

Crystallochromy and Reversible-Phase Transition in 2,6-Diamino-benzo[1,2-b:4,5-b']difuran-3,7-diethyl Ester Single Crystals: Experimental and Theoretical Insights

Giovanni Pierri, Rosita Diana,* Consiglia Tedesco,* Ludovica Milzi, Antonio Carella, Marianna Pannico, Francesco Silvio Gentile, and Barbara Panunzi



Cite This: *Cryst. Growth Des.* 2026, 26, 1525–1535



Read Online

ACCESS |



Metrics & More

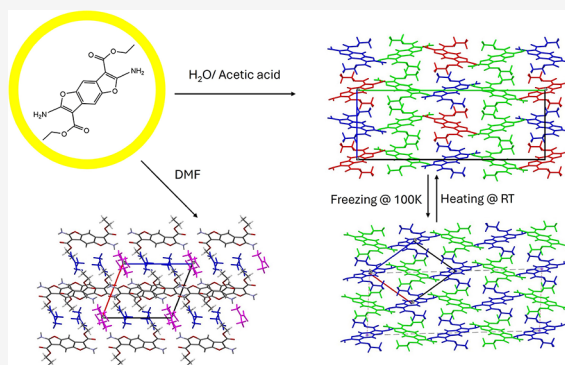


Article Recommendations



Supporting Information

ABSTRACT: The benzo[1,2-b:4,5-b']difuran core has emerged as a building block for the development of electronic and optoelectronic compounds, pharmacologically active molecules, and even antiproliferative tools for different cancer cell lines. In our past research articles, we analyzed the properties of a series of diaminobenzo[1,2-b:4,5-b']difuran derivatives with different substituents, both from the functional and crystallographic points of view. We herein have investigated the effect of different crystallization conditions on 2,6-diamino-benzo[1,2-b:4,5-b']difuran-3,7-diethyl ester. We both obtained the known colorless crystalline structure **1a(RT)** and another violet colored crystal form containing DMF as guest molecules, named **1b**. On the other hand, we recorded the ability of **1a(RT)** to change into another colorless crystal form named **1a(LT)** at 100 K, undergoing a reversible-phase transformation accompanied by a reversible twinning/detwinning process. The solid-state assembly of the three crystal forms was deeply examined; specific absorption curves and colorimetric coordinates were studied, and the energetic characteristics were derived by computational methods.



1. INTRODUCTION

Polymorphism in crystals has attracted significant scientific and technological attention over the years.¹ Small changes in crystallization conditions might lead to different polymorphs or solvatomorphs with different physical, chemical, and mechanical properties. The transformation of one crystalline phase into another can be due to a transition caused by environmental conditions such as temperature, pressure, or a chemical environment. Single-crystal to single-crystal (SCSC) polymorphic transformations are relatively rare. Even more, reversible SCSC transitions are unusual, as changes in the crystal structure commonly lead to the destruction of the parent crystal. A reversible SCSC transformation implies no destruction of the crystal lattice and occurs when the changes in the molecular conformation and packing arrangement are usually very small in the phase transition,² though notable exceptions were reported recently, and dramatic reversible conformational changes in the solid state were observed through cooperative molecular movements.^{1,3–5}

In organic molecules in solution or as crystals, the color is derived from the light not absorbed, which is the light observable by the naked eye. The absorbed light results from the excitation of electrons from the occupied to unoccupied orbitals of the molecule. Color change between polymorphs is increasingly studied for its possible applications in different domains, such as pigment, sensor, and technology industries.⁶

Based on recent articles and reviews, a few different compound families exhibit this special type of polymorphism. The ten polymorphs of 5-methyl-2-((2-nitrophenyl)amino)thiophene-3-carbonitrile (ROY) with its red, orange, and yellow crystals, are the best example of the color polymorphism phenomenon.⁷

Less investigated despite being interesting for its potential technological applications is the color change between solvatomorphs.⁸

To the best of our knowledge, there are no examples of an in-depth investigation into color changes upon solvate formation and reversible-phase transformation in benzodifuran-based molecules.^{9–14}

Benzodifuran (BDF) scaffolds are aromatic tricyclic compounds consisting of a central benzene ring symmetrically fused to two heterocyclic furan rings. Diamino-BDF molecules can be obtained by reaction of 1,4-benzoquinone with a cyanoacetic ester in alcoholic ammonia,^{15–17} which leads to functionalized derivatives with a wide choice of substituents in

Received: July 18, 2025

Revised: January 23, 2026

Accepted: January 26, 2026

Published: February 5, 2026



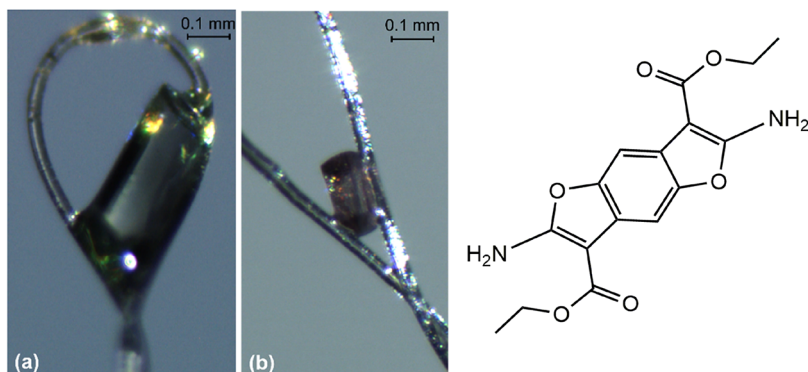


Figure 1. Analyzed crystals of form **1a**(RT) (a) and form **1b** (b) for the BDF-ethyl compound, whose formula is on the right.

the 3,7-positions. By varying the 3,7-substituent groups, chemical–physical (including color and emission) and biological properties can be tuned. Diamino-BDF molecules have emerged as efficient building blocks for the development of novel functional molecules, polymers, and COF and MOF materials.¹⁸ Due to the unique electronic and optoelectronic properties, BDF units have been used as active materials in OLEDs and OPCs¹⁹ variously functionalized to modulate the absorption/emission spectral properties.¹⁸ On the other hand, BDF compounds are key motifs in bioorganic and medical fields. BDF-based synthetic hallucinogens have a longer action than most of the other phenethylamines.²⁰ Their antimicrobial, antifungal,^{21–23} antiparasitic,²⁴ anti-inflammatory,²⁵ and analgesic activities²⁶ are largely examined. Nonetheless, their most interesting application is perhaps the antiproliferative effects on different cancer cell lines and cell-selective activity.^{27,28}

In the search for new responsive materials, we focused our attention on BDF compounds as building blocks for the synthesis of novel molecular and polymeric functional tools.^{29,30} Specifically, we analyzed the properties of a series of diamino-BDF derivatives with different R substituents³¹ and also determined the crystal structures of several derivatives using single-crystal X-ray diffraction analysis, including 2,6-diamino-benzo[1,2-b:4,5-b']difuran-3,7-dicarboxylic acid diethyl ester,³² (BDF-ethyl, [Figure 1](#)). Herein, we investigated the effect of different crystallization conditions on the derivative BDF-ethyl. By varying the crystallization conditions, we both reobtained the crystalline structure **1a(RT)** previously described¹⁸ and a new DMF solvatomorph **1b**. Interestingly, the crystals of the novel solvatomorph **1b** show a violet color at difference with the previously reported colorless crystals of the pure form **1a(RT)**. On the other hand, single crystals of **1a(RT)** transforms into a new polymorph **1a(LT)** at low temperatures. Interestingly, the transformation is accompanied by a reversible nonmerohedral twinning, since two crystal domains of form **1a(LT)** revert back into a single crystal of **1a(RT)** by increasing the temperature.

1a(RT) and **1b** show specific absorption curves and thermal behavior. Current computational methods were used to account for the energetic characteristics of the three different crystal forms, aiming to link the peculiar chemical and physical properties to the solid-state assembly of the studied crystal forms.

2. MATERIALS AND METHODS

2.1. Materials and Identification Methods

Commercially available starting products were supplied by Sigma-Aldrich (20151 Milano (MI), Italy). ^1H NMR spectra were recorded in 1,1,2,2-tetrachloroethane- d_2 (TCE) with a Bruker ADVANCE II 400 MHz apparatus by Bruker Corporation, Billerica, MA, USA. Mass spectrometry measurements were carried out using a Q-TOF Premier instrument (Waters, Milford, MA, USA) with an electrospray ion source and a hybrid quadrupole-time-of-flight analyzer. Optical observations were performed using a Zeiss AxioScope polarizing microscope by Carl Zeiss, Oberkochen, Germany, equipped with an FP90 Mettler microfurnace by Mettler-Toledo International INC MTD, Columbus, OH, USA.

