We are IntechOpen, the world's leading publisher of Open Access books
Built by scientists, for scientists

6,900
Open access books available

186,000
International authors and editors

200M
Downloads

154
Countries delivered to

Our authors are among the

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities

CLARIVATE ANALYTICS
BOOK CITATION INDEX
INDEXED

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

Thermodynamic Properties and Crystallization Behavior of Pesticide Imidacloprid

Zhou Cairong
School of Chemical Engineering& Energy, Zhengzhou University
People's Republic of China

1. Introduction

A large quantity of pesticide is produced and consumed in all the world. Pesticide industry plays more and more important role in economy of agriculture. With the updating of pesticide products, traditional pesticide, due to its high toxic residue and poor performance, has been gradually replaced by new generation pesticide which is more friendly to environment and mankind. Imidacloprid has become a typical representative of the new generation pesticide for which gives due weight to its great efficiency, low toxicity and low residue, and has been developed since the 1990s. Imidacloprid (1-[(6-chloro-3- pyridinyl) methyl]-4,5–dihydro–N–nitro-1H-imidazol-2-amine, molecular formula $C_9H_{10}ClN_5O_2$, CAS Registry No.138261–4-3)，acts on the diverse acetylcholine receptor (nAchR) of insect origin, is a new, selective, long-acting neonicotioid insecticide which can be used with reasonable environmental safety (PAN Y. M. et al., 2000; Kagabu, S. et al.,1997; Heijb roek W. et al., 1995). Imidacloprid is a commercial example of the chloronicotinyl insecticides acting at the nicotinyl acetylcholine receptor (Bai et al., 1991; Moriya et al., 1992; Leicht, 1993), is reported as highly active insecticide for homopteran pests (Iwaya and Tsuboi, 1992; Shiokawa et al., 1994; Gourment et al., 1996; Jian Zhong et al., 1996; Sannino, 1997; Ramaprasad et al., 1998; Kumar et al., 2000a) and for some speces of the order coleoptera, diptera and lepidoptera (Elbert et al., 1990, 1991). It has recently been registered in the world for plant protection practices. Its bioefficacy and persistence has been studied on few crops like wheat, barley, rice, cotton, chilli, okra, mustard and sugar beet (Dewar and Read 1990; Rike et al,. 1993; Ishii et al., 1994; Jarande and Dethe, 1994; Rouchaud et al., 1994; Iwaya et al., 1998; Kumar, 1999; Kumar et al., 2000a; Dikshit et al., 2000). So far, it has been one of the new competitive pesticides in the world market (A.W.M. Huiijbrgts et al., 1995; KONG et al., 2008). However, the original pesticide of imidacloprid contains huge amounts of 2-Nitroaminoimidazoline(4,5-Dihydro-N-nitro-1H-imidazol-2-amine, CAS Registry No. 5465-96-3, ab. NIM) and by-products (2-Nitriminoimidazolidine,1,1'- (2,5-pyridinediyl)bis-, ab. NMP) which affect the quality of imidacloprid in the producing process. Crystallization technology for the separation and purification of organic materials is used widely because of low energy consumption and higher purity. So the solid–liquid equilibriums are of interest for the development of theoretical models and in application of the chemical industry (Kojima et al.,1997; Matsuoka et al.1989; Dalmazzone et al., 2002; Shibuya et al., 1993; Khimeche et al., 2006; DING et al., 2000). As long as crystallization behavior is observed and

the data for the pure substances are known it is possible to use the data obtained in any solid-liquid equilibrium experiment to calculate the activity coefficient in the liquid phase. The study of solid-liquid equilibrium of binary/ternary mixtures provides information on both the intermolecular forces between solvent and solute and also on the nature of the intermolecular compounds in the solid phase(Yamamoto I., 1996). In the paper, the thermodynamic properties of the solid-liquid equilibrium on imidacloprid, 2-Nitroaminoimidazoline and NMP have been studied in order to solve the problem of the separation and purification of imidacloprid. In addition, the crystallization metastable zone width and crystallization behavior in some solvents and purification to the second powder concentrated of imidacloprid have been also determined.

2. Standard combustion enthalpy and thermal capacity of imidacloprid and some nitrogenous organisms

During the production process of imidacloprid, the yield and quality of product are influenced by 2-Nitroaminoimidazoline and accessory substance NMP. The structural formula of them are written in Fig.1.
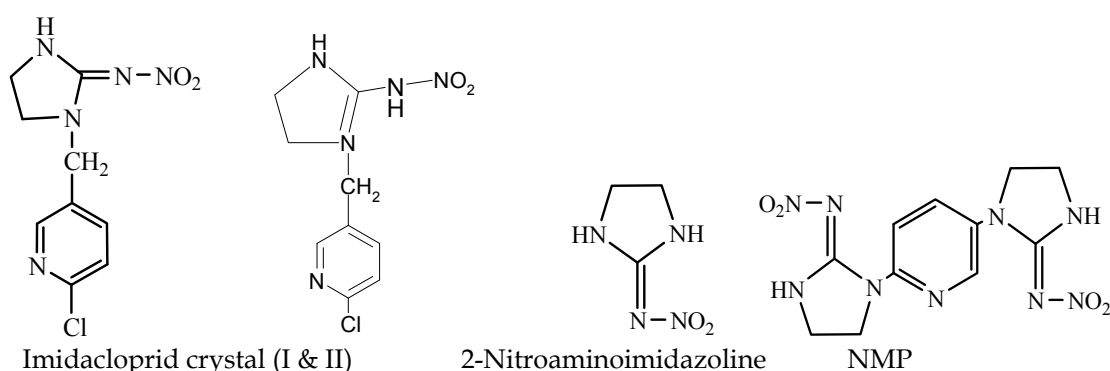

Fig. 1. The compound structure

The constant-volume combustion energies of three pure substance can be determined by a precision oxygen bomb calormeter. The standard molar enthalpies of combustion and formation can be calculated on the basis of thermodynamic theory. Moreover, The relationship between the specific heat capacity and temperature could be discussed by mathematics according to the experimental data. The related studies can provide a thermodynamic basis for imidacloprid further application, and it will play an important role on gainning high-yield purification of imidacloprid and be available for the exploiting new synthesis method, engineering design and industry production of imidacloprid.

2.1 Medicines and experiment apparatus

The crystals both imidacloprid and NMP are purified by recrystallization with pure organic solvents, respectively, to obtain the purity of 99.9 %（mass fractions） by high performance liquid chromatography. The melting points of them are separately 416.80±0.05K and 423.85±0.05K by DSC-60 (Japan Shimadzu Co.), which agrees well with the literature value of (416.95±0.50 K) for imidacloprid (LIU, 2000). And NMP's melting point has been reported

(CHEN et al., 2009; ZHOU et al., 2010).   2-Nitroaminoimidazoline purchased from Jiangsu Tianze Chemical Industrial Co. Ltd, China (purity ≥ 99.00 %) has used as delivered without further purification, and the melting point of it is 495.13±0.05K by DSC-60. Benzoic acid used in the experiment is of AR grade with mass fraction purity of over 99.5% and purchased from Shanghai chemical reagent company, R.. P. China. α-Al₂O₃ is the powder for DSC Standard Material，provided by the Shimadzu company in Japan.

DSC-60 differential scanning calorimetry and DTG-60 thermogravimetric-differential scanning calorimetry are provided by the Shimadzu company in Japan. The error of electronia balance and microthermometer is, respectively, 0.1mg and ±0.01℃. SPN-500 nitrogen generator (the HP analysis technology research institute in Beijing, China.) is used to provides nitrogen atmosphere for the experiment of thermal analysis.

2.2 Principle of enthalpy of combustion determined

Based on the first law of thermodynamics, when a **s**ubstance is burnt completely，the combustion energy of material at constant volume is shown in Eq.(1) (CHEN et al., 2009; Duane, 2000; Sergy, 1998; JIANG et al., 2005; ZHOU et al., 2002; AN et al., 2007).

$$Q_V = \Delta_C U_m \tag{1}$$

or if it is under constant pressure, the combustion enthalpy of material is shown in Eq.(2):

$$Q_p = \Delta_C H_m \tag{2}$$

Where,

$$\Delta_C H_m = Q_p = Q_V + \Delta n RT \tag{3}$$

Here Δn represents the change of mole number for gaseous materials when the combustion reaction occurs. R and T represent the universal gas constant 8.314 J·mol⁻¹·K⁻¹ and the Kelvin temperature. When the sample is combusted completely, temperature of both the oxygen bomb calorimeter and surrounding medium (usually, that is water) rise because it give off quantity of heat. The temperature variation (ΔT) is determined by experiment. The combustion reaction heat Q_v can be obtained for the material at constant volume by Eq. (4) after the specific heat of Oxygen Bomb Calorimeter (ε_{calar}) is defined.

$$mQ_V = \left(3200 C_{water} + \varepsilon_{calar}\right)\Delta T + Q_f \tag{4}$$

Where m is amounts of the sample, g; C_{water} is specific heat capacity of water, 4.18 J·g⁻¹·K⁻¹; ε_{calar} is the specific heat of calorimeter, J·K⁻¹; Q_f is an attach heat quantity generated by air of which is in the calorimeter, it is 0 J at the ideal state. Q_v is the energy of combustion. On the basis of the standard substance Q_v (26460 J·g⁻¹) of benzoic acid (Sergey, 1998; JIANG et al., 2005; ZHOU. et al., 2002; AN. et al, 2007) , the heat of calorimeter (ε_{calar}) can be obtained from the Eq. (4), and the standard molar energy of combustion ($\Delta_c U_m^\theta$) can calculaed by experimental data from Eq.(4). The standard moler enthalpy of the substance($\Delta_c H_m^\theta$)is referred to be the change of combustion enthalpy in the ideal combustiong reaction according to Eq.(3) at 298.15K and 101.325kPa.

