Acta Cryst. (1978). B**34**, 3475–3477

3-Methoxy-2-aza-1,3,5(10)-estratrien-17*β*-yl Acetate

By Douglas C. Rohrer and William L. Duax

Medical Foundation of Buffalo, Inc., 73 *High Street, Buffalo, New York* 14203, *USA*

(*Received* 10 *February* 1978; *accepted* 18 *July* 1978)

Abstract. $C_{20}H_{27}NO_3$, M_r = 329·45, orthorhombic, $P2_12_12_1$, a = 9·1806 (5), b = 29·817 (2), c = 6·5273 (4) Å, (λ = 1·5418 Å, room temperature), V = 1786·66 Å^3, Z = 4, ρ_x = 1·228 g cm^{-3}. The steroid *A* ring is perfectly planar with all torsion angles 0·0°. The *B* ring conformation is intermediate between a 7*α*,8*β*-half chair and an 8*β*-sofa. The *D* ring has an intermediate 13*β*,14*α*-half-chair/13*β*-envelope conformation.

Introduction. The structure of the title compound was determined to evaluate the effect that introduction of the 2-aza into the *A* ring has on the overall conformation of the steroid backbone and the exocyclic substituents.

Crystal data were measured on a crystal of dimensions 0·10 × 0·20 × 0·38 mm on an Enraf–Nonius CAD-4 diffractometer using Ni-filtered Cu $K\alpha$ radiation. The conditions $h = 2n$, $k = 2n$ and $l = 2n$ limiting the $h00$, $0k0$ and $00l$ reflections determine the space group to be $P2_12_12_1$. The lattice parameters were refined by a least-squares fit to measured 2θ values of 39 reflections in the range $40 < 2\theta < 56°$. Integrated relative intensities for 2141 independent reflections with $2\theta < 150°$ were measured using ω–2θ scans; 1569 of these intensities were determined to be observed above background ($I > 2\sigma_I$).

The intensities were reduced to structure factor amplitudes, and phase angles sufficient to locate the nonhydrogen atoms were derived using the direct methods program *MULTAN* (Germain, Main & Woolfson, 1971). The H atoms were located on a difference electron density map prepared at an intermediate stage of least-squares refinement of the structural parameters. In the final cycles of full-matrix least-squares refinement, the positional parameters for all atoms, anisotropic thermal parameters for the nonhydrogen atoms and isotropic thermal parameters for the H atoms were determined. The quantities $1/\sigma_F^2$, where σ_F was defined by Stout & Jensen (1968, p. 457, equation *H*14) but with an instability factor of 0·06, were used to weight the least-squares differences for the observed data; the unobserved data were given zero weight. The final values of the residual, $R = \sum||F_o| - |F_c||/\sum|F_o|$, were 0·042 for the observed data and 0·069 for all data measured, the weighted residual was

Table 1. *Atomic coordinates of* 3-*methoxy*-2-*aza*-1,3,5(10)-*estratrien*-17*β*-*yl acetate*

