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Supporting Information

Progress in Predicting Ionic Cocrystal Formation: The Case of Ammonium Nitrate

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SI 1. Experimental

Ammonium nitrate (AN), 4-pyridone, parabanic acid, 2-methylbenzimidazole, imidazole, and 5-aminotetrazole were obtained from Sigma Aldrich. 5-Amino-1,2,4-triazole and barbituric acid were obtained from Alfa Aesar. 4-Cyanoimidazole, 2-pyridone, 2-imidazolidone, cyanuric acid, 2-methylimidazole, 5-nitro-2(1H)-pyridone, 3,5-diamino-1,2,4-triazole, picolinic acid, and benzimidazole were obtained from Acros Organics. 2-Nitroimidazole, 4-chloropyrazole, and 6-hydroxy-4(1H)-pyrimidinone were obtained from Oakwood Chemical. 3-Nitro-1,2,4-triazole was obtained from Chem-Impex International. 3,5-Dimethylpyrazole was obtained from TCI. 1H-1,2,4-Triazole, methanol, and acetonitrile were obtained from Fisher Scientific. Disposable syringe filters (0.45 µm, polytetrafluoroethylene) were obtained from Macherey-Nagel.

Cocrystal Screening and Synthesis

Each coformer was subjected to several cocrystallization methods with AN: cooling crystallization in water and in methanol, evaporative crystallization in methanol, slurry crystallization in acetonitrile, and liquid-assisted grinding (LAG) with acetonitrile. Cooling crystallization experiments were prepared in 4 mL vials by the addition of excess coformer to 1 mL of a stock saturated solution of AN in water or methanol. The co-saturated liquid was syringe filtered into a fresh 4 mL vial, sealed, and then stored in a refrigerator for up to one week. Evaporative crystallization experiments were prepared with stoichiometric quantities of AN and the coformer in 1:1, 2:1, and 1:2 ratios dissolved in 2 mL of methanol and allowed to evaporate at ambient. Slurry crystallization experiments were prepared by the addition of approximately 120 µL co-saturated acetonitrile to ground stoichiometric mixtures of AN and the coformer (1:1, approximately 0.001 mol) in 1.5 mL vials. Slurries were placed on an orbital shaker for one week. LAG was carried out with stoichiometric mixtures of AN and the coformer (1:1, approximately 0.001 mol) in a small mortar and pestle. The mixtures were ground immediately after the addition of 5 µL of acetonitrile. The stoichiometry of the mixtures was adjusted as needed based on PXRD results to obtain phase pure cocrystals.

Table S1. Methods successfully used to generate each cocrystal.

Cocrystal	Cooling (H_2O)	Cooling (MeOH)	Evap. (MeOH)	Slurry (MeCN)	LAG (MeCN)
AN:4-pyridone (4P)		✓		✓	✓
AN:picolinic acid (PA)		✓	✓	✓	
AN:cyanuric acid (CYA)			✓	✓	
AN:5-aminotriazole (5AT)	✓			✓	
AN:4-cyanoimidazole (4CI)				✓	✓
AN:2-pyridone (2P)				✓	✓
AN:2-imidazolidone (2IM)				✓	✓
AN:5-nitro-2(1H)-pyridone (5N2P)	✓	✓		✓	✓

Characterization

Single-Crystal Structure Determination

Single-crystal X-ray diffraction data were collected using a Rigaku XtaLAB Synergy-S X-ray diffractometer with a kappa goniometer geometry configuration. The X-ray source is a PhotonJet-S microfocus Cu source (λ = 1.54184 Å) operated at 50 kV and 1 mA. X-ray intensities were measured with a HyPix-6000HE detector held 34 mm from the sample. The data were processed using CrysAlisPro v40.82 (Rigaku Oxford Diffraction) and were corrected for absorption. The structures were determined and refined using OLEX2[1] v1.5-ac5-024 with SHELXT[2] and SHELXL[3]. With the exception of the disorder in AN:5AT and AN:5N2P, all non-hydrogen atoms were refined anisotropically with hydrogen atoms located in a combination of refined and idealized positions.

Powder X-Ray Diffraction

All powder pattern data were collected using a Panalytical Empyrean system utilizing Cu-Kα radiation (λ = 1.54184 Å) and operating at 45 kV and 40 mA. The system uses a Bragg-Brentano HD X-ray optic and an X'Celerator Scientific detector operating in a continuous 1D scan mode. Scans were conducted according to the following parameters: 2θ = 5° to 50°, step size = 0.008°, and step speed = 20 seconds. The data were plotted using Origin Pro 9.85.

Differential Scanning Calorimetry (DSC)

Differential scanning calorimetry (DSC) thermograms were recorded on a TA Instruments Q20 DSC instrument. Experiments were carried out at a heating rate of 5 °C/min, covering a temperature range of 5 °C to 400 °C. Samples were prepared in Tzero™ hermetic aluminum DSC pans. The instrument was calibrated using an indium standard, all DSC thermograms were analyzed using TA Universal Analysis 2000, V4.5A, build 4.5.0.5 and plotted using Origin Pro 9.85.

Computational Analysis

AN and all coformer molecules were modeled using Spartan '20 v1.0.0. Equilibrium geometries were optimized by DFT (B3LYP) calculations with the 6-311+G** basis set. Electrostatic potential maps were generated with a 0.002 e/au isosurface.

Table S2. Computed properties for all coformers. CSD codes are the structures for which packing coefficient was calculated. Packing coefficients were calculated for RT structures, aside from four molecules for which only low temperature collections were available (4-chloropyrazole, 4-pyridone, 4-cyanoimidiazole, and 2-nitroimidazole). Low temperature structures may have a packing coefficient up to 2.5% higher than at RT, based on the known relationship between temperature and cell volume.[4] Accounting for this difference does not change the observed trend in packing coefficient. Other properties were calculated from DFT optimized geometries.

