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Polymorphism in a benzo[*b*][1,4]diazepine derivative: crystal structure, phase behavior and selective influence of solvents

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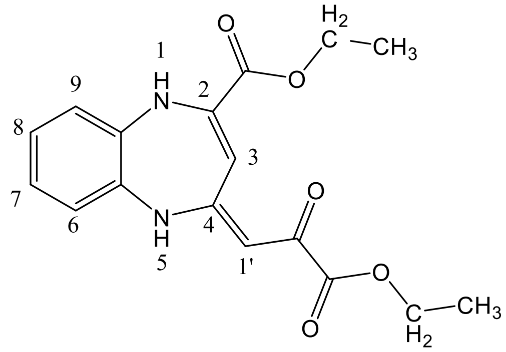
Synthesis of ethyl 4-[(*Z*)-3-ethoxy-2,3-dioxopropylidene]-4,5-dihydro-1*H*-benzo[*b*][1,4]diazepine-2-carboxylate

The studied compound has been obtained as the by-product from the reaction of *o*-phenylenediamine and diethoxalylacetone (dimethyl 2,4,6-trioxoheptanedioate) in methanol. A black precipitated solid was filtered off from the reaction mixture and recrystallised from chloroform.

Yeild 33%, melting point 146-148 °C. Found, %: C 61.72; H 5.46; N 8.59. $C_{17}H_{18}N_2O_5$. Calculated, %: C 61.81; H 5.49; N 8.48. ^{1}H NMR spectrum (DMSO-d_6), δ, p.p.m., *J*/Hz, 600.13 MHz): 1.23-1.31 (m, 6H, $2CH_2\underline{CH_3}$); 4.17-4.28 (m, 4H, $2\underline{CH_2}CH_3$); 5.26 (s, 1H, H(3)); 5.75 (s, 1H, H(1′)); 6.48-6.51 (m, 1H, H(9)); 6.78-6.83 (m, 2H, H(7)+H(8)); 6.90-6.93 (m, 1H, H(6)); 7.90 (brs, 1H, NH(1)); 11.50 (brs, 1H, NH(5)).



Scheme S1. Structural formula of ethyl 4-[(*Z*)-3-ethoxy-2,3-dioxopropylidene]-4,5-dihydro-1*H*-benzo[*b*][1,4]diazepine-2-carboxylate

Single crystal photos

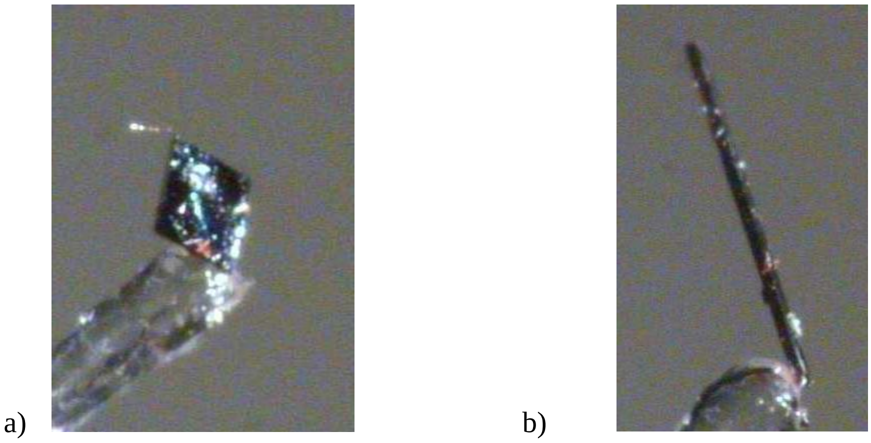


Figure S1. Different shapes of the single crystals of two polymorphic modifications: a) α-phase; b) β-phase.

Differential scanning calorimetry experiments

The thermograms were measured on a Netzsch DSC 204 F1 Phoenix differential scanning calorimeter (τ-sensor) using sealed 25 µl aluminum crucibles in a temperature range of 20-170 °C with the heating and cooling rates of 20 °C min^{-1} while purging with nitrogen (20 ml min^{-1}). Temperature scale and heat flux were calibrated against the melting data for phenol, naphthalene, benzil, acetanilide, benzoic acid, and indium. The mass of the samples usually amounted to ca. 1.5 mg, which was controlled with a Sartorius CPA-2P microbalance.

