Direct correlation among crystal structure, mechanical behaviour and tabletability in a trimorphic molecular compound

Partha Pratim Bag,[a] Miles Chen,[b] Changquan Calvin Sun*[b] and C. Malla Reddy*[a]

[a] *Indian Institute of Science Education and Research, Kolkata, 741252 West Bengal, India. Fax: +91-33-25873020; Tel: +91-33-25873118, Ext: 238; E-mail: cmallareddy@gmail.com; cmreddy@iiserkol.ac.in*

[b] *Department of Pharmaceutics, College of Pharmacy, University of Minnesota, 9-127B Weaver-Densford Hall, 308 Harvard Street S.E., Minneapolis, MN 55455, USA Fax: 612-626-2125; Tel: 612-624-3722; E-mail: sunx0053@umn.edu*

Experimental Method:

Powder X-Ray Diffraction (PXRD): The PXRD patterns were collected on a Rigaku SmartLab with a Cu Kα radiation (1.540 Å). The tube voltage and amperage were set at 40 kV and 50 mA respectively. Each sample was scanned between 5 and 50° 2θ with a step size of 0.02°. The instrument was previously calibrated using a silicon standard.

Differential Scanning Calorimetry (DSC): DSC was conducted on a Mettler-Toledo DSI1 STAR^e instrument. Accurately weighed samples (4-6 mg) were placed in hermetically sealed aluminium crucibles (40 μL) and scanned in the range of 30 °C to 300 °C at a heating rate of 5 °C/min under a dry nitrogen atmosphere (flow rate 80 mL/min). The data were managed by STAR^e software.

Thermo gravimetric Analysis: TGA was performed on a Mettler-Toledo TGA/SDTA 851^e instrument. Approximately 6-8 mg of the sample was added to an aluminium crucible and heated from 30 to 350 °C at a rate of 10 °C/min under continuous nitrogen purge.

FT-IR Spectroscopy (KBr): Fourier transmission infrared spectra of the solids were obtained using a Fourier–transform infrared spectrometer (PerkinElmer 502 or SHIMADZU FTIR-8400S). KBr samples (2 mg in 20 mg of KBr) were prepared and 5 scans were collected at 4 cm-1 resolution for each sample. The spectra were measured over the range of 4000-400 cm^{-1}.

Table S1. Conditions used at rotary evaporator for the preparation of 6-chloro-2,4-dinitroaniline (**cda**) polymorphs. In the initial milligram scale batches, 200 mg of **cda** (0.9192 mmol; Sigma-Aldrich) was used in all cases for preparing the polymorphs. The weight of **cda** used in the large batches was 5 gm (22.9811 mmol).

Solvent	**Pressure (mbar)**	**Temperature of water bath (°C)**	**Revolution speed of round bottom flask (rpm)**	**Polymorph obtained**
Acetone	430	50	130	Polymorph I*
Dichloromethane (DCM)	900	50	130	Polymorph II
Ethyl Acetate (EA)	300	50	130	Polymorph III*

*It was also noticed occasionally that the polymorph I and III may also form from ethyl acetate and acetone, respectively, by the FE method.

