THE STRUCTURE OF ECHITAMINE IODIDE

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ECHITAMINE ($C_{22}H_{28}O_4N_2$) the major alkaloid derived from the bark of *Alstonia scholaris*, has been attracting the attention of the organic chemist in recent months and its structure has been the subject of some controversy.[1-6] The determination of its X-ray, crystal structure was undertaken by the present writers at the instance of Prof. T. R. Govindachari who was kind enough to prepare for them the quarternary iodide and the chloride ($C_{22}H_{29}O_4N_2I$, Cl). Goodson and Henry[7] report that the iodide crystallises in the anhydrous state while the chloride crystallises as "stumpy prisms" with one molecule of water when crystallised slowly from water but as long anhydrous needles when crystallised rapidly. Chemical analysis of the iodide by Prof. Govindachari gave the formula $C_{22}H_{29}O_4N_2I$. No analysis was done on the chloride but the needle shape of the crystals was taken to indicate the absence of any water of crystallisation.

Rotation and Weissenberg photographs gave the space group to be $P2_12_12_1$ with the following axial dimensions in Ångstrom units :

	a	*b*	*c*
Echitamine iodide ..	18·45	13·83	8·48
Echitamine chloride ..	17·29	14·97	7·94

The measured value of the density in the case of the iodide ($d = 1{\cdot}583$) gave four molecules in the unit cell and confirmed the anhydrous nature of the crystals. The density of the chloride was not determined. The differences in the axial dimensions suggest that the isomorphism between the two compounds may not be exact.

Intensity data were collected for the *hko*, *hk*L (L = 1 to 5) and *hol* reflexions using the multiple film technique of Robertson and the intensities were accurately measured visually using calibrated scales. In the *hko* zone there were 196 reflexions of measurable intensity for the iodide and 166 for the chloride. The L.P. and absorption corrections were applied and the approximate scale factors determined by the Wilson method.

An *hko* Patterson projection gave the iodine position to be $x = 0{\cdot}067$, $y = 0{\cdot}190$ in fractional co-ordinates. By the heavy atom and the isomorphous replacement method the phases of 70 reflexions for the iodide and 52 reflexions for the chloride could be deduced with some certainty. However, it was decided to proceed only with the solution of structure of the iodide. A Fourier projection using these 70 amplitudes not only confirmed the iodine position but also showed a large number of other peaks. From the structure factor computation made on putting 17 carbon atoms at the peaks in the Fourier, 66 additional signs could be assigned. A Fourier with these terms included showed better resolution, a phenyl and a five-membered ring being easily distinguishable. The iterative process of Fourier synthesis was continued till all the 28 atoms of the molecule (excluding the hydrogens) could be put in at the Fourier peaks. The structure factor calculations with all the atoms assumed to have the scattering factor of carbon gave the signs of about 169 reflexions and the R factor was 0·28.

A subtraction Fourier projection with the temperature corrected iodine contribution removed showed very much better resolution and with the movement of the atoms to the peaks the R-factor came down to 0·22. A Difference-error synthesis indicated that six atoms had been placed in wrong positions. On moving them to high positive regions not only did the R-factor come down to 0·19, but most of the "bad" reflexions became very much better. This was followed by two subtraction Fouriers and one difference projection and the subsequent structure factor calculation gave the phases of 192 out of 196 observable reflexions. Of the 23 reflexions whose phases were obtained in the later stages of the iterative process there were a few of medium intensity (*e.g.*, 210 : $F_0 = +21{\cdot}5$, $F^1_{calc.} = -35$) whose signs came out opposite to those deduced by the heavy atom method. These had a considerable effect in not only resolving the peaks in the iodine removed Fourier but also in completely suppressing many spurious peaks.

The iodine removed *hko* Fourier projection is given in Fig. 1. A very small peak persists at the iodine position but each one of the 28