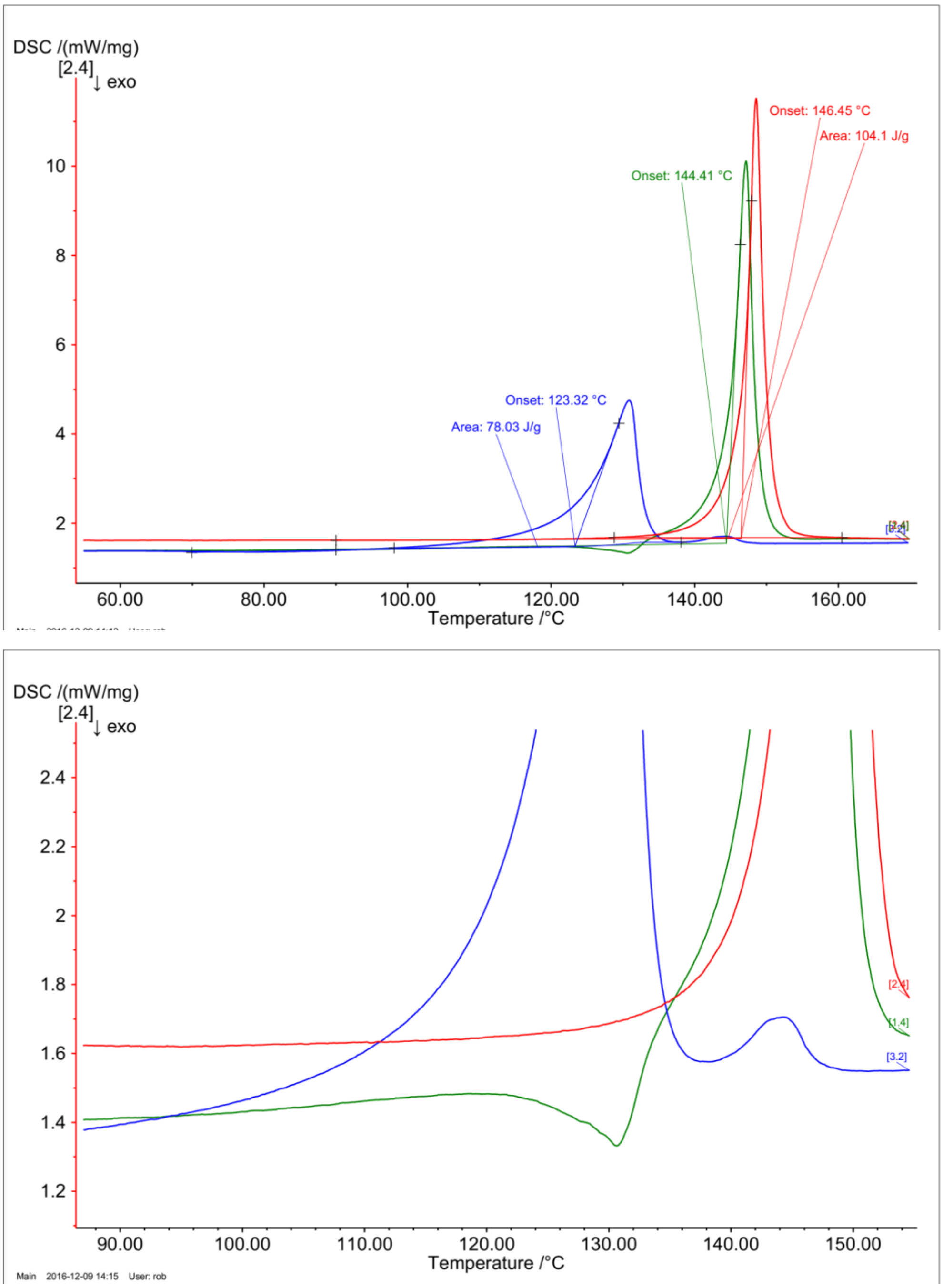
