and 2. The well individualized thiocation is pyramidal, suggesting an sp^3 hybridation state for the S atom; it possesses only one symmetry plane (for $y = 0{\cdot}25$ or $0{\cdot}75$), in which the S, O and C(1) atoms are located; but it approximates very much to the $3m$ symmetry assigned to the free ion. The bond distances S—C(1) and S—C(2) are equal and the bond angles C(1)—S—C(2) and C(2)—S—C(2) are slightly different.

This work was carried out at the 'Centre de Diffractométrie de l'Université de Bourgogne'.

References

COULDER, L. C., GANTZEL, P. K. & MCCULLOUGH, J. D. (1963). *Acta Cryst.* **16**, 676–681.

Enraf–Nonius (1977). *Structure Determination Package.* Enraf–Nonius, Delft, The Netherlands.

MAIN, P., LESSINGER, L., WOOLFSON, M. M., GERMAIN, G. & DECLERCQ, J.-P. (1977). *MULTAN77. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data.* Univs. of York, England, and Louvain, Belgium.

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

ZIMMERMANN, I. C., BARLOW, M. & MCCULLOUGH, J. D. (1963). *Acta Cryst.* **16**, 883–887.

Acta Cryst. (1991). C**47**, 1689–1693

Non-Natural 14-Hydroxy Steroids. II. 13α,14α and 13β,14β Isomers of Methyl 14-Hydroxy-1,7,17-trioxo-5β-androst-8-ene-19-oate

BY MARC DROUIN

Laboratoire de chimie structurale, Université de Sherbrooke, Sherbrooke, Québec, Canada J1K 2R1

RÉJEAN RUEL

Laboratoire de synthèse organique, Université de Sherbrooke, Sherbrooke, Québec, Canada J1K 2R1

AND ANDRÉ G. MICHEL*

Laboratoire de chimie structurale, Université de Sherbrooke, Sherbrooke, Québec, Canada J1K 2R1

(*Received* 25 *June* 1990; *accepted* 17 *December* 1990)

Abstract. $C_{20}H_{24}O_6$, $M_r = 360{\cdot}41$, λ(Cu $K\alpha$) = 1·54056 Å, room temperature. (I) (5β,10β,13α,14α)-Methyl 14-hydroxy-1,7,17-trioxoandrost-8-ene-19-oate, triclinic, $P\bar{1}$, $a = 7{\cdot}9514$ (5), $b = 9{\cdot}2892$ (5), $c = 12{\cdot}8534$ (12) Å, $\alpha = 81{\cdot}256$ (6), $\beta = 75{\cdot}796$ (6), $\gamma = 77{\cdot}908$ (5)°, $V = 894{\cdot}85$ (11) Å^3, $Z = 2$, $D_x = 1{\cdot}338$ Mg m^{-3}, $\mu = 0{\cdot}77$ mm^{-1}, $F(000) = 383{\cdot}96$, final $R = 0{\cdot}043$ for 2912 observed reflections. (II) (5β,10β,13β,14β)-Methyl 14-hydroxy-1,7,17-trioxoandrost-8-ene-19-oate, monoclinic, $P2_1/n$, $a = 12{\cdot}8704$ (9), $b = 10{\cdot}4481$ (9), $c = 13{\cdot}1482$ (5) Å, $\beta = 104{\cdot}103$ (5)°, $V = 1714{\cdot}77$ (20) Å^3, $Z = 4$, $D_x = 1{\cdot}396$ Mg m^{-3}, $\mu = 0{\cdot}81$ mm^{-1}, $F(000) = 767{\cdot}92$, final $R = 0{\cdot}055$ for 2516 observed reflections. These two non-natural steroids bear a methoxycarbonyl group at C(10). In both molecules the relative stereochemistry is *cis* for the *A*/*B* ring junction and *cis* for the *C*/*D* ring junction. The relative orientations of MeO_2C—C(10) and HO—C(14) are *anti* for (I) and *syn* for (II). The methoxycarbonyl group lies at the axial position for (I) and equatorial for (II), relative to ring *A*. The energies of possible conformations for (I) and (II) are evaluated, wherein the *A* rings adopt a chair conformation.

Introduction. Cardioactive steroids used in the treatment of heart disease have the ability to slow the heart rate and, at the same time, increase the contractility of the muscle. However, the natural steroids used exhibit a dangerously high toxicity, while most patients receive 60% of the toxic dose in order to obtain the desired therapeutic response (Weisner & Tsai, 1986). The synthesis of new cardioactive steroids having a wider margin of safety has thus become a major goal shared by many research groups. Furthermore, the synthesis of such non-natural 14-hydroxy steroids, and subsequent analyses of their activity will hopefully allow a better understanding of the structure–activity relationships.

