Electronic Supplementary Information

For

Crystal structure and optical properties of a pharmaceutical co-crystal - the case of melamine-barbital addition compound

M. Gryl,[a] K. Stadnicka,[a] T. Seidler,[a] I. Matulková [b], I. Němec [b], N. Tesařová [c], P. Němec[c]

[a] Jagiellonian University, Faculty of Chemistry, Department of Crystal Chemistry and Crystal Physics, Ingardena 3, 30-060 Kraków, Poland. Email: gryl@chemia.uj.edu.pl

[b] Charles University in Prague, Faculty of Science, Department of Inorganic Chemistry, Hlavova 2030, 128 40 Prague 2, Czech Republic.

[c] Charles University in Prague, Faculty of Mathematics and Physics, Department of Chemical Physics and Optics, Ke Karlovu 3, 121 16 Prague 2, Czech Republic.

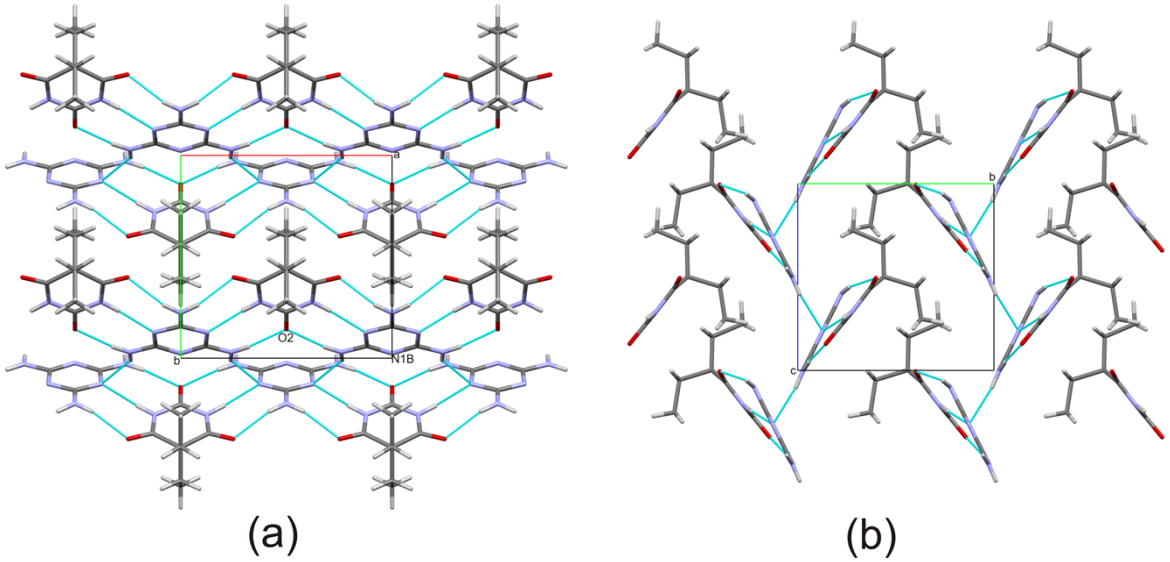


Fig. S1 (a) Packing of the melamine and barbital molecules viewed along [001]. The infinite crinkled tapes are running along [100]. (b) View of crystal structure along [100] direction. Polar twofold axis is parallel to c. Drawings were prepared in Mercury (C. F. Macrae, P. R. Edgington, P. McCabe, E. Pidcock, G. P. Shields, R. Taylor, M. Towler and J. van de Streek, J. Appl. Crystallogr., 2006, 39, 453.).

