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SUPPORTING INFORMATION

Polymorphism control in mechanochemical and solution based synthesis of a thermochromic Schiff base

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1. EXPERIMENTAL DETAILS

1.1. Materials

All reagents, solvents and filtering papers were purchased from commercial sources and used as received. Table S2 comprises all starting materials and solvents used for syntheses, crystallization or liquid-assisted grinding experiments.

Table S1 Starting materials used for various experiments.

Name	Acronym	Manufacturer
***Ortho*-vanillin**	*ovan*	Acros Organics
3-aminoacetophenone	3aa	Merck
Ethanol, 96%	EtOH, 96 %	Alkaloid Skopje
Ethanol, 99.5%	AtOH, abs	GRAM-MOL
Acetone	ace	CLARO-PROM
Acetonitrile	MeCN	J.T.Baker
Cyclohexanol	ChxOH	Kemika

The filtering papers used for filtration of ethanolic solutions of 3-aminoacetophenone were selected in order to assure various pore sizes and therefore different amounts of impurities that remain in the mother liquor (Table S2).

Table S2 Filtering papers used for filtration.

Full name of filtering paper	Manufacturer	Reference
Student grade 21N	**Munktell Ahlstrom, Germany**	http://www.ahlstrom.com/en/Munktell/Munktell-products/Brochure/?productId=4649
White ribbon 615	**MACHEREY-NAGEL GmbH & Co., Germany**	ftp://ftp.mn-net.com/filtration/filter_paper_data_sheets/MN-615-Pd.pdf
Blue ribbon 619	**MACHEREY-NAGEL GmbH & Co., Germany**	ftp://ftp.mn-net.com/filtration/filter_paper_data_sheets/MN-619-Pd.pdf

1.2. Synthesis accompanied by ex situ PXRD experiments

Syntheses of compound **1** were performed by means of solution-based and mechanochemical methods as described below. All products obtained were characterized by means of Powder X-Ray diffraction measurements, PXRD (for details see further in text).

1.3. Solution based syntheses and crystallization experiments

All solution based syntheses were performed using equimolar quantities of reactants *i.e.* 0.153 g (1 mmol) of *o*-vanillin dissolved in 2 mL and 0.135 g (1 mmol) of 3-aminoacetophenone in 5 mL of corresponding boiling ethanol.

1.3.1. Solution based syntheses of compound **1**, form **I**

1.3.1.1. Room temperature experiments

Form **I** can be obtained from a boiling ethanol (96 % or absolute) mixture of *o*-vanillin and 3-aminoacetophenone solutions left overnight at 25 °C when 3aa solution is not filtered (Figure S1). The solution of 3-aminoacetophenone is blurry and was therefore filtered using:

1. student grade,
2. white ribbon
3. and blue ribbon filtering paper before adding into the solution of *o*-vanillin,

and then the resulting mixture was left semi-closed overnight at 25 °C.

Orange rod-like crystals of form **I** suitable for SCXRD were obtained by means of slow evaporation of mother liquor and can be seen in Figure S1.

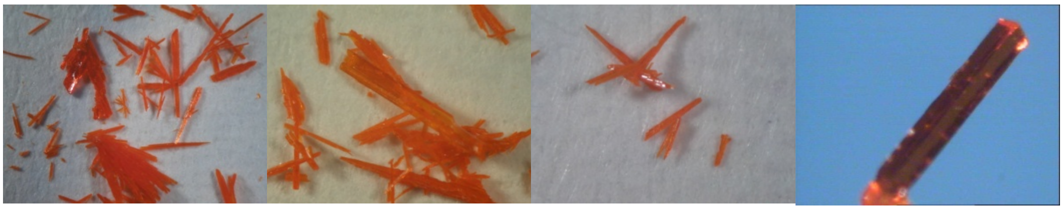


Figure S1 Crystals of polymorph **I** at 25 °C and the single crystal used for SCXRD obtained from 96 % ethanol at RT when filtration of 3aa solution was not performed.

1.3.1.2. Low temperature experiments

If 3-aminoacetophenone is dissolved in boiling EtOH, 96 % and filtered using blue ribbon filtering paper and then poured in the boiling EtOH, 96 %, solution of *o*van and the mixture is left at 8 °C overnight form **I** of compound **1** is obtained. If student grade filtering paper is used but the solutions of reactants are made using absolute EtOH, slow overnight evaporation of solvent results again in compound **1**, form **I**.

1.3.2. Solution based syntheses of compound **1**, form **I** and **II** obtained as concomitant polymorphs

1. Reactants were dissolved in boiling 96 % ethanol. 3aa solution was filtered using student grade filtering paper and poured into *o*van solution. The resulting mixture was left semi-closed overnight at 8 °C.
2. Reactants were dissolved in boiling 1:2 mixture of 96 % ethanol and distilled water. 3aa solution was filtered using blue ribbon filtering paper and poured into *o*van solution. The resulting mixture was left semi-closed overnight at 8 °C.
3. Reactants were dissolved in boiling 2:1 mixture of 96 % ethanol and distilled water. 3aa solution was filtered using blue ribbon filtering paper and poured into *o*van solution. The resulting mixture was left semi-closed overnight at 8 °C.

1.3.3. Solution based syntheses of compound **1**, form **II**

Form **II** of compound **1** was obtained unaccompanied by form **I** only in three synthetic procedures at 8 °C as follows:

1. Reactants were dissolved in boiling 96 % ethanol. 3aa solution was filtered using white ribbon filtering paper and poured into *o*van solution. The resulting mixture was left semi-closed overnight at 8 °C.
2. Reactants were dissolved in boiling absolute ethanol. 3aa solution was filtered using white ribbon filtering paper and poured into *o*van solution. The resulting mixture was left semi-closed overnight at 8 °C.
3. Reactants were dissolved in boiling 1:1 mixture of 96 % ethanol and distilled water. 3aa solution was filtered using white ribbon filtering paper and poured into *o*van solution. The resulting mixture was left semi-closed overnight at 8 °C.

Light orange needle-like crystals of form **II** suitable for SCXRD were obtained by means of slow evaporation of mother liquor and can be seen in Figure S2.

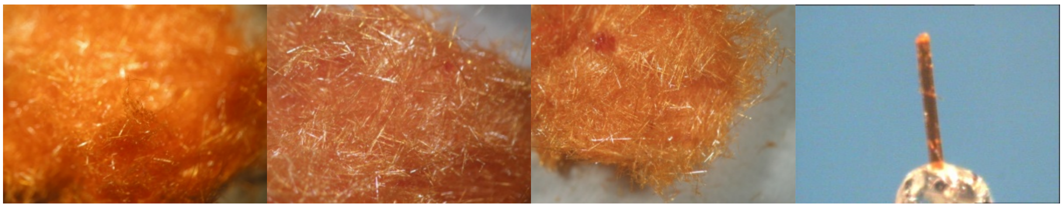


Figure S2 Crystals of polymorph **II** at 25 °C and the single crystal used for SCXRD obtained from 96 % ethanol at LT when filtration was performed using white ribbon filtering paper.

1.3.4. Solution based syntheses of compound **1**, form **III**

We were able to obtain form **III** of compound **1** only in one solution based method. Reactants were dissolved in boiling absolute ethanol. 3aa solution was filtered using student grade filtering paper and poured into *o*van solution. The resulting mixture was left semi-closed overnight at 25 °C.

Dark orange, almost red brick-like crystals of form **III** suitable for SCXRD were obtained by means of slow evaporation of mother liquor and can be seen in Figure S3.

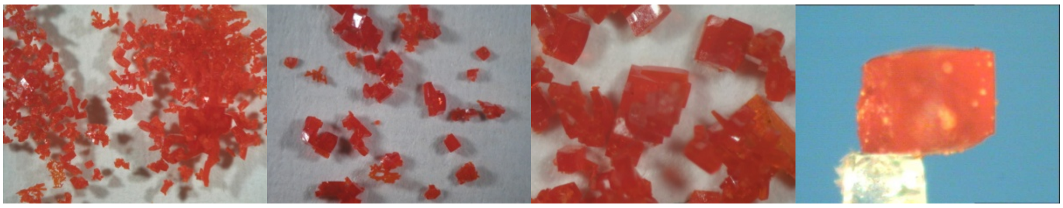


Figure S3 Crystals of polymorph **III** at 25 °C and the single crystal used for SCXRD.

The syntheses were doubled to check the reproducibility.

1.4. Mechanochemical syntheses

All grinding experiments were performed in an agate mortar at RT and 40-50 % relative humidity. The required grinding time in the agate mortar was determined empirically when the colour of the reaction mixture stopped changing. *Ex–situ* PXRD experiments were performed on all powder products obtained by grinding to check if the condensation reaction of the aldehyde and amine yielded in compound **1**.

1.4.1. Neat grinding experiments

Equimolar quantities of ***o*van** (0.153 g, 1 mmol) and **3aa** (0.135 g, 1 mmol) were ground in an agate mortar at 25 °C as can be seen in Figure S4. After 40 s of NG the reaction mixture starts to change its colour and after 60 s an orange paste appears. The paste starts to solidify after 2 min of grinding. After 3.5 min an orange powder was obtained. The PXRD data on the obtained powder revealed that the used procedure is efficient enough since there are no traces of reactants in the powder product.


t = 0 s *t* = 20 s *t* = 40 s *t* = 45 s *t* = 60 s *t* = 120 s *t* = 180 s *t* = 210 s

Figure S4 Neat ginding of ***ovan*** and **3aa** in an agate mortar.

1.4.2. Liquid-assisted grinding experiments

1. Equimolar quantities of ***ovan*** (0.153 g, 1 mmol), **3aa** (0.135 g, 1 mmol) and 40 µL of 96 % ethanol were put in an agate mortar at 25 °C and ground for 8 min in total.

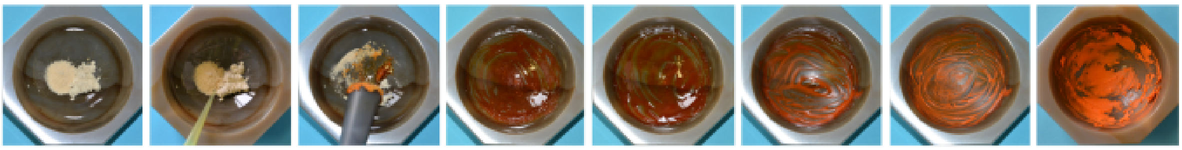

t = 0 s *t* = 30 s *t* = 60 s *t* = 2 min *t* = 2.5 min *t* = 3.5 min *t* = 4 min *t* = 8 min

Figure S5 Liquid-assisted grinding of ***ovan*** and **3aa** monitored using a photo camera.

After one minute of grinding in presence of a catalytic amount of EtOH, 96%, the reaction mixture starts to change its colour and orange paste appears almost instantaneously. The paste starts to solidify after 2.5 min of grinding but remains present up to the fourth minute. After 8 min an orange powder was obtained. The PXRD data on the obtained powder revealed that the used procedure is efficient enough since there are no traces of reactants in the powder product.

2. Equimolar quantities of ***ovan*** (0.153 g, 1 mmol) and **3aa** (0.135 g, 1 mmol) were ground at 25 °C up until a paste was formed like in NG experiments. At this point 40 µL of 96 % ethanol was added in the reaction mixture and ground for 9 min in total until an orange powder was obtained since the paste solidifies gradually with time. The PXRD data on the obtained powder revealed that the used procedure is efficient enough since there are no traces of reactants in the powder product.

1.4.3. Seeding-assisted grinding experiments

1. ***ovan*** (0.153 g, 1 mmol) and seeds of form **II** (0.048 g, 0.2 mmol) were ground in an agate mortar at 25 °C for 2.5 min resulting in light orange powder. At this point **3aa** (0.135 g, 1

mmol) was added to the mixture and ground. 20 s after that point a paste forms and after another 2.5 min the reaction mixture starts to solidify. The grinding process lasted 6 minutes in overall until dry orange powder wasn't obtained. The PXRD data on the obtained powder revealed that the used procedure is efficient to convert form **II** to form **I** using mechanochemical method.

2. ***o*van** (0.153 g, 1 mmol) and **III** (0.048 g, 0.2 mmol) were ground in an agate mortar at 25 °C for 2.5 min. At this point **3aa** (0.135 g, 1 mmol) was added to the mixture and ground for another 60 s when an orange paste forms. By further grinding the paste gradually solidifies. After 5.5 min from **3aa** addition again orange dry powder was obtained.

1.5. Synthesis by ageing of the reaction mixture – *In-situ* PXRD monitoring

In order to monitor the advancement of the reaction using *in situ* PXRD (for details see further in text) merely by putting the reactants used as purchased in close contact and leaving the reaction mixture to age, equimolar quantities of aldehyde and amine (1:1) were gently mixed in a mortar with a spatula to provide homogeneity of the reaction mixture and to ensure no (or minimal) mechanic force was used. The reaction mixture was transferred into an aluminium holder, evened and then put into the instrument.

In another similar experiment the reactants were first pre-ground separately for *approx.* 2-3 minutes and then mixed to provide homogeneity, transferred into an aluminium holder, evened and then put into the instrument.

1.6. Polymorph interconversion study

1.6.1. Heating experiments

The measurements were performed on a Mettler Toledo DSC823^e module in sealed aluminium pans (40 µL), heated in flowing nitrogen (200 mL min^{-1}) at a rate of 10 °C min^{-1}. The data collection and analysis was performed using the program package STAR^e Software 9.01.[i].

1. Samples of forms **I**, **II** and **III**, were heated from 25 to 500 °C on a Mettler Toledo TGA/SDTA and DSC823^e module in sealed aluminium pans (40 µL), heated in flowing nitrogen (200 mL min^{-1}) at a rate of 10 °C min^{-1}. Data analyses on DSC measurements

revealed that form **I** and **III** show one strong endothermic peak with an onset at 103 and 118 °C, respectively that corresponds to their melting onset which is in accordance with their TGA/SDTA curves. On the other hand, form **II** of compound **1** has three endothermic peak onsets in the DSC curve (77, 101 and 117 °C) and for that reason isothermal experiments described below were performed.

TGA/SDTA curves are in good agreement with the ones obtained by DSC measurements confirming that all three samples (form **I**, **II** and **III**) go through an exothermic decomposition after *approx.* 220 °C.

2. Samples of compound **1**, form **I**, were heated from 25 to 98 and 100 °C and then kept at those selected temperatures for 2 minutes. After that, the samples were cooled to 25 °C and PXRD measurements on the obtained material were done revealing that form **I** doesn’t undergo a temperature induced transformation.
3. Samples of compound **1**, form **I**, were heated from 25 to 82, 101, 106 and 116 °C and then kept at those selected temperatures for 2 minutes. After that, the samples were cooled back to 25 °C and PXRD measurements on the obtained material were done revealing that form **II** undergoes a temperature induced transformation to form **III** even at 82 °C.
4. Samples of compound **1**, form **III**, were heated from 25 to 80, 95 and 108 °C and then cept at that selected temperature for 2 minutes. After that, the samples were cooled to 25 °C and PXRD measurements on the obtained material were done revealing that form **III**, like form **I** as well, doesn’t undergo a temperature induced transformation.

1.6.2. Liquid-assisted grinding of mixtures of polymorphs

Three combinations of polymorph mixtures i.e. I and II, I and III, II and III, in mass ratio of 1:1 (cca 0.015 g of each per experiment) were ground in a mortar with addition of 20 µL of five solvents [acetone (ace), acetonitrile (MeCN), ethanol (EtOH, 96 %), cyclohexanol (ChxOH) and water (H2O)] until the solvent evaporated when PXRD experiments were done. The ex situ PXRD tests were performed on the obtained material after 3 weeks as well.

1.6.3. Ethanol vapour digestion experiments

Open test tubes containing *cca* 100 mg of forms **I**, **II**, **I** and **II** obtained concomitantly by solution based synthesis, and **III** were exposed at 25 °C to vapour of ethanol (96 % and absolute, respectively) by placing the tube in a bottle containing ethanol so that there is no direct contact between the crystals and the liquid phase. The efficiencies were monitored by means of PXRD. Crystals of form **II** convert spontaneously into form **I** in the period of three hours. On the other hand, there is no influence of ethanol vapour to neither form **I** nor form **III** in the same period of vapour digestion.

1.7. FT-IR spectroscopy

Infrared spectra were recorded on a PerkinElmer Spectrum Two FTIR spectrophotometer using the KBr pellet method. The data collection and analysis was performed using the program package PerkinElmer Spectrum 10.4.2.279[ii] Table S3 comprises data for the characteristic stretching bands for **I**, **II** and **III**.

Table S3 Characteristic stretching bands for **I**, **II** and **III** found in the FT-IR spectra.

