Structural landscape of multicomponent solids based on sulfa drugs

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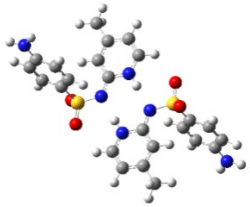
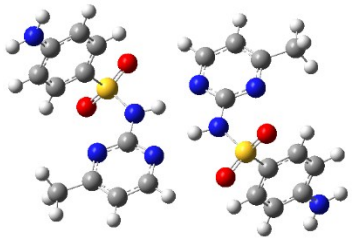
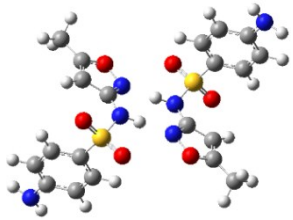
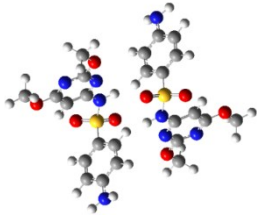
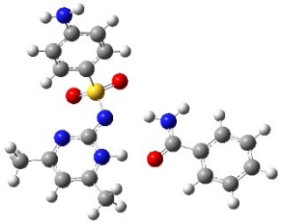
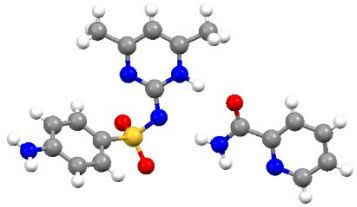
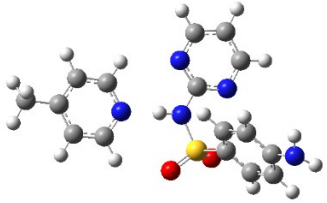
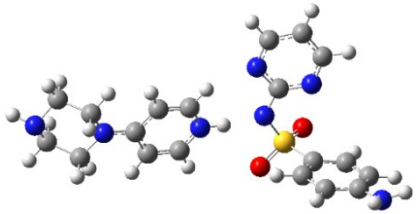
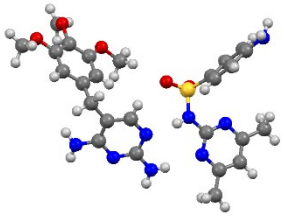
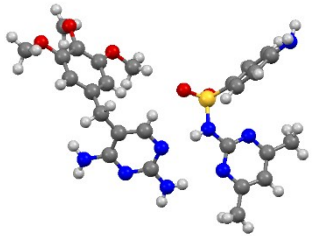
Table S1: Synthons considered for the calculation of energies as listed in Table 6.

 **SUTHAZ29**	 **XIFKON01**	 **SLFNMA03**	 **SLFNMB05**
 **SFDMOX04**	 **SLFNMD10**	 **EXAPAV**	 EXAPEZ
 **TICREE**	 **TICSAB**	 **RASSUZ**	 SMZTMP

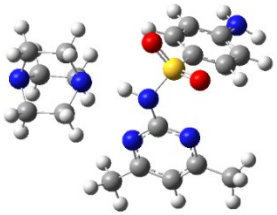
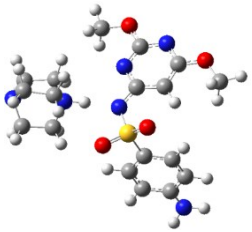
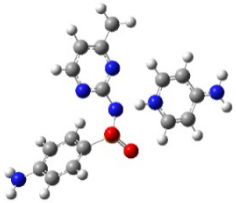
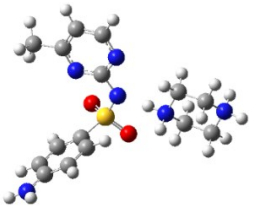
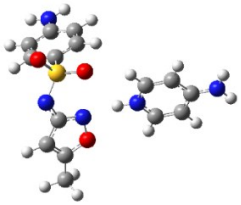
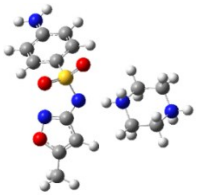
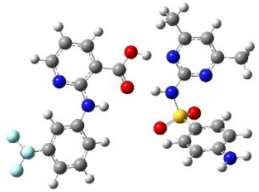
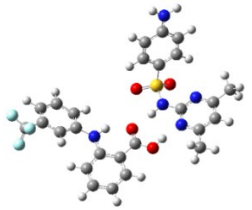
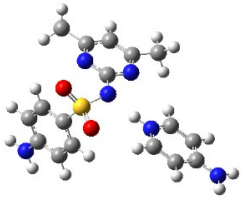
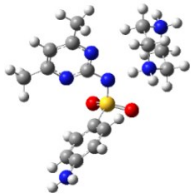
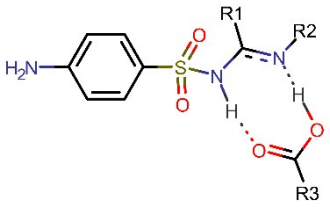
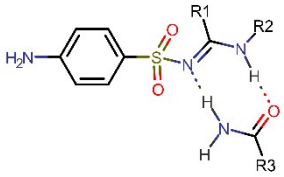
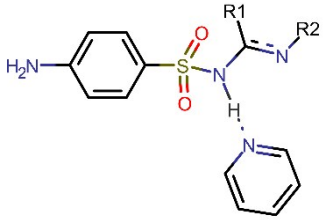
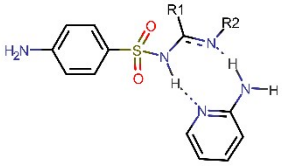
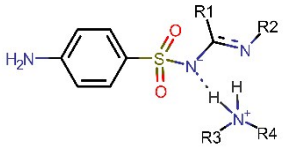
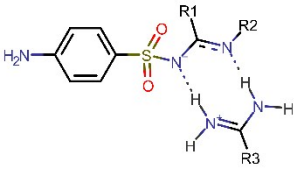
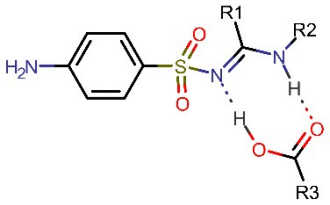
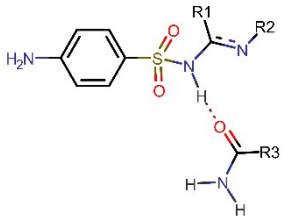
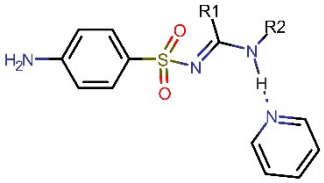
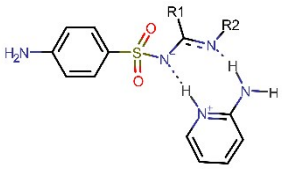
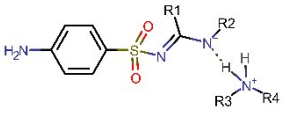
 VIPXOJ	 VACBUZ	 SOLID1	 SOLID2
 SOLID3	 SOLID4	 SOLID5	 SOLID6
 SOLID7	 SOLID8		

