/4) varying from  $\sim 90/10$  at  $40^\circ C$  to  $\sim 30/70$  at  $-70^\circ C$ . This sensitivity of product ratio to temperature may be a reflection of the distribution of pseudoaxial: pseudoequatorial (4'-trimethylstannyl)butyl side-chain conformers coupled with the relative facility and product selective mode of cyclization of each side-chain conformer.<sup>4</sup>

An additional entry into the 4-substituted cyclohexenyl cation manifold (cf. 2) is via the ionization of 6-substituted 2-cyclohexen-1-ol precursors. Thus, when allyl alcohols 5<sup>3</sup> were subjected to non-aqueous acidic reaction conditions, cis- and trans-9-methyl- $\Delta^{1,2}$ -octalins 6 and 7 were obtained. The octalin product ratio was again independent of the stereochemistry of the cyclohexenol precursor 5 and sensitive to variation in reaction temperature. The differential in product ratio with temperature (6/7)  $\cong$  95/5 at 40°C and  $\cong$  55/45 at -70°C) was smaller than in the cyclization of cyclohexenols 1, which we attribute to a diminished conformational preference for the pseudoequatorial position of the (4'-trimethylstannyl)butyl pendant side chain (which we postulate progresses preferentially to the trans ring junction product<sup>4b</sup>) due to the geminal ring methyl substituent.

However, when the site adjacent to the (4'-trimethylstannyl)butyl side chain in the 4-cyclohexenyl cation is tertiary, an alternate reaction course transpires. Thus, cyclohexenols 5 (H = Me) upon electrophilic activation undergo exclusive transfer of hydride in the position  $\beta$  to the trimethylstannyl unit generating a single, stereoisomeric cyclohexene to which we tentatively assign structure 8<sup>3</sup> (78%). In the formation of six-membered rings via this alkylin mediated strategy, the balance between carbon-carbon bond formation and  $\beta$ -hydride transfer for a variety of carbon centered electrophiles is sensitive to several reaction conditions and substrate structural parameters.<sup>1b</sup> Under the conditions employed in the cyclization of cyclohexenols 1 and 5, secondary-carbocationic sites favor carbon-carbon bond formation and tertiary-carbocations favor  $\beta$ -hydride transfer.



$\beta$ -Hydride transfer does not appear to be a competitive reaction mode during the formation of five-membered rings via these tetraalkyltin mediated processes, even when carbocyclization requires approach to a trisubstituted carbocation. Thus, cyclohexenols 9 (R = H, Me) undergo smooth acid catalyzed cyclization to afford cis-4-methylhydrindene 10 (R = H, Me). This mode of reaction occurs under catalysis by a variety of Lewis and protic acids in methylene chloride. As in our previous investigation of  $\alpha$ -enone initiated tin(IV)-mediated carbocyclization,<sup>1a</sup> the formation of a five-membered ring relative to the homologous six-membered ring appears qualitatively to be a kinetically faster and less sterically sensitive reaction process. Furthermore, in the cyclopentannulation of substrates with identical requirements, alkyl substitution at the electrophilic site for carbon-tin bond attack appears to retard carbon-carbon bond formation, but not to alter the course of reaction (eg. to  $\beta$ -hydride transfer). The facile formation of quaternary carbon-carbon bonds during the generation of five-membered carbocycles has been established by the examination of several carbocyclic systems. [For example: the direct synthesis of spirocycle 11 via internal carbon-tin bond attack at a trisubstituted site of the intermediate cation (82%).]

Both internal tetraalkyltin-mediated reactions with carbon-centered electrophiles - carbon-carbon bond formation and  $\beta$ -hydride transfer - are useful synthetic transformations. We are continuing our synthetic and mechanistic investigations of these processes.

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#### Notes and References

† Research Fellow of the Alfred P. Sloan Foundation.

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- (c) See also: Stork, G.; Taber, D. F.; Mark, M. ibid 1978, 2445 and references therein.

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