	$V_{s,min}$ (kJ mol^{-1})	$V_{s,max}$ (kJ mol^{-1})	ΔV_s (kJ mol^{-1})	Dipole (D)	Packing Coefficient	FNO	Polar surface area (Å^2)	Ovality	S/L	CSD code
5-nitrotriazole	-172.16	346.64	518.80	7.18	0.7766	0.750	74.34	1.20	0.476	CIFROY
benzimidazole	-207.25	263.78	471.03	3.48	0.7850	0.222	20.54	1.17	0.423	BZDMAZ
pyrazole	-187.54	246.72	434.26	2.38	0.7867	0.400	25.06	1.10	0.576	PYRZOL38
3,5-dimethylpyrazole	-200.28	228.21	428.49	2.55	0.7890	0.286	25.06	1.21	0.430	DASXEA
4-chloropyrazole	-163.58	270.90	434.48	2.52	0.7951	0.333	25.00	1.15	0.497	EZOQES
3,5-diaminotriazole	-188.57	249.91	438.48	3.18	0.8017	0.714	84.10	1.21	0.480	DAMTRZ10
5-aminotetrazole	-208.68	314.52	523.20	6.40	0.8143	0.833	77.35	1.16	0.580	EJIQEU
methyl benzimidazole	-206.83	262.24	469.07	3.63	0.8167	0.200	20.48	1.22	0.413	KOWYEA02
barbituric acid	-136.04	258.62	394.66	0.10	0.8181	0.556	66.25	1.19	0.525	BARBAC
parabanic acid	-148.00	299.59	447.59	2.32	0.8204	0.625	68.08	1.17	0.523	PARBAC11
1h-1,2,4-triazole	-186.06	283.41	469.47	2.93	0.8333	0.600	33.81	1.10	0.606	TRAZOL
5-aminotriazole	-183.25	263.56	446.81	2.05	0.8374	0.800	58.89	1.16	0.548	AMTRAZ
5-nitro-2(1H)-pyridone	-165.01	294.95	459.96	1.85	0.8409	0.500	64.81	1.22	0.421	ELOXOS
cyanuric acid	-133.00	276.28	409.28	0.01	0.8436	0.667	77.23	1.20	0.500	CYURAC10
4-pyridone	-246.70	298.62	545.32	7.09	0.8650	0.286	26.24	1.14	0.497	MOKYER01
4-cyanoimidazole	-199.45	324.30	523.75	7.61	0.8722	0.429	35.69	1.16	0.471	FOHHOA
2-nitroimidazole	-184.31	296.00	480.31	5.85	0.8759	0.625	59.91	1.19	0.503	CELBAW
4,6-dihydroxypyrimidine	-204.36	268.93	473.29	4.27	0.8801	0.500	53.11	1.17	0.500	UHUMEP
picolinic acid	-288.63	226.83	515.46	10.98	0.8907	0.333	36.81	1.18	0.435	PICOLA02
2-imidazolidone	-221.53	192.60	414.13	4.61	0.8953	0.500	39.74	1.15	0.655	SUNKAO
2-pyridone	-221.87	234.22	456.09	4.51	0.9067	0.286	25.99	1.14	0.491	PYRIDO

SI 2. Crystallographic Data

Table S3. Crystallographic parameters for each ionic cocrystal.

	AN:4P	AN:PA	AN:CYA	AN:5AT	AN:4Cl	AN:2P	AN:2IM	AN:5N2P
stoichiometry	1:2	2:1	1:1	1:1	1:2	1:1	1:2	1:3
space group	$P2_1/c$	Cc	$P\bar{1}$	$P2_1/m$	$P\bar{1}$	$P2_1/c$	$P\bar{1}$	$P2_1$
a (Å)	3.86408(5)	9.61462(12)	6.76481(14)	6.5851(19)	3.7722(4)	9.9973(4)	9.1336(3)	10.9432(4)
b (Å)	30.6073(4)	19.00259(18)	7.16424(15)	7.2682(15)	12.2587(6)	7.2473(4)	10.8390(5)	6.7898(4)
c (Å)	10.88731(14)	7.33411(10)	9.02720(18)	7.4500(15)	13.9110(4)	12.0757(4)	14.4537(5)	14.6238(5)
α (°)	90	90	69.8056(19)	90	75.545(4)	90	97.721(3)	90
β (°)	99.6371(13)	110.5335(14)	78.0107(17)	102.53(3)	89.971(5)	102.732(4)	96.105(3)	100.331(3)
γ (°)	90	90	87.3711(17)	90	85.889(5)	90	108.826(4)	90
Volume (Å^3)	1269.46(3)	1254.83(3)	401.490(15)	348.07(15)	621.31(7)	853.41(7)	1233.21(9)	1068.96(8)
ρ_{calc} (g cm^{-3})	1.414	1.499	1.73	1.566	1.423	1.363	1.359	1.555
formula	$C_{10}H_{14}N_4O_5$	$C_6H_{13}N_5O_8$	$C_3H_7N_5O_6$	$C_2H_8N_6O_3$	$C_8H_{10}N_8O_3$	$C_5H_9N_3O_4$	$C_{12}H_{32}N_{12}O_{10}$	$C_{15}H_{16}N_8O_{12}$
fW (g/mol)	270.242	283.196	209.118	164.123	266.217	175.143	504.457	500.334
crystal system	monoclinic	monoclinic	triclinic	monoclinic	triclinic	monoclinic	triclinic	monoclinic
Z	4	4	2	4	2	4	2	2
$R_{int.}$ (%)	2.93	2.83	3.18	4.92	6.05	3.49	3.96	2.98
R_1/R_{W2} (%)	3.62/10.64	3.37/9.26	3.36/9.71	7.36/21.20	5.63/15.14	4.84/14.87	5.95/17.85	6.87/20.21
deposit #	2232413	2232415	2232414	2232408	2232409	2232410	2232411	2232412