Table S2. Occurrences of various SD−coformer synthons in the previously reported multicomponent solid forms of SDs with distinct organic coformers.

SD−Carboxylic acid	SD−amide	SD−pyridine	SD−2-aminopyridine	SD−amine	SD−banzamidine
 16	 5	 6	 3	 6	 2
 2	 1	 2	 1	 8	

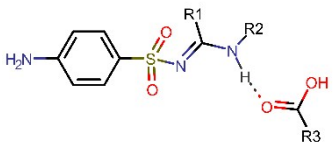
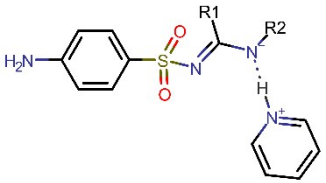
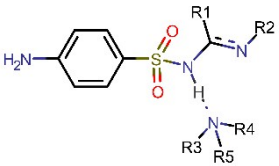
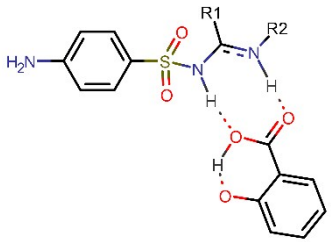
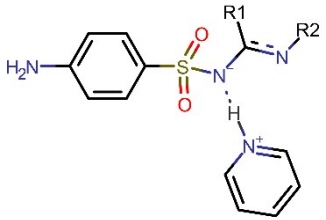
 3		 1		 1	
 2		 3			

Table S3. Occurrences of various SD-coformer synthons in the previously reported SD based solids and those reported in the present study(red colored), and the type of SD-SD synthons present in the input SDs. Various possible SD−coformer synthons are shown in Table 1 and Scheme 1.

Sulfa drug (SD)	**SD−SD synthon present in the most stable form of the parent SD**	**SD-coformer synthon type (see Scheme 1)**					
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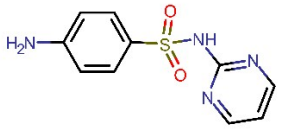
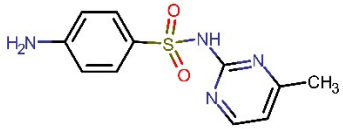
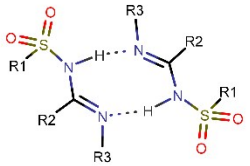
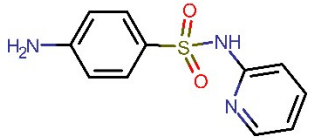
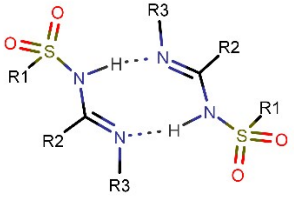
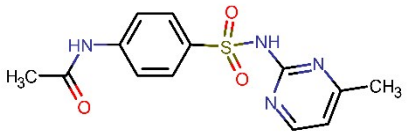
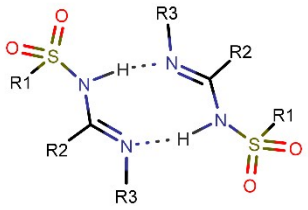
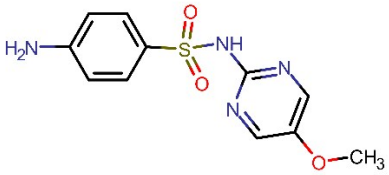
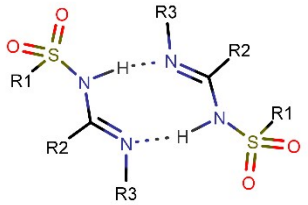
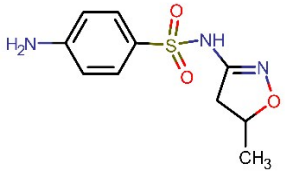
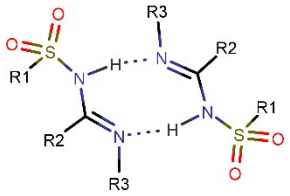
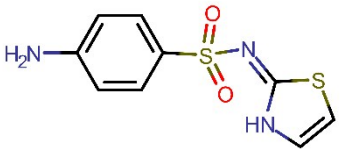
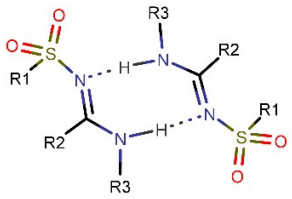
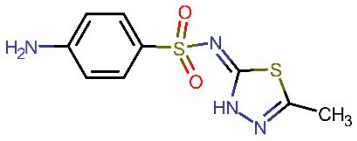
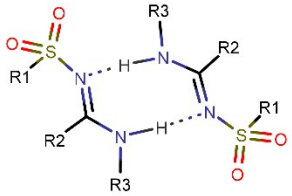
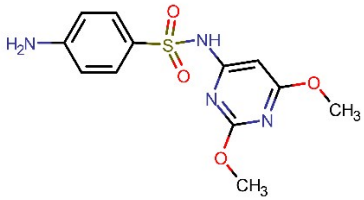
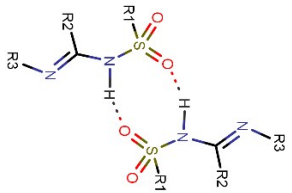
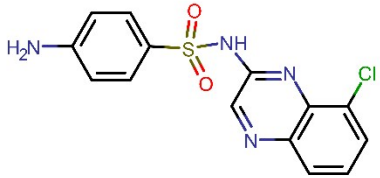
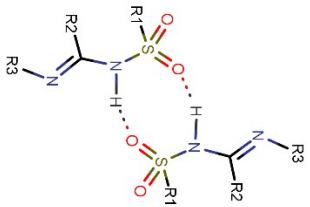
Sulfadiazine (sdz) 				5		1	
Sulfamerazine (smr) 				1		1	1
Sulfapyridine 						1	

