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Attorneys for Plaintiff
Bristol-Myers Squibb Company

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

BRISTOL-MYERS SQUIBB COMPANY, Plaintiff, v. AUROBINDO PHARMA U.S.A., INC. and AUROBINDO PHARMA LTD., Defendants.	)	CA. No. _____ *Electronically Filed*

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiff Bristol-Myers Squibb Company ("BMS"), through its attorneys, hereby alleges as follows:

Nature of the Action

1. This is an action for patent infringement of United States Patent No. 6,087,383 ("the '383 patent") against defendants Aurobindo Pharma Ltd. and Aurobindo Pharma U.S.A., Inc. (collectively "Aurobindo"). This action relates to Abbreviated New Drug Application ("ANDA") No. 204806 filed by Aurobindo Pharma Ltd. with the United States Food and Drug Administration ("FDA") for approval to market a generic version of BMS's Reyataz® drug product. This action arises under the patent laws of the United States, 35 U.S.C. § 100, *et seq*.

Parties

2. BMS is a Delaware corporation having its corporate headquarters at 345 Park Avenue, New York, New York.

3. BMS is engaged in the business of creating, developing, and bringing to market revolutionary biopharmaceutical products to help patients prevail in their fight against serious diseases.

4. Upon information and belief, Aurobindo Pharma Ltd. is a company organized and existing under the laws of India, having a place of business at Maitri Vihar, Plot #2, Ameerpet, Hyderabad - 500038, Andhra Pradesh, India.

5. On information and belief, Aurobindo Pharma U.S.A., Inc. is a corporation organized and existing under the laws of the State of Delaware, having its principal place of business at 6 Wheeling Road, Dayton, New Jersey 08810 (Middlesex County). On information and belief, Aurobindo Pharma U.S.A. is a wholly-owned subsidiary of Aurobindo Pharma Ltd.

Jurisdiction and Venue

6. This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. §§ 1331, 1338(a), 2201, and 2202.

7. Venue is proper in this judicial district pursuant to, *inter alia*, 28 U.S.C. §§ 1391(b) and 1400(b).

8. This Court has jurisdiction over the defendants because, upon information and belief, Aurobindo Pharma U.S.A., Inc. has a principal place of business in New Jersey and is the subsidiary and agent of Aurobindo Pharma Ltd. Upon information and belief, Aurobindo Pharma U.S.A., Inc. is acting as the agent of Aurobindo Pharma Ltd. with respect to ANDA No. 204806.

9. This Court has jurisdiction over Aurobindo Pharma Ltd. because it has corporate offices in Dayton, New Jersey, and Dayton, New Jersey is also the center of its U.S. operations. Aurobindo Pharma Ltd. has at least three significant subsidiaries based in Dayton, New Jersey.

10. In the alternative, this Court has jurisdiction over Aurobindo Pharma Ltd. because the requirements of Federal Rule of Civil Procedure 4(k)(2)(A) are met.

11. This Court also has jurisdiction over the defendants because, *inter alia*, this action arises from actions of the defendants directed toward New Jersey, and because the defendants have purposefully availed themselves of the rights and benefits of New Jersey law by engaging in systematic and continuous contacts with New Jersey. Upon information and belief, the defendants regularly and continuously transact business within the state of New Jersey, including by selling pharmaceutical products in New Jersey, either on their own or through affiliates. Upon information and belief, the defendants derive substantial revenue from the sale of those products in New Jersey and have availed themselves of the privilege of conducting business within the State of New Jersey.

12. The defendants have previously been sued in this judicial district without objecting on the basis of lack of personal jurisdiction and have availed themselves of New Jersey courts through the assertion of counterclaims.

13. For these reasons, and for other reasons that will be presented to the Court if jurisdiction is challenged, the Court has personal jurisdiction over the defendants.

BMS's Reyataz® Product and the '383 Patent

14. On July 11, 2000, the U.S. Patent and Trademark Office duly and legally issued the '383 patent, titled "Bisulfide Salt of HIV Protease Inhibitor." A true and correct copy of the '383 patent is attached as Exhibit A. The claims of the '383 patent are valid and enforceable.

15. BMS is the owner of the '383 patent.

16. The expiration date of the '383 patent is December 21, 2018.

17. BMS is the holder of New Drug Application ("NDA") No. 21-567, by which the FDA granted approval for atazanavir sulfate capsules (Eq. 100 mg base, Eq., 150 mg base, Eq. 200 mg base, and Eq. 300 mg base). BMS markets and sells atazanavir sulfate capsules in the United States under the trade name Reyataz®.

18. The Food and Drug Administration Center for Drug Equivalence Evaluations (the "Orange Book") lists the '383 patent for each of the strengths of Reyataz® approved by the FDA under NDA No. 21-567.

Aurobindo's ANDA Filing and Notice Letter

19. Upon information and belief, Aurobindo filed with the FDA ANDA No. 204806 (the "Aurobindo ANDA") under Section 505(j) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 355(j)), seeking approval to engage in the commercial manufacture, use, or sale of Atazanavir Sulfate Capsules (Eq. 100 mg, 150 mg, 200 mg, and 300mg base) (the "Aurobindo ANDA Products") – generic versions of the FDA-approved Reyataz® capsules, Eq. 100 mg, 150 mg, 200 mg, and 300 mg base – before the expiration date of the '383 patent.

20. Upon information and belief, the Aurobindo ANDA Products contain atazanavir bisulfate.

21. Upon information and belief, the Aurobindo ANDA Products will be manufactured by, or at the direction of, Aurobindo.

22. Upon information and belief, Aurobindo intends to – directly or indirectly – manufacture, use, market, sell, offer for sale, and distribute the Aurobindo ANDA products, including within this District, upon regulatory approval.

23. By letter dated April 24, 2014 ("Aurobindo Notice Letter"), Aurobindo notified BMS that it had filed an ANDA for the Aurobindo ANDA Products, including a "Paragraph IV

certification" asserting that the '383 patent is invalid, unenforceable, and/or will not be infringed by the commercial manufacture, use, and sale of the Aurobindo ANDA products, and that it sought approval of its ANDA prior to the expiration date of the '383 patent.

24. BMS received the Aurobindo Notice Letter on or about April 25, 2014.

25. This action is being commenced before the expiration of forty-five days from the date BMS received the Aurobindo Notice Letter.

