Electronic Supplementary Material (ESI) for CrystEngComm

Electronic Supporting Information

Supramolecular constructs and thermodynamic stability of four polymorphs and a co-crystal of pentobarbital (nembutal)

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1. Preparation methods

Table S1 Preparation methods of polymorphs of Nbtl as described in the literature (for each form, the range of reported melting points is given).

Polymorphic form, preparation,	Reference
*Nbtl-**I** (m.p. 129−131 °C)*	
Evaporation of a solution in chloroform, by blowing a jet of air over the solution	Cleverley & Williams, 1959 [1]
Precipitation from xylene/petroleum ether or ethanol/water	Schulte, 1980 [2]
Sublimation (needles)	Fischer, 1939 [3]
Annealing of the melt at 70−80 °C	Brandstätter-Kuhnert & Aepkers, 1962 [4]
Heating of any other Nbtl-form to 120 °C	Mesley, 1970 [5]
*Nbtl-**II** (m.p. 124−126 °C)*	
Evaporating the solvent of a solution in diethylether or dichloromethane or tetrachloromethane under reduced pressure sample temperature: ca. 10 °C	Schulte, 1980 [2]
Precipitation from Nbtl sodium salt, dissolved in water with diluted hydrochloric acid	Huang, 1951 [6]
Evaporation of a solution in carbon tetrachloride, by blowing a jet of air over the solution	Cleverley & Williams, 1959 [1]
*Nbtl-**III** (m.p. 113 °C)*	
Stirring of Nbtl-**I** in water or benzene at 10 °C for 24 hours	Schulte, 1980 [2]
Sublimation	Brandstätter-Kuhnert & Aepkers, 1962 [4]
*Nbtl-**IV** (m.p. 109 °C)*	
Spontaneous from the melt (concomitantly with Nbtl-**I**)	Brandstätter-Kuhnert & Aepkers, 1962 [4]
Rotavapor: from chloroform (12−13 °C) under vacuum	Schulte, 1980 [2]

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2. Polarised light photomicrographs of forms of Nbtl

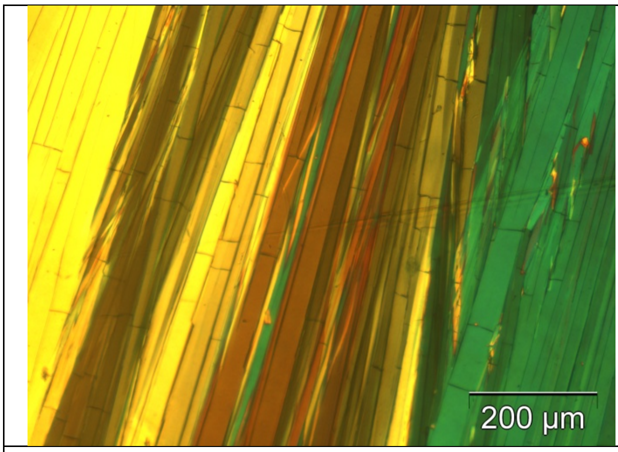

Fig. S1 Melt film preparation of Nbtl-**I** produced by cooling the melt to about 80 °C

