Supporting Information

Title: *Altering physical properties of pharmaceutical co-crystals in a systematic manner*

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Table 1. Crystallographic data for **1-6.**

Compound	**1**	**2**	**3**	**4**	**5**	**6**
Formula moiety	$(C_{16}H_{18}N_4O_2)$ $(C_6H_{10}O_4)$	$(C_{16}H_{18}N_4O_2)$ $(C_8H_{14}O_4)$	$(C_{20}H_{26}N_4O_2)$ $(C_4H_6O_4)$	$(C_{20}H_{26}N_4O_2)$ $(C_6H_{10}O_4)$	$(C_{20}H_{26}N_4O_2)$ $(C_8H_{14}O_4)$	$(C_{20}H_{26}N_4O_2)$ $(C_{10}H_{18}O_4)$
Empirical formula	$C_{22}H_{28}N_4O_6$	$C_{24}H_{32}N_4O_6$	$C_{24}H_{32}N_4O_6$	$C_{26}H_{36}N_4O_6$	$C_{28}H_{40}N_4O_6$	$C_{30}H_{44}N_4O_6$
Molecular weight	444.48	472.54	472.54	500.59	528.64	556.69
Color, Habit	gold prism	colourless plate	colourless plate	colourless plate	colourless prism	colourless plate
Crystal system	Triclinic	Triclinic	Triclinic	Triclinic	Triclinic	Triclinic
Space group, Z	P-1, 1	P-1, 1	P-1, 1	P-1, 1	P-1, 1	P-1, 1
a, Å	5.1160(4)	5.1221(4)	5.1072(4)	5.1403(3)	5.1420(4)	5.1264(6)
b, Å	5.1957(4)	5.2045(4)	5.1171(4)	5.2489(3)	5.2541(4)	5.2432(6)
c, Å	19.5042(16)	21.5019(14)	22.119(2)	22.9829(15)	24.624(2)	26.127(3)
α, °	90.704(2)	94.963(2)	96.134(6)	93.859(4)	89.785(4)	85.874(4)
β, °	93.362(2)	95.404(2)	94.037(6)	95.267(4)	87.095(4)	89.354(4)
γ, °	91.346(2)	91.630(2)	91.340(6)	91.289(4)	88.590(4)	88.356(4)
Volume, $Å^3$	517.36(7)	568.12(7)	573.05(8)	615.82(6)	664.20(9)	700.11(14)
X-ray wavelength	0.71073	0.71073	0.71073	0.71073	0.71073	0.71073
μ, mm-1	0.105	0.100	0.099	0.097	0.093	0.092
Crystal size, mm x mm x mm	0.32 x 0.22 x 0.14	0.32 x 0.24 x 0.08	0.24 x 0.14 x 0.08	0.25 x 0.10 x 0.05	0.20 x 0.15 x 0.10	0.32 x 0.18 x 0.06
Absorption corr	none	none	none	multi-scan	multi-scan	none
Reflections						
collected	8119	10539	5484	10595	11236	11866
independent	3505	3669	5484	3955	4009	4577
observed	3032	3070	4617	3054	2949	3014
Threshold expression	$>2\sigma(I)$	$>2\sigma(I)$	$>2\sigma(I)$	$>2\sigma(I)$	$>2\sigma(I)$	$>2\sigma(I)$
R_1 (observed)	0.0375	0.0429	0.0471	0.0402	0.0473	0.0614
wR_2 (all)	0.1132	0.1303	0.1230	0.1154	0.1384	0.1827
S	1.057	1.064	1.032	1.045	1.005	1.084
$\Delta\rho$ max / min	0.507 / -0.245	0.458 / -0.237	0.403 / -0.250	0.439 / -0.213	0.420 / -0.235	0.555 / -0.342
Θ_{full}, °	30.0	27.50	31.64	31.41	25.00	27.50
Completeness to Θ_{full}	0.986	0.971	0.984	0.970	0.972	0.967

