

Polymorphism of urea–barbituric acid co-crystals

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The crystal structures of three polymorphs found for the addition complex of urea and barbituric acid are described and compared. Two polymorphs are monoclinic, space groups $P2_1/c$ and Cc , whereas the third is triclinic, $P1$. The displacement of electron density towards the mesomeric forms, corresponding to the tautomeric forms of higher stability, of the barbituric acid molecule seem to influence the type of hydrogen bonds formed, which in turn determines the different packing topology in the polymorphs. While the polymorphic forms can be easily differentiated at the first-level graph-set analysis of their hydrogen-bonding patterns, a higher-level analysis enables important features of the mutual spatial arrangement of the structural components to be revealed.

1. Introduction

The current interest in the polymorphism phenomena is due to its potential applications in designing new solids with specific physical and chemical properties. The ability of a chemical compound to form two or more different crystal structures provides an opportunity to study the correlation between three-dimensional structures and material properties. The crystal engineering of polymorphic forms often utilizes the capability of starting components to create a variety of hydrogen-bond patterns, provided that the components possess suitable hydrogen-bond donors and acceptors. Three-dimensional structure formation is also affected by crystallization conditions such as molar ratio, type of solvent, ionic forces, temperature range, pressure *etc.*, which can lead to polymorphic modifications.

Polymorphism is quite common among derivatives of barbituric acid. Anhydrous barbituric acid itself is known to form three polymorphs (Lewis *et al.*, 2004; Braga *et al.*, 2006). Two of them, for which the crystal structures were determined by X-ray diffraction, belong to the same space group and differ mainly in hydrogen-bond patterns. Moreover, barbituric acid was reported to form pseudo-polymorphs such as barbituric acid dihydrate (Nichol & Clegg, 2005a) or hemi-tri-(1,4)-dioxane solvate (Al-Saqqar *et al.*, 2004).

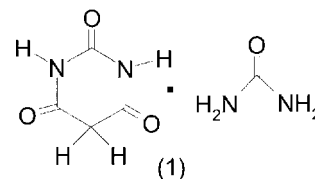
Many derivatives of barbituric acid also crystallize in various polymorphic forms. For example, barbital (5,5-diethylbarbituric acid) was reported to form four polymorphs with crystal structures determined for three of them (Craven *et al.*, 1969; Caillet & Claverie, 1980), whereas for violuric acid, a 5-substituted derivative of barbituric acid [pyrimidine-2,4,5,6-(1*H*,3*H*)-tetrone monohydrate], two polymorphic modifications were found: an orthorhombic one (Craven & Mascarenhas, 1964; Craven & Takei, 1964; Nichol & Clegg, 2005b) and a monoclinic one (Guille *et al.*, 2007).

Recently, the possible polymorphs of phenobarbital (5-ethyl-5-phenylbarbituric acid) were predicted using atomistic (force-field) and density-functional theory (DFT) calculations from which, in addition to the polymorphs already characterized by their specific crystal structures, the existence of new polymorphs has been suggested (Day *et al.*, 2007).

The formation of co-crystals of barbituric acid and melamine derivatives has been widely investigated by Zerkowski *et al.* (1990, 1994) and Zerkowski & Whitesides (1994) to clarify the interactions that underlie molecular recognition and self-assembly of these components, and to design optically and electronically active organic solids. Among them were polar phases, which are interesting from the point of view of non-linear optical (NLO) materials.

The observed properties make barbituric acid a perfect component in the crystal engineering of polar co-crystals, especially with such a molecule as urea, because of the compatibility of their hydrogen-bond donor and acceptor spatial distributions. Crystals of urea ($P4_2m$) are known as an NLO material (SHG – second-harmonic generation – nonlinear coefficient $d_{14} = 1.4 \text{ pm V}^{-1}$; Boulanger & Zyss, 2003). The polar molecule of urea (dipole moment $12.78 \times 10^{-30} \text{ Cm}$) can be the donor of four hydrogen bonds, its carbonyl oxygen usually accepts two and in some cases even four hydrogen bonds (*e.g.* in the urea–oxalic acid addition

compound: Harkema *et al.*, 1972; in urea: Birkedal *et al.*, 2004) and its amine N atoms, in some cases, can serve as additional acceptors of relatively weak hydrogen bonds owing to their lone-pair electrons (Zhou *et al.*, 1986).



Scheme 1

The aim of this work was to design crystal phases containing barbituric acid and urea molecules with a view towards polar materials and to investigate the influence of hydrogen-bond patterns on the formation of polymorphic modifications of their addition compounds (see Scheme 1) using Etter's empirical hydrogen-bond rules (Etter, 1990) and graph-set theory (Etter *et al.*, 1990; Bernstein *et al.*, 1995).

2. Experimental

2.1. Structure design

The detailed analysis of the structure of known barbituric acid polymorphs (see Fig. 1) revealed several types of synthons formed by the hydrogen bonds of the N–H...O type. Those are: fused rings forming a two-dimensional structure in polymorph (I) ($P2_1/c$), both also found in polymorph (I) of butobarbital (Gelbrich *et al.*, 2007), and typical for the layers found in polymorph (II) ($P2_1/c$). In the pseudo-polymorph $\text{C}_4\text{H}_4\text{N}_2\text{O}_3 \cdot 2\text{H}_2\text{O}$ ($Pnma$), where water molecules serve as the additional donors of two hydrogen bonds and as acceptors, there are three possible graph-sets of hydrogen bonds.

