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Three solid forms of chlorantraniliprole: Structure, characterization, and phase transformation

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ABSTRACT

Chlorantraniliprole is one of the most widely used broad-spectrum pesticides. This paper studied three solid forms of chlorantraniliprole, among which two novel solvates were introduced, as well as their crystal structures. Form 2 and form 3 are defined as DME solvate in the triclinic space group $P\bar{1}$ ($Z = 4$) and pyridine solvate in the triclinic space group $P\bar{1}$ ($Z = 2$), respectively. All of the three forms were characterized and identified by powder X-ray diffraction, thermal analysis (DSC and TG), vibrational spectroscopy (IR and Raman), electron microscopy and particle size distribution. Solid-state stability and transformation relationship of the solid forms were also investigated. Besides, the insecticidal activities of form 1 and form 2 were examined.

1. Introduction

Polymorphism is important in pharmaceutical industry and new functional material design. Polymorphs in different active pharmaceutical ingredients may exhibit differences in physical or chemical properties, such as melting point, bulk density, solubility, stability, and bioavailability [1–5]. Thus, the characterization of polymorphs has recently become one of the most important activities and high useful interest in the field of crystal engineering [6]. For example, recent years discoveries of new polymorphs of phenobarbital [7], 5-nitrofurazone [8], and metacetamol [9], which means that there is chance for traditional screening methods to be used in polymorph searching. Moreover, because of the inclusion of solvent molecules, solvate, normally defined as pseudopolymorph, exhibits many different physical properties when compared with its non-solvent formation [10,11]. In the past decades, solid form screening [12] was widely used in the field of pharmaceutical industry. However, such research on pesticide field did not cause enough attention and there are few literature report.

Chlorantraniliprole (3-bromo-*N*-[4-chloro-2-methyl-6-(methylcarbamoyl) phenyl]-1-(3-chloropyridin-2-yl)-1*H*-pyrazole-5-carboxamide, Fig. 1) is a new generation efficient anthranilic diamides insecticide developed by DuPont in 2000 [13,14]. It is an excellent representative of ryanicide receptor with many advantages such as high efficiency, low toxicity, broad spectrum, long persistence and low residue [15,16]. It has been reported to exhibit excellent efficacy against *lepidoptera* insects [17] such as *noctuidae*, *pyralidae*, *carposinidae*, *tortricidae*, powder moth, *plutellidae*, *gelechiidae*, and fine moth [18]) and non-lepidopteran pests (such as *curculionidae* and *chrysomelidae* [19] of *coleoptera*, *diptera agromyzidae*, and *bemisia tabaci* [20]). The revenue of chlorantraniliprole was 1.48 billion dollars in 2014, which was in the first place of all insecticide. Now it is being sold in global agriculture. Nie [21] reported the single crystal structure of chlorantraniliprole in 2014, which was defined as form 1 in the context.

In this study, two solvates of chlorantraniliprole, *i.e.* form 2 and form 3, were introduced. The single crystal and X-ray diffraction data of the solvates were also obtained. The different hydrogen interaction mode in chlorantraniliprole different polymorphs resulted in varies solid forms (forms 1, 2, and 3). Stability and

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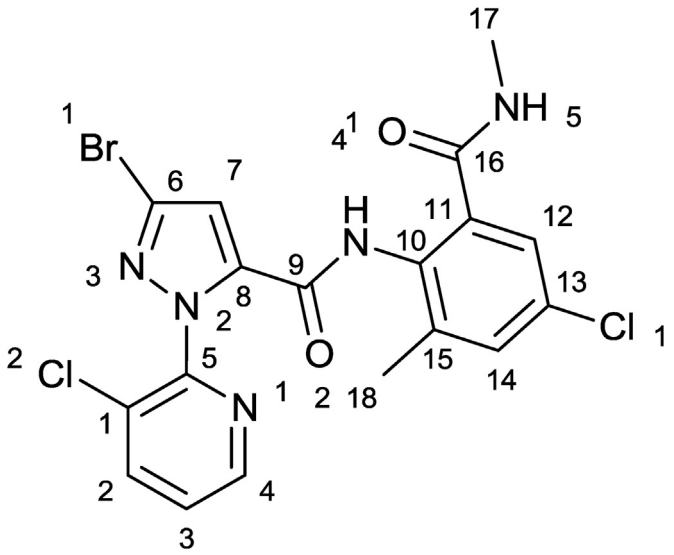

Fig. 1. Molecular structure of chlorantraniliprole.

transformation relationship of them were investigated as well. Furthermore, indoor insecticide biological activity test of form 1 and form 2 was also performed, with the result that the insecticidal activity of form 2 is slightly higher than that of form 1.