Table 1 (cont). Crystallographic data for **7-11.**

Compound	**7**	**8**	**9**	**10**	**11**
Formula moiety	$(C_{18}H_{22}N_4O_2)$ $(C_4H_6O_4)$	$(C_{18}H_{22}N_4O_2)$ $(C_6H_{10}O_4)$	$(C_{18}H_{22}N_4O_2)$ $(C_8H_{14}O_4)$	$(C_{18}H_{22}N_4O_2)$ $(C_{10}H_{18}O_4)$	$(C_{18}H_{22}N_4O_2)$ $(C_{12}H_{22}O_4)$
Empirical formula	$C_{22}H_{28}N_4O_6$	$C_{24}H_{32}N_4O_6$	$C_{26}H_{36}N_4O_6$	$C_{28}H_{40}N_4O_6$	$C_{30}H_{44}N_4O_6$
Molecular weight	444.48	472.54	500.59	528.64	556.69
Color, Habit	colourless prism	colourless needle	colourless plate	colourless rod	colourless needle
Crystal system	Triclinic	Triclinic	Triclinic	Triclinic	Triclinic
Space group, Z	P-1, 1	P-1, 1	P-1, 1	P-1, 1	P-1, 1
a, Å	5.0275(6)	5.0282(6)	5.1671(13)	4.9817(4)	4.9821(4)
b, Å	6.9253(9)	6.7877(8)	11.646(3)	6.8634(6)	6.8797(6)
c, Å	16.058(2)	17.522(2)	11.779(4)	20.0493(16)	21.4410(17)
α, °	89.749(6)	98.124(3)	67.873(11)	93.097(4)	87.936(6)
β, °	81.536(5)	97.604(3)	80.585(12)	90.233(4)	86.223(6)
γ, °	80.893(6)	94.605(3)	79.827(12)	98.285(4)	81.469(5)
Volume, $Å^3$	545.92(12)	583.82(12)	642.6(3)	677.32(10)	724.93(10)
X-ray wavelength	0.71073	0.71073	0.71073	0.71073	0.71073
μ, mm-1	0.100	0.098	0.093	0.092	0.089
Crystal size, mm x mm x mm	0.25 x 0.25 x 0.15	0.36 x 0.16 x 0.18	0.28 x 0.18 x 0.08	0.25 x 0.15 x 0.10	0.28 x 0.12 x 0.06
Absorption corr	multi-scan	none	none	multi-scan	multi-scan
Reflections					
collected	14151	8477	9851	11823	14792
independent	4361	3487	3328	4462	4826
observed	3593	2567	1959	3482	3271
Threshold expression	$>2\sigma(I)$	$>2\sigma(I)$	$>2\sigma(I)$	$>2\sigma(I)$	$>2\sigma(I)$
R_1 (observed)	0.0431	0.0487	0.0563	0.0517	0.0510
wR_2 (all)	0.1305	0.1400	0.1599	0.1571	0.1478
S	1.041	1.084	1.070	1.091	1.017
$\Delta\rho$ max / min	0.473 / -0.225	0.367 / -0.281	0.251 / -0.293	0.626 / -0.322	0.479 / -0.300
Θ_{full}, °	25.00	30.49	27.50	31.64	31.50
Completeness to Θ_{full}	0.997	0.978	0.962	0.976	0.997

Datasets were collected on a SMART APEX II system with Mo radiation (**1**, **2**, **6**, **8**) or a Bruker Kappa APEX II system (**3**, **4**, **5**, **7**, **9**, **10**, **11**).[1] With the exception of **9**, whose dataset was collected at ambient temperature, an Oxford Croystream 700 low-temperature device set to 120 ° K was used to control temperature. Initial cell constants were found by small widely separated "matrix" runs. Data collection strategies were determined using COSMO.[2] Scan speeds and scan widths were chosen based on scattering power and peak rocking curves.

Unit cell constants and orientation matrices were improved by least-squares refinement of reflections thresholded from the entire dataset. Integrations were performed with SAINT,[3] using these improved unit cells as a starting point. Precise unit cell constants were calculated in SAINT from the final merged datasets. Lorenz and polarization corrections were applied. Absorption corrections was applied using SADABS unless otherwise noted.[4]

Datasets were refined with SHELXTL.[5] The structures were solved by direct methods without incident. Unless otherwise noted, coordinates for the amide and carboxylic acid hydrogens were allowed to refine. All other hydrogens were assigned to idealized positions and were allowed to ride. Isotropic thermal parameters for the hydrogen atoms were constrained to be 1.5x (methyl) / 1.2x (all other) that of the connected atom.

3 The crystal was a nonmerohedral twin, and the data were processed with TWINABS[6] to produce an HKLF 5 file.

7 The dicarboxylic acid was disordered over two sites. The ratio of the two species was allowed to refine, and eventually converged to ~ 88% : 12%. The geometry of the disordered species was restrained using DFIX commands, and thermal parameters for closely located atoms were pairwise constrained using the EADP command. The carboxylic acid hydrogen atoms were assigned to idealized positions and were allowed to ride.

1. APEX2 v2013.10-0, © 2005-2013, Bruker AXS Inc., Madison, WI.

2. COSMO v1.61, © 1999 - 2009, Bruker AXS Inc., Madison, WI.

3. SAINT v8.34a, © 1997 - 2013, Bruker AXS Inc., Madison, WI.

4. SADABS v2012/1, © 2012, Bruker AXS Inc., Madison, WI.

5. SHELXTL v2013/4, © 2013, Bruker AXS Inc., Madison, WI.

6. TWINABS v2012.1 © © 2012, Bruker AXS Inc., Madison, WI.