	$\tilde{\nu}$ / cm^{-1}							
	X–H, X = N or O	**C_{ar}–H, C–H**	**C=N**	**C_{ar}–O**	**C_{ar}– C_{ar}**	**C_{ar}–N**	**C_{ar}-O-CH_3**	**C=O**
I	3445	3059, 2997	1615	1256 (1469)	1574	1358	1186	1677
II	3450	3056, 2951	1614	1256 (1466)	1572	1371	1183	1678
III	3449	3056, 2951	1614	1256 (1466)	1570	1371	1183	1678

1.8. Single crystal X-Ray diffraction experiments

Crystal and molecular structures of **II** and **III** at 25 and of **I** at –73 °C were determined using single crystal X-ray diffraction. Diffraction measurements were made on an Oxford Diffraction Xcalibur Kappa CCD X-ray diffractometer with graphite-monochromated MoK_α (λ = 0.71073 Å) radiation [iii]. The data sets were collected using the ω scan mode over the 2θ range up to 54°. The structures were solved by direct methods and refined using the SHELXS and SHELXL programs, respectively [iv]. The structural refinement was performed on F^2 using all data. The hydrogen atoms not involved in hydrogen bonding were placed in calculated positions and treated as riding on their parent atoms [C–H = 0.93 Å and $U_{iso}(H) = 1.2\ U_{eq}(C)$; C–H = 0.97 Å and $U_{iso}(H) = 1.2\ U_{eq}(C)$] while the others were located from the electron difference map. All calculations were performed using the WinGX crystallographic suite of programs [v]. The data concerning the results of the crystallographic experiments of until now unreported structures are listed in Table S2. Further details are available from the Cambridge Crystallographic Centre [vi]. Molecular structures of compounds are presented by ORTEP-3 [vii] and their packing diagrams were prepared using Mercury [viii].

1.9. Powder X-Ray diffraction experiments

1.9.1. *Ex-situ* experiments

The powder X-ray diffraction (PXRD) experiments were performed on a PHILIPS PW 1840 X-ray diffractometer with Cu$K_{\alpha 1}$ (1.54056 Å) radiation at 40 mA and 40 kV. The scattered intensities were measured with a scintillation counter. The angular range (2θ) was from 5 to 45° with steps of 0.02°, and the measuring time was 0.5 s per step. The data collection and analysis were performed using the program package *Philips X'Pert* [ix,x,xi].

1.9.2. *In-situ* experiments

The powder X-ray diffraction (PXRD) experiments were performed on a PHILIPS PW 1840 X-ray diffractometer with Cu$K_{\alpha 1}$ (1.54056 Å) radiation at 40 mA and 40 kV. The scattered intensities were measured with a scintillation counter. The angular range (2θ) was selected according to the reactants diffraction maxima from 10.0 to 20.0° with steps of 0.02°, and the measuring time was 0.5 s per step for reactants used as purchased. The measurements were repeated in 40 cycles. In the case of the *in-situ* monitoring of the contact reaction when reactants were separately ground prior to contact, the angular range (2θ) was also selected according to the reactants diffraction maxima from 11.5 to 15.0° with steps of 0.02°, and the measuring time was 0.5 s per step. The measurements were repeated in 110 cycles. The data collection and analysis were performed using the program package *Philips X'Pert* [xii,xiii,xiv].

2. RESULTS

2.1. Results of Single crystal X-ray experiments

Table S4 General and crystallographic data for **I**, **II** and **III**.

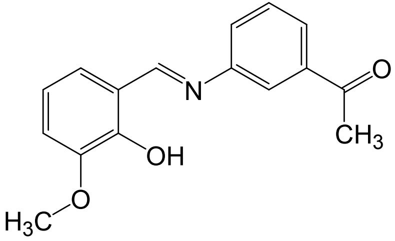
Structural formula			
Molecular formula	$C_{16}H_{15}NO_3$		
M_r	269.30		
Polymorph	**I**	**II**	**III**
Temperature / K	200	298	
Crystal system	Orthorhombic		
Space group	$P\ na2_1$	$P\ 2_12_12_1$	$P\ 2_12_12_1$
Crystal data:			
a / Å	19.139(3)	4.8773(5)	7.4681(3)
b / Å	5.3140(13)	13.7541(14)	13.1048(5)
c / Å	26.000(5)	20.3950(18)	13.9995(5)
V / Å^3	2644.3(9)	1368.2(2)	1370.10(9)
Z	8	4	4
D_{calc} / g cm^{-3}	1.353	1.307	1.305
$\lambda(\mathrm{Mo}K_\alpha)$ / Å	0.71073		
μ / mm^{-1}	0.094	0.091	0.091
Crystal size / mm	0.96 × 0.18 × 0.16	0.60 × 0.08 × 0.04	0.56 × 0.48 × 0.44
$F(000)$	1136	568	568
Refl. collected/unique	16801 / 5701	5046 / 2651	10075 / 2966
No. of restraints	5	2	0
Parameters	372	187	187
$\Delta\rho_{max}, \Delta\rho_{min}$ / e Å^{-3}	0.549, –0.516	0.125, –0.128	0.608, –0.205
$R[F^2 \geq 2\sigma(F^2)]$	0.0996	0.0382	0.0705
$wR(F^2)$	0.2945	0.0830	0.2302
Goodness-of-fit, S	1.047	0.681	1.038

Table S5 Values of O1–C2 and N1–C7 bond lengths used for tautomer determination.

		Polymorph			
		I		**II**	**III**
Interatomic distance, *d* / Å	O1–C2	1.361(7)	1.336(6)	1.345(4)	1.355(4)
	N1–C7	1.295(7)	1.282(7)	1.275(4)	1.280(4)

Table S6 Intramolecular Hydrogen-bond geometry (Å, °). *D* – donor atom, *A* – acceptor atom..

Polymorph	H-bond type	*d(D···A) / Å*	∡(*D*–H···*A*) / °
I	O11–H11···N11	2.617(6)	123(4)
	O21–H21···N21	2.613(6)	138(4)
II	O1–H1···N1	2.557(3)	150(2)
III	O1–H1···N1	2.618(4)	130(4)

Table S7 Intermolecular Hydrogen-bond geometry (Å, °). *D* – donor atom, *A* – acceptor atom.

Polymorph	H-bond type	*d(D···A) / Å*	∡(*D*–H···*A*) / °	Symmetry operator
I*	C116–H11E···O21	3.447(7)	120.06(38)	*x, y, z*
	C213–H213···O12	3.468(7)	156.63(35)	
	C17–H17···O23^{i}	3.501(7)	163.91(33)	(i) –*x* + ½, +*y* – ½, +*z* + ½
	C115–H11a···O13^{ii}	3.563(8)	162.55(38)	(ii) *x*, +*y* –1, +*z*
	C215–H21c···O23^{ii}	3.578(7)	154.60(37)	
	C27–H27···O13^{iii}	3.488(7)	161.81(34)	(iii) –*x* + ½, +*y* + ½ + 1, +*z* – ½
	C211–H211···O22^{iv}	3.586(7)	132.40(36)	(iv) *x* – ½, –*y* + ½ + 1, +*z*
II	C15–H15c···O2^{i}	3.411(5)	140.62(25)	(i) *x* – ½ – 1, –*y* + ½ + 1, –*z*
	C7–H7···O3^{ii}	3.571(4)	167.43(19)	(ii) –*x*, +*y* + ½, –*z* + ½
III	C13–H13···O1^{i}	3.441(4)	142.30(21)	(i) *x* + ½, –*y* + ½, –*z* + 1
	C16–H16b···O1^{ii}	3.395(6)	121.48(28)	(i) *x* – ½, –*y* + ½, –*z*
	C6–H6···O3^{iii}	3.416(5)	149.09(23)	(iii) *x* – ½, –*y* + ½, –*z*
	C7–H7···O3^{iii}	3.356(4)	153.56(20)	

* Data at 200 K

2.2. Thermal ellipsoid plots with crystallographic labelling scheme

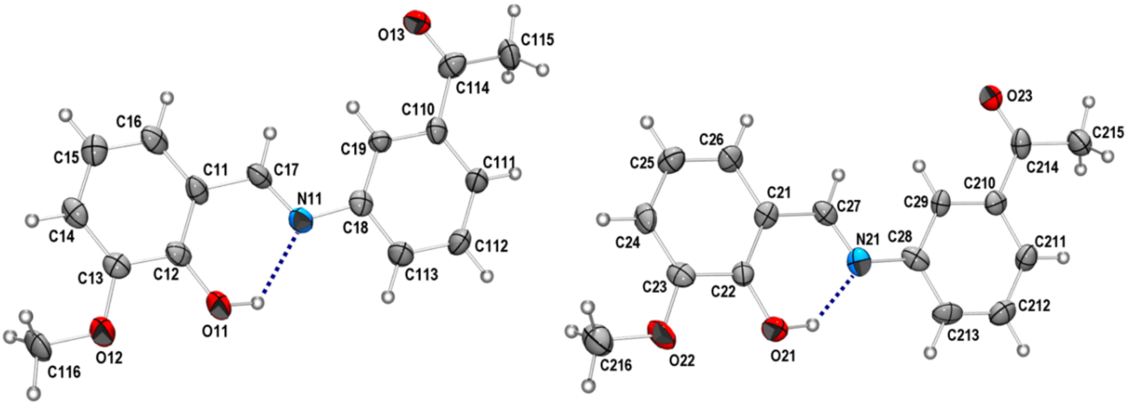


Figure S6 Thermal ellipsoids (50 %) plot of two crystallographically independent molecules in the asymmetric unit of form **I** showing the atom-labelling schemes. Dashed lines indicate intramolecular interactions. Data obtained at –73 °C.

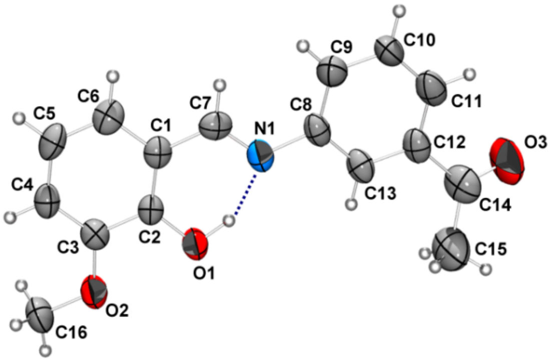


Figure S7 Thermal ellipsoid (50 %) plot of form **II** showing the atom-labelling scheme. Dashed line indicates intramolecular interaction. Data obtained at 25 °C.

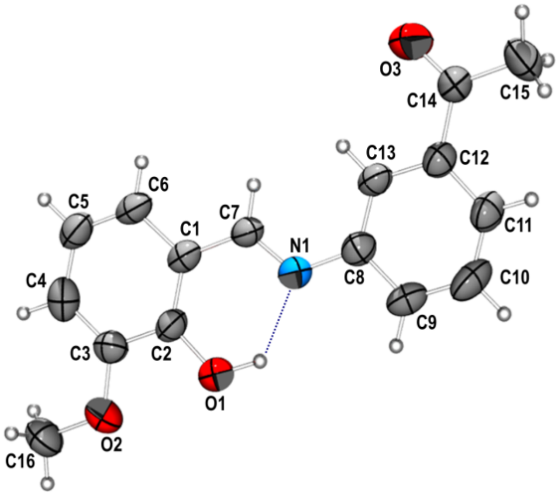
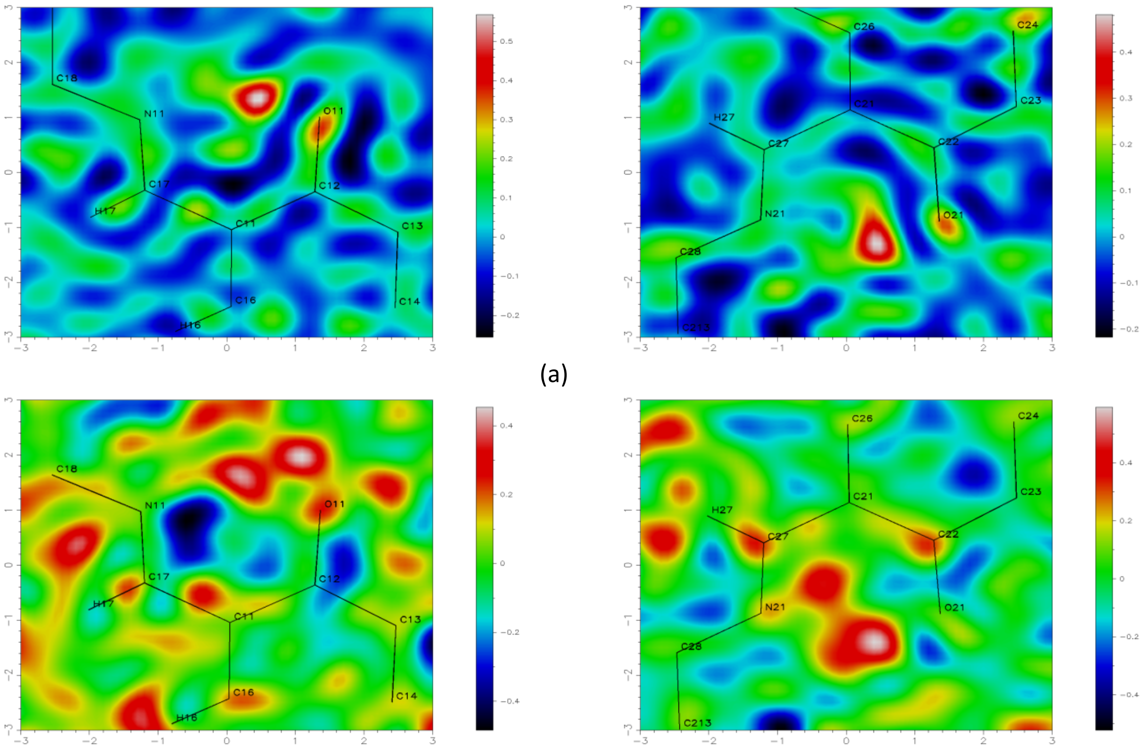


Figure S8 Thermal ellipsoid (50 %) plot of form **III** showing the atom-labelling scheme. Dashed line indicates intramolecular interaction. Data obtained at 25 °C.

2.3. *δ*F maps



(a)

(b)

Figure S9 *δ*F maps calculated through N1–C7–C1–C2–O1 chelate ring of **I** at (a) 110 and (b) 200 K.

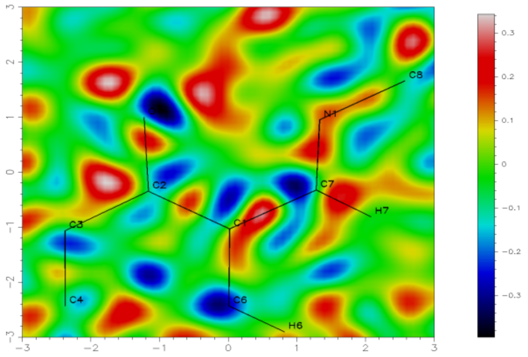


Figure S10 *δ*F maps calculated through N1–C7–C1–C2–O1 chelate ring of **II** at 298 K.

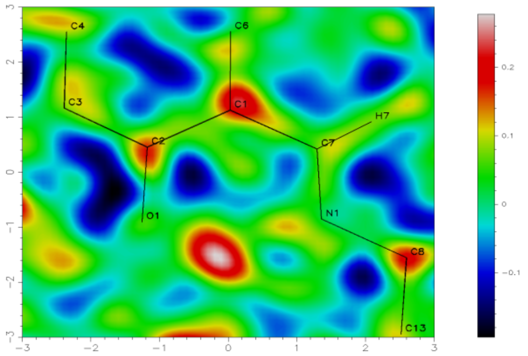


Figure S11 *δ*F maps calculated through N1–C7–C1–C2–O1 chelate ring of **III** at 298 K.