	x	y	z
C(1)	0·0739 (4)	0·28084 (9)	0·9576 (5)
N(2)	0·0616 (3)	0·32538 (8)	0·9217 (4)
C(3)	0·1216 (4)	0·33957 (9)	0·7502 (5)
C(4)	0·1935 (3)	0·31212 (10)	0·6129 (6)
C(5)	0·2058 (3)	0·26716 (9)	0·6531 (5)
C(6)	0·2834 (4)	0·23621 (11)	0·5023 (5)
C(7)	0·3107 (3)	0·18948 (10)	0·5816 (5)
C(8)	0·1794 (3)	0·17152 (9)	0·6995 (4)
C(9)	0·1529 (3)	0·20111 (9)	0·8906 (4)
C(10)	0·1432 (3)	0·25008 (10)	0·8340 (4)
C(11)	0·0220 (3)	0·18368 (10)	1·0163 (5)
C(12)	0·0337 (3)	0·13404 (10)	1·0695 (4)
C(13)	0·0607 (3)	0·10492 (8)	0·8795 (4)
C(14)	0·1970 (3)	0·12318 (9)	0·7696 (4)
C(15)	0·2369 (4)	0·08665 (10)	0·6171 (5)
C(16)	0·1959 (4)	0·04263 (11)	0·7245 (5)
C(17)	0·1114 (3)	0·05664 (9)	0·9190 (4)
C(18)	−0·0739 (3)	0·10432 (10)	0·7389 (5)
C(19)	0·0368 (5)	0·41198 (12)	0·8420 (7)
C(20)	−0·0516 (4)	0·01569 (9)	1·1362 (5)
C(21)	−0·1616 (4)	−0·02176 (11)	1·1385 (6)
O(3)	0·1115 (3)	0·38409 (7)	0·7022 (4)
O(17*β*)	−0·0042 (2)	0·02411 (6)	0·9471 (3)
O(20)	−0·0111 (3)	0·03532 (9)	1·2852 (3)
H(1)	0·031 (3)	0·2729 (9)	1·083 (5)
H(4)	0·228 (4)	0·3278 (10)	0·490 (5)
H(6*B*)	0·372 (4)	0·2522 (12)	0·462 (6)
H(6*A*)	0·211 (4)	0·2318 (10)	0·380 (6)
H(7*A*)	0·397 (4)	0·1900 (9)	0·679 (5)
H(7*B*)	0·335 (3)	0·1662 (8)	0·461 (4)
H(8*B*)	0·090 (3)	0·1711 (8)	0·608 (5)
H(9*A*)	0·237 (3)	0·1993 (8)	0·980 (4)
H(11*B*)	−0·057 (4)	0·1901 (10)	0·941 (5)
H(11*A*)	0·009 (4)	0·2032 (10)	1·154 (6)
H(12*B*)	−0·055 (4)	0·1255 (11)	1·134 (6)
H(12*A*)	0·114 (4)	0·1312 (11)	1·169 (5)
H(14*A*)	0·273 (4)	0·1210 (10)	0·865 (5)
H(15*A*)	0·353 (4)	0·0895 (10)	0·578 (6)
H(15*B*)	0·177 (3)	0·0911 (9)	0·483 (4)
H(16*A*)	0·273 (4)	0·0277 (10)	0·763 (5)
H(16*B*)	0·129 (4)	0·0241 (9)	0·632 (5)
H(17*A*)	0·176 (4)	0·0542 (9)	1·040 (5)
H(18*A*)	−0·099 (4)	0·1407 (10)	0·704 (5)
H(18*B*)	−0·056 (4)	0·0878 (12)	0·600 (7)
H(18*C*)	−0·151 (4)	0·0948 (10)	0·823 (5)
H(19*A*)	0·087 (5)	0·4081 (12)	0·984 (6)
H(19*B*)	0·038 (4)	0·4421 (11)	0·799 (6)
H(19*C*)	−0·063 (4)	0·4035 (10)	0·853 (6)
H(21*A*)	−0·129 (5)	−0·0467 (12)	1·087 (7)
H(21*B*)	−0·181 (4)	−0·0304 (12)	1·266 (5)
H(21*C*)	−0·247 (6)	−0·0150 (12)	1·050 (6)

0·061. Final positional parameters are listed in Table 1.*

Discussion. The observed structure of the molecule is shown in Fig. 1. The intramolecular dimensions involving the nonhydrogen atoms are given in Fig. 2. The 27 C—H bond distances range from 0·87 to 1·13 Å. All of the bond lengths and angles in this structure are within the range of values observed for other structures of this type (Duax & Norton, 1975). The two nonbonded contacts less than 3·5 Å both involve O(20) with C(15) and C(16) of a molecule translated one unit cell in the z direction and are 3·495 and 3·447 Å respectively.

The planarity of the A ring is enhanced by the N substituent in contrast to most estra-1,3,5(10)-triene structures in which the A ring torsion angle generally ranges between ±2°. The largest displacement from the least-squares plane calculated for the six atoms is 0·003 Å. The B ring is intermediate between a 7α,8β-half chair and an 8β-sofa conformation as indicated by the ΔC_2(C5—C10) and ΔC_s(C5) asymmetry parameters (Duax, Weeks & Rohrer, 1976); see Fig. 2. The C ring has a chair conformation and the D ring has a conformation intermediate between a 13β,14α-half chair and a 13β-envelope.

The 3-methoxy substituent is synperiplanar to N(2) forming a torsion angle, N(2)—C(3)—O(3)—C(19), of 0·0°. In three other similar structures, 3-methoxy-8β-methyl-1,3,5(10)-estratrien-17β-yl bromoacetate (Tsukuda, Itazaki, Nagata, Sato, Shiro & Koyama, 1969), 3-methoxyestrone (Rohrer, Blessing, Strong, Duax & Segaloff, 1978) and 3-methoxy-14-dehydroestrone (Rohrer, Blessing, Duax & Segaloff, 1978), the 3-methoxy group has an antiperiplanar conformation to C(2) with C(2)—C(3)—O(3)—C(19) torsion angles of −166·2, −176·5 and 177·6° respectively. From these data it seems that the 2-aza may shift the conformational preference from *anti* to *syn* relative to the 2 position.