2. Experimental section

2.1. Materials and methods

Chlorantraniliprole form 1 (purity > 95%) was provided by RuDong ZhongYi Chemical Co., Ltd. (China). Organic solvents of analytical or chromatographic grade were purchased from Sinopharm Chemical Reagent Co., Ltd. (China) and used without further purification. Water used in the experiments was purified from a deionizer with mixed bed purification system (Merck Millipore D 24 UV, Germany).

2.2. Preparation of chlorantraniliprole solid forms

Chlorantraniliprole Form 2. Form 2 was obtained upon dissolving 100 mg of chlorantraniliprole (form 1) in 10 ml of 1,2-dimethoxyethane (DME) followed by ultrasonic treatment for 1 h, the clear solution was evaporated slowly to precipitate. The precipitate was filtered and dried over 24 h in vacuum oven at room temperature to give chlorantraniliprole form 2. Faint yellow rod-shaped crystals suitable for X-ray diffraction were obtained after 15–17 days through slow evaporation of the above solution.

Chlorantraniliprole Form 3. Form 3 was obtained upon dissolving 10 mg of chlorantraniliprole (form 1) in 1 ml of pyridine, after adding 5 ml dibutyl ether followed by 4 days' standing, lots of solids precipitated. The precipitate was filtered and dried over 24 h in vacuum oven at room temperature to give chlorantraniliprole form 3. Needle-shaped crystals suitable for X-ray diffraction were obtained by standing a solution of 10 mg of chlorantraniliprole (form 1) in 1 ml of pyridine and 2 ml of dibutyl ether for 24 h under ambient conditions.

2.3. X-ray crystallography

X-ray diffraction data were collected on Bruker SMART-APEX DUO diffractometer (USA) equipped with a graphite monochromator and Mo-Kα fine-focus sealed tube ($\lambda = 0.71073$ Å). Data processing was performed using Bruker SAINT Software. Intensities were corrected for absorption using SADABS [22], and the structure was refined using SHELXL-97 [23]. All non-hydrogen atoms were refined anisotropically [24]. Hydrogen atoms on heteroatoms were located from different electron density maps and all C–H hydrogens were fixed geometrically. Hydrogen bond geometries were determined in Platon. X-Seed was used to prepare packing diagrams. Related crystallographic data have been deposited in the Cambridge Crystallographic Data Centre (CCDC Nos. 1505332, 1505333).

2.4. Powder X-ray diffraction (PXRD)

PXRD patterns were recorded using a Rigaku Ultima IV diffractometer (Japan) with Cu-Kα radiation [25] (40 kV, 40 mA) scanned at 20°/min over a 2θ angular range of 5°–45°.

2.5. Differential scanning calorimetry (DSC)

DSC was performed on a TA DSC Q2000 instrument (Waters, USA). Samples were placed in crimped and sealed aluminium sample pans [26]. The typical sample size is 2–5 mg, and the temperature range is 30–300 °C at a heating rate of 10 °C/min. The instrument was calibrated against with the melting properties of indium according to standard procedure. Each sample was analysed in triplicate with RSD <2%.

2.6. Thermogravimetric (TG) analysis

Thermogravimetric properties were determined using a TA TGA Q500 instrument (Waters, USA) within platinum pans at a heating rate of 10 °C/min under nitrogen gas flow [27]. The instrument was calibrated with mass and temperature according to standard procedure. Each sample was analysed in triplicate with RSD <2%.

2.7. Vibrational spectroscopy

IR and Raman spectra were recorded by Thermo-Nicolet 6700 Fourier transform infrared spectrophotometer [28] with NXR-Fourier transform Raman [29] module (Thermo Scientific, USA). IR spectra were recorded on samples with KBr pellets. Raman spectra were recorded on samples contained in a gold-coated sample holder. Experimental data were analysed using the Omnic software.

2.8. Field emission scanning electron microscopy (FESEM)

The shapes and morphologies of the three forms were examined on a Carl Zeiss model Merlin Compact 6027 FESEM (Germany) with a beam voltage of 3.0 kV [30]. The sample was spread on a carbon-coated copper grid. Prior to FESEM imaging. In order to enhance the conductivity of the sample, an ultrathin layer of gold was coated on the sample.

2.9. Particle size distribution (PSD)

PSD was measured using a Mastersizer 2000 laser diffraction particle size analyser (UK). Dry sample was introduced by Scirocco 2000 automatic sampler and measured for three times.