IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	ATAI Life Sciences AG	Confirmation No.: 2263
Serial No.:	18/116,195	Group No.:
Filing or 371(c) Date:	01 March 2023	Examiner:

Entitled: STABLE POLYMORPH OF R-MDMA HCL

THIRD-PARTY PRE-ISSUANCE SUBMISSION

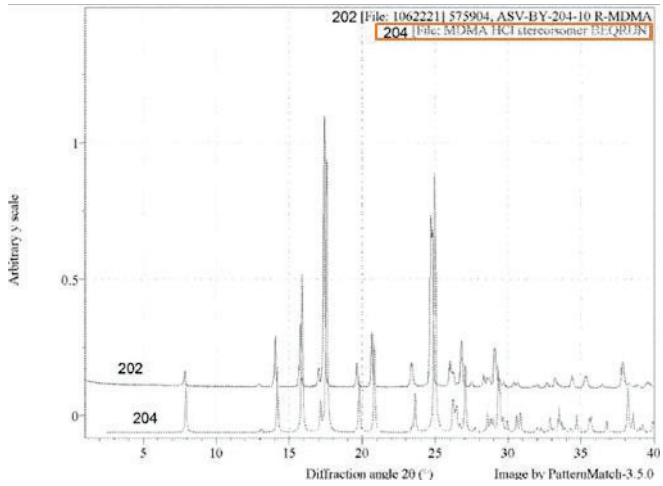
Examiner:

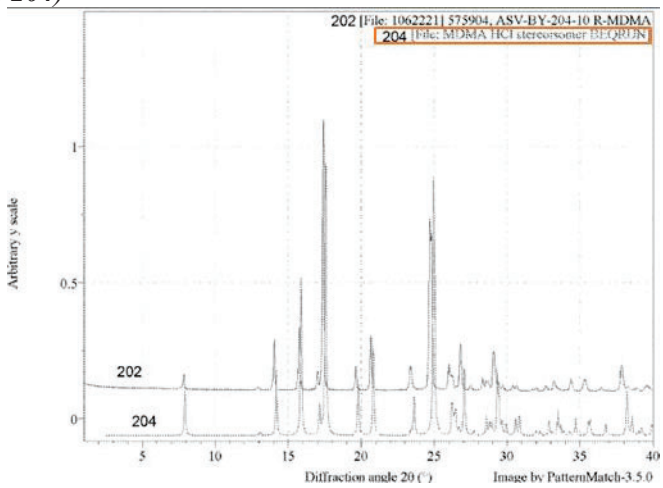
The following documents, which are also identified in the Form PTO/SB/429 filed herewith, are submitted for your consideration as being of potential relevance to the examination of the present application.

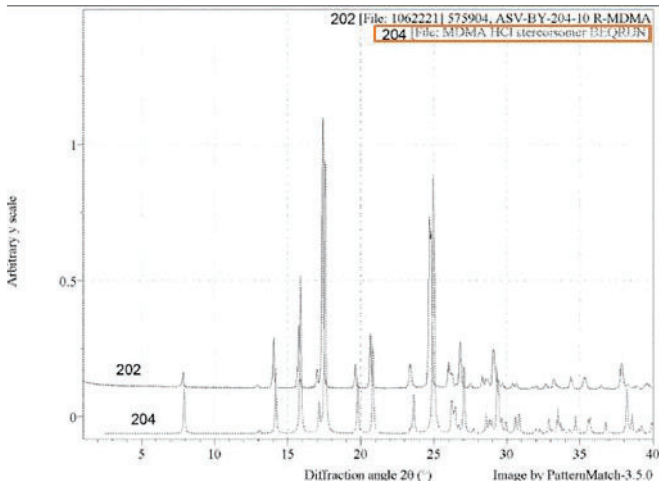
1. Skelton (2018) “CSD Entry: BEQRUN” Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published

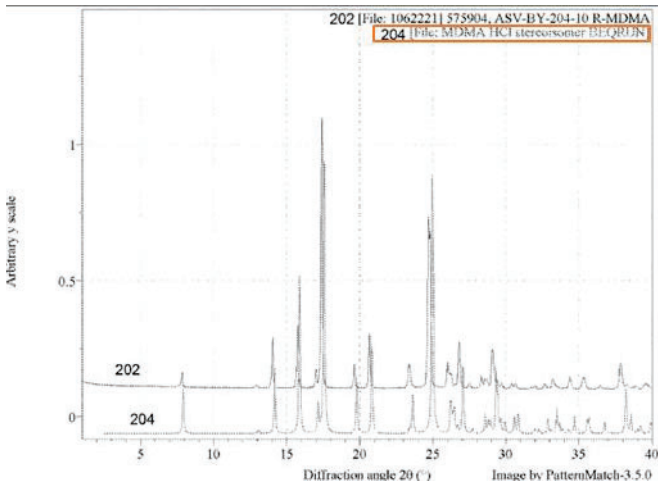
2. Buttonwood (2017) “Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment” Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o