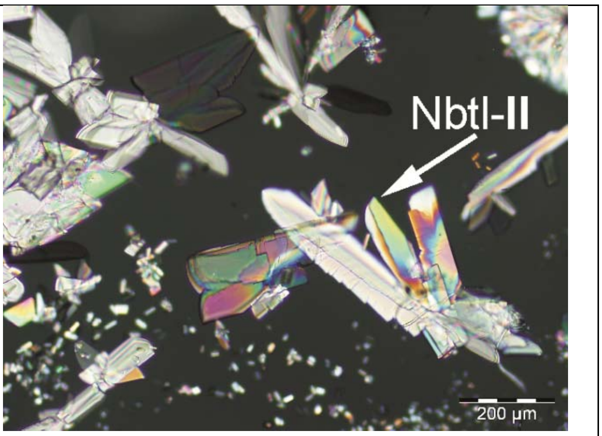

Fig. S2 Crystals of Nbtl-**II** (large crystals) grown from the melt at 85 °C

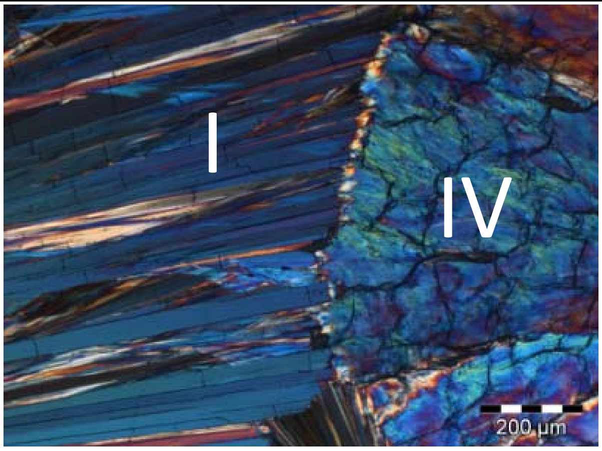

Fig. S3 Melt-film preparation showing Nbtl-**I** (left) and Nbtl-**IV** (right) produced by annealing the supercooled melt at about 70 °C

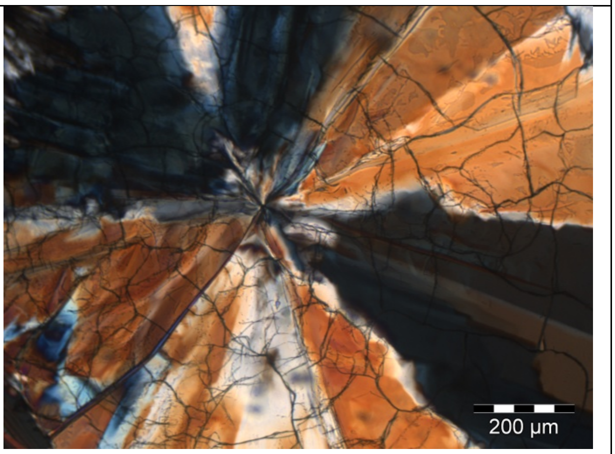

Fig. S4 Melt film preparation of Nbtl-**IV** produced by annealing the supercooled melt at about 100 °C

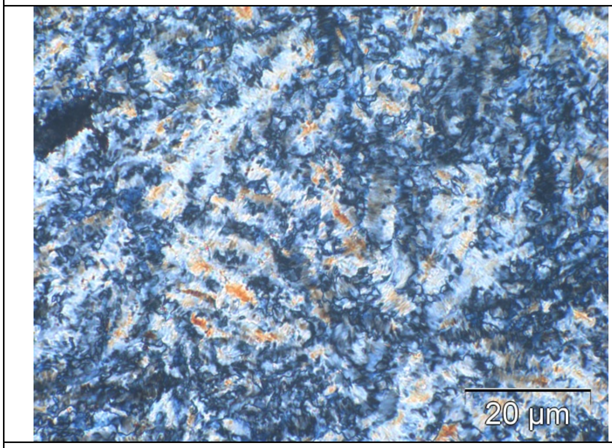

Fig. S5 Melt film preparation of Nbtl produced by keeping the supercooled melt at RT for several hours containing Nbtl-**I** and Nbtl-**II**

