

Solubility study and thermal stability analysis of calcium propionate

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Abstract

The solubilities in water within a temperature range between 10°C and 80°C and the thermal behavior of the frequently used food additive calcium propionate were investigated in order to clarify deviations in published data. Furthermore, solubilities in ethanol/water mixtures with the ethanol fraction range between 0% and 80% at 30°C were measured. Material purified by recrystallization was used to exclude that impurities have no influence on the solubility data. Consideration of the dissociation process of calcium propionate in aqueous solution shows that the particular shapes of the solubility curves can not be attributed to changes in pH. The thermal stability and phase behavior of calcium propionate was investigated using TG-DSC and DSC combined with temperature-resolved XRPD. The substance initially provided turned out to be a mixture of the monohydrate and the anhydrous calcium propionate. The solid phases obtained under equilibrium conditions in the solubility experiments in water and also in the mixed solvents were identified as the monohydrate. The conversion of the monohydrate to anhydrous calcium propionate is connected with a dehydration enthalpy of $\sim 46.5 \text{ kJ mol}^{-1}$. A new polymorph of the anhydrous calcium propionate was found and characterized. The results obtained in this study provide a better understanding of calcium propionate and support the development of improved crystallization processes.

Key words: calcium propionate; solubility; solid-state characterization; thermal analysis

1 Introduction

Calcium propionate appears as a white crystalline solid or powder with odors resembling propionate acids [1, 2]. It is mainly used as preservative in a broad variety of products, especially in the manufacturing of baked goods. The antimicrobial action of calcium propionate is based on its dissociation process to produce undissociated propionate acid, which could diffuse across the cytoplasmic membrane and on the one hand releases a proton to increase the energy consumption of the organism for removing the proton out, while on the other hand accumulates in the cell and blocks metabolism by inhibiting enzymes [3]. Therefore the pH value of the substance to be preserved is of great importance to the antimicrobial action [2]. Typical concentration of calcium propionate used in bread producing is 0.2% based on the flour weight [4]. No flavor or lip feel is detectable when the concentration of calcium propionate in aqueous solutions ranges between 30 and 50 mM, which could be used with chlorinated water as a sanitary treatment for fresh-cut melon [5]. Calcium propionate is more widely used than propionic acid because it is easier to handle the solid salt than the corrosive liquid acid [3, 4]. The common method employed for the preparation of calcium propionate is the neutralization of propionic acid with calcium hydroxide in aqueous solution. The methods to achieve the solid products include spray drying, evaporation crystallization in aqueous solution or a solvent-free process, which could cause environment pollution and

high costs or strong aggregation problems [6]. So improving the solid-liquid separation process, which includes the design of an optimal crystallization process to produce calcium propionate with desired CSD, shape and solid-state form as well as with low energy consumption and simplified procedures, is of crucial importance.

Crystallization is a key technology used as a purification and isolation process both on a laboratory and an industrial scale in a wide variety of chemical engineering fields. The solids produced in crystallization processes based on different operation could have various physical and chemical properties such as crystal size distribution (CSD), crystal morphology and solid-state form, which have a strong effect on the final product properties (e.g. dissolution behavior, bioavailability, density, etc.), as well as on the efficiency of the downstream processes (such as filtration, drying etc.) [7, 8]. It is well known that equilibria between solid and liquid phases are of crucial importance for the design of industrial crystallization processes [9]. Solubility values of the substance in a specified solvent provide information of supersaturation, which mainly determines the crystallization dynamics such as nucleation and growth behavior, as well as yield. If a single solvent cannot satisfy the request of the crystallization process, the combination of two or more intermiscible solvents would be chosen and the solid phases in the mixed solvents are necessary to be determined [10].

The solubility data of calcium propionate in water was determined by Krasnicki in 1887, who obtained the results from experiments made by heating and also by cooling a solution to the desired saturation temperature (heating and cooling method rep.) [11]. In 1902 Lumsden [12] determined solubility data and found a broad deviation from the results of Krasnicki. In Lumsden's solubility experiments, a thermostat to achieve a constant temperature was suggested, and a device used to remove the suspensions out with subsequent vacuum filtration to obtain the saturated solid-free liquid was devised [12, 13]. Lumsden [12] also analyzed the solids in contact with the solution by weighing the mass of solids and then converting the calcium propionate into calcium sulfate and subsequently weighing the mass of calcium sulfate. His results showed that the solids contained 1 mole of water. Furthermore, Walker and Fyffe [14] also obtained quite different results from those of Krasnicki for determining the solubility of barium acetate. They also verified that Krasnicki's results for the higher temperature were not valid. In study of Seidel [15], Krasnicki's solubility results for barium acetate were considered as incorrect as well. Wing and Thompson [13] examined the solubility data of Krasnicki for barium propionate and got a significantly different solubility curve which was convex to the temperature axis, and not concave as Krasnicki described. Obviously in [16] the solubility of calcium propionate in water was cited from ref. [12]. One patent [17] describes that calcium propionate has got a solubility minimum at 55°C, while another one [6] expresses this minimum solubility to be at 50°C. To clarify the observed deviations of the solubility behavior, the comprehensive solubilities of calcium propionate in water were re-examined in this paper. XRPD were performed to characterize the solid-state form in solubility experiments.

It is well known that impurities may affect the solubility of a solute. Microimpurities can influence phenomena at crystal-liquid interfaces [9, 18]. In this work, the specific solubility behavior of calcium propionate raises obvious concerns regarding the effect of microimpurities on the solubility data. Since the purity of the substance received from the supplier was specified with > 98%, recrystallization of calcium propionate was performed to further increase the purity and to analyze the influence of the microimpurities on the solubility data.

It is clear now that the change of the pH value leads to a shift of the equilibrium of ionization process, which causes an increase or decrease of solubility of calcium propionate [19]. Thus the dissociation behavior of calcium propionate aqueous solution with regard to temperature was studied to analyze the effect of ionization process on the solubility of calcium propionate in water.

In order to evaluate the solid phase behavior at higher temperatures and also to obtain the information of occurrence of further solid phases, thermal behavior and solid phase identity of a substance should be analyzed. Researchers [20, 21, 22, 23] have studied the thermal properties of calcium propionate using TG, DTA, and DSC. However, the solid phase behavior of calcium propionate with respect to temperature is not clear and the identity of the solid phases is still missing. In this paper, thermal stability and solid phase behavior of calcium propionate was analyzed by simultaneous TG-DSC and separately performed DSC in a closed crucible both under dry helium. Complementary temperature-resolved XRPD studies were performed to elaborate the solid-state behavior and the phase identity at different temperatures.

2 Experimental

2.1 Materials and analytical methods

Anhydrous calcium propionate was purchased from ACROS ORGANICS Company, 98% + purity, CAS No. 4075-81-4. According to the impurities information provided by the supplier, the content of water insoluble materials and heavy metals in the substance purchased are less than 0.3% and 0.01%, respectively. Deionized water and ethanol (purity \geq 99.7%, VWR Chemicals) were used as solvents during solubility measurements. The substances were used as obtained.

X-Ray powder diffraction (XRPD) measurements were performed on an X'Pert Pro diffractometer (PANalytical GmbH, Germany) with Cu-K α radiation. XRPD scans were recorded in continuous mode with a step size of 0.017° and a counting time of 50 s per step over an angular range of 3-40° 2Theta. Samples were prepared on background-free sample holders. In order to analyze the phase behavior with respect to temperature, temperature-resolved XRPD measurements in a temperature range of 30-305°C were applied. A typical heating-cooling program is as follows: the samples were heated stepwise from 30°C to 305°C with a heating rate of 5 K/min, and subsequently cooled with a cooling rate of 5 K/min from 305°C to 140°C and 10 K/min from 140°C to 30°C. At certain temperatures (30°C, 140°C, 230°C, 305°C), the samples were kept isothermal for equilibrium and to measure the diffraction patterns at this temperature. The temperatures were selected on the basis of the DSC and TG-DSC results.

