Radical Cyclization of Epoxyketones *via* a 1,5-$Bu^n{}_3Sn$ Group or a 1,5-H Atom Transfer

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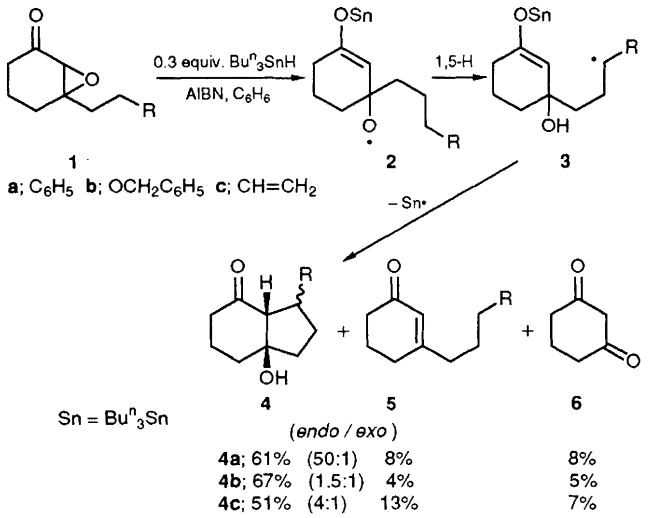
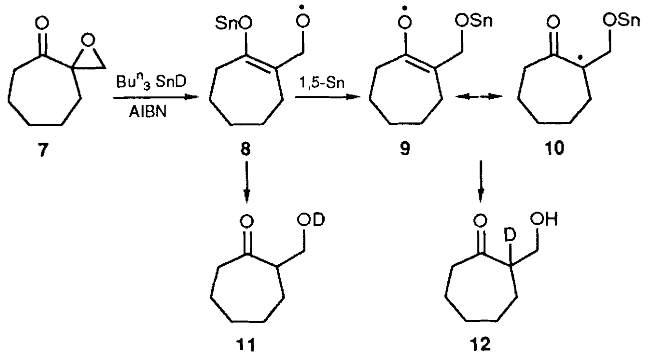
Radical cyclization of epoxyketones is initiated by $Bu^n{}_3Sn$ radical addition to epoxyketones, followed by epoxide fragmentation, 1,5-H- or 1,5-$Bu^n{}_3Sn$ transfer, and cyclization.

The importance of radical cyclization as a powerful synthetic tool for the formation of five- and six-membered rings has been well recognized in recent years.[1] In general, alkyl, allyl and vinyl radicals, generated directly from the corresponding radical precursors, undergo intramolecular addition to double and triple bonds. However, there are a few reports in which the radical cyclization takes place at the radical site, which is generated *via* radical translocation by 1,5-H atom transfer.[2]

In connection with our research programme on radical cyclizations,[3] we have studied the radical reaction of epoxyketones and report here radical cyclizations of epoxyketones *via* radical translocations by a 1,5-$Bu^n{}_3Sn$ group or a 1,5-H atom transfer, depending on the structural nature of the epoxyketones. Our initial study was carried out with a bicyclo epoxyketone. As shown in Scheme 1, our approach relied on $Bu^n{}_3Sn$ radical addition to the epoxyketone,[4] the epoxide



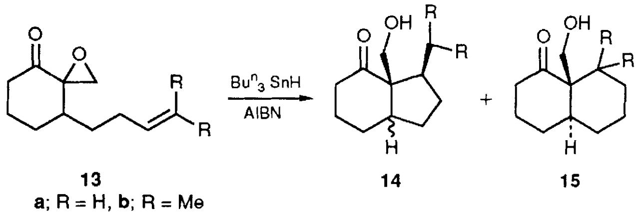
Scheme 1



Scheme 2

fragmentation, 1,5-H transfer, cyclization, and elimination of Bu$^n_3$Sn radical.[5] Reaction of **1a** with 0.3 equiv. of Bu$^n_3$SnH and 0.05 equiv. of AIBN (azoisobutyronitrile) in refluxing benzene afforded the desired *cis*-fused bicyclic compound **4a** with high diastereoselectivity in 61% yield along with 8% of **5** and 8% of **6**. Apparently, **6** resulted from β-fragmentation of **2a** and **5** would be produced *via* conversion of the *O*-metallated form **3** into the *C*-metallated form, followed by thermal 1,2-elimination.[6] Similar radical cyclizations were achieved with **1b** and **1c**, but relatively low diastereoselectivities were obtained. A similar phenomenon has recently been reported.[7] The stereochemistry of **4** was assigned by NOE (nuclear Overhauser enhancement) experiment.

Our attention next turned to a spiro epoxyketone **7**. Only one example of 1,5-Bu$^n_3$Sn group transfer from enoxyl oxygen to alkoxy oxygen has previously been reported but no synthetic applications have yet been explored.[8] As shown in Scheme 2, it was expected that the radical reaction of **7** with Bu$^n_3$Sn radical would generate the stable α-carbonyl-substituted radical **10** *via* 1,5-Bu$^n_3$Sn group transfer from **8** to **9**. Thus, the addition of a 0.1 mol dm^{-3} benzene solution of Bu$^n_3$SnD (1.1 equiv.) and AIBN (0.1 equiv.) by a syringe pump over 3 h to a 0.05 mol dm^{-3} refluxing benzene solution of **7** with additional stirring for 1 h afforded a mixture of **12** and **11** in 83% yield in a ratio of 95 : 5. We have examined two spiro epoxyketones to see whether radical cyclization *via* radical translocation by a 1,5-Bu$^n_3$Sn group transfer could be effected. Slow addition of a 0.1 mol dm^{-3} benzene solution of Bu$^n_3$SnH (1.1 equiv.) and AIBN (0.1 equiv.) by a syringe pump over 3 h to a 0.05 mol dm^{-3} refluxing benzene solution of **13a** led to a mixture of **14a** and **15a** in 31 and 9% yield, respectively. Similarly, **13b** gave 26% of **14b** along with 15% of **15b** under similar conditions (Scheme 3). In the case of **14**, the ring junction stereochemistry could not be determined by ^{1}H NMR spectroscopic analysis, although *cis*-fusion is anticipated.[9]



Scheme 3

In conclusion, we have shown that radical reactions of epoxyketones proceed *via* radical translocation by a 1,5-Bu$^n_3$Sn group or 1,5-H atom transfer and provide a useful method for the synthesis of a variety of cyclic compounds.

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