2.2. Synthesis of BDF-Ethyl

To obtain compound **1a**, 2,6-diamino-benzo[1,2-b:4,5-b']difuran-3,7-dicarboxylic acid diethyl ester³² ethyl cyanoacetate (3.0 mL, 26.5 mmol) was added slowly to a solution of 1,4-benzoquinone (2.0 g, 18.5 mmol) in absolute ethanol (40 mL), with stirring at room temperature. By addition of 30% w/w aqueous solution of ammonia (7.0 mL), an exothermic reaction (temperature rises to 40 °C) starts with the precipitation of a gray solid, which was kept under stirring for 30 min. The solid was recovered by filtration, washed three times with ethanol, and obtained by recrystallization from DMF/water (9:1). Yield = 44%; mp = 278 °C with decomposition, in good agreement with the literature.³² C₁₆H₁₆N₂O₆ (332.310): C, 57.83; H, 4.85; N, 8.43; found: C, 57.80; H, 4.88; N, 8.47. ¹H NMR (200 MHz, DMSO-d₆, 25 °C): δ = 7.61 (s, 4H), 7.32 (s, 2H), 4.24 (q, J = 6.7 Hz, 4H), 1.32 (t, J = 6.7 Hz, 6H) ppm. ¹³C NMR (200 MHz, DMSO-d₆, 25 °C): δ = 195.0, 158.3, 153.0, 126.6, 123.2, 123.1, 34.9, 8.2 ppm.

2.3. UV–Vis Spectroscopy

Solid-state UV–vis spectroscopy used a JASCO V-750 spectrophotometer by JASCO Inc., Easton, MD, USA, at a scanning rate of 200 nm·min⁻¹ at room temperature. Crystalline solid samples were crushed within a mortar before insertion into a 2 mm wide quartz sample holder.

2.4. Calculation of the CIE Chromaticity Coordinates

The color display was investigated by employing the CIE 1931 RGB (Red, Green, Blue) color space (International Commission on Illumination, 1931). CIE color space is a quantitative link between distributions of wavelengths in the visible spectrum and physiologically perceived colors in human color vision. CIE calculation was performed using Spectragryph, a spectroscopy software tool analyzing data taken from spectrometers.³³

2.5. Computational Modeling

Calculations were carried out using the CRYSTAL17 software package, which employs the Linear Combination of Atomic Orbitals (LCAO) method with Gaussian (centered over the nucleus positions) orbitals to represent the electronic structure of the molecules. This method is suited for large systems where precise electronic structure

Table 1. Relevant Crystallographic Data for 1a(RT), 1a(LT), and 1b Crystal Forms

	form 1a(RT)	form 1a(LT)	form 1b
CCDC code	2392622	2392623	2464337
formula	C ₁₆ H ₁₆ N ₂ O ₆	C ₁₆ H ₁₆ N ₂ O ₆	C ₁₆ H ₁₆ N ₂ O ₆ ·2(C ₃ H ₇ NO)
<i>D</i> _{calc} /g cm ^{−3}	1.426	1.464	1.320
μ /mm ^{−1}	0.935	0.960	0.851
formula weight	332.31	332.31	478.50
color	clear, colorless	clear, colorless	light violet
size/mm ³	0.37 × 0.15 × 0.07	0.37 × 0.15 × 0.07	0.22 × 0.12 × 0.04
<i>T</i> /K	298	100	100
crystal system	monoclinic	triclinic	triclinic
space group	<i>P</i> 2 ₁ / <i>c</i>	$\bar{P}$ 1	$\bar{P}$ 1
<i>a</i> /Å	9.1922(6)	9.0596(3)	9.994(6)
<i>b</i> /Å	30.256(2)	9.1701(3)	10.962(5)
<i>c</i> /Å	14.0393(10)	9.6087(3)	12.102(4)
α /°	90	89.168(3)	100.35(2)
β /°	127.561(2)	71.197(3)	109.11(4)
γ /°	90	85.804(3)	98.10(4)
<i>V</i> /Å ³	3095.2(4)	753.60(4)	1203.7(10)
<i>Z</i>	8	2	2
$\Theta_{\min}$ /°	2.921	4.836	3.983
$\Theta_{\max}$ /°	71.833	77.048	74.483
measured Refl's	44900	5648	17269
Refl's $I \geq 2 \sigma(I)$	4893	5023	3934
parameters	469	237	330
restraints	0	0	0
largest peak	0.25	0.43	0.25
deepest hole	−0.23	−0.43	−0.26
GooF	1.128	1.098	1.067
<i>wR</i> ₂ (all data)	0.1408	0.2129	0.1129
<i>wR</i> ₂	0.1355	0.1996	0.0971
<i>R</i> ₁ (all data)	0.0658	0.0710	0.0462
<i>R</i> ₁	0.0555	0.0650	0.0368

calculations are required. The electronic interactions described by the B3LYP functional ensured accuracy in predicting the geometry and energy of the molecular systems. This functional combines Becke's three-parameter exchange functional within the Lee–Yang–Parr correlation functional, providing reliable results for both molecular and crystal calculations. The presence of 20% Fock exchange avoids the effects of the electron self-interaction. The GRIMME D3 dispersion correction accounts for van der Waals interactions in the organic crystal lattices. For the electronic structure calculations, the Ahlrichs def2-SVP basis set was used, which strikes an excellent balance between computational efficiency and accuracy, as demonstrated in previous studies.^{34,35} To ensure precision, the integral tolerances (TOLINTEG) were set to 8 8 8 16, ensuring the required level of accuracy while optimizing the resource efficiency. Finally, for the DFT calculations, a pruned XXL integration grid was employed. This grid is specifically designed to provide high accuracy in the numerical integration of the exchange–correlation functional and is advantageous for systems with complex electronic structures.^{36–38}

2.6. Crystallization

As previously reported,¹⁸ single crystals of 1a(RT) were obtained by slow evaporation of a solution of acetic acid (0.025 mmol·mL^{−1}) at room temperature in a glass crystallizer. The form 1a(LT) was obtained by freezing a single crystal of form 1a(RT) at 100 K.

Crystals of form 1b were obtained in dimethylformamide (DMF). In particular, crystallization (0.01 mmol, 8 mL of DMF) was carried out for 72 h at 90 °C in hydrothermal synthesis reactors consisting of a hermetic stainless-steel body (working pressure up to 2 MPa) and an inner liner in Teflon. Crystals large enough to analyze via single-crystal X-ray diffraction were produced via slow cooling down at room temperature (within 5 h).

2.7. Single-Crystal X-ray Diffraction Data Collection, Integration, and Structural Refinement

Suitable single crystals for data collection were selected, mounted on a cryoloop with paratone oil (Figure 1) and measured with a Bruker D8 QUEST diffractometer equipped with a PHOTON detector using Cu-K α radiation (λ = 1.54178 Å). Crystals of form 1a(LT) and form 1b were collected at 100 K, while data collection on crystals of form 1a(RT) was performed at 298 K.

Data indexing, integration, reduction, and absorption correction of data collection of form 1a(RT) and form 1b were performed using APEX3 software suite (APEX3, version 2015.5-2; Bruker AXS Inc., 2016, Madison, Wisconsin, USA; SAINT, version 8.34A; Bruker AXS Inc., 2013, Madison, Wisconsin, USA; SADABS, version 2014/5; Bruker AXS Inc., 2014, Madison, Wisconsin, USA.).

Regarding the data collection performed on the crystal of form 1a(LT), the data were processed using CrysAlisPro ver. 1.171.43.111a (Rigaku Oxford Diffraction), a CrysAlisPro Software system (Rigaku Oxford Diffraction, 2015). Empirical absorption correction was performed with CrysAlisPro ver. 1.171.43.111a using spherical harmonics, implemented in the SCALE3 ABSPACK scaling algorithm. The crystal shows nonmerohedral twinning with two equal components rotated by 180° around the [3/4, 0, 2/3] direction in direct space.

All of the crystal structures were solved using SHELXS³⁹ and refined using full matrix least-squares based on *F*² using the program SHELXL⁴⁰ and OLEX2⁴¹ as the graphical user interface.

Non-hydrogen atoms were refined anisotropically. Hydrogen atoms attached to the nitrogen atoms were localized from the difference in electron density maps and refined, whereas the remaining hydrogen atoms were positioned geometrically and included in the structure

factor calculations but not refined. Relevant crystallographic data and refinement details are reported in Table 1.

2.8. Thermal Analysis

DSC analysis was performed using a TA DSC-Q20 instrument under a purified N_2 flow (50 mL min^{-1}) with a rate of 5 K/min . 1.0 mg of crystals of **1a(RT)** was dried up with a filter paper and sealed in an aluminum pan, cooled to 113 K , and then heated to 573 K .

2.9. Lattice Energy Calculations

The MiCMoS package was used to perform lattice energy calculations.⁴² In particular, the CLP-PIXEL^{43–45} module was used with a pixel condensation level of 4, partitioning the interaction energies for molecular pairs into Coulombic, polarization, dispersion, and repulsion terms. For pixel calculations, the electron density was calculated *ab initio* using the MP2 method and 6-31G(d,p) basis set. Since the PIXEL module can handle only two independent molecules in the asymmetric unit, the lattice energy calculations on the crystal form **1a(RT)** were performed by considering two molecules at a time. This allowed us to obtain the interaction energies for all three molecules.