As part of a study aimed at the synthesis of various natural and non-natural 14-hydroxy steroids, (I) and (II) (Fig. 1) were obtained upon alkaline treatment (Cs_2CO_3, CH_3CN, reflux) of tetraketone (III) as a 3:2 mixture (Ruel & Deslongchamps, 1990).

* To whom correspondence should be addressed.

0108-2701/91/081689-05$03.00

The present crystallographic analyses were undertaken to confirm the structure of steroids (I) and (II). The observation of two different conformations for ring *A* [the methoxycarbonyl is axial for (I) and equatorial for (II)] prompted us to evaluate the relative conformational energies of possible conformations for both steroids.

Experimental. Enraf–Nonius CAD-4 diffractometer, graphite-monochromator, Cu $K\bar{\alpha}$ radiation, the $\omega/2\theta$ scan mode was used for the data collection at a constant speed of 2·7° min^{-1}. Two standard reflections were monitored every 60 min without significant deviation. Cell parameters were obtained by least-squares procedure on 24 reflections with 2θ in the range 60–80°. (I) Crystal: 0·30 × 0·30 × 0·20 mm; *hkl* range: −9,9; 0,10; −15,15. 3472 unique reflections were measured and 2912 were considered observed with $I_{net} > 2{\cdot}5\sigma I_{net}$; $2\theta_{max} = 143{\cdot}3°$. (II) Crystal: 0·20 × 0·20 × 0·20 mm; *hkl* range: −15,15; 0,12; 0,16. 3357 unique reflections were measured and 2516 were considered observed with $I_{net} > 3{\cdot}0\sigma I_{net}$; $2\theta_{max} = 143{\cdot}5°$. The *NRCVAX* (Gabe, Lee & Le Page, 1985) system was used for all calculations. Both structures were solved by the application of direct methods and refined by full-matrix least squares on *F*. Anisotropic thermal parameters were refined for all non-H atoms. Function minimized: $\sum w(|F_o| - |F_c|)^2$, where $w = 1/\sigma^2(F)$. All H-atom positional parameters were calculated and refined except for the hydroxy H atom which was found by a difference Fourier map in both molecules. The final residuals obtained at convergence were for (I): $R = 0{\cdot}043$, $wR = 0{\cdot}033$ and $S = 2{\cdot}589$, max. Δ/σ ratio was 0·001. In the last difference map, the deepest hole was −0·17 e Å^{-3} and the highest peak 0·23 e Å^{-3}. The secondary-extinction coefficient was 0·21 (1) (Larson, 1967; Zachariasen, 1963). For (II): $R = 0{\cdot}055$, $wR = 0{\cdot}040$, and $S = 3{\cdot}230$; max. Δ/σ ratio was 0·049. In the last difference map, the deepest hole was −0·32 e Å^{-3} and the highest peak 0·33 e Å^{-3}. The secondary-extinction coefficient was 0·31 (2). Atomic scattering factors as stored in the *NRCVAX* program are those of Cromer & Waber (*International Tables for X-ray Crystallography*, 1974, Vol. IV).

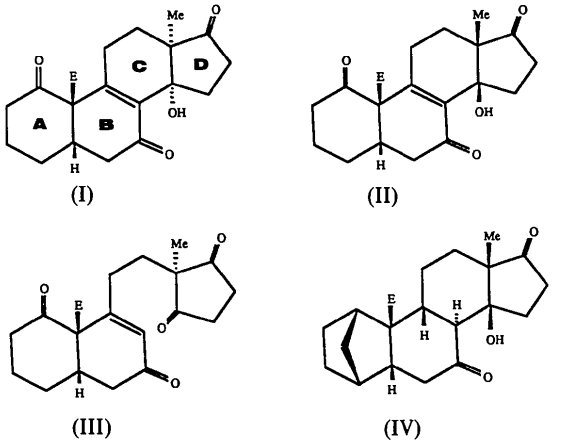
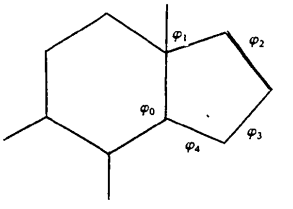


Fig. 1. Molecular formulae (E = $COOCH_3$).