SI 3. Thermal Ellipsoid plots at 50% probability

AN:4P

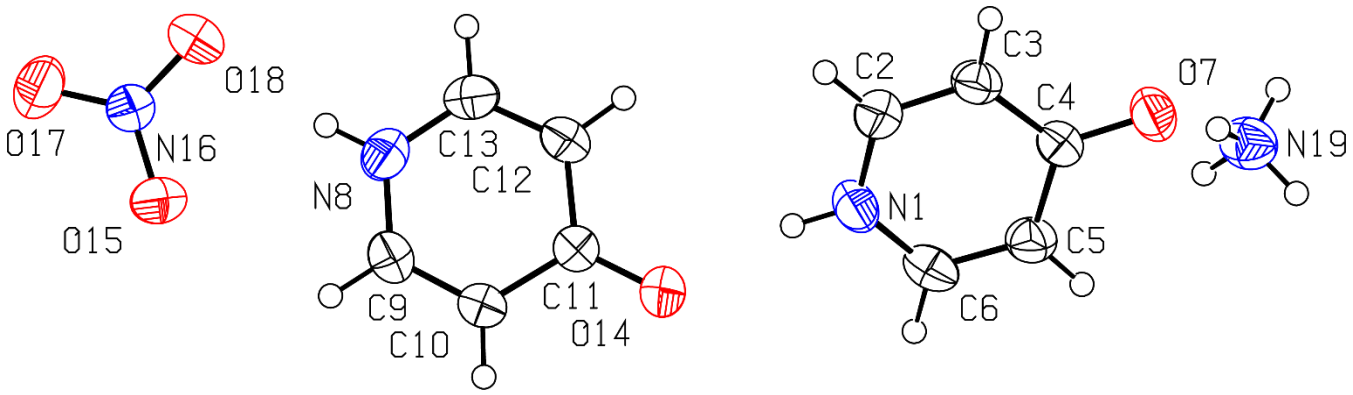

Figure S1. Thermal ellipsoid plot for **AN:4P** at 293(2) K.

AN:PA

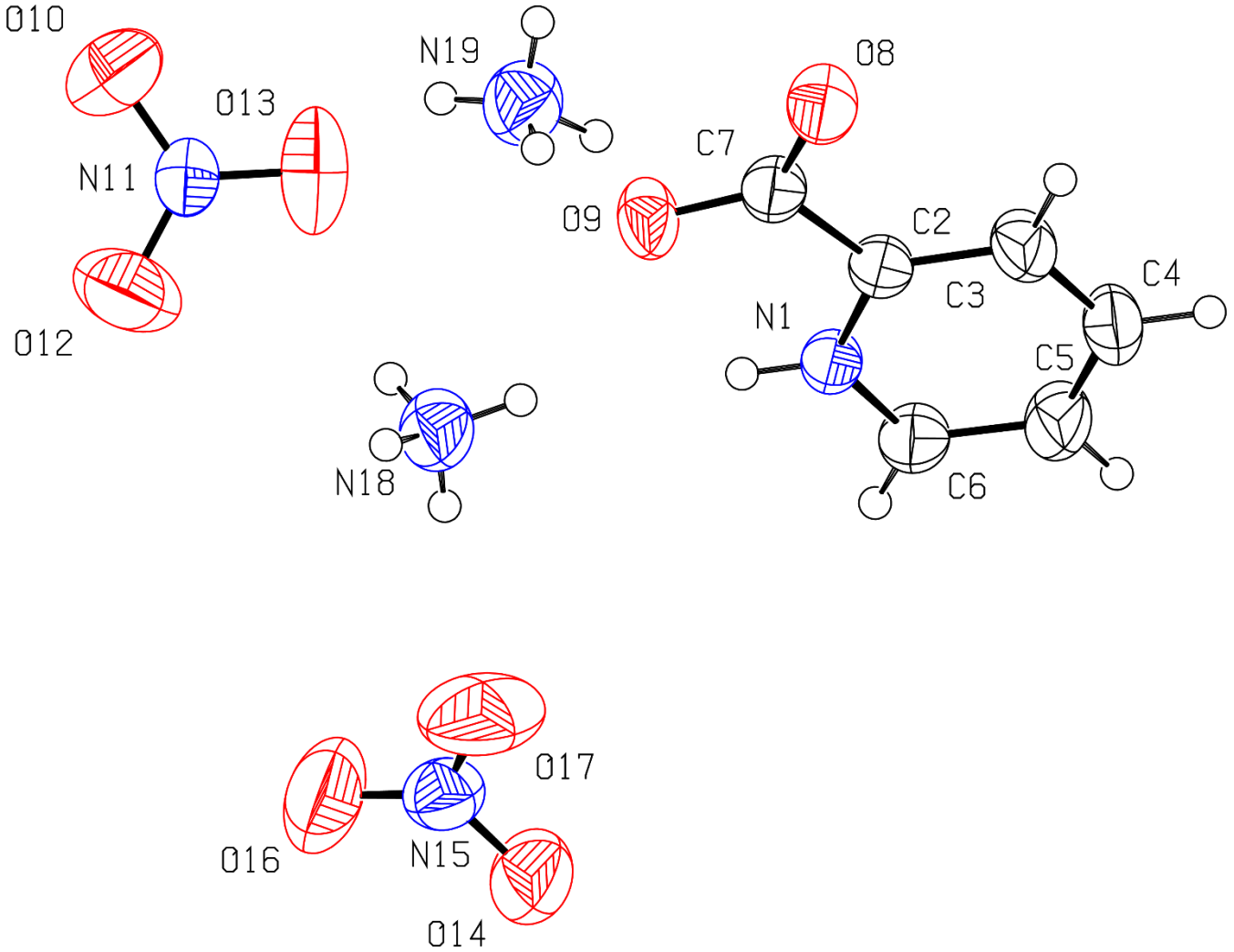

Figure S2. Thermal ellipsoid plot for **AN:PA** at 293(2) K.