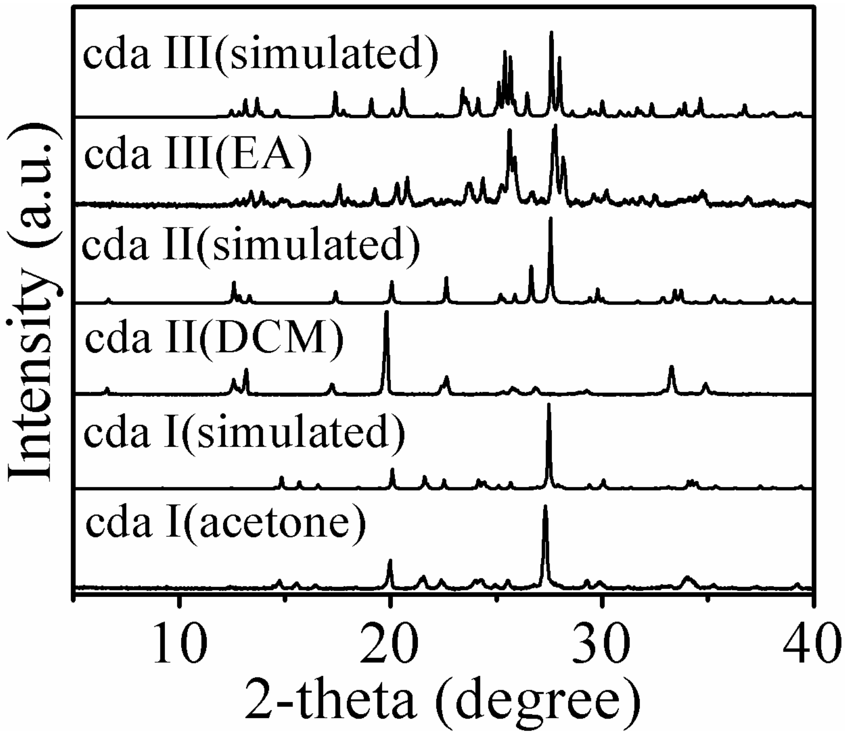


Figure S1. PXRD patterns of the three **cda** solid forms obtained from acetone (Form I), dichloromethane (Form II) and ethyl acetate (Form III) by FE method using rotary evaporator and corresponding simulated patterns. The PXRD patterns of all the FE products match well with the simulated PXRD patterns. In the experimental PXRD of Form II, a prominent peak at 27.5° could not be detected, probably due to particle preferred orientation effects.

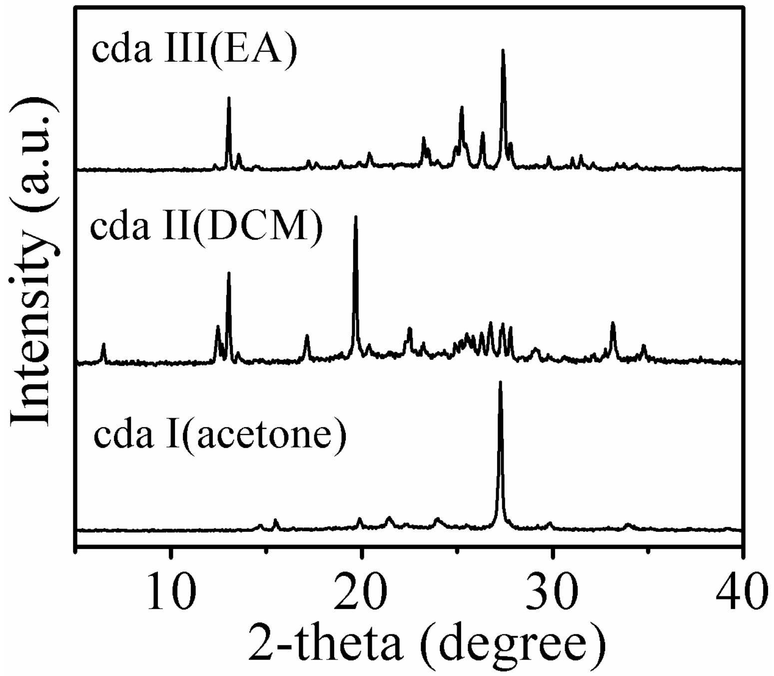


Figure S2. PXRD patterns of three **cda** solid forms, after grinding by mortar and pestle.

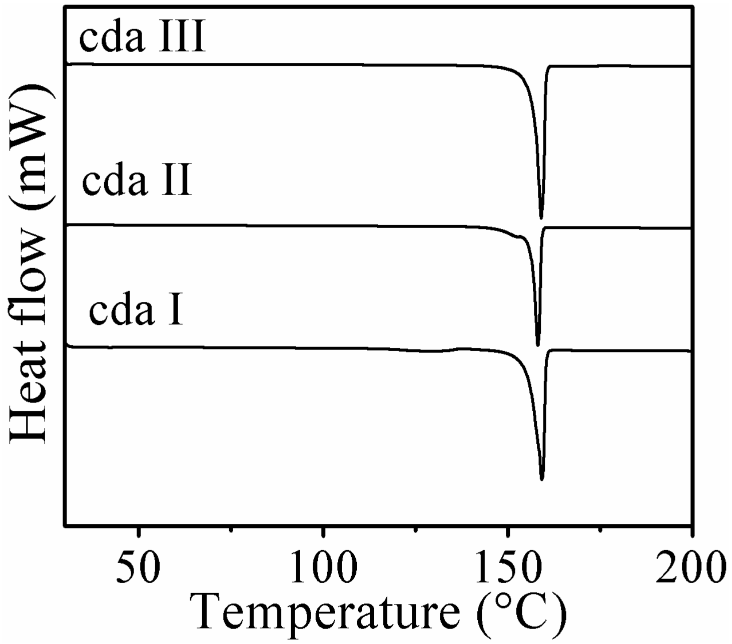


Figure S3: DSC of three forms of **cda** single crystals obtained by slow evaporation method. The powder samples obtained by the FE method showed a good agreement with this.

