Tetrahedron Letters No. 23, pp. 2061-2064, 1971. Pergamon Press. Printed in Great Britain.

GARDNERIA ALKALOIDS - VII[1)]

THE CRYSTAL STRUCTURE OF GARDNERAMINE CYANOBROMIDE

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(Received in Japan 31 March 1971; received in UK for publication 4 May 1971)

The structure of gardneramine (I), a novel type indolic alkaloid of Gardneria nutans[2)] and G. multiflora[3)] (Loganiaceae), has been elucidated in the preceeding communication[1)], remaining the geometry of the side chain double bond and the absolute configuration of the molecule undetermined. The difficulty in clarifying these structural features with chemical methods and the novelty of the structure possessing an imino-ether ring which hitherto has not been found in naturally occurring indolic alkaloids stimulated us to the present X-ray crystallographical study. The material chosen was gardneramine cyanobromide (II)[1)], $C_{24}H_{28}N_3O_5Br$ (MW 518.4), mp 214°, which regenerates the mother base on treatment with acetic acid to prove no skeletal change has occurred in its formation from I. Repeated recrystallization from acetone afforded colorless prisms, which were shown to be orthorhombic with unit cell dimensions of a=12.24, b=25.70 and c=7.34 Å, and belong to space group $P2_12_12_1$. The density measured by the floatation method using CCl_4-n-hexane is 1.500 $g\cdot cm^{-3}$, which agreed with the calculated value of 1.497 $g\cdot cm^{-3}$ based on the presence of four molecules in a unit cell.

Three dimensional reflexions of 0kl - 5kl and hk0 - hk5 were recorded with Cu Kα radiation on the equi-inclination Weissenberg photographs using the multiple film technique, and their intensities were measured photometrically to give a total of 1448 independent non-zero observed structure factors. The coordinate of the bromine atom was determined to be (0.0043, 0.4171 0.3662) by the Patterson synthesis and there appeared a pseudo mirror plane through x = 0 on the Fourier map. The conventional heavy atom method, however, was carried out successfully by the careful selection of the correct peaks from their mirror images, and successive use of Fourier and difference Fourier syntheses enabled us to assign the structure (II) shown in Fig.1 to gardneramine cyanobromide. Refinement of the structural parameters was carried out by the block-matrix least-squares calculations including anisotropic thermal parameters for each atom, and the final R-factor was 0.113. The absolute configuration was determined by using the anomalous dispersion effect of the bromine atom for Cu Kα radiation. Ten sets of hkl and h$\bar{k}$l reflexions on the c - axis 1st layer Weissenberg photographs showed clearly that the absolute configuration is as shown in Fig. 1.

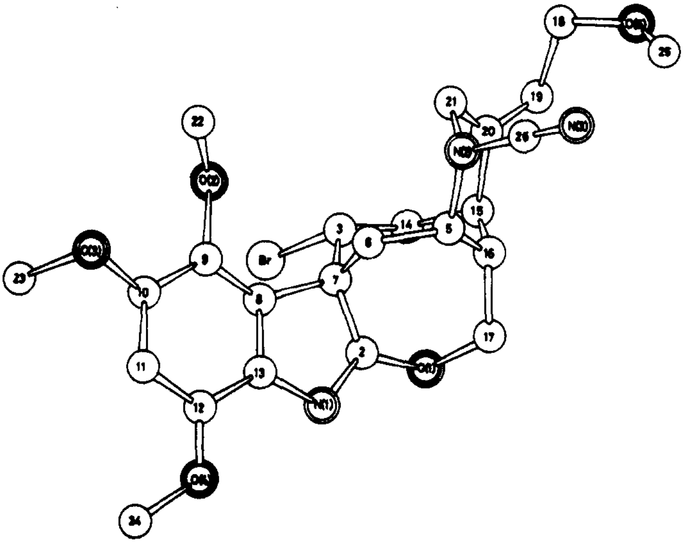
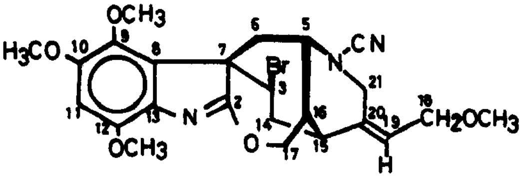


Fig.1



(II)

