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STEREOSPECIFIC CYCLOPROPANE SYNTHESIS FROM γ-STANNYL ALCOHOLS[1]

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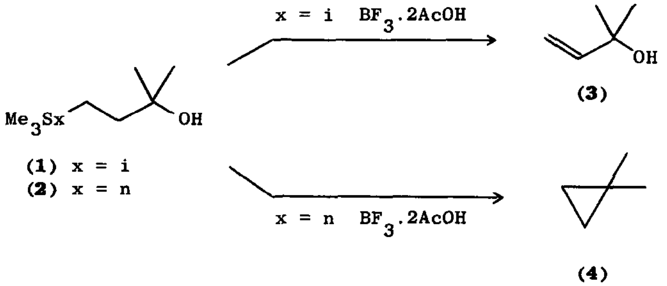
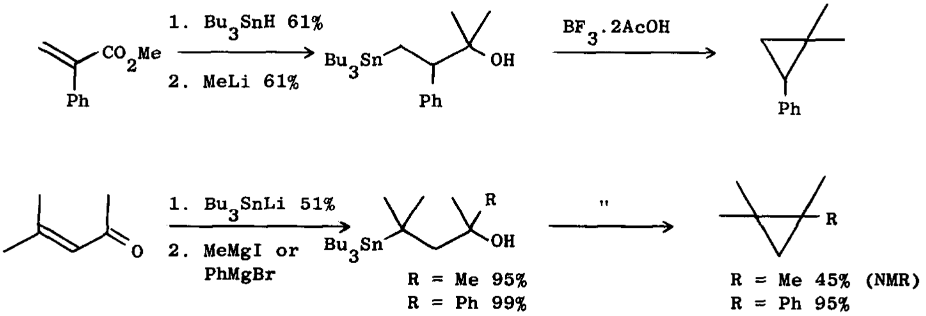
Summary—Tertiary and benzyl alcohols with a γ-trialkyltin group form cyclopropanes stereospecifically on treatment with acid, with inversion of configuration at both carbon atoms.

We have reported earlier[2,3] several examples of silicon-controlled carbonium ion rearrangement, of which the most simple was the hydride shift (**1** → **3**).[2] In contrast, there were several indications[4-6] that the corresponding tin compounds would give cyclopropanes, a reaction we have almost never[7] seen in the silicon series. Thus solvolysis of the tertiary chloride corresponding to the alcohol (**2**) was known[4] to give the cyclopropane (**4**). We were not surprised, therefore, to find that the alcohol (**2**) gave the cyclopropane (**4**) on treatment with acid under the same conditions that we had used for the alcohol (**1**). We have now investigated this cyclopropane-forming reaction in more detail, and find that it is both high-yielding and amenable to a high level of stereocontrol.



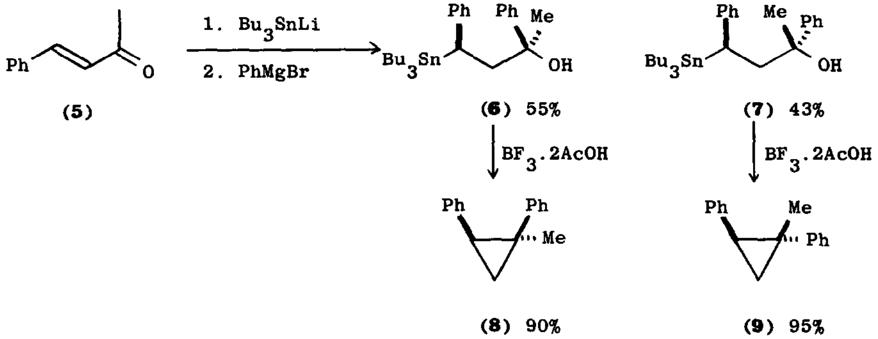
The reactions in Scheme 1 illustrate methods for the synthesis of simple γ-stannyl alcohols using hydrostannation[8] or conjugate addition of tin-lithium reagents.[9] The acid-catalysed formation of the cyclopropanes takes place in high yield, even when the carbon-carbon bond is formed between fully-substituted centres.

