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THE STEREOSPECIFIC SYNTHESIS OF D,L-WINTERIN

Gottfried Brieger
Chemistry Department
Oakland University
Rochester, Michigan

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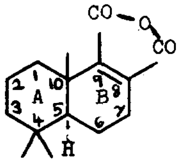
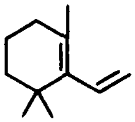
Winterin (I), is one member of a series of closely related bicyclofarnesol derivatives found in the bark extracts of D.winterin (1). A recent paper (2) illustrates one approach to the synthesis of drimanic sesquiterpenes.

We were interested in a generally useful synthetic route to these compounds as well as to structurally related diterpenes. Our approach, which introduces the entire A ring directly, is illustrated by a stereospecific synthesis of winterin.



I.



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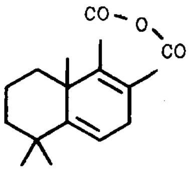

III.

The olefin, 1-vinyl-2,2,6-trimethylcyclohexene (II), is readily prepared by thermal decarboxylation of β-cyclocitrylideneacetic acid (3).

A Diels-Alder reaction with acetylenedicarboxylic acid was effected in diglyme at 97°C for 24 hours. After removal of the solvent in vacuo and cooling, the adduct III, as the anhydride, can be isolated directly. After recrystallization from ether, III exhibits a m.p. of 142-143°C.*

The yield of nicely crystalline product is 4%. The infrared spectrum of adduct III closely resembles that of winterin (4), having strong absorbtions at 5.45 and 5.69μ (anhydride C=O) and two weak bands at 5.95 and 6.18μ (C=C stretching).

The n.m.r. spectrum is also consistent with the assigned structure, having absorbtions at 1.14 and 1.20 p.p.m., assigned to the C_4 gem dimethyl protons; 1.47 p.p.m. (C_{10} methyl protons); a doublet at 3.06 p.p.m. (J_5cps) assigned to the allylic methylene group at C_7; and a triplet at 5.71 p.p.m. (J=5 cps) assigned to the C_6 vinyl proton, ($CHCl_3$, TMS standard).

Catalytic hydrogenation in glacial acetic acid with 10% Pd/C, followed by preparative thin-layer chromatography on silica gel G, gave a crystalline product, m.p. 153-154°C.* in 30% yield. A mixed m.p. with authentic (4) winterin (I) gave no depression. Its infrared, ultraviolet, and n.m.r. spectrum as well as its TLC behavior is identical with winterin. The only other product observed on hydrogenation was the tetrahydro derivative of III. The hydrogenation must therefore have followed a stereospecific

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* Satisfactory analyses were obtained on all new compounds.

course leading only to the trans A/B ring juncture. There is adequate precedent for the steric outcome of catalytic hydrogenation of related compounds in the literature (5). The stereochemistry of winterin has already been deduced by comparison with confertifolin (1).

We are continuing to explore this approach.

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