Synthesis and *X*-Ray Structure of the 8,13-Diaza-steroid System

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OUR previous Communication[1] reported the first total synthesis *via* (Ia) and (Ib) of the 8,13-diaza-steroid system in the form of $\Delta^{8(14)}$-immonium salts [(IIa) and (IIb)]. Subsequent work has resulted in the conversion of these immonium salts to the 8,13-diaza-18-noroestrone methyl ethers [(IVa) and (IVb)] by reductive procedures using sodium borohydride or PtO_2.

By a one-step reductive cyclization of (Ia), indicated earlier as our objective,[2] Taylor and Lenard recently prepared (IVa) by means of PtO_2-reduction in ethanol.[3] The (IVa) obtained by this method proved to be identical with that prepared from the immonium salt (IIa).[†] We have found that sodium borohydride will also reductively cyclize (Ia) to (IVa).

With PtO_2 catalyst in ethanol, the unsubstituted compound (IVd) was prepared as the HCl salt (m.p. 269—273°, decomp.), as was the 3-benzyl ether (IVc) (m.p. 174—176°). 8,13-Diaza-18-noroestrone (IVe), the analogue of oestrone itself, was readily obtained from the benzyl ethers [(Ic) or (IVc)] with Pd–C in ethanol (m.p. 230—232°, decomp.). Reduction of the lactams [(IVa) and (IVb)] was readily accomplished with an excess of lithium aluminium hydride to give the cyclic *gem*-diamines (IIIa) and (IIIb) (m.p. 123—124° and 77—79°, respectively).

The structures of (IV) have been uncertain, particularly the configuration at positions 9 and 14. Hence an *X*-ray crystal structure determination of (IVa) was undertaken. The compound crystallizes in space group $P2_1/n$ with cell parameters $a = 7\cdot531$, $b = 29\cdot917$, $c = 7\cdot637$ Å, $\beta = 116\cdot9^\circ$, and $Z = 4$. A total of 2154 measurable reflections were recorded on a Supper–Dates diffractometer. The structure has been refined to $R = 0\cdot068$. The result, shown as an ORTEP drawing[4] in the Figure, agrees with structure (IVa). The hydrogens at positions 9 and 14 are both α. The overall molecular structure is similar to that of 4-bromooestrone[5] except for the following differences: the

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[†] Taylor and Lenard (ref. 2) report m.p. 166—167° for the dimethyl ether (IVa). We found a higher m.p., 171—172°.