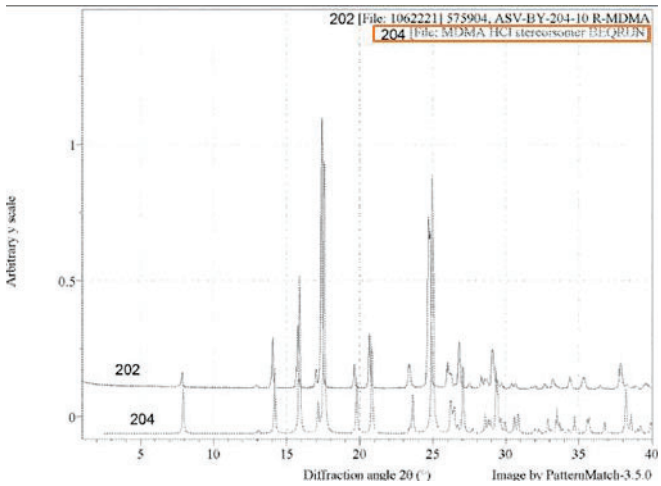
Attached hereto is a claim chart providing a concise description of the relevance of each reference in the document list to the elements of the presently pending claims.

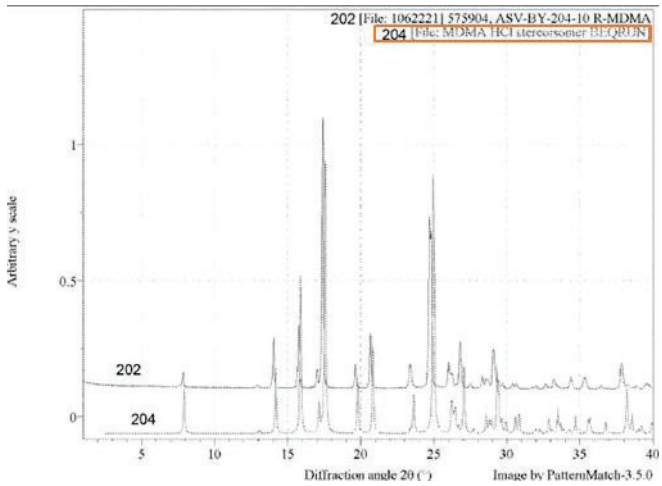
U.S.S.N.#18/116,195 Pending Claims	References
1. (R)-3,4-methylenedioxymethamphetamine HCl **Form I**.	*From the application of interest 18/116,195 paragraph [0117]:* *"FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*  1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published From **webpage** " Deposition Number 1825511 Data Citation Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9 Additional Database Identifiers BEQRUN01 Deposited on 23/02/2018" 2. Buttonwood (2017) "Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment" Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretrical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."

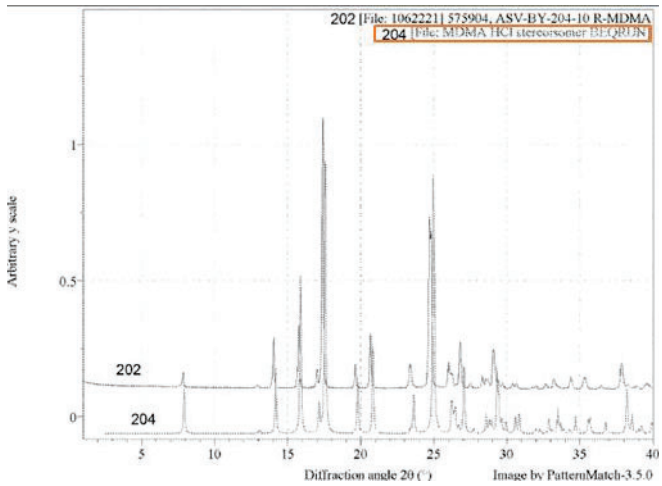
2. The composition of claim 1, wherein (R)-3,4-methylenedioxymethamphetamine HCl **Form I is characterized by an X-ray Powder Diffraction (XPRD) pattern substantially similar to 204 in FIG. 2A.**	*From the application of interest 18/116,195 paragraph [0117]:* *"FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*  1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published From **webpage** " Deposition Number 1825511 Data Citation Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9 Additional Database Identifiers BEQRUN01 Deposited on 23/02/2018" 2. Buttonwood (2017) "Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment" Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretrical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."

