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 β-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. However, this type of cyclizations is reversible, and the reverse reaction is generally faster than the cyclization. In the cases of acylgermanes, acylsilanes, thioesters, and selenoesters, 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. Herein, we wish to report the intramolecular cyclization of a formyl group with an α-stannyl radical (eq 1). In this cyclization, a novel homolytic 1,3-stannyl shift from carbon to oxygen serves as the driving force.

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

converted to α-stannyl bromides using carbon tetrabromide and triphenylphosphine. The dithiane moiety was then deprotected to give aldehydes in mild yields over three steps. Treatment of aldehyde with tributyltin hydride (Scheme 1) followed by quenching the reaction with benzoyl chloride gave cyclopentyl benzoate (3) in 57% yield. Uncyclized reduction product aldehyde 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 first. This radical then cyclizes with the formyl group to generate γ-stannyl alkoxy radical. Because radical cyclizations of carbonyl compounds are generally reversible, 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 is stronger than the C–Sn bond by about 25 kcal/mol. 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. 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 allyltetrahydride (4 equiv) in the presence of hexabutylditin (0.2 equiv) and initiated by photolysis of long wavelength UV light (12 h), we were able to isolate alcohol 10 in 35% yield. This reaction provided evidence that indeed radical 8 was formed. In the case of a 6-exo cyclization (eq 3), aldehyde 2b reacted with tributyltin hydride 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 allyltetrahydride (eq 4). Along with alcohol 14 (10%), we obtained a 50% yield of aldehyde 15 that contains an allyl group at the R-position of the carbonyl group. This result indicates that a 1,5-hydrogen transfer occurs after generation of the R-stannyl radical from aldehyde 2b. This process leads to formation of an α-carbonyl radical. The α-carbonyl radical is then trapped by allyltetrahydride 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 xanthes 16 and 17 for our studies. The reaction of xanthe...
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

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

Scheme 3

(18) A Rayonet photochemical reactor equipped with 3500 Å lamps was used.
investigation. In the tandem cyclizations, the α-stannyl xanthate moiety serves as a novel gem-diyyl equivalent.\(^{27}\)

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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.

\(^{(27)}\) For the use of gem-dihalide as gem-diyyl equivalent, see ref 22.