

A Short Synthesis of (\pm)-Hirsutene involving the Use of an Organoselenium-mediated Cyclization Reaction

Steven V. Ley* and P. John Murray

Department of Chemistry, Imperial College, London SW7 2AY, U.K.

A short synthesis of the sesquiterpene hirsutene (**1**) has been developed in which the key step involved intramolecular cyclization of a β -oxoester to an alkene using *N*-phenylselenophthalimide and tin tetrachloride.

Recently the synthesis of fused pentacyclic systems has stimulated considerable interest.¹ Here we show how one such compound, hirsutene (**1**),² can be prepared by a short route involving the use of a novel organoselenium-mediated cyclization³ as the key synthetic step.

The unsaturated bromide (**2**),[†] *via* its cuprate, was added conjugatively to methyl 2-oxocyclopentanecarboxylate⁴ to give (**3**)[‡] in 74% yield (ν_{\max} 1756, 1724, and 1650 cm^{-1}).

Upon treatment with *N*-phenylselenophthalimide (NPSP),⁵ and 1 equiv. of SnCl_4 for 2.5 h at room temperature, compound (**3**) was smoothly cyclized to a readily separable mixture of the *anti*-isomer (**4**), m.p. 106–108 °C, and the *syn*-isomer (**5**) m.p. 109–112 °C in 45% yield of each. The structural proof of these compounds follows from careful

spectroscopic analysis, X-ray crystallographic determination,[§] and later conversion of (**4**) into the natural product (**1**).

In order to facilitate the synthesis of the final target compound, it was decided firstly to remove the phenylselenomoiety from (**4**) and then selectively transform the ester group into the desired angular methyl substituent. This was achieved by initial reduction of (**4**) with Raney-nickel followed by protection of the ketone as its enolate⁶ and reduction with lithium aluminium hydride to give (**6**) in 65% overall yield (ν_{\max} 3430 and 1730 cm^{-1}).

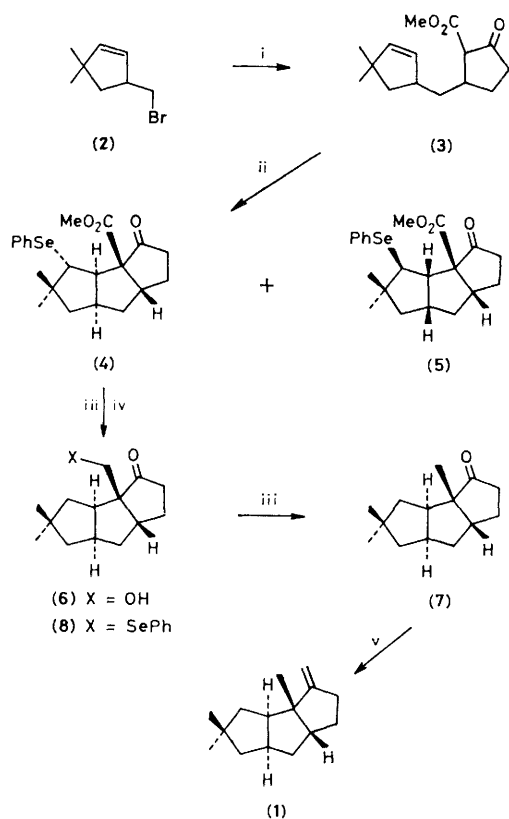
Final elaboration of (**6**) to the known ketone (**7**)^{2a} required conversion of the primary hydroxy-group into the corresponding phenylselenide (**8**) (62%) using NPSP-Buⁿ₃P⁷ and Raney-nickel reduction (83%).

The ketone (**7**) was treated with $\text{Ph}_3\text{P}=\text{CH}_2$ to give a 70% yield of (\pm)-hirsutene (**1**)^{2a} which was identical in all respects with previously synthesised material.

[†] Details for the preparation of this simple bromide will be reported in full later.

[‡] All new compounds were fully characterised by spectroscopic and microanalytical methods.

[§] We thank Dr. D. J. Williams, Imperial College, for this determination.



Scheme 1. Reagents and conditions: i, Mg, CuBr·Me₂S, methyl 2-oxocyclopentanecarboxylate, -30 to 0 °C; ii, NPSP (1.1 equiv.), SnCl₄ (1.0 equiv.), CH₂Cl₂, room temp., 2.5 h; iii, Raney-nickel, EtOH, 50 °C, 20 min; iv, lithium di-isopropylamide, tetrahydrofuran at -45 °C for 45 min then LiAlH₄ added, warmed to room temp. over 1.3 h; v, Ph₃P=CH₂, Me₂SO.

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