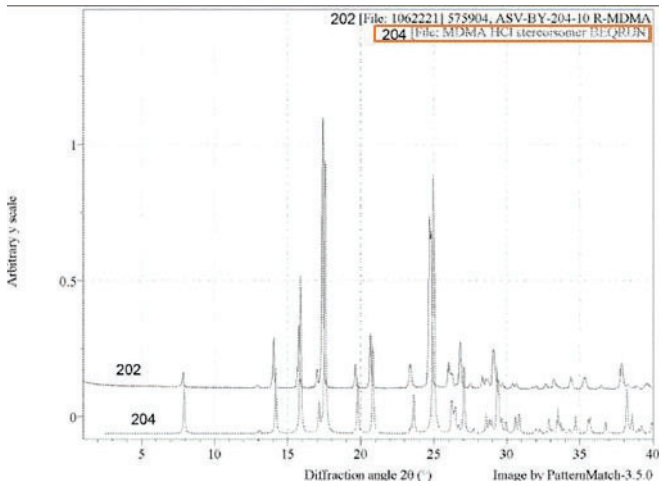
3. The composition of claim 1, wherein (R)-3,4-methylenedioxymethamphetamine HCl **Form I is characterized by peaks in an XPRD pattern at 17.5±0.2, 24.8±0.2, and 15.8±0.2° of 2θ.**	*From the application of interest 18/116,195 paragraph [0117]:* *"FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*  1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published From **webpage** " Deposition Number 1825511 Data Citation Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9 Additional Database Identifiers BEQRUN01 Deposited on 23/02/2018" 2. Buttonwood (2017) "Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment" Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretrical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."

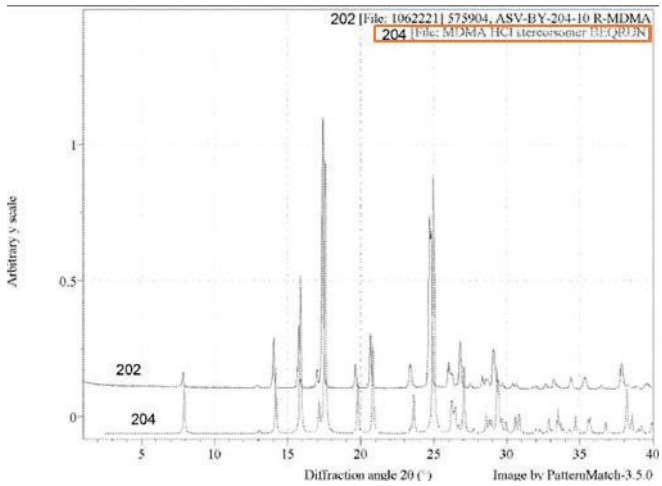
4. The composition of claim 1, wherein (R)-3,4-methylenedioxymethamphetamine HCl **Form I is characterized by peaks in an XPRD pattern at 17.5±0.2, 24.8±0.2, 15.8±0.2, 20.5±0.2, 14.0±0.2, 26.7±0.2, 29.0±0.2, 37.9±0.2, 7.9±0.2° of 2θ.**	*From the application of interest 18/116,195 paragraph [0117]:* *"FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*  1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published From **webpage** " Deposition Number 1825511 Data Citation Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9 Additional Database Identifiers BEQRUN01 Deposited on 23/02/2018" 2. Buttonwood (2017) "Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment" Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretrical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."

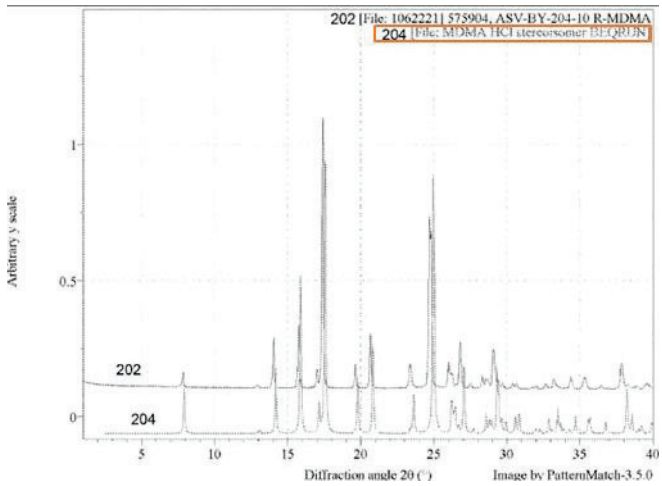
5. The composition of claim 1, wherein (R)-3,4-methylenedioxymethamphetamine HCl **Form I exhibits a monoclinic crystal system with cell parameters of a=7.17±0.05 Å, b=7.61±0.05 Å, c=11.75±0.05 Å, α=90±1°, β=107±1°, γ=90±1°, V=612±5 Å 3/cell.**	*From the application of interest 18/116,195 paragraph [0117]: "FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*  1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published From **webpage** " Deposition Number 1825511 Data Citation Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9 Additional Database Identifiers BEQRUN01 Deposited on 23/02/2018" 2. Buttonwood (2017) "Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment" Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretrical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."