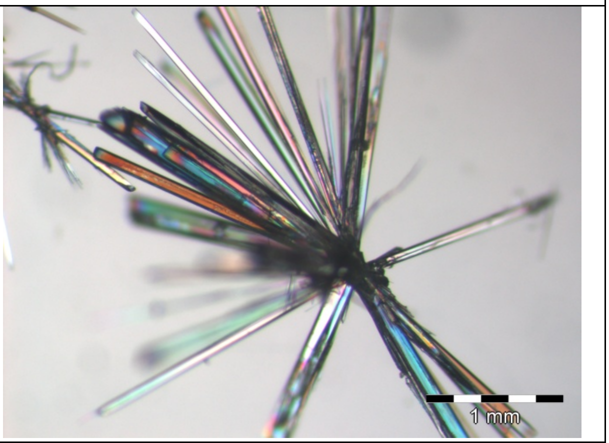

Fig. S6 Co-crystal of Nbtl·Pbtl produced from mesitylen

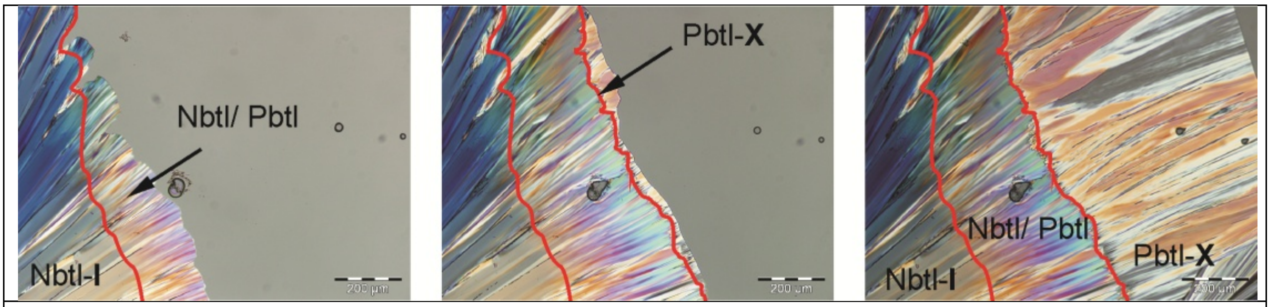

Fig. S7 Microscopic image of a contact preparation of Nbtl (left part of the image) with Pbtl (right part of the image). Left: sample at 90 °C showing the growth of Nbtl-**I** into the contact zone forming the co-crystal Nbtl·Pbtl with similar morphological features. Centre and right: the Nbtl-Pbtl co-crystal grows within the contact zone (between the red lines) and induces the formation of Pbtl-X which is isomorphic to the co-crystal (sample at 95 °C and 105 °C).

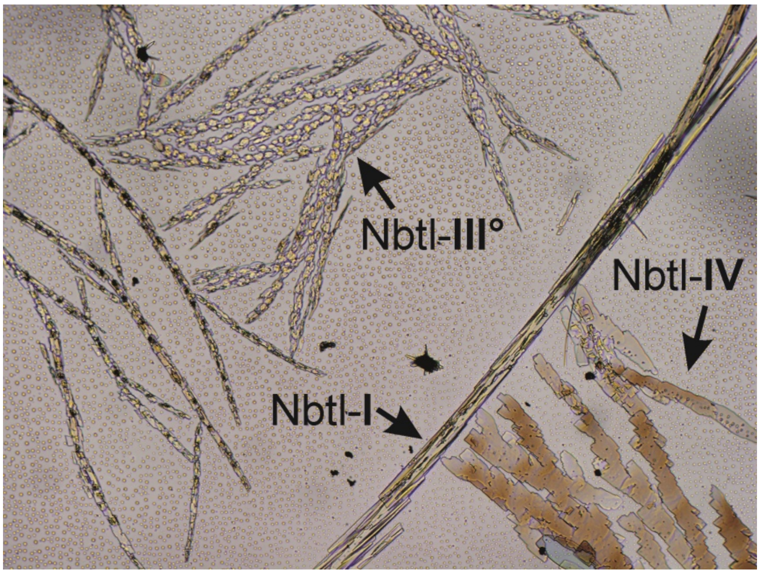

Fig. S8 Photomicrograph of sublimates of Nbtl forms. The samples were sublimed from one object slide to another (90 °C, Kofler hot-bench), using a glass ring with a height of 5 mm.

