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

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Summary: A short synthesis of danaidone (6,7-dihydro-1-methyl-5H-pyrrolizidine-7-one), the major pheromone component of several species of Danainae butterflies, is described. Monocrotaline, the principal pyrrolizidine alkaloid of Crotalaria retusa L. (Leguminosae), is used as the starting material.

The relationship between butterflies of the subfamily Danainae and plants containing pyrrolizidine alkaloids (PA) is well known[2], altough the exact function of these substances has not been precisely determined. Use in defense mechanisms or as 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 Danaus, Amauris and Lycorea species.

We became interested in undertaking the synthesis of 1 starting from monocrotaline 2[5] in order to show in vitro the possibility that this substrate 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, 2[6] was hydrolyzed to the necinic base retronecine 4[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 (Ra-Ni, EtOH, rt, 96%)[8] and submitted to the sequence monotosylation-acetylation (TsCl, leq., Py, 0-10°C, 90 min. solvent removal; Ac_2O, 4-DMAP cat., rt, 2h) to give as the only product in 75% yield the acetate 3b[9]. With compound 3b secured, it 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[12], afforded in 90% yield the derivative 7a[9] as a crystalline compound, which was sufficiently stable even at room temperature (inert dry atmosphere) to permit the 9-deoxygenation step. We were pleased to find that immediate reduction (LAH, THF, rt) of the unstable tosylate 7b, prepared from 7a (TsCl 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 danaidone 1 (20-45%). The spectral properties of this synthetic compound were in accord with those reported by Meinwald[14].

In conclusion, a short synthesis of danaidone 1 from monocrotaline 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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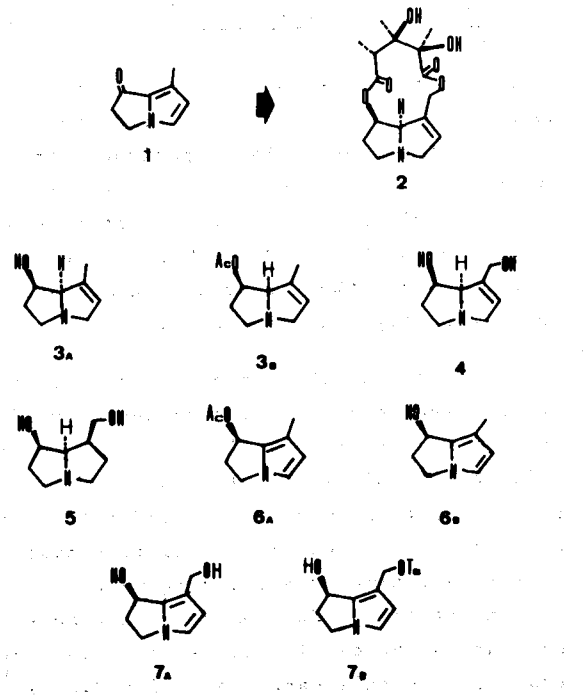

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