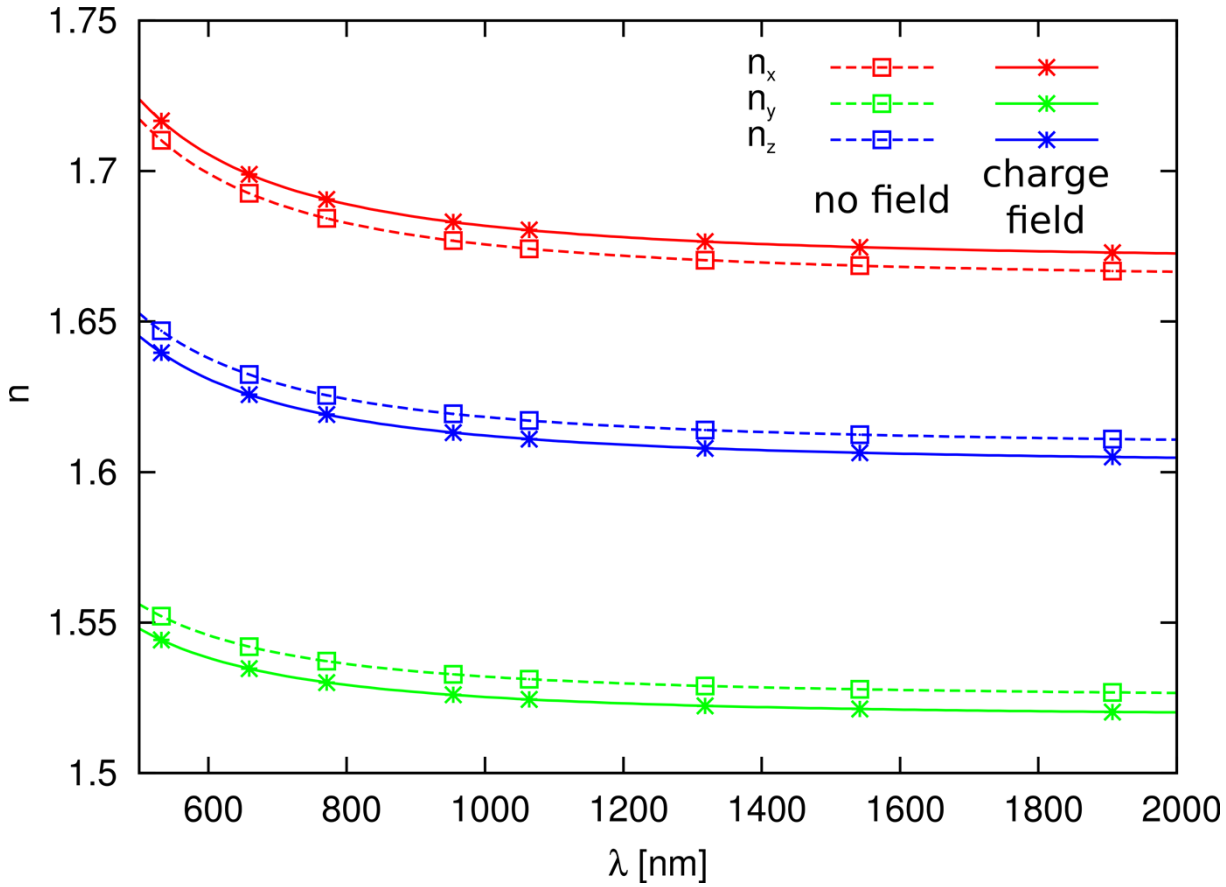


Fig. S2 Theoretically predicted refractive indices for the investigated crystal at MP2 level of theory (geometry II).

Table S1 Hydrogen bonds for I [Å,°]

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(4B)-H(4B)...O(4A)#1	0.95(1)	2.04(1)	2.972(1)	167(1)
N(2B)-H(2B2)...O(2A)	0.97(1)	1.98(1)	2.950(1)	173(1)
N(1A)-H(1A)...N(3B)	0.99(1)	1.93(1)	2.912(1)	175(1)
N(2B)-H(2B1)...N(3B)#3	0.95(1)	2.36(1)	3.170(1)	144(1)

Symmetry transformations used to generate equivalent atoms:

#1 -x,y,z #2 -x+1,y,z #3 -x+1/2,-y,z-1/2

Table S2 Selected (a) bond lengths, (b) valence angles (c) torsion angles at the experimental, A and B geometry.