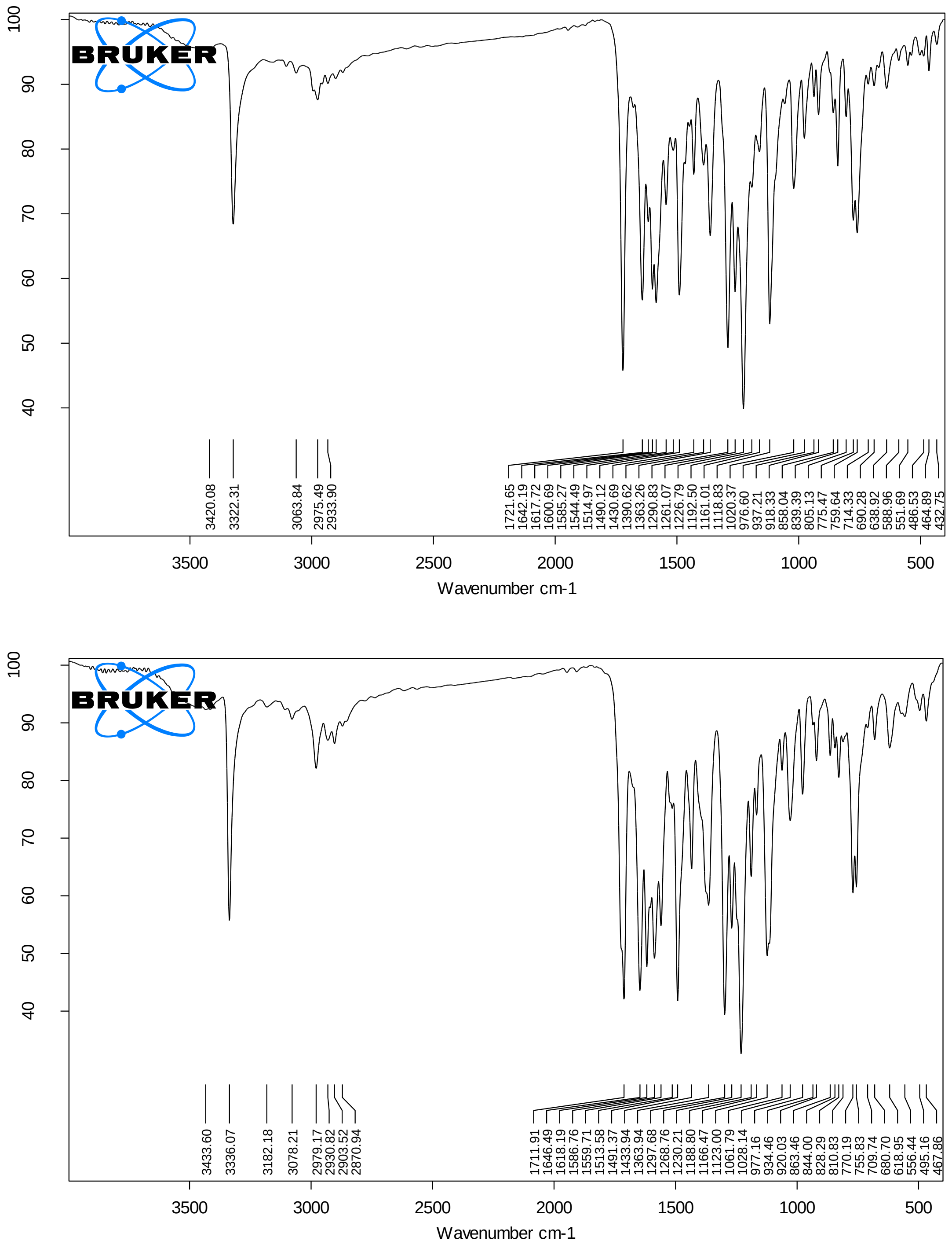