AN:CYA

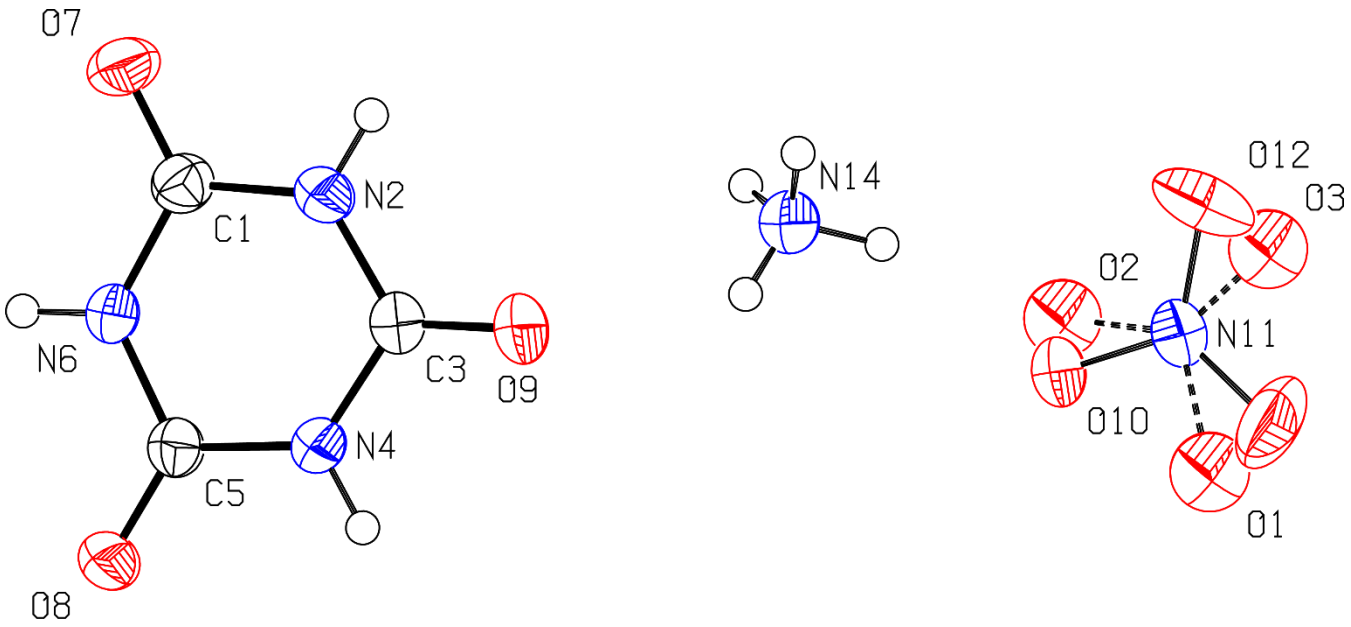

Figure S3. Thermal ellipsoid plot for **AN:CYA** at 293(2) K.

AN:5AT

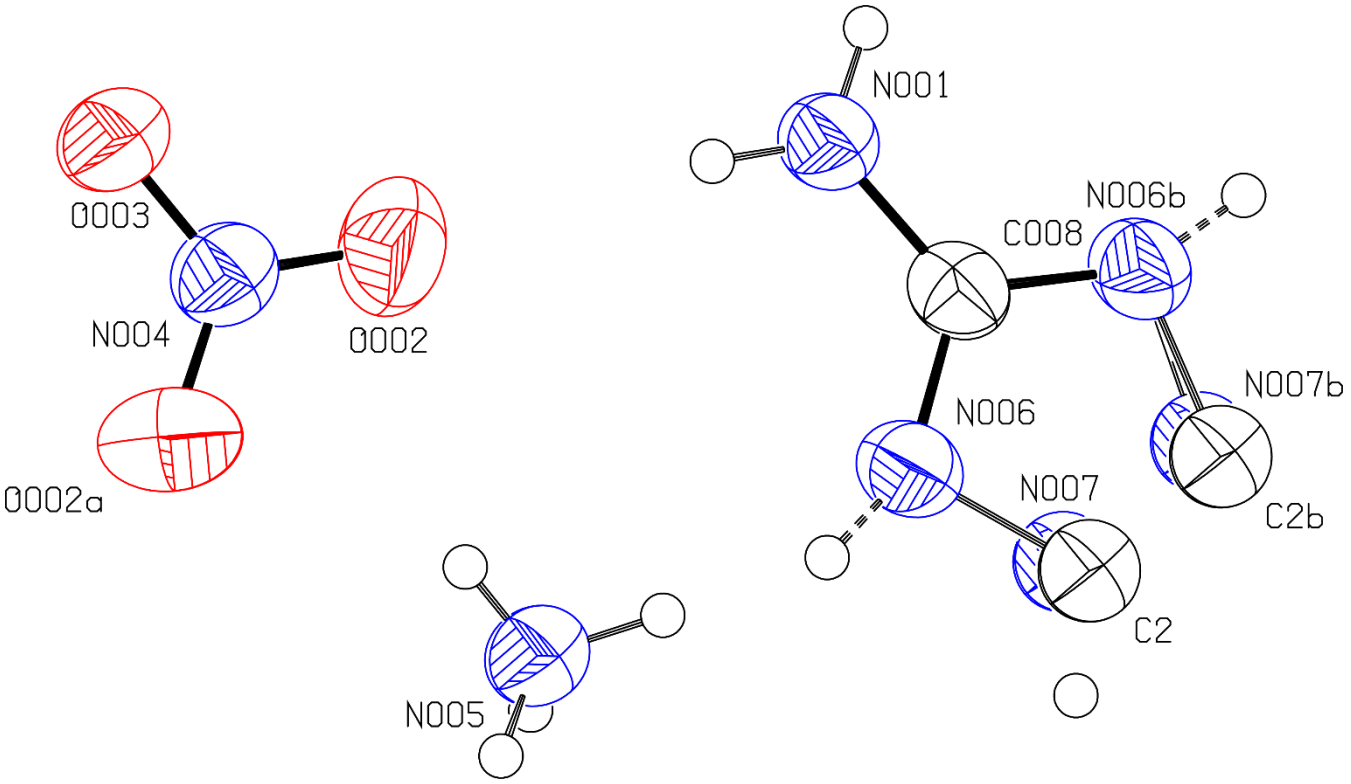

Figure S4. Thermal ellipsoid plot for **AN:5AT** at 293(2) K.

