

A Novel 1,3-Stannyl Shift Promoted Intramolecular Cyclizations of α -Stannyl Radicals with a Formyl Group

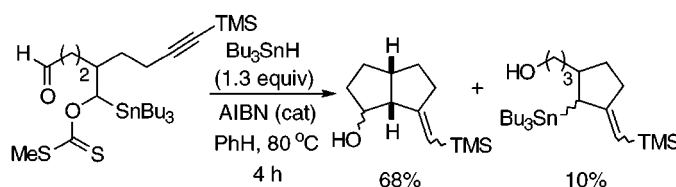
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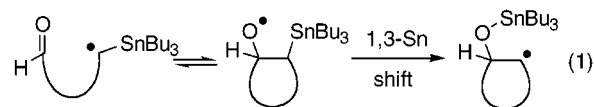
ABSTRACT



Reactions of α -stannyl bromides and xanthates with tributyltin hydride generate α -stannyl radicals. Intramolecular cyclizations of these radicals with a formyl group afford γ -stannyl alkoxy radicals that undergo a 1,3-stannyl shift from carbon to oxygen. The carbon radicals obtained can be trapped inter- or intramolecularly. Approximately, the rates of 5-*exo* cyclizations of α -stannyl radicals with a formyl group and terminal olefin are similar.

Intramolecular radical addition to a carbonyl to give a cyclic alcohol is a potentially useful reaction.¹ However, this type of cyclizations is reversible, and the reverse reaction is generally faster than the cyclization.² In the cases of acylgermanes,³ acylsilanes,¹ thioesters,⁴ and selenoesters,⁴ intramolecular radical additions to the carbonyl moieties in these compounds are followed by irreversible processes. Therefore, these cyclizations can be stopped at the cyclization side.⁵ Herein, we wish to report the intramolecular cyclization

of a formyl group with an α -stannyl radical⁶ (eq 1). In this cyclization, a novel homolytic 1,3-stannyl shift from carbon to oxygen^{7–10} serves as the driving force.



As shown in eq 2, aldehydes **1**¹¹ were coupled with tributyltin lithium,¹² and the resulting α -stannyl alcohols were

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(3) (a) Curran, D. P.; Liu, H. *J. Org. Chem.* **1991**, *56*, 3463–3465. (b) Curran, D. P.; Palovich, M. *Synlett* **1992**, 631–632. (c) Curran, D. P.; Diederichsen, U.; Palovich, M. *J. Am. Chem. Soc.* **1997**, *119*, 4797–4804. (d) Diederichsen, U.; Curran, D. P. *J. Organomet. Chem.* **1997**, *531*, 9–12.

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(6) Tsai, Y.-M.; Chang, S.-Y. *J. Chem. Soc., Chem. Commun.* **1995**, 981–982.

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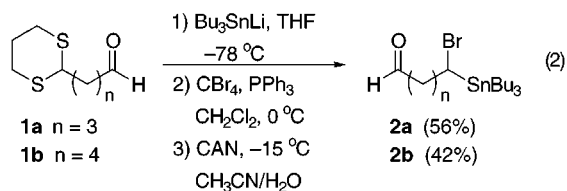
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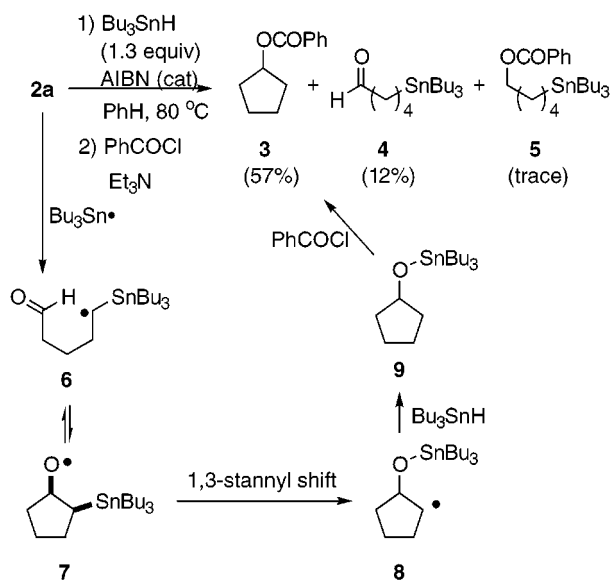
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converted to α -stannyl bromides using carbon tetrabromide and triphenylphosphine.¹³ The dithiane moiety was then deprotected¹⁴ to give aldehydes **2** in mild yields over three steps. Treatment of aldehyde **2a** with tributyltin hydride¹⁵ (Scheme 1) followed by quenching the reaction with benzoyl

Scheme 1



chloride gave cyclopentyl benzoate (**3**) in 57% yield. Uncyclized reduction product aldehyde **4** was also isolated in 12% yield along with a trace amount of benzoate **5**. Benzoate **5** was presumably derived from over-reduction of aldehyde **4** by excess tributyltin hydride followed by benzoate formation.