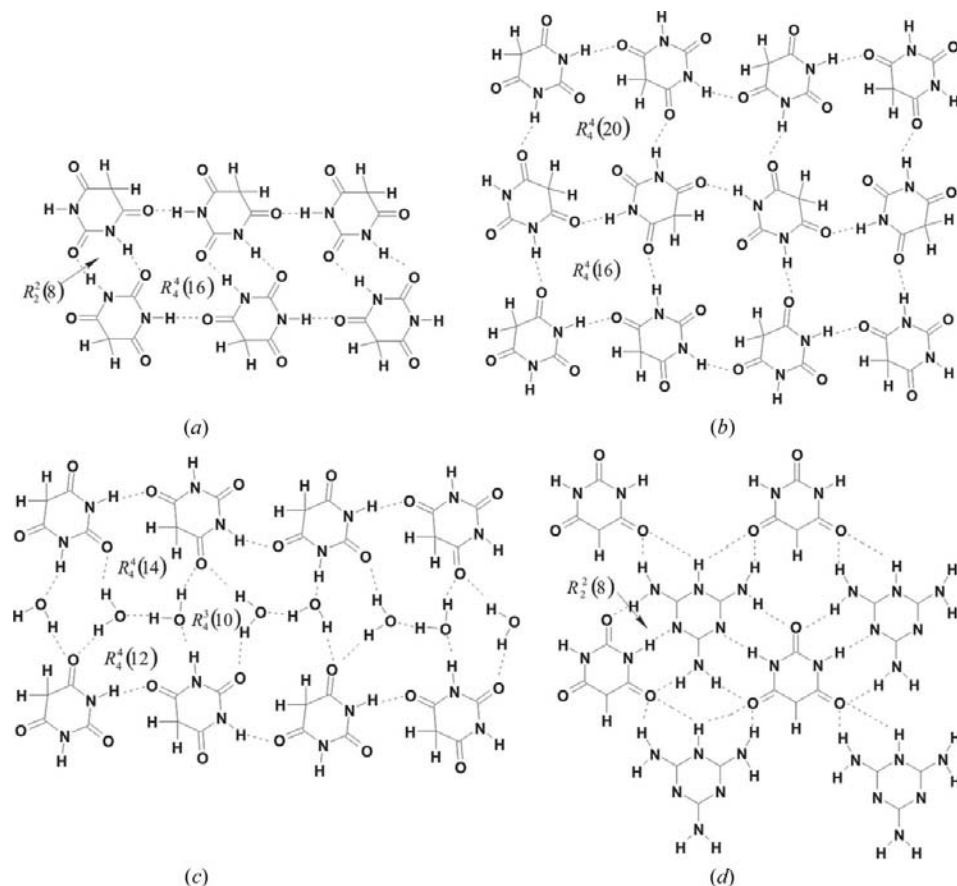


Figure 1

The synthons formed by N–H...O hydrogen bonds in the known barbituric acid polymorphs: (a) polymorph (I), $P2_1/c$; (b) polymorph (II), $P2_1/c$; (c) pseudo-polymorph–barbituric acid dihydrate, $Pnma$; (d) melamine barbiturate, $Ccc2$.

containing barbituric acid and urea molecules. The results of such an approach (shown in Fig. 2) indicated that the appropriate proportion of the components, barbituric acid and urea used for co-crystallization should be: 2:1 (*a–c,g*), 1:2 (*d,e*) and 1:1 (*f*). The case of the molar ratio 1:1 was omitted because it would lead to a centrosymmetric structure.

2.2. Sample preparation

Co-crystals of barbituric acid and urea, with the chemical formula $C_4H_4N_2O_3 \cdot CH_4N_2O$, were obtained in three polymorphic forms, depending on the crystallization conditions. Form (I) crystallizes in the space group $P2_1/c$ from a methanol solution of barbituric acid and urea in the molar ratios 2:1 or 3:1. Form (II), space group Cc , was obtained from an ethanol solution of barbituric acid and urea in the molar ratio 1:2,

whereas form (III), space group $P\bar{1}$, was found in the sample crystallizing from a methanol solution of barbituric acid and urea (molar ratio 1:2). All solutions were prepared at a temperature of *ca* 323 K using a water bath and were left to crystallize by slow evaporation of the solvent at room temperature. The crystals of the three polymorphs were stable in the temperature range 295–100 K, whereas left in the solutions at room temperature (293 K) over several weeks crystals of (I) and (II) were transformed into polymorph (III), which indicates that (III) is the most stable form of the addition compound at ambient conditions.

2.3. Crystal structure determination

The structures of all three polymorphs were determined by single-crystal X-ray diffraction analysis. Measurements were performed on a Nonius KappaCCD diffractometer at 293 (2) K. The standard strategies were used for data collection (Nonius, 1997), cell refinement and data processing: *HKL DENZO* and *SCALEPACK* (Otwinowski & Minor, 1997). *SIR92* (Altomare *et al.*, 1994) was used to solve the structures and *SHELXL97* (Sheldrick, 2008) was employed for structure refinement. Space groups were assigned from the systematic absences observed in the diffraction patterns. In the case of polymorph (II), the $|E|$ distribution and $N(z)$ test clearly indicated the non-centrosymmetric space group Cc as opposed to the centrosymmetric space group $C2/c$ with the same systematic absences. The structures were refined by full-matrix least-squares against F^2 using all data. The H atoms of the amino and amido groups were found on difference-Fourier maps and refined in a riding model assuming $U_{iso} = 1.2U_{eq}$ of the parent atom. The H atoms of the methylene group (both H atoms were observed on the difference-Fourier map) were included in geometrically calculated positions and refined using a riding model with $U_{iso}(H) = 1.2U_{eq}(C5)$. For structural drawings the following programs were used: *ORTEP3* for Windows (Farrugia, 1997), *MERCURY1.4.2* (Macrae *et al.*, 2006). Selected crystal data and