2.4. Results of *ex-situ* PXRD experiments on materials obtained by solution based syntheses

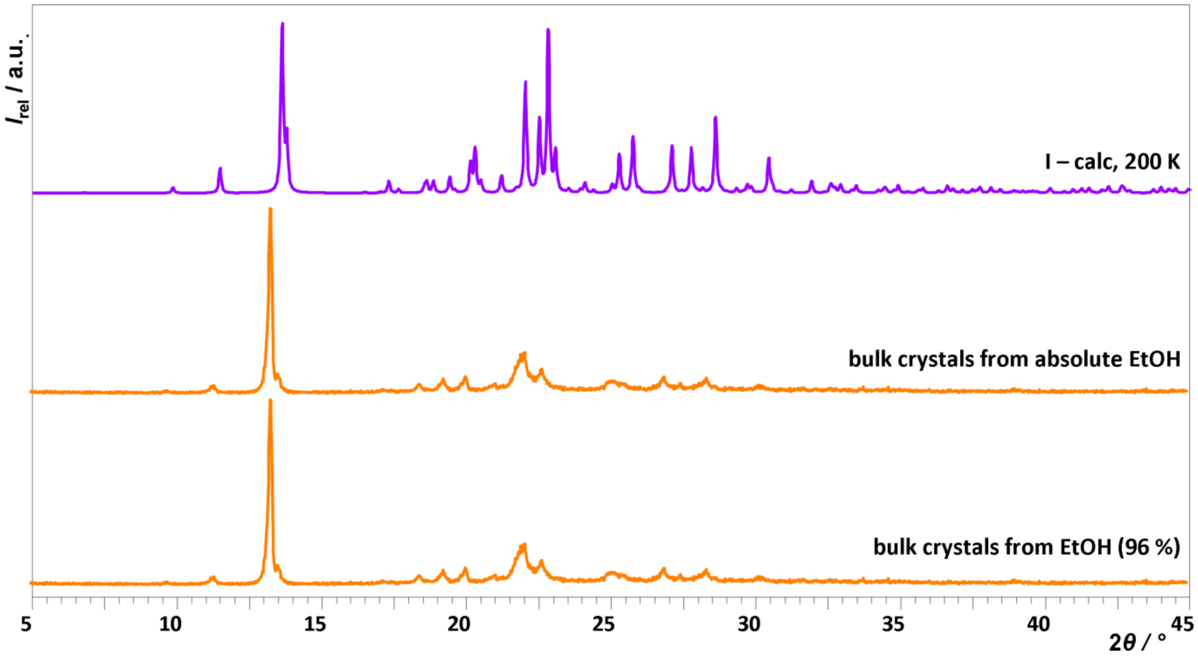


Figure S12 PXRD patterns of bulk crystals obtained at 25 °C by crystallization from 96 % and from absolute ethanol when filtration wasn't performed and the calculated pattern of **I**.

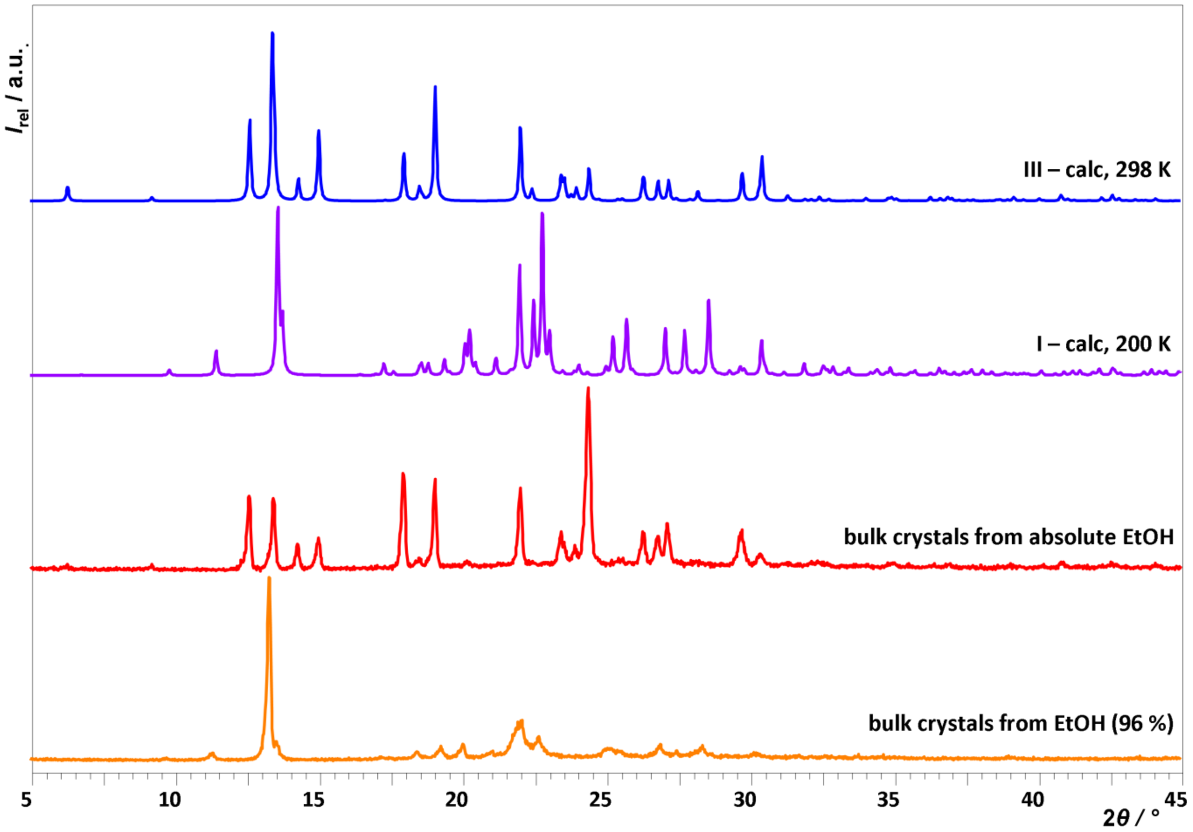


Figure S13 PXRD patterns of bulk crystals obtained at 25 °C by crystallization from 96 % and from absolute ethanol when filtration was performed using student grade filtering paper and the calculated patterns of form **I** and **III**.

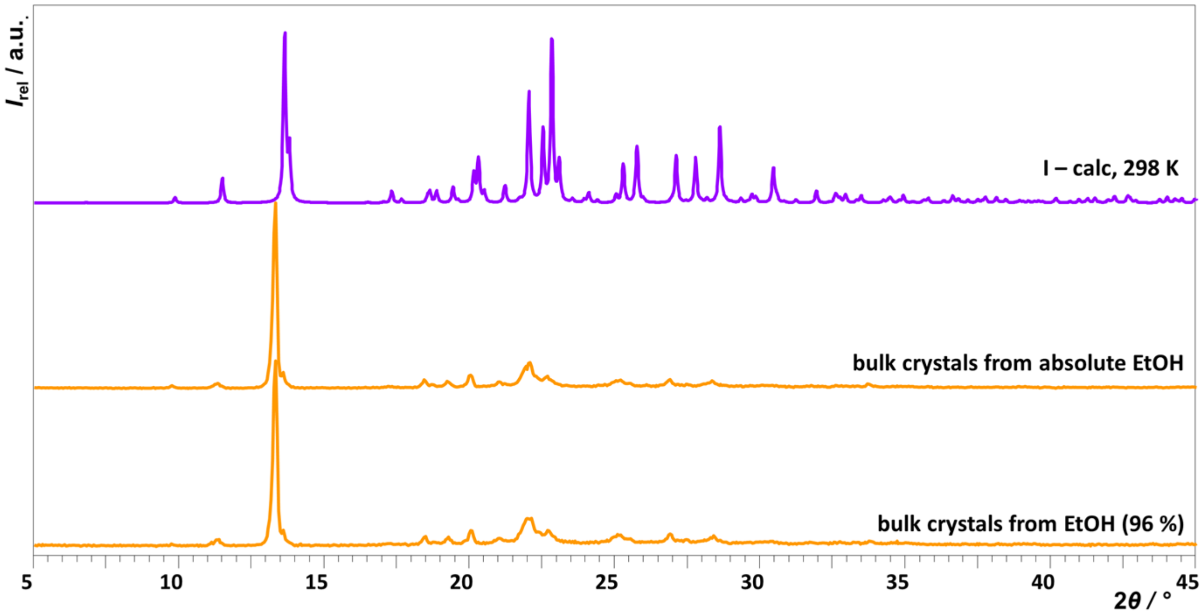


Figure S14 PXRD patterns of bulk crystals obtained at 25 °C by crystallization from 96 % and from absolute ethanol when filtration was performed using white ribbon filtering paper and the calculated pattern of form **I**.

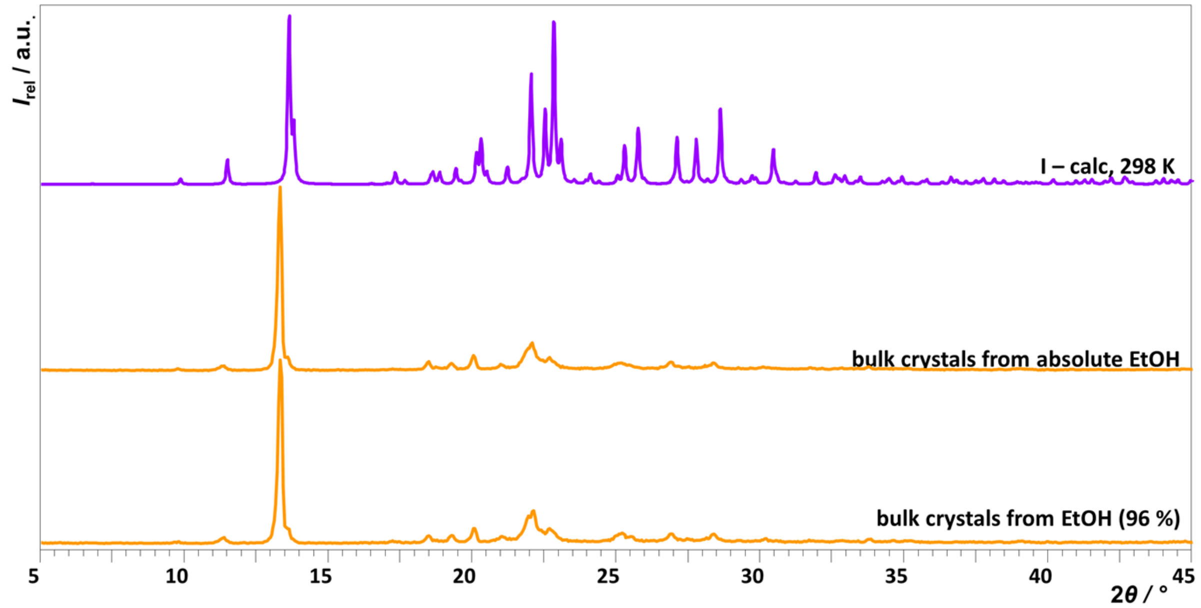


Figure S15 PXRD patterns of bulk crystals obtained at 25 °C by crystallization from 96 % and from absolute ethanol when filtration was performed using blue ribbon filtering paper and the calculated pattern of form **I**.

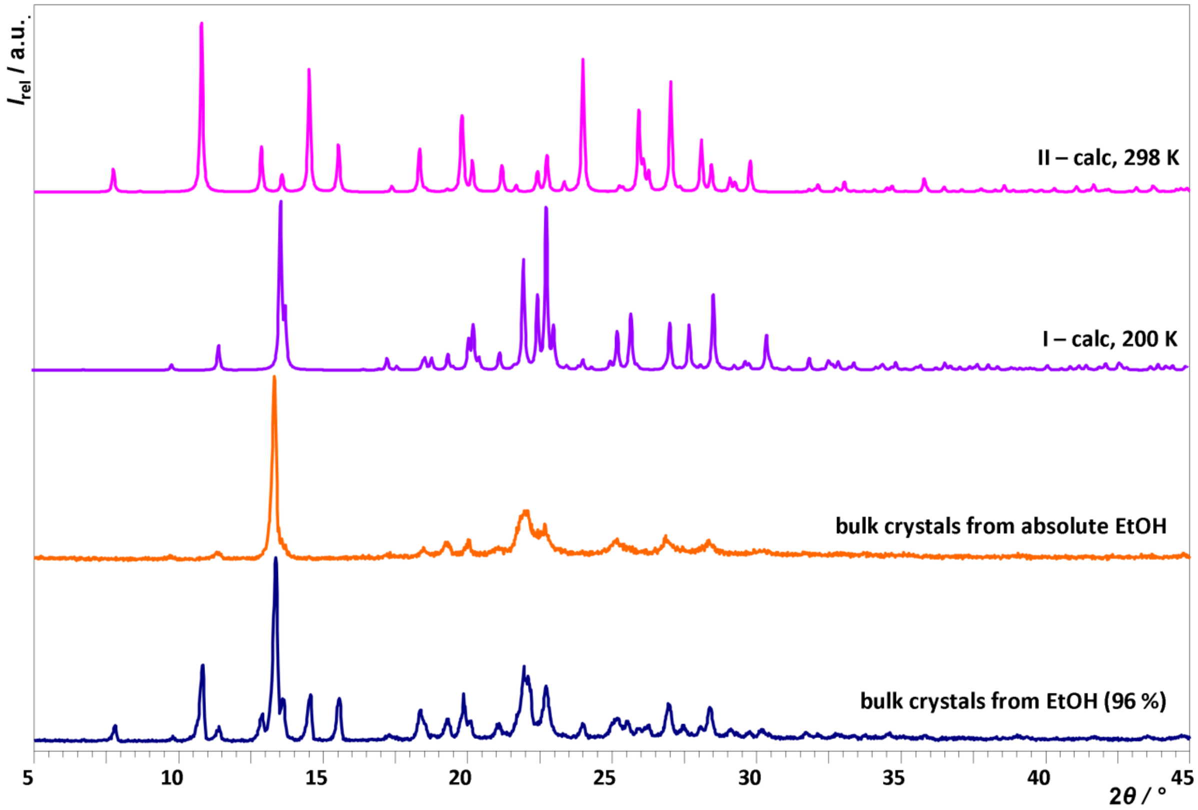


Figure S16 PXRD patterns of bulk crystals obtained at 8 °C by crystallization from 96 % and from absolute ethanol when filtration was performed using student grade filtering paper and the calculated patterns of form **I** and **II**.

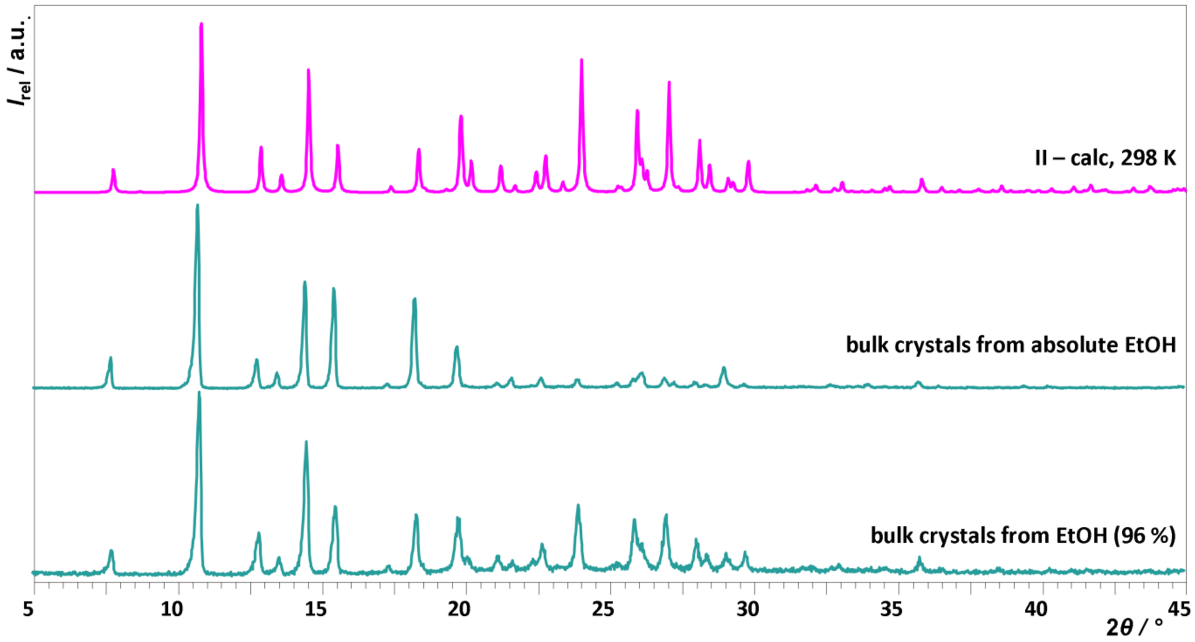


Figure S17 PXRD pattern of bulk crystals obtained at 8 °C by crystallization from 96 % and from absolute ethanol when filtration was performed using white ribbon filtering paper and the calculated pattern of form **II**.

