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STRUCTURAL EVOLUTION OF THE METASTABLE POLYMORPH OF PARA-CRESOL

Time-dependent polymorphic transformations of para-cresol, a compound known for its multiple crystalline forms and diverse applications, were investigated. The behavior of the metastable form III of para-cresol, which is obtained as a result of relaxation of the metastable form II, was examined using differential scanning calorimetry. Thermal analysis showed that the transformation of the metastable form III of para-cresol is slow, heterogeneous, and probabilistic in nature. The multi-peak decomposition of the melting curves indicates the coexistence of three polymorphs in the samples for a relatively long time. These results demonstrate that metastable forms of para-cresol can persist far longer than would normally be expected for thermodynamically unfavorable phases.

Keywords: para-cresol, differential scanning calorimetry, polymorphism, phase transitions, relaxation.

1. Introduction

Polymorphism is the ability of a substance to exist in different crystalline forms that differ in molecular packing and intermolecular interactions [1]. *Para*-cresol (*p*-cresol) is one of such compounds and is of considerable scientific and practical interest due to its various applications, particularly as an antioxidant and disinfectant in pharmaceuticals [2]. Batisai *et al.* [3] demonstrated that *p*-cresol exists in two crystalline forms, I and II, and determined their crystal structures. They reported that the stable phase (form I) melts at $T_{\text{melt}} = 309.2$ K, whereas the metastable phase (form II) melts at $T_{\text{melt}} = 307.9$ K. It was also noted in [3] that once form II is formed, it readily converts to form I when stored at room temperature for several days. The transition from an unstable state (form II) to the most stable state (form I) is known as Ostwald's rule [4].

Various techniques have been used to identify *p*-cresol polymorphs, including crystallography [3, 5], thermal analysis [3], and spectroscopy [6–12]. In our recent work [11], we showed that forms I and II of *p*-cresol can be obtained simply by cooling melted *p*-cresol under our cooling conditions. Crystallization of the stable phase (form I) develops preferentially above 260 K, while crystallization of the metastable phase (form II) occurs below 260 K. The stable form I melts at 309.3 K, and metastable form II melts at 307.4 K, in contrast to the method reported in [3], where forms I and II were obtained from chloroform (form I) and acetone (form II) solutions, respectively. Most notably, we unexpectedly discovered a third crystalline form of *p*-cresol (form III), which melts at 302.9 K, in addition to forms I and II.

After obtaining metastable form II from the melt at low temperature, we obtained a behavior that contradicts Ostwald's rule [4]: instead of transforming into the stable phase, metastable form II transformed overnight into another metastable phase (form III). This represents a rare case in which a metastable form does not convert to the stable form.

The conversion of metastable form II into metastable form III was also confirmed by our FT-IR

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spectroscopy studies, in which we examined the FT-IR spectra and temperature dependences of the stable and two metastable crystalline forms of *p*-cresol from 300 K to 12 K [11, 12]. This raises the question of what subsequently happens to form III. Will its transformation involve the formation of additional metastable phases, or will it eventually convert to the stable phase?

This question is important because *p*-cresol is used in the pharmaceutical industry, where the phase stability is crucial and the presence of different polymorphs can significantly alter various physico-chemical properties of the substance. Understanding these transformations is essential for designing stable forms of pharmaceutical products. No similar study on long-term treatments of *p*-cresol polymorphs has been conducted previously. These considerations motivated our investigation of the time-dependent structural evolution of form III. Specifically, we sought to determine how form III changes over time, how long the transformation process takes place, and which phase it ultimately form? To answer these questions, we used differential scanning calorimetry (DSC) to study the temperature evolution of form III.

2. Experimental

p-Cresol, the *para*-isomer of methylphenol, was purchased from Aldrich (99% purity) and was used without further purification. *p*-Cresol is an aromatic organic compound with the chemical formula C_7H_8O or, more precisely, $CH_3C_6H_4OH$. Its structure consists of a six-carbon aromatic ring, with the hydroxyl group at position 1 and the methyl group at position 4 of the ring (Fig. 1).

Calorimetric measurements were performed using differential scanning calorimeter (Perkin-Elmer DSC 8000) equipped with the CLN2 low-temperature accessory. Samples of ~ 7 mg were enclosed in aluminium sample pans, hermetically sealed using a sample encapsulating press. Measurements were performed under dry helium to improve the thermal conductivity. Liquid nitrogen was used as a coolant, and the measurements were carried out in the temperature range of 104–350 K. To calibrate the equipment, both in temperature and enthalpy, certified indium was used. All measurements comprised three heating curves, to test the reproducibility among them.