Figure S2. DSC curves registered at the heating of polymorphs α (red) and β (green) and the sample obtained after crystallization from the melt (rescan; blue). The heating rate is 20 °C min^{-1}.

IR spectra

IR spectra were recorded on an FTIR spectrometer Tensor 27 (Bruker) in the 400-4000 cm^{-1} range at optical resolution of 4 cm^{-1}. Solid samples were prepared as KBr pellets.



(a)

(b)

Figure S3. IR spectra of α-**1** (a) and β-**1** (b) polymorphs.

Powder diffraction experiments

The PXRD patterns were collected using an automated Bruker D8 Advance X-ray diffractometer equipped with a Vario setup and a Vantec linear coordinate detector. The Cu$K\alpha_1$ radiation monochromated by a curved Johansson monochromator (λ = 1.5406 Å) was used, and the performance mode of the X-ray tube was 40 kV, 40 mA. Experiments were carried out at room temperature in the Bragg–Brentano geometry with a flate sample. The patterns were recorded in the 2θ range between 3° and 60°, in 0.008° steps, with a step time of 0.3-0.5 s. The obtained diffraction data were processed using the EVA program package.

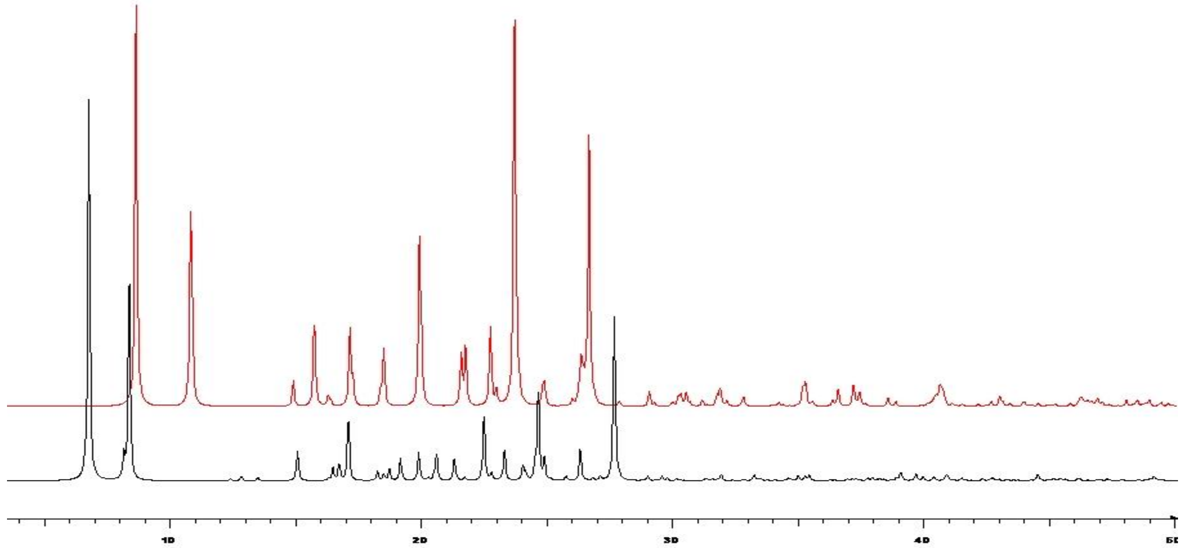


Figure S4. Comparison of theoretical powder diffraction patterns of α-polymorph (red curve) and β-polymorph (black curve).

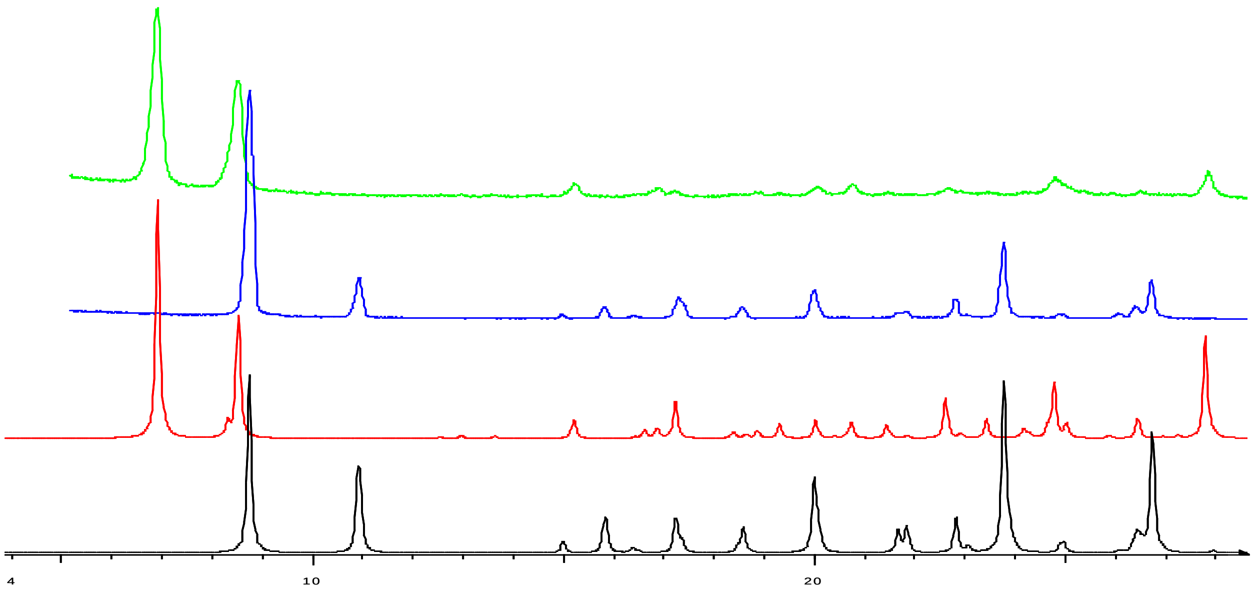


Figure S5. Theoretical powder diffraction patterns of α-polymorph (black) and β-polymorph (red) and experimental patterns of the crystalline samples obtained from ethanol (blue) and chloroform (green) solutions after fast solvent evaporation at r.t.

