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(54) Benævnelse: **FREMGANGSMÅDE TIL FREMSTILLING AF KRYSTALLINSK DTPMP**

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# Process for the preparation of crystalline DTPMP

The present invention relates to crystallisates of the pure aminoalkylenephosphonic acid DTPMP in three crystal modifications and a process for the solid recovery of crystalline DTPMP by a preferably single-stage crystallisation from an aqueous product mixture containing DTPMP.

For many decades, aminoalkylenephosphonic acids have been used worldwide at a rate of approx. 100.000 tons of active substance molecule per year. The main fields of application are the detergents and cleaning agent industry as well as various water treatment technologies in which aminoalkylenephosphonic acids and their salts act as multi-functional additives.

For manufacturing reasons, aminoalkylenephosphonic acids are predominantly marketed as aqueous solutions. The solid aminoalkylene phosphonic acids required for special applications, such as use in powder, lump or paste formulations, must be produced from the aqueous synthesis solutions in additional process steps. The group of aminoalkylenephosphonic acids includes la large number of liquid products based on diethylenetriaminepenta (methylenephosphonic acid) (DTPMP), which crystallizes from aqueous solutions only with difficulty.

The reason for this is the very good complexing power for a large number of metal ions, an excellent stabilisation of water hardness, combined with a pronounced dispersing capacity of solid particles and the protection of metallic surfaces against corrosion. This results in a wide variety of applications for DTPMP, such as in washing and cleaning processes, as a chelating agent in the stabilisation of peroxide bleaches and as an additive in the treatment of drinking water, industrial process water and oilfield water treatment.

There is therefore a great demand for DTPMP products, which are preferably free of accompanying ions and discolourations and which can be supplied not only as aqueous solutions, but also as solids, in order to open up a multitude of new application possibilities for the formulator.

Processes for the production of DTPMP are known and disclosed in detail e.g. in DE 3128755 A1 or EP 1 838 720 B1. However, the products based on DTPMP which are commercially available at the present time have inadequate purities and are only available as aqueous products.

DTPMP is only commercially available in aqueous solutions. However, the aqueous products currently on the market are not free of by-products and contain significant amounts of impurities, so that they always have a brownish colour and a pronounced characteristic odour. This restricts the practical applicability of aminoalkylenephosphonic acid, which is extraordinarily flexible from an application standpoint.

For example, an exclusively aqueous DTPMP concentrate is known from US 4,477,390 A, which is storage-stable at room temperature, wherein the DTPMP is to be kept in solution only in admixture with its lesser substituted representatives (D3A and D4A) and by the addition of high concentrations of at least from 18 to 22 percent by mass of non-oxidising mineral acids (e.g. HCl).

The literature contains a large number of attempts to improve the product qualities of aqueous solutions of aminoalkylenephosphonic acids and to increase the product variety. In addition to a wide range of variants for synthesis optimisation, attempts at subsequent purification and the technical production of solids are also known.

JP 2002 105089 A discloses a process for purifying aminophosphonic acids, wherein an aqueous solution of the contaminated aminophosphonic acid is mixed with a polar organic solvent, reducing the solubility of the acid in the mixture and initiating its precipitation. A disadvantage of precipitation is that all substances insoluble in the solvent mixture are precipitated by reducing the solubility, for example by adding methanol.
RU 2 434 875 C1, which describes the production of aminoalkylphosphonic acids by reacting ammonium compounds with formaldehyde and phosphonic acids, is similar. Larger amounts of methanol are added to the aqueous reaction solution which is constricted at the end of the reaction in order to initiate precipitation of the product.

However, no pure and crystalline aminoalkylenephosphonic acid is obtained; rather the precipitation product is an amorphous mixture of all substances insoluble in the solvent mixture.

EP 0 225 409 A1 discloses the production of radio-labelled complexes of aminoalkyphosphonic acids, including DTPMP. The free acid is first generated in aqueous solution from the reaction of phosphorous acid, amine and formaldehyde by boiling under reflux. The product precipitates during cooling. The disadvantage is that a crude product is also produced which, in addition to the desired aminoalkylenephosphonic acid, also contains less substituted by-products and impurities.

EP 0411941 B1 discloses in this connection a chemical separation process for the purification of aminomethylene phosphonic acids using an acid-base reaction. After dissolving the respective aminoalkylenephosphonic acid in an aqueous base, the aminoalkylenephosphonic acid is recrystallized by the stepwise addition of an acid. The resulting precipitate is then filtered and washed with water. EP 0411941 B1 expressly mentions that the claimed process is not suitable for the purification of DTPMP.

EP 724576 B1 discloses a process for the non-alkaline purification of aminoalkylene phosphonic acids. In this process, the raw products, after being suspended in water, are heated to reflux at a neutral or acid pH value. After the heat treatment, the precipitate is filtered and washed with water. The described process is suitable for the purification of EDTMP and DOTMP, for example. Since the solubility of DTPMP increases sharply at elevated temperatures between 60 and 70°C, the process is not suitable for suspending DTPMP in water to isolate it under reflux conditions. Consequently, recrystallization by cooling the solution also does not lead to industrially usable quantities.

Typical, commercially available pH-acidic DTPMP products are only available as liquid products, as pH-acidic DTPMP solids cannot be manufactured in a storage-stable manner without the aid of stabilisers due to the impurities they contain as a result of synthesis. Stabilisation of pH-acidic DTPMP liquid products against uncontrolled precipitation is

imperative. This is carried out either by partial neutralisation, at least the trisodium salt or by adding foreign acids (e.g. at least 10 % HCl by mass).

Granulated sodium salts of DTPMP are mixed with additives due to the production process, so that the proportion of DTPMP in these solids is significantly less than 40 % by mass.

Conventional drying processes such as spray drying or granulation either lead to extremely hygroscopic powders or use technologies in which the active ingredient content of the poorly drying aminoalkylenephosphonic acid DTPMP is reduced by additives, which in turn limits the range of application of the dry matter. The upshot is that solid DTPMP products have hitherto been unable to establish themselves on the market, as is the case, for example, with the widespread powdered and granular products of hydroxybisphosphonic acid HEDP.

Since the processes described above for the purification of aminoalkylenephosphonic acids containing large amounts of accompanying substances and impurities are not suitable for purifying and obtaining solid DTPMP for technical, economic or environmental reasons, there is therefore a great need for such a process.

It is therefore the task of the invention to provide a process for purifying and obtaining solid pure aminoalkylenephosphonic acid DTPMP.

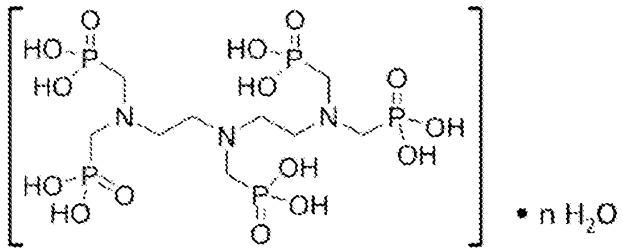
According to the invention, the task is solved by a process for solid recovery of crystalline DTPMP as a pure acid of the general formula (I) from an aqueous crude product containing DTPMP and having a pH value of less than 4, preferably less than 3 (hereinafter referred to as aqueous crude product) by means of the following steps:

a. Introduction of seed crystals containing DTPMP into an aqueous crude product containing DTPMP in a total proportion in the range of from 10 to 65 % by mass up to a suspension density in the range from 1 to 25%;
b. Inputting kinetic energy into the aqueous crude product, for example by intensive stirring and/or shaking and/or the input of vibrations, whereby a

crystal layer grows from the seed crystals so that a crystallisate of the general formula (I) containing DTPMP as pure acid with a total content of at least 75% by mass is formed and precipitates;

c. Separation of the crystallisate formed from the aqueous crude product by sedimentation and/or filtration,

wherein the crystallisate of the pure acid DTPMP has the general formula (I):



(I)

where n is a number between 0 and 2.

The advantage of the process according to the invention is that DTPMP, as an aminoalkylenephosphonic acid which has a high tendency to supersaturation and at the same time a low nucleation rate and crystal growth rate and is therefore difficult to crystallize from aqueous solutions, is obtained as a solid end product in the form of a crystallisate via a preferably quasi-continuous process. Unwanted impurities are separated off advantageously by the process, preferably during the crystallisation of DTPMP, so that the crystallisate has a high degree of purity. Most advantageously, crystallisates containing DTPMP obtained by the process according to the invention have a substantially lower hygroscopy in comparison with solids containing DTPMP obtained by conventional methods.

Particularly advantageously, the aminoalkylenephosphonic acid is obtained as a solid in the form of a crystallisate by complete crystallisation without inorganic or organic impurities, such as cytotoxic lead impurities and synthesis-related secondary products and unreacted raw materials, for example.

Further advantageously, the process also achieves high degrees of purity, which satisfy requirements such as low toxicity, no corrosivity, no colouring due to impurities for applications in the detergent sand cleaning agent industry, as well as the high purity requirements for chemicals for the electronics industry and metal treatment.

Fortunately, it has also been shown that the process according to the invention is more economical and environmentally friendly than conventional methods for obtaining solid aminoalkylenephosphonic acids, as it is advantageous to dispense with the use of other chemicals or expensive downstream process steps.

The present invention is based on the recently gained knowledge that the solubility and the tendency to supersaturation of the aminoalkylenephosphonic acid DTPMP decrease with increasing degree of purification (i.e. with decreasing proportion of impurities).

The skilled person already knows from US 4,477,390 A (Monsanto Company, 16.10.1984; columns 5 and 6, examples 1 to 34) that the solubility of the DTPMP is increased by the addition of high concentrations of accompanying ions (e.g. HCl, $H_2SO_4$). According to the teaching of the patent, the concentration of added HCl should be at least 15 percent by mass to provide an aqueous storage-stable DTPMP concentrate (i.e. without the input of kinetic energy) containing up to 40 percent by mass phosphonate. By the combined use of several accompanying ions, e.g. HCl and H2SO4, even liquid DTPMP products with up to 60% DTPMP in solution can be obtained.

Due to synthesis, the aqueous crude product of DTPMP usually contains residual amounts of chloride ions, e.g. after its production with HCl as acid catalyst (up to 18 % by mass). Surprisingly, however, it has now been found that chloride ions at relatively low concentrations in the range of from 1 to 4 % by mass lead to a further decrease in solubility and/or a reduction in the supersaturation tendency of the DTPMP (cf. Fig. 13).

Suspensions (hereinafter also referred to as slurry, i.e. a heterogeneous mixture of solid particles containing DTPMP and the aqueous crude product) from production processes

with acid catalysts alternative to HCl, such as methanesulphonic acid (up to 25%) or sulphuric acid (up to 25%), also exhibit comparable solubility behaviour.

It is presumed that at equimolar substance ratios in solution a salt formation takes place via at least one nitrogen atom of the aminoalkylenephosphonic acid DTPMP (e.g. DTPMP hydrochloride DTPMP*HCl), as a result of which the steric mobility of the DTPMP molecules is restricted, so that the solubility is reduced. It is all the more surprising that the free aminoalkylenephosphonic acid crystallizes and not its salt DTPMP*HCl. The purification effect is therefore advantageously not hindered. This behaviour can be used particularly advantageously to increase the yield of crystallisate by deliberately leaving residual amounts of mineral acid (e.g. from 1 to 5 % by mass chloride ions) in the DTPMP slurry or by adding chloride contents which are comparable to the chloride contents of DTPMP products which are customary on the market (synthesis-related substance ratio of a typical DTPMP slurry).

By definition, the solubility of a substance is the maximum amount of a substance that is homogeneously distributed in a solvent without the substance being present as a solid phase (solid) as a result of crystallisation. The solubility indicates how many grams (g) of this substance in its pure form can be dissolved in 100 g of solvent.

The aminoalkylenephosphonic acid DTPMP, however, has a tendency, when a saturated solution cools slowly, to easily pass over the onset of crystallisation, which leads to the formation of a solid phase of DTPMP, so that crystallisation does not take place to the extent necessary to maintain the thermodynamic equilibrium and also occurs with a time delay. The crystallisation and nucleation rate of DTPMP are very low, which is why even when a small amount of solid particles (0.1-2.0 % by mass) containing DTPMP is introduced into a saturated solution (i.e. seeded) and subsequently incubated (i.e. without the input kinetic energy), no significant amounts of DTPMP precipitate as a solid even after days, weeks or months. Only the active sites of the added solid particles are saturated and the further crystallisation process comes to a halt.

By definition, exceeding the maximum soluble amount of a substance, which does not lead to crystallisation by the time the equilibrium state is reached, is referred to as supersaturation. A supersaturated solution is accordingly in a metastable state, wherein little or no crystallisation occurs.

Particularly advantageously, undesirable accompanying substances and impurities are separated from the aminoalkylenephosphonic acid DTPMP by the process according to the invention because they either remain undissolved from the outset and can therefore readily be separated from an aqueous crude product even before the process according to the invention or, even if they do go into solution, they remain in the aqueous crude product due to their low concentration when the crystallisate has already precipitated.

Further developments, advantages and possible applications of the invention are also apparent from the following description. All the characteristics described, either individually or in any desired combination, form the subject-matter of the invention, irrespective of their combination in the claims or their appendancies.

The starting point of the process according to the invention is a crude product containing at least DTPMP which is present in the form of dry substance, in dissolved form and/or as a suspension, preferably in water. The crude product preferably contains DTPMP with a concentration of at least 5 % by mass, preferably between 10 and 90 % by mass, particularly preferably between 20 and 80 % by mass.

The data in percent by mass (wt. %) are derived from the mass fraction w of the respective component in the (aqueous) solution and are given as 100 times this value (m %=100*w). The mass fraction of the respective component is determined as the fraction of the mass of this component in the mass of the total solution after mixing, i.e. the masses of all components dissolved in the solvent plus the mass of the solvent itself.

Within the meaning of the invention, the term "aqueous crude product" means that the crude product to be purified is preferably homogeneously dissolved and/or suspended in water or a water - containing solution at the beginning of the purifying process according to the invention. In addition to DTPMP, the aqueous crude product may contain impurities

in the form of by-products and/or unreacted educts. Secondary products are inorganic secondary products such as phosphates and organic secondary products. Unreacted educts are e.g. chlorides and phosphorous acid ($H_3PO_3$).

The organic secondary products can be subdivided into lesser substituted products and condensation products. Lesser substituted products are formed during incomplete reaction of the primary or secondary amine (e.g. with formaldehyde and phosphorous acid $H_3PO_3$), wherein some N-H functionalities are retained or N-$CH_3$ functionalities are formed.

Condensation products can form between $H_3PO_3$ and the formaldehyde and are e.g. hydroxymethanephosphonic acid.

In addition, educts such as formaldehyde or $H_3PO_3$ may be present in a concentration between 0 and 15 % by mass. Phosphoric acid $H_3PO_4$, which is also present, is formed by oxidation of the phosphorous acid $H_3PO_3$ as a secondary reaction.

As a result of synthesis, an aqueous crude product contains acids, for example HCl, $H_2SO_4$, $H_3PO_3$, $H_3PO_4$ and/or methanesulphonic acid, in a total concentration relative to DTPMP of between 0 and 30 % by mass.

In one embodiment according to the invention, the aqueous crude product contains impurities in the form of secondary products and/or unreacted educts in addition to DTPMP.

The crude product may contain lesser substituted DTPMP derivatives in a concentration of from 0 to 15% by mass, preferably between 0.1 and 10 % by mass, and/or other secondary products (e.g. phosphoric acid, hydroxymethanephosphonic acid, etc.) which were formed during an incomplete conversion of the chemical reaction. In the case of incomplete synthesis, the crude product may also contain residues of unreacted starting materials (e.g. formaldehyde, hydrochloric acid, phosphorous acid, etc.) with a concentration of 0 to 15 % by mass, preferably 0.1 to 10 % by mass.

The advantage of the process according to the invention lies in the selective separation of the DTPMP from the mentioned impurities. Although the inorganic secondary products can be separated off by known methods of precipitation with solvents, the molecularly similar and comparably soluble organic secondary products cannot be completely separated off by these methods.

The aqueous crude product preferably contains DTPMP with a total proportion in the range of from 10 to 65 % by mass, more preferably from 15 to 65 % by mass, and most preferably in the range of from 20 to 60 % by mass.

The mass fraction of a component (e.g. an aminoalkylenephosphonic acid) in solution can be determined by various methods known to the skilled person, for example by gravimetric methods, complexometric titration or acid-base titration.

An aqueous crude product to be purified can be suitably prepared preferably analogously to the work of Moedritzer and Irani (*J. Org. Chem*. 1966, 31, 1603-1607).

In the presence of a strong acid (e.g. hydrochloric acid (HCl), sulphuric acid), preferably primary amines (e.g. ammonia, aminoethane, 1,2-diaminoethane, aminoethanol, etc.), phosphorous acid ($H_3PO_3$) and formaldehyde are converted to phosphonic acids, taking into account the stoichiometric ratios necessary for a complete conversion of all N-H functionalities. As an alternative to the use of H3PO3 and HCl, it is also possible to work with phosphorus trichloride and water. With a phosphonomethylation carried out in this way, the fully substituted aminoalkylenephosphonic acid as the main product is usually obtained with a purity of from 75 - 85%.

Alternatively, an aqueous crude product containing DTPMP can also be obtained by a nucleophilic substitution reaction based on a Michaelis-Arbuzov reaction (Berichte [*German Chemical Society Reports*] 1898, 31, 1048) followed by acid hydrolysis. Commercial aqueous solutions containing DTPMP with a total content of between 20 and 60 % by mass, which for example are sold under trade names such as CUBLEN® DNC 450,

CUBLEN® D5000 from Zschimmer & Schwarz) as well as partially neutralised and neutralised commercial products in the form of sodium salt, such as Cublen D 5113 (pH 2-3) Cublen D 4217 (pH 6 -8), can be preferably be used as aqueous crude products.