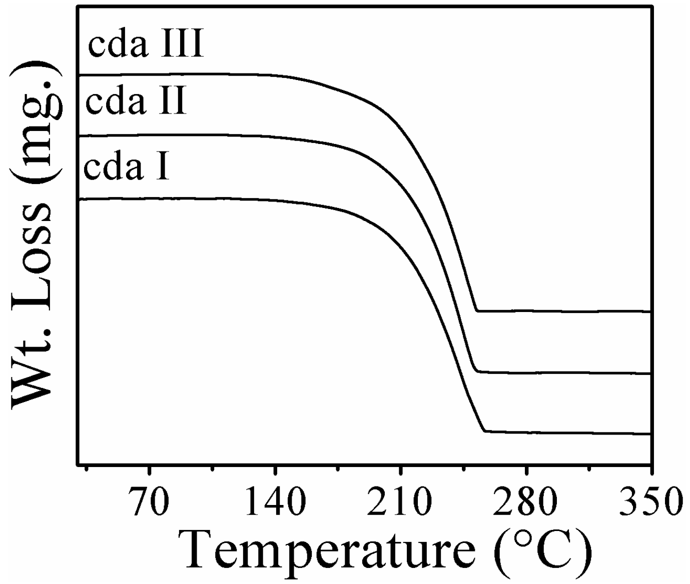
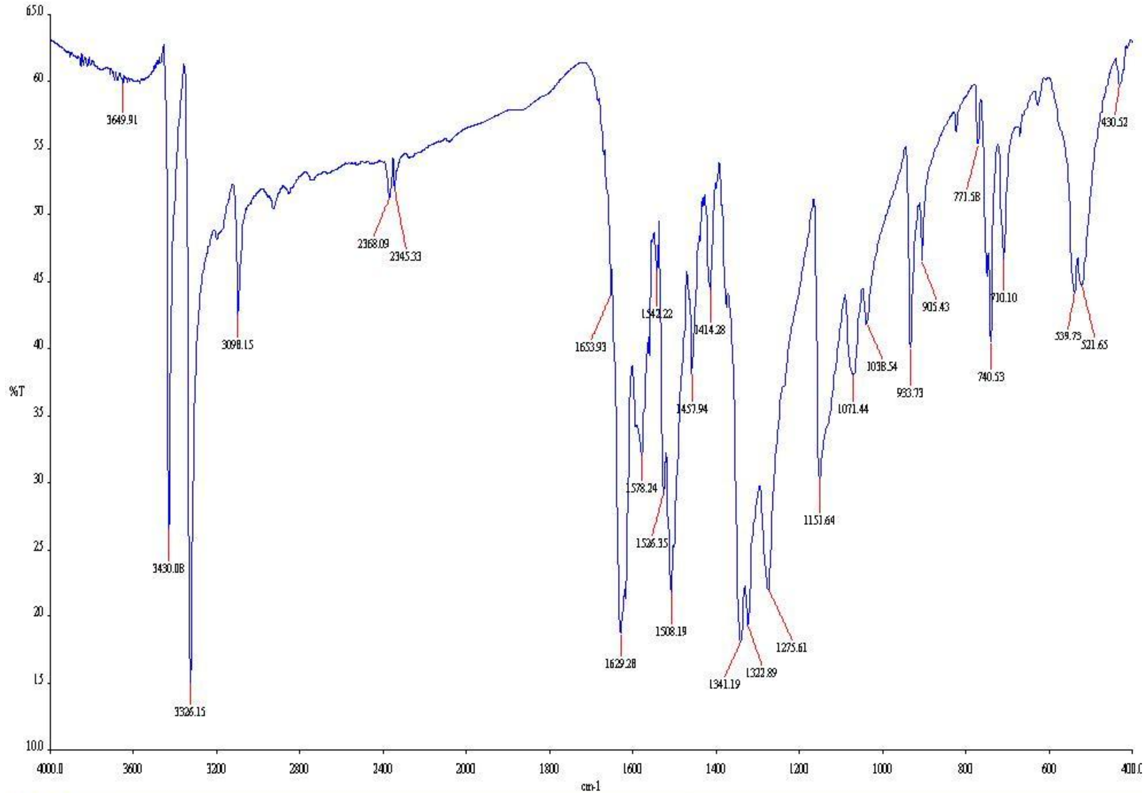
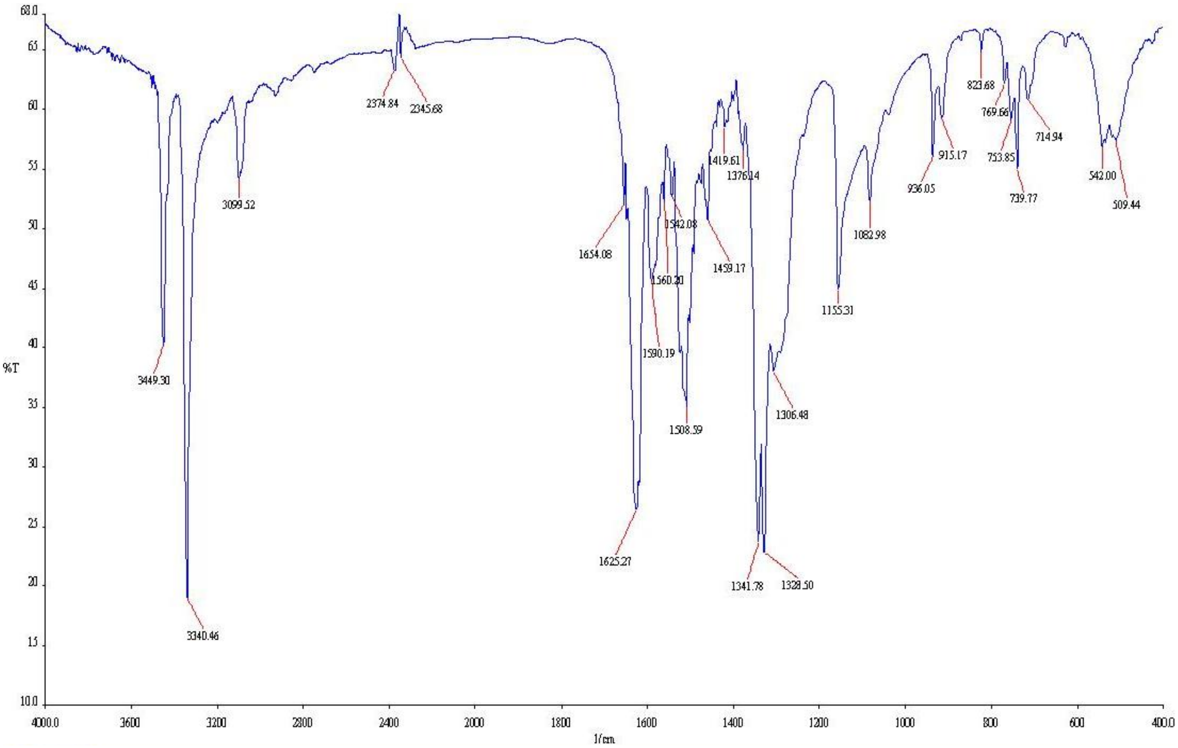


