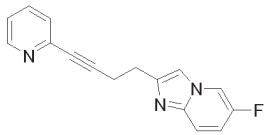
MONO-PHOSPHATE SALT OF 6-FLUORO-2-[4-(PYRIDIN-2-YL)BUT-3-YN-1 -YL] IMIDAZO[1 ,2A]PYRIDINE AND POLYMORPHS THEREOF AS NEGATIVE ALLOSTERIC MODULATOR OF MGLU5 RECEPTOR

SUMMARY OF THE INVENTION

The present invention relates to crystalline and amorphous forms of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate salt and methods of making these solid forms thereof. The invention compounds are modulators of $mGlu_5$ receptors which are useful for the treatment or prevention of central nervous system disorders as well as other disorders modulated by $mGlu_5$ receptors. The invention is also directed to pharmaceutical compositions and the use of such compounds in the manufacture of medicaments, as well as to the use of such compounds for the prevention and treatment of such diseases in which $mGlu_5$ receptors are involved.

BACKGROUND TO THE INVENTION

6-Fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine is described in PCT patent application WO05123703 (Example 74) as a negative allosteric modulator of the metabotropic glutamate receptor 5 ($mGluR_5$). The compound has the following structure:



The present invention is based on the discovery that the mono-phosphate of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine exhibits surprisingly much better solubility characteristics as compared to the corresponding free base. The free base has

an aqueous solubility of 0.5 mg/mL whereas the mono-phosphate salt has an aqueous solubility of 21.0 to 32.5 mg/mL, at all relevant physiological pH. Thus the increase of the solubility of at least 40 times of the mono-phosphate salt will greatly improve the pharmacological properties of the active compound.

In a first aspect, the present invention relates to the mono-phosphate salt of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine.

In another aspect, the present invention relates to two distinct crystalline forms, Polymorph I and Polymorph II of the 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate salt, respectively.

In yet another aspect, the present invention relates to the amorphous form of the 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate salt.

The aforementioned salt and its crystalline and amorphous forms can be distinguished by physical and chemical properties that can be characterized by X-ray powder diffraction patterns, infrared spectra, melting behavior or glass transition temperatures.

In another aspect, the invention provides a process of preparing the Polymorph I and the Polymorph II of the 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate salt.

The invention also includes pharmaceutical compositions comprising a therapeutically effective amount of a 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate salt in a crystalline or in an amorphous form, together with one or more pharmaceutically acceptable carrier, diluent or excipient therefor.

In accordance with the invention the abovementioned crystalline or amorphous forms of the 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate salt can be used for the preparation of medicaments useful in the control or the prevention of disorders based on the $mGlu_5$ receptor.

DEFINITION OF TERMS

The term "amorphous" as used herein denotes a physical state which is not crystalline and may be verified by X-ray diffraction and other means including but not limited to observation with a polarized light microscope and differential scanning calorimetry (DSC). More particularly, an amorphous salt in accordance with the present invention is preferably essentially free from any crystalline form of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate salt.

"Pharmaceutically acceptable" means substantially non-toxic to the subject to which the pharmaceutically acceptable material is administered.

"Therapeutically effective amount" means an amount that is effective to prevent, alleviate or ameliorate the symptoms of disease or prolonge the survival of the subject being treated.

"IR" is used herein as an acronym of InfraRed.

"NMR" is used herein as an acronym of Nuclear Magnetic Resonance.

"XRPD" is used herein as an acronym of X-Ray Powder Diffraction.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows an XRPD pattern of a typical lot of Polymorph I of the mono-phosphate of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine.

Figure 2 shows an IR spectrum of a typical lot of Polymorph I of the mono-phosphate of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine.

Figure 3 shows an XRPD pattern of a typical lot of Polymorph II of the mono-phosphate of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine.

DETAILED DESCRIPTION OF THE INVENTION

6-Fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine may be prepared as described in PCT patent application WO05123703, which is incorporated by reference herein in its entirety. WO05123703 describes methods of making and using the aforesaid compound.

As already mentioned hereinabove, the present invention relates to novel mono-phosphate salt and to crystalline and amorphous forms of the mono-phosphate salt of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine.

It has been found that 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine can be isolated, depending upon the method of preparation, as a mono-phosphate salt

and that such a salt has an unexpectedly and excellent solubility as a solid and satisfactorily serves as a pharmaceutical.

A further aspect of the present invention is the identification of two different crystal forms of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate, identified herein as Polymorphs I and II, respectively.

The mono-phosphate salt of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine can be prepared by salt formation of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine with phosphoric acid in methanol with subsequent spontaneous precipitation.