SCHEME 1

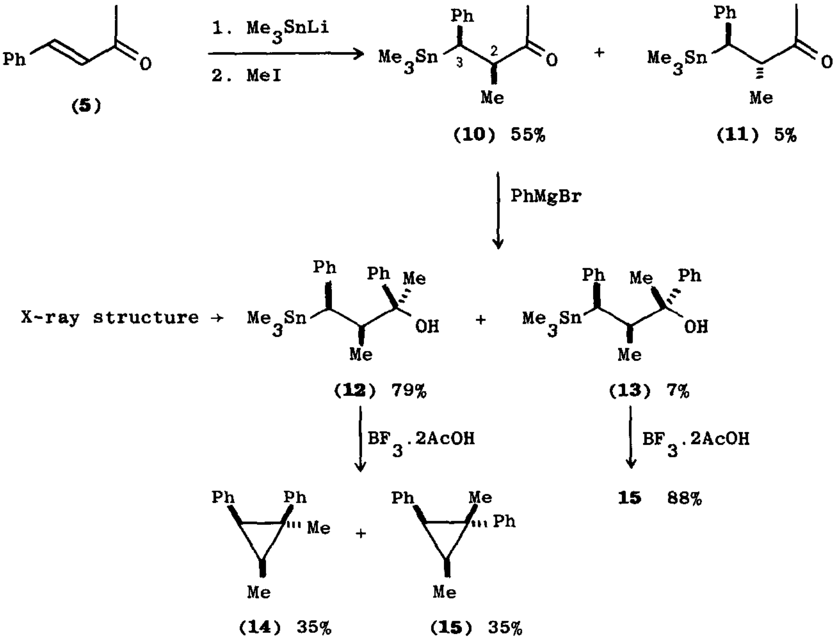


The reactions in Scheme 2 illustrate the stereospecificity of the reaction, each diastereoisomer (**6** or **7**) giving a different cyclopropane (**8** or **9**). The stereospecificity at the hydroxyl-bearing carbon is remarkable in view of its tertiary benzylic nature. That the reactions actually take place with inversion of configuration at both centres, as illustrated, was only proved in the more complicated case below (Scheme 3). Conjugate addition of trimethyltin-lithium to the enone (**5**), followed by methylation of the intermediate enolate, gave the ketones (**10** and **11**) with high diastereoselectivity.[10] The reaction of the phenyl Grignard reagent on the major ketone gave the alcohols (**12** and **13**), also with high diastereoselectivity.[11] Proof of structure was provided by an X-ray structure determination[12] on the major alcohol (**12**).

SCHEME 2

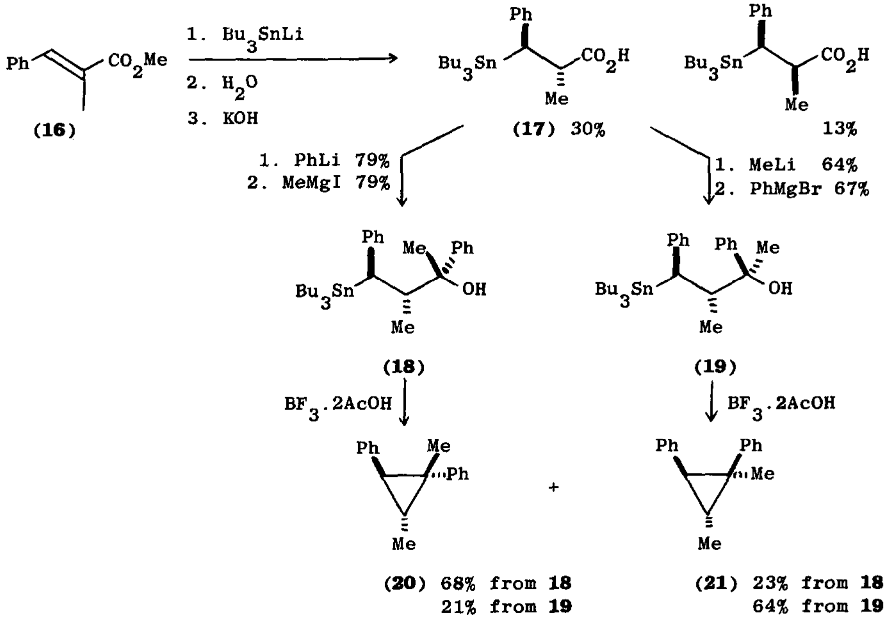


SCHEME 3



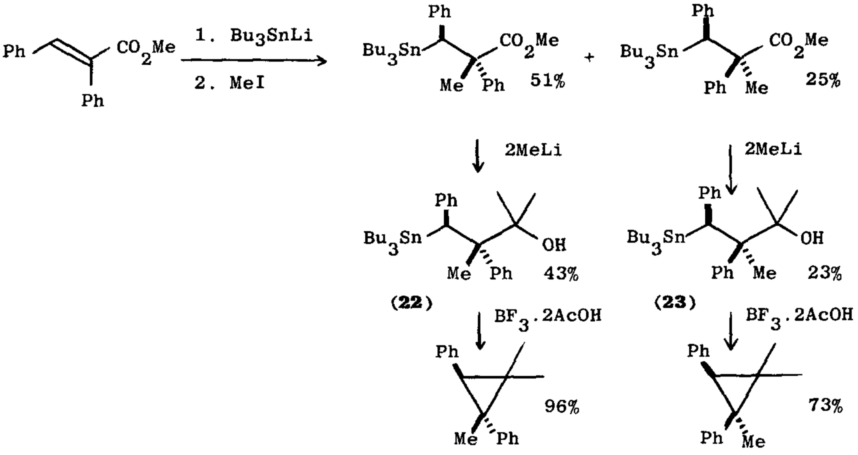
Treatment of this alcohol with acid gave two cyclopropanes (**14** and **15**), whereas the minor alcohol gave only the cyclopropane (**15**). Although the stereospecificity with inversion of configuration at both centres is now proved,[13] it is no longer complete at the hydroxyl-bearing carbon of **12**. The sequence of reactions (**5** → **10** → **12**) is a highly stereocontrolled and effective synthesis of the cyclopropanes (**14** and **15**), and it is easily possible to adapt it for the synthesis of the stereoisomeric cyclopropanes (**20** and **21**). Thus conjugate addition (Scheme 4) to the ester (**16**), followed by protonation[10] and ester hydrolysis, gave largely the acid (**17**). Successive treatment with phenyl-lithium and the methyl Grignard reagent gave largely[15] the alcohol (**18**), and the alternative order, methyl-lithium and the phenyl Grignard reagent, gave largely the alcohol (**19**). Each of these alcohols cyclised with high but incomplete stereospecificity to give the cyclopropanes (**20** and **21**).

