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

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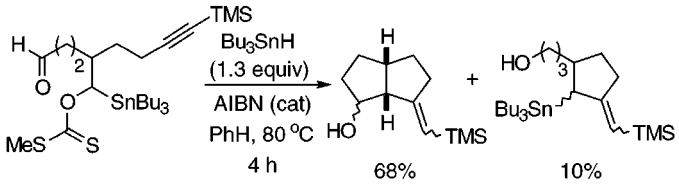
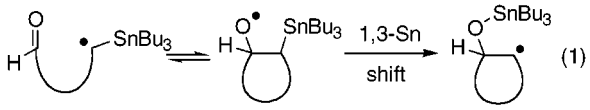
ABSTRACT



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 radical[6] (eq 1). In this cyclization, a novel homolytic 1,3-stannyl shift from carbon to oxygen[7−10] serves as the driving force.



(1)

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

(1) Chang, S.-Y.; Jiaang, W.-T.; Cherng, C.-D.; Tang, K.-H.; Huang, C.-H.; Tsai, Y.-M. *J. Org. Chem.* **1997**, *62*, 9089−9098 and references therein.

(2) (a) Beckwith, A. L. J.; Hay, B. P. *J. Am. Chem. Soc.* **1989**, *111*, 230−234. (b) Beckwith, A. L. J.; Hay, B. P. *J. Am. Chem. Soc.* **1989**, *111*, 2674−2681. (c) Beckwith, A. L. J.; Raner, K. D. *J. Org. Chem.* **1992**, *57*, 4954−4962.

(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.

(4) Kim, S.; Jon, S. Y. *J. Chem. Soc., Chem. Commun.* **1996**, 1335−1336.

(5) For other strategies to drive the equilibrium, see: (a) Hays, D. S.; Fu, G. C. *J. Org. Chem.* **1998**, *63*, 6375−6381. (b) Kim, S.; Oh, D. H. *Synlett* **1998**, 525−527. (c) Batey, R. A.; MacKay, D. B. *Tetrahedron Lett.* **1998**, *39*, 7267−7270.

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

(7) For homolytic 1,5-stannyl shift from carbon to oxygen, see: (a) Kim, S.; Lee, S.; Koh, J. S. *J. Am. Chem. Soc.* **1991**, *113*, 5106−5107. (b) Kim, S.; Lim, K. M. *Tetrahedron Lett.* **1993**, *34*, 4851−4854.

(8) For homolytic 1,6-stannyl shift from carbon to oxygen, see: (a) Kim, S.; Lim, K. M. *J. Chem. Soc., Chem. Commun.* **1993**, 1152−1153. (b) Kim, S.; Do, J. Y.; Lim, K. M. *Chem. Lett.* **1996**, 669−670.

(9) For homolytic 1,4-stannyl shift from oxygen to oxygen, see: Alberti, A.; Hudson, A. *Chem. Phy. Lett.* **1977**, *48*, 331−333.

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(12) Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481−1487.

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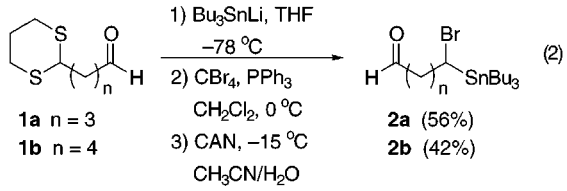
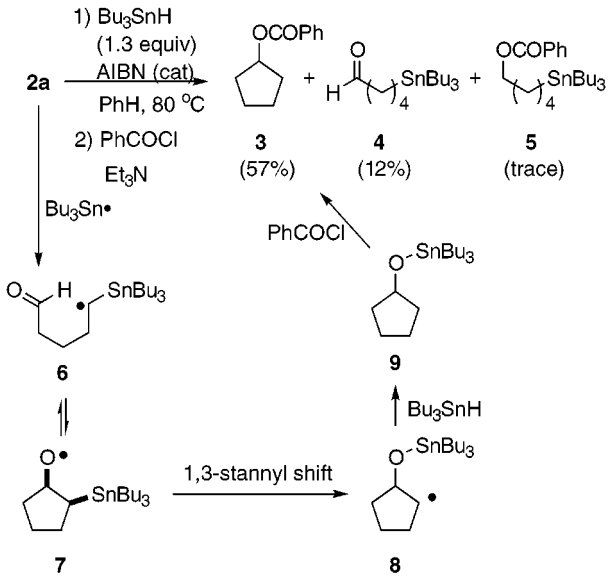


converted to α-stannyl bromides using carbon tetrabromide and triphenylphosphine.[13] The dithiane moiety was then deprotected[14] to give aldehydes **2** in mild yields over three steps. Treatment of aldehyde **2a** with tributyltin hydride[15] (Scheme 1) followed by quenching the reaction with benzoyl

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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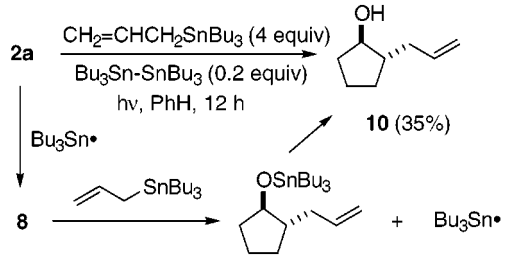
(14) (a) Ho, T.-L.; Ho, H. C.; Wong, C. M. *J. Chem. Soc., Chem. Commun.* **1972**, 791−791. (b) Ho, H. C.; Ho, T.-L.; Wong, C. M. *Can. J. Chem.* **1972**, *50*, 2718−2721.