DSC and simultaneous TG-DSC measurements were performed on a DSC 131 and a Sensys Evo (both Setaram, France) system respectively. The samples were taken from an freshly opened bottle, carefully crushed in an agate mortar and about 12 mg thereof weighted into an Al-pan. The sample crucible is open for TG-DSC and closed for separately performed DSC. Samples are then subjected to heating from 30°C to 450°C with a heating rate of 5 K/min, while purging with helium at flow rates of 40 mL/min and 20 mL/min, respectively.

pH-values were measured using a pH meter (SevenExcellence, Mettler Toledo, Switzerland). It allows measurements of both pH value (\pm 0.002) and temperature (\pm 0.1°C). Calibration was performed before the measurements. Around 7 g calcium propionate and around 70 g deionized water were dissolved in a beaker under magnetic stirring. The temperature of the beaker was controlled using a double jacketed

vessel connected with a thermostat. A PT100 ($\pm 0.1^\circ\text{C}$) was used for in-line monitoring the temperature. At each point, the temperature measured by pH device and PT 100 was compared. In aqueous solution, calcium propionate dissociates into calcium and propionate ions. The latter is seen as the conjugate base of propionic acid. Ionized part can be calculated based on the values of pKa and pH of 10% calcium propionate aqueous solution (w/w) [24, 25].

Ion chromatography was performed on a DIONEX ICS-1100 system (Thermo Scientific, USA) to analyze the composition of the commercial substance and recrystallized materials in particular to identify and quantify potential ionic impurities, as e. g. Li^+ , NH_4^+ , K^+ cations and sulfate anions (that might form sparingly soluble salts with e. g. Ba or Sr present.). The columns used were IonPac CG16 (3 \times 50 mm) and IonPac CS16 (3 \times 250 mm), respectively. The eluent applied were 30 mM methanesulfonic acid solution and 4.5 mM Na_2CO_3 /1.4 mM NaHCO_3 solution at flow rates of 0.4 and 1.2 mL/min, respectively.

2.2 Solubility measurements of calcium propionate in water and ethanol/water mixtures

The solubilities of calcium propionate were measured gravimetrically with an isothermal method. The substance bought was used as the starting material. Around 100 g deionized water or ethanol/water mixtures were put in a 250 mL double jacketed crystallizer equipped with mechanical agitation and a thermostat. A PT 100 ($\pm 0.1^\circ\text{C}$) was used for in-line monitoring and adjusting a certain temperature for the solubility measurement. Temperature stability was $\pm 0.1^\circ\text{C}$. After the temperature was stable, excess solute was added gradually, and then the suspension was well mixed for at least 24 h. When the solid-liquid system had reached equilibrium, the wet solids separated from the suspension were directly analyzed by XRPD to check the solid-state form for correlation with the solute in equilibrium in the saturated solution. Solution was drawn using a syringe and filtered via a micro-filter, put in small vessels and dried in the oven at 150°C under atmospheric pressure for 4 h. The clear saturated solution and dried solids were weighted respectively. Similarly, the dried solids were analyzed by XRPD as soon as taken from oven. At each data point, the experiments were repeated for three times, and the relative deviations of solubility values were estimated to be less than 0.5%. Solubilities are then specified as g calcium propionate per 100 g solvent. Pure deionized water and solvent mixtures of ethanol and water with ethanol contents of 20%, 40%, 60% and 80% (w/w) respectively were used as solvents in the experiments. The solubilities in water were measured in a temperature range between 10°C and 80°C , in ethanolic solutions solubilities refer to 30°C .

2.3 Recrystallization of calcium propionate

Around 90 g original substance bought and 250 g deionized water were added into a crystallizer and dissolved under stirring for several hours by using a magnetic stirrer. The solution was filtered in order to remove the insoluble matter. The filtrate was then transferred to a glass beaker and put in the oven at 120°C under atmospheric pressure for a certain time. Then the temperature was decreased to 70°C and the beaker kept in the oven overnight. The solid-liquid suspensions were filtered and the filter cake was washed using 80% ethanol/20% water (w/w), then the solids were put into oven with 150°C for drying. The dry solid was weighed (18 g), analyzed by ion chromatography and used in solubility experiments in water at 30°C and 60°C .

3 Results and discussion

3.1 Solubilities in water

The solid phase should be properly characterized before and after the solubility measurement [26]. The powder patterns of solids from solubility measurements are shown in Fig. 1. The curve labelled with “bottle” refers to calcium propionate sampled from a fresh opened bottle bought from ACROS ORGANICS Company as presented before. The pattern shows three main sharp peaks at $\sim 7^\circ$, $\sim 8^\circ$ and $\sim 9^\circ$, and compared to the reference patterns of anhydrous calcium propionate and calcium propionate monohydrate [27, 28], the substance bought is clearly a mixture of both the anhydrous calcium propionate and the monohydrate. The curves of wet samples prepared from suspended solids during solubility measurements between 10°C and 80°C (labelled as “10-80°C wet” in Fig. 1) exhibit many characteristic peaks, for example the sharp peak at $\sim 7^\circ$. All patterns show the presence of the same phase, small shifts in the 2 Theta positions are caused by the sample preparation procedure (some mg of wet unground samples). Comparison of the patterns with data from reported literature [27] verifies that monohydrate is the stable phase of calcium propionate in aqueous solution from 10°C to 80°C . So the solubility data presented in the following relate to monohydrate (H) as solid phase. The dry samples included in Fig. 1 were obtained by putting the solid-free saturated solution into oven at 150°C for 4 hours under atmospheric pressure, that was combination of recrystallization to obtain solids and drying at the same time. The patterns of dry samples (labelled as “10-80°C dry” in Fig. 1) contain two sharp peaks at $\sim 8^\circ$ and $\sim 9^\circ$, indicating the dry samples were anhydrous calcium propionate (A) [28]. Thus, a drying method to achieve anhydrous calcium propionate can be derived then.

The solubilities of calcium propionate determined in this work and from literature [11, 12] are presented in Tab. 1 and illustrated in Fig. 2. It can be seen that all solubility curves are markedly convex to the temperature axis with minimal solubility values. The results from refs. [11, 12] indicate that the solubility decreases with increasing the temperature at low temperatures until reaching about 55°C . Above this temperature, the solubility increases monotonously. In this work the solubility decreased when the temperature was increased from 10°C to 45°C reaching a minimal value at about 45°C . Between 45°C and 60°C , the solubility values kept almost constant. Above 60°C , the solubility increased with increasing the temperature. The XRPD results shown in Fig. 1 verify that the solid-state form on the descending and ascending parts of the solubility curve is always the same, the monohydrate of calcium propionate.

It is found that our measured solubility values are lower than those in refs. [11, 12], with the Lumsden values [12] being the highest. By comparing our results with Lumsden's, we can find that relative deviations range from $\sim 2\%$ to $\sim 5\%$, e.g. at 55°C , the solubility values are 36.4 and 38.2 g/100 g water, respectively, with the deviation reached 4.8%. The deviation and possible causes are discussed in the following. First, in Lumsden's solubility experiments, the substance was obtained by the reaction of dilute propionic acid and calcium carbonate with the subsequent recovery of products by evaporating the liquid over a water-bath and drying in air [12, 13]. The purity of final products was not given. Possible acid residuals or other impurities could influence the solubility results. Also, the solubility of calcium propionate in ref. [12] was determined by converting the calcium propionate into calcium sulfate and subsequently weighing the mass of calcium sulfate. It is known that calcium sulfate occurs in three different forms: gypsum ($\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$), hemihydrate ($\text{CaSO}_4 \cdot 0.5\text{H}_2\text{O}$) and anhydrite (CaSO_4). The transition temperatures of gypsum-anhydrite and gypsum-hemihydrate vary within a range of $42\text{--}60^\circ\text{C}$ and $80\text{--}100^\circ\text{C}$ [28, 29], showing that anhydrite easily tends to moisture absorption. It is obvious that the

solubility result measured at a certain temperature point would be higher than the real one if solvates generated during weighing the mass of calcium sulfate.