AN:4Cl

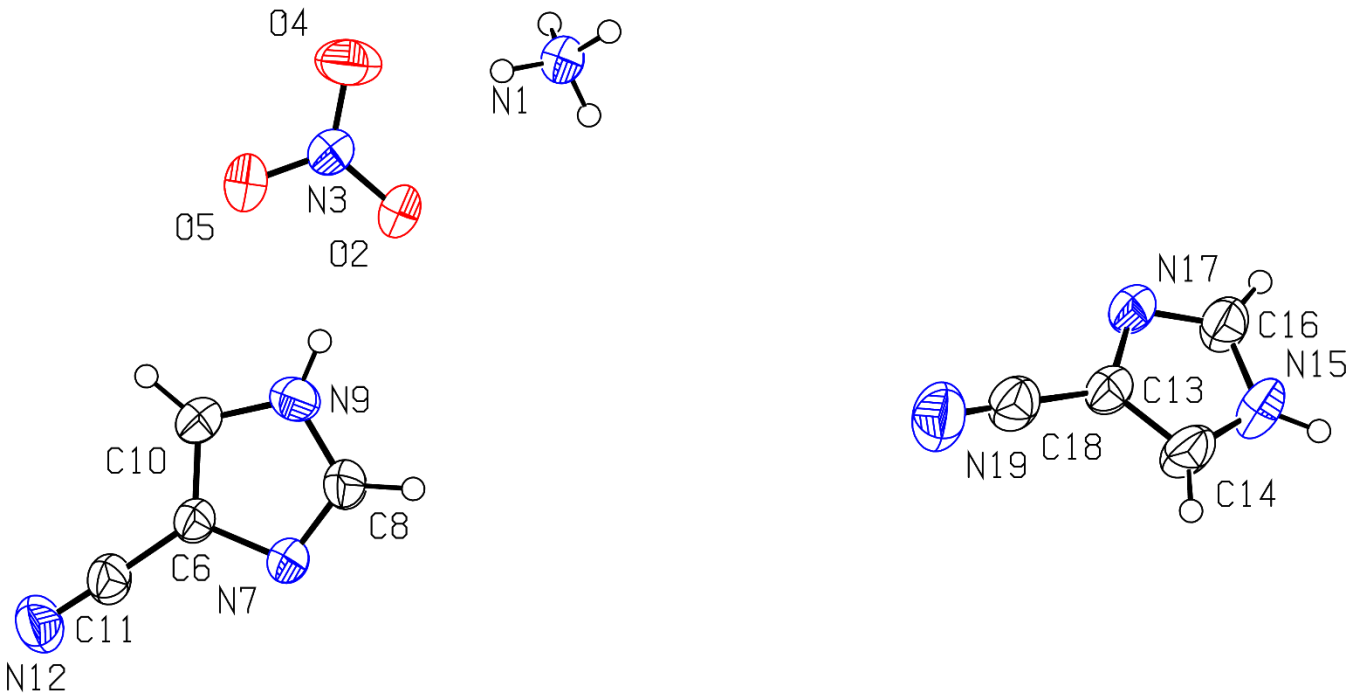

Figure S5. Thermal ellipsoid plot for **AN:4Cl** at 293(2) K.