Alternatively, a water-containing crude product may preferably be prepared by dissolving and/or suspending a solid containing DTPMP in water or a water-containing solution. The solid is preferably dissolved and/or suspended in one or more aqueous solvents with heating to a temperature of more than 30°C, more preferably to a temperature between 30 and 100°C, most preferably to between 35 and 60°C.

A portion of undesired impurities advantageously remains undissolved during the DTPMP dissolution process and can thus be separated from the water-containing crude product by filtration and/or sedimentation prior to the crystallisation process.

Preferably an aqueous crude product has a pH value of less than 5, preferably less than 4, most preferably less than 3. The pH range of the water-containing crude product can optionally be adjusted by adding an acid (e.g. hydrohalic acid, $H_3PO_4$) and/or a base (e.g. alkali, alkaline earth lye). Methods for determining the pH value are well known to persons skilled in the art.

The mass fraction of a component (e.g. an aminoalkylenephosphonic acid) in solution can be determined in various ways known to the skilled person, for example by gravimetric methods, by complexometric titration or by acid-base titration.

According to the invention, a seed crystal is a particulate solid which induces the crystallisation and maturation of the crystallisates as a substrate and thus serves as a matrix material for the growth of the crystal layer for recovering a solid (i.e. crystallisation) containing DTPMP, so that the crystallisate is formed. Seeding therefore means the introduction of seed crystals into a solution to initiate crystallisation after exceeding the saturation concentration. These seed crystals preferably consist of type-specific crystallisate, i.e. crystals or fragments of crystals which were obtained in advance under comparable conditions.

A seed crystal is preferably a type-specific crystalline solid which contains DTPMP in a proportion by mass relative to the seed crystal of between 50 and 100% by mass, particularly preferably from 70 to 100% by mass, most preferably from 75 to 95% by mass. Within the meaning of the invention, a mass fraction of a component of 100 % by mass means that the fraction of other components is below the detection limit. The seed crystal is preferably type-specific and has a high specific surface area. The seed crystals preferably have an edge length in the range of from 0.1 to 100 µm, particularly preferably 0.5 to 50 µm.

It may be of particular importance in this connection that the seed crystals produced in the pre-crystallisation step are present in a desired stable type-specific crystal modification. For the process according to the invention, these are the so-called α, β and γ crystal modifications of pure DTPMP.

A suspension (also referred to as a slurry, i.e. a heterogeneous mixture of solid particles containing DTPMP and the aqueous crude product) is formed by introducing seed crystals into the aqueous crude product. The aqueous crude product serves as a carrier liquid in which the solid particles are coarsely dispersed and therefore tend to sediment.
Due to the high specific surface area of the added solid particles, crystallisation is advantageously accelerated. Crystallisation here means the growth of ions, molecules or ion and molecular aggregates containing DTPMP from the aqueous solution at the contact surface of the seed crystal and/or the crystallisate by adsorption.
The virtually non-existent tendency of DTPMP to self-nucleation and the extremely low crystallisation rate are circumvented by a specified high specific surface area in the form of added solid particles.

It is known in principle to the skilled person that they can initiate the crystallisation of common aminoalkylene phosphonic acids by introducing very small amounts (suspension density less than 0.5 % by mass) of seed crystals, whereby an ordered crystal growth up to or almost up to the equilibrium point, i.e. with only very little residual supersaturation, can be achieved with only small amounts. On the other hand, the inventors have now

surprisingly found that this is not the case for aminoalkylenephosphonic acid DTPMP. Rather, the ordered crystallisation of the DTPMP requires substantially larger seed quantities up to close to the respective equilibrium point.

The amount of seed crystals introduced into the aqueous crude product can be advantageously used to accelerate the time until the transition to the steady-state operation. The aqueous crude product is preferably contacted with a seed crystal quantity in the form of seed crystals containing DTPMP up to a suspension density of between 0.1 and 25 % by mass, more preferably between 0.2 and 20 % by mass, most preferably between 1 and 20 %.

According to a preferred embodiment of the present invention, seed crystal quantities with a suspension density of 1 to 25% by mass, more preferably from 5 to 20 % by mass, most preferably between 10 to 20 % have proved to be particularly suitable.

A suspension is a heterogeneous mixture of solid particles of the seed crystals and/or the crystallisate in water or an aqueous solution. The water or an aqueous solution serves as a carrier liquid in which the solid particles of the seed crystals and/or the crystallisate are coarsely or finely dispersed, preferably finely dispersed.

In order to ensure that a suspension of solid particles (i.e. seed crystals and/or crystallisates) in a carrier liquid is flowable and pumpable, the suspension density of a suspension of seed crystals and/or crystallisates in an aqueous solution is preferably a maximum of 70%, especially preferably a maximum of 60%, most preferably in the range of 20 and 55%. The suspension density is a measure of the solids content in a suspension and is defined as the proportion of suspended solid particles in kg per $m^3$ of carrier liquid (%).

For obtaining a solid (precipitating the crystallisate), the aqueous crude product preferably has a temperature in the range from 0 to 85°C, particularly preferably from 15 to 80°C, more preferably from 25 to 75°C, since the solubility of DTPMP in the aqueous crude product is disadvantageously too high above 85°C .

The aqueous crude product is preferably set in motion by the input of kinetic energy during and after the introduction of seed crystals, so that the seed crystals and/or crystallisates are kept suspended in the aqueous suspension. The input of kinetic energy advantageously effects an intensive and complete mixing of the aqueous crude product and the possibly present seed crystals in the reaction chamber, which ensures a homogeneous distribution of the components and a constant material transport in the aqueous solution.

In this context, material transport means that growth of the crystallisates is accelerated by adsorption by the diffusion of individual ions, molecules or ion and molecular aggregates containing DTPMP from the aqueous solution at the contact surface of the seed nucleus and/or the crystallisate.

Advantageously, after diffusion of the ions, molecules or ion and molecular aggregates containing DTPMP at the contact surface of the seed nucleus and/or of the crystallisate and adsorption thereof at the contact surface thereof, surface diffusion of the precursors takes place, which favours the process of controlled crystallisation of the solid particles containing DTPMP.

It is generally known to the skilled person that the input of kinetic energy is not necessary for crystallisation, i.e. that the system is at rest.

Surprisingly, it has now been shown that the formation of the crystallisate, in particular the growth of the crystal layer by adsorption, is facilitated by the presence of seed crystals and/or crystallisates which have fractured edges which differ from the ideal crystal forms. The input of kinetic energy thereby advantageously effects mechanical disintegration at the surface of the seed crystal and/or the crystallisate, whereby secondary nucleation occurs. As a result of the mechanical disintegration at the surface of the seed crystal and/or the crystallisates, new active sites are advantageously constantly formed, which are saturated by the constant diffusion and adsorption of individual ions, molecules or ion and molecular aggregates containing DTPMP from the aqueous solution at the contact

surface of the seed nucleus and/or the crystallisate. Therefore, the entry of kinetic energy is essential for carrying out the process according to the invention.

According to a preferred embodiment of the present invention, kinetic energy is introduced advantageously in such a way that mechanical disintegration takes place at the surface of the seed crystal and/or crystallisate and secondary nuclei are formed, the Reynolds number of the stirring elements preferably being above Re (stirring) = 10, more preferably in a characteristic number range from 50 to 4000.

The effect of the mechanical breaking of seed crystals and/or crystallisates which have been introduced can also be increased in a beneficial manner by increasing the suspension density and/or modification of the stirrer geometry. This advantageously increases the probability of effective collisions between the seed crystals and/or crystallisates.

The process of crystallisation in the form of the growth of a crystal layer on the seed crystal or crystallisate can be monitored, for example, by microscopic, electron microscopic, thermogravimetric analysis methods and laser diffraction. The composition of crystalline solids can be determined, for example, by means of high-resolution nuclear magnetic resonance spectroscopy (NMR) or X-ray diffraction. The active content of DTPMP in the aqueous crude product is determined, for example, by complexometric titration or acid-base titration. Contents of other components such as chloride ions and phosphorus-containing impurities can be determined, for example, by argentometric and/or iodometric titration, capillary electrophoresis or spectrophotometry.

According to a preferred embodiment of the process according to the invention, kinetic energy is introduced into the system by stirring and/or shaking and/or ultrasonic treatment in order to advantageously ensure an intensive mixing of the system.

The speeds during stirring and/or shaking are preferably infinitely variable in order to allow for the optimal adjustment of the desired stirring or shaking movement. The input of kinetic energy advantageously increases the highly diffusion-controlled material transport during the formation of the crystallisate. Diffusion-controlled material transport

in this case means that by diffusion of individual ions, molecules or ion and molecular aggregates containing DTPMP from a solution at the contact surface of the seed crystals or crystallisates an ordered growth thereof and the formation of crystalline structures is accelerated.

According to the invention, the term crystallisate is understood to mean a preferably particulate crystalline solid which, in dried form, contains the DTPMP as the pure acid with a total proportion of more than 75% by mass, preferably more than 80% by mass, particularly preferably at least 85% by mass, for example determined with an NMR spectrometer, by capillary electrophoresis or by means of complexometric titration. A crystallisate preferably has an edge length in the range of 20 to 1000 µm, particularly preferably from 30 to 500 µm, most preferably from 30 to 200 µm.

The crystallisates obtained following the process according to the invention are obtained as lance-shaped, plate-like or cuboid crystals containing DTPMP as the pure acid.

A crystallisate preferably comprises impurities (as described above) only with a total proportion of less than 1.0 % by mass, particularly preferably less than 0.5 % by mass, but most preferably less than 0.3 % by mass. However, the skilled person knows that individual impurities with a proportion below the detection limit may be present.
A crystallisate preferably comprises the aminoalkylenephosphonic acid DTPMP in the form of the crystalline anhydrate (i.e. the pure acid DTPMP in which all phosphonic acid groups are protonated), the mono- or dihydrate of the acid DTPMP, particularly preferably in the form of the monohydrate of the acid DTPMP.

Within the meaning of the invention, the term "monohydrate" or “dihydrate” denotes a crystallisate of the free acid DTPMP, wherein the crystallisate is present in the form of a solid addition compound ("solvate"), in which one or two water molecules ("water of crystallisation") are attached to a molecule of the acid DTPMP, so that the water molecules form part of the crystal structure of the crystallisate.

The term "anhydrate", however, refers to a crystallisate of the acid DTPMP free of water of crystallisation, wherein the term “crystallisate-free” means that mathematically (based on one crystallisate) less than 0.4, preferably less than 0.3, more preferably less than 0.2 water molecules are attached to a molecule of the acid DTPMP. Stoichiometrically, the monohydrate has 3 % by mass water in the crystallisate, the dihydrate 5.9 % by mass water in the crystallisate.

By definition, retained water is defined as the sum of capillary and adsorption water. Adsorption water refers to water deposited on the surface of crystallisates, whereby a film of water molecules forms. Capillary water is the amount of water retained in the capillaries of a solid (pore diameter to a maximum of 0.2 µm) by adhesion and cohesion (corresponding to suction tension). The skilled person knows that the amount of water that forms a surface film or fills the capillaries varies depending on the ambient parameters (e.g. temperature, pressure, water tension).

Methods for the chemical analysis of solids are well known to the skilled person and are based, for example, on thermal analysis (DTA/TG). The skilled person is also familiar with methods of structural analysis which are based, for example, on X-ray crystal structure analyses (e.g. powder diffraction, single-crystal structure analysis) or the evaluation of epitaxial effects.

According to a preferred embodiment of the present invention, the crystallisates obtained by the procedure according to the invention are plate-like or quadratic and have an aspect ratio (length to width) in the range from 1:1 to 10:1.

According to an alternative embodiment of the present invention, the crystallisates obtained by the process according to the invention are preferably lance-shaped and have an aspect ratio of at least 3:1.

According to a preferred embodiment of the process according to the invention, the seed crystal is a comminuted crystallisate with identical composition thereto.

The crystallisate is preferably separated from the aqueous crude product by sedimentation (e.g. by centrifugation) and/or filtration (e.g. using a Büchner funnel).

According to a particularly preferred embodiment of the invention, the crystallisate is separated from the aqueous crude product via filtering centrifugation, such that residues of mother liquor (i.e. of the aqueous crude product) are advantageously separated from the crystallisate and its surface by the combination of centrifugal force and filtration.

It may optionally be provided that the separated crystallisate after separation is washed several times with cold distilled water and/or a water-containing solution containing e.g. 5 to 20 % by mass ethanol or 5 to 10 % by mass hydrochloric acid.

In particular, repeated washing with a water-containing solution containing, for example, 5 to 20 % by mass ethanol, a loss of separated crystallisate due to washing is reduced because the pure acid DTPMP is only slightly soluble therein.

After separation of the crystallisate from the water-containing crude product, the separated crystallisate is present in the form of a crystalline solid containing DTPMP in the form of the pure acid, wherein the separated crystallisate contains DTPMP with a dry matter content of at least 75% by mass, preferably more than 80% by mass, particularly preferably between 85% by mass and 99% by mass.

According to a preferred embodiment of the present invention, the process comprises at least one isothermal process stage in which the conditions for obtaining solid crystalline DTPMP are selected such that the temperature difference in the aqueous crude product is constant over a defined period of time of the input of kinetic energy, i.e. a maximum of 2.5 K, preferably a maximum of 2 K, particularly preferably a maximum of 1 K. This exact isothermal process control advantageously permits the extraction of crystallisates with a high degree of purity. Alternatively, the temperature can be pulsed to stimulate crystal growth and nucleation.

According to a preferred embodiment of the process according to the invention, the temperature of the aqueous crude product is reduced between the isothermal process stages with a defined temperature profile of from 1 to 7 K per day (i.e. 24 h), preferably from 2 to 6 K per day, particularly preferably from 2 to 5 K per day. The temperature-dependent solubility product of the DTPMP, which has a tendency to supersaturation, in the aqueous crude product is reduced by a stepwise or gradual reduction of the temperature, whereby the tendency to crystallisation of the dissolved DTPMP to DTPMP in the form of a crystalline solid is increased. Reducing the temperature advantageously has the effect of shortening the time required to accumulate larger quantities of crystalline solids containing DTPMP.

According to a particularly preferred embodiment of the process in accordance with the invention, the defined temperature profile of the single-stage process is divided into at least two stages, wherein the process temperature:

a) for the introduction of the seed crystals is first adjusted to a temperature in the range from 25 to 85°C, particularly preferably from 30 to 80°C, most preferably from 35 to 75°C;

b) is then reduced stepwise or gradually by 1 to 7 K per day, preferably from 2 to 6 K per day, most preferably from 2 to 5 K per day, and

c) is subsequently kept constant (isothermal) over a defined period of time.

The process according to the invention for quasi-continuous obtaining of a solid is preferably completed in steady state operation under constant process conditions (constant temperature). The term “quasi-continuous” within the meaning of the invention means that the process for obtaining solid crystalline DTPMP is designed in such a way that, after a partial separation of accumulated crystallisate from the aqueous crude product, the process is continued and/or performed at least once more. At certain intervals, in particular every 0.5 to 12 h, a partial withdrawal of a quantity of aqueous crude product in the range of 10 to 50 % by mass is carried out, whereby the proportion of the withdrawn quantity is replaced by the addition of an identical quantity of fresh aqueous crude product (as defined above). It may thereby be provided that seed crystals are purposively added to the quantity of fresh aqueous crude product. In any case, the

suspension density of the aqueous crude product during quasi-continuous recovery of a solid is in the range of 20 to 55%.

The matured crystallisate is separated from the removed amount of aqueous crude product as described above.

The removal of at least a portion of aqueous crude product and the addition of an identical quantity of fresh aqueous crude product preferably take place within the isothermal process stage.

The process according to the invention for the quasi-continuous recovery of a solid is preferably carried out as a batch process in a stirred vessel.

The skilled person knows that a start-up phase is arranged between seeding and the steady state operating phase. By definition, the start-up phase comprises the time interval from seeding to reaching the steady state.

Within the meaning of the present invention, the time interval of the start-up phase (i.e. the period until the transition to the steady-state operating state) is between 1 and 48 hours.

According to a preferred embodiment of the process according to the invention, the crystallisate is dried after separation so that the separated crystallisate after drying contains water with a maximum mass content of 25 % by mass, preferably not more than 15% by mass, wherein water and optionally other volatile compounds (e.g. alcohols or ethers) are preferably removed.

Drying is preferably carried out at a temperature above 40°C, particularly preferably at temperatures above 50°C. Optionally or additionally, the separated crystallisate is dried by applying a vacuum.

If the dry matter content of the separated crystallisate containing DTPMP is less than 60 % by mass, the solid starts to dissolve in the residual moisture that is present from a

temperature of approx. 40-50°C, which necessitates additional upstream pre-drying in industrial processes which is expensive in terms of energy and apparatus.

Preferably, therefore, after separation from the aqueous solution, only crystallisates with a dry matter content of more than 65 % by mass are used for the drying.

The specific surface area of the separated crystallisate containing DTPMP is preferably kept high by the comminution of larger aggregates during the drying process. It can thereby be optionally provided that the dried crystallisate is coarsely or finely comminuited after the drying process for better packaging and storage. A crystallisate with a homogeneous particle size distribution is thus advantageously obtained. The grain size range can be adjusted by sieving, for example by means of a vibrating screen. Through the parallel use of two sieve nets, individual grain fractions can be purposively obtained.