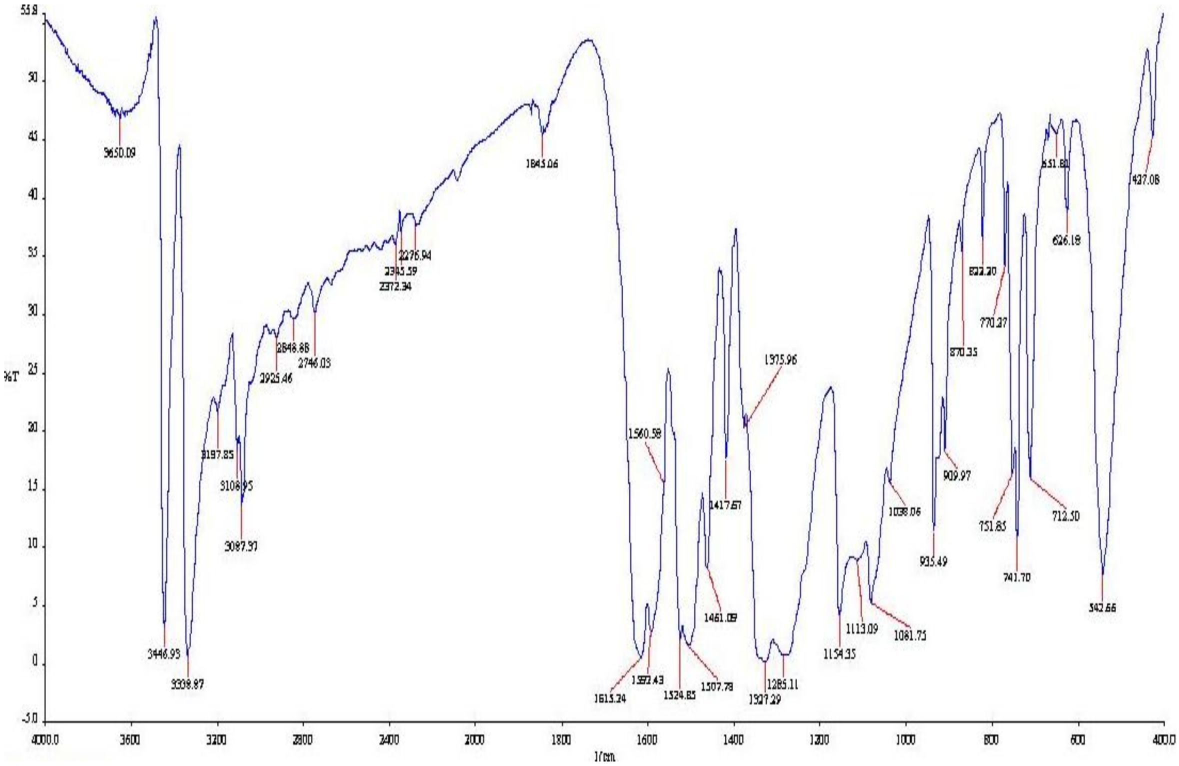
Figure S4: TGA of three **cda** forms obtained by FE method.



