Conformations of D-Nor-steroids by *X*-Ray Analysis

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Summary *X*-Ray analysis of the *p*-bromobenzenesulphonate esters of 16β-hydroxy-3-methoxy-D-noroestra-1,3,5(10)-triene and 16α-hydroxy-3-methoxy-D-noroestra-1,3,5(10)-triene has established molecular geometries of these model compounds containing conformationally rigid cyclobutane rings.

THE synthesis of D-nor-steroids has been stimulated by interest in their biological activity and by their use as models for studies of carbonium ion rearrangements[1] since this class of compounds possesses cyclobutane rings which are held in a fixed conformation by their *trans*-fusion to adjacent ring C. In order to establish the detailed conformations of these systems we have elucidated the crystal structures of epimeric 16β-hydroxy-3-methoxy-D-noroestra-1,3,5(10)-triene *p*-bromobenzenesulphonate (I) and 16α-hydroxy-3-methoxy-D-noroestra-1,3,5(10)-triene *p*-bromobenzenesulphonate (II).

U.v. irradiation of 16-diazo-oestrone methyl ether in ether–dioxan–water produced a mixture of epimeric 16-carboxylic acids. The derived mixture of methyl ethers, after column chromatography, gave the 16β-carboxylic methyl ester (III), m.p. 105—106° (major product) and the 16α-ester (IV), m.p. 89—90°. Ester (III) yielded *p*-bromobenzenesulphonate (I), m.p. 151—153°, by way of the 16β-hydroxymethyl derivative (V), m.p. 139—140°. Ester (IV) furnished *p*-bromobenzenesulphonate (II), m.p. 122—124°, *via* the 16α-hydroxymethyl derivative (VI), m.p. 79—80°.

Compound (I) crystallizes from ethyl acetate in the orthorhombic system, space group $P2_12_12_1$, with a = 13·49, b = 29·71, c = 5·69 Å, and Z = 4. Three-dimensional *X*-ray data were recorded by equi-inclination Weissenberg photography. The structure was solved by the heavy-atom method, and the atomic parameters were refined by full-matrix least-squares calculations to R = 0·104 over 1791 independent reflexions. Crystals of (II) from ether–hexane are orthorhombic, space group $P2_12_12_1$, with a = 7·44, b = 39·78, c = 7·90 Å, and Z = 4. Intensity data were obtained photographically, and the structure was solved by a combination of the heavy-atom method and tangent-formula refinement,[2] the latter being employed to remove pseudo-symmetry arising from an accidental special relationship between the bromine and sulphur positions. Atomic positional and thermal parameters were refined by full-matrix least-squares calculations to the present R of 0·120 over 2077 observed reflexions.

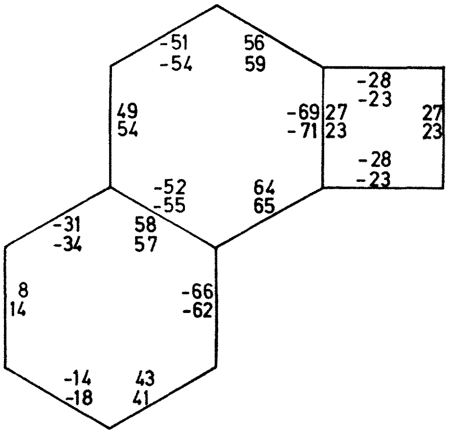


FIGURE 1 *Torsion angles for the* B, C, *and* D *rings of* (I), *upper, and* (II), *lower*.

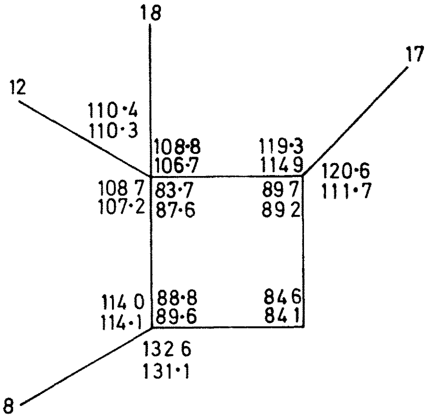
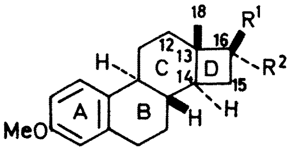


FIGURE 2 *Valency angles* (*e.s.d.* 1·1°) *at the cyclobutane ring carbon atoms for* (I) *upper, and* (II), *lower*. *Angles not shown above are* C(12)C(13)C(16) = 128·3° *and* C(14)C(13)C(18) = 114·2° *in* (I) *the corresponding values in* (III) *are* 128·7 *and* 114·6°.

Torsion angles[3] for the B, C, and D rings of (I) and (II) are recorded in Figure 1, and the valency angles at the cyclobutane ring carbon atoms are in Figure 2. The average valency angles in the cyclobutane rings of (I) and (II) are 87 and 88°, respectively, and the rings are puckered appreciably with a slightly larger (14)(15)(16)–(13)(15)(16) di-



(I) R^1 = p-$BrC_6H_4SO_3CH_2$, R^2 = H
(II) R^1 = H, R^2 = p-$BrC_6H_4SO_3CH_2$
(III) R^1 = CO_2Me, R^2 = H
(IV) R^1 = H, R^2 = CO_2Me
(V) R^1 = CH_2OH, R^2 = H
(VI) R^1 = H, R^2 = CH_2OH

hedral angle of 40° in (I) compared with that of 33° in (II). Significantly larger exocyclic angles occur around C(16) in (I), the increased values resulting from a minimisation of the nonbonded interactions between the C(17) methylene group and the C(18) methyl group to give a C(17) $\cdots$ C(18) separation of 2·97 Å. The exocyclic (17)–(16)–(13)–(18) torsion angles are -39 and $-155°$ in (I) and (II), respectively.

The C(16) configurations found in these *X*-ray studies are in accord with previous assignments in D-nor-steroids based on mechanistic considerations (in the oestrone series[4]) and on circular dichroism measurements (in the androst-5-ene series[5]).

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