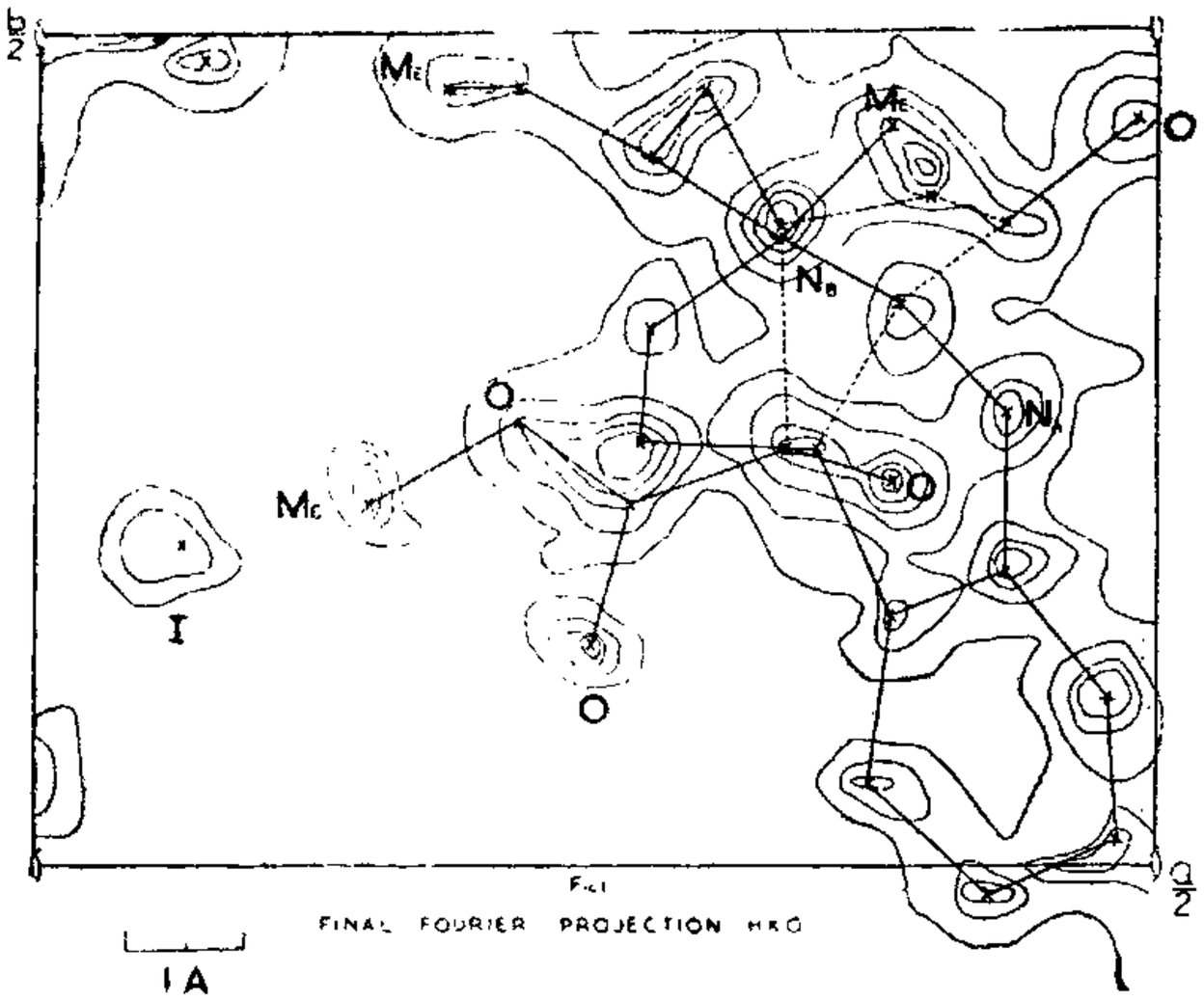


FIG. 1

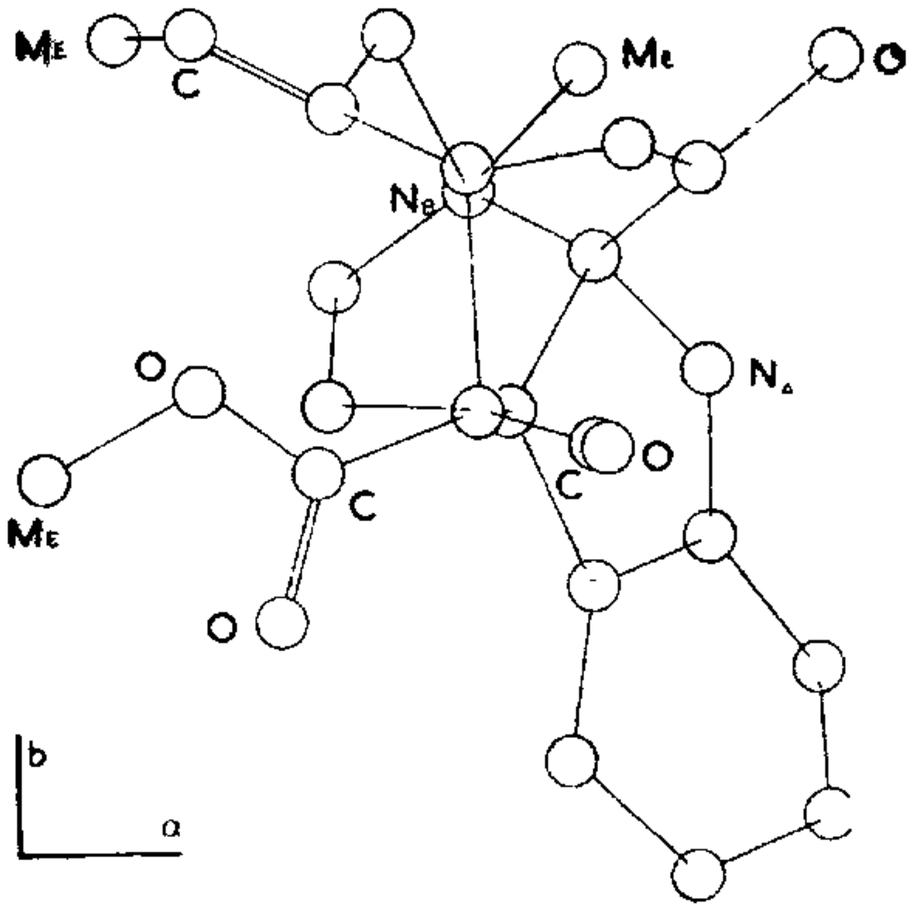
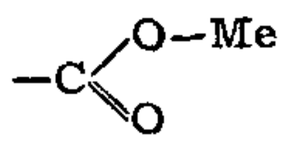