Discussion. Table 1 gives the final atomic parameters with their *B* values for (I) and (II).* Fig. 1 gives the molecular formulae for both molecules. Fig. 2 shows the crystallographic atom numbering and an *ORTEP* perspective view of the two synthetic hydroxy steroids. Bond lengths and angles are given in Tables 2(*a*) and 2(*b*). The crystal structures of (I) and (II) show for both compounds that the *A* ring adopts two different chair conformations, the *C*/*D* ring junction is *cis*, and the *D* ring is in a C(14) envelope conformation. In (I) the methoxycarbonyl group (*E*) at C(10) has an axial orientation relative to ring *A* [Fig. 2(*a*)] compared to an equatorial orientation for (II) [Fig 2(*b*)]. Fig. 3 shows the observed hydrogen bonding in the crystal packing of (I) and (II). In (I), two hydrogen bonds are geometrically possible (Table 2). The first intermolecular hydrogen bond occurs between the O(2) oxygen and the hydroxy O(3^i)—H atom. The second one is an intramolecular hydrogen bond between O(2) and O(3)—H contributing to stabilization of the molecular structure. In (II) only an intramolecular hydrogen bond is observed between O(2) and O(3)—H. Ring *B* is held as a pseudo-chair to accommodate the planarity of the *B*/*C* junction. The torsional angles, φ_D, in (I) and (II) defined by C(17)—C(13)—C(14)—C(15) are relatively small for both steriods [32·6 (2) and 29·1 (2)° for (I) and (II) respectively] compared to the standard value of 46·3° (Altona, Geise & Romers, 1968). This is explained by the presence of a double bond between C(8) and C(9). The puckering constants for ring *D*, Δ (phase angle of pseudorotation) and φ_m (maximum angle of torsion)† (Altona, Geise & Romers, 1968) values are given in Table 2.



* Lists of structure factors, anisotropic thermal parameters, torsion angles and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 53842 (45 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

† $\tan(\Delta/2) = [(\varphi_2 + \varphi_4) - (\varphi_1 + \varphi_3)]/(3{\cdot}0777\varphi_0)$, $\varphi_m = \varphi_0/\cos(\Delta/2)$.

Table 1. *Final coordinates and B values for non-H atoms with e.s.d.'s in parentheses*

