Tetrahedron Letters No.51, pp. 5373-5375, 1968. Pergamon Press. Printed in Great Britain.

THE STRUCTURE OF VERTICINONE METHOBROMIDE

Shô Itô, Yoshimasa Fukazawa and Tomoko Okuda

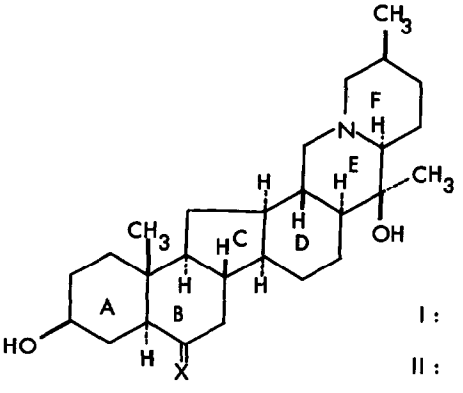
Department of Chemistry, Tohoku University, Sendai

and Yoichi Iitaka

Faculty of Pharmaceutical Sciences, University of Tokyo, Tokyo, Japan

(Received in Japan 22 August 1968; received in UK for publication 2 September 1968)

In our previous paper (1) we have provided the evidence which enabled us to formulate the structure of verticine and verticinone, the alkaloids of Fritillaria verticillata WILD. var. Thunbergii BAKER., as that indicated in I and II, respectively. Since the stereochemistry suggested for the ring junctures B/C, C/D and D/E was based on analogy and on biogenetic considerations, we have carried out an X-ray analysis in order to establish these points.



The material used for this study was verticinone methobromide III, $C_{28}H_{45}ON_3Br$, m.p. 287°C, derived from II by quaternization with methyl bromide.

This compound crystallized from methanol is thin flakes with well-developed {100} faces. The crystal belongs to the monoclinic system with the space group $P2_1$ and the cell dimensions, a=12.49 Å, b=12.02 Å, c=9.12 Å and β=92.4°

Three-dimensional intensity data for hk0 - hk4 and h0ℓ - h6ℓ reflections were collected from the equi-inclination Weissenberg photographs taken with copper Kα radiation, and intensities were estimated by visual comparison with the calibulated intensity scale. A total of 2074 independent structure factors were evaluated for the analysis. The positions of bromine atoms were determined by the calculation of the three-dimensional sharpened Patterson synthesis.

Several cycles of calculations of Fourier and difference Fourier synthesis with the use of the heavy atom method, revealed the whole structure. The parameters were refined by several cycles of least-squares calculations. At the present stage of refinement the R factor is 9.9%. The molecular structure of verticinone methobromide is shown in Figs. I and II.

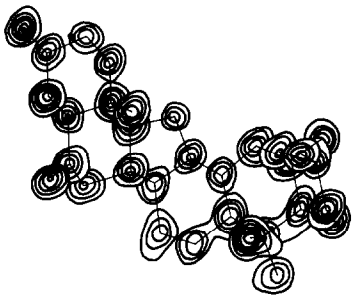


FIG. I

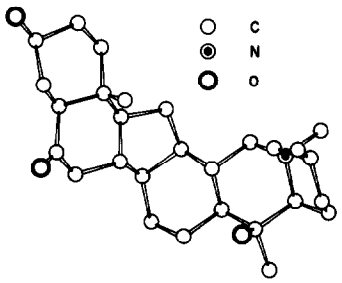
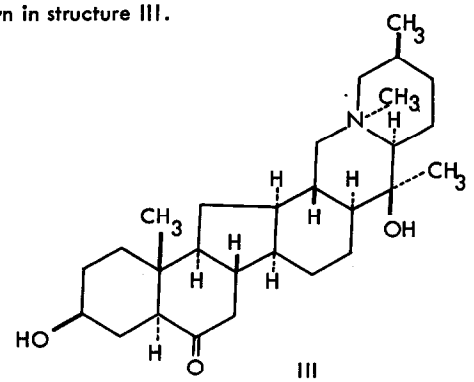


FIG. II

As is clear from Fig. II, all six-membered rings in this compound are in the chair conformation, with the ring fusions as follows: A/B trans; B/C trans; C/D cis; D/E trans and E/F cis.

The absolute configuration was determined by the anomalous dispersion effect of bromine atoms for copper Kα radiation and is as shown in structure III.



III

Since the presence of a trans quinolizidine ring system in I and II is already established (1) and since the configurational change from trans to cis quinolizidine upon the quarternization is well established (2), the alkaloids, verticine and verticinone, should thus be represented by the structures I and II, in agreement with our original proposal.

The calculations were performed on the HITAC 5020E computor in the University of Tokyo.

References

1) S. Itô, M. Kato, K. Shibata and T. Nozoe, Chem. Pharm. Bull., 11, 1337 (1963).

2) T. M. Moynehan, K. Schofield, Richard A. Y. Jones and A. R. Katritzky, J. Chem. Soc., 2637 (1962).