Combustion calorimetry. The constant-volume combustion energy of sample can be determined by a precise thermal isolation oxygen bomb calorimeter (XRY-1C, shanghai changji geology apparatus Ltd., R. P. China), in which fitted with a stirred water bath. An amount of benzonic acid (BA) is taken and preformed by hand driven tablet machine. The preforming sample is placed in stainless steel pot, and a metal wire used as ignition is binded on a couple of electrode before oxygen is put into the oxygen bomb calorimeter, which is bured in oxygen at pressure 3.00 ± 0.50 MPa. Then the oxygen bomb is put into a bucket contained 3200mL water (at 298.15K). Stir is opened before the apparatus records automatically. After 5 min, the metal wire is ignited. Meanwhile, it is that the sample starts combustion when temperature quickly rised. Temperature readings are taken at 5s intervals before and after the ignition. After temperature reach at the most height point and continue 10min, the test could be stopped automatically.

2.3 Principle and procedure of specific heat capacity determined

To determine the specific heat capacity of sample by DSC, heat flow signal from the sample is compared to the DSC signal of a standard material of known specific heat (CHEN et al., 2009). Both curves are corrected by a zero line or base line to correction experiment. Where empty crucibles of both a reference and sample are separately placed in the furnace，the system signal drift is measured under identical experimental conditions.

The specific heat capacity of sample determined is accomplished according to three step technique progess at a linear heating rate by DSC-60:(i)assumes that the identical instrument settings and conditions are used for each experimental step. (ii) the same empty reference crucible is used for all steps and not removed from the DSC furnace. (iii) The three main steps defined as follows are done by DSC.

Step 1: empty sample crucible is scanned to obtain DSC sign of zero line determined.

Step 2: to scan sample crucible where contains zinc and indium used as the substance of calibration standard.

Step 3: to scan sample crucible in which contains the sample measured.

The experiments are done for each of them at least three times. Specific heat capacity C_p of the substance is then calculated by Eq.(5) as follows:

$$C_{p,\text{sample}} = \frac{M_{\text{standard}}}{M_{\text{sample}}} \times \frac{\varphi_{\text{sample}}(T) - \varphi_0(T)}{\varphi_{\text{standard}}(T) - \varphi_0(T)} \times C_{p,\text{standard}} \qquad (5)$$

Where C_p, M, and φ are , respectively, specific heat capacity，mass of sample, and DSC output signal as heat flow rate of substance；subscript symbols, such as sample, standard and 0, are respectively, sample measured, standard chemical substance (e.g.zinc, indium), and zero line.

A small amount of powdery solid sample (3 to 5mg) is taken and sealed in an aluminum pan of DSC-60 for the analysis. The measurements are made under fixed conditions of which is the constant heating rate of 5 ℃ · min⁻¹ and under nitrogen atmosphere (40 mL·min⁻¹). α-Al₂O₃（standard material）is used as reference material in the process of the analysis. Before the samples are analyzed, it is necessary that the DSC-60 is calibrated with indium (purity=99.99%, T_m=429.78 K, $\Delta_m H$ =28.45 J·g⁻¹) and zincum (purity=99.99%, T_m=419.58K, $\Delta_m H$=100.50J·g⁻¹) (Japan Shimadzu Co.). Data acquisition and online processing could be done with TA-60WS Collection Monitor software.

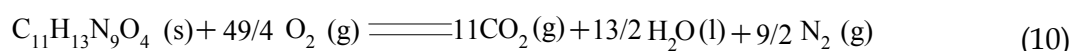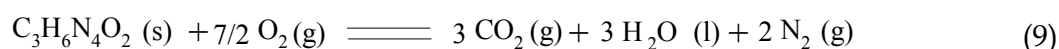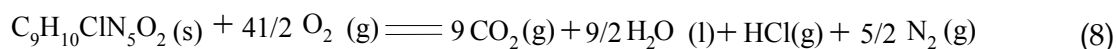## 2.4 Standard molar enthalpy combustion and formation of imidacloprid and some nitrogenous organisms

The detailed procedure has been described above-mentioned method. Freshly circular sheet solid sample is prepared for determining the combustion heat of substance. Smooth curves are fitted to the pre and after-period temperatures and the corrected temperature rise is calculated by means of data processing soft-ware in the oxygen bomb calorimeter working station using the Dickinson method (JIANG et al., 2005; ZHOU et al., 2002; AN et al, 2007), in which ΔT is the ordinate that encloses equal areas above and below the reaction curve. The energy equivalent of the calorimenter ε_{calar} could be determined with a standard reference sample of benzoic acid. From three experimental dada ε_{calar} is measured to be 15245 J·K-1. On the basis of thermodynamics principle，the standard molar enthalpy of combustion is

$$\Delta_C H_m^\theta (298.15K) = \Delta H_1 + \Delta_C H_m(T) + \Delta H_2 = \Delta H_1 + Q_V + \Delta nRT + \Delta H_2 \qquad (6)$$

Which

$$\Delta H_1 = \int_{298.15}^{T} \sum \left(a_j c_{p,j}\right)_{reactant} dT \quad , \quad \Delta H_2 = \int_{T}^{298.15} \sum \left(b_k c_{p,k}\right)_{product} dT \qquad (7a,b)$$

The individual values of both the standard molar energy and enthalpy of combustion are listed in Table 1 together with the mean. The combustion reaction equations of imidacloprid, NIM and NMP, can be written as Eq.(8) to Eq. (10):

$$C_9H_{10}ClN_5O_2 (s) + 41/2\ O_2\ (g) = 9\ CO_2 (g) + 9/2\ H_2O\ (l) + HCl(g) + 5/2\ N_2\ (g) \qquad (8)$$

$$C_3H_6N_4O_2 (s) + 7/2\ O_2 (g) = 3\ CO_2 (g) + 3\ H_2O\ (l) + 2\ N_2\ (g) \qquad (9)$$

$$C_{11}H_{13}N_9O_4\ (s) + 49/4\ O_2\ (g) = 11CO_2 (g) + 13/2\ H_2O (l) + 9/2\ N_2\ (g) \qquad (10)$$

and, $\Delta_c H_m = Q_v + \Delta nRT$ where Δn = -6, 1.5, -9, accordingly. Hence, the standard molar enthalpy of combustion can be obtained for various samples by Eq. (3) , and the results are listed in Table1. The obtained values are, respectively, -5536.34 kJ·mol-1, -2017.64 kJ·mol-1, -7976.88 kJ·mol-1 for imidacloprid, NIM and NMP.

The standard molar enthalpy of formation, $\Delta_f H_m^\theta$, can be calculated by Hess's law(Sergey, 1998), according to the thermochemical equations (8) to (10) as follows:

$$\Delta_f H_m^\theta [C_9H_{10}ClN_5O_2, s] = \left[9\Delta_f H_m^\theta (CO_2, g) + 9/2\Delta_f H_m^\theta (H_2O, l) + \Delta_f H_m^\theta (HCl, g) \right] - \Delta_C H_m^\theta [C_9H_{10}ClN_5O_2, s] \qquad (11)$$

$$\Delta_f H_m^\theta [C_3H_6N_4O_2, s] = \left[3\Delta_f H_m^\theta (CO_2, g) + 3\Delta_f H_m^\theta (H_2O, l) \right] - \Delta_C H_m^\theta [C_3H_6N_4O_2, s] \qquad (12)$$

$$\Delta_f H_m^\theta [C_{11}H_{13}N_9O_4, s] = \left[11\Delta_f H_m^\theta (CO_2, g) + 6.5\Delta_f H_m^\theta (H_2O, l) \right] - \Delta_C H_m^\theta [C_{11}H_{13}N_9O_4, s] \qquad (13)$$

Where

$$\Delta_f H_m^\theta \left(CO_2, g \right) = \left(-393.52 \pm 0.13 \right) kJ \cdot mol^{-1}, \quad \Delta_f H_m^\theta \left(H_2O, l \right) = \left(-285.83 \pm 0.04 \right) kJ \cdot mol^{-1},$$

$$\Delta_f H_m^\theta \left(HCl_2, g \right) = \left(-92.307 \right) kJ \cdot mol^{-1}$$

(CHEN et al., 2009; Duane, 2000; George et al., 2006; WANG et al., 2002; ZHOU et al., 2010). The standard molar enthalpy of formation for imidacloprid, NIM and NMP are calculated to be –(616.12)kJ·mol-1, –(20.41) kJ·mol-1 and 1789.94 kJ·mol-1, respectively, based on the standard molar enthalpies of combustion.

In the literature (CHEN et al., 2009), that the standard molar enthalpy of combustion $\Delta_c H_m$ is (-5153.9 kJ·mol-1) for naphthalene agrees very closely with experimentally derived value of (-5158.43 kJ·mol-1) in the work, the relative error is 0.088%. The result shows that $\Delta_c H_m$ value of reliability prediction is superior.