N-4acetyl sulfamerazine 							
5-methoxy-sulfadiazine (smd) 		1					
Sulfamethoxazole (smx) 				1	2	1 1	
Sulfathiazole 		2	1	1		7	1

Sulfamethiazole 		1	1	1			
Sulfadimethoxine 			1	2		5	
							

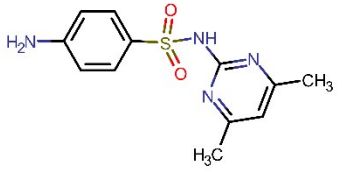
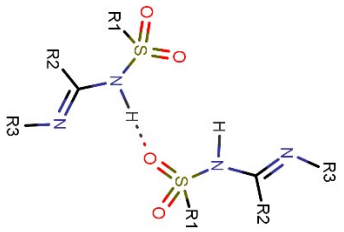
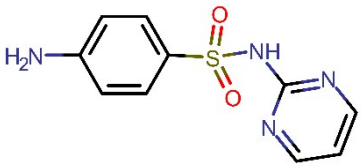
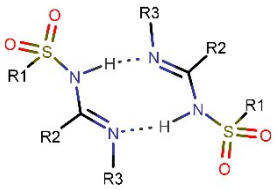
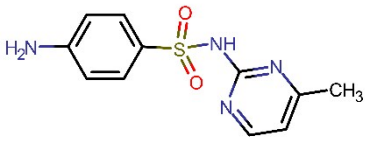
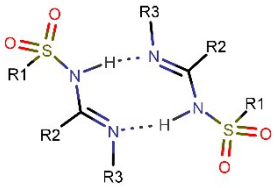
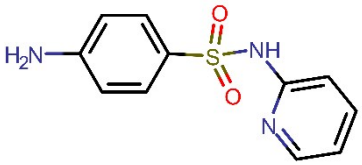
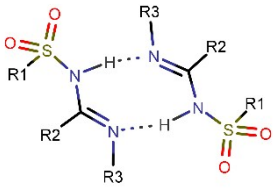
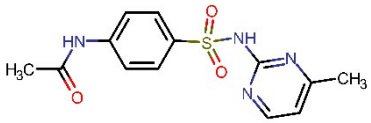
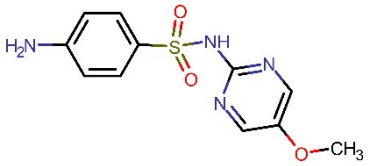
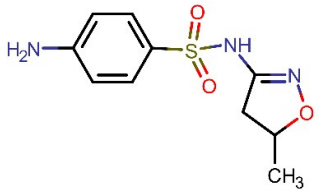
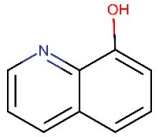
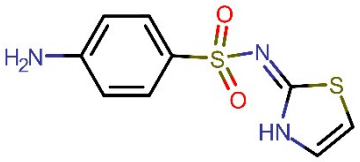
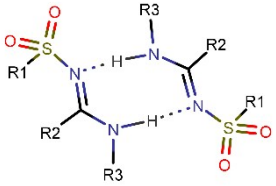
Sulfamethazine (smz) 		19 2	3	3 1	2	1 1	

Table S4. Classification of the previously reported SD based solids with various coformers that do not fit in Table S1 and those with various solvents based on whether or not the coformer/solvent disrupt the key SD−SD synthon present in the input SD. The reported salts with strong organic and inorganic acids shown in the last column are not considered in the analysis.

Sulfa drug	**SD−SD synthon present in the most stable form of the parent SD**	**Coformer**		**Solvate**		**Salt former (anion)**
		SD−SD disrupted	SD−SD undisrupted	SD−SD disrupted	SD−SD undisrupted	
Sdz 			(E)-1,2-bis(4-pyridyl)ethylene & 1,2-bis(4-pyridyl)acetylene			I^-, BF_4^-, NO_3^-, CH_3-CH_2-SO_3^-, HO-C_6H_6-SO_3^-, Cl^-
Smr 			2-methyl-1,4-nephthoquinone		1,4-dioxane (Form I & II), DMF, DMAc, Cyclopentanone, 3-methylpyridine, CH3CN + Crown Ether and Tetrahydrofuran	
Sulfapyridine 					Nitromethane, oxalic acid dibutyl ester, DMSO	

N-4acetyl sulfamerazine 					H_2O, CH_3OH CH_3COOH & 1-4 dioxane	
5 methoxy-sulfadiazine 					CH_3CN, 1-4 dioxane & THF	
Smx 		3.5 di nitro salicylic acid, Cl^-				
Sulfathiazole 		Oxalic acid	4-nitrobenzoic acid, 4-amino sulfonamide,	CH_3CN + crown ether	CH_3CN, DMF, formyl piperidine & 1-4 dioxane	NO_3^-

