

- HANSON, H. P., HERMAN, F., LEA, J. D. & SKILLMAN, S. (1960). *Acta Cryst.* **17**, 1040–1044.
- JOHNSON, C. K. (1971). *ORTEP*. Report ORNL-3794. Second revision with supplemental instructions. Oak Ridge National Laboratory, Tennessee.
- KLYNE, W. & PRELOG, V. (1960). *Experientia*, **16**, 521–523.
- LAPP, R. L. & JACOBSON, R. A. (1979). *ALLS. A Generalized Crystallographic Least-Squares Program*. Ames Laboratory (DOE) and Iowa State Univ., Ames, Iowa.
- LAWTON, S. & JACOBSON, R. A. (1968). *Inorg. Chem.* **7**, 2124–2134.
- MAIN, P., WOOLFSON, M. M. & GERMAIN, G. (1976). *MULTAN. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.
- PAULING, L. (1960). *The Nature of the Chemical Bond*. Ithaca: Cornell Univ. Press.
- POPLE, J. A. & BEVERIDGE, D. L. (1970). *Approximate Molecular Orbital Theory*. New York: McGraw-Hill.
- POWELL, D. R. & JACOBSON, R. A. (1980). *FOUR. A Generalized Fourier Program*. Ames Laboratory (DOE) and Iowa State Univ., Ames, Iowa.

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Structure of the Monohydrate of 17 α -Hydroxy-3,11,20-trioxo-4-pregnen-21-yl Acetate (Cortisone Acetate, Modification *Vaq*)

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Abstract. $C_{23}H_{30}O_6 \cdot H_2O$, $M_r = 420.51$, orthorhombic, $P2_12_12_1$, $a = 7.548$ (4), $b = 9.863$ (1), $c = 30.648$ (6) Å, $V = 2282$ (1) Å³, $Z = 4$, $D_x = 1.224$ g cm⁻³, $\lambda(\text{Mo } K\alpha) = 0.71069$ Å, $\mu(\text{Mo } K\alpha) = 0.8$ cm⁻¹, $F(000) = 904$, room temperature, $R = 0.083$ for 1781 unique reflections with $I \geq 2.5\sigma(I)$. Under humid conditions the unstable methanol solvate of cortisone acetate is converted into a stable isomorphous hydrate. The water molecule acts as an acceptor in a hydrogen bond with the 17 α -hydroxyl group of the steroid molecule and as a donor in a weak hydrogen bond with the 3-oxo atom. In the crystal-structure analysis no account could be taken of some additional interstitial water, with a mean occupancy in the bulk of 0.23 molecules water in the asymmetric unit. The conformation of the steroid molecule is the same as was observed in the acetone solvate and anhydrous modification I.

Introduction. The methanol solvate of cortisone acetate, usually characterized by its IR spectra and in literature known as form V (CA V) (Mesley, 1968), can be obtained by crystallization from dry methanol. However, CA V obtained from a mixture of carbon tetrachloride and methanol has been described as hydrates by Callow & Kennard (1961)* and Carless, Moustafa & Rapson (1966). So there seems to be

confusion, because CA V desolvates quickly and attracts water (van Geerestein, Kanters, van Dijck & van Wendel de Joode, 1985). The present paper reports the analysis of the isomorphous hydrate of CA V, which will be called modification *Vaq* (CA *Vaq*).

Experimental. Crystals of CA *Vaq* were obtained through the Scientific Development Group of Organon, Oss, The Netherlands. Samples of crystals of CA V were kept in small loosely closed brown flasks for about nine months, after which the opaque crystals were analysed by analytical techniques. Methanol could not be detected by NMR, and Karl Fisher analysis resulted in 5.20 wt% water, corresponding to 1.23 molecules of water in the asymmetric unit. Differential thermal analysis and thermogravimetry experiments indicated that one water molecule is tightly bound and the additional water only loosely attached. Density measurement by flotation in hexane/carbon tetrachloride showed that the crystals were variable in density ($D_m = 1.21$ – 1.24 g cm⁻³). So the experimentally determined water content of 1.23 can only be considered as a mean value. A crystal of dimensions $0.3 \times 0.3 \times 0.2$ mm was selected for data collection on an Enraf–Nonius CAD-4 diffractometer with Zr-filtered Mo $K\alpha$ radiation; lattice parameters were refined by least-squares fitting of 2θ values of 25 reflections in the range $16 < 2\theta < 32^\circ$; ω - 2θ scan mode, $\Delta\omega = (1.00 + 0.35 \tan\theta)^\circ$; 3774 reflections measured up to $\theta = 30^\circ$, h, k, l (max. range 10, 13, 43); 1781 of these were considered observed [$I \geq 2.5\sigma(I)$] and used for structure refinement. Two