2.5 The specific heat capacity of imidacloprid and some nitrogenous organisms

The specific heat capacity of imidacloprid could be measured by means of DSC-60 Differential Scanning Calorimeter in the hermetically sealed chamber. The conditions of scanning: α-Al₂O₃ is used as the reference material，scanned area is between room temperature and melting temperature of the sample measured，sample mass is about 5mg，heating rate is 5℃·min-1. The specific heat capacity is measured at least three times. Fig.2 shows the relationship between the specific heat capacity with temperature for the substances measured. The results indicate that a sequence of the specific heat capacity for the substance determined at same temperature is NIM, imidacloprid, benzoic acid, NIM. And the higher temperature is, the bigger the specific heat capacity is for the substances of nitrogenous organisms measurated. At the same time, the bigger the relative molecular weight is for the nitrogenous organisms, the bigger the specific heat capacity is also. Relationship between the specific heat capacity and temperature can be obtained with the least square method at solid phase states, and represented by Eq.s (14) to (17) (CHEN et al., 2009).

$$C_p(\text{imidacloprid}) = 2.04708 - 0.01949T + 5.77744 \times 10^{-5}T^2 \tag{14}$$

$$(R^2 = 0.99559, \ SD = 0.034)$$

$$C_p(\text{NIM}) = 2.56469 - 0.01224T + 2.26134 \times 10^{-5}T^2 \tag{15}$$

$$(R^2 = 0.98341, \ SD = 0.01001)$$

$$C_p(\text{NMP}) = 92.03739 - 0.86937T + 0.00272T^2 - 2.7657 \times 10^{-6}T^3 \tag{16}$$

$$(R^2 = 0.9916, \ SD = 0.02746)$$

$$C_p(\text{benzoic acid}) = 11.62525 - 0.07464T + 1.33277 \times 10^{-4}T^2 \tag{17}$$

$$(R^2 = 0.99495, \ SD = 0.02768)$$

Where R is the multiple correlation coefficient, SD is the standard deviation. The abovemented logistic equations accord with the statistical precision in mathematics so that it is believable.
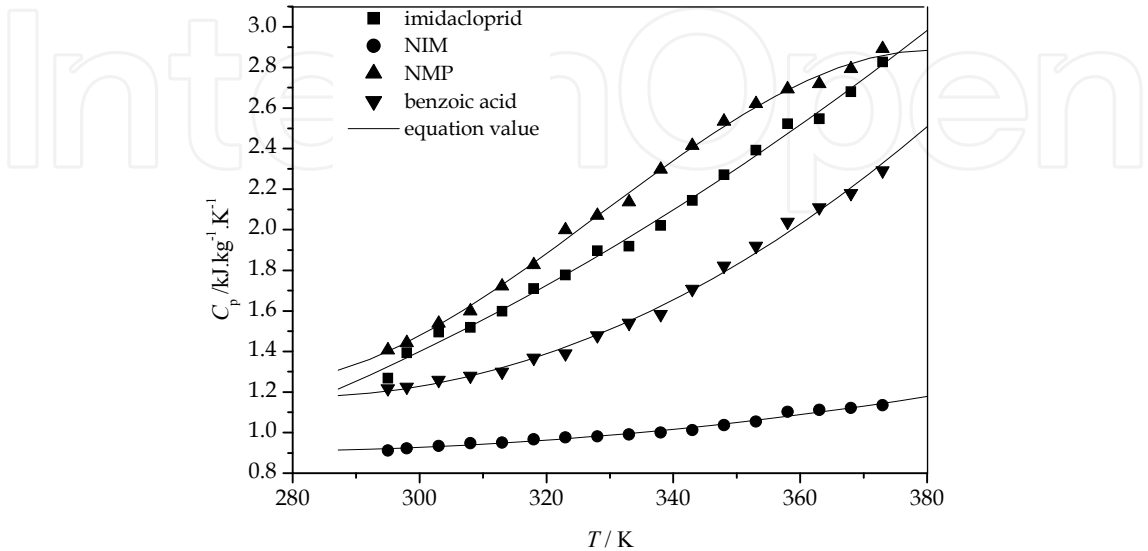

Fig. 2. Change curve specific heats as temperature for different matters

2.6 Melting temperature and the melting enthalpy of imidacloprid and some nitrogenous organisms

The melting temperatures and melting enthalpies of imidacloprid, NIM, NMP could be measured by DSC. The values of them are given to be 416.8K, 495.13K, 423.85K， and -109.93, -265.55, -102.22 J·g⁻¹, respectvely, in Fig.3. The thermal decomposition of the substances have been studied by thermogravimetric analysis. The results of thermal decomposition (in Fig.4~6) show that the heat stability of NIM and NMP is not good because they are decomposed as soon as melting, but imidacloprid has good heat stability. The decomposition temperature is, respectively, 525.10K, 495.13K, 450.25K for imidacloprid, NIM, NMP(CHEN et al., 2009) .

In conclusion, the thermodynamic properties of imidacloprid, NIM, NMP are listed in table 1.

Substances	T_m/K	ΔH_m J·g⁻¹	T_d/K	$\Delta_c H_m^\theta$ /kJ·mol⁻¹	$\Delta_f H_m^\theta$ /kJ·mol⁻¹	C_p=a+bT+cT^2+dT^3/kJ·kg⁻¹·K⁻¹			
						a	b	c×10⁵	d×10⁶
imidacloprid	416.80	109.93	525.10	5536.34	-616.12	2.04708	-0.01949	5.77744	0
NIM	495.13	265.53	495.13	2017.64	-20.41	2.56469	-0.01224	2.26134	0
NMP	423.85	102.22	450.25	7976.55	1789.94	92.03739	-0.86937	272	-2.7657

Table 1. The thermodynamic properties of imidacloprid, NIM and NMP
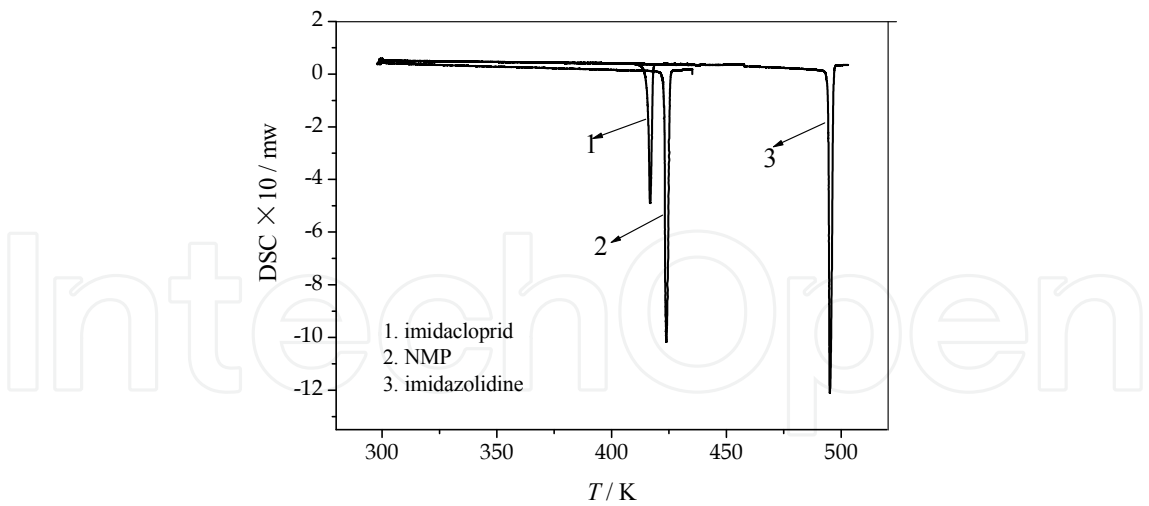
Fig. 3. The DSC melting curve of imidacloprid , NIM and NMP
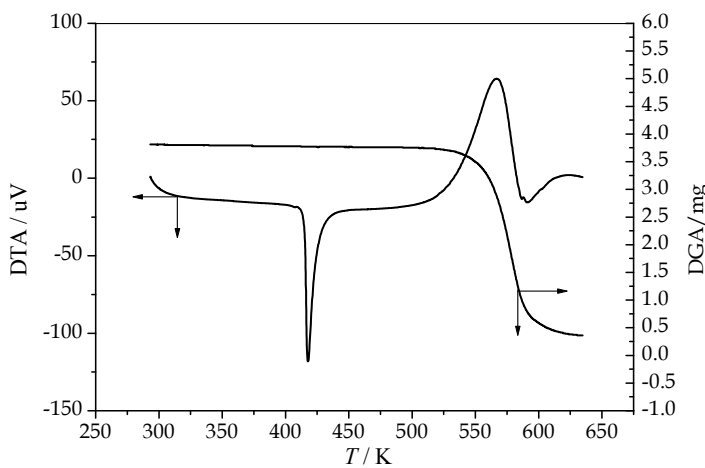

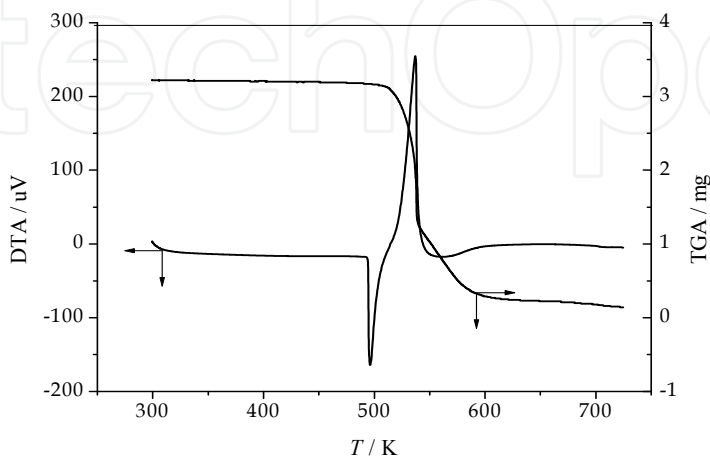
Fig. 4. The DTA-TGA curve of imidacloprid
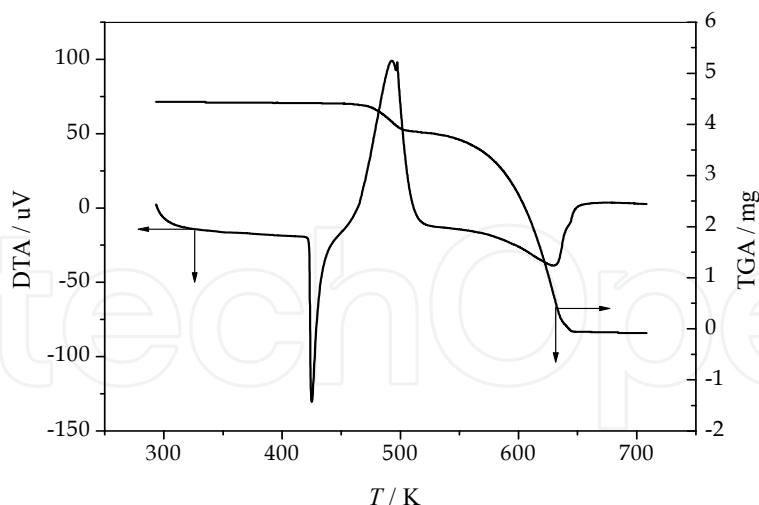