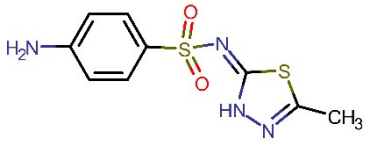
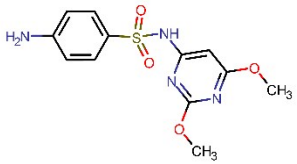
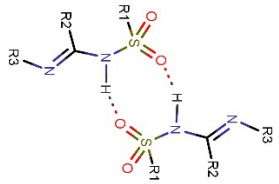
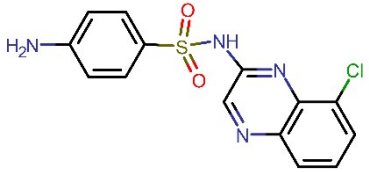
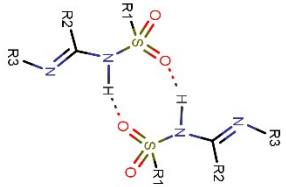
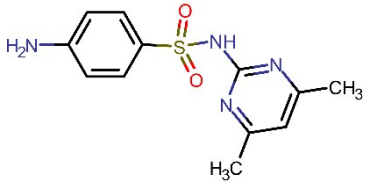
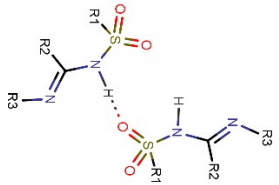
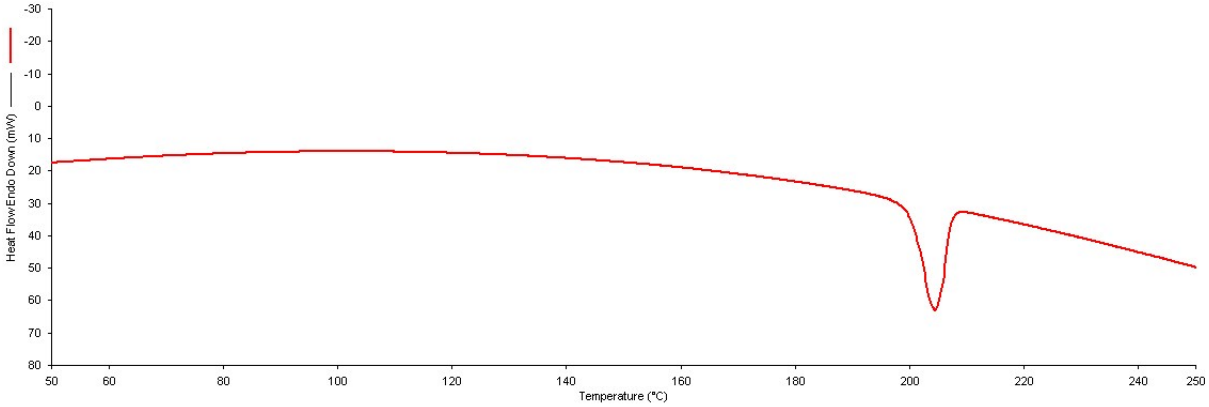
Sulfamethiazole 		Vanillic acid	Oxalic acid, adipic acid, suberic acid & 4-amino benzoic acid			SO_4^{2-}
Sulfadimethoxine 						
					CH_3CN	
Sulfamethazine (smz) 		2,4,6-trinitro phenol & saccharin		CH_3OH		

Table S5. Δ*p*Ka values of SD based solids forms reported in the present study.

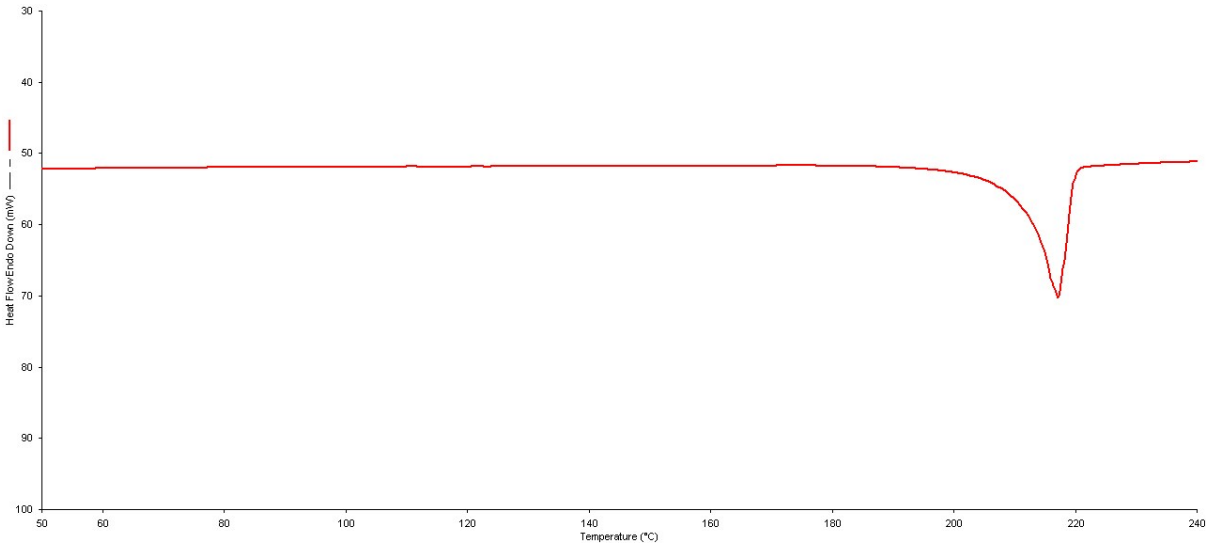
Solid	*p*Ka of SD	*p*Ka of coformer	Δ*p*Ka = *p*Ka(base) – *p*Ka(acid)	solid form
1	6.99	8.95	1.96	Salt
2	6.99	9.56	2.57	Salt
3	6.16	8.95	2.79	Salt
4	6.16	9.56	3.4	Salt
5	-1.97	1.88	-3.85	Cocrystal
6	-1.97	3.88	-5.85	Cocrystal
7	6.99	8.95	1.96	Salt
8	6.99	9.56	2.57	Salt

pKa of SD's and coformers were calculated using ChemAxon calculator, Marvin 15.2.16.0 (http://www.chemaxon.com).

