Electronic Supplementary Material (ESI) for CrystEngComm.

A Late Appearing Polymorph of Nutraceutical Pterostilbene

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Electronic Supplementary Information

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1. Experimental methods

1.1. Synthesis of Pterostilbene (Form IV)

Synthesis of the new anhydrous form IV of Pterostilbene was conducted by liquid assisted grinding and crystallization methodologies. Details of synthesis are as follows:

Bulk powder

Pterostilbene (Form II) (20 mg, 0.0780 mmol) and acetone (one drop) were grinded using a Retsch MM 2000 grinding mill. The sample was placed in 2 mL volume stainless steel jars, along with two stainless tungsten grinding balls of 3 mm diameter. Grinding was performed for 15 minutes, with a mill frequency of 30 Hz at 25 ºC. The sample was collected immediately without prior drying for PXRD analysis. The formation of a new solid form (Form IV) was confirmed by comparison of PXRD patterns of Pterostilbene polymorphs (Forms I, II and III).

Single crystal

Pterostilbene Form IV (50 mg, 0.195 mmol) was dissolved in toluene (0.7 mL) at 90 °C. Then, the solution was kept sealed and allowed to cool down to room temperature. After 57 days, the obtained crystals were analyzed by single crystal X-ray diffraction.

1.2. X-ray crystallographic analysis.

Powder X-ray diffraction pattern of Pterostilbene Form IV was obtained on a PANalytical X'Pert PRO MPD diffractometer in transmission configuration using Cu Kα1+2 radiation (λ = 1.5406 Å) with a focalizing elliptic mirror and a PIXcel detector working at a maximum detector's active length of 3.347°. Configuration of convergent beam with a focalizing mirror and a transmission geometry with flat sample sandwiched between low absorbing films measuring from 1 to 40 ° in 2θ, with a step size of 0.026° and a total measuring time of 30 minutes.

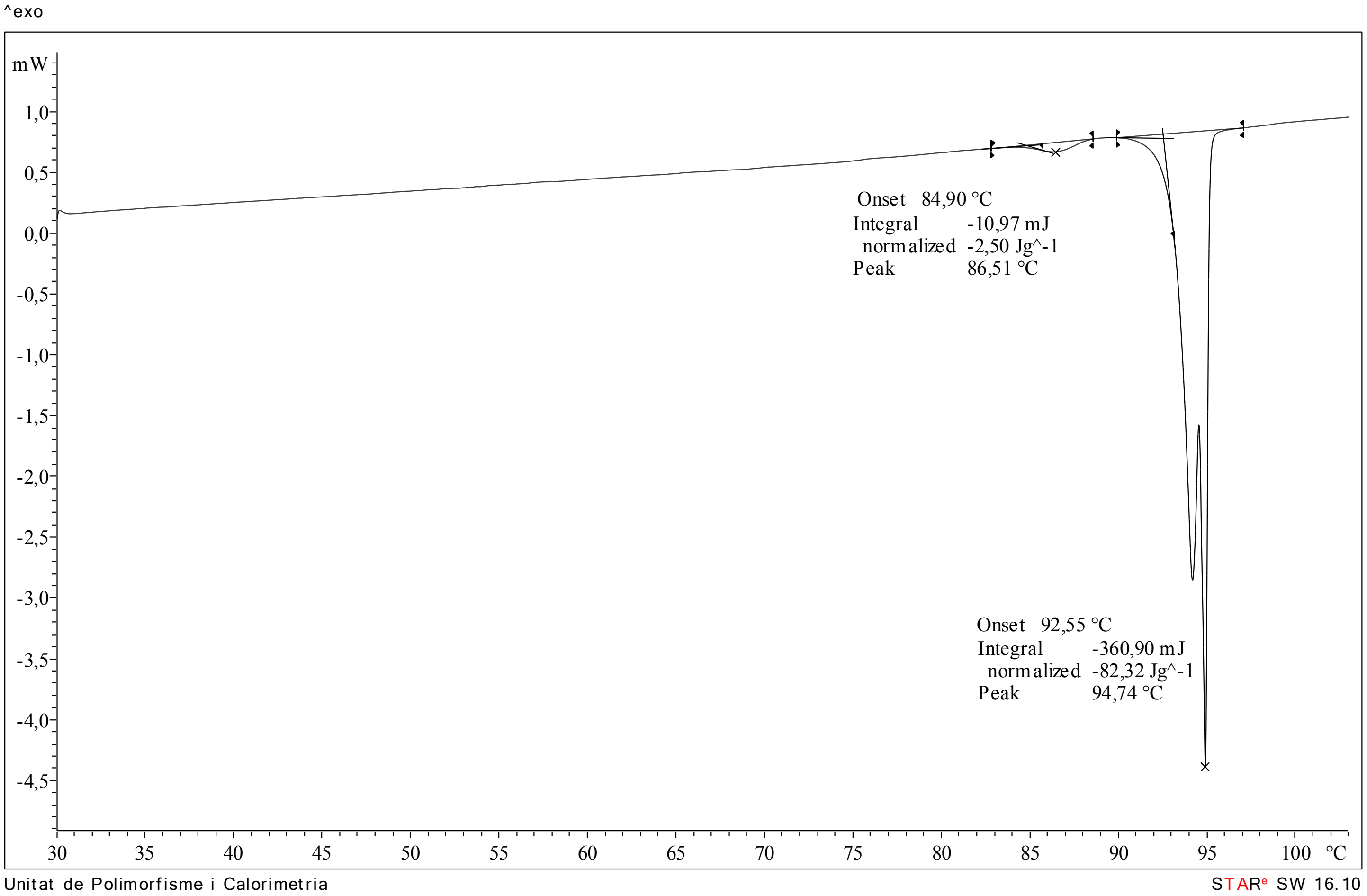
1.3 Single X-ray crystallographic analysis

