A FACILE SYNTHESIS OF DENDROLASIN

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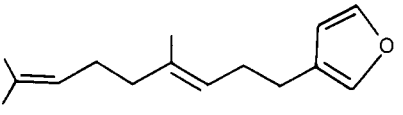
ABSTRACT.—A new convenient synthesis of dendrolasin (**1**) is reported. The synthesis formally consists of the coupling of geraniol with the third isoprene unit containing the preformed furane ring.

Dendrolasin was first isolated from the ant *Lasius (Dendrolasius) fuliginosus* Latr. in 1957 (1) and subsequently has been isolated in plant sources, *i.e.*, in the oil from *Torreya nucifera* Sieb Zucc. (2) and sweet-potato fusel oil (3). It has been assigned the structure **1**, a furane sesquiterpenoid formed by the normal isoprene head-to-tail union.

A biological role of dendrolasin has not yet been definitively established, but it has been suggested that it may be a defense (4) or an alarm (5) substance.

Since its isolation, a number of dendrolasin syntheses have been established (6-11). We now report a new, facile synthesis of this compound that, in a formal sense, consists of the coupling of geraniol **2a** with the third isoprene unit containing the preformed furane ring.



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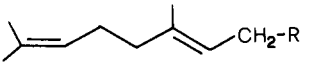
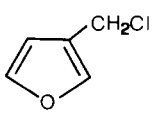


2a R=OH
2b R=Br
2c R=O-Ø

In such a scheme, the crucial C-C bond formation implies alkylation of 3-chloromethylfurane (**3**) by an organometallic derivative (**4**).

Due to its allylic nature, direct conversion of geranyl bromide (**2b**) into **4** could be anticipated to give a very poor result. On the other hand, it has been reported that lithium allyl derivatives may be obtained easily by lithium cleavage of allylphenyl ethers (12). Therefore, geraniol (**2a**) was transformed (via geranyl bromide [**2b**]) into phenyl-ether (**2c**) (13), and this latter was treated with lithium in tetrahydrofurane. Reaction with 3-chloromethylfurane (**3**) (14) then smoothly gave dendrolasin (**1**). As it might be expected (15), the reaction occurred with complete retention of configuration at the trisubstituted double bond, but led to the formation of minor amounts of the allylic isomer (**5**).



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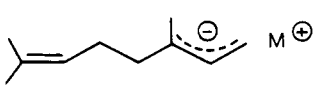

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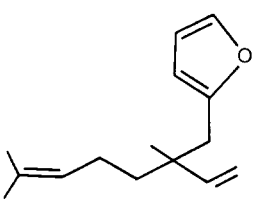

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Pure dendrolasin, however, could be easily isolated by silica gel column chromatography in a 52% yield. All physical constants and ir and nmr spectra were identical to those reported (16).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURE.—The nmr spectra were performed on a Brüker WH270 FT spectrometer with ASPECT 2000 computer in $CDCl_3$ solutions using TMS as internal standard. The ms spectra were determined with an MS9 (AEI) spectrometer.

GERANYL PHENYLETHER (**2c**).—Title compound was obtained by room temperature reaction (12 h) between geranyl bromide (**2b**) (0.90 g) and sodium phenoxide prepared from phenol (0.80 g) and sodium hydride (0.35 g; 55% dispersion in paraffin) in THF (20 ml). Usual work-up and distillation afforded pure **2c** (1.0 g) bp, 128-131°/1.5 mm.

DENDROLASIN (**1**) AND ISODENDROLASIN (**5**).—To a solution of geranyl phenyl ether (**2c**) (620 mg, 2.7 mmol) in ether (1.5 ml, distilled from $LiAlH_4$ directly into the reaction vessel) and THF (2.5 ml, distilled from $LiAlH_4$ directly into the reaction vessel) lithium (38 mg, 5.4 mmol, thin slices) was added.

The mixture was stirred at room temperature under oxygen-free, dry (17) N_2 until the lithium was consumed (approx 3 h). The deep red reaction mixture was cooled with an ice-bath, and 3-chloromethylfurane (**3**) (348 mg, 3 mmol) was added dropwise in 5 min. The colorless mixture was stirred for 2 min at room temperature; then, a few drops of water were added, and the mixture was diluted with hexane (10 ml). The organic layer was washed first with 2 N NaOH and then with water. It was dried ($MgSO_4$) and evaporated *in vacuo* at room temperature to give an oily residue (700 mg). Column chromatography (silica gel, hexane) of the residue gave dendrolasin (**1**) (308 mg; 52% yield) showing physical constants and spectra identical to those reported (1,16) and isodendrolasin (**5**) (148 mg; 25% yield), ms 218 *m/e*; nmr (δ, $CDCl_3$) 7.31 (1H, br s), 7.18 (1H, br s), 6.23 (1H, br s), 5.77 (1H, m, X part of an ABX system), 5.08 (1H, m), 4.97 (m, AB part of an ABX system), 2.41 (2H, br s), 1.90 (2H, m), 1.67 (3H, s), 1.58 (3H, s), 1.28 (2H, m), 0.96 (3H, s).

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