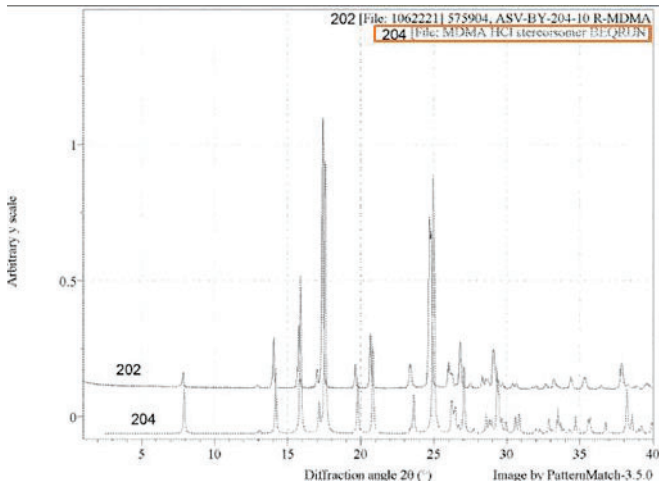
6. The composition of claim 1, wherein (R)-3,4-methylenedioxymethamphetamine HCl **Form I** exhibits a solubility of >110 mg/mL in water.	*From the application of interest 18/116,195 paragraph [0117]:* *"FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*  1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published From **webpage** " Deposition Number 1825511 Data Citation Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9 Additional Database Identifiers BEQRUN01 Deposited on 23/02/2018" 2. Buttonwood (2017) "Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment" Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretrical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."

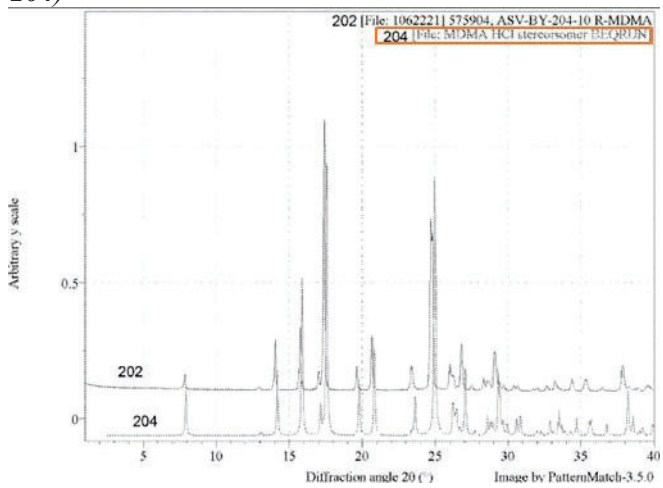
7. The composition of claim 1, wherein (R)-3,4-methylenedioxymethamphetamine HCl **Form I** exhibits a Differential Scanning Calorimetry (DSC) thermogram comprising an endotherm peak with an onset at 185° C.	*From the application of interest 18/116,195 paragraph [0117]:* *"FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*  1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published From **webpage** " Deposition Number 1825511 Data Citation Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9 Additional Database Identifiers BEQRUN01 Deposited on 23/02/2018" 2. Buttonwood (2017) "Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment" Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretrical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."

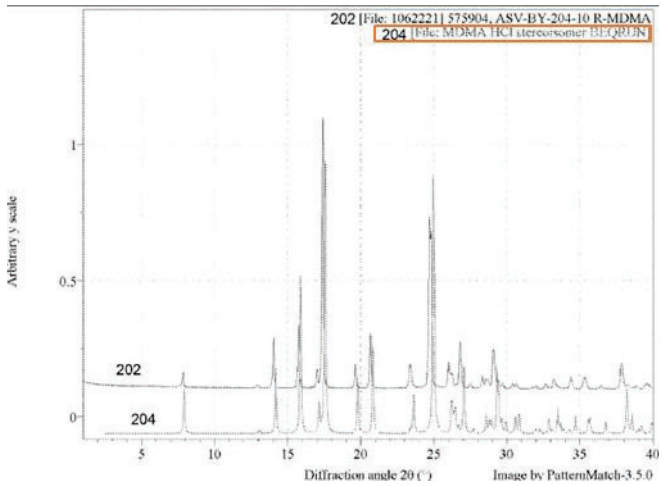
8. The composition of claim 1, wherein (R)-3,4-methylenedioxymethamphetamine HCl **Form I** exhibits a DSC thermogram comprising an endothermic peak at 186° C.	*From the application of interest 18/116,195 paragraph [0117]:* *"FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*  1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published From **webpage** " Deposition Number 1825511 Data Citation Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9 Additional Database Identifiers BEQRUN01 Deposited on 23/02/2018" 2. Buttonwood (2017) "Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment" Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretrical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."

