Supporting Information

Cocrystals of the Antiandrogenic Drug Bicalutamide: Screening, Crystal Structures, Formation Thermodynamics and Lattice Energies

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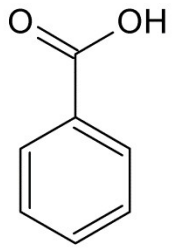
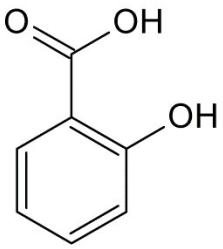
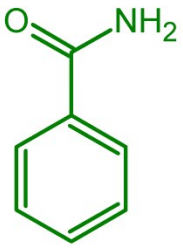


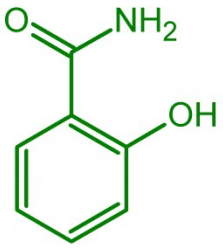
Benzoic acid



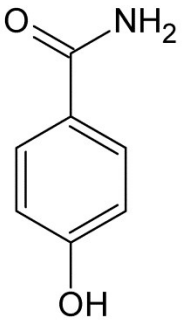
Salicylic acid



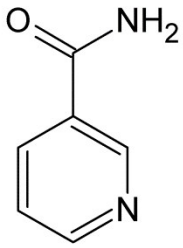
Benzamide



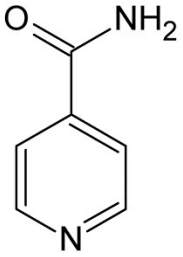
Salicylamide



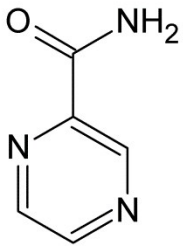
4- Hydroxybenzamide



Nicotinamide



Isonicotinamide



Pyrazinamide

Figure S1. Molecular structures of cocrystal formers used for screening experiments. The coformers that provided cocrystals are colored in green.

