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Research Article

POLYMORPHIC BEHAVIOR OF AN ORGANIC COMPOUND USING A DYNAMIC THERMAL AND X-RAY DIFFRACTION TECHNIQUE 2'-CHLORO-4-METHOXY-3-NITRO BENZIL

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ABSTRACT

Objective: Polymorphic crystals were exhibited in many organic compounds. The frequency changes, relative intensities, band contours, and number of bands were observed in the spectra of different polymorphism which may be due to molecule-molecule interactions in the crystal unit cells. The shape of a molecule at its site in the unit cell is distorted by molecular interactions.

Methods: The identification of a pure crystal form and to quantify a mixture of two forms infrared and Raman spectra of different crystalline forms of the same organic compound can be used. 2'-chloro-4-methoxy-3-nitro benzil (1) was synthesized and its two polymorphic forms were obtained by recrystallization from the solvents acetone/chloroform and ethanol. The polymorphism present in the compound was confirmed by single crystal X-ray crystallography and differential scanning calorimetry.

Results: The polymorph 1.1 crystallizes as triclinic P-1 space group in the solvent acetone – chloroform and the polymorph 1.2 crystallizes as monoclinic P21/c space group in the solvent ethanol.

Discussion: The intermolecular lattice energy and the interplay of molecular conformation in the crystallization and stability of polymorphs are identified by X-ray crystal structures of conformational polymorphs.

Keywords: Conformational polymorphism, Organic compounds, Single crystal growth, X-ray diffraction.

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INTRODUCTION

Organic compounds can crystallize in more than one crystal form. During recent years industries as well as the academic side has shown much interest in an exciting phenomenon polymorphism [1,2]. Different physical and chemical properties are exhibited for the different polymorphic crystal in the solid state. Many systems are known to show polymorphism, although the difficulty still remains as to obtaining reproducibly one or more polymorphs (e.g., the disappearing polymorph problem) [3-5]. The structure-property relationship has been investigated by the presence of polymorphic structures since the different intermolecular interactions could exert spectacular effect on the consequent solid materials [6].

Polymorphism is exhibited for the organic compounds with flexible torsions and low energy conformers because.

1. New hydrogen bonding and close packing modes were obtained from different conformations.
2. The tradeoff reduces the total energy difference between alternative crystal structures.

Different polymorphs were obtained from different crystallization procedures which lead to two polymorphs precipitating similarly in the same crystallization experiment. New polymorphs were formed by different crystallization solvents, temperatures or rates of crystallization [7,8]. The organic molecules were crystallized by hydrogen bonding which is a most important discriminating cohesive force [9]. In organic and biological structures the nature of strong or conventional hydrogen bonds such as O-H-O and N-H-O or O-H-N is well studied [10]. Weak hydrogen bonds C-H-O, C-H-N, and N-H-π are equally considerable in crystal packing [11-13]. Both polymorphs 1a and 1b, exhibit interestingly different intermolecular interactions in the solid state and therefore different photo physical properties [14,15]. The behavior of form 1a and 1b was fully characterized through thermogravimetric - differential thermal analysis (TG-DTA) analysis. The results of single crystal X-ray diffraction applied to the forms 1a and 1b are reported.

EXPERIMENTAL

Synthesis and crystal growth of polymorph

The title compound was synthesized by the formation of benzoin condensation followed by oxidation (Scheme 1). 4 g of KCN was dissolved in 75 ml of water in a 1 l flask. To this was added 6.8 g (0.05 mole) of anisaldehyde, 7 g (0.05 mole) of 2-chloro benzaldeyde, and 75 ml of 95% ethanol. The mixture formed a solution at the boiling temperature and was refluxed for ½ hrs. Steam was then passed through the solution until all the alcohol, and the unchanged aldehydes were removed. The condensed water was decanted from the product and later set away to crystallize. The product was then pressed as free as possible from oily material on a suction funnel and by washing with cold alcohol yields about 10 g of crude product. The crude mixture was dissolved in hot alcohol and allowed to crystallize slowly. The 2'chloro -4-methoxy benzoin crystallises out as colorless, hexagonal crystals. From the benzoin about 1 g was taken and treated with concentrated nitric acid by heating in a water bath inside a fume cupboard for about 3 hrs until it is free from the smell of nitrates. It is then cooled, and the obtained benzil is recrystallized using chloroform/acetone in the ratio 3:1. Pure crystals of benzil 1.1 separate out. The yield is about 70-80%. The melting point of the benzil was found to be 123.3°C. The another polymorph 1.2 of the crystal is obtained by recrystallization using hot ethanol. The melting point of the benzil was found to be 141.5°C. The molecular formula and structure of the benzil were determined by infrared (IR), nuclear magnetic resonance, and mass spectral analysis. The thermal behavior of the crystal was analyzed using thermogravimetric analysis. The crystal structure was confirmed by single crystal XRD analysis for the compound 1.1 and 1.2.