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3. Comparison of PXRD patterns

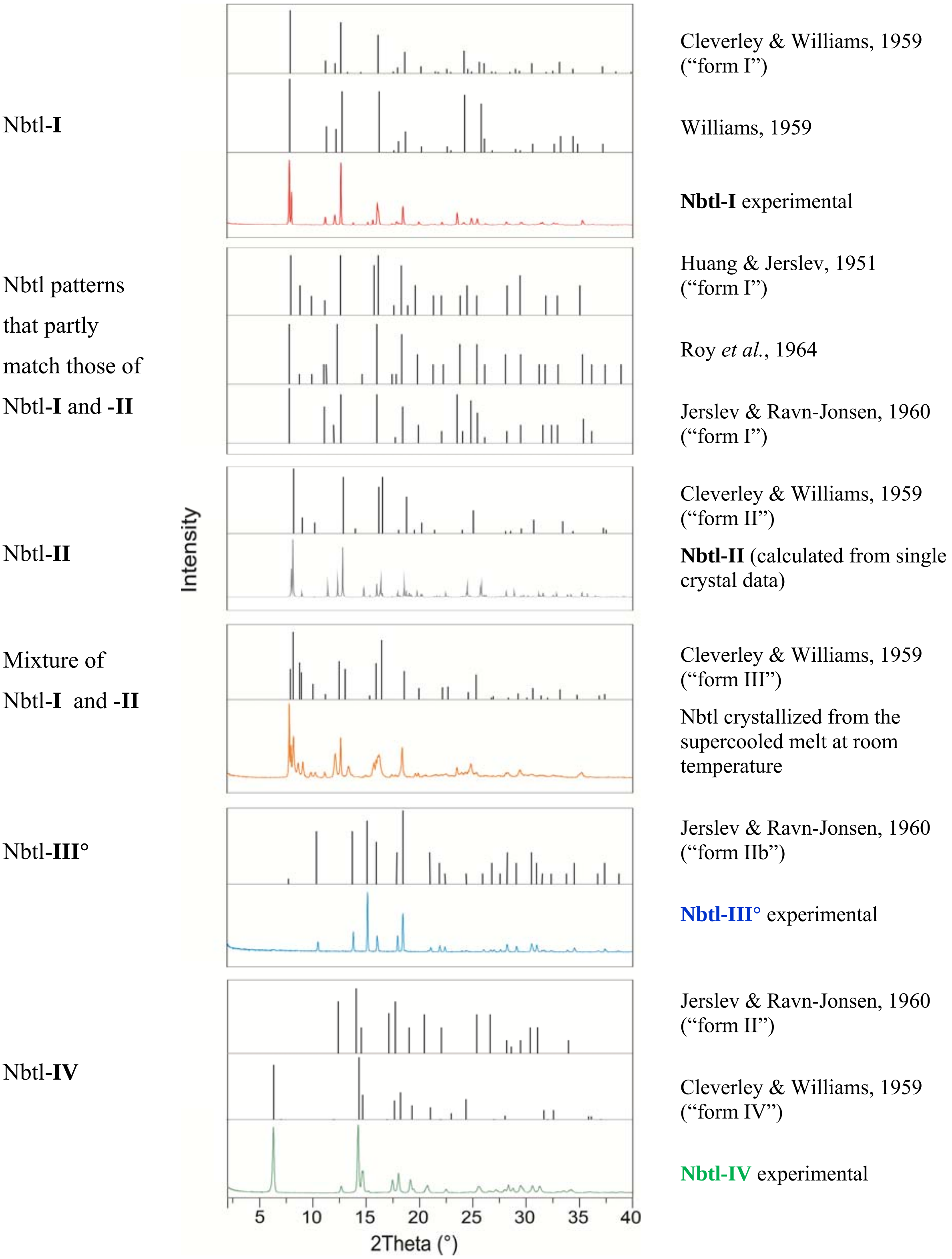


Fig. S9: Summary of X-ray powder diffraction patterns of Nbtl from different literature sources (see also Table S1) in comparison with the reference patterns for the polymorphs characterised in the present study.