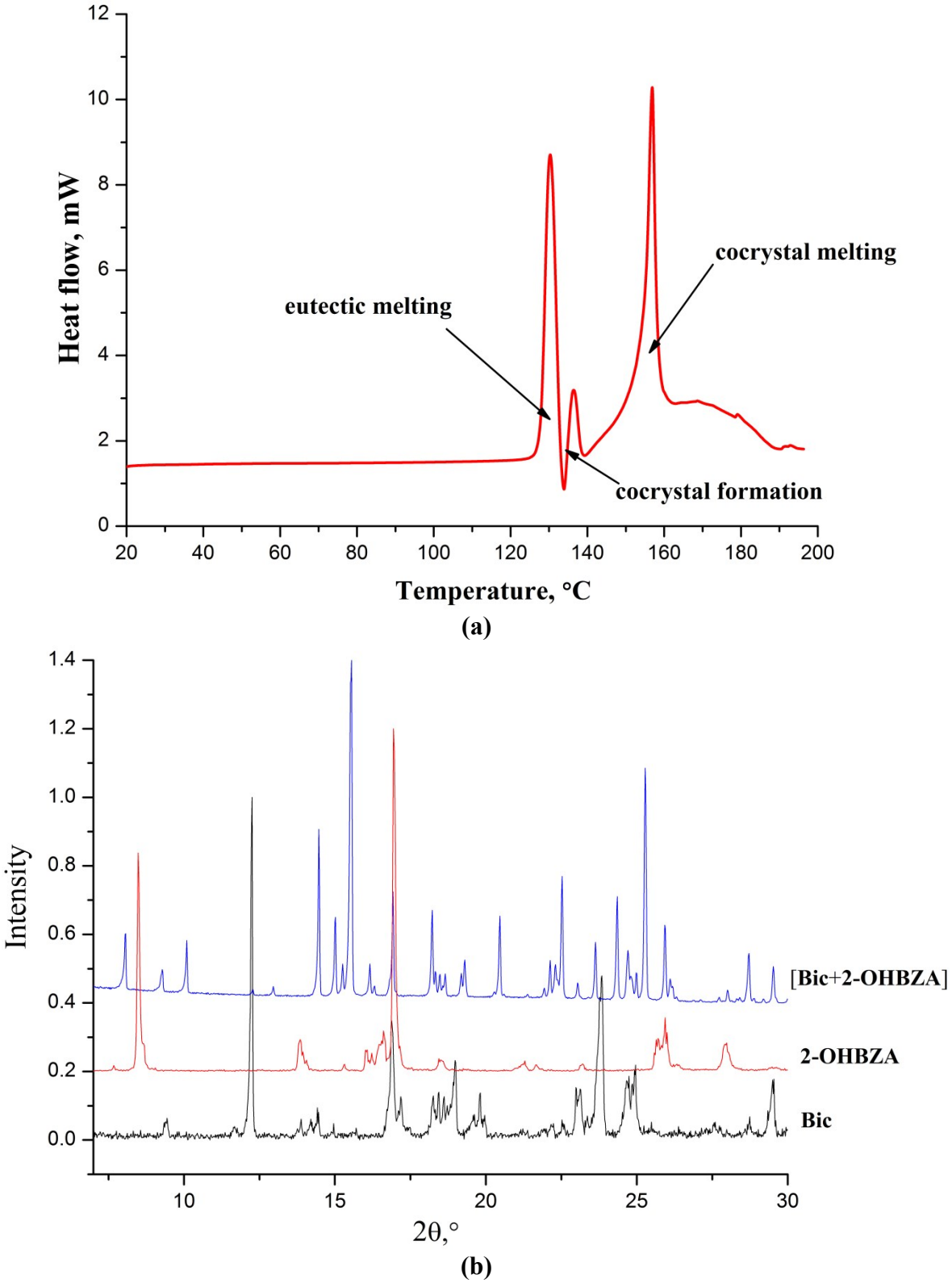


Figure S2. (a) DSC traces for (bicalutamide + salicylamide) physical mixture in 1:1 molar ratio recorded at at 10°C·min^{-1} heating rate; **(b)** PXRD analysis of [**Bic**+**2OHBZA**] (1:1) after liquid-assisted grinding, pure bicalutamide (**Bic**) and pure salicylamide (**2OHBZA**).

