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trans Ring-fused Bicyclic Structures by 6-*exo*-Trigonal Radical Closure: Use of the Triethylborane–Stannane–Air System for Intramolecular Radical Addition to Aldehydes

Derrick L. J. Clive* and Maarten H. D. Postema
Chemistry Department, University of Alberta, Edmonton, Alberta T6G 2G2, Canada

Selenium-containing aldehydes of type **5** are easily made by alkylation of bicyclic lactones **1**, and they undergo 6-*exo*-trigonal radical cyclization on treatment with triphenyltin hydride in the presence of triethylborane and air to give products convertible into *trans* ring-fused bicyclic ketones **7**.

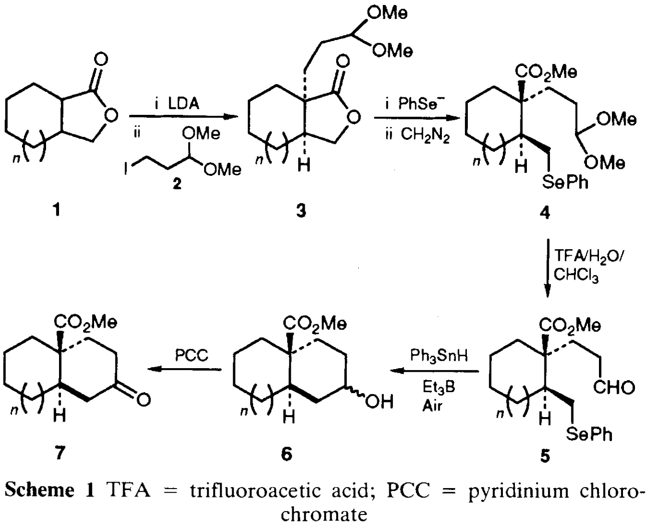
We report a method (Scheme 1) for preparing bicyclic compounds of type **7**. The essential features of the scheme are (*a*) the fact that alkylation of lactones **1** proceeds[1] so as to place the new substituent *syn* to the adjacent ring fusion hydrogen **1** → **3** and (*b*) our observation that radical closure of a carbon chain onto an aldehyde—hitherto restricted to closure of iodides under special conditions[2]—can, be carried out also with selenides, by use of the stannane–triethylborane–air[3] system.

The starting lactones **1** are available by a number of routes,[1a,4] while the iodoacetal **2** can be made by sequential treatment of acrolein with iodotrimethylsilane and a stoichiometric amount of methanol.[5] Lactone opening **3** → **4** with phenylselenide anion[6] proceeds normally[1a,7] and the intermediate acids are immediately esterified with diazomethane. Finally, mild acid hydrolysis (trifluoroacetic acid–water–chloroform[8]) **4** → **5** affords the substrates for radical cyclization.

When selenide **5b** (*n* = 1) (Table 1) was treated under conditions reported[2] for radical closure of ω-iodo aldehydes then, as expected, very little cyclization tool place. Prior work[2] had indicated the requirement for a weak homolysable bond (*e.g.* C–I),[9] and a sufficiently high stannane concentration to ensure capture of the intermediate alkoxy radical. In the case of selenides, RSePh, a high concentration of stannane results in premature reduction of the radical R$^\bullet$. We have found, however, that when the reaction is done at room temperature[†] by the stannane–triethylborane–air method,[3] which involves addition of all the stannane in one portion, then acceptable yields of closure product are obtained, provided the concentration of substrate is low (*ca.* 0.01–0.008 mol dm^{-3}).[‡] The reaction sequence **1** → **7** is general, as indicated by the examples collected in Table 1. In all our experiments we obtained alcohol mixtures from the radical closure and in the one case we examined in detail (Table 1, entry ii) the equatorial alcohol was the major (*ca.* 65% of total) product. We found it convenient to oxidize the crude alcohols directly to the corresponding ketones as these are very much more easily purified.

As far as we are aware, radical closure onto an aldehyde carbonyl, starting from a selenide, has been reported only once[10] and that case had the helpful feature[§] that a heteroatom was present at a ring fusion position in the product. The present work shows that aldehyde closure in all-carbon systems is not restricted to iodides and that the very useful phenylseleno group[12] can be employed routinely in this regard.

It is not clear whether the successful use of triethylborane is due to effects of Lewis acid complexation or to the fact that the



Scheme 1 TFA = trifluoroacetic acid; PCC = pyridinium chlorochromate

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[†] We have not investigated lower temperatures.