Count 1

(Infringement of United States Patent No. 6,087,383)

26. BMS incorporates the preceding paragraphs as if fully set forth herein.

27. Aurobindo's submission of the Aurobindo ANDA to obtain approval to engage in the commercial manufacture, use, offer to sell, or sale of the Aurobindo ANDA Products prior to the expiration of the '383 patent constitutes infringement of claims 1 and 2 of the '383 patent under 35 U.S.C. § 271(e)(2)(A).

28. Aurobindo's commercial manufacture, use, offer to sell, sale, or importation of the Aurobindo ANDA Products prior to the expiration of the '383 patent, and its inducement of and/or contribution to such conduct, would further infringe claims 1 and 2 of the '383 patent under 35 U.S.C. §§ 271(a), (b) and/or (c).

29. Upon FDA approval of the Aurobindo ANDA, Aurobindo will infringe claims 1 and 2 of the '383 patent by making, using, offering to sell, selling, or importing the Aurobindo ANDA Products in the United States, and by actively inducing and/or contributing to infringement by others, unless enjoined by this Court.

30. BMS will be irreparably harmed if Aurobindo's infringement is not enjoined. BMS does not have an adequate remedy at law.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs pray that this Court grant the following relief:

A. A declaration that the ’383 patent is valid and enforceable;

B. A declaration that Aurobindo has infringed a claim or claims of the ’383 patent by submitting the aforesaid ANDA and certification, and that Aurobindo’s making, using, offering to sell, selling, or importing the Aurobindo ANDA Products and its inducement of and/or contribution to such conduct by others, will infringe the ’383 patent;

C. An Order providing that the effective date of any approval of the Aurobindo ANDA shall be a date which is not earlier than the expiration of the ’383 patent and all exclusivities to which Plaintiff is or becomes entitled;

D. An Order permanently enjoining Aurobindo and its affiliates and subsidiaries, and each of its officers, agents, servants, and employees, from making, using, offering to sell, selling, or importing the Aurobindo ANDA Products and from inducing or contributing to such conduct by others, until after expiration of the ’383 patent and all exclusivities to which Plaintiff is or becomes entitled;

E. Damages or other monetary relief to BMS if Aurobindo engages in the commercial manufacture, use, offer to sell, sale, or importation of the Aurobindo ANDA Products, or inducing or contributing to such conduct by others, prior to expiration of the ’383 patent and all exclusivities to which Plaintiff is or becomes entitled, and that any such damages or monetary relief be awarded to BMS with prejudgment interest; and,

F. Such further and other relief as this Court deems proper and just, including any appropriate relief under 35 U.S.C. § 285.

Dated: June 4, 2014

CONNELL FOLEY LLP

/s/ Liza M. Walsh

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RULE 11.2 CERTIFICATION

I hereby certify that, to the best of my knowledge, the matter in controversy is not the subject of any other pending or anticipated litigation in any court or arbitration proceeding, nor are there any non-parties known to Plaintiff that should be joined to this action. In addition, I recognize a continuing obligation during the course of this litigation to file and to serve on all other parties and with the Court an amended certification if there is a change in the facts stated in this original certification.

Dated: June 4, 2014

CONNELL FOLEY LLP

/s/ Liza M. Walsh

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RULE 201.1 CERTIFICATION

I hereby certify that the above-captioned matter is not subject to compulsory arbitration in that the Plaintiff seeks, *inter alia*, injunctive relief.

Dated: June 4, 2014

CONNELL FOLEY LLP

/s/ Liza M. Walsh

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EXHIBIT A

US006087383A

United States Patent [19]

Singh et al.

[11] Patent Number: 6,087,383

[45] Date of Patent: Jul. 11, 2000

[54] **BISULFATE SALT OF HIV PROTEASE INHIBITOR**

[75] Inventors: **Janak Singh**, Lawrenceville; **Madhusudhan Pudipeddi**, Plainsboro; **Mark D. Lindrud**, Basking Ridge, all of N.J.

[73] Assignee: **Bristol-Myers Squibb Company**, Princeton, N.J.

[21] Appl. No.: **09/217,538**

[22] Filed: **Dec. 21, 1998**

Related U.S. Application Data

[60] Provisional application No. 60/071,968, Jan. 20, 1998.

[51] **Int. Cl.**[7] **A61K 31/44**; C07D 213/56

[52] **U.S. Cl.** **514/357**; 546/332

[58] **Field of Search** 546/332; 514/357

[56] **References Cited**

U.S. PATENT DOCUMENTS

5,849,911 12/1999 Fassler et al. 544/335

FOREIGN PATENT DOCUMENTS

WO97/40029 10/1997 WIPO .

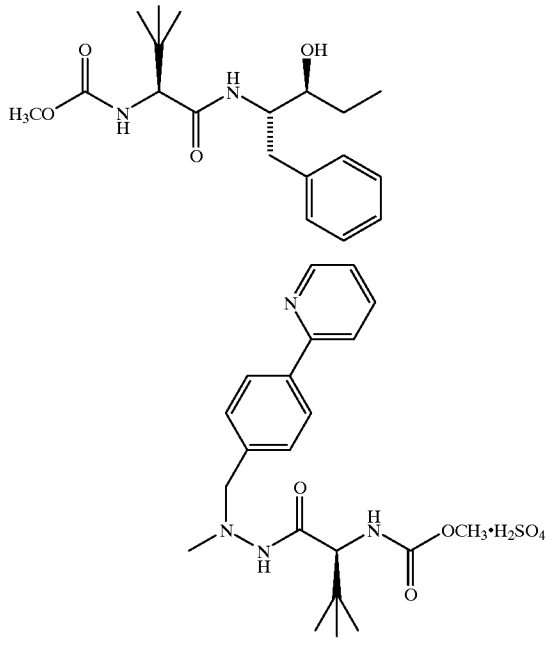
Primary Examiner—Bernard Dentz

Attorney, Agent, or Firm—David M. Morse

[57] **ABSTRACT**

The present invention provides the crystalline bisulfate salt of the formula

II



which is found to have unexpectedly high solubility/dissolution rate and oral bioavailability relative to the free base form of this azapeptide HIV protease inhibitor compound.

