SYNTHESIS OF THE ALKALOID HAPLOBUCHARINE[+]

Pietro Venturella* and Aurora Bellino

Institute of Organic Chemistry, University of Palermo
20, via Archirafi- 90123 Palermo (Italy)

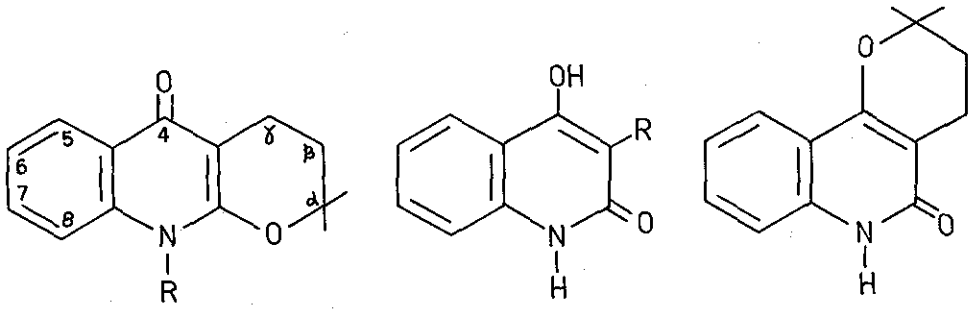
A simple synthesis of haplobucharine [I], an alkaloid isolated from Haplophillum bucharicum was described.

The structure [I] has been assigned[1] to the alkaloid haplobucharine $C_{19}H_{23}NO_2$ from Haplophillum bucharicum (Rutaceae) , mainly on the basis of spectroscopic evidence. The above product is a representative of the class of linear pyranoquinoline alkaloids with the γ,γ-dimethylallyl group attached to the aromatic system through the heteroatom.

Continuing our synthetic work on the alkaloids occurring in plants of Rutaceae family, we report here an easy synthesis of [I] by isoprenylation at nitrogen atom of 3,4,5,10-tetrahydro-2,2-dimethyl-5-oxo-2H-pyrano [2,3-b] quinoline [II] (kaplofoline), another alkaloid isolated from Haplophillum foliosum[2].

The preparation of the intermediate [II] was performed according to the procedure of Bowman and Grundon[3]: 4-hydroxy-3-(γ,γ-dimethylallyl)-2-quinolone [III] was refluxed with 6N-hydrochloric acid in ethanol for 3 hr.

It gave the pyranoquinoline [II] and its angular isomer [IV] which were separated with 20% aqueous hydroxide.



[I] R=$CH_2CH=C(CH_3)_2$ [III] R=$CH_2CH=C(CH_3)_2$ [IV]

[II] R=H

A solution of [II] (200 mg) in dry acetone (60 ml) was treated with anhydrous potassium carbonate (400 mg) and γ,γ-dimethylallyl bromide (1.5 ml) and the resulting mixture was refluxed for 6 hr. After filtration, the solution was concentrated under reduced pressure and the crude product was chromatographed on silica gel. Elution with chloroform-ethyl acetate (9/1) gave the alkaloid [I] (60 mg, 30%), m.p.126-127° (from ethyl acetate), (lit.[1] m.p.126°); uv (EtOH) λ max (log ε) 238 nm (4.18), 250 (sh, 3.95), 317 (3.78), 329 (3.76); m/e 297 (M^+), 229,228,214,212,186,174,69,43; nmr (90 MHz, $CDCl_3$) δ 1.42 (6H, s, $>C(CH_3)_2$), 1.80 (2H, t, J 7.0 Hz, Hβ), 2.75 (2H, t, J 7 Hz, Hγ), 1.72 and 1.88 (s, 3H each $=C(CH_3)_2$), 4.82 (2H, d J 7.3 Hz, $C\underline{H}_2$-CH=), 5.18 (1H, t, J 7.3 Hz, CH_2-C<u>H</u>=), 7.45 (3H, H-6,H-7,H-8), 8.50 (1H, q, J_o 9 Hz, J_m 2.5 Hz, H-5).

The data of synthetic [I] are in good agreement with those reported[1] for natural haplobucharine, thus confirming the structure proposed for the alkaloid.

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+ This paper is Part IX in the series of " Synthesis of Quinoline Alkaloids". For previous papers see (4-11).

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