



Cyclopentanoid Allylsilanes in Synthesis: A Facile Construction of the 5-8 Fused Carbon Framework of Asteriscanolide

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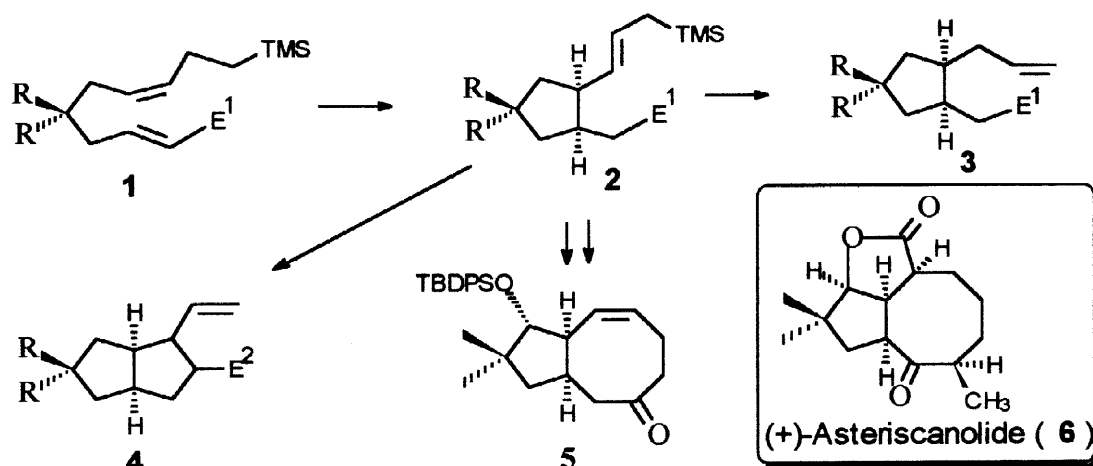
Abstract: A short synthesis of the 5-8 fused carbocyclic system of asteriscanolide, a novel cyclooctane sesquiterpene is described which entails a 5-(3,4) ene cyclization, an allylsilane induced lactone formation and a [3,3] sigmatropic rearrangement in the key steps of the synthesis.

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Key words: Cyclopentanoid allylsilanes; sigmatropic rearrangement; cyclooctane sesquiterpenes

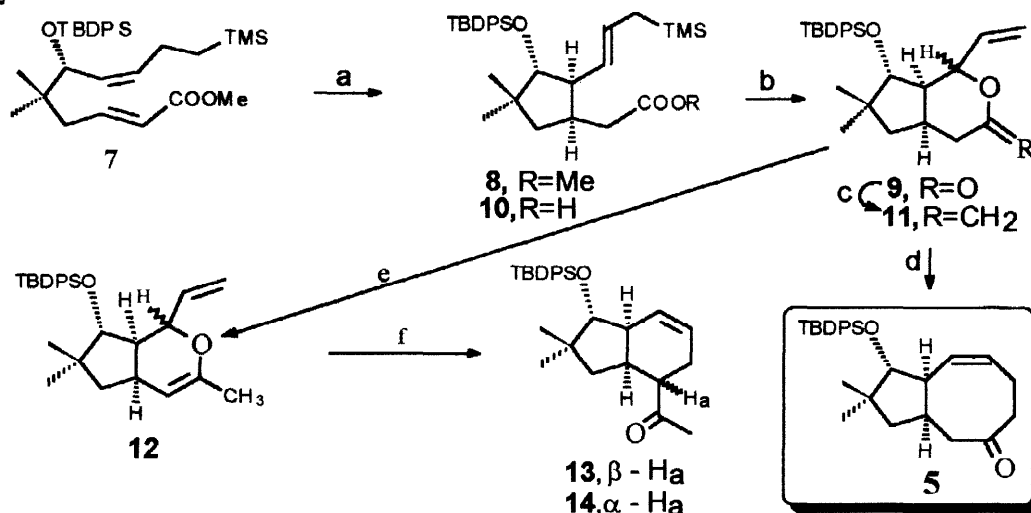
In a series of papers,^{1,2} we have recently described the synthesis of cyclopentanoid allylsilanes, *e.g.*, **2** ($R=H/Me$) by intramolecular ene reaction³ of suitably functionalized 1,6-dienes **1** with a built-in homoallylsilane moiety as the ene donor. We have shown the versatility of the allylsilane side chain in the products by protodesilylation **2**→**3** and allylsilane induced ring closure **2**→**4** leading to differentially substituted cyclopentanes and diquinanes, respectively (Scheme 1). This new methodology has also allowed us to achieve concise syntheses of several cyclopentanoid natural products of considerable contemporary importance.^{4,9} Herein, we report another variation of the theme to utilize the allylsilane functionality of species such as **2** to access the *cis* 5-8 fused ring system **5** representing the carbocyclic core of asteriscanolide (**6**), a cyclooctane sesquiterpene isolated from *Asteriscus aquaticus* L.¹⁰