SCHEME 4



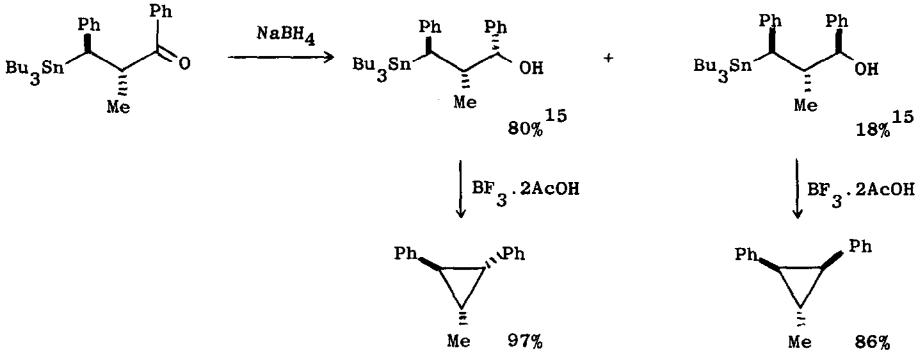
The reactions in Scheme 5 were carried out to give the alcohols (**22** and **23**) a highly favourable opportunity to undergo rearrangement by phenyl shift with formation of a tertiary cation. This did not take place, demonstrating vividly the contrast between the tin and the silicon series. Finally, the reactions in Scheme 6 show that secondary benzyl alcohols give cyclopropanes with complete stereospecificty.

SCHEME 5



We have met two failures in our attempts to extend this cyclopropane synthesis. One limit is that simple secondary alcohols with a γ-stannyl group decompose without noticeable cyclopropane formation. The other is more serious: we have failed[16] to make the reaction work in such a way as to fuse a gem-dimethylcyclopropane onto a five-, six-, or seven-membered ring. This was disappointing in view of the analogous reaction,[17] in which five- and six-membered rings have been fused onto six-membered rings using a functionally isolated carbon-tin bond as the carbon nucleophile.

SCHEME 6



NOTES and REFERENCES

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6. D. C. McWilliam, T. R. Balasubramanian, and H. G. Kuivila, *J. Am. Chem. Soc.*, **100**, 6407 (1978); Y. Ueno, M. Ohata, and M. Okawara, *Tetrahedron Lett.*, **23**, 2577 (1982); D. J. Peterson, M. D. Robbins, and J. R. Hansen, *J. Organomet. Chem.*, **73**, 237 (1974).
7. When the silyl group is γ to a primary or secondary electron-deficient centre, cyclopropane formation is common,[18] but with tertiary alcohols we have found cyclopropanes only when we were trying to persuade a methoxycarbonyl group to migrate.
8. G. J. M. Van der Kirk, J. G. Noltes, and J. G. A. Luijten, *J. Appl. Chem.*, **7**, 356 (1957).
9. W. C. Still, *Tetrahedron Lett.*, 2659 (1978).
10. The high diastereoselectivity in this step is the same as that which we had already observed in the silicon series.[19]
11. The high diastereoselectivity in this step is remarkable for being anti-Cram. See note 15.
12. P. Raithby, to be published.
13. Inversion at the tin-bearing C was in line with analogies in tin[5] and boron[20] chemistry.
14. We speculate that the formation of a cyclopropane **(14)** with two phenyl groups and one methyl group, all *cis* to each other, provides the barrier to smooth S_N2-like behaviour at the hydroxyl-bearing carbon of **12**.
15. These reactions follow Cram's rule, in contrast to the reaction of the ketone **(10)**. It looks, superficially, as though the tin-bearing chiral centre (C-3) controls the diastereoselectivity more powerfully than the chiral centre (C-2) adjacent to the ketone group. However, when C-3 is the only chiral centre, as in the ketone used for the preparation of **6** and **7**, it exerts a negligible effect (56:44).
16. We speculate that the high stereospecificity demands a *trans*-diaxial arrangement of the tributylstannyl and the dimethylcarbinol groups, and this is, quite reasonably, not populated. We made both *cis* and *trans* isomers with each ring size, and none gave any noticeable cyclopropane products.
17. T. L. Macdonald and S. Mahalingam, *J. Am. Chem. Soc.*, **102**, 2113 (1980) and **103**, 6767 (1981).
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