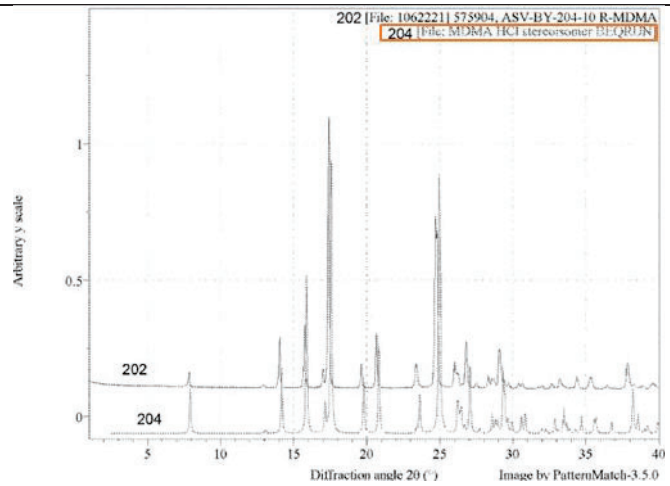
9. The composition of claim 1, wherein (R)-3,4-methylenedioxymethamphetamine HCl **Form I** exhibits 0.2±0.1% weight loss between 52-231° C. as measured by thermogravimetric (TGA) analysis.	*From the application of interest 18/116,195 paragraph [0117]:* *"FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*  1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published From **webpage** " Deposition Number 1825511 Data Citation Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9 Additional Database Identifiers BEQRUN01 Deposited on 23/02/2018" 2. Buttonwood (2017) "Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment" Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretrical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."

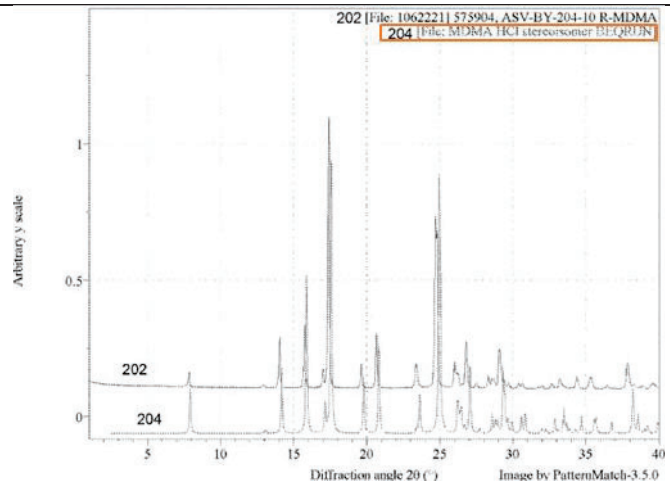
10. The composition of claim 1, wherein (R)-3,4-methylenedioxymethamphetamine HCl **Form I** exhibits 5.28±0.02% weight gain from 5-95% relative humidity (RH) and a 5.35±0.02% weight loss from 95-5% RH at 10% RH increments under a nitrogen purge as measured by Dynamic Vapor Sorption (DVS).	*From the application of interest 18/116,195 paragraph [0117]:* *"FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*  1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published From **webpage** " Deposition Number 1825511 Data Citation Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9 Additional Database Identifiers BEQRUN01 Deposited on 23/02/2018" 2. Buttonwood (2017) "Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment" Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretrical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."

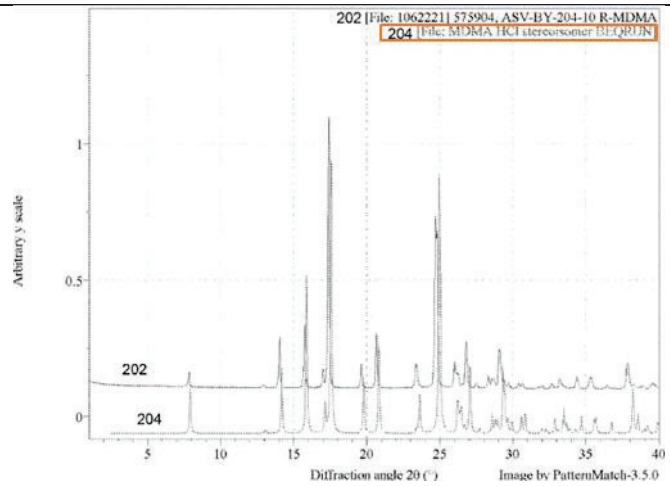
11. The composition of claim 1, wherein (R)-3,4-methylenedioxymethamphetamine HCl **Form I** exhibits physical stability upon stressing at 97% RH for 6 days.	*From the application of interest 18/116,195 paragraph [0117]:* *"FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*  1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published From **webpage** " Deposition Number 1825511 Data Citation Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9 Additional Database Identifiers BEQRUN01 Deposited on 23/02/2018" 2. Buttonwood (2017) "Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment" Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretrical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."