The methods for comminution and/or pulverisation of crystallisates are known to the skilled person and include, for example, coarse grain crushers, pin mills and roller mills.
In addition, it has now been recognized that during the drying of separated crystallisates containing DTPMP in the form of the pure acid by means of spray drying in the temperature range between 125-140°C, an incongruent melting of the solid takes place with the elimination of water. Known methods for drying solids containing DTPMP thus permit only the drying of sodium-containing DTPMP solids, wherein the DTPMP obtained after synthesis is neutralised by the addition of sodium hydroxide solution, with a stoichiometric Na/DTPMP ratio of at least 2 to 1. The solid mixtures obtained thereby disadvantageously always contain DTPMP in the form of a $Na_x$DTPMP salt (where x is a number in the range from 2 to 10), such that it is not possible to isolate a solid that comprises DTPMP only in the form of an acid.

Surprisingly, however, it has now been found that drying below 125°C until a stoichiometric Na/DTPMP ratio of 2 to 1 is present results in the obtaining of a solid containing DTPMP in the form of the acid.

According to an alternative embodiment of the process according to the invention, drying is therefore carried out by spray drying at a temperature below 125°C, particularly preferably below 120°C, most preferably in the temperature range from 90 to 120°C.

It has also been surprisingly found that the crystallisation of the DTPMP and the formation of the crystallisate are advantageously accelerated in an aqueous crude product containing up to 5% by mass of a strong acid.

Strong acids are preferably selected from the group of mineral acids and/or organic acids, which are contained in the aqueous crude product either as a result of synthesis or by purposive addition.

According to an embodiment according to the invention, the aqueous crude product contains strong acids, preferably mineral acid, such as, for example, a hydrohalic acid, carboxylic acid, phosphoric acid or sulphuric acid, in particular a hydrohalic acid, particularly preferably hydrochloric acid, with a total content in the range from 1 to 5 % by mass, preferably in the range from 1 to 4.5 % by mass. However, aqueous crude products with a total content of mineral acids in the range of 1 to 4 % by mass are also used.

The addition of a highly concentrated acid preferably effects the defined adjustment of the pH value, so that DTPMP is advantageously present in the aqueous crude product in the form of an electrically neutral derivative and/or in the form of a positively charged derivative. The five phosphonic acid groups ($-PO_3^{2-}$) of DTPMP are preferably present completely or at least partially in their protonated form, wherein the amino groups are advantageously present in protonated form as the quaternary amine.

The crystallisate obtained by the method according to the invention is optionally obtained by single or multiple recrystallization and optionally by intermediate synthesis processes to minimise synthesis secondary products.

Methods of recrystallization are very well known to the skilled person, whereby the solution from which the DTPMP obtained by a process according to the invention is recrystallized is preferably contacted with a sufficient quantity of seed crystal and the input of kinetic energy takes place at the same time.

The aminoalkylenephosphonic acid DTPMP is known per se. However, a solid of the pure acid DTPMP has not been described at the present time, nor is there any information about crystal modifications thereof.

When solids are used industrially as chemical raw materials, they are generally in the form of loose bulk materials. Quality parameters of these solids such as easy metering and storage stability are essential prerequisites for their successful use.

However, the high adhesive tendency which occurs during the drying process of commercially available DTPMP grades (e.g. sodium salts) limits the application of thermal drying processes considerably. Modern fluidised bed processes can thus only be carried out with a low drying performance and with the addition of carriers (accompanying substances). These carriers are intended to reduce the adhesion of individual product grains during production and to reduce the hygroscopicity during storage, but at the same time they introduce foreign and usually undesirable accompanying substances (e.g. silicates) into the product which are of a type different from the active substance DTPMP and also considerably reduce the active content of the product.

Due to their extremely high hygroscopicity, spray-dried powders cake in a very short time and can therefore no longer be metered. For these reasons, DTPMP solids produced by thermal drying processes have not yet been able to establish themselves on an industrial scale.

Particularly disadvantageously, known solids of the salts of DTPMP (e.g. sodium salts) contain high proportions of additives (accompanying substances) and equally low proportions (less than 40 % by mass) of DTPMP in these solids due to their production. Nevertheless, the solids of the salts of the DTPMP are disadvantageously strongly

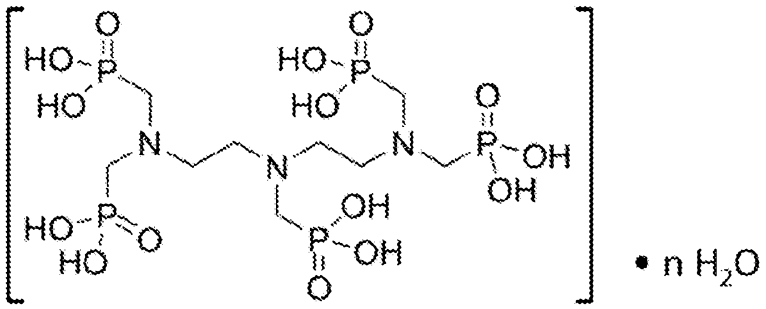
hygroscopic, such that dried solids clump together even in a closed container to form a pasty mass (so-called adhesive tendency). As a result, portioning is more difficult for the formulator, which in turn limits the scope of application of known dried substances.

Therefore it is also the task of the invention to provide a solid of the pure acid DTPMP.

Chemical compounds can exist in different crystal modifications and thereby tend to form a wide variety of particulate structures, such as needles or plates, which differ in their macroscopic properties. Needles, for example, have a significantly lower bulk density than plates, which is a particular disadvantage for the storage or transport of this compound.

Another important aspect for an industrial application is whether a chemical compound is present in the form of a crystalline or amorphous material, the latter having the disadvantageous tendency to form large, irregular agglomerates. Essential factors for economic and technical usability are crystallisate size (i.e. the larger the crystallisate, the more favourable it is, given that the proportion of the surface area in the volume is small) and crystal form (i.e. compact crystallisates are better to handle than forms which tend to generate texture, e.g. needles or plates), as these directly influence the specific surface area and filterability, washability, dryability and hygroscopicity.

Surprisingly, three crystal modifications of the pure acid DTPMP have now been found, wherein the pure acid DTPMP, preferably in the form of the pure hydrate, is present according to the general formula (I):




where n is a number between 0 and 2, preferably between 0.5 and 1.5.

The three crystal modifications of pure DTPMP are characterized by the characteristic chemical shifts in a $^{1}$H-NMR spectrum or $^{31}$P-NMR spectrum (measured at pH 6.5) shown in Fig. 1 and listed below:

$^{1}$H NMR (500 MHz, $D_2O$; ppm): Δ = 3.52 (t, J = 6.3 Hz, 4H), 3.19 (d, *J* = 11.6 Hz, 8H), 3.01 (t, *J* = 6.2 Hz, 4H), 2.66 (d, *J* = 11.2 Hz, 2H).

$^{31}$P NMR (202 MHz, $D_2O$; ppm): Δ = 16.58 (t, *J* = 11.1 Hz), 7.40 (t, *J* = 11.5 Hz)

It has been shown particularly advantageously that the crystallisates according to the invention containing DTPMP as the pure acid are not hygroscopic and therefore, in contrast to the salts of DTPMP, do not clump together to form a pasty mass. The DTPMP is therefore easier to portion, which opens up a wide range of new applications for the formulator.

By definition, the term "hygroscopicity" refers to the ability of solids to absorb moisture from the environment, i.e. to react to the relative moisture content of the air at a given temperature by absorbing or releasing water vapour. Most moisture-absorbing solids undesirably dissolve or clump together through water absorption.

The crystallisate of the pure acid DTPMP according to the invention, in particular the α, β and γ crystal modifications preferably exhibits a hygroscopicity of less than 1% by mass of water per 10 days at a temperature of 22°C and a relative humidity of 55% by mass. Particularly preferably, the hygroscopicity of the crystallisate according to the invention under the aforementioned conditions is less than 1 % by mass water per 20 days.

Against this background it is an additional object of the present invention to provide a first crystal modification of the pure acid DTPMP under the name α crystal modification according to the invention, wherein the corresponding X-ray diffraction diagram of the α crystal modification (obtained by Cu-$K_\alpha$radiation [1.54178 Å] at 25°C) is distinguished by characteristic reflections at the following double diffraction angles 2Θ (in degrees) and lattice plane spacings d in Å-1, wherein all the reflection positions are affected by an uncertainty of ± 0.2°:

| α crystal modification | | |
|---|---|---|
| **2 Θ** | **d** | **rel. intensity** |
| 6.8 | 13.00 | 38.00% |
| 17.9 | 5.0 | 35.60% |
| 20.2 | 4.40 | 41.00% |
| 22.2 | 4.00 | 45.80% |
| 22.5 | 3.95 | 100.00% |
| 23.0 | 3.86 | 72.60% |
| 23.1 | 3.84 | 39.10% |
| 25.0 | 3.6 | 64.30% |

An X-ray diffraction diagram of crystallisates of the α crystal modification according to the invention recorded with Cu-$K_\alpha 1$ radiation is shown in Fig. 2 and proves the absence of another crystal modification. The absence of another crystal modification means that neither the β nor γ crystal modification of the pure acid DTPMP is detectable by known analytical methods.

The α crystal modification preferably comprises DTPMP in the form of the crystalline monohydrate of the pure acid DTPMP (i.e. in which all phosphonic acid groups are protonated). The crystallisates of the α crystal modification according to the invention can contain water molecules in the crystal lattice, normally up to 4% by mass, based on the total weight.

Surprisingly, it has been found that (as opposed to crystallisates of the β crystal modification) only crystallisates of the α crystal modification grow epitaxially on crystallisates of the γ crystal modification. The epitaxial growth can be advantageously be utilised for the targeted crystallisation of compact crystallisates at moderate temperatures by using the crystallisates of the γ crystal modification as the seed material,

but the crystallisation process takes place in the existential range of the α crystal modification. This epitaxy is also a clear and unambiguous distinguishing feature for delimiting the β and γ crystal modifications from each other.

The α crystal modification is preferably obtained by a procedure according to the invention. A pure or predominantly pure α crystal modification is particularly preferably formed when an aqueous solution with a pH value of less than 2 is used. The aqueous crude product preferably contains DTPMP with a total proportion in the range of 10 to 35% by mass, particularly preferably from 10 to 30% by mass.

The aqueous crude product for the production of the α crystal modification preferably has a temperature in the range from 0 to 40°C, particularly preferably from 5 to 35°C.
Surprisingly, it has been found that for the production of crystallisates of the α crystal modification, which only have an edge length of a maximum of 20 µm, it is sufficient to use a seed material with a total proportion of DTPMP in the range of 30 to 95 % by mass as the seed crystal.

Crystallisates of the α crystal modification are preferably plate-like and have an aspect ratio (length to width) in the range from 1:1 to 10:1 and a width to depth ratio of at least 5:1. The volume-based specific surface area of crystallisates of the α crystal modification is preferably above 1.0 $m^2/m^3$

The volume-based specific surface area of a body is defined as the ratio of its surface area (in $m^2$) to its volume (in $m^3$).

Hygroscopicity refers to the affinity of a substance to absorb water. It is known to the skilled person that hygroscopicity is substance-specific and depends both on purity (i.e. the purer the substance, the lower the hygroscopicity) and on the volume-based surface area (the smaller the specific surface area, the lower the hygroscopicity).

According to a preferred embodiment of the present invention, crystallisates of the α crystal modification can be obtained, for example, by a process in which a multi-stage

purification process takes place directly after the synthesis of the DTPMP, so that preliminary purification by precipitation at approx. 30°C occurs first. The resulting precipitate is separated from the reaction solution and again converted into a solution in concentrated form in a downstream reactor. After recrystallization, the solid obtained is isolated and subjected to drying. The solid obtained consists of plate-like crystallisates, which have an edge length of approx. 20 µm and some of which have grown together to aggregates.

Surprisingly, it has also been found that a second, hitherto unknown crystal modification of the pure acid DTPMP is formed by a process according to the invention at a slightly elevated pH. The second crystal modification is referred to as the β crystal modification.

Accordingly, the present invention provides a β crystal modification of the pure acid DTPMP, wherein the corresponding X-ray diffraction diagram of the β crystal modification (obtained by Cu-Kα radiation) is distinguished by characteristic reflections at the following double diffraction angles 2Θ (in degrees) and lattice plane spacings d in Å-1, wherein all the reflection positions are affected by an uncertainty of ± 0.2°:

| β crystal modification | | |
|---|---|---|
| **2 Θ** | **d** | **rel. intensity** |
| 6.7 | 13.17 | 41.30% |
| 18.6 | 4.77 | 43.80% |
| 19.6 | 4.5 | 36.50% |
| 20.0 | 4.4 | 39.80% |
| 22.1 | 4.0 | 65.10% |
| 22.5 | 3.9 | 79.10% |
| 23.0 | 3.9 | 76.80% |
| 24.8 | 3.6 | 50.60% |
| 25.2 | 3.5 | 35.70% |

An X-ray diffraction diagram of crystallisates of the β crystal modification according to the invention recorded with Cu-$K_\alpha 1$ radiation is shown in Fig. 4 and proves the absence of another crystal modification. The absence of another crystal modification means that neither the α nor γ crystal modification of the pure acid DTPMP is detectable by known analytical methods.

The β crystal modification preferably comprises DTPMP in the form of the crystalline monohydrate of the pure acid DTPMP (i.e. in which all phosphonic acid groups are protonated). The crystallisates of the β crystal modification according to the invention can contain water molecules in the crystal lattice, normally up to 4% by mass, based on the total weight.

The β crystal modification is preferably obtained by a procedure according to the invention. A pure or predominantly pure β crystal modification is particularly preferably formed when an aqueous solution with a pH value of less than 4, preferably less than three is used. The pH value is preferably adjusted by adding a highly concentrated caustic solution, preferably an alkaline solution such as sodium hydroxide solution. The aqueous crude product preferably contains DTPMP with a total content in the range of 15 to 55% by mass, particularly preferably from 15 to 50% by mass. A range from 20 to 40% by mass is most preferred.

The aqueous crude product for the production of the β crystal modification preferably has a temperature in the range from 5 to 60°C, particularly preferably from 35 to 55°C.
Crystallisates of the β crystal modification are preferably lance-shaped (i.e. cutter-shaped) and have an aspect ratio (length to width) of at least 3:1, particularly preferably at least 10:1 and a width-to-depth ratio of at least 5:1.

The volume-based specific surface area of crystallisates of the β crystal modification is in the range from 0.2 to 1.2 $m^2/m^3$, such that only a small amount of retained water remains on the surface of separated crystallisates.

Thus it is advantageous to completely or at least partially dispense with subsequent drying (as described above) for crystallisates of the β crystal modification.

This invention also provides a third, hitherto unknown triclinic crystal modification of the pure acid DTPMP. The third crystal modification is referred to as the γ crystal modifications.

The X-ray diffraction diagram of the γ crystal modification (obtained by Cu-$K_\alpha$ radiation) is distinguished by characteristic reflections at the following double diffraction angles 2Θ (in degrees) and lattice plane spacings d in Å-1, wherein all the reflection positions are affected by an uncertainty of ± 0.2°:

| γ crystal modification | | |
|---|---|---|
| **2 Θ** | **d** | **rel. intensity** |
| 13.0 | 6.8 | 48.10% |
| 17.9 | 4.9 | 37.20% |
| 22.0 | 4.0 | 39.20% |
| 22.4 | 4.0 | 100.00% |
| 23.1 | 3.8 | 64.40% |
| 23.3 | 3.8 | 44.90% |
| 25.1 | 3.6 | 92.60% |
| 26.1 | 3.4 | 36.00% |

An X-ray diffraction diagram of crystallisates of the γ crystal modification according to the invention recorded with Cu-$K_\alpha$1 radiation is shown in Fig. 6 and proves the absence of another crystal modification. The absence of another crystal modification means that neither the α nor β crystal modification of the pure acid DTPMP is detectable by known analytical methods.

The γ crystal modification preferably comprises DTPMP in the form of the crystalline monohydrate of the pure acid DTPMP (i.e. in which all phosphonic acid groups are protonated). The crystallisates of the γ crystal modification according to the invention can contain water molecules in the crystal lattice, normally up to 4% by mass, based on the total weight.

The γ crystal modification is preferably obtained by a procedure according to the invention. A pure or predominantly pure γ crystal modification is particularly preferably formed when an aqueous solution with a pH value of less than 4, preferably less than 3 is used. The pH is preferably adjusted by adding a highly concentrated caustic solution, preferably an alkaline solution such as sodium hydroxide solution. The aqueous crude product preferably contains DTPMP with a total proportion of at least 45% by mass, particularly preferably in the range from 45 to 60% by mass, most preferably from 45 to 55% by mass.

The γ crystal modification is preferably obtained by heating an aqueous solution to a temperature in the range of 40 to 85°C, particularly preferably from 50 to 80°C, most preferably to above 55°C.

Crystallisates of the γ crystal modification are preferably cuboid to column-shaped and have an aspect ratio (length to width) in the range from 1:1 to 10:1 and a maximum width-to-depth ratio of 5:1. The volume-based specific surface area of crystallisates of the γ crystal modification is preferably less than 0.3 $m^2/m^3$, so that only little or no retained water remains on the surface of separated crystallisates. Thus, the subsequent drying (as described above) of crystallisates of the γ crystal modification can be advantageously dispensed with completely. Most advantageously, crystallisates of the γ crystal modification can be processed simply by pelletizing. Particularly advantageously, high degrees of purity can also be achieved for crystallisates of the γ crystal modification, which have only a small volume-based specific surface area, even without washing after separation.

The present invention also relates to an aqueous solution containing crystallisates of the pure acid DTPMP according to the general formula (I), preferably in the α crystal modification and/or β crystal modification and/or γ crystal modification.

An aqueous solution within the meaning of the invention is preferably obtainable by a method according to the invention.