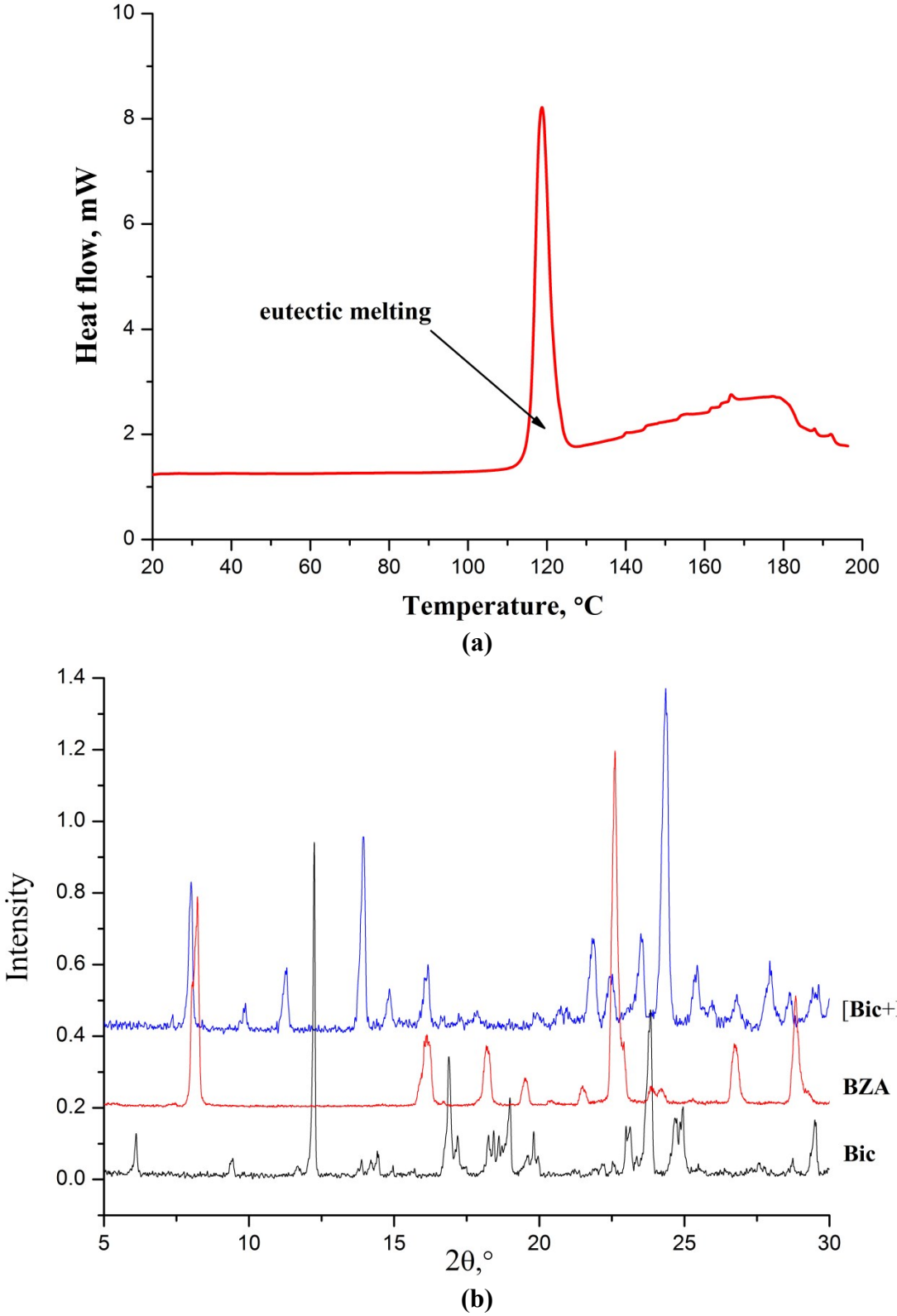
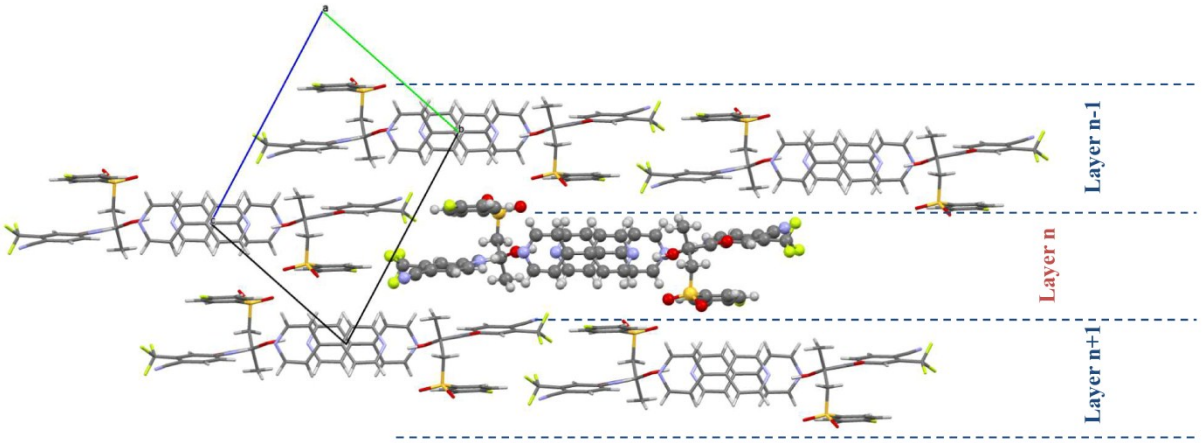
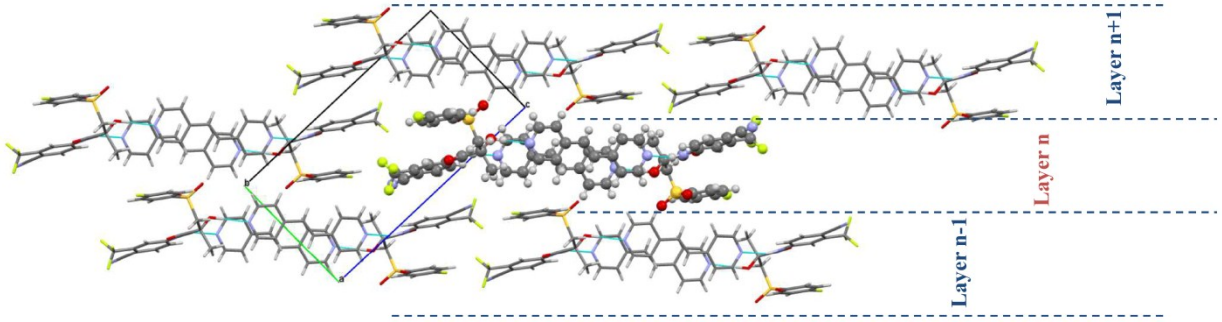


Figure S3. (a) DSC traces for (bicalutamide + benzamide) physical mixture in 1:1 molar ratio recorded at at 10°C·min^{-1} heating rate; **(b)** PXRD analysis of [**Bic**+**BZA**] (1:1) after liquid-assisted grinding, pure bicalutamide (**Bic**) and pure benzamide (**BZA**).