2.10. Energy Framework Analysis

The energy framework analysis was carried out with CrystalExplorer 21.5.⁴⁶ In this specific case, lattice energy calculations were performed using the B3LYP method and the 6-31G(d,p) basis set, accounting for electrostatic, polarization, dispersion, and exchange-repulsion terms.^{47,48}

The CrystalExplorer total lattice energy was obtained by multiplying the single contributions using the following scale factors: $k_{\text{ele}} = 1.057$, $k_{\text{pol}} = 0.740$, $k_{\text{disp}} = 0.871$, and $k_{\text{rep}} = 0.618$.⁴⁸

For calculations, all of the X–H bond lengths were normalized using the standard X–H distances (X=C, O, N),^{49,50} the reported X–H distances and X $\cdots$ H contacts differ from those determined from the original cif files.⁵¹

3. RESULTS AND DISCUSSION

3.1. SC-XRD Analysis

As previously reported,¹⁸ **1a(RT)** crystal form crystallizes in a monoclinic space group $P2_1/c$ with three independent molecules in the asymmetric unit: type A molecule (green in Figure 2), type B molecule (blue in Figure 2), and type C

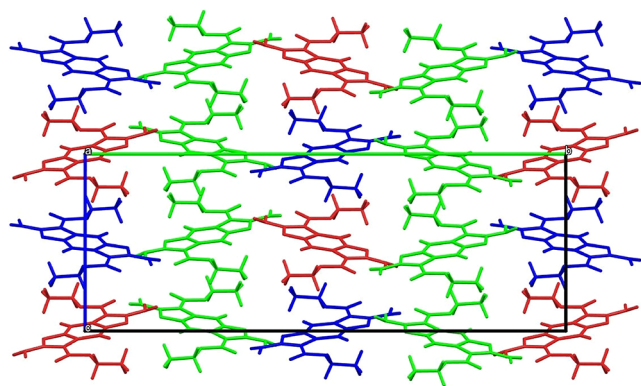


Figure 2. Crystal packing of form **1a(RT)** as viewed along the a axis with type A molecules in green, type B molecules in red, and type C molecules in blue.

molecule (red in Figure 2). Two molecules (type B and type C) are localized on two inversion centers, while the third one is in a general position although it exhibits a noncrystallographic inversion center and is crossed by the crystallographic glide plane, which occurs very rarely for molecular organic

compounds. This is due both to the planarity of the BDF moiety and to the presence of a molecular inversion center.

The molecular overlay performed with Mercury software⁵² confirms that the three molecules do not differ significantly from one another (type A vs type B RSMD = $0.041\text{ \AA}$; type A vs type C RSMD = $0.039\text{ \AA}$; type B vs type C RSMD = $0.029\text{ \AA}$, see Figures S2 and S3 in the Supporting Information).

The quality of the newly collected X-ray diffraction data allowed us to localize NH_2 hydrogen atoms in the Fourier difference map and refine their coordinates. Therefore, the nitrogen atom pyramidalization can be appreciated quite effectively.

By performing single-crystal diffraction measurements on the same crystal at 100 K , we obtained a new polymorph of compound **1**. The new crystal form, indicated as **1a(LT)**, features a triclinic unit cell with two independent molecules ($Z' = 2$): type A (green) and type B (blue) molecules (Figure 3). In this case, both independent molecules are localized on

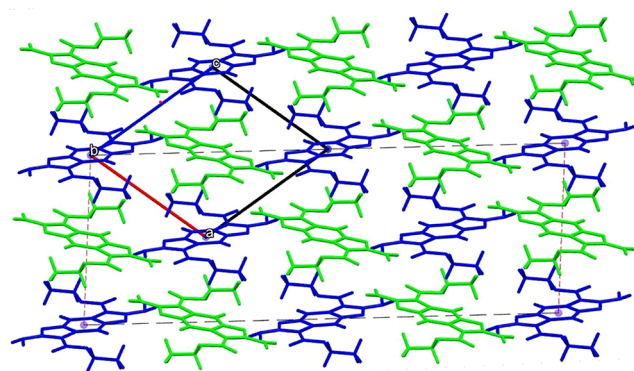


Figure 3. Crystal packing of form **1a(LT)** as viewed along the b axis. **1a(LT)** type A molecules are depicted in green and **1a(LT)** type B molecules are depicted in blue. The triclinic unit cell is depicted with solid lines, and the supercell is depicted with dashed lines.

an inversion center. By increasing the temperature at 298 K , we obtained again form **1a(RT)** confirming that the transformation is reversible.

In particular, at 100 K , the crystal exhibits nonmerohedral twinning and the monoclinic unit cell obtained⁵³ at temperature to 298 K twinning completely disappears.

Reversible transformation associated with crystal twinning and detwinning was reported in intermetallic compounds,⁵⁴ and only recently they start being reported for organic⁵³ and organometallic compounds.⁵⁵

Form **1b** is the only solvated crystal form of compound **1** obtained so far, exhibiting a 1:2 host:guest ratio (Figure 4). The crystal structure adopts a layered structure, where the layers of guest and host molecules alternate. As for form **1a(RT)** type A molecule, it exhibits a noncrystallographic inversion center.

ORTEP drawings for crystal structures of **1a(RT)** type A molecule, type B molecule, and type C molecule; **1a(LT)** type A molecule and type B molecule; **1b** are reported in Figure S1 (Supporting Information).

3.2. Crystal Packing Analysis

The reversible transformation from **1a(RT)** to **1a(LT)** was investigated in-depth using CLP-PIXEL and CrystalExplorer. Tables 2 and 3 report the intermolecular distances, angles, and interaction energies for both crystal forms obtained with

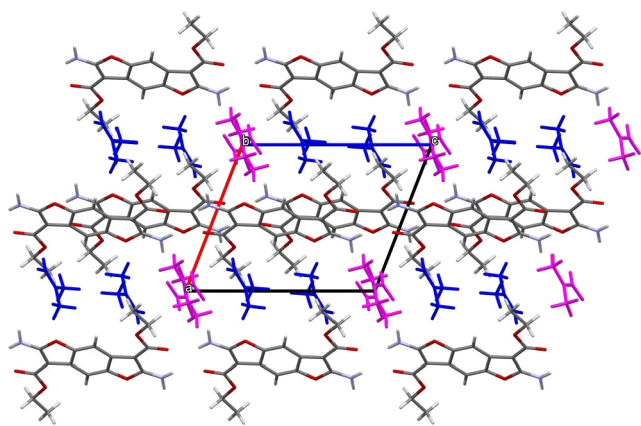


Figure 4. Crystal packing of form **1b** as viewed along the *b* axis. Crystallographically independent DMF guest molecules are colored magenta and blue.

CrystalExplorer (Tables S2 and S3 in the Supporting Information the energy values obtained with CLP-PIXEL are also reported).

Both polymorphs exhibit a very efficient packing, as confirmed by the Kitaigorodskii packing index⁵⁶ calculated using the Platon software (69.0% for form **1a(RT)** and 71.4% for form **1a(LT)**).⁵⁷

By visually inspecting the crystal packing of **1a(RT)**, as viewed along the *a* axis, and the crystal packing of **1a(LT)**, as viewed along the *b* axis, it is possible to appreciate the packing similarities between the two crystal forms (Figures 2 and 3).

Notably, the *a* axis in **1a(RT)** and the *b* axis in **1a(LT)** feature very similar values of 9.1922(6) and 9.1768(2) Å, respectively. Along these directions, the molecules assemble through CH–π interactions, motifs II A–A, I B–B, and I C–C in **1a(RT)** and motifs II A–A and I B–B in **1a(LT)** with very similar energy values.

In detail:

- in **1a(RT)**, type A molecules (green) give rise to the II A–A motif by means of CH–π interactions between the side-chain methylene hydrogen atoms and the π orbitals of the furan moiety; also, type B molecules (red) assemble into I B–B motif molecules through CH–π interactions between the side-chain methylene hydrogen atoms and the π orbitals of the furan moiety; finally, type C (blue) molecules assemble into the I C–C motif through CH–π interactions involving both side-chain methylene and methyl hydrogen atoms and furan and carbonyl π systems although at a longer distance (slightly greater than 3.00 Å).
- in **1a(LT)**, type A molecules give rise to the II A–A motif by means of CH–π interactions between methyl hydrogens and the carbonyl double bond of the side

Table 2. List of Intermolecular Distances (Å), Angles (°), and Interaction Energies (kJ/mol) in Form **1a(RT)**^a