Single crystal X-ray diffraction (SCXRD) intensity data of the crystal form of Pterostilbene (Form IV) was collected using a D8 Venture system equipped with a multilayer monochromator and a Mo microfocus (λ = 0.71073 Å). Frames were integrated with the Bruker SAINT software package using a SAINT algorithm. Data were corrected for absorption effects using the multi-scan method (SADABS).[1] The structure was solved and refined using the Bruker SHELXTL Software Package, a computer program for automatic solution of crystal structures and refined by full-matrix least-squares method with ShelXle Version 4.8.0, a Qt graphical user interface for SHELXL computer program.[2]

1.4 Differential Scanning Calorimetry (DSC). Differential scanning calorimetry analysis was carried out by means of a Mettler-Toledo DSC-822e calorimeter. Experimental conditions: aluminum crucibles of 40 μL volume, atmosphere of dry nitrogen with 50 mL/min flow rate, heating rate of 10 °C/min. The calorimeter was calibrated with indium of 99.99% purity (m.p.: 156.8 ºC; ΔH: 28.47 J/g).

2.- Characterization of the new Pterostilbene polymorph (Form IV)

Figure S1: DSC of Form IV: DSC analysis shows a first endothermic phenomenon starting at 84.9 ºC with an associated heat of 2.5 J/g and a second endothermic phenomenon (overlapping of two phenomena) starting at 92.5 ºC with an associated heat of 82.3 J/g. First phenomenon suggests an endothermic polymorph transition between Form IV and presumably Form I which melts approximately at 93 ºC (in concordance with DSC reported for Form I from the reference 4 of the article, figure S2)



