crystals

MDPI

Supporting Information for

Born out of Fire and Ice: Polymorph studies of the Antiviral Famciclovir

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1. X-ray Powder Diffraction Experiments

Experimental

Powder X-ray diffraction data were collected on a STOE Stadi P diffractometer, equipped with a linear position detector, using Cu K_α radiation (40 kV, 40 mA).

Measurements were carried out in the range $3° < 2\theta < 60°$ with a PSD step of 0.5°; 80s/step. Samples were filled in a 0.7 mm capillary and rotated throughout the experiment. A Oxford Cryosystems 700 was used to collect variable temperature data.

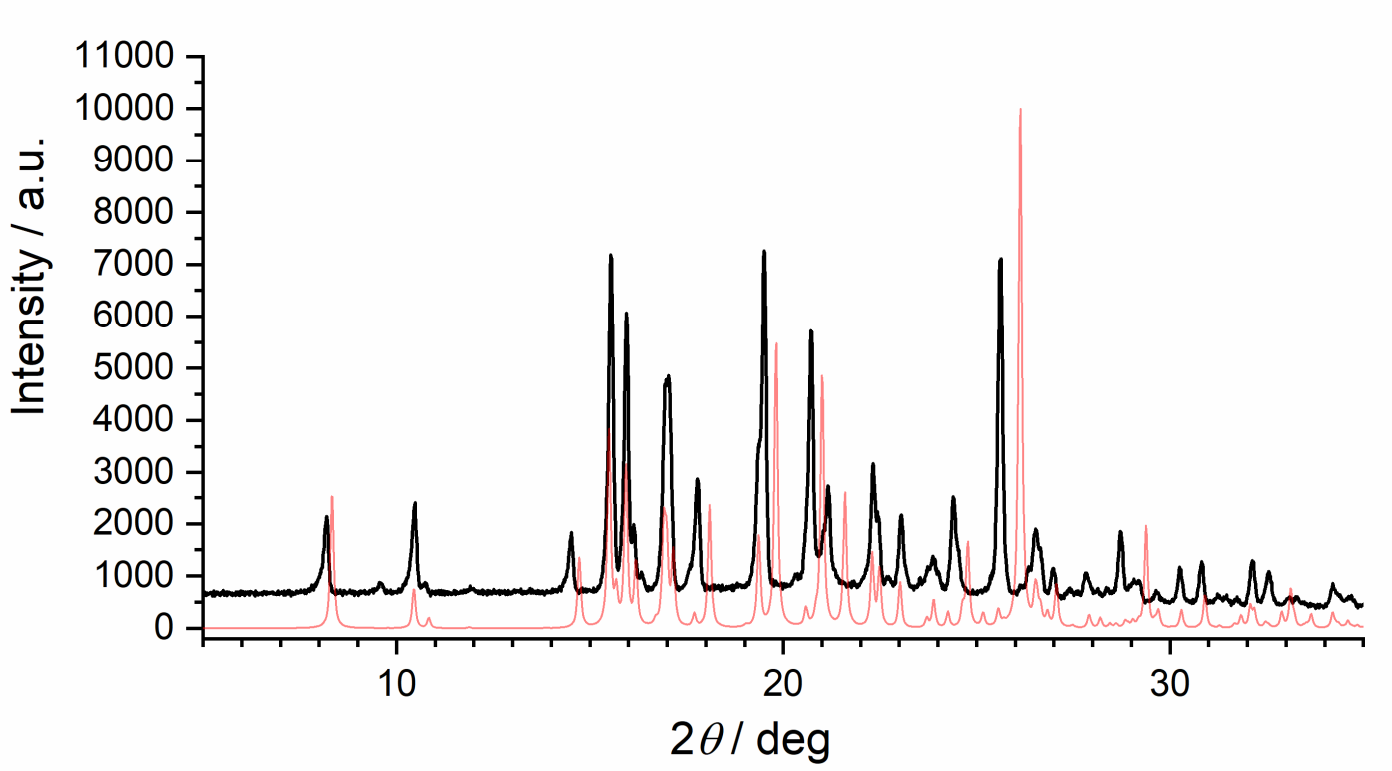

Figure S1. Powder X-ray pattern of Form 1 collected at room temperature (black) compared to the calculated pattern from single-crystal data obtained from a crystal from the same sample collected at -123°C (red)