(a)			
	exp	**A**	**B**
O2A - C2A	1.224(2)	1.231	1.209
C4A - O4A	1.218(1)	1.224	1.211
N1A - H1A	0.990(1)	1.377	1.013
N3B - C2B	1.357(1)	1.359	1.341
N4B - H4B	0.952(1)	1.018	1.006
N1A - C4A	1.374(1)	1.377	1.389
N1A - C2A	1.371(1)	1.374	1.388
C5A - C4A	1.514(1)	1.521	1.531
C5A-C7A	1.562(2)	1.570	1.558
C5A-C8A	1.549(2)	1.550	1.558
C7A - H71	0.996(1)	1.093	1.092
C8A - H81	0.992(1)	1.093	1.092
C9A - H91	0.988(1)	1.094	1.094
C10A- H11	0.979(1)	1.093	1.094
N2B - C2B	1.336(1)	1.340	1.359
N2B - H2B2	0.967(1)	1.017	1.006
N2B-H2B1	0.948(1)	1.017	1.006
N1B - C2B	1.344(1)	1.344	1.341
N3B - C4B	1.349(1)	1.352	1.340
N4B - C4B	1.339(2)	1.340	1.360
C7A - C10A	1.524(3)	1.529	1.531
C8A - C9A	1.525(3)	1.528	1.531
C9A - H92	0.985(1)	1.093	1.092
C10A-H11	0.979(1)	1.093	1.094
C10A- H12	0.997(1)	1.095	1.093

(b)			
	exp	**A**	**B**
C2A-N1A-C4A	125.5(1)	125.5	127.9
C5A-C4A-O4A	121.7(1)	121.6	122.3
O2A-C2A-N1A	121.4(1)	121.4	122.8
C5A-C4A-N1A	118.2(1)	118.0	117.5
N1A-C4A-O4A	120.0(1)	120.3	120.1
C4A-C5A-C8A	110.1(1)	110.4	108.3
C4A-C5A-C7A	107.2(1)	106.9	108.3
C8A-C5A-C7A	108.3(1)	108.4	108.9
C9A-C8A-C5A	114.4(2)	115.5	115.2
C10A-C7A-C5A	115.8(1)	117.0	115.2
C4B-N3B-C2B	114.7(1)	115.1	115.2
N3B-C4B-N4B	117.5(1)	117.8	116.9
N3B-C2B-N2B	116.7(1)	116.7	116.9
N1B-C2B-N2B	117.8(1)	118.2	116.9
N3B-C2B-N1B	125.5(1)	125.1	126.1