3. DSC thermograms of the other Pterostilbene polymorphs

Figure S2: DSC of Form I

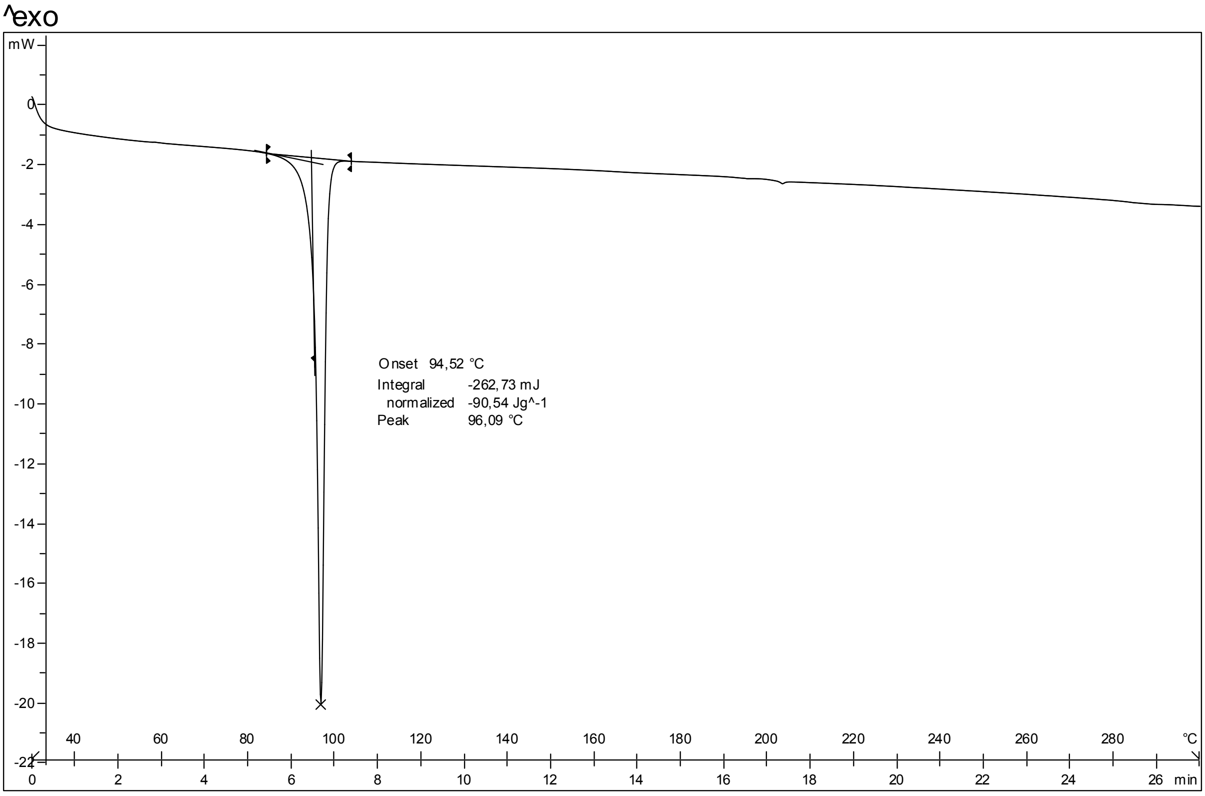