4. Disorder models

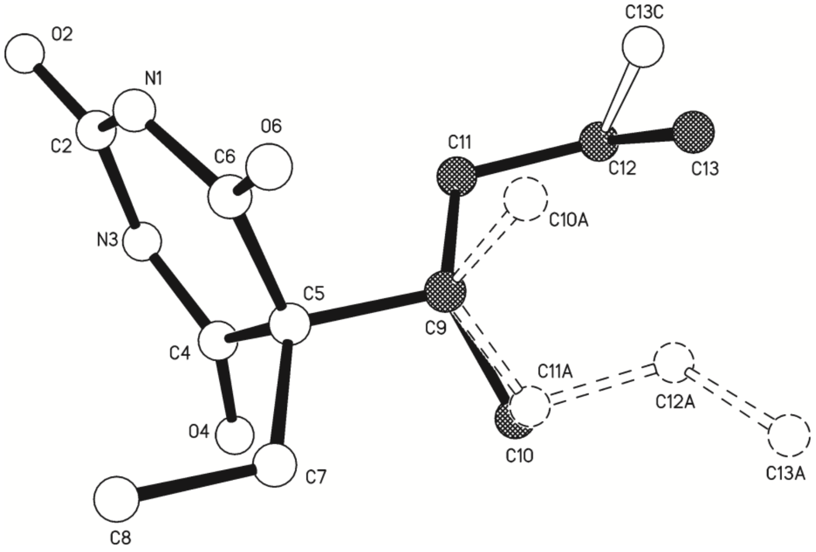


Fig. S10 Crystal structure of Nbtl-**II**: disorder model for the 1-methylbutyl group of molecule A: C10−C9−C11−C12−C13 (42%) and C10−C9−C11−C12−C13C (43%), C10A−C9A−C11A−C12A−C13A (15%).

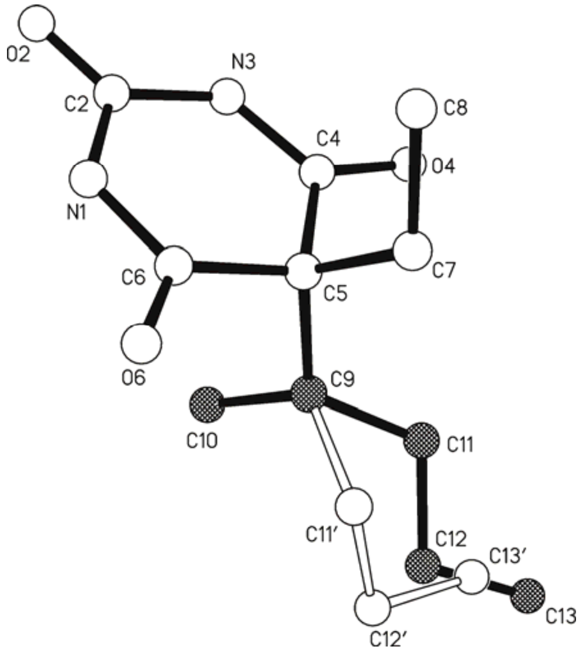


Fig. S11 Crystal structure of Nbtl-**IV**: disorder model for the 1-methylbutyl group: C10−C9−C11−C12−C13 (59%) and C10−C9−C11’−C12’−C13’ (41%).