3. Results

As briefly noted in the Introduction, metastable form III is obtained only as a result of the transformation of form II, and form II itself can be obtained by strong supercooling of liquid *p*-cresol. Crystallization of metastable form II from the melt is favored at temperatures lower than those at which form I crystallizes [11]. With this in mind, the samples were prepared as follows. A sufficiently large amount of the substance was placed into a container, melted, and then the container with the melt was rapidly immersed in liquid nitrogen. This low-temperature treatment promoted crystallization into metastable form II. Based on the results of [11], it was expected that form II would transform into form III overnight. Therefore, the DSC measurements were started the following day. Three samples were taken from the container to ensure statistical reliability and their DSC curves were recorded (Fig. 2). The procedure was repeated two days later, and again two weeks later (Figs. 3 and 4, respectively). All measurements were carried out at a scanning rate of 10 K/min.

Fig. 2 shows the melting curves of three samples with masses of 7.06, 7.09, and 6.54 mg (curves 1,

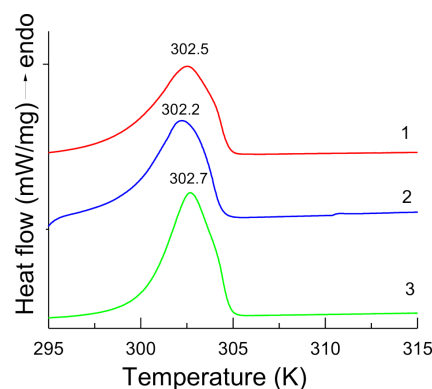
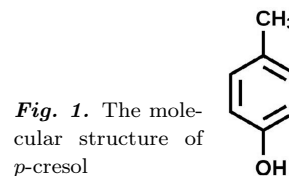


Fig. 2. DSC curves of the metastable form III of *p*-cresol recorded at a heating rate of 10 K/min. Details are given in the text

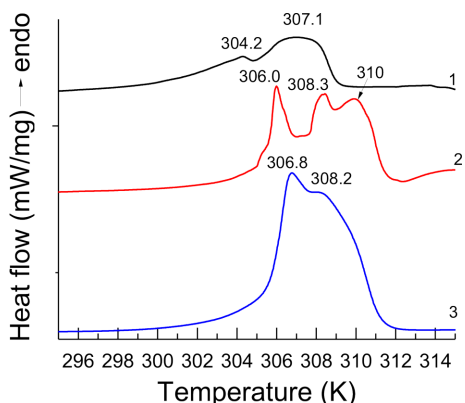


Fig. 3. DSC curves of the metastable phase III of *p*-cresol were obtained two days after its formation, at a heating rate of 10 K/min. Details are given in the text

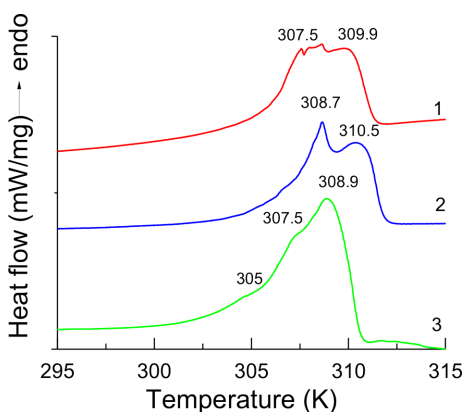


Fig. 4. DSC curves of the metastable form III of *p*-cresol were obtained two weeks after its formation, at a heating rate of 10 K/min. Details are given in the text

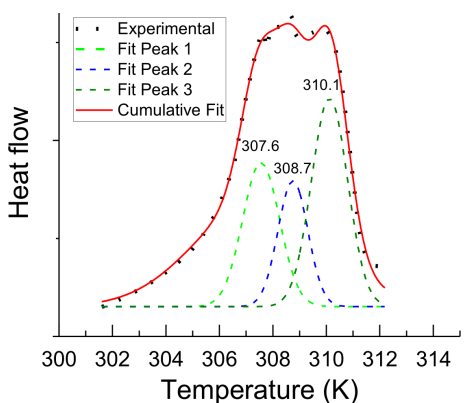


Fig. 5. Gaussian decomposition of the melting curve 1 from Fig. 4. Experimental data are plotted as black circles, and the fit is plotted as a solid line. Dashed lines represent Gaussian bands used to fit the experimental spectra

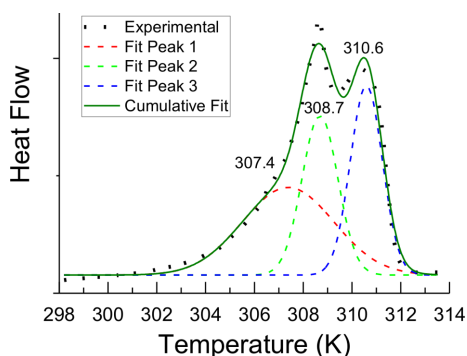


Fig. 6. Gaussian decomposition of the melting curve 2 from Fig. 4. Experimental data are plotted as black circles, and the fit is plotted as a solid line. Dashed lines represent Gaussian bands used to fit the experimental spectra