FIG. 2

heavier atoms of the molecule could be easily identified. The structure factor calculation gave an R-factor of 0·15 for 196 observed *hko* reflexions. The unobserved reflexions also calculated quite low.

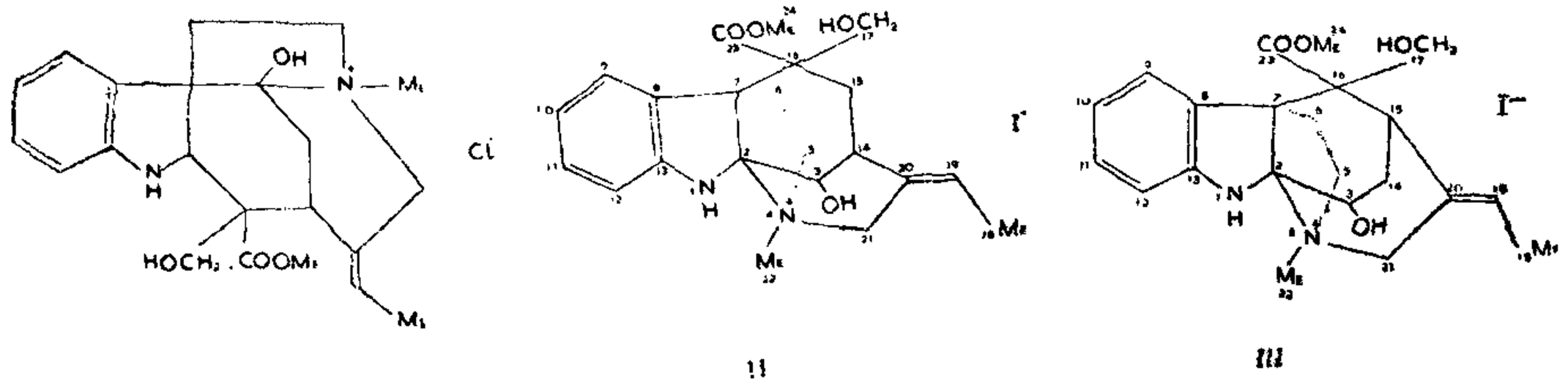
The configuration of any molecule can be assigned without ambiguity only if its crystal structure has been solved in at least two projections. However as the iodine subtracted *hko* projection (Fig. 1) shows very good resolution it should be possible to deduce the molecular structure from it making use of some of the well-established chemical data about the compound.

It became increasingly clear during the progress of this work that the structure (I) suggested by Conroy[4] or its modification due to Robinson *et al.*[5] are incompatible with the Fourier projection. In the *hko* projection (Fig. 1) the following features may be clearly discerned: (1) A phenyl ring with a five-membered ring fused to it; (2) this five-membered ring is fused on to two other rings—one five-membered and one six-membered boat-shaped ring (dotted lines in Fig. 1)—along a common bond; (3) the carbomethoxy group



is attached to the six-membered boat at the equatorial position; (4) the heavy peak at the centre of the first five-membered ring is due to two atoms and is therefore presumably the carbon and the oxygen of the CH_2OH. This group is attached to the same carbon atom of the boat as the carbomethoxy group; (5) an oxygen atom (probably the OH group) is attached to the opposite point of the boat.

