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FREE RADICAL MEDIATED RING EXPANSION OF VINYL EPOXIDES

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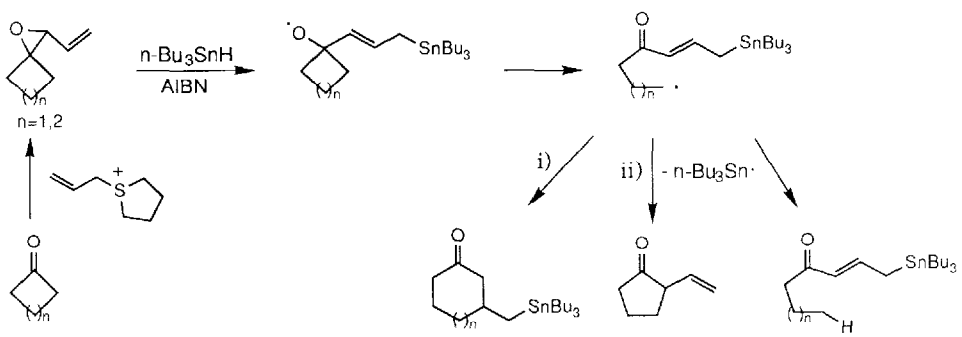
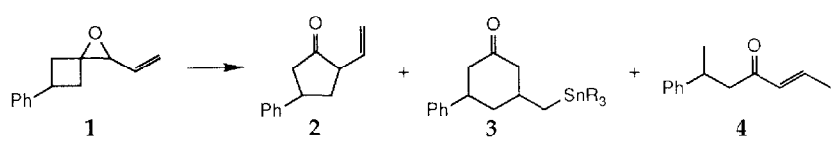
Summary: Free radical mediated ring expansion of vinyl epoxides occurred smoothly via n-Bu$_3$Sn or PhS radical addition to vinyl epoxides, epoxide fragmentation, β-cleavage of alkoxy radicals, cyclization, and elimination.

The synthetic importance of free radical reactions has been well recognized in recent years[1] and several free radical ring expansion reactions have been recently developed.[2] Our interest in ring expansion reactions[3] led to us to investigate a conceptually new ring expansion reaction via radical chain process.



Scheme 1

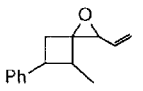
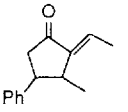
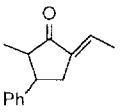
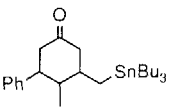
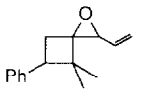
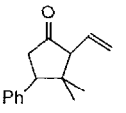
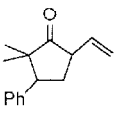
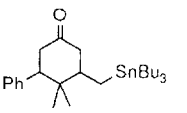
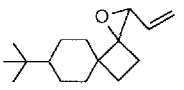
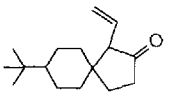
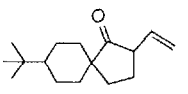
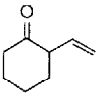
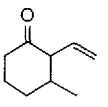
The radical reaction was originally initiated by n-Bu$_3$Sn radical addition to the vinyl epoxide,[4,5] followed by epoxide fragmantion to the alkoxy radical,[6] β–cleavage to produce the carbon-centered radical, and cyclization. As shown in Scheme 1, the cyclization reaction would be expected to proceed via two pathways: (i) conjugate addition and reduction and/or (ii) addition and termination through ejection of n-Bu$_3$Sn radical.



1 **2** **3** **4**

Vinyl epoxides were readily prepared by the reaction of cycloalkanones with allyl sulfur ylide derived from allyl sulfonium salt.[7] The reaction of vinyl oxaspirohexane **1** with n-Bu$_3$SnH (0.3 equiv) and AIBN (10 mol %) in refluxing benzene for 2 h afforded 2-vinylcyclopentanone **2** in 56% yield

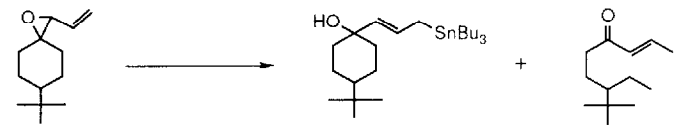
Table 1. Free Radical Mediated Ring Expansion of Vinyl Epoxides

entry	vinyl epoxide	method [a]	product (%)[c]		
1					
		A[b]	82	10	
		B[b]	81	8	3
2					
		A	83 (66 : 17)	<2	
		B	85	<2	5
3					
		A	60 (50 : 10)	<2	
4					
		A	82		
		C	81		
5					
		A	85 (46 : 37)		
		C	87		

[a] method A: PhSSPh/AIBN, hv. method B: Ph_3SnH/AIBN. method C: Bu_3SnH/AIBN.
[b] The products were completely isomerized to α, β–enones. [c] The numbers in parenthesis indicate the ratio of diastereomeric mixtures.