The solubilities measured for the recrystallized substance are also shown in Tab. 1 and Fig. 2 (data at 30°C and 60°C). The results of ion chromatography showed that besides calcium ions only ~0.45% sodium ions were present in the original substance purchased. No other cations or anions in accessible amounts were detected. After recrystallization more than 68% of the sodium (residual content ~0.14%) and also the insoluble matter were removed as purification results. The relative deviation between the solubility data of the original substance bought from company and the recrystallized materials is 0.6% and 0.7% for the two temperatures, respectively. This agrees with “microimpurities may generally have an impact on phenomena at the crystal-liquid interface but not solubility data” that is illustrated in ref. [18]. Thus the original substance could be used for measuring the solubility of calcium propionate.

Fig. 3 shows the values of pKa of propionic acid calculated [24], values of pH measured, and values of ionized part of 10% calcium propionate in water (w/w) at different temperatures [25]. The values of pKa increase very slightly from 4.9 at 32°C to 5.0 at 76°C, while pH values are found to fluctuate at around 7.2 as the temperature increases. The part of propionate ionized form remains around 99.5% with the maximum value being 99.6% at 41°C. The results indicate that calcium and propionate ionized forms predominate in calcium propionate aqueous solution. It is worthwhile noted that the relative deviations of % ionized values at different temperatures are extremely small, with the maximum value being around 0.06%, further verifying the shape of the solubility curve of calcium propionate not be attributed to the change of pH.

The measured solubility data of calcium propionate monohydrate in water are fitted and could be expressed by the following quadratic equation:

$$\frac{C^i}{[g \text{ calcium propionate} / 100 g \text{ water}]} = 0.0019 \left(\frac{T}{^\circ\text{C}} \right)^2 - 0.2056 \left(\frac{T}{^\circ\text{C}} \right) + 41.82 \quad R^2 = 0.993 \quad (1)$$

3.2 Solubilities in ethanol/water mixtures

Results similar to works are observed investigating the solid phase behavior of calcium propionate in ethanol/water mixtures, as shown in Fig. 4. In all ethanol/water mixtures monohydrate is the stable phase in equilibrium. Thus the solubility data in ethanol/water mixtures relate to monohydrate as solid phase. Dry solids after recrystallization and drying of solution with ethanol fractions of 20%-80% (w/w) are anhydrous calcium propionate. However, when the solvent was changed to pure ethanol, the solids suspended in ethanol were mixture of the anhydrous calcium propionate and the monohydrate, with main portion being the anhydrous phase as in the starting material. The dry solids provided by recrystallization and drying of saturated ethanol solution show different phase behavior in pattern, for example, the splitting peaks rang between 8° and 9°, were not observed in the patterns of anhydrous and monohydrate or their mixture.

Fig. 5 shows the solubilities of calcium propionate in ethanol/water mixtures with fractions of ethanol of 0%, 20%, 40%, 60% and 80% (w/w) at 30°C. In comparison to the solubilities in pure water at 30°C, the solubility of calcium propionate monohydrate in ethanol/water mixtures decreases significantly with increasing ethanol content, e.g. only 16.93 g calcium propionate is dissolved at an ethanol fraction of

60%, which is around 55% of the original value in water. It is worthwhile to be noted that the solubility of calcium propionate shows a strong dependence on the fraction of ethanol and decreases nearly linearly with the ethanol mass fraction, indicating the possibility of an anti-solvent crystallization process by adding ethanol into an aqueous solution to create supersaturation. This crystallization process will be investigated in future studies.

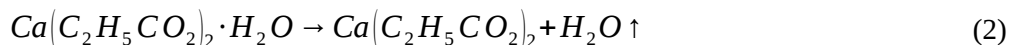
3.3 Thermal stability and phase behavior of calcium propionate

In order to investigate the solid phase of calcium propionate with respect to temperature, temperature-resolved XRPD measurements following the temperature profile as presented before were performed and the results are shown in Fig. 6. When the temperature was increased from 30°C to 140°C, the characteristic peak of the monohydrate at $\sim 7^\circ$ disappeared, that is the hydrate water is released and only anhydrous material remained. The dehydrated form remained stable at 230°C, but when heating to 305°C, a new pattern appeared, with a very sharp peak observed between 8° and 9° . This pattern looks similar to those of dry solids recrystallized from pure ethanol (Fig. 4). This might be a new polymorph of the anhydrous phase, but this cannot be derived clearly before discussing the TG-DSC results. With decreasing the temperature the backward transition was observed.

Fig. 7 presents the TG-DSC curve of original calcium propionate (as bought), Fig. 8 the related DSC curve measured separately in a closed crucible both under dry helium.

The first endothermic effect between 67°C and 112°C is connected with a mass loss of 0.82% observed in the TG plot shown in Fig. 7. Based on the XRPD curves in Fig. 6, it is linked to the loss of the hydrate water. That means although the substance was sold as anhydrous calcium propionate it contained around 9% mass percentage of the monohydrate. As already mentioned above calcium propionate easily tends to moisture absorption. A second drastic mass loss started from around 342°C, causing a mass loss of around 27% until the final measurement accomplished. The decomposition process of calcium propionate has been studied by E. Gobert-Ranchoux and Niu [20, 23]. During this process, gaseous product 3-pentanone $C_2H_5CO C_2H_5$ was emitted and calcium carbonate $CaCO_3$ was left. Because the heating process was stopped when the temperature reached 450°C, only parts of anhydrous salts decomposed into calcium carbonate, causing a smaller mass loss of around 27% than the theoretical one of 46.3%.

The heat flow curves shown in Fig. 7 and Fig. 8 can be divided into four stages. The first stage contains an endothermic peak with peak temperature of 83°C and 92.6°C, respectively. This peak corresponds to the loss of hydrate water. This dehydration process could be confirmed by temperature-resolved XRPD measurements. As shown in Fig. 7, the XRPD curve at 30°C changed to the one at 140°C when the substance was heated from 30°C to 140°C. The phase change is shown below:

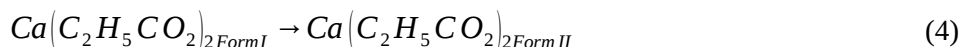


The dehydration process caused a heat effect of $\sim 21 \text{ J g}^{-1}$ (mean value). The dehydration enthalpy of calcium propionate monohydrate can be obtained based on the heat consumed and the weight fraction of the monohydrate in the samples. E. Gobert-Ranchoux [20] stated that the dehydration heat value measured by DTA was $52.97 \text{ kJ mol}^{-1}$. In this work the mean value of the dehydration enthalpy is calculated as 46.5 kJ mol^{-1} using TG-DSC and DSC in a closed crucible, which is close to the reported value [20].

As the temperature increased, small exothermic peaks were observed with peak temperatures of 198.9°C and 211.7°C in TG-DSC and 191.3°C and 211.8°C in separately performed DSC, respectively. These exothermic peaks are not accompanied by a mass loss shown in Fig. 7. Comparison between XRPD curves at 140°C and 230°C in Fig. 6, show that there is no change of the particular solid phase in that temperature region. Thus these effects can be attributed to change in crystallinity, i.e. recrystallization of some amorphous phase still present after dehydration. Since the sample was a heterogeneous mixture of monohydrate and anhydrate, no ‘homogeneous’ recrystallization occurred but rather two small events. A similar effect was also observed by E. Gobert-Ranchoux [20], according to the following reaction:



A second endothermic peak is observed at 272.1°C (T_{peak}) in TG-DSC (Fig. 7) and at 272.6°C (T_{peak}) in separate DSC (Fig. 8). The heat consumed is 4.4 J g⁻¹ and 5.4 J g⁻¹ for TG-DSC and DSC, respectively. No mass loss is observed from TG curve shown in Fig. 7. The study of temperature-resolved XRPD indicated a solid-phase transition occurring between 230°C and 305°C. By combining the results of TG-DSC, DSC and temperature-resolved XRPD, it can be concluded that a polymorphic transformation of the anhydrous phase occurred and a new polymorph was obtained. The new polymorph is represented as anhydrous calcium propionate Form II (simplified as Form II in Fig. 9) compared to anhydrous calcium propionate Form I (Form I in Fig. 9). Thus this polymorphic transformation of the anhydrous calcium propionate of Form I → Form II is:



As shown in Fig. 6, when the temperature decreased from 305°C to 230°C, the backward transition of this polymorphic transformation was observed, showing the transition process between Form I and Form II to be reversible; thus these two polymorphs are related enantiotropically.