$B_{eq} = (8\pi^2/3)\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$

	x	y	z	B_{eq}(Å^2)
(I)				
C(1)	0·4923 (3)	0·8849 (2)	0·1736 (2)	3·38 (9)
C(2)	0·6336 (3)	0·7555 (2)	0·1365 (2)	4·40 (11)
C(3)	0·8117 (3)	0·80430 (2)	0·0840 (2)	4·98 (12)
C(4)	0·8603 (3)	0·89374 (2)	0·1572 (2)	4·19 (11)
C(5)	0·7194 (2)	1·0294 (2)	0·1877 (2)	3·00 (8)
C(6)	0·6992 (3)	1·1430 (2)	0·0911 (2)	3·45 (9)
C(7)	0·5630 (3)	1·2760 (2)	0·1211 (2)	3·14 (9)
C(8)	0·4021 (2)	1·2534 (2)	0·2047 (1)	2·74 (8)
C(9)	0·3918 (2)	1·1210 (2)	0·2634 (1)	2·67 (8)
C(10)	0·5381 (2)	0·9853 (2)	0·2437 (1)	2·60 (8)
C(11)	0·2304 (3)	1·0989 (2)	0·3513 (2)	3·48 (9)
C(12)	0·1155 (3)	1·2424 (2)	0·3870 (2)	3·70 (9)
C(13)	0·0799 (2)	1·3554 (2)	0·2902 (2)	3·14 (9)
C(14)	0·2576 (2)	1·3894 (2)	0·2211 (2)	2·98 (8)
C(15)	0·3055 (3)	1·5018 (2)	0·2814 (2)	3·90 (11)
C(16)	0·1299 (3)	1·59542 (2)	0·3300 (2)	5·07 (13)
C(17)	−0·0069 (3)	1·5011 (2)	0·3360 (2)	4·21 (11)
C(18)	−0·0334 (3)	1·3047 (3)	0·2293 (2)	4·80 (13)
C(19)	0·5572 (3)	0·8998 (2)	0·3535 (2)	2·94 (9)
C(20)	0·4535 (3)	0·7156 (2)	0·4884 (2)	4·48 (11)
O(1)	0·35182 (20)	0·9129 (2)	0·1472 (1)	4·91 (8)
O(2)	0·5821 (2)	1·4000 (2)	0·0781 (1)	4·64 (7)
O(3)	0·2176 (2)	1·4597 (2)	0·1212 (1)	4·19 (7)
O(4)	−0·1630 (2)	1·5370 (2)	0·3722 (2)	6·90 (10)
O(5)	0·6465 (2)	0·9247 (2)	0·4084 (1)	4·23 (7)
O(6)	0·4560 (2)	0·7951 (1)	0·3813 (1)	3·59 (6)
(II)				
C(1)	0·2323 (3)	0·2727 (3)	0·3629 (2)	2·91 (15)
C(2)	0·2091 (4)	0·4138 (4)	0·3585 (3)	3·89 (19)
C(3)	0·3105 (4)	0·4923 (4)	0·4027 (3)	4·19 (21)
C(4)	0·3626 (3)	0·4498 (3)	0·5135 (3)	3·46 (17)
C(5)	0·3919 (3)	0·3076 (3)	0·5180 (2)	2·67 (14)
C(6)	0·4405 (3)	0·2646 (4)	0·6300 (3)	3·36 (17)
C(7)	0·3628 (3)	0·2700 (3)	0·6966 (2)	3·02 (16)
C(8)	0·2458 (3)	0·2466 (3)	0·6464 (2)	2·22 (13)
C(9)	0·2165 (2)	0·2153 (3)	0·5431 (2)	2·18 (13)
C(10)	0·2943 (3)	0·2206 (3)	0·4721 (2)	2·25 (13)
C(11)	0·1036 (3)	0·1737 (3)	0·4934 (2)	2·67 (15)
C(12)	0·0455 (3)	0·1271 (3)	0·5738 (3)	2·92 (15)
C(13)	0·0525 (3)	0·2230 (3)	0·6620 (2)	2·47 (14)
C(14)	0·1691 (3)	0·2582 (3)	0·7174 (2)	2·48 (14)
C(15)	0·1620 (3)	0·3993 (3)	0·7507 (3)	3·25 (17)
C(16)	0·0765 (3)	0·4603 (4)	0·6621 (3)	4·07 (19)
C(17)	0·0039 (3)	0·3497 (3)	0·6168 (2)	3·21 (15)
C(18)	−0·0112 (4)	0·1775 (5)	0·7382 (3)	4·39 (22)
C(19)	0·3365 (3)	0·0872 (3)	0·4504 (2)	2·70 (14)
C(20)	0·3133 (4)	−0·1363 (4)	0·4604 (3)	4·01 (22)
O(1)	0·2073 (2)	0·2023 (2)	0·2890 (2)	4·58 (13)
O(2)	0·3925 (2)	0·2885 (2)	0·7919 (2)	4·34 (13)
O(3)	0·2034 (2)	0·1766 (2)	0·8079 (2)	3·54 (13)
O(4)	0·0818 (2)	0·3601 (2)	0·5541 (2)	4·58 (13)
O(5)	0·4082 (2)	0·0725 (2)	0·4093 (2)	4·09 (12)
O(6)	0·2815 (2)	−0·0066 (2)	0·4809 (2)	3·34 (11)

In both molecules φ_m is found to be lower than in the natural steriod skeleton. The phase angles (Δ) for (I) and (II) are relatively low which corresponds to a C(14) envelope conformation. The resulting overall conformation is viewed in Fig. 4. The α-hydroxy steroid (I) is in an extended conformation compared to the β conformation of (II) which is folded on the α face resulting in a compact structure similar to a related compound (IV) (Douglas, Sawyer & Yates, 1987). The mean planes through ring *A* and ring *D* for (I) make angles with the mean plane through the *B*/*C* rings of 60·9 (1) and 55·1 (1)° respectively. For (II) these angles are 79·1 (1) and 93·0 (1)° respectively. No abnormally short contacts were observed for (I) and (II).

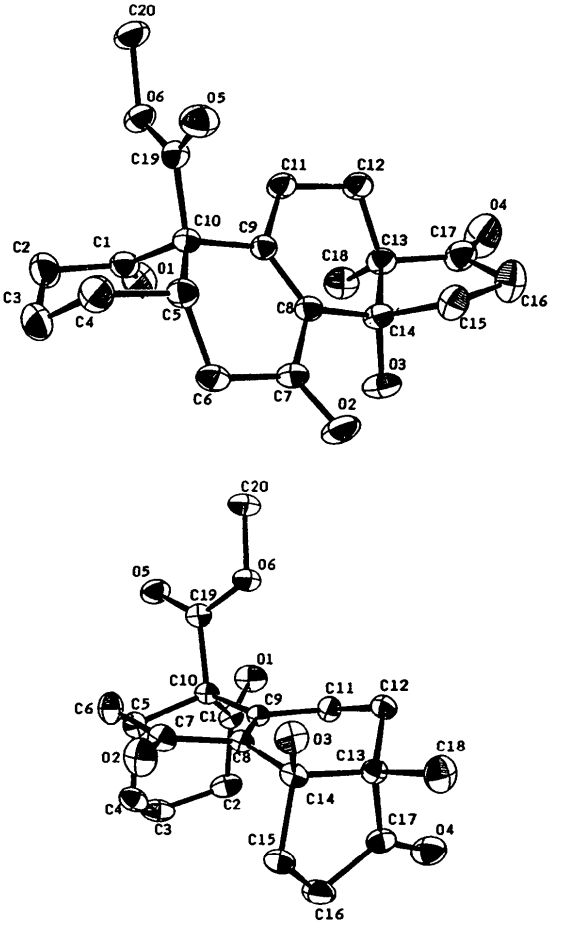


Fig. 2. *ORTEP* perspective view and atom numbering of (I) top view and (II) bottom view.

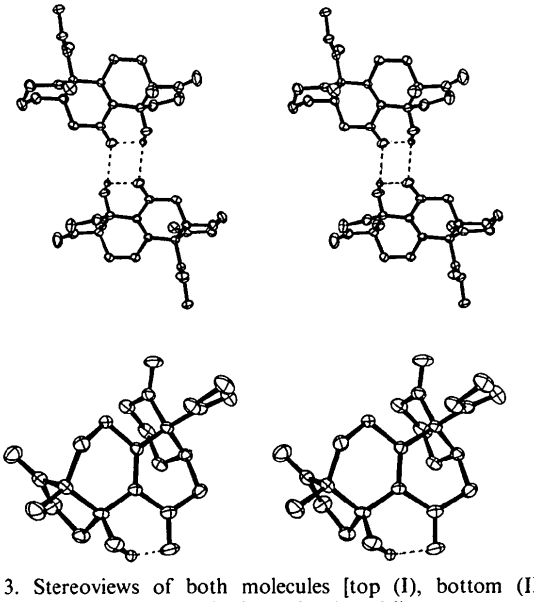


Fig. 3. Stereoviews of both molecules [top (I), bottom (II)]. Hydrogen bonds shown by dotted lines.

Table 2. *Molecular geometry*

(*a*) Bond lengths (Å) with e.s.d.'s in parentheses

	(I)	(II)		(I)	(II)
C(1)—C(2)	1·510 (3)	1·502 (5)	C(10)—C(19)	1·536 (3)	1·547 (4)
C(1)—C(10)	1·540 (3)	1·561 (4)	C(11)—C(12)	1·514 (3)	1·516 (5)
C(1)—O(1)	1·211 (3)	1·200 (4)	C(12)—C(13)	1·543 (3)	1·518 (4)
C(2)—C(3)	1·540 (3)	1·532 (6)	C(13)—C(14)	1·539 (3)	1·544 (4)
C(3)—C(4)	1·508 (3)	1·515 (5)	C(13)—C(17)	1·518 (3)	1·522 (5)
C(4)—C(5)	1·529 (3)	1·531 (5)	C(13)—C(18)	1·511 (3)	1·518 (5)
C(5)—C(6)	1·520 (3)	1·522 (5)	C(14)—C(15)	1·547 (3)	1·547 (4)
C(5)—C(10)	1·5536 (25)	1·548 (4)	C(14)—O(3)	1·4266 (22)	1·443 (3)
C(6)—C(7)	1·493 (3)	1·481 (5)	C(15)—C(16)	1·525 (3)	1·533 (5)
C(7)—C(8)	1·485 (3)	1·510 (5)	C(16)—C(17)	1·515 (3)	1·514 (5)
C(7)—O(2)	1·2223 (22)	1·233 (3)	C(17)—O(4)	1·207 (3)	1·209 (4)
C(8)—C(9)	1·348 (3)	1·358 (4)	C(19)—O(5)	1·1919 (24)	1·189 (4)
C(8)—C(14)	1·521 (3)	1·519 (4)	C(19)—O(6)	1·3427 (23)	1·326 (4)
C(9)—C(10)	1·531 (3)	1·524 (4)	C(20)—O(6)	1·4570 (24)	1·460 (4)
C(9)—C(11)	1·515 (3)	1·508 (4)			

(*b*) Valence angles (°) with e.s.d.'s in parentheses

	(I)	(II)		(I)	(II)
C(2)—C(1)—C(10)	116·5 (2)	115·5 (3)	C(9)—C(10)—C(19)	108·3 (1)	113·1 (2)
C(2)—C(1)—O(1)	122·5 (2)	124·0 (3)	C(9)—C(11)—C(12)	113·5 (2)	112·2 (3)
C(10)—C(1)—O(1)	120·9 (2)	120·5 (3)	C(11)—C(12)—C(13)	112·0 (2)	111·9 (3)
C(1)—C(2)—C(3)	111·6 (2)	111·6 (3)	C(12)—C(13)—C(14)	108·6 (2)	112·8 (3)
C(2)—C(3)—C(4)	110·5 (2)	110·1 (3)	C(12)—C(13)—C(17)	106·4 (2)	109·5 (3)
C(3)—C(4)—C(5)	112·9 (2)	111·6 (3)	C(12)—C(13)—C(18)	111·6 (2)	110·9 (3)
C(4)—C(5)—C(6)	112·3 (2)	111·2 (3)	C(14)—C(13)—C(17)	102·8 (2)	103·7 (2)
C(4)—C(5)—C(10)	111·0 (2)	112·7 (3)	C(14)—C(13)—C(18)	114·8 (2)	112·5 (3)
C(6)—C(5)—C(10)	109·7 (2)	107·9 (3)	C(17)—C(13)—C(18)	112·1 (2)	107·1 (3)
C(5)—C(6)—C(7)	112·3 (2)	112·6 (3)	C(8)—C(14)—C(13)	114·0 (2)	113·1 (2)
C(6)—C(7)—C(8)	118·0 (2)	118·7 (3)	C(8)—C(14)—C(15)	111·9 (2)	110·0 (3)
C(6)—C(7)—O(2)	121·3 (2)	121·3 (3)	C(8)—C(14)—O(3)	111·6 (2)	110·2 (2)
C(8)—C(7)—O(2)	120·7 (2)	119·9 (3)	C(13)—C(14)—C(15)	104·5 (2)	104·1 (3)
C(7)—C(8)—C(9)	120·7 (2)	118·5 (3)	C(13)—C(14)—O(3)	104·3 (1)	108·4 (3)
C(7)—C(8)—C(14)	115·5 (2)	116·5 (2)	C(15)—C(14)—O(3)	110·1 (2)	110·9 (2)
C(9)—C(8)—C(14)	123·7 (2)	124·9 (3)	C(14)—C(15)—C(16)	105·2 (2)	105·2 (3)
C(8)—C(9)—C(10)	122·5 (2)	122·8 (3)	C(15)—C(16)—C(17)	105·0 (2)	104·0 (3)
C(8)—C(9)—C(11)	120·9 (2)	120·3 (3)	C(13)—C(17)—C(16)	110·5 (2)	110·7 (3)
C(10)—C(9)—C(11)	116·6 (2)	116·9 (2)	C(13)—C(17)—O(4)	124·9 (2)	124·4 (3)
C(1)—C(10)—C(5)	109·0 (1)	109·7 (2)	C(16)—C(17)—O(4)	124·6 (2)	124·9 (3)
C(1)—C(10)—C(9)	110·5 (2)	108·1 (3)	C(10)—C(19)—O(5)	124·9 (2)	123·1 (3)
C(1)—C(10)—C(19)	109·9 (2)	105·6 (2)	C(10)—C(19)—O(6)	111·0 (2)	111·9 (3)
C(5)—C(10)—C(9)	111·9 (1)	111·9 (2)	O(5)—C(19)—O(6)	124·1 (2)	124·9 (3)
C(5)—C(10)—C(19)	107·1 (2)	108·2 (3)	C(19)—O(6)—C(20)	115·3 (2)	115·9 (3)

(*c*) Hydrogen-bond distances (Å) and angles (°) between donor (O—H) and acceptor (C=O) atoms with e.s.d.'s in parentheses

Hydrogen bond	O···O	O—H	O···H	O—H < O
(I) O(2)—O(3)	2·764 (2)	0·877 (20)	2·216 (18)	125·0 (16)
O(2)—O(3^{i})	2·941 (2)	0·877 (20)	2·201 (20)	141·8 (15)
(II) O(2)—O(3)	2·753 (4)	0·850 (40)	1·980 (40)	149·0 (30)

Equivalent position (i) $1-x, 3-y, -z$.

(*d*) Maximum torsional angle (φ_m°) and phase angle of pseudorotation (Δ°)

	Molecule (I)	Molecule (II)	Standard*
φ_m	34·4	32·4	46·7
Δ	−37·1	−53·4	

* Altona, Geise & Romers (1968).

Fig. 5 presents the four possible conformations of (I) and (II), considering the two chair orientations of ring *A*. Corresponding conformational energies were computed using the *SYBYL* Molecular Modeling System (Tripos Associates Inc., 1989). Structure (I*a*) shows the methoxycarbonyl group (*E*) equatorial relative to ring *A* and in (I*b*) *E* is axial, which corresponds to the minimized X-ray structure. (II*a*) shows the minimized X-ray structure, *E* being equatorial relative to *A* and in (II*b*) *E* is axial. Conformation (I*a*) is 1·6 kcal mol^{-1} (6·69 kJ mol^{-1}) more

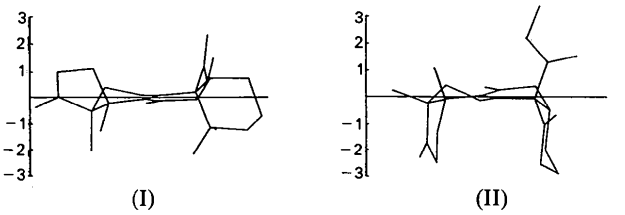


Fig. 4. Overall conformation of both steriods, viewed parallel to the least-squares mean plane through *B* and *C* rings (scale in Å).

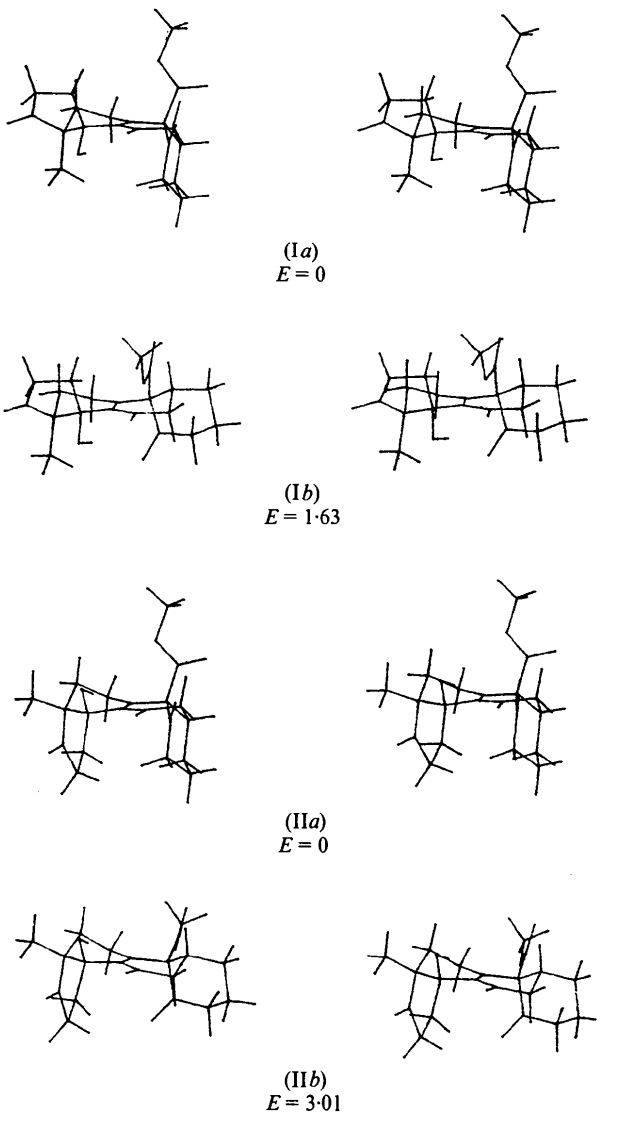


Fig. 5. Stereoviews of minimized conformations of (I) and (II) with their relative energies. (I*a*) Minimized structure of (I) where *E* is equatorial relative to ring *A*. (I*b*) Minimized X-ray structure of (I) where *E* is axial relative to ring *A*. (II*a*) Minimized X-ray structure of (II) where *E* is equatorial relative to ring *A*. (II*b*) Minimized structure of (II) where *E* is axial relative to ring *A*.

stable than (I*b*), while structure (II*a*) is 3·0 kcal mol^{-1} (12·6 kJ mol^{-1}) more stable than (II*b*). For (I), the presence of an intermolecular hydrogen bond can easily explain that (I*b*), while higher in energy, is the preferred structure in the crystalline state. For compound (II), (II*a*), which is lower in energy, corresponds to the X-ray structure. No major interactions are found in the crystal of (II).

References

ALTONA, C., GEISE, H. J. & ROMERS, C. (1968). *Tetrahedron*, **24**, 13–32.

DOUGLAS, S. P., SAWYER, J. F. & YATES, P. (1987). *Acta Cryst.* C**43**, 1372–1375.

GABE, E. J., LEE, F. L. & LEPAGE, Y. (1985). *The NRCVAX Crystal Structure System.* In *Crystallographic Computing* 3; *Data Collection, Structure Determination, Proteins and Databases*, edited by G. M. SHELDRICK, C. KRÜGER & R. GODDARD, pp. 167–174. Oxford: Clarendon Press.

LARSON, A. C. (1967). *Acta Cryst.* **23**, 664–665.

RUEL, R. & P. DESLONGCHAMPS. (1990). *Can. J. Chem.* **68**, 1917–1922.

Tripos Associates Inc. (1989). *SYBYL. Molecular Modeling Software*, Version 5.22. Tripos Associates Inc., St. Louis, Missouri, USA.

WEISNER, K. & TSAI, T. Y. R. (1986). *Pure Appl. Chem.* pp. 799–810.

ZACHARIASEN, W. H. (1963). *Acta Cryst.* **16**, 1139–1144.

Acta Cryst. (1991). C**47**, 1693–1697

Structures of the 1-(2-Deoxy-2-fluoro-β-D-arabinopyranosyl)thymine–Water Complex and 1-(2-Deoxy-2-fluoro-β-D-arabinopyranosyl)-5-ethyluracil*

BY H. L. DE WINTER, N. M. BLATON, O. M. PEETERS AND C. J. DE RANTER†

Laboratorium voor Analytische Chemie en Medicinale Fysicochemie, Instituut voor Farmaceutische Wetenschappen, Katholieke Universiteit Leuven, Van Evenstraat 4, *B*-3000 *Leuven, Belgium*

AND A. VAN AERSCHOT AND P. HERDEWIJN

Laboratorium voor Farmaceutische Chemie, Rega Institute for Medical Research, Katholieke Universiteit Leuven, B-3000 *Leuven, Belgium*

(*Received* 20 *October* 1990; *accepted* 20 *December* 1990)

Abstract. (I) 1-(2-Deoxy-2-fluoro-β-D-arabinopyranosyl)thymine–water complex, $C_{10}H_{13}FN_2O_5.H_2O$, $M_r = 278{\cdot}24$, monoclinic, $P2_1$, $a = 8{\cdot}669\ (4)$, $b = 6{\cdot}395\ (3)$, $c = 10{\cdot}713\ (7)$ Å, $\beta = 103{\cdot}73\ (5)°$, $V = 576{\cdot}9\ (6)$ Å^3, $Z = 2$, $D_m = 1{\cdot}60$, $D_x = 1{\cdot}602$ Mg m^{-3}, graphite-monochromated Mo $K\alpha$ radiation, $\lambda = 0{\cdot}71069$ Å, $\mu = 0{\cdot}134$ mm^{-1}, $F(000) = 292$, room temperature, final $R = 0{\cdot}030$ for 1307 unique observed [$F \geq 4\sigma(F)$] reflections. (II) 1-(2-Deoxy-2-fluoro-β-D-arabinopyranosyl)-5-ethyluracil, $C_{11}H_{15}FN_2O_5$, $M_r = 274{\cdot}25$, hexagonal, $P6_5$, $a = 10{\cdot}108\ (7)$, $c = 19{\cdot}48\ (1)$ Å, $V = 1724\ (2)$ Å^3, $Z = 6$, $D_m = 1{\cdot}54$, $D_x = 1{\cdot}585$ Mg m^{-3}, graphite-monochromated Mo $K\alpha$ radiation, $\lambda = 0{\cdot}71069$ Å, $\mu = 0{\cdot}127$ mm^{-1}, $F(000) = 864$, room temperature, final $R = 0{\cdot}026$ for 694 unique observed [$F \geq 4\sigma(F)$] reflections. The geometries of molecules (I) and (II) show a close similarity. In both structures the sugar ring adopts a slightly distorted chair conformation and for both molecules the fluorine and one of the hydroxyl substituents are placed in an axial position on the ring. The *N*-glycosidic torsion angle χ between the pyranose ring and the pyrimidine base is oriented $-ac$ for both molecules. The terminal C of the ethyl group in (II) deviates from the base least-squares plane. The packing in both crystals is determined by intermolecular hydrogen bonds and base-stacking forces. In (I) the solvent water is kept from being disordered by a dense network of strong hydrogen bonds. In (II) the molecules are packed in such a way that a single stranded left-handed helix is formed which resembles the structure of the 6_1 poly(2′-*O*-methylcytidine) single stranded helix. No intramolecular hydrogen bonds are present. The conformational parameters are in accordance with the IUPAC–IUB Joint Commission on Biochemical Nomenclature (1983) guidelines.

Introduction. The crystal structures of the title compounds have been determined as part of a continuing program of investigation of potentially anti-viral

* Structural Studies of Modified Nucleosides. X. Part IX: Everaert, Peeters, Blaton, De Ranter, Van Aerschot & Herdewijn (1991).

† To whom correspondence should be addressed.

0108-2701/91/081693-05$03.00