The 17β-acetate substituent is planar with torsion angles along O(17β)—C(20) of −174·8° for C(17) with C(21) and 4·8° for C(17) with O(20). The conformation of the acetate relative to the D ring directs it away from the steroid backbone minimizing the steric interactions; see Fig. 1. The C(17)—O(17β) torsion angles are −92·0° for C(13) with C(20) and 151·1° for C(16) with C(20).

This work was supported in part by Grant No. CA-10906 from the National Cancer Institute, DHEW.

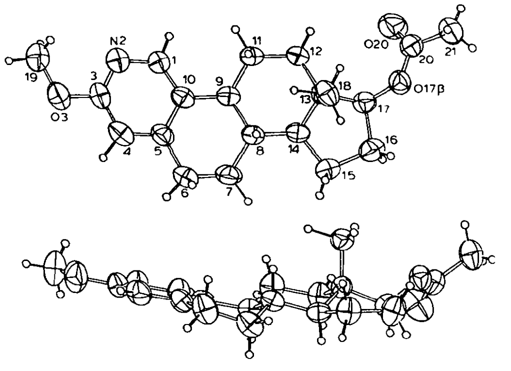

Fig. 1. *ORTEP* (Johnson, 1965) drawings of 3-methoxy-2-aza-1,3,5(10)-estratrien-17β-yl acetate. Thermal ellipsoids for nonhydrogen atoms are scaled to 60% probability and hydrogen atoms are represented as spheres equivalent to $B = 1$ Å².

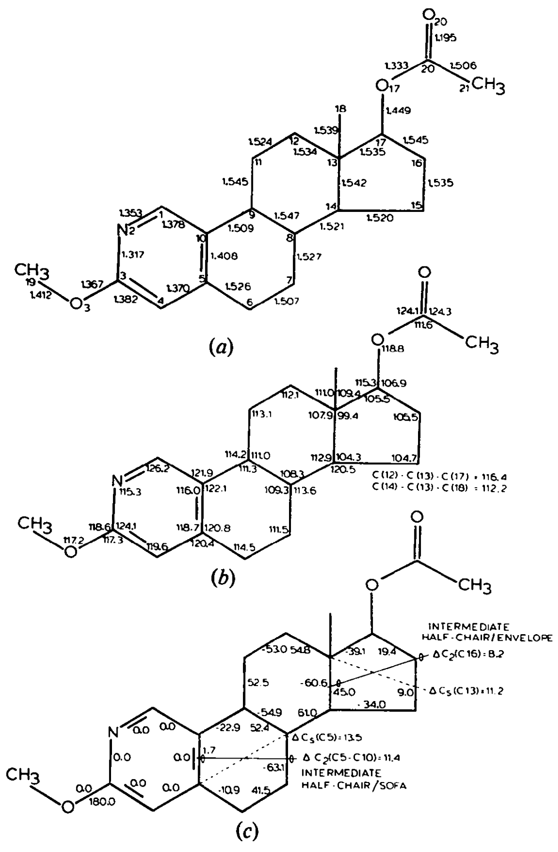

Fig. 2. Intramolecular dimensions of 3-methoxy-2-aza-1,3,5(10)-estratrien-17β-yl acetate. (a) Bond distances (Å); σ range = 0·003–0·005 Å. (b) Bond angles (°); σ range = 0·2°. (c) Endocyclic torsion angles; a torsion angle α–β–γ–δ is positive if, when viewed down the β—γ bond, the α—β bond will eclipse the γ—δ bond when rotated less than 180° in a clockwise direction.

---

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33790 (12 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

DUAX, W. L. & NORTON, D. A. (1975). *Atlas of Steroid Structure*, Vol. I. New York: Plenum.

DUAX, W. L., WEEKS, C. M. & ROHRER, D. C. (1976). *Topics in Stereochemistry*, Vol. 9, edited by E. L. ELIEL & N. ALLINGER, pp. 271–383. New York: John Wiley.

GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1971). *Acta Cryst.* A**27**, 368–376.

JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee.

ROHRER, D. C., BLESSING, R. H., DUAX, W. L. & SEGALOFF, A. (1978). *Acta Cryst.* Submitted.

ROHRER, D. C., BLESSING, R. H., STRONG, P., DUAX, W. L. & SEGALOFF, A. (1978). *Acta Cryst.* Submitted.

STOUT, G. H. & JENSEN, L. H. (1968). *X-ray Structure Determination*. New York: Macmillan.

TSUKUDA, Y., ITAZAKI, H., NAGATA, W., SATO, T., SHIRO, M. & KOYAMA, H. (1969). *J. Chem. Soc. B*, pp. 336–341.