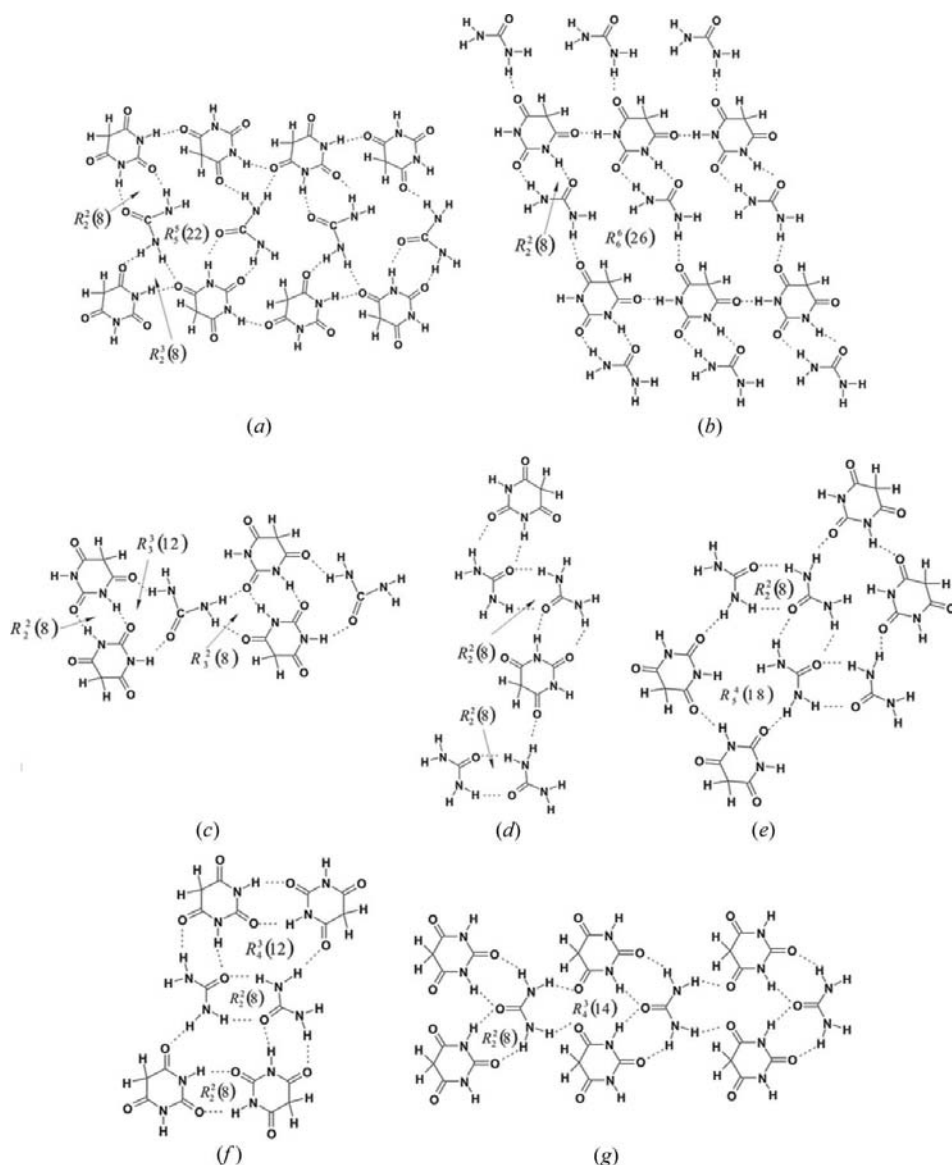


Figure 2

The possible frameworks of hydrogen bonds, designed for barbituric acid and urea co-crystals, consisting of graph sets: (a) $R_2^2(8)$, $R_3^3(8)$, $R_5^5(22)$; (b) $R_2^2(8)$, $R_6^6(26)$; (c) $R_2^2(8)$, $R_3^3(8)$; (d) $R_2^2(8)$; (e) $R_2^2(8)$, $R_5^5(18)$; (f) $R_2^2(8)$, $R_3^3(12)$; (g) $R_2^2(8)$, $R_4^4(14)$.

Table 1
Experimental details for (I), (II) and (III).

	(I)	(II)	(III)
Crystal data			
Chemical formula	C ₅ H ₈ N ₄ O ₄	C ₅ H ₈ N ₄ O ₄	C ₅ H ₈ N ₄ O ₄
<i>M_r</i>	188.15	188.15	188.15
Crystal system, space group	Monoclinic, <i>P</i> 2 ₁ / <i>c</i>	Monoclinic, <i>Cc</i>	Triclinic, <i>P</i> $\bar{1}$
Temperature	293 (2)	293 (2)	293 (2)
<i>a</i> , <i>b</i> , <i>c</i> (Å)	7.8857 (3), 6.920 (2), 14.4283 (6)	15.9423 (7), 5.0984 (3), 10.5534 (5)	8.1588 (4), 9.1117 (4), 10.9268 (5)
α , β , γ (°)	90, 98.027 (1), 90	90, 110.570 (2), 90	100.248 (2), 91.515 (2), 99.192 (2)
<i>V</i> (Å ³)	784.36 (5)	803.09 (7)	787.82 (6)
<i>Z</i>	4	4	4
<i>D_x</i> (Mg m ⁻³)	1.593	1.556	1.586
Radiation type	Mo <i>K</i> α	Mo <i>K</i> α	Mo <i>K</i> α
μ (mm ⁻¹)	0.14	0.14	0.14
Crystal form, color	Plate, yellowish	Block, colorless	Block, colorless
Crystal size (mm)	0.30 × 0.22 × 0.05	0.32 × 0.22 × 0.12	0.35 × 0.13 × 0.13
Data collection			
Diffractometer	KappaCCD	KappaCCD	KappaCCD
Data collection method	ω scans at $\chi = 55^\circ$	ω scans at $\chi = 55^\circ$	ω scans at $\chi = 55^\circ$
Absorption correction	Multi-scan†	Multi-scan†	Multi-scan†
<i>T_{min}</i>	0.960	0.958	0.953
<i>T_{max}</i>	0.993	0.984	0.982
No. of measured, independent and observed reflections	3177, 1775, 1334	3691, 1169, 1099	4828, 3584, 2380
Criterion for observed reflections	<i>I</i> > 2σ(<i>I</i>)	<i>I</i> > 2σ(<i>I</i>)	<i>I</i> > 2σ(<i>I</i>)
<i>R_{int}</i>	0.025	0.016	0.017
θ_{\max} (°)	27.5	30.0	27.5
Refinement			
Refinement on	<i>F</i> ²	<i>F</i> ²	<i>F</i> ²
<i>R</i> [<i>F</i> ² > 2σ(<i>F</i> ²)], <i>wR</i> (<i>F</i> ²), <i>S</i>	0.043, 0.113, 1.03	0.033, 0.085, 1.06	0.053, 0.137, 1.03
No. of reflections	1775	1169	3584
No. of parameters	118	118	235
H-atom treatment	Constrained‡	Constrained‡	Constrained‡
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0535P)^2 + 0.1825P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0491P)^2 + 0.0769P]$, where $P = (F_o^2 + 2F_c^2)/3$	$w = 1/[\sigma^2(F_o^2) + (0.0476P)^2 + 0.2967P]$, where $P = (F_o^2 + 2F_c^2)/3$
(Δ/σ) _{max}	< 0.001	< 0.001	< 0.001
$\Delta\rho_{\max}$, $\Delta\rho_{\min}$ (e Å ⁻³)	0.21, -0.19	0.15, -0.17	0.22, -0.19

Computer programs used: *KappaCCD* (Nonius, 1997), *DENZO* and *SCALEPACK* (Otwinowski & Minor, 1997), *SIR92* (Altomare *et al.*, 1994), *SHELXL97* (Sheldrick, 2008), *PLATON* (Spek, 2003), *ORTEP3* (Farrugia, 1997), *MERCURY* (Macrae *et al.*, 2006). † Multi-scan based on symmetry-related measurements. ‡ Constrained to parent site.

experimental details are summarized in Table 1.¹

3. Results and discussion

3.1. Molecular geometry

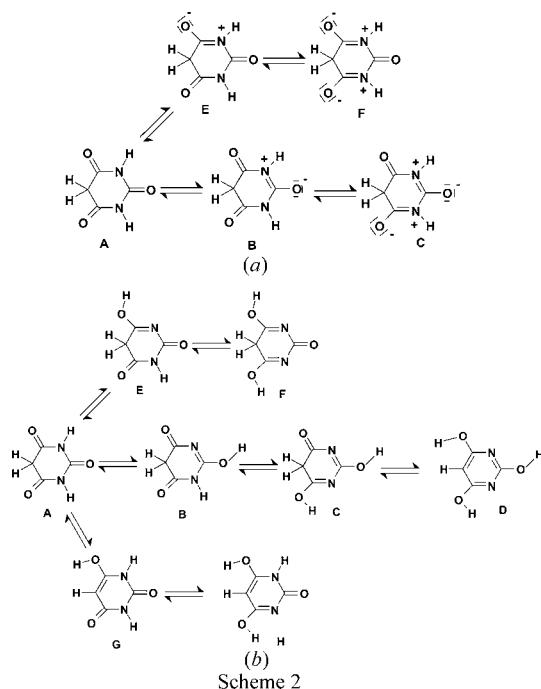
The crystal phases studied, with the chemical formula C₄H₄N₂O₃·CH₄N₂O, differ in the mutual arrangement of the barbituric acid and urea molecules. Form (I) crystallizes in the *P*2₁/*c* space group and the asymmetric unit contains one barbituric acid molecule and one urea molecule, which are parallel to each other as shown in Fig. 3(*a*). Form (II) of the space group *Cc* has the same content as the asymmetric unit but, contrary to (I), the barbituric acid and urea molecule are oriented antiparallel to each other (Fig. 3*b*). The structure is polar. Form (III) crystallizes in the *P*1 space group with two symmetry-independent addition compounds (two barbituric acid and two urea molecules) in the asymmetric unit, as shown in Fig. 3(*c*). The appropriate bond lengths and angles of the