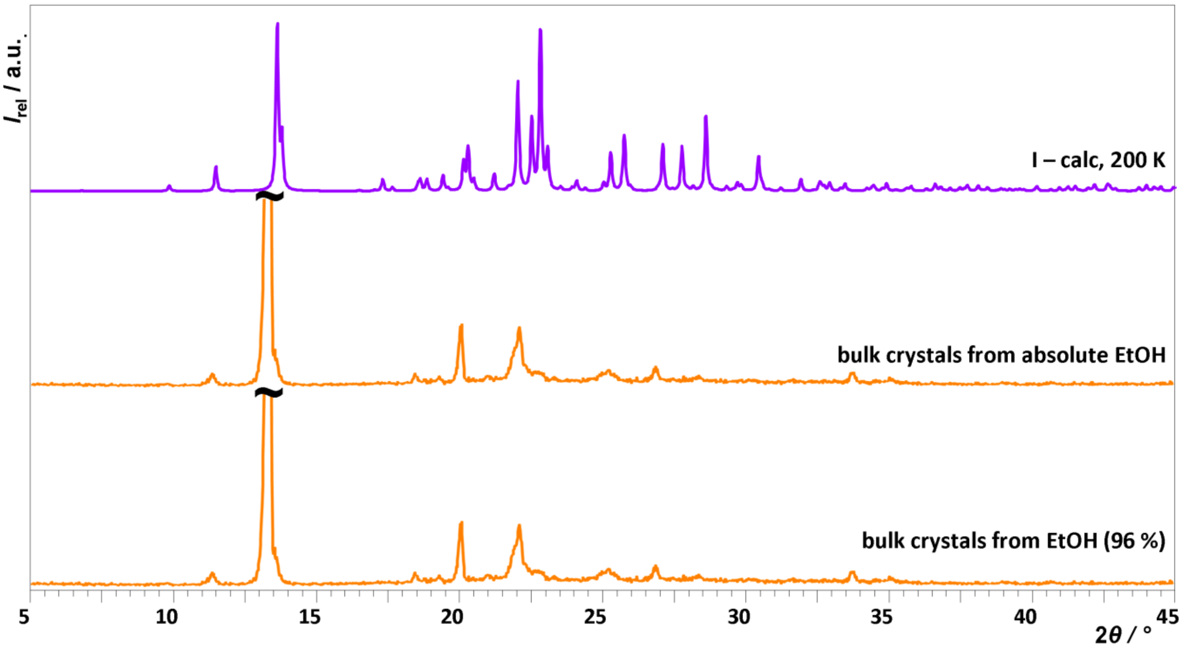


Figure S18 PXRD pattern of bulk crystals obtained at 8 °C by crystallization from 96 % and from absolute ethanol when filtration was performed using blue ribbon filtering paper and the calculated pattern of form **I**.

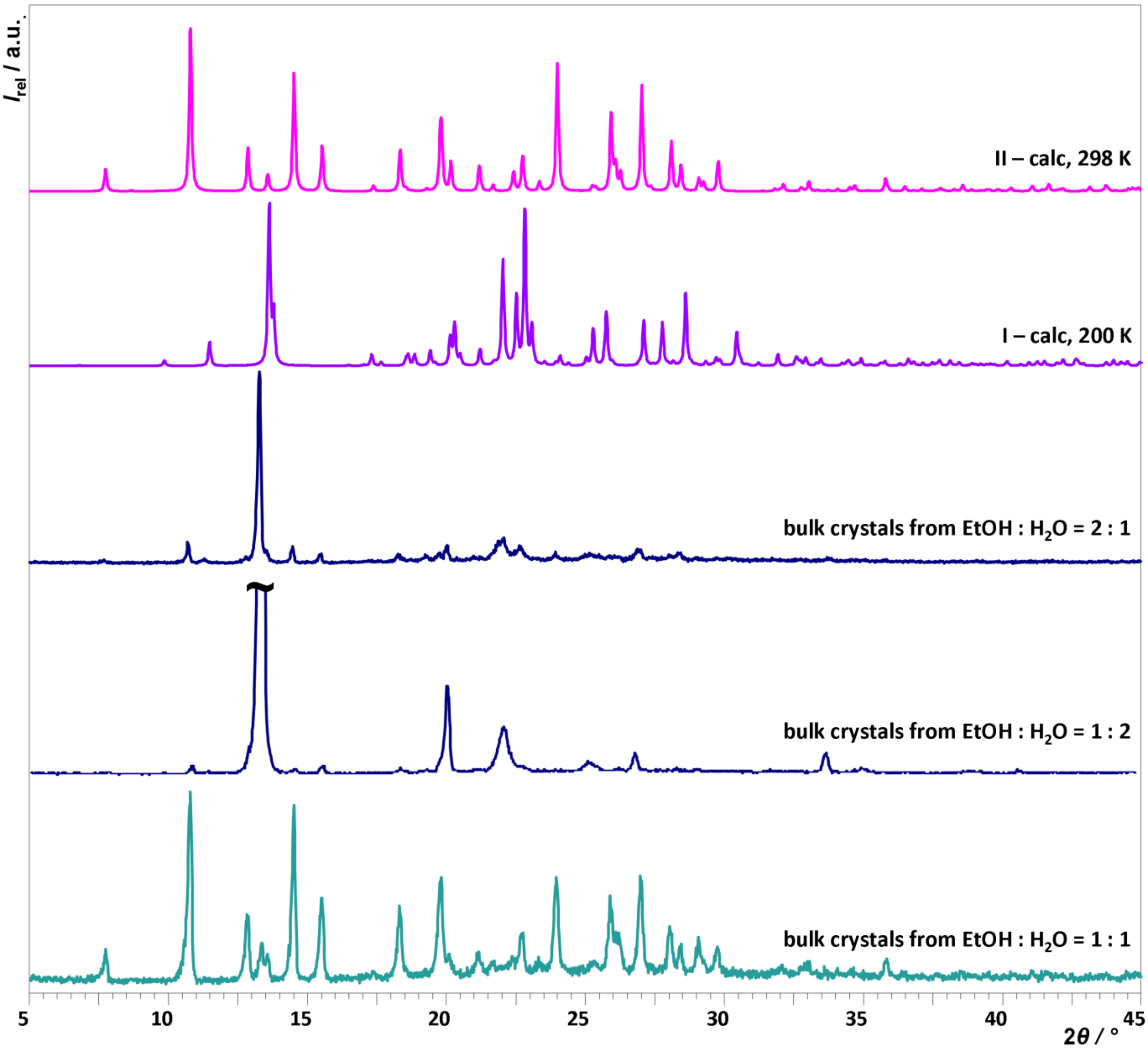


Figure S19 PXRD pattern of bulk crystals obtained at 8 °C by crystallization from a mixture of 96 % ethanol and distilled water in volume ratio 1:1, 1:2 and 2:1, respectively, when filtration was performed using blue ribbon filtering paper and the calculated patterns of forms **I** and **II**.

2.5. Results of *ex-situ* PXRD experiments on materials obtained by mechanochemical methods

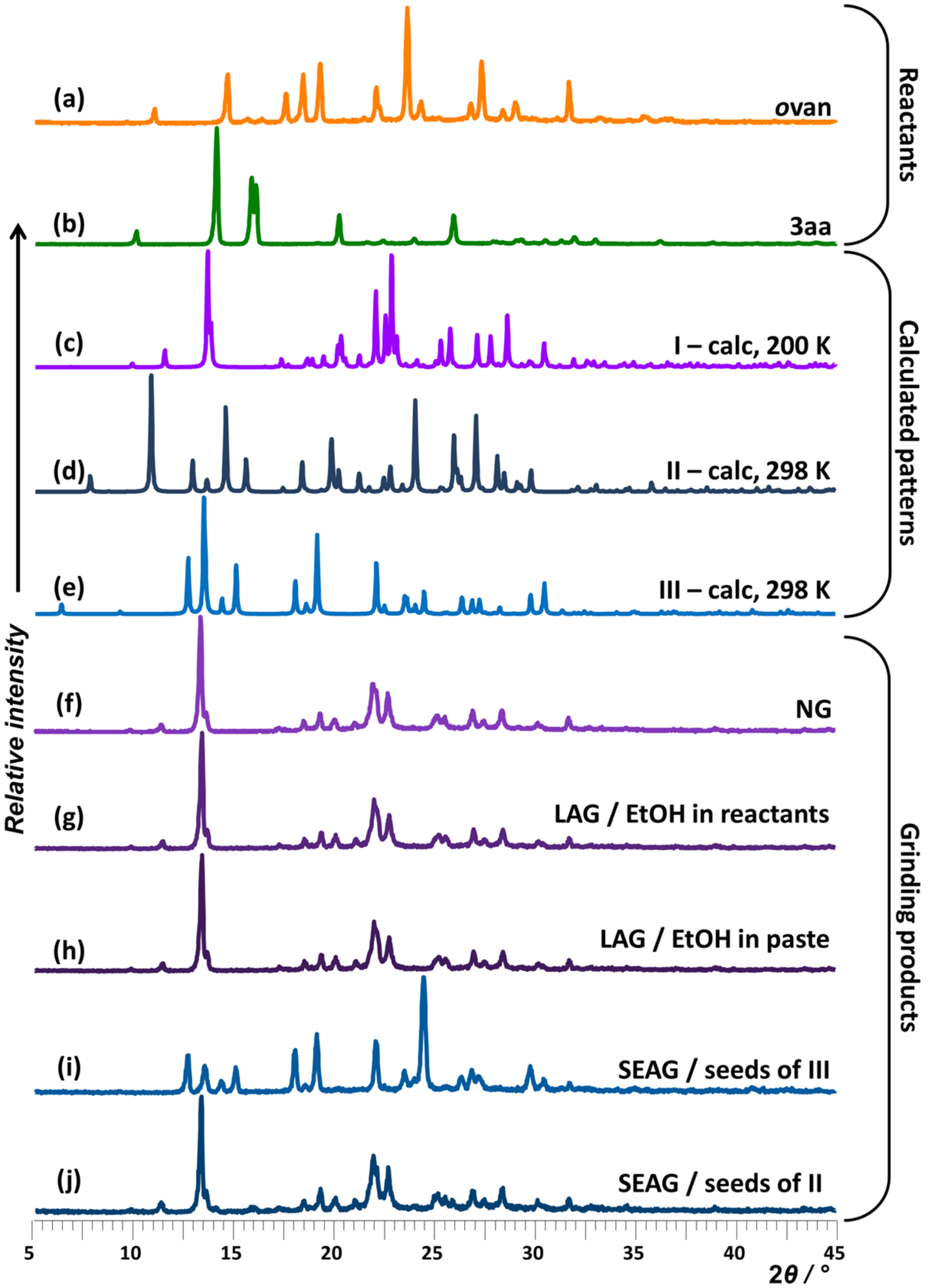
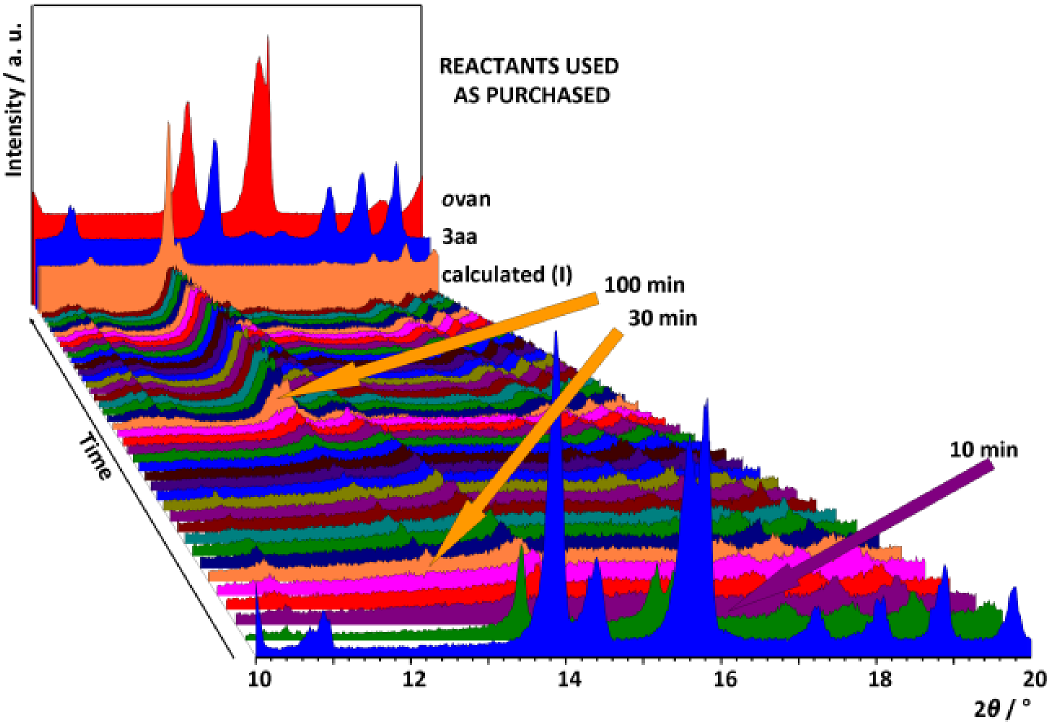
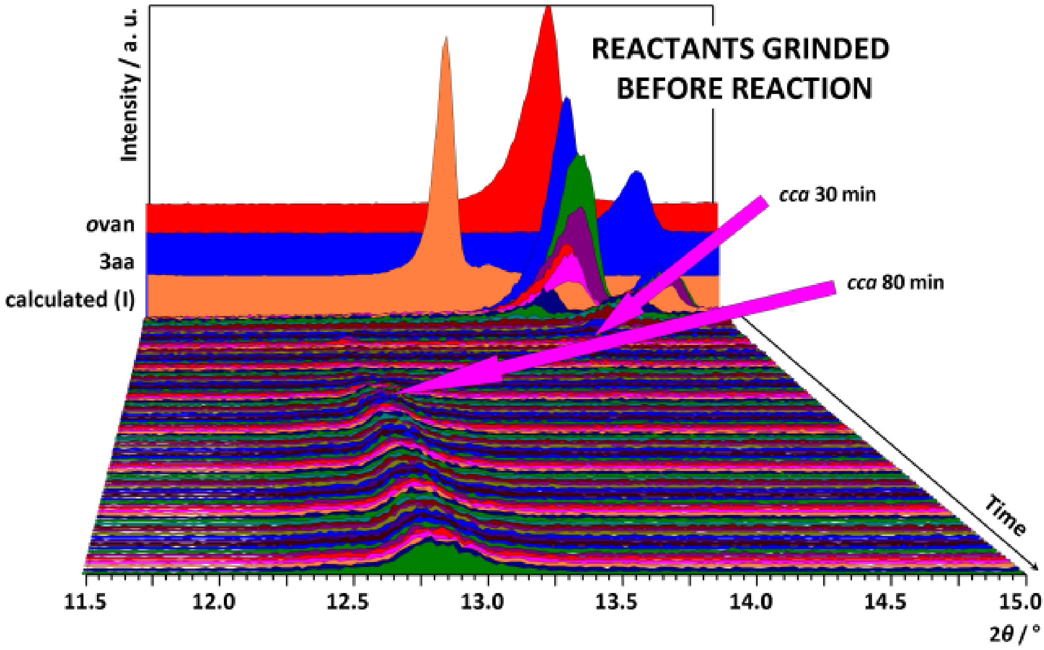


Figure S20 PXRD patterns of (a) *o*-vanillin, (b) 3-aminoacetophenone, calculated pattern of (c) form **I**, (d) form **II**, (e) form **III**, **I** prepared by (f) neat and liquid-assisted grinding when EtOH was (g) added in reactants and (h) in the paste, (i) **III** obtained by seeding-assisted grinding when seeds of **III** were added and (j) **I** obtained by seeding-assisted grinding when seeds of **II** were added.

2.6. Results of *in-situ* PXRD experiments of ageing of the reaction mixtures of *o*van and 3aa



(a)



(b)

Figure S21 PXRD patterns observed by in-situ monitoring of the formation of polymorph I by close contact reaction when (a) reactants used as purchased and (b) reactants ground separately prior to reaction to ensure smaller particles and better homogeneity. [Time headed (a) from and (b) towards reader for better visibility.]

