# Terpenoid Precursors *via* Steroid Degradation: Synthesis of (−)-Warburganal

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The sesquiterpene (−)-warburganal was prepared from a (1*S*)-1-methoxycarbonyl-2,5,5,8a-tetramethyldecahydronaphthalene (**4**) obtained by degradation of commercial glycyrrhetinic acid.

Terpenoids and steroids still command considerable interest as synthetic targets as a consequence of their diverse architecture and potent biological activities.[1] As part of a programme addressing current problems in polyisoprenoid total synthesis, we sought to develop a generation of functionalized synthetic intermediates[2] by excising appropriate subunits from the chiral pool of commercial natural products. Reported here is the preparation of a versatile, chiral precursor for the common structural unit (**1**) and its exploitation in the synthesis of (−)-warburganal,[3] an insect antifeedant, antimicrobial sesquiterpene.

Irradiation†[4] of the homo-diene (**2**), available[5] in 75% yield from glycyrrhetinic acid, furnished the triene (**3**)‡ (90—95%) (Scheme 1). Oxidation of the tetrasubstituted olefins with peroxy acid gave a labile bis-epoxide which led to the ester (**4**) (45%) upon exhaustive ozonolysis, esterification with diazomethane, and chromatographic purification.

The chiral precursor (**4**) readily isomerized with acid to give the allylic alcohol (**5**) (80%). Removal of the acetoxy group by methanolysis of the acetate and Barton's radical deoxygenation sequence using the corresponding *O*-phenyl thiocarbonate and di-t-butyl peroxide[6] afforded (**6**) (67%). Consecutive allylic oxidation with selenium dioxide, ester reduction with lithium aluminium hydride (LAH), and Swern oxidation[7] of the primary alcohols yielded (−)-warburganal (**7**) (65%).

Additional chiral precursors and their conversion into natural products, *e.g.* forskolin, will be reported in due course.

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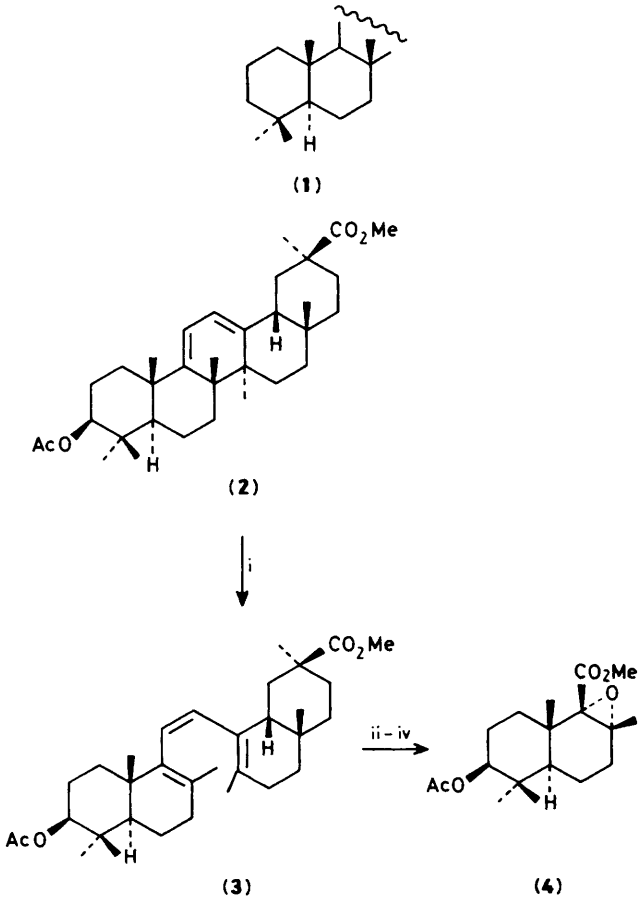
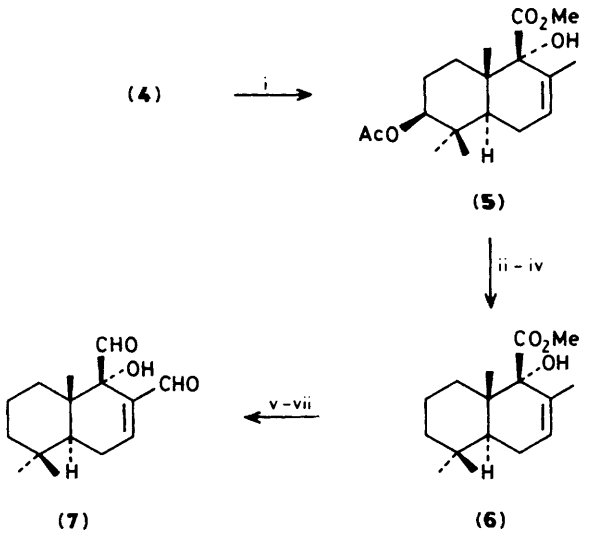



**Scheme 1.** *Reagents:* i, *hν*, EtOH; ii, *m*-$ClC_6H_4CO_3H$, $Na_2CO_3$, $CH_2Cl_2$; iii, $O_3$, EtOAc, −5 °C, 4 h, then $Me_2S$; iv, $CH_2N_2$, $Et_2O$.

† Irradiated in a borosilicate flask using a 100 W high-pressure Hg street lamp with the outermost glass shell removed.

‡ (**3**): m.p. 163—164 °C ($Et_2O$–hexane); $[\alpha]_D^{24}$ + 209° (*c* 1.0, $CHCl_3$). (**4**): m.p. 112—113 °C (hexane); $[\alpha]_D^{24}$ + 85° (*c* 1.35, $CHCl_3$); $\delta_H$ (90 MHz, $CDCl_3$) 0.84 (3H, s), 0.88 (3H, s), 1.20 (3H, s), 1.28 (3H, s), 2.02 (3H, s), 1.30—2.20 (9H, m), 3.68 (3H, s), and 4.30—4.52 (1H, m). (**5**): m.p. 142—143 °C ($Et_2O$–hexane). (**6**): $[\alpha]_D^{22}$ −64° (*c* 1.5, $CHCl_3$). (**7**): m.p. 105—106 °C (lit.,[3b] 106—107 °C); $[\alpha]_D^{22}$ −260° (*c* 0.45, $CHCl_3$) [lit.,[3b] $[\alpha]_D^{24}$ −260° (*c* 0.22, $CHCl_3$)].




**Scheme 2.** *Reagents:* i, 47% HI/$Et_2O$ (1 : 16), 25 °C, 2 h; ii, NaOMe, MeOH, 25 °C, 8 h; iii, PhOC(S)Cl, pyridine, $CH_2Cl_2$; iv, $Bu_3SnH$, $(Bu^tO)_2$, 110 °C, 4 h; v, $SeO_2$, dioxane, 100 °C, 4 h; vi, $LiAlH_4$, tetrahydrofuran, 24 °C, 24 h; vii, $Me_2SO$, $(ClCO)_2$, $Et_3N$, $CH_2Cl_2$, −60 to 25 °C, 2 h.

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