Acta Cryst. (1978). B**34**, 3477–3479

N,N'-Biphthalimide

BY M. C. APREDA,* C. FOCES-FOCES, F. H. CANO AND S. GARCÍA-BLANCO

Departamento de Rayos X, Instituto de Química-Física 'Rocasolano', Serrano 119, *Madrid*-6, *Spain*

(*Received* 10 *May* 1978; *accepted* 18 *July* 1978)

Abstract. $C_{16}H_8N_2O_4$, monoclinic, space group $P2_1/c$, $a = 8{\cdot}473\ (1)$, $b = 13{\cdot}404\ (1)$, $c = 11{\cdot}604\ (1)$ Å, $\beta = 92{\cdot}79\ (1)°$, $Z = 4$, $D_x = 1{\cdot}47$ g cm^{-3}. $R = 5{\cdot}1\%$ for 1390 observed reflexions. The pseudo symmetry of the molecule is 222; the two halves of the dimer are twisted through 78°.

Introduction. The title compound was obtained during attempts to recrystallize an intermediate in the synthesis of tetracycline analogues. It was decided to undertake the determination of the structure by X-ray diffraction methods.

The intensities were collected from a crystal of dimensions 0·29 × 0·20 × 0·20 mm on a Philips PW 1100 four-circle diffractometer with graphite-monochromated Mo $K\alpha$ radiation and an $\omega/2\theta$ scan. 2310 reflexions were recorded up to $\theta = 25°$. 1390 obeyed the condition $I > 2\sigma(I)$ and were considered observed. The intensities were corrected for Lorentz and polarization factors. Absorption corrections were not applied ($\mu = 1{\cdot}17$ cm^{-1}). The structure was solved with *MULTAN* 77 (Main, Lessinger, Woolfson, Germain & Declercq, 1977) and refined in the usual way (Foces-Foces, Cano & Garcia-Blanco, 1978). The final R was 5·1%. Weights were applied by adjusting curves as functions of sin θ/λ and F_o. R_w was 5·7%. The final difference synthesis showed no electron density >0·26 e Å^{-3}.

Table 1. *Final positional parameters with their e.s.d.'s*

	x	y	z		x	y	z
N(1)	0·2916 (4)	0·2173 (2)	0·3979 (3)	N(1′)	0·2556 (4)	0·3162 (2)	0·4116 (3)
C(2)	0·4414 (4)	0·1838 (3)	0·3662 (3)	C(2′)	0·1725 (4)	0·3726 (3)	0·3272 (3)
C(3)	0·4261 (4)	0·0742 (3)	0·3633 (3)	C(3′)	0·1653 (4)	0·4734 (3)	0·3785 (3)
C(4)	0·5389 (5)	0·0028 (3)	0·3430 (3)	C(4′)	0·0952 (5)	0·5590 (3)	0·3339 (4)
C(5)	0·4933 (5)	−0·0955 (3)	0·3481 (3)	C(5′)	0·1013 (5)	0·6434 (3)	0·4033 (4)
C(6)	0·3398 (5)	−0·1222 (3)	0·3717 (3)	C(6′)	0·1794 (5)	0·6430 (3)	0·5099 (4)
C(7)	0·2274 (5)	−0·0504 (3)	0·3922 (3)	C(7′)	0·2543 (5)	0·5579 (3)	0·5528 (4)
C(8)	0·2735 (4)	0·0479 (2)	0·3891 (3)	C(8′)	0·2432 (4)	0·4727 (3)	0·4865 (3)
C(9)	0·1827 (4)	0·1392 (3)	0·4121 (3)	C(9′)	0·3017 (5)	0·3706 (3)	0·5120 (3)
O(10)	0·0483 (3)	0·1507 (2)	0·4363 (3)	O(10′)	0·3716 (4)	0·3365 (2)	0·5940 (3)
O(11)	0·5503 (3)	0·2374 (2)	0·3493 (2)	O(11′)	0·1244 (4)	0·3417 (2)	0·2356 (3)
H(4)	0·647 (5)	0·024 (3)	0·332 (3)	H(4′)	0·036 (5)	0·554 (3)	0·253 (4)
H(5)	0·567 (5)	−0·143 (3)	0·332 (3)	H(5′)	0·063 (5)	0·713 (5)	0·366 (4)
H(6)	0·303 (5)	−0·193 (4)	0·371 (4)	H(6′)	0·193 (4)	0·708 (4)	0·555 (3)
H(7)	0·121 (6)	−0·067 (3)	0·406 (4)	H(7′)	0·311 (6)	0·553 (4)	0·633 (5)

---

* On leave from Dept. de Fisica, Facultad de Ciencias Exactas, UNLP, calle 115, esq. 49, La Plata, Buenos Aires, Argentina.