Carbocyclic Ring Expansion Reactions *via* Radical Chain Processes

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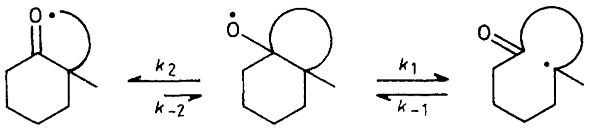
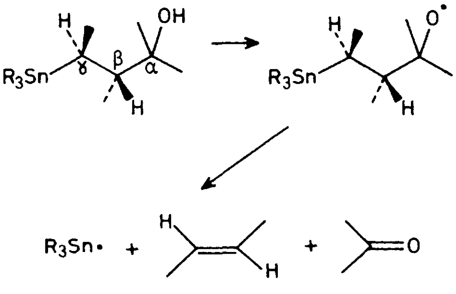
Free radical mediated ring expansion of *cis*- and *trans*-α-substituted-β-stannylcyclohexanones provides efficient routes to *cis*- and *trans*-cyclononenones and cyclodecenones; the *cis*-/*trans*-geometry of the precursor controls the alkene geometry of the ring-expanded product.

Since γ-hydroxystannanes undergo stereospecific oxidative fragmentations to olefins and ketones *via anti*-conformations, Scheme 1,[1,2] and also since alkyl radicals can add in an intramolecular sense to ketones, generating alkoxy-radicals albeit in an unfavourable equilibrium, Scheme 2,[3,4] then it follows that a combination of these processes should provide a method of carbocyclic ring expansion under essentially neutral conditions by way of a radical chain reaction, Scheme 3. As such a chain process would require only catalytic tin hydride/azoisobutyronitrile (AIBN) for initiation, undesired direct reduction before expansion of (**1**) would be minimized.†

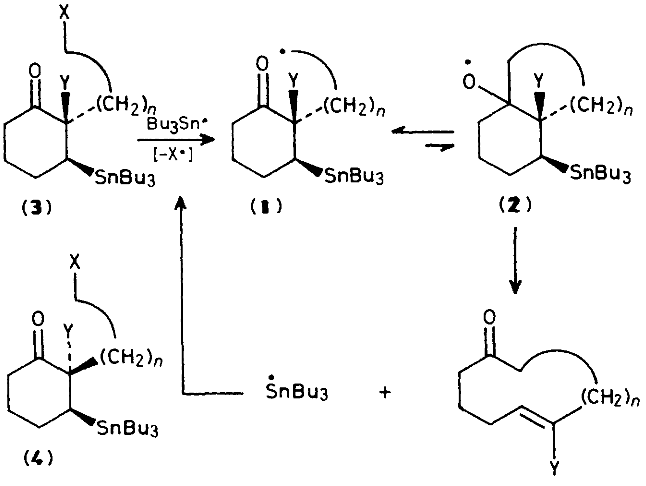


$k_1 \approx k_{-1} > k_2 > k_{-2}$

Scheme 2



Scheme 1



Scheme 3

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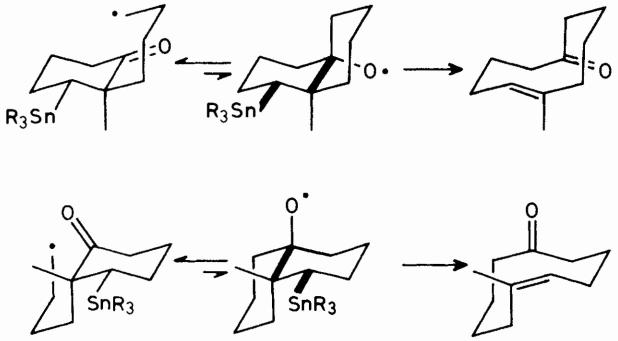
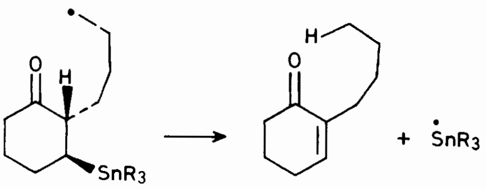
† Competitive expansion followed by reduction, and direct reduction without expansion, especially when expansion required unfavourable intermediates, *i.e.*, (**2**: $n \neq 1, 3, 4$) was observed by Dowd[4] in related systems.

Access to suitable precursors (**3**) and (**4**) was readily achieved by two methods, A and B. The first, Method A, provides a *trans*-relationship between the stannyl group and the pendant chain and involves Michael addition of tri-n-butylstannyl-lithium to a cyclohexenone [tetrahydrofuran/hexamethylphosphoric triamide (THF/HMPA) (1 : 1), −78 °C, 30 min] followed by alkylation of the derived enolate with a 1,*n*-di-iodide or a 1-iodo-*n*-phenylselenoalkane (50—60%).[5] The corresponding *cis*-isomers were obtained by Method B, involving Michael addition of tri-n-butylstannyl-lithium to a preformed α-(*n*-phenylselenoalkyl)cyclohexenone (THF/HMPA, −30 °C, 2 h) followed by alkylation or protonation of the derived enolate (50—60%). The observed coupling constants $^3J(^{119}Sn-^{13}C)$ between the tin atom and the carbonyl carbon of *ca.* 30 Hz for *cis*-(**4**) and *ca.* 45 Hz for *trans*-(**3**), Scheme 3, were in general consistent with reported values.[2]