The largest endothermic transition, which is sharp and narrow with peak temperature of 394.5°C in TG-DSC and 393.5°C in DSC, corresponds to the melting of anhydrous calcium propionate. A series of narrow and fluctuating peaks follows this sharp effect, characterizing the subsequent decomposition process of the sample, confirmed also by the rapid mass loss in the TG curve.

The XRPD patterns of the four different materials investigated in this work together with their preparation procedure are summarized in Fig. 9.

4 Summary and Conclusions

In this work the solubility and thermal behavior of calcium propionate was investigated. In solubility experiments an isothermal method was applied combined with gravimetric measurements. Solubilities of calcium propionate in water in the range between 10°C and 80°C were determined. The solubility in water decreases when the temperature is increased from 10°C to 45°C. Between 45°C and 60°C, the solubility values kept almost constant. Above 60°C, the solubility increases with increasing temperature. Material purified by recrystallization was used in additional solubility experiments at 30°C and 60°C to evaluate possible effects of small amounts of impurities. It is turned out that the materials purchased and used without further purification (specified with > 98% purity) could be used for solubility determination of calcium propionate.

The dissociation process of 10% calcium propionate aqueous solution (w/w) was also studied at different temperatures. The results obtained show that the ionized forms remain stable in the temperature range between 32°C and 76°C. The particular shape of the solubility curve of calcium propionate is not attributed to changes of pH. Solubilities of calcium propionate in ethanol/water mixtures with the ethanol fraction range between 0% and 80% (w/w) at 30°C were also measured. It is shown that the solubility decreases nearly linearly with increasing the fraction of ethanol. These results suggest applying low energy consuming crystallization processes using mixed solvents.

XRPD was used for allocating the solid-state form in solubility experiments. It is verified that monohydrate is the stable phase of calcium propionate in aqueous solution from 10°C to 80°C and at 30°C in ethanol/water mixtures within the ethanol fraction range between 0% and 80% (w/w).

Thermal behavior and solid-phase identity of calcium propionate was analyzed using TG-DSC and temperature-resolved XRPD. The thermal behavior of calcium propionate in dry helium could be divided into four parts: dehydration process (i.e. conversion of the monohydrate to the anhydrous calcium propionate), recrystallization of residual amorphous calcium propionate in the anhydrous phase formed, polymorphic transformation of the anhydrous phase and melting with subsequent decomposition. It is turned out that the substance purchased was a mixture of the anhydrous calcium propionate and the monohydrate. The dehydration enthalpy of the monohydrate was measured about 46.5 kJ mol⁻¹. A new polymorph of the anhydrous phase was found and characterized (anhydrous calcium propionate Form II). The polymorphic phase transition is reversible and occurs at ~270°C (onset temperature of TG-DSC/DSC). The two polymorphs are related enantiotropically. Fusion occurred at ~391°C (onset temperature of TG-DSC/DSC) directly followed by decomposition.

The results obtained in the current study contribute to better understand calcium propionate. They are seen as of importance for the development of improved crystallization processes providing calcium propionate.

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Figure legends

Figure 1. Overlay of XRPD patterns of calcium propionate solid phases from solubility measurements in water. Temperatures refer to saturation temperatures in solubility measurements. “10-80°C wet” represents XRPD curves of solids in equilibrium in solubility experiments; “10-80°C dry” represents XRPD curves of dry solids obtained by putting the solid-free saturated solution into oven at 150°C for 4 hours under atmospheric pressure; “Bottle” represents the XRPD curve of the original substance bought. Below available powder diffraction patterns of calcium propionate monohydrate from ref. [27] and anhydrous calcium propionate from ref. [28] are plotted for comparison. (PDF database, PANalytical GmbH, Germany). For easy identification of the present phases, symbols “H” for Monohydrate and “A” for Anhydrate are introduced.

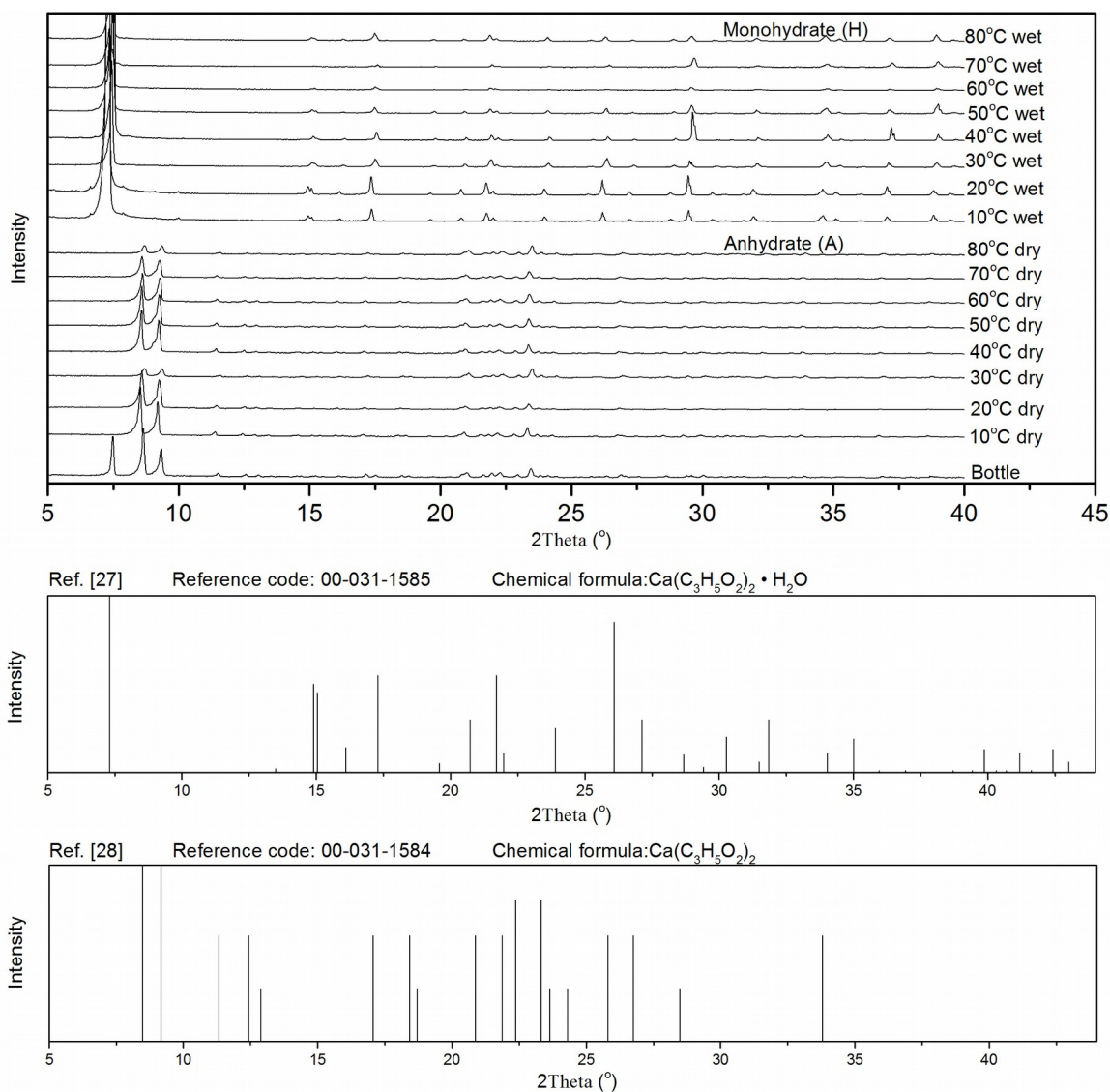


Figure 2. Solubilities of calcium propionate monohydrate in water as a function of temperature T: (□) ref. [12], (◻) ref. [11] cooling method, (◻) ref. [11] heating method, (◻) this work without further purification, (◻) this work purified by recrystallization.