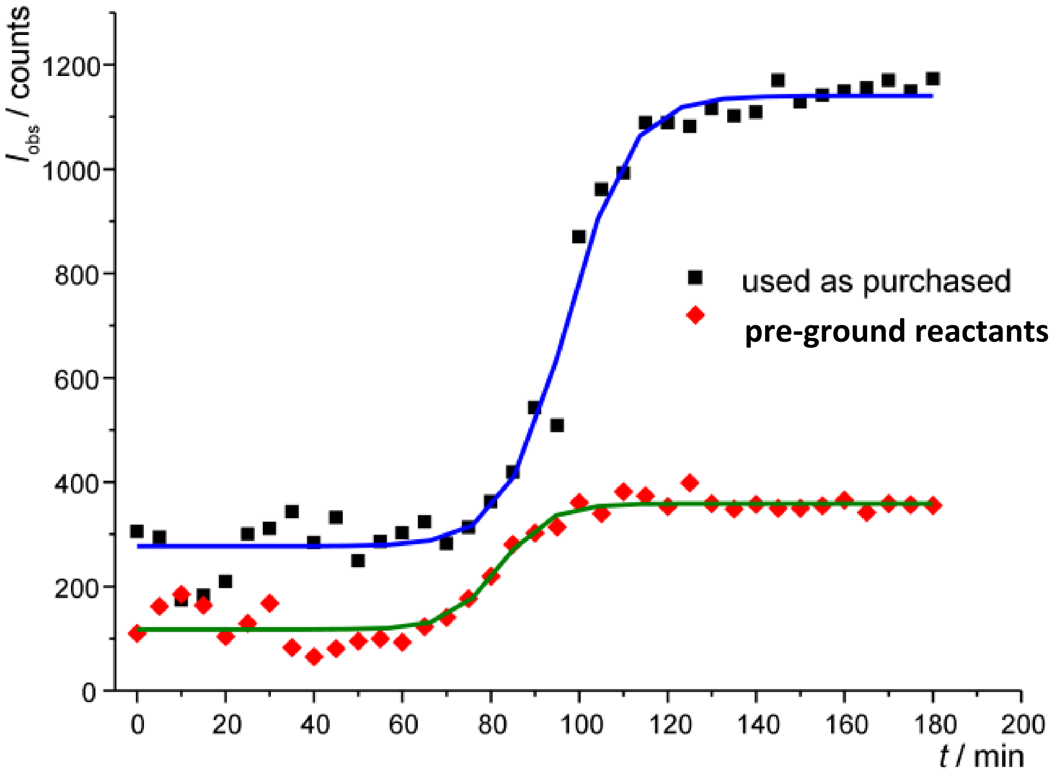
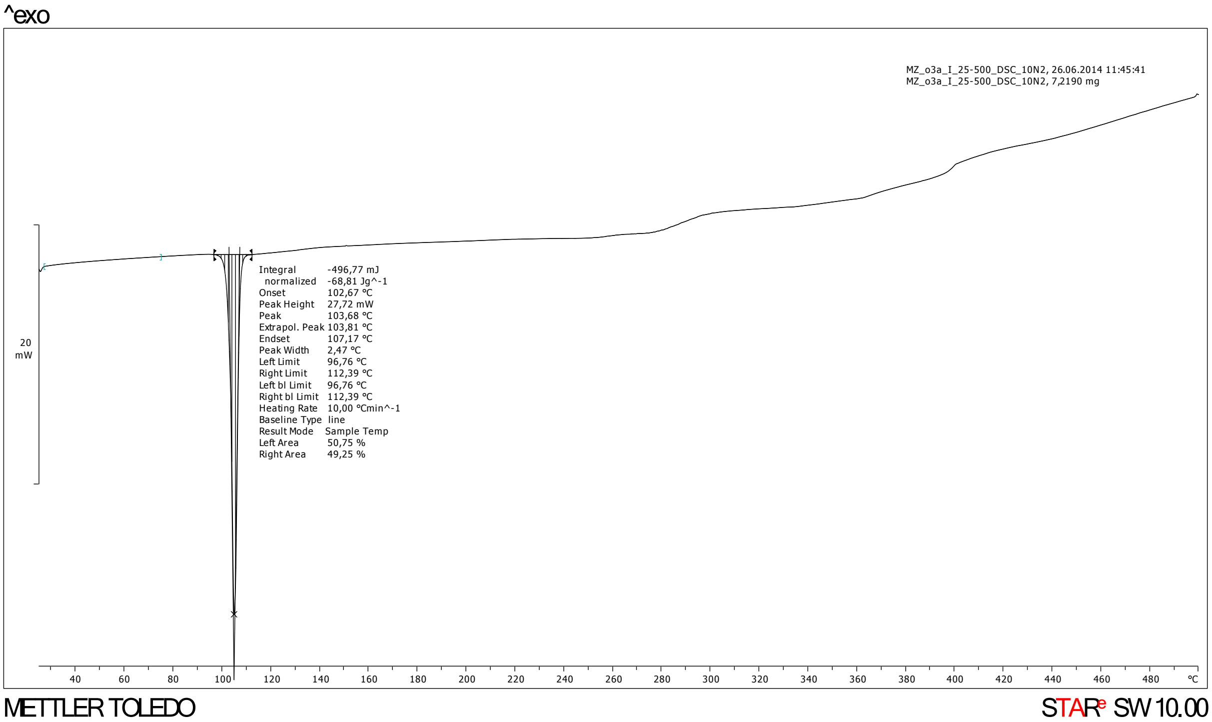


Figure S22 Intensity of diffraction *vs*. time diagram.

2.7. Thermal study on samples of form I



```
MZ_o3a_I_25-500_DSC_10N2, 26.06.2014 11:45:41
MZ_o3a_I_25-500_DSC_10N2, 7,2190 mg
```

```
Integral          -496,77 mJ
  normalized      -68,81 Jg^-1
Onset             102,67 °C
Peak Height       27,72 mW
Peak              103,68 °C
Extrapol. Peak    103,81 °C
Endset            107,17 °C
Peak Width        2,47 °C
Left Limit        96,76 °C
Right Limit       112,39 °C
Left bl Limit     96,76 °C
Right bl Limit    112,39 °C
Heating Rate      10,00 °Cmin^-1
Baseline Type     line
Result Mode       Sample Temp
Left Area         50,75 %
Right Area        49,25 %
```

Figure S23 DSC curve of polymorph **I**.

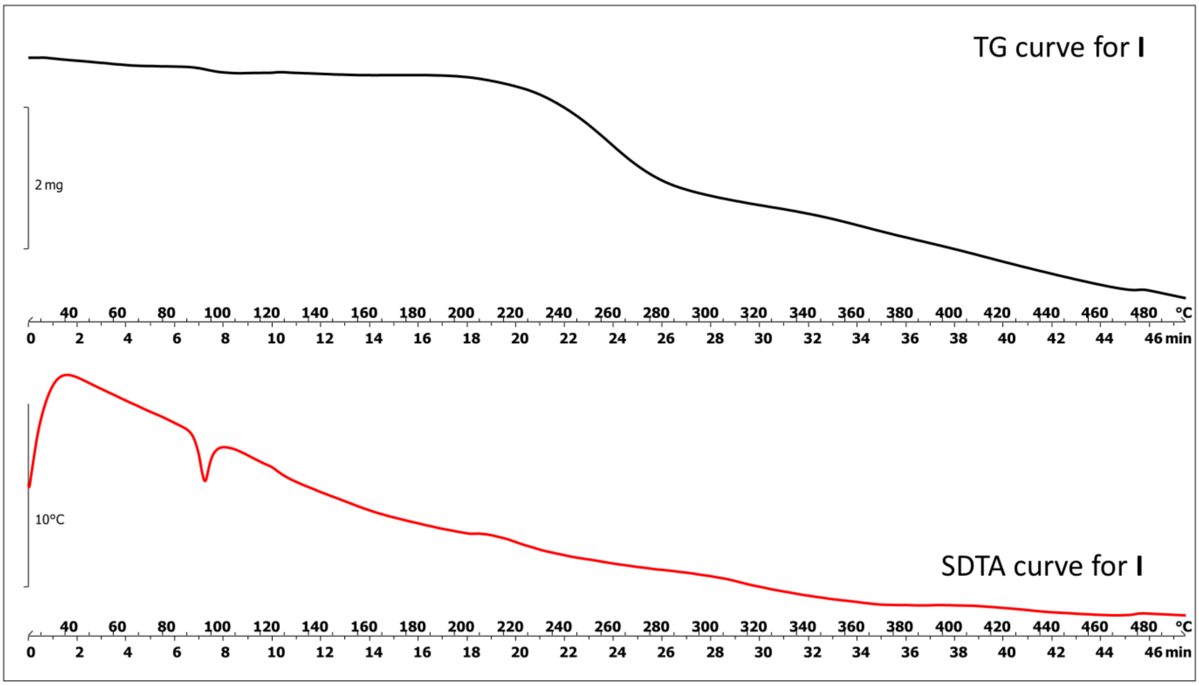


Figure S24 TGA and SDTA curve for bulk crystals of **I**.

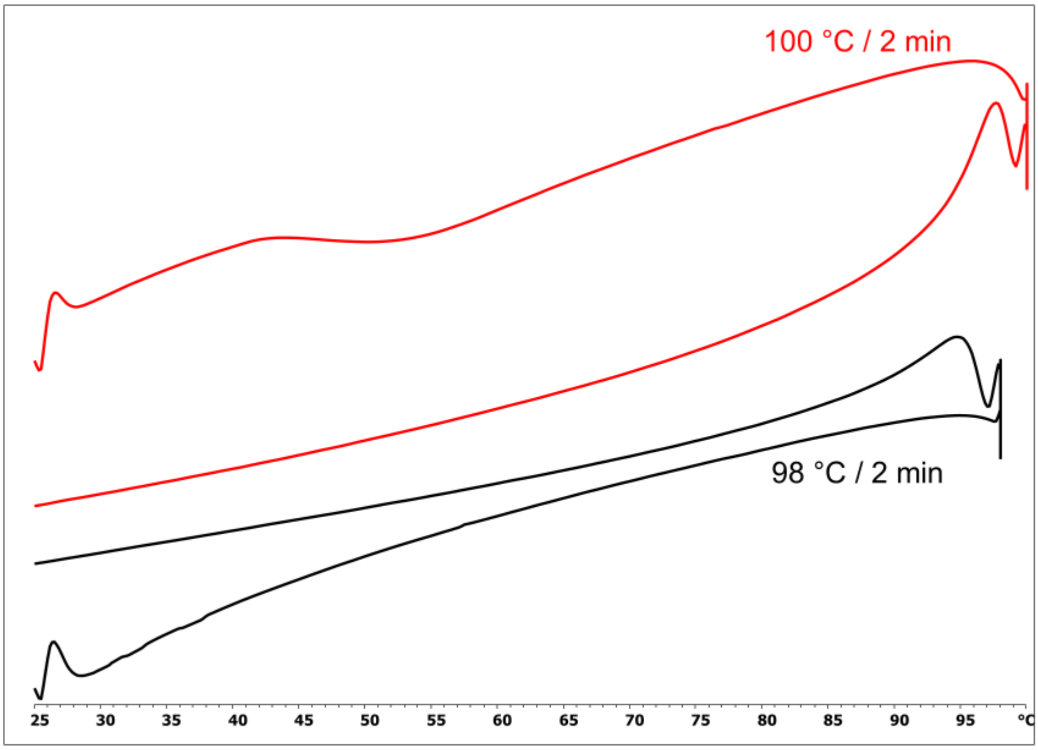


Figure S25 Curves of isothermal DSC experiments on polymorph **I**.

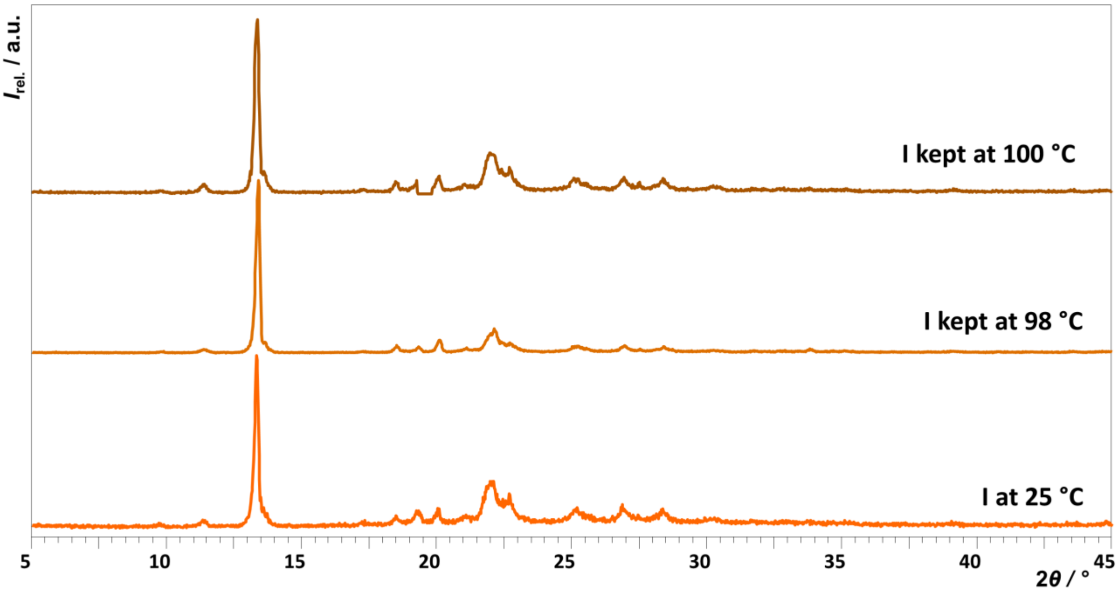


Figure S26 PXRD patterns of polymorph **I** at 25 °C and patterns of material obtained by keeping samples of **I** at 98 and 100 °C for 2 minutes and cooling them to 25 °C.

2.8. Thermal study on samples of form II

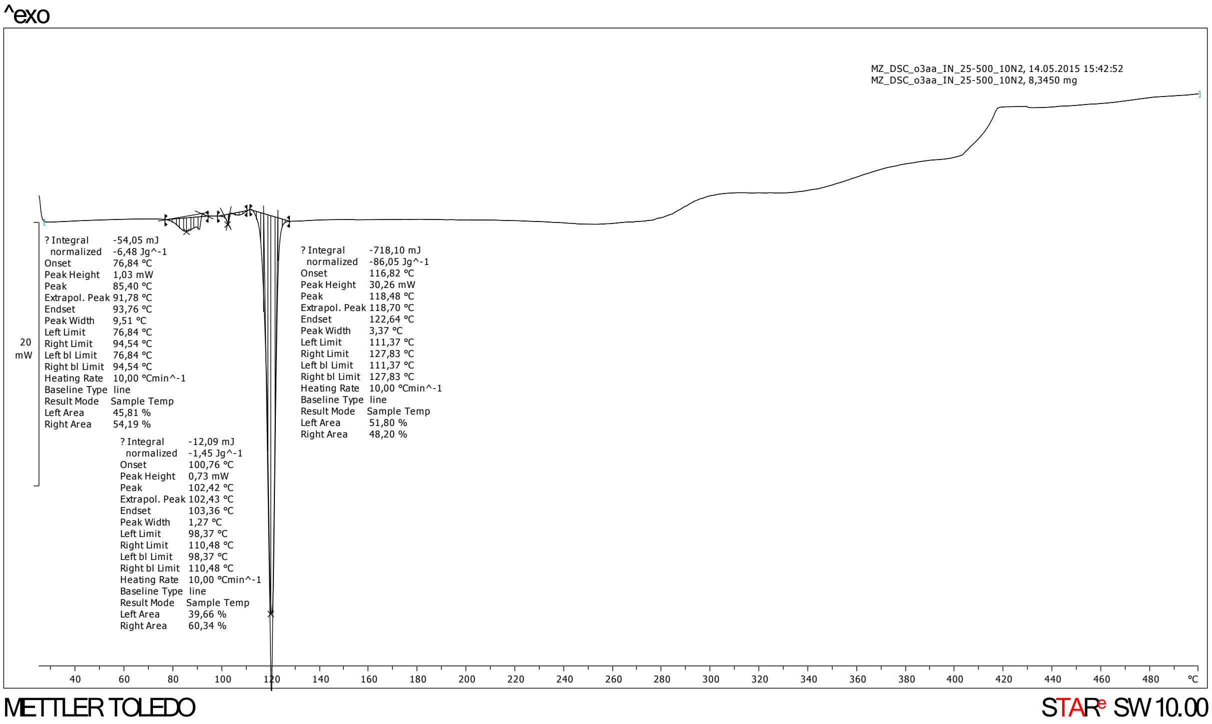


Figure S27 DSC curve of polymorph **II**.

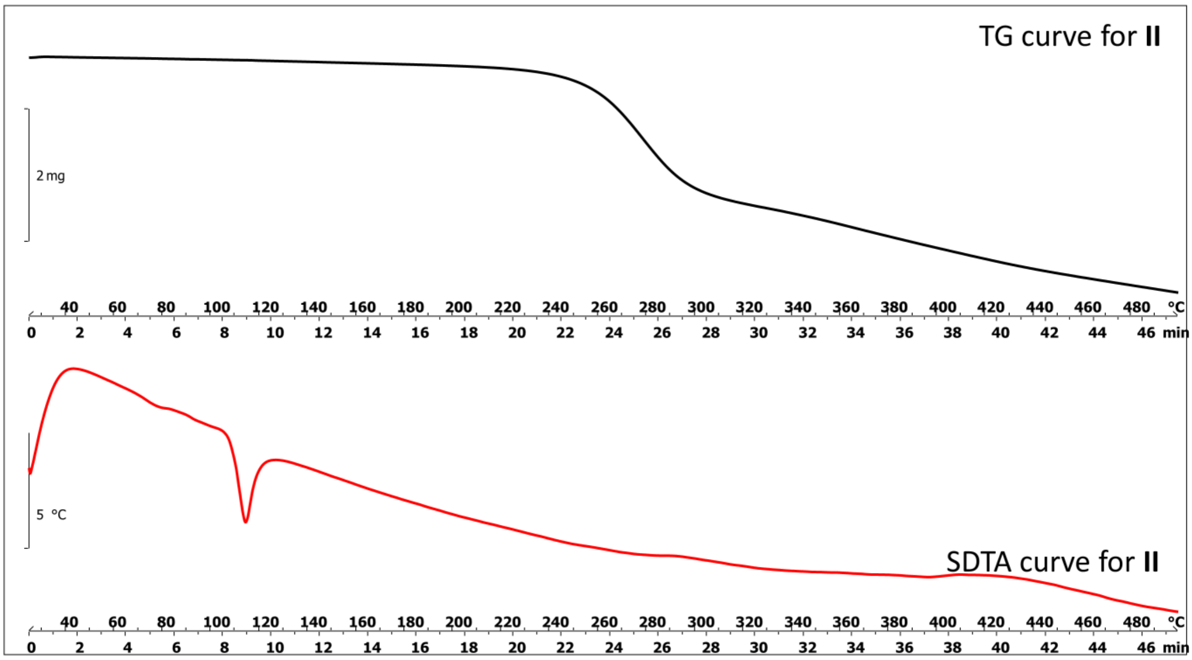


Figure S28 TGA and SDTA curve for bulk crystals of **II**.