2 Claims, 5 Drawing Sheets

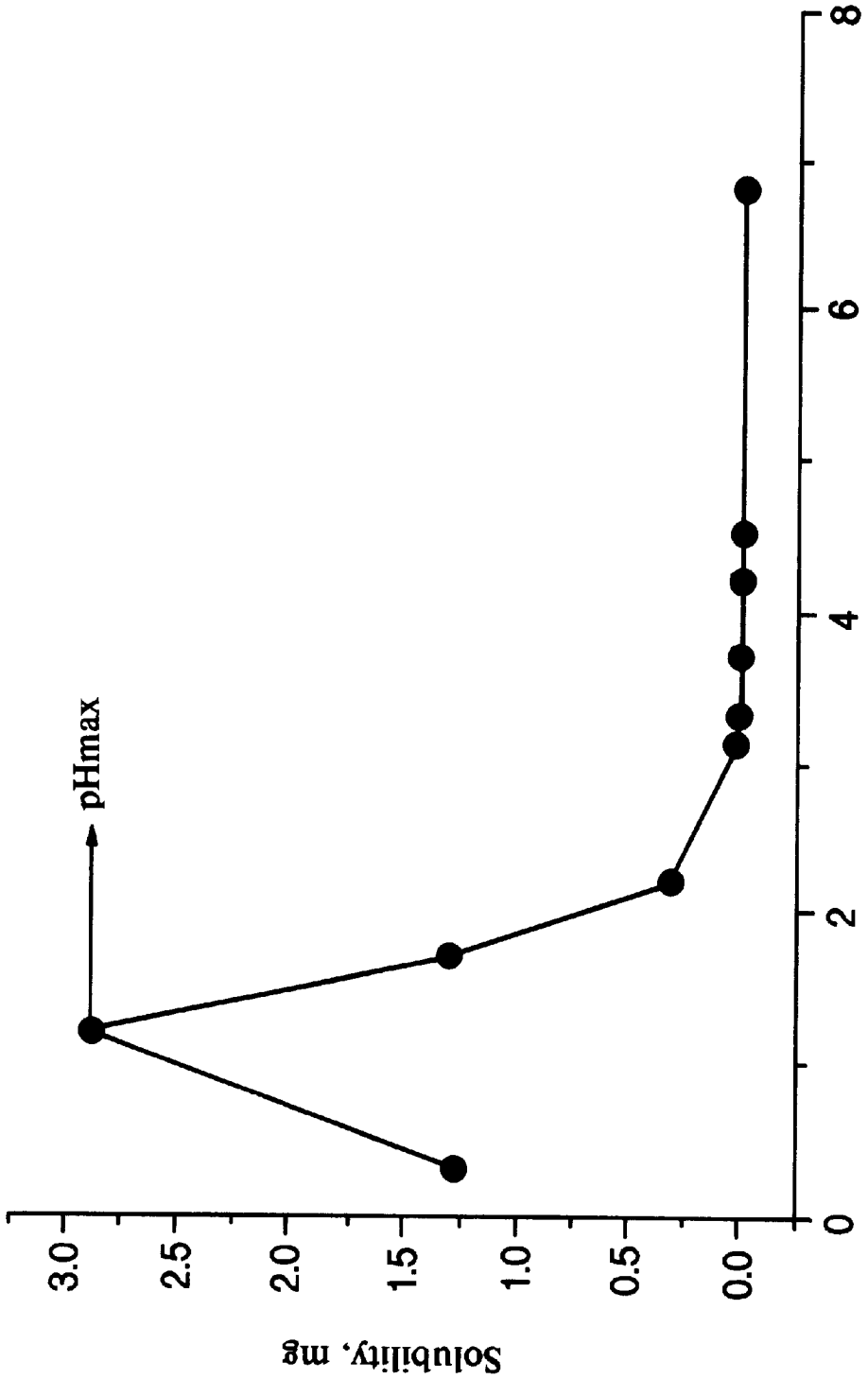


FIG. 1

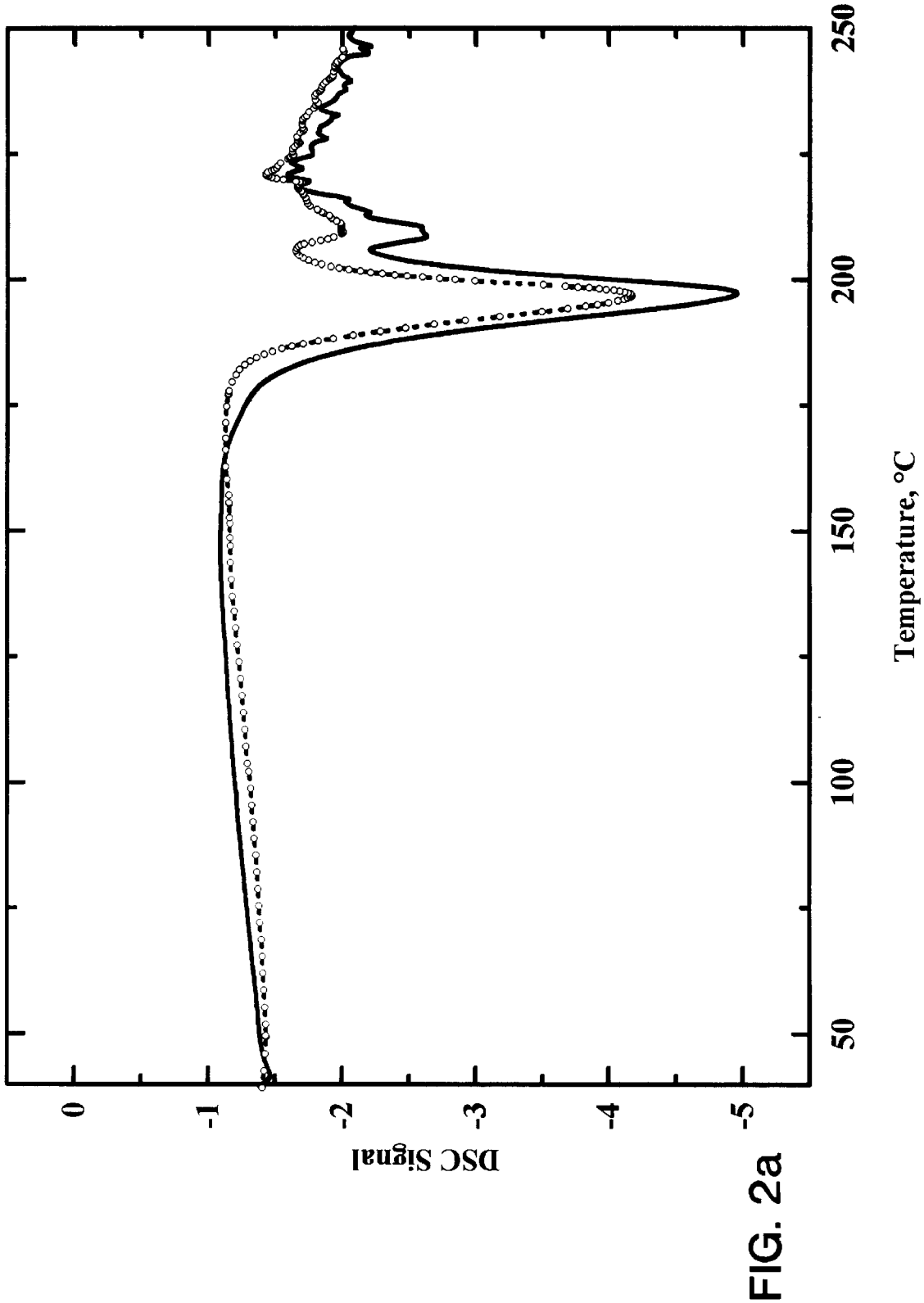


FIG. 2a

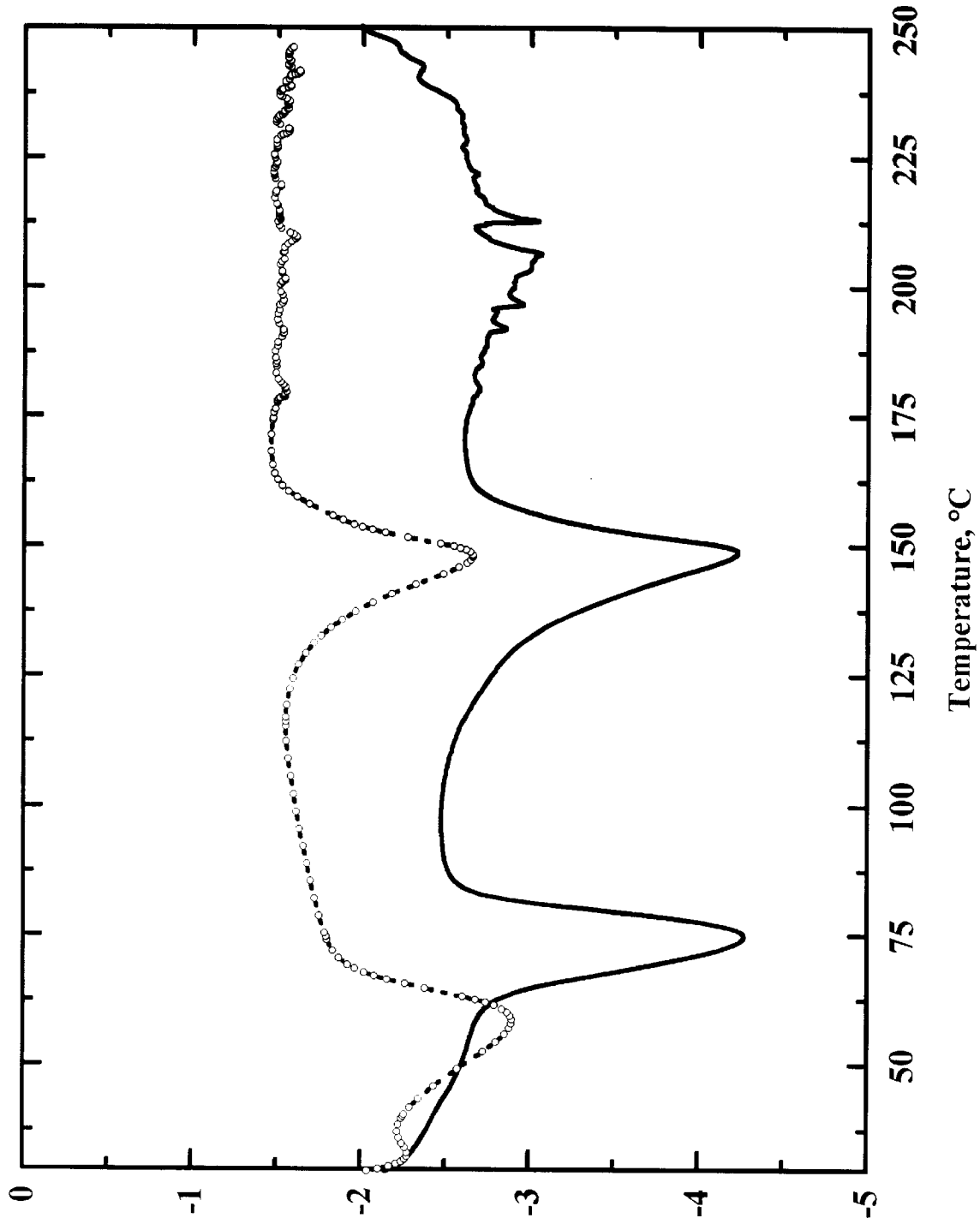

DSC Signal
0
-1
-2
-3
-4
-5
50
75
100
125
150
175
200
225
250
Temperature, °C

FIG. 2b

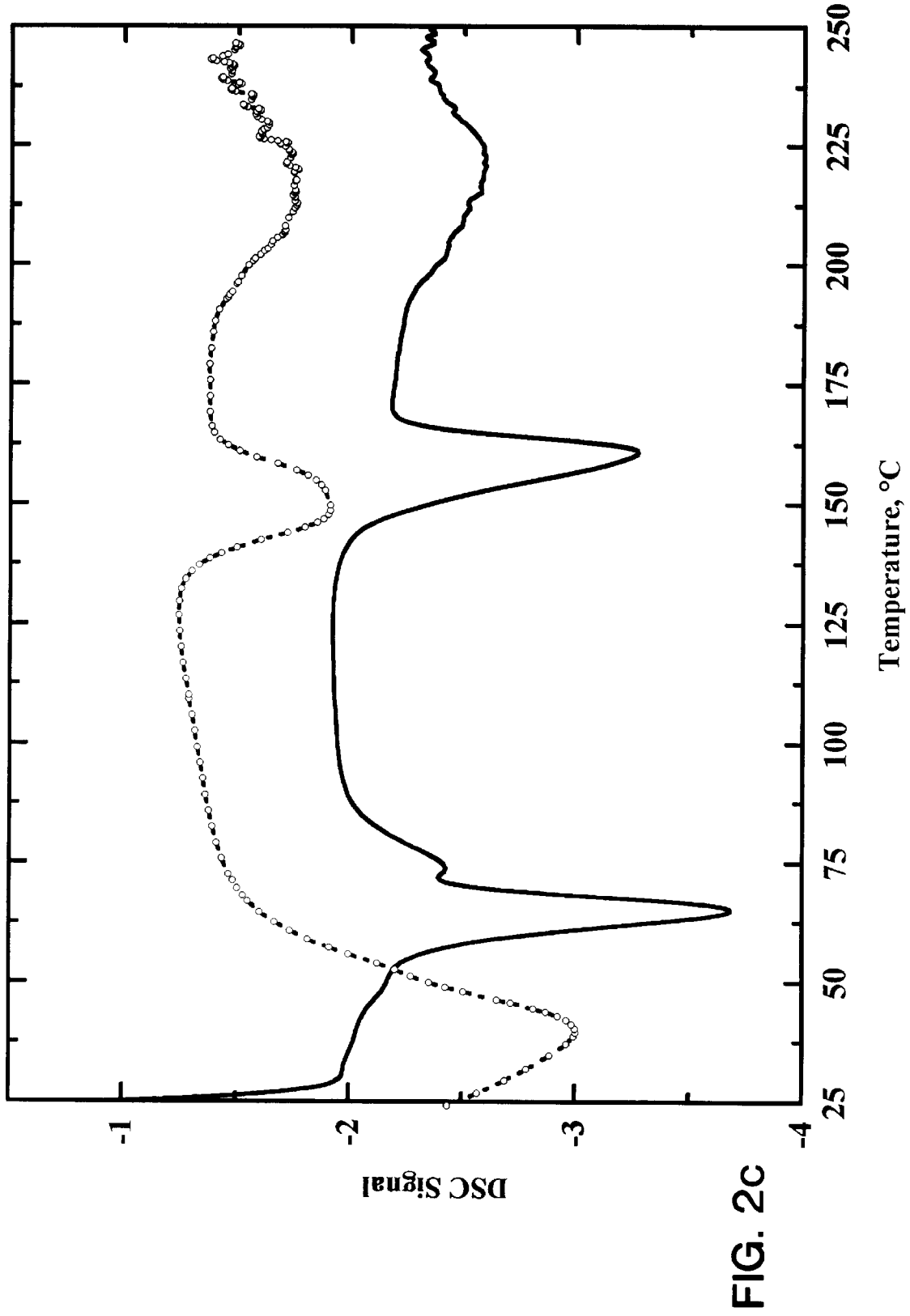

DSC Signal
-1
-2
-3
-4
25
50
75
100
125
150
175
200
225
250
Temperature, °C

FIG. 2C

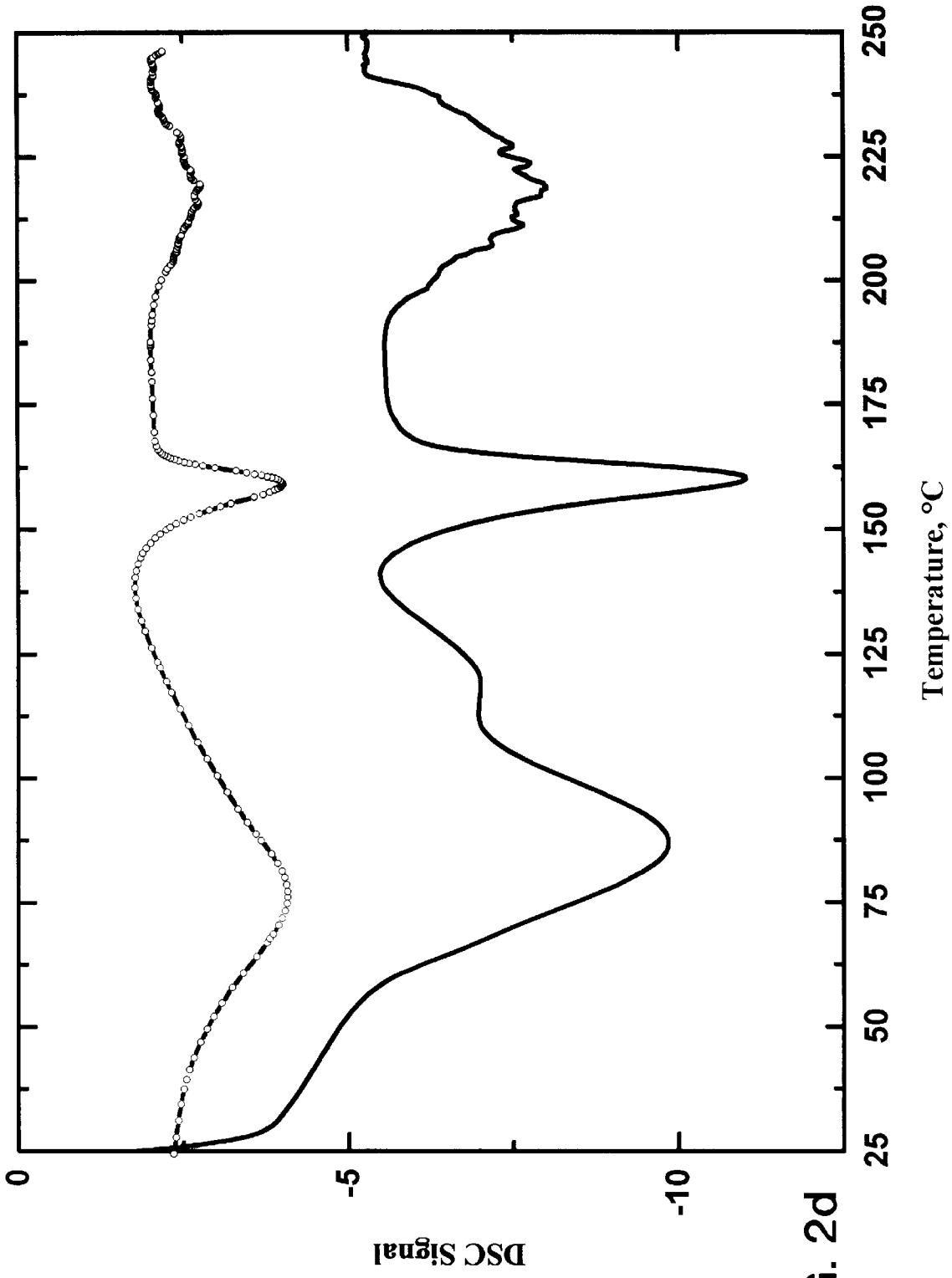

0
-5
-10
DSC Signal
25
50
75
100
125
150
175
200
225
250
Temperature, °C

FIG. 2d

BISULFATE SALT OF HIV PROTEASE INHIBITOR

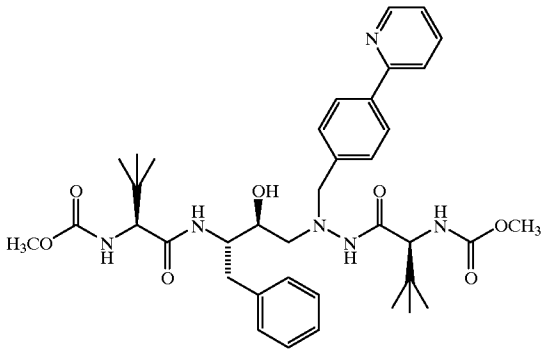
This application claims priority from Provisional Application 60/071,968 filed Jan. 20, 1998.

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention provides the novel crystalline bisulfate salt of the azapeptide HIV protease inhibitor of the formula

I