Motif	D–H...A	H...A (Å)	∠D–H...A (°)	Symm. Op.	Centr. Dist. (Å)	E_{Coul} (kJ/mol)	E_{Pol} (kJ/mol)	E_{Disp} (kJ/mol)	E_{Rep} (kJ/mol)	E_{Tot} (kJ/mol)
I A–A				$x, 3/2 - y, -1/2 + z$ $x, 3/2 - y, 1/2 + z$	7.025	−7.3	−3.1	−71.2	38.4	−48.3
II A–A				$-1 + x, y, z$ $1 + x, y, z$	9.192	−7.2	−1.4	−38.8	18.5	−31.0
I B–B				$-1 + x, y, z$ $1 + x, y, z$	9.192	−7.1	−1.4	−39.2	19.2	−30.8
I C–C				$-1 + x, y, z$ $1 + x, y, z$	9.192	−7.7	−1.4	−38.2	19.1	−31.4
I A–B	N1A–H1AB...O2B	2.04	161.1	x, y, z	8.848	−34.4	−6.3	−25.6	36.8	−40.7
	N1B–H1BB...O1A	2.39	128.7							
II A–B	N1B–H1BA...O3A	2.05	157.1	$-1 + x, y, z$	8.640	−29.8	−5.7	−23.0	28.7	−38.0
	N1A–H1AA...O1B	2.53	119.2	$1 + x, y, z$						
I A–C	N1C–H1CA...O5A	2.02	161.1	$1 - x, 1/2 + y, 1/2 - z$	9.086	−31.4	−6.3	−22.5	31.8	−37.8
	N2A–H2AA...O1C	2.45	127.7	$1 - x, -1/2 + y, 1/2 - z$						
II A–C	N2A–H2AB...O2C	2.04	159.1	$-x, 1/2 + y, 1/2 - z$	8.884	−29.0	−5.9	−20.3	27.0	−36.0
	N1C–H1CB...O2A	2.57	117.8	$-x, -1/2 + y, 1/2 - z$						
III A–C	N1A–H1AA...O2C	2.57	141.4	$-1 + x, y, z$	12.511	−24.5	−3.4	−9.0	0.0	−36.3
	N1C–H1CB...O3A	2.61	149.0	$1 + x, y, z$						
I B–C				x, y, z $x, y, 1 + z$ $x, y, -1 + z$	7.020	−6.4	−3.2	−71.1	38.7	−47.1
IV A–B					13.340	−8.2	−0.6	−2.9	0.0	−11.7

^aThe CrystalExplorer total lattice energy is obtained by multiplying the single contributions by the following scale factors: $k_{\text{ele}} = 1.057$, $k_{\text{pol}} = 0.740$, $k_{\text{disp}} = 0.871$, and $k_{\text{rep}} = 0.618$.

Table 3. List of Intermolecular Distances (Å), Angles (°), and Interaction Energies (kJ/mol) in Form **1a**(LT)^a

motif	D–H...A	H...A (Å)	∠D–H...A (°)	Symm. Op.	centroid distance (Å)	E_{Coul} (kJ/mol)	E_{Pol} (kJ/mol)	E_{Disp} (kJ/mol)	E_{Rep} (kJ/mol)	E_{Tot} (kJ/mol)
I A–A	N1A–H1AA...O2A	2.41	149.7	$-1+x, 1+y, z$ $1+x, -1+y, z$	12.410	−32.4	−4.8	−10.2	0.0	−46.7
II A–A				$x, -1+y, z$ $x, 1+y, z$	9.170	−8.0	−1.4	−40.0	21.2	−31.3
I B–B				$x, -1+y, z$ $x, 1+y, z$	9.170	−9.4	−1.6	−44.2	27.0	−33.0
I A–B	N1A–H1AA...O2B	2.00	163.9	x, y, z	9.074	−34.8	−6.9	−25.0	38.6	−39.8
	N1B–H1BA...O1A	2.39	129.0	$1+x, 1+y, 1+z$ $-1+x, -1+y, -1+z$						
II A–B	N1B–H1BB...O2A	2.06	152.6	$x, 1+y, z$	8.659	−28.4	−5.8	−22.3	28.5	−36.1
	N1A–H1AB...O1B	2.58	115.9	$1+x, y, 1+z$ $-1+x, y, -1+z$ $x, -1+y, z$						
III A–B				$x, 1+y, 1+z$ $1+x, y, z$ $-1+x, y, z$ $x, -1+y, -1+z$	6.942	−10.4	−3.5	−80.8	52.8	−51.4

^aThe CrystalExplorer total lattice energy is obtained by multiplying the single contributions by the following scale factors: $k_{\text{ele}} = 1.057$, $k_{\text{pol}} = 0.740$, $k_{\text{disp}} = 0.871$, and $k_{\text{rep}} = 0.618$.⁴⁸

chains, while type B molecules assemble into the I B–B motif molecules through CH–pi interactions between the side-chain methylene hydrogen atoms and the pi orbitals of the furan moiety.

In **1a**(RT), the molecular assembly along the *c* axis (=14.0393(10) Å) corresponds to the molecular assembly along the minor body diagonal of the triclinic cell (=13.884 Å) in **1a**(LT).

Thus, in **1a**(LT), type A (green) and B (blue) molecules are connected with a centroid distance of 6.942 Å along the minor body diagonal of the triclinic cell; in **1a**(RT), type B (blue) and C (red) molecules are connected with a centroid distance of 7.020 Å, and type A (green) and type A (green) are connected with a centroid distance of 7.025 Å.

In particular, in **1a**(RT) motifs I A–A and I B–C (−48.3 kJ mol^{−1} and −47.1 kJ mol^{−1}) and in **1a**(LT) motif III A–B (−51.4 kJ mol^{−1}), they are based on pi–pi and CH–pi interactions with a strong dispersive character.

Noteworthy, parallel to the *c* axis direction in **1a**(RT), gliding provided by the *c* glide symmetry plane occurs, and the detachment of type A molecules from the glide symmetry plane determines the occurrence of the twinning in **1a**(LT), as shown by the observed twin law, which highlights the emergence of a symmetry plane perpendicular to the *b* axis in **1a**(LT) (forbidden in the P1 space group).

Differences in solid-state assembly can be detected by observing the corresponding energy frameworks for **1a**(RT) and **1a**(LT), as shown in Figures 5 and 6, respectively, and also in the movie provided in the Supporting Information (Movie 1).

The most striking feature is the occurrence of a strong interaction (−46.7 kJ/mol) in **1a**(LT), with a prevalent Coulombic contribution, between type A molecules, I A–A motif (Table 3). This interaction involves type A molecules, whose centroids are at a distance of 12.410 Å and are located along the triclinic *C* face's minor diagonal. This is a prototypical supramolecular synthon as the amino group

hydrogen atoms and carbonyl oxygen atoms of two A type molecules face each other along the crystallographic inversion centers located in the middle of the triclinic *c* axis.

I A–A interactions in **1a**(LT) substitutes III A–C and IV A–B motifs in **1a**(RT) with a significant increase in the interaction energies (from −11.7 kJ mol^{−1} and −36.3 kJ mol^{−1} to −46.7 kJ mol^{−1}, respectively) and the corresponding tightening of the hydrogen bonding donor and acceptor groups (Table S1 in the Supporting Information).

3.3. Crystal Packing Analysis of **1b** Crystal Form

In the crystal packing analysis of **1b**, we first investigated the host–host interactions, followed by the host–guest interactions. In Table 4, we list the results of PIXEL and CrystalExplorer calculations (Tables 4 and S4 in the Supporting Information). Since the unit cell contains two independent DMF molecules in the asymmetric unit, host–guest interactions are reported as H–GA and H–GB to identify the two guest molecules, while host–host interactions are reported as H–H.

Host molecules in **1b** form ribbons parallel to the *c* axis via NH...OC hydrogen bonds between amino groups and side-chain carbonyl groups (motif I H–H, Table 4), similar to motif I A–A in **1a**(LT) and III A–C in **1a**(RT). Noteworthy, in **1b**, the BDF moieties belong to the same plane, and the distances between amino group H atoms and oxygen atoms decrease from 2.6 Å in III A–C in **1a**(RT) and 2.4 Å in I A–A in **1a**(LT) to 2.0 Å with the corresponding increase of the interaction energies.

The ribbons in **1b** assemble together along the *b* axis by dispersive interactions, including CH...π contacts (motifs II H–H and III H–H, Table 4). Notably, the assembly of the host molecules along the third direction (*a* axis) occurs only through bridging DMF guest molecules, as shown in Figure 7.

Crystal form **1b** highlights those intermolecular host–host interactions, whose strength can compete with the surrounding DMF molecules (see assembly motifs I H–H in **1b**, I A–A in

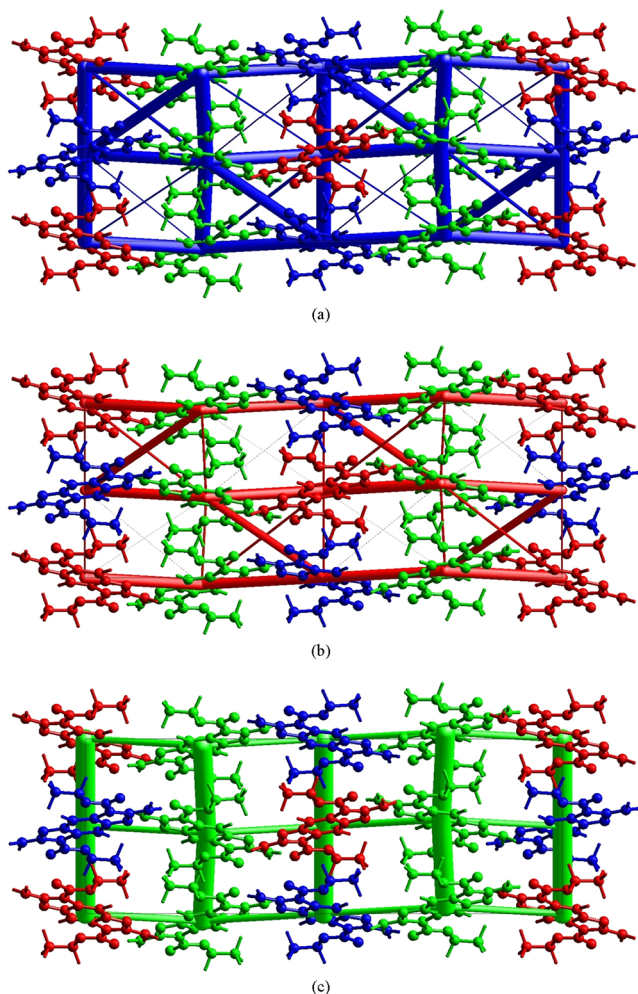


Figure 5. Energy frameworks for **1a(RT)** as viewed along the *a* axis: (a) total interaction (blue), (b) electrostatic (red), and (c) dispersion (green) energy contributions. The tube size is proportional to the energy values and is set to 100, and interaction energies with magnitudes greater than -10 kJ mol^{-1} have been omitted.