polymorphs are given in Table 2. The observed differences in the values of C=O and C5–C4/C5–C6 bond lengths could be correlated with a tendency of barbituric acid to form several resonance structures shown in Scheme 2(*a*) (mesomeric effect). Although the real structure is a hybrid that includes contribution from a few canonical forms, the most interesting are the resonance structures which correspond to some of the keto-enol tautomers (Scheme 2*b*), especially those of higher stability. The stability of the tautomeric forms of barbituric acid, as predicted by DFT and *ab initio* studies, could be arranged in the following order: *A* > *G* > *E* > *B* > *D* > *H* > *C* > *F* (Delchev, 2004) and 1 (*A*) > 2 (*G*) > 3 (*E*) > 4 (*B*) > 11 (*D*) > 8 > 5 (*H*) > 10 (*C*) > 6 (*F*) (Senthilkumar & Kolan-daivel, 2002).

The presence of H atoms at N1 and N3 is confirmed by the C–N–C valence angles with the average value of 125.6°. Although both H atoms of the methylene group were observed on the difference-Fourier maps in the positions close to those found from geometrical constraints, the value of the endocyclic angle C4–C5–C6 is rather large (116.6–118.2°). Electron displacement in the barbituric acid molecule towards mesomeric form *E* could be responsible for a particular

¹ Supplementary data for this paper are available from the IUCr electronic archives (Reference: BS5065). Services for accessing these data are described at the back of the journal.

hydrogen-bond system in polymorph (I), $P2_1/c$. In the structure of polymorph (III), $P1$, molecules *a* and *b* represent the mesomers *E* and *A* (see Scheme 2*a*), respectively. In the structure of polymorph (II), Cc , the relatively less stable form B could be recognized. The properties of the barbituric acid molecule (relatively strong acid), together with the influence of urea (weak base), seem to be responsible for the different hydrogen-bond systems found in the polymorphs studied. The hydrogen-bond geometry is given in Table 3 and hydrogen-bond systems are described in detail in §3.3.



3.2. Packing arrangements

The packing of molecules in polymorph (I) contains alternate layers parallel to *ab*, as shown in Fig. 4. The barbituric acid molecules in the pseudo-bilayer are joined together by only moderate (Jeffrey, 1997) $N3-H3 \cdots O4$ hydrogen bonds (Table 3) around a twofold screw axis, whereas the urea layers are built of centrosymmetric dimers with $N2-H2 \cdots O1$ hydrogen bonds. The methylene group of barbituric acid is the donor of two weak interactions (of the $C-H \cdots O$ type) to urea and to adjacent barbituric acid molecules (Table 4*a*). The short distance of the centre $Cg1$ of the barbituric heterocyclic ring to the $O6$ atom of the barbituric acid molecule related by the twofold screw axis ($-x, y - \frac{1}{2}, -z + \frac{1}{2}$) suggests a deficiency of the negative charge at the centre of the ring (Table 4*b*). The urea $C1=O1$ carbonyl group on the other side of the ring is in a similar position. It is worth noting that the $O6$ atom is not involved as an acceptor in any hydrogen bond.

Form (II) is built of alternating layers of barbituric acid and urea molecules, parallel to *bc*. The packing diagrams shown in Figs. 5(*a*) and (*b*) reveal a pseudo-hexagonal arrangement of the molecules. The structure belongs to crystal class *m*. Each barbituric acid molecule interacts *via* hydrogen bonds of the $N-H \cdots O$ type with the adjacent urea molecules and *vice*

Table 2

Bond lengths (Å) and angles (°) for all studied polymorphs.

	(I)	(II)	(III <i>a</i>)	(III <i>b</i>)
Barbituric acid				
N1—C2	1.366 (2)	1.369 (2)	1.371 (2)	1.362 (2)
N1—C6	1.379 (2)	1.367 (2)	1.357 (2)	1.359 (2)
N3—C2	1.379 (2)	1.367 (2)	1.368 (3)	1.375 (2)
N3—C4	1.360 (2)	1.371 (2)	1.376 (3)	1.367 (3)
C2—O2	1.216 (2)	1.224 (2)	1.215 (2)	1.218 (2)
C4—O4	1.224 (2)	1.216 (2)	1.211 (2)	1.215 (2)
C6—O6	1.208 (2)	1.215 (2)	1.221 (2)	1.214 (2)
C4—C5	1.487 (2)	1.503 (2)	1.485 (3)	1.491 (3)
C5—C6	1.487 (2)	1.499 (2)	1.482 (3)	1.491 (3)
Urea				
N2—C1	1.331 (2)	1.333 (2)	1.327 (3)	1.331 (3)
N4—C1	1.334 (2)	1.331 (2)	1.340 (3)	1.319 (3)
C1—O1	1.250 (2)	1.257 (2)	1.244 (2)	1.243 (2)
Barbituric acid				
C2—N1—C6	125.7 (1)	125.5 (1)	125.7 (2)	125.7 (2)
C4—C5—C6	118.2 (1)	116.6 (1)	118.0 (2)	117.8 (2)
C4—N3—C2	125.5 (1)	125.4 (1)	125.8 (2)	125.5 (2)
N1—C2—N3	117.2 (1)	117.8 (1)	117.2 (2)	117.6 (2)
O2—C2—N1	121.8 (1)	120.9 (1)	120.7 (2)	121.2 (2)
O2—C2—N3	121.0 (1)	121.3 (1)	122.2 (2)	121.2 (2)
N3—C4—C5	116.6 (1)	116.6 (1)	116.2 (2)	116.3 (3)
O4—C4—C5	122.4 (1)	122.5 (1)	122.9 (2)	123.0 (2)
O4—C4—N3	121.0 (1)	120.7 (1)	120.9 (2)	120.7 (2)
N1—C6—C5	116.2 (1)	116.6 (1)	117.0 (2)	116.9 (2)
O6—C6—N1	120.8 (1)	120.6 (1)	120.1 (2)	120.6 (2)
O6—C6—C5	123.0 (1)	122.8 (1)	122.9 (2)	122.5 (2)
Urea				
N2—C1—N4	116.7 (1)	116.7 (1)	116.2 (2)	116.3 (2)
O1—C1—N2	118.2 (1)	117.5 (1)	121.4 (2)	121.2 (2)
O1—C1—N4	121.2 (1)	121.2 (1)	121.0 (2)	120.7 (2)

versa (Table 3). All possible donor and acceptor groups are involved in the moderate hydrogen bonds. Contrary to polymorph (I), in (II) there are no moderate hydrogen bonds between molecules of the same type. The only interactions between barbituric acid molecules are those of $C5-H5b \cdots O6(x, y + 1, z)$ weak hydrogen bonds (Table 4*a*). The short distance between the centre of the barbituric ring and the $O1$ atom of urea, which is approaching the ring from one side, confirms the negative charge deficiency at the ring centre (Table 4*b*). On the other side of the ring two oxygen atoms, $O4$ and $O6$, are situated at distances of 3.487 and 3.547 Å, respectively, equivalent to van der Waals interactions.