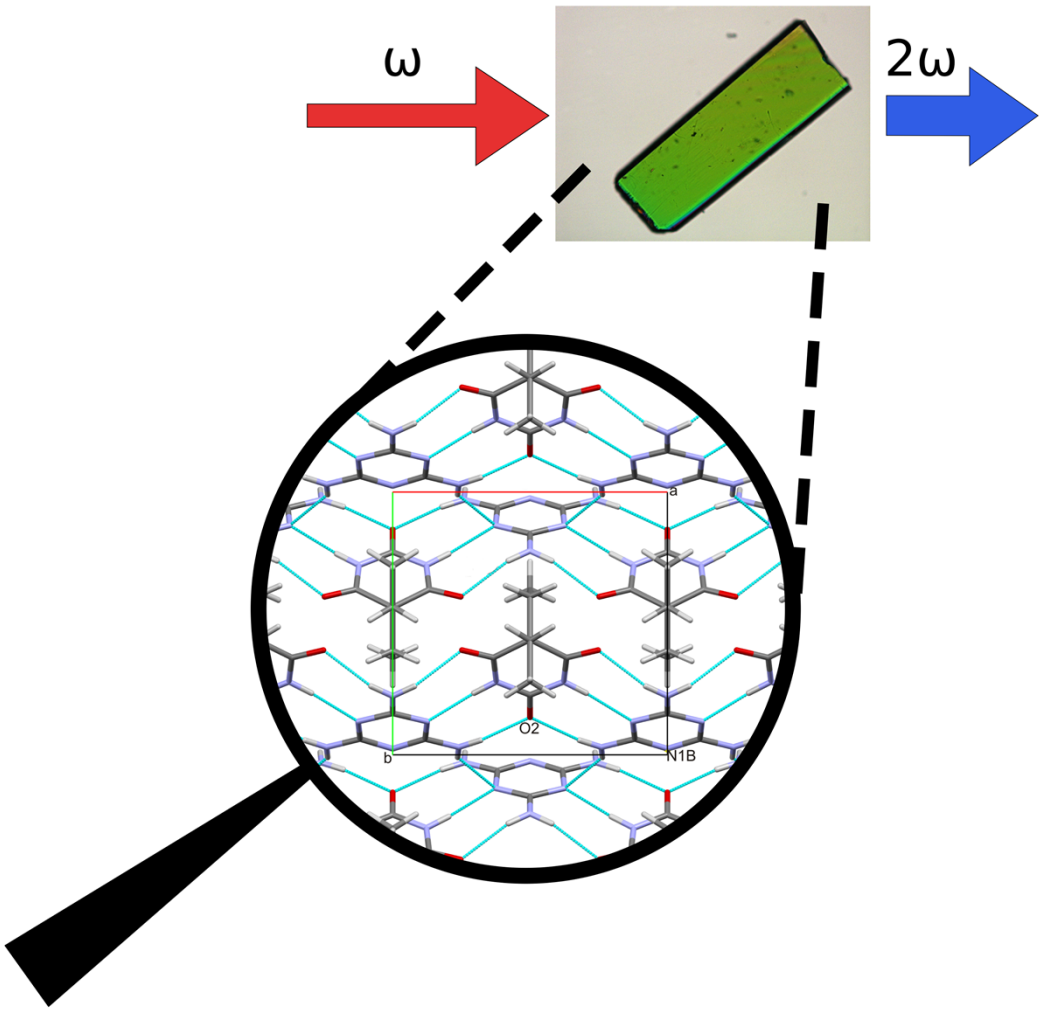
(c)			
	exp	**A**	**B**
O2A - C2A - N1A - C4A	177.8(1)	176.9	-180
C2A - N1A - C4A - C5A	9.0(1)	10.3	0.0
C2A - N1A - C4A - O4A	-173.9(1)	-173.1	180.0
C2B - N3B - C4B - N4B	179.9(1)	179.6	178.3
C4B - N3B - C2B - N1B	-1.0(1)	-0.9	-0.2
C4B - N3B - C2B - N2B	179.2(1)	179.0	178.8

Table S3 Effect of the electric field on the selected molecular properties of melamine and barbital as obtained at MP2/6-311++G(d,p) level of theory. The average electric field strength is of the order of ca. 0.5 and 2.5 GV/m for barbital and melamine, respectively .Polarizability α [Å^3], first hyperpolarizability β [10^{-30} esu] and dipol moment μ [D].

molecule	electrcic field	α_{iso}	$\lvert\underline{\beta}_{vec}\rvert$	$\lvert\underline{\mu}\rvert$
melamine	no field (A)	12.8	0.07	0.42
	no field (B)	12.8	0.20	1.14
	charge field (geometry B)	12.9	0.36	1.54
barbital	no field (geometry A)	16.8	0.95	0.96
	no field (geometry B)	16.9	0.91	1.09
	charge field (geometry B)	16.9	0.99	1.69

Table S4 RLFTn calculations results for $\chi(2)$ tensor components (in pm/V) for the investigated cocrystal.

method	λ / nm	$\chi^{(2)}_{113}=\chi^{(2)}_{311}$	$\chi^{(2)}_{233}=\chi^{(2)}_{322}$	$\chi^{(2)}_{333}$
MP2 (A)	∞	-5.4	0.3	3.5
	1064	-7.6	0.5	4.9
MP2 (B)	∞	-5.5	0.5	2.7
	1064	-8.0	0.9	4.1
MP2 (B)	∞	-6.4	0.8	2.7
	1064	-8.1	0.9	3.4



Graphical Abstract

Pleochroic crystal of melamine barbital addition compound viewed under the polarizing microscope in transmitted light under 100x magnification. Red and Blue arrows indicate incident and second harmonic beam respectively. A fragment of crystal packing showing mutual orientation of melamine and barbital molecules, viewed along the **c** direction is presented under the magnifier.