Powder X-ray diffraction of altrenogest, $C_{21}H_{26}O_2$

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The crystal structure of altrenogest has been solved and refined using synchrotron X-ray powder diffraction data, and optimized using density functional techniques. Altrenogest crystallizes in space group $P2_12_12_1$ (#19) with $a = 7.286\,916(16)$, $b = 10.580\,333(19)$, $c = 22.266\,08(7)$ Å, $V = 1716.671(6)$ Å^3, and $Z = 4$ at 295 K. Thermal expansion between 113 and 295 K is anisotropic. An O–H···O hydrogen bond links the molecules into chains along the *c*-axis. The powder pattern has been submitted to ICDD for inclusion in the Powder Diffraction File™ (PDF®). [doi:10.1017/S0885715622000331]

Key words: altrenogest, Altren, powder diffraction, Rietveld refinement, density functional theory

Altrenogest (Figure 1; sold under the brand names Swinemate, Altren, and Regumate) is a steroidal progestin that is widely used in veterinary medicine to suppress estrus (female sexual activity) in mammals. The systematic name (CAS Registry Number 850-52-2) is (8S,13S,14S,17R)-17-hydroxy-13-methyl-17-prop-2-enyl-1,2,6,7,8,14,15,16-octahydrocyclopenta[*a*]phenanthren-3-one. This work was carried out as part of a project to determine the crystal structures of large-volume commercial pharmaceuticals, and include high-quality powder diffraction data for them in the Powder Diffraction File (Gates-Rector and Blanton, 2019).

The synchrotron pattern (measured at 11-BM at APS using a wavelength of 0.458 208 Å) of a commercial reagent (purchased from TargetMol, lot #113704) was indexed on a primitive orthorhombic unit cell having $a = 7.285\,45$, $b = 10.608\,36$, $c = 22.293\,64$ Å, $V = 1723.0$ Å^3, and $Z = 4$ using JADE Pro 8.1 (MDI, 2021). The suggested space group was $P2_12_12_1$ (#19). The structure was solved by Monte Carlo simulated annealing techniques as implemented in EXPO2014 (Altomare *et al.*, 2013), with a success rate of ~30%; 30% of the trials yielded an essentially identical correct structure. The structure was refined using GSAS-II (Toby and Von Dreele, 2013) and optimized using VASP (Kresse and Furthmüller, 1996). After refinement, a repeated reduced cell search in the Cambridge Structural Database (Groom *et al.*, 2016) yielded a very recent private communication to the CSD (Cui, 2021; Refcode OPOGIM) of the structure of altrenogest at 113 K.

The powder pattern of altrenogest calculated from the 113 K structure of OPOGIM exhibits significant peak shifts, compared with the pattern measured at ambient conditions (Figure 2). The thermal expansion is anisotropic (Table I). It is largest in the *b*-direction, along which the molecules are stacked. The smallest expansion is along the *c*-axis, which represents end-to-end contacts. There is one traditional hydrogen bond (Table II) between the hydroxyl group O1–H41 and the carbonyl group O2. These link the molecules into chains parallel to the *c*-axis with a graph set *C1,1(12)* (Etter, 1990; Bernstein *et al.*, 1995; Shields *et al.*, 2000). Two C–H···O and one C–H···C hydrogen bonds also contribute to the lattice energy.

I. DEPOSITED DATA

The Crystallographic Information Framework (CIF) files containing the results of the Rietveld refinement (including the raw data) and the DFT geometry optimization were deposited with the ICDD. The data can be requested at info@icdd.com.

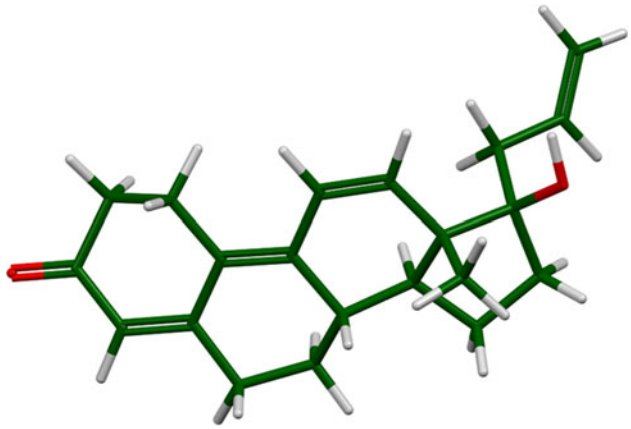

Figure 1. The molecular structure of altrenogest.

