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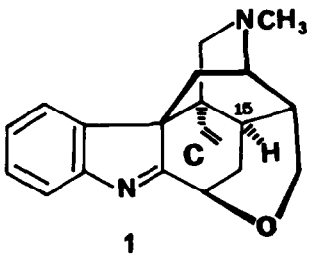
STRUCTURE OF KOUMINE, AN ALKALOID FROM GELSEMIUM ELEGANS BENTH

Françoise KHUONG-HUU, Angèle CHIARONI and Claude RICHE

Institut de Chimie des Substances Naturelles, CNRS, 91190 Gif-sur-Yvette, France

Abstract - The structure of koumine, an indole alkaloid from Gelsemium elegans Benth., was determined by a X-ray crystallographic study.

Koumine, 1, is an indole alkaloid which has been isolated for the first time by T.Q. Chou [1] in 1931 and by Chi, Kao and Huang [2] in 1932, from a Chinese Loganiaceae, Gelsemium elegans Benth, of which Kou-wen is the chinese name. Its structure had never been determined. From this species, gelsemine [2] (from the kouminine fraction of T.Q. Chou [1]), sempervirine [3] and kouminidine [1,2] were also obtained.



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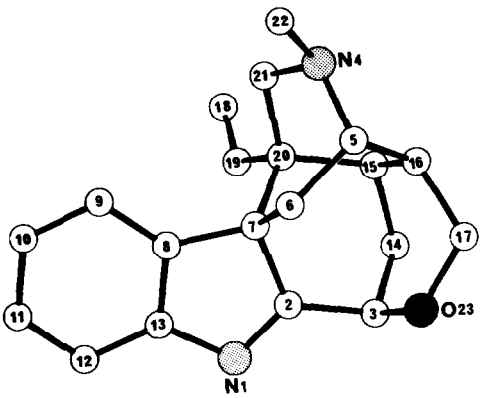

The isolation of a crystalline sample from a fraction of a chromatographic separation effected on the mother liquors of koumine which was extracted in 1953 by Janot, Goutarel and al. [3] from South-Annam G.elegans, allowed us to perform a X-ray crystallographic study of this alkaloid.

The physical data of koumine, $C_{20}H_{22}N_2O$, are the following : F 172° (acetone), $(\alpha)_D$ - 272° ; UV (EtOH) $\lambda_{max.nm}$ 220, 262, log ε 4.32, 3.84 [3] ; IR (nujol) 1700 cm^{-1} (C=N) ; MS M^+ 306 (main peak), no noticeable fragmentations ; ^1H NMR (400 MHz) ($CDCl_3$) : 2.61 (3H, 1, N-CH_3), 3.09 and 3.13 (2H, AB, J=11 Hz, CH_2-21 [4], 3.62 (1H, ABX, JAB=11 Hz, JAX ~ 0, H_A-17), 4.29 (1H, ABX, JAB=11 Hz, JBX=4 Hz, H_B-17), 4.69-4.80 (3H, ABC, -CH=CH_2), 5.03 (1H, m, H-3), 7.24 and 7.38 (2H, 2t, J=8Hz, H-10 and H-11), 7.58 and 7.62 (2H, 2d, J=8Hz, H-9 and H-12).

Crystal data : monoclinic system, space group $P2_1$, Z=2, a=7.676 (2), b=13.122 (3), c=7.988 (2) Å, β=103.32 (2)°, V=782.95 $Å^3$, Dc=1.28 gcm^{-3}, λ=1.5418 Å.

Intensity data were collected on a PW1100 Philips diffractometer. Of the 1469 measured reflexions, 1133 were considered as observed ($I>3\sigma(I)$).

The structure was solved by direct methods and refined by full-matrix last-squares using anisotropic temperature factors. All the hydrogen atoms were located on difference Fourier syntheses and replaced at their theoretical positions except those of the nitrogen atom N(1) and carbon atoms C(18) and C(22) [4]. The final R value was 0.036 for the observed reflexions. Atomic coordinates ($\times 10^4$) of the non-hydrogen atoms are listed in Table :

ATOM	X	Y	Z
N(1)	-3124 (3)	3733 (3)	9427 (4)
C(2)	-1702 (4)	4287 (3)	9684 (4)
C(3)	-1185 (4)	4914 (4)	8319 (4)
N(4)	2696 (3)	5400 (3)	13606 (3)
C(5)	2609 (3)	4842 (3)	11994 (4)
C(6)	1315 (4)	3949 (3)	11805 (4)
C(7)	-645 (3)	4356 (3)	11548 (3)
C(8)	-1817 (4)	3702 (3)	12384 (4)
C(9)	-1731 (4)	3422 (3)	14070 (5)
C(10)	-3112 (5)	2822 (4)	14429 (5)
C(11)	-4506 (4)	2486 (4)	13106 (6)
C(12)	-4580 (4)	2746 (4)	11422 (6)
C(13)	-3238 (4)	3351 (4)	11071 (4)
C(14)	-1103 (5)	6008 (4)	8911 (5)
C(15)	211 (4)	6088 (3)	10680 (4)
C(16)	2055 (4)	5625 (3)	10563 (4)
C(17)	2017 (5)	5210 (4)	8778 (4)
C(18)	-2664 (7)	6675 (6)	13067 (9)
C(19)	-2315 (4)	5916 (4)	12236 (5)
C(20)	-503 (3)	5506 (3)	12094 (4)
C(21)	862 (4)	5610 (3)	13813 (4)
C(22)	3778 (4)	4899 (4)	15099 (4)
O(23)	532 (3)	4555 (3)	8091 (3)

Koumine 1 belongs to the corynantheine group alkaloids and has been represented with at C-15 the absolute configuration common to all alkaloids known of this type and in agreement with a biogenetic hypothesis of its formation from corynantheine.

The molecule exhibits a cage-like structure were all the rings are almost boat-shaped except cycle C with adopts a chair conformation.

References

1. T.Q. Chou, Chinese J. of physiology, 1931, 5, 32 ; Chem.Abstr., 1932, 26, 806.
2. Y.F. Chi, Y.S. Kao and Y.T. Huang, J. Am. Chem. Soc., 1938, 60, 1728.
3. M.M. Janot, R. Goutarel, and M.C. Perezamador, Y.Barron, Ann. Pharm. Fr., 1953, 11, 602.
4. The nomenclature used is that from J. Le Men and W.I. Taylor, Experientia, 1965, 21, 509.

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