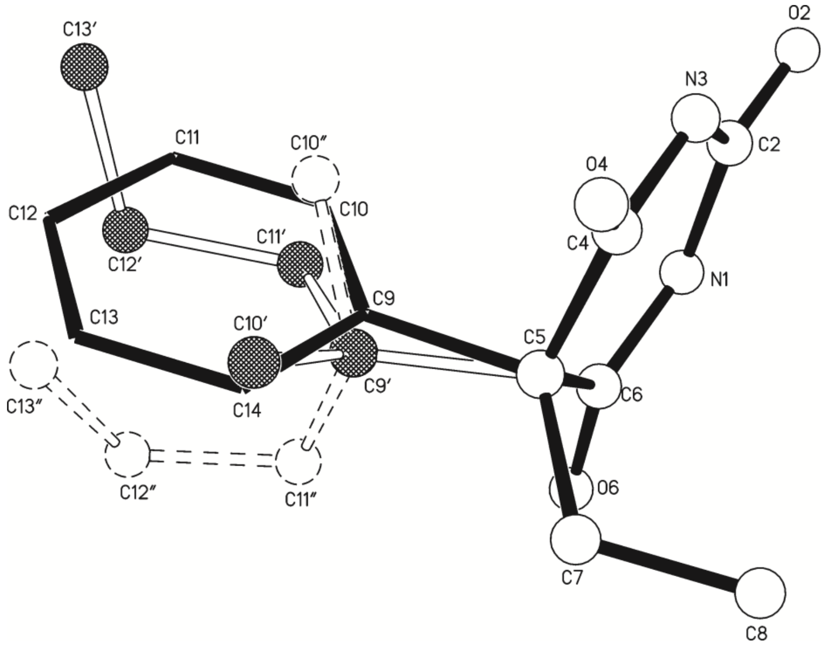


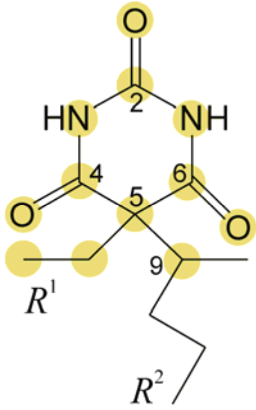
Fig. S12 Co-crystal Nbtl·Pbtl: disorder between the phenyl ring of Pbtl (50%; solid bonds) and two orientations (open bonds and dashed open bonds) of 1-methylbutyl.

5. *XPac* comparison of crystal structures

5.1. General

Structure comparisons were carried out with version 2.0 of the program *XPac*.[7] Molecules were represented by the positions of the p = 12 non-H atoms highlighted in Scheme S1. Atoms of the R^2 group were not considered, except for the carbon atom bonded to the C-5 position of the barbiturate ring. Results from these calculations were therefore not directly affected by differences in the composition and conformation of the R^2 group and the obtained dissimilarity indices x (for p = 12) account primarily account for changes in the relative arrangement of molecules.

Additional comparisons between Nbtl-**I** and Nbtl-**II** (with each independent molecule by represented as by one disorder fragment) and between Nbtl-**IV** and form I of vinbarbital[8] (CSD refcode VINBAR) were carried out, in which all p = 16 non-H atomic positions per molecule were used. The dissimilarity index x obtained from these calculations (i.e. for p = 16) accounts for the entirety of geometrical differences between two crystal structures, including conformational differences between R^2 groups.



Scheme S1

5.2. Nbtl-I, Nbtl-II Nbtl·Pbtl and the "Pbtl-X group"

The *XPac* comparisons show that the complete 3D molecular packing arrangement in the co-crystal Nbtl·Pbtl agrees with that of those structures which form the Pbtl-X group: AMYTAL11, FUFTAG and BECLIE, despite different space group symmetries. The corresponding lattice vectors and other parameters are compiled Table S2. The calculated dissimilarity indices x were 6.0, 6.2 and 10.6 for the p = 12 comparisons of Nbtl·Pbtl with AMYTAL11, FUFTAG and BECLIE, respectively. Fig. S13 shows an *XPac* plot for the comparison between Nbtl·Pbtl and AMYTAL11.

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Table S2 Corresponding lattice parameters within the “Pbtl-X group” of isostructures and parameters in the structures of Nbtl-**I** and Nbtl-**II** which are associated with the common 2D SC (see Fig. S13).

Structure	Spgr.	*Z'*	Lattice vectors			Distances / Å			Angles / °			Reference
			$\mathbf{t}_1$	$\mathbf{t}_2$	$\mathbf{t}_3$	d_1	d_2	d_3	($\mathbf{t}_2$,$\mathbf{t}_3$)	($\mathbf{t}_1$,$\mathbf{t}_2$)	($\mathbf{t}_2$,$\mathbf{t}_3$)	
AMYTAL11 [a,b]	$P2_1/c$	2	100	001	010	10.28	11.68	22.60	109.1	90	90	9
Nbtl·Pbtl [a,c]	$C2/c$	1	001	$\bar{1}0\bar{1}$	$0\bar{1}0$	10.25	11.91	20.69	110.7	90	90	This study
FUFTAC [a,b]	$C2/c$	1	001	$\bar{1}0\bar{1}$	010	10.28	11.82	17.37	110.6	90	90	10
BECLIE [a,b]	$P2_1/c$	2	001	100	$0\bar{1}0$	10.20	11.59	22.19	109.0	90	90	11
Nbtl-**I**	$P2/c$	1	001	100	–	10.19	11.74	–	110.2	–	–	This study
Nbtl-**II**	$P2_1/c$	2	001	100	–	10.22	11.87	–	110.5	–	–	This study