Figure S3: DSC of Form II

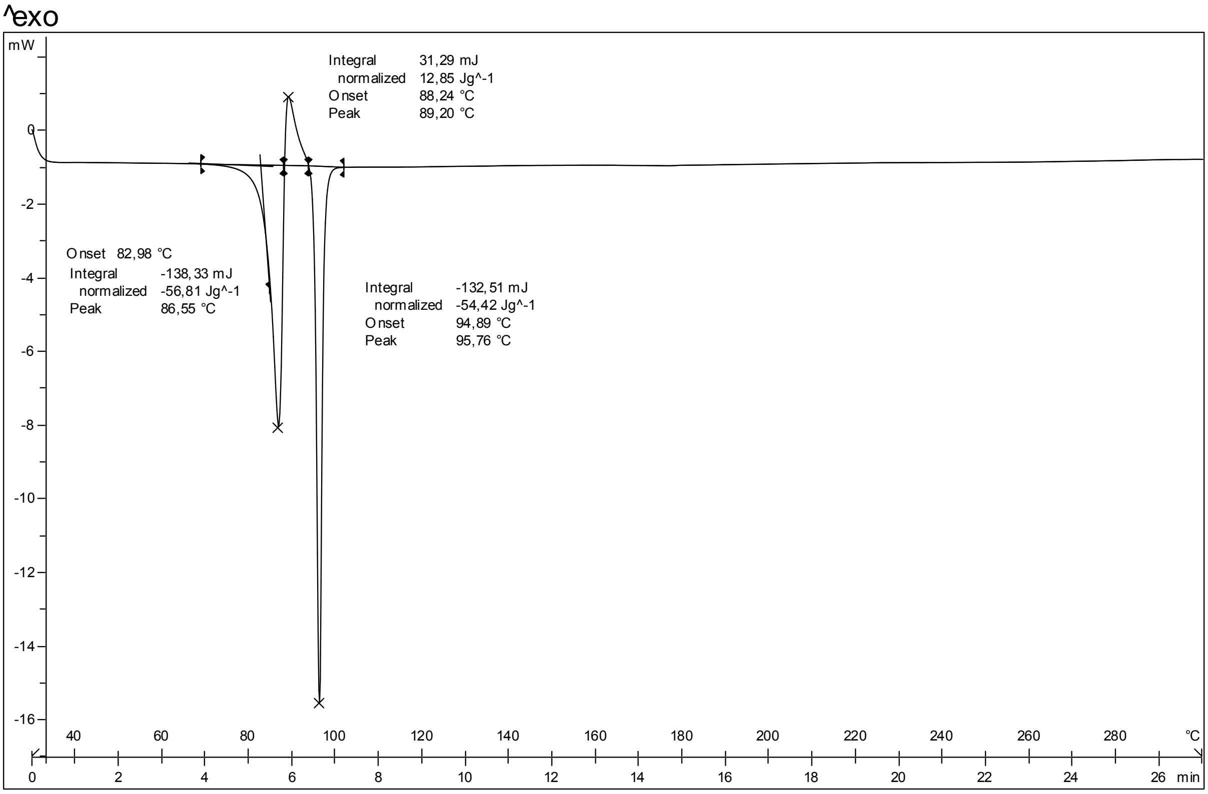
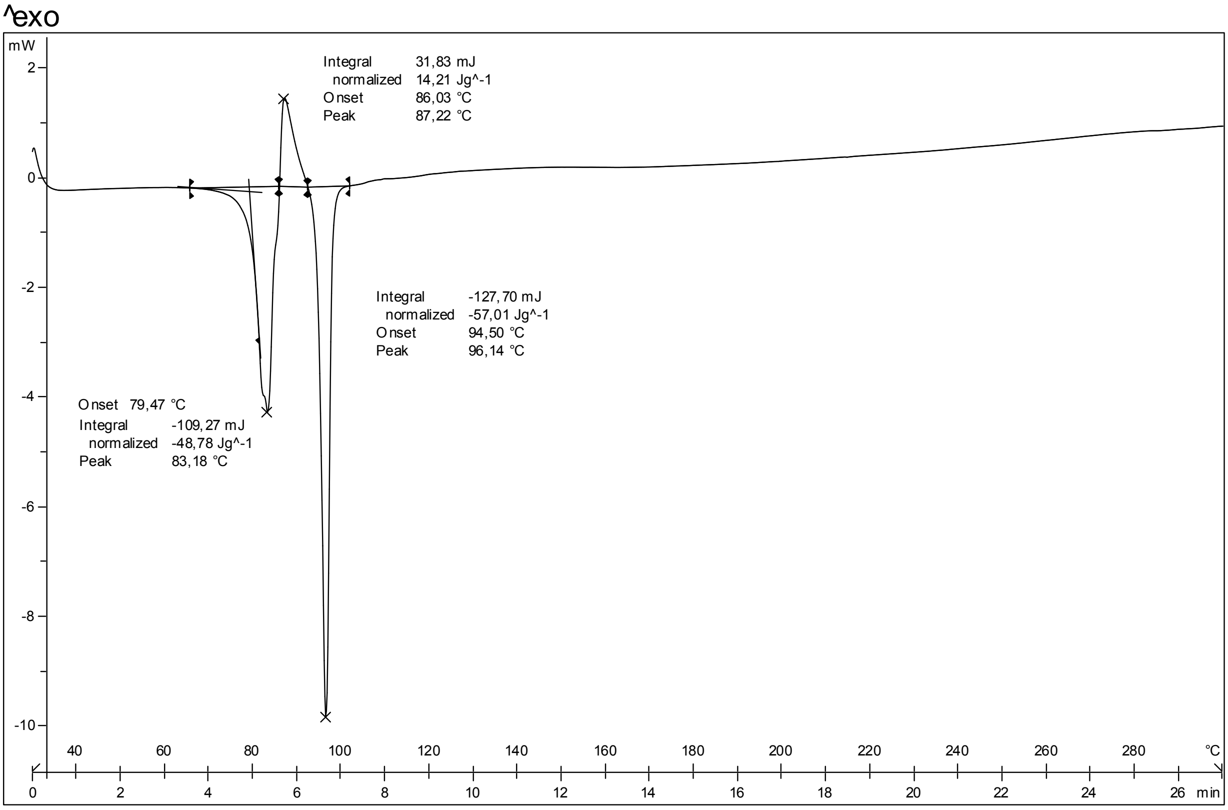