* Callow & Kennard have interchanged the X-ray data of modification IV (ethanolate) and V (methanolate); however, their relevant IR data are correct and consistent with literature and our IR spectra.

periodically measured standard reflections ($\bar{3}2\bar{7}$, $\bar{1}\bar{1}$, 12) showed no significant changes; Lp corrections, no correction for absorption.

The structure was solved with a preliminary version of the *PATSEE* Patterson search program (Egert & Sheldrick, 1985) using the fused *A*, *B* and *C* rings of CA II (Declercq, Germain & Van Meerssche, 1972) as a search fragment. H atoms of the steroid molecule were placed on calculated positions, except the hydroxyl-group H atom which was located on a difference map. In the final cycles of full-matrix least-squares refinement on *F*, using *SHELX76* (Sheldrick, 1976), 270 parameters were varied, including overall scale factor, positional and individual anisotropic thermal parameters for C and O atoms, positional parameters for the hydroxyl-group H atom and O(aq) and overall thermal parameter for H atoms and an isotropic thermal parameter for O(aq). The H atoms of the water molecule were located in the final difference Fourier map, but not refined. No parameters could be ascribed to the additional 0.23 molecules of water and this is expressed in the value of the final *R* index. The refinement on *F* converged at $R = 0.083$ and $wR = 0.077$, where $w = 1/\sigma^2(F)$. The m.s. amplitude of vibration for the H atoms refined to 0.70 (5) Å². $\Delta/\sigma_{av} = 0.003$ (3) and $\Delta/\sigma_{max} = 0.022$ for all refined parameters; $-0.28 < \Delta\rho < 0.35$ e Å⁻³. The final difference Fourier map showed some peaks, which had no atom contacts less than 3.0 Å and these densities possibly originate from the additional interstitial water molecules. Scattering factors were taken from Cromer & Mann (1968) for C and O atoms and from Stewart, Davidson & Simpson (1965) for H atoms.

Discussion. The final atomic parameters are given in Table 1.* The conformation of the steroid molecule and atom numbering are shown in Fig. 1. The bond lengths and bond angles involving non-H atoms are given in Table 2 and correspond to those observed in the other modifications: anhydrous forms CA I (Declercq, Germain & Van Meerssche, 1972) and CA II (Kanters, de Koster, van Geerestein & van Dijck, 1985) and the acetone solvate CA IVac (van Geerestein & Kanters, 1987). The conformation of the steroid molecule is similar to that found in CA IVac and we refer to this paper for a comparison with CA I and CA II. The *A* ring has a distorted 1 α -sofa conformation, as indicated by the asymmetry parameter $\Delta C_s[C(1)] = 10.4$ (8)^o (Duax & Norton, 1975); the *B* and *C* rings have chair conformations and the *D* ring has a 13 β -envelope conformation [$\Delta C_s[C(13)] = 1.0$ (8)^o]; for CA IVac

* Lists of structure factors, anisotropic thermal parameters, H-atom parameters and torsion angles have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 43615 (17 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. *Positional and equivalent isotropic thermal parameters* (Å²) *for non-H atoms with e.s.d.'s in parentheses*

