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.[†]



[†] 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 Dowd⁴ in related systems.



Scheme 2



Scheme 3

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-nbutylstannyl-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-butylstannyllithium 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 ${}^{3}J({}^{119}Sn{}^{-13}C)$ 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, Bu₃SnH (10 mol %), benzene, reflux] of these substrates gave the conversions



Method B







Conditions: Initial; substrate (5 mmolar in benzene), AIBN (0.2 mol. equiv.), Bu₃SnH (0.1 mol. equiv.), reflux, 2—72 h. Prolonged; add AIBN (0.2 mol. equiv.) every 12—24 h. * E:Z Isomer ratio greater than 95:5. * Z:E Isomer ratio greater than 95:5. * Z:E Isomer ratio a: 90: 10. d Z:E Isomer ratio = 90: 10. * Ratio after 14 h reaction. The exomethylene isomer predominates in prolonged products. All new compounds have been characterized by analytical and/or spectroscopic techniques.

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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

Received, 29th April 1988; Com. 8/01697F

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

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