Figure S4: DSC of Form III



4.- Crystal data and structure refinement

4.1 Pterostilbene Form IV (mo_023XB92_0m_a): 1986003

Table S1. Crystal data and structure refinement for mo_023XB92_0m_a.

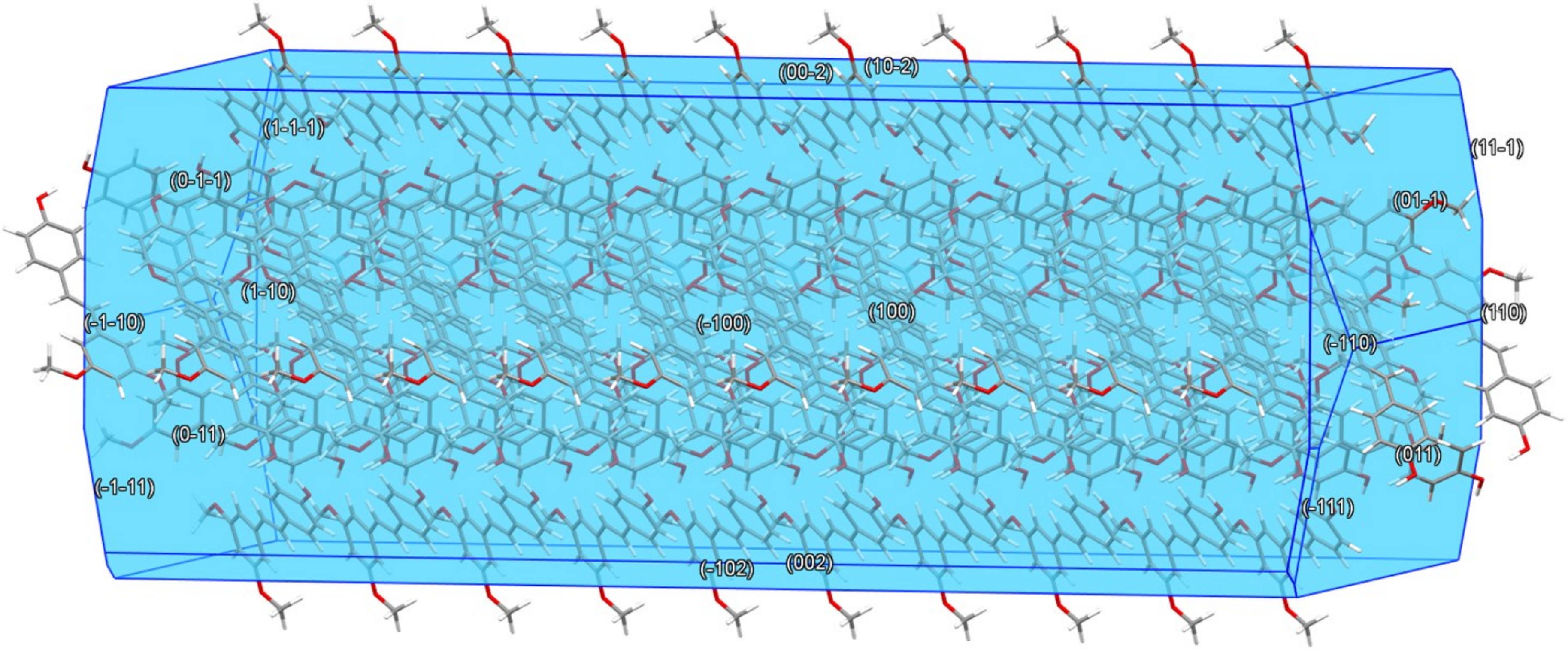
Identification code	mo_023XB92_0m_a	
Empirical formula	C16 H16 O3	
Formula weight	256.29	
Temperature	298(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C 2/c	
Unit cell dimensions	a = 17.282(10) Å	α= 90°.
	b = 7.629(4) Å	β= 98.812(17)°.
	c = 41.71(2) Å	γ = 90°.
Volume	5435(5) Å^3	
Z	16	
Density (calculated)	1.253 Mg/m^3	
Absorption coefficient	0.086 mm^{-1}	
F(000)	2176	
Crystal size	0.305 x 0.192 x 0.106 mm^3	
Theta range for data collection	2.385 to 26.423°.	
Index ranges	-21<=h<=21, -9<=k<=9, -52<=l<=52	
Reflections collected	31746	
Independent reflections	5555 [R(int) = 0.0498]	
Completeness to theta = 25.242°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7454 and 0.6692	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5555 / 1 / 351	
Goodness-of-fit on F^2	1.063	
Final R indices [I>2sigma(I)]	R1 = 0.0489, wR2 = 0.1029	
R indices (all data)	R1 = 0.0746, wR2 = 0.1173	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.282 and -0.163 e.Å^{-3}	

Table S2. Hydrogens bonds for mo_023XB92_0m_a [Å and °]

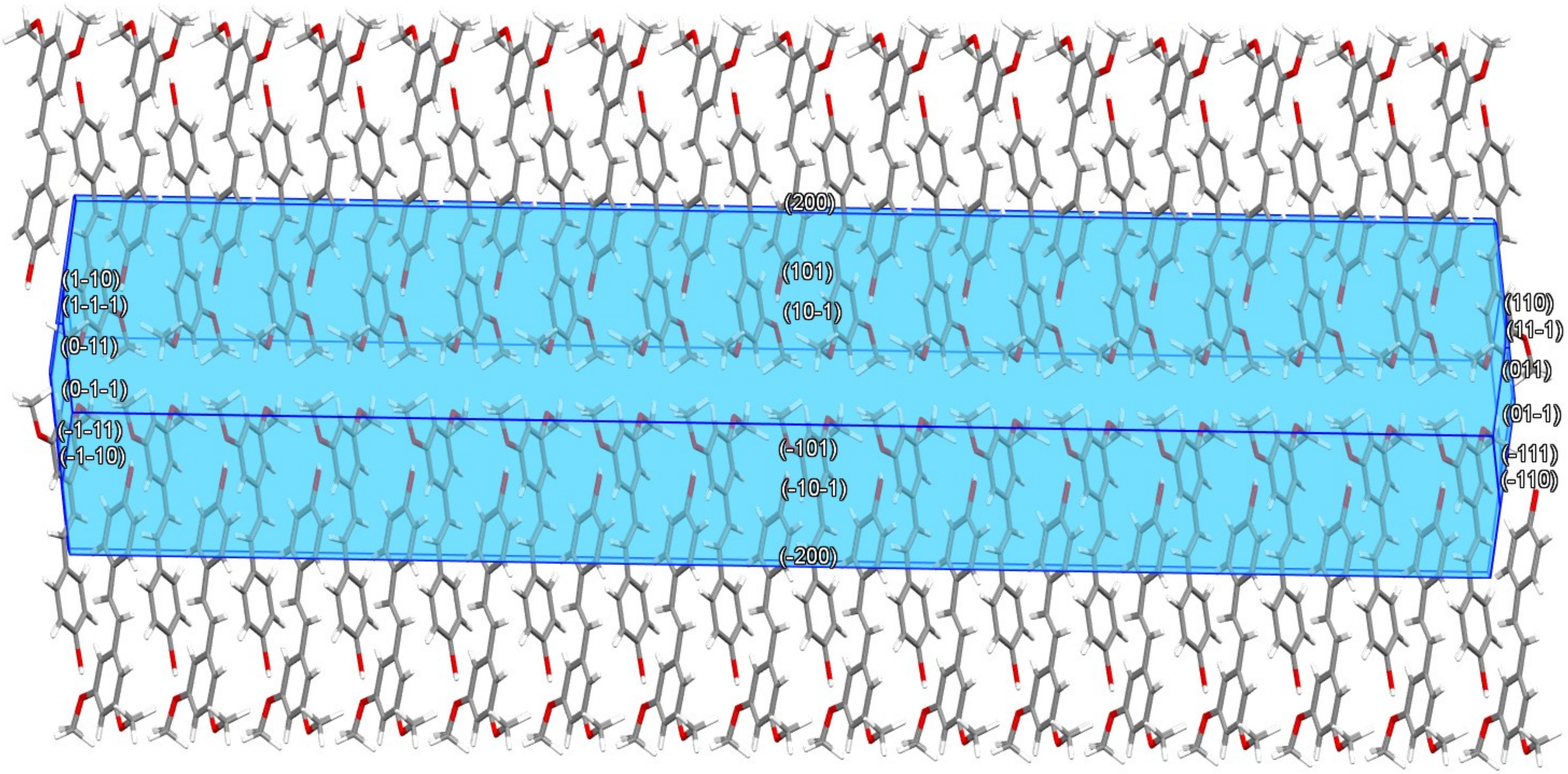
Res Donor --- H....Acceptor	[ARU]	d(D – H)	d(H...A)	d(D...A)	<(D - H...A)
O(1A) --H(1A)...O(2B)	[ ]	0.87(3)	1.93(2)	2.773(3)	163.8(16)
O(1B) --H(1B)...O(2A)	[1/2+x,1/2-y,-1/2+z]	0.90(2)	1.97(3)	2.857(3)	166(2)

