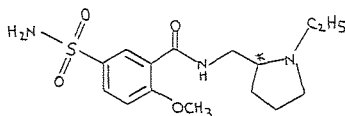


**03.3-09** THE CRYSTAL STRUCTURE OF SULPIRIDE, AN ANTI-PSYCHOTIC AGENT. By Lilian Y.Y. Chan and Norman Camerman, Department of Biochemistry, University of Toronto, Toronto, Ont., Canada, and Arthur Camerman, Departments of Medicine (Neurology) and Pharmacology, University of Washington, Seattle, Wash., U.S.A.

Crystals of the active stereoisomer of the antipsychotic drug sulpiride are orthorhombic with cell dimensions  $a=12.037(6)$ ,  $b=24.163(4)$ ,  $c=11.536(6)$ , space group  $P2_12_12_1$  with eight formula units per unit cell. The two independent molecules in the asymmetric unit are related by a pseudo centre of symmetry, and conventional direct phasing methods failed to determine the structure completely. Specifically, the atomic positions of the five-membered ring containing the asymmetric carbon atom could not be unambiguously identified in both molecules, and refinement stopped at  $R=13.5\%$ . The crystal and molecular structure of the racemate (space group  $P\bar{1}$ ) was then determined, and was used to solve the noncentrosymmetric structure by molecular fitting and Fourier methods. Subsequent refinement of the noncentrosymmetric structure converged at  $R=6.5\%$  ( $R$  for racemic sulpiride= $7.9\%$ ). The absolute configuration of the active isomer was determined to be  $S$ , in accordance with chemical results. The stereochemical characteristics of  $S$ -sulpiride will be compared with those of other neuroleptics.



**03.3-10** THE CRYSTAL STRUCTURE OF FREE BASE COCAINE,  $C_{17}H_{21}NO_4$ . By Ronald J. Hrynchuk, Richard J. Barton and Beverly E. Robertson, Faculty of Science, University of Regina, Regina, Saskatchewan, S4S 0A2 Canada.

The crystal structure of free base cocaine has been determined in order to compare the conformation with that observed in salts, and to clarify the powder pattern of the pure compound. Crystals of cocaine are monoclinic, space group  $P2_1$ ,  $a = 10.130(1)$ ,  $b = 9.866(2)$ ,  $c = 8.445(1)$  Å,  $\beta = 106.92(1)^\circ$ ,  $Z = 2$ ,  $D_x = 1.25$  g cm $^{-3}$ . Data were collected with  $M\alpha$  radiation on a modified Picker diffractometer using the NRCC diffractometer control system. (D.F. Grant and E.J. Gabe, Am. Cryst. Assoc. Abstracts 2, 245 (1974)). The structure was solved by direct methods and refined by least squares to a final weighted  $R$  factor of 0.067 ( $w = 1/\sigma^2$ ) using the 1662 independent reflections with  $\sin \theta/\lambda < 0.70$  and  $I/\sigma(I) > 2.0$ .

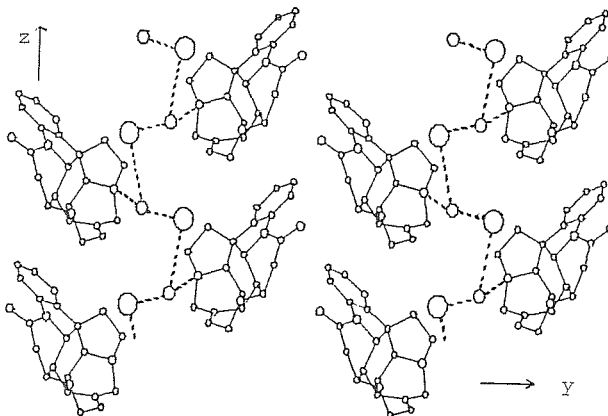
The free base exists in a piperidine chair conformation similar to the methiodide salt (M. Shen, J.R. Ruble and G. Hite, Acta Cryst. B31, 2706 (1975)) and the hydrochloride salt (E.J. Gabe and W.H. Barnes, Acta Cryst. 16, 796 (1963)). However, the piperidine ring carbon-nitrogen bonds in the free base are shorter than those in the salts: 1.46(1) and 1.47(1) in the free base compared to 1.55(2) and 1.51(2) in the methiodide salt and 1.50(1) and 1.49(1) in the hydrochloride salt. Although the benzyloxy side chain and the methyl on the piperidine nitrogen atom are both equatorial in the free base, as in the salts, the orientation of the benzyloxy side chain with respect to the piperidine ring is different from that common to both salts. Thus the free base is conformationally less rigid. The orientation of the carbomethoxy group also differs from that found in both salts.

**03.3-11** CRYSTAL PACKING OF STRYCHNINE SALTS. By Anne Cleasby, R.O. Gould, Nicola Moulden and M.D. Walkinshaw, Department of Chemistry, University of Edinburgh, Edinburgh EH9 3JJ, Scotland.

Investigation of crystals of strychnine hydrochloride and hydriodide shows a clear relationship between their unit cells and those of the previously determined structures of the hydrobromide (Beever and Robertson, Acta Cryst. (1951) 4, 270) and the sulphate (Bokhoven, Schoone and Bijvoet, Acta Cryst. (1951) 4, 275). Unit cell data for these compounds, arranged to show the similarities, are as follows:

| Acid                 | HI               | HCl                              | HBr               | $\frac{1}{2}H_2SO_4$             |
|----------------------|------------------|----------------------------------|-------------------|----------------------------------|
| Hydration            | H <sub>2</sub> O | 1 $\frac{1}{2}$ H <sub>2</sub> O | 2H <sub>2</sub> O | 2 $\frac{1}{2}$ H <sub>2</sub> O |
| $a/\text{Å}$         | 7.750            | 7.833                            | 7.70              | 7.84                             |
| $b/\text{Å}$         | 16.19            | 32.22                            | 33.20             | 34.34                            |
| $c/\text{Å}$         | 7.580            | 7.558                            | 7.64              | 7.56                             |
| $\alpha/^\circ$      | 90               | 90                               | 90                | 90                               |
| $\beta/^\circ$       | 90               | 90.82                            | 90                | 90                               |
| $\gamma/^\circ$      | 92.57            | 90                               | 90                | 94.75                            |
| Space Group          | $P2_1$           | $P2_1$                           | $P2_12_12_1$      | I2                               |
| Z                    | 2                | 4                                | 4                 | 4                                |
| $UZ^{-1}/\text{Å}^3$ | 475              | 478                              | 488               | 507                              |

In all of the compounds, the structure consists essentially of double layers of sheets of strychnine cations alternating with sheets of anions and water molecules. This arrangement, shown in the diagram for the hydriodide, is always perpendicular to the long axis of the cell (b). The symmetry relating one layer to another, however, differs markedly in the four compounds. The structural parameters of the strychnine moiety in this and other compounds will be discussed.



100 projection of strychnine HI, showing hydrogen bonding.