Fig. 5. The DTA-TGA curve of NIM

Fig. 6. The DTA-TGA curve of NMP

3. The mixed crystal of imidacloprid

The spatial disposition is different for the molecule or atom of substance in crystal lattice when they are crystallized. The reason is that the intermolecular bonding manner take place change and make different crystal structures formed by effect of various factors on crystallization precess, that is polymorphism. Only that the substance is dissolved or is melted make the lattice structure change can the polymorphism disappear. Therefore, this necessitated field experiments to study on pharmaceutical polymorphism is in favour of establish biological activity and bioavailability of chemical compound, can promote corresponding technology optimization, selection of the route of administration and dosage form, enhance the pharmaceutical quality and stability(WANG, 2005).

3.1 The method of polycrystallinity transformation
3.1.1 The recrystal method

Recrystallization can prepare corresponding crystal form by using different solvents, such as non-polar solvent aether, petroleum ether, chloroform, benzene, and polar solvent water, acetic acid, pyridine, as well as medium polar solvent methanol, alcohol, acetone and the mixture of organic solvent and water. To change and control the conditions of crystallization, such as concentration, temperature, and the rate of crystal, can obtain different crystal form (XIU, 1996). Only suitable solvent is used can the main crystal form be obtained.

3.1.2 The melting method

In general, the crystal form of low melting is able to translated into the crystal form of higt melting temperature at a suitable temperature. So we can use the melting method by heating the crystal form of low melting to reach an aim of crystal form transformed. For example, metoclopramine has a couple of endothermic peaks by using differential thermal analysis(DTA), which is 125 to129℃ and 147 to 150℃, respectively. The first peak is solid – solid transforming endothermic peak of which metoclopramine (I) change crystal form (II) ,

another is solid –liquid endothermic peak of crystal form (II). If the substance is heated 15min at 135℃, the secongd peak will only appear when reusing differential thermal analysis(DTA). It shows that metoclopramine (I) could be quickly changed into crystal form (II) as long as above metoclopramine (I) melting temperature(XIU , 1996).

3.1.3 The sublimation method
Pharmaceutical is put into an evaporating dish, covered with the glass hopper, heated little and little, a large number sublimated crystal can be get in upper and border of the glass hopper. The method can make pyrimethaimine (crystal form A) transformed into crystal form (B) (ZHANG , 1995).

3.1.4 The smashing and grinding method
When using the smashing and grinding method，strong mechanical force made the surface crystal structure of crystal grain diminish and the local energy level of particle surface increase, so that lead to the misalignment and boundary deformation of crystal form. Commonly, the metastabletype crystal form could be changed into the stability type of crystal. There is also an exception to this rule, such as anhydrous caffieine is apt to make stability type transform into metastabletype when it is smashed and grinded (Pirttimaki Jukka and Laine Ensio, 1994).

3.2 Determine to imidacloprid polymorphism
To make clear a crystal substance is whether there is in polymorphism, the methods are commonly used as (1) melting pointmethod; (2) Thermal analysis; (3) X-ray diffraction; (4) infrared spectrometry; (5) nuclear magnetic resonance method. The polymorphism of imidacloprid has been determined by using thermal analysis method. The DSC melting curves of imidacloprid before and after crystal formation changed show in Fig. 7 and Fig. 8
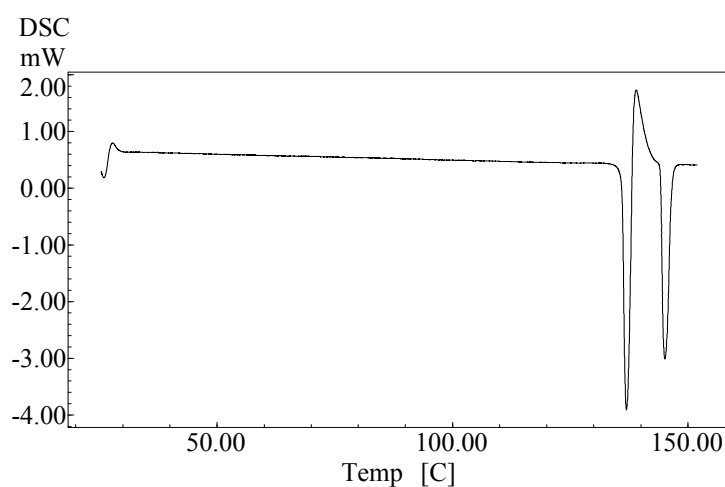

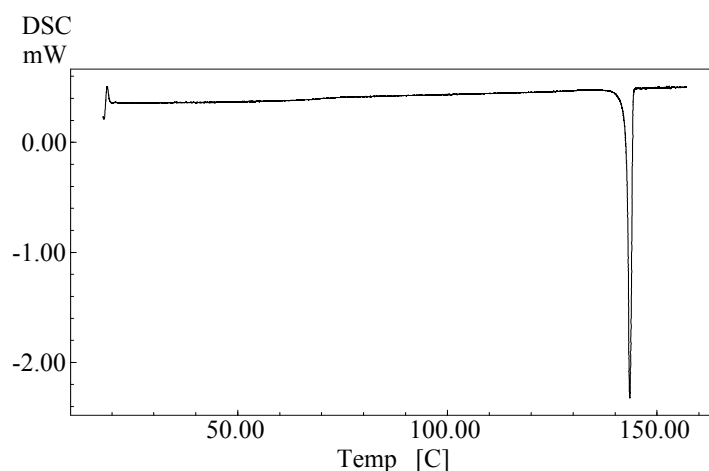Fig. 7. The DSC melting curve of imidacloprid before changed crystal formation

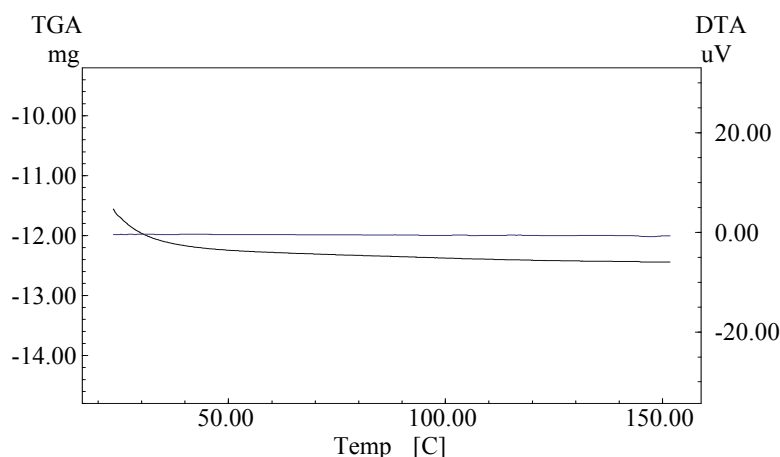Fig. 8. The DSC melting curve of imidacloprid after changed crystal formation

Fig. 9. The TGA melting curve of imidacloprid before and after recrystal

It is observed that there are two endothermic processes at 136.13℃ to 138.29℃ and 144.37℃ to 146.23℃ , and has a strong exothermic process in 138.29℃ to 144.37℃ according to Fig.7. Combining with Fig.9, there is no a significant change for TGA curve at 136.23℃ to 146.23 ℃, i.e. no weightlessness, so it show that the first peak is solid –solid transforming endothermic peak of which imidacloprid (I) change into crystal form (II) , another is solid – liquid endothermic peak of crystal form (II) in Fig.7.

By means of the recrystal method, imidacloprid could be dissolved in boiling water, then dissolved out crystal when it is cooled. This recrystal sample has been analyzed by DSC, in Fig.9, only there is a solid–liquid endothermic peak. And the TGA curves of imidacloprid are same before and after recrystal. The result indicates also that the crystal form of imidacloprid has been changed into a single form by solvent processing.

4. Crystallization metastable zone of imidacloprid in organic solvents

4.1 The solubility and supersolubility of imidacloprid

Materials. The process of recrystallization for imidacloprid is designed according to its the physical and chemical properties and obtained the solubility data in the laboratory

previously. The purity of imidaclaprid is analyzed by the melting point method, differential scanning calorimetry and high performance liquid chromtography. The simple physical method that is boiling water is used for transfering the mixed crystallization into a single crystal. Eventually, the purity of products meets the requirements of the factory for the first grade products(over 99%). Ethanol, acetone, 2-butanone, dichloromethane and 1,2-dichoroethane used for the experiments were of analytical reagent grade. Distilled deionized water of HPLC grade is used.

Apparatus and Procedure. The solubility and supersolubility of imidacloprid in different solvents is measured by the synthetic method (dynamic method). The laser monitoring observation technique is used to determine the dissolution temperature of the solid-liquid mixture of known composition. The laser monitoring system consists of a laser generator, a photoelectric transformer, and a light intensity display. The experiments are carried out in a jacketed glass vessel with a magnetic stirrer, a constant temperature (± 0.02 K) is maintained at the required temperature by circulating water through the outer jacket from a thermoelectric controller. The vessel has a perforated rubber cover plate to prevent the solvent from evaporating, through which a mercury glass thermometer is inserted into the inner chamber of the vessels for the measurement of the temperature. The uncertainty of temperature is ± 0.05 K at least.

