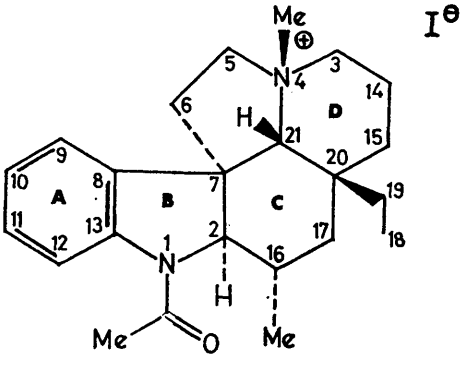
The Crystal Structure of (±)-1-Acetyl-16-methylaspidospermidine-4-methiodide

By OLGA KENNARD,*† K. ANN KERR, D. G. WATSON, and J. K. FAWCETT
(*University Chemical Laboratory, Cambridge*)
and L. RIVA DI SANSEVERINO
(*Istituto di Mineralogia et Petrografia, Universita di Bologna, Italy*)

BARTON and HARLEY-MASON[1] have reported the total synthesis of (±)-1-acetyl-16-methylaspidospermidine-4-methiodide (I) by a route involving a novel and elaborate rearrangement. Remarkably, the synthesis appeared to be entirely stereospecific. Since direct comparison with material from natural sources was not possible, the main structural evidence was derived from mass spectroscopy. *X*-Ray crystallographic analysis of the methiodide was undertaken to confirm the structure of the product and to determine its stereochemistry.‡

Crystal data: $C_{23}H_{33}ON_2^+ I^-$; $M = 480{\cdot}4$; triclinic; $a = 16{\cdot}21$, $b = 14{\cdot}53$, $c = 11{\cdot}08$ Å, $\alpha = 102{\cdot}10°$, $\beta = 108{\cdot}95°$, $\gamma = 102{\cdot}75°$, $U = 2292$ Å^3, $D_c = 1{\cdot}385$ g./cc., $Z = 4$, F(000) = 984; μ(Mo-K_α) = 15 cm.$^{-1}$. Because the compound was known to be a racemate, the centrosymmetric space group, $P\bar{1}$, was chosen. This choice implies that there are two molecules in the asymmetric unit and was confirmed by the subsequent solution and refinement of the structure.



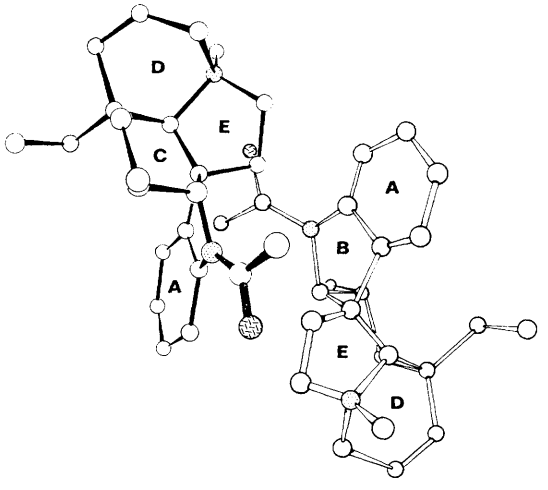


FIGURE. (±)-1-*Acetyl*-16-*methylaspidospermidine*-4-*methiodide*.

The structure was solved by the heavy-atom method using three-dimensional Patterson and Fourier syntheses. Minimal chemical assumptions were used and the molecules treated as essentially of unknown structure. Most of the atoms were located from a series of five three-dimensional electron-density maps and the remaining ones were revealed by a "difference" synthesis. Five cycles of least-squares refinement with anisotropic temperature parameters for the heavy atoms and isotropic parameters for the light atoms have reduced the *R* value to 13·6% for 3084 independent, visually estimated, non-zero reflections (*hk*0–*hk*7). The correlation factors between the layers were included as variables in the refinement.

The structure and stereochemistry of the two molecules of the asymmetric unit are shown in the Figure. Both molecules have the same relative stereochemistry, but the configuration at equivalent carbon atoms is reversed. Thus we have an

† External staff, Medical Research Council.

‡ Dr. J. Harley-Mason (private communication) comments that this stereochemistry is the same as that of aspidospermine (J. F. D. Mills and S. C. Nyburg, *J. Chem. Soc.*, 1960, 1458) and that very recently a similar rearrangement has led to the stereospecific synthesis of aspidospermidine (J. Harley-Mason and M. Kaplan, *Chem. Comm.*, 1967, 915), identified in this case by comparison with natural material. Thus it seems that rearrangements of this type in strongly acid media lead solely to the product having the "natural" stereochemistry which corresponds to the arrangement having maximum thermodynamic stability.

enantiomorphic pair of molecules related by a centre of symmetry to another pair to give a total of four molecules per unit cell.

The conformation of the molecule is particularly interesting because all of the ring junctions other than the CE ring junction are *cis*. This allows ring C to maintain a slightly twisted chair conformation but forces ring D into a boat conformation. A detailed conformational analysis will be possible when the refinement of the structure is complete.

We thank Dr. J. Harley-Mason for his collaboration at various stages in this work, Dr. J. Baldwin of the Atlas Computer Laboratory, Chilton, for help with computing, Imperial College, London, for time on the 7090 computer and the Office for Scientific and Technical Information for some of the financial support.

(*Received, October 25th*, 1967; *Com.* 1147.)

[1] J. E. D. Barton and J. Harley-Mason, *Chem. Comm.*, 1965, 298.