Optionally, an aqueous solution containing crystallisates in one of the crystal modifications according to the invention may also be obtained by suspending crystallisates of at least one crystal modification according to the invention in water or a water-containing solution. This is the case, for example, when, after separation, crystallisates are washed or dissolved in water or a solution containing water for a potential application of the DTPMP.

It may also be provided that the crystallisates of the pure acid DTPMP in the α crystal modification and/or β crystal modification and/or γ crystal modification are introduced into water or a water containing solution for long-term storage and/or for transport.

It is also an object of the invention to provide the use of a process according to the invention for the purification of an aqueous crude product containing DTPMP in pure form with a total content of at least 5% by mass, preferably between 10 and 85% by mass, particularly preferably between 20 and 80% by mass.

A particularly advantageous use of the process according to the invention consists of applying it directly after a preparation process for the synthesis of DTPMP.

The aqueous solution containing DTPMP to be purified is thereby fed directly to the process according to the invention or via an intermediate storage after the last reaction step. According to a particularly advantageous embodiment of the process according to the invention, the quasi-continuous recovery of solids takes place in a stirrer vessel.

A process according to the invention is preferably used to produce a pure acid DTPMP crystallisate according to the general formula (I), preferably in the α crystal modification and/or β crystal modification and/or γ crystal modification, with a total DTPMP content in pure form of at least 75% by mass, preferably at least 80% by mass, preferably on an industrial scale.

A crystallisate obtained by the process according to the invention for obtaining solid can be used directly as a solid or by dissolving or suspending it in water or an aqueous solution. The form in which the crystallisate is used depends on the wishes and needs of the formulator at the respective place of use. The crystallisate obtained may be prepared by spray drying, agglomeration or pelletizing.

The following figures and embodiments are intended to explain the invention in more detail, without restricting the invention thereto.

**Fig. 1**: top: $^{1}$H-NMR of DTPMP crystallisates; below: $^{31}$P-NMR of DTPMP crystallisates.

**Fig. 2**: Powder diffractogram of crystallisates of the α crystal modification.

**Fig. 3**: top: Light micrograph of plate-like crystallisates of the α crystal modification; bottom: SEM micrographs thereof.

**Fig. 4**: Powder diffractogram of crystallisates of the β crystal modification.

**Fig. 5**: top: Light micrograph of plate-like crystallisates of the α crystal modification; bottom: SEM micrographs thereof.

**Fig. 6**: Calculated powder diffractogram of crystallisates of the γ crystal modification.

**Fig. 7**: top: Light micrograph of plate-like crystallisates of the γ crystal modification; bottom: SEM micrographs thereof.

**Fig. 8**: Thermogravimetry of crystallisates of the α, β and γ crystal modification.

**Fig. 9**: DSC/TG coupled IR gas analysis for the determination of the water content of DTPMP crystallisates.

**Fig. 10**: Reflection positions of crystallisates of the α, β and γ crystal modification and of the calculated γ crystal modification in the powder diffractogram with relative intensities as bubble diameter.

**Fig. 11**: Thermo-optical analysis of the β crystal modification; heating regime: 120-140°C, heating rate 0.1K/minute; hot stage: FP82HT hot stage/Mettler Toledo, Software analySIS DOCU/Olympus Soft Imaging GmbH

**Fig. 12**: Drying behaviour of crystals as a function of purity and residual moisture

**Fig. 13**: Solubility of the DTPMP at room temperature as a function of the concentration of sodium ions or chloride ions in % by mass.

**Fig. 14**: Water absorption capacity of the crystallisates according to the invention in comparison to amorphous DTPMP solids of different qualities.

**Fig. 15**: Water absorption capacity of purified DTPMP acid in comparison to its sodium salts ($Na_7$-DTPMP, $Na_3$-DTPMP, $Na_{0.5}$-DTPMP)

Example 1 - Isothermal Procedure

A starting quantity of 4.5 kg slurry containing 40 % by mass DTPMP and 3 % by mass chloride in water is placed in a double-walled 5 litre stirred tank reactor with a 14 cm

anchor agitator. Seeding was carried out with 0.2kg of solid containing 85 % by mass DTPMP and 0.1 % by mass chloride with a main particle size of 20 µm. A calculated initial suspension density of 4% by mass was obtained. Precipitation took place at a constant stirring speed of 150 rpm.

A temperature profile is specified during the quasi-continuous process, whereby the temperature of the aqueous solution is first raised continuously over a period of 18 hours to a temperature of 58°C, and then the temperature is cooled continuously over a period of 72 hours by 1K per 8 hours to a temperature of 46°C and then kept constant for 70 hours. Samples of the slurry were taken at different times and both the solution and the suspended solid were tested for their DTPMP and chloride contents.

| Test time | Temperature [°C] | Suspension density [% by mass] | DTPMP Solution [% by mass] | Chloride Solution [% by mass] | DTPMP Solid [% by mass] | Chloride Solid [% by mass] |
|---|---|---|---|---|---|---|
| 0.5 | 58 | 14 | 38.9 | 3.0 | 55.2 | 2.1 |
| 18 | 58 | 16 | 39.6 | 3.1 | 53.1 | 2.2 |
| 24 | 58 | 16 | 38.9 | 3.1 | 54.3 | 2.2 |
| 42 | 55 | 21 | 39.2 | 3.1 | 53.2 | 2.2 |
| 48 | 54 | 21 | 39.8 | 3.2 | 52 | 2.3 |
| 66 | 51 | 30 | 36.3 | 3.2 | 50.8 | 2.4 |
| 72 | 50 | 33 | 37.5 | 3.2 | 52.6 | 2.4 |
| 90 | 46 | 44 | 34.3 | 3.4 | 49.5 | 2.4 |
| 96 | 46 | 48 | 33.9 | 3.4 | 48.8 | 2.5 |
| 115 | 46 | 59 | 31.8 | 3.6 | 47.4 | 2.5 |
| 140 | 46 | 67 | 29.6 | 3.7 | 49 | 2.6 |
| 161 | 46 | 73 | 29 | 3.9 | 45.8 | 2.6 |

Separation of the crystallisate from the aqueous solution takes place in a filtering centrifuge with a perforated drum with a filtering area of 235 $cm^2$ and at a centrifugation

speed of 6500 rpm for 2 minutes. This centrifugation speed of 6500 rpm corresponds to a separating capacity of 3500 g.

Three washing operations with washing water (corresponding to half the amount of solid, divided into 3 equal amounts) are then carried out. Finally, the separated crystallisate is dried for 5 minutes at a centrifugation speed of 10,000 rpm.

This centrifugation speed of 10,000 rpm corresponds to a separating capacity of 8400 g. The particle sizes of the DTPMP crystallisates are determined by means of a laser diffraction particle size analyser LS 13 320/Beckmann Coulter at a wavelength of 780 nm.

| | |
|---|---|
| Mean [µm] | 60 |
| $d_{10}$ [µm] | 17 |
| $d_{90}$ [µm] | 113 |

For characterising the breadth of a particle size distribution, the $d_{10}$ and the $d_{90}$ value are used in addition to the $d_{50}$ value. The $d_{50}$ value (mean) indicates the mean particle diameter, i.e. exactly 50% of the particles are larger than or smaller than the indicated particle diameter, and is referred to as the main particle size below. The $d_{10}$ value refers to the particle diameter at which 10% of the particles are smaller than this limit value. Correspondingly, the $d_{90}$ value indicates a particle diameter at which 90% of the particles are smaller than the indicated limit value.

The crystallisates of the isolated solid have a cutter shape with an edge length from 50 to 120 µm, a width of from 10 to 50 µm, and a thickness in the range of from 1 to 5 µm (cf. Fig. 5, top left image).

Following the test, the contents of DTPMP and chloride in the individual components were determined by complexometric titration and by argentometric titration, respectively.

| | Amount obtained, based on the amount of slurry | DTPMP content [% by mass] | Chloride content [% by mass] |
|---|---|---|---|
| Slurry | 4.5 [kg] | 40 | 3 |
| Solid unwashed | 34 [% by mass] | 83.6 | 0.6 |
| Solid washed | 23 [% by mass] | 87.2 | 0.1 |
| | | | |
| Filtrate | 65 [% by mass] | 26.9 | 3.8 |
| Washing water | 29 [% by mass] | 12.1 | 1.5 |

Example 2 - Continuous Procedure

For continuous long-term production in the state over a total period of 8 weeks on an industrial scale, a starting amount of 10 kg of slurry, containing 40% by mass DTPMP and 3% by mass chloride in water, is placed in a 10-litre stirred tank reactor having an 11 cm propeller mixer. Seeding is carried out once by the introduction of 2 kg of solid containing 85% by mass DTPMP and 0.1% by mass chloride and characterised by a main particle size of 35 )m. A calculated initial suspension density of 14% by mass is obtained. A calculated initial suspension density of 4% by mass was obtained. Precipitation occurred at a constant temperature of 40° C and at a constant stirring speed of 280 rpm.

During quasi-continuous long-term production, 2.5 kg of suspension are removed every 12 hours, the amount removed being replaced by the addition of an identical amount of fresh suspension (40% DTPMP by mass and 3% chloride by mass). Depending on the time at which the samples are removed, the suspension density, determined gravimetrically by means of centrifugation at 6500 rpm/2 minutes, is from 30 to 45%. This centrifugation speed of 6500 rpm corresponds to a separating capacity of 3500 g.

The crystallisate is separated from the amount of slurry removed in a filtering centrifuge having a perforated drum with a filtering area of 235 cm2 and at a centrifugation speed of 6500 rpm for 2 minutes. This centrifugation speed of 6500 rpm corresponds to a

separating capacity of 3500 g. Three washing operations with washing water (corresponding to half the amount of solid, divided into 3 equal amounts) are then carried out. Finally, the separated crystallisate is dried for 5 minutes at a centrifugation speed of 10,000 rpm. This centrifugation speed of 10,000 rpm corresponds to a separating capacity of 8,400 g.

The particle sizes of the DTPMP crystallisates are determined by means of a laser diffraction particle size analyser LS 13 320/Beckmann Coulter at a wavelength of 780 nm. The crystallisates of the isolated solid have a lance shape with an edge length of from 50 to 100 µm, a width of from 10 to 50 µm and a thickness in the range of from 1 to 5 µm (cf. Fig. 5; SEM micrograph).

| | |
|---|---|
| $d_{50}$ [µm] | 50 |
| $d_{10}$ [µm] | 10 |
| $d_{90}$ [µm] | 95 |

Following the test, the contents of DTPMP and chloride in the individual components were determined analogously to Example 1.

Example 3 - Influence of Seeding and Kinetic Energy Input

In order to determine the influences of seeding and kinetic energy input on the stirring speed and the space-time yield (amount of crystallisate formed per crystallisation volume and per unit time), the tests described below were carried out as follows.

A 250 ml screw-top jar clamped in a stand and provided with a perforated lid in order to reduce evaporative losses was equipped with a propeller mixer with a 4 cm agitator driven by an agitator mechanism. The experimental setup was operated at room temperature in a fume cupboard.

The slurry used was an aqueous solution containing 25 % by mass DTPMP. The solid DTPMP acid used to produce the slurry had, upon initial weighing, a content of 49.6 % by

mass DTPMP acid, a chloride content of 1.7 % by mass and 0.2 % by mass orthophosphate and a main particle size of 15 µm. This material was also used as the seed material. For seeding the slurry, the amount of solid DTPMP acid specified for the test was made into a suspension in a few millilitres of the slurry and introduced into the precipitation vessel by means of a pipette. The amount used was calculated as g of seed material per 100 g of slurry.

The progress of crystallisation is determined by repeated measurements (according to the following table) of the DTPMP content in the filtrate.
To determine the DTPMP content remaining in the slurry, samples were taken via a 45 µm syringe filter and analysed by complexometric titration.

**Result**:

As shown in the following table, the combination of high stirring speed plus a large amount of seed material in test 1-1 results in the quickest depletion of the mother liquor and thus produces the greatest yield of crystallisate per unit time.

Tests 2-1 and 3-1 here demonstrate that stirring, i.e. the input of kinetic energy, is the dominant factor. At a constantly high stirring speed, tests 1-1, 2-1 and 3-1 show a clear advantage for the larger amounts of seed material.

Example 4 - Process for the production of the γ crystal modification, isothermal at 70°C and 60°C

A starting amount of 2 kg of slurry, containing 55% by mass DTPMP, 3.9% by mass chloride and 0.7% by mass ortho-phosphate, is placed in a double-walled 3-litre stirred reactor with a 14 cm anchor agitator. Seeding was carried out once with 140 g (about 7% by mass) of crystallisate of the j crystal modification comprising 82.5% by mass DTPMP and 0.09% by mass chloride and having a main particle size of 50 µm. Precipitation took place at a constant stirring speed of 180 rpm.

| Test no. | 1-1 | 2-1 | 2-3 | 3-1 | 3-2 | 3-3 |
|---|---|---|---|---|---|---|
| Seed amount [% by mass] | 5 | 0.5 | 0.5 | 0.1 | 0.1 | 0.1 |
| Resulting initial suspension density [% by mass] | 2.4 | 0.25 | 0.25 | 0.05 | 0.05 | 0.05 |
| Stirring [rpm] | 160 | 160 | 0 | 160 | 40 | 0 |
| | | | | | | |
| Run time [h] | DTPMP in the Filtrate [% by mass | DTPMP in the Filtrate [% by mass | DTPMP in the Filtrate [Ma.-% | DTPMP in the Filtrate [Ma.-% | DTPMP in the Filtrate [Ma.-% | DTPMP in the Filtrate [Ma.-% |
| 0 | 25.0 | 25.0 | 25.0 | 25.0 | 25.0 | 25.0 |
| 2 | | | 25.0 | | | |
| 4 | | | | | 23.6 | 23.6 |
| 15 | 7.5 | | | 18.4 | | |
| 16 | | 10.5 | | | | |
| 21 | | | 14.6 | | 17.1 | 19.8 |
| 23 | 7.5 | 8.8 | | 14.4 | | |
| 24 | | | | | 15.4 | 19.7 |
| 26 | | | 13.7 | | | |
| 28 | | | | | 13.9 | 19.6 |
| 39 | 7.1 | | | | | |
| 40 | | 7.4 | | 8.6 | | |
| 46 | | | | 8.6 | | |
| 47 | 7.5 | 7.4 | | | | |
| 63 | 6.9 | | | | | |
| 64 | | 7.2 | | 7.4 | | |
| 69 | | | 10.8 | | 7.7 | 17.8 |
| 71 | 6.9 | 7.6 | | 7.1 | | |
| 94 | | | | | | 17.1 |
| 99 | | | | | | 16.8 |
| 140 | | | | 6.7 | | |
| 165 | | | | | | 15.0 |

The quasi-continuous process is left isothermal over a period of 19 days. First, the crystallisation is left at a constant initial temperature of 70°C for 7 days, then the temperature is reduced to 60°C and left for a remaining period of 12 days. The matured crystallisate is separated from the aqueous solution in a filtering centrifuge with a perforated drum with a filtering area of 235 cm2 and at a centrifugation speed of 6800 rpm for 2 min. This centrifugation speed of 6500 rpm corresponds to a separation performance of 3500 g. Three washing cycles are then carried out with washing water (half the quantity of solids, divided into 3 equal parts). Finally, the separated crystallisate is dried for 5 minutes at a centrifugation speed of 10,000 rpm. This centrifugation speed of 10,000 rpm corresponds to a separating capacity of 8,400 g.

The suspension density, i.e. the solids content of the suspension in % by mass, is determined gravimetrically via a benchtop centrifuge in 12 ml vials at 6500 rpm. This centrifugation speed of 6500 rpm corresponds to a separating capacity of 3500 g.

Analytical values during isothermal procedure at 70°C:

| | DTPMP content [% by mass] | Chloride content [% by mass] | Chloride fraction in DTPMP [% by mass] | Amount [g] |
|---|---|---|---|---|
| Filtrate | 49.8 | 2.69 | 5.2 | 789 |
| Solid unwashed | 90.9 | 0.28 | 0.31 | 1290 |
| Solid washed | 93.8 | 0.06 | 0.06 | 941 |

Analytical values during isothermal procedure at 60°C:

| | DTPMP content [% by mass] | Chloride content [% by mass] | Chloride fraction in DTPMP [% by mass] | Amount [g] |
|---|---|---|---|---|
| Filtrate | 48.7 | 2.94 | 6.03 | 511 |
| Solid unwashed | 89.8 | 0.4 | 0.45 | 1470 |
| Solid washed | 92.8 | 0.03 | 0.03 | 895 |

The particle size of the DTPMP crystallisates is then determined by means of a laser diffraction particle size analyser LS 13 320/Beckmann Coulter at a wavelength of 780 nm. The average growth rate (in [µm/h]) of the crystallisates was determined for an isothermal procedure at 70° C as 0.15.

| | Start | End |
|---|---|---|
| $d_{50}$ [µm] | 50 | 68 |
| $d_{10}$ [µm] | 22 | 39 |
| $d_{90}$ [µm] | 88 | 103 |

For characterising the breadth of a particle size distribution, the $d_{10}$ and the $d_{90}$ value are used in addition to the $d_{50}$ value. The $d_{50}$ value (mean) indicates the mean particle diameter, i.e. exactly 50% of the particles are larger than or smaller than the indicated particle diameter, and is referred to as the main particle size below. The $d_{10}$ value refers to the particle diameter at which 10% of the particles are smaller than this limit value. Correspondingly, the $d_{90}$ value indicates a particle diameter at which 90% of the particles are smaller than the indicated limit value.

Because of the small specific surface area of crystallisates of the γ crystal modification, both tests, 60° C. and 70° C., for obtaining the γ crystal modification advantageously yield, even without washing, very pure solids which, as a result of the low residual moisture contents of <10% by mass, can be dried significantly more efficiently than is the case with the other crystal forms.