5. Morphologies prediction of Pterostilbene crystal forms

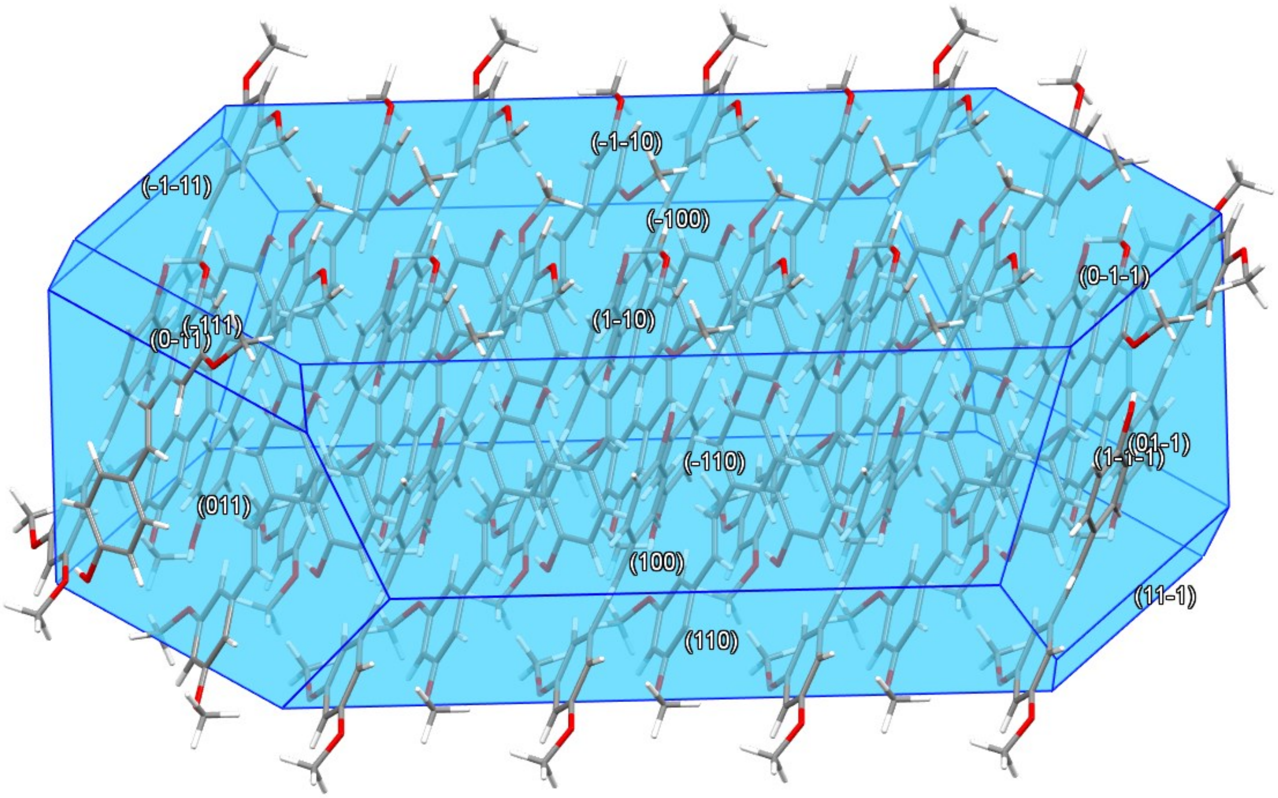
5.1. BFDH morphology prediction of Pterostilbene (Form I)