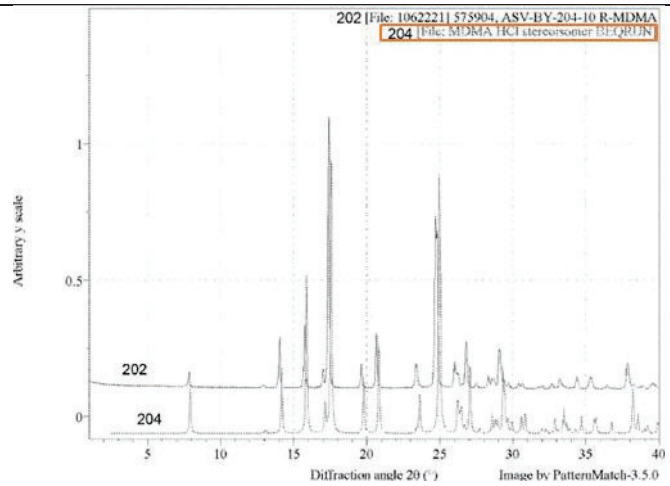
A process for the preparation of (R)-3,4-methylenedioxymethamphetamine HCl **Form 1**, the process comprising: i) reacting an organometallic reagent prepared from a compound of Formula (I): with a compound of Formula (IIa): wherein R 3 is alkyl; and ii) converting the product of step i) to (R)-3,4-methylenedioxymethamphetamine, wherein X is a halogen; R 1 is a protecting group, R 2 is a protecting group or R 1 and R 2 together with the atoms to which they are attached form a 5-membered heterocycle.	*From the application of interest 18/116,195 paragraph [0117]:* *"FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*  1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published From **webpage** " Deposition Number 1825511 Data Citation Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9 Additional Database Identifiers BEQRUN01 Deposited on 23/02/2018" 2. Buttonwood (2017) "Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment" Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."

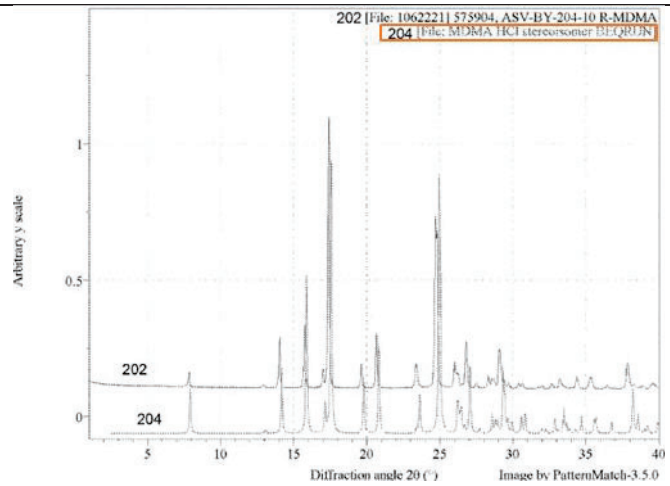
13. The process of claim 12, wherein the compound of Formula (I) is a compound of Formula (Ia):	*From the application of interest 18/116,195 paragraph [0117]:* *"FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*  1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published From **webpage** " Deposition Number 1825511 Data Citation Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9 Additional Database Identifiers BEQRUN01 Deposited on 23/02/2018" 2. Buttonwood (2017) "Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment" Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretrical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."
14. The process of claim 12, wherein X is bromine.	*From the application of interest 18/116,195 paragraph [0117]:* *"FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*

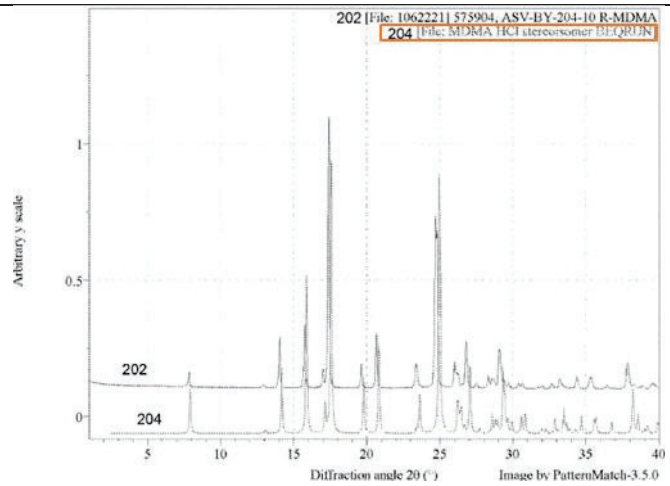
	 1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published From **webpage** " Deposition Number 1825511 Data Citation Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9 Additional Database Identifiers BEQRUN01 Deposited on 23/02/2018" 2. Buttonwood (2017) "Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment" Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretrical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."
15. The process of claim 12, wherein R 3 is tert-butyl.	*From the application of interest 18/116,195 paragraph [0117]: "FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*