Polymorph (III), similar to (I) and (II), has a layered structure (Fig. 6*a*), but this time the layers are perpendicular to $[110]$ and contain alternate dimers of barbituric acid and urea molecules arranged in tapes due to moderate hydrogen bonds of the $N-H \cdots O$ type (Table 3). All barbituric acid donor groups, but not all acceptors, are involved in hydrogen bonds. The methylene $C5a$ atom forms a weak hydrogen bond to $O1b$, with both donor and acceptor belonging to the same tape (Table 4*a*). Carbonyl atoms $O6a$ and $O6b$ are not acceptors for any good hydrogen bond. Instead, the $O6a$ atom lies a short distance (3.242 Å) from the centre of the barbituric acid ring of molecule (*a*) from the neighbouring layer (Fig. 6*b*, Table 4*b*). The barbituric heterocyclic ring of molecule (*b*) interacts with the urea atom $O1a$, also from an adjacent layer (Fig. 6*c*). As can be deduced from intermolecular distances

between tapes there are only weak van der Waals interactions between them.

3.3. Graph-set analysis of hydrogen-bond patterns

The presence of numerous hydrogen bonds in the polymorphs studied results in characteristic arrays which may be described by graph-set analysis (Etter *et al.*, 1990; Bernstein *et al.*, 1995). The type of hydrogen bond is defined by the chemical nature of the functional groups forming hydrogen bonds, their nearest neighbourhood and crystallographic description. Taking into account these criteria, in the structures (I) and (II) there are six types of hydrogen bonds,

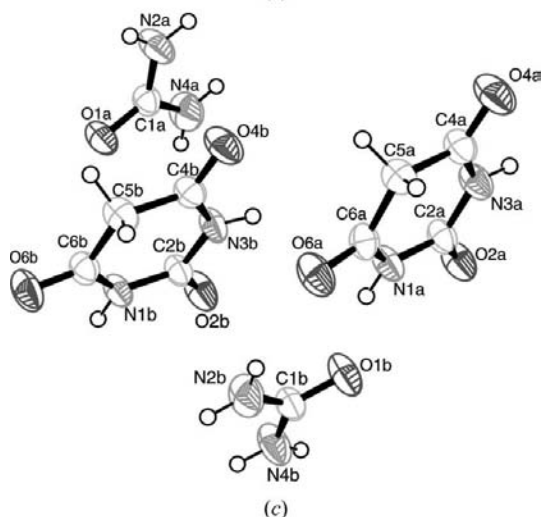
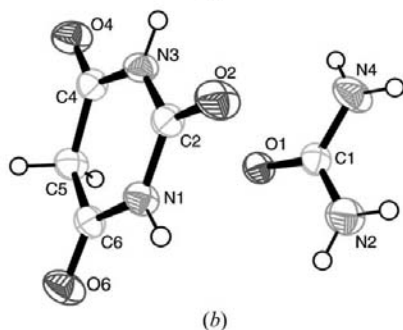
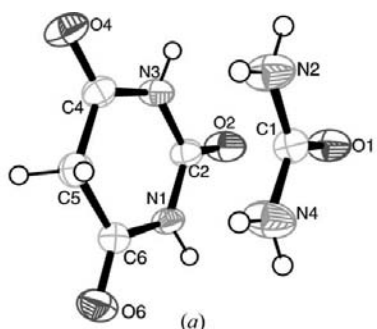


Figure 3
An ORTEP3 (Farrugia, 1997) view of the contents of the asymmetric unit with atom-labelling scheme for: (a) polymorph (I), (b) polymorph (II) and (c) polymorph (III). Atomic displacement ellipsoids are drawn at the 50% probability level.

Table 3
Moderate hydrogen-bond geometry (Å, °) for the studied polymorphs.

Hydrogen-bond descriptors for the graph-set analysis are given in parentheses.

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	∠ <i>DHA</i>
(I)				
N1—H1...O1 ⁱ (<i>e</i>)	0.86	1.95	2.779 (2)	160
N2—H2a...O1 ⁱⁱ (<i>a</i>)	0.86	2.06	2.903 (2)	168
N2—H2b...O4 ⁱⁱⁱ (<i>b</i>)	0.86	2.44	3.223 (2)	151
N3—H3...O4 ^{iv} (<i>f</i>)	0.86	2.09	2.895 (2)	156
N4—H4a...O2 ^v (<i>d</i>)	0.86	2.16	3.005 (2)	165
N4—H4b...O2 ^v (<i>c</i>)	0.86	2.25	2.916 (2)	135
(II)				
N1—H1...O1 ^{vi} (<i>e</i>)	0.86	1.94	2.793 (3)	172
N2—H2a...O2 ^{vii} (<i>a</i>)	0.86	2.14	2.992 (2)	169
N2—H2b...O4 ^{viii} (<i>b</i>)	0.86	2.15	3.005 (2)	175
N3—H3...O1 ^{ix} (<i>f</i>)	0.86	1.99	2.811 (2)	158
N4—H4a...O2 ^v (<i>c</i>)	0.86	2.17	3.019 (2)	169
N4—H4b...O6 ^x (<i>d</i>)	0.86	2.09	2.884 (2)	153
(III)				
N1a—H1a...O1b (<i>a</i>)	0.86	1.85	2.682 (2)	164
N1b—H1b...O1a ^{xi} (<i>c</i>)	0.86	1.87	2.719 (2)	167
N2a—H2a1...O1b ^v (<i>e</i>)	0.86	2.24	3.077 (2)	165
N2a—H2a2...O4b ^{xiii} (<i>f</i>)	0.86	2.25	3.088 (2)	164
N3a—H3a...O2b ^{xiii} (<i>b</i>)	0.86	2.00	2.842 (2)	166
N3b—H3b...O2a ^{xiii} (<i>d</i>)	0.86	2.01	2.841 (2)	162
N4b—H4b1...O1a ^{vi} (<i>g</i>)	0.86	2.21	3.055 (3)	167
N4b—H4b2...O4a ^{xiv} (<i>h</i>)	0.86	2.31	3.135 (3)	160

Symmetry codes: (i) $-x, -y, -z$; (ii) $-x+1, -y, -z$; (iii) $-x+1, -y+\frac{1}{2}, -z+\frac{1}{2}$; (iv) $-x+1, y-\frac{1}{2}, -z+\frac{1}{2}$; (v) $x, y+1, z$; (vi) $x, y-1, z$; (vii) $x, -y, z+\frac{1}{2}$; (viii) $x-\frac{1}{2}, y-\frac{1}{2}, z$; (ix) $x, -y+1, z-\frac{1}{2}$; (x) $x-\frac{1}{2}, y+\frac{1}{2}, z-\frac{1}{2}$; (xi) $-x+1, -y+1, -z+2$; (xii) $-x+1, -y+1, -z+1$; (xiii) $-x+1, -y, -z+1$; (xiv) $x, y, z+1$.