Crystal structure determination

Single crystal X-ray diffraction using monochromatized MoK\a radiation (0.71073A^0) data were collected at room temperature (25°C), on a Bruker axs kappa apex2 CCD diffractometer for forms 1a and 1b. The structures were solved using program SIR92 (Altornare *et al*., 1993) and refined using the full matrix LS procedure with SHELXL-97 (Sheldrick, 2008).

TG-DTA studies were conducted with a NETZSCH STA 409 C/CD instrument. Samples weighing 3-5 mg were heated in opened platinum pans at a rate of 10 K/minutes under nitrogen gas flow of 40 ml/minutes.

IR spectra were recorded on a Perkin Elmer Spectrum RX I spectrometer with KBr discs in the 4000-450 cm^{-1} region. For diffuse reflectance analysis, samples weighing approximately 2 mg were mixed with 200 mg KBr by means of an agate mortar and pestle, and placed in sample cups for fast sampling.

FT-RAMAN spectrometer is a Bruker 110/S spectrometer with a multiRAM, stand alone model. The spectral range is 4000-50/cm^{-1}. The laser source is Nd: YAG 1064 nm. The spectrometer has a large sample compartment to accommodate different sample formats, from powder to liquid in vials.

RESULT AND DISCUSSION

Synthesis and spectral characterization

The polymorph 1.1 and 1.2 were obtained by recrystallization using chloroform/acetone in the ratio 3:1 and hot ethanol, respectively. The melting point of the benzil 1.1 and 1.2 was found to be 123.3°C and 141.5°C, respectively. Both polymorphs are insoluble in water, but soluble in ethanol, chloroform, and acetone. Crystals of both compounds were found to be yellow cubes. Compound 1.1 crystallizes in triclinic P-1 space group and 1.2 in monoclinic P21/c space group.

Crystal structures

The structures 1.1 and 1.2 were determined crystallographically, and the crystallographic data, selected bond distances, bond, and torsion angles were collected, and the details of the data collection and refinement are presented in Table 1. The polymorph 1.1 crystallizes in the triclinic space group P-1 and the another polymorph 1.2 was found to crystallize in the monoclinic space group P21/c. Thus, the molecules exhibit conformational polymorphism as the conformations of the molecule are described by the different sequence of torsion angles listed in Table 1.

The title compound contains two ring systems, *viz,* chlorophenyl and methoxy phenyl moiety. The torsional angle between the C=O groups was found to be O(1)-C(7)-C(8)-O(2) -119.03(16), and O(1)-C(7)-C(8)-O(2) 122.1(2) for 1.1 and 1.2, respectively. The torsional angles between Cl(1)-C(1)-C(2)-C(3) 176.25(12), N(1)-C(11)-C(12)-O(3) -3.3(2) and Cl(1)-C(1)-C(2)-C(3) -177.85(19), and N(1)-C(11)-C(12)-O(3) 0.4(2) for 1.1 and 1.2 shows a wide difference denoting the presence of polymorphism. The bond angle for the compound 1.1 and 1.2 slightly differs as C(6)-C(7)-C(8) 119.31(12) and C(6)-C(7)-C(8) 118.64(14), respectively. ORTEP diagram of the complex is presented in Fig. 1 and crystal packing diagram is illustrated in Fig. 2. Polymorphic structures stabilized by strong O-H-O interactions and close packing were considered. The compound 2'-chloro-4-methoxy-3-nitro benzil has distance angle scatter plots of O-H-O hydrogen bonds extracted from the Cambridge structural database indicate that polymorphs with a large number of symmetry independent molecules (high Z') generally have better interactions when compared with the polymorphs with lower Z' values with the implication that these symmetry independent molecules have different independent conformations.