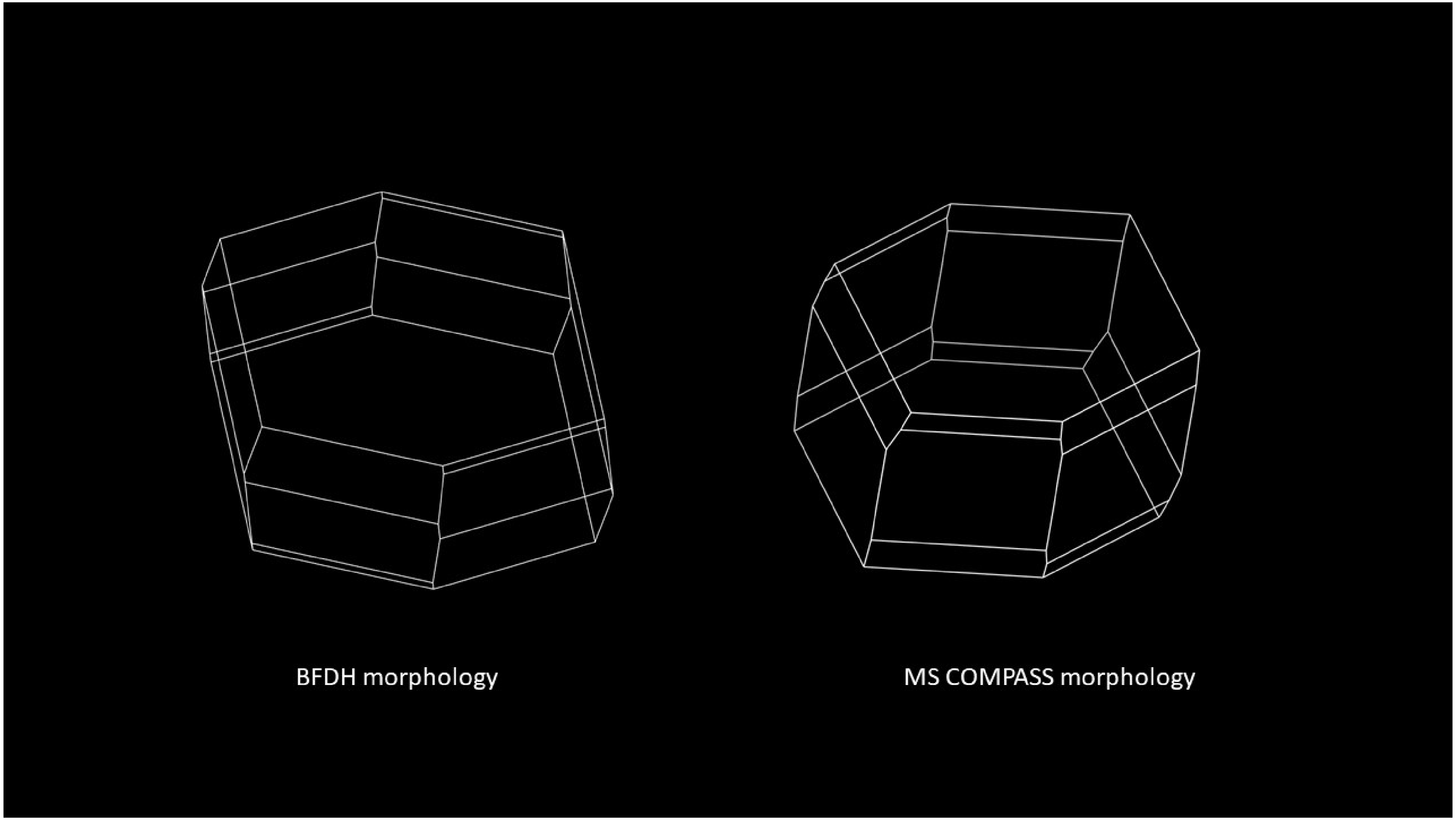
5.2. BFDH morphology prediction of Pterostilbene (Form II)



