A SIMPLE SYNTHESIS OF DANAIDONE (6,7-DIHYDRO-1-METHYL-5H-PYRROLIZIDINE-7-ONE) FROM THE PYRROLIZIDINE ALKALOID MONOCOTALINE. 1

Anibal L. Pereira 5 and Eliezer J. Barreiro *

5Núcleo de Pesquisas de Produtos Naturais, Universidade de Federal do Rio de Janeiro, Departamento de Química, CP 676, Universidade Federal de São Carlos, S.P., Brazil.

Summary: A short synthesis of danai done (6,7-dihydro-1-methyl-5h-pyrrrolizidine-7-one), the major pheromone component of several species of Danaeae butterflies, is described. Monocotamine, the principal pyrrolizidine alkaloid of Crotalaria retusa L. (Leguminoseae), is used as the starting material.

The relationship between butterflies of the subfamily Danaeae and plants containing pyrrolizidine alkaloids (PA) is well known 2, although the exact function of these substances has not been precisely determined. Use in defense mechanisms or as a precursor of sexual pheromones has been suggested 3. In the latter instance, one of the substances thought to be an important pheromonal component is the title compound 1, present in Danaea, Amauris and Lycocoeus species.

We became interested in undertaking the synthesis of 1 starting from monocotamine 2 5 in order to show in vitro the possibility that this substance could perhaps in vivo serve as the precursor of 1.

Our initial synthetic approach to 1 required a derivative such as compound 3a, that through oxidation at C-7 followed by aromatization of the saturated ring would afford the desired pheromone 1.

Thus, 4 6 was hydrolyzed to the necine base tetronene 6, with appeared to be a potential precursor of the 9-deoxy derivative 3a. Despite several attempts we could not accomplish, in adequate yield, the hydrogenolysis of the primary hydroxyl group of 4 7. In light of this result, platynecine 5 was obtained by hydrogenation of 4 (Na-Ni, EtOH, rt, 96%) 8 and submitted to the sequence monosubstitution-acetylation (TSCl, Ieq., Py, 0-10°C, 90 min. solvent removal; AcOEt, 4-DMAP cat., rt, 2h) to give the only product in 75% yield the acetate 5a. With compound 3b secured, we was hoped that it might be possible to obtain the aromatic ring of 1 by dehydrogenation of 3b to give 6a. However, in spite of trying several dehydrogenation conditions we could not satisfactorily accomplish this transformation 10.

In light of this failure, our initial synthetic plan was changed in order to prepare the base 7a. In fact, oxidation of 4 with chloranil followed by treatment with aqueous sodium borohydride 11 afforded in 90% yield the derivative 4b 9 as a crystalline compound, which was sufficiently stable even at room temperature (inert dry atmosphere) to permit the 9-deoxygation step. We were pleased to find that immediate reduction (LAH, THF, rt) of the unstable tosylate 7b, prepared from 7a (TscCL 0.95 eq., Py, 0-5°C, ca 70-85%) 13, afforded the desired compound 6b 9 in an overall yield as high as 60% from the natural alkaloid 2.

The remaining step of the synthesis of 1 14 was accomplished by cautious oxidation of the unstable alcohol 6b with pyridinium chlorochromate on alumina 15 to give the danai done 1 (20-45%). The spectral properties of this synthetic compound were in accord with those reported by Weinwald 14.

In conclusion, a short synthesis of danai done 1 from monocotamine 2 has been effected which leads one to speculate that perhaps the biosynthesis of 1 involves an aromatization-oxidation of a derivative from 2 3.

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REFERENCES AND NOTES


9. All compounds showed spectral properties in accord with the assigned structure.

10. The methods tried in this step include: chloranil in chloroform; DDQ in benzene; 30% H2O2 in MeOH in the presence of NaF and FeSO4;11 PD/C.12


13. Purification of this compound was not possible. The yield for this step was estimated from the NMR spectrum of the final product, which suffered partial decomposition during the analysis.