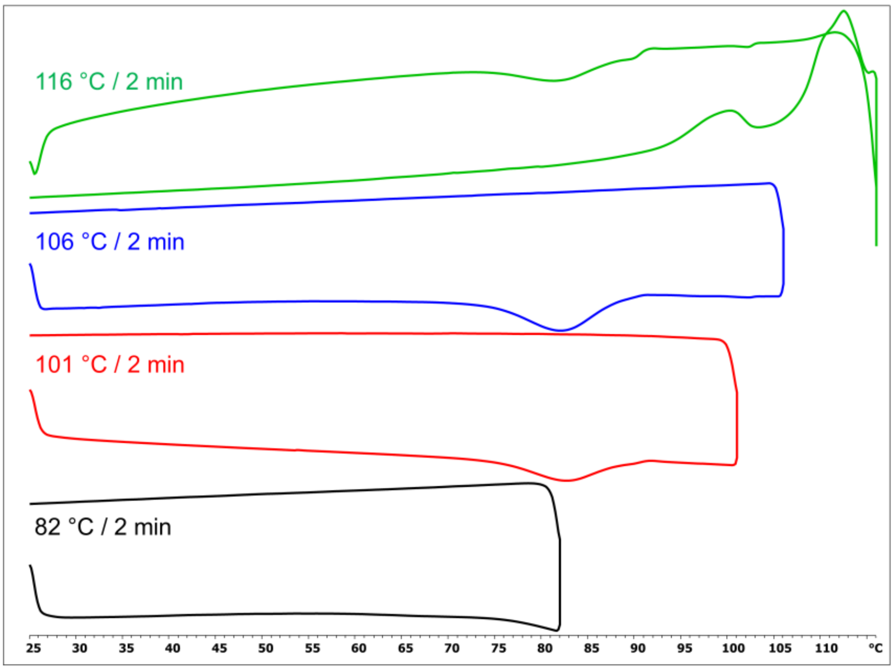


Figure S29 Curves of isothermal DSC experiments on polymorph **II**.

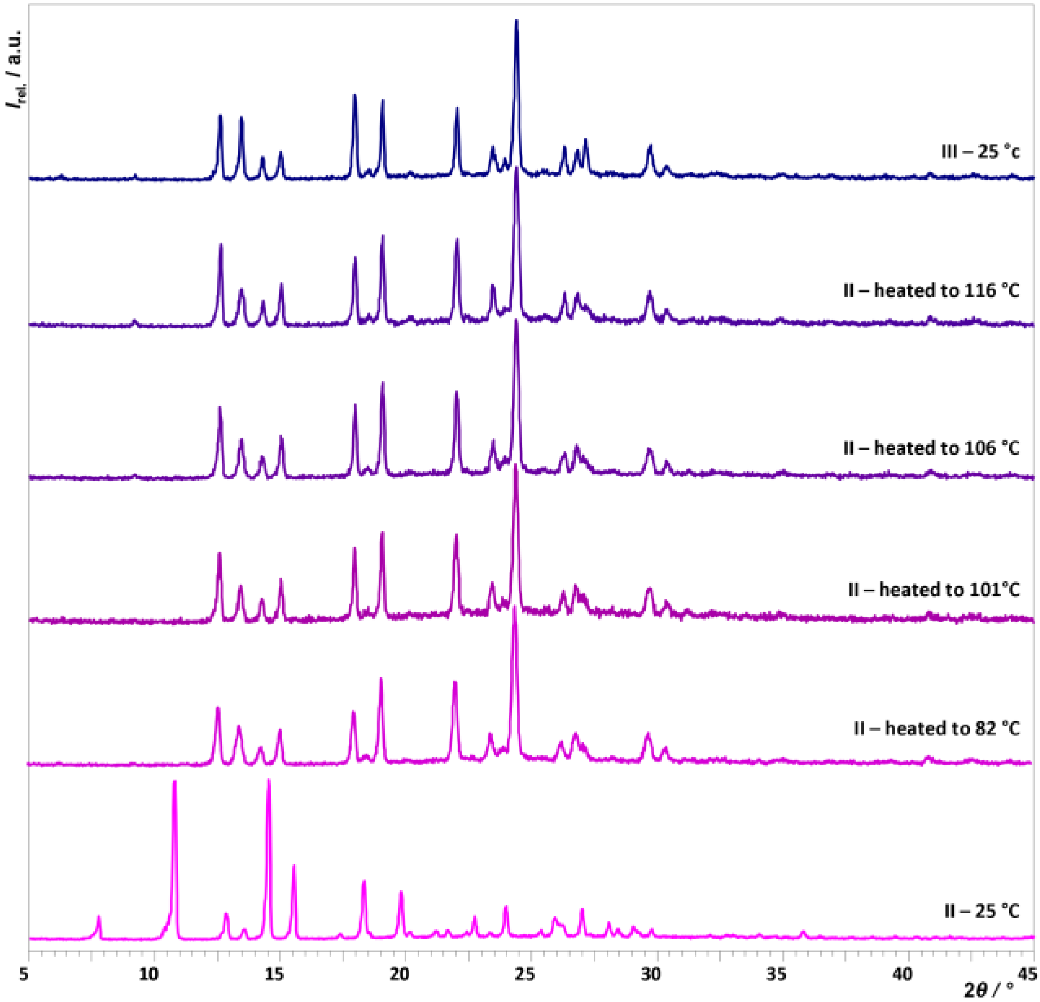


Figure S30 PXRD patterns of polymorph **II** and **III** at 25 °C and patterns showing polymorph transition of **II** to **III** obtained by keeping samples of **II** at 82, 101, 106 and 116 °C for 2 minutes and cooling them to 25 °C.

2.9. Thermal study on samples of form III

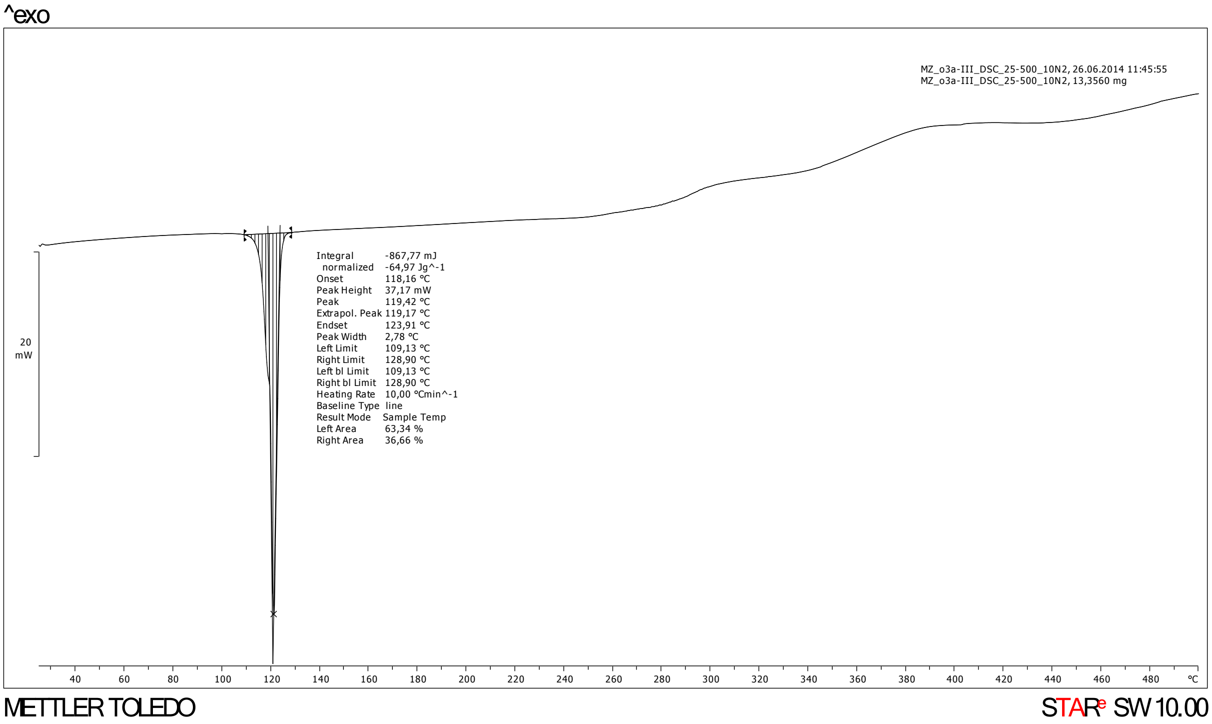


Figure S31 DSC curve of polymorph **III**.

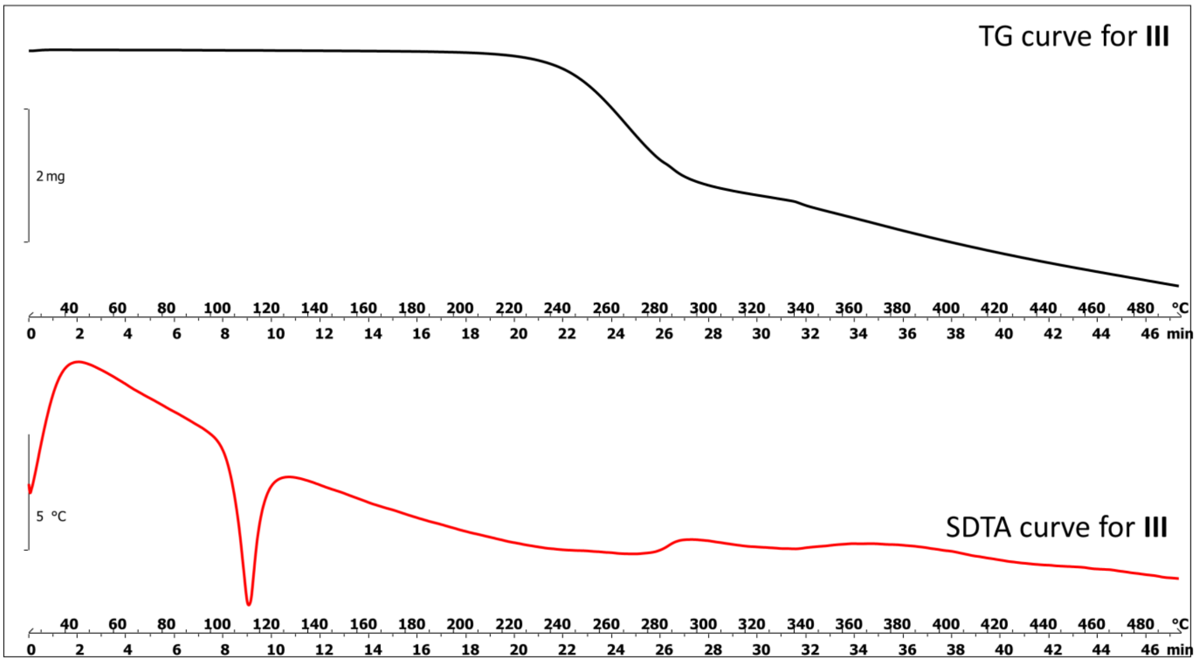


Figure S32 TGA and SDTA curve for bulk crystals of **III**.

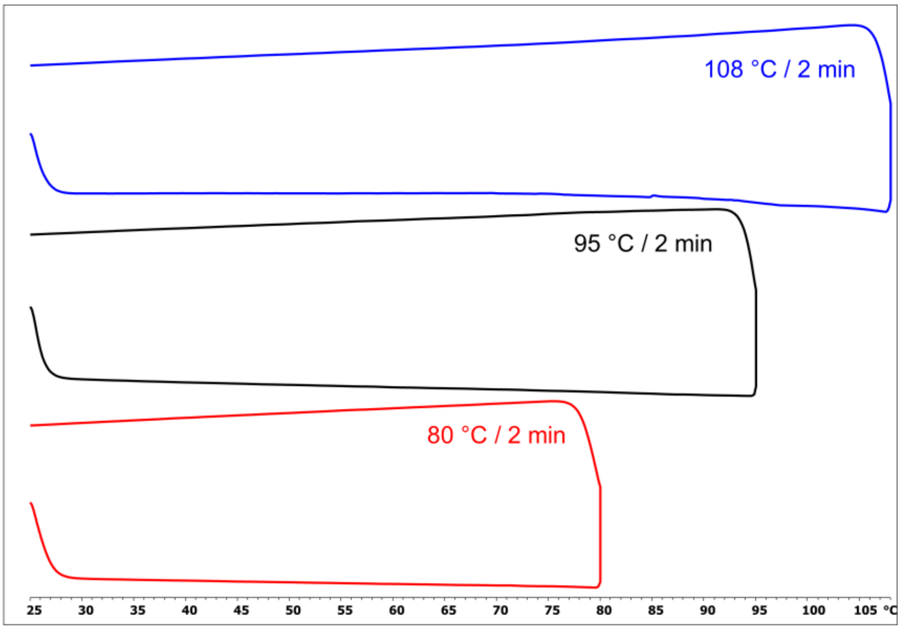


Figure S33 Curves of isothermal DSC experiments on polymorph **III**.

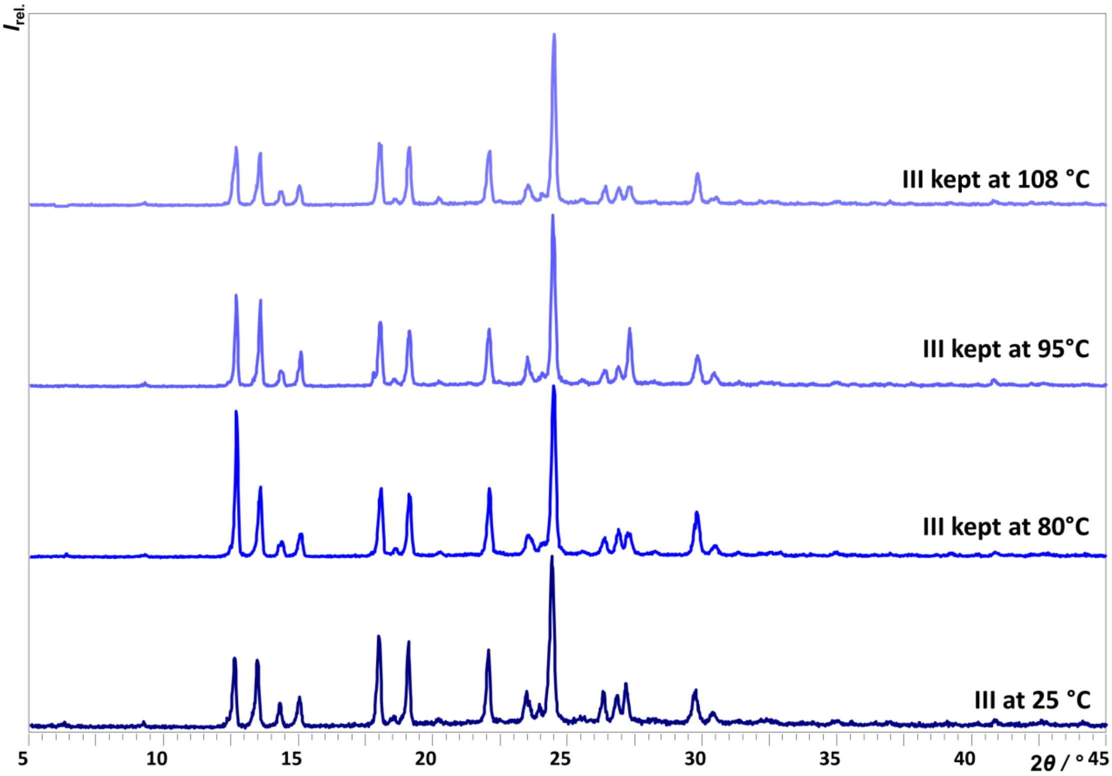


Figure S34 PXRD patterns of polymorph **III** at 25 °C and patterns of material obtained by keeping samples of **III** at 80, 95 and 108 °C for 2 minutes and cooling them to 25 °C.

