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BIOMIMETIC FORMATION OF 5,6-DIHYDROFLAVOPEREIRINE FROM 4,21-DEHYDROGEISSOSCHIZINE

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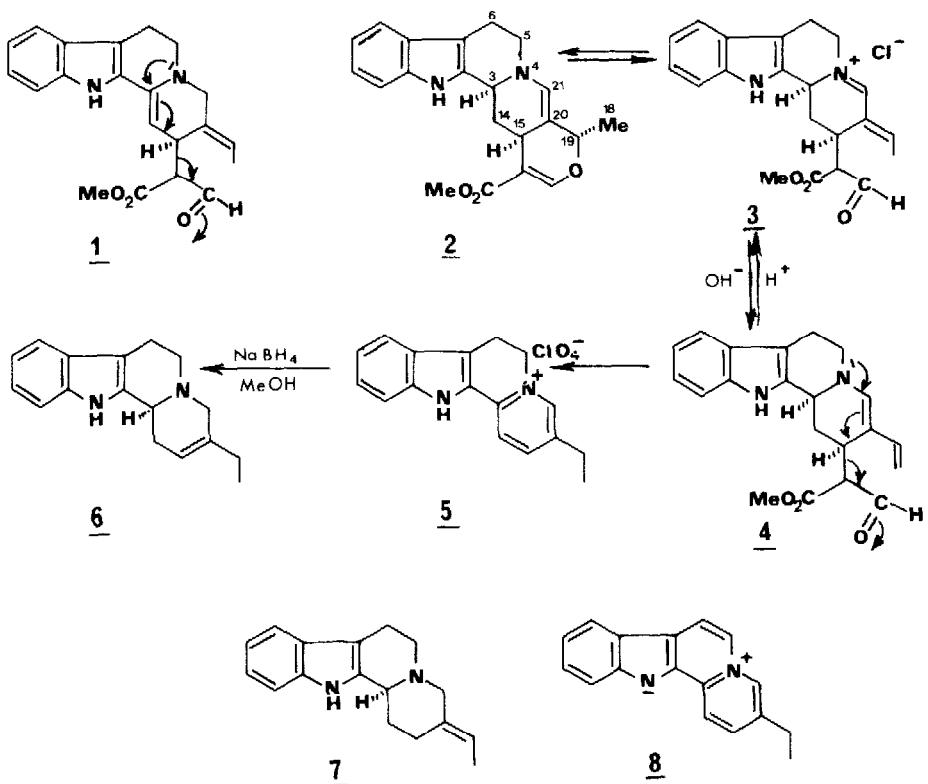
Summary : Indole alkaloids lacking the three carbon unit at C-15 such as deplancheine 7 and flavopereirine 8 can be biogenetically related to 4,21-dehydrogeissoschizine 3. A biomimetic transformation of 3 into 5,6-dihydroflavopereirine 5 supports this proposal.

The three carbon atoms usualy borne at the C-15 position of the Corynanthé group of indole alkaloids are missing in flavopereirine 8[1] and deplancheine 7[2]. A retro-Mannich reaction of synthetic 3,14-dehydrogeissoschizine 1 has been proposed as a model for the biogenesis of flavopereirine[3].



1 2 3 4 5 6 7 8

We report in this paper that the natural 4,21-dehydrogeissoschizine hydrochloride 3[4] can be easily converted in high yield into this series of alkaloids.

We previously demonstrated the versatile reactivity of the key biosynthetic intermediates 2 and 3[4,5]. This reactivity is highly dependant on the reaction conditions.

The means for the conversion of 3 into dihydroflavopereirine 5 have now been found. 4,21-dehydrogeissoschizine 3 (1 g) in N KOH methanol solution (500 ml) was stirred at room temperature for 24 hours. The solution was then neutralized with HCl, the precipitated salt was filtered off and the filtrate was concentrated to 50 ml in vacuo. An aqueous solution of sodium perchlorate was added to the cooled methanolic solution. The filtered precipitate was crystallized from ethanol (0.219 g). The yellow crystals were identical with 5,6-dihydroflavopereirine perchlorate 5[6]. Furthermore sodium borohydride reduction of the crystals gave 6[6] in accordance with the proposed structure for 5. Sodium borohydride reduction of the methanolic neutralized solution containing 5 afforded a nearly quantitative yield of crude compound 6 indicating a high yield for the transformation of 3 into 5.

Retro 1,4 addition of the malonic unit on a conjugated iminium salt followed by double bond migrations must be invoked for the formation of 5. The high dilution is a crucial factor allowing the formation of 5 instead of the self condensation product of 2 or 3 observed in concentrated solution.

Indeed, dimeric compounds of non established structures were isolated as major products beside dihydroflavopereirine 5 in experiments where high dilution conditions were not employed.

Cathenamine 2 as well as 3 led to the formation of 5. These results confirmed the previously postulated equilibrium between 2, 3 and 4[5].

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REFERENCES

1 - N.A. HUGHES and H. RAPOPORT, J. Am. Chem. Soc., 1958, 80, 1604.

2 - R. BESSELIEVRE, J.-P. COSSON, B.-C. DAS and H.-P. HUSSON, Tetrahedron Lett., 1980, 63.

3 - A.-I. SCOTT, Bioorganic Chemistry, 1974, 3, 398.

4 - C. KAN FAN and H.-P. HUSSON, J.C.S. Chem. Comm., 1979, 1015.

5 - C. KAN FAN and H.-P. HUSSON, Tetrahedron Lett., 1980, 1463.

6 - E. WENKERT, R.-A. MASSY-WESTROPP and R.-G. LEWIS, J. Am. Chem. Soc., 1962, 84, 3732.

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