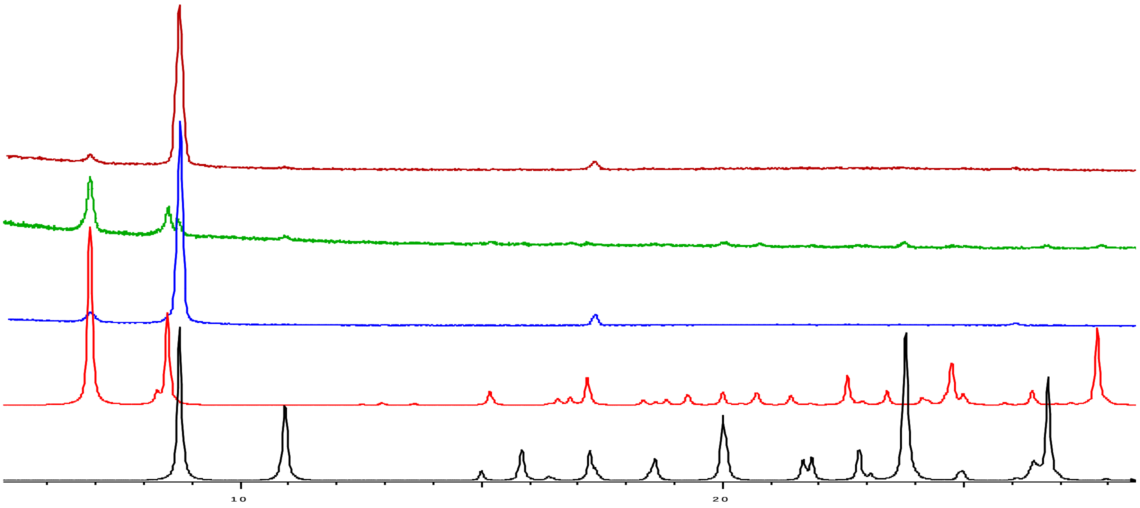


Figure S6. Theoretical powder diffraction patterns of α-polymorph (black) and β-polymorph (red) and experimental patterns of the crystalline samples obtained from acetone (blue), methylene chloride (green), and diethyl ether (brown) solutions after fast solvent evaporation at r.t.

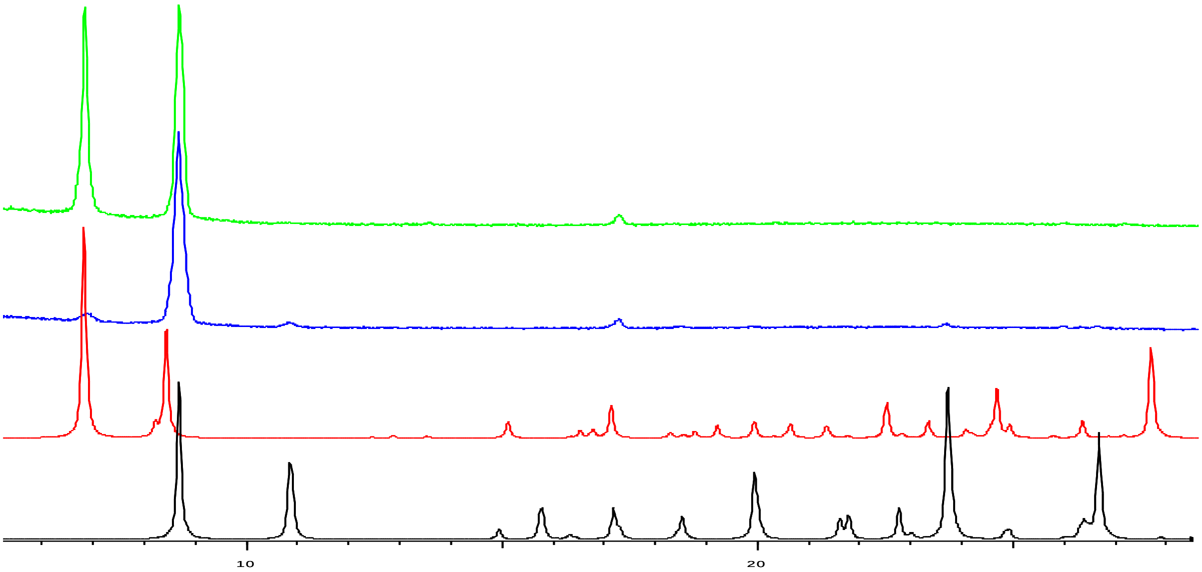


Figure S7. Theoretical powder diffraction patterns of α-polymorph (black) and β-polymorph (red) and experimental patterns of the crystalline samples obtained from a toluene solution (blue and green) after fast solvent evaporation at r.t.