2.10. Results of LAG of mixtures of polymorphs

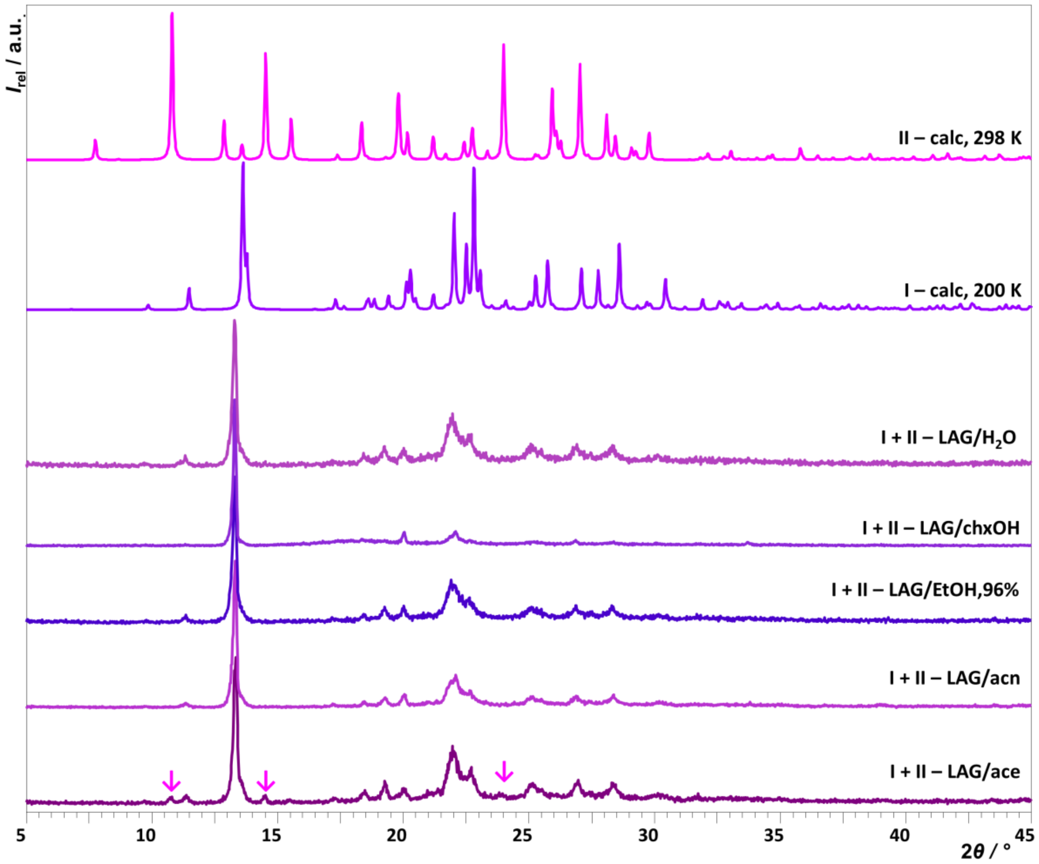


Figure S35 PXRD patterns of samples of mixtures of forms **I** and **II** ground in agate mortar at RT with addition of several solvents compared to calculated patterns of **I** and **II**. Pink arrow (↓) indicates positions of diffraction maxima of **II** in grinding product.

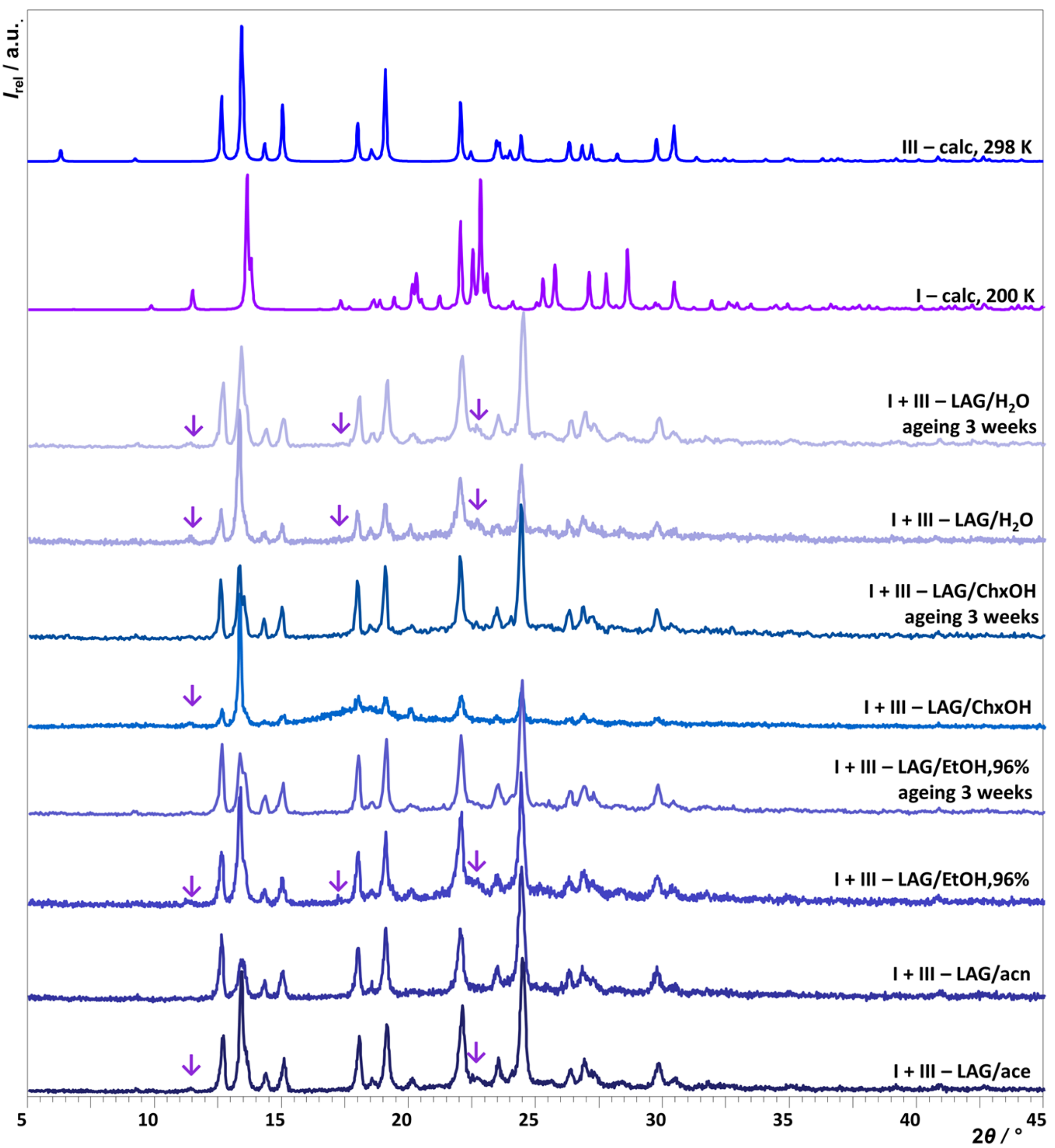


Figure S36 PXRD patterns of samples of mixtures of forms **I** and **III** ground in agate mortar at RT with addition of several solvents compared to calculated patterns of **I** and **III**. Violet arrow (↓) indicates positions of diffraction maxima of **I** in grinding products.

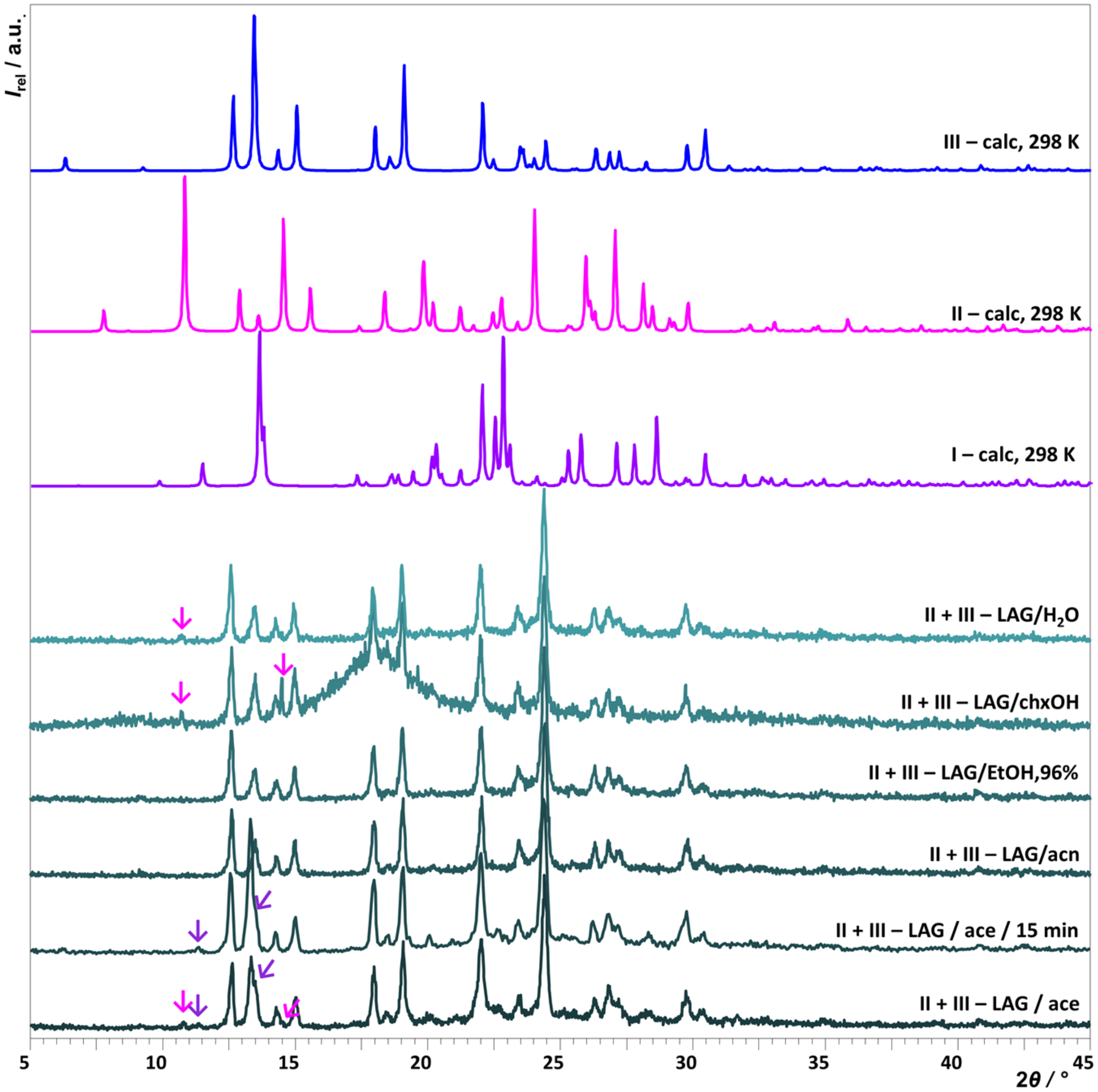


Figure S37 PXRD patterns of samples of mixtures of forms **II** and **III** ground in agate mortar at RT with addition of several solvents compared to calculated patterns of **II** and **III**. Pink and violet arrows (↓ and ↓) indicate positions of diffraction maxima of **II** and **I** in grinding products, respectively.

2.11. Results of vapour digestion experiments

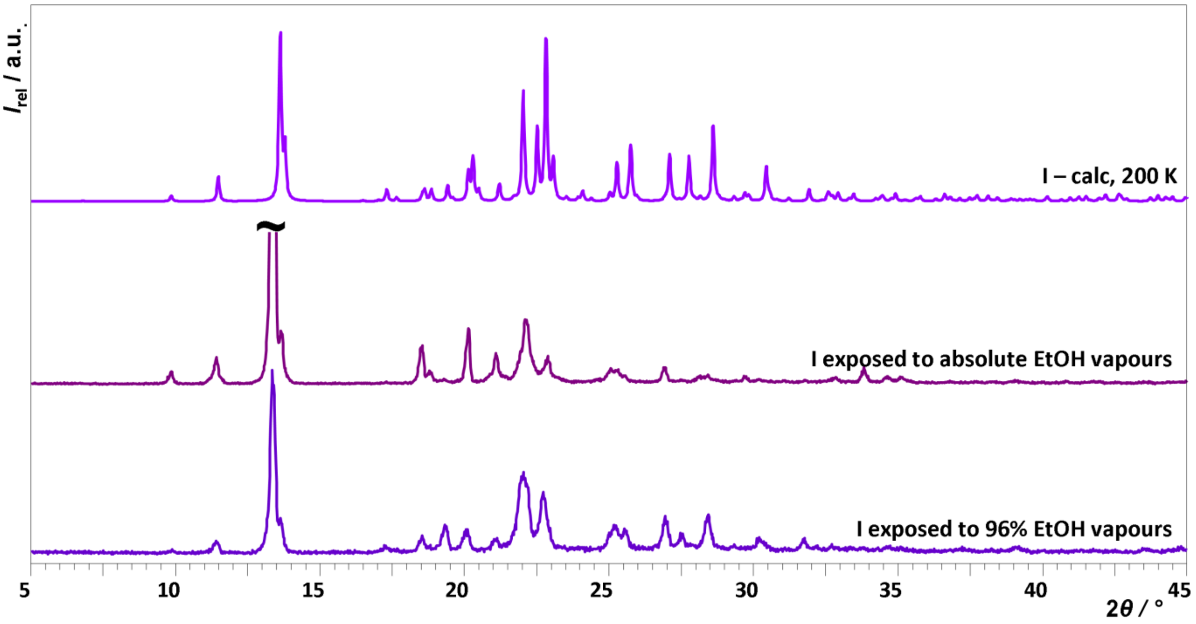


Figure S38 PXRD patterns of samples of form **I** exposed to vapours of 96 % and absolute ethanol and calculated pattern of **I**.

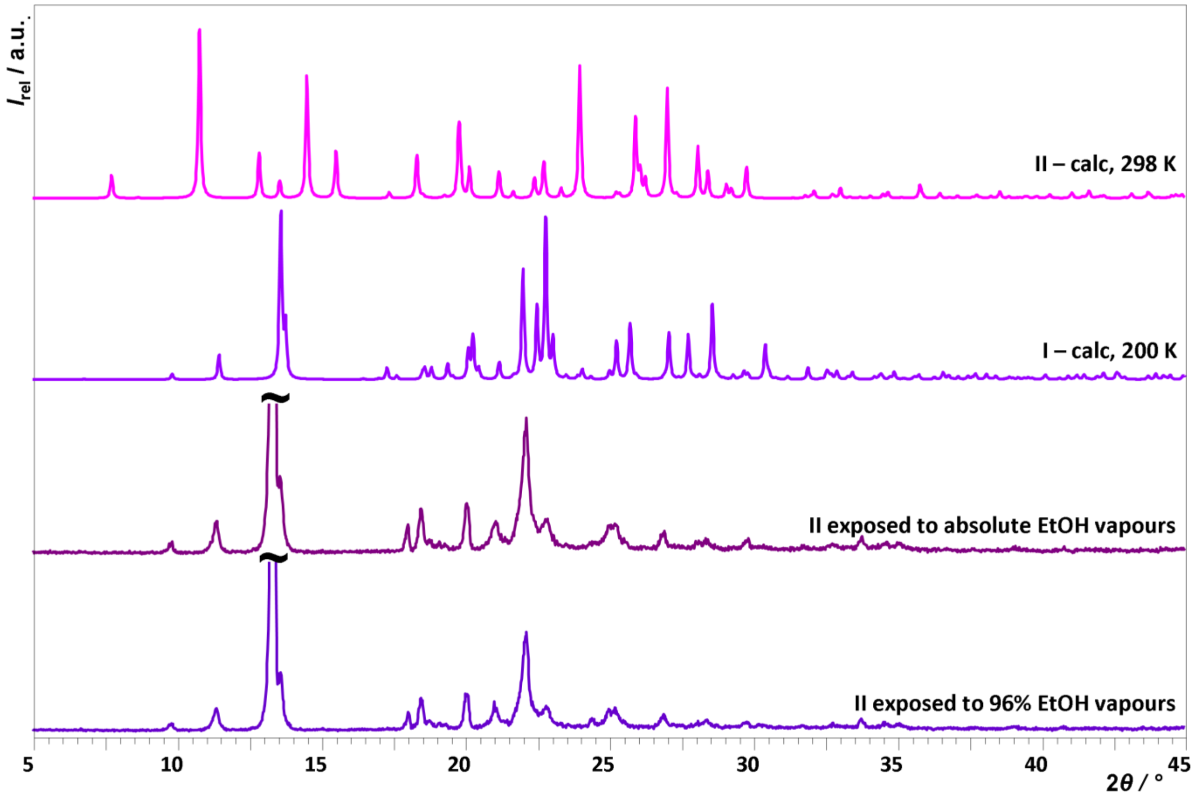


Figure S39 PXRD patterns of samples of form **II** exposed to vapours of 96 % and absolute ethanol and calculated patterns of **I** and **II**, respectively.