When the filter cake of crystallisates of the γ crystal modification is washed analogously to examples 5 and 6, residual moisture and impurities can advantageously be reduced further.

The powder diffractogram calculated from the structural data of a single-crystal structure analysis of the γ crystal modification by means of PowderCell software (Bundesanstalt für Materialforschung und-prüfung Berlin) is shown in Fig. 6, wherein the characteristic reflections are found in Table 3. The single-crystal X-ray diffractometer IPDS 2T (Stoe) was

used for structure determination. A comparison of the reflection positions in Fig. 10 between the calculated and the measured powder diffractogram proves the absence of another crystal modification.

Table 3: Characteristic reflections of crystallisates of the γ crystal modification

| γ crystal modification | | |
|---|---|---|
| **2 Θ** | **d** | **rel. intensity** |
| 8.939 | 9.8849 | 33.80% |
| 10.652 | 8.2986 | 12.80% |
| 11.673 | 7.5753 | 13.50% |
| 13.008 | 6.8005 | 48.10% |
| 16.280 | 5.4403 | 16.40% |
| 17.914 | 4.9476 | 37.20% |
| 20.128 | 4.408 | 27.70% |
| 21.768 | 4.0794 | 17.00% |
| 21.960 | 4.0443 | 39.20% |
| 22.432 | 3.9602 | 100.00% |
| 23.113 | 3.845 | 64.40% |
| 23.311 | 3.8128 | 44.90% |
| 25.058 | 3.5508 | 92.60% |
| 26.131 | 3.4074 | 36.00% |
| 26.909 | 3.3107 | 20.50% |

Example 5 - Process for the preparation of the α crystal modification

A starting amount of 24.3 kg of slurry, as detailed in the following table, is placed in a pilot plant having a 10-litre stirred tank reactor and an 11 cm propeller mixer. Seeding is carried out with 2.4 kg % by mass DTPMP crystallisates of the n crystal modification comprising 50% by mass DTPMP, 1.5% by mass chloride and having a main particle size of 20 )m, at a reaction temperature of 30° C. A calculated initial suspension density of 5% by mass is obtained. Precipitation took place at a constant stirring speed of 170 rpm.

The suspension density, i.e. the solids content of the suspension in % by mass, is determined gravimetrically via a benchtop centrifuge in 12 ml vials at 6500 rpm. This centrifugation speed of 6500 rpm corresponds to a separating capacity of 3500 g.
After a test duration of 15.5 hours, the solid is separated from the liquid via a porcelain suction filter (50 mbar, on filter paper), the unwashed solid and the filtrate having the contents of DTPMP, chloride and ortho-phosphate indicated in the following table.

| | Amount [kg] | DTPMP content [% by mass] | Chloride content [% by mass] | Chloride fraction in DTPMP [% by mass] | Ortho-phosphate content [% by mass] |
|---|---|---|---|---|---|
| Slurry | 24.3 | 46.5 | 3.3 | 7.1 | 0.6 |
| Solid unwashed | 8.5 | 59.5 | 2.6 | 4.4 | 0.4 |
| Filtrate | 15.8 | 32.8 | 3.8 | 11.6 | 0.5 |

As the suspension density increases, the thin crystal plates increasingly rub together and are thereby destroyed mechanically. This leads to new nuclei, so that the suspension density increases further as they heal. As a result, no further significant crystal growth is observed, but the crystals remain at crystal sizes of about 20 µm. These small crystal sizes, combined with the plate form typical of crystal form A, result in high specific surface areas. This leads to extremely high residual moisture contents and washing losses.

The grain growth to be observed by means of laser diffraction on a macroscopic scale takes place primarily via the formation of agglomerates (see Fig. 3, bottom right image), which are visible by means of a scanning electron microscope. Although the

agglomeration has a favourable effect on the sedimentation behaviour and thus also on the filtration behaviour, the inclusion of mother liquor reduces the purification effect.

A two-step process appears to be expedient here. The solid precipitated and separated off by filtration in the first step is dissolved again, without being washed, and recrystallized in a second step in a mother liquor which is now purer and, on account of its higher purity, advantageously less supersaturated. After filtration, this solid is washed and shows significantly better purification. How- ever, the high content of residual moisture of >60% by mass disadvantageously remains. If this material is to be dried energy-efficiently at temperatures >60° C, it forms aggregates by rolling up or even begins to dissolve in the residual moisture. In order to counteract this, it is necessary to carry out drying beforehand to residual moisture contents <40% by mass with significantly lower energy inputs, that is to say at temperatures of about 40°C.

This dependence is shown by the following example for determining the drying behaviour of crystallisates in dependence on residual moisture and product purity.

A DTPMP solid isolated by recrystallization is characterised by residues of adhering mother liquor via the quality parameters listed in the following table. The determination of the residual moisture by means of HB 43 S / Mettler Toledo halogen dryer is carried out isothermally at the specified temperature using switch-off criterion 4 (AK4 = mean weight reduction is < 1mg per 90 seconds):

| | DTPMP content [% by mass] | Chloride content [% by mass] | Inorg. $PO_4$ [% by mass] | $H_3PO_3$ [% by mass] | Residual moisture 130°C AK4 |
|---|---|---|---|---|---|
| Unwashed sample | 47.7 | 1.8 | 0.13 | 3 | 45.6 |

After a purification step, which consists of suspending the solid in water and then separating it off by means of a filtering centrifuge, the following quality criteria are obtained:

| | DTPMP content [% by mass] | Chloride content [% by mass] | Inorg. $PO_4$ [% by mass] | $H_3PO_3$ [% by mass] | Residual moisture 130°C AK4 |
|---|---|---|---|---|---|
| Washed sample | 50.9 | 0.7 | 0.15 | 1.5 | 44.8 |

The adhering residual moisture is gradually removed from these solid samples in a rotary evaporator at 40°C and 5 mbar vacuum, so that a series of samples with decreasing residual moisture content is prepared from each of the two purity grades (unwashed and washed).

| Unwashed Sample no. | Residual moisture [% by mass] | Unwashed sample | Residual moisture [% by mass] |
|---|---|---|---|
| 1 | 53 | 1 | 51 |
| 2 | 47 | 2 | 47 |
| 3 | 36 | 3 | 40 |
| 4 | 32 | 4 | 36 |
| 5 | 26 | 5 | 31 |
| 6 | 14 | 6 | 24 |
| 7 | 11 | 7 | 19 |

4 ml borosilicate vials are filled with this sample material and the filling level is adjusted to 2/3 of the glass by gentle tapping. To minimize evaporation losses, the screw caps of each vial are additionally sealed with a polyethylene film. All samples are shaken in parallel in a tempering block on a Quantifoil Instruments GmbH ThermoTwister comfort heating/cooling shaker for a defined period at a defined temperature and then visually evaluated. Classification is carried out according to the following points system:

5 points = sample unchanged

4 points = sample compacted/started to dissolve

3 points = sample visibly started to dissolve

2 points = sample cloudy highly viscous solution

1 point = sample dissolved to clear solution

The following two tables summarize the observations made at the end of each tempering step, and photographs taken (see Fig. 12) complete the overview.

Table of samples of unwashed quality:

| Test duration [h] | 24 | 24 | 24 | 24 | 24 | 24 | 5 | 5 | 5 | 5 | 5 | 5 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Temperature [°C] | 35 | 40 | 45 | 50 | 55 | 60 | 65 | 70 | 75 | 80 | 85 | 90 |
| 51 [% by mass] residual moisture | 5 | 5 | 5 | 5 | 5 | 2 | 1 | 1 | 1 | 1 | 1 | 1 |
| 47 [% by mass] residual moisture | 5 | 5 | 5 | 5 | 5 | 3 | 1 | 1 | 1 | 1 | 1 | 1 |
| 40 [% by mass] residual moisture | 5 | 5 | 5 | 5 | 5 | 3 | 1 | 1 | 1 | 1 | 1 | 1 |
| 36 [% by mass] residual moisture | 5 | 5 | 5 | 5 | 5 | 3 | 1 | 1 | 1 | 1 | 1 | 1 |
| 31 [% by mass] residual moisture | 5 | 5 | 5 | 5 | 4 | 3 | 1 | 1 | 1 | 1 | 1 | 1 |
| 24 [% by mass] residual moisture | 5 | 5 | 5 | 4 | 4 | 3 | 2 | 1 | 1 | 1 | 1 | 1 |
| 19 [% by mass] residual moisture | 5 | 5 | 5 | 5 | 5 | 4 | 2 | 2 | 2 | 2 | 2 | 2 |

Table of samples of “washed quality”:

| Test duration [h] | 24 | 24 | 24 | 24 | 24 | 24 | 5 | 5 | 5 | 5 | 5 | 5 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Temperature [°C] | 35 | 40 | 45 | 50 | 55 | 60 | 65 | 70 | 75 | 80 | 85 | 90 |
| 53 [% by mass] residual moisture | 5 | 5 | 5 | 5 | 5 | 3 | 1 | 1 | 1 | 1 | 1 | 1 |
| 47 [% by mass] residual moisture | 5 | 5 | 5 | 5 | 5 | 5 | 3 | 1 | 1 | 1 | 1 | 1 |
| 36 [% by mass] residual moisture | 5 | 5 | 5 | 5 | 5 | 5 | 3 | 1 | 1 | 1 | 1 | 1 |
| 32 [% by mass] residual moisture | 5 | 5 | 5 | 5 | 5 | 5 | 4 | 3 | 3 | 2 | 2 | 2 |
| 26 [% by mass] residual moisture | 5 | 5 | 5 | 5 | 5 | 5 | 4 | 3 | 3 | 2 | 2 | 2 |
| 14 [% by mass] residual moisture | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| 11 [% by mass] residual moisture | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |

The photographs of the samples taken at the end of each tempering step show very clearly that samples with high residual moisture contents and at the same time low purity compact at only low temperatures and dissolve partially or even completely in their own residual moisture. This property significantly complicates economic process management, i.e. high product yields due to the input of a lot of drying energy.
On the other hand, DTPMP solid qualities with less than 0.7% chloride and less than 40% residual moisture prove to be advantageous with regard to their drying behaviour.

The X-ray diffraction diagram of the α crystal modification according to the invention recorded with Cu-Kα1 radiation is shown in Fig. 2, wherein the characteristic reflections are found in Table 1, and proves the absence of another crystal modification. The D8 Discover (Bruker) high-resolution X-ray diffractometer was used to record the X-ray diffraction diagram.

Table 1: Characteristic reflections of crystallisates of the α crystal modification.

| 2Θ | d | Rel. intensity |
|---|---|---|
| 6.796 | 12.99626 | 38.00% |
| 12.534 | 7.05661 | 21.70% |
| 12.937 | 6.83779 | 24.10% |
| 17.9 | 4.9513 | 35.60% |
| 18.641 | 4.75618 | 26.50% |
| 18.981 | 4.67183 | 22.00% |
| 20.152 | 4.40287 | 41.00% |
| 20.94 | 4.23896 | 27.60% |
| 21.276 | 4.17267 | 10.20% |
| 21.854 | 4.06371 | 21.30% |
| 22.229 | 3.99591 | 45.80% |
| 22.52 | 3.94501 | 100.00% |
| 23.031 | 3.85863 | 72.60% |
| 23.119 | 3.84415 | 39.10% |
| 25 | 3.55902 | 64.30% |

Example 6 - Procedure for the production of the β crystal modification

A starting amount of 4.49 kg of slurry, containing 38.9% by mass DTPMP and 3.0% by mass chloride, is placed in a double-walled 5-litre stirred tank reactor with a 14 cm anchor agitator. Seeding was carried out once with 0.2 kg of crystallisate of the β crystal modification comprising 85% by mass DTPMP and 0.1% by mass chloride and with a main particle size of 30 µm. A calculated initial suspension density of 3.6% by mass was obtained. Precipitation took place at a constant stirring speed of 150 rpm.

The process is left isothermal for a period of 3 days. The crystallisation is first left at a constant initial temperature of 58° C for 24 hours and then the temperature is lowered

continuously to 46° C. with a temperature profile of about 1 K per 6 hours and left for a remaining period of 71 hours. The matured crystallisate is separated from the aqueous solution in a filtering centrifuge having a perforated drum with a filtering area of 235 $cm^2$ and at a centrifugation speed of 6800 rpm for 2 minutes.

This centrifugation speed of 6800 rpm corresponds to a separating capacity of 3500 g. Three washing operations with washing water (corresponding to half the amount of solid, divided into 3 equal amounts) are then carried out. Finally, the separated crystallisate is dried for 5 minutes at a centrifugation speed of 10,000 rpm. This centrifugation speed of 10,000 rpm corresponds to a separating capacity of 8400 g.

| | Quantity [g] | DTPMP [% by mass] | Chloride [% by mass] | Chloride in DTPMP [% by mass] |
|---|---|---|---|---|
| Slurry | 4492 | 38.9 | 3.0 | 7.7 |
| Solid unwashed | 1509 | 83.6 | 0.6 | 0.7 |
| Solid washed 1 x | | 85.4 | 0.36 | 0.4 |
| Solid washed 2 x | | 86.0 | 0.3 | 0.4 |
| Solid washed 3 x | 1017 | 87.2 | 0.09 | 0.1 |
| Filtrate: | 2915 | 26.9 | 3.8 | 14.1 |
| Washing water: | 1312 | 12.1 | 1.54 | 12.7 |

The particle size of the DTPMP crystallisates is then determined by means of a laser diffraction particle size analyser LS 13 320/Beckmann Coulter at a wavelength of 780 nm.

| | End |
|---|---|
| $d_{50}$ [µm] | 60 |
| $d_{10}$ [µm] | 17 |
| $d_{90}$ [µm] | 113 |

The average particle size at the end of the test is determined using a microscope and Olympus visualisation software (cf. Fig. 5):

| | |
|---|---|
| Length [µm] | 50-120 |
| Width [µm] | 10-50 |
| Thickness [µm]: | 1-5 |

Crystallisates of the β crystal modification can be obtained with comparable yields and degrees of purification over a wide temperature range. Cooling crystallisation requires low cooling rates to avoid supersaturation. An isothermal reduction of supersaturation is possible both in the upper existence range of the β crystal modification and in the lower existence range of the β crystal modification.

The X-ray diffraction diagram of the β crystal modification according to the invention recorded with Cu-Kα1 radiation is shown in Fig. 4, wherein the characteristic reflections are found in Table 1, and proves the absence of another crystal modification. The D8 Discover (Bruker) high-resolution X-ray diffractometer was used to record the X-ray diffraction diagram.

Table 2: Characteristic reflections of crystallisates of the β crystal modification

| 2Θ | d | Rel. intensity |
|---|---|---|
| 6.707 | 13.1694 | 41.30% |
| 12.464 | 7.09618 | 33.30% |
| 13.512 | 6.54779 | 22.10% |
| 14.553 | 6.08179 | 32.50% |
| 18.596 | 4.76749 | 43.80% |
| 18.894 | 4.69305 | 29.40% |
| 19.614 | 4.52231 | 36.50% |
| 20.02 | 4.43159 | 39.80% |
| 20.854 | 4.25612 | 32.00% |
| 21.204 | 4.18675 | 27.70% |
| 22.12 | 4.01534 | 65.10% |
| 22.522 | 3.94466 | 79.10% |
| 22.988 | 3.86569 | 76.80% |
| 24.8 | 3.58726 | 50.60% |
| 25.166 | 3.53581 | 35.70% |

Example 7 - Thermal Analysis of the Crystals

In a drying cabinet, crystallisates of the α, β and γ crystal modification are pre-dried at 80° C. for 24 hours to residual moisture contents of <10% by mass. Thermogravimetric analysis is carried out by placing the samples in a platinum crucible under a heating regime of 30° C. to 230°C with a constant heating rate of 1.0 K/min in a TG/DTA 220 (Seiko Instruments). Melting of the samples in a temperature range between 130 and 140°C is detectable thermo-optically (Fig. 11). The crystallisates of the α crystal modification begin to melt at 130° C, the β crystal modification melts at 135° C and melting begins at 140° C

for crystallisates of the γ crystal modification. The γ crystal modification can thus advantageously be dried with higher energy inputs and thus more energy efficiently than crystallisates of the α or β crystal modification, while retaining the solid state of aggregation.

By means of DSC/TG coupled IR gas analysis (Fig. 9), the loss of mass of 3 to 5% by mass which occurs upon melting can be attributed to water. This amount of water corresponds to 1 mol of water per mol of DTPMP plus a negligible amount of retained water of residual moisture deposited on the surface. The analysis is the proof that a crystallisate of DTPMP is present in the form of the crystalline monohydrate of the acid DTPMP.

Example 8 - Determination of hygroscopicity

To determine the hygroscopicity, solid samples were stored in 25 ml glass beakers in a desiccator under constant humidity. Via a saturated magnesium nitrate solution with precipitate (about 1/3 precipitate in 2/3 of the solution), a relative humidity of 55% by mass becomes established at 22 ± 2° C. The water absorption of the samples was determined gravimetrically once daily as mass difference over a period of 12 days (cf. Fig. 14).

Two spray-dried powders were tested in comparison to crystallisate samples of the α, β and γ crystal modifications.

A DTPMP synthesis product with the quality parameters from Table 4 used as the starting slurry for the crystallisation was spray dried with a Büchi-Mini Spray Dryer B-290.

The second spray-dried powder was obtained from re-dissolved crystallisate of the α crystal modification and thus showed the same low degree of impurity as the crystallisate of the α crystal modification.

The composition of the samples used and the relative water absorption [in % by mass] are given in Table 4 below.