Crystallization experiments

Slow solvent evaporation. The compound was dissolved in different solvents at room temperature (23 °C). Flasks were covered and a few small holes were made to allow the solvent to evaporate slowly. **Fast solvent evaporation**. The compound was dissolved in different solvents at room temperature (23 °C). The solution was evaporated at room temperature on the glass plate. The solid products were analyzed by PXRD for the identification of polymorphic composition.

Table S1. Results of crystallization for obtaining polymorphic modification from the fast and slow evaporation.

Method	ethanol	chloroform	toluene	diethyl ether	acetone	methylene chloride	tetrachloro-methane
Fast evaporation	α**	β**	α, β**	α (primary), β**	α (primary), β**	β (primary), α**	β (primary), α**
Slow evaporation	α, β***	β**	α*	α*	α*	β**	n/a

* single crystals were obtained;

** powder was obtained;

*** at the first stage, crystals of two types are observed but over time (3 months) the needles (β) disappeared while the number of prisms (α) increased. The same situation is observed if the compound crystallized from a mixture of ethanol and chloroform.

Single crystal X-ray diffraction data

Table S2. Crystal data and structure refinement for α-**1**.

Empirical formula	$C_{17}H_{18}N_2O_5$	
Formula weight	330.33	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 11.4514(6) Å	α = 90°
	b = 13.4050(8) Å	β = 118.7410(10)°.
	c = 11.6910(7) Å	γ = 90°
Volume	1573.54(16) $Å^3$	
Z	4	
Density (calculated)	1.394 mg m^{-3}	
Absorption coefficient	0.104 mm^{-1}	
F(000)	696	
Crystal size	0.556 × 0.373 × 0.265 mm^3	
Theta range for data collection	2.028° to 28.780°	
Index ranges	$-15 \leq h \leq 15$, $-17 \leq k \leq 18$, $-15 \leq l \leq 15$	
Reflections collected	18441	
Independent reflections	4028 [$R_{int} = 0.0236$, $R_\sigma = 0.0199$]	
Completeness to θ_{max}	98.5 %	
Absorption correction	Numerical	
Max. and min. transmission	0.9489 and 0.9018	
Data / $I > 2\sigma(I)$ / restraints / parameters	4028 / 3429 / 0 / 227	
Goodness-of-fit on F^2	1.041	
Final *R* indices [$I > 2\sigma(I)$]	$R1 = 0.0366$, $wR2 = 0.0923$	
R indices (all data)	$R1 = 0.0445$, $wR2 = 0.0971$	
Largest diff. peak and hole	0.326 and –0.217 e $Å^{-3}$	

Table S3. Crystal data and structure refinement for β-**1**.

Empirical formula	$C_{17}H_{18}N_2O_5$	
Formula weight	330.33	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	$P\bar{1}$	
Unit cell dimensions	a = 5.425(3) Å	α = 113.388(9)°
	b = 11.666(7) Å	β = 95.061(9)°.
	c = 14.060(9) Å	γ = 96.102(8)°
Volume	803.7(9) $Å^3$	
Z	2	
Density (calculated)	1.365 mg m^{-3}	
Absorption coefficient	0.102 mm^{-1}	
F(000)	348	
Crystal size	0.561 × 0.063 × 0.040 mm^3	
Theta range for data collection	1.925° to 25.343°	
Index ranges	$-6 \leq h \leq 6$, $-13 \leq k \leq 14$, $-15 \leq l \leq 16$	
Reflections collected	6709	
Independent reflections	2900 [R_{int} = 0.0612, R_{σ} = 0.0891]	
Completeness to θ_{max}	98.4 %	
Absorption correction	Numerical	
Max. and min. transmission	0.9580 and 0.6217	
Data / $I > 2\sigma(I)$ / restraints / parameters	2900 / 1667 / 103 / 267	
Goodness-of-fit on F^2	0.997	
Final *R* indices [$I > 2\sigma(I)$]	$R1$ = 0.0550, $wR2$ = 0.1222	
R indices (all data)	$R1$ = 0.1094, $wR2$ = 0.1456	
Largest diff. peak and hole	0.233 and –0.281 e $Å^{-3}$	

Table S4. Hydrogen bonds for α-**1** [Å and °].