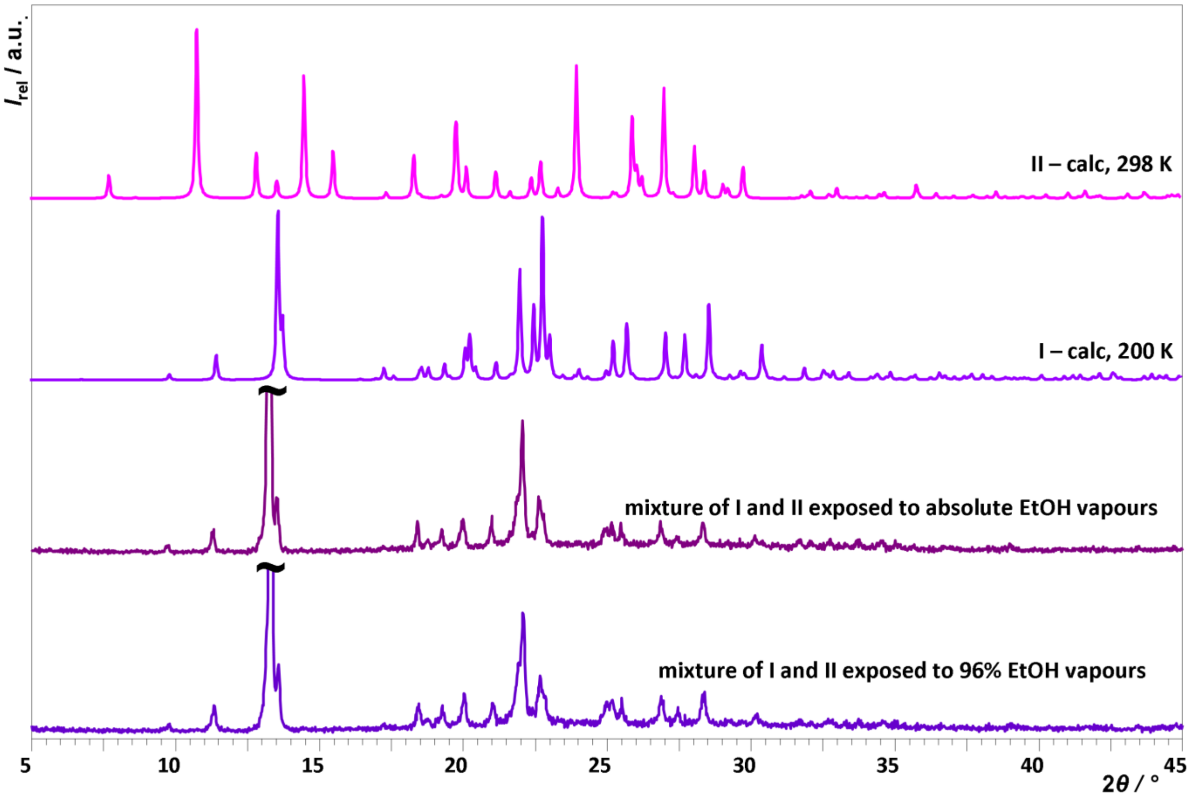


Figure S40 PXRD patterns of samples of the mixture of form **I** and **II** exposed to vapours of 96 % and absolute ethanol and calculated patterns of **I** and **II**, respectively.

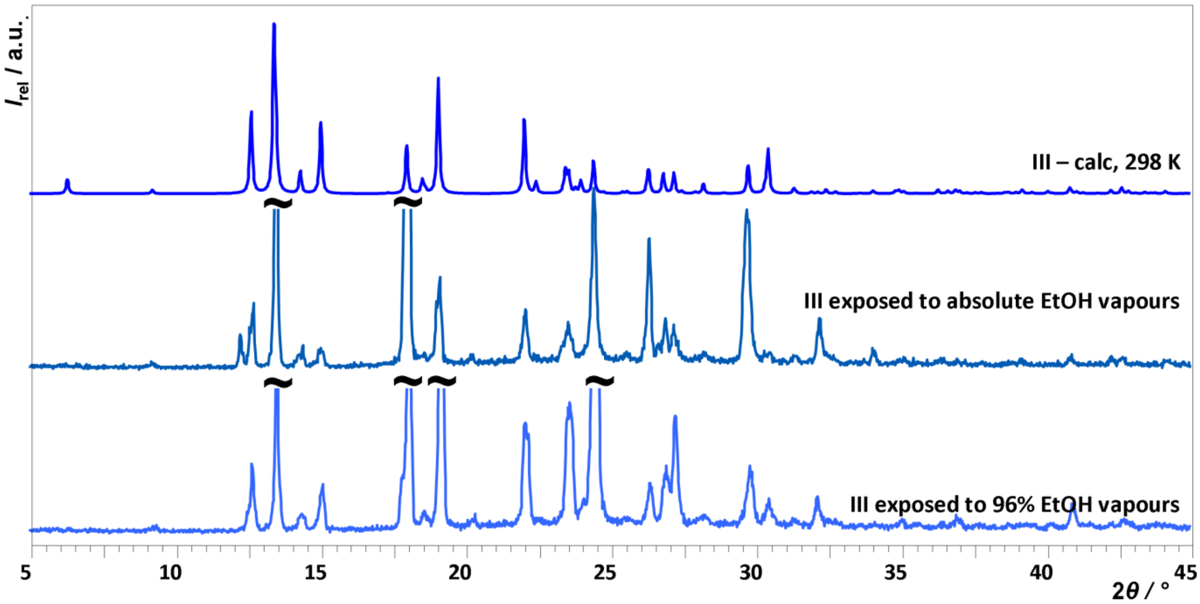


Figure S41 PXRD patterns of samples of form **III** exposed to vapours of 96 % and absolute ethanol and calculated pattern of **III**.

2.12. Results of FT-IR spectroscopic measurements

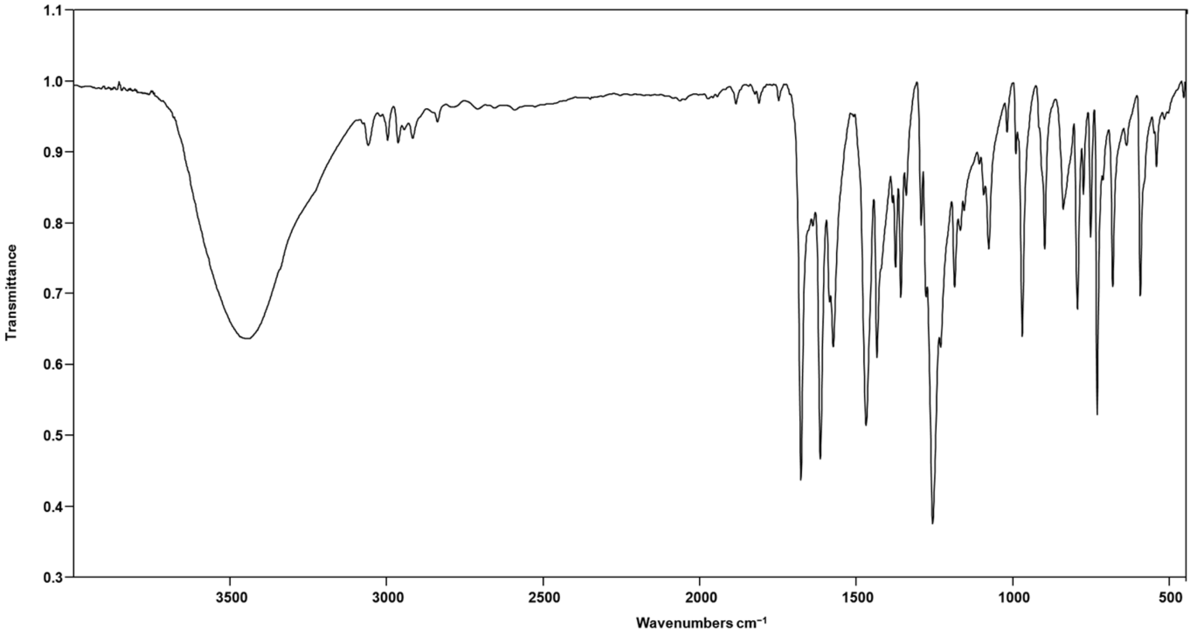


Figure S42 IR spectrum for **I**.

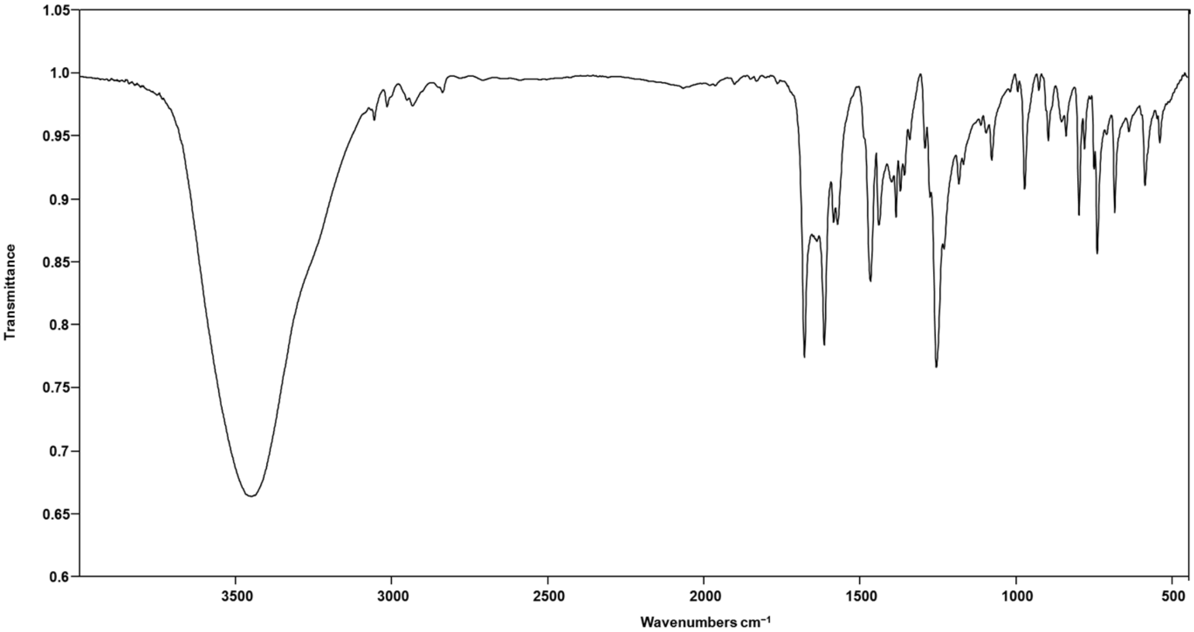


Figure S43 IR spectrum for **II**.

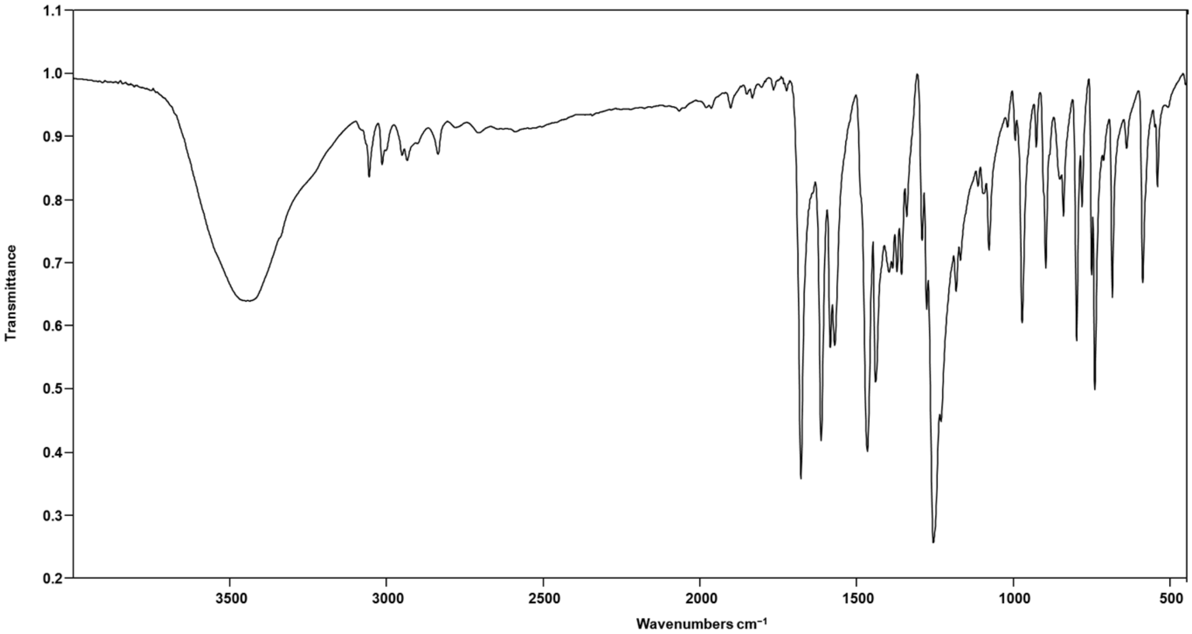


Figure S44 IR spectrum for **III**.

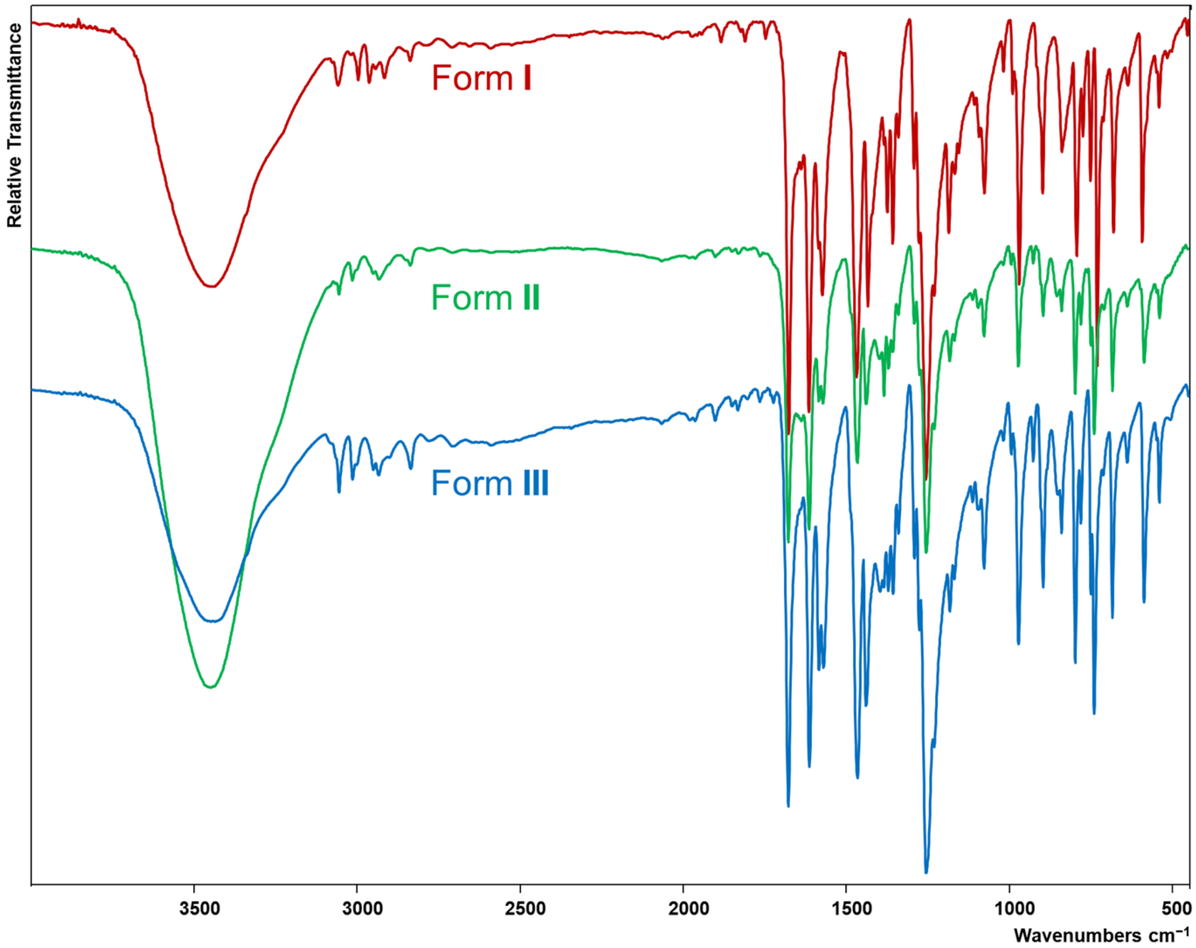


Figure S45 IR spectra for **I**, **II** and **III**.

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