$$U_{eq} = (U_{11} + U_{22} + U_{33})/3.$$

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{eq}
O(3)	0.068 (1)	0.6690 (7)	0.1769 (2)	0.079 (3)
O(11)	0.3186 (8)	0.4113 (6)	-0.0086 (2)	0.057 (2)
O(17)	0.0445 (9)	0.6679 (6)	-0.1398 (2)	0.048 (2)
O(20)	0.019 (1)	0.3570 (7)	-0.1939 (2)	0.077 (3)
O(21)	0.355 (1)	0.4159 (8)	-0.2153 (2)	0.073 (3)
O(22)	0.410 (1)	0.2944 (8)	-0.1557 (2)	0.087 (3)
C(1)	0.220 (1)	0.5395 (9)	0.0731 (2)	0.041 (3)
C(2)	0.219 (1)	0.536 (1)	0.1226 (3)	0.053 (3)
C(3)	0.064 (1)	0.6140 (9)	0.1410 (3)	0.054 (3)
C(4)	-0.097 (1)	0.6167 (9)	0.1143 (3)	0.050 (3)
C(5)	-0.109 (1)	0.5555 (8)	0.0741 (3)	0.037 (3)
C(6)	-0.286 (1)	0.548 (1)	0.0524 (3)	0.046 (3)
C(7)	-0.278 (1)	0.5875 (8)	0.0044 (3)	0.043 (3)
C(8)	-0.1374 (9)	0.5078 (8)	-0.0194 (2)	0.033 (3)
C(9)	0.0449 (9)	0.5311 (7)	0.0034 (2)	0.031 (2)
C(10)	0.047 (1)	0.4903 (7)	0.0518 (2)	0.029 (2)
C(11)	0.200 (1)	0.4765 (8)	-0.0245 (2)	0.034 (3)
C(12)	0.199 (1)	0.5126 (9)	-0.0724 (2)	0.036 (3)
C(13)	0.022 (1)	0.4755 (8)	-0.0923 (2)	0.036 (3)
C(14)	-0.125 (1)	0.5487 (8)	-0.0675 (2)	0.035 (3)
C(15)	-0.291 (1)	0.5316 (9)	-0.0962 (2)	0.042 (3)
C(16)	-0.217 (1)	0.520 (1)	-0.1425 (3)	0.051 (3)
C(17)	-0.015 (1)	0.5309 (8)	-0.1394 (3)	0.039 (3)
C(18)	0.001 (1)	0.3203 (8)	-0.0917 (3)	0.045 (3)
C(19)	0.027 (1)	0.3356 (7)	0.0573 (3)	0.047 (3)
C(20)	0.077 (1)	0.454 (1)	-0.1754 (3)	0.044 (3)
C(21)	0.260 (1)	0.510 (1)	-0.1887 (3)	0.066 (4)
C(22)	0.427 (1)	0.309 (1)	-0.1938 (4)	0.069 (4)
C(23)	0.535 (2)	0.220 (1)	-0.2240 (4)	0.115 (5)
O(aq)	0.089 (1)	0.7844 (8)	-0.2141 (2)	0.092 (2)*

* Kept isotropic.

Table 2. *Bond distances* (Å) *and bond angles* (°) *for non-H atoms with e.s.d.'s in parentheses*