D–H···A	d(D–H)	d(H···A)	d(D···A)	∠(DHA)
N(1)–H(1)···O(42)[#1]	0.884(15)	2.179(15)	2.9665(12)	148.2(12)
N(5)–H(5)···O(21)[#2]	0.867(15)	2.593(14)	3.1171(12)	119.9(11)
N(1)–H(1)···O(21)	0.884(15)	2.225(14)	2.6575(12)	109.8(11)
N(5)–H(5)···O(42)	0.867(15)	1.918(15)	2.6563(12)	142.1(13)

Symmetry transformations used to generate equivalent atoms:

#1 1–*x*, *y*–½ , ½–*z* #2 1–*x*, *y*+½ , ½–*z*

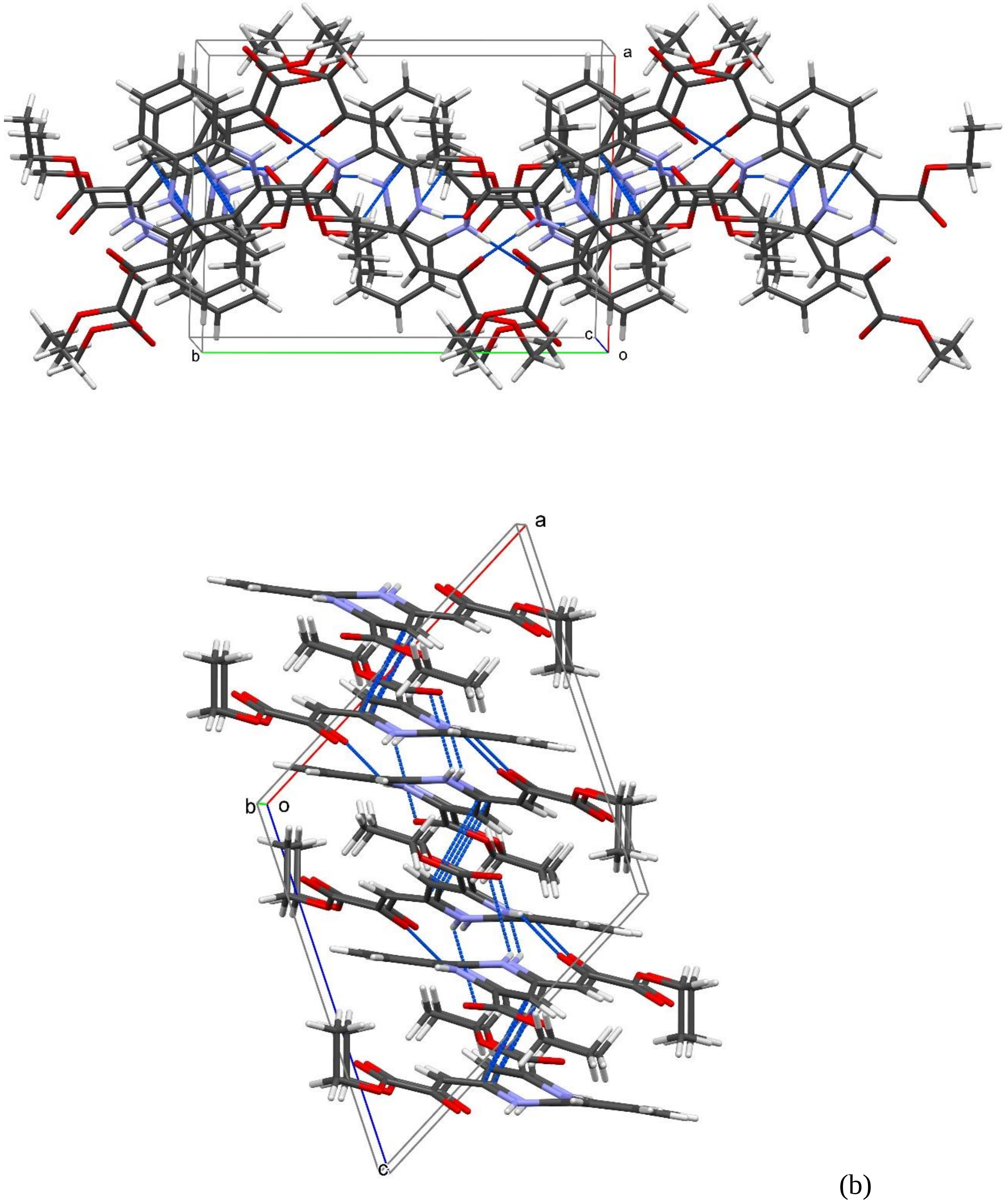
Table S5. Hydrogen bonds for β-**1** [Å and °].