2. Single-crystal X-ray Structure Determination

Experimental

Single crystals of $C_{14}H_{19}N_5O_4$ [Famciclovir (Form I)] were obtained directly from the commercially obtained solid. A suitable crystal was selected and mounted on a glass pin

in inert oil on a Xcalibur, Atlas, Gemini ultra diffractometer. The crystal was kept at 150.01(10) K during data collection. Using Olex2 [1], the structure was solved with the ShelXS [2] structure solution program using Direct Methods and refined with the

1. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. (2009), J. Appl. Cryst. 42, 339-341.
2. Sheldrick, G.M. (2008). Acta Cryst. A64, 112-122.
3. Sheldrick, G.M. (2015). Acta Cryst. C71, 3-8.

Table S1. Crystal data and structure refinement for Famciclovir (Form I).

Empirical formula	$C_{14}H_{19}N_5O_4$
Formula weight/g mol^{-1}	321.34
Temperature/K	150.01(10)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	11.0760(3)
b/Å	12.7697(3)
c/Å	11.7933(4)
α/°	90
β/°	106.751(3)
γ/°	90
Volume/Å^3	1597.23(8)
Z	4
ϱ_{calc} g/cm^3	1.336
μ/mm^{-1}	0.839
F(000)	680.0
Crystal size/mm^3	0.6365 × 0.6161 × 0.0531
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.336 to 132.51
Index ranges	-13 ≤ h ≤ 13, -15 ≤ k ≤ 14, -13 ≤ l ≤ 13
Reflections collected	26895
Independent reflections	2779 [R_{int} = 0.0391, R_{sigma} = 0.0134]
Data/restraints/parameters	2779/0/218
Goodness-of-fit on F^2	1.053
Final R indexes [I>=2σ (I)]	R_1 = 0.0391, wR_2 = 0.1019
Final R indexes [all data]	R_1 = 0.0431, wR_2 = 0.1059
Largest diff. peak/hole / e Å^{-3}	0.32/-0.22

Table S2. Crystal data and structure refinement for Famciclovir (Form I).

Empirical formula	$C_{14}H_{19}N_5O_4$
Formula weight/g mol^{-1}	321.34
Temperature/K	150.01(10)

Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	11.0760(3)
b/Å	12.7697(3)
c/Å	11.7933(4)
α/°	90
β/°	106.751(3)
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Volume/Å^3	1597.23(8)
Z	4
ρ_{calc} g/cm^3	1.336
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Goodness-of-fit on F^2	1.053
Final R indexes [I>=2σ (I)]	R_1 = 0.0391, wR_2 = 0.1019
Final R indexes [all data]	R_1 = 0.0431, wR_2 = 0.1059
Largest diff. peak/hole / e Å^{-3}	0.32/-0.22

Table S2 Fractional Atomic Coordinates (×104) and Equivalent Isotropic Displacement Parameters (Å2×103) for Famciclovir (Form I). Ueq is defined as 1/3 of the trace of the orthogonalised UIJ tensor.