(a)

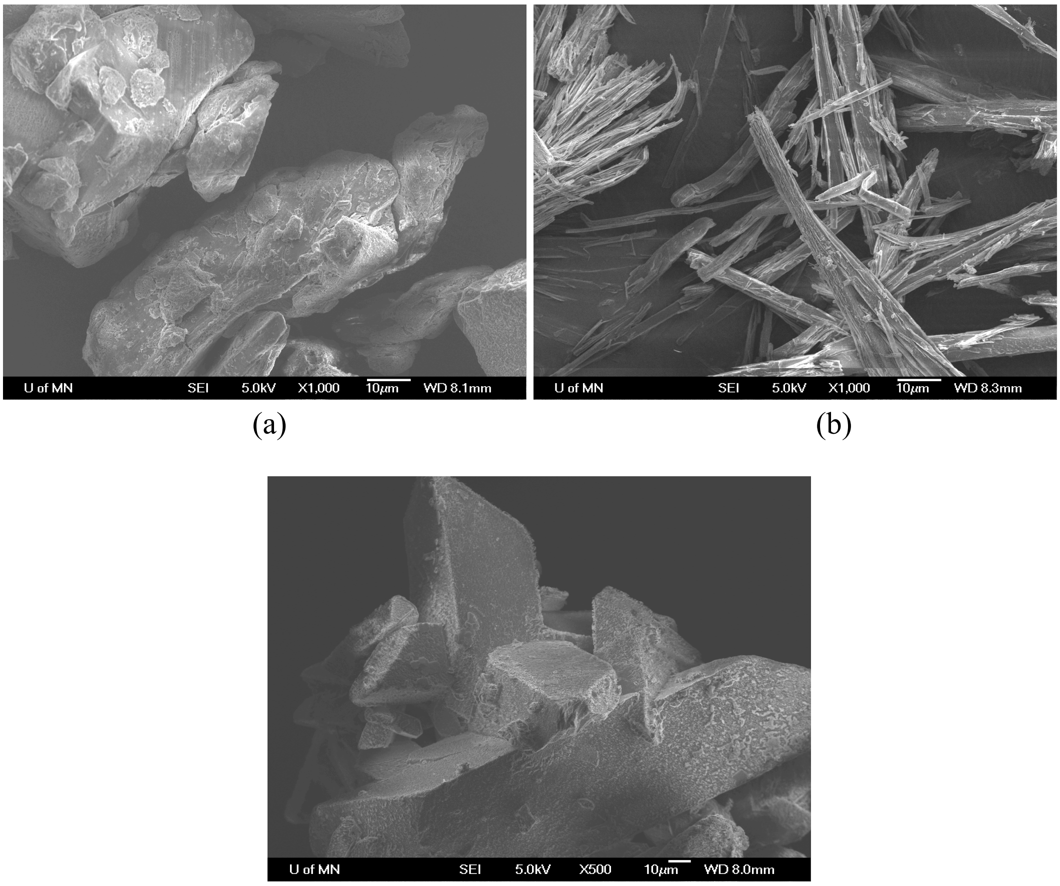


(b)