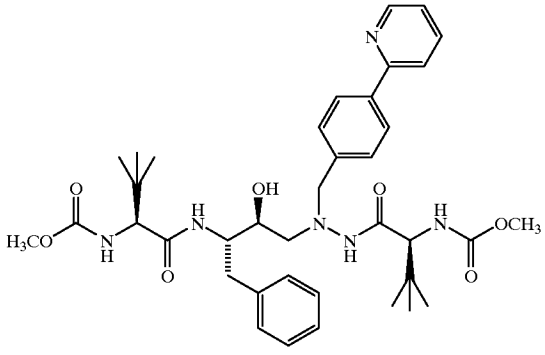


which exhibits unexpectedly superior aqueous solubility/dissolution behavior compared to other salts, and significantly improved oral bioavailability in animals compared to the free base. The bisulfate salt is thus useful for pharmaceutical dosage forms of the above-indicated protease inhibitor, particularly oral dosage forms.

2. Background Art

Published PCT patent application WO 97/40029 discloses a series of azapeptide HIV protease inhibitors reported to have a high degree of inhibitory activity against the HIV virus. One of the agents included within the scope of WO 97/40029 is the compound having the structural formula

I



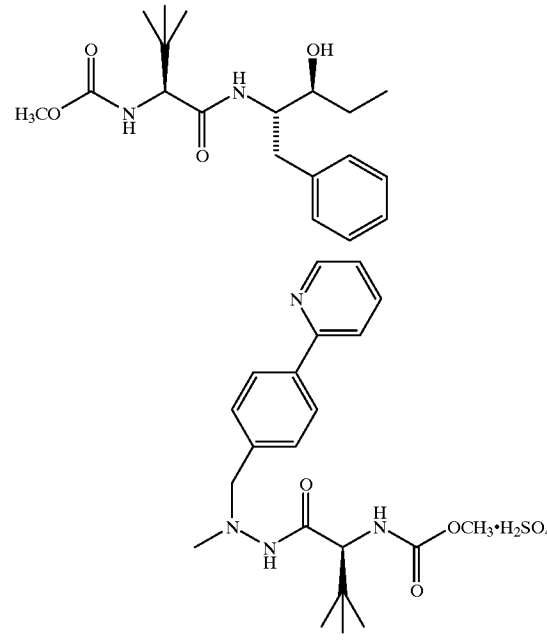
and the chemical name [3S-(3R*, 8'R*, 9'R*, 12R*)]-3,12-bis(1,1-dimethylethyl)-8-hydroxy-4,11-dioxo-9-(phenylmethyl)-6-[[4-(2-pyridinyl)phenylmethyl]-2,5,6,10,13-pentaazatetradecanedioic] acid, dimethyl