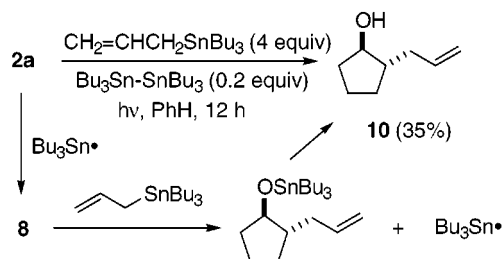
Mechanistically, this cyclization reaction occurs through formation of α -stannyl radical **6** first. This radical then cyclizes with the formyl group to generate γ -stannyl alkoxy radical **7**. Because radical cyclizations of carbonyl compounds are generally reversible,² it is likely that the oxygen radical and stannyl group may have a chance to adopt a *syn*-relationship as shown in **7**. Alkoxy radical **7** presumably undergoes a 1,3-stannyl shift from carbon to oxygen to generate carbon radical **8**. It is known that the O–Sn bond

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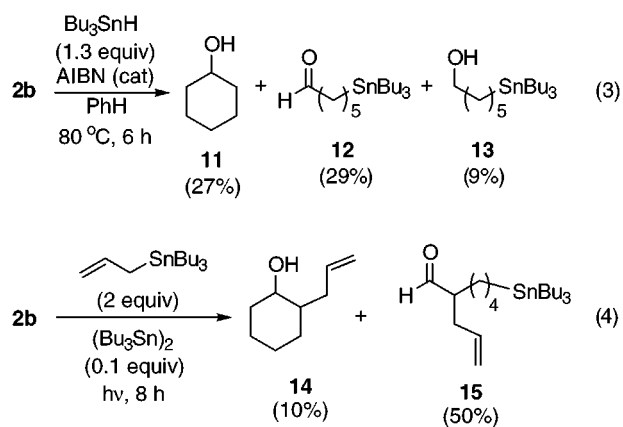
(15) The cyclization reaction was performed by slow addition (4 h) via syringe pump of a benzene solution of tributyltin hydride (1.3 equiv, 0.13 M in benzene) and AIBN (0.05 equiv) to a solution of the bromide (0.1 M) in refluxing benzene.

Scheme 2

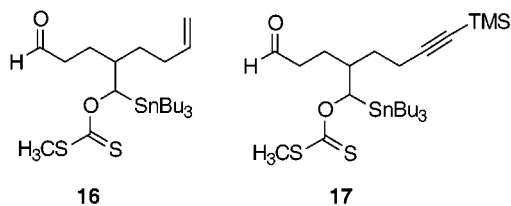


is stronger than the C–Sn bond by about 25 kcal/mol.¹⁶ This big difference provides a strong thermodynamic driving force to trap alkoxy radical **7**. Abstraction of hydrogen from tributyltin hydride by radical **8** gives stannyl ether **9**. The oxygen atom in stannyl ethers is known to be quite nucleophilic.¹⁷ Therefore, for the convenience of isolation and identification, stannyl ether **9** was converted directly to the corresponding benzoate **3**.

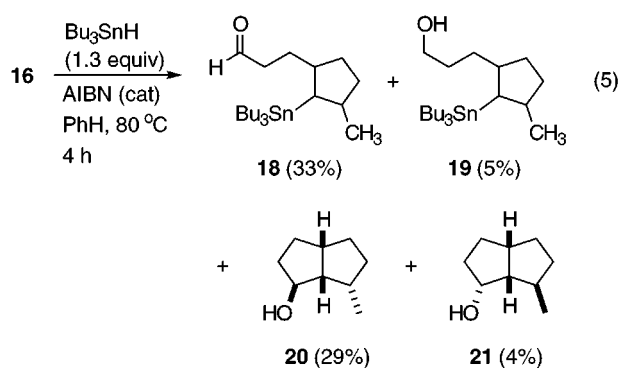
When aldehyde **2a** (Scheme 2) was treated with allyltributyltin (4 equiv) in the presence of hexabutylditin (0.2 equiv) and initiated by photolysis of long wavelength UV light¹⁸ (12 h), we were able to isolate alcohol **10**¹⁹ in 35% yield. This reaction provided evidence that indeed radical **8** was formed. In the case of 6-*exo* cyclization (eq 3), aldehyde **2b** reacted with tributyltin hydride¹⁵ and gave 27% of cyclohexanol (**11**), 29% of uncyclized reduction product aldehyde **12**, and 9% of over-reduction product alcohol **13**. The problem of this reaction was revealed by the reaction of aldehyde **2b** with allyltributyltin (eq 4). Along with alcohol **14**²⁰ (10%), we obtained a 50% yield of aldehyde **15** that contains an allyl group at the α -position of the carbonyl group. This result indicates that a 1,5-hydrogen transfer²¹ occurs after generation of the α -stannyl radical from aldehyde **2b**. This process leads to formation of an α -carbonyl radical. The α -carbonyl radical is then trapped by allyltributyltin to give aldehyde **15**.