Solvents for the solubility and supersolubility of measurement are prepared using an electronic balance with an accuracy of ± 0.0001 g. Predetermined amounts of imidacloprid and the solvents are weighed and transferred into the vessel. The contents of the vessel are heated very slowly at rates $1℃·h^{-1}$when the system would arrive balance. In the early stage of the experiment, the laser beam is blocked by the unsolved particles of imidacloprid in the solution, so the intensity of the laser beam penetrating the vessel is lower. The intensity increased gradually along with the increase of the amount of imidacloprid dissolved. When the last portion of imidacloprid just disappeared, the intensity of the laser beam penetrating the vessel reached the maximum, and the temperature is recorded, and the solubility expressed in mole fraction is calculated as follows

$$x_1 = \frac{\dfrac{m_1}{M_1}}{\dfrac{m_1}{M_2} + \dfrac{m_2}{M_2}} \tag{18}$$

In which m_1 and m_2 represent the masses of solute and solvent. M_1 and M_2 are the molecular weights of solute and solvent.

The contents of the vessel are heated continuely and temperature is rise 2 to 3℃ when the solid solute is dissolved completely. Then the contents of the vessel are cooled slowly at rates 4 to $5℃·h^{-1}$ by temperature of circulating water controlled through the outer jacket. The cooling rate is not too quickly toensure thermometer value in accord with them of actual system. When the last portion of imidacloprid just appeared, the intensity of the laser beam penetrating the vessel minished suddenly, and the temperature is recorded and obtain the supersolubility of the solute. The difference in temperature is expressed to be the crystallization metastable zone at the concentration.

4.2 The relationship of both the solubility and supersolubility with temperature for imidacloprid

Extraction-crystallization process is frequently used for the separation and purificaton of imidacloprid in industry. The relationships of both the solubility (w) and supersolubility

(w^*) with temperature have been showed in Fig.10 and Fig.11 for imidacloprid in ethanol, acetone, 2-butanone, dichloromethane and 1,2-dichoroethane (ZHOU et al., 2010). They indicate that the solvent of having the most solubility is 2-butanone at same temperature, and in turn, acetone, dichloromethane, 1,2-dichoroethane and ethanol. So 2-butanone can used as extraction agent, and ethanol can used as washing agent to eliminate impurities of which are liable to dissolve in imidacloprid. In common with dissolution rule for a lot of crystal systems, it is found that the solubility and supersolubility of imidacloprid in solvents increase with temperature increase.
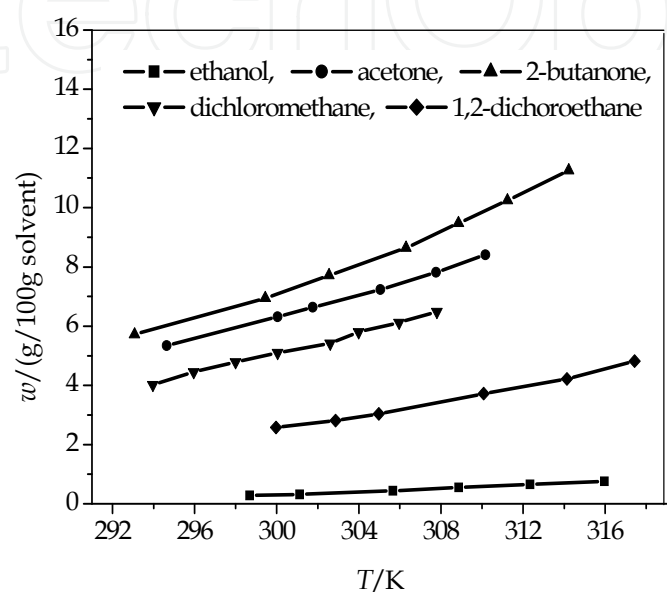

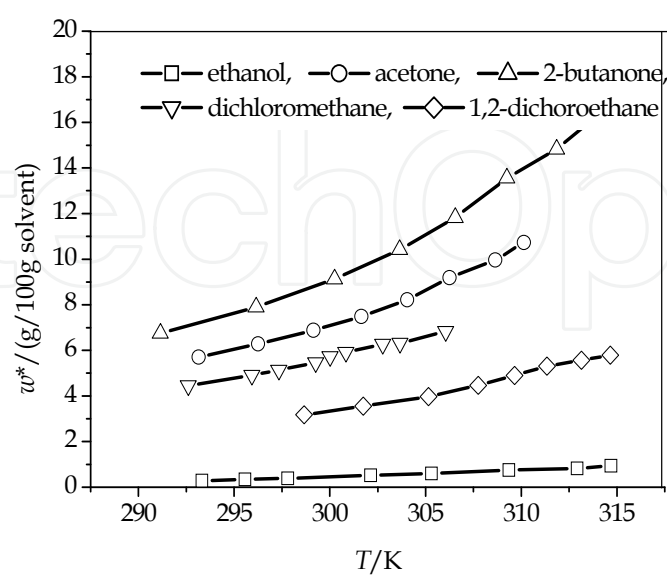
Fig. 10. THe solubility of imidaclprid in organic solvents

Fig. 11. THe supersolubility of imidaclprid in organic solvents

4.3 Crystallization metastable zone width of imidacloprid

In order to produce crystals with a specified purity and crystal size distribution at minimum cost, it is necessary to operate the crystallizer at the optimum supersaturation within the metastable zone. In generally, only the actual metastable zone of substance is known can the nucleation and the rate of crystallizing process be controlled in industry production (ZHOU et al., 2002; AN et al., 2007). The operational condition of crystallization must be controlled within metastable zone to ensure the quality of the crystal.

The metastable zone width is an experimentally measurable quantity and it depends mainly on the cooling rate, temperature, concentration, presence of impurities and mechanical effects. The metastable zone width is expressed as a maximum undercooling ΔT_{max} , which is given by

$$\Delta T_{max} = T_s - T_n \tag{19}$$

In which T_n and T_s are respectively, the temperatures corresponding to the onset of nucleation and the saturation. The relation of maximum supersaturation to the maximum undercooling can be expressed by

$$\Delta w_{max} = \int_{T_p}^{T_s} \left(\frac{dw^*}{dT} \right) dT \tag{20}$$

Since the maximum undercooling is generally not very large, the temperature dependence of dw^*/dT can be assumed constant over the temperature range examined. Thus, the maximum supersaturation can be siven by the following equation (Soloway et al., 1978):

$$\Delta w_{max} = \left(dw^* \middle/ dT \right) \Delta T_{max} \tag{21}$$

Where w^* is the equilibrium concentration of substance in soild-liquid phase，dw^*/dT is the slope factor of some temperature point in the curve of relation between solubility and temperature.
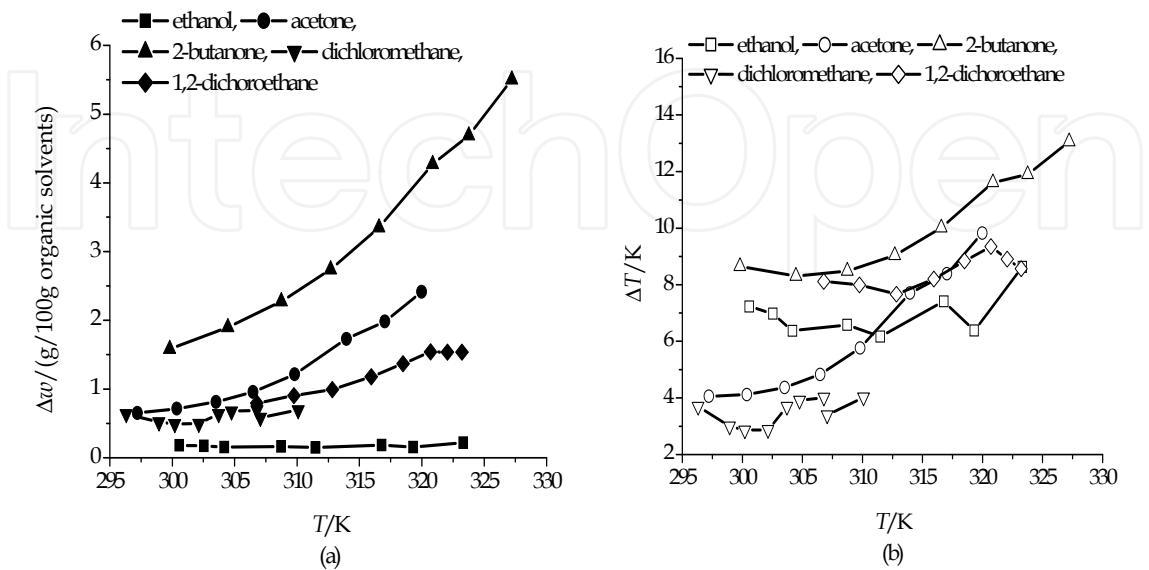

Fig. 12. The metastable zone width of imidacloprid in organic solvents

The saturate and supersaturate characteristics of imidacloprid in ethanol, acetone, 2-butanone,dichloromethane and 1,2-dichoroethane at different temperature are investigated by using laser detection technique. The crystallization metastable zone width of imidacloprid in mentioned above solvents are also determined. The solubility, super-solubility and crystallization metastable zone width (Δw) of imidacloprid in mentioned above solvents increase with temperature rising, and those properties of imidacloprid in 2-butanone are high compared with other solvents. The crystallization metastable zone width (ΔT) of imidacloprid is about 4.4℃，5.8℃，1.2℃，1.8℃ and 2.4℃ in 2-butanone , acetone , dichloromethane, 1,2-dichoroethane and ethanol at the same agitation rate, respectively, in Fig.s 12(a), (b). (ZHOU et al., 2010)