whereas in (III) there are eight. Each type of hydrogen bond forms a pattern which is called a motif. The sum of all motifs gives the first-level (unitary) graph set, designated by N_1 . With

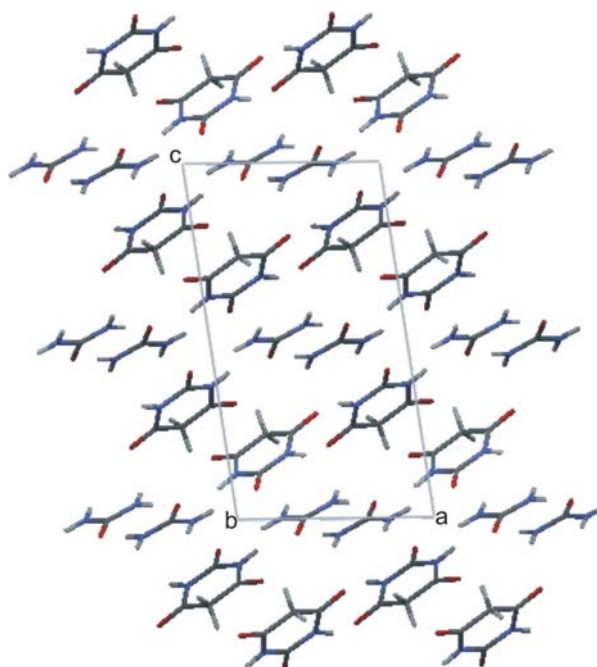


Figure 4
Packing arrangement of the molecules in polymorph (I) viewed along [010]. Alternate urea and barbituric acid layers are parallel to *ab*.

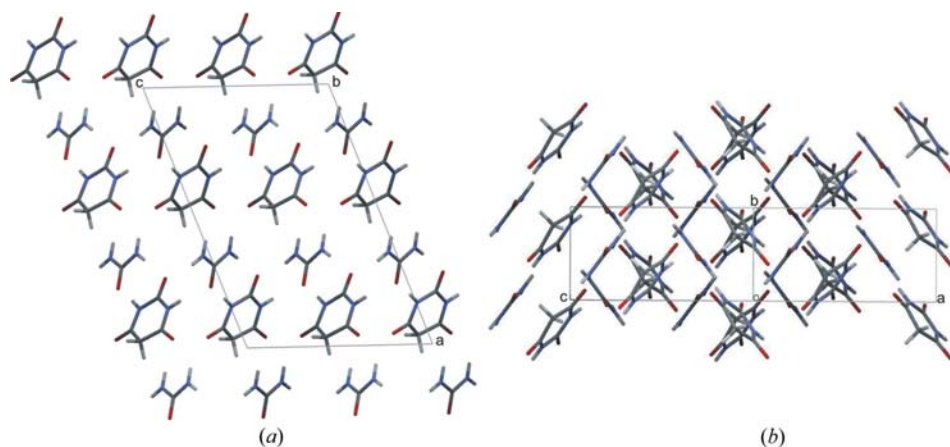


Figure 5
Pseudo-hexagonal molecular arrangement in polymorph (II): (a) view along [010]; (b) view along [101].

Table 4

Geometry of weak interactions (\AA , $^\circ$) in the studied polymorphs: (a) $C-H \cdots O$; (b) $Cg \cdots O/C$, where Cg is the gravity centre of the heterocyclic ring of the barbituric acid molecule.

$D-H \cdots A$	$D-H$	$H \cdots A$	$D \cdots A$	$\angle DHA$
(a)				
(I)				
$C5-H5a \cdots O1$	0.97	2.59	3.43	145
$C5-H5b \cdots O4$	0.97	2.66	3.55	152
(II)				
$C5-H5b \cdots O6^i$	0.97	2.57	3.44	148
(III)				
$C5a1-H5a1 \cdots O1b$	0.97	2.49	3.39	154
<hr/>				
	$D \cdots A$	$d(\perp)$	Offset	
(b)				
(I)				
$Cg1 \cdots O1$	3.485	3.138	1.518	
$Cg1 \cdots C1$	3.323	3.297	0.415	
$Cg1 \cdots O6^{ii}$	2.897	2.877	0.340	
(II)				
$Cg1 \cdots O1$	3.099	3.064	0.464	
(III)				
$Cg1 \cdots O6a^{iii}$	3.242	3.151	0.738	
$Cg2 \cdots O1a$	2.958	2.958	0.000	

Symmetry codes: (i) $x, y+1, z$; (ii) $-x, y-\frac{1}{2}, -z+\frac{1}{2}$; (iii) $-x+2, -y, -z+1$.

more than one type of hydrogen bond, upper-level graph sets can also be specified.

In (I) there are six possible motifs, as shown in Figs. 7(a) and (b). Hydrogen bonds of type *a* form a ring array with the $R_2^2(8)$ descriptor. Hydrogen bonds *b*, *c*, *d* and *e* all form the discrete motifs of type *D*. The chain array occurs for *f*-type hydrogen bonds designated by the $C(4)$ descriptor. These six hydrogen-bond motifs give the full description of the unitary graph set $N_1 = R_2^2(8)DDDDC(4)$. Turning to the second-level graph set, there are 6^2 combinations of all types of hydrogen bonds as presented in Table 5. Further assembling the motifs exhibits complicated but more characteristic hydrogen-bond patterns.

Two rings $R_2^2(8)$, composed of *b* and *e* hydrogen bonds, assembled with an $R_2^2(8)$ ring of type *a*, form finite patterns which are joined by hydrogen bonds of the *f*-type and build a two-dimensional periodic layer parallel to the $(\bar{1}03)$ plane (Fig. 7a). The layers connected by hydrogen bonds of *c* and *d* types form a three-dimensional structure. The mutual set of all hydrogen-bond types can be seen in a general projection in Fig. 7(b).

In the case of (II) there are also six possible motifs, but all hydrogen bonds are involved in discrete motifs *D* giving the description of the unitary graph set: $N_1 = DDDDD$. Patterns of

the second-level graph-set are listed in Table 6. Nevertheless, it seems to be more appropriate to analyse the whole set of hydrogen bonds rather than individual graph-set levels. Characteristic features of the hydrogen-bond pattern are two-dimensional periodic networks of fused rings formed by five types of hydrogen bonds (all except those of *f* type) parallel to $(\bar{3}11)$ with channels running along [010], as shown in Fig. 8(a).