ester and is under evaluation as a possible second generation HIV protease inhibitor.

WO 97/40029 discloses the free base form of azapeptide derivatives such as compound I and also various pharmaceutically acceptable acid addition salts. While several organic and inorganic acids are mentioned as possible salt-forming agents, including sulfuric acid, there is no mention of the particular bisulfate salt which is the subject of the present application.

SUMMARY OF THE INVENTION

The present invention provides the bisulfate salt of compound I above having the structural formula

II



DETAILED DESCRIPTION OF THE INVENTION

Compound I as disclosed above is a weak organic base with an aqueous solubility of less than 1 μg/mL at 24±3° C. The crystalline free base form as a suspension in water or oil has poor oral bioavailability in animals, probably because of its extremely low solubility in these vehicles.

For development of pharmaceutical formulations, particularly oral dosage forms, the active ingredient must have sufficient oral bioavailability. Since the free base form of compound I did not possess such bioavailability, acid addition salts were explored by the present inventors. A number of commonly used acid addition salts such as the hydrochloride, benzenesulfonate, methanesulfonate, p-toluenesulfonate, phosphate, nitrate, 1,2-ethanedisulfonate, isethionate and sulfate were evaluated, in addition to the bisulfate salt of the present invention. All of these salts in their crystalline form exhibited lower aqueous solubility (1–3 mg/mL or less at 24±3° C.) than the bisulfate which had a solubility under the same conditions of approximately 4–5 mg/mL.

