Construction of a linear triquinane skeleton by an *O*-stannyl ketyl radical rearrangement

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An *O*-stannyl ketyl ring scission–cyclization of a rigid tricyclo[3.3.0.0^{2,8}]octan-3-one ring system bearing an alkene tether results in the synthesis of a linear triquinane skeleton.

The linear-fused triquinanes represent an important class of natural products.[1] There have been many innovative approaches to the preparation of the interesting tricyclic skeleton of the triquinanes and often the framework itself serves as a vehicle to demonstrate new synthetic methodology in fused cyclopentane construction. We have recently become interested in a radical-based synthetic strategy towards this goal through the use of unique strained ring precursors, in particular, the novel ring-scission of a tricyclo[3.3.0.0^{2,8}]octan-3-one ring system by an *O*-stannyl ketyl.[2,3]

Here we will detail a new and unusual application of the α-ketocyclopropane fragmentation of this tricycle which afforded a linear triquinane skeleton. An antithetic analysis which shows how this synthetic methodology might be implimented is shown in Scheme 1. Annulation of one ring of the triquinane **1** by a hex-5-enyl radical cyclization is established by ring scission of the rigid cyclopropane moiety of **4**. *O*-Stannyl ketyl intermediate **4** is formed from tributyltin radical addition to ketone **5**. Although reactions of α-cyclopropyl radical ring scissions have been examined prior to these studies, most previous efforts focused on a halide, phenyl selenide or a thionocarbonyl ester for the radical precursor, rather than a simple ketone.[4] The viability of the tandem scission–cyclization approach can be readily tested because the precursor diketone **6**, the diquinane portion of the strained tricyclo[3.3.0.0^{2,8}]octan-3-one **5**, contains a σ-plane of symmetry.

To study this series of reactions, a model linear triquinane was constructed as shown in Scheme 2. A cyclopropane ring would be first installed in commercial diquinane **7** using a two-step method of monoiodination, followed by treatment with DBU.[5] The labile iodide intermediate was not characterized but was directly used in next step after workup. The dehydrohalogenation constructed the symmetrical tricyclodione **8** in a 52% overall yield.†

Next, the reaction of **8** with the Grignard reagent of 4-bromobutene gave **9** as the sole stereoisomer which was isolated in 64% yield. Although addition to the *exo*-face of the tricycle was expected, it was interesting that none of the *endo*-product due to the steric hindrance of the two ring-fusion methyl groups was obtained. Stereoselective addition of the Grignard reagent to the most accessible face of the carbonyl in **8** gave **9** with the appropriate stereochemistry for elaboration to the normal cis,anti,cis configuration of the linear triquinane skeleton.

Prior to the *O*-stannyl ketyl scission–cyclization studies of **9**, we examined preliminary fragmention studies on tricycloketone model compounds lacking an alkene appendage and found that the cleavage of the 'a' or 'b-bond' is possible.[3] If the *O*-stannyl ketyl was generated in **9**, only radical-stabilizing functions (R^1 = ester) would direct the cleavage of the 'a-bond' of the cyclopropane. Moreover, the 'b-bond' was expected to have better orbital overlap with the orbital of the adjacent ketyl.[3] It was therefore predicted that stereoelectronically favoured cleavage of the 'b-bond' would predominate, leading to the desired 5-*exo-trig* radical cyclization.

In support of this prediction, treatment of **9** with Bu_3SnH afforded the linear triquinane **11** in 83% yield as the only isolable product. Some measure of stereochemical control was realized in the 5-*exo-trig* radical cyclization where the *endo*:*exo* stereoselectivity ratio, determined by capillary GC, was > 4:1. A Beckwith chair-like intermediate **10** readily explains the stereochemistry of the *endo*-methyl in **11**.[6] The *endo*-methyl group in **11** was established by comparison with previous ^{13}C NMR studies of closely related fused-cyclopentanes.[7] The *endo*-methyl in **11** was observed at δ_C 14 by ^{13}C NMR which is closer to Whitesell's reported average value of δ_C 15 for an *endo*-methyl rather than δ_C 20 for an *exo*-methyl substituent.

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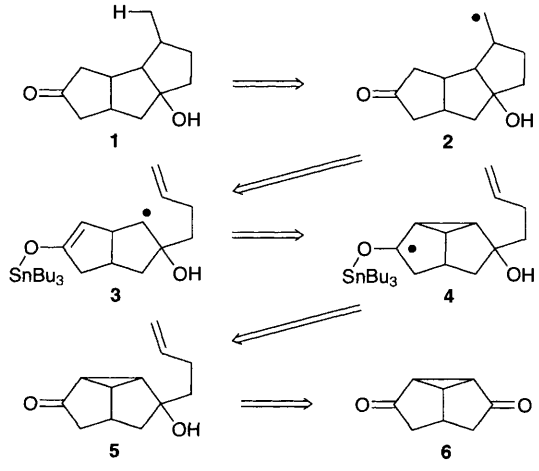
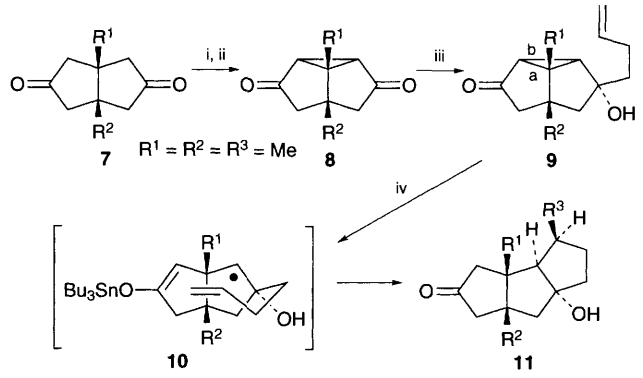


Scheme 1



Scheme 2 *Reagents and conditions*: i, I_2, $HgCl_2$ CH_2Cl_2; ii, DBU, MeCN; 51% (2 steps); iii, $BrMgCH_2CH_2CH{=}CH_2$, THF; 64%; iv, Bu_3SnH, AIBN, PhH, 80 °C; 83%

Footnote

† All new compounds exhibited ^{1}H and ^{13}C NMR, IR and combustion analysis consistent with the structure shown.

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