AN:2P

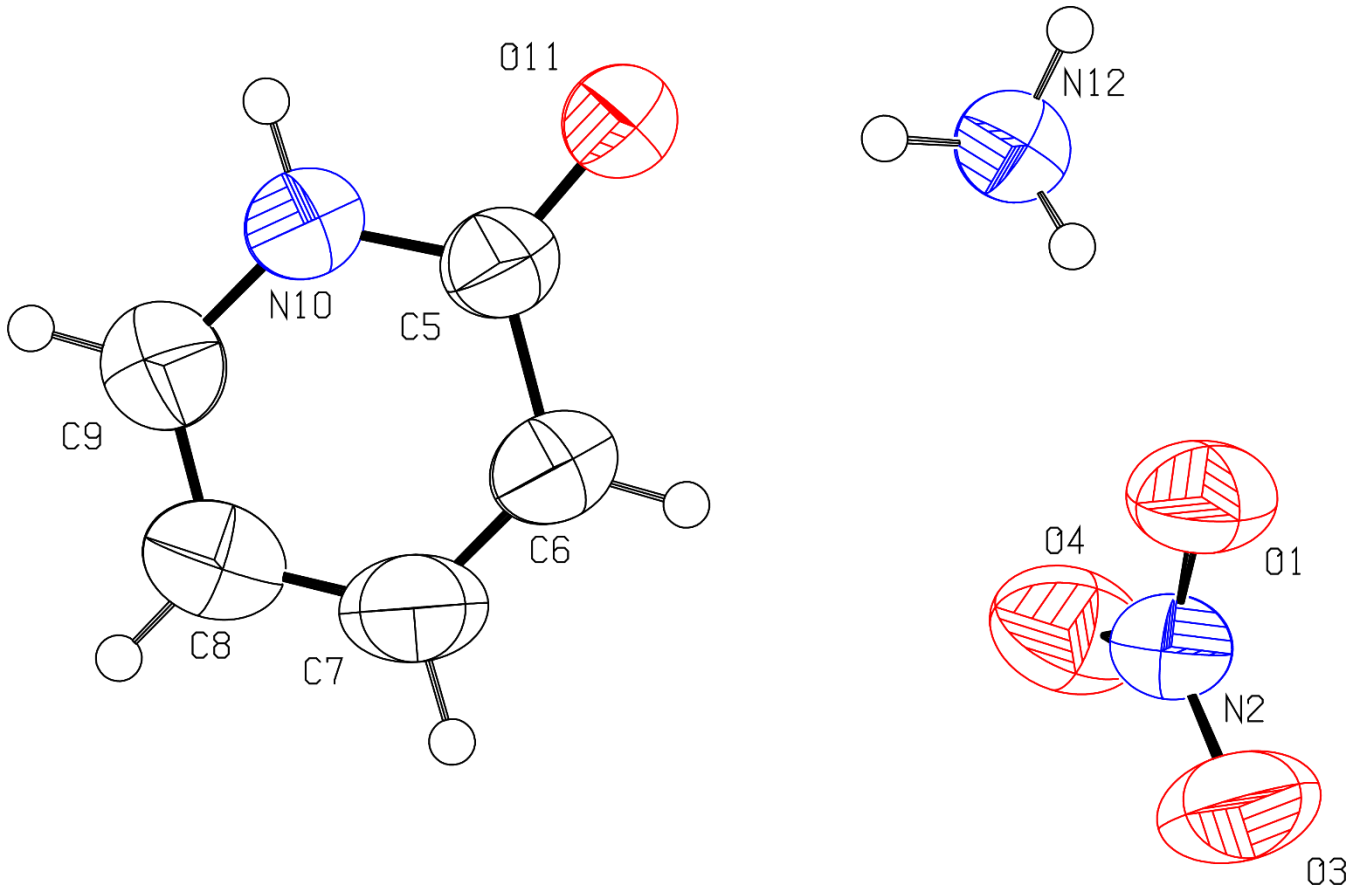

Figure S6. Thermal ellipsoid plot for **AN:2P** at 293(2) K.

AN:2IM

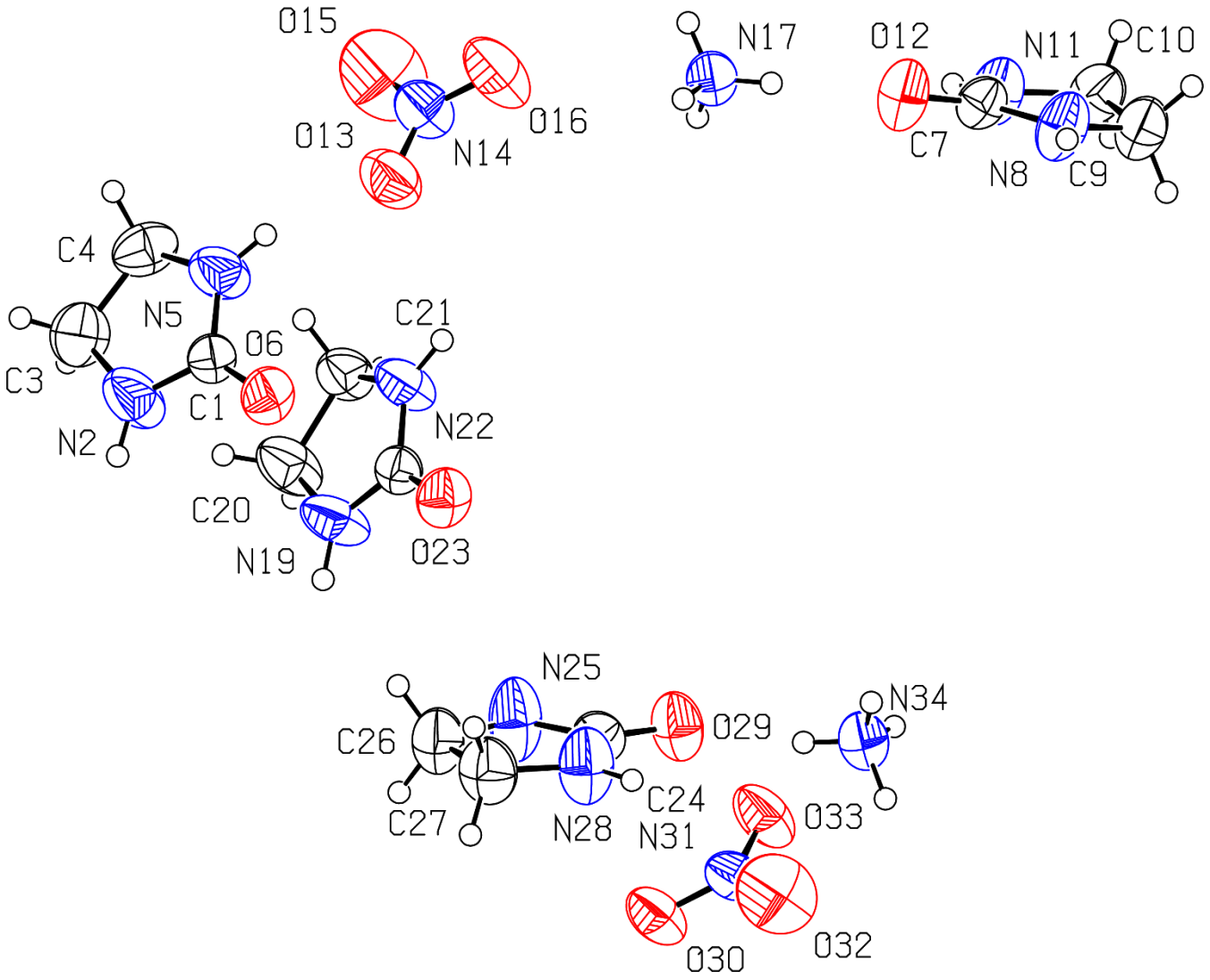

Figure S7. Thermal ellipsoid plot for **AN:2IM** at 293(2) K.

