STEREOSELECTIVE SYNTHESIS OF NATURAL (4S,6S,7S)-SERRICORNIN STARTING WITH (3S,4S)-4-HYDROXY-3-METHYL-1-HEXENE

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(4S,6S,7S)-Serricornin has been synthesized in three steps starting with (3S,4S)-4-hydroxy-3-methyl-1-hexene.

Serricornin (1) is the sex pheromone of cigarette beetle (Lasioderma serricone F) which is a major pest of cured tobacco leaves. (1) Recently, the absolute stereochemistry of the natural stereoisomer of serricornin (1), as its open-chain acetate 2, has been established by Mori et al. as 4S,6S,7S. Because of the practical value of serricornin, its synthesis has been attracted much attention. (1b,2,3)

We wish to report here a new method for preparation of 1 (Scheme 1) starting with the optically acitve (3S,4S)-4-hydroxy-3-methyl-1-hexene (3) (>95% ee), which can be prepared from (R)-2-methyl-3-trimethylsilyl-3-butenal by the diastereoselective addition of ethylmagnesium bromide followed by protodesilylation. Hydromagnesiation of 3 with isobutylmagnesium chloride in the presence of a catalytic amount of Cp_2TiCl_2 (10 mol%) in THF (room temp, 3 h), treatment with gaseous CO_2 (1 atm, -60 °C, 30 min then room temp, 4 h), and addition of formic acid to the reaction mixture afforded the lactone 4 in 54% yield. It should be noted here that the lactone 4 would also be synthesized via hydroformylation of 3 and subsequent oxidation of the resulting cyclic hemiacetal. Methylation of the lactone enolate derived from 4 (MeI, LiN(SiMe_3)_2, THF-HMPA) proceeded diastereoselectively affording the lactone 5 exclusively in 86% yield ([α] because the context of the second of 5 with ethylmagnesium bromide (-40 °C \rightarrow -30 °C, 1.5 h, THF) afforded (4S,6S,7S)-serricornin (1). The crude 1 was converted into its acetate 2 ([α] because 1 h and 13 C (co.168, hexane), lit. here

NMR spectral data were in accord with values reported in the literature. 2b) Thus, the present procedure provides the very short synthesis of natural serricornin (1). In addition, this result strongly indicates that the acyclic stereoselection using relative 1,2-asymmetric induction 4) provides a simple, direct tool for the synthesis of acyclic natural products.

Scheme 1.

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