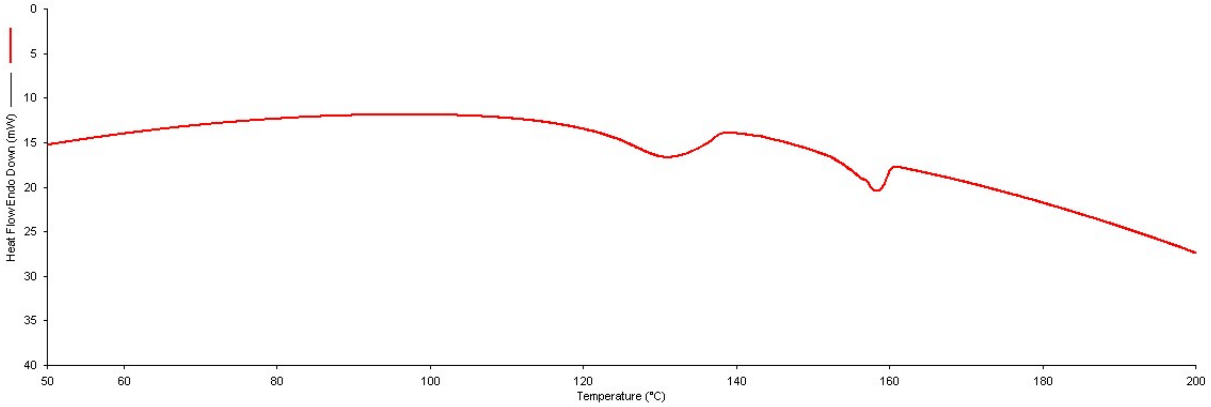
Solid 1



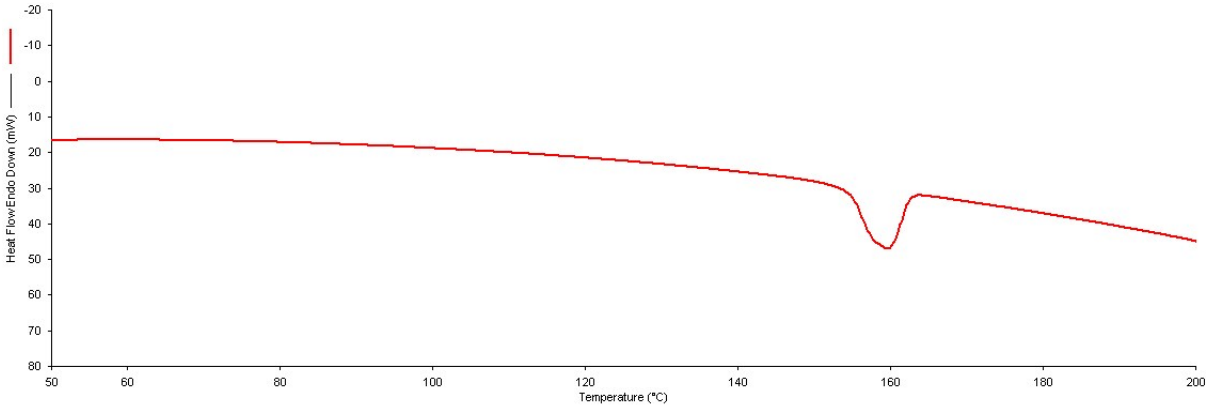
Solid 2



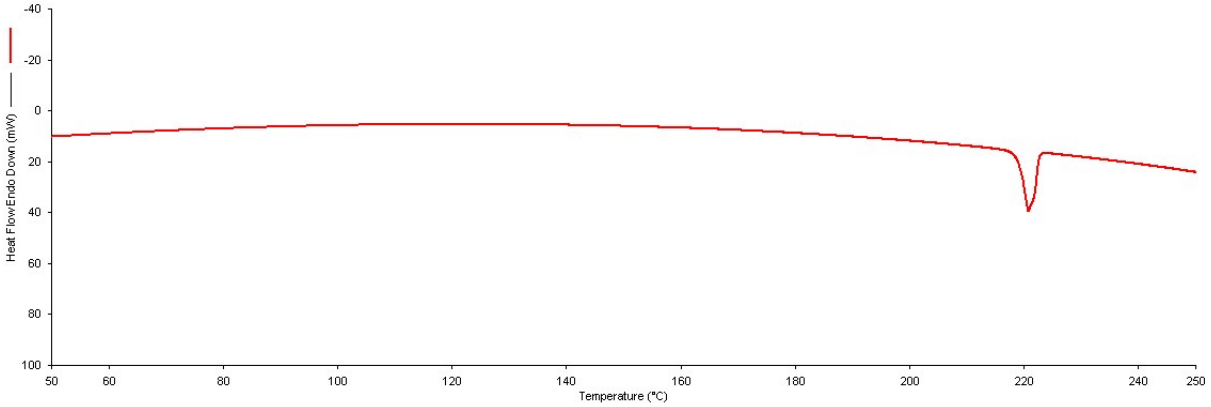
Solid 3



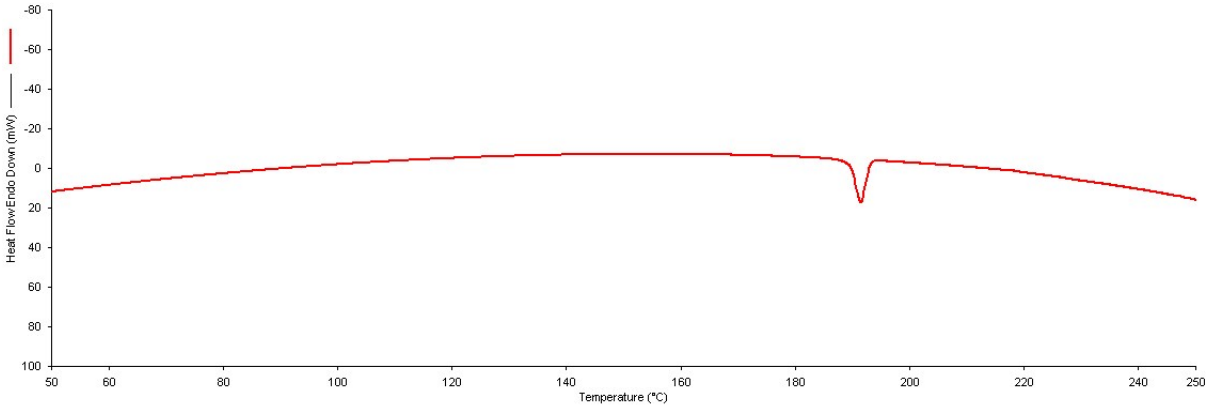
Solid 4