AN:5N2P

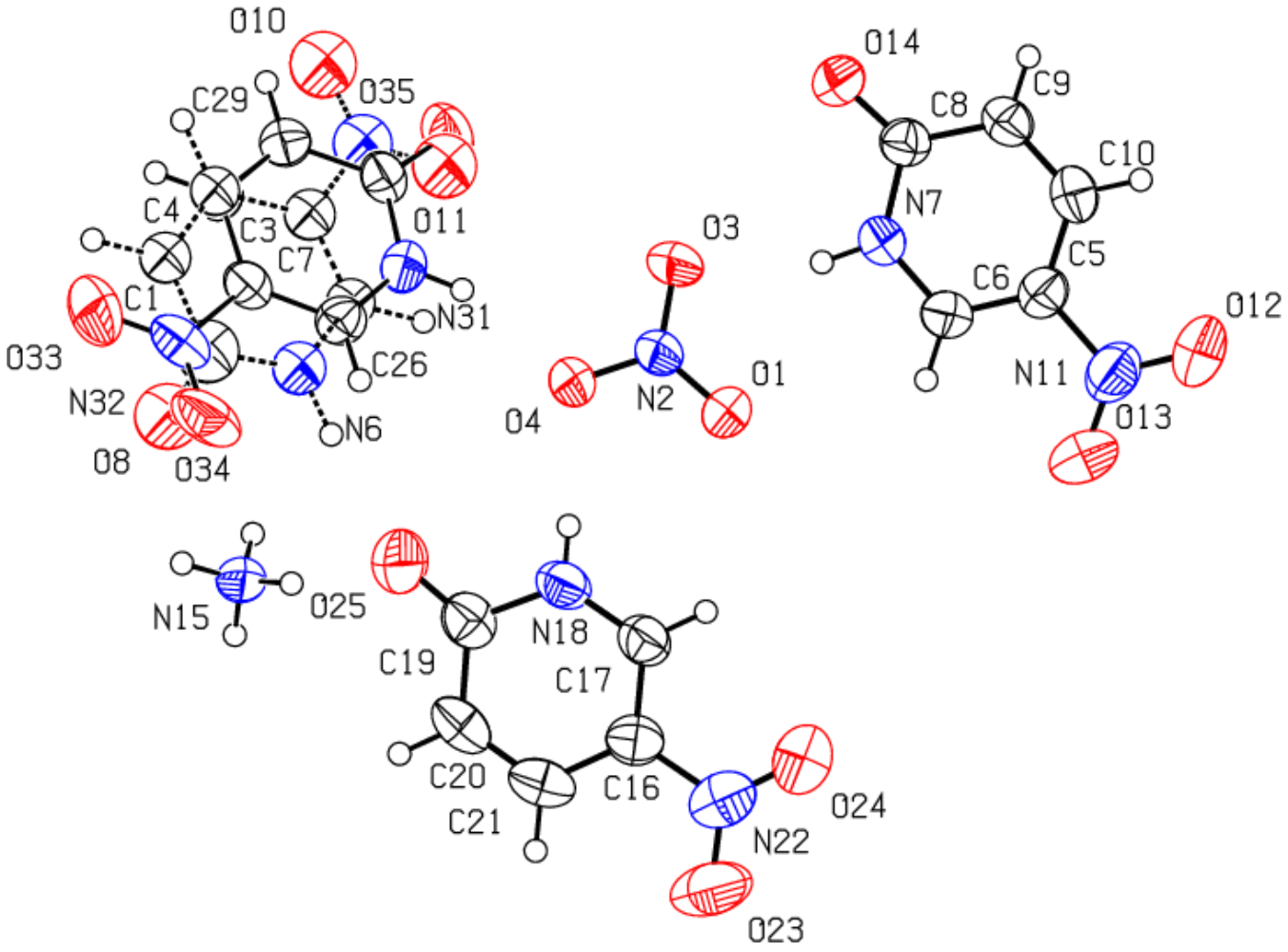

Figure S8. Thermal ellipsoid plot for **AN:5N2P** at 293(2) K.