1a(LT), and III A–C in **1a(RT)** in the [Supporting Information](#)).

3.4. Thermal Behavior, UV–Vis Analysis, and Calculation of CIE Coordinates

Optical observations of the phase transitions were performed on single crystals by using a polarizing light optical microscope equipped with a microfurnace. The optical observations confirmed the endothermal event at $278\text{--}280^\circ\text{C}$ for **1a(RT)**.¹⁸ A low amount of decomposition impedes regular recrystallization after melting. Similar behavior is recorded for **1b**, whose single crystal melts at 269°C , with decomposition. This broad phenomenon is also related to the release of DMF solvent.

We also characterized the transformation from **1a(RT)** to **1a(LT)** by differential scanning calorimetry (DSC). A few crystals of **1a(RT)** were cooled down to 113 K and then heated up to 573 K. The DSC profile ([Figure S4](#) in the Supporting Information) allows us to appreciate that the **1a(LT)** crystal form undergoes transformations into **1a(RT)** at 118 K with only a slightly exothermal process ($\Delta H_{\text{tr}} = -9.75 \text{ kJ/mol}^{-1}$) and starts melting at 545 K ($\Delta H_{\text{fus}} = +78.89 \text{ kJ/mol}^{-1}$).

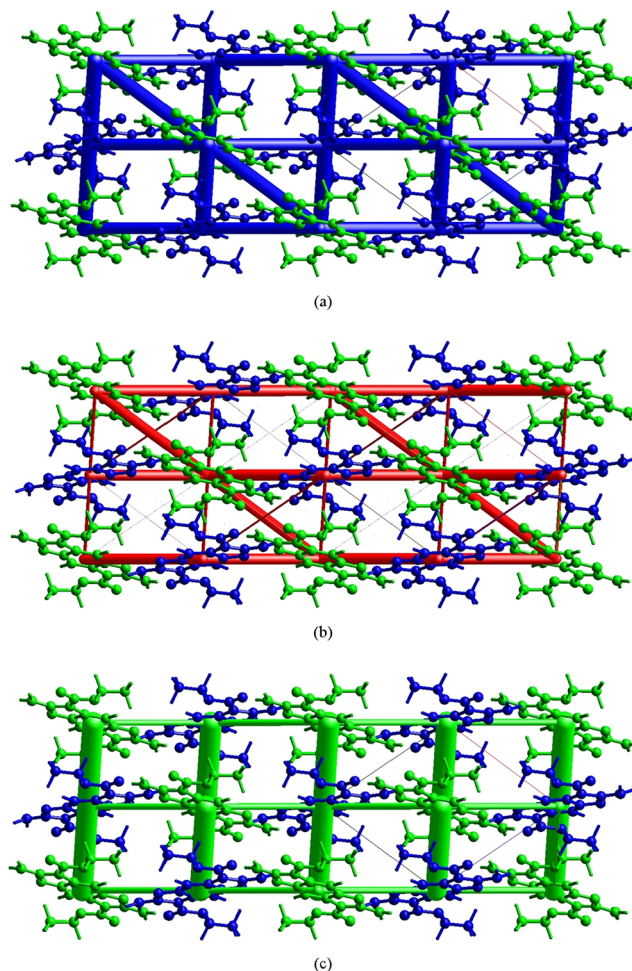


Figure 6. Energy frameworks for **1a(LT)** as viewed along the *b* axis: (a) total interaction (blue), (b) electrostatic (red), and (c) dispersion (green) energy contributions. The tube size is proportional to the energy values and is set to 100.

Physiologically perceived colors in human vision fall in the range of 380 to 760 nm. The range can be extended to 310–1050 nm under artificial conditions.^{58–61} In our case, the color of the crystals was perceived under irradiation light of the microscope, expanding our selective color detection capability. On the other hand, the absorption spectrum recorded by a spectrophotometer is an absolute measure of color. Substances that absorb in the visible range are colored with a complementary color to absorbed radiation. The longest-wavelength excitation (lowest energy) is the most relevant in the chromophore pattern of a molecule. While all or most of the shorter-wavelength light will be absorbed, light with longer wavelengths will be reflected or transmitted and will mainly contribute to the observed color. The UV–vis absorption of the **1a(RT)** and **1b** polymorphs in the solid state was analyzed and compared. [Figure 8](#) shows the absorption spectra recorded on the powdered crystal samples. The UV–vis spectral pattern can be related to perceived crystallochromy. The main absorption band of light violet of **1b** is related to the two-band pattern. The lower band at 323 nm contributes little to the color, while the upper band at 375 nm is crucial for a perceivable colorimetric response.

The CIE 1931 color spaces are defined as quantitative links between distributions of wavelengths in the electromagnetic

Table 4. List of Intermolecular Distances (Å), Angles (°), and Interaction Energies (kJ/mol) in Form 1b^a

motif	D–H...A	H...A (Å)	∠D–H...A (°)	Symm. Op.	centroid distance (Å)	E_{Coul} (kJ/mol)	E_{Pol} (kJ/mol)	E_{Disp} (kJ/mol)	E_{Rep} (kJ/mol)	E_{Tot} (kJ/mol)
I H–H	N1–H1B...O5	2.01	148.1	$x, y, -1 + z$	12.102	−50.9	−10.7	−14.6	0.0	−74.4
	N2–H2B...O2	2.00	148.5	$x, y, 1 + z$						
II H–H	C13–H13C...O5	2.67	150.0	$1 - x, -y, 1 - z$	5.491	−6.0	−2.8	−51.4	21.6	−39.9
				$1 - x, 1 - y, 1 - z$	7.775	−9.4	−1.7	−48.2	31.7	−33.6
I H–GA	C3S–H3SC...O3	2.50	164.7	$1 - x, 1 - y, 2 - z$	8.127	−36.0	−9.0	−5.9	31.0	−30.8
	C1S–H1S...C2	2.56	166.8							
II H–GA	N1–H1A...O1S	1.92	165.1	x, y, z	4.797	−9.3	−2.2	−25.8	24.2	−18.9
I H–GB	N2–H2A...O2S	1.94	154.4	$-1 + x, -1 + y, -1 + z$	7.871	−30.8	−8.1	−6.5	28.7	−26.5
				$1 + x, 1 + y, 1 + z$						

^aThe CrystalExplorer total lattice energy is obtained by multiplying the single contributions by the following scale factors: $k_{\text{ele}} = 1.057$, $k_{\text{pol}} = 0.740$, $k_{\text{disp}} = 0.871$, and $k_{\text{rep}} = 0.618$.⁴⁸

visible spectrum and physiologically perceived colors in the human eye. Here, we defined CIE chromaticity coordinates as the unique color reference derived from the UV–vis spectrum of **1b**. In the CIE diagram (see the insert in Figure 8), the black point indicates the coordinates (0.270, 0.234) in the lilac-violet region. The CIE coordinates cannot be evaluated for the **1a(RT)** colorless crystal forms.

3.5. TD-DFT Calculation of Formation Energies

This study examines the energetic characteristics of the three BDF-ethyl crystals obtained under various conditions, beginning with their crystallographic information. Specifically, the **1a(LT)** crystal form, stable at 100 K, exhibits the $P\bar{1}$ space group with 40 atoms in the asymmetric unit (80 atoms in the crystallographic unit cell); the **1a(RT)** crystal, stable at 298 K with the $P2_1/c$ space group contains 40 atoms in the asymmetric unit, 80 atoms in the conventional unit cell, and 320 atoms in the crystallographic unit cell; the **1b** violet crystal incorporating two DMF molecules also exhibits the $P\bar{1}$ space group, with 64 atoms in the asymmetric unit, where 40 atoms correspond to the BDF moiety and 24 atoms to two DMF molecules (128 atoms in the crystallographic unit cell).

The stability of the three different crystals was examined based on their formation energies (FEs). The energy was evaluated as the difference: $E_{\text{crystal}} - nE_{\text{singlemolecules}}$, where n is the number of molecules in the unit cell. Therefore, the FE indicates the energetic advantage of the molecules to organize themselves in a specific crystallite structure. FE values were calculated using two methods:

- **MOLSPLIT method.** This method expands the crystal lattice by a factor of 100, scaling the fractional coordinates to eliminate intermolecular interactions while preserving the internal geometry of the molecules. A standard wave function calculation was performed on this expanded lattice, allowing for the evaluation of the energy of isolated molecules within the crystal structure.
- **Optimized Isolated Molecule (OIM) method,** where the energy of each molecule was optimized in a vacuum to determine its intrinsic energy without any interactions.