Solid state transformation was observed when the other acid addition salts mentioned above were suspended in water, probably due to their dissociation to form the free base. In the majority of cases, this transformation was accompanied by gel formation. Unlike the other salts mentioned above, the extra proton of the bisulfate salt prevents the conversion to the free base which, as mentioned above, is very insoluble in water and has poor oral bioavailability. The unusual solubility behavior of the bisulfate salt in water is further elaborated in the following.

In general, conversion of salts to the unionized form or vice versa can be explained on the basis of pH-solubility theory. The solubility of the free base in water was determined as a function of pH at 24±3° C. and is shown below. The pH at which the compound exhibits the highest solubility is referred to as pH_{max} and was found to be approximately 1.2. It has been reported in the literature that at $pH>pH_{max}$ of a weakly basic organic compound, the equilibrium solid phase in an aqueous suspension of the compound is the free base. At $pH<pH_{max}$ the equilibrium solid converts to the corresponding salt form. The term "equilibrium solid phase" refers to the undissolved or excess solid in a suspension of the compound in water after sufficient equilibration time. When a salt of a weak base is equilibrated in water in an amount exceeding its solubility limit (i.e., a suspension of the salt in water), the resulting pH of the suspension may fall on either side of the pH_{max} depending on the strength of the acid among other factors. When the resulting pH is greater than the pH_{max}, the suspended solid converts to the free base.

Studies conducted with methane sulfonate and hydrochloride salts, in particular, of the free base confirmed the above described general findings reported in the literature. Amounts in excess of the solubility of these salts were equilibrated in water at 24±3° C. for at least 24 hours. The pH of the suspensions after equilibration was 2.1±0.1 which is greater than the pH_{max}. The undissolved solids from these suspensions were isolated, air-dried, and characterized. By thermal and elemental analysis the undissolved solids from these suspensions were identified as the free base. This behavior was expected based on the pH-solubility profile shown in FIG. **1** and the studies reported in the literature.

When an excess amount of the bisulfate salt was equilibrated in water a modification occurred in the solid phase in equilibrium with solution. However, the undissolved solid phase after equilibration was not the free base, although the pH (1.9±0.2) of the suspension was greater than the pH_{max} and comparable to the pH of the suspensions of methane sulfonate and hydrochloride salts described above. The solid phase after at least 24 hours of equilibration was identified by elemental analysis as a hydrated form of 2:1 salt of the free base form and sulfuric acid (referred to as the sulfate salt). This behavior of the bisulfate salt is unexpected based on pH-solubility theory.

When an excess amount of the sulfate salt, in turn, was equilibrated in water a modification occured in the solid phase in equilibrium with solution. The undissolved solid from this suspension was isolated, air-dried, and characterized. Thermal and elemental analysis of this undissolved solid phase was similar to that of the free base although the conversion of the sulfate salt to the free base was not as definitive as that of the methane sulfonate and hydrochloride salts. From a pharmaceutical point of view the propensity of salts to convert to the free base in an aqueous environment is not desirable due to the low oral bioavailability of the free base. Thus, the bisulfate salt due its unique solubility behavior in water offered unexpected superiority.

The solubility behavior of the bisulfate salt in water was also unexpected considering the interaction of compound I free base and sulfuric acid in water. For example, the free base exhibited a solubility of less than 1 mg/mL in water at a pH of ~1.8 adjusted with sulfuric acid, compared to 4–5 mg/mL solubility of the bisulfate salt in water at comparable pH conditions. Based on pH-solubility theory the free base and the salt are expected to exhibit similar solubility at a given pH.

The enhanced solubility/dissolution behavior of the bisulfate contributes to its improved oral bioavailability in animals relative to the free base. The absolute oral bioavailability of the bisulfate salt was found to be approximately 20% in dogs when administered in unformulated solid form placed in a gelatin capsule. In comparison, the crystalline free base had minimal oral bioavailability in dogs.

In addition to optimal solubility, satisfactory physical stability in the solid-state is another desirable property of pharmaceutical salt forms. The term physical stability indicates the ability of the salt form to retain its crystal structure (including solvents of crystallization, if any) under storage/stress conditions. Significant changes in the physical nature of the salt form as indicated by thermal methods such as differential scanning calorimetry are undesirable. The bisulfate salt exhibited excellent solid-state physical stability when stored at 40° C./75% relative humidity (RH) for as long as 9 months as shown in FIG. **2***a*. Differential scanning calorimetry revealed no significant changes in the thermal behavior of the stressed sample of the bisulfate salt compared to that of the unstressed sample (stored at 2–8° C. in a closed container). The methane sulfonate, hydrochloride, and the sulfate salts, on the other hand, showed significant changes in their thermal behavior when stored at 40° C./75% RH for as little as two weeks as shown in FIGS. **2***b, c,* and *d.* While differences in physical stability of salt forms is not unusual, the propensity of a particular salt to form solvates (or crystal modifications) and its ability to retain the solvent of crystallization (the physical stability of crystal modifications) under storage/stress conditions cannot be predicted apriori.

FIG. **2***a* represents Physical stability of the bisulfate salt. The solid line represents the unstressed material. The dotted line represents the material stressed at 40° C./75% RH for 9 months.

FIG. **2***b* represents Physical Stability of the hydrochloride salt. The solid line represents the unstressed material. The dotted line represents the material stressed at 40° C./75% RH for two weeks.

FIG. **2***c* represents Physical stability of the methane sulfonate salt. The solid line represents the unstressed material. The dotted line represents the material stressed at 40° C./75% RH for two weeks

FIG. **2***d* represents Physical stability of the sulfate salt. The solid line represents the unstressed material. The dotted line represents the material stressed at 40° C./75% RH for two weeks.

The bisulfate salt may be prepared by forming a solution of free base of compound I with sulfuric acid in solvents such as acetonitrile, isopropanol, ethanol, or acetone and then isolating the so-produced bisulfate salt.

Because of its high bioavailability as well as its good crystallinity and stability, the bisulfate salt is very useful in preparing oral dosage forms of compound I. The examples which follow illustrate preparation of representative oral formulations.

The bisulfate salt, and formulations thereof, are used as described in WO 97/40029 for the treatment of diseases caused by viruses, especially retroviruses such as the HIV virus.