SI 4. PXRD Data

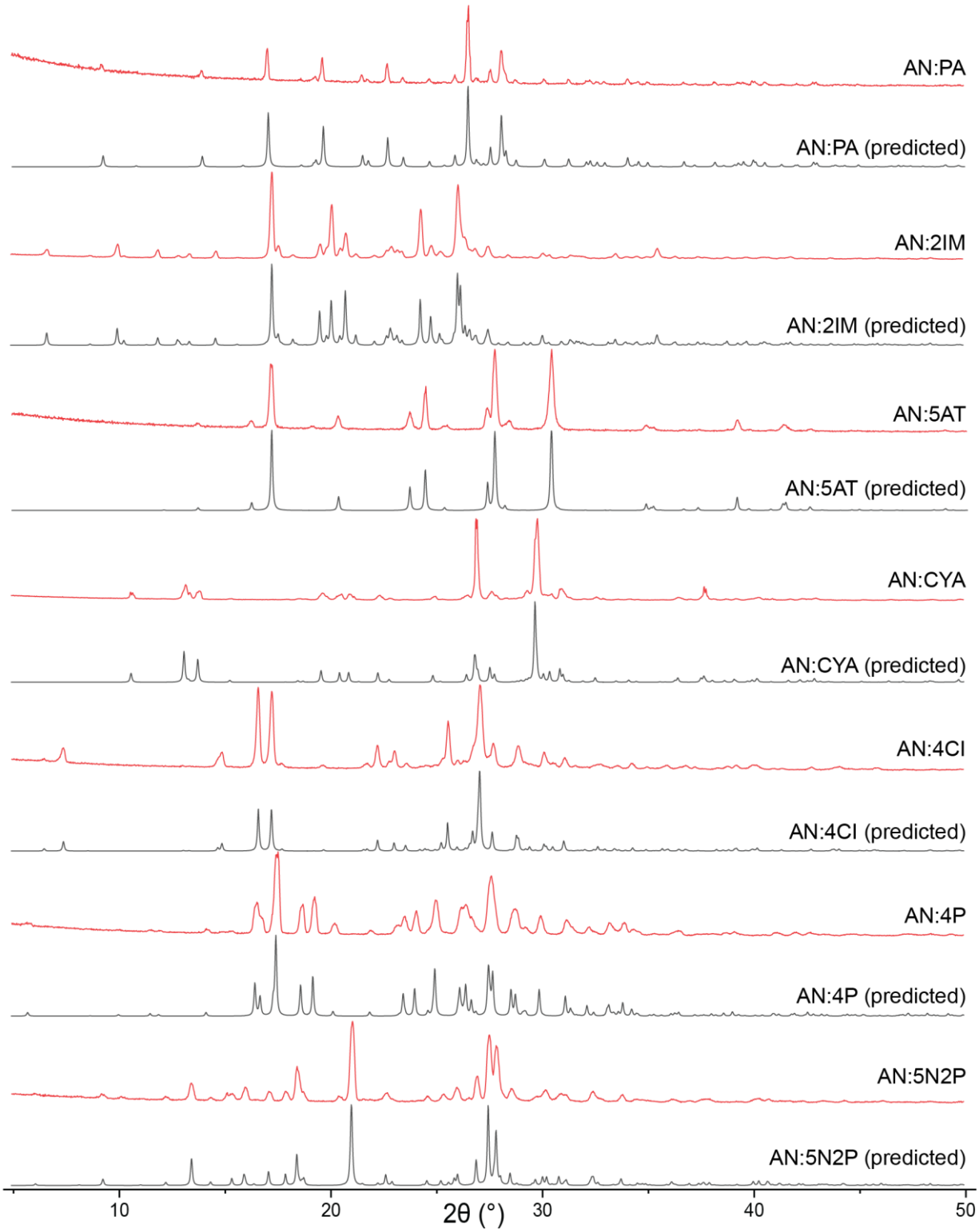

Figure S9. Experimental and predicted PXRD data for all obtained ionic cocrystals except for AN:2-pyridone, which deteriorates rapidly under ambient conditions.

SI 5. DSC Data

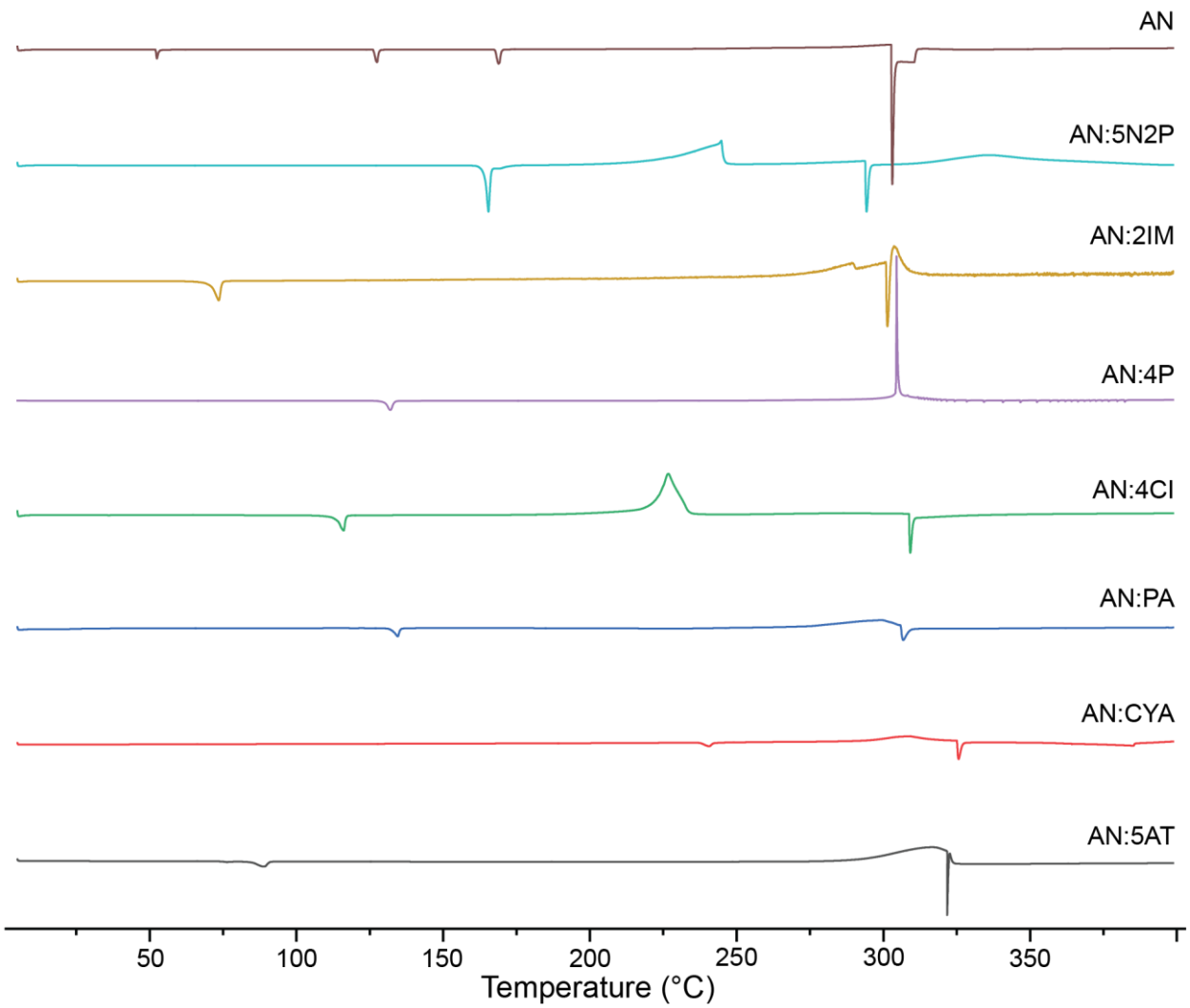

Figure S10. DSC traces (exotherm up) for AN and all obtained cocrystals except for AN:2-pyridone, which deteriorates rapidly under ambient conditions. The IV to III phase transition of AN, visible here at 53 °C, has been eliminated in each cocrystal.

SI 6. CSD Search Parameters

Nitrate-containing cocrystals

Search conducted using ConQuest.2020.11 [5.42] on March 16th, 2022. The search was conducted with the following requirements:

1) Nitrate ion
2) Number of residues >=3
3) 3D coordinates determined
4) Only single crystal structures
5) Only organics

The search was then refined to include only structures with nitrate···H-N contacts (default ConQuest contact value).

SI 7. References

[1] O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. a. K. Howard, H. Puschmann, *J. Appl. Crystallogr.* **2009**, *42*, 339–341.
[2] G. M. Sheldrick, *Acta Crystallogr. Sect. Found. Adv.* **2015**, *71*, 3–8.
[3] G. M. Sheldrick, *Acta Crystallogr. Sect. C Struct. Chem.* **2015**, *71*, 3–8.
[4] M. Kaźmierczak, E. Patyk-Kaźmierczak, A. Katrusiak, *Cryst. Growth Des.* **2021**, *21*, 2196–2204.