Atom	*x*	*y*	*z*	U(eq)
O15	2784.3(10)	6711.6(8)	2721.4(9)	36.5(3)
O18	2282.8(16)	7831.6(10)	1205.3(13)	67.7(4)
O20	5357.6(10)	5460.8(9)	1879.3(10)	40.8(3)
O24	5588.0(16)	7181.8(12)	2284.4(16)	74.9(5)
N1	1543.1(12)	4210.3(9)	4626.4(10)	29.1(3)
N3	1096.8(12)	4208.7(9)	6374.6(10)	31.9(3)
N6	371.5(11)	1424.8(9)	5503.5(10)	26.7(3)
N8	1086.2(11)	2400.1(8)	4058.4(10)	25.2(3)
N10	657.5(13)	639.2(9)	3837.3(11)	32.3(3)
C2	1474.5(15)	4761.5(11)	5606.3(13)	32.8(3)
C4	890.4(13)	3213.3(10)	5863.3(12)	25.9(3)
C5	455.7(13)	2276.9(10)	6179.3(12)	27.1(3)
C7	706.5(13)	1518.7(10)	4481.5(12)	24.4(3)
C9	1170.0(13)	3210.8(10)	4783.0(11)	24.5(3)
C11	1852.4(14)	4616.5(11)	3584.2(12)	31.9(3)
C12	3259.1(15)	4717.2(12)	3763.7(13)	34.0(3)
C13	3590.2(14)	4991.9(11)	2617.6(13)	31.2(3)
C14	2772.9(14)	5856.9(11)	1911.7(13)	30.7(3)
C16	2509.6(15)	7664.9(12)	2249.8(16)	39.8(4)
C17	2531.9(19)	8464.4(13)	3177.1(19)	52.5(5)
C19	4985.1(15)	5261.1(14)	2935.3(15)	42.4(4)
C21	5621.4(16)	6461.0(14)	1648.3(18)	47.9(4)
C22	5932(2)	6522.0(18)	505(2)	62.1(6)

Table S3 Bond Lengths for Famciclovir (Form I)

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O15	C14	1.4479(17)	N6	C7	1.3648(17)
O15	C16	1.3365(18)	N8	C7	1.3468(17)
O18	C16	1.203(2)	N8	C9	1.3286(17)
O20	C19	1.4430(19)	N10	C7	1.3482(17)
O20	C21	1.355(2)	C4	C5	1.3798(19)
O24	C21	1.195(2)	C4	C9	1.3952(19)
N1	C2	1.3738(18)	C11	C12	1.516(2)
N1	C9	1.3704(17)	C12	C13	1.540(2)
N1	C11	1.4628(17)	C13	C14	1.5160(19)

N3	C2	1.3087(19)	C13	C19	1.521(2)
N3	C4	1.3971(18)	C16	C17	1.491(2)
N6	C5	1.3360(18)	C21	C22	1.487(3)

Table S4 Hydrogen Atom Coordinates (Å×10⁴) and Isotropic Displacement Parameters (Å²×10³) for Famciclovir (Form I).

Atom	*x*	*y*	*z*	U(eq)
H2	1683.53	5483.2	5716.9	39
H5	212.64	2237.59	6887.69	33
H11A	1455.39	5312.78	3382.66	38
H11B	1490.64	4144.03	2905.64	38
H12A	3672.82	4048.19	4079.29	41
H12B	3599.64	5267.8	4361.4	41
H13	3450.54	4350.12	2110.38	37
H14A	3111.64	6092.75	1263.96	37
H14B	1900.89	5601.81	1559.97	37
H17A	2457.4	8115.18	3893.83	79
H17B	1825.2	8950.1	2885.53	79
H17C	3327.63	8853.38	3361.27	79
H19A	5155.41	5888.64	3449.87	51
H19B	5487.07	4672.95	3379.89	51
H22A	5892.4	5819.79	160.68	75
H22B	5324.47	6979.98	-41.76	75
H22C	6783.94	6806.29	641.89	75
H22D	6108.14	7250.92	346.53	75
H22E	6676.07	6090.72	548.97	75
H22F	5216.6	6264.41	-134.68	75
H10A	397(16)	51(15)	4083(15)	36(4)
H10B	841(16)	676(14)	3141(17)	39(5)

Table 8 Atomic Occupancy for Famciclovir (Form I).

Atom	*Occupancy*	Atom	*Occupancy*	Atom	*Occupancy*
H22A	0.60(2)	H22B	0.60(2)	H22C	0.60(2)
H22D	0.40(2)	H22E	0.40(2)	H22F	0.40(2)