The two approaches are different but contribute synergistically to explaining the trend. In the MOLSPLIT calculation, the geometry of BDF-ethyl is constrained by the position of its crystalline structure. The distances between molecules are increased to eliminate intermolecular interactions, but the

internal geometry of each molecule is fixed to maintain the optimized form within the crystal. This constraint prevents complete geometric relaxation that the molecule would experience if it were isolated, as in the case of vacuum optimization. Geometric relaxation in an isolated environment, such as in the vacuum (OIM), allows the molecule to adapt to energetic minimization by reorganizing its bonds and angles and lowering the total energy. On the other hand, the presence of interatomic forces and geometric constraints imposed by the lattice symmetry prevent the molecule from fully relaxing, forcing it to maintain a geometry that may not be the most energetically favorable.

The formation energies, normalized per molecule in the unit cell, are summarized in Table 5.

The results indicate that all crystals exhibit favorable formation energies. The energetic difference between the MOLSPLIT calculations and the molecule optimized in the vacuum ($\Delta E_{\text{MOLSPLIT-OIM}}$, third column) highlights the effect of the geometric relaxation of BDF-Ethyl in a crystalline environment compared with its isolated form. The energy differences between $E(\text{MOLSPLIT})$ and $E(\text{OIM})$ in the vacuum indicate how the crystal structure influences the geometry of the molecule. The formation energy difference ΔE (approximately 27.2–31.4 kJ/mol) observed between the two methods suggests that the crystal represents a relatively stable structure, but the geometric relaxation of the molecule in the vacuum allows for a more energetically favorable configuration. The difference reflects the effect of the crystal's interactions and its geometric limitations in determining the overall stability of the molecule in a confined environment. Furthermore, this energy value is a measure of the energy required to “release” the molecule from the constraints imposed by its position within the crystal and represents an indication of the “rigidity” the crystal imposes on the molecular geometry. The influence of these differences could also be relevant for the thermodynamic behavior and stability of the crystals, particularly when considering temperature or solvent effects that might favor the geometric relaxation of the molecule.

The similar FE values of structures **1a(RT)** and **1a(LT)** support the ability to undergo a reversible transformation. On the other hand, the violet crystal **1b** shows the most significant stabilization, in both the MOLSPLIT and the OIM calculations. In this case, a crucial role of DMF molecules in

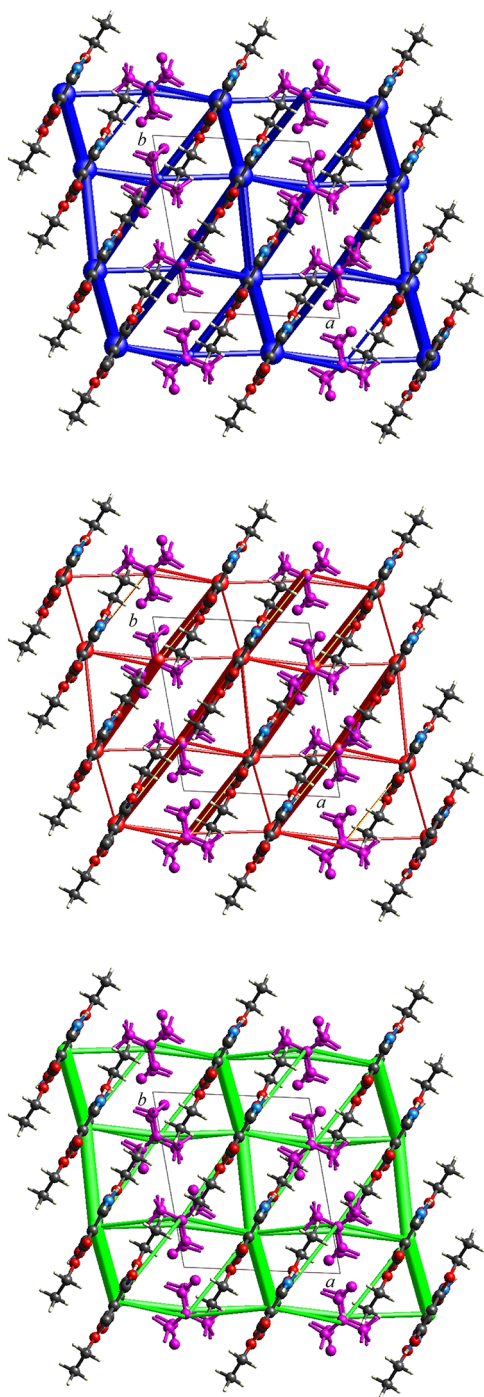


Figure 7. Energy frameworks of form **1b** view along the *c* axis. DMF molecules are depicted in magenta. Electrostatic contributions are represented as red cylinders; dispersive contributions are represented as green cylinders, and total interaction energies are represented as blue cylinders. The tube size is set to 100.

the crystal structure can be speculated to enhance stability. That is, the interactions between the BDF-ethyl units and the DMF molecules plausibly contribute to a lower formation energy, reinforcing the crystal's cohesion.

4. CONCLUSIONS

In our previous research papers, we highlighted the capabilities of diaminobenzo[1,2-*b*:4,5-*b'*]difuran to produce interesting functional responses in both the solution and the solid state.

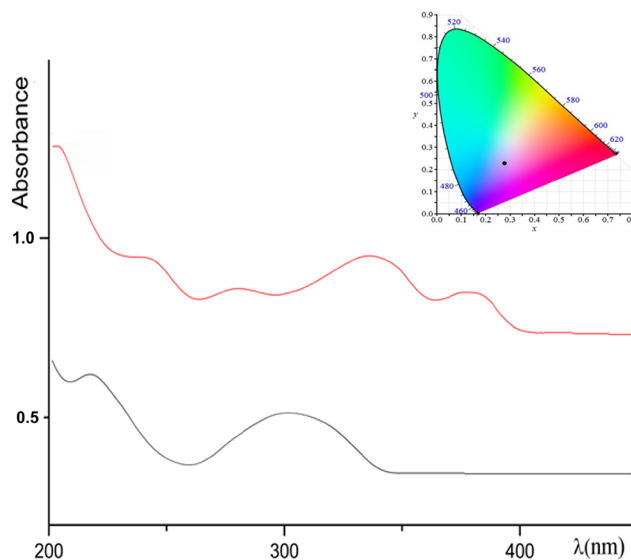


Figure 8. UV-vis absorption of crystalline powders of **1a(RT)** (black line) and **1b** (red line, moved +1). On the right: related CIE coordinates for **1b**.

Table 5. Formation Energies Calculated for the Three Different Crystals and Their Difference $|\Delta E_{\text{MOLSPPLIT-OIM}}|$ in Absolute Value

BDF-Ethyl	MOLSPPLIT (kJ/mol)	OIM (kJ/mol)	$ \Delta E_{\text{MOLSPPLIT-OIM}} $ (kJ/mol)
1a(LT)	−427.43	−400.26	27.17
1a(RT)	−425.59	−395.19	30.40
1b	−647.07	−617.13	29.94

Here, we detected a rare reversible polymorphic transformation involving 2,6-diaminobenzo[1,2-*b*:4,5-*b'*]difuran-3,7-dicarboxylic acid diethyl ester. The known colorless crystalline structure of **1a(RT)** changes below 126 K into another colorless form named **1a(LT)** fully characterized at 100 K. The transformation of **1a(RT)** to **1a(LT)** occurs by loss of a glide symmetry plane that leads to the splitting of the single crystal of **1a(RT)** into a twinned triclinic crystal, which reversibly transforms back to a monoclinic single crystal upon increasing the temperature. The interplay between van der Waals interactions and hydrogen bonding ensures the reversibility of the transformation, and the crystal packing relies both on the presence of relatively strong dispersive intermolecular interactions and medium-to-weak hydrogen bonds.

Moreover, the same BDF-ethyl compound crystallizes from DMF solutions as violet DMF solvate crystals, named **1b**. Driven by this singular and complex behavior, we have deepened the structural aspects, adding the examination of the chromatic properties of the room-temperature polymorph **1a(RT)** and the solvatomorph **1b**.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.cgd.5c01056>.

Energy frameworks for **1a(RT)** and **1a(LT)** (MP4)
ORTEP drawings for crystal structures **1a(RT)**, **1a(LT)**,
and **1b**; molecular overlay for **1a(RT)** and **1a(LT)**; DSC

results; intermolecular interactions in crystal forms **1a(RT)** and **1a(LT)**; intermolecular distances, angles, and interaction energies in **1a(RT)**, **1a(LT)**, and **1b**; and assembly motifs in **1a(RT)**, **1a(LT)**, and **1b** (PDF)

Accession Codes

Deposition Numbers 2392622–2392623 and 2464337 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via the joint Cambridge Crystallographic Data Centre (CCDC) and Fachinformationszentrum Karlsruhe [Access Structures service](#).