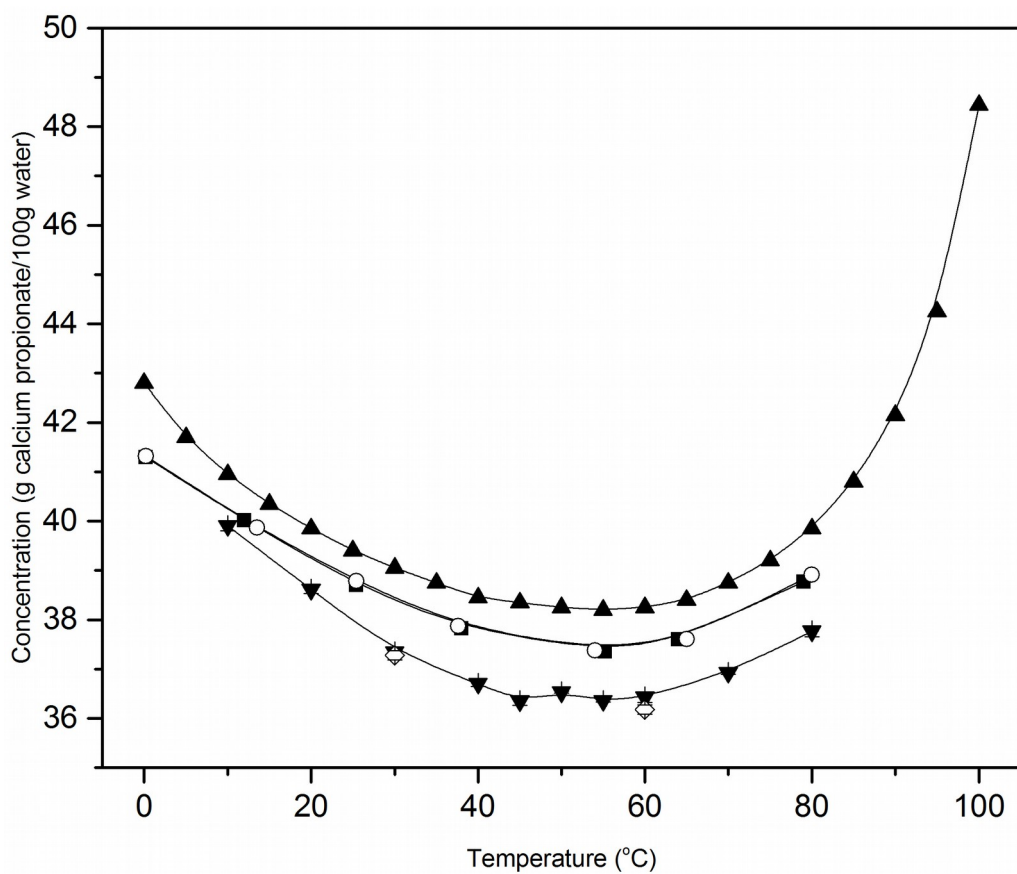


Figure 3. (■) Values of pKa of propionic acid calculated [30], (●) pH of 10% calcium propionate/water (w/w) solution measured, (◇) ionized part of 10% calcium propionate/water (w/w) solution, with temperature.

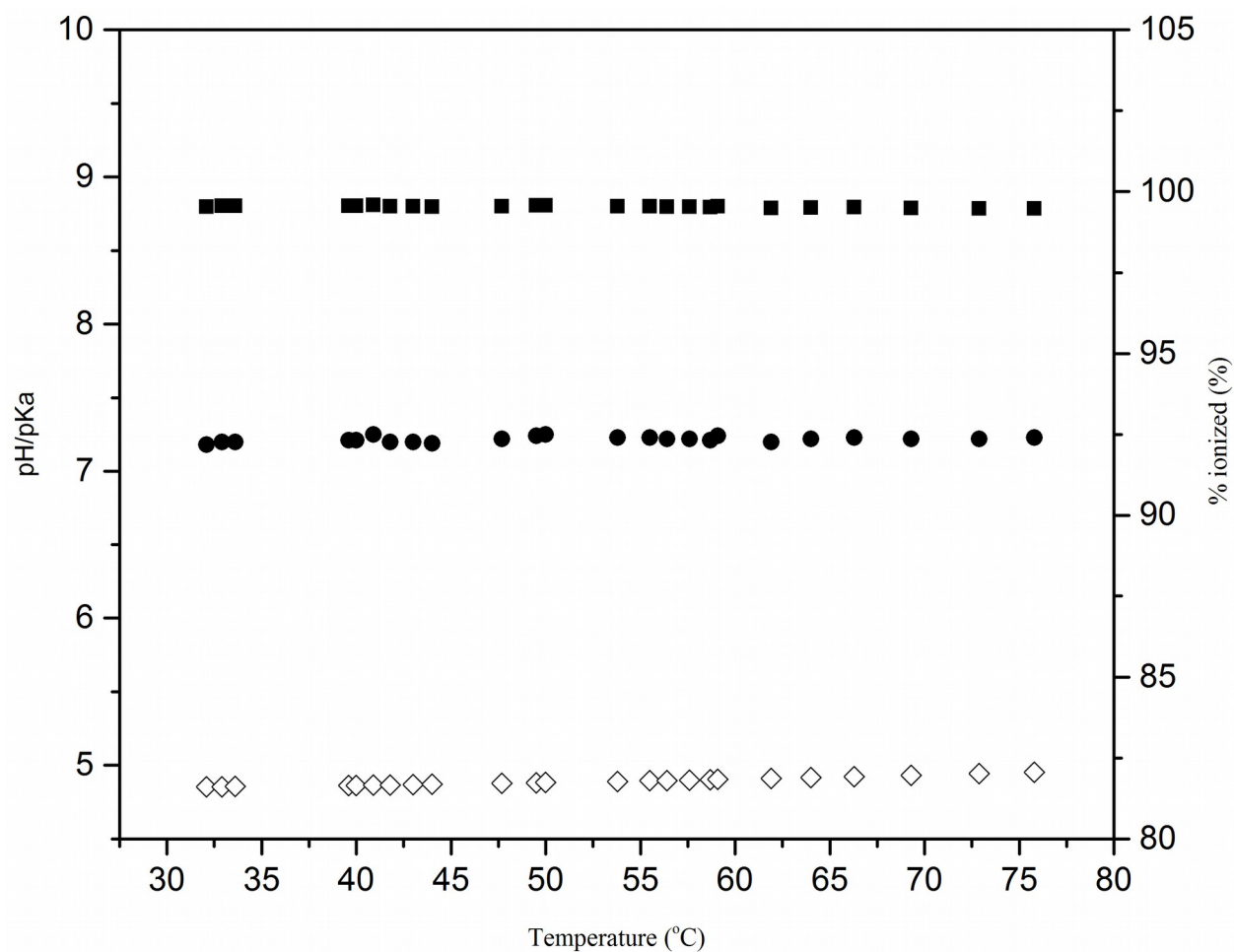


Figure 4. Overlay of XRPD patterns of calcium propionate from solubility measurements in ethanol/water mixtures at 30°C. “20%-80% wet and dry” represent XRPD curves of samples from the suspended solids and dry solids after recrystallization and drying of solution with ethanol fractions of 20%-80%; “ethanol wet and dry” represent XRPD curves with pure ethanol as solvent; “30°C water wet” and “30°C water dry” XRPD curves with pure water as solvent. “H” and “A” represent monohydrate and anhydrous calcium propionate phases, respectively.