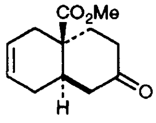
[‡] *Typical procedure*: Triphenyltin hydride (333.0 mg, 0.947 mmol) in hexane (4 ml plus 1 ml rinse) and triethylborane (2.0 ml, 1 mol dm^{-3} solution in hexane, 2.0 mmol) were added simultaneously over *ca.* 15 s to a solution of aldehyde **5b** (248.6 mg, 0.677 mmol) in hexane (80 ml). Air (20 ml) was then bubbled through the solution (over a few seconds) and the mixture was stirred for 4 h with exposure to the atmosphere. At this point the reaction was still incomplete (TLC control, silica, 30% ethyl acetate–hexane). Triphenyltin hydride (50.0 mg, 0.142 mmol) in hexane (3 ml plus 1 ml rinse) and triethylborane (0.88 ml, 1 mol dm^{-3} solution in hexane, 0.88 mmol) were added as before and stirring was continued. Addition of stannane and borane was repeated once again after 3 h, and stirring was continued for an additional 8 h. Evaporation of the solvent and flash chromatography of the residue over silica gel (2 × 20 cm) using 10% ethyl acetate–hexane gave the epimeric alcohols **6b**, which were oxidized directly to ketone **7b** (73% overall yield).

[§] Radical closures are generally faster when the chain contains a heteroatom. See ref. 11.

Table 1[a]

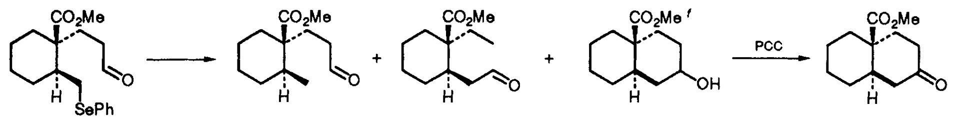
Entry	Lactone[b] **1**	Alkylated lactone **3**	Selenide **4**	Aldehyde **5**	Ketone[c] **7**
(i)	**1a** $n = 0$	**3a** $n = 0$, 40%	**4a** $n = 0$, 39%, (62%)[d]	**5a** $n = 0$, 86%	**7a** $n = 0$, 58% (64%)[e,f]
(ii)	**1b** $n = 1$	**3b** $n = 1$, 76%	**4b** $n = 1$, 77%	**5b** $n = 1$, 88%	**7b** $n = 1$, 73%
(iii)	**1c** $n = 1$; $\Delta^{5,6}$	**3c** $n = 1$, $\Delta^{5,6}$ 71%	**4c** $n = 1$, double bond 62%	**5c** $n = 1$, double bond 95%	**7c** $n = 1$, double bond[g] 71%
(iv)	**1d** $n = 2$	**3d** $n = 2$, 77%	**4d** $n = 2$, 50%	**5d** $n = 2$, 98%	**7d** $n = 2$, 80%
(v)	**1e** $n = 3$	**3e** $n = 3$, *ca.* 63%	**4e** $n = 3$, 45%, (61%)[d]	**5e** $n = 3$, 93%	**7e** $n = 3$, 77%

[a] All yields refer to pure isolated compounds. [b] All lactones **1** have a saturated carbocycle except for $n = 1$, in which case both the saturated and $\Delta^{5,6}$ unsaturated [*i.e.* *cis*-3a,4,7,7a-tetrahydro-1(3*H*)-isobenzofuranone] compounds were studied. [c] Overall yield for **5** → **7**. [d] Corrected for recovered starting lactone. [e] Corrected for recovered aldehyde **5a**. [f] Some reduced product (i.e. PhSe replaced by H) is also formed: 28% yield; 31% corrected for recovered starting material (**5a**, $n = 0$). [g]



7c

Table 2[a]



Ph_3SnH, Et_3B, hexanes, 25 °C	Only a trace, if any	Only a trace, if any	—[e]	73[c]
Ph_3SnH, AIBN, benzene, 80 °C	24[b]	11[b]	34[b,g]	—[d]
Ph_3SnH, AIBN, Et_3B, benzene, 80 °C	26[b]	Only a trace, if any	—[e]	43[b,c]
Ph_3SnH, AIBN, $Ti(OPr^i)_4$, benzene, 80 °C	—	—	—[e]	11[b,c]

[a] Yields refer to isolated products. [b] Yield based on recovered starting material. [c] Yield over two steps (cyclization and oxidation). [d] Experiments not tried. [e] Oxidation was carried out directly. [f] Isomer composition (axial or equatorial alcohol) not established. [g] One isomer [axial OH, δ ^{13}C for CH(OH) = 66.63] only was isolated.

reactions are done at a much lower temperature than those reported for ω-iodo aldehydes.¶ The detailed mechanism by which triethylborane behaves in the generation of carbon radicals has not been examined, but the experiments summarized in Table 2 show clearly the advantage of using the borane.

All new compounds for which yields are given were fully characterized by spectroscopic measurements and, usually, also by combustion analysis.

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