2, and 3, respectively). The first sample (curve 1) melts at $T_{\text{melt}} = 302.5$ K with an enthalpy $\Delta H = 73.56 \text{ Jg}^{-1}$, the second one melts at 302.2 K with an enthalpy $\Delta H = 66.93 \text{ Jg}^{-1}$, and the third sample melts at 302.7 K with an enthalpy $\Delta H = 90.15 \text{ Jg}^{-1}$. As expected, the melting temperatures correspond to those of form III. Thus, the metastable form III of *p*-cresol is uniformly distributed throughout the volume of the container.

Fig. 3 presents the melting curves of three samples taken from the container two days later, with masses of 7.17, 7.29, and 6.74 mg (curves 1, 2, and 3, respectively). In DSC curve 1 for the first sample, two peaks appear at 304.2 and 307.1 K, with a total melting enthalpy $\Delta H = 80.92 \text{ Jg}^{-1}$. DSC curve 2 for the second sample shows three melting peaks at 306.0, 308.3 and 310.0 K, with a total melting enthalpy $\Delta H = 109.27 \text{ Jg}^{-1}$. Curve 3 of the third sample shows two melting peaks at 306.8 and 308.2 K, with a total melting enthalpy $\Delta H = 98.75 \text{ Jg}^{-1}$.

Fig. 4 shows the melting curves of samples taken from the container after two weeks with masses of 7.59, 7.48, and 7.15 mg (curves 1, 2, and 3, respectively). The first sample (curve 1) melts over a broad range from 307 to 310 K, with a total melting enthalpy $\Delta H = 85.5 \text{ Jg}^{-1}$. DSC curve 2 for the second sample exhibits two melting peaks at 308.7 and 310.5 K, with a total melting enthalpy $\Delta H = 96.45 \text{ Jg}^{-1}$. Curve 3 of the third sample shows the main melting peak at 308.9 K accompanied by two shoulders on the low-temperature side at 305.0 and 307.5 K, with a total melting enthalpy $\Delta H = 72.23 \text{ Jg}^{-1}$.

4. Discussion

We analyze the transformation of the metastable form III of *p*-cresol using the data presented in Figs. 2–4. It is evident that the transformation of metastable form III into other phases is slow, heterogeneous, and probabilistic in nature.

Immediately after the formation, form III is distributed relatively uniformly throughout the entire container (Fig. 2, curves 1–3). However, after two days, form III transforms into a mixture of polymorphs, and the exact composition varies between samples taken from different locations (Fig. 3). In the first sample, the two melting peaks at 304.2 and 307.1 K indicate the presence of forms III and II, respectively (Fig. 3, curve 1). In the second sample, the melting peak of form III is absent, while a peak at 310 K, indicates the presence of stable form I (Fig. 3, curve 2). Additionally, curve 2 shows a melting peak at 306 K, corresponding to a previously unknown polymorph (Fig. 3, curve 2). The third sample contains two polymorphs with melting points at 306.8 and 308.2 K (Fig. 3, curve 3).

After two weeks, the polymorphic composition shifts further toward more stable forms II and I (Fig. 4, curves 1 and 2). However, even after two weeks, the metastable polymorphs had not completely transformed into a stable polymorph. In the third sample, there is no melting peak at 310 K at all, indicating the absence of stable form I (Fig. 4, curve 3). This result is rather unexpected, demonstrating that metastable phases can persist for an extended period.

Figs. 5–7 show Gaussian multi-peak fitting decomposition of the melting curves 1–3 from Fig. 4. The software package Origin 5.0 was used. Experimental curves are shown as black circles. The fit is plotted as a solid line. Dashed lines represent Gaussian bands used to fit the experimental curves. The fits confirm that even two weeks after the formation of form III, the contents of the container remain a mixture of several polymorphs. The first sample contains polymorphs melting at 307.8, 308.7, and 310.1 K (Fig. 5). The second sample contains polymorphs melting at 307.4, 308.7, and 310.6 K (Fig. 6). It can be observed that although their experimental melting curves 1 and 2 in Fig. 4 differ, according to the decomposition results, these samples contain the same polymorphs in different proportions, with the sta-