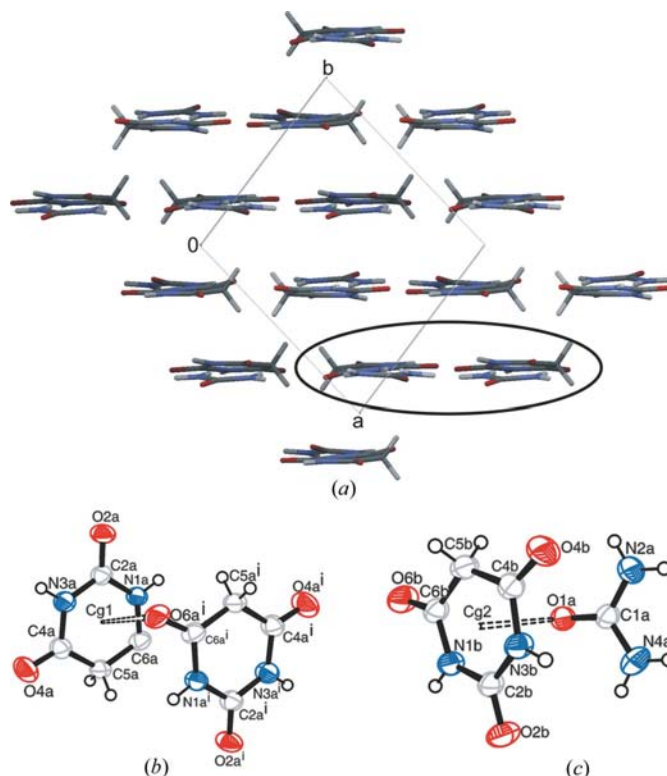


Figure 6
Packing arrangement of the molecules in polymorph (III): (a) view along [001] – layers are perpendicular to $[110]$; a single tape built of *a* and *b* molecules running along *c* is marked by an oval shape; (b) carbonyl $O6a$ atom interacts with the barbituric acid *a* ring; (c) urea $O1a$ atom interacts with the barbituric acid *b* ring. Symmetry code: (i) $-x+2, -y, -z+1$.

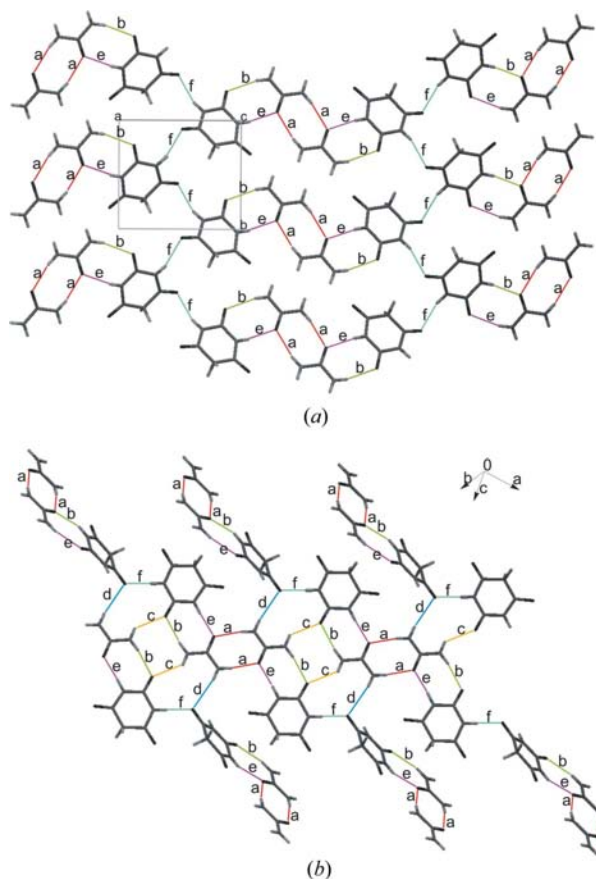


Figure 7
Graph-set assignment of the unitary, secondary and higher levels for (I): (a) view along [001]; (b) the best view of all the possible hydrogen bonds. Different hydrogen bonds as defined in Table 3 are distinguished by different colors: *a* – red, *b* – green, *c* – yellow, *d* – blue, *e* – violet, *f* – cadet blue.

Such two-dimensional networks are connected in the third dimension owing to sixth-type hydrogen bonds (*f* type), as illustrated in Fig. 8(b) in projection along [011̄].

The corresponding graph-set analysis for (III) shows that, in analogy to polymorph (II), all hydrogen bonds are involved in

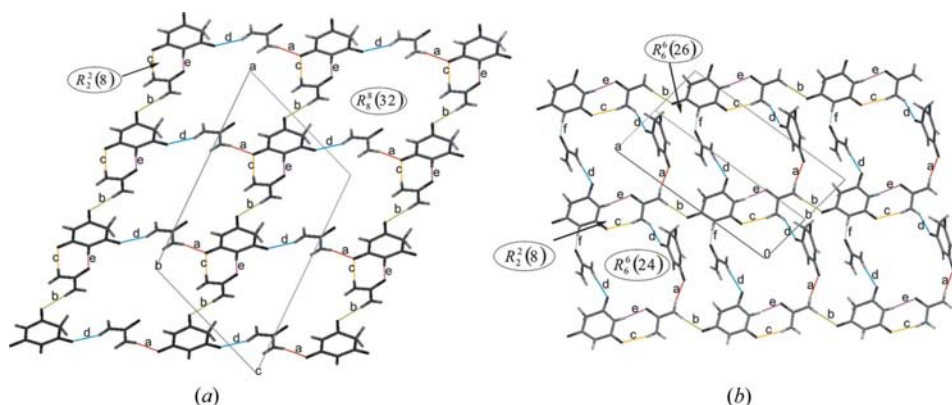


Figure 8
Hydrogen-bond patterns for polymorph (II): (a) in the layer parallel to (311) viewed along [010]; (b) in the layer parallel to (312) viewed along [011]. Different hydrogen bonds defined in Table 3 are distinguished by different colors: *a* – red, *b* – green, *c* – yellow, *d* – blue, *e* – violet, *f* – cadet blue.

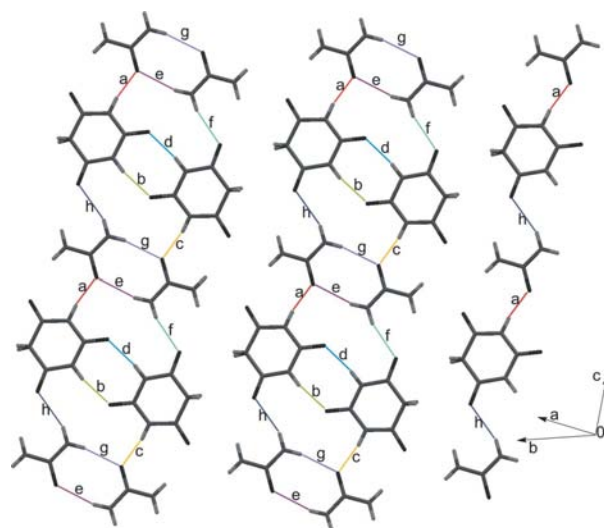


Figure 9
Hydrogen-bond patterns for polymorph (III) in the single layer built of parallel tapes running along [001]. Different hydrogen bonds defined in Table 3 are distinguished by different colors: *a* – red, *b* – green, *c* – yellow, *d* – blue, *e* – violet, *f* – cadet blue, *g* – plum, *h* – navy blue.

discrete motifs *D* leading to the description of the unitary graph set as $N_1 = DDDDDDD$. All patterns of the binary graph set are listed in Table 7. The *b* and *d* hydrogen bonds are involved in a locally (non-crystallographic) centrosymmetric ring array of barbituric acid molecules. The ring is designated by the $R_2^2(8)$ descriptor. The same pattern, $R_2^2(8)$, is formed between urea molecules through *e* and *g* hydrogen bonds. Between barbituric and urea molecules four types of hydrogen bond are present. The *a* and *h* as well as *c* and *f* hydrogen bonds form identical chains parallel to [001]. The hydrogen bonds of all types build one-dimensional ladder-like ribbons, as shown in Fig. 9.