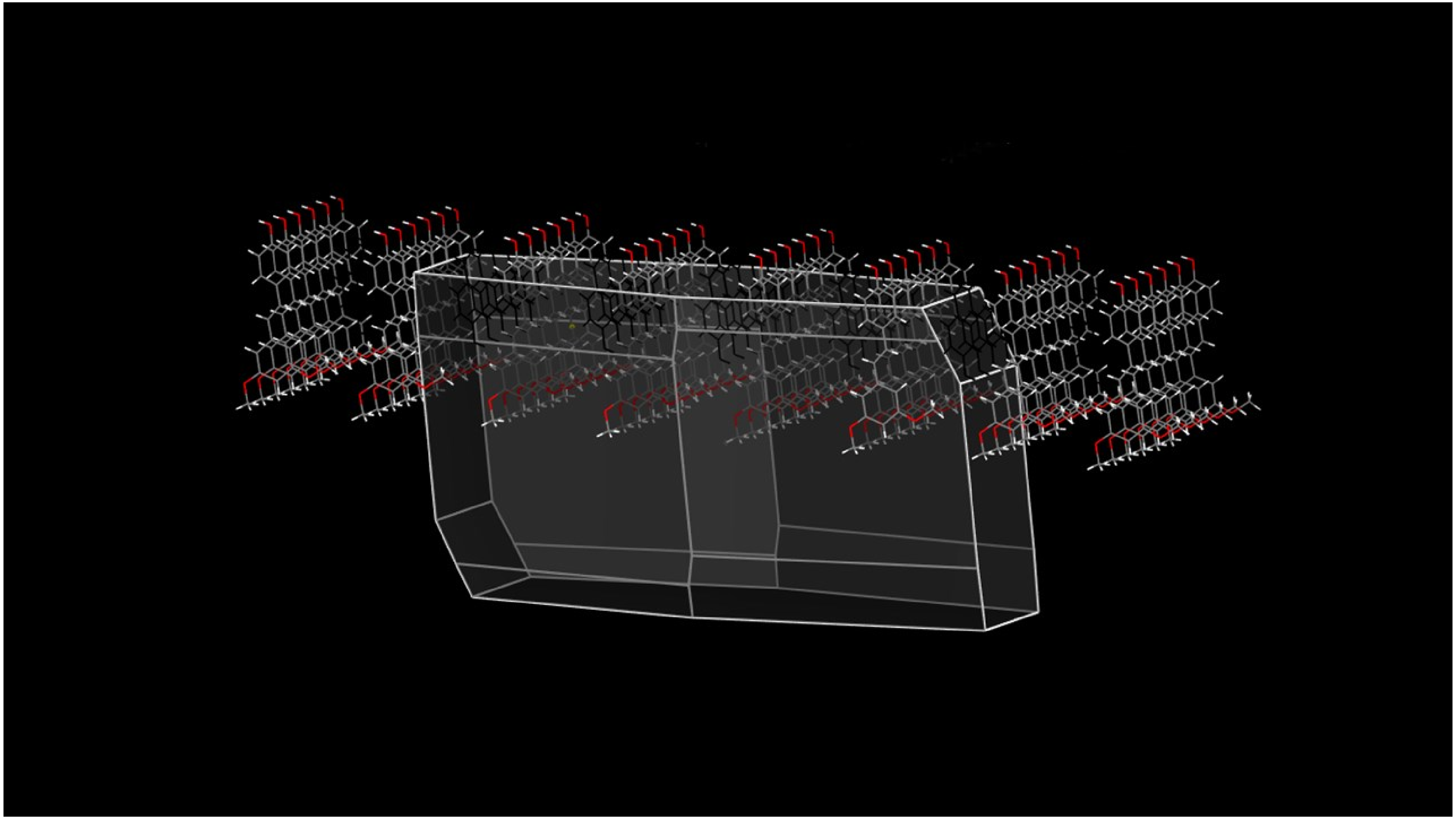
5.3. BFDH morphology prediction of Pterostilbene (Form III)



5.4 Comparative of Pterostilbene (Form IV) morphologies: BFDH morphology (left) and MS COMPASS morphology (right)



5.5 Pterostilbene (Form IV) MS COMPASS morphology prediction: It shows Pterostilbene molecules with the phenol groups pointing out of the surface in a similar way as BFDH morphology prediction



6. Theoretical methods

All DFT calculations were carried out using the Gaussian-16 program[3] at the PBE1PBE[4]-D3[5]/def2-TZVP[6] level of theory and using the crystallographic coordinates, unless otherwise noted. For instance, the isomers A and B of Figure 5 (main text) have been fully optimized. The formation energies of the assemblies have been evaluated by calculating the difference between the total energy of the assembly and the sum of the monomers that constitute the assembly, which have been maintained frozen. The molecular electrostatic potential was computed at the same level of theory and plotted onto the 0.001 a.u. isosurface. and Atoms-in-Molecules (AIM)[7] analysis was carried out at the same level of theory. The calculation of AIM properties was done using the AIMAll program and the same level of theory.[8]

7. References

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