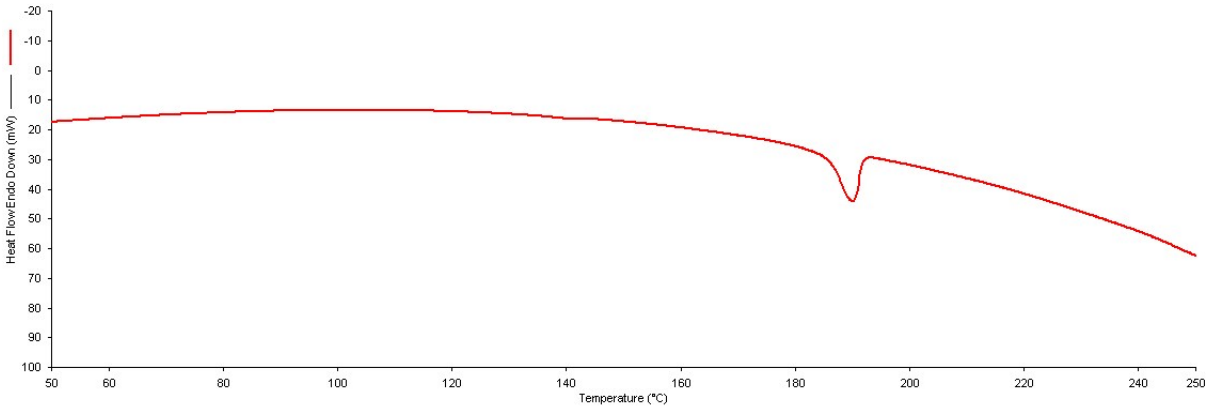
Solid 5



Solid 6



Solid 7



Solid 8

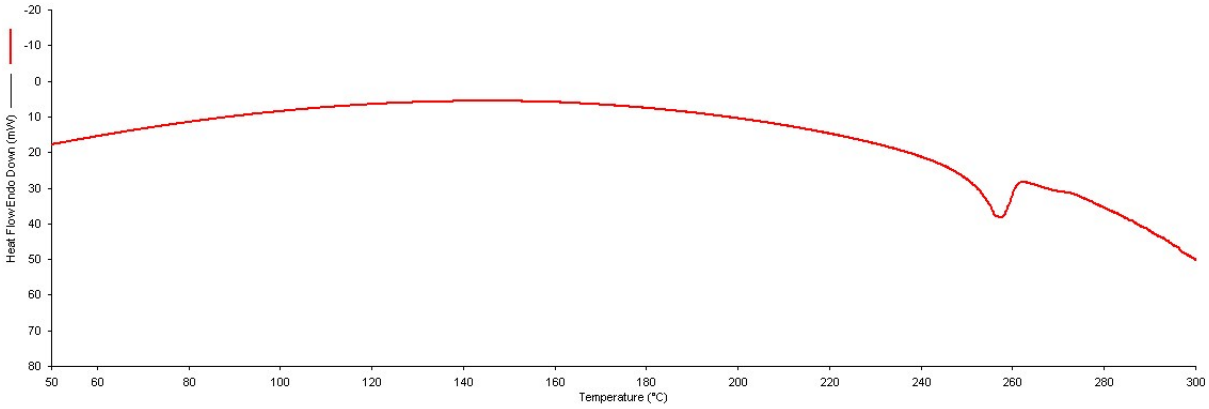
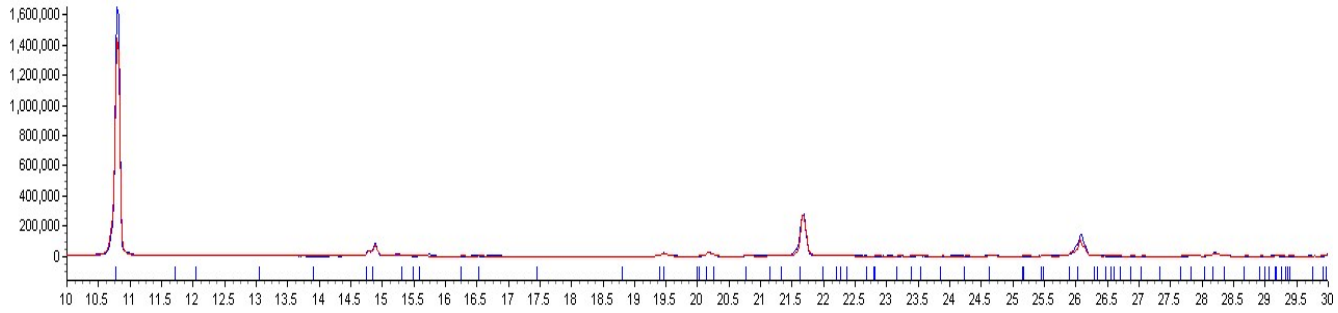
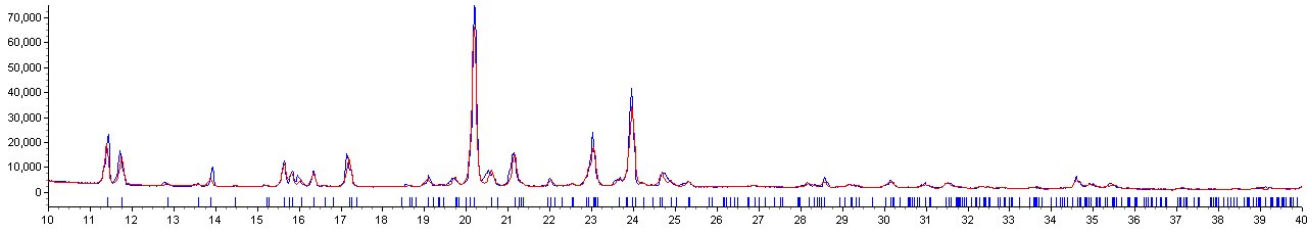