This stannyl shift that promotes the radical cyclization reaction can be employed in a tandem cyclization mode. Instead of using α -stannyl bromides, we synthesized xanthates **16** and **17** for our studies.⁶ The reaction of xanthate

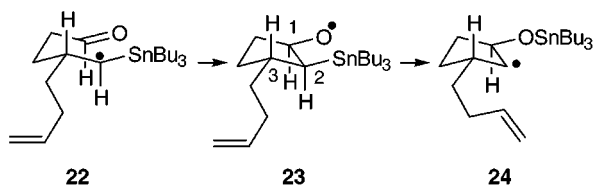


16 with tributyltin hydride¹⁵ (eq 5) gave monocyclic aldehyde **18** in 33% yield. This aldehyde was derived from the addition of an α -stannyl radical to the olefin first. Alcohol **19** (5%) was also obtained. This material was presumably derived from reduction of aldehyde **18** by excess tributyltin hydride. Bicyclic alcohol **20** was isolated in 29% yield. Small amounts of the benzoate derived from bicyclic alcohol **21** were detected in 4% yield through benzylation of the crude cyclization mixture. The benzoates derived from alcohols **20** and **21** thus obtained are identical to that reported by Wilcox et al.²² The stereochemistry of alcohols **20** and **21**



can therefore be determined. There appeared to be other stereoisomers of the alcohols **20** and **21**; however, the amount was very small and we were not able to identify these minor isomers. Bicyclic alcohols **20** and **21** are tandem cyclization products derived from the addition of α -stannyl radical **22** (Scheme 3) to the formyl group first. The cyclization

Scheme 3



presumably prefers to adopt a chair transition state²³ with the large groups located at the equatorial position as shown in **22**. This leads to the formation of the alkoxy radical **23** with a predominant *trans*-1,3-relationship. The stannyl shift

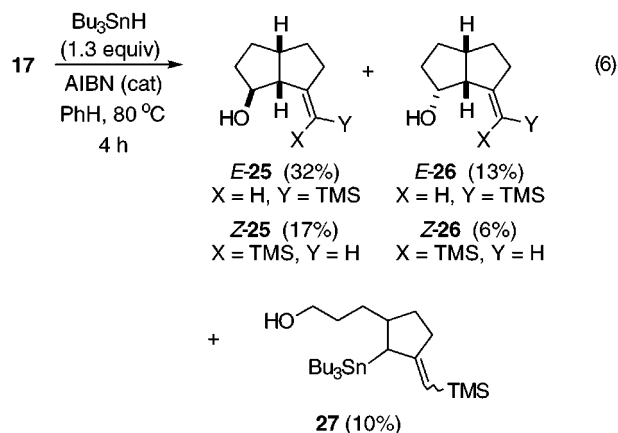
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(17) Pereyre, M.; Quintard, J.-P.; Rahm, A. *Tin in Organic Synthesis*; Butterworths: London, 1997; Chapter 11, p 261.

(18) A Rayonet photochemical reactor equipped with 3500 Å lamps was used.

of alkoxy radical **23** gives radical **24**. This radical cyclizes with the olefin to give bicyclic alcohol **20** as the major isomer with known *endo*-selectivity.²⁴

The rates for the addition of an α -stannyl radical to an olefin and a formyl group appear to be similar because the total yield of monocyclic products **18** and **19** is close to that of bicyclic alcohols **20** and **21**. With this information available, it is possible to attenuate the tandem system to favor the bicyclic product. For example, it is known that 5-*exo* cyclization of 5-hexynyl radical is slower than the corresponding 5-hexenyl radical cyclization by nearly 10-fold.²⁵ Therefore, for xanthate **17**, one would expect carbonyl cyclization to be faster than alkyne cyclization. As shown in eq 6, cyclization of xanthate **17** gave four isomeric bicyclic alcohols **25** and **26** in a combined yield of 68%.²⁶ Monocyclic alcohol **27** was isolated in 10% yield. The ratio of carbonyl addition products versus alkyne addition products was about 7:1.



In conclusion, a 1,3-stannyl shift promoted cyclization of an α -stannyl radical with a formyl group was developed. This process is successful for 5-*exo* cyclization. In comparison, the corresponding 6-*exo* cyclization seriously competes with a 1,5-hydrogen transfer reaction. Approximately, 5-*exo* cyclizations of an α -stannyl radical with a formyl group or with a terminal olefin have similar rates. This information will be useful in the design of tandem cyclizations. However, the reversibility of formyl group cyclization requires further

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(26) The stereochemistry of these compounds were determined by NOE experiments.

investigation. In the tandem cyclizations, the α -stannyl xanthate moiety serves as a novel *gem*-diyl equivalent.²⁷

Acknowledgment. Financial support by the National Science Council of the Republic of China is gratefully acknowledged.

(27) For the use of *gem*-dihalide as *gem*-diyl equivalent, see ref 22.

Supporting Information Available: Synthetic schemes for **16** and **17**. Details of compound characterization of **2a,b**, **4**, **12**, **13**, **15–20**, and **25–27**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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