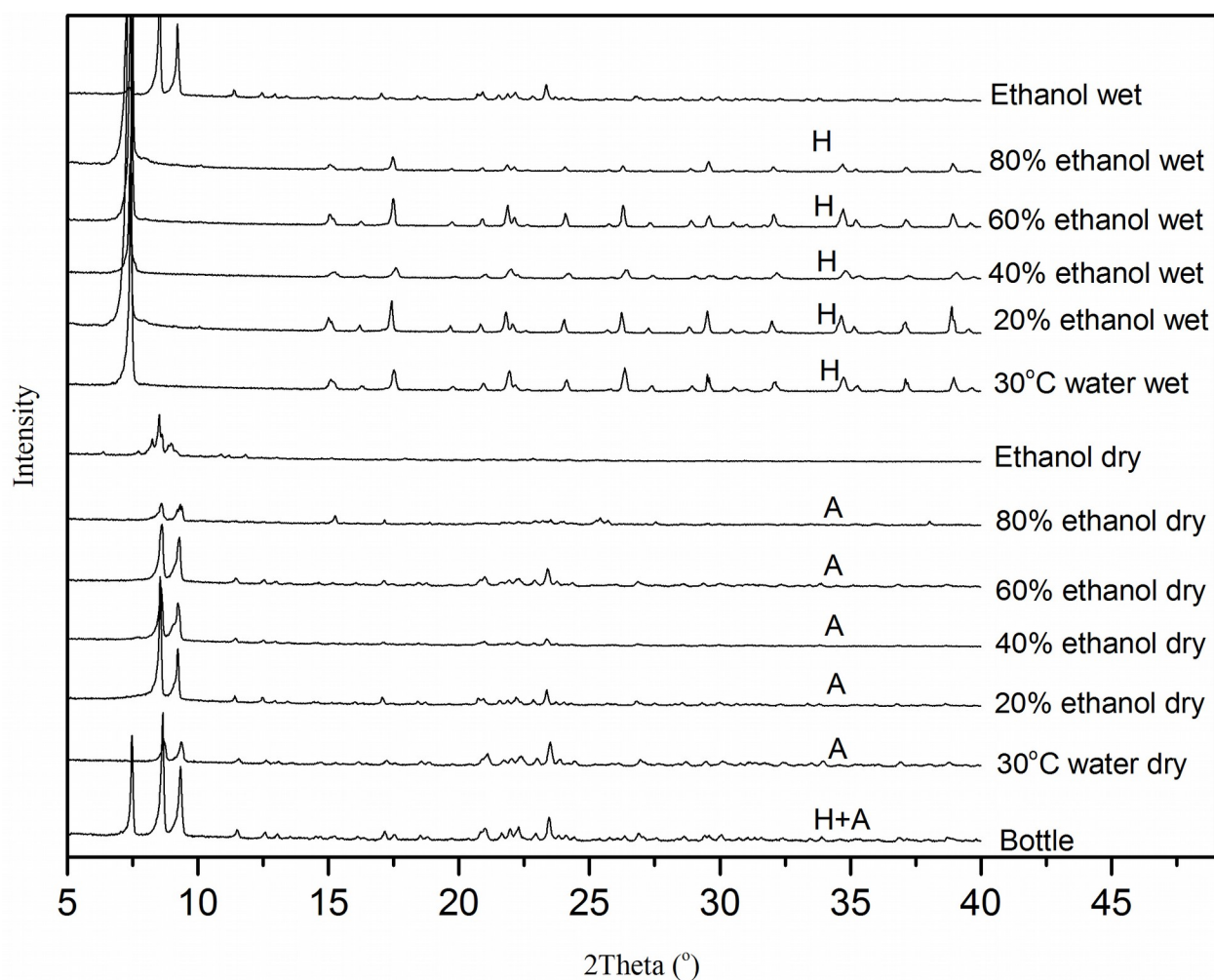


Figure 5. Solubilities of calcium propionate in ethanol/water mixtures at 30°C.

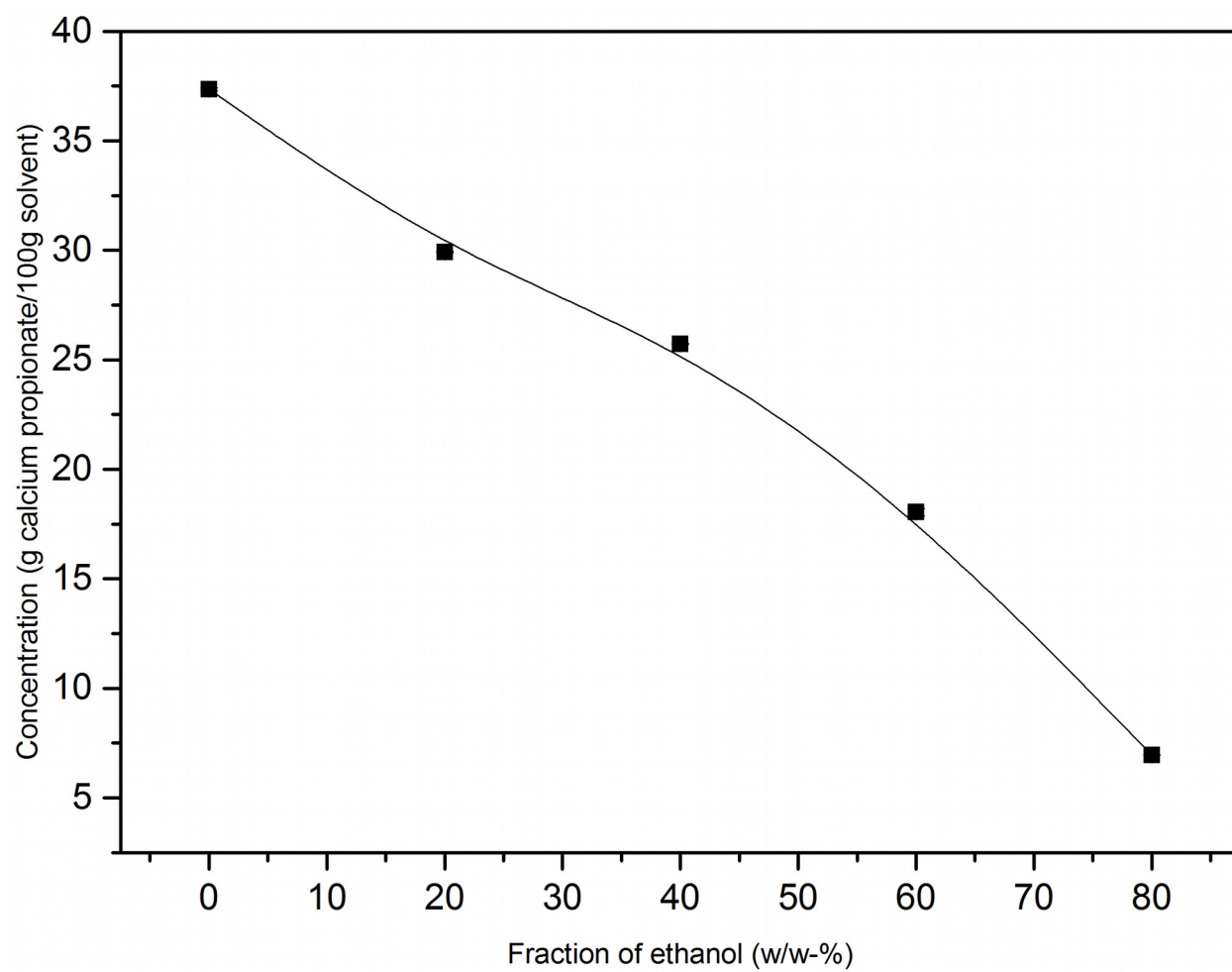


Figure 6. XRPD patterns of calcium propionate (as bought) at different temperatures on heating and cooling (from bottom to top) for studying the solid-state behavior with regard to temperature. “H” and “A” represent monohydrate and anhydrous calcium propionate phases, respectively.