IR analysis

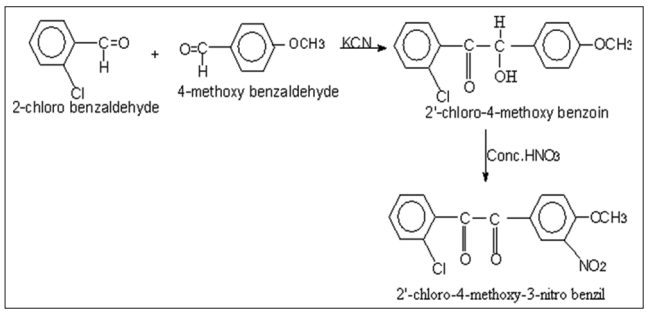
The IR analysis for the compound 3(1) and 3(2) shows a number of relative intensity differences in the IR fingerprint region below 1700 cm^{-1} and especially between 800 and 900 cm^{-1} which shows the existence of polymorphism in the title compound. The analysis also gives the existence of –C=O group at 1609 and 1673 cm^{-1} and 1667 and 1602 cm^{-1} for the polymorphic structure 1.1 and 1.2, respectively.

Thermal analysis

The TG-DTA curve 4(1) and 4(2) shows the melting point at 123.3°C for the polymorph 1.1 and that of 141.5°C for the form 1.2, respectively. The difference in the temperature could be associated with the different crystal morphology of forms 1.1 and 1.2.

Raman analysis

The Raman spectrum of the two polymorphs 5(1) and 5(2) are different in the C-H stretching region at ~3000 cm^{-1}, ~1600 cm^{-1}, and ~800 cm^{-1}



Scheme 1: Preparation of 2'-chloro-4-methoxy-3-nitro benzil

Table 1: Crystal data and summary of data collection and refinement details

Crystal data	1.1	1.2
Emperical formula	$C_{15}H_{10}ClNO_5$	$C_{15}H_{10}ClNO_5$
Formula weight (g mol^{-1})	319.69	319.69
Temperature (K)	293(2)	293(2)
Wavelength(^{0}A)	0.71073	0.71073
Crystal system	Triclinic	Monoclinic
Space group	P-1	P21/c
a(^{0}A)	7.8559(2)	8.541(5)
b(^{0}A)	8.1003(2)	14.903(5)
c(^{0}A)	12.4961(3)	11.135(5)
α(^{0})	74.8930(10)	90.000(5)
β(^{0})	74.8090(10)	92.779(5)
γ(^{0})	68.5930(10)	90.000(5)
Volume (^{0}A^3)	702.32(3)	1415.7(11)
Z	2	4
D_{calc} (M g^{-3})	1.512	1.500
Absorption coefficient (mm^{-1})	0.296	0.294
F(0 0 0)	328	656
Crystal size (mm)	0.30×0.20×0.20	0.30×0.20×0.20
θ Range for data collection (^{0})	2.75-29.64	2.28-25.00
Limiting indices	−10<=h<=10 −11<=k<=10 −12<=l<=17	−10<=h<=10 −17<=k<=1 −13<=l<=13
Reflections collected /independent[R (int)]	17487/3937 [0.0207]	12500/2488 [0.0226]
Completeness to θ = 29.64^0	99.6%	100.0%
Maximum and minimum transmission	0.951 and 0.892	0.9643 and 0.9056
Data/restraints/parameters	3937/0/200	2488/0/200
Goodness-of-fit on F^2	1.059	1.040
Final R indices [I>2σ(I)]	R1=0.0423 wR2=0.1198	R1=0.0342 wR2=0.0889
R indices (all data)	R1=0.0537 wR2=0.1283	R1=0.0450 wR2=0.0987
Largest diff. peak and hole (^{0}A^{-3})	0.484 and −0.408	0.282 and −0.275