A fisrt polymorph described as "Polymorph I" of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate is a solvent-free, crystalline form and may be produced by a process described herein.

Therefore, one aspect of the invention provides a process of preparing Polymorph I of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate.

The Polymorph I of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate can be obtained by re-crystallization of the mono-phosphate salt in solvent comprising but not limited to ethanol:water (80:20), methanol, isopropyl alcohol:water (80:20), acetonitrile:water (80:20), methanol:dioxane (80:20), methanol:methyl ethyl ketone (80:20 or 60:40), methanol:acetonitrile (60:40), 2-butanone and water:dioxane (10:90).

The Polymorph I of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate can be characterized by at least 3 peaks selected from X-Ray

diffraction peaks obtained with a $Cu_{K\alpha}$ radiation at 2 θ (2 Theta (deg)) = 8.4, 10.2, 12.5, 15.7, 16.8, 18.6, 20.5, 21.3, 28.1, 29.4.

The Polymorph I of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate can also be characterized by the X-Ray powder diffraction pattern shown on Figure 1.

The Polymorph I of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate can also be characterized by an infrared spectrum having sharp bands at 3059, 2937, 2233, 1592, 1564, 1537, 1515, 1477, 1429, 1317, 1262, 1168, 1162, 1117, 863, 819, 772, 691.

The Polymorph I of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate can also be characterized by the infrared spectrum shown on Figure 2.

A second polymorph described as "Polymorph II" of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate is a solvent-free, crystalline form and may be produced by a process described herein.

Therefore, one aspect of the invention provides a process of preparing Polymorph II of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate.

The Polymorph II of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate can be obtained by re-crystallization of the mono-phosphate salt in solvent comprising but not limited to ethanol:water (60:40 or 20:80), methanol:water (20:80), propanol:water (40:60 or 20:80), acetonitrile:water (60:40 or 40:60 or 20:80), acetone:water (20:80) or THF:water (20:80).

The Polymorph II of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate can be characterized by at least 3 peaks selected from X-Ray diffraction peaks obtained with a $Cu_{K\alpha}$ radiation at 2 θ (2 Theta (deg)) = 8.5, 10.0, 12.5, 15.8, 17.1, 18.2, 18.7, 19.4, 20.2, 20.8, 25.7, 27.6.

The Polymorph II of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate can also be characterized by the X-Ray powder diffraction pattern shown on Figure 3.

A further aspect of the invention provides a combination of two of the polymorphs described herein.

In accordance with the invention, the crystalline or amorphous forms of the mono-phosphate salt of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine can be used for the preparation of medicaments useful in the treatment or prevention of disorders in which the $mGlu_5$ receptor plays a role. Such disorders include, but are not limited to: epilepsy, ischemia, neuropathic or inflammatory pain, psychiatric disorders such as psychotic disorders, central nervous system disorders selected from addiction, tolerance or dependence, affective disorders, such as depression and anxiety, attention-deficit/hyperactivity disorder, bipolar disorder, movement disorders, neuroprotection, migraine, neurological disorders such as neurodegeneration, neurotoxicity, Parkinson's disease, PD-LID, dystonia, memory impairment, Alzheimer's disease, dementia, delirium tremens, attentional disorders, eating disorders, mood disorders, cognitive disorders, personality disorders, behavioural disorders, substance of abuse related disorders, including alcohol, nicotine, cocaine, amphetamine, benzodiazepine, analgesics, opiate or other substance tolerance or dependence, bulimia nervosa, anorexia nervosa, gambling dependence, sex dependence, obsessive compulsive disorders, panic disorder, phobia, post-traumatic stress disorder, generalized anxiety disorder, seasonal affective disorders, acute stress disorder, inherited disorders such as Fragile X syndrome, autism, obesity and gastrointestinal disorders, for example, gastro-esophageal reflux disease (GERD), lower esophageal sphincter diseases or disorders,

diseases of gastrointestinal motility, colitis, Crohn's disease or irritable bowel syndrome (IBS).

In one preferred embodiment, the polymorphs of the mono-phosphate salt of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine can be used for the treatment or prevention of dystonia.

In one preferred embodiment, the polymorphs of the mono-phosphate salt of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine can be used for the treatment or prevention of Parkinson's disease L-DOPA induced dyskinesia.

In one preferred embodiment, the polymorphs of the mono-phosphate salt of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine can be used for the treatment or prevention of movement disorders.

In one preferred embodiment, the polymorphs of the mono-phosphate salt of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine can be used for the treatment or prevention of autism.

In one preferred embodiment, the polymorphs of the mono-phosphate salt of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine can be used for the treatment or prevention of Fragile X.

