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SYNTHESIS OF DENDROLASIN

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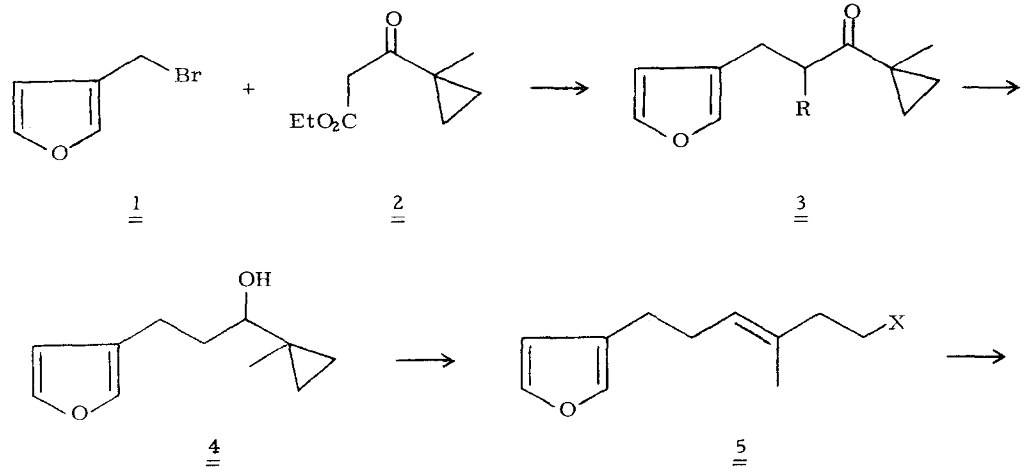
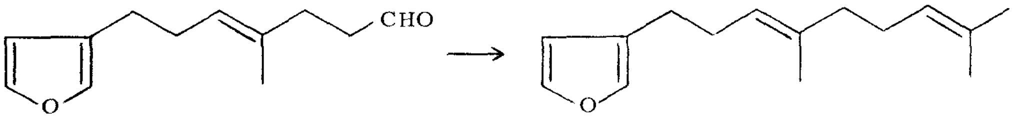
The isolation[1] and proof of structure[2,3] of dendrolasin (7), the major product of the mandibular gland of the ant *Lasius* (*Dendrolasius*) *fulginosus* Latr., were reported in 1956. Since then, dendrolasin has been isolated from other natural sources.[4,5] Its biological function has not yet been defined. It has been reported to have juvenile hormone properties;[6] however, it has been suggested[7] that the observed activity may have been due to the presence of farnesal as an impurity in the specimen which was tested. On the other hand the hypothesis has been advanced that dendrolasin is an alarm[8] and defense[1] substance. In the present communication we are disclosing a stereospecific total synthesis of dendrolasin, which utilizes the highly stereoselective rearrangement of a cyclopropylcarbinyl to the homoallylic system,[9] i.e., 4→5 (X = Br), for the production of the *trans* trisubstituted internal olefinic bond.





6 7

3-Furfuryl bromide (1), n_D^{20} 1.5283, prepared by treatment of 3-furfuryl alcohol[10] with phosphorus tribromide and pyridine in ether, was treated with the sodium enolate of the keto ester 2[9] in tetrahydrofuran. The resulting alkylation product 3 (R = CO_2Et), λ_{max}^{film} 5.73 (ester C = O), 5.91 (ketone C = O), 3.18 (furan CH), 9.77, 11.41, and 12.68 μ (furan), n_D^{20} 1.4835, on heating with barium hydroxide in aqueous ethanol followed by acidification, suffered decarbethoxylation giving the ketone 3 (R = H), λ_{max}^{film} 5.91 μ (ketone C = O), n_D^{20} 1.4916, which was converted, on treatment with lithium aluminum hydride in ether, into the carbinol 4, λ_{max}^{film} 2.86 μ (OH), n_D^{20} 1.4871. This carbinol was submitted to the two-stage treatment involving phosphorus tribromide, then zinc bromide,[9] which afforded the *trans* homoallylic bromide 5 (X = Br), n_D^{20} 1.5155. The 60 mc nmr spectrum of this substance in carbon tetrachloride exhibited absorption for three protons as singlets at δ = 7.27, 7.15, and 6.21 ppm (furan protons), one proton as an unresolved multiplet centered at 5.27 (vinyl proton), two protons as a triplet (J = 7 Hz) centered at 3.39 ($-CH_2Br$), six protons as a broad unresolved multiplet centered at 2.4 (allylic protons) and three protons as a singlet at 1.62 (vinyl methyl). There was no detectable contamination by the *cis* isomer which would have exhibited vinyl methyl absorption in the 1.68 ppm region.[9] The rearranged bromide appeared to be homogeneous by vpc.

The bromide 5 (X = Br) was heated with sodium cyanide in dimethylsulfoxide,[11] to give the nitrile 5 (X = CN), λ_{max}^{film} 4.41 μ (CN), n_D^{20} 1.4896, which was converted, by hydrolysis with potassium hydroxide in ethylene glycol, into the carboxylic acid 5 (X = CO_2H), λ_{max}^{film} 5.83 μ (C = O), n_D^{20} 1.4938. Treatment of this acid with lithium aluminum hydride in refluxing tetrahydrofuran gave the alcohol 5 (X = CH_2OH), λ_{max}^{film} 2.95 μ (OH), n_D^{20} 1.4945, which was smoothly transformed, upon treatment at room temperature with excess Collins reagent,[12] into the aldehyde **6**, λ_{max}^{film} 3.68 (aldehyde CH) and 5.78 μ (C = O), n_D^{20} 1.4907. This aldehyde was allowed to interact with isopropylidenetriphenylphosphorane in dimethylsulfoxide.[13,14] The product was purified by preparative tlc to give dendrolasin that was 95% pure by vpc, n_D^{20} 1.4921. Further purification was effected by preparative vpc. The infrared, nmr, and mass spectra and the tlc and vpc behavior of the synthetic material were identical with the corresponding spectral and physical properties of authentic natural dendrolasin.

All new substances described in this communication gave satisfactory combustion analyses. Mass spectra, recorded on a CEC Type 21-103C spectrometer at 70 ev showed a molecular ion peak for each new compound.

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