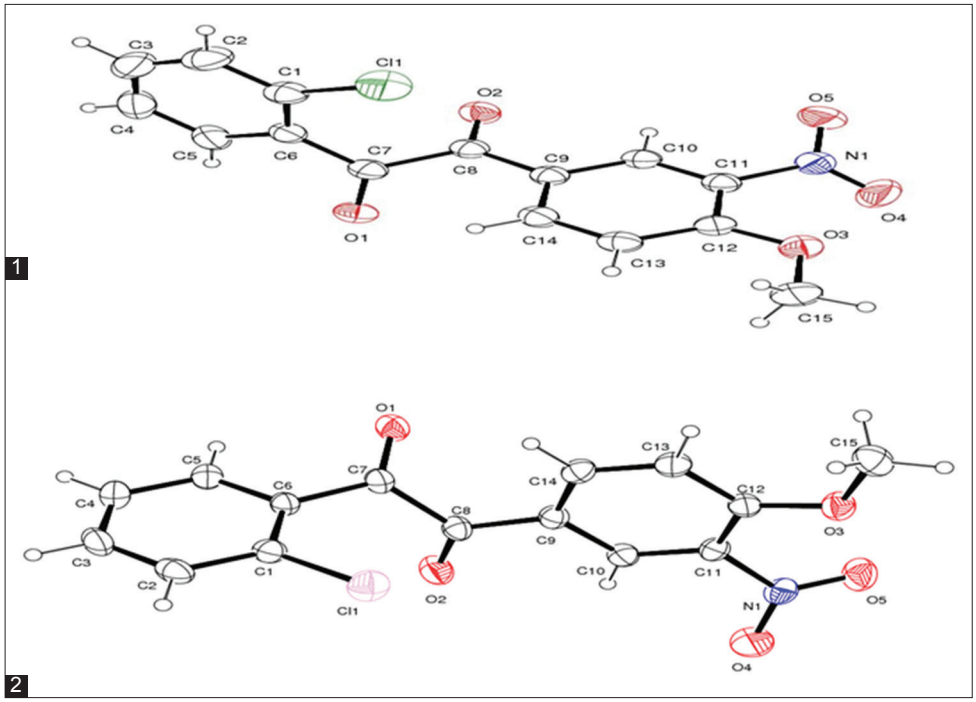


Fig. 1: Ortep diagram of (1) polymorph 1.1 and (2) polymorph 1.2

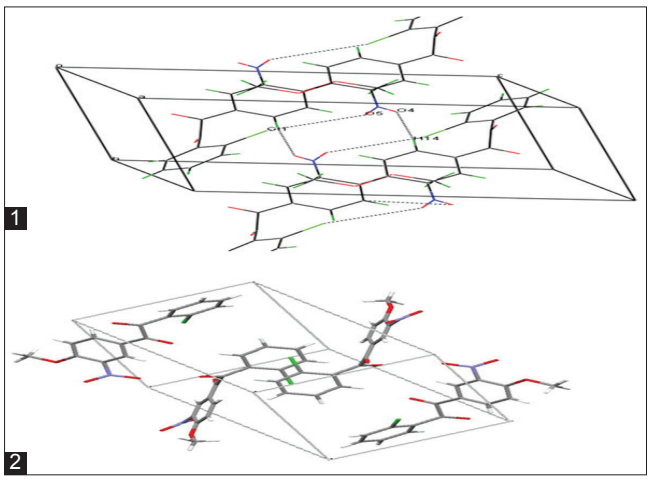


Fig. 2: Crystal packing diagram of (1) polymorph 1.1 and (2) polymorph 1.2

and many small pattern differences in the Raman spectra below 1700 cm^{-1} which indicates the presence of polymorphism.

CONCLUSION

The physical, organic, inorganic, metal-organic, supramolecular, computational, and pharmaceutical chemists throw much interest in polymorphism. IR and Raman spectra of the polymorphic forms of large pharmaceutical molecules can be used to identify the form. Attractions and repulsions of different chemical functional groups can change the intensities and frequencies of bands. Moreover, attractions can lead to coupling of molecules, which can alter the number and frequencies of bands due to in-phase and out-of-phase conditions. Systematic effects wherein high-energy conformers are stabilized by stronger hydrogen bonds or more efficient close packing in crystal structures are not a one-off occurrence. They are frequently observed in polymorphic crystal structures. The compensation of conformer destabilization by the crystal environment increases the likelihood of polymorphism in molecules with flexible torsions. This observation is of significant relevance in pharmaceutical polymorphism because typical drug molecules represent a confluence of conformational mobility and functional complexity [16,17].

Supplementary material

CCDC 817058 and 879618 contain the supplementary crystallographic data for 1a and 1b, respectively. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: Deposit@ccdc.cam.ac.uk.

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