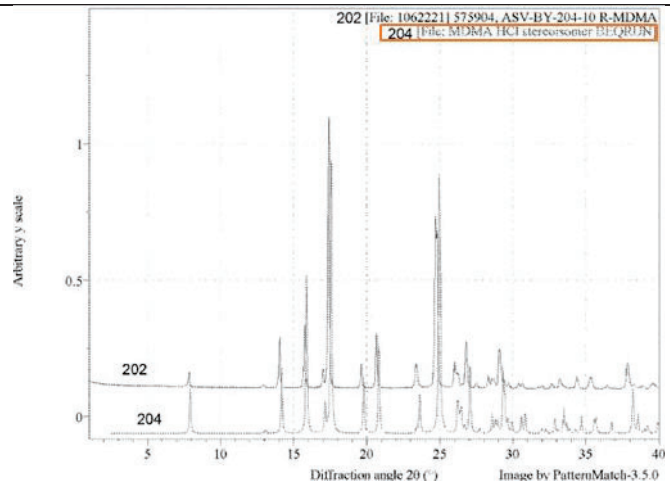
	 1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published From **webpage** " Deposition Number 1825511 Data Citation Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9 Additional Database Identifiers BEQRUN01 Deposited on 23/02/2018" 2. Buttonwood (2017) "Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment" Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretrical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."
16. The process of claim 12, wherein step i) comprises reacting the compound of Formula (I) or Formula (Ia) with magnesium.	*From the application of interest 18/116,195 paragraph [0117]:* *"FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*

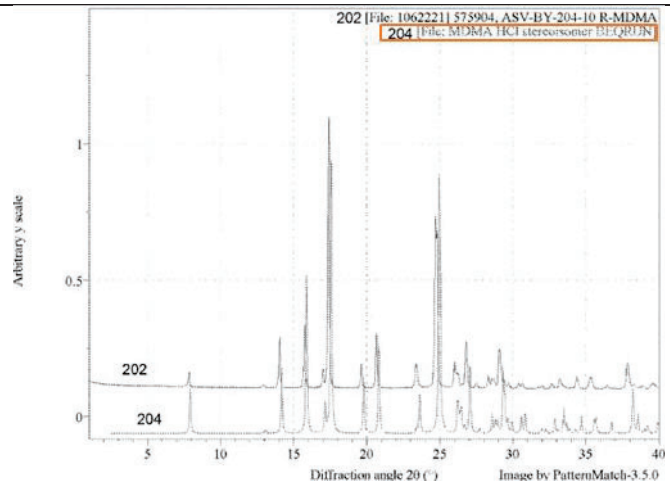
	 1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published From **webpage** " Deposition Number 1825511 Data Citation Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9 Additional Database Identifiers BEQRUN01 Deposited on 23/02/2018" 2. Buttonwood (2017) "Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment" Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretrical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."
17. The process of claim 16, wherein the step i) further comprises adding a copper (I) salt (e.g., CuI) to the reaction mixture.	*From the application of interest 18/116,195 paragraph [0117]: "FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*

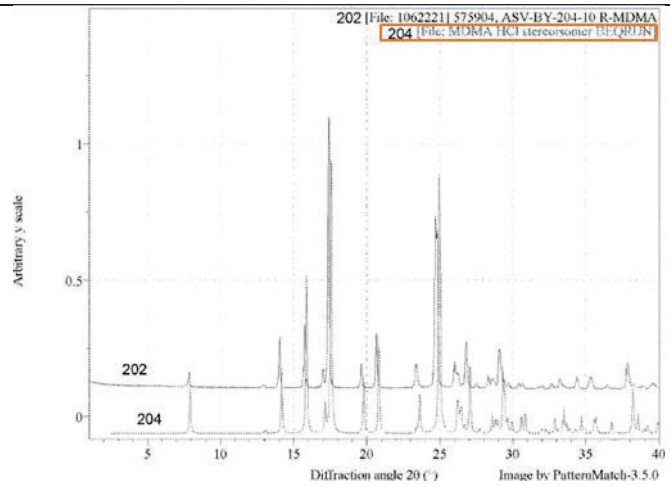
	 1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published From **webpage** " Deposition Number 1825511 Data Citation Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9 Additional Database Identifiers BEQRUN01 Deposited on 23/02/2018" 2. Buttonwood (2017) "Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment" Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretrical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."
18. The process of claim 12, wherein the product of step i) is a compound of Formula (IIIb):	*From the application of interest 18/116,195 paragraph [0117]:* *"FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*

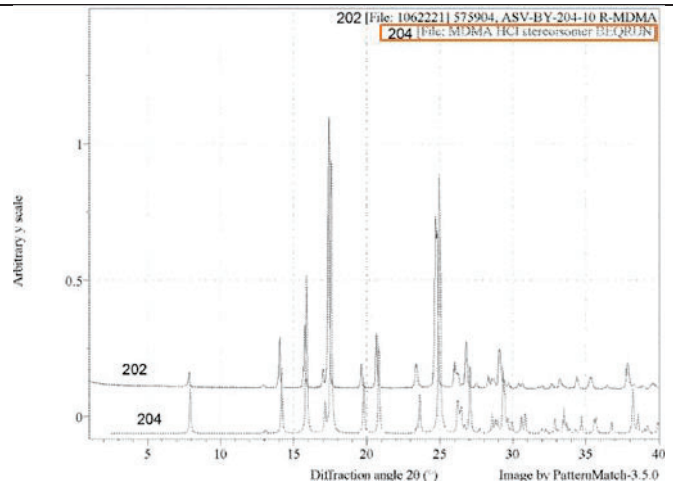
	 1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published From **webpage** " Deposition Number 1825511 Data Citation Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9 Additional Database Identifiers BEQRUN01 Deposited on 23/02/2018" 2. Buttonwood (2017) "Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment" Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretrical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."
19. The process of claim 12, wherein the product of step i) is a compound of Formula (IIIb′):	*From the application of interest 18/116,195 paragraph [0117]: "FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*