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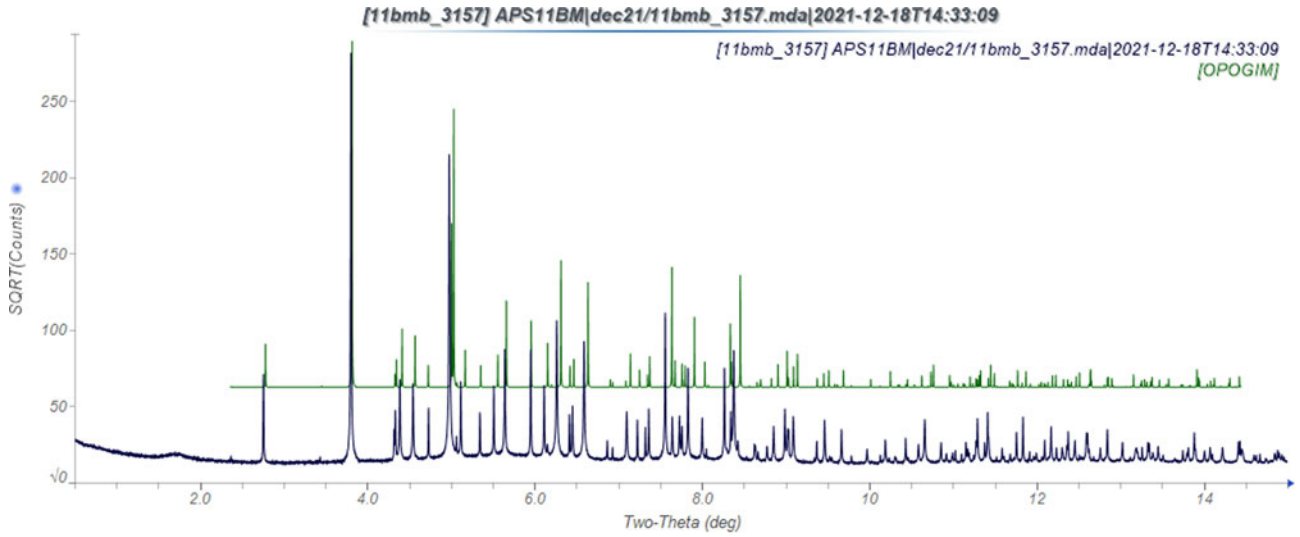

Figure 2. The observed synchrotron X-ray powder pattern of altrenogest at 295 K (black), compared with that calculated from the single crystal structure at 113 K (green). Note that the *y*-axis is the square root of the intensity, to highlight the weaker peaks.

TABLE I. Lattice parameters of altrenogest (space group $P2_12_12_1$).

Temperature (K)	113	295	Ratio 295/113
Source	Cui (2021)	This work	
a, Å	7.2501(15)	7.286 916(16)	1.00508
b, Å	10.452(2)	10.580 333(19)	1.01228
c, Å	22.252(5)	22.266 08(7)	1.00063
V, Å^3	1686.213	1716.671(6)	1.01806

TABLE II. Hydrogen bonds (CRYSTAL17; Dovesi *et al.*, 2018) in altrenogest.

H-bond	D–H (Å)	H···A (Å)	D···A (Å)	D–H···A (°)	Overlap (*e*)	*E* (kcal mol^{-1})
O1–H41···O2	0.996	1.848	2.836	171.2	0.062	13.6
C21–H47···O1	1.096	2.328	3.245	140.0	0.025	
C20–H45···O1	1.094	2.682	3.712	156.8	0.016	
C16–H39···C23	1.106	2.745	3.679	141.9	0.010	

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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