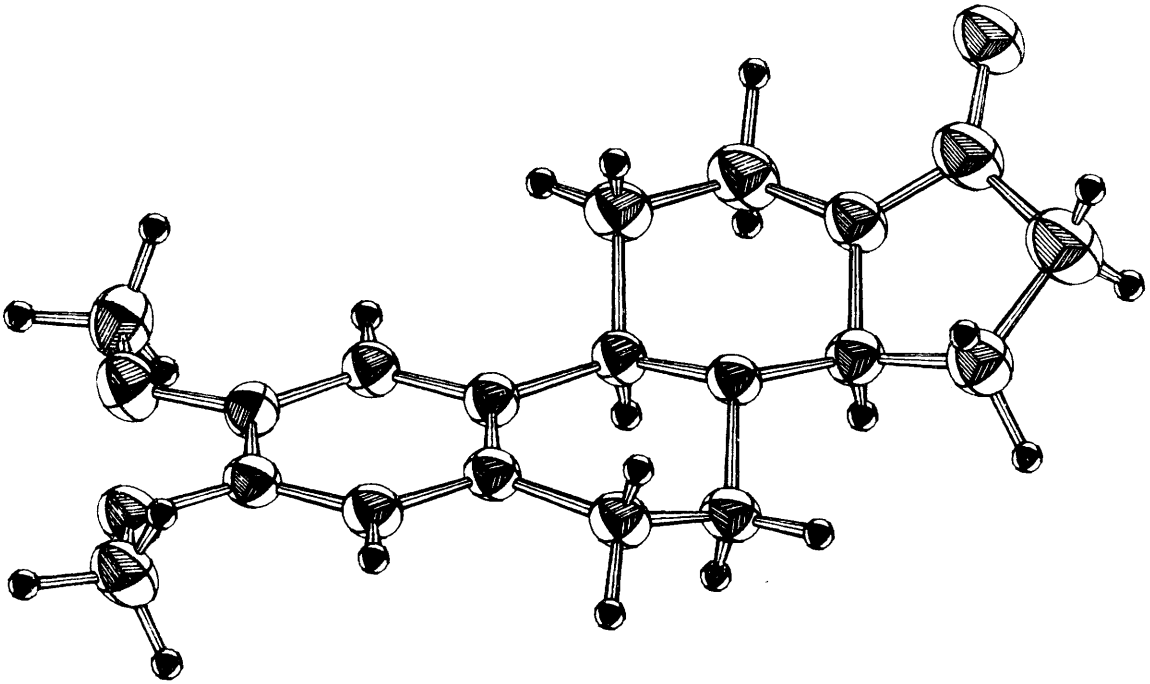

FIGURE. *ORTEP drawing of the molecule viewed at an angle of* 60° *from the normal to ring-*A. *The ellipsoids express the thermal motion of the non-hydrogen atoms.*

amide character of atoms C-14, N-13, C-17, C-16, and the oxygen at C-17 is demonstrated by the fact that they are nearly coplanar and their bond angles and bond distances agree with those found in amide groups. The D-ring has a β-envelope configuration with C-15 0·34 Å above the plane defined by the other D-ring atoms as compared with the α envelope configuration with C-14 below the D-ring plane found in 4-bromo-oestrone. The C-ring is a slightly distorted chair form with C-9 0·71 Å below and N-13 0·53 Å above a least-square plane through C-14, N-8, C-12, C-11. The B-ring, which approaches the half-chair configuration, differs from 4-bromo-oestrone, which is in an envelope configuration.

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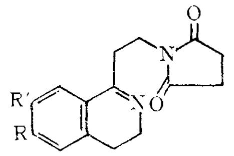
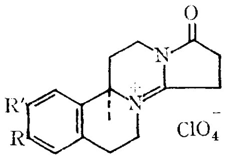
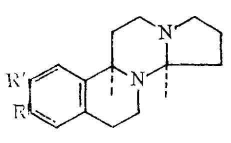


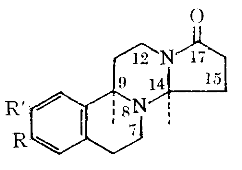
(Ia) R=R'=OMe
(Ib) R=OMe,R'=H
(Ic) R=OCH$_2$Ph,R'=H
(Id) R=R'=H



(IIa) R=R'=OMe
(IIb) R=OMe,R'=H



(IIIa) R=R'=OMe
(IIIb) R=OMe,R'=H



(IVa) R=R'=OMe
(IVb) R=OMe,R'=H
(IVc) R=OCH$_2$Ph,R'=H
(IVd) R=R'=H
(IVe) R=OH,R'=H

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[1] J. H. Burckhalter and H. N. Abramson, *Chem. Comm.*, 1966, 805.

[2] H. N. Abramson, Ph.D. Thesis, The University of Michigan, Ann Arbor, Michigan, U.S., 1966; H. N. Abramson and J. H. Burckhalter, Abstracts of Papers presented at the 152nd Meeting, American Chemical Society, New York, Sept. 12—15, 1966, p. 43.

[3] E. C. Taylor and K. Lenard, *Chem. Comm.*, 1967, 97.

[4] C. K. Johnson, "ORTEP: A Fortran Thermal-Ellipsoid Plot Program for Crystal Structure Illustrations", Oak Ridge National Laboratory, Report ORNL-3794.

[5] D. A. Norton, G. Kartha, and C. T. Lu, *Acta Cryst.*, 1963, **16**, 89.