[a] “Pbtl-X group” of isostructures

[b] CSD refcode

c The asymmetric unit contains one barbiturate molecule. However because of the disorder between Nbtl and Pbtl, Z’ = 0.5 with respect to the composition Nbtl·Pbtl

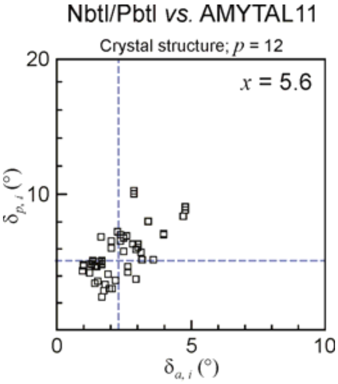

Fig. S13 *XPac* plot for the comparison between the structures of Nbtl·Pbtl and AMYTAL11, which confirms that they are isostructural, *i.e.* they display the same complete 3D arrangement of molecules.

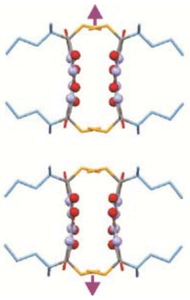

Fig. S14 The common 2D SC that is present in the crystal structures of the “Pbtl-X group” of isostructures (including the co-crystal Nbtl·Pbtl), in Nbtl-**I** and Nbtl-**II** (see also Fig. 6). The layer is viewed parallel to the translation of the N−H···O=C-bonded chain, i.e. along the lattice vector t_1 (with t_2 running in vertical direction as indicated by the arrows).

5.3. Nbtl-IV and form I of vinbarbital

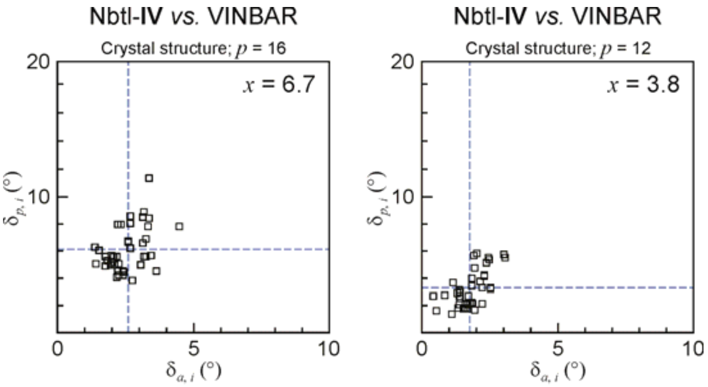

Fig. S15 *XPac* plots for the comparison of Nbtl-**IV** (R^1 = ethyl, R^2 = 1-methylbutyl) with form I of vinbarbital[8] (CSD: VINBAR; R^1 = ethyl, R^2 = 1-methylbutenyl). Left: The match of representative cluster with $n = 14$ neighbour molecules based on geometrical parameters calculated from $p = 16$ non-H atoms gave an overall dissimilarity index x of 6.7. Right: The analogous procedure gives a significantly lower value of $x = 3.8$ if the R^2 groups are not included except for the carbon atom attached to the C-5 atom of the barbiturate ring.

Table S3 Corresponding lattice parameters of Nbtl-**IV** and form I of vinbarbital.

Structure	Space group	*a*/Å	*b*/Å	*c*/Å	*β*/°	Ref.
Nbtl-**IV**	$P2_1/c$	14.514	6.834	12.497	104.76	This study
VINBAR	$P2_1/c$	14.395	6.822	12.540	107.43	8

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