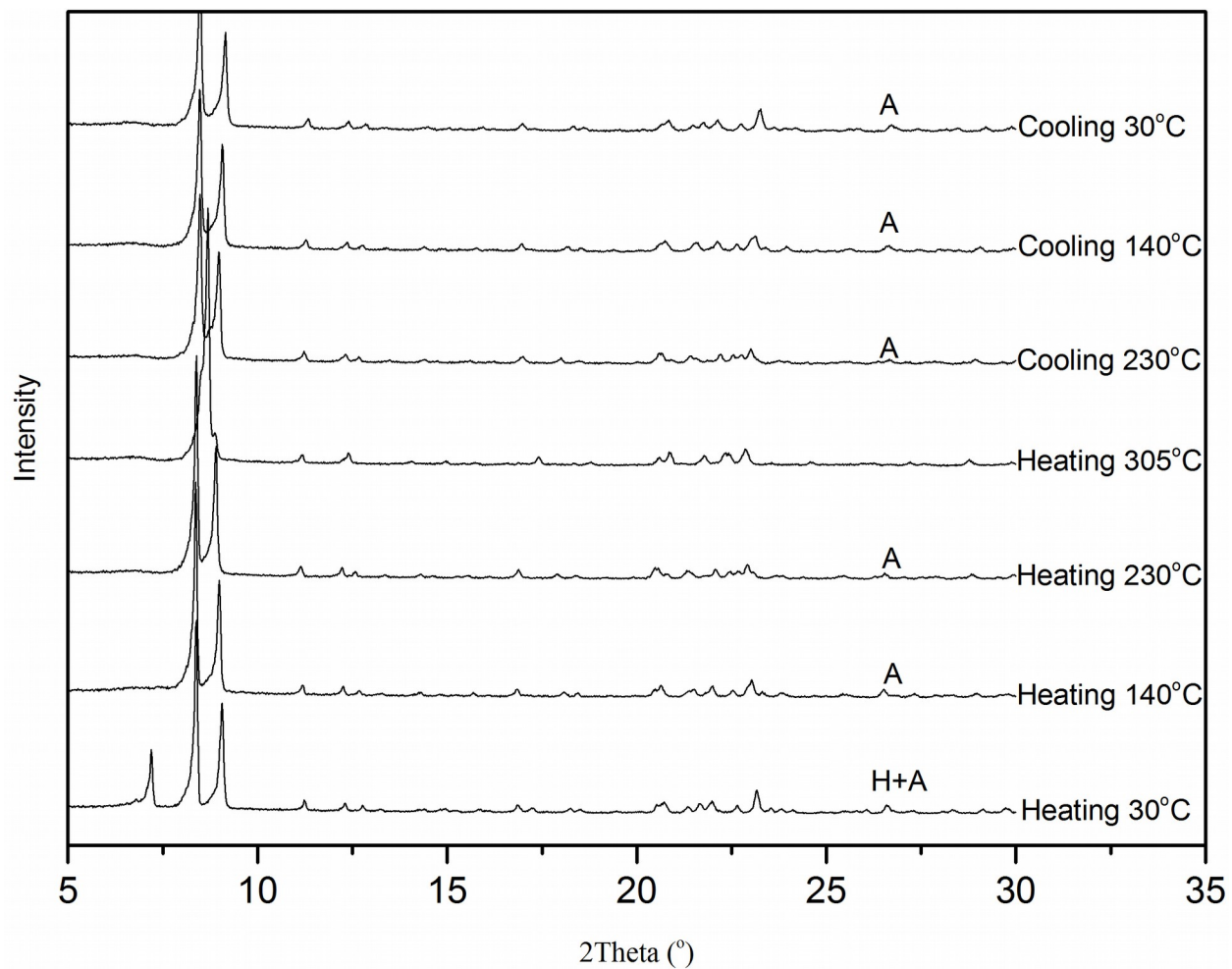


Figure 7. TG-DSC curve of calcium propionate (as bought).

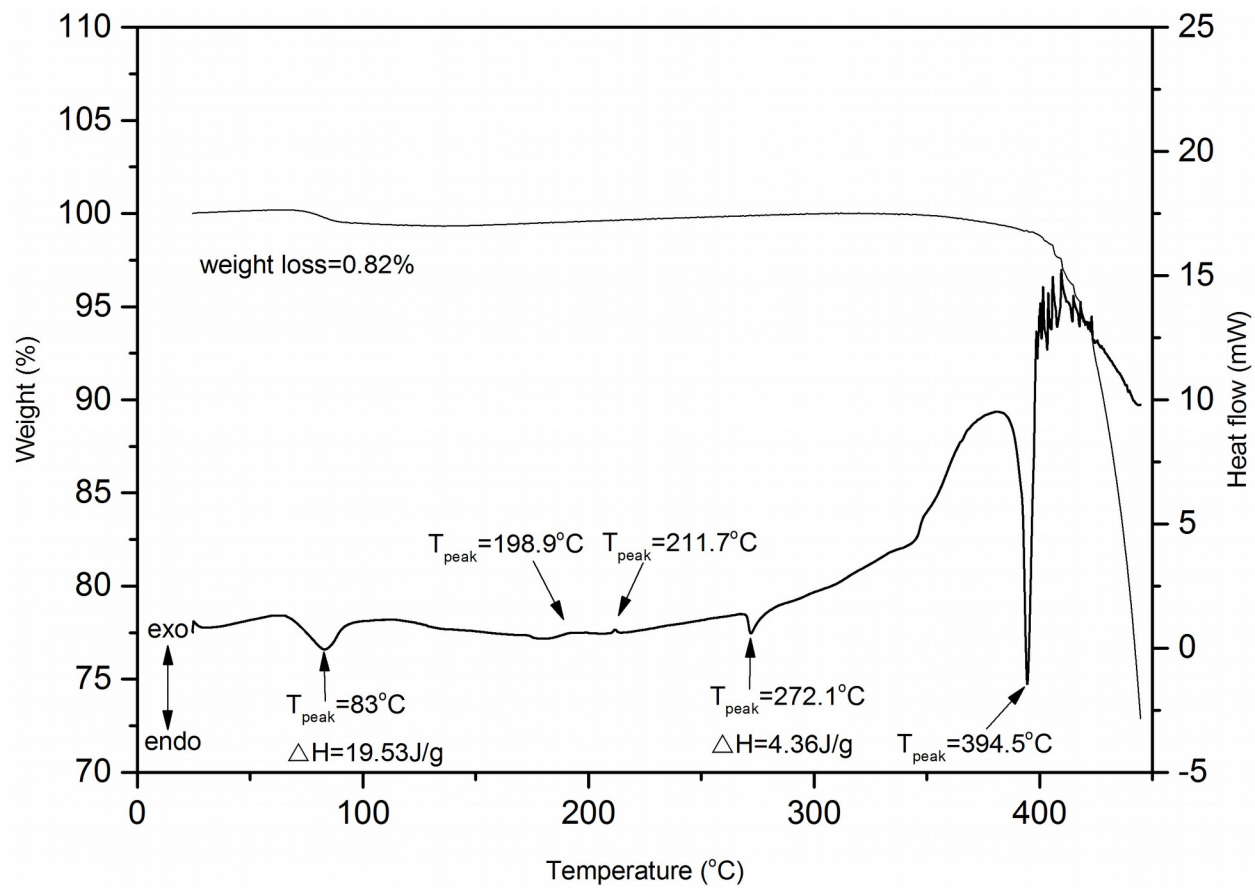


Figure 8. Overlay of DSC curve of calcium propionate (as bought).