(c)

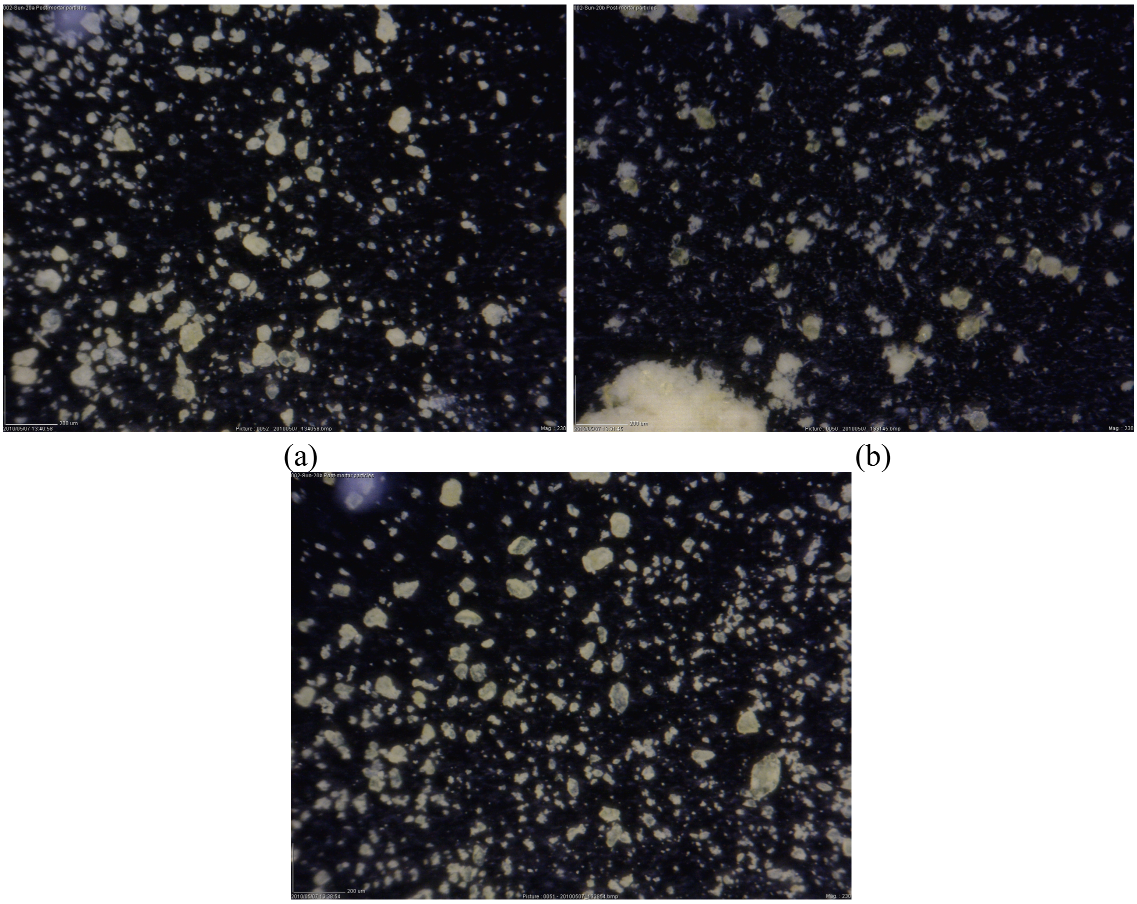
Figure S5: Infrared spectra of the three **cda** forms (a) **I**, (b) **II** and (c) **III**, obtained by FE method.



(a) (b)

(c)

Figure S6: SEM image of **cda** Form I (a), Form II (b) and Form III (c) before grinding. Notice similar (block) morphology in Form I and III while Form II has needle morphology.



(a) (b)

(c)

Figure S7. Optical microscopy images of powder samples of 6-chloro-2,4-dinitroaniline (**cda**) after grinding. (a) Form I, (b) Form II and (c) Form III prepared by the fast evaporation (FE) technique (rotary evaporation). Notice similar particle size and morphology achieved in all the three forms on grinding.