Powder X-ray diffraction of fluorometholone, $C_{22}H_{29}FO_4$

Diana Gonzalez,[1] Joseph T. Golab,[1] James A. Kaduk,[2,3,a)] Amy M. Gindhart,[4] and Thomas N. Blanton[4]
[1]*Illinois Mathematics and Science Academy, 1500 Sullivan Rd., Aurora, Illinois 60506-1000, USA*
[2]*Illinois Institute of Technology, 3101 S. Dearborn St., Chicago, Illinois 60616, USA*
[3]*North Central College, 131 S. Loomis St., Naperville, Illinois 60540, USA*
[4]*ICDD, 12 Campus Blvd., Newtown Square, Pennsylvania 19073-3273, USA*

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Commercial fluorometholone, CAS #426-13-1, crystallizes in the monoclinic space group $P2_1$ (#4) with $a = 6.40648(2)$, $b = 13.43260(5)$, $c = 11.00060(8)$ Å, $\beta = 92.8203(5)°$, $V = 945.517(5)$ Å^3, and $Z = 2$. A reduced cell search in the Cambridge Structural Database yielded one previous structure determination, using single-crystal data at 292 K. In this work, the sample was ordered from the United States Pharmacopeial Convention (Lot # R032K0) and analyzed as-received. The room temperature (295 K) crystal structure was refined using synchrotron ($\lambda = 0.412826$ Å) powder diffraction data and optimized using density functional theory (DFT) techniques. Hydrogen positions were included as a part of the structure and were re-calculated during the refinement. The diffraction data were collected on beamline 11-BM at the Advanced Photon Source, Argonne National Laboratory, and the powder X-ray diffraction pattern of the compound has been submitted to ICDD® for inclusion in the Powder Diffraction File™. The agreement of the Rietveld-refined and DFT-optimized structures is excellent; the root-mean-square Cartesian displacement is 0.060 Å. In addition to the O–H···O hydrogen bonds observed by Park *et al.* (Park, Y. J., Lee, M. Y., and Cho, S. I. (**1992**). "Fluorometholone," J. Korean Chem. Soc. **36**, 812–817), C–H···O hydrogen bonds contribute to the crystal energy. © *2020 International Centre for Diffraction Data.*
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Key words: fluorometholone, Efflumidex®, X-ray diffraction, Powder Diffraction File

Fluorometholone (brand names: Efflumidex, Flucon, FML Forte, and FML) is a prescription drug classified as a synthetic glucocorticoid used to treat optical inflammation or diseases. Commercial fluorometholone, CAS #426-13-1, crystallizes in the monoclinic space group $P2_1$ (#4) with $a = 6.40648(2)$, $b = 13.43260(5)$, $c = 11.00060(8)$ Å, $\beta = 92.8203(5)°$, $V = 945.517(5)$ Å^3, and $Z = 2$. A reduced cell search in the Cambridge Structural Database (Groom *et al.*, 2016) yielded one previous structure determination (Park *et al.*, 1992), using single-crystal data at 292 K.

In this work, the sample was ordered from the United States Pharmacopeial Convention (Lot # R032K0) and analyzed as-received. The diffraction data were collected on beamline 11-BM at the Advanced Photon Source, Argonne National Laboratory. The room temperature (295 K) crystal structure was refined using synchrotron ($\lambda = 0.412826$ Å) powder diffraction data and optimized using density functional theory (DFT) techniques. Hydrogen positions were included as a part of the structure and were re-calculated during the refinement (Figure 1).

The agreement of the Rietveld-refined and DFT-optimized structures is excellent; the root-mean-square Cartesian displacement is 0.060 Å. In addition to the O–H···O hydrogen bonds observed by Park *et al.* (1992), C–H···O hydrogen bonds contribute to the crystal energy (Table I). The powder X-ray diffraction pattern of the compound has been submitted to ICDD® for inclusion in the Powder Diffraction File™.

DEPOSITED DATA

CIF and/or RAW data files were deposited with ICDD. You may request this data from ICDD at info@icdd.com.

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[a)] Author to whom correspondence should be addressed. Electronic mail: kaduk@polycrystallography.com

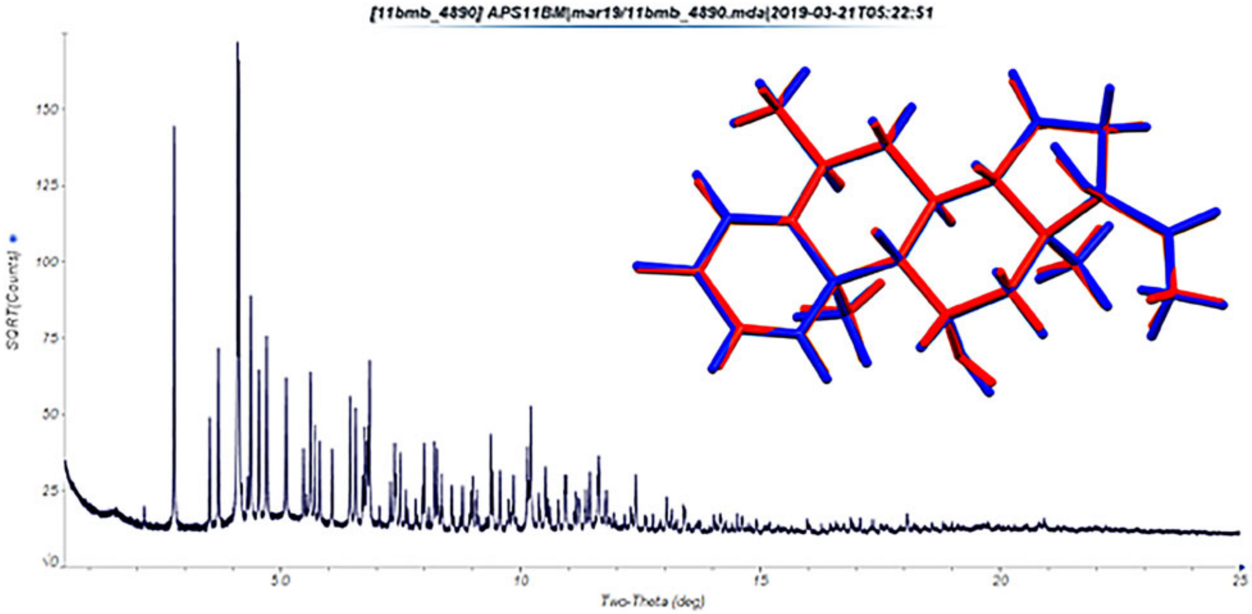

Figure 1. Powder X-ray diffraction pattern of fluorometholone. The Rietveld-refined structure is indicated in red, and the DFT-optimized structure is indicated in blue.

TABLE I. Hydrogen bonds (CRYSTAL14) in fluorometholone.

H-bond	D–H (Å)	H···A (Å)	D···A (Å)	D–H···A (°)	Overlap (*e*)	*E* (kcal mol^{-1})
O3–H29···O1	0.980	1.784	2.753	169.1	0.050	12.2
O2–H28···O3	0.979	1.892	2.835	160.7	0.059	13.3
C22–H27···O4	1.094	2.599	3.686	172.5	0.012	[a]
C21–H23···O1	1.096	2.525	3.567	158.5	0.017	[a]
C16–H14···O4	1.091	2.387[b]	2.840	103.1	0.014	[a]
C1–H1···O4	1.087	2.515	3.598	173.4	0.020	[a]

[a] Correlation between overlap population and hydrogen bond energy not yet available for C–H···O hydrogen bonds.

[b] Intramolecular.