In one preferred embodiment, the polymorphs of the mono-phosphate salt of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine can be used for the treatment or prevention of anxiety.

In one preferred embodiment, the polymorphs of the mono-phosphate salt of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine can be used for the treatment or prevention of depression.

In one preferred embodiment, the polymorphs of the mono-phosphate salt of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine can be used for the treatment or prevention of pain.

In use for therapy in a mammalian patient, the polymorphs ot amorphous forms of the mono-phosphate of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine defined herein may be administered in the form of a pharmaceutical composition by any route including ingestion, administration by oral, intramuscular, subcutaneous, topical, intranasal, intraperitoneal, intrathoracical, intravenous, epidural, intrathecal, intracerebroventricular routes and by injection into the joints.

In a particular embodiment of the invention, the route of administration may be by ingestion or by an oral, intravenous or intramuscular route.

For preparing pharmaceutical composition from the polymorphs or the amorphous salt of the mono-phosphate of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine defined herein, inert, pharmaceutically acceptable carriers can be either solid or liquid. Solid form preparations include powders, tablets, dispersible granules, capsules, cachets and suppositories.

A solid carrier can be one or more substance, which may also act as a diluent, a flavoring agent, a solubilizer, a lubricant, a suspending agent, a binder, or a tablet-disintegrating agent; it can also be an encapsulating material.

In powders, the carrier is a finely divided solid, which is a mixture with the finely divided amorphous salt or polymorphs of the mono-phosphate of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine. In tablets, the active component is mixed with a carrier having the necessary binding properties in suitable proportions and compacted in the shape and size desired.

For preparing suppository compositions, a low-melting wax such as a mixture of fatty acid glycerides and cocoa butter is first melted and the active ingredient is dispersed therein by, for example, stirring. The molten homogeneous mixture is then placed in suitable sized moulds and allowed to cool and solidify.

Suitable carriers are magnesium carbonate, magnesium stearate, talc, lactose, sugar, pectin, dextrin, starch, tragacanth, methyl cellulose, sodium carboxymethyl cellulose, a low-melting wax, cocoa butter, and the like.

Tablets, powders, cachets, and capsules can be used as solid dosage forms suitable for oral administration by ingestion.

Liquid form compositions include solutions, suspensions, and emulsions. For example, sterile water or water propylene glycol solutions of the active compounds may be liquid preparations suitable for parenteral administration. Liquid compositions can also be formulated in solution in aqueous polyethylene glycol solution.

Aqueous solutions for oral administration can be prepared by dissolving the active component in water and adding suitable colorants, flavouring agents, stabilizers, and thickening agents as desired. Aqueous suspensions for oral use can be made by dispersing the finely divided component in water together with a viscous material such as natural synthetic gums, resins, methyl cellulose, sodium carboxymethyl cellulose, and other suspending agents known to the person skilled in the art.

Depending on the mode of administration, the pharmaceutical composition will preferably include from 0.05% to 99% (per cent by weight), more preferably from 0.10 to 50%w, of the amorphous salt or the polymorphs of the mono-phosphate of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine, alll percentages by weight being based on total composition.

The dosage at which the polymorphs or the amorphous salt of the mono-phosphate of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine according to the invention are administered can vary within wide limits and will, of course, have to be adjusted to the individual requirements in each particular case.

Within the scope of the invention is the use of the polymorphs or the amorphous form of the mono-phosphate of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine for the manufacture of a medicament.

Also within the scope of the invention is the use of the polymorphs or the amorphous form of the mono-phosphate salt of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine for the manufacture of a medicament for the therapy of: epilepsy, ischemia, neuropathic or inflammatory pain, psychiatric disorders such as psychotic disorders, central nervous system disorders selected from addiction, tolerance or dependence, affective disorders, such as depression and anxiety, attention-deficit/hyperactivity disorder, bipolar disorder, movement disorders, neuroprotection, migraine, neurological disorders such as neurodegeneration, neurotoxicity, Parkinson's disease, PD-LID, dystonia, memory impairment, Alzheimer's disease, dementia, delirium tremens, attentional disorders, eating disorders, mood disorders, cognitive disorders, personality disorders, behavioural disorders, substance of abuse related disorders, including alcohol, nicotine, cocaine, amphetamine, benzodiazepine, analgesics, opiate or other substance tolerance or dependence, bulimia nervosa, anorexia nervosa, gambling dependence, sex dependence, obsessive compulsive disorders, panic disorder, phobia, post-traumatic stress disorder, generalized anxiety disorder, seasonal affective disorders, acute stress disorder, inherited disorders such as

Fragile X syndrome, autism, obesity and gastrointestinal disorders, for example, gastro-esophageal reflux disease (GERD), lower esophageal sphincter diseases or disorders, diseases of gastrointestinal motility, colitis, Crohn's disease or irritable bowel syndrome (IBS).