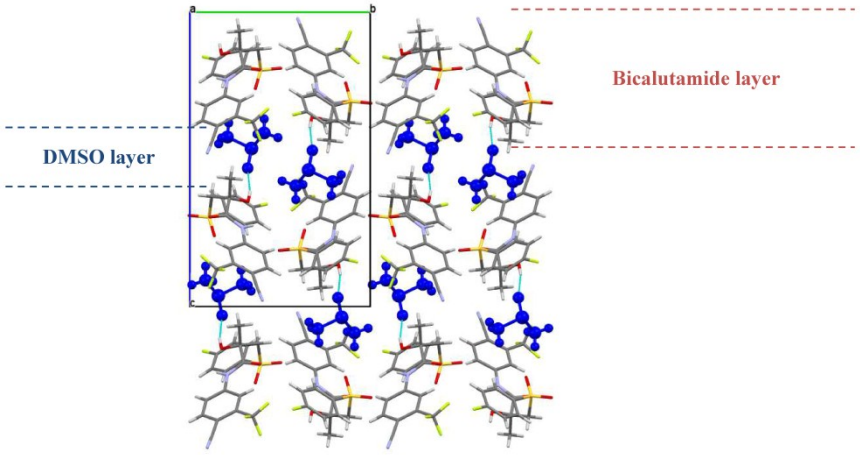
[Bic+4,4'-bipyridine] (1:1)

(a)



[Bic+trans-1,2-bis(4-pyridyl)ethene] (1:1)

(b)



[Bic+DMSO] (1:1)

(c)

Figure S4. Molecular packing projections for (**a**) [**Bic+4,4'-bipyridine**] (1:1), (**b**) [**Bic+trans-1,2-bis(4-pyridyl)ethene**] (1:1) and (c) [**Bic+DMSO**] (1:1). [**Bic+BZA**] and [**Bic+2OHBZA**] cocrystals. The supramolecular tetrameric unit in the cocrystals is shown in ball and stick style. The layers are separated by dash lines. The DMSO molecules in [**Bic+DMSO**] are colored in blue.

Table S1. Solubility values of bicalutamide, benzamide, salicylamide (in mol·L^{-1}) and solubility ratios in the selected organic solvents

Solvent	S^{Bic}	S^{BZA}	S^{2OHBZA}	S^{BZA}/S^{Bic}	S^{2OHBZA}/S^{Bic}
Methanol	0.04 ± 0.01	1.70 ± 0.05	0.86 ± 0.02 (0.89)[a]	39.5	20.1
Acetonitrile	0.11 ± 0.02	0.48 ± 0.02 (0.48)[a]	0.58 ± 0.01 (0.59)[a]	4.6	5.5
Ethyl acetate	0.07 ± 0.01	0.37 ± 0.02	0.74 ± 0.02 (0.73)[a]	5.0	10.1
Acetone	0.30 ± 0.03	0.85 ± 0.02	1.45 ± 0.03 (1.49)[a]	2.8	4.8

[a]Values in the brackets indicate the literature data taken from ref. [1S].

Table S2. Temperature dependence (in °C) of solubility, S ($mol \cdot L^{-1}$), of bicalutamide, benzamide, salicylamide and the corresponding cocrystals in chloroform.

Temp.	**Bic**	**BZA**	**2OHBZA**	[**Bic**+**BZA**]		[**Bic**+**2OHBZA**]	
	$S \cdot 10^3$	S	$S \cdot 10^2$	$S \cdot 10^3$	$K_{sp} \cdot 10^4$	$S \cdot 10^3$	$K_{sp} \cdot 10^4$
18.0	5.6 ± 0.2	0.16 ± 0.05	3.8 ± 0.1	13.9 ± 0.5	1.9	8.8 ± 0.3	0.8
22.0	6.2 ± 0.2	0.19 ± 0.03	4.4 ± 0.1	16.6 ± 0.3	2.8	10.8 ± 0.5	1.0
25.0	6.7 ± 0.1	0.21 ± 0.05	4.9 ± 0.1	18.9 ± 0.3	3.6	11.7 ± 0.4	1.4
30.0	7.7 ± 0.3	0.24 ± 0.06	6.0 ± 0.1	23.1 ± 0.7	5.4	14.3 ± 0.5	2.0

References:

(1S) Jouyban, A. *Handbook of solubility data for pharmaceuticals*; CRC Press: Boca Raton, 2010.