Scheme 1



Our point of departure was the cyclopentanoid allylsilane **8**, a high-yielding synthesis of which was reported earlier *via* thermal 5-(3,4) ene cyclization of **7**⁷ (Scheme 2). Exposure of **8** to MCPBA followed by stirring of the crude product with silica gel (100–200 mesh) in dichloromethane gave the desired lactone **9** in 46% yield. Attempts to increase the yield in the step **8** → **9** by carrying out the reaction on the corresponding acid **10** was not, however, successful. Although, **9** appeared to be practically a single diastereomer (¹H- & ¹³C-NMR), no attempt was made to determine the

Scheme 2



a) 235°C, toluene, 18h, 96%; b) MCPBA / Na₂HPO₄ / CH₂Cl₂, r.t., then SiO₂ / CH₂Cl₂, r.t., 46%; c) Cp₂TiMe₂ / THF, 65°C, 24h, 65%; d) 180°C, toluene, 24h, and then prep. HPLC, 36%; e) SiO₂ / CH₂Cl₂, 85%; f) 180°C, toluene, 24h.

configuration at the newly created stereogenic centre as this has no bearing on the synthesis of the target molecule. Methylenation of 9 with dimethyltitanocene under the usual conditions¹¹ afforded the extremely labile enol ether 11 (65%). Incidentally, the slightest provocation of 11 e.g., exposure to silica gel, caused the π -bond of the enol ether unit to move into the *endo* position leading to the undesired product 12. Thermolysis of 11 in a sealed tube coated with NaOH, followed by chromatography, gave a mixture (50%) of the long-sought-after ketone 5, contaminated with the 5-6 fused ring systems 13 and 14 (5:13:14=50:38:12). Purification of the mixture by preparative HPLC gave pure 5¹³ (36%) as an oil along with 13 and somewhat impure 14 (containing ~25% of 13). The structure and relative stereochemistry of 5, 13 and 14 rest on ¹H- & ¹³C-NMR as well as nOe studies. Formation of 13 and 14 is explicable in terms of partial isomerization of 11 to 12 followed by an alternative Claisen rearrangement. In fact, when *endo* enol ether 12 was heated at 180°C for 24h, a mixture of 13 and 14 (13/14=1:1) was formed uncontaminated with any trace of 5.

In conclusion, we have achieved a short synthesis of the bicyclic carbon framework of asteriscanolide via a 5-(3,4) ene cyclization, allylsilane induced lactonization and [3,3]sigmatropic rearrangement as the pivotal steps of the synthesis. Further transformation involving inversion of the hydroxy group after O-Si bond cleavage in 5, five-membered lactone formation via radical reaction of the corresponding S-alkoxycarbonyl dithiocarbonate¹² and other necessary elaboration would complete the synthesis of the target molecule and efforts in that direction are currently underway in this laboratory.

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13) Selected spectral data for 5: ν_{max} 1703 cm^{-1} . ¹H NMR (400MHz, CDCl₃) δ : 7.61(m, 4H), 7.32(m, 6H), 5.57(m, 1H), 4.99(m, 1H), 3.72(d, 1H, $J=3.2$ Hz), 2.64(m, 1H), 2.46(m, 1H), 2.40(m, 1H), 2.28(m, 2H), 2.02(m, 1H), 1.95(m, 1H), 1.75(m, 1H), 1.50(m, 1H), 1.07(s, 3H), 1.02(s, 9H), 1.00(m, 1H), 0.88(s, 3H). ¹³C NMR (75MHz) δ : 213.93(s), 136.10(d, 4C), 134.31(s), 134.00(s), 132.76(d), 129.51(d), 129.42(d), 129.26(d), 127.43(d, 2C), 127.36(d, 2C), 89.36(d), 48.23(d), 47.16(t), 45.01(t), 44.25(t), 42.29(s), 37.07(d), 28.75(q), 27.09(q, 3C), 23.49(t), 23.18(q), 19.37(s). MS m/z 389(M-Me₃C, 30%), 199(100%).