	 1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published From **webpage** " Deposition Number 1825511 Data Citation Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9 Additional Database Identifiers BEQRUN01 Deposited on 23/02/2018" 2. Buttonwood (2017) "Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment" Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretrical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."
20. The process of claim 12, wherein the step ii) comprises reacting a group of Formula (IVa) with a reducing agent to provide a group of	*From the application of interest 18/116,195 paragraph [0117]: "FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*

Formula (Va), or a pharmaceutically acceptable salt thereof:	 1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published From **webpage** " Deposition Number 1825511 Data Citation Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9 Additional Database Identifiers BEQRUN01 Deposited on 23/02/2018" 2. Buttonwood (2017) "Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment" Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretrical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."
21. The process of claim 20, wherein the reducing agent is lithium aluminum hydride.	*From the application of interest 18/116,195 paragraph [0117]:* *"FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*

	 1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published From **webpage** " Deposition Number 1825511 Data Citation Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9 Additional Database Identifiers BEQRUN01 Deposited on 23/02/2018" 2. Buttonwood (2017) "Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment" Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretrical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."
22. The process of claim 12, wherein the process provides (R)-3,4-methylenedioxymethamphetamine HCl **Form 1**	*From the application of interest 18/116,195 paragraph [0117]:* *"FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*

in an enantiomeric excess of at least 99.5%.	 1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published From **webpage** " Deposition Number 1825511 Data Citation Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9 Additional Database Identifiers BEQRUN01 Deposited on 23/02/2018" 2. Buttonwood (2017) "Single crystal x-ray diffraction experiment backwards: from CIF to genuine set of raw data without performing actual experiment" Chemistry Stack Exchange. Edited 28 June 2017. URL:https://chemistry.stackexchange.com/questions/76950/single-crystal-x-ray-diffraction-experiment-backwards-from-cif-to-genuine-set-o From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretrical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."
23. (R)-3,4-methylenedioxymethamphetamine HCl **Form 1** prepared by a process of claim 12.	*From the application of interest 18/116,195 paragraph [0117]: "FIG. 2A: XRPD overlap of **Form I** patterns (experimental 202 vs. **literature 204**)"*



1. Skelton (2018) "CSD Entry: BEQRUN" Cambridge Crystallographic Data Centre. Available 20 April 2018. URL:https://www.ccdc.cam.ac.uk/structures/Search?Ccdcid=BEQRUN&DatabaseToSearch=Published

From **webpage** "

Deposition Number	1825511
Data Citation	Brian W. Skelton, Matthew J. Piggott CCDC 1825511: Experimental Crystal Structure Determination, 2018, DOI: 10.5517/ccdc.csd.cc1z8lg9
Additional Database Identifiers	BEQRUN01
Deposited on	23/02/2018"

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From **page 2** "If the crystallographic model is completed (in layman's terms, **if there is a *.cif file**), than it is easy to predict a theoretical powder diffraction pattern. Programs like CCDC Mercury just ask about the wavelength to consider …. **Such a theoretrical diffractogram is then compared with an experimentally recorded one; for example to check the newly prepared sample's phase identity (polymorphism) and purity**."

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APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/116,195	**02/15/2024 10:56:37 AM Z ET**	

Title of Invention

Application Information

APPLICATION TYPE		PATENT #	
CONFIRMATION #		FILED BY	Steven Schmid
PATENT CENTER #	64331386	FILING DATE	03/01/2023
CUSTOMER #	–	FIRST NAMED INVENTOR	
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	-

Documents

TOTAL DOCUMENTS: 7

DOCUMENT		PAGES	DESCRIPTION	SIZE (KB)
third-party-preissuance-submission.pdf		2	Third-Party Submission Under 37 CFR 1.290	46 KB
Third-party-notification-request.pdf		1	Request for Notification of Non-compliant Third-Party Submission	13 KB
Concise-description-generated.pdf		2	Concise Description of Relevance	26 KB
Claim_chart.pdf		24	-	304 KB
Claim_chart-3P.RELEVANCE.pdf	(1-24)	24	Concise Description of Relevance	304 KB
Claim_chart-3P.RELEVANCE.pdf	(1-24)	24	Concise Description of Relevance	304 KB
1_SKELTON_FORMATTED.pdf		2	-	333 KB

1_SKELTON_FORMATTED-NPL.pdf	(1-2)	2	Non Patent Literature	325 KB
2_BUTTONWOOD_FORMATTED.pdf		6	-	741 KB
2_BUTTONWOOD_FORMATTED-NPL.pdf	(1-6)	6	Non Patent Literature	732 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
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64216ACA7D12C41545398142FEBD24

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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.