AUTHOR INFORMATION

Corresponding Authors

Rosita Diana – Department of Agriculture, University of Napoli Federico II, Portici, NA 80055, Italy; [orcid.org/0000-0001-5672-2297](#); Email: rosita.diana@unina.it

Consiglia Tedesco – Department of Chemistry and Biology “A. Zambelli”, University of Salerno, Fisciano 84084, Italy; [orcid.org/0000-0001-6849-798X](#); Email: ctedesco@unisa.it

Authors

Giovanni Pierri – Department of Chemistry and Biology “A. Zambelli”, University of Salerno, Fisciano 84084, Italy; [orcid.org/0000-0001-5433-6077](#)

Ludovica Milzi – Department of Agriculture, University of Napoli Federico II, Portici, NA 80055, Italy

Antonio Carella – Department of Chemical Sciences, University of Napoli Federico II, Napoli 80126, Italy

Marianna Pannico – Institute on Polymers Composites and Biomaterials, National Research Council, Pozzuoli 80078, Italy

Francesco Silvio Gentile – Department of DICMaPI, University of Napoli Federico II, Napoli 80125, Italy; [orcid.org/0000-0002-2853-5643](#)

Barbara Panunzi – Department of Agriculture, University of Napoli Federico II, Portici, NA 80055, Italy

Complete contact information is available at: <https://pubs.acs.org/10.1021/acs.cgd.5c01056>

Notes

The authors declare no competing financial interest.

REFERENCES

- (1) Cruz-Cabeza, A. J.; Reutzel-Edens, S. M.; Bernstein, J. Facts and fictions about polymorphism. *Chem. Soc. Rev.* **2015**, *44* (23), 8619–8635.
- (2) Takanabe, A.; Katsufuji, T.; Johmoto, K.; Uekusa, H.; Shiro, M.; Koshima, H.; Asahi, T. Reversible Single-Crystal-to-Single-Crystal Phase Transition of Chiral Salicylidenebenzylthylamine. *Crystals* **2017**, *7* (1), No. 7, DOI: [10.3390/cryst7010007](#).
- (3) Brog, J.-P.; Chanez, C.-L.; Crochet, A.; Fromm, K. M. Polymorphism, what it is and how to identify it: a systematic review. *RSC Adv.* **2013**, *3* (38), 16905–16931.
- (4) Takahashi, H.; Ito, Y. Low-temperature-induced reversible single-crystal-to-single-crystal phase transition of 3, 4-dichloro-2', 4', 6'-triethylbenzophenone. *CrystEngComm* **2010**, *12* (5), 1628–1634.
- (5) Liu, G.; Liu, J.; Liu, Y.; Tao, X. Oriented Single-Crystal-to-Single-Crystal Phase Transition with Dramatic Changes in the Dimensions of Crystals. *J. Am. Chem. Soc.* **2014**, *136* (2), 590–593.
- (6) Nogueira, B. A.; Castiglioni, C.; Fausto, R. Color polymorphism in organic crystals. *Commun. Chem.* **2020**, *3* (1), No. 34.
- (7) Nogueira, B. A.; Lopes, S. M. M.; Milani, A.; André, V.; Paixão, J. A.; Eusébio, M. E. S.; Pinho e Melo, T. M. V. D.; Duarte, M. T.; Castiglioni, C.; Fausto, R. Color Polymorphs of ROY-ol. *Cryst. Growth Des.* **2022**, *22* (9), 5375–5389.
- (8) Jha, K. K.; Kumar, A.; Munshi, P. Solvatochromism and Reversible Solvent Exchange Phenomena in Solvatomorphic Organic Chromophore Crystals. *Cryst. Growth Des.* **2023**, *23* (4), 2922–2931.
- (9) Cruz-Cabeza, A. J.; Feeder, N.; Davey, R. J. Open questions in organic crystal polymorphism. *Commun. Chem.* **2020**, *3* (1), No. 142.
- (10) Belviso, B. D. Crystal Polymorphism. In *Encyclopedia of Membranes*; Drioli, E.; Giorno, L., Eds.; Springer Berlin Heidelberg: Berlin, Heidelberg, 2015; pp 1–3.
- (11) Griesser, U. J. Importance of Solvates. In *Polymorphism*; Wiley, 2006; pp 211–233.
- (12) Boothroyd, S.; Kerridge, A.; Broo, A.; Buttar, D.; Anwar, J. Why Do Some Molecules Form Hydrates or Solvates? *Cryst. Growth Des.* **2018**, *18* (3), 1903–1908.
- (13) Cruz-Cabeza, A. J.; Day, G. M.; Motherwell, W. D. S.; Jones, W. Prediction and observation of isostructurality induced by solvent incorporation in multicomponent crystals. *J. Am. Chem. Soc.* **2006**, *128* (45), 14466–14467.
- (14) Cruz-Cabeza, A. J.; Wright, S. E.; Bacchi, A. On the entropy cost of making solvates. *Chem. Commun.* **2020**, *56* (38), 5127–5130.
- (15) Huo, L.; Huang, Y.; Fan, B.; Guo, X.; Jing, Y.; Zhang, M.; Li, Y.; Hou, J. Synthesis of a 4,8-dialkoxy-benzo[1,2-b:4,5-b']difuran unit and its application in photovoltaic polymer. *Chem. Commun.* **2012**, *48* (27), 3318–3320.
- (16) King, T. J.; Newall, C. E. 175. The chemistry of colour reactions. The craven reaction. *J. Chem. Soc.* **1965**, 974–977.
- (17) Obushak, M. D.; Martyak, R. L.; Matychuk, V. S. Synthesis of heterocycles on the basis of arylation products of unsaturated compounds. Part 9. Dialkyl 2,6-diamino-4-arylfuro[2',3':4,5]benzo-[b]furan-3,7-dicarboxylates from 2-aryl-1,4-benzoquinones and cyanoacetic esters. *Pol. J. Chem.* **2002**, *76* (10), 1419–1424.
- (18) Caruso, U.; Panunzi, B.; Roviello, G. N.; Roviello, G.; Tingoli, M.; Tuzi, A. Synthesis, structure and reactivity of amino-benzodifurane derivatives. *C. R. Chim.* **2009**, *12* (5), 622–634.
- (19) Moussallem, C.; Gohier, F.; Frère, P. Extended benzodifuran–thiophene systems connected with azomethine junctions: synthesis and electronic properties. *Tetrahedron Lett.* **2015**, *56* (36), 5116–5119.
- (20) Barcelo, B.; Gomila, I. Pharmacology and Literature Review Based on Related Death and Non-Fatal Case Reports of the Benzofurans and Benzodifurans Designer Drugs. *Curr. Pharm. Des.* **2017**, *23* (36), 5523–5529.
- (21) Alper-Hayta, S.; Arisoy, M.; Temiz-Arpaci, Ö.; Yildiz, I.; Aki, E.; Özkan, S.; Kaynak, F. Synthesis, antimicrobial activity, pharmacophore analysis of some new 2-(substitutedphenyl)benzyl)-5-[(2-benzofuryl)carboxamido]benzoxazoles. *Eur. J. Med. Chem.* **2008**, *43* (11), 2568–2578.
- (22) Soni, J. N.; Soman, S. S. Synthesis and antimicrobial evaluation of amide derivatives of benzodifuran-2-carboxylic acid. *Eur. J. Med. Chem.* **2014**, *75*, 77–81.
- (23) Ashok, D.; Sudershan, K.; Khalilullah, M. Solvent-free microwave-assisted synthesis of E-(1)-(6-benzoyl-3,5-dimethylfuro-[3',2':4,5]benzo[b]furan-2-yl)-3-(aryl)-2-propen-1-ones and their antibacterial activity. *Green Chem. Lett. Rev.* **2012**, *5* (2), 121–125.
- (24) Thévenin, M.; Thoret, S.; Grellier, P.; Dubois, J. Synthesis of polysubstituted benzofuran derivatives as novel inhibitors of parasitic growth. *Bioorg. Med. Chem.* **2013**, *21* (17), 4885–4892.
- (25) Feng, Z.; Mohapatra, S.; Klimko, P. G.; Hellberg, M. R.; May, J. A.; Kelly, C.; Williams, G.; McLaughlin, M. A.; Sharif, N. A. Novel benzodifuran analogs as potent 5-HT_{2A} receptor agonists with ocular hypotensive activity. *Bioorg. Med. Chem. Lett.* **2007**, *17* (11), 2998–3002.
- (26) Wang, Y.-N.; Liu, M.-F.; Hou, W.-Z.; Xu, R.-M.; Gao, J.; Lu, A.-Q.; Xie, M.-P.; Li, L.; Zhang, J.-J.; Peng, Y.; et al. Bioactive benzofuran derivatives from cortex mori radices, and their neuroprotective and