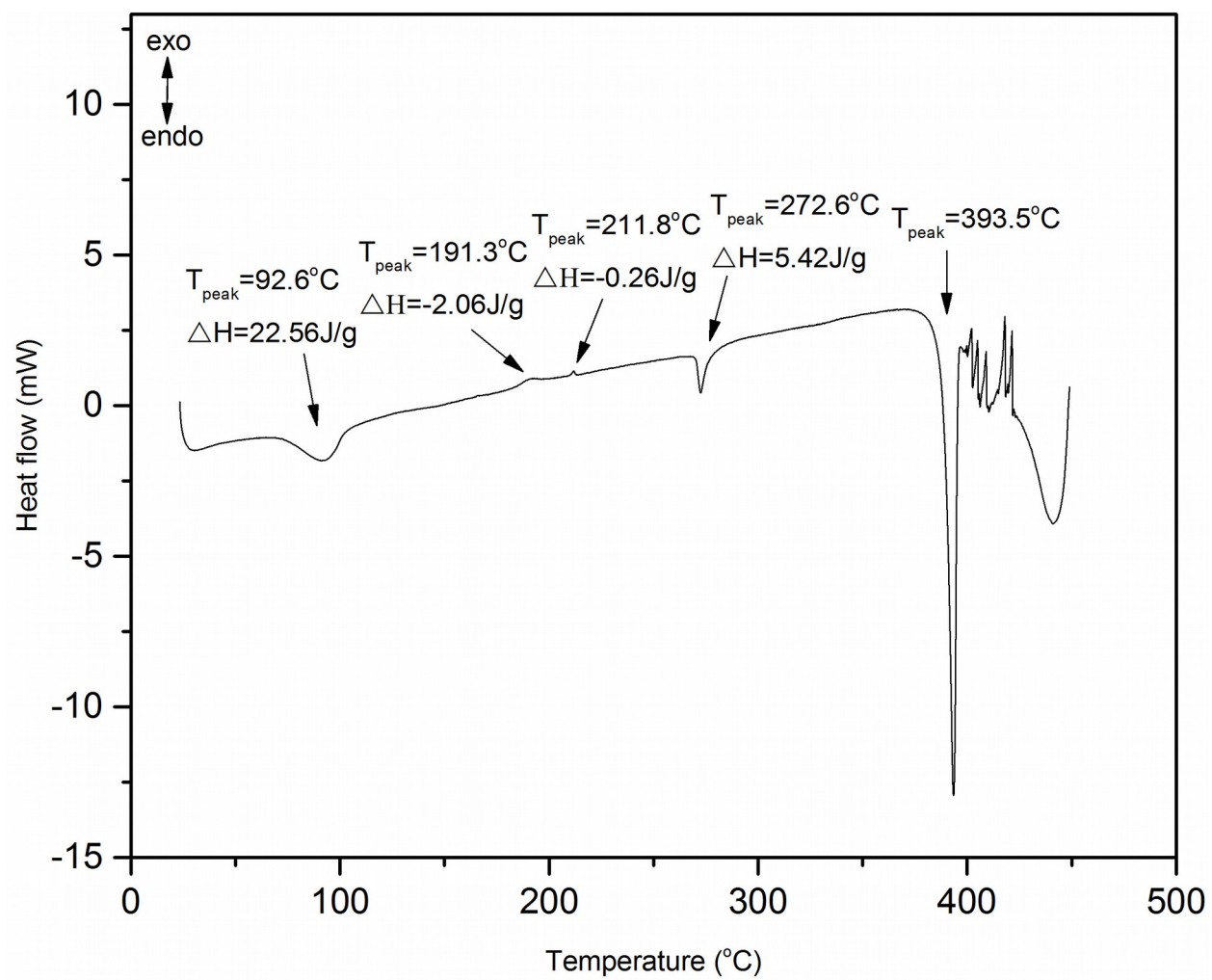
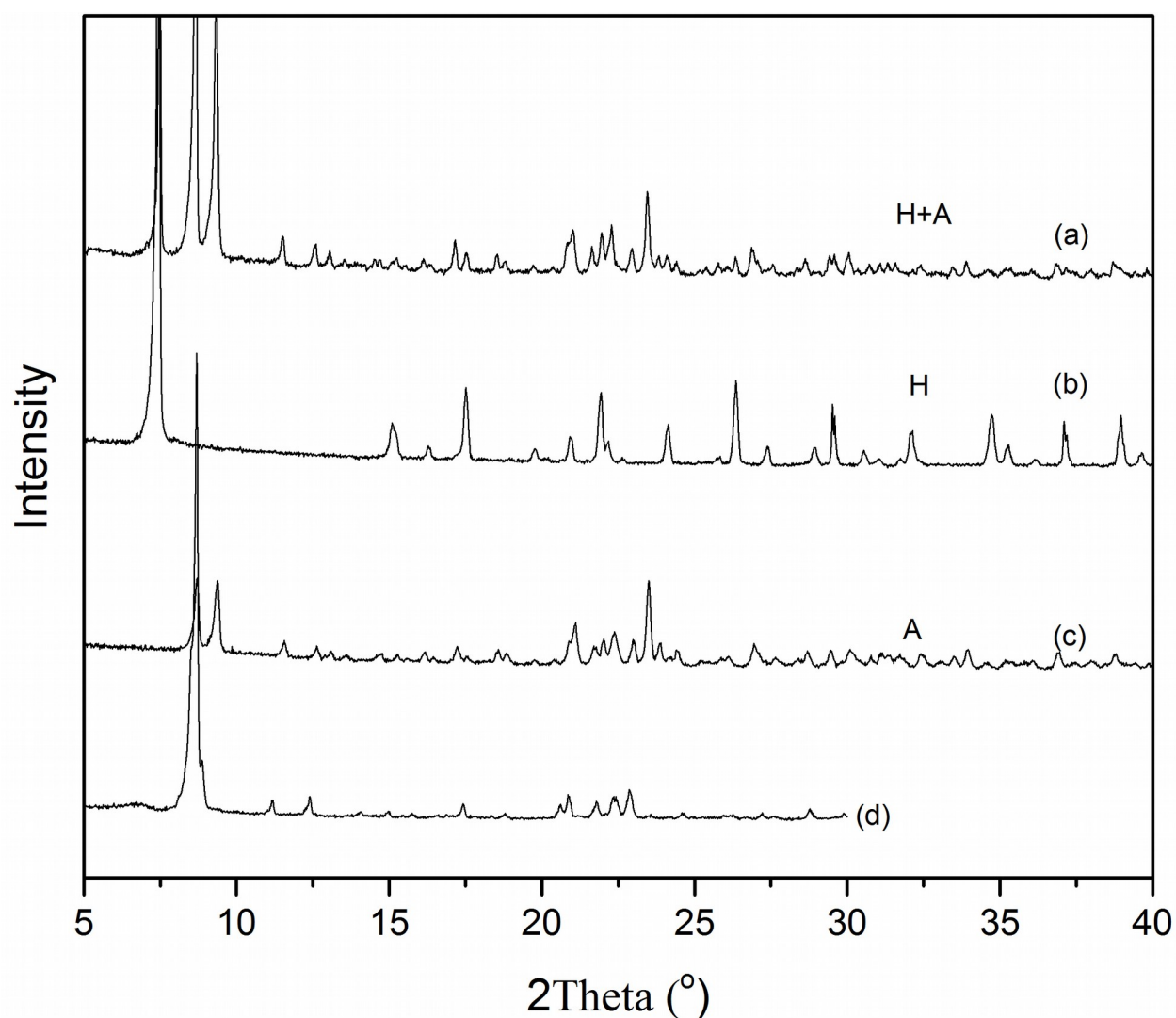


Figure 9. Four different materials investigated in this work: (a) mixture of the anhydrous calcium propionate Form I and the monohydrate as taken from bottle bought from company; (b) monohydrate obtained from solids suspended in aqueous solution at 30°C; (c) anhydrous calcium propionate Form I prepared by recrystallization and drying of saturated aqueous solution at 30°C in oven at 150°C and under atmospheric pressure; (d) anhydrous calcium propionate Form II that is formed when calcium propionate is heated up to 305°C with a phase transition temperature of around 270°C (T_{onset} of TG-DSC/DSC); The mixture of the anhydrous calcium propionate Form I and the monohydrate was used as starting materials in the experiments. “H” and “A” represent monohydrate and anhydrous calcium propionate phases, respectively.



Tables

Table 1. Solubilities of calcium propionate in water / (g calcium propionate/ 100 g water)

Temperature /(°C)	Krasnicki ref. [11]		Lumsden ref. [12]	This work	
	Cooling method	Heating method		Without further purification	Purification by recrystallization
0			42.8		
0.2	41.2986	41.3216			
5			41.7		
10			40.95	39.90	
12	40.0212				
13.5		39.8713			
15			40.35		
20			39.85	38.61	
25			39.4		
25.4	38.7072	38.7851			
30			39.05	37.35	37.28
35			38.75		
37.6		37.8760			
38	37.8247				
40			38.45	36.70	
45			38.35	36.35	
50			38.25	36.53	
54		37.3806			
55			38.2	36.36	
55.2	37.3598				
60			38.25	36.43	36.18
64	37.6014				
65		37.6123	38.4		
70			38.75	36.93	
75			39.2		
79	38.7736				
80		38.9132	39.85	37.77	
85			40.8		
90			42.15		
95			44.25		
100			48.44		