A further aspect of the invention is a method for therapy of a patient suffering from any of the conditions discussed above, whereby an effective amount of a polymorph or the amorphous form defined herein is administered to a patient in need of such therapy.

Additionally, there is provided a pharmaceutical composition comprising at least one of the polymorphs or the amorphous form of the mono-phosphate of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine in association with a pharmaceutically acceptable carrier.

Particularly, there is provided a pharmaceutical composition comprising at least one of a polymorph defined herein in association with a pharmaceutically acceptable carrier for therapy, more particularly for therapy of the conditions mentioned herein.

Further, there is provided a pharmaceutical composition comprising at least one of the polymorphs or the amorphous form of the mono-phosphate of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine in association with a pharmaceutically acceptable carrier use in any of the conditions mentioned herein.

EXPERIMENTAL METHODS

X-Ray-Powder Diffraction (XRPD)

The X-ray powder diffractions pattern was collected using a Philips PW3710 diffractometer (wavelength α_1: 1.5406 Å, wavelength α_2: 1.54439 Å, Cu source,

Voltage 45kV, filament emission 30 mA). Samples were scanned from 5-50° 2θ and a 2.5 s per step time count.

Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry was performed using a Pyris Diamond DSC (Perkin Elmer). A sample (approximately 1-3 mg) was weighed into an aluminium sample pan and transferred to the DSC. The instrument was purged with helium at a flow rate of 20mL/min and data collected between 30°C and 250°C, using a heating rate of 10°C/minute.

Examples

The invention will further be described in more detail by the following Examples which describe methods whereby compounds of the present invention may be prepared, purified and analyzed, and which are not to be construed as limiting the invention.

Example 1: Preparation of the mono-phosphate salt form of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine

51.0 mg of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine was dissolved in 2.0 mL of methanol (192.2 μmol). 2.5 mL of 0.1 M Phosphoric acid solution (0.25 mmol of H_3PO_4) was added to the methanolic solution of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine under constant stirring. A clear solution was obtained which then turned into a milky liquid due to the precipitation of the mono-phosphate salt form of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine. The salt was then allowed to settle down and the supernatant liquid was decanted. The precipitate was dried under the flow of nitrogen and then washed with methanol. The dry solid mono-phosphate salt of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine was then obtained.

MS *m/z* ES^+= 266.2; ^{1}H-NMR (500MHz, DMSO-d_6) δ: 10.15 (3H, br s), 8.79-8.75 (1H, m), 8.51 (1H, d), 7.86 (1H, s), 7.76 (1H, t), 7.59 (1H, dd), 7.43 (1H, d), 7.36-7.29 (2H,

m), 3.02 (2H, t), 2.88 (2H, t); ^{13}C-NMR (125.76MHz, DMSO-d_6) δ: 18.49, 27.40, 80.79, 89.89, 111.51, 113.18, 113.51, 116.11, 116.31, 116.45, 116.52, 122.86, 126.84, 136.51, 141.65, 142.73, 145.79, 145.80, 149.74, 151.38, 153.22; IR (cm^{-1}): 3102, 3060, 2937, 2915, 2688, 2233, 1592, 1565, 1537, 1515, 1477, 1262, 1169, 819, 772, 752.

Example 2: Preparation of Polymorph-I of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate

The mono-phosphate salt of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine (9.5 mg, 26 μmol) was dissolved in 200 mL of a mixture of ethanol:water (80:20) with continuous stirring and gentle warming (30-35°C) and then filtered to obtain a clear solution. This was then left to crystallize at 5-6°C. The crystallized solid was filtered out and then dried under vacuum to yield the title compound (7.0 mg, 74%).

Example 3: Preparation of Polymorph-II of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate

6-Fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine mono-phosphate (10.0 g, 27.3 mmol) was dissolved in 200 mL of a mixture water:acetone (80:20) and was left to stir at 40°C for an hour, until a clear solution was obtained. Then the solution was kept at 4-6°C to allow crystallization. The crystals precipitated, then the supernatant was decanted and finally the crystals were dried under vacuum for 12 hours to yield the title compound.

CLAIMS

1. A crystalline form of the mono-phosphate salt of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine.

2. A crystalline form of the mono-phosphate salt of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine characterized by at least 3 peaks selected from X-Ray diffraction peaks obtained with a $CuK\alpha$ radiation at 2 θ (2 Theta (deg)) = 8.4, 10.2, 12.5, 15.7, 16.8, 18.6, 20.5, 21.3, 28.1, 29.4.

