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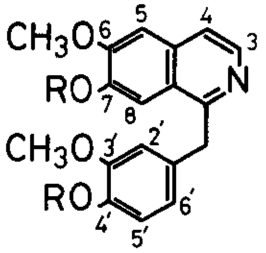
STRUCTURE OF CRISTADINE; A NEW BENZYLISOQUINOLINE ALKALOID

Motoharu Ju-ichi*, Yukari Fujitani
Faculty of Pharmaceutical Sciences, Mukogawa Women's University,
Nishinomiya, Hyogo 663, Japan
Hiroshi Furukawa
Faculty of Pharmacy, Meijo University,
Yagoto, Tempaku-ku, Nagoya 468, Japan

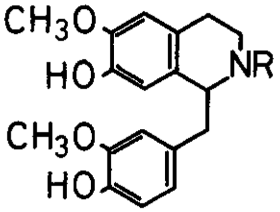
Abstract —— Cristadine (I), a new benzylisoquinoline alkaloid, was isolated from the leaves of Erythrina crista-galli Linn. (Leguminosae) and its structure was elucidated by chemical and spectral studies as (I).

Although many erythrinan alkaloids have been isolated from Erythrina species (Leguminosae), the presence of the other type of alkaloids in this species is rare1). On the phenolic alkaloid constituents of the leaves of Erythrina crista-galli Linn., erysodine, erybidine and N-nororientaline have been isolated2). During the course of our investigation of alkaloid constituents of the leaves of this plant, we isolated a new benzylisoquinoline alkaloid named cristadine. In this communication, we wish to report the structure elucidation of this alkaloid.

Cristadine (I), mp 128-129°, formed colorless cubes, $C_{18}H_{17}NO_4$, optically inactive; IR (KBr, cm^{-1}): 3400 (OH); NMR (DMSO-d_6, δ): 3.69, 3.91 (each 3H, s, OCH_3), 4.31 (2H,s), 6.55 (1H, dd, J=1.5, 8.1 Hz, aromatic-H), 6.62 (1H, d, J=8.1 Hz, aromatic-H), 6.86 (1H, d, J=1.5 Hz, aromatic-H), 7.28, 7.44 (each 1H, s, aromatic-H), 7.49, 8.19 (each 1H, d, J=5.6 Hz, aromatic-H), 8.72, 9.83 (each 1H, s, OH). These data suggested the presence of two methoxyl groups, two phenolic hydroxyl groups and seven aromatic protons in (I). No signal due to an NH or an N-methyl group in the NMR and IR spectra was observed. Information relating to the skeletal structure of (I) was obtained from its UV spectrum [λ_{max}^{EtOH} nm (log ε): 240 (4.80), 282 (3.88), 322 (3.57), 332 (3.74)] which showed the characteristic absorption for the 1-benzylisoquinoline chromophore. Methylation of (I) with diazomethane afforded O-methylcristadine (II), which was identical with an authentic sample of papaverine (II) in a comparison with MS, IR, NMR spectra and TLC behaviors. The position of two phenolic hydroxyl groups was assumed to be



(I) R=H
(II) R=CH_3



(III) R=H
(IV) R=CH_3

situated at C_7 and $C_{4'}$ positions, by considering two hydroxyl groups of N-nor-orientaline (III) isolated from this plant. To confirm this assumption, cristadine (I) was treated with CH_3I, followed by reduction with $NaBH_4$3) to afford *dl*- orientaline (IV), which was identified with an authentic specimen by MS, IR, NMR spectral and TLC comparisons. On the basis of above results, the whole structure of cristadine was assigned as 1-(4'-hydroxy-3'-methoxybenzyl)-7-hydroxy-6-methoxyisoquinoline (I).

Most of benzylisoquinoline alkaloids of papaverine type are isolated from Papaveraceae plants, and cristadine (I) is the first example of this type alkaloid isolated from Leguminosae. From the biogenetic point of view, it is of interest that the presence of cristadine (I) and its precursor (III) in the same plant suggests similar pathways to the biosynthesis of papaverine (II) in Papaveraceae plants4).

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