Table 4:

| | **Total ($H_3PO_4$ + $H_3PO_3$) / DTPMP** | **Chloride/DTPMP** | **Bulk density** | **Relative water absorption** |
|---|---|---|---|---|
| Product | % by mass | % by mass | [g/ml] | % by mass/day |
| Amorphous powder from spray drying of an unpurified DTPMP synthesis product | 6.5 | 3.5 | 0.27 | 0.40 |
| Amorphous powder from spray drying of a DTPMP acid purified by recrystallization | 3.3 | 1.3 | 0.27 | 0.29 |
| Crystal form α, purified quality | 3.3 | 1.3 | 0.36 | 0.03 |
| Crystal form β, purified quality | 1.1 | 0.3 | 0.49 | 0.04 |
| Crystal form γ, purified quality | 0.95 | 0.05 | 0.59 | 0.003 |

A clear differentiation is possible after only a short time. Spray-dried powders of the unpurified DTPMP synthesis product (amorphous structure) exhibit the greatest hygroscopicity. The DTPMP quality purified by recrystallization and spray dried (amorphous structure) exhibits a lower water absorption capacity than the unpurified crude product while having the same very high specific surface area.

By contrast, the crystallisates of α, β and γ crystal modifications according to the invention are distinguished by consistently low water absorption, crystal form γ exhibiting by far the lowest hygroscopicity. This appears to be due to the compact, cuboid crystal form, which results in a high purification success and low hygroscopicity.

Example 9 - Hygroscopicity of acids and salts

In a further test, the influence of the degree of neutralisation of the phosphonic acid DTPMP on the hygroscopicity was studied, on account of its industrial relevance, especially the sodium salts. To that end, 10 g of sample were stored in four crystallisation dishes of equal size in a desiccator under constant humidity. Via a saturated magnesium nitrate solution with precipitate (about 1/3 precipitate in 2/3 of the solution), about 55% by weight humidity is established at 22° C. The water absorption of the samples was determined gravimetrically twice daily as a mass difference over a period of 22 days (cf. Fig. 15).

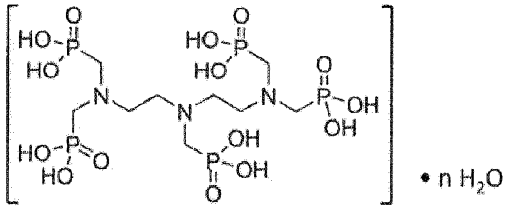
A crystallisate of the α crystal modification with a foreign acid content of 3.8% chloride by weight and in total 6.6% $H_3PO_4$ and $H_3PO_3$ by mass per 100% DTPMP by mass was dissolved again. Portions were neutralised with sodium hydroxide solution to pH (1% strength) =1.7 for the $Na_{0.5}$-DTPMP salt, pH (1% strength) = 2.1 for the $Na_3$-DTPMP salt and pH (1% strength) = 6.6 for the $Na_7$-DTPMP salt. These aqueous solutions were spray dried using a Büchi-Mini Spray Dryer B-290.

After only half the test time, the powder samples neutralised to pH 7 are visibly contracting to form a block. After 22 days, the powdered structure of the DTPMP acid is still recognisable, the sample of the Na salt has liquefied.

This shows that, with the same, low degree of impurity, solids of DTPMP acid are stable to storage, while this is not the case for the sodium salts of DTPMP.

**Patentkrav**

**1.** Krystallisat af den rene syre DTPMP ifølge den generelle formel (I) eller en tautomer form deraf:




(I)

hvor n er et tal mellem 0 og 2,

**kendetegnet ved, at** krystallisatet har mindst en krystalmodificering valgt fra *α, β* og *γ*,

hvor *α*-krystalmodificeringen er **kendetegnet ved** følgende karakteristiske reflektioner i røntgendiffraktionsdiagrammet, målt under anvendelse af Cu-$K_\alpha$ stråling:

| **2Θ** | **d** |
|---|---|
| 6,8 | 13,00 |
| 17,9 | 5,0 |
| 20,2 | 4,40 |
| 22,2 | 4,00 |
| 22,5 | 3,95 |
| 23,0 | 3,86 |
| 23,1 | 3,84 |
| 25,0 | 3,6 |

hvor *β*-krystalmodificeringen er **kendetegnet ved** følgende karakteristiske reflektioner i røntgendiffraktionsdiagrammet, målt under anvendelse af Cu-$K_\alpha$ stråling:

| **2Θ** | **d** |
|---|---|
| 6,7 | 13,17 |

| **2Θ** | **d** |
|---|---|
| 18,6 | 4,77 |
| 19,6 | 4,5 |
| 20,0 | 4,4 |
| 22,1 | 4,0 |
| 22,5 | 3,9 |
| 23,0 | 3,9 |
| 24,8 | 3,6 |
| 25,2 | 3,5 |

og hvor *γ*-krystalmodificeringen er **kendetegnet ved** følgende karakteristiske reflektioner i røntgendiffraktionsdiagrammet, målt under anvendelse af Cu-$K_\alpha$ stråling:

| **2Θ** | **d** |
|---|---|
| 13,0 | 6,8 |
| 17,9 | 4,9 |
| 22,0 | 4,0 |
| 22,4 | 4,0 |
| 23,1 | 3,8 |
| 23,3 | 3,8 |
| 25,1 | 3,6 |
| 26,1 | 3,4 |

**2.** Fremgangsmåde til at opnå faststof af krystallinsk DTPMP som en ren syre med den generelle formel (I) ifølge det foregående krav fra et vandigt råprodukt, indeholdende DTPMP med en pH-værdi på mindre end 4 med følgende trin:

a. at anbringe podekrystaller, indeholdende DTPMP, i et vandigt råprodukt, indeholdende DTPMP med et samlet indhold i området fra 10 til 65 ma.%, op til en opslæmningstykkelse på mellem 1 til 25%,

b. at indføre kinetisk energi i det vandige råprodukt, hvorved et krystallisat, indeholdende DTPMP som en ren syre med et samlet indhold på mindst 75 ma.%, udfældes,
c. at separere krystallisatet fra det vandige råprodukt ved hjælp af sedimentering og/eller filtrering.

**3.** Fremgangsmåde ifølge krav 2, **kendetegnet ved, at** det vandige råprodukt indeholder urenheder i form af biprodukter og/eller ikke-omsatte udgangsprodukter.

**4.** Fremgangsmåde ifølge krav 2 eller krav 3, **kendetegnet ved, at** den kinetiske energi indføres i form af omrøring og/eller rystning og/eller ultrasonisk behandling.

**5.** Fremgangsmåde ifølge kravene 2 til 4, **kendetegnet ved, at**, for at opnå et faststof, har det vandige råprodukt en temperatur i området fra 25 til 85°C.

**6.** Fremgangsmåde ifølge et hvilket som helst af kravene 2 til 5, **kendetegnet ve, at** et separeret krystallisat har et faststofindhold på mindst 65%.

**7.** Fremgangsmåde ifølge et hvilket som helst af kravene 2 til 6, **kendetegnet ved, at** fremgangsmåden omfatter mindst et isotermisk procestrin, hvor temperaturforskellen i det vandige råprodukt er konstant i løbet af et defineret tidsrum for introduktion af kinetisk energi.

**8.** Fremgangsmåde ifølge krav 7, **kendetegnet ved, at** temperaturen af det vandige råprodukt reduceres mellem det definerede tidsrum på to isotermiske procestrin med en temperaturprofil på fra 1 til 7 K per dag.

**9.** Fremgangsmåde ifølge et hvilket som helst af kravene 2 til 8, **kendetegnet ved, at** fremgangsmåden udføres i en kvasikontinuerlig drift.

**10.** Fremgangsmåde ifølge et hvilket som helst af kravene 2 til 6, **kendetegnet ved, at**, for at opnå et faststof, har det vandige råprodukt en stærk syre i

området fra 1 til 4,5 ma.%.

**11.** Anvendelse af en fremgangsmåde ifølge et hvilket som helst af kravene 2 til 10 til oprensning af et vandholdigt råprodukt, indeholdende DTPMP, med et samlet indhold på mindst 10 ma.%.

**12.** Anvendelse af en fremgangsmåde ifølge et hvilket som helst af kravene 2 til 6 til fremstilling af et krystallisat af den rene syre DTPMP ifølge den generelle formel (I) ifølge krav 1.

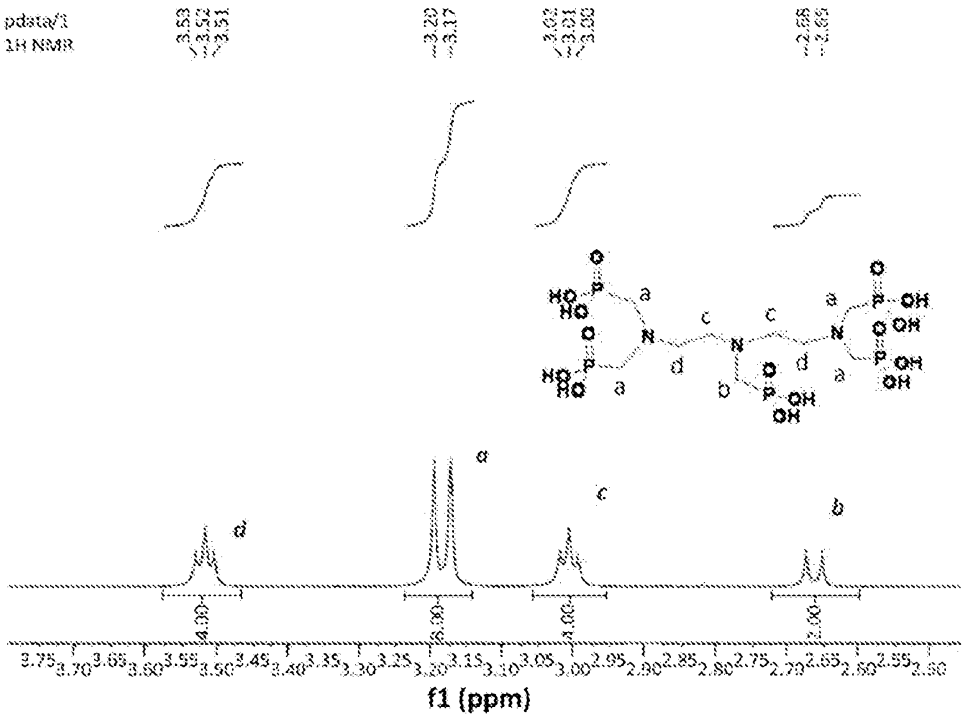

pdata/1
1H NMR
3.53
3.52
3.51
3.20
3.17
3.02
3.01
2.98
2.66
2.65
a
b
c
d
4.00
6.00
4.00
2.00
f1 (ppm)

Fig. 1

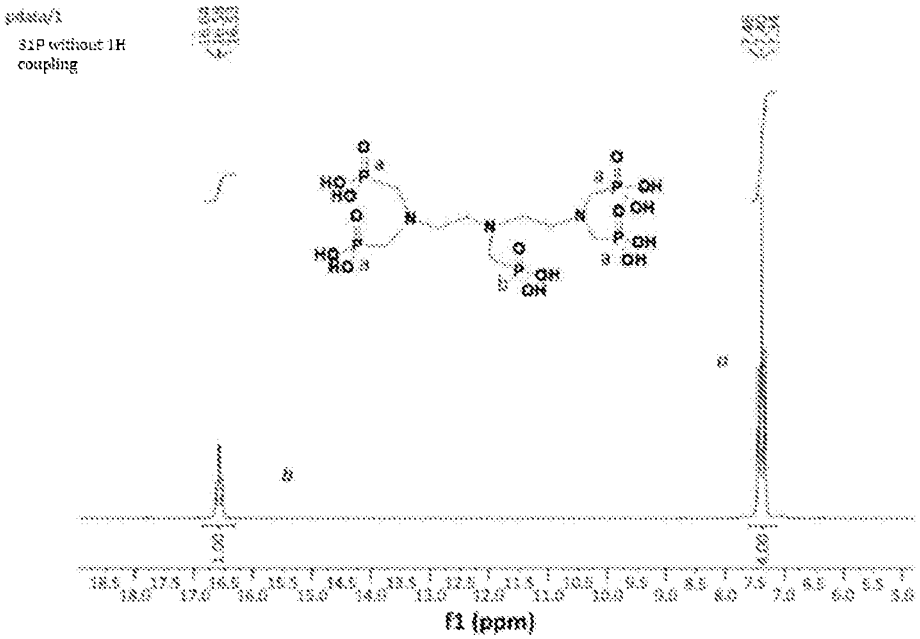



Fig. 1 (continued)

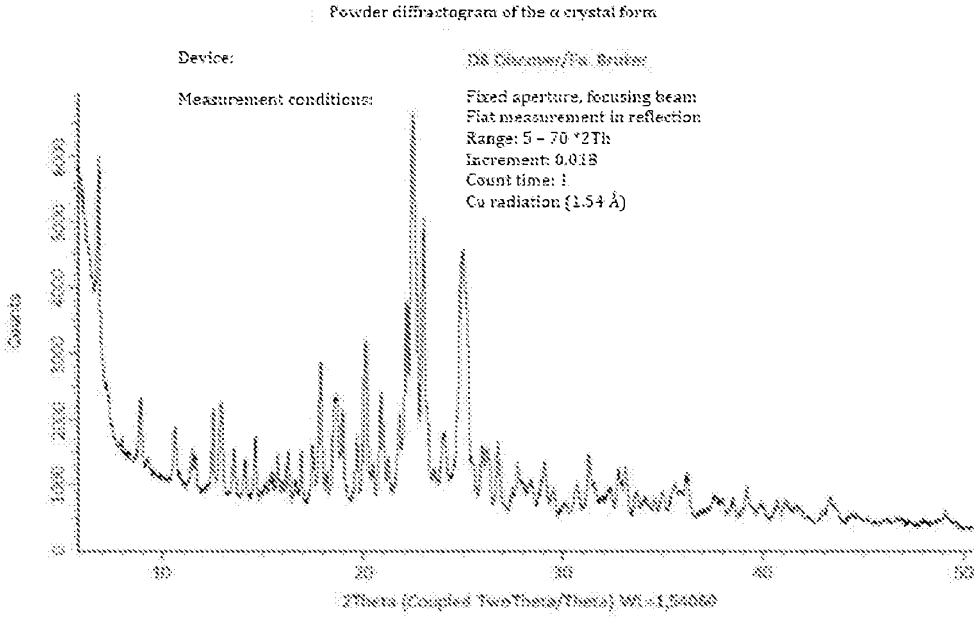

Powder diffractogram of the α crystal form
Device:
Measurement conditions:
Fixed aperture, focusing beam
Flat measurement in reflection
Range: 5 - 70 °2Th
Increment: 0.018
Count time: 1
Cu radiation (1.54 Å)
Counts
2Theta (Coupled TwoTheta/Theta) WL=1.54060

Fig. 2

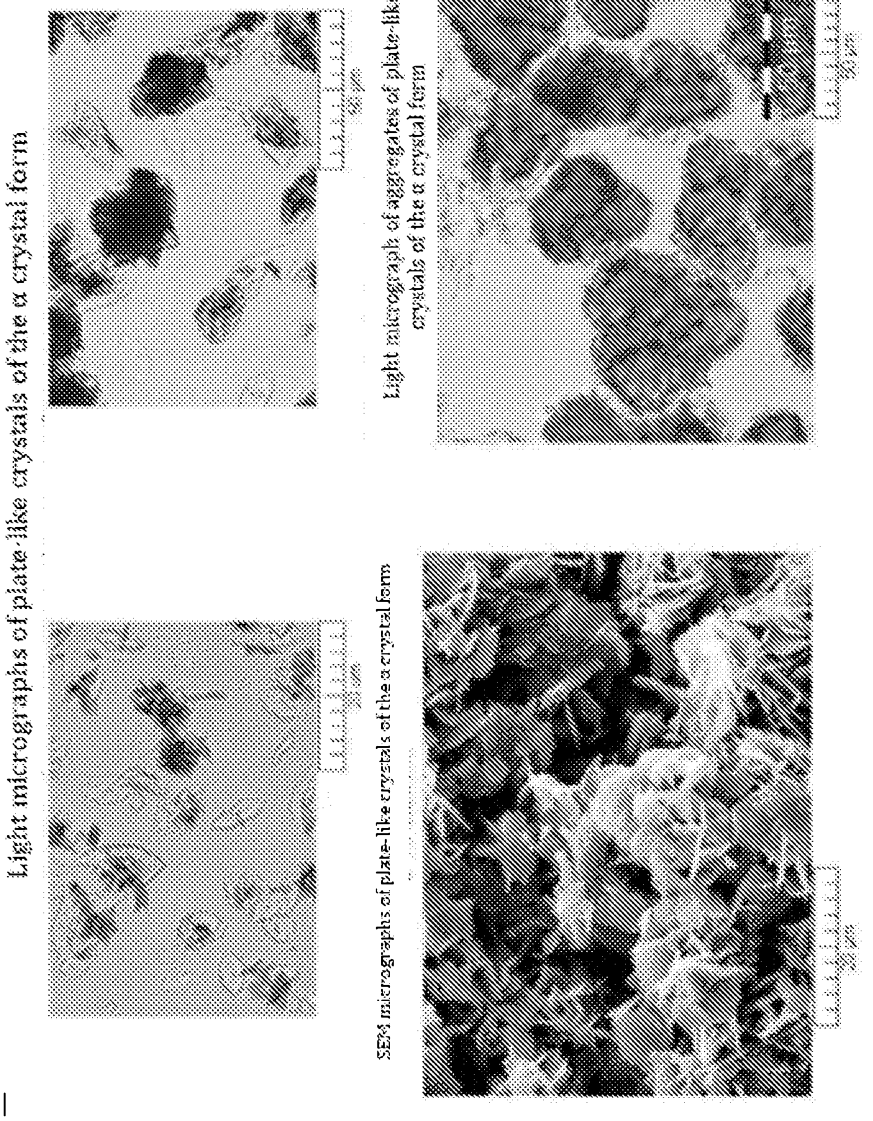

Light micrographs of plate-like crystals of the α crystal form
Light micrograph of aggregates of plate-like crystals of the α crystal form
SEM micrographs of plate-like crystals of the α crystal form