Figure S1. DSC scans of Sulfa drugs based solids 1–8 showing a single endothermic peak, except for the solid 3.

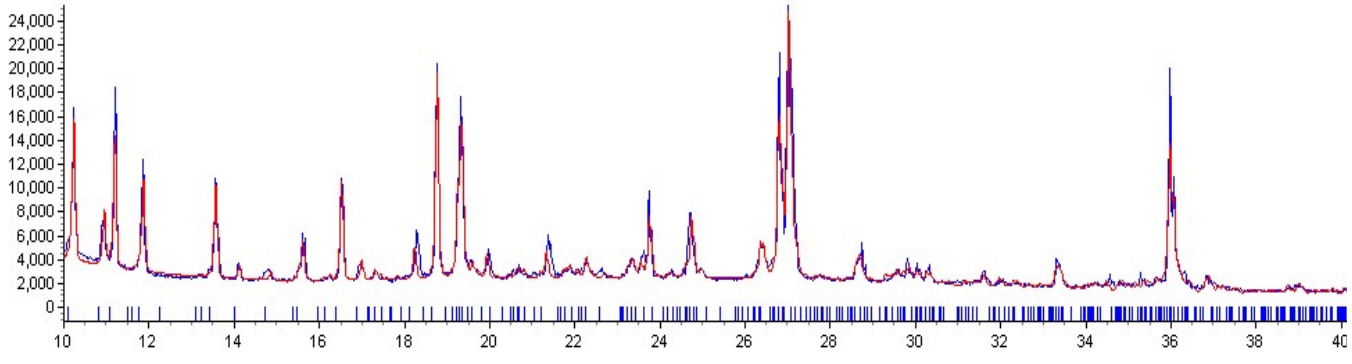
Solid 1



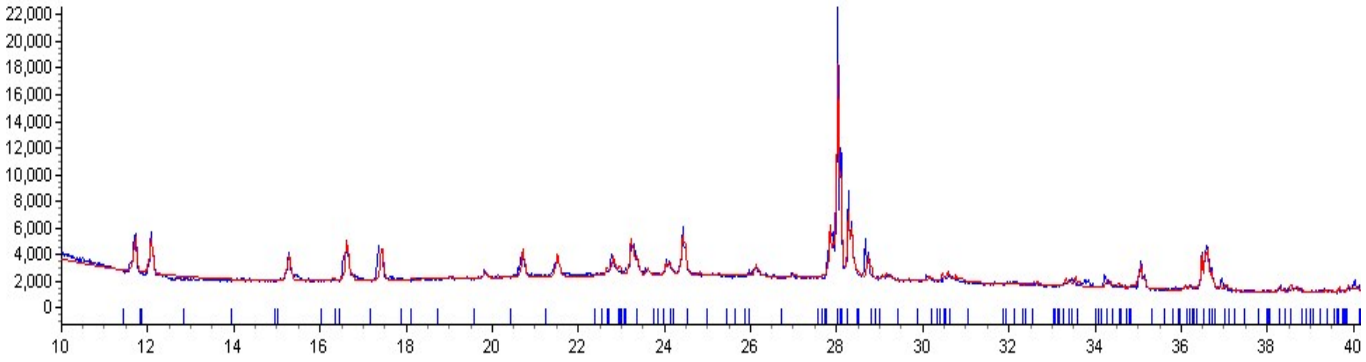
Solid 2



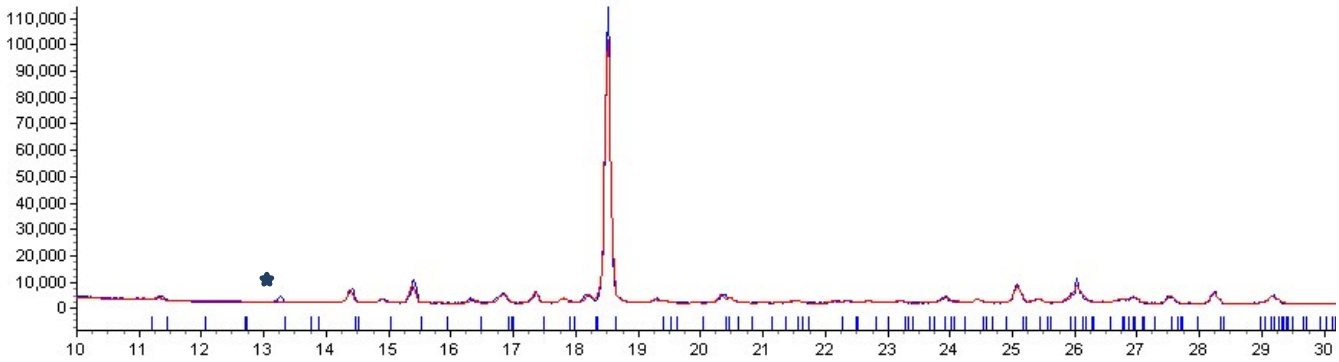
Solid 3



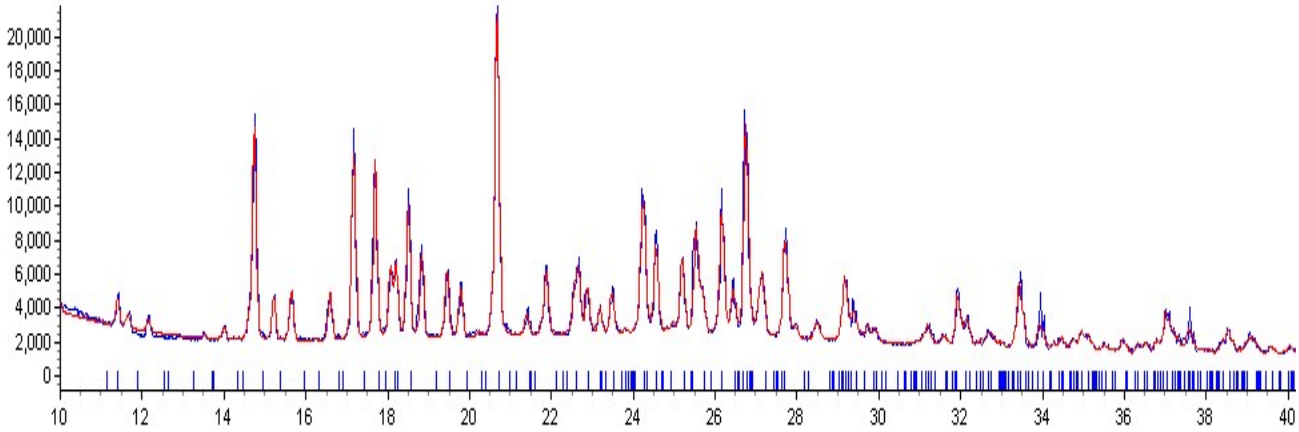
Solid 4



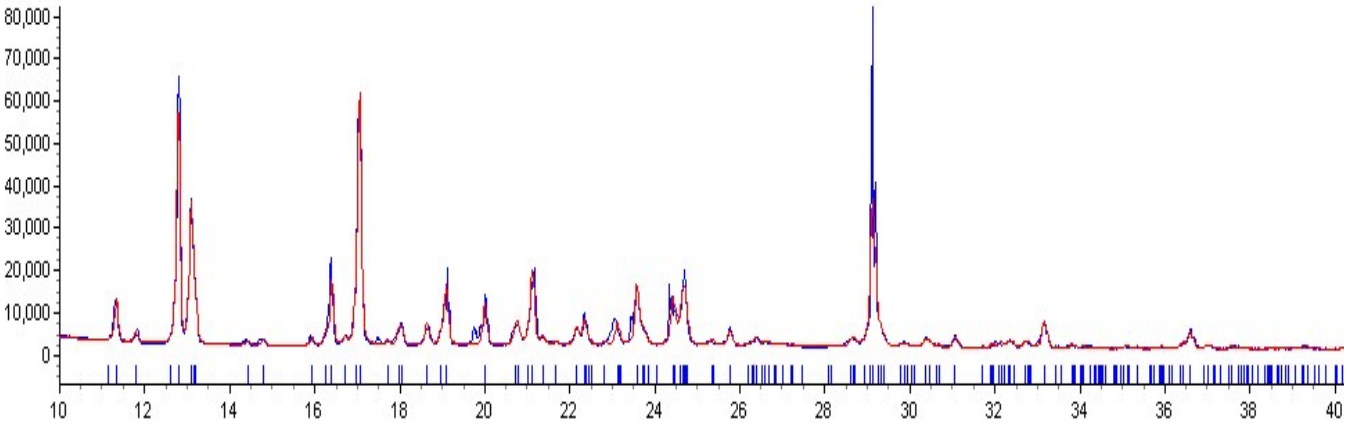
Solid 5



Solid 6