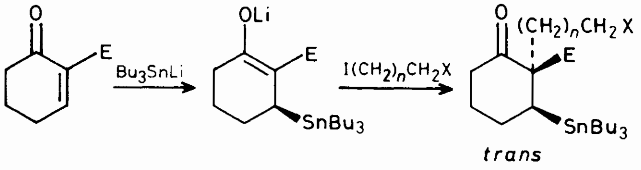
Radical-initiated chain reactions [AIBN, Bu_3SnH (10 mol %), benzene, reflux] of these substrates gave the conversions



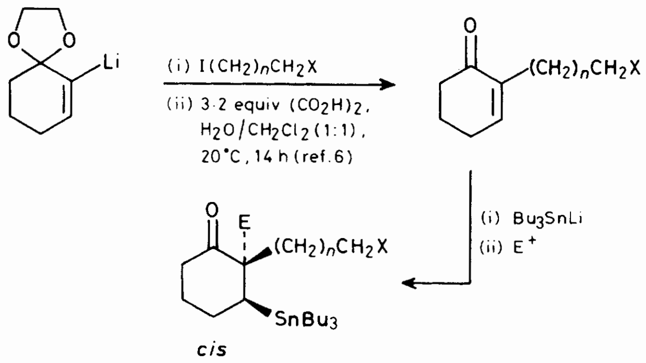
Scheme 4



Scheme 5

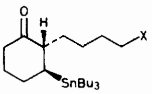
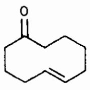
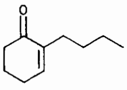
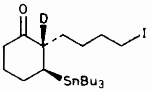
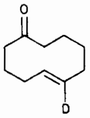
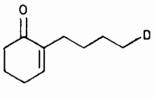
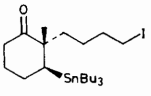
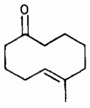
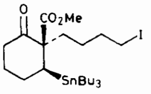
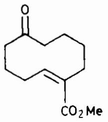
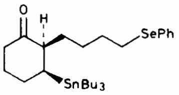
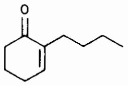
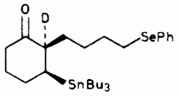
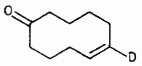
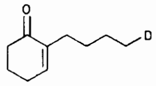
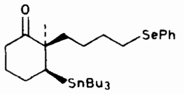
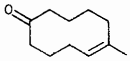
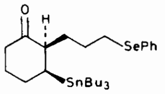
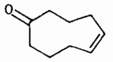
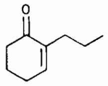
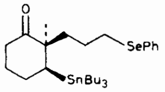
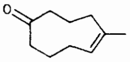
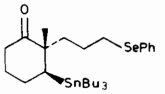
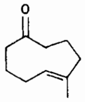
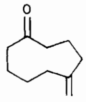


Method A



Method B

Table 1.

Entry (ref.[f])	Precursor	Product (% isolated)	
1 (7)		 (a) X = I (47)[a] (b) X = SePh (42)[a]	 (36) (33)
2 (7)		 (75)[a]	 (10)
3 (8)		 (85)[a]	only
4 (-)		 (72)[b]	only
5 (-)		 (86)	only
6 (7)		 (21)[b]	 (58)
7[c] (8)		 (89)[d]	only
8 (9)		 (87)[b]	 (4)
9 (10)		 (87)[b]	only
10 (10)		 (44)[a]	 (36)[e]

Conditions: Initial; substrate (5 mmolar in benzene), AIBN (0.2 mol. equiv.), Bu_3SnH (0.1 mol. equiv.), reflux, 2—72 h. Prolonged; add AIBN (0.2 mol. equiv.) every 12—24 h. [a] *E* : *Z* Isomer ratio greater than 95 : 5. [b] *Z* : *E* Isomer ratio greater than 95 : 5. [c] *Cis* : *trans* precursor ratio *ca.* 90 : 10. [d] *Z* : *E* Isomer ratio = 90 : 10. [e] Ratio after 14 h reaction. The exomethylene isomer predominates in prolonged reactions. [f] References to ring-expanded products. All new compounds have been characterized by analytical and/or spectroscopic techniques.

listed in Table 1. Several points emerge from the data. First, it is evident that the olefin geometry is controlled by the stereochemistry of the precursor, *i.e., trans* gives *trans* and *cis* gives *cis*, as expected for the preferred *anti*-relationship, as shown in Scheme 4.‡ Secondly, if the carbonyl α-carbon bears hydrogen then reduction competes with ring expansion (entries 1 and 5). This reduction process was not favoured by 10-fold concentration and appears to be intramolecular, Scheme 5. If the α-carbon is substituted by deuterium an isotope effect depresses this pathway (entry 2 *vs.* entry 1). Also if the geometry for intramolecular hydrogen abstraction is unfavourable, *i.e.*, 5-membered instead of 6-membered transition state, then the reduction process is disfavoured (entry 8 *vs.* entry 5). This dependence on ring size for hydrogen abstraction has been observed previously.[11]

In conclusion, we have found that carbocyclic ring expansions can be mediated through radical chain processes and are effective alternatives to existing heterolytic procedures.[12]

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‡ Similar stereospecificity has been observed in related systems, see refs. 1, 2.

References

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