D–H···A	d(D–H)	d(H···A)	d(D···A)	∠(DHA)
N(1)–H(1)···O(21)[#1]	0.86(2)	2.42(3)	3.255(3)	163(3)
N(1)–H(1)···O(21)	0.86(2)	2.22(3)	2.669(3)	112(2)
N(5)–H(5)···O(41)	0.87(2)	2.03(3)	2.727(3)	136(2)

Symmetry transformations used to generate equivalent atoms:

#1 –*x*, 2–*y*, 1–*z*

Molecular packing in the crystals of the polymorphs



(a)

(b)

Figure S8. Two projections of the 2D layer forming in the crystal of the polymorph α due to hydrogen bonds N–H···O and π…π contacts.

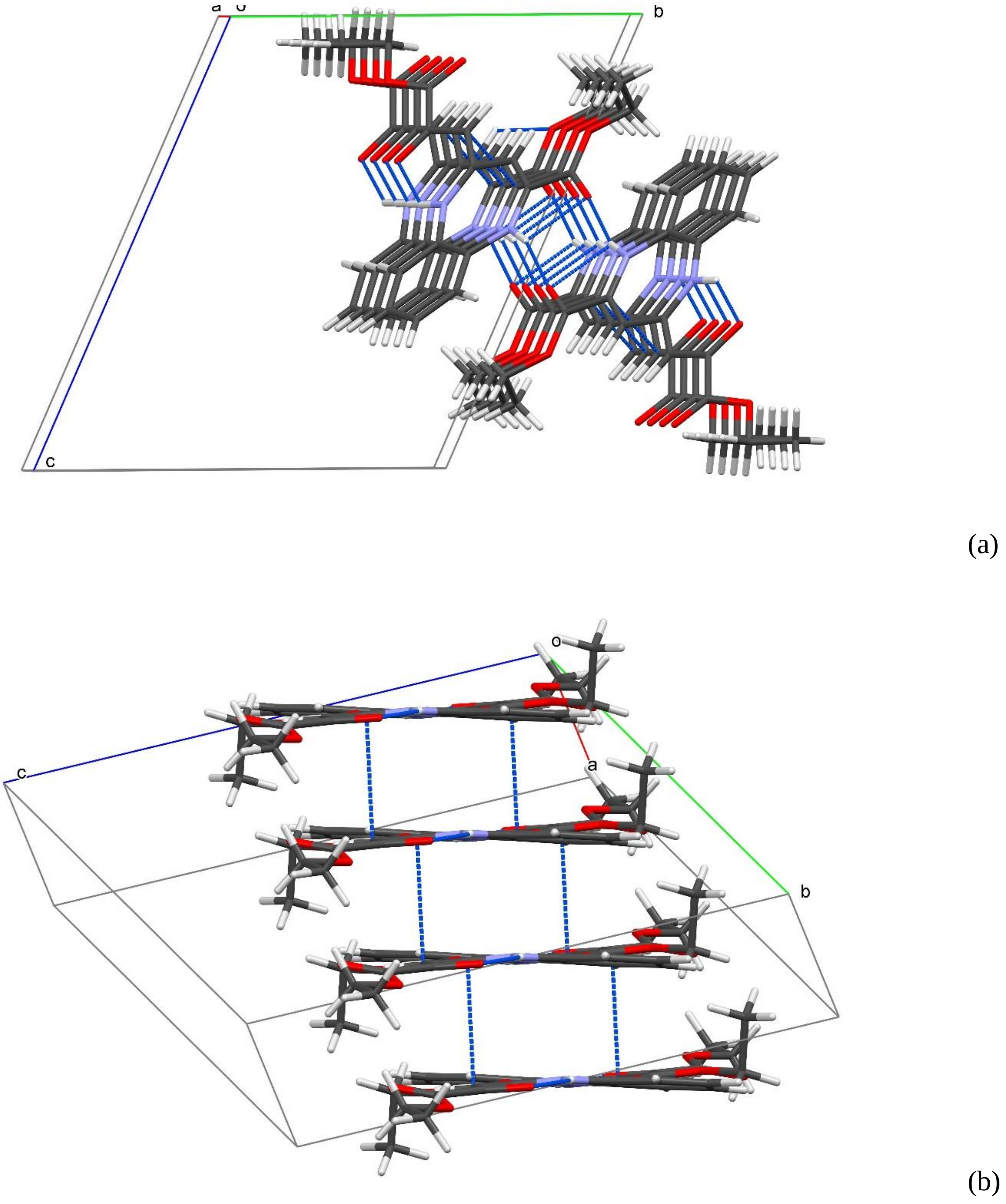


Figure S9. Two projections of the 1D ribbon forming in the crystal of the polymorph β due to hydrogen bonds N–H···O and π…π contacts.