4.4 The solid-liquid equilibrium data of binary and ternary organic systems for imidacloprid+2-nitroaminoimidazoline +NMP by DSC

A complete data obtained by DSC of solid-liquid equilibriums(SLE) for (MIP+ NIM), (IMIP + NMP), (NIM + NMP) and (NIM + NMP+ IMIP) systems are reported to solve the problems of separation and purification in the production of imidacloprid. (ZHOU et al., 2011)

Procedure. Products (purity ≥99 .00%) were used directly. A series of binary systems of IMIP+ NIM, IMIP + NMP, NIM + NMP were prepared in the following method. The samples were weighed by electronic analytical balance (type BS110S, Germany) with the accuracy of ±0.1mg. Usually, the sample is prepared as follows: the compounds at some molar ratio are heated very slowly inside a glass cell above the melting temperature of the major component. Then the liquefied sample with continuous stirring was solidified. The solvent-soluble method was selected for obtained an intimate mixture sample to avoid the substances sublimation or decomposition above the melting temperature of the major component. The sample at some molar ratio was put into amount of organic solvent. Then the solution was stirred continuously, heated very slowly to ensure crystals dissolved. And the glass cell was put into vacuum dryer at constant temperature 45℃ until the solvent was evaporated completely. The solidified sample was grinded to be powdery in a glass mortar box with mortar pestle before the sample was kept in a desiccator with silica gel. Then a small amount of powdery solid (3 to 4mg) is taken and sealed in an aluminum pan of DSC-60 for the analysis.

Solid-liquid phase diagrams (SLPD) for binary systems were measured by DSC. Fig. 13 to 15 show the relationship for three binary systems between the experimental temperatures of solid–liquid equilibrium and molar fraction of components. There were eutectic point for the binary systems of (IMIP+NIM), (NIM+NMP) and (IMIP+NMP) because that there were the characteristics of which first peak appeared at the constant temperature(Teu), and the second peak temperature(Tsl) was change with molar ratio of components. The area of the eutectic peak in a DSC curve was affected by both the amount of the sample and heat of fusion of the melting component. The corresponding eutectic molar composition (xeu, 1) was 0.4962, 0.4229, 0.5506 , and the eutectic temperatures (Teu) was 402.41 K, 407.46 K and 383.13K, respectively.

Moreover, solid-liquid phase diagram (SLPD) was investigated for the ternary system of (NMP (1) +NIM (2) +IMIP (3)) mixtures with the above-mentioned method. The results showed that it was also the eutectic type, the molar eutectic composition (xeu, 1) and eutectic temperatures(Teu) is 0.3507 and 373.77K at x3/x2=1.857 , respectively, and are presented in Fig. 16.
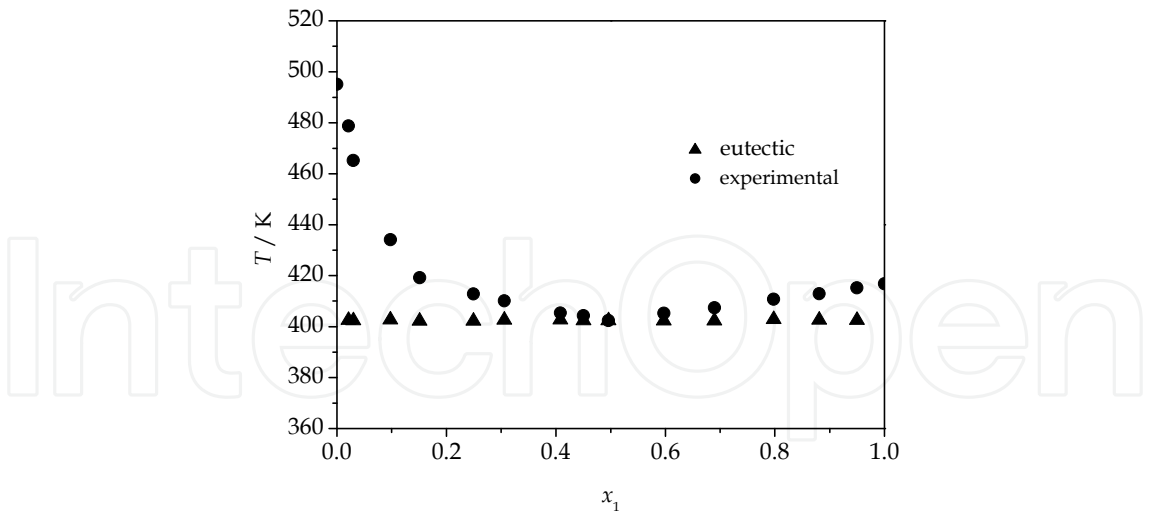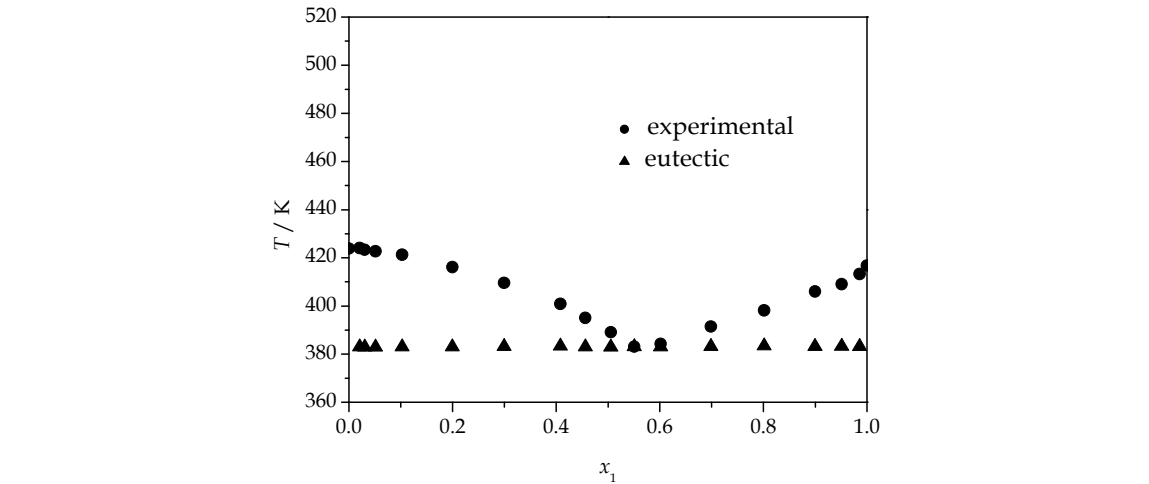
Fig. 13. Determined SLE for IMIP (1) + NIM (2)
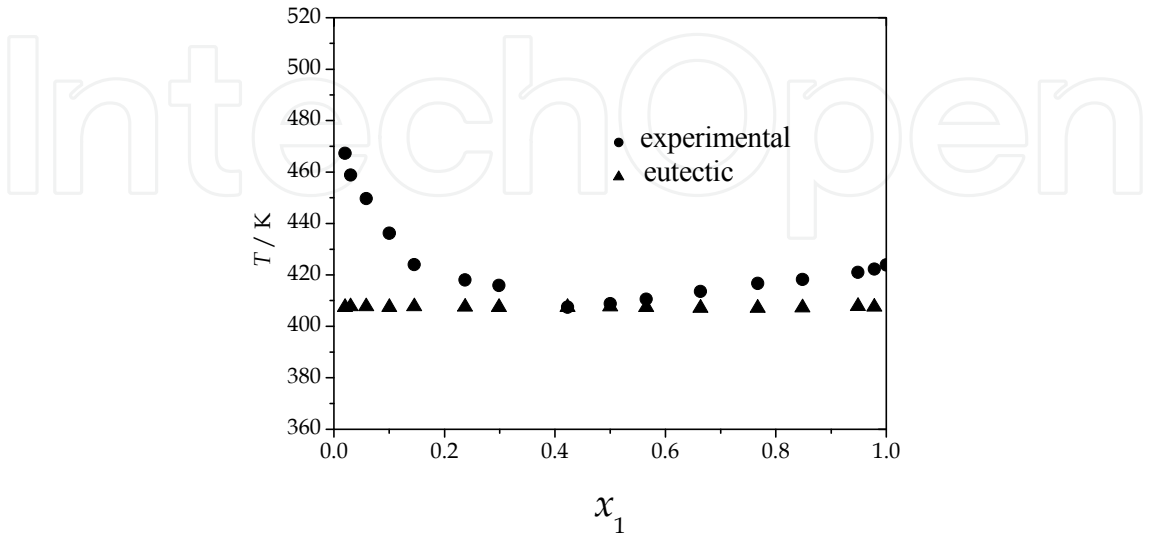

Fig. 14. Determined SLE for IMIP (1) + NMP (2)

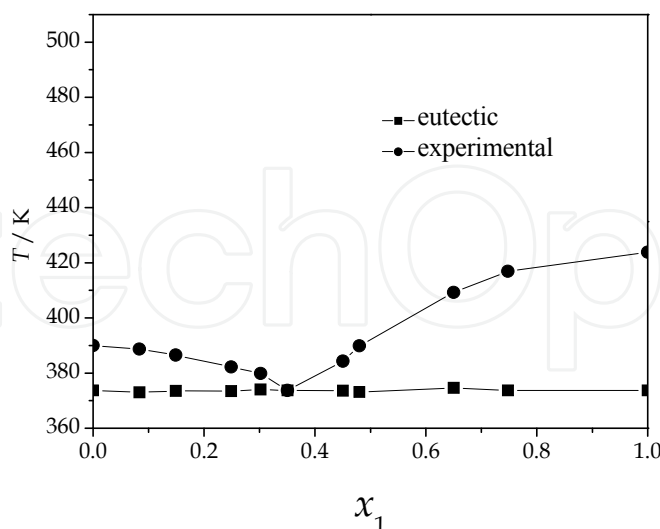Fig. 15. Determined SLE for NMP (1) + NIM (2)

Fig. 16. Phase diagram of SLE for NMP (1) + IMIP(2) + NIM (3)

5. Purification to the second powder concentrated of imidacloprid

So far, studies on to purifiy the second powder concentrated of imidacloprid have not been conducted. Because imidacloprid has the solid state with by-products, filtering method cannot reach an aim of it purified. For distillation, due to (i) imidacloprid has two kinds of crystal form and the boiling point of them is much the same; (ii) imidacloprid has high boiling point, long time and high temperature distillation process could make material easily coked and breaked down in the kettle bottom, so also cannot be used. If separation purification technology of crystallization is employed, not only it can simplify the process flow, is apt to do mass production, but also it improve the quality of crystal, can effectively reduce the production cost. Combined with the features of raw material of imidacloprid, this experiment method of solvent extraction - recrystallization could be used to separate and purify imidacloprid from the mixture of the second powder.