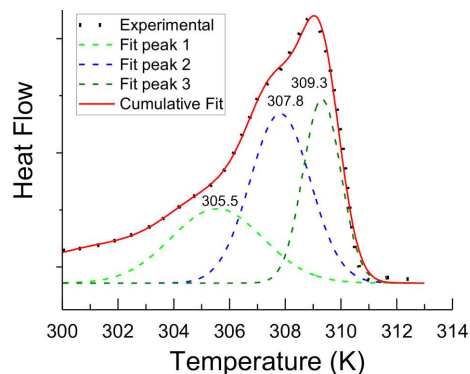


Fig. 7. Gaussian decomposition of the melting curve 3 from Fig. 4. Experimental data are plotted as black circles, and the fit is plotted as a solid line. Dashed lines represent Gaussian bands used to fit the experimental spectra

ble form I ($T \sim 310$ K) predominating (Figs. 5 and 6, Fit peak 3). The fitting peaks at 308.7 K probably correspond to the incomplete transformation of form II into a stable form I. The third sample contains polymorphs with melting points at 305.5, 307.8, and 309.3 K (Fig. 7). The fitting peak 1 at 305.5 K likely corresponds to an incompletely transformed residue of form III, distinguishing this sample from the others.

5. Conclusion

In conclusion, our extensive DSC measurements demonstrate that the transformation of metastable form III of *p*-cresol is slow, heterogeneous, and probabilistic in nature. Although form III is initially distributed uniformly, its conversion into more stable polymorphs proceeds irregularly, leading to significant sample-to-sample variations even within the same container. After two weeks, the *p*-cresol sample still consists of a mixture of several polymorphs. These findings indicate that metastable forms of *p*-cresol can persist far longer than would normally be expected for thermodynamically unfavorable phases. The results obtained improve our understanding of the thermodynamics and kinetics of polymorphic transitions in *p*-cresol and are useful for applications where the phase stability is important.

1. J. Bernstein. *Polymorphism in Molecular Crystals* (Oxford University Press, 2002).
2. H. Fiege. Cresols and Xylenols. In *Ullmann's Encyclopedia of Industrial Chemistry* (Wiley-VCH, 2007).

3. E. Batisai, V.J. Smith, S.A. Bourne, N.B. Báthori. Solid state structures of *p*-cresol revisited *Cryst. Eng. Comm.* **17**, 5134 (2015).
4. W.Z. Ostwald. Studien über die Bildung und Umwandlung fester Körper. *Z. Phys. Chem.* **22**, 289 (1897).
5. P.C. Bois. Structure du *p*-crésol à basse température. *Acta Crystallogr. B* **26**, 2086 (1970).
6. M.M. Ilczyszyn, M. Ilczyszyn, M. Selent. Structure and stability of *p*-cresol – xenon clathrate: Raman spectroscopy study *J. Mol. Struct.* **1212**, 128147 (2020).
7. H. Takeuchi, N. Watanabe, I. Harada. Vibrational spectra and normal coordinate analysis of *p*-cresol and its deuterated analogs. *Spectrochim. Acta A* **44**, 749 (1988).
8. J.H.S. Green, D.J. Harrison, W. Kynaston. Vibrational spectra of benzene derivatives – XIV: Mono substituted phenols. *Spectrochim. Acta A* **27**, 2199 (1971).
9. R.J. Jakobsen. The vibrational spectra of *p*-cresol. *Spectrochim. Acta* **21**, 433 (1965).
10. Balachandran, M. Murugan, A. Nataraj, M. Karnan, G. Ilango. *Spectrochim. Acta A* **132**, 538 (2014).
11. J. Baran, N.A. Davydova, M. Drozd. New phase transition of *p*-cresol studied by DSC analysis and FT-IR spectroscopy. *Spectrochim. Acta A* **326**, 125252 (2025).
12. J. Baran, N.A. Davydova, M. Drozd, V.Ya. Reznichenko. Spectroscopic studies of conformational polymorphism in 4-methylphenol. *Low Temp. Phys.* **51**, 162 (2025).

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СТРУКТУРНА ЕВОЛЮЦІЯ МЕТАСТАБІЛЬНОГО ПОЛІМОРФУ ПАРА-КРЕЗОЛУ

Досліджено залежні від часу поліморфні перетворення пара-крезолу, сполуки, відомої своїми численними кристалічними формами й різноманітним застосуванням. Поведінка метастабільної форми III пара-крезолу, яка утворюється в результаті релаксації метастабільної форми II, досліджувалася за допомогою диференціальної сканувальної калориметрії. Термічний аналіз показав, що перетворення метастабільної форми III пара-крезолу відбувається повільно, гетерогенно й має ймовірнісний характер. Розкладання кривих плавлення на багато піків вказує на співіснування трьох поліморфів у зразках протягом досить тривалого часу. Ці результати демонструють, що метастабільні форми пара-крезолу можуть зберігатися набагато довше, ніж звичайно очікується для термодинамічно нестійких фаз.

Ключові слова: пара-крезол, диференціальна сканувальна калориметрія, поліморфізм, фазові переходи, релаксація.