Solid 7



Solid 8

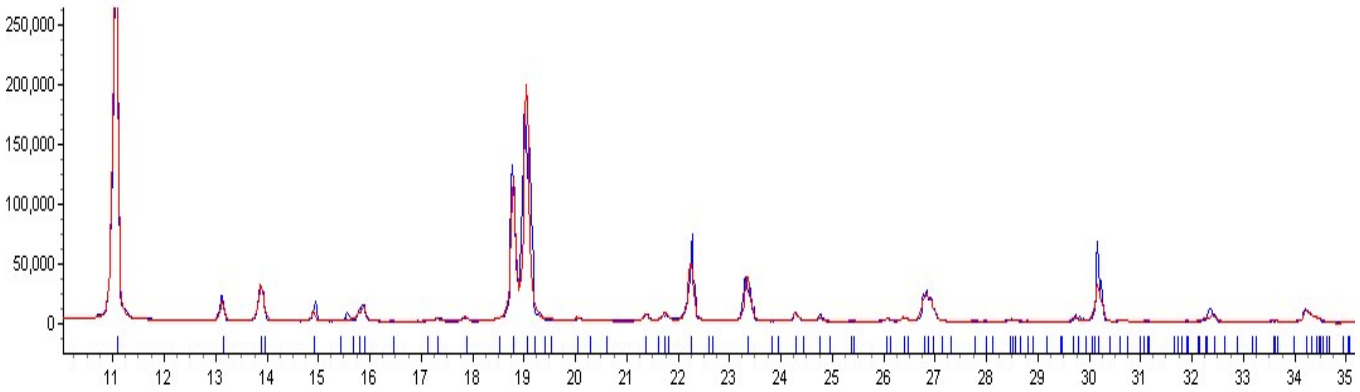


Figure S2. Rietveld refinement plots for **1–8**, indicating the homogeneity of the bulk samples. The plot shows the experimental powder XRD profile (blue line), the calculated (red line), and blue tick lines shows Bragg positions in the bottom.

Footnote: *Peak(s) marked with star correspond to an unidentified phase.