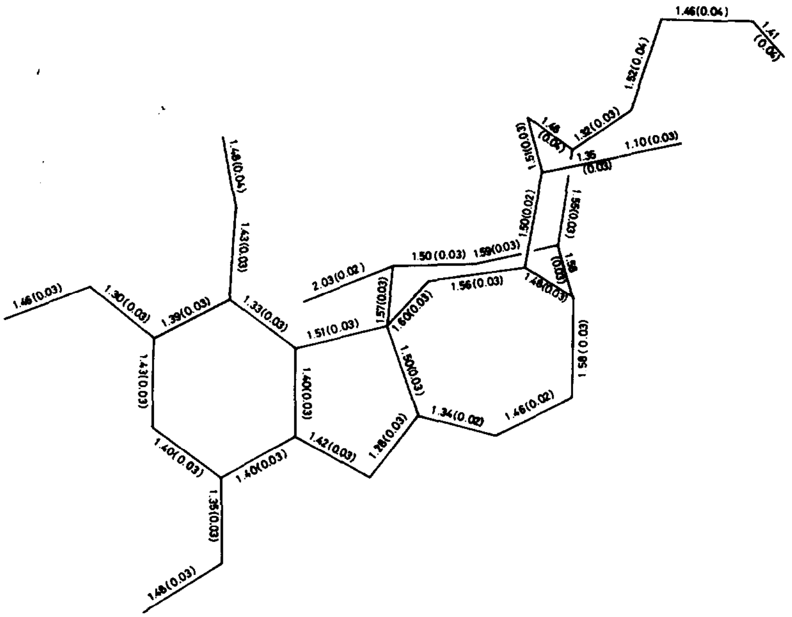


Fig.2 Bond lengths in Å. Standard deviations are shown in parentheses.

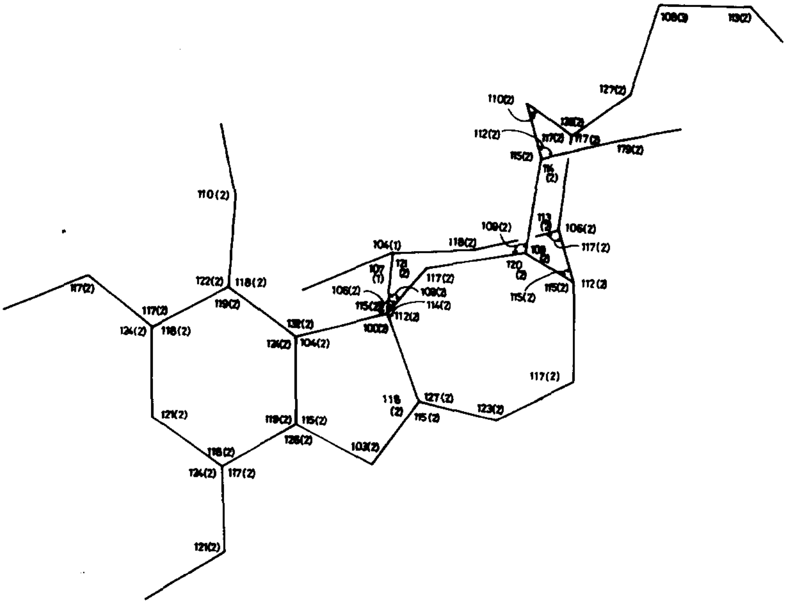
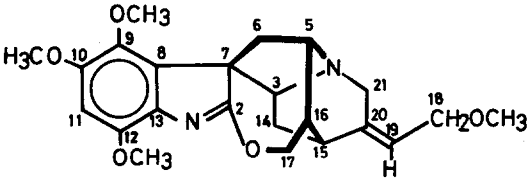


Fig.3 Bond angles in degrees. Standard deviations are shown in parentheses.

The chemically deduced gross structure of gardneramine (I)[1] has been confirmed by the present study. At the same time, the structural features which remained obscure have now been fully revealed. Thus the three methoxyl groups are located at $C_{(9)}$, $C_{(10)}$ and $C_{(12)}$ on the benzene ring, and the configuration of the $>C_{(19)}=C_{(20)}<$ system is Z form, that is $C_{(18)}$ is oriented cis to $C_{(21)}$. It is interesting to note the difference of these structural features from those of three other bases, gardnerine (III), gardnutine (IV) and hydroxygardnutine (V), which are coexisting in the same plant.[4,5] Thus I is oxygenated at all aromatic carbons in its indole nucleus except $C_{(11)}$, which is the only aromatic carbon carrying the oxygen function in III, IV and V. In addition, the configuration of the $>C_{(19)}=C_{(20)}<$ system in I is opposite to that of III and IV.

Gardneramine (I) is the first natural indolic alkaloid having an imino-ether ring in its molecule. A possible biosynthetical role of imino-ether system derived from oxindole has been suggested by Scott.[6] Oxindole alkaloids with a quinuclidine system in the alicyclic moiety are quite few, the only precedent being voacharotine oxindole.[7]



GARDNERAMINE (I)

ACKNOWLEDGEMENT : A part of the expences of this work was supported by a Grant-in-Aid from the Ministry of Education, Japan, to which our thanks are due.

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