Fig. 3

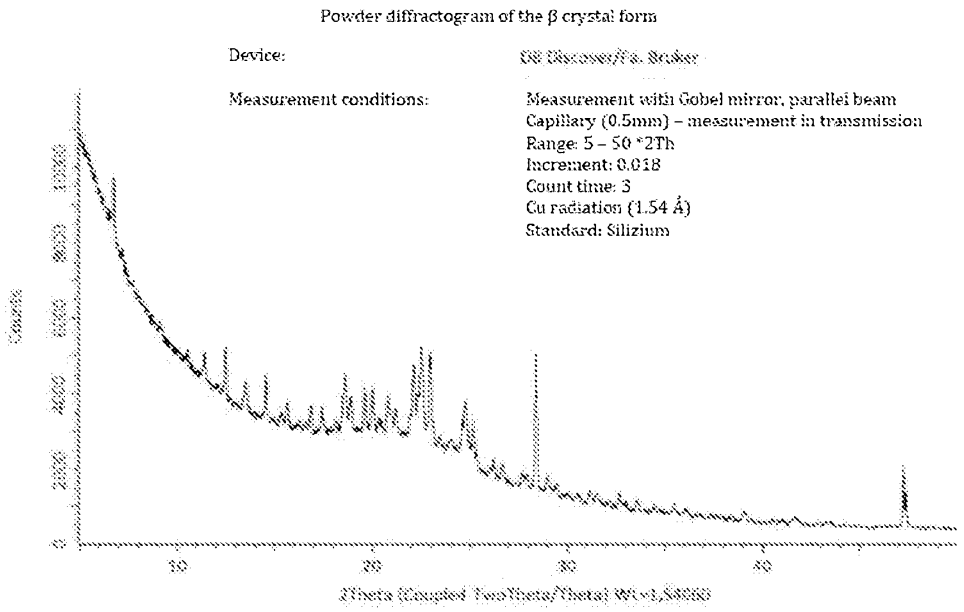
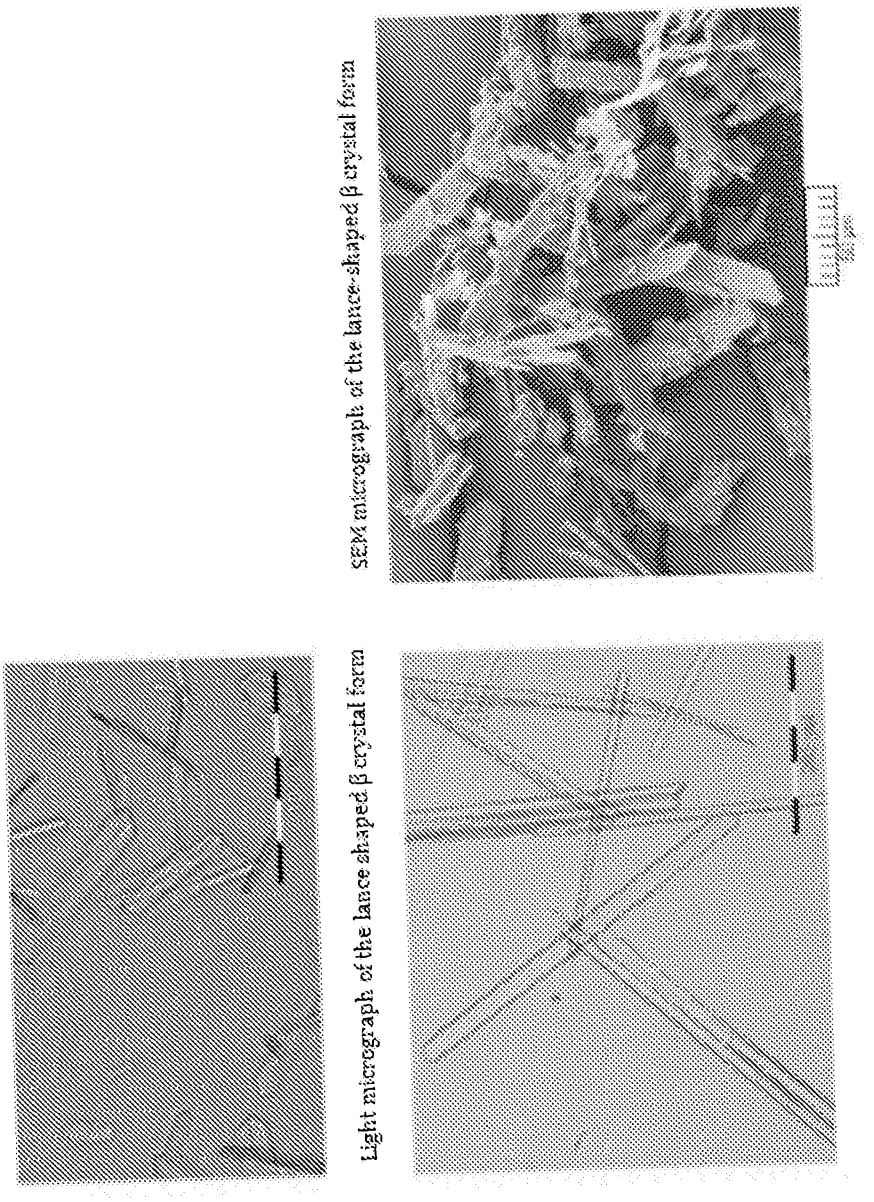

Powder diffractogram of the β crystal form
Device:
Measurement conditions:
Measurement with Gobel mirror, parallel beam
Capillary (0.5mm) – measurement in transmission
Range: 5 – 50 °2Th
Increment: 0.018
Count time: 3
Cu radiation (1.54 Å)
Standard: Silizium
10
20
30
40

Fig. 4

Fig. 5


SEM micrograph of the lance-shaped β crystal form
Light micrograph of the lance shaped β crystal form

Powder diffractogram of the γ crystal form calculated using PowderCell

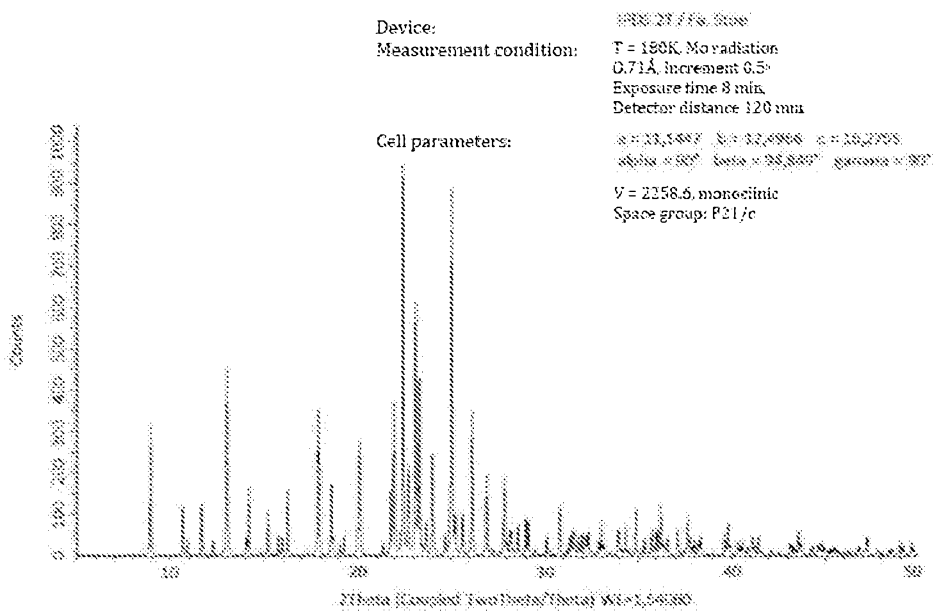



Fig. 6

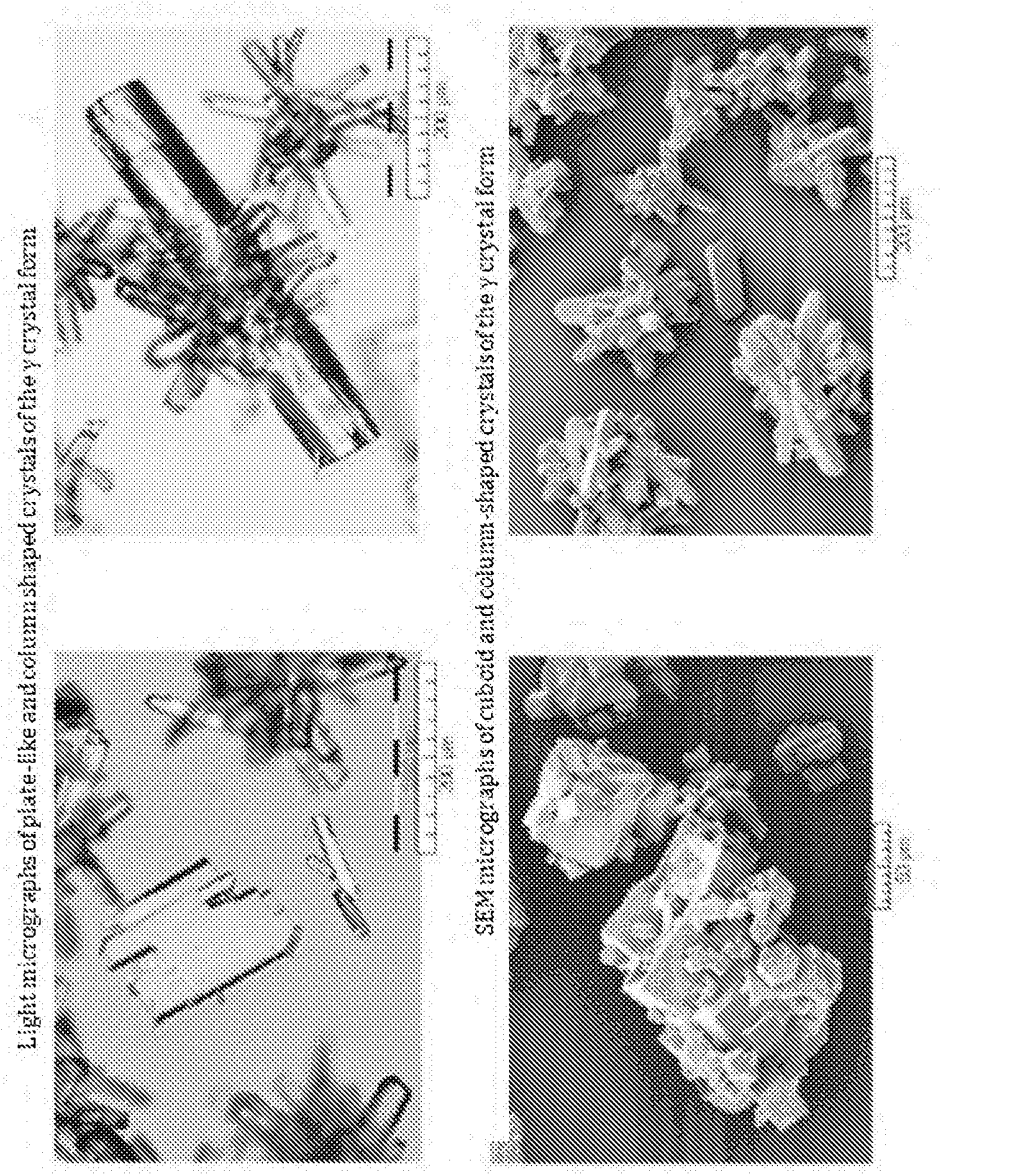

Light micrographs of plate-like and column-shaped crystals of the γ crystal form
SEM micrographs of cuboid and column-shaped crystals of the γ crystal form

Fig. 7

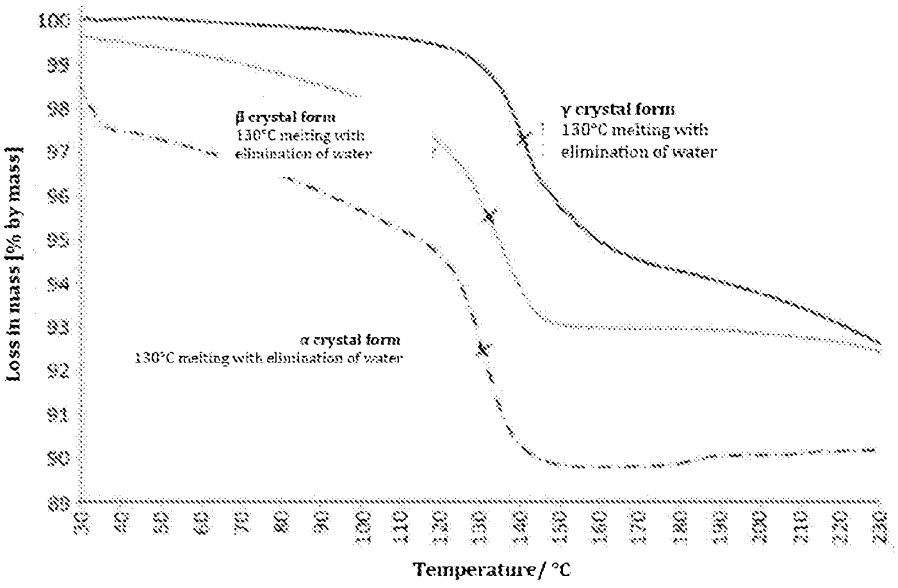
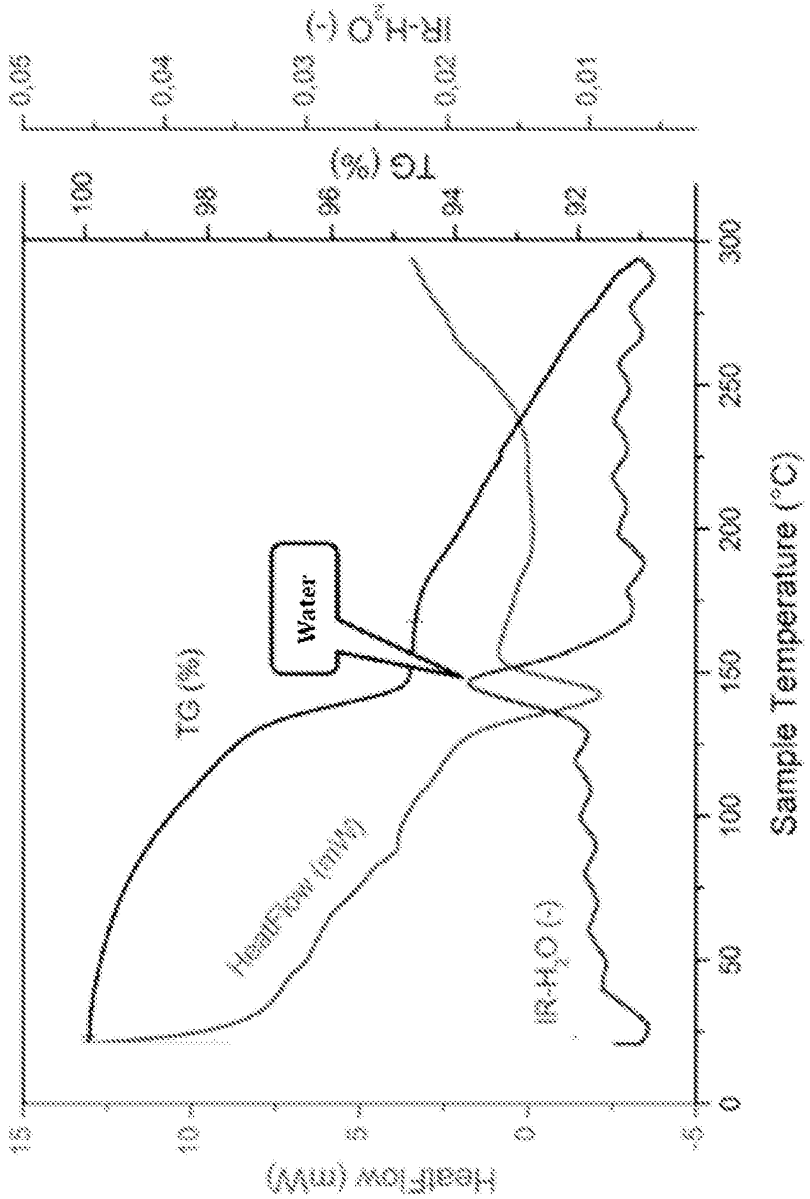

Loss in mass [% by mass]
100
99
98
97
96
95
94
93
92
91
90
89
β crystal form
130°C melting with
elimination of water
γ crystal form
130°C melting with
elimination of water
α crystal form
130°C melting with elimination of water
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
230
Temperature / °C

Fig. 8

Fig. 9


Water
TG (%)
HeatFlow (mW)
IR-H2O (-)
Sample Temperature (°C)
HeatFlow (mW)
TG (%)
IR-H2O (-)