5.1 Experimental process flow
The experimental procedure is designed as follows on the basis of the preliminary experiments:
Experimental operation steps: (i)take a certain amount of raw material (second powder of imidacloprid) and put into a certain proportion of material and organic solvent A , stired at room temperature for 20 minutes to remove impurities and decoloring part; (ii)after filtrated, liquid is placed in bottle, filter cake dried is put in ing boiling water for 30 minutes; (iii) filtrated in heating state, cleaning filter cake dried with organic solvent B to remove the impurities of some soluble in B; (iv) according to steps (ii) after filter cake dried is put in organic solvent C and heat to 60℃, natural cooling until crystallization dissolved out. The crystal dried is used continuely recrystalled at least three times by the organic solvent C; (v) after filtrated, liquid is evaporated by totating evaporator to recover solvent, filter cake is imidacloprid.
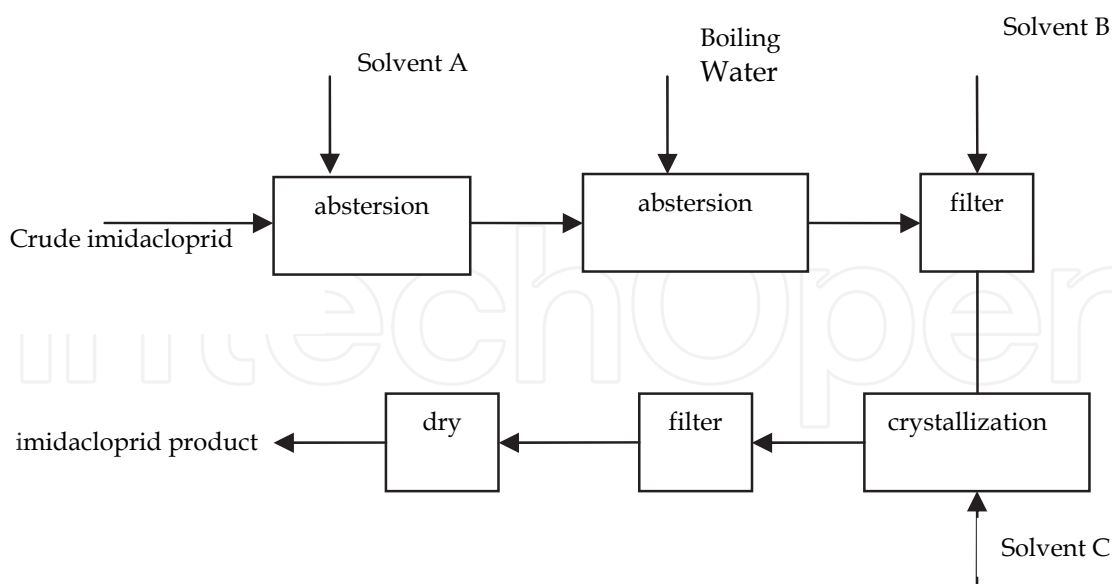
Fig. 17. The process chart of purification technology

5.2 Imidacloprid analysis

Imidacloprid used as standard substance (99.3%) 0.2 g (accurate to 0.1 mg) is put in a volumetric flash (50mL), add methanol to scale shake and make it completely dissolved . They are used as reserve. Using a pipette take 1mL to put in a volumetric flash (25mL) from above prepared reserve liquid, add a mobile phase make it diluted to scale, shake well, filtrate it with 45 μm filter membrane to prepare for analysis by HPLC. And this is identical for the sample of product imidacloprid.

Agilent1100 high-performance liquid chromatography, and 4.6×250mm，C18 DOS Chromatographic column, Chemical Station chromatographic data workstations, are used to analyzed product imidacloprid. Chromatographic analysis conditions are as follow: column temperature 25℃; methanol (gc) : pure water (double steamed water) = 40:60 (mL/mL) as mobile phase; velocity 1.0mL·min^{-1}; detected wavelength 260nm; sampling volume 20 0μL .

The external standard method is used to calculate an amount of imidacloprid, and can be expressed by

$$x = \frac{A_2 \times C_1}{A_1 \times C_2} \times 100\% \tag{22}$$

Where C_1, C_2 is , respectively, concentration of standard substance and sample product for imidacloprid（mg·L^{-1}）; A_1, A_2 is , respectively, chromatographic peak area of them. The analysis results are listed in table 2. Sensitivity experiments showed that the minimum amount of detecting substance found to be 5×10^{-14}g (SNR ≥ 3) in HPLC for standard imidacloprid solution in the above conditions, so that it is a method of high sensitivity, cando with the analysis of residues.

To determine the accuracy of the above methods, were analyzed at least five for a sample. The results showed the standard deviation is 0.28, and the coefficient of variation is 0.32%.

sample	Peak area ofHPLC	Product purity ,%
Standard sample of imidacloprid	1811.66	99.70
The first batch of imidacloprid products	1790.00	99.69
The second batch of imidacloprid products	1750.00	99.24
The third batch of imidacloprid products	1730.00	99.73

Table 2. The results of analytical reagent for the purity of the Imidacloprid and NMP

5.3 Polycrystal transformation

The separation extracted of imidacloprid can get the crystals mixed, but not satisfy a single effective crystal, so we could use recrystallization method to change its polycrystal. At present, it is still not seen have to imidacloprid more crystal phenomenon reported.

We can take the experimental procedure: (i) take a quantitative products to join in a glass container of which quantitative of cold water has been accommodated, heat to a nearly boiling in a boiling water bath, then take the container to make natural cooling at room temperature before filtrated and dried; (ii) take quantitative products to join separately in glass container where a quantitative of solvent B, methylene dichloride, 1,2-dichloroethane, chloroform, acetone, butanone, make solid dissolved completely after natural cooling to room temperature, recrystallization, and filtrated and dried ; (iii) analyze the product respectively with melting point instrument, thermoanalysis and HPLC on the qualitative and quantitative analysis.

According to the above experiment steps, the test results see table 3.

solvents	Crystal form	Content of imidacloprid ,%
boiling water	II	95.3
Solvent B	I	96.5
methylene dichloride	I	97.4
1,2-dichloroethane	I	96.4
chloroform	I	96.4
acetone	I	97.2
butanone	I	97.5

Table 3. Crystallization of mixed polymorph in deferent solvents

6. Conclusion

The enthalpy of combustion is a measure of the energy available from a substance. An appropriate knowledge of this value is essential for providing the basis of a commercial conttact between producer and user. Physical chemistry texts provide the necesssary tools needed to calculate the combustion enthalpy of pure substances. Using DSC differential scanning calorimetric, the thermodynamic basic data such as the melting point, melting enthalpie of taurine and specific heat capacity, were examined. Relationship between the specific heat capacity of taurine and temperature was accomplished with DSC. So these thermodynamic basic data are available for the exploiting new synthesis method, engineering design and industry production of imidacloprid. The results obtained in this work indicate that solubility of imidacloprid can be determined accurately by laser

monitoring technique. From the experimental data, it can be found that the solubility data of imidacloprid in the organic solvents over the temperature range from 293.00 K to 323.0 K increased with increasing temperature. And 2-butanone was a better solvent for the purification of imidacloprid. The solid-liquid equilibrium data of both three binary systems and one ternary system had been determined for imidacloprid, 2-Nitroaminoimidazoline, NMP by DSC. All of them are identified as eutectic type. The SLE data can be successfully applied on separation and purification processes of the substances.

There are two kinds of crystal forms for imidacloprid. Using the boiling water, the crystal form(I) can be transformed crstal form(II) for the imidacloprid product mixed crystal. The separation technology of extraction-crystallization employed the purity of imidacloprid could reached over 99% for the second powder concentrated of which is produced in industry process.