The $=C-Me$ can also be identified although



II III

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the manner in which it is joined to the main structure is not so clear. For deducing this a model given by II which satisfies all the five points mentioned above was first tried. The model appeared to have the further merit in having (*a*) the $\phi - N - C - N$ system advocated by Govindachari[1] and Birch[6]; (*b*) the same number of five-membered and six-membered

rings as in the structure due to Conroy and Robinson *et al.* When the three-dimensional model was made it was found that it could explain all but two of the peaks in the Fourier projection.*

However, when the bond connecting C_{20} to C_{14} was shifted to C_{20}—C_{15} as in III (making the lower six-membered ring of II into a seven-membered ring), all the atomic peaks could be most satisfactorily explained. It appears therefore that III is the most probable structure of echitamine iodide. Figure 2 gives the identification of the Fourier peaks in Fig. 1, according to the structure III. The solution of the *hol* projection and the refinement of the parameters are in progress.

The authors wish to record their grateful thanks to Prof. T. R. Govindachari of the Presidency College, Madras, for preparing the compounds and for the invaluable discussions they had with him. Thanks are due to Prof. D. K. Banerjee and Mr. G. Bagavant of the Indian Institute of Science with whom the authors were in constant consultation. Thanks are also due to Prof. R. S. Krishnan for his very kind interest in this problem.

* At this stage Prof. T. R. Govindachari intimated one of us (S. R.) that he had received a letter from Prof. J. Monteath Robertson stating that he had solved the structure of echitamine bromide and that it corresponded to III. Model III was tried only after the receipt of this information.

1. Govindachari, T. R. and Rajappa, S., *Proc. Chem. Soc.*, 1959, 134; *Chem. and Ind.*, 1959, 1154 and 1549.
2. Birch, A. J., Hodson, H. F. and Smith, G. F., *Proc. Chem. Soc.*, 1959, 224.
3. Chatterjee, A., Ghosal, S. and Majumdar, S. G., *Chem. and Ind.*, 1960, 265.
4. Conroy, H., Bernasconi, R., Brook, P. R., Ikan, R., Kurtz, R. and Robinson, K. W., *Tetrahedron Letters*, 1960, No. 6, 1.
5. Chakravarthi, D., Chakravarthi, R. N., Ghose, R. and Sir Robert Robinson, *Ibid.*, 1960, No. 10, 10; No. 11, 25; No. 12, 33.
6. Birch, A. J., Hodson, H. F., Moore, B., Potts, H. and Smith, G. F., *Ibid.*, 1960, No. 19, 36.
7. Goodson, J. A. and Henry, T. A., *Jour. Chem. Soc.*, 1925, **127**, 1640.
   Goodson, J. A., *Ibid.*, 1932 (2), 2626.

Note added in Proof: Prof. J. M. Robertson has kindly informed us that the compound used by him for solving the structure was ecnitamine bromide with a molecule of methanol as solvate.

VARENNA SUMMER SCHOOL ON RADIOFREQUENCY SPECTROSCOPY

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THE "Enrico Fermi" International School of Physics sponsored by the Italian Physical Society, under the joint auspices of the Italian Ministry of Public Instruction and the Italian National Council of Research, held its Seventeenth International Summer School Course entitled "Topics on Radiofrequency Spectroscopy" at the Villa Monastero, Varenna, on Lake Como from 1st August to 17th August 1960. Professor A. Gozzini (Pisa) was the Director of this Course.

The subjects discussed in the School can be broadly classified under the following headings: **(1) Radiofrequency spectroscopy of optically oriented atoms; (2) Study of nuclear and atomic ground states by atomic beams; (3) Masers and maser spectroscopy; (4) Double irradiation in magnetic resonance.** The lectures were delivered in French and in English.

The Course commenced with a general exposition by Professor Brossel (Paris) on optical pumping. The subject of optical methods in magnetic resonance was discussed in a series of twelve lectures by Professor A. Kastler, Professor J. Brossel, Dr. C. Cohen-Tannoudji and Dr. A. D. May (all from Ecole Normale Superieure, Paris) and Professor T. Skalinski (Warsaw). The aspects of optical pumping which covered these lectures were (*i*) the experimental methods for optical pumping and the detection of nuclear magnetic resonance; (*ii*) a theoretical discussion of the phenomenon of coherence in optical resonance study of the fundamental states and optically excited states of atoms; (*iii*) measurement of lifetimes of excited states; (*iv*) study of collisions; and (*v*) investigations of excited states produced by electronic bombardment.

Professor W. A. Nierenberg (Berkeley) dealt with the study of atomic and nuclear ground states by atomic beams. After a heuristic discussion of the hyperfine Hamiltonian, the Breit-Rabi diagram and the atomic magnetic moment, he described the computational methods for determining the parameters a, b, g_J *and* g_I. The results so far obtained on Pu^{239}, Pu^{238}, Tm^{170} and Pa^{233} were presented.