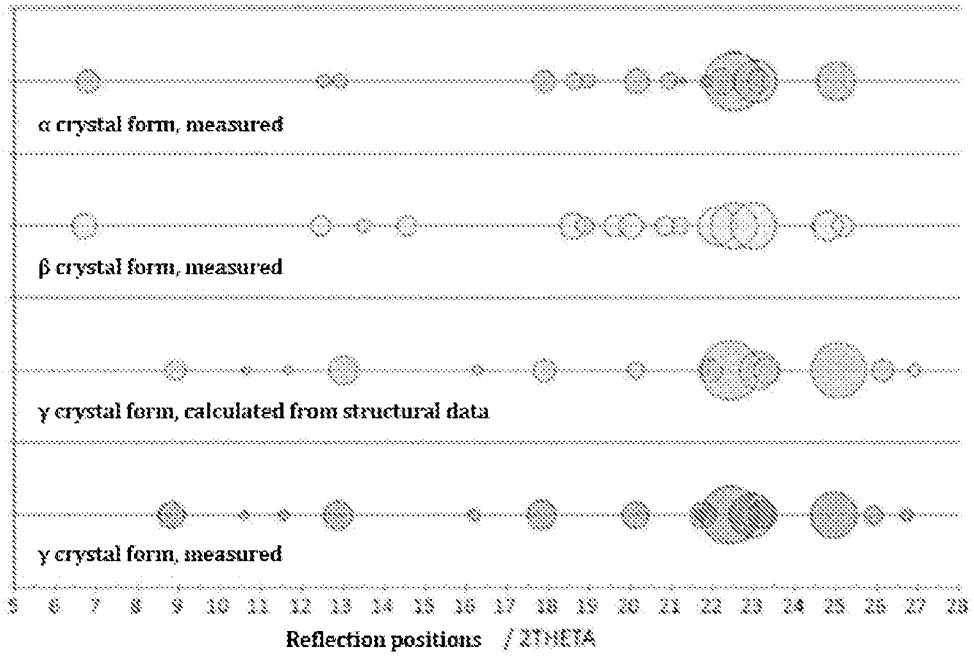

α crystal form, measured
β crystal form, measured
γ crystal form, calculated from structural data
γ crystal form, measured
5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28
Reflection positions / 2THETA

Fig. 10

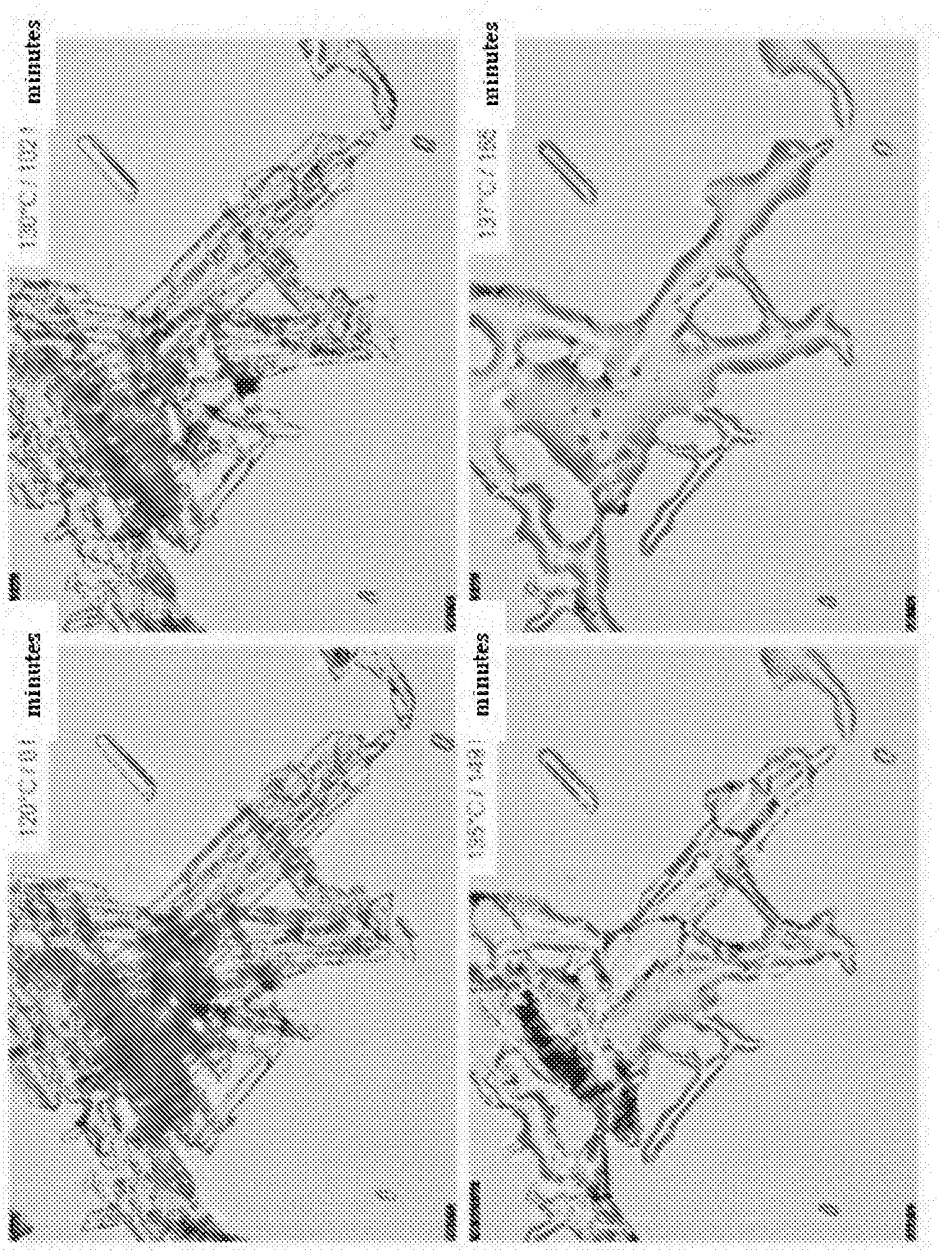



Fig. 11

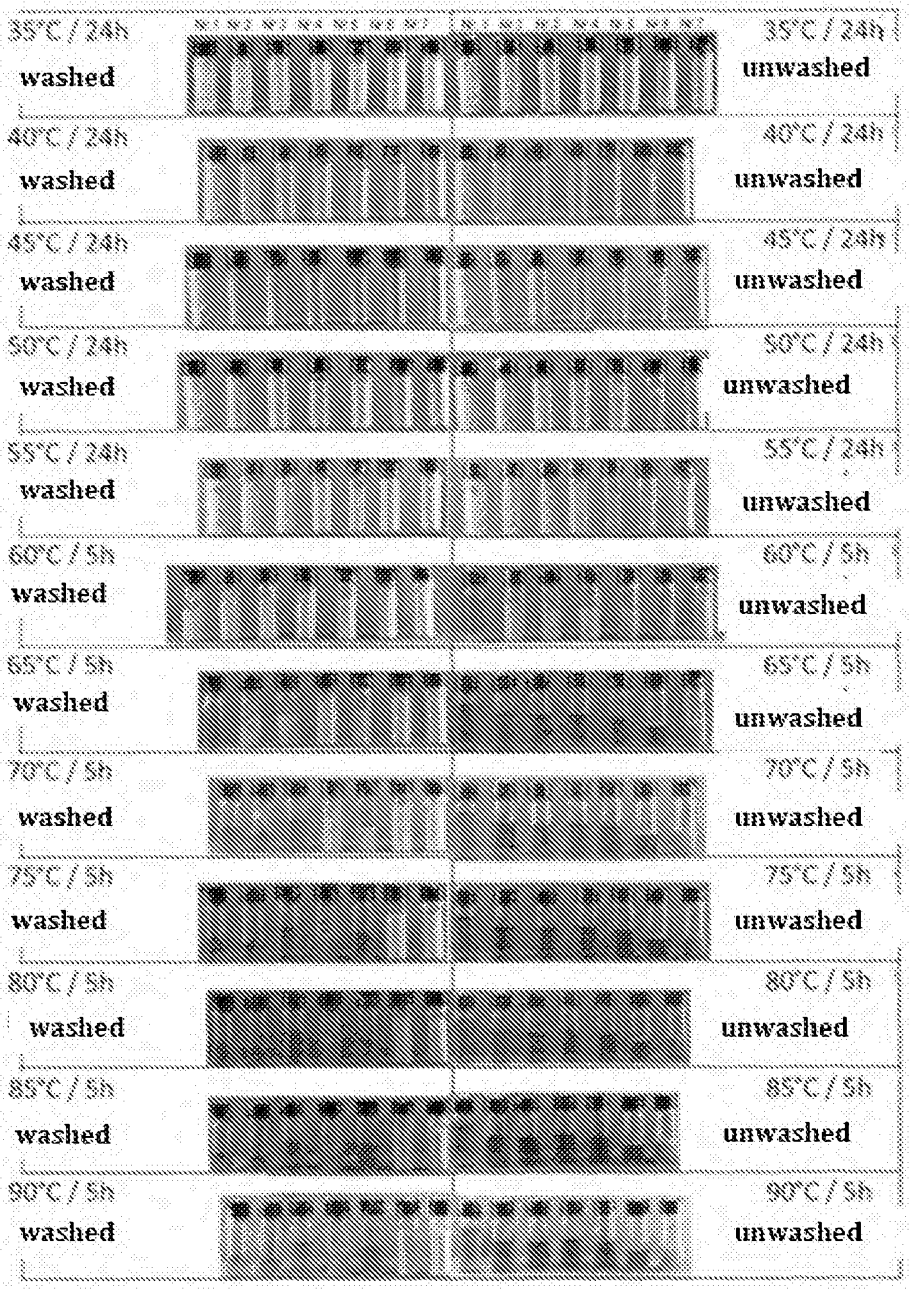

35°C / 24h
washed
35°C / 24h
unwashed
40°C / 24h
washed
40°C / 24h
unwashed
45°C / 24h
washed
45°C / 24h
unwashed
50°C / 24h
washed
50°C / 24h
unwashed
55°C / 24h
washed
55°C / 24h
unwashed
60°C / 5h
washed
60°C / 5h
unwashed
65°C / 5h
washed
65°C / 5h
unwashed
70°C / 5h
washed
70°C / 5h
unwashed
75°C / 5h
washed
75°C / 5h
unwashed
80°C / 5h
washed
80°C / 5h
unwashed
85°C / 5h
washed
85°C / 5h
unwashed
90°C / 5h
washed
90°C / 5h
unwashed

Fig. 12

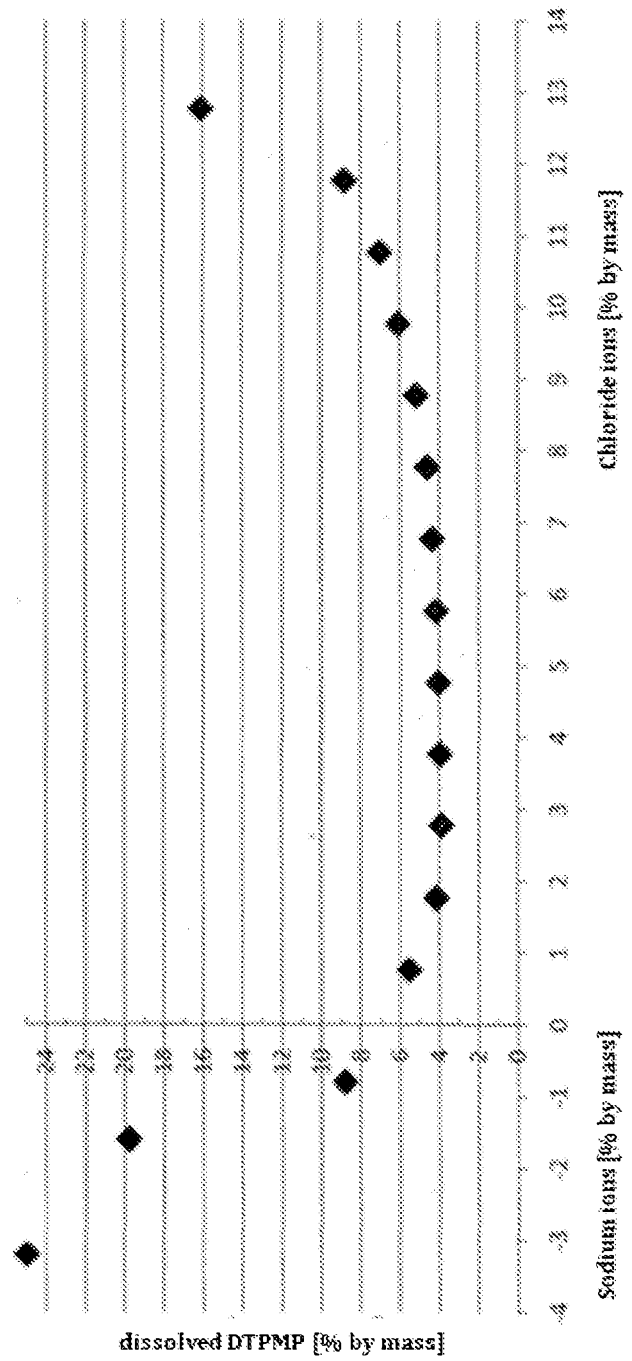

dissolved DTPMP [% by mass]
Sodium ions [% by mass]
Chloride ions [% by mass]

Fig. 13

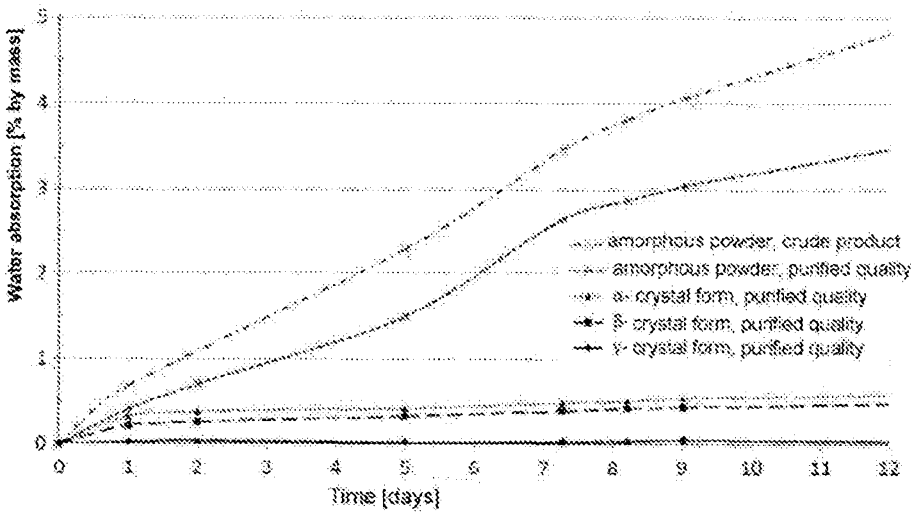

Water absorption [% by mass]
Time [days]
amorphous powder, crude product
amorphous powder, purified quality
α- crystal form, purified quality
β- crystal form, purified quality
γ- crystal form, purified quality

Fig. 14

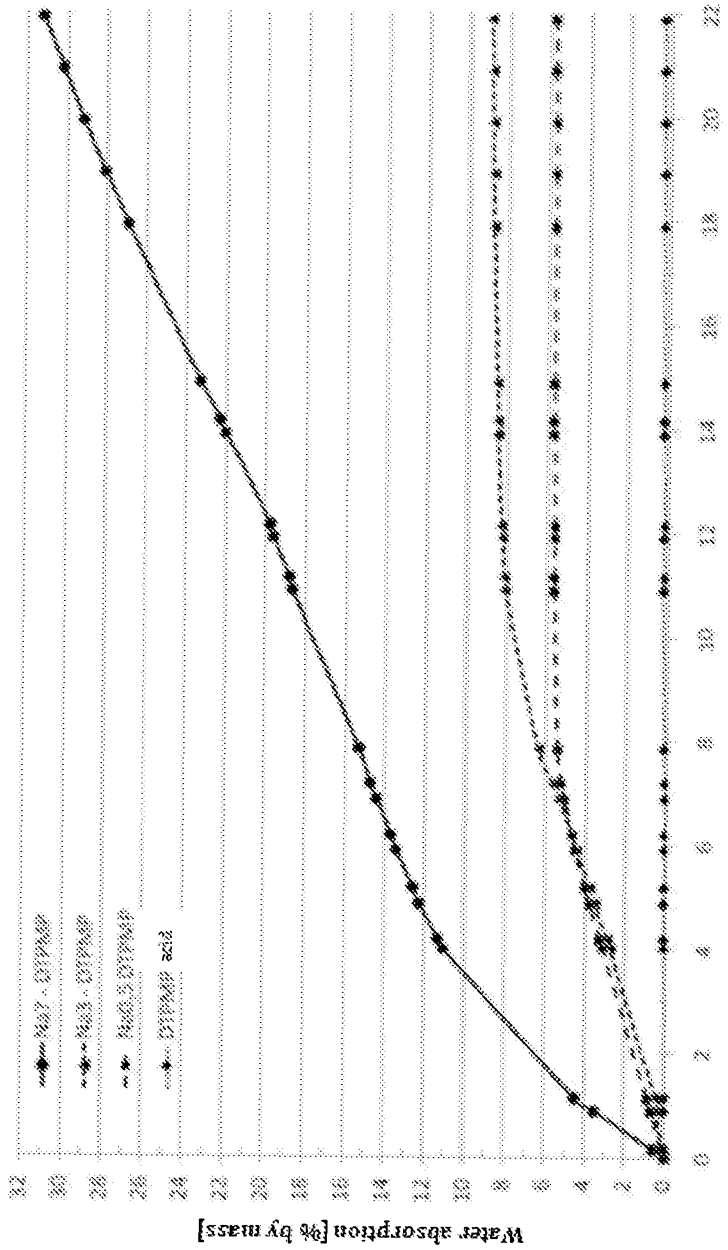

Water absorption [% by mass]
Time [Days]
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
32

Fig. 15