3. A crystalline form of the mono-phosphate salt of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine characterized by the X-Ray powder diffraction pattern shown on Figure 1.

4. A crystalline form of the mono-phosphate salt of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine characterized by an infrared spectrum having sharp bands at 3059, 2937, 2233, 1592, 1564, 1537, 1515, 1477, 1429, 1317, 1262, 1168, 1162, 1117, 863, 819, 772, 691.

5. A crystalline form of the mono-phosphate salt of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine characterized by an infrared spectrum shown on Figure 2.

6. A crystalline form of the mono-phosphate salt of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine characterized by at least 3 peaks selected from X-Ray diffraction peaks obtained with a $CuK\alpha$ radiation at 2 θ (2 Theta (deg)) = 8.5, 10.0, 12.5, 15.8, 17.1, 18.2, 18.7, 19.4, 20.2, 20.8, 25.7, 27.6.

7. A crystalline form of the mono-phosphate salt of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine characterized by the X-Ray powder diffraction pattern shown on Figure 3.

8. A process for the preparation of a compound according to claims 2 to 5, comprising the steps of a) salt formation of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine with phosphoric acid with subsequent spontaneous

precipitation, and re- crystallization of the product of step a) in ethanol:water (80:20).

9. A process for the preparation of a compound according to claims 6 and 7, comprising the steps of a) salt formation of 6-fluoro-2-[4-(pyridin-2-yl)but-3-yn-1-yl]imidazo[1,2-a]pyridine with phosphoric acid with subsequent spontaneous precipitation, and re- crystallization of the product of step a) in water:acetone (80:20).

10. A pharmaceutical composition comprising a therapeutically effective amount of a compound according to claims 1 to 7, or a combination of two of the polymorph forms of a compound according to claims 1 to 7, and at least one pharmaceutically acceptable carrier, diluent or excipient.

11. Use of a compound according to claims 1 to 7, or a composition according to claim 10, in the manufacture of a medicament for treating or preventing disorders in which the mGlu5 receptor plays a role, wherein the disorders are selected from the group consisting of: epilepsy, ischemia, neuropathic or inflammatory pain, psychiatric disorders such as psychotic disorders, central nervous system disorders selected from addiction, tolerance or dependence, affective disorders, such as depression and anxiety, attention-deficit/hyperactivity disorder, bipolar disorder, movement disorders, neuroprotection, migraine, neurological disorders such as neurodegeneration, neurotoxicity, Parkinson's disease, PD-LID, dystonia, memory impairment, Alzheimer's disease, dementia, delirium tremens, attentional disorders, eating disorders, mood disorders, cognitive disorders, personality disorders, behavioural disorders, substance of abuse related disorders, including alcohol, nicotine, cocaine, amphetamine, benzodiazepine, analgesics, opiate or other substance tolerance or dependence, bulimia nervosa, anorexia nervosa, gambling dependence, sex dependence, obsessive compulsive disorders, panic disorder, phobia, post-traumatic stress disorder, generalized anxiety disorder, seasonal affective disorders, acute stress disorder, inherited disorders such as Fragile X syndrome, autism, obesity and gastrointestinal disorders, for example, gastro-esophageal reflux disease (GERD), lower esophageal sphincter diseases or disorders, diseases of gastrointestinal motility, colitis, Crohn’s disease or irritable bowel syndrome (IBS).

12. Use of a compound according to claims 1 to 7, or a composition according to claim 10, in the manufacture of a medicament for treating or preventing dystonia.

13. Use of a compound according to claims 1 to 7, or a composition according to claim 10, in the manufacture of a medicament for treating or preventing Parkinson's disease L-DOPA dyskinesia.

14. Use of a compound according to claims 1 to 7, or a composition according to claim 10, in the manufacture of a medicament for treating or preventing movement disorders.

15. Use of a compound according to claims 1 to 7, or a composition according to claim 10, in the manufacture of a medicament for treating or preventing autism.

16. Use of a compound according to claims 1 to 7, or a composition according to claim 10, in the manufacture of a medicament for treating or preventing Fragile X.

17. Use of a compound according to claims 1 to 7, or a composition according to claim 10, in the manufacture of a medicament for treating or preventing anxiety.

18. Use of a compound according to claims 1 to 7, or a composition according to claim 10, in the manufacture of a medicament for treating or preventing depression.

19. Use of a compound according to claims 1 to 7, or a composition according to claim 10, in the manufacture of a medicament for treating or preventing pain.

20. A composition according to claim 10 for use in treating or preventing a disorder as defined in any of claims 11 to 19.