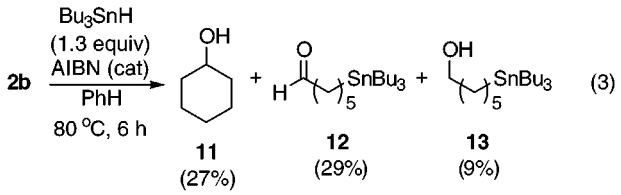
(15) The cyclization reaction was performed by slow addition (4 h) via syringe pump of a benzene solution of tributyltin hydride (1.3 equiv, 0.13 M in benzene) and AIBN (0.05 equiv) to a solution of the bromide (0.1 M) in refluxing benzene.

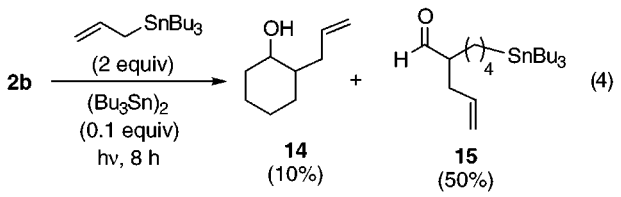
Scheme 2



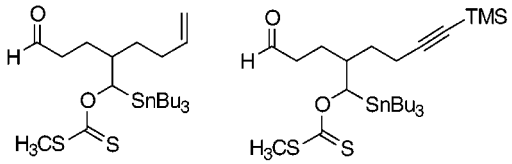
is stronger than the C−Sn bond by about 25 kcal/mol.[16] This big difference provides a strong thermodynamic driving force to trap alkoxy radical **7**. Abstraction of hydrogen from tributyltin hydride by radical **8** gives stannyl ether **9**. The oxygen atom in stannyl ethers is known to be quite 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 light[18] (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 hydride[15] 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 transfer[21] 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**.



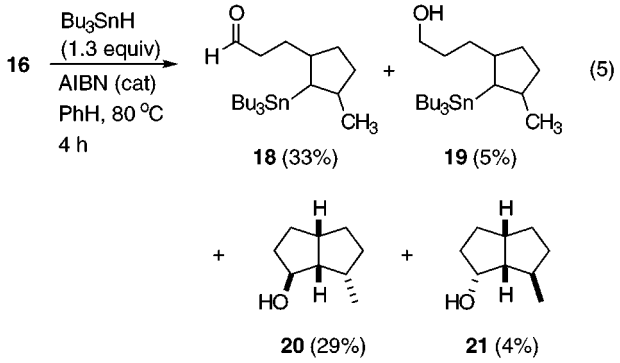


This stannyl shift that promotes the radical cyclization reaction can be employed in a tandem cyclization mode. Instead of using α-stannyl bromides, we synthesized xanthates **16** and **17** for our studies.[6] The reaction of xanthate



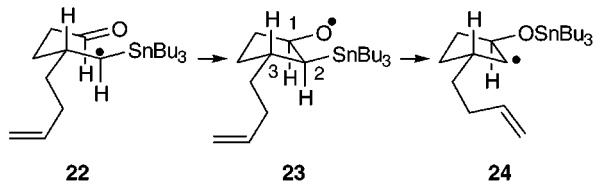
16 17

16 with tributyltin hydride[15] (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 benzoylation 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**



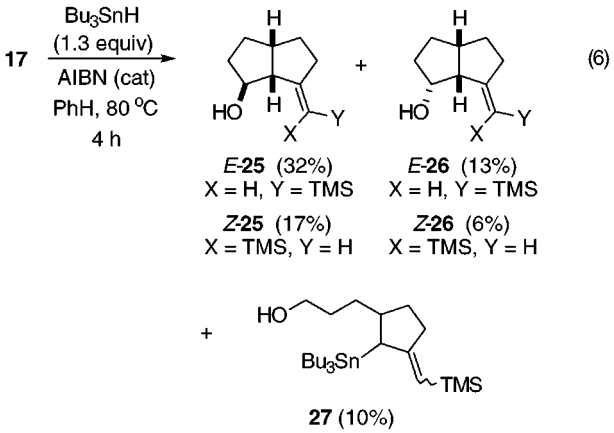
can therefore be determined. There appeared to be other stereoisomers of the alcohols **20** and **21**; however, the amount was very small and we were not able to identify these minor isomers. Bicyclic alcohols **20** and **21** are tandem cyclization products derived from the addition of α-stannyl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

Scheme 3



presumably prefers to adopt a chair transition state[23] 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 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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(25) Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073−3100.
(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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