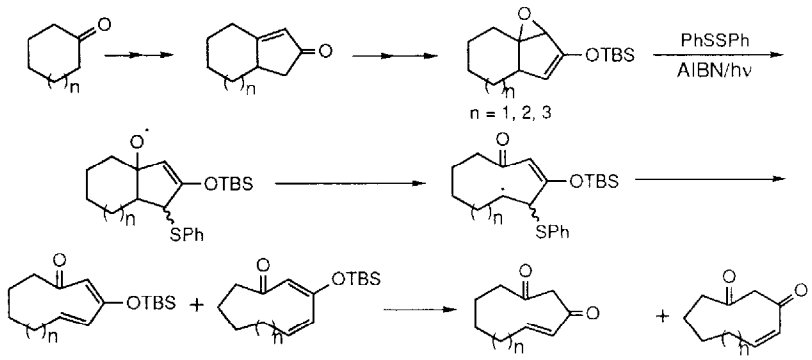
along with 18% of the conjugate addition product **3** and 4% of the reduction product **4**. It was found that Ph_3SnH gave much better results, yielding 85% of **2** along with 10% of **3** without any formation of **4**. Since the use of n-Bu_3SnH as a radical trapping agent would cause the formation of **3**, hexamethylditin was employed along with AIBN in refluxing benzene, but no reaction took place. However, the use of PhS radical obviated the undesired reactions and afforded only **2** in 75% yield, suggesting that such chain process would require a catalytic amount of PhS radical.[8] Thus, remaining reactions were carried out with PhSSPh (0.3 equiv) and AIBN (10 mol%)/hv[9] and/or Ph_3SnH or Bu_3SnH (0.3 equiv) and AIBN (10 mol%) in refluxing benzene for 3 h. Some of our experimental results are shown in Table 1 and several noteworthy features are apparent. First, ring expansion of vinyl oxaspiroheptanes with n-Bu_3SnH and AIBN proceeded cleanly, yielding 2-vinylcyclohexanones

in high yields (entries 4 and 5) due to the strong preference of 6-exo ring closure over 7-endo closure.[10] Second, β–cleavage of alkoxy radicals occurred at the more highly substituted carbon. (entries 1, 2, 3, and 5)[11] Finally, ring expansion of vinyl oxaspirooctane failed due to unfavorable β–cleavage of the alkoxy radical[12] and 7-exo closure. Thus, radical reaction of **5** with n-Bu_3SnH (1.0 equiv) and AIBN (10 mol%) in refluxing benzene for 2 h afforded **6** and **7** in 23 % and 29%, respectively.



5 **6** 23 % **7** 29 %

We also investigated the possibility of three carbon ring expansion reactions. The reaction of epoxy enol silyl ethers with PhS radical occurred smoothly, yielding initially alkoxy radicals. β–Cleavage of alkoxy radicals proceeded rapidly and cleanly, yielding the carbon-centered radicals which underwent fragmentation via ejection of PhS radical as shown in Scheme 2.



n = 1		85 %
2	38 %	49 %
3	72 %	16 %

Scheme 2

The reaction of epoxy enol silyl ethers[13] with PhSSPh (0.3 equiv) and AIBN(10 mol%)/hv in refluxing benzene for 5 h afforded three carbon expanded products in high yields. The products were desilylated to some extent during silica gel column chromatographic separation and they were isolated as a keto form.[14]

In conclusion, we have found that radical reactions of vinyl spiro epoxides are useful for ring expansion of cyclobutanone and cyclopentanone derivatives and provide a useful entry into the preparation of three carbon ring expanded 1,3-diones.

Acknowledgment: We thank Lucky Ltd. and the Organic Chemistry Research Center sponsored by KOSEF for financial support.

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13. Epoxy enol silyl ethers were prepared from cycloalkanones in five steps (LDA, 2,3-dibromopropene / $Hg(OAc)_2$, NaCl(aq) / KOH(alcohol) / NaOH, H_2O_2 / LDA, TMSOTf)
14. The product was completely hydrolyzed with aqueous acetic acid during work-up.

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