7. Acknowledgment

List of symbols

ε_{calar}	— the specific heat of calorimeter
C	— heat capacity，$J \cdot g^{-1} \cdot K^{-1}$ or $J \cdot mol^{-1} \cdot K^{-1}$
DS C	— DSC signal for sample curve at temperature, mV
H	— enthalpy，$J \cdot mol^{-1}$ or $kJ \cdot mol^{-1}$
m	— mass of sample, mg
M	— relative molecular mass of substance, or an amount of sample
n	— mole number
Q	— quantity of heat，$J \cdot mol^{-1}$ or $kJ \cdot mol^{-1}$
R	— the universal gas constant，$8.314J \cdot mol^{-1} \cdot K^{-1}$
t	— time，min
T	— Kelvin temperature，K
U	— energe of thermodynamics，$J \cdot mol^{-1}$ or $kJ \cdot mol^{-1}$
w	— mass fration, or mass number
x	— molar fration

Greek symbol

φ	— DSC output signal
Δ	— variable quantity

superscript

θ	— standard state
*	— phase equilibrium state

Subscript

c	— combustion heat
f	— reaction heat
lit	— literature
m	— material, or melting enthalpy
max	— the maximum value
n	— the onset of nucleation.
p	— constant pressure

s	— saturation
sample	— substance measured
standard	— substance used as the standard
V	— constant volume
0	— zero line of DSC

8. Reference

PAN, Y. M. ; CHEN, W. N.; MO, X. Z; et al, (2000) . Synthesis and simple in secticide test of the new pesticide 1-Substituent-2-Nitroiminoimidazolidines. Pesticides , Vol.39, No.1, (January 2000), pp. 16-17, ISSN 1006-0413

Kagabu, S.; Matsuno, H. (1997). Chloroni- cotinyl insecticides. 8. Crystal and molec- ular structures of imidacloprid and anal- ogous compounds. J. Agric. Food Chem., Vol. 45, No.1, (January 1997), pp.276-281, ISSN 0021-8561.

Heijbroek, W.; Huijbregts, A. W. M. (1995). Fungicides and insecticides applied to pelleted sugar-beet seeds—III. Control of insects in soil. Crop Protection, Vol. 14, No.5, (May 1995) , pp.363–366, ISSN 0261-2194

Huijbregts, A. W. M.; Gijssel P. D.; Heijbroek, W. (1995). Fungicides and insecticides applied to pelleted sugar-beet seeds -- I. Dose, distribution, stability and release patterns of active ingredients. Crop Protection, Vol. 14, No.5, (May 1995) , pp.355–362, ISSN 0261-2194.

KONG M. Z.; SHI X. H.; CAO Y. C.; ZHOU C. R. (2008). Solubility of Imidacloprid in Different Solvent. J. Chem. Eng. Data，Vol.53, No.3, (February 2008), pp.615-618, ISSN 0021-9568

Kojima, K. (1997). Compilation of group-contribution prediction of VLE and excess enthalpy. Fluid Phase Equilibria, Vol.136, No.1-2,(November 1997), pp.63-77, ISSN 0378-3812.

Matsuoka, M.; Ozawa, R. (1989). Determination of S-L Phase Equilibria of Binary Organic Systems by DSC. J. Crys. Growth, Vol.96, No.3, (July 1989), pp.596-604, ISSN 0022-0248.

Dalmazzone, D.; Kharrat, M.; Lachet, V. ; Fouconnier B. ; Clausse, D. (2002). DSC and PYT measurement. Journal of Thermal Analysis and Calorimetry, Vol.70, No.2, (February 2002), pp.493-505, ISSN 1418-2874.

Shibuya, H.,; Suzuki, Y..; Yamaguchi, K.; Arai, K; Saito, S. (1993). Measurement and prediction of solid-liquid phase equilibria of organic compound mixtures Fluid Phase Equilibria, Vol.82, (February 1993), pp.397-405, ISSN 0378-3812.

Khimeche, K.; Dahmani , A. (2006). Determination by DSC of solid–liquid diagrams for polyaromatic – 4,4'diaminodiphenylmethane binary systems. Journal of Thermal Analysis and Calorimetry, Vol.84, No.1, (January 2006), pp.47-52, ISSN 1418-2874.

DING, M.S.; XU, K.; JOW, T. R. (2000). Phase Diagram of EC—DMC Binary System and Enthalpic Determination of Its Eutectic Composition. Journal of Thermal Analysis and Calorimetry, Vol.62, No.1, (October 2000), pp.177-186, ISSN 1418-2874.

Yamamoto, I. (1996). Neonicotinoids- Mode of action and selectivity.Agrochem. Jpn. Vol.68, pp.1-14, ISSN 0919-5505.

LIU, C. L. (2000). World agricultural chemicals information manual, Chemical Industry Press, ISSN 750252786, Beijing, China

CHEN, L. L.; ZHOU, C. R.; SHI, X. H. (2009). Standard Combustion Enthalpy and Thermal Capacity of Some Nitrogenous Organisms. J. Chem. Eng. of Chinese Univ., Vol.23, No.5, (october 2009), pp.729-735, ISSN 1003-9015

ZHOU, C. R.; SHI, X. H.; CHEN, L. L.WANG H. F. (2011). The measurement of solid-liquid equilibrium data of binary and ternary organic systems for imidacloprid + 2-Nitroaminoimidazoline + NMP by DSC. Fluid Phase Equilibria, Vol.302, No.(1-2), (March 2011), pp.123-126, ISSN 0378-3812.

Duane, R. Kirklin, (2000). Enthalpy of combustion of acetylsalicylic acid. J. chem. Thermodymanics, Vol.32, No.6, (June 2000), pp.701-709, ISSN 0021-9614.

Sergey p. Verevkin, (1998). Experimental Enthalpies of Formation and Strain of the Methylated 1-Amino-2-phenylethanes. Strctural Chemistry, Vol.9, No. 1, (January 1998), pp. 1-7, ISSN 1040-0400.

JIANG, D.G., ZHOU, C. R.,WANG, F., et al. (2005). Study on standard combustion enthalpy and heat capacity for cis- and thans-1,2-cyclohexanediol . Chemical Engineering, Vol.33, No. 4, (April 2005) pp.63-67 , ISSN 1005-9954.

ZHOU, C. R. ;PENG, G. S.; ZHANG, Y. D.; et al. (2002). Study on thermodynamics properties of cis- and trans-1, 2-cyclohexanediol. J. Chem. Eng. of Chinese Univ., Vol.16, No. 3, （June 2002）pp.237-241, ISSN 1003-9015.

AN, N.; SHI, X. H.; ZHOU, C. R.; et al, (2007). Determination of the standard combustion enthalpy of trans-ferulic acid . Chemical Engineering, Vol.35, No.7, (July 2007) pp.43-44, ISSN 1005-9954.

George, W.; Gokel, D. (2006). Handbook of Origanic Chemistry, (2nd Edition), McGraw-Hill Education (Asia)Co. and Chemical Industry Press, ISSN 9787502585570 , Beijing, China

Wang, Z. L.; Zhou, Y. P. (2002) . Physical Chemistry, Higher Education Press , (4nd Edition), ISSN 7-04-010161-0, Beijing , China

ZHOU, C. R.; SHI, X. H.; KONG, W. L.; WANG, H. F. (2010). Study on Crystallization Metastable Zone of Imidacloprid in Organic Solvents. J. Zhengzhou University Natural Science Edition, Vol.42, No.4, (December 2010), pp67-70 , ISSN 1671-6841

WANG, Z. Q. (2005). Polymorphism and Drug Availability. Chinese Journal of Pharmaceuticals, Vol.36, No. 7, (July 2005), pp.442-446, ISSN 1001-8255

XIU, J. (1996). Studies on the Characteristics of Polymorphs of Metoclopramide. Journal of China Pharmaceutical University, Vol.27, No. 12, (December1996), pp.722-725, ISSN 1000-5048

ZHANG, X. S. (1995). Study on IR and Crystal of Pyrimethamine. Chinese Journal of Pharmaceutical Analysis, Vol.15, No. 1, (January 1995), pp.57-58, ISSN 0254-1793

Pirttimaki, Jukka; Laine, Ensio. (1994). The transformation of anhydrate forms of caffeine at 100%RH and RH. Eur J Pharm Sci, Vol.1, No. 4, (February 1994), pp. 203-208, ISSN 0928-0987

Soloway, S. B.; Henry, A. C.; Kollmeyer, W.D.; et al. (1978). Advaces in Pesticide Science, Part 2, ed. (2nd Edition), H gessibueheler, GT Brooks and P C Kearney, Pergamon Press, pp206-217, Oxford
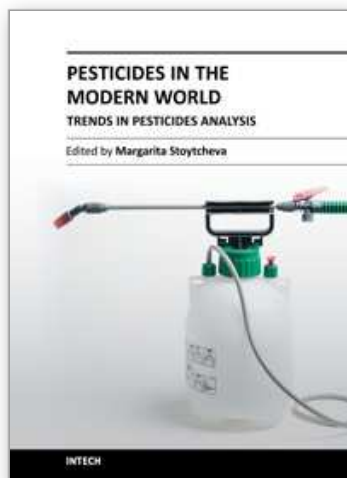
Pesticides in the Modern World - Trends in Pesticides Analysis

Edited by Dr. Margarita Stoytcheva

ISBN 978-953-307-437-5

Hard cover, 514 pages

Publisher InTech

Published online 21, October, 2011

Published in print edition October, 2011

The book offers a professional look on the recent achievements and emerging trends in pesticides analysis, including pesticides identification and characterization. The 20 chapters are organized in three sections. The first book section addresses issues associated with pesticides classification, pesticides properties and environmental risks, and pesticides safe management, and provides a general overview on the advanced chromatographic and sensors- and biosensors-based methods for pesticides determination. The second book section is specially devoted to the chromatographic pesticides quantification, including sample preparation. The basic principles of the modern extraction techniques, such as: accelerated solvent extraction, supercritical fluid extraction, microwave assisted extraction, solid phase extraction, solid phase microextraction, matrix solid phase dispersion extraction, cloud point extraction, and QuEChERS are comprehensively described and critically evaluated. The third book section describes some alternative analytical approaches to the conventional methods of pesticides determination. These include voltammetric techniques making use of electrochemical sensors and biosensors, and solid-phase spectrometry combined with flow-injection analysis applying flow-based optosensors.

INTECH

open science | open minds