DESCRIPTION OF SPECIFIC EMBODIMENTS

Example 1

Preparation of Bisulfate Salt from Ethanol

To a 500 mL three-necked round bottomed flask equipped with an overhead stirrer and dropping funnel, 15.013 g

(0.0213 mole) of free base compound I and 113 mL of 200 proof ethanol were added with stirring. To this suspension, 1.28 mL concentrated sulfuric acid was added dropwise over 90 seconds. After the addition of sulfuric acid, a clear amber-colored solution was obtained. The solution was polish filtered using #1 Whatman filter paper and washed with 5 mL of 200 proof ethanol. To this solution was added 58 mL of heptane and 37.5 mg (0.25 wt %) of seed crystals of the compound of formula II followed by 55 mL of additional heptane. The resulting mixture was stirred for 6 hours at 300 rpm. The resulting crystal slurry was filtered and washed with 50 mL ethanol/heptane (1:1) solution and dried under vacuum at 60° C. overnight to afford 15.11 g of the desired crystalline bisulfate salt (88.4 mole % yield) having formula II above.

Characterizing Properties of Bisulfate Salt

Anal. Calcd. for $C_{38}H_{52}N_6O.1.0\ H_2SO_4$: C, 56.84; H, 6.78; N, 10.37; S, 3.99. Found: C, 56.72; H, 6.65; N, 10.41; S, 3.83. m.p. 195.0°, H_2O=0.28% (KF).

Example 2

Preparation of Bisulfate Salt from Acetone

5M H_2SO_4 (8.52 mL, 42.6 mM) was added dropwise to a suspension of the free base compound of formula I (30.0 g., 42.6 mM) in acetone (213 mL) stirred mechanically in a 50° C. oil-bath. A clear solution was obtained almost immediately. The solution was seeded with crystals of the free base compound of formula II. After two minutes, a precipitate formed which became a paste. The mixture was stirred at 50° C. for one hour, at 25° C. for 30 minutes and at 0° C. for 2 hours. The solid was filtered and the first filtrate was used to transfer the remaining material in the flask to the filtration funnel. The product was washed with acetone, then heptane, and dried under vacuum overnight to give 31.48 g (corrected yield 92%) of the bisulfate salt of formula II, m.p. 198–199° C. dec.

Anal. Calcd. $C_{38}H_{52}N_6O_7.1.0\ H_2SO_4.0.2\ H_2O$: C, 56.59; H, 6.80; N, 10.42; S, 3.98; H_2O, 0.45. Found: C, 56.66; H, 6.78; N, 10.50; S, 4.20; H_2O, 0.45 (KF).

Example 3

Preparation of Bisulfate Salt from Isopropanol

Aqueous sulfuric acid (5.0 M, 0.20 mL, 1 mM) was added to a suspension of the free base compound of formula I (0.704 g, 1.00 mM) in isopropanol (4.0 mL) chilled in an ice-bath. The ice-bath was removed and the mixture stirred at room temperature. The suspension had dissolved after 15 minutes. The solution was seeded with crystals prepared as in Examples 1 or 2 above and stirred for 5 hours. The solid was filtered and the filtrate was used to transfer the solid from the flask to the funnel. The product was washed with heptane and dried under vacuum to give 0.752 g of crystalline bisulfate salt of formula II, yield 90%, m.p. 160–190° C., dec.

Anal. Calcd. for $C_{38}H_{52}N_6O_7.1.0\ H_2SO_4.2.0\ H_2O$; C, 54.40; H, 6.97; N, 10.02; S, 3.82; H_2O, 4.29. Found: C, 54.25; H, 6.73; N, 10.02; S, 3.67; H_2O, 4.53 (KF).

The crystals obtained from isopropanol showed a powder x-ray diffraction pattern different from the crystals obtained from acetonitrile, ethanol-heptane or acetone. They are now referred to as Type-II crystals. The Type-I crystals appear to be an anhydrous/desolvated crystalline material while the Type-II crystals are a hydrated, hygroscopic crystalline form.

Example 4

Preparation of Capsule Formulations of Bisulfate Salt

A. Capsules (50 and 200 mg free base equivalent)

Capsules are provided for oral administration in which the capsule is a size #0, gray, opaque, hard gelatin capsule containing the bisulfate salt of formula II formulated as a wet granulation with lactose, crospovidone and magnesium stearate.

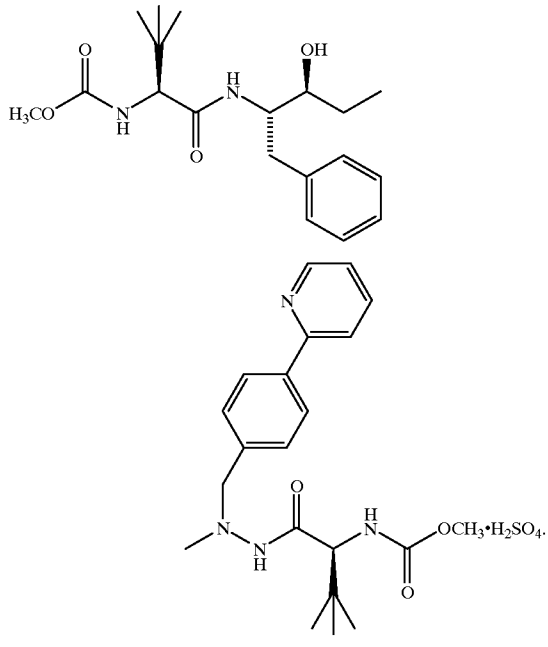
B. Capsules (100 mg free base equivalent)

Capsules are provided for oral administration in which the capsule is a size #0, gray, opaque, hard gelatin capsule containing the bisulfate salt of formula II suspended in Gelucire 44/14. Gelucire 44/14 is a saturated polyglycolized glyceride consisting of mono-, di- and triglycerides and mono- and di-fatty acid esters of polyethylene glycol. Capsules are prepared by melting Gelucire 44/14 at 45–70° C. followed by addition of the bisulfate salt with stirring. The molten mixture is filled into hard gelatin capsules and allowed to cool and solidify.

We claim:

1. The bisulfate salt having the formula

II



2. A pharmaceutical dosage form comprising the bisulfate salt of claim **1** and a pharmaceutically acceptable carrier.

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