4. Conclusions

By varying the crystallization conditions three polymorphs of barbituric acid and urea co-crystals were obtained. The polymorphism phenomenon seems to have its origin in the resonance structures of barbituric acid molecule stabilized by the influence of urea.

It was possible to recognize electron displacement in the barbituric acid molecules towards mesomeric forms:

- (i) *E* in polymorph (I) – space group $P2_1/c$;
- (ii) *E* and *A* in polymorph (III) – space group $P\bar{1}$, for two symmetrically-independent barbituric acid molecules;
- (iii) *B* in polymorph (II) – polar space group Cc .

Table 5

Quantitative graph-set descriptors of the first and second levels for the structure of polymorph (I).

	<i>a</i>	<i>b</i>	<i>c</i>	<i>d</i>	<i>e</i>	<i>f</i>
<i>a</i>	$R_2^2(8)$	$D_3^3(9)$	$D_3^3(11)$	$D_3^3(11)$	$D_3^2(7)$	–
<i>b</i>	$D_3^3(9)$	D	$C_2^2(10)$	$C_2^2(10)$	–	$D_3^2(7)$
<i>c</i>	$D_3^3(11)$	$C_2^2(10)$	D	$R_4^4(8)$	$R_2^2(8)$	$D_3^3(11)$
<i>d</i>	$D_3^3(11)$	$C_2^2(10)$	$R_4^4(8)$	DD	$R_4^4(16)$	$D_3^3(11)$
<i>e</i>	$D_3^2(7)$	$C_2^2(10)$	$R_2^2(8)$	$R_4^4(16)$	D	$D_3^3(13)$
<i>f</i>	–	$D_3^3(7)$	$D_3^3(11)$	$D_3^3(11)$	$D_3^3(13)$	$C(4)$

Table 6

Quantitative graph-set descriptors of the first and second levels for the structure of polymorph (II).

	<i>a</i>	<i>b</i>	<i>c</i>	<i>d</i>	<i>e</i>	<i>f</i>
<i>a</i>	$R_2^2(8)$	$D_3^3(9)$	$D_3^3(11)$	$D_3^3(11)$	$D_3^2(7)$	–
<i>b</i>	$D_3^3(9)$	D	$C_2^2(10)$	$C_2^2(10)$	–	$D_3^2(7)$
<i>c</i>	$D_3^3(11)$	$C_2^2(10)$	D	$R_4^4(8)$	$R_2^2(8)$	$D_3^3(11)$
<i>d</i>	$D_3^3(11)$	$C_2^2(10)$	$R_4^4(8)$	DD	$R_4^4(16)$	$D_3^3(11)$
<i>e</i>	$D_3^2(7)$	$C_2^2(10)$	$R_2^2(8)$	$R_4^4(16)$	D	$D_3^3(13)$
<i>f</i>	–	$D_3^3(7)$	$D_3^3(11)$	$D_3^3(11)$	$D_3^3(13)$	$C(4)$

Table 7

Quantitative graph-set descriptors of the first and second levels for the structure of polymorph (III).

	<i>a</i>	<i>b</i>	<i>c</i>	<i>d</i>	<i>e</i>	<i>f</i>	<i>g</i>	<i>h</i>
<i>a</i>	D	$D_2^2(7)$	–	$D_2^2(6)$	$D_2^1(3)$	–	$D_2^2(6)$	$C_2^2(10)$
<i>b</i>	$D_2^2(7)$	D	$D_2^2(6)$	$R_2^2(8)$	–	$D_2^2(7)$	–	$D_2^2(6)$
<i>c</i>	–	$D_2^2(6)$	D	$D_2^2(7)$	$D_2^2(6)$	$C_2^2(10)$	$D_2^1(3)$	–
<i>d</i>	$D_2^2(6)$	$R_2^2(8)$	$D_2^2(7)$	D	–	$D_2^2(6)$	–	$D_2^2(7)$
<i>e</i>	$D_2^1(3)$	–	$D_2^2(6)$	–	D	$D_2^2(5)$	$R_2^2(8)$	$D_2^2(6)$
<i>f</i>	–	$D_2^2(7)$	$C_2^2(10)$	$D_2^2(6)$	$D_2^2(5)$	D	$D_2^2(6)$	–
<i>g</i>	$D_2^2(6)$	–	$D_2^1(3)$	–	$R_2^2(8)$	$D_2^2(6)$	D	$D_2^2(5)$
<i>h</i>	$C_2^2(10)$	$D_2^2(6)$	–	$D_2^2(7)$	$D_2^2(6)$	–	$D_2^2(5)$	D

To justify the presence of a particular mesomeric form in the structure of each reported polymorph, experimental charge-density studies were undertaken for all three polymorphs. In all the polymorphs a significant deficiency of electron density at the centre of the barbituric heterocyclic ring was observed (Gryl *et al.*, 2008; Krawczuk *et al.*, 2008), in agreement with the results of the experimental charge-density investigation for polymorph (II) of 5,5-diethylbarbituric acid (barbital) at 198 K (Craven *et al.*, 1982).

All the studied polymorphs have layered structures but they are built of different species:

(i) in polymorph (I) urea dimers and chains of barbituric acid molecules are observed;

(ii) in polymorph (II) no direct interactions, through moderate hydrogen bonds, between species of the same type were detected;

(iii) in polymorph (III) dimers of urea and dimers of barbituric acid molecules alternate in one-dimensional tapes.

Due to the complementarity of the donor and acceptor functional groups of urea and barbituric acid components, the moderate hydrogen bonds dominate while the resonance structures of barbituric acid are responsible for the different hydrogen-bond systems observed in the polymorphs. The hydrogen-bond systems were described in terms of graph-set analysis (Etter, 1990; Etter *et al.*, 1990; Bernstein *et al.*, 1995) at

the first, second and higher levels. Most of the polymorphs do not differ at the first-level graph sets so it is necessary to turn to higher levels to distinguish between the polymorphs. In the case of the studied structures it was not necessary to use upper-level analysis because the differentiation of polymorphs (I), (II) and (III) could be established at first level. Nevertheless, higher-level analysis was useful to reveal the specific behaviour of hydrogen-bond systems responsible for the mutual arrangement of the structural components.

Polymorph (II) of the crystal class *m* will be further investigated towards the possible polar physical properties.

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