- analgesic activities mediated by mGluR1. *Molecules* **2017**, *22* (2), No. 236.
- (27) Diana, R.; Schibeci, M.; Arciello, A.; Sessa, L.; Concilio, S.; Piotto, S.; Caruso, U.; Panunzi, B. Two series of benzofuran and benzodifuran chelating chromophores with DR/NIR emission and anticancer activity. *Dyes Pigm.* **2024**, *224*, No. 112034.
- (28) Vicidomini, C.; Cioffi, F.; Broersen, K.; Roviello, V.; Riccardi, C.; Montesarchio, D.; Capasso, D.; Gaetano, S. D.; Musumeci, D.; Roviello, G. N. Benzodifurans for Biomedical Applications: BZ4, a Selective anti-proliferative and anti-amyloid Lead Compound. *Future Med. Chem.* **2019**, *11* (4), 285–302.
- (29) Diana, R.; Schibeci, M.; Arciello, A.; Sessa, L.; Concilio, S.; Piotto, S.; Caruso, U.; Panunzi, B. Two series of benzofuran and benzodifuran chelating chromophores with DR/NIR emission and anticancer activity. *Dyes Pigm.* **2024**, *224*, No. 112034, DOI: 10.1016/j.dyepig.2024.112034.
- (30) Diana, R.; Caruso, U.; Gentile, F. S.; Di Costanzo, L.; Turrà, D.; Vitale, S.; Panunzi, B. Benzodifuran-based fluorescent brighteners: A novel platform for plant cell wall imaging. *Dyes Pigm.* **2022**, *199*, No. 110071, DOI: 10.1016/j.dyepig.2021.110071.
- (31) Vitoria, P.; Wéry, A. S. J.; San Felices, L.; Bravo-García, L.; Ruiz-Bilbao, E.; Laza, J. M.; Vilas-Vilela, J. L.; Gutiérrez-Zorrilla, J. M. Reversible First-Order Single Crystal to Single Crystal Thermal Phase Transition in [(CH₃)₃CNH₃]₄[V₄O₁₂]. *Materials* **2022**, *15* (16), No. 5663, DOI: 10.3390/ma15165663.
- (32) King, T. J.; Newall, C. E. 175. The chemistry of colour reactions. The Craven reaction. *J. Chem. Soc.* **1965**, No. 0, 974–977.
- (33) Menges, F. *Spectragryph - Optical Spectroscopy Software*.
- (34) Pascale, F.; D'Arco, P.; Silvio Gentile, F.; Dovesi, R. Strategies for the optimization of the structure of crystalline compounds. *J. Comput. Chem.* **2022**, *43* (3), 184–196.
- (35) Centore, R.; Borbone, F.; Carella, A.; Causà, M.; Fusco, S.; Gentile, F. S.; Parisi, E. Hierarchy of Intermolecular Interactions and Selective Topochemical Reactivity in Different Polymorphs of Fused-Ring Heteroaromatics. *Cryst. Growth Des.* **2020**, *20* (2), 1229–1236.
- (36) Mirzaei, A.; Bina Jorshari, Y.; Jananshir, S.; Noori, M.; Mahdavi, M. Colorimetric pH-sensitive hydrogel film based on kappa-carrageenan containing quercetin or eucalyptus leaf extract for freshness monitoring of chicken meat. *Food Chemistry: X* **2024**, *22*, No. 101307.
- (37) Diana, R.; Caruso, U.; Di Costanzo, L.; Bakayoko, G.; Panunzi, B. A novel DR/NIR T-shaped aiegen: Synthesis and x-ray crystal structure study. *Crystals* **2020**, *10* (4), No. 269, DOI: 10.3390/cryst10040269.
- (38) Diana, R.; Caruso, U.; Di Costanzo, L.; Gentile, F. S.; Panunzi, B. Colorimetric recognition of multiple first-row transition metals: A single water-soluble chemosensor in acidic and basic conditions. *Dyes Pigm.* **2021**, *184*, No. 108832, DOI: 10.1016/j.dyepig.2020.108832.
- (39) Sheldrick, G. M. A short history of SHELX. *Found. Crystallogr.* **2008**, *64* (1), 112–122.
- (40) Sheldrick, G. M. SHELXT—Integrated space-group and crystal-structure determination. *Found. Crystallogr.* **2015**, *71* (1), 3–8.
- (41) Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H. OLEX2: a complete structure solution, refinement and analysis program. *J. Appl. Crystallogr.* **2009**, *42* (2), 339–341.
- (42) Gavezzotti, A.; Presti, L. L.; Rizzato, S. Molecular dynamics simulation of organic materials: structure, potentials and the MiCMoS computer platform. *CrystEngComm* **2022**, *24* (5), 922–930.
- (43) Gavezzotti, A. Calculation of Intermolecular Interaction Energies by Direct Numerical Integration over Electron Densities. 2. An Improved Polarization Model and the Evaluation of Dispersion and Repulsion Energies. *J. Phys. Chem. B* **2003**, *107* (10), 2344–2353.
- (44) Gavezzotti, A. Calculation of lattice energies of organic crystals: the PIXEL integration method in comparison with more traditional methods. *Z. Kristallogr. - Cryst. Mater.* **2005**, *220* (5–6), 499–510.
- (45) Gavezzotti, A. Efficient computer modeling of organic materials. The atom–atom, Coulomb–London–Pauli (AA-CLP) model for intermolecular electrostatic-polarization, dispersion and repulsion energies. *New J. Chem.* **2011**, *35* (7), 1360–1368.
- (46) Spackman, P. R.; Turner, M. J.; McKinnon, J. J.; Wolff, S. K.; Grimwood, D. J.; Jayatilaka, D.; Spackman, M. A. CrystalExplorer: a program for Hirshfeld surface analysis, visualization and quantitative analysis of molecular crystals. *J. Appl. Crystallogr.* **2021**, *54* (Pt 3), 1006–1011.
- (47) Turner, M. J.; Thomas, S. P.; Shi, M. W.; Jayatilaka, D.; Spackman, M. A. Energy frameworks: insights into interaction anisotropy and the mechanical properties of molecular crystals. *Chem. Commun.* **2015**, *51* (18), 3735–3738.
- (48) Mackenzie, C. F.; Spackman, P. R.; Jayatilaka, D.; Spackman, M. A. CrystalExplorer model energies and energy frameworks: extension to metal coordination compounds, organic salts, solvates and open-shell systems. *IUCrJ.* **2017**, *4* (Pt5), 575–587.
- (49) Prince, E. *International Tables for Crystallography, Vol. C: Mathematical, Physical and Chemical Tables*; Springer Science & Business Media, 2004.
- (50) *International Tables for Crystallography*; Allen, F. H.; W, D. G.; Brammer, L.; Orpen, A. G.; Taylor, R.; Prince, E., Eds.; Springer Netherlands: Dordrecht, 2004; pp 790–811.
- (51) Caruso, U.; Panunzi, B.; Roviello, G. N.; Roviello, G.; Tingoli, M.; Tuzi, A. Synthesis, structure and reactivity of amino-benzodifurane derivatives. *C. R. Chim.* **2009**, *12* (5), 622–634.
- (52) Macrae, C. F.; Sovago, I.; Cottrell, S. J.; Galek, P. T. A.; McCabe, P.; Pidcock, E.; Platings, M.; Shields, G. P.; Stevens, J. S.; Towler, M.; Wood, P. A. Mercury 4.0: from visualization to analysis, design and prediction. *J. Appl. Crystallogr.* **2020**, *53* (Pt 1), 226–235.
- (53) Li, L.; Commins, P.; Al-Handawi, M. B.; Karothu, D. P.; Halabi, J. M.; Schramm, S.; Weston, J.; Rezgui, R.; Naumov, P. Martensitic organic crystals as soft actuators. *Chem. Sci.* **2019**, *10* (31), 7327–7332.
- (54) Dudka, A.; Nesterenko, S.; Tursina, A. Multi-temperature X-ray diffraction study of a reversible structural phase transition in the high-temperature polymorph of Ce₂Rh₂Ga compound. *J. Alloys Compd.* **2022**, *890*, No. 161759.
- (55) Vušak, D.; Naumov, P.; Jelcic, Ž.; Matković-Čalogović, D.; Prugovečki, B. Thermally Induced Reversible Martensitic Phase Transition and Self-Healing in Nickel Glycinamide Crystals. *Angew. Chem., Int. Ed.* **2025**, *64* (12), No. e202421769, DOI: 10.1002/anie.202421769.
- (56) Kitaigorodsky, A. *Molecular Crystals and Molecules*; Elsevier, 2012; Vol. 29.
- (57) Spek, A. L. checkCIF validation ALERTS: what they mean and how to respond. *Acta Crystallogr., Sect. E: Crystalllogr. Commun.* **2020**, *76* (Pt 1), 1–11.
- (58) Sliney, D. H. What is light? The visible spectrum and beyond. *Eye* **2016**, *30* (2), 222–229.
- (59) Cecie, S.; Christine, E.; Lisa, S. *Biology: Concepts and Applications* Cole: Thomson Brooks, 2005; pp 160–161.
- (60) Diana, R.; Caruso, U.; Piotto, S.; Concilio, S.; Shikler, R.; Panunzi, B. Spectroscopic Behaviour of Two Novel Azobenzene Fluorescent Dyes and Their Polymeric Blends. *Molecules* **2020**, *25*, No. 1368, DOI: 10.3390/molecules25061368.
- (61) Panunzi, B.; Diana, R.; Caruso, U. A highly efficient white luminescent zinc (II) based metallopolymer by RGB approach. *Polymers* **2019**, *11* (10), No. 1712, DOI: 10.3390/polym11101712.