O(3)-C(3)	1.23 (1)	C(8)-C(9)	1.560 (9)
O(11)-C(11)	1.21 (1)	C(8)-C(14)	1.531 (9)
O(17)-C(17)	1.42 (1)	C(9)-C(11)	1.55 (1)
O(20)-C(20)	1.20 (1)	C(9)-C(10)	1.537 (9)
O(21)-C(22)	1.36 (1)	C(10)-C(19)	1.54 (1)
O(21)-C(21)	1.43 (1)	C(11)-C(12)	1.511 (9)
O(22)-C(22)	1.18 (1)	C(12)-C(13)	1.51 (1)
C(1)-C(10)	1.54 (1)	C(13)-C(14)	1.53 (1)
C(1)-C(2)	1.52 (1)	C(13)-C(17)	1.57 (1)
C(2)-C(3)	1.51 (1)	C(13)-C(18)	1.54 (1)
C(3)-C(4)	1.47 (1)	C(14)-C(15)	1.54 (1)
C(4)-C(5)	1.37 (1)	C(15)-C(16)	1.53 (1)
C(5)-C(6)	1.49 (1)	C(16)-C(17)	1.53 (1)
C(5)-C(10)	1.51 (1)	C(17)-C(20)	1.51 (1)
C(6)-C(7)	1.52 (1)	C(20)-C(21)	1.54 (1)
C(7)-C(8)	1.51 (1)	C(22)-C(23)	1.51 (2)
C(21)-O(21)-C(22)	115.4 (7)	O(11)-C(11)-C(12)	121.5 (7)
C(2)-C(1)-C(10)	114.4 (6)	C(11)-C(12)-C(13)	109.8 (6)
C(1)-C(2)-C(3)	111.5 (7)	C(14)-C(13)-C(18)	112.9 (6)
O(3)-C(3)-C(4)	120.9 (8)	C(12)-C(13)-C(17)	116.3 (6)
C(2)-C(3)-C(4)	116.3 (8)	C(14)-C(13)-C(17)	99.4 (6)
O(3)-C(3)-C(2)	122.8 (8)	C(17)-C(13)-C(18)	109.8 (6)
C(3)-C(4)-C(5)	123.2 (7)	C(12)-C(13)-C(14)	109.1 (6)
C(4)-C(5)-C(10)	122.9 (7)	C(12)-C(13)-C(18)	109.1 (6)
C(4)-C(5)-C(6)	118.7 (7)	C(8)-C(14)-C(15)	118.1 (6)
C(6)-C(5)-C(10)	118.4 (7)	C(13)-C(14)-C(15)	104.8 (5)
C(5)-C(6)-C(7)	112.4 (7)	C(8)-C(14)-C(13)	113.5 (6)
C(6)-C(7)-C(8)	111.2 (6)	C(14)-C(15)-C(16)	103.9 (6)
C(7)-C(8)-C(9)	109.1 (6)	C(15)-C(16)-C(17)	107.5 (7)
C(7)-C(8)-C(14)	111.8 (6)	O(17)-C(17)-C(16)	112.3 (7)
C(9)-C(8)-C(14)	109.8 (6)	O(17)-C(17)-C(13)	106.4 (7)
C(8)-C(9)-C(11)	111.6 (5)	C(16)-C(17)-C(20)	112.2 (7)
C(10)-C(9)-C(11)	115.8 (6)	O(17)-C(17)-C(20)	109.0 (7)
C(8)-C(9)-C(10)	113.7 (6)	C(13)-C(17)-C(16)	102.1 (7)
C(5)-C(10)-C(9)	108.6 (6)	C(13)-C(17)-C(20)	114.6 (7)
C(1)-C(10)-C(9)	109.6 (6)	O(20)-C(20)-C(17)	125.5 (8)
C(1)-C(10)-C(19)	110.4 (6)	C(17)-C(20)-C(21)	115.2 (8)
C(5)-C(10)-C(19)	107.2 (6)	O(20)-C(20)-C(21)	119.3 (8)
C(1)-C(10)-C(5)	109.7 (6)	O(21)-C(21)-C(20)	111.6 (8)
C(9)-C(10)-C(19)	111.3 (6)	O(21)-C(21)-C(23)	112. (1)
C(9)-C(11)-C(12)	116.8 (6)	O(22)-C(22)-C(23)	126.2 (9)
O(11)-C(11)-C(9)	121.6 (6)	O(21)-C(22)-O(22)	122.0 (9)

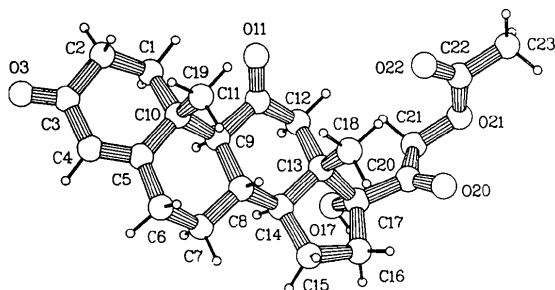


Fig. 1. Perspective view of the molecule with atom numbering.

these parameters were 7.9 (6) and 5.0 (5) $^\circ$ respectively. The conformation of the side chain of CA is given by torsion angles $C(17)-C(20)-C(21)-O(21) = 166.7$ (7), $O(20)-C(20)-C(21)-O(21) = -14$ (1), $C(20)-C(21)-O(21)-C(22) = -75.8$ (9), $C(21)-O(21)-C(22)-C(23) = -176.2$ (8), $C(21)-O(21)-C(22)-O(22) = -1$ (1) $^\circ$ and its orientation with respect to the steroid skeleton is given by the torsion angles about $C(17)-C(20)$, e.g. $C(13)-C(17)-C(20)-C(21) = -92.2$ (9) $^\circ$. The orientations of the side chains of CA *Vaq* and CA *IVac* are almost the same with the mean difference of the six $C(17)-C(20)$ torsion angles amounting to only 1 (1) $^\circ$. Fig. 2 shows a stereoview down *a*. The water molecule is an acceptor in a hydrogen bond with $O(17)$ and a donor in a rather poor hydrogen bond to $O(3\{-\frac{1}{2}+x, \frac{3}{2}-y, -z\})$, with distances $O(17)\cdots O(aq) = 2.742$ (9) and $O(aq)\cdots O(3) = 2.87$ (1) \AA and angles $O(17)-H\cdots O(aq) = 167$ (8) and $O(aq)-H\cdots O(3) = 115$ $^\circ$. This latter angle and the $H\cdots O(3)$ distance of 2.3 \AA indicate the rather poor geometry of this H bond, but this may be due to the approximate coordinates of the H atom, which could not be refined satisfactorily. The packing is different from those of the other described modifications and can

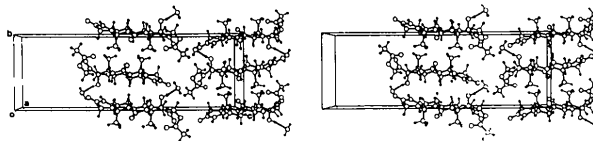


Fig. 2. Stereo packing diagram viewed down *a*. Hydrogen bonds are indicated.

be described as $O b_1 a_9 c_3$ 212 (Duax & Norton, 1975), indicating that the molecules are packed two thick, one wide and two long, with the steroid length parallel to *c*.

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References

- CALLOW, R. K. & KENNARD, O. (1961). *J. Pharm. Pharmacol.* **13**, 723–733.
 CARLESS, J. E., MOUSTAFA, M. A. & RAPSON, H. D. (1966). *J. Pharm. Pharmacol.* **18**, 190s–197s.
 CROMER, D. T. & MANN, J. B. (1968). *Acta Cryst.* **A24**, 321–324.
 DECLERCQ, J.-P., GERMAIN, G. & VAN MEERSSCHE, M. (1972). *Cryst. Struct. Commun.* **1**, 59–62.
 DUAX, W. L. & NORTON, D. A. (1975). *Atlas of Steroid Structure*, Vol. I, pp. 16–25. New York: IFI/Plenum.
 EGERT, E. & SHELDRIK, G. M. (1985). *Acta Cryst.* **A41**, 262–268.
 GEERESTEIN, V. J. VAN & KANTERS, J. A. (1987). *Acta Cryst.* **C43**, 136–139.
 GEERESTEIN, V. J. VAN, KANTERS, J. A., VAN DIJCK, L. A. & VAN WENDEL DE JOODE, M. D. (1985). Ninth Eur. Crystallogr. Meet., Torino, Italy. Abstracts, pp. 402–403.
 KANTERS, J. A., DE KOSTER, A., VAN GEERESTEIN, V. J. & VAN DIJCK, L. A. (1985). *Acta Cryst.* **C41**, 760–763.
 MESLEY, R. J. (1968). *J. Pharm. Pharmacol.* **20**, 877–878.
 SHELDRIK, G. M. (1976). *SHELX76*. Program for crystal structure determination. Univ. of Cambridge, England.
 STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

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Absolute Configuration and Structure of Ethyl 2-(3-Methyl-1,4-dioxoperhydrocyclopenta[4,5]pyrrolo[1,2-*a*]pyrazin-2-yl)-4-phenylbutyrate

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Abstract. $C_{23}H_{30}N_2O_4$, $M_r = 398.5$, orthorhombic, $P2_12_12_1$, $a = 9.145$ (2), $b = 12.602$ (1), $c = 18.782$ (3) \AA , $V = 2164.5$ \AA^3 , $Z = 4$, $F(000) = 856$, $D_m = 1.21$ (flotation in aqueous K_2HgI_4 solution), $D_x = 1.223$ Mg m^{-3} , $\lambda(\text{Mo K}\alpha) = 0.71069$ \AA , $\mu =$

0108-2701/87/050938-04\$01.50

0.078 cm^{-1} , $T = 293$ K, $R = 0.11$, $wR = 0.040$ for 2297 reflections [$F^2 > \sigma(F^2)$]. Solution of the phase problem was